The Different Behaviors of Photoredox Catalysts in Visible Light Promoted Organic Transformations

Dissertation

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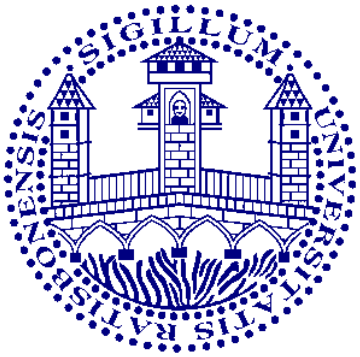

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Table of Contents

Table of Contents

Table of Contents

Table of Contents

Abbreviations

A	acceptor; ampere
Ac	acetyl
Act	activating group
AIBN	2,2′-azobis(2-methyl propionitrile)
anh.	anhydrous
APCI	atmospheric pressure chemical ionization
Ar	aryl
ATRA	atom transfer radical addition
aq.	aqueous
binc	bis(2-isocyanophenyl) phenyl phosphonate
Bn	benzyl ($PhCH_2$)
Boc	*tert*-butyloxycarbonyl
bpm	2,2′-bipyrimidine
bpy	2,2’-bipyridine
bpz	2,2′-bipyrazine
brsm	based on recovered starting material
bs	broad singlet (spectral)
BTMG	2-*tert*-butyl-1,1,3,3-tetramethylguanidine
Bu	butyl
^{t}Bu	*tert*-butyl
Bz	benzoyl (PhCO)
°C	degree celsius
c	centi (10^{-2}); concentration
c	cyclo
CFL	compact fluorescent lamp
cf	conferatur (*Latin*: compare)
*m*CPBA	*meta*-chloroperoxybenzoic acid
D	donor
d	doublet (spectral)
δ	chemical shift
dr	diastereomeric ratio
dap	2,9-bis(*para*-anisyl)-1,10-phenanthroline
dba	dibenzalaceton
DBU	1,8-diazabicyclo-[5.4.0]undec7-ene
dCF_3bpy	4,4'-bis(trifluoromethyl)-2,2'-bipyridine
$dF(CF_3)ppy$	2-(2,4-difluorophenyl)-5-(trifluoromethyl) pyridine
DHQD	hydroquinidine
DIPEA	*N,N*-diisopropylethylamine
DMAP	4-dimethylaminopyridine
DME	dimethoxyethane
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
dmp	2,9-dimethyl-1,10-phenanthroline
dpdmp	2,9-diphenyl-4,7-dimethyl-1,10-phenanthroline
DPEphos	bis(2-(diphenylphospha-nyl) phenyl)ether
dpp	2,9-diphenyl-1,10-phenanthroline
dppb	1,4-bis(diphenyl-phosphino)butane
dtbbpy	4,4’-di-*tert*-butyl-2,2’-bipyridine
ee	enantiomeric excess

Abbreviations

e.g.	exempli gratia (*Latin*: for example)
E/Z	entgegen / zusammen
$E_{1/2}$	standard reduction potential
EDTA	ethylenediaminetetra-acetic acid
EI	electron ionization
eq	equation
equiv	equivalent
ESI	electrospray ionization
Et	ethyl
EtOAc	ethyl acetate
et al.	et alia (*Latin*: and others)
EWG	electron withdrawing group
EY	eosin Y
F	fluorescence
fac	facial
Fmoc	Fluorenylmethyloxy-carbonyl
FTIR	Fourier transform infrared spectroscopy
g	gram
glyme	1,2-dimethoxyethane
GP	general procedure
h	hour
h	Planck constant
hept	septet (spectral)
HOMO	highest occupied molecular orbital
HPLC	high pressure liquid chromatography
HRMS	high resolution mass spectroscopy
HSAB	hard and soft acids and bases
Hz	Hertz
IC	Internal conversion
IR	infrared spectroscopy
ISC	intersystem crossing
J	coupling constant (spectroscopy)
K_{SV}	Stern-Volmer-constant
L	ligand; liter
λ	wavelength
λ_{max}	wavelength of maximum
LED	light emitting diode
LMCT	ligand-to-metal charge-transfer
LRMS	low resolution mass spectroscopy
LUMO	lowest unoccupied molecular orbital
M	molar (mol L^{-1}); mega (10^6)
m	milli (10^{-3}); multiplet (spectral)
μ	micro (10^{-6})
m	meta
m/z	mass to charge ratio
Me	methyl
MeCN	acetonitrile
min	minute
mol	mole
mol%	mole percent
MLCT	metal-to-ligand charge-transfer
mp	melting point
MS	mass spectroscopy
n	nano (10^{-9})
ν	frequency

Abbreviations

NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser effect spectroscopy
o	ortho
p	quintet (spectral)
p	para
Pc	photocatalyst
Pg	protecting group
PHAL	1,4-phthalazinediyl
phen	1,10-phenanthroline
PIB	polyisobutylene
PMMA	poly(methyl methacrylate)
ppm	parts per million
Ph	phenyl
^{i}Pr	*iso*-propyl
ppy	2-phenylpyridine
PS	photosensitizer
Q	quencher
q	quartet (spectral)
Q-TOF	quadrupole time-of-flight
Φ	quantum yield
R	arbitrary rest
rac.	racemic
redox	reduction-oxidation
R_f	retardation factor
rt	room temperature
s	singlet (spectral)
SCE	standard calomel electrode
SET	single electron transfer
sex	sextet (spectral)
SOMO	singly occupied molecular orbital
t	time; triplet (spectral)
T	temperature
τ	lifetime
TEMPO	(2,2,6,6-tetramethyl-piperidin-1-yl)oxyl
Tf	triflyl (= trifluoro methanesulfonyl)
Ts	tosyl (= toluenesulfonyl)
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
TOCSY	total correlation spectroscopy
Tol	toluene
UV	ultra violet
V	Volt
VIS	visible light
VLIH	visible light initiated homolysis
vs	versus (Latin: against)
W	Watt
wt%	weight percent
X	arbitrary heteroatom

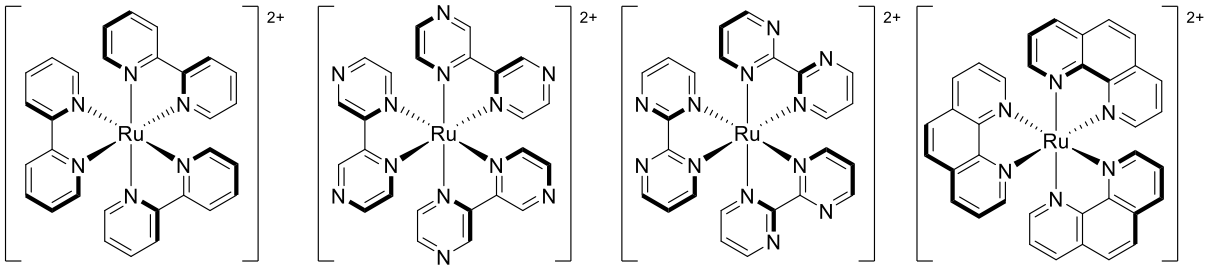
A. Introduction

1. The Evolution of the Photoredox Catalysts in Organic Synthesis

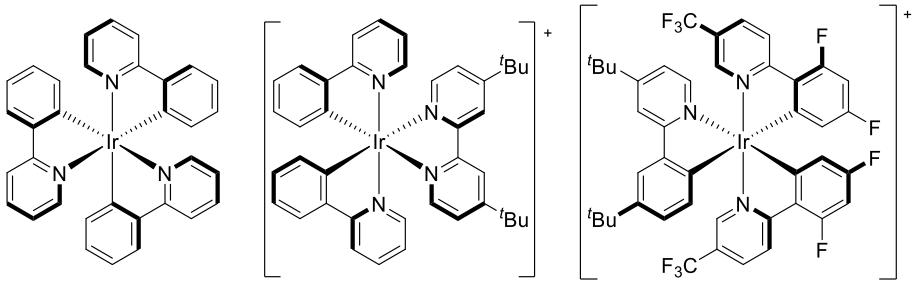
In 1886, Giacomo Ciamician and Paul Silber reported their observations of sunlight promoted transformations of quinone to hydroquinone and nitrobenzene to aniline, both in the presence of ethanol. The oxidation of alcohol to the corresponding aldehyde was identified as the reductant for the quinone and nitrobenzene.[1] On the peak of the industrial revolution, driven by fossil fuels, the role of sunlight as an alternative energy source and reagent in chemical reactions was not strongly considered. However, in 1912 Giacomo Ciamician described his vision for the use of sunlight as the main energy source and reagent in organic synthesis thus making the mankind independent of ending fossil fuels such as coal.[2] Indeed, in the 20th century, the increasing role of radical chemistry elevated the importance of the UV-light as a versatile tool for organic synthesis.[3] However, the use of the high energy UV-light has several disadvantages. In general, the generation of high-energy UV-light requires specialized equipment, making the performance of the reactions more difficult, although recently this problem was solved by introduction of UV-LED. Moreover, the irradiation of organic molecules with high energy UV-light can, in the worst case, lead to an undesired bond cleavage and thus to the destruction of the organic compound before reacting in the desired way.[4] To avoid these difficulties the use of low-energy visible light in combination with photocatalysts was discovered for many chemical transformations. Surprisingly, in addition to the mild reaction conditions, a variety of new synthetic pathways were enabled giving access to a broad range of new organic molecules.[5] In the view of the increasing importance of sustainability and environmental friendliness for the modern society, the research field of visible-light photocatalysis moved strongly into the focus of chemists around the world. In recent years, a remarkable amount of visible-light promoted photoredox transformations, utilizing a broad selection of photocatalysts, have been presented. This synthetic progress is described in a large number of chemical reviews[6] and development is still ongoing, resulting in a variety of publications every year. The success of visible-light mediated chemical transformations is strongly dependent on the employed photocatalyst and thus the generation of new catalytic systems is an important research field. Therefore, the requirements for the new photocatalysts are multifaceted.[7] Beside the photophysical properties and the efficiency in the desired transformation, other properties are gaining in importance. Considering resource depletion, sustainability and as a consequence thereof the price disparity, the employment of metal-free catalysts[6f], complexes based on earth abundant metals[6j] or recyclable photocatalysts[8] was extended in the recent years.

In general, there are three groups of catalysts that are frequently used in photoredox catalysis induced by visible-light. An important group of visible light photocatalysts, commonly used

under blue light irradiation (455 nm), are complexes of ruthenium(II) and iridium(III) in combination with bipyridine, phenylpyridine and phenanthroline ligands. In 1978, Kellogg introduced $[Ru(bpy)_3]Cl_2$ as catalyst for the photoredox catalyzed reduction of sulfonium ions to the corresponding alkanes and thioethers in the presence of *N*-substituted 1,4-dihydropyridines as the terminal reductant.[6g, 9] Due to the promising photochemical properties and the good availability, these complexes were extensively explored in a broad range of organic transformations e.g. atom transfer radical addition (ATRA) reactions[10], carbonyl reactions[11], decarboxylations[12] and more[6a, 6c, 6g, 6k, 6l].



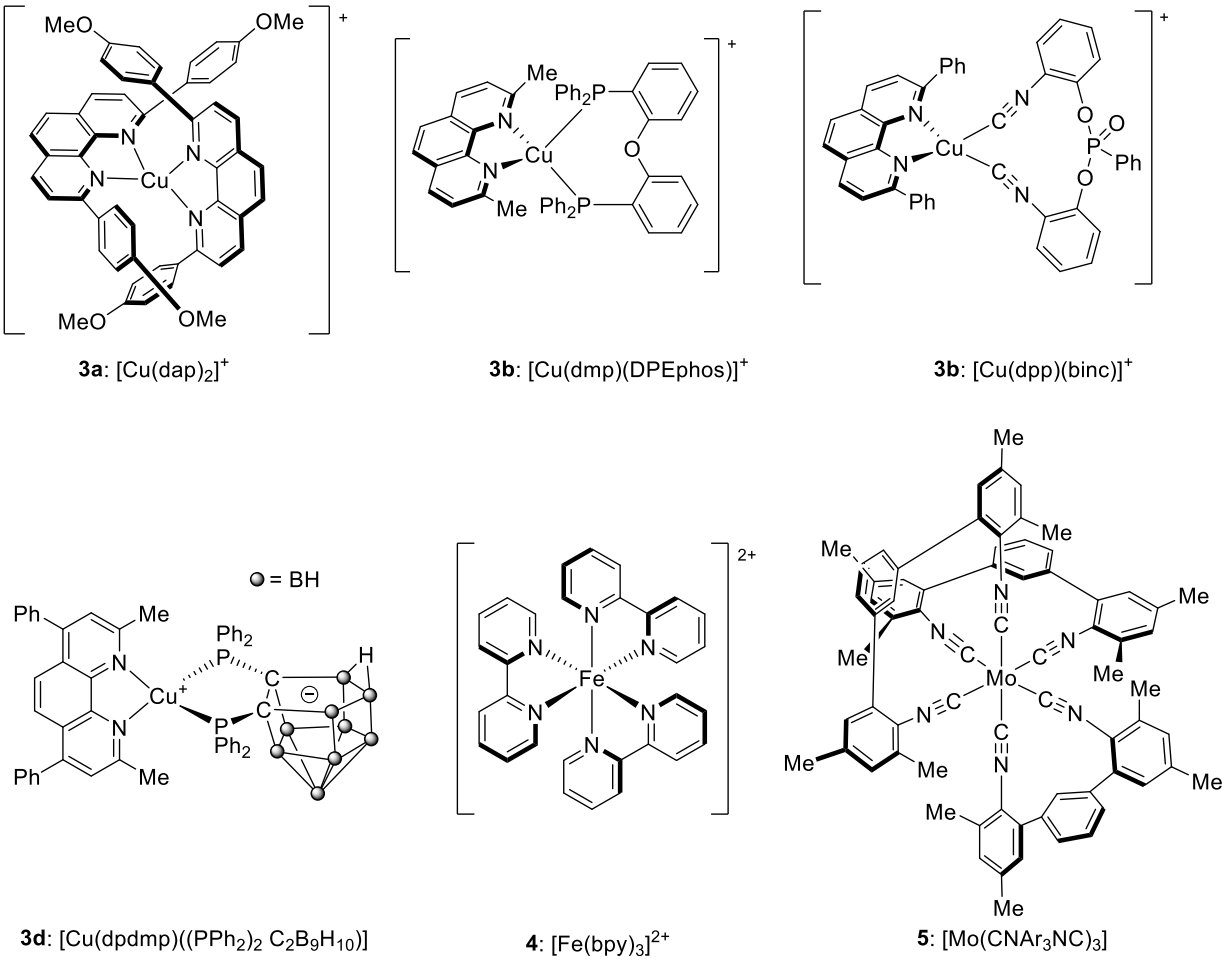
1a: $[Ru(bpy)_3]^{2+}$ **1b**: $[Ru(bpz)_3]^{2+}$ **1c**: $[Ru(bpm)_3]^{2+}$ **1d**: $[Ru(phen)_3]^{2+}$



2a: *fac*-$Ir(ppy)_3$ **2b**: $[Ir(ppy)_2(dtbbpy)]^+$ **2c**: $[Ir(dF(CF_3)ppy)_2(dtbbpy)]^+$

Figure 1. Commonly used ruthenium- and iridium-based photocatalysts.

In 1987, Sauvage et al.[13] introduced $[Cu(dap)_2]^+$ (**3a**) as catalyst in the visible-light photoredox catalyzed dimerization reaction of 4-nitrobenzyl bromide, being the starting shot for the development of photoredox catalysts based on inexpensive earth-abundant metals such as copper, iron, chromium, molybdenum and more.[6j]



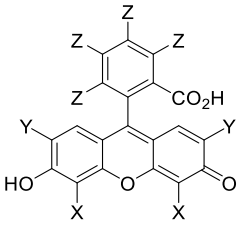
3a: $[Cu(dap)_2]^+$ **3b**: $[Cu(dmp)(DPEphos)]^+$ **3b**: $[Cu(dpp)(binc)]^+$

3d: $[Cu(dpdmp)((PPh_2)_2\ C_2B_9H_{10})]$ **4**: $[Fe(bpy)_3]^{2+}$ **5**: $[Mo(CNAr_3NC)_3]$

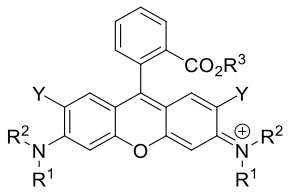
Figure 2. Commonly used photoredox catalysts based on earth-abundant metal centers.

Especially the employment of copper-based catalysts delivered excellent results and often enabled new types of organic transformations. In particular the high efficiency in atom transfer radical addition (ATRA) reactions, initiated by activation of carbon-halogen or heteroatom-halogen bonds established these catalysts as versatile tools in visible-light photoredox catalysis.[14]

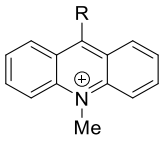
The last important group of photocatalysts are non-metal based organic dyes. With continuous exploration of radical reactions induced by visible-light irradiation the attempts towards prevention of metal-based catalysts and exchange of those by organic dyes gained in importance. The most established organic dyes in photochemistry are derivatives of fluorescein such as Eosin Y and Rose Bengal, rhodamines and acridinium-based organic catalysts also known as Fukuzumi-catalyst[15]. The latter is known to be an excellent oxidant, as was impressively demonstrated by Nicewicz group in the direct catalytic anti-Markovnikov hydroetherification of alkenols with alkene oxidation as mechanistic key step.[6f, 16]



6a: Fluorescein (X, Y, Z = H)
6b: Eosin Y (X, Y = Br; Z = H)
6c: Rose Bengal (X, Y = I; Z = Cl)



7a: Rhodamine B (Y,R^3 = H; R^1,R^2 = Et)
7b: Rhodamine 6G (Y = Me; R^2 = H; R^1,R^3 = Et)



8a: 10-methylacridinium (R = H)
8b: 10-methyl-9-phenylacridinium (R = Ph)
8c: 10-methyl-9-mesitylacridinium (R = mesityl)

Figure 3. Commonly used organic dyes for photoredox catalysis.

2. Photophysics

In general, the application of photocatalysts in organic transformations is based on the ability of metal complexes and organic dyes to interact after excitation with visible light in single-electron-transfer (SET) processes or energy transfer reactions with organic molecules. The wavelengths of visible spectrum range from 380 to 740 nm. The high-energy UV-light is characterized by wavelength below 380 nm, while low-energy infrared light exhibits wavelength higher than 740 nm. The function of the photocatalyst as mediator, that can absorb visible light and utilize the energy for organic reactions is of great importance, because only a rather small selection of organic molecules is able to directly absorb the visible light. Therefore, the irradiation of the reaction mixture ideally results only in excitation of catalyst with no direct energy transfer to the substrate. Moreover, it is important that the reaction of the excited state of the catalyst and the substrate results in only small modifications of the catalyst structure, thus enabling the recovery of its original state by a second reaction on the electronic ground state.[17] For this purpose it is crucial for the photocatalyst to be stable under irradiation with visible-light and only undergo reversible processes. The simplified analysis of the photophysics of the photocatalyst in the absence of the substrate is described by a Jablonsky diagram.[17] Therein, the transitions between different electronic states can occur either by absorption or emission of radiation or as radiationless transition. In Figure 4 the radiative transitions are described by straight lines, whereas the nonradiative transitions are shown as curly lines. The irradiation of the photocatalyst with visible-light leads to the absorption ($h\nu_A$) and the excitation of the photocatalyst from the ground state to the energetically higher excited state. For this process the energy of the photon must be high enough to reach the S_1 stage and be in line with resonance condition. Since the relaxation from the higher excited states e.g. S_2 occur very fast, the energy of S_1 is the maximum that is available for the diffusion controlled photoreaction.[17] Please notice that in the presented simplified diagram no vibrational levels are drawn and the internal conversion (IC) is shown as a summarized relaxation process. From the excited S_1 level the photocatalyst can go through different routes. Beside the described internal conversion (IC), the direct emission of energetically poor light with longer wavelengths

from excited singlet state called fluorescence ($h\nu_F$) is possible. Moreover, the transition from one electronic state to another with a different spin multiplicity e.g. singlet state S_1 to triplet state T_1 is called inter system crossing (ISC). This type of transition is analogue to the internal conversion (IC) with additional spin factor which must be considered for the transition probability.[17] From the excited triplet state T_1 another inter system crossing (ISC) process is possible. Alternatively, the radiative transition from this triplet state to the ground state S_0, called phosphorescence ($h\nu_{Ph}$) can take place.

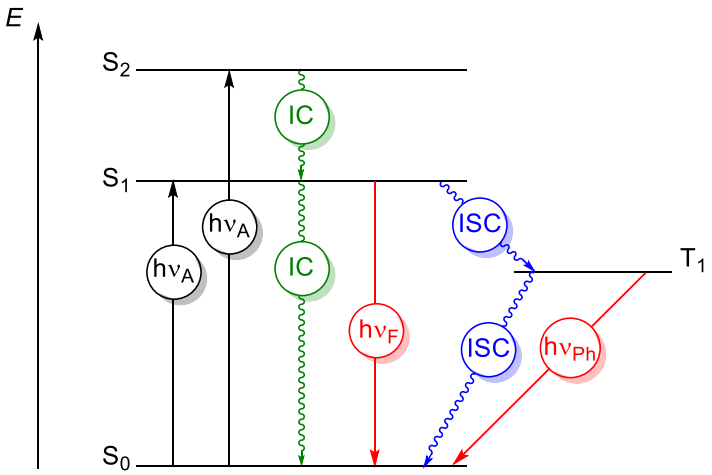


Figure 4. Simplified Jablonsky diagram for a photoredox catalyst in the absence of substrate.

For a successful photochemical transformation, the employed photocatalyst must be able to absorb light, which is energetically rich enough to reach the singlet state S_1 and the lifetime of this excited state shall be long enough to enable the electron transfer or energy transfer between the catalyst and the substrate. Typical emission wavelengths of commonly used LEDs and other light sources are in the region of 400-700 nm. To ensure the generation of excited state catalyst by visible-light the UV-VIS-spectrum of the complex should be determined. In Table 1 the values for the excitation maximum and lifetime of the excited state are described for the commonly used photocatalysts.

In general, the excitation maxima λ_{max} for the ruthenium-, iridium-, copper-, and molybdenum-based photocatalysts **1**-**5** are in the range of 375-454 nm (Table 1, entries 1-14). For the organic dyes **6**-**8** a slight shift of excitation maxima λ_{max} towards longer wavelengths of 424-550 nm can be observed (Table 1, entries 15-20). The lifetime analysis of the Ru- and Ir-based catalysts indicates that the variation of the electronic structure of the ligand leads to a significant change of lifetime values for the ruthenium-based catalysts **1a**-**1c** (entries 1-3). $[Ru(bpy)_3]^{2+}$ (**1a**), *fac*-$Ir(ppy)_3$ (**2a**) and $[Ir(dF(CF_3)ppy)_2(dtbbpy)]^+$ (**2c**) show the longest excited state lifetimes in the range of more than 1 µs (entries 1, 5 and 7). The group of photocatalysts based on earth-abundant metals shows big differences in lifetime values (Table 1, entries 8-14).

Table 1. Lifetime, excitation and emission values for selected photoredox catalysts.[a]

Entry	Photocatalyst	Lifetime τ [ns]	Excitation λ_{max} [nm]	Emission λ_{max} [nm]	Ref.
1	$[Ru(bpy)_3]^{2+}$ (**1a**)	1100	452	615	6a
2	$[Ru(bpz)_3]^{2+}$ (**1b**)	740	443	591	6a
3	$[Ru(bpm)_3]^{2+}$ (**1c**)	131[b]	454	639[b]	6a
4	$[Ru(phen)_3]^{2+}$ (**1d**)	500	422	610[c]	6a
5	*fac*-$Ir(ppy)_3$ (**2a**)	1900	375	494[d]	6a
6	$[Ir(ppy)_2(dtbbpy)]^+$ (**2b**)	557		581	6a
7	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]^+$ (**2c**)	2300	380	470	6a
8	$[Cu(dap)_2]^+$ (**3a**)	270/560[e]	437	670[f]	6a, 13-14
9	$[Cu(dmp)(DPEphos)]^+$ (**3b**)	14300	383	570	18
11	$[Cu(dpp)(binc)]^+$ (**3c**)	17000[e]	450[f]	560	14a
12	$[Cu(dpdmp)((PPh_2)_2\ C_2B_9H_{10})]$ (**3d**)	1300	449[f]	602	19
13	$[Fe(bpy)_3]^{2+}$ (**4**)	0.7			20
14	$[Mo(CNAr_3NC)_3]$ (**5**)	74[g]	420	617[g]	21
15	Eosin Y (**6b**)	2.1	520		6f
16	Rose Bengal (**6c**)	0.5	550		6f
17	Rhodamine B (**7a**)	2.5	550		6f
18	Rhodamine 6G (**7b**)	4.1	530		6f
19	10-methyl-9-phenylacridinium (**8b**)	1.5	424		6f
20	10-methyl-9-mesitylacridinium (**8c**)	6	425		6f

[a]Measurements were performed in acetonitrile at room temperature unless otherwise noted. [b]Determined in propylene carbonate. [c]Determined in aqueous solution. [d]Determined in 1:1 ethanol/methanol glass at 77 K. [e]Determined in PMMA (poly(methyl methacrylate)). [f]Determined in CH_2Cl_2. [g]Determined in THF.

In contrast to the commonly employed $[Cu(dap)_2]^+$ (**3a**) photocatalyst the copper-based complexes $[Cu(dmp)(DPEphos)]^+$ (**3b**) and $[Cu(dpp)(binc)]^+$ (**3c**) have very long excited state lifetimes of more than 14 µs. These values are more than six times higher compared to the long-lived excited state of $[Ir(dF(CF_3)ppy)_2(dtbbpy)]^+$ (**2c**). However, the broad application of $[Cu(dap)_2]^+$ (**3a**) in photoredox reactions indicates that the value of 270 ns is sufficient for the successful photoredox mediated transformations. The molybdenum-based photocatalyst **5** introduced by Wenger et al. in 2016 demonstrated catalytic activity in rearrangement of acyl cyclopropane to 2,3-dihydrofuran[21], although the lifetime of the excited state was only 74 ns. Surprisingly, the iron(II)-based complex $[Fe(bpy)_3]^{2+}$ (**4**) with 0.7 ns lifetime for the excited state showed excellent catalytic activity[22]. Even though this complex is a d^6-analogue of the commonly employed $[Ru(bpy)_3]^{2+}$ (**1a**), the application of the iron-complex **4** in a variety of organic reactions is not possible so far. In general, the lifetime of the excited singlet state of the organic dyes is very short with values in the range of <1-45 ns[6f]. In contrast, the lifetimes for excited triplet states are in the range of microseconds to milliseconds. This difference in lifetimes is based on the fact that the $T_1 \rightarrow S_0$ transition is symmetry forbidden.[6f]

3. Interaction Between Photocatalyst and Substrate

To understand the interaction process between the photocatalyst and the substrate, it is of great importance to analyze the molecular orbitals of the metal-based photocatalysts. For this purpose, the simplified molecular orbital diagrams for d^6-complex *fac*-Ir(ppy)$_3$ (**2a**) and for d^{10}-complexes [Cu(dap)$_2$]Cl (**3a**) and [Cu(dpdmp)((PPh$_2$)$_2$ C$_2$B$_9$H$_{10}$)] (**3d**) are shown in Figure 5 and Figure 6. The octahedral complex *fac*-Ir(ppy)$_3$ (**2a**) shows a low-spin configuration with six paired electrons in the t_{2g}-orbitals.[6g] Under irradiation with visible-light the complex undergoes metal to ligand charge transfer (MLCT) in combination with inter system crossing to form the excited triplet state of the catalyst.

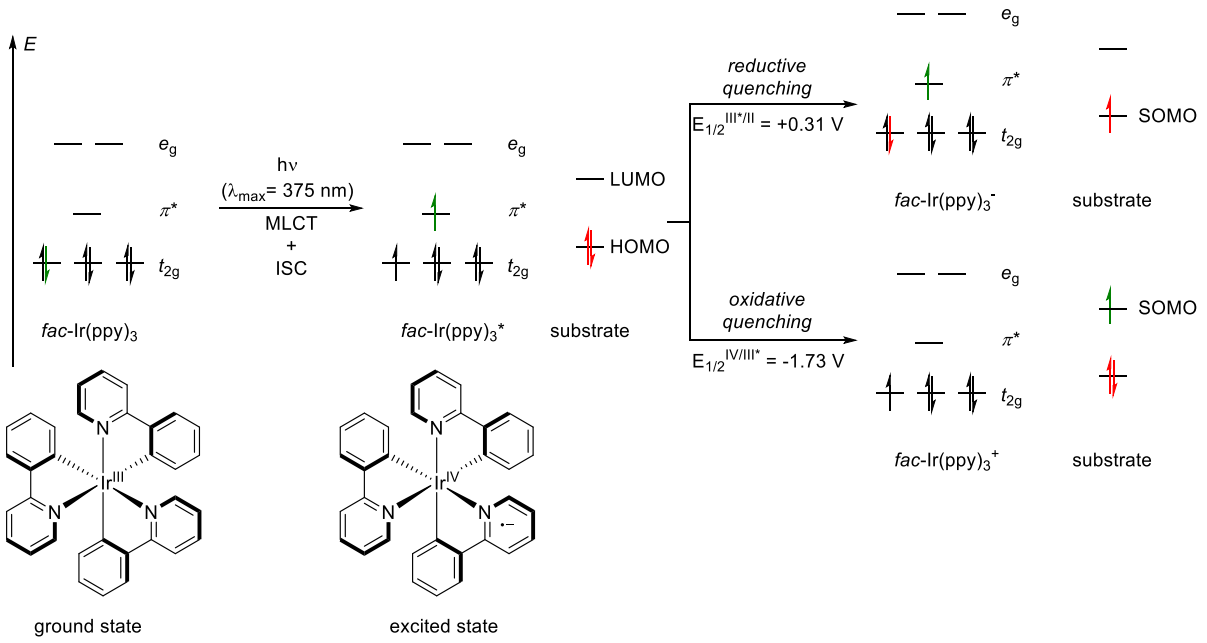


Figure 5. Simplified molecular orbital depiction of octahedral low-spin d^6-complex *fac*-Ir(ppy)$_3$ (**2a**).

In the presence of a substrate this species can run through two different processes. In the oxidative quenching the electron from the π*-orbital can be transferred to the LUMO of the substrate resulting in the formation of a new SOMO. In contrast, the reductive quenching leads to an electron transfer from the substrate to the single occupied t_{2g}-orbital of the complex, thus transforming the HOMO of the substrate into SOMO. The unique character of the d^6-ruthenium- and iridium-based photocatalysts arise from the ability to act as both oxidant and reductant. In Figure 6 the simplified molecular orbital depiction of tetrahedral d^{10}-complexes $[Cu(dap)_2]^+$ (**3a**) and [Cu(dpdmp)((PPh$_2$)$_2$ C$_2$B$_9$H$_{10}$)] (**3d**) with completely occupied *e*- and t_2-orbitals is shown. Similar to the d^6-complexes (Figure 5), under irradiation with visible-light the complexes undergo metal to ligand charge transfer (MLCT) with subsequent inter system crossing (ISC) forming the excited triplet state species. The nature of the copper-based catalyst is responsible for the route the catalyst can run through in the presence of the substrate.

The well established $[Cu(dap)_2]^+$ (**3a**) is known to be a strong reductant applying the oxidative quenching. In this case the electron from the π*-orbital can be transferred to the LUMO of the substrate to form the SOMO.

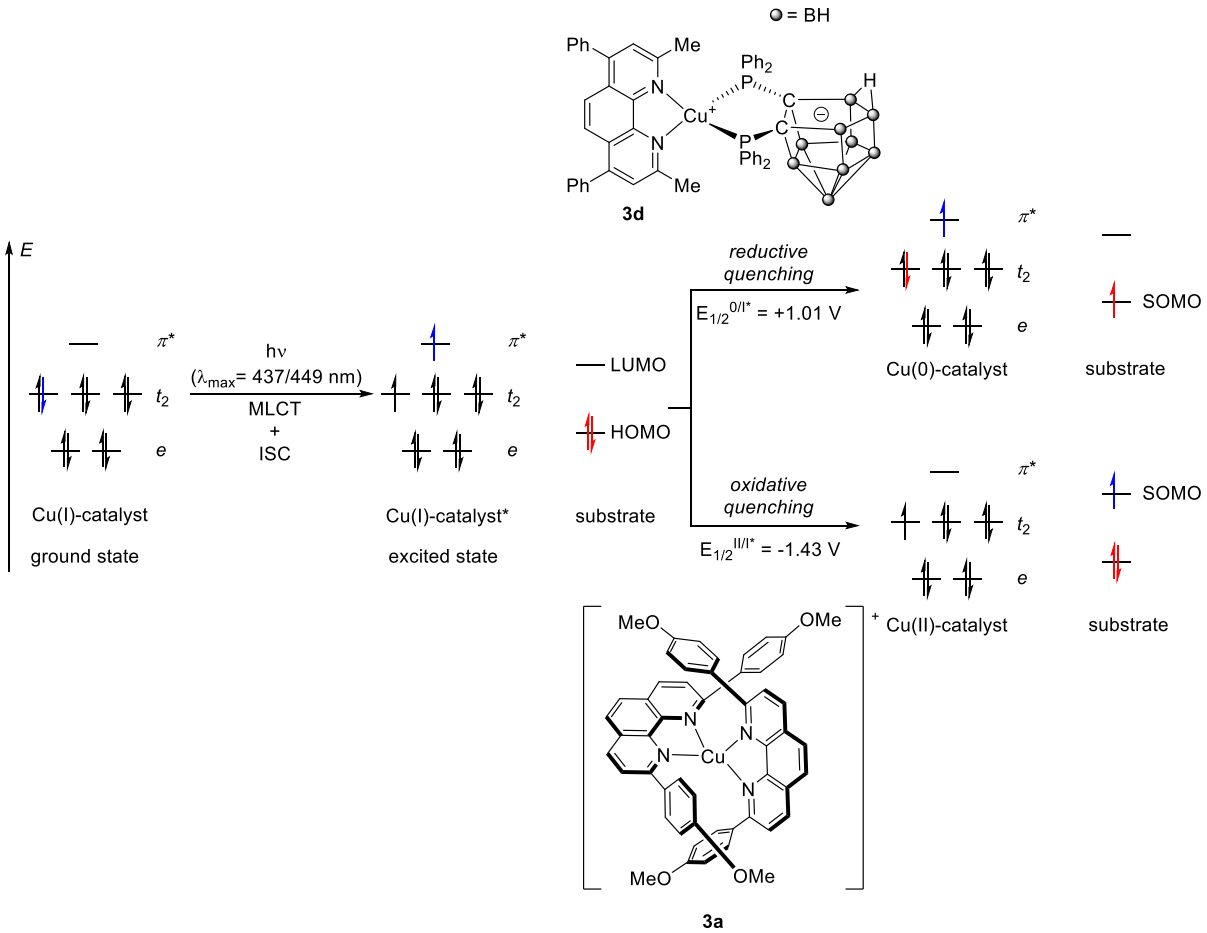
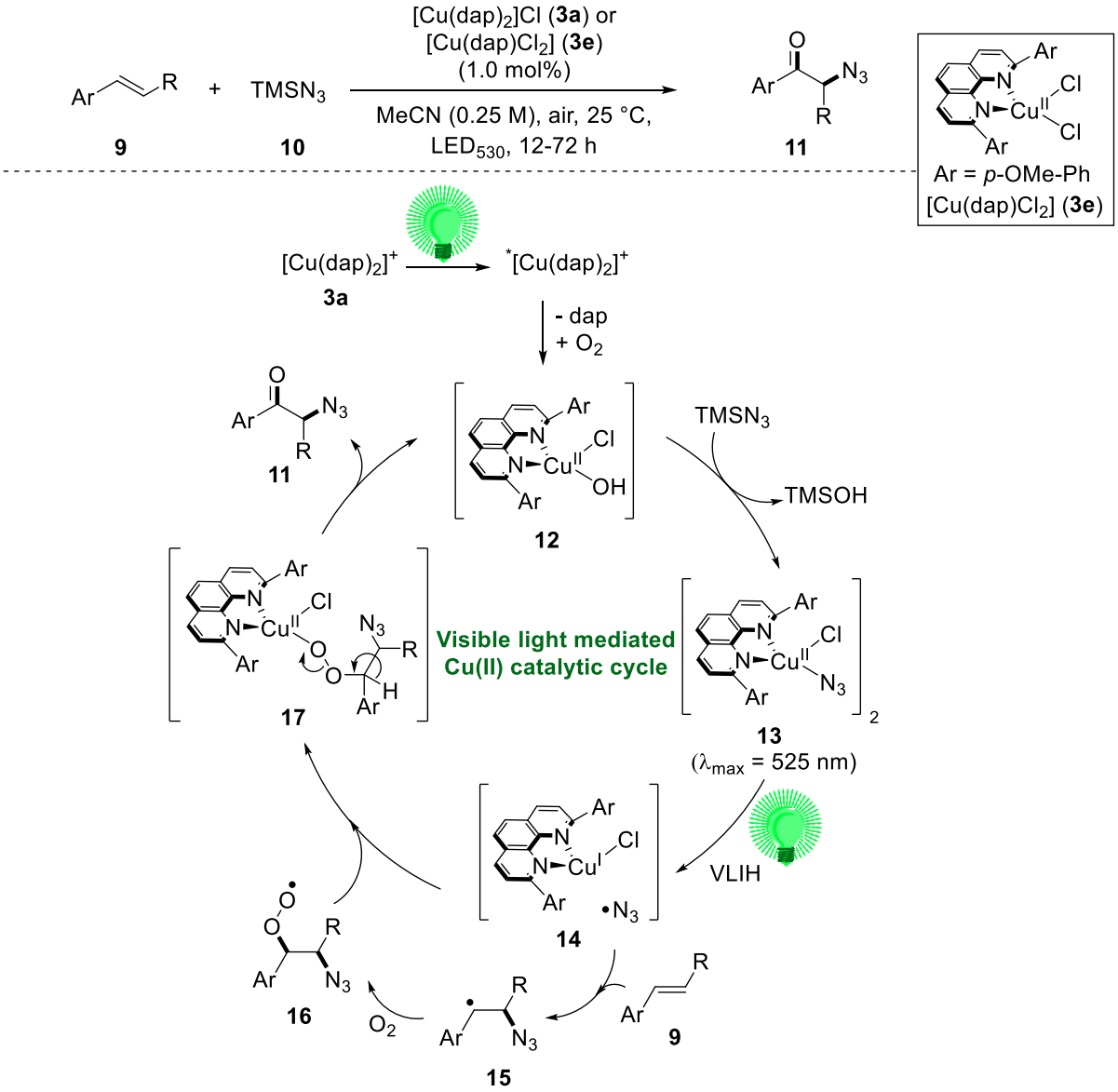


Figure 6. Simplified molecular orbital depiction of tetrahedral d^{10}-complexes $[Cu(dap)_2]^+$ (**3a**) and $[Cu(dpdmp)((PPh_2)_2\ C_2B_9H_{10})]$ (**3d**).

Due to the low stability of the resulting Cu(0)-species, the reductive quenching cycle is not favored in the case of Cu-photocatalysts. However, in 2015 Chen and coworkers[19] presented $[Cu(dpdmp)((PPh_2)_2C_2B_9H_{10})]$ (**3d**) as copper catalyst for the reductive quenching. This complex has a zwitterionic character and a long-lived excited state, thus the reduction of the Cu(I)-center to Cu(0) is possible. The single electron transfer occurs from the HOMO of the substrate to the t_2-orbital of the complex forming the Cu(0)-species. Compared to the ruthenium- and iridium-based catalysts that show the ability to go through both reductive and oxidative quenching cycle, the copper-based catalysts are limited to only one type of quenching.

The concept of metal to ligand charge transfer (MLCT) described in Figure 5 and Figure 6 is commonly used in the literature for the explanation of catalytic photoredox properties. In contrast, the ligand to metal charge transfer (LMCT) process is less common in photocatalysis and enables the oxidation of the employed nucleophiles by metal coordination. Recently,

Reiser and Rehbein confirmed this concept in the efficient oxo-azidation of alkenes employing $[Cu(dap)_2]^+$ (**3a**) and Cu(II)-catalyst $[Cu(dap)Cl_2]$ (**3e**) (Scheme 1).[23] The proposed mechanism includes the formation of Cu(II)-species **12** which can be transformed into the dimer **13** by a ligand exchange. The irradiation of the latter with green light results in visible light initiated homolysis (VLIH) and thus in the formation of azide radical which can be trapped by alkene **9** followed by oxygen to give radical **16**. The VLIH concept is based on the UV-light promoted homolysis of $CuCl_2$ to CuCl and Cl-radical described by Kochi.[24] The catalytic cycle is closed by recombination of the radical **16** with complex **14** providing Cu(II)-species **17** and after elimination the final product **11**. The unique coordination properties of copper are discussed in section “Electron Transfer vs. Coordination” (*vide infra*).



Scheme 1. Cu(II)-catalysis as example for ligand to metal charge transfer (LMCT).

4. Quenching and Quantum Yield

Beside the analysis of excited state lifetimes, extintions, emissions and molecular orbitals of the employed catalysts, it is also important to analyze the spectroscopic characteristics of the reaction mixture. For example, some substrates or intermediates can undergo a quenching process of the excited state of the catalyst, thus blocking the desired reaction pathway. Hence, for determination of this property it is mandatory to measure a Stern-Volmer-plot, which describes the quenching of the excited species dependent on the concentration of the potential quencher. In 1919, Otto Stern and Max Volmer presented their work in this field and described the physical principles for their observations.[25] The general fluorescence quenching process, also called Stern-Volmer-relationship, is described by equation 1 with F_0 as fluorescence measured in the absence of a potential quencher, F as fluorescence determined in the presence of a quenching species with concentration [Q] and K_{SV} as Stern-Volmer-constant.

$$\frac{F_0}{F} = 1 + K_{SV} \cdot [Q] \qquad \text{(eq. 1)}$$

The transformation of equation 1 to equation 2 provides the direct linear proportionality between the measured fluorescence F and the concentration of the quencher [Q] simplifying graphical analysis for practical use (Figure 7 right side).

$$\frac{F_0}{F} - 1 = K_{SV} \cdot [Q] \qquad \text{(eq. 2)}$$

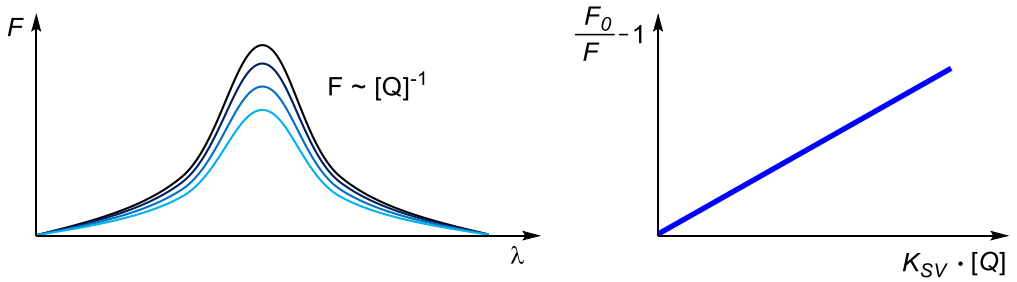


Figure 7. Fluorescence spectrum with different quencher concentrations [Q] (left side) and exemplary Stern-Volmer-plot (right side).

In general, there are two different ways of the quenching process. The direct collision of the fluorescent species in the excited state and the quencher is called dynamic quenching and leads to the radiationless energy transfer from excited singlet state compound A* to the quencher Q (eq. 3). In this process the lifetime τ of the excited singlet state of compound A is dependent on the concentration of the quencher Q. The longer the lifetime τ of the excited

state, the higher is the propability for the collision of the quencher Q with the excited state fluorophore A*.

dynamic quenching: $A^* + Q \rightleftharpoons A + Q$ $\frac{F_0}{F} = \frac{\tau_0}{\tau} = 1 + K_d \cdot [Q]$ (eq. 3)

Alternatively, the quencher Q can recombine with the fluorophore A forming a new non-fluorescent species AQ (eq. 4). This process is called static quenching and is based on the law of mass action for complex formation (eq. 5). The quenching of the fluorescence evolves from the blocking of the potential fluorophore A. Therefore, in this quenching process the lifetime τ of the fluorophore stays untouched resulting in equation 6.

static quenching: $A + Q \rightleftharpoons AQ$ $\frac{F_0}{F} = 1 + K_s \cdot [Q]$ (eq. 4)

with $K_s = \frac{[AQ]}{[A][Q]}$ (eq. 5) and $\frac{\tau_0}{\tau} = 1$ (eq. 6)

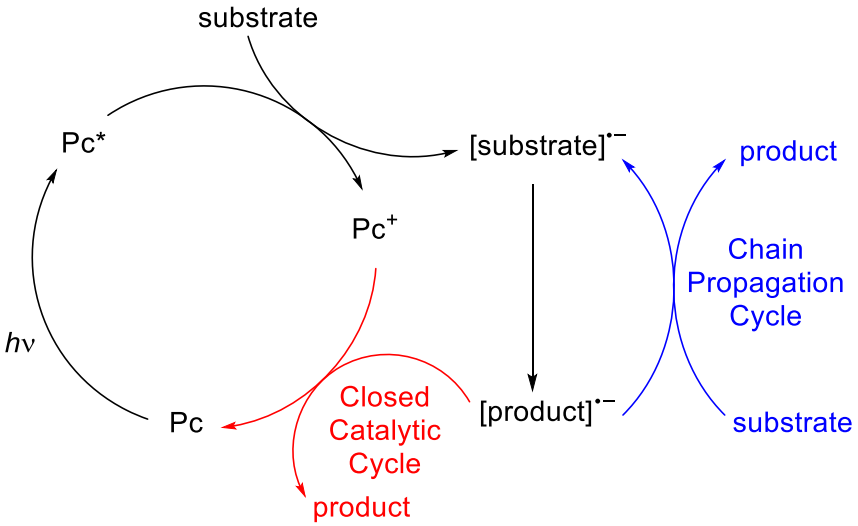
The simplified equation 1 is only valid when two assumptions are fulfilled. The quencher should have approximately identical access to all molecules of the investigated fluorophore, and it should undergo only one type of quenching (*cf*. eq. 3 and eq. 4). Otherwise the Stern-Volmer-equation must be adjusted.[26]

Furthermore, the efficiency of photoabsorption can give important indications about the nature of the radical process in the investigated reaction. The quantum yield Φ describes the relationship between the amount of product molecules formed after time t_x and the number of absorbed photons in this time (eq. 7).

$$\Phi = \frac{N_{prod}}{N_{ph,abs}} = \frac{moles\ of\ product\ formed\ after\ t_x}{moles\ of\ photons\ absorbed\ in\ t_x} \quad \text{(eq. 7)}$$

In general, there are two established mechanistic pathways for the photoredox mediated transformations based on initial single electron transfer (Scheme 2).[27] Herein, the oxidative quenching cycle of the photocatalyst Pc is used for the demonstration of the different mechanistic routes, however, similar considerations can also be made for the reductive quenching cycle. Both routes start with excitation of the photocatalyst Pc by visible-light irradiation forming the excited state species Pc* which can transfer a single electron to the substrate providing the substrate radical anion and oxidized photocatalyst Pc^+. Subsequent transformation of the substrate radical anion to the product radical anion enables two conclusive reactions. In the closed catalytic cycle (depicted in red) Pc^+ can act as oxidant, thus forming the desired product and regenerating the photocatalyst Pc. In contrast, in the chain

propagation cycle (depicted in blue) the product radical anion reacts with another substrate molecule to form the final product and regenerate substrate radical anion.



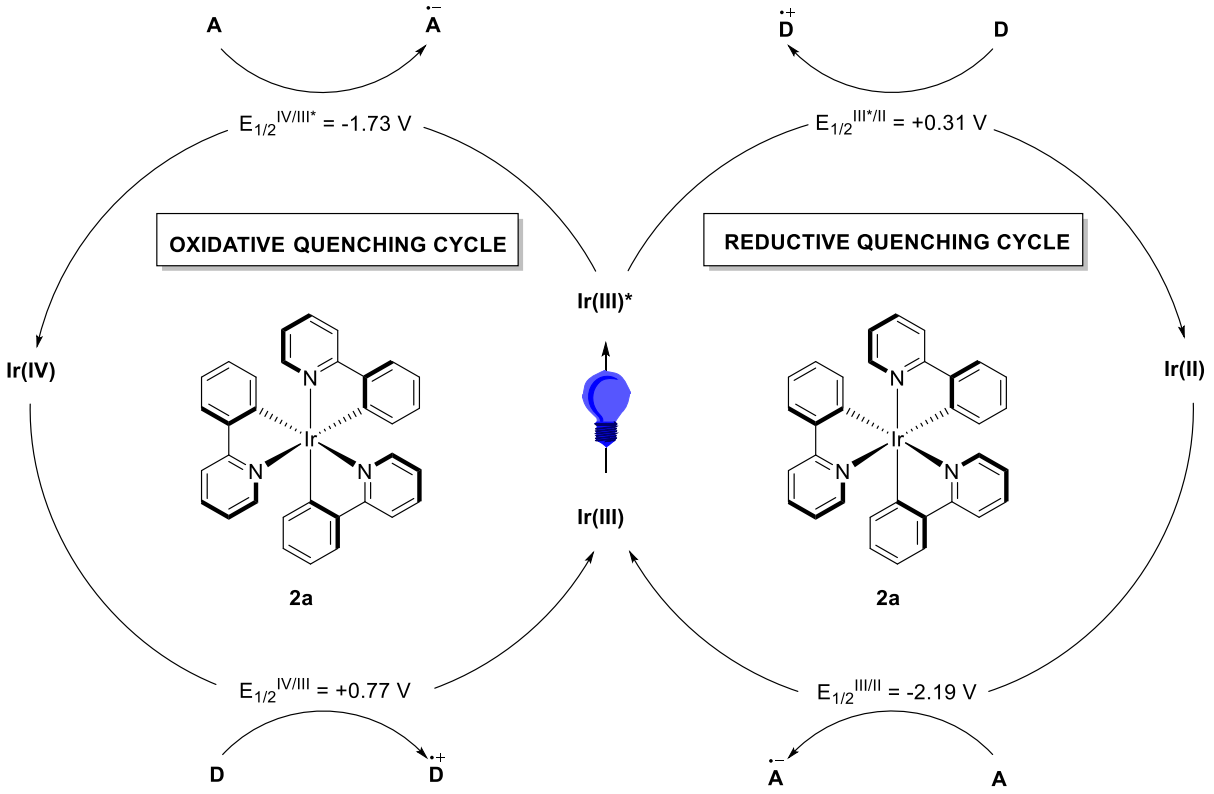
Scheme 2. General mechanistic pathways for the oxidative quenching cycle.

In the case of closed catalytic cycle, the quantum yield can reach at most the value $\Phi = 1$ indicating that every photon absorbed by the photocatalyst leads to the formation of one product molecule. The occurence of events induced by photon uptake which do not lead to the formation of product molecules e.g. phosphorescence, internal conversion, or back electron transfer would only decrease the quantum yield to the values $0 < \Phi < 1$.[27] In contrast, the chain propagation processes are characterized by the ability of one absorbed photon to generate more than one product molecule $\Phi > 1$. Therefore, processes with $\Phi << 1$ include catalytic cycle character, whereas transformations with $\Phi >> 1$ indicate the presence of radical chain propagation. However, the interpretations based on quantum yield should be taken into account very carefully, because the analysis based on yield of the desired product and absorbed photons does not consider the participation of other photomediated transformations that do not lead to the desired product.[27]

5. Photoredox Properties

Based on the described photophysics the general catalytic cycles for different photoredox catalysts can be described as follows. In Scheme 3 the oxidative and reductive quenching cycles for *fac*-Ir(ppy)$_3$ (**2a**) as representative for the ruthenium- and iridium-based d^6-complexes are described. The irradiation with blue LED leads to the generation of the photoexcited Ir(III)*-species with enormously changed redox properties. The photoexcited *fac*-$Ir^{III}(ppy)_3$* is a stronger oxidant ($E_{1/2}^{III*/II}$ = +0.31 V vs. the saturated calomel electrode (SCE)) and reductant ($E_{1/2}^{IV/III*}$ = -1.73 V vs. SCE) as compared to its respective electronic ground state with values of $E_{1/2}^{III/II}$ = -2.19 V vs. SCE and $E_{1/2}^{IV/III}$ = +0.77 V vs. SCE, respectively.

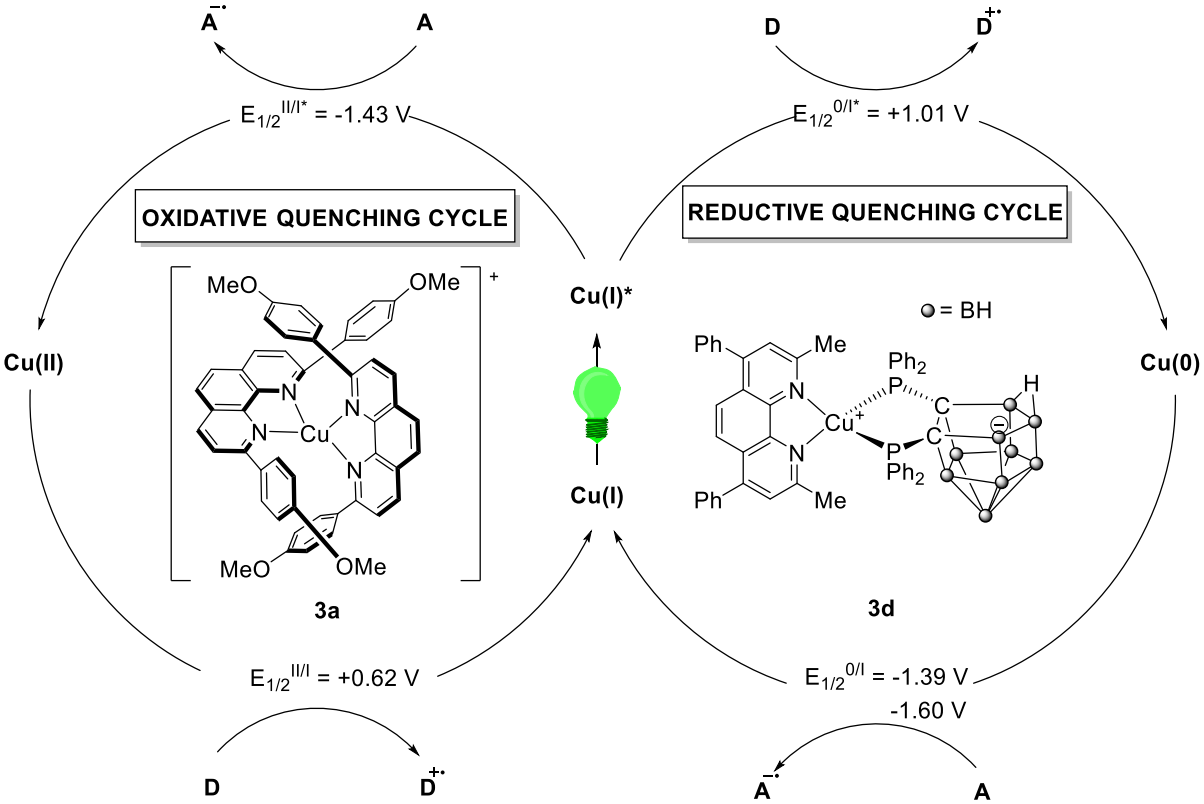
Therefore, this catalyst can interact with both types of substrates, oxidants and reductants. The strong reduction potentials are sufficient for a broad range of organic substrates.[28] In general, the reduction potential of the reduced ruthenium- and iridium-based photocatalysts in the reductive quenching cycle is significantly higher compared to the reduction potential of the photoexcited catalyst. Therefore, this group of photoredox catalysts is often used in the presence of sacrificial electron donors e.g. amines. However, also the substrate derived reduction of the catalyst is well known in the literature.[6a]



Scheme 3. Oxidative and reductive quenching cycles described for *fac*-Ir(ppy)$_3$ (**2a**) photocatalyst with A as electron acceptor and D as electron donor.

In contrast, the photoredox character of the copper-based photocatalysts differs from the one described for ruthenium- and iridium-based complexes. In general, the photoexcited Cu(I)*-species can exclusively undergo one quenching cycle. Compared to its ground state ($E_{1/2}^{II/I}$ = +0.62 V vs. SCE) the excited state of the $[Cu(dap)_2]^+$ (**3a**) is known to be a strong reductant ($E_{1/2}^{II/I*}$ = -1.43 V vs. SCE) employing oxidative quenching cycle under irradiation with green LED ($h\nu$ = 530 nm). However, the reductive quenching cycle is not accessible for this catalyst due to the low stability of the proposed Cu(0)-species. In order to get access to the reductive quenching cycle, the modification of the employed ligands is necessary. In 2015 Chen and coworkers[19] introduced the photostable zwitterionic copper-based photocatalyst [Cu(dpdmp)((PPh_2)$_2$ $C_2B_9H_{10}$)] (**3d**) which can run through the reductive quenching cycle with Cu(0)-intermediate. This catalyst demonstrates strong oxidation potential ($E_{1/2}^{0/I*}$ = +1.01 V vs.

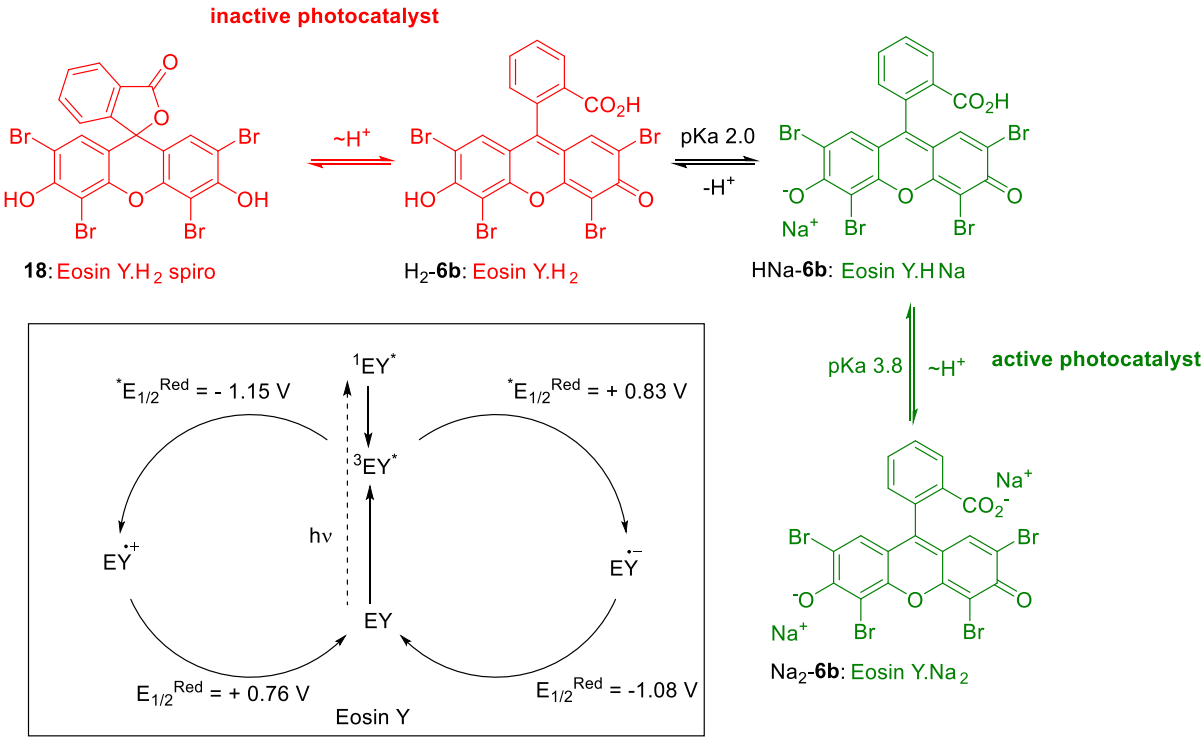
SCE) and strong reduction potential ($E_{1/2}^{0/I}$ = -1.39 V/ -1.60 V vs. SCE). Therefore, the main difference between the copper-based photocatalysts and the d^6-configurated ruthenium- and iridium-catalysts is the ability of the latter to run through both the oxidative and reductive quenching cycles, whereas the former are limited to only one of them.



Scheme 4. Oxidative and reductive quenching cycles described for copper-based photocatalysts **3a** and **3d** with A as electron acceptor and D as electron donor.

In general, the photoredox properties of organic dyes are like those of the metal-based photocatalysts including oxidative and reductive quenching cycles. In literature, the redox potentials of both singlet and triplet states of the photoexcited organic dyes are known.[6f] However, in experimental studies it was shown that the overall efficiency for the formation of free ions was higher when electron transfer occurred from triplet state of the catalyst. Therefore, for reactions whose efficiencies suffer from back electron transfer, the triplet excited state of the employed photoredox catalyst is the most important one.[6f] In contrast to metal-based photocatalysts, organic dyes often have acid-base character. The control of the pH-value is very important due to the formation of inactive catalyst-species which are not able to perform the desired transformations. In Scheme 5 the four major structures of Eosin Y are shown. Beside the photocatalytically inactive H_2-spiro-structure **18** and the ring-opened H_2-structure **6b**, the active mono- and dianionic forms HNa-**6b** and Na_2-**6b** are known. The photophysical properties of the long-wavelength absorbing xanthene core can be influenced by the negative charge of the conjugated substituents. Under acidic conditions the spirocyclic form is present which has no connected xanthenoid π-system, thus enabling the absorption of

the visible light and the subsequent electron transfer.[6i] In literature, also disactivation of the reduced Na_2-**6b** species by full $2e^-/2H^+$ reduction is described.[29] Therefore, in order to ensure the optimal pH-value and thus the formation of the photoactive catalyst structure it is often crucial to use additives such as amines. Similar observations are also described for other representatives of the organic dyes e.g. rhodamines.[6f]



Scheme 5. pH-dependance[6i] and photoredox properties of Eosin Y (**6b**).

The determination of the redox potentials in the ground state occurs by electrochemical measurement such as cyclovoltammetry. Therefore, the solution of the catalyst or investigated compound is analyzed in the presence of electrodes e.g. standard calomel electrode (SCE). The variation of the potential at the electrode leads to oxidation or reduction of the investigated compound and in this way gives the information about the redox potential. The estimation of the excited state redox potentials can then be obtained by calculation using excited state energy to correct the measured ground state redox potentials.[30] In Table 2 the redox potentials of commonly employed photocatalysts are described. The group of ruthenium- and iridium-based photocatalysts demonstrate excellent redox potentials for both the reductive and oxidative quenching cycles. For example, *fac*-Ir(ppy)$_3$ (**2a**) is the strongest representative of this group with the reduction potentials of -1.73 V and -2.19 V. The commonly employed copper-based photocatalyst $[Cu(dap)_2]^+$ (**3a**) is a strong reductant ($E_{1/2}^{II/I*}$= -1.43 V) for a wide range of organic molecules.[28] However, in 2015 Reiser et al. introduced $[Cu(dpp)(binc)]^+$ (**3c**) with longer excited state lifetime and stronger reduction potential of -1.88 V employing oxidative quenching cycle.[14a] Therefore, in reaction with no sacrificial substrates this catalyst is a stronger reductant compared to *fac*-Ir(ppy)$_3$ (**2a**). In 2016, Wenger group demonstrated the

catalytic applicability of the molybdenum-based [Mo(CNAr$_3$NC)$_3$] (**5**) catalyst with very strong excited state reduction potential of -2.0 V to -2.2 V for the Mo(0)/Mo(I) pair.[21] In the case of organic dyes the reduction potentials shown in Table 2 refer to the excited triplet states of the catalyst due to the photophysical properties described in literature[6f].

Table 2. Redox potentials for selected photoredox catalysts.[a]

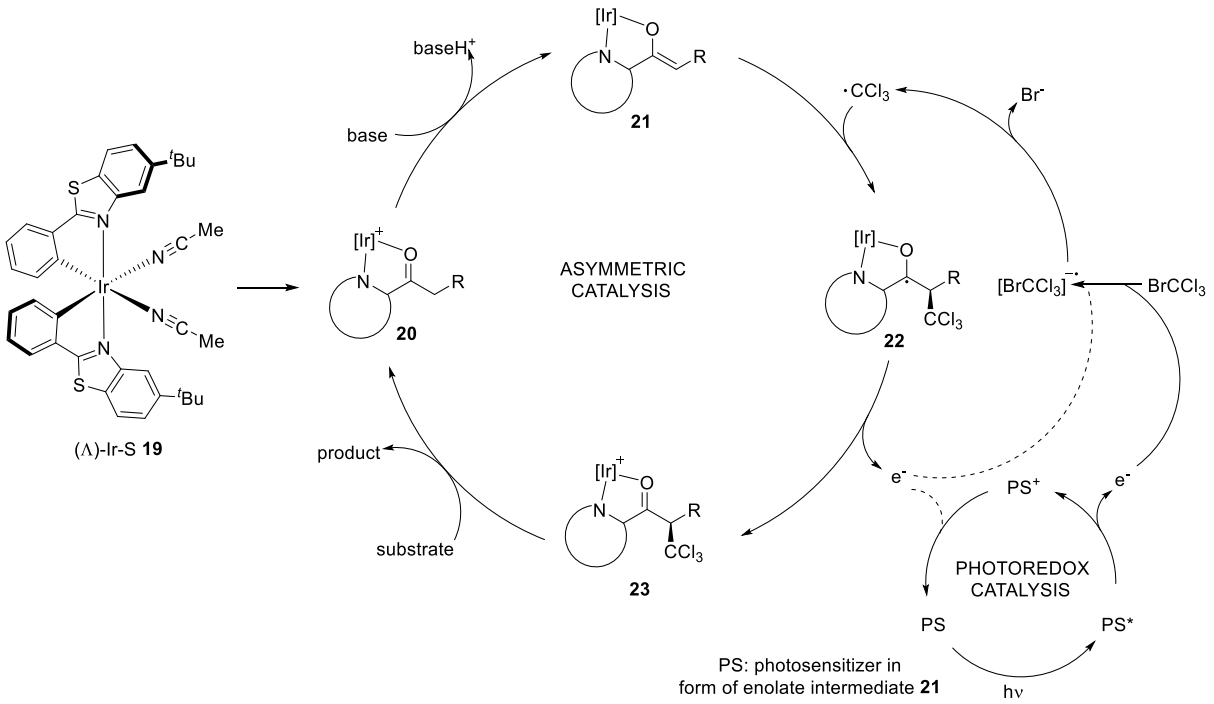
Entry	Photocatalyst	$E_{1/2}$ (Pc^+/Pc^*) [V]	$E_{1/2}$ (Pc^+/Pc) [V]	$E_{1/2}$ (Pc^*/Pc^-) [V]	$E_{1/2}$ (Pc/Pc^-) [V]	Ref
1	$[Ru(bpy)_3]^{2+}$ (**1a**)	-0.81	+1.29	+0.77	-1.33	6a
2	$[Ru(bpz)_3]^{2+}$ (**1b**)	-0.26	+1.86	+1.45	-0.80	6a
3	$[Ru(bpm)_3]^{2+}$ (**1c**)	-0.21	+1.69	+0.99	-0.91	6a
4	$[Ru(phen)_3]^{2+}$ (**1d**)	-0.87	+1.26	+0.82	-1.36	6a
5	*fac*-Ir(ppy)$_3$ (**2a**)	-1.73	+0.77	+0.31	-2.19	6a
6	$[Ir(ppy)_2(dtbbpy)]^+$ (**2b**)	-0.96	+1.21	+0.66	-1.51	6a
7	$[Ir(dF(CF_3)ppy)_2(dtbbpy)]^+$ (**2c**)	-0.89	+1.69	+1.21	-1.37	6a
8	$[Cu(dap)_2]^+$ (**3a**)	-1.43	+0.62			13
9	$[Cu(dpp)(binc)]^+$ (**3c**)	-1.88	+0.69			14a
10	[Cu(dpdmp)($(PPh_2)_2C_2B_9H_{10}$)] (**3d**)			+1.01	-1.39, -1.60	19
11	$[Mo(CNAr_3NC)_3]$ (**5**)	-2.0/ -2.2	-0.02			21, 31
12	Eosin Y (**6b**)	-1.15[b]	-1.08[b]	+0.83[b]	+0.76[b]	6f
13	Rose Bengal (**6c**)	-0.96[b]	-0.99[b]	+0.81[b]	+0.84[b]	6f
14	Rhodamine B (**7a**)	-0.89[b]	-0.96[b]	+0.84[b]	+0.91[b]	6f
15	Rhodamine 6G (**7b**)	-0.86	-1.14	+0.95	+1.23	6f
16	10-methyl-9-phenyl-acridinium (**8b**)		-0.54[c]			6f
17	10-methyl-9-mesityl-acridinium (**8c**)		-0.49	+1.45		6f

[a]All potentials are given in volts versus the saturated calomel electrode (SCE). Pc: Photocatalyst. Measurements were performed in acetonitrile at room temperature unless otherwise noted. [b]In MeOH. [c]In DMF.

6. Electron Transfer vs. Coordination

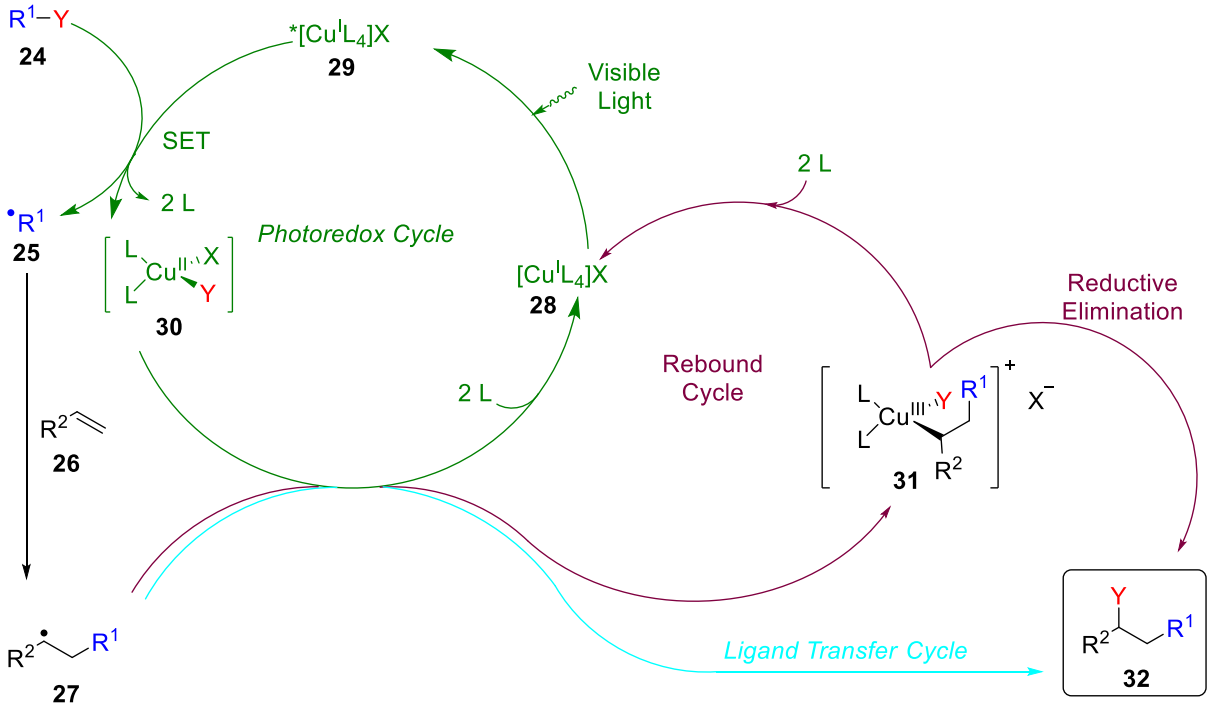
As already mentioned in the description of reductive quenching cycle, amines can be used as sacrificial electron donors or hydrogen-atom sources. Beside this group of molecules, there is a range of further additives like ascorbic acid, Hantzsch ester, 2,6-lutidine and more which can help the photocatalyst to go through the desired transformation. Interestingly, the employment of the photocatalysts is also compatible with the use of chiral additives known from organocatalysis.[6g] This type of cocatalysis was impressively demonstrated e.g. by utilization of chiral amines for the in situ generation of enamines and subsequent radical addition derived from single electron transfer of the employed photocatalyst.[32] Moreover, the use of chiral

Brønsted acid as cocatalyst in photocatalysis was demonstrated to give rise to high enantiomeric excess in the reaction of imines with *N*-arylamines.[33] In this type of cocatalysis the function of the photocatalyst was limited to the single-electron-transfer with no direct coordination of the substrate. In contrast, Meggers group presented an efficient transformation of α,β-unsaturated carbonyl compounds with allyl sulfones to the corresponding chiral products employing chiral metal-based lewis acid and Hantzsch ester as single-electron donor.[34] In this reaction the role of the metal-complex was the coordination to the substrate and in this way the formation of the better electron acceptor. Moreover, iridium-based photocatalyst (Λ)-Ir-S **19** was introduced by Meggers et al. to act as both, chiral lewis acid and the photoredox catalyst as single-electron-donor (Scheme 6).[35]



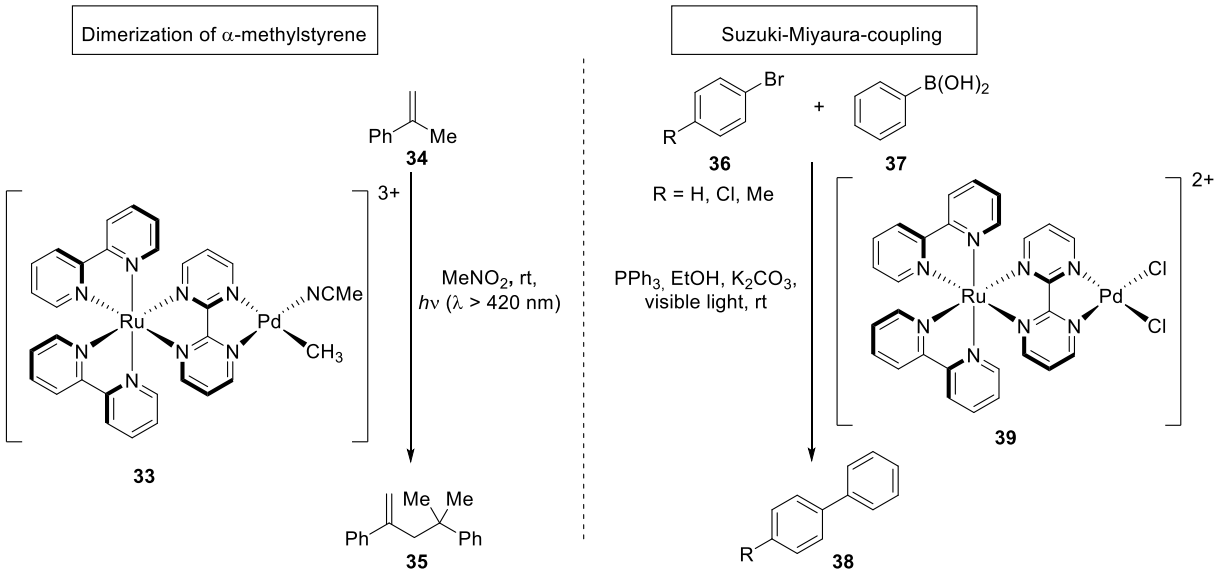
Scheme 6. Chiral iridium-based photocatalyst for enantioselective functionalization of carbonyl compounds.[35]

In contrast, to the ruthenium- and iridium-based photocatalysts which are known to utilize closed catalytic cycle or radical chain propagations (see quantum yield section), copper can run through additional mechanistic pathways. The formation of Cu(III)-intermediates by oxidative additions or direct radical trapping processes demonstrate the unique character of copper-based photocatalysts and enables a variety of organic transformations. In several reports[14a, 14b, 14d, 14e, 36], the employed copper catalysts are shown to go through inner-sphere mechanisms including trapping of the intermediary radical to form Cu(III)-species or direct ligand transfer process. In Scheme 7 these two mechanistic pathways are described exemplary for an atom transfer radical addition (ATRA) reaction.



Scheme 7. Alternative mechanistic pathways for copper-based photocatalysts.

The variation of the ligands employed in established photocatalysts (*vide supra*) enables the synthesis of bimetallic complexes as was shown by Inagaki and coworkers.[37] The described complex **33** contained photoactive ruthenium center and catalytically active palladium center and demonstrated excellent results in the dimerization of α-methylstyrene (**34**) suppressing the polymerization of the substrate. Interestingly when mononuclear catalysts $Ru(bpy)_3^{2+}$ and $[(bpy)PdMe(MeCN)]^+$ were used separately or as mixture no reaction was observed.

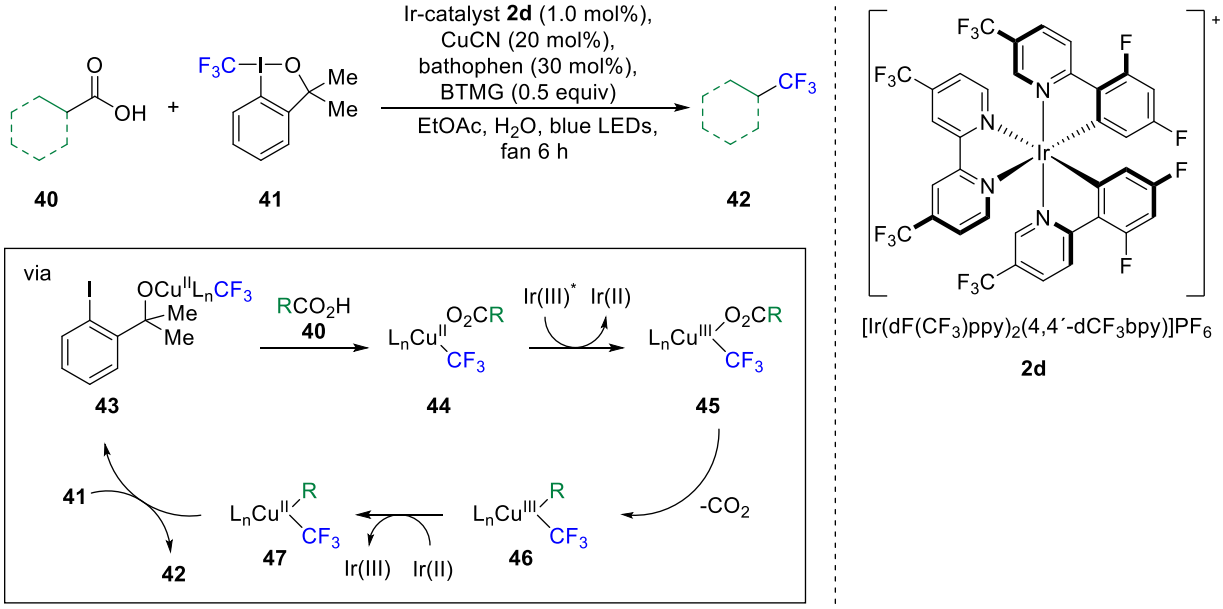


Scheme 8. Dimerization of α-methylstyrene (**34**)[37d] and Suzuki-Miyaura coupling[38] by bimetallic Ru/Pd-complexes **33** and **39**.

In 2014, Mori et al. demonstrated visible-light enhanced Suzuki-Miyaura coupling reaction employing bimetallic complex **39**.[38] In this reaction the electron transfer from photoexcited

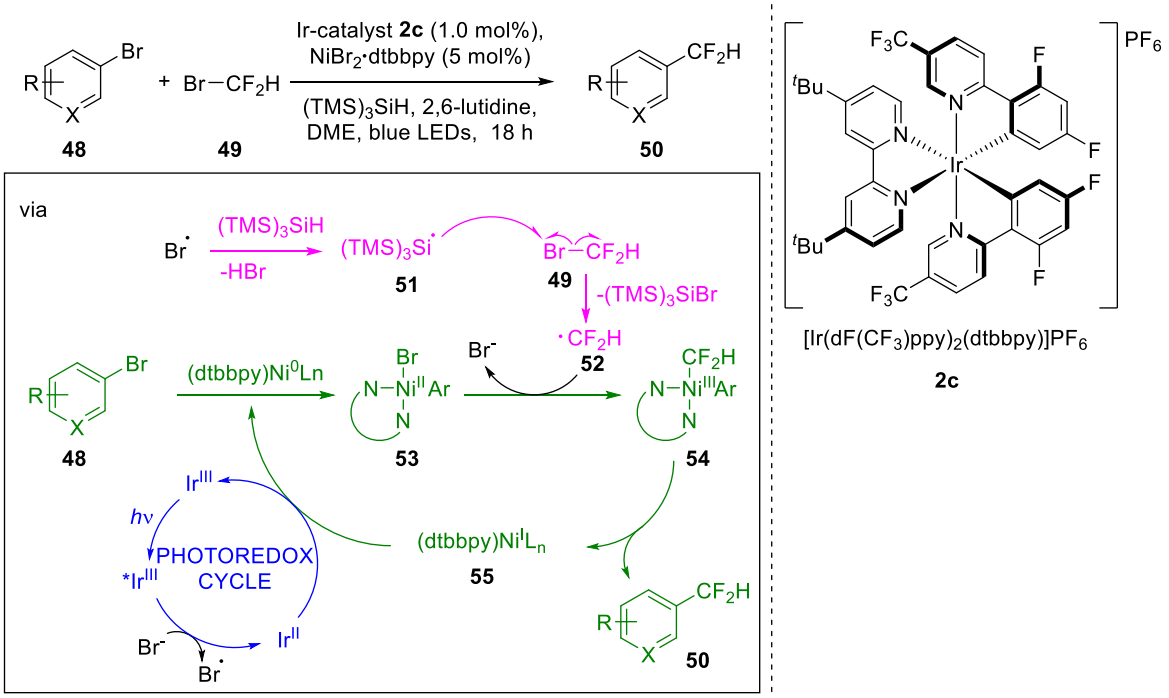
Ru(II)-catalyst to palladium center forms the catalytically active and electron rich Pd(0)-species, thus facilitating the oxidative addition of the aryl halide **36**.

The variety of the photochemical transformations performed with different types of catalyst indicate the unique character of each photocatalyst. Therefore, in recent years the research interest focused on the combination of different types of catalysts.[6h] The two selected examples are presented in Scheme 9 and Scheme 10.



Scheme 9. Iridium(III)-copper(I)-cocatalysis.[39]

In 2018, the photomediated decarboxylative trifluoromethylation of aliphatic carboxylic acids was presented by MacMillan group (Scheme 9).[39] In this reaction the employed iridium photocatalyst acts as the electron acceptor, whereas the use of copper cocatalyst is important for activation of carboxylic acid, thus facilitating the oxidative decarboxylation and coordination of the coupling partners CF_3 and R. After insertion into Togni´s reagent **41** and ligand exchange the Cu(II)-species **44** is formed coordinating CF_3 and carboxylic acid. Photochemical oxidation of Cu(II) to Cu(III)-species **45** with subsequent extrusion of CO_2 results in formation of Cu(III)-complex **46**, which is finally reduced by iridium photocatalyst and undergoes reductive elimination to give the desired product **42** and to regenerate the Cu(II)-species **43**. In the same year, MacMillan et al. employed Ir(III)-Ni(0) catalyst pair for the difluoromethylation of aryl bromides (Scheme 10).[40] In the similar way as described for the Ir(III)-Cu(I)-cocatalysis, in this reaction the function of nickel metal was the coordination of the coupling partners. For this purpose, the Ni(0)-complex undergoes oxidative addition to the aryl bromide **48** forming a Ni(II)-species **53**. The bromide ligand is exchanged by difluoromethyl-radical **52** forming Ni(III)-intermediate **54** which can subsequently form the final product **50** and release Ni(I)-complex **55**.



Scheme 10. Iridium-nickel(0)-cocatalysis.[40]

The latter is finally reduced by iridium-photocatalyst regenerating the Ni(0)-species. The regeneration of the photocatalyst occurs through oxidation of bromide to the bromine radical which is necessary for the formation of the difluoromethyl radical **52**.

7. Sustainability

Compared to the metal-free organic dyes and photocatalysts based on earth-abundant metals, the main disadvantage of the iridium- and ruthenium-based photocatalysts is the relatively high price of the employed metals. This argument is often used when the same reactions can be also carried out by alternative catalysts. In order to increase the attractivity of the very efficient and variable Ir-/Ru-catalysts many efforts have been made to develop recyclable variations of the commonly used photocatalysts. The main strategies are based on the use of immobilized photocatalysts in ionic liquids[41] or by introduction of polymer chains[8] and alkyl chains[42] at the ligands of the catalysts. Bergbreiter et al. developed a recyclable version of $[Ru(bpy)_3]^{2+}$ by installation of polyisobutylene (PIB) chains at the bpy-ligand. The separation and reuse of the synthesized catalyst was achieved by selective precipitation of the polymeric reaction product from the reaction solution.[8a, 43] Moreover, a recyclable version of $[Ir(ppy)_2(dtbbpy)]^+$ photocatalyst was obtained by Kobayashi et al. through the use of the well-established suspension polymerization method leading to the iridium catalyst **2e** with partially cross-linked acrylates. The separation and reuse of the catalyst was ensured by simple filtration from the reaction solution.[8b] In 2016, Reiser and coworkers presented a recyclable version of the strongly reducing *fac*-$Ir(ppy)_3$ catalyst by installation of polyisobutylene (PIB) chain at one of

the ligands. The homogeneous catalyst allows automatic recovery and reuse in flow systems, employing thermomorphic or biphasic solvent systems.[8c]

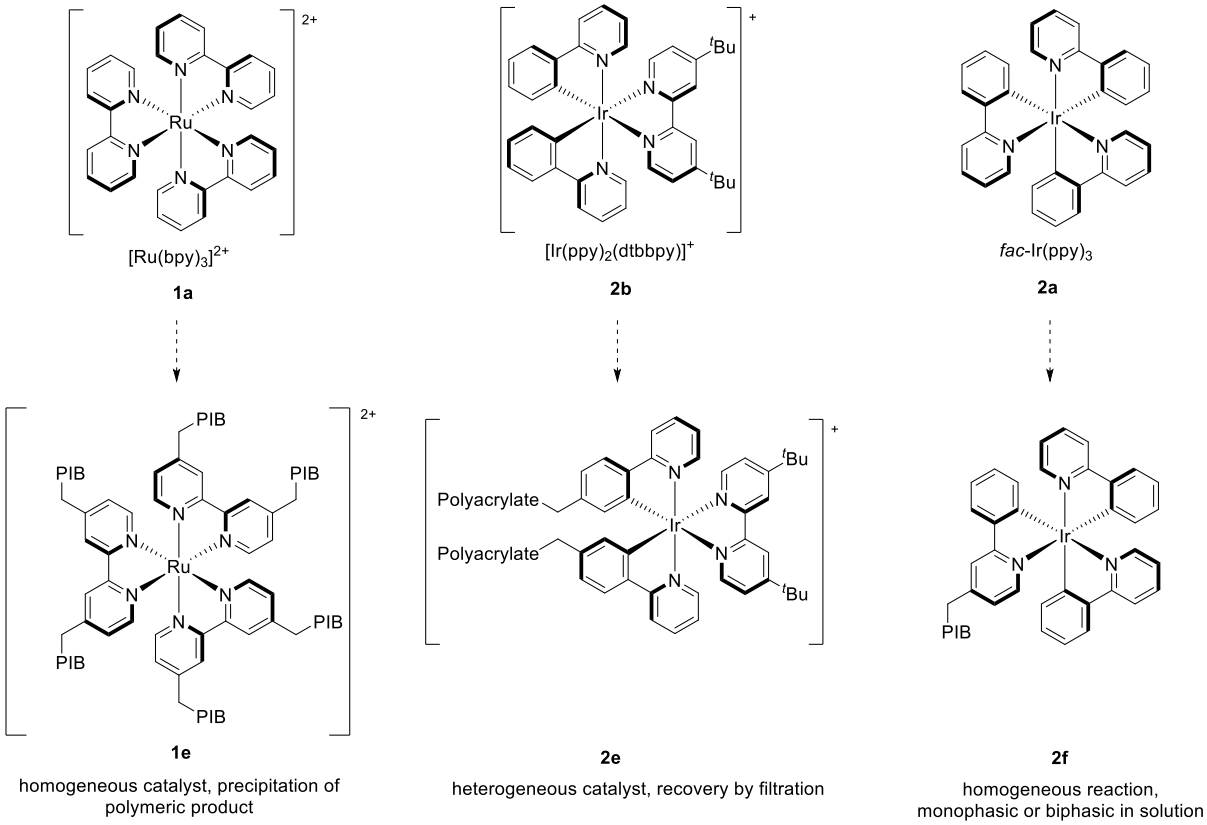


Figure 8. Recyclable representatives of the commonly used photocatalysts.[8]

8. Aim of the work

In the present work four types of transformations were investigated employing different photocatalysts. The differences in the catalytic properties of the catalysts were of great importance for the unique characters of the investigated reactions. In chapter B, *fac*-Ir(ppy)$_3$ was used in the visible-light mediated deoxygenation of activated amino alcohols to give polysubstituted *N*-heterocycles, which are important key structures in natural products and pharmaceuticals. In chapter C the performance of Cu(II)-based photocatalyst [Cu(dap)Cl$_2$] in the iodoperfluoroalkylation reaction of alkenes was compared with the established [Cu(dap)$_2$]Cl and plausible mechanistic pathways for copper based catalysts were investigated. In chapter D the copper-based catalysts were used for the transformation of sulfonylchlorides and unactivated alkenes into chlorosulfonylation products in the presence of inorganic base underlining the unique character of copper catalysis. Finally, in chapter E the visible-light induced reaction between commercially available allyl bromides and sulfonyl chlorides provided allylsulfones, being an important substrate class in organic synthesis.

9. References

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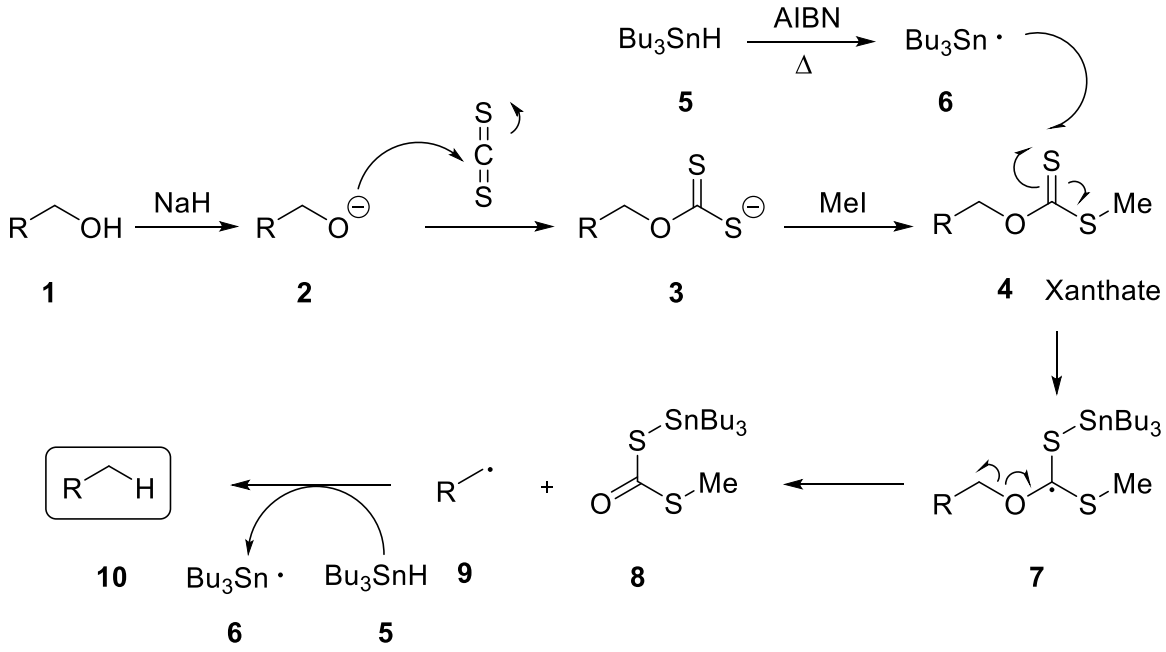
B. Synthesis of Heterocycles via Photoredox Mediated Deoxygenation Reaction‡

1. Introduction

In 1975 Derek H. R. Barton and Stuart W. McCombie presented an efficient method for deoxygenation of alcohols by reductive carbon-oxygen bond cleavage.[1] For this purpose, the strong C-O bond was activated by the formation of thiocarbonyl derivatives (Scheme 1). First, the hydroxy group of the substrate **1** is deprotonated by a strong base such as NaH and the resulting alkoxide **2** reacts with CS_2 to form anion **3**. The subsequent methylation of this anion yields the desired xanthate **4**, which has a high reactivity to tributylstannyl radical **6** formed by reaction of tributyltin hydride (**5**) with AIBN. The formation of the very stable S-Sn bond acts as the driving force for this reaction.[2] The resulting radical **7** undergoes a homolytical bond cleavage of the C-O bond providing alkyl radical **9** and tributyltin xanthate **8**. In the final step, radical **9** abstracts a hydrogen atom from tributyltin hydride (**5**) to give the desired deoxygenation product **10** and regenerating a new tributylstannyl radical **6**.



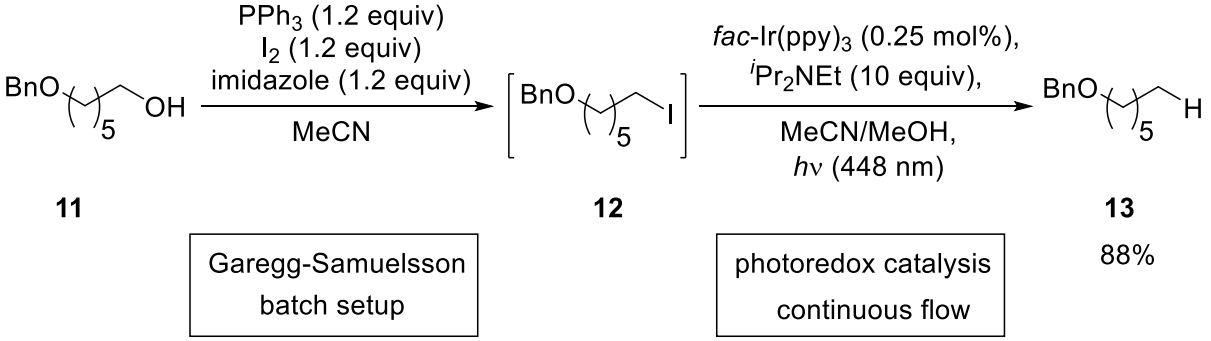
Scheme 1. General mechanism of Barton-McCombie deoxygenation reaction.[3]

Although the Barton-McCombie reaction is an efficient strategy for deoxygenating a wide range of alcohols, it contains some difficulties and limitations. For example, the preparation of *S*-methyl dithiocarbonates requires prolonged use of alkali, so stable *O*-benzyl ethers must be used as protecting groups.[4]

‡This chapter is partially based on Rackl, D.; Kais, V.; Lutsker, E.; Reiser; O. *Eur. J. Org. Chem.* **2017,** *2017* (15), 2130-2138.

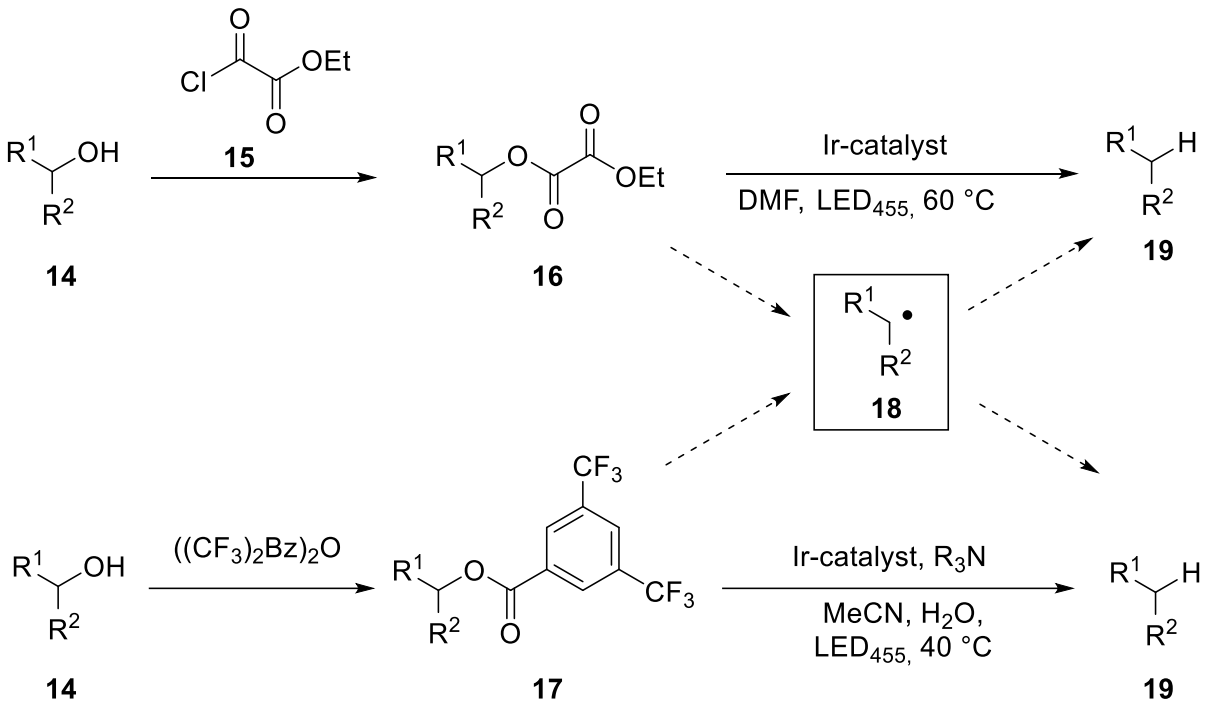
In 1981 Robins et al.[5] solved this problem by employment of *O*-phenoxythiocarbonyl derivatives, which make sensitive natural products such as ribonucleosides and 2'-deoxynucleosides suitable substrates for the desired reaction.

In addition, the employment of tributylstannane (**5**) has the disadvantage that stoichiometric amounts of toxic tin-containing byproducts are formed.[6] For this reason, Stephenson et al.[7] presented in 2013 a deoxygenation protocol for alcohols by in situ conversion into alkyl iodides with subsequent hydrodeiodination reaction (Scheme 2). The alcohol **11** was converted by Garegg-Samuelsson reaction in a batch setup into the corresponding iodine **12** and then by photoredox catalyzed reaction in microflow setup to give the deoxygenated product **13** in high yields. This one-pot deoxygenation protocol is applicable to primary and secondary alcohols, can be carried out under mild reaction conditions and tolerates the presence of a wide range of functional groups.[3, 7]



Scheme 2. Deoxygenation reaction by Stephenson et al.[7] via transformation of alcohol into alkylhalide and subsequent dehalogenation.

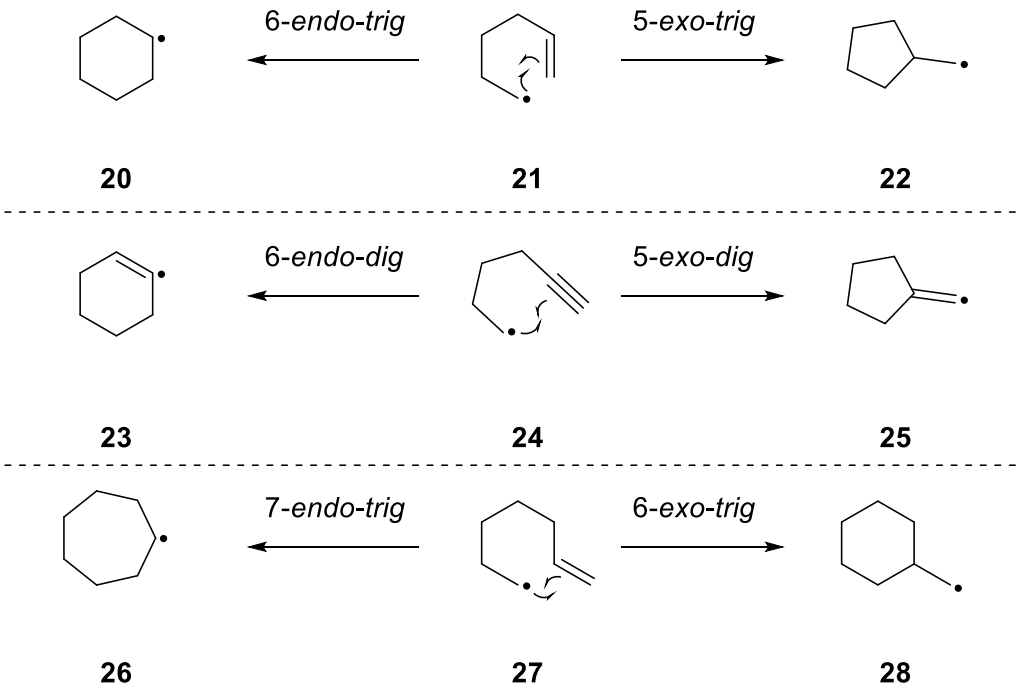
However, the protocol presented by Stephenson and coworkers[7] also has the disadvantage, that an equimolar amount of halides is produced as a byproduct during the transformation. In order to solve this problem D. Rackl and V. Kais from the Reiser group developed efficient protocols for the halide free deoxygenation of primary and secondary alcohols (Scheme 3).[8]



Scheme 3. Deoxygenation strategies developed in Reiser group.[8b, 8c]

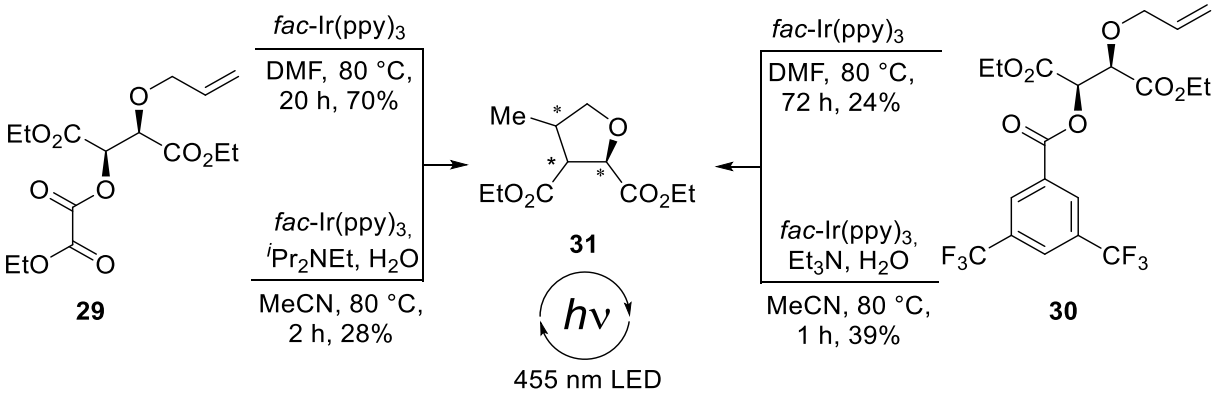
Both synthetic pathways are based on the activation of the hydroxy group by esterification to the corresponding ethyl oxalates **16** or 3,5-bis(trifluoromethyl)benzoates **17**. Afterwards, the intermediary radical **18** is formed by the homolytical C-O bond cleavage under photoredox conditions using an iridium photocatalyst. Fanally, radical **18** abstracts a hydrogen atom from a hydrogen source such as DMF or amine as sacrificial electron donor to form the deoxygenated product **19**.

In 1976 J. E. Baldwin[9] published a series of rules allowing to predict the possibility of ring closure reactions. The ease of the ring formations depends on the stereochemical requirements of the transition states for the various ring constructions. First, the size of the formed ring is described by a numerical prefix. Secondly, the shortened terms *tet* (tetrahedral = sp^3), *trig* (trigonal = sp^2) or *dig* (diagonal = sp) describe the hybridization of the atom attacked by a nucleophile, radical or electrophile. Finally, the way in which the bonds are broken during the cyclization process is described by the terms endocyclic (*endo* = a bond is broken within the newly formed ring) or exocyclic (*exo* = a bond is broken outside the newly formed ring). The trend shows that sp^2-hybridized carbons can undergo 3- to 7-*exo*-*trig*-reactions and 6- to 7-*endo*-*trig* processes, while 3- to 5-*endo*-*trig* reactions are disfavored. In contrast, 5- to 7-*exo*-*dig*-reactions and 3- to 7-*endo*-*dig* processes are favored for the sp-hybridized carbons, whereas 3- and 4-*exo*-*dig*-reactions are disfavored (Scheme 4).[9] In the present work especially 5-/6-*exo*-*trig* and 5-*exo*-*dig* ring closures are particularly important.



Scheme 4. Baldwin´s rule for 5-hexenyl- (**21**), 5-hexynyl- (**24**) and 6-heptenyl radicals (**27**).

Further investigations on the use of the intermediary radical **18** led to the idea of intramolecular trapping via a radical 5-*exo*-*trig* cyclization reaction. Therefore, commercially available tartaric acid ester was monoallylated and *O*-activated providing substrates **29** and **30**. Under photoredox conditions in the presence of the strong reductant *fac*-Ir(ppy)$_3$, substituted tetrahydrofuran **31** was formed in good yields (Scheme 5).



Scheme 5. Photomediated cyclization via deoxygenation reaction.[10]

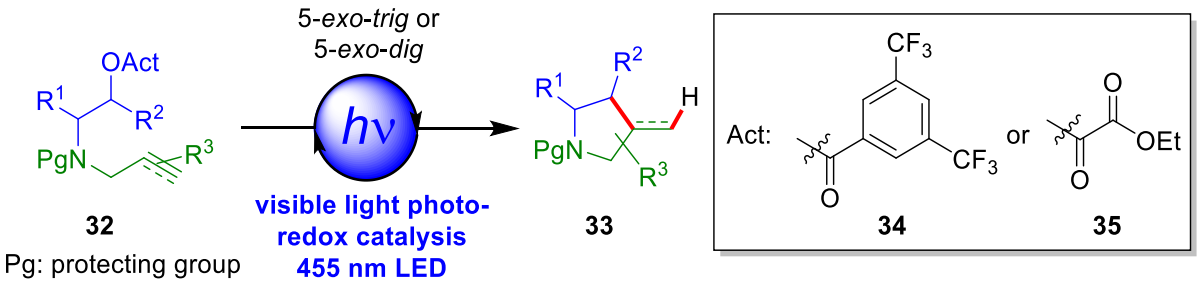
Based on the results from dissertations of D. Rackl[8b] and V. Kais[8c], first efforts towards photomediated synthesis of substituted *N*-heterocycles were undertaken in my master thesis[3]. Thereby, the determination of the optimized reaction conditions and the successful synthesis of several pyrrolidines, mostly derived from ethyl oxalates, were performed. Tetrahydrofurans[11] and pyrrolidines[12] are important key structures in numerous natural products and pharmaceuticals. Many synthetic strategies towards these important classes of heterocycles have been reported, among them visible light photocatalysis.[13] In contrast to the reported

protocols, which include the ring closure by the formation of carbon-heteroatom bond, the synthesis of heterocycles by C-C bond formation has been achieved in the present work.[10] The aim of this work was to investigate the substrate scope for the photomediated synthesis of polysubstituted pyrrolidines with a focus on the two activation groups ethyl oxalate **16** and 3,5-bis(trifluoromethyl)benzoate **17**. In addition, the extension of the developed protocol to the synthesis of further *N*-heterocycles was explored.

2. Synthesis of Substituted Pyrrolidines

2.1. Preparation of Starting Materials

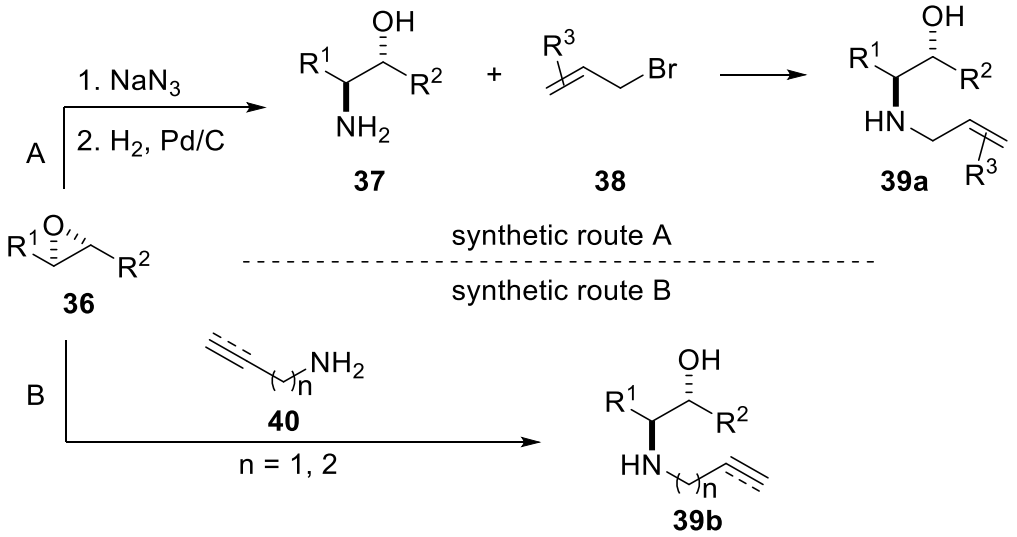
The present study is linked to the results of my master thesis[3]. The focus of this project was on the synthesis of a broad substrate pool of ethyl oxalates as well as 3,5-bis(trifluoromethyl)benzoates and their employment in the photoredox catalyzed cyclization reaction. In general, the target starting material should contain several properties: Besides the activated C-O bond next to a radical stabilizing group e.g. carbonyl, aryl or cyano[8a], the molecule needs a double or triple bond, with an *N*-protected nitrogen as bridge between the two described parts in order to undergo a radical ring closure reaction (Scheme 6). The protection of the nitrogen is necessary due to the risks of oxidation of the lone pair and thus acting as a sacrificial electron donor for the catalyst. Such an oxidation process would lead to irreversible destruction of the starting material which would be incapable of performing the desired ring closure reaction. The employment of designed 1,2-amino alcohols **32** is required to obtain access to substituted pyrrolidines **33** via favored 5-*exo*-*trig* or 5-*exo*-*dig* reactions.



Scheme 6. Proposed cyclization strategy.

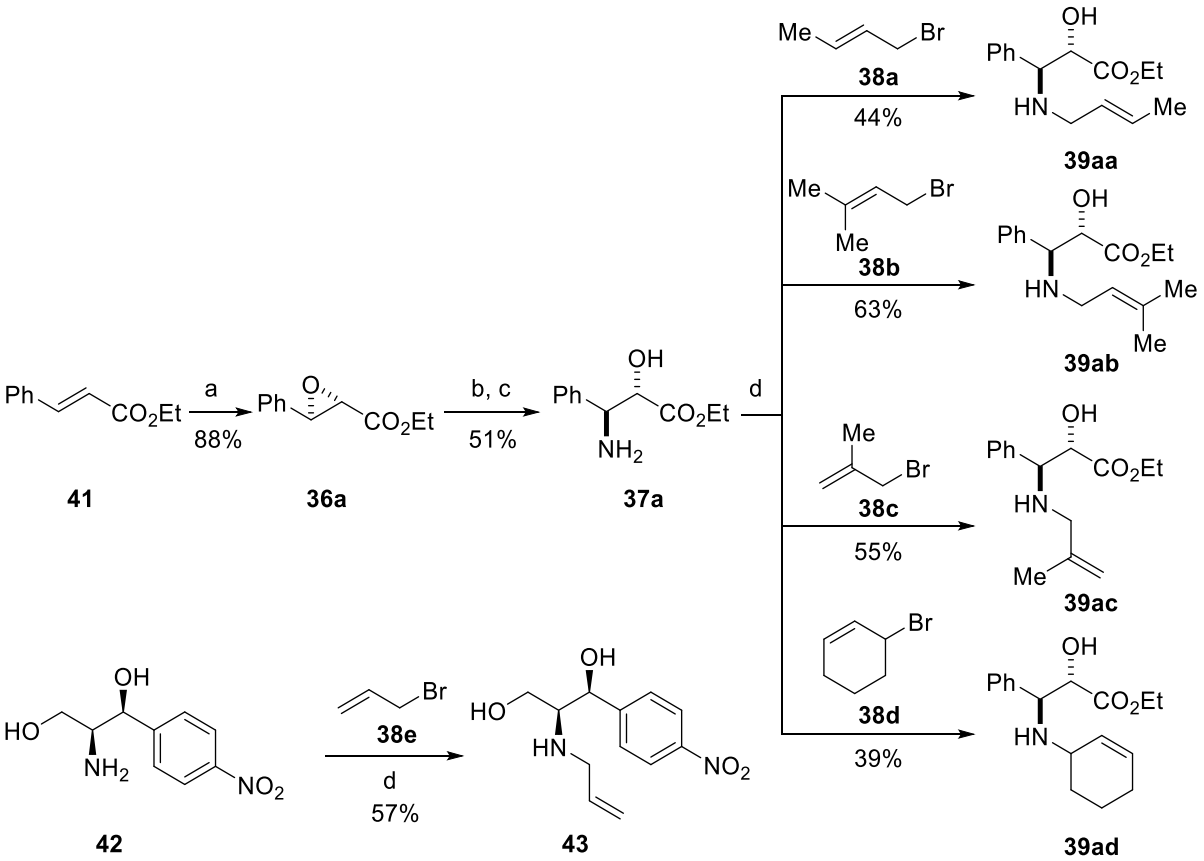
Due to the low stability of ethyl oxalyl esters and 3,5-bis(trifluoromethyl) benzoates under basic conditions necessary for *N*-alkylation and *N*-protection steps, *O*-activation is identified as the final synthetic step. The protection of nitrogen by an electron withdrawing group such as Boc- or Ac-group, leads to a strongly decreased nucleophilic character of the heteroatom making the subsequent alkylation of this atom more difficult. For this reason, the *N*-protection should be carried out after the allylation/propargylation step. In general, there are two feasible routes to the *N*-alkylated 1,2-amino alcohols **39** (Scheme 7). The synthetic pathway B is based on the ring opening reaction of epoxide **36** with alkylamine such as allylamine (**40a**) or propargylamine (**40b**), which leads in two steps to the *anti*-configurated product **39b**, starting from commercially available alkenes.[3, 14] This strategy is advantageous due to the small number of synthesis steps and allows the variation of the non-allylic part of the molecule (Scheme 6, blue part of compound **32**). However, the limited number of commercially available substituted allylamines illustrates the disadvantage of this route. For this purpose, synthetic route A must be used starting from commercially available alkenes. After the formation of epoxide **36** followed by ring opening using sodium azide, the subsequent hydrogenation provides the 1,2-amino alcohol

37.[3, 14a, 15] Next, the desired product **39a** can be obtained under basic conditions in the presence of allyl bromide **38**. This synthetic pathway enables the variation of the allylic part of the molecule (Scheme 6, green part of compound **32**) due to the commercial and synthetic availability of substituted allyl bromides **38** (Scheme 7).



Scheme 7. Synthetic routes towards alkylamino alcohols **39a** and **39b** starting from epoxide **36**.

First, literature known epoxide **36a** was transformed into the 1,2-amino alcohol providing key compound **37a** for the subsequent allylations reactions using synthetic route A (Scheme 8). The variation of the allylic part included the introduction of methyl groups at different positions of the alkene leading to alkylamino alcohols **39aa**, **39ab** and **39ac**, as well as the introduction of sterically demanding cyclohexene moiety leading to compound **39ad**. Moreover, the same allylation strategy was applied to the commercially available enantiopure 2-amino-1,3-diol **42** resulting in product **43**. All reaction showed moderate yields of 39-63% without significant sterical effect of additional groups at the alkene moiety.

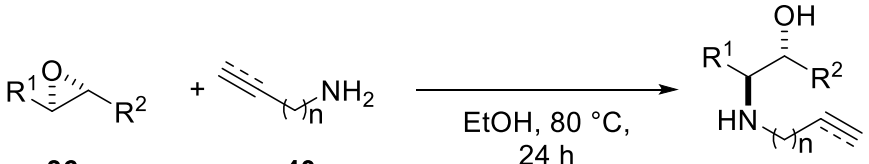


Scheme 8. Allylation reaction of amino alcohols.
Reagents and conditions: (a)[14a] *m*CPBA (1.5 equiv), CH_2Cl_2, reflux, 5 d, 88%; (b)[15a] NaN_3 (1.4 equiv), NH_4Cl (1.4 equiv), EtOH/H_2O (3:11), reflux , 42 h, 51%; (c)[15b] Pd/C (10 wt%), H_2 (1 atm), EtOH, rt, 24 h, 99%; (d)[3] alkyl bomide (**38a**-**38e**) (1.0-2.0 equiv), DBU (1.0-2.0 equiv), toluene, 60 °C , 96 h, 39%-63%.

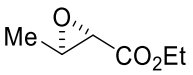
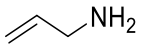
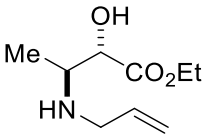
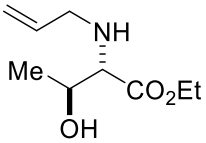
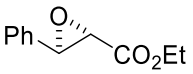
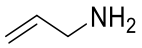
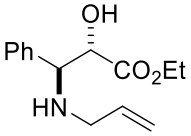
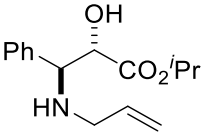
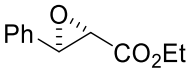
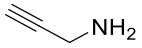
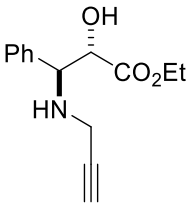
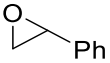
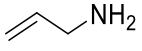
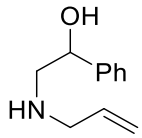
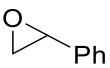
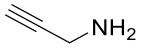
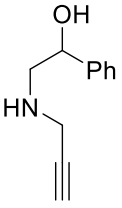
The ring opening reaction of various epoxides with allylamine **40a** and propargylamine **40b** provided a series of *N*-alkylated amino alcohols **39b** (Table 1). In general, the equimolar amount of the corresponding alkylamine was used for epoxides containing ester moiety to avoid the formation of amides, while 2.0 equivalents of the alkylamine were used for other epoxides. In the case of epoxide **36b**, derived from commercially available ethyl (*E*)-but-2-enoate, the reaction with allylamine (**40a**) provided the desired product **39ba** only as minor diastereomer in 24% yield (Table 1, entry 1). The obtained major diastereomer **39ba´** was not a suitable substrate for the next synthetic steps as there was no radical stabilizing group next to the carbon containing the hydroxy group. The employment of epoxide **36a**, which can be obtained from commercially available ethyl cinnamate (**41**), in combination with allylamine (**40a**) provided the desired product **39bb** in 56% as a single diastereomer. The subsequent transesterification gave rise to isopropyl ester **39bc** in 52% overall yield (entry 2). Switching allylamine (**40a**) to propargylamine (**40b**) resulted in comparable yields for the alkylation product **39bd** (entry 3). According to the reported procedure[14c] compound **39be** was synthesized in very good yield, but surprisingly the reaction of propargylamine (**40b**) with the same epoxide provided the desired alkylamino alcohol **39bf** only in 27% yield (entries 4 and 5). In contrast to entry 4 with high isolated yield, the reaction of the epoxide **36d** derived from

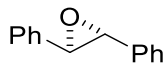
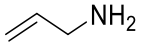
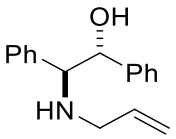
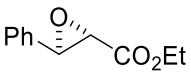
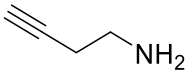
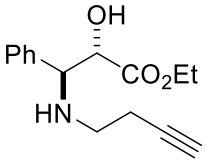
trans-stilbene delivered the desired product **39bg** in only 48% yield. To demonstrate the synthesis of 6-membered rings via 6-*exo*-*dig* cyclization reaction, but-3-yn-1-amine (**40c**) was used as alkylamine in combination with epoxide **36a**, giving rise to the formation of product **39bh** in 46% yield (entry 7). The analysis of both the nucleophilicity of corresponding amines and sterical hindrance of the carbon backbone does not provide a clear explaination for the different yields.

Table 1. Synthesis of alkylamino alcohols via epoxide ring opening reacion.



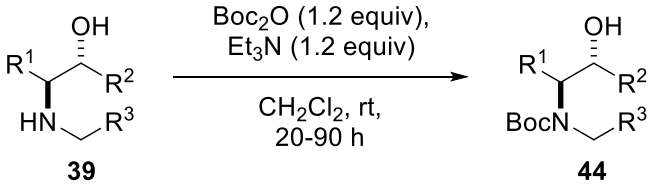
36 **40** n = 1, 2 **39b** n = 1, 2

Entry	Epoxide	Alkylamine	Product	
1				
	36b (1.0 equiv)	**40a** (1.0 equiv)	**39ba,** 24%	**39ba´,** 32%
2				
	36a (1.0 equiv)	**40a** (1.0 equiv)	**39bb**, 56%	**39bc**, 52%[a]
3				
	36a (1.0 equiv)	**40b** (1.0 equiv)	**39bd**, 54%	
4				
	36c (1.0 equiv)	**40a** (2.0 equiv)	**39be**, 93%	
5				
	36c (1.0 equiv)	**40b** (2.0 equiv)	**39bf**, 27%	

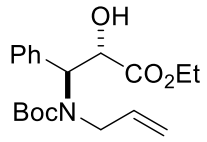
6			
	36d (1.0 equiv)	**40a** (2.0 equiv)	**39bg**, 48%
7			
	36a (1.0 equiv)	**40c** (1.0 equiv)	**39bh**, 46%

Reagents and conditions: epoxide (**36a**-**36d**) (1.0 equiv), alkyl amine (**40**) (1.0-2.0 equiv), EtOH, 80 °C, 24 h, 24%-93%. [a]Product **39bc** was obtained after acid catalyzed transesterification of compound **39bb** in 93% yield.

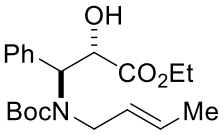
Next, the protection of the amine moiety was carried out employing the combination of Boc_2O and triethylamine.[3] To avoid double protection of the alkylamino alcohol, only a slight excess of di-*tert*-butyldicarbonat should be used (Scheme 9). For the compound **44a** and the monoalkylated derivative **44b** good yields of 65% and 74% were obtained. The introduction of an additional methyl group to the alkene moiety provided the Boc-protected product **44c** in excellent yield. Surprisingly, switching the methyl group to the other carbon of the double bond resulted in strong decrease of the yield for the product **44d**.



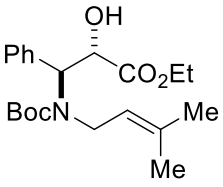
39 **44**



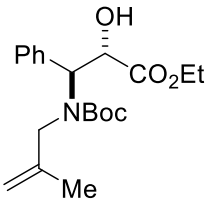
44a, 65%



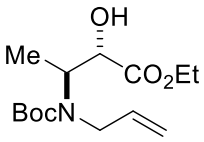
44b, 74%



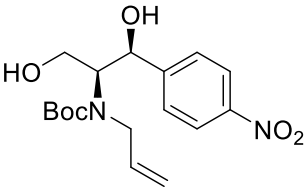
44c, 98%



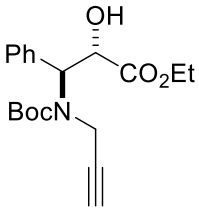
44d, 29%



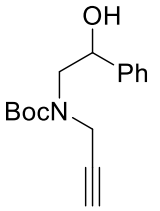
44e, 78%



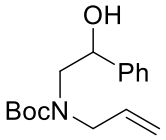
44f, 71%[a]



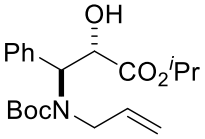
44g, 33%



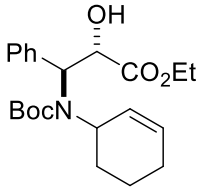
44h, 97%



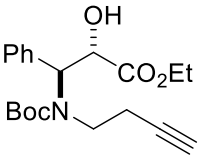
44i, 59%



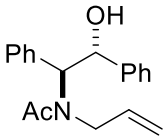
44j, 63%



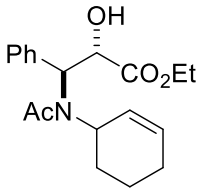
44k, 0%



44l, 0%



44m, 70%[b]



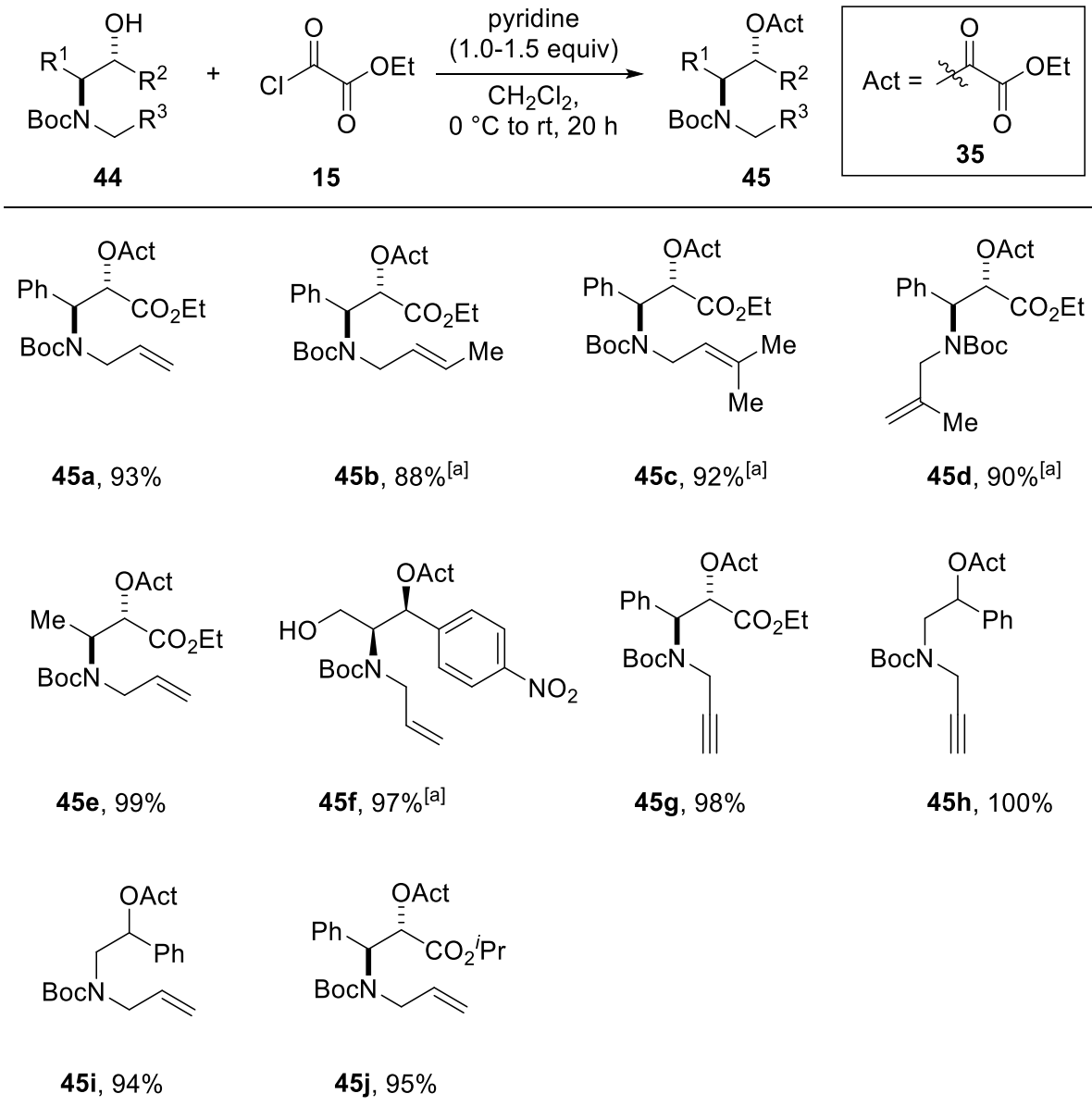
44n, 0%[b]

Scheme 9. Substrate scope of *N*-protected alkylamino alcohols.
Reagents and conditions: alkylamino alcohol (**39**) (1.0 equiv), Boc_2O (1.2 equiv), Et_3N (1.2 equiv), CH_2Cl_2, rt, 20-90 h, 29%-97%. [a] The product was synthesized starting from substrate **43**. [b]The product **44m** was obtained using Ac_2O (2.1 equiv) and Et_3N (2.2 equiv).

This result can be explained by the steric interaction of the methyl group and the sterically demanding Boc-group. However, the low yield of the propargylated compound **44g** cannot be explained by this argument. In further protection reactions, the desired products **44e, 44f**, **44i** and **44j** were obtained in moderate to good yields, whereas the product **44h** was formed in excellent yield of 97%. For the formation of product **44m** acetic anhydride was used instead of Boc_2O as a result of the obtained observations during the master thesis showing no product

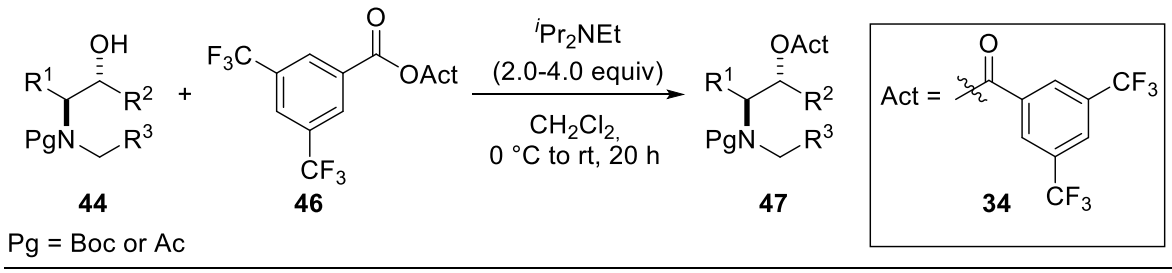
formation with the sterically demanding Boc-group.[3] Unfortunatelly, the protection reaction to the compounds **44k**, **44l** and **44n** failed, resulting in very low conversion.

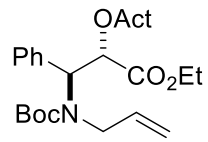
As the final step of the synthesis, the strong C-O bond was activated by esterification to the appropriate ethyl oxalyl esters and 3,5-bis(trifluoromethyl) benzoates.



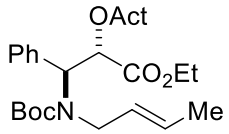
Scheme 10. Substrate scope of ethyl oxalates **45**.
Reagents and conditions: alcohol **44** (1.0 equiv), ethyl 2-chloro-2-oxoacetate (**15**) (1.0-1.5 equiv), pyridine (1.0-1.5 equiv), CH_2Cl_2, 0 °C to rt, 20 h, 88%-100%. [a]The products were synthesized during the master thesis[3].

The esterification reactions employing ethyl 2-chloro-2-oxoacetate (**15**) in the presence of pyridine showed high yields for all substrates applying the method developed during my master thesis[3] (Scheme 10). Similarly excellent results with very high yields in the range of 91-100% were obtained employing 3,5-bis(trifluoromethyl)benzoic anhydride (**45**) in the presence of *N*,*N*-diisopropylethylamine (Scheme 11).

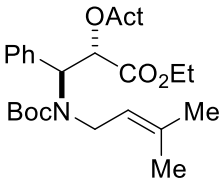




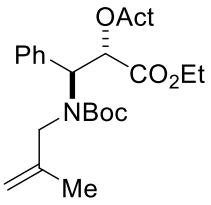
47a, 100%



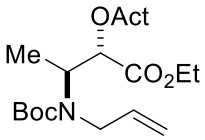
47b, 99%



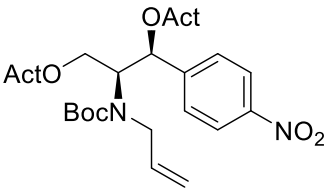
47c, 97%



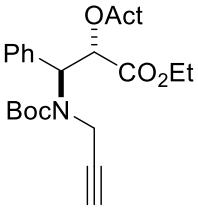
47d, 97%



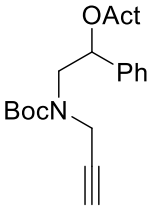
47e, 98%



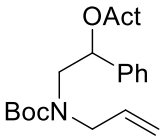
47f, 99%



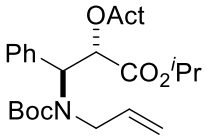
47g, 96%



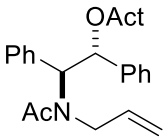
47h, 98%



47i, 95%



47j, 97%



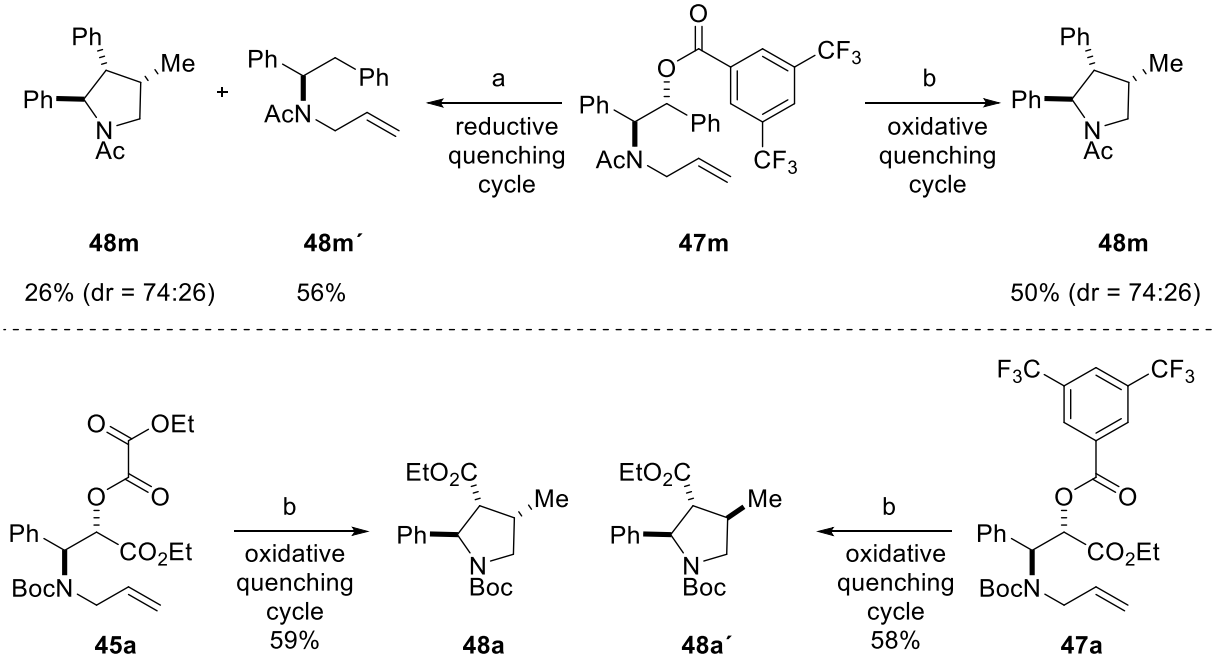
47m, 91%[a]

Scheme 11. Substrate scope of 3,5-bis(trifluoromethyl)benzoates **47**.
Reagents and conditions: alcohol **44** (1.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (1.2-2.4 equiv), *N*,*N*-diisopropylethylamine (2.0-4.0 equiv), CH_2Cl_2, rt, 20 h, 91%-100%. [a]The product was synthesized during the master thesis[3].

2.2. Photomediated Deoxygenation Reactions

The first attempt to synthesize pyrrolidine derivatives from ethyl oxalate activated *N*-allylated compounds was performed during my master thesis with substrate **45a**.[3] The reaction was carried out in a microflow reactor setup under irradiation with blue light and heating at 80 °C using the oxidative quenching cycle of *fac*-Ir(ppy)$_3$ in DMF. Apart from the starting material **45a**, photocatalyst and solvent no further additives were necessary. In contrast, the initial reaction with 3,5-bis(trifluoromethyl)benzoate **47m** was carried out analogously to the procedure developed by D. Rackl[8b]. Employing a batch setup, the starting material **47m** was converted in the presence of a sacrificial amine, water and MeCN as solvent at 80 °C using the reductive quenching cycle of photocatalyst. In specific, the main disadvantage of this pathway was the formation of the undesired deoxygenated acyclic side product **48m´** in 56% yield in addition to

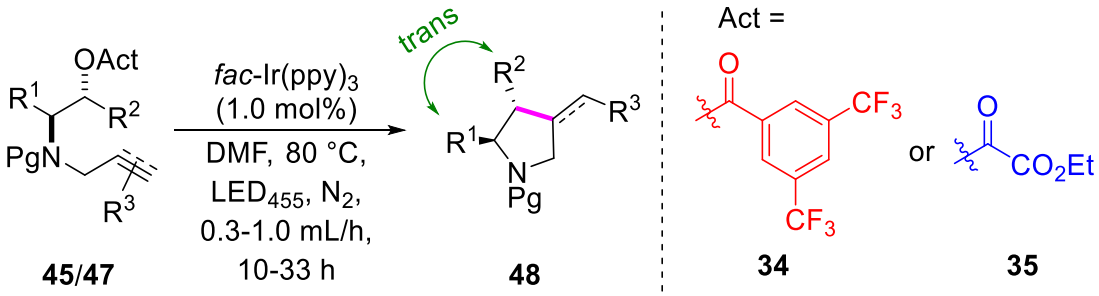
the low yield of the desired cyclic product **48m**. Interestingly, submitting the substrate **47m** to the oxidative quenching cycle showed a yield of 50% of the desired pyrrolidine **48m** and no formation of deoxygenated open-chain product **48m´**. Optimizing the reaction conditions for the pyrrolidine synthesis revealed that the oxidative quenching cycle was the best choice for both activation groups. 3,5-Bis(trifluoromethyl)benzoate **47a** and ethyl oxalate **45a** showed comparable yields and diastereomeric ratios (Scheme 12).



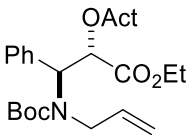
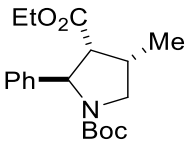
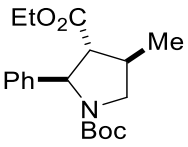
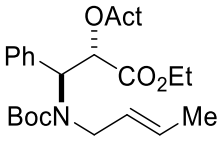
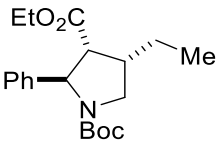
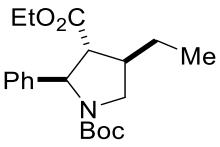
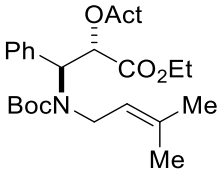
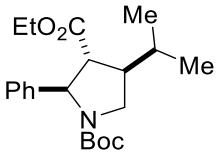
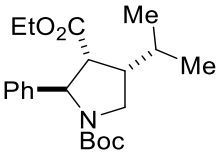
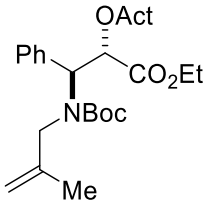
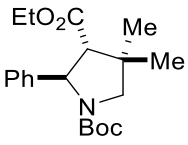
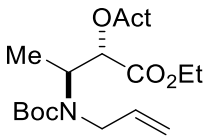
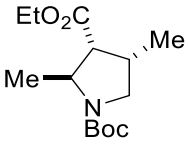
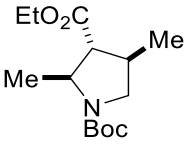
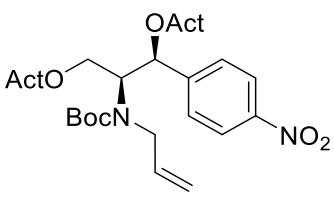
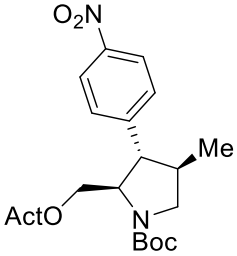
Scheme 12. Investigation of oxidative quenching cycle for substrates activated as 3,5-bis(trifluoromethyl)benzoates.
Reagents and conditions: a) reductive quenching cycle, substrate **47m** (1.0 equiv), *fac*-Ir(ppy)$_3$ (1.0 mol%), Et_3N (5.0 equiv), H_2O (100.0 equiv), MeCN, 80 °C, 2 h. Reaction was carried out during the master thesis[3]. b) Oxidative quenching cycle, substrate **45a**/**47a** or **47m** (1.0 equiv), *fac*-Ir(ppy)$_3$ (1.0 mol%), DMF (0.1 M), 80 °C, 455 nm LED irradiation under N_2 atmosphere in a microflow reactor setup 1.0 mL/h.

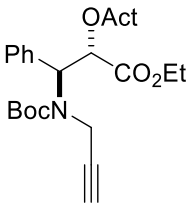
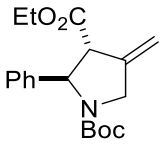
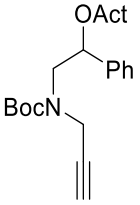
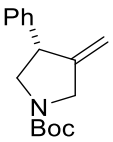
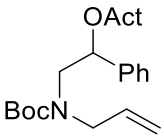
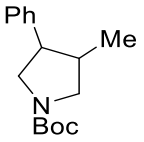
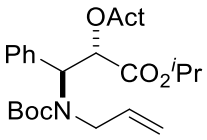
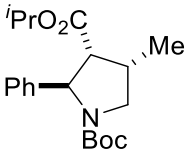
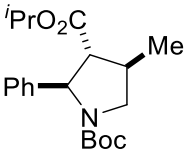
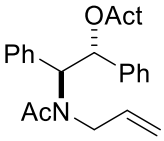
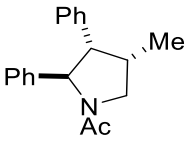
With these results in hand, the photoredox catalyzed cyclization reactions with ethyl oxalates **45** and 3,5-bis(trifluoromethyl)benzoates **47** were carried out using the oxidative quenching cycle of *fac*-Ir(ppy)$_3$ in the microflow reactor, resulting in a series of substituted pyrrolidines (Table 2). The reduction potentials of other commonly used photocatalysts were not sufficient for the successful transformation.[3] The yields and diastereomeric ratios are in general similar for both benzoates **47** or oxalates **45**, and in the cases where diastereomers are formed, they can be easily separated. Using substrates **45a** or **47a** showed the formation of two separable diastereomers **48a** and **48a'** in 61-62% yield (Table 2, entry 1).

Table 2. Photoredox catalyzed cyclization reaction towards substituted pyrrolidines.



45/47 **48** **34** **35**

Entry	Substrate	Major product	Minor product	Total yield and dr [a]
1				**47a**: 61% (61:39) **45a**: 62% (63:37)
	45a or **47a**	**48a** (38-39%)	**48a´** (23%)	
2				**47b**: 52% (79:21) **45b**: 47% (81:19) [b]
	45b or **47b**	**48b** (38-41%)	**48b´** (9-11%)	
3				**47c**: 53% (53:47) [b], [c] **45c**: 48% (52:48) [b], [c]
	45c or **47c**	**48c** (25-28%)	**48c´** (23-25%)	
4			/	**47d**: 45% (>99:01) **45d**: 38% (>99:01) [b]
	45d or **47d**	**48d** (38-45%)		
5				**47e**: 66% (53:47) [d] **45e**: 66% (53:47)
	45e or **47e**	**48e** (35%)	**48e´** (31%)	
6			not isolated	**47f**: 28% (68:32) [d] **45f**: 30% (73:27) [d]
	45f or **47f**	**48f** (18-21%)		

7	 **45g** or **47g**	 **48g** (45-47%)	/	**47g**: 45% (>99:01) **45g**: 47% (>99:01)
8	 **45h** or **47h**	 **48h** (38-39%)	/	**47h**: 40% (>99:01) **45h**: 41% (>99:01)
9	 **45i** or **47i**	 **48i** (33-37%)	not isolated	**47i**: 70% (62:38) [e] **45i**: 64% (60:40) [e]
10	 **45j** or **47j**	 **48j** (34%)	 **48j´** (25%)	**47j**: 59% (57:43) **45j**: 59% (57:43)
11	 **47m**	 **48m**	not isolated	**47m**: 50% (74:26) [e]

Reagents and conditions: 3,5-bis(trifluoromethyl) benzoate ester **47** or oxalate ester **45** (0.4 - 1.0 mmol), *fac*-Ir(ppy)$_3$ (1.0 mol%), and DMF (0.1 M) at 80 °C under 455 nm LED irradiation under N_2 atmosphere in a flow setup (flow rate 0.30-1.0 mL/h, 10-33 h); [a]isolated yield; [b]synthesized during master thesis[3]. [c]After hydrogenation, initial alkane/alkene ratio 23:77 for **47c**, 15:85 for **45c**. [d]Flowrate of 0.15 mL/h. [e]dr determined by ^{1}H NMR integration, unseparable diastereomers.

The introduction of an additional methyl group in γ-position of the allyl system had a significant effect on yield and diastereoselectivity (entries 2 and 3). The diastereomeric ratio of products **48b** and **48b´** rised up to 81:19, while the yield of benzoate **47b** dropped from 61% to 52% and of oxalate **45b**[3] from 62% to 47% (entry 2). The introduction of an additional methyl group in γ-position did not lead to any further reduction of reaction yield with loss of stereo control at the *iso*-propyl bearing stereocenter (entry 3). The photoredox catalyzed transformation gave rise to larger amounts of the alkenes, which were subsequently hydrogenated with H_2 and Pd/C to give rise to the desired products **48c** and **48c´** in 48-53% yield. Methyl substitution in β-position in **45d**[3] and **47d** gave pyrrolidine **48d** with moderate yield, but excellent diastereomeric induction (entry 4). Only slightly higher yield and low diastereoselectivity were obtained when the aryl group in 1-position was replaced by a methyl group (entry 5). Employing

substrates **45f**[3] or **47f**, synthesized from commercially available, enantiopure (1*S*,2*S*)-2-amino-1-(4-nitrophenyl)propane-1,3-diol (**42**), gave rise to low yields of 28-30% and slightly higher diastereoselectivity (entry 6). An additional purification step via column chromatography was necessary to isolate the major diastereomer **48f**. Moreover, 5-*exo*-*dig* cyclization reaction of substrates **45g** and **47g** gave rise to corresponding pyrrolidine **48g** in 45-47% yield and excellent diastereoselectivity (entry 7). The comparison of this result with entry 1 shows clearly that exchange of the allylic moiety for a propargyl group leads to a reduction in yield but to an increase in diastereoselectivity. The introduction of hydrogen for a phenyl group, which reduces the steric bulk of the substrate, showed comparable yield and control of stereochemistry (entry 8) whereas a higher yield was obtained with allylic moiety (entry 9). However, in this case low diastereoselectivity was observed with hardly separable diastereomers. The comparison of sterically more demanding isopropyl ester (entry 10) and ethyl ester (entry 1) showed similar yields and diastereomeric ratios. Moreover, as already shown in Scheme 7, employing substrate **47m** with an additional phenyl group instead of ester had only a moderate effect on diastereoselectivity and allowed to obtain **48m** in 50% yield (entry 11).

2.3. Mechanistic Studies

The spectroscopic analysis of the successful cyclization process was performed with the 2D-NMR experiment TOCSY (Figure 1). The colored spin systems (blue and green) are isolated in the starting material but combined after cyclization reaction (red: breaking bond in substrate, new formed bond in cyclization product). The evidence for the resulting cyclization is provided by correlation signals of each proton of the spin system to the other protons of the same spin system.[3] Moreover 2D-NMR experiment NOESY was used to determine the absolute configuration of synthesized pyrrolidines (for details see Experimental Part).

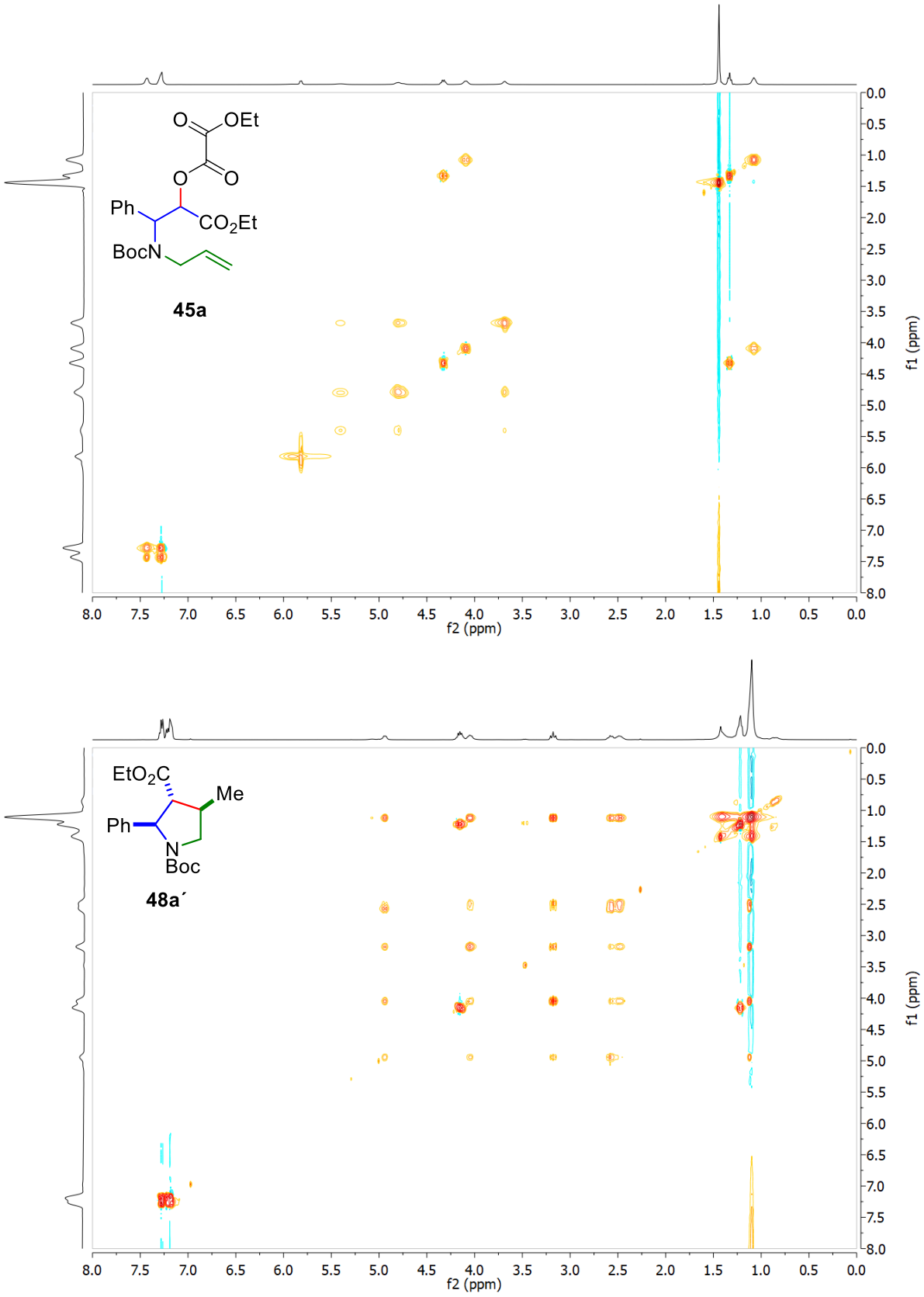
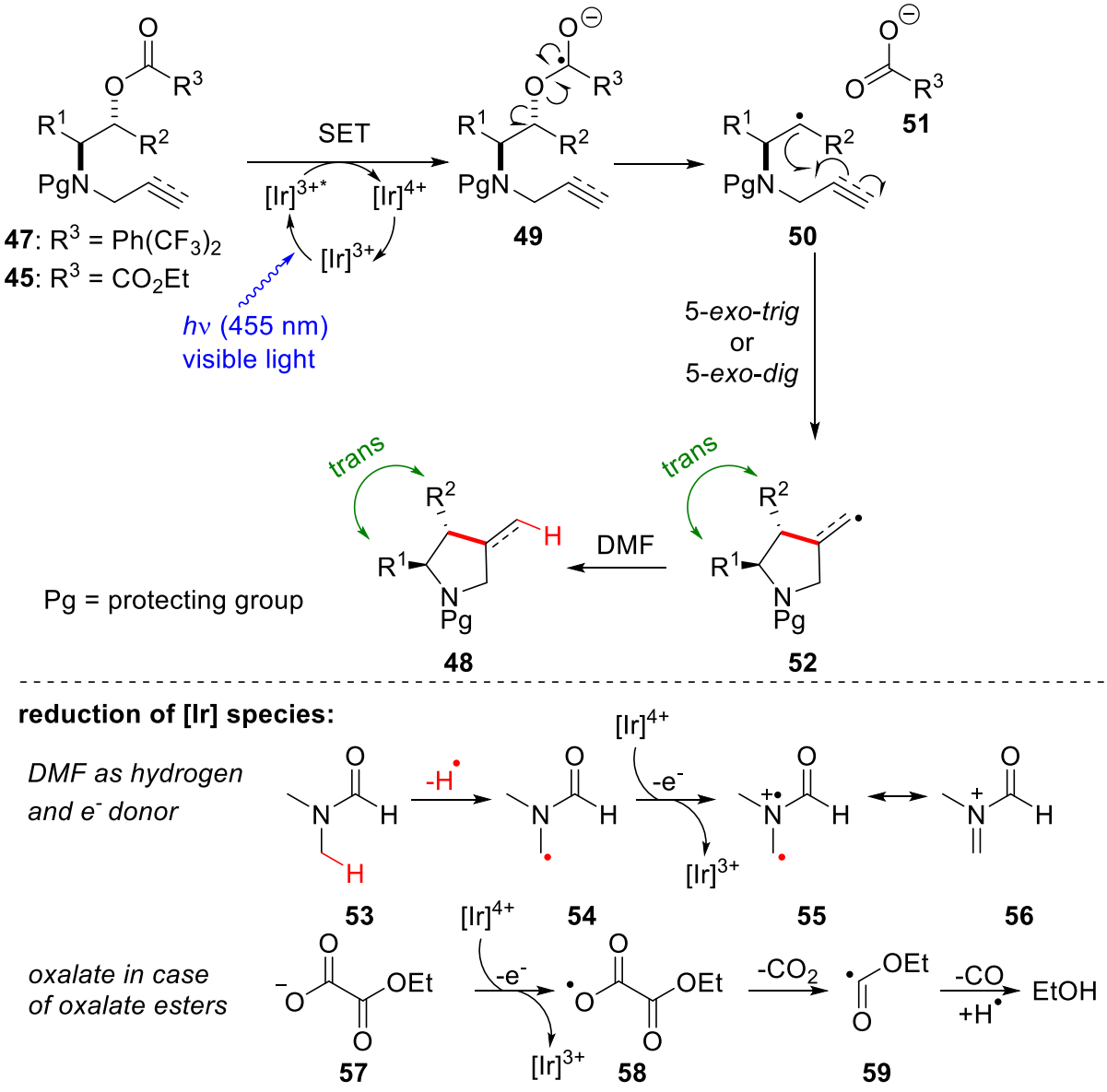


Figure 1. TOCSY analysis as evidence for successful ring closure.[3]

The proposed mechanism for both deoxygenation protocols starts with a single electron uptake from the photoexcited Ir^{3+*} species thus activating the strong C-O bond for homolytical

cleavage leading to a carbon-centered radical **50** (Scheme 13). This radical can undergo either 5-*exo-trig* or 5-*exo-dig* cyclization to give the desired pyrrolidine radical **52**, or it can be trapped by hydrogen atom abstraction, leading to undesired simple deoxygenation (not depicted) as occured when reductive quenching cycle was used (Scheme 12).[3] This undesired reduction process is facilitated when strong sacrificial electron donors such as Et_3N or $^{i}Pr_2NEt$ are present. In the final step, the thus formed primary radical **52** undergoes a hydrogen trapping from DMF to form the final pyrrolidine **48**. There are two plausible ways to regenerate the photocatalyst: on the one hand the electron uptake from the dehydrogenated DMF radical **54** takes place with the formation of DMF cation **55**, on the other hand in the case of ethyl oxalates the cleaved ester **57** can be oxidized to radical **58** and finally decompose to CO_2, CO and EtOH.[10, 16b-d]



Scheme 13. Proposed mechanism for a visible light mediated deoxygenated cyclization reaction.[10]

The hydrogen abstraction from the solvent was verified by V. Kais with a deuteration experiment using DMF-d_7 as solvent providing the monodeuteration of the product at the terminal methyl group.[8c]

For all obtained pyrrolidines, including various diastereomers (Table 2), the relative stereochemistry between C1 and C2 was *trans*. This result is very interesting due to the fact, that during the photoredox catalyzed C-O bond cleavage the intermediary radical is located on the C2 position thus destroying the stereocenter. In general, the formation of two new stereocenters can result in generation of four diastereomers. It is obvious, that the fixed stereocenter on the C1 carbon controls the stereochemistry on the adjacent C2 carbon and thus only allows the formation of two diastereomers. For a deeper understanding of this process, especially of the obtained major products and diastereomeric ratios, it is helpful to analyze the cyclization step. For this purpose, the results of cyclization reactions with different steric bulk groups at γ-position of allyl group were analyzed (Table 1, entries 1-3, oxalate results). The low diastereoselectivity does not allow to develop a universal explaination for the obtained results, but the present analysis serves as a basis for a plausible mechanistic approach. As shown in Figure 2, there are two plausible conformations of the carbon-centered radical that lead to the cyclization product. The concept is based on the discussion of analogous radical cyclizations to cyclopentanes.[17] The more stable chair conformation **60** leads to the formation of *cis*-product **48a**, **48b** or **48c´** if the 1,3-diaxial strain can be avoided where applicable. This is possible for substrates without a methyl group and with one methyl group at γ-position. Further increase of steric bulk at this position by introduction of an additional methyl group leads to a strong 1,3-diaxial strain, thus making the less stable boat conformation favorable giving rise to all-*trans* products **48a´**, **48b´** or **48c**.

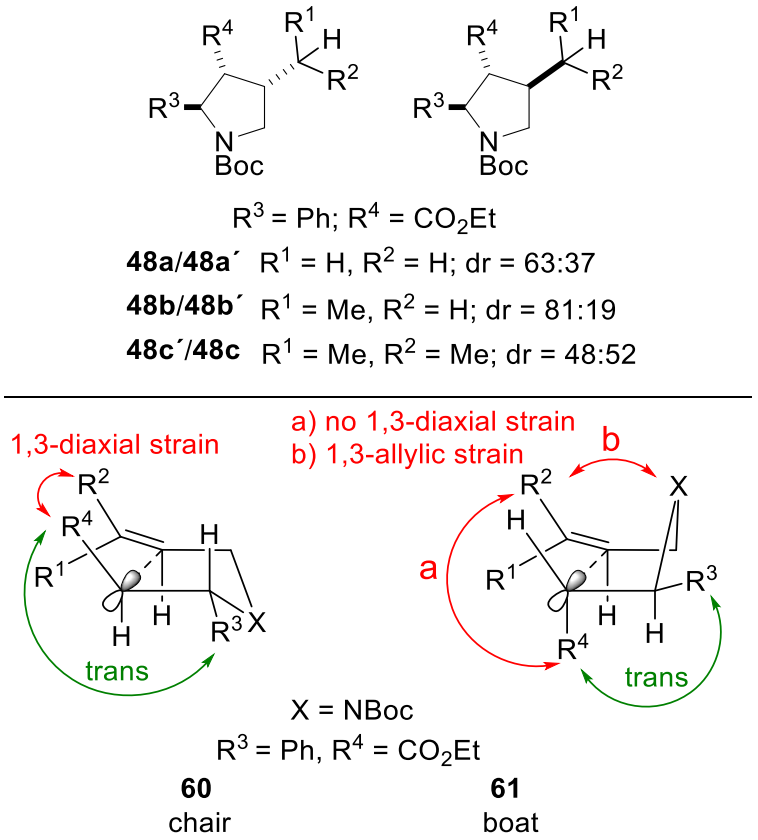
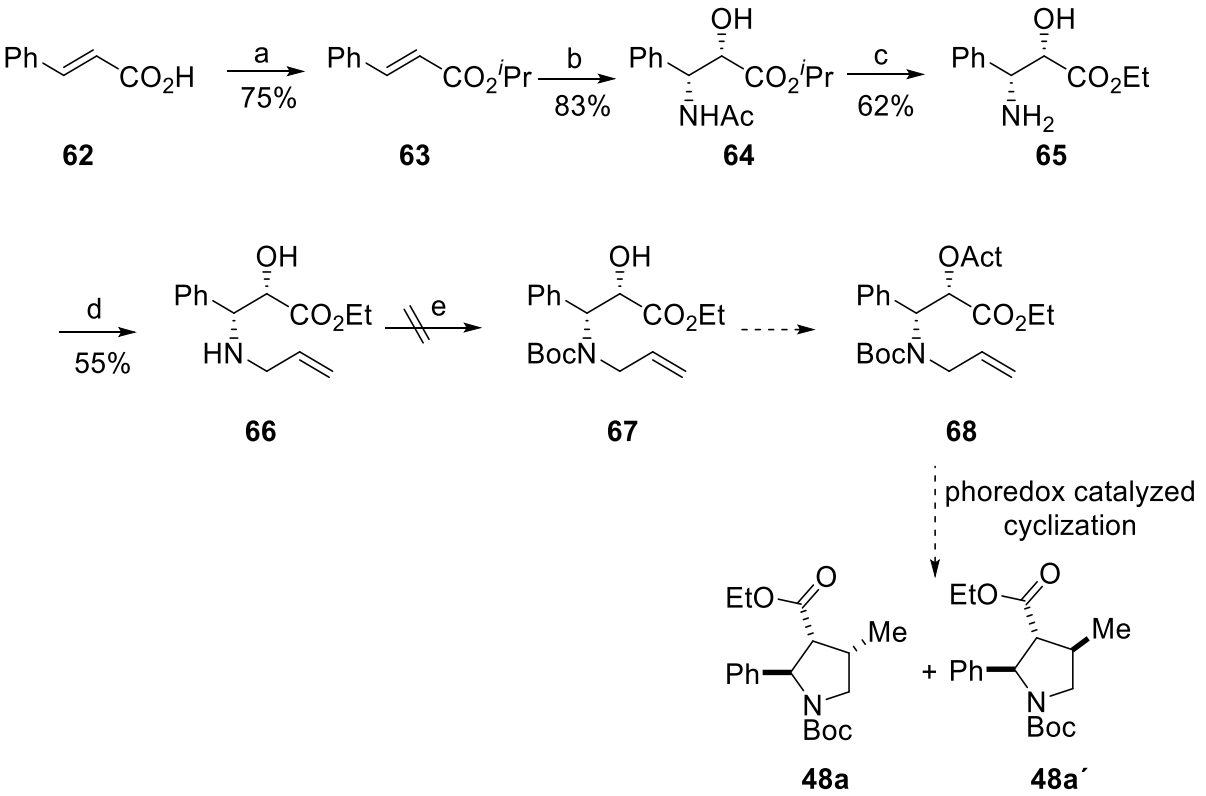


Figure 2. Analysis of cyclization step forming two diastereomers.[10]

2.4. Synthesis of Enantiopure Pyrrolidines

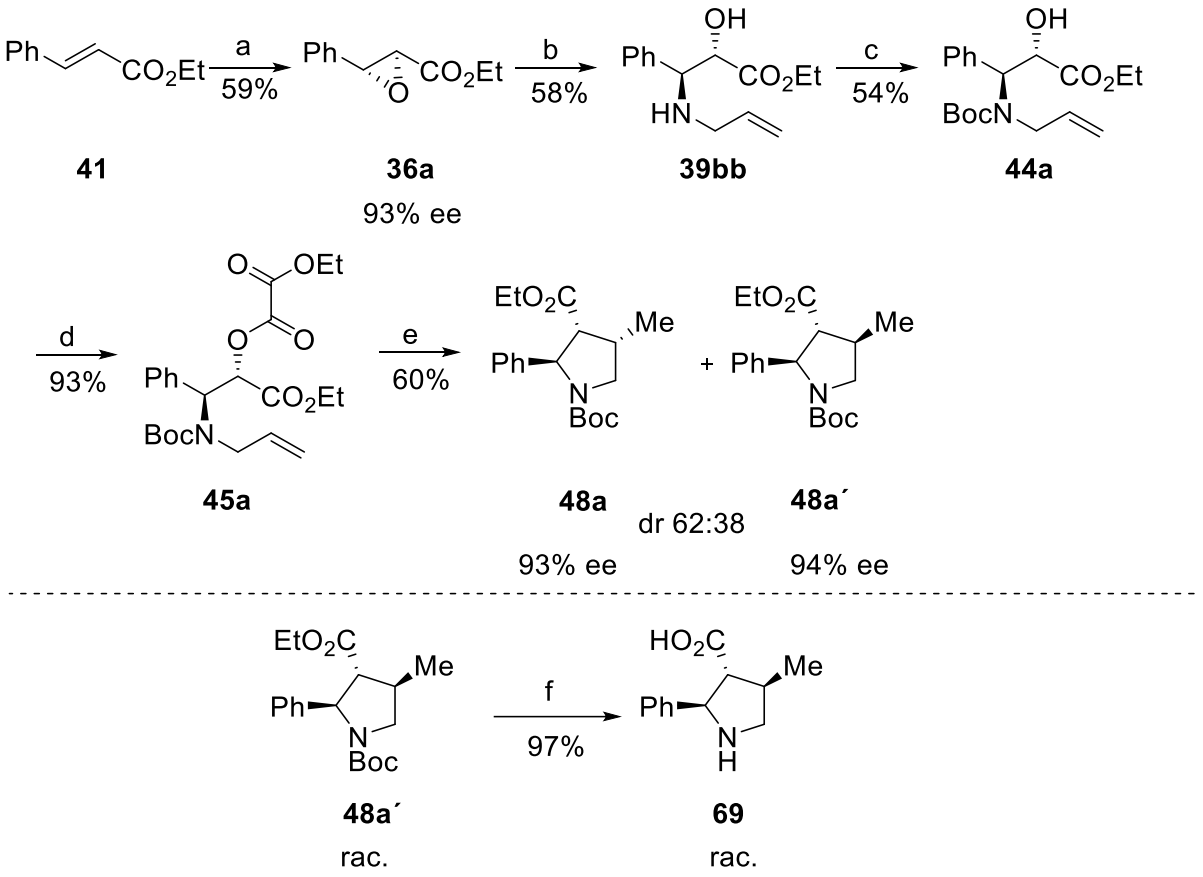
The method presented here leads to epimers with respect to the stereocenter that forms when cyclization into a prochiral allyl group takes place. The enantioselective synthesis of starting materials enables access to enantiopure pyrrolidines. For this purpose, Sharpless Aminohydroxylation[18] reaction of isopropyl cinnamate (**63**)[19] derived from cinnamic acid (**62**) by an acid catalyzed esterification reaction was carried out forming the desired *N*-acetylated *syn*-1,2-amino alcohol **64** in 83% yield (Scheme 14). Under acidic reaction conditions compound **64** was deprotected and transesterificated to give *syn*-1,2-amino alcohol **65** in 62% yield.[18] Submission of this compound to the standard allylation protocol (*vide supra*) delivered *syn*-1,2-allylamino alcohol **66** in 55% yield. Surprisingly, the Boc-protection step failed, thus disabling to continue the synthesis towards enantiopure pyrrolidines **48a** and **48a´**.



Scheme 14. Synthesis of enantiopure pyrrolidines via asymmetric Sharpless Aminohydroxylation reaction.

Reagents and conditions: (a)[19] isopropanol, HCl (cat.), reflux, 12 h, 75%; (b)[18] $(DHQD)_2PHAL$ (5.0 mol%), $K_2[OsO_2(OH)_4]$ (4.0 mol%), $CH_3CONHBr$ (1.1 equiv), LiOH (1.0 equiv), $^tBuOH/H_2O$ (1.5:1), 0 °C, 4 h, 83%; (c)[18] HCl (10%), H_2O, reflux, 24 h; H_2SO_4 (cat.), EtOH, cyclohexane, reflux, 24 h, 62%; (d) Allyl bromide (**38e**) (1.1. equiv), Et_3N (1.1 equiv), rt, 48 h, 55%; (e) Boc_2O (1.2 equiv), Et_3N (1.2 equiv), CH_2Cl_2, rt, 48 h, complex reaction mixture.

A plausible explaination for this result can be the intramolecular attack of the free hydroxy group on the newly formed carbamate, which leads to a complex reaction mixture. In contrast to the presented racemic synthesis with *anti*-configuration, Sharpless Aminohydroxylation only forms *syn*-amino alcohols. To solve this problem a new strategy with asymmetric Shi-Epoxidation was applied (Scheme 15).[20] In the first step epoxide **36a** was formed in 59% yield and 93% ee. After the ring-opening reaction with allylamine and Boc-protection step compound **44a** was obtained in a moderate yield. Finally, this compound was esterified to form ethyl oxalate **45a** in 93% yield. The standard photocyclization protocol derived the two separable diastereomers **48a** and **48a´** in 60% overall yield and diastereomeric ratio of 62:38. Chiral HPLC analysis of epoxide **36a** and pyrrolidines **48a** and **48a´** confirmed similar enantiomeric excesses of 93-94% (for details see Experimental Part). In this way enantiomerically and diastereomerically pure pyrrolidines with biologically relevant core structures, e.g. α- and β-prolines, can be easily prepared. To demonstrate the formation of deprotected β-prolines, racemic pyrrolidine **48a´** was treated with hydrochloric acid to give unprotected product **69** in excellent yield.

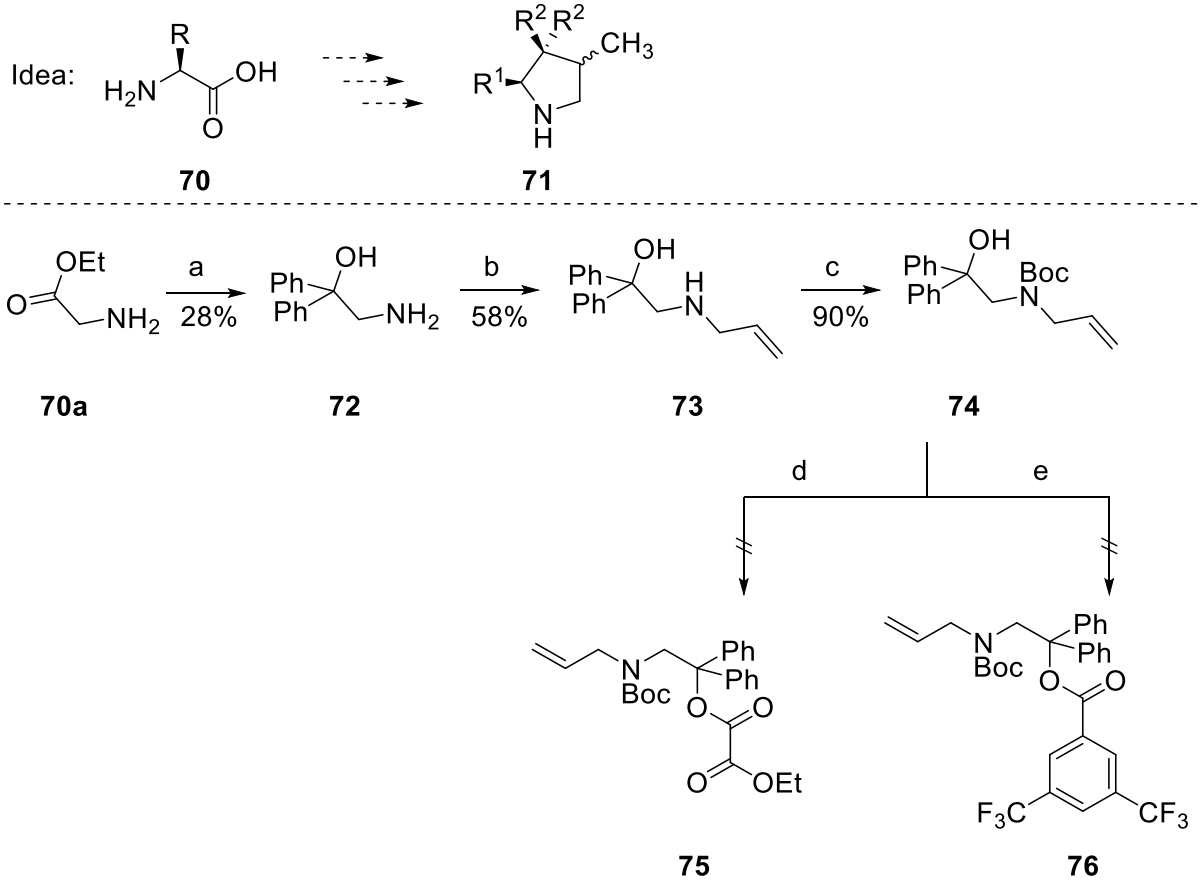


Scheme 15. Strategy towards enantiopure substituted β-proline derivatives including the photoredox catalyzed cyclization reaction as the key step.[10]
Reagents and conditions: (a)[20a] Shi-catalyst (0.3 equiv), $Na_2(EDTA)$ ($4x10^{-5}$M), Bu_4NHSO_4 (0.06 equiv), oxone (5.0 equiv), $NaHCO_3$ (15.5 equiv), CH_3CN/H_2O, 0 °C to rt, 24 h, 59%; (b)[14c] allylamine (1.0 equiv), EtOH, reflux , 24 h, 58%; (c) Boc_2O (1.2 equiv), Et_3N (1.2 equiv), CH_2Cl_2, rt, 24 h, 54%; (d) ethyl oxalyl chloride (1.5 equiv), pyridine (1.5 equiv), CH_2Cl_2, 0 °C to rt, 20 h, 93%; (e) *fac*-$Ir(ppy)_3$ (1.0 mol%), LED (455 nm), DMF, 80 °C, 1.0 mL/h, 60%; (f) HCl (6.0 M), rt, 24 h, 97%.

3. Amino Acids as Starting Materials for the Photomediated Pyrrolidine Synthesis

Amino acids are commercially available and accessible compounds that can be obtained as enantiopure starting materials in high quality and quantity. Based on the efficient transformation of corresponding ethyl oxalates and 3,5-bis(trifluoromethyl)benzoates to substituted pyrrolidines, the next idea was to synthesize starting materials derived from amino acids and thus enabling the enantioselective product formation (Scheme 16, top part). The study began with the ester of the achiral amino acid glycine **70a** due to the smallest possible complications resulting from steric bulk and functional group tolerance during the synthesis (Scheme 16, bottom part). First, following common literature procedure[21] the substrate **70a** reacted with phenyl Grignard reagent to form amino alcohol **72** in 28% yield. The amino moiety was then alkylated with allyl bromide to form compound **73** in 58% yield followed by Boc-protection to give alcohol **74** in 90% yield. The esterification step failed for both activating

groups resulting in a very low conversion of the starting material. Prolongation of the reaction time nor increase in temperature gave rise to the desired products. This result can be traced back to the steric bulk of the tertiary alcohol **74**, which disables the esterification to the corresponding ester.

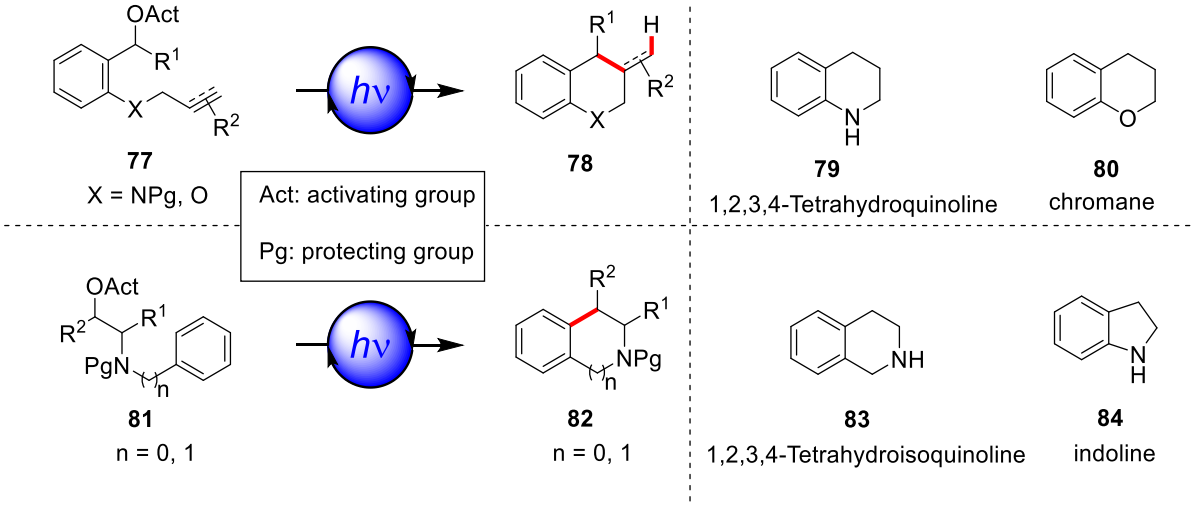


Scheme 16. Synthesis of starting material for photoredox mediated deoxygenation starting from amino acids.

Reagents and conditions: (a)[21] PhMgBr (6.0 equiv), THF, reflux, 24 h, 28%; (b) allyl bromide (1.5 equiv), DBU (1.5 equiv), toluene, 60 °C, 48 h, 58%; (c) Boc_2O (1.2 equiv), Et_3N (1.2 equiv), CH_2Cl_2, rt, 72 h, 90%; (d) ethyl oxalyl chloride (**15**) (3.6 equiv), pyridine (3.6 equiv), CH_2Cl_2, 4 °C to rt, 48 h; (e) $((CF_3)_2Bz)_2O$ (**46**) (1.2 equiv), DIPEA (2.0 equiv), CH_2Cl_2, rt, 72 h.

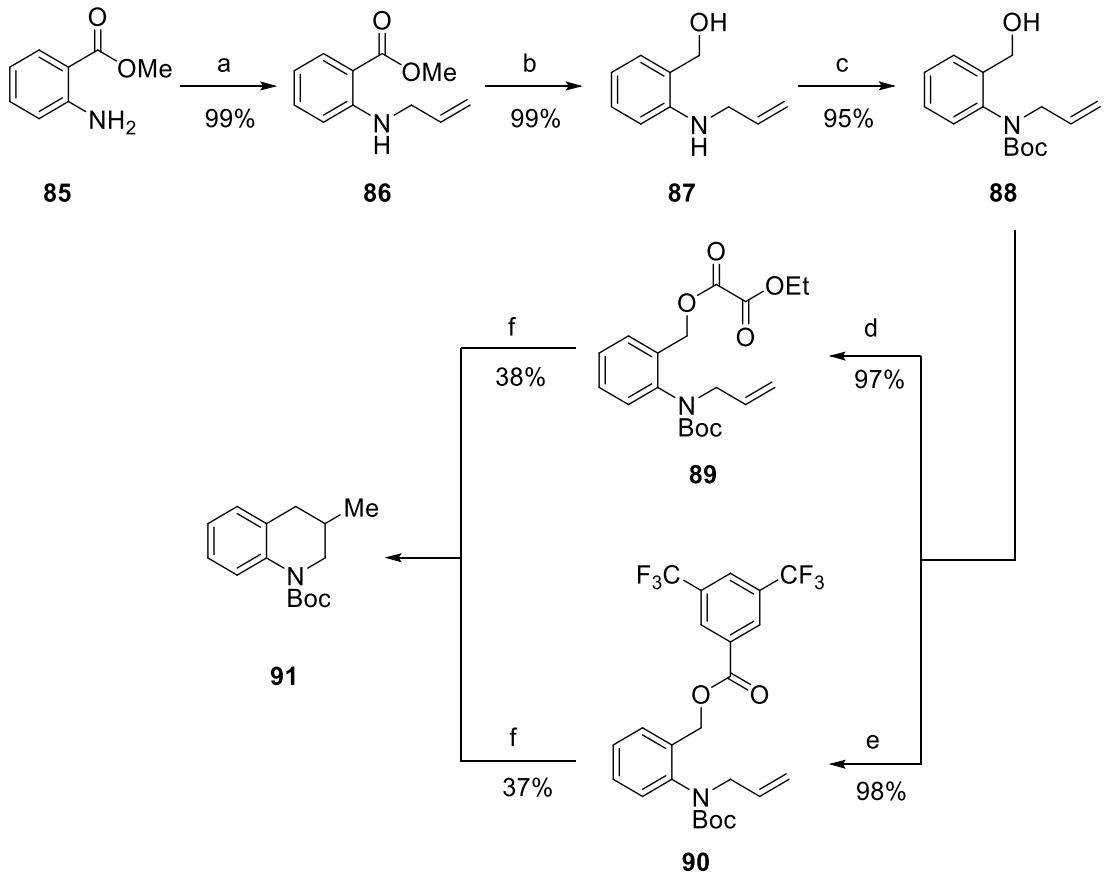
4. Photomediated Synthesis of Bicyclic Compounds

As a consequence of the successful photoredox catalyzed synthesis of substituted pyrrolidines, a number of different bicyclic compounds such as tetrahydroquinolines[22], tetrahydroisoquinolines[22], chromanes and indolines were selected to be synthesized with the here developed cyclization protocol (Scheme 17). The tetrahydroquinoline[23] key structure **79**, tetrahydroisoquinoline[24] skeleton **83**, chromane[25] and indoline cores **80** and **84** can be found in various drugs and natural products, e.g. viratmycin[26], tubocurarine[27], nomifensine[28], diclofensine[29], tocopherol[30] or silodosin[31].



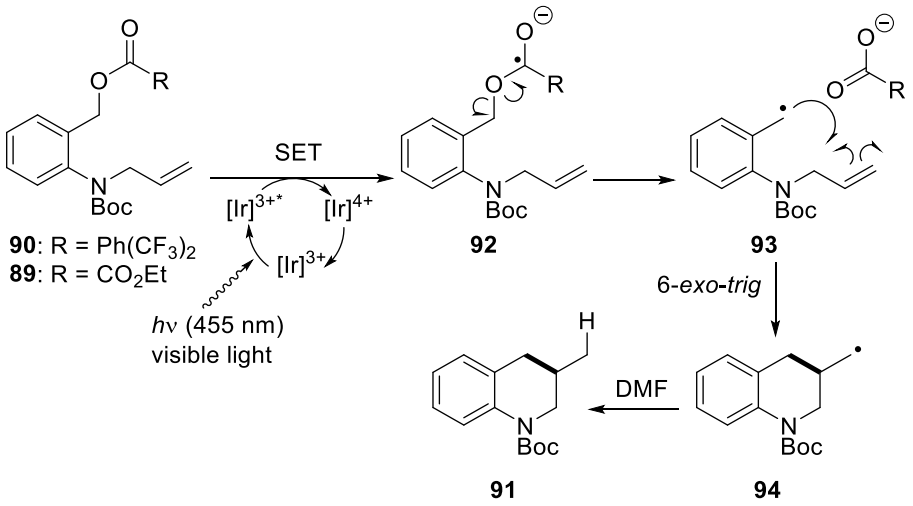
Scheme 17. Planned bicyclic compounds.

Starting from commercially available ethyl anthranilate (**85**) the allylation product **86** was synthesized according to the procedure described in literature (Scheme 18).[32] After reduction with $LiAlH_4$ and Boc-protection step[33], benzylic alcohol **88** was obtained in excellent yield. Both ethyl oxalate and 3,5-bis(trifluoromethyl)benzoate were used as activating groups to form compounds **89** and **90** as starting materials for the desired photoredox catalyzed cyclization reaction. The photoreaction was carried out in a microreactor setup under irradiation with blue light and heating at 80 °C using the oxidative quenching cycle of photocatalyst. Apart from the starting material **89** or **90**, solvent DMF and *fac*-$Ir(ppy)_3$ as photocatalyst no other additives were required. For both activating groups moderate yields of 37-38% were obtained for the 6-*exo-trig* product **91**. The relatively low yield can be caused by an unfavorable geometry of the generated radical during the cyclization process.



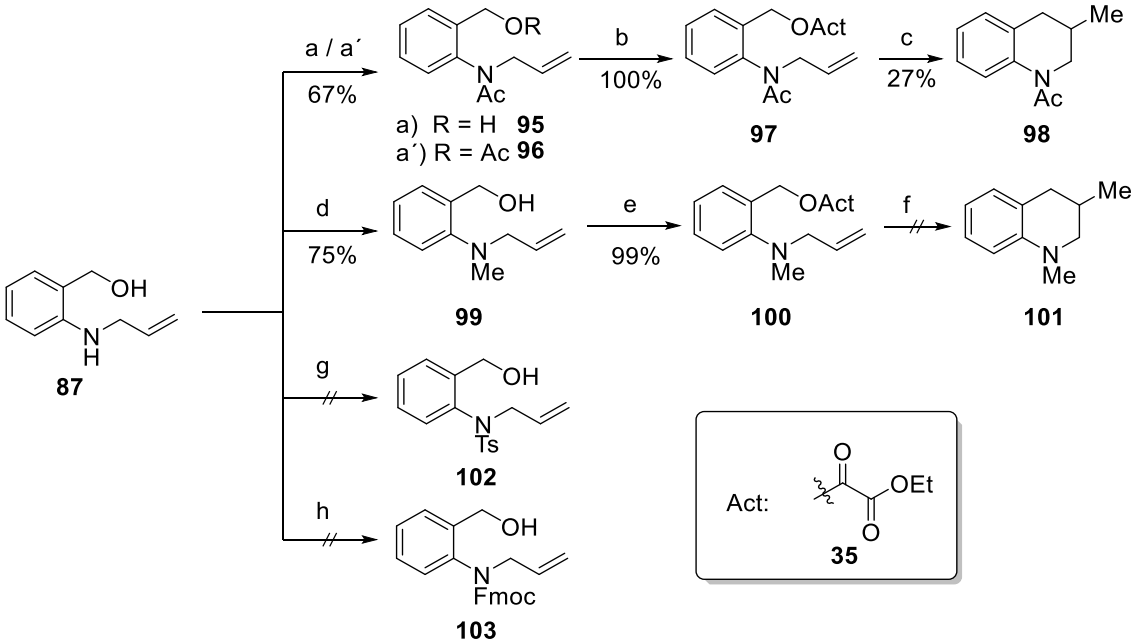
Scheme 18. Synthetic pathway towards monosubstituted 1,2,3,4-tetrahydroquinoline **91**.
Reagents and conditions: (a)[32] allyl bromide (0.5 equiv), DMF, 0 °C to 40 °C, 20 h, 99%; (b) $LiAlH_4$ (4.0 equiv), THF, 0 °C to rt, 2 h, 99%; (c)[33] Boc_2O (1.5 equiv), EtOH, 50 °C, 16 h, 95%; (d) ethyl oxalyl chloride (**15**) (2.0 equiv), pyridine (2.0 equiv), CH_2Cl_2, 0 °C to rt, 20 h, 97%; (e) 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (1.2 equiv), *N*,*N*-diisopropylethylamine (2.0 equiv), CH_2Cl_2, rt, 4 h, 98%; (f) *fac*-Ir(ppy)$_3$ (1.0 mol%), 455 nm, DMF, 80 °C, 0.15-0.30 mL/h, 37-38%.

The proposed mechanism for this reaction is based on the previously described mechanism for the pyrrolidine formation (*vide supra*, Scheme 13). After single electron transfer from photoexcited Ir^{3+*} species and subsequent dissociation of corresponding ester the benzylic radical **93** is formed which can undergo the more favorable 6-*exo*-*trig* cyclization reaction to form primary *N*-heterocyclic radical **94**. Finally, after trapping with DMF as hydrogen source the desired 1,2,3,4-tetrahydroquinoline **91** can be formed. The regeneration of the catalyst is described in Scheme 13.



Scheme 19. Proposed mechanism for a visible light mediated deoxygenative cyclization reaction towards corresponding tetrahydroquinoline **91**.

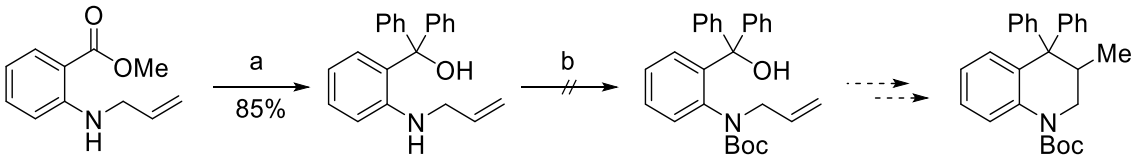
The investigations of the steric effect on the cyclization process included the variation of the protecting group and the increase of the steric bulk of the benzylic alcohol. For this purpose, benzylic alcohol **87** was subjected to several *N*-protection reactions (Scheme 20). Acetylation of substrate **87** by acetyl chloride delivered compound **95** in 67% yield followed by a quantitative synthesis of the corresponding ethyl oxalate **97**. In contrast the reaction of substrate **87** with acetic anhydride yielded in double acetylation product **96**.



Scheme 20. Variation of protecting groups in substrates for tetrahydroquinoline synthesis.
Reagents and conditions: (a) AcCl (1.0 equiv), $NaHCO_3$ (1.2 equiv), CH_2Cl_2, 0 °C to rt, 16 h, 67%; (a´) Ac_2O (1.5 equiv), Et_2O, 0 °C to rt, 18 h, 66%; (b) ethyl oxalyl chloride (2.0 equiv), pyridine (2.0 equiv), CH_2Cl_2 , 0 °C to rt, 20 h, 100%; (c) *fac*-Ir(ppy)$_3$ (1.0 mol%), 455 nm, DMF, 80 °C, 0.30 mL/h, 27%; (d) CH_3I (1.1 equiv), K_2CO_3 (1.5 equiv), DMF, rt, 20 h, 75%; (e) ethyl oxalyl chloride (2.0 equiv), pyridine (2.0 equiv), CH_2Cl_2 , 0 °C to rt, 20 h, 99%; (f) *fac*-Ir(ppy)$_3$ (1.0 mol%), 455 nm, DMF, 80 °C, 0.30 mL/h, complex reaction mixture; (g) TsCl (1.0 equiv), Et_3N (1.0 equiv), CH_2Cl_2, rt, 48 h, no reaction; (h) FmocCl (1.0 equiv), Et_3N (1.0 equiv), CH_2Cl_2, rt, 48 h, complex reaction mixture.

Submission of this substrate **97**, containing a less sterically demanding protecting group, to photoredox catalyzed deoxygenation reaction provided *N*-heterocycle **98** in 27% yield. The methylation of nitrogen provided the alkylated alcohol **99** in 75% yield and after esterification step the desired ethyl oxalate **100** in quantitative yield. The subsequent photoreaction led to the formation of complex reaction mixture. In this case, the absence of electron withdrawing group on the nitrogen acting as a sacrificial electron donor may be the reason for the unsuccessful reaction. Interestingly, the two small protecting groups acetyl and methyl could not improve the formation of the desired tetrahydroquinoline. Furthermore, the reaction of allyl amino alcohol **87** with TsCl showed no reaction and the use of the Fmoc protecting group resulted in the formation of a complex reaction mixture.

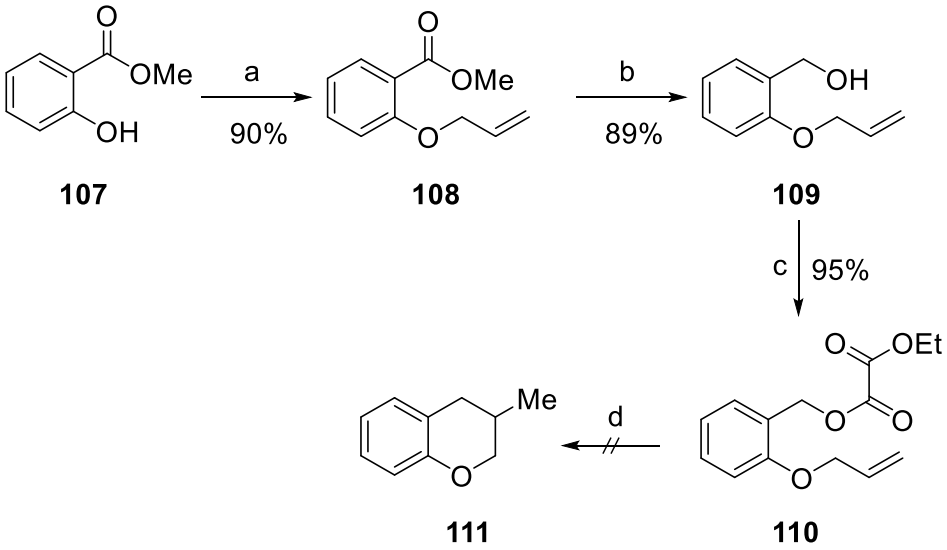
The variation of the benzylic alcohol position was carried out by reaction of methyl benzoate **86** and phenyl Grignard reagent to form alcohol **104** in 85% yield (Scheme 21). This transformation should facilitate the formation of the highly stable benzylic radical in the photoreaction. However, the subsequent Boc-protection step failed, even if the reaction conditions were varied, showing very low conversion of the starting material. For this reason, it was not possible to perform the desired reaction to product **106**.



86 **104** **105** **106**

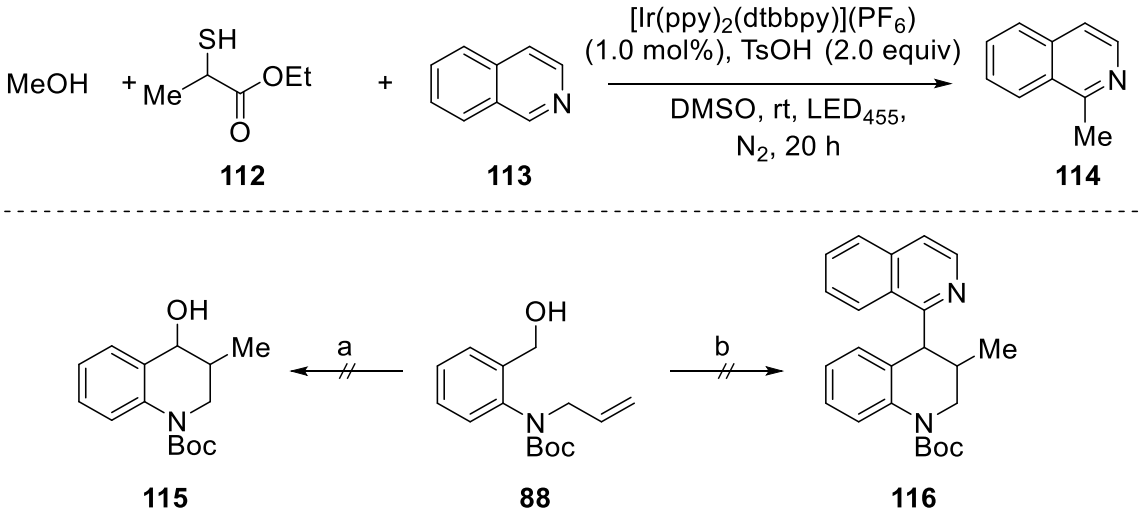
Scheme 21. Variation of steric bulk at benzylic alcohol position.
Reagents and conditions: (a) PhMgBr (3.2 equiv), THF, 0 °C to rt, 2 h, 85%; (b) Boc_2O (1.2 equiv), Et_3N (1.2-2.4 equiv), EtOH, 40-60 °C, 24-72 h, no reaction.

Next, the starting material for the formation of chromane **111** was synthesized (Scheme 22). The synthetic route began with the allylation reaction of commercially available methyl salicylate (**107**) to form compound **108** in 90% yield.[34] The subsequent reduction to the corresponding benzyl alcohol **109** and esterification with ethyl oxalyl chloride (**15**) gave the desired starting material **110** in high yield. However, the photomediated transformation to substituted chromane **111** failed resulting in the formation of a complex reaction mixture. Due to the unsuccessful transformation of the simplest *O*-substrate **110** no further variations of this substrate type were carried out.



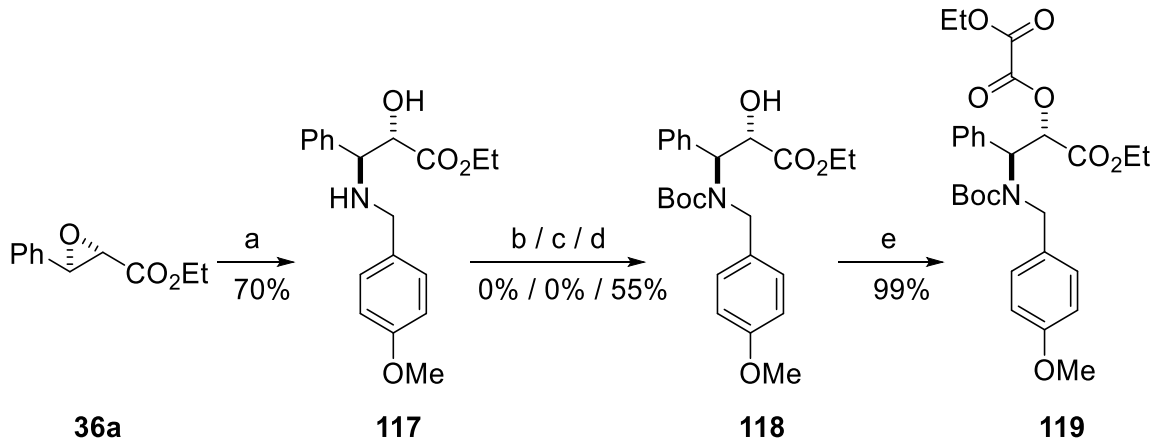
Scheme 22. Synthesis of 3,4-dihydrochromene **111**.
Reagents and conditions: (a)[34] allyl bromide (1.3 equiv), K_2CO_3 (2.0 equiv), DMF, rt, 24 h, 90%; (b) $LiAlH_4$ (4.0 equiv), THF, 0 °C to rt, 2 h, 89%; (c) ethyl oxalyl chloride (2.0 equiv), pyridine (2.0 equiv), CH_2Cl_2, 0 °C to rt, 20 h, 95%; (d) *fac*-$Ir(ppy)_3$ (1.0 mol%), 455 nm, DMF, 80 °C, 0.30 mL/h, complex reaction mixture.

In 2015 the MacMillan group[35] presented a protocol for photoredox mediated methylation of several *N*-heterocycles e.g. quinolines and pyridines with methanol as alkylating agent (Scheme 23, top part). In this procedure $[Ir(ppy)_2(dtbbpy)](PF_6)$ was used as photocatalyst, ethyl 2-mercaptopropanoate (**106**) and TsOH as additives, and the reaction was carried out in DMSO at room temperature. Methanol as alkylation agent was added in hundredfold excess. The proposed reaction mechanism describes the formation of α-oxy methyl radical that adds to the protonated electrondeficient heteroarene in a Minisci-type pathway to afford the aminyl radical cation. After deprotonation of acidic α-C-H bond with subsequent water dissociation, the desired alkylated product is formed.[35] The previously synthesized benzyl alcohol **88** was subjected to the reaction conditions employed by MacMillan due to the idea that formation of α-oxy radical should be easier facilitated compared to methanol in benzylic position. The formation of this radical can then lead to a cyclization reaction forming product **115** (Scheme 23, Reaction a) and cyclization reaction by addition to the additive quinoline (**116**) (Scheme 23, Reaction b). However, both photocatalytic transformations resulted in complex reaction mixtures with no sign of the proposed products **115** and **116**. A conceivable reason can be, that in contrast to methanol benzyl alcohol **88** was not used in a large excess, which is necessary to form the high concentration of the α-oxo radical to perform the alkylation process.



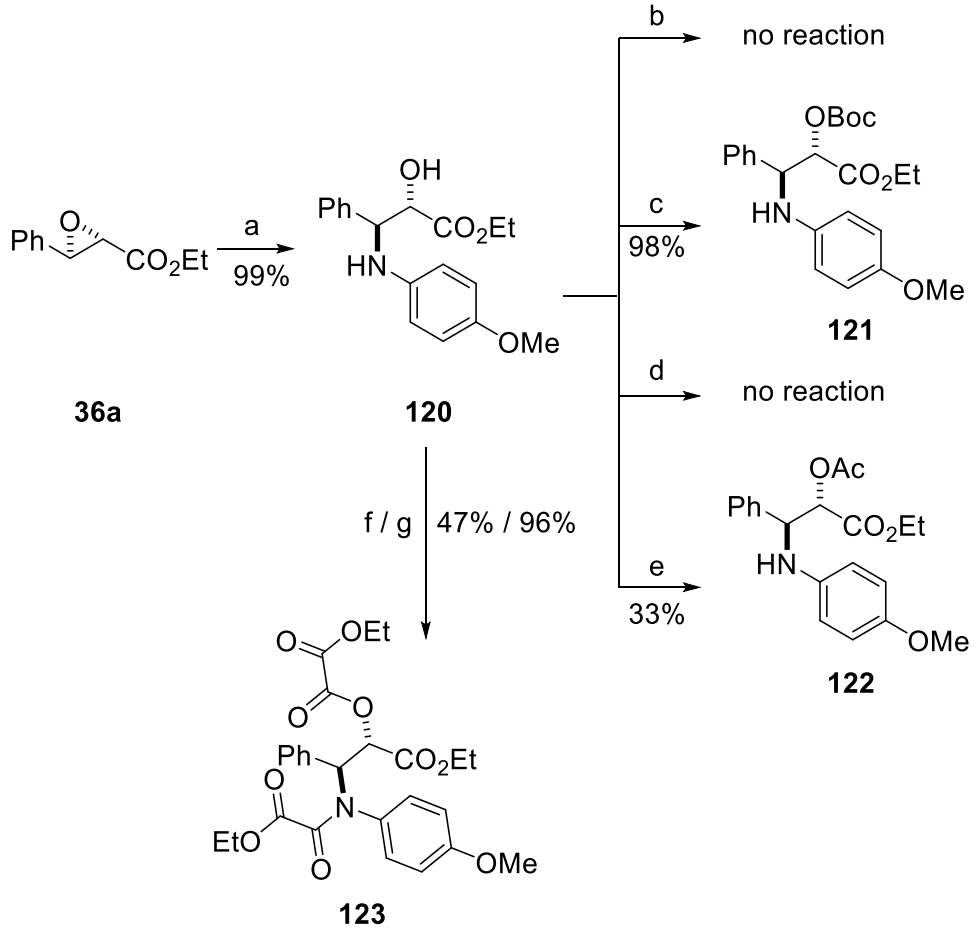
Scheme 23. Application of protocol by MacMillan[35] for deoxygenation of benzylic alcohol **88**.
Reagents and conditions: (a) benzyl alcohol **88** (1.0 equiv), $Ir(ppy)_2(dtbbpy)(PF_6)$ (1.0 mol%), TsOH (2.0 equiv), ethyl 2-mercaptopropanoate (**112**) (5.0 mol%), DMSO, rt, 20 h, complex reaction mixture; (b) benzyl alcohol **88** (1.0 equiv), $Ir(ppy)_2(dtbbpy)(PF_6)$ (1.0 mol%), TsOH (2.0 equiv), isoquinoline (**113**) (1.0 equiv), ethyl 2-mercaptopropanoate (**112**) (5.0 mol%), DMSO, rt, 20 h, complex reaction mixture.

Based on the insignificant success in the synthesis of the bicyclic compounds a new strategy towards *N*-containing polycycles was developed. Starting from the previously introduced epoxide **36a** (*vide supra*) the amino alcohol **117** was obtained in 70% yield using 4-methoxybenzylamine as nucleophile for the epoxide ring-opening reaction as depicted in Scheme 24.



Scheme 24. Synthesis of starting material for photoredox catalyzed formation of 1,2,3,4-tetrahydroisoquinoline.
Reagents and conditions: (a) *p*-methoxybenzylamine (1.0 equiv), EtOH, reflux, 24 h, 70%. (b) Boc_2O (1.2 equiv), Et_3N (1.2 equiv), CH_2Cl_2, rt, 72 h, no reaction; (c) Boc_2O (1.2 equiv), Et_3N (1.2 equiv), DMAP (10 mol%), CH_2Cl_2, rt, 72 h, complex reaction mixture; (d) Boc_2O (1.2 equiv), EtOH, 60 °C, 48 h, 55%; (e) ethyl oxalyl chloride (1.5 equiv), pyridine (1.5 equiv), CH_2Cl_2 , 0 °C → rt, 20 h, 99%.

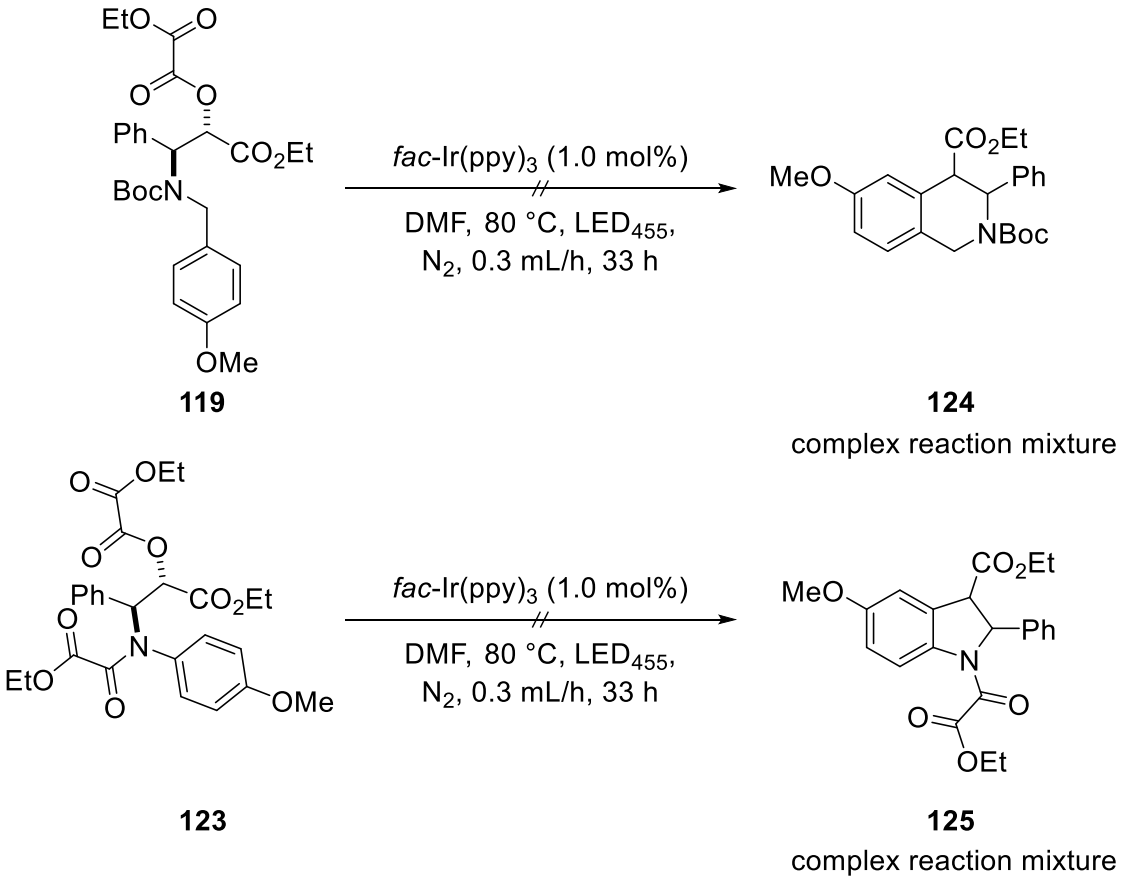
The protection of the amine moiety proved to be a demanding synthetic step: First the reaction was carried out using established conditions described in the synthesis of pyrrolidines (Scheme 9). These conditions led to a complete reisolation of the starting material. The addition of DMAP for a strong activation of the Boc-group resulted in the formation of a complex reaction mixture. Finally, the desired Boc-protected product **118** was obtained in 55% yield using Boc_2O in ethanol at 60 °C. The subsequent reaction of compound **118** with ethyl oxalyl chloride (**15**) resulted in the formation of substrate **119** in 99% yield. Analogously, starting from the epoxide **36a** the reaction with 4-methoxyaniline provided the amino alcohol **120** in quantitative yield (Scheme 25). Again, the protection step turned out to be a challenge.



Scheme 25. Synthesis of starting material for photoredox catalyzed formation of indoline.
Reagents and conditions: (a) *p*-methoxyaniline (1.0 equiv), EtOH, reflux, 24 h, 79%; (b) Boc_2O (1.2 equiv), Et_3N (1.2 equiv), CH_2Cl_2, rt, 72 h, no reaction; (c) Boc_2O (1.2 equiv), Et_3N (1.2 equiv), DMAP (2 mol%), CH_2Cl_2, rt, 72 h, 98%; (d) Boc_2O (1.2 equiv), EtOH, 60 °C, 48 h, no reaction; (e) AcCl (2.0 equiv), Et_3N (2.0 equiv), CH_2Cl_2, 0 °C to rt, 24 h, 33%; (f) ethyl oxalyl chloride (1.2 equiv), pyridine (1.2 equiv), CH_2Cl_2, 4 °C to rt, 20 h, 47%; (g) ethyl oxalyl chloride (2.4 equiv), pyridine (2.4 equiv), CH_2Cl_2, 4 °C to rt, 20 h, 96%.

No conversion of the starting material was observed when carrying out the reaction under the established conditions described in the synthesis of pyrrolidines (Scheme 9). In contrast, the addition of DMAP resulted in the formation of the Boc-protected product **121** in 98% yield. Analysis of the product by 2D-NMR spectroscopy envisioned that the Boc-group was located

at oxygen and not at nitrogen. The reaction of the substrate **120** with Boc_2O in ethanol at 60 °C showed no significant conversion. Changing the sterically demanding Boc-group to the smaller acetyl protecting group gave rise to *O*-Ac product **122** in 33% yield. Based on these results the protection step was skipped and a direct activation of the amino alcohol **120** was performed. Interestingly, when 1.2 equivalents of ethyl oxalalyl chloride (**15**) were used no full conversion and 47% of the product **123** with ethyl oxalyl groups at oxygen and nitrogen were obtained. Increasing the amount of ethyl oxalyl chloride (**15**) to 2.4 equivalents resulted in full conversion and 96% yield of the compound **123**. The application of the photomediated deoxygenation protocol to the synthesized substrates **119** and **123** in both cases provided the formation of complex reaction mixtures (Scheme 26). Due to the challenging synthetic transformations and low chance of success for the variation of the substrates the synthesis towards substituted bicycles was stopped at this point.

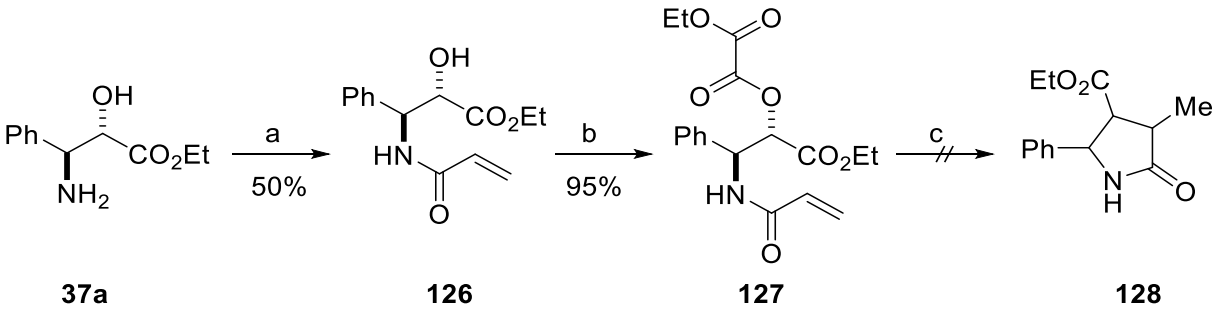


Scheme 26. Attempts towards tetrahydroisoquinoline **124** and indoline **125**.

5. Synthesis of Substituted Lactames

The 5-membered lactames such as 2-pyrrolidones[36] are important key structures in a variety of pharmaceutical drugs e.g. Cotinine[37], Doxapram[38] and Piracetam[39]. As demonstrated for the substituted pyrrolidines, the protoredox catalyzed cyclization reaction opens the door to new derivatives of substituted heterocycles which are not accessible by convential synthetic

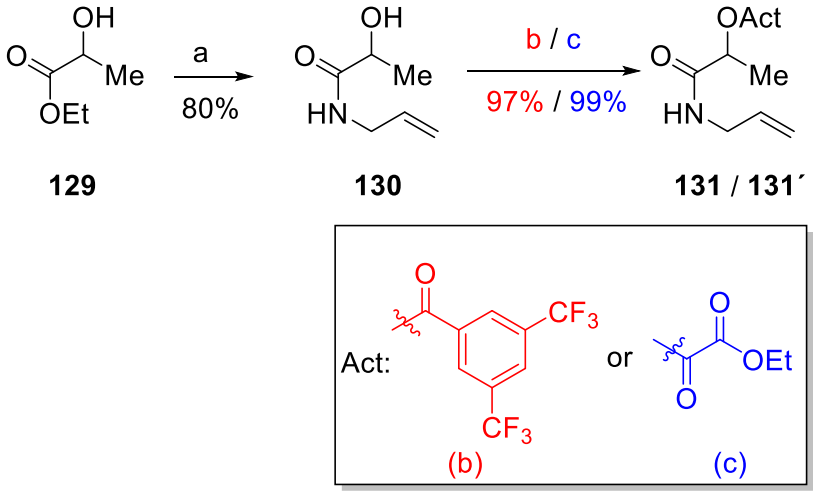
strategies. The starting material **126** for the initial reaction was synthesized from literature known amino alcohol **37a**[14a, 15]. Subsequent esterification with ethyl oxalyl chloride (**15**) resulted in the formation of substrate **127** in high yield. However, the photomediated deoxygenation reaction failed, leading to a complex reaction mixture (Scheme 27).



37a **126** **127** **128**

Scheme 27. Synthetic pathway towards substituted lactames via photoredox mediated deoxygenation. *Reagents and conditions*: (a) acroylchloride (1.1 equiv), CH_2Cl_2, 0 °C to rt, 72 h, 50%; (b) ethyl oxalyl chloride (1.1 equiv), pyridine (1.1 equiv), CH_2Cl_2, 4 °C to rt, 20 h, 95%; (c) *fac*-Ir(ppy)$_3$ (1.0 mol%), DMF, 455 nm, 80 °C, 0.3 mL/h, complex reaction mixture.

Another strategy for the synthesis of starting material for the cyclization reaction is shown in Scheme 28. The amidation reaction of ethyl lactate (**129**) with allylamine (**40a**) gave rise to allyl amido alcohol **130** in 80% yield.[40] Afterwards, ester formation provided 3,5-bis(trifluoromethyl)benzoate **131** and ethyl oxalate **131´** in excellent yields.



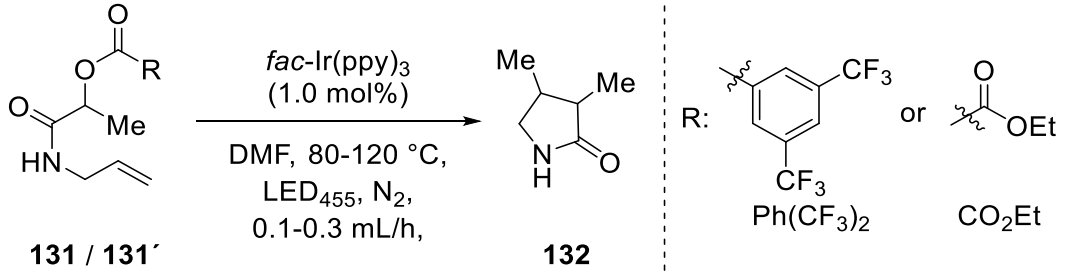
129 **130** **131 / 131´**

Scheme 28. Synthetic pathway towards substituted lactames via photoredox mediated deoxygenation. *Reagents and conditions*: (a)[40] allylamine (**40a**) (1.3 equiv), reflux, 72 h, 80%; (b) $((CF_3)_2Bz)_2O$ (**46**) (1.2 equiv), DIPEA (2.0 equiv), CH_2Cl_2, rt, 72 h, 97 %; (c) ethyl oxalyl chloride (1.2 equiv), pyridine (1.2 equiv), CH_2Cl_2, 4 °C to rt, 20 h, 99%.

Both starting materials were then subjected to the photoredox catalyzed process (Table 3). The standard reaction conditions for the photoinduced cyclization reaction did not lead to the successful reaction resulting in low conversion and only formation of complex reaction mixtures (Table 3, entries 1 and 4). The low conversion of the here employed substrate **131´** is surprising due to the similar redox potential (E_{Red} = -1.81 V vs SCE in DMF) compared to the starting

material **45a** (E_{Red} = -1.76 V vs SCE in DMF) being successfully transformed into the corresponding pyrrolidines **48a** and **48a´** (Table 2, entry 1). Lowering the flow rate of the microflow setup from 0.3 mL/h to 0.1 mL/h resulted in no significant change of the conversion and showed no product formation (Table 3, entries 2 and 5). In order to ensure the rotational freedom for all bonds of the substrates the reaction temperature was increased from 80 °C to 120 °C (Table 3, entries 3 and 6). Again, no significant change of conversion was achieved, and the desired cyclization product was not detected. In all reactions, only starting materials and complex reaction mixtures were obtained.

Table 3. Variation of reaction parameters for lactame synthesis.

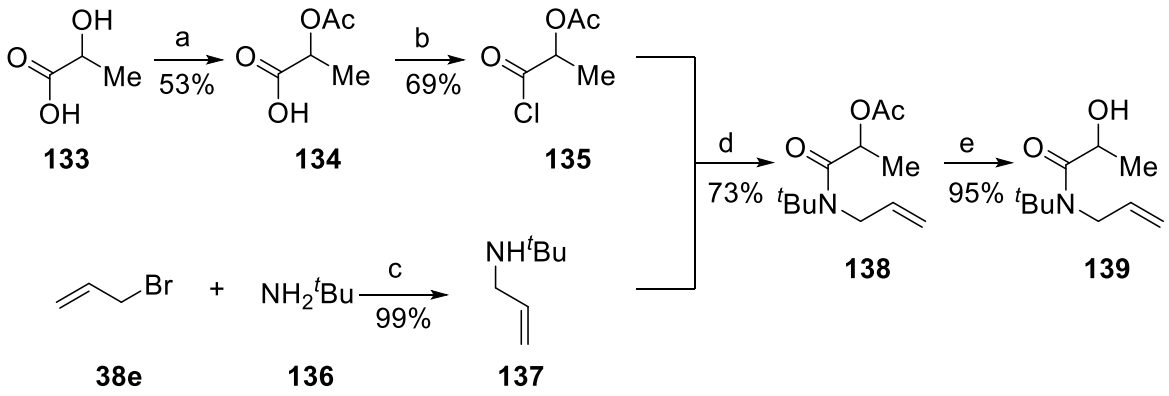


Entry	R	T [°C]	Flow Rate [mL/h]	Conversion [%]	Yield [%]	Result
1	CO_2Et	80	0.3	31	0	substrate and complex reaction mixture
2	CO_2Et	80	0.1	42	0	substrate and complex reaction mixture
3	CO_2Et	120	0.3	45	0	substrate and complex reaction mixture
4	$Ph(CF_3)_2$	80	0.3	26	0	substrate and complex reaction mixture
5	$Ph(CF_3)_2$	80	0.1	34	0	substrate and complex reaction mixture
6	$Ph(CF_3)_2$	120	0.3	40	0	substrate and complex reaction mixture

Reagents and conditions: 3,5-bis(trifluoromethyl) benzoate ester **131** or oxalate ester **131´** (0.2-0.5 mmol), *fac*-Ir(ppy)$_3$ (1.0 mol%), and DMF (0.1 M) at 80-120 °C under 455 nm LED irradiation under N_2 atmosphere in a flow setup (flow rate 0.1-0.3 mL/h).

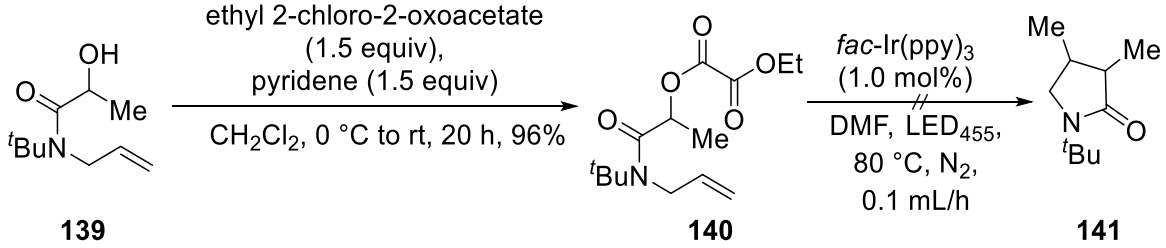
In order to ensure the preferred conformation for the cycle formation the steric bulk at the nitrogen was increased. For this purpose, the desired amide **138** was synthesized by the reaction of *N*-protected allylamine **137**[41] and acid chloride **135** in 73% yield. The synthesis of both building blocks is depicted in Scheme 29: Starting from lactic acid (**133**) the acylation reaction led to the formation of product **134**[42] followed by the subsequent reaction with $SOCl_2$ to form acid chloride **135**. In parallel *N*-protected allylamine **137**[41] was obtained by the reaction

of allyl bromide (**38e**) and *tert*-butylamine **136** providing the desired allyl amine **137** in quantitative yield. The amide **138** was deprotected giving rise to the alcohol **139** that was subsequently esterified to give ethyl oxalate **140** in an overall yield of 91% over two steps.



Scheme 29. Synthesis of *N*-alkylated alcohol **139**.
Reagents and conditions a)[42] AcCl (2.2 equiv), THF, rt, 24 h, 53%; (b) $SOCl_2$ (1.2 equiv), DMF (5 mol%), CH_2Cl_2, rt, 24 h, 69%; (c)[41] reflux, 48 h, 99%; (d) Et_3N (2.0 equiv), DMAP (2 mol%), CH_2Cl_2, rt, 20 h, 73%; (e) K_2CO_3 (4.0 equiv), MeOH/H_2O (2:1), rt, 24 h, 95%.

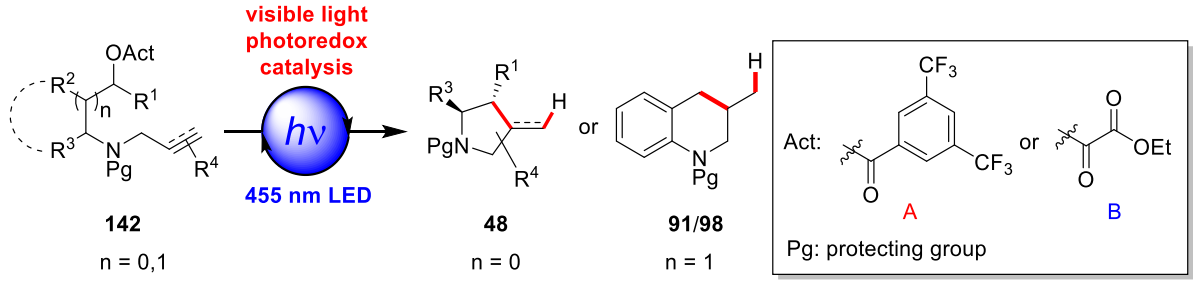
With ethyl oxalate **140** in hand, the subsequent photoredox process showed only the formation of complex reaction mixture and no full conversion (Scheme 30). Again, the reduction potential of *fac*-Ir(ppy)$_3$ ($E_{1/2}^{IV/*III}$ = -1.73 V vs SCE)[43] should be sufficient for transfering an electron to the oxalate ester moiety of substrate **140** (E_{Red} = -1.82 V vs SCE in DMF). Due to the unsuccessful transformation of all substrates in lactame synthesis no further investigations towards this product group were conducted.

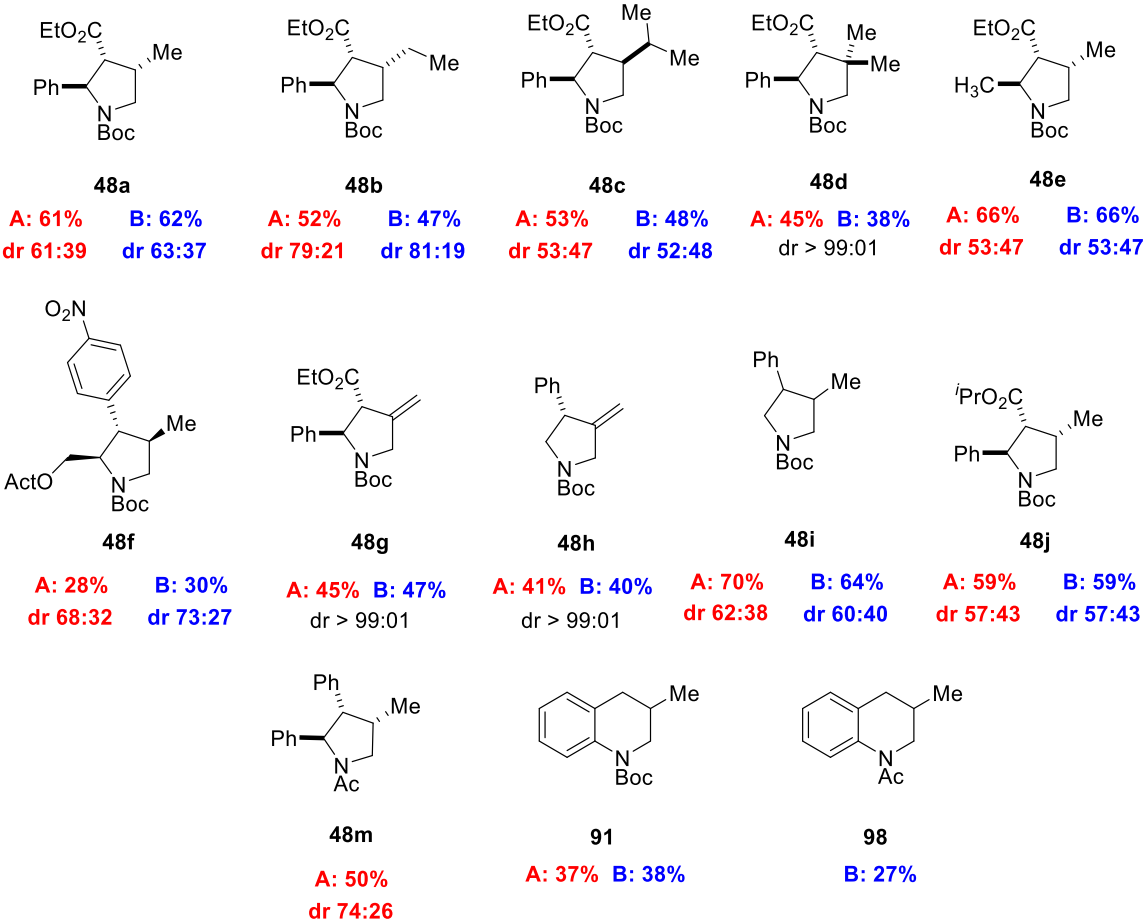


Scheme 30. Activation of *N*-alkylated alcohol **139** and subsequent photoredox catalyzed reaction of substrate **140**.

6. Summary

In conclusion an efficient protocol for the synthesis of substituted pyrrolidines is shown. Starting from commercially available starting materials various substrates for the photochemical transformation were synthesized in several simple steps. The polysubstituted pyrrolidines **48** were obtained under photoredox conditions using microflow reactor at 80 °C in the presence of *fac*-Ir(ppy)$_3$ as catalyst with the strong reduction potential. In contrast to the obtained yields being in moderate to good range, the diastereoselectivity could be increased to selective formation of only one diastereomer by reducing the number of stereocenters from three to two (products **48d**, **48g** and **48h**).





Scheme 31. Overview of the successful photoredox mediated deoxygenative cyclization transformations (only major products are shown).

For all products the stereoselective formation of *trans*-configuration between C1 and C2 carbons was determined. Moreover, the successful photomediated synthesis of enantiopure substituted pyrrolidines was shown employing asymmetric Shi-Epoxidation as key step. The application of the developed protocol to the synthesis of bicyclic products failed, except the examples **91** and **98**. Likewise, the synthesis of substituted 2-pyrrolidinons was not successful.

7. References

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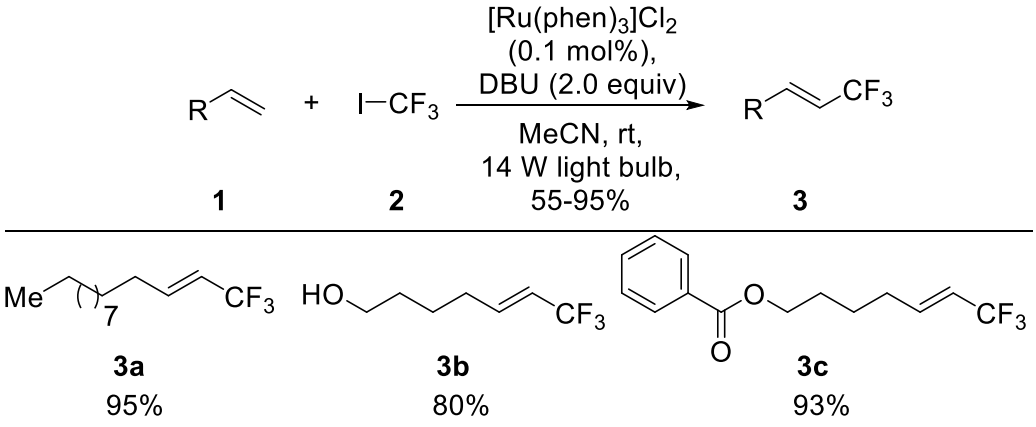
C. Copper Mediated Photochemical Iodoperfluoro-alkylation‡

1. Introduction

The introduction of fluorine or fluorine containing alkyl chains strongly influence the chemical, physical or biological properties of the target molecules which are impressively demonstrated for example in medicinal chemistry or in the synthesis of pharmaceuticals.[1] Thus, for the design of new drugs with improved biological half-life, bioabsorption and pharmaceutical effectiveness the selective introduction of fluorine or fluorine containing groups is an important synthetic challenge.[2] Furthermore, in 2001 the advantage of fluorinated compounds was demonstrated in the synthetic approach of Curran and coworkers, who presented an efficient technique for the synthesis of mixtures of various organic compounds solving both separation and identification problems at the same time.[3] This protocol increased the value of reactions introducing perfluorinated tags to the highly functionalized target molecules. As a result, many methods for efficient perfluorination processes were reported[4] in recent years, including the photoredox catalyzed transformations[5] with various photocatalytic systems.

In 2012 Cho et al.[6] presented the photomediated trifluoromethylation of alkenes employing $[Ru(phen)_3]Cl_2$ catalyst in the presence of a strong organic amine base acting as both sacrificial electron donor for regeneration of ruthenium-catalyst and base for the elimination reaction forming alkene **3** (Scheme 1). A broad substrate scope with high yields and diastereoselectivities was presented including, alcohols, amides, esters, ketones, and aldehydes. However, the reaction of styrene derivatives was not reported.

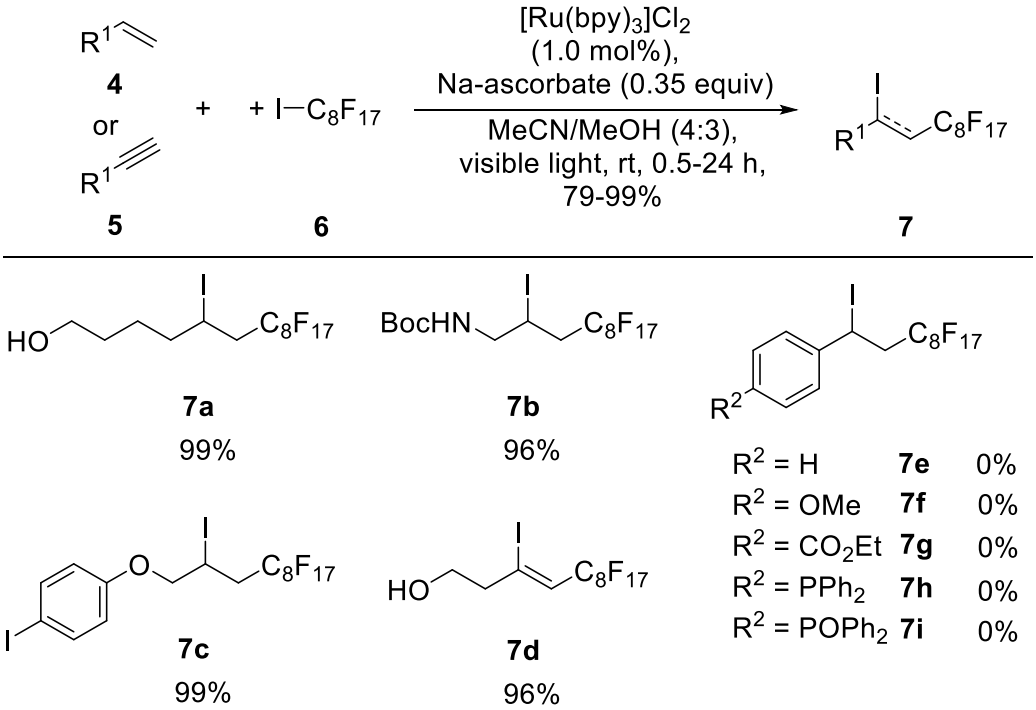


Scheme 1. Photomediated trifluoromethylation of alkenes reported by Cho and coworkers.[6]

In the same year Stephenson and coworkers[7] published a protocol for the photoredox catalyzed addition of perfluoroalkyl iodide **6** to alkenes **4** and alkynes **5** (Scheme 2).

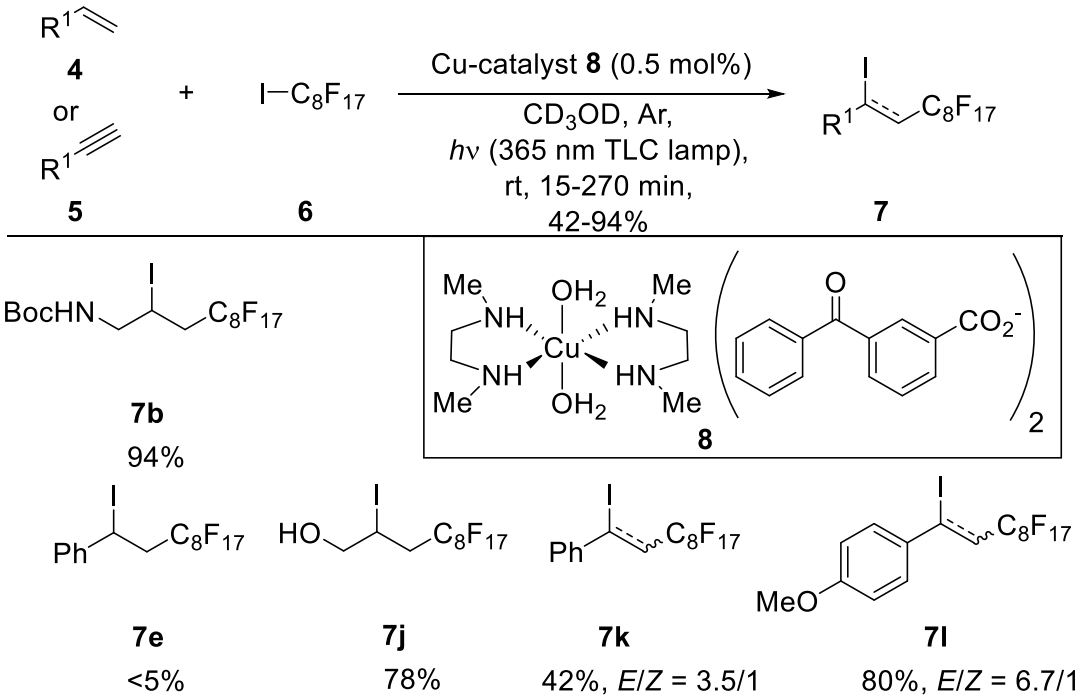
‡This chapter is partially based on Rawner, T.; Lutsker, E.; Kaiser, C. A.; Reiser, O., *ACS Catal.* **2018,** *8* (5), 3950-3956.

The reductive quenching cycle of $[Ru(bpy)_3]Cl_2$ was used employing sodium ascorbate as sacrificial electron donor. The reaction delivered high yields for the desired ATRA products **7** tolerating a broad range of functional groups. Nevertheless, all efforts to utilize styrenes as starting materials for this transformation resulted in complex reaction mixtures.[7]



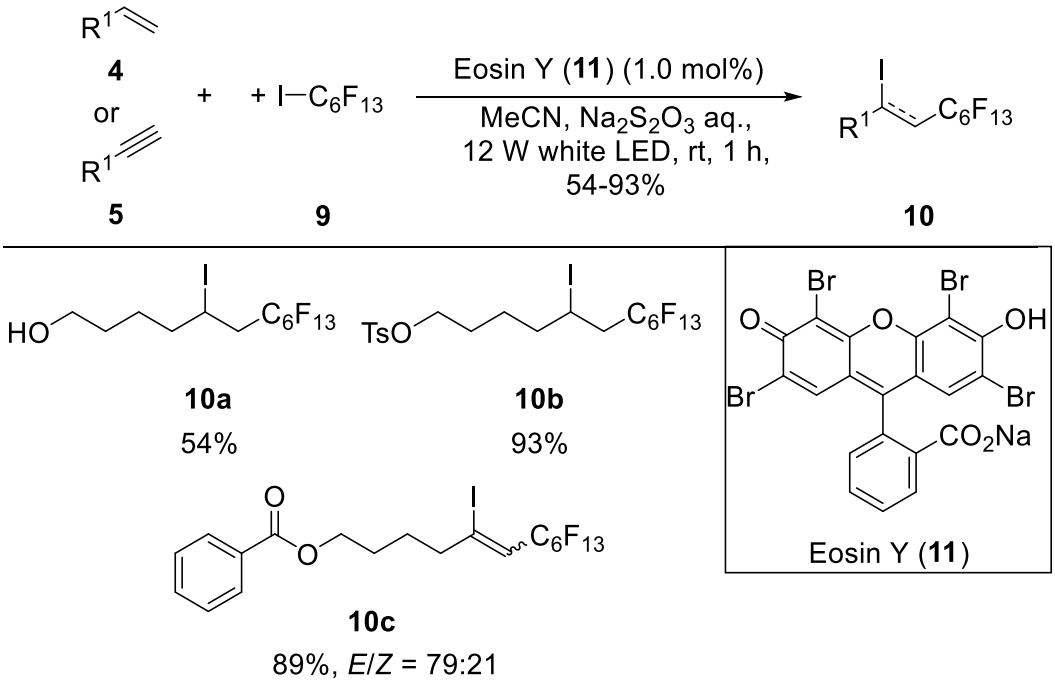
Scheme 2. Photoredox catalyzed iodoperfluoroalkylation of alkenes and alkynes reported by Stephenson and coworkers.[7]

Furthermore, in 2016 Vincent et al.[8] presented an efficient protocol for an UV-light-promoted ATRA reaction employing copper/benzophenone catalyst **8** (Scheme 3). While under reported reaction conditions the unactivated alkenes were successfully transformed into the corresponding ATRA products, the reaction with styrene again showed only trace amounts of the desired photoproduct **7e**. Moreover, several activated and unactivated alkynes **5** were suitable substrates for the iodoperfluoroalkylation reaction.



Scheme 3. UV-light-promoted copper catalyzed ATRA reaction of perfluoroalkyl iodides **6** to alkenes **4** and alkynes **5** by Vincent and coworkers.[8]

In 2017 Yajima et al.[9] investigated successfully the iodoperfluoroalkylation of unactivated alkenes and alkynes in the presence of organic dyes such as Eosin Y (**11**) (Scheme 4). However, the reaction of styrenes was not described by the authors, assuming that styrenes were no suitable substrates. Another protocol was described by Yu et al., who presented a metal-free halogen-bond-promoted ATRA reaction of terminal alkynes with perfluoroalkyl iodides under visible light irradiation in the presence of sacrificial amine.[10]



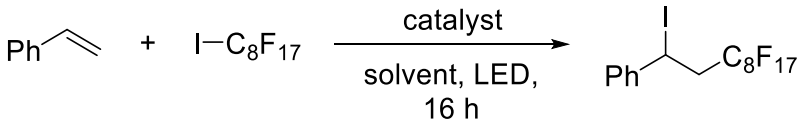
Scheme 4. Eosin Y (**11**) as catalyst for the visible light mediated reaction of perfluoroalkyl iodide **9** with alkenes / alkynes.[9]

These literature reports show that styrenes are in principle an interesting substrate class with unique requirements for the employed catalyst. In 2016 T. Rawner described the successful generation of styrene derived ATRA products of perfluorooctyl iodides[11] showing the unique character of copper catalyst under visible light irradiation. With these results in hand, the investigation of the newly synthesized Cu(II)-catalyst [Cu(dap)Cl_2] (**47**)[12] in iodoperfluoroalkylation reaction of alkenes, including styrenes was carried out. The aim of this chapter was the comparison with the results obtained with the Cu(I)-catalyst and proposition of plausible mechanistic pathways for both catalysts taking all experimental results into account.

2. Preliminary Studies with Styrene and Perfluorooctyl Iodide

This study started with the investigation of the optimized reaction conditions for the new [Cu(dap)Cl_2] (**47**) (Table 1). In 2012 Stephenson et al. reported that the reaction of styrene (**12a**) and perfluorooctyl iodide (**6**) in the presence of [Ru(bpy)$_3$]Cl_2 catalyst resulted in the formation of complex reaction mixture.[7] The validation of this result was done according to the literature protocols using once the oxidative quenching cycle (entry 1) as well as the reductive quenching cycle with sodium ascorbate as sacrificial electron donor (entry 2) in MeCN/MeOH solvent mixture. As expected, both reactions provided the desired product **7e** in very low yields. Employing [Ru(bpy)$_3$]Cl_2 and *fac*-Ir(ppy)$_3$ as photocatalysts showed low yields with both the blue light (λ_{max}= 455 nm) and the green light (λ_{max}= 530 nm) (entries 3-5). The reaction with [Cu(dap)$_2$]Cl (**45**) photocatalyst and 2.0 equivalents of perfluorooctyl iodide (**6**) in MeCN under irradiation with green light gave the iodoperfluoroalkylation product **7e** in 88% yield (entry 6). This result was in accordance with the results presented by T. Rawner in his dissertation.[11] Employing similar reaction conditions for the [Cu(dap)Cl_2] (**47**) provided the photoproduct **7e** in 92% yield (entry 7). This result was surprising due to the fact, that the UV absorption of the new Cu(II)-catalyst was much lower compared to the Cu(I)-catalyst (for details see Experimental Part). With this result in hand further investigations were carried out to find the parameters which were disadvantageous for the reaction. When the catalyst loading was lowered to 0.1 mol% only 17% yield was observed (entry 8), whereas using equimolar amount of perfluorooctyl iodide (**6**) resulted in moderate yield of 47% (entry 9). Variation of solvents revealed CH_2Cl_2 and DMF as feasible alternatives for MeCN with 93% and 88% yields, whereas the yield with DMSO as solvent dropped to 36% (entries 10-12). Employing $CuCl_2$ without ligand or vice versa, dap ligand without copper salt as well as the absence of light showed no reaction or only low yields (entries 13-15). Similarly, the reaction without catalyst showed no reaction (entry 16) and carrying out the reaction without prior degassing gave only 30% yield (entry 17). The latter indicates the quenching of the photoexcited catalyst by oxygen. The initiation of the reaction with AIBN under thermal conditions led to a complex reaction mixture and only trace amounts of the product **7e** were detected (entry 18). Hu et al.[13] reported iron-catalyzed 1,2-addition of perfluoroalkyl iodides to alkenes and alkynes, however, also under these conditions only traces of the desired product **7e** were obtained (entry 19). While switching the light source to blue light (λ_{max}= 455 nm) gave the desired product only in 13% yield (entry 20), the employment of the energetically lower powered turquoise light (λ_{max}= 505 nm) delivered the ATRA product **7e** in 69% yield (entry 21). In addition, it was shown that both Cu(I)- and Cu(II)-catalysts can be formed in situ with similar catalytic activity (entries 22 and 23).

Table 1. Determination of the optimized reaction conditions for iodoperfluoroalkylation of sytrene (**12a**).



12a **6** **7e**

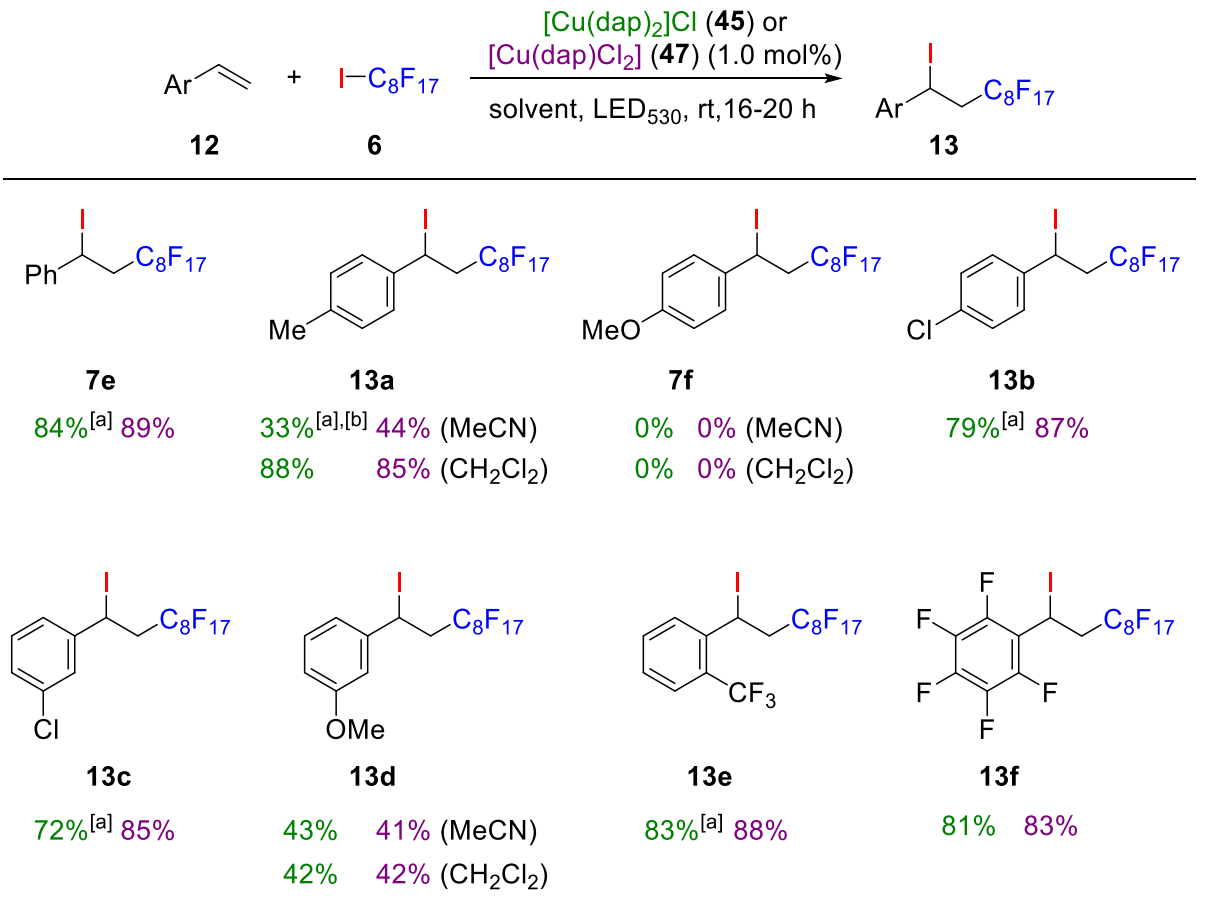
Entry	Catalyst / Conditions	Solvent	Yield [%][a]
1[b]	$[Ru(bpy)_3]Cl_2$	MeCN/MeOH (4:3)	2
2[b], [c]	$[Ru(bpy)_3]Cl_2$	MeCN/MeOH (4:3)	3
3	$[Ru(bpy)_3]Cl_2$	MeCN	9
4[b]	$[Ru(bpy)_3]Cl_2$	MeCN	10
5[b]	*fac*-$Ir(ppy)_3$	MeCN	16
6	$[Cu(dap)_2]Cl$ (**45**)	MeCN	88
7	$[Cu(dap)Cl_2]$ (**47**)	MeCN	92
8[d]	$[Cu(dap)Cl_2]$ (**47**)	MeCN	17
9[e]	$[Cu(dap)Cl_2]$ (**47**)	MeCN	47
10	$[Cu(dap)Cl_2]$ (**47**)	CH_2Cl_2	93
11	$[Cu(dap)Cl_2]$ (**47**)	DMF	83
12	$[Cu(dap)Cl_2]$ (**47**)	DMSO	36
13	$CuCl_2$	MeCN	n.r.
14[f]	$[Cu(dap)Cl_2]$ (**47**)	MeCN	n.r.
15	dap	MeCN	11
16	no catalyst	MeCN	n.r.
17	not degassed	MeCN	30
18[f], [g]	AIBN	MeCN	2
19[f], [h]	$FeBr_2/Cs_2CO_3$	MeCN	3
20[b]	$[Cu(dap)Cl_2]$ (**47**)	MeCN	13
21[i]	$[Cu(dap)Cl_2]$ (**47**)	MeCN	69
22	CuCl/dap (1:2)	MeCN	86
23	$CuCl_2$/dap (1:1)	MeCN	89

Reaction conditions: styrene (0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (1.0 mmol, 2.0 equiv), catalyst (1.0 mol%) in solvent (anh., degassed, 1.0 mL), N_2, irradiation at 530 nm (green LED) for 16 h. [a]Determined by NMR with diphenoxymethane as an internal standard. [b]Irradiation at 455 nm (blue LED). [c]Sodium ascorbate (0.35 mmol, 0.35 equiv), reductive quenching cycle. [d]Catalyst loading 0.1 mol%. [e]$C_8F_{17}I$ (1.0 mmol, 1.0 equiv). [f]Dark reaction. [g]AIBN (10 mol%), 80 °C. [h]$FeBr_2$(0.10 mmol, 10 mol%) and Cs_2CO_3 (0.8 mmol, 0.8 equiv). [i]Irradiation at 505 nm (turquious LED).

3. Substrate Scope

With the optimized reaction conditions in hand the substrate scope was investigated. Scheme 5 shows the comparison between Cu(I)- and Cu(II)-catalysts. The results were obtained using 1.0 equivalents of styrene derivative **12** and 2.0 equivalents of $C_8F_{17}I$ (**6**) in the presence of $[Cu(dap)_2]Cl$ (**45**) or $[Cu(dap)Cl_2]$ (**47**). The reaction of styrene (**12a**) provided the ATRA product **7e** in 89% yield. The introduction of methyl group in *para*-position resulted in a moderate yield of 44% for product **13a**. Since MeCN and CH_2Cl_2 showed comparable results during the investigation of optimized reaction conditions the reactions with low product yields were additionally carried out in CH_2Cl_2. Interestingly, when the reaction of 1-methyl-4-

vinylbenzene with soft electron donating group was performed in CH_2Cl_2 the yield for the corresponding product **13a** strongly increased to 85-88% for both copper catalysts. Further increase of electron donor properties by using 4-methoxystyrene resulted in no product formation for both tested catalysts and solvents. In these reactions only polymerization of the staring material was obtained.

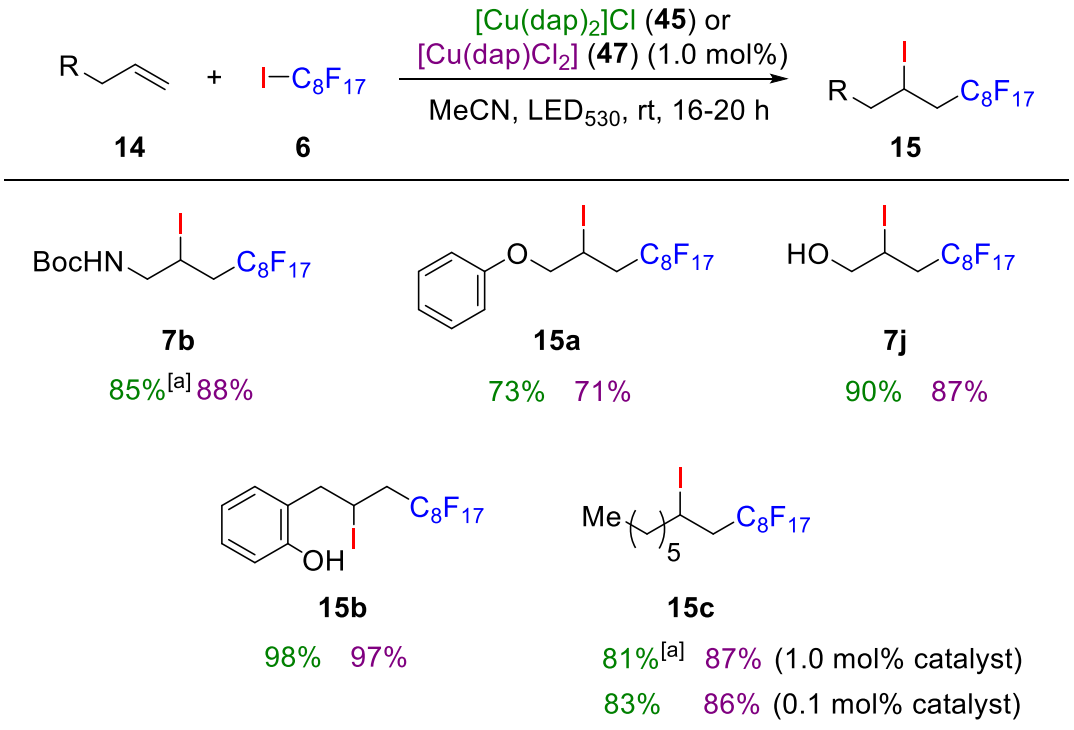


Scheme 5. Substrate scope of copper catalyzed iodoperfluoroalkylation of styrene derivatives **12**. *Reaction conditions*: alkene (0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (1.0 mmol, 2.0 equiv), $[Cu(dap)_2]Cl$ (**45**) or $[Cu(dap)Cl_2]$ (**47**) (1.0 mol%) in MeCN (anh., degassed, 1.0 mL), N_2, irradiation at 530 nm (green LED) for 16-20 h. [a]Result obtained by T. Rawner.[11] [b]HI elimination product in 20% yield isolated.

The reaction of 4-chlorostyrene gave rise to the ATRA product **13b** in 87% yield demonstrating the tolerance towards soft electron withdrawing groups. Switching the chlorine-substituent to *meta*-position gave product **13c** in comparable yield to *para*-substitution. In contrast to the *para*-methoxy substitution, when the methoxy group was switched to *meta*-position, a moderate yield was obtained for product **13d**, both for the catalyst variation and for the solvent change. Moreover, the introduction of CF_3-group at *ortho*-position provided the desired product **13e** in 88% yield being in accordance with the result obtained with 4-chlorostyrene. Further increase of electron withdrawing character showed no negative effect on yield, giving pentasubstituted ATRA product **13f** in 81% and 83% yield. For all styrene derivatives **12** no

significant differences in yield or reactivity between [Cu(dap)$_2$]Cl (**45**) or [Cu(dap)Cl$_2$] (**47**) were observed.

Next, the investigation of the substrate scope for unactivated alkenes **14** was carried out. For this purpose similar reaction conditions which were already employed for the styrene derivatives (Scheme 5), were used as depicted in Scheme 6. The tolerance towards amine moiety was demonstrated by the reaction of *tert*-butyl allylcarbamate with perfluorooctyl iodide (**6**) providing the desired ATRA product **7b** in 88% yield. Furthermore, employing allyl phenylether delivered ATRA compound **15a** in good yields. The presence of a free hydroxy group showed no negative effect on the photoredox catalyzed transformation giving rise to product **7j** in 90% and 87% yield. Moreover, when 2-allylphenol was used the corresponding ATRA product **15b** was obtained in excellent yields.

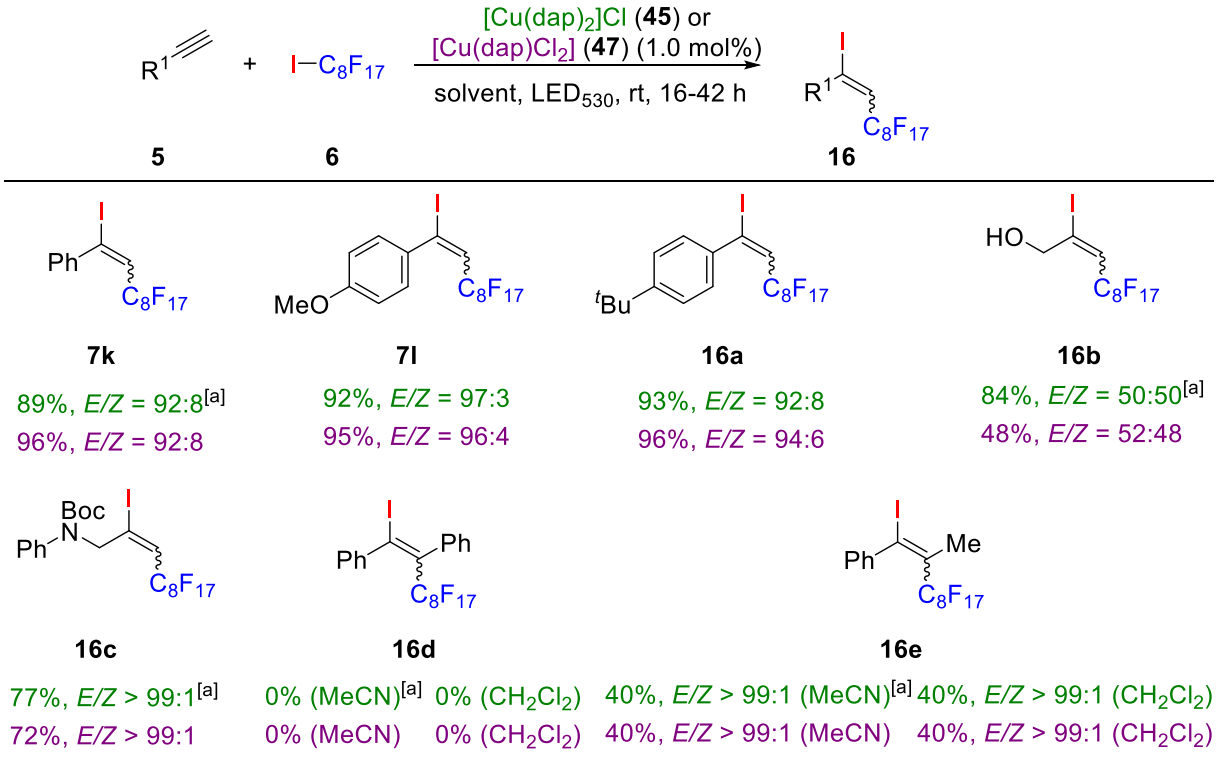


Scheme 6. Substrate scope of copper catalyzed iodoperfluoroalkylation of alkenes **14**.
Reaction conditions: alkene (0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (1.0 mmol, 2.0 equiv), [Cu(dap)$_2$]Cl (**45**) or [Cu(dap)Cl$_2$] (**47**) (1.0 mol%) in MeCN (anh., degassed, 1.0 mL), N_2, irradiation at 530 nm (green LED) for 16-20 h. [a]Result obtained by T. Rawner.[11]

Surprisingly, no cyclization product was formed, although the ring closure process towards a five membered ring was conceivable. This result provides evidence about the absence of cationic intermediate during the ATRA process (*vide infra*). Additionally, the photoredox mediated atom transfer radical addition reaction of perfluorooctyl iodide (**6**) with 1-octene showed very good yields for both catalysts. In contrast to the results obtained for styrene (**12a**) (Table 1, entry 8) lowering the catalyst loading to 0.1 mol% showed no yield decreasing effect,

providing the desired product **15c** in 83-86% yield. As expected, comparable results for unactivated alkenes **14** (Scheme 6) were obtained for both copper-catalysts **45** and **47**.

Next, a range of alkynes was subjected to the photomediated ATRA reaction employing the new type catalyst [Cu(dap)Cl_2] (**47**) (Scheme 7). When phenylacetylene was used as a substrate the desired product **7k** was obtained in 96% yield with an *E*/*Z* ratio of 92:8. In contrast to *para*-methoxy styrene (Scheme 5), employing 1-ethynyl-4-methoxybenzene provided the desired ATRA product **7l** in excellent yields and diastereomeric ratios. When *tert*-butyl group was introduced in *para*-position of the aryl ring, again excellent yields and diastereoselectivities were observed for product **16a**.



Scheme 7. Substrate scope of copper catalyzed iodoperfluoroalkylation of alkynes **5**.
Reaction conditions: alkyne (0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (1.0 mmol, 2.0 equiv), [Cu(dap)$_2$]Cl (**45**) or [Cu(dap)Cl_2] (**47**) (1.0 mol%) in MeCN (anh., degassed, 1.0 mL), N_2, irradiation at 530 nm (green LED) for 16-42 h. *E*/*Z* ratio was determined via NMR spectroscopy. [a]Result obtained by T. Rawner.[11]

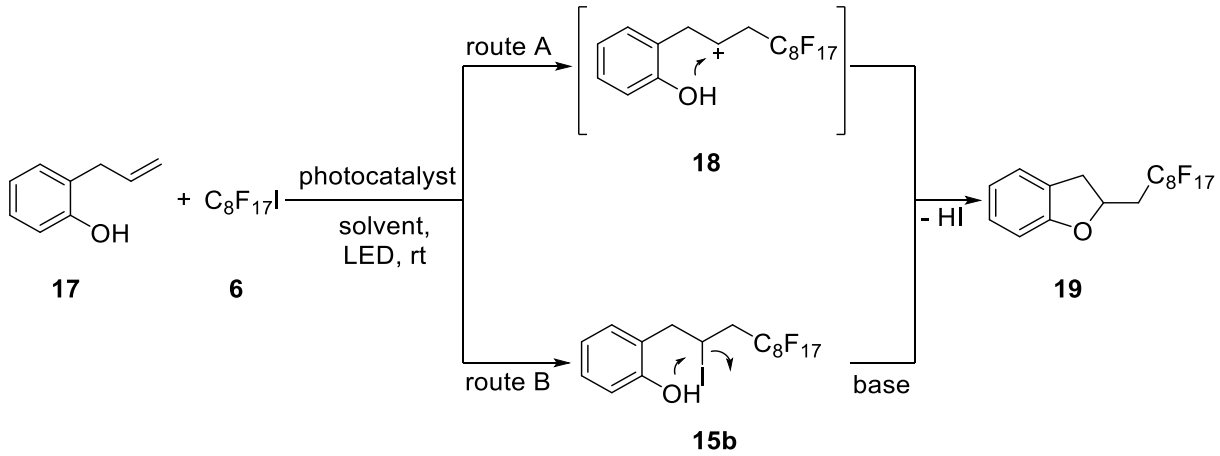
Surprisingly, a free hydroxy group like in propargyl alcohol lowered the yield of the corresponding ATRA product **16b** from 84% to 48% when [Cu(dap)Cl_2] (**47**) was used as photocatalyst, whereas in the presence of protected amine moiety comparably good yields and excellent *E*/*Z* ratios for product **16c** were observed for both copper catalysts. No conversion was observed when the symmetrical 1,2-diphenylethyne was subjected to the reaction conditions in both MeCN and CH_2Cl_2. It was assumed that steric bulk of the additional phenyl group prevented the addition of perfluoroalkyl radical to the triple bond (*vide infra*). Consequently, the use of substrate with the smaller methyl group furnished the desired ATRA product **16e** in 40% yield and an excellent diastereomeric ratio of >99:1. However, the

employment of CH_2Cl_2 as solvent showed no change in yield and *E*/*Z* ratio. With the exception of propargyl alcohol for all alkyne substrates **5**, similar results were observed with $[Cu(dap)_2]Cl$ (**45**) or $[Cu(dap)Cl_2]$ (**47**).

4. Cyclization Reaction via ATRA

4.1. Initial Reaction

Further investigation was focused on the substrates which in principle can undergo atom transfer radical addition reaction with subsequent ring closure forming heterocycles.[14] The proposed transformation of 2-allylphenol (**17**) is shown in Scheme 8. Established mechanistic proposal for ATRA processes is the addition of the radical to the corresponding alkene with subsequent oxidation of the newly formed carbon centered radical to give cationic intermediate **18** which can be attacked by a nucleophile to form the desired product.[5a] For substrate **17** the intramolecular nucleophilic attack of hydroxy group is conceivable (route A). Another possibility is the intramolecular nucleophilic substitution reaction of hydroxy group of the formed ATRA product **15b** at the iodine containing carbon (route B). In these ways the formation of substituted 2,3-dihydrobenzofuran **19** can be achieved.

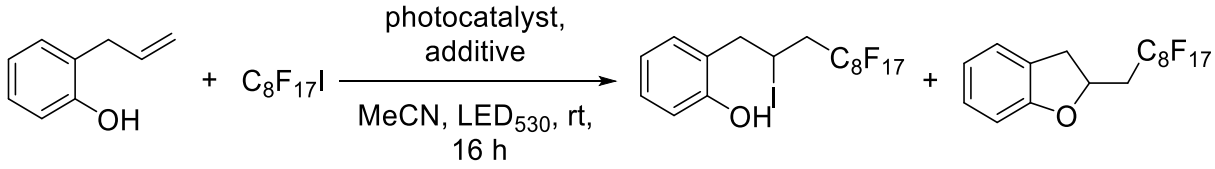


Scheme 8. Expectable mechanistic pathway for the cyclization process.

The presence of bases should be advantageous for both mechanistic pathways. Based on the previous result that no ring closure occurred at **15b**, assuming that route B is preferred, a short screening of catalysts and especially additives (e.g. bases), was carried out (Table 2). The addition of weak bases such as $NaHCO_3$ and K_2HPO_4 provided the ATRA product **15b** almost quantitatively (Table 2, entries 1 and 2). Increasing the basicity of the added base led to lower yield for ATRA product and an inseparable product mixture with no generation of cyclic compound **19** (entry 3). The use of a strong organic base also showed no cyclization reaction with low yield of ATRA product **15b**. $CuCl_2$ is known to be able to act as radical trapping reagent[15]. It is conceivable that $CuCl_2$ can trap the carbon-centered radical to form Cu(III)-species that can undergo the intramolecular ring closure via reductive elimination to form Cu(I)-

halide. However, this reaction resulted in a complex reaction mixture (entry 5). The strongly reductive *fac*-Ir(ppy)$_3$ is known to undergo ATRA processes via oxidation of the carbon centered radical to form the corresponding cation.[5a] The reaction of 2-allylphenol (**17**) with $C_8F_{17}I$ (**6**) delivered 54% yield for the ATRA product **15b** and trace amounts of the desired cyclization product **19**. To improve the nucleophilicity of the hydroxy group $NaHCO_3$ was added to the reaction mixture with *fac*-Ir(ppy)$_3$ photocatalyst. However, again only traces of 2,3-dihydrobenzofuran **19** were obtained (entry 7).

Table 2. Efforts towards cyclization product **19**.



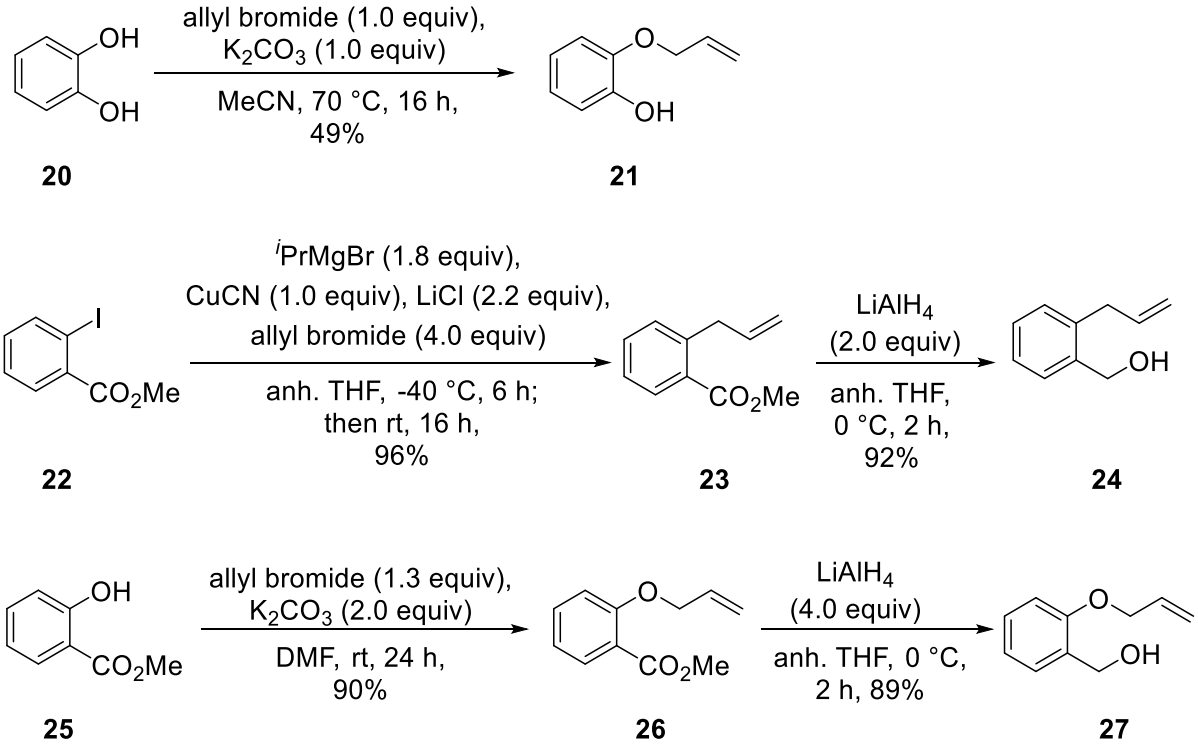
17 **6** **15b** **19**

Entry	Catalyst [1.0 mol%]	Additive [1.0 equiv]	Yield [%][a] **15b**:**19**
1	[Cu(dap)$_2$]Cl (**45**)	$NaHCO_3$	96:0
2	[Cu(dap)$_2$]Cl (**45**)	K_2HPO_4	95:0
3	[Cu(dap)$_2$]Cl (**45**)	Na_2CO_3	54:0
4	[Cu(dap)$_2$]Cl (**45**)	DBU	21:0
5	[Cu(dap)$_2$]Cl (**45**)	$CuCl_2$	complex reaction mixture
6[b]	*fac*-Ir(ppy)$_3$	/	54:5
7[b]	*fac*-Ir(ppy)$_3$	$NaHCO_3$	52:4

Reaction conditions: 2-allylphenol (**17**) (0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (1.0 mmol, 2.0 equiv), catalyst (1.0 mol%) and additive (1.0 equiv) in MeCN (anh., 1.0 mL), N_2, irradiation at 530 nm (green LED) for 16 h. [a]Isolated yield. [b]Irradiation at 455 nm (blue LED).

4.2. Synthesis of Starting Materials for Cyclization Reaction

Surprisingly, the addition of bases to the reaction mixture showed no positive effect on the formation of the cyclization product. To exclude the option that the investigated substrate **17** had the wrong geometry for a successful ring closure, various substrates for the cyclization process were synthesized (Scheme 9). Starting from commercially available catechol (**20**) the monoallylated alcohol **21** was obtained in 49% yield using allyl bromide under basic conditions.[16] Next, methyl 2-iodobenzoate (**22**) was treated with ^{i}PrMgBr in the presence of CuCN and LiCl to form soft cuprate being able to undergo nucleophilic substitution reaction to form allylbenzene **23** in 96% yield.[17] Subsequently, the ester moiety was reduced by $LiAlH_4$ to the corresponding benzylic alcohol to give the desired starting material **24** in 92% yield.[18] Finally, methyl salicylate (**25**) reacted with allyl bromide under basic reaction conditions providing product **26** in 90% yield[19], which was reduced in the next step to form the benzylic alcohol **27** in 89% yield.



Scheme 9. Synthesis of starting materials for cyclization reactions.

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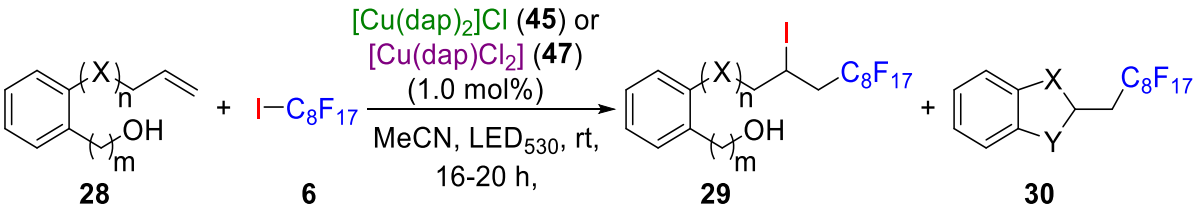
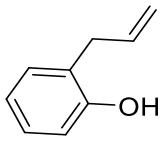
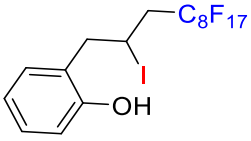
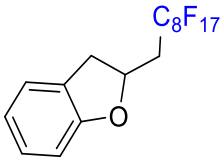
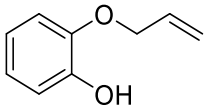
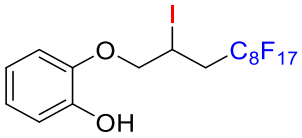
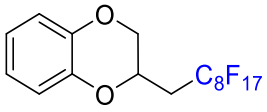
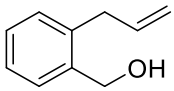
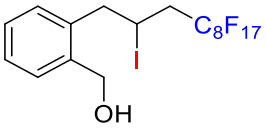
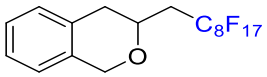
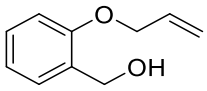
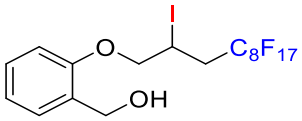
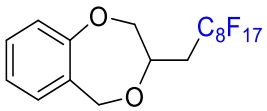
4.3. Photoreactions

The prepared starting materials were consequently employed in the photoredox catalyzed iodoperfluoroalkylation reaction using $[Cu(dap)_2]Cl$ (**45**) or $[Cu(dap)Cl_2]$ (**47**) as photocatalysts. In all cases no desired cyclization products **30a**-**30d** were obtained whereas only the formation of ATRA products **15b**, **29a**, **29b** and **29c** was observed. The yields for both employed catalysts were similar. As a result of no successful cyclization reaction no further investigations were carried out towards the described cyclic product groups.

Table 3. Photoinduced addition of perfluorooctyl iodide (**6**) to arenes **28**.

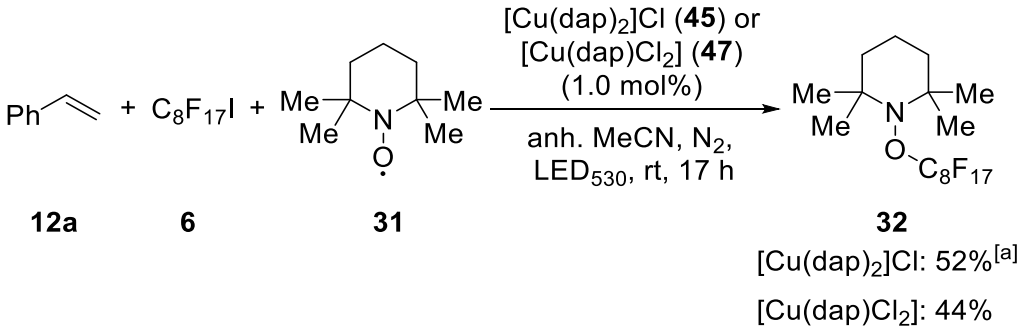


Entry	Substrate	ATRA product	Cyclization product
1			
	17	**15b**	**30a**
		98% 97%	0% 0%
2			
	21	**29a**	**30b**
		73% 70%	0% 0%
3			
	24	**29b**	**30c**
		69% 65%	0% 0%
4			
	27	**29c**	**30d**
		56% 61%	0% 0%

Reaction conditions: alkene **28** (0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (1.0 mmol, 2.0 equiv), catalyst (1.0 mol%) in MeCN (anh., degassed, 1.0 mL), N_2, irradiation at 530 nm (green LED) for 16 h.

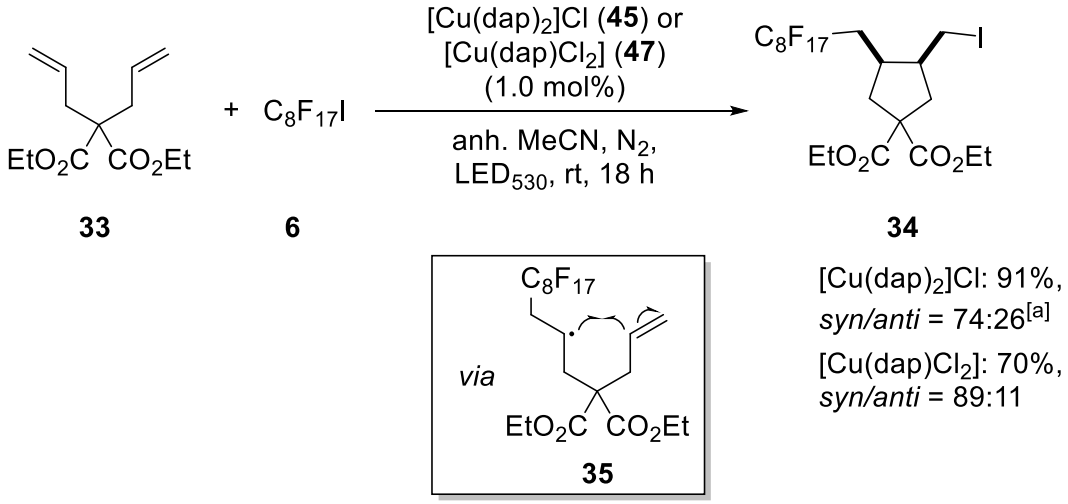
5. Mechanistic Studies

In order to get a deeper insight into the mechanism of the iodoperfluoroalkylation reaction a series of experiments was carried out. First, several mechanistic experiments were done using $[Cu(dap)Cl_2]$ (**47**) and the obtained results were compared with the results for $[Cu(dap)_2]Cl$ (**45**) described by T. Rawner[11]. In line with a radical pathway of the perfluorination reaction the addition of TEMPO (**31**) provided exclusively the radical trapping product **32** in 44% yield (Scheme 10). However, no other intermediates could be identified by this experiment.



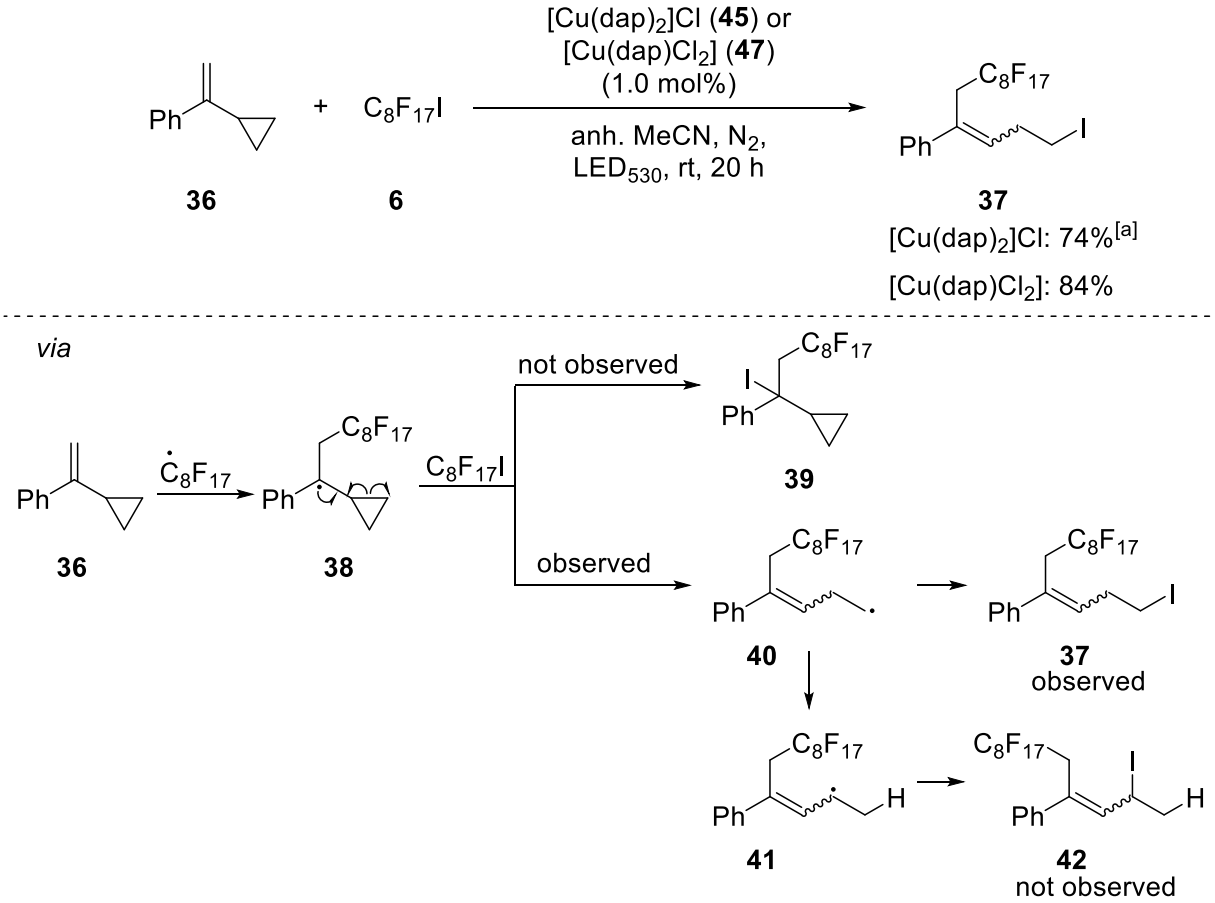
Scheme 10. Radical trapping reaction with TEMPO (**31**).
[a]Result obtained by T. Rawner.[11]

Moreover, the radical character of the reaction was confirmed by 5-*exo-trig* cyclization reaction. Employing diallyl ester **33** as starting material led after perfluorooctyl radical addition to the formation of intermediary radical **35** which can undergo the favored 5-*exo-trig* cyclization to form cyclopentane **34** in 70% yield (Scheme 11). The reaction occured with high diastereoselectivity as confirmed by 2D-NMR towards the formation of *syn*-product which is in accordance with literature[11, 20]



Scheme 11. Mechanistic study: Radical 5-*exo-trig* ring closure.
[a]Result obtained by T. Rawner.[11]

Furthermore, the radical clock experiment was carried out using substrate **36** under optimized reaction conditions (Scheme 12). In the first step perfluorooctyl radical adds to the double bond of the substrate **36** forming benzylic radical **38**. The presence of the radical next to the cyclopropane ring resulted in ring opening process leading to the product **37**, whereas the formation of cyclopropane product **39** was not observed.[21] In addition, no indication for the 1,2-hydride shift resulting in the formation of allyl radical **41** was detected being in agreement with the results obtained by T. Rawner[11].

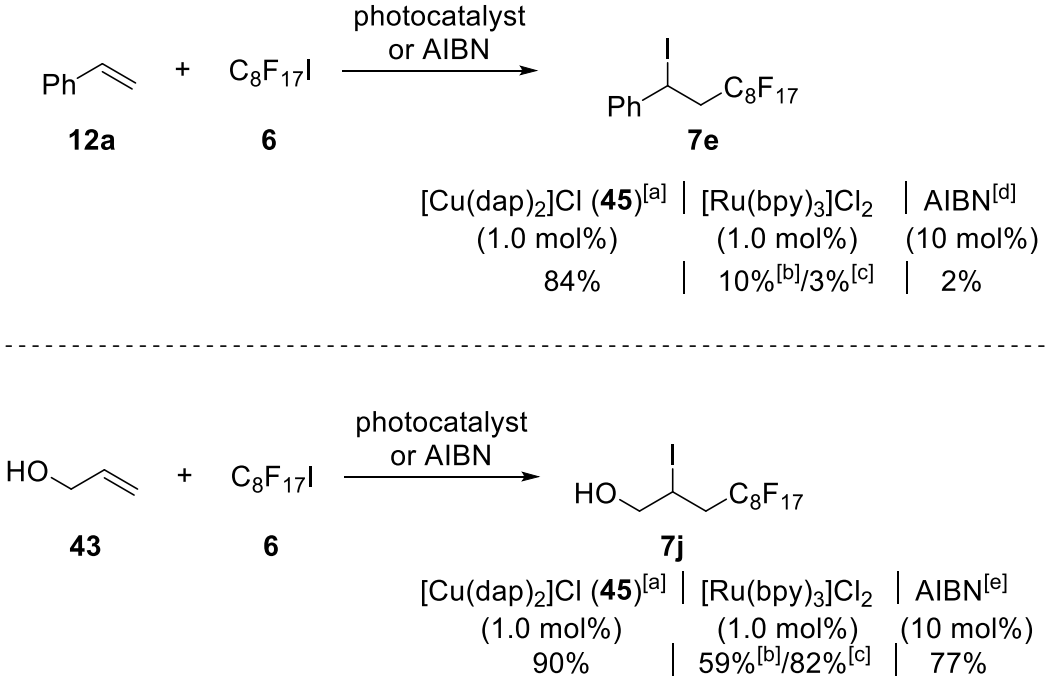


Scheme 12. Mechanistic study: radical clock experiment.
[a]Result obtained by T. Rawner.[11]

Since the results for [Cu(dap)Cl_2] (**47**) and [Cu(dap)$_2$]Cl (**45**) were similar for all mechanistic studies so far, further investigations were only carried out with [Cu(dap)$_2$]Cl (**45**). Next, it was established that the formed ATRA products are stable under photoredox conditions. Therefore, the product **7e** was firstly stirred under irradiation with blue light in the presence of [Ru(bpy)$_3$]Cl_2. Secondly, additional styrene was added to the reaction mixture of the ATRA product and irradiated with blue light in the presence of [Ru(bpy)$_3$]Cl_2. These experiments were important in order to exclude the possibility of subsequent product decomposition or a second ATRA reaction with styrene in the presence of [Ru(bpy)$_3$]Cl_2. Similar studies were carried out for [Cu(dap)$_2$]Cl (**45**). All reactions demonstrated the high stability of the ATRA products under photoredox conditions.[12a]

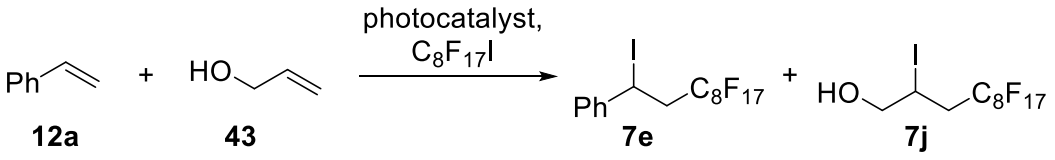
The ATRA reaction between allyl alcohol (**43**) or styrene **12a** and perfluorooctyl iodide (**6**) illustrates the different mechanistic pathways that are involved depending on the catalyst employed. The reaction of allyl alcohol (**43**) delivers the desired product **7j** in good yields employing visible light photoredox catalysis either by [Ru(bpy)$_3$]Cl_2 or by [Cu(dap)$_2$]Cl (**45**). Moreover, the reaction is successful under thermal conditions using AIBN as radical initiator (Scheme 13). In contrast, neither AIBN nor [Ru(bpy)$_3$]Cl_2 are able to promote this transformation for styrene (**12a**), whereas [Cu(dap)$_2$]Cl (**45**) provides the desired product in

very good yield. These results indicate different mechanistic pathways for the investigated catalysts.



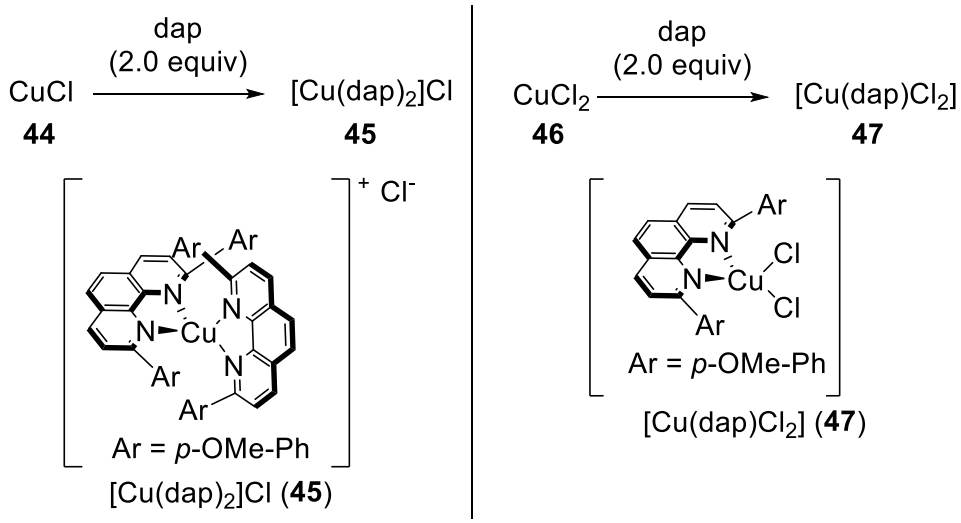
Scheme 13. Comparison between reactions with styrene (**12a**) and allyl alcohol (**43**).[12a]
Reaction conditions: **12a**/**43** (1.0 mmol), **6** (2.0 equiv). [a][$Cu(dap)_2$]Cl (**45**) (1.0 mol%) in MeCN (anh., degassed, 0.5 mL), N_2, irradiation at 530 nm for 17 h. [b][$Ru(bpy)_3$]Cl_2 (1.0 mol%) in MeCN (anh., degassed, 0.5 mL), N_2, irradiation at 455 nm for 17 h. [c]**12a**/**43** (0.25 mmol), **6** (1.3 equiv), sodium ascorbate (0.35 equiv), [$Ru(bpy)_3$]Cl_2 (1.0 mol%) in MeCN/MeOH (anh., degassed, 4:3, 3.5 mL), N_2, irradiation at 455 nm for 2 h. [d]**12a** (1.0 mmol), **6** (1.0 equiv), AIBN (10 mol%) in MeCN (anh., degassed, 0.5 mL), N_2, at 80 °C for 16 h. [e]**43** (2.0 mmol, 1.15 equiv), **6** (1.0 equiv), AIBN (10 mol%) at 80 °C for 14 h.

With these results in hand a competitive reaction between styrene (**12a**) and allyl alcohol (**43**) was carried out using [$Cu(dap)_2$]Cl (**45**) and [$Ru(bpy)_3$]Cl_2 (Scheme 14). When the reaction was performed in the presence of copper catalyst 69% of styrene derived product **7e** and 13% of alcohol **7j** were obtained indicating the higher reactivity of styrene (**12a**) compared to the unactivated alkene **43**. Interestingly, when the catalyst was switched to [$Ru(bpy)_3$]Cl_2 both photoproducts **7e** and **7j** were obtained in very low yields. These observations indicate, that the higher reactivity of styrene (**12a**) provides the formation of benzylic radical but only leads to the desired ATRA product when copper catalyst is present. To exclude the possibility of simple quenching of the ruthenium catalyst with styrene (**12a**) fluorescence measurements were carried out in cooperation with C. Kaiser (for details see Experimental Part).



Scheme 14. Competitive reaction between styrene (**12a**) and allyl alcohol (**43**).[12a]
Reaction conditions: **12a** (1.0 mmol), **43** (1.0 mmol), $C_8F_{17}I$ (**6**) (2.0 equiv): [a]$[Cu(dap)_2]Cl$ (**45**) (1.0 mol%) MeCN (anh., degassed, 0.5 mL), N_2, irradiation at 530 nm for 17 h. [b]Sodium ascorbate (0.35 equiv), $[Ru(bpy)_3]Cl_2$ (1.0 mol%) in MeCN/MeOH (anh., degassed, 4:3, 3.5 mL), N_2, irradiation at 455 nm for 2 h**.**

The exclusive formation of $[Cu(dap)Cl_2]$ (**47**) upon treatment of $CuCl_2$ (**44**) with 2.0 equivalents of dap ligand indicates, that the $[Cu(dap)_2]Cl$ (**45**) should lose one dap ligand when transferring a single electron to perfluorooctyl iodide (**6**), thus forming a Cu(II) species (Scheme 15).



Scheme 15. Formation of $[Cu(dap)_2]Cl$ (**45**) and $[Cu(dap)Cl_2]$ (**47**) in the presence of 2.0 equivalents dap ligand.[12a]

This assumption was confirmed by a ^1H NMR experiment in $CDCl_3$ using styrene (**12a**) (0.2 mmol), $C_8F_{17}I$ (**6**) (0.4 mmol), $[Cu(dap)_2]Cl$ (**45**) (20 mol%) in MeCN (anh., degassed, 1.0 mL), after irradiation for 16 h with 530 nm LED (green LED). The analyzed reaction mixture showed clearly the formation of free ligand after the ATRA-reaction (Figure 1). Control experiment without styrene (**12a**) and $C_8F_{17}I$ (**6**), thus preventing the Cu(I) → Cu(II) transition, showed no free ligand formation (Figure 2).

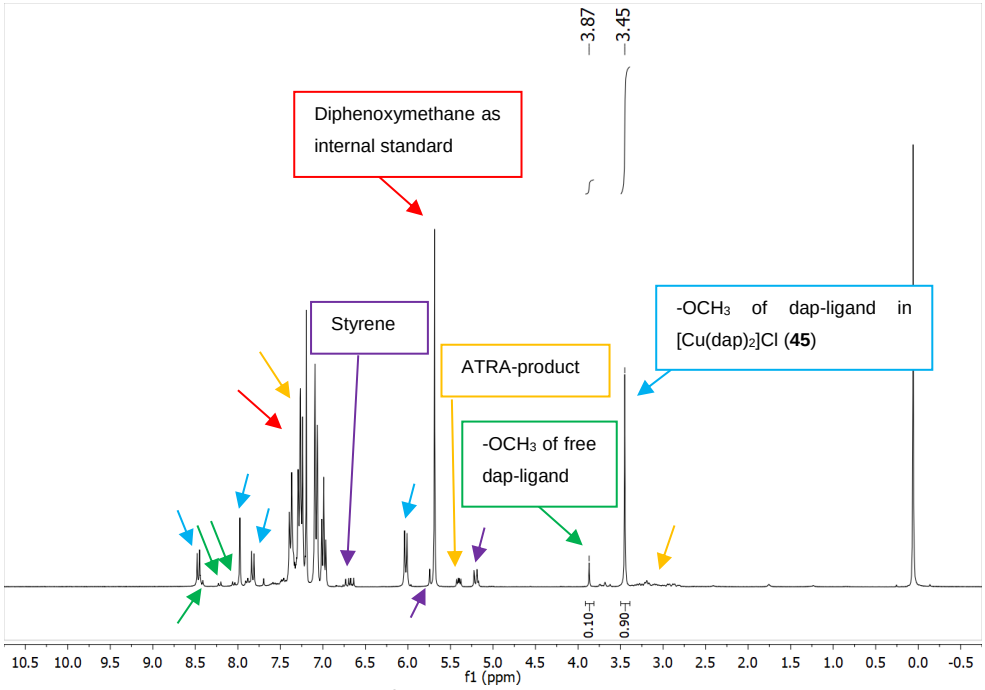


Figure 1. Ligand dissociation experiment.[12a]

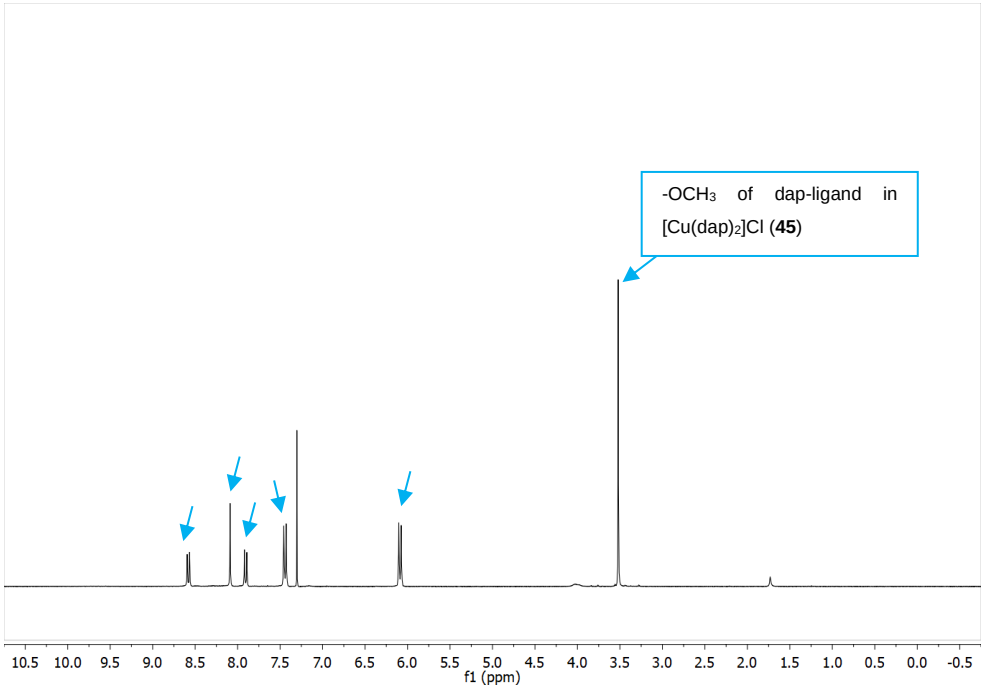
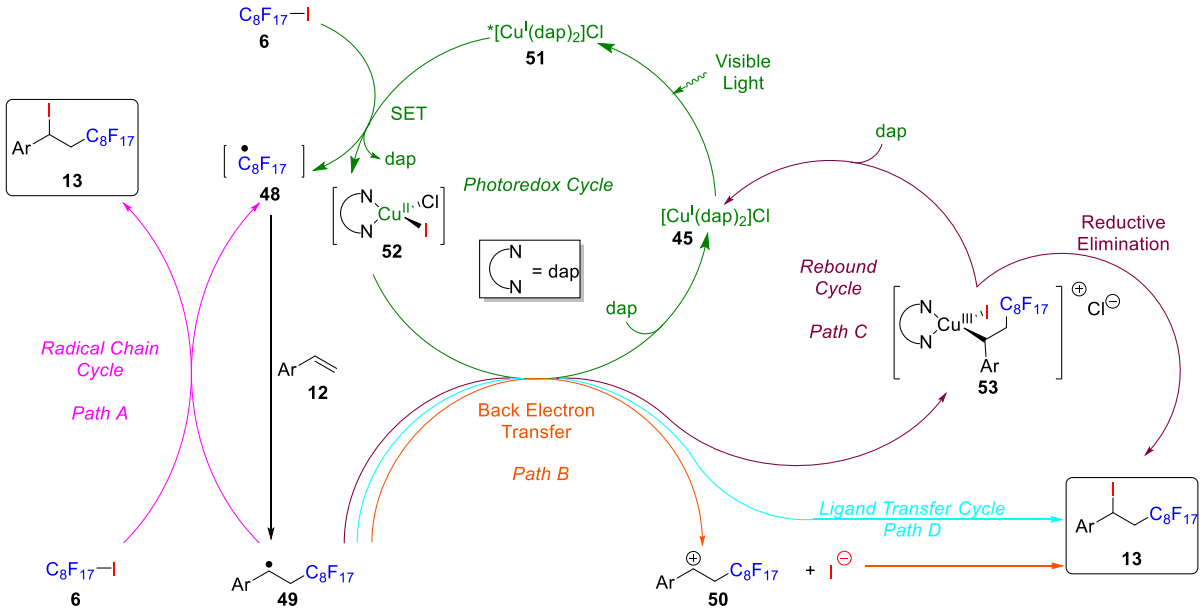


Figure 2. Control experiment for ligand dissociation.[12a]

6. Proposed Mechanism

Taking all observations into account, the following mechanistic pathways can be proposed[12a]: The two commonly discussed and generally accepted mechanistic proposals for ATRA reactions are either a radical chain[22] or a photoredox cycle[5a, 5c, 7, 23]. The ATRA process starts with initial generation of perfluoroalkyl radical **48** e.g. thermally in the presence of radical starter

AIBN or via single electron transfer from the photoexcited catalyst. Perfluoroalkyl iodides are accessible substrates for both types of initiation. AIBN mediated ATRA reactions of perfluroalkyl iodides with a wide range of alkyl substituted alkenes have been described in the literature.[24] In the case of photoredox process the reduction potentials of both, $[Ru(bpy)_3]Cl_2$ (reductive quenching cycle: $Ru^{2+}/Ru^{+} = -1.33$ V vs SCE)[5a] and $[Cu(dap)_2]Cl$ (**45**) (oxidative quenching cycle: $Cu^{2+/}Cu^{+*} = -1.43$ V vs SCE)[5a] are strong enough for the reduction of $C_8F_{17}I$ (**6**) (–1.32 V vs SCE)[7] to generate a perfluoroalkyl radical **48**. This radical can then add to the alkene **12** to form carbon centered radical **49**. Subsequently the radical **49** can undergo a radical chain propagation by abstraction of iodine from $C_8F_{17}I$ (**6**) forming the desired product **13** and regenerating perfluoroalkyl radical **48** (Scheme 16, Path A). Alternatively, radical **49** can be oxidized by the photoredox catalyst forming carbocation **50** and regenerating the catalyst. This mechanistic pathway is closed by subsequent recombination of iodide and carbocation **50** giving rise to the desired ATRA compound **13** (Scheme 16, Path B). Both mechanistic pathways are not totally in agreement with the experimental results obtained for the iodoperfluoroalkylation of styrenes. On the one hand the radical chain mechanism (Scheme 16, Path A) appears not to be plausible because the corresponding thermally initiated reaction with AIBN showed only traces of the ATRA product (Table 1, entry 18). On the other hand the quantum yield[25] for this reaction catalyzed by $[Cu(dap)_2]Cl$ (**45**) or $[Cu(dap)Cl_2]$ (**47**) was determined to be 0.48 and 0.52, respectively, which is not characteristic for a radical chain propagation. However, the interpretations based on quantum yield should be considered very carefully as the analysis based on yield of the desired product and absorbed photons does not take into account the participation of other photomediated transformations that do not lead to the desired ATRA product (for detailed calculation of quantum yield see Experimental Part).[26]

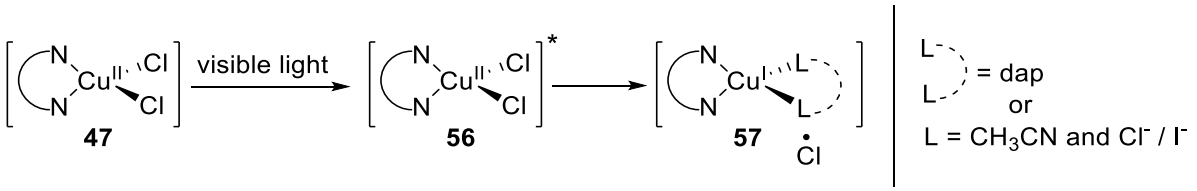


Scheme 16. Mechanistic pathways for the ATRA reaction of perfluoroalkyl iodide **6** and alkene **12**.[12a]

Moreover, the photoredox cycle with included oxidation of radical to the corresponding carbocation is not plausible due to the failure of $[Ru(bpy)_3]Cl_2$ in the transformation of styrene (**12a**) and $C_8F_{17}I$ (**6**) (Table 1, entries 1-4). The oxidation of benzyl radicals ($PhCH_2^+/PhCH_2^\bullet$ = +0.73 V vs SCE)[27] and ($PhCH^+CH_3$/ $PhCH^\bullet CH_3$ = +0.37 V vs SCE)[27] to the corresponding cations should be in principle possible by $[Ru(bpy)_3]Cl_2$ (reductive quenching cycle: Ru^{2+}/ Ru^+ = +0.77 V vs SCE)[5a]. As consequence, it can be assumed that the recombination of benzylic cation and iodide is not working well in this reaction, thus stopping the reaction at this stage of the transformation. This observation is in accordance with the competitive reaction of styrene (**12a**) and allyl alcohol (**43**) (Scheme 13 and Scheme 14).

As an alternative, two additional plausible mechanistic pathways can be described that are in agreement with the experimental observations. Again, the catalytic cycles start with single electron transfer from the photoexcited copper catalyst **51** to perfluroalkyl iodide **6** resulting in the formation of radical **48**, iodide and oxidized Cu(II) species **52** which undergoes a ligand dissociation process as was described earlier (*vide supra*). The analogy between the Cu(II)-species **52** and the stable and catalytically active $[Cu(dap)Cl_2]$ (**47**) is obvious (Scheme 15). Subsequent radical addition to alkene **12** forms the benzyl radical **49** which can undergo two different pathways, rebound mechanism (Scheme 16, Path C) and ligand transfer cycle (Scheme 16, Path D). The radical **49** can be trapped directly by the Cu(II)-center of complex **52** thus forming four coordinated Cu(III) species **53** which can undergo a reductive elimination to form the desired ATRA product **13** and $[Cu(dap)_2]Cl$ (**45**) (Scheme 16, Path C). Monomeric Cu(III)-complexes are known to have the favored coordination number four, whereas the five coordinated complexes are rare.[28] Alternatively, the intermediary radical **49** adds to the iodine ligand of Cu(II)-species **52**, with simultaneous homolytic Cu-I bond cleavage and the formation of ATRA compound **13** and regenerated copper(I)-complex **45** (Scheme 16, Path D). The considerations for the proposed mechanistic pathways base on the concepts of an inner sphere mechanism for copper-catalyzed transformations, which were described in the literature[29].

Finally, to understand the successful transformation of alkenes with $C_8F_{17}I$ (**6**) using $[Cu(dap)Cl_2]$ (**47**) following mechanistic proposal was developed (Scheme 17). When irradiated with visible light the photoexcited Cu(II)-complex **56** is formed which can undergo homolytic Cu(II)-Cl bond cleavage to form Cu(I) intermediate **57** and chlorine.[12c]

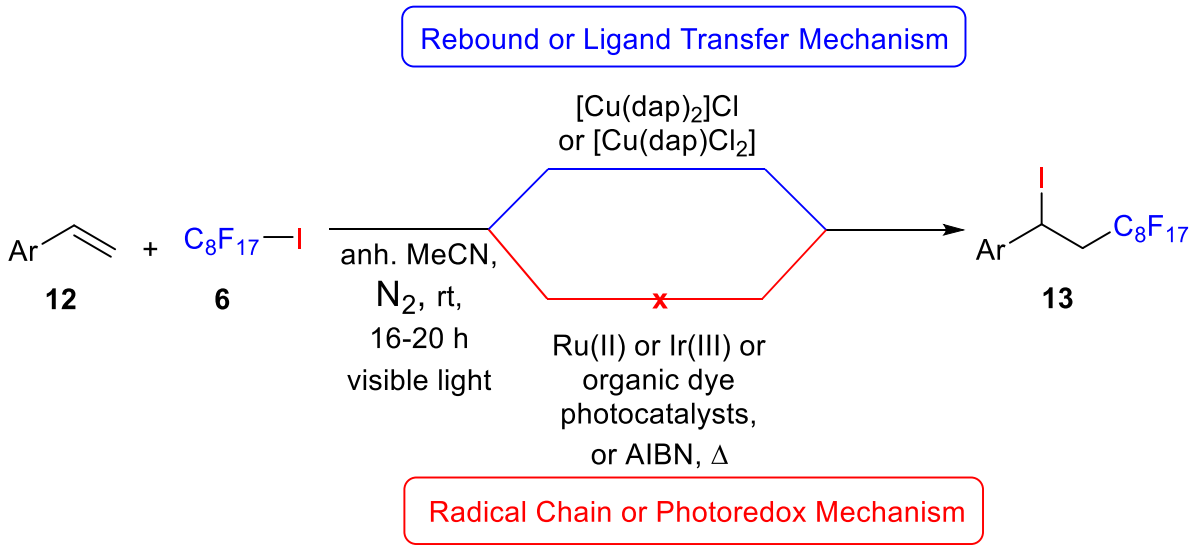


Scheme 17. Transformation of Cu(II)-catalyst **47** into catalytically active Cu(I)-species **57**.[12c]

The coordination of the newly formed copper species occurs by another dap ligand and chloride counteranion, thus resulting in the formation of catalytically active $[Cu(dap)_2]Cl$ (**45**) which can act as described in Scheme 16. Another possibility is the coordination of Cu(I)-center by solvent[30] or halides. Moreover, the transformation of Cu(II)-catalyst into the $[Cu(dap)_2]Cl$ (**45**) is a plausible explanation for the similarity of the obtained yields and diastereoselecivities for the most of the investigated substrates.

7. Summary

In summary, an efficient atom transfer radical addition (ATRA) reaction of perfluorooctyl iodide (**6**) with a broad range of alkenes and alkynes is described employing [Cu(dap)Cl_2] (**47**) as photocatalyst. The comparison with the results obtained with [Cu(dap)$_2$]Cl (**45**) showed similar yields and diastereoselectivities for the most of the substrates. Mechanistic studies for both catalytic systems provided an extensive proposal for the mechanistic behavior of the current ATRA reaction. The unique character of copper catalysts was shown by presenting two alternative mechanistic pathways: ligand transfer cycle with homolytic Cu-halide bond cleavage and a rebound mechanism including a Cu(III)-intermediate. These mechanisms are especially important for the explanation of the reaction with styrene derivatives that are not accessible substrates for thermally initiated AIBN reaction and photoredox catalyzed transformation with [Ru(bpy)$_3$]Cl_2.[12a] Moreover, the explanation for the successful Cu(II)-catalyzed process was proposed including homolytic Cu-Cl bond cleavage and the formation of the catalytically active Cu(I)-species.[12c]



Scheme 18. The unique mechanistic pathways of copper catalysts.[12a]

8. References

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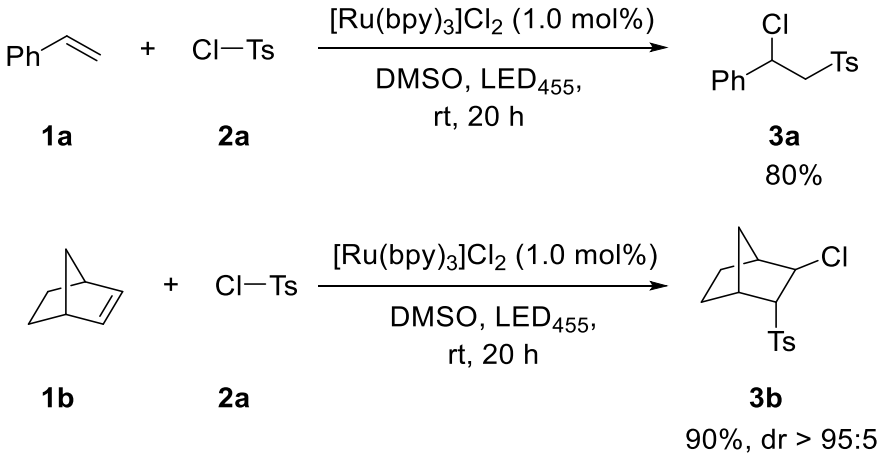
D. Copper Mediated Chlorosulfonylation of Alkenes‡

1. Introduction

Sulfones are important motifs in a variety of natural products and pharmaceuticals.[1] The importance of the direct introduction of this functional group is reflected by a broad range of publications.[1b-d, 2] The incorporation to the highly functionalized substrates can be challenging, making soft and non-destructive methods necessary. In recent years, photoredox catalysis with visible light became an important technique in the organic synthesis, demonstrating outstanding advantages in comparison with UV-light mediated reactions.[3] For example, irradiation of functionalized organic molecules with high energy UV-light in the worst case can destroy them before reacting in the desired way. Recent progress in the successful synthesis of important class of sulfones by visible-light mediated photoredox catalysis was described in several literature reports.[1b] In 2012 Stephenson and coworkers[4] demonstrated efficient ATRA reaction of tosyl chloride (**2a**) with styrene (**1a**) and norbornene (**1b**) (Scheme 1). The reactions showed high yields employing oxidative quenching cycle with no need for additives like sacrificial amines. However, only these two examples were presented.

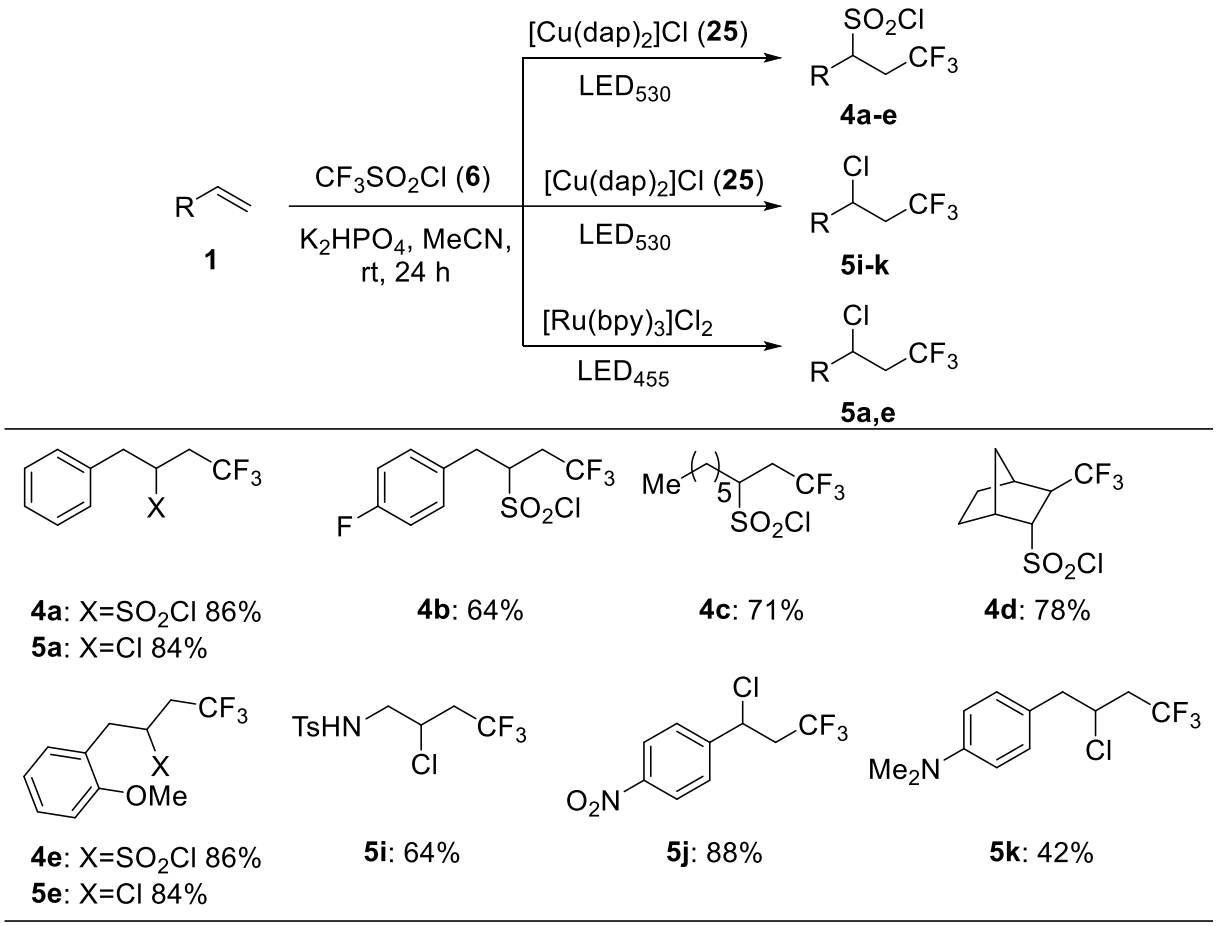


Scheme 1. Atom transfer radical addition reaction of tosyl chloride (**2a**) with styrene (**1a**) and norbornene (**1b**) by Stephenson and coworkers.[4]

In 2015, the unique character of copper-based photocatalysts was demonstrated by Reiser group in trifluoromethylchlorosulfonylation reaction of alkenes (Scheme 2).[5] In contrast to the $[Ru(bpy)_3]Cl_2$ catalyst which provided trifluoromethylchlorination products **5a** and **5e** $[Cu(dap)_2]Cl$ (**25**) was able to prevent the SO_2 excursion for a variety of substrates giving rise to trifluoromethylchlorosulfonylation products **4a**-**4e**.

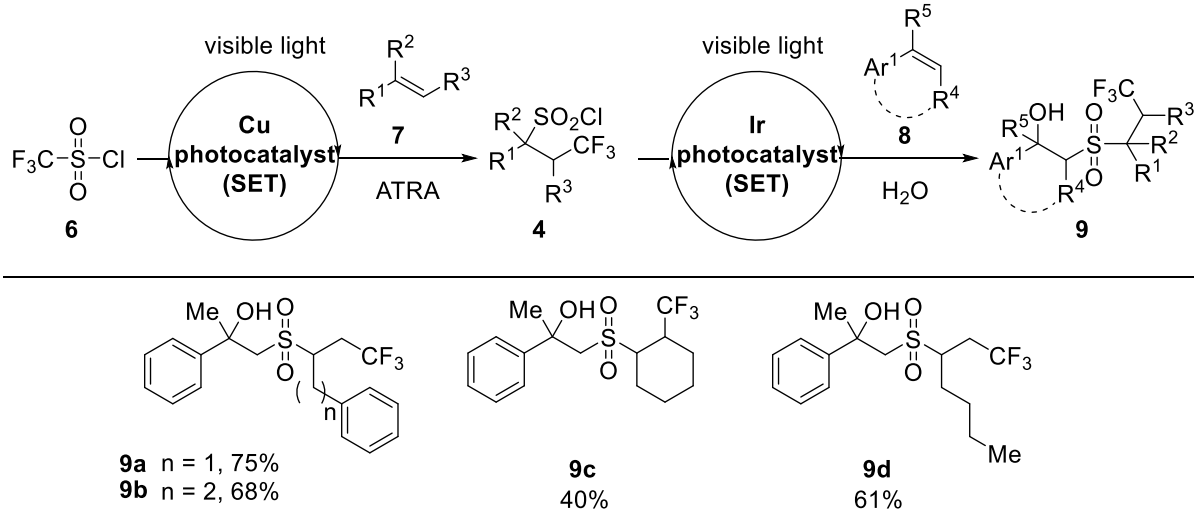
‡This chapter is partially based on Hossain, A.; Engl, S.; Lutsker, E.; Reiser, O., *ACS Catal.* **2019,** *9* (2), 1103-1109.

However, also with copper catalyst for some substrates only the trifluoromethylchlorination products **5i**-**5k** were obtained. The generation of sulfonylchloride products enabled interesting follow-up chemistry as was reported recently for the synthesis of substituted sultones.[6]



Scheme 2. Trifluoromethylchlorosulfonylation versus trifluoromethylchlorination of alkenes **1** by Reiser and coworkers[5].

Moreover, the exclusive formation of SO_2-products in the presence of copper-based photocatalyst was exploited to form sulfonyl chlorides **4** which were subsequently transformed into corresponding β-hydroxysulfones **9** via iridium-mediated photoreaction (Scheme 3).[7]



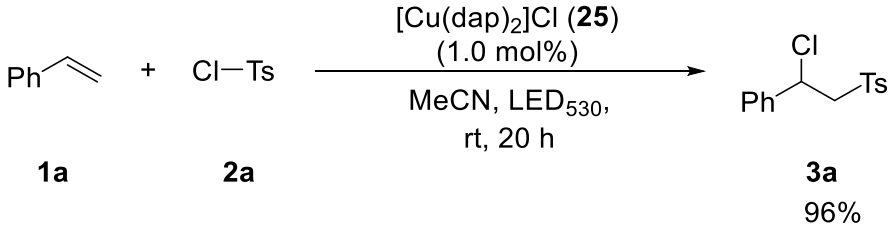
Scheme 3. Photoredox catalyzed synthesis of β-hydroxysulfones from sulfonyl chlorides by Reiser and coworkers[7].

This procedure was an outstanding demonstration for the consecutive formation of two C-S-bonds via photoredox catalysis, forming highly substituted sulfones.

Recently, the reaction conditions developed by Stephenson et al.[4] (Scheme 1) were used by Niu and Ni to explore the substrate scope of the ruthenium catalyzed chlorosulfonylation of alkenes.[8] However, only few successful transformations of unactivated alkenes were described and interestingly the results obtained for product **3a** were even not consistent with the results presented by Stephenson and coworkers. Moreover, for several examples only the elimination products were formed. Due to the ability of copper to provide successful chlorosulfonylation reaction of alkenes under thermal conditions as was demonstrated by the pioneering studies with CuCl and $CuCl_2$[9], the employment of copper catalyst as an alternative to ruthenium complex was promising. The aim of this chapter was the investigation of visible light mediated photoredox catalyzed chlorosulfonylation of alkenes using $[Cu(dap)_2]Cl$ (**25**) and $[Cu(dap)Cl_2]$ (**27**) photocatalysts demonstrating the unique character and advantages of copper-mediated photocatalysis.

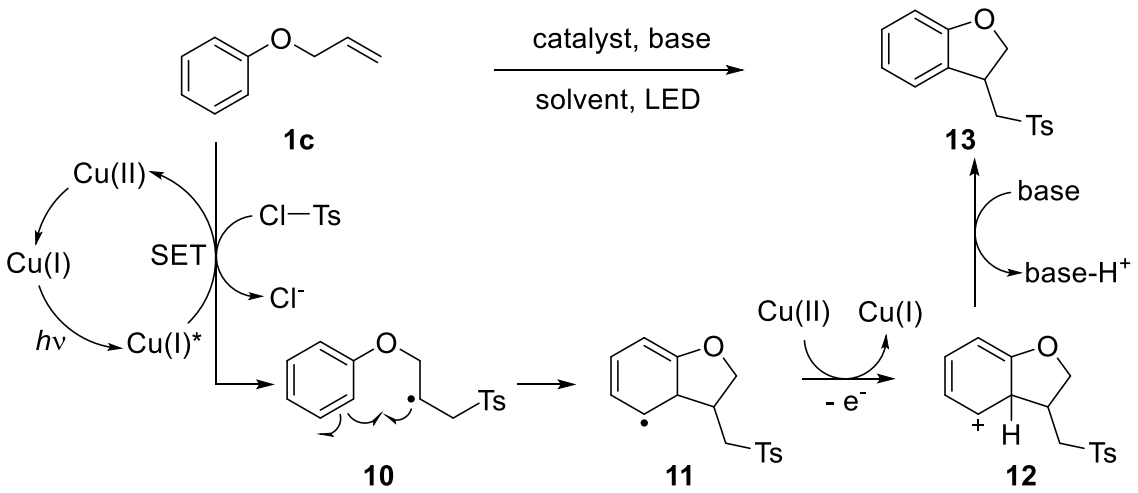
2. Preliminary Studies with Tosyl Chloride and Styrene or Allyl Phenyl Ether

The initial reaction for this project was a control experiment carried out during the study of the iodoperfluoroalkylation reaction of styrenes (chapter C). Due to the proposed mechanism of this reaction, including the impossibility of recombination between iodide and benzylic cation (for details see mechanistic discussion of chapter C), a plausible explanation was the HSAB concept, which describes the favorable reactions between Lewis acids and Lewis bases.[10] It was proposed that softer copper catalyst undergoes exclusively the rebound mechanism or ligand exchange pathway with the softer iodide and thus enables the creation of the carbon-iodine bond. Switching the anion from the softer iodide to the harder chloride should lead to a lower yield, which confirms the described assumption for copper catalysis. However, the reaction between styrene (**1a**) and tosyl chloride (**2a**) resulted in the formation of chlorosulfonylation product **3a** in excellent yield (Scheme 4). The comparison of the obtained results with the reported literature[4] showed a higher catalytic activity compared to the established $[Ru(bpy)_3]Cl_2$. The responsibility for the investigation of chlorosulfonylation reaction of styrene derivatives employing copper photocatalysis was then transferred to S. Engl as the project for his master thesis[11].



Scheme 4. Initial copper catalyzed chlorosulfonylation of styrene (**1a**).

Further investigation of the chlorosulfonylation reaction focused on unactivated alkenes, especially substrates which could possibly undergo a cyclization process forming heterocyclic products[12] (Scheme 5). For this purpose, allyl phenyl ether (**1c**) was synthesized according to the protocol described in the literature[13]. The idea for the cyclization reaction was based on the copper mediated photoinduced generation of sulfonyl radical, which can add to the alkene **1c** and forms the carbon-centered radical **10**. Due to the favorable intramolecular process, which should be faster compared to the intermolecular ATRA product formation, the radical **10** can cyclize into the aryl system to form compound **11** which is subsequently oxidized by Cu(II)-complex to regenerate the catalyst and to form cation **12**. Finally, the deprotonation of compound **12** leads to the rearomatization and the formation of the substituted 2,3-dihydrobenzofuran **13**. To ensure the success of the aromatization step base was added as an additive to the reaction mixture.

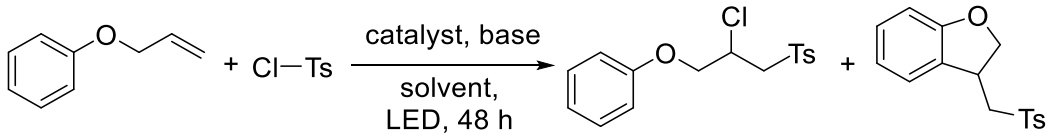


Scheme 5. Proposed photomediated cyclization reaction.

The investigation of the photomediated process started with the reaction of 2.0 equivalents allyl phenyl ether (**1c**) and 1.0 equivalent tosyl chloride (**2a**) in the presence of 1.0 equivalent $NaHCO_3$ and $[Cu(dap)_2]Cl$ (**25**) in MeCN under irradiation with green LED (Table 1, entry 1). This reaction gave no desired cyclization product **13** but only the ATRA product **3c** in 15% yield. When different alkali metal carbonates were employed as additives no cyclization product could be obtained, but the yield of the ATRA product **3c** was interesting. While lithium carbonate (entry 2) and potassium carbonate (entry 4) showed only 23% and 11% yield respectively, the reaction with caesium carbonate showed no product formation at all (entry 5). Surprisingly, the reaction with sodium carbonate delivered the ATRA product in 78% yield (entry 3). These results are unexpected as the basicities of these alkali metal carbonates do not differ much. Further increase of basicity by employing NaOH as base resulted in no product formation (entry 6), whereas low yield of the addition product **3c** was obtained by using organic amine base (entry 7). In order to understand the reason for the strongly increased product yield when using sodium carbonate, two experiments were carried out. On the one hand when sodium chloride as sodium source was used no conversion was observed, thus indicating the need of a basic additive (entry 8). On the other hand, when sodium chloride was used in combination with potassium carbonate only 13% yield was obtained (entry 9). This result shows, that the function of sodium carbonate in the successful transformation does not only refer to its behaviour as sodium and as a base source. Interestingly, reducing the amount of the base to 0.2 equivalents resulted in lower yield (entry 10) and when no base was added to the reaction mixture no conversion of the starting material was observed (entry 11). This result is curious due to the fact, that several other ATRA reactions catalyzed by $[Cu(dap)_2]Cl$ (**25**) were carried out successfully without addition of base. Furthermore, it was not possible to reduce the reaction time from 48 h to 24 h resulting in only 46 % yield (entry 12). When the amount of alkene **1c** was decreased to only 1.0 equivalent or 2.0 equivalents of TsCl (**2a**) were used, the yield dropped to 43% and 49%, respectively (entries 13 and 14). Next, the light

source for the irradiation was switched from a green LED (λ_{max} = 530 nm) to a blue LED (λ_{max} = 455 nm), generating slightly lower yield of the desired product **3c** (entry 15). Variation of the solvents demonstrated that the reaction did not work in DMF and DMSO (entries 16 and 17), whereas only low amounts of the ATRA product **3c** were formed in CH_2Cl_2 (entry 18). Furthermore, different catalytic systems were employed in the current reaction.

Table 1. Determination of optimal reaction conditions.



1c **2a** **3c** **13**

Entry	Conditions	Product **3c**[a]	Product **13**[a]
1	$NaHCO_3$ (1.0 equiv)	15	0
2	Li_2CO_3 (1.0 equiv)	23	0
3	Na_2CO_3 (1.0 equiv)	78	0
4	K_2CO_3 (1.0 equiv)	11	0
5	Cs_2CO_3 (1.0 equiv)	0	0
6	NaOH (1.0 equiv)	0	0
7	NEt_3 (1.0 equiv)	6	0
8	NaCl (1.0 equiv)	0	0
9	K_2CO_3 (1.0 equiv) + NaCl (1.0 equiv)	13	0
10	Na_2CO_3 (0.2 equiv)	61	0
11	no base	0	0
12	24 h	46	0
13	TsCl (2.0 equiv)	43	0
14	alkene (1.0 equiv)	49	0
15[b]	455 nm LED	64	0
16	DMF	0	0
17	DMSO	0	0
18	CH_2Cl_2	24	0
19	$[Cu(dap)Cl_2]$ (**27**) (1.0 mol%)	76	0
20	CuCl (10 mol%)	2	0
21[b]	$[Ru(bpy)_3]Cl_2$ (1.0 mol%)	31	0
22[b]	$[Ru(bpy)_3]Cl_2$ (1.0 mol%) + Na_2CO_3 (1.0 equiv)	32	0
23[b]	*fac*-Ir(ppy)$_3$ (1.0 mol%)	28	0
24[b]	*fac*-Ir(ppy)$_3$ (1.0 mol%) + Na_2CO_3 (1.0 equiv)	26	0
25	no catalyst	0	0
26	no light	0	0

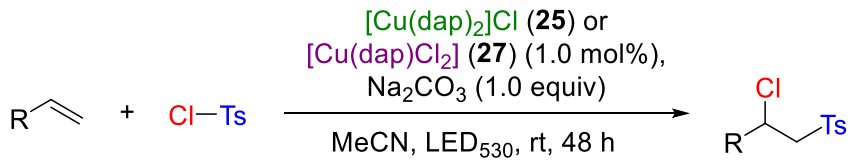
Reaction conditions: alkene **1c** (1.0 mmol, 2.0 equiv), TsCl (**2a**) (0.5 mmol, 1.0 equiv), Na_2CO_3 (1.0 equiv), $[Cu(dap)_2]Cl$ (**25**) (1.0 mol%) in MeCN (anh., degassed, 2.0 mL), irradiation at 530 nm (green LED) for 48 h. [a]Determined by NMR with diphenoxymethane as an internal standard. [b]Irradiation at 455 nm (blue LED).

When the copper(II)-catalyst $[Cu(dap)Cl_2]$ (**27**) was used, the desired ATRA product **3c** was obtained in 76% yield (entry 19), whereas the reaction with CuCl in the absence of dap ligand gave only trace amounts of the product (entry 20). The reactions with $[Ru(bpy)_3]Cl_2$ in the

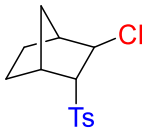
presence and in the absence of equimolar amount of sodium carbonate delivered product **3c** in only low yields (entries 21 and 22). Similar results were obtained when *fac*-Ir(ppy)$_3$ was used (entries 23 and 24). Moreover, the control experiments without the catalyst as well as with no light showed no conversion of the starting material indicating the photoredox character of the investigated reaction. Although the formation of the desired cyclization product was not observed for any entry, particularly the comparison of copper catalysts with [Ru(bpy)$_3$]Cl$_2$ and *fac*-Ir(ppy)$_3$ demonstrated interesting results. Furthermore, the unique role of sodium carbonate in this transformation was curious.

3. Substrate Scope

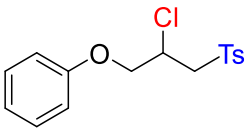
With the optimized reaction conditions in hand the substrate scope for the atom transfer radical addition reaction of sulfonyl chlorides with unactivated alkenes was explored employing both [Cu(dap)$_2$]Cl (**25**) and [Cu(dap)Cl$_2$] (**27**) photocatalysts (Scheme 6). The product **3c** which was also used for the screening reactions was isolated in 73% and 70% yield. Employing allyl benzene (**1d**) as substrate in the presence of copper(I)-catalyst **25** provided the desired product **3d** in 86% yield, whereas with copper(II)-catalyst **29** a slightly lower yield was obtained. When the *N*-Boc protected allylamine **1e** was submitted to the reaction conditions high yields of 75-80% for the desired product **3e** were observed. The successful transformation of allyl alocohol (**1f**) to the corresponding ATRA product **3f** demonstrated high functional group tolerance towards free hydroxy groups. Moreover, 1-octen (**1g**) as representative of substrates with a long alkyl chain showed very good yields for both catalytic systems. The primary bromide **1h** was a feasible substrate for the photoredox catalyzed reaction forming the desired ATRA product **3h** in very good yield. To achieve the full consumption of the starting material, it was necessary to increase the amount of alkene from 2.0 equivalents to 4.0 equivalents. In contrast to the obtained result for allyl alcohol (**1f**), when 2-allylphenol (**1i**) was applied to the present reaction no photoproduct formation was observed. This observation can be explained by the stronger acidity of phenol compared to the allyl alcohol (**1f**), thus leading to the fast acid-base reaction between phenol **1i** and sodium carbonate. The consumption of sodium carbonate results in low activity of the catalyst and in this way the slower photoreaction is blocked. To solve this problem and to verify the explanation, 2-allylphenol (**1i**) was methylated according to the procedure described in the literature[14]. The obtained substrate **1j** was transformed in the presence of [Cu(dap)$_2$]Cl (**25**) and [Cu(dap)Cl$_2$] (**27**) to the desired ATRA product **3j** in 83% and 69% yield, respectively.



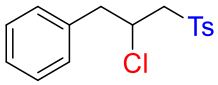
1 **2a** **3**



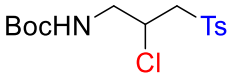
3b
91% 80%



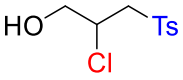
3c
73% 70%



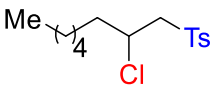
3d
86% 74%



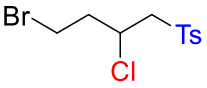
3e
80% 75%



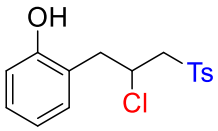
3f
77% 72%



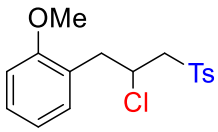
3g
84% 86%



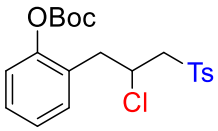
3h
96%[a] 86%[a]



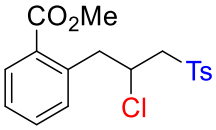
3i
0% 0%



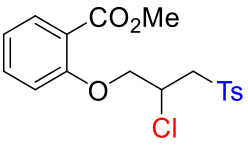
3j
83% 69%



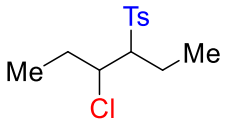
3k
53% (77% brsm)[b]
35% (57% brsm)[b]



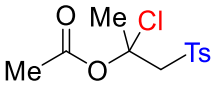
3l
57% (74% brsm)[b]
69% (78% brsm)[b]



3m
52% (73% brsm)[b]
76% (83% brsm)[b]



3n
0% 0%

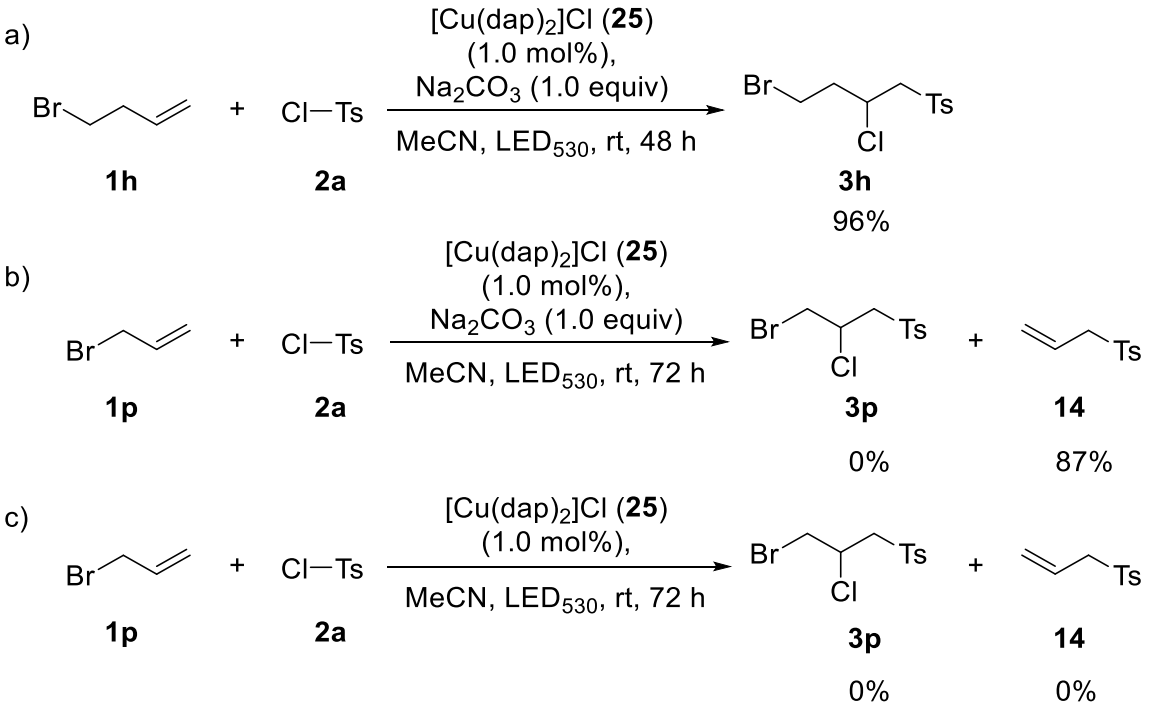


3o
0% 0%

Scheme 6. Substrate scope for the visible light mediated chlorosulfonylation of unactivated alkenes. *Reaction conditions*: alkene **1** (1.0 mmol, 2.0 equiv), TsCl (**2a**) (0.5 mmol, 1.0 equiv), Na_2CO_3 (1.0 equiv), $[Cu(dap)_2]Cl$ (**25**) or $[Cu(dap)Cl_2]$ (**27**) (1.0 mol%) in MeCN (anh., degassed, 2.0 mL), irradiation at 530 nm (green LED) for 48 h. [a]Alkene (2.0 mmol, 4.0 equiv). [b]Reaction time 72 h.

The variation of the *O*-protecting group showed, that when the substrate with the sterically demanding Boc-group[15] was used, the yields for both catalysts dropped dramatically. In both cases even after 72 h no full conversion of the starting material was achieved, thus leading to the reisolation of the remained substrate **1k**. The yields based on the recovered starting material are given in parenthesis. Moreover, no full conversion was obtained when the products **3l** and **3m** were synthesized. For both substrates $[Cu(dap)Cl_2]$ (**27**) showed higher isolated yields, but the analysis of the yield based on recovered starting material revealed quite similar results fo both catalytic systems. When norbornene (**1b**) was employed as the starting material the corresponding ATRA product **3b** was obtained in very good yields. Similar results

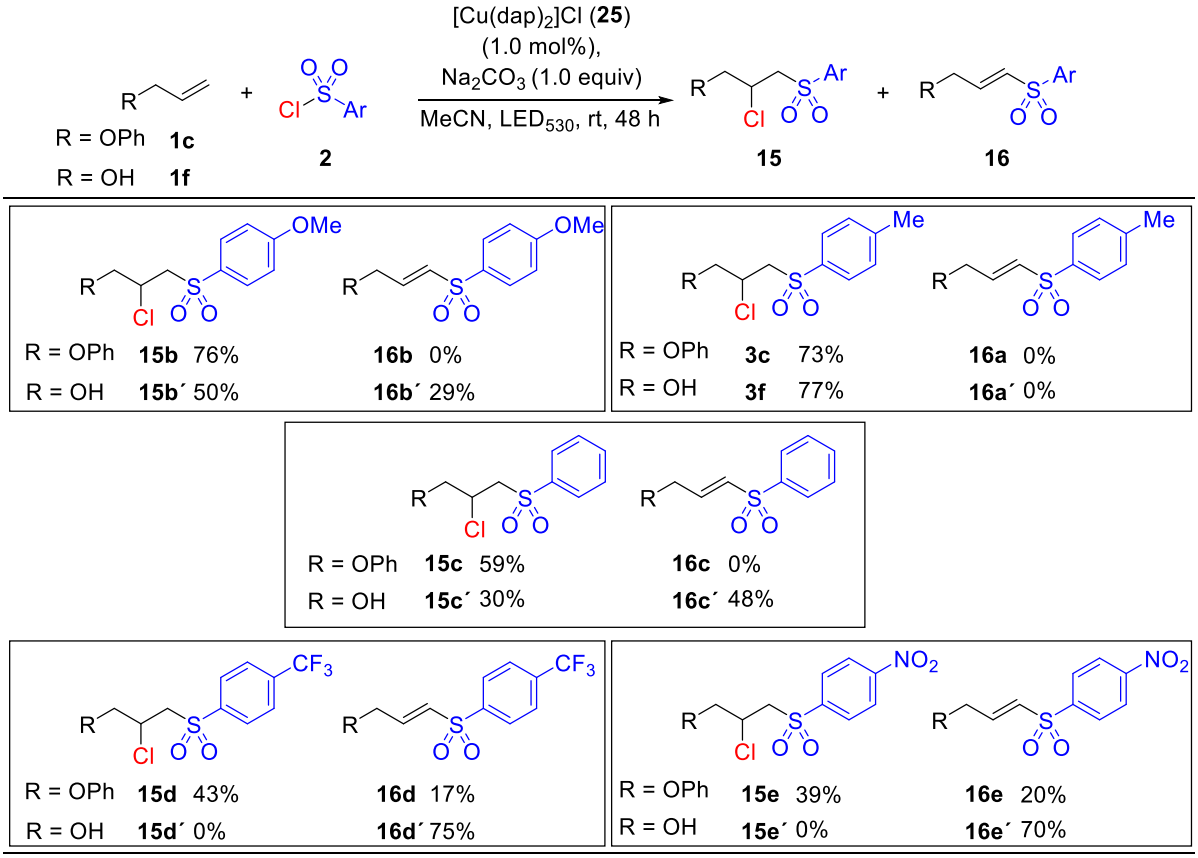
were observed by Stephenson et al. using $[Ru(bpy)_3]Cl_2$, indicating that the high ring strain in norbornene[16] facilitates the atom transfer radical addition reaction. Besides, two additional unsuccessful transformations were performed. The developed protocol does not tolerate internal alkenes e.g. 3-hexene (**1n**) and vinyl esters like prop-1-en-2-yl acetate (**1o**). Interestingly, when the reaction was carried out using allyl bromide (**1p**) instead of 4-bromobut-1-ene (**1h**) full conversion of the starting material but no ATRA product formation were observed (Scheme 7, reaction b). The obtained product was identified as the allylsulfone **14** which was obtained in 87% yield. Carrying out the reaction without adding sodium carbonate showed no conversion of the starting material (Scheme 7, reaction c). Since both allyl bromide (**1p**) and tosyl chloride (**2a**) are electrophiles, a simple nucleophilic attack can be excluded as the reason for the formation of product **14**. Further investigations of this allylation reaction are shown in chapter E.



Scheme 7. Allyl bromide (**1p**) as substrate for the ATRA reaction.

Similarly to the comparison of the results between $[Cu(dap)_2]Cl$ (**25**) and $[Cu(dap)Cl_2]$ (**27**) in chapter C no clear differences in yield were observed for the chlorosulfonylation reaction of unactivated alkenes. Due to this fact, the variation of sulfonyl chlorides **2** was carried out focusing on $[Cu(dap)_2]Cl$ (**25**) photocatalyst (Scheme 8). The reactions were carried out once with allyl phenyl ether (**1c**) and with allyl alcohol (**1f**) in order to test the functional group tolerance towards different sulfonyl chlorides. When the reaction was carried out with *O*-protected alkene **1c** and electron rich 4-methoxybenzenesulfonyl chloride (**2b**) the desired ATRA product **15b** was obtained in 76% yield, whereas the reaction of unprotected allyl alcohol

(**1f**) with this sulfonyl chloride showed only 50% yield of the ATRA product **15b´** and additional 29% of the elimination product **16b´**. Surprisingly, decreasing the electronic densitiy in the aryl ring by using 4-methylbenzenesulfonyl chloride (**2a**) resulted only in the formation of ATRA products **15a** and **15a´** in good yields for both employed alkenes with no generation of elimination compounds. This result is unexpectable because the acidity of the proton next to the sulfonyl moiety should be increased by a lower electronic density of the aryl ring. Next, phenylsulfonyl chloride (**2c**) was used as ATRA reagent bearing no functional group which can influence the electronic density in the aryl ring. The reaction of allyl phenyl ether (**1c**) with this sulfonyl chloride gave the desired ATRA compound **15c** in 59% yield with no formation of elimination product **16c**. In contrast the reaction of alcohol **1f** provided the product **15c´** in only 30% yield with additional 48% of the alkene **16c´**.



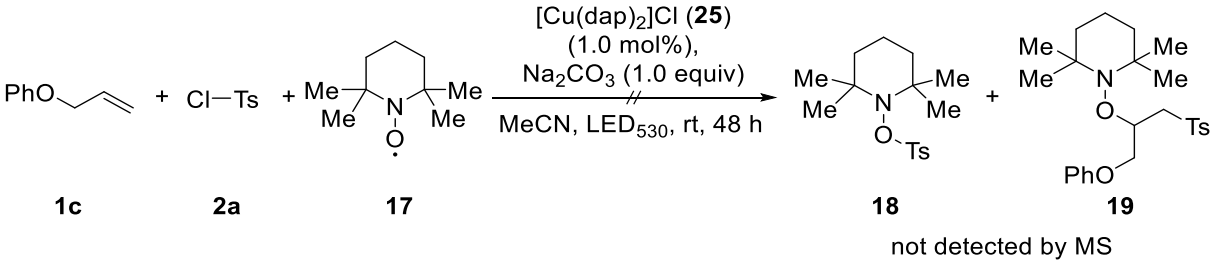
Scheme 8. Variation of sulfonyl chlorides **2** for the ATRA reaction with unactivated alkenes **1c** and **1f**. *Reaction conditions*: alkene **1c** or **1f** (1.0 mmol, 2.0 equiv), sulfonyl chloride **2** (0.5 mmol, 1.0 equiv), Na_2CO_3 (1.0 equiv), $[Cu(dap)_2]Cl$ (**25**) (1.0 mol%) in MeCN (anh., degassed, 2.0 mL), irradiation at 530 nm (green LED) for 48 h.

Moreover, when electron withdrawing CF_3 group was employed in combination with allyl phenyl ether (**1c**), 17% of the elimination product **16d** and 43% of ATRA product **15d** were obtained. Interestingly, when allyl alcohol (**1f**) was employed in the reaction with 4-trifluoromethylbenzenesulfonyl chloride (**2d**) the formation of the elimination product **16d´** occurred selectively with 75% yield. Further increase of the electron withdrawal by introducing

nitro group in *para*-position resulted in the formation of both the ATRA product **15e** and elimination product **16e** in 39% yield and 20% yield, respectively. Again, the reaction of allyl alcohol (**1f**) showed only the generation of the alkene **16e´** in 70% yield. The formation of the elimination products can be favored by the initial deprotonation of the free hydroxy group of allyl alcohol which can easily abstract the acidic proton next to the sulfonyl group. This effect is enhanced when electron withdrawing groups are present which can stabilize the resulting anion. The easy elimination of hydrochloric acid in chlorosulfonylated products was demonstrated by S. Engl[11] thus underlining the acidic character of this compound class. The amount of the elimination product rises from electron rich to electron poor substrates. However, the result obtained with tosyl chloride (**2a**) is not in accordance wih this proposal, thus indicating additional mechanistic reasons responsible for the elimination process.

4. Mechanistic Studies

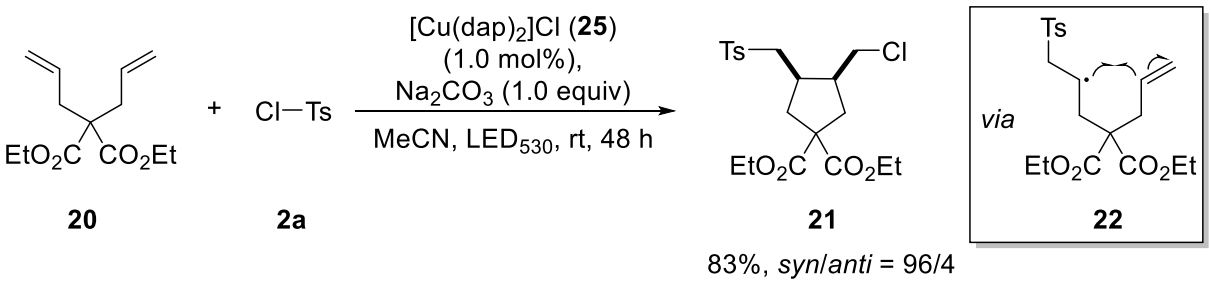
In order to get a deeper insight into the mechanism of the photoinduced chlorosulfonylation reaction several mechanistic studies were performed in cooperation with S. Engl and A. Hossain. To bring the reaction in line with a radical pathway of the chlorosulfonylation reaction, the radical trapping experiment with TEMPO (**17**) was carried out. However, no radical could be trapped during this reaction (Scheme 9). Conceivably, the basic reaction conditions lead to the decomposition of the formed TEMPO trapping products **18** and **19**. In contrast, S. Engl observed the formation of benzylic radical, when the reaction of styrene (**1a**) with tosyl chloride (**2a**) in the presence of TEMPO (**17**) was investigated.[11]



Scheme 9. Radical trapping experiment using TEMPO (**17**).

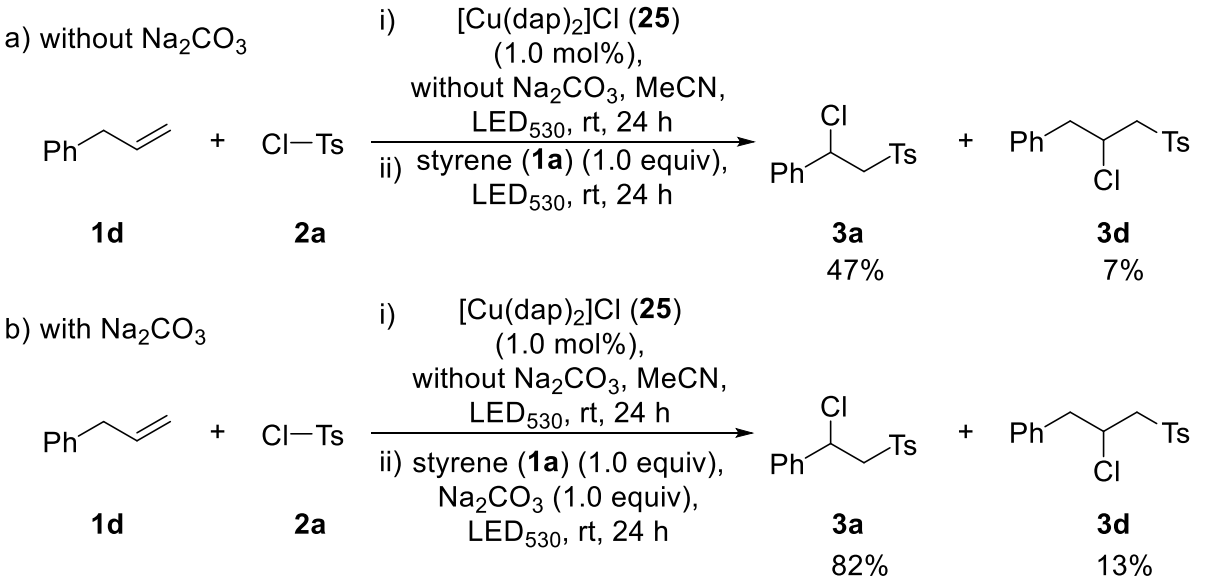
Furthermore, when diallyl ester **20** was applied to the optimized reaction conditions the cyclic product **21** was obtained in 83% yield and excellent *syn*/*anti* ratio of 96:4 (Scheme 10). The cyclization occurs by addition of the formed tosyl radical to the double bond of substrate **20** forming free intermediary radical **22**. This radical can undergo a 5-*exo*-*trig* cyclization to form substituted cyclopentane **21**. Another evidence for the free radical pathway was delivered by S. Engl, when he carried out the radical clock experiment. Moreover, he demonstrated the ligand dissociation during the ATRA process and determined the quantum yield of the reaction to be 9%.[11] These results were in accordance with the experimental data which were obtained

for the iodoperfluoroalkylation reaction (see chapter C), thus indicating analogue inner sphere mechanisms.[17]



Scheme 10. Light promoted radical cyclization reaction.

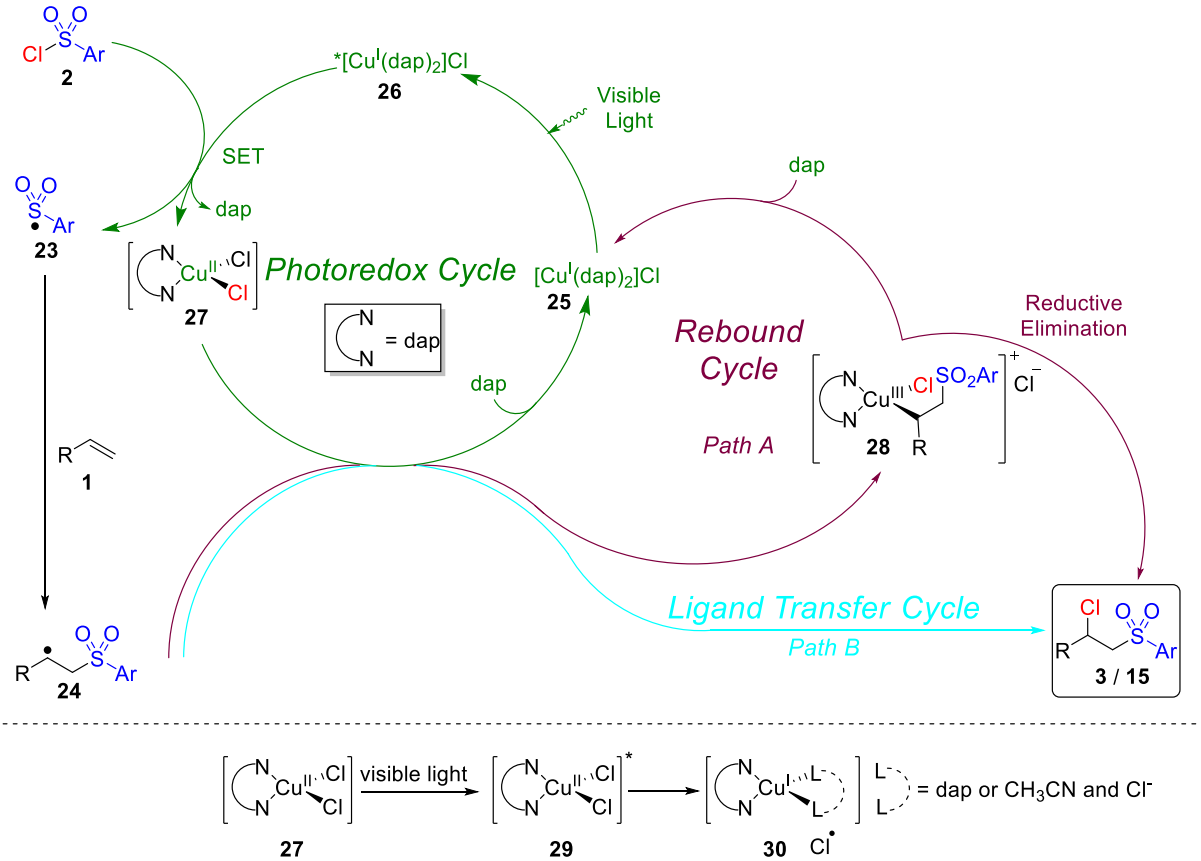
Finally, the role of sodium carbonate, which has also been shown to be beneficial in other reported copper mediated photoredox catalyzed transformations towards alkylsulfones[5, 18], was investigated by A. Hossain.[19] For this purpose he used allyl benzene (**1d**) under standard reaction conditions without adding sodium carbonate (Scheme 11, reaction a, conditions i). After 24 h styrene (**1a**) was added and the reaction mixture was stirred for additional 24 h (Scheme 11, reaction a, conditions ii). The NMR analysis of reaction mixture detected the ATRA products **3a** and **3d** in 47% yield and 7% yield, respectively. The yield obtained for product **3a** is much lower compared to the reaction of styrene (**1a**) with tosyl chloride (**2a**) (Scheme 4), thus suggesting poisoning of the catalyst in the presence of unactivated alkenes without sodium carbonate. When the reaction was repeated, but Na_2CO_3 was added in combination with styrene (**1a**) (Scheme 11, reaction b, conditions ii) both ATRA products were obtained in higher yields. These results indicate the protective or regenerative character of the sodium carbonate for the copper catalyst. The higher yields for product **3a** can be explained by a higher reactivity of styrene compared to unactivated alkene (*cf*. chapter C).



Scheme 11. Mechanistic studies carried out by A. Hossain.[19]

5. Proposed Mechanism

With all the experimental results in hand the mechanism of chlorosulfonylation reaction of alkenes can be described as follows. The presence of radical chain mechanism can be excluded through the failure of performing the reaction under thermal conditions in the presence of AIBN[11, 19] and a quantum yield of 9%[11, 19] which is not characteristic for a radical chain propagation. However, the interpretations based on quantum yield should be taken very carefully into account because the analysis based on yield of the desired product and absorbed photons does not consider the participation of other photomediated transformations that do not lead to the desired ATRA product.[20] Since Stephenson et al.[4] demonstrated that $[Ru(bpy)_3]Cl_2$ (oxidative quenching cycle: Ru^{3+}/Ru^{2+*} = -0.81 V vs SCE)[21] is capable to generate sulfonyl radical (Scheme 1), both the highly reductive *fac*-$Ir(ppy)_3$ (oxidative quenching cycle: Ir^{4+}/Ir^{3+*} = -1.73 V vs SCE)[21] and $[Cu(dap)_2]Cl$ (**25**) (oxidative quenching cycle: $Cu^{2+/}Cu^{+*}$ = -1.43 V vs SCE)[21] should also be able to generate this radical. However, the simple back electron transfer mechanism, including oxidation of the radical to cation is also not plausible, due to the low yields obtained with highly oxidative $[Ru(bpy)_3]Cl_2$ (oxidative quenching cycle: Ru^{3+}/ Ru^{2+} = +1.29 V vs SCE)[21] and *fac*-$Ir(ppy)_3$ (oxidative quenching cycle: Ir^{4+}/ Ir^{3+} = +0.77 V vs SCE)[21] compared to $[Cu(dap)_2]Cl$ (**25**) (Cu^{2+}/ Cu^{+} = +0.62 V vs SCE)[21]. In the similar way as described in chapter C for iodoperfluoroalkylation reaction, two plausible mechanisms can be proposed as follows (Scheme 12).[17] After single electron transfer from the photoexcited copper catalyst **26** to sulfonyl chloride **2** sulfur-centered radical **23** is formed which adds to alkene **1** to give carbon-centered radical **24**. As the consequence of the catalyst oxidation one dap ligand is replaced by two chlorines forming the copper(II)-species **27**. Radical **24** can now undergo two different pathways, rebound mechanism (Scheme 12, Path A) and ligand transfer cycle (Scheme 12, Path B). In the rebound pathway radical **24** adds directly to Cu(II)-center of **27** forming Cu(III)-species **28** with coordination number four (Scheme 12, Path A). Monomeric Cu(III)-complexes are known to have the favored coordination number four, whereas the five coordinated complexes are rare.[22] For this purpose, one chloride leaves the coordination sphere of copper and acts as counteranion. Subsequent reductive elimination provides the desired ATRA product **3** / **15** and regenerates $[Cu(dap)_2]Cl$ (**25**) photocatalyst.

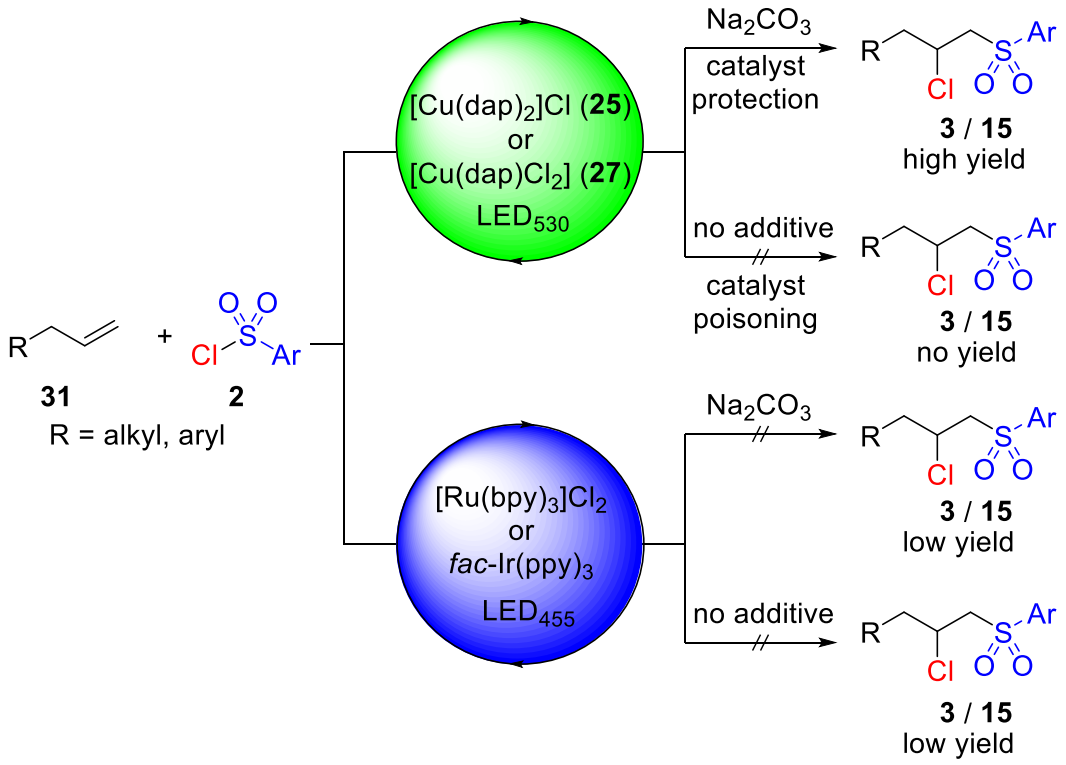


Scheme 12. Proposed mechanism for the chlorosulfonylation reaction of alkenes.

Alternatively, the intermediary radical **24** adds to the chlorine ligand of Cu(II) complex **27**, thus forming the desired product **3** / **15** through a homolytical copper-chlorine bond cleavage and regenerating [Cu(dap)$_2$]Cl (**25**) (Scheme 12, Path B). Similarly to the discussion in chapter C, the mechanistic pathway for [Cu(dap)Cl$_2$] (**27**) is described to start with photoexcitation and generation of Cu(II)-complex **29** This complex can undergo homolytic Cu(II)-Cl bond cleavage to form Cu(I)-species **30** and chlorine.[19] In the new formed complex **30** another dap ligand, solvent[23] or halide coordinate to the copper center and chloride acts as counteranion, thus forming the catalytically active Cu(I)-species **30**. The transformation of Cu(II)-catalyst **27** into Cu(I)-species **30** is a plausible way to explain the similarity of the obtained yields for both catalytic systems.

6. Summary

In summary, an efficient protocol for chlorosulfonylation of unactivated alkenes was described. Compared to the commonly used photocatalysts $[Ru(bpy)_3]Cl_2$ and *fac*-$Ir(ppy)_3$ the employed copper catalysts $[Cu(dap)_2]Cl$ (**25**) and $[Cu(dap)Cl_2]$ (**27**) demonstrated higher yields with excellent functional group tolerance. However, for the successful transformation the addition of equimolar amount of sodium carbonate was crucial. In collaboration with S. Engl and A. Hossain plausible inner sphere mechanisms were proposed and verified by various mechanistic experiments thus underlining the unique attributes of copper catalysts in photoredox catalysis. The use of the inorganic base was determined to have protective or regenerative function for the copper catalyst.[19]



Scheme 13. Copper mediated photoredox catalyzed chlorosulfonylation of unactivated alkenes.

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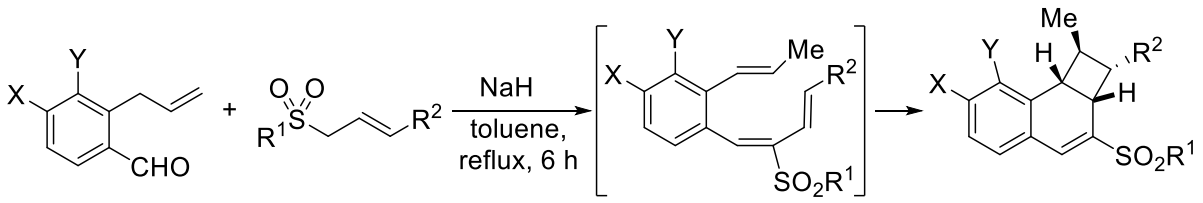
E. Copper Mediated Light Promoted Synthesis of Allylsulfones

1. Introduction

A variety of natural products and phamaceuticals contain sulfone key structures[1] including cyclic allyl sulfones which are known to act as antibacterial agents.[2] In organic synthesis allyl sulfones play a relevant role as synthetic building blocks due to the unique properties of this substrate class. For example the allyl sulfones have electrophilic character and can react as equivalents to a 1,3- or 1,1-dipoles as demonstrated by Trost and coworkers.[3] Under basic conditions the carbon next to the sulfonyl group can be deprotonated to produce a nucleophile that can undergo coupling reactions or Julia olefinations.[1a, 4] In general, allyl sulfone nucleophiles can add to carbonyls or other electrophiles, thus acting as building blocks for example in the synthesis of polycyclic products[5] as shown in Scheme 1 or heterocycles[6].



1 **2** **3** **4**

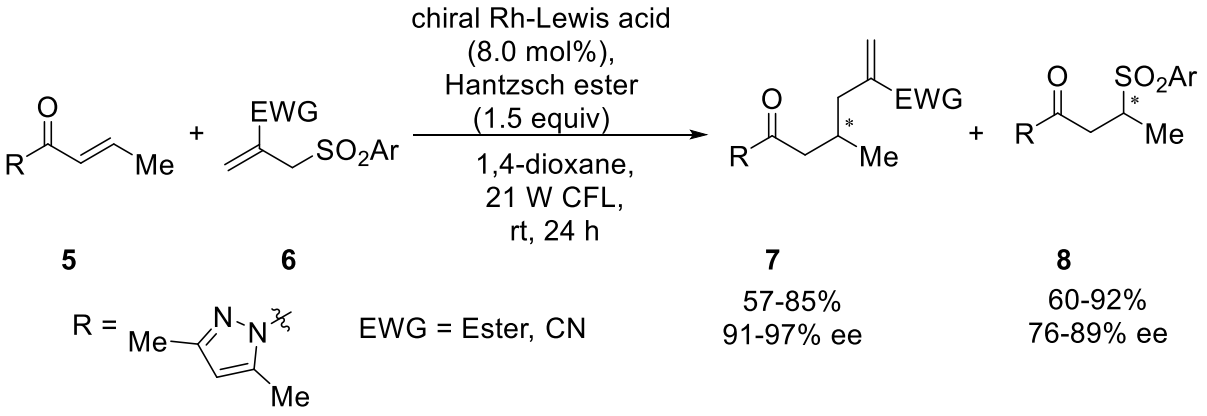
X, Y = MeO, BnO, *c*-C_5H_9O

R^1, R^2 = alkyl, aryl

75-87%

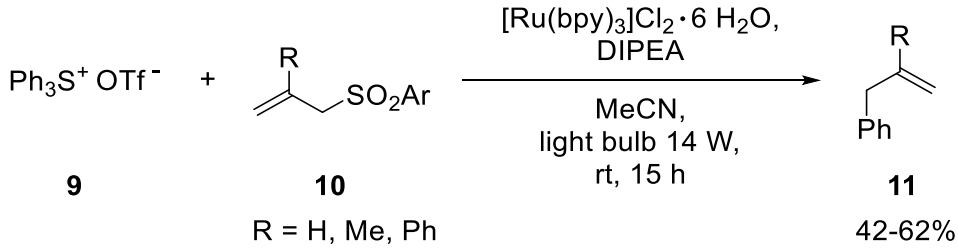
Scheme 1. Allylsulfones as building blocks in the synthesis of polycyclic compounds by Chang and coworkers.[5]

In 2017 Meggers et al.[7] presented enantioselective addition of allylsulfones to α,β-unsaturated double bonds employing chiral Rhodium-Lewis acid and Hantzsch ester under irradiation with 21 W compact fluorescent lamp (CFL) (Scheme 2). In this reaction the allylsulfone **6** was used as a nucleophile providing the desired products **7** and **8** in good yield and high enantiomeric excess. Further examples for enantioselective synthesis employing allyl sulfones are described in the literature[8].



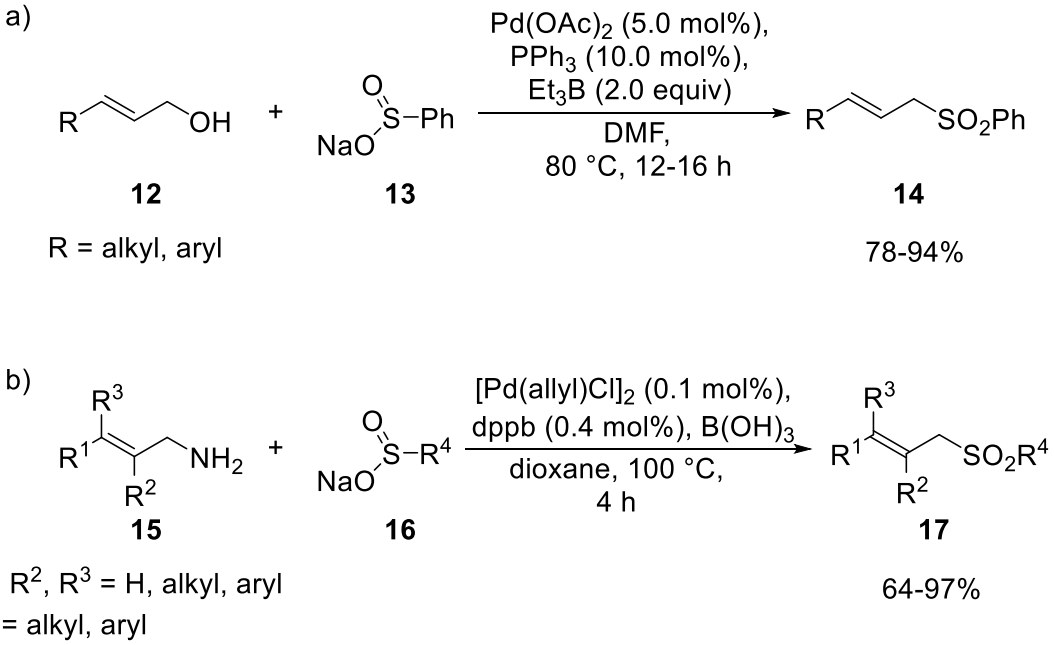
Scheme 2. Synthesis of chiral compounds using allylsulfones as nucleophiles reported by Meggers and coworkers.[7]

Moreover, allylsulfones can be used in radical allylation reactions as demonstrated by Fensterbank and coworkers[9]. In this reaction sulfone moiety acts as a leaving group after the addition of aryl radical to the double bond of the allyl group, thus enabling the formation of monoallylated arenes **11** (Scheme 3).



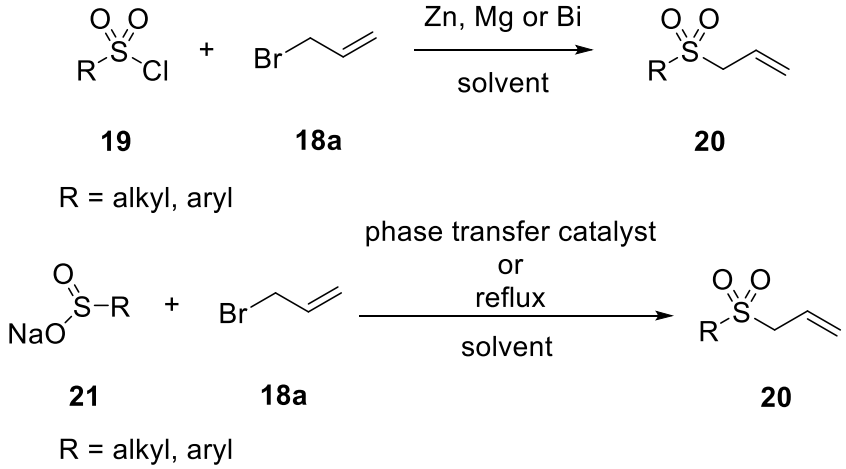
Scheme 3. Photoredox catalyzed addition of aryl radicals to allyl sulfones by Fensterbank and coworkers[9].

The most commonly used strategy for the synthesis of allyl sulfones is the oxidation of corresponding sulfides with peracids or with tetra-*n*-butylammonium oxone.[10] Furthermore, the compound class of allylsulfones can be obtained by palladium catalyzed reactions of allyl alcohols[11] (**12**) and allyl amines[12] (**15**) with oxcess of sodium sulfinates (Scheme 4). In these reactions the boron-based lewis acids coordinate to the hydroxy or amine moieties and enable the formation of Pd-coordinated allyl cation which is finally attacked by sulfinate **13**/**16** as a nucleophile to form the allyl sulfones **14** and **17**.



Scheme 4. Pd-catalyzed synthesis of allylsulfones starting from allyl alcohols[11] and allyl amines[12].

Furthermore, the generation of allyl sulfones from allyl bromide can be usually achieved through two synthetic strategies (Scheme 5): First, initial transformation of allyl bromide (**18a**) to the corresponding metal organyl, using zinc[13], magnesium[14] or bismuth[10], can be used for the subsequent nucleophilic attack on sulfonyl chlorides **19** to form the final product (Scheme 5, upper part). Secondly, sodium sulfinate **21** can be employed as nucleophile in the direct reaction with allyl bromide (**18a**) under reflux[15] or in the presence of phase transfer catalyst[16] (Scheme 5, bottom part).

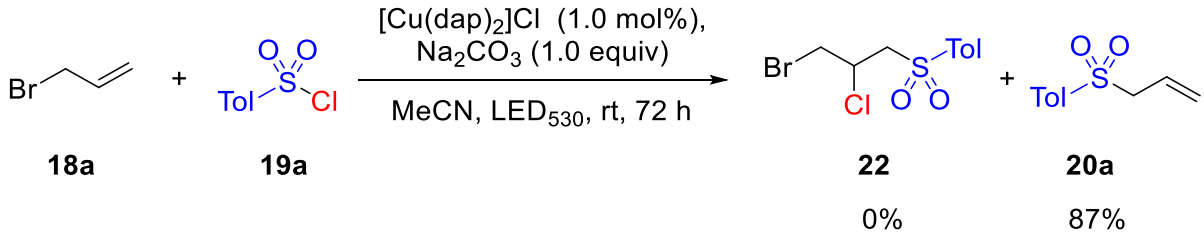


Scheme 5. Synthetic pathways towards allylsulfones starting from allyl bromide.

Aim of this project was the investigation of the unexpected photoreaction of allyl bromide (**18a**) with tosyl chloride (**19a**) (*cf*. chapter D) forming allylsulfone product **20a** and subsequent development of photoredox catalyzed procedure for the synthesis of allylsulfones employing $[Cu(dap)_2]Cl$ and other commonly used photocatalysts.

2. Preliminary Studies with Tosyl Chloride and Allyl Bromide

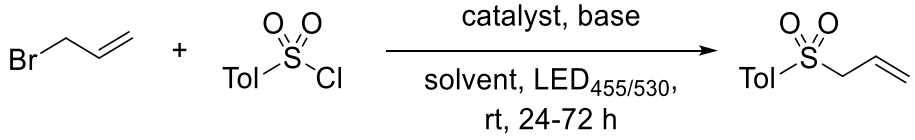
The initial reaction for this project was carried out in chapter D when allyl bromide (**18a**) was used as the alkene for the chlorosulfonylation reaction with tosyl chloride (**19a**) (Chapter D, Scheme 7). Surprisingly, instead of the desired ATRA product **22** the formation of the allyl sulfone **20a** was obtained in 87% isolated yield.



Scheme 6. Allyl bromide (**18a**) as substrate for the ATRA reaction.

With this first result in hand, the optimized reaction conditions using allyl bromide (**18a**) and tosyl chloride (**19a**) as benchmark substrates were determined (Table 1). The monitoring of the reaction time showed that after 24 h the allylation product **20a** was formed in 71% yield (entry 2), whereas the increase of the reaction time to 72 h resulted in a similar yield as after 48 h (entries 1 and 3). The variation of solvent showed low yield for CH_2Cl_2 (entry 4) and no conversion for DMF and DMSO (entries 5 and 6). The reaction in the absence of sodium carbonate resulted in 9% yield indicating a key function of the base during the transformation (entry 7). When the amount of sodium carbonate was lowered to 0.5 equivalents or even 0.1 equivalents excellent yields were obtained (entries 8 and 9). Further decrease of base loading to 0.01 equivalents resulted in only 24% yield (entry 10). In contrast to the results obtained in chapter D, where only sodium carbonate was a suitable inorganic base, the here presented allylation reaction showed good results with potassium carbonate and very high yields employing $NaHCO_3$ (entries 11 and 12). When the excess of allyl bromide (**18a**) was decreased, lower yields for the desired product **20a** were observed (entries 13-15). While the reduction of the catalyst loading to 0.5 mol% gave only slightly lower yield (entry 16), a further decrease of catalyst amount resulted in only 38% yield (entry 17). As expected, the reaction with $[Cu(dap)Cl_2]$ photocatalyst showed similar yield as with copper(I)-catalyst (entry 18). This result is in accordance with the outcomes obtained in the previous chapters C and D. In the presence of $[Ru(bpy)_3]Cl_2$ only 52% yield were observed, whereas the employment of *fac*-$Ir(ppy)_3$ resulted in 85% yield (entries 19 and 20). The results for *fac*-$Ir(ppy)_3$ were further improved when the reaction was carried out in the absence of the base, suggesting no positive effect of inorganic base for the iridium-catalyzed reaction (entry 21).

Table 1. Determination of optimal reaction conditions for the photoredox catalyzed synthesis of allylsulfones.



18a **19a** **20a**

Entry	Conditions	Yield [%][a]
1	/	90
2	24 h	71
3	72 h	92
4	CH_2Cl_2	28
5	DMF	0
6	DMSO	0
7	no base	9
8	Na_2CO_3 (0.5 equiv)	96
9	Na_2CO_3 (0.1 equiv)	95
10	Na_2CO_3 (0.01 equiv)	24
11	K_2CO_3 (1.0 equiv)	62
12	$NaHCO_3$ (1.0 equiv)	90
13	Allyl bromide (2.0 equiv)	36
14	Allyl bromide (4.0 equiv)	62
15	Allyl bromide (5.0 equiv)	80
16	$[Cu(dap)_2]Cl$ (0.5 mol%)	85
17	$[Cu(dap)_2]Cl$ (0.1 mol%)	38
18	$[Cu(dap)Cl_2]$ (1.0 mol%)	90
19	$[Ru(bpy)_3]Cl_2$ (1.0 mol%)	52
20	*fac*-$Ir(ppy)_3$ (1.0 mol%)	85
21	*fac*-$Ir(ppy)_3$ (1 mol%), no base	95
22[b]	no catalyst, 530 nm LED	24
23[b]	no catalyst, 455 nm LED	42
24[b]	no catalyst, 455 nm LED, no base	10
25	no light	2
26	AIBN	29
27	dap (2.0 mol%) 455nm	38
28	dap (2.0 mol%) 530nm	16
29	CuCl (10.0 mol%) 455nm	10
30	CuCl (10.0 mol%) 530nm	4
31	$CuCl_2$ (10.0 mol%) 455nm	12
32	$CuCl_2$ (10.0 mol%) 530nm	5
33	O_2-atmosphere	55
34	air-atmosphere, not degassed	90

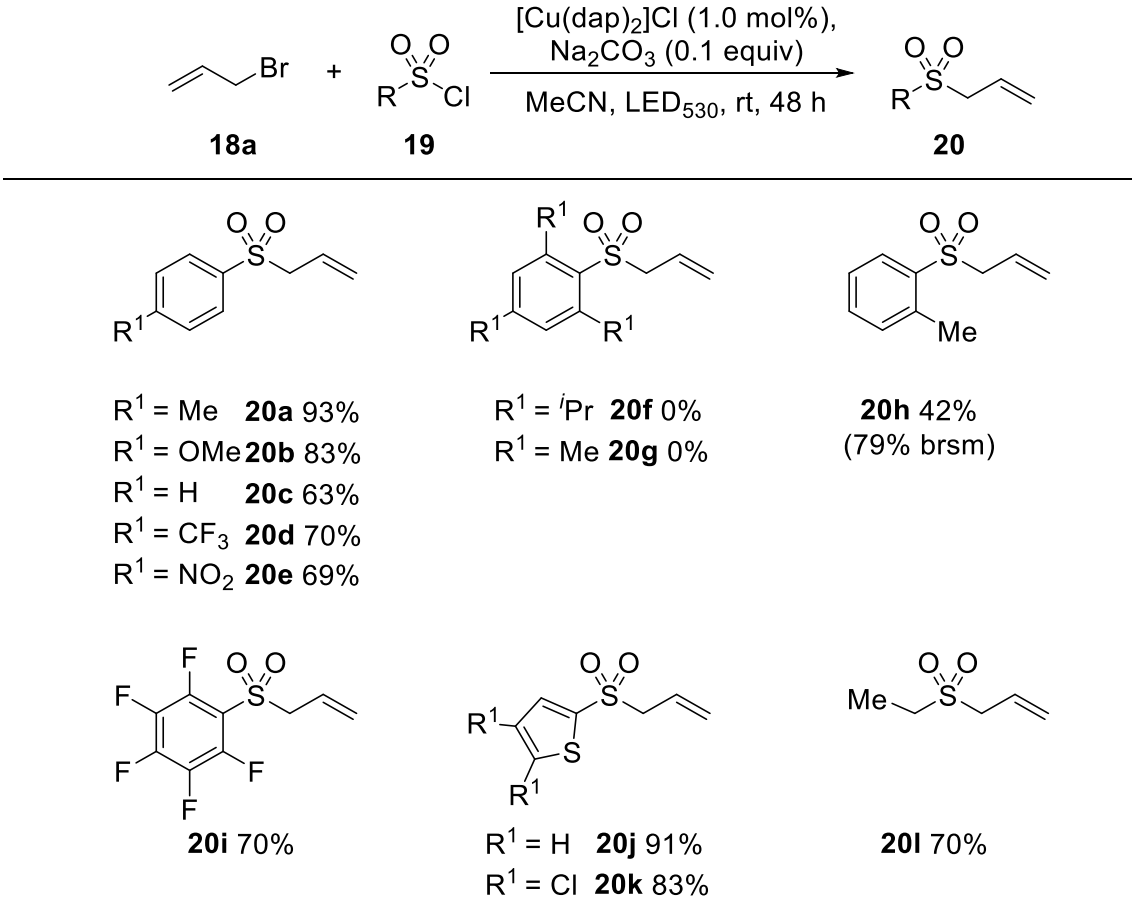
Reaction conditions: allyl bromide (**18a**) (3.0 mmol, 6.0 equiv), TsCl (**19a**) (0.5 mmol, 1.0 equiv), Na_2CO_3 (1.0 equiv), $[Cu(dap)_2]Cl$ (1.0 mol%) in MeCN (dry, degassed, 2.0 mL), irradiation at 530 nm (green LED) for 48 h. [a] Determined by NMR with 1,1,2,2-tetrachloroethane as an internal standard. [b] 72 h reaction time.

The reactions with no photocatalyst using green light (530 nm LED) and blue light (455 nm LED) provided the allylation product **20a** in 24% yield and 42% yield, respectively (entries 22

and 23). Although the reaction time for these experiments was increased to 72 h it is an important result for the understanding of the mechanism (*vide infra*). However, carrying out the reaction in the absence of photocatalyst and sodium carbonate gave only 10% yield, thus again demonstrating the important role of base additive (entry 24). The key role of light was underlined by the dark reaction resulting in only 2% yield (entry 25) and thermal initiation of the reaction in the presence of AIBN, which provided the desired product in only 29% yield (entry 26). The usage of free dap ligand under irradiation with blue light (455 nm LED) or green light (530 nm LED) resulted in very low yields (entries 27 and 28). Likewise, the reactions with copper chloride salts in the absence of dap ligand produced only low amounts of the desired allylsulfone **20a** (entries 29-32). Finally, it was demonstrated, that the reaction is not very sensitive to oxygen. While the reaction with O_2-saturated solution, under oxygen atmosphere gave 55% yield, the reaction with no degassed solution under air atmosphere provided the desired product in very good yield (entries 33 and 34).

3. Substrate Scope

With the optimized reaction conditions in hand the substrate scope for the photoredox catalyzed synthesis of allyl sulfones **20** was explored (Scheme 7 and Table 3). First, the variation of sulfonyl chlorides **19** was carried out using allyl bromide (**18a**) as allylation reagent (Scheme 7). The reaction of 4-methoxybenzenesulfonyl chloride (**19b**) with methoxy-moiety as strong electron donating group provided the desired allylation product **20b** in 83% yield. Likewise, employing electron rich tosyl chloride (**19a**) gave product **20a** in very good yield of 93%. When the electron donating group in *para*-position was removed, the yield for the corresponding allylsulfone **20c** dropped to 63%. Decreasing the electronic density in the aryl ring by introducing trifluoromethyl group resulted in 70% yield for the desired product **20d** and the employment of the strongly withdrawing nitro group led to the formation of the product **20e** in 69% yield. Likewise, the use of pentafluorobenzenesulfonyl chloride (**19i**) provided sulfone **20i** in 70% yield. When sterically hindered 2,4,6-triisopropylbenzenesulfonyl chloride (**19f**) was investigated in this reaction, no conversion of the starting material was observed. A similar result was obtained when using the sterically less hindered 2,4,6-trimethylbenzenesulfonyl chloride (**19g**). In order to prove the steric argument for the unsuccessful transformation, 2-methylbenzenesulfonyl chloride (**19h**) was employed as starting material, having similar electronic properties compared to the tosyl chloride (**19a**) which showed excellent yield for the allylsulfone **20a**. Interestingly, when the methyl group was switched to the *ortho*-position of the aryl ring the yield of product **20h** dropped to 42% with no full consumption of the starting material. However, based on recovered starting material 79% yield was achieved being in accordance with the result for the tosyl chloride (**19a**). This result indicates a strong steric effect of the methyl group in *ortho*-position.



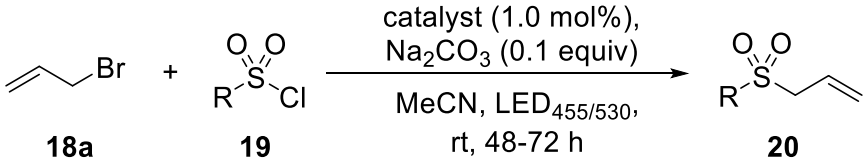
Scheme 7. Substrate scope for the photomediated synthesis of allylsulfones **20**.
Reaction conditions: Alkene (3.0 mmol, 6.0 equiv), TsCl (0.5 mmol, 1.0 equiv), Na_2CO_3 (0.1 equiv), $[Cu(dap)_2]Cl$ (1.0 mol%) in MeCN (dry, degassed, 2.0 mL), irradiation at 530 nm (green LED) for 48 h.

In addition, the reactions with thiophenesulfonyl chlorides **19j** and **19k** showed very good yields for the desired allylsulfones **20j** and **20k** in 91% yield and 83% yield, respectively. Finally, the successful transformation of ethylsulfonyl chloride (**19l**) to the corresponding allylsulfone **20l** was demonstrated in 70% yield. Particularly, this result is important for the understanding of the mechanism of the present reaction (*vide infra*).

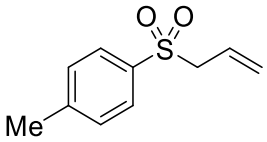
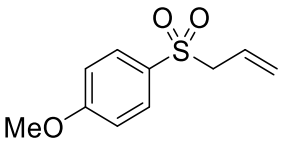
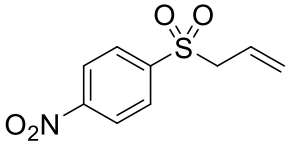
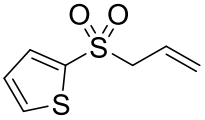
Next, selected reactions with *fac*-$Ir(ppy)_3$ (*cf*. Table 1, entry 21) as photocatalyst or in the absence of the catalyst (*cf*. Table 1, entry 23) were carried out in addition to the results of copper catalysis. The comparison of these results is summarized in Table 2. In the case of the electron rich allylsulfones **20a** and **20b** copper and iridium catalysts showed similar yields, while in the absence of the catalyst only moderate yields were obtained (entries 1-6). These results in combination with the control experiments (*cf*. Table 1, entry 24 and 25) indicate that aromatic sulfonyl chlorides can interact with visible light and thus are able to initiate the allylation reaction even in the absence of the catalyst. However, the photocatalysts have a significant effect on the reaction time and yield. Even with the prolonged reaction time of 72 h no full conversion was obtained in the absence of photocatalyst. The formation of *para*-nitro substituted allylsulfone **20e** in 65% yield in the absence of photocatalyst compared to 70%

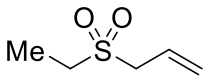
yield for copper catalysis confirmed the assumption that aromatic sulfonyl chlorides can initiate the reaction via visible-light absorption (entries 7-9). However, for the heterocyclic allylsulfone **20j** again only moderate yield was observed when no photocatalyst was added to the reaction mixture (entries 10-12). Furthermore, when ethylsulfonyl chloride was employed in the allylation reaction no product was formed in the absence of the catalyst, whereas in the presence of $[Cu(dap)_2]Cl$ or *fac*-$Ir(ppy)_3$ good yields of the desired product **20l** were observed (entries 13-15). In summary the ability of product formation in the absence of photocatalyst was limited to aromatic sulfonyl chlorides. Moreover, the iridium catalyst and copper catalyst showed comparable results for all substrates.

Table 2. Comparison of yields obtained in the absence of photocatalyst and in the presence of $[Cu(dap)_2]Cl$ and *fac*-$Ir(ppy)_3$.



18a **19** **20**

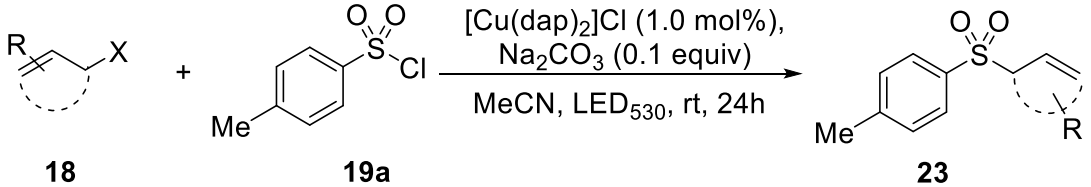
Entry	Product	Catalyst	Yield [%]
1[a]		No catalyst	42
2[b]		$[Cu(dap)_2]Cl$	93
3[c]	**20a**	*fac*-$Ir(ppy)_3$	95
4[a]		No catalyst	44
5[b]		$[Cu(dap)_2]Cl$	83
6[c]	**20b**	*fac*-$Ir(ppy)_3$	87
7[a]		No catalyst	65
8[b]		$[Cu(dap)_2]Cl$	70
9[c]	**20e**	*fac*-$Ir(ppy)_3$	87
10[a]		No catalyst	41
11[b]		$[Cu(dap)_2]Cl$	91
12[c]	**20j**	*fac*-$Ir(ppy)_3$	90

13[a]		No catalyst	0
14[b]		$[Cu(dap)_2]Cl$	70
15[c]	**20l**	*fac*-$Ir(ppy)_3$	68

Reaction conditions: [a]allyl bromide (**18a**) (3.0 mmol, 6.0 equiv), sulfonyl chloride (**19**) (0.5 mmol, 1.0 equiv), Na_2CO_3 (0.1 equiv) in MeCN (dry, degassed, 2.0 mL), irradiation at 455 nm (blue LED) for 72 h. [b] Allyl bromide (**18a**) (3.0 mmol, 6.0 equiv), sulfonyl chloride (**19**) (0.5 mmol, 1.0 equiv), Na_2CO_3 (0.1 equiv), $[Cu(dap)_2]Cl$ (1.0 mol%) in MeCN (dry, degassed, 2.0 mL), irradiation at 530 nm (green LED) for 48 h. [c] Allyl bromide (**18a**) (3.0 mmol, 6.0 equiv), sulfonyl chloride (**19**) (0.5 mmol, 1.0 equiv), *fac*-$Ir(ppy)_3$ (1.0 mol%) in MeCN (dry, degassed, 2.0 mL), irradiation at 455 nm (blue LED) for 48 h.

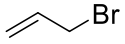
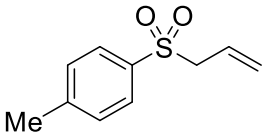
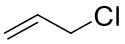
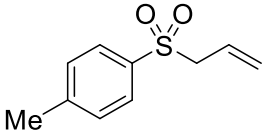
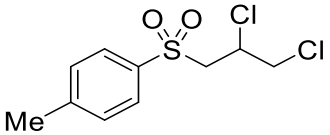
In the next step, the variation of alkyl halides **18** with tosyl chloride (**19a**) as model substrate was performed (Table 3). Using allyl chloride (**18b**) instead of allyl bromide (**18a**) full conversion of the starting material was observed, but only 17% of the desired allylsulfone **20a** were obtained (entry 2) besides the ATRA product **24** in 56% yield. Increasing the steric demand of the double bond by introducing methyl group in 2-position of allyl bromide resulted in the formation of the expected allylsulfone **23c** in excellent yield (entry 3). However, when the methyl group was switched to the 3-position using crotyl bromide (**18d**) two types of product were formed (entry 4). On the one hand the inseparable *E*/*Z* mixture of product **23d** was generated in 31% yield and diastereomeric ratio of 74:26. On the other hand, the product **23d´** was obtained in 50% yield. The latter was in accordance with results obtained by Reiser and coworkers[17] in 2015.

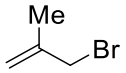
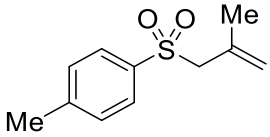
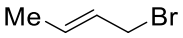
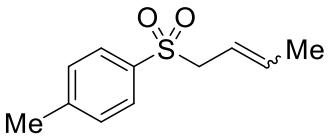
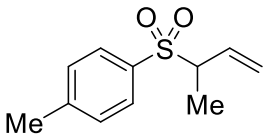
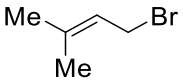
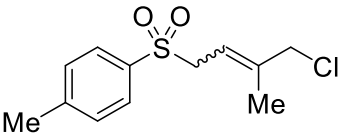
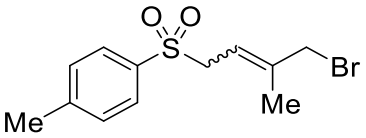
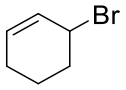
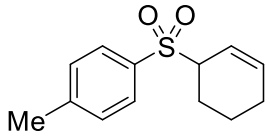
Table 3. Variation of alkyl halides **18** in photoredox catalyzed synthesis of allylsulfones **23**.



18 **19a** **23**

X = Cl, Br

Entry	Alkene	Product Yield	
1			
	18a	**20a** 93%	
2			
	18b	**20a** 17%	**24** 56%

3				
	18c	**23c**		
		92%		
4				
	18d	**23d**	**23d´**	
		31% *E*/*Z* =74/26	50%	
5				
	18e	**23e**	**23e´**	
		overall 40-46%		
6				
	18f	**23f**		
		0%		

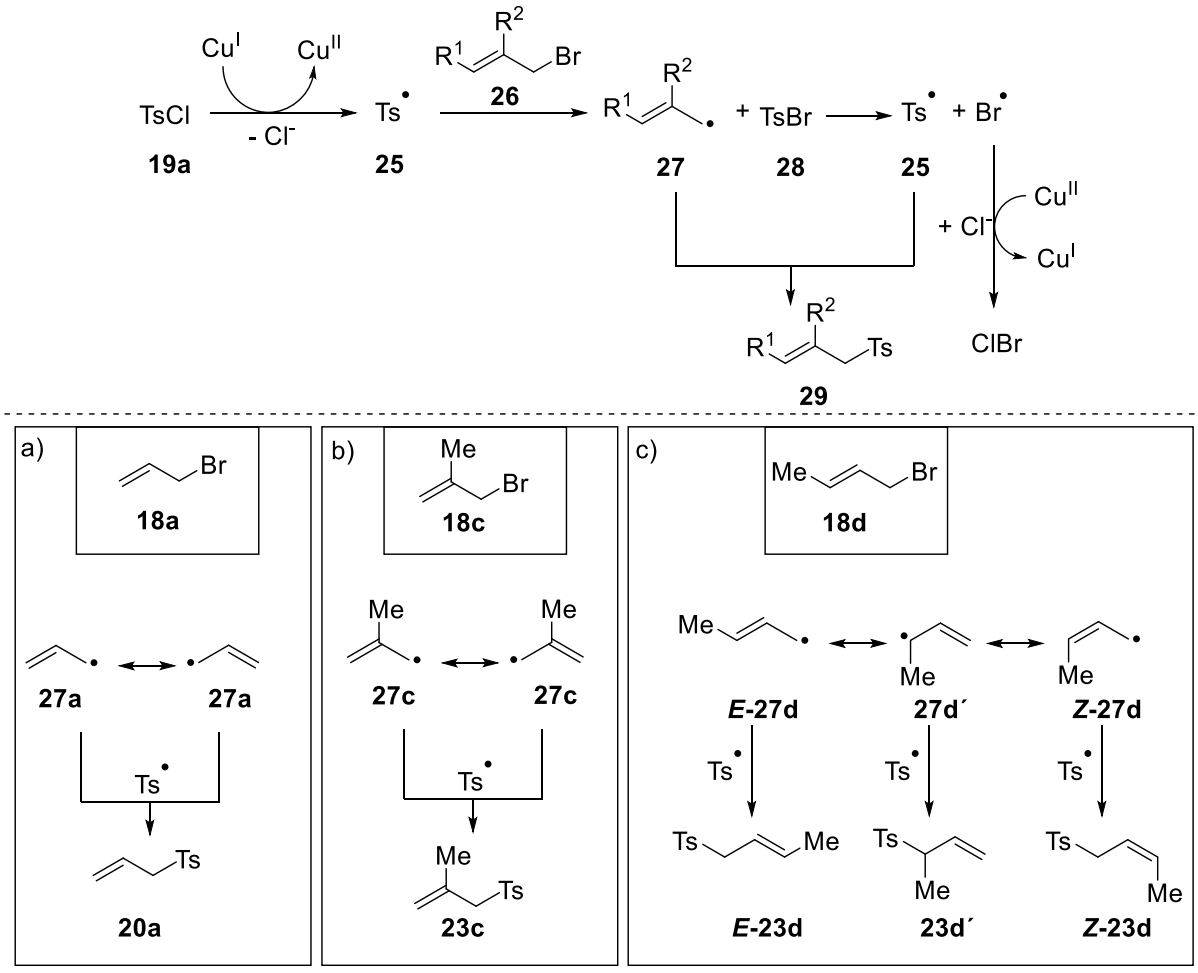
Reaction conditions: Alkyl halide (**18**) (3.0 mmol, 6.0 equiv), TsCl (**19a**) (0.5 mmol, 1.0 equiv), Na_2CO_3 (0.1 equiv), $[Cu(dap)_2]Cl$ (1.0 mol%) in MeCN (dry, degassed, 2.0 mL), irradiation at 530 nm (green LED) for 48 h.

Unexpectedly, when introducing the additional methyl group into the double bond, no desired product was obtained but the formation of an inseparable mixture of halogenated allylsulfones **23e** and **23e´** in 40-46% yield and indeterminable ratio was observed (entry 5). Moreover, the employment of the sterically demanding 1-bromocyclohexene (**18f**) resulted in no product formation and low conversion of the starting material (entry 6). The variation of the alkyl halides demonstrated the strong limitation of the presented protocol.

4. Proposed Mechanism

Scheme 8 describes the proposed mechanisms for the formation of products **20a**, **23c** and **23d**/**23d´**. All three mechanisms are based on a free radical proposal. In the presence of copper photocatalyst the tosyl radical **25** is formed through a single electron transfer from $[Cu(dap)_2]Cl$. This radical can abstract the bromine from the allyl bromide **26** generating allyl radical **27** and TsBr (**28**). The latter is known to undergo a homolytical S-Br bond cleavage in the presence of radicals providing bromine radical and regenerating tosyl radical **25**.[18] The tosyl radical **25** can then undergo a radical recombination reaction with allyl radical **27** to form the desired product **29**. Finally, the bromine radical can recombine with chloride forming ClBr and simultaneously reduce the Cu(II)-species to $[Cu(dap)_2]Cl$. In the case of allyl bromide (**18a**) the formed allyl radical is symmetrical, thus both mesomeric structures **27a** are identical. This

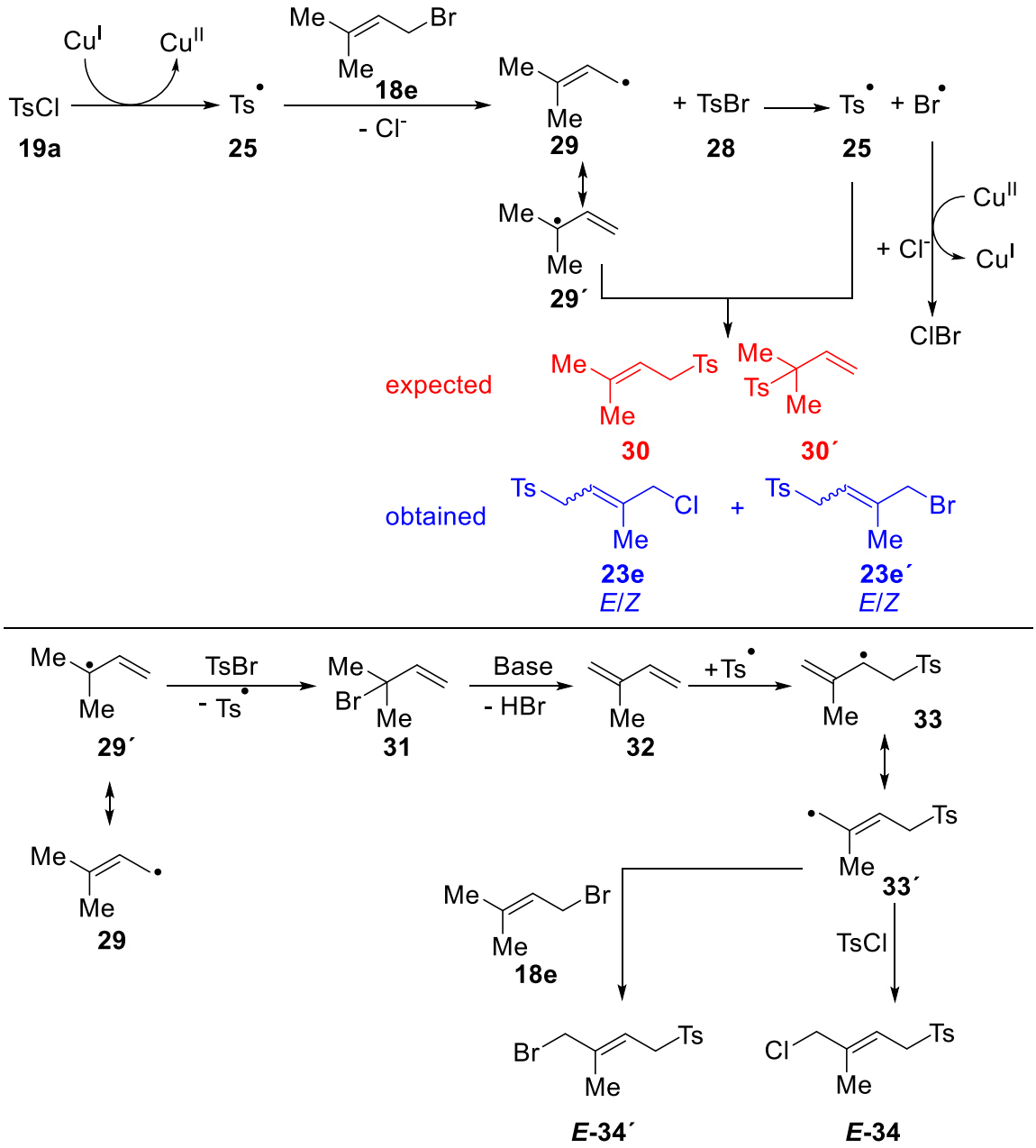
is the reason for the selective formation of only one allylsulfone product (Scheme 8, pathway a). When 3-bromo-2-methylpropene (**18c**) is used in the reaction, the formation of the allyl radical **27c** occurs. Also, for this radical both mesomeric structures are identical, thus leading to the same allyl sulfone **23c** in excellent yield (Scheme 8, pathway b). In contrast, the employment of crotyl bromide (**18d**) results in the formation of allyl radical with three different mesomeric structures (Scheme 8, pathway c). The recombination of tosyl radical **25** with allyl radicals ***E*-27d** and ***Z*-27d** results in the formation of *E*/*Z* mixture of the desired allyl sulfone **23d**, whereas the reaction with allyl radical **27d´** generates the major product **23d´**. The ratio of the three products can be explained by the different stability of the intermediary allyl radical[19]. The major product **23d´** is formed via more stable secondary radical **27d´**, whereas the *E*/*Z* products **23d** result from less stable primary radicals ***E*-27d** and ***Z*-27d**. However, the stability of the radical can also be unfavorable for a successful reaction if the radical is not reactive enough.[19c]



Scheme 8. Mechanistic analysis for different alkyl bromides.

As depicted in Scheme 9 a proposed mechanism for the reaction between tosyl chloride (**19a**) and 3,3-dimethylallyl bromide (**18e**) explains the unexpected outcome for the generation of the inseparable product mixture **23e** and **23e´**. After formation of the mesomeric structures **29** and

29´ like in the above proposed mechanism for other allyl bromides the generation of two products **30** and **30´** was expected. However, instead of the expected allyl sulfones the halogenated allyl sulfones **23e** and **23e´** were obtained as inseparable product mixture. The mesomeric structure **29´** of the allyl radical undergoes a bromine abstraction from TsBr[18] (**28**) forming allyl bromide **31**. Subsequent elimination of HBr in the presence of a base provides the formation of 1,3-diene **32** that can be consequently attacked by a tosyl radical **25** forming carbon centered radical **33**/**33´**. Due to its mesomeric structure **33´** a chlorine can be abstracted from TsCl (**19a**) or a bromine from 3,3-dimethylallyl bromide (**18e**), thus forming the halogenated allyl sulfones *E*-**34** and *E*-**34´**. Although the secondary radical **33** should be more stable than the primary radical **33´**, the latter leads to the formation of products with higher substituted double bond and thus forms the thermodynamically more stable product. This observation is consistent with the higher reactivity of radical **33´** compared to the more stable radical **33**, but is not in agreement with the results observed for the reaction of crotyl bromide (*cf*. Scheme 8).

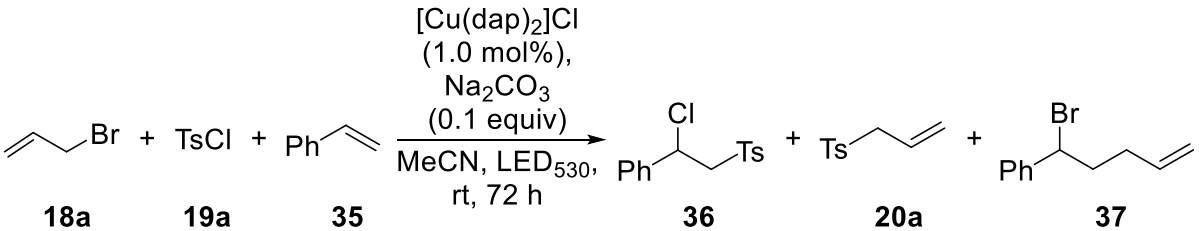


Scheme 9. Proposed mechanism for the reaction of 3,3-dimethylallyl bromide (**18e**) with tosyl chloride (**19a**).

Further mechanistic investigations were focused on trapping the intermediary allyl radical **27a** with excess of styrene (**35**) to form ATRA type product **37** (Table 4). When the reaction was carried out with 1.0 equivalent allyl bromide (**18a**), 1.0 equivalent TsCl (**19a**) and 5.0 equivalents styrene (**35**) in the presence of $[Cu(dap)_2]Cl$ and sodium carbonate in MeCN under irradiation with green LED, only the ATRA product **37** was obtained in 95% yield (entry 1). In order to prevent the undesired formation of ATRA product **37**, the amount of allyl bromide (**18a**) was drastically increased to 6.0 equivalents. However, again only ATRA product **37** was obtained in quantitative yield (entry 2). When no tosyl chloride (**19a**) was used no conversion of the starting material was observed (entry 3). The obtained results underline the

role of tosyl radical as initiator for the allylation reaction. However, the allylation process seems to be much slower compared to the atom transfer radical addition reaction, thus losing the competition between these reactions.

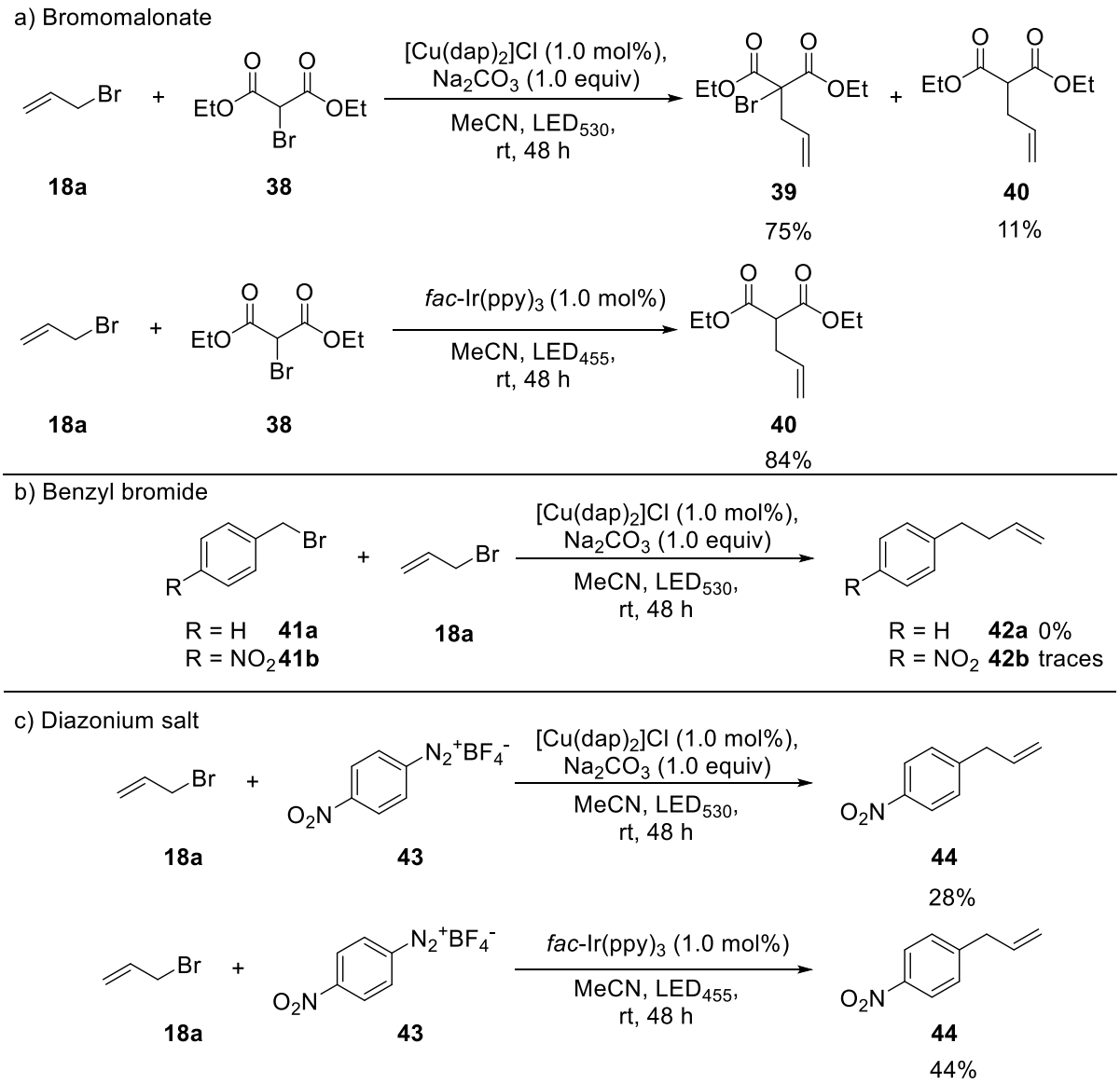
Table 4. Efforts towards trapping of allyl radical.



18a **19a** **35** **36** **20a** **37**

Entry	**18a** [equiv]	**19a** [equiv]	**35** [equiv]	**36** [%]	**20a** [%]	**37** [%]
1	1.0	1.0	5.0	95	0	0
2	6.0	1.0	6.0	99	0	0
3	1.0	0.0	1.0	0	0	0

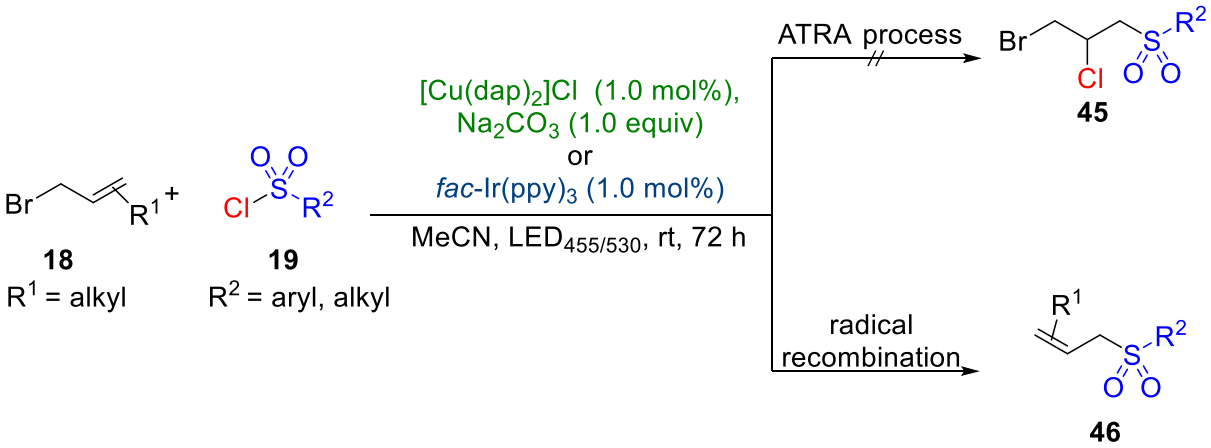
Furthermore, the allylation reaction was investigated with other radical sources in visible light mediated processes established in the literature[20] (Scheme 10). The reaction of diethyl bromomalonate (**38**) under established reaction conditions led to the formation of product **39** in 75% yield, derived from the nucleophilic attack of deprotonated malonate on sp^3-center of allyl bromide (**18a**). Additionally, only 11% of the desired photoproduct **40** were obtained. Nevertheless, when the reaction was carried out with *fac*-Ir(ppy)$_3$ in the absence of sodium carbonate the allylated photoproduct **40** was formed in 84% yield. This reaction shows an additional limitation of the copper-mediated process, disabling the employment of substrates with acidic protons. Moreover, the reaction of benzyl bromides **41a** and **41b** showed only low conversion and traces of the desired products **42a** and **42b**. These results are somehow surprising, because the reaction of 4-nitrobenzyl bromide (**41b**) with alkenes catalyzed by copper catalyst is well known and thus the generation of benzyl radical by [Cu(dap)$_2$]Cl should be possible.[17, 21] Finally, the allylation reaction was carried out employing diazonium salts **44**.[20d] The purpose of this reaction was to develop a protocol for the selective monoallylation of arenes without disadvantage like polyalkylation, which are known in Friedel-Crafts-alkylation reactions. The reaction with copper catalyst and additional inorganic base provided the monoallylated arene **45** in 28% yield. Employing iridium photocatalyst in the absence of base additive delivered the product **45** in slightly higher yield of 44%. Although both reactions gave the desired product, the obtained yields were too low for further investigation of this transformation.



Scheme 10. Variation of radical source for the photoinitiated allylation reaction.

5. Summary

In conclusion an efficient protocol for the photoredox catalyzed synthesis of allylsulfones **46** was developed employing copper- and iridium-photocatalysts (Scheme 11). The variation of sulfonyl chlorides **19** showed high functional group tolerance, whereas the variation of alkyl halides **18** was strongly limited to allylbromide (**18a**) and substrates with symmetrical mesomeric structures of the intermediary allyl radical. The proposed mechanism is assumed on the recombination of free radicals, thus explaining the results obtained in the absence of photocatalyst (*vide supra*). The comparison of the results obtained by copper catalysis and iridium catalysis showed slight advantages in the use of iridium catalyst as no base addition is required. Nevertheless, the present reaction again underlined the protective character of sodium carbonate for the $[Cu(dap)_2]Cl$ catalyst. The extension of the protocol to other radical sources known in visible light photoredox catalysis showed additional limitation of copper catalyst (e.g. reaction of diethyl bromomalonate) or only low yields of the desired allylation products obtained in the presence of both photocatalysts (reactions with benzyl bromides and diazonium salts).



Scheme 11. Photoredox catalyzed synthesis of allylsulfones **46**.

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F. Summary

1. Summary in English

The present PhD thesis demonstrates the unique character of the employed photoredox catalysts in organic transformations. In chapter A the introduction into the field of photocatalysis is given by an overview about the commonly employed photocatalysts and the most important properties of photoredox catalysts such as photophysics, redox behavior and coordination ability.

Chapter B “Synthesis of Heterocycles via Photoredox Mediated Deoxygenation Reaction” is directly linked to the results obtained during my master thesis and is focused on the synthesis of substituted *N*-heterocycles via photoredox catalyzed C-O bond activation. Due to the strongly negative reduction potentials of the employed ethyl oxalates and 3,5-bis(trifluoromethyl)benzoates, a catalyst with strong reduction potential such as *fac*-Ir(ppy)$_3$ is crucial for the successful transformation. While the synthesis of the polysubstituted pyrrolidines was successful, the limitations of the developed protocol were revealed by the failure in the synthesis of bicyclic compounds and lactames.

In chapter C “Copper Mediated Photochemical Iodoperfluoroalkylation” the new photocatalyst [Cu(dap)Cl$_2$] is employed in the copper mediated iodoperfluoroalkylation of alkenes and alkynes, which was already reported by T. Rawner employing [Cu(dap)$_2$]Cl. After determination of the optimized reaction conditions and the investigation of the substrate scope, several mechanistic studies were performed. Both catalysts show outstanding results in the transformation of styrene derivatives which are no suitable substrates for other catalytic systems reported in the literature. Moreover, the enhanced mechanistic investigation provided information about the unique character of copper-based photocatalysts and the plausible mechanism for this transformation including rebound pathway and ligand exchange process.

Chapter D “Copper Mediated Chlorosulfonylation of Alkenes” demonstrates the protective role of sodium carbonate for the copper catalyst in efficient chlorosulfonylation reaction of unactivated alkenes. In contrast to the commonly used ruthenium- and iridium-based photocatalysts, showing only low yields of the desired product, the employment of copper catalysts enables the formation of chlorosulfonylated compounds in high yields. In cooperation with S. Engl and A. Hossain the mechanistic studies were performed providing information about plausible mechanism. Analogous to the results described in chapter C the inner sphere mechanisms of copper catalysts are proposed.

Finally, in chapter E “Copper Mediated Light Promoted Synthesis of Allylsulfones” the investigation of the unexpected reaction between allyl bromide and sulfonyl chloride obtained in chapter D is performed. After determination of optimal reaction conditions, the investigation of the substrate scope was carried out resulting in excellent yields for the variation of sulfonyl chlorides and strong limitations when modifying the alkyl halide part. The plausible mechanism for this photoinduced reaction includes radical recombination. Application of the developed protocol to other radical sources commonly used in photoredox catalysis resulted in low yields, thus demonstrating the limitations of the employed protocol.

2. Summary in German (Zusammenfassung)

Die vorliegende Doktorarbeit besteht aus vier Projekten und befasst sich mit der Untersuchung der photoredox-katalysierten Reaktionen für deren Erfolg universelle Eigenschaften der eingesetzten Photokatalysatoren entscheidend sind. Zu Beginn werden in Kapitel A verschiedene gängige Katalysatortypen vorgestellt, die in photochemischen Reaktionen verwendet werden und die wichtigsten Eigenschaften von Photokatalysatoren beschrieben. Dabei wird unter anderem auf photophysikalische Eigenschaften, Redoxverhalten und Koordinationsfähigkeit eingegangen.

Kapitel B “Synthesis of Heterocycles via Photoredox Mediated Deoxygenation Reaction” knüpft direkt an die Resultate meiner Masterarbeit und beschäftigt sich mit der Synthese von *N*-Heterozyklen mittels photoredox-katalysierten Aktivierung der C-O Bindung. Aufgrund der stark negativen Redoxpotentiale der eingesetzten Ethyloxalate und 3,5-Bis(trifluoromethyl)benzoate ist der Einsatz eines stark reduzierenden Photokatalysators wie *fac*-Ir(ppy)$_3$ für eine erfolgreiche Reaktion unabdingbar. Neben der erfolgreichen Synthese polysubstituierter Pyrrolidine wurde zudem die Limitierung des entwickelten Protokolls während der Synthese von Bizyklen und Lactam-Derivaten ermittelt.

Im Kapitel C “Copper Mediated Photochemical Iodoperfluoroalkylation” wurde der neu entwickelte Photokatalysator [Cu(dap)Cl$_2$] in der Iodoperfluoroalkylierungsreaktion von Alkenen und Alkinen untersucht. Die erhaltenen Ergebnisse wurden dabei mit den Resultaten von T. Rawner verglichen die beim Einsatz des etablierten [Cu(dap)$_2$]Cl Katalysators erhalten wurden. Im Anschluss an die Bestimmung der optimalen Reaktionsbedingungen und der Substratbreite, wurden mehrere mechanistische Untersuchungen durchgeführt, um die universellen Eigenschaften von Kupferkatalysatoren zu belegen. Im Gegensatz zu den gängigen Katalysatoren, die in der photochemischen Iodoperfluoroalkylierung eingesetzt werden, zeigen kupferbasierte Komplexe herausragende Ergebnisse bei der Umsetzung von Styrolderivaten. Diese universelle Eigenschaft wurde durch mechanistische Studien belegt und Rebound Mechanismus mittels postulierter Cu(III)-Spezies, sowie Ligandenaustausch Mechanismus als plausible Erklärungen für die erhaltenen Resultate präsentiert.

Kapitel D “Copper Mediated Chlorosulfonylation of Alkenes” beschreibt die schützende Wirkung von Natriumcarbonat für Kupferkatalysatoren bei der effizienten Chlorosulfonylierungsreaktion von unaktivierten Alkenen. Im Gegensatz zu gängigen ruthenium- und iridiumbasierten Photokatalysatoren, die lediglich niedrige Ausbeuten des erwünschten Produkts liefern, zeigt Kupfer herausragende katalytische Aktivität in der beschriebenen Reaktion. In Kooperation mit S. Engl und A. Hossain wurden zudem

mechanistische Untersuchungen durchgeführt und analog zum Kapitel C Mechanismen postuliert, die auf der koordinierenden Funktion des Kupfers basieren.

Abschließend wurde im Kapitel E “Copper Mediated Light Promoted Synthesis of Allylsulfones” die photochemische Synthese von Allylsulfonen aus Allylbromid und Sulfonylchloriden untersucht. Nach erfolgter Bestimmung optimaler Reaktionsbedingungen wurde die Substratbreite der beschriebenen Reaktion untersucht. Dabei wurde bei der Variation von Sulfonylchloriden Toleranz gegenüber einer Reihe von funktionellen Gruppen ermittelt. Bei der Modifizierung der Allylbromide wurden jedoch starke Limitierungen der verwendeten Reaktionsbedingungen deutlich und der vorliegende Mechanismus als Rekombination freier Radikale beschrieben. Zudem wurde beim Einsatz weiterer in der Photoredoxchemie gängiger Radikalquellen zusätzliche Schwächen der entwickelten Methode deutlich.

G. Experimental Part

1. General Information

Commercially available chemicals were purchased in high quality and were used without further purification. All reactions were carried out in flame dried glassware under atmospheric conditions unless otherwise stated. Reactions with moisture or oxygen sensitive reagents were carried out in flame dried glassware under an atmosphere of predried nitrogen. Anhydrous solvents were prepared by established laboratory procedures[1]. DCM, EtOAc and hexanes (40-60 °C) for chromatography were distilled prior to use. All photochemical reactions were carried out in flame dried glassware applying three consecutive freeze-pump-thaw cycles. The reported yields are referred to the isolated compounds unless otherwise stated.

Chromatography

Thin layer chromatography was performed with TLC precoated aluminum sheets (Merck) Silica gel 60 F254, 0.2 mm layer thickness. Visualization was done with UV light (λ= 254 nm) and staining with vanillin (6 g vanillin, 100 mL ethanol (95%), 1 mL conc. sulfuric acid), ninhydrin (300 mg ninhydrin, 3 mL conc. acetic acid, 100 mL ethanol) or potassium permanganate (1.0 g $KMnO_4$, 2 g Na_2CO_3, 100 mL water) followed by heating. Column chromatography was performed with silica gel (Merck, 0.063-0.200 mm particle size) and flash silica gel 60 (Merck, 0.040-0.063 mm particle size).

NMR-Spectroscopy

^{1}H NMR spectra were recorded on FT-NMR-spectrometer of the type Bruker Avance 300 (300 MHz for ^{1}H, 75 MHz for ^{13}C, 282 MHz for ^{19}F) or BRUKER Avance III 400 “Nanobay” (400 MHz for ^{1}H, 100 MHz for ^{13}C, 386 MHz for ^{19}F). Chemical shifts for ^{1}H NMR were reported as δ, parts per million (ppm), relative to the signal of $CHCl_3$ at 7.26 ppm, H_2O at 4.79 ppm, relative to the center line signal of the CH_3CN quintet at 1.94 ppm and relative to the center line signal of the DMSO quintet at 2.50 ppm. Spectra were evaluated in 1st order and coupling constants *J* were reported in Hertz (Hz). The following notations indicate the multiplicity of the signals: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, p = quintet, sex = sextet, hept = septet, and m = multiplet, and combinations thereof. Chemical shifts for ^{13}C NMR were reported as δ, parts per million (ppm), relative to the center line signal of the $CDCl_3$ triplet at 77.2 ppm, CD_3CN singlet at 118.3 and DMSO-d_6 septet at 39.5 ppm. NMR yields were determined using diphenoxymethane or 1,1,2,2-tetrachloroethane as internal standards.

IR-Spectroscopy

FTIR spectroscopy was carried out on a Cary 630 FTIR Spectrometer. Solid and liquid compounds were measured neatly, and the wave numbers are reported as cm^{-1}.

Mass Spectrometry

Mass spectra were recorded by the Central Analytical Laboratory (University of Regensburg) using Jeol AccuTOF GCX and Agilent Q-TOF 6540 UHD. High-resolution mass spectra were measured using atmospheric pressure chemical ionization (APCI), electron ionization (EI), electrospray ionization (ESI) with a quadrupole time-of-flight (Q-TOF) detector.

Polarimetry

Determination of optical rotation was carried out on a MCP 500 Modular Circular Polarimeter by Anton Paar using 589 nm (Na-D-line) as measurement wavelength.

Light Source

Blue light irradiation in batch processes was performed using light emitting diodes OSLO 80 rb (700 mA, 3 W, λ_{max} = 455 nm), OSLO SSL 80 (700 mA, 3 W, λ_{max} = 455 nm), CREE XP rb LED (700 mA, 3 W, λ_{max} = 455 nm). Green light irradiation in batch processes was performed using a light emitting diode OSLON SSL 80 (700 mA, 3 W, λ_{max} = 530 nm). In microreactor processes eight light emitting diodes OSRAM OSLON Black Series LD H9GP (700 mA, 3W, λ_{max} = 455±10 nm) were employed.

HPLC

Enantiomeric excess was determined by chiral HPLC (Phenomenex Lux Cellulose-2, 4.6 x 250 mm, particle size 5 µm).

Melting Point Apparatus

The measurement of melting point was carried out on a MPA100 - Automated melting point system by OptiMelt using a ramp rate of 1K/min.

Cyclic Voltammetry

Cyclic voltammetry measurements were carried out on an Autolab PGSTAT 302N set-up at 20 °C in the stated solvent containing tetrabutyl ammonium tetrafluoroborate as the supporting electrolyte under an argon atmosphere with use of a conventional undivided electrochemical cell, a glassy carbon working electrode, platinum wire as the counter electrode and silver wire as the reference electrode. The solvent was degassed by vigorous argon bubbling prior to the

measurements. Redox potentials were referenced against ferrocene as internal standard. For better comparsion all values are reported in reference to the SCE electrode. The values were converted according to reference[2].

2. Chapter B: Synthesis of Heterocycles via Visible Light Mediated Deoxygenation Reaction

2.1. Synthesis of Literature Known Compounds and Reagents

The following compounds were synthesized according to the reported literature procedures. The spectral data were in agreement with the data reported: *fac*-Ir(ppy)$_3$[3], rac. ethyl 3-phenyloxirane-2-carboxylate (**36a**)[4], ethyl 3-methyloxirane-2-carboxylate (**36b**)[4], 2,3-diphenyloxirane (**36d**)[5], rac. ethyl (2*S*,3*S*)-3-amino-2-hydroxy-3-phenylpropanoate (**37a**)[4, 6], 2-(allylamino)-1-phenylethan-1-ol (**39be**)[7], isopropyl cinnamate (**63**)[8], *N*-bromoacetamide[9], isopropyl (2*S*,3*R*)-3-acetamido-2-hydroxy-3-phenylpropanoate (**64**)[10], Shi-catalyst[11], 2-amino-1,1-diphenylethan-1-ol (**72**)[12], methyl 2-aminobenzoate (**85**)[13], methyl 2-(allylamino)benzoate (**108**)[14], 2-acetoxypropanoic acid (**134**)[15], *N*-(*tert*-butyl)prop-2-en-1-amine (**137**)[16].

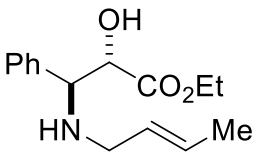
2.2. Compound Characterization

2.2.1. Preparartion of Starting Materials for the Synthesis of Pyrrolidines

General Procedure (GP-1) for the Synthesis of Alkylated Amino Alcohols via Allylation

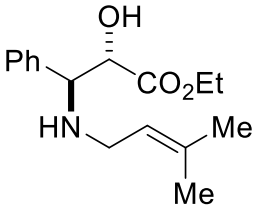
A 500 mL round bottom flask equipped with a magnetic stir bar and reflux condenser was charged with rac. ethyl (2*R*,3*R*)-3-amino-2-hydroxy-3-phenylpropanoate (**37a**) (2.6 mmol, 1.0 equiv), DBU (5.2 mmol, 2.0 equiv) and toluene (200 mL). Alkyl bromide (5.2 mmol, 2.0 equiv) was added dropwise at room temperature and the reaction mixture was stirred for 96 h at 60 °C. After addition of water (100 mL) the mixture was extracted with EtOAc (2x 100 mL). The combined organic layers were washed with water (3x 100 mL), dried over anhydrous Na_2SO_4, the solvent was evaporated *in vacuo* and the residue purified by silica gel column chromatography to give monoalkylated amino alcohol.

rac. Ethyl (2*S*,3*S*)-3-(((*E*)-but-2-en-1-yl)amino)-2-hydroxy-3-phenylpropanoate (39aa)



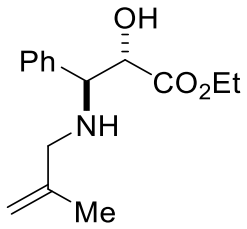
Following general procedure GP-1, using rac. ethyl (2*S*,3*S*)-3-amino-2-hydroxy-3-phenylpropanoate (**37a**) (1.1 g, 5.1 mmol, 1.0 equiv), DBU (1.5 mL, 1.5 g, 10.1 mmol, 2.0 equiv), crotyl bromide (**38a**) (1.2 mL, 1.37 g, 10.1 mmol, 2.0 equiv) and toluene (200 mL) gave 586 mg (2.2 mmol, 44%) of rac. ethyl (2*S*,3*S*)-3-(((*E*)-but-2-en-1-yl)amino)-2-hydroxy-3-phenylpropanoate (**39aa**) as a colorless oil after purification by silica gel column chromatography (hexanes / EtOAc, 2:1 to 1:1). R_f (hexanes / EtOAc, 1:1) = 0.20, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 – 7.01 (m, 5H), 5.62 – 5.35 (m, 2H), 4.50 (d, *J* = 4.0 Hz, 1H), 4.07 – 3.92 (m, 3H), 3.25 (bs, 2H), 3.12 – 2.91 (m, 2H), 1.72 – 1.34 (m, 3H), 1.08 (t, *J* = 7.2 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$): δ 172.5, 137.8, 137.7, 128.7, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 126.6, 73.2, 73.1, 63.5, 63.4, 61.1, 61.1, 48.7, 42.9, 17.7, 13.9, 12.8. IR (neat): 3329, 3064, 3027, 2982, 2919, 1733, 1454, 1368, 1260, 1200, 1103, 1025, 969, 936, 861, 753 cm^{-1}. HRMS (ESI) m/z calculated for $C_{15}H_{22}NO_3$ ($[M+H]^+$) 264.1594, found 264.1597.

rac. Ethyl (2*S*,3*S*)-2-hydroxy-3-((3-methylbut-2-en-1-yl)amino)-3-phenylpropanoate (39ab)



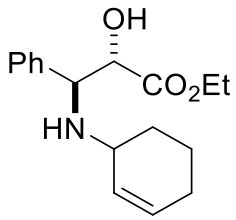
Following general procedure GP-1, using rac. ethyl (2*S*,3*S*)-3-amino-2-hydroxy-3-phenylpropanoate (**37a**) (1.4 g, 6.9 mmol, 1.0 equiv), DBU (2.1 mL, 2.1 g, 13.8 mmol, 2.0 equiv), 1-bromo-3-methyl-but-2-ene (**38b**) (1.7 mL, 2.1 g, 13.8 mmol, 2.0 equiv) and toluene (200 mL) gave 1.2 g (4.3 mmol, 63%) of rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((3-methylbut-2-en-1-yl)amino)-3-phenylpropanoate (**39ab**) as a yellowish oil after purification by silica gel column chromatography (hexanes / EtOAc, 2:1 to 1:2). R_f (hexanes / EtOAc, 1:1) = 0.15, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.09 (m, 5H), 5.21 (t, *J* = 7.0 Hz, 1H), 4.50 (d, *J* = 4.0 Hz, 1H), 4.15 – 3.86 (m, 3H), 3.33 (bs, 2H), 3.08 (dd, *J* = 13.0, 6.7 Hz, 1H), 3.01 (dd, *J* = 13.0, 7.2 Hz, 1H), 1.65 (s, 3H), 1.43 (s, 3H), 1.07 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.5, 137.9, 134.7, 128.1, 127.8, 127.6, 122.2, 73.2, 63.7, 61.1, 44.3, 25.6, 17.7, 13.9. IR (neat): 3317, 3064, 3030, 2978, 2915, 2859, 1733, 1454, 1372, 1267, 1238, 1197, 1115, 1025, 932, 865, 753 cm^{-1}. HRMS (ESI) m/z calculated for $C_{16}H_{24}NO_3$ ($[M+H]^+$) 278.1751, found 278.1751.

rac. Ethyl (2*S*,3*S*)-2-hydroxy-3-((2-methylallyl)amino)-3-phenylpropanoate (39ac)



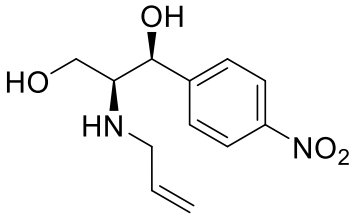
Following general procedure GP-1, using rac. ethyl (2*S*,3*S*)-3-amino-2-hydroxy-3-phenylpropanoate (**37a**) (2.1 g, 10.2 mmol, 1.0 equiv), DBU (2.3 mL, 2.3 g, 15.3 mmol, 1.5 equiv), 3-bromo-2-methylprop-1-ene (**38c**) (1.6 mL, 2.1 g, 15.7 mmol, 1.5 equiv) and toluene (300 mL) gave 1.5 g (5.6 mmol, 55%) of rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((2-methylallyl)amino)-3-phenylpropanoate (**39ac**) as a yellowish oil after purification by silica gel column chromatography (hexanes / EtOAc, 2:1 to 1:2). R_f (hexanes / EtOAc, 1:1) = 0.19, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 – 7.14 (m, 5H), 4.81 (d, *J* = 6.8 Hz, 2H), 4.49 (d, *J* = 4.1 Hz, 1H), 4.15 – 3.87 (m, 3H), 3.23 – 2.79 (m, 4H), 1.70 (s, 3H), 1.09 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.5, 143.3, 137.9, 128.1, 127.7, 111.2, 73.4, 63.4, 61.1, 52.6, 20.7, 13.9. IR (neat): 3314, 3083, 3038, 2974, 2847, 2796, 1748, 1655, 1457, 1433, 1372, 1249, 1207, 1129, 1029, 977, 898, 824, 757, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{15}H_{22}NO_3$ ($[M+H]^+$) 264.1594, found 264.1597.

rac. Ethyl (2*S*,3*S*)-3-(cyclohex-2-en-1-ylamino)-2-hydroxy-3-phenylpropanoate (39ad)



A 500 mL round bottom flask equipped with a magnetic stir bar and reflux condenser was charged with ethyl 3-amino-2-hydroxy-3-phenylpropanoate (**37a**) (1.7 g, 7.9 mmol, 1.0 equiv), DBU (1.2 mL, 1.2 g, 7.9 mmol, 1.0 equiv) and toluene (300 mL). 3-bromocyclohex-1-ene (**38d**) (1.3 g, 8.2 mmol, 1.0 equiv) was added dropwise at room temperature and the reaction mixture was stirred for 72 h at 60 °C. After addition of water (100 mL) the mixture was extracted with EtOAc (2x 100 mL). The combined organic layers were washed with water (3x 100 mL), dried over anhydrous Na_2SO_4, the solvent was evaporated in vacuo and the residue purified by silica gel column chromatography (hexanes / EtOAc, 2:1 to 1:1) to give 900 mg (3.1 mmol, 39%) of rac. ethyl (2*S*,3*S*)-3-(cyclohex-2-en-1-ylamino)-2-hydroxy-3-phenylpropanoate (**39ad**) as a colorless oil. R_f (hexanes / EtOAc, 1:1) = 0.33, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.20 (m, 5H), 5.85 – 5.46 (m, 2H), 4.45 (dd, *J* = 4.2, 3.0 Hz, 1H), 4.20 (dd, *J* = 13.1, 4.2 Hz, 1H), 4.10 – 3.92 (m, 2H), 3.23 – 2.55 (m, 3H), 2.06 – 1.84 (m, 2H), 1.73 (dddd, *J* = 19.8, 16.8, 7.5, 3.4 Hz, 2H), 1.59 – 1.36 (m, 2H), 1.10 (td, *J* = 7.2, 1.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.6, 138.6, 138.2, 129.7, 129.6, 129.2, 128.9, 128.4, 128.4, 128.0, 127.9, 73.8, 73.4, 62.0, 61.9, 61.4, 61.4, 50.3, 49.8, 30.5, 29.1, 25.3, 20.3, 19.7, 14.1. IR (neat): 3299, 3027, 2933, 2866, 2837, 1703, 1495, 1454, 1398, 1364, 1297, 1264, 1234, 1129, 1088, 1021, 980, 902, 839, 763 cm^{-1}. HRMS (ESI) m/z calculated for $C_{17}H_{24}NO_3$ ($[M+H]^+$) 290.1751, found 290.1756.

(1*S*,2*S*)-2-(allylamino)-1-(4-nitrophenyl)propane-1,3-diol (43)

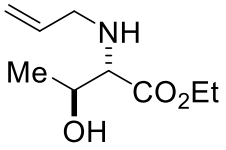


Following general procedure GP-1, using (*1S*,*2S*)-2-amino-1-(4-nitrophenyl)propane-1,3-diol (**42**) (4.6 g, 21.6 mmol, 1.0 equiv), DBU (3.2 mL, 3.3 g, 21.6 mmol, 1.0 equiv), allyl-bromide (**38e**) (1.9 mL, 2.7 g, 22.2 mmol, 1.0 equiv) and toluene (200 mL) gave 3.1 g (12.4 mmol, 57%) of (1*S*,2*S*)-2-(allylamino)-1-(4-nitrophenyl)propane-1,3-diol (**43**) as a yellow oil after 4 h reaction time and purification by silica gel column chromatography (CH_2Cl_2 / MeOH, 9:1). R_f (CH_2Cl_2 / MeOH, 9:1) = 0.18, Staining: Ninhydrin (UV active). Specific Rotation: $[\alpha]_D^{25}$ = + 49.1 °. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (dd, *J* = 8.6, 1.4 Hz, 2H), 7.53 (d, *J* = 8.5 Hz, 2H), 5.74 (ddt, *J* = 16.3, 11.0, 5.7 Hz, 1H), 5.11 – 5.00 (m, 2H), 4.71 (d, *J* = 6.7 Hz, 1H), 3.73 – 3.60 (m, 1H), 3.47 – 3.24 (m, 4H), 3.19 (ddd, *J* = 14.0, 5.8, 1.0 Hz, 1H), 3.05 (ddd, *J* = 14.1, 6.0, 0.9 Hz, 1H), 2.73 – 2.62 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 150.1, 147.3, 135.9, 127.4, 123.5, 116.7, 72.1, 63.8, 59.8, 50.1. IR (neat): 3310, 3079, 2881, 1644, 1603, 1513, 1410, 1401, 1341, 1200, 1107, 1043, 995, 921, 853, 823, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{12}H_{17}N_2O_4$ ($[M+H]^+$) 253.1183, found 253.1186.

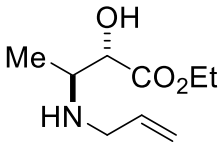
General Procedure (GP-2) for Epoxide Ring Opening with Alkyl Amines

A 500 mL round bottom flask equipped with a magnetic stir bar and reflux condenser was charged with appropriate epoxide **36** (46.3 mmol, 1.0 equiv), alkylamine **40** (46.3 mmol, 1.0 equiv) and EtOH (250 mL). The resulting mixture was refluxed for 24 h at 80 °C. Afterwards the solvent was evaporated *in vacuo*, and the residue was purified by silica gel column chromatography (hexanes / EtOAc) to give monoalkylated amino alcohol **39b**.

rac. Ethyl allyl-D-allothreoninate (39ba´, major) and rac. ethyl (2*S*,3*S*)-3-(allylamino)-2-hydroxybutanoate (39ba, minor)



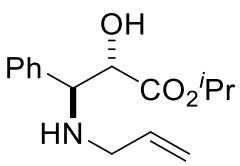
major



minor

Following general procedure GP-2, using ethyl 3-methyloxirane-2-carboxylate (**36b**) (3.1 g, 23.8 mmol, 1.0 equiv), allylamine (**40a**) (1.8 mL, 1.4 g, 23.8 mmol, 1.0 equiv) and EtOH (125 mL) gave 1.4 g (7.6 mmol, 32%) of rac. ethyl allyl-D-allothreoninate (**39ba´**) and 1.1 g (5.7 mmol, 24%) of rac. ethyl (2*S*,3*S*)-3-(allylamino)-2-hydroxybutanoate (**39ba**) as colorless oils after purification by silica gel column chromatography (hexanes / EtOAc, 2:1 to 1:3). R_f (**39ba´**, hexanes / EtOAc, 1:1) = 0.30, R_f (**39ba**, hexanes / EtOAc, 1:1) = 0.08, Staining: Ninhydrin (UV active). ^{1}H NMR (**39ba´**, 300 MHz, $CDCl_3$) δ 5.88 (ddt, *J* = 17.2, 10.2, 6.0 Hz, 1H), 5.18 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.08 (dq, *J* = 10.2, 1.3 Hz, 1H), 4.29 (d, *J* = 3.4 Hz, 1H), 4.23 (qd, *J* = 7.2, 0.7 Hz, 2H), 3.28 (dt, *J* = 6.0, 1.5 Hz, 2H), 3.05 (qd, *J* = 6.6, 3.4 Hz, 1H), 2.49 (bs, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H). ^{1}H NMR (**39ba**, 400 MHz, $CDCl_3$) δ 5.85 – 5.70 (m, 1H), 5.11 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.03 (dq, *J* = 10.1, 1.4 Hz, 1H), 4.21 – 4.08 (m, 2H), 3.97 – 3.89 (m, 1H), 3.32 – 3.20 (m, 2H), 3.07 (ddt, *J* = 13.8, 6.1, 1.4 Hz, 1H), 2.61 (bs, 2H), 1.22 (td, *J* = 7.2, 3.9 Hz, 3H), 1.03 (dd, *J* = 6.6, 1.4 Hz, 3H). ^{13}C NMR (**39ba´**, 75 MHz, $CDCl_3$) δ 173.8, 136.6, 116.3, 71.2, 61.6, 54.6, 49.6, 15.0, 14.3. ^{13}C NMR (**39ba**, 101 MHz, $CDCl_3$) δ 173.2, 136.1, 116.7, 67.3, 65.3, 60.9, 51.3, 18.9, 14.3. IR (**39ba´**, neat): 3497, 3332, 3079, 2982, 2937, 1730, 1644, 1450, 1372, 1301, 1260, 1185, 1156, 1096, 1021, 921, 857, 775 cm^{-1}. IR (**39ba**, neat): 3317, 3079, 2978, 2937, 1730, 1644, 1450, 1372, 1252, 1204, 1129, 1029, 917, 865, 753 cm^{-1}. HRMS (**39ba´**, ESI) m/z calculated for $C_9H_{18}NO_3$ ([M+H]$^+$) 188.1281, found 188.1284. HRMS (**39ba**, ESI) m/z calculated for $C_9H_{18}NO_3$ ([M+H]$^+$) 188.1281, found 188.1286.

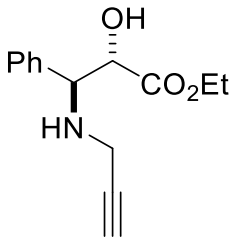
rac. Isopropyl (2*S*,3*S*)-3-(allylamino)-2-hydroxy-3-phenylpropanoate (39bc)



A 500 mL round bottom flask equipped with a magnetic stir bar and reflux condenser was charged with ethyl 3-phenyloxirane-2-carboxylate (**36a**) (8.9 g, 46.3 mmol, 1.0 equiv), allylamine (**40a**) (3.5 mL, 2.6 g,

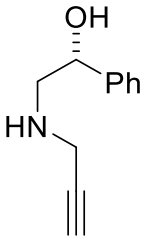
46.3 mmol, 1.0 equiv) and EtOH (250 mL). The resulting mixture was refluxed for 24 h at 80 °C. Afterwards the solvent was evaporated *in vacuo*, and the residue was purified by silica gel column chromatography (hexanes / EtOAc, 2:1 to 1:1) to give 6.5 g (26.1 mmol, 56%) of rac. ethyl (2*S*,3*S*)-3-(allylamino)-2-hydroxy-3-phenylpropanoate (**39bb**) as a colorless oil. Spectral data were in agreement with those reported in literature.[7] A 250 mL round bottom flask equipped with a magnetic stir bar was charged with rac. ethyl (2*S*,3*S*)-3-(allylamino)-2-hydroxy-3-phenylpropanoate (**39bb**) (1.4 g, 5.7 mmol, 1.0 equiv) and isopropanol (200 mL). H_2SO_4 (conc., 2.0 mL) was added dropwise while stirring and the resulting mixture was refluxed for 72 h, neutralized with solid $NaHCO_3$ and filtered off. The solvent was evaporated under reduced pressure and the obtained residue was purified by silica gel column chromatography (hexanes / EtOAc, 10:1 to 3:1) to yield 1.4 g (5.3 mmol, 93%) of rac. Isopropyl (2*S*,3*S*)-3-(allylamino)-2-hydroxy-3-phenylpropanoate (**39bc**) as colorless oil. R_f (hexanes / EtOAc, 1:1) = 0.31, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.22 (m, 5H), 5.89 (ddt, *J* = 17.1, 10.2, 6.0 Hz, 1H), 5.20 – 5.04 (m, 2H), 4.89 (sex, *J* = 6.3 Hz, 1H), 4.50 (d, *J* = 4.0 Hz, 1H), 4.05 (d, *J* = 3.9 Hz, 1H), 3.22 (ddt, *J* = 13.9, 5.8, 1.5 Hz, 1H), 3.08 (ddt, *J* = 14.0, 6.3, 1.5 Hz, 1H), 2.78 (bs, 2H), 1.13 (d, *J* = 6.3 Hz, 3H), 1.10 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 137.7, 136.3, 128.4, 128.1, 128.0, 116.5, 77.6, 77.2, 76.7, 73.4, 69.6, 63.7, 49.7, 21.8, 21.7. IR (neat): 3474, 3332, 3064, 3030, 2982, 2933, 1722, 1644, 1495, 1454, 1375, 1271, 1241, 1208, 1103, 995, 913, 824, 749 cm^{-1}. HRMS (ESI) m/z calculated for $C_{15}H_{22}NO_3$ ([M+H]$^+$) 264.1594, found 264.1598.

rac. Ethyl (2*S*,3*S*)-2-hydroxy-3-phenyl-3-(prop-2-yn-1-ylamino)propanoate (39bd)



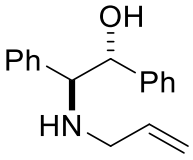
Following general procedure GP-2, using ethyl 3-phenyloxirane-2-carboxylate (**36a**) (4.0 g, 20.9 mmol, 1.0 equiv), propargylamine (**40b**) (1.3 mL, 1.2 g, 20.9 mmol, 1.0 equiv) and EtOH (150 mL) gave 2.8 g (11.3 mmol, 54%) of rac. ethyl (2*S*,3*S*)-2-hydroxy-3-phenyl-3-(prop-2-yn-1-ylamino) propanoate (**39bd**) as a colorless oil after purification by silica gel column chromatography (hexanes / EtOAc, 2:1 to 1:1). 1.4 g (7.4 mmol, 35%) of starting material could be isolated. Based on the uncomplete conversion the yield of the desired product is 84%. R_f (hexanes / EtOAc, 1:1) = 0.43, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.22 (m, 5H), 4.53 (d, *J* = 4.0 Hz, 1H), 4.24 (d, *J* = 4.0 Hz, 1H), 4.08 (qd, *J* = 7.1, 1.9 Hz, 2H), 3.41 (dd, *J* = 16.8, 2.5 Hz, 1H), 3.20 (dd, *J* = 16.8, 2.5 Hz, 1H), 2.75 (bs, 2H), 2.21 (t, *J* = 2.5 Hz, 1H), 1.15 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 137.0, 128.4, 128.2, 81.5, 73.4, 71.9, 63.3, 61.7, 35.8, 14.1. IR (neat): 3474, 3288, 3064, 3030, 2982, 2933, 2840, 1730, 1454, 1368, 1264, 1200, 1115, 1025, 939, 861, 753 cm^{-1}. HRMS (ESI) m/z calculated for $C_{14}H_{18}NO_3$ ([M+H]$^+$) 248.1281, found 248.1283.

1-phenyl-2-(prop-2-yn-1-ylamino)ethan-1-ol (39bf)



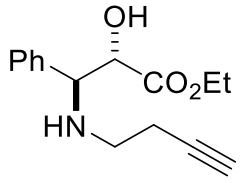
Following general procedure GP-2, using 2-phenyloxirane (**36c**) (2.4 g, 20.0 mmol, 1.0 equiv), propargylamine (**40b**) (2.6 mL, 2.2 g, 40.0 mmol, 2.0 equiv) and EtOH (200 mL) gave 932 mg (5.3 mmol, 27%) of 1-phenyl-2-(prop-2-yn-1-ylamino) ethan-1-ol (**39bf**) as a brownish oil after 72 h and purification by silica gel column chromatography (hexanes / EtOAc, 5:1 to 1:2). R_f (hexanes / EtOAc, 1:1) = 0.13, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.18 (m, 5H), 4.75 (dd, *J* = 8.9, 3.6 Hz, 1H), 3.44 (dd, *J* = 2.5, 1.1 Hz, 2H), 2.98 (ddd, *J* = 12.2, 3.6, 1.5 Hz, 1H), 2.91 – 2.64 (m, 3H), 2.22 (t, *J* = 2.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 128.5, 127.7, 126.0, 81.7, 72.0, 71.9, 56.0, 37.9. IR (neat): 3310, 3203, 3064, 2911, 2851, 2743, 1491, 1435, 1342, 1215, 1111, 1062, 1025, 943, 898, 857, 760 cm^{-1}. HRMS (ESI) m/z calculated for $C_{11}H_{14}NO$ ($[M+H]^+$) 176.1070, found 176.1067.

rac. (1*R*,2*S*)-2-(allylamino)-1,2-diphenylethan-1-ol (39bg)



Following general procedure GP-2, using 2,3-diphenyloxirane (**36d**) (4.7 g, 23.7 mmol, 1.0 equiv), allylamine (**40a**) (3.6 mL, 2.7 g, 47.4 mmol, 2.0 equiv) and EtOH (350 mL) gave 2.9 g (11.3 mmol, 48%) of rac. (1*R*,2*S*)-2-(allylamino)-1,2-diphenylethan-1-ol (**39bg**) as a white solid after purification by silica gel column chromatography (hexanes / EtOAc, 1:2). R_f (hexanes / EtOAc, 1:2) = 0.25, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.20 (m, 6H), 7.19 – 7.08 (m, 4H), 5.80 (ddt, *J* = 15.7, 10.0, 5.9 Hz, 1H), 5.12 – 4.99 (m, 2H), 4.84 (d, *J* = 5.7 Hz, 1H), 3.95 (d, *J* = 5.7 Hz, 1H), 3.17 (dd, *J* = 14.3, 5.5 Hz, 1H), 3.04 (dd, *J* = 14.2, 6.3 Hz, 1H), 1.72 (br, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 140.7, 139.2, 136.5, 128.4, 128.3, 128.1, 127.8, 127.7, 126.9, 116.2, 76.7, 68.0, 49.7. IR (neat): 3213, 3153, 3080, 3032, 2900, 2886, 2857, 2845, 2056, 1987, 1490, 1450, 1423, 1360, 1197, 1100, 1050, 996, 958, 926, 880, 841, 767, 698, 663, 598, 509 cm^{-1}. HRMS (ESI) m/z calculated for $C_{17}H_{20}NO$ ($[M+H]^+$) 254.1539, found 254.1547. mp: 117 °C.

rac. ethyl (2*S*,3*S*)-3-(but-3-yn-1-ylamino)-2-hydroxy-3-phenylpropanoate (38bh)



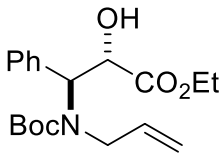
Following general procedure GP-2, using ethyl 3-phenyloxirane-2-carboxylate (**36a**) (1.4 g, 7.3 mmol, 1.0 equiv), but-3-yn-1-amine (**40c**) (501 mg, 7.3 mmol, 1.0 equiv) and EtOH (50 mL) gave 880 mg (3.4 mmol, 46%) of rac. ethyl (2*S*,3*S*)-3-(but-3-yn-1-ylamino)-2-hydroxy-3-phenylpropanoate (**39bh**) as a colorless oil purification by silica gel column chromatography (hexanes / EtOAc, 2:1 to 1:1). R_f (hexanes / EtOAc, 1:1) = 0.44, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.19 (m, 5H), 4.50 (d, *J* = 4.0 Hz, 1H), 4.15 – 3.98 (m, 3H), 2.77 – 2.59 (m, 2H), 2.43 – 2.32 (m, 2H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 137.8, 128.5, 128.0, 127.8, 82.4, 73.5, 69.8, 64.4, 61.5, 45.6, 19.9, 14.1. IR (neat): 3288, 3068, 3038, 2989, 2911, 2870, 2771, 1748, 1491, 1435, 1372, 1297, 1256, 1204, 1129, 1092, 1029, 980, 947, 906, 839, 764, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{15}H_{20}NO_3$ ([M+H]$^+$) 262.1438, found 262.1439.

General Procedure (GP-3) for *N*-Protection of Monoalkylated Amino Alcohols

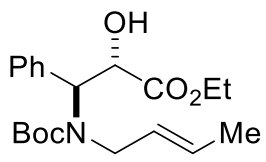
A 50 mL round bottom flask equipped with a magnetic stir bar was charged with monoalkylated amino alcohol **39** (4.0 mmol, 1.0 equiv), triethylamine (4.7 mmol, 1.2 equiv) and CH_2Cl_2 (20 mL). After addition of di-*tert*-butyl-dicarbonate (4.6 mmol, 1.2 equiv) the solution was stirred for 20 h at room temperature. The solvent was evaporated under reduced pressure and the obtained residue was purified by silica gel column chromatography to give monoalkylated and *N*-protected amino alcohol **44**.

rac. Ethyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoate (44a)



Following general procedure GP-3, using rac. ethyl (2*S*,3*S*)-3-(allylamino)-2-hydroxy-3-phenylpropanoate (**39bb**) (5.40 g, 21.7 mmol, 1.0 equiv), triethylamine (3.5 mL, 2.6 g, 25.3 mmol, 1.2 equiv), di-*tert*-butyl dicarbonate (5.4 g, 24.9 mmol, 1.2 equiv) and CH_2Cl_2 (70 mL) gave 4.9 g (14.1 mmol, 65%) of rac. ethyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoate (**44a**) as a colorless oil after purification by silica gel column chromatography (hexanes / EtOAc, 5:1 to 4:1). R_f (hexanes / EtOAc, 5:1) = 0.23, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.22 (m, 5H), 5.58 (br, 1H), 5.41 (br, 1H), 4.92 (d, *J* = 11.3 Hz, 2H), 4.82 (t, *J* = 4.9 Hz, 1H), 4.19 (q, *J* = 6.5 Hz, 2H), 3.93 – 3.67 (m, 2H), 3.52 (br, 1H), 1.43 (s, 9H), 1.20 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.3, 155.8, 136.9, 135.2, 129.0, 128.4, 127.9, 116.1, 80.6, 72.0, 62.2, 61.8, 48.7, 28.5, 14.1. IR (neat): 3445, 3067, 2978, 2932, 1734, 1686, 1454, 1393, 1366, 1300, 1270, 1251, 1166, 1144, 1128, 1096, 1021, 913, 887, 755, 701, 652, 624, 537, 498 cm^{-1}. HRMS (ESI) m/z calculated for $C_{19}H_{28}NO_5$ ([M+H]$^+$) 350.1962, found 350.1960.

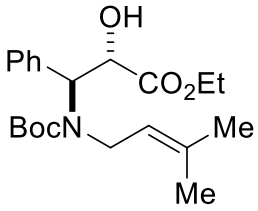
rac. Ethyl (2*S*,3*S*)-3-(((*E*)-but-2-en-1-yl)(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoate (44b)



Following general procedure GP-3, using rac. ethyl (2*S*,3*S*)-3-(((*E*)-but-2-en-1-yl)amino)-2-hydroxy-3-phenylpropanoate (**39aa**) (280 mg, 1.1 mmol, 1.0 equiv), triethylamine (172 µL, 126 mg, 1.2 mmol, 1.2 equiv), di-*tert*-butyl dicarbonate (267 mg, 1.2 mmol, 1.2 equiv) and CH_2Cl_2 (5 mL) gave 285 mg (784 µmol, 74%) of rac. ethyl (2*S*,3*S*)-3-(((*E*)-but-2-en-1-yl)(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoate (**44b**) as a colorless oil after stirring for

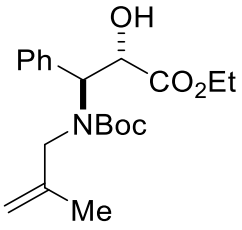
48 h and purification by silica gel column chromatography (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 5:1) = 0.33, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 – 7.23 (m, 5H), 5.57 – 5.01 (m, 3H), 4.84 (t, *J* = 5.5 Hz, 1H), 4.20 (qd, *J* = 7.2, 2.6 Hz, 2H), 3.96 – 3.36 (m, 3H), 1.56 (d, *J* = 5.9 Hz, 3H), 1.43 (s, 9H), 1.22 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, *E*/*Z*-isomers present): δ 173.4, 155.8, 137.0, 135.1, 128.9, 128.4, 128.4, 128.0, 127.8, 127.6, 80.5, 80.4, 72.0, 62.2, 62.0, 48.4, 43.1, 28.5, 17.8, 14.1, 13.0. IR (neat): 3437, 2978, 2937, 1737, 1670, 1454, 1401, 1364, 1282, 1249, 1163, 1129, 1096, 1021, 965, 887, 861, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{20}H_{30}NO_5$ ([M+H]$^+$) 364.2118, found 364.2118.

rac. Ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(3-methylbut-2-en-1-yl)amino)-2-hydroxy-3-phenylpropanoate (44c)



Following general procedure GP-3, using rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((3-methylbut-2-en-1-yl)amino)-3-phenylpropanoate (**39ab**) (285 mg, 1.0 mmol, 1.0 equiv), triethylamine (167 µL, 122 mg, 1.2 mmol, 1.2 equiv), di-*tert*-butyl dicarbonate (258 mg, 1.2 mmol, 1.2 equiv) and CH_2Cl_2 (10 mL) gave 380 mg (1.0 mmol, 98%) of rac. ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(3-methylbut-2-en-1-yl)amino)-2-hydroxy-3-phenylpropanoate (**44c**) as a colorless oil after stirring for 90 h and purification by silica gel column chromatography (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 5:1) = 0.33, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.16 (m, 5H), 5.26 (bs, 1H), 5.01 (s, 1H), 4.83 (t, *J* = 5.6 Hz, 1H), 4.31 – 4.10 (m, 2H), 3.92 – 3.48 (m, 3H), 1.61 (s, 3H), 1.49 (s, 3H), 1.42 (s, 9H), 1.23 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.3, 156.0, 137.1, 133.8, 128.7, 128.3, 127.7, 121.9, 80.4, 72.2, 62.3, 62.1, 44.6, 28.5, 25.7, 17.8, 14.1. IR (neat): 3437, 2978, 2933, 1737, 1689, 1454, 1402, 1364, 1313, 1252, 1159, 1126, 1096, 1021, 947, 891, 775, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{21}H_{32}NO_5$ ([M+H]$^+$) 378.2275, found 378.2281.

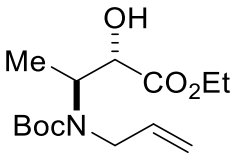
rac. Ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(2-methylallyl)amino)-2-hydroxy-3-phenylpropanoate) (44d)



Following general procedure GP-3, using rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((2-methylallyl)amino)-3-phenylpropanoate (**39ac**) (305 mg, 1.2 mmol, 1.0 equiv), triethylamine (188 µL, 137 mg, 1.4 mmol, 1.2 equiv), di-*tert*-butyl dicarbonate (291 mg, 1.3 mmol, 1.2 equiv) and CH_2Cl_2 (10 mL) gave 120 mg (330 µmol, 29%) of rac. ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(2-methylallyl)amino)-2-hydroxy-3-phenylpropanoate) (**44d**) as a colorless oil after stirring for 72 h and purification by silica gel column chromatography (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 5:1) = 0.25, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.11 (m, 5H), 5.28 (bs, 1H), 4.84 (d, *J* = 4.6 Hz, 1H), 4.70 (s, 1H), 4.65 (s, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.97 – 3.64 (m, 3H), 1.55 (s, 3H), 1.40 (s, 9H), 1.19 (t, *J* = 8.2

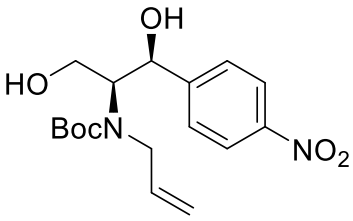
Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.9, 156.0, 142.2, 128.8, 128.2, 127.7, 110.6, 80.5, 72.4, 62.6, 62.0, 52.0, 28.3, 20.1, 14.1. IR (neat): 3444, 2978, 2933, 1737, 1685, 1454, 1394, 1368, 1249, 1163, 1111, 1021, 943, 891, 861, 813, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{20}H_{29}NNaO_5$ ([M+Na]$^+$) 386.1938, found 386.1944.

rac. Ethyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxybutanoate (44e)



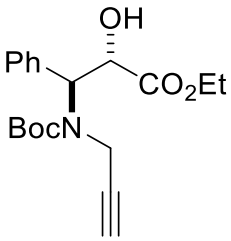
Following general procedure GP-3, using rac. ethyl (2*S*,3*S*)-3-(allylamino)-2-hydroxybutanoate (**39ba**) (773 mg, 4.1 mmol, 1.0 equiv), triethylamine (670 µL, 489 mg, 4.8 mmol, 1.2 equiv), di-*tert*butyl dicarbonate (1.0 g, 4.8 mmol, 1.2 equiv) and CH_2Cl_2 (40 mL) gave 920 mg (3.2 mmol, 78%) of rac. ethyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxybutanoate (**44e**) as a colorless oil after stirring for 48 h and purification by silica gel column chromatography (hexanes / EtOAc, 5:1 to 4:1). R_f (hexanes / EtOAc, 3:1) = 0.38, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (ddt, *J* = 17.2, 10.5, 5.5 Hz, 1H), 5.16 – 5.00 (m, 2H), 4.44 – 4.00 (m, 4H), 3.95 – 3.48 (m, 3H), 1.43 (s, 9H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.20 – 1.11 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.4, 156.0, 135.8, 115.6, 80.2, 74.1, 62.1, 54.4, 47.9, 28.5, 14.3, 12. IR (neat): 3448, 3083, 2982, 2937, 1733, 1689, 1450, 1402, 1368, 1327, 1249, 1148, 1096, 1018, 913, 865, 775 cm^{-1}. HRMS (APCI) m/z calculated for $C_{14}H_{26}NO_5$ ([M+H]$^+$) 288.1805, found 288.1812.

***tert*-butyl allyl((1*S*,2*S*)-1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl)carbamate (44f)**



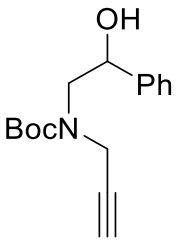
Following general procedure GP-3, using (1*S*,2*S*)-2-(allylamino)-1-(4-nitrophenyl)propane-1,3-diol (**43**) (3.1 g, 12.4 mmol, 1.0 equiv), triethylamine (2.0 mL, 1.5 g, 14.5 mmol, 1.2 equiv), di-*tert*-butyl dicarbonate (3.1 g, 14.2 mmol, 1.2 equiv) and CH_2Cl_2 (75 mL) gave 3.1 g (8.8 mmol, 71%) of *tert*-butyl allyl((1*S*,2*S*)-1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl)carbamate (**44f**) as a white solid after purification by silica gel column chromatography (CH_2Cl_2 / MeOH, 9:1). R_f (CH_2Cl_2 / MeOH, 9:1) = 0.49, Staining: Ninhydrin (UV active). Specific Rotation: $[\alpha]_D^{25}$ = + 91.9 °. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.8 Hz, 2H), 7.51 (d, *J* = 8.7 Hz, 2H), 5.44 – 5.14 (m, 2H), 5.07 – 4.89 (m, 2H), 4.22 – 4.08 (m, 1H), 3.84 (dd, *J* = 11.4, 6.6 Hz, 1H), 3.68 – 3.48 (m, 2H), 3.37 – 3.22 (m, 1H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6, 150.1, 147.4, 133.6, 127.1, 123.5, 117.9, 81.8, 72.8, 67.0, 60.8, 54.3, 28.4. IR (neat): 3504, 3384, 2982, 2937, 2911, 1659, 1637, 1521, 1461, 1416, 1353, 1320, 1274, 1148, 1081, 1047, 992, 913, 857, 828, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{17}H_{24}N_2NaO_6$ ([M+Na]$^+$) 375.1527, found 375.1529. mp: 97 °C.

rac. Ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-2-hydroxy-3-phenylpropanoate (44g)



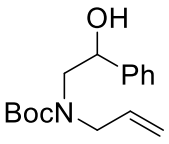
Following general procedure GP-3, using rac. ethyl (2*S*,3*S*)-2-hydroxy-3-phenyl-3-(prop-2-yn-1-ylamino)propanoate (**39bd**) (2.0 g, 8.2 mmol, 1.0 equiv), triethylamine (1.3 mL, 972 mg, 9.6 mmol, 1.2 equiv), di-*tert*-butyl dicarbonate (2.1 g, 9.4 mmol, 1.2 equiv) and CH_2Cl_2 (80 mL) gave 950 mg (2.7 mmol, 33%) of rac. ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-2-hydroxy-3-phenylpropanoate (**44g**) as a yellow oil after stirring for 72 h and purification by silica gel column chromatography (hexanes / EtOAc, 5:1 to 4:1). R_f (hexanes / EtOAc, 3:1) = 0.36, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 2H), 7.36 – 7.23 (m, 3H), 5.47 (bs, 1H), 4.91 (s, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.11 – 3.92 (m, 2H), 3.29 (bs, 1H), 2.06 (s, 1H), 1.46 (s, 9H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 155.1, 136.3, 128.9, 128.5, 128.0, 110.1, 81.3, 80.8, 72.2, 70.5, 62.3, 61.2, 35.4, 28.4, 14.1. IR (neat): 3444, 3295, 3064, 2982, 2937, 1733, 1689, 1446, 1394, 1368, 1252, 1159, 1125, 941, 887, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{19}H_{25}NNaO_5$ ([M+Na]$^+$) 370.1625, found 370.1628.

***tert*-butyl-(2-hydroxy-2-phenylethyl)(prop-2-yn-1-yl)carbamate (44h)**



Following general procedure GP-3, using 1-phenyl-2-(prop-2-yn-1-ylamino)ethan-1-ol (**39bf**) (339 mg, 1.9 mmol, 1.0 equiv), triethylamine (322 µL, 235 mg, 2.3 mmol, 1.2 equiv), di-*tert*-butyl dicarbonate (507 mg, 2.3 mmol, 1.2 equiv) and CH_2Cl_2 (60 mL) gave 517 mg (1.9 mmol, 97%) of *tert*-butyl-(2-hydroxy-2-phenylethyl)(prop-2-yn-1-yl)carbamate (**44h**) as a yellowish solid after stirring for 72 h and purification by silica gel column chromatography (hexanes / EtOAc, 15:1 to 2:1). R_f (hexanes / EtOAc, 1:1) = 0.86, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.25 (m, 5H), 4.99 (t, *J* = 5.8 Hz, 1H), 4.28 – 3.76 (m, 2H), 3.56 (d, *J* = 6.4 Hz, 2H), 2.25 (t, *J* = 2.5 Hz, 1H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.2, 128.6, 127.8, 125.9, 81.5, 79.6, 74.0, 71.9, 55.5, 38.6, 28.5. IR (neat): 3440, 3247, 3064, 3012, 2982, 2937, 2113, 1685, 1457, 1394, 1368, 1312, 1252, 1189, 1155, 1129, 1029, 954, 887, 849, 783, 757, 705 cm^{-1}. HRMS (ESI) m/z calculated for $C_{16}H_{21}NNaO_3$ ([M+Na]$^+$) 298.1414, found 298.1410.

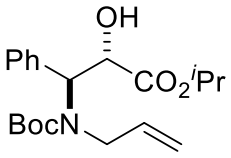
***tert*-butyl allyl(2-hydroxy-2-phenylethyl)carbamate (44i)**



Following general procedure GP-3, using 2-(allylamino)-1-phenylethan-1-ol (**39be**) (1.7 g, 9.8 mmol, 1.0 equiv), triethylamine (1.6 mL, 1.2 g, 11.7 mmol, 1.2 equiv), di-*tert*-butyl dicarbonate (2.6 g, 11.7 mmol, 1.2 equiv) and CH_2Cl_2 (80 mL) gave 1.6 g (5.8 mmol, 59%) of *tert*-butyl allyl(2-hydroxy-2-phenylethyl)carbamate

(**44i**) as a yellow oil after stirring for 48 h and purification by silica gel column chromatography (hexanes / EtOAc, 9:1 to 3:1). R_f (hexanes / EtOAc, 3:1) = 0.53, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.25 (m, 5H), 5.78 – 5.61 (m, 1H), 5.20 – 5.00 (m, 2H), 4.92 (dt, *J* = 7.6, 3.6 Hz, 1H), 4.41 (bs, 1H), 3.98 – 3.22 (m, 4H), 1.47 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 142.5, 133.8, 128.5, 127.6, 125.9, 116.6, 80.8, 74.4, 55.8, 51.9, 28.5. IR (neat): 3429, 3064, 2978, 2933, 1670, 1457, 1409, 1364, 1249, 1163, 1100, 1059, 995, 917, 872, 753, 701cm^{-1}. HRMS (ESI) m/z calculated for $C_{16}H_{23}NNaO_3$ ([M+Na]$^+$) 300.1570, found 300.1577.

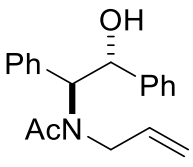
rac. isopropyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenyl-propanoate (44j)



Following general procedure GP-3, using rac. isopropyl (2*S*,3*S*)-3-(allylamino)-2-hydroxy-3-phenylpropanoate (**39bc**) (1.4 g, 5.2 mmol, 1.0 equiv), triethylamine (865 µL, 632 mg, 6.2 mmol, 1.2 equiv), di-*tert*-butyl dicarbonate (1.4 g, 6.2 mmol, 1.2 equiv) and CH_2Cl_2 (60 mL) gave 1.2 g (3.3 mmol, 63%) of rac. isopropyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenyl-propanoate (**44j**) as a colorless oil after stirring for 48 h and purification by silica gel column chromatography (hexanes / EtOAc, 7:1 to 3:1). R_f (hexanes / EtOAc, 3:1) = 0.53, Staining: Ninhydrin, $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.36 (m, 2H), 7.27 (dq, *J* = 6.6, 5.5, 4.5 Hz, 3H), 5.56 (s, 2H), 5.01 (p, *J* = 6.2 Hz, 1H), 4.90 (d, *J* = 12.2 Hz, 2H), 4.79 (t, *J* = 4.8 Hz, 1H), 3.88 (t, *J* = 7.6 Hz, 2H), 3.60 – 3.20 (m, 1H), 1.44 (s, 9H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.06 (bs, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 155.9, 137.1, 135.3, 129.2, 128.4, 127.9, 115.9, 80.5, 72.3, 70.2, 61.2, 48.7, 28.5, 21.8, 21.5. IR (neat): 3444, 3068, 2982, 2937, 1730, 1685, 1454, 1394, 1368, 1252, 1167, 1103, 992, 910, 820, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{20}H_{29}NNaO_5$ ([M+Na]$^+$) 386.1938, found 386.1950.

***N*-Ac Protection**

rac. *N*-allyl-*N*-((1*S*,2*R*)-2-hydroxy-1,2-diphenylethyl)acetamide (44m)



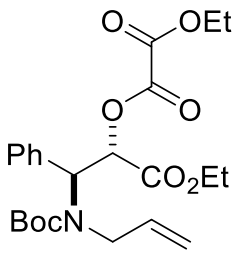
A 100 mL round bottom flask equipped with a magnetic stir bar was charged with rac. (1*S*,2*R*)-2-(allylamino)-1,2-diphenylethan-1-ol (**39bg**) (2.1 g, 8.4 mmol, 1.0 equiv), triethylamine (2.6 mL, 1.9 g, 18.5 mmol, 2.2 equiv) and CH_2Cl_2 (60 mL). Acetic anhydride (1.6 mL, 1.8 g, 17.3 mmol, 2.1 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 30 h at room temperature. The resulting solution was washed with water (30 mL), 1M HCl (40 mL) and brine (30 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexanes / EtOAc, 2:1) to give 1.7 g (5.9 mmol, 70%) of rac. *N*-allyl-*N*-((1*S*,2*R*)-2-hydroxy-1,2-

diphenylethyl)acetamide (**44m**) as a white solid. R_f (hexanes / EtOAc, 1:1) = 0.44, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.23 (m, 10H), 5.54 – 5.41 (m, 2H), 5.18 – 5.05 (m, 2H), 4.93 (d, *J* = 5.0 Hz, 1H), 4.38 (bs, 1H), 3.84 (dd, *J* = 17.5, 5.0 Hz, 1H), 3.67 (dd, *J* = 17.5, 5.2 Hz, 1H), 2.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.4, 141.8, 136.6, 133.3, 129.7, 128.3, 128.2, 128.0, 127.8, 126.9, 117.3, 74.2, 69.6, 52.2, 22.9. IR (neat): 3247, 3019, 2870, 1603, 1500, 1424, 1320, 1275, 1178, 1066, 1033, 915, 771, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{19}H_{22}NO_2$ ([M+H]$^+$) 296.1645, found 296.1650. mp: 98 °C.

General Procedure (GP-4) for the Preparation of Ethyl Oxalyl Esters via Acylation with Ethyl 2-chloro-2-oxoacetate

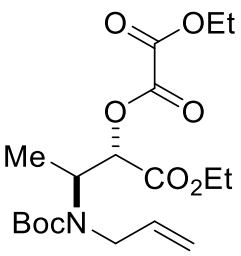
A 50 mL round bottom flask equipped with a magnetic stir bar was charged with *N*-alkylated and protected amino alcohol **44** (10.8 mmol, 1.0 equiv) and pyridine (10.8 mmol, 1.0 equiv) in CH_2Cl_2 (50 mL). The solution was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (**15**) (10.8 mmol, 1.0 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. The reaction mixture was washed with water (3x 20 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to give ethyl oxalyl ester **45**.

rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (45a)



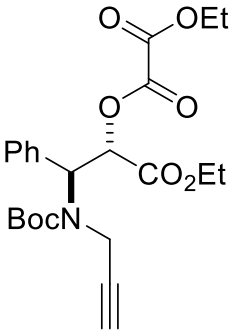
Following general procedure GP-4, using rac. ethyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoate (**44a**) (3.8 g, 10.8 mmol, 1.0 equiv), pyridine (869 µL, 851 mg, 10.8 mmol, 1.0 equiv), ethyl 2-chloro-2-oxoacetate (**15**) (1.2 mL, 1.5 g, 10.8 mmol, 1.0 equiv) and CH_2Cl_2 (50 mL) gave 4.5 g (10.1 mmol, 93%) of rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (**45a**) as a colorless oil. R_f (hexanes / EtOAc, 3:1) = 0.59, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 – 7.39 (m, 2H), 7.35 – 7.27 (m, 3H), 6.16 – 5.70 (m, 2H), 5.42 (s, 1H), 4.99 – 4.65 (m, 2H), 4.42 – 4.28 (m, 2H), 4.19 – 4.02 (m, 2H), 3.70 (bs, 2H), 1.46 (s, 9H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.10 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.7, 156.8, 156.8, 135.3, 134.9, 129.5, 128.6, 128.4, 115.7, 81.0, 75.2, 63.5, 62.2, 58.9, 48.0, 28.4, 14.0, 13.9. IR (neat): 3034, 2981, 2936, 2910, 2878, 1775, 1747, 1690, 1499, 1476, 1453, 1393, 1368, 1351, 1309, 1271, 1250, 1153, 1094, 1018, 954, 921 884, 860, 771, 755, 701, 606 cm^{-1}. HRMS (ESI) m/z calculated for $C_{23}H_{32}NO_8$ ([M+H]$^+$) 450.2122, found 450.2122.

rac. (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-1-ethoxy-1-oxobutan-2-yl ethyl oxalate (45e)



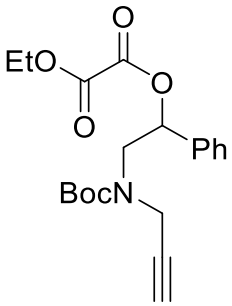
Following general procedure GP-4, using rac. ethyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxybutanoate (**44e**) (200 mg, 696 µmol, 1.0 equiv), pyridine (165 µL, 162 mg, 1.3 mmol, 1.8 equiv), ethyl 2-chloro-2-oxoacetate (**15**) (139 µL, 171 mg, 1.3 mmol, 1.8 equiv) and CH_2Cl_2 (10 mL) gave 268 mg (692 µmol, 99%) of rac. (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-1-ethoxy-1-oxobutan-2-yl ethyl oxalate (**45e**) as a colorless oil. R_f (hexanes / EtOAc, 3:1) = 0.55, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 – 5.69 (m, 1H), 5.26 (s, 1H), 5.15 – 4.99 (m, 2H), 4.74 (rotamer, bs, 1H), 4.37 (qd, *J* = 7.1, 1.3 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.96 – 3.71 (m, 2H), 1.52 – 1.40 (m, 9H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.32 – 1.23 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, rotamers present) δ 167.1, 157.0, 155.3, 154.6, 135.8, 135.0, 116.4, 115.5, 80.9, 80.5, 76.9, 63.5, 62.1, 52.8, 51.4, 48.0, 46.9, 28.5, 14.0, 13.5. IR (neat): 2982, 2941, 1744, 1692, 1450, 1392, 1368, 1316, 1252, 1148, 1018, 917, 861, 775 cm^{-1}. HRMS (ESI) m/z calculated for $C_{18}H_{29}NNaO_8$ ($[M+Na]^+$) 410.1785, found 410.1790.

rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (45g)



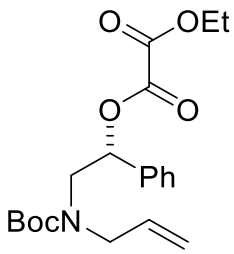
Following general procedure GP-4, using rac. ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-2-hydroxy-3-phenylpropanoate (**44g**) (401 mg, 1.2 mmol, 1.0 equiv), pyridine (183 µL, 179 mg, 1.4 mmol, 1.2 equiv), ethyl 2-chloro-2-oxoacetate (**15**) (154 µL, 189 mg, 1.4 mmol, 1.2 equiv) and CH_2Cl_2 (20 mL) gave 504 mg (1.1 mmol, 98%) of rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (**45g**) as a colorless oil. R_f (hexanes / EtOAc, 3:1) = 0.58, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.46 (m, 2H), 7.39 – 7.27 (m, 3H), 6.01 (bs, 1H), 5.84 (d, *J* = 4.7 Hz, 1H), 4.37 (qd, *J* = 7.1, 1.9 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 4.00 – 3.60 (m, 2H), 1.97 (s, 1H), 1.50 (s, 9H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, rotamers present) δ 166.5, 156.8, 156.5, 154.6, 134.8, 129.2, 128.8, 128.5, 81.8, 81.1, 75.5, 70.3, 63.5, 62.3, 58.2, 34.7, 28.4, 14.0, 14.0. IR (neat): 3288, 2982, 2937, 1748, 1696, 1443, 1394, 1368, 1308, 1252, 1156, 1018, 958, 883, 820, 772, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{23}H_{29}NNaO_8$ ($[M+Na]^+$) 470.1785, found 470.1785.

2-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-1-phenylethyl ethyl oxalate (45h)



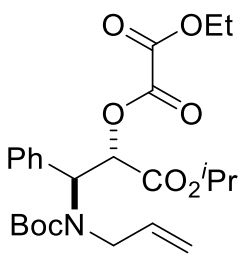
Following general procedure GP-4, using *tert*-butyl-(2-hydroxy-2-phenylethyl)(prop-2-yn-1-yl)carbamate (**44h**) (205 mg, 745 µmol, 1.0 equiv), pyridine (72 µL, 71 mg, 893 µmol, 1.2 equiv), ethyl 2-chloro-2-oxoacetate (**15**) (100 µL, 122 mg, 893 µmol, 1.2 equiv) and CH_2Cl_2 (10 mL) gave 279 mg (743 µmol, 100%) of 2-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-1-phenylethyl ethyl oxalate (**45h**) as a colorless oil. R_f (hexanes / EtOAc, 3:1) = 0.63, Staining: Vanillin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.31 (m, 5H), 6.18 – 6.05 (m, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.21 – 3.94 (m, 2H), 3.86 – 3.61 (m, 2H), 2.28 – 2.13 (m, 1H), 1.46 (s, 9H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, rotamers present) δ 157.6, 157.0, 154.9, 154.7, 136.6, 129.0, 126.6, 81.2, 81.1, 79.7, 79.4, 77.6, 72.2, 71.7, 63.4, 63.3, 51.6, 51.3, 38.2, 37.3, 28.4, 14.1. IR (neat): 3288, 2982, 2937, 1760, 1744, 1696, 1463, 1405, 1368, 1305, 1245, 1156, 1129, 1003, 932, 865 760, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{20}H_{25}NNaO_6$ ([M+Na]$^+$) 398.1574, found 398.1580.

2-(allyl(*tert*-butoxycarbonyl)amino)-1-phenylethyl ethyl oxalate (45i)



Following general procedure GP-4, using *tert*-butyl allyl(2-hydroxy-2-phenylethyl)carbamate (**44i**) (411 mg, 1.5 mmol, 1.0 equiv), pyridine (179 µL, 176 mg, 2.2 mmol, 1.5 equiv), ethyl 2-chloro-2-oxoacetate (**15**) (248 µL, 303 mg, 2.2 mmol, 1.5 equiv) and CH_2Cl_2 (15 mL) gave 526 mg (1.4 mmol, 94%) of 2-(allyl(*tert*-butoxycarbonyl)amino)-1-phenylethyl ethyl oxalate (**45i**) as a colorless oil. R_f (hexanes / EtOAc, 3:1) = 0.63, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.30 (m, 5H), 6.23 – 6.01 (m, 1H), 5.73 (ddd, *J* = 16.2, 10.7, 5.3 Hz, 1H), 5.21 – 5.00 (m, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 3.98 – 3.75 (m, 2H), 3.74 – 3.40 (m, 2H), 1.50 – 1.42 (m, 9H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, rotamers present) δ 157.8, 157.6, 157.2, 157.1, 155.6, 155.1, 136.8, 133.8, 128.9, 128.8, 126.6, 117.0, 116.3, 80.6, 80.3, 63.4, 63.3, 51.9, 51.5, 51.3, 50.5, 28.5, 14.1. IR (neat): 2982, 2937, 1769, 1751, 1692, 1457, 1405, 1305, 1249, 1144, 999, 924, 865, 757, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{20}H_{27}NNaO_6$ ([M+Na]$^+$) 400.1731, found 400.1739.

rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-isopropoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (45j)

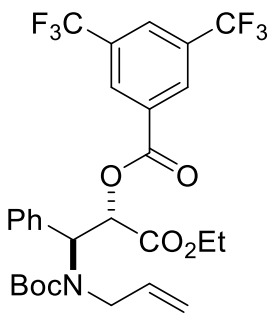


Following general procedure GP-4, using rac. isopropyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenyl-propanoate (**44j**) (408 mg, 1.1 mmol, 1.0 equiv), pyridine (175 µL, 133 mg, 1.7 mmol, 1.5 equiv), ethyl 2-chloro-2-oxoacetate (**15**) (187 µL, 230 mg, 1.7 mmol, 1.5 equiv) and CH_2Cl_2 (11 mL) gave 494 mg (1.1 mmol, 95%) of rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-isopropoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (**45j**) as a orange oil. R_f (hexanes / EtOAc, 3:1) = 0.55, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (bs, 2H), 7.38 – 7.26 (m, 3H), 6.10 – 5.69 (m, 2H), 5.55 – 5.22 (m, 1H), 5.04 – 4.62 (m, 3H), 4.37 (dt, *J* = 7.9, 6.5 Hz, 2H), 3.86 – 3.54 (m, 2H), 1.46 (s, 9H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.19 (d, *J* = 6.3 Hz, 3H), 0.90 (bs, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 156.9, 156.8, 135.3, 134.9, 129.6, 128.6, 128.4, 115.3, 80.9, 75.4, 70.2, 63.5, 58.5, 47.7, 28.5, 21.6, 21.3, 14.0. IR (neat): 2982, 2937, 1774, 1744, 1689, 1454, 1394, 1308, 1252, 1144, 1103, 1000, 913, 880, 820, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{24}H_{33}NNaO_8$ ([M+Na]$^+$) 486.2098, found 486.2104.

General Procedure (GP-5) for the Preparation of 3,5-Bis(trifluoromethyl)benzoate Esters via Benzoylation with 3,5-Bis(trifluoromethyl)benzoic Anhydride

A flame dried 50 mL Schlenk flask equipped with a magnetic stir bar was charged with *N*-alkylated and protected amino alcohol **44** (1.1 mmol, 1.0 equiv) and dry CH_2Cl_2 (20 mL). *N*,*N*-diisoproylethylamine (2.2 mmol, 2.0 equiv) was added followed by the addition of 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (1.3 mmol, 1.2 equiv). After stirring for 16 h at room temperature, CH_2Cl_2 (40 mL) was added and the organic layer was washed with Na_2CO_3 (aq. 10%, 20 mL) and water (20 mL). The organic phase was dried over anhydrous Na_2SO_4 and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography to give the 3,5-bis(trifluoromethyl)benzoate ester **47**.

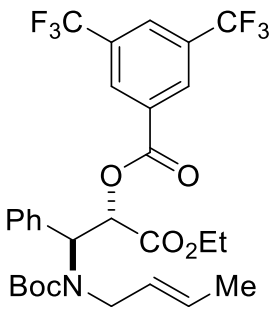
rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47a)



Following general procedure GP-5**,** using rac. ethyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoate (**44a**) (1.1 g, 3.0 mmol, 1.0 equiv), *N*,*N*-diisoproylethylamine (1.0 mL, 775 mg, 6.0 mmol, 2.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (1.8 g, 3.6 mmol, 1.2 equiv) and dry CH_2Cl_2 (60 mL) gave 1.8 g (3.0 mmol, 100%) of rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoro- methyl)benzoate (**47a**) as colorless oil after purification by flash chromatography (hexanes / EtOAc, 3:1). R_f

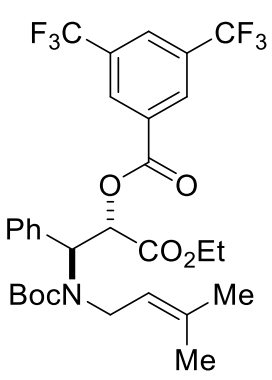
(hexanes / EtOAc, 3:1) = 0.75, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (s, 2H), 8.04 (s, 1H), 7.48 – 7.41 (m, 2H), 7.38 – 7.30 (m, 3H), 6.01 (d, *J* = 8.0 Hz, 1H), 5.79 (bs, 1H), 5.51 (bs, 1H), 4.99 – 4.78 (m, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.87 – 3.66 (m, 2H), 1.48 (s, 9H), 1.24 (t, *J* = 7.0 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.62 (s, 6F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.1, 163.2, 136.1, 134.7, 132.5 (q, *J* = 34.1 Hz), 131.5, 130.0 (d, *J* = 3.3 Hz), 128.8, 128.5, 127.1 – 126.8 (m), 127.3 – 118.4 (m), 116.4, 81.1, 73.6, 62.3, 59.6, 48.6, 28.5, 14.1. IR (neat): 3071, 2982, 1741, 1692, 1625, 1454, 1394, 1367, 1279, 1249, 1174, 1133, 1033, 954, 913, 883, 846, 816, 757, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{28}H_{29}F_6NNaO_6$ ([M+Na]$^+$) 613.1824, found 613.1827.

rac. (1*S*,2*S*)-1-(((*E*)-but-2-en-1-yl)(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47b)



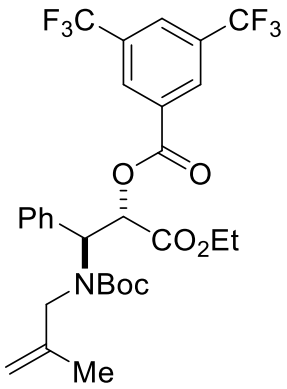
Following general procedure GP-5**,** using rac. ethyl (2*S*,3*S*)-3-(((*E*)-but-2-en-1-yl)(*tert*-butoxycarbonyl) amino)-2-hydroxy-3-phenylpropanoate (**44b**) (204 mg, 561 µmol, 1.0 equiv), *N,N*-diisoproylethylamine (191 µL, 145 mg, 1.1 mmol, 2.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (336 mg, 674 µmol, 1.2 equiv) and dry CH_2Cl_2 (60 mL) gave 336. mg (557 µmol, 99%) of rac. (1*S*,2*S*)-1-(((*E*)-but-2-en-1-yl)(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoro-methyl)benzoate (**47b**) as colorless oil after purification by flash chromatography (hexanes / EtOAc, 3:1). R_f (hexanes / EtOAc, 3:1) = 0.88. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, CDCl3): δ 8.31 (s, 2H), 8.03 (s, 1H), 7.54 – 7.21 (m, 5H), 6.03 (d, *J* = 8.1 Hz, 1H), 5.95 – 4.87 (m, 3H), 4.22 (q, *J* = 12.0, 6.0 Hz, 2H), 3.96 – 3.44 (m, 2H), 1.45 (s, 12H), 1.22 (t, *J* = 6.0 Hz, 3H). ^{19}F NMR (376 MHz, CDCl3): δ -63.69 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$, *E*/*Z*-isomers present) δ 168.2, 163.2, 163.2, 155.2, 136.3, 132.4 (q, *J* = 34.2 Hz), 131.5, 130.1 – 129.9 (m), 128.8, 128.7, 128.4, 128.3, 127.2, 127.0 – 126.7 (m), 122.8 (q, *J* = 272.9 Hz), 80.8, 73.7, 73.5, 62.2, 59.7, 48.1, 28.4, 17.6, 14.1, 12.7. IR (neat): 2982, 2937, 1741, 1692, 1454, 1394, 1368, 1279, 1174, 1133, 1036, 962, 910, 846, 816, 768, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{29}H_{31}F_6NNaO_6$ ([M+Na]$^+$) 626.1948, found 626.1956.

rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(3-methylbut-2-en-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47c)



Following general procedure GP-5**,** using rac. ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl) (3-methylbut-2-en-1-yl)amino)-2-hydroxy-3-phenylpropanoate (**44c**) (203 mg, 538 µmol, 1.0 equiv), *N,N*-diisoproylethylamine (183 µL, 139 mg, 1.1 mmol, 2.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (322 mg, 645 µmol, 1.2 equiv) and dry CH_2Cl_2 (60 mL) gave 321 mg (520 µmol, 97%) of rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(3-methylbut-2-en-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (**47c**) as colorless oil after purification by flash chromatography (hexanes / EtOAc, 3:1). R_f (hexanes / EtOAc, 6:1) = 0.63. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 2H), 8.03 (s, 1H), 7.49 – 7.25 (m, 5H), 6.04 (d, *J* = 7.8 Hz, 1H), 5.68 (bs, 1H), 4.90 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.93 – 3.55 (m, 2H), 1.47 (s, 12H), 1.38 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -63.67 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 163.2, 155.2, 136.3, 132.4 (q, *J* = 34.2 Hz), 131.5, 130.0 (d, *J* = 3.1 Hz), 128.7, 128.3, 127.0 – 126.7 (m), 128.4 – 117.1 (m), 122.0, 121.9, 80.8, 73.8, 62.2, 59.7, 44.3, 28.5, 25.5, 17.6, 14.1. IR (neat): 3068, 2982, 2937, 1741, 1692, 1625, 1454, 1394, 1368, 1279, 1249, 1178, 1137, 1029, 954, 913, 846, 760, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{30}H_{33}F_6NNaO_6$ ([M+Na]$^+$) 640.2104, found 640.2109.

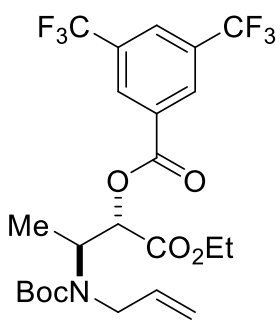
rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(2-methylallyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47d)



Following general procedure GP-5**,** using rac. ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(2-methylallyl)amino)-2-hydroxy-3-phenylpropanoate) (**44d**) (70 mg, 193 µmol, 1.0 equiv), *N,N*-diisopropylethylamine (66 µL, 50 mg, 385 µmol, 2.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (115 mg, 231 µmol, 1.2 equiv) and dry CH_2Cl_2 (60 mL) gave 113 mg (187 µmol, 97%) of rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(2-methylallyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (**47d**) as colorless oil after purification by flash chromatography (hexanes / EtOAc, 3:1). R_f (hexanes / EtOAc, 6:1) = 0.63. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (s, 2H), 8.04 (s, 1H), 7.52 – 7.26 (m, 5H), 6.06 (d, *J* = 7.3 Hz, 1H), 5.73 (bs, 1H), 4.61 (d, *J* = 9.2 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.98 – 3.50 (m, 2H), 1.47 (s, 9H), 1.41 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (376 MHz, CDCl3): δ -63.63 (s, 6F). ^{13}C NMR (75 MHz, CDCl3): δ 168.1, 163.1, 155.5, 141.6, 136.1, 132.4 (q, *J* = 34.2 Hz), 131.6, 130.1 – 129.8 (m), 129.0, 128.7, 128.4, 127.0 – 126.7 (m), 122.8 (q, *J* = 272.9 Hz), 111.1, 81.0, 73.9, 62.3, 60.0, 51.8, 28.4, 20.0, 14.1. IR (neat): 3071, 2982,

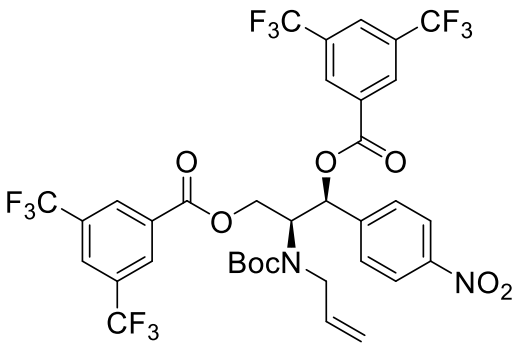
2937, 1744, 1696, 1625, 1454, 1394, 1372, 1279, 1249, 1174, 1137, 1029, 958, 913, 846, 816, 768, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{29}H_{31}F_6NNaO_6$ ($[M+Na]^+$) 626.1948, found 626.1951.

rac. (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-1-ethoxy-1-oxobutan-2-yl 3,5-bis(trifluoromethyl)benzoate (47e)



Following general procedure GP-5**,** using rac. ethyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxybutanoate (**44e**) (298 mg, 1.0 mmol, 1.0 equiv), *N*,*N*-diisoproylethylamine (529 µL, 402 mg, 3.1 mmol, 3.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (930 mg, 1.9 mmol, 1.8 equiv) and dry CH_2Cl_2 (20 mL) gave 535 mg (1.0 mmol, 98%) of rac. (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-1-ethoxy-1-oxobutan-2-yl 3,5-bis(trifluoromethyl)benzoate (**47e**) as yellow oil after purification by flash chromatography (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 3:1) = 0.74, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 2H), 8.10 (s, 1H), 5.77 (td, *J* = 10.7, 5.2 Hz, 1H), 5.45 (d, *J* = 6.1 Hz, 1H), 5.16 – 4.99 (m, 2H), 4.76 (rotamer, bs, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.05 – 3.66 (m, 2H), 1.57 – 1.43 (m, 9H), 1.40 (d, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -63.64 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$, rotamers present) δ 168.3, 168.0, 163.3, 155.3, 154.7, 140.7, 135.5, 134.9, 132.5 (q, *J* = 34.1 Hz), 131.7, 129.97 (d, *J* = 3.9 Hz), 127.08 – 126.76 (m), 122.9 (q, *J* = 272.9 Hz), 126.9, 116.6, 115.7, 81.0, 80.5, 76.1, 62.0, 53.2, 51.9, 48.6, 47.3, 28.4, 15.4, 14.2. IR (neat): 2982, 2941, 1741, 1696, 1625, 1454, 1368, 1323, 1279, 1245, 1174, 1133, 1018, 913, 860, 768, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{23}H_{27}F_6NNaO_6$ ($[M+Na]^+$) 550.1635, found 550.1649.

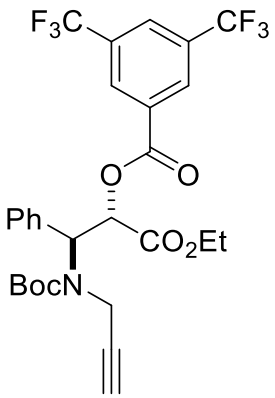
(1*S*,2*S*)-2-(allyl(*tert*-butoxycarbonyl)amino)-1-(4-nitrophenyl)propane-1,3-diyl bis(3,5-bis(trifluoro-methyl)benzoate) (47f)



Following general procedure GP-5**,** using *tert*-butyl allyl((1*S*,2*S*)-1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl)carbamate (**44f**) (238 mg, 675 µmol, 1.0 equiv), *N*,*N*-diisoproylethylamine (459 µL, 349 mg, 2.7 mmol, 4.0 equiv), 3,5-bis(trifluoromethyl)-benzoic anhydride (**46**) (808 mg, 1.6 mmol, 2.4 equiv) and dry CH_2Cl_2 (20 mL) gave 554 mg (665 µmol, 99%) of (1*S*,2*S*)-2-(allyl(*tert*-butoxycarbonyl)amino)-1-(4-nitrophenyl)propane-1,3-diyl bis(3,5-bis(trifluoro-methyl)benzoate) (**47f**) as yellow oil after purification by flash chromatography (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 6:1) = 0.67, Staining: $KMnO_4$ (UV active). Specific Rotation: $[\alpha]_D^{25}$ = + 22.7 °. ^{1}H NMR (400 MHz, $CDCl_3$) δ

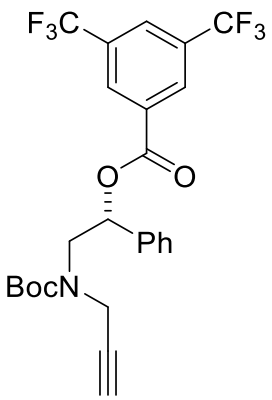
8.55 – 8.41 (m, 2H), 8.35 – 8.20 (m, 4H), 8.08 (d, *J* = 17.8 Hz, 2H), 7.70 (dd, *J* = 21.6, 8.4 Hz, 2H), 6.76 – 6.07 (m, 1H), 5.97 – 5.67 (m, 1H), 5.43 – 3.72 (m, 7H), 1.35 (s, 9H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -63.52 (s, 6F), -63.60 (s, 6F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 162.7, 148.5, 143.5, 134.4, 132.9, 132.7, 132.6, 132.4, 131.6, 130.0, 129.7, 128.6, 126.9, 124.5, 127.4 – 118.6 (m), 81.4, 74.7, 62.9, 58.2, 50.4, 28.1. IR (neat): 3090, 2982, 1737, 1700, 1610, 1528, 1457, 1349, 1279, 1238, 1179, 1133, 992, 962, 913, 846, 768, 682 cm^{-1}. HRMS (ESI) m/z calculated for $C_{35}H_{28}F_{12}N_2NaO_8$ ([M+Na]$^+$) 855.1546, found 855.1545.

rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47g)



Following general procedure GP-5**,** using rac. ethyl (2*S*,3*S*)-3-((*tert* butoxycarbonyl)(prop-2-yn-1-yl)amino)-2-hydroxy-3 phenylpropanoate (**44g**) (324 mg, 933 µmol, 1.0 equiv), *N*,*N*-diisoproylethylamine (317 µL, 241 mg, 1.9 mmol, 2.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (558 mg, 1.1 mmol, 1.2 equiv) and dry CH_2Cl_2 (20 mL) gave 527 mg (897 µmol, 96%) of rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (**47g**) as yellow oil after purification by flash chromatography (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 3:1) = 0.75, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 2H), 8.06 (s, 1H), 7.54 – 7.45 (m, 2H), 7.43 – 7.30 (m, 3H), 6.09 (d, *J* = 6.6 Hz, 1H), 5.89 (bs, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 4.07 – 3.64 (m, 2H), 1.90 (s, 1H), 1.51 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.63 (s, 6F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 163.2, 154.6, 135.4, 132.4 (q, *J* = 34.2 Hz), 131.8, 130.2 – 129.9 (m), 129.0, 128.6, 127.0 – 126.8 (m), 127.0 – 118.6 (m), 81.9, 80.3, 74.0, 70.9, 62.4, 59.3, 35.2, 28.4, 14.1. IR (neat): 3314, 2982, 1741, 1700, 1443, 1394, 1372, 1279, 1249, 1174, 1133, 1033, 910, 883, 846, 760, 682 cm^{-1}. HRMS (ESI) m/z calculated for $C_{28}H_{27}F_6NNaO_6$ ([M+Na]$^+$) 610.1635, found 610.1638.

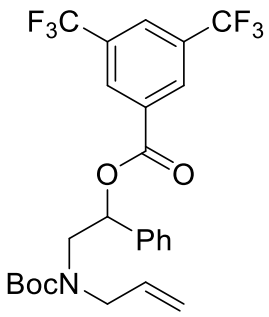
2-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-1-phenylethyl 3,5-bis(trifluoromethyl)-benzoate (47h)



Following general procedure GP-5**,** using *tert*-butyl-(2-hydroxy-2-phenylethyl)(prop-2-yn-1-yl)carbamate (**44h**) (149 mg, 541 µmol, 1.0 equiv), *N*,*N*-diisoproylethylamine (184 µL, 140 mg, 1.1 mmol, 2.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (324 mg, 649 µmol, 1.2 equiv) and dry CH_2Cl_2 (20 mL) gave 274 mg (532 µmol, 98%) of 2-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-1-phenylethyl 3,5-bis(trifluoromethyl)benzoate (**47h**) as colorless oil after purification by flash chromatography (hexanes / EtOAc, 12:1 to 3:1). R_f (hexanes /

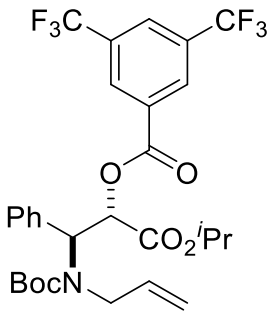
EtOAc, 3:1) = 0.89, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (s, 2H), 8.08 (s, 1H), 7.59 – 7.32 (m, 5H), 6.43 – 6.21 (m, 1H), 4.34 – 3.88 (m, 3H), 3.84 – 3.57 (m, 1H), 2.24 (d, *J* = 9.1 Hz, 1H), 1.43 (d, *J* = 13.1 Hz, 9H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -63.44 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 163.2, 154.9, 154.8, 137.4, 137.3, 133.1, 132.5, 132.1, 130.3 – 129.7 (m), 129.0, 126.6, 123.0 (q, *J* = 273.0 Hz), 81.2, 81.0, 79.3, 79.2, 76.2, 76.0, 72.8, 72.2, 51.2, 37.6, 37.2, 28.3. IR (neat): 3314, 3071, 2982, 2937, 1733, 1700, 1625, 1454, 1409, 1368, 1279, 1241, 1174, 1133, 1010, 913, 846, 764, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{25}H_{23}F_6NNaO_4$ ([M+Na]$^+$) 538.1423, found 538.1420.

2-(allyl(*tert*-butoxycarbonyl)amino)-1-phenylethyl 3,5-bis(trifluoromethyl)benzoate (47i)



Following general procedure GP-5***,*** using *tert*-butyl allyl(2-hydroxy-2-phenylethyl)carbamate (**44i**) (300 mg, 1.1 mmol, 1.0 equiv), *N*,*N*-diisoproylethylamine (378 µL, 280 mg, 2.2 mmol, 2.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (647 mg, 1.3 mmol, 1.2 equiv) and dry CH_2Cl_2 (22 mL) gave 532 mg (1.0 mmol, 95%) of 2-(allyl(*tert*-butoxycarbonyl)amino)-1-phenylethyl 3,5-bis(trifluoromethyl)benzoate (**47i**) as yellow oil after 24 h stirring and purification by flash chromatography (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 3:1) = 0.75, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.37 (m, 2H), 8.18 – 7.90 (m, 1H), 7.58 – 7.31 (m, 5H), 6.41 – 6.15 (m, 1H), 5.72 (ddd, *J* = 14.6, 10.9, 5.5 Hz, 1H), 5.25 – 4.98 (m, 2H), 4.11 – 3.40 (m, 4H), 1.54 – 1.27 (m, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.45 (s, 6F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 163.1, 155.7, 155.2, 137.6, 133.9, 132.6, 132.2, 130.1, 129.9, 128.9, 128.9, 126.7, 126.6, 127.3 – 118.7 (m), 117.1, 116.5, 80.6, 80.3, 76.2, 51.6, 51.6, 50.8, 50.5, 28.5, 28.3. IR (neat): 3090, 2982, 2933, 1733, 1696, 1457, 1409, 1368, 1279, 1241, 1174, 1133, 1003, 913, 846, 764, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{25}H_{25}F_6NNaO_4$ ([M+Na]$^+$) 540.1580, found 540.1587.

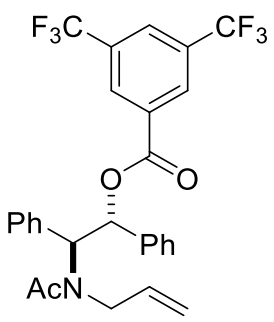
rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-isopropoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47j)



Following general procedure GP-5***,*** using rac. isopropyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl) amino)-2-hydroxy-3-phenyl-propanoate (**44j**) (420 mg, 1.2 mmol, 1.0 equiv), *N*,*N*-diisoproylethylamine (415 µL, 299 mg, 2.3 mmol, 2.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (691 mg, 1.4 mmol, 1.2 equiv) and dry CH_2Cl_2 (22 mL) gave 677 mg (1.1 mmol, 97%) of rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-isopropoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (**47j**) as yellow oil after 24 h stirring and purification by flash chromatography (hexanes / EtOAc, 5:1). R_f (hexanes / EtOAc, 3:1) = 0.83,

Staining: $KMnO_4$ (UV active). ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.26 (m, 2H), 8.05 (dt, *J* = 2.0, 1.0 Hz, 1H), 7.51 – 7.39 (m, 2H), 7.40 – 7.26 (m, 3H), 5.99 (d, *J* = 7.6 Hz, 1H), 5.90 – 5.30 (m, 2H), 5.05 (p, *J* = 6.2 Hz, 1H), 4.93 – 4.68 (m, 2H), 3.94 – 3.54 (m, 2H), 1.48 (s, 9H), 1.29 (d, *J* = 6.3 Hz, 3H), 1.11 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.61 (s, 6F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 163.3, 155.3, 136.2, 134.7, 132.5 (q, *J* = 34.2 Hz), 131.6, 130.1 – 130.0 (m), 128.8, 128.5, 127.1 – 126.8 (m), 127.1 – 118.7 (m), 116.4, 81.1, 73.9, 70.2, 59.5, 48.7, 28.5, 21.8, 21.6. IR (neat): 3071, 2982, 2937, 1741, 1696, 1454, 1394, 1279, 1249, 1179, 1133, 1036, 962, 913, 846, 760, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{29}H_{31}F_6NNaO_6$ ($[M+Na]^+$) 626.1948, found 626.1954.

rac. (1*R*,2*S*)-2-(*N*-allylacetamido)-1,2-diphenylethyl 3,5-bis(trifluoro-methyl)benzoate (47m)



Following general procedure GP-5**,** using rac. *N*-allyl-*N*-((1*R*,2*S*)-2-hydroxy-1,2-diphenylethyl)acetamide (**44m**) (317 mg, 1.1 mmol, 1.0 equiv), *N*,*N*-diisoproylethylamine (367 µL, 277 mg, 2.2 mmol, 2.0 equiv), 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (642 mg, 1.3 mmol, 1.2 equiv) and dry CH_2Cl_2 (20 mL) gave 521 mg (973 µmol, 91%) of rac. (1*R*,2*S*)-2-(*N*-allylacetamido)-1,2-diphenylethyl 3,5-bis(trifluoromethyl)benzoate (**47m**) as a colorless oil after purification by flash chromatography (hexanes / EtOAc, 3:1). R_f (hexanes/ EtOAc, 3:1) = 0.30, Staining: Ninhydrin (UV active). ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (s, 2H), 7.96 (s, 1H), 7.66 – 7.52 (m, 4H), 7.45 – 7.27 (m, 6H), 6.92 (d, *J* = 10.6 Hz, 1H), 6.13 (d, *J* = 10.6 Hz, 1H), 5.10 (ddd, *J* = 16.6, 10.5, 5.5 Hz, 1H), 4.92 (dd, *J* = 10.3, 1.0 Hz, 1H), 4.84 (dd, *J* = 17.1, 1.0 Hz, 1H), 3.84 – 3.76 (m, 1H), 3.66 (dd, *J* = 17.4, 6.2 Hz, 1H), 1.81 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.04 (s, 6F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.5, 163.0, 137.4, 136.8, 133.6, 132.3, 132.2 (q, *J* = 34.0 Hz), 129.7 (d, *J* = 3.3 Hz), 129.3, 128.9, 128.9, 128.6, 128.4, 128.1, 126.6 – 126.4 (m), 127.1 – 118.6 (m), 117.5, 76.0, 61.4, 49.8, 22.3. IR (neat): 3092, 3068, 3036, 3010, 2988, 2975, 2938, 2905, 1732, 1651, 1498, 1456, 1406, 1366, 1334, 1278, 1245, 1176, 1131, 1077, 1032, 989, 968, 947, 912, 871, 845, 831, 756, 697, 681, 623, 610, 542 cm^{-1}. HRMS (ESI) m/z calculated for $C_{28}H_{24}F_6NO_3$ ($[M+H]^+$) 536.1655, found 536.1662.

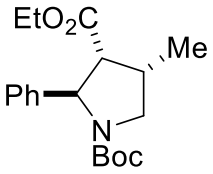
2.2.2. Deoxygenative Cyclization Towards Substituted Pyrrolidines

General Procedure (GP-6) for Reaction of Ethyl Oxalyl Esters and 3,5-Bis(trifluoromethyl)benzoate Esters to Pyrrolidine Derivatives

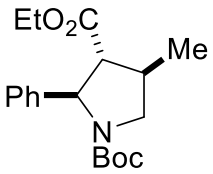
A flame dried Schlenk tube equipped with a magnetic stir bar was charged with ethyl oxalate ester **45** or 3,5-bis(trifluoromethyl)benzoate ester **47**, *fac*-$Ir(ppy)_3$ (1.0 mol%) and DMF (0.1 M). The reaction mixture was degassed by three freeze-pump-thaw-cycles and pumped through a

previously N_2 purged micro reactor equipped with eight LED's at a flow rate of 0.15-1.00 mL/h *via* a syringe pump while heated at 80 °C. Afterwards, the reaction mixture was diluted with diethyl ether (150 mL) and washed with brine (3x 100 mL). The combined organic layers were dried over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure and the residue purified by flash column chromatography.

rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (48a) and rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (48a´)



major 48a



minor 48a´

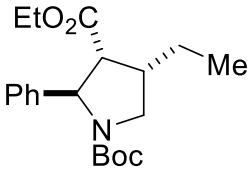
From oxalate ester: Following general procedure GP-6, using rac. (1*R*,2*R*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (**45a**) (456 mg, 1.0 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (6.6 mg, 10.0 µmol, 1.0 mol%) and DMF (10 mL, 0.1 M) at a flow rate of 1.00 mL/h gave 131 mg (393 µmol, 39%) of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48a**) and 79 mg (237 µmol, 23%) of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48a´**) as colorless oils after flash column purification (diethyl ether / *n*-pentane, 1:20 to 1:3), (dr = 63:37).

From 3,5-bis(trifluoromethyl) benzoate ester: Following general procedure GP-6, using rac. (1*R*,2*R*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoro- methyl)benzoate (**47a**) (593 mg, 1.0 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (6.6 mg, 10.0 µmol, 1.0 mol%) and DMF (10 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 126 mg (378 µmol, 38%) of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48a**) and 76 mg (228 µmol, 23%) of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48a´**) as colorless oils after flash column purification (diethyl ether / *n*-pentane, 1:20 to 1:3), (dr = 61:39).

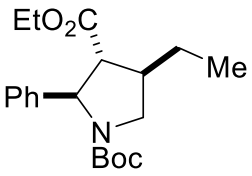
R_f (**48a**, diethyl ether / *n*-pentane, 1:3) = 0.20, Staining: Ninhydrin (UV active). R_f (**48a´**, diethyl ether / *n*-pentane, 1:3) = 0.25, Staining: Ninhydrin (UV active). ^{1}H NMR (**48a**, 400 MHz, $CDCl_3$): δ 7.33 – 7.14 (m, 5H), 5.06 (m, 1H), 4.25 – 3.98 (m, 2H), 3.84 – 3.66 (m, 1H), 3.58 – 3.33 (m, 1H), 3.06 – 2.82 (m, 1H), 2.71 – 2.54 (m, 1H), 1.45 (bs, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.12 (m, 6H), 1.01 (d, *J* = 7.0 Hz, 3H). ^{1}H NMR (**48a´**, 400 MHz, $CDCl_3$): δ 7.35 – 7.11 (m, 5H), 5.16 – 4.85 (m, 1H), 4.24 – 3.98 (m, 3H), 3.18 (t, *J* = 10.7 Hz, 1H), 2.63 – 2.40 (m, 2H), 1.46 – 1.01 (m, 15H). ^{13}C NMR (**48a**, 101 MHz, $CDCl_3$): δ 172.2, 171.6, 154.6, 143.8, 128.4, 127.1, 127.1, 126.0, 125.6, 79.6, 62.3, 61.0, 60.8, 57.9, 53.5, 33.9, 28.6, 28.2, 14.6, 14.4. ^{13}C NMR (**48a´**, 101 MHz, $CDCl_3$): δ 172.3, 154.1, 143.9, 128.4, 127.1, 125.9, 79.7, 65.2, 61.9, 61.0, 54.6, 37.4, 28.1, 16.0, 14.4. IR (**48a**, neat): 2974, 2930, 1730, 1685, 1480, 1398, 1282, 1256,

1230, 1185, 1141, 1036, 1006, 887, 760, 701 cm^{-1}. IR (**48a´**, neat): 2978, 2933, 1733, 1692, 1480, 1394, 1279, 1163, 1126, 1025, 951, 895, 861, 760, 701 cm^{-1}. HRMS (**48a**, ESI) m/z calculated for $C_{19}H_{28}NO_4$ ($[M+H]^+$) 334.2013, found 334.2020. HRMS (**48a´**, ESI) m/z calculated for $C_{19}H_{27}NNaO_4$ ($[M+Na]^+$) 356.1832, found 356.1838.

rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-ethyl-2-phenylpyrrolidine-1,3-dicarboxylate (48b) and rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-ethyl-2-phenylpyrrolidine-1,3-dicarboxylate (48b´)



major 48b

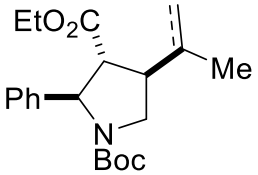


minor 48b´

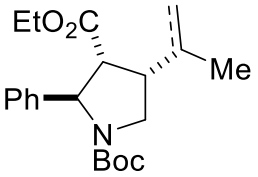
From 3,5-bis(trifluoromethyl) benzoate ester: Following general procedure GP-6, using rac. (1*R*,2*R*)-1-(((*E*)-but-2-en-1-yl) (*tert*-butoxycarbonyl) amino)-3-ethoxy-3-oxo-1 phenyl-propan-2-yl 3,5-bis(trifluoro-methyl)benzoate (**47b**) (446 mg, 739 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (4.9 mg, 7.4 µmol, 1.0 mol%) and DMF (7.5 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 106 mg (305 µmol, 41%) of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-ethyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48b**) and 27 mg (78 µmol, 11%) of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-ethyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48b´**) as colorless oils after flash column purification (diethyl ether / *n*-pentane, 1:20 to 1:1), (dr = 79:21).

R_f (**48b**, diethyl ether / *n*-pentane, 1:3) = 0.33, Staining: Ninhydrin (UV active). R_f (**48b´**, diethyl ether / *n*-pentane, 1:3) = 0.40, Staining: Ninhydrin (UV active). ^{1}H NMR (**48b**, 400 MHz, $CDCl_3$): δ 7.34 – 7.16 (m, 5H), 5.29 – 4.93 (m, 1H), 4.18 (m, 2H), 3.84 – 3.61 (m, 1H), 3.58 – 3.29 (m, 1H), 3.09 – 2.81 (m, 1H), 2.38 (q, *J* = 7.2 Hz, 1H), 1.53 – 1.08 (m, 14H), 0.98 – 0.84 (m, 3H). ^{1}H NMR (**48b´**, 400 MHz, $CDCl_3$): δ 7.36 – 7.12 (m, 5H), 5.08 – 4.81 (m, 1H), 4.22 – 4.02 (m, 3H), 3.20 (t, *J* = 10.7 Hz, 1H), 2.63 (t, *J* = 10.0 Hz, 1H), 2.47 – 2.31 (m, 1H), 1.74 – 1.53 (m, 2H), 1.51 – 1.30 (m, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.10 (s, 6H), 0.92 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (**48b**, 101 MHz, $CDCl_3$): δ 172.2, 154.6, 143.6, 142.5, 128.6, 128.4, 127.1, 125.8, 125.6, 79.6, 63.7, 63.3, 60.7, 56.7, 55.2, 51.4, 50.8, 41.2, 40.8, 28.6, 28.2, 22.2, 14.4, 14.3, 12.7, 12.2. ^{13}C NMR (**48b´**, 101 MHz, $CDCl_3$): δ 172.7, 154.2, 143.9, 128.5, 127.1, 125.8, 79.8, 65.5, 61.0, 60.4, 52.9, 44.0, 28.2, 25.0, 14.4, 12.2. IR (**48b**, neat): 2989, 2930, 2863, 1733, 1681, 1480, 1405, 1279, 1163, 1074, 1014, 928, 898, 865, 768, 705 cm^{-1}. IR (**48b´**, neat): 3034, 2989, 2930, 2866, 1733, 1685, 1480, 1405, 1279, 1163, 1107, 1070, 1010, 961, 928, 895, 764, 705 cm^{-1}. HRMS (**48b**, ESI) m/z calculated for $C_{20}H_{29}NNaO_4$ ($[M+Na]^+$) 370.1989, found 370.1992. HRMS (**48b´**, ESI) m/z calculated for $C_{20}H_{29}NNaO_4$ ($[M+Na]^+$) 370.1989, found 370.1991.

rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxy-late (48c) / rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-2-phenyl-4-(prop-1-en-2-yl)pyrrolidine-1,3-dicarboxylate (48cS1) and rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxylate (48c´) / rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-2-phenyl-4-(prop-1-en-2-yl)pyrrolidine-1,3-dicarboxylate (48c´S1)



major 48c/48cS1

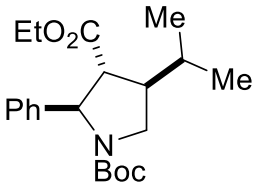


minor 48c´/48c´S1

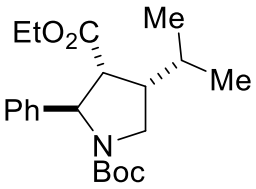
From 3,5-bis(trifluoromethyl) benzoate ester: Following general procedure GP-6, using rac. (1*R*,2*R*)-1-((*tert*-butoxycarbonyl)(3-methylbut-2-en-1-yl) amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)-benzoate (**47c**) (351 mg, 568 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (3.7 mg, 5.7 µmol, 1.0 mol%) and DMF (5.7 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 57 mg (158 µmol, 28%) of a mixture of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxy-late (**48c**) / rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-2-phenyl-4-(prop-1-en-2-yl)pyrrolidine-1,3-dicarboxylate (**48cS1**) and 51 mg (140 µmol, 25%) of a mixture of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48c´**) / rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-2-phenyl-4-(prop-1-en-2-yl)pyrrolidine-1,3-dicarboxylate (**48c´S1**) as colorless oils after flash column purification (diethyl ether / *n*-pentane, 1:20 to 1:1). (Alkene/Alkane ratio 77:23 for **47c** (dr = 53:47).

R_f (**48c**/**48cS1**, diethyl ether / *n*-pentane, 1:3) = 0.35, Staining: Ninhydrin (UV active). R_f (**48c´**/**48c´S1**, diethyl ether / *n*-pentane, 1:3) = 0.40, Staining: Ninhydrin (UV active). ^{1}H NMR (**48cS1**, 400 MHz, $CDCl_3$): δ 7.40 – 7.07 (m, 5H), 5.10 – 4.74 (m, 3H), 4.11 (ddq, *J* = 11.0, 7.1, 3.7 Hz, 3H), 3.43 (t, *J* = 11.0 Hz, 1H), 3.14 (td, *J* = 11.4, 7.6 Hz, 1H), 2.96 (t, *J* = 10.5 Hz, 1H), 1.75 (s, 3H), 1.48 – 1.35 (m, 2H), 1.23 – 1.01 (m, 10H). ^{1}H NMR (**48c´S1**, 400 MHz, $CDCl_3$): δ 7.37 – 7.19 (m, 5H), 5.19 (d, *J* = 56.1 Hz, 1H), 4.81 (d, *J* = 33.6 Hz, 2H), 4.28 – 4.02 (m, 2H), 3.82 (dd, *J* = 12.0, 7.1 Hz, 2H), 3.18 – 2.95 (m, 2H), 1.72 (s, 3H), 1.47 (s, 2H), 1.32 – 1.13 (m, 10H). ^{13}C NMR (**48cS1**, 101 MHz, $CDCl_3$): δ 172.1, 154.1, 143.5, 141.4, 128.5, 127.3, 125.8, 113.3, 79.9, 65.4, 61.0, 58.1, 51.6, 49.2, 28.1, 20.0, 14.3. ^{13}C NMR (**48c´S1**, 101 MHz, $CDCl_3$): δ 171.6, 154.5, 143.5, 142.0, 128.5, 127.2, 125.7, 112.6, 79.8, 63.5, 60.8, 56.5, 49.3, 45.2, 28.6, 28.2, 22.2, 21.2, 14.3. IR (neat): 3034, 2967, 1733, 1696, 1476, 1390, 1370, 1274, 1261, 1163, 1126, 1018, 951, 898, 768, 701 cm^{-1}. HRMS (ESI) m/z calculated for major product $C_{21}H_{29}NNaO_4$ ([M+Na]$^+$) 382.1989, found 382.1994.

rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4 isopropyl-2-phenylpyrrolidine-1,3-dicarboxy-late (48c) and rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxylate (48c´)



major 48c

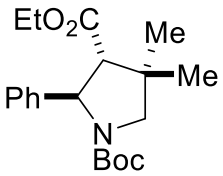


minor 48c´

A 5 mL Schlenk tube was charged with a mixture of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxy-late (**48c**) / rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-2-phenyl-4-(prop-1-en-2-yl) pyrrolidine-1,3-dicarboxylate (**48cS1**) (57 mg, 158 µmol, 1.0 equiv), Pd/C (10 wt%, 34 mg, 0.25 equiv) and dry EtOH (1.0 mL). The atmosphere was exchanged to hydrogen (3 times), a balloon of hydrogen gas was fitted to the Schlenk flask and the mixture was stirred for 24 h at room temperature. The reaction mixture was evaporated under reduced pressure to give 56 mg (155 µmol, 98%) of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxy-late (**48c**) as a colorless oil. In an analogue way rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48c´**) (49 mg, 137 µmol, 97%) was obtained. (dr = 53:47).

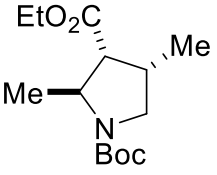
R_f (**48c**, diethyl ether / *n*-pentane, 1:3) = 0.35, Staining: Ninhydrin (UV active). R_f (**48c´**, diethyl ether / *n*-pentane, 1:3) = 0.40, Staining: Ninhydrin (UV active). ^{1}H NMR (**48c**, 400 MHz, $CDCl_3$): δ 7.35 – 7.04 (m, 5H), 4.98 – 4.77 (m, 1H), 4.13 (ddq, *J* = 10.8, 7.2, 3.7 Hz, 2H), 4.07 – 3.91 (m, 1H), 3.29 (t, *J* = 10.9 Hz, 1H), 2.71 (t, *J* = 9.9 Hz, 1H), 2.40 (tt, *J* = 10.9, 7.6 Hz, 1H), 1.68 (dd, *J* = 13.7, 6.6 Hz, 1H), 1.50 – 1.35 (m, 2H), 1.20 (t, *J* = 7.1 Hz, 3H), 1.09 (s, 7H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H). ^{1}H NMR (**48c´**, 400 MHz, $CDCl_3$): δ 7.36 – 7.14 (m, 5H), 5.11 (d, *J* = 65.5 Hz, 1H), 4.30 – 4.07 (m, 2H), 3.76 (dt, *J* = 45.3, 9.5 Hz, 1H), 3.44 (td, *J* = 10.7, 4.0 Hz, 1H), 2.91 (dd, *J* = 14.8, 6.6 Hz, 1H), 2.17 – 2.00 (m, 1H), 1.64 – 1.51 (m, 1H), 1.47 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.22 (s, 6H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (**48c**, 101 MHz, $CDCl_3$): δ 173.4, 154.2, 143.8, 128.5, 127.2, 125.7, 79.7, 66.5, 61.0, 58.8, 50.8, 48.4, 30.3, 28.1, 21.0, 19.9, 14.3. ^{13}C NMR (**48c´**, 101 MHz, $CDCl_3$): δ 172.9, 172.8, 154.7, 154.5, 143.2, 142.3, 128.6, 128.4, 128.4, 127.2, 127.1, 125.6, 125.5, 79.7, 79.6, 64.7, 60.7, 60.7, 55.0, 50.1, 47.0, 46.1, 28.9, 28.9, 28.7, 28.3, 21.8, 21.6, 21.6, 14.4. IR (**48c**, neat): 3034, 2967, 1733, 1696, 1476, 1390, 1275, 1163, 1126, 1018, 951, 898, 865, 768, 701 cm^{-1}. IR (**48c´**, neat): 2967, 2937, 1730, 1696, 1476, 1390, 1256, 1215, 1163, 1115, 1040, 943, 902, 772, 701 cm^{-1}. HRMS (**48c**, ESI) m/z calculated for $C_{21}H_{31}NNaO_4$ ([M+Na]$^+$) 384.2145, found 384.2159. HRMS (**48c´**, ESI) m/z calculated for $C_{21}H_{31}NNaO_4$ ([M+Na]$^+$) 384.2145, found 384.2154.

rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*)-4,4-dimethyl-2-phenylpyrrolidine-1,3-dicarboxylate (48d)

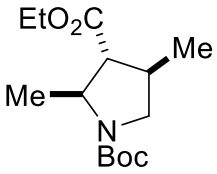


From 3,5-bis(trifluoromethyl) benzoate ester: Following general procedure GP-6, using rac. (1*R*,2*R*)-1-((*tert*-butoxycarbonyl)(2-methylallyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl) benzoate (**47d**) (230 mg, 381 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (2.5 mg, 3.8 µmol, 1.0 mol%) and DMF (3.8 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 59 mg (170 µmol, 45%) of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*)-4,4-dimethyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48d**) as a colorless oil after flash column purification (diethyl ether / *n*-pentane, 1:7 to 1:1). R_f (diethyl ether / *n*-pentane, 1:3) = 0.29, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$, rotamers present): δ 7.40 – 7.09 (m, 5H), 5.11 (d, *J* = 9.5 Hz, 1H), 4.30 – 3.98 (m, 2H), 3.69 (d, *J* = 10.8 Hz, 1H), 3.38 (d, *J* = 10.7 Hz, 1H), 2.74 (d, *J* = 9.5 Hz, 1H), 1.41 (s, 2H), 1.26 – 1.19 (m, 6H), 1.09 (s, 7H), 1.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.5, 154.4, 144.1, 128.3, 127.0, 126.1, 79.6, 64.0, 62.8, 61.0, 60.7, 40.6, 28.5, 28.1, 25.3, 22.4, 14.4. IR (neat): 3034, 2974, 2933, 2874, 1730, 1692, 1457, 1394, 1364, 1297, 1264, 1226, 1185, 1156, 1007, 1028, 898, 861, 757, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{20}H_{29}NNaO_4$ ([M+Na]$^+$) 370.1989, found 370.1995.

rac. 1-(*tert*-butyl) 3-ethyl (2*S*,3*R*,4*S*)-2,4-dimethylpyrrolidine-1,3-dicarboxylate (48e) and rac. 1-(*tert*-butyl) 3-ethyl (2*S*,3*R*,4*R*)-2,4-dimethylpyrrolidine-1,3-dicarboxylate (48e´)



major 48e



minor 48e´

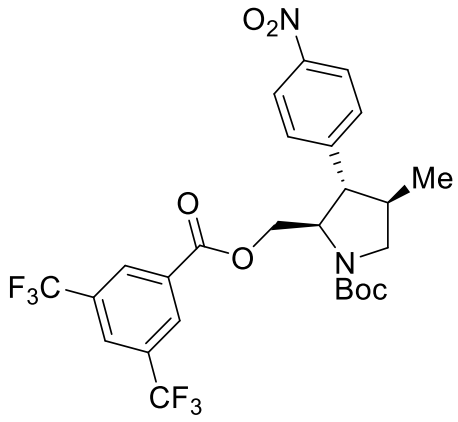
From oxalate ester: Following general procedure GP-6, using rac. (2*R*,3*R*)-3-(allyl(*tert*-butoxycarbonyl) amino)-1-ethoxy-1-oxobutan-2-yl ethyl oxalate (**45e**) (330 mg, 852 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (5.6 mg, 8.5 µmol, 1.0 mol%) and DMF (8.5 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 80 mg (295 µmol, 35%) of rac. 1-(*tert*-butyl) 3-ethyl (2*S*,3*R*,4*S*)-2,4-dimethylpyrrolidine-1,3-dicarboxylate (**48e**) and 71 mg (262 µmol, 31%) of rac. 1-(*tert*-butyl) 3-ethyl (2*S*,3*R*,4*R*)-2,4-dimethylpyrrolidine-1,3-dicarboxylate (**48e´**) as colorless oils after flash column purification (diethyl ether / *n*-pentane, 1:20 to 1:3), (dr = 53:47).

From 3,5-bis(trifluoromethyl) benzoate ester: Following general procedure GP-6, using rac. (2*R*,3*R*)-3-(allyl(*tert*-butoxycarbonyl)amino)-1-ethoxy-1-oxobutan-2-yl 3,5-bis(trifluoromethyl)-benzoate (**47e**) (268 mg, 508 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (3.4 mg, 5.1 µmol, 1.0 mol%) and DMF (5.1 mL, 0.1 M) at a flow rate of 0.15 mL/h gave 48 mg (177 µmol, 35%) of rac. 1-(*tert*-butyl) 3-ethyl (2*S*,3*R*,4*S*)-2,4-dimethylpyrrolidine-1,3-dicarboxylate (**48e**) and 43 mg (158 µmol, 31%) of rac. 1-(*tert*-butyl) 3-ethyl (2*S*,3*R*,4*R*)-2,4-dimethylpyrrolidine-1,3-

dicarboxylate (**48e´**) as colorless oils after flash column purification (diethyl ether / *n*-pentane, 1:20 to 1:3), (dr = 53:47).

R_f (**48e**, diethyl ether / *n*-pentane, 1:3) = 0.29, Staining: Ninhydrin (UV active). R_f (**48e´**, diethyl ether / *n*-pentane, 1:3) = 0.40, Staining: Ninhydrin (UV active). ^{1}H NMR (**48e**, 400 MHz, $CDCl_3$) δ 4.11 (qq, *J* = 10.1, 6.4, 4.7 Hz, 3H), 3.44 (dd, *J* = 10.6, 6.7 Hz, 1H), 3.21 (s, 1H), 2.55 (td, *J* = 16.1, 13.7, 9.3 Hz, 2H), 1.43 (s, 9H), 1.29 – 1.19 (m, 6H), 0.94 (d, *J* = 6.7 Hz, 3H). ^{1}H NMR (**48e´**, 400 MHz, $CDCl_3$) δ 4.15 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 1H), 3.80 (s, 1H), 2.82 (t, *J* = 10.7 Hz, 1H), 2.31 (tt, *J* = 10.6, 6.6 Hz, 1H), 2.20 (dd, *J* = 10.8, 8.4 Hz, 1H), 1.42 (s, 9H), 1.30 (d, *J* = 6.0 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (**48e**, 101 MHz, $CDCl_3$) δ 172.4, 154.6, 79.2, 60.5, 55.0, 52.6, 33.8, 28.6, 20.7, 14.4, 14.1. ^{13}C NMR (**48e´**, 101 MHz, $CDCl_3$) δ 172.8, 154.2, 79.4, 60.9, 59.8, 57.0, 53.2, 36.5, 28.6, 21.03, 16.2, 14.4. IR (**48e**, neat): 2974, 2937, 2878, 1733, 1692, 1457, 1390, 1282, 1252, 1174, 1107, 1062, 1029, 954, 869, 775 cm^{-1}. IR (**48e´**, neat): 2974, 2933, 2878, 1733, 1692, 1457, 1394, 1290, 1256, 1163, 1096, 1033, 910, 869, 772 cm^{-1}. HRMS (**48e**, ESI) m/z calculated for $C_{14}H_{25}NNaO_4$ ($[M+Na]^+$) 294.1676, found 294.1678. HRMS (**48e´**, ESI) m/z calculated for $C_{14}H_{25}NNaO_4$ ($[M+Na]^+$) 294.1676, found 294.1683.

tert-butyl (2*R*,3*S*,4*R*)-2-(((3,5-bis(trifluoromethyl)benzoyl)oxy)methyl)-4-methyl-3-(4-nitrophenyl)pyrrolidine-1-carboxylate (48f)

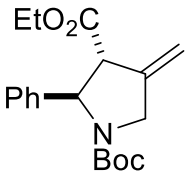


major

From 3,5-bis(trifluoromethyl) benzoate ester: Following general procedure GP-6, using (1*S*,2*S*)-2-(allyl(*tert*-butoxycarbonyl)amino)-1-(4-nitrophenyl)propane-1,3-diyl bis(3,5-bis(trifluoro-methyl)benzoate) (**47f**) (458 mg, 550 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (3.6 mg, 5.5 µmol, 1.0 mol%) and DMF (5.5 mL, 0.1 M) with a flow rate of 0.15 mL/h gave 88 mg (153 µmol, 28%) of diastereomeric mixture of *tert*-butyl -2-(((3,5-bis(trifluoromethyl) benzoyl) oxy)-methyl)-4-methyl-3-(4-nitrophenyl)pyrrolidine-1-carboxylate (d.r. = 68:32) as a colorless oil after flash column purification (diethyl ether / *n*-pentane, 1:2). An additional column chromatography gave 56 mg (97 µmol, 18%) of *tert*-butyl (2*R*,3*S*,4*R*)-2-(((3,5-bis(trifluoromethyl)benzoyl)oxy)methyl)-4-methyl-3-(4-nitrophenyl)pyrrolidine-1-carboxylate (**48f**) as a single diastereomer. R_f (**48f**, diethyl ether / *n*-pentane, 1:1) = 0.61, Staining: Ninhydrin (UV active). Specific Rotation: $[\alpha]_D^{25}$ = + 2.5 °. ^{1}H NMR (**48f**, 400 MHz, $CDCl_3$) δ 8.23 – 8.08 (m, 4H), 8.01 (s, 1H), 7.40 (d, *J* = 8.7 Hz, 2H), 4.71 (dd, *J* = 10.9, 3.6 Hz, 1H), 4.65 – 4.43 (m, 1H), 4.42 – 4.19 (m, 1H), 4.19 – 3.97 (m, 1H), 3.07 – 2.72 (m, 2H), 2.34 – 2.19 (m, 1H), 1.50 (s, 9H), 0.92 (d, *J* = 6.4 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -63.62 (s,

6F). ^{13}C NMR (**48f**, 101 MHz, $CDCl_3$) δ 163.5, 154.5, 153.9, 147.7, 147.3, 132.3 (q, *J* = 34.2 Hz), 129.6, 128.9, 126.6, 124.2, 121.5, 81.1, 80.6, 66.7, 66.1, 63.1, 58.5, 57.6, 54.6, 54.0, 42.0, 41.6, 28.6, 14.9. IR (**48f**, neat): 2971, 2930, 2874, 1733, 1692, 1603, 1525, 1457, 1394, 1349, 1279, 1249, 1170, 1133, 984, 913, 846, 753 cm^{-1}. HRMS (**48f**, ESI) m/z calculated for $C_{26}H_{26}F_6N_2NaO_6$ ([M+Na]$^+$) 599.1587, found 599.1587.

rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*)-4-methylene-2-phenylpyrrolidine-1,3-dicarboxylate (48g)

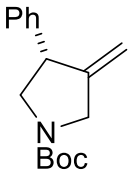


From oxalate ester: Following general procedure GP-6, using rac. (1*R*,2*R*)-1-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (**45g**) (405 mg, 905 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (6.0 mg, 9.1 µmol, 1.0 mol%) and DMF (9.1 mL, 0.1 M) at a flow rate of 0.40 mL/h gave 140 mg (422 µmol, 47%) of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*)-4-methylene-2-phenylpyrrolidine-1,3-dicarboxylate (**48g**) as a colorless oil after flash column purification (diethyl ether / *n*-pentane, 1:7 to 1:1).

From 3,5-bis(trifluoromethyl) benzoate ester: Following general procedure GP-6, using rac. (1*R*,2*R*)-1-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (**47g**) (386 mg, 657 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (4.3 mg, 6.6 µmol, 1.0 mol%) and DMF (6.6 mL, 0.1 M) at a flow rate of 0.40 mL/h gave 97 mg (294 µmol, 45%) of rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*)-4-methylene-2-phenylpyrrolidine-1,3-dicarboxylate (**48g**) as a colorless oil after flash column purification (diethyl ether / *n*-pentane, 1:7 to 1:1).

R_f (diethyl ether / *n*-pentane, 1:3) = 0.34, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.04 (m, 5H), 5.39 – 5.13 (m, 3H), 4.36 (dq, *J* = 15.0, 2.2 Hz, 1H), 4.28 – 4.12 (m, 3H), 3.46 (s, 1H), 1.56 – 1.13 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 154.1, 143.1, 142.0, 128.5, 127.3, 125.7, 111.2, 79.9, 65.9, 63.9, 61.4, 58.4, 51.2, 28.3, 14.2. IR (neat): 3064, 2978, 2933, 2870, 1733, 1696, 1454, 1390, 1320, 1252, 1159, 1111, 1033, 898, 753, 701 cm^{-1}. HRMS (APCI) m/z calculated for $C_{19}H_{26}NO_4$ ([M+H]$^+$) 332.1856, found 332.1861.

***tert*-butyl-3-methylene-4-phenylpyrrolidine-1-carboxylate (48h)**

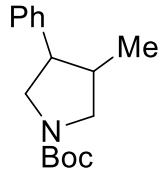


From oxalate ester: Following general procedure GP-6, using 2-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-1-phenylethyl ethyl oxalate (**45h**) (203 mg, 541 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (3.6 mg, 0.54 µmol, 1.0 mol%) and DMF (5.4 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 56 mg (216 µmol, 40%) of *tert*-butyl-3-methylene-4-phenylpyrrolidine-1-carboxylate (**48h**) as a colorless oil after flash column purification (diethyl ether / *n*-pentane, 1:9 to 1:2).

From 3,5-bis(trifluoromethyl) benzoate ester: Following general procedure GP-6, using 2-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-1-phenylethyl 3,5-bis(trifluoromethyl)benzoate (**47h**) (258 mg, 501 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (3.3 mg, 0.50 µmol, 1.0 mol%) and DMF (5.0 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 53 mg (204 µmol, 41%) of *tert*-butyl-3-methylene-4-phenylpyrrolidine-1-carboxylate (**48h**) as a colorless oil after flash column purification (diethyl ether / *n*-pentane, 1:9 to 1:2).

R_f (diethyl ether / *n*-pentane, 1:3) = 0.50, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.15 (m, 5H), 5.06 (d, *J* = 12.4 Hz, 1H), 4.67 (s, 1H), 4.24 – 4.04 (m, 2H), 4.03 – 3.79 (m, 2H), 3.55 – 3.35 (m, 1H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5, 150.2, 149.3, 140.4, 128.7, 128.4, 127.1, 108.5, 108.2, 79.7, 53.9, 53.0, 51.1, 50.8, 49.8, 49.1, 28.6. IR (neat): 3064, 3030, 2974, 2930, 2870, 1696, 1539, 1476, 1394, 1252, 1163, 1107, 980, 892, 876, 753 cm^{-1}. HRMS (ESI) m/z calculated for $C_{16}H_{21}NNaO_2$ ([M+Na]$^+$) 282.1465, found 282.1470.

tert-butyl 3-methyl-4-phenylpyrrolidine-1-carboxylate (48i)

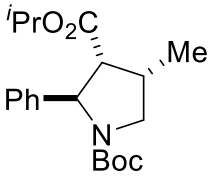


From oxalate ester: Following general procedure GP-6, using 2-(allyl(tert-butoxycarbonyl)amino)-1-phenylethyl ethyl oxalate (**45i**) (350 mg, 927 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (6.1 mg, 0.93 µmol, 1 mol%) and DMF (9.3 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 156 mg (597 µmol, 64%) of a diastereomeric mixture of *tert*-butyl 3-methyl-4-phenylpyrrolidine-1-carboxylate (**48i**) (dr = 60:40) as a colorless oil after flash column purification (diethyl ether / *n*-pentane, 1:10). Additional flash column purification (diethyl ether / *n*-pentane, 1:20 to 1:10) gave 80 mg (306 µmol, 33%) of *tert*-butyl 3-methyl-4-phenylpyrrolidine-1-carboxylate (**48i**) as single diastereomer.

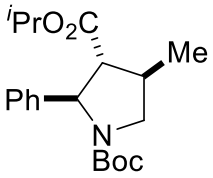
From 3,5-bis(trifluoromethyl) benzoate ester: Following general procedure GP-6, using 2-(allyl(tert-butoxycarbonyl)amino)-1-phenylethyl 3,5-bis(trifluoromethyl)benzoate (**47i**) (391 mg, 756 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (5.0 mg, 0.76 µmol, 1 mol%) and DMF (7.6 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 138 mg (529 µmol, 70%) of a diastereomeric mixture of *tert*-butyl 3-methyl-4-phenylpyrrolidine-1-carboxylate (**48i**) (dr=62:38) as a colorless oil after flash column purification (diethyl ether / *n*-pentane, 1:19 to 1:10). Additional flash column purification (diethyl ether / *n*-pentane, 1:20 to 1:10) gave 74 mg (283 µmol, 37%) of *tert*-butyl 3-methyl-4-phenylpyrrolidine-1-carboxylate (**48i**) as single diastereomer. R_f (diethyl ether / *n*-pentane, 1:3) = 0.38, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.19 (m, 5H), 3.78 (ddd, *J* = 21.7, 10.8, 7.8 Hz, 2H), 3.35 (t, *J* = 10.8 Hz, 1H), 2.99 (t, *J* = 10.4 Hz, 1H), 2.80 (td, *J* = 10.6, 7.9 Hz, 1H), 2.38 – 2.22 (m, 1H), 1.47 (s, 9H), 0.95 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5, 140.1, 128.8, 127.8, 127.1, 79.3, 66.0, 53.6, 53.4, 52.3, 40.6, 28.7, 15.7. IR (neat): 2974, 2933, 2874, 1692, 1480, 1402, 1252, 1174, 1148, 1085, 965,

924, 876, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{16}H_{23}NNaO_2$ ([M+Na]$^+$) 284.1621, found 284.1624.

rac. 1-(*tert*-butyl) 3-isopropyl (2*R*,3*R*,4*S*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (48j) and rac. 1-(*tert*-butyl) 3-isopropyl (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (48j´)



major 48j



minor 48j´

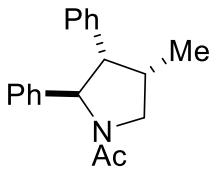
From oxalate ester: Following general procedure GP-6, using rac. (1*S*,2*S*)-1-(allyl(*tert* butoxycarbonyl) amino)-3-isopropoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (**45j**) (400 mg, 863 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (5.7 mg, 0.86 µmol, 1.0 mol%) and DMF (8.6 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 101 mg (291 µmol, 34%) of rac. 1-(*tert*-butyl) 3-isopropyl (2*R*,3*R*,4*S*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48j**) and 76 mg (219 µmol, 25%) of rac. 1-(*tert*-butyl) 3-isopropyl (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48j´**) as colorless oils after flash column purification (diethyl ether / *n*-pentane, 1:10), (dr = 57:43).

From 3,5-bis(trifluoromethyl) benzoate ester: Following general procedure GP-6, using rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-isopropoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (**47j**) (602 mg, 997 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (6.6 mg, 1.0 µmol, 1.0 mol%) and DMF (10 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 117 mg (337 µmol, 34%) of rac. 1-(*tert*-butyl) 3-isopropyl (2*R*,3*R*,4*S*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48j**) and 88 mg (253 µmol, 25%) of rac. 1-(*tert*-butyl) 3-isopropyl (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48j´**) as colorless oils after flash column purification (diethyl ether / *n*-pentane, 1:19 to 1:10), (dr = 57:43).

R_f (**48j**, diethyl ether / *n*-pentane, 1:3) = 0.28, Staining: Ninhydrin (UV active). R_f (**48j´**, diethyl ether / *n*-pentane, 1:3) = 0.35, Staining: Ninhydrin (UV active). ^{1}H NMR (**48j**, 400 MHz, $CDCl_3$): δ 7.37 – 7.14 (m, 5H), 5.31 – 4.92 (m, 2H), 3.85 – 3.64 (m, 1H), 3.57 – 3.34 (m, 1H), 3.03 – 2.78 (m, 1H), 2.68 – 2.44 (m, 1H), 1.50 – 1.41 (m, 2H), 1.28 – 1.21 (m, 7H), 1.19 – 1.12 (m, 6H), 1.02 (d, *J* = 7.0 Hz, 3H). ^{1}H NMR (**48j´**, 400 MHz, $CDCl_3$): δ 7.32 – 7.13 (m, 5H), 5.13 – 4.84 (m, 2H), 4.15 – 3.93 (m, 1H), 3.17 (t, *J* = 10.6 Hz, 1H), 2.63 – 2.35 (m, 2H), 1.48 – 0.99 (m, 18H). ^{13}C NMR (**48j**, 101 MHz, $CDCl_3$): δ 171.1, 154.6, 143.9, 128.4, 127.0, 126.0, 79.6, 68.4, 62.3, 58.0, 53.6, 34.0, 28.2, 22.0, 14.5.^{13}C NMR (**48j´**, 101 MHz, $CDCl_3$): δ 171.8, 154.1, 144.0, 128.4, 127.1, 125.8, 79.7, 68.5, 65.2, 62.1, 54.5, 37.4, 28.1, 22.0, 16.0. IR (**48j**, neat): 2974, 2937, 2878, 1730, 1696, 1454, 1390, 1256, 1223, 1170, 1141, 1103, 984, 906, 861, 824, 757, 701 cm^{-1}. IR (**48j´**, neat): 2978, 2933, 2878, 1730, 1692, 1454, 1402, 1364, 1279, 1215, 1168, 1103, 992, 990, 951, 861, 820, 760, 701 cm^{-1}. HRMS (**48j**, ESI) m/z

calculated for $C_{20}H_{30}NO_4$ ([M+H]$^+$) 348.2169, found 348.2178. HRMS (**48j´**, ESI) m/z calculated for $C_{20}H_{29}NNaO_4$ ([M+Na]$^+$) 370.1989, found 370.1999.

rac. 1-((2*R*,3*S*,4*S*)-4-methyl-2,3-diphenylpyrrolidin-1-yl)ethan-1-one (48m)

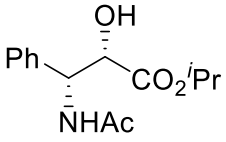


major 48m

Following general procedure GP-6, using rac. (1*S*,2*R*)-2-(*N*-allylacetamido)-1,2-diphenylethyl 3,5-bis(trifluoromethyl)benzoate (**47m**) (315 mg, 588 µmol, 1.0 equiv), *fac*-Ir(ppy)3 (3.9 mg, 5.9 µmol, 1.0 mol%), and DMF (8.5 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 82 mg (294 µmol, 50%) of rac. 1-((2*R*,3*S*,4*S*)-4-methyl-2,3-diphenylpyrrolidin-1-yl)ethan-1-one (**48m**) (dr = 74:26) as a colorless oil after flash silica gel column chromatography (diethyl ether / *n*-pentane, 1:1). R_f (diethyl ether / *n*-pentane, 1:1) = 0.13, Staining: Ninhydrin (UV active). ^{1}H NMR (Major Diastereomer, 400 MHz, $CDCl_3$): δ 7.40 – 7.08 (m, 10H), 5.12 (s, 1H), 3.99 (dd, *J* = 12.1, 7.9 Hz, 1H), 3.41 (dd, *J* = 12.1, 10.2 Hz, 1H), 3.25 – 3.18 (m, 1H), 2.82 – 2.62 (m, 1H), 1.91 (s, 3H), 0.68 (d, *J* = 6.8 Hz, 3H). ^{1}H NMR (Minor Diastereomer, 400 MHz, $CDCl_3$): δ 7.40 – 7.08 (m, 10H), 5.50 (s, 1H), 3.89 (dd, *J* = 9.9, 7.6 Hz, 1H), 3.32 (t, *J* = 10.0 Hz, 1H), 3.25 – 3.18 (m, 1H), 2.82 – 2.62 (m, 1H), 2.24 (s, 3H), 0.70 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (Major Diastereomer, 101 MHz, $CDCl_3$): δ 170.6, 142.8, 140.4, 129.1, 128.9, 128.1, 127.7, 127.2, 125.6, 69.1, 58.7, 52.4, 33.2, 22.5, 13.9. ^{13}C NMR (Minor Diastereomer, 101 MHz, $CDCl_3$): δ 169.5, 142.6, 139.9, 128.7, 128.6, 128.2, 127.1, 127.0, 125.5, 66.5, 56.5, 53.9, 35.0, 23.0, 13.9. IR (neat): 3064, 3030, 2963, 2930, 2874, 1722, 1648, 1495, 1454, 1409, 1357, 1279, 1245, 1178, 1137, 1081, 1029, 973, 913, 865, 801, 749, 701 cm^{-1}. HRMS (APCI) m/z calculated for $C_{19}H_{22}NO$ ([M+H]$^+$) 280.1696, found 280.1702.

2.2.3. Synthesis of Starting Materials for enantiopure Pyrrolidines

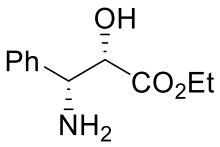
Isopropyl (2*S*,3*R*)-3-acetamido-2-hydroxy-3-phenylpropanoate (64)



A 100 mL round bottom flask equipped with a magnetic stir bar was charged with $K_2OsO_4{\cdot}2H_2O$ (176 mg, 0.5 mmol, 4.0 mol%) and dissolved in 36 mL of an aqueous solution of $LiOH{\cdot}H_2O$ (514 mg, 12.2 mmol, 1.0 equiv.). After addition of ^{t}BuOH (72 mL), $(DHQD)_2PHAL$ (468 mg, 0.6 mmol, 5.0 mol%) was added and the mixture was stirred for 10 min to give a clear pink solution. Subsequently, water (72 mL) was added and the mixture was immersed in an ice bath. Isopropyl cinnamate (**63**) (2.3 g, 12.0 mmol, 1.0 equiv.) was added in one portion followed by *N*-bromoacetamide (1.8 g, 13.2 mmol, 1.1 equiv.) which resulted in an immediate color change to green. The mixture was stirred while still cooling by an ice bath for 20 h. After full conversion as judged by TLC analysis and pH control at pH 7, Na_2SO_3 (6.0 g) was added in one portion and the resulting mixture was stirred at room temperature for 30 min. EtOAc (60 mL) was added, the organic layer was separated, and the aqueous phase was extracted

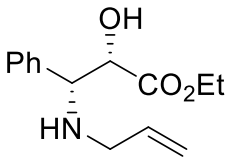
with EtOAc (3x 120 mL). The combined organic layers were washed with brine (60 mL), dried over anhydrous $MgSO_4$, filtered and the solvent evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (hexanes / EtOAc, 1:1) to give 2.9 g (10.9 mmol, 90%, 99% ee) of isopropyl (2*S*,3*R*)-3-acetamido-2-hydroxy-3-phenylpropanoate (**64**) as a white solid. Spectral data are in agreement with those reported in literature. R_f (hexanes / EtOAc, 2:3) = 0.40, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46 – 7.21 (m, 5H), 6.51 (d, J = 9.4 Hz, 1H), 5.54 (dd, J = 9.4, 2.3 Hz, 1H), 5.09 (hept, J = 6.3 Hz, 1H), 4.46 (d, J = 2.3 Hz, 1H), 3.41 (bs, 1H), 1.96 (s, 3H), 1.27 (dd, J = 9.0, 6.3 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.5, 169.6, 139.0, 128.7, 127.8, 127.0, 73.4, 70.8, 54.5, 23.2, 21.8, 21.6.

Ethyl (2*S*,3*R*)-3-amino-2-hydroxy-3-phenylpropanoate (65)



A 100 mL round bottom flask equipped with a magnetic stir bar and reflux condenser was charged with isopropyl (2*S*,3*R*)-3-acetamido-2-hydroxy-3-phenylpropanoate (**64**) (1.6 g, 5.9 mmol, 1.0 equiv) and HCl (aq., 10%, 60 mL) and the reaction mixture was refluxed for 16h. After evaporating the solvent in vacuo, the obtained white solid was transferred into a Dean-Stark-apparatus and dissolved in EtOH (60 mL). After Addition of H_2SO_4 (98%, 0.5 mL) the reaction mixture was refluxed for 16 h. After evaporating the solvent, the residue was dissolved in EtOAc (20 mL) and washed with Na_2CO_3 solution (10%, 20 mL). The aqueous phase was extracted wih EtOAc (3x 20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. After the evaporation of the solvent the obtained residue was purified by silica gel column chromatography (EtOAc/Et_3N, 99:1) to give 640 mg (3.1 mmol, 52%) of ethyl (2*S*,3*R*)-3-amino-2-hydroxy-3-phenylpropanoate (**65**) was obtained as white solid. R_f (EtOAc / NEt_3, 99:1) = 0.28, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 – 7.21 (m, 5H), 4.41 – 4.05 (m, 4H), 2.42 (s, 3H), 1.24 (t, J = 6.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 142.3, 128.6, 127.7, 126.9, 75.2, 61.9, 58.1, 14.2.

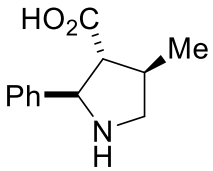
Ethyl (2*S*,3*R*)-3-(allylamino)-2-hydroxy-3-phenylpropanoate (66)



A 100 mL round bottom flask equipped with a magnetic stir bar was charged with ethyl (2*S*,3*R*)-3-amino-2-hydroxy-3-phenylpropanoate (**65**) (548 mg, 2.62 mmol, 1.0 equiv) and triethylamine (399 µL, 292 mg, 2.9 mmol, 1.1 equiv) in THF (1 mL). Allyl bromide (**38e**) (245 µL, 333 mg, 2.8 mmol, 1.1 equiv) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. Additional triethylamine (399 µL, 292 mg, 2.9 mmol, 1.1 equiv) and allyl bromide (**38e**) (245 µL, 333 mg, 2.8 mmol, 1.1 equiv) were added and the mixture was stirred for 24 h. The white precipitate was filtered off and the solvent was evaporated under reduced

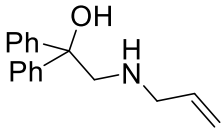
pressure. The crude product was purified by silica gel column chromatography (hexanes / EtOAc, 2:1 to 0:1) to give 285 mg (1.1 mmol, 44%) of ethyl (2*S*,3*R*)-3-(allylamino)-2-hydroxy-3-phenylpropanoate (**66**) as a colorless oil. R_f (hexanes / EtOAc, 1:1) = 0.31, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 – 7.26 (m, 5H), 5.90 – 5.69 (m, 1H), 5.18 – 5.00 (m, 2H), 4.30 – 4.09 (m, 3H), 3.98 (d, *J* = 3.2 Hz, 1H), 3.28 – 3.14 (m, 1H), 2.99 (dd, *J* = 12.0, 8.0 Hz, 1H), 2.79 (bs, 2H), 1.20 (t, *J* = 8.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.5, 139.7, 136.6, 128.6, 127.9, 127.8, 116.3, 74.9, 63.9, 61.8, 49.5, 14.2. IR (neat): 3403, 3202, 3064, 2982, 2851, 1737, 1580, 1502, 1402, 1100,1021, 924, 760, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{14}H_{20}NO_3$ ([M+H]$^+$) 250.1438, found 250.1440.

rac. (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-3-carboxylic acid (69)



A 10 mL round bottom flask equipped with a magnetic stir bar was charged with rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (**48a´**) (89 mg, 267 µmol, 1.0 equiv) and hydrochloric acid (6M, aq., 10 mL). The resulting mixture was stirred for 24 h at room temperature. The solvent was removed in vacuo and the residue was dissolved in hydrochloric acid (0.1M, aq., 5 ml). The solution was loaded on to a Dowex 50X8 (H^+) ion exchange column, washed with water (250 mL) and the column was eluted with ammonium hydroxide solution (16%, aq.,) until the product was detected by TLC analysis (Staining: Ninhydrin). The solvent was removed in vacuo and lyophilised to afford 53 mg (258 µmol, 97%) of rac. (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-3-carboxylic acid (**69**) as white solid. ^{1}H NMR (400 MHz, D_2O) δ 7.54 – 7.42 (m, 5H), 4.74 (d, *J* = 11.4 Hz, 1H), 3.68 (dd, *J* = 11.7, 8.4 Hz, 1H), 3.10 (dd, *J* = 11.7, 10.1 Hz, 1H), 2.89 (t, *J* = 11.1 Hz, 1H), 2.66 (tdd, *J* = 10.3, 8.4, 6.6 Hz, 1H), 1.24 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, D_2O) δ 177.6, 133.4, 129.8, 129.3, 127.6, 66.5, 59.5, 50.9, 38.1, 15.4. IR (neat): 2960, 2874, 2363, 2110, 1644, 1558, 1498, 1461, 1379, 1267, 1197, 1144, 1100, 1006, 962, 865, 760, 731 cm^{-1}. HRMS (ESI) m/z calculated for $C_{12}H_{16}NO_2$ ([M+H]$^+$) 206.1176, found 206.1177.

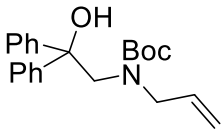
2-(allylamino)-1,1-diphenylethan-1-ol (73)



A 250 mL round bottom flask equipped with a magnetic stir bar and reflux condenser was charged with 2-amino-1,1-diphenylethan-1-ol (**72**) (639 mg, 3.0 mmol, 1.0 equiv), DBU (670 µL, 684 mg, 4.5 mmol, 1.5 equiv) and toluene (150 mL). 3-bromoprop-1-ene (**38e**) (388 µL, 544 mg, 4.5 mmol, 1.5 equiv) was added dropwise at room temperature and the reaction mixture was stirred for 72 h at 60 °C. After addition of water (100 mL) the mixture was extracted with EtOAc (2x 100 mL). The combined organic layers were washed with water (3x 100 mL), dried over anhydrous Na_2SO_4, the solvent was evaporated in vacuo and the residue purified by silica gel column chromatography

(hexanes / EtOAc, 2:1 to 1:1) to give 440 mg (1.7 mmol, 58%) of 2-(allylamino)-1,1-diphenylethan-1-ol (**73**) as a colorless oil. R_f (hexanes / EtOAc, 1:1) = 0.45, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 – 7.43 (m, 4H), 7.39 – 7.29 (m, 4H), 7.28 – 7.17 (m, 2H), 5.84 (ddt, *J* = 17.2, 10.2, 6.0 Hz, 1H), 5.24 – 5.00 (m, 2H), 3.33 (s, 2H), 3.28 (dt, *J* = 6.0, 1.4 Hz, 2H), 2.83 (bs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.7, 136.5, 128.4, 127.1, 126.2, 116.6, 76.3, 58.1, 52.4. IR (neat): 3302, 3068, 2937, 2878, 2822, 1644, 1603, 1495, 1450, 1327, 1275, 1230, 1200, 1144, 1103, 1066, 1025, 910, 869, 820, 772 cm^{-1}. HRMS (ESI) m/z calculated for $C_{17}H_{20}NO$ ($[M+H]^+$) 254.1539, found 254.1541.

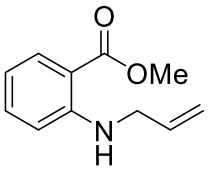
***tert*-butyl allyl(2-hydroxy-2,2-diphenylethyl)carbamate (74)**



A 25 mL round bottom flask equipped with a magnetic stir bar was charged with 2-(allylamino)-1,1-diphenylethan-1-ol (**73**) (342 mg, 1.4 mmol, 1.0 equiv), triethylamine (225 µL, 164 mg, 1.6 mmol, 1.2 equiv) and CH_2Cl_2 (20 mL). After addition of di-tertbutyl dicarbonate (354 mg, 1.6 mmol, 1.2 equiv) the solution was stirred for 20 h at room temperature. After the addition of CH_2Cl_2 (20 mL) and 1M HCl (15 mL), the mixture was partitioned. The organic layer was washed with 1M HCl (2x 15 mL) solution, dried over anhydrous Na_2SO_4, and the solvent evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexanes / EtOAc, 9:1 to 6:1) to give 429 mg (1.2 mmol, 90%) of *tert*-butyl allyl(2-hydroxy-2,2-diphenylethyl)carbamate (**74**) as a colorless oil. R_f (hexanes / EtOAc, 6:1) = 0.54, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 – 7.40 (m, 4H), 7.36 – 7.15 (m, 6H), 5.76 (bs, 1H), 5.61 – 5.41 (m, 1H), 5.04 (d, *J* = 10.0 Hz, 1H), 4.90 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.06 (s, 2H), 3.17 (s, 2H), 1.45 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 145.8, 133.5, 128.1, 127.1, 126.6, 116.5, 81.2, 78.7, 57.3, 51.9, 28.4. IR (neat): 3355, 3064, 2978, 2933, 1659, 1599, 1454, 1409, 1364, 1308, 1252, 1163, 1062, 995, 857, 753 cm^{-1}. HRMS (ESI) m/z calculated for $C_{22}H_{27}NNaO_3$ ($[M+Na]^+$) 376.1883, found 376.1890.

2.2.4. Synthesis of Bicyclic Products

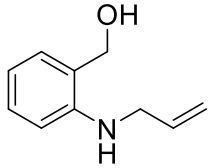
Methyl 2-(allylamino)benzoate (86)



A 100 mL round bottom flask equipped with a magnetic stir bar was charged with methyl 2-aminobenzoate (**85**) (21.2 g, 140 mmol, 2.0 equiv) in dry DMF (15 mL) and cooled to 0 °C. Allyl bromide (**38e**) (6.2 mL, 8.5 g, 70.0 mmol, 1.0 equiv) was added dropwise and the reaction mixture was stirred 16 h at 40 °C. After the addition of H_2O (50 mL) the mixture was extracted with EtOAc (3x 50 mL). The organic layer was washed with H_2O (2x 25 mL), dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexanes / EtOAc, 19:1 to 10:1) to give 13.2 g (69.0 mmol, 99%) of

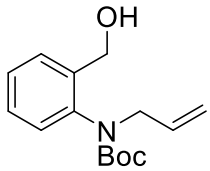
methyl 2-(allylamino)benzoate (**86**) as a colorless oil. R_f (hexanes / EtOAc, 9:1) = 0.60, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 8.0, 1.8 Hz, 2H), 7.35 (ddd, *J* = 8.7, 7.1, 1.7 Hz, 1H), 6.74 – 6.54 (m, 2H), 5.97 (ddt, *J* = 17.1, 10.2, 5.0 Hz, 1H), 5.31 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.19 (dq, *J* = 10.3, 1.6 Hz, 1H), 3.94 – 3.80 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 151.0, 134.6, 134.6, 131.7, 116.1, 114.8, 111.6, 110.1, 51.6, 45.3.

(2-(allylamino)phenyl)methanol (87)



A 100 mL round bottom flask equipped with a magnetic stir bar was charged with methyl 2-(allylamino)benzoate (**86**) (4.2 g, 22.0 mmol, 1.0 equiv) in dry THF (100 mL). A solution of $LiAlH_4$ (3.3 g, 87.9 mmol, 4.0 equiv) in THF (100 mL) was added dropwise while the temperature was maintained at 0 °C. The resulting mixture was allowed to warm to room temperature and was stirred for 2 h. The mixture was then hydrolyzed by addition of H_2O (100 mL), the resulting suspension was filtered, and the precipitate was washed with EtOAc (3x 100 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and solvent evaporated under reduced pressure to give 3.5 g (21.7 mmol, 99%) of (2-(allylamino)phenyl)methanol (**87**) as yellow oil. R_f (hexanes / EtOAc, 3:1) = 0.40, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (td, *J* = 8.0, 1.6 Hz, 1H), 7.07 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.78 – 6.59 (m, 2H), 5.99 (ddt, *J* = 17.2, 10.4, 5.3 Hz, 1H), 5.30 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.18 (dq, *J* = 10.3, 1.5 Hz, 1H), 4.68 (s, 2H), 3.83 (dt, *J* = 5.2, 1.7 Hz, 2H), 3.29 (bs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.4, 135.4, 129.7, 129.2, 124.5, 116.7, 116.2, 111.1, 64.8, 46.1. IR (neat): 3384, 3079, 3012, 2922, 2870, 1644, 1606, 1513, 1461, 1312, 1260, 1193, 1074, 992, 921, 850, 798 cm^{-1}. HRMS (APCI) m/z calculated for $C_{10}H_{14}NO$ ($[M+H]^+$) 164.1070, found 164.1073.

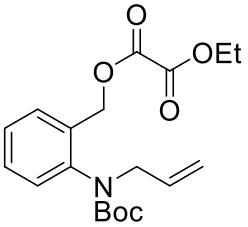
***tert*-butyl allyl(2-(hydroxymethyl)phenyl)carbamate (88)**



A 100 mL round bottom flask equipped with a magnetic stir bar and a reflux condenser was charged with (2-(allylamino)phenyl)methanol (**87**) (979 mg, 6.0 mmol, 1.0 equiv) and di-*tert*butyl dicarbonate (2.0 g, 9.0 mmol, 1.5 equiv) in ethanol (70 mL) and the solution was stirred for 16 h at 50 °C. After evaporation of solvent under reduced pressure the obtained residue was purified by silica gel column chromatography (hexanes / EtOAc, 9:1 to 4:1) to give 1.5 g (5.7 mmol, 95%) of *tert*-butyl allyl(2-(hydroxymethyl)phenyl)carbamate (**88**) as a white solid. R_f (hexanes / EtOAc, 6:1) = 0.25, Staining: Ninhydrin, $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.47 (m, 1H), 7.32 – 7.27 (m, 2H), 7.16 (bs, 1H), 5.90 (ddt, *J* = 16.7, 10.2, 6.4 Hz, 1H), 5.24 – 5.01 (m, 2H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.44 – 4.32 (m, 1H), 4.26 – 3.92 (m, 2H), 3.44 (s, 1H), 1.71 – 1.20 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.6, 133.7, 131.0, 129.1, 128.0, 127.5, 118.0, 81.3, 61.9, 54.2, 28.4, 27.5. IR (neat): 3433, 3075, 2978, 2930,

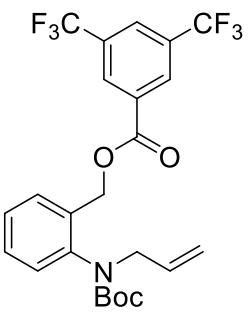
1674, 1491, 1454, 1390, 1305, 1275, 1148, 1044, 1006, 924, 857, 760, 731 cm^{-1}. HRMS (APCI) m/z calculated for $C_{15}H_{22}NO_3$ ($[M+H]^+$) 264.1594, found 264.1599. mp: 56 °C.

2-(allyl(*tert*-butoxycarbonyl)amino)benzyl ethyl oxalate (89)



A 50 mL round bottom flask equipped with a magnetic stir bar was charged with *tert*-butyl allyl(2-(hydroxymethyl)phenyl)carbamate (**88**) (206 mg, 782 µmol, 1.0 equiv), dry pyridine (126 µL, 124 mg, 1.6 mmol, 2.0 equiv) and dry CH_2Cl_2 (10 mL). The solution was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (**15**) (174 µL, 214 mg, 1.6 mmol, 2.0 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. CH_2Cl_2 (50 mL) was added and the reaction mixture was washed with water (3x 20 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 268 mg (269 mg, 740 µmol, 95%) of 2-(allyl(*tert*-butoxycarbonyl)amino)benzyl ethyl oxalate (**89**) as a colorless oil. R_f (hexanes / EtOAc, 6:1) = 0.42, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 1H), 7.38 – 7.27 (m, 2H), 7.23 – 7.09 (m, 1H), 5.95 (ddt, *J* = 16.8, 12.1, 6.4 Hz, 1H), 5.26 (q, *J* = 12.8 Hz, 2H), 5.16 – 5.03 (m, 2H), 4.40 – 4.26 (m, 3H), 4.00 (bs, 1H), 1.54 – 1.25 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.8, 157.7, 154.5, 141.2, 133.6, 132.6, 129.6, 129.3, 128.5, 127.7, 118.3, 80.8, 64.9, 63.3, 53.1, 28.4, 14.1. IR (neat): 3079, 2982, 2937, 1767, 1740, 1696, 1498, 1457, 1368, 1305, 1148, 1010, 928, 861, 760 cm^{-1}. HRMS (ESI) m/z calculated for $C_{19}H_{29}N_2O_6$ ($[M+NH_4]^+$) 381.2020, found 381.2028.

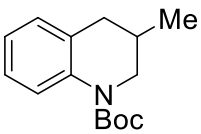
2-(allyl(tert-butoxycarbonyl)amino)benzyl 3,5-bis(trifluoromethyl)benzoate (90)



A 100 mL Schlenk flask equipped with a magnetic stir bar was charged with *tert*-butyl allyl(2-(hydroxymethyl)phenyl)carbamate (**88**) (308 mg, 1.2 mmol, 1.0 equiv) and dissolved in dry CH_2Cl_2 (12 mL). *N*,*N*-diisoproylethylamine (398 µL, 302 mg, 2.3 mmol, 2.0 equiv) was added followed by 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (699 mg, 1.4 mmol, 1.2 equiv). After stirring for 4 h at room temperature, CH_2Cl_2 (60 mL) was added and the organic layer was washed with Na_2CO_3 (aq. 10%, 60 mL) and water (60 mL). The organic phase was dried over Na_2SO_4 and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography (hexanes / EtOAc, 5:1 to 3:1) to give 575 mg (1.1 mmol, 98%) of 2-(allyl(tert-butoxycarbonyl)amino)benzyl 3,5-bis(trifluoromethyl)-benzoate (**90**) as colorless oil. R_f (hexanes / EtOAc, 6:1) = 0.75, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 2H), 8.07 (s, 1H), 7.50 (d, *J* = 7.3 Hz, 1H), 7.40 – 7.30 (m, 2H), 7.20 (bs, 1H), 6.05 – 5.89 (m, 1H), 5.42 (s, 2H), 5.12 (d, *J* = 11.6 Hz, 2H), 4.33 (dd, *J* = 15.2, 6.1 Hz, 1H), 4.07 (bs, *J* =

15.3 Hz, 1H), 1.57 – 1.27 (m, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.55 (s, 6F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 154.5, 141.0, 133.7, 133.3, 132.4 (q, *J* = 34.1 Hz), 132.4, 130.0 – 129.8 (m), 129.4, 129.1, 128.5, 127.8, 126.7 – 126.5 (m), 123.0 (q, *J* = 272.9 Hz), 118.1, 117.6, 80.7, 64.2, 53.2, 28.3. IR (neat): 3083, 2982, 2933, 1733, 1700, 1625, 1498, 1457, 1368, 1279, 1241, 1174, 1133, 992, 943, 913, 846, 764, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{24}H_{23}F_6NNaO_4$ ([M+Na]$^+$) 526.1423, found 526.1424.

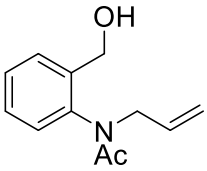
tert-butyl 3-methyl-3,4-dihydroquinoline-1(2H)-carboxylate (91)



From oxalate ester: A flame dried Schlenk tube was charged with 2-(allyl(*tert*-butoxycarbonyl)amino)benzyl ethyl oxalate (**89**) (206 mg, 567 µmol, 1.0 equiv) in DMF (5.7 mL). After addition of *fac*-Ir(ppy)$_3$ (3.8 mg, 0.57 µmol, 1 mol%) the reaction mixture was degassed by freeze-pump-thaw cycles (3x) and pumped through a micro reactor (which was sparged with N_2 too) equipped with 8 LED's at a flow rate of 0.30 mL/h via a syringe pump while heated at 80 °C. Afterwards, the reaction mixture was diluted with diethyl ether (80 mL) and extracted with water (3x 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (diethyl ether / *n*-pentane, 1:10 to 1:1) to give *tert*-butyl 3-methyl-3,4-dihydroquinoline-1(2H)-carboxylate (**91**) (53 mg, 214 µmol, 38%) as colorless oil.

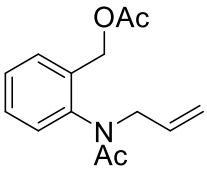
From 3,5-bis(trifluoromethyl) benzoate ester: Following the procedure described for oxalate ester **84** using 2-(allyl(*tert*-butoxycarbonyl)amino)benzyl 3,5-bis(trifluoromethyl)benzoate (**90**) (311 mg, 618 µmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (4.1 mg, 6.2 µmol, 1.0 mol%) and DMF (6.2 mL, 0.1 M) at a flow rate of 0.30 mL/h gave 57 mg (230 µmol, 37%) of *tert*-butyl 3-methyl-3,4-dihydroquinoline-1(2H)-carboxylat (**91**) as a colorless oil after flash column purification (diethyl ether / *n*-pentane, 1:10 to 1:1). R_f (diethyl ether / *n*-pentane, 1:9) = 0.50, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.2 Hz, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 7.06 (d, *J* = 7.0 Hz, 1H), 6.97 (td, *J* = 7.4, 1.2 Hz, 1H), 3.97 (ddd, *J* = 12.6, 4.2, 1.4 Hz, 1H), 3.10 (dd, *J* = 12.6, 9.8 Hz, 1H), 2.87 (dd, *J* = 16.2, 5.4 Hz, 1H), 2.42 (dd, *J* = 16.2, 9.6 Hz, 1H), 2.12 – 1.97 (m, 1H), 1.53 (s, 9H), 1.06 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 138.4, 129.3, 128.9, 125.7, 124.0, 123.3, 80.9, 51.1, 36.1, 29.2, 28.5, 19.1. IR (neat): 2960, 2930, 2874, 1700, 1491, 1457, 1368, 1297, 1252, 1211, 1156, 1036, 1006, 982, 861, 753 cm^{-1}. HRMS (ESI) m/z calculated for $C_{15}H_{21}NNaO_2$ ([M+Na]$^+$) 270.1465, found 270.1460.

N-allyl-*N*-(2-(hydroxymethyl)phenyl)acetamide (95)



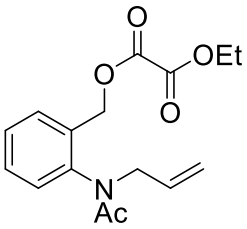
A 50 mL Schlenk flask equipped with a magnetic stir bar was charged while cooling at 0 °C with (2-(allylamino)phenyl)methanol (**87**) (330 mg, 2.0 mmol, 1.0 equiv), acetyl chloride (144 µL, 159 mg, 2.0 mmol, 1.0 equiv) and $NaHCO_3$ (200 mg, 2.4 mmol, 1.2 equiv) in dry CH_2Cl_2 (20 mL) and the solution was stirred for 4 h at 0 °C and then 16 h at room temperature. The organic phase was washed with water (3x 20 mL), the aqueous phase was extracted with CH_2Cl_2 (2x 20 mL) and the organic phase was dried with anhydrous Na_2SO_4. After evaporation of solvent under reduced pressure the obtained residue was purified by silica gel column chromatography (hexanes / EtOAc, 5:1 to 1:1) to give 276 mg (1.3 mmol, 67%) of *N*-allyl-*N*-(2-(hydroxymethyl)phenyl)acetamide (**95**) as a colorless oil. R_f (hexanes / EtOAc, 1:1) = 0.14, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 – 7.57 (m, 1H), 7.44 – 7.29 (m, 2H), 7.08 (dt, *J* = 7.8, 1.2 Hz, 1H), 5.89 (ddddd, *J* = 17.1, 10.1, 7.0, 6.0, 1.0 Hz, 1H), 5.16 – 4.99 (m, 2H), 4.66 – 4.49 (m, 3H), 3.87 (ddd, *J* = 14.4, 7.3, 1.5 Hz, 1H), 2.62 (bs, 1H), 1.77 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 140.4, 138.4, 132.9, 129.5, 129.3, 129.0, 128.9, 118.8, 60.8, 52.0, 22.6. IR (neat): 3377, 3079, 2922, 2874, 1629, 1491, 1431, 1394, 1282, 1230, 1144, 1115, 1040, 984, 924, 820, 775, 742, 664 cm^{-1}. HRMS (ESI) m/z calculated for $C_{12}H_{16}NO_2$ ($[M+H]^+$) 206.1176, found 206.1178.

2-(*N*-allylacetamido)benzyl acetate (96)



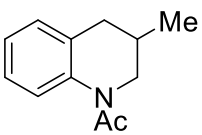
A 50 mL round bottom flask equipped with a magnetic stir bar was charged while cooling at 0 °C with (2-(allylamino)phenyl)methanol (**87**) (179 mg, 1.1 mmol, 1.0 equiv) and acetic anhydride (156 µL, 168 mg, 1.7 mmol, 1.5 equiv) in diethyl ether (20 mL) and the solution was stirred for 2 h at 0 °C and then 18 h at room temperature. After evaporation of solvent under reduced pressure the obtained residue was purified by silica gel column chromatography (hexanes / EtOAc, 5:1 to 1:1) to give 180 mg (728 µmol, 66%) of 2-(*N*-allylacetamido)benzyl acetate (**96**) as a colorless oil. R_f (hexanes / EtOAc, 3:1) = 0.13, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 – 7.45 (m, 1H), 7.43 – 7.35 (m, 2H), 7.16 – 7.08 (m, 1H), 5.89 (dddd, *J* = 17.2, 10.1, 7.4, 5.9 Hz, 1H), 5.16 – 4.98 (m, 4H), 4.67 (ddt, *J* = 14.4, 5.9, 1.4 Hz, 1H), 3.77 (ddt, *J* = 14.3, 7.3, 1.1 Hz, 1H), 2.09 (s, 3H), 1.79 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 170.6, 141.5, 133.8, 132.7, 130.7, 129.9, 129.8, 129.0, 118.9, 62.5, 52.0, 22.6, 21.0. IR (neat): 3079, 2982, 1737, 1659,1495, 1454, 1379, 1279, 1223, 1081, 1029, 977, 924, 887, 839, 779, 753, 664 cm^{-1}. HRMS (ESI) m/z calculated for $C_{14}H_{17}KNO_3$ ($[M+K]^+$) 286.0840, found 286.0840.

2-(*N*-allylacetamido)benzyl ethyl oxalate (97)



A 50 mL round bottom flask equipped with a magnetic stir bar was charged with *N*-allyl-*N*-(2-(hydroxymethyl)phenyl)acetamide (**95**) (170 mg, 828 µmol, 1.0 equiv), dry pyridine (134 µL, 131 mg, 1.7 mmol, 2.0 equiv) and dry CH_2Cl_2 (10 mL). The solution was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (184 µL, 226 mg, 1.7 mmol, 2.0 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. CH_2Cl_2 (50 mL) was added and the reaction mixture was washed with water (3x 20 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 252 mg (825 µmol, 100%) of 2-(*N*-allylacetamido)benzyl ethyl oxalate (**97**) as a colorless oil. R_f (hexanes / EtOAc, 1:1) = 0.43, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 – 7.51 (m, 1H), 7.45 – 7.39 (m, 2H), 7.19 – 7.12 (m, 1H), 5.89 (dddd, *J* = 17.3, 10.0, 7.4, 5.9 Hz, 1H), 5.24 (s, 2H), 5.12 (dd, *J* = 10.1, 1.4 Hz, 1H), 5.05 (dd, *J* = 17.1, 1.4 Hz, 1H), 4.66 (ddt, *J* = 14.3, 6.0, 1.3 Hz, 1H), 4.34 (q, *J* = 7.2 Hz, 2H), 3.83 (ddt, *J* = 14.4, 7.4, 1.1 Hz, 1H), 1.81 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 157.5, 157.3, 141.9, 132.6, 132.2, 131.1, 130.6, 130.1, 129.1, 119.1, 64.6, 63.5, 52.1, 22.6, 14.0. IR (neat): 3079, 2986, 2937, 1767, 1744, 1662, 1454, 1405, 1383, 1297, 1156, 1115, 1014, 980, 932, 861, 757, 664 cm^{-1}. HRMS (ESI) m/z calculated for $C_{16}H_{20}NO_5$ ($[M+H]^+$) 306.1336, found 306.1340.

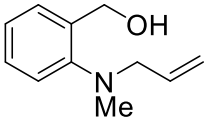
1-(3-methyl-3,4-dihydroquinolin-1(2H)-yl)ethan-1-one (98)



A flame dried Schlenk tube was charged with 2-(*N*-allylacetamido)benzyl ethyl oxalate (**97**) (231 mg, 757 µmol, 1.0 equiv) in DMF (7.6 mL). After addition of *fac*-Ir(ppy)3 (5.0 mg, 0.76 µmol, 1 mol%) the reaction mixture was degassed by freeze-pump-thaw cycles (3x) and pumped through a micro reactor (which was sparged with N_2 too) equipped with 8 LED's at a flow rate of 0.30 mL/h via a syringe pump while heated at 80 °C. Afterwards, the reaction mixture was diluted with diethyl ether (100 mL) and extracted with water (3x 60 mL). The combined organic layers were dried over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure and the residue purified by flash column chromatography (diethyl ether / *n*-pentane, 1:10 to 1:1) to give 1-(3-methyl-3,4-dihydroquinolin-1(2H)-yl)ethan-1-one (**98**) (38 mg, 201 µmol, 27%) as colorless oil. R_f (hexanes / EtOAc, 4:1) = 0.19, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.06 (m, 4H), 4.03 (s, 1H), 3.21 (dd, *J* = 12.6, 9.7 Hz, 1H), 2.85 (dd, *J* = 15.8, 5.5 Hz, 1H), 2.38 (dd, *J* = 15.8, 9.7 Hz, 1H), 2.24 (s, 3H), 2.06 (dq, *J* = 9.9, 4.3 Hz, 1H), 1.08 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 139.1, 128.8, 126.1, 125.1, 124.4, 49.9, 35.7, 30.5, 23.3, 19.6. IR (neat): 3027, 2956, 2930, 2874, 1655, 1491, 1457, 1372, 1327, 1279,

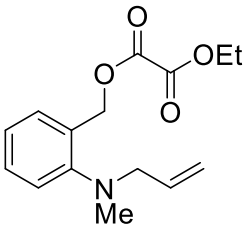
1204, 1122, 1085, 1040, 984, 951, 857, 798, 760 cm^{-1}. HRMS (ESI) m/z calculated for $C_{12}H_{16}NO$ ($[M+H]^+$) 190.1226, found 190.1226.

(2-(allyl(methyl)amino)phenyl)methanol (99)



A 50 mL round bottom flask equipped with a magnetic stir bar was charged with (2-(allylamino)phenyl)methanol (**87**) (326 mg, 2.0 mmol, 1.0 equiv) and K_2CO_3 (415 mg, 3.0 mmol, 1.5 equiv) and dry DMF (10 mL). The solution was cooled to 0 °C and iodomethane (137 µL, 312 mg, 2.2 mmol, 1.1 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. CH_2Cl_2 (50 mL) was added and the reaction mixture was washed with water (3x 50 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 267 mg (1.5 mmol, 75%) of (2-(allyl(methyl)amino)phenyl)methanol (**99**) as a colorless oil. R_f (hexanes / EtOAc, 3:1) = 0.45, Staining: Vanillin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 1H), 7.21 – 7.15 (m, 2H), 7.09 (td, *J* = 7.3, 1.3 Hz, 1H), 5.87 (ddt, *J* = 16.7, 10.1, 6.4 Hz, 1H), 5.39 (bs, 1H), 5.24 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.19 (dt, *J* = 10.1, 1.4 Hz, 1H), 4.81 (s, 2H), 3.53 (dt, *J* = 6.6, 1.3 Hz, 2H), 2.69 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.2, 135.9, 134.5, 128.7, 128.2, 124.8, 121.5, 118.6, 64.9, 60.2, 41.7. IR (neat): 3340, 3071, 2982, 2948, 2848, 2796, 1644, 1599, 1491, 1454, 1420, 1347, 1223, 1170, 1085, 1025, 999, 917, 828, 764, 723 cm^{-1}. HRMS (ESI) m/z calculated for $C_{11}H_{16}NO$ ($[M+H]^+$) 178.1226, found 178.1230.

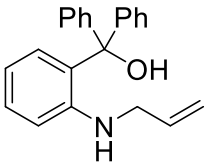
2-(allyl(methyl)amino)benzyl ethyl oxalate (100)



A 50 mL round bottom flask equipped with a magnetic stir bar was charged with (2-(allyl(methyl)amino)phenyl)methanol (**99**) (150 mg, 846 µmol, 1.0 equiv), dry pyridine (137 µL, 134 mg, 1.7 mmol, 2.0 equiv) and dry CH_2Cl_2 (10 mL). The solution was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (188 µL, 231 mg, 1.7 mmol, 2.0 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. CH_2Cl_2 (50 mL) was added and the reaction mixture was washed with water (3x 20 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 234 mg (844 µmol, 100%) of 2-(allyl(methyl)amino)benzyl ethyl oxalate (**100**) as a colorless oil. R_f (hexanes / EtOAc, 6:1) = 0.53, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.36 – 7.30 (m, 1H), 7.17 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.11 (td, *J* = 7.5, 1.2 Hz, 1H), 5.85 (ddt, *J* = 17.2, 10.2, 6.1 Hz, 1H), 5.45 (s, 2H), 5.24 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.15 (dq, *J* = 10.2, 1.4 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.52 (d, *J* = 6.1 Hz, 2H), 2.69 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 157.9, 152.7, 135.1, 130.5, 129.7, 129.7, 124.1, 121.4, 117.5, 65.4, 63.2, 60.9,

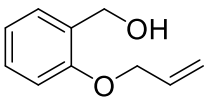
42.1, 14.1. IR (neat): 3075, 2982, 2851, 2796, 1767, 1741, 1677, 1644, 1603, 1495, 1454, 1379, 1305, 1230, 1178, 1018, 980, 928, 865, 760, 731, 678 cm^{-1}. LRMS (ESI) showed no product signal, but hydrolysis product: m/z calculated for $C_{11}H_{16}NO$ ($[M+H]^+$) 178.1226, found 178.1223 and methanolysis product: m/z calculated for $C_{12}H_{18}NO$ ($[M+H]^+$) 192.1383, found 192.1388. These results indicate the lability of the product during the HPLC purification.

(2-(allylamino)phenyl)diphenylmethanol (104)



A 250 mL round bottom flask equipped with a magnetic stir bar was charged with methyl 2-(allylamino)benzoate (**86**) (1.2 g, 6.0 mmol, 1.0 equiv) in dry THF (100 mL). A solution of phenylmagnesium bromide (3.5 g, 19.2 mmol, 3.2 equiv) in THF (100 mL) was added dropwise while the temperature was maintained at 0 °C. The resulting mixture was allowed to warm to room temperature and was stirred for 2 h. The mixture was then hydrolyzed by addition of H_2O (100 mL), the resulting suspension was filtered, and the precipitate was washed with EtOAc (3x 100 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and solvent evaporated under reduced pressure to give 1.6 g (5.1 mmol, 85%) of (2-(allylamino)phenyl)diphenylmethanol (**104**) as yellow oil after purification with column chromatography (hexanes / EtOAc, 9:1). R_f (hexanes / EtOAc, 9:1) = 0.38, Staining: $KMnO_4$ (UV active). ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 10H), 7.27 – 7.20 (m, 1H), 6.81 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.67 (td, *J* = 7.6, 1.2 Hz, 1H), 6.53 (dd, *J* = 7.8, 1.6 Hz, 1H), 5.75 (ddt, *J* = 17.3, 10.3, 5.0 Hz, 1H), 5.02 (dq, *J* = 10.5, 1.5 Hz, 1H), 4.96 (dq, *J* = 17.2, 1.7 Hz, 1H), 4.72 (bs, 2H), 3.61 (dt, *J* = 5.0, 1.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.8, 145.6, 134.8, 132.7, 130.1, 129.0, 128.2, 127.9, 127.5, 118.0, 115.9, 114.3, 82.8, 46.5. IR (neat): 3340, 3291, 3056, 3030, 2874 1580, 1521, 1487, 1446, 1323, 1115, 1003, 924, 846, 794 cm^{-1}. HRMS (ESI) m/z calculated for $C_{22}H_{22}NO$ ($[M+H]^+$) 316.1696, found 316.1698.

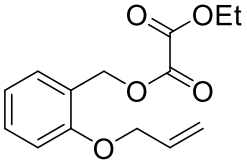
(2-(allyloxy)phenyl)methanol (109)



A 250 mL round bottom flask equipped with a magnetic stir bar was charged with methyl 2-(allylamino)benzoate (**108**) (1.0 g, 5.2 mmol, 1.0 equiv) in dry THF (50 mL). A solution of $LiAlH_4$ (790 mg, 20.8 mmol, 4.0 equiv) in THF (50 mL) was added dropwise while the temperature was maintained at 0 °C. The resulting mixture was allowed to warm to room temperature and was stirred for 2 h. The mixture was then hydrolyzed by addition of H_2O (100 mL), the resulting suspension was filtered, and the precipitate was washed with EtOAc (3x 100 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and solvent evaporated under reduced pressure to give 650 mg (4.0 mmol, 76%) of (2-(allyloxy)phenyl)methanol (**109**) as pale yellow oil after purification with column chromatography (hexanes / EtOAc, 6:1). R_f (hexanes / EtOAc, 6:1) = 0.24, Staining: $KMnO_4$

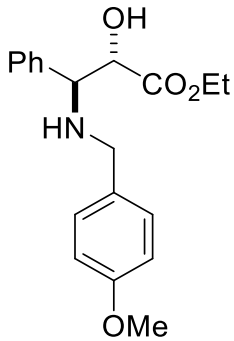
(UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.19 (m, 2H), 6.96 (td, *J* = 7.4, 1.1 Hz, 1H), 6.88 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.07 (ddt, *J* = 17.3, 10.4, 5.2 Hz, 1H), 5.43 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.31 (dq, *J* = 10.5, 1.5 Hz, 1H), 4.72 (s, 2H), 4.59 (dt, *J* = 5.2, 1.6 Hz, 2H), 2.50 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.5, 133.1, 129.5, 128.9, 128.8, 120.9, 117.7, 111.5, 68.8, 62.2.

2-(allyloxy)benzyl ethyl oxalate (110)



A 50 mL round bottom flask equipped with a magnetic stir bar was charged with (2-(allyloxy)phenyl)methanol (**109**) (207 mg, 1.3 mmol, 1.0 equiv), dry pyridine (204 µL, 199 mg, 2.5 mmol, 2.0 equiv) and dry CH_2Cl_2 (10 mL). The solution was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (**15**) (280 µL, 344 mg, 2.5 mmol, 2.0 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. CH_2Cl_2 (50 mL) was added and the reaction mixture was washed with water (3x 20 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 280 mg (1.1 mmol, 84%) of 2-(allyloxy)benzyl ethyl oxalate (**110**) as a colorless oil. R_f (hexanes / EtOAc, 9:1) = 0.38, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.22 (m, 2H), 6.96 (td, *J* = 7.5, 1.1 Hz, 1H), 6.88 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.04 (ddt, *J* = 17.3, 10.3, 5.1 Hz, 1H), 5.45 – 5.36 (m, 3H), 5.27 (dq, *J* = 10.6, 1.5 Hz, 1H), 4.58 (dt, *J* = 5.1, 1.6 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 158.0, 156.8, 133.1, 130.4, 130.3, 123.0, 120.8, 117.5, 112.0, 69.0, 64.3, 63.2, 14.1. IR (neat): 2986, 1778, 1741, 1607, 1495, 1454, 1379, 1308, 1249, 1152, 1018, 924, 809, 801, 753 cm^{-1}. HRMS (ESI) m/z calculated for $C_{14}H_{16}NaO_5$ ($[M+Na]^+$) 287.0890, found 287.0891.

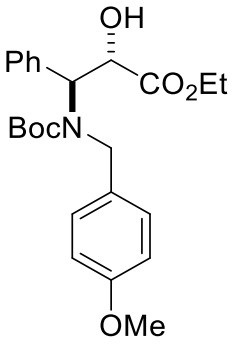
rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((4-methoxybenzyl)amino)-3-phenylpropanoate (117)



A 100 mL round bottom flask equipped with a magnetic stir bar and reflux condenser was charged with ethyl 3-phenyloxirane-2-carboxylate (**36a**) (980 mg, 5.1 mmol, 1.0 equiv), (4-methoxyphenyl)methanamine (666 µL, 699 mg, 5.1 mmol, 1.0 equiv) and EtOH (50 mL). The resulting mixture was refluxed for 24 h at 80 °C. Afterwards the solvent was evaporated in vacuo, and the residue was purified by silica gel column chromatography (hexanes / EtOAc, 9:1 to 1:1) to give 1.2 g (3.6 mmol, 70%) of rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((4-methoxybenzyl)amino)-3-phenylpropanoate (**117**) as white solid. R_f (hexanes / EtOAc, 1:1) = 0.34, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.12 (m, 7H), 6.96 – 6.75 (m, 2H), 4.52 (d, *J* = 4.1 Hz, 1H), 4.12 – 3.99 (m, 3H), 3.80 (s, 3H), 3.71 (d, *J* = 12.8 Hz, 1H), 3.56 (d, *J* = 12.8 Hz, 1H), 1.13 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 158.8, 137.8, 131.8, 129.6, 129.6, 128.5, 128.0, 128.0, 113.9, 73.5,

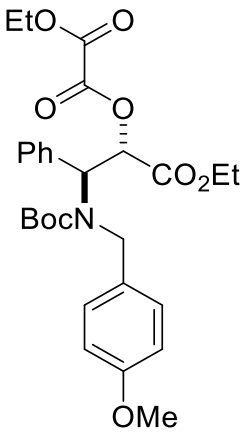
63.7, 61.5, 55.4, 50.4, 14.2. IR (neat): 3474, 3329, 3064, 3030, 2982, 2836, 1730, 1610, 1584, 1513, 1454, 1367, 1301, 1245, 1204, 1111, 1029, 932, 813, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{19}H_{24}NO_4$ ($[M+H]^+$) 330.1700, found 330.1706. mp: 54 °C.

rac. ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(4-methoxybenzyl)amino)-2-hydroxy-3-phenylpropanoate (118)



A 250 mL round bottom flask equipped with a magnetic stir bar and a reflux condenser was charged with rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((4-methoxybenzyl)amino)-3-phenylpropanoate (**117**) (2.7 g, 8.3 mmol, 1.0 equiv) and di-*tert*butyl dicarbonate (2.0 g, 9.1 mmol, 1.1 equiv) in ethanol (150 mL) and the solution was stirred for 48 h at 60 °C. After evaporation of solvent under reduced pressure the obtained residue was purified by silica gel column chromatography (hexanes / EtOAc, 9:1 to 3:1) to give 2.7 g (6.2 mmol, 75%) of rac. ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(4-methoxybenzyl)amino)-2-hydroxy-3-phenylpropanoate (**118**) as a colorless oil. R_f (hexanes / EtOAc, 3:1) = 0.32, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.19 (m, 5H), 7.03 – 6.93 (m, 2H), 6.77 – 6.71 (m, 2H), 5.36 (bs, 1H), 4.82 (t, *J* = 5.0 Hz, 1H), 4.58 – 4.29 (m, 2H), 4.16 (qd, *J* = 7.1, 2.5 Hz, 2H), 3.75 (s, 3H), 1.38 (s, 9H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 158.5, 156.2, 136.9, 131.3, 128.9, 128.4, 127.8, 113.6, 80.8, 72.3, 62.6, 62.1, 55.3, 49.6, 28.4, 14.1. IR (neat): 3444, 3064, 2978, 2937, 2840, 1737, 1685, 1614, 1513, 1454, 1394, 1364, 1301, 1245, 1159, 1118, 1033, 943, 891, 850, 816, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{24}H_{31}NNaO_6$ ($[M+Na]^+$) 452.2044, found 452.2051.

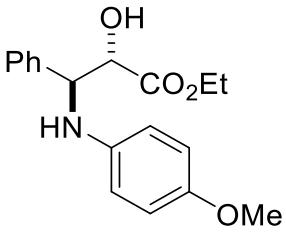
rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(4-methoxybenzyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (119)



A 25 mL round bottom flask equipped with a magnetic stir bar was charged with rac. ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(4-methoxybenzyl)amino)-2-hydroxy-3-phenylpropanoate (**118**) (859 mg, 2.0 mmol, 1.0 equiv), dry pyridine (242 µL, 237 mg, 1.5 mmol, 1.5 equiv) and dry CH_2Cl_2 (30 mL). The solution was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (**15**) (341 µL, 410 mg, 1.5 mmol, 1.5 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. CH_2Cl_2 (100 mL) was added and the reaction mixture was washed with water (3x 20 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 1.1 g (2.0 mmol, 99%) of rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(4-methoxybenzyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate

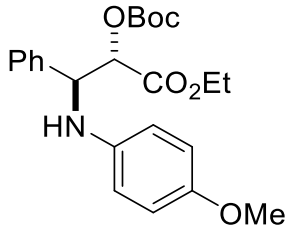
(**119**) as a colorless oil. R_f (hexanes / EtOAc, 3:1) = 0.45, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 – 7.20 (m, 5H), 7.05 – 6.49 (m, 4H), 6.26 – 5.54 (m, 2H), 4.58 – 4.18 (m, 4H), 4.09 (qd, *J* = 7.2, 1.1 Hz, 2H), 3.74 (s, 3H), 1.61 – 1.21 (m, 12H), 1.09 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 158.4, 156.5, 156.4, 135.3, 129.6, 128.6, 128.4, 113.5, 81.2, 75.3, 63.4, 62.2, 55.3, 28.4, 14.0, 13.9. IR (neat): 2982, 2840, 1748, 1689, 1614, 1513, 1454, 1394, 1368, 1305, 1245, 1156, 1021, 962, 924, 887, 857, 820, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{28}H_{35}NNaO_9$ ([M+Na]$^+$) 552.2204, found 552.2200.

rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((4-methoxyphenyl)amino)-3-phenylpropanoate (120)



A 500 mL round bottom flask equipped with a magnetic stir bar and reflux condenser was charged with ethyl 3-phenyloxirane-2-carboxylate (**36a**) (5.0 g, 26.0 mmol, 1.0 equiv), 4-methoxyaniline (3.2 mg, 26.0 mmol, 1.0 equiv) and EtOH (250 mL). The resulting mixture was refluxed for 24 h at 80 °C. Afterwards the solvent was evaporated in vacuo, and the residue was purified by silica gel column chromatography (hexanes / EtOAc, 9:1 to 1:1) to give 8.1 g (25.7 mmol, 99%) of rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((4-methoxyphenyl)amino)-3-phenylpropanoate phenylpropanoate (**120**) as a brown solid. R_f (hexanes / EtOAc, 1:1) = 0.63, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.21 (m, 5H), 6.74 – 6.67 (m, 2H), 6.64 – 6.56 (m, 2H), 4.79 (d, *J* = 3.5 Hz, 1H), 4.67 (d, *J* = 3.5 Hz, 1H), 4.15 (qd, *J* = 7.2, 2.6 Hz, 2H), 3.69 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 152.7, 140.1, 137.2, 128.5, 128.1, 127.7, 115.7, 114.9, 73.5, 62.0, 60.8, 55.8, 14.2. IR (neat): 3384, 3280, 3064, 3034, 2989, 2945, 2907, 2833, 1707, 1513, 1454, 1409, 1342, 1297, 1215, 1096, 1029, 906, 864, 813, 753, 697 cm^{-1}. HRMS (ESI) m/z calculated for $C_{18}H_{22}NO_4$ ([M+H]$^+$) 316.1543, found 316.1544.

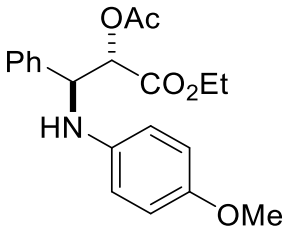
rac. ethyl (2*S*,3*S*)-2-((*tert*-butoxycarbonyl)oxy)-3-((4-methoxyphenyl)amino)-3-phenylpropanoate (121)



A 50 mL round bottom flask equipped with a magnetic stir bar was charged with ethyl 2-hydroxy-3-((4-methoxyphenyl)amino)-3-phenylpropanoate (**120**) (358 mg, 1.1 mmol, 1.0 equiv), triethylamine (189 µL, 138 mg, 1.4 mmol, 1.2 equiv), di-*tert*butyl dicarbonate (297 mg, 1.4 mmol, 1.2 equiv) and DMAP (3 mg, 23 µmol, 0.02 equiv) in CH_2Cl_2 (30 mL). and the solution was stirred for 72 h at room temperature. The solvent was evaporated under reduced pressure and the obtained residue was purified by silica gel column chromatography (hexanes / EtOAc, 9:1 to 3:1) to give 460 mg (1.1 mmol, 98%) of rac. ethyl (2*S*,3*S*)-2-((*tert*-butoxycarbonyl)oxy)-3-((4-methoxyphenyl)amino)-3-phenylpropanoate (**121**) as a brown solid. R_f (hexanes / EtOAc, 1:1) = 0.58, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.21 (m, 5H), 6.71

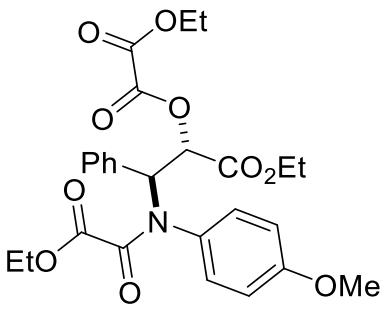
(d, *J* = 8.9 Hz, 2H), 6.56 (d, *J* = 9.0 Hz, 2H), 5.22 (d, *J* = 4.8 Hz, 1H), 4.86 (d, *J* = 4.8 Hz, 1H), 4.42 (bs, 1H), 4.09 (qd, *J* = 7.2, 5.4 Hz, 2H), 3.70 (s, 3H), 1.48 (s, 9H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 152.7, 140.2, 137.8, 128.6, 128.1, 127.7, 115.6, 114.8, 83.6, 77.0, 61.6, 59.5, 55.8, 27.8, 14.0. IR (neat): 3355, 2982, 2837, 1744, 1710, 1513, 1457, 1394, 1290, 1234, 1200, 1159, 1115, 1021, 872, 824, 798, 753, 701, 664 cm^{-1}. HRMS (ESI) m/z calculated for $C_{23}H_{30}NO_6$ ([M+H]$^+$) 416.2068, found 416.2069. mp: 86 °C.

rac. ethyl (2*S*,3*S*)-2-acetoxy-3-((4-methoxyphenyl)amino)-3-phenylpropanoate (122)



A 50 mL Schlenk flask equipped with a magnetic stir bar was charged while cooling at 0 °C with rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((4-methoxyphenyl)amino)-3-phenylpropanoate phenylpropanoate (**120**) (136 mg, 431 µmol, 1.0 equiv), acetyl chloride (31 µL, 34 mg, 431 µmol, 1.0 equiv) and triethylamine (60 µL, 44 mg, 431 µmol, 1.0 equiv) in dry CH_2Cl_2 (20 mL) and the solution was stirred for 4 h at 0 °C and then 44 h at room temperature. After evaporation of solvent under reduced pressure the obtained residue was purified by silica gel column chromatography (hexanes / EtOAc, 12:1 to 3:1) to give 51 mg (143 µmol, 33%) of rac. ethyl (2*S*,3*S*)-2-acetoxy-3-((4-methoxyphenyl)amino)-3-phenylpropanoate (**122**) as a yellow oil. R_f (hexanes / EtOAc, 3:1) = 0.39, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.22 (m, 5H), 6.77 – 6.67 (m, 2H), 6.62 – 6.51 (m, 2H), 5.32 (d, *J* = 5.0 Hz, 1H), 4.84 (d, *J* = 5.1 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.70 (s, 3H), 2.13 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 168.2, 152.8, 140.4, 138.0, 128.7, 128.2, 127.6, 115.5, 114.9, 75.0, 61.7, 59.6, 55.8, 20.8, 14.0. IR (neat): 3377, 2986, 2937, 2832, 1737, 1618, 1513, 1454, 1372, 1223, 1129, 1092, 1029, 939, 857, 820, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{20}H_{24}NO_5$ ([M+H]$^+$) 358.1649, found 358.1650.

rac. (2*S*,3*S*)-1-ethoxy-3-(2-ethoxy-*N*-(4-methoxyphenyl)-2-oxoacetamido)-1-oxo-3-phenylpropan-2-yl ethyl oxalate (123)

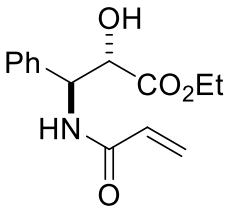


A 50 mL round bottom flask equipped with a magnetic stir bar was charged with rac. ethyl (2*S*,3*S*)-2-hydroxy-3-((4-methoxyphenyl) amino)-3-phenylpropanoate phenyl-propanoate (**120**) (315 mg, 1.0 mmol, 1.0 equiv), dry pyridine (194 µL, 190 mg, 2.4 mmol, 2.4 equiv) and dry CH_2Cl_2 (20 mL). The solution was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (**15**) (269 µL, 328 mg, 2.4 mmol, 2.4 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. CH_2Cl_2 (50 mL) was added and the reaction mixture was washed with water (3x 20 mL), dried over anhydrous $MgSO_4$ and the

solvent was evaporated under reduced pressure to yield 493 mg (956 µmol, 96%) of rac. (2*S*,3*S*)-1-ethoxy-3-(2-ethoxy-*N*-(4-methoxyphenyl)-2-oxoacetamido)-1-oxo-3-phenylpropan-2-yl ethyl oxalate (**123**) as a brownish oil. R_f (hexanes / EtOAc, 1:1) = 0.34, Staining: Ninhydrin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.10 (m, 6H), 7.09 – 6.41 (m, 3H), 6.26 (d, *J* = 7.9 Hz, 1H), 5.86 (d, *J* = 7.9 Hz, 1H), 4.30 – 4.14 (m, 4H), 3.93 (q, *J* = 7.1 Hz, 2H), 3.74 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 162.7, 162.1, 160.1, 156.5, 133.3, 132.4, 130.1, 129.0, 128.8, 128.5, 113.8, 73.2, 63.5, 62.8, 61.7, 59.2, 55.5, 14.0, 13.9, 13.8. IR (neat): 3064, 2986, 2941, 2844, 1760, 1744, 1670, 1607, 1510, 1457, 1405, 1372, 1301, 1252, 1178, 1018, 921, 842, 801, 734, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{26}H_{30}NO_{10}$ ($[M+H]^+$) 516.1864, found 516.1870.

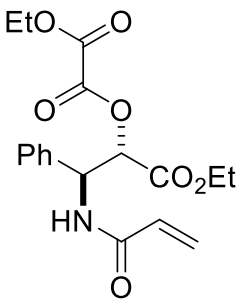
2.2.5. Preparation of Straing Materials for the Synthesis of Lactames

rac. Ethyl (2*S*,3*S*)-3-acrylamido-2-hydroxy-3-phenylpropanoate (126)



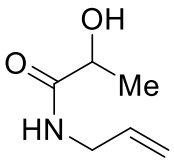
A 100 mL round bottom flask equipped with a magnetic stir bar and reflux condenser was charged with ethyl 3-amino-2-hydroxy-3-phenylpropanoate (**37a**) (244 mg, 1.2 mmol, 1.0 equiv), acryloyl chloride (100 µL, 111 mg, 1.2 mmol, 1.1 equiv) and CH_2Cl_2 (50 mL). The reaction mixture was stirred for 72 h at rt, after addition of water (100 mL) the mixture was extracted with CH_2Cl_2 (2x 100 mL). The combined organic layers were washed with water (3x 100 mL), dried over anhydrous Na_2SO_4, the solvent was evaporated in vacuo and the residue purified by silica gel column chromatography (hexanes / EtOAc, 2:1 to 1:1) to give 154 mg (585 µmol, 50%) of rac. ethyl (2*S*,3*S*)-3-acrylamido-2-hydroxy-3-phenylpropanoate (**126**) as a colorless oil. R_f (hexanes / EtOAc, 1:1) = 0.30, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.17 (m, 5H), 6.78 (d, *J* = 8.7 Hz, 1H), 6.31 (dd, *J* = 17.0, 1.7 Hz, 1H), 6.16 (dd, *J* = 16.9, 10.0 Hz, 1H), 5.65 (dd, *J* = 10.0, 1.7 Hz, 1H), 5.51 (dd, *J* = 8.8, 3.5 Hz, 1H), 4.59 (d, *J* = 3.5 Hz, 1H), 4.13 (qd, *J* = 7.1, 3.1 Hz, 2H), 3.16 (bs, 1H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 164.8, 136.5, 130.6, 128.6, 128.4, 127.8, 127.3, 72.9, 62.3, 55.2, 14.2. IR (neat): 3310, 3064, 3034, 2982, 1730, 1655, 1521, 1409, 1372, 1267, 1211, 1107, 1021, 984, 861, 805, 753, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{14}H_{18}NO_4$ ($[M+H]^+$) 264.1230, found 264.1232.

rac. (1*S*,2*S*)-1-acrylamido-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (127)



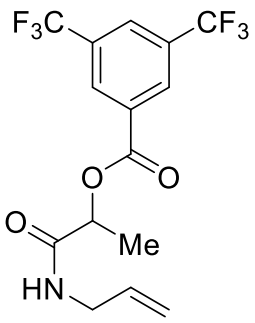
A 50 mL round bottom flask equipped with a magnetic stir bar was charged with rac. ethyl (2*S*,3*S*)-3-acrylamido-2-hydroxy-3-phenylpropanoate (**126**) (139 mg, 528 µmol, 1.0 equiv), dry pyridine (47 µL, 46 mg, 581 µmol, 1.1 equiv) and dry CH_2Cl_2 (10 mL). The solution was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (**15**) (64 µL, 79 mg, 581 µmol, 1.1 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. CH_2Cl_2 (50 mL) was added and the reaction mixture was washed with water (3x 20 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 183 mg (504 µmol, 95%) of rac. (1*S*,2*S*)-1-acrylamido-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (**127**) as a colorless oil. R_f (hexanes / EtOAc, 1:1) = 0.45, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 2H), 7.38 – 7.30 (m, 3H), 6.36 – 6.29 (m, 2H), 6.13 (dd, *J* = 17.0, 10.2 Hz, 1H), 5.75 (dd, *J* = 8.2, 4.5 Hz, 1H), 5.69 (dd, *J* = 10.2, 1.5 Hz, 1H), 5.60 (d, *J* = 4.4 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 4.07 (qd, *J* = 7.1, 1.7 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 164.8, 156.9, 156.7, 135.7, 130.2, 129.0, 128.9, 128.0, 128.0, 75.6, 63.7, 62.3, 53.5, 14.0, 14.0. IR (neat): 3370, 3280, 3034, 2986, 2941, 1744, 1659, 1629, 1525, 1405, 1372, 1308, 1178, 1088, 1018, 913, 857, 805, 753, 701, 667 cm^{-1}. HRMS (ESI) m/z calculated for $C_{18}H_{22}NO_7$ ($[M+H]^+$) 364.1391, found 364.1395.

N-allyl-2-hydroxypropanamide (130)



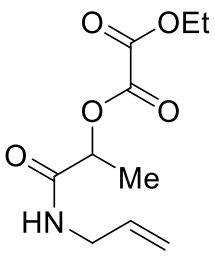
A 100 mL round bottom flask equipped with a magnetic stir bar and reflux condenser was charged with ethyl 2-hydroxypropanoate (**129**) (11.8 g, 100.0 mmol, 1.0 equiv) and allylamine (**40a**) (10.2 mL, 7.7 g, 135.2 mmol, 1.3 equiv) and the mixture was refluxed for 72 h. After evaporation of all volatile compounds under reduced pressure the obtained residue was destilled (134 °C, 3 mbar) to give 10.4 g (80.3 mmol, 80%) of *N*-allyl-2-hydroxypropanamide (**130**) as a yellow oil. R_f (hexanes / EtOAc, 1:1) = 0.14, Staining: $KMnO_4$, Ninhydrin (UV inactive). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.97 (s, 1H), 5.81 (ddt, *J* = 17.3, 10.4, 5.5 Hz, 1H), 5.26 – 5.04 (m, 2H), 4.20 (q, *J* = 6.8 Hz, 2H), 3.85 (ddt, *J* = 5.7, 3.3, 1.7 Hz, 2H), 1.40 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.1, 133.8, 116.5, 68.4, 41.5, 21.3.

1-(allylamino)-1-oxopropan-2-yl 3,5-bis(trifluoromethyl)benzoate (131)



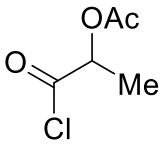
A 50 mL Schlenk flask equipped with a magnetic stir bar was charged with *N*-allyl-2-hydroxypropanamide (**130**) (129 mg, 1.0 mmol, 1.0 equiv) and dissolved in dry CH_2Cl_2 (20 mL). *N*,*N*-diisoproylethylamine (349 µL, 258 mg, 2.0 mmol, 2.0 equiv) was added followed by 3,5-bis(trifluoromethyl)benzoic anhydride (**46**) (598 mg, 1.2 mmol, 1.2 equiv). After stirring for 20 h at room temperature, CH_2Cl_2 (30 mL) was added and the organic layer was washed with Na_2CO_3 (aq. 10%, 20 mL) and water (20 mL). The organic phase was dried over Na_2SO_4 and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography (hexanes / EtOAc, 5:1 to 3:1) to give 357 mg (967 µmol, 97%) of 1-(allylamino)-1-oxopropan-2-yl 3,5-bis(trifluoromethyl)benzoate (**131**) as white solid. R_f (hexanes / EtOAc, 1:1) = 0.70, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 2H), 8.11 (s, 1H), 6.11 (bs, 1H), 5.84 (ddt, *J* = 17.2, 10.2, 5.6 Hz, 1H), 5.46 (q, *J* = 6.9 Hz, 1H), 5.27 – 5.12 (m, 2H), 3.94 (tt, *J* = 5.7, 1.6 Hz, 2H), 1.66 (d, *J* = 6.9 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -63.47 (s, 6F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 163.2, 133.6, 132.6 (q, *J* = 34.2 Hz), 131.7, 130.0 (d, *J* = 3.1 Hz), 127.3 – 126.9 (m), 122.9 (q, *J* = 273.1 Hz), 117.0, 72.4, 41.9, 17.9. IR (neat): 3291, 3097, 2993, 1733, 1662, 1566, 1454, 1387, 1282, 1245, 1174, 1129, 1044, 995, 917, 816, 772, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{15}H_{14}F_6NO_3$ ([M+H]$^+$) 370.0872, found 370.0870.

1-(allylamino)-1-oxopropan-2-yl ethyl oxalate (131´)



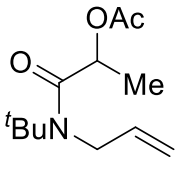
A 50 mL round bottom flask equipped with a magnetic stir bar was charged with *N*-allyl-2-hydroxypropanamide (**130**) (646 mg, 5.0 mmol, 1.0 equiv), dry pyridine (484 µL, 475 mg, 6.0 mmol, 1.2 equiv) and dry CH_2Cl_2 (30 mL). The solution was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (**15**) (671 µL, 819 mg, 6.0 mmol, 1.2 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. CH_2Cl_2 (50 mL) was added and the reaction mixture was washed with water (3x 20 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 1.1 g (5.0 mmol, 99%) of 1-(allylamino)-1-oxopropan-2-yl ethyl oxalate (**131´**) as a brownish oil. R_f (hexanes / EtOAc, 1:1) = 0.48, Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.40 (s, 1H), 5.83 (ddt, *J* = 17.2, 10.3, 5.6 Hz, 1H), 5.34 (q, *J* = 6.8 Hz, 1H), 5.25 – 5.12 (m, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 3.91 (tt, *J* = 5.7, 1.6 Hz, 2H), 1.58 (d, *J* = 6.9 Hz, 3H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 157.2, 156.2, 133.5, 116.9, 73.2, 63.8, 41.7, 17.9, 14.0. IR (neat): 3276, 3094, 2989, 2941, 1744, 1655, 1569, 1454, 1420, 1383, 1338, 1252, 1197, 1096, 1014, 924, 850, 768, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{10}H_{16}NO_5$ ([M+H]$^+$) 230.1023, found 230.1020.

1-chloro-1-oxopropan-2-yl acetate (135)



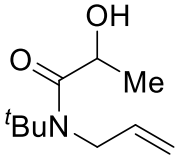
A 100 mL round bottom flask equipped with a magnetic stir bar was charged with 2-acetoxypropanoic acid (**134**) (5.3 g, 40.0 mmol, 1.0 equiv), sulfurous dichloride (3.5 mL, 5.7 g, 48.0 mmol, 1.2 equiv) and *N*,*N*-dimethylformamide (154 µL, 146 mg, 2.0 mmol, 0.05 equiv) in CH_2Cl_2 (50 mL) while cooling in an ice bath. The mixture was allowed to come to room temperature and stirred overnight. All volatiles were evaporated under reduced pressure and the product was destilled under reduced pressure to yield 4.1 g (27.4 mmol, 69%) of 1-chloro-1-oxopropan-2-yl acetate (**135**) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.20 (q, *J* = 7.1 Hz, 1H), 2.16 (s, 3H), 1.61 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 170.1, 75.1, 20.5, 16.4.

1-(allyl(*tert*-butyl)amino)-1-oxopropan-2-yl acetate (138)



A 50 mL round bottom flask equipped with a magnetic stir bar was charged with 1-chloro-1-oxopropan-2-yl acetate (**135**) (151 mg, 1.0 mmol, 1.0 equiv) and *N*-(*tert*-butyl)prop-2-en-1-amine (**137**) (113 mg, 1.0 mmol, 1.0 equiv) while cooling in an ice bath. The mixture was allowed to come to room temperature and stirred overnight. CH_2Cl_2 (100 mL) was added and the reaction mixture was washed with water (3x 50 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure and the residue was purified by column chromatography (hexanes/ EtOAc, 9:1 to 3:1) to yield 175 mg (770 µmol, 77%) of 1-(allyl(*tert*-butyl)amino)-1-oxopropan-2-yl acetate (**138**) as a colorless oil. R_f (hexanes / EtOAc, 4:1) = 0.30 Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 – 5.82 (m, 1H), 5.31 – 5.17 (m, 2H), 5.11 (qd, *J* = 6.6, 1.0 Hz, 1H), 4.20 – 4.07 (m, 1H), 3.95 – 3.84 (m, 1H), 2.07 (s, 3H), 1.43 – 1.32 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 170.9, 136.3, 116.5, 68.9, 58.0, 46.9, 28.5, 21.0, 17.8. IR (neat): 2982, 1737, 1659, 1454, 1409, 1364, 1297, 1241, 1197, 1133, 1085, 1036, 977, 947, 801, 738, 697 cm^{-1}. HRMS (ESI) m/z calculated for $C_{12}H_{22}NO_3$ ($[M+H]^+$) 228.1594, found 228.1595.

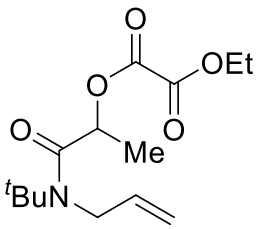
N-allyl-*N*-(*tert*-butyl)-2-hydroxypropanamide (139)



A 100 mL round bottom flask equipped with a magnetic stir bar was charged with 1-(allyl(*tert*-butyl)amino)-1-oxopropan-2-yl acetate (**138**) (2.5 g, 10.9 mmol, 1.0 equiv) and K_2CO_3 (6.0 g, 43.6 mmol, 4.0 equiv) in MeOH/H_2O (2:1, 50 mL) and the reaction mixture was stirred for 40 h. H_2O (120 mL) was added, the reaction mixture was extracted with EtOAc (3x 100 mL), dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure to give the crude product. After purification by column chromatography (hexanes / EtOAc, 4:1) 1.9 g (10.3 mmol, 94%) of *N*-allyl-*N*-(*tert*-butyl)-2-hydroxypropanamide (**139**) were obtained as a colorless oil.

R_f (hexanes / EtOAc, 4:1) = 0.33, Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (dddd, *J* = 17.2, 10.7, 5.0, 4.2 Hz, 1H), 5.23 – 5.13 (m, 2H), 4.25 (q, *J* = 6.4 Hz, 1H), 3.95 (ddt, *J* = 18.7, 5.1, 1.8 Hz, 1H), 3.82 (ddt, *J* = 18.7, 4.2, 2.1 Hz, 1H), 3.73 (bs, 1H), 1.41 (s, 9H), 1.25 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 135.6, 116.6, 65.5, 58.2, 46.3, 28.6, 22.1. IR (neat): 3422, 2974, 2930, 1778, 1741, 1640, 1454, 1364, 1260, 1200, 1118, 1077, 1029, 977, 921, 794, 746 cm^{-1}. HRMS (ESI) m/z calculated for $C_{10}H_{20}NO_2$ ($[M+H]^+$) 186.1489, found 186.1489.

1-(allyl(*tert*-butyl)amino)-1-oxopropan-2-yl ethyl oxalate (140)

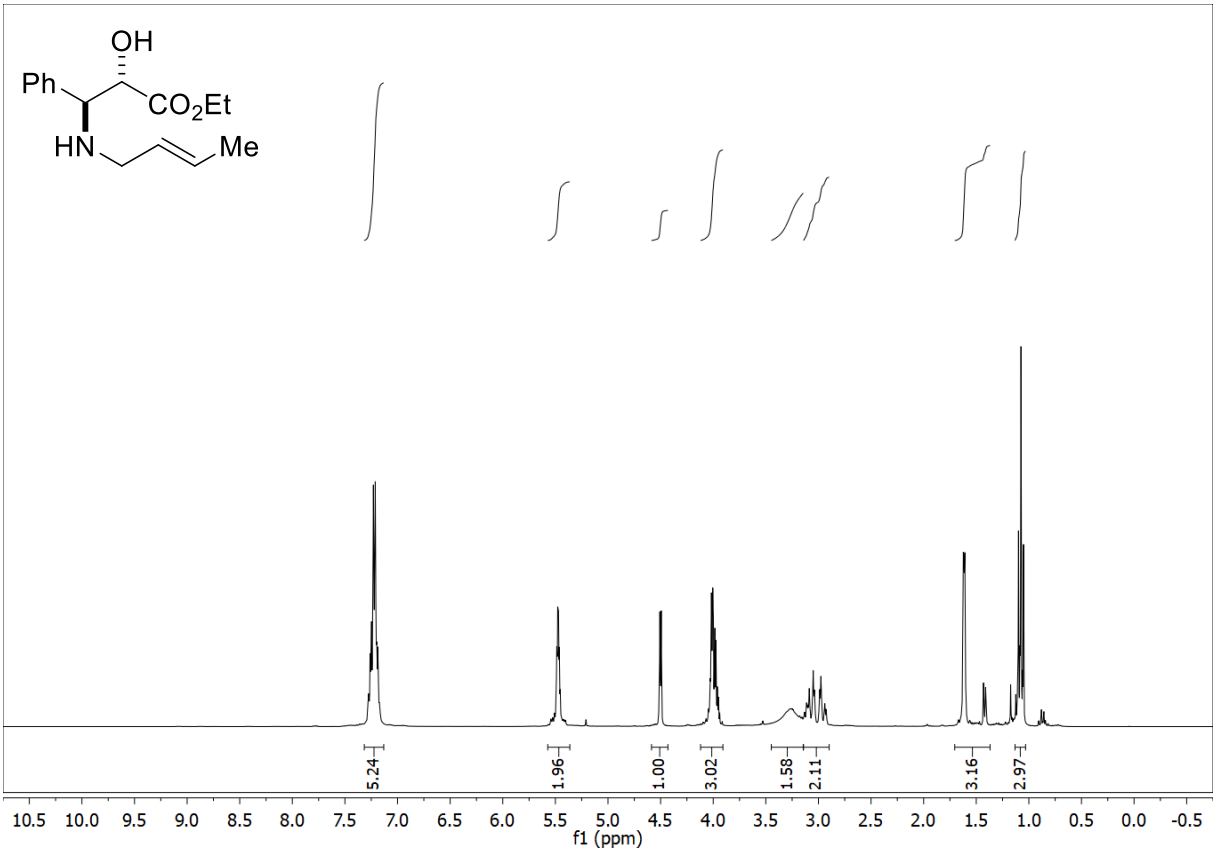


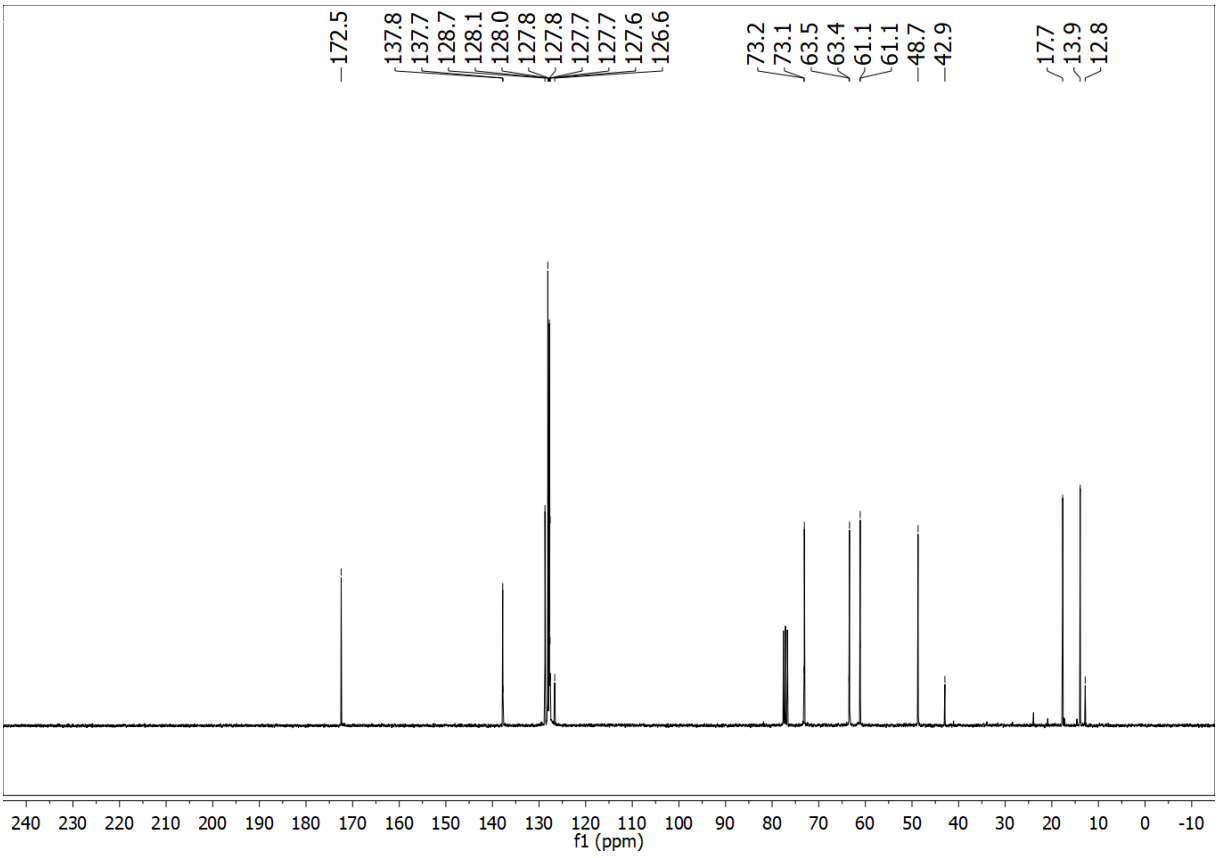
A 50 mL round bottom flask equipped with a magnetic stir bar was charged with *N*-allyl-*N*-(*tert*-butyl)-2-hydroxypropanamide (**139**) (185 mg, 1.0 mmol, 1.0 equiv), dry pyridine (121 µL, 119 mg, 1.5 mmol, 1.5 equiv) and dry CH_2Cl_2 (20 mL). The solution was cooled to 0 °C and ethyl 2-chloro-2-oxoacetate (**15**) (170 µL, 205 mg, 1.5 mmol, 1.5 equiv) was added over 1 h. Afterwards, the mixture was stirred in an ice bath for 4 h, allowed to come to room temperature and stirred overnight. CH_2Cl_2 (50 mL) was added and the reaction mixture was washed with water (3x 20 mL), dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 274 mg (960 µmol, 96%) of 1-(allyl(*tert*-butyl)amino)-1-oxopropan-2-yl ethyl oxalate (**140**) as a colorless oil. R_f (hexanes / EtOAc, 1:1) = 0.33, Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.91 (dddd, *J* = 17.3, 10.5, 5.4, 3.7 Hz, 1H), 5.36 – 5.14 (m, 3H), 4.33 (q, *J* = 7.2 Hz, 2H), 4.13 (ddt, *J* = 19.1, 5.4, 1.8 Hz, 1H), 3.89 (ddt, *J* = 19.1, 3.7, 2.2 Hz, 1H), 1.51 (d, *J* = 6.6 Hz, 3H), 1.41 (s, 9H), 1.35 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 157.5, 157.4, 135.7, 116.9, 71.5, 63.4, 58.3, 46.8, 28.4, 17.6, 14.0. IR (neat): 3083, 2982, 2941, 1741, 1662, 1450, 1409, 1361, 1327, 1256, 1182, 1118, 1081, 1014, 939, 909, 857, 801, 727, 690 cm^{-1}. LRMS (ESI) showed no product signal, but hydrolysis product: m/z calculated for $C_{10}H_{20}NO_2$ ($[M+H]^+$) 186.1489, found 186.1493 This result indicates the lability of the product towards methanol during the HPLC purification.

2.3. NMR Spectra

^{1}H NMR	first image
^{13}C NMR	second image
^{19}F NMR	third image

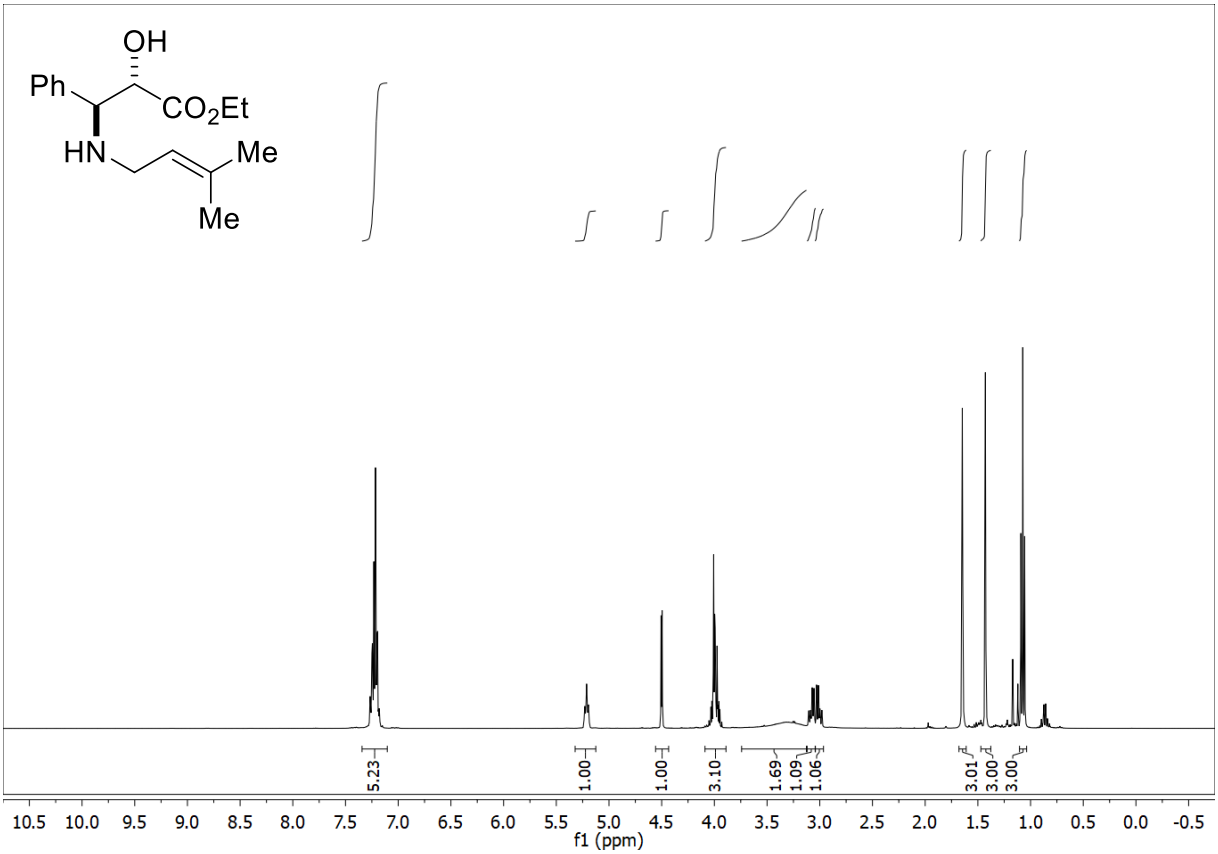
rac. Ethyl (2*S*,3*S*)-3-(((*E*)-but-2-en-1-yl)amino)-2-hydroxy-3-phenylpropanoate (39aa)

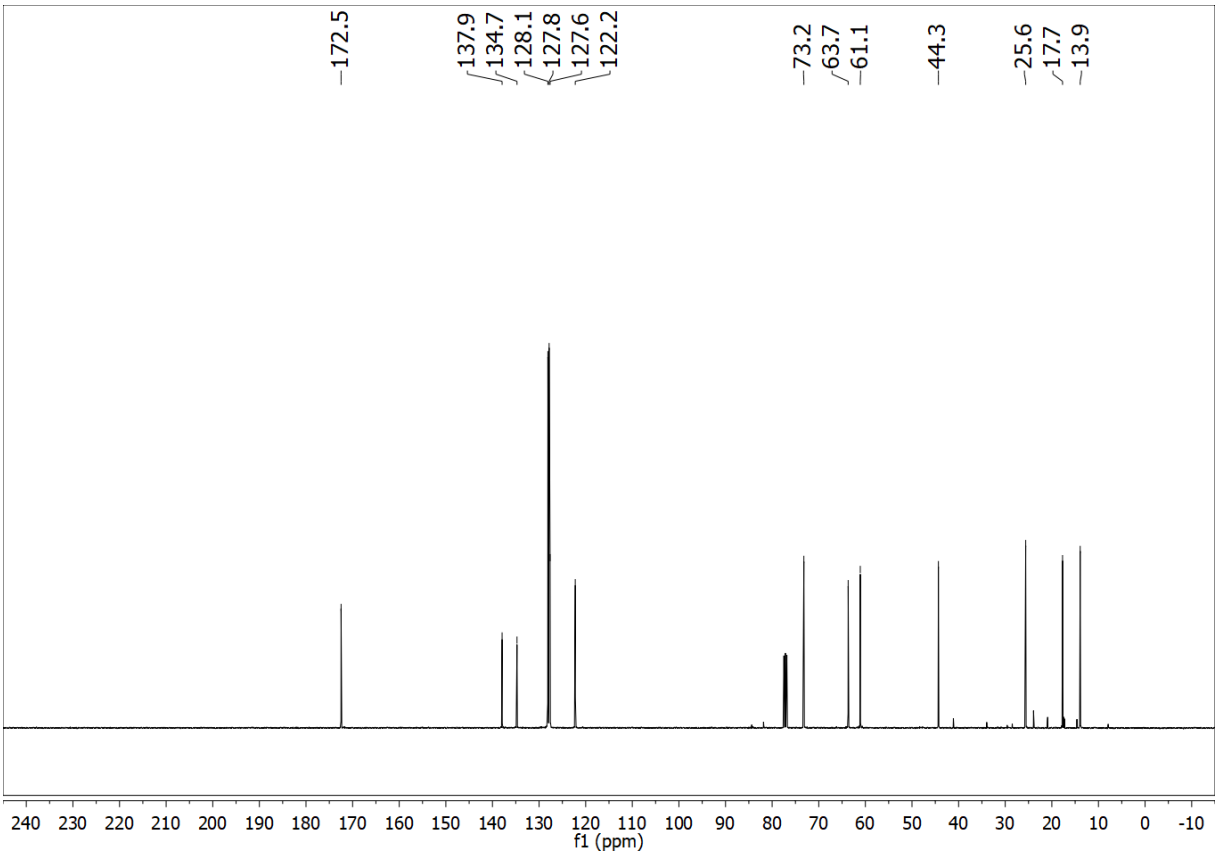




NMR-Solvent: $CDCl_3$

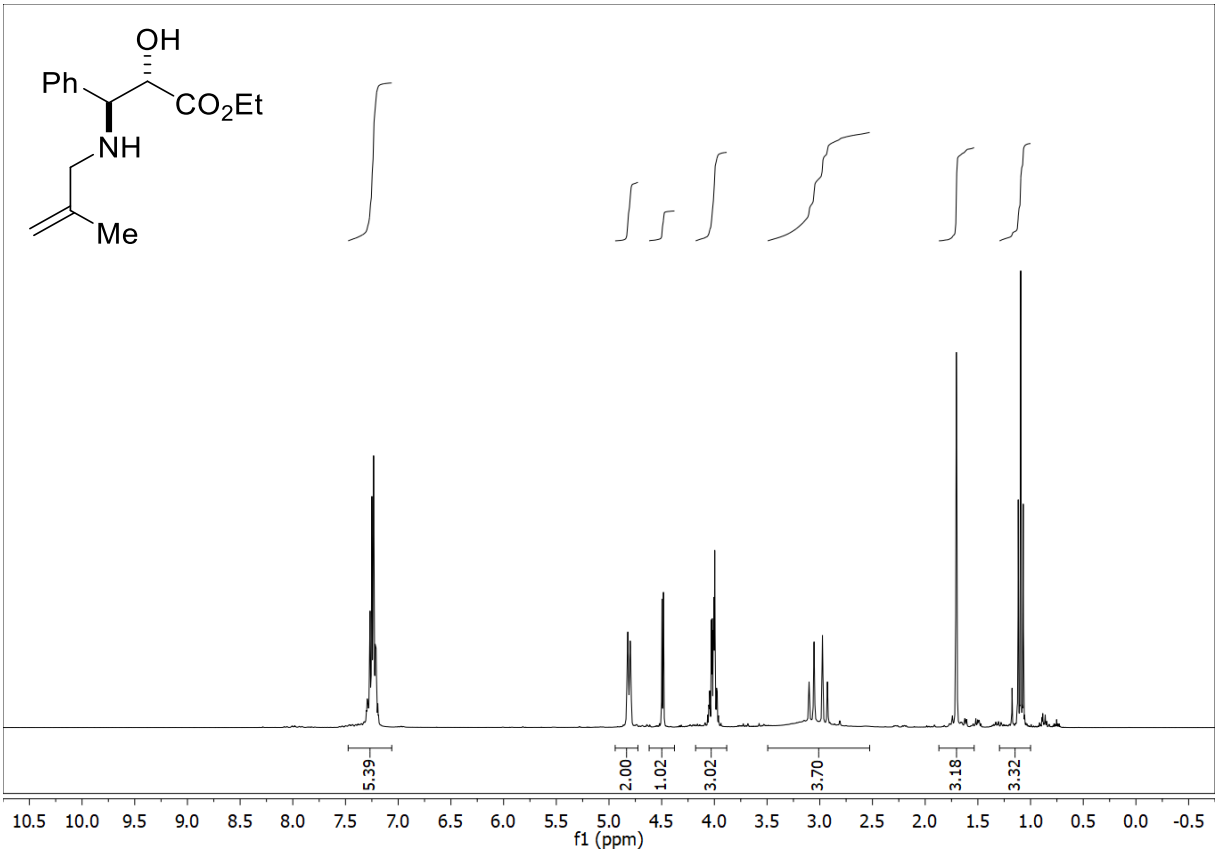
rac. Ethyl (2*S*,3*S*)-2-hydroxy-3-((3-methylbut-2-en-1-yl)amino)-3-phenylpropanoate (39ab)

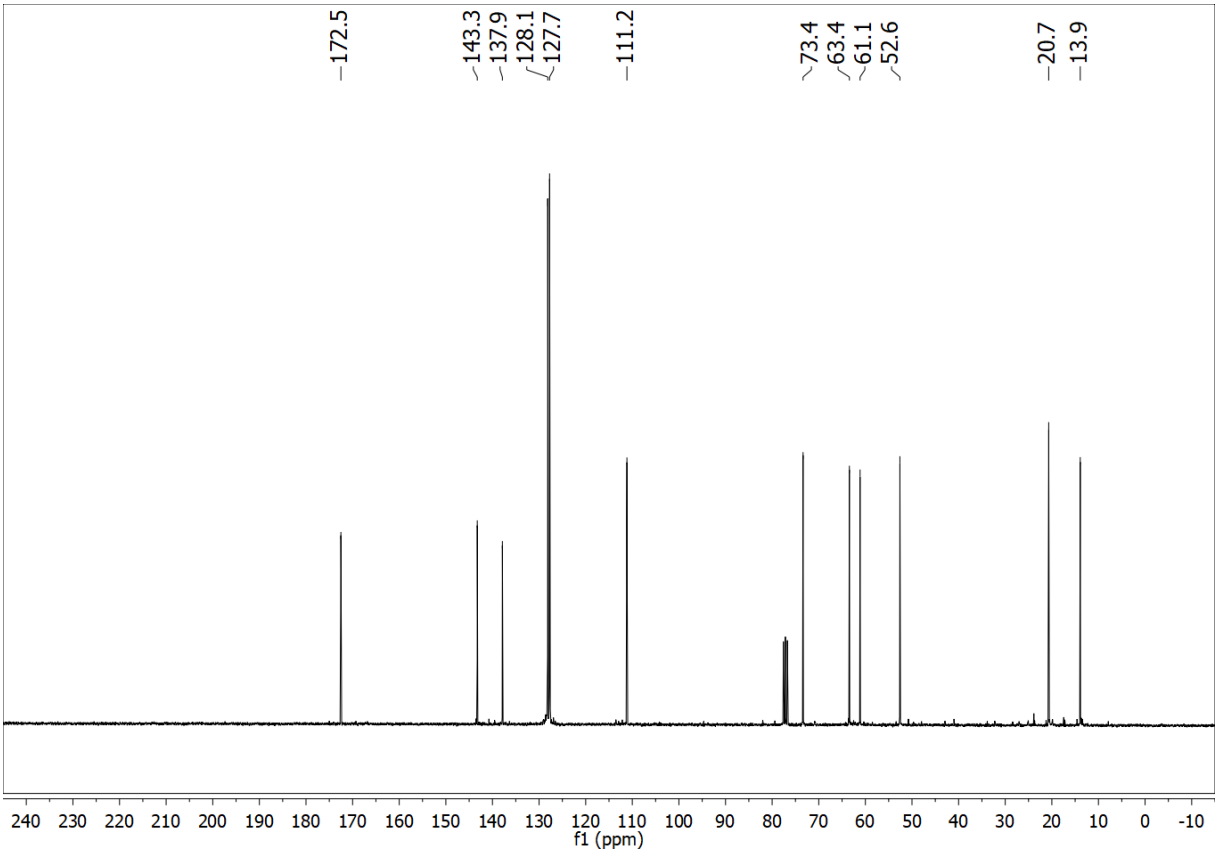




NMR-Solvent: $CDCl_3$

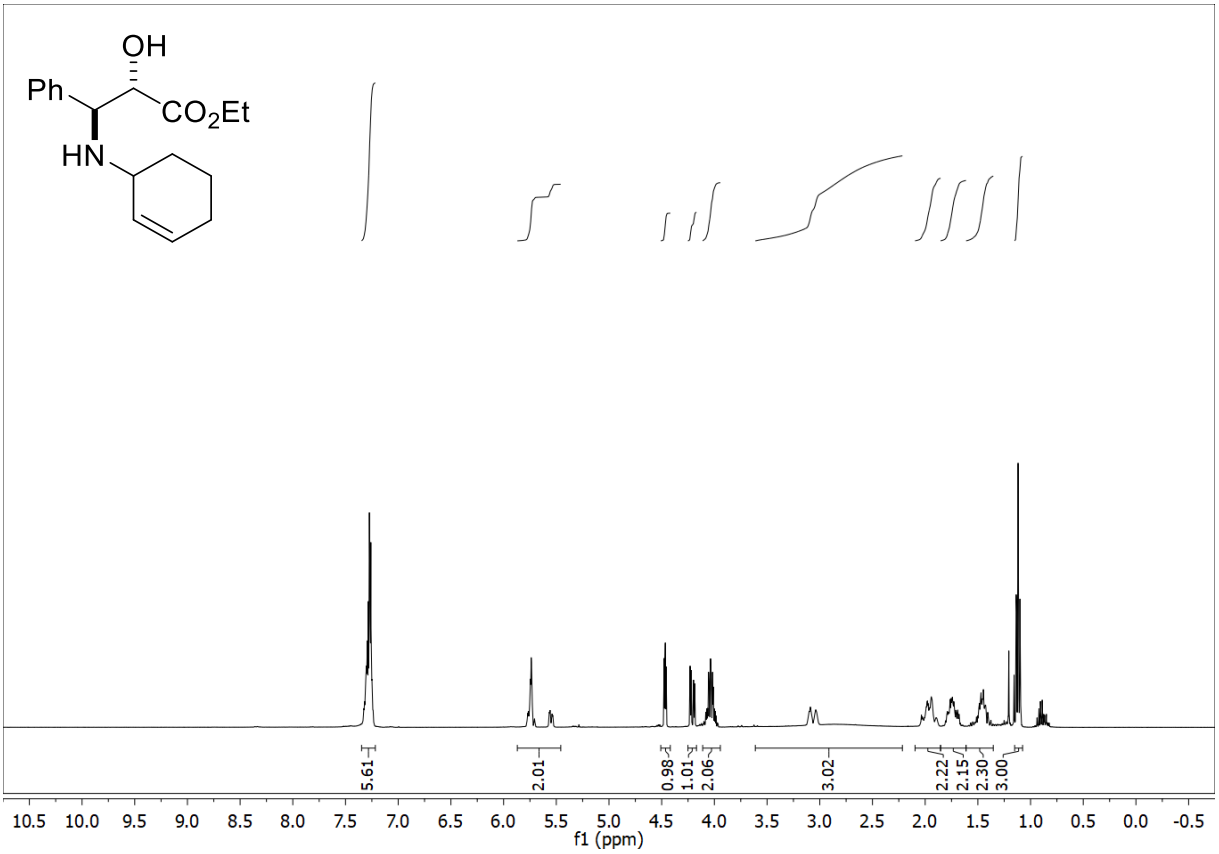
rac. Ethyl (2*S*,3*S*)-2-hydroxy-3-((2-methylallyl)amino)-3-phenylpropanoate (39ac)

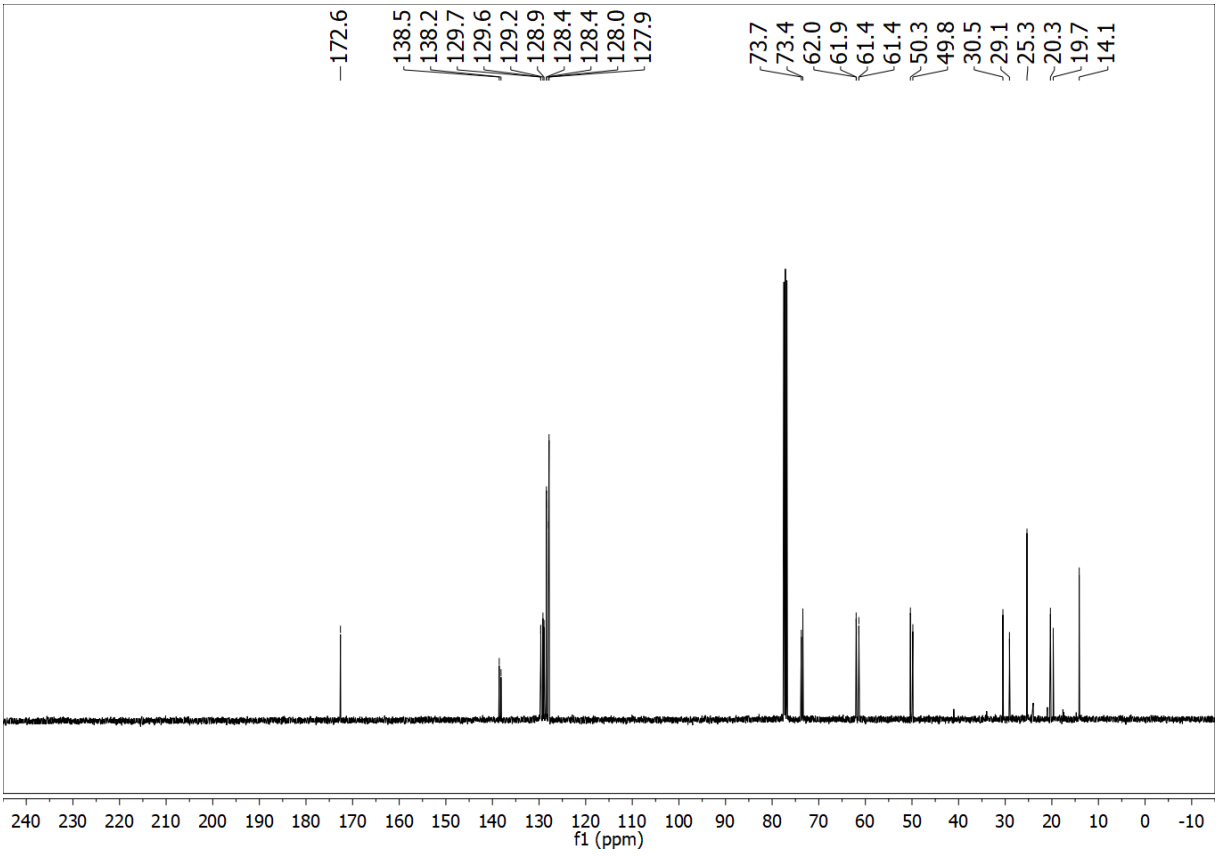




NMR-Solvent: $CDCl_3$

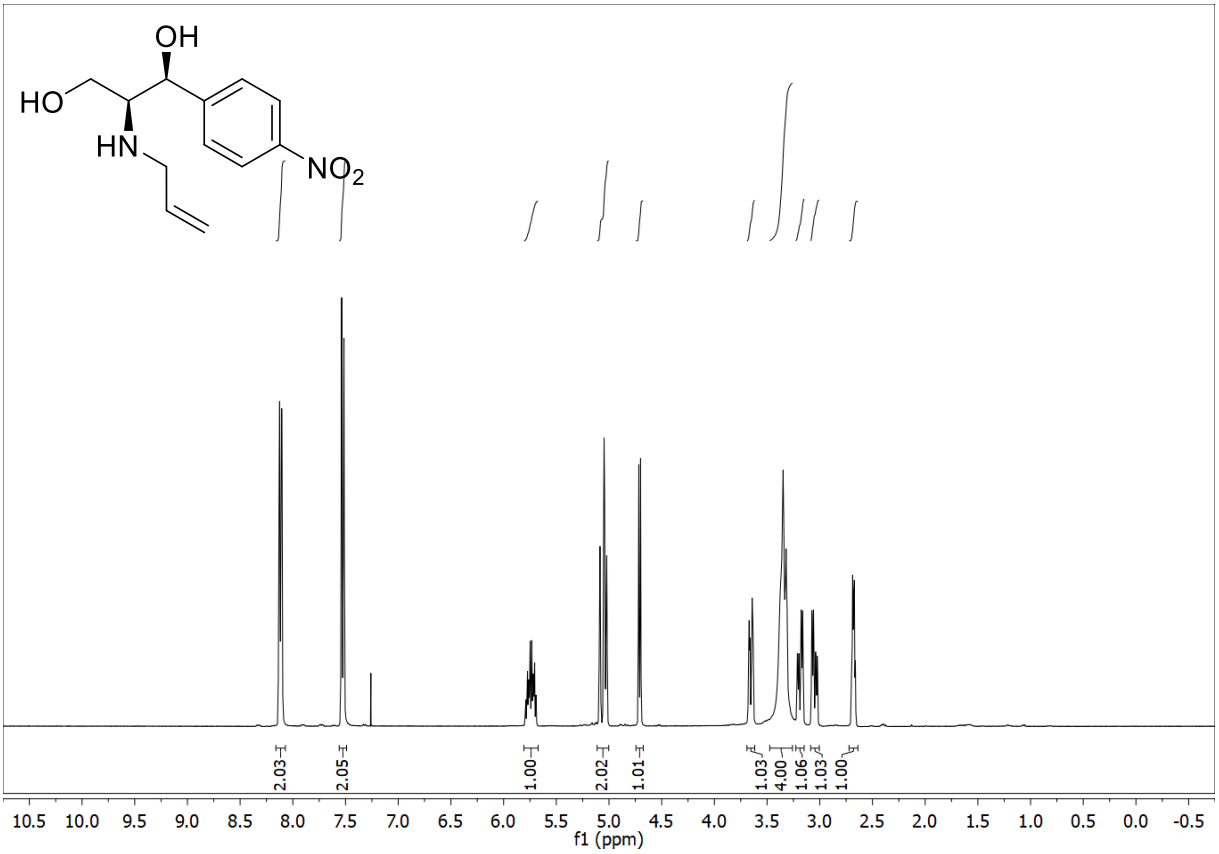
rac. Ethyl (2*S*,3*S*)-3-(cyclohex-2-en-1-ylamino)-2-hydroxy-3-phenylpropanoate (39ad)

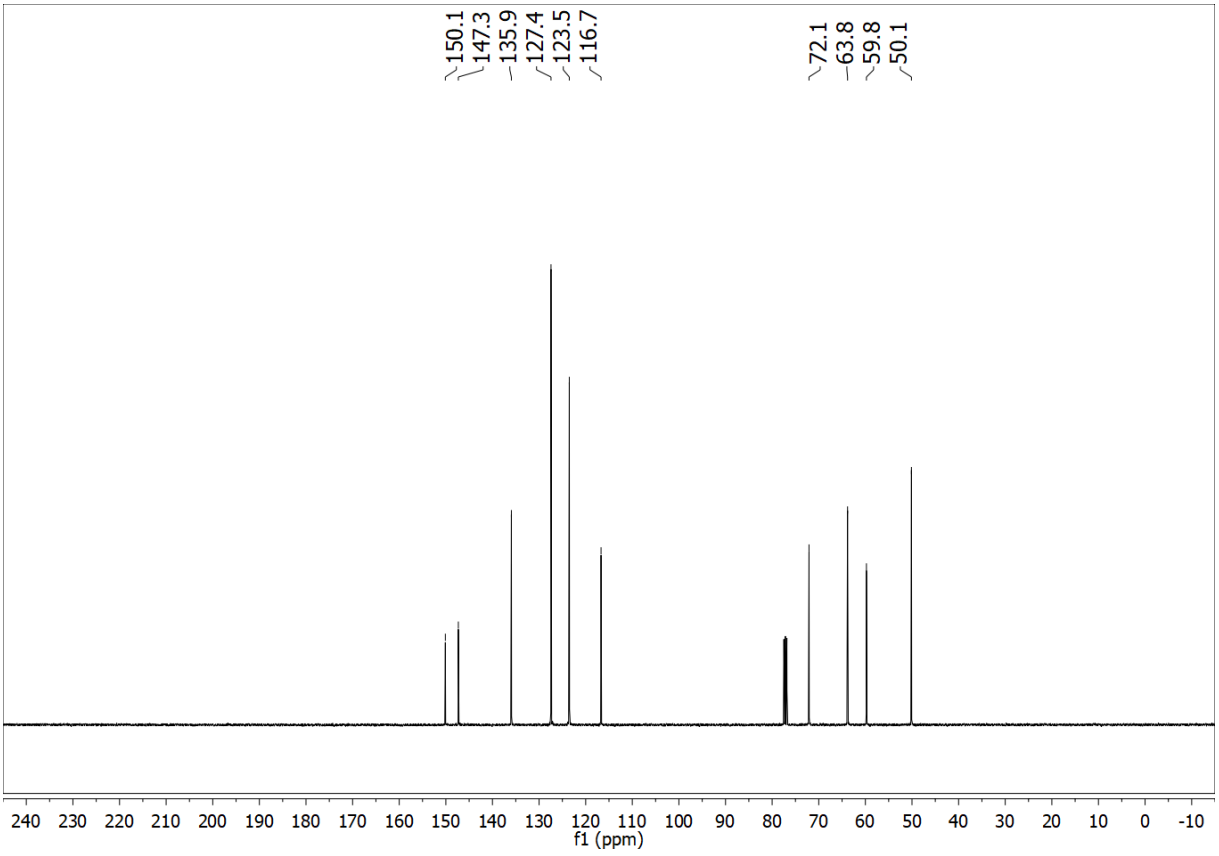




NMR-Solvent: $CDCl_3$

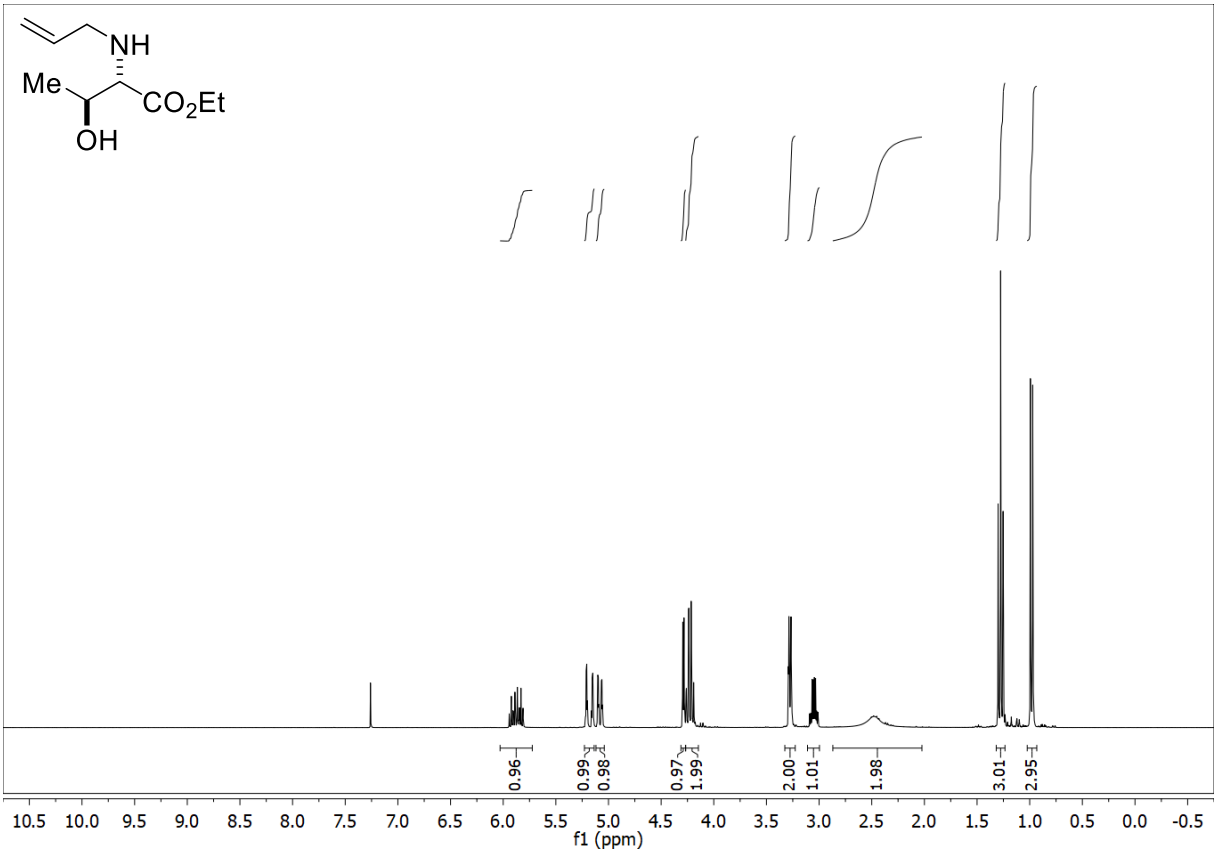
(1*S*,2*S*)-2-(allylamino)-1-(4-nitrophenyl)propane-1,3-diol (43)

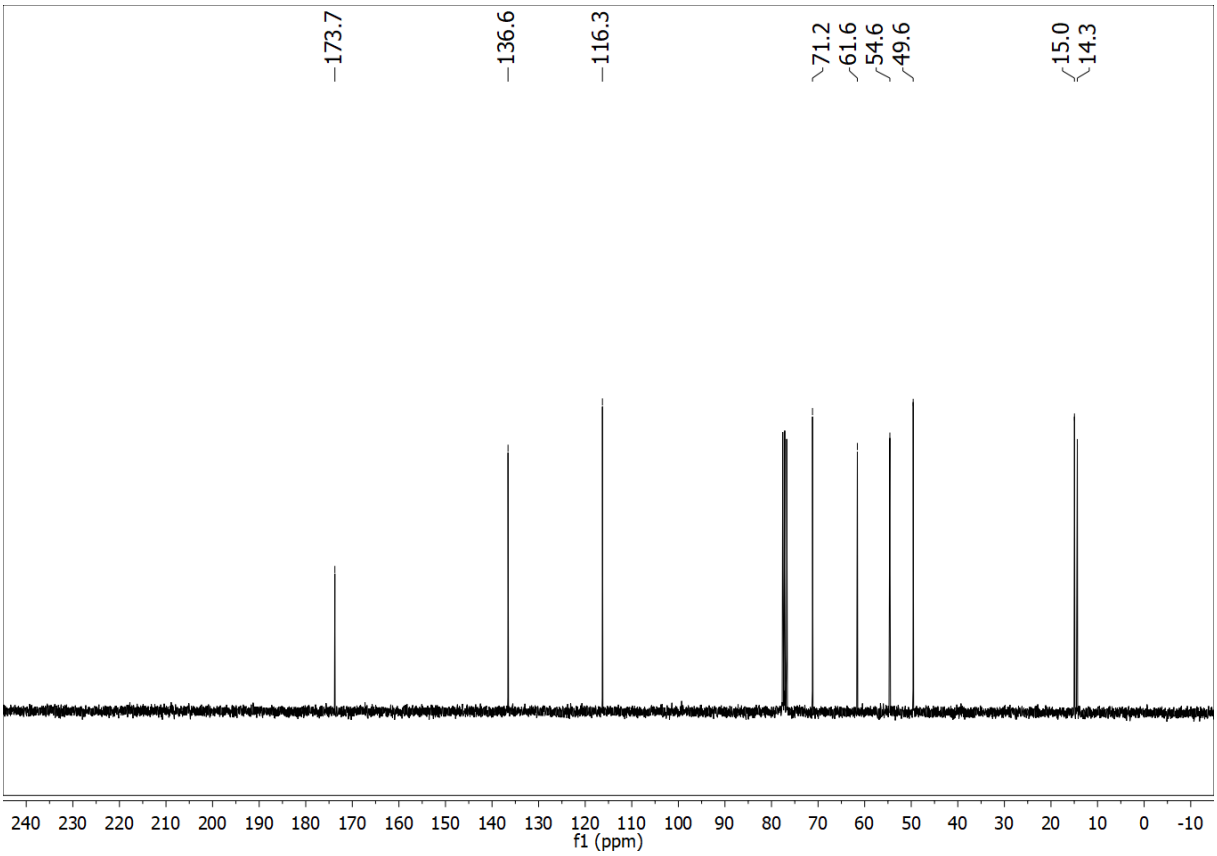




NMR-Solvent: $CDCl_3$

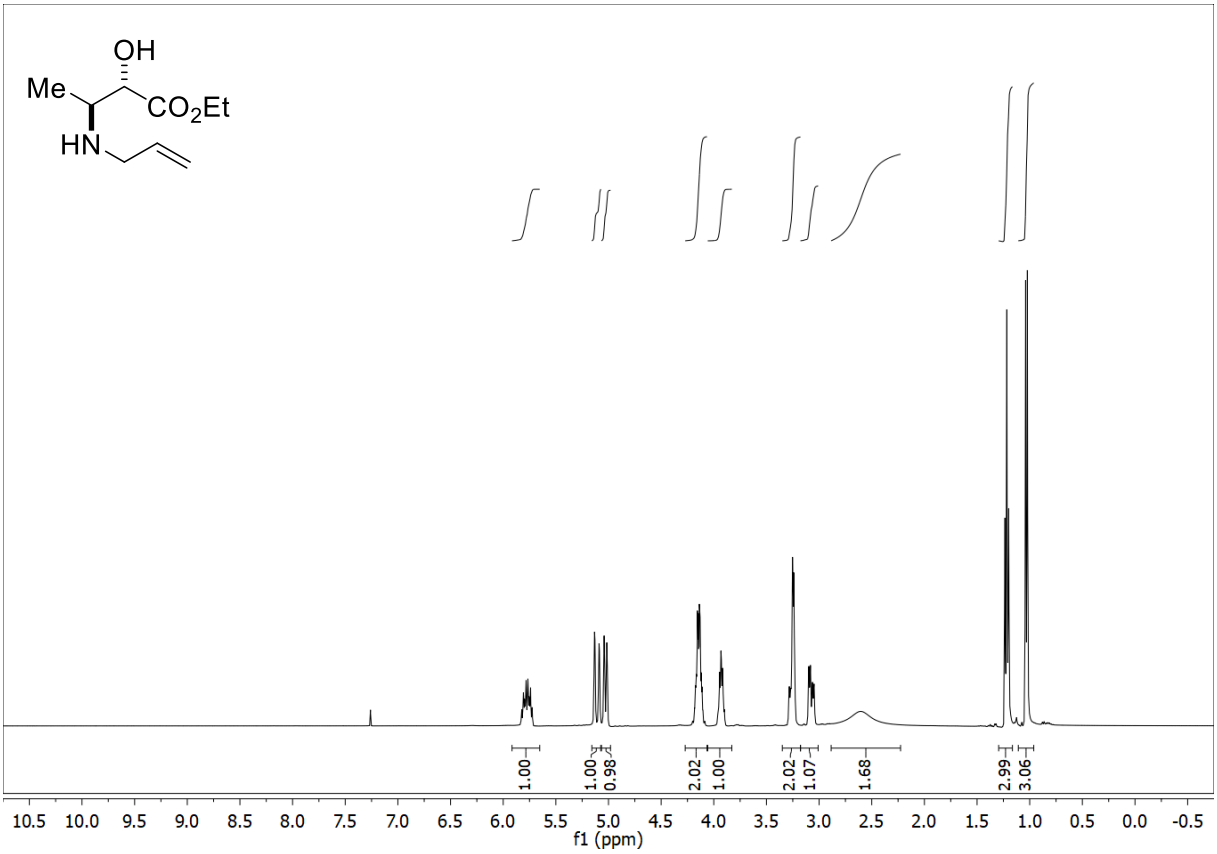
rac. Ethyl allyl-D-allothreoninate (39ba´)

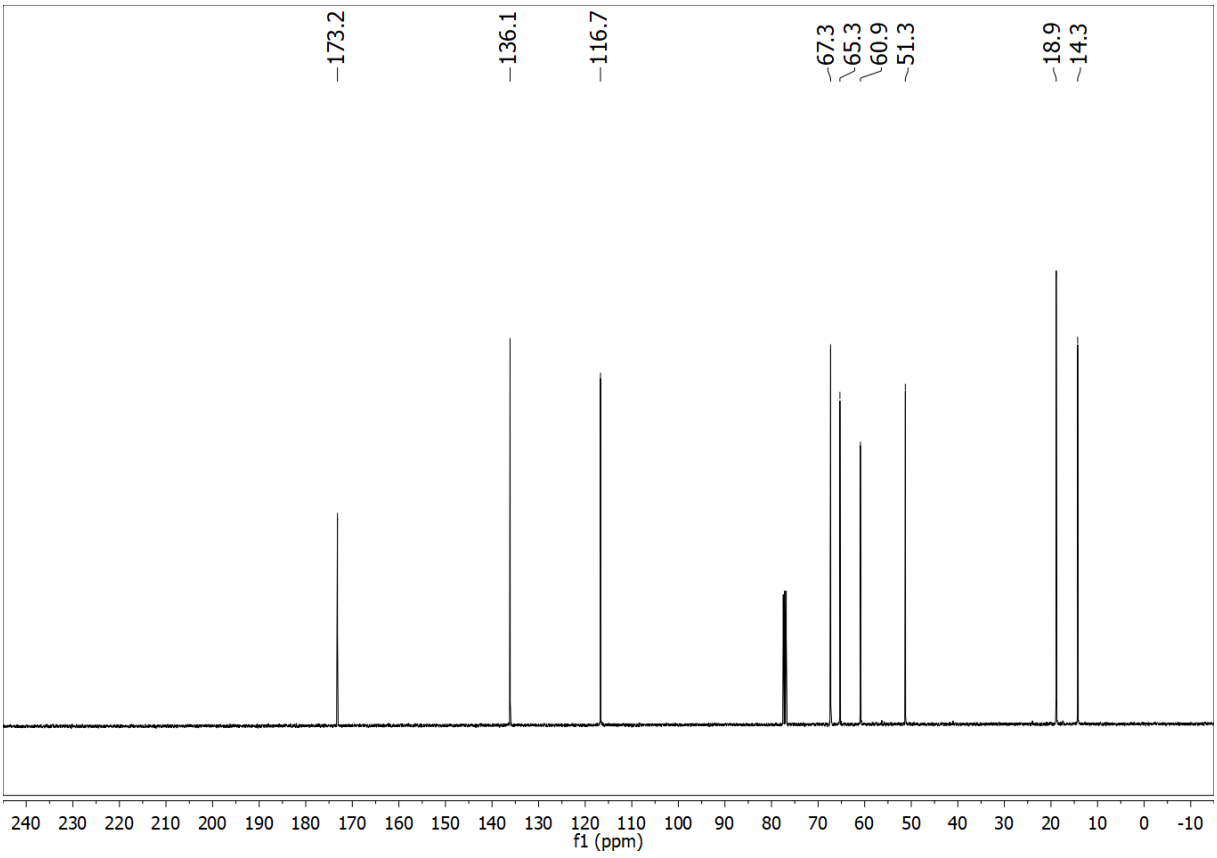




NMR-Solvent: $CDCl_3$

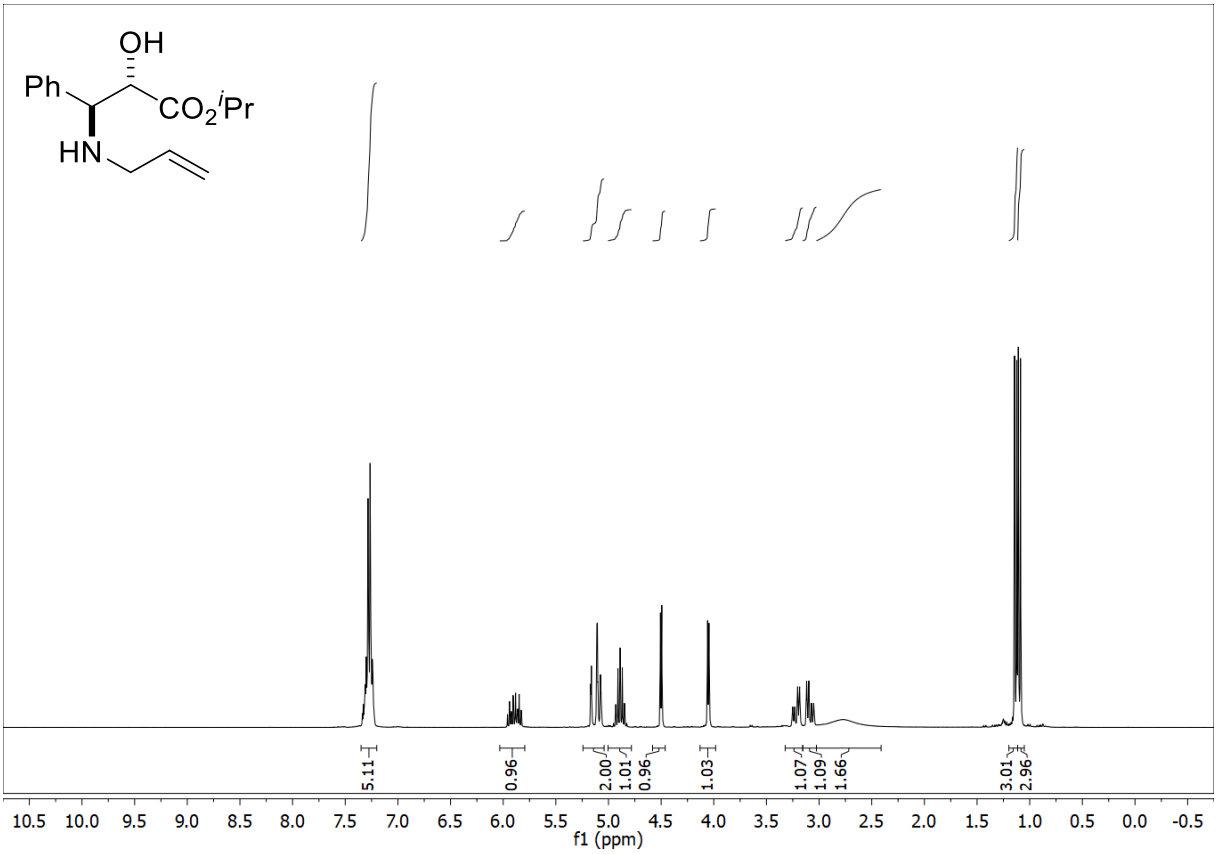
rac. Ethyl (2*S*,3*S*)-3-(allylamino)-2-hydroxybutanoate (39ba)

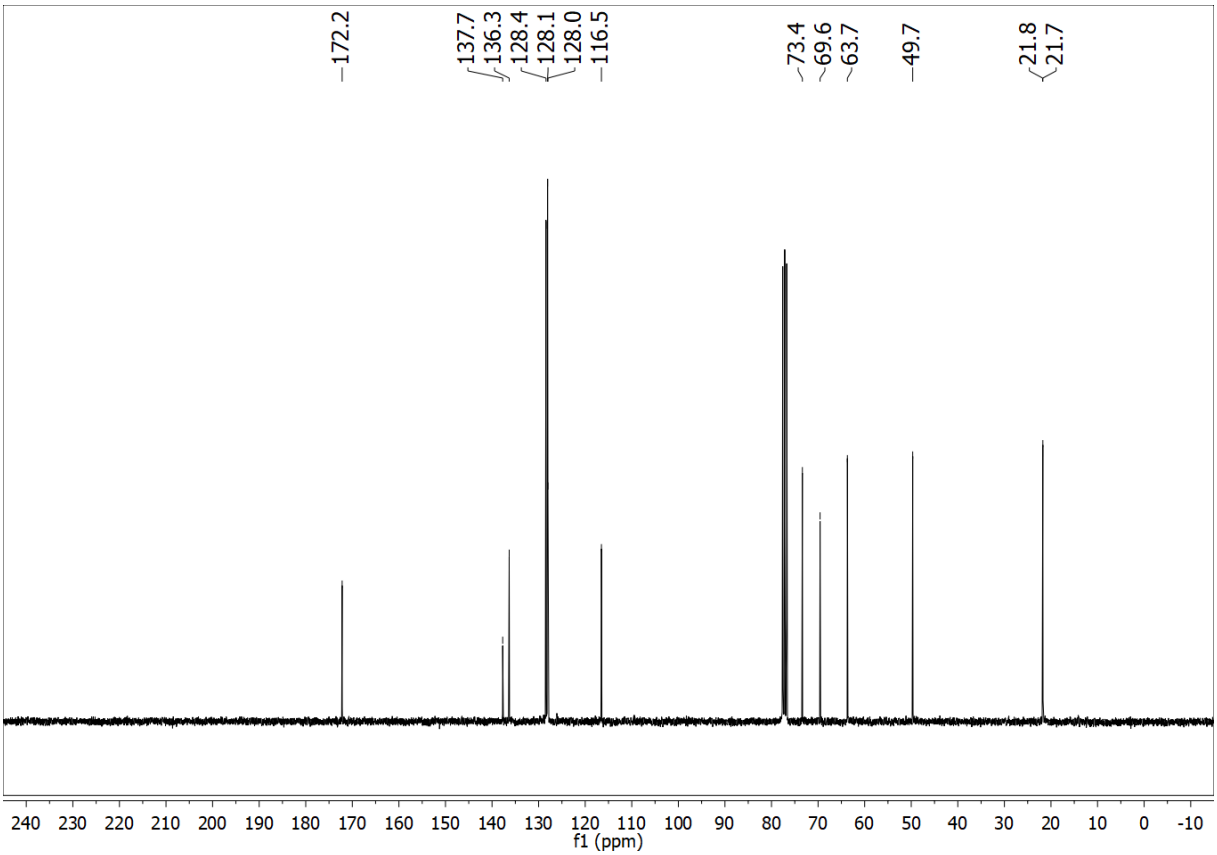




NMR-Solvent: $CDCl_3$

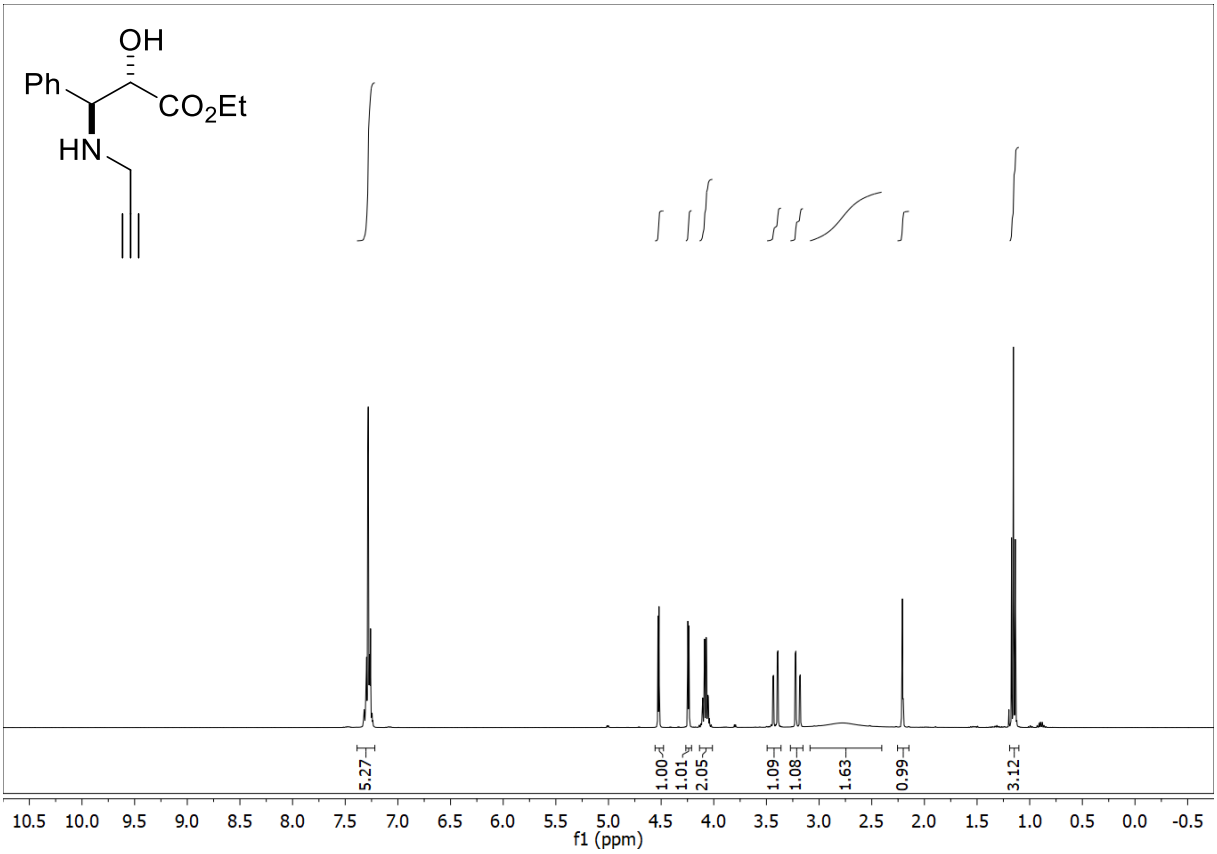
rac. Isopropyl (2*S*,3*S*)-3-(allylamino)-2-hydroxy-3-phenylpropanoate (39bc)

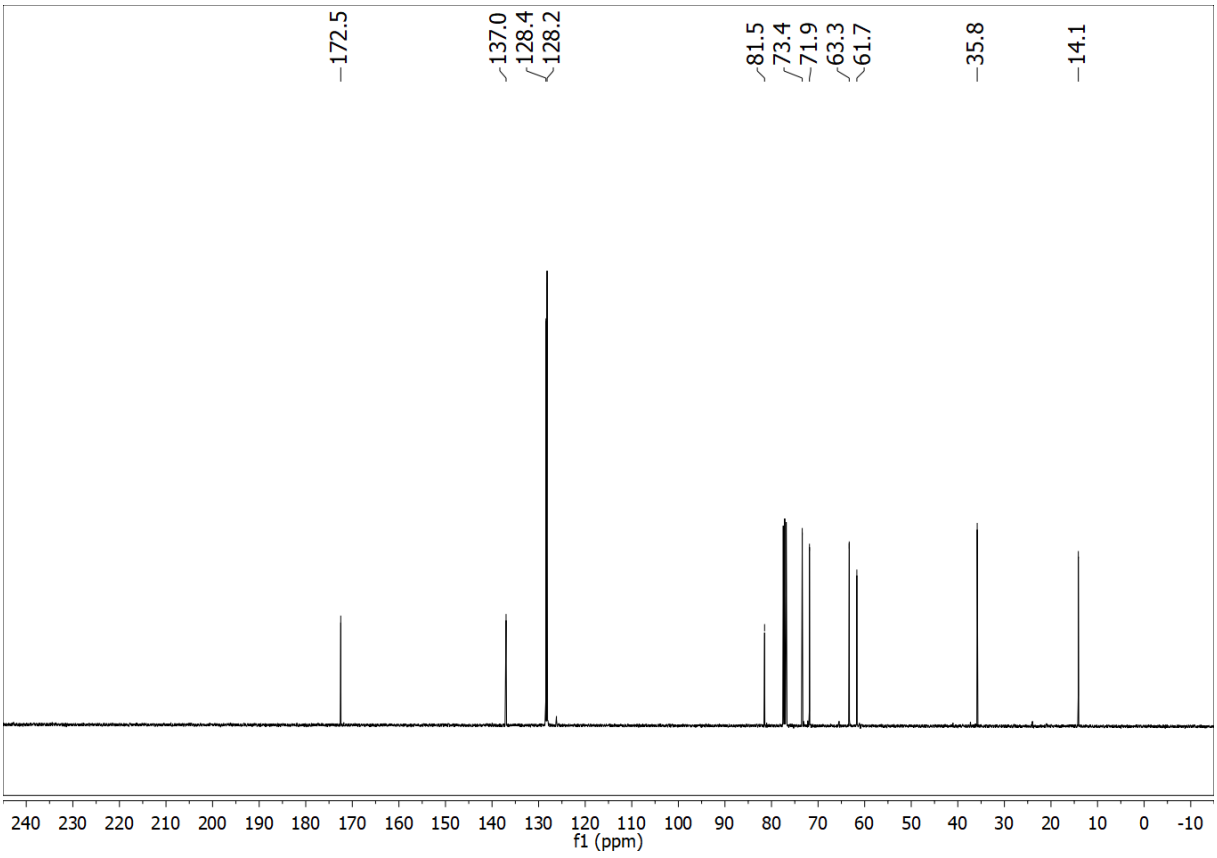




NMR-Solvent: $CDCl_3$

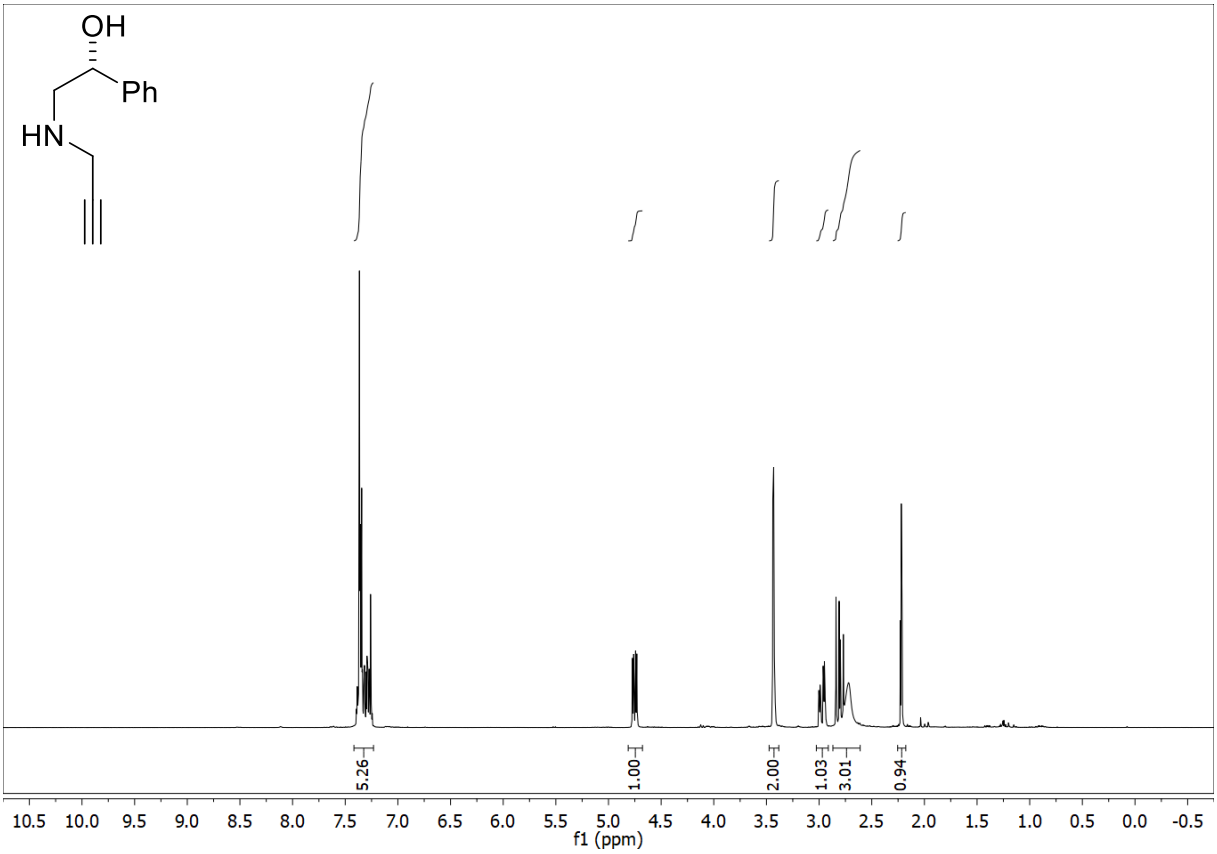
rac. Ethyl (2*S*,3*S*)-2-hydroxy-3-phenyl-3-(prop-2-yn-1-ylamino)propanoate (39bd)

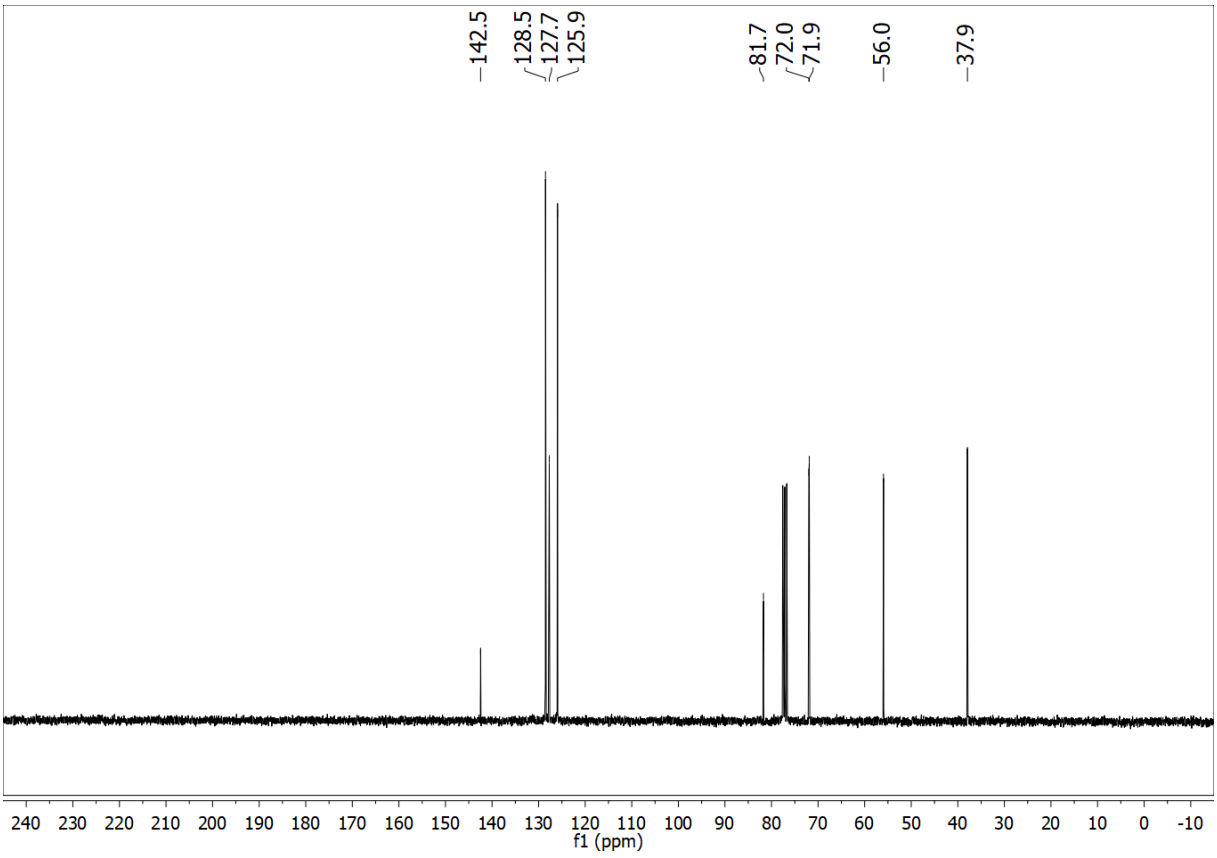




NMR-Solvent: $CDCl_3$

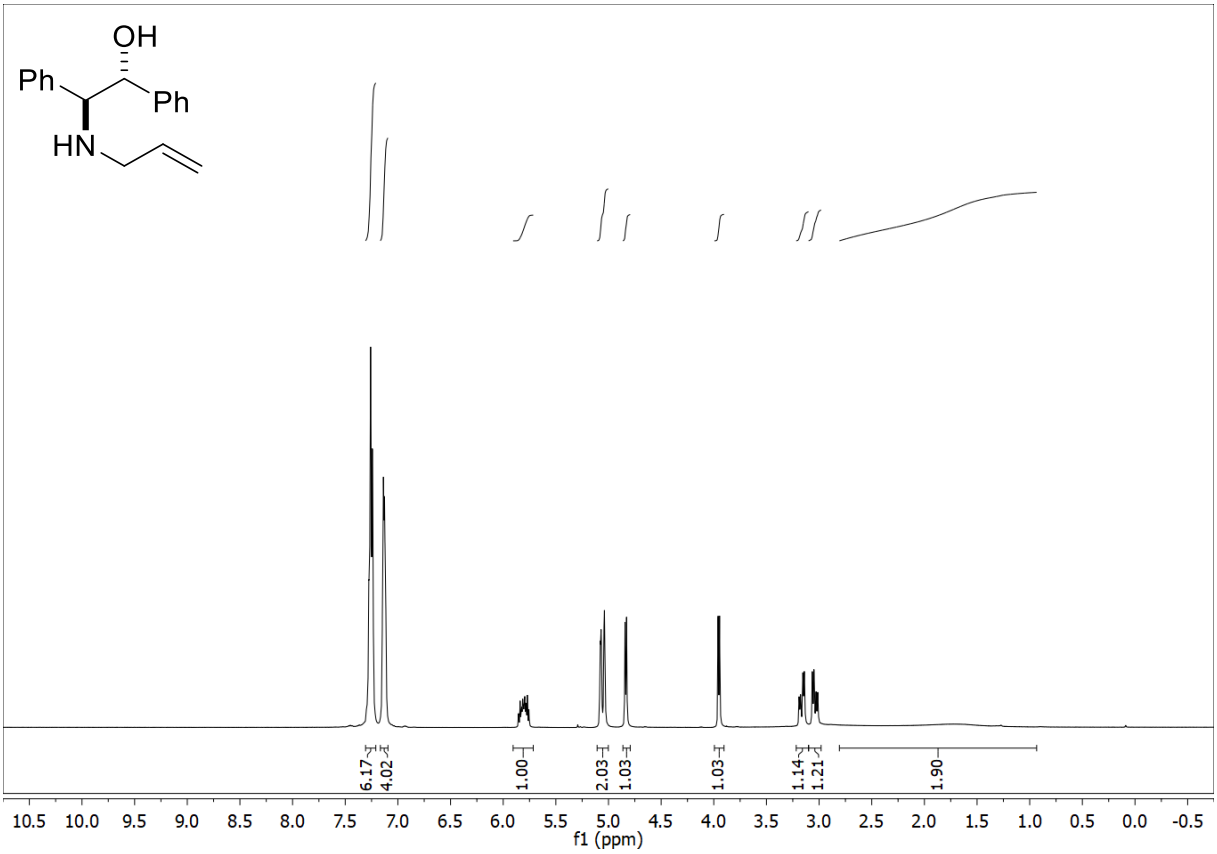
1-Phenyl-2-(prop-2-yn-1-ylamino)ethan-1-ol (39bf)

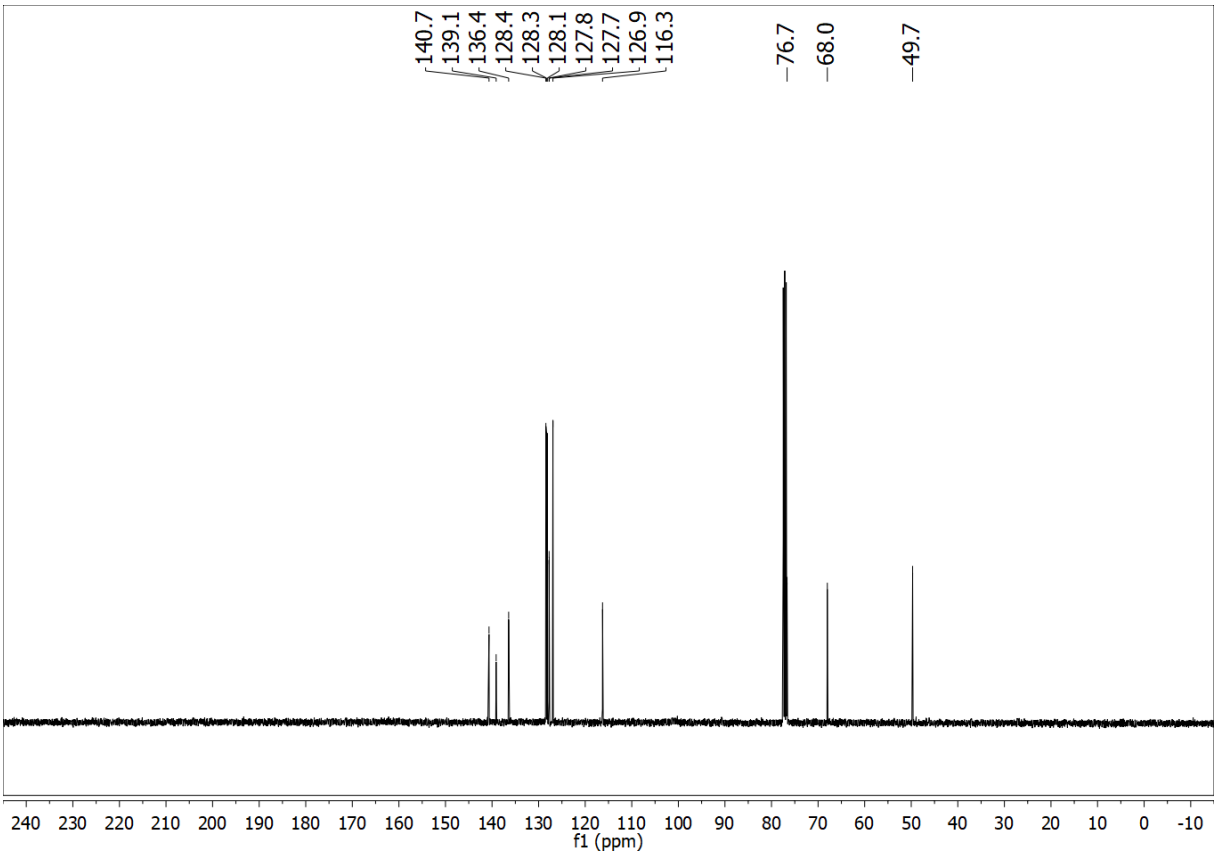




NMR-Solvent: $CDCl_3$

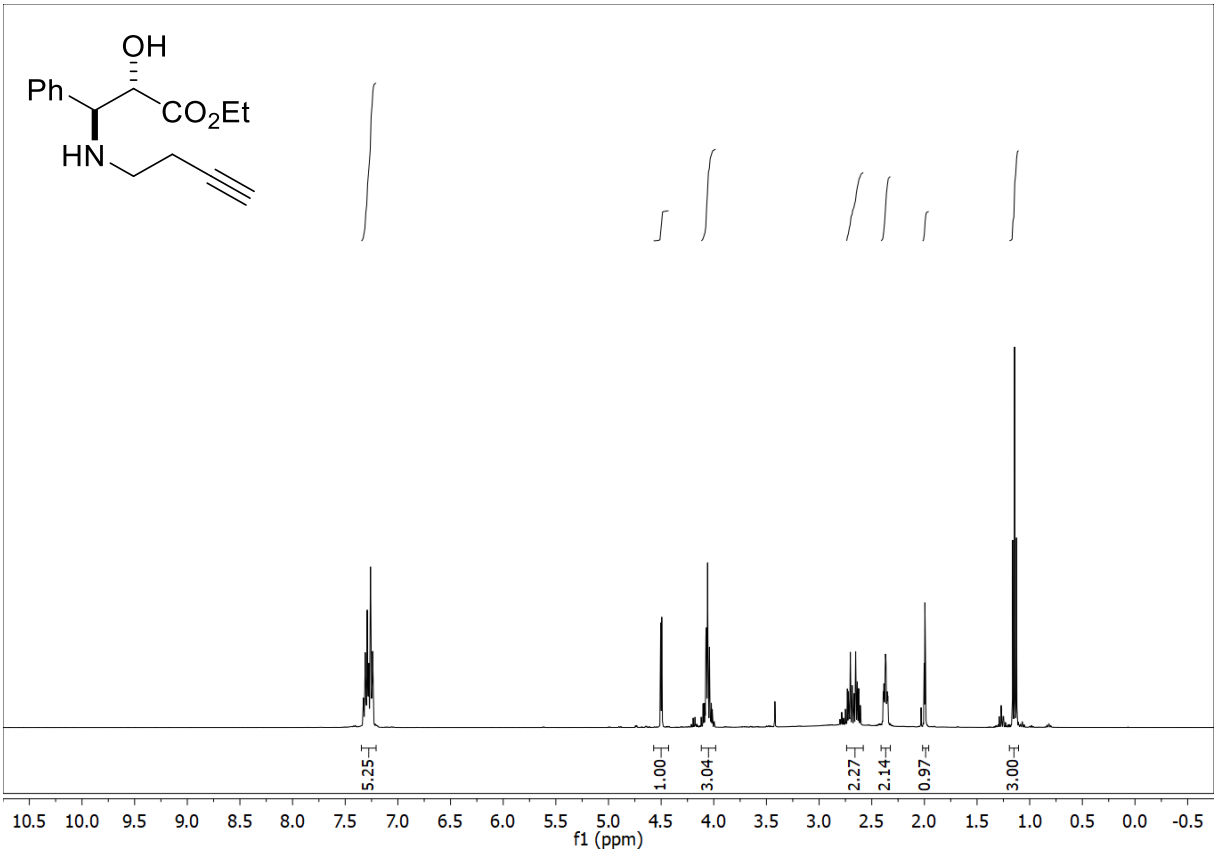
rac. (1*R*,2*S*)-2-(allylamino)-1,2-diphenylethan-1-ol (39bg)

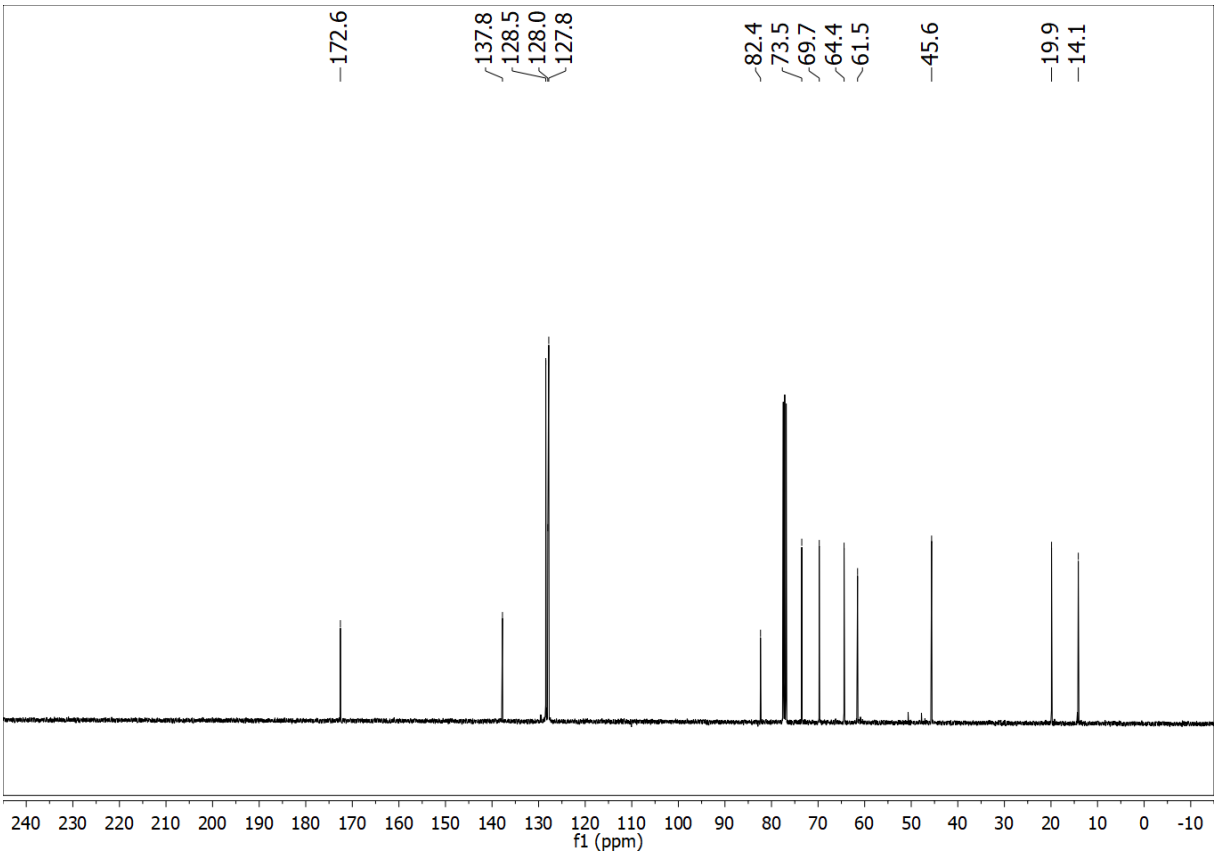




NMR-Solvent: $CDCl_3$

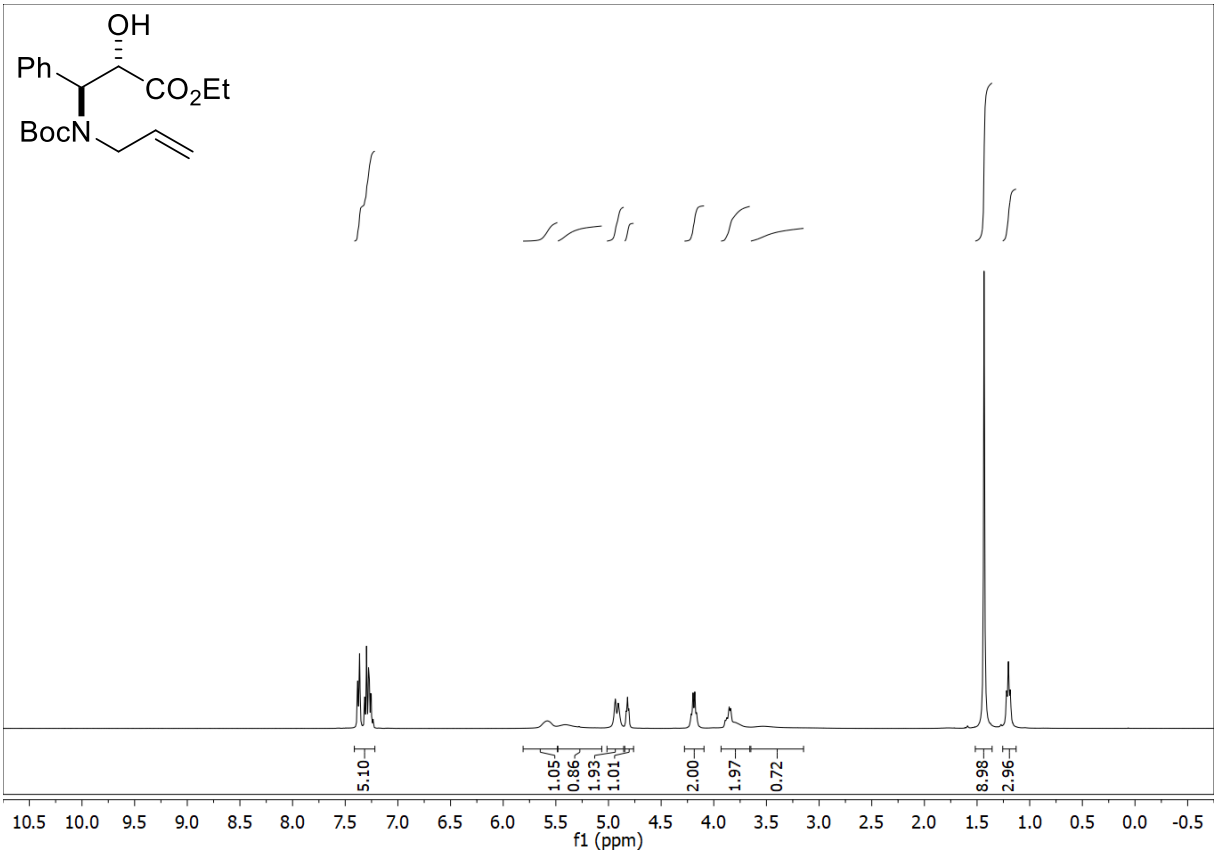
rac. Ethyl (2*S*,3*S*)-3-(but-3-yn-1-ylamino)-2-hydroxy-3-phenylpropanoate (39bh)

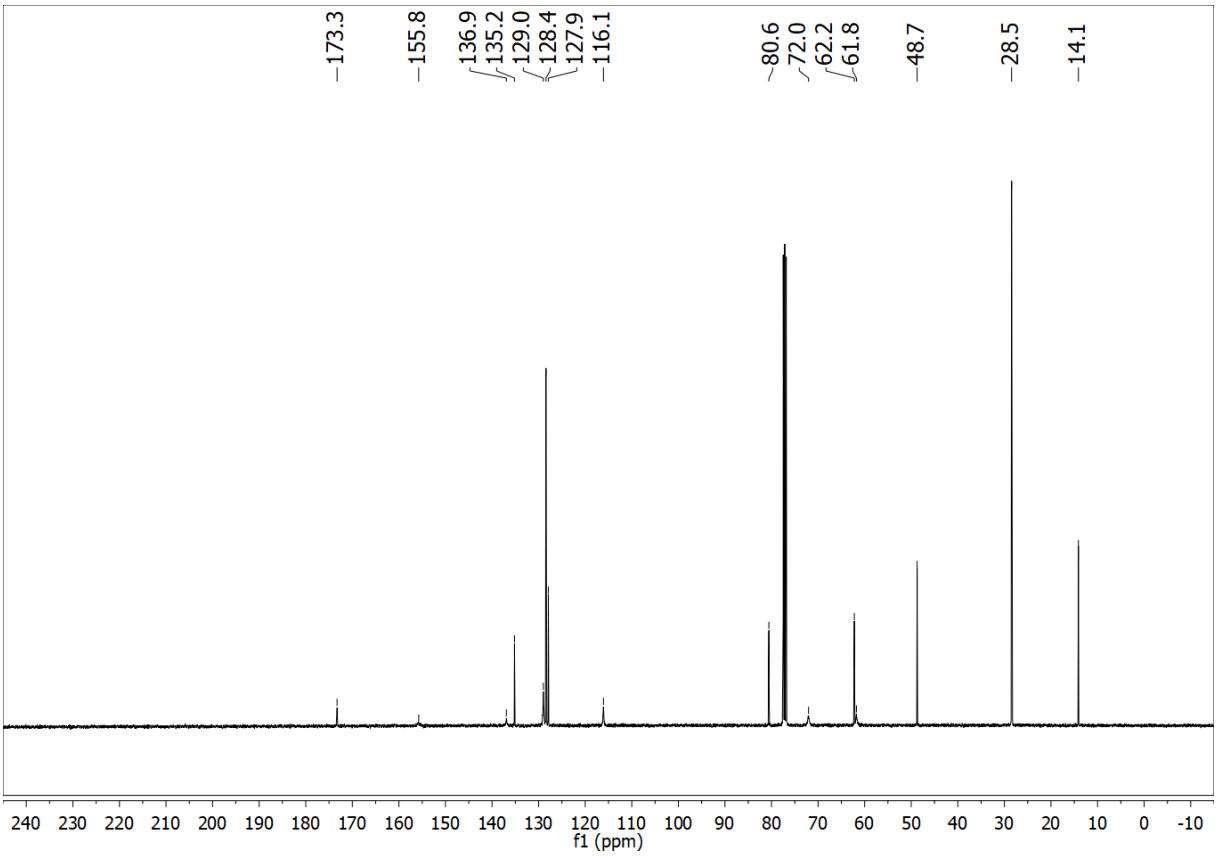




NMR-Solvent: $CDCl_3$

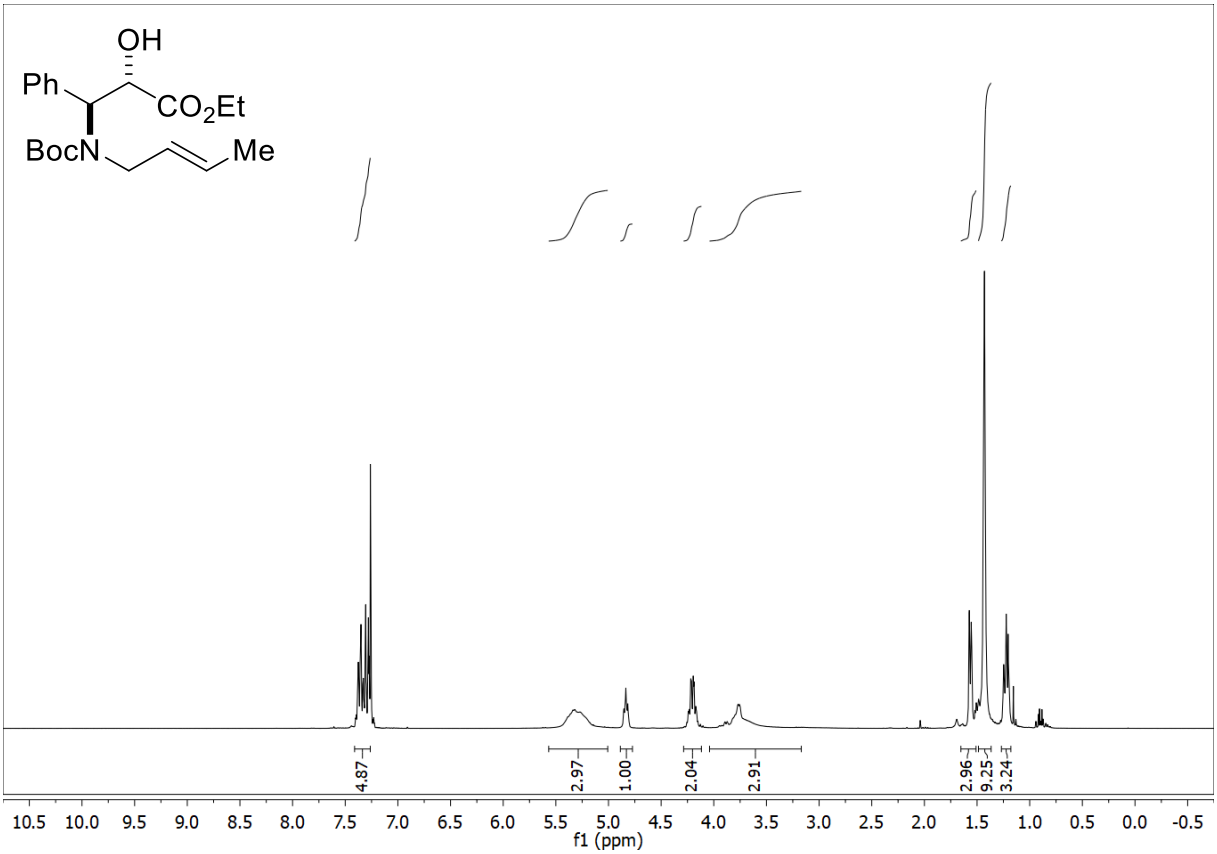
rac. Ethyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoate (44a)

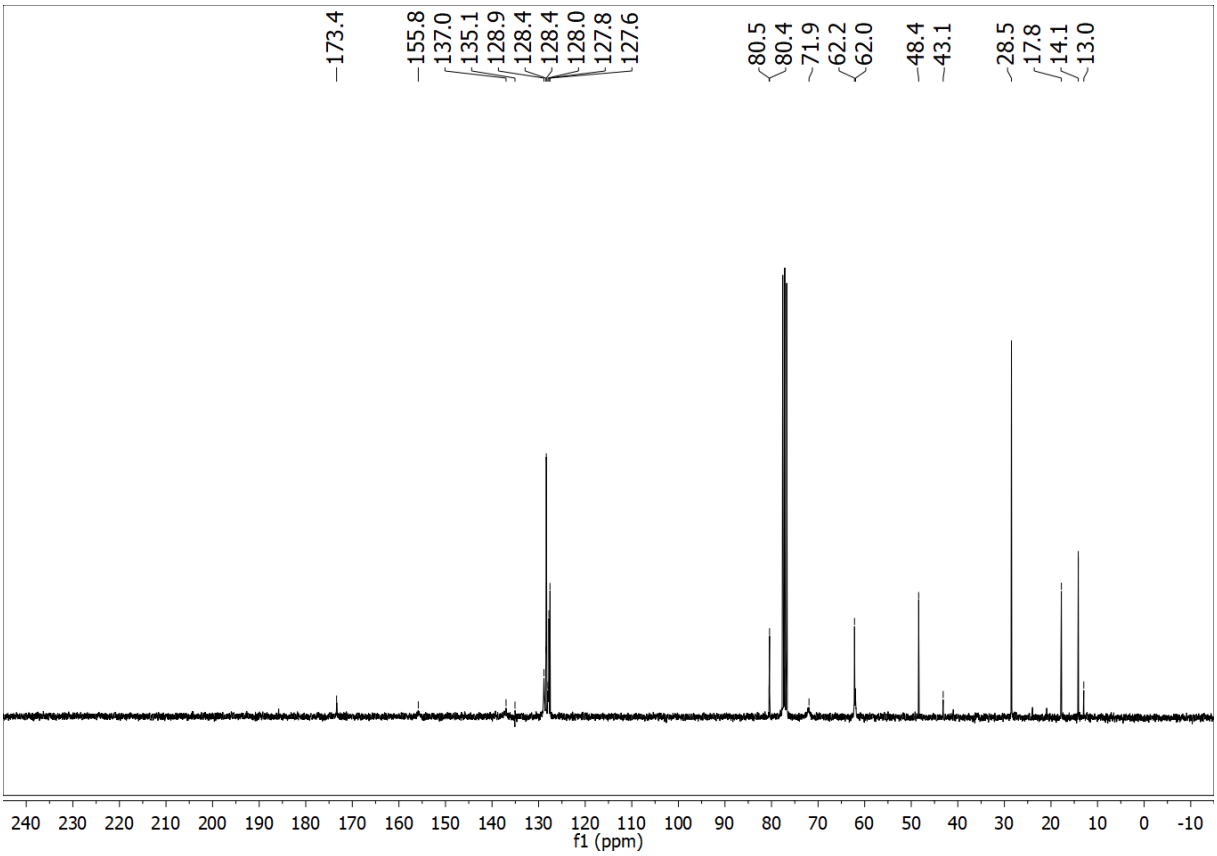




NMR-Solvent: $CDCl_3$

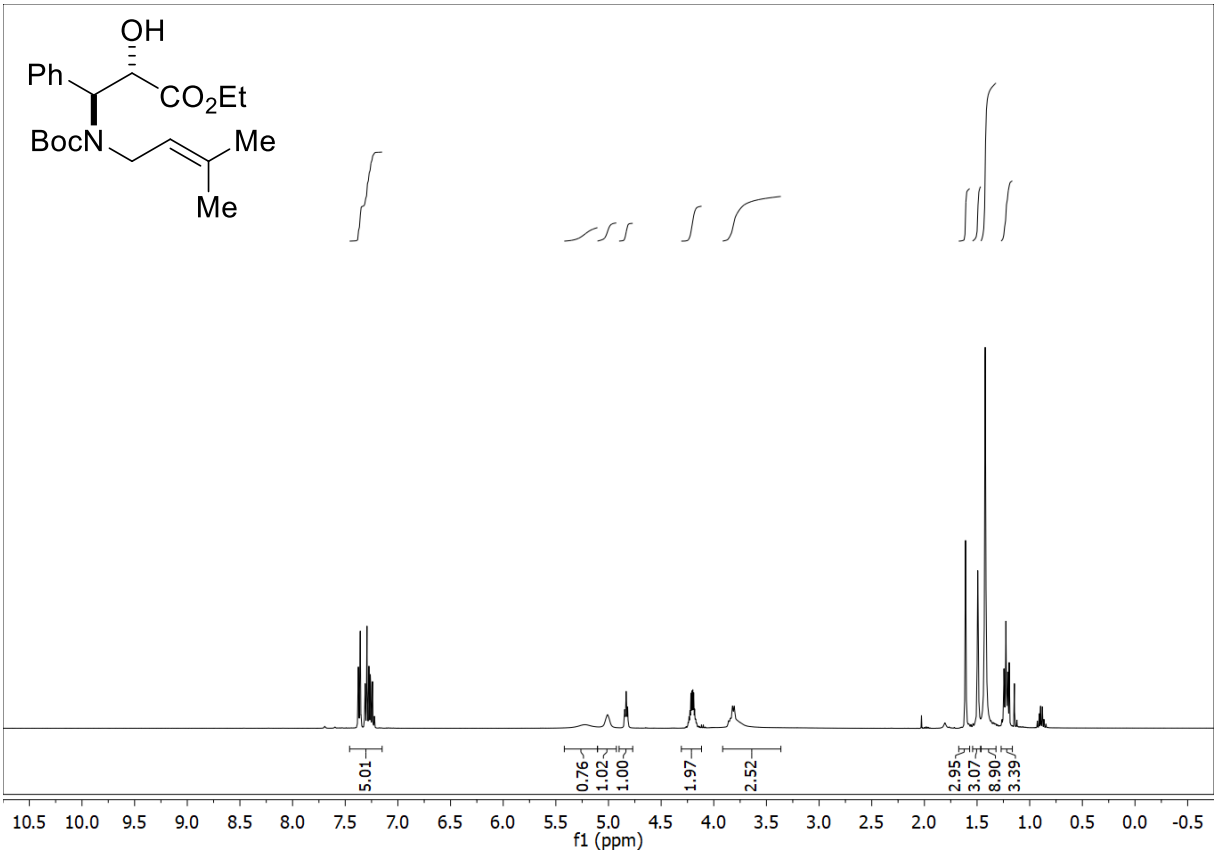
rac. Ethyl (2*S*,3*S*)-3-(((*E*)-but-2-en-1-yl)(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenylpropanoate (44b)

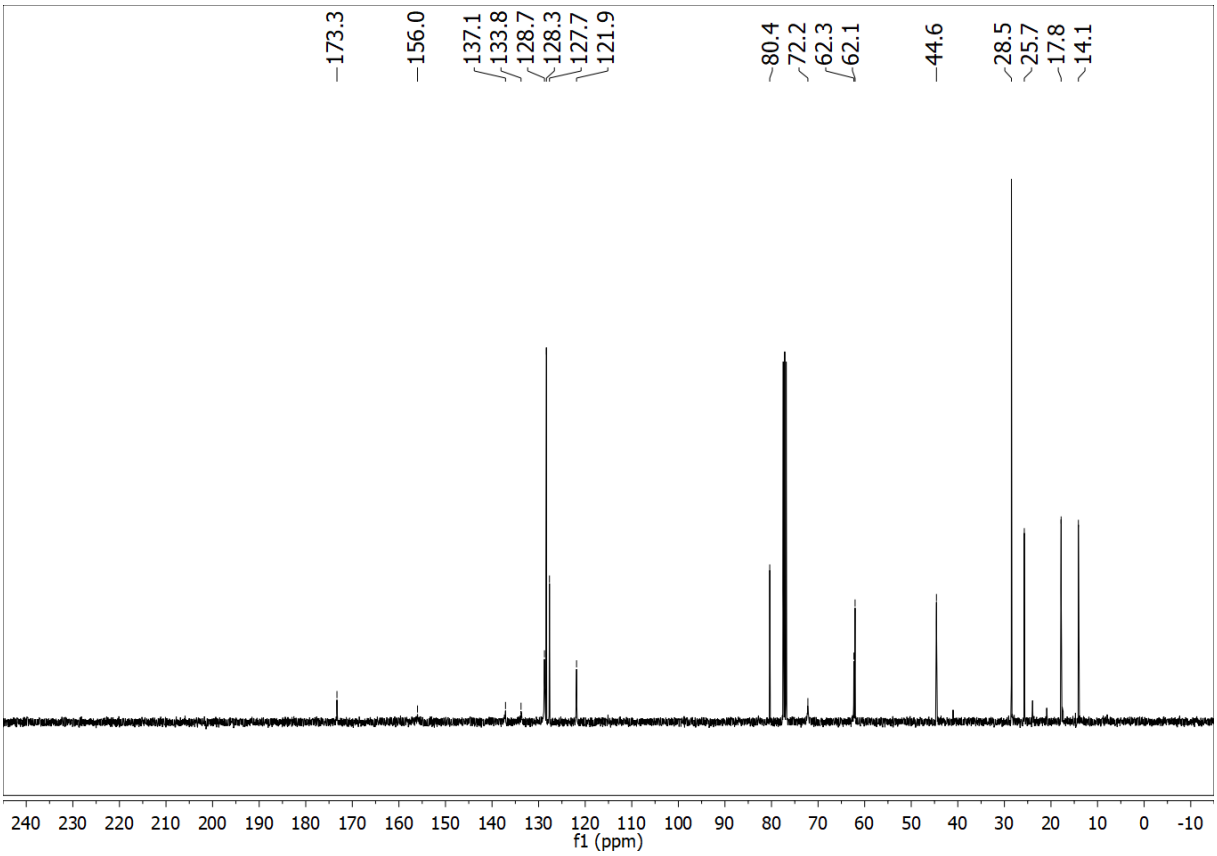




NMR-Solvent: $CDCl_3$

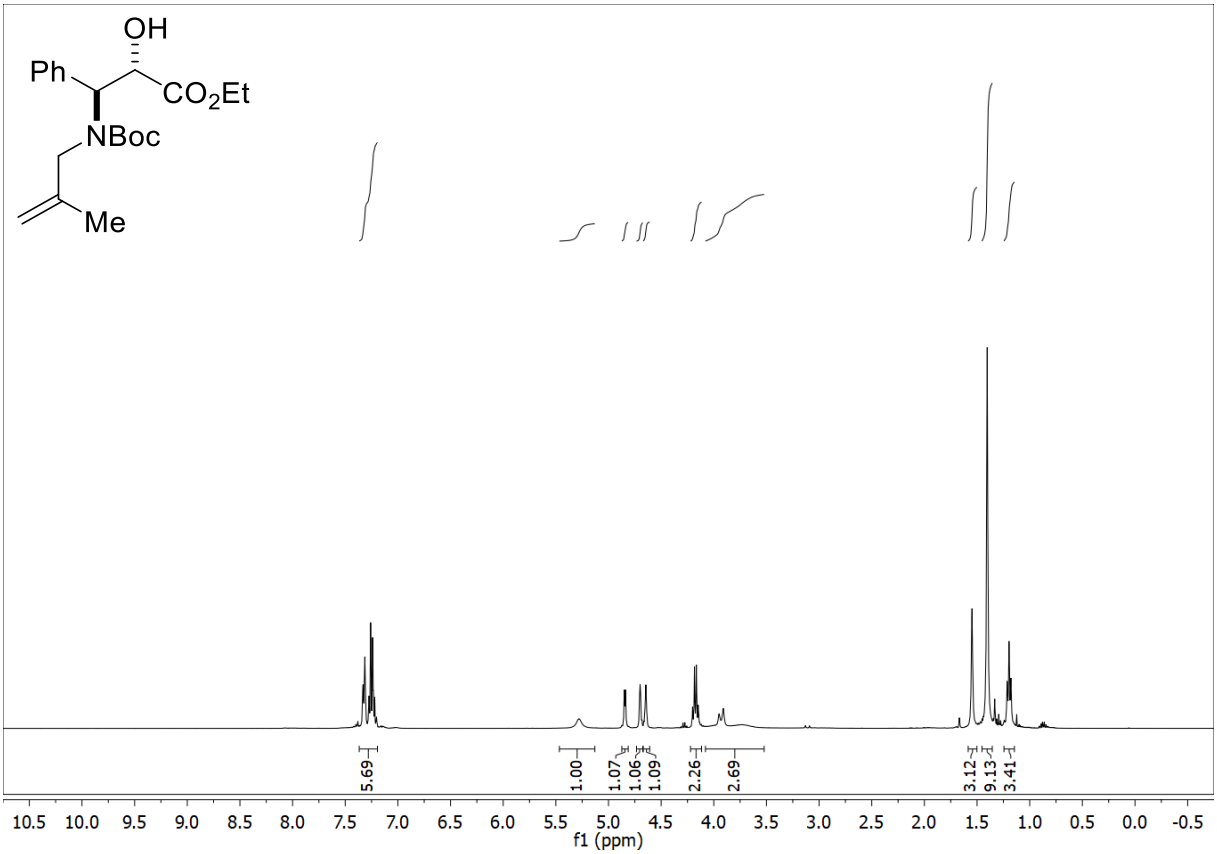
rac. Ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(3-methylbut-2-en-1-yl)amino)-2-hydroxy-3-phenylpropanoate (44c)

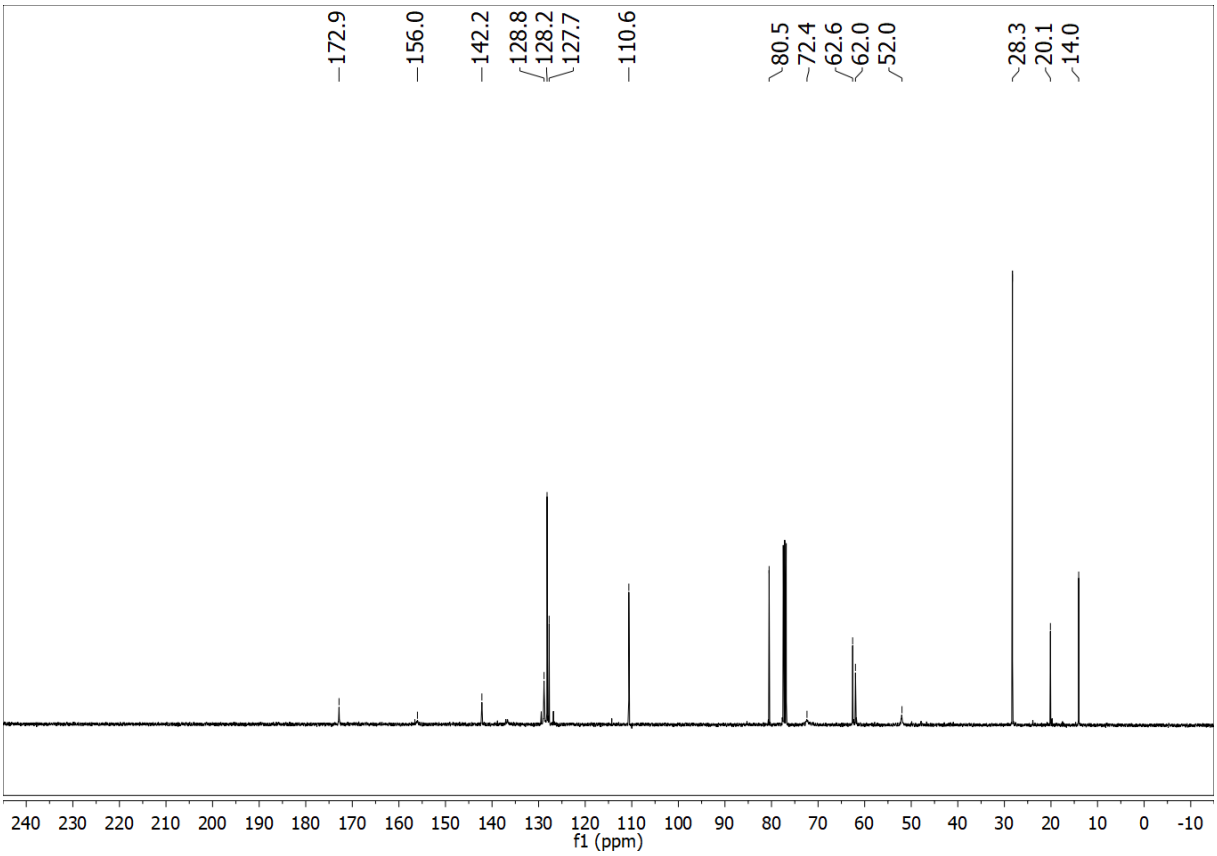




NMR-Solvent: $CDCl_3$

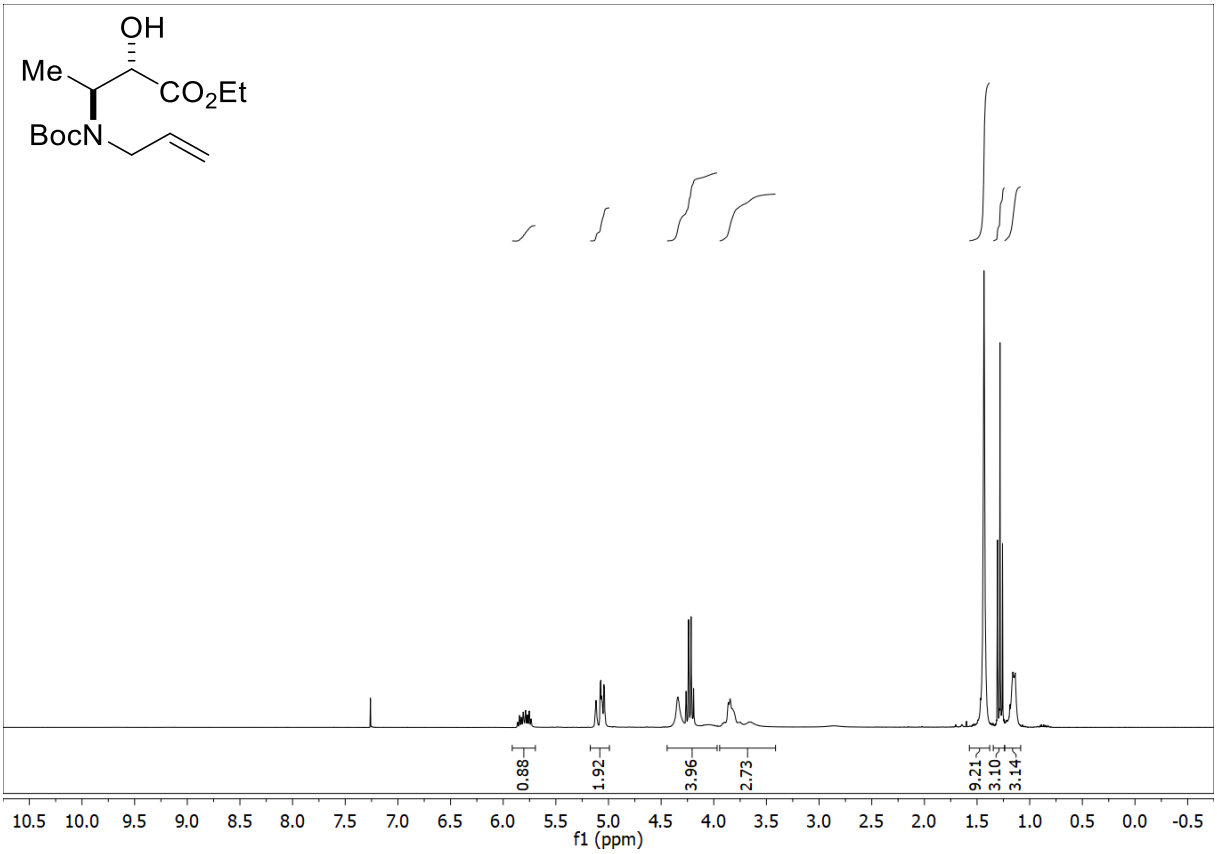
rac. Ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(2-methylallyl)amino)-2-hydroxy-3-phenyl-propanoate) (44d)

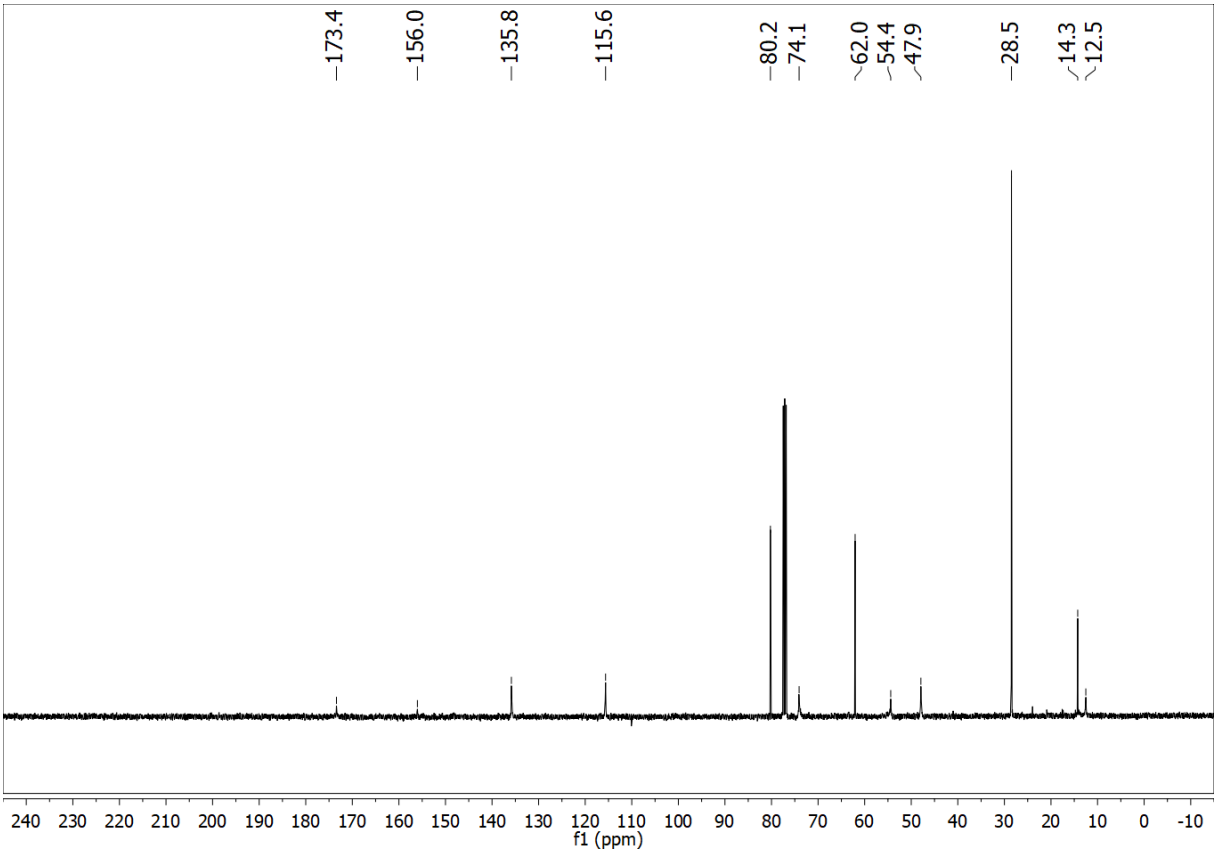




NMR-Solvent: $CDCl_3$

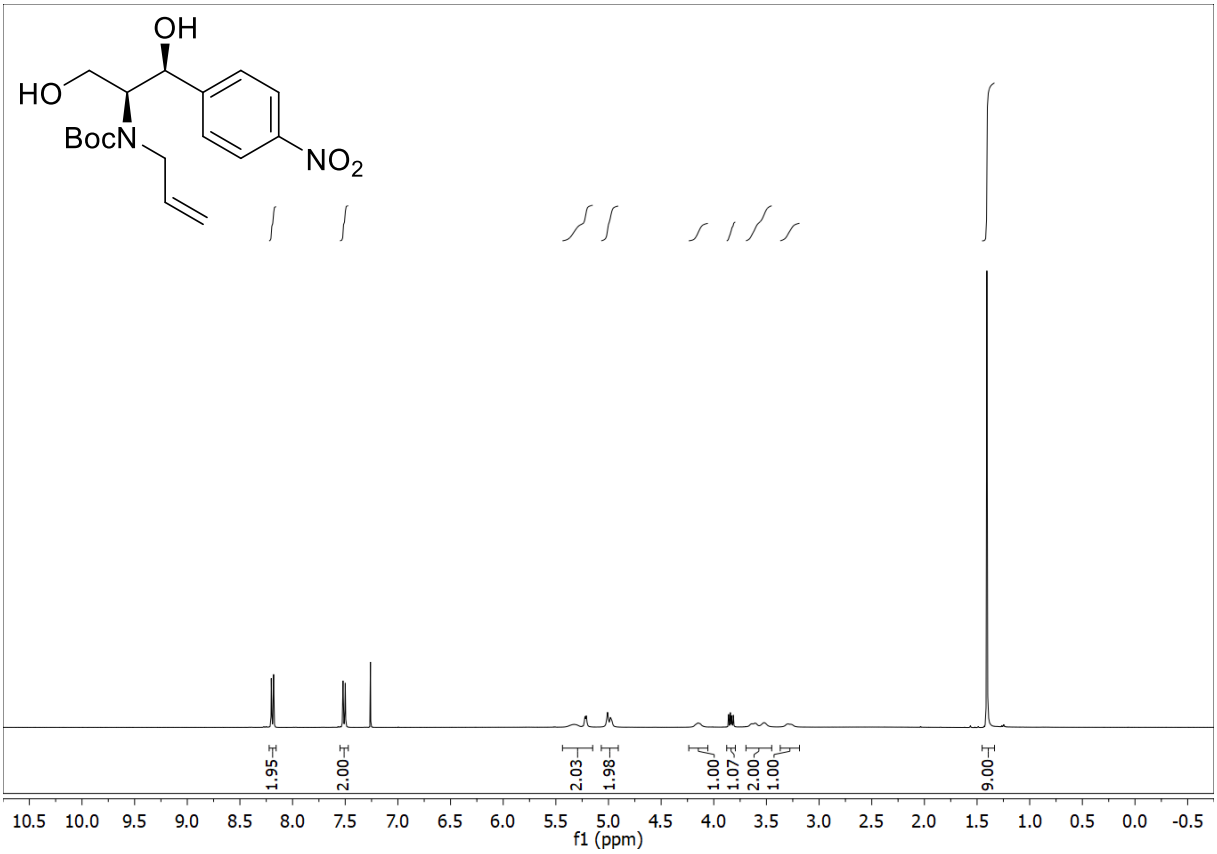
rac. Ethyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxybutanoate (44e)

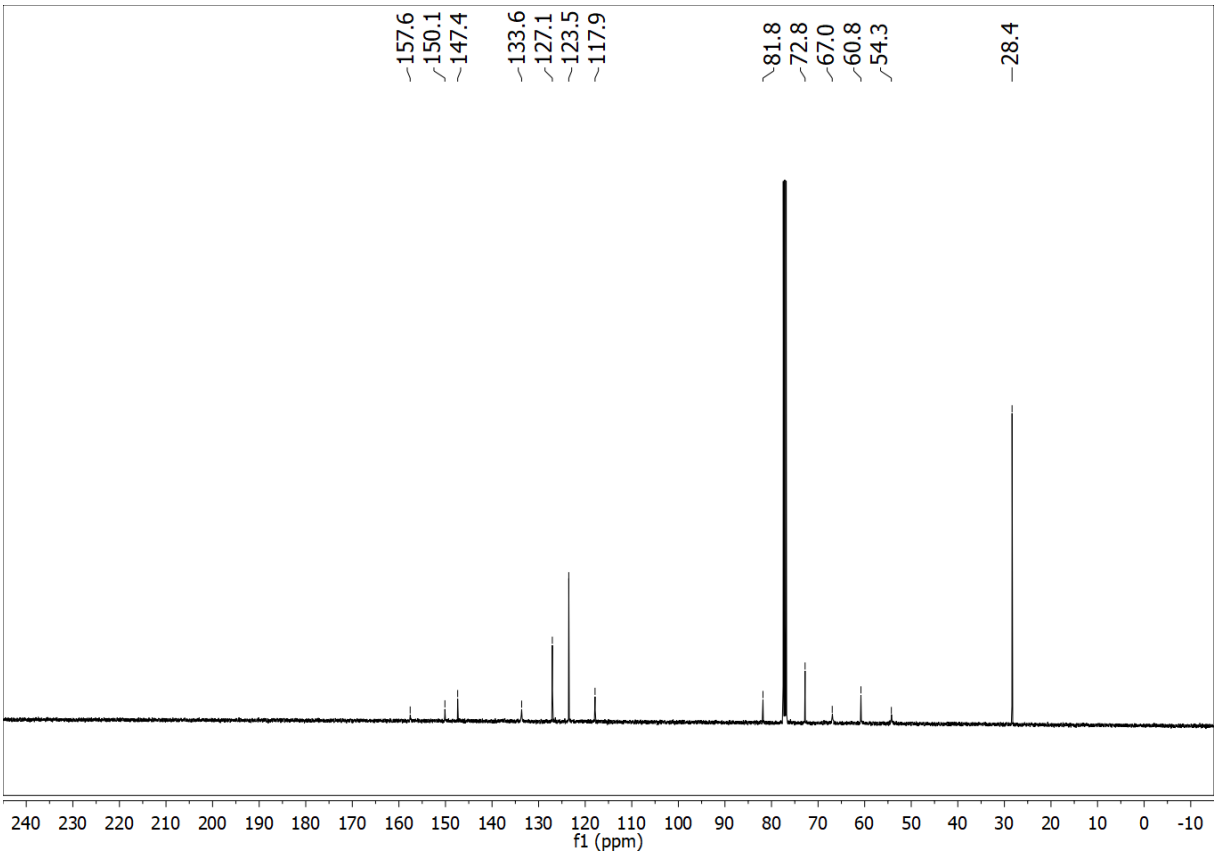




NMR-Solvent: $CDCl_3$

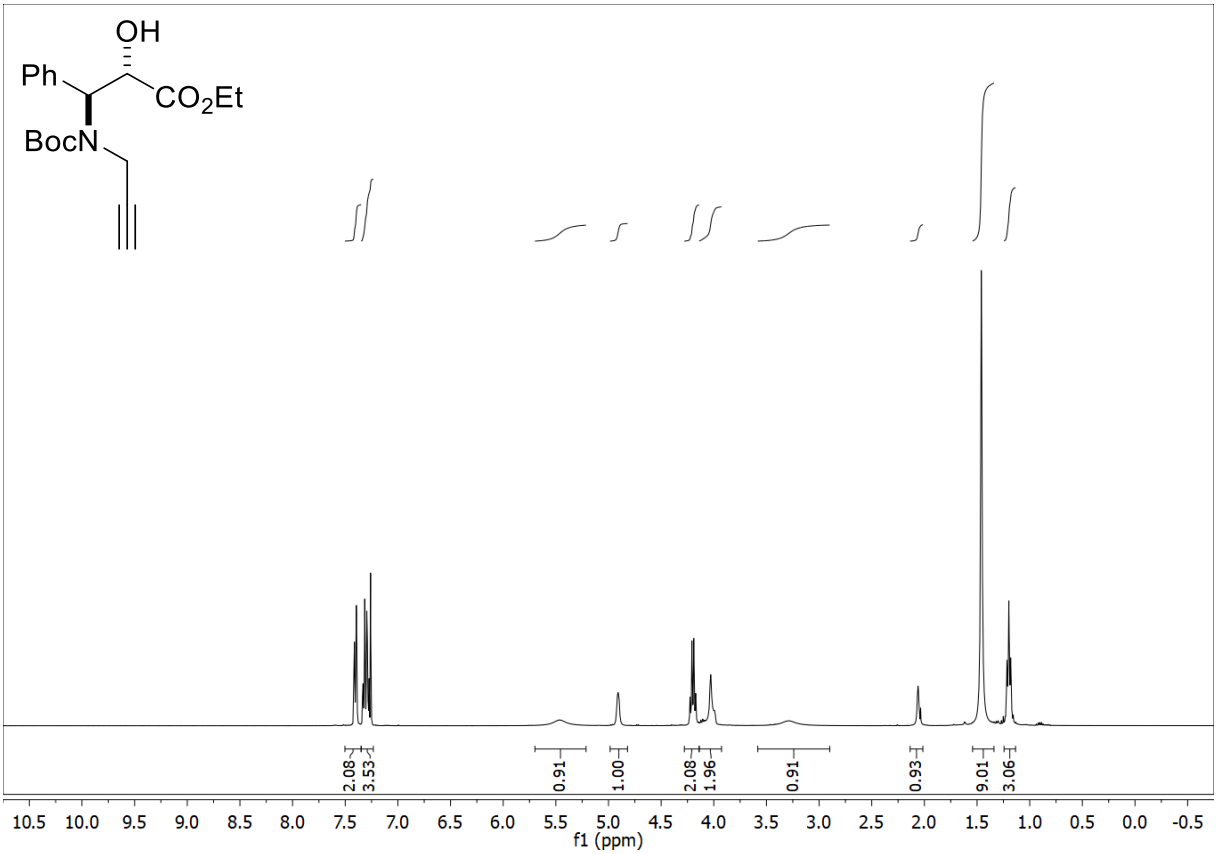
tert-Butyl allyl((1*S*,2*S*)-1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl)carbamate (44f)

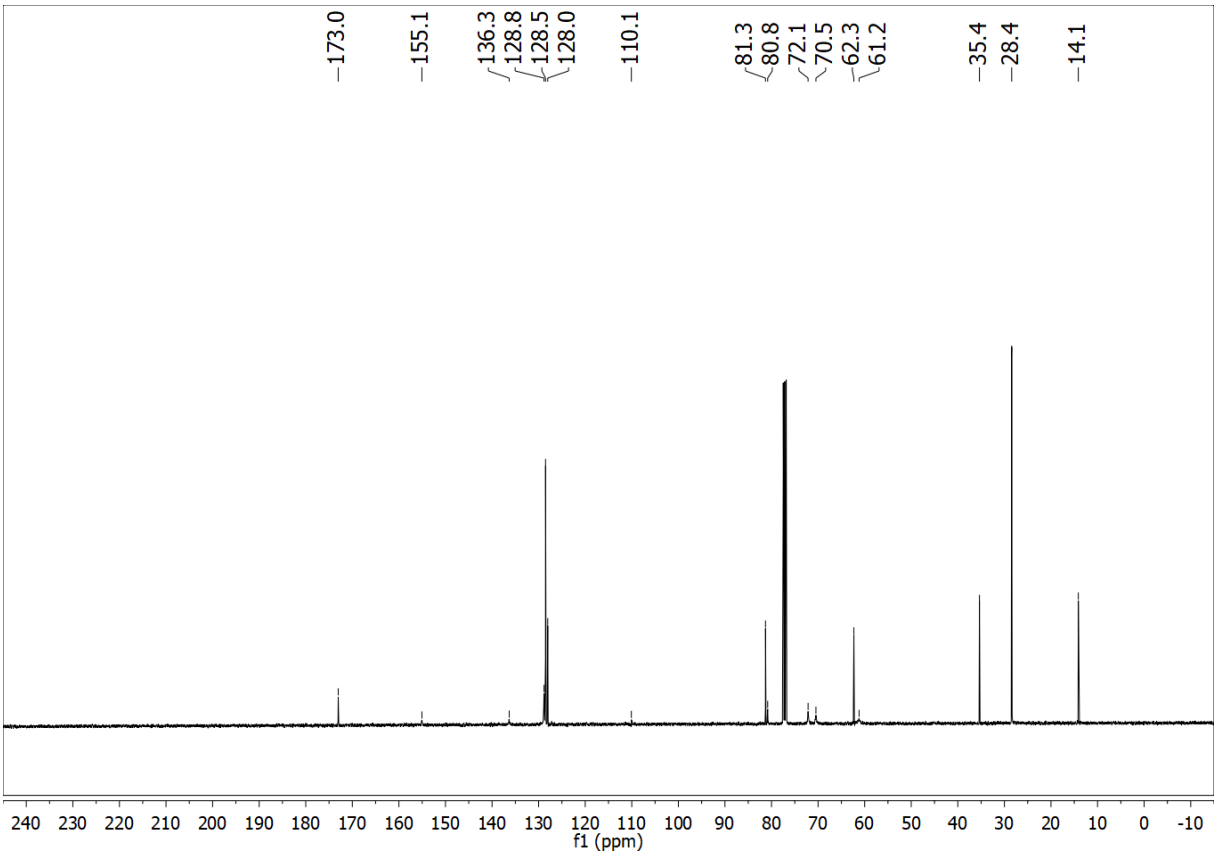




NMR-Solvent: $CDCl_3$

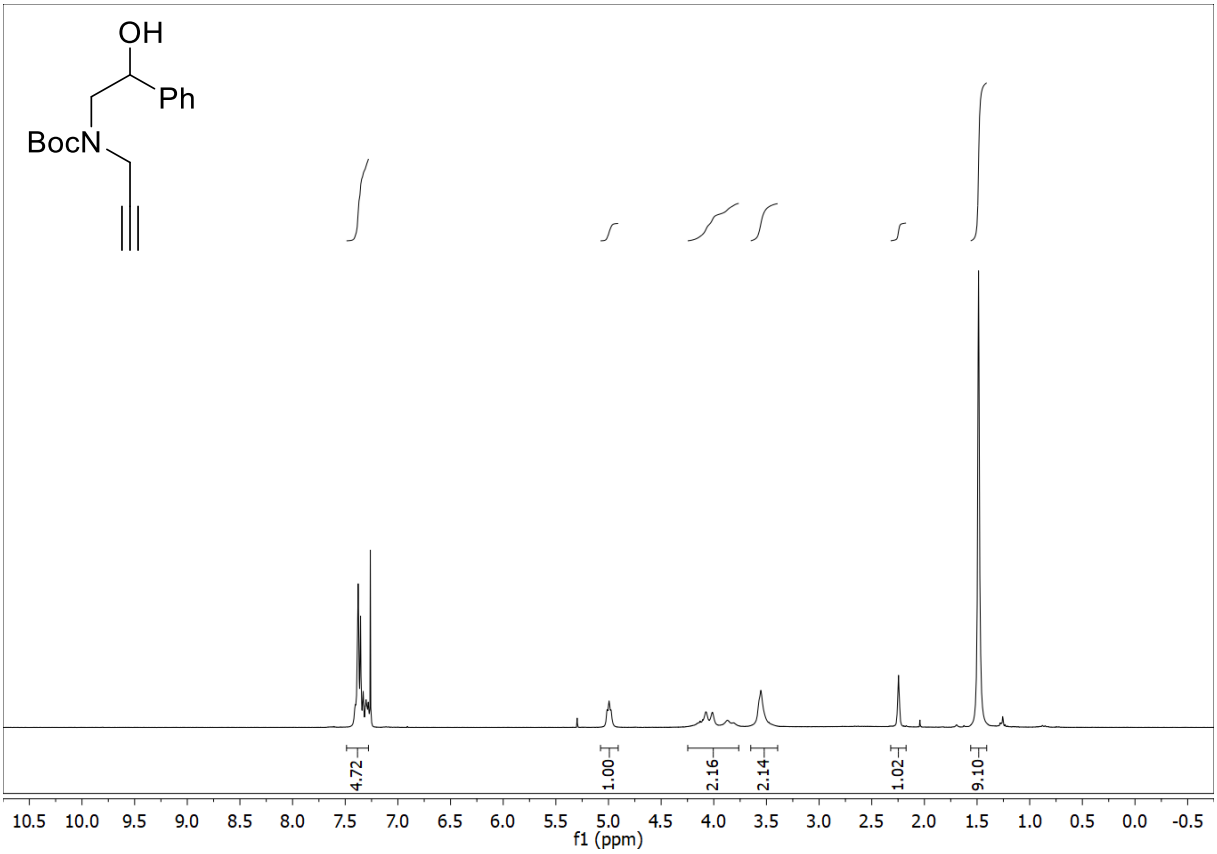
rac. Ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-2-hydroxy-3-phenylpropanoate (44g)

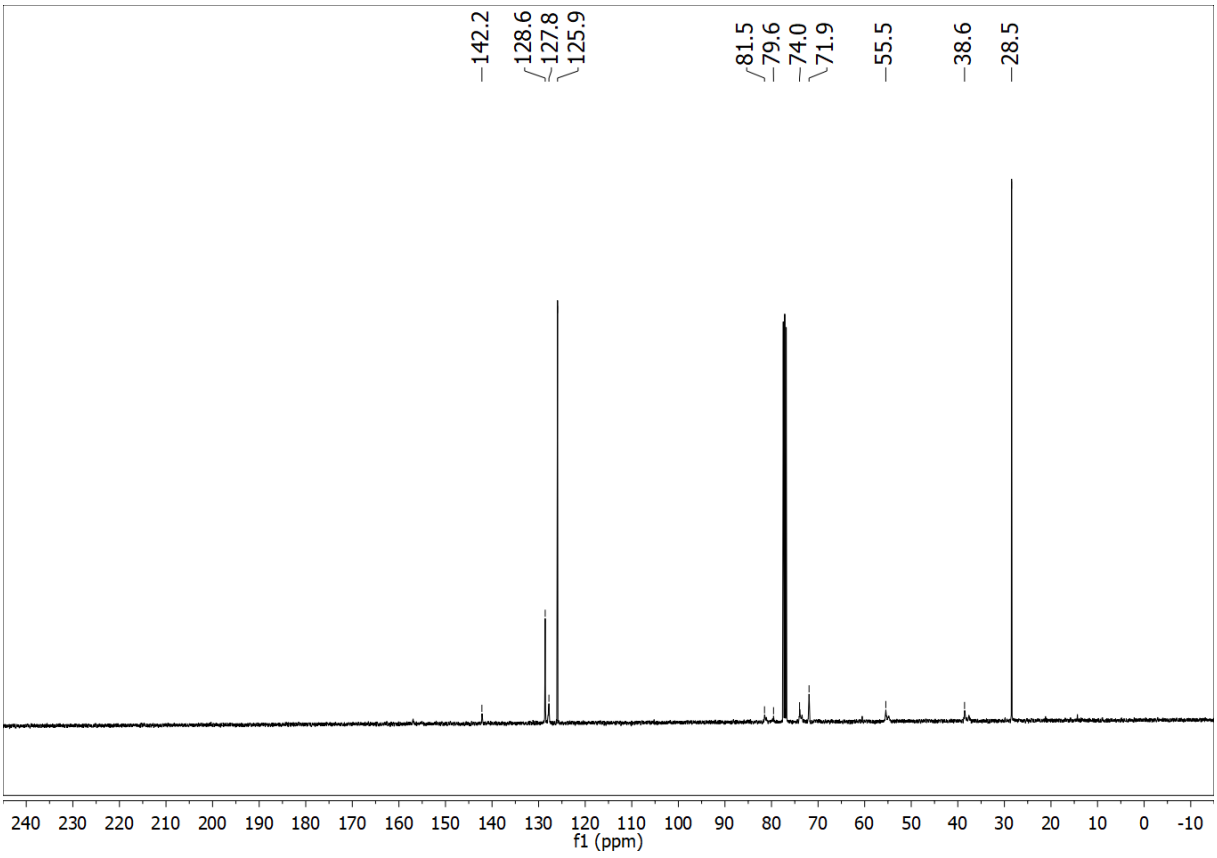




NMR-Solvent: $CDCl_3$

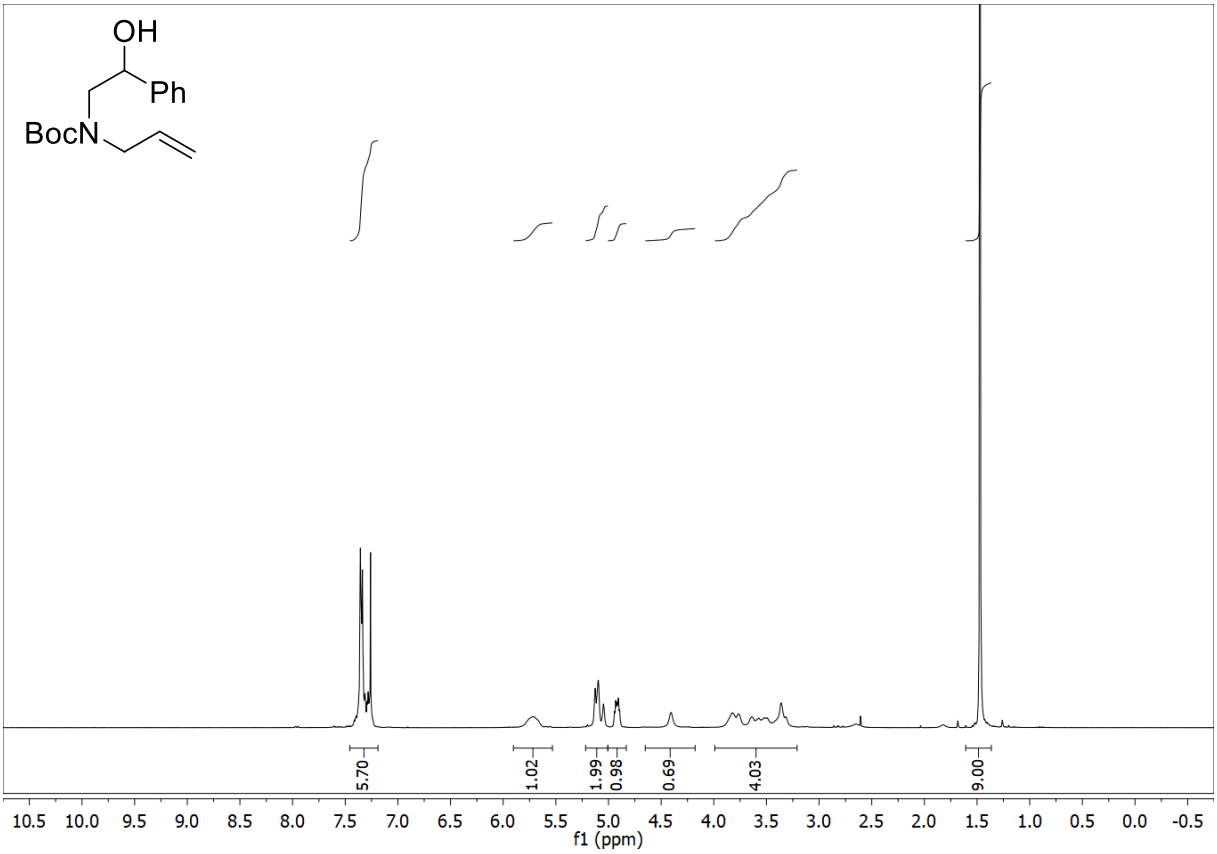
tert-Butyl-(2-hydroxy-2-phenylethyl)(prop-2-yn-1-yl)carbamate (44h)

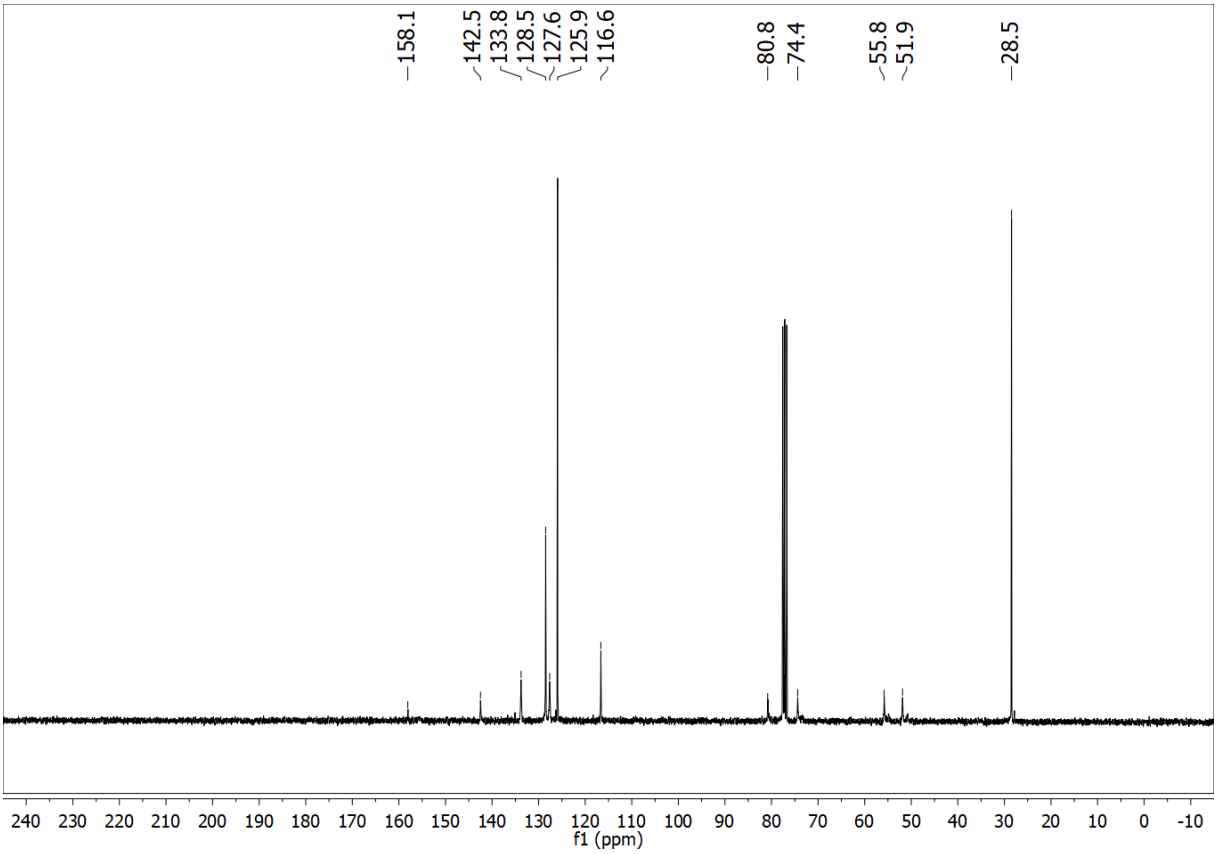




NMR-Solvent: $CDCl_3$

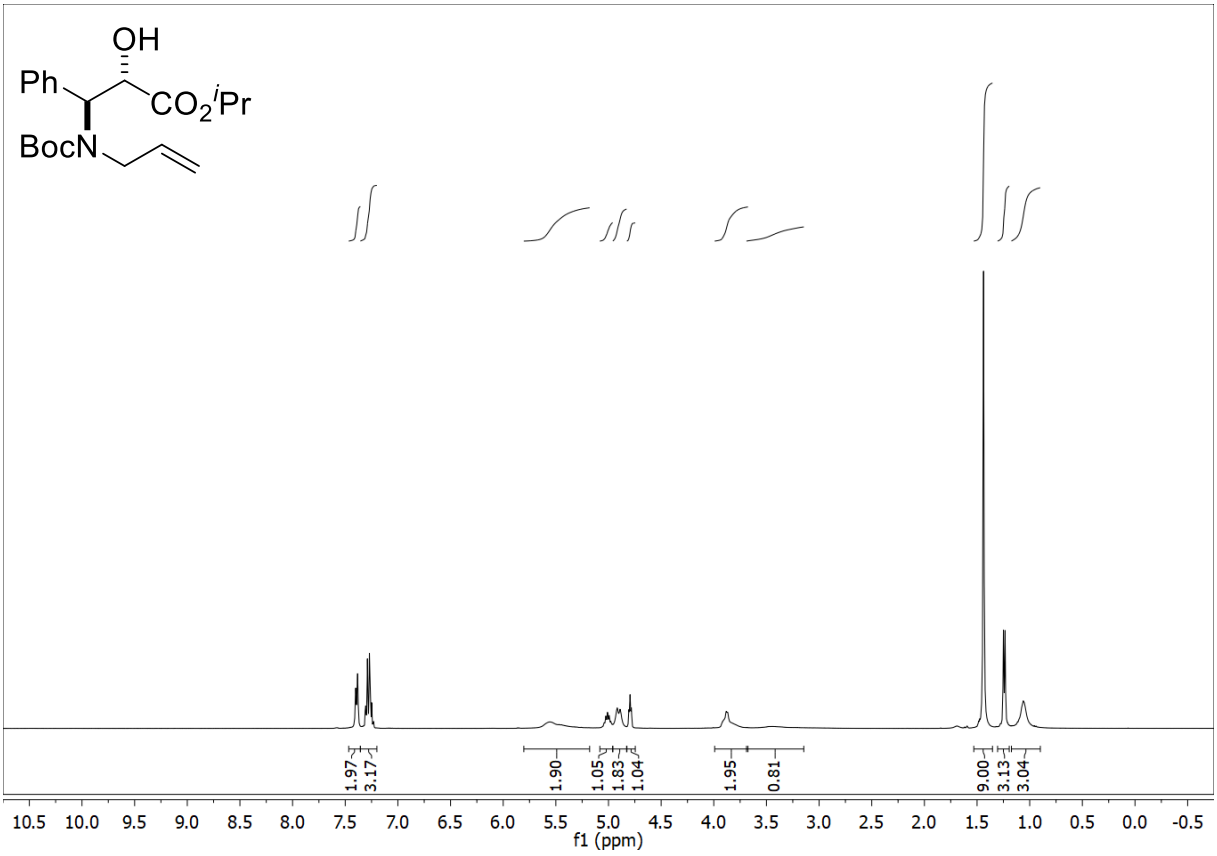
tert-Butyl allyl(2-hydroxy-2-phenylethyl)carbamate (44i)

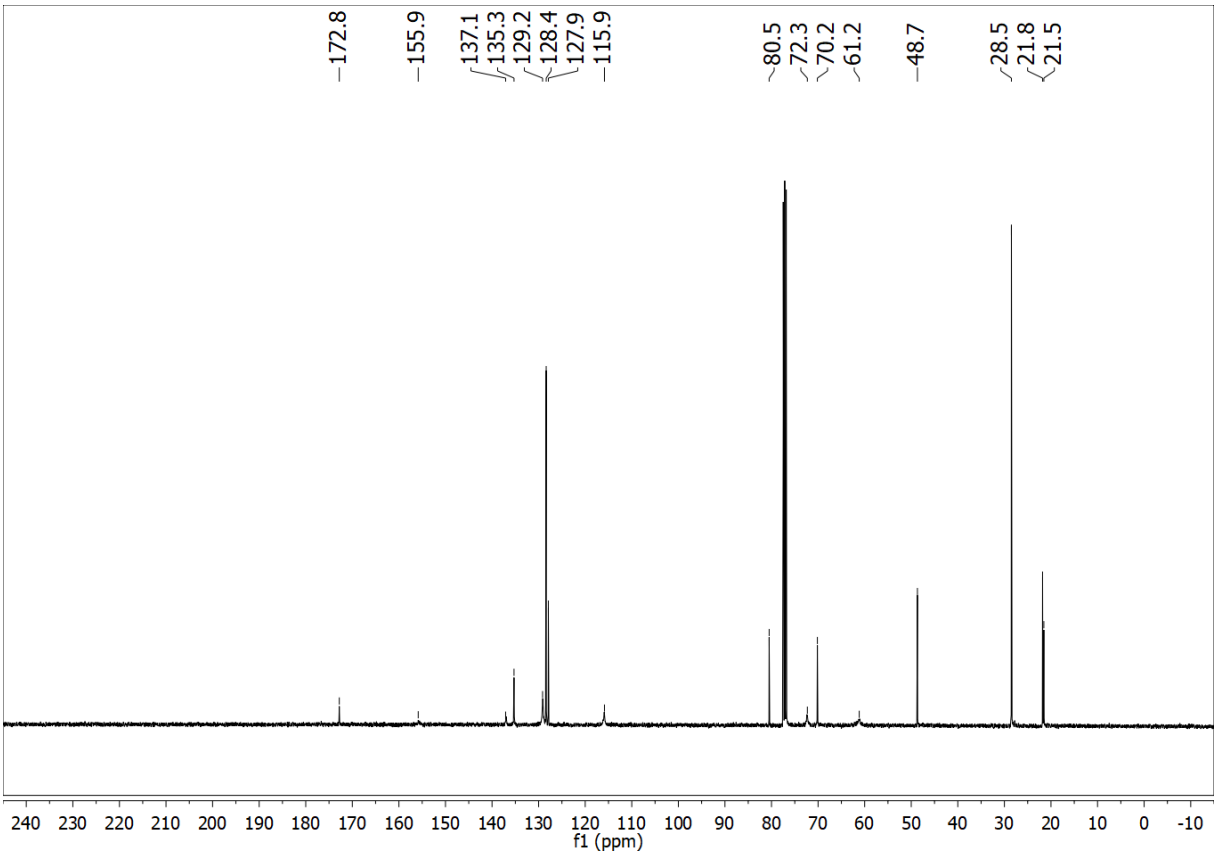




NMR-Solvent: $CDCl_3$

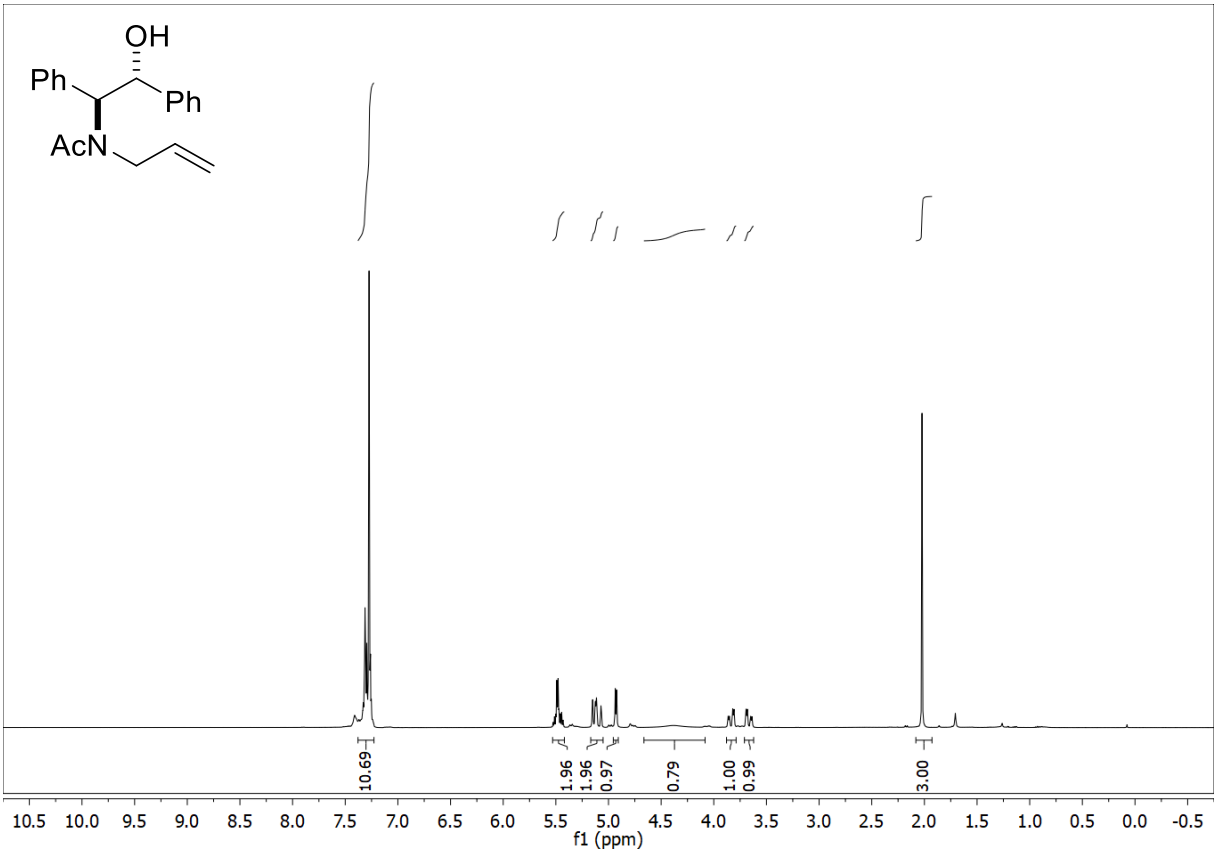
rac. Isopropyl (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-2-hydroxy-3-phenyl-propanoate (44j)

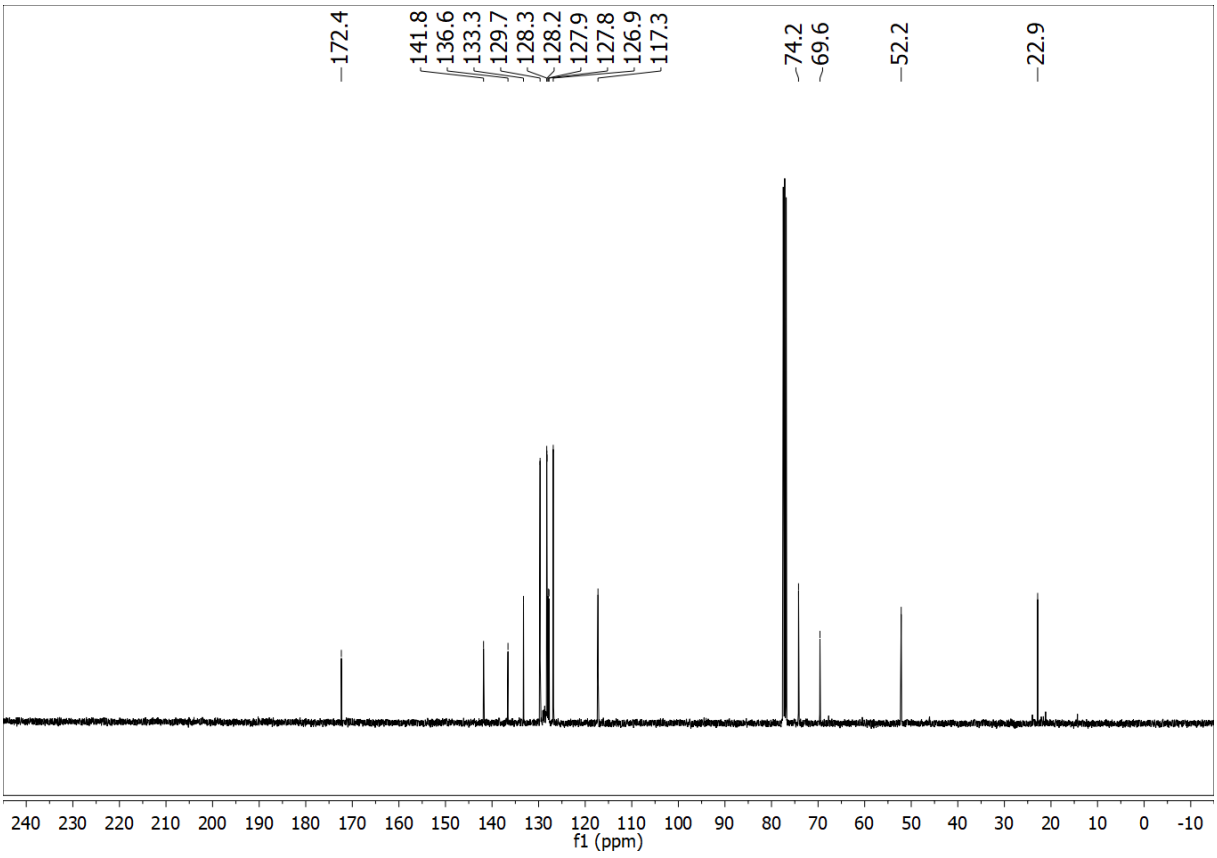




NMR-Solvent: $CDCl_3$

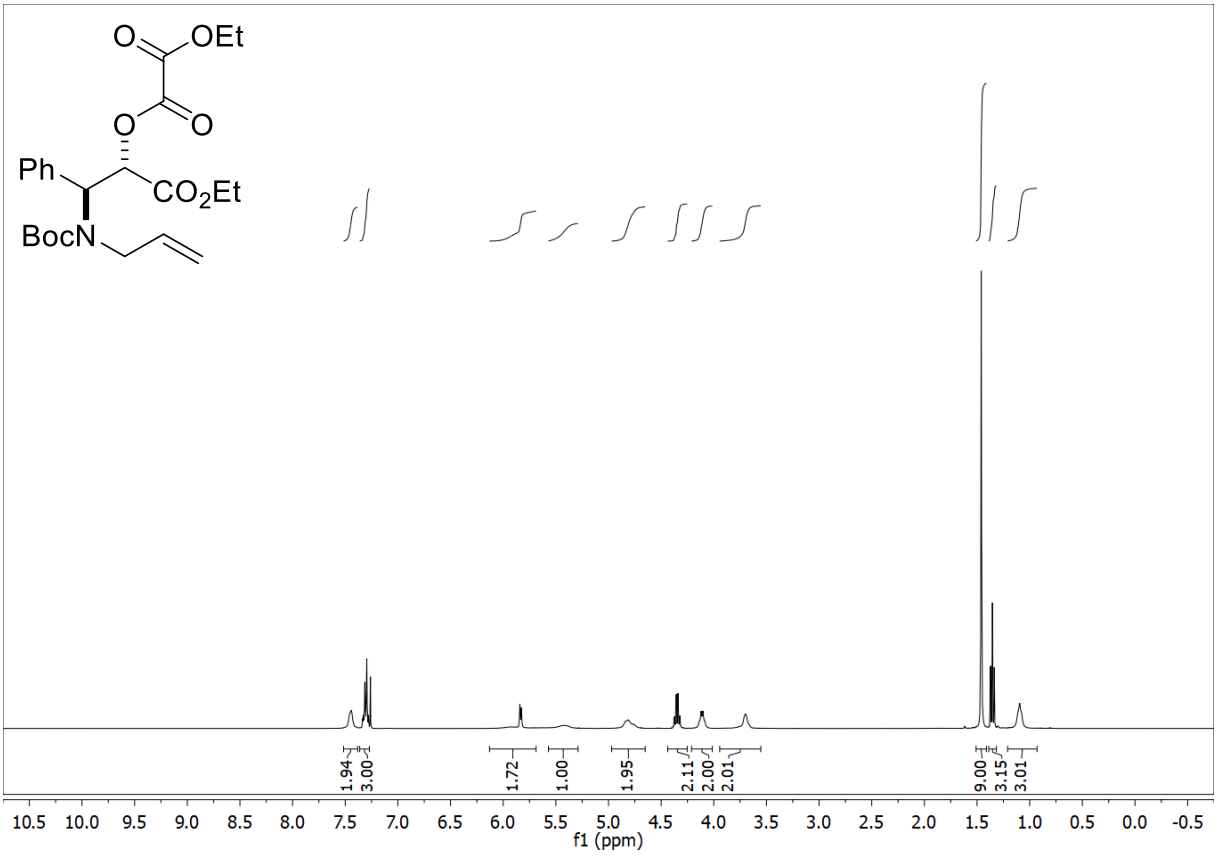
rac. *N*-allyl-*N*-((1*S*,2*R*)-2-hydroxy-1,2-diphenylethyl)acetamide (44m)

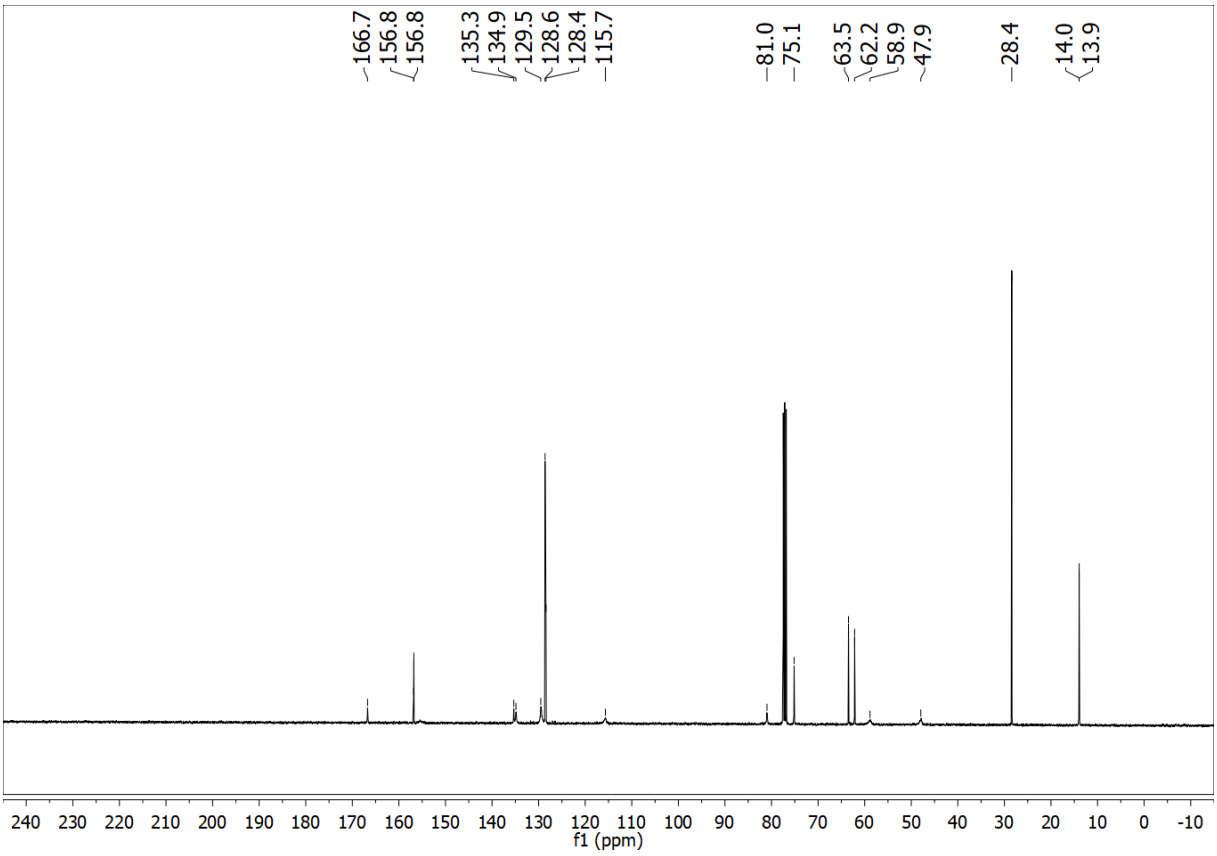




NMR-Solvent: $CDCl_3$

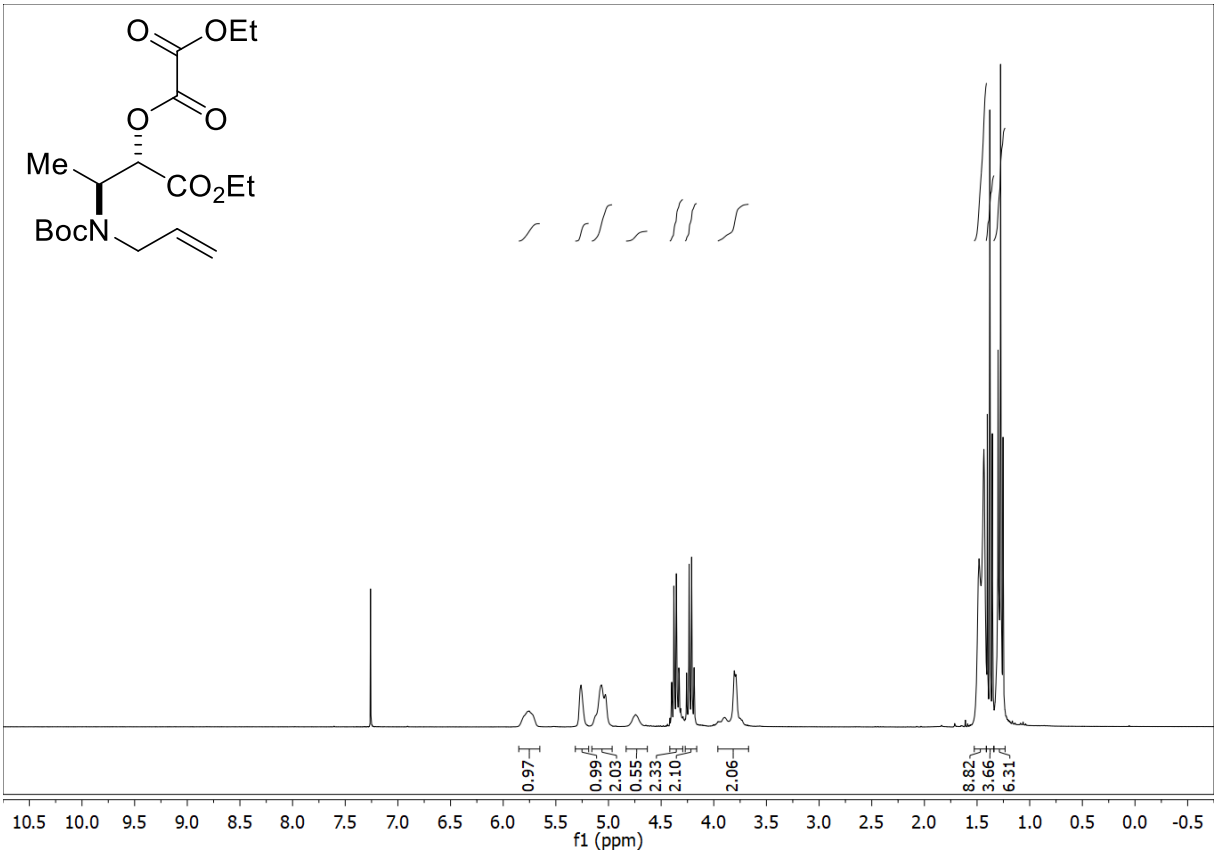
rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (45a)

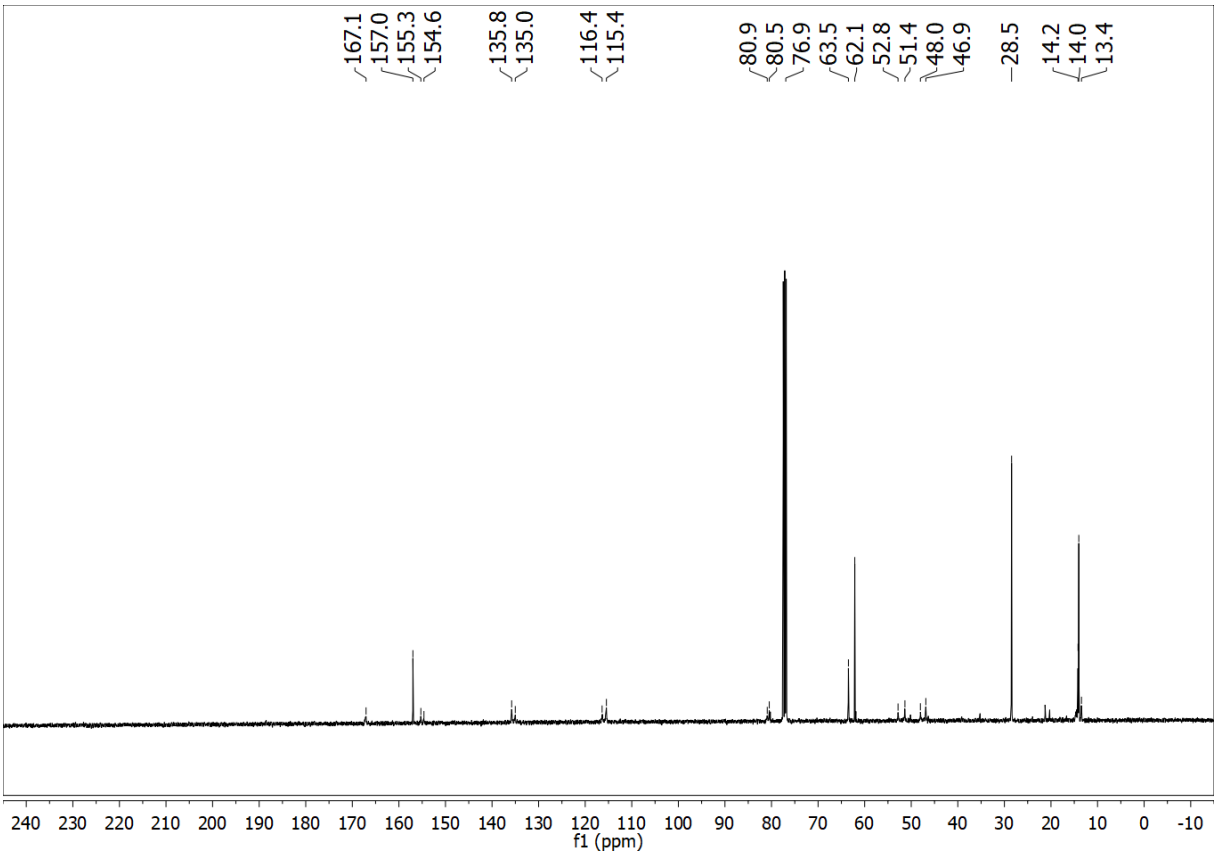




NMR-Solvent: $CDCl_3$

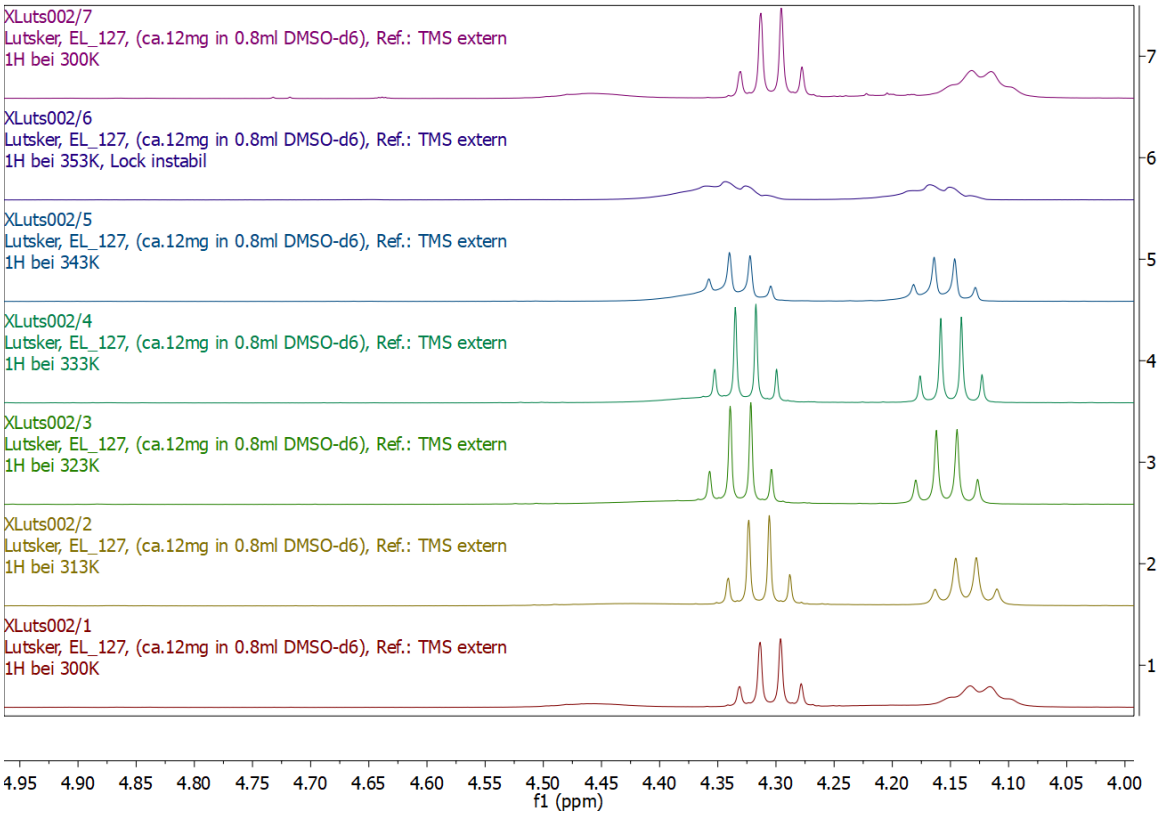
rac. (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-1-ethoxy-1-oxobutan-2-yl ethyl oxalate (45e)





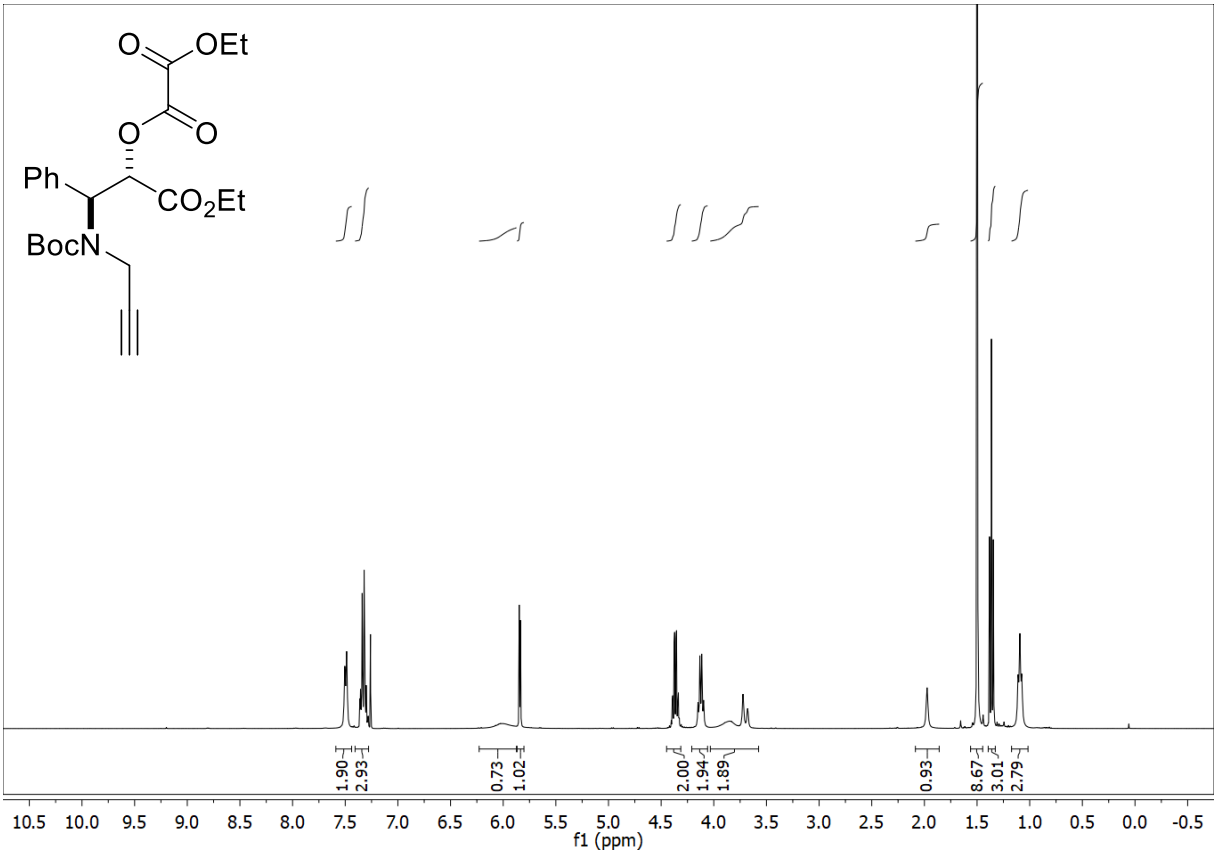
NMR-Solvent: $CDCl_3$

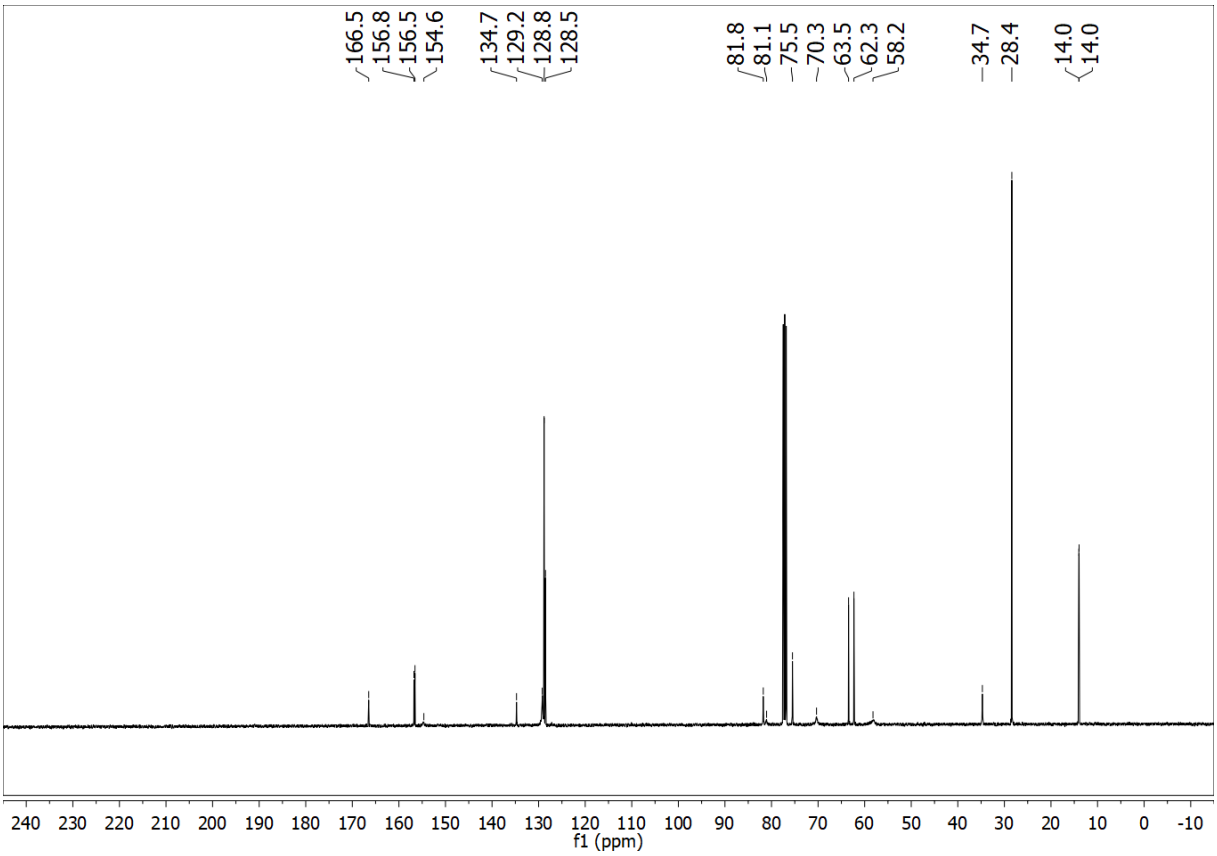
Rotamer measurement



NMR-Solvent: DMSO-d_6

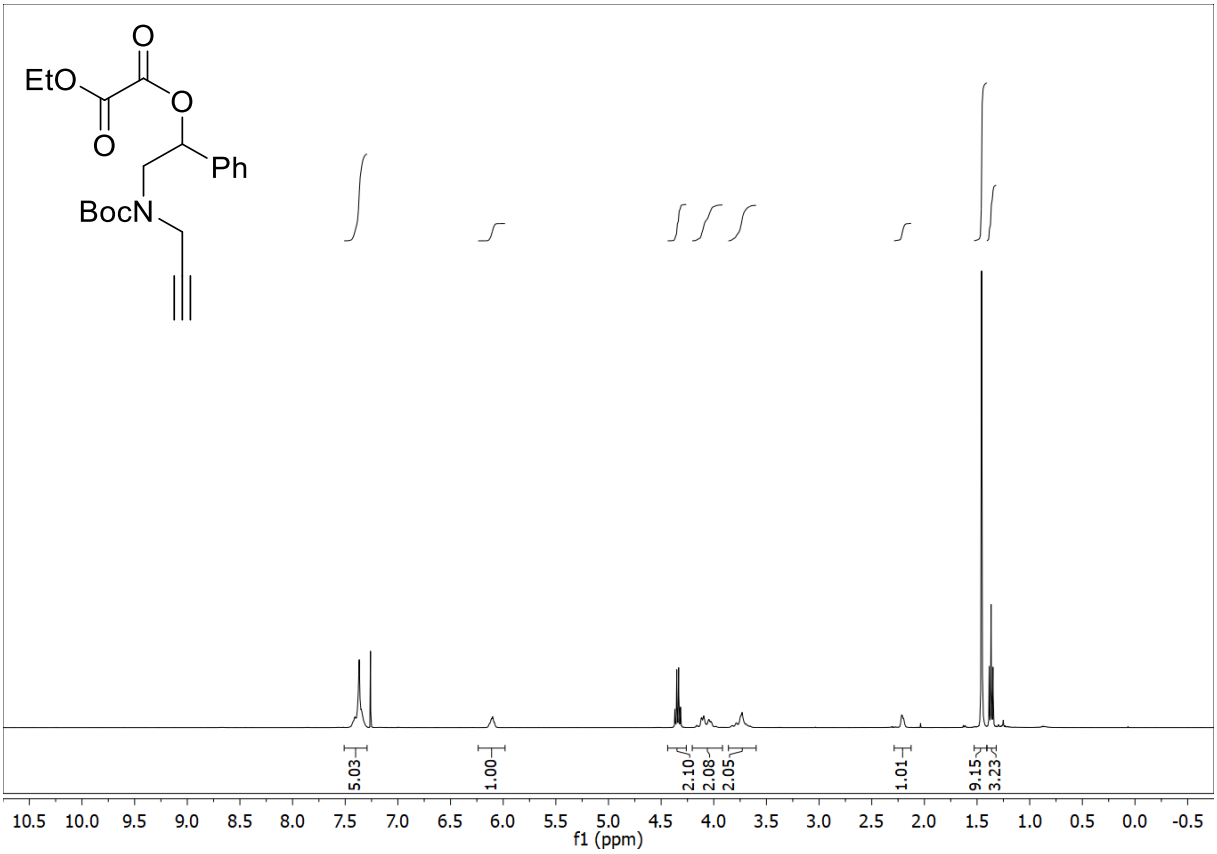
rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (45g)

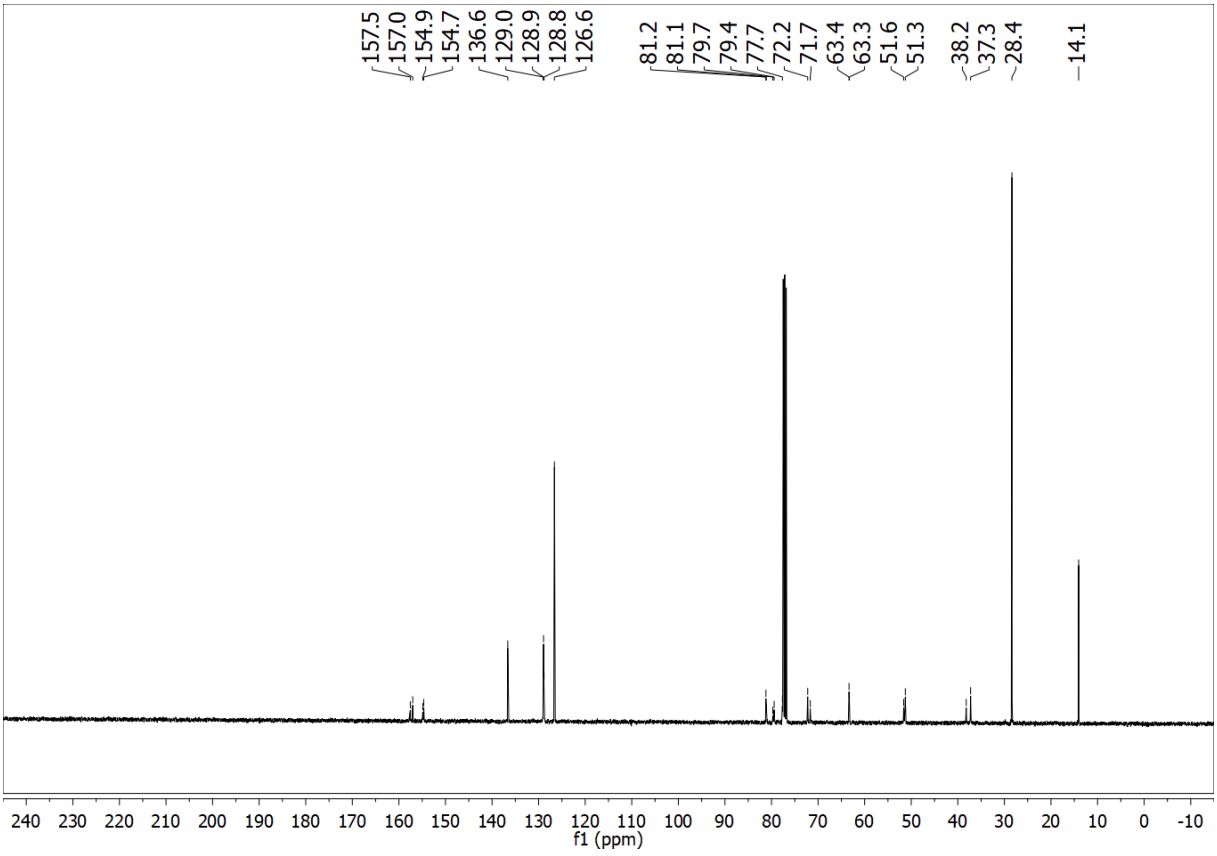




NMR-Solvent: $CDCl_3$

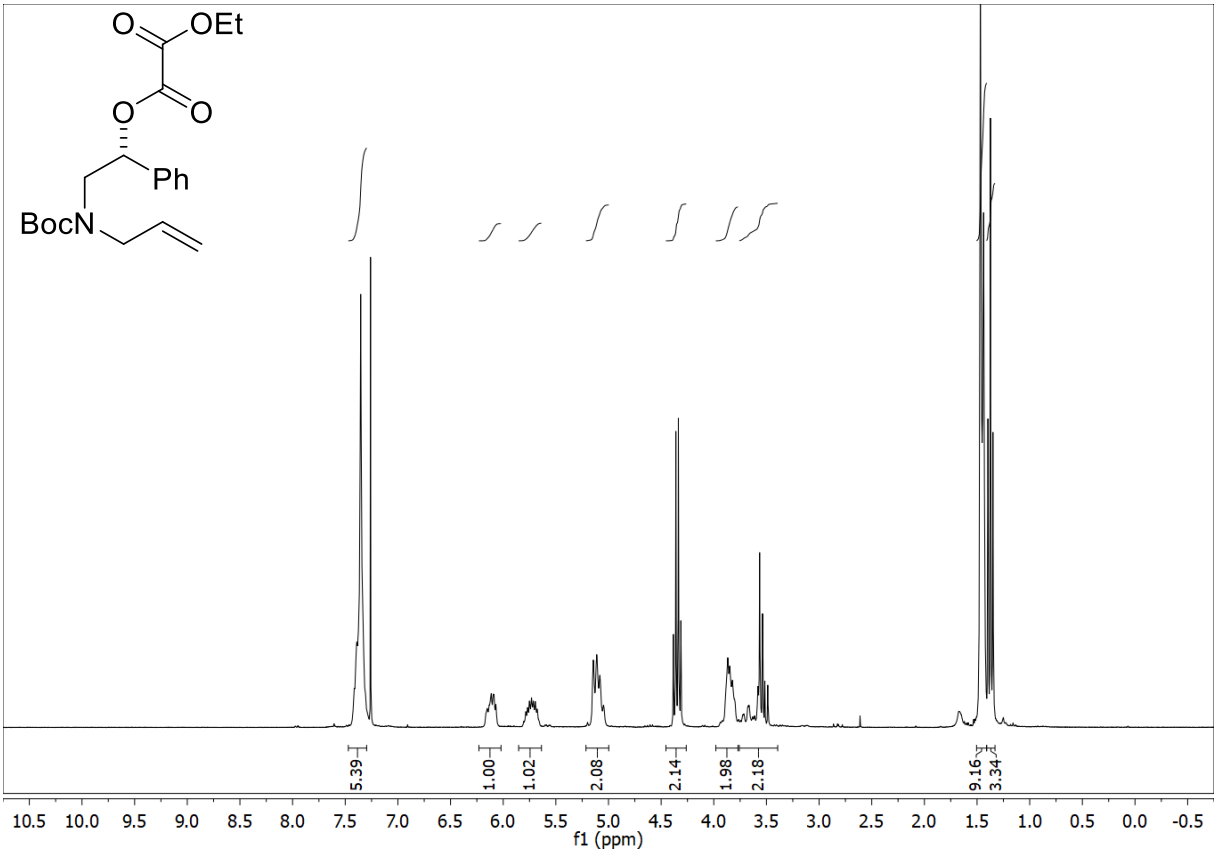
2-((*tert*-Butoxycarbonyl)(prop-2-yn-1-yl)amino)-1-phenylethyl ethyl oxalate (45h)

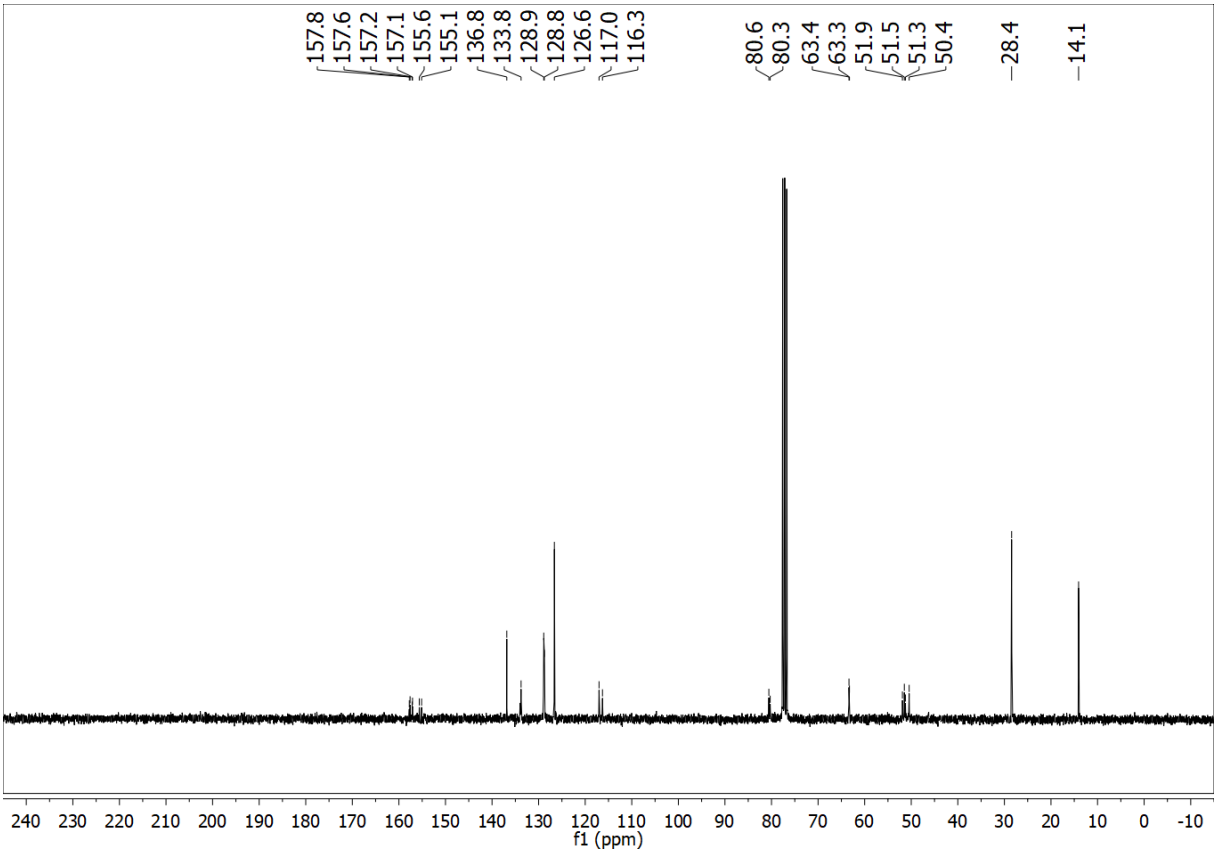




NMR-Solvent: $CDCl_3$

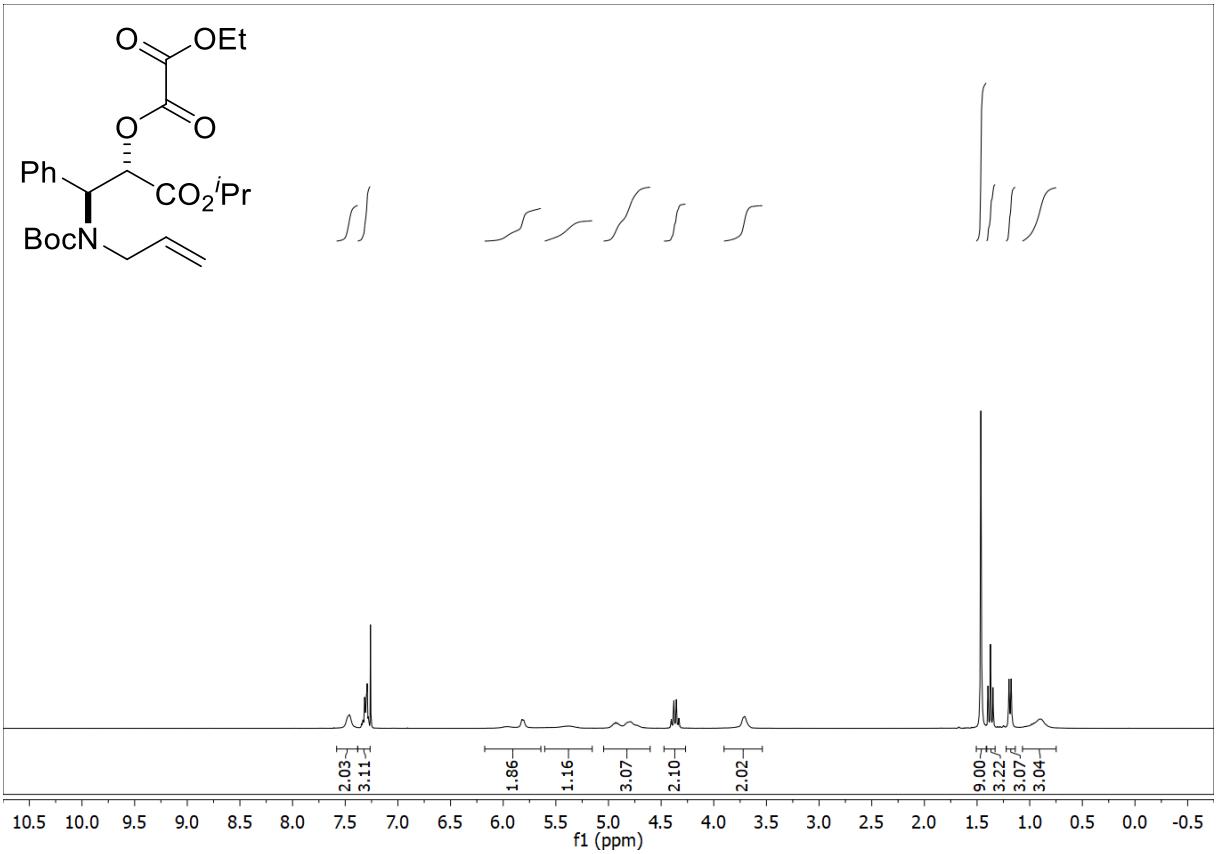
2-(Allyl(*tert*-butoxycarbonyl)amino)-1-phenylethyl ethyl oxalate (45i)

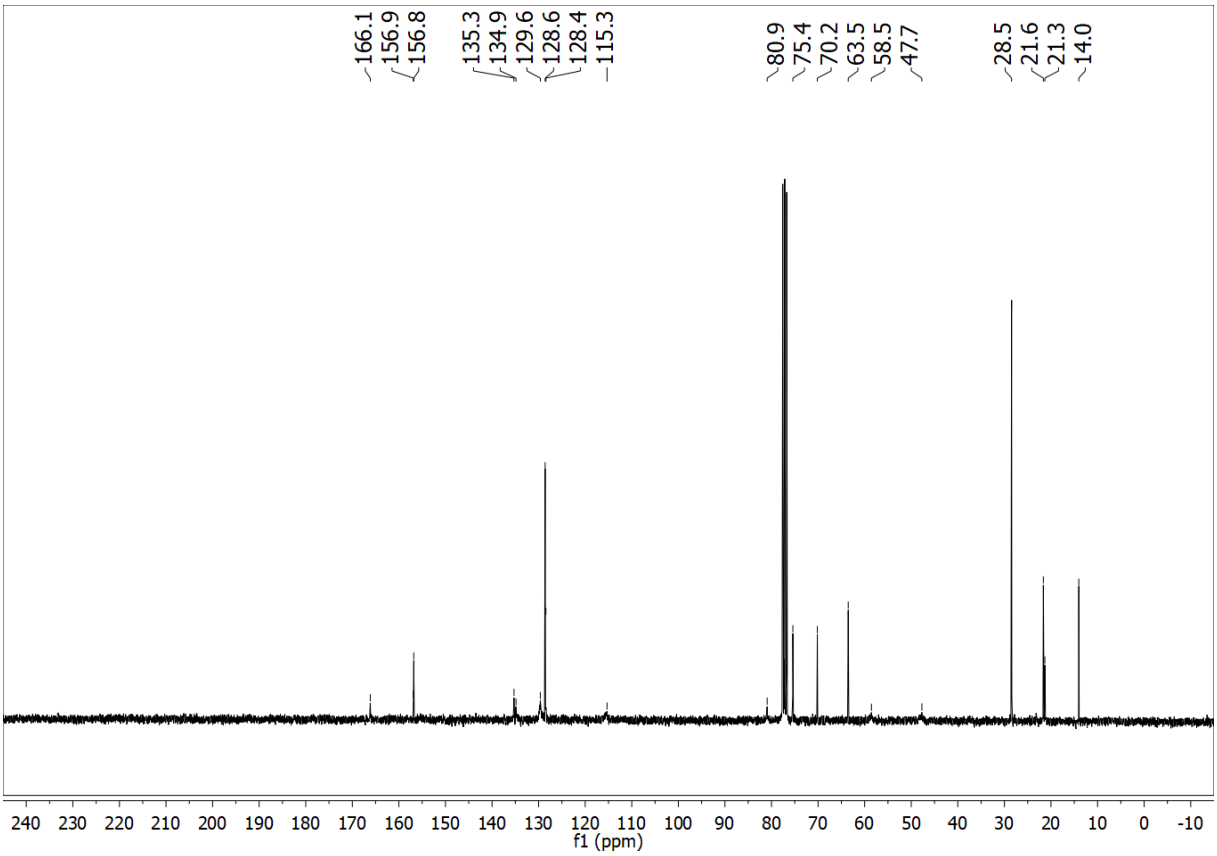




NMR-Solvent: $CDCl_3$

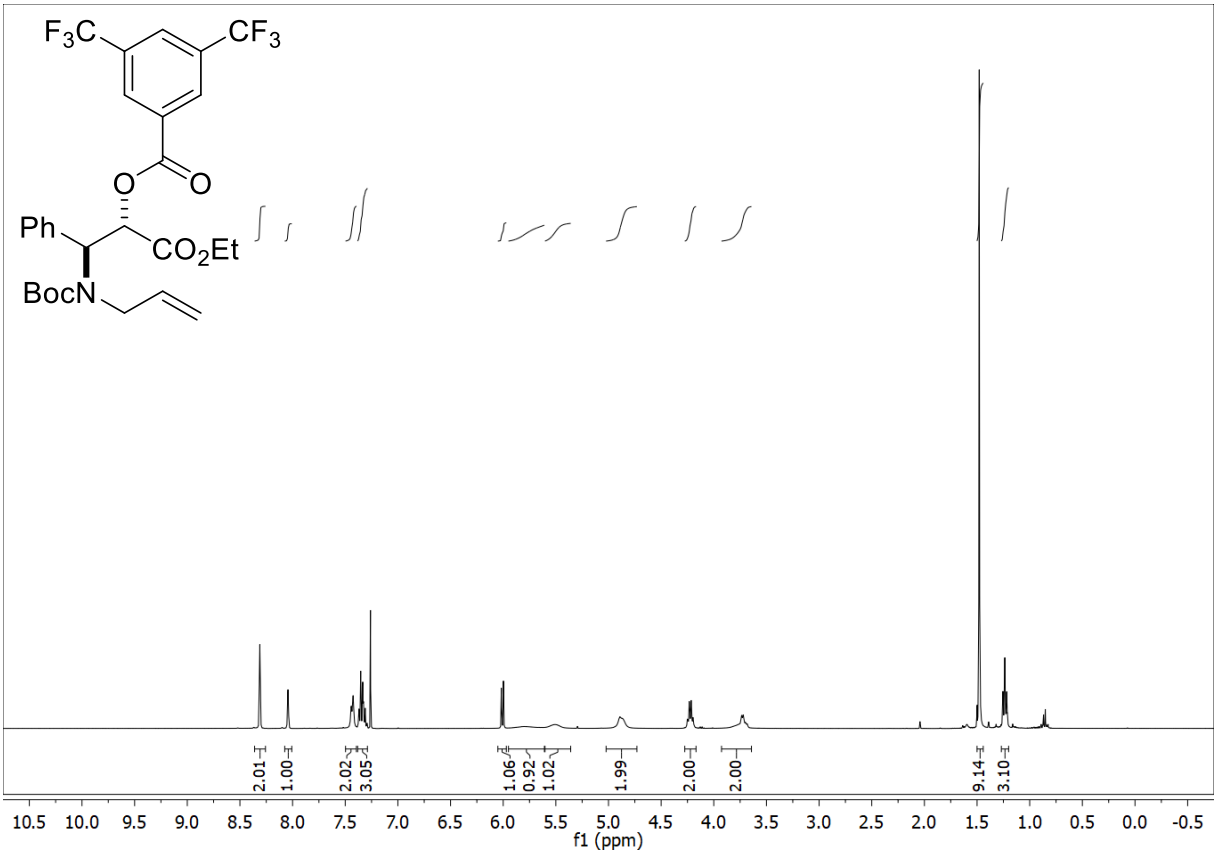
rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-isopropoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (45j)

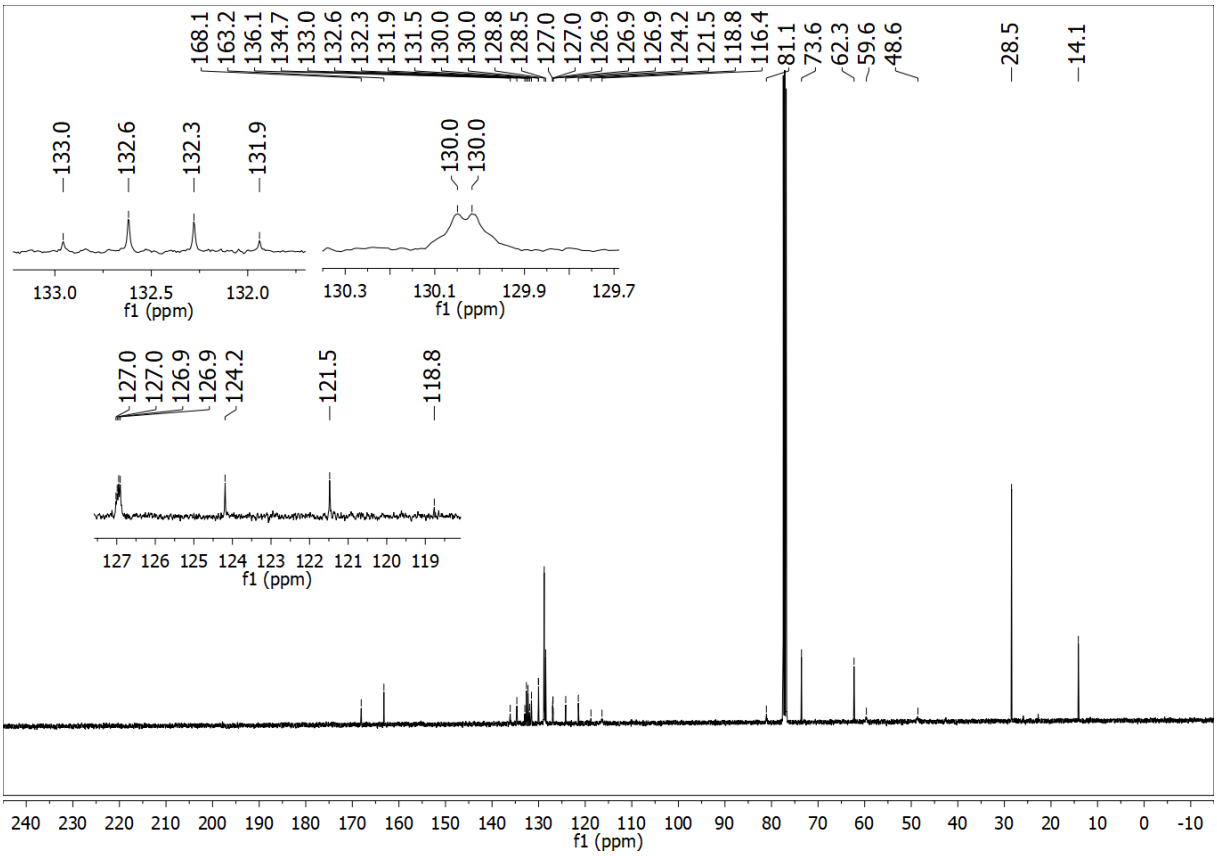


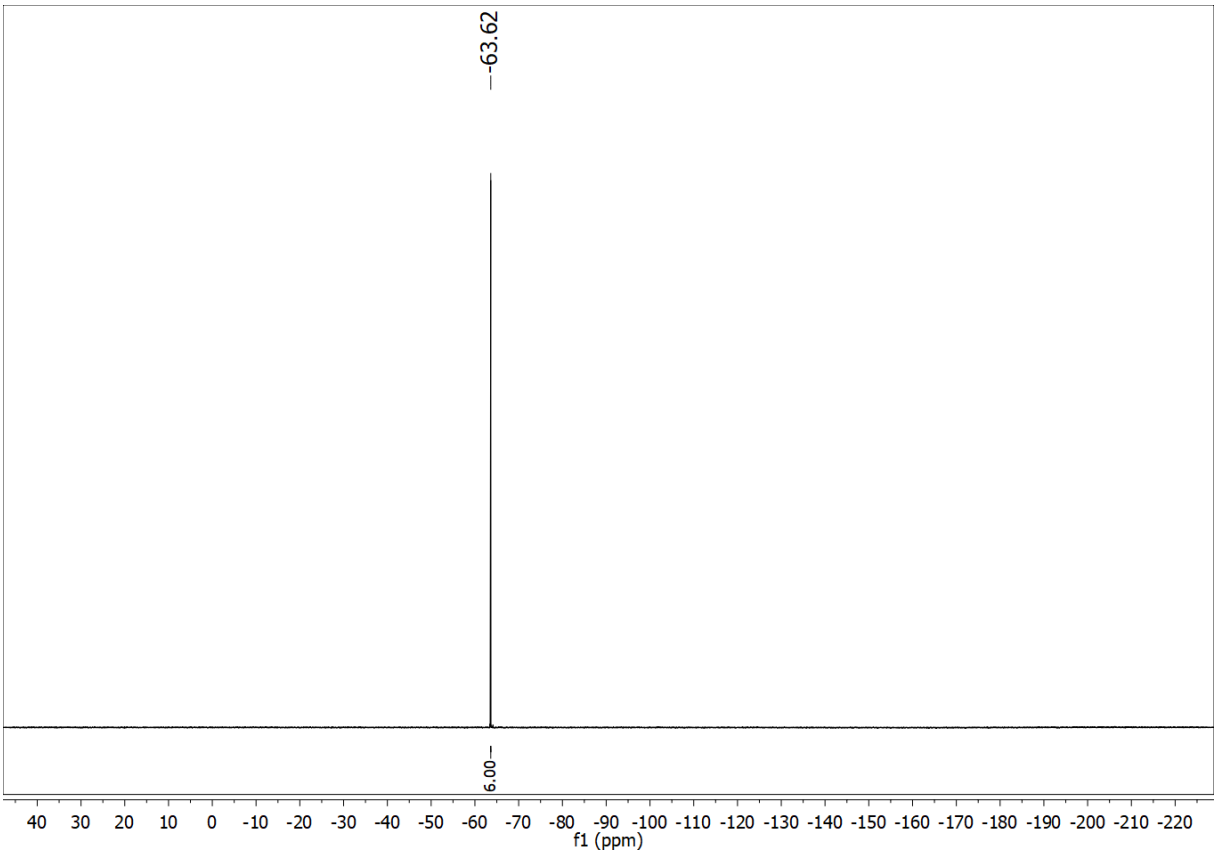


NMR-Solvent: $CDCl_3$

rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47a)

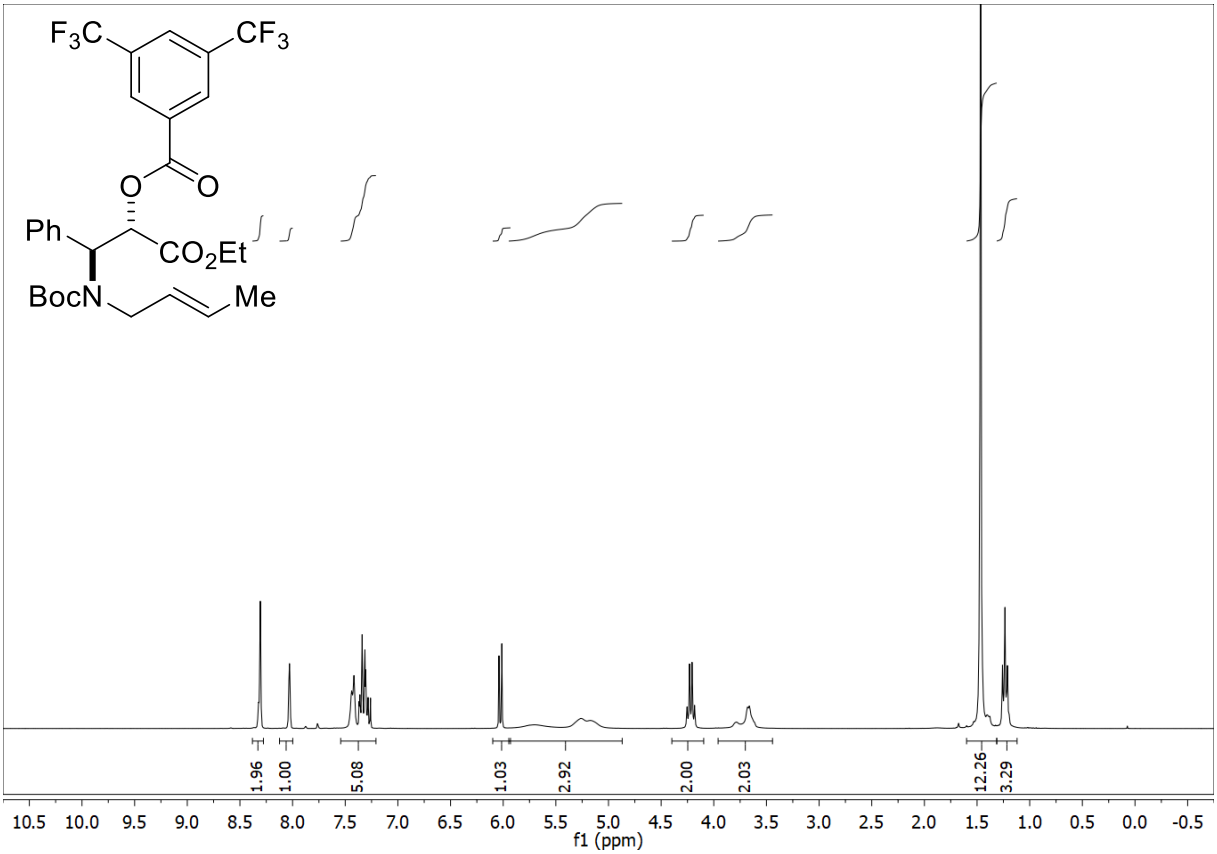


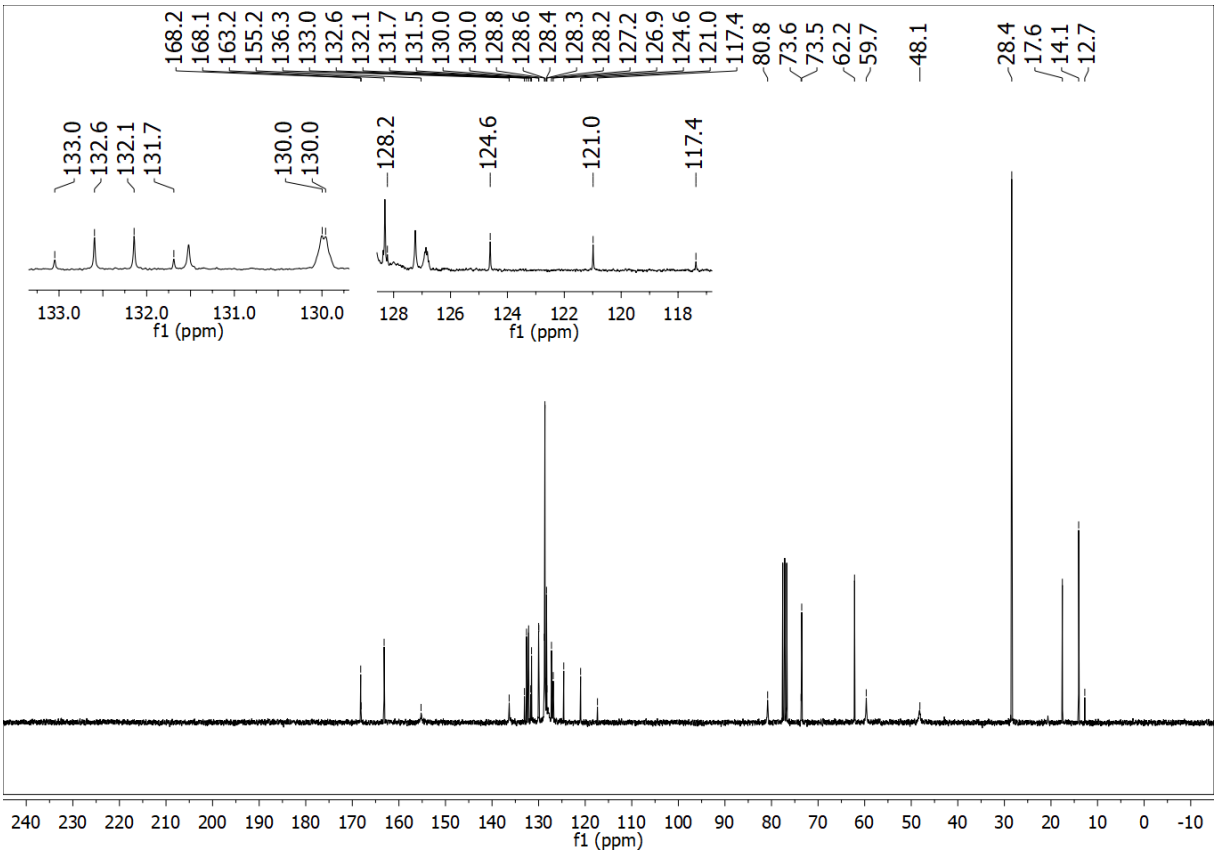


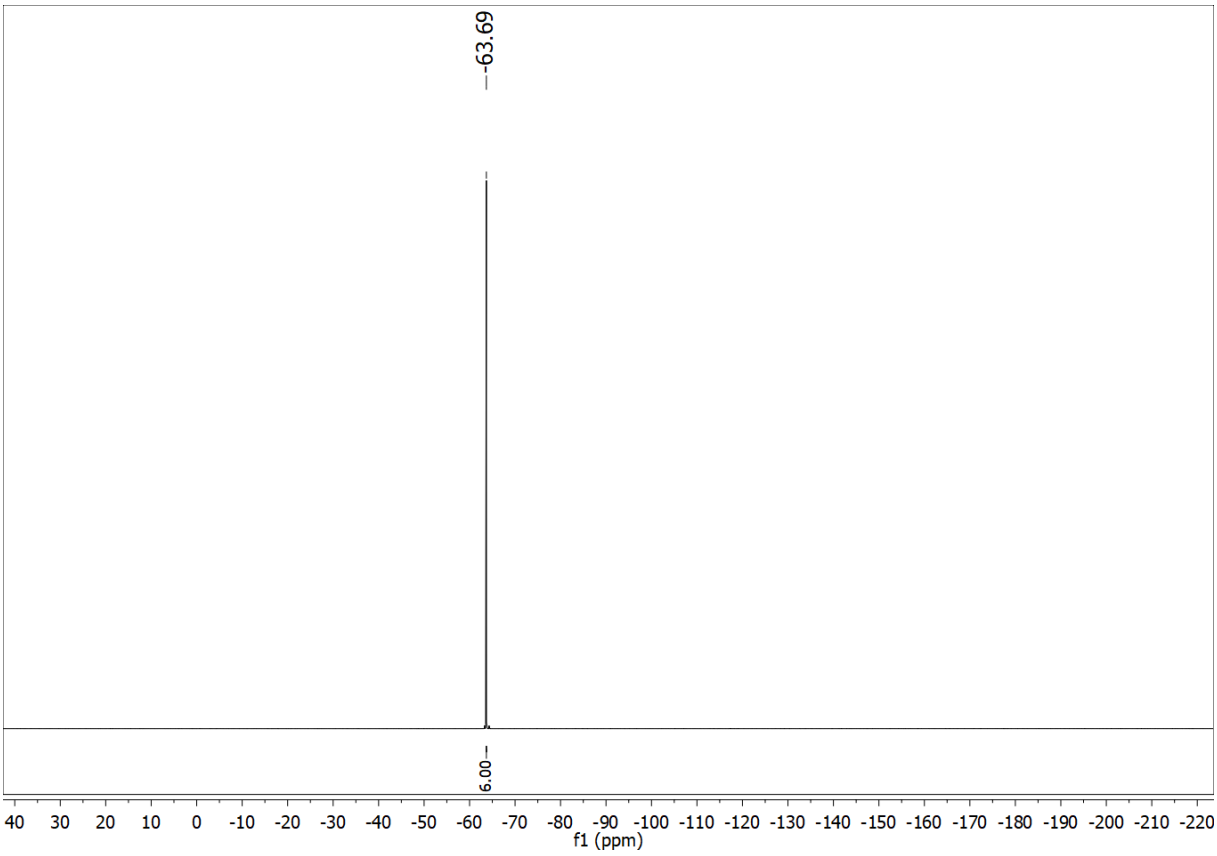


NMR-Solvent: $CDCl_3$

rac. (1*S*,2*S*)-1-(((*E*)-but-2-en-1-yl)(*tert*-butoxycarbonyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47b)

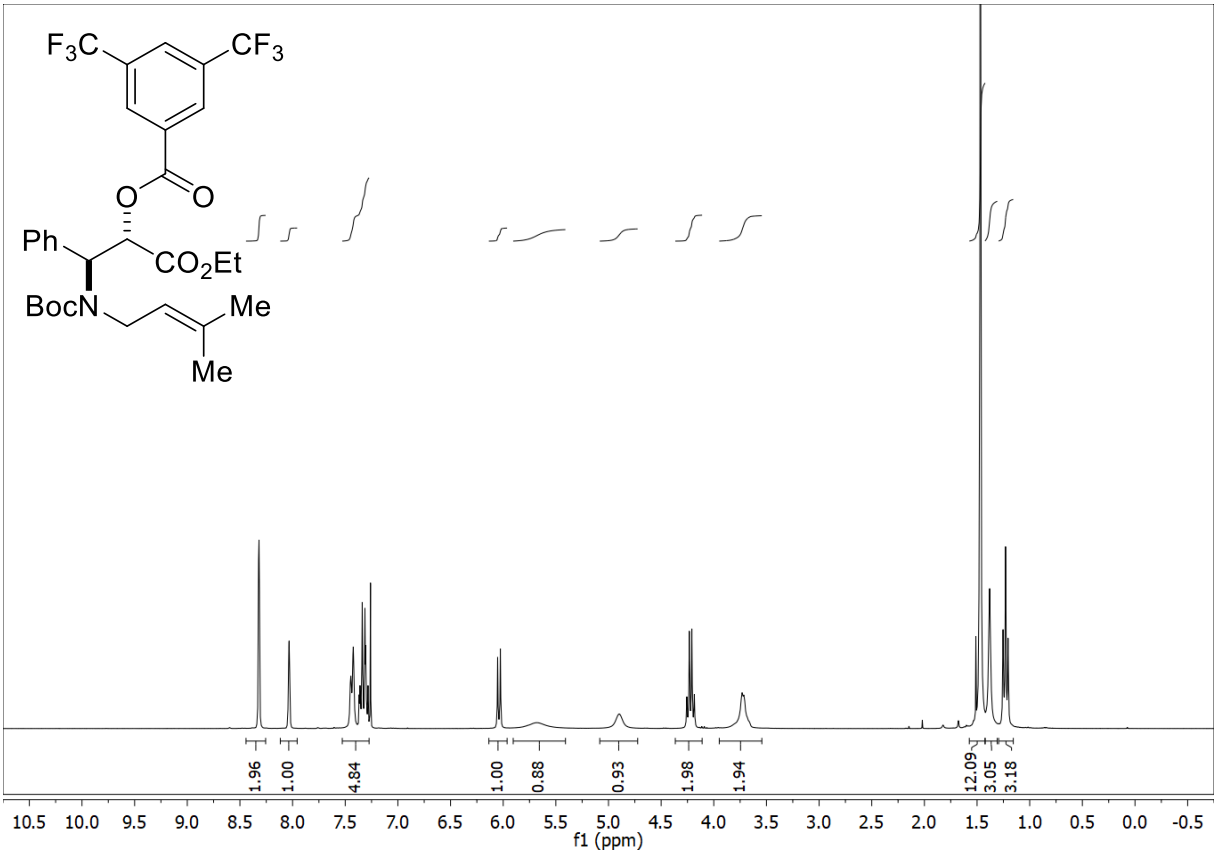


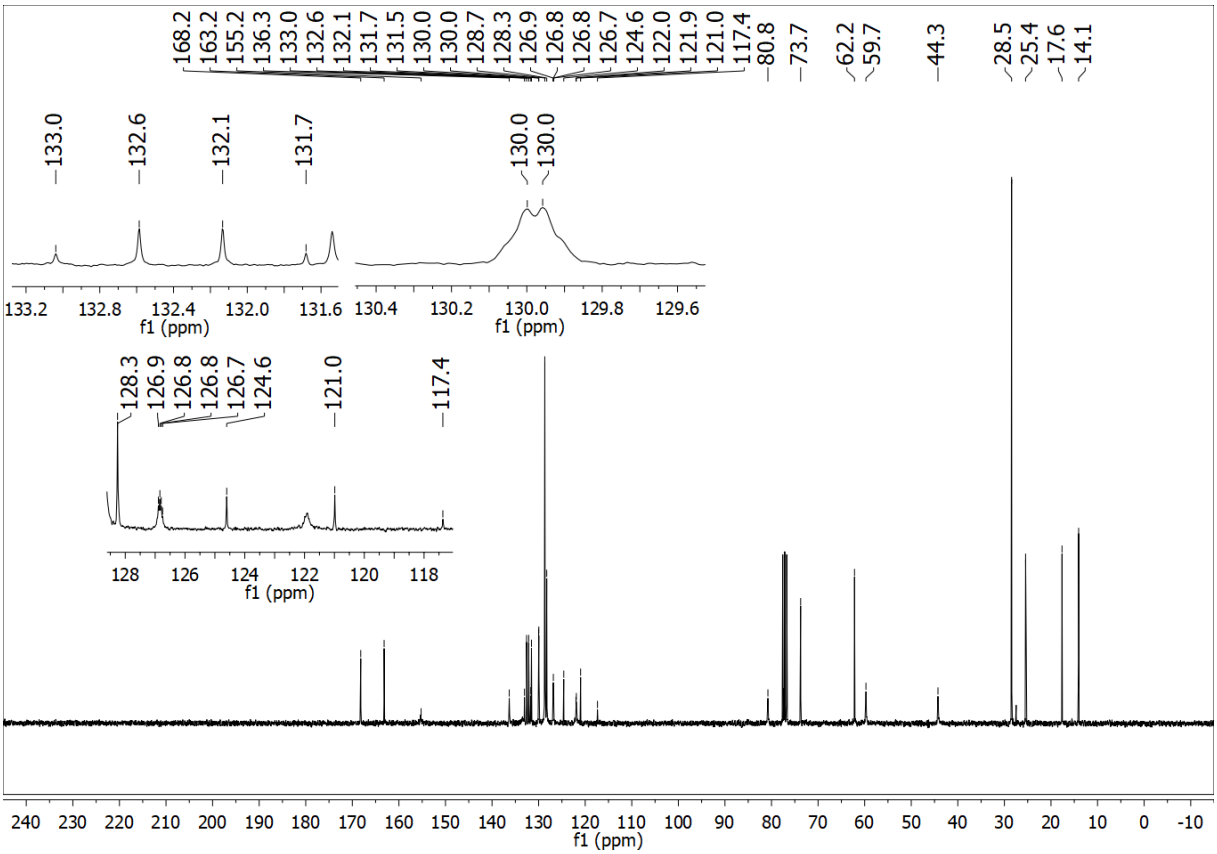


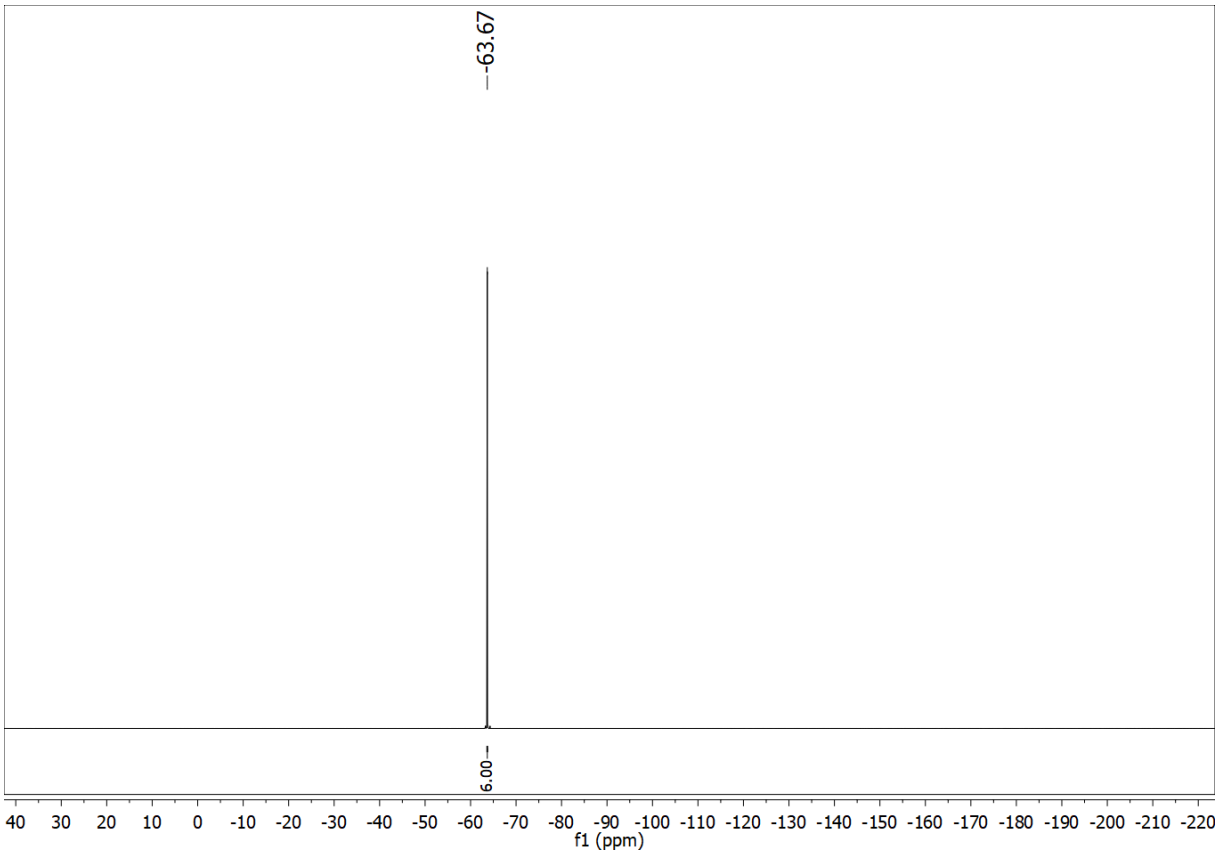


NMR-Solvent: $CDCl_3$

rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(3-methylbut-2-en-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47c)

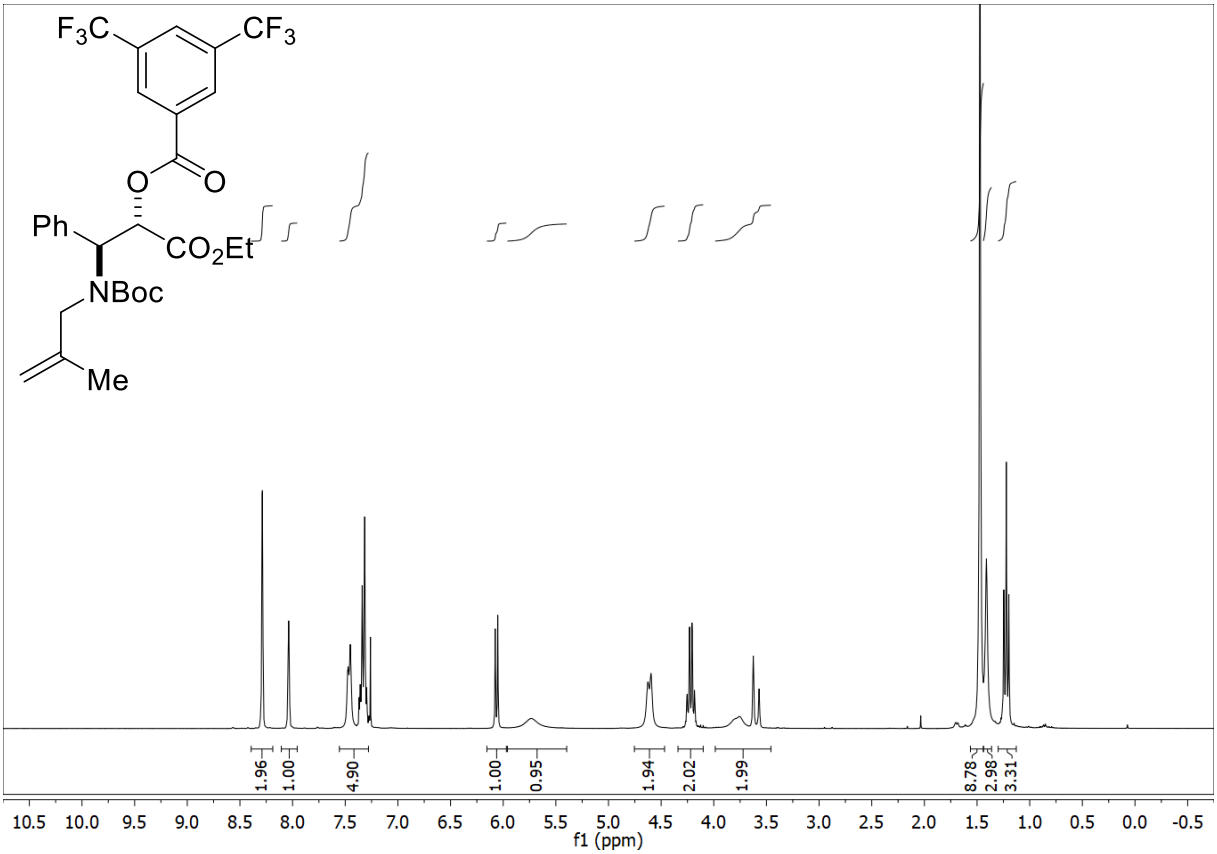


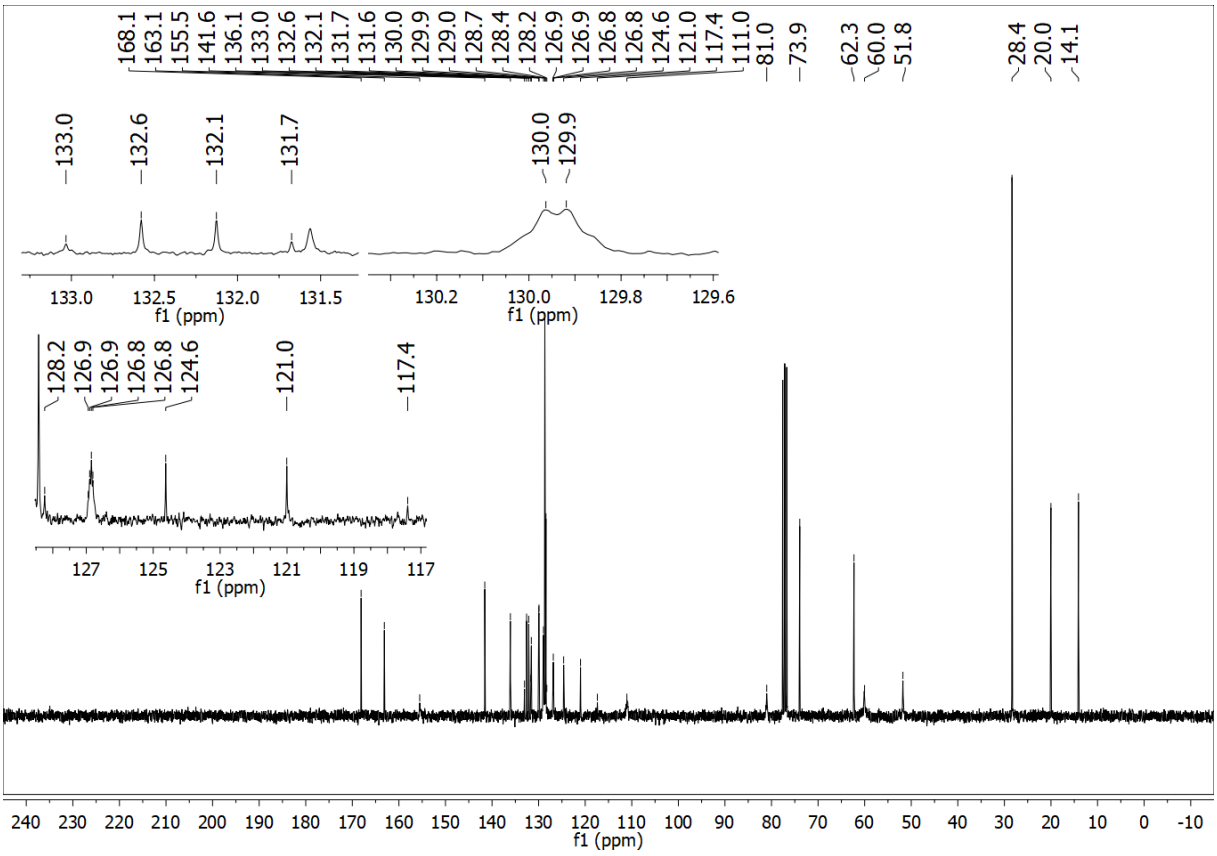


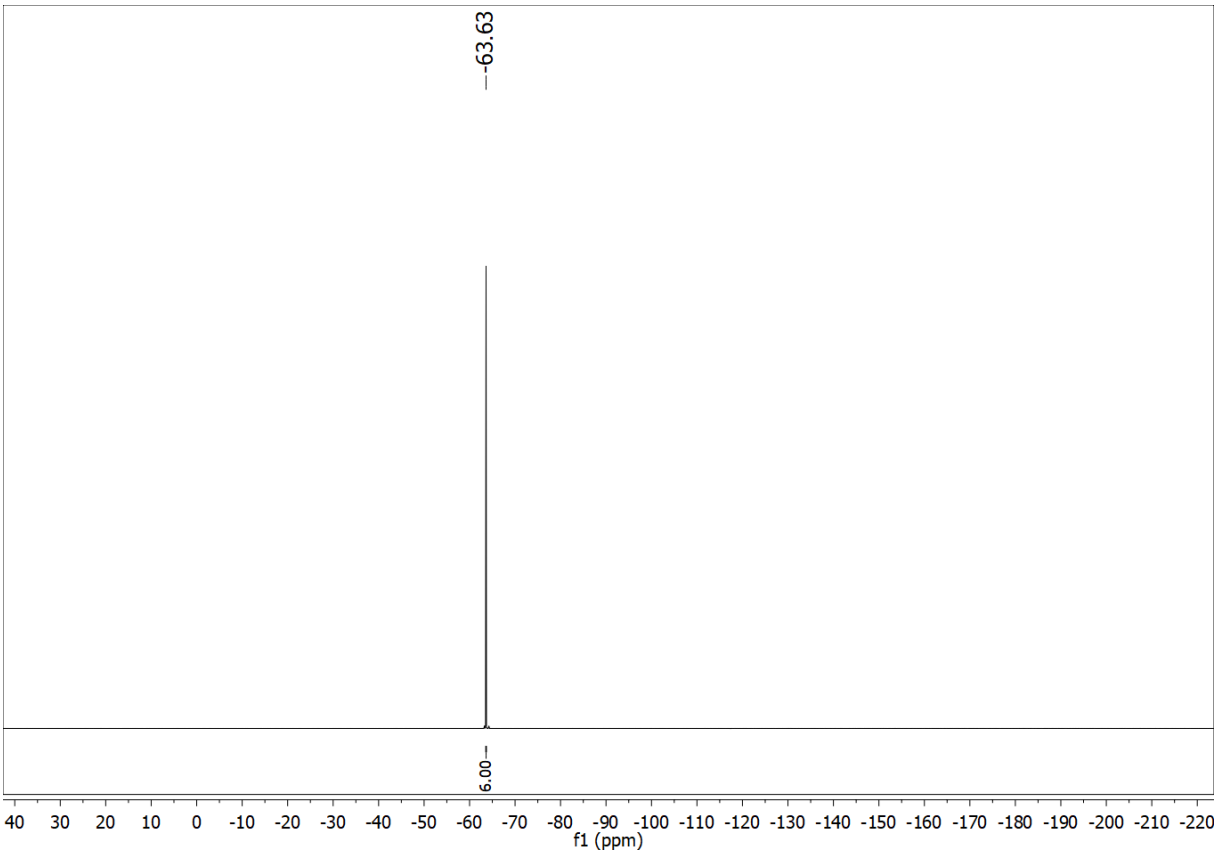


NMR-Solvent: $CDCl_3$

rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(2-methylallyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47d)

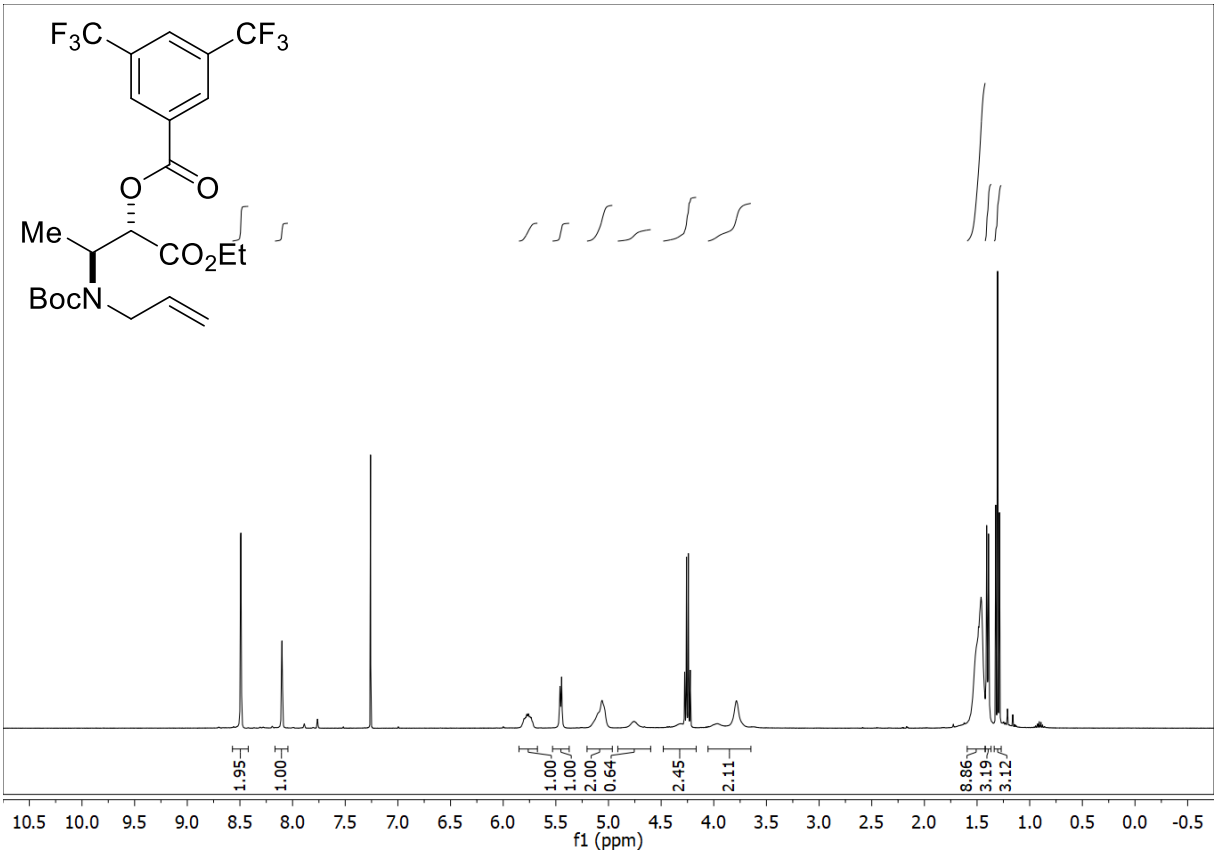


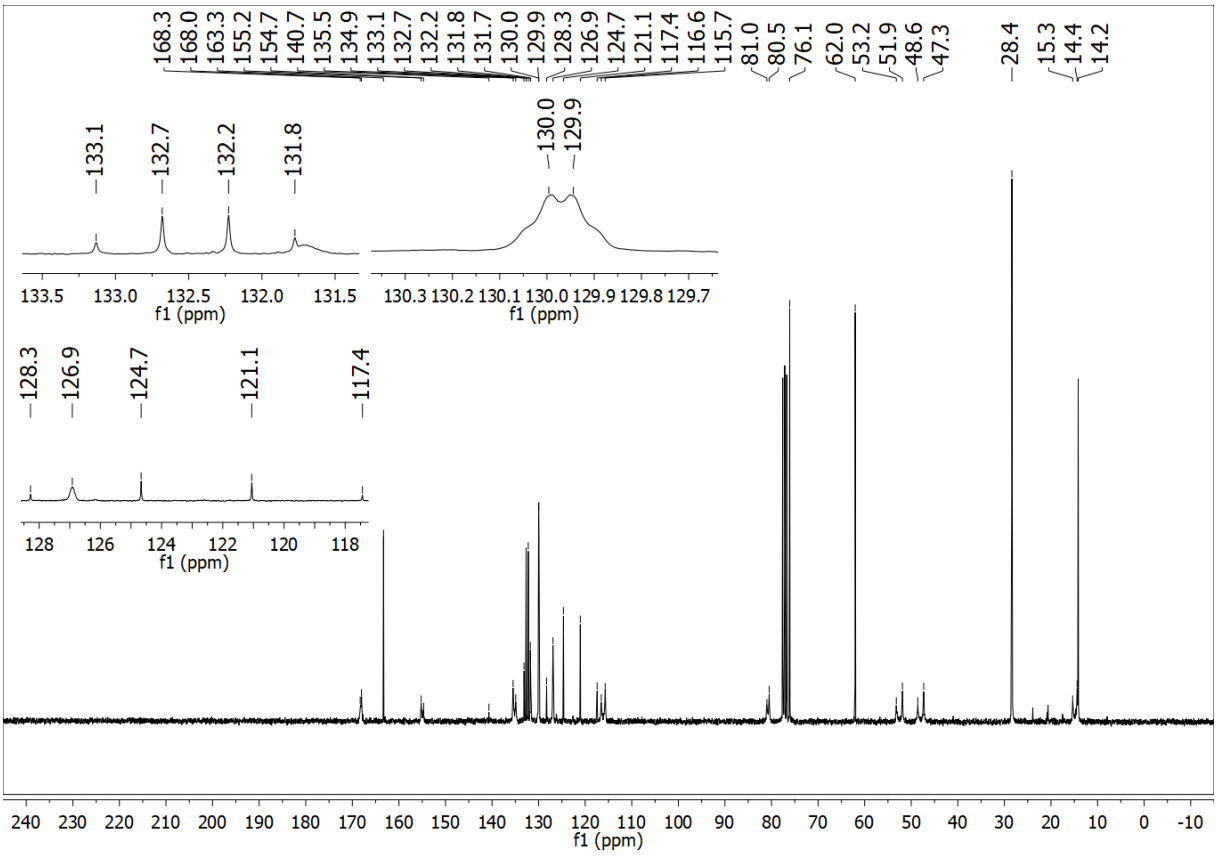


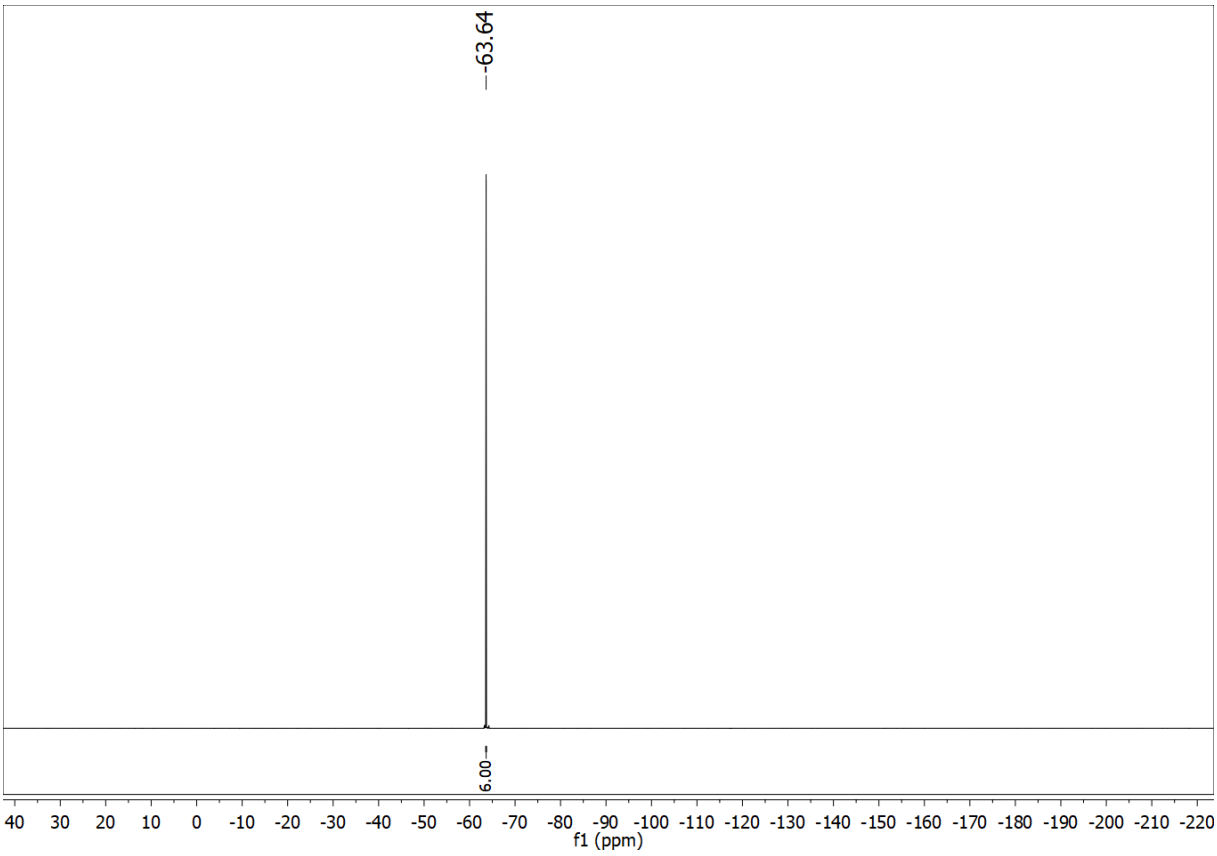


NMR-Solvent: $CDCl_3$

rac. (2*S*,3*S*)-3-(allyl(*tert*-butoxycarbonyl)amino)-1-ethoxy-1-oxobutan-2-yl 3,5-bis(trifluoromethyl)benzoate (47e)

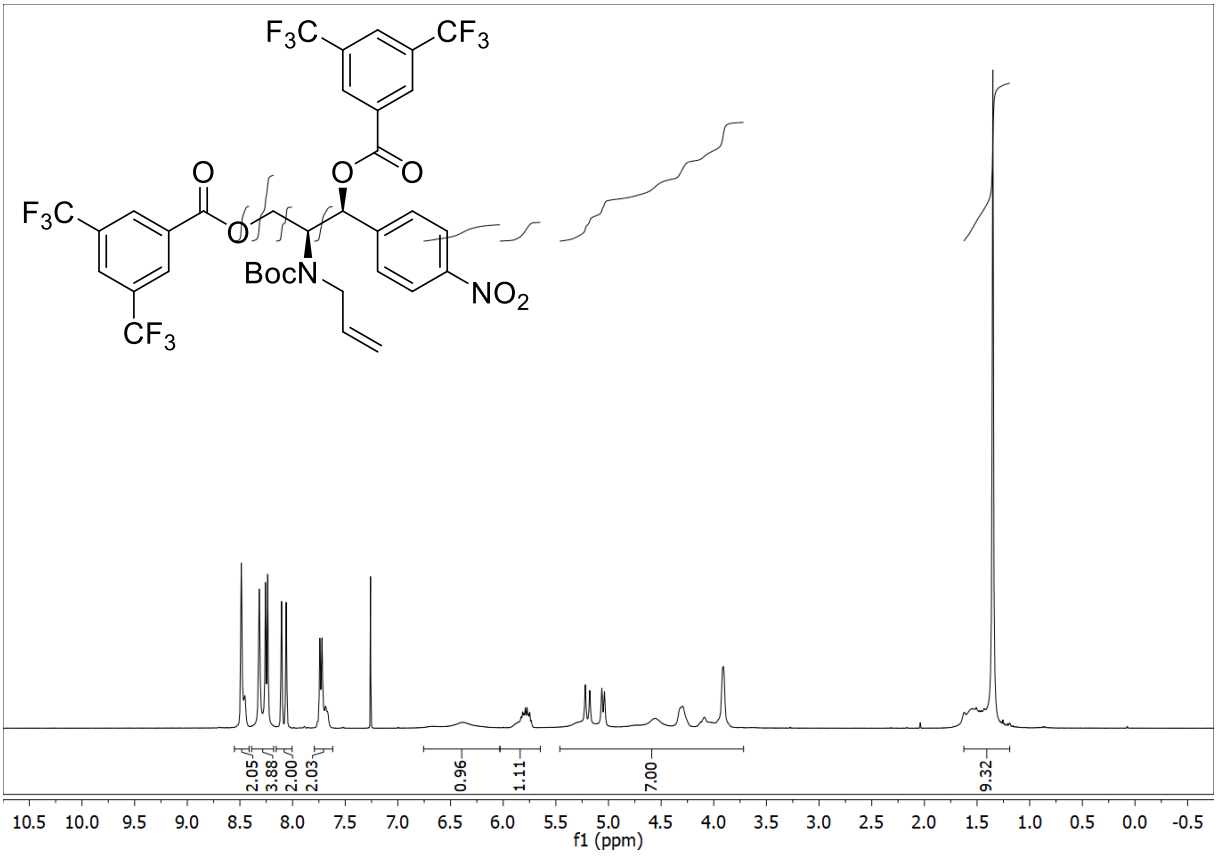


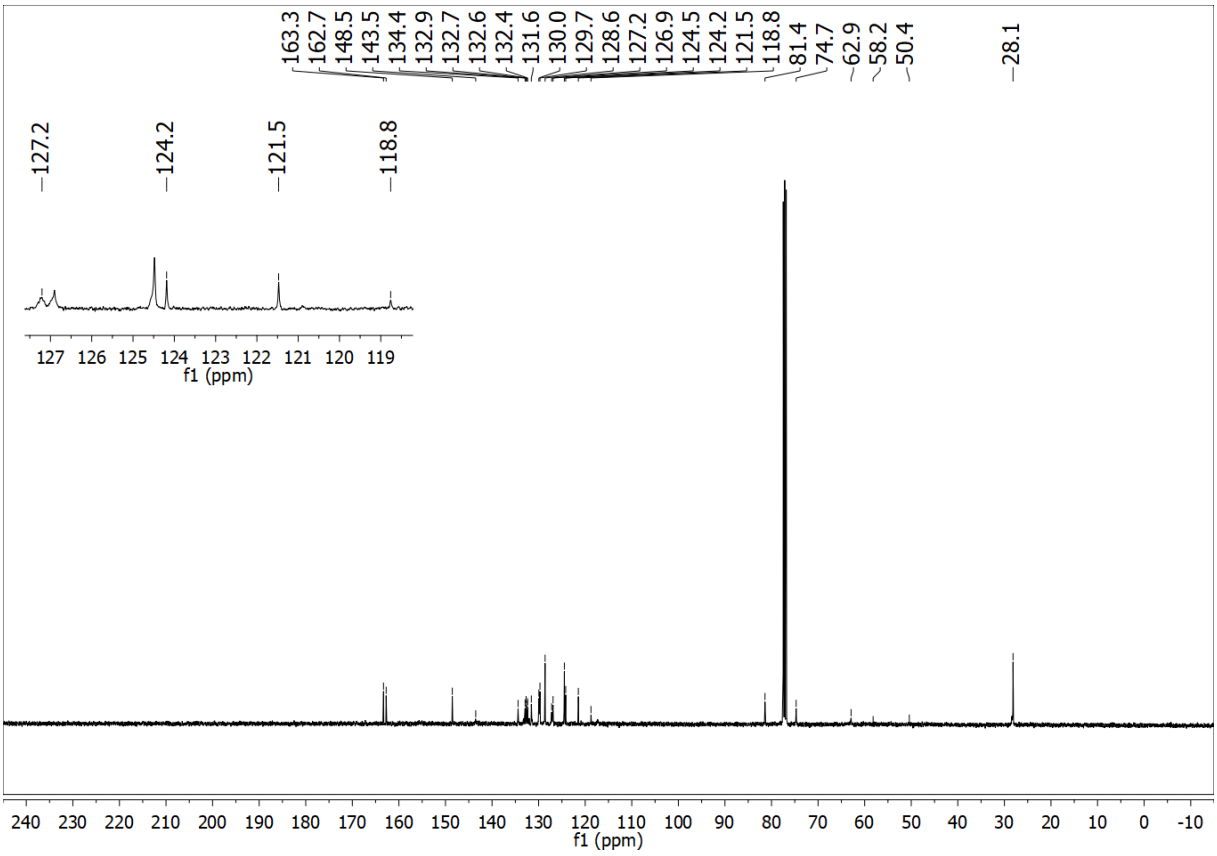


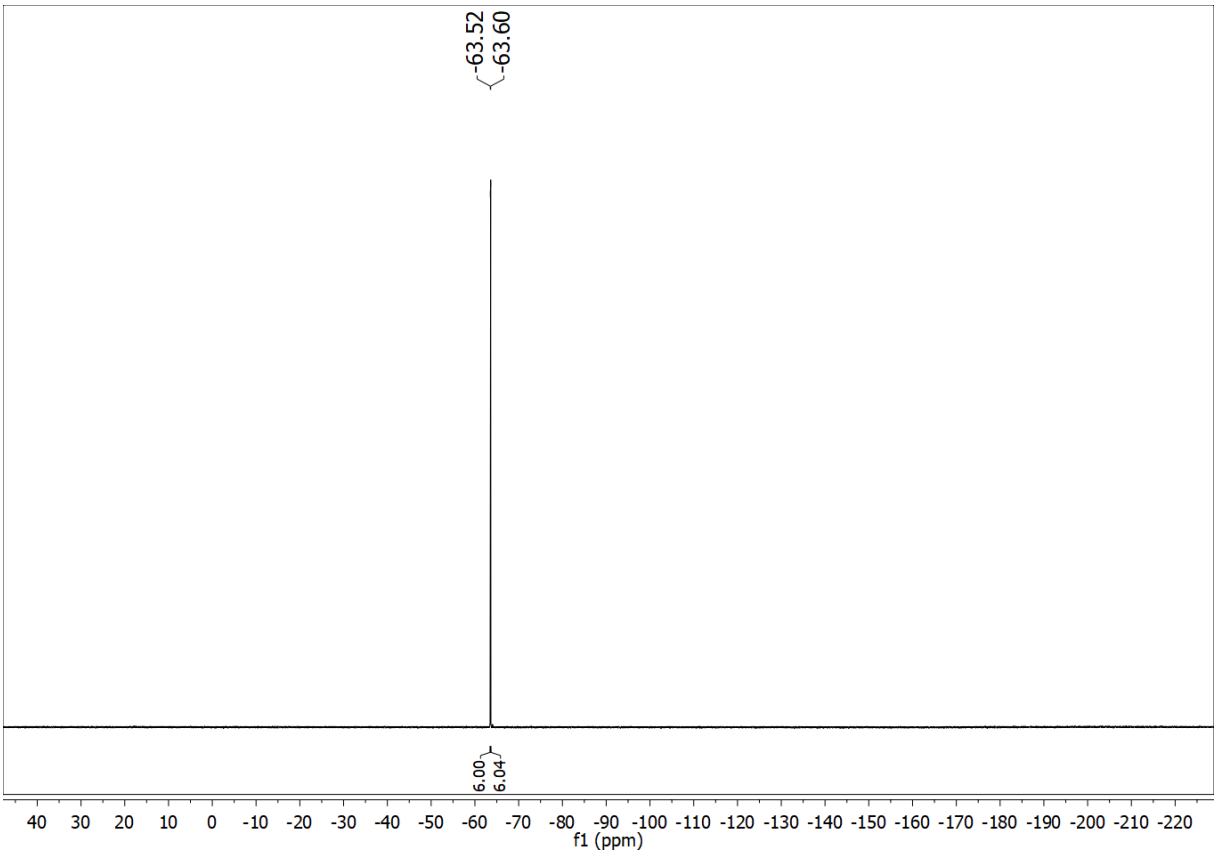


NMR-Solvent: $CDCl_3$

(1*S*,2*S*)-2-(allyl(*tert*-butoxycarbonyl)amino)-1-(4-nitrophenyl)propane-1,3-diyl bis(3,5-bis(trifluoro-methyl)benzoate) (47f)

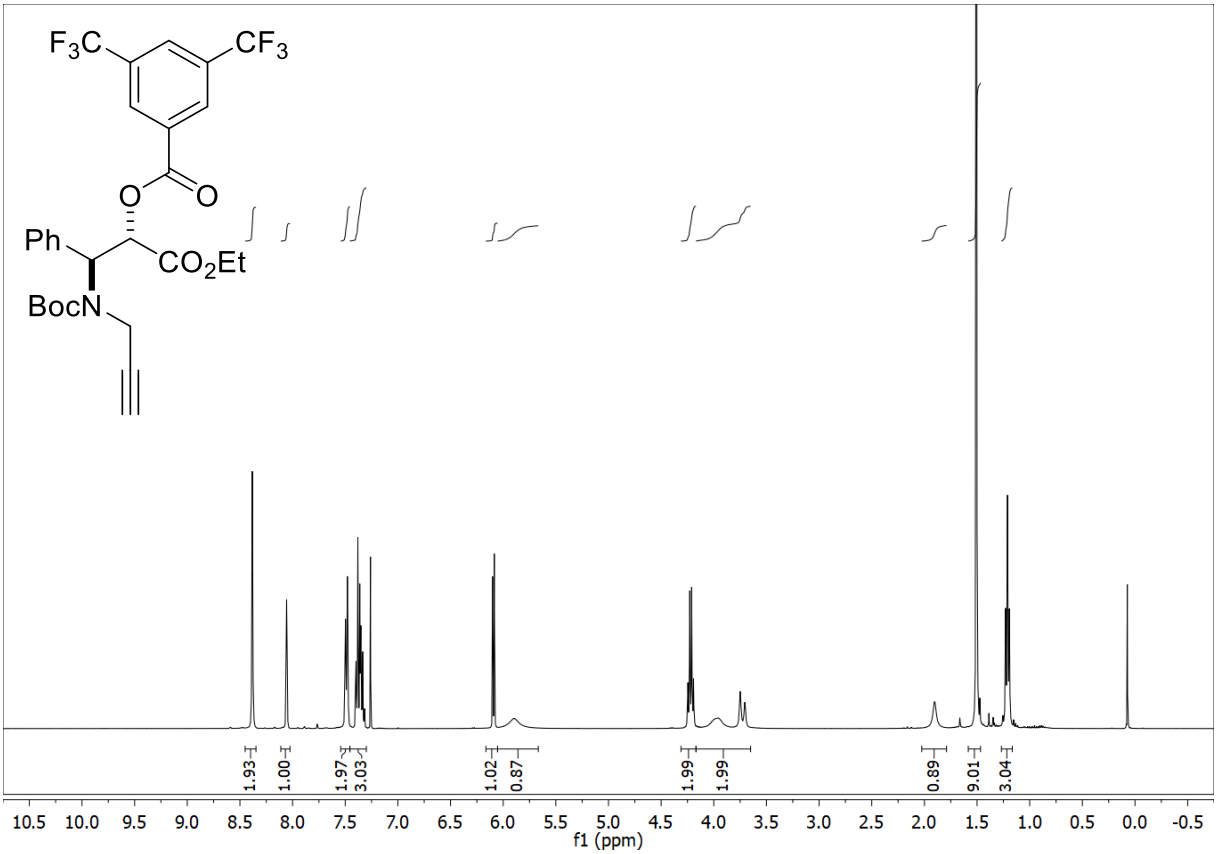


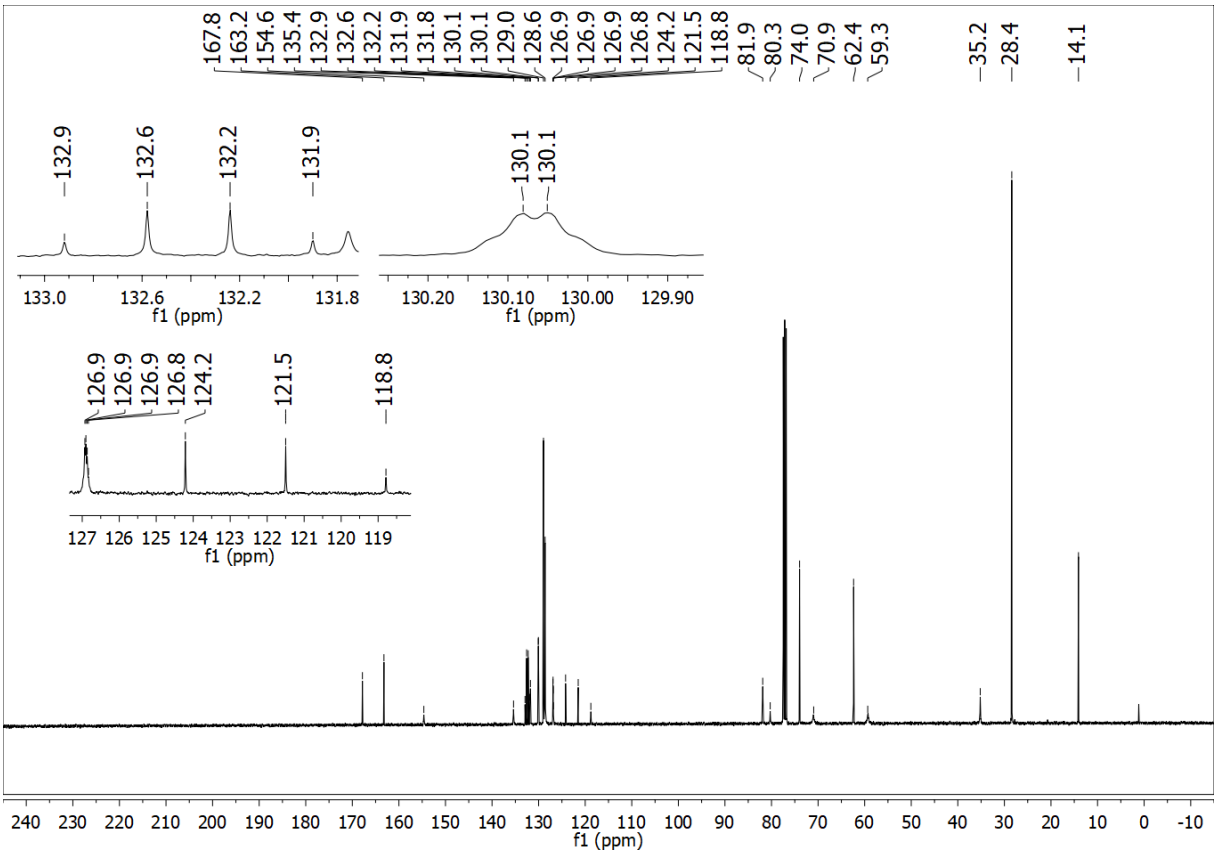


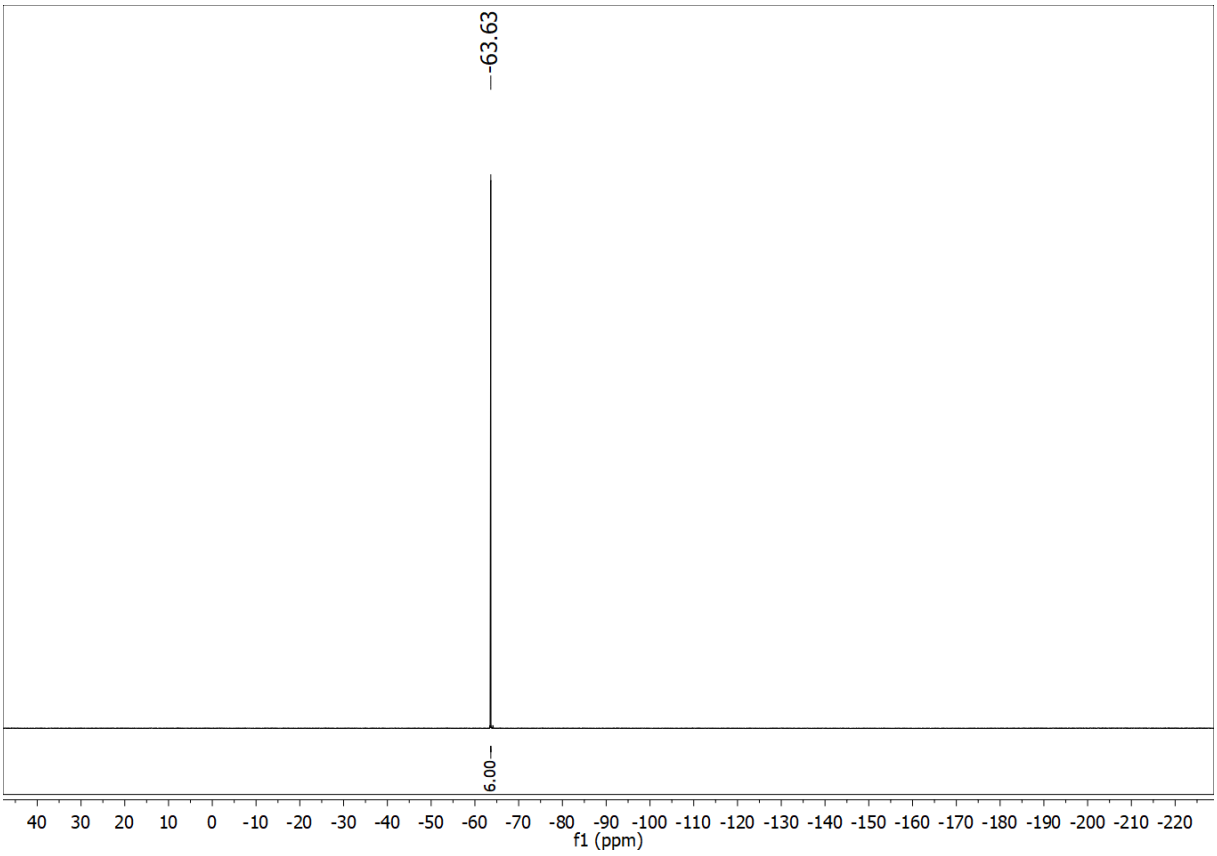


NMR-Solvent: $CDCl_3$

rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47g)

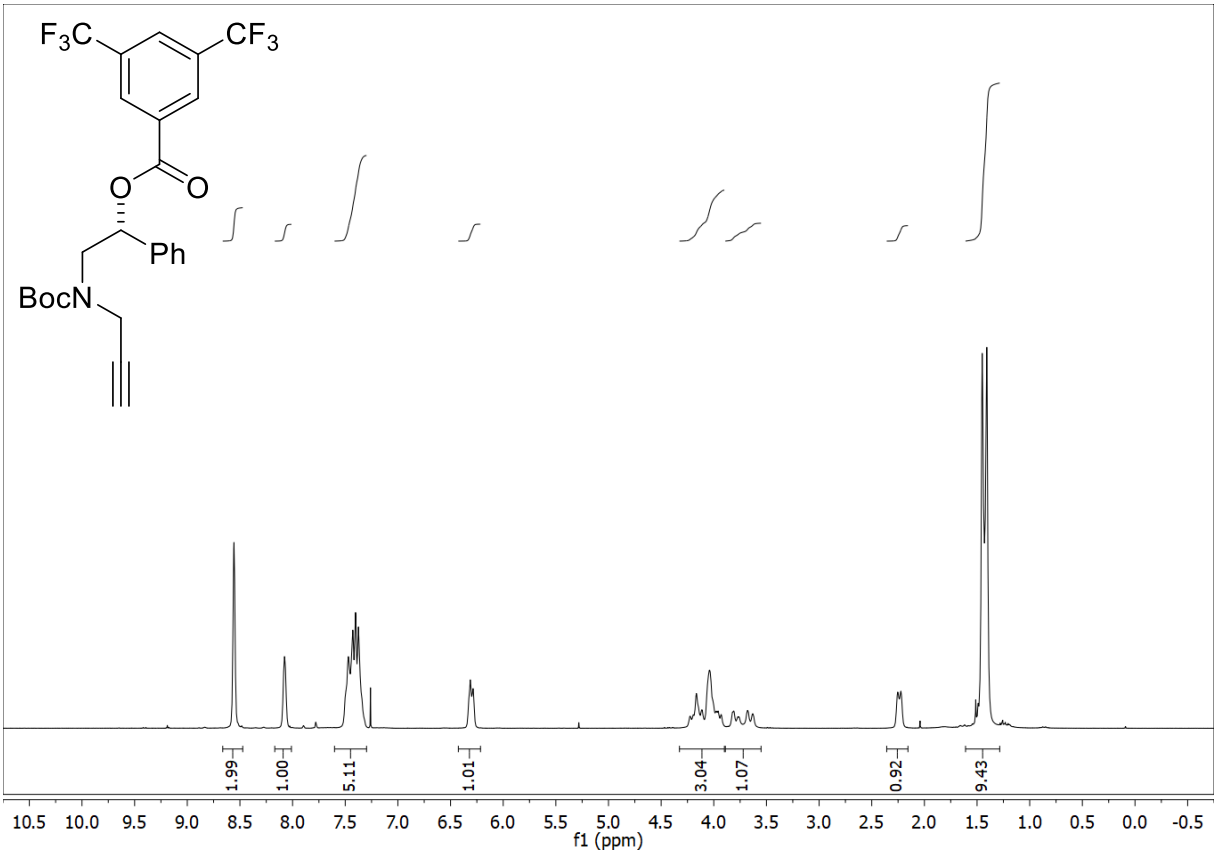


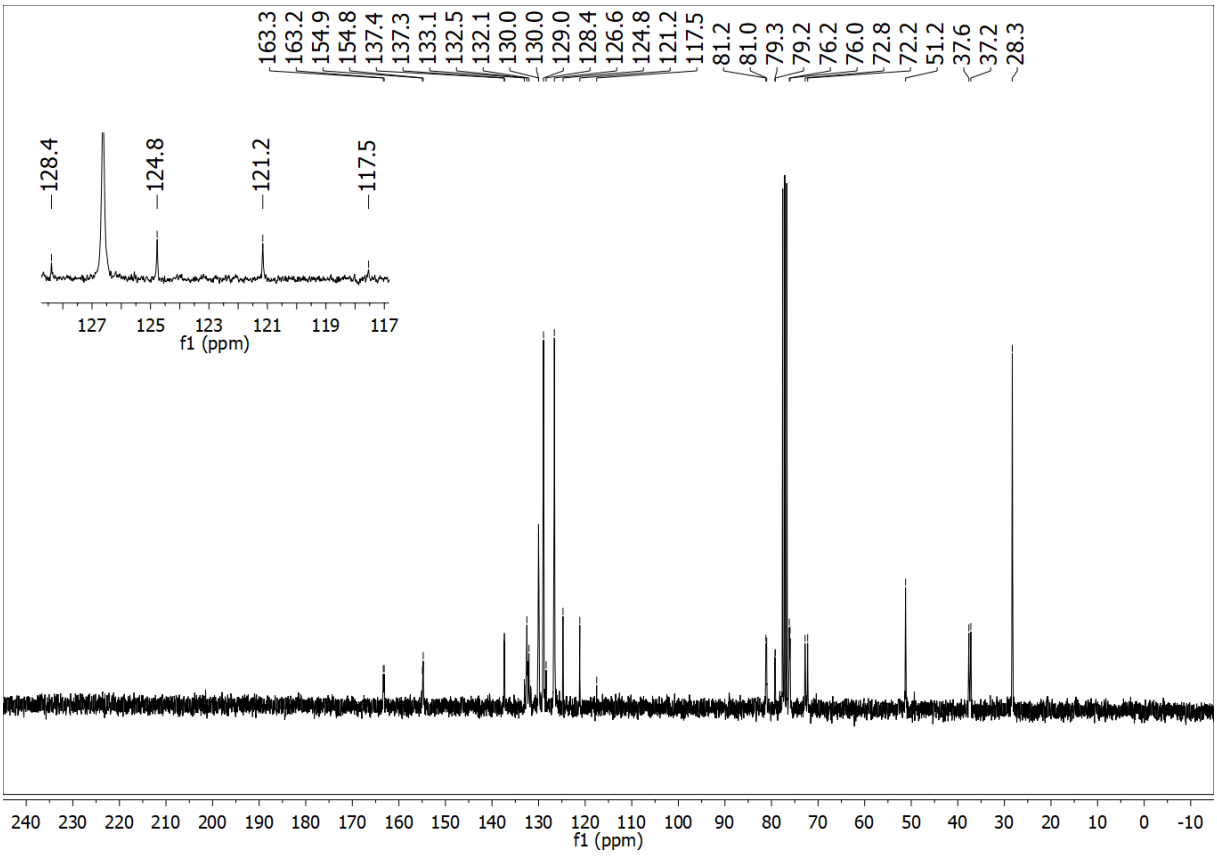


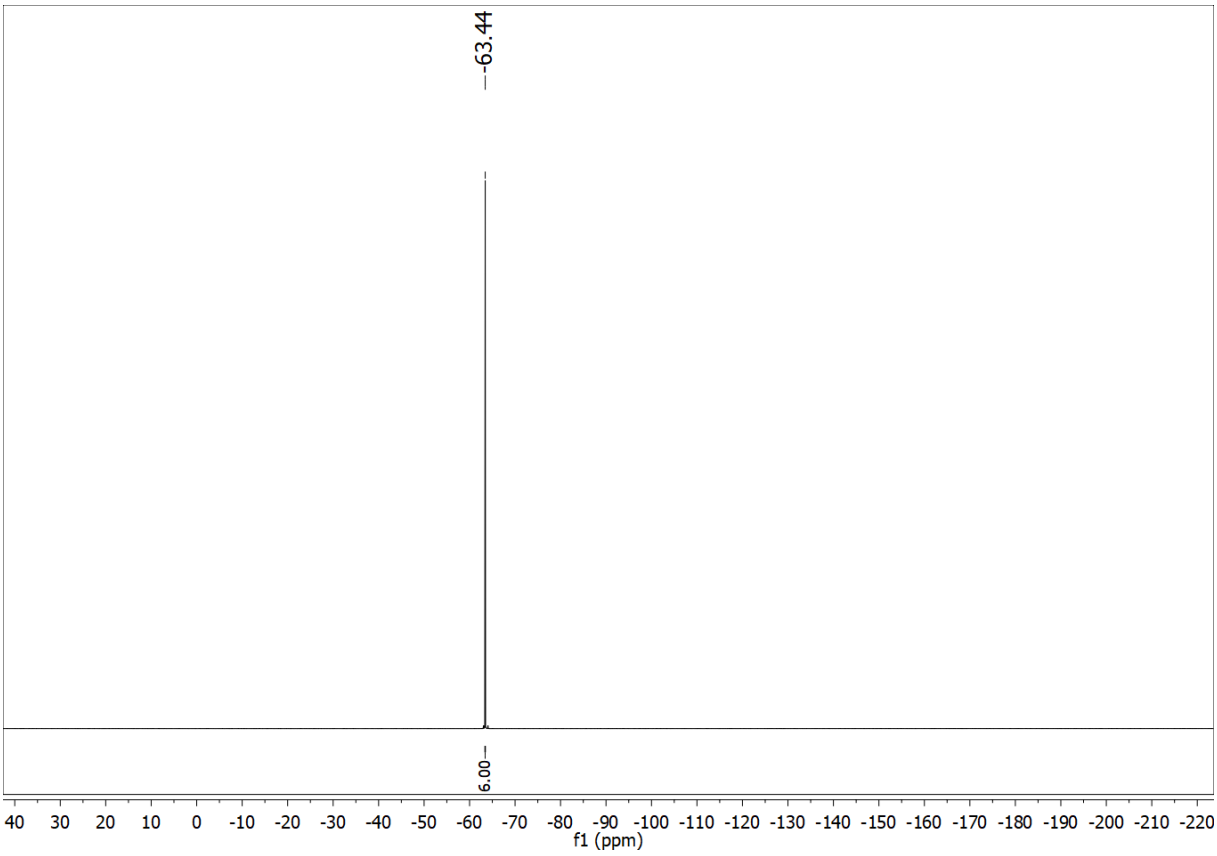


NMR-Solvent: $CDCl_3$

2-((*tert*-Butoxycarbonyl)(prop-2-yn-1-yl)amino)-1-phenylethyl 3,5-bis(trifluoromethyl)benzoate (47h)

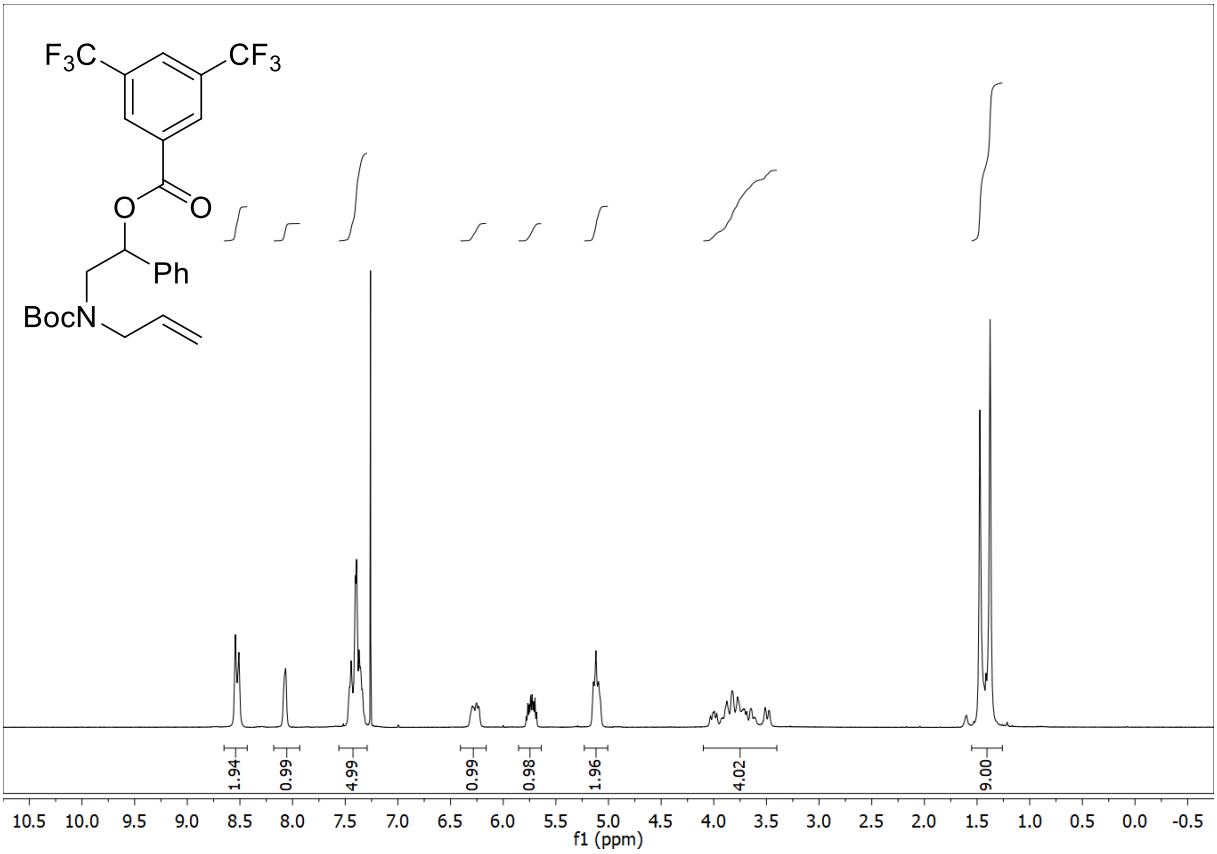


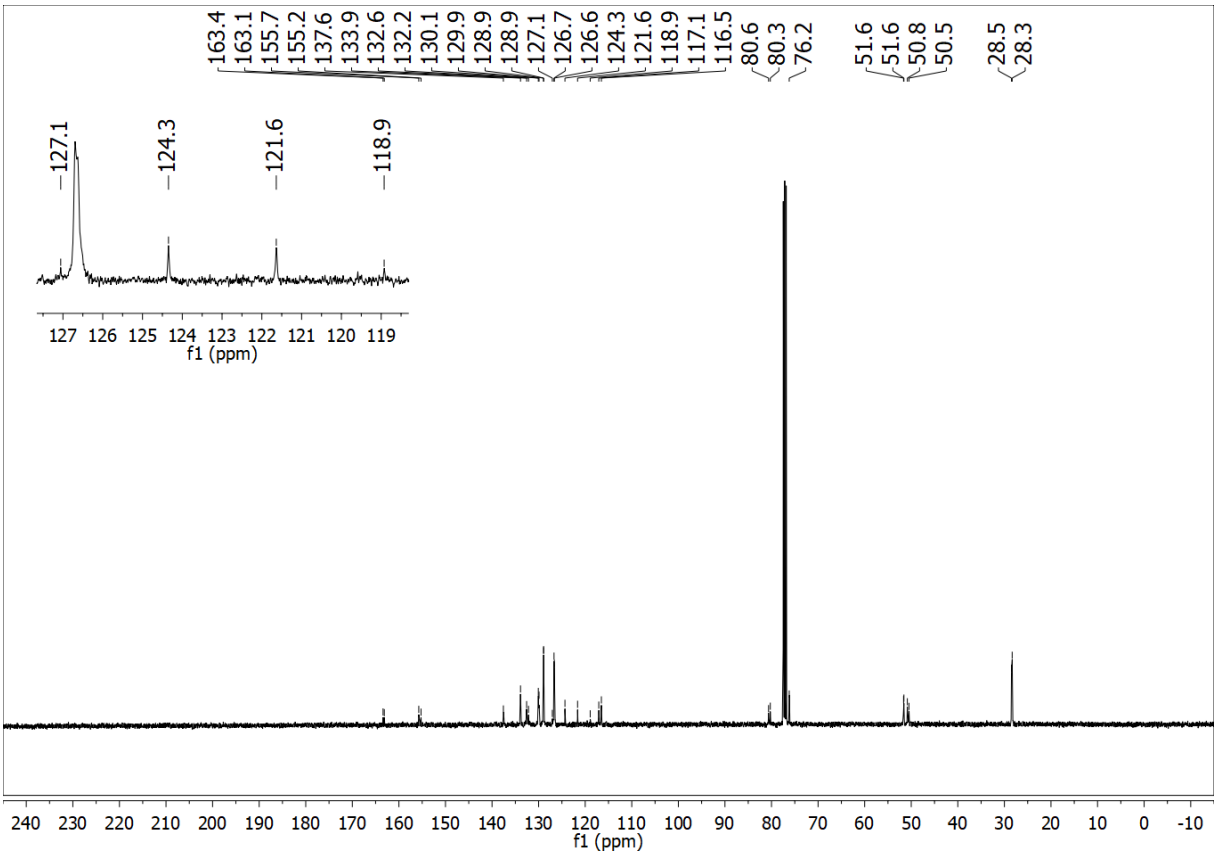


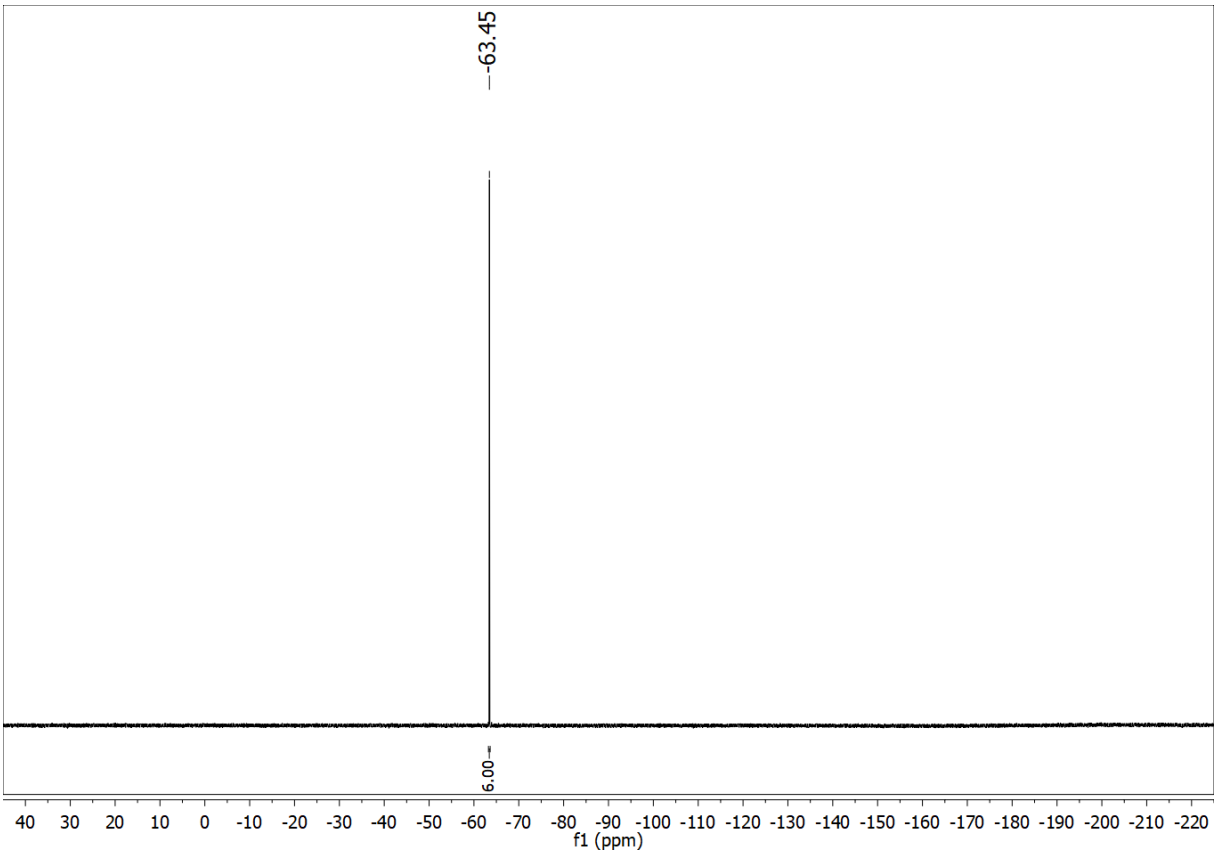


NMR-Solvent: $CDCl_3$

2-(Allyl(*tert*-butoxycarbonyl)amino)-1-phenylethyl 3,5-bis(trifluoromethyl)benzoate (47i)

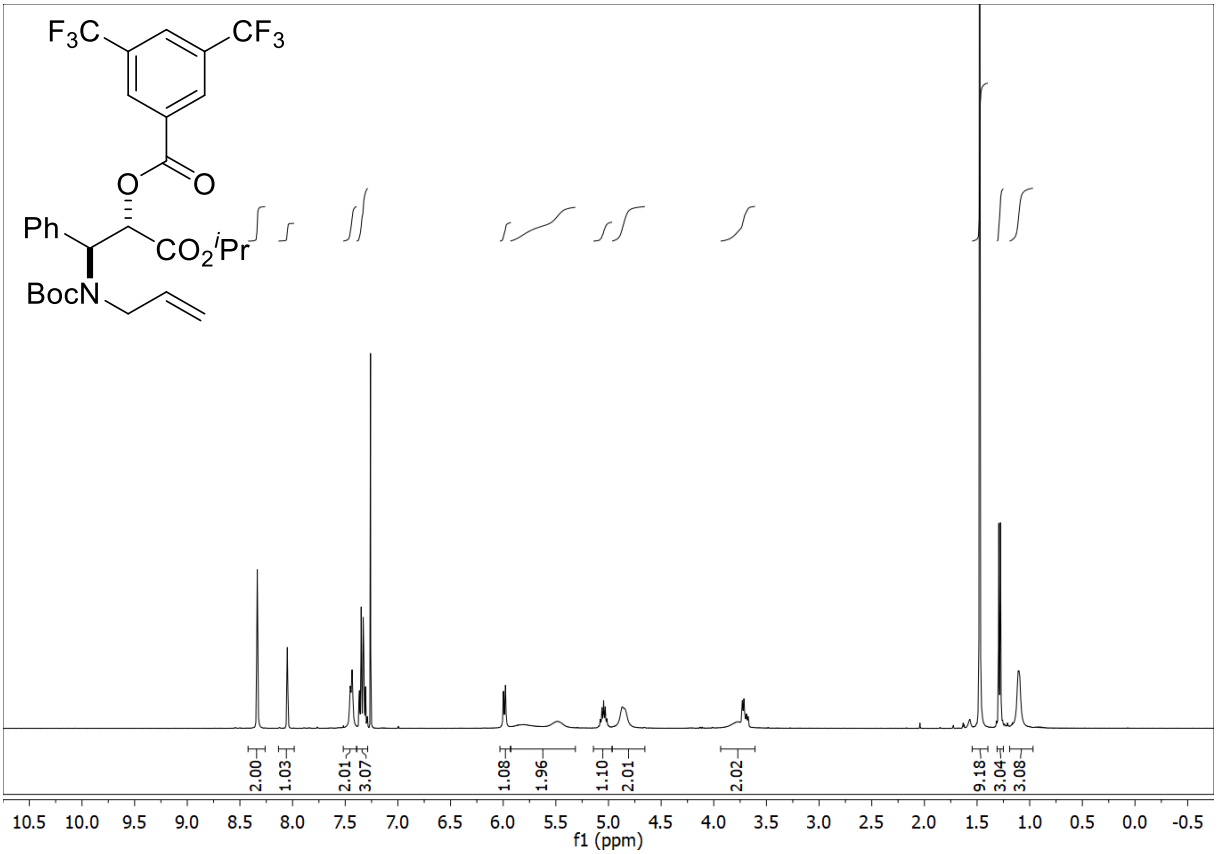


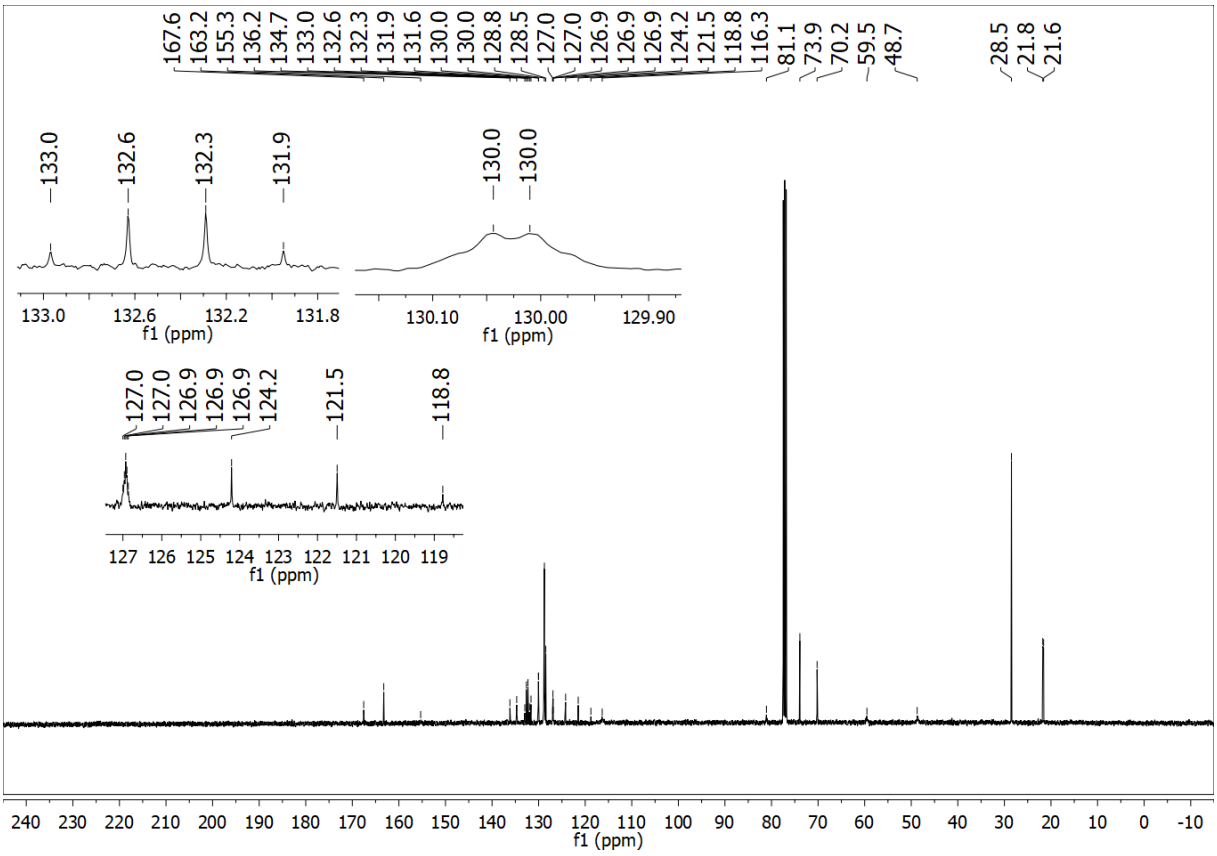


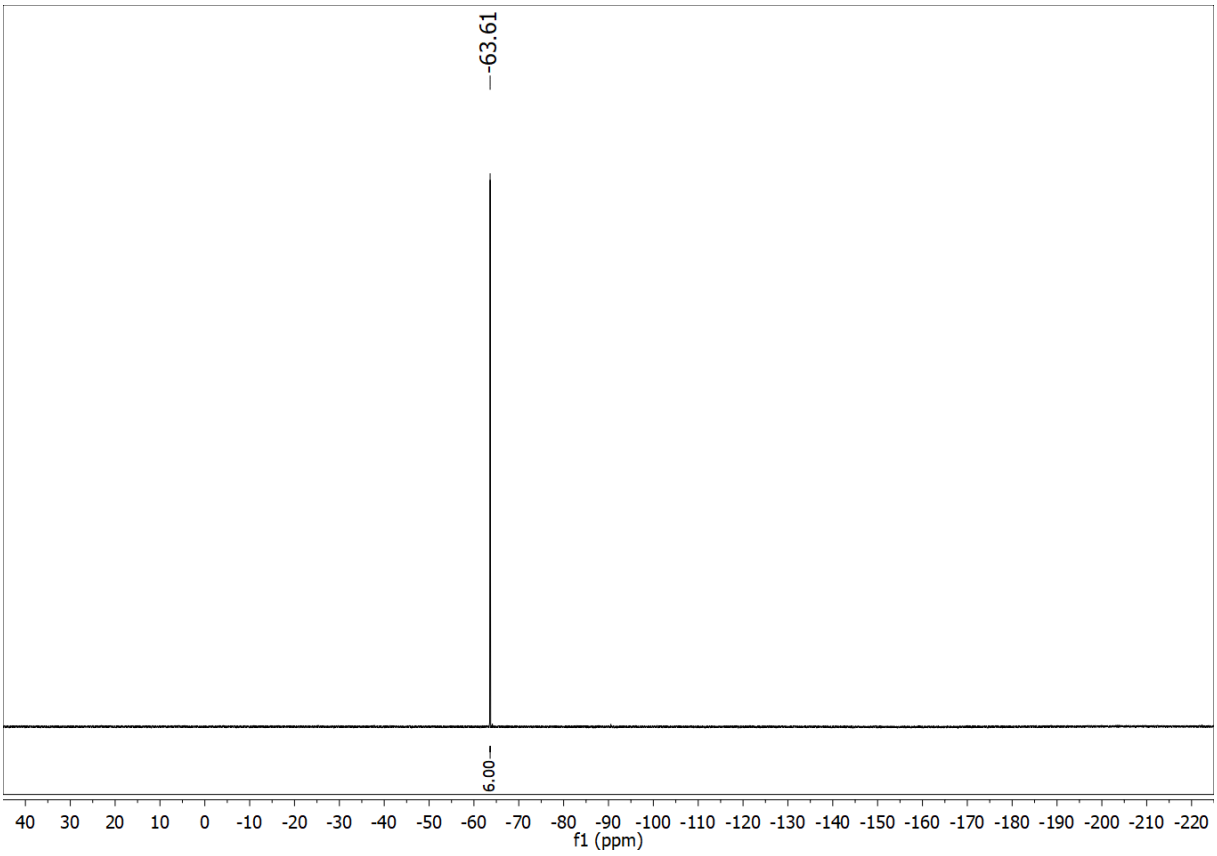


NMR-Solvent: $CDCl_3$

rac. (1*S*,2*S*)-1-(allyl(*tert*-butoxycarbonyl)amino)-3-isopropoxy-3-oxo-1-phenylpropan-2-yl 3,5-bis(trifluoromethyl)benzoate (47j)

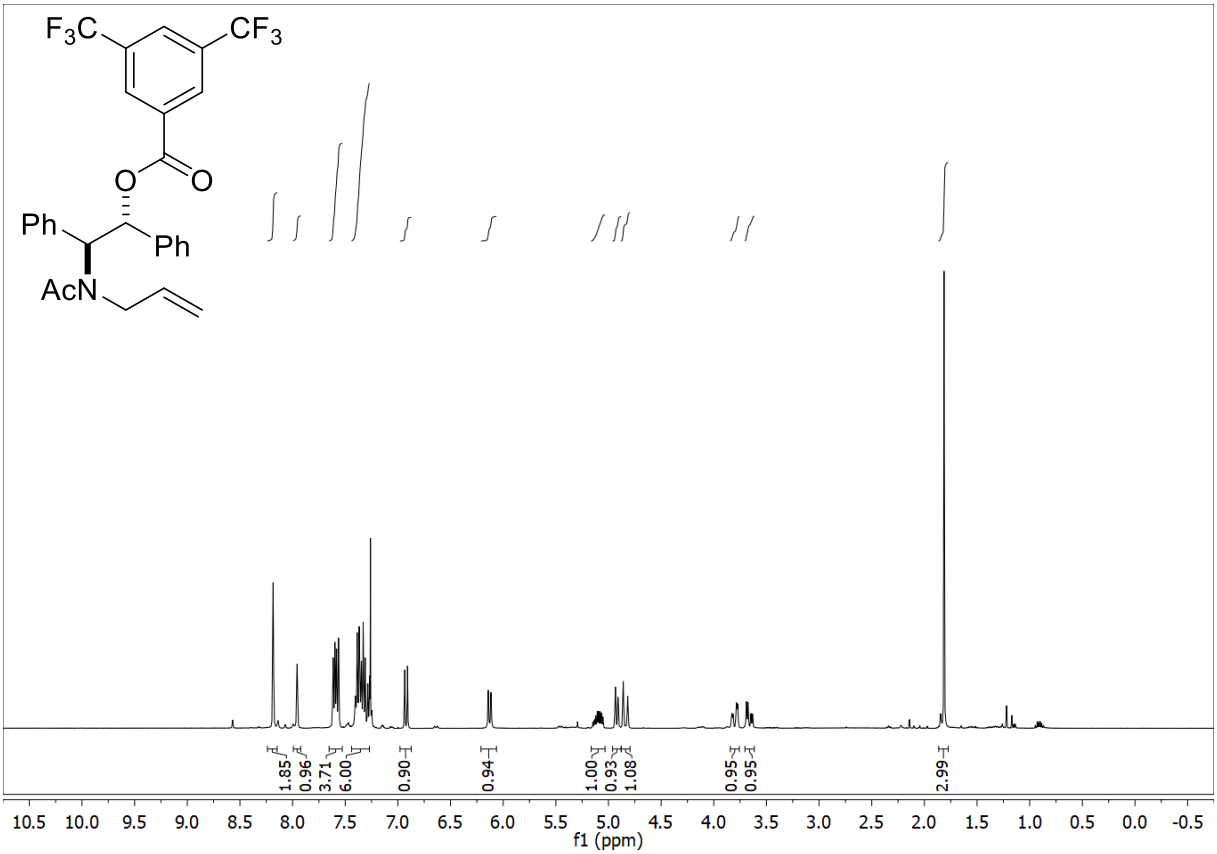


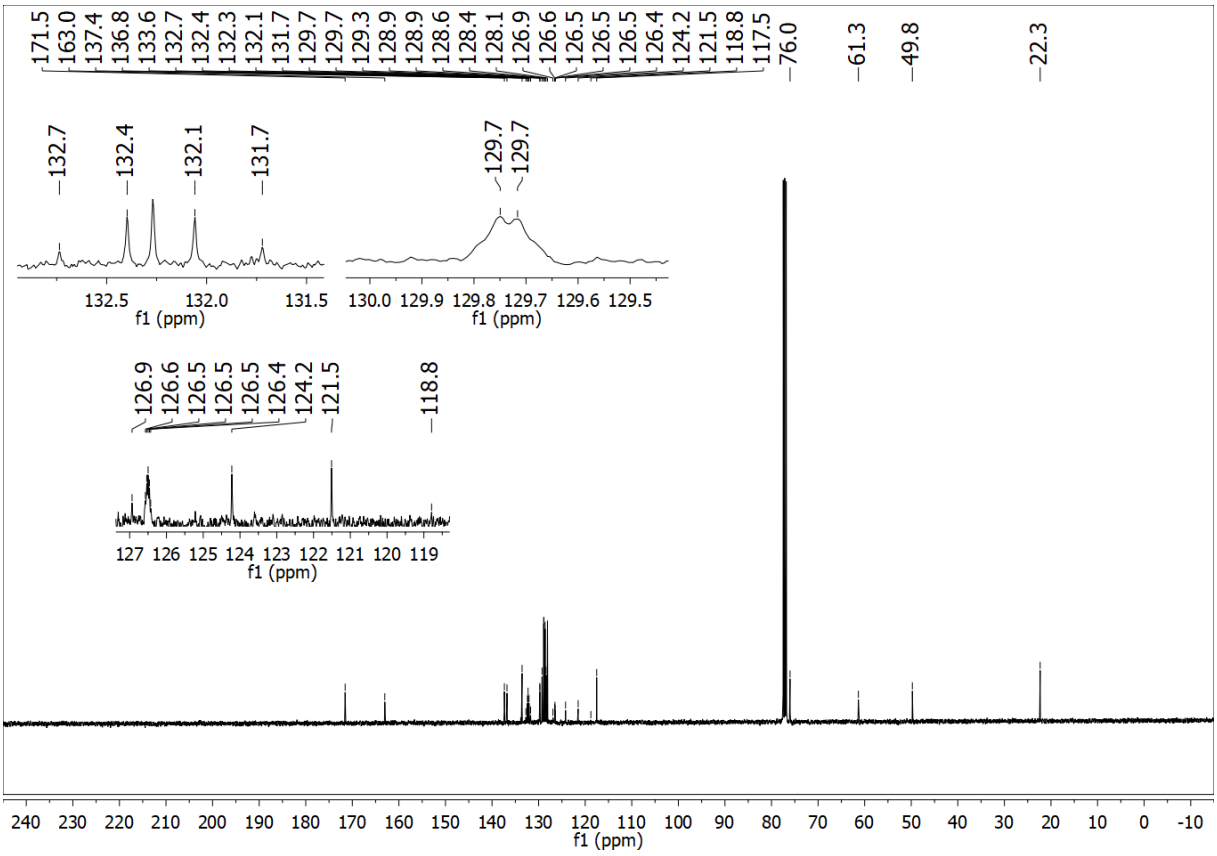


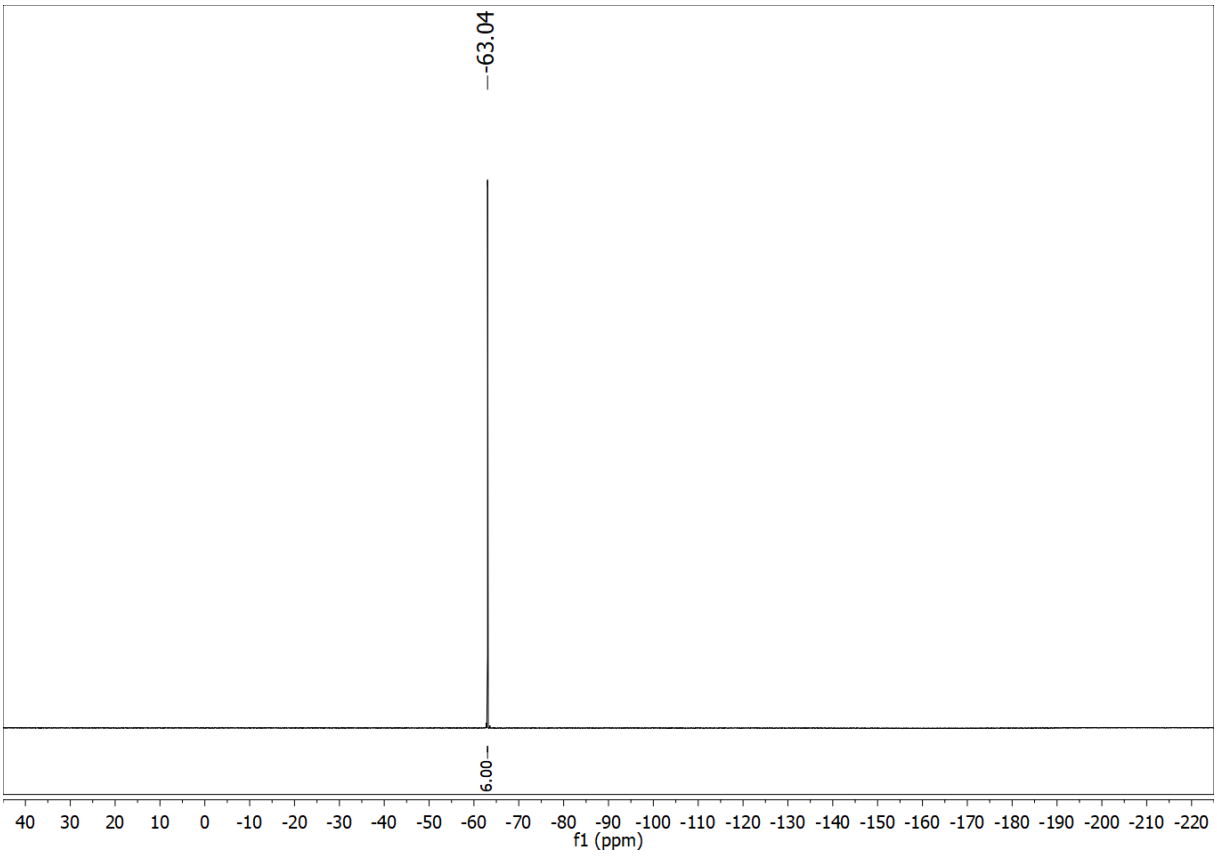


NMR-Solvent: $CDCl_3$

rac. (1*R*,2*S*)-2-(*N*-allylacetamido)-1,2-diphenylethyl 3,5-bis(trifluoro-methyl)benzoate (47m)

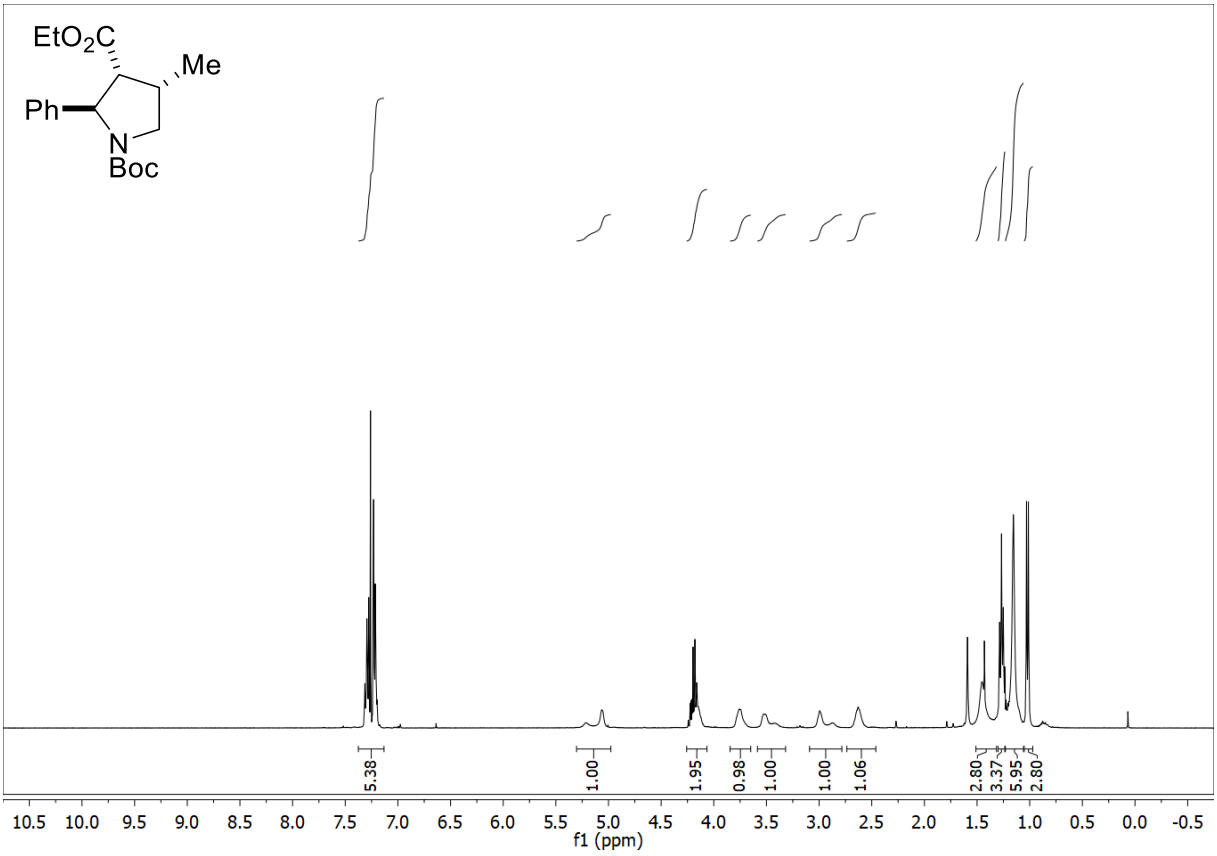


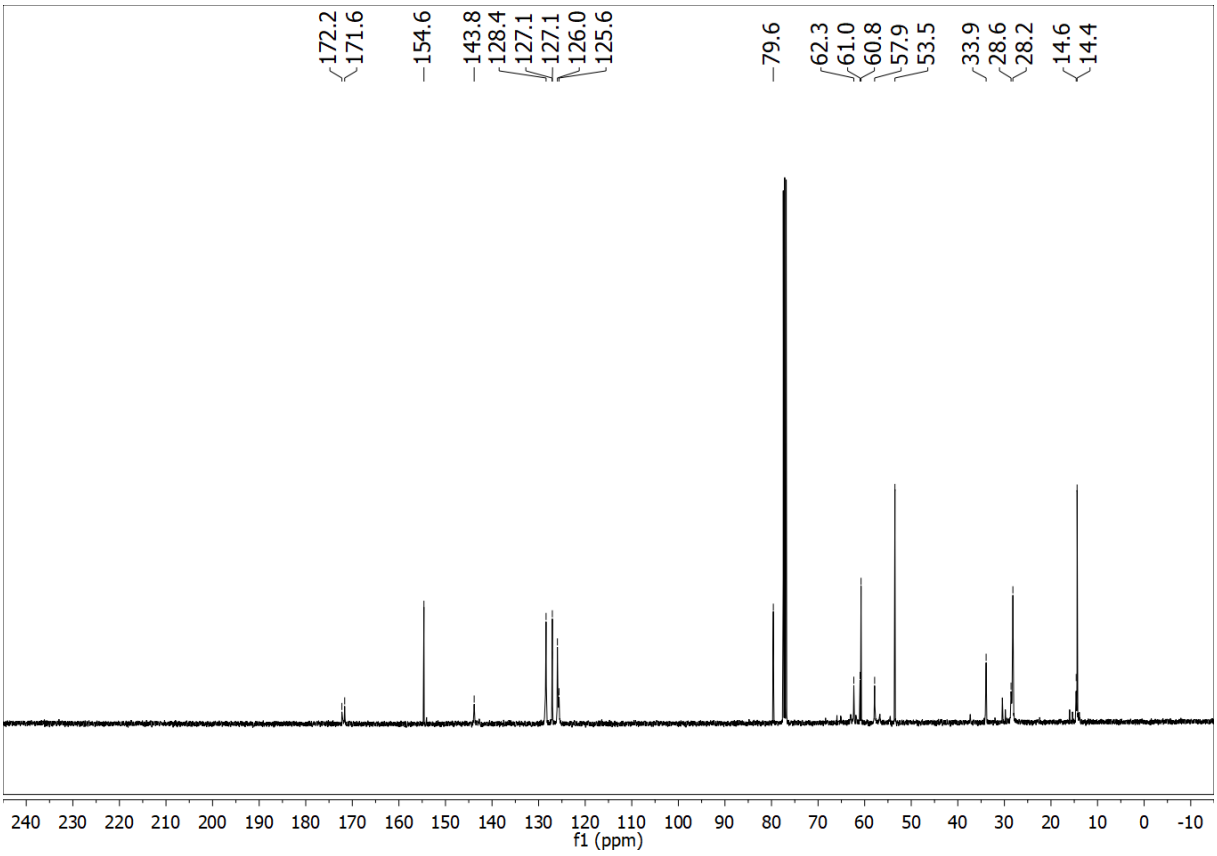




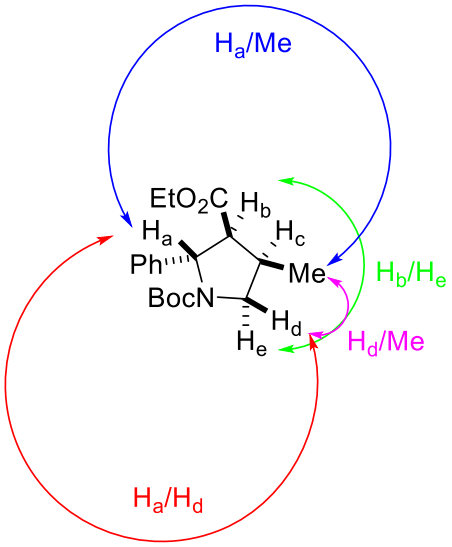
NMR-Solvent: $CDCl_3$

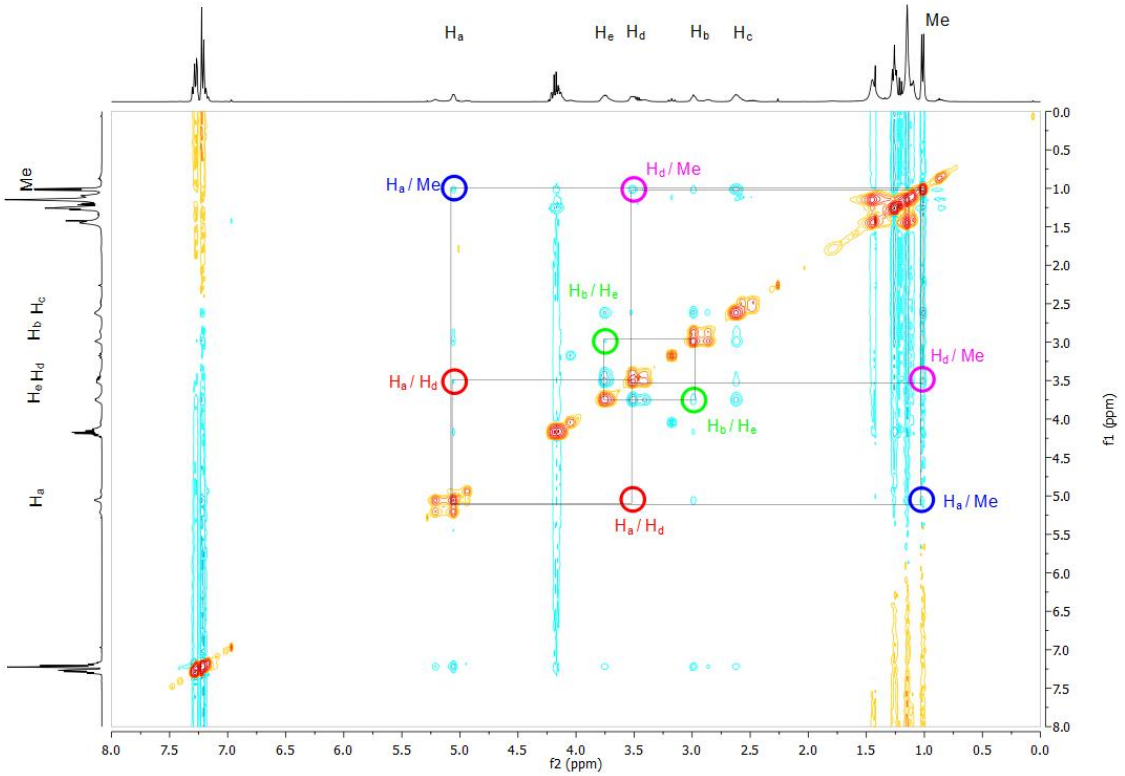
rac. 1-(*tert*-Butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (48a)





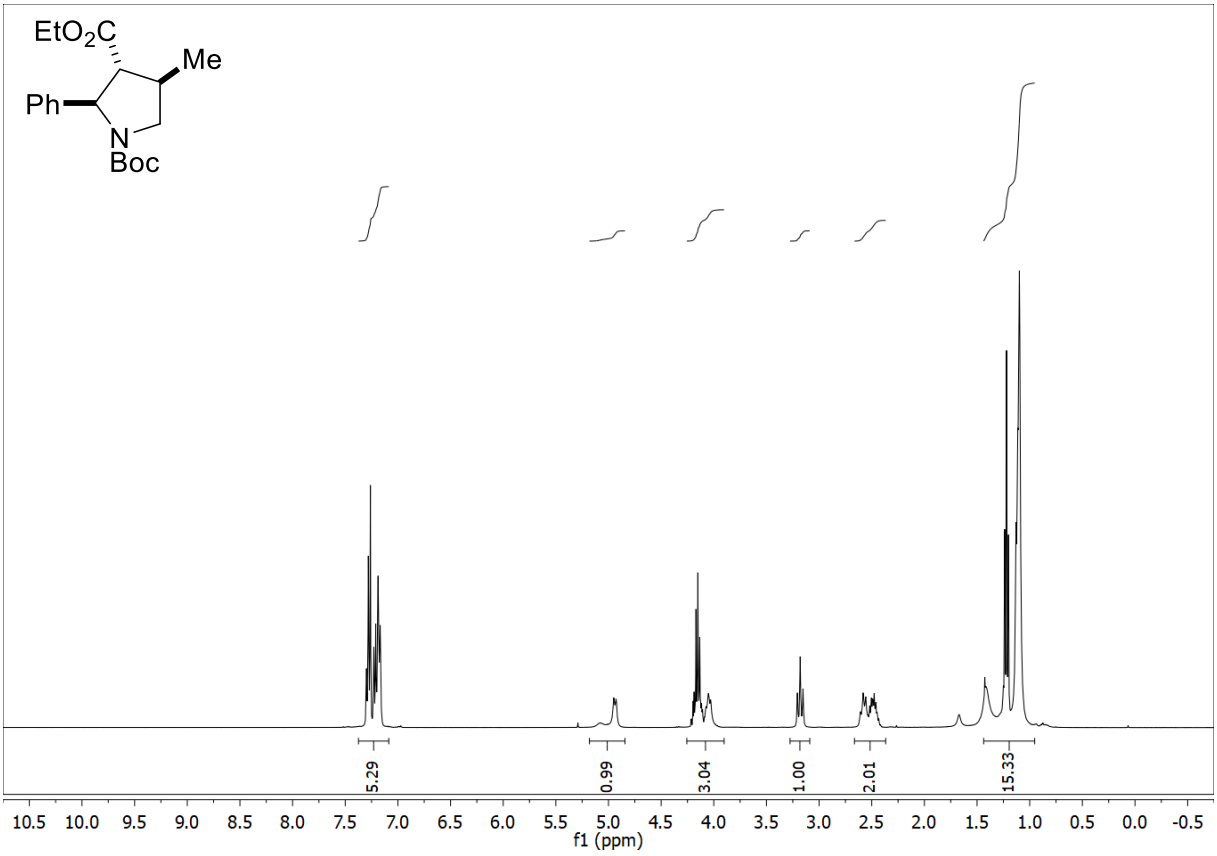
NMR-Solvent: $CDCl_3$

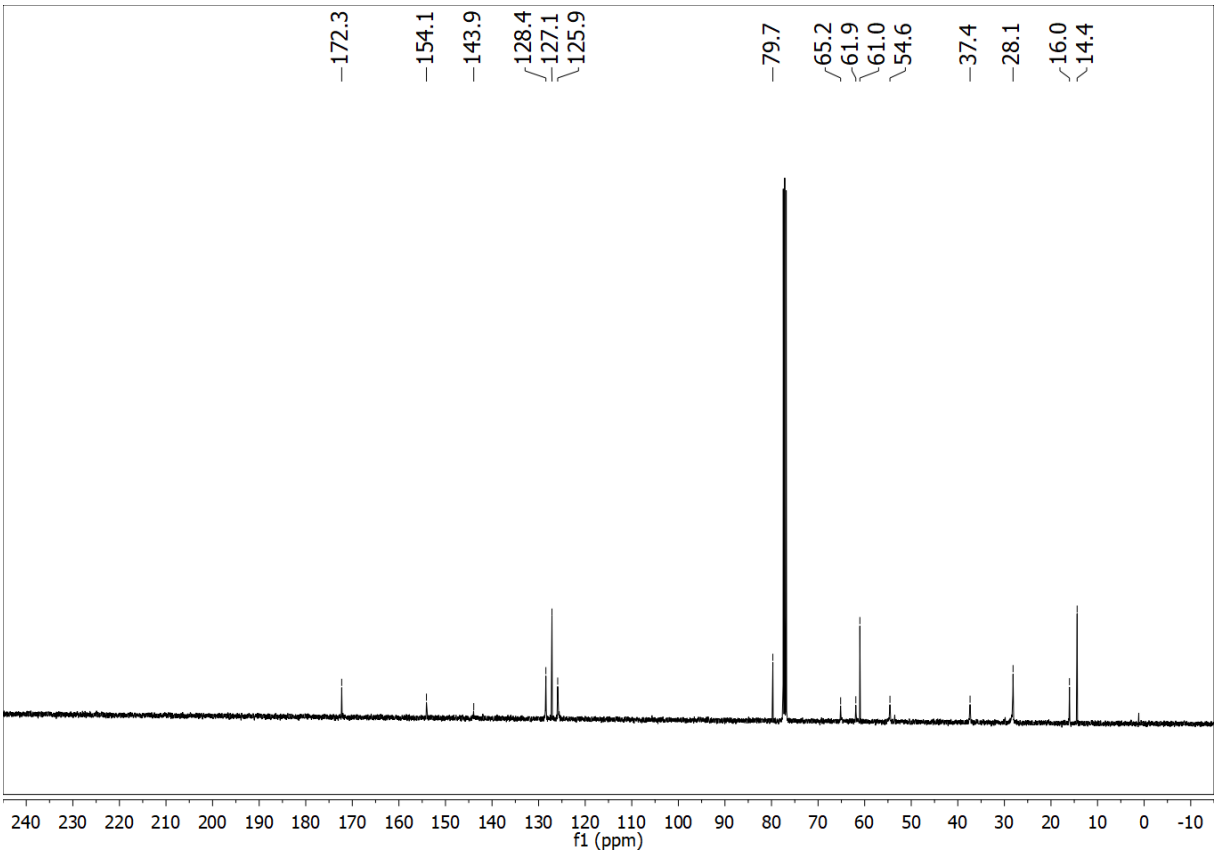




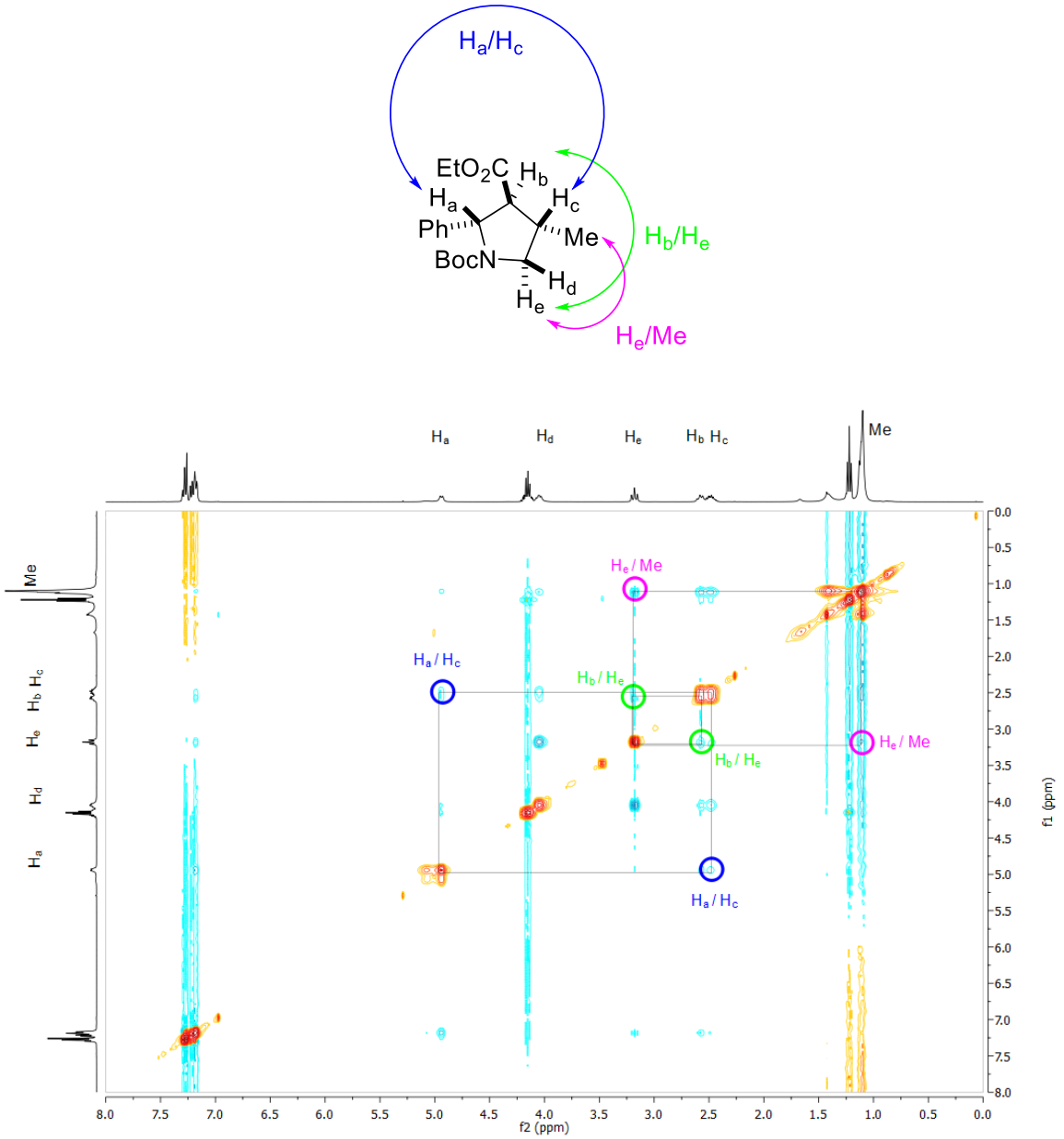
NOESY Analysis

rac. 1-(*tert*-Butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (48a´)



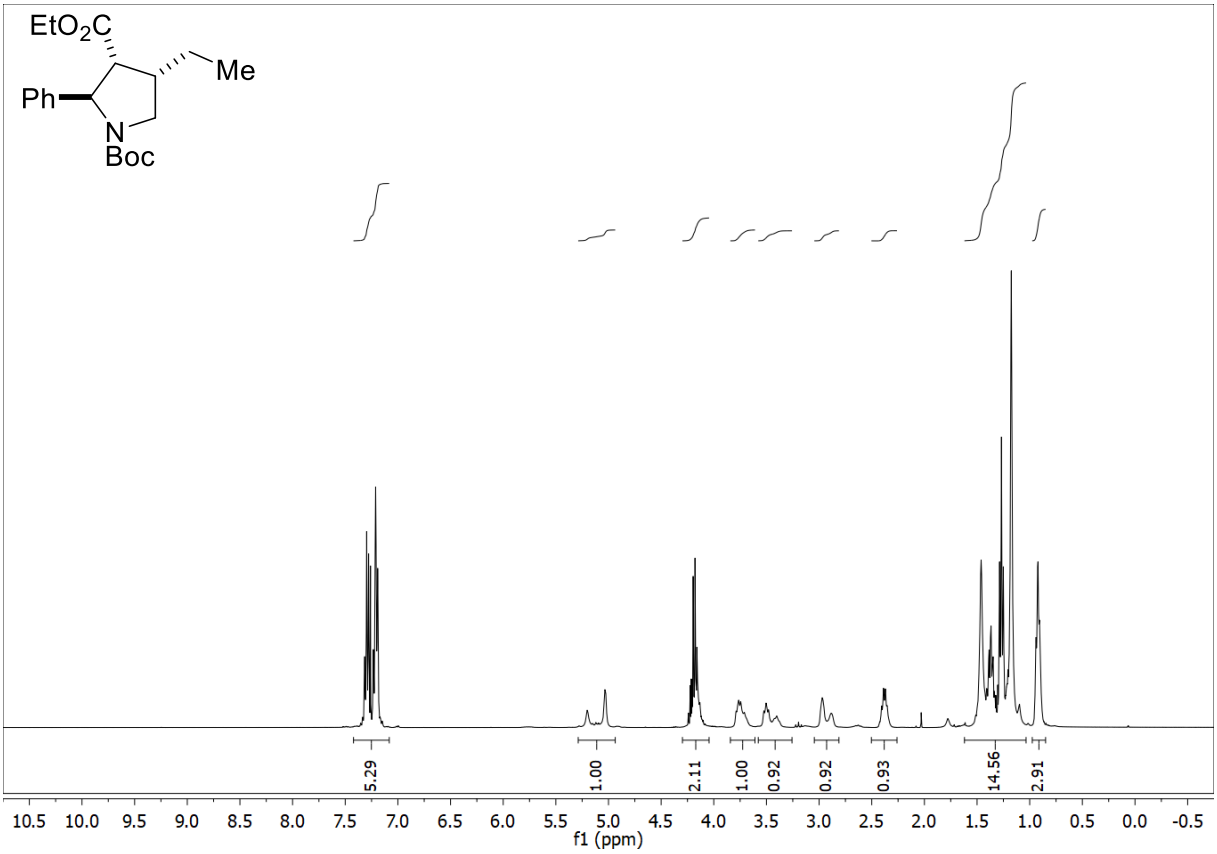


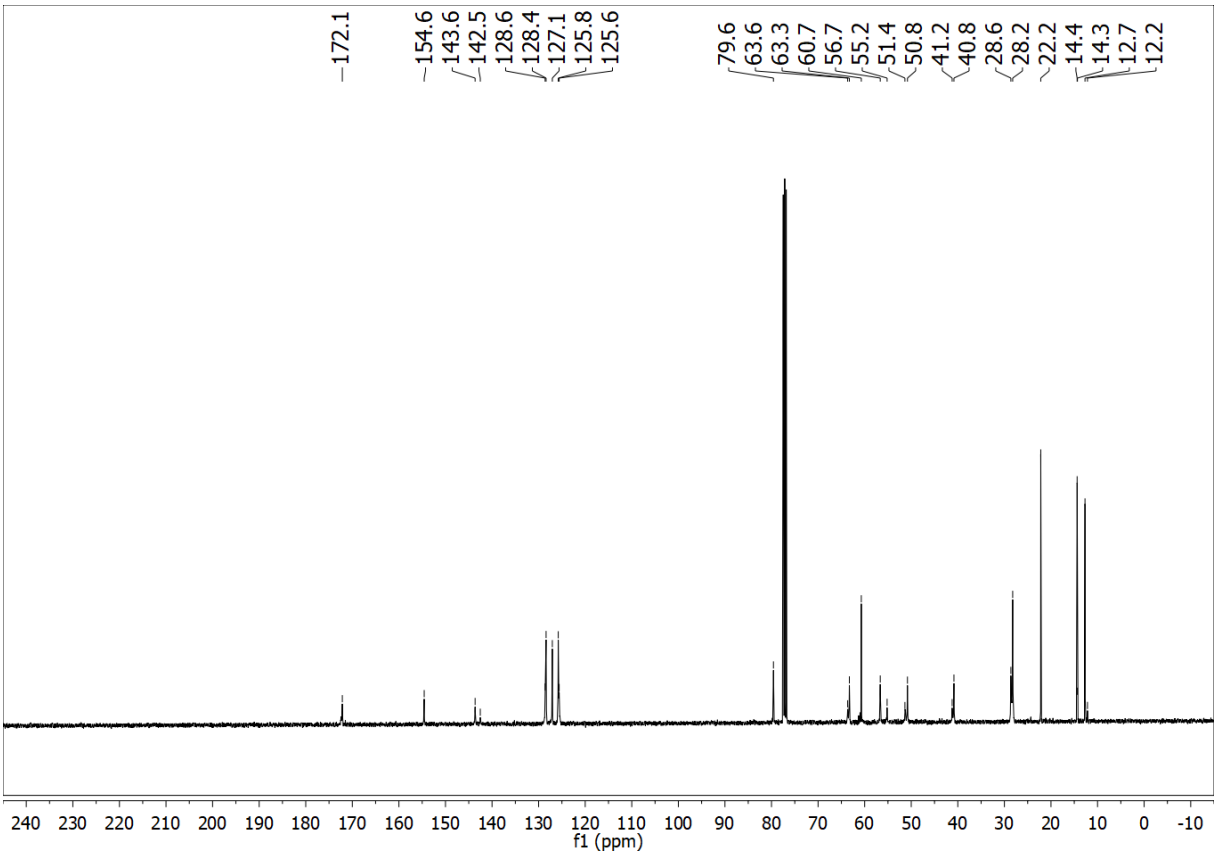
NMR-Solvent: $CDCl_3$



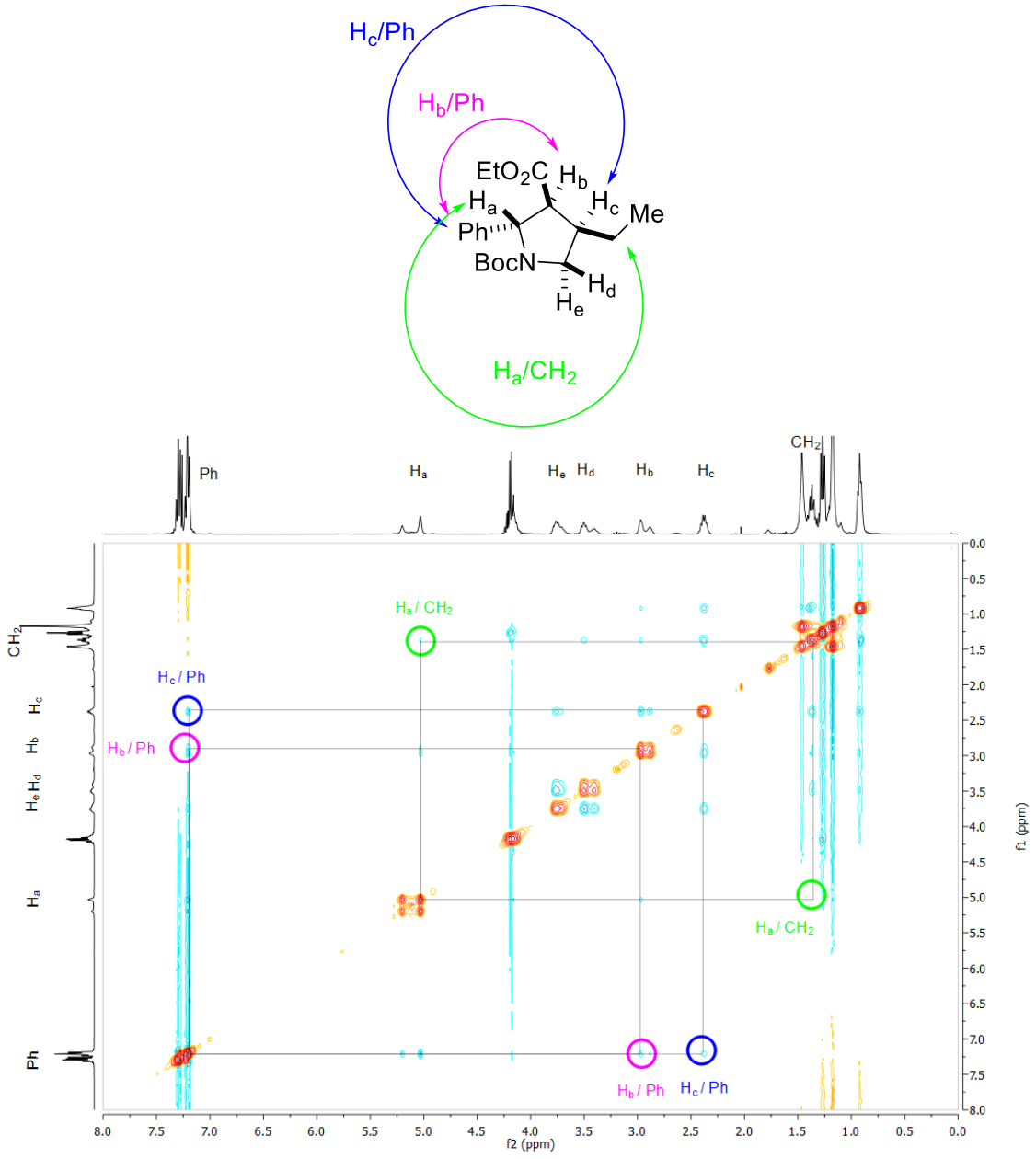
NOESY Analysis

rac. 1-(*tert*-Butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-ethyl-2-phenylpyrrolidine-1,3-dicarboxylate (48b)



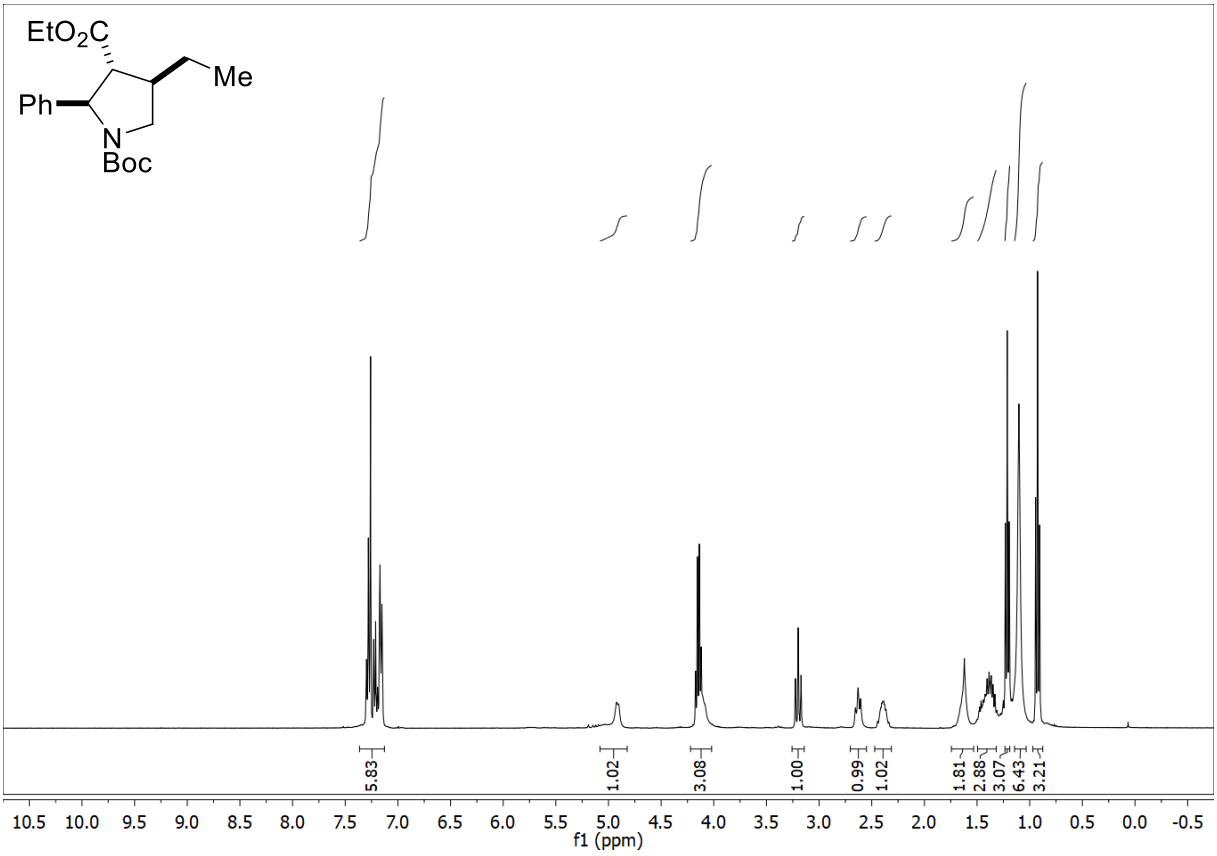


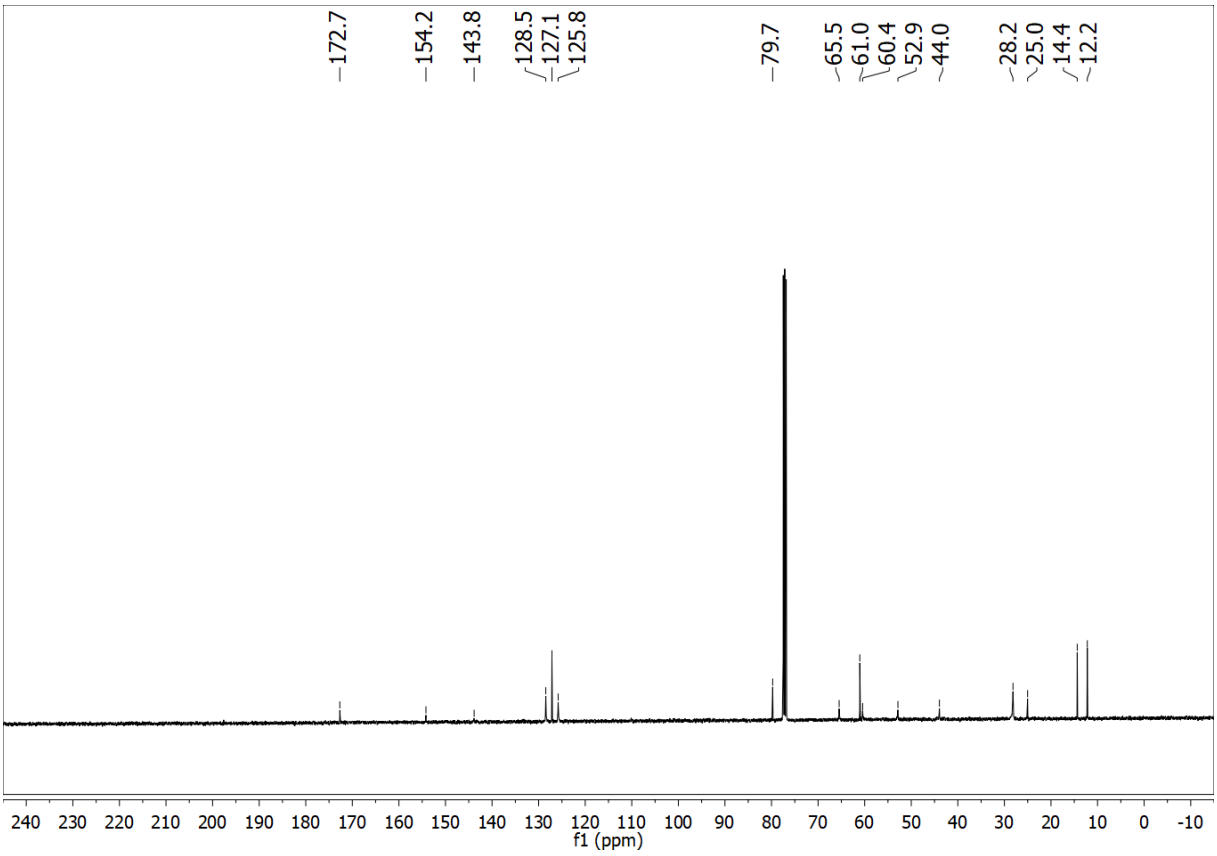
NMR-Solvent: $CDCl_3$



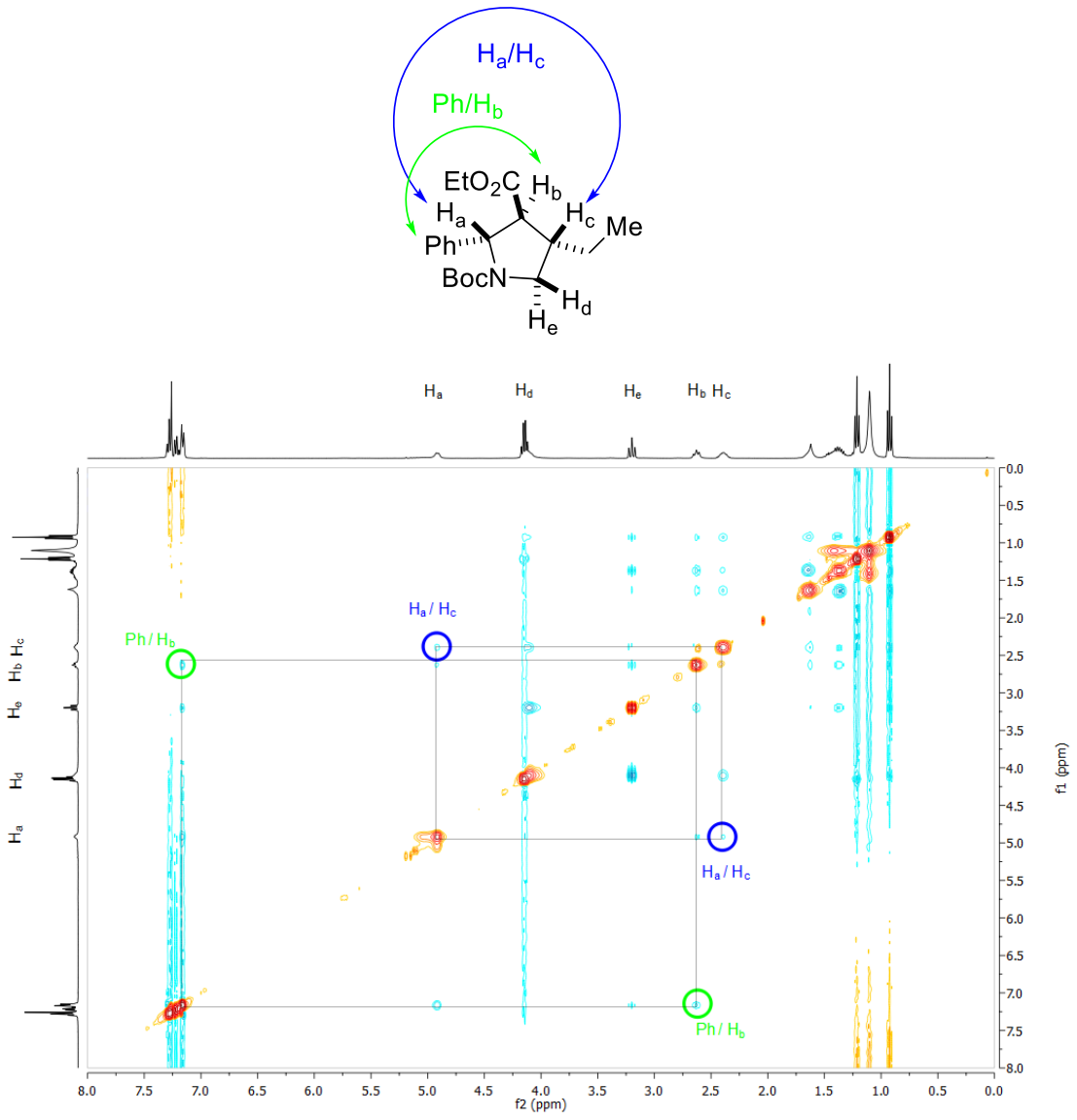
NOESY Analysis

rac. 1-(*tert*-Butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-ethyl-2-phenylpyrrolidine-1,3-dicarboxylate (48b´)



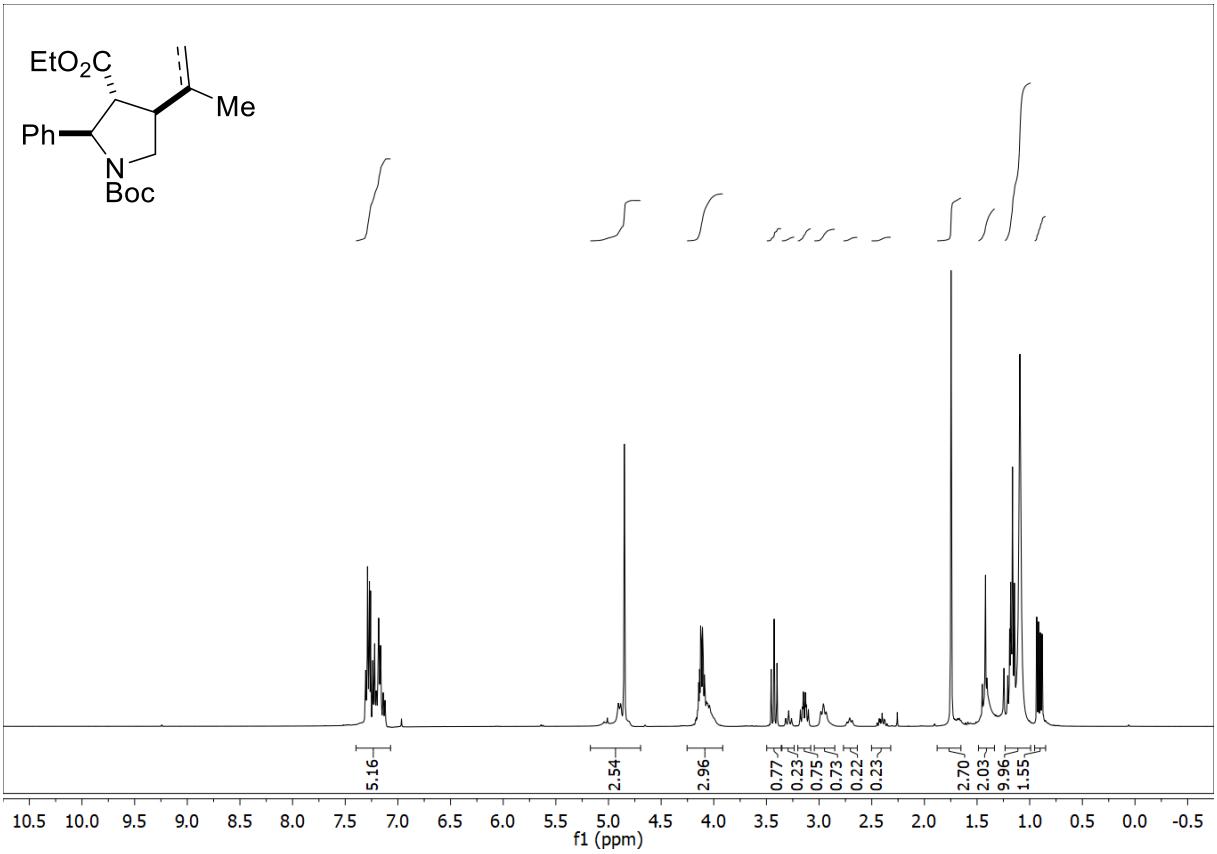


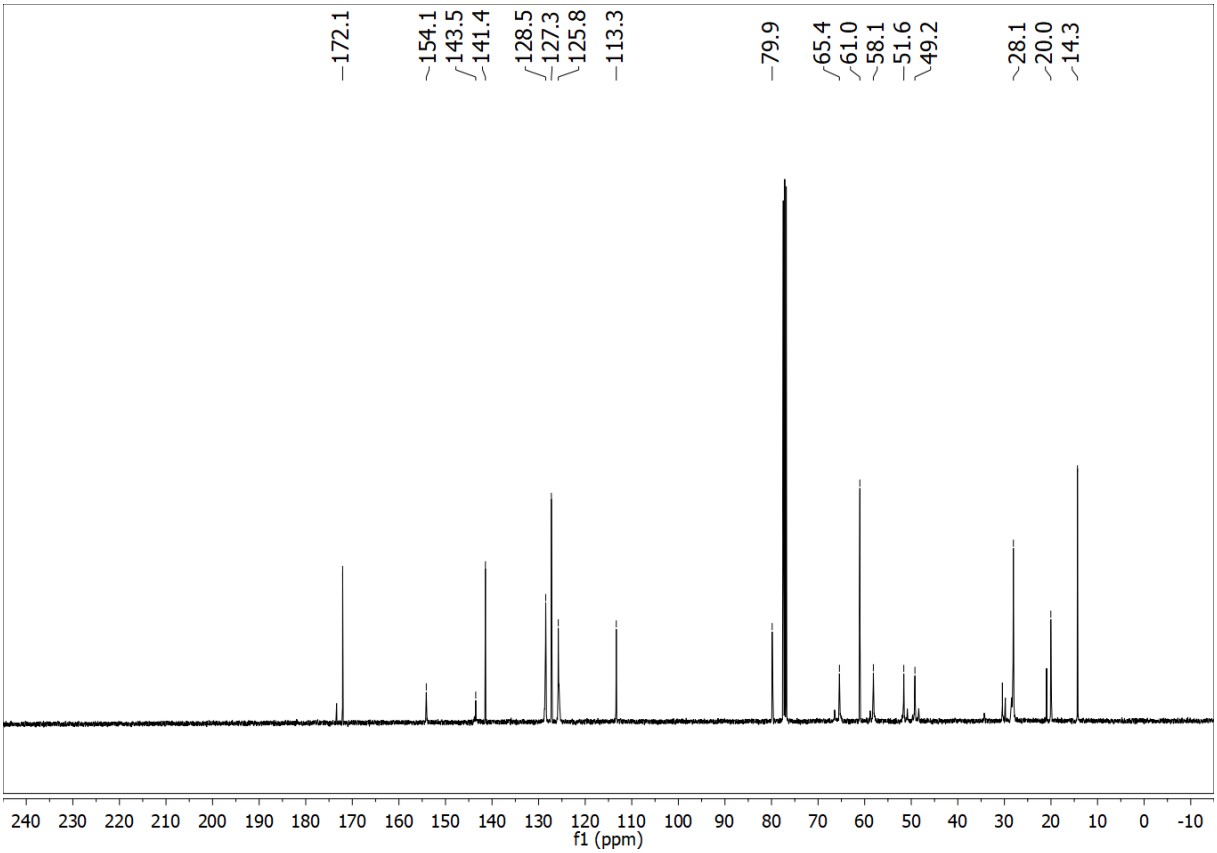
NMR-Solvent: $CDCl_3$



NOESY Analysis

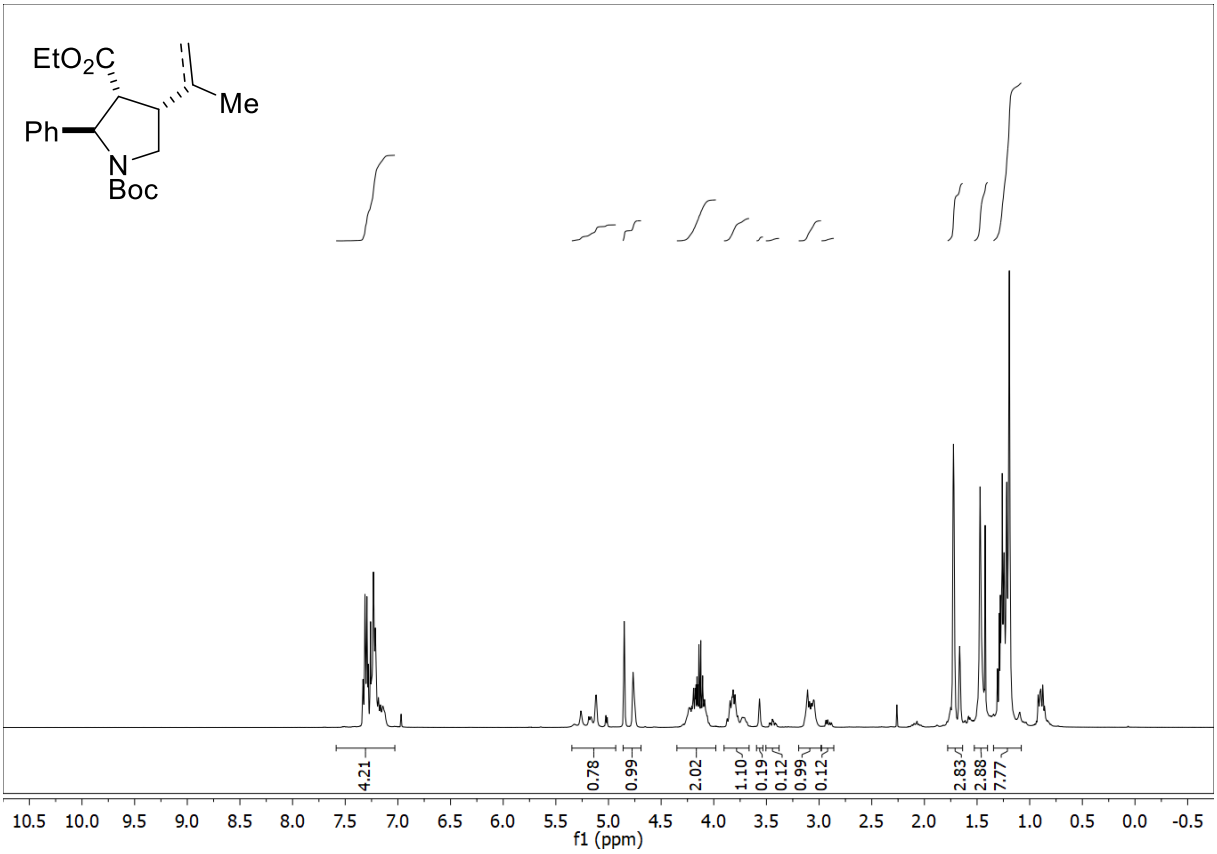
rac. 1-(*tert*-Butyl) 3-ethyl (2*R*,3*R*,4*R*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxy-late (48c) / rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*S*)-2-phenyl-4-(prop-1-en-2-yl)pyrrolidine-1,3-dicarboxylate (48cS1)

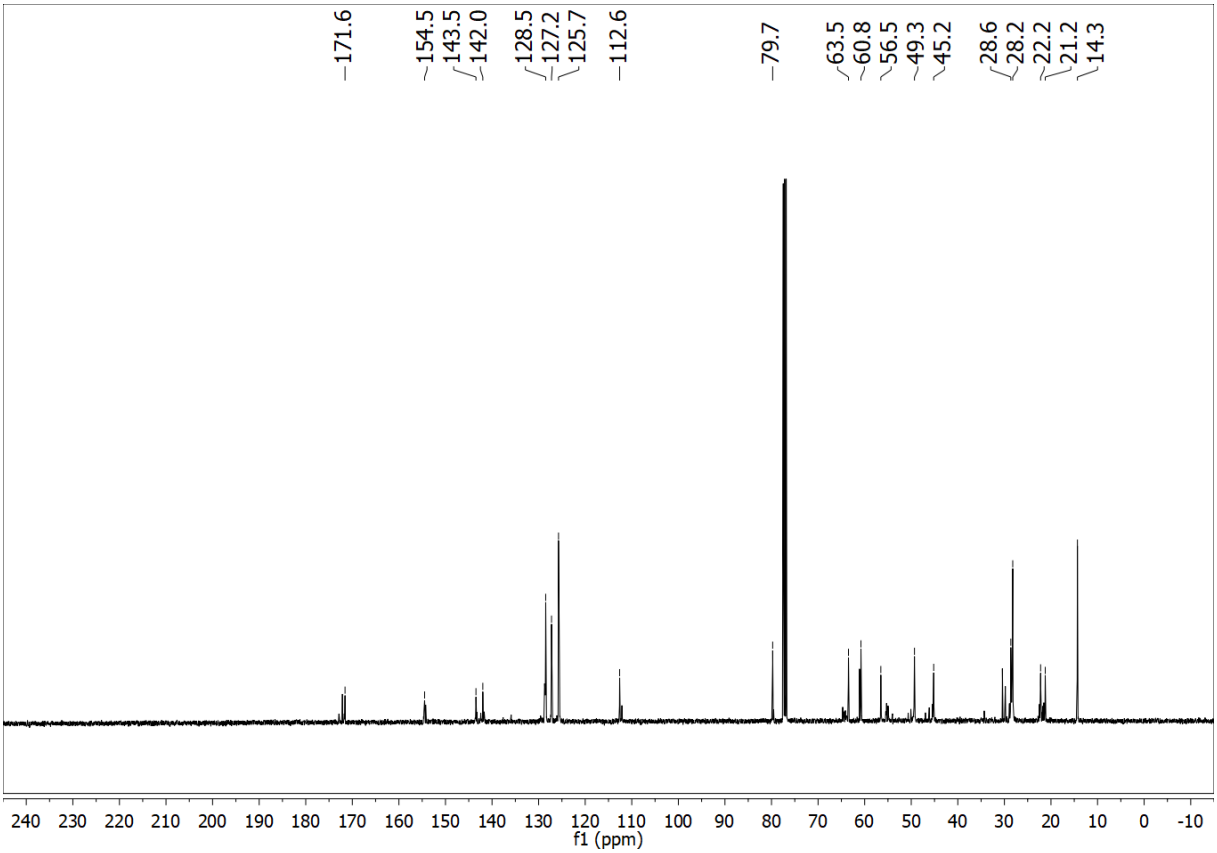




NMR-Solvent: $CDCl_3$

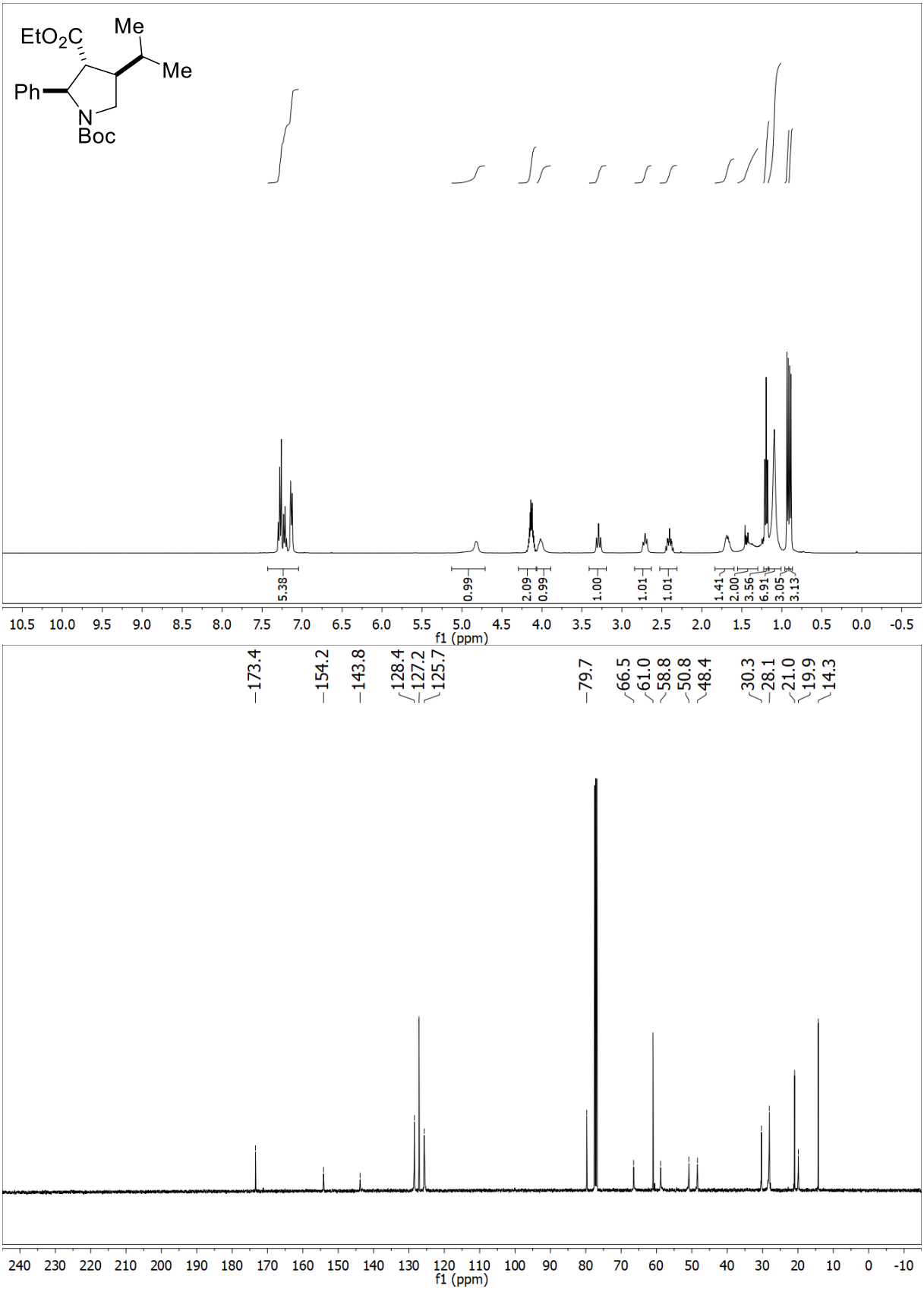
rac. 1-(*tert*-Butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxylate (48c´) / rac. 1-(*tert*-butyl) 3-ethyl (2*R*,3*R*,4*R*)-2-phenyl-4-(prop-1-en-2-yl)pyrrolidine-1,3-dicarboxylate (48c´S1)



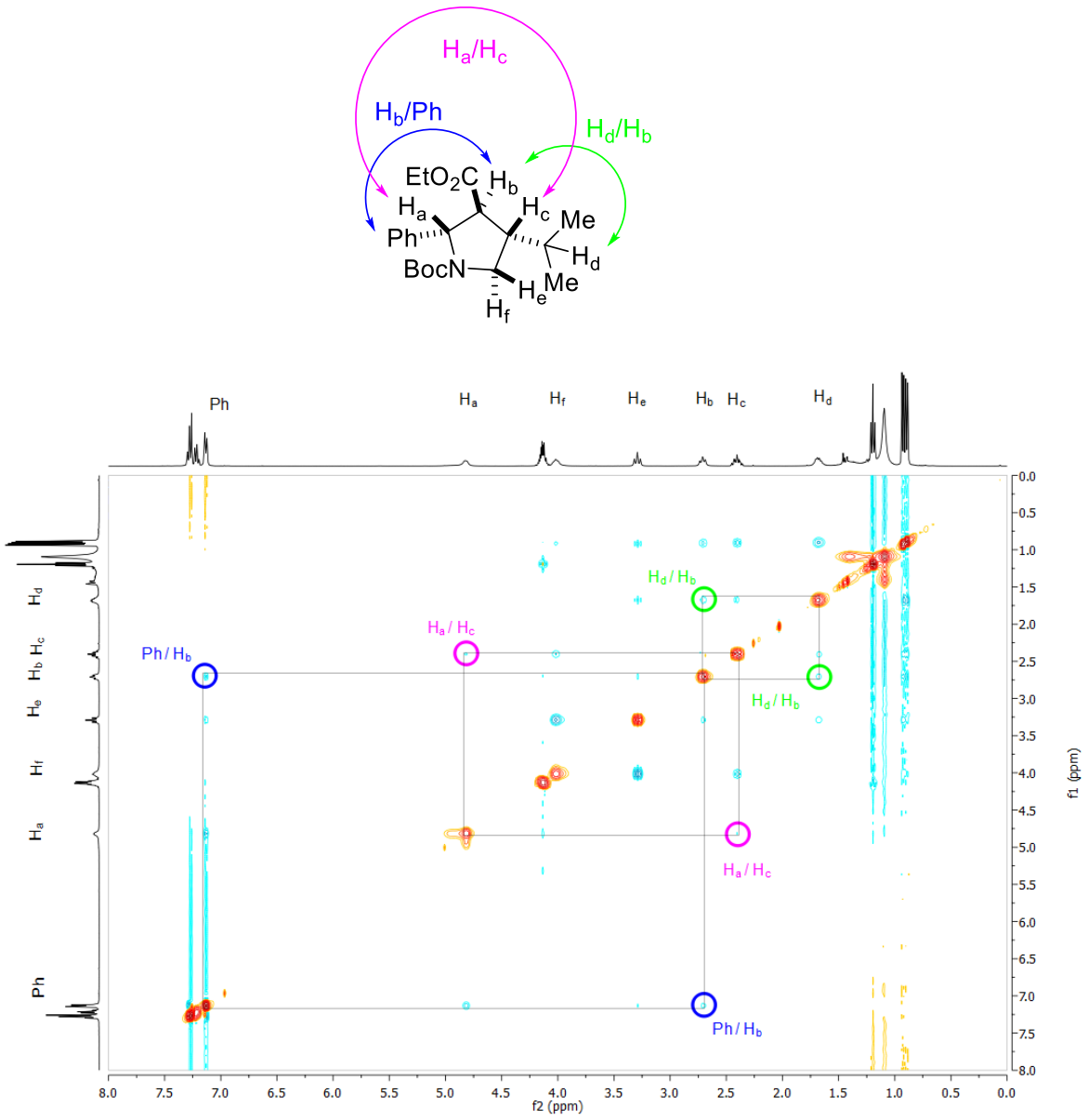


NMR-Solvent: $CDCl_3$

rac. 1-(*tert*-Butyl) 3-ethyl (2*R*,3*R*,4*R*)-4 isopropyl-2-phenylpyrrolidine-1,3-dicarboxy-late (48c)

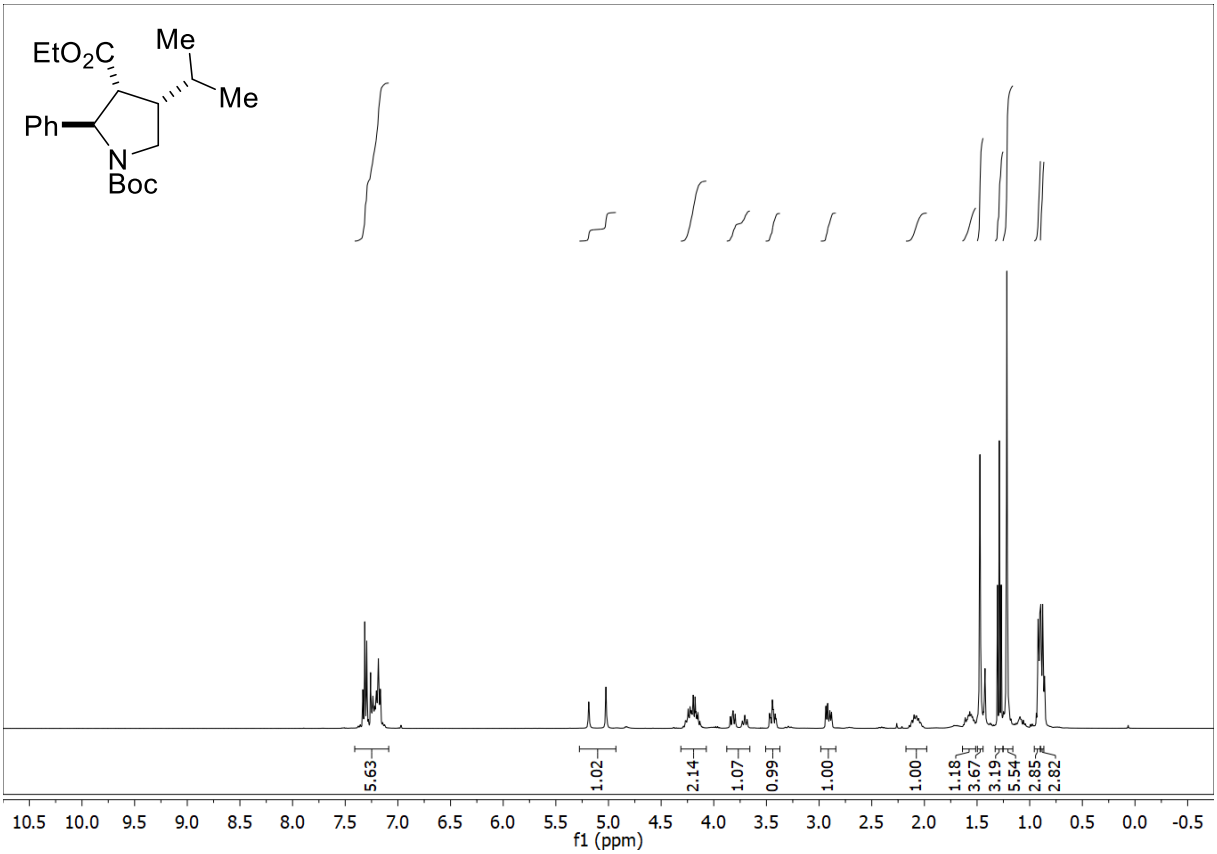


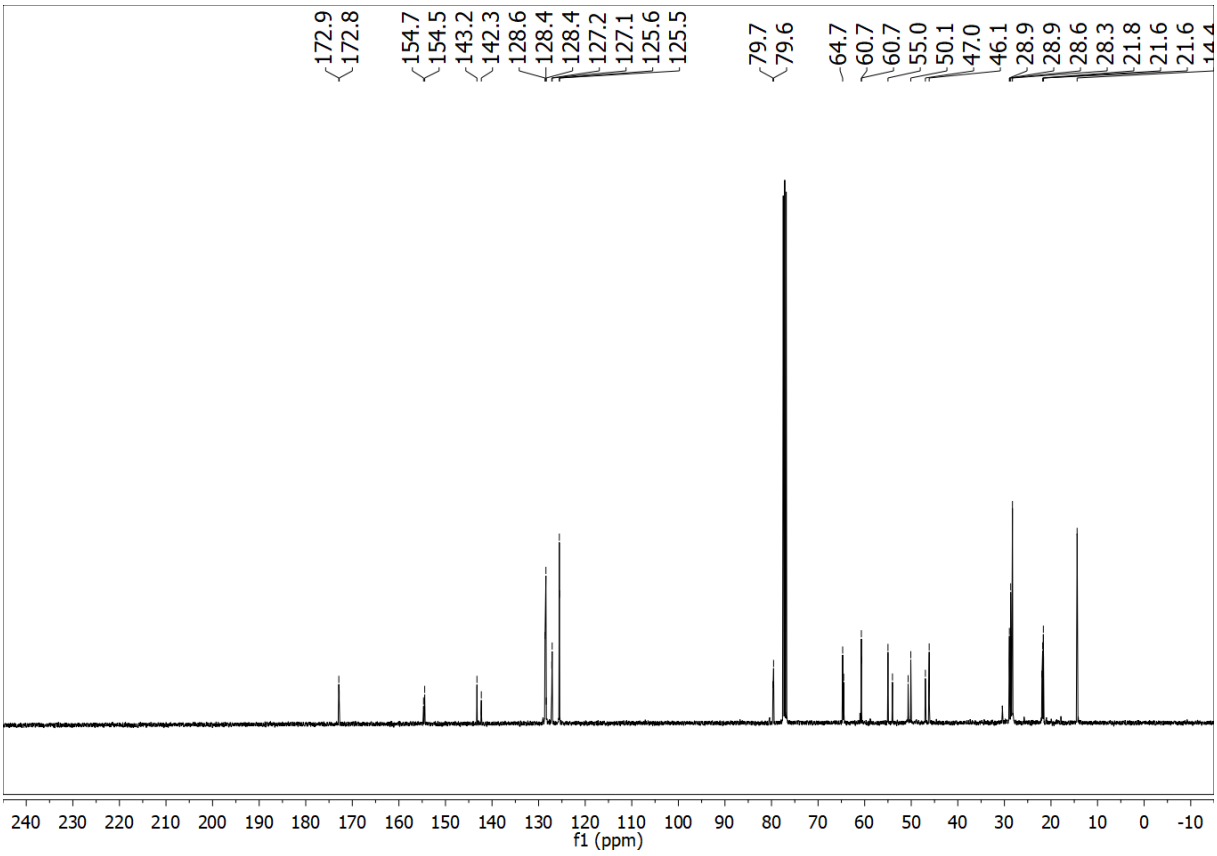
NMR-Solvent: $CDCl_3$



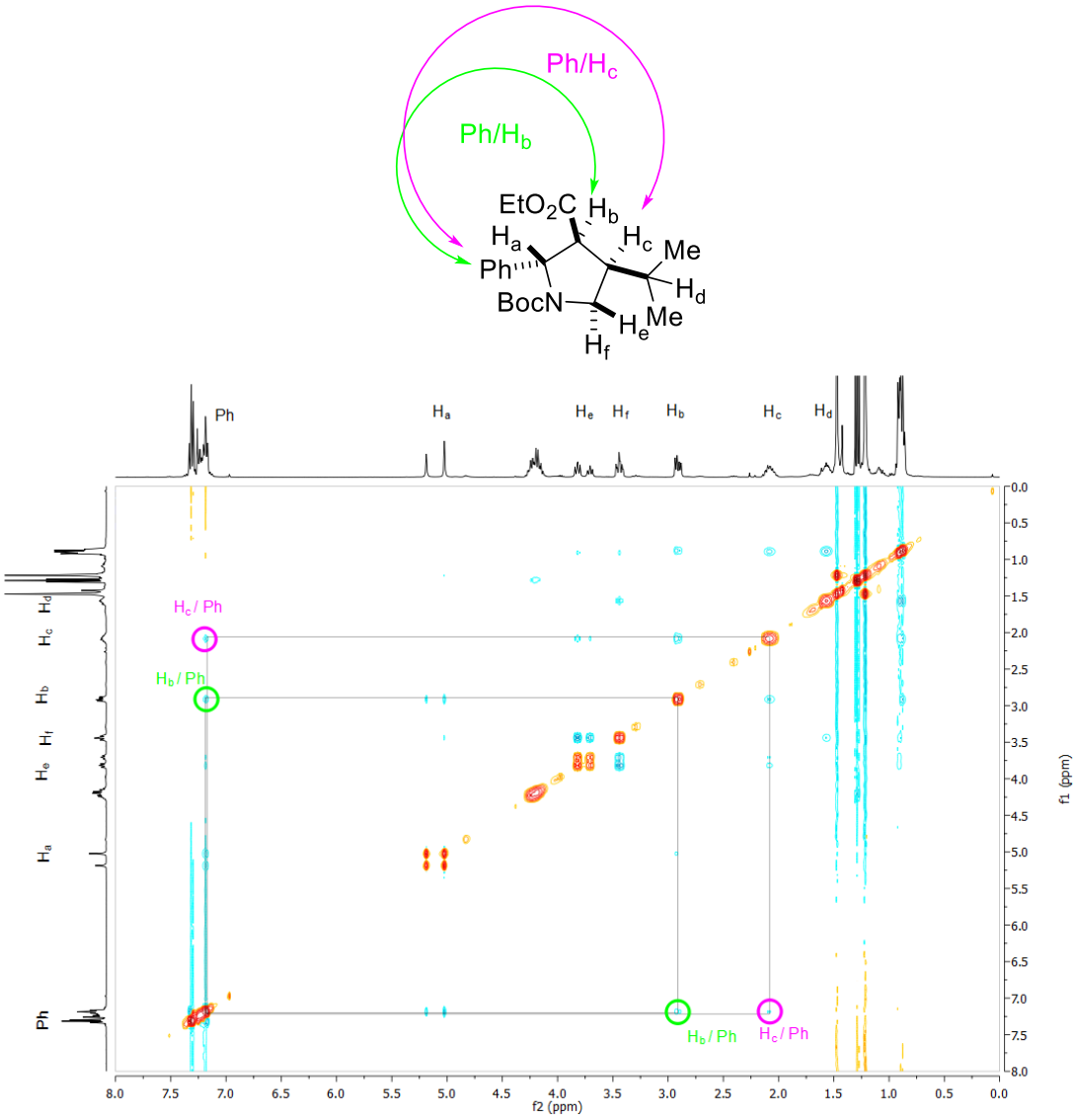
NOESY Analysis

rac. 1-(*tert*-Butyl) 3-ethyl (2*R*,3*R*,4*S*)-4-isopropyl-2-phenylpyrrolidine-1,3-dicarboxylate (48c´)



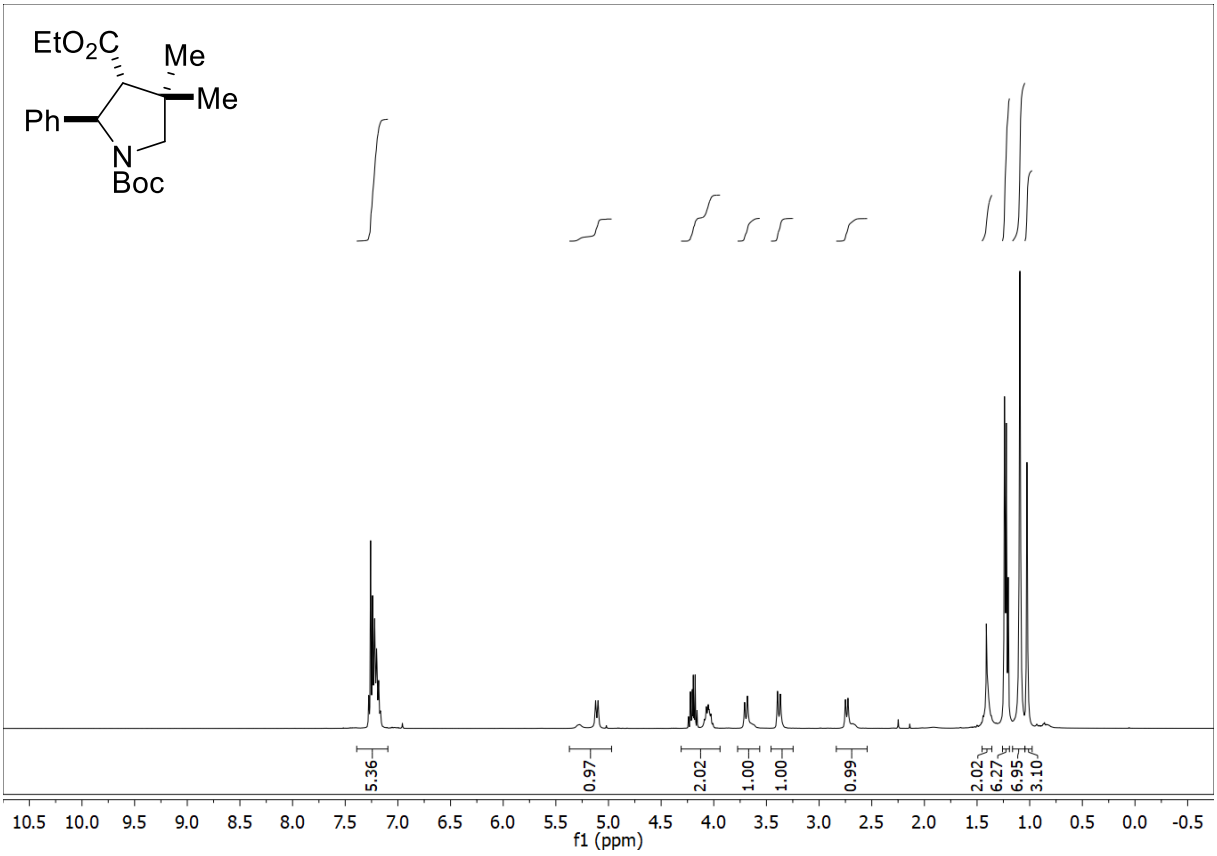


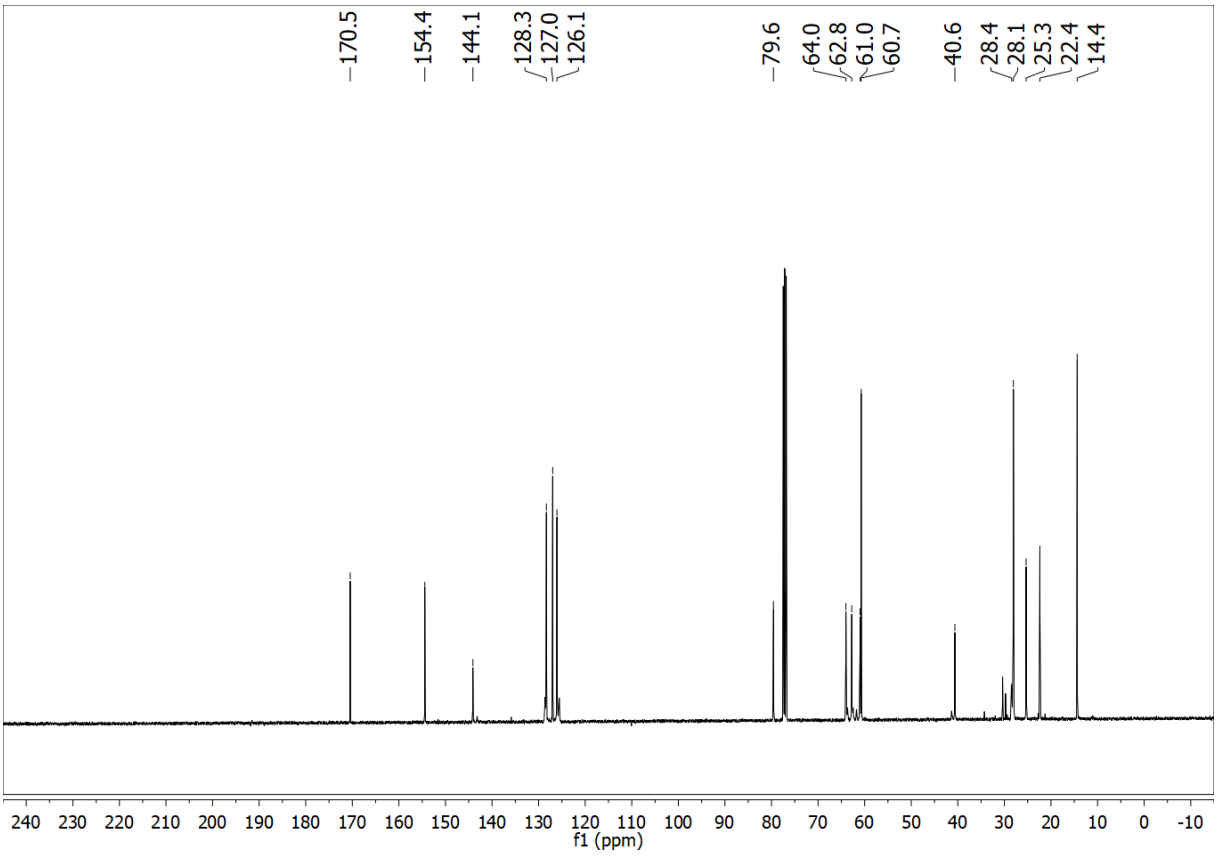
NMR-Solvent: $CDCl_3$



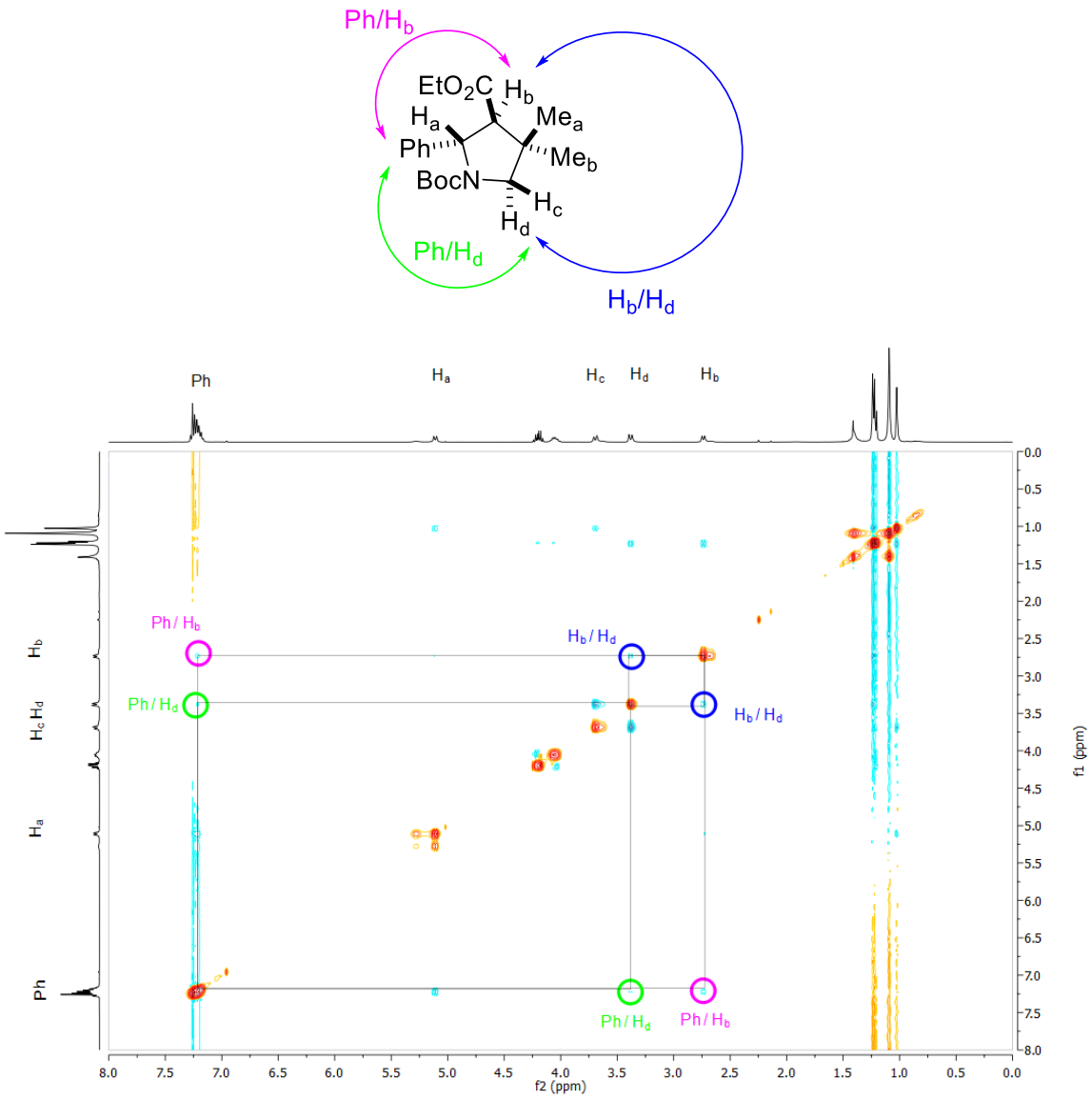
NOESY Analysis

rac. 1-(*tert*-Butyl) 3-ethyl (2*R*,3*R*)-4,4-dimethyl-2-phenylpyrrolidine-1,3-dicarboxylate (48d)



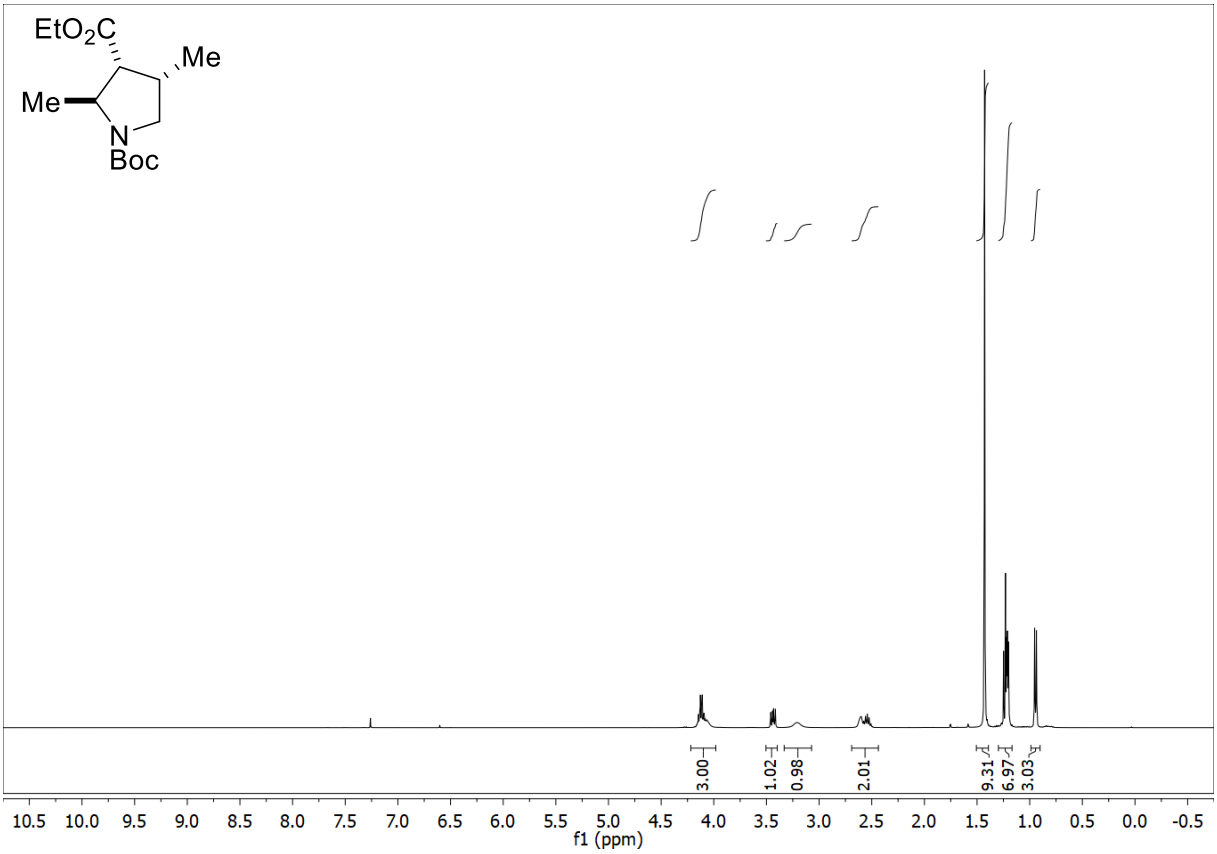


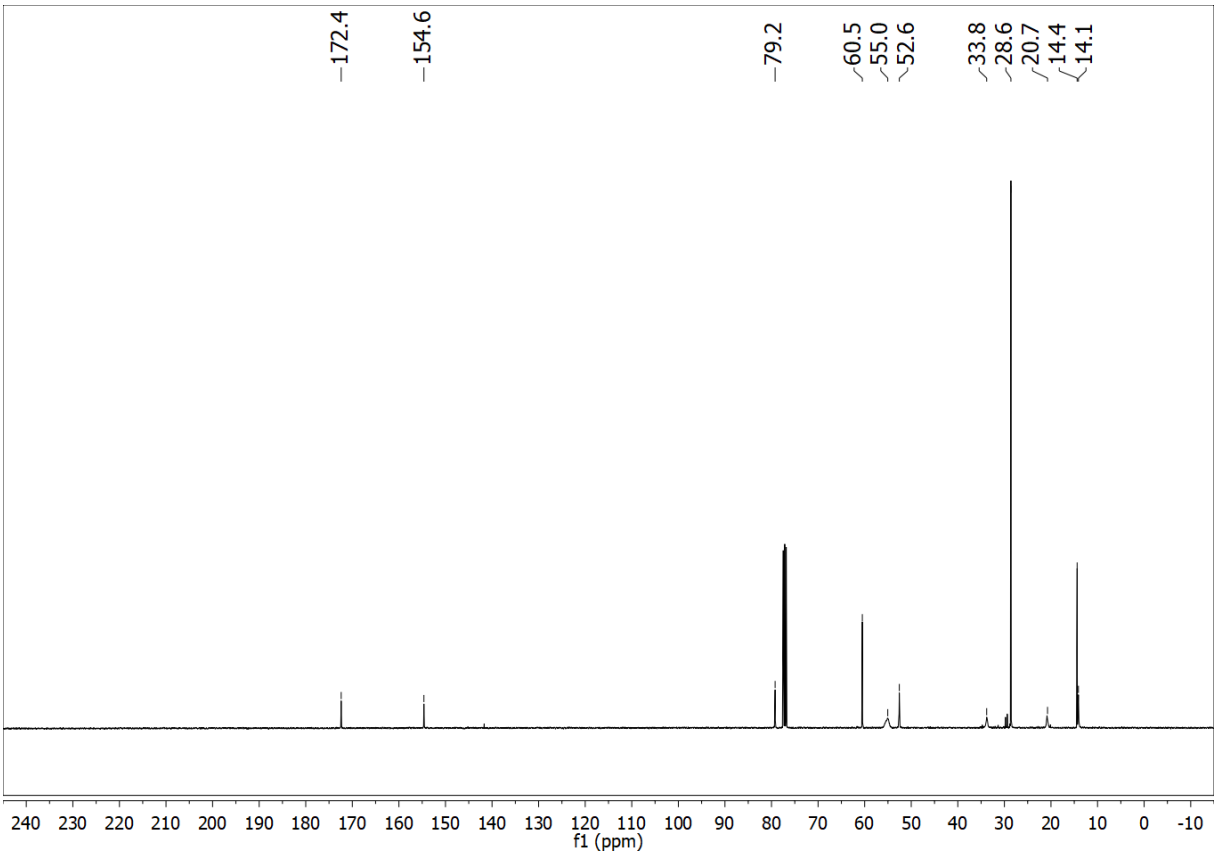
NMR-Solvent: $CDCl_3$



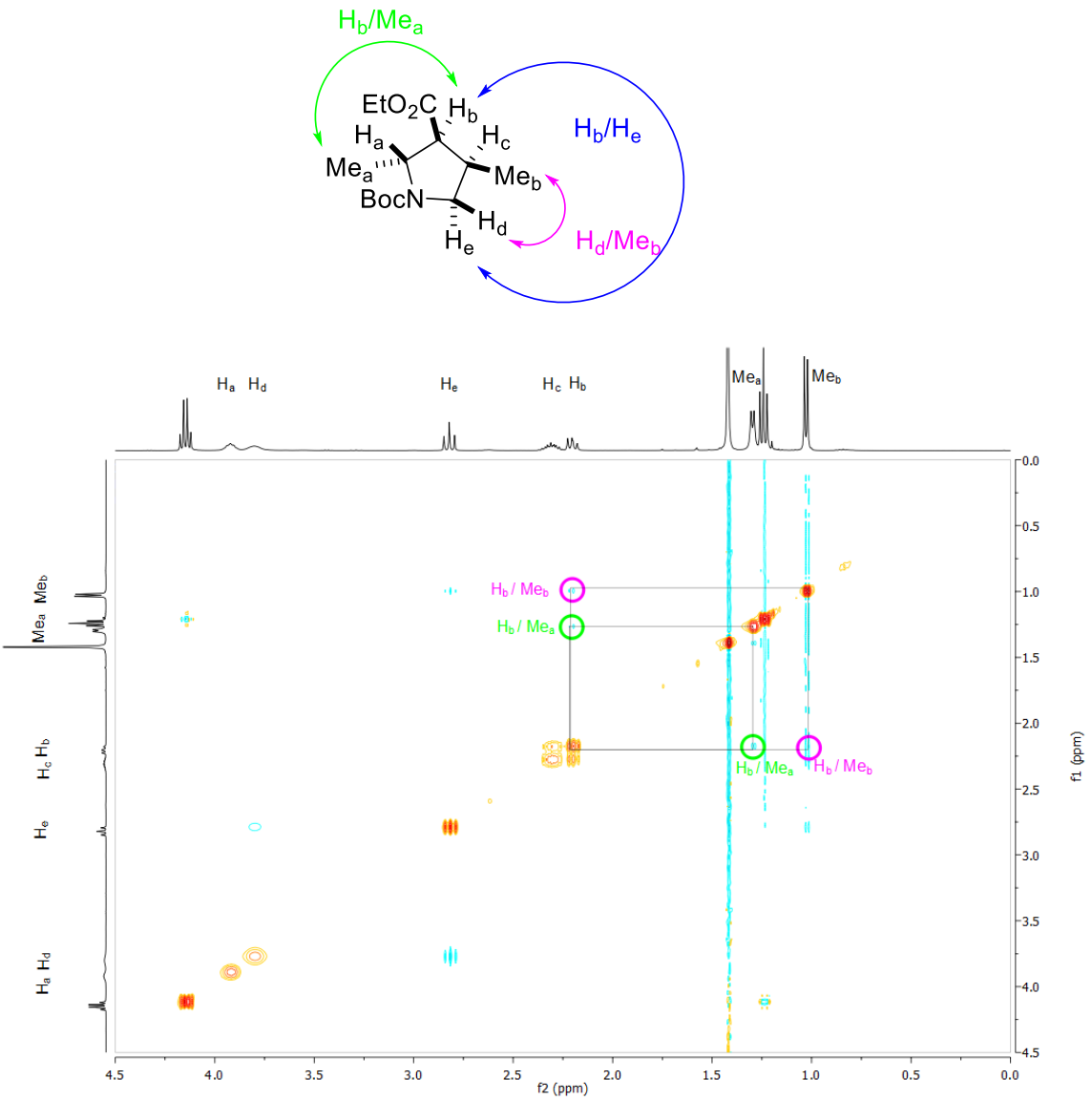
NOESY Analysis

rac. 1-(*tert*-Butyl) 3-ethyl (2*S*,3*R*,4*S*)-2,4-dimethylpyrrolidine-1,3-dicarboxylate (48e)



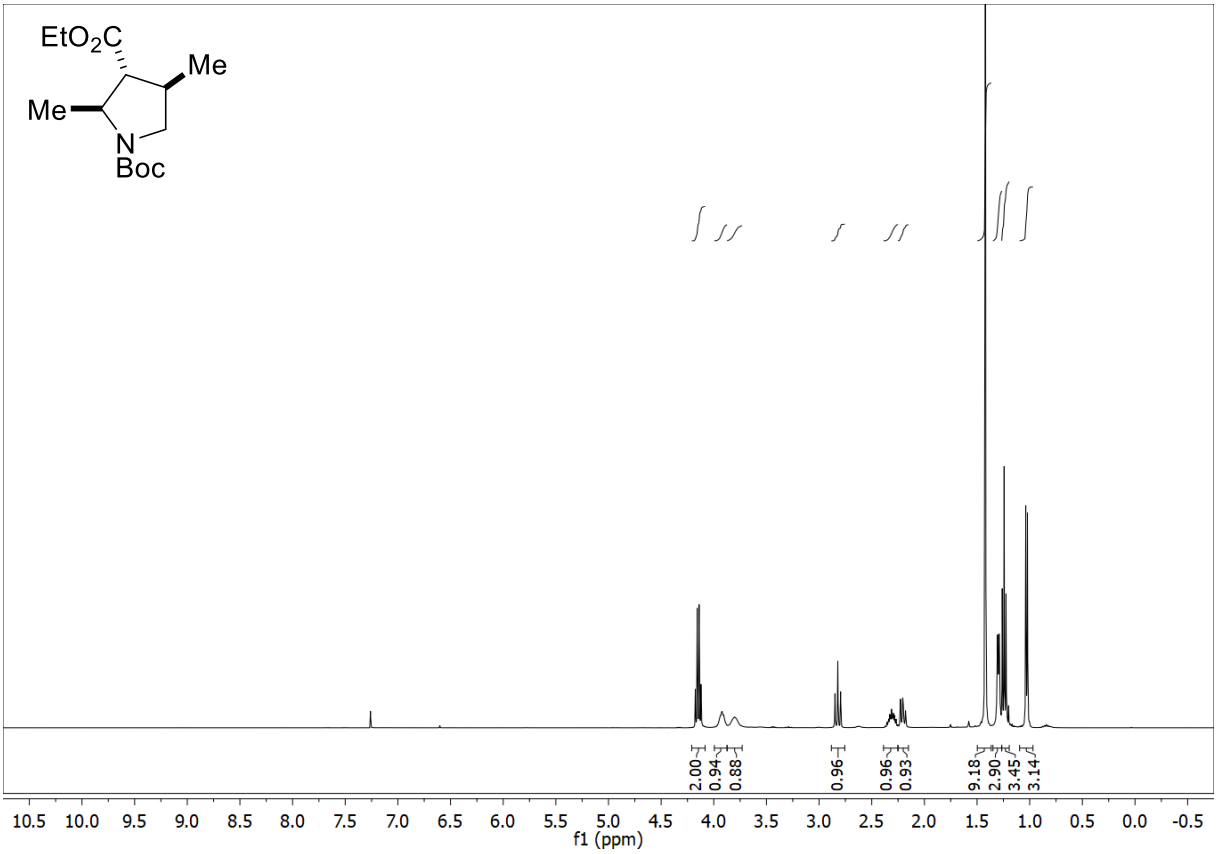


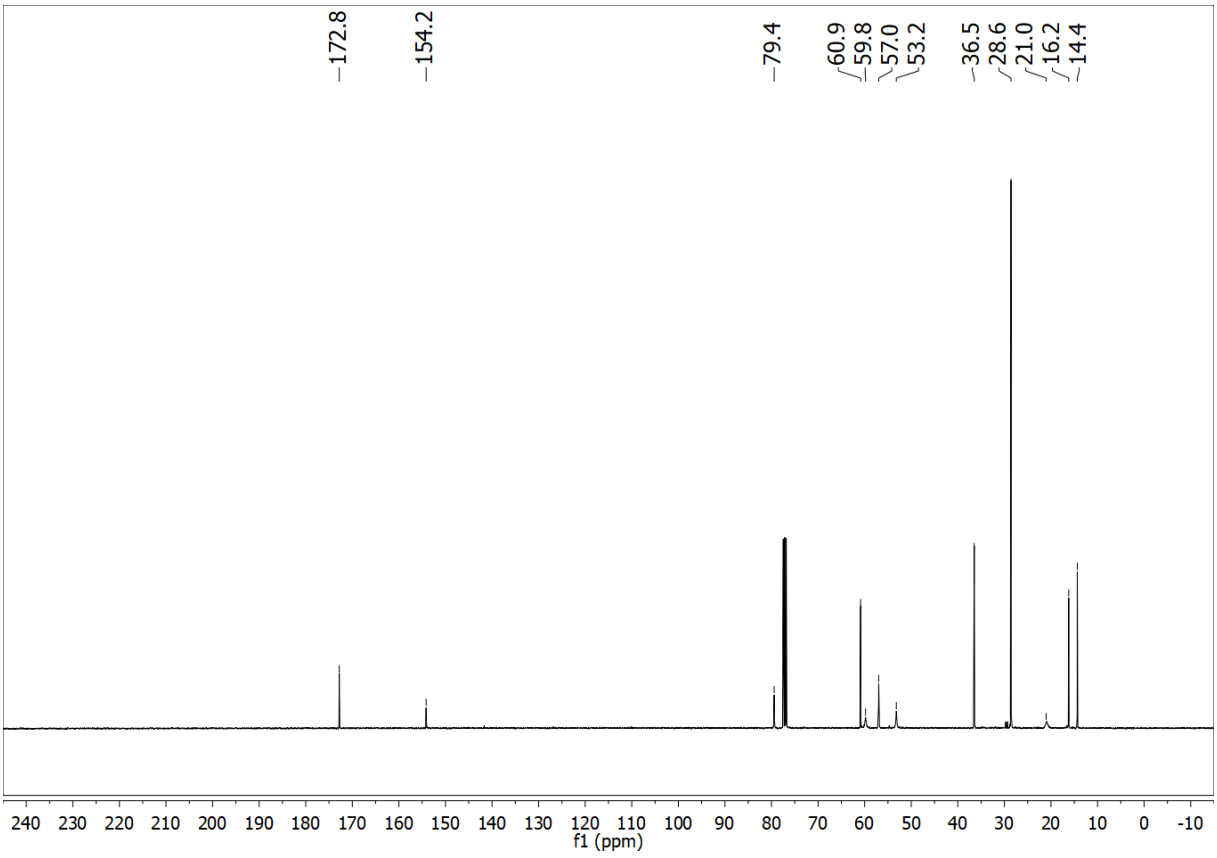
NMR-Solvent: $CDCl_3$



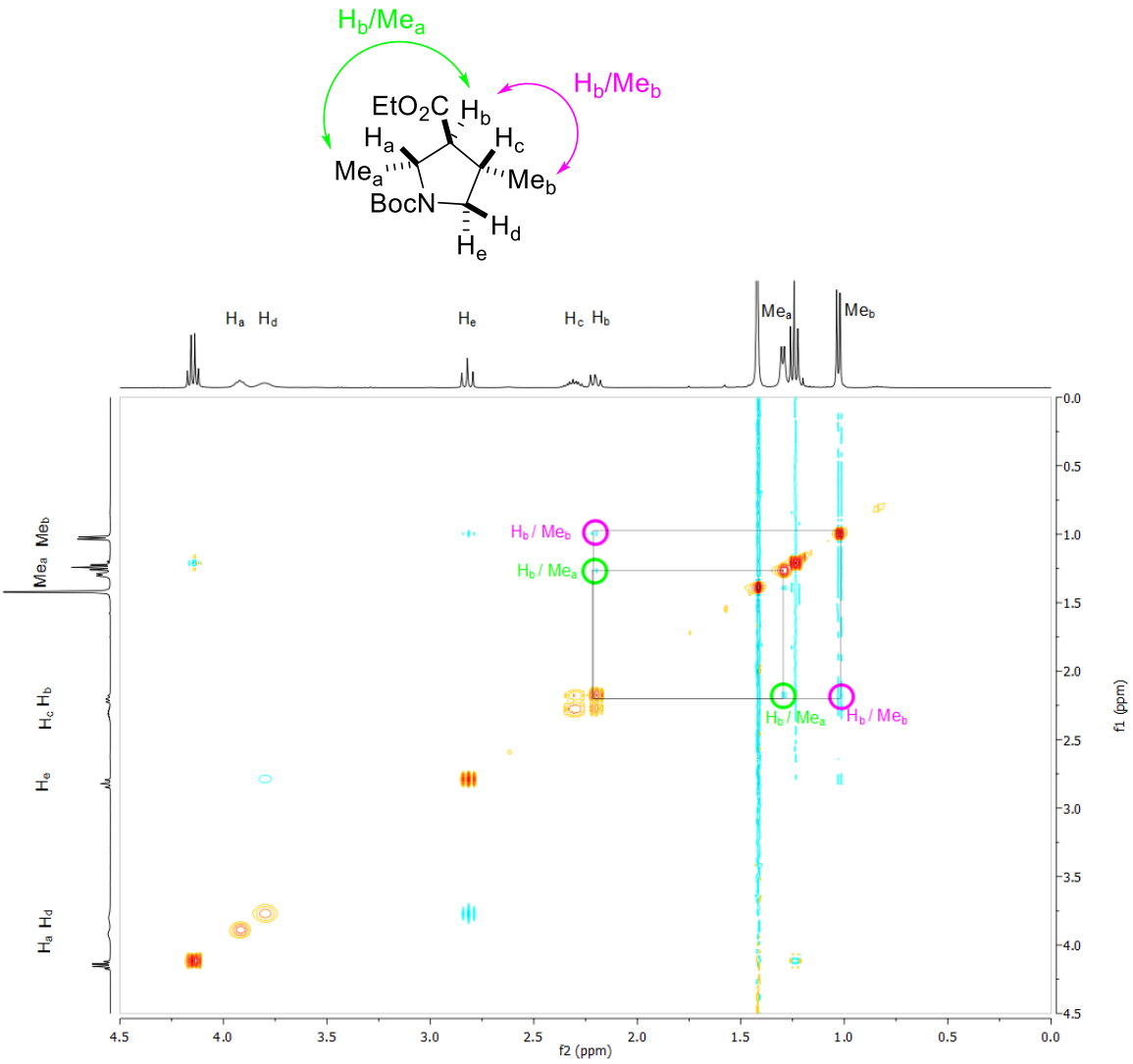
NOESY Analysis

rac. 1-(*tert*-Butyl) 3-ethyl (2*S*,3*R*,4*R*)-2,4-dimethylpyrrolidine-1,3-dicarboxylate (48e´)



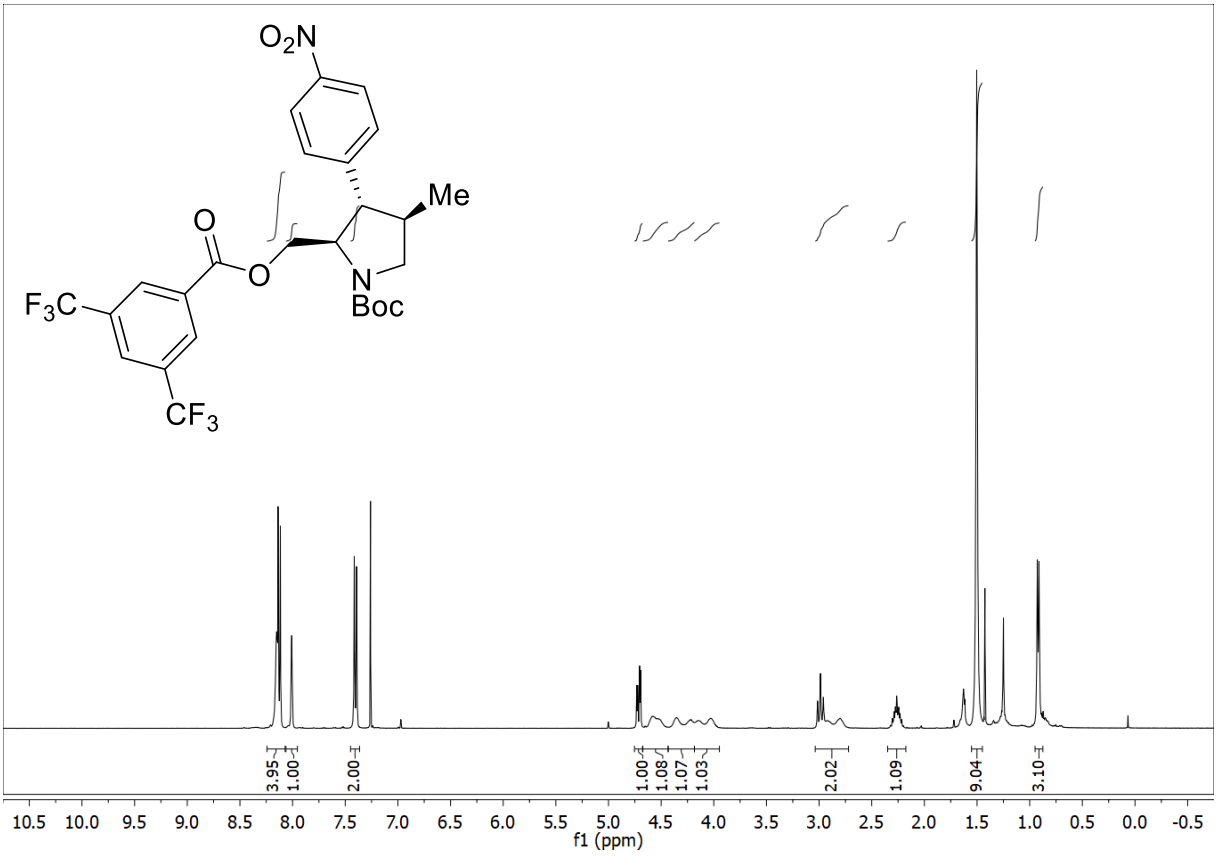


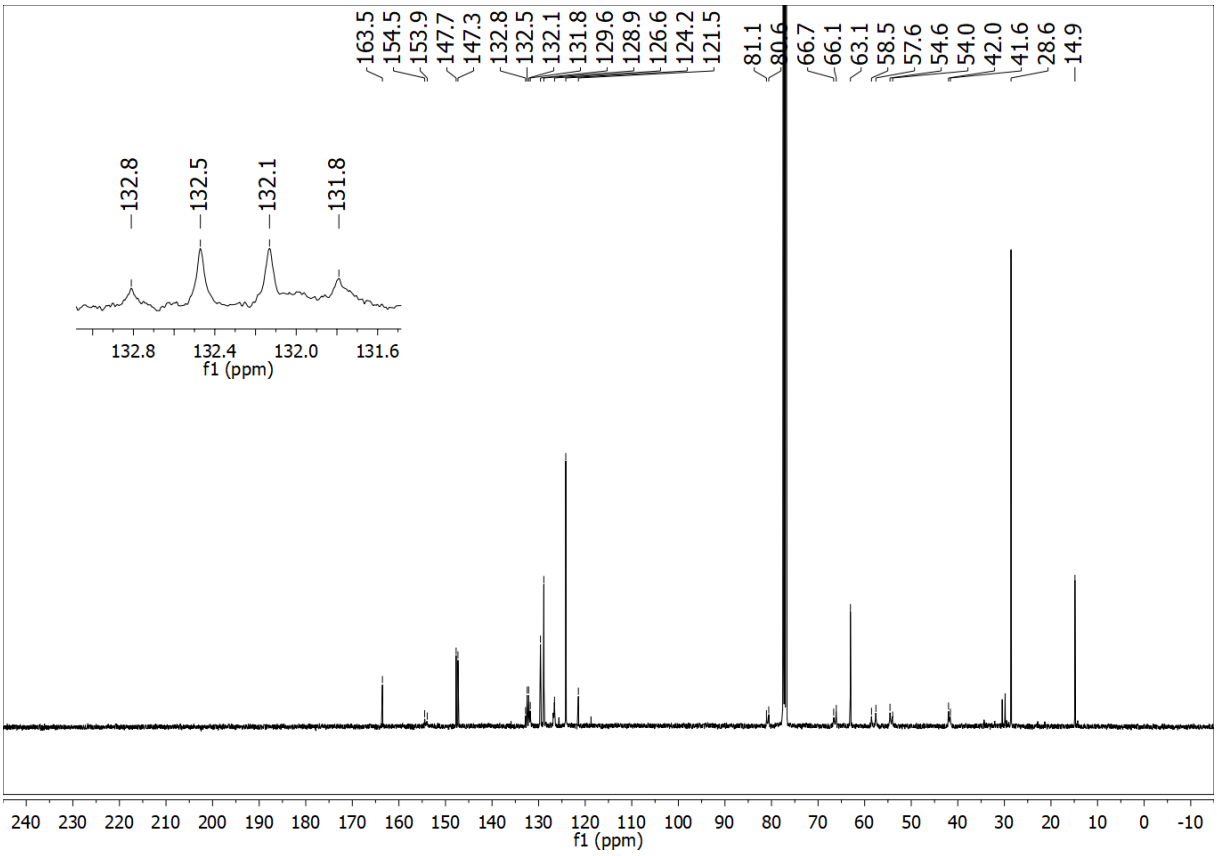
NMR-Solvent: $CDCl_3$

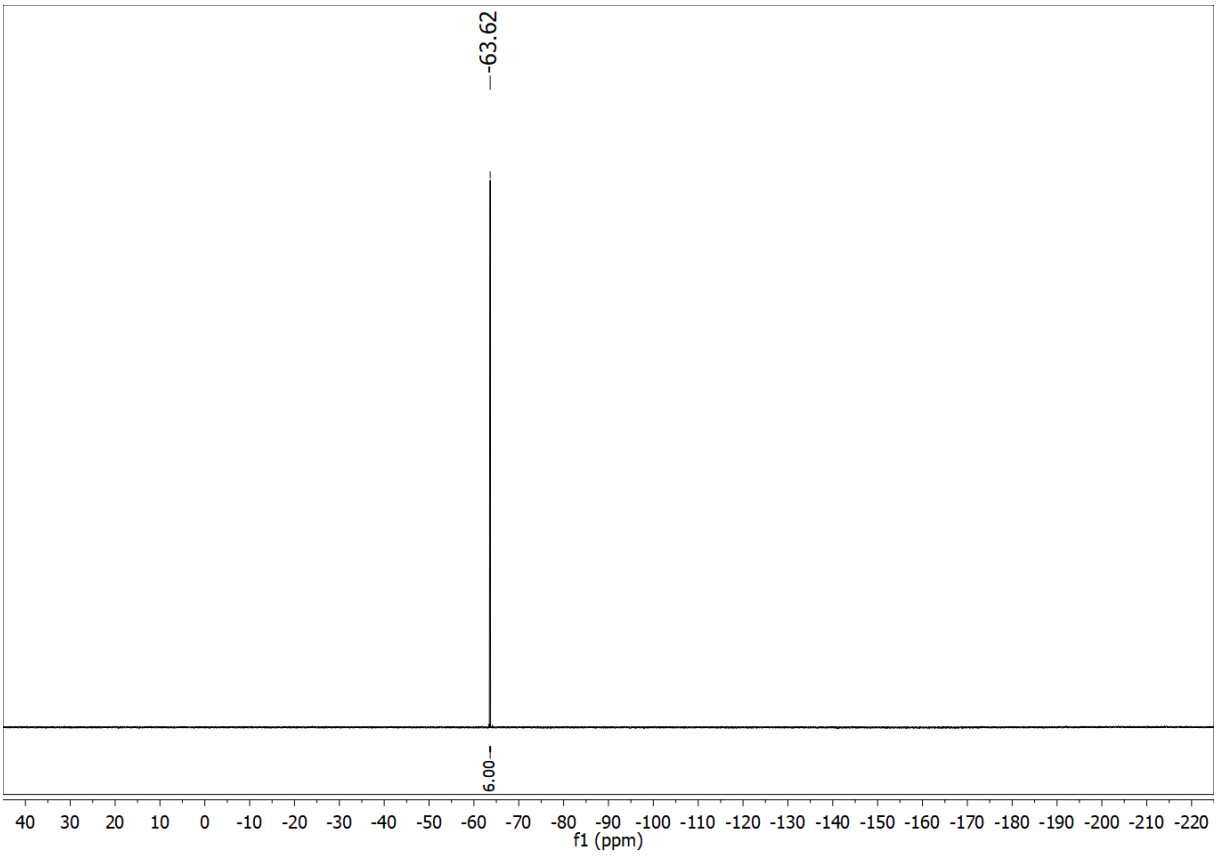


NOESY Analysis

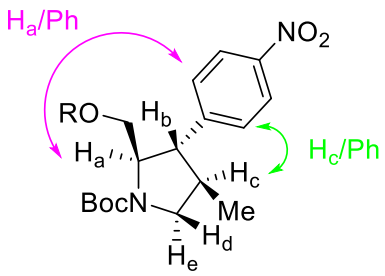
***tert*-Butyl (2*R*,3*S*,4*R*)-2-(((3,5-bis(trifluoromethyl)benzoyl)oxy)methyl)-4-methyl-3-(4-nitrophenyl)pyrrolidine-1-carboxylate (48f)**

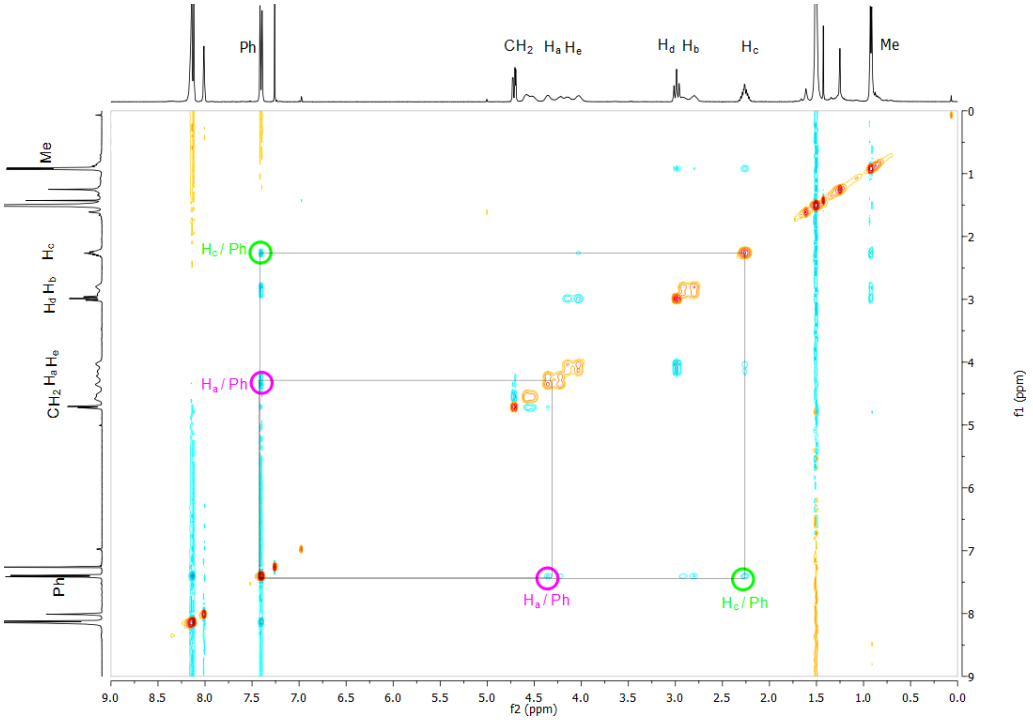




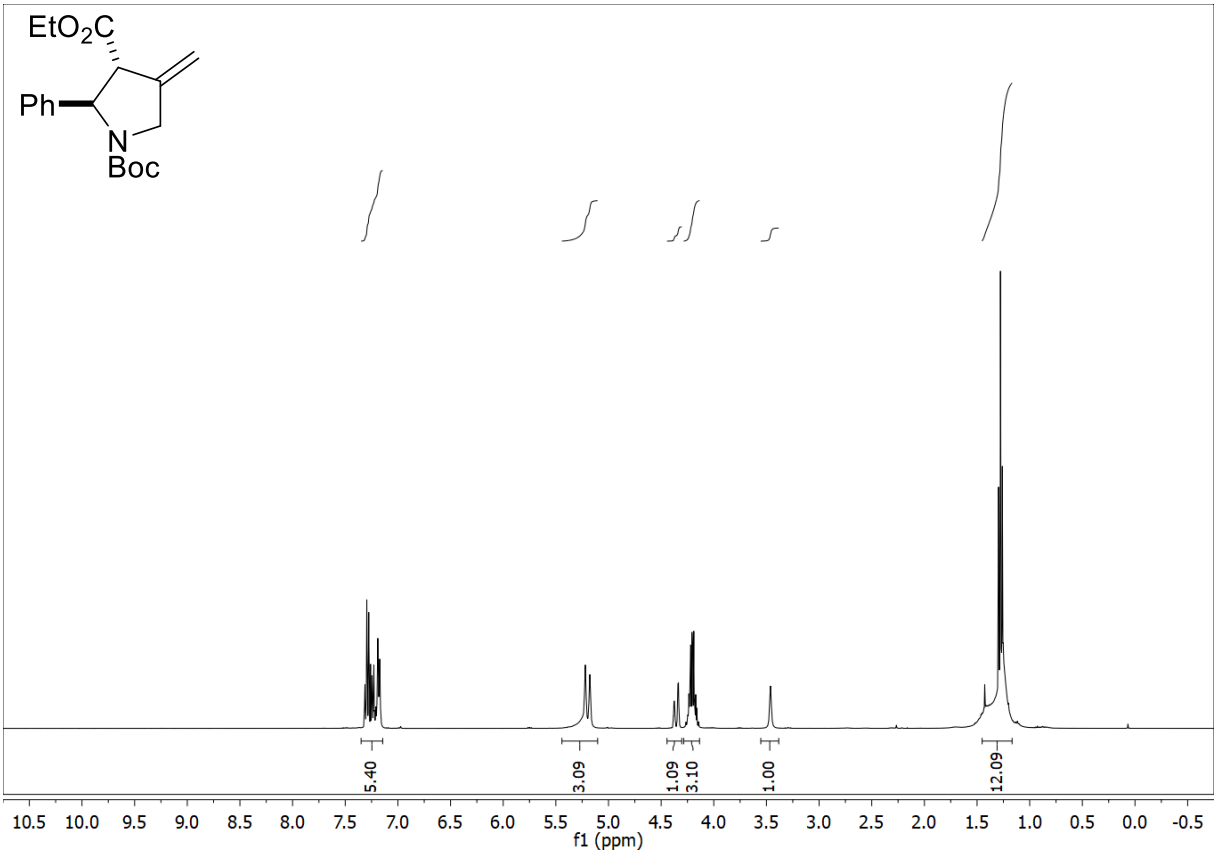


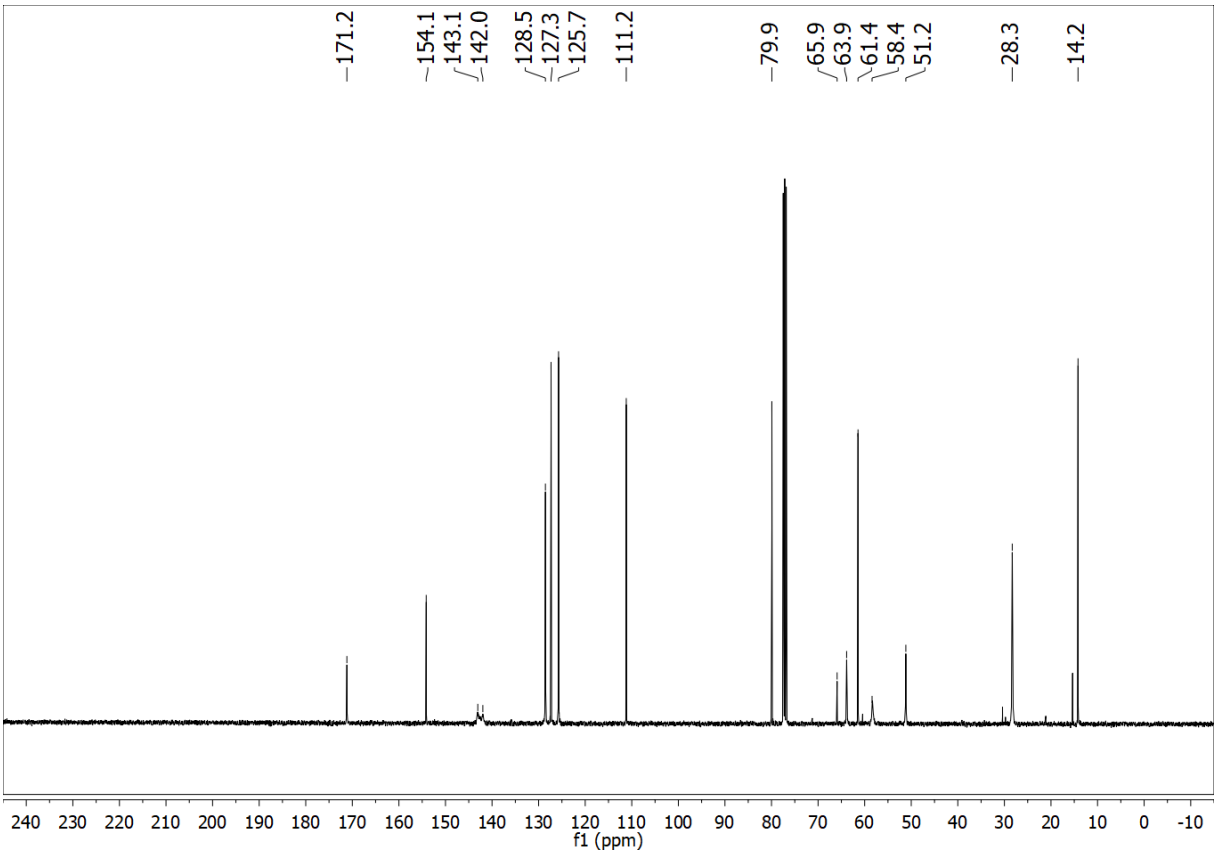
NMR-Solvent: $CDCl_3$



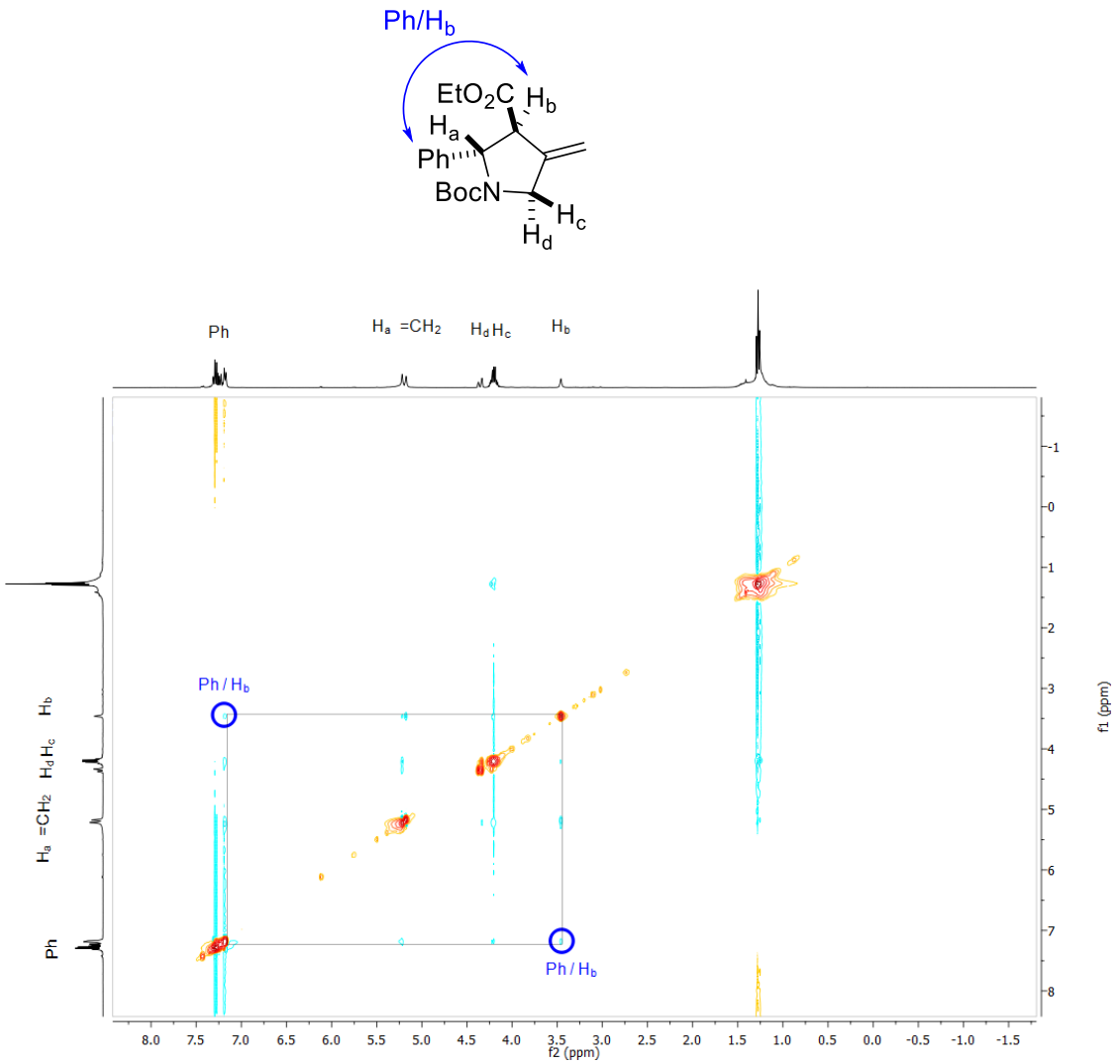


rac. 1-(*tert*-Butyl) 3-ethyl (2*R*,3*R*)-4-methylene-2-phenylpyrrolidine-1,3-dicarboxylate (48g)



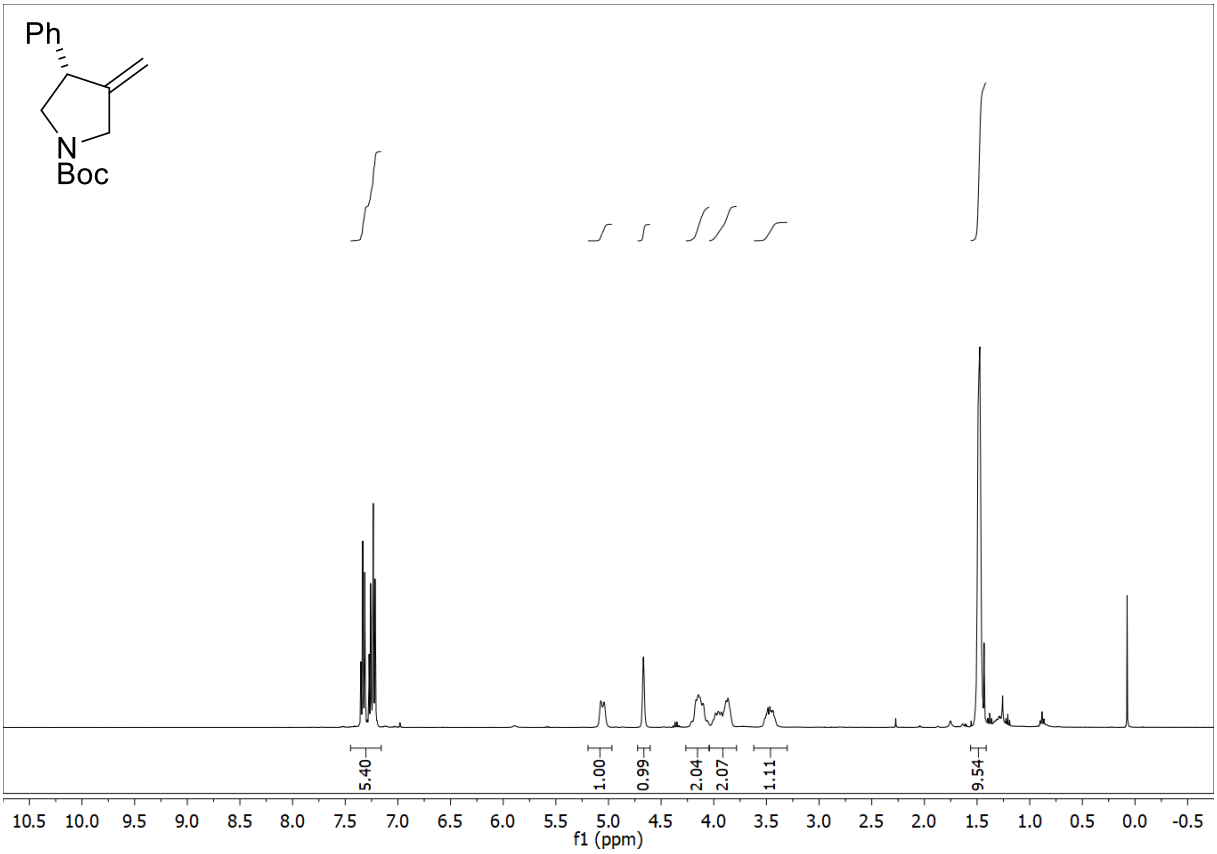


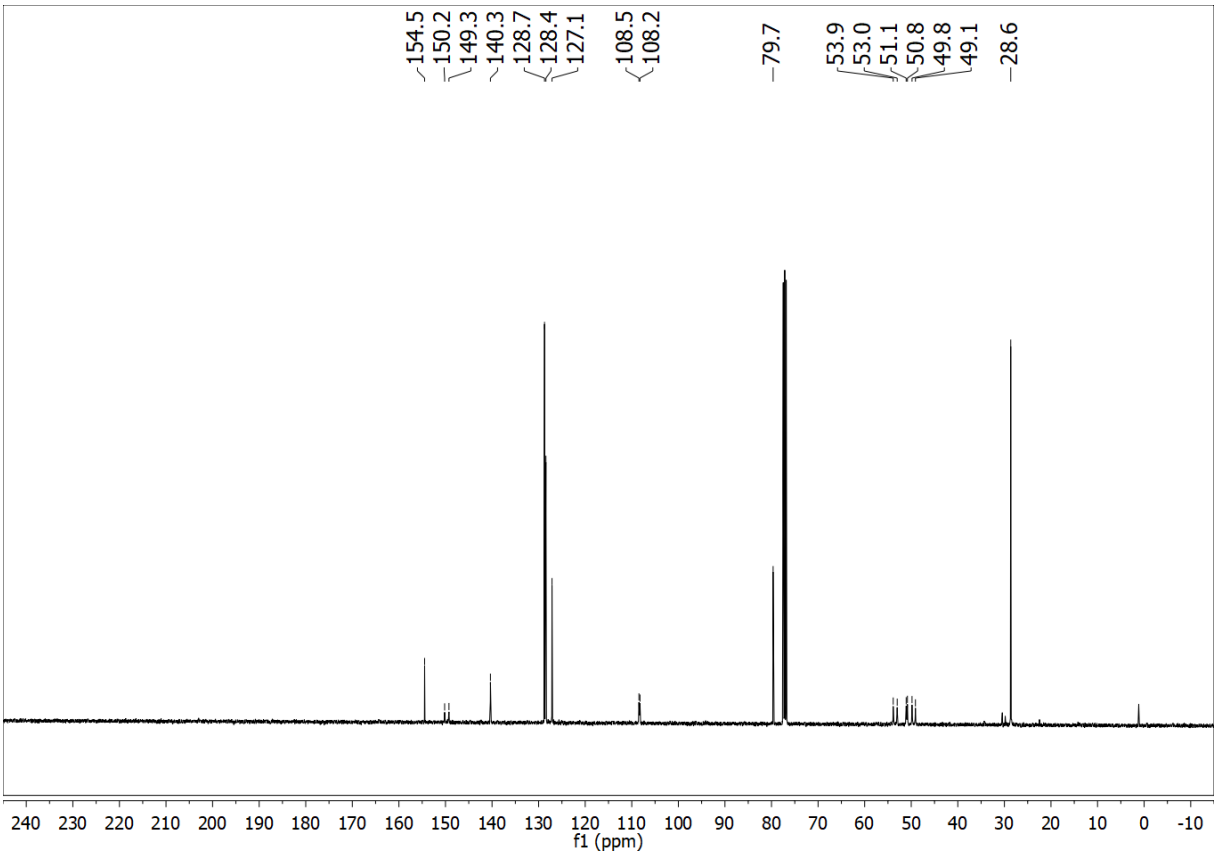
NMR-Solvent: $CDCl_3$



NOESY Analysis

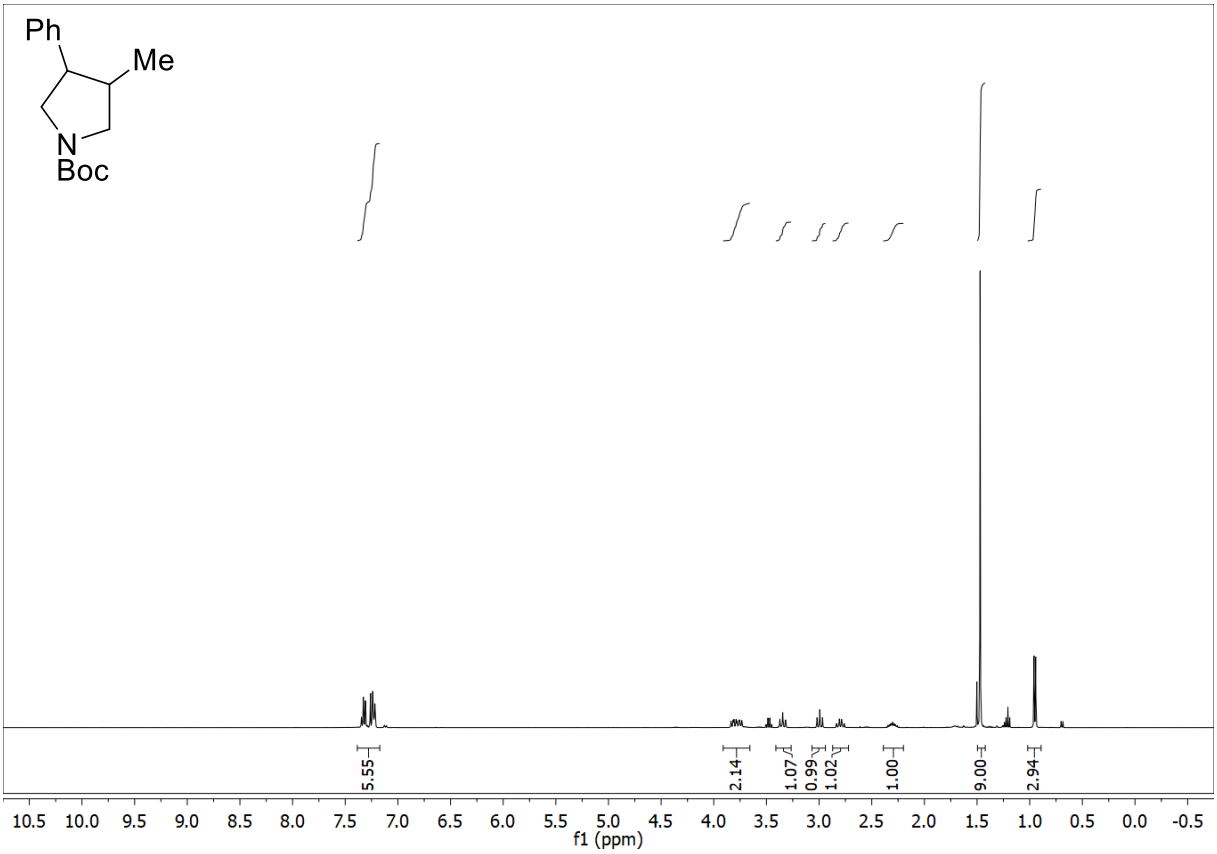
tert-Butyl-3-methylene-4-phenylpyrrolidine-1-carboxylate (48h)

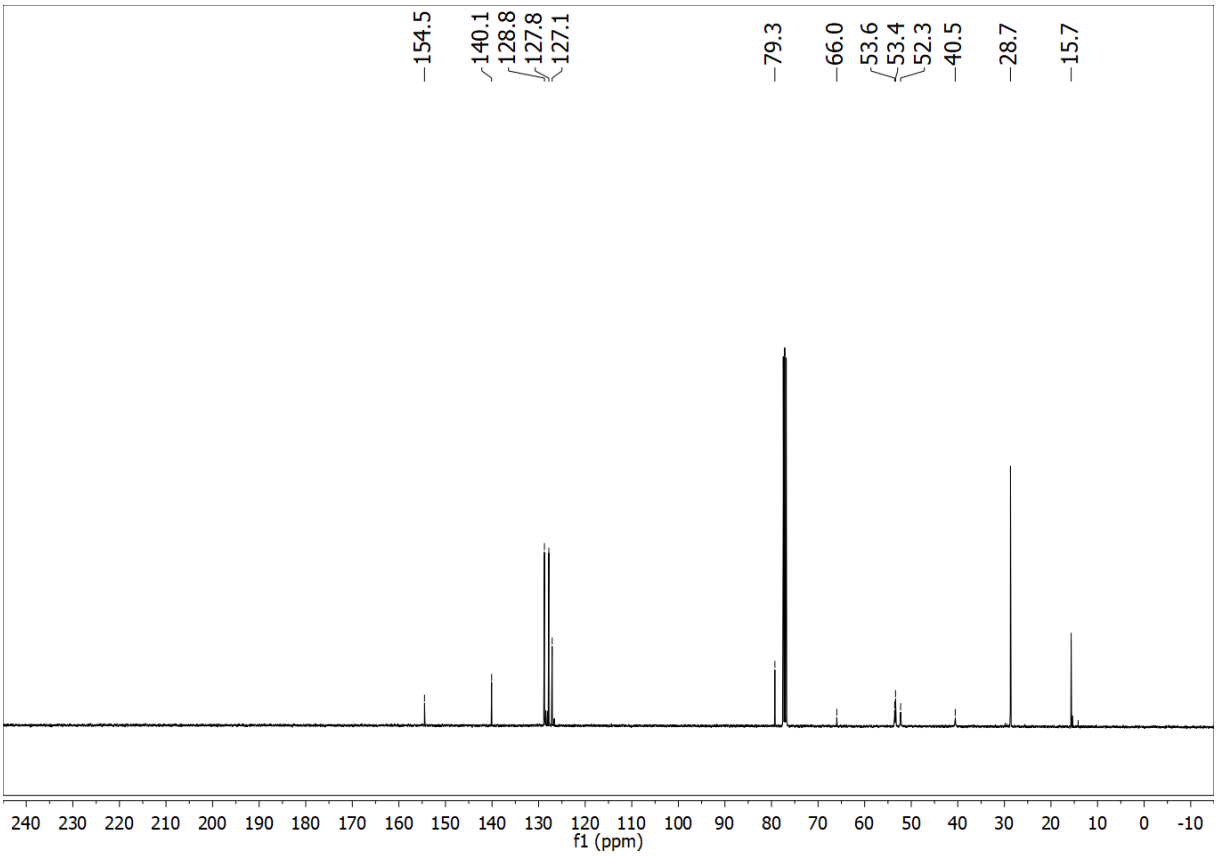




NMR-Solvent: $CDCl_3$

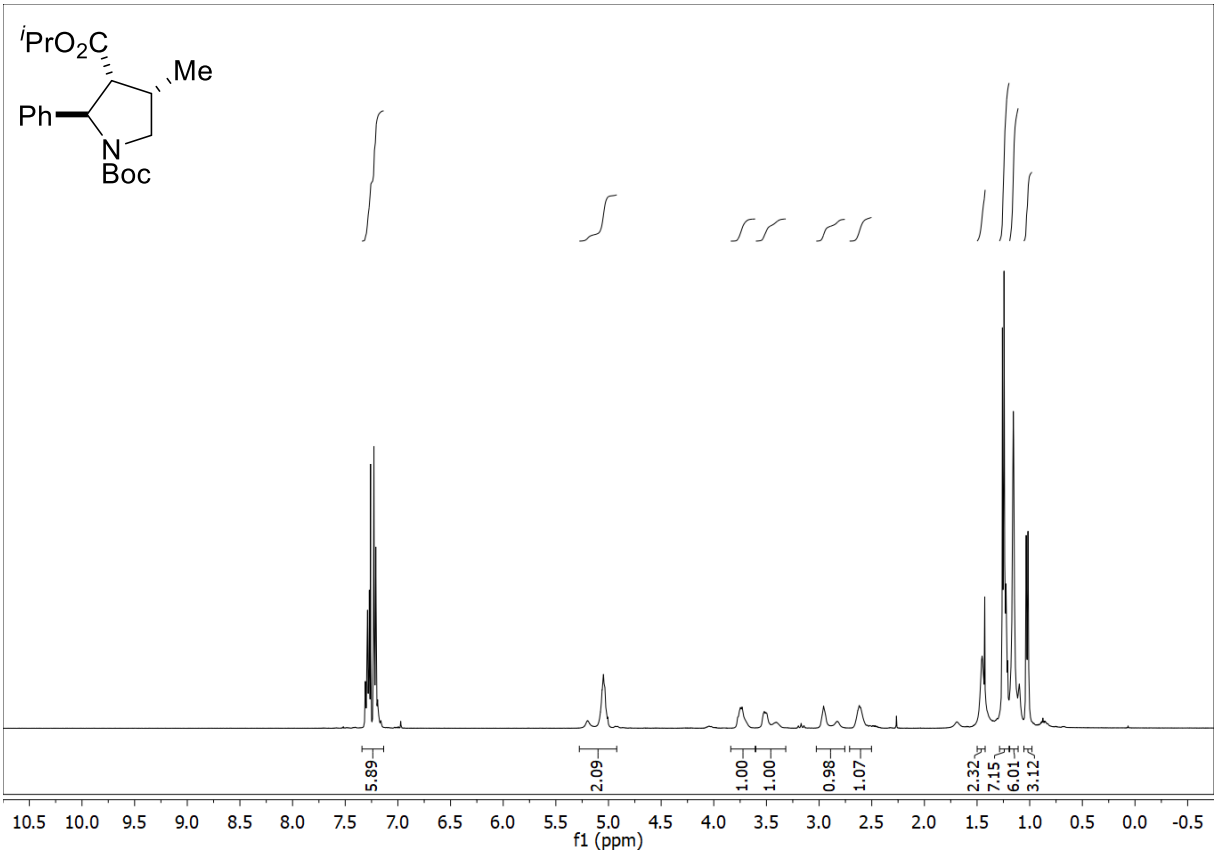
tert-butyl 3-methyl-4-phenylpyrrolidine-1-carboxylate (48i)

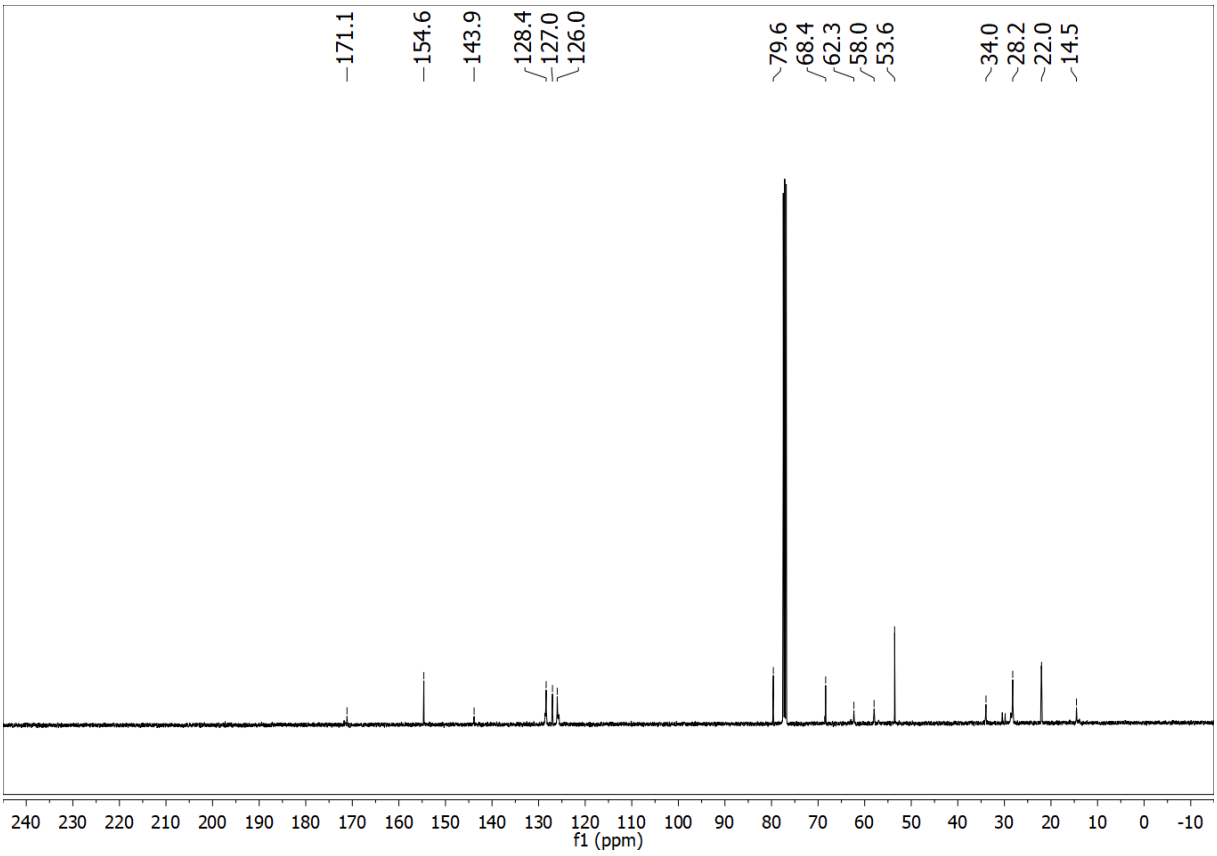




NMR-Solvent: $CDCl_3$

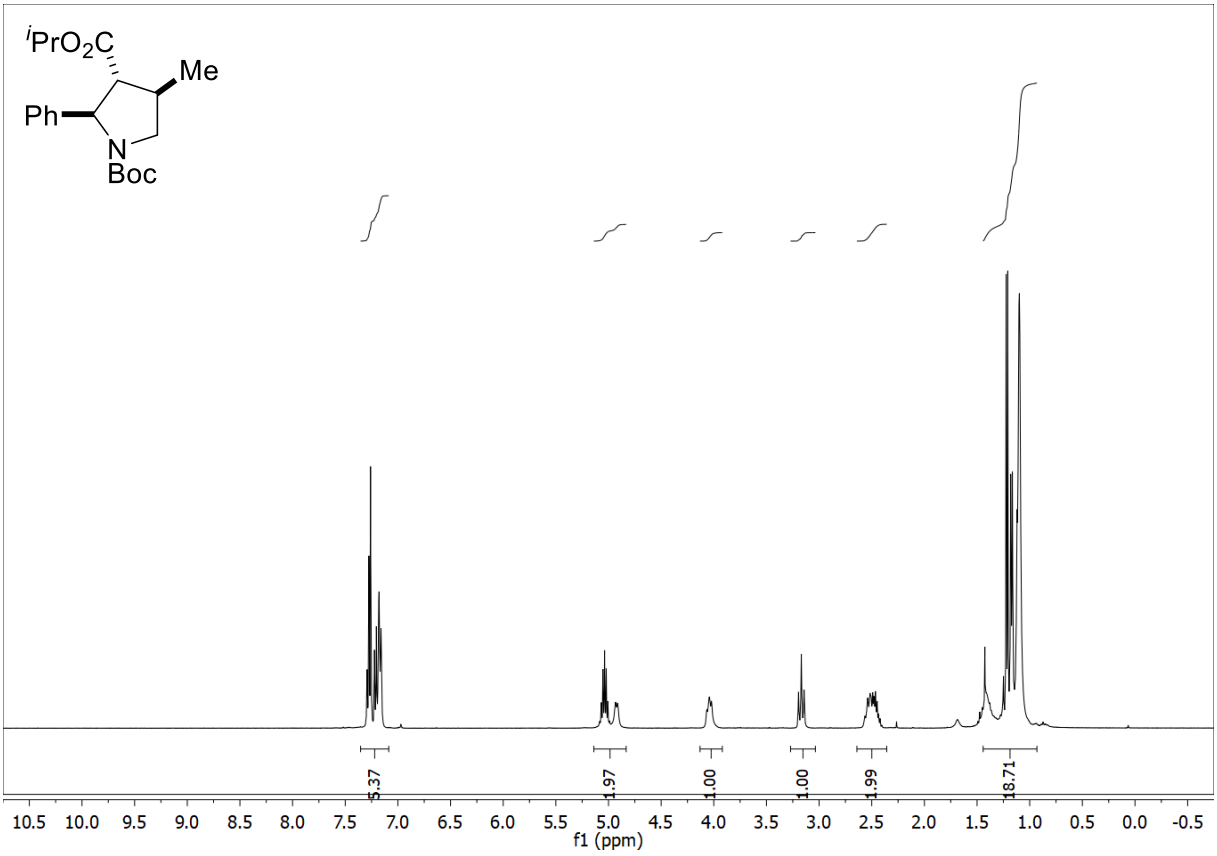
rac. 1-(*tert*-Butyl) 3-isopropyl (2*R*,3*R*,4*S*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (48j)

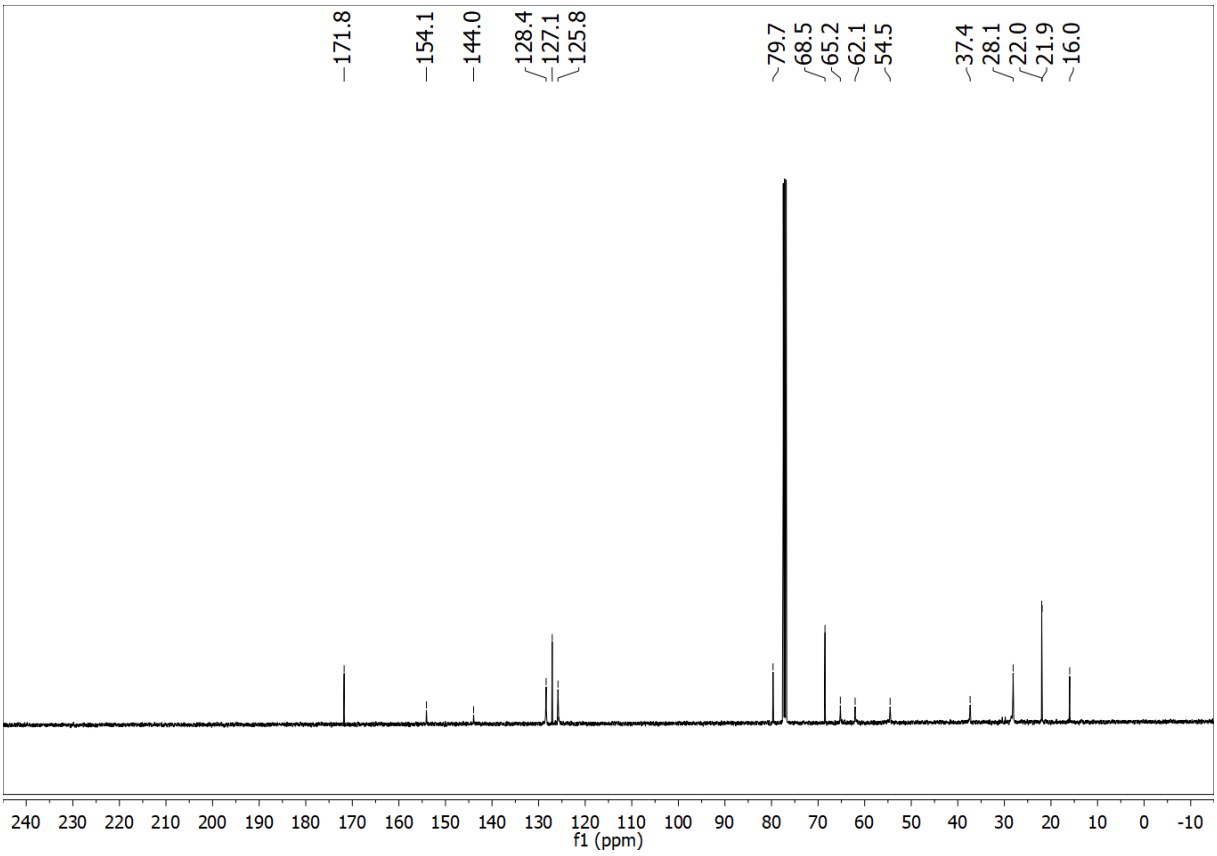




NMR-Solvent: $CDCl_3$

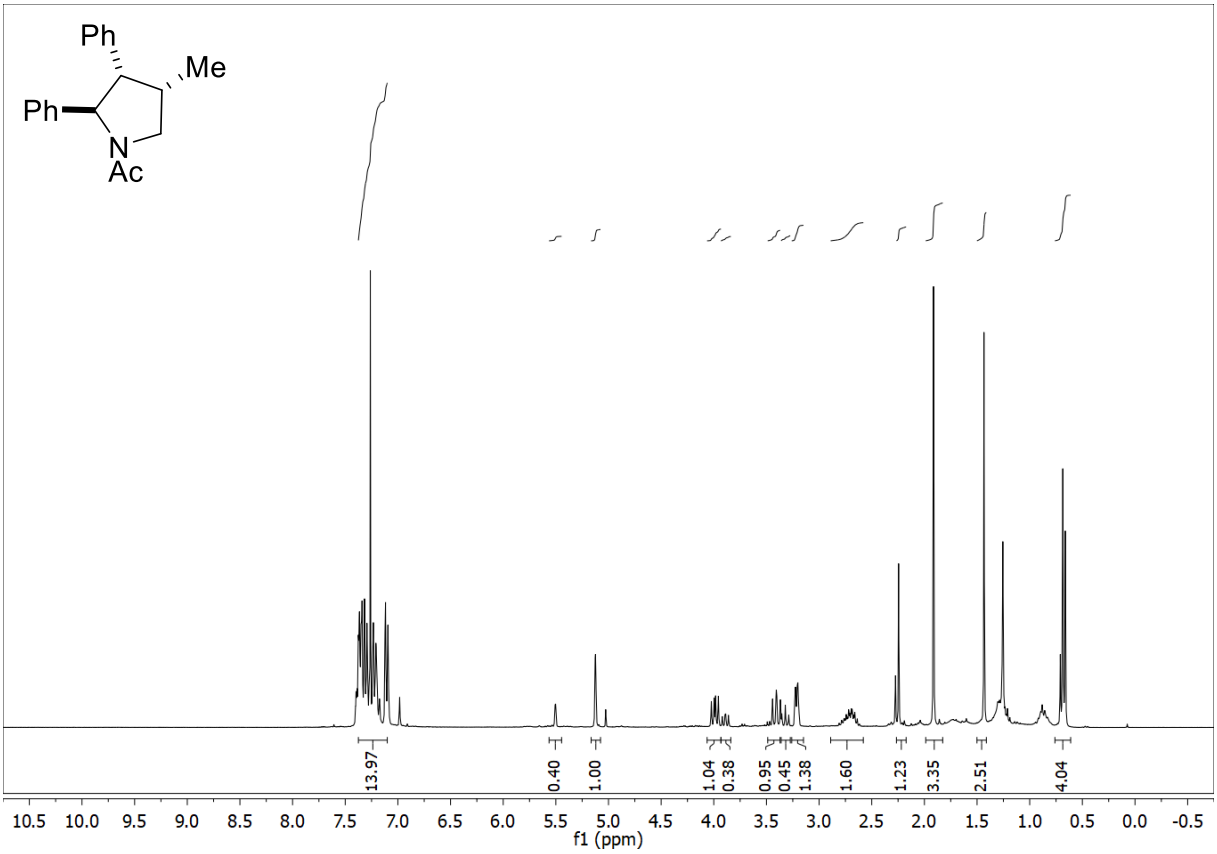
rac. 1-(*tert*-Butyl) 3-isopropyl (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-1,3-dicarboxylate (48j´)

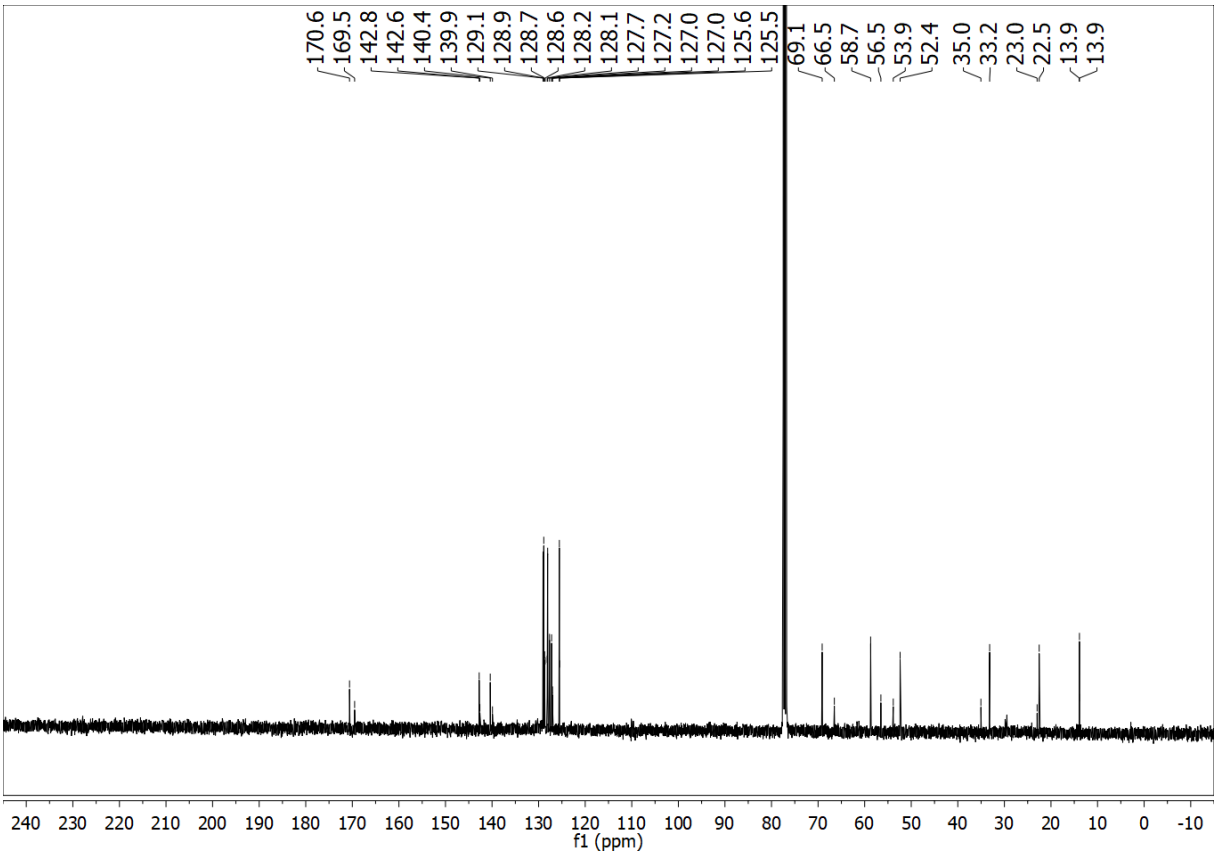




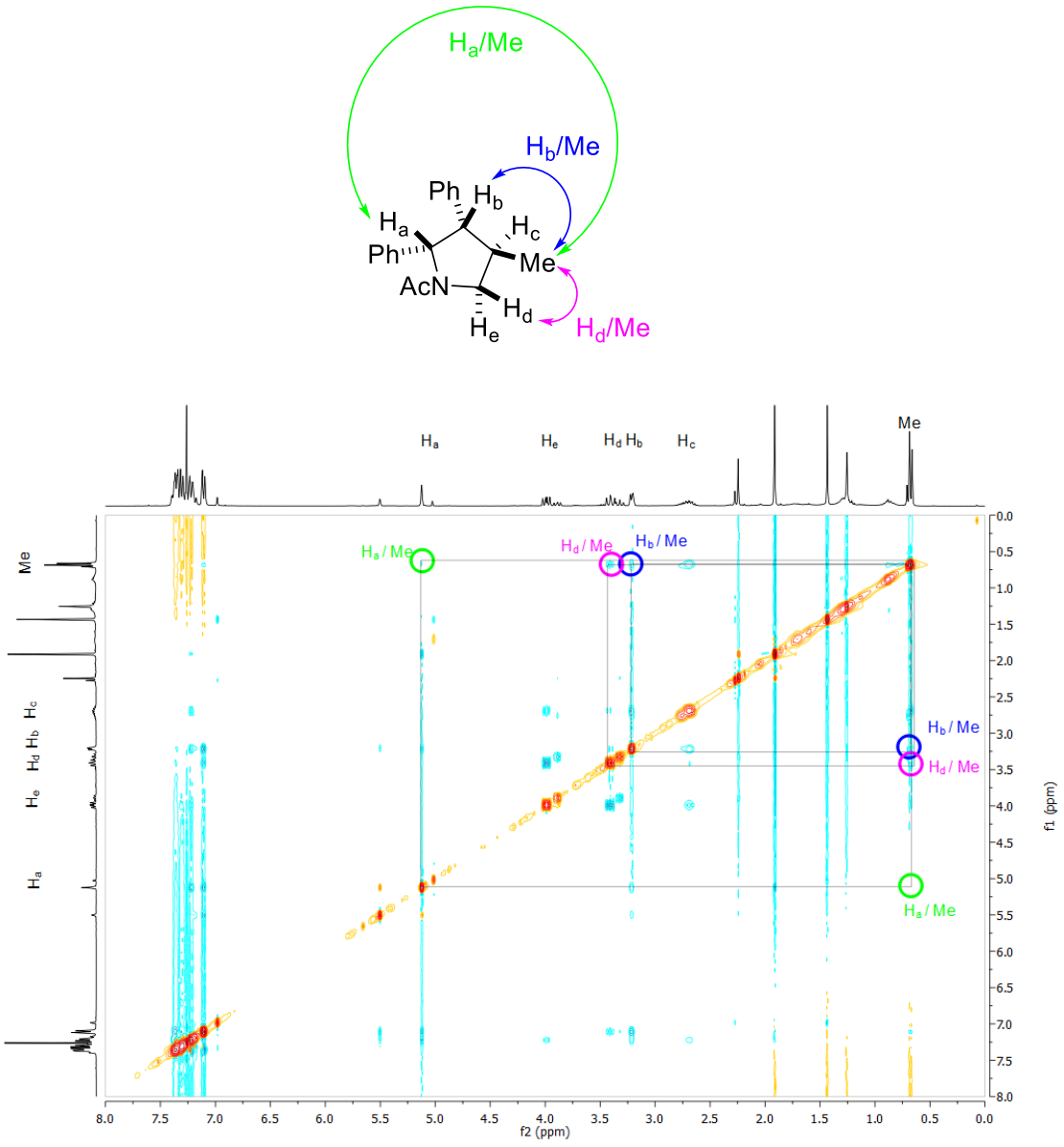
NMR-Solvent: $CDCl_3$

rac. 1-((2*R*,3*S*,4*S*)-4-methyl-2,3-diphenylpyrrolidin-1-yl)ethan-1-one (48m)



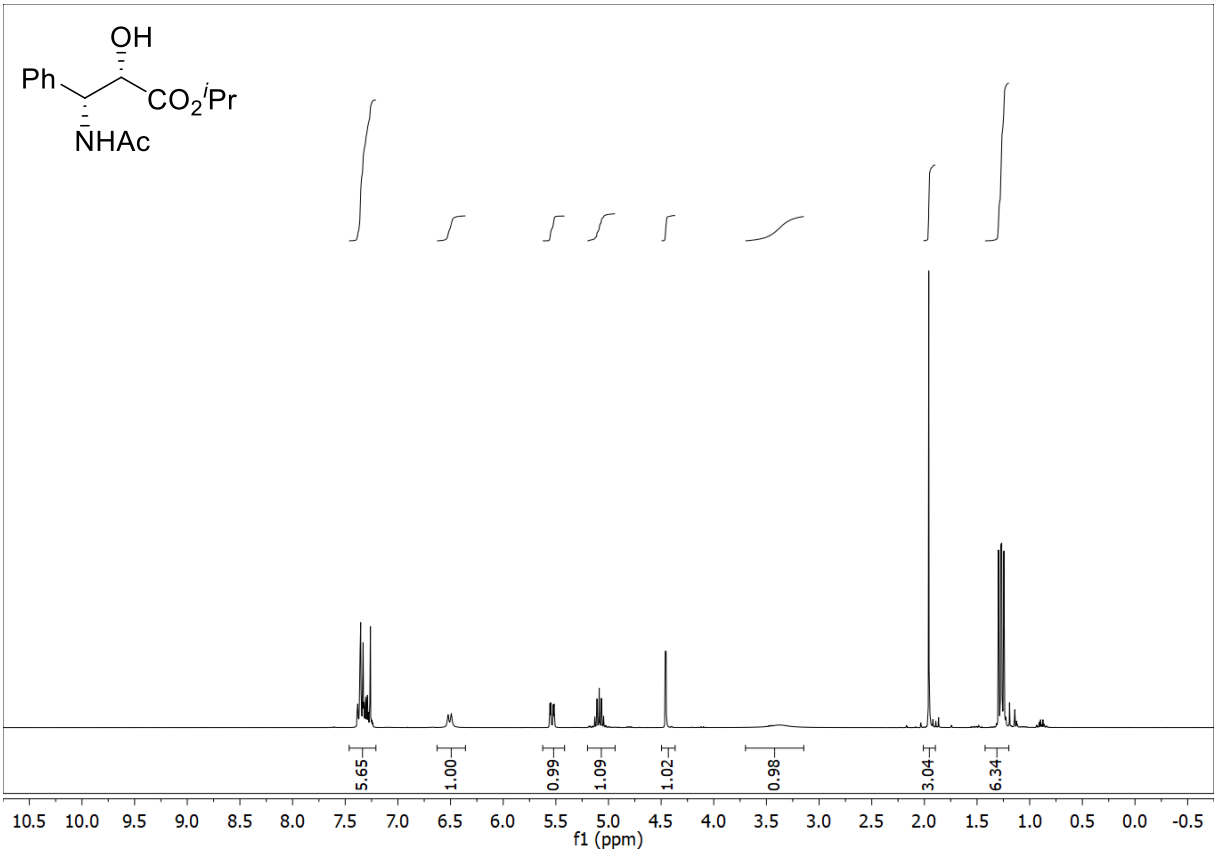


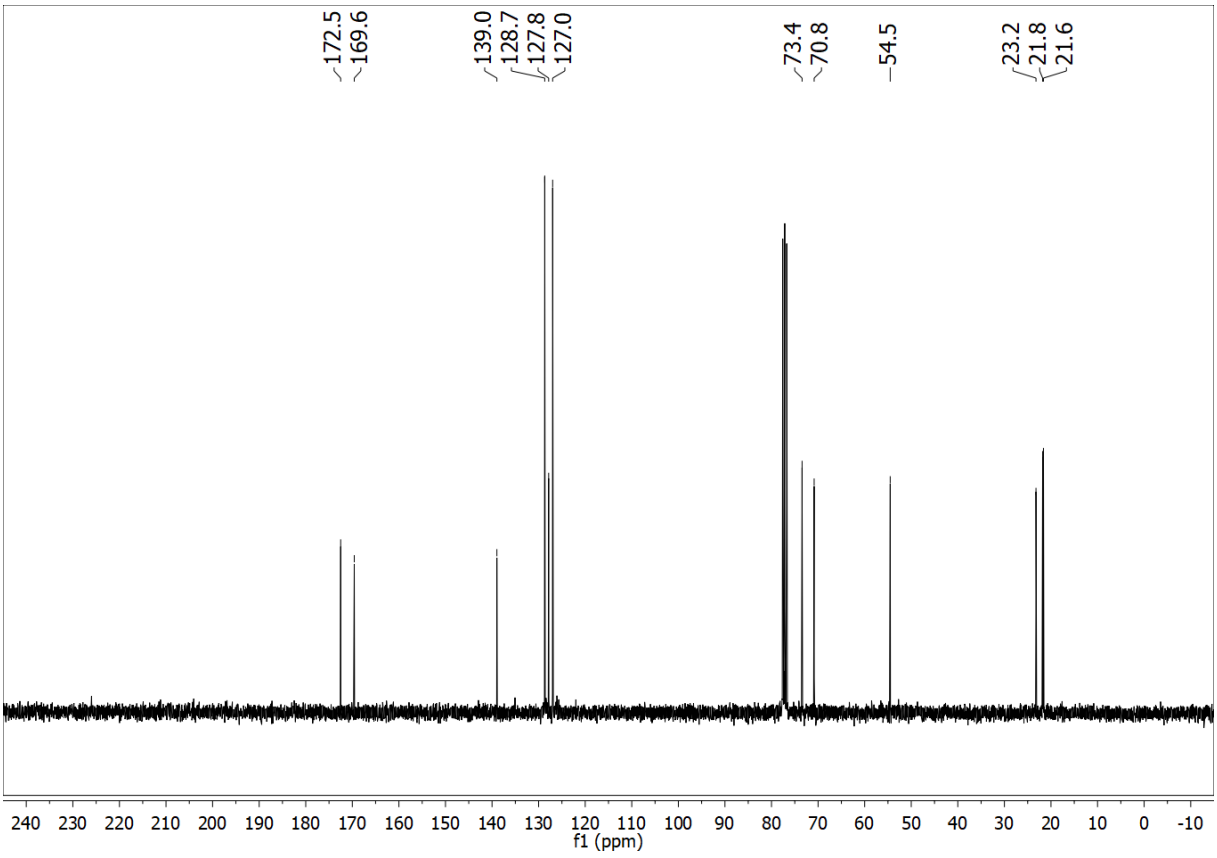
NMR-Solvent: $CDCl_3$



NOESY Analysis

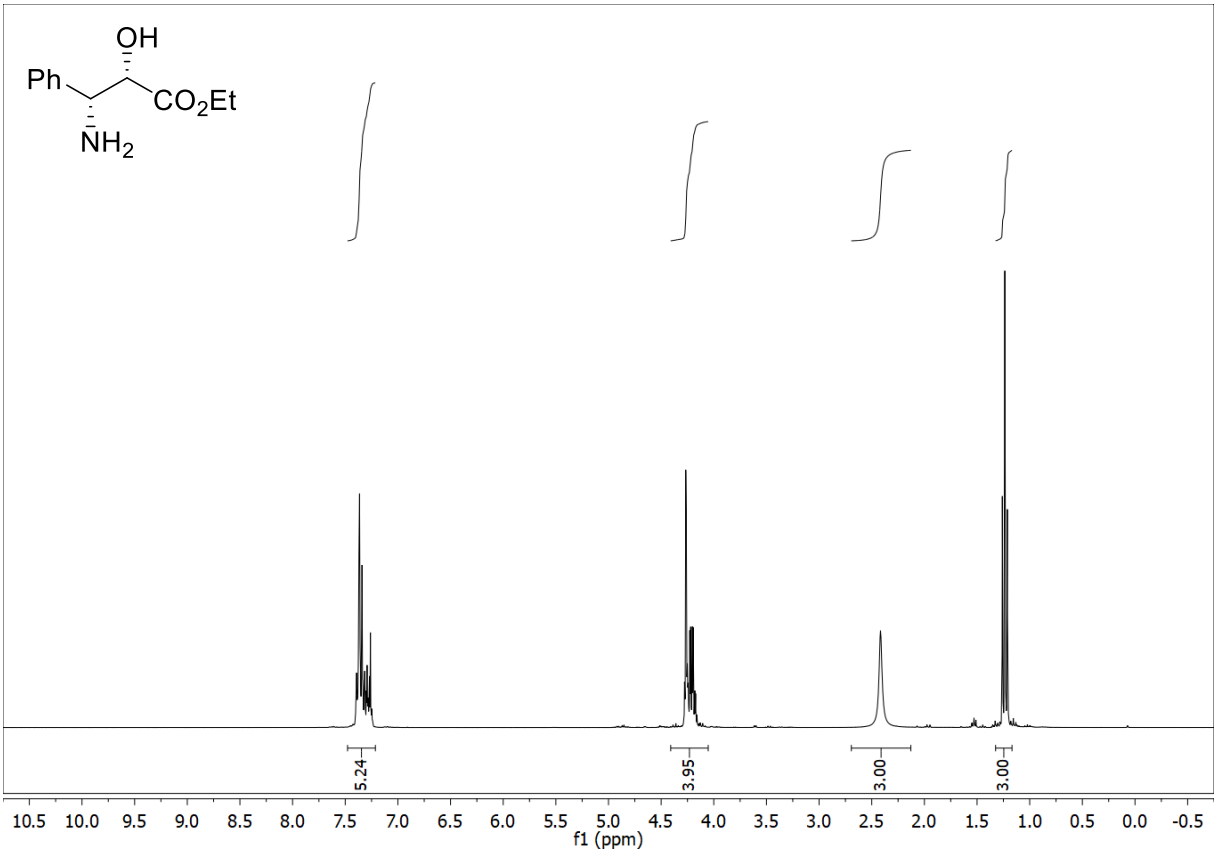
Isopropyl (2*S*,3*R*)-3-acetamido-2-hydroxy-3-phenylpropanoate (64)

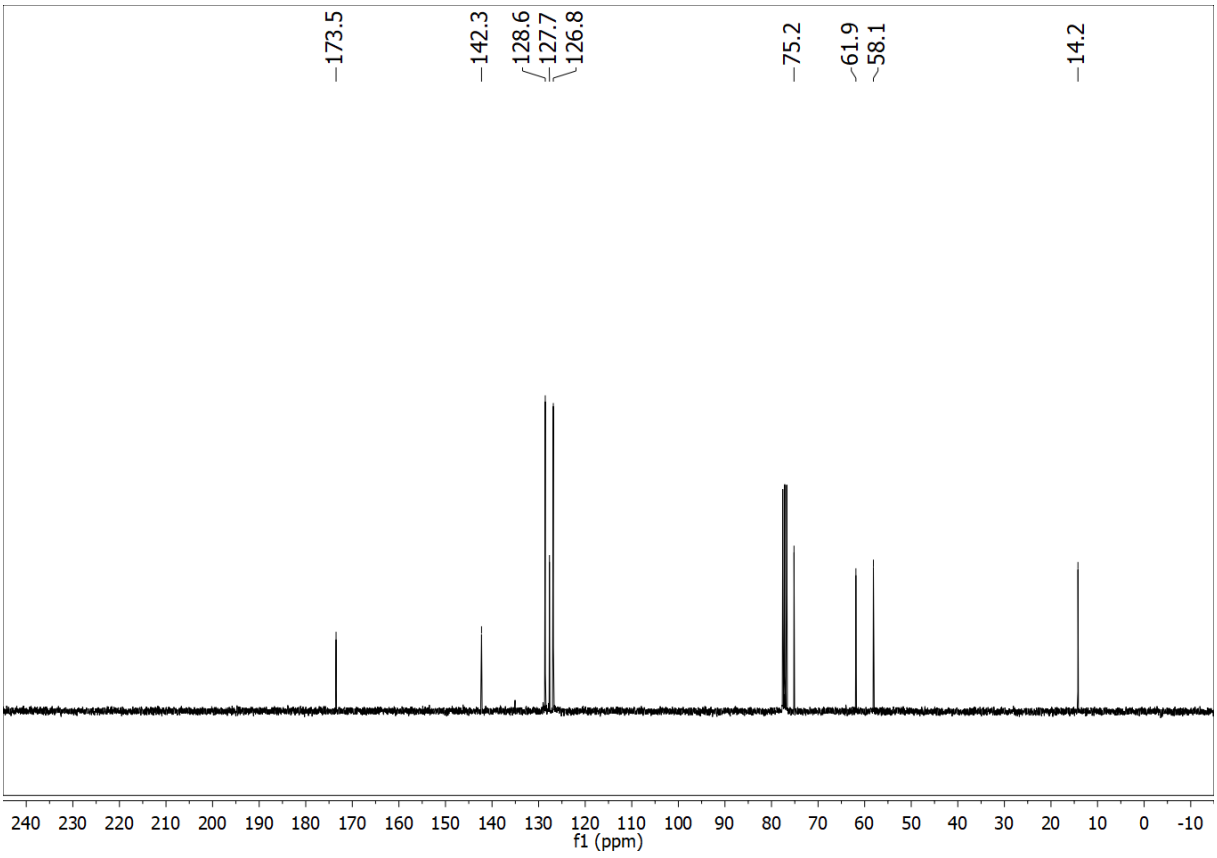




NMR-Solvent: $CDCl_3$

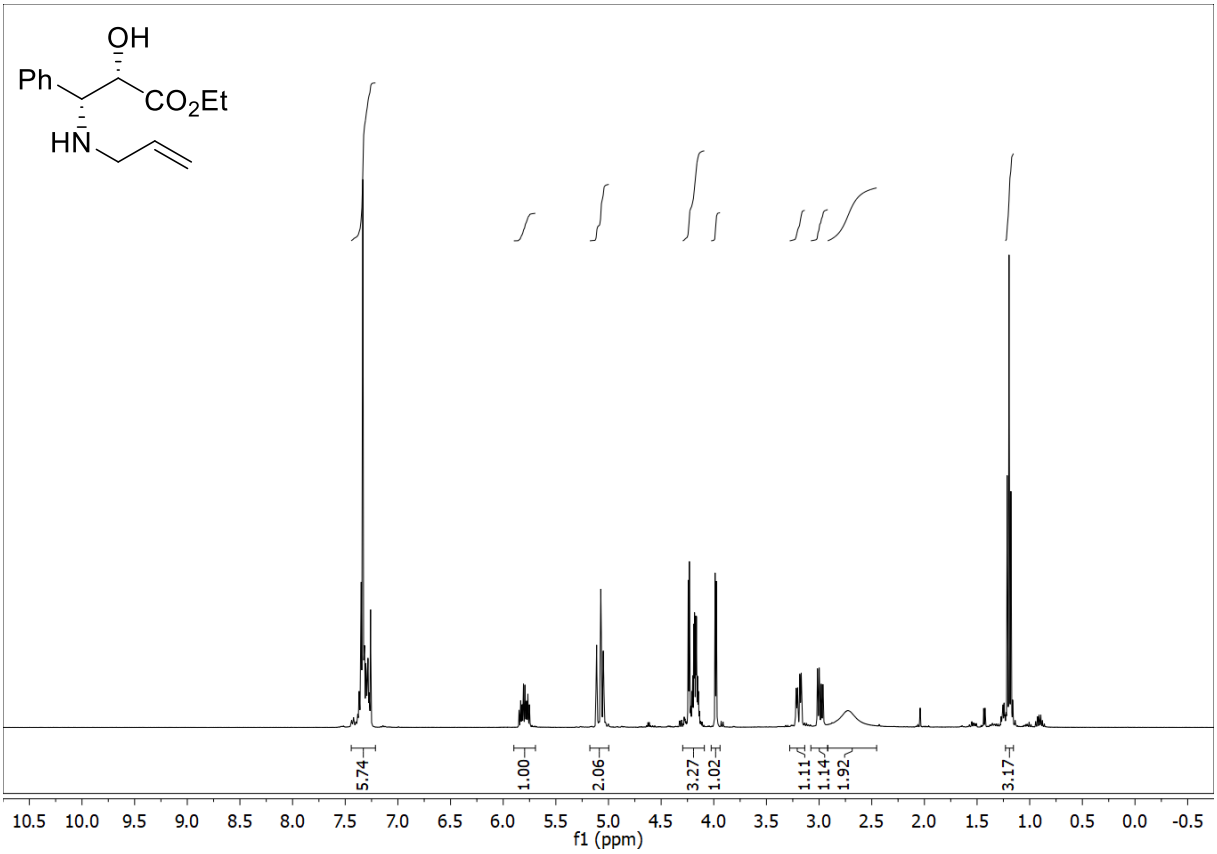
Ethyl (2*S*,3*R*)-3-amino-2-hydroxy-3-phenylpropanoate (65)

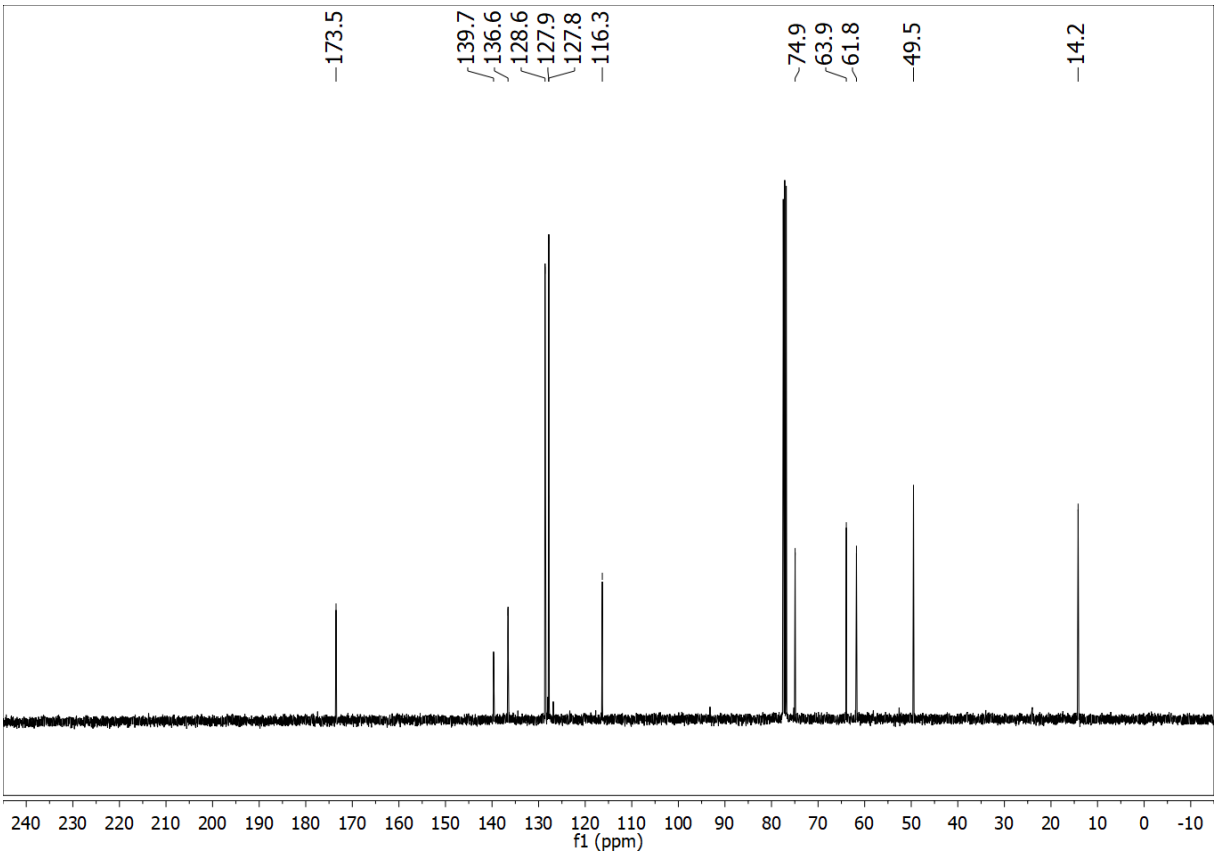




NMR-Solvent: $CDCl_3$

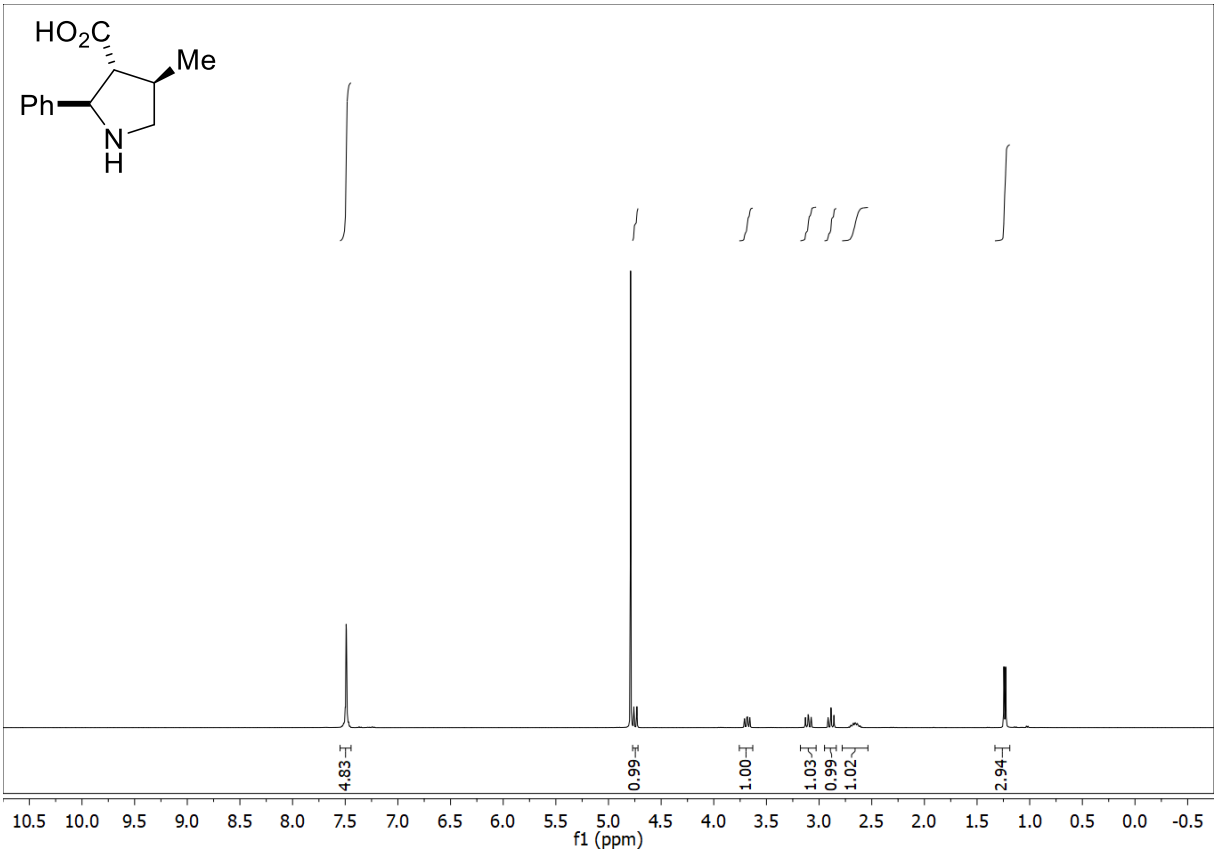
Ethyl (2*S*,3*R*)-3-(allylamino)-2-hydroxy-3-phenylpropanoate (66)

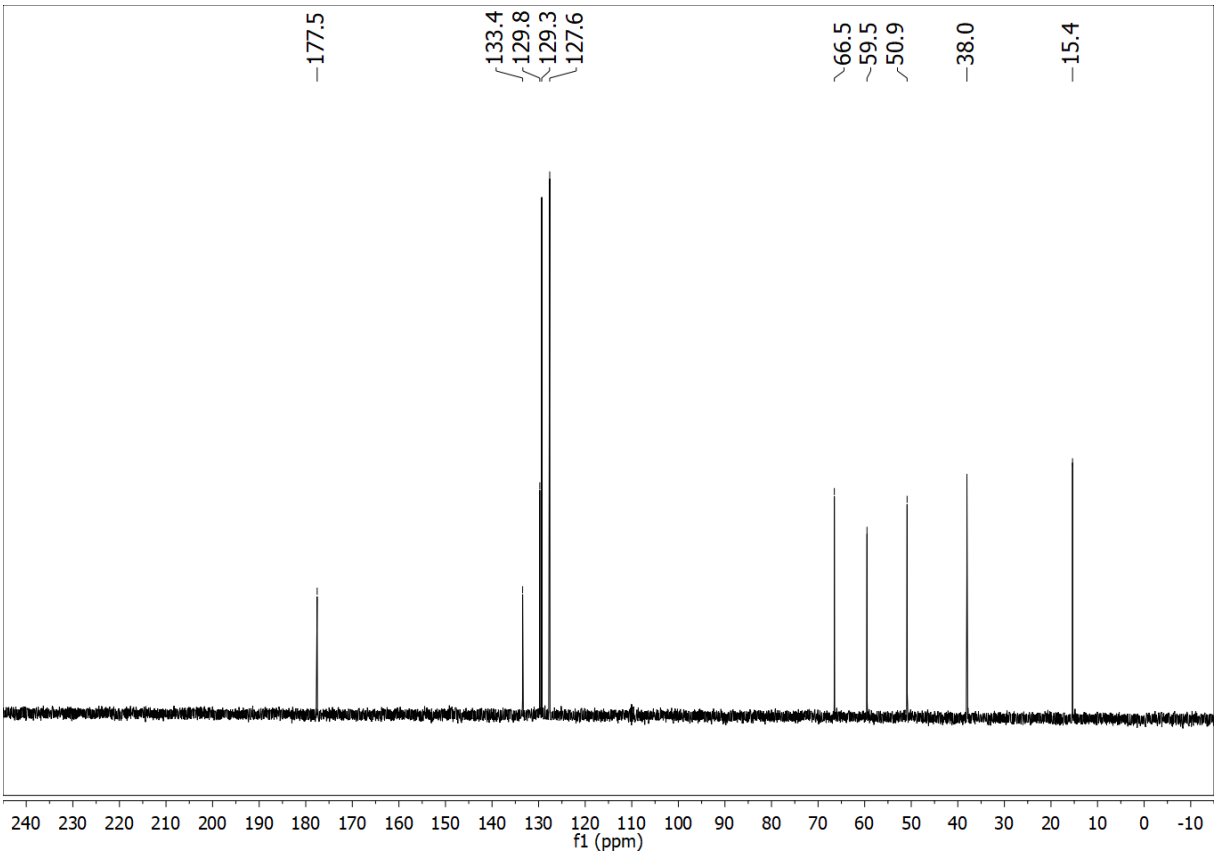




NMR-Solvent: $CDCl_3$

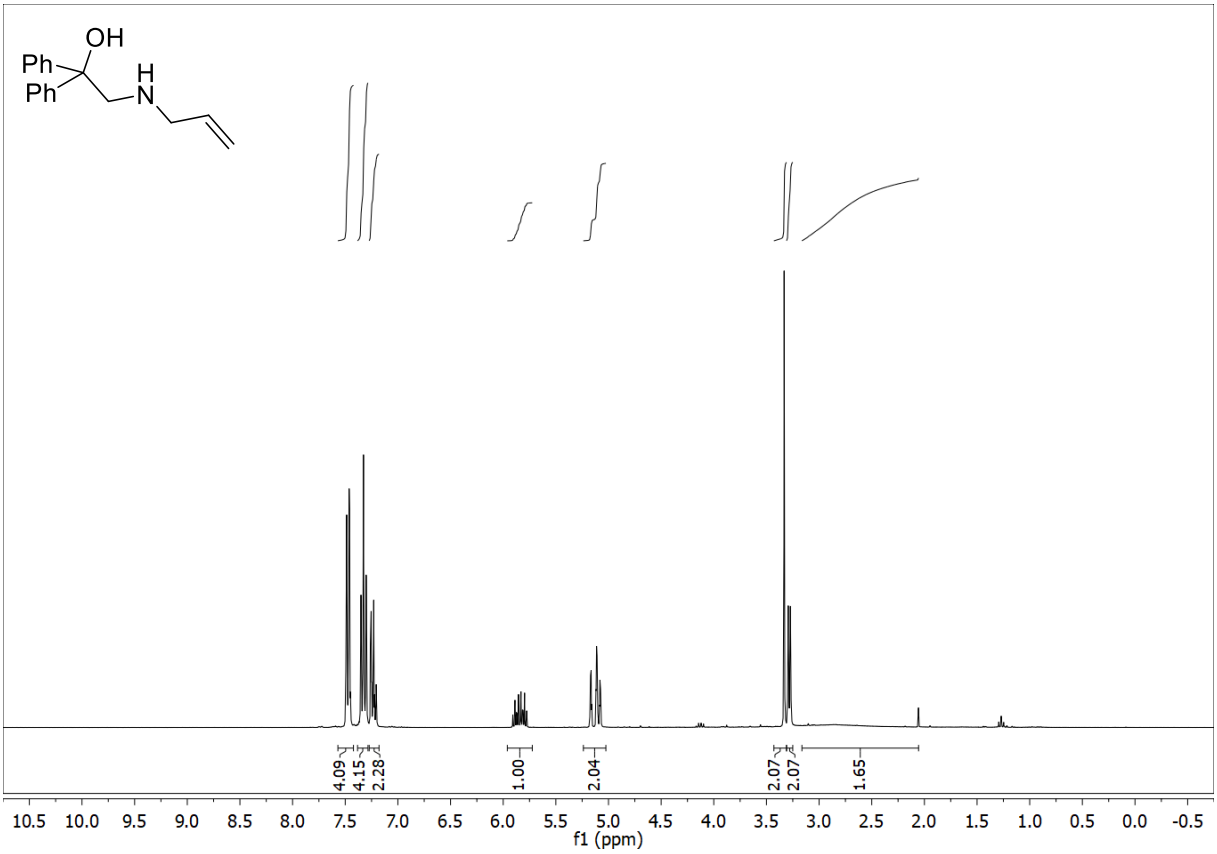
rac. (2*R*,3*R*,4*R*)-4-methyl-2-phenylpyrrolidine-3-carboxylic acid (69)

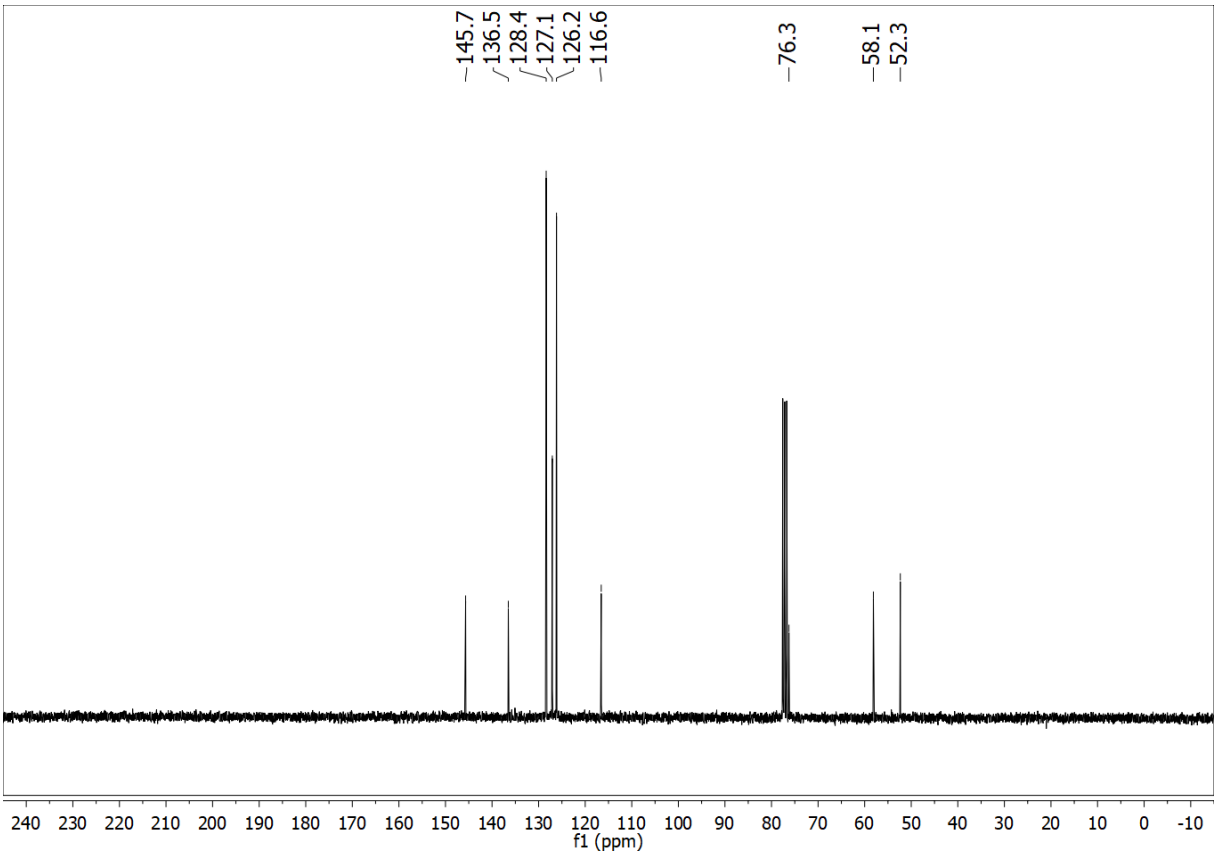




NMR-Solvent: D_2O

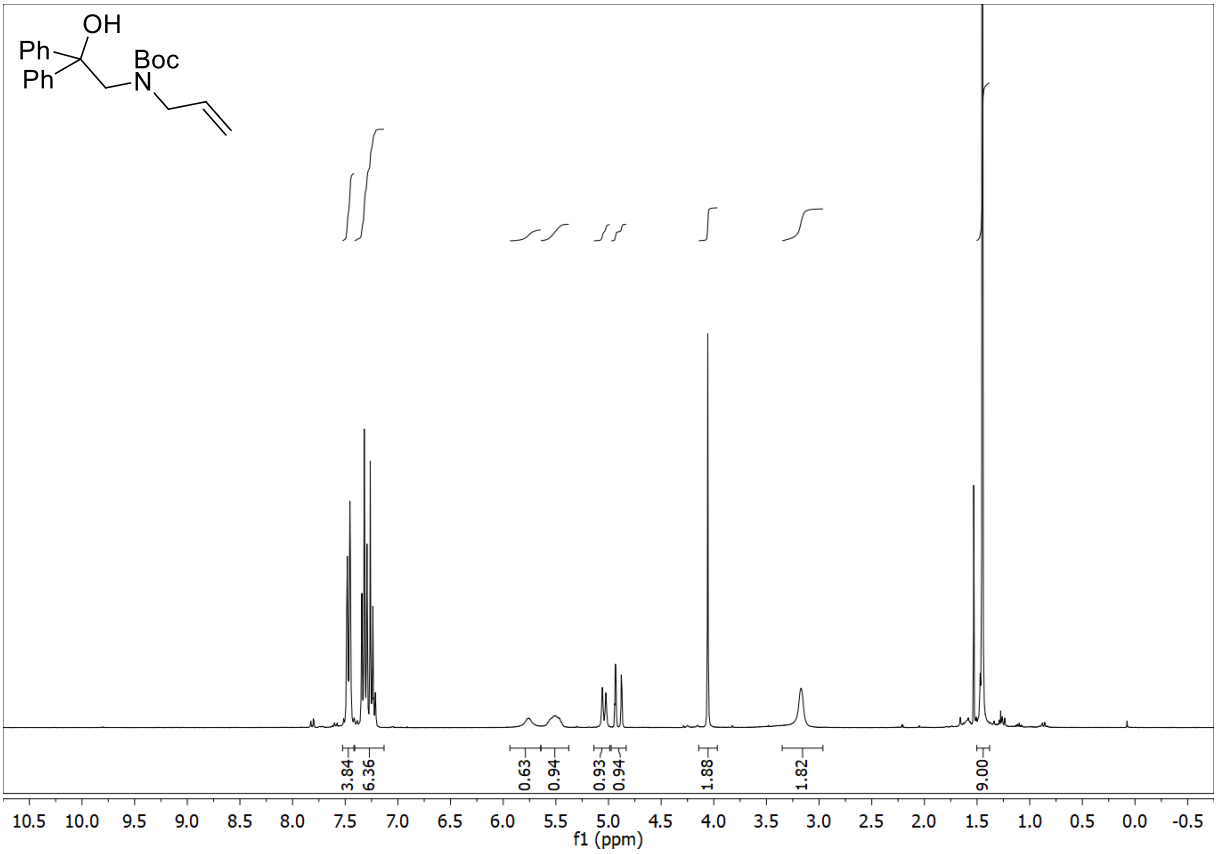
2-(Allylamino)-1,1-diphenylethan-1-ol (73)

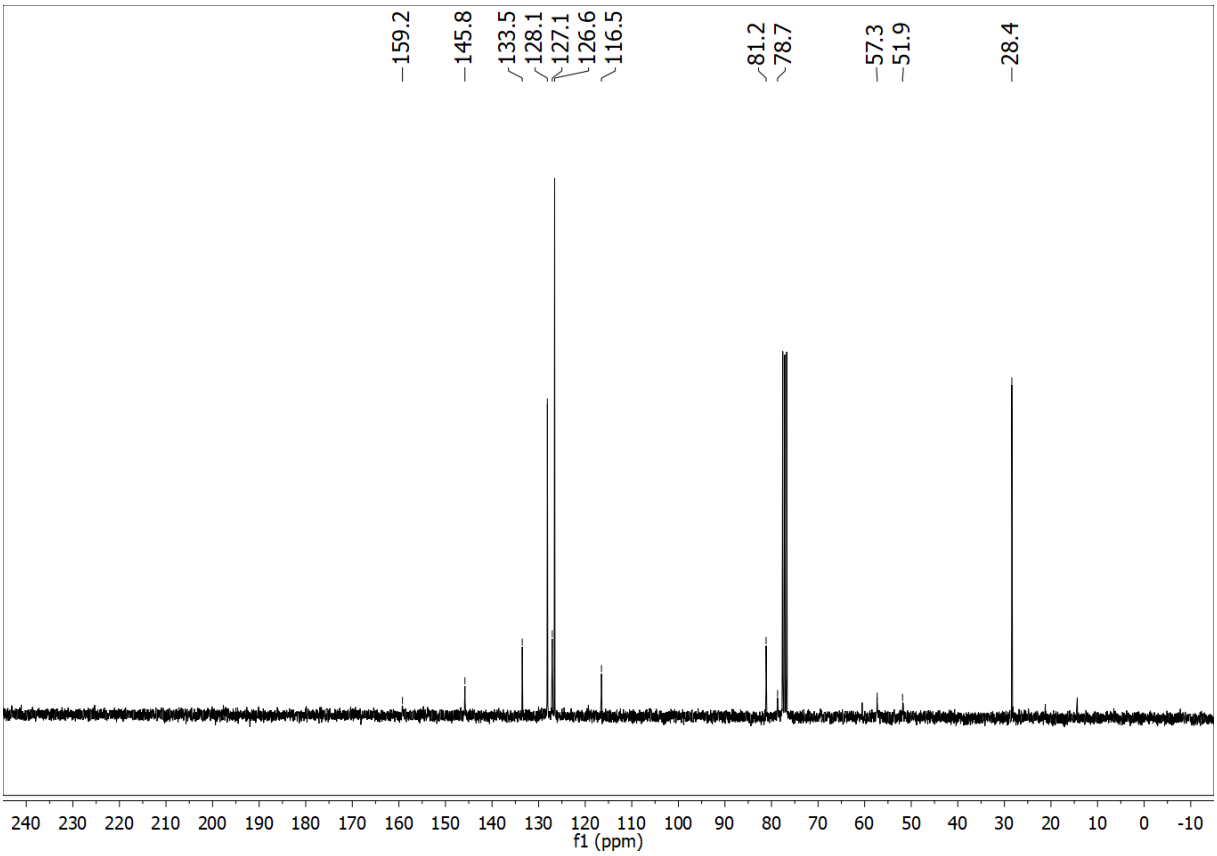




NMR-Solvent: $CDCl_3$

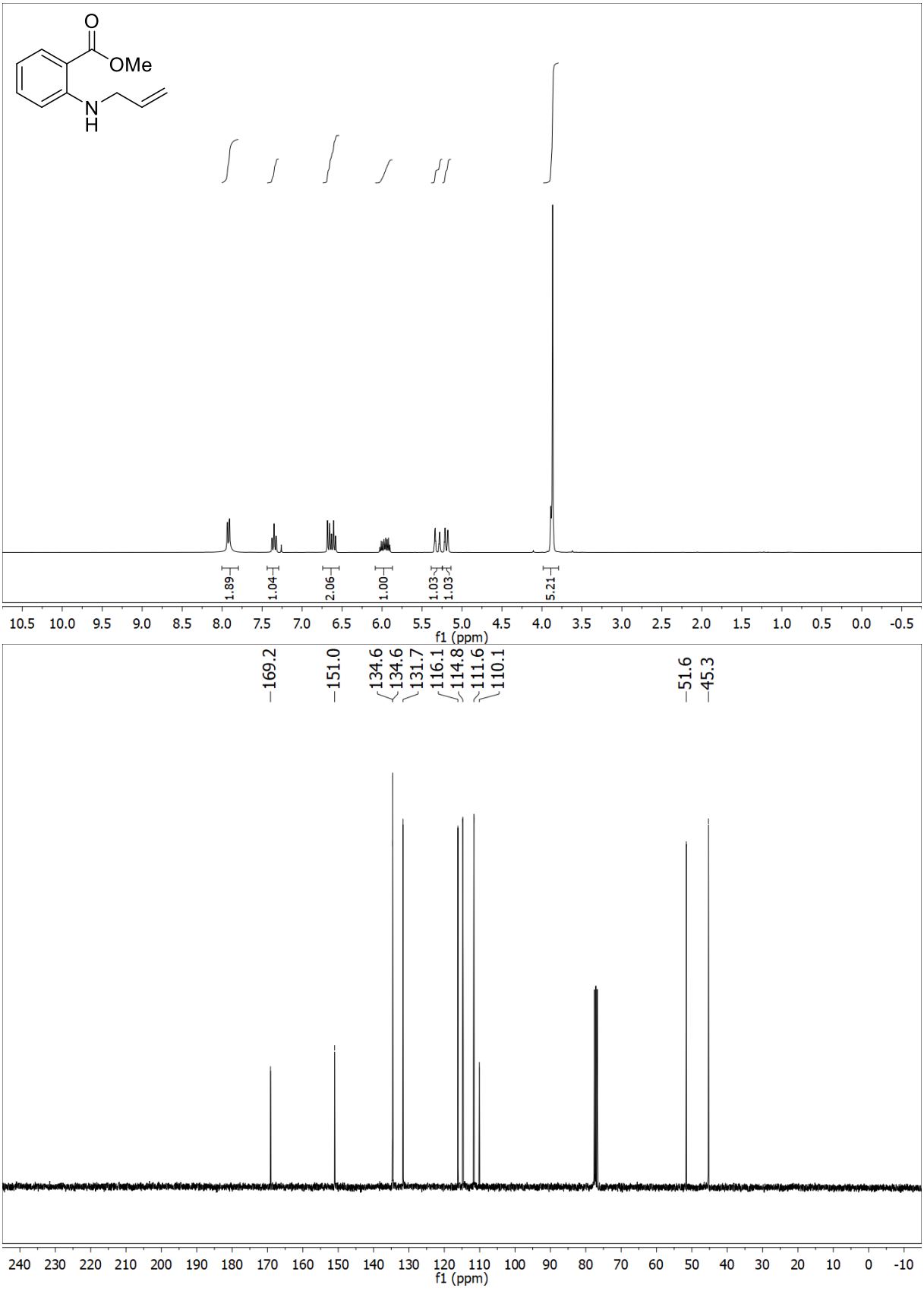
tert-Butyl allyl(2-hydroxy-2,2-diphenylethyl)carbamate (74)





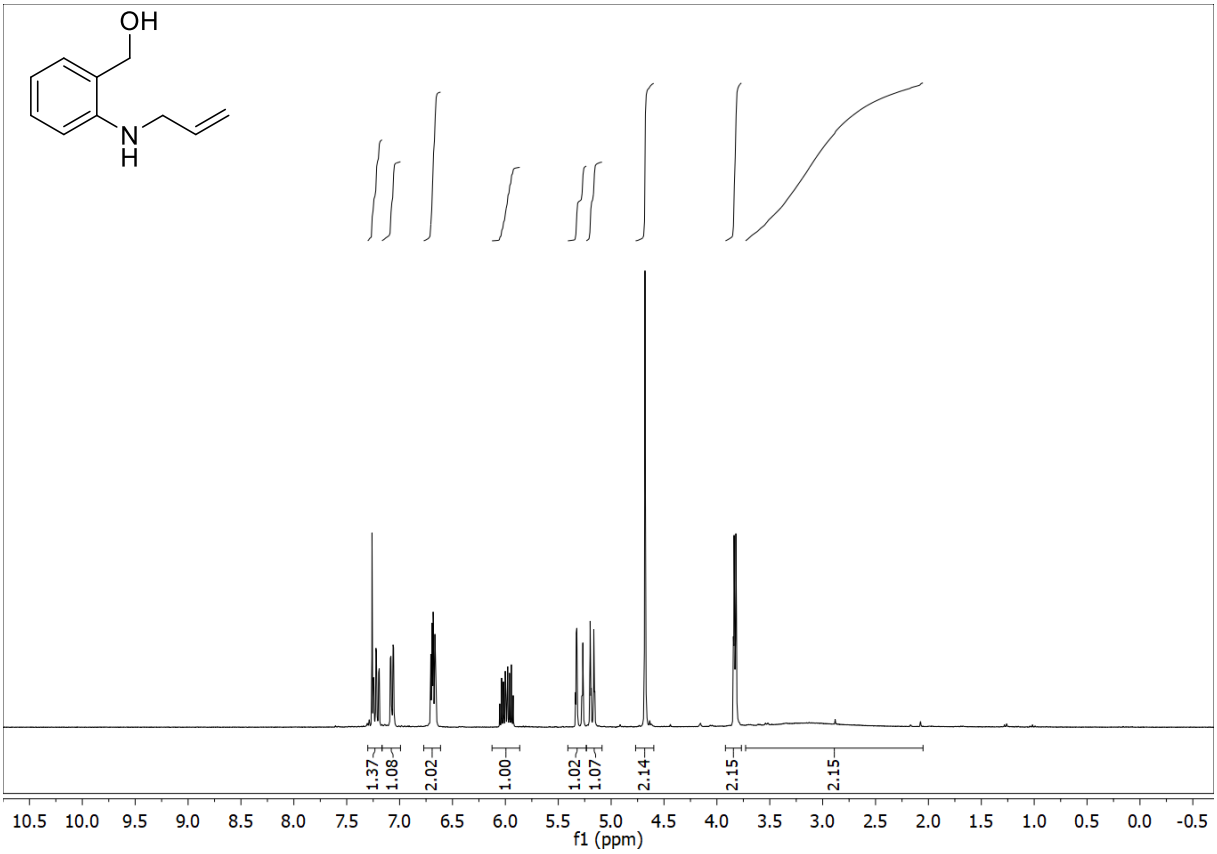
NMR-Solvent: $CDCl_3$

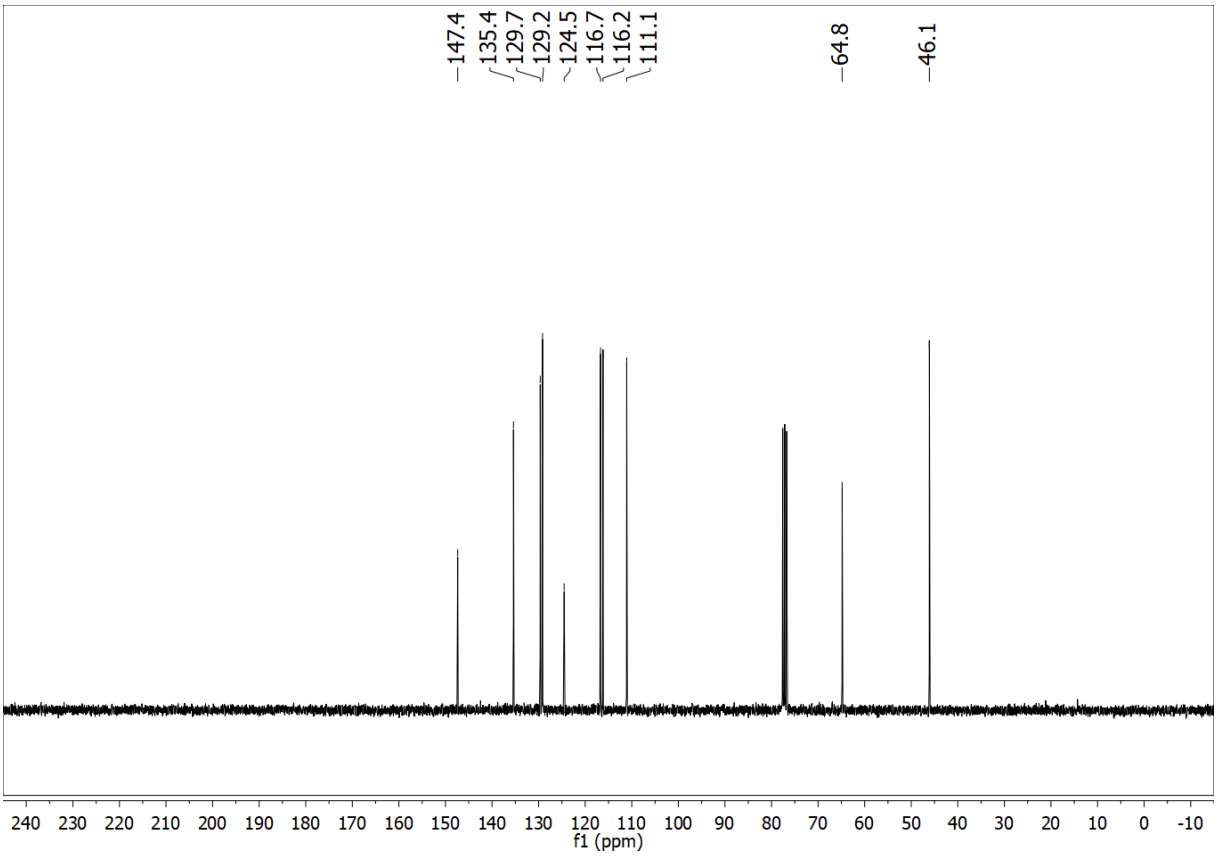
Methyl 2-(allylamino)benzoate (86)



NMR-Solvent: $CDCl_3$

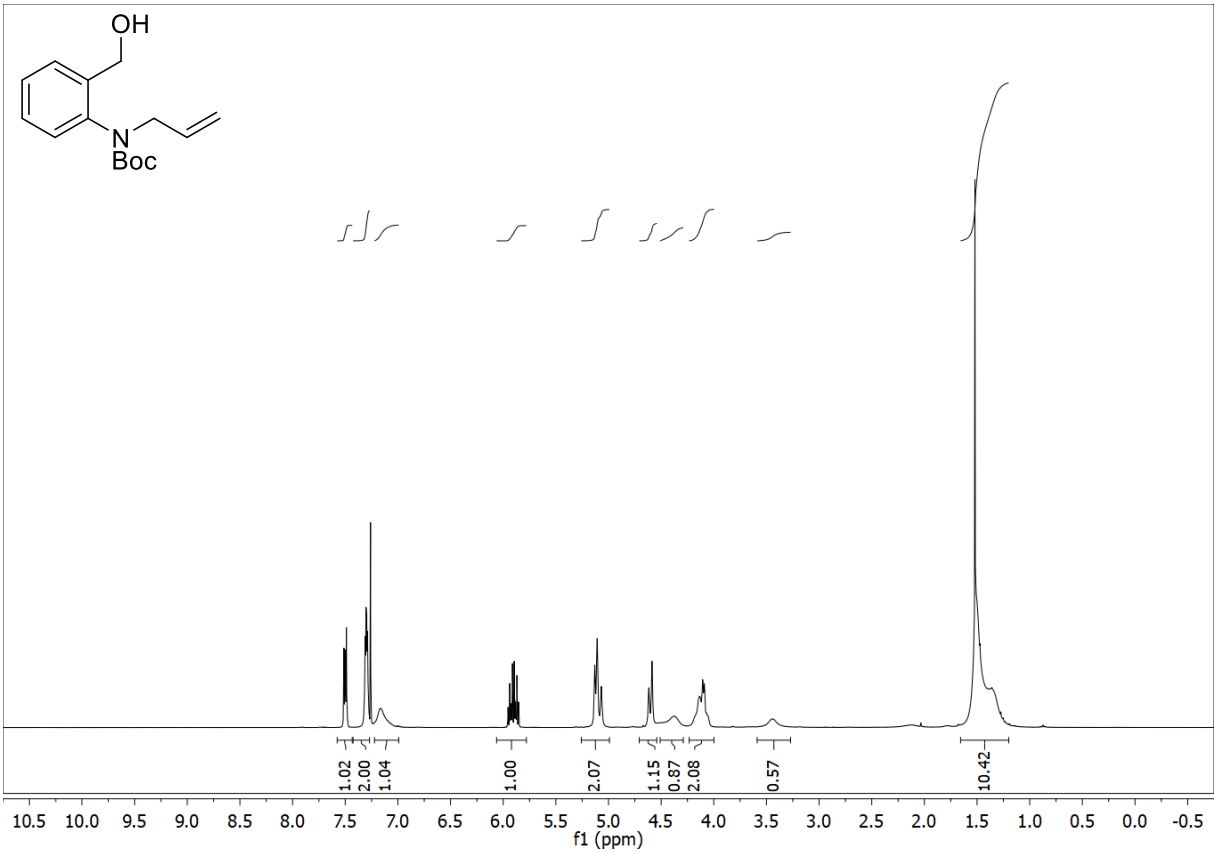
(2-(Allylamino)phenyl)methanol (87)

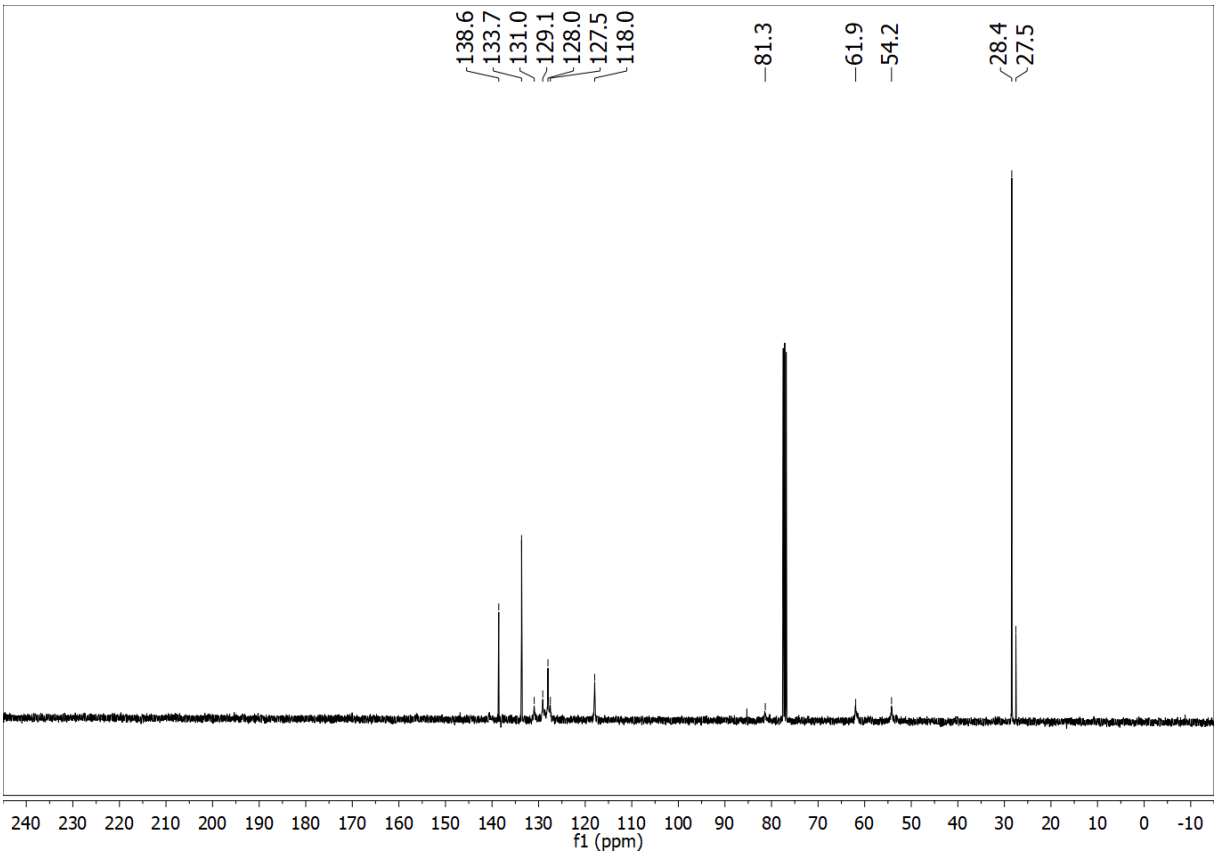




NMR-Solvent: $CDCl_3$

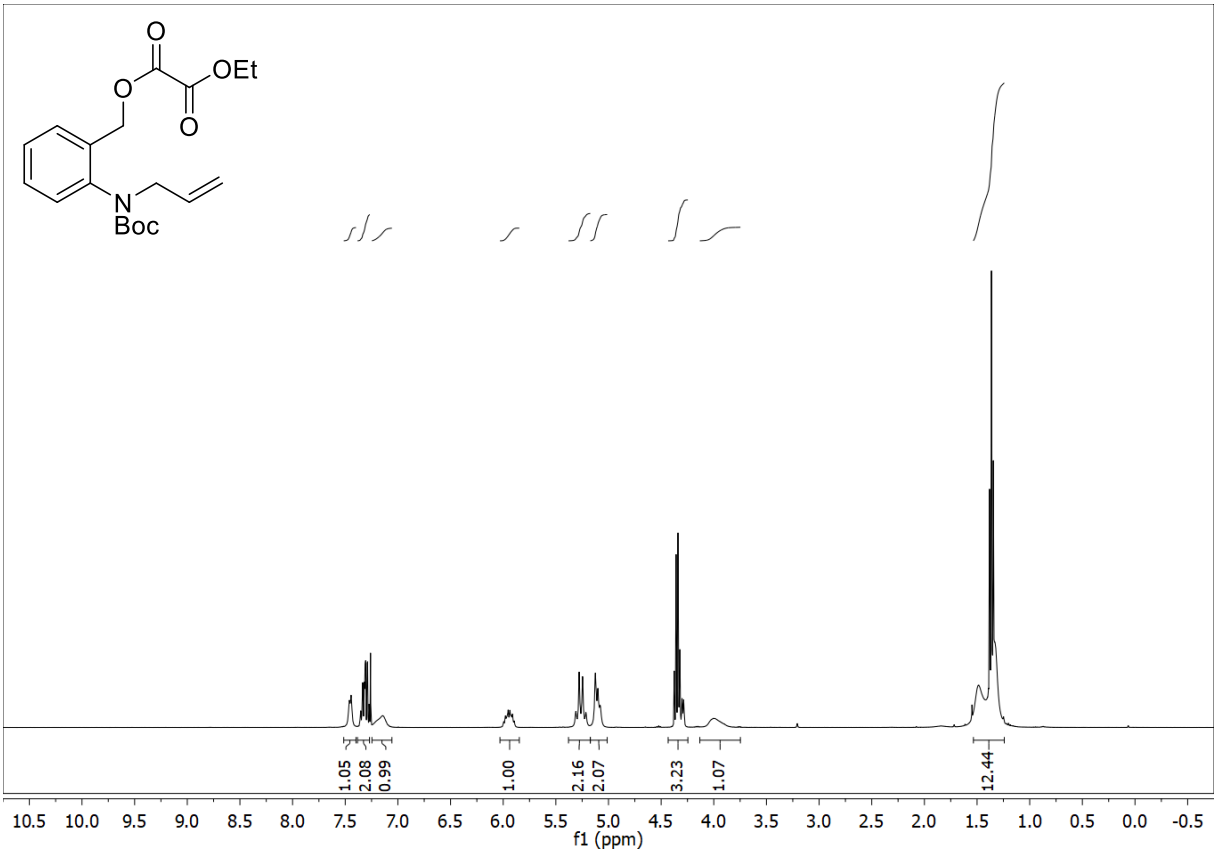
tert-Butyl allyl(2-(hydroxymethyl)phenyl)carbamate (88)

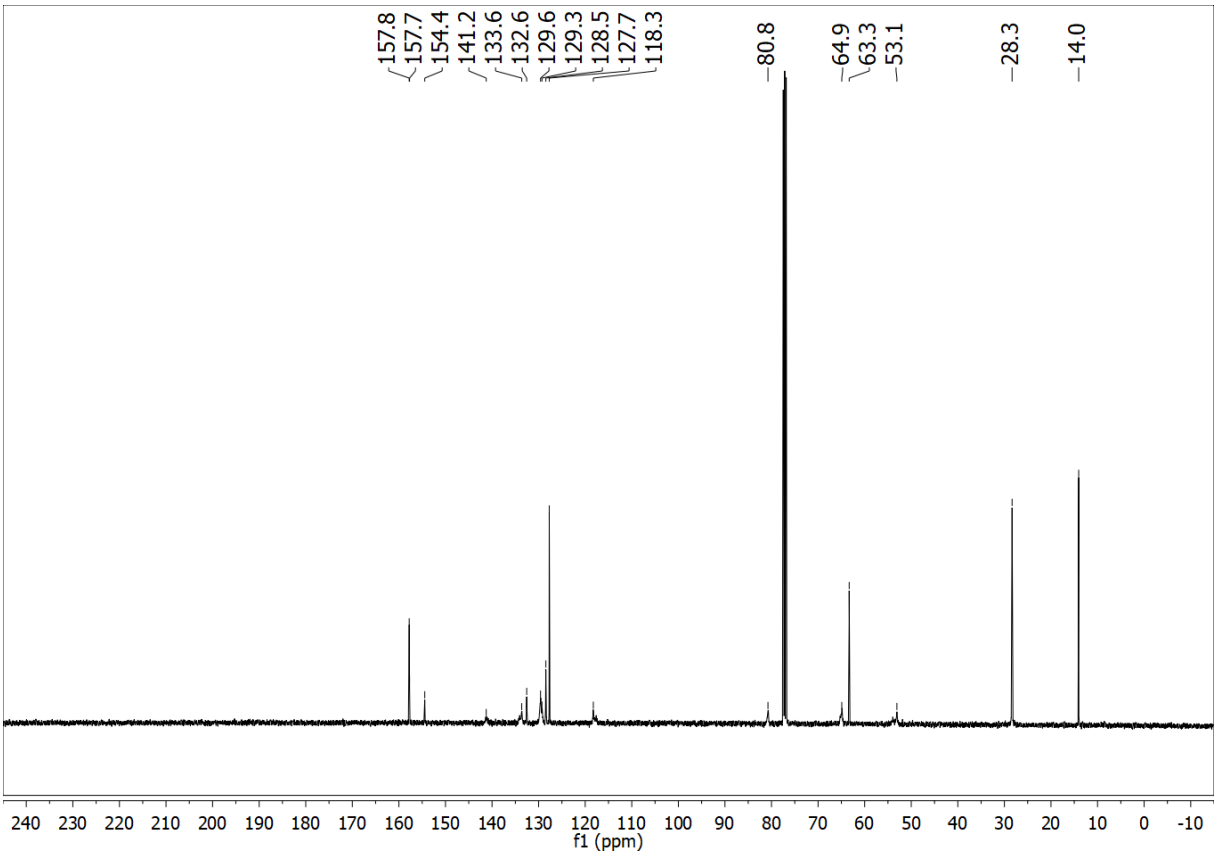




NMR-Solvent: $CDCl_3$

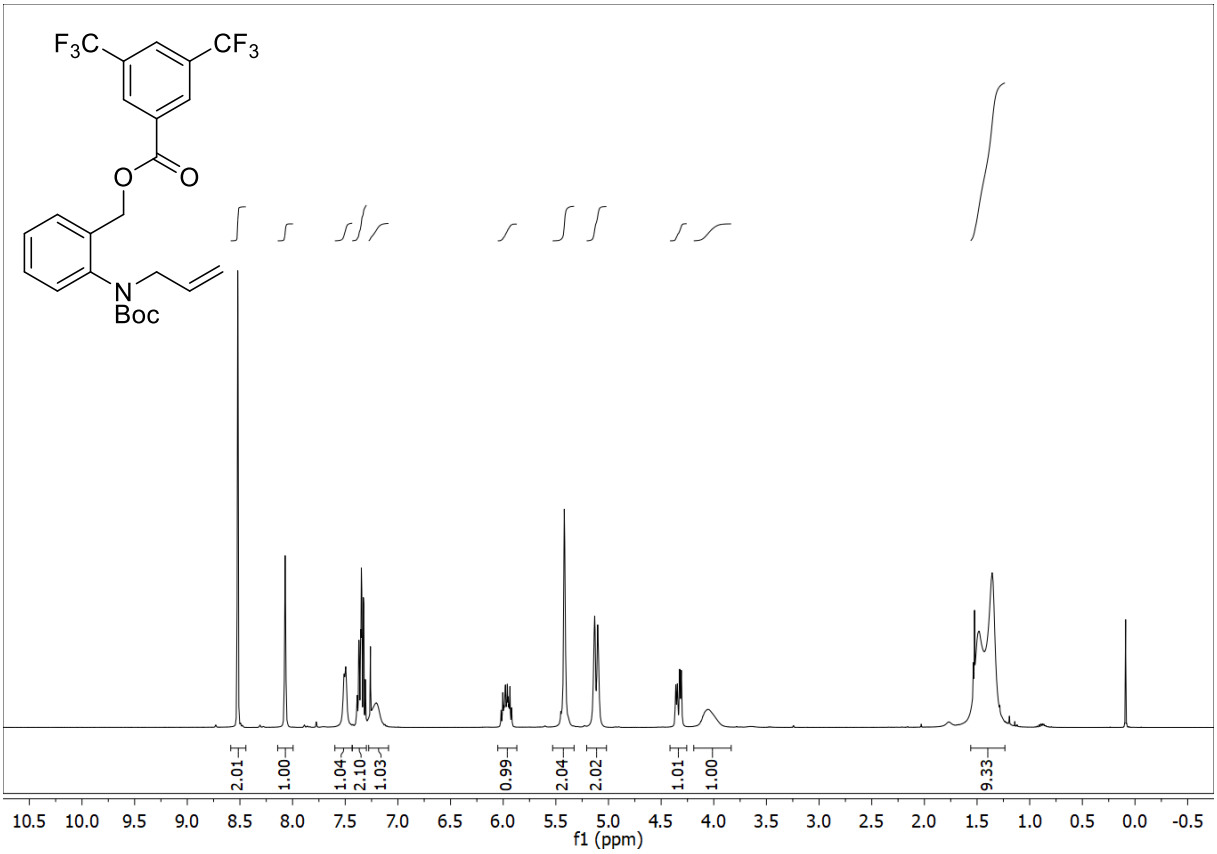
2-(Allyl(*tert*-butoxycarbonyl)amino)benzyl ethyl oxalate (89)

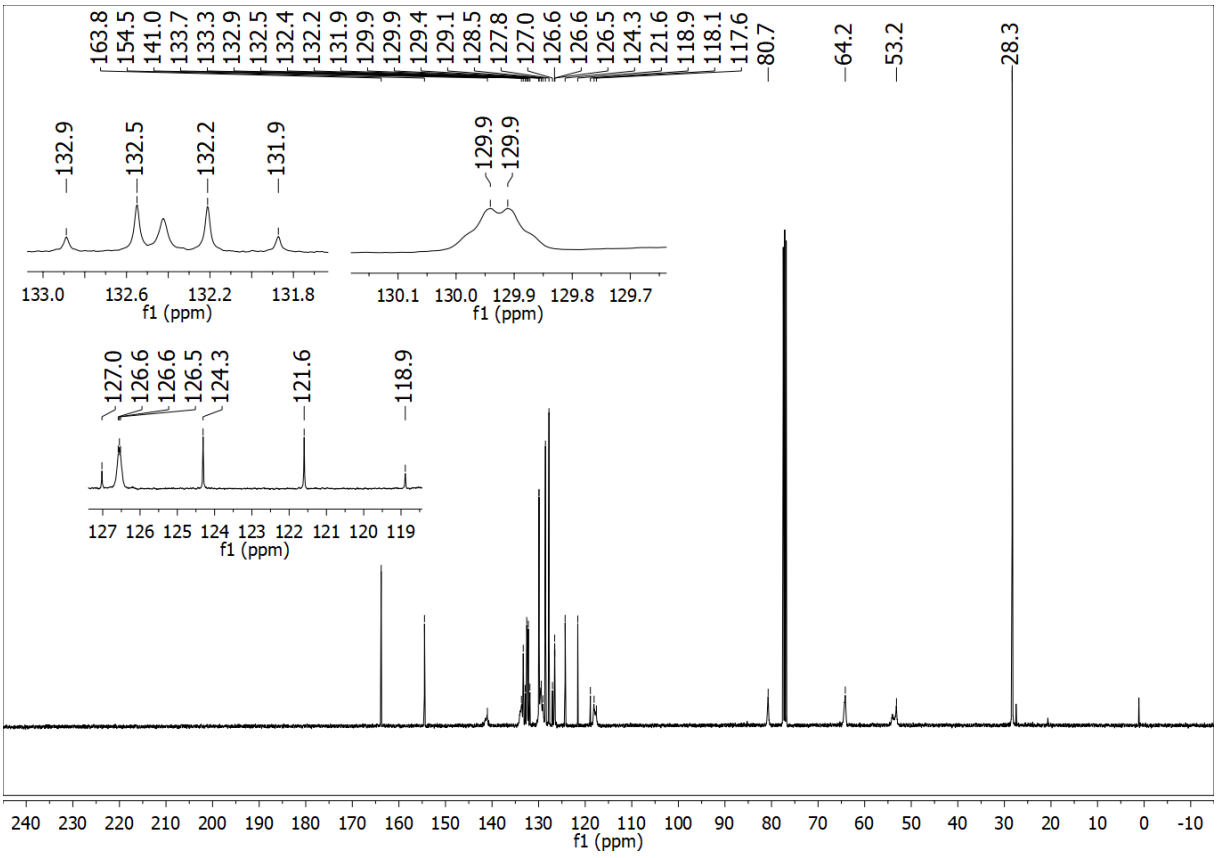


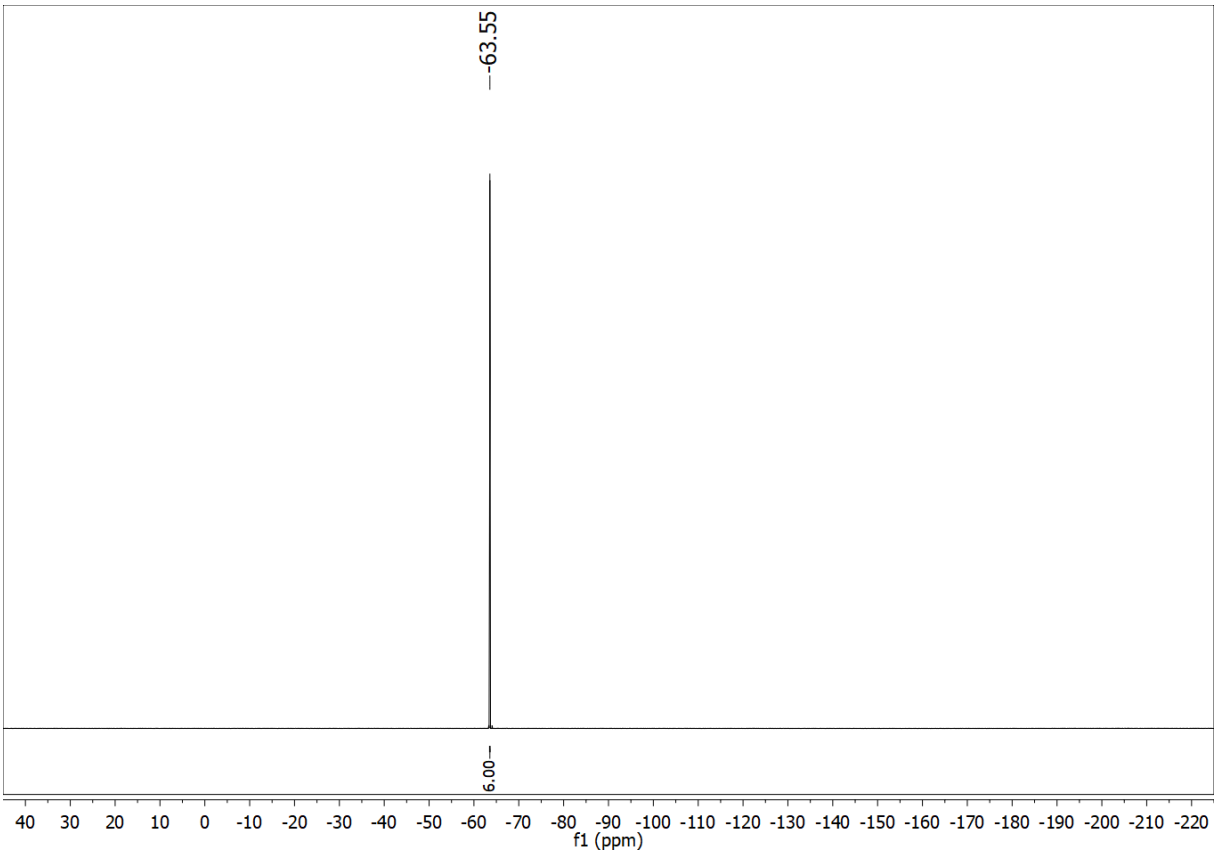


NMR-Solvent: $CDCl_3$

2-(Allyl(*tert*-butoxycarbonyl)amino)benzyl 3,5-bis(trifluoromethyl)benzoate (90)

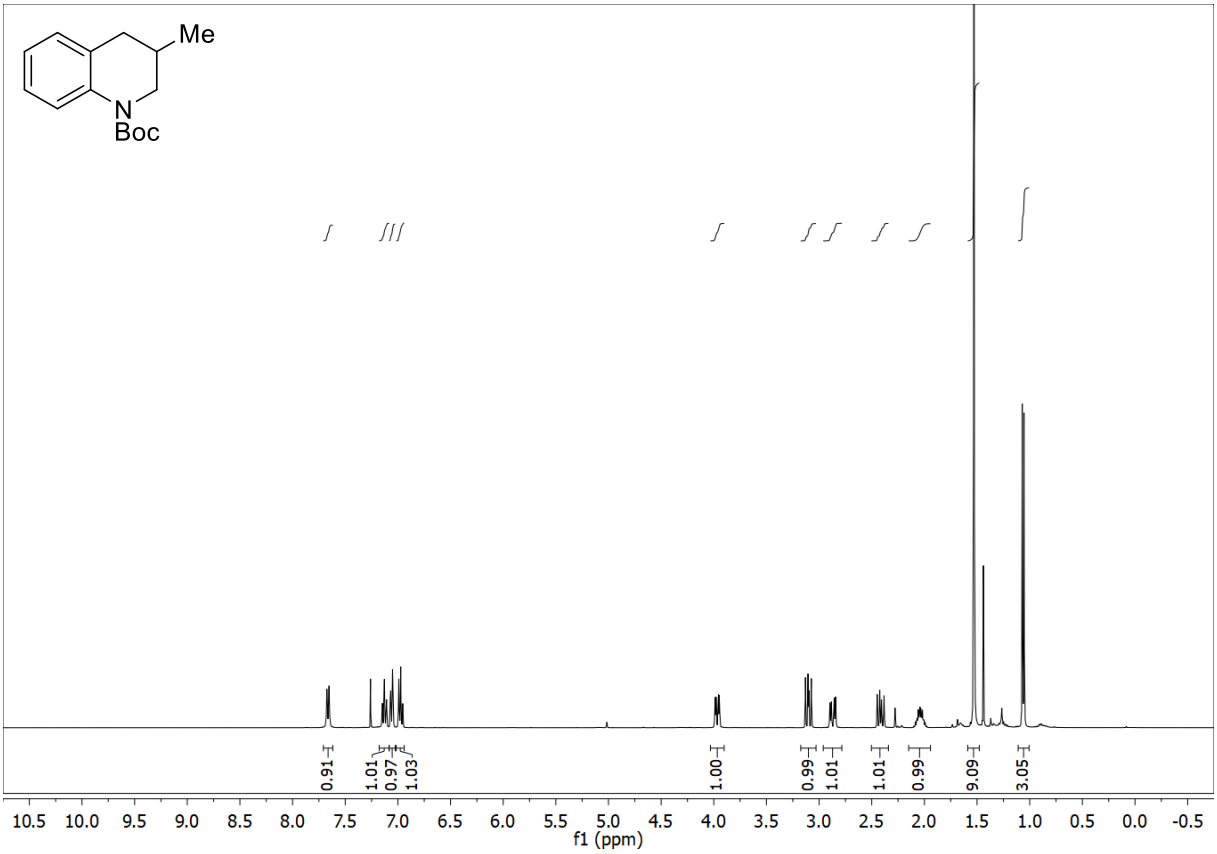


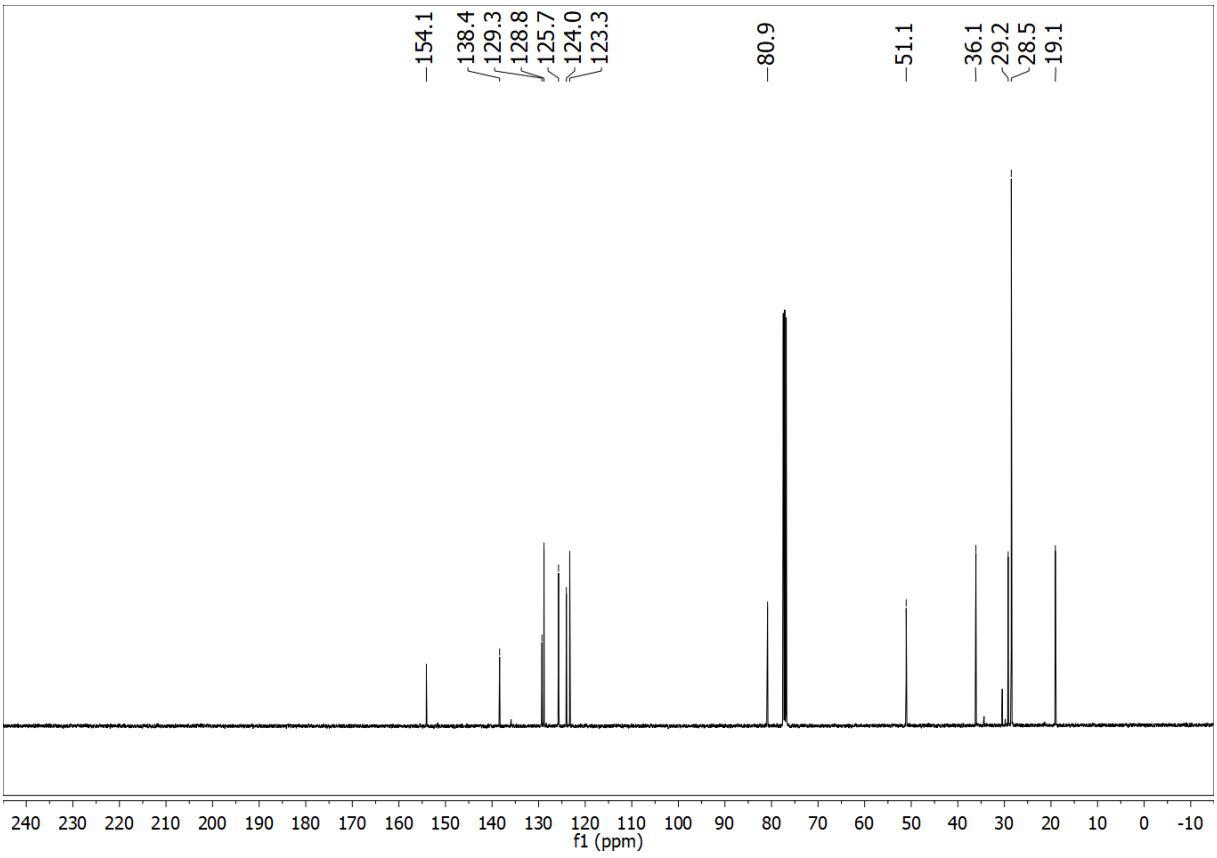




NMR-Solvent: $CDCl_3$

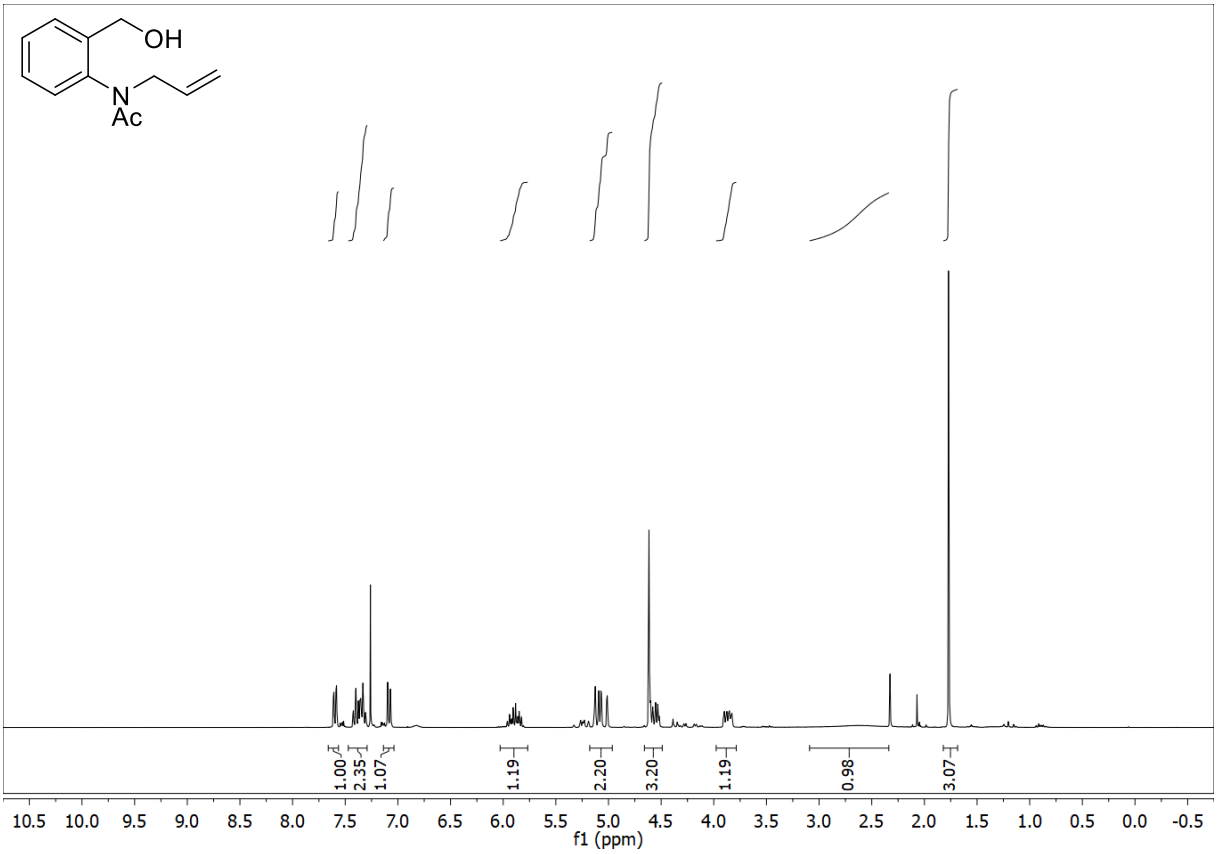
tert-Butyl 3-methyl-3,4-dihydroquinoline-1(2H)-carboxylate (91)

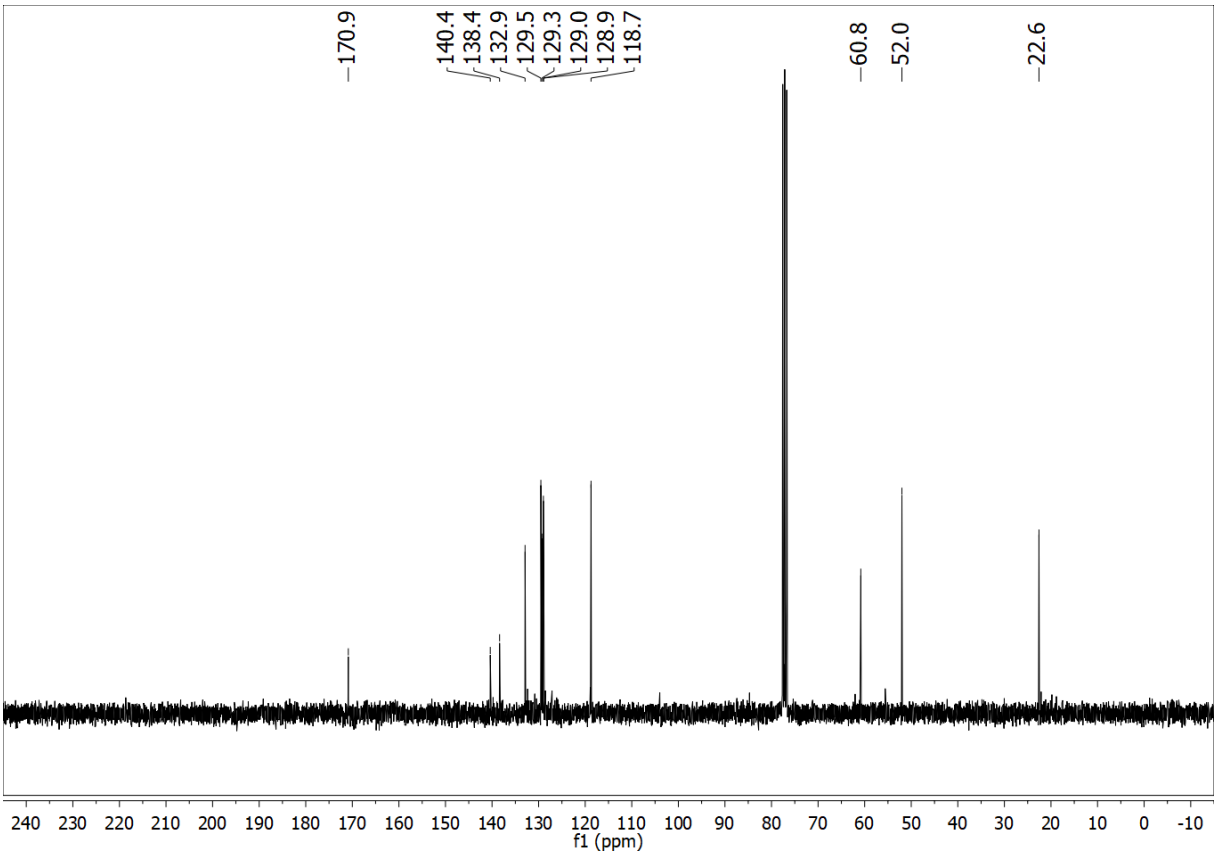




NMR-Solvent: $CDCl_3$

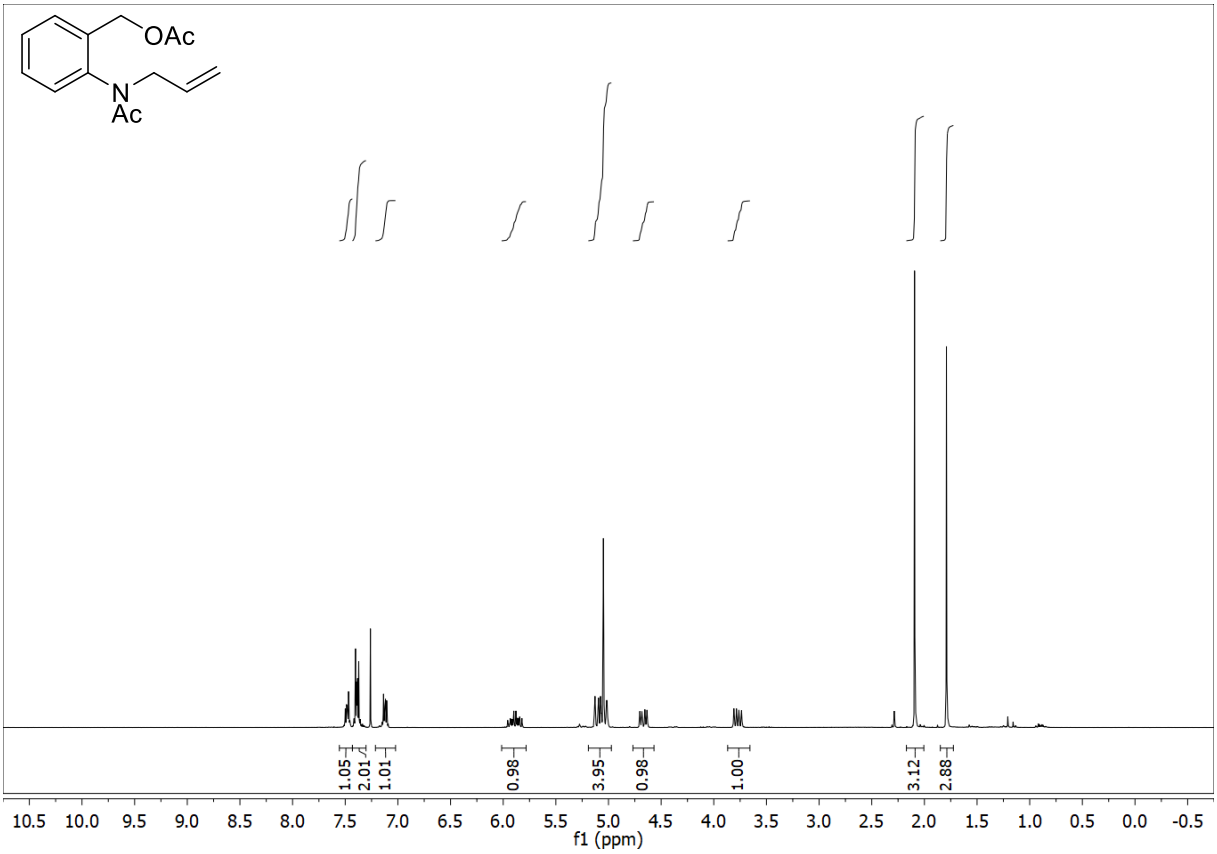
N-allyl-*N*-(2-(hydroxymethyl)phenyl)acetamide (95)

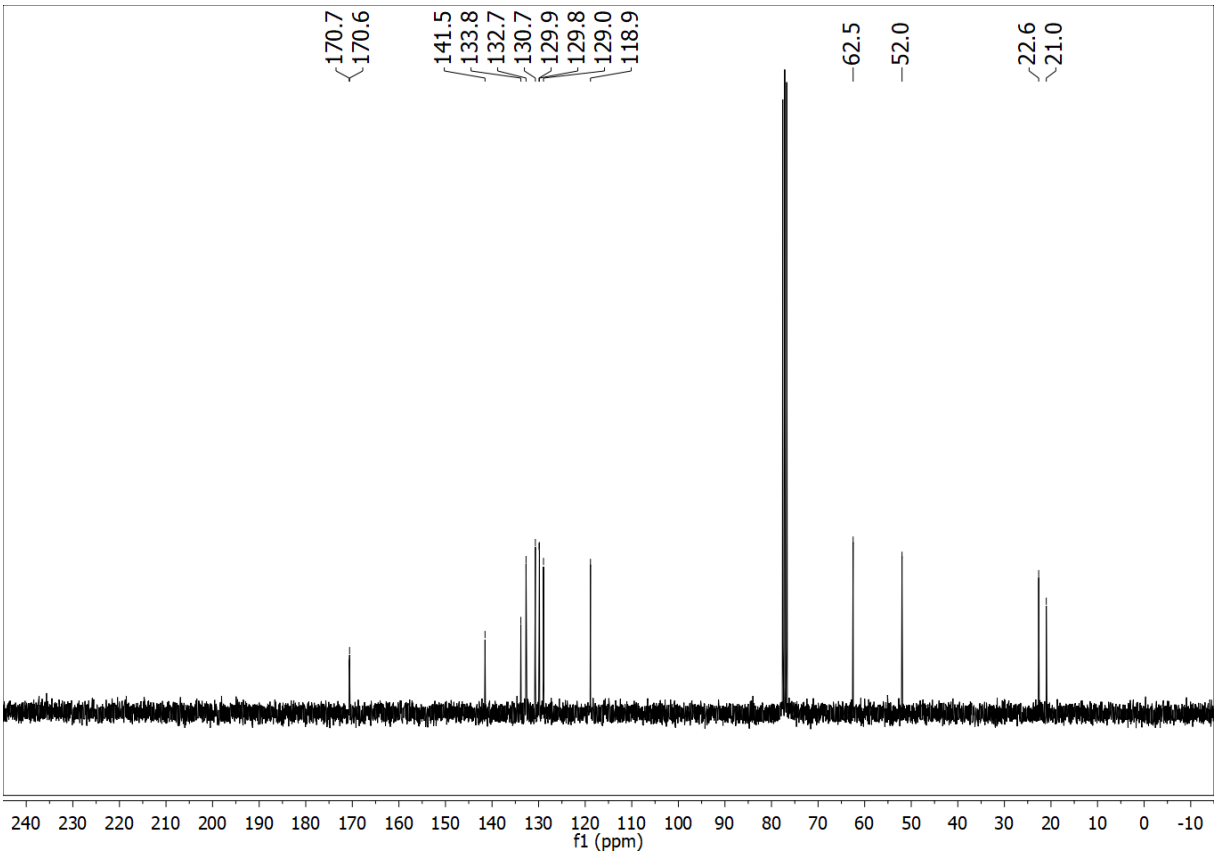




NMR-Solvent: $CDCl_3$

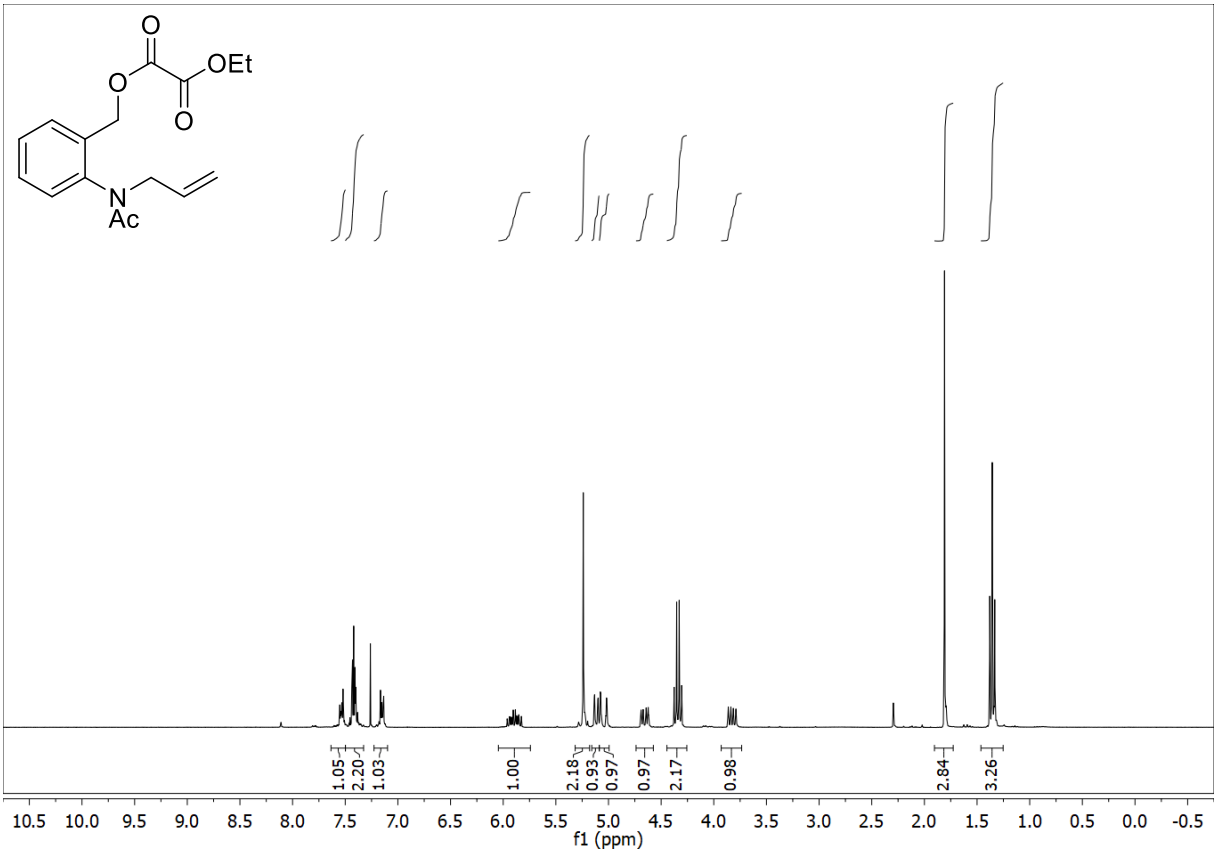
2-(*N*-allylacetamido)benzyl acetate (96)

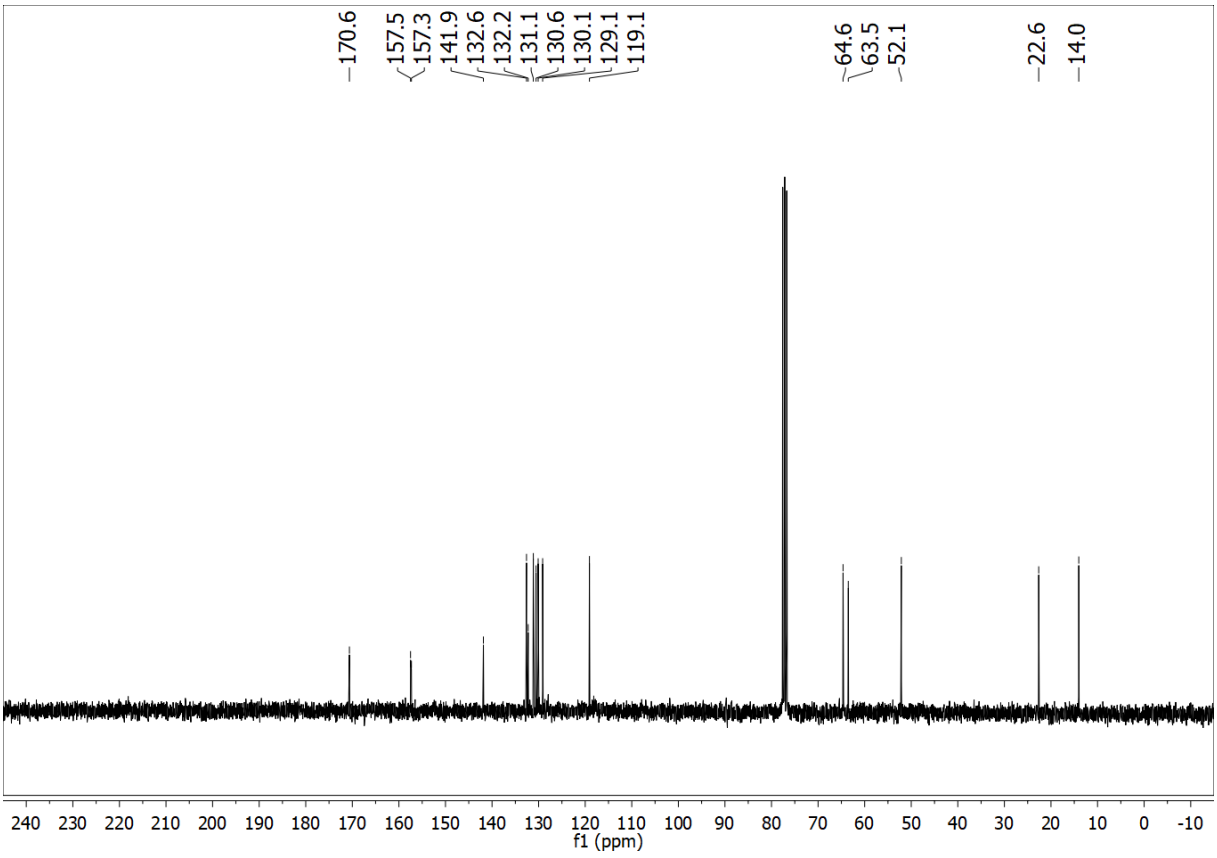




NMR-Solvent: $CDCl_3$

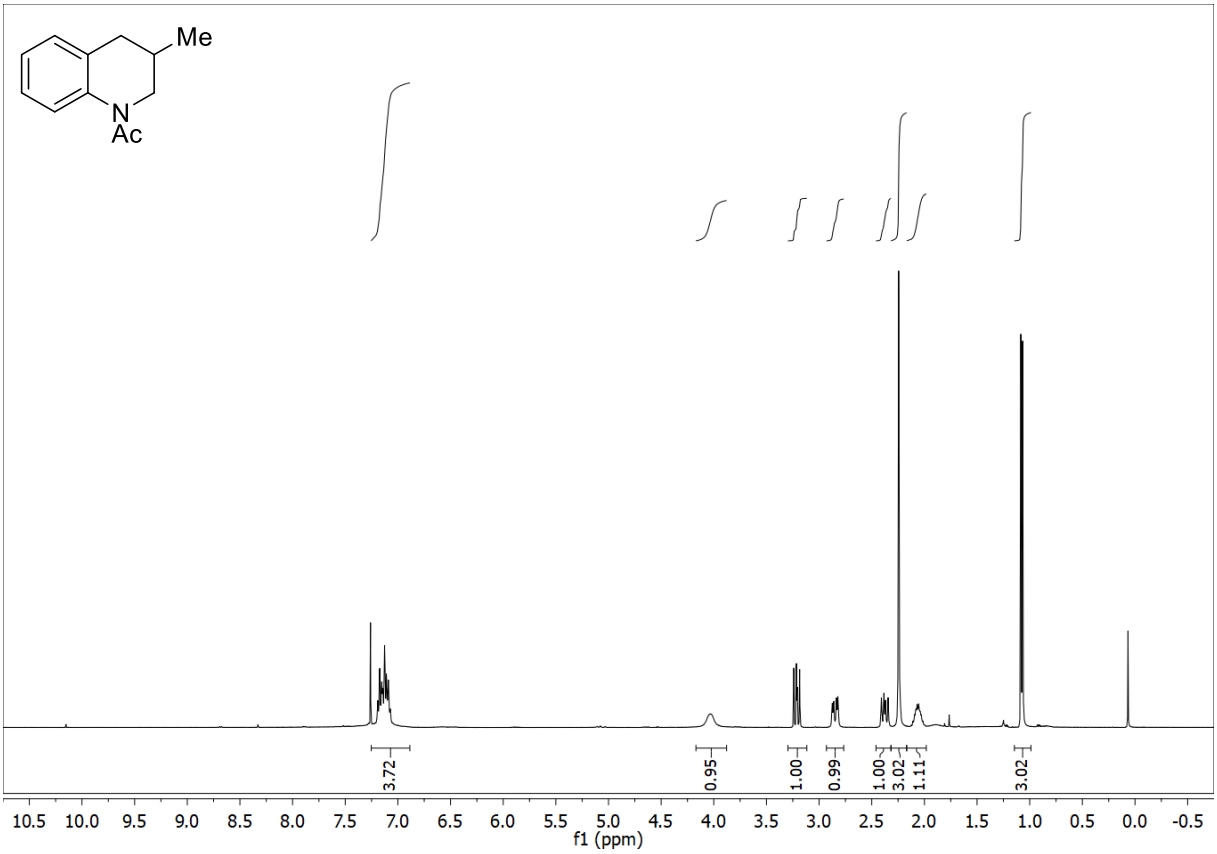
2-(*N*-allylacetamido)benzyl ethyl oxalate (97)

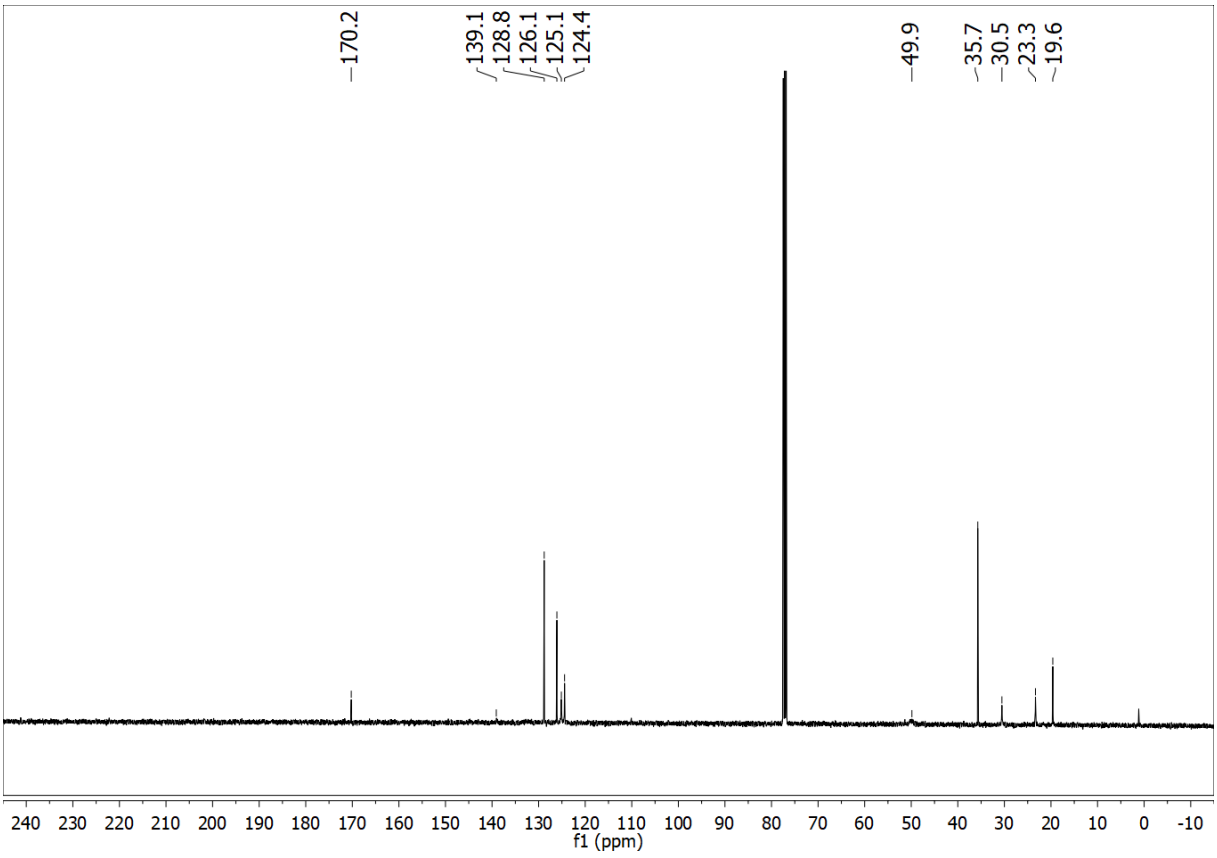




NMR-Solvent: $CDCl_3$

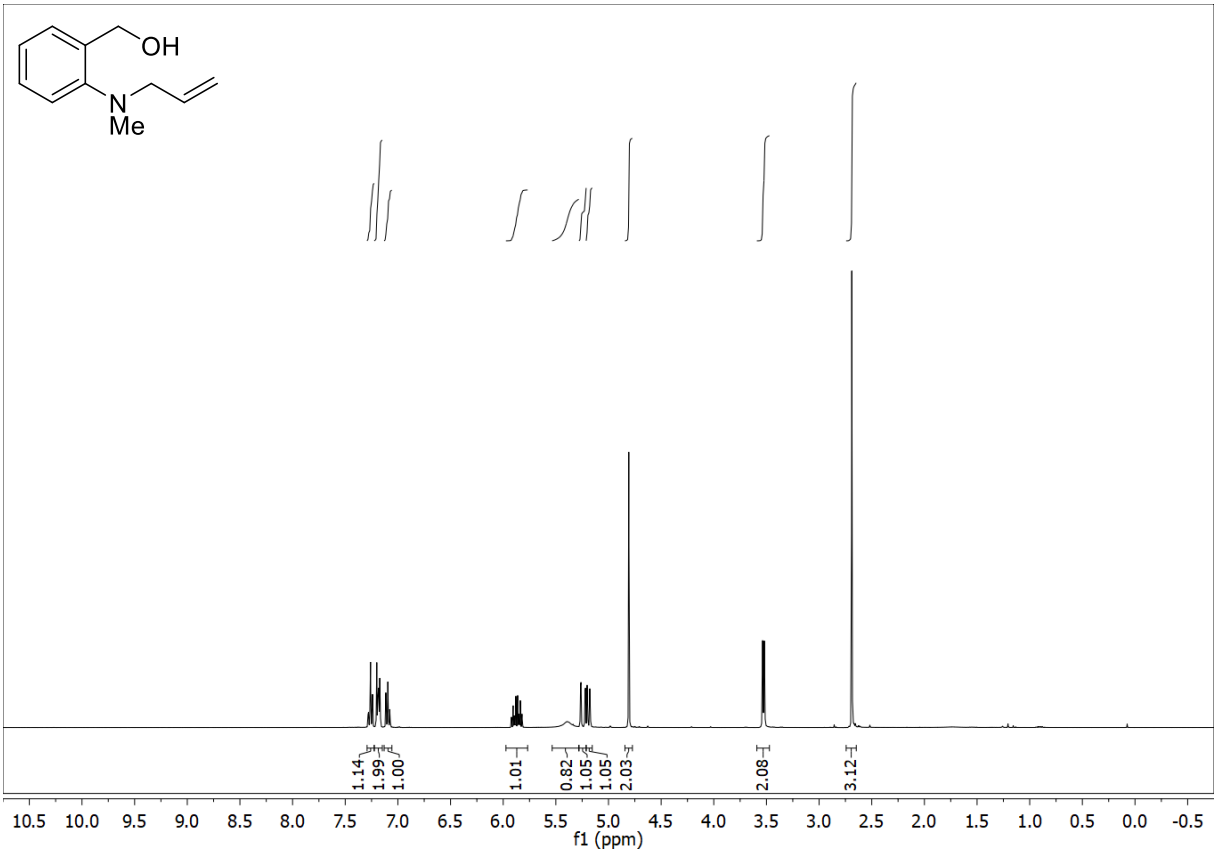
1-(3-Methyl-3,4-dihydroquinolin-1(2H)-yl)ethan-1-one (98)

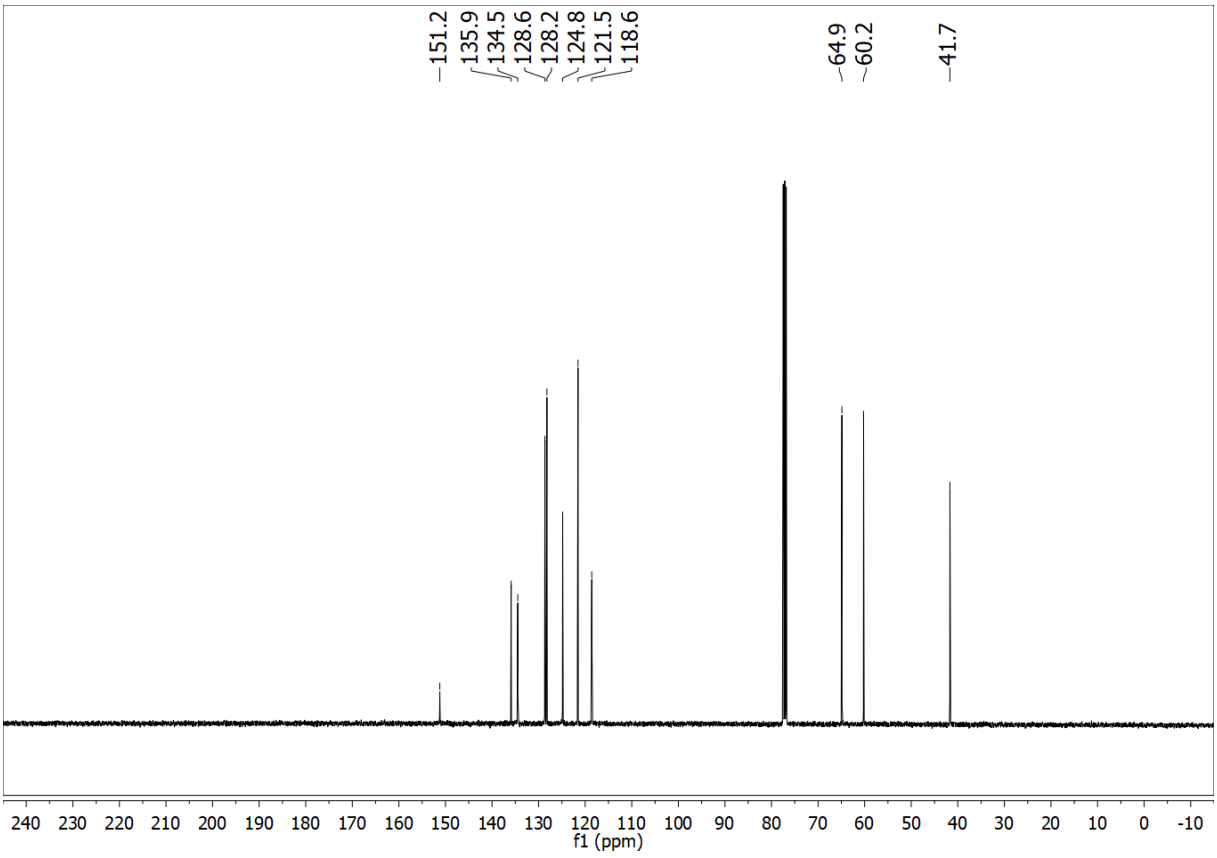




NMR-Solvent: $CDCl_3$

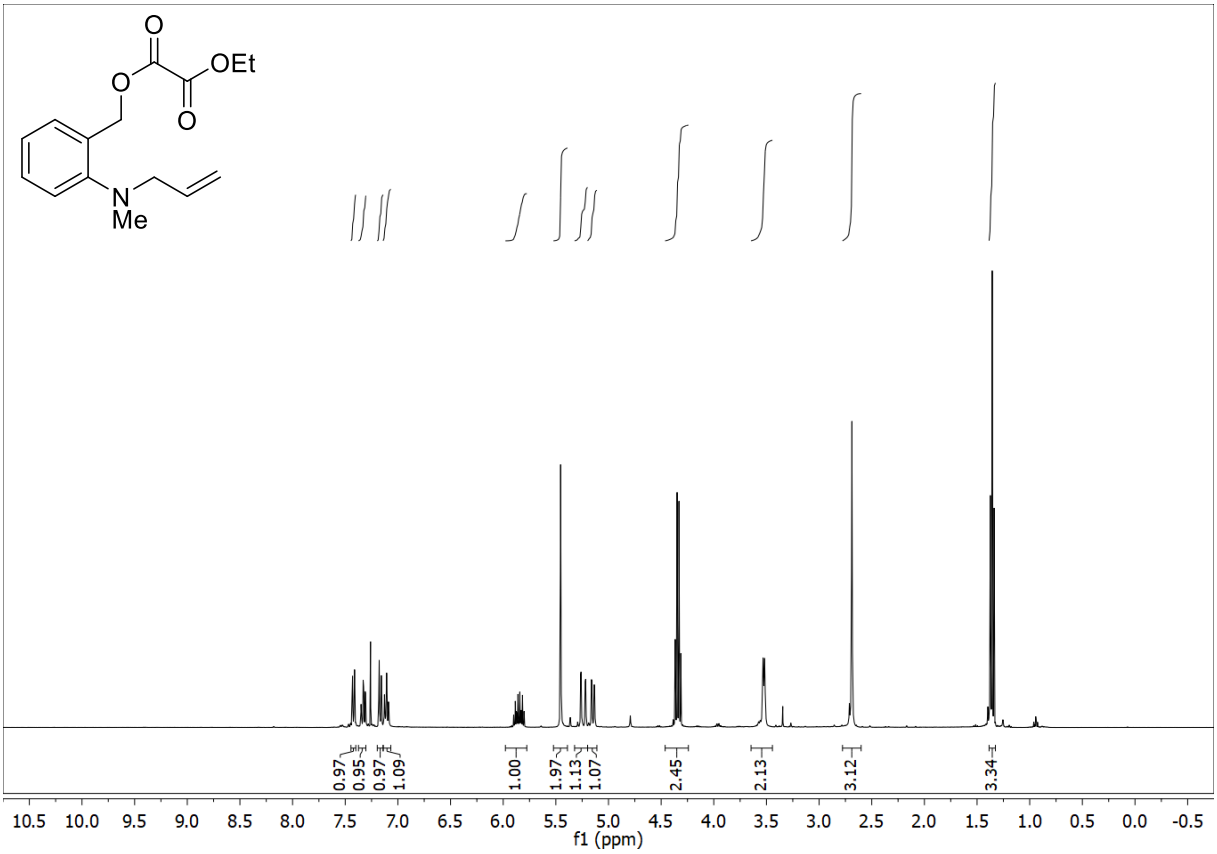
(2-(Allyl(methyl)amino)phenyl)methanol (99)

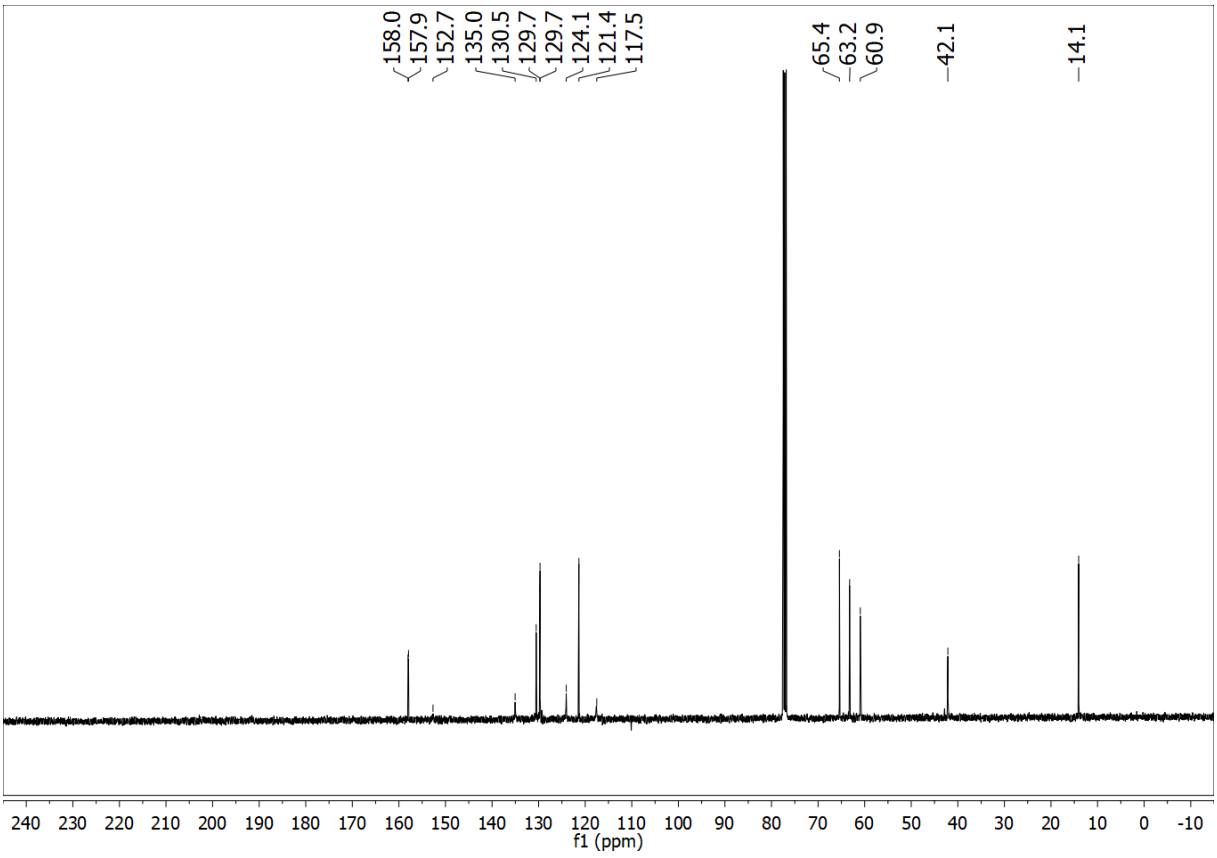




NMR-Solvent: $CDCl_3$

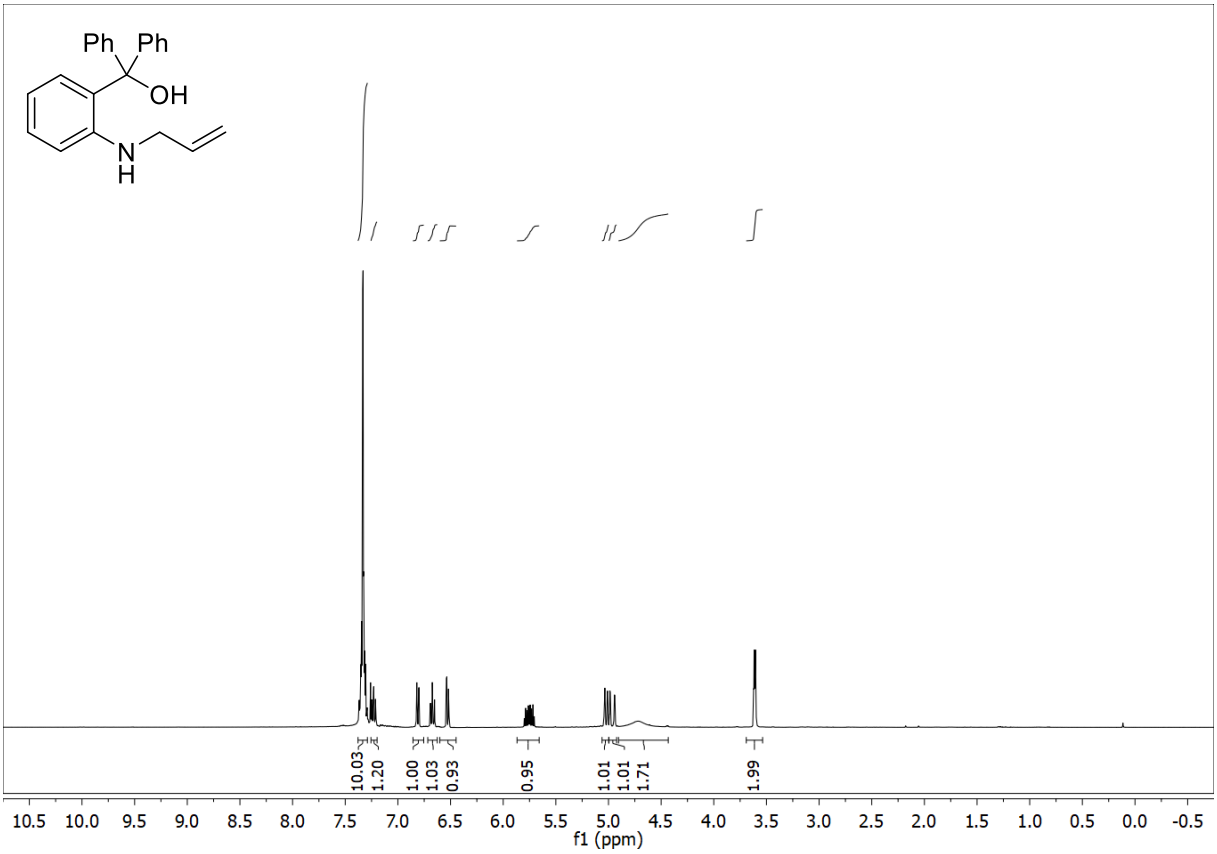
2-(Allyl(methyl)amino)benzyl ethyl oxalate (100)

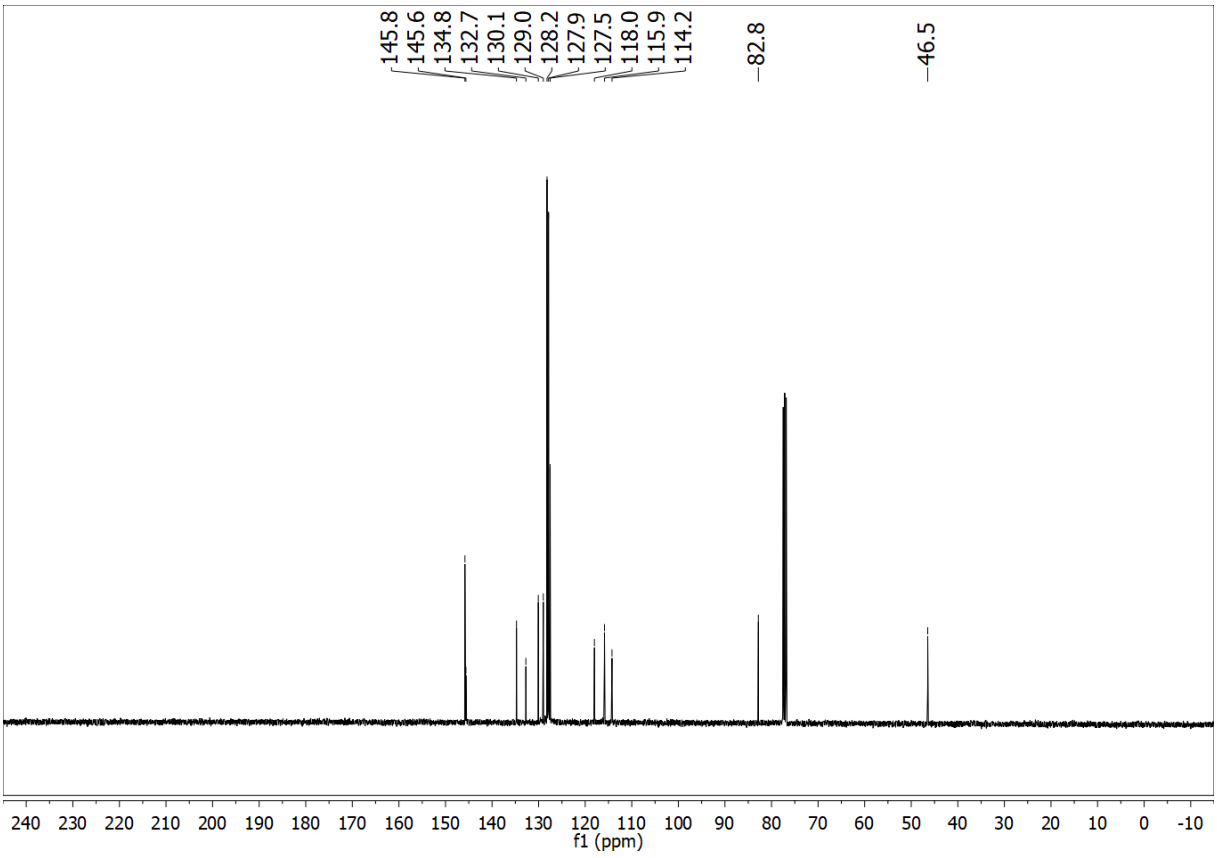




NMR-Solvent: $CDCl_3$

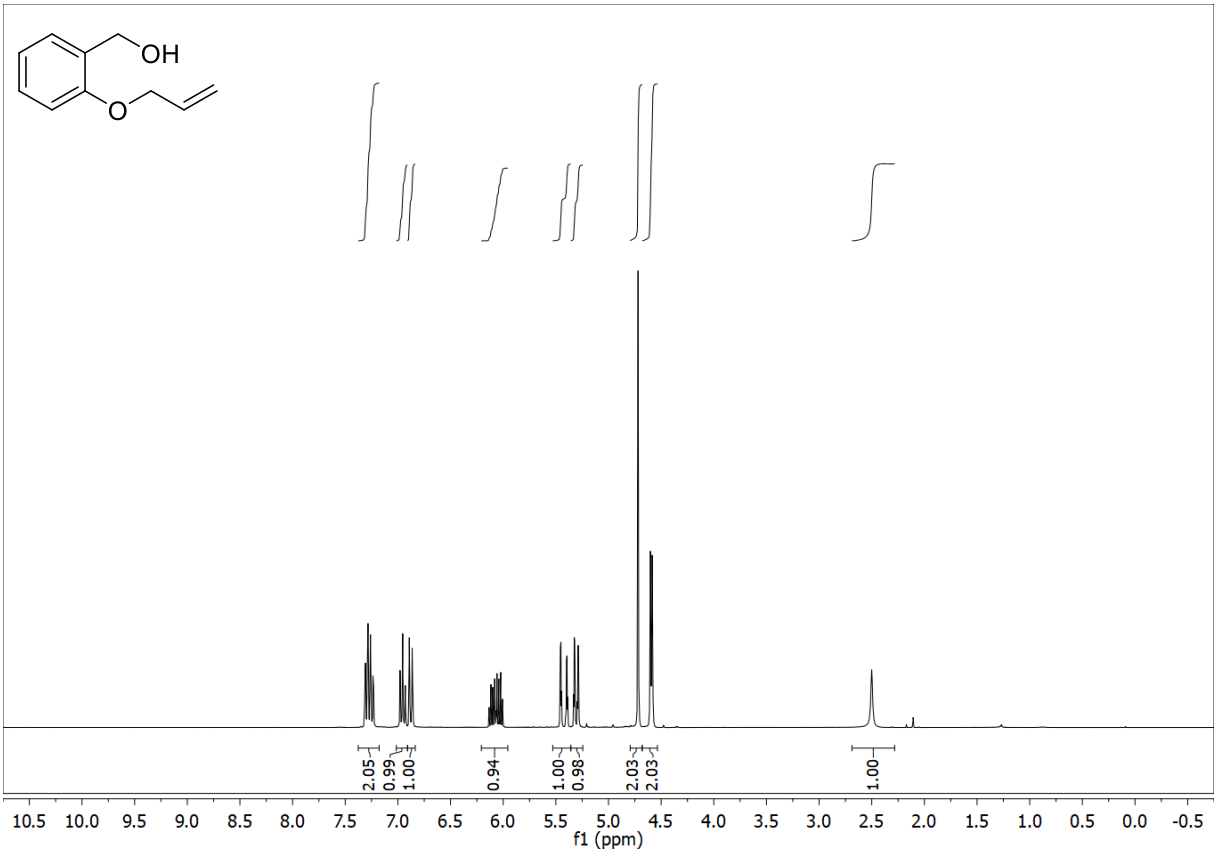
(2-(Allylamino)phenyl)diphenylmethanol (104)

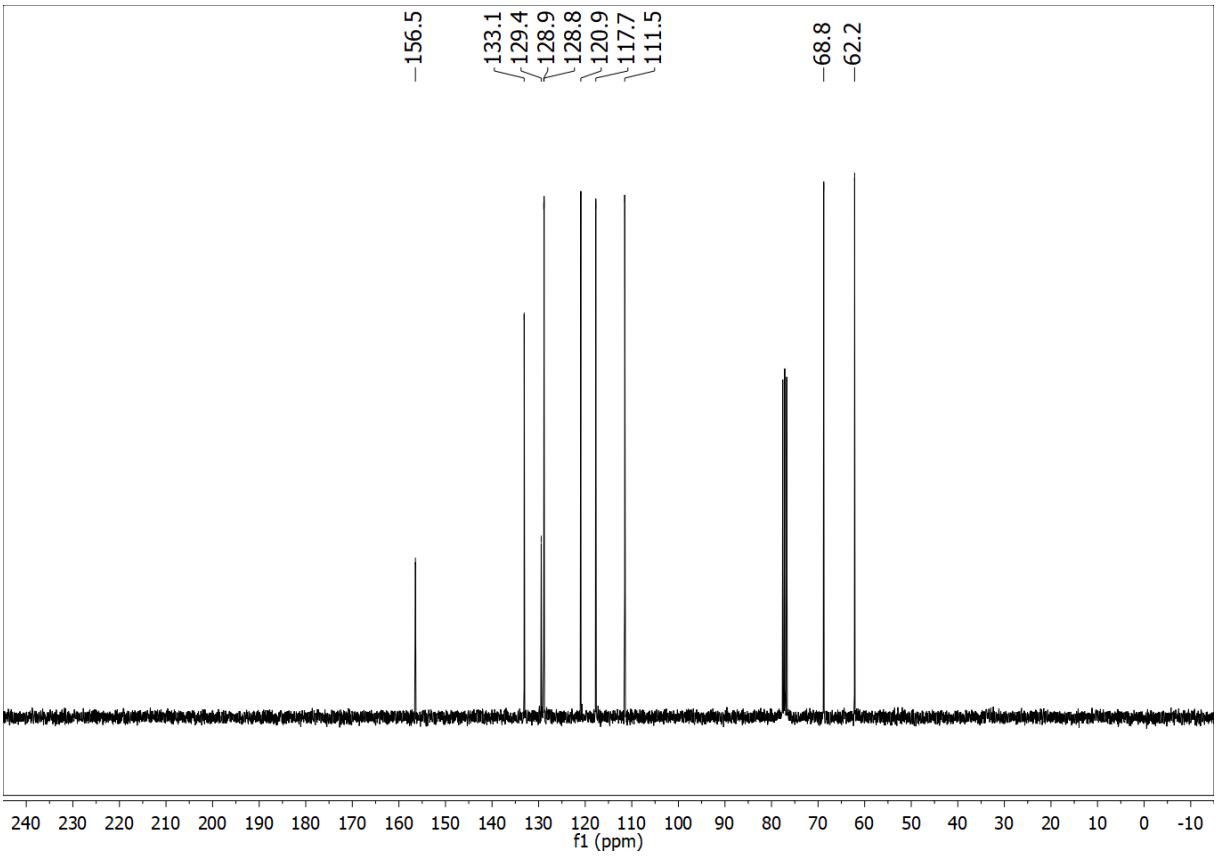




NMR-Solvent: $CDCl_3$

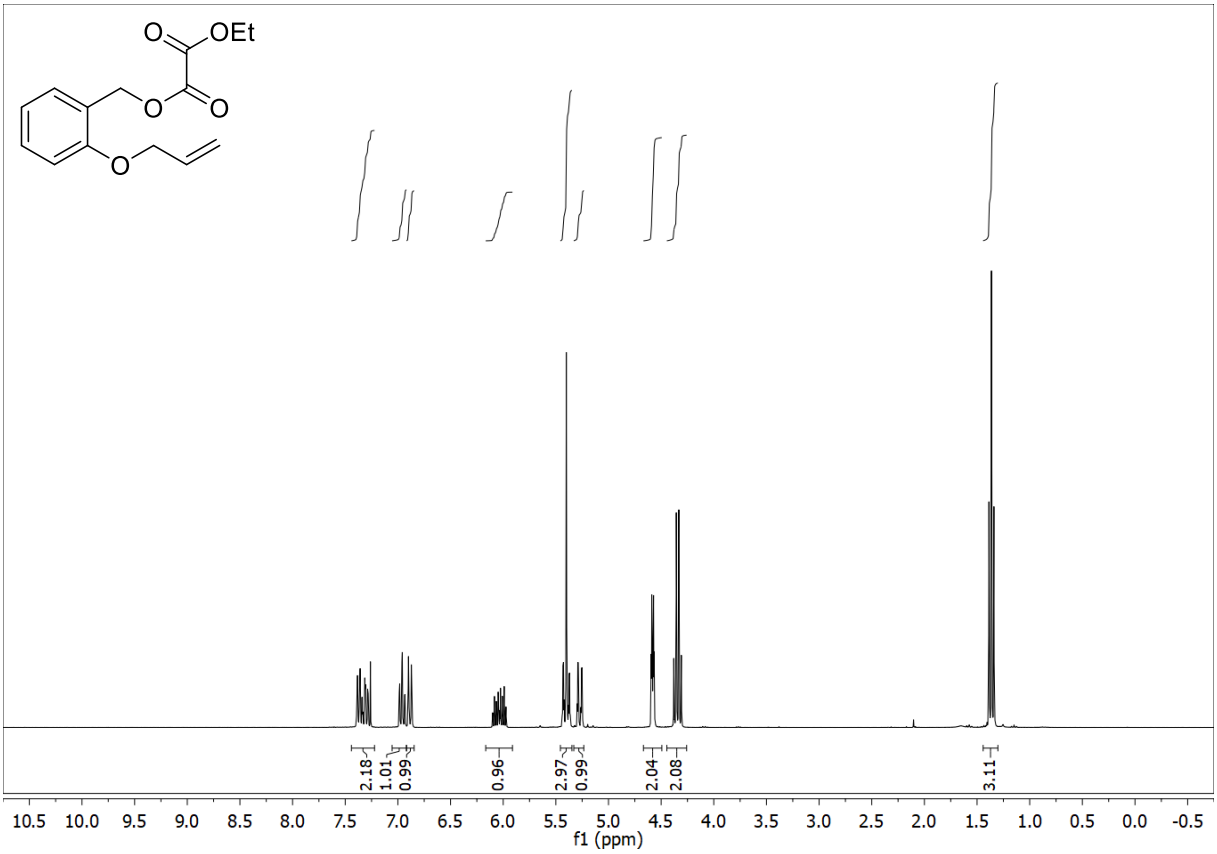
(2-(Allyloxy)phenyl)methanol (109)

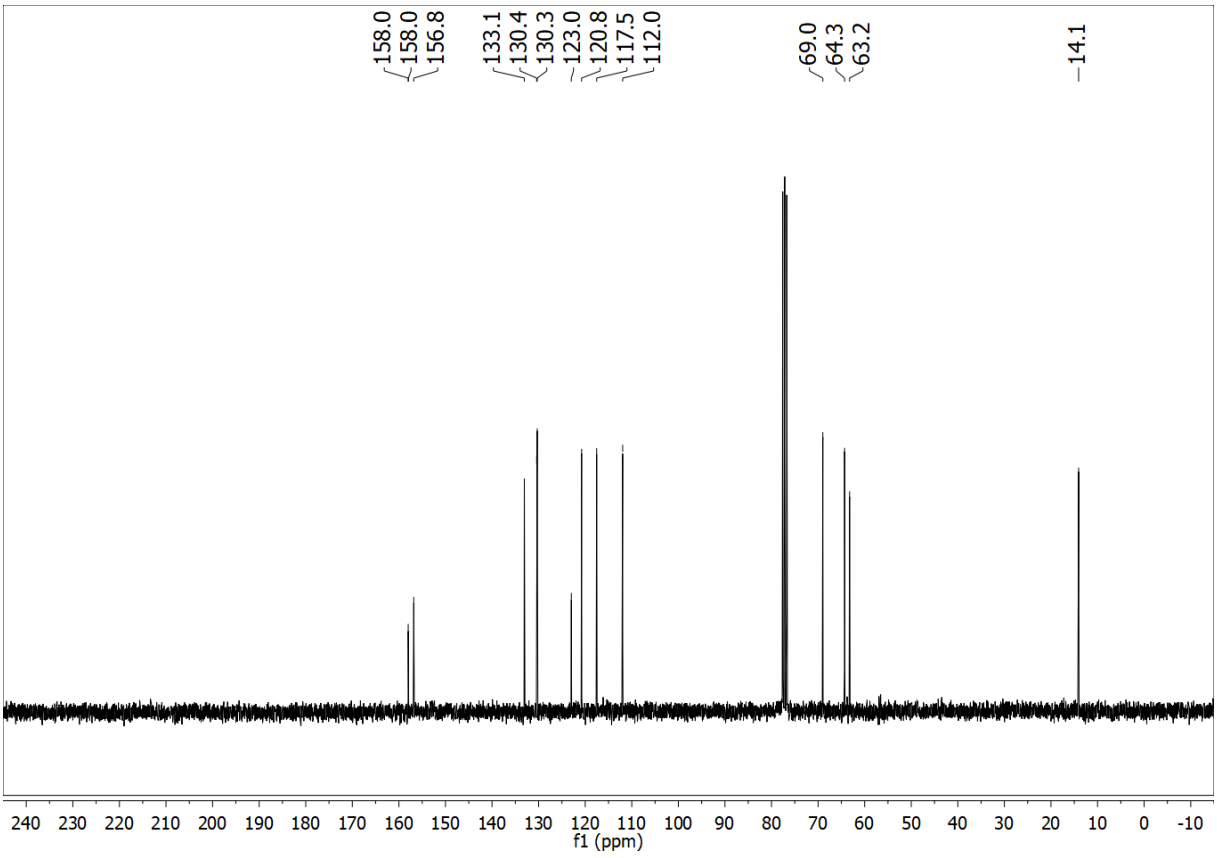




NMR-Solvent: $CDCl_3$

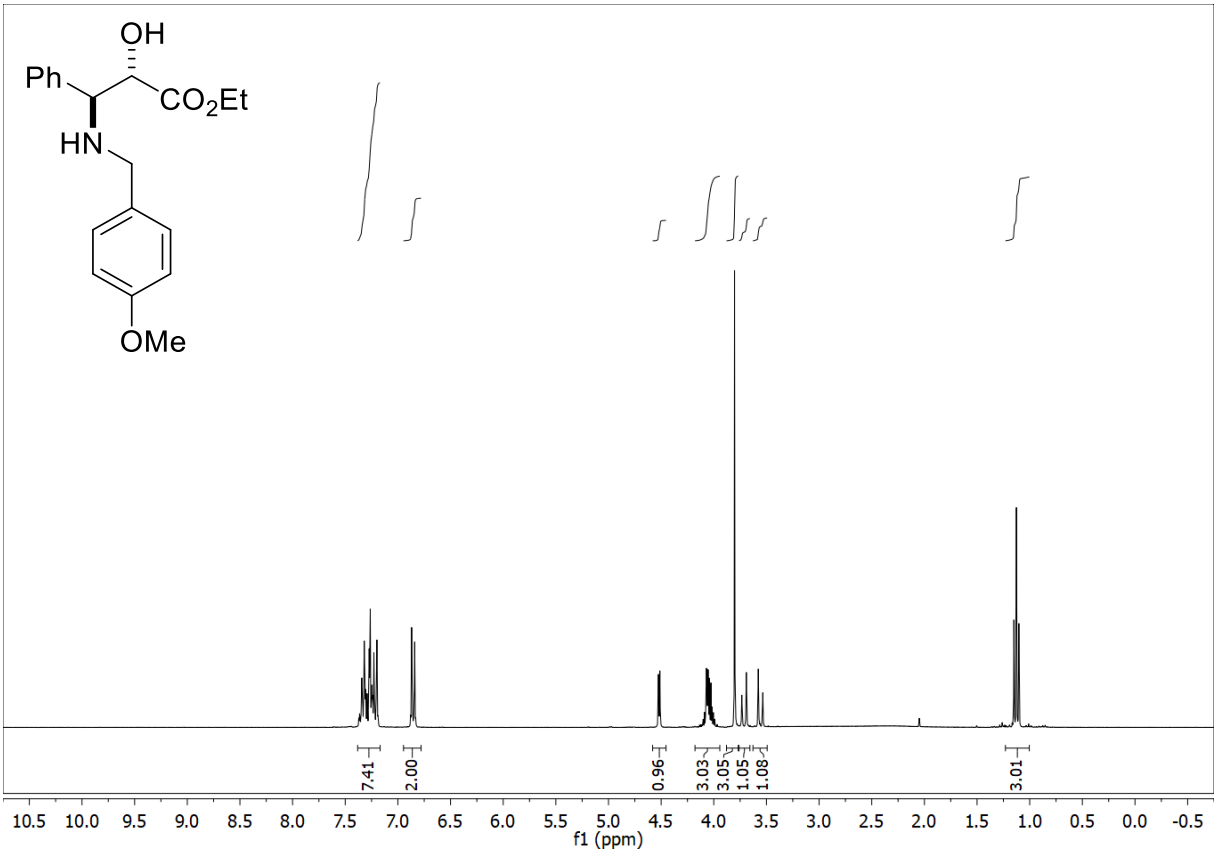
2-(Allyloxy)benzyl ethyl oxalate (110)

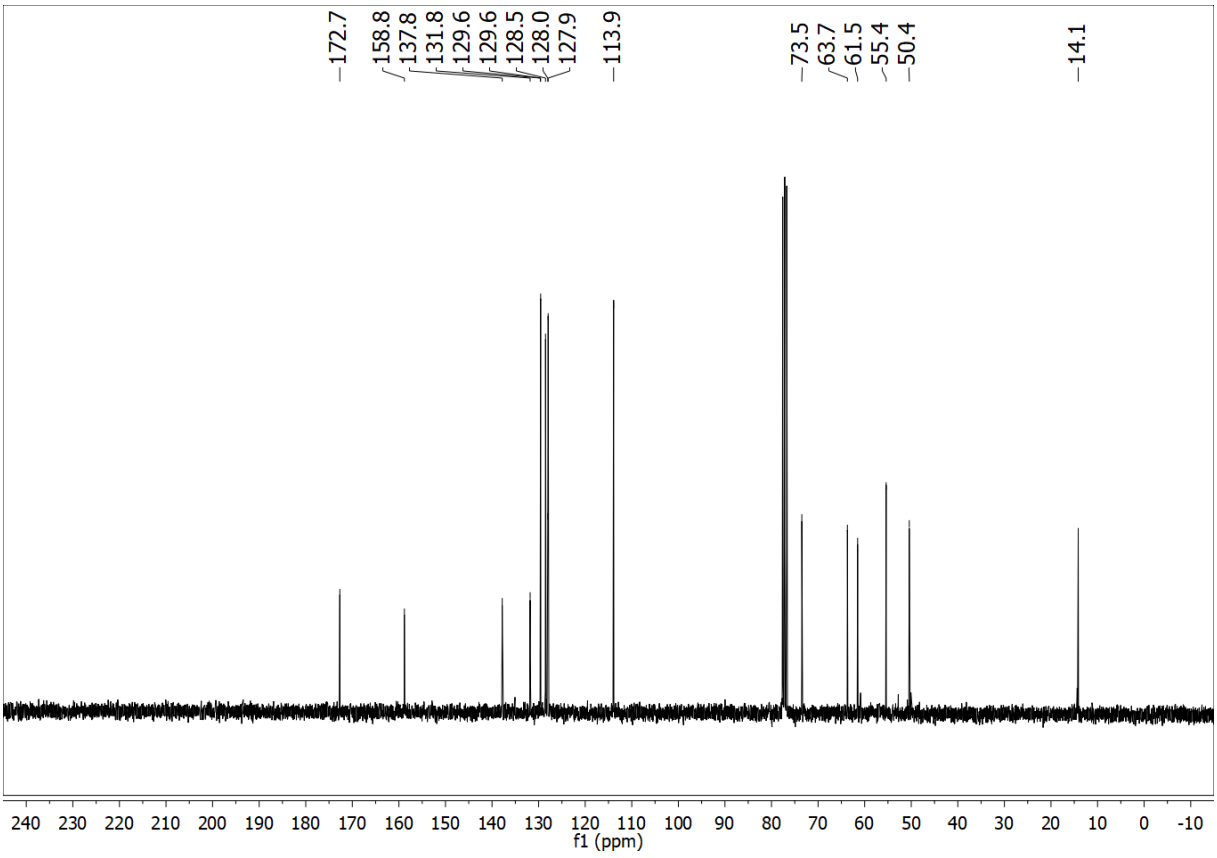




NMR-Solvent: $CDCl_3$

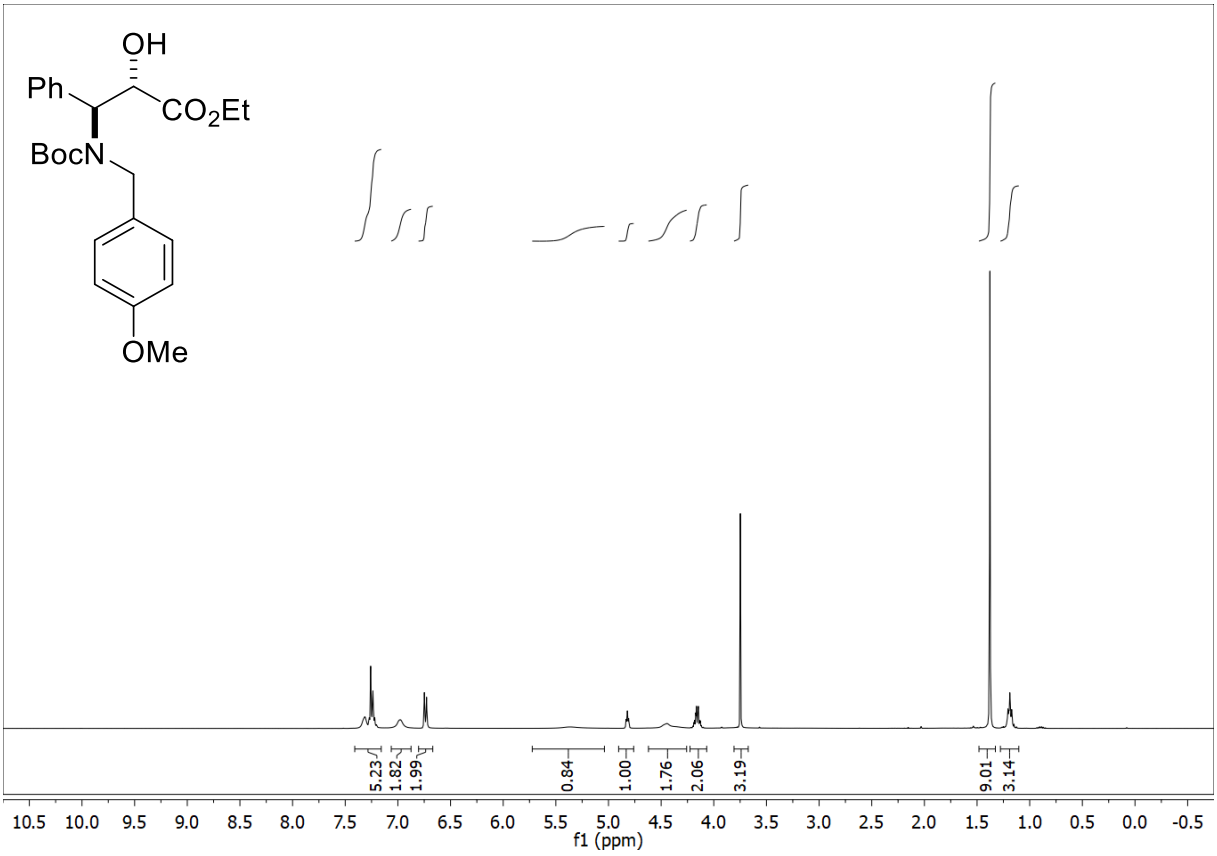
rac. Ethyl (2*S*,3*S*)-2-hydroxy-3-((4-methoxybenzyl)amino)-3-phenylpropanoate (117)

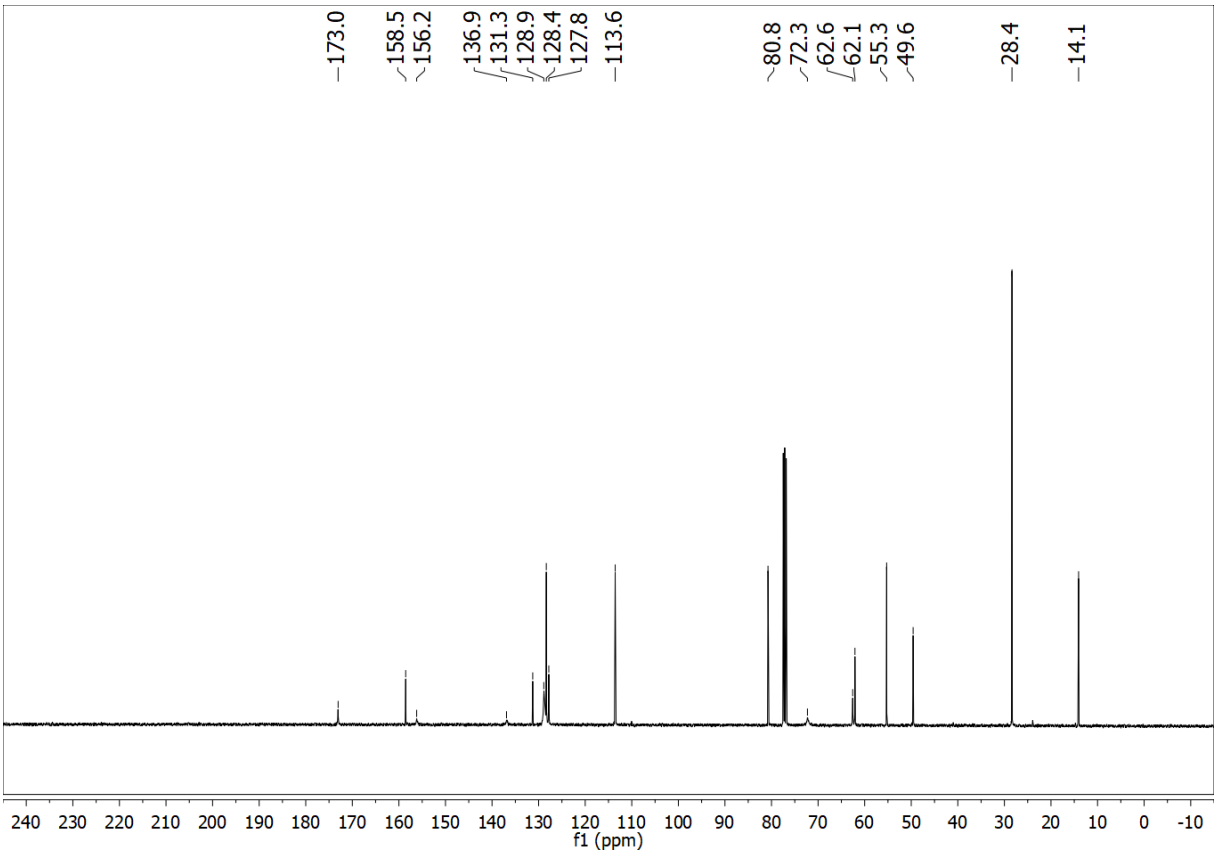




NMR-Solvent: $CDCl_3$

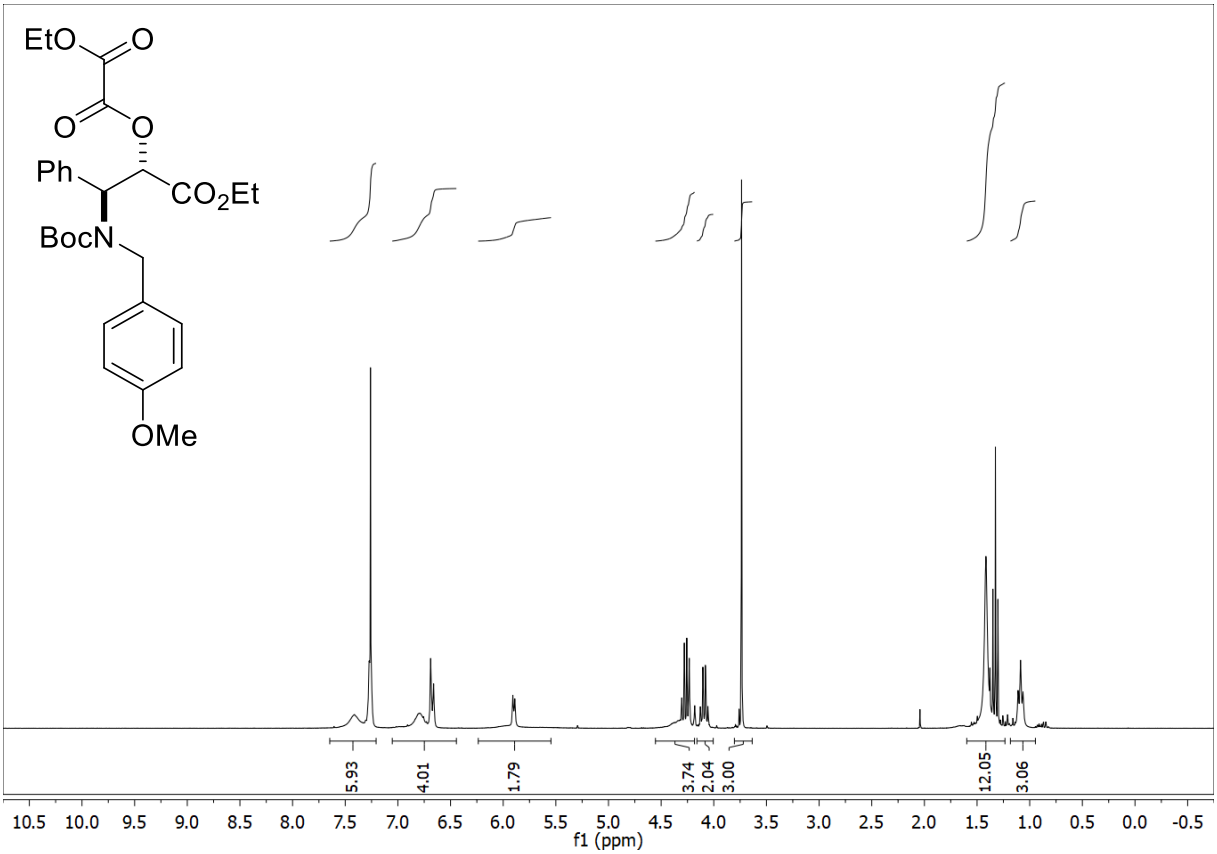
rac. Ethyl (2*S*,3*S*)-3-((*tert*-butoxycarbonyl)(4-methoxybenzyl)amino)-2-hydroxy-3-phenylpropanoate (118)

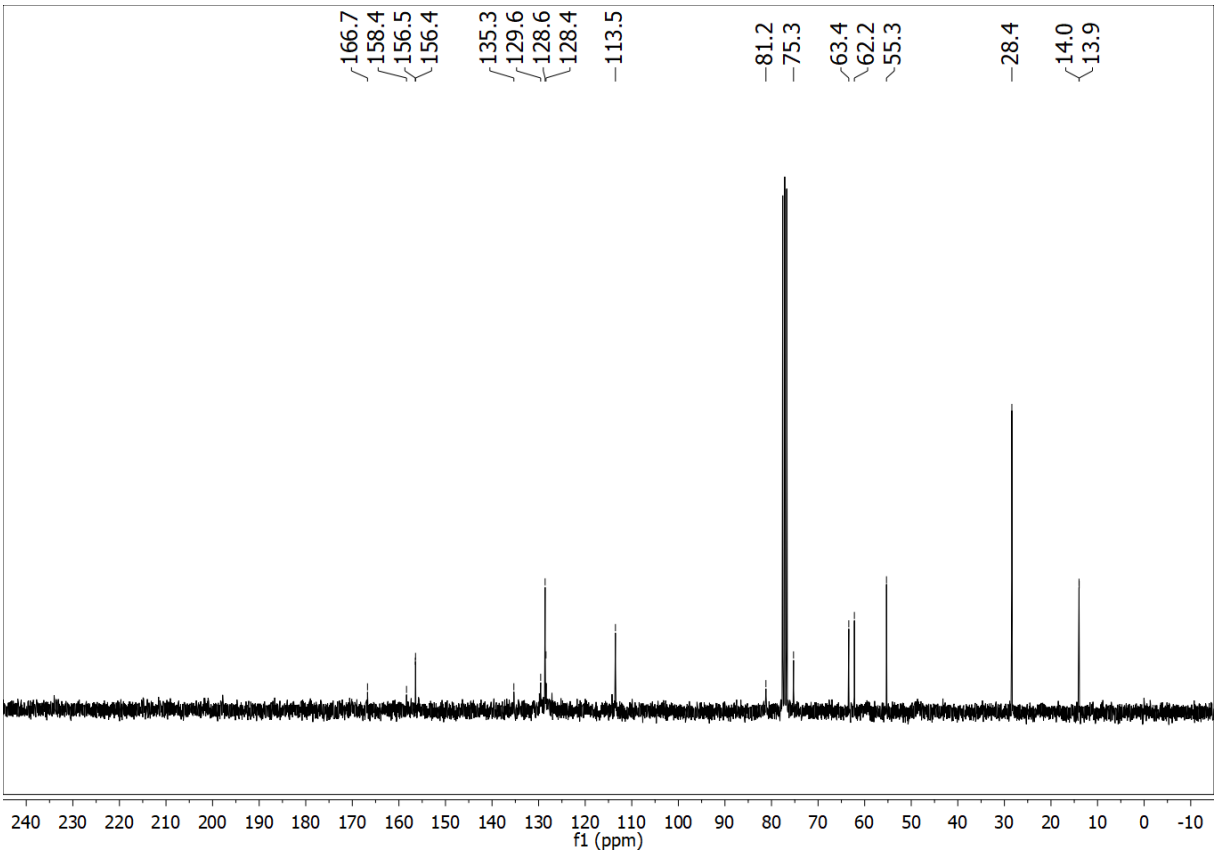




NMR-Solvent: $CDCl_3$

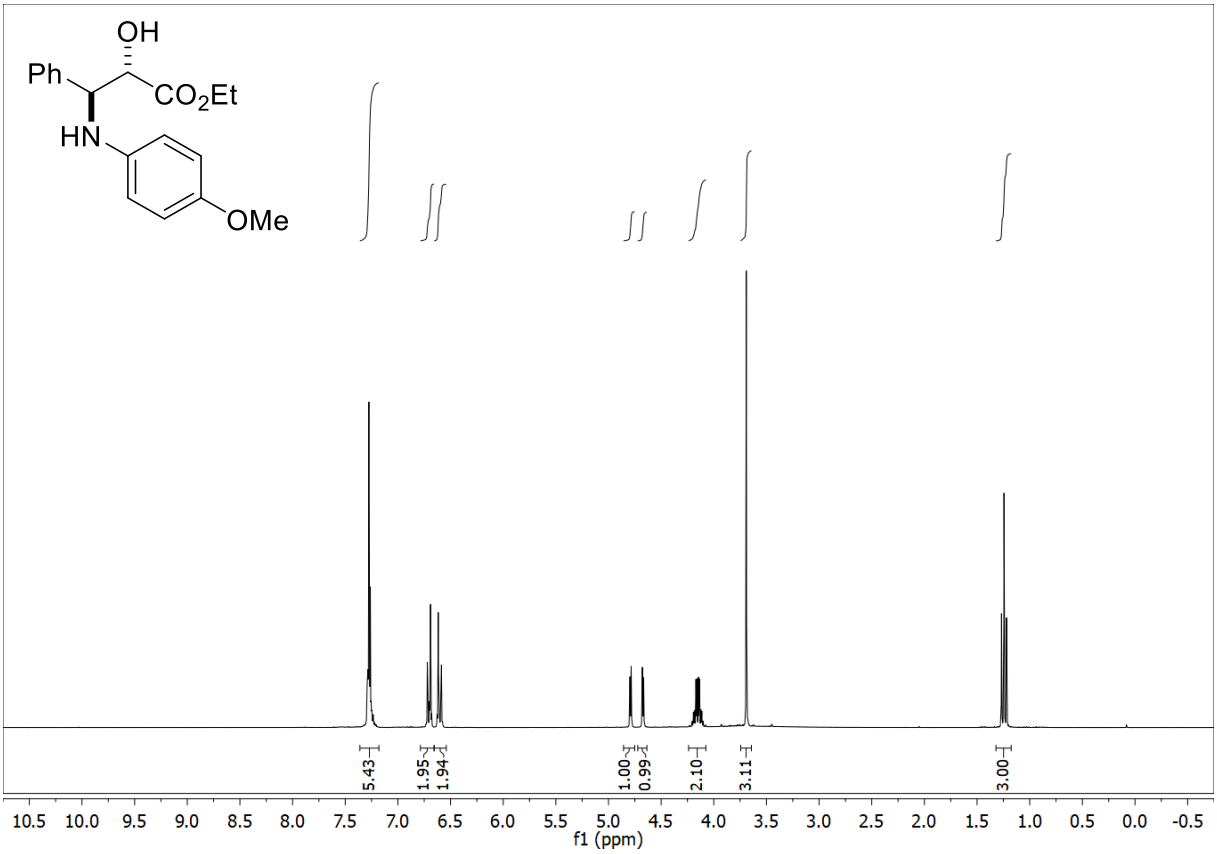
rac. (1*S*,2*S*)-1-((*tert*-butoxycarbonyl)(4-methoxybenzyl)amino)-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (119)

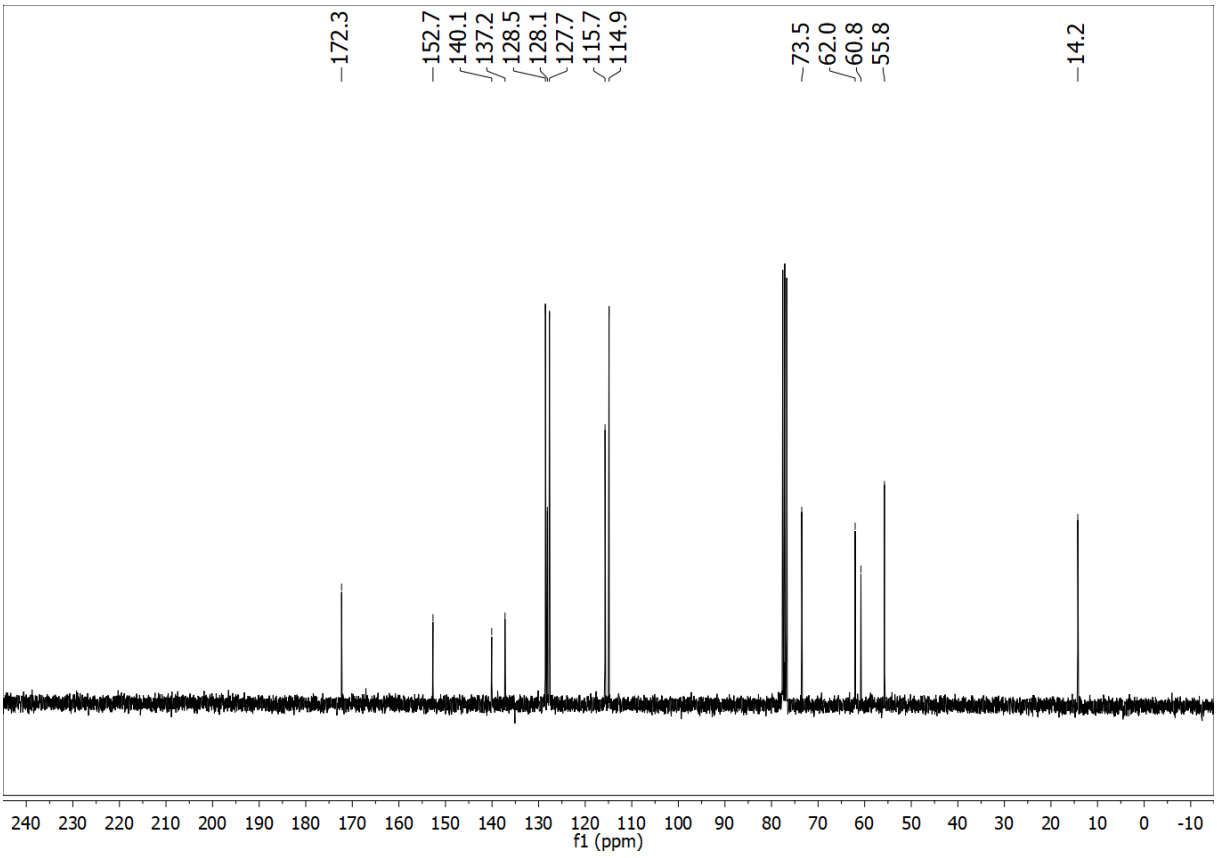




NMR-Solvent: $CDCl_3$

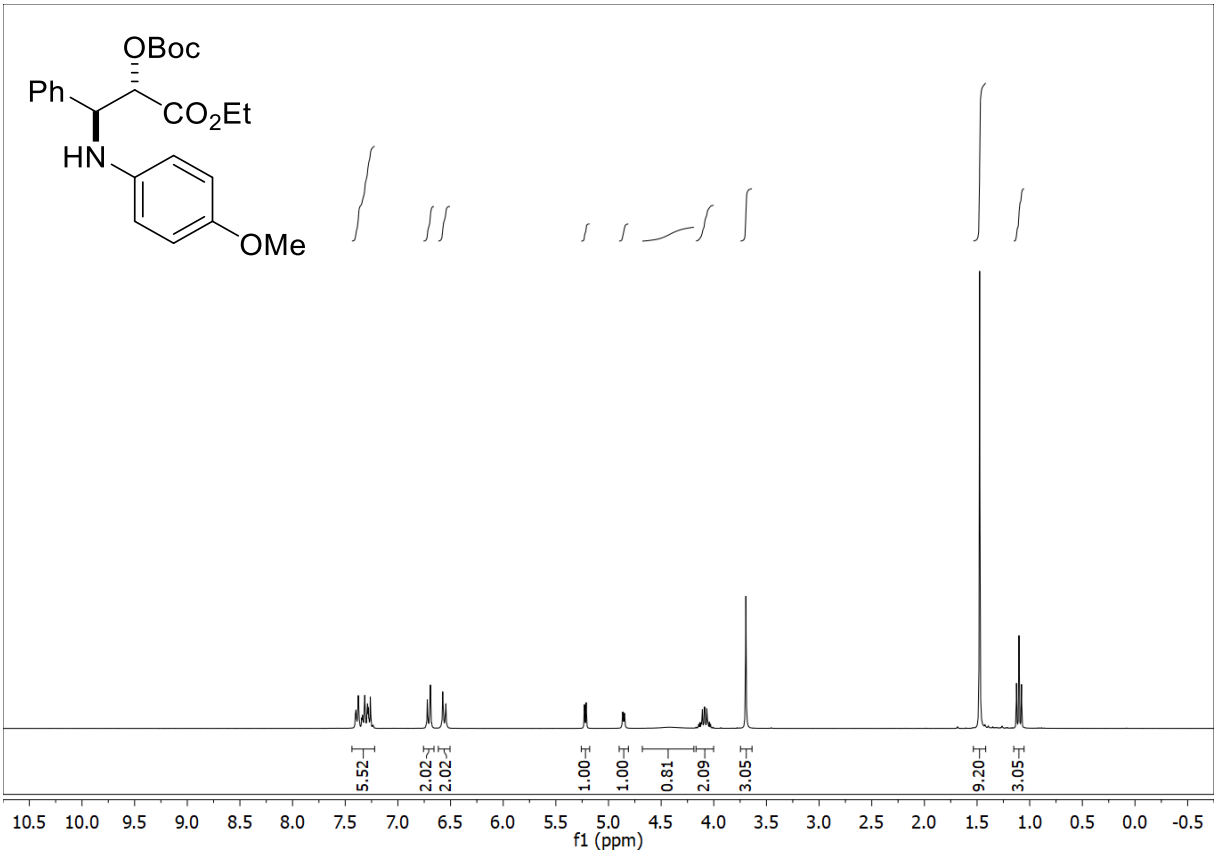
rac. Ethyl (2*S*,3*S*)-2-hydroxy-3-((4-methoxyphenyl)amino)-3-phenylpropanoate (120)

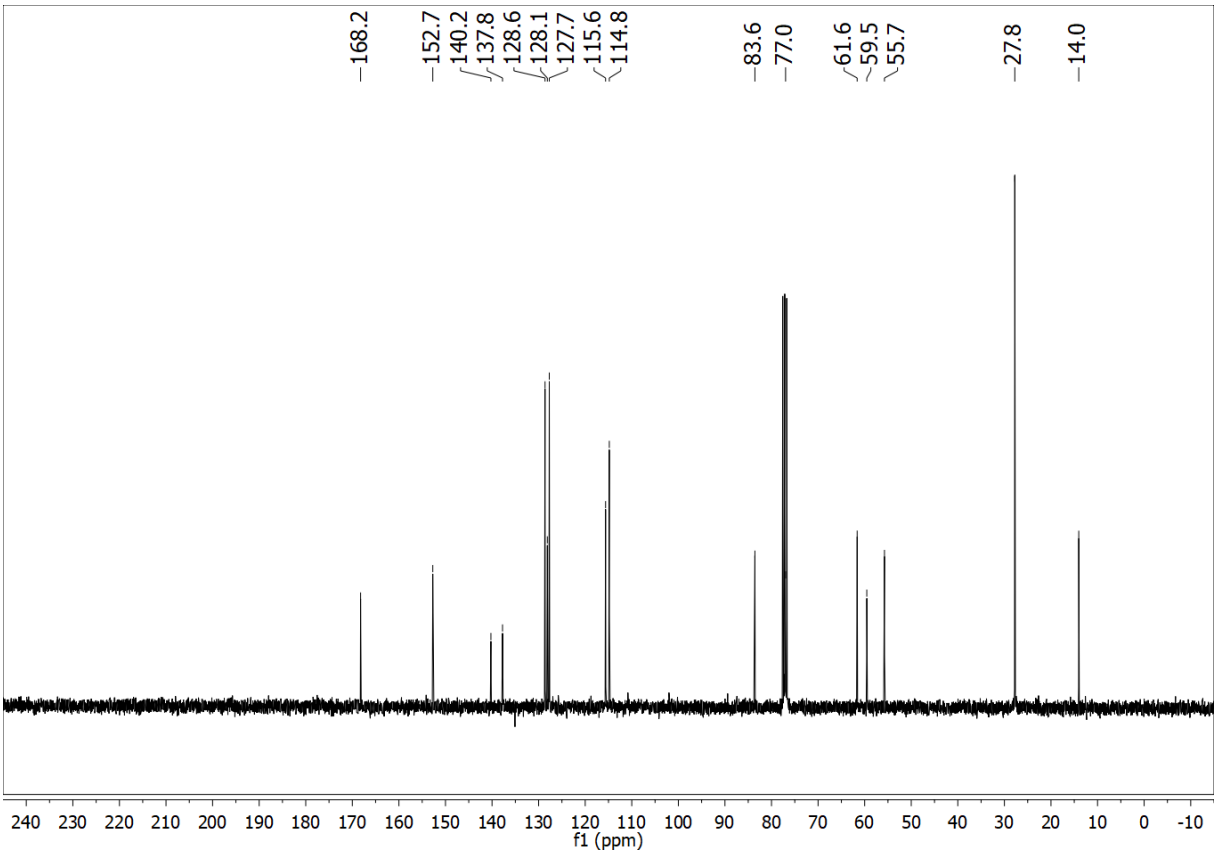




NMR-Solvent: $CDCl_3$

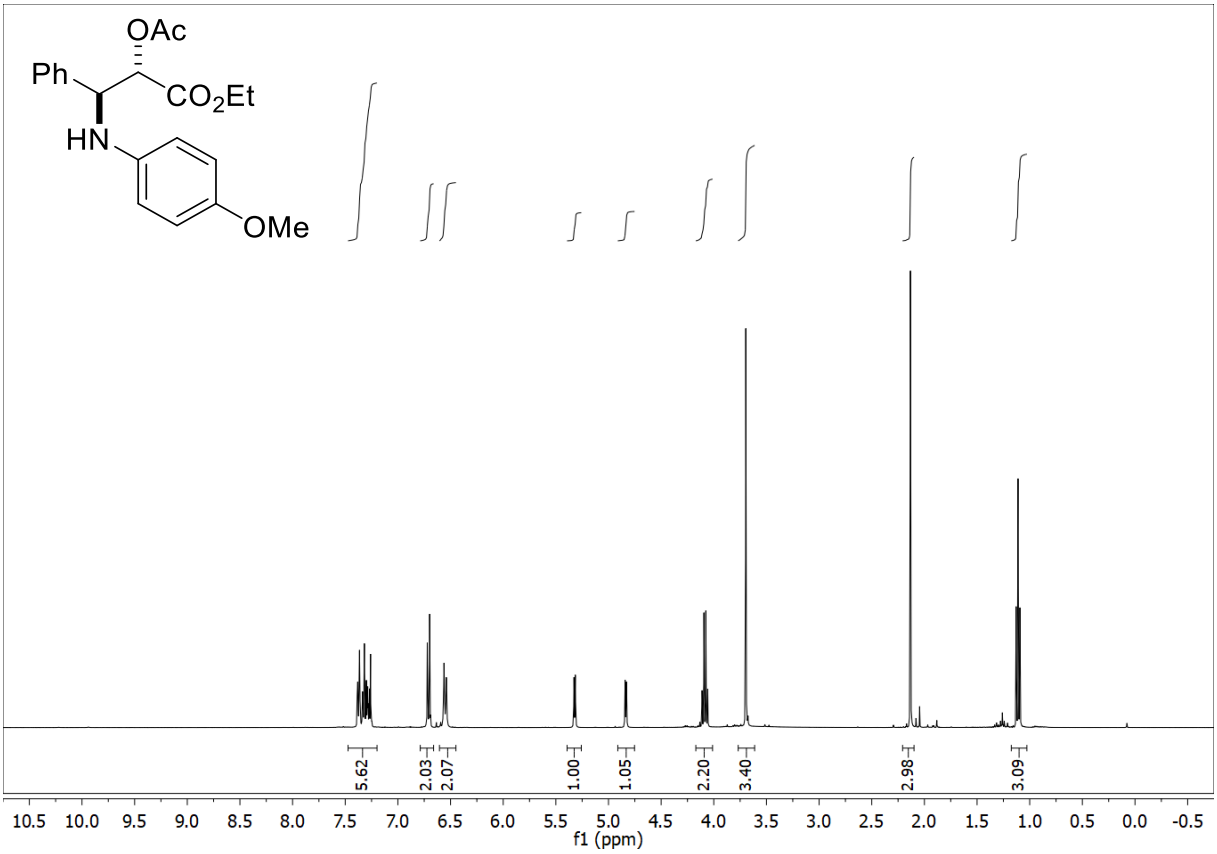
rac. Ethyl (2*S*,3*S*)-2-((*tert*-butoxycarbonyl)oxy)-3-((4-methoxyphenyl)amino)-3-phenylpropanoate (121)

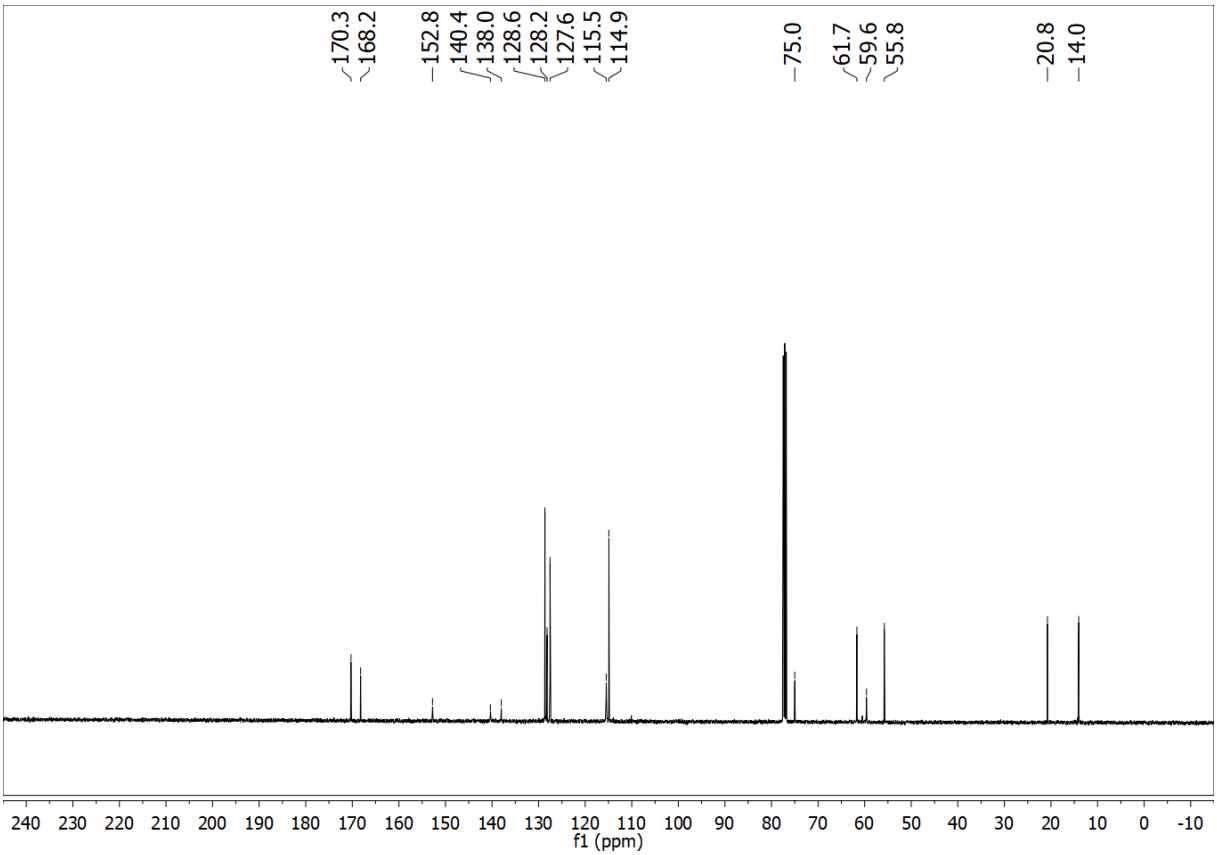




NMR-Solvent: $CDCl_3$

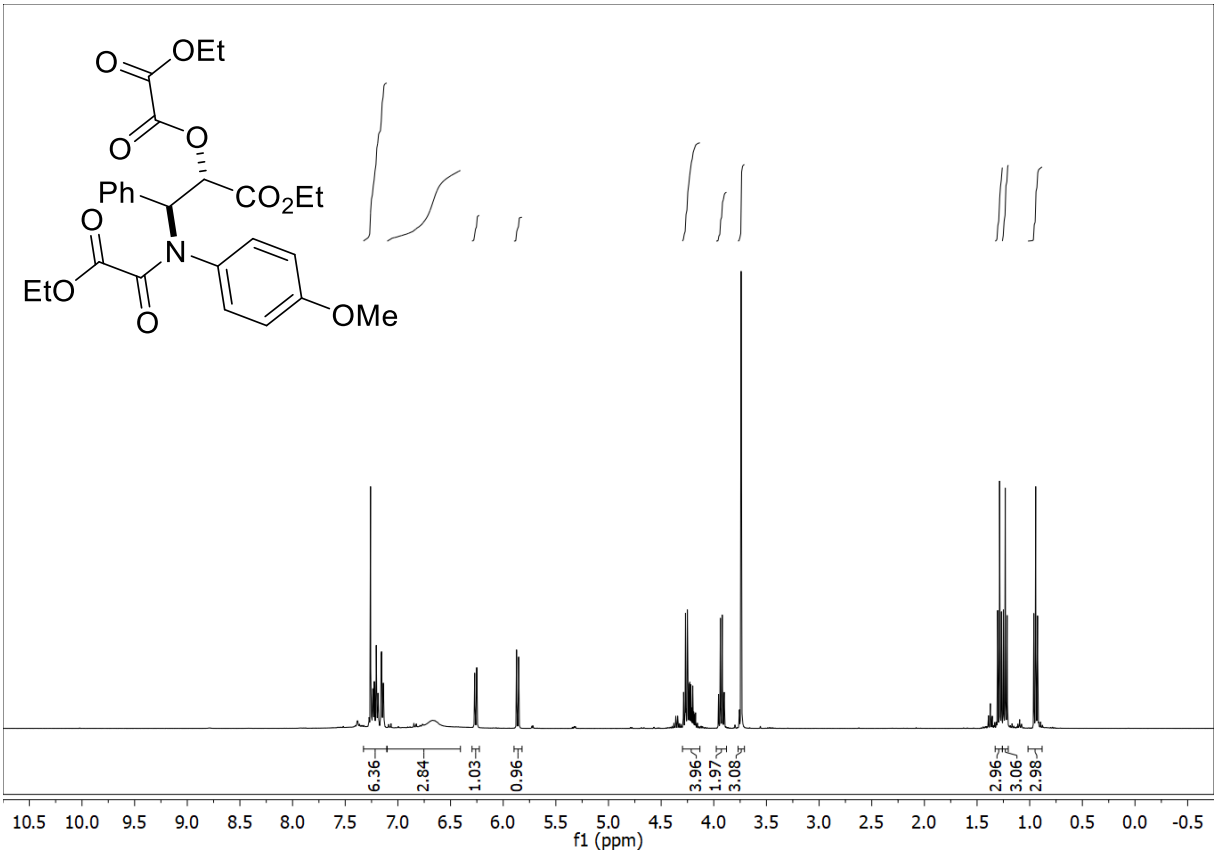
rac. Ethyl (2*S*,3*S*)-2-acetoxy-3-((4-methoxyphenyl)amino)-3-phenylpropanoate (122)

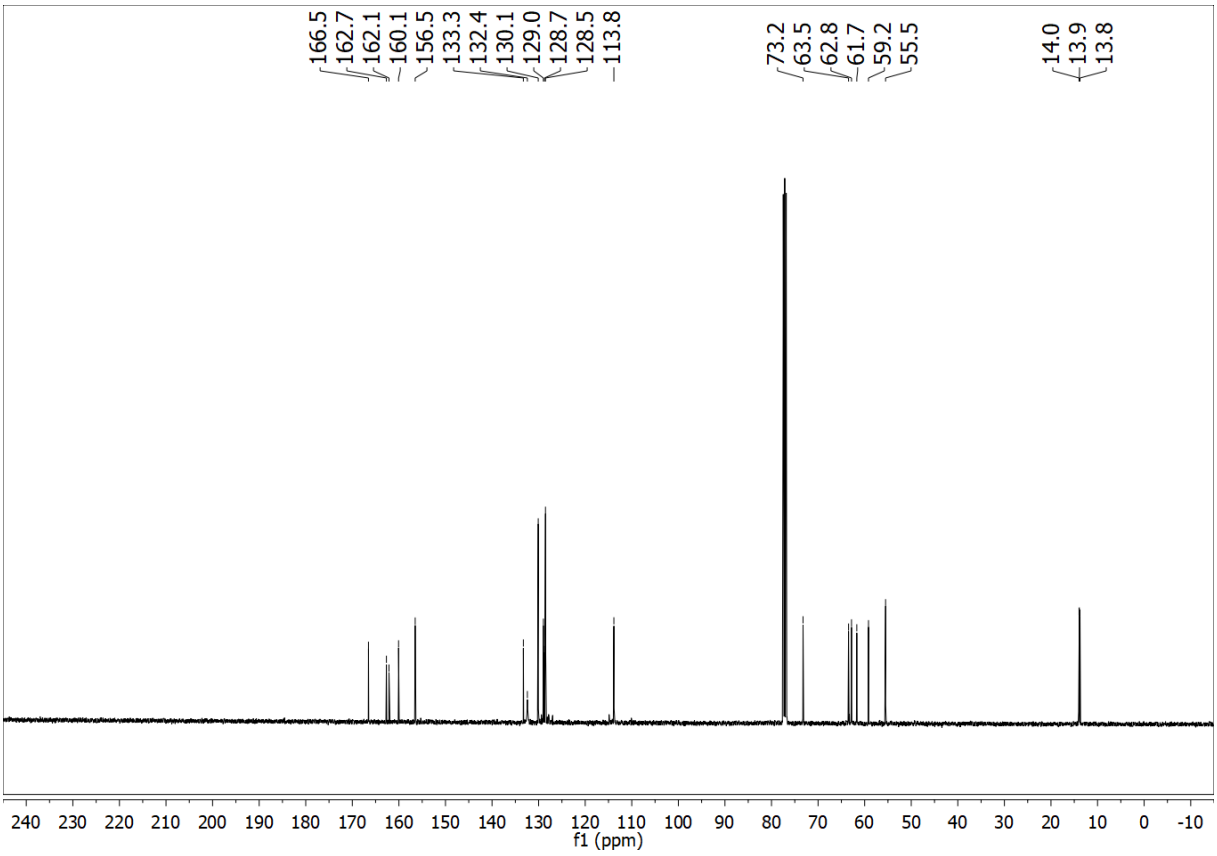




NMR-Solvent: $CDCl_3$

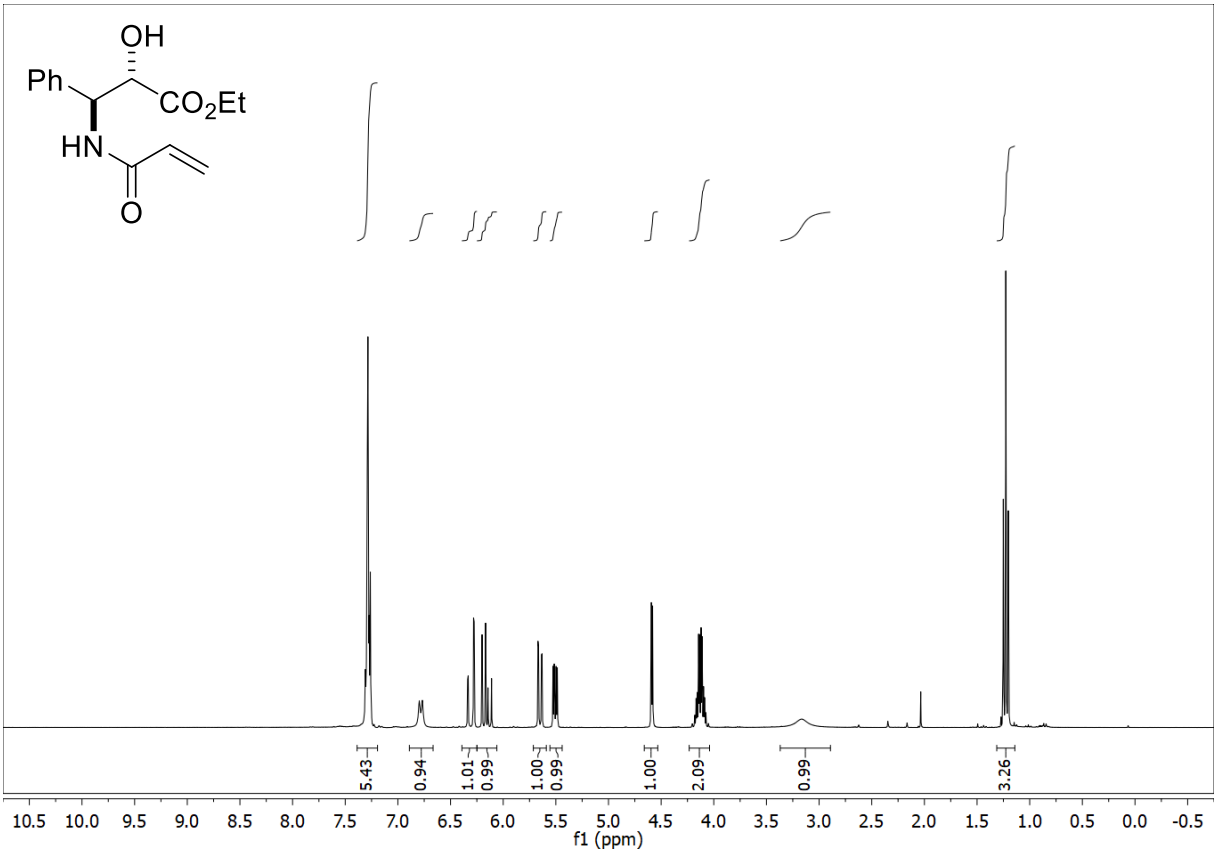
rac. (2*S*,3*S*)-1-ethoxy-3-(2-ethoxy-*N*-(4-methoxyphenyl)-2-oxoacetamido)-1-oxo-3-phenylpropan-2-yl ethyl oxalate (123)

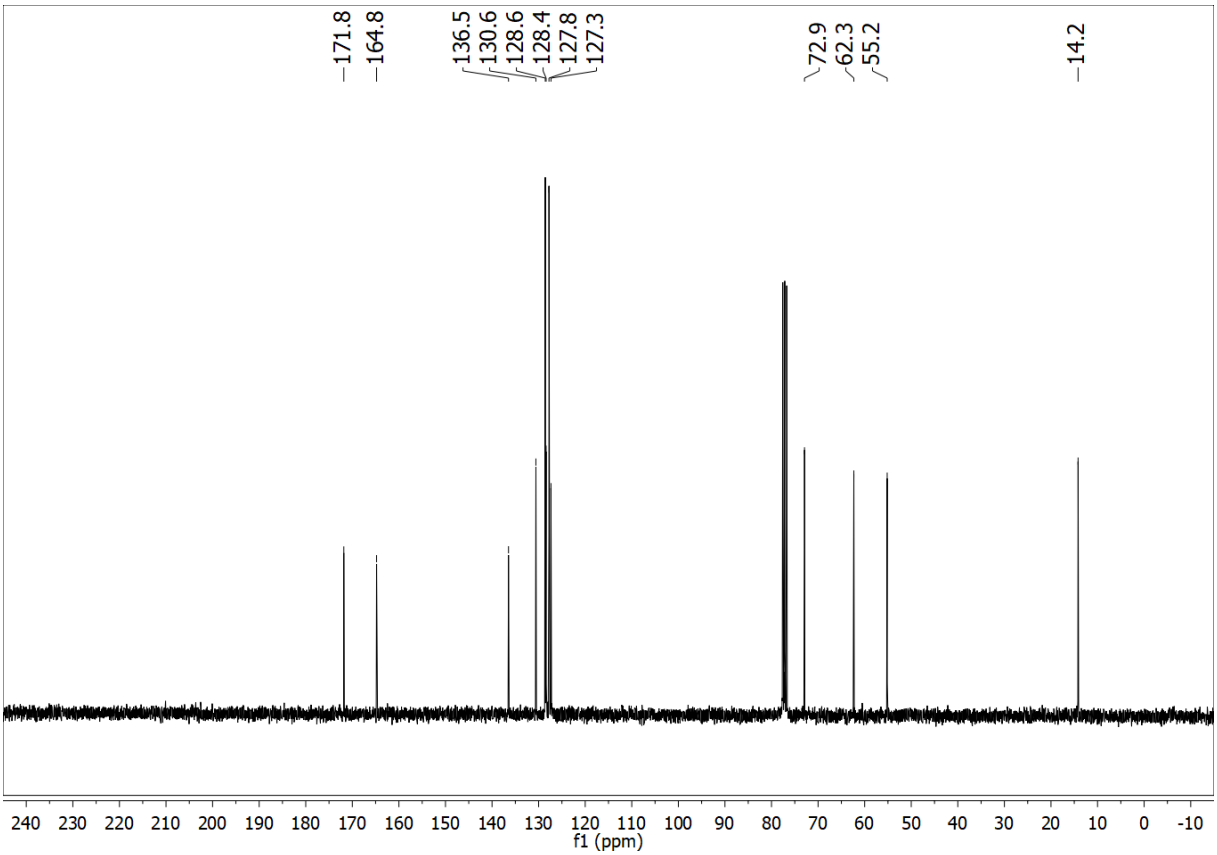




NMR-Solvent: $CDCl_3$

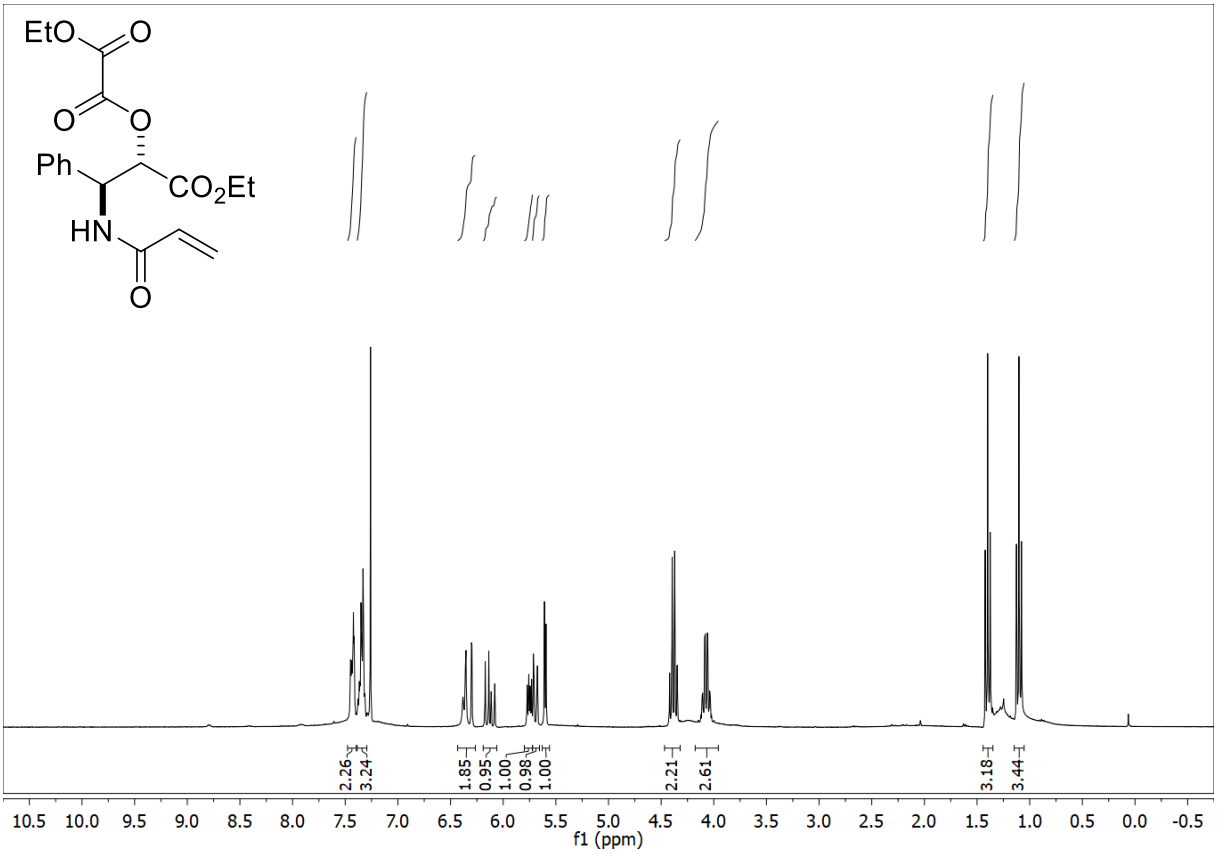
rac. Ethyl (2*S*,3*S*)-3-acrylamido-2-hydroxy-3-phenylpropanoate (126)

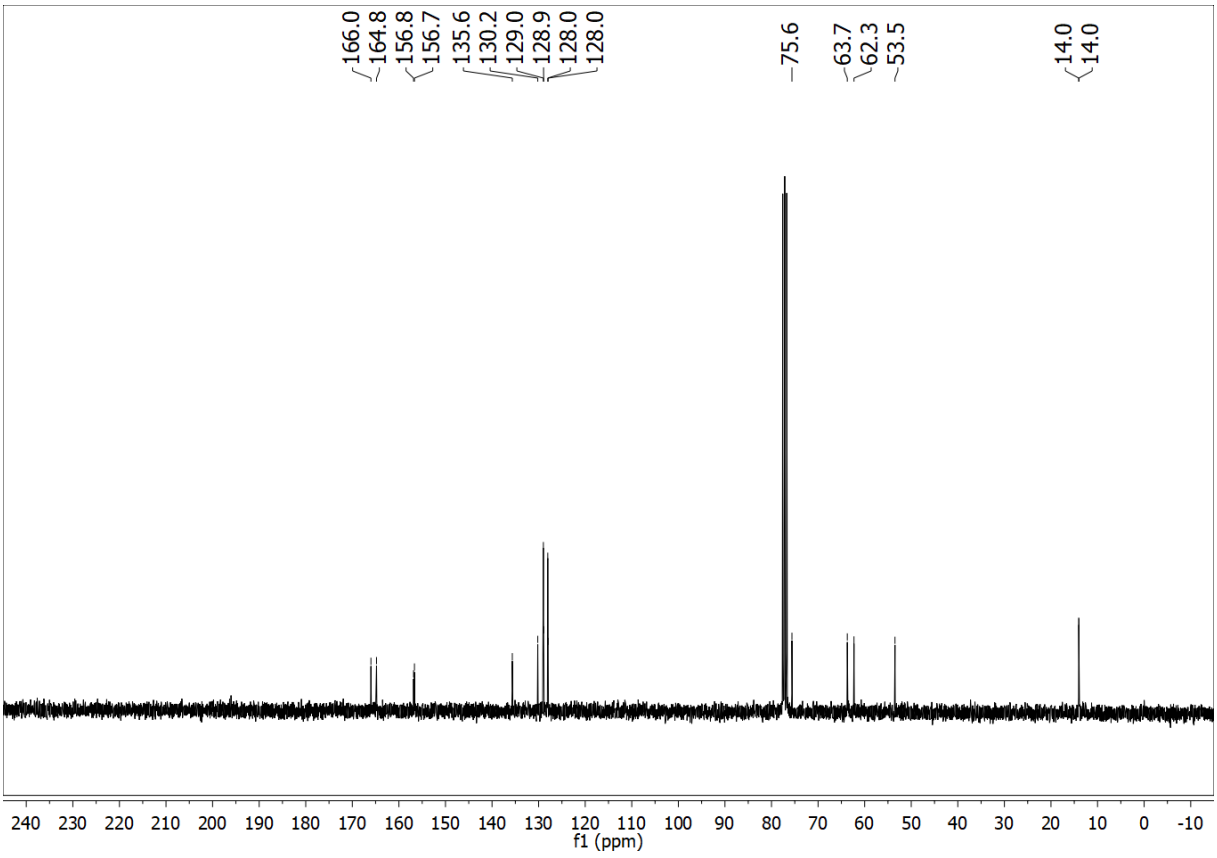




NMR-Solvent: $CDCl_3$

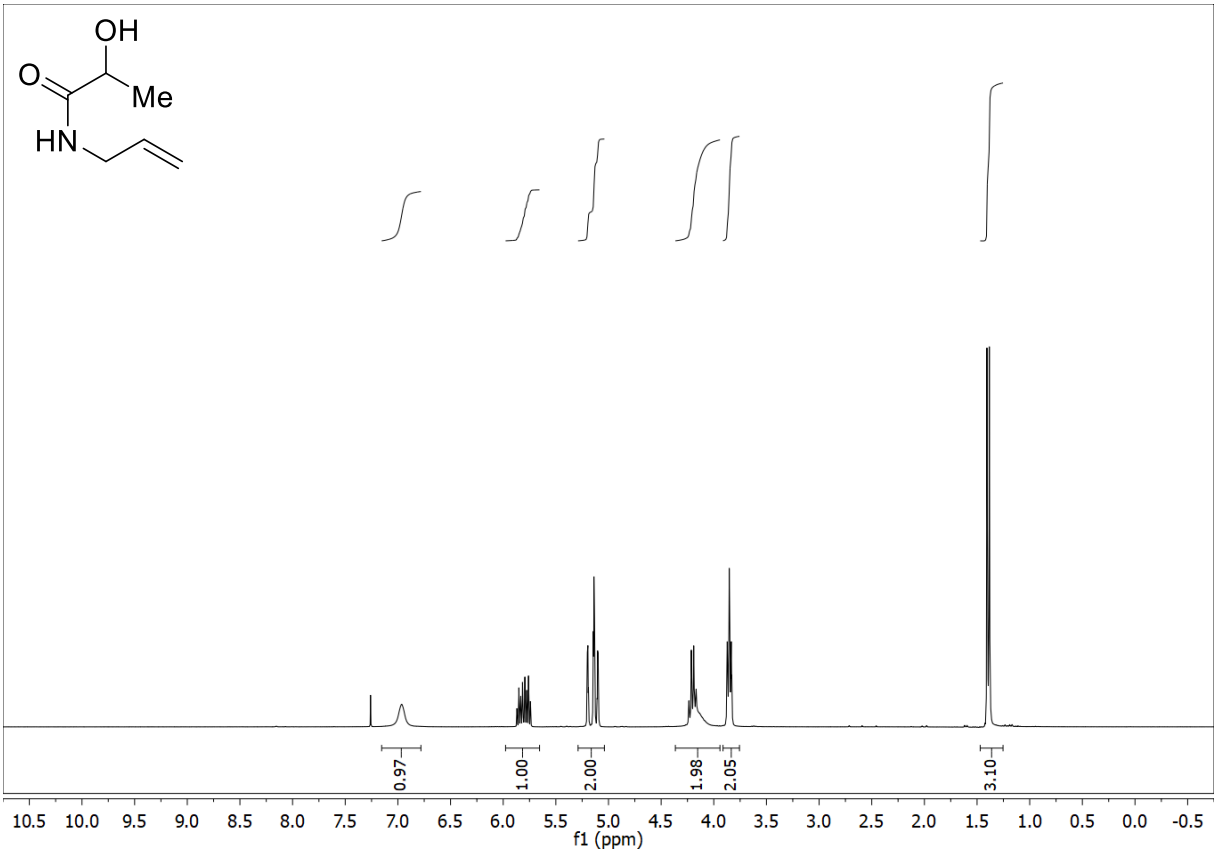
rac. (1*S*,2*S*)-1-acrylamido-3-ethoxy-3-oxo-1-phenylpropan-2-yl ethyl oxalate (127)

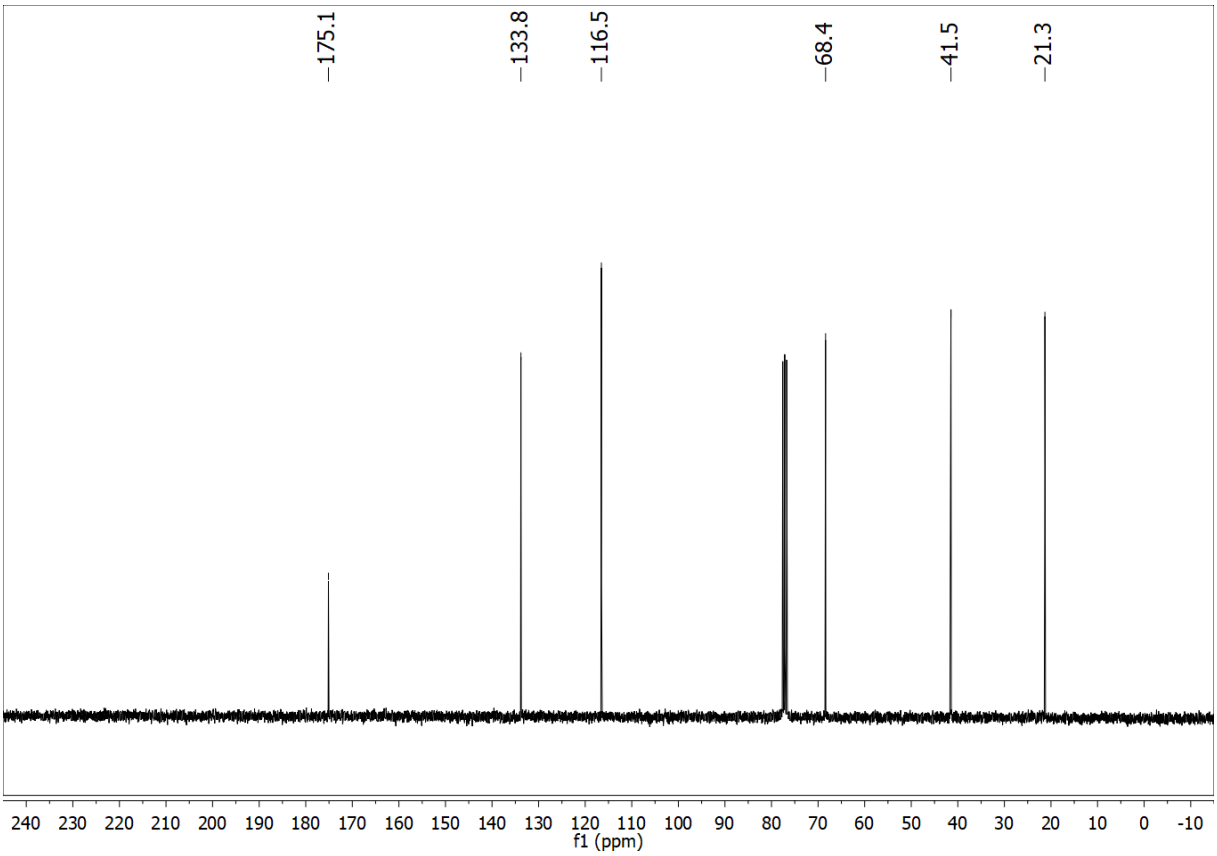




NMR-Solvent: $CDCl_3$

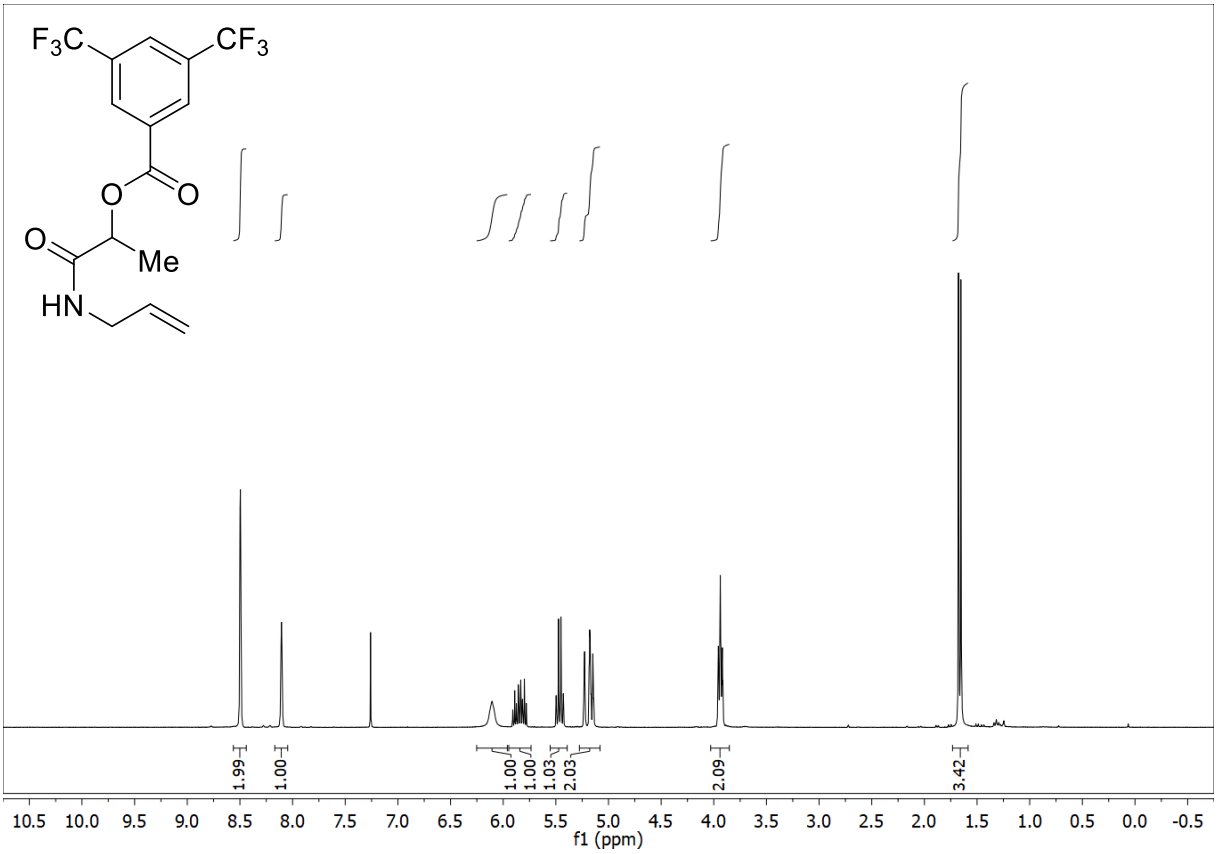
N-allyl-2-hydroxypropanamide (130)

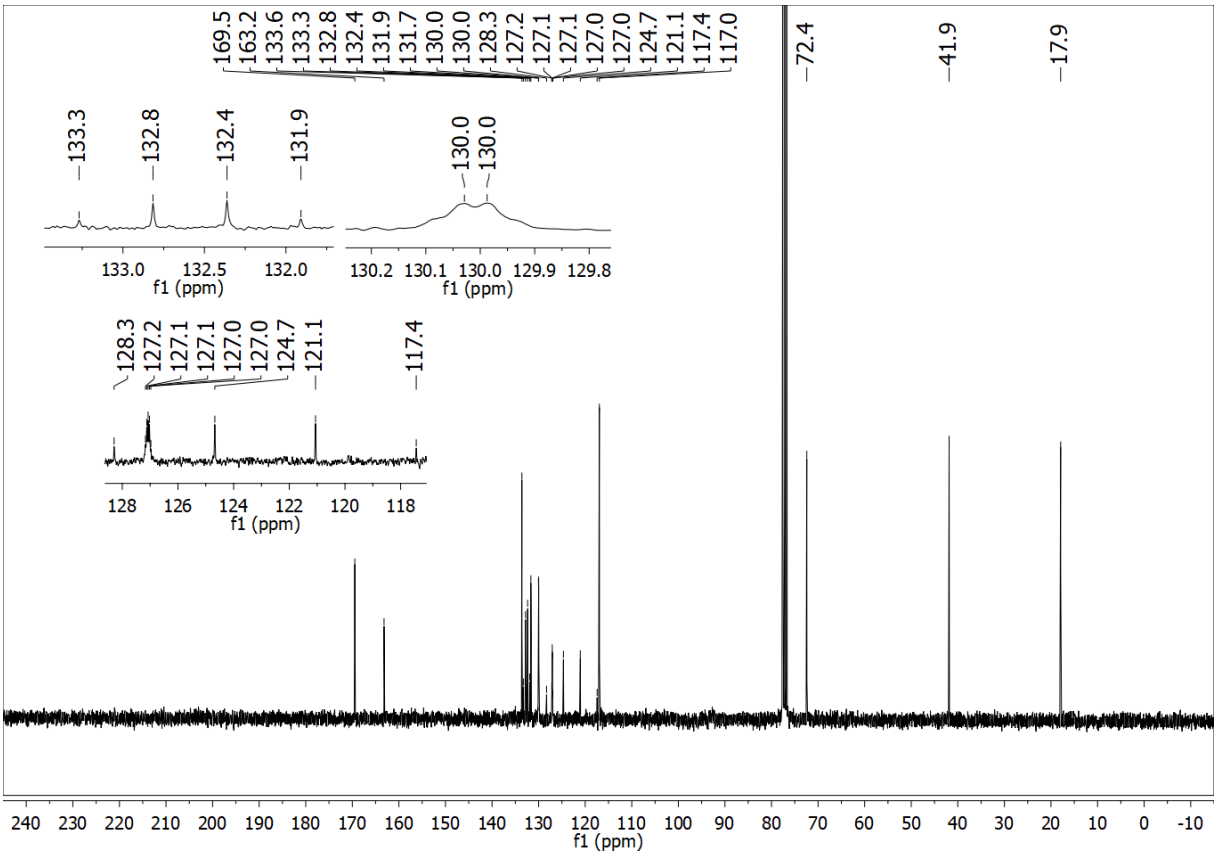


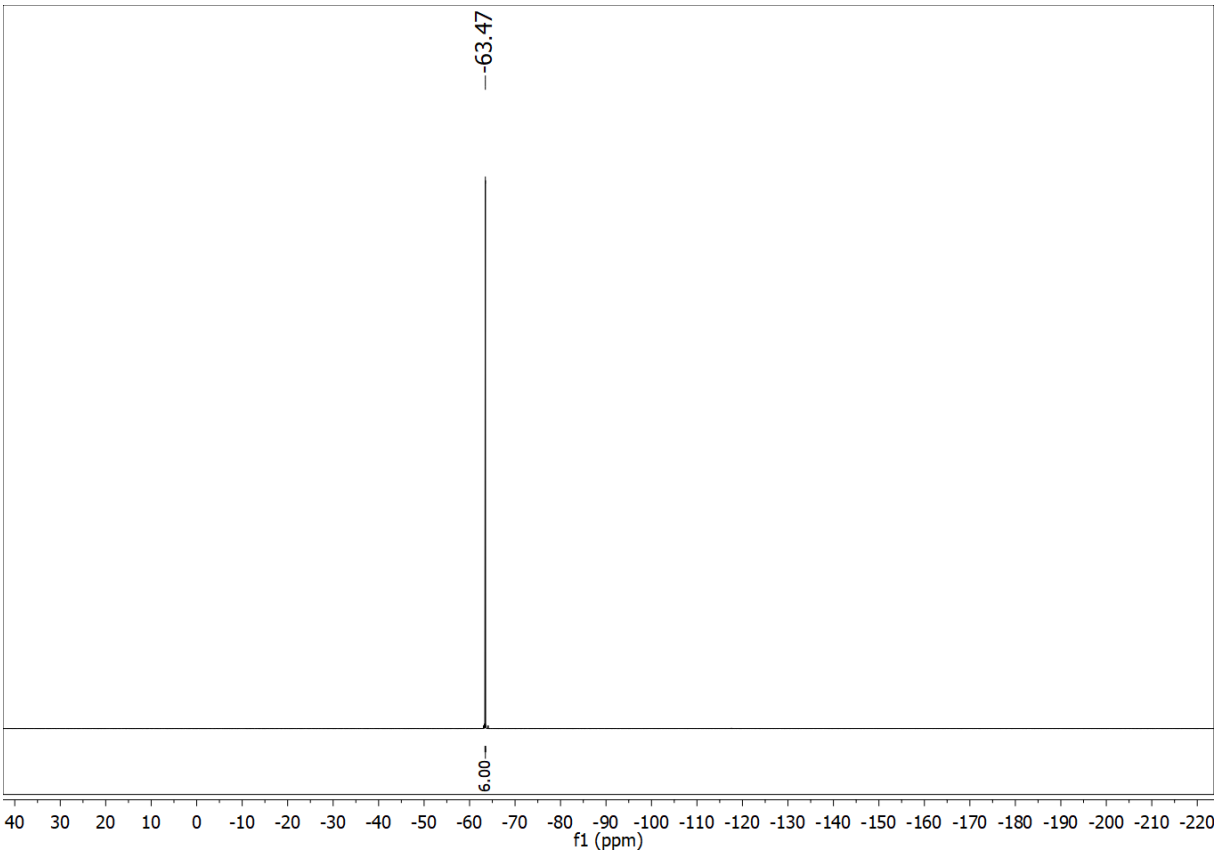


NMR-Solvent: $CDCl_3$

1-(Allylamino)-1-oxopropan-2-yl 3,5-bis(trifluoromethyl)benzoate (131)

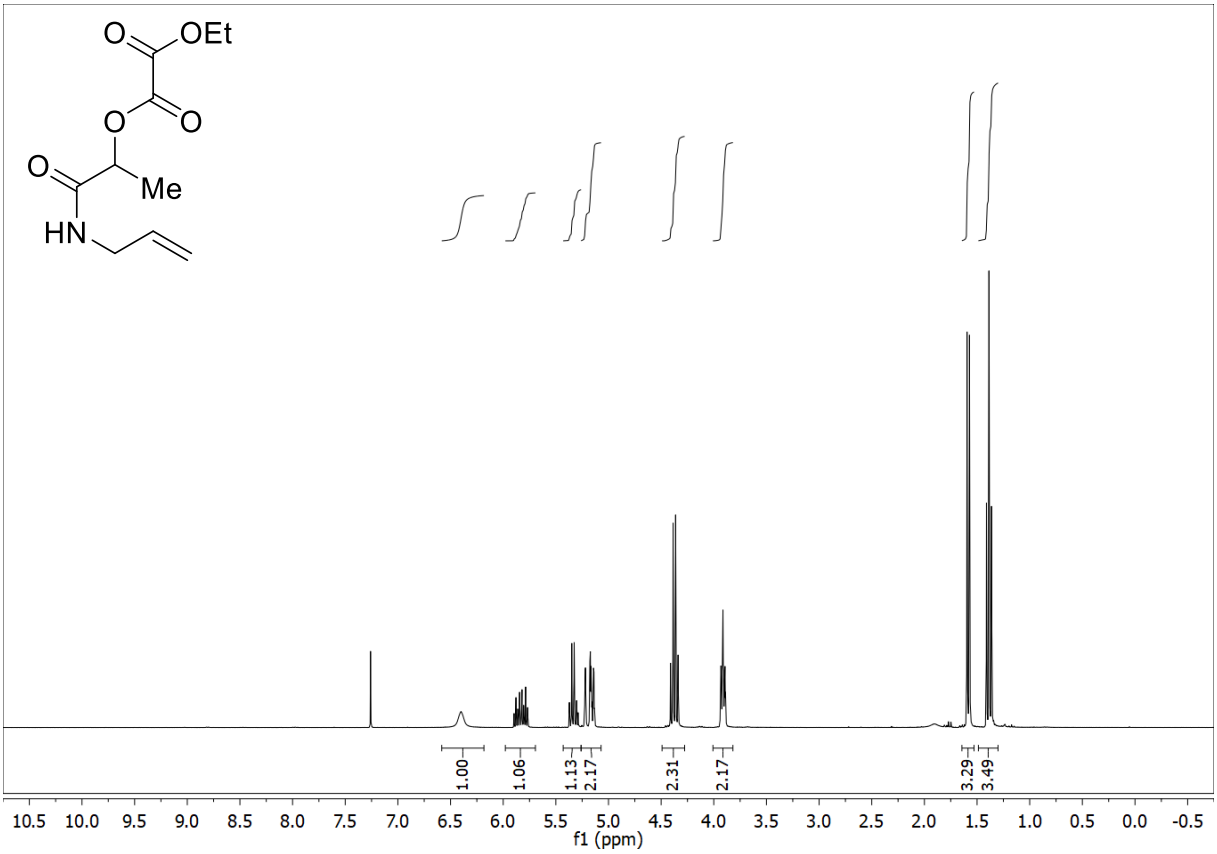


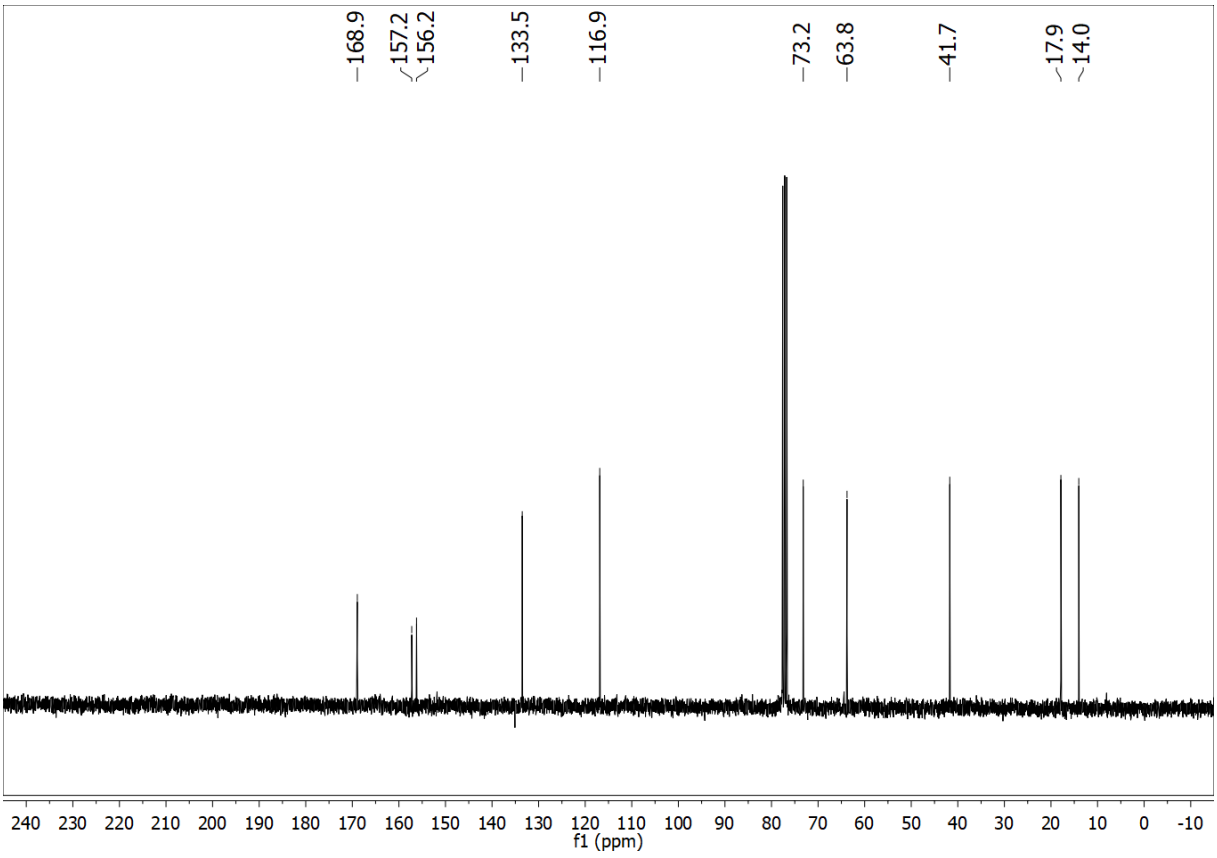




NMR-Solvent: $CDCl_3$

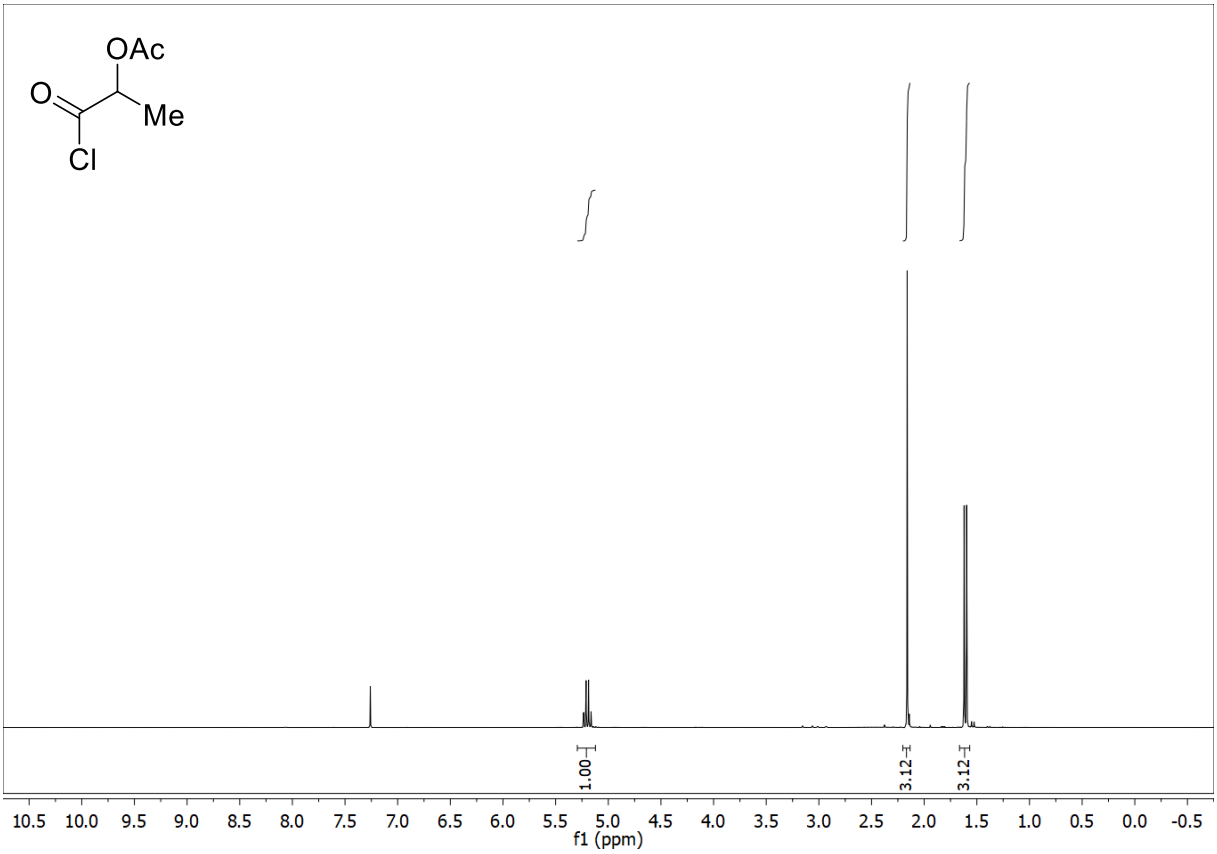
1-(Allylamino)-1-oxopropan-2-yl ethyl oxalate (131´)

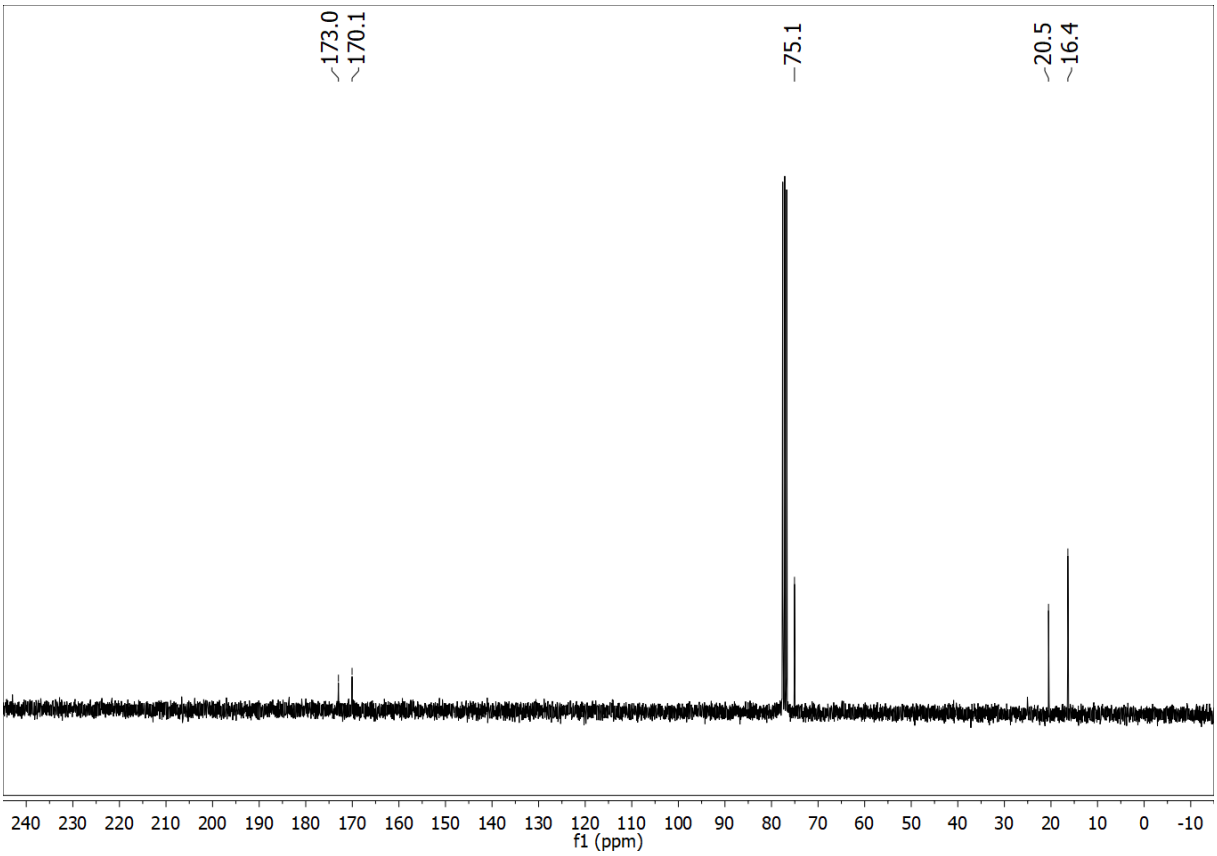




NMR-Solvent: $CDCl_3$

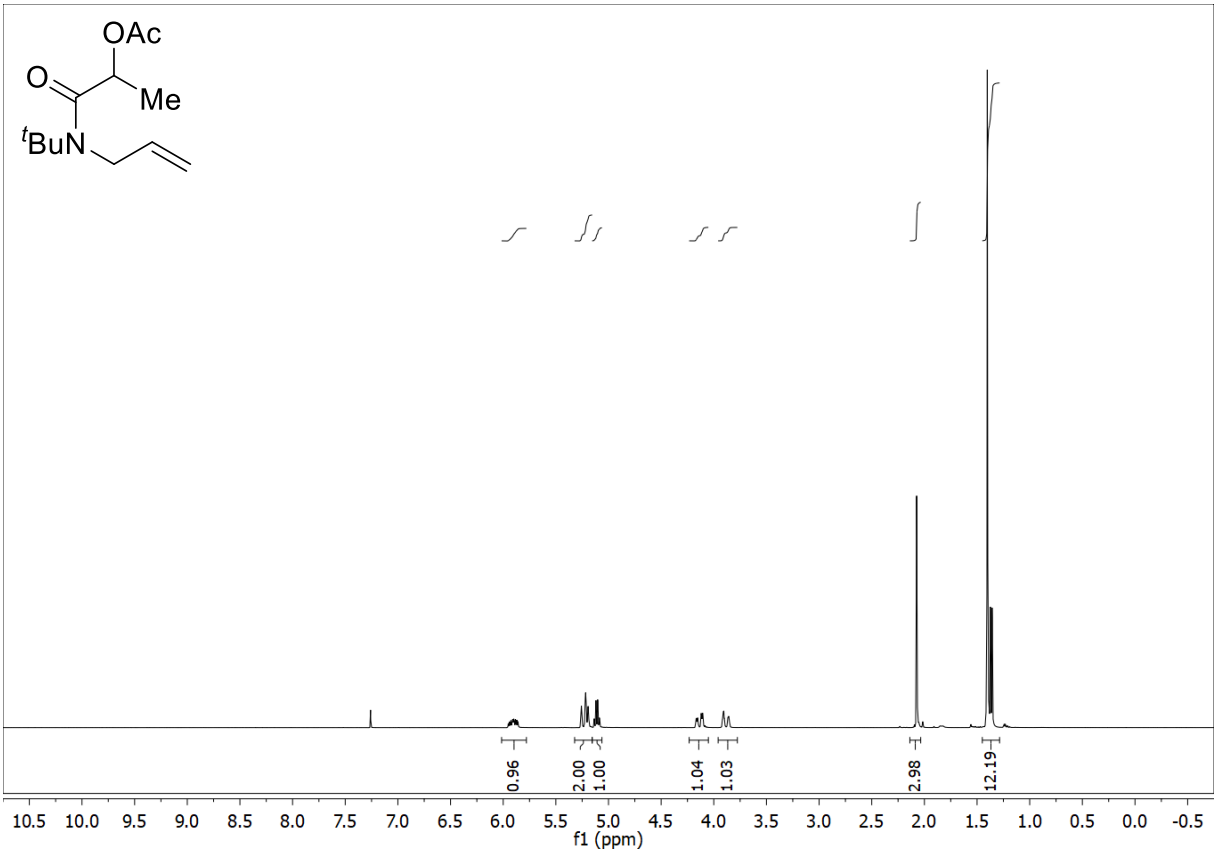
1-Chloro-1-oxopropan-2-yl acetate (135)

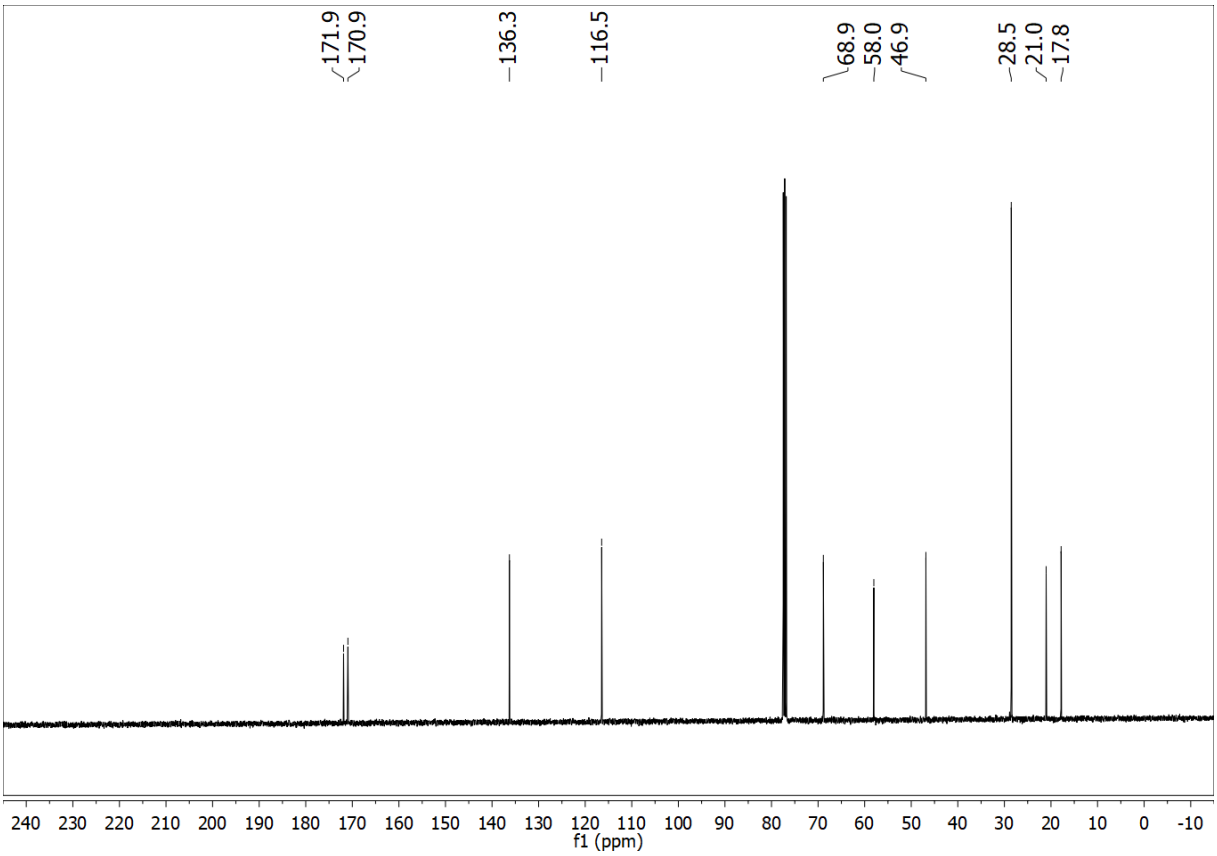




NMR-Solvent: $CDCl_3$

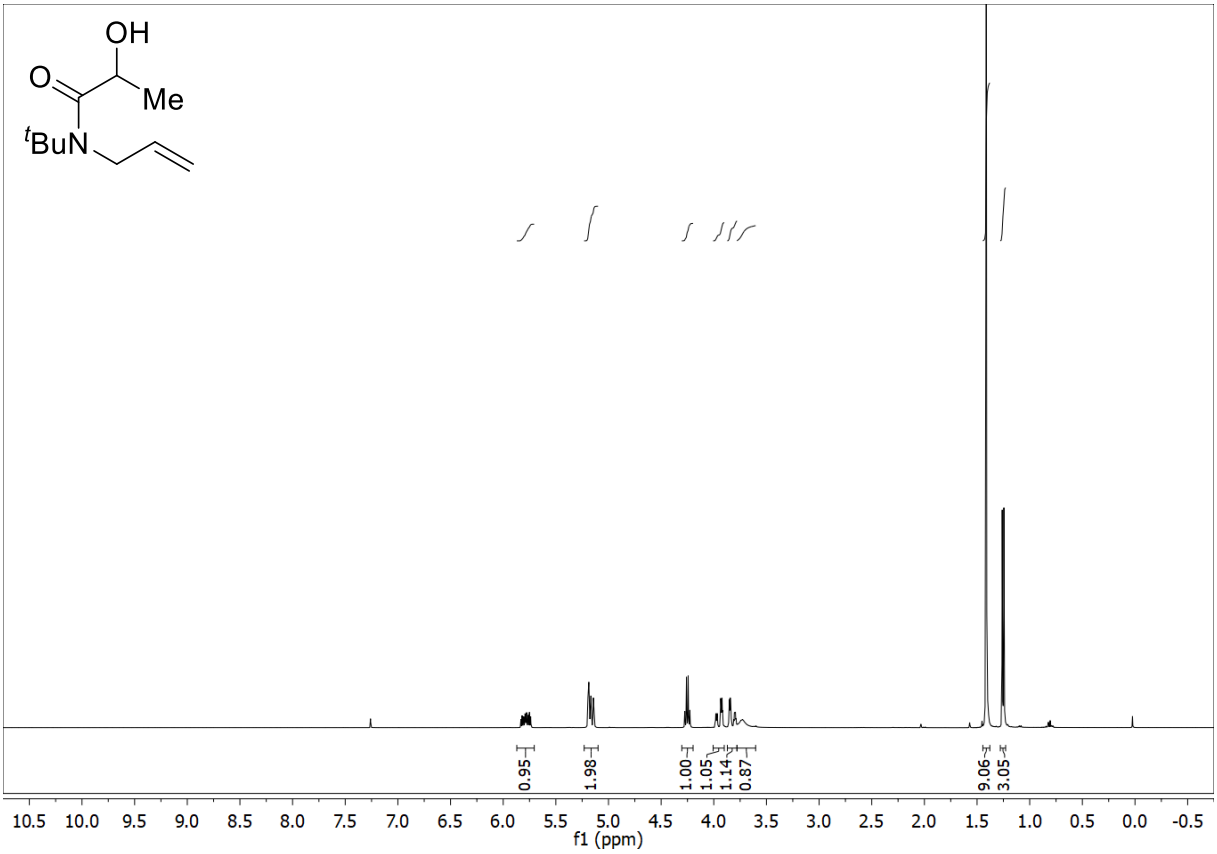
1-(Allyl(*tert*-butyl)amino)-1-oxopropan-2-yl acetate (138)

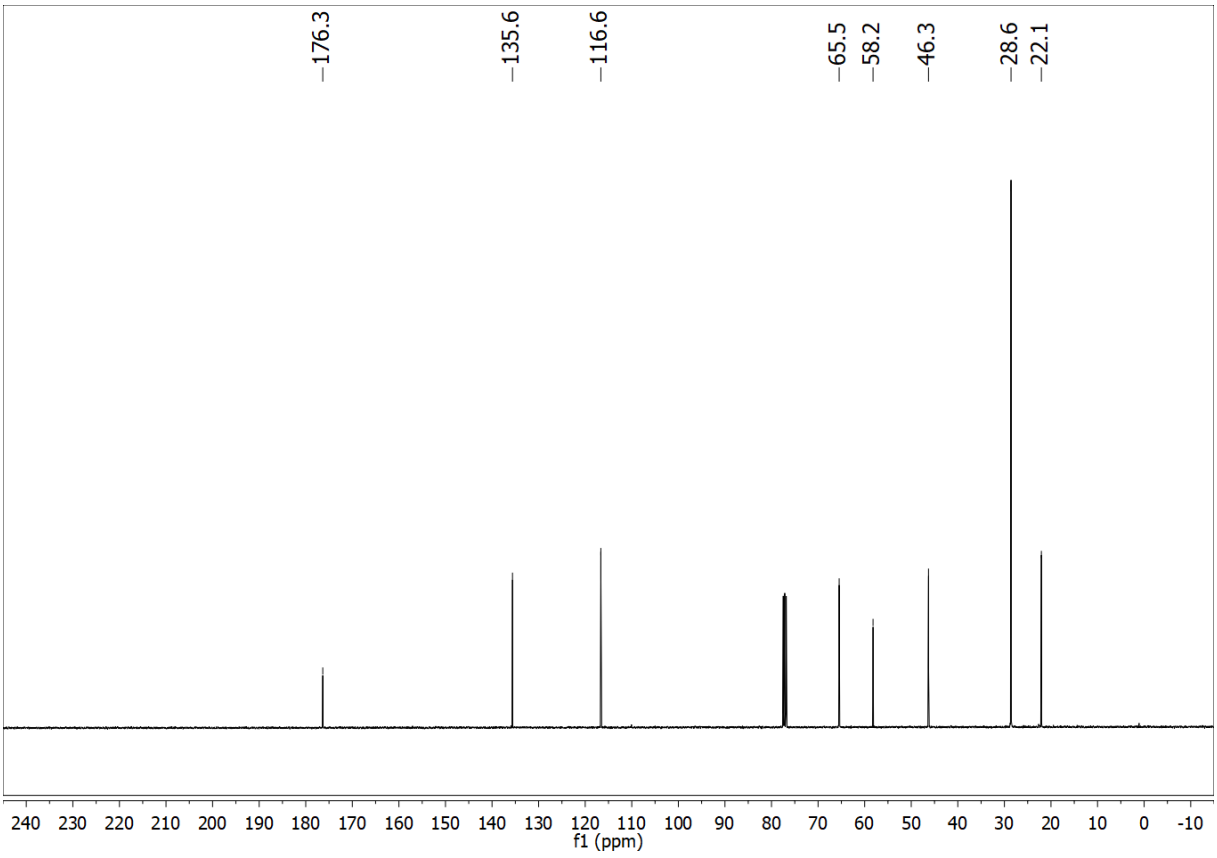




NMR-Solvent: $CDCl_3$

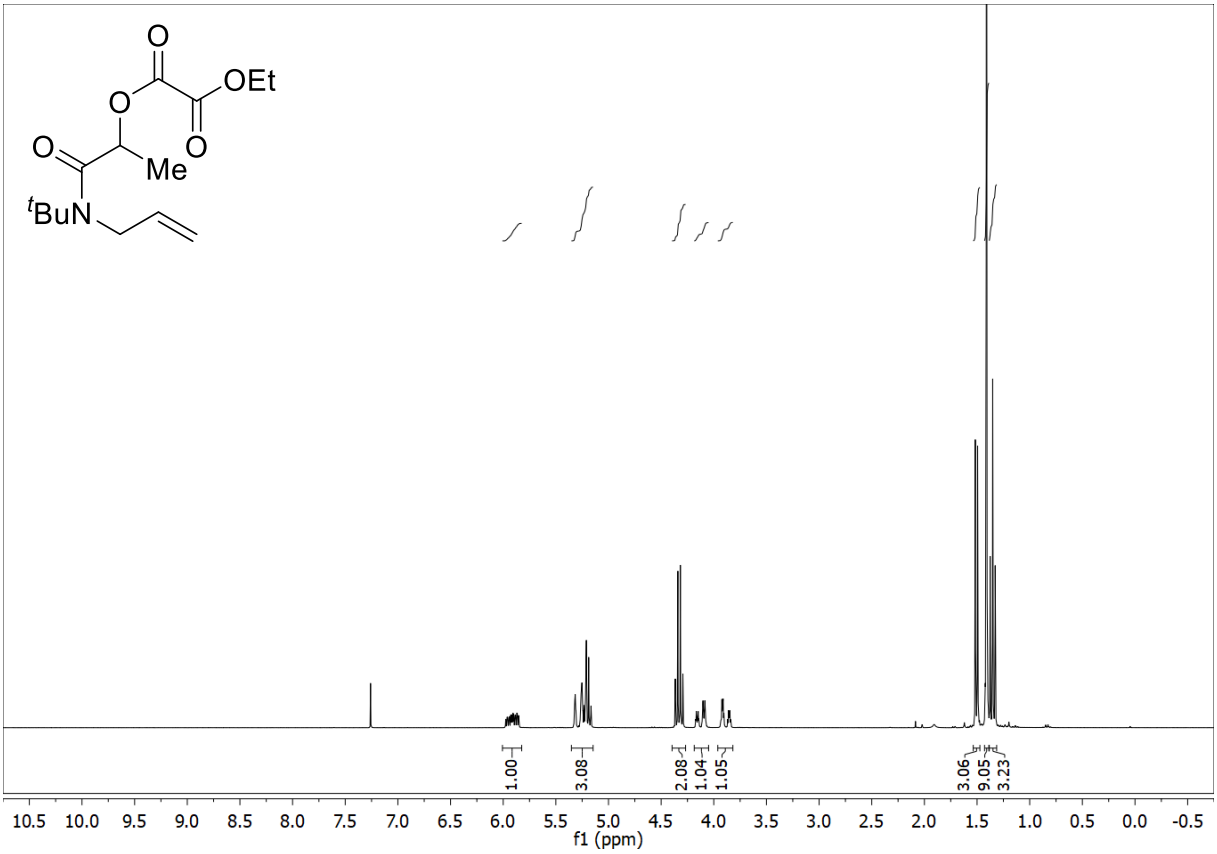
N-allyl-*N*-(*tert*-butyl)-2-hydroxypropanamide (139)

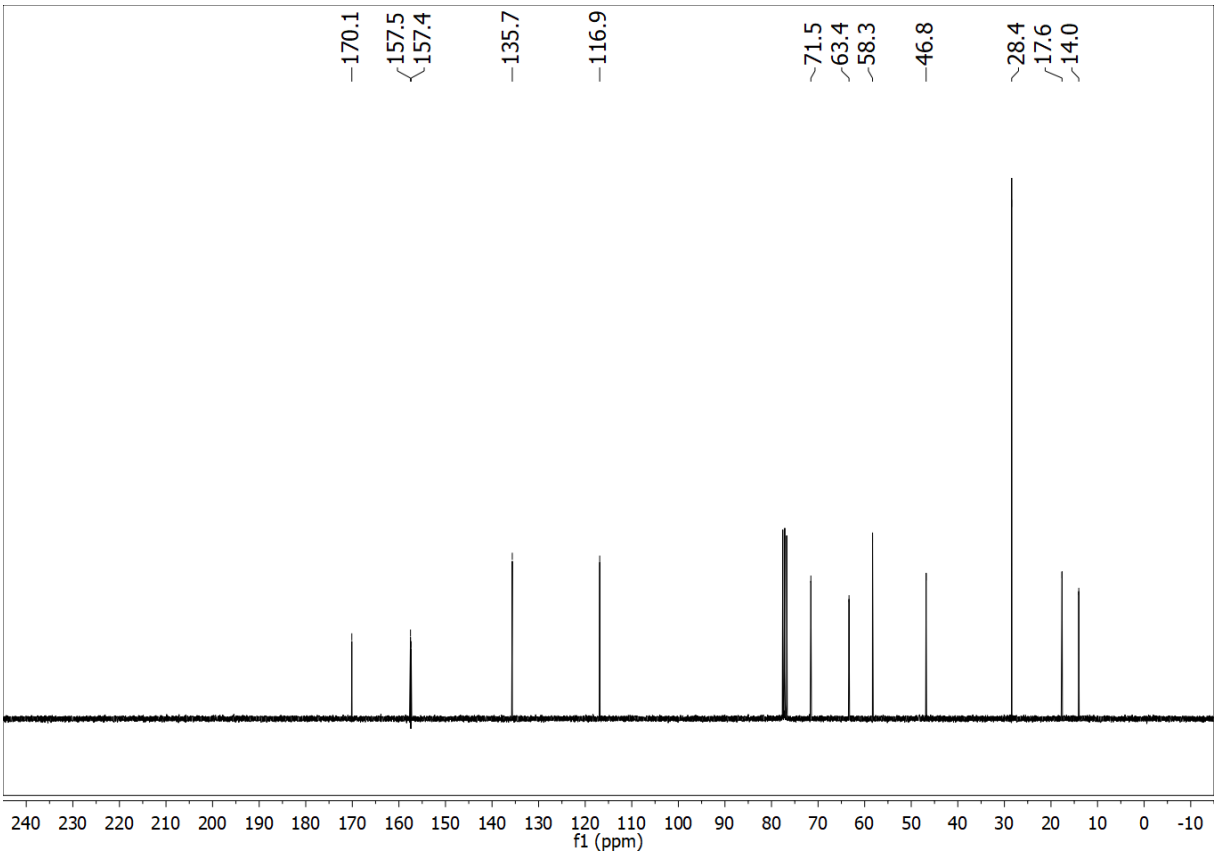




NMR-Solvent: $CDCl_3$

1-(Allyl(*tert*-butyl)amino)-1-oxopropan-2-yl ethyl oxalate (140)

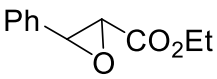




NMR-Solvent: $CDCl_3$

2.4. HPLC Analysis

Determination of enantiomeric excess by chiral HPLC analysis

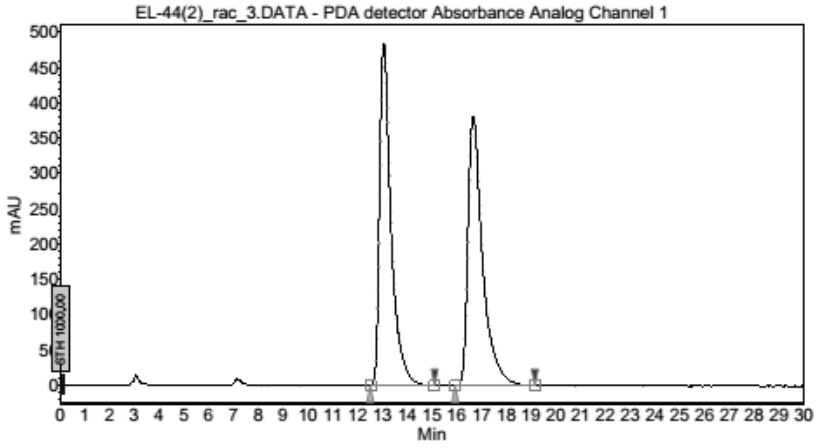


36a
racemic

Vail : 175
Method : Phex-Cel2_99-1
Run time : 30,00 min
Inj. vol. : 10,000 µl

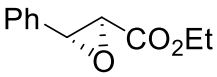
λ : 215 nm

Column : Phenomenex Lux Cellulose-2,
4.6 x 250 mm, 5 µm
Eluents : A = n-Heptane
B = i-Propanol
Flow : 1.0 ml/min



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	13,05	49,88	486,2	260,7	49,882
2	UNKNOWN	16,66	50,12	382,7	261,9	50,118
Total			100,00	869,0	522,6	100,000

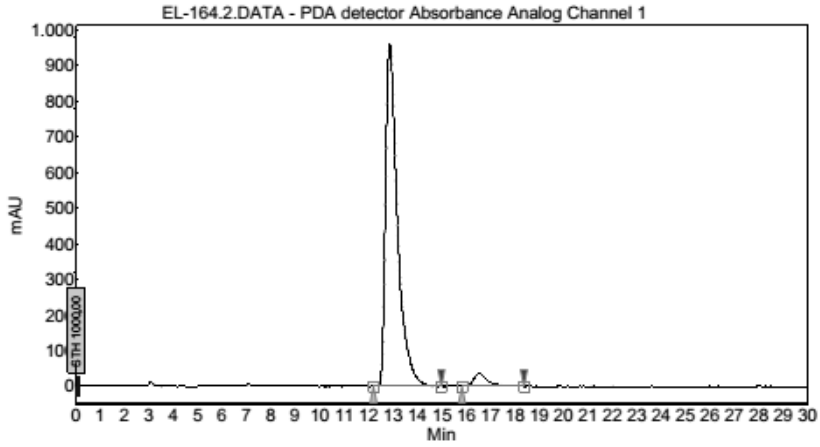


36a
92% ee

Vail : 176
Method : Phex-Cel2_99-1
Run time : 30,00 min
Inj. vol. : 10,000 µl

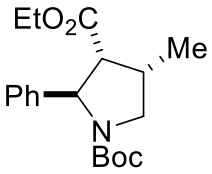
λ : 215 nm

Column : Phenomenex Lux Cellulose-2,
4.6 x 250 mm, 5 µm
Eluents : A = n-Heptane
B = i-Propanol
Flow : 1.0 ml/min



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	12,86	95,83	963,9	544,8	95,834
2	UNKNOWN	16,52	4,17	36,2	23,7	4,166
Total			100,00	1000,2	568,5	100,000

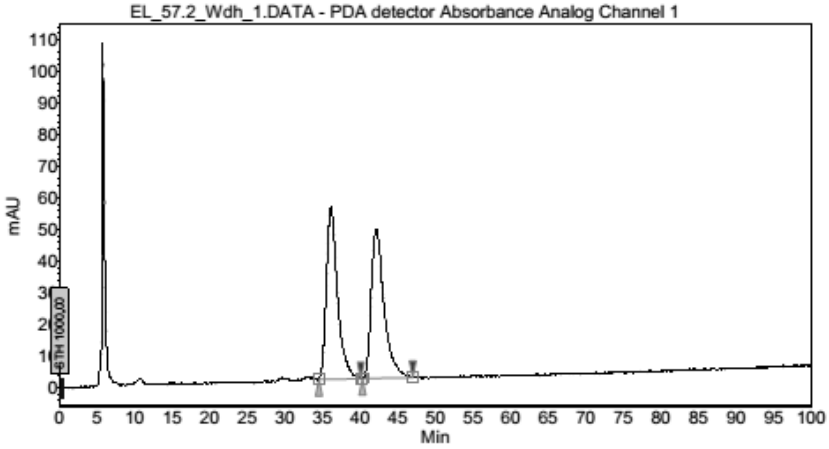


48a
racemic

Vail : 118
Method : Phex-Cel2_99-1_0.5
Run time : 100,00 min
Inj. vol. : 10,000 µl

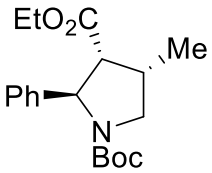
λ : 215 nm

Column : Phenomenex Lux Cellulose-2,
4.6 x 250 mm, 5 µm
Eluents : A = n-Heptane
B = i-Propanol
Flow : 0.5 ml/min



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	36,11	50,07	54,4	93,1	50,073
2	UNKNOWN	42,12	49,93	47,0	92,9	49,927
Total			100,00	101,4	186,0	100,000

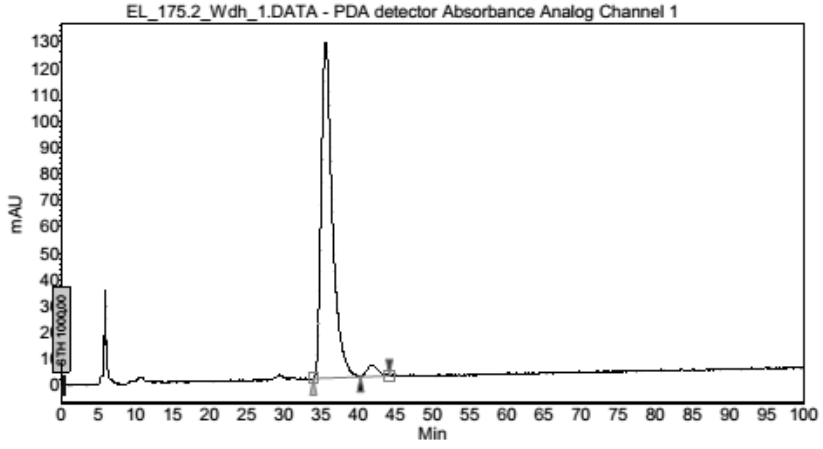


48a
93% ee

Vail : 117
Method : Phex-Cel2_99-1_0.5
Run time : 100,00 min
Inj. vol. : 10,000 µl

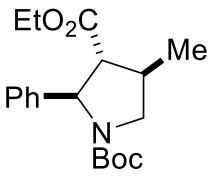
λ : 215 nm

Column : Phenomenex Lux Cellulose-2,
4.6 x 250 mm, 5 µm
Eluents : A = n-Heptane
B = i-Propanol
Flow : 0.5 ml/min



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	35,61	96,69	127,1	220,7	96,688
2	UNKNOWN	41,83	3,31	4,3	7,6	3,312
Total			100,00	131,4	228,2	100,000

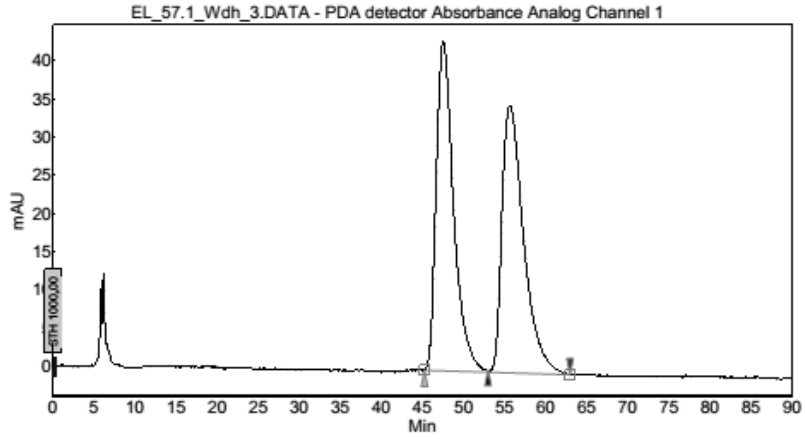


48a´
racemic

Vail : 116
Method : Phex-Cel2_99-1_0.5
Run time : 90,00 min
Inj. vol. : 10,000 µl

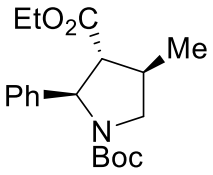
λ : 215 nm

Column : Phenomenex Lux Cellulose-2,
4.6 x 250 mm, 5 µm
Eluents : A = n-Heptane
B = i-Propanol
Flow : 0.5 ml/min



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	47,51	49,68	43,1	105,9	49,679
2	UNKNOWN	55,68	50,32	35,0	107,2	50,321
Total			100,00	78,1	213,1	100,000

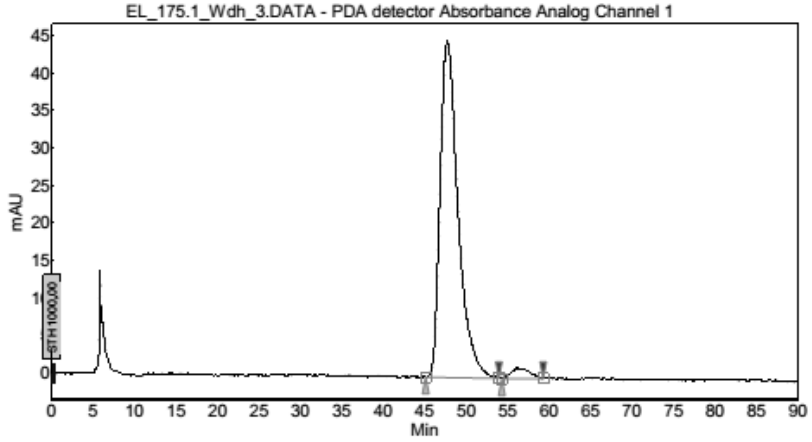


48a´
94%ee

Vail : 115
Method : Phex-Cel2_99-1_0.5
Run time : 90,00 min
Inj. vol. : 10,000 µl

λ : 215 nm

Column : Phenomenex Lux Cellulose-2,
4.6 x 250 mm, 5 µm
Eluents : A = n-Heptane
B = i-Propanol
Flow : 0.5 ml/min



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	47,71	97,04	44,9	112,7	97,043
2	UNKNOWN	56,38	2,96	1,4	3,4	2,957
Total			100,00	46,3	116,1	100,000

3. Chapter C: Copper Mediated Photochemical Iodoperfluoroalkylation

3.1. Synthesis of Literature Known Compounds and Reagents

The following compounds were synthesized according to the reported literature procedures. The spectral data were in agreement with the data reported: *tert*-butyl allylcarbamate[17], (allyloxy)benzene[18], *tert*-butyl phenyl(prop-2-yn-1-yl)carbamate[19], 2-(allyloxy)phenol (**21**)[20], methyl 2-allylbenzoate (**23**)[21], methyl 2-(allyloxy)benzoate (**26**)[14], diethyl 2,2-diallylmalonate (**33**)[22], (1-cyclopropylvinyl)benzene (**36**)[23].

For the synthesis of (2-(allyloxy)phenyl)methanol (**27**) see Chapter B: Synthesis of Heterocycles via Visible Light Mediated Deoxygenation Reaction.

3.2. Quantum Yield Determination

The quantum yield **Φ** of the visible light driven perfluorination of styrene (**12a**) with $C_8F_{17}I$ (**6**) was determined using a method developed by E. Riedle et al.[24] For irradiation, a green LED (500 mA operating current, λ_{max} = 528 nm, OSRAM LTCP7P-KXKZ) was used. The radiant power was measured with a commercial power meter (PowerMax USB - PS19Q Power Sensor from Coherent) using computer-aided read out with PowerMax software.

A flame dried pressure tube was charged with $C_8F_{17}I$ (**6**) (2120 µL, 8.0 mmol, 2.0 equiv) and $[Cu(dap)_2]Cl$ (**45**) (35.2 mg, 40.0 µmol, 1.0 mol%) or $[Cu(dap)Cl_2]$ (**47**) (21.0 mg, 40.0 µmol, 1.0 mol%) under nitrogen atmosphere. Anhydrous MeCN (4.0 mL) was added and the reaction mixture was degassed by three freeze-pump-thaw cycles. Styrene (**12a**) (416 mg, 4.0 mmol, 1.0 equiv) was added under a slight nitrogen overpressure. A flame dried fluorescence cuvette equipped with a stirring bar and a septum was flushed with nitrogen. Immediately prior to the quantum yield measurement, 2.0 mL of the reaction solution (corresponding to 2.0 mmol of styrene (**12a**)) was transferred to the measuring cuvette under a nitrogen atmosphere. In order to minimize ambient light, the measurement was accomplished in a dark room. The radiant power of light transmitted by the cuvette with a blank solution (P_{ref}) was measured. The cuvette with the blank solution was exchanged by the cuvette containing the reaction mixture and the transmitted radiant power (P_{sample}) was determined. The transmitted radiant power was monitored during the whole irradiation and remained constant. The sample was irradiated for the indicated time (*cf*. Table 1) and the yield was determined by ^{1}H NMR analysis using diphenoxymethane as internal standard.

The quantum yield **Φ** was calculated as follows:

$$\Phi = \frac{N_{prod}}{N_{ph,abs}} = \frac{n_{prod} * N_A * h * c}{P_{abs} * \Delta t * \lambda} = \frac{n_{prod} * N_A * h * c}{\left(P_{ref} - P_{sample}\right) * f * \Delta t * \lambda}$$

Here, Φ is quantum yield, N_{prod} is the number of molecules created, $N_{ph,\ abs}$ is the number of photons absorbed, N_A is Avogadro´s constant in mol^{-1}, n_{prod} is the molar amount of product molecules created in mol, P_{abs} is the radiant power absorbed in Watt, Δt is the irradiation time in seconds, h is Planck´s constant in Js, c is the speed of light in ms^{-1}, λ is the wavelength of the irradiation source in meters, P_{ref} is the radiant power transmitted by a blank cuvette in Watt, P_{sample} is the radiant power transmitted by the cuvette with the reaction mixture in Watt and f

is a correction factor. The correction factor ***f*** depends on the reflection coefficient ***R*** of the air-glass-interface. Neglecting second order effects, ***f*** can be calculated from:

$$f = \frac{1 + R * \frac{P_{sample}}{P_{ref}}}{1 - R}$$

For a fused silica cuvette and λ = 528 nm, R = 0.0357.

$$P_{abs} = \left(P_{ref} - P_{sample}\right) * f$$

Calculation using the data of entry 1 (Table 1):

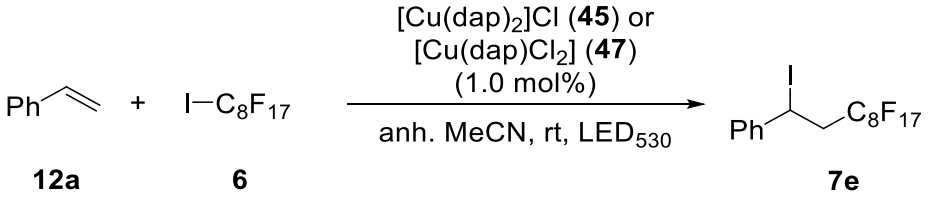
$$f = \frac{1 + R * \frac{P_{sample}}{P_{ref}}}{1 - R} = \frac{1 + 0.0357 * \frac{13.2mW}{25.5mW}}{1 - 0.0357} = 1.056$$

$$\Phi = \frac{n_{prod} * N_A * h * c}{\left(P_{ref} - P_{sample}\right) * f * \Delta t * \lambda} =$$

$$= \frac{0.80 * 10^{-3}mol * 6.022 * 10^{23}mol^{-1} * 6.626 * 10^{-34} * 2.998 * 10^{8}ms^{-1}}{(25.5 - 13.2) * 10^{-3}Js^{-1} * 1.056 * 28800s * 528 * 10^{-9}m} = 0.484$$

$$\cong 48\%$$

Table 1. Results of quantum yield measurement.



12a **6** **7e**

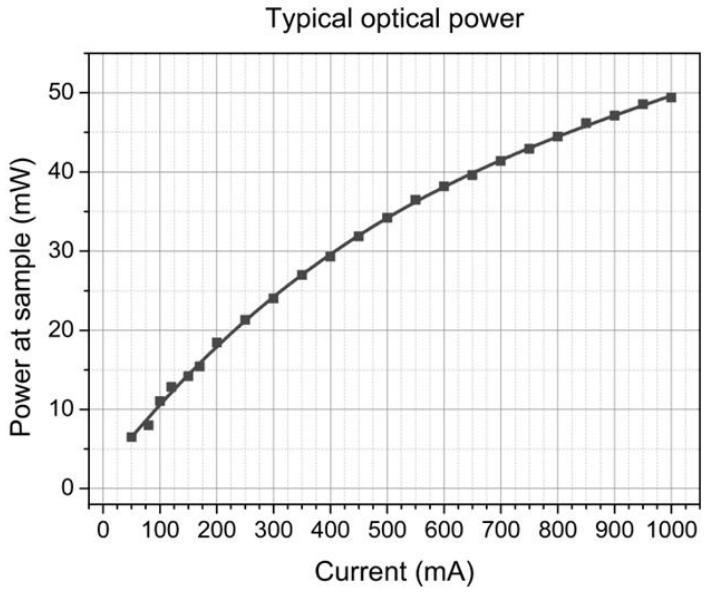
Entry	Catalyst	Δt / h	P_{ref} / mW	P_{sample} / mW	P_{abs} / mW	NMR Yield	Φ
1	[Cu(dap)$_2$]Cl (**45**)	8	25.5	13.2	13.0	40%	48%
2	[Cu(dap)Cl$_2$] (**47**)	8	25.8	16.1	10.3	34%	52%

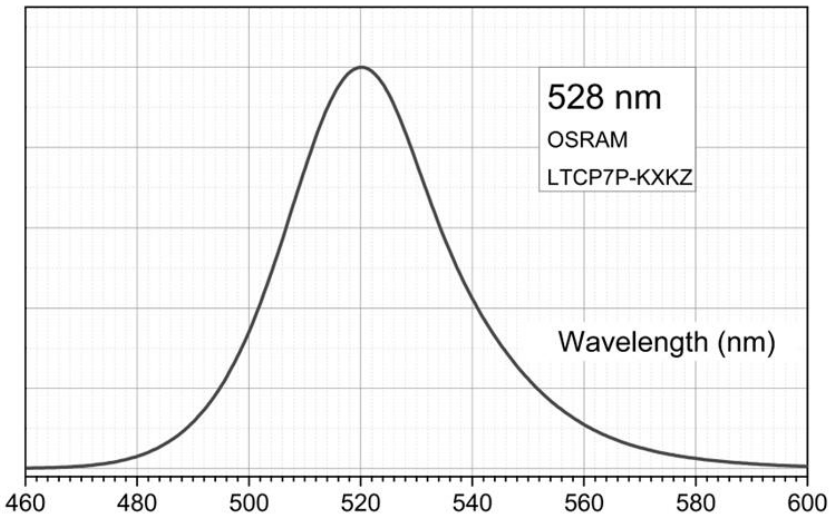
Reaction conditions: styrene (**12a**) (2.0 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (4.0 mmol, 2.0 equiv), [Cu(dap)$_2$]Cl or [Cu(dap)Cl$_2$] (1.0 mol%), degassed anh. MeCN (2.0 mL), irradiation with green LED (530 nm), stirred reaction mixture. The NMR yields were determined by ^{1}H NMR using diphenoxymethane as internal standard.

Data sheet for LED

Quantum Yield Determination Setup
ag-riedle

Serial No.:	409		
Manufacturer:	OSRAM	Model:	LTCP7P-KXKZ
Date:	25.11.2015	Tested by:	M. Götz
Power @ 500 mA:	34 mW		



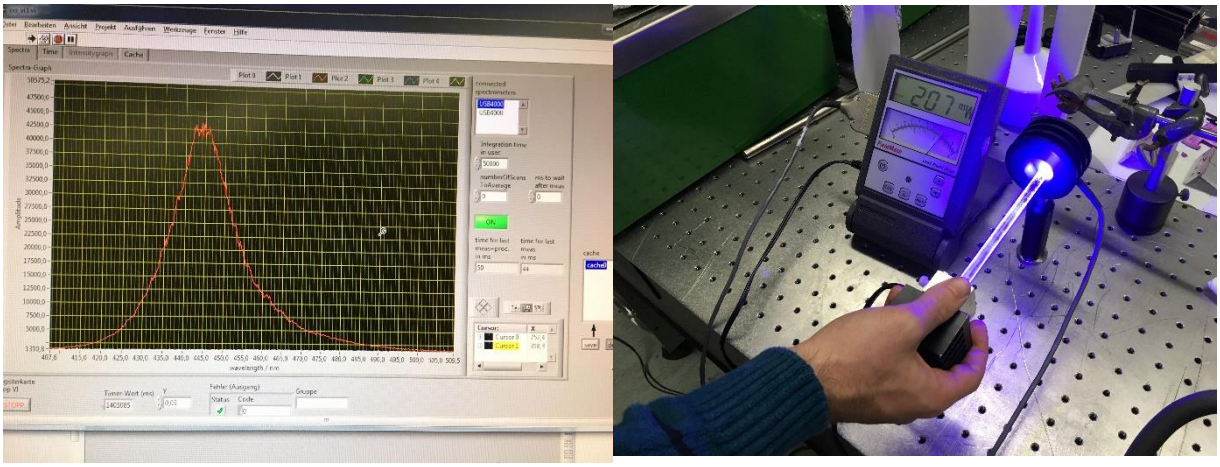


ag-Riedle LS für BioMolekulare Optik, Uni München 11/15

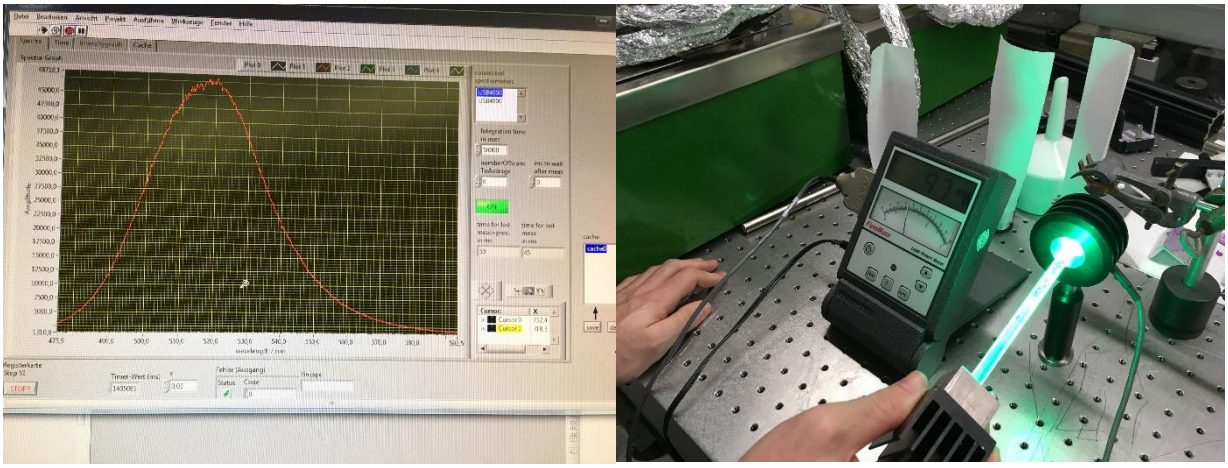
3.3. LED Power Measurement

The light transmitted power of the LEDs used for ATRA reaction was determined using the COHERENT FieldMate Laser Power Meter. The combined apparatus of the LED with the glas stick was measured.

Blue LED wavelength emission: ca. 445 nm. Blue LED with glas stick: 207 mW.

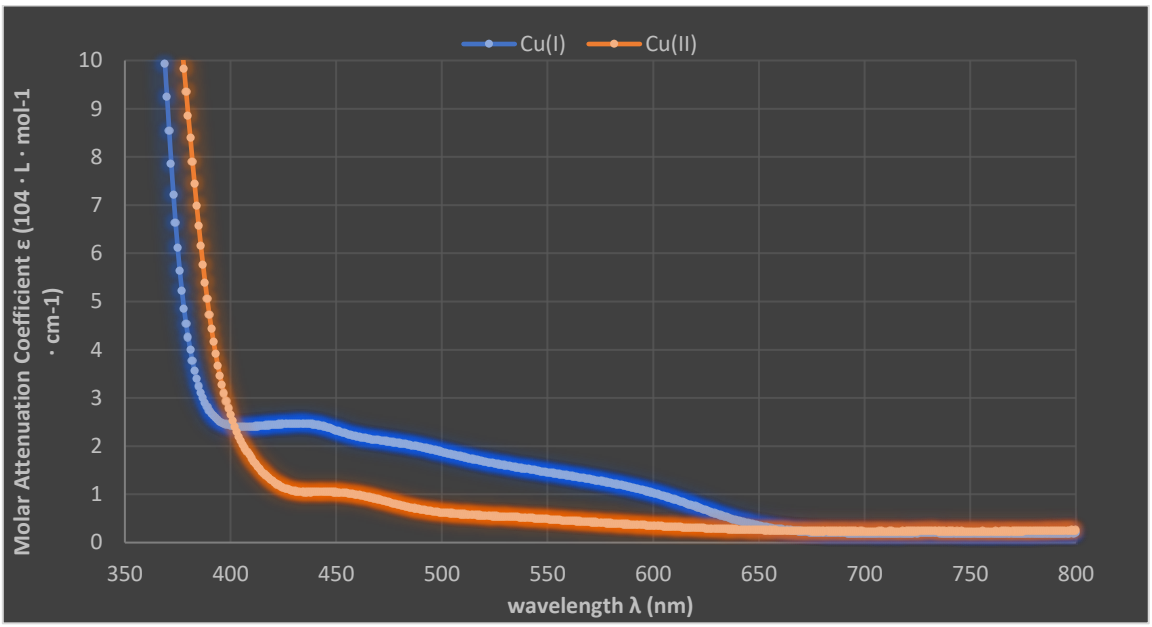


Green LED wavelength emission: ca. 520 nm. Green LED with glas stick: 97 mW.



3.4. UV-Spectra of $[Cu(dap)_2]Cl$ (45) and $[Cu(dap)Cl_2]$ (47)

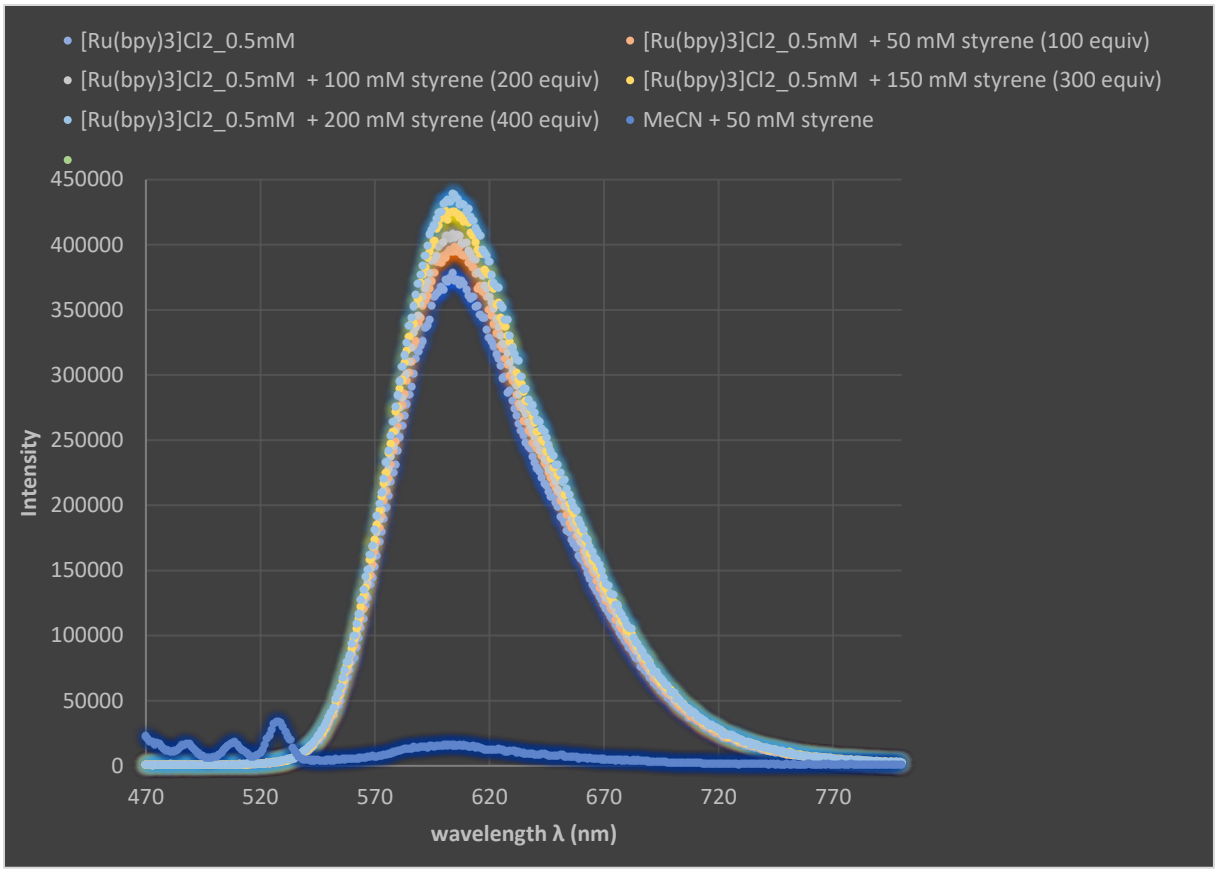
The UV-spectra of the Cu-catalysts $[Cu(dap)_2]Cl$ (**45**) (Cu(I)) and $[Cu(dap)Cl_2]$ (**47**) (Cu(II)) (each 0.02 mM in anh. MeCN) were measured with Agilent Technologies Cary Series 100 UV-Vis-Spectrometer.

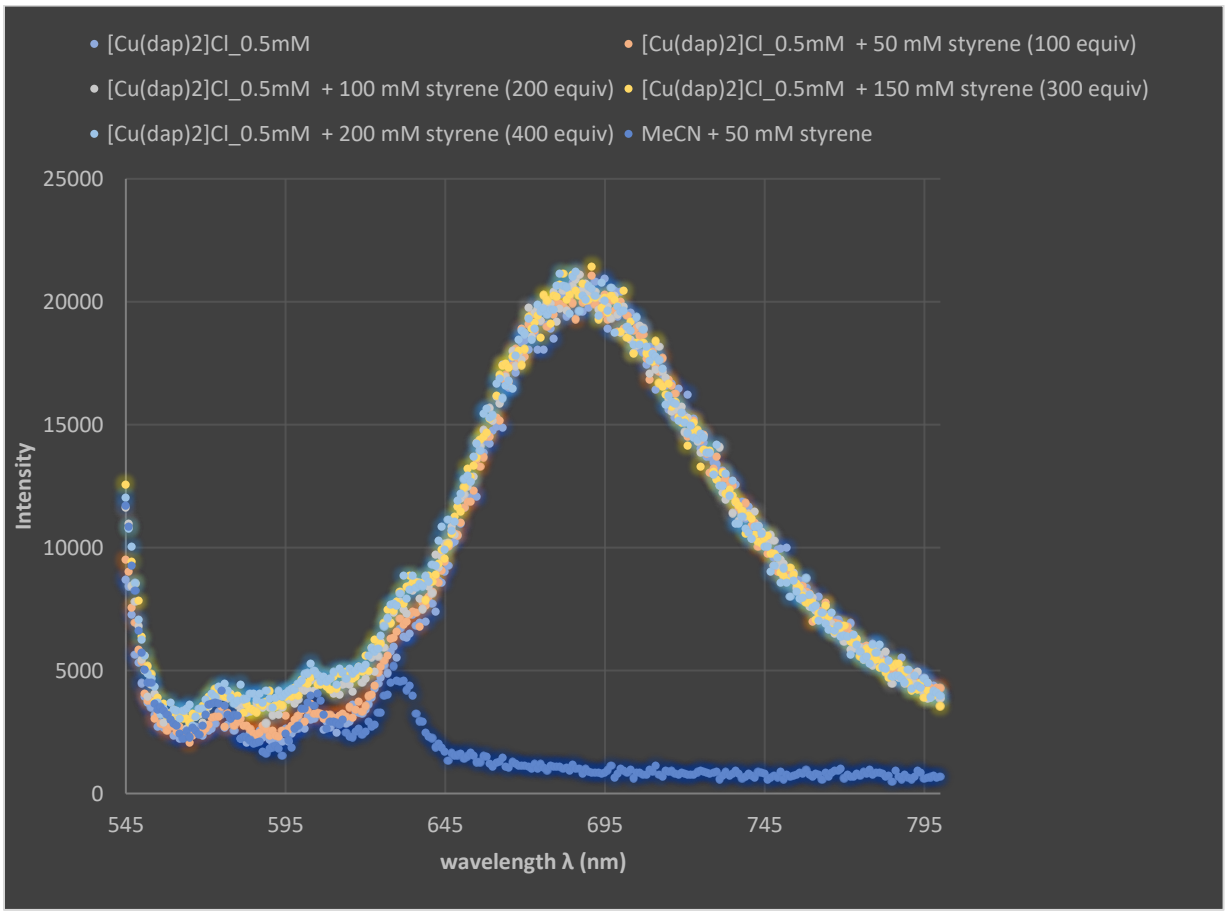


3.5. Fluorescence Measurement of $[Cu(dap)_2]Cl$ (45) and $[Ru(bpy)_3]Cl_2$

For the following measurements a Horiba Scientific FluoroMax®-4 & FluoroMax®-4P with USB was used.

In a cuvette with septum for fluorescent measurements 2 mL of dry, degassed MeCN was used with respective photocatalyst $[Cu(dap)_2]Cl$ (**45**) (1 µmol, 0.5 mM) or $[Ru(bpy)_3]Cl_2$ (1 µmol, 0.5 mM) and respective amount of styrene (see spectra). The solutions with $[Cu(dap)_2]Cl$ were excited at a wavelength of 530 nm, the solutions with $[Ru(bpy)_3]Cl_2$ were excited at a wavelength of 455 nm.

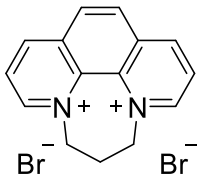

[Ru(bpy)3]Cl2_0.5mM
[Ru(bpy)3]Cl2_0.5mM + 50 mM styrene (100 equiv)
[Ru(bpy)3]Cl2_0.5mM + 100 mM styrene (200 equiv)
[Ru(bpy)3]Cl2_0.5mM + 150 mM styrene (300 equiv)
[Ru(bpy)3]Cl2_0.5mM + 200 mM styrene (400 equiv)
MeCN + 50 mM styrene
Intensity
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
470
520
570
620
670
720
770
wavelength λ (nm)


[Cu(dap)2]Cl_0.5mM
[Cu(dap)2]Cl_0.5mM + 50 mM styrene (100 equiv)
[Cu(dap)2]Cl_0.5mM + 100 mM styrene (200 equiv)
[Cu(dap)2]Cl_0.5mM + 150 mM styrene (300 equiv)
[Cu(dap)2]Cl_0.5mM + 200 mM styrene (400 equiv)
MeCN + 50 mM styrene
Intensity
25000
20000
15000
10000
5000
0
545
595
645
695
745
795
wavelength λ (nm)

3.6. Compound Characterization

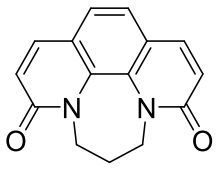
Synthesis of Cu-catalysts [Cu(dap)$_2$]Cl (45) and [Cu(dap)Cl$_2$] (47)

6,7-Dihydro-5*H*-[1,4]diazepino[1,2,3,4-*lmn*][1,10]phenanthroline-4,8-diium bromide (45S1)



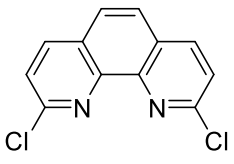
A three-neck flask equipped with a magnetic stirring bar, dropping funnel and a reflux condenser was charged with 1,10-phenanthroline (10.6 g, 58.8 mmol, 1.0 equiv) and dissolved in nitrobenzene (80 mL). Afterwards, 1,3-dibromopropane (31 mL, 306 mmol, 5.2 equiv) was dropwise added and the mixture was stirred at 130 °C for 5 h. During the reaction, the product precipitated from the reaction mixture. Then, the mixture was allowed to cool to room temperature and the precipitate was collected by filtration, washed with hexanes and dried over $CaCl_2$ in a desiccator overnight to yield the product **45S1** as a yellowish solid (22.5 g, 57.6 mmol, 98%). ^{1}H NMR (400 MHz, D_2O) δ 9.71 (dd, *J* = 5.8, 1.3 Hz, 2H), 9.49 (dd, *J* = 8.5, 1.3 Hz, 2H), 8.63 (s, 2H), 8.59 (dd, *J* = 8.4, 5.8 Hz, 2H), 5.19 (t, *J* = 7.0 Hz, 4H), 3.47 (p, *J* = 7.0 Hz, 2H). ^{13}C NMR (101 MHz, D_2O) δ 150.9, 147.4, 134.2, 133.5, 130.3, 127.4, 60.5, 31.0.

6,7-Dihydro-5*H*-[1,4]diazepino[1,2,3,4-*lmn*][1,10]phenanthroline-3,9-dione (45S2)



A mixture of compound **45S1** (30.0 g, 78.5 mmol, 1.0 equiv) and KO^{t}Bu (37.0 g, 329.7 mmol, 4.2 equiv) in *tert*-butyl alcohol (400 mL) was stirred at 40 °C overnight in an open flask. Afterwards, oxygen was bubbled once to the suspension via a balloon. Then, water (100 mL) and $CHCl_3$ (100 mL) was added and extracted with $CHCl_3$ (5x 50 mL). The combined organic layers were washed with brine (2x 100 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to yield the pure product **45S2** as a brown solid (18.8 g, 74.6 mmol, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 9.5 Hz, 2H), 7.36 (s, 2H), 6.81 (d, *J* = 9.5 Hz, 2H), 4.31 (s, 4H), 2.45 (p, *J* = 6.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 139.0, 132.2, 123.2, 123.0, 122.9, 45.9, 25.9.

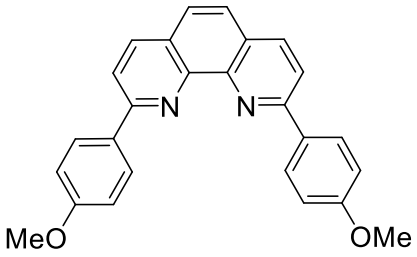
2,9-Dichloro-1,10-phenanthroline (45S3)



A flame dried three-neck flask equipped with a magnetic stirring bar and a reflux condenser was charged with compound **45S2** (18.8 g, 74.5 mmol, 1.0 equiv.) and PCl_5 (31.0 g, 149 mmol, 2.0 equiv) under nitrogen atmosphere. After addition of $POCl_3$ (300 mL) the mixture was stirred overnight at 145 °C. The excess of $POCl_3$ was removed by distillation. The resulting brown residue was cooled to 0 °C and quenched carefully by the addition of ice followed by aqueous NH_3 (1 M) until neutral pH. Then, the dark solution was extracted with CH_2Cl_2 (4x 75 mL). The

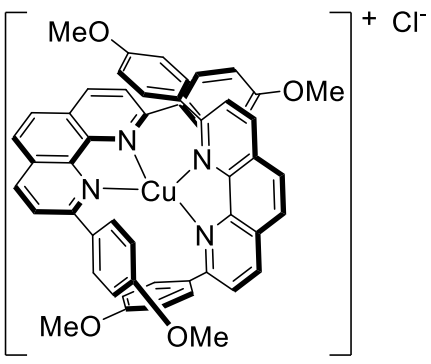
combined organic layers were washed with brine (1x 100 mL), dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2) to afford **45S3** as a yellowish solid (13.4 g, 53.6 mmol, 72%). R_f (CH_2Cl_2) = 0.53. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.4 Hz, 2H), 7.81 (s, 2H), 7.63 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.0, 145.0, 138.9, 127.8, 126.4, 125.0.

2,9-Bis(4-methoxyphenyl)-1,10-phenanthroline (45S4)



A flame dried three-neck round bottom flask equipped with a reflux condenser was charged with 2,9-dichloro-1,10-phenanthroline (**45S3**) (2.5 g, 10.0 mmol, 1.0 equiv), (4-methoxyphenyl)boronic acid (3.3 g, 22.0 mmol, 2.2 equiv), PPh_3 (131 mg, 500 µmol, 5.0 mol%) and Pd_2dba_3 (100 mg, 109 µmol, 1.2 mol%) in freshly distilled glyme (80 mL) under nitrogen atmosphere. The reaction mixture was degassed by three freeze-pump-thaw cycles. Afterwards, a solution of K_2CO_3 (3.0 g, 22.0 mmol, 2.2 equiv) in H_2O (8 mL) was added and the mixture was degassed by one freeze-pump-thaw cycle. The resulting solution was stirred for 48 h at 100 °C. Then, the mixture was allowed to cool to room temperature and extracted with CH_2Cl_2 (4x 50 mL). The combined organic layers were washed with brine (4x 50 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2 followed by CH_2Cl_2-MeOH, 95:5) followed by recrystallization from hot toluene to afford the product **45S4** as a yellowish solid (3.3 g, 8.4 mmol, 84%). R_f (CH_2Cl_2 / MeOH, 9:1) = 0.82. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.9 Hz, 4H), 8.26 (d, *J* = 8.5 Hz, 2H), 8.09 (d, *J* = 8.4 Hz, 2H), 7.74 (s, 2H), 7.12 (d, *J* = 8.9 Hz, 4H), 3.93 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 156.3, 145.5, 137.2, 131.9, 129.1, 127.6, 125.7, 119.6, 114.3, 55.5.

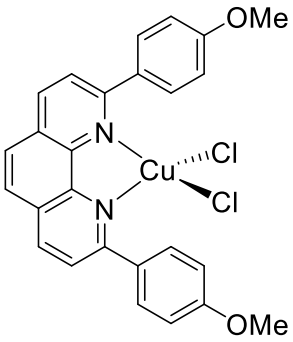
[Cu(dap)$_2$]Cl (45)



In a 100 mL round bottom flask 2,9-Bis-(4-methoxy-phenyl)-[1,10]phenanthroline (**45S4**) (1.0 g, 2.6 mmol, 2.0 equiv.) was dissolved in chloroform (30 mL) and stirred at room temperature for 20 min. CuCl (126 mg, 1.3 mmol, 1.0 equiv.) was added slowly and the mixture was stirred for 20 min. The violet solution was stirred at 60 °C for 20 min, the solvent was removed under reduced pressure and the product **45** was isolated as violet-black solid (1.1 g, 1.3 mmol, > 99 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.0 Hz, 4H), 8.03 (s, 4H), 7.86 (d,

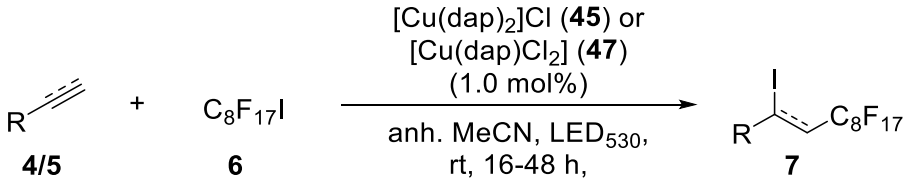
J = 7.8 Hz, 4H), 7.40 (d, *J* = 8.1 Hz, 8H), 6.05 (d, *J* = 8.1 Hz, 8H), 3.48 (s, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 156.3, 143.5, 137.2, 131.1, 129.2, 127.9, 126.2, 124.5, 112.6, 55.4.

[Cu(dap)Cl$_2$] (47)



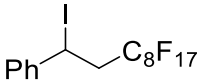
In a round bottom flask, $CuCl_2$ (8.8 mg, 65 µmol, 1.0 equiv) was suspended in chloroform (0.7 mL) and sonicated at room temperature for 3 min. To the stirred solution, 2,9-bis(para-anisyl)-1,10-phenanthroline (dap) (**45S4**) (25.3 mg, 65 µmol, 1.0 equiv) and 0.3 mL chloroform were added. The mixture was sonicated at room temperature for 3 min, and stirred for 60 min. After evaporation of the solvent the resulting solid was recrystallized from chloroform and diethyl ether. The crystallization was completed in a freezer. This procedure afforded compound **47** as brownish green crystals (23.0 mg, 44 µmol, 68%).

General Procedure for Iodoperfluoroalkylation of Alkenes/Alkynes with [Cu(dap)$_2$]Cl (45) or [Cu(dap)Cl$_2$] (47) (GP-1)



A flame dried Schlenk tube equipped with a magnetic stir bar was charged with alkene/alkyne **4**/**5** (0.5 mmol, 1.0 equiv), perfluorooctyl iodide **6** (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)$_2$]Cl (**45**) / [Cu(dap)Cl$_2$] (**47**) (5.0 µmol, 1.0 mol%) in anh. MeCN (1.0 mL). The reaction mixture was degassed by three freeze-pump-thaw cycles, placed under N_2-atmosphere and irradiated with a green LED (λ_{max} = 530 nm) at room temperature. After completion of the reaction (judged by TLC), the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel to yield pure product **7**.

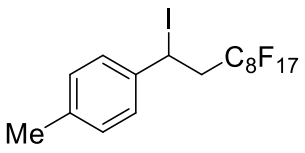
(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododecyl)benzene (7e)



Cu(II)-catalysis: Following general procedure GP-1, using styrene (**12a**) (57 µL, 52 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl$_2$] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 288 mg (443 µmol, 89%) of **7e** as a white solid after flash column purification (hexanes). R_f (hexanes) = 0.51. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.39 (m, 2H), 7.39 – 7.21 (m, 3H), 5.45 (dd, *J* = 9.6, 5.1 Hz, 1H), 3.40 – 3.06 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.36 (t, *J* = 10.1 Hz, 3F), -112.45 – -115.70 (m, 2F), -121.97 – -122.76 (m, 6F), -123.27 (s, 2F), -124.05

(s, 2F), -126.66 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.9, 129.1, 128.7, 126.9, 122.9 – 107.0 (m), 42.7 (t, *J* = 20.6 Hz), 16.7.

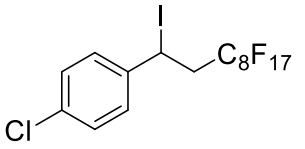
1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododecyl)-4-methylbenzene (13a)



Cu(I)-catalysis: Following general procedure GP-1, using 1-methyl-4-vinylbenzene (66 µL, 59 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)_2]Cl$ (**45**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 291 mg (438 µmol, 88%, DCM as solvent) of **13a** as a white solid after flash column purification (hexanes).

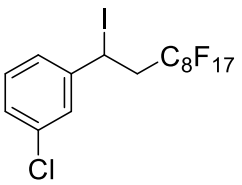
Cu(II)-catalysis: Following general procedure GP-1, using 1-methyl-4-vinylbenzene (66 µL, 59 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)Cl_2]$ (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 281 mg (423 µmol, 85%, DCM as solvent/ 145 mg, 218 µmol, 44%, MeCN as solvent) of **13a** as a white solid after flash column purification (hexanes). R_f (hexanes) = 0.59. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 5.49 (dd, *J* = 9.7, 5.2 Hz, 1H), 3.46 – 3.06 (m, 2H), 2.34 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.55 (t, *J* = 10.0 Hz, 3F), -112.92 (dt, *J* = 271.1, 14.6 Hz, 1F), -114.68 – -116.02 (m, 1F), -122.00 – -122.91 (m, 6F), -123.42 (s, 2F), -124.17 (s, 2F), -126.68 – -127.04 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1, 138.8, 129.7, 129.6 – 127.3 (m), 126.7, 126.0 – 104.0 (m), 42.7 (t, *J* = 20.5 Hz), 21.3, 17.2.

1-Chloro-4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-iododecyl)benzene (13b)



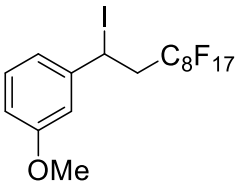
Cu(II)-catalysis: Following general procedure GP-1, using 1-chloro-4-vinylbenzene (60 µL, 69 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)Cl_2]$ (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 298 mg (435 µmol, 87%) of **13b** as a white solid after flash column purification (hexanes). R_f (hexanes) = 0.54. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 2H), 7.33 – 7.27 (m, 2H), 5.41 (dd, *J* = 10.0, 5.1 Hz, 1H), 3.39 – 3.02 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.30 (t, *J* = 9.9 Hz, 3F), -111.84 – -113.11 (m, 1F), -114.56 – -115.84 (m, 1F), -121.92 – -122.67 (m, 6F), -123.26 (s, 2F), -123.84 – -124.15 (m, 2F), -126.51 – -126.80 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.4, 134.4, 129.3, 130.3 – 127.1 (m), 128.2, 121.0 – 107.4 (m), 42.7 (t, *J* = 20.6 Hz), 15.3.

1-Chloro-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-iododecyl)benzene (13c)



Cu(II)-catalysis: Following general procedure GP-1, using 1-chloro-3-vinylbenzene (65 µL, 69 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 295 mg (431 µmol, 86%) of **13c** as a white solid after flash column purification (hexanes). R_f (hexanes) = 0.52. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (q, *J* = 1.5 Hz, 1H), 7.35 – 7.22 (m, 3H), 5.36 (dd, *J* = 9.6, 5.3 Hz, 1H), 3.41 – 3.00 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.36 (t, *J* = 9.9 Hz, 3F), -112.08 – -113.36 (m, 1F), -115.21 (dt, *J* = 271.2, 13.7 Hz, 1F), -121.85 – -122.77 (m, 6F), -123.30 (s, 2F), -123.83 – -124.20 (m, 2F), -126.54 – -126.92 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7, 134.7, 130.3, 128.9, 127.1, 125.1, 42.5 (t, *J* = 20.6 Hz), 14.7.

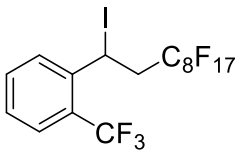
1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-iododecyl)-3-methoxybenzene (13d)



Cu(I)-catalysis: Following general procedure GP-1, using 1-methoxy-3-vinylbenzene (138 µL, 134 mg, 1.0 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (530 µL, 1.09 g, 2.0 mmol, 2.0 equiv) and [Cu(dap)$_2$]Cl (**45**) (8.8 mg, 10.0 µmol, 1.0 mol%) gave 290 mg (426 µmol, 43%, MeCN as solvent/ 283 mg, 416 µmol, 42%, DCM as solvent) of **13d** as a colorless oil after 72 h and flash column purification (hexanes).

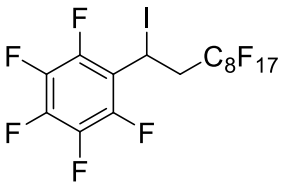
Cu(II)-catalysis: Following general procedure GP-1, using 1-methoxy-3-vinylbenzene (69 µL, 67 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 139 mg (204 µmol, 41% (66% brsm), MeCN as solvent/ 150 mg, 221 µmol, 42% (66% brsm), DCM as solvent) of **13d** as a colorless oil after 72 h and flash column purification (hexanes). R_f (hexanes / EtOAc, 4:1) = 0.78. Staining: $KMnO_4$, Vanillin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (t, *J* = 8.0 Hz, 1H), 7.03 (ddd, *J* = 7.7, 1.8, 0.9 Hz, 1H), 6.97 (t, *J* = 2.1 Hz, 1H), 6.83 (ddd, *J* = 8.3, 2.5, 0.9 Hz, 1H), 5.42 (dd, *J* = 9.5, 5.3 Hz, 1H), 3.84 (s, 3H), 3.40 – 3.07 (m, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.37 (t, *J* = 10.0 Hz, 3F), -113.16 (dt, *J* = 271.0, 14.5 Hz, 1F), -114.57 – -115.69 (m, 1F), -121.99 – -122.23 (m, 2F), -122.30 – -122.68 (m, 4F), -123.29 (s, 2F), -124.06 (s, 2F), -126.48 – -126.89 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 144.3, 130.1, 119.2, 122.4 – 107.4 (m), 114.0, 112.9, 55.4, 42.6 (t, *J* = 20.6 Hz), 16.6 – 16.2 (m). IR (neat): 3015, 2952, 2848, 1599, 1491, 1465, 1435, 1372, 1331, 1200, 1144, 1044, 954, 876, 779, 746, 716 cm^{-1}. LRMS (EI) *m/z* (%): 553.0 ([M-I]$^{+\bullet}$, 100), 134.1 (30), 554.1 (26), 183.1 (13), 534.1 (11), 135.1 (7), 139.1 (7). HRMS (EI) m/z calculated for $C_{17}H_{10}OF_{17}I$ ([M]$^{+\bullet}$) 679.9499, found 679.9497.

1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododecyl)-2-(trifluoromethyl) benzene (13e)



Cu(II)-catalysis: Following general procedure GP-1, using 1-(trifluoromethyl)-2-vinylbenzene (73 µL, 86 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 307 mg (428 µmol, 86%) of **13e** as a colourless oil after flash column purification (hexanes). R_f (hexanes) = 0.53. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.37 (ddt, *J* = 8.4, 7.6, 1.0 Hz, 1H), 5.83 (dd, *J* = 9.5, 5.2 Hz, 1H), 3.55 – 3.05 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -60.50 (s, 3F), -81.51 (t, *J* = 10.0 Hz, 3F), -114.5 – -114.9 (m, 2F), -122.1 – -122.4 (m, 2F), -122.4 – -122.8 (m, 4F), -123.40 (s, 2F), -124.0 – -124.4 (m, 2F), -126.6 – -127.0 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9 – 141.6 (m), 132.8, 130.2, 128.5, 127.7, 126.2 (q, *J* = 5.8 Hz), 126.0 – 125.2 (m), 121.2 – 105.5 (m), 42.7 (t, *J* = 20.6 Hz), 9.2 – 9.0 (m).

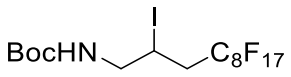
1,2,3,4,5-pentafluoro-6-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-iododecyl)benzene (13f)



Cu(I)-catalysis: Following general procedure GP-1, using 1,2,3,4,5-pentafluoro-6-vinylbenzene (138 µL, 194 mg, 1.0 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (530 µL, 1.09 g, 2.0 mmol, 2.0 equiv) and [Cu(dap)$_2$]Cl (**45**) (8.8 mg, 10.0 µmol, 1.0 mol%) gave 600 mg (811 µmol, 81%) of **13f** as a colorless oil after flash column purification (hexanes).

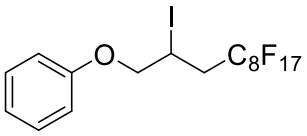
Cu(II)-catalysis: Following general procedure GP-1, using 1,2,3,4,5-pentafluoro-6-vinylbenzene (69 µL, 97 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 308 mg (416 µmol, 83%) of **13f** as a colorless oil after flash column purification (hexanes). R_f (hexanes) = 0.90. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.68 (dd, *J* = 11.4, 4.6 Hz, 1H), 3.57 – 3.37 (m, 1H), 3.18 – 2.99 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.54 (t, *J* = 10.0 Hz, 3F), -113.48 – -114.99 (m, 1F), -116.46 (dt, *J* = 271.4, 14.0 Hz, 1F), -122.07 – -122.90 (m, 6F), -123.42 (s, 2F), -124.15 (s, 2F), -126.64 – -127.04 (m, 2F), -139.81 (bs, 1F), -143.83 (bs, 1F), -153.50 (tt, *J* = 20.9, 2.7 Hz, 1F), -161.44 (td, *J* = 21.4, 7.9 Hz, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1 – 136.1 (m), 122.1 – 119.8 (m), 118.8 (t, *J* = 33.0 Hz), 117.7 (t, *J* = 32.3 Hz), 116.5 (td, *J* = 14.4, 4.3 Hz), 115.9 (t, *J* = 33.1 Hz), 115.3 – 106.9 (m), 40.6 (t, *J* = 20.6 Hz), -3.9. IR (neat): 1733, 1651, 1505, 1427, 1357, 1312, 1238, 1200, 1148, 1047, 992, 951, 883, 827, 723 cm^{-1}. LRMS (EI) *m/z* (%): 613.0 ([M-I]$^{+\bullet}$, 100), 199.0 (95), 243.0 (54), 181.0 (54), 197.0 (50), 194.0 (49), 195.0 (27), 69.0 (24), 614.0 (24), 200.0 (9), 28.0 (9), 119.0 (9), 131.0 (8), 244.0 (7), 205.0 (7). HRMS (EI) m/z calculated for $C_{16}H_3F_{22}$ ([M-I]$^+$) 612.9878, found 612.9874 .

tert-Butyl (4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl) carbamate (7b)



Cu(II)-catalysis: Following general procedure GP-1, using *tert*-butyl allylcarbamate[17] (79 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)Cl_2]$ (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 310 mg (441 µmol, 88%) of **7b** as a brown solid after flash column purification (hexanes). R_f (hexanes / EtOAc, 5:1) = 0.72. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.11 – 4.68 (rotamer present, m, 1H), 4.38 (p, *J* = 6.6 Hz, 1H), 3.69 – 3.36 (m, 2H), 2.98 – 2.66 (m, 2H), 1.45 (s, 9H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.28 (t, *J* = 9.9 Hz, 3F), -112.42 – -115.05 (m, 2F), -121.82 – -122.65 (m, 6F), -123.25 (s, 2F), -124.14 (s, 2F), -126.53 – -126.83 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7, 124.2 – 102.6 (m), 80.4, 49.1, 38.8 (t, *J* = 21.1 Hz), 28.4, 18.8.

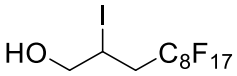
((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)oxy)benzene (15a)



Cu(I)-catalysis: Following general procedure GP-1, using (allyloxy)benzene[18] (67 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)_2]Cl$ (**45**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 248 mg (365 µmol, 73%) of **15a** as a colorless oil after flash column purification (hexanes/EtOAc 100:0 to 15:1).

Cu(II)-catalysis: Following general procedure GP-1, using (allyloxy)benzene[18] (67 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)Cl_2]$ (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 243 mg (357 µmol, 71%) of **15a** as a colorless oil after flash column purification (hexanes/EtOAc 100:0 to 15:1). R_f (hexanes) = 0.35. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 2H), 7.09 – 7.00 (m, 1H), 6.98 – 6.90 (m, 2H), 4.54 (qd, *J* = 6.7, 5.1 Hz, 1H), 4.31 (dd, *J* = 10.4, 4.9 Hz, 1H), 4.20 (dd, *J* = 10.4, 6.8 Hz, 1H), 3.36 – 3.07 (m, 1H), 2.98 – 2.66 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.53 (t, *J* = 10.0 Hz, 3F), -114.16 (dt, *J* = 41.6, 13.8 Hz, 2F), -122.04 – -122.33 (m, 2F), -122.34 – -122.75 (m, 4F), -123.08 – -123.65 (m, 2F), -123.88 – -124.35 (m, 2F), -126.61 – -127.10 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 129.8, 122.0, 115.1, 122.0 – 106.3 (m), 72.9, 37.9 (t, *J* = 21.1 Hz), 13.1 – 12.8 (m). IR (neat): 1599, 1498, 1465, 1368, 1331, 1200, 1148, 1077, 1047, 883, 820, 753, 705 cm^{-1}. LRMS (EI) *m/z* (%): 219.9 (100), 93.0 (68), 94.0 (67), 679.9 (65), 586.9 (57), 65.0 (34), 77.0 (24), 69.0 (18), 172.9 (16). HRMS (EI) m/z calculated for $C_{17}H_{10}OF_{17}I$ ($[M]^{+\bullet}$) 679.9499, found 679.9484.

4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecan-1-ol (7j)

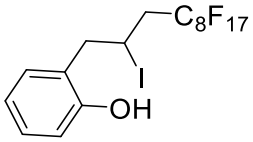


Cu(I)-catalysis: Following general procedure GP-1, using allyl alcohol (**43**) (68 µL, 58 mg, 1.0 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (530 µL, 1.1 g, 2.0 mmol, 2.0 equiv) and $[Cu(dap)_2]Cl$ (**45**) (8.8 mg, 10.0 µmol, 1.0 mol%) gave 54 mg (902 µmol, 90%) of **7j** as a white solid after flash column purification (hexanes/EtOAc = 7:1).

Cu(II)-catalysis: Following general procedure GP-1, using allyl alcohol (**43**) (34 µL, 29 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)Cl_2]$ (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 263 mg (435 µmol, 87%) of **7j** as a white solid after flash column purification (hexanes/EtOAc = 7:1).

AIBN reaction: A Schlenk tube equipped with a magnetic stir bar was charged with allyl alcohol (**43**) (137 µL, 116 mg, 2.0 mmol, 1.15 equiv), $C_8F_{17}I$ (**6**) (477 µL, 981 mg, 1.8 mmol, 1.0 equiv) and AIBN (28.6 mg, 173 µmol, 10 mol%) under N_2-atmosphere and stirred for 14 h at 80 °C. After completion of the reaction (judged by TLC), the volatile components were evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 7:1) to yield pure product **7j** as a white solid (813 mg, 1.35 mmol, 77%). NMR-Spectra were in accordance with those reported in literature. R_f (hexanes) = 0.45. Staining: $KMnO_4$ (UV inactive). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.44 (ddt, *J* = 7.3, 6.1, 4.9 Hz, 1H), 3.91 – 3.74 (m, 2H), 3.15 – 2.89 (m, 1H), 2.89 – 2.64 (m, 1H), 2.05 (s, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.35 (t, *J* = 10.0 Hz, 3F), -112.33 – -113.82 (m, 1F), -114.08 – -115.56 (m, 1F), -121.82 – -122.73 (m, 6F), -122.99 – -123.58 (m, 2F), -123.75 – -124.26 (m, 2F), -126.47 – -126.95 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.1 (d, *J* = 2.4 Hz), 37.6 (t, *J* = 21.0 Hz), 22.0.

2-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)phenol (15b)

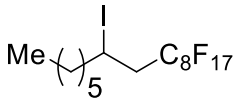


Cu(I)-catalysis: Following general procedure GP-1, using 2-allylphenol (**17**) (65 µL, 67 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)_2]Cl$ (**45**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 334 mg (491 µmol, 98%) of **15b** as a white solid after flash column purification (hexanes).

Cu(II)-catalysis: Following general procedure GP-1, using 2-allylphenol (**17**) (65 µL, 67 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)Cl_2]$ (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 330 mg (485 µmol, 97%) of **15b** as a white solid after flash column purification (hexanes). R_f (hexanes / EtOAc) = 0.45. Staining: Vanillin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 – 7.10 (m, 2H), 6.93 (td, *J* = 7.4, 1.1 Hz, 1H), 6.75 (dd, *J* = 8.0, 1.1 Hz, 1H), 4.84 (s, 1H), 4.71 (dq, *J* = 8.9, 6.4 Hz, 1H), 3.37 (dd, *J* = 14.3, 6.1 Hz, 1H), 3.22 (dd, *J* = 14.3, 8.9 Hz, 1H), 2.92 (dddd, *J* = 25.0, 12.0, 6.3, 3.2 Hz, 2H). ^{19}F NMR (282

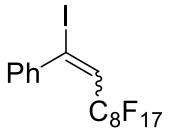
MHz, $CDCl_3$) δ -81.46 (t, *J* = 10.0 Hz, 3F), -112.39 – -115.29 (m, 2F), -121.93 – -122.77 (m, 6F), -123.36 (s, 2F), -124.22 (s, 2F), -126.62 – -127.00 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6, 131.7, 128.9, 125.8, 121.2, 115.7, 115.0 – 102.3 (m), 42.7 (d, *J* = 2.1 Hz), 41.1 (t, *J* = 21.6 Hz), 18.7 – 18.3 (m). IR (neat): 3530, 2937, 1595, 1506, 1457, 1372, 1327, 1200, 1144, 1044, 954, 876, 828, 749 cm^{-1}. LRMS (EI) *m/z* (%): 553.0 ([M-I]$^{+\bullet}$, 100), 133.1 (55), 552.0 (47), 119.0 (39), 107.0 (37), 533.0 (25), 554.0 (22), 91.1 (20), 69.0 (13), 105.1 (12), 534.0 (12), 164.1 (10), 134.1 (9), 77.0 (9), 120.1 (9), 127.9 (8), 680.0 (7). HRMS (EI) m/z calculated for $C_{17}H_{10}OF_{17}I$ ([M]$^+$) 679.9499, found 679.9502.

1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-Heptadecafluoro-10-iodohexadecane (15c)



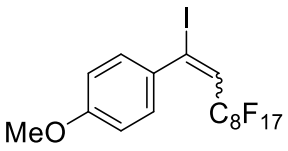
Cu(II)-catalysis: Following general procedure GP-1, using oct-1-ene (79 µL, 56 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.7 mg, 5.0 µmol, 1.0 mol%) gave 305 mg (463 µmol, 93%) of **15c** as a colourless oil after flash column purification (hexanes). R_f (hexanes) = 0.80. Staining: $KMnO_4$ (UV inactive). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.40 – 4.27 (m, 1H), 3.06 – 2.65 (m, 2H), 1.92 – 1.69 (m, 2H), 1.63 – 1.49 (m, 1H), 1.45 – 1.22 (m, 7H), 0.95 – 0.84 (m, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.43 (t, *J* = 10.0 Hz, 3F), -112.32 (dt, *J* = 269.9, 14.7 Hz, 1F), -114.65 – -115.88 (m, 1F), -121.90 – -122.32 (m, 2F), -122.32 – -122.74 (m, 4F), -123.34 (s, 2F), -124.20 (s, 2F), -126.50 – -127.00 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 123.5 – 106.5 (m), 41.9 (t, *J* = 20.8 Hz), 40.5 (d, *J* = 2.1 Hz), 31.7, 29.7, 28.4, 22.7, 21.0, 14.1.

(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododec-1-en-1-yl)benzene (7k)



Cu(II)-catalysis: Following general procedure GP-1, using ethynylbenzene (55 µL, 51 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 312 mg (481 µmol, 96%) of **7k** in a diastereomeric ratio of *E*/*Z* = 94:06 as a white solid after flash column purification (hexanes). R_f (hexanes) = 0.73. Staining: Vanilin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.27 (m, 5H), 6.60 (t, *J* = 13.5 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.34 (t, *J* = 9.9 Hz, 3F), -105.75 (t, *J* = 13.1 Hz, 2F), -121.85 – -122.20 (m, 2F), -122.27 – -122.66 (m, 4F), -123.05 – -123.58 (m, 4F), -126.48 – -126.91 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.5, 129.4, 128.2, 127.4, 127.2, 127.0 (t, *J* = 2.6 Hz), 119.7 – 107.4 (m).

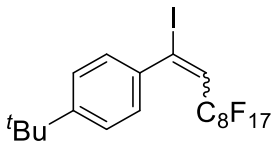
1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododec-1-en-1-yl)-4-methoxy benzene (7l)



Cu(I)-catalysis: Following general procedure GP-1, using 1-ethynyl-4-methoxybenzene (65 µL, 66 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)_2]Cl$ (**45**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 313 mg (462 µmol, 92%) of **7l** in a diastereomeric ratio of *E*/*Z* = 97:03 as a white solid after 42 h and flash column purification (hexanes).

Cu(II)-catalysis: Following general procedure GP-1, using 1-ethynyl-4-methoxybenzene (65 µL, 66 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)Cl_2]$ (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 322 mg (475 µmol, 95%) of **7l** in a diastereomeric ratio of *E*/*Z* = 95:05 as a white solid after 42 h and flash column purification (hexanes). R_f (hexanes) = 0.26. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.57 (t, *J* = 13.5 Hz, 1H), 3.82 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.58 (t, *J* = 10.0 Hz, 3F), -105.45 (t, *J* = 13.3 Hz, 2F), -122.11 (s, 2F), -122.34 – -122.79 (m, 4F), -123.31 – -123.60 (m, 4F), -126.64 – -127.02 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 133.8, 130.1, 129.0 (t, *J* = 2.6 Hz), 126.6 (t, *J* = 21.8 Hz), 113.5, 123.1 – 105.6 (m), 55.4.

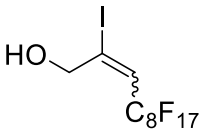
1-(*tert*-Butyl)-4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-iododec-1-en-1-yl)benzene (16a)



Cu(I)-catalysis: Following general procedure GP-1, using 1-(*tert*-butyl)-4-ethynylbenzene (90 µL, 79 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)_2]Cl$ (**45**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 328 mg (466 µmol, 93%) of **16a** in a diastereomeric ratio of *E*/*Z* = 93:07 as a white solid after flash column purification (hexanes).

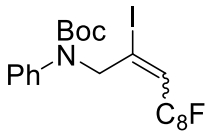
Cu(II)-catalysis: Following general procedure GP-1, using 1-(*tert*-butyl)-4-ethynylbenzene (90 µL, 79 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)Cl_2]$ (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 339 mg (481 µmol, 96%) of **16a** in a diastereomeric ratio of *E*/*Z* = 93:07 as a white solid after flash column purification (hexanes). R_f (hexanes) = 0.67. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.32 (m, 2H), 7.29 – 7.21 (m, 2H), 6.59 (t, *J* = 13.5 Hz, 1H), 1.33 (s, 9H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.5 (t, *J* = 10.0 Hz, 3F), -105.6 (t, *J* = 13.1 Hz, 2F), -121.8 – -122.2 (m, 2F), -122.3 – -122.8 (m, 4F), -123.1 – -123.7 (m, 4F), -126.5 – -127.1 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 138.5, 127.0 (t, *J* = 2.1 Hz), 126.7, 126.5, 125.1, 119.7 – 107.1 (m), 34.9, 31.3.

4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoro-2-iodoundec-2-en-1-ol (16b)



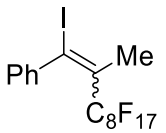
Cu(II)-catalysis: Following general procedure GP-1, using prop-2-yn-1-ol (30 µL, 28 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 147 mg (244 µmol, 49%, DCM as solvent/ 144 mg, 239 µmol, 48%, MeCN as solvent) of **16b** in a diastereomeric ratio of *E*/*Z* = 52:48 as a yellow solid after flash column purification (hexanes/EtOAc 100:0 to 7:1). R_f (hexanes / EtOAc, 7:1) = 0.27. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.80 (tt, *J* = 13.4, 1.8 Hz, 1H), 6.47 (t, *J* = 14.6 Hz, 1H), 4.35 (s, 4H), 2.33 (s, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.48 (t, *J* = 10.0 Hz, 6F), -105.49 – -105.76 (m, 2F), -108.78 (t, *J* = 13.2 Hz, 2F), -121.87 – -122.26 (m, 4F), -122.26 – -122.80 (m, 8F), -123.17 – -123.59 (m, 6F), -123.61 – -123.88 (m, 2F), -126.58 – -127.04 (m, 4F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 127.5 (t, *J* = 24.9 Hz), 122.9 (t, *J* = 5.9 Hz), 120.2 (t, *J* = 24.0 Hz), 118.7 (t, *J* = 33.2 Hz), 115.9 (t, *J* = 32.8 Hz), 115.2 – 107.4 (m), 72.7, 65.0 (t, *J* = 4.8 Hz).

***tert*-Butyl-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundec-2-en-1-yl)(phenyl)carbamate (16c)**



Cu(II)-catalysis: Following general procedure GP-1, using *tert*-butyl phenyl(prop-2-yn-1-yl)carbamate[19] (116 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 280 mg (360 µmol, 72%) of **16c** in a diastereomeric ratio of *E*/*Z* = 73:27 as a colourless oil after flash column purification (hexanes). R_f (hexanes / EtOAc, 5:1) = 0.72. Staining: Vanilin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$, rotamers present) δ 7.42 – 7.14 (m, 5H), 6.49 (t, *J* = 12.7 Hz, 1H), 4.74 – 4.56 (m, 2H), 1.46 (s, 9H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.42 (t, *J* = 9.9 Hz, 3F), [-106.23 (minor diastereomer, s, 2F), -108.90 (major diastereomer, s, 2F)], -121.78 – -122.22 (m, 2F), -122.22 – -122.77 (m, 4F), -123.10 – -123.89 (m, 4F), -126.53 – -126.98 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 141.8, 129.1, 128.9, 127.4, 126.9, 126.6, 125.9, 121.6 (t, *J* = 23.8 Hz), 118.7 (t, *J* = 33.0 Hz), 115.9 (t, *J* = 33.1 Hz), 114.2 – 113.2 (m), 113.1 – 107.4 (m), 81.9, 64.1, 28.4 (minor diastereomer), 28.2 (major diastereomer).

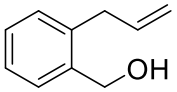
(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iodo-2-methyldec-1-en-1-yl) benzene (16e)



Cu(II)-catalysis: Following general procedure GP-1, using prop-1-yn-1-ylbenzene (63 µL, 58 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 134 mg (202 µmol, 40%, DCM as solvent/ 133 mg, 201 µmol, 40%, MeCN as solvent) of **16e**

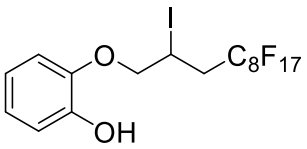
in a diastereomeric ratio of *E*/*Z* > 99:01 as a white solid after flash column purification (hexanes). R_f (hexanes) = 0.68. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.22 (m, 3H), 7.21 – 7.15 (m, 2H), 2.29 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.33 (t, *J* = 10.0 Hz, 3F), -103.73 (s, 2F), -119.78 – -120.27 (m, 2F), -122.5 (s, 6F), -123.3 (s, 2F), -126.7 (s, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3, 130.2 (t, *J* = 20.5 Hz), 128.8, 128.3, 127.8, 126.9, 119.3 – 105.1 (m), 26.8 (p, *J* = 3.5 Hz).

(2-allylphenyl)methanol (24)



A 100 mL round bottom flask equipped with a magnetic stir bar was charged with methyl 2-allylbenzoate (**23**)[21] (881 mg, 5.0 mmol, 1.0 equiv) in dry THF (30 mL). A solution of $LiAlH_4$ (380 mg, 10.0 mmol, 2.0 equiv) in THF (20 mL) was added dropwise while the temperature was maintained at 0 °C. The resulting mixture was allowed to warm to room temperature and was stirred for 2 h. The mixture was then hydrolyzed by addition of H_2O (70 mL), the resulting suspension was filtered, and the precipitate was washed with EtOAc (3x 70 mL). The combined organic layer was dried over anh. Na_2SO_4 and solvent evaporated under reduced pressure to give 679 mg (4.6 mmol, 92%) of (2-allylphenyl)methanol (**24**)[25] as pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.35 (m, 1H), 7.30 – 7.19 (m, 3H), 6.01 (ddt, *J* = 17.2, 10.1, 6.2 Hz, 1H), 5.09 (dq, *J* = 10.1, 1.6 Hz, 1H), 5.01 (dq, *J* = 17.0, 1.8 Hz, 1H), 4.69 (s, 2H), 3.48 (dt, *J* = 6.3, 1.7 Hz, 2H), 1.99 (bs, 1H).

2-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)oxy)phenol (29a)

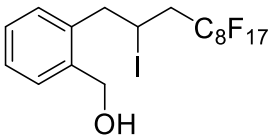


Cu(I)-catalysis: Following general procedure GP-1, using 2-(allyloxy)phenol (**21**)[20] (75 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)_2]Cl$ (**45**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 254 mg (365 µmol, 73%) of **29a** as a colorless oil after flash column purification (hexanes/EtOAc 100:0 to 15:1).

Cu(II)-catalysis: Following general procedure GP-1, using 2-(allyloxy)phenol (**21**)[20] (75 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)Cl_2]$ (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 244 mg (351 µmol, 70%) of **29a** as a colorless oil after flash column purification (hexanes/EtOAc 100:0 to 15:1). R_f (hexanes / EtOAc 15:1) = 0.50. Staining: Vanillin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.07 – 6.91 (m, 2H), 6.86 (dd, *J* = 3.5, 1.2 Hz, 2H), 5.65 (s, 1H), 4.60 (dq, *J* = 7.6, 5.6 Hz, 1H), 4.33 – 4.18 (m, 2H), 3.20 – 2.78 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -80.70 (t, *J* = 10.0 Hz, 3F), -111.24 – -112.60 (m, 1F), -114.26 (dt, *J* = 269.3, 14.1 Hz, 1F), -121.05 – -122.16 (m, 6F), -122.67 (s, 2F), -123.31 (s, 2F), -125.79 – -126.43 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.3, 144.8, 123.3, 120.5, 115.7, 113.4, 73.7 (d, *J* = 2.5 Hz), 38.5 (t, *J* = 21.5 Hz), 13.9. IR (neat): 3370, 1599, 1513, 1461, 1431,

1372, 1331, 1238, 1193, 1141, 1111, 1070, 1010, 917, 895, 842, 790, 742, 705 cm^{-1}. LRMS (EI) *m/z* (%): 109.0 (100), 586.9 (43), 84.0 (32), 49.0 (31), 110.0 (29), 85.9 (21), 121.0 (19), 91.0 (16), 51.0 (16), 81.0 (15), 69.0 (13), 172.9 (11), 695.9 (10), 568.0 (7), 235.9 (7). HRMS (EI) m/z calculated for $C_{17}H_{10}O_2F_{17}I$ ($[M]^{+\bullet}$) 695.9449, found 695.9450.

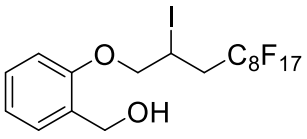
(2-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)phenyl)-methanol (29b)



Cu(I)-catalysis: Following general procedure GP-1, using (2-allylphenyl)methanol (**24**) (74 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)_2]Cl$ (**45**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 240 mg (346 µmol, 69%) of **29b** as a colorless oil after flash column purification (hexanes/EtOAc 100:0 to 10:1).

Cu(II)-catalysis: Following general procedure GP-1, using (2-allylphenyl)methanol (**24**) (74 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)Cl_2]$ (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 224 mg (323 µmol, 65%) of **29b** as a colorless oil after flash column purification (hexanes/EtOAc 100:0 to 15:1). R_f (hexanes / EtOAc 15:1) = 0.29. Staining: Vanillin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.33 – 7.27 (m, 1H), 7.04 (td, *J* = 7.5, 1.0 Hz, 1H), 6.84 (dd, *J* = 8.2, 1.0 Hz, 1H), 4.78 (q, *J* = 12.9 Hz, 2H), 4.64 (dq, *J* = 7.2, 5.5 Hz, 1H), 4.29 (h, *J* = 5.3 Hz, 2H), 3.27 – 3.06 (m, 1H), 3.03 – 2.81 (m, 1H), 2.35 (s, 1H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -80.96 (t, *J* = 10.0 Hz, 3F), -112.43 (dt, *J* = 269.6, 14.5 Hz, 1F), -114.35 (dt, *J* = 269.6, 14.1 Hz, 1F), -121.29 – -122.35 (m, 6F), -122.83 (s, 2F), -123.17 – -123.82 (m, 2F), -126.02 – -126.53 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 129.7, 129.3, 129.2, 122.0, 111.4, 72.3 (d, *J* = 2.4 Hz), 61.7, 38.4 (t, *J* = 21.3 Hz), 13.7 – 13.6 (m). IR (neat): 3317, 1491, 1431, 1368, 1331, 1200, 1148, 1044, 999, 880, 824, 749, 705 cm^{-1}. LRMS (EI) *m/z* (%): 549.0 ($([M\text{-}I\text{-}H_2O]^{+\bullet}$,100), 567.1 (35), 129.1 (24), 84.0 (22), 550.1 (21), 49.0 (20), 86.0 (15), 130.1 (14), 115.1 (13), 105.1 (13), 116.1 (12), 160.1 (11), 128.1 (9), 69.0 (9), 119.0 (7), 568.1 (7), 77.0 (7), 51.0 (7), 135.1 (7), 120.1 (7), 133.1 (7). HRMS (EI) m/z calculated for $C_{18}H_{12}OF_{17}I$ ($[M]^{+\bullet}$) 693.9656, found 693.9654.

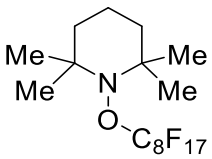
(2-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)oxy)phenyl)-methanol (29c)



Cu(I)-catalysis: Following general procedure GP-1, using (2-(allyloxy)phenyl)methanol (**27**) (82 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and $[Cu(dap)_2]Cl$ (**45**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 200 mg (282 µmol, 56%) of **29c** as a colorless oil after flash column purification (hexanes/EtOAc 100:0 to 14:1).

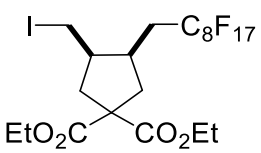
Cu(II)-catalysis: Following general procedure GP-1, using (2-(allyloxy)phenyl)methanol (**27**) (82 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 217 mg (306 µmol, 61%) of **29c** as a colorless oil after flash column purification (hexanes/EtOAc 100:0 to 14:1). R_f (hexanes / EtOAc 14:1) = 0.30. Staining: Vanillin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 1H), 7.34 – 7.29 (m, 2H), 7.25 – 7.20 (m, 1H), 4.77 – 4.66 (m, 2H), 4.61 (dq, *J* = 9.3, 6.4 Hz, 1H), 3.44 – 3.26 (m, 2H), 3.14 – 2.77 (m, 2H), 1.96 (s, 1H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.00 (t, *J* = 10.0 Hz, 3F), -111.84 (dt, *J* = 269.3, 14.5 Hz, 1F), -113.49 – -114.59 (m, 1F), -121.50 – -121.79 (m, 2F), -121.79 – -122.27 (m, 4F), -122.68 – -123.08 (m, 2F), -123.50 – -123.86 (m, 2F), -126.13 – -126.51 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 137.8, 130.2, 129.5, 128.4, 127.9, 122.1 – 107.1 (m), 43.6 (d, *J* = 2.1 Hz), 41.5 (t, *J* = 20.7 Hz), 20.0 – 19.8 (m). IR (neat): 3355, 2878, 1603, 1491, 1454, 1368, 1331, 1200, 1148, 1044, 861, 828, 753, 705 cm^{-1}. LRMS (EI) *m/z* (%): 95.1 (100), 106.0 (99), 249.9 (98), 107.0 (60), 77.0 (59), 710.0 (([M]$^{+\bullet}$,45), 123.0 (31), 121.0 (30), 586.9 (29). HRMS (EI) m/z calculated for $C_{18}H_{12}O_2F_{17}I$ ([M]$^{+\bullet}$) 709.9605, found 709.9598.

2,2,6,6-tetramethyl-1-((perfluorooctyl)oxy)piperidine (32)



Cu(II)-catalysis: Following general procedure GP-1, using styrene (**12a**) (57 µL, 52 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv), 2,2,6,6-Tetramethylpiperidinyloxyl (78 mg, 0.5 mmol, 1.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 144 mg (222 µmol, 44%) of **32** as a colorless oil after flash column purification (hexanes). R_f (hexanes) = 0.55. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.62 – 1.54 (m, 5H), 1.42 – 1.33 (m, 1H), 1.18 (s, 12H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -78.89 – -79.09 (m, 2F), -81.26 (t, *J* = 9.9 Hz, 3F), -121.96 – -122.59 (m, 6F), -123.04 – -123.41 (m, 2F), -123.92 – -124.24 (m, 2F), -126.42 – -126.77 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 62.1, 40.6, 33.6 (t, *J* = 5.4 Hz), 20.8, 17.0. IR (neat): 3012, 2945, 1539, 1469, 1372, 1334, 1238, 1200, 1133, 999. 880, 816, 783, 727, 664 cm^{-1}. HRMS (ESI) m/z calculated for $C_{17}H_{19}F_{17}NO$ ([M+H]$^+$) 576.1190, found 576.1203.

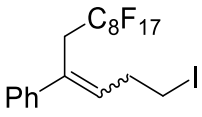
rac. Diethyl (3*R*,4*R*)-3-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononyl)-4-(iodomethyl)cyclopentane-1,1-dicarboxylate (34)



Cu(II)-catalysis: Following general procedure GP-1, using diethyl 2,2-diallylmalonate (**33**)[22] (120 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 275 mg (350 µmol, 70%) of **34** in a diastereomeric ratio of cis/trans = 92:08 as a yellow solid after flash column purification (hexanes/EtOAc 100:0 to 7:1). R_f (hexanes / EtOAc, 5:1) = 0.58. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.25 – 4.14 (m,

4H), 3.16 (dd, *J* = 9.8, 5.3 Hz, 1H), 3.04 (t, *J* = 9.6 Hz, 1H), 2.69 – 2.44 (m, 4H), 2.37 – 1.99 (m, 4H), 1.25 (td, *J* = 7.1, 3.4 Hz, 6H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.32 (t, *J* = 9.9 Hz, 3F), -112.12 – -113.49 (m, 1F), -114.97 (dt, *J* = 270.1, 13.8 Hz, 1F), -121.85 – -122.74 (m, 6F), -123.27 (s, 2F), -123.73 – -124.20 (m, 2F), -126.49 – -126.97 (m, 2F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 172.1, 122.4 – 107.2 (m), 62.1, 62.0, 58.4, 45.6, 39.9, 38.5 (d, *J* = 2.5 Hz), 35.5, 30.2 – 29.5 (m), 14.1, 14.1, 5.7.

(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-Heptadecafluoro-1-iodotridec-3-en-4-yl) benzene (37)

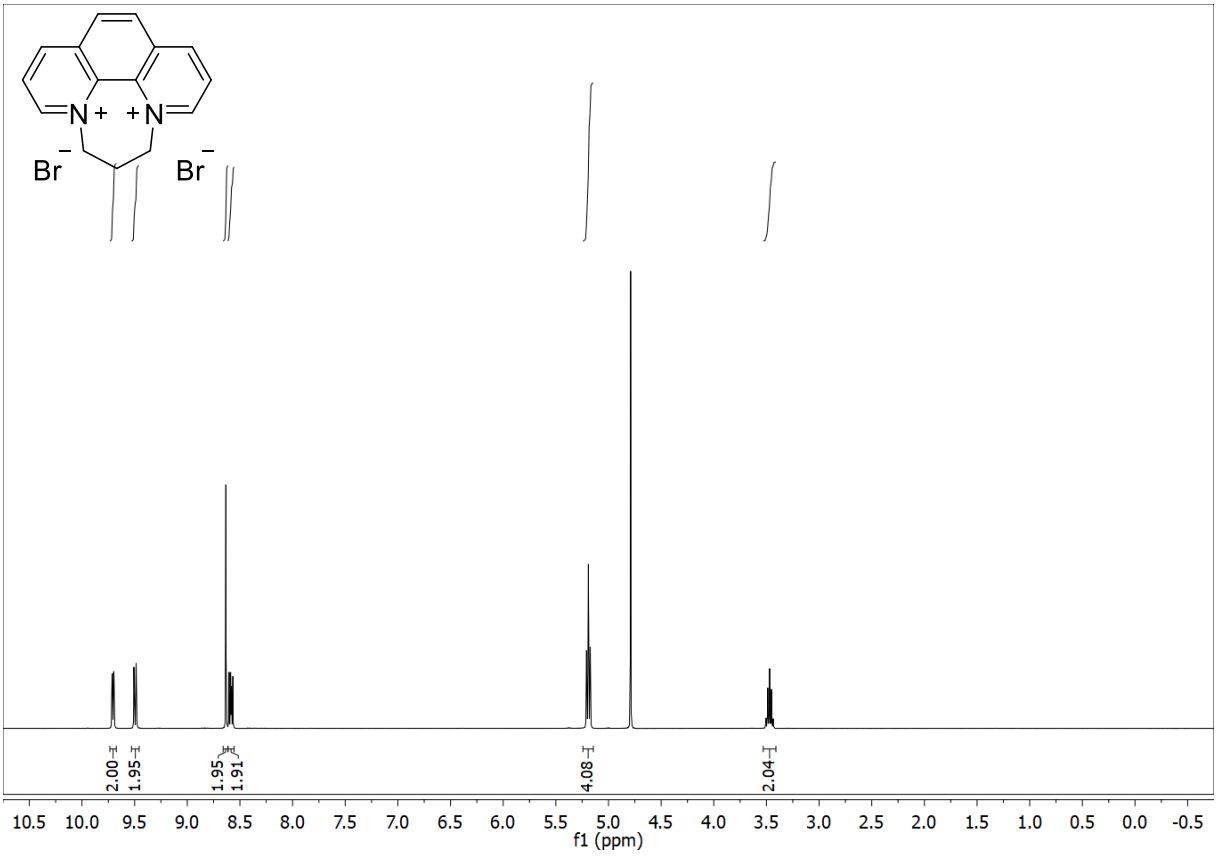


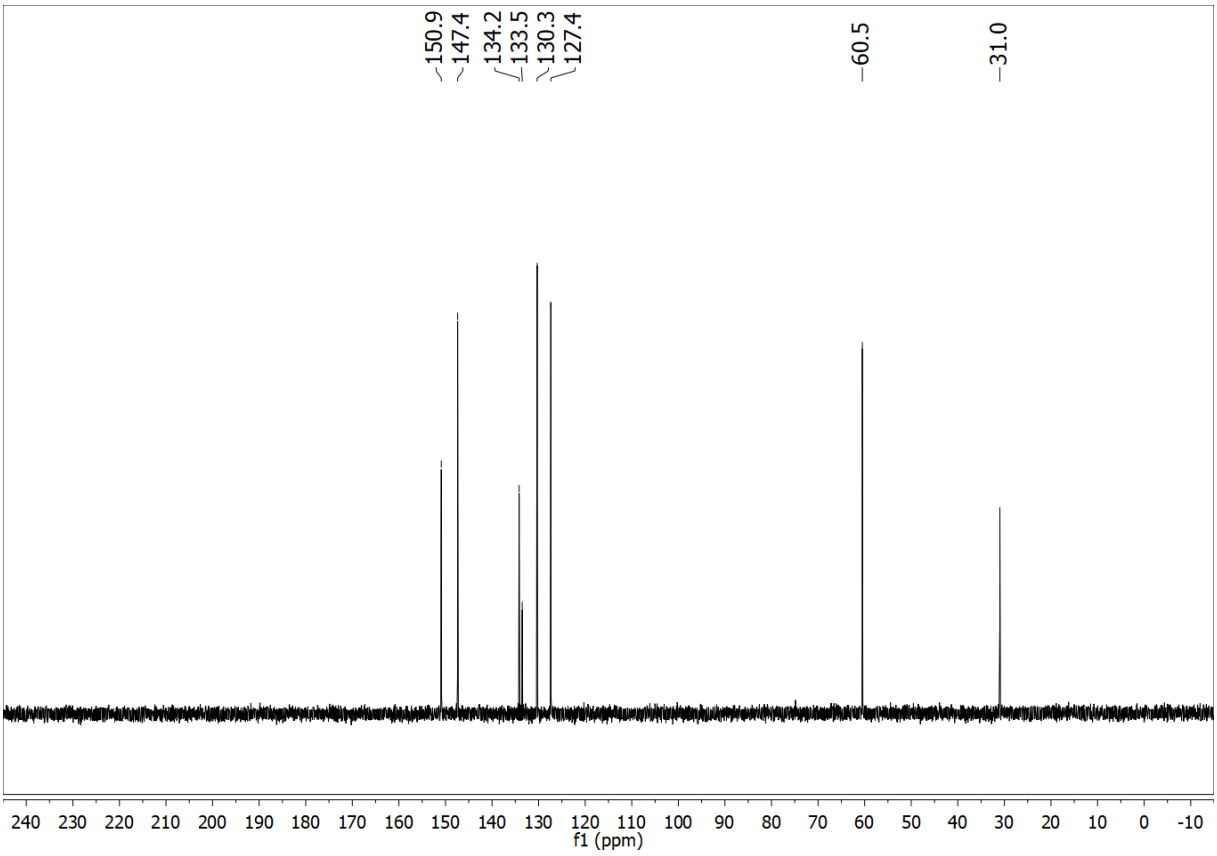
Cu(II)-catalysis: Following general procedure GP-1, using (1-cyclopropylvinyl)benzene (**36**)[23] (72 mg, 0.5 mmol, 1.0 equiv), $C_8F_{17}I$ (**6**) (265 µL, 546 mg, 1.0 mmol, 2.0 equiv) and [Cu(dap)Cl_2] (**47**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 290 mg (420 µmol, 84%) of **37** in a diastereomeric ratio of *E/Z* = 96:04 as a colourless oil after flash column purification (hexanes). R_f (hexanes) = 0.35. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 5H), 6.01 (t, *J* = 7.3 Hz, 1H), 3.44 – 3.21 (m, 4H), 2.85 (q, *J* = 7.0 Hz, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.53 (t, *J* = 10.0 Hz, 3F), -111.89 (t, *J* = 14.2 Hz, 2F), -121.93 – -122.34 (m, 2F), -122.34 – -122.79 (m, 4F), -123.21 – -123.56 (m, 2F), -123.57 – -123.91 (m, 2F), -126.64 – -126.99 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.2, 135.0, 130.9, 128.7, 127.8, 126.5, 122.3 – 106.1 (m), 33.1, 31.7 (t, *J* = 22.1 Hz), 4.2.

3.7. NMR Spectra

^{1}H NMR	first image
^{13}C NMR	second image
^{19}F NMR	third image

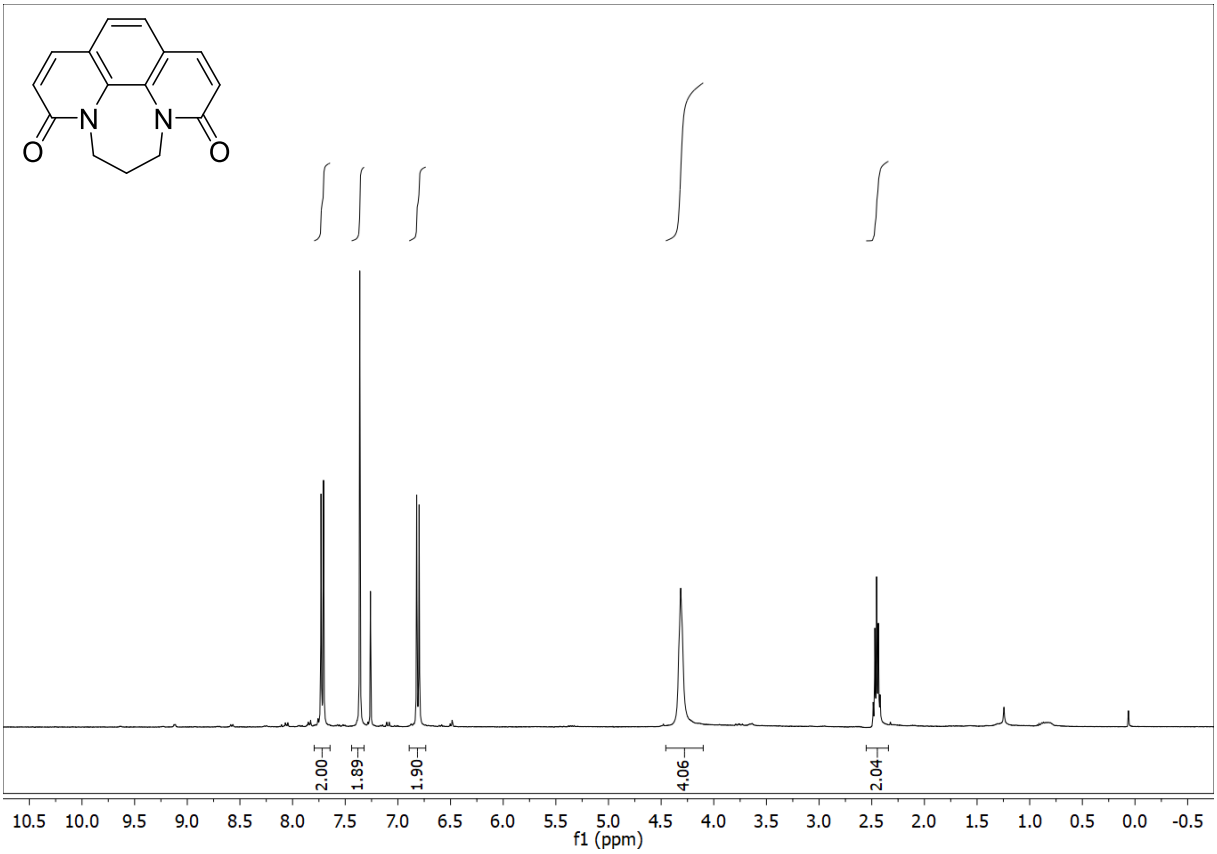
6,7-Dihydro-5*H*-[1,4]diazepino[1,2,3,4-*lmn*][1,10]phenanthroline-4,8-diium bromide (45S1)

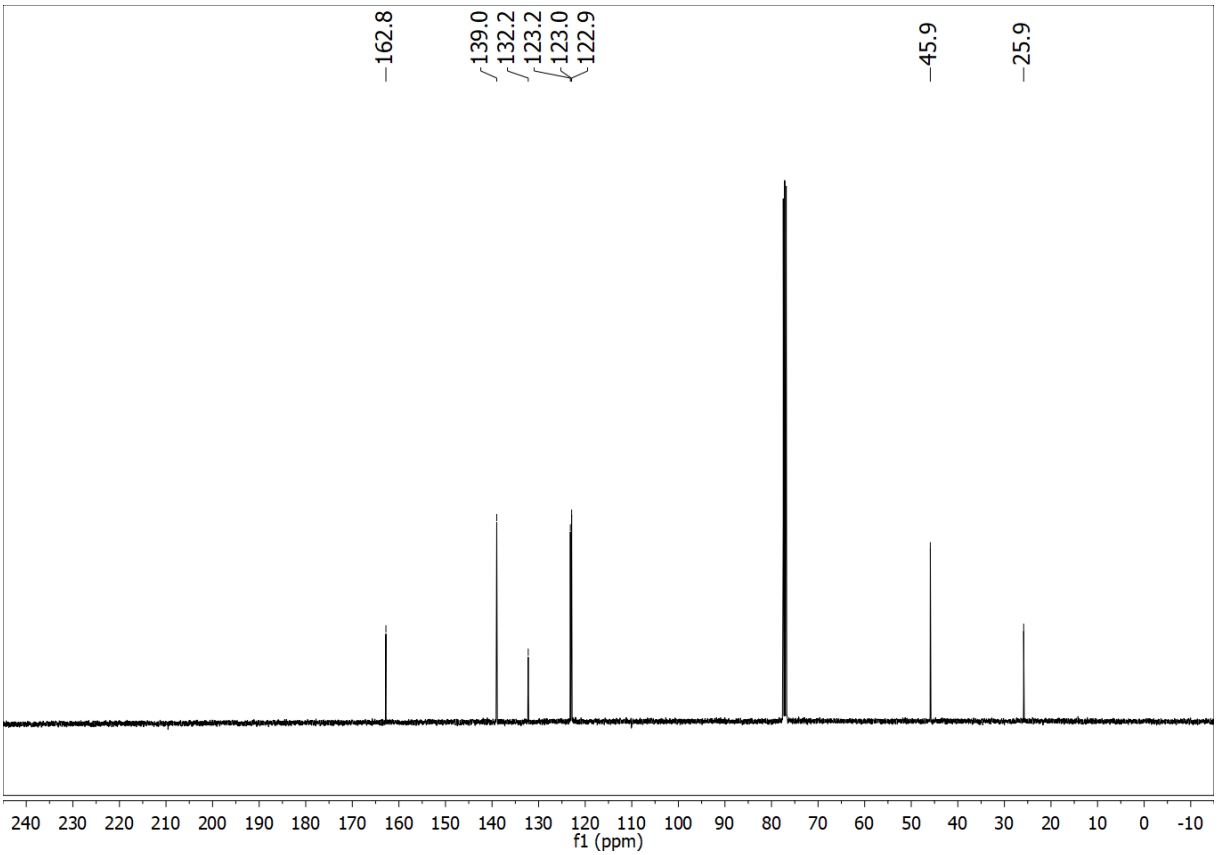




NMR-Solvent: D_2O

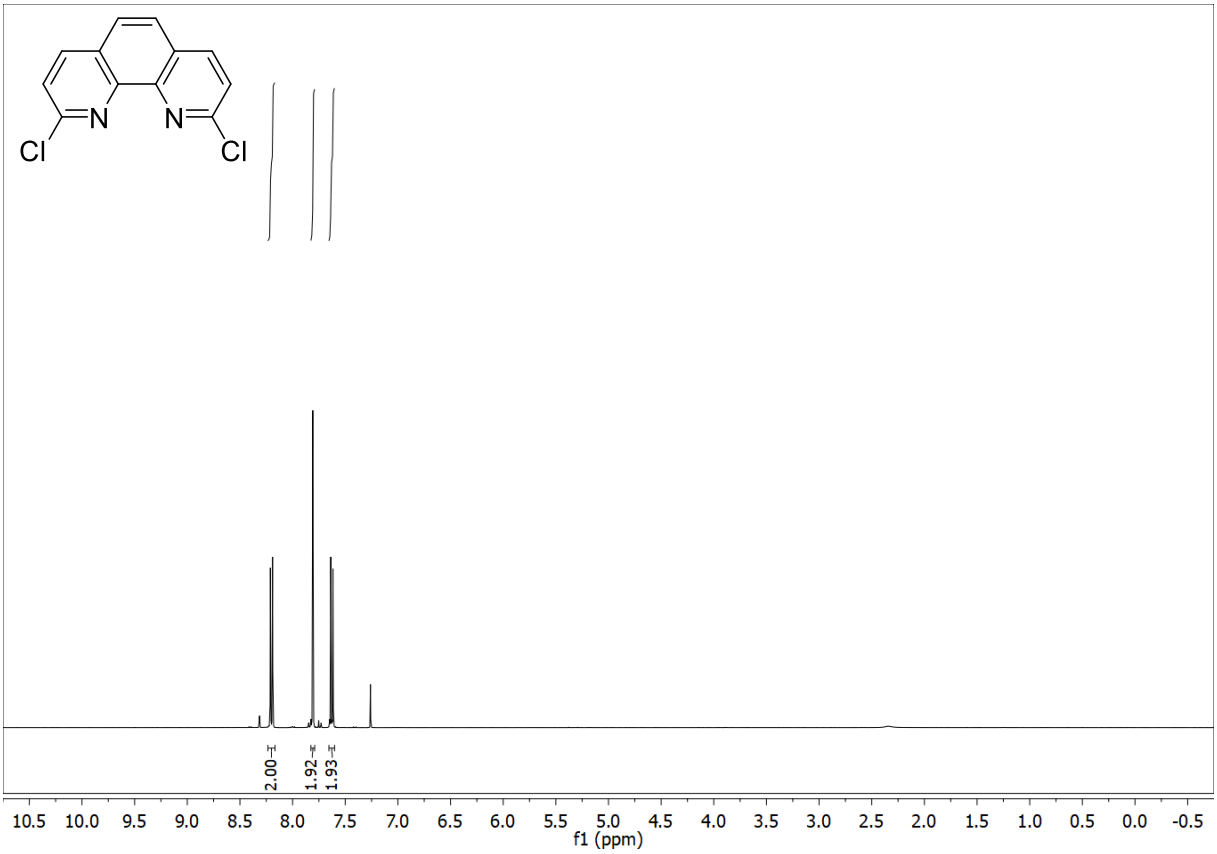
6,7-Dihydro-5*H*-[1,4]diazepino[1,2,3,4-*lmn*][1,10]phenanthroline-3,9-dione (45S2)

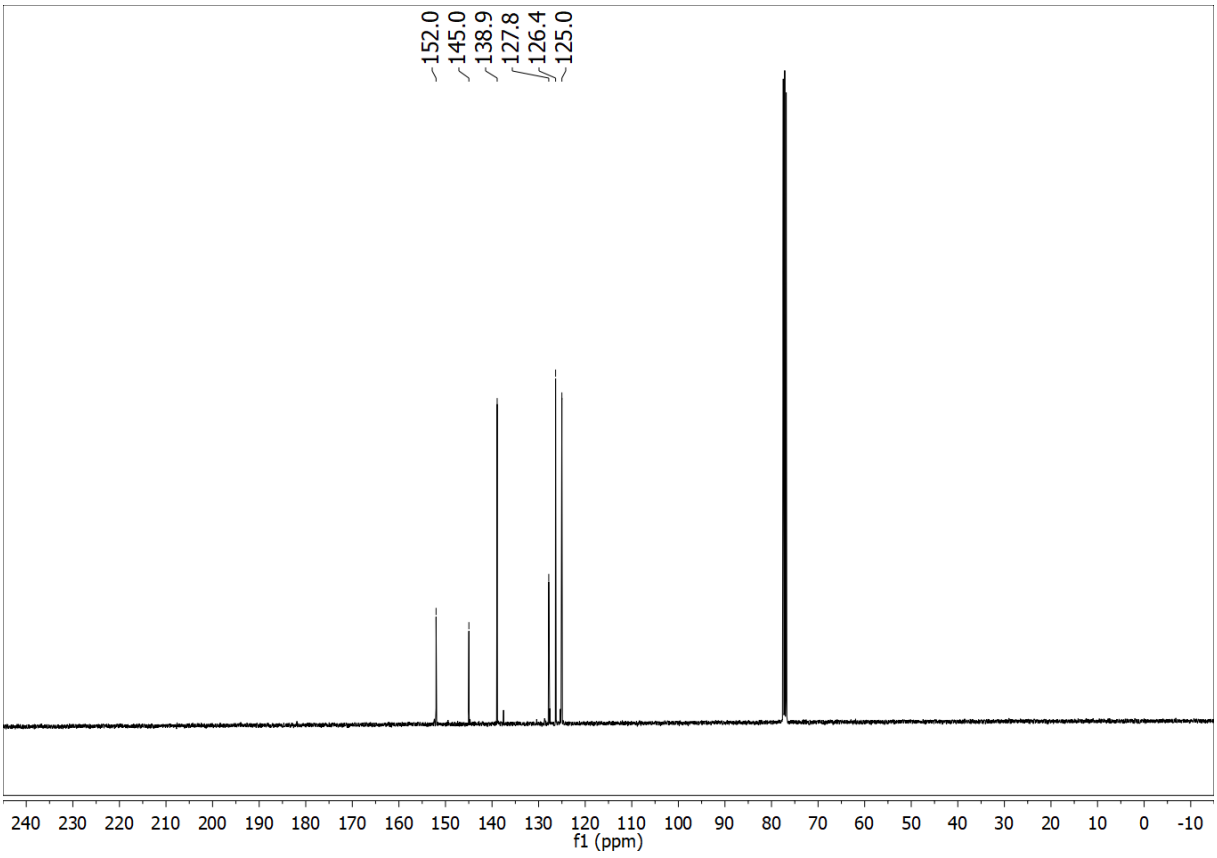




NMR-Solvent: $CDCl_3$

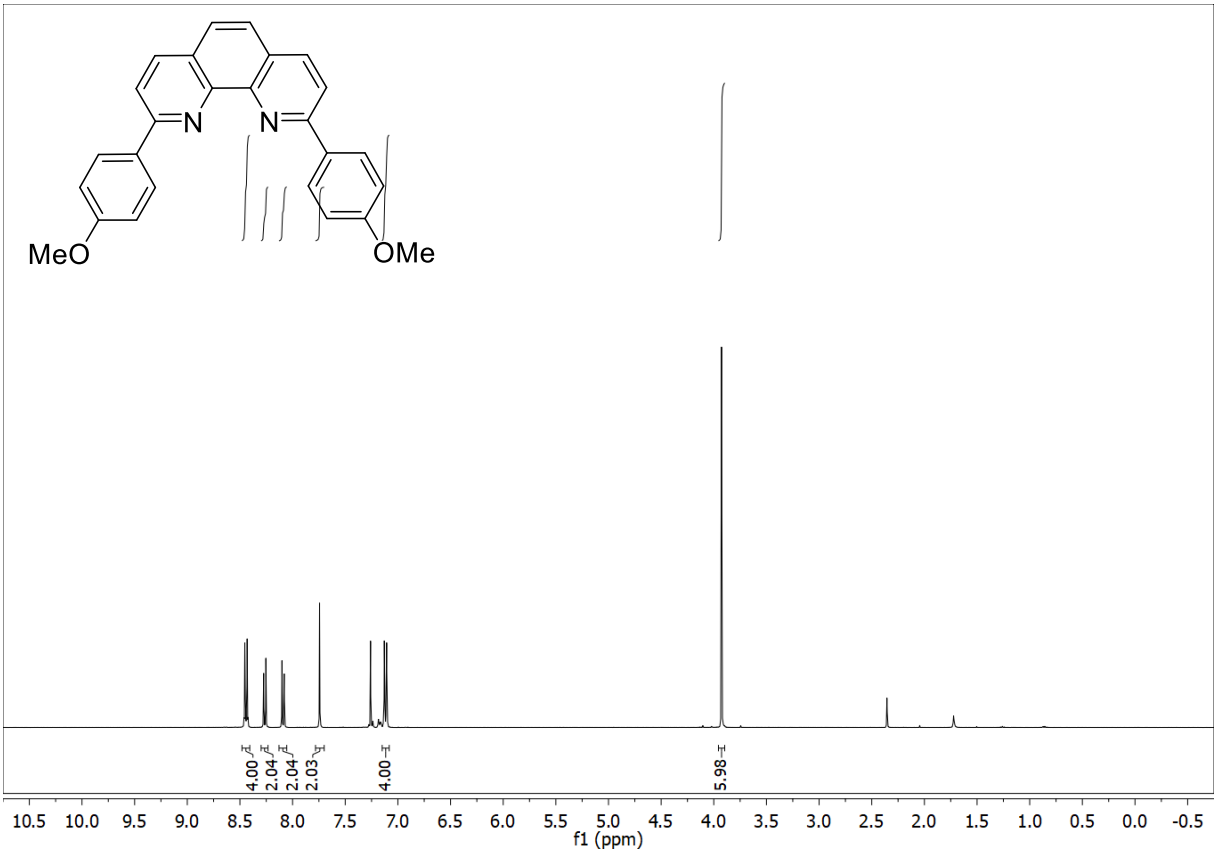
2,9-Dichloro-1,10-phenanthroline (45S3)

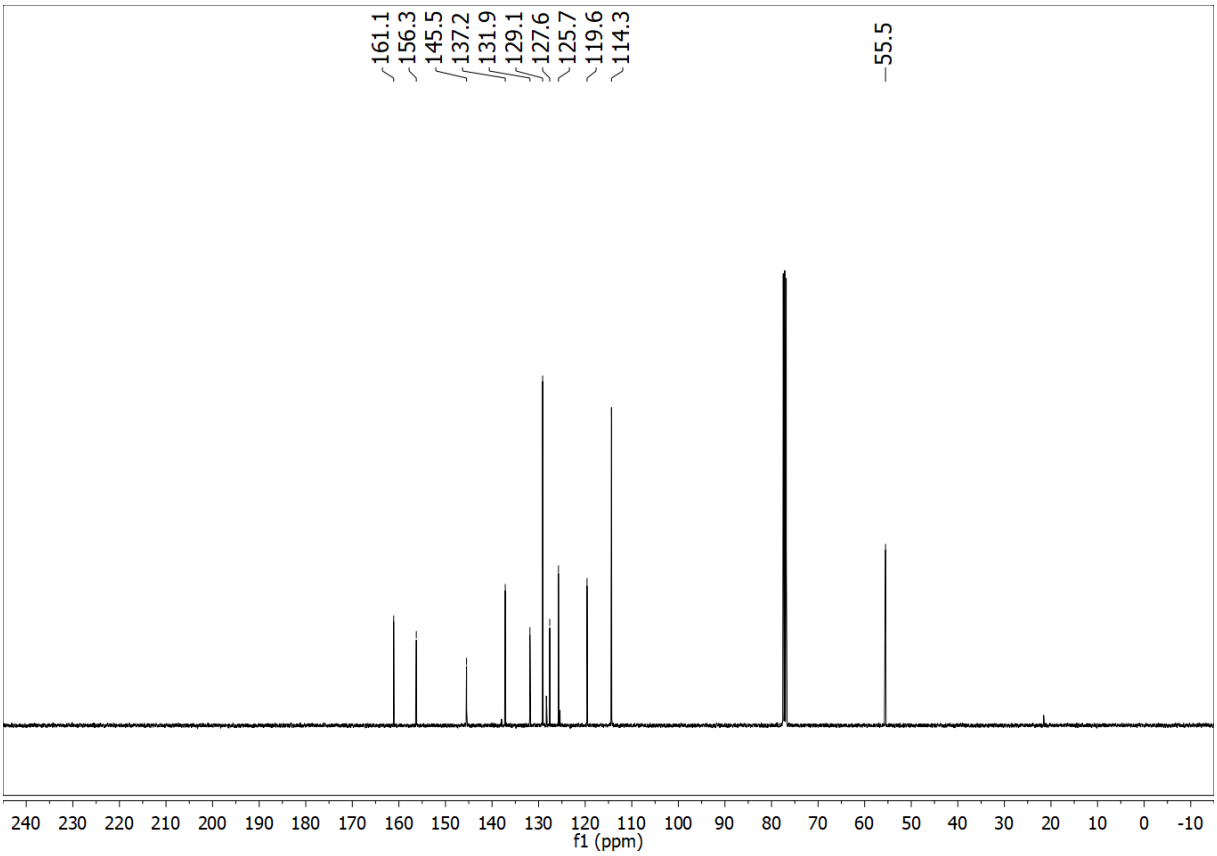




NMR-Solvent: $CDCl_3$

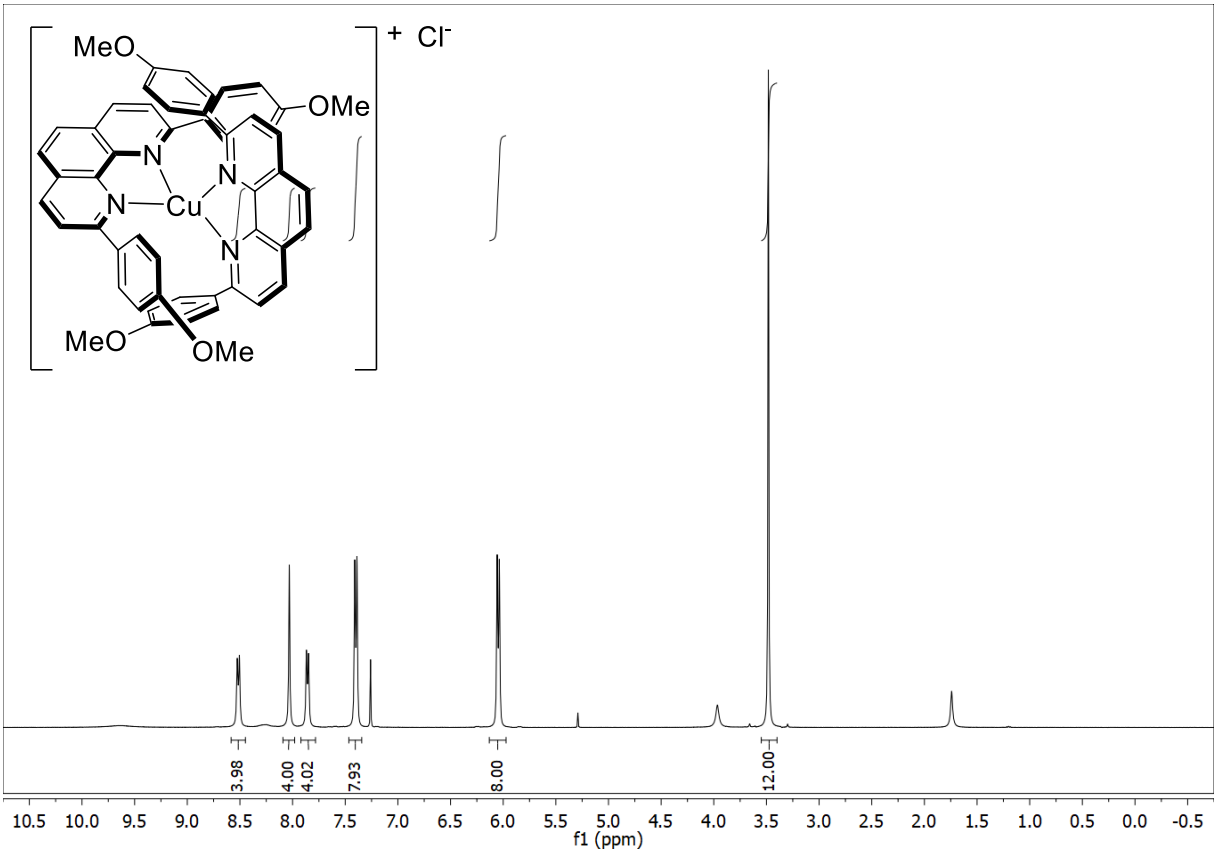
2,9-Bis(4-methoxyphenyl)-1,10-phenanthroline (45S4)

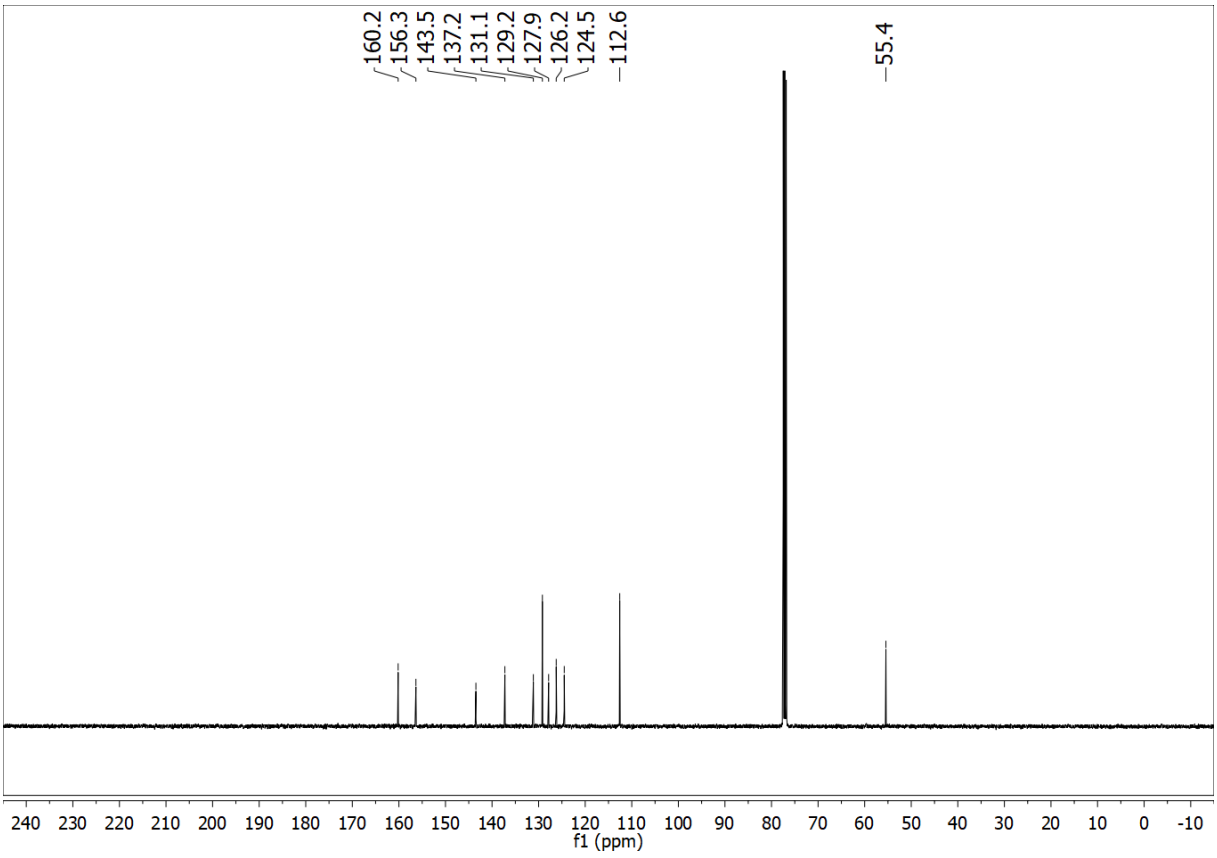




NMR-Solvent: $CDCl_3$

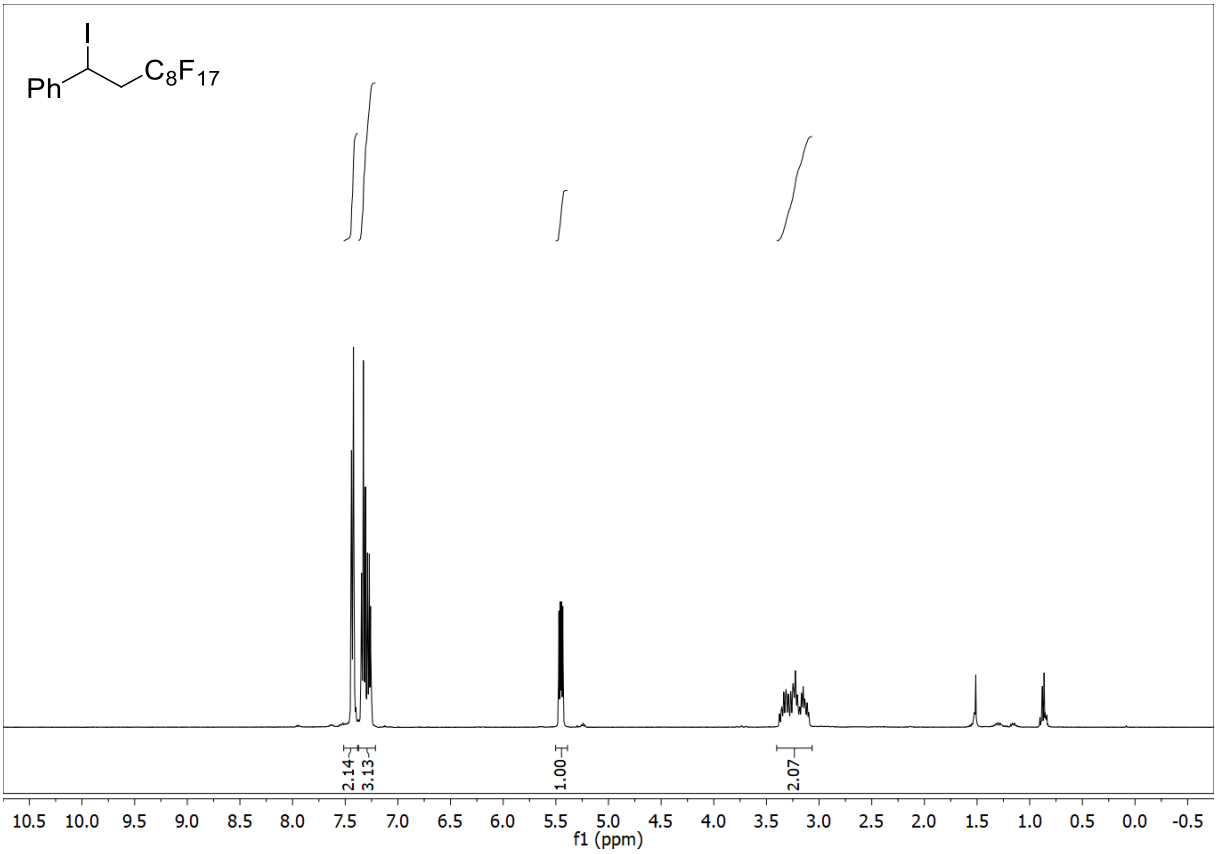
[Cu(dap)$_2$]Cl (45)

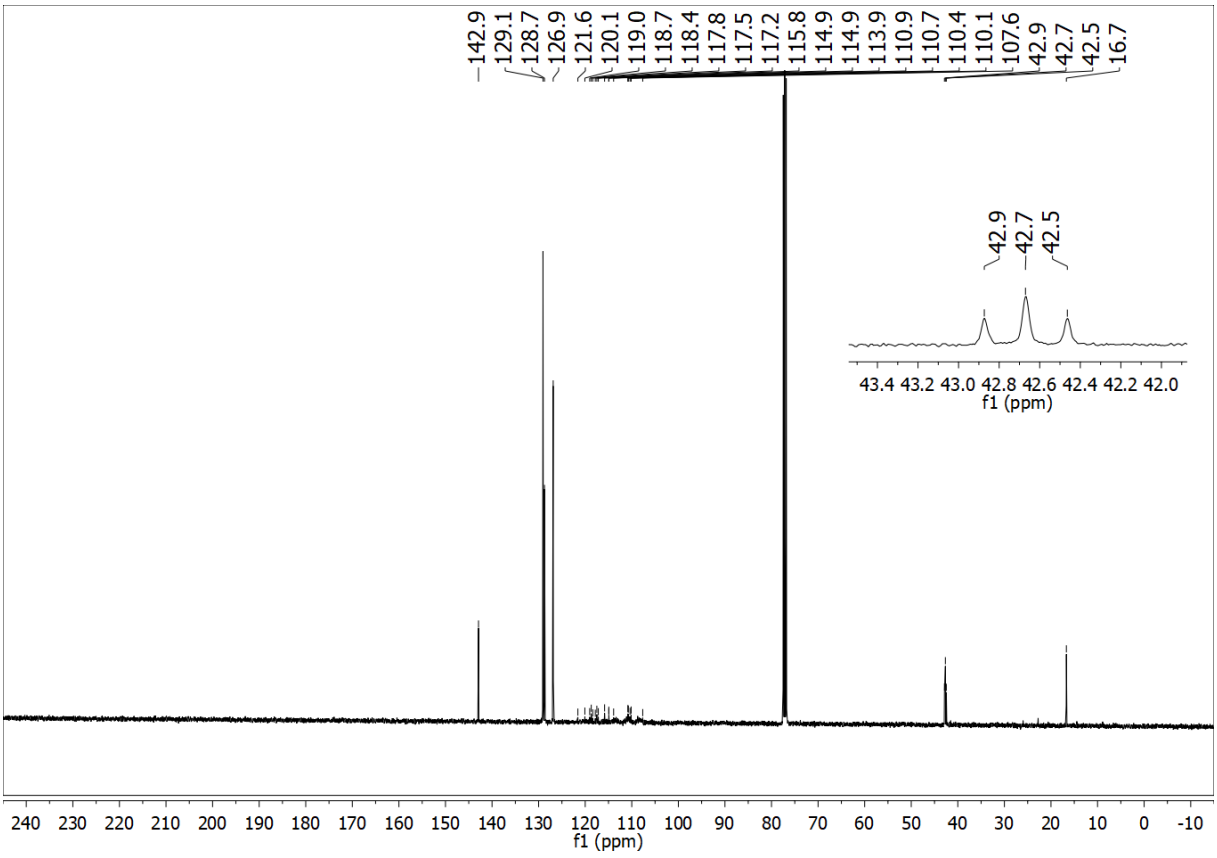


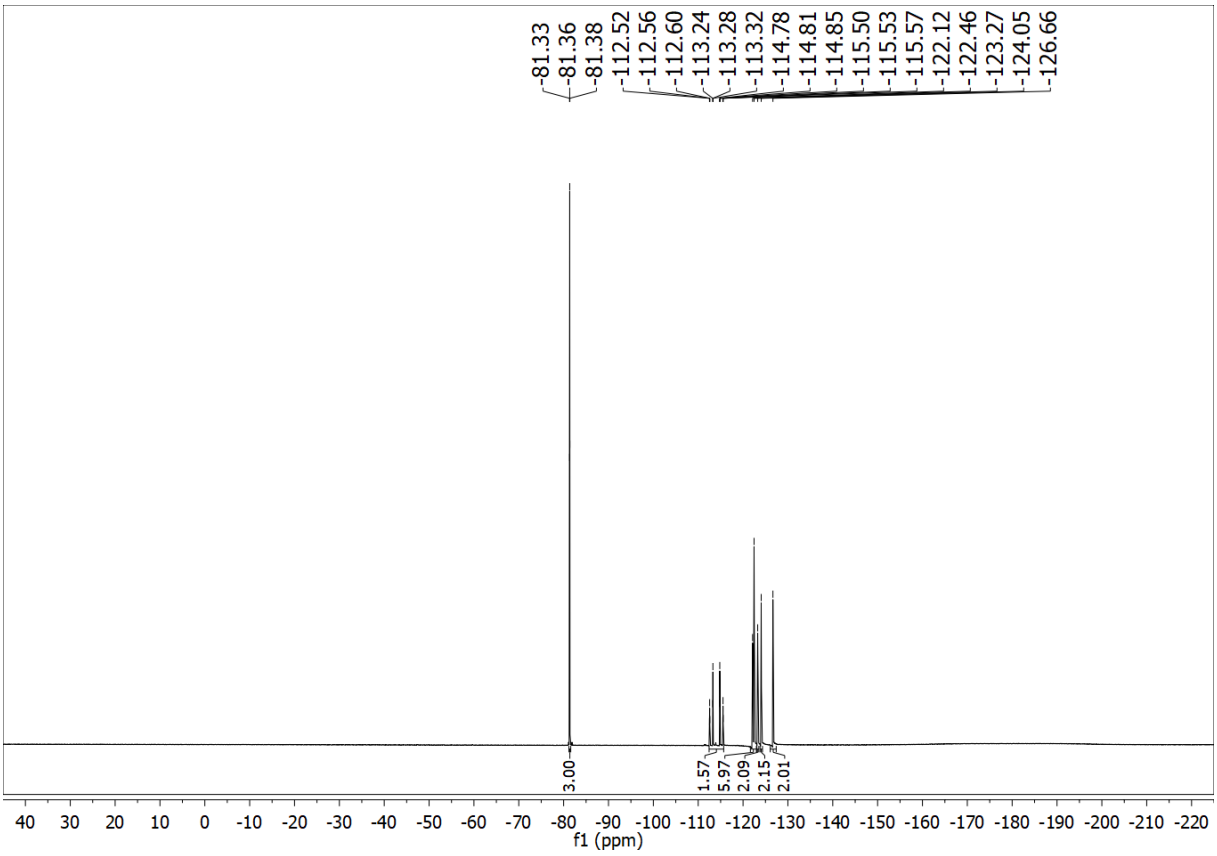


NMR-Solvent: $CDCl_3$

(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododecyl)benzene (7e)

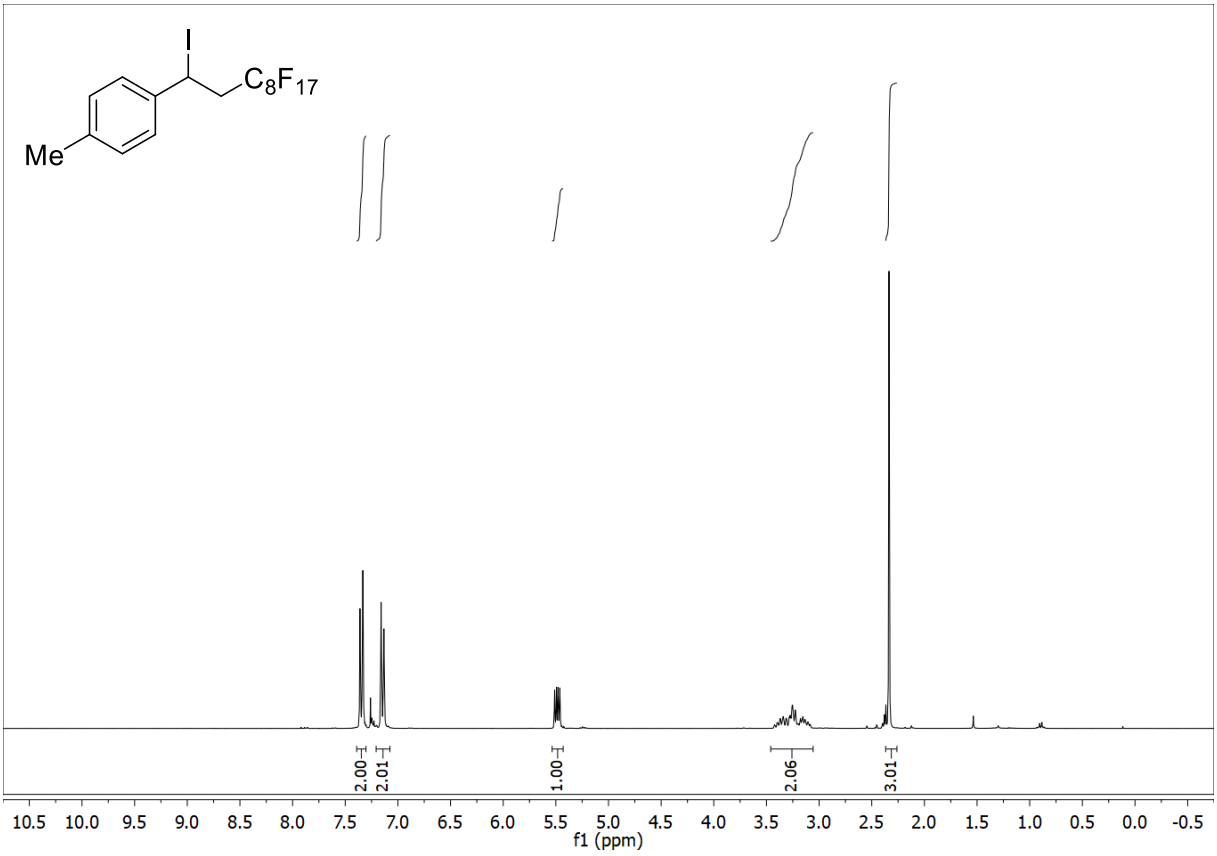


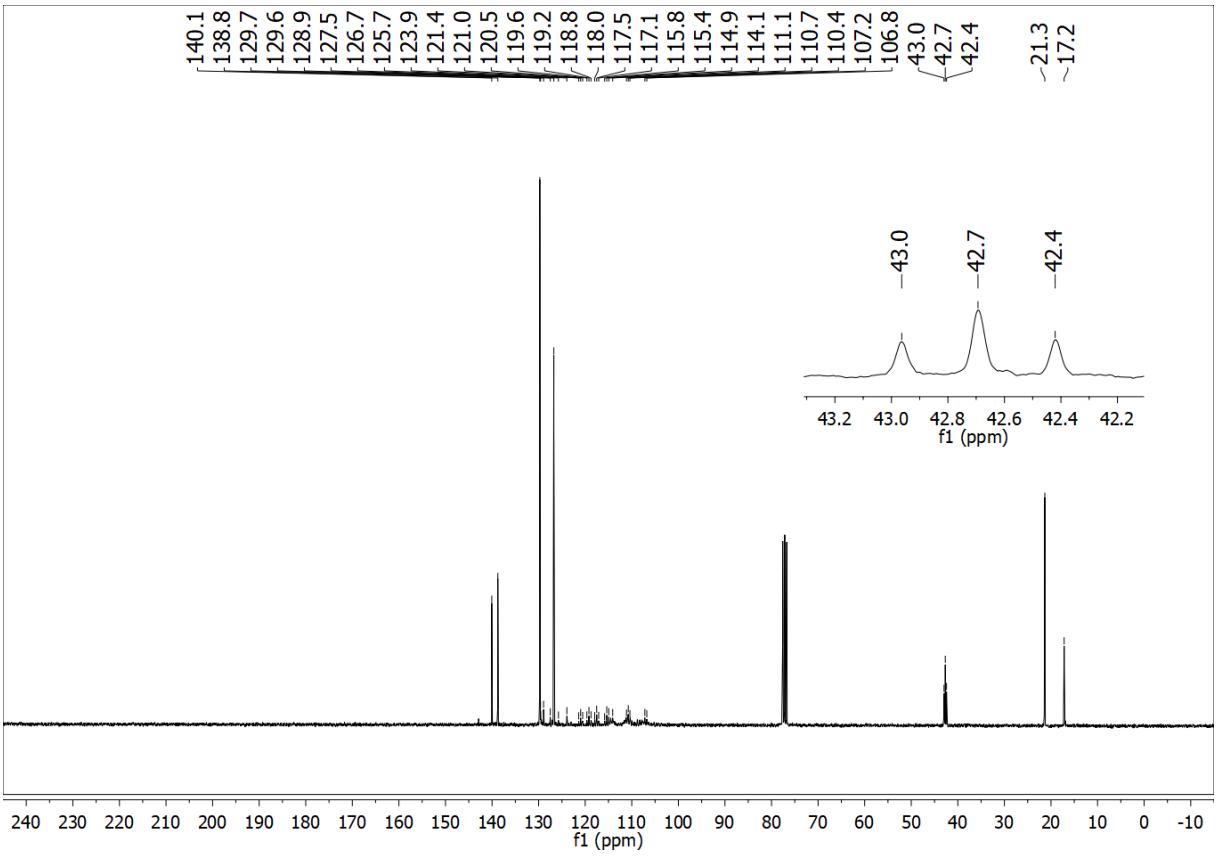


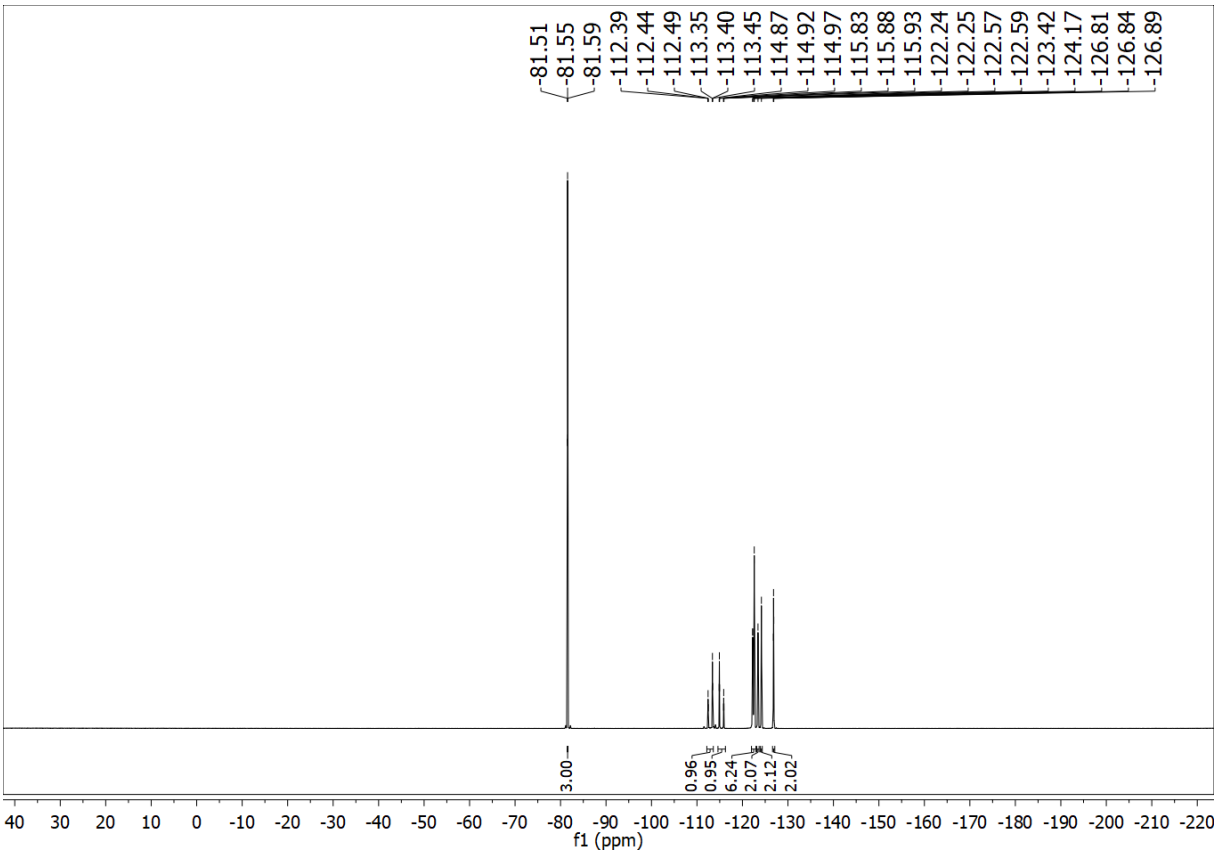


NMR-Solvent: $CDCl_3$

1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododecyl)-4-methylbenzene (13a)

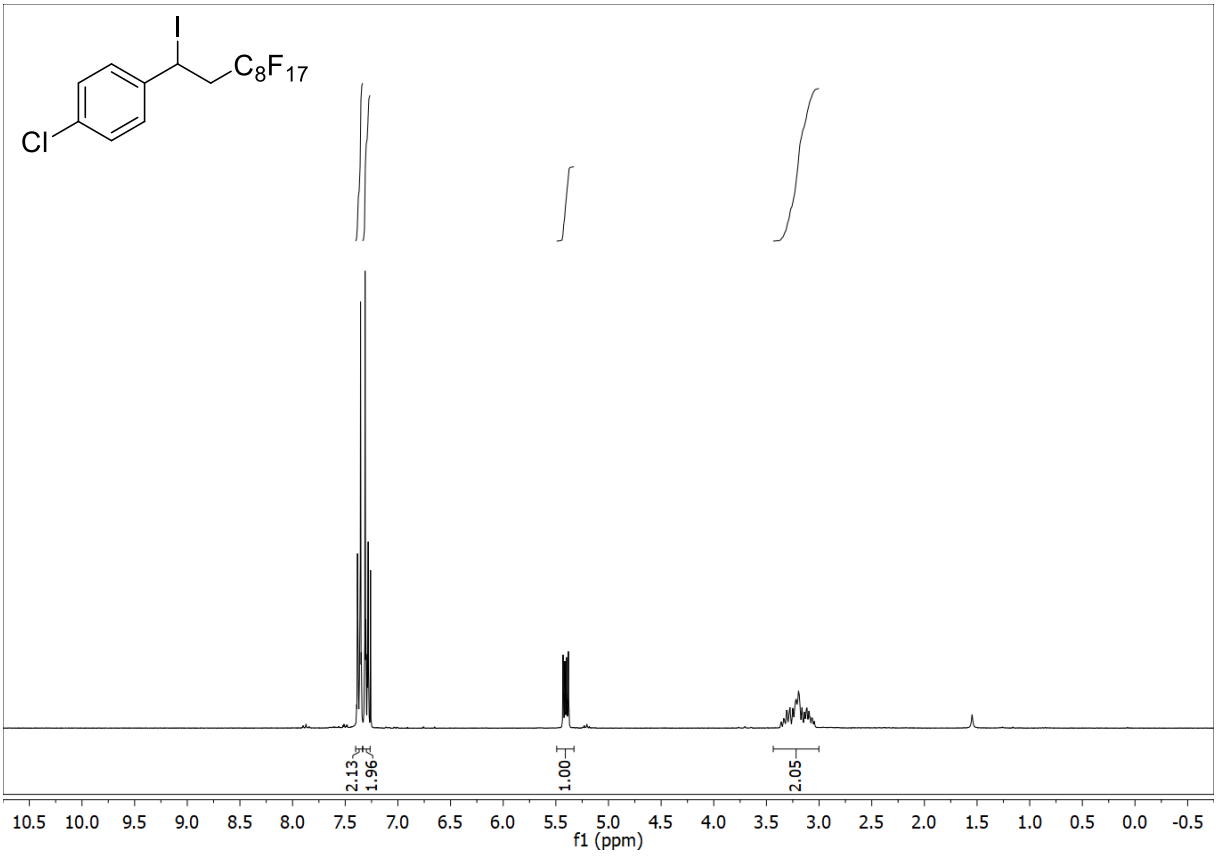


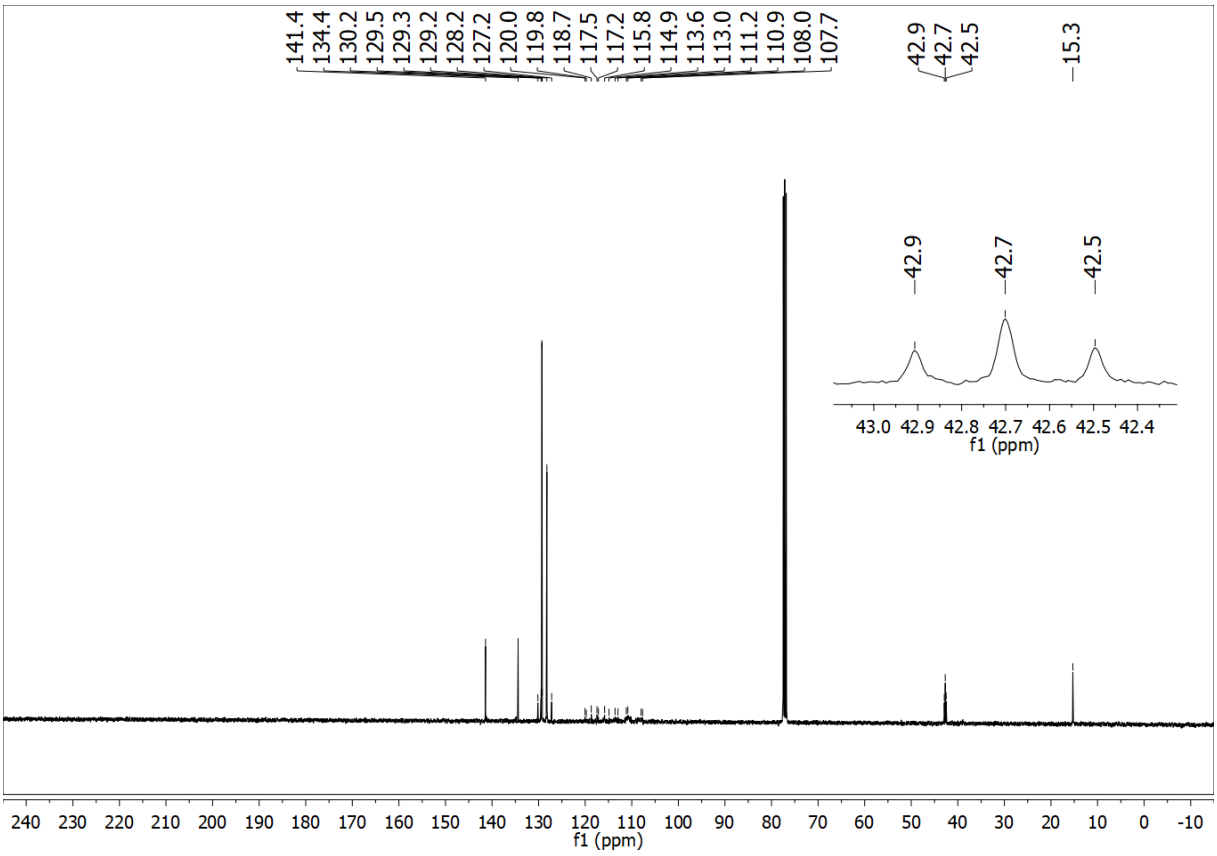


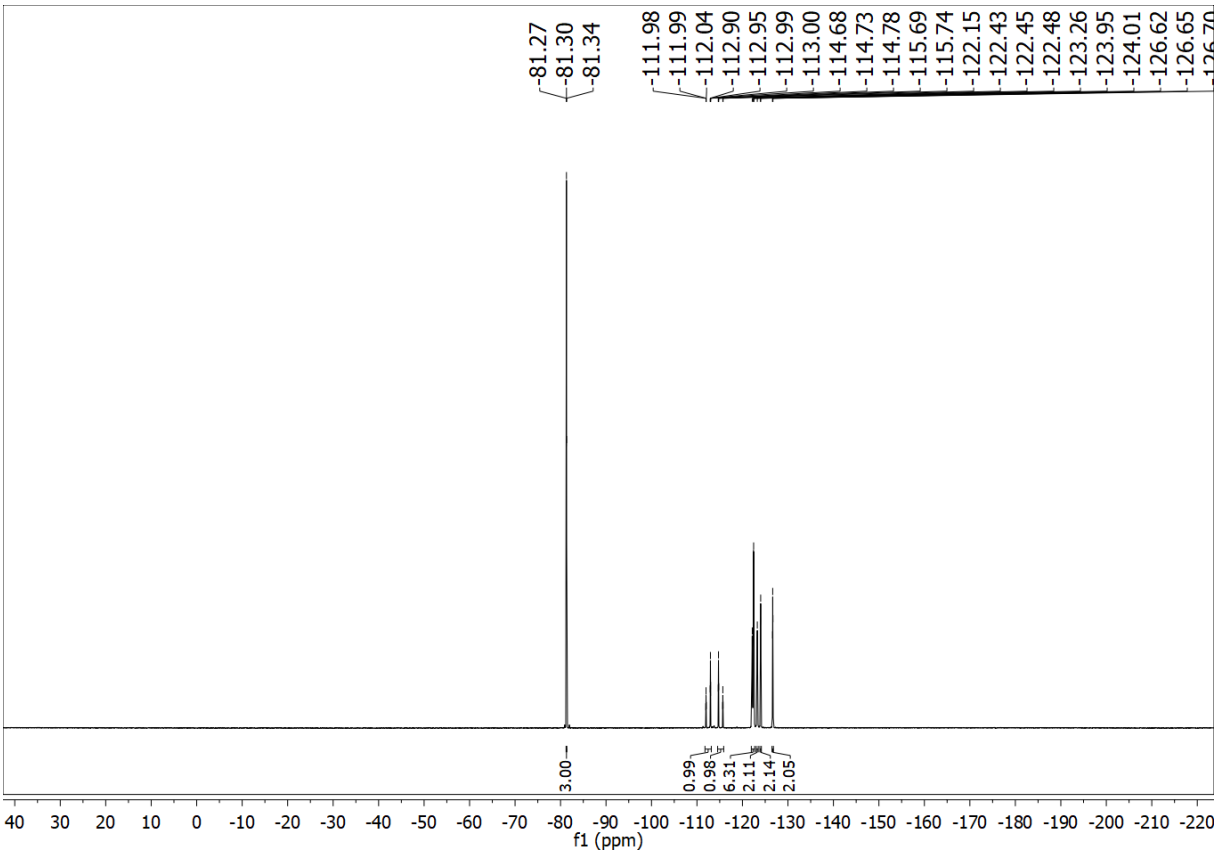


NMR-Solvent: $CDCl_3$

1-Chloro-4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-iododecyl)benzene (13b)

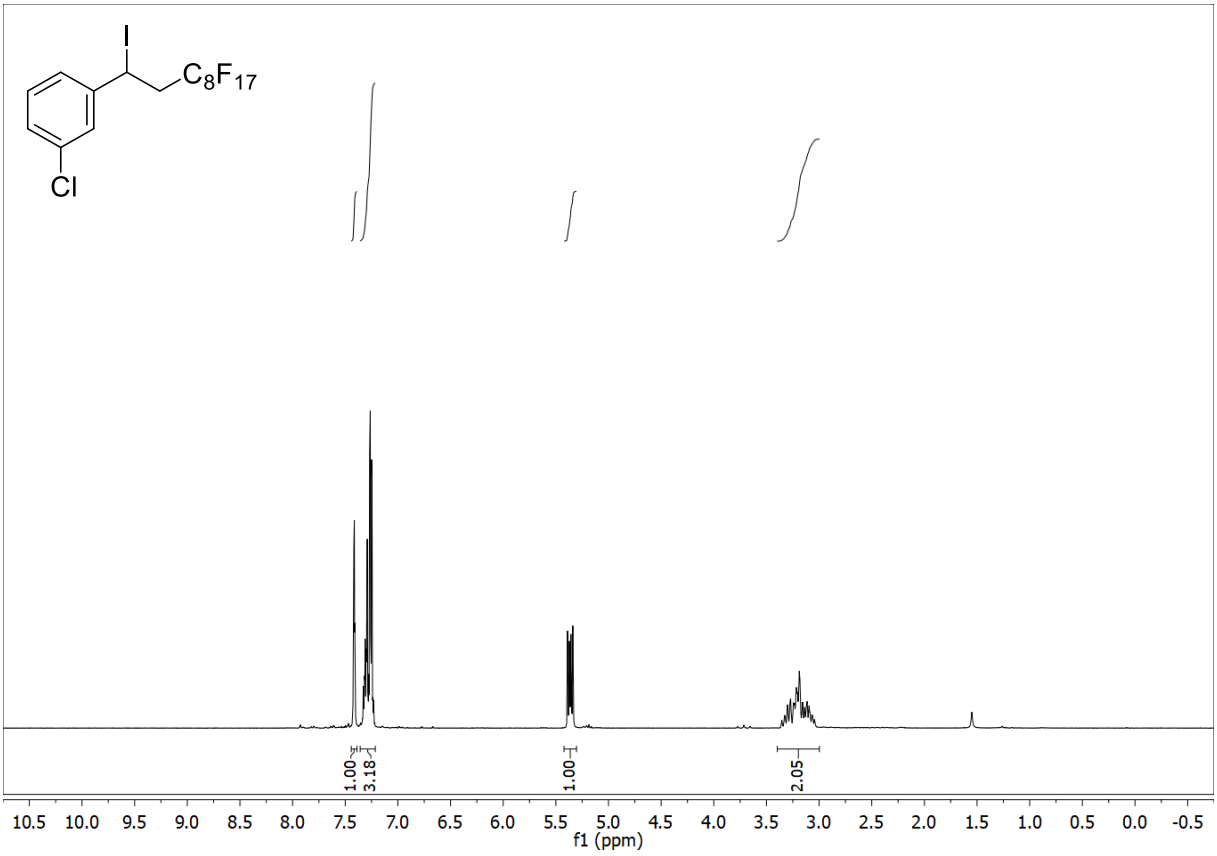


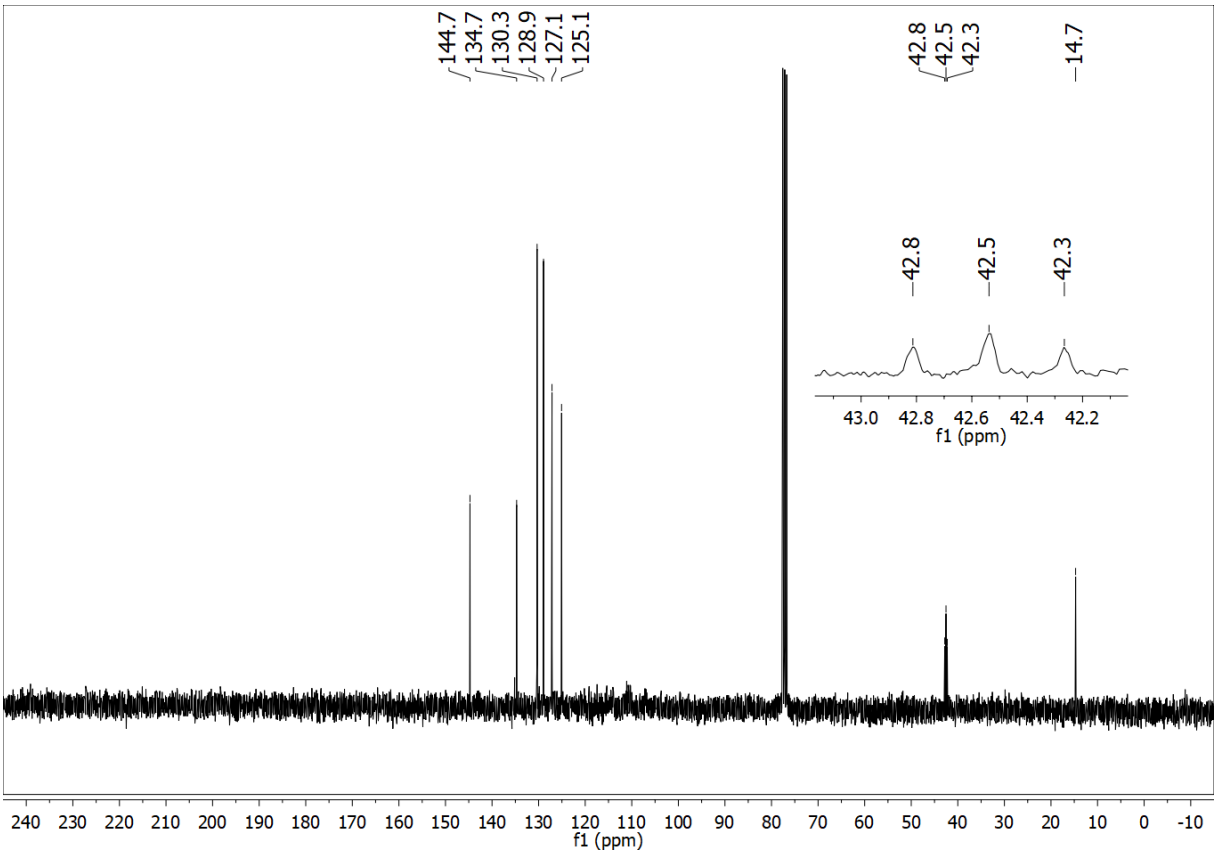


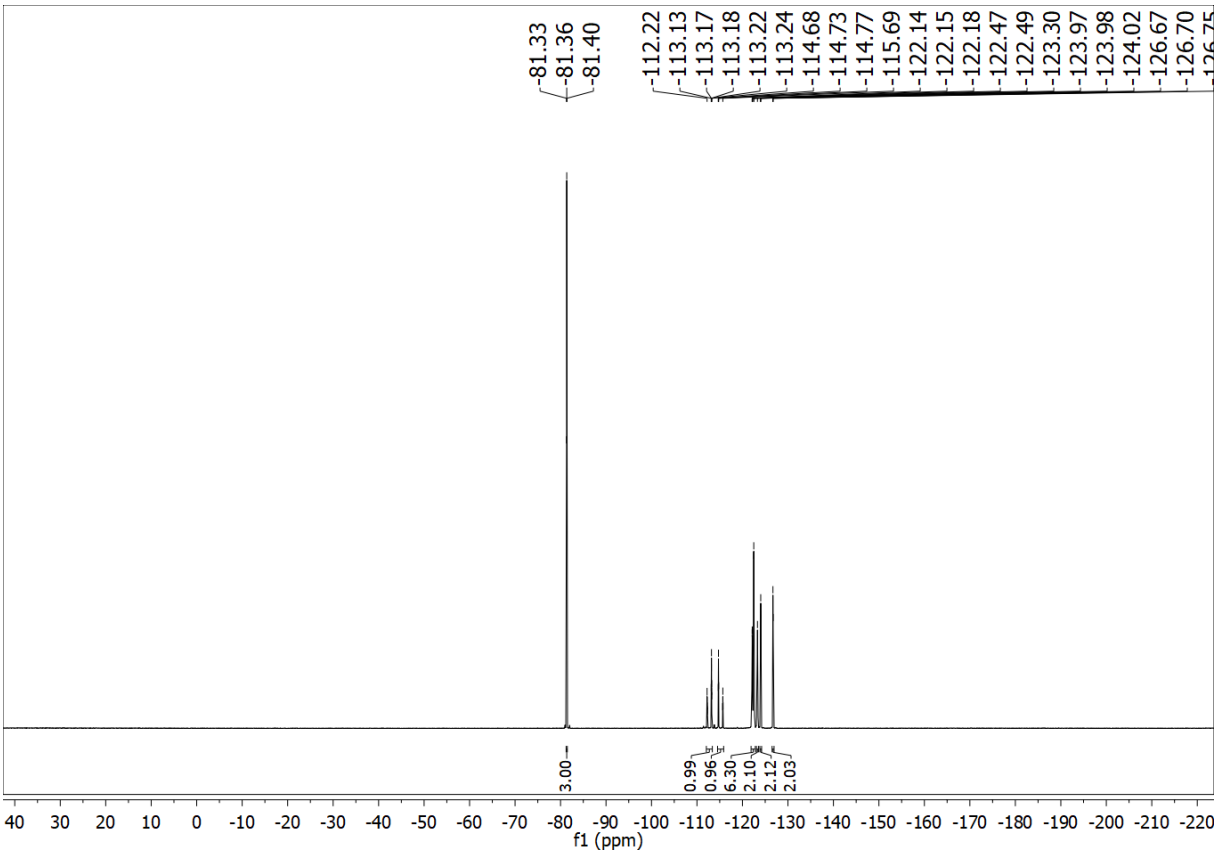


NMR-Solvent: $CDCl_3$

1-Chloro-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-iododecyl)benzene (13c)

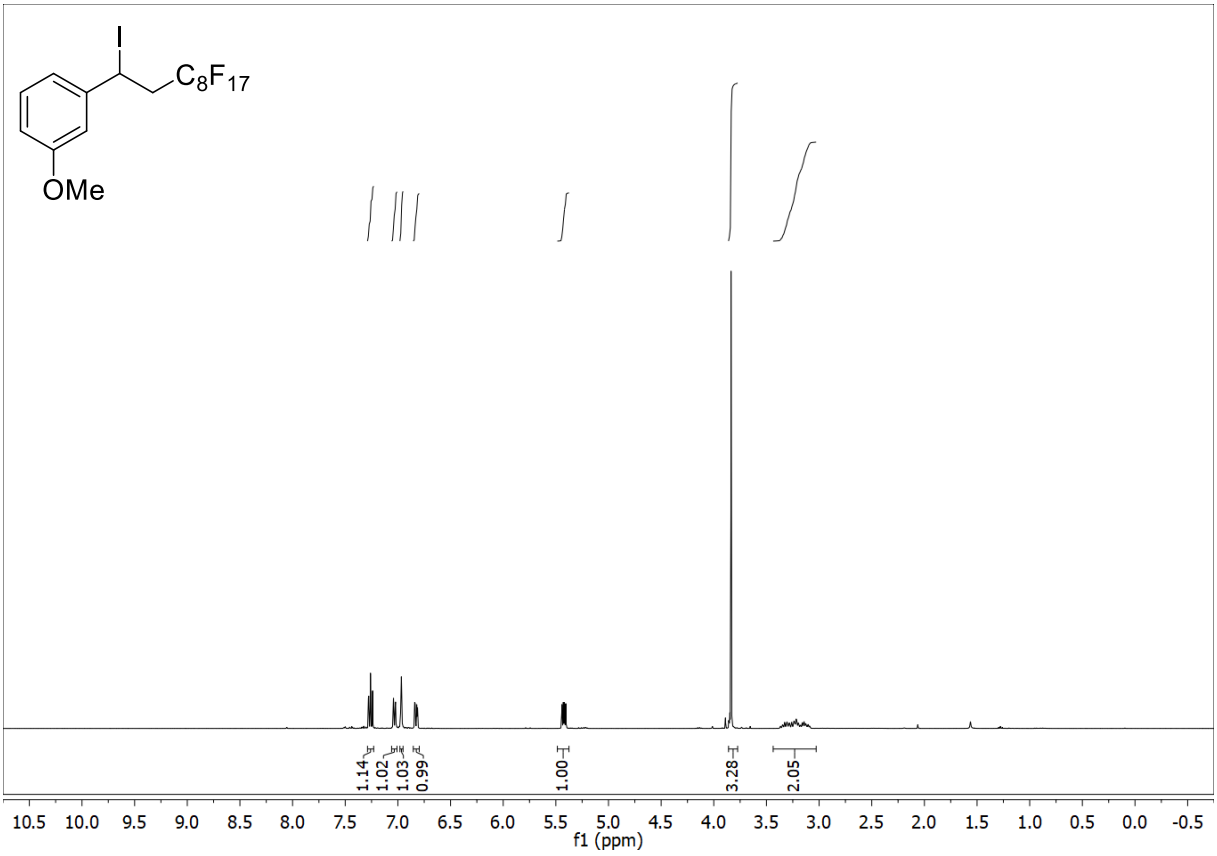


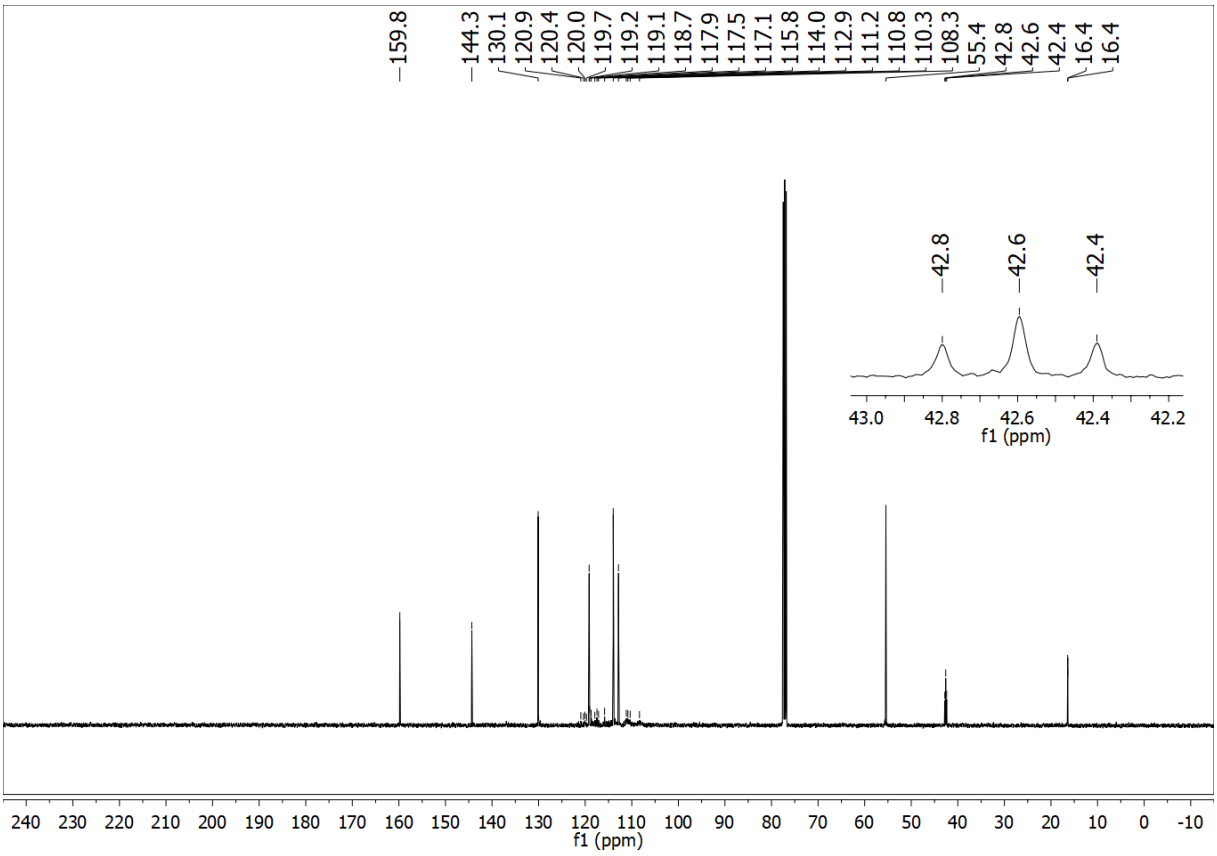


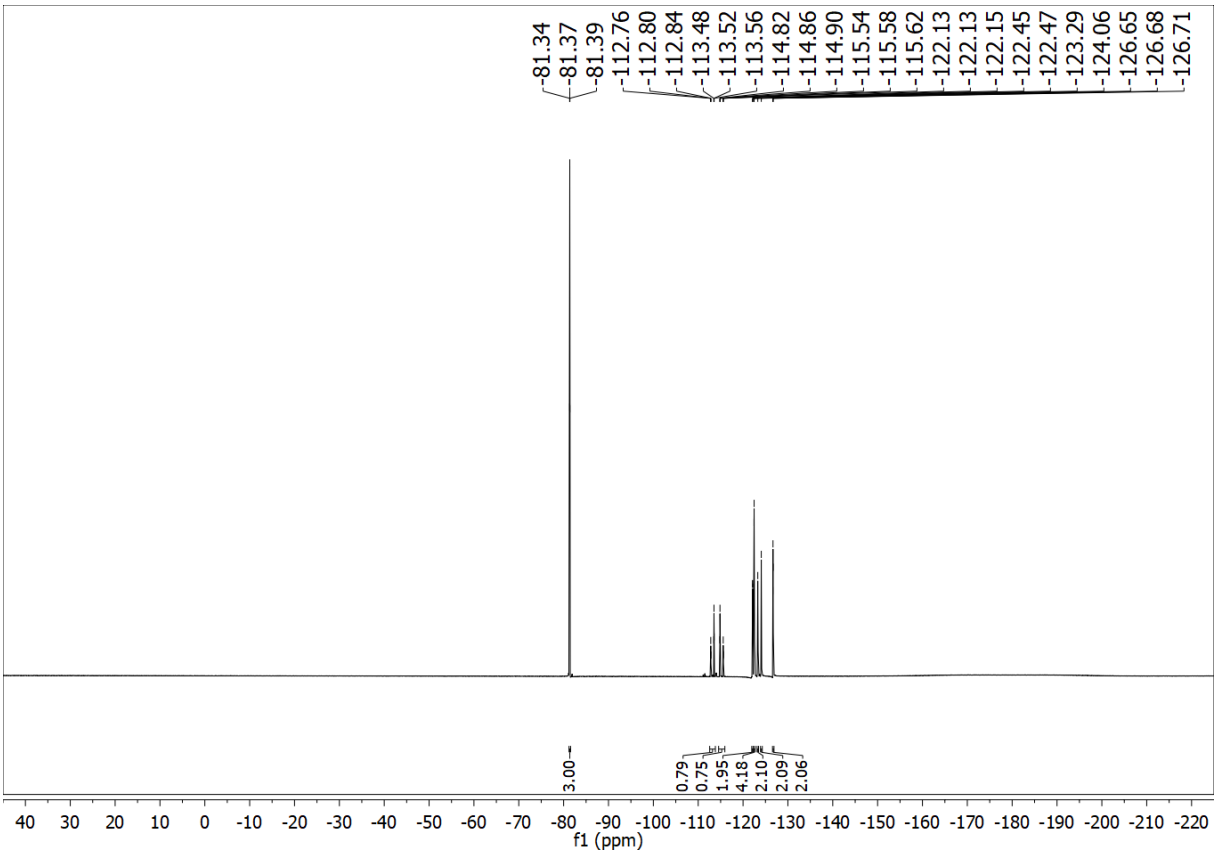


NMR-Solvent: $CDCl_3$

1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-iododecyl)-3-methoxybenzene (13d)

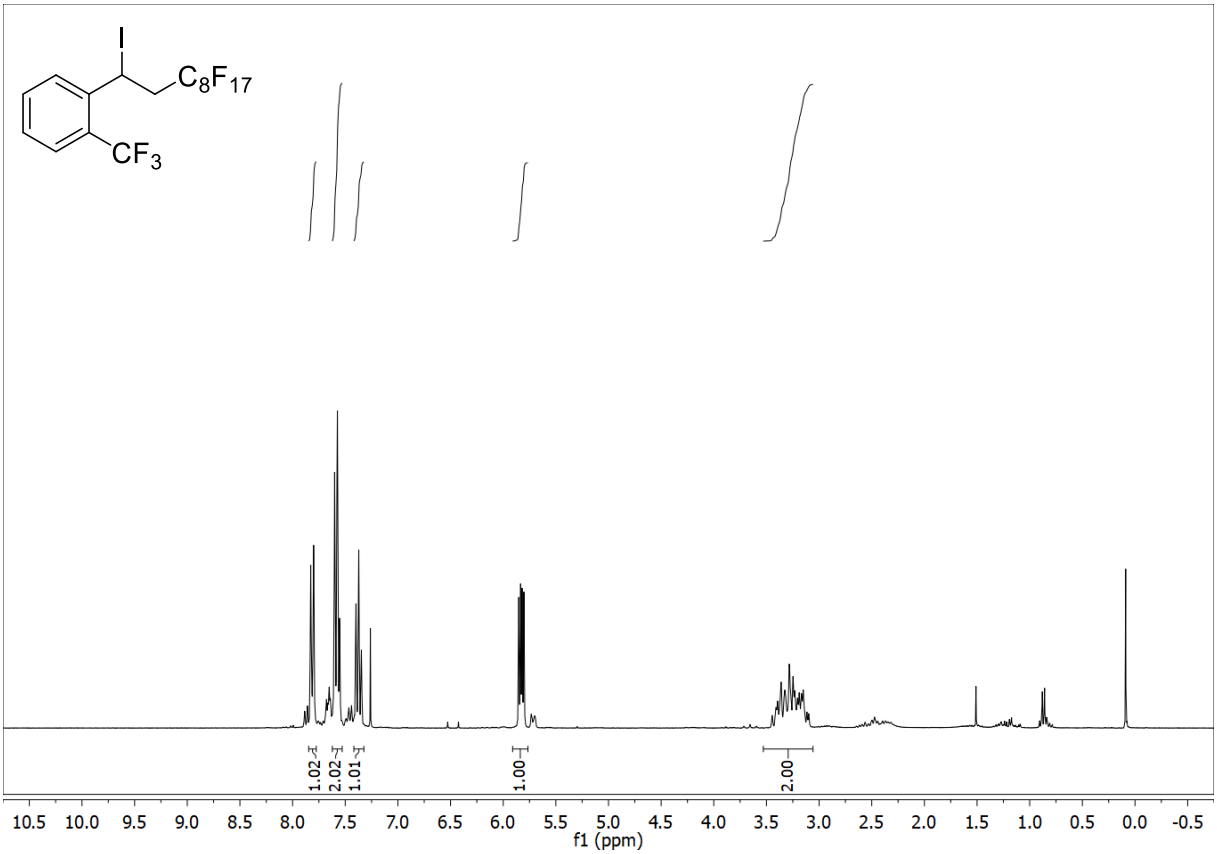


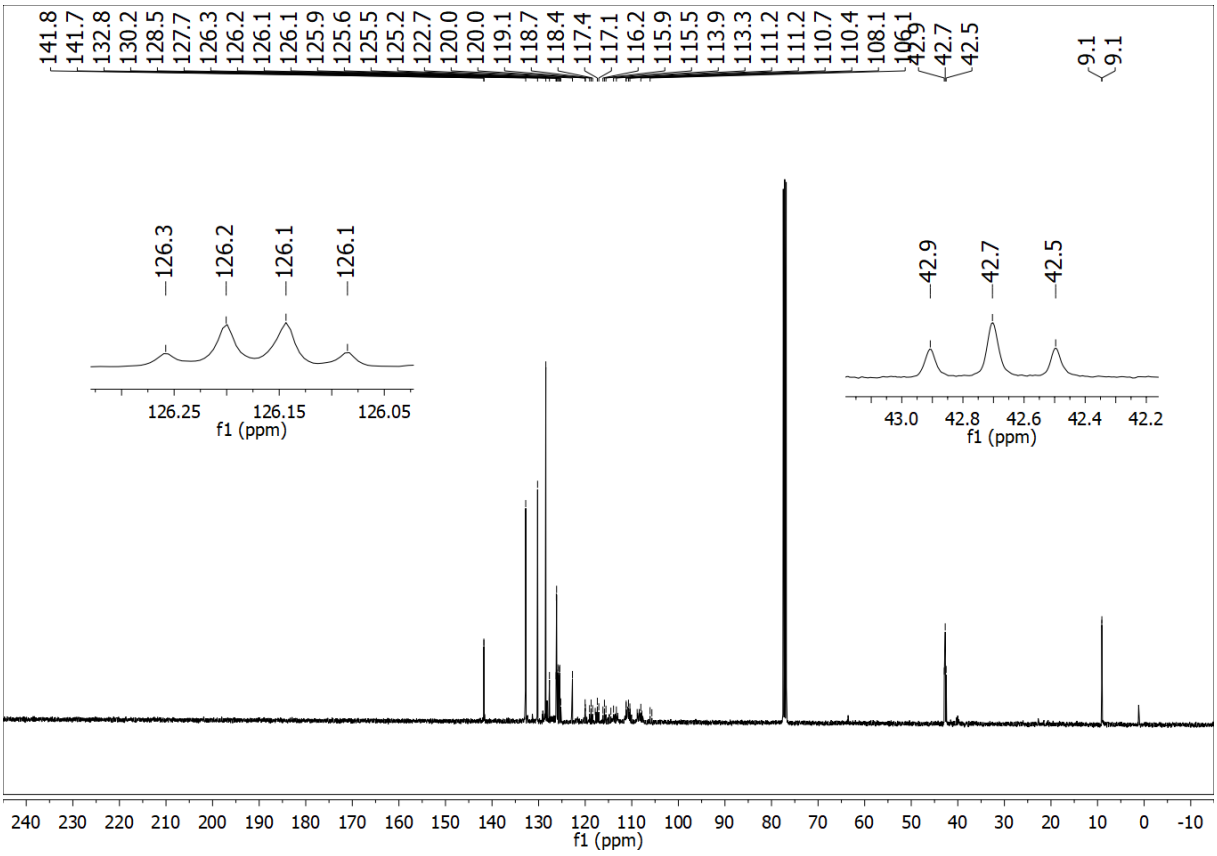


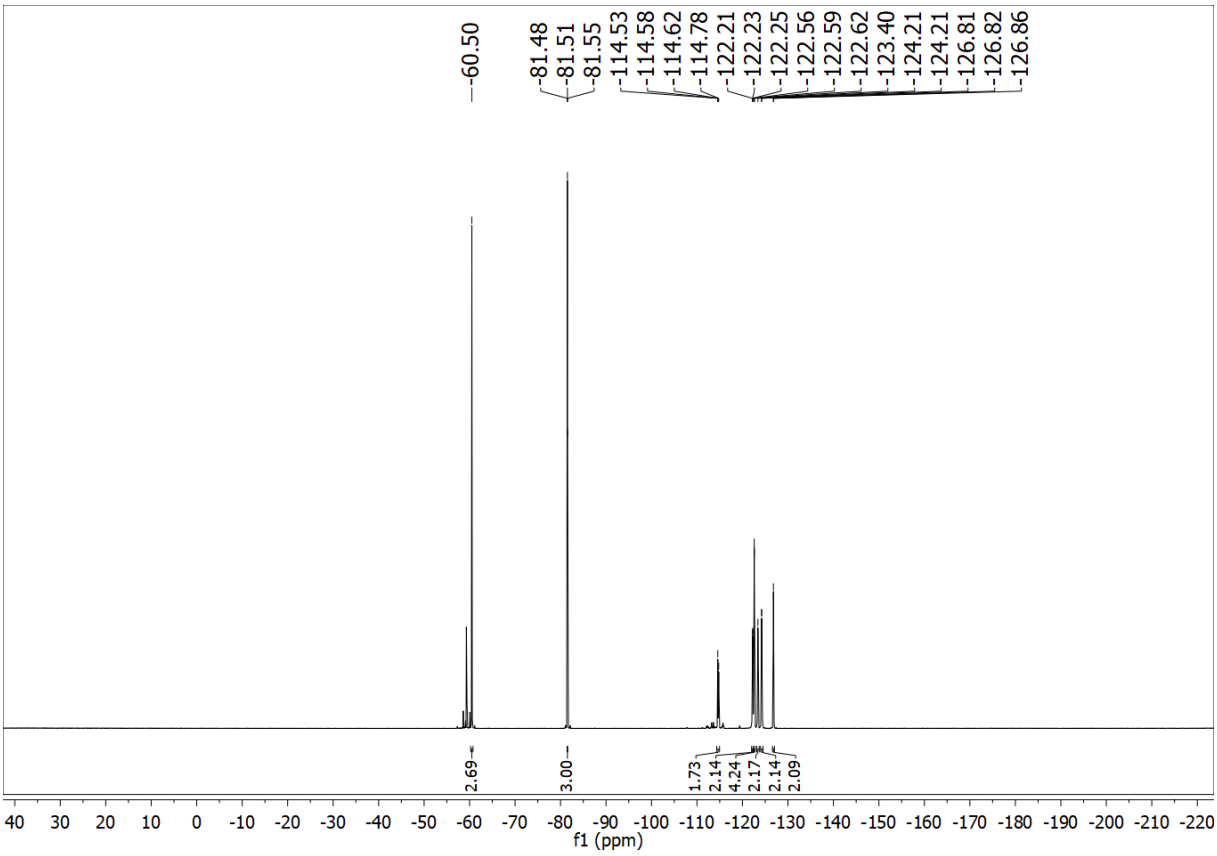


NMR-Solvent: $CDCl_3$

1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododecyl)-2-(trifluoromethyl) benzene (13e)

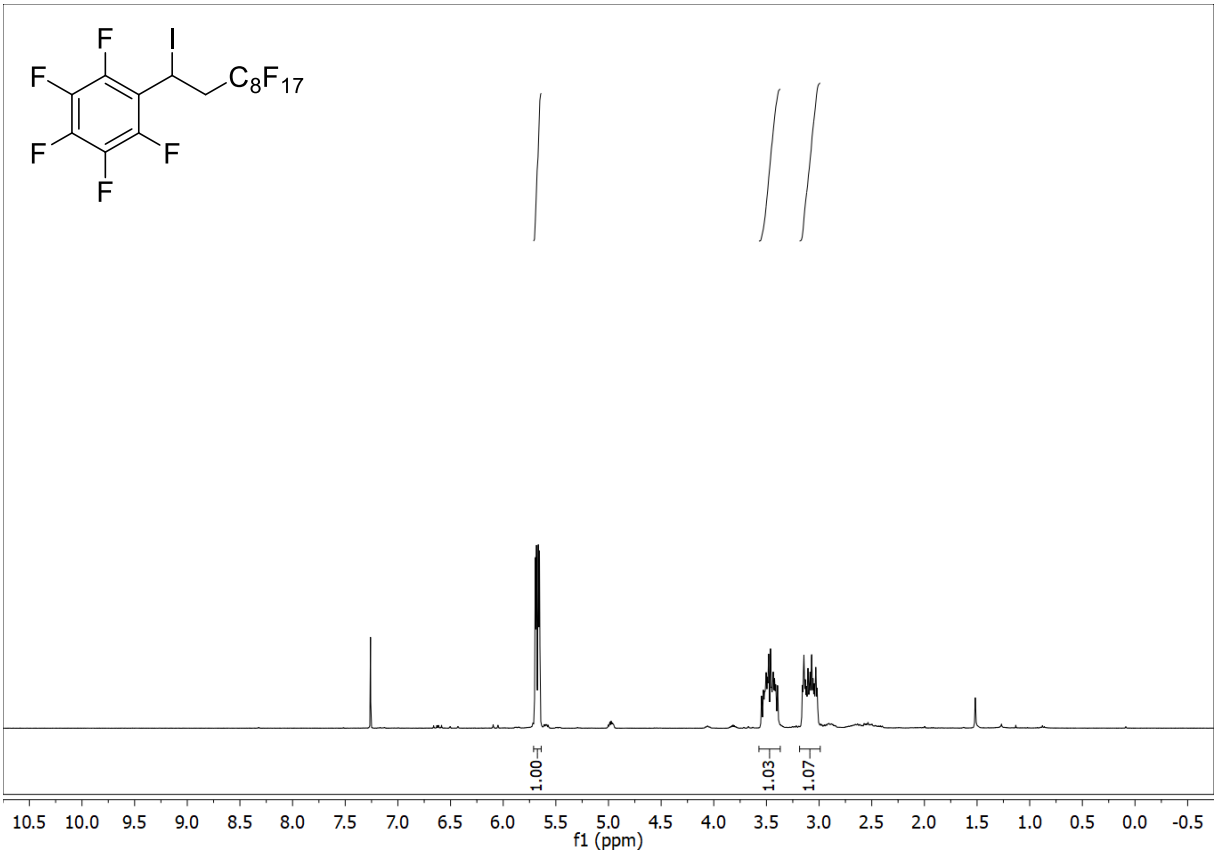


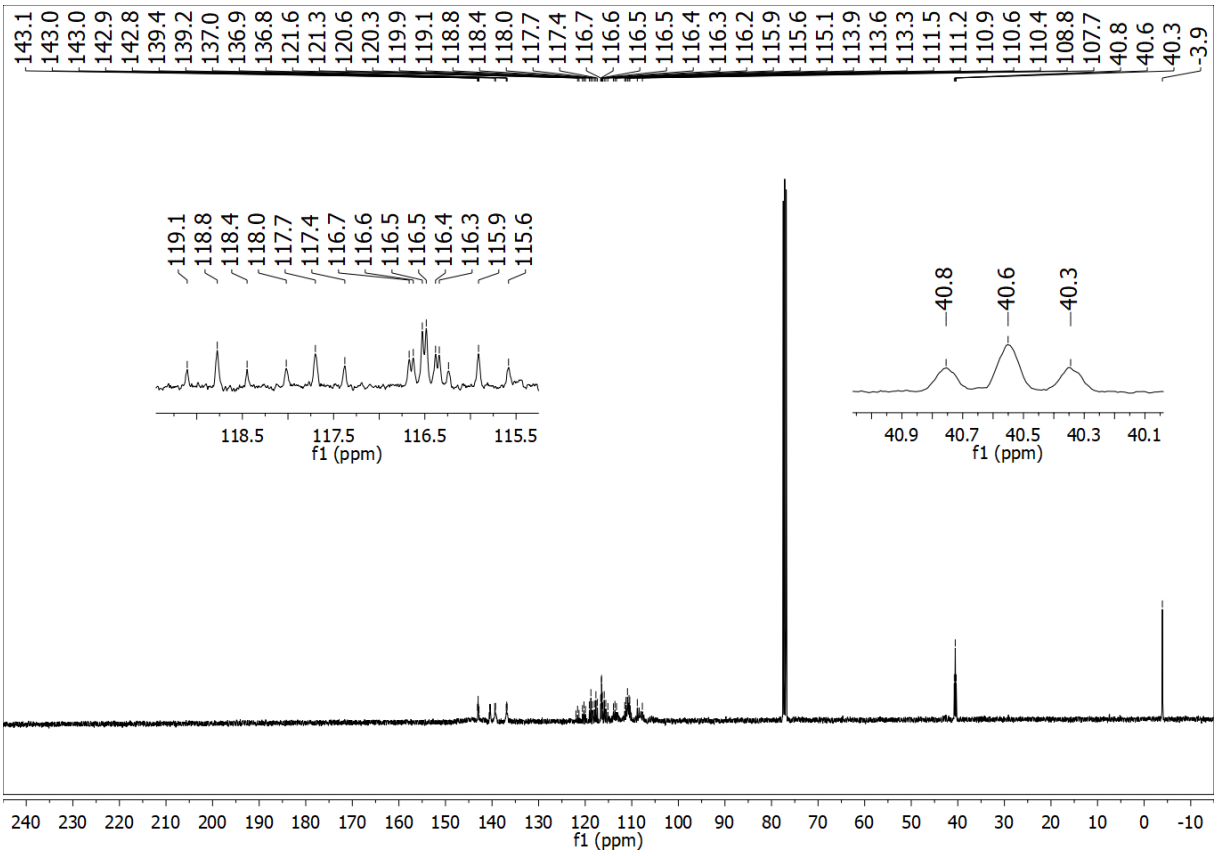


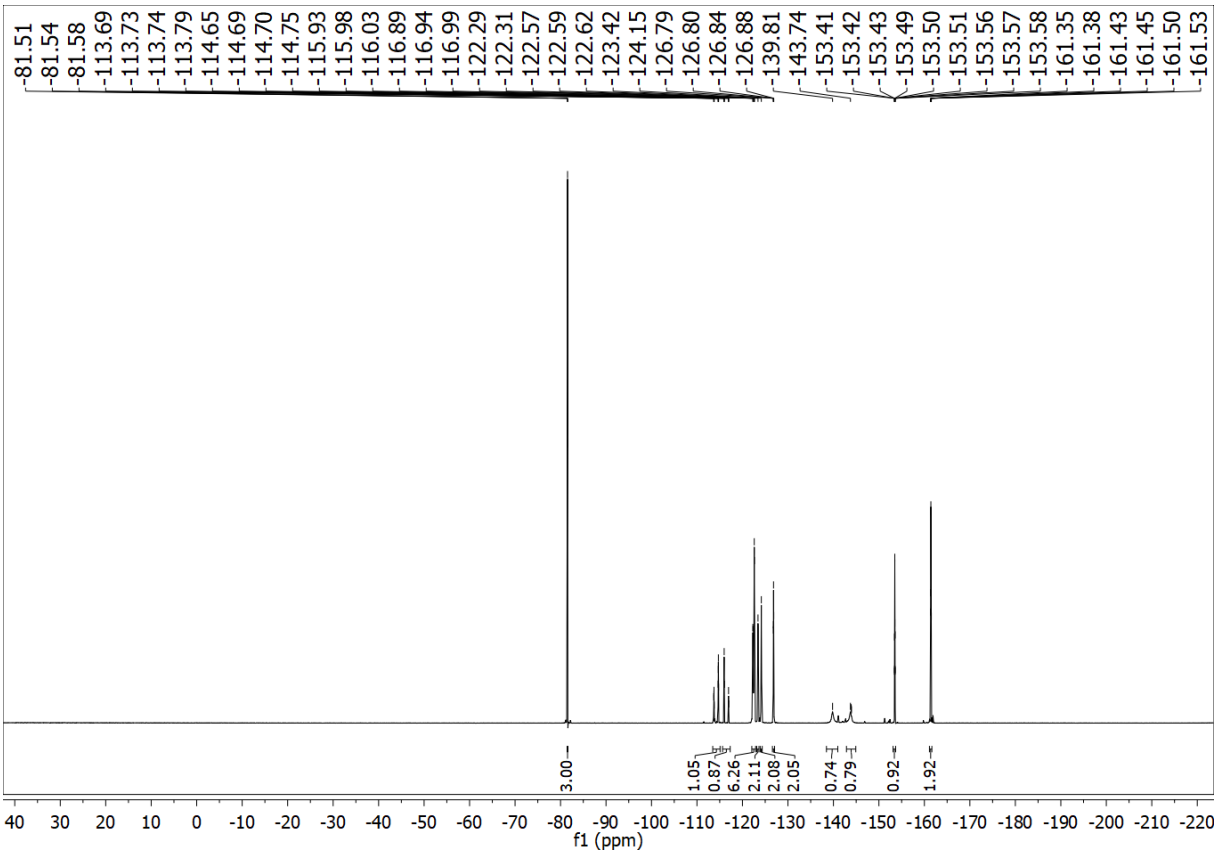


NMR-Solvent: $CDCl_3$

1,2,3,4,5-pentafluoro-6-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-iododecyl)benzene (13f)

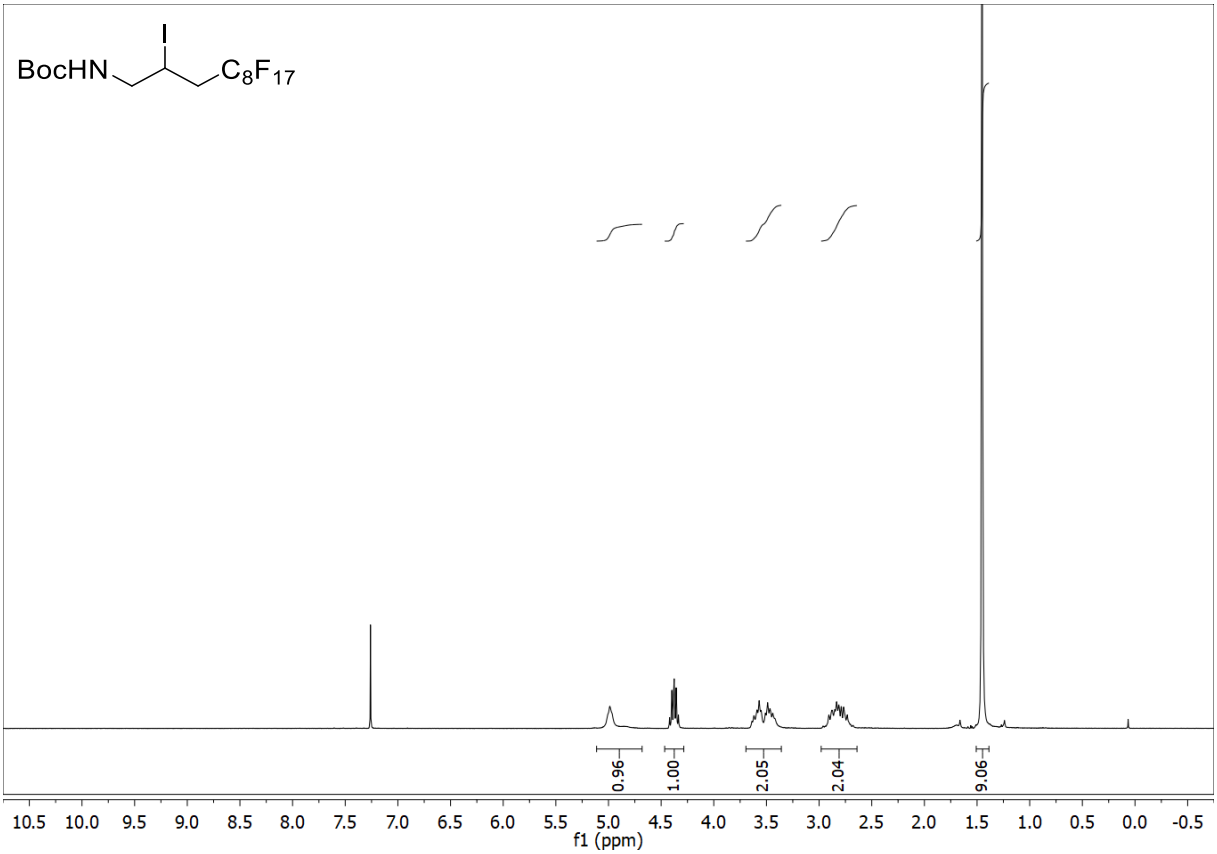


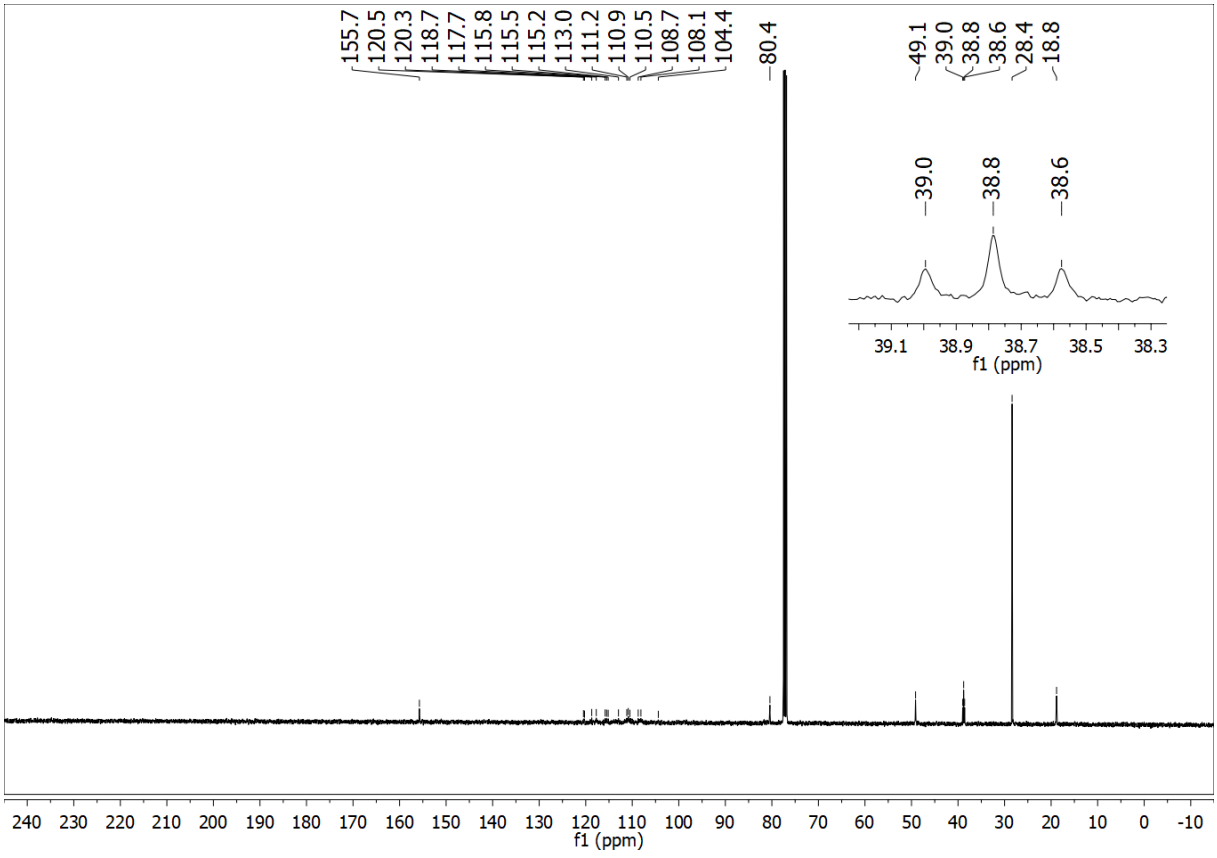


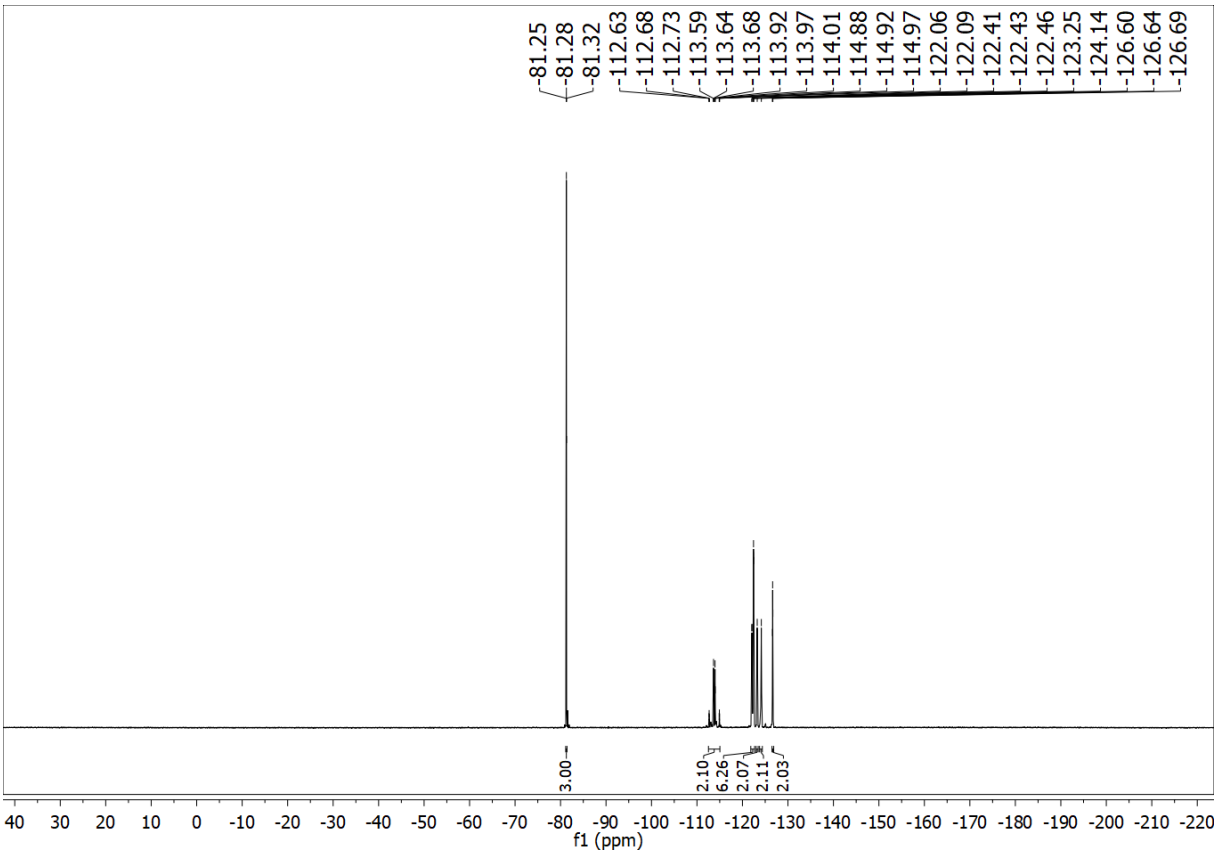


NMR-Solvent: $CDCl_3$

***tert*-Butyl (4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl) carbamate (7b)**

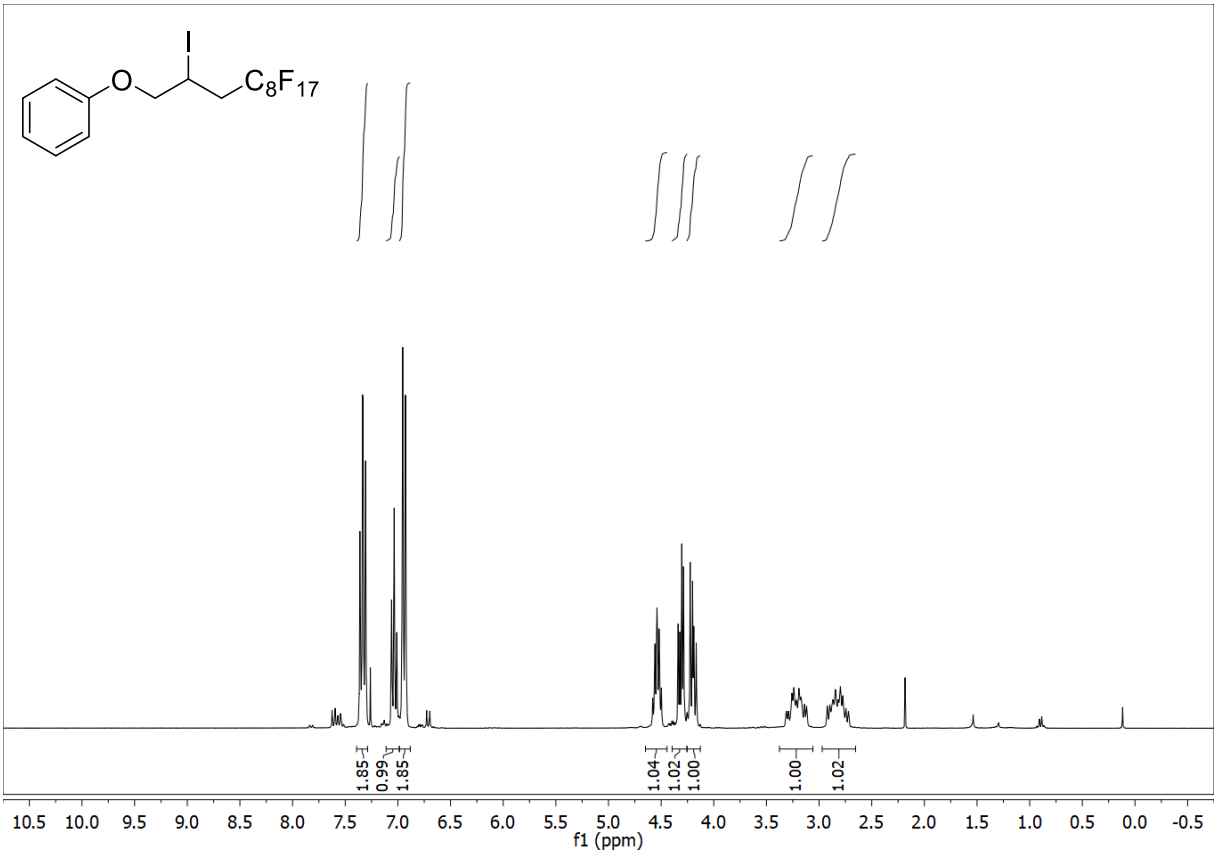


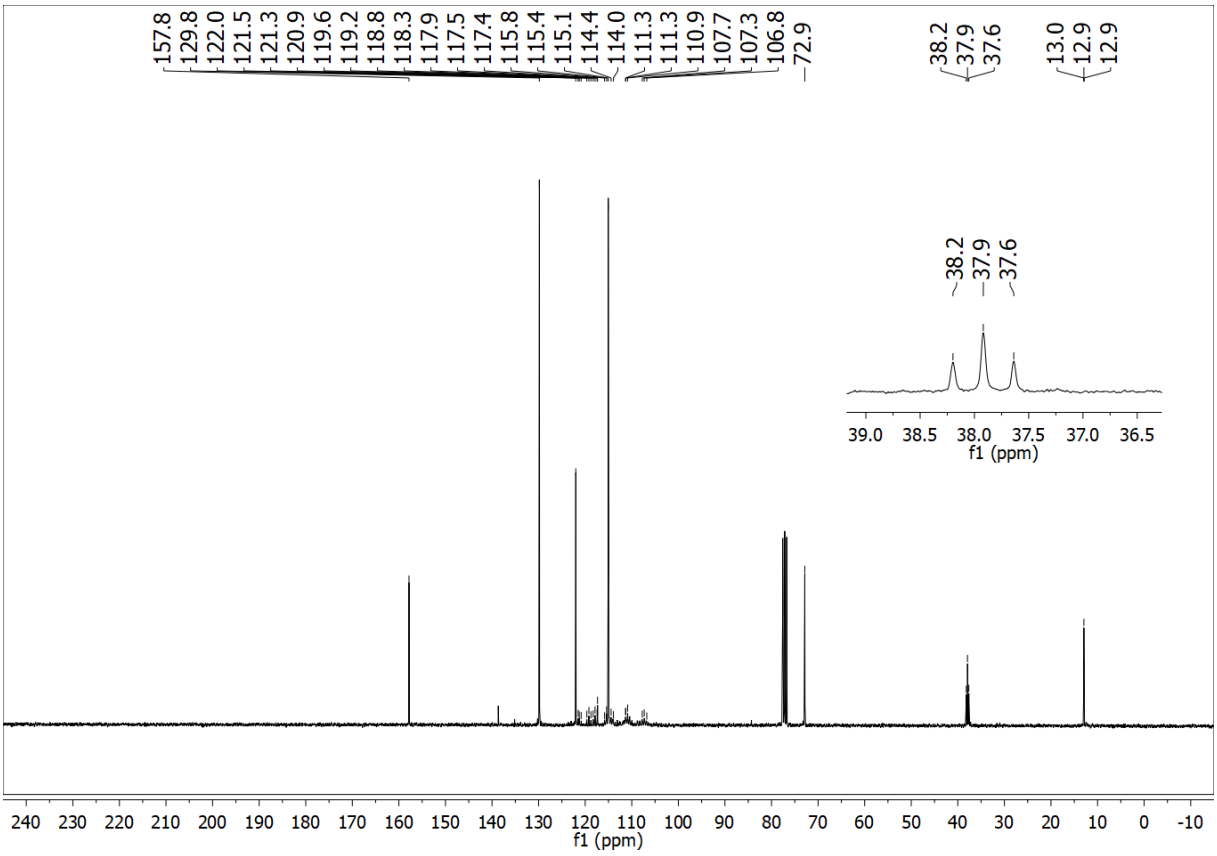


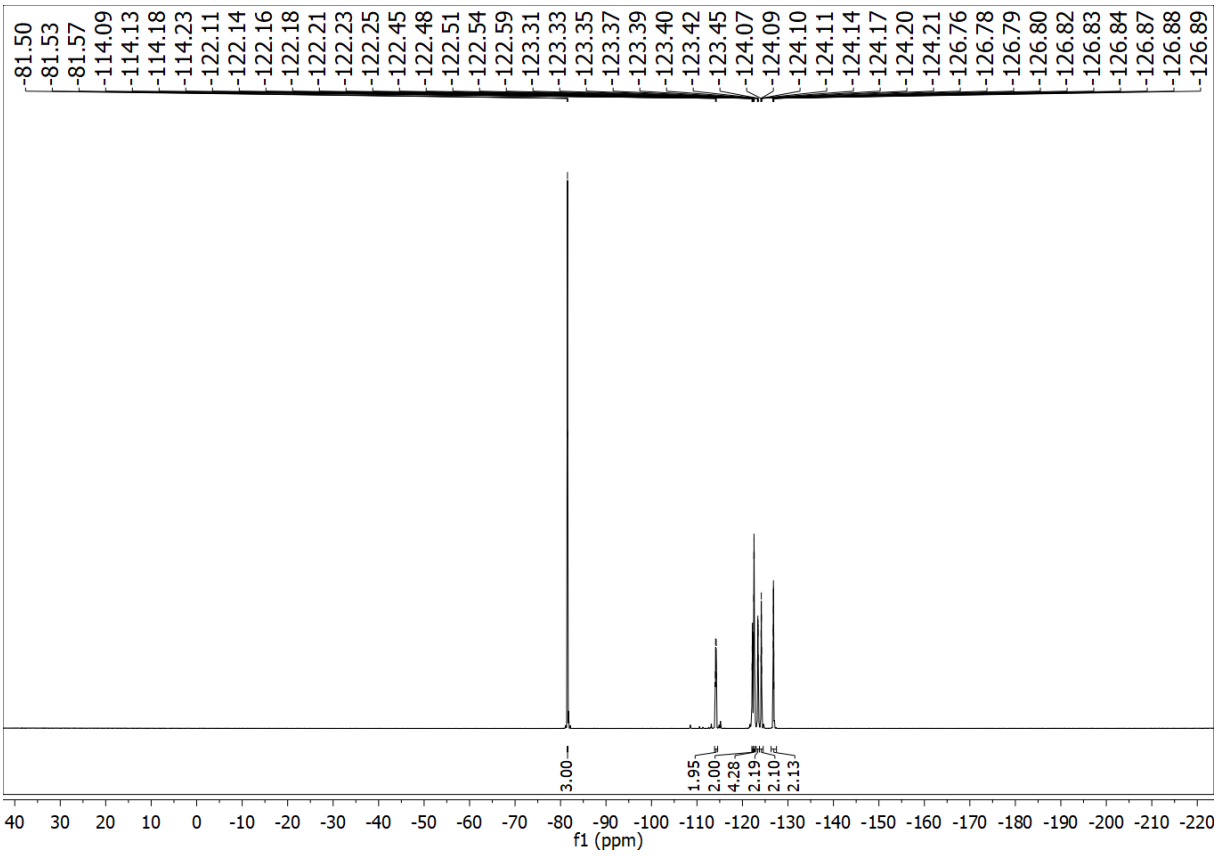


NMR-Solvent: $CDCl_3$

((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)oxy)benzene (15a)

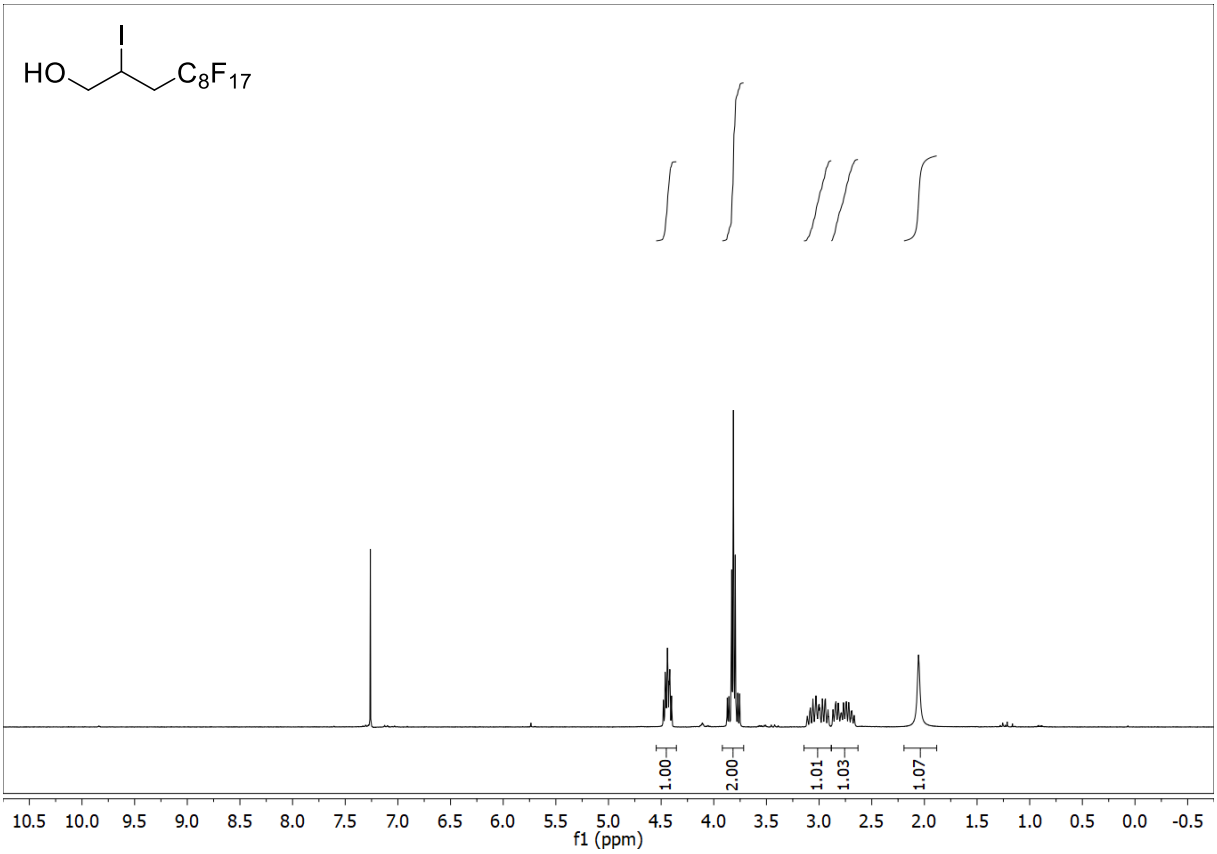


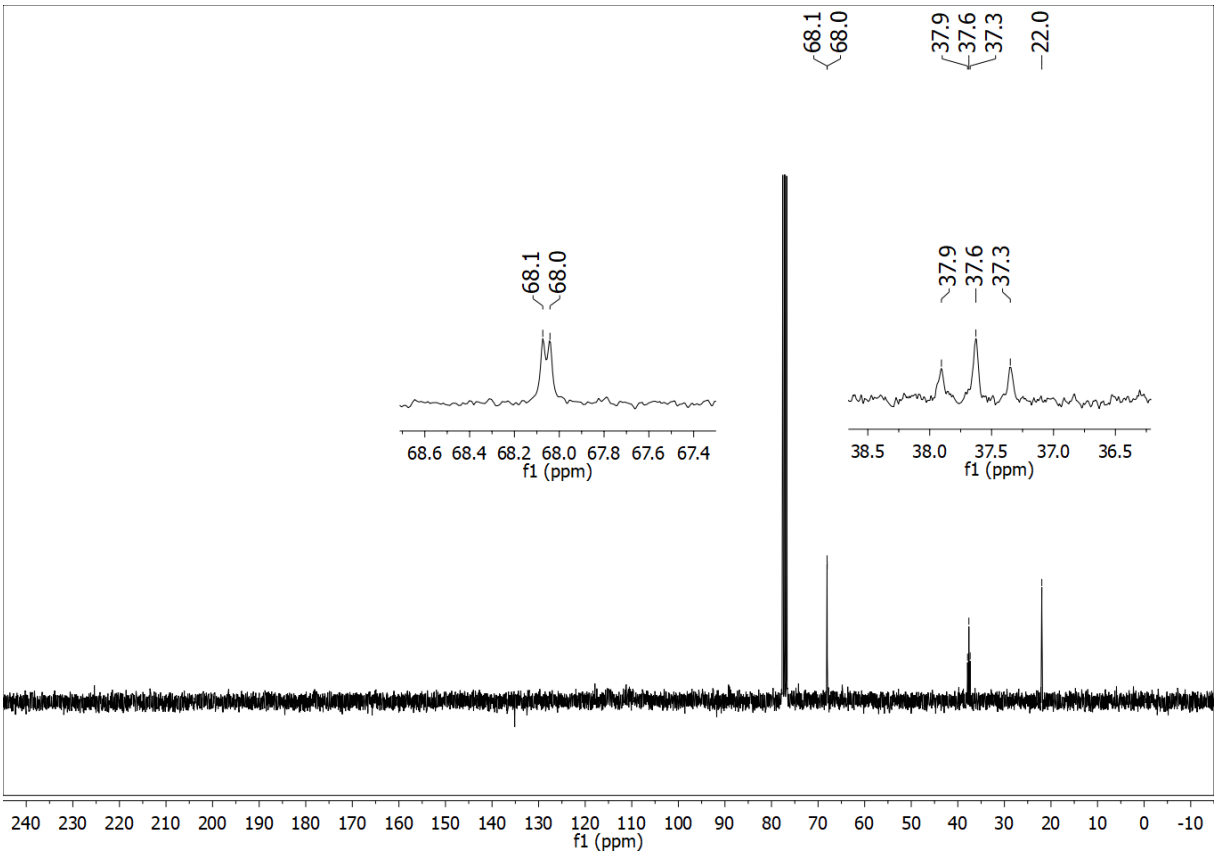


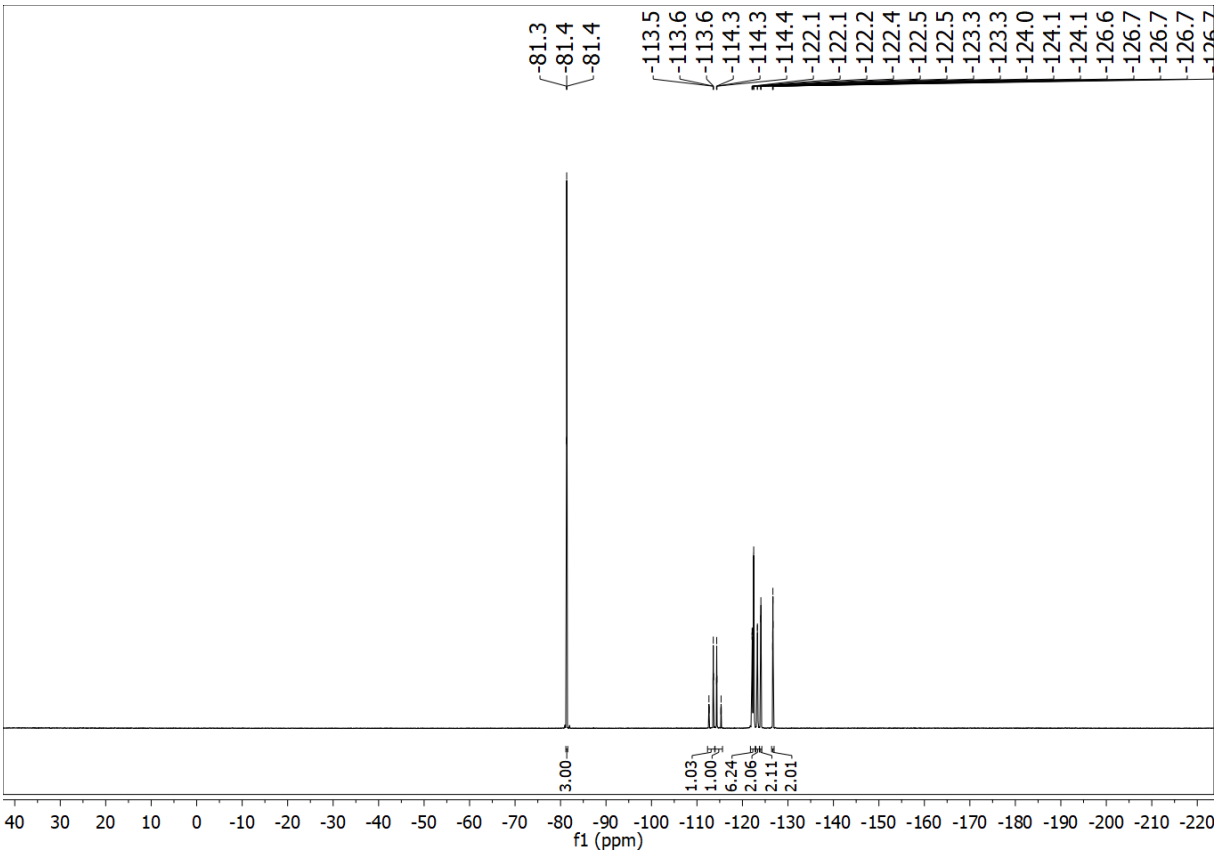


NMR-Solvent: $CDCl_3$

4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecan-1-ol (7j)

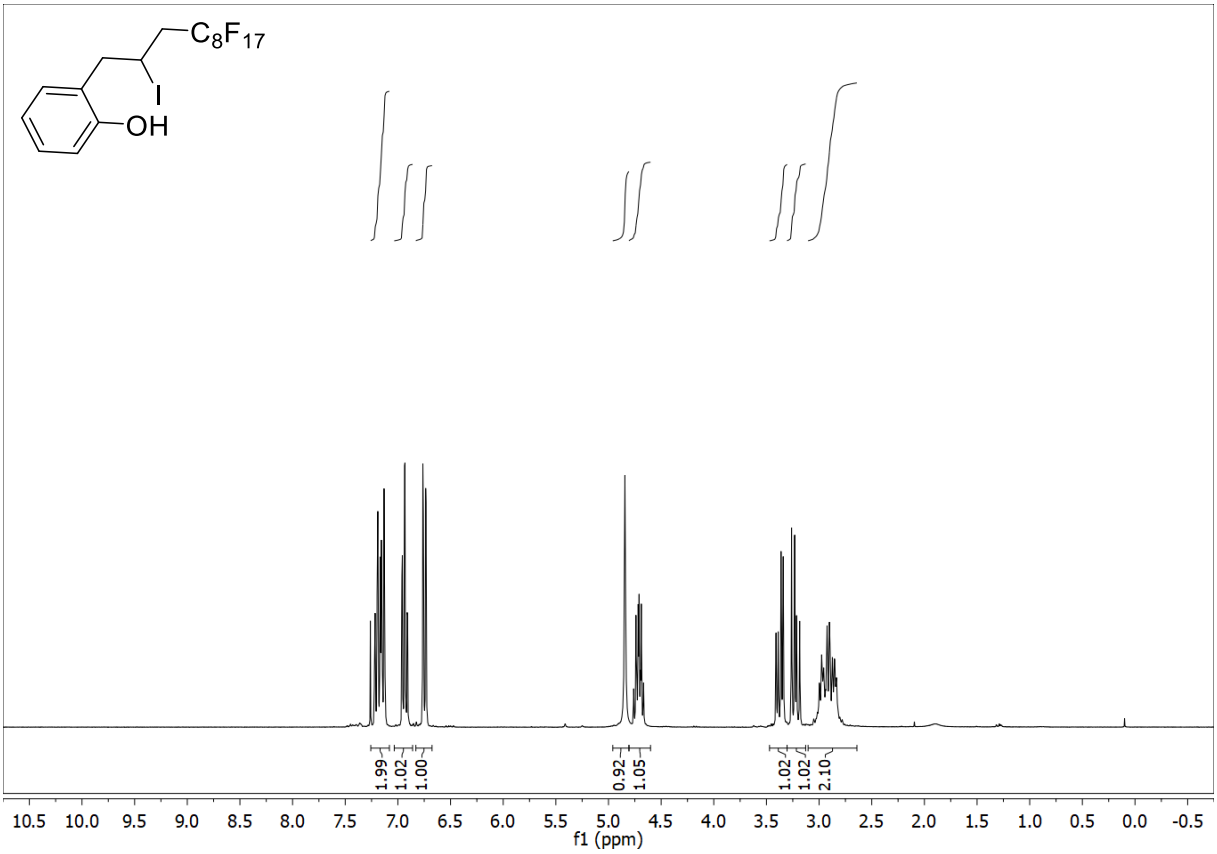


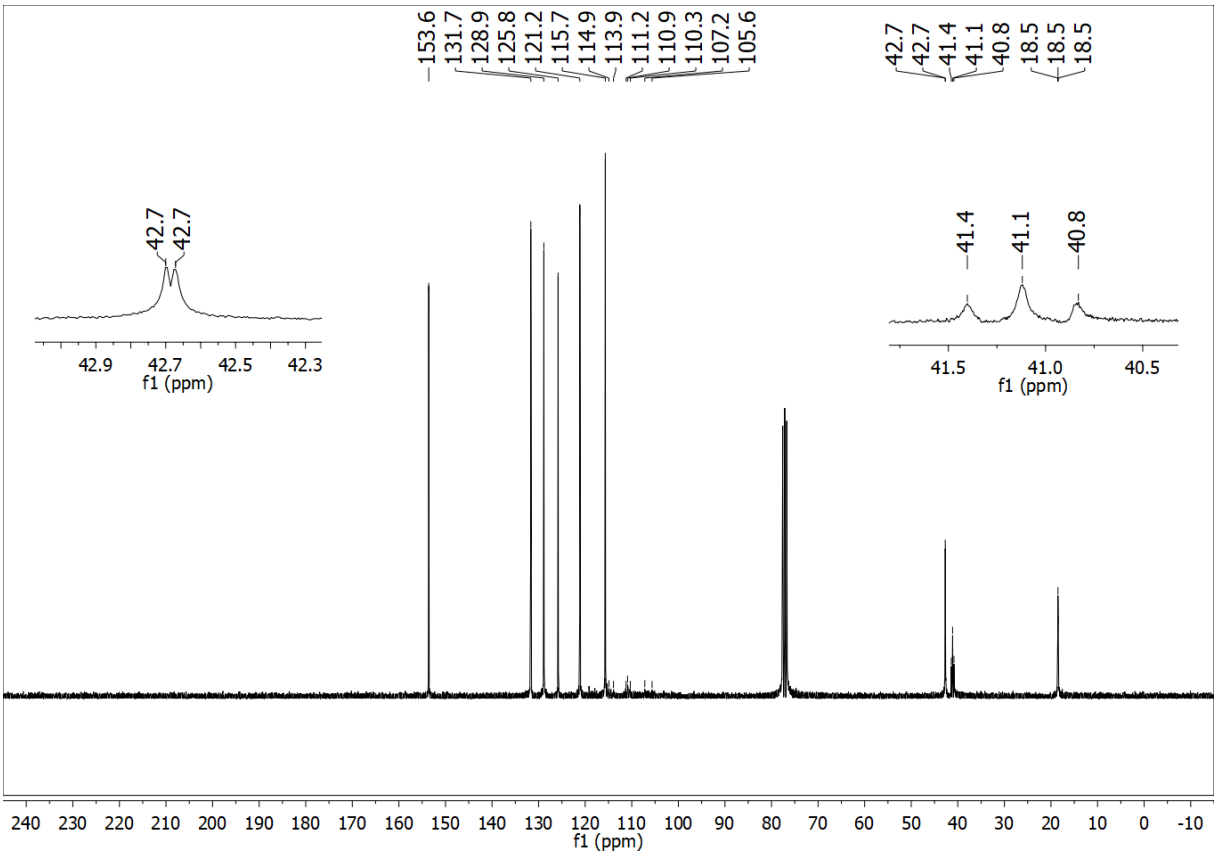


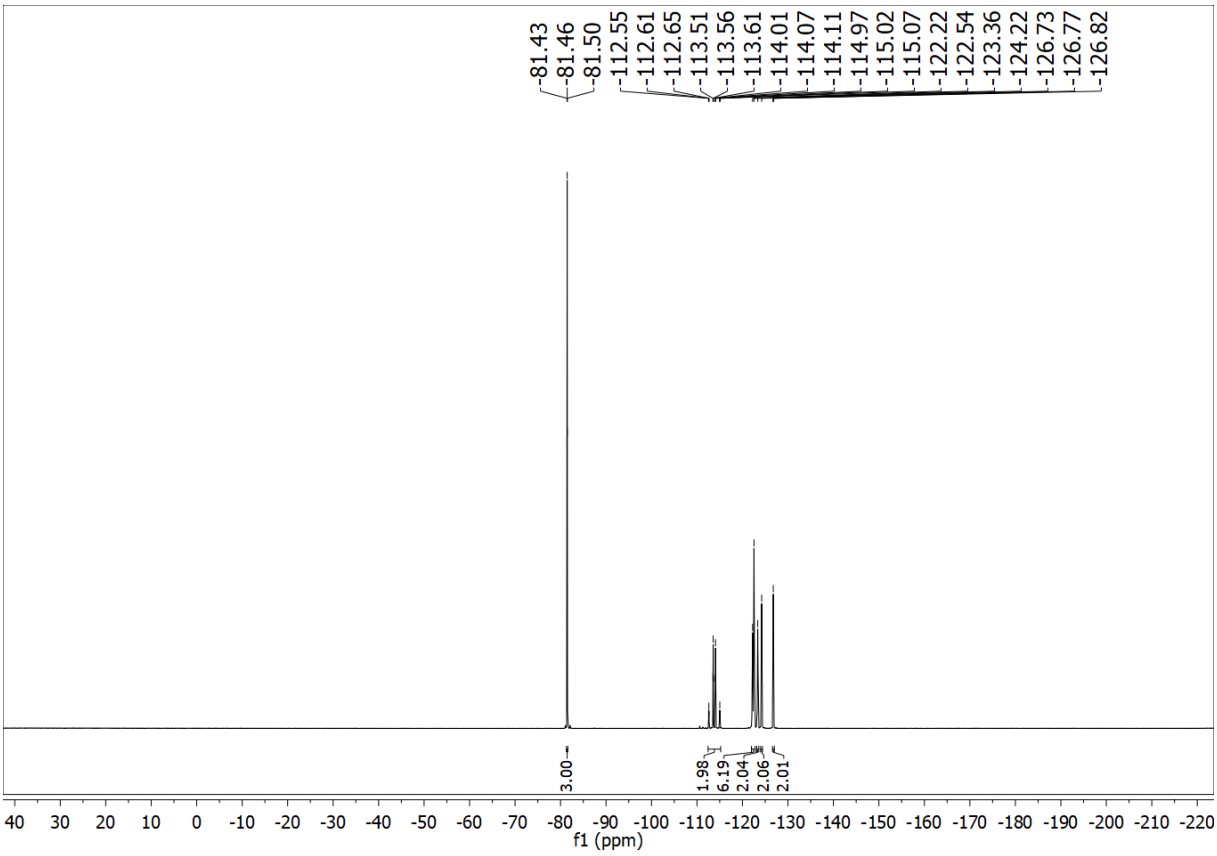


NMR-Solvent: $CDCl_3$

2-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)phenol (15b)

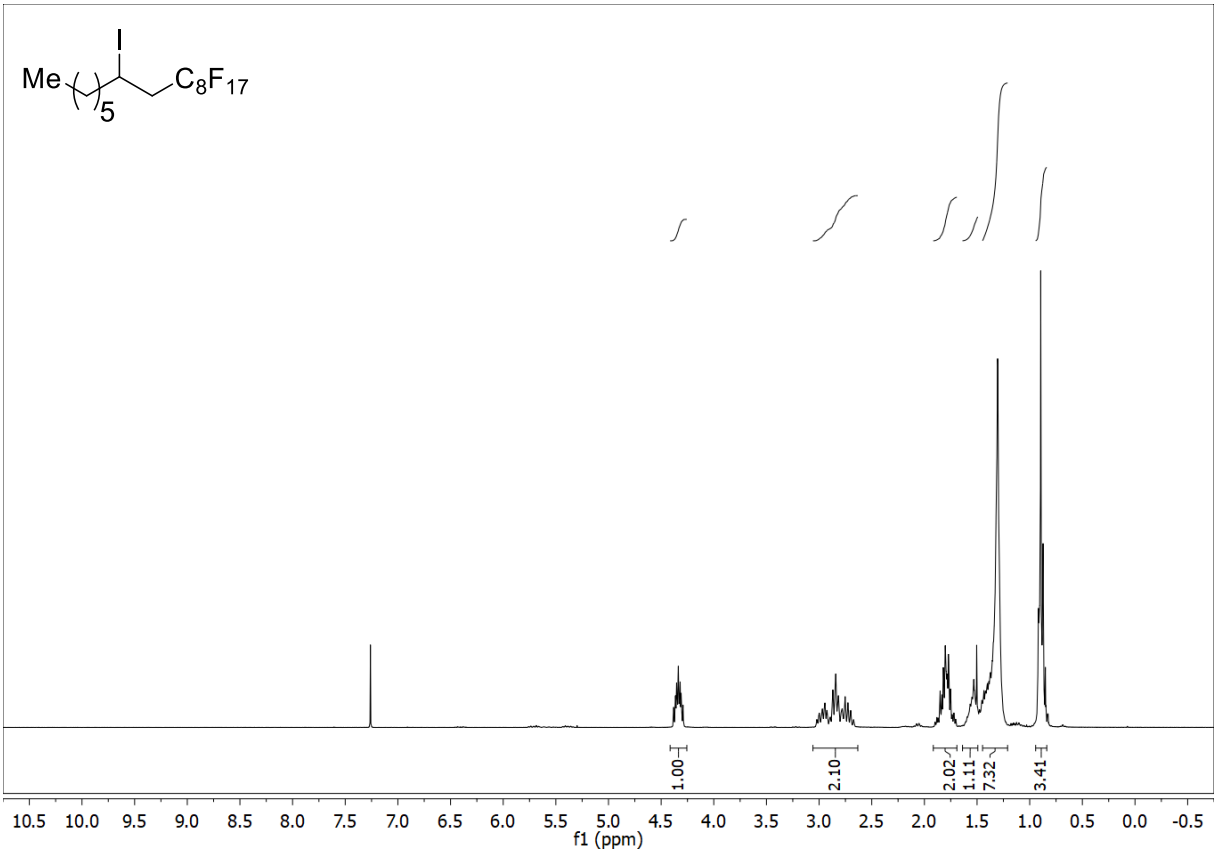


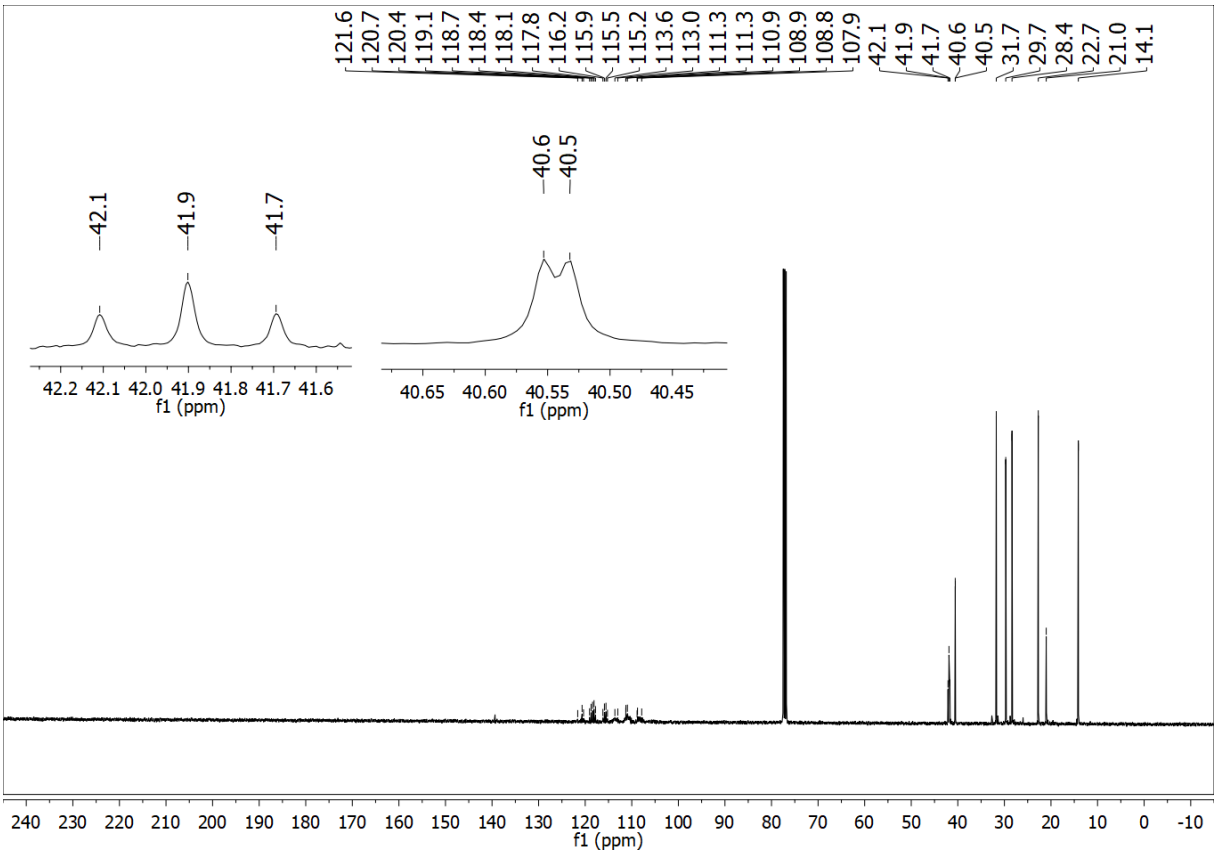


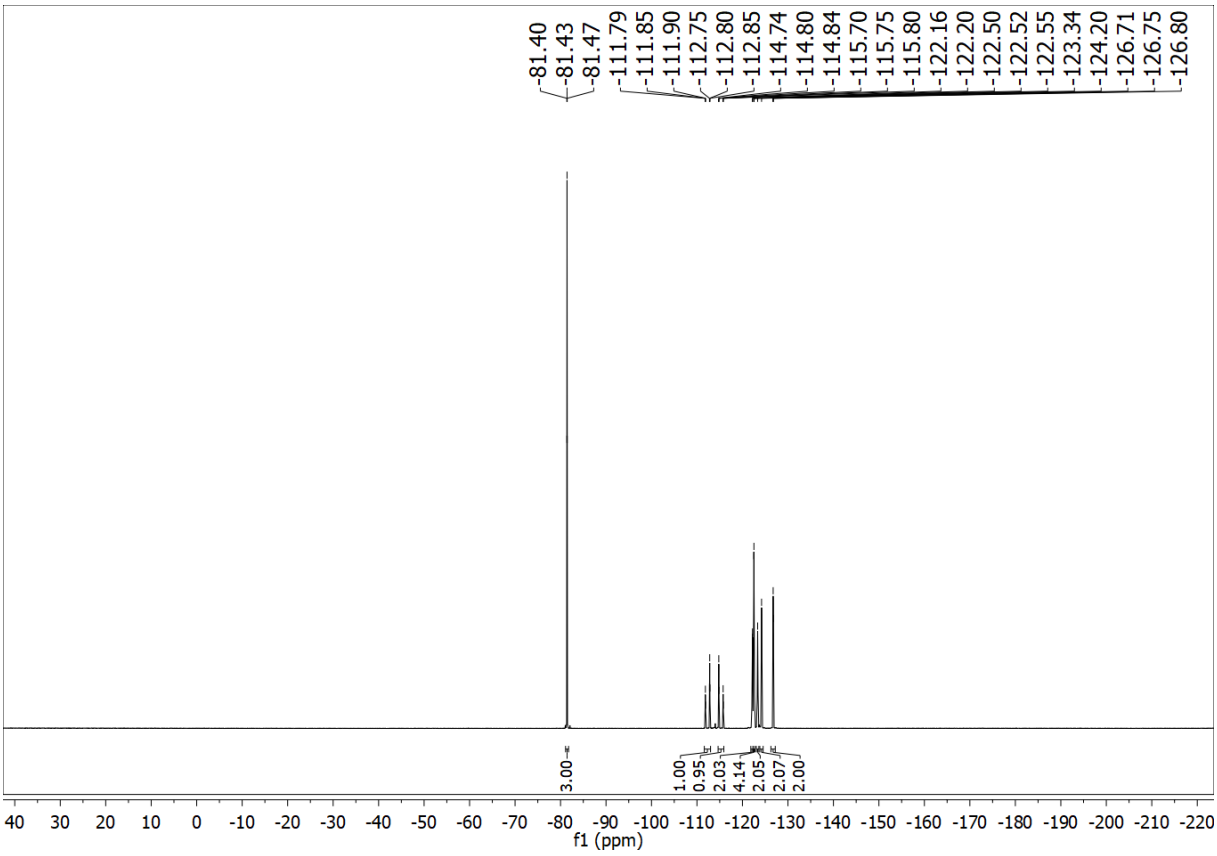


NMR-Solvent: $CDCl_3$

1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-Heptadecafluoro-10-iodohexadecane (15c)

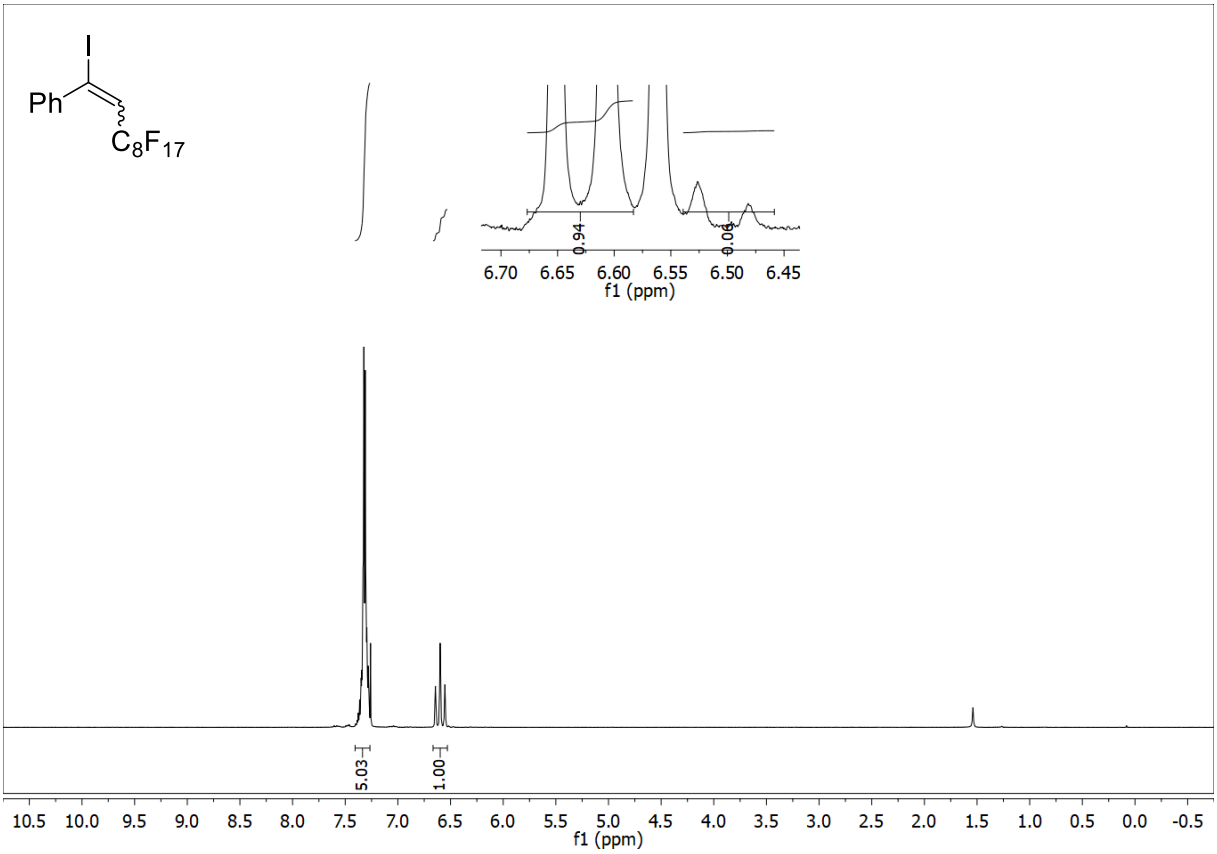


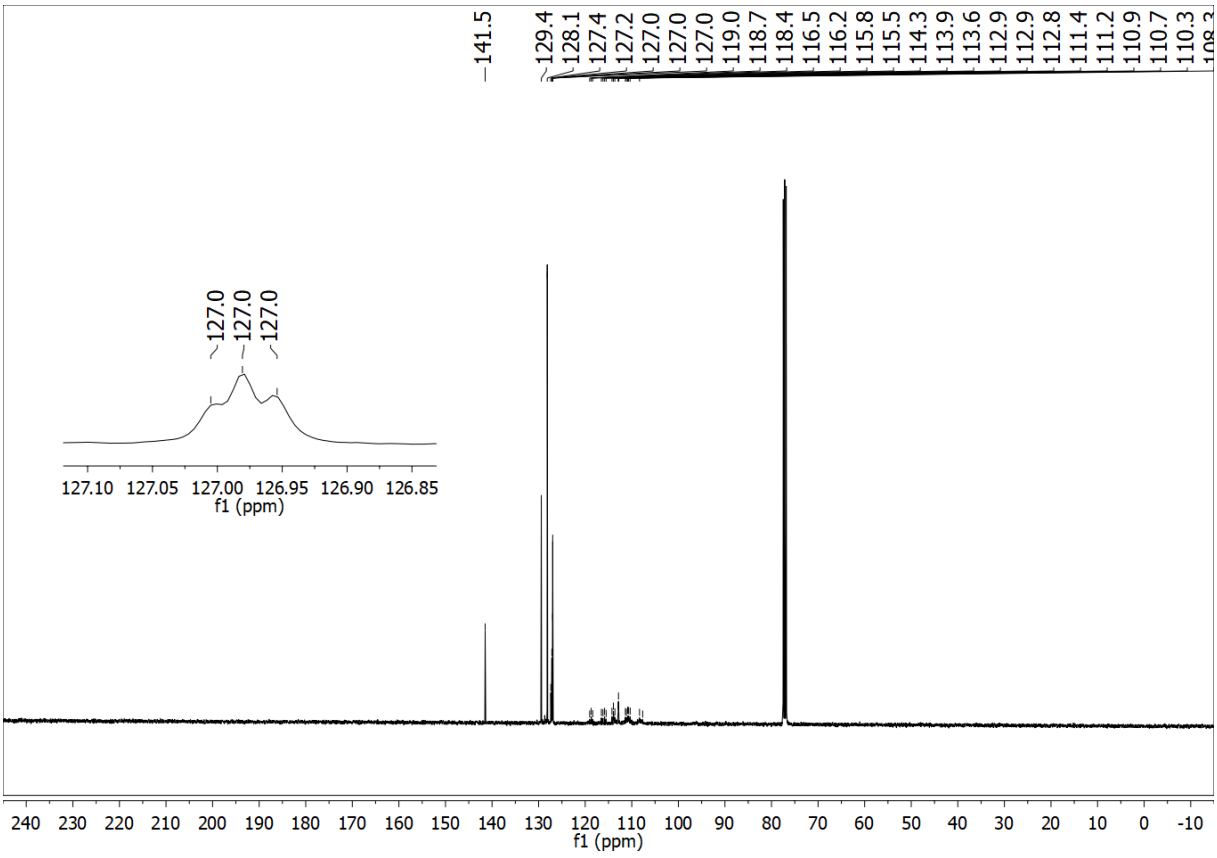


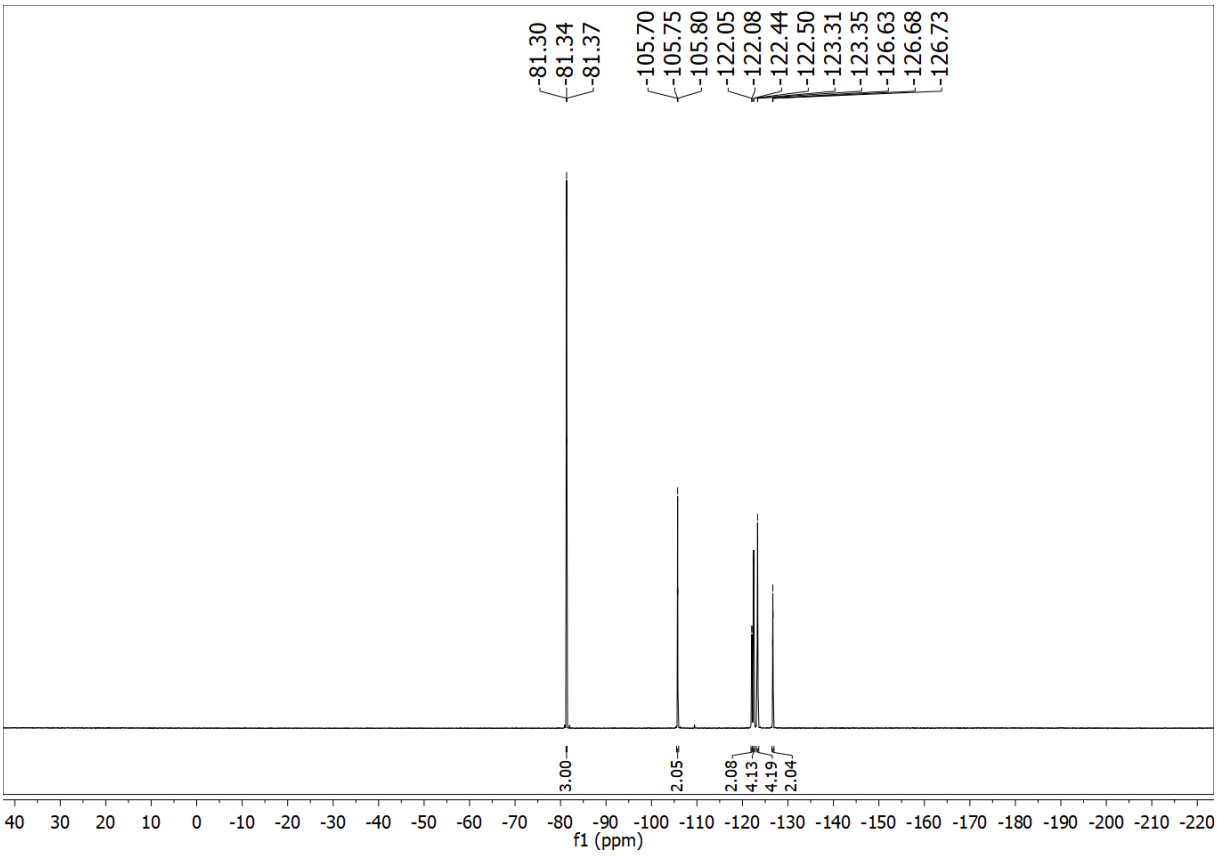


NMR-Solvent: $CDCl_3$

(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododec-1-en-1-yl)benzene (7k)

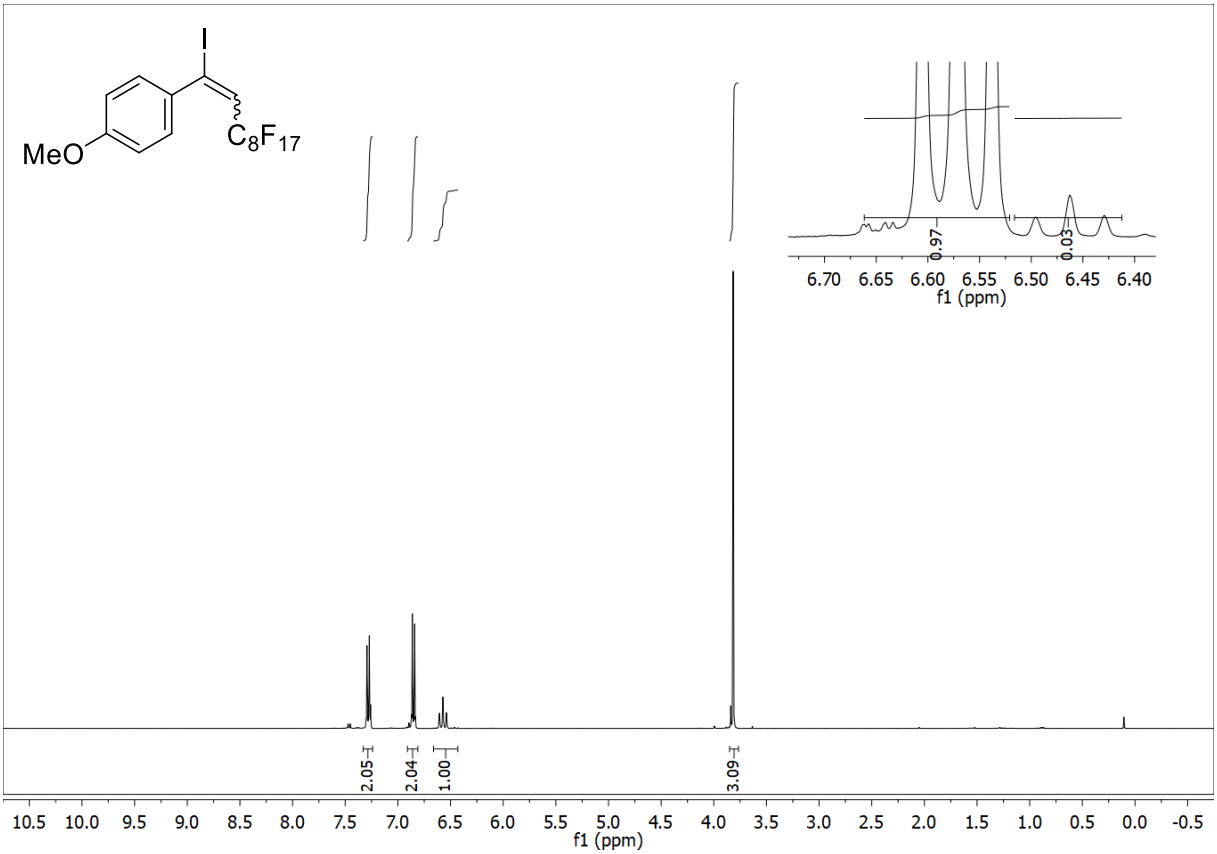


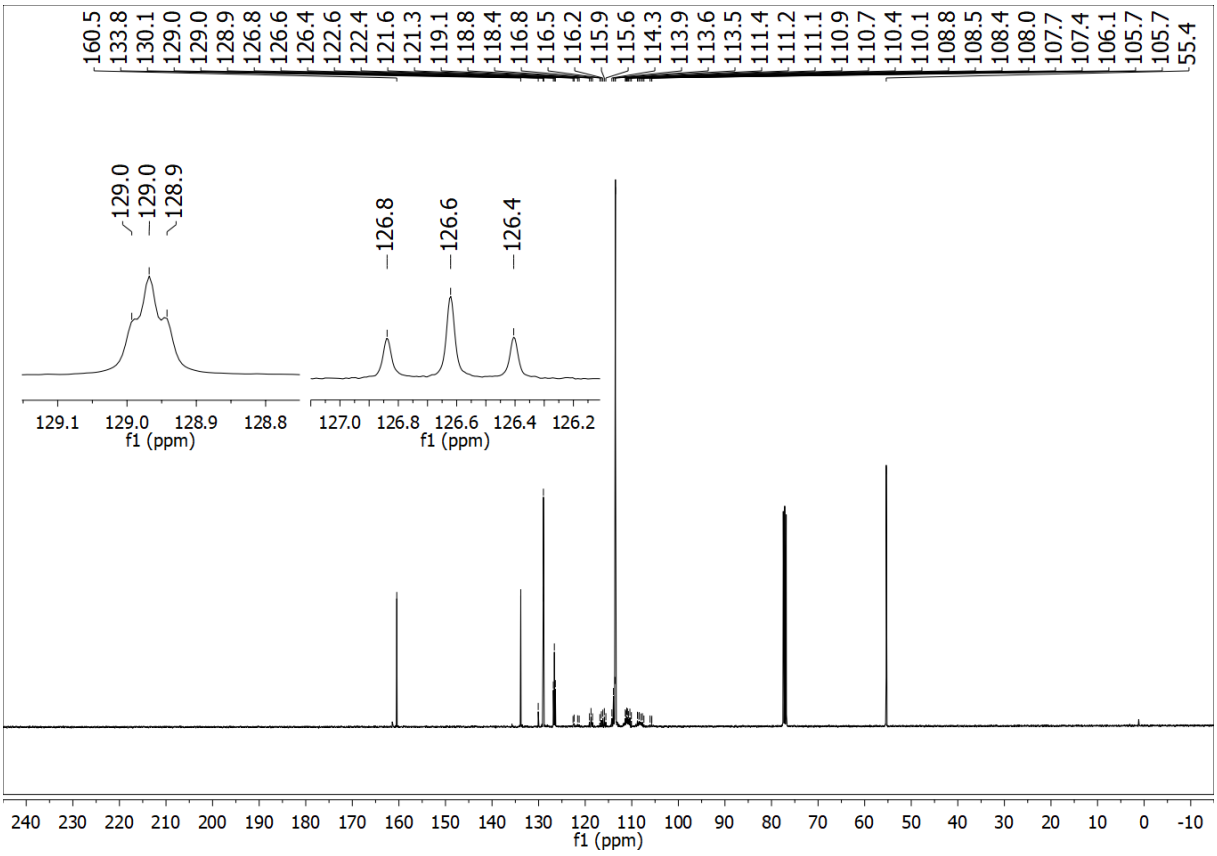


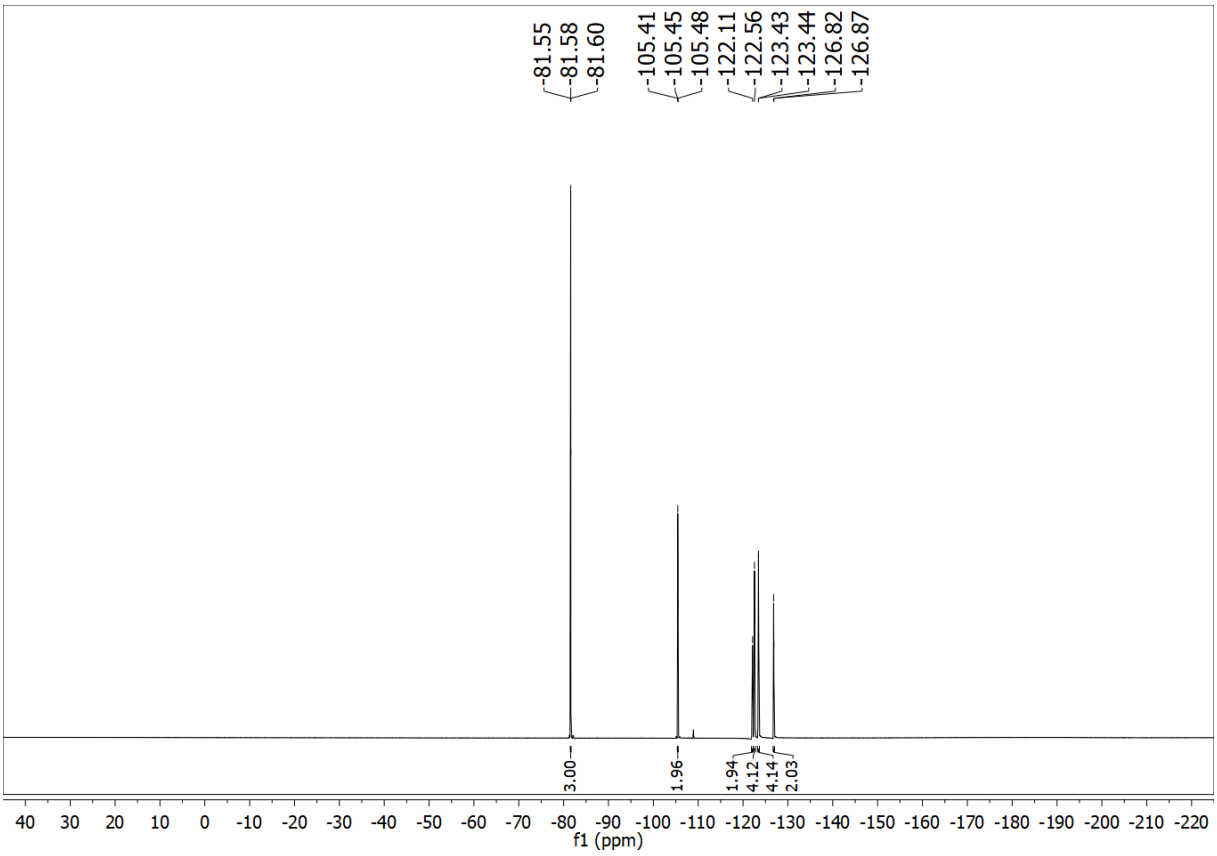


NMR-Solvent: $CDCl_3$

1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iododec-1-en-1-yl)-4-methoxy benzene (7l)

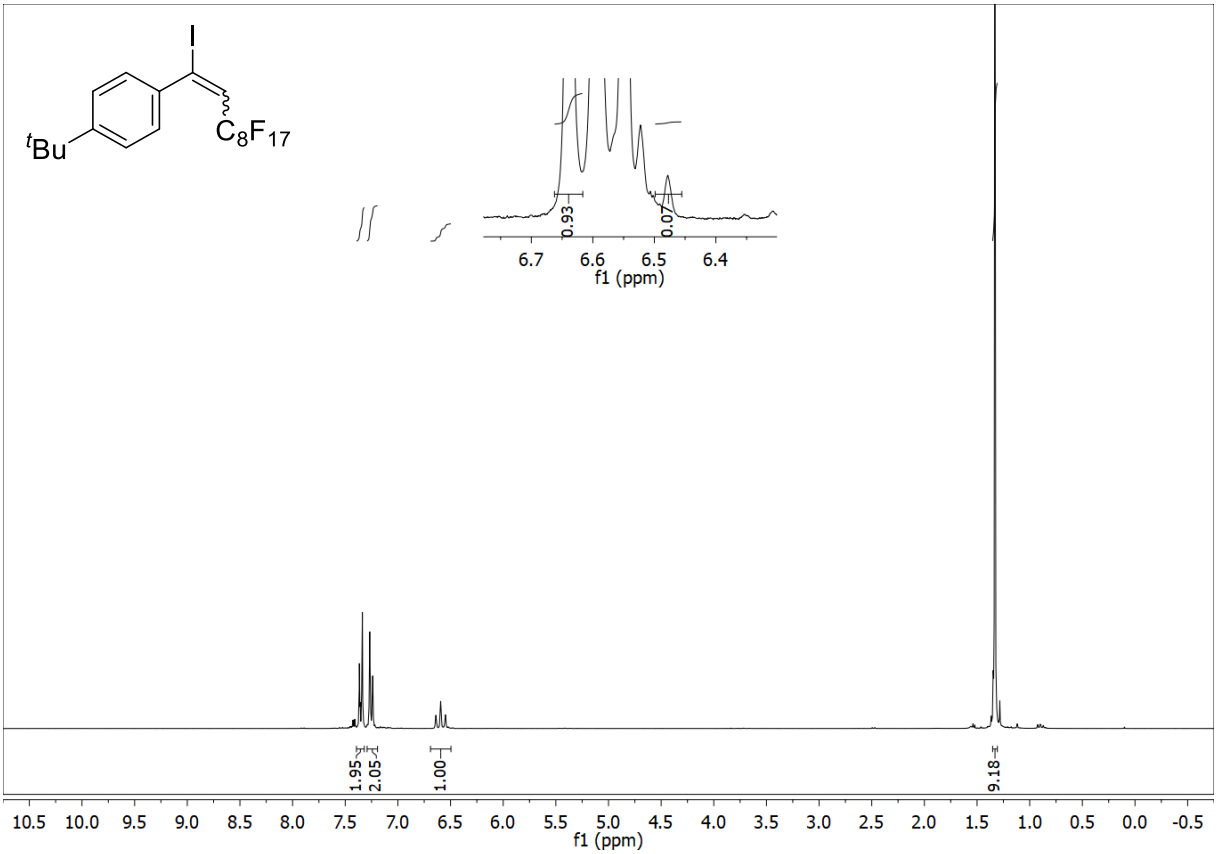


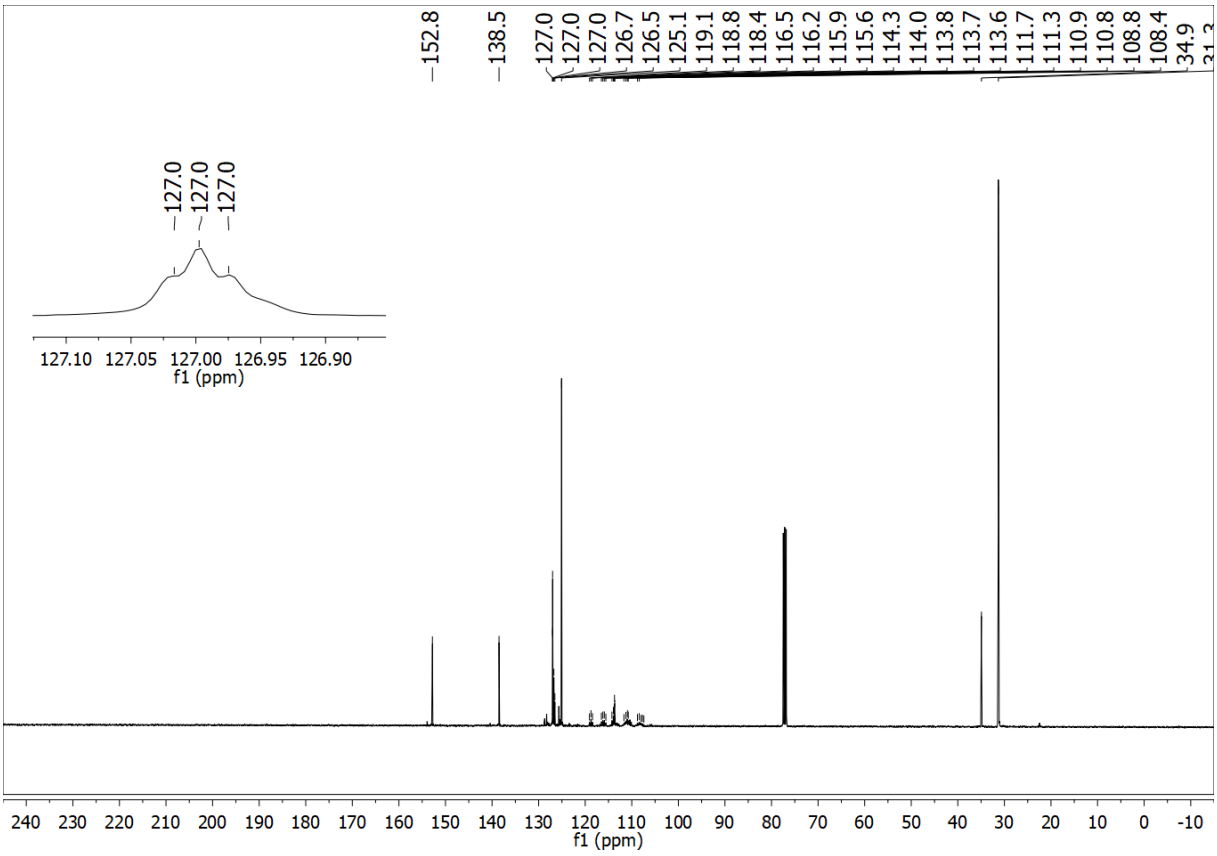


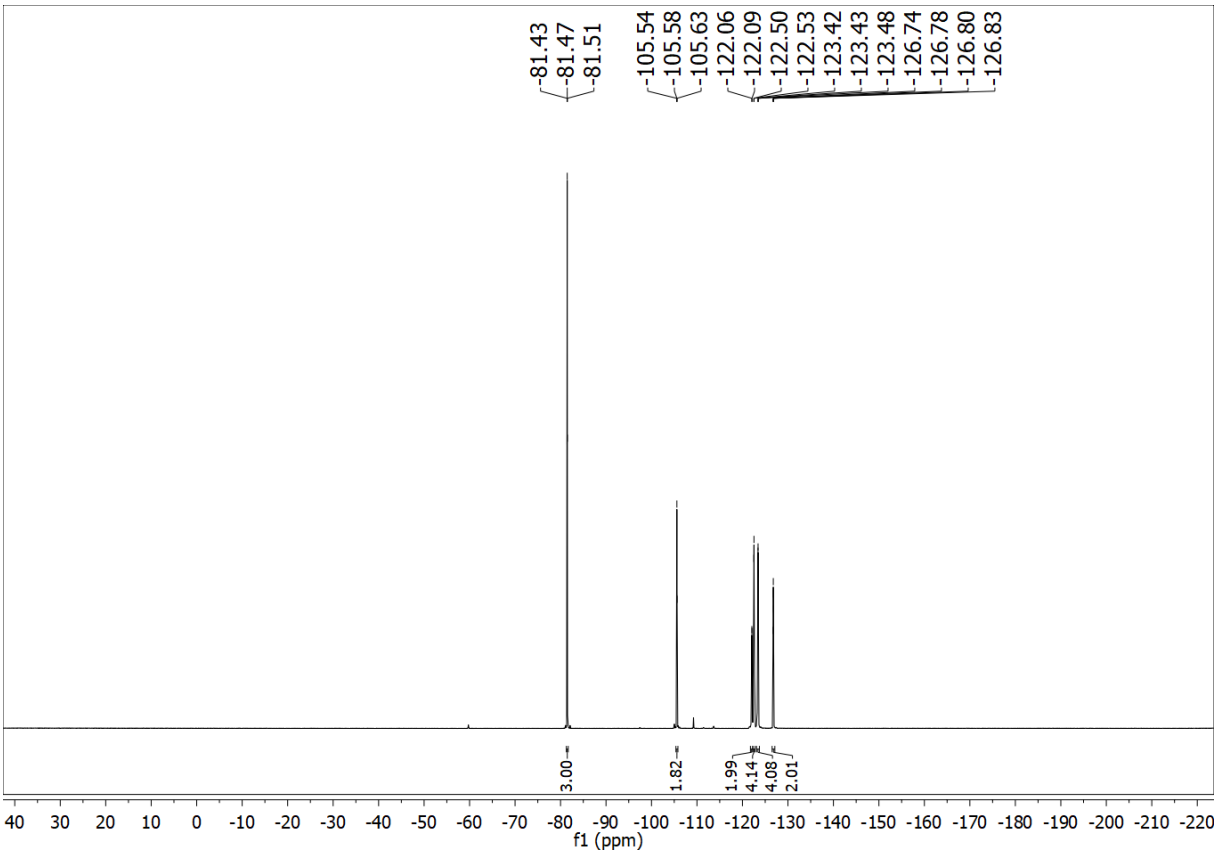


NMR-Solvent: $CDCl_3$

1-(*tert*-Butyl)-4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-1-iododec-1-en-1-yl)benzene (16a)

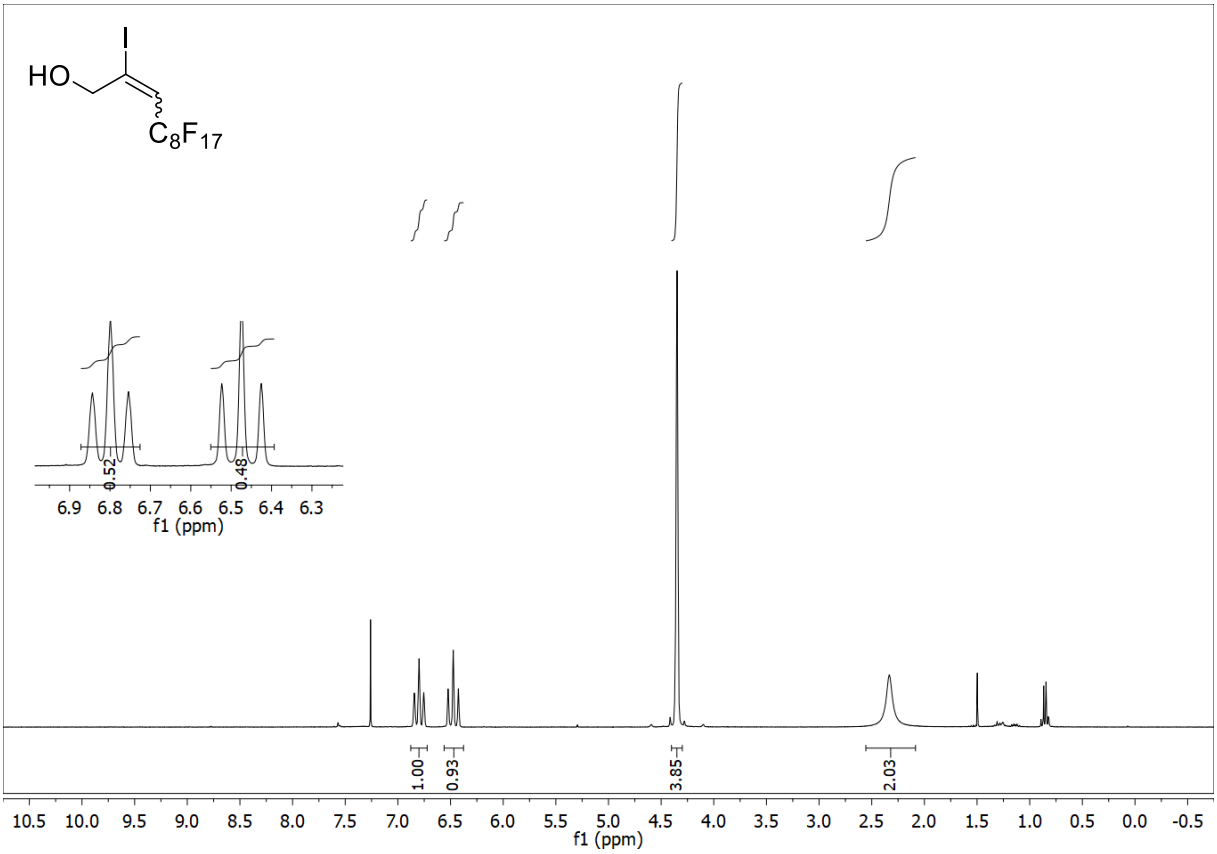


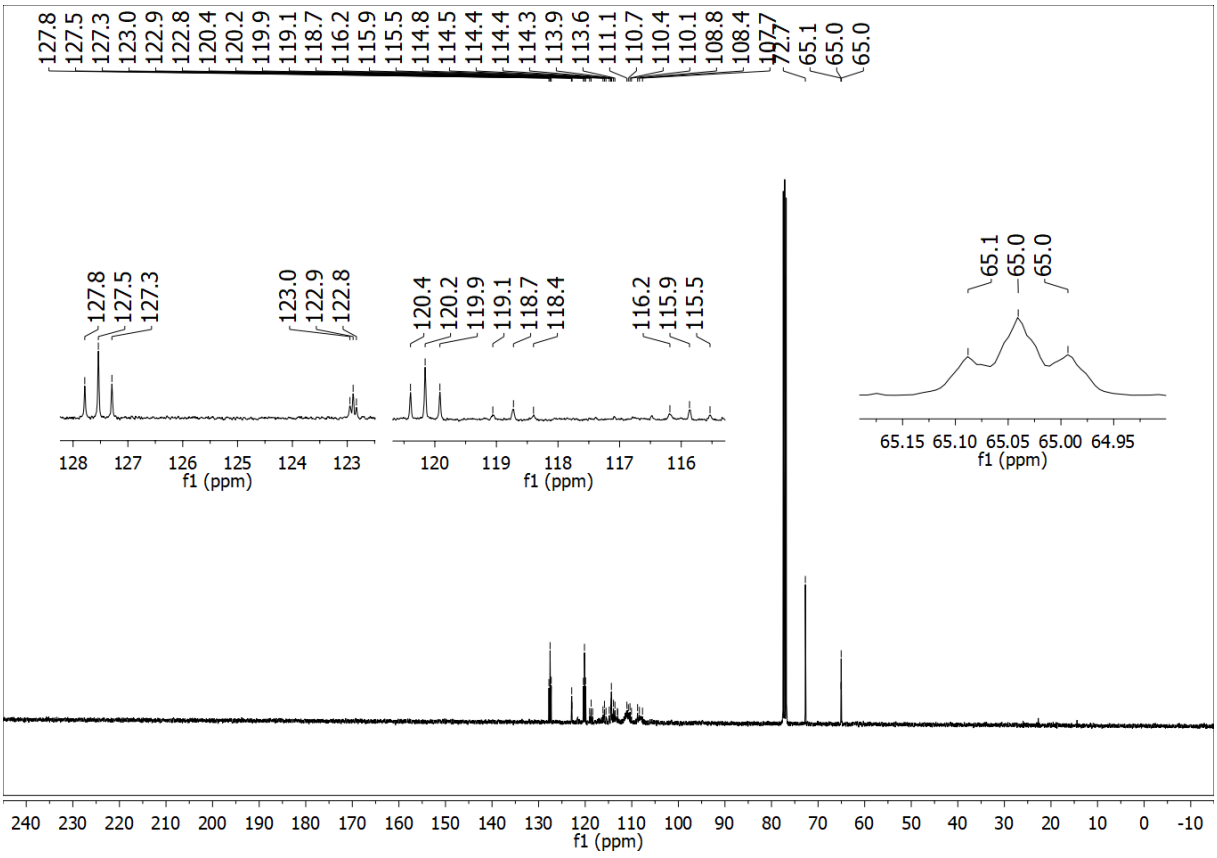


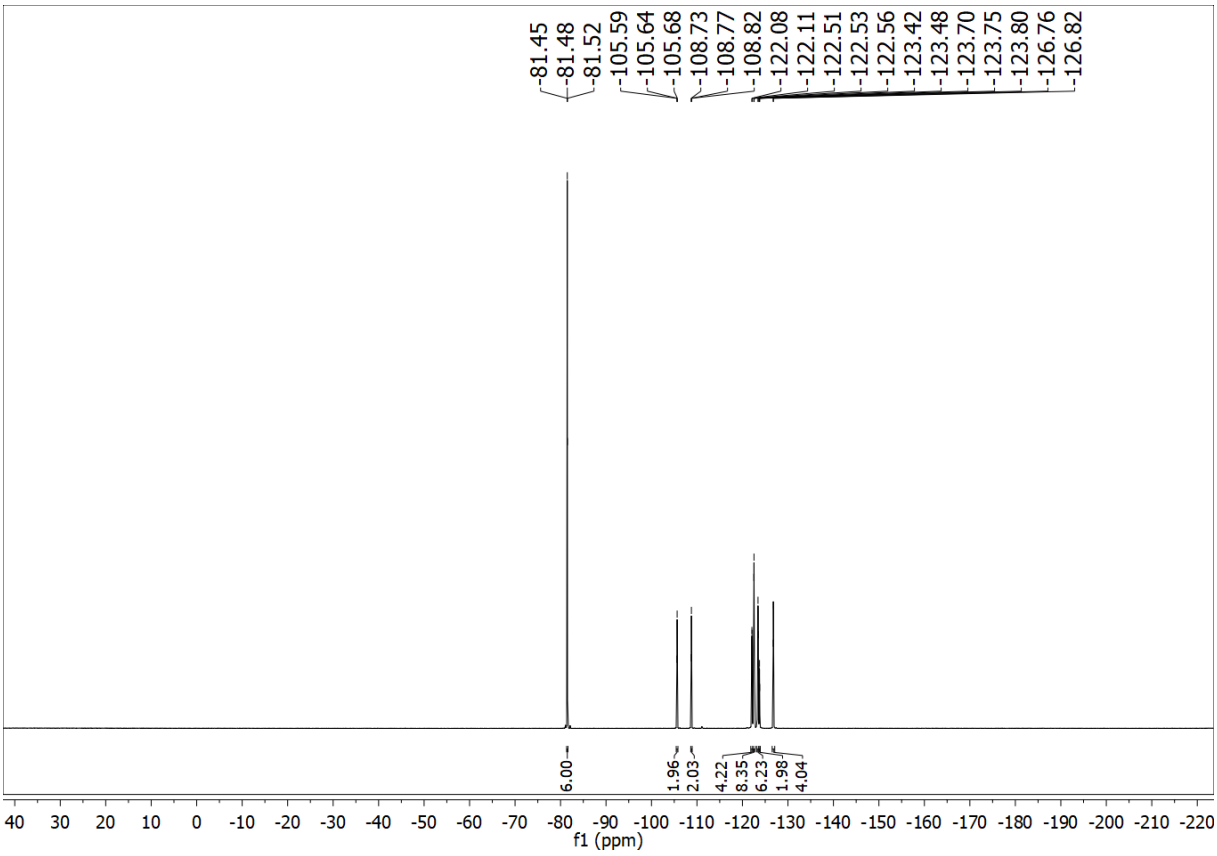


NMR-Solvent: $CDCl_3$

4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoro-2-iodoundec-2-en-1-ol (16b)

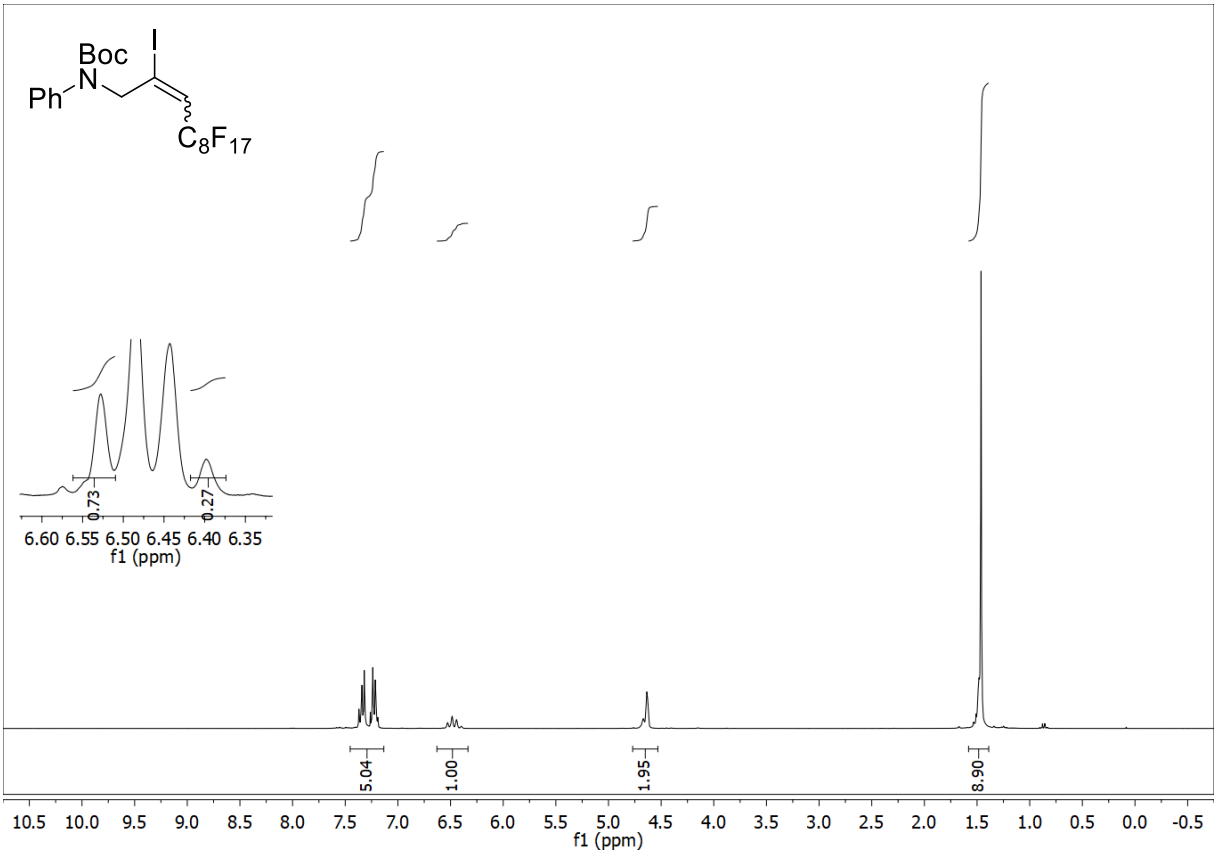


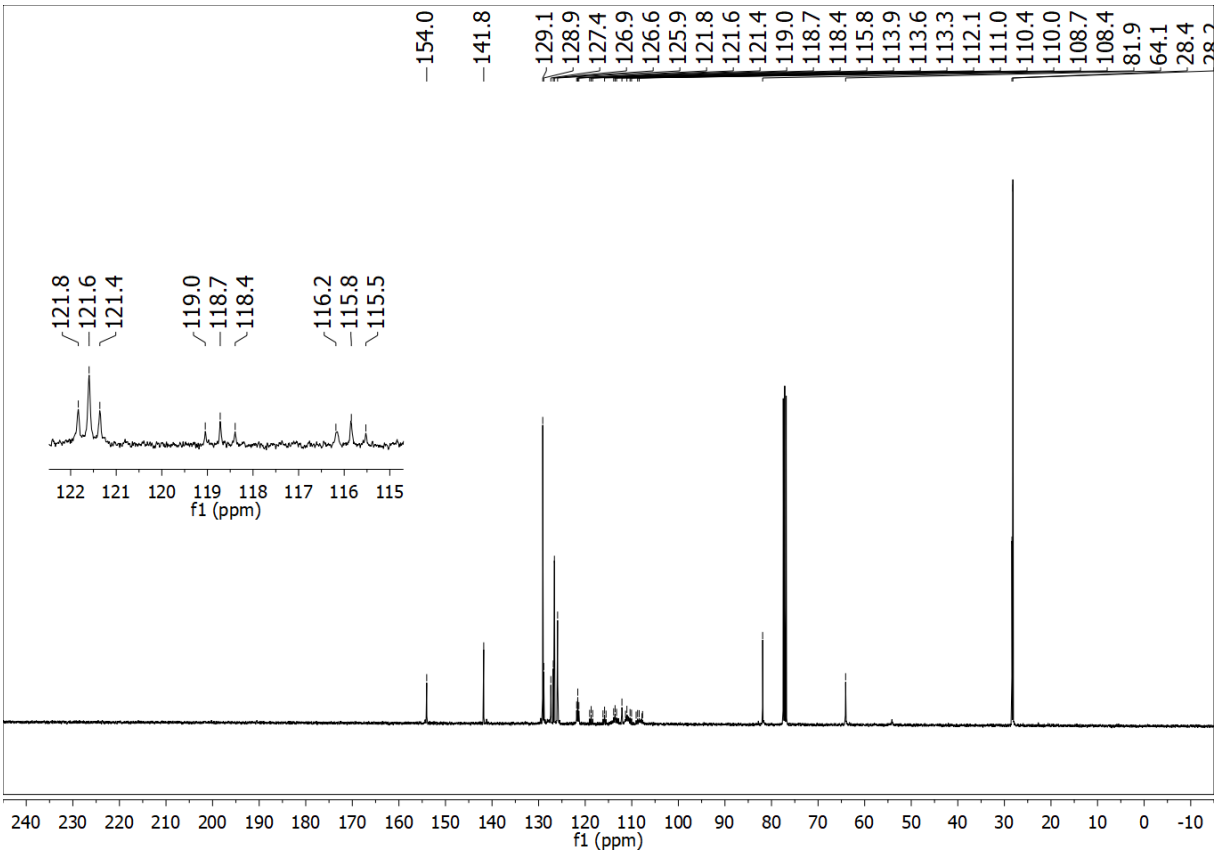


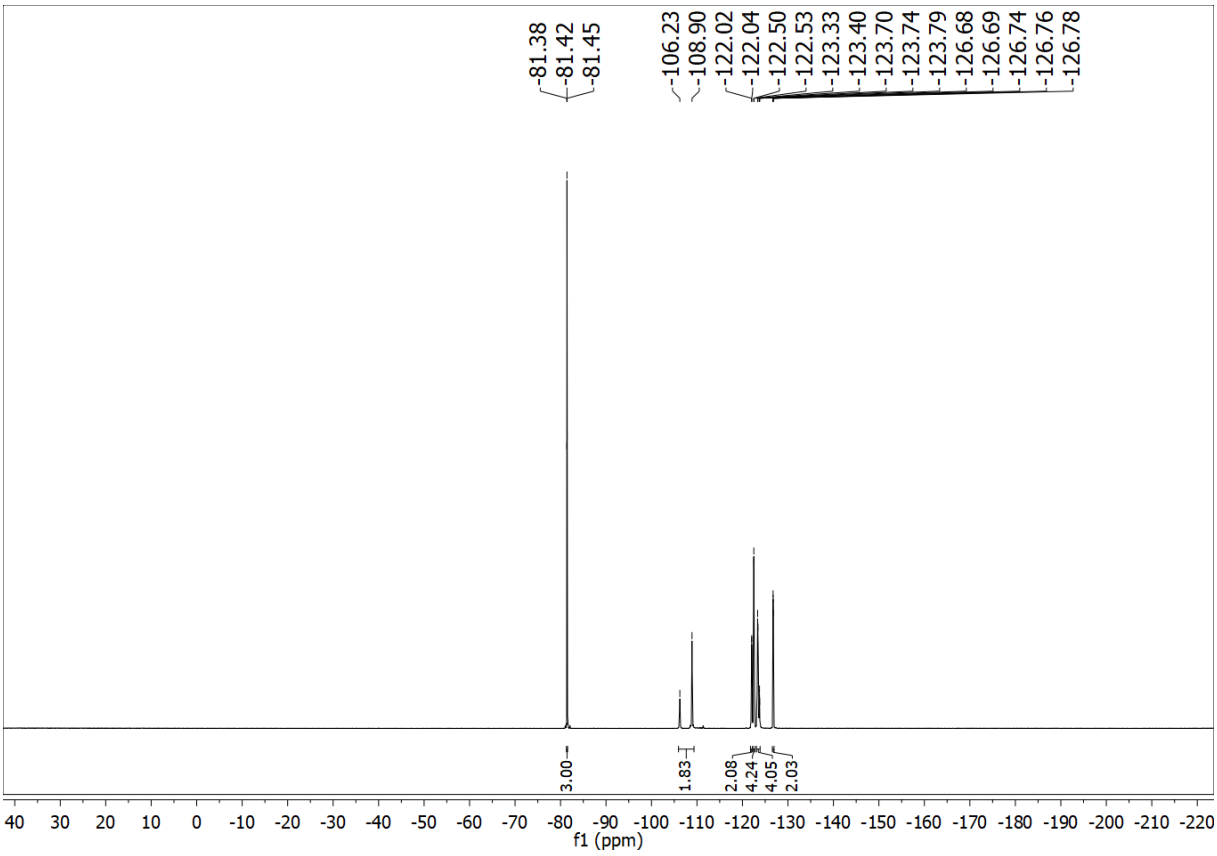


NMR-Solvent: $CDCl_3$

***tert*-Butyl-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundec-2-en-1-yl)(phenyl)carbamate (16c)**

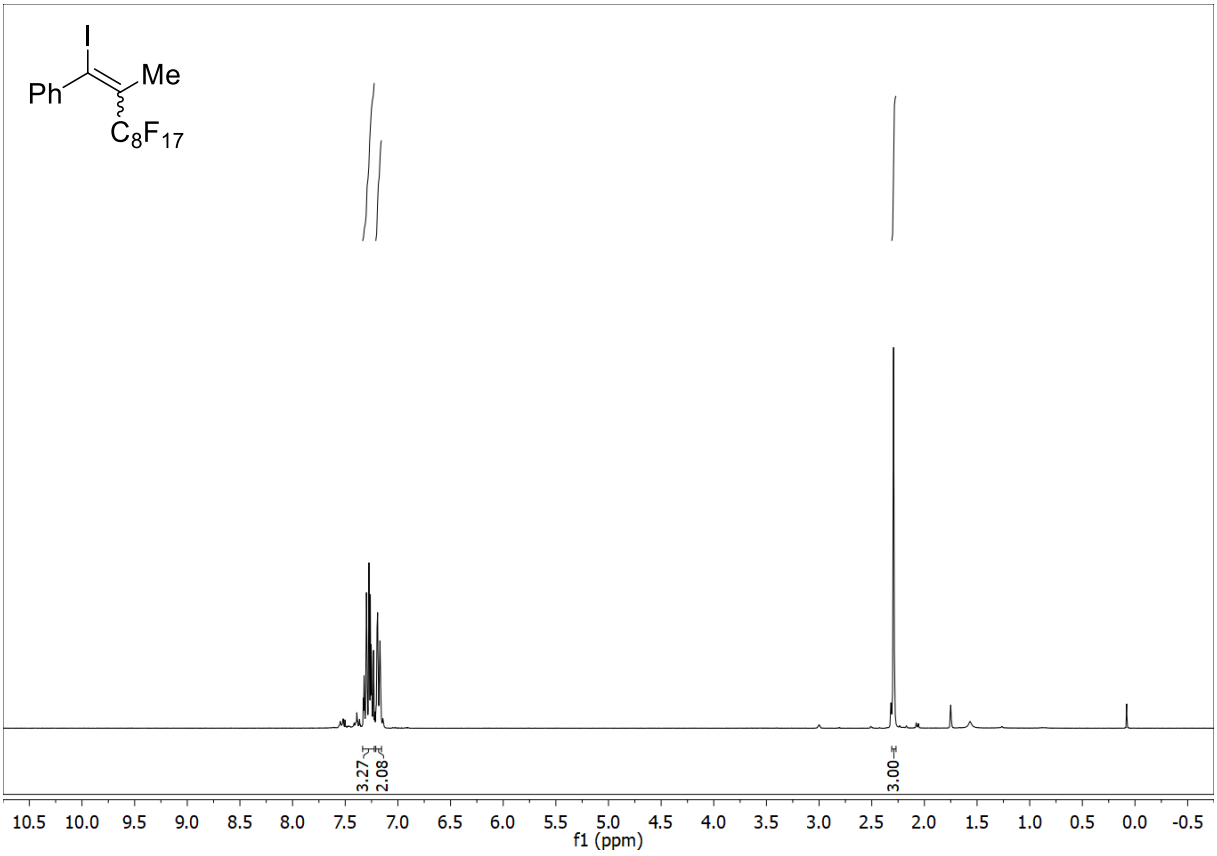


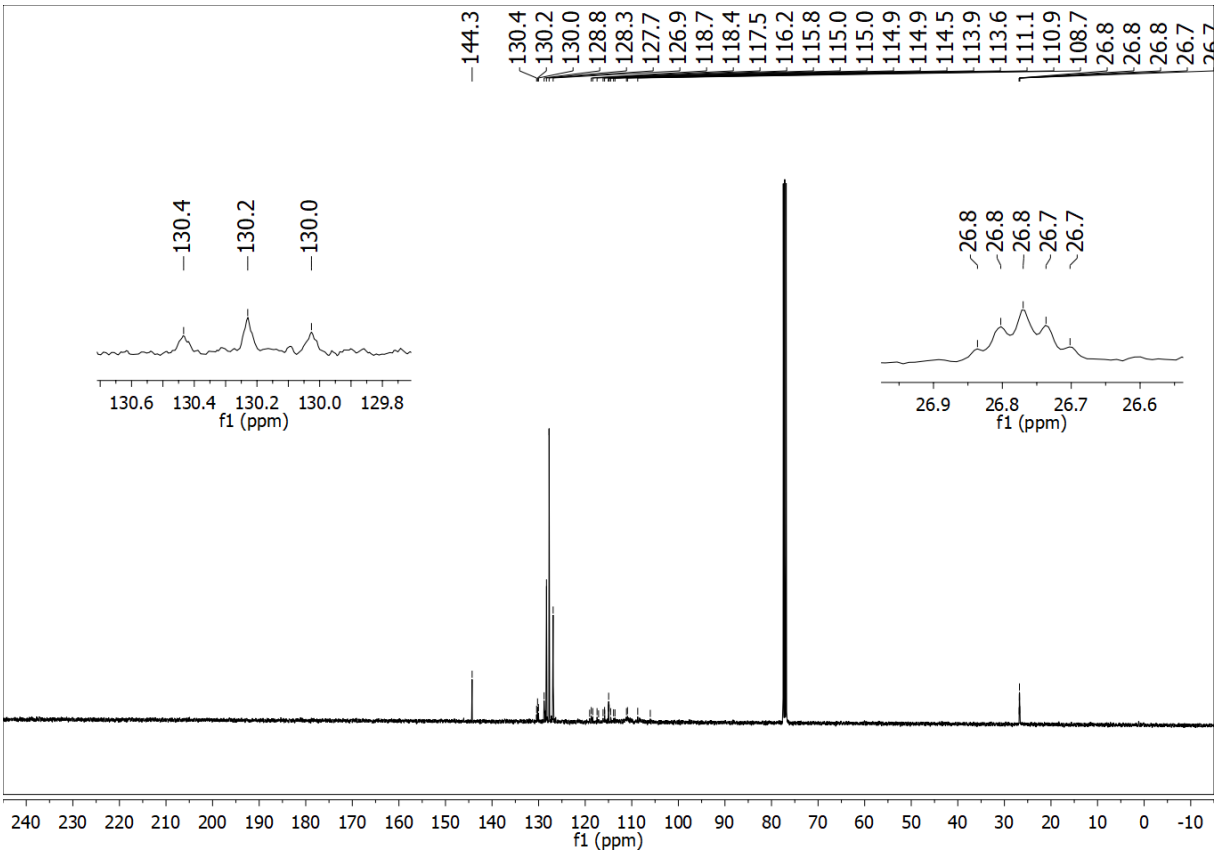


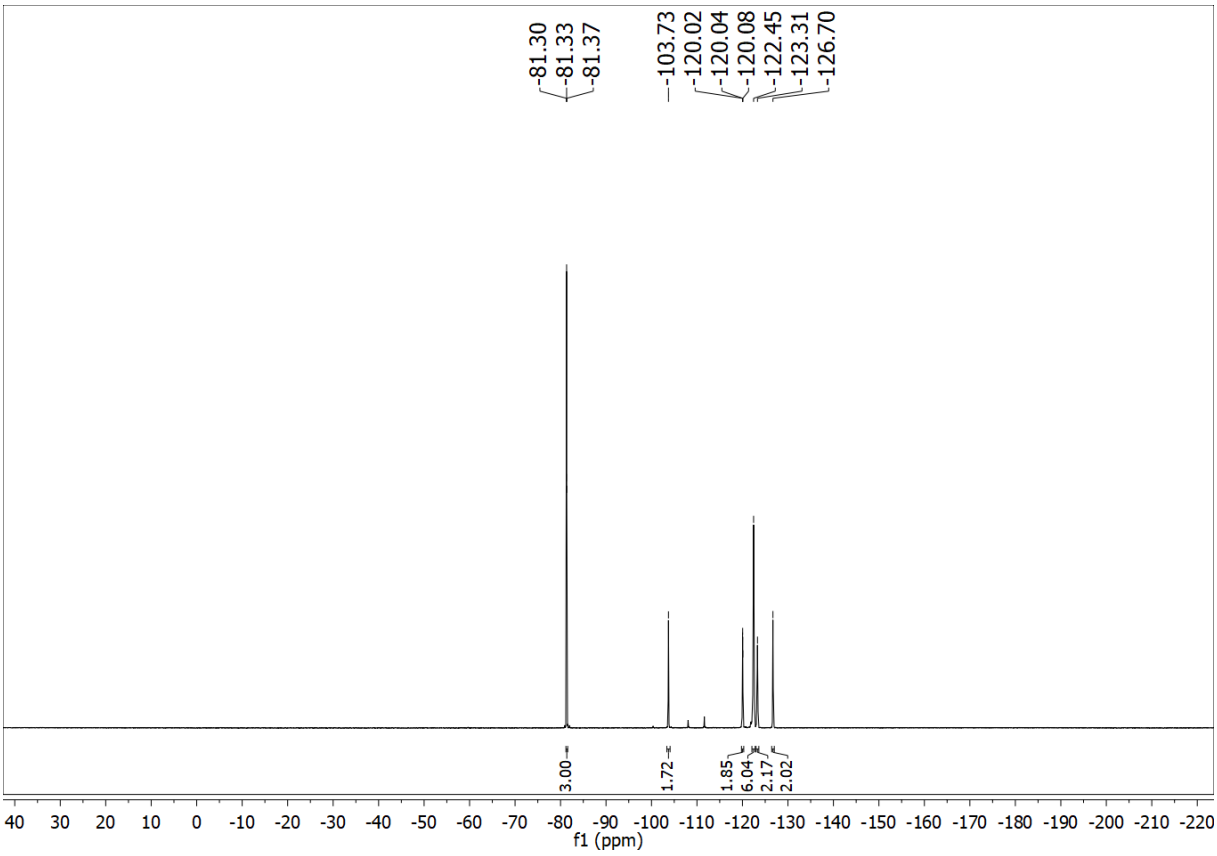


NMR-Solvent: $CDCl_3$

(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-iodo-2-methyldec-1-en-1-yl) benzene (16e)

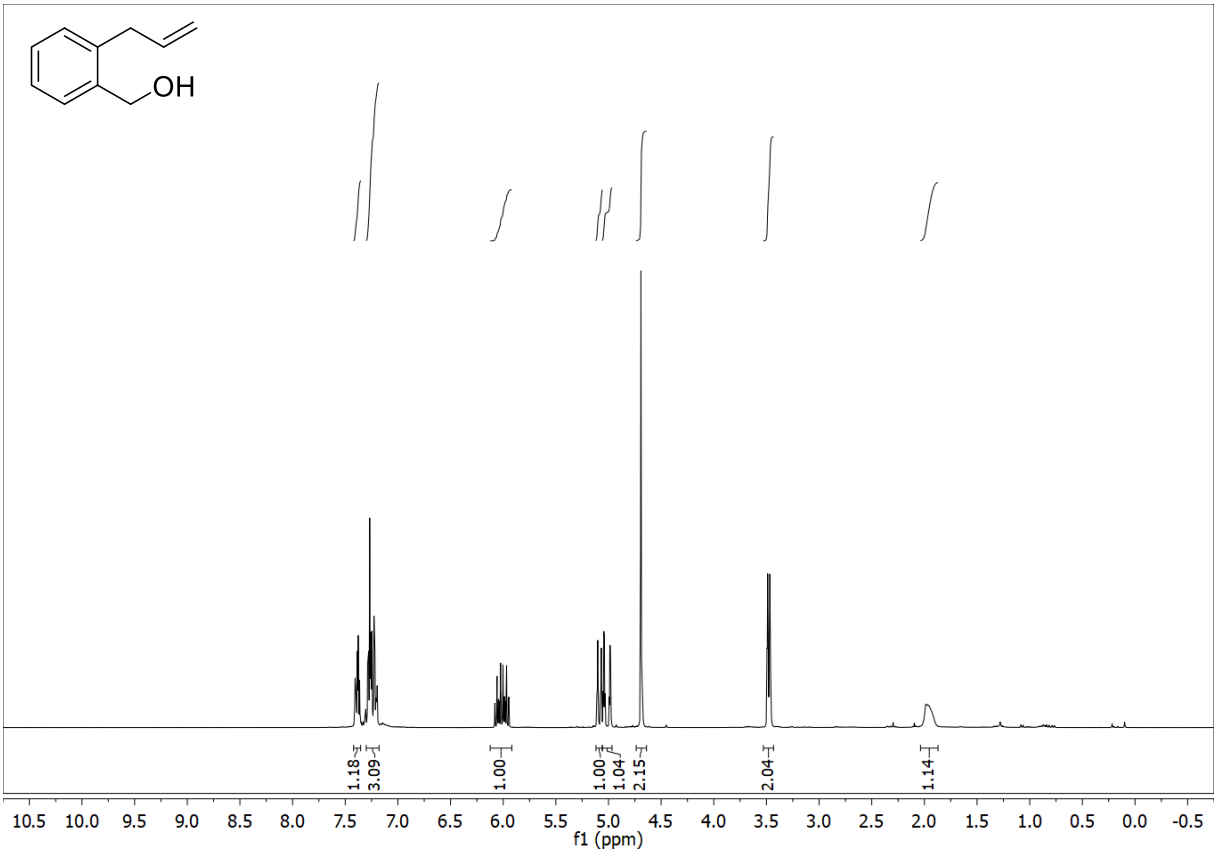






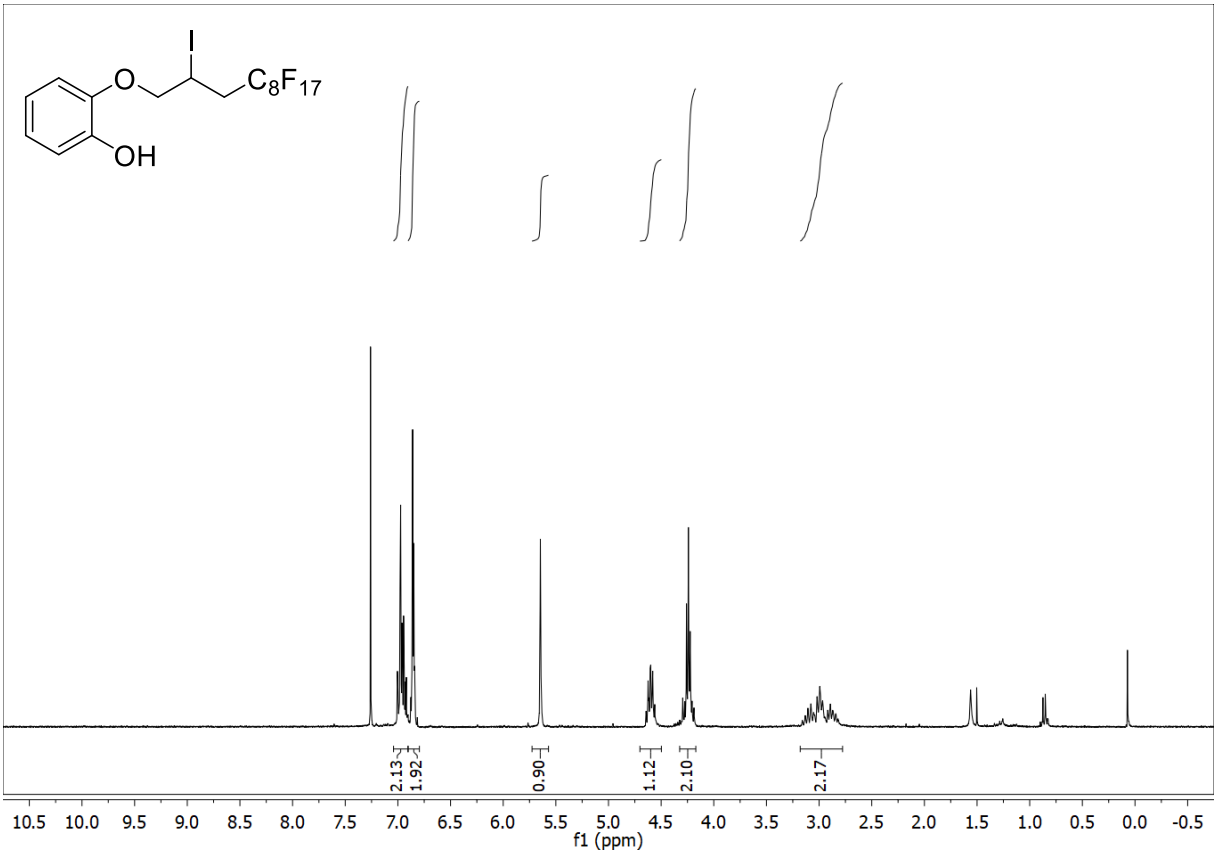
NMR-Solvent: $CDCl_3$

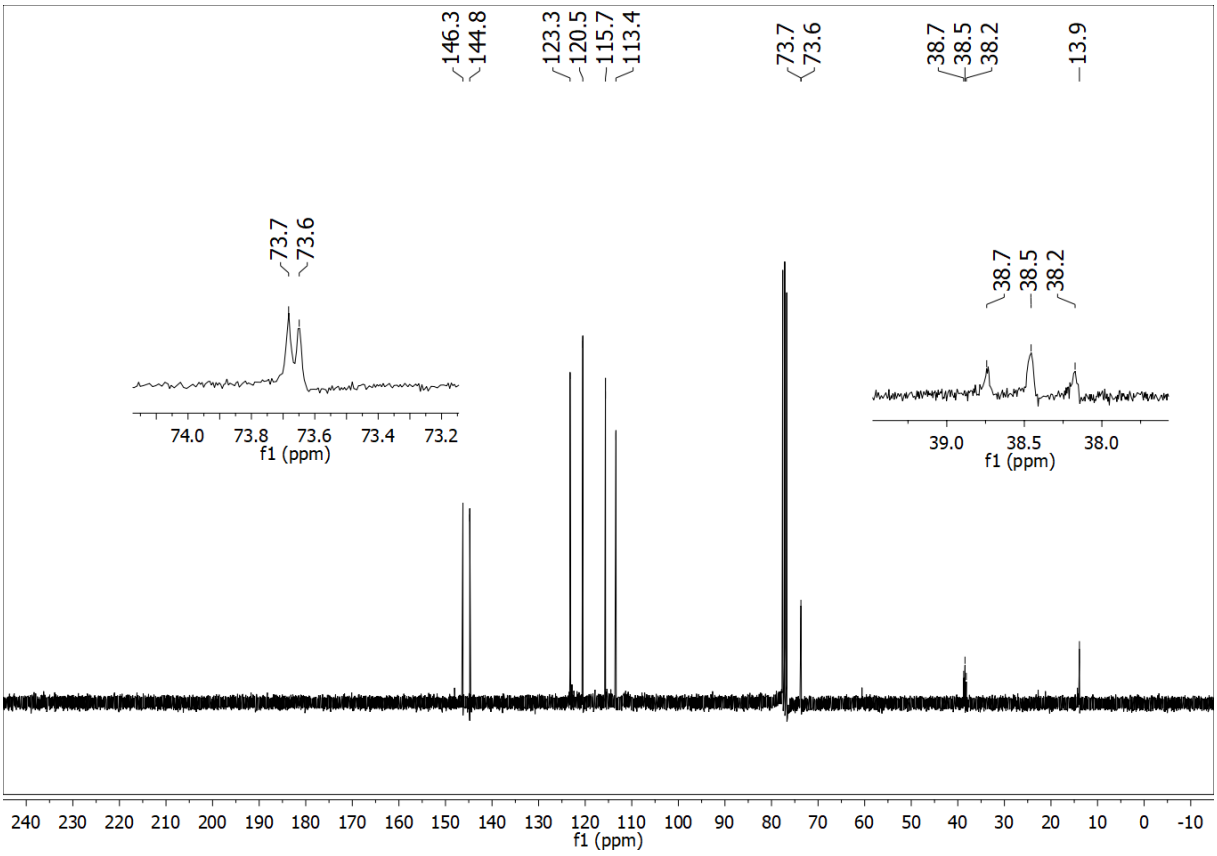
(2-allylphenyl)methanol (24)

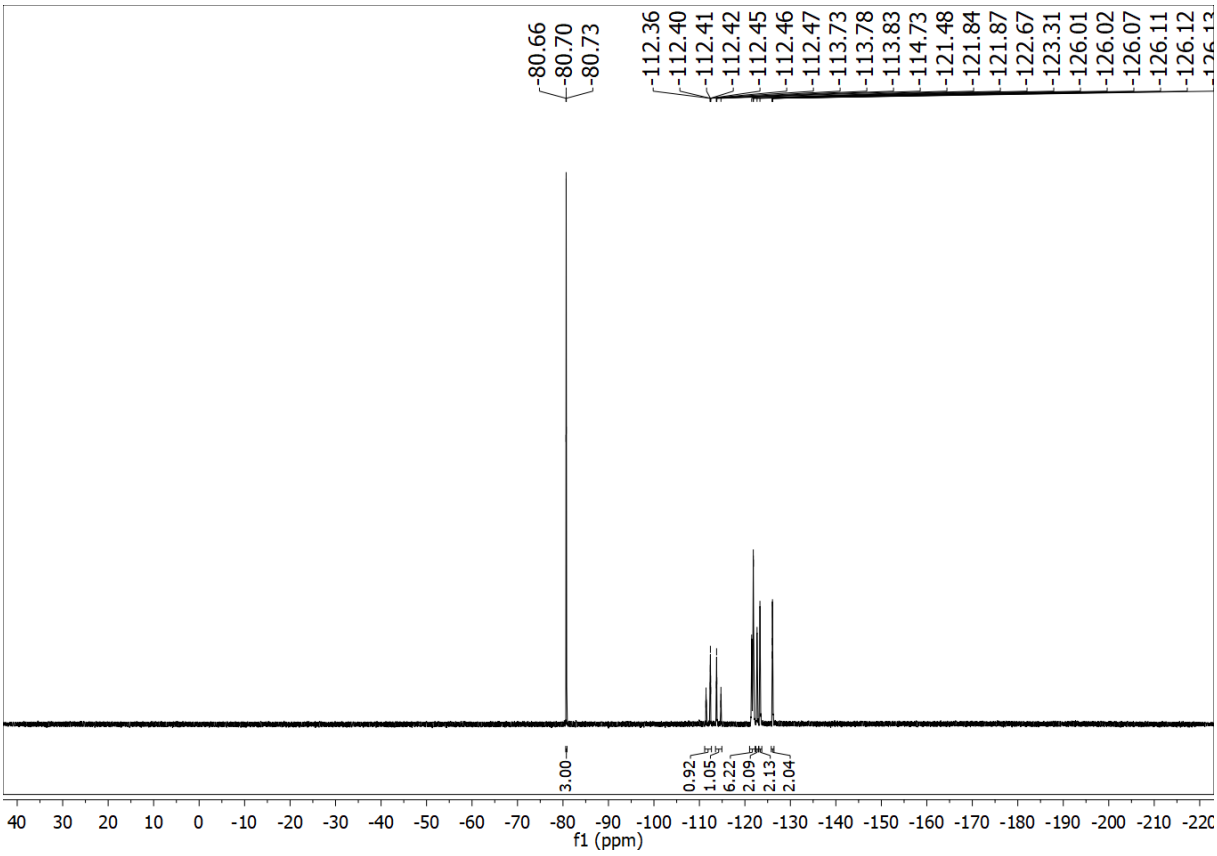


NMR-Solvent: $CDCl_3$

2-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)oxy)phenol (29a)

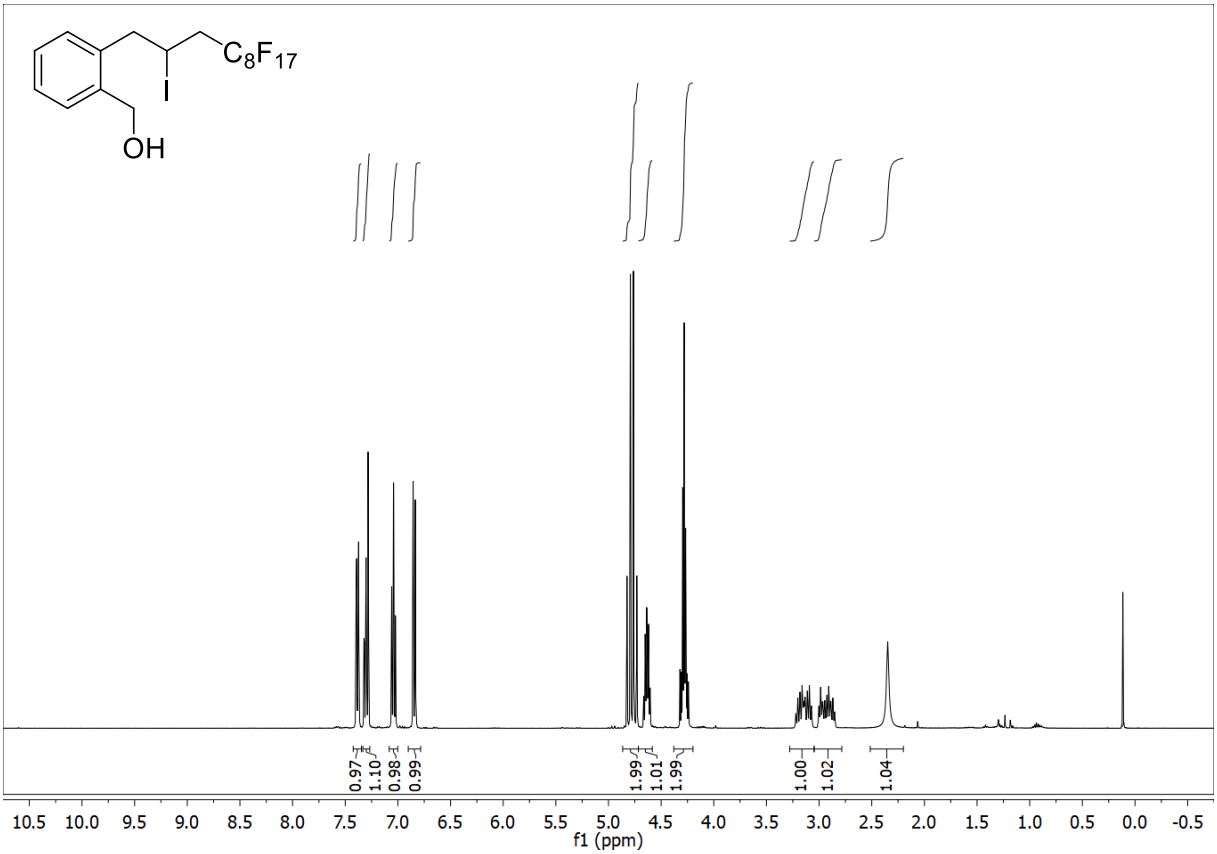


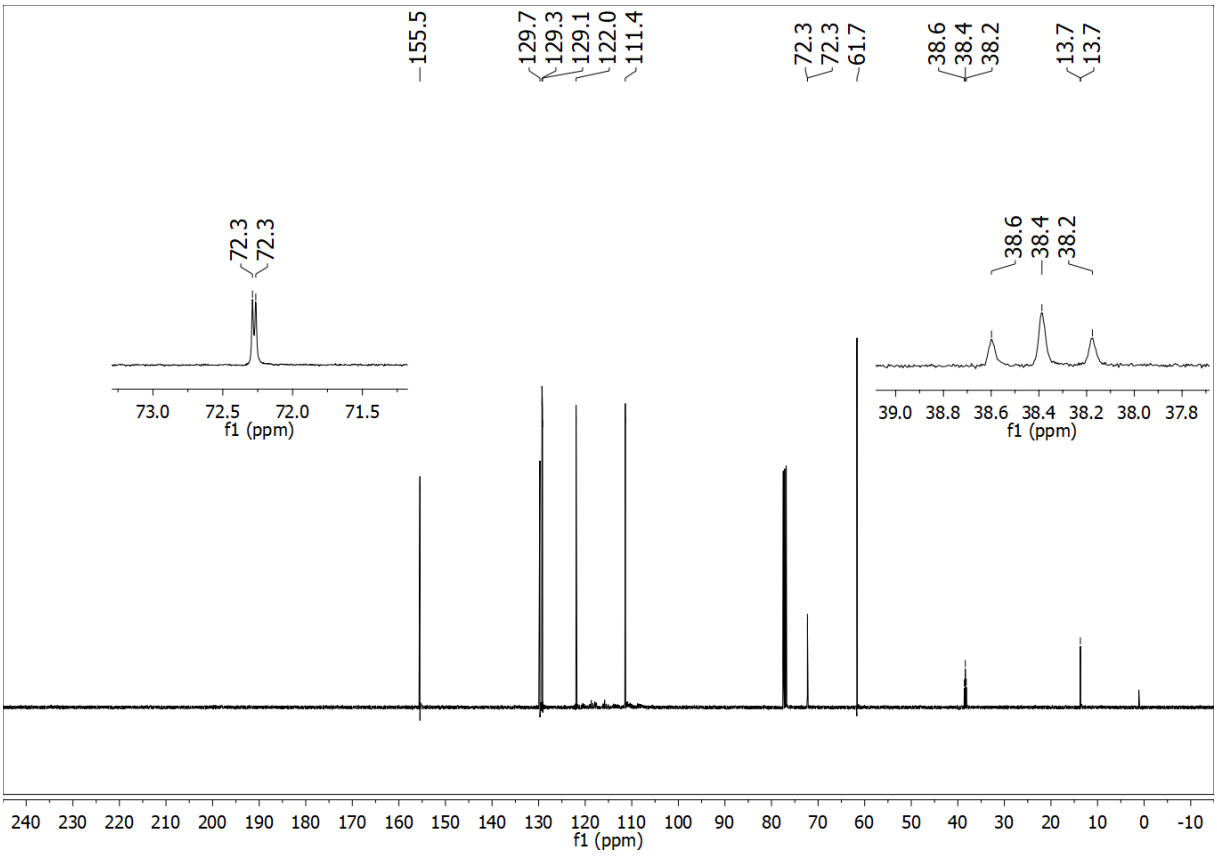


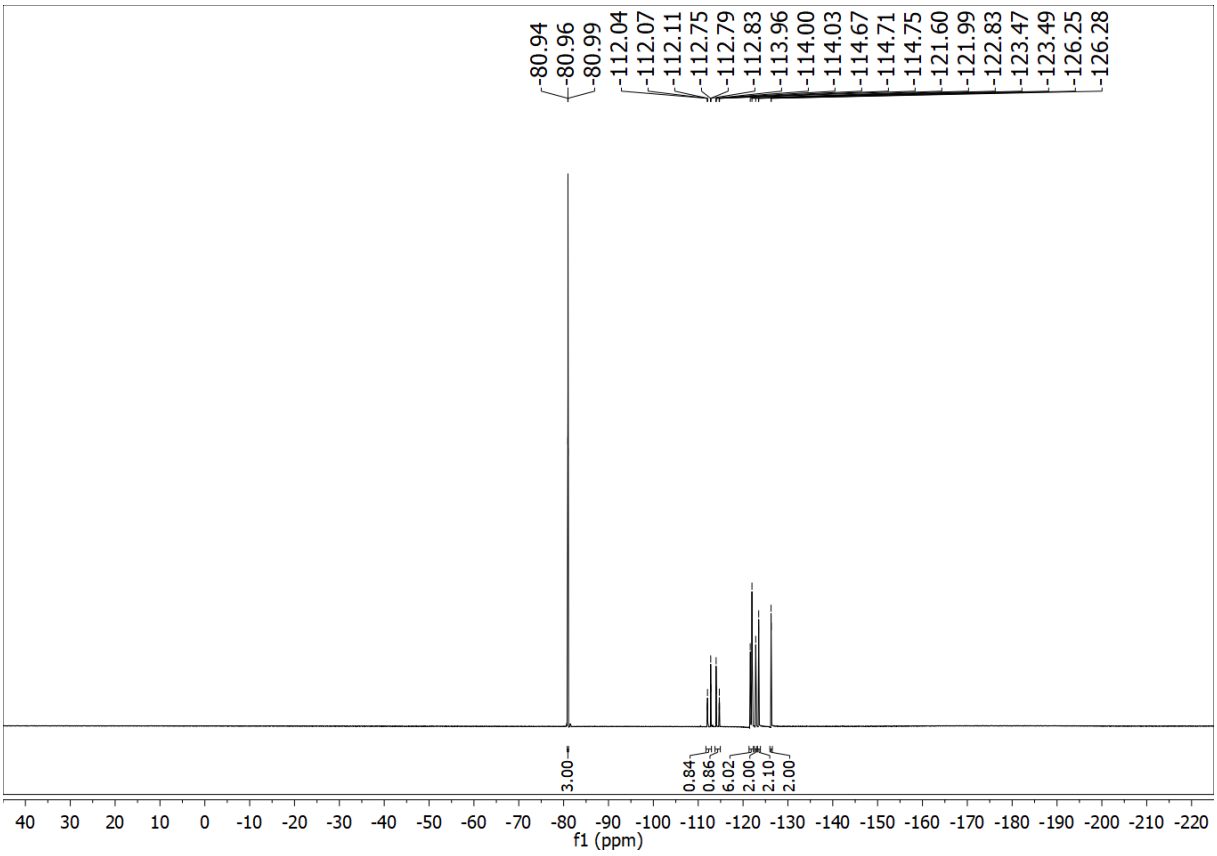


NMR-Solvent: $CDCl_3$

(2-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)phenyl)-methanol (29b)

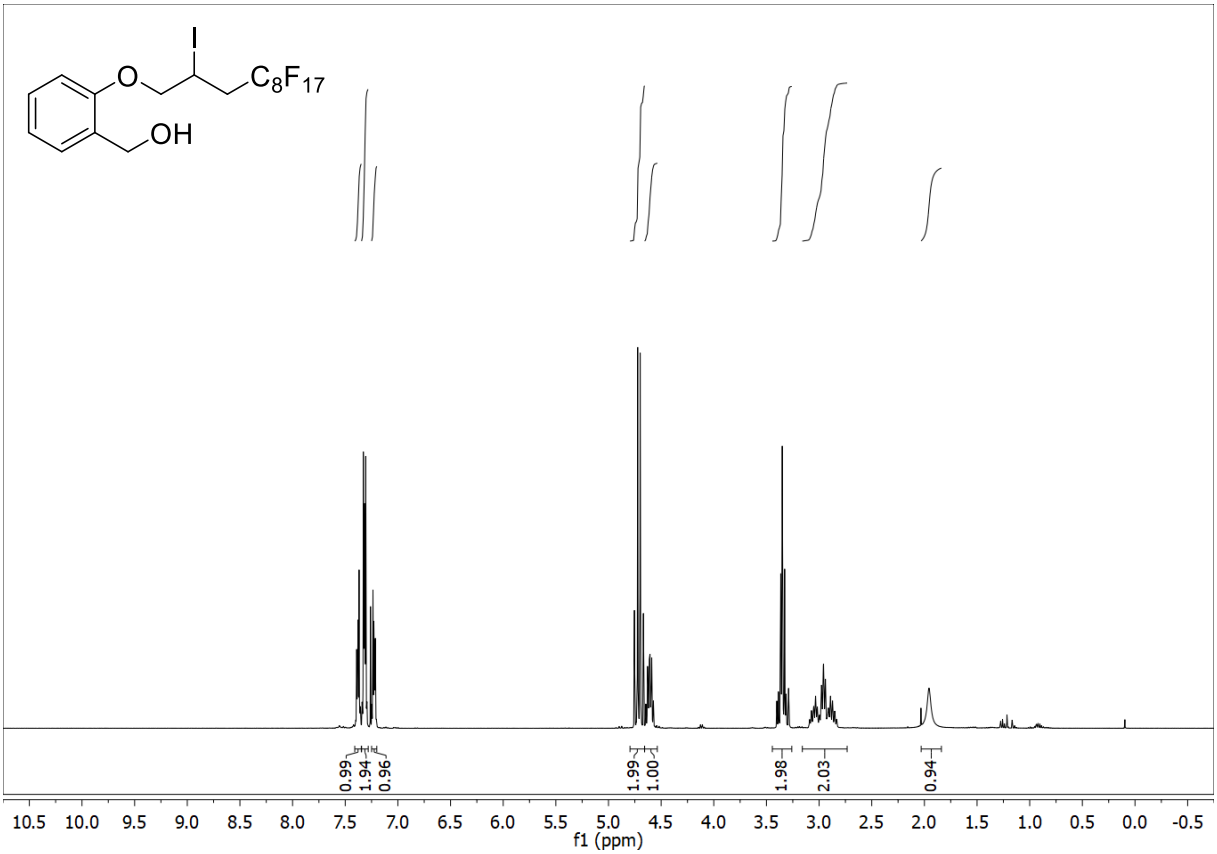


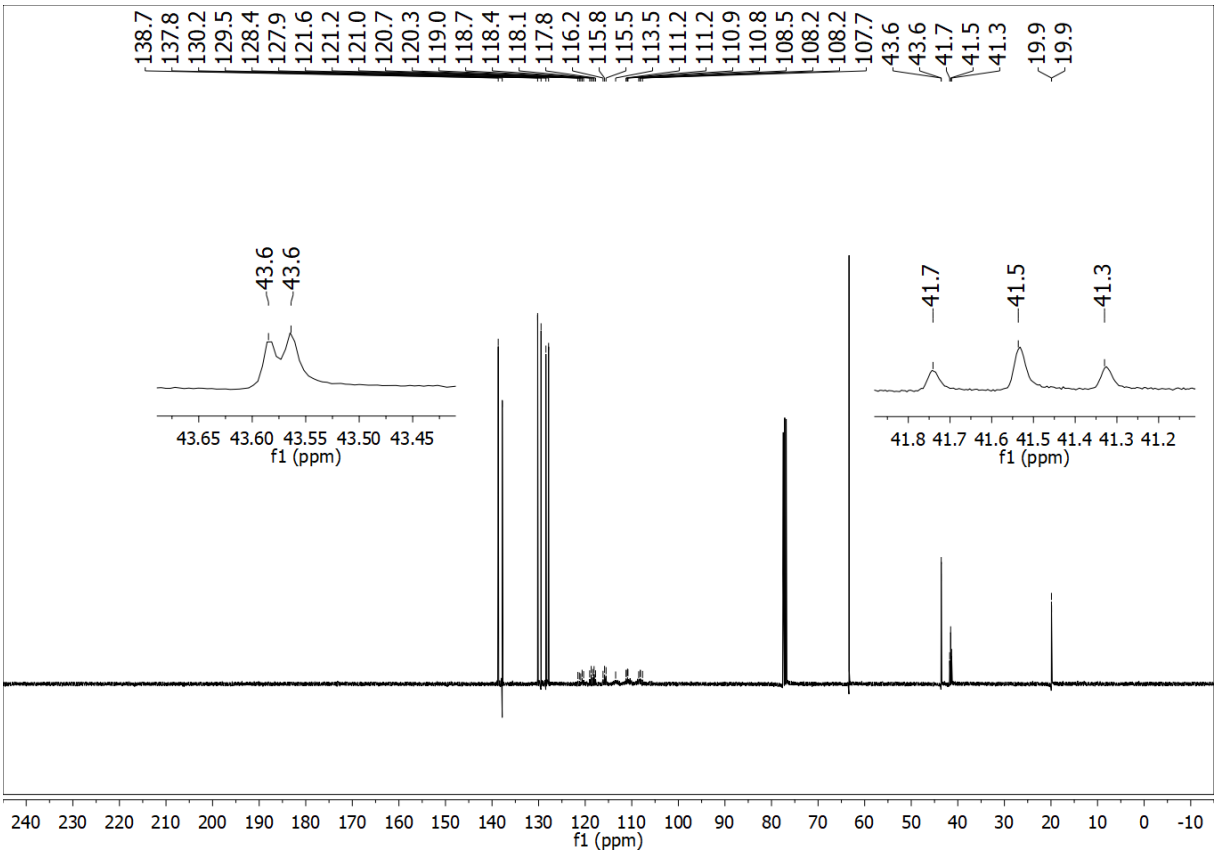


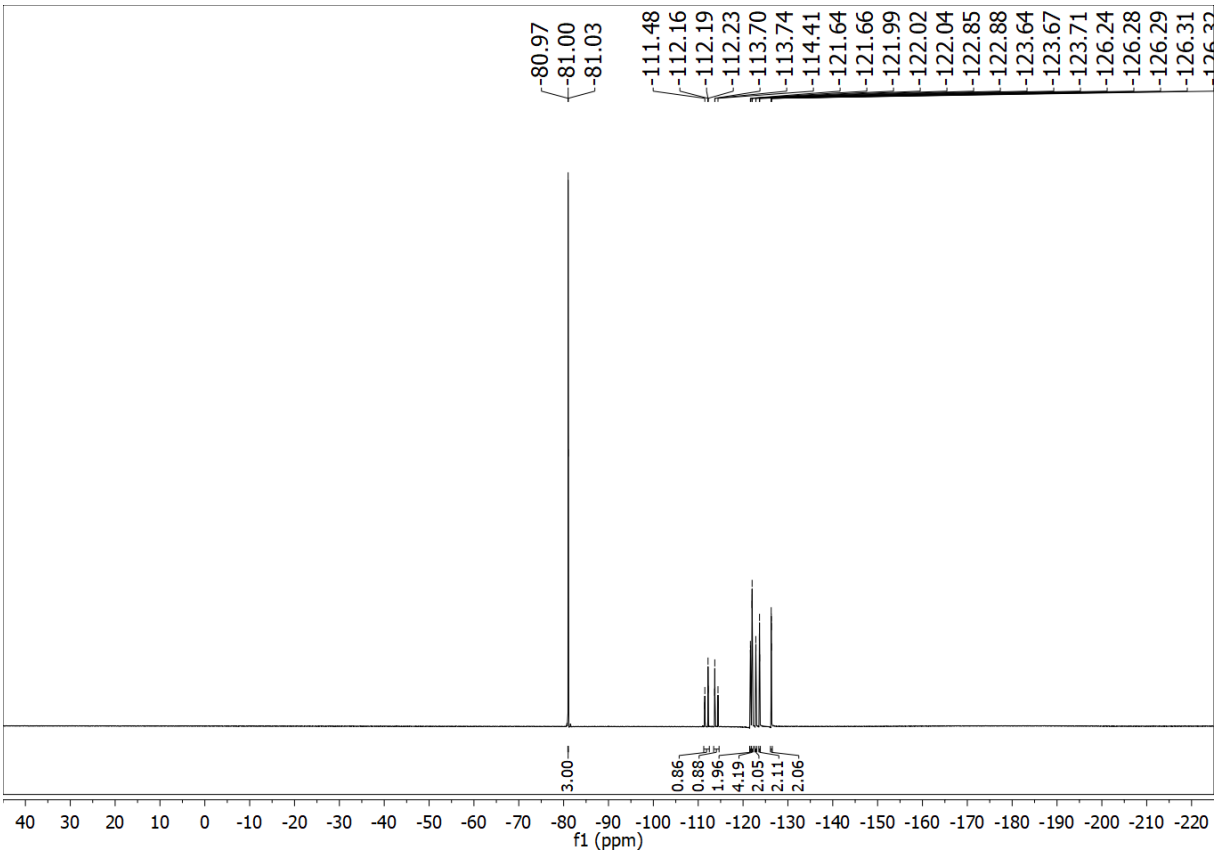


NMR-Solvent: $CDCl_3$

(2-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)oxy)phenyl)-methanol (29c)

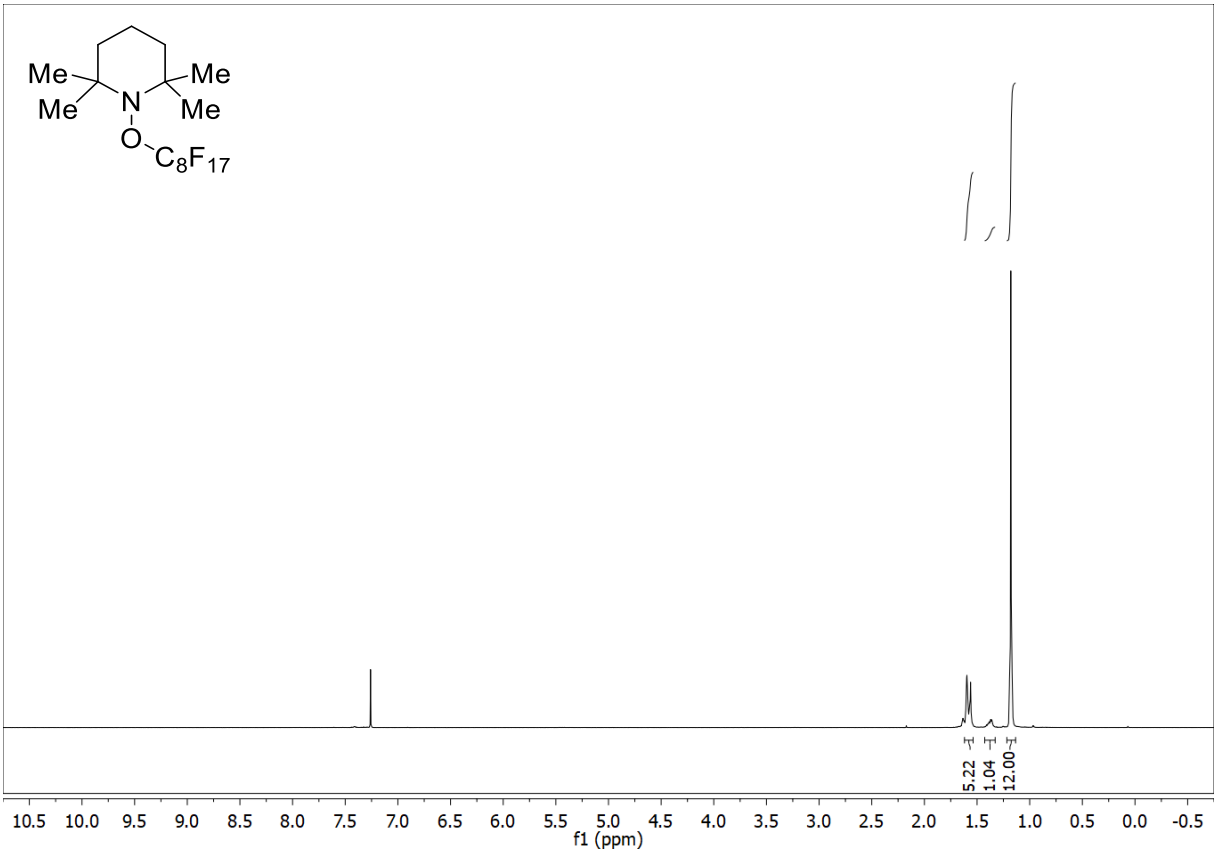


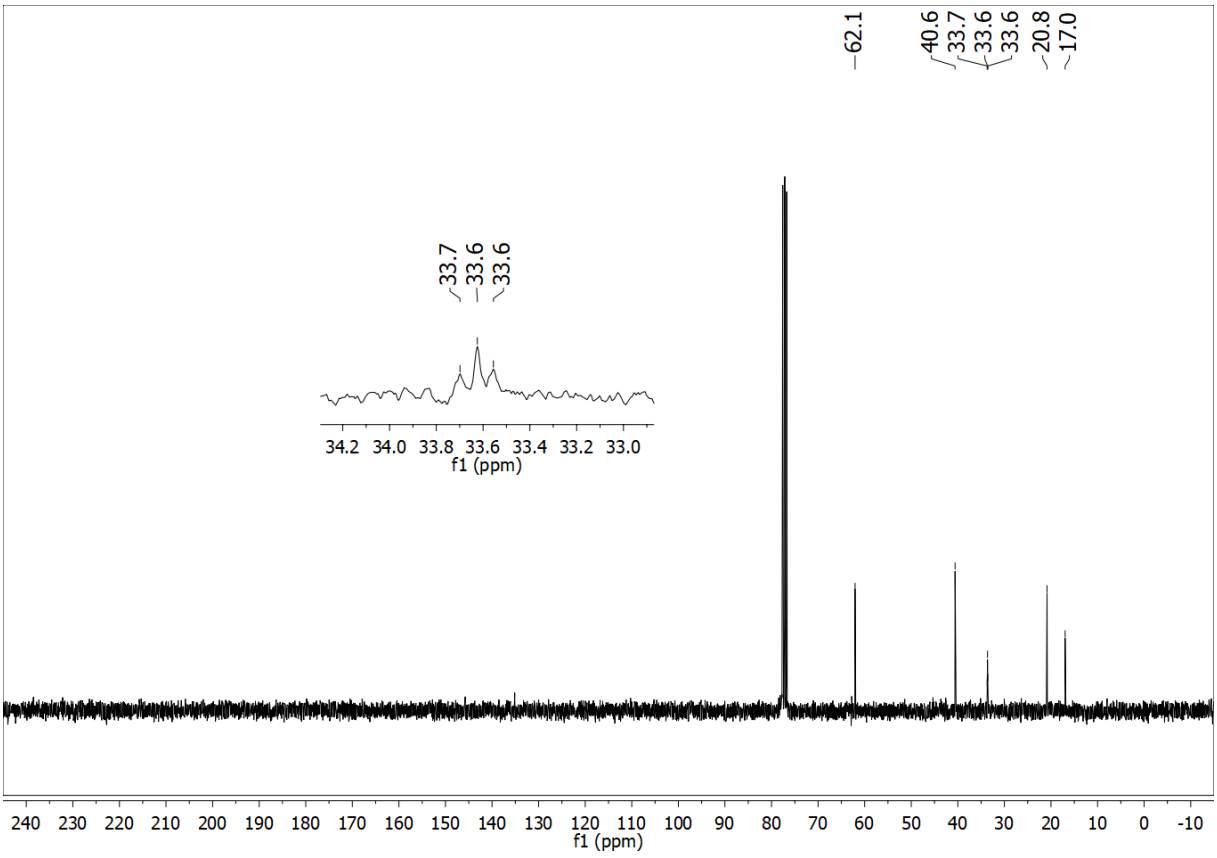


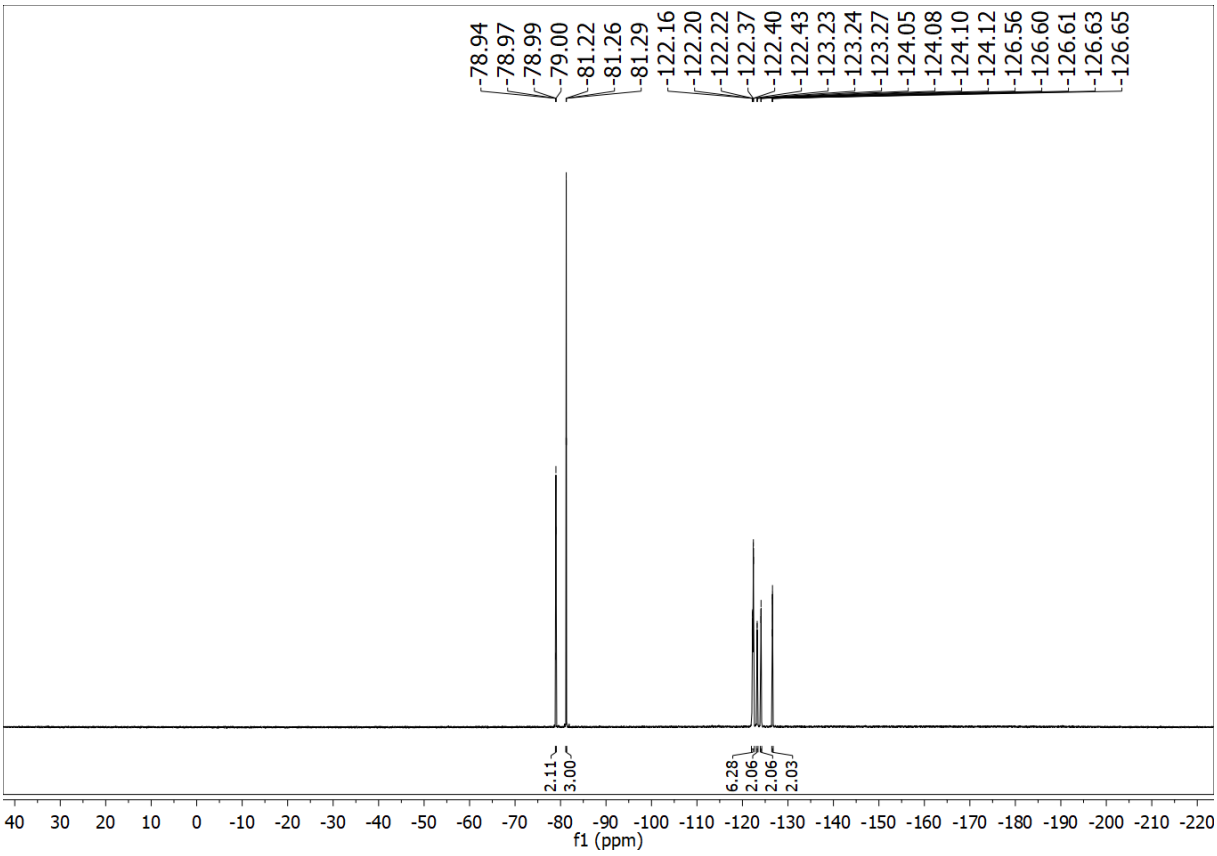


NMR-Solvent: $CDCl_3$

2,2,6,6-tetramethyl-1-((perfluorooctyl)oxy)piperidine (32)

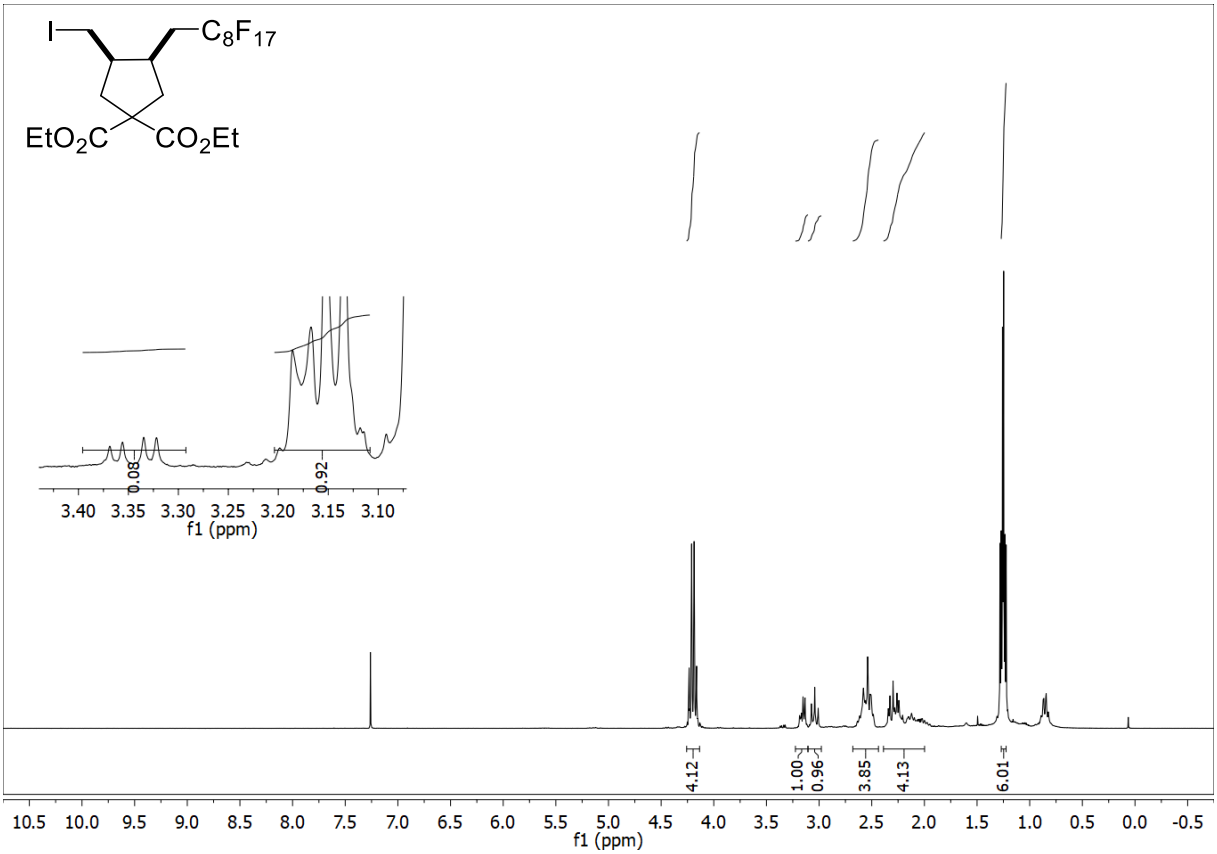


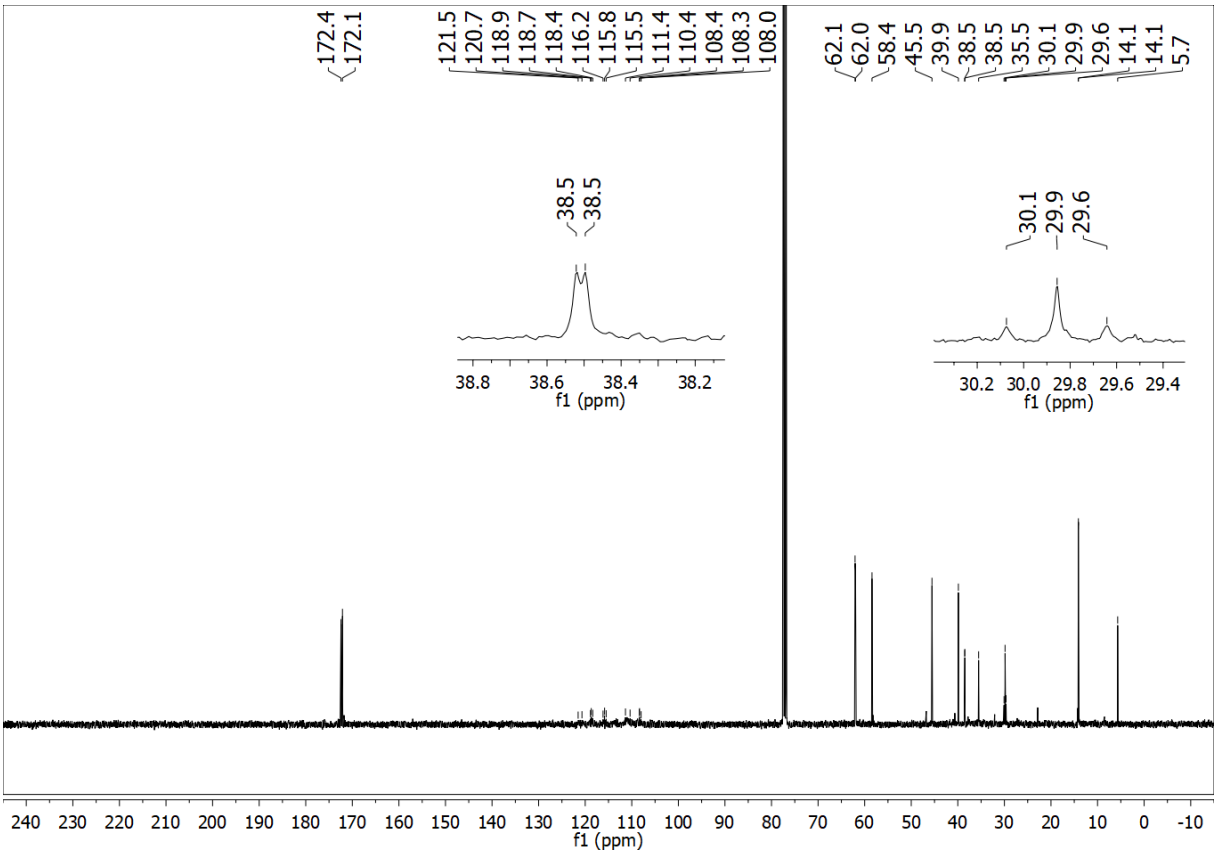


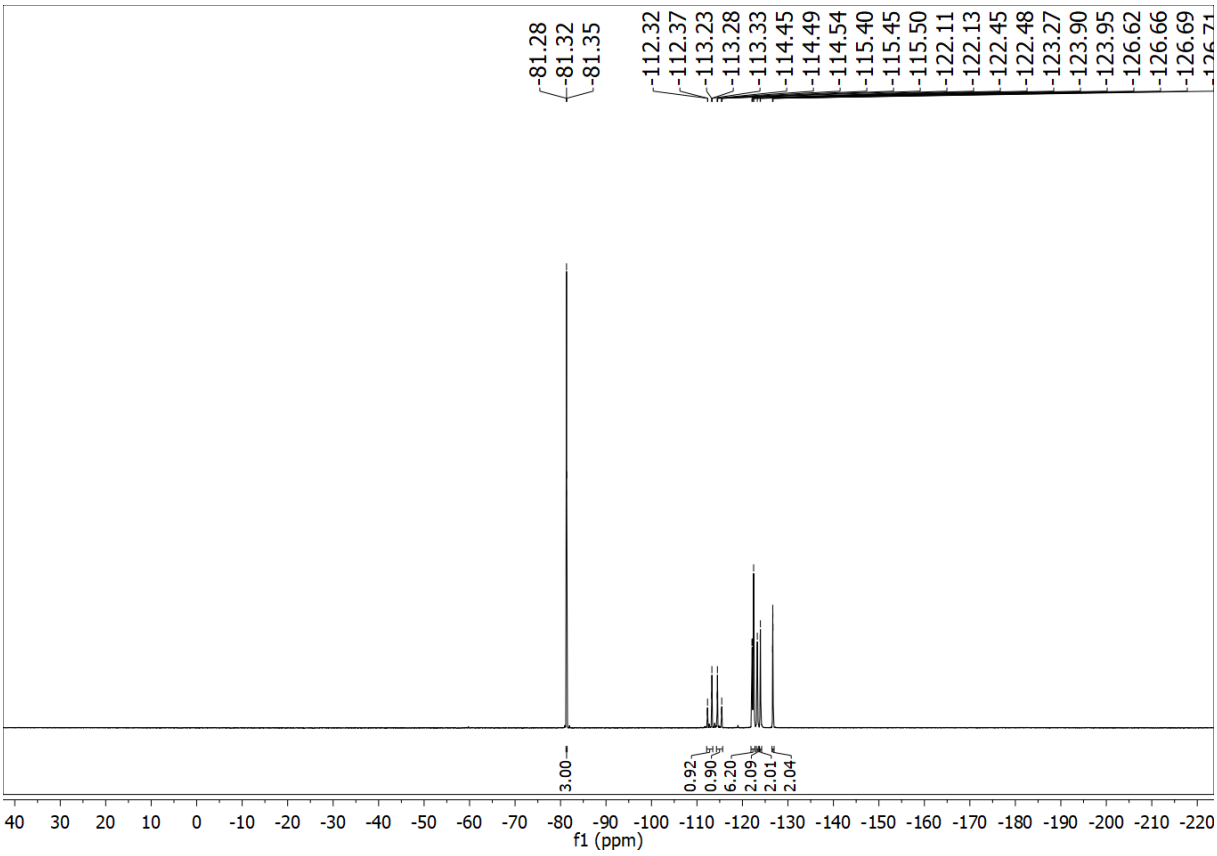


NMR-Solvent: $CDCl_3$

rac. Diethyl (3*R*,4*R*)-3-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononyl)-4-(iodomethyl)cyclopentane-1,1-dicarboxylate (34)

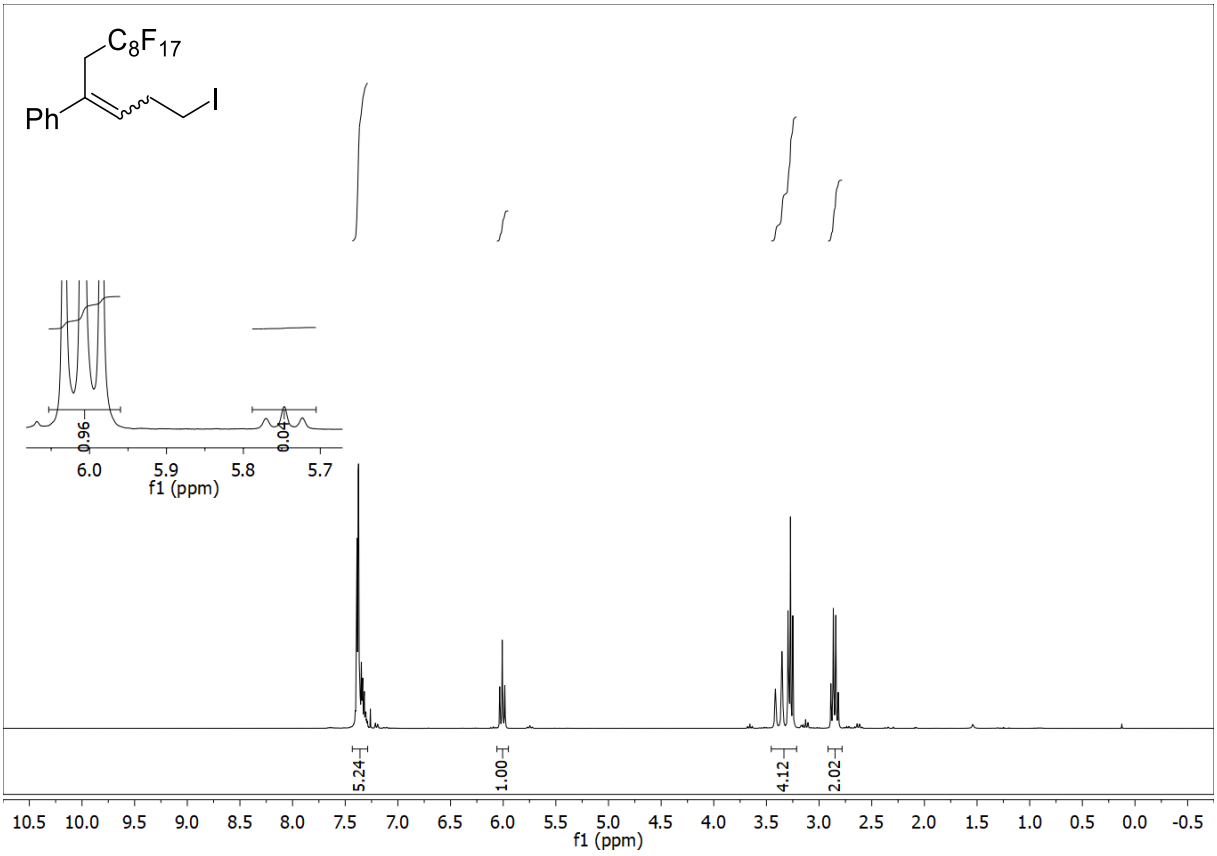


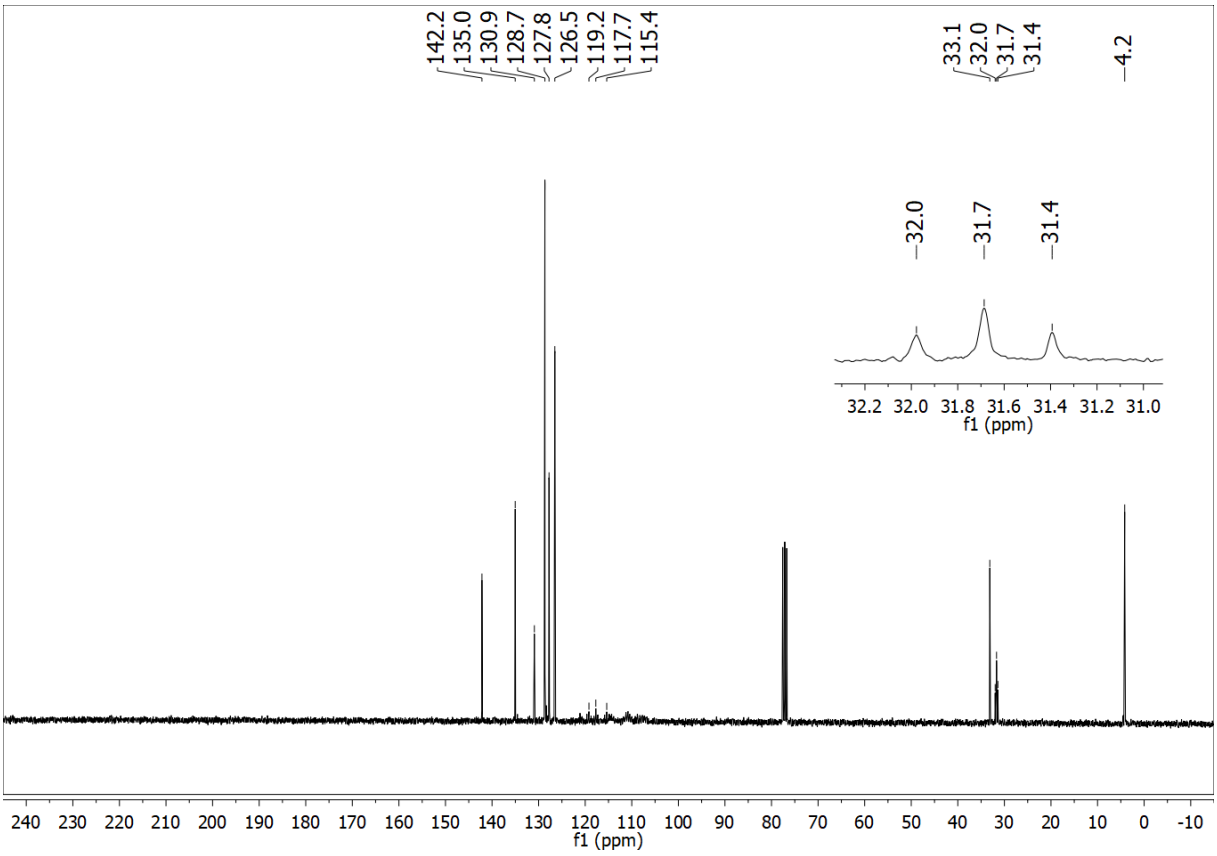


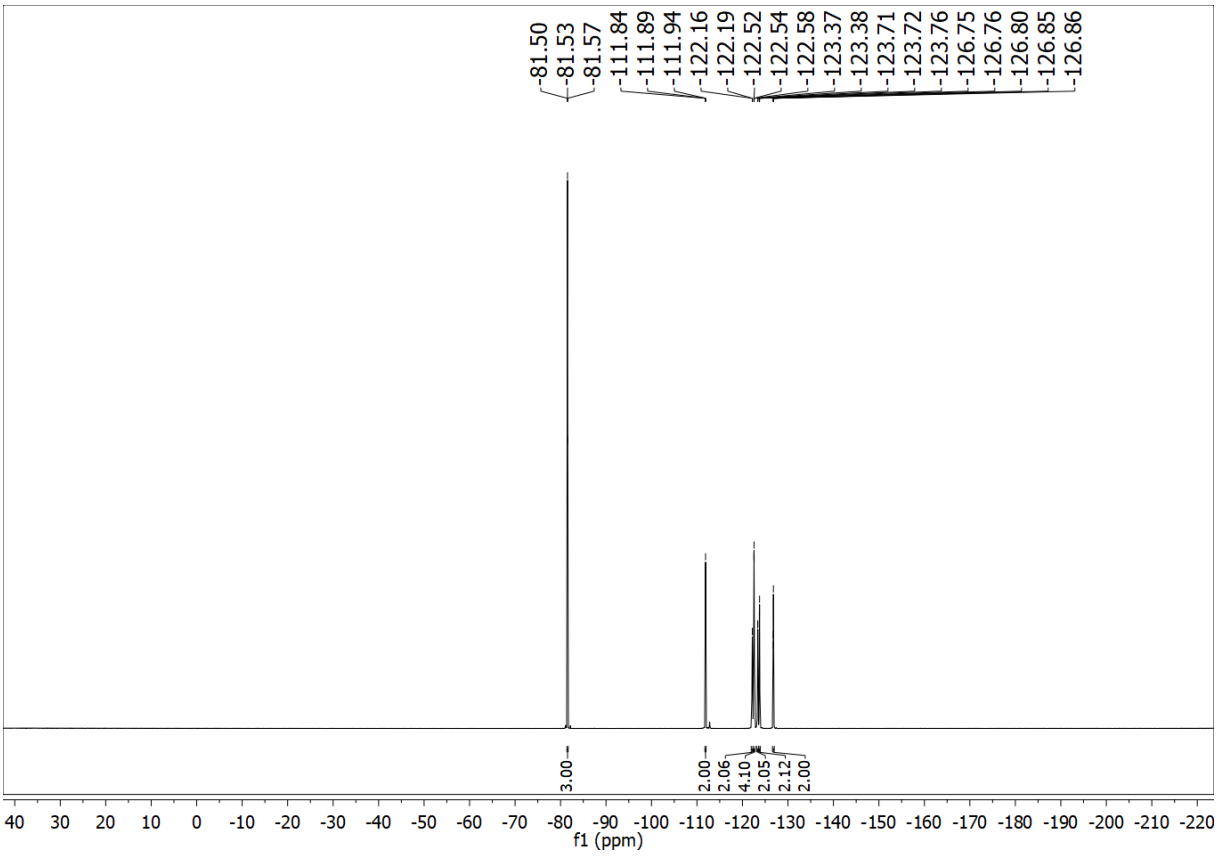


NMR-Solvent: $CDCl_3$

(6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-Heptadecafluoro-1-iodotridec-3-en-4-yl) benzene (37)







NMR-Solvent: $CDCl_3$

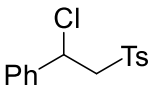
4. Chapter D: Copper Mediated Chlorosulfonylation of Alkenes

4.1. Synthesis of Literature Known Compounds and Reagents

The following compounds were synthesized according to the reported literature procedures. The spectral data were in agreement with the data reported: *tert*-butyl allylcarbamate (**1e**)[17], (allyloxy)benzene (**1c**)[18], 1-allyl-2-methoxybenzene (**1j**)[26], 2-allylphenyl *tert*-butyl carbonate (**1k**)[27], methyl 2-allylbenzoate (**1l**)[21], methyl 2-(allyloxy)benzoate (**1m**)[14], diethyl 2,2-diallylmalonate (**21**)[22].

4.2. Compound Characterization

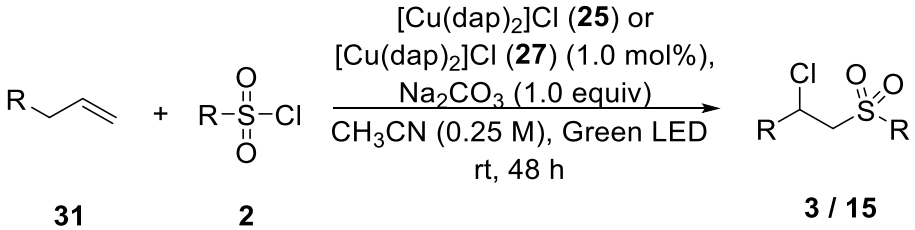
1-((2-chloro-2-phenylethyl)sulfonyl)-4-methylbenzene (3a)



Cu(I)-catalysis: A Schlenk tube equipped with a magnetic stir bar was charged with 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) in anh. MeCN (2.0 mL). The reaction mixture was degassed by three freeze-pump-thaw cycles and placed under N_2-atmosphere. Styrene (**1a**) (57 µL, 52 mg, 0.5 mmol, 1.0 equiv) was added and the reaction mixture was irradiated with a green LED (λ_{max} = 530 nm) at room temperature for 20 h. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexanes / EtOAc 9:1 to 4:1) to yield 140 mg (475 µmol, 95%) of rac. 1-((2-chloro-2-phenylethyl)sulfonyl)-4-methylbenzene (**3a**) as a white solid.

Cu(II)-catalysis: A Schlenk tube equipped with a magnetic stir bar was charged with 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)Cl_2]$ (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) in anh. MeCN (2.0 mL). The reaction mixture was degassed by three freeze-pump-thaw cycles and placed under N_2-atmosphere. Styrene (**1a**) (57 µL, 52 mg, 0.5 mmol, 1.0 equiv) was added and the reaction mixture was irradiated with a green LED (λ_{max} = 530 nm at room temperature for 20 h. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexanes / EtOAc 9:1 to 4:1) to yield 138 mg (468 µmol, 94%) of rac. 1-((2-chloro-2-phenylethyl)sulfonyl)-4-methylbenzene (**3a**) as a white solid. R_f (hexanes / EtOAc) = 0.29. Staining: Vanillin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.3 Hz, 2H), 7.29 – 7.19 (m, 7H), 5.33 (t, *J* = 6.9 Hz, 1H), 3.94 (dd, *J* = 14.8, 6.9 Hz, 1H), 3.84 (dd, *J* = 14.8, 6.9 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 138.7, 136.3, 129.8, 129.1, 129.0, 128.2, 127.2, 64.2, 55.2, 21.7.

General Procedure for Chlorosulfonylation of Unactivated Olefins (GP-1):

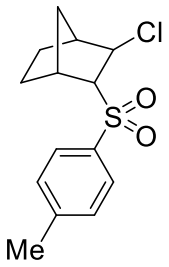


31 **2** **3 / 15**

A Schlenk tube equipped with a magnetic stir bar was charged with sulfonyl chloride derivative **2** (0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) / $[Cu(dap)Cl_2]$ (**27**) (5.0 µmol, 1.0 mol%) in anh. MeCN (2.0 mL). The reaction mixture was degassed by three freeze-pump-thaw cycles and placed under N_2-atmosphere. Alkene **31**

(1.0 mmol, 2.0 equiv) was added and the reaction mixture was irradiated with a green LED (λ_{max} = 530 nm) at room temperature. After completion of the reaction (judged by TLC, usually 48 h), the reaction mixture was washed with brine solution (20 mL) and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic fractions were dried over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel to yield pure product **3** / **15**.

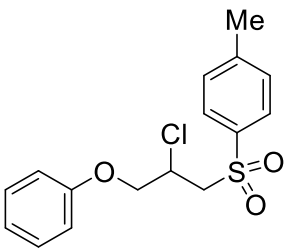
rac. (1*S*,2*R*,3*R*,4*R*)-2-chloro-3-tosylbicyclo[2.2.1]heptane (3b)



Cu(I)-catalysis: Following general procedure GP-1, using rac. (1*R*,4*S*)-bicyclo[2.2.1]hept-2-ene (**1b**) (94.2 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95.3 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53.0 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 130 mg (456 µmol, 91%) of **3b** as a white solid after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Cu(II)-catalysis: Following general procedure GP-1, using rac. (1*R*,4*S*)-bicyclo[2.2.1]hept-2-ene (**1b**) (94.2 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95.3 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53.0 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)Cl_2]$ (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 118 mg (414 µmol, 83%) of **3b** as a white solid after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.49. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 4.41 (ddd, *J* = 5.6, 4.1, 1.8 Hz, 1H), 2.88 (dd, *J* = 5.2, 2.2 Hz, 1H), 2.82 (d, *J* = 4.1 Hz, 1H), 2.54 – 2.48 (m, 1H), 2.44 (s, 3H), 2.04 – 1.96 (m, 1H), 1.89 (dddd, *J* = 12.8, 9.3, 4.9, 2.3 Hz, 1H), 1.69 (tt, *J* = 12.3, 4.6 Hz, 1H), 1.51 (dtd, *J* = 12.6, 4.1, 1.8 Hz, 1H), 1.41 (dq, *J* = 10.8, 1.8 Hz, 1H), 1.36 – 1.25 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 135.3, 130.0, 128.6, 75.3, 59.8, 44.0, 39.3, 36.1, 29.7, 21.8, 21.5. HRMS (EI) m/z calculated for $C_{14}H_{17}O_2SCl$ ($[M]^{+\bullet}$) 284.0632, found 284.0628.

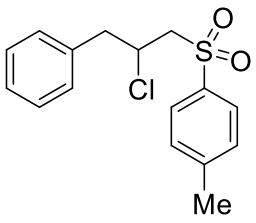
1-((2-chloro-3-phenoxypropyl)sulfonyl)-4-methylbenzene (3c)



Cu(I)-catalysis: Following general procedure GP-1, using (allyloxy)benzene (**1c**) (134 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv), and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 118 mg (363 µmol, 73%) of **3c** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Cu(II)-catalysis: Following general procedure GP-1, using (allyloxy)benzene (**1c**) (134 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv), and [Cu(dap)Cl_2] (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 115 mg (354 µmol, 71%) of **3c** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.41. Staining: Vanillin (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.31 – 7.24 (m, 2H), 7.04 – 6.95 (m, 1H), 6.89 – 6.81 (m, 2H), 4.60 (p, *J* = 5.4 Hz, 1H), 4.25 (dd, *J* = 10.3, 4.8 Hz, 1H), 4.18 (dd, *J* = 10.3, 5.4 Hz, 1H), 3.88 (dd, *J* = 14.8, 5.9 Hz, 1H), 3.58 (dd, *J* = 14.8, 6.8 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 145.4, 136.3, 130.1, 129.7, 128.2, 121.9, 114.8, 70.1, 60.0, 51.3, 21.8. IR (neat): 3042, 2930, 1599, 1495, 1461, 1398, 1290, 1238, 1141, 1085, 1044, 928, 842, 816, 753, 690 cm^{-1}. LRMS (EI) *m/z* (%): 133.1 (100), 91.1 (87), 155.0 (46), 139.0 (45), 77.0 (32), 231.0 ([M]$^{+\bullet}$-$C_6H_5O^\bullet$,17), 195.0 ([M]$^{+\bullet}$-$C_6H_5O^\bullet$-HCl,15), 324.1 (([M]$^{+\bullet}$,3), 288.1 ([M]$^{+\bullet}$-HCl, 2). HRMS (EI) m/z calculated for $C_{16}H_{17}O_3SCl$ ([M]$^{+\bullet}$) 324.0581, found 324.0588.

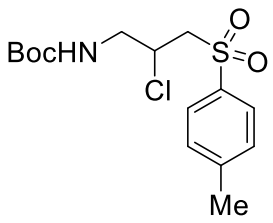
1-((2-chloro-3-phenylpropyl)sulfonyl)-4-methylbenzene (3d)



Cu(I)-catalysis: Following general procedure GP-1, using allyl benzene (**1d**) (132 µL, 118 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv), and [Cu(dap)$_2$]Cl (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 117 mg (379 µmol, 76%) of **3d** as a white solid after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Cu(II)-catalysis: Following general procedure GP-1, using allyl benzene (**1d**) (132 µL, 118 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv), and [Cu(dap)Cl_2] (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 111 mg (359 µmol, 72%) of **3d** as a white solid after 72 h and flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc) = 0.48. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.21 (m, 5H), 7.20 – 7.15 (m, 2H), 4.46 (dq, *J* = 7.7, 6.1 Hz, 1H), 3.48 (d, *J* = 6.3 Hz, 2H), 3.25 (dd, *J* = 14.3, 5.5 Hz, 1H), 3.06 (dd, *J* = 14.3, 7.7 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.3, 136.4, 136.0, 130.1, 129.7, 128.7, 128.3, 127.4, 62.4, 54.6, 43.9, 21.8. IR (neat): 3042, 2989, 2911, 1595, 1495, 1454, 1390, 1342, 1297, 1185, 1137, 1088, 895, 820, 768, 701 cm^{-1}. HRMS (ESI) m/z calculated for $C_{16}H_{21}ClNO_2S$ ([M+NH_4]$^+$) 326.0976, found 326.0980.

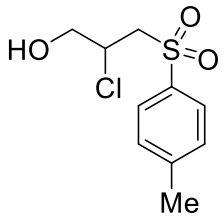
***tert*-butyl (2-chloro-3-tosylpropyl)carbamate (3e)**



Cu(I)-catalysis: Following general procedure GP-1, using *tert*-butyl allylcarbamate (**1e**) (157 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 140 mg (402 µmol, 80%) of **3e** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Cu(II)-catalysis: Following general procedure GP-1, using *tert*-butyl allylcarbamate (**1e**) (157 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)Cl_2]$ (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 131 mg (377 µmol, 75%) of **3e** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.25. Staining: Ninhydrin (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 5.15 – 4.70 (m, 1H, rotamer present), 4.34 (p, *J* = 5.7 Hz, 1H), 3.76 – 3.38 (m, 4H), 2.45 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.8, 145.4, 136.3, 130.2, 128.4, 80.3, 60.9, 53.7, 46.5, 28.4, 21.8. IR (neat): 3377, 3001, 2915, 1700, 1599, 1521, 1457, 1431, 1394, 1334, 1290, 1167, 1006, 943, 883, 805, 705 cm^{-1}. HRMS (ESI) m/z calculated for $C_{15}H_{26}ClN_2O_4S$ ($[M+NH_4]^+$) 365.1296, found 365.1297.

2-chloro-3-tosylpropan-1-ol (3f)

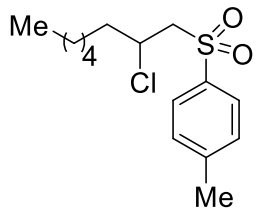


Cu(I)-catalysis: Following general procedure GP-1, using prop-2-en-1-ol (**1f**) (68 µL, 58 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 96 mg (386 µmol, 77%) of **3f** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Cu(II)-catalysis: Following general procedure GP-1, using prop-2-en-1-ol (**1f**) (68 µL, 58 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)Cl_2]$ (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 90 mg (362 µmol, 72%) of **3f** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.11. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 4.38 (tt, *J* = 6.4, 4.6 Hz, 1H), 3.92 (dd, *J* = 12.3, 4.7 Hz, 1H), 3.84 (dd, *J* = 12.3, 4.5 Hz, 1H), 3.71 (dd, *J* = 14.6, 6.5 Hz, 1H), 3.49 (dd, *J* = 14.7, 6.3 Hz, 1H), 2.71 (bs, 1H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.5, 136.1, 130.2, 128.2, 65.6, 59.7, 54.8, 21.8; IR (neat): 3493, 3064, 2926, 2881, 1595, 1495,

1454, 1402, 1290, 1137, 1085, 972, 898, 854, 813, 760, 708, 667 cm^{-1}. HRMS (APCI) m/z calculated for $C_{10}H_{17}ClNO_3S$ ($[M+NH_4]^+$) 266.0612, found 266.0611.

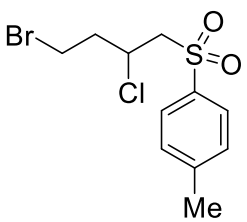
1-((2-chlorooctyl)sulfonyl)-4-methylbenzene (3g)



Cu(I)-catalysis: Following general procedure GP-1, using oct-1-ene (**1g**) (157 µL, 112 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 127 mg (419 µmol, 84%) of **3g** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Cu(II)-catalysis Following general procedure GP-1, using oct-1-ene (**1g**) (157 µL, 112 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)Cl_2]$ (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 130 mg (429 µmol, 86%) of **3g** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.68. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 – 7.76 (m, 2H), 7.40 – 7.33 (m, 2H), 4.29 (dtd, *J* = 8.8, 6.3, 3.9 Hz, 1H), 3.55 (dd, *J* = 14.6, 6.2 Hz, 1H), 3.45 (dd, *J* = 14.6, 6.5 Hz, 1H), 2.45 (s, 3H), 1.96 (dddd, *J* = 14.0, 9.9, 5.8, 3.9 Hz, 1H), 1.84 – 1.66 (m, 1H), 1.56 – 1.16 (m, 8H), 0.94 – 0.81 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.3, 136.6, 130.1, 128.3, 63.6, 54.7, 38.0, 31.6, 28.5, 25.8, 22.6, 21.8, 14.1. IR (neat): 2930,2859, 1595, 1495, 1461, 1402, 1305, 1141, 1088, 1040, 924, 891, 842, 816, 757, 693 cm^{-1}. HRMS (APCI) m/z calculated for $C_{15}H_{27}ClNO_2S$ ($[M+NH_4]^+$) 320.1446, found 320.1450.

1-((4-bromo-2-chlorobutyl)sulfonyl)-4-methylbenzene (3h)

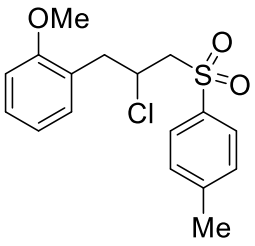


Cu(I)-catalysis: Following general procedure GP-1, using 4-bromobut-1-ene (**1h**) (203 µL, 270 mg, 2.0 mmol, 4.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 156 mg (479 µmol, 96%) of **3h** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Cu(II)-catalysis: Following general procedure GP-1, using 4-bromobut-1-ene (**1h**) (203 µL, 270 mg, 2.0 mmol, 4.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)Cl_2]$ (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 140 mg (430 µmol, 86%) of **3h** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.50. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.3 Hz, 2H), 7.43 – 7.36 (m, 2H), 4.46 (dddd, *J* =

10.4, 8.0, 5.3, 2.8 Hz, 1H), 3.68 – 3.44 (m, 4H), 2.65 (dddd, *J* = 15.1, 8.9, 7.0, 2.9 Hz, 1H), 2.47 (s, 3H), 2.31 – 2.14 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.6, 136.0, 130.3, 128.4, 63.1, 52.7, 40.1, 29.0, 21.9; IR (neat): 3049, 2974, 2926, 1595, 1495, 1439, 1402, 1301, 1256, 1215, 1141, 1085, 1036, 988, 939, 876, 813, 757, 705, 671 cm^{-1}. HRMS (ESI) m/z calculated for $C_{11}H_{18}BrClNO_2S$ ($[M+NH_4]^+$) 341.9925, found 341.9929.

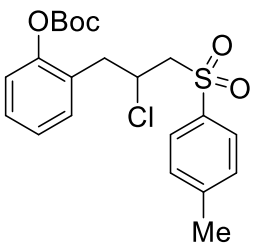
1-(2-chloro-3-tosylpropyl)-2-methoxybenzene (3j)



Cu(I)-catalysis: Following general procedure GP-1, using 1-allyl-2-methoxybenzene (**1j**) (148 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 140 mg (413 µmol, 83%) of **3j** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Cu(II)-catalysis: Following general procedure GP-1, using 1-allyl-2-methoxybenzene (**1j**) (148 mg, 1.00 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)Cl_2]$ (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 117 mg (345 µmol, 69%) of **3j** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.22. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.37 – 7.30 (m, 2H), 7.29 – 7.22 (m, 1H), 7.09 (dd, *J* = 7.4, 1.8 Hz, 1H), 6.92 – 6.80 (m, 2H), 4.65 – 4.51 (m, 1H), 3.79 (s, 3H), 3.53 (dd, *J* = 6.2, 1.5 Hz, 2H), 3.22 (dd, *J* = 13.8, 6.8 Hz, 1H), 3.04 (dd, *J* = 13.8, 7.5 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.5, 145.0, 136.5, 131.6, 129.9, 128.9, 128.4, 124.4, 120.6, 110.6, 62.9, 55.3, 53.4, 39.8, 21.8. IR (neat): 3004, 2922, 2840, 1737, 1599, 1495, 1402, 1401, 1320, 1290, 1245, 1137, 1088, 1029, 943, 861, 816, 753, 667 cm^{-1}. HRMS (ESI) m/z calculated for $C_{17}H_{23}ClNO_3S$ ($[M+NH_4]^+$) 356.1082, found 356.1086.

***tert*-butyl (2-(2-chloro-3-tosylpropyl)phenyl) carbonate (3k)**

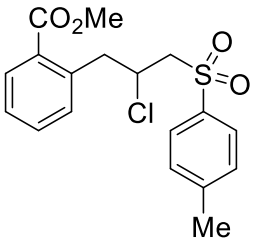


Cu(I)-catalysis: Following general procedure GP-1, using 2-allylphenyl *tert*-butyl carbonate (**1k**) (234 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 112 mg (264 µmol, 53% (brsm 77%)) of **3k** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Cu(II)-catalysis: Following general procedure GP-1, using 2-allylphenyl *tert*-butyl carbonate (**1k**) (234 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol,

1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and [Cu(dap)Cl_2] (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 75 mg (177 µmol, 35%, (brsm 57%)) of **3k** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.43. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.3 Hz, 2H), 7.38 – 7.11 (m, 6H), 4.48 (dtd, *J* = 8.4, 6.2, 5.4 Hz, 1H), 3.54 (dd, *J* = 6.3, 1.3 Hz, 2H), 3.41 (dd, *J* = 14.3, 5.5 Hz, 1H), 2.98 (dd, *J* = 14.4, 8.4 Hz, 1H), 2.44 (s, 3H), 1.56 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.8, 149.6, 145.2, 136.4, 131.7, 130.1, 128.7, 128.4, 128.4, 126.1, 122.6, 84.1, 62.9, 53.7, 38.8, 27.7, 21.8. IR (neat): 2982, 2933, 1756, 1595, 1491, 1454, 1398, 1327, 1275, 1226, 1141, 1047, 1014, 947, 891, 865, 816, 749, 664 cm^{-1}. HRMS (ESI) m/z calculated for $C_{21}H_{29}ClNO_5S$ ([M+NH_4]$^+$) 442.1449, found 442.1458.

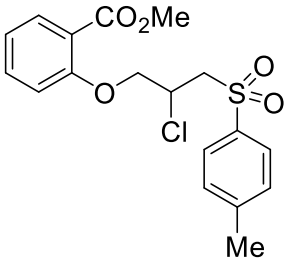
Methyl 2-(2-chloro-3-tosylpropyl)benzoate (3l)



Cu(I)-catalysis: Following general procedure GP-1, using methyl 2-allylbenzoate (**1l**) (176 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and [Cu(dap)$_2$]Cl (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 104 mg (283 µmol, 57% (brsm 74%)) of **3l** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Cu(II)-catalysis: Following general procedure GP-1, using methyl 2-allylbenzoate (**1l**) (176 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and [Cu(dap)Cl_2] (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 126 mg (343 µmol, 69%, (brsm 78%)) of **3l** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.30. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.45 (td, *J* = 7.5, 1.5 Hz, 1H), 7.38 – 7.23 (m, 4H), 4.57 (dddd, *J* = 8.5, 7.5, 5.5, 4.8 Hz, 1H), 3.87 (s, 3H), 3.75 – 3.51 (m, 3H), 3.32 (dd, *J* = 13.6, 8.4 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.4, 145.0, 138.0, 136.5, 132.7, 132.3, 131.3, 129.9, 129.6, 128.4, 127.6, 63.0, 54.7, 52.3, 42.8, 21.8. IR (neat): 3027, 2952, 1715, 1599, 1491, 1435, 1402, 1260, 1189, 1137, 1081, 1018, 962, 906, 857, 813, 749, 708, 664 cm^{-1}. HRMS (ESI) m/z calculated for $C_{18}H_{23}ClNO_4S$ ([M+NH_4]$^+$) 384.1031, found 384.1038.

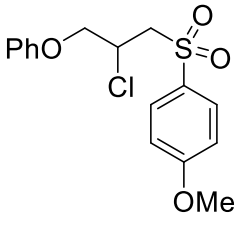
Methyl 2-(2-chloro-3-tosylpropoxy)benzoate (3m)



Cu(I)-catalysis: Following general procedure GP-1, using methyl 2-(allyloxy)benzoate (**1m**) (192 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 100 mg (261 µmol, 52% (brsm 73%)) of **3m** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1).

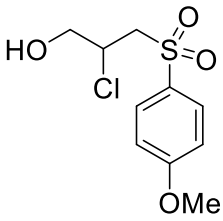
Cu(II)-catalysis: Following general procedure GP-1, using methyl 2-(allyloxy)benzoate (**1m**) (192 mg, 1.00 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)Cl_2]$ (**27**) (2.6 mg, 5.0 µmol, 1.0 mol%) gave 145 mg (379 µmol, 76%, (brsm 83%)) of **3m** as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.26. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85 – 7.76 (m, 3H), 7.42 (ddd, *J* = 8.3, 7.4, 1.8 Hz, 1H), 7.31 – 7.23 (m, 2H), 7.01 (td, *J* = 7.6, 1.0 Hz, 1H), 6.82 (dd, *J* = 8.3, 1.0 Hz, 1H), 4.64 (tdd, *J* = 6.4, 5.3, 4.1 Hz, 1H), 4.40 – 4.15 (m, 3H), 3.87 (s, 3H), 3.58 (dd, *J* = 14.7, 6.6 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.2, 157.3, 145.2, 136.4, 133.7, 132.1, 130.0, 128.2, 121.5, 120.5, 113.8, 70.7, 59.4, 52.1, 51.1, 21.7. IR (neat): 2952, 1722, 1599, 1491, 1454, 1402, 1305, 1245, 1137, 1085, 1051, 962, 936, 906, 880, 842, 816, 753, 705 cm^{-1}. HRMS (ESI) m/z calculated for $C_{18}H_{20}ClO_5S$ ($[M+H]^+$) 383.0714, found 383.0718.

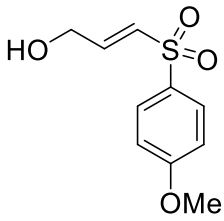
1-((2-chloro-3-phenoxypropyl)sulfonyl)-4-methoxybenzene (15b)



Cu(I)-catalysis: Following general procedure GP-1, using (allyloxy)benzene (**1c**) (134 mg, 1.0 mmol, 2.0 equiv), 4-methoxybenzenesulfonyl chloride (**2b**) (103 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.50 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 130 mg (381 µmol, 76%) of 1-((2-chloro-3-phenoxypropyl)sulfonyl)-4-methoxybenzene (**15b**) as colorless oil after flash column purification (hexanes / EtOAc 9:1 to 3:1). R_f (hexanes / EtOAc, 4:1) = 0.25. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.9 Hz, 2H), 7.32 – 7.23 (m, 2H), 7.03 – 6.94 (m, 3H), 6.89 – 6.81 (m, 2H), 4.59 (dq, *J* = 6.7, 5.5 Hz, 1H), 4.21 (qd, *J* = 10.3, 5.1 Hz, 2H), 3.92 – 3.80 (m, 4H), 3.58 (dd, *J* = 14.8, 6.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 157.8, 130.7, 130.5, 129.7, 121.9, 114.9, 114.7, 70.2, 60.3, 55.8, 51.4. IR (neat): 3064, 2933, 2840, 1595, 1495, 1461, 1413, 1297, 1238, 1137, 1088, 1021, 928, 835, 753, 693 cm^{-1}. HRMS (ESI) m/z calculated for $C_{16}H_{21}ClNO_4S$ ($[M+NH_4]^+$) 358.0874, found 358.0882.

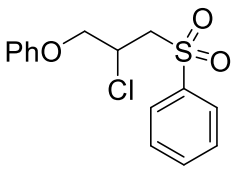
2-chloro-3-((4-methoxyphenyl)sulfonyl)propan-1-ol (15b´) and (*E*)-3-((4-methoxyphenyl)-sulfonyl)prop-2-en-1-ol (16b´)





Cu(I)-catalysis: Following general procedure GP-1, using prop-2-en-1-ol (**1f**) (68 µL, 58 mg, 1.0 mmol, 2.0 equiv), 4-methoxybenzenesulfonyl chloride (**2b**) (103 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 66 mg (249 µmol, 50%) of 2-chloro-3-((4-methoxyphenyl)sulfonyl)propan-1-ol (**15b´**) and 33 mg (145 µmol, 29%) of (*E*)-3-((4-methoxyphenyl)sulfonyl)prop-2-en-1-ol (**16b´**) as colorless oils after flash column purification (hexanes / EtOAc 9:1 to 1:2). R_f (**15b´**, hexanes / EtOAc, 2:1) = 0.13. Staining: $KMnO_4$ (UV active). R_f (**16b´**, hexanes / EtOAc, 2:1) = 0.08. Staining: $KMnO_4$ (UV active). ^{1}H NMR (**15b´**, 300 MHz, $CDCl_3$) δ 7.88 – 7.79 (m, 2H), 7.06 – 6.97 (m, 2H), 4.38 (tt, *J* = 6.4, 4.5 Hz, 1H), 3.98 – 3.80 (m, 5H), 3.70 (dd, *J* = 14.6, 6.6 Hz, 1H), 3.48 (dd, *J* = 14.6, 6.2 Hz, 1H), 2.57 (bs, 1H). ^{1}H NMR (**16b´**, 300 MHz, $CDCl_3$) δ 7.81 – 7.75 (m, 2H), 7.02 – 6.92 (m, 3H), 6.62 (dtd, *J* = 15.0, 2.2, 0.5 Hz, 1H), 4.35 (dd, *J* = 3.2, 2.3 Hz, 2H), 3.86 (s, 3H), 2.36 (s, 1H). ^{13}C NMR (**15b´**, 75 MHz, $CDCl_3$) δ 164.3, 130.5, 114.8, 65.7, 60.0, 55.9, 55.0. ^{13}C NMR (**16b´**, 75 MHz, $CDCl_3$) δ 163.7, 144.5, 131.7, 130.1, 130.0, 114.7, 61.0, 55.8. IR (**15b´**, neat): 3499, 3101, 2937, 2844, 1595, 1498, 1461, 1416, 1297, 1260, 1133, 1088, 1021, 973, 902, 835, 805, 768, 693 cm^{-1}. IR (**16b´**, neat): 3496, 3064, 2974, 2848, 1633, 1595, 1498, 1461, 1435, 1357, 1312, 1264, 1193, 1133, 1085, 1018, 943, 828, 805, 764, 671 cm^{-1}. HRMS (**15b´**, ESI) m/z calculated for $C_{10}H_{17}ClNO_4S$ ($[M+NH_4]^+$) 282.0561, found 282.0565. HRMS (**16b´**, ESI) m/z calculated for $C_{10}H_{16}NO_4S$ ($[M+NH_4]^+$) 246.0795, found 246.0797.

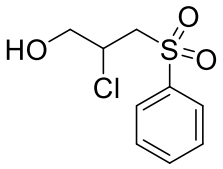
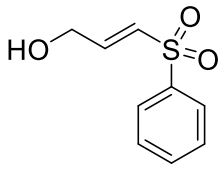
(2-chloro-3-(phenylsulfonyl)propoxy)benzene (15c)



Cu(I)-catalysis: Following general procedure GP-1, using (allyloxy)benzene (**1c**) (134 mg, 1.0 mmol, 2.0 equiv), benzenesulfonyl chloride (**2c**) (88 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 91 mg (293 µmol, 59%) of (2-chloro-3-(phenylsulfonyl)propoxy)benzene (**15c**) as colorless oil after flash column purification (hexanes / EtOAc 9:1 to 3:1). R_f (hexanes / EtOAc, 4:1) = 0.35. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 – 7.91 (m, 2H), 7.71 – 7.62 (m, 1H), 7.61 – 7.52 (m, 2H), 7.34 – 7.24 (m, 2H), 7.04 – 6.96 (m, 1H), 6.90 – 6.83 (m, 2H), 4.69 – 4.57 (m, 1H), 4.27 (dd, *J* = 10.3, 4.8 Hz, 1H), 4.19 (dd, *J* = 10.3, 5.5 Hz, 1H), 3.90 (dd, *J* = 14.8, 5.7 Hz, 1H), 3.61 (dd, *J* = 14.8, 7.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 139.3, 134.3, 129.7, 129.6, 128.3, 122.0, 114.9, 70.2, 60.1, 51.2. IR (neat): 3064, 2930, 1599,

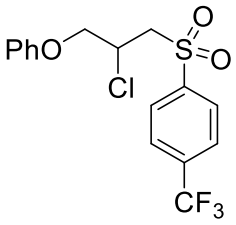
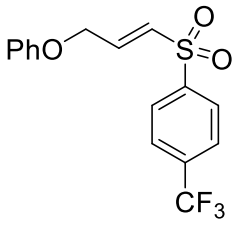
1495, 1446, 1390, 1305, 1238, 1141, 1085, 1044, 928, 883, 842, 820, 787, 749, 686 cm^{-1}. HRMS (ESI) m/z calculated for $C_{15}H_{19}ClNO_3S$ ($[M+NH_4]^+$) 328.0769, found 328.0774.

2-chloro-3-(phenylsulfonyl)propan-1-ol (15c´) and (*E*)-3-(phenylsulfonyl)prop-2-en-1-ol (16c´)

Cu(I)-catalysis: Following general procedure GP-1, using prop-2-en-1-ol (**1f**) (68 µL, 58 mg, 1.0 mmol, 2.0 equiv), benzenesulfonyl chloride (**2c**) (88 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 35 mg (149 µmol, 30%) of 2-chloro-3-(phenylsulfonyl)propan-1-ol (**15c´**) and 48 mg (242 µmol, 48%) of (*E*)-3-(phenylsulfonyl)prop-2-en-1-ol (**16c´**) as colorless oils after flash column purification (hexanes / EtOAc 9:1 to 1:1). R_f (**15c´**, hexanes / EtOAc, 2:1) = 0.18. Staining: $KMnO_4$ (UV active). R_f (**16c´**, hexanes / EtOAc, 2:1) = 0.13. Staining: $KMnO_4$ (UV active). ^{1}H NMR (**15c´**, 300 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.74 – 7.66 (m, 1H), 7.64 – 7.55 (m, 2H), 4.43 (ddt, *J* = 6.7, 6.1, 4.4 Hz, 1H), 4.02 – 3.84 (m, 2H), 3.73 (dd, *J* = 14.6, 6.8 Hz, 1H), 3.53 (dd, *J* = 14.6, 6.1 Hz, 1H), 2.31 (bs, 1H). ^{1}H NMR (**16c´**, 300 MHz, CD_3CN) δ 7.91 – 7.84 (m, 2H), 7.74 – 7.53 (m, 3H), 7.03 (dt, *J* = 15.1, 3.2 Hz, 1H), 6.64 (dt, *J* = 15.0, 2.2 Hz, 1H), 4.25 (dt, *J* = 5.0, 2.8 Hz, 2H), 3.25 (s, 1H). ^{13}C NMR (**15c´**, 75 MHz, $CDCl_3$) δ 139.1, 134.4, 129.6, 128.2, 65.7, 59.7, 54.9. ^{13}C NMR (**16c´**, 75 MHz, CD_3CN) δ 148.3, 141.7, 134.4, 130.4, 129.5, 128.2, 61.0. IR (**15c´**, neat): 3489, 3064, 2930, 1588, 1446, 1394, 1305, 1141, 1085, 977, 902, 854, 787, 749, 686 cm^{-1}. IR (**16c´**, neat): 3489, 3056, 2922, 2851, 1629, 1390, 1275, 1226, 1197, 1137, 1081, 1018, 943, 842, 760, 716 cm^{-1}. HRMS (**15c´**, ESI) m/z calculated for $C_9H_{15}ClNO_3S$ ($[M+NH_4]^+$) 252.0456, found 252.0459. HRMS (**16c´**, ESI) m/z calculated for $C_9H_{14}NO_3S$ ($[M+NH_4]^+$) 216.0689, found 216.0692.

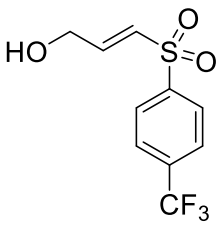
1-((2-chloro-3-phenoxypropyl)sulfonyl)-4-(trifluoromethyl)benzene (15d) and (*E*)-1-((3-phenoxyprop-1-en-1-yl)sulfonyl)-4-(trifluoromethyl)benzene (16d)

Cu(I)-catalysis: Following general procedure GP-1, using (allyloxy)benzene (**1c**) (134 mg, 1.0 mmol, 2.0 equiv), 4-(trifluoromethyl)benzenesulfonyl chloride (**2d**) (122 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 82 mg (216 µmol, 43%) of 1-((2-chloro-3-phenoxypropyl)sulfonyl)-4-(trifluoromethyl)benzene (**15d**) and 29 mg (85 µmol, 17%) of (*E*)-1-((3-phenoxyprop-1-en-1-yl)sulfonyl)-4-(trifluoromethyl)benzene (**16d**) as colorless oils after flash column purification (hexanes / EtOAc 9:1 to 3:1). R_f (**15d**, hexanes / EtOAc, 4:1) = 0.47. Staining: $KMnO_4$ (UV active). R_f (**16d**, hexanes / EtOAc, 4:1) = 0.43. Staining: $KMnO_4$ (UV active). ^{1}H NMR (**15d**,

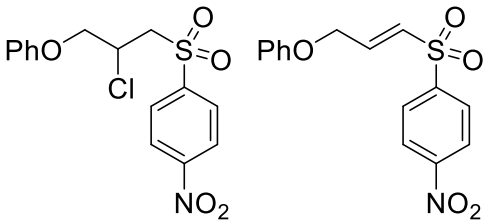
400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.28 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.87 – 6.80 (m, 2H), 4.64 (ddt, *J* = 7.5, 5.9, 4.8 Hz, 1H), 4.27 (dd, *J* = 10.3, 4.5 Hz, 1H), 4.15 (dd, *J* = 10.3, 5.9 Hz, 1H), 3.95 (dd, *J* = 15.0, 5.0 Hz, 1H), 3.66 (dd, *J* = 15.0, 7.5 Hz, 1H). ^{1}H NMR (**16d**, 400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.30 – 7.23 (m, 2H), 7.18 (dt, *J* = 15.0, 3.3 Hz, 1H), 6.97 (t, *J* = 7.4 Hz, 1H), 6.87 – 6.82 (m, 2H), 6.77 (dt, *J* = 15.0, 2.2 Hz, 1H), 4.73 (dd, *J* = 3.3, 2.2 Hz, 2H). ^{19}F NMR (**15d**, 377 MHz, $CDCl_3$) δ -63.72 (s, 3F). ^{19}F NMR (**16d**, 377 MHz, $CDCl_3$) δ -63.72 (s, 3F). ^{13}C NMR (**15d**, 101 MHz, $CDCl_3$) δ 157.6, 143.0 – 142.9 (m), 135.9 (q, *J* = 33.3 Hz), 129.8, 129.0, 126.7 (q, *J* = 3.6 Hz), 123.1 (q, *J* = 273.2 Hz), 122.1, 114.8, 70.0, 60.1, 50.9. ^{13}C NMR (**16d**, 101 MHz, $CDCl_3$) δ 157.6, 143.9 – 143.8 (m), 142.5, 135.4 (q, *J* = 33.2 Hz), 130.6, 129.8, 128.5, 126.6 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 273.1 Hz), 122.0, 114.7, 65.6. IR (**15d**, neat): 3101, 3068, 2997, 2945, 2889, 1599, 1498, 1402, 1320, 1290, 1245, 1167, 1122, 1085, 1059, 924, 887, 850, 799, 753, 693 cm^{-1}. IR (**16d**, neat): 3105, 3056, 2915, 2885, 1640, 1588, 1495, 1439, 1402, 1320, 1234, 1163, 1118, 1014, 951, 869, 829, 805 cm^{-1}. HRMS (**15d**, ESI) m/z calculated for $C_{16}H_{18}ClF_3NO_3S$ ($[M+NH_4]^+$) 396.0643, found 396.0640. HRMS (**16d**, ESI) m/z calculated for $C_{16}H_{17}F_3NO_3S$ ($[M+NH_4]^+$) 360.0876, found 360.0870.

(*E*)-3-((4-(trifluoromethyl)phenyl)sulfonyl)prop-2-en-1-ol (16d´)



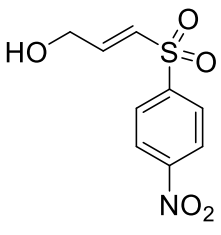
Cu(I)-catalysis: Following general procedure GP-1, using prop-2-en-1-ol (**1f**) (68 µL, 58 mg, 1.0 mmol, 2.0 equiv), 4-(trifluoromethyl)benzenesulfonyl chloride (**2d**) (122 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 100 mg (376 µmol, 75%) of (*E*)-3-((4-(trifluoromethyl)phenyl)sulfonyl)prop-2-en-1-ol (**16d´**) as colorless oil after flash column purification (hexanes / EtOAc 9:1 to 1:1). R_f (hexanes / EtOAc, 4:1) = 0.09. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 8.2 Hz, 2H), 7.11 (dt, *J* = 15.0, 3.0 Hz, 1H), 6.66 (dt, *J* = 14.9, 2.2 Hz, 1H), 4.40 (dd, *J* = 3.1, 2.3 Hz, 2H), 2.49 (bs, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -63.16 (s, 3F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.6, 143.8 (q, *J* = 1.6 Hz), 135.3 (q, *J* = 33.3 Hz), 128.7, 128.4, 126.6 (q, *J* = 3.9 Hz), 125.0, 121.4, 61.0. IR (neat): 3496, 3064, 1633, 1439, 1405, 1320, 1290, 1223, 1163, 1126, 1085, 1014, 948, 857, 790, 738 cm^{-1}. HRMS (ESI) m/z calculated for $C_{10}H_{10}F_3O_3S$ ($[M+H]^+$) 267.0297, found 267.0303.

1-((2-chloro-3-phenoxypropyl)sulfonyl)-4-nitrobenzene (15e) and (*E*)-1-nitro-4-((3-phenoxyprop-1-en-1-yl)sulfonyl)benzene (16e)



Cu(I)-catalysis: Following general procedure GP-1, using (allyloxy)benzene (**1c**) (134 mg, 1.0 mmol, 2.0 equiv), 4-nitrobenzenesulfonyl chloride (**2e**) (111 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 69 mg (194 µmol, 39%) of 1-((2-chloro-3-phenoxypropyl)sulfonyl)-4-nitrobenzene (**15e**) and 32 mg (100 µmol, 20%) of (*E*)-1-nitro-4-((3-phenoxyprop-1-en-1-yl)sulfonyl)benzene (**16e**) as colorless oils after flash column purification (hexanes / EtOAc 9:1 to 2:1). R_f (**15e**, hexanes / EtOAc, 4:1) = 0.33. Staining: $KMnO_4$ (UV active). R_f (**16e**, hexanes / EtOAc, 4:1) = 0.28. Staining: $KMnO_4$ (UV active). ^{1}H NMR (**15e**, 400 MHz, $CDCl_3$) δ 8.40 – 8.33 (m, 2H), 8.18 – 8.11 (m, 2H), 7.31 – 7.23 (m, 2H), 6.99 (td, *J* = 7.3, 1.0 Hz, 1H), 6.84 – 6.78 (m, 2H), 4.64 (ddt, *J* = 7.7, 6.1, 4.5 Hz, 1H), 4.26 (dd, *J* = 10.3, 4.4 Hz, 1H), 4.12 (dd, *J* = 10.3, 6.2 Hz, 1H), 3.99 (dd, *J* = 15.2, 4.7 Hz, 1H), 3.69 (dd, *J* = 15.2, 7.8 Hz, 1H).^{1}H NMR (**16e**, 400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.8 Hz, 2H), 8.10 (d, *J* = 8.8 Hz, 2H), 7.33 – 7.21 (m, 3H), 7.00 (tt, *J* = 7.2, 1.0 Hz, 1H), 6.87 (dt, *J* = 7.9, 1.0 Hz, 2H), 6.80 (dt, *J* = 14.9, 2.2 Hz, 1H), 4.78 (dd, *J* = 3.2, 2.2 Hz, 2H). ^{13}C NMR (**15e**, 101 MHz, $CDCl_3$) δ 157.4, 151.1, 145.0, 129.9, 129.8, 124.7, 122.2, 114.7, 69.8, 60.2, 50.9. ^{13}C NMR (**16e**, 101 MHz, $CDCl_3$) δ 157.5, 150.8, 146.0, 143.5, 130.1, 129.9, 129.3, 124.7, 122.1, 114.7, 65.6. IR (**15e**, neat): 3109, 3071, 3038, 2930, 2870, 1603, 1528, 1491, 1387, 1349, 1305, 1230, 1156, 1081, 1044, 902, 854, 760, 738, 690 cm^{-1}. IR (**16e**, neat): 3109, 3079, 2904, 2859, 1640, 1599, 1543, 1491, 1443, 1349, 1305, 1238, 1182, 1141, 1085, 1021, 872, 757, 682 cm^{-1}. HRMS (**15e**, ESI) m/z calculated for $C_{15}H_{18}ClN_2O_5S$ ($[M+NH_4]^+$) 373.0619, found 373.0619. HRMS (**16e**, ESI) m/z calculated for $C_{15}H_{17}N_2O_5S$ ($[M+NH_4]^+$) 337.0853, found 337.0853.

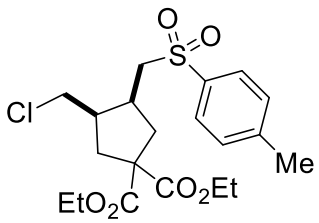
(*E*)-3-((4-nitrophenyl)sulfonyl)prop-2-en-1-ol (16e´)



Cu(I)-catalysis: Following general procedure GP-1, using prop-2-en-1-ol (**1f**) (68 µL, 58 mg, 1.0 mmol, 2.0 equiv), 4-nitrobenzenesulfonyl chloride (**2e**) (111 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 85 mg (349 µmol, 70%) of (*E*)-3-((4-nitrophenyl)sulfonyl)prop-2-en-1-ol (**16e´**) as colorless oil after flash column purification (hexanes / EtOAc 9:1 to 1:2). R_f (hexanes / EtOAc, 2:1) = 0.15. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, CD_3CN) δ 8.36 (d, *J* = 8.9 Hz, 2H), 8.08 (d, *J* = 8.9 Hz, 2H), 7.16 (dtd, *J* = 14.8, 3.0, 1.1 Hz, 1H), 6.70 (dt, *J* = 15.0, 2.3 Hz, 1H), 4.28 (s, 2H), 3.30 (s, 1H). ^{13}C NMR (75 MHz, CD_3CN) δ 151.0, 147.2, 129.8, 128.2, 125.5, 61.1. IR (neat): 3481, 3101, 3068, 3038, 2930, 2855, 1633, 1603, 1528, 1431, 1398, 1349, 1275, 1141,

1081, 1006, 939, 835, 764, 686 cm^{-1}. HRMS (ESI) m/z calculated for $C_9H_{10}NO_5S$ ($[M+H]^+$) 244.0274, found 244.0279.

rac. Diethyl (3*R*,4*S*)-3-(chloromethyl)-4-(tosylmethyl)cyclopentane-1,1-dicarboxylate (21)

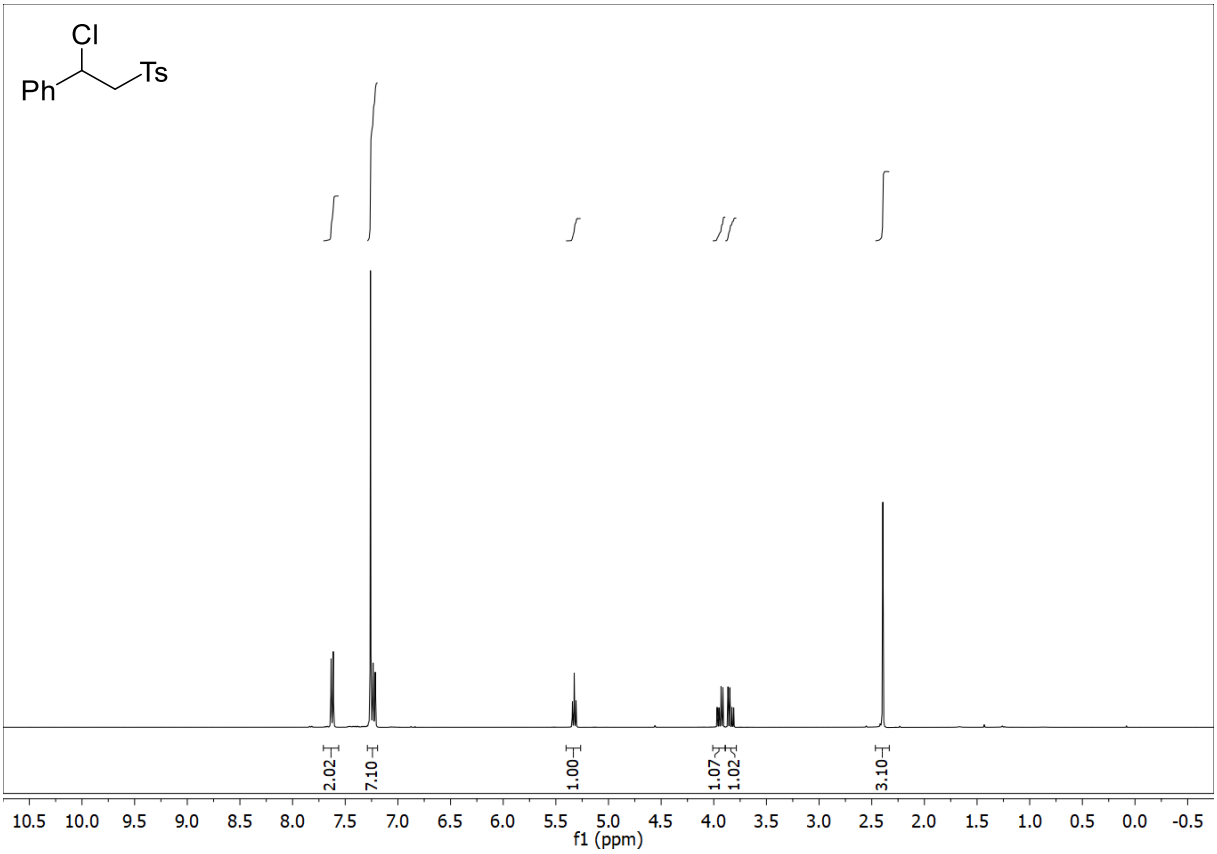


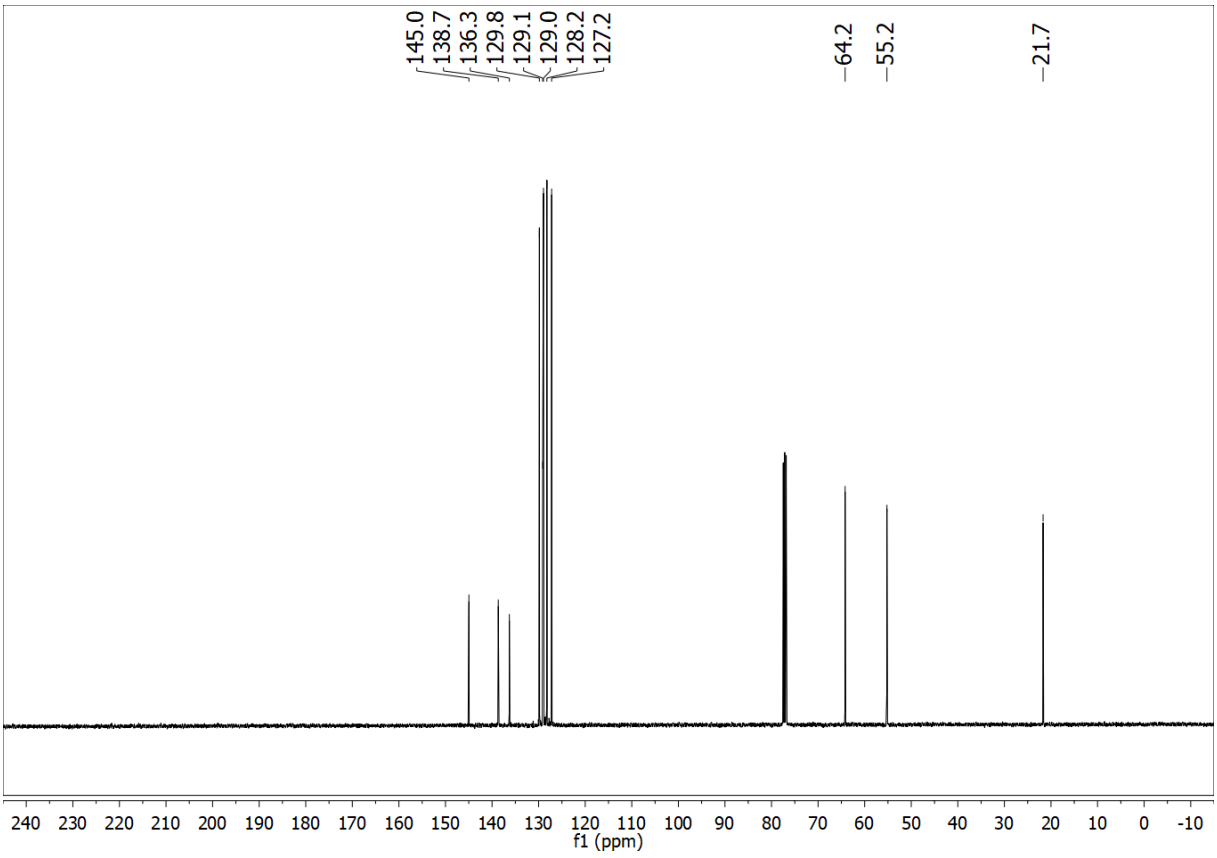
Cu(I)-catalysis: Following general procedure GP-1, using diethyl 2,2-diallylmalonate (**20**) (240 mg, 1.0 mmol, 2.0 equiv), 4-methylbenzenesulfonyl chloride (**2a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (53 mg, 0.5 mmol, 1.0 equiv) and $[Cu(dap)_2]Cl$ (**25**) (4.4 mg, 5.0 µmol, 1.0 mol%) gave 178 mg (413 µmol, 83%) of **21** in a diastereomeric ratio of 96:04 colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc, 4:1) = 0.31. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.38 – 7.31 (m, 2H), 4.16 (qd, *J* = 7.1, 1.9 Hz, 4H), 3.45 (d, *J* = 6.5 Hz, 2H), 3.23 (dd, *J* = 14.0, 5.0 Hz, 1H), 3.09 (dd, *J* = 14.0, 8.4 Hz, 1H), 2.65 – 2.17 (m, 9H), 1.22 (td, *J* = 7.1, 2.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.1, 171.9, 145.1, 136.5, 130.2, 128.2, 62.0, 61.9, 58.7, 56.0, 44.5, 43.9, 38.5, 37.1, 36.0, 21.8, 14.2; IR (neat): 2982, 1722, 1599, 1446, 1398, 1368, 1301, 1256, 1182, 1141, 1088, 1059, 861, 816, 760, 667 cm^{-1}. HRMS (ESI) m/z calculated for $C_{20}H_{28}ClO_6S$ ($[M+H]^+$) 431.1290, found 431.1300.

4.3. NMR Spectra

^{1}H NMR	first image
^{13}C NMR	second image
^{19}F NMR	third image

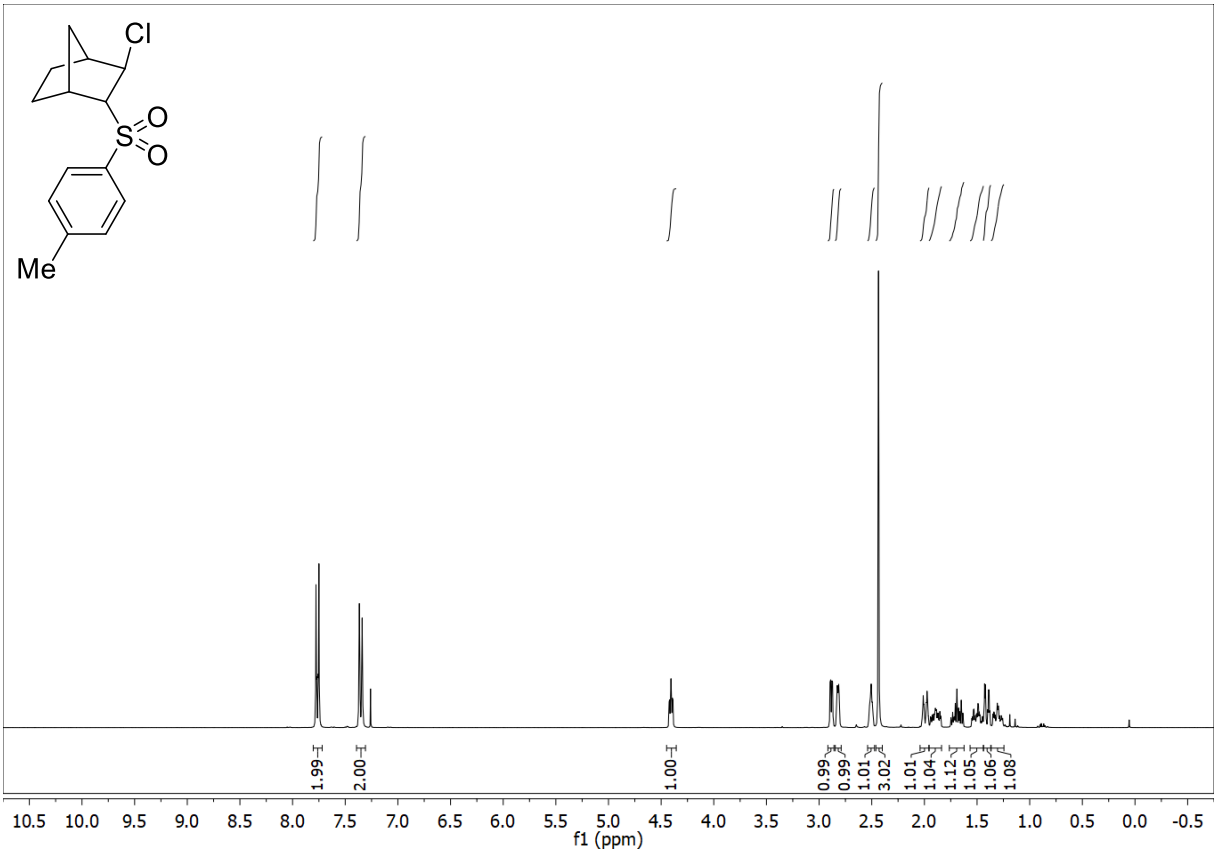
1-((2-Chloro-2-phenylethyl)sulfonyl)-4-methylbenzene (3a)

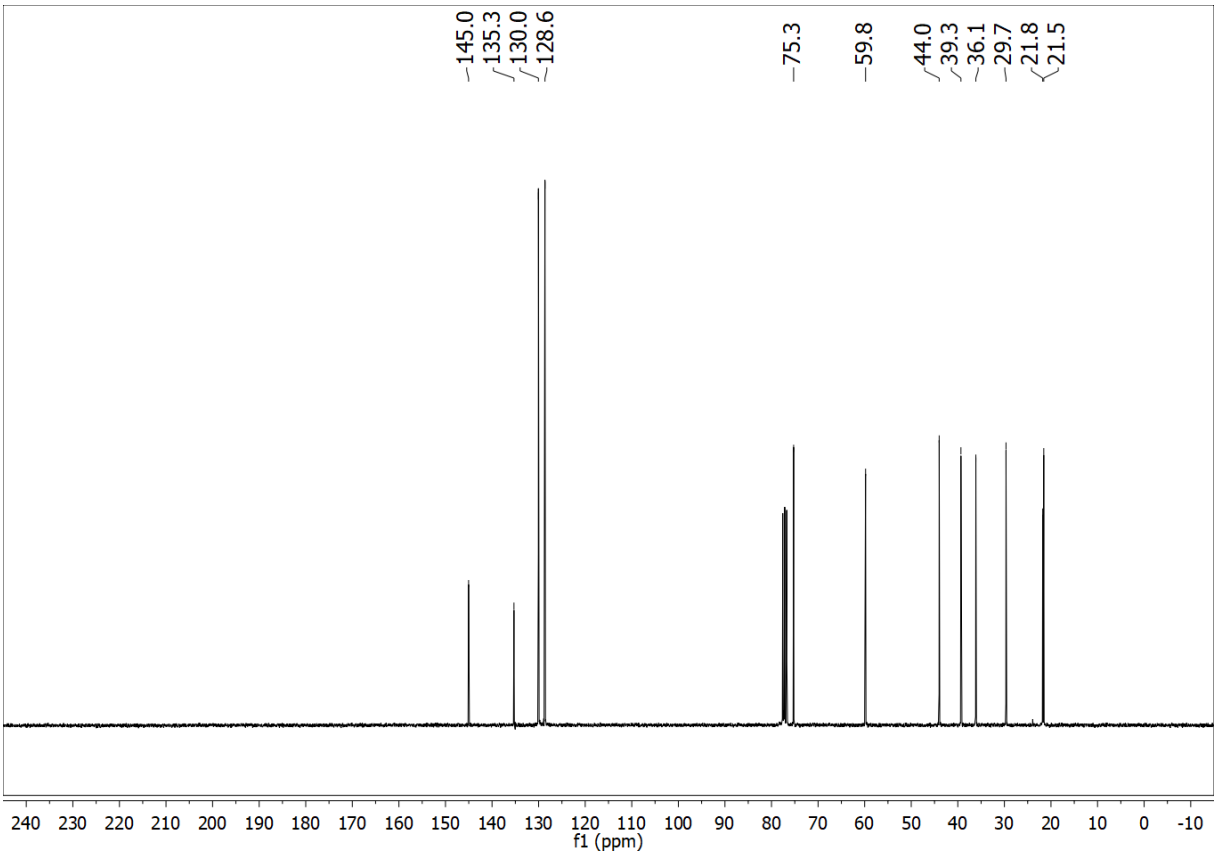




NMR-Solvent: $CDCl_3$

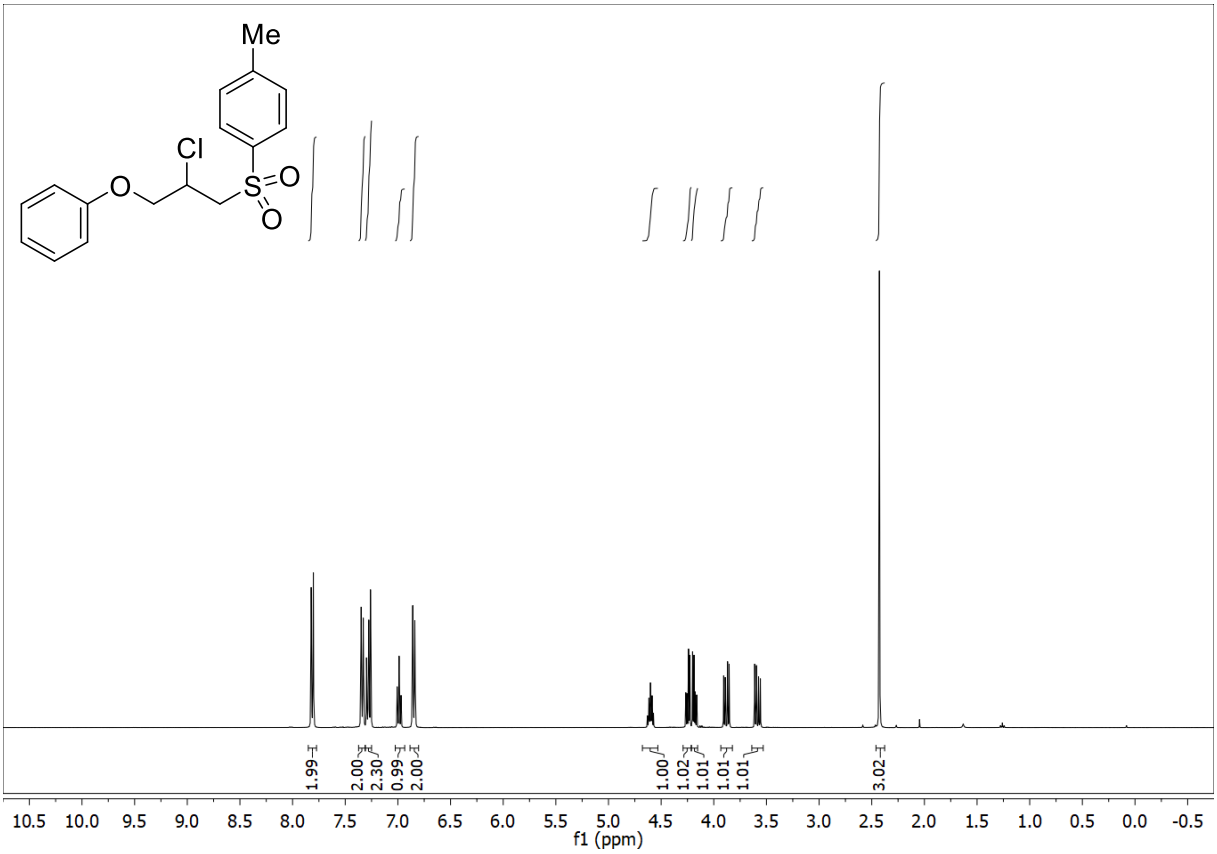
rac. (1*S*,2*R*,3*R*,4*R*)-2-Chloro-3-tosylbicyclo[2.2.1]heptane (3b)

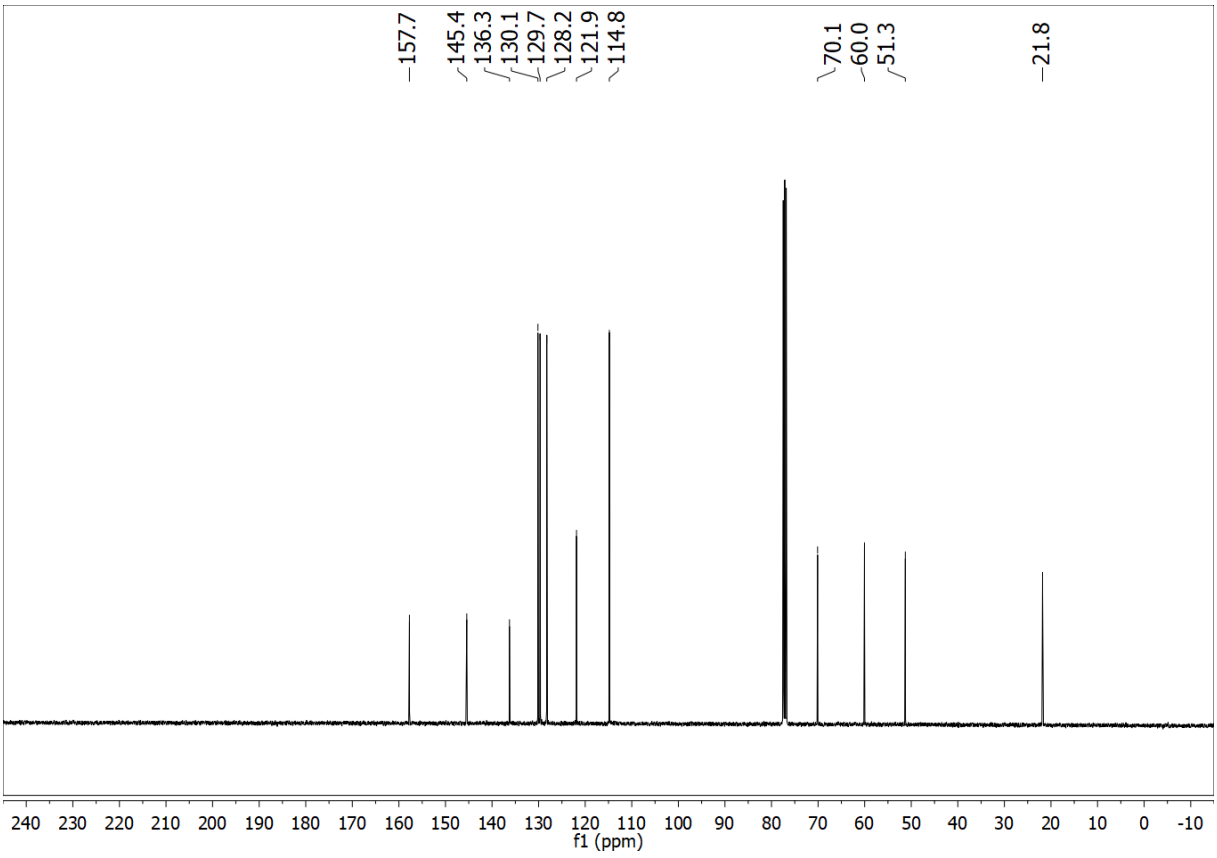




NMR-Solvent: $CDCl_3$

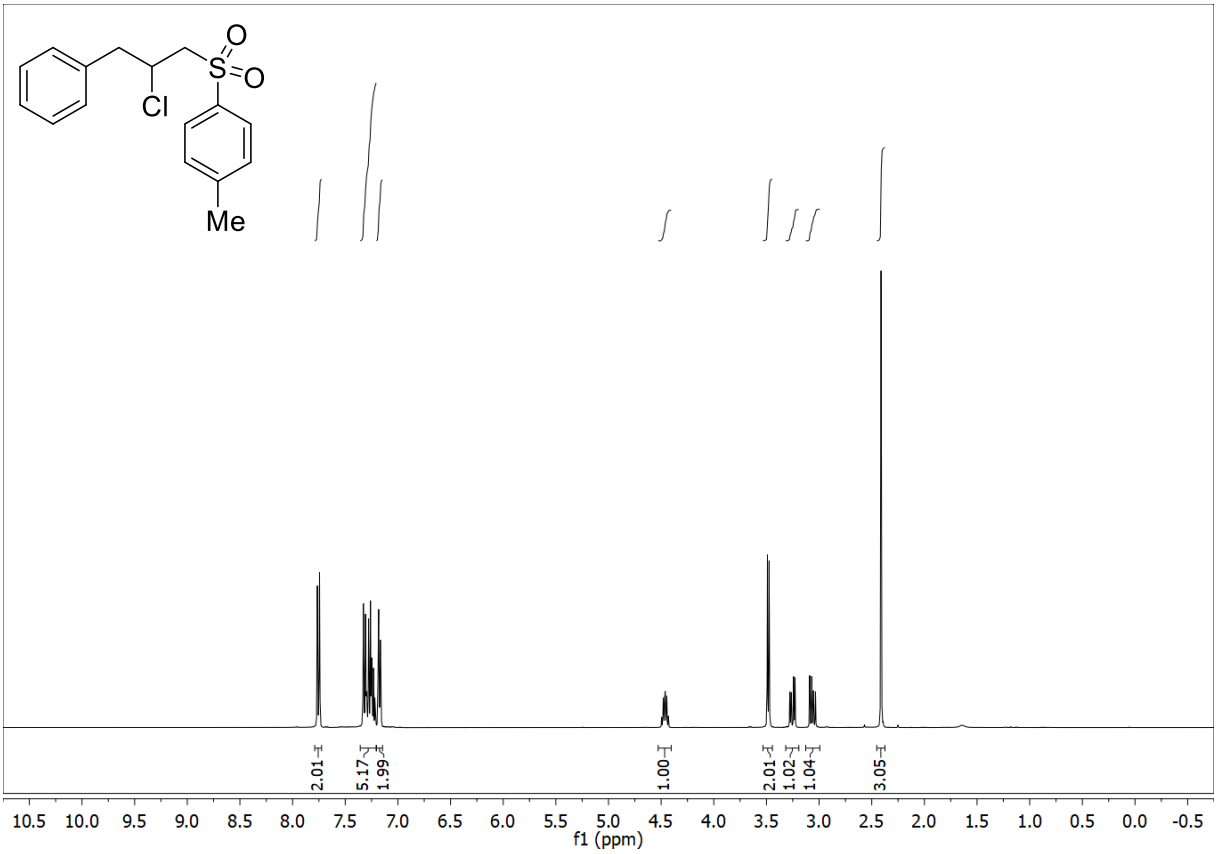
1-((2-Chloro-3-phenoxypropyl)sulfonyl)-4-methylbenzene (3c)

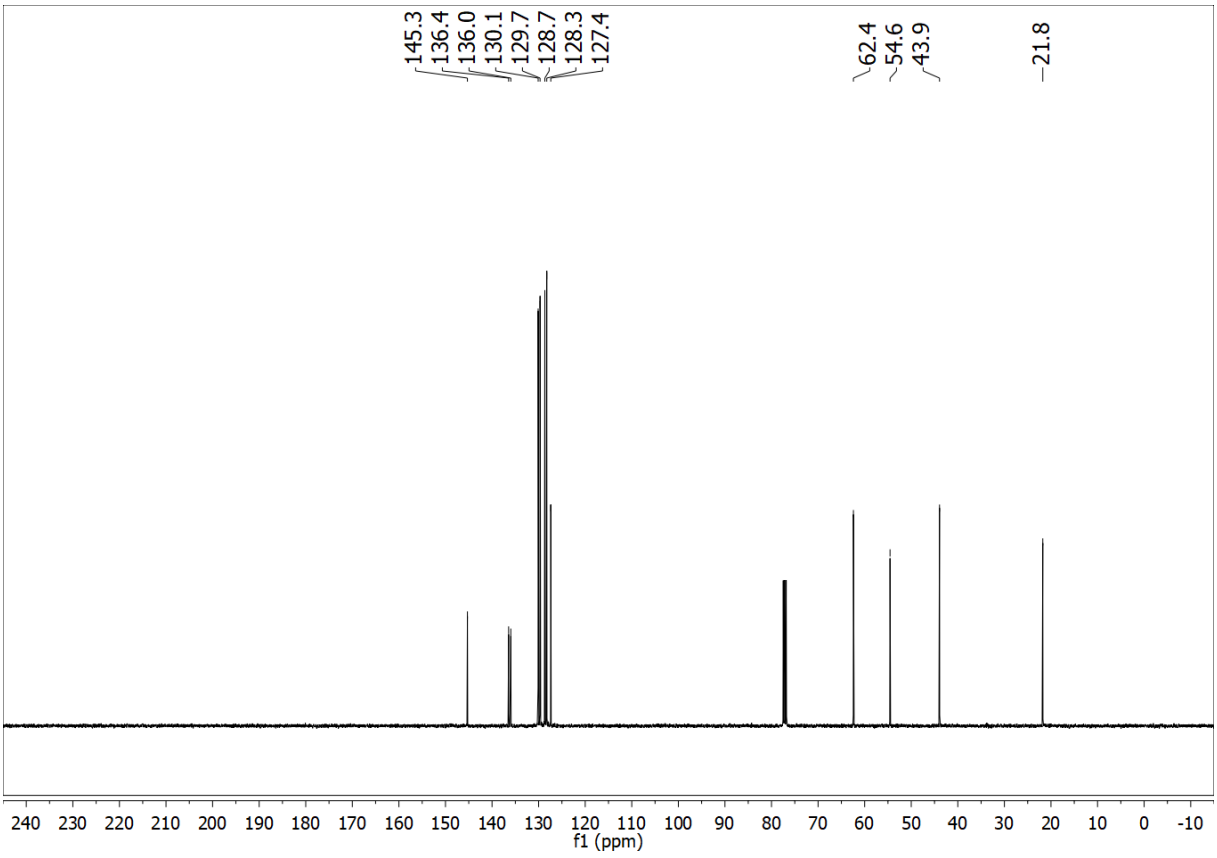




NMR-Solvent: $CDCl_3$

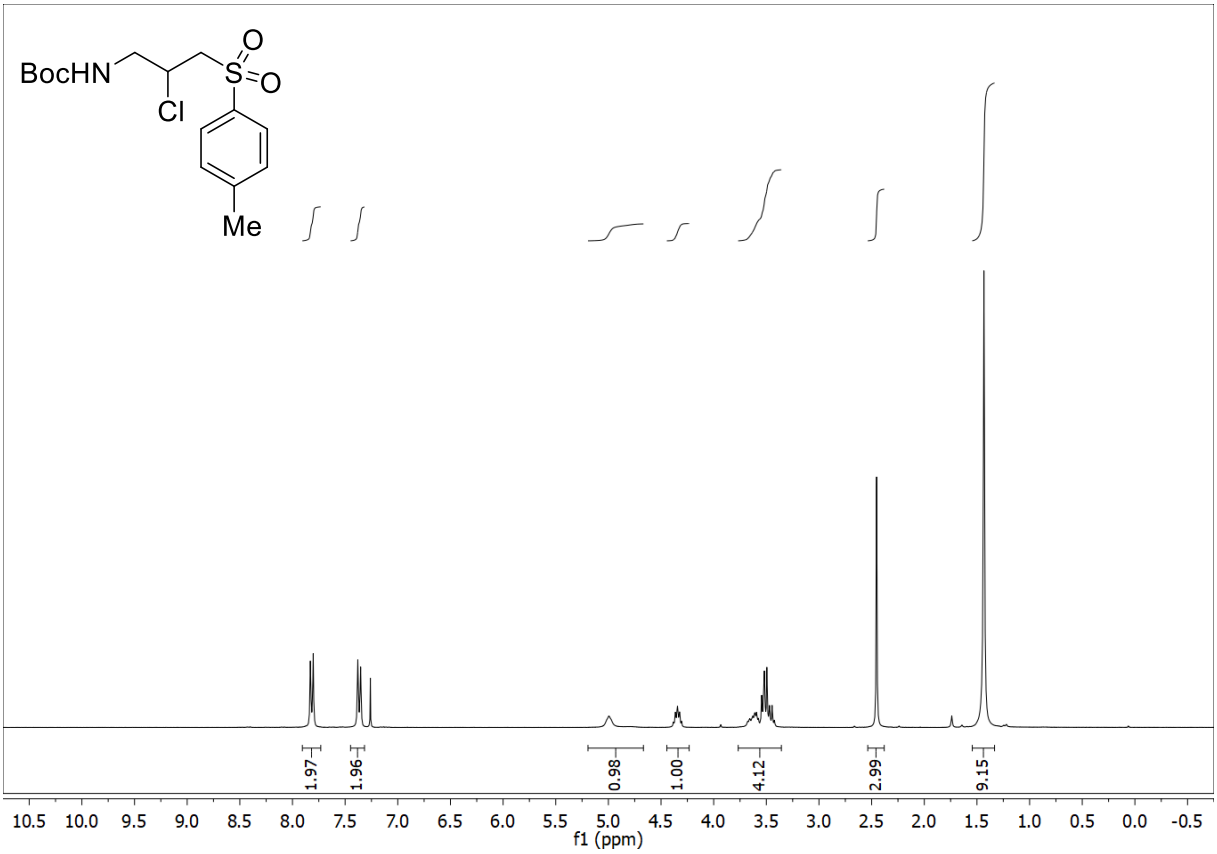
1-((2-Chloro-3-phenylpropyl)sulfonyl)-4-methylbenzene (3d)

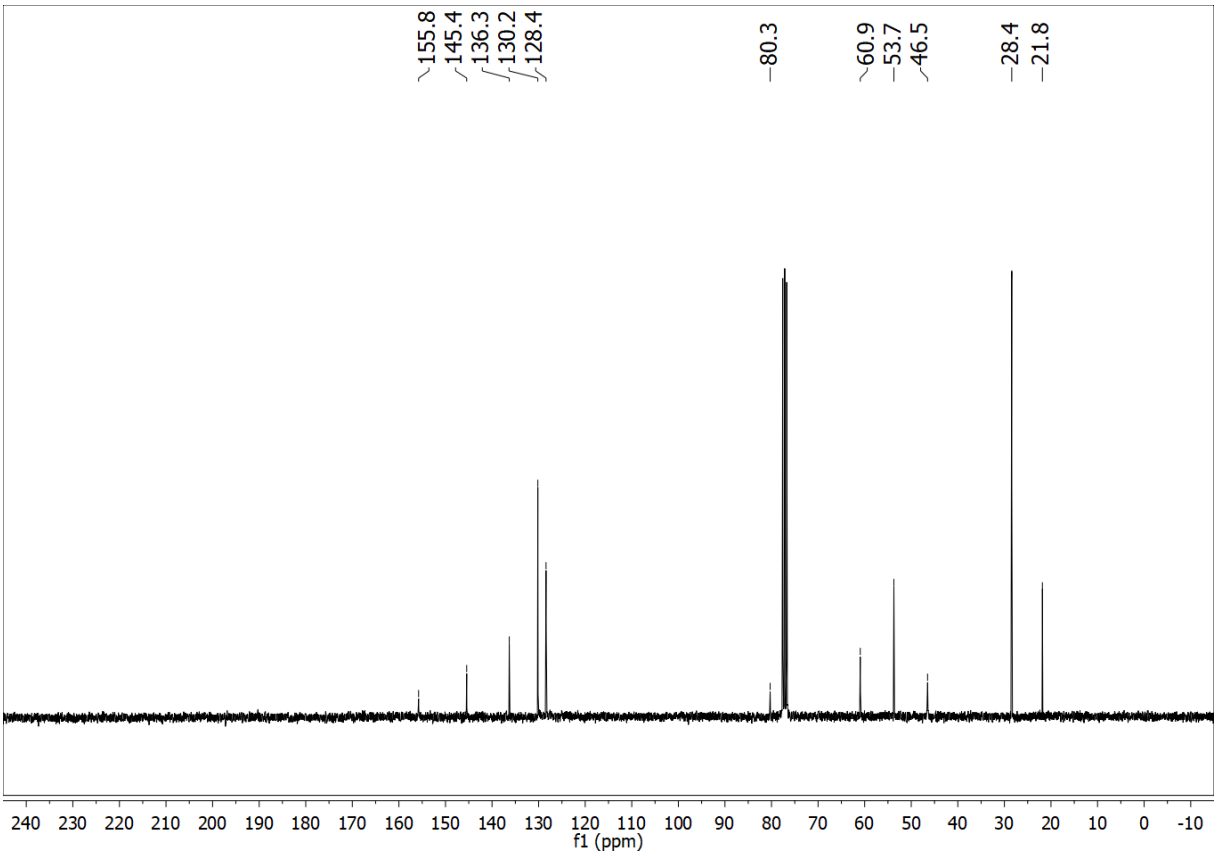




NMR-Solvent: $CDCl_3$

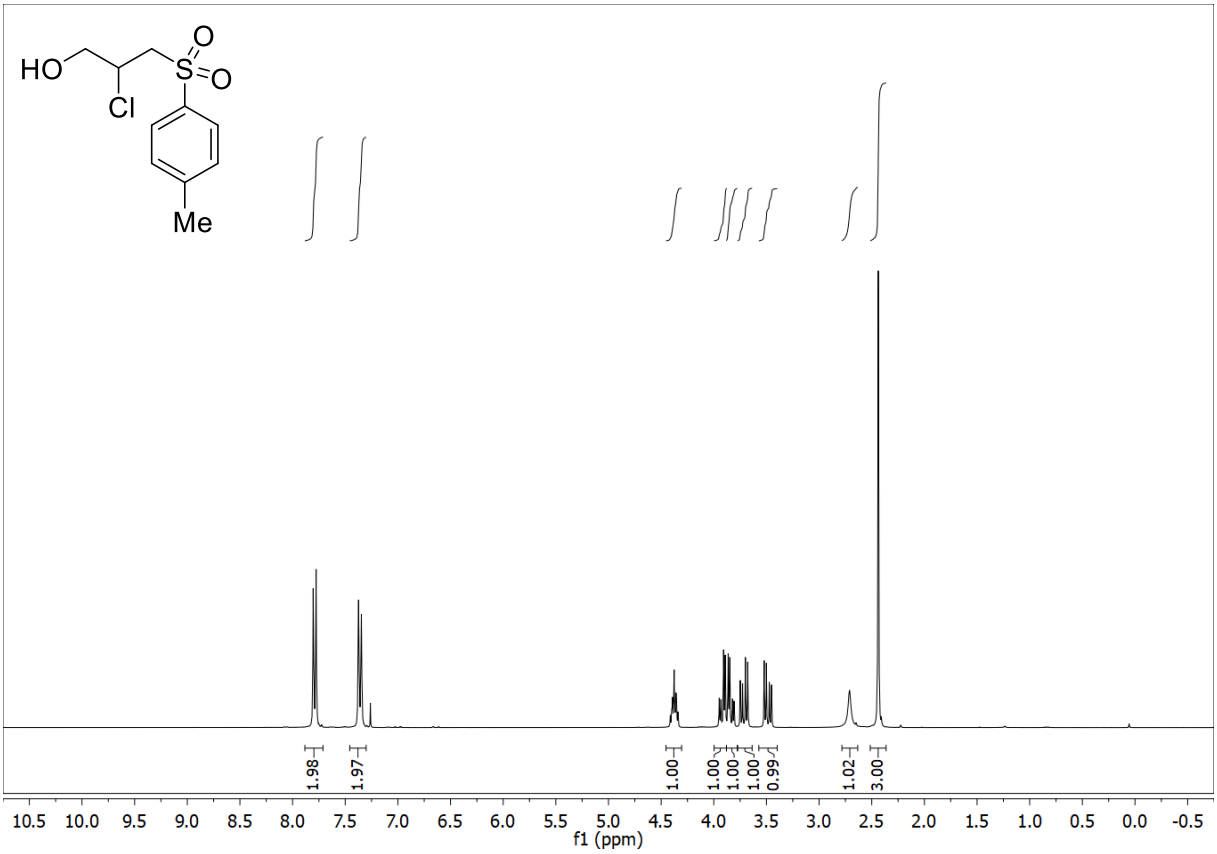
tert-Butyl (2-chloro-3-tosylpropyl)carbamate (3e)

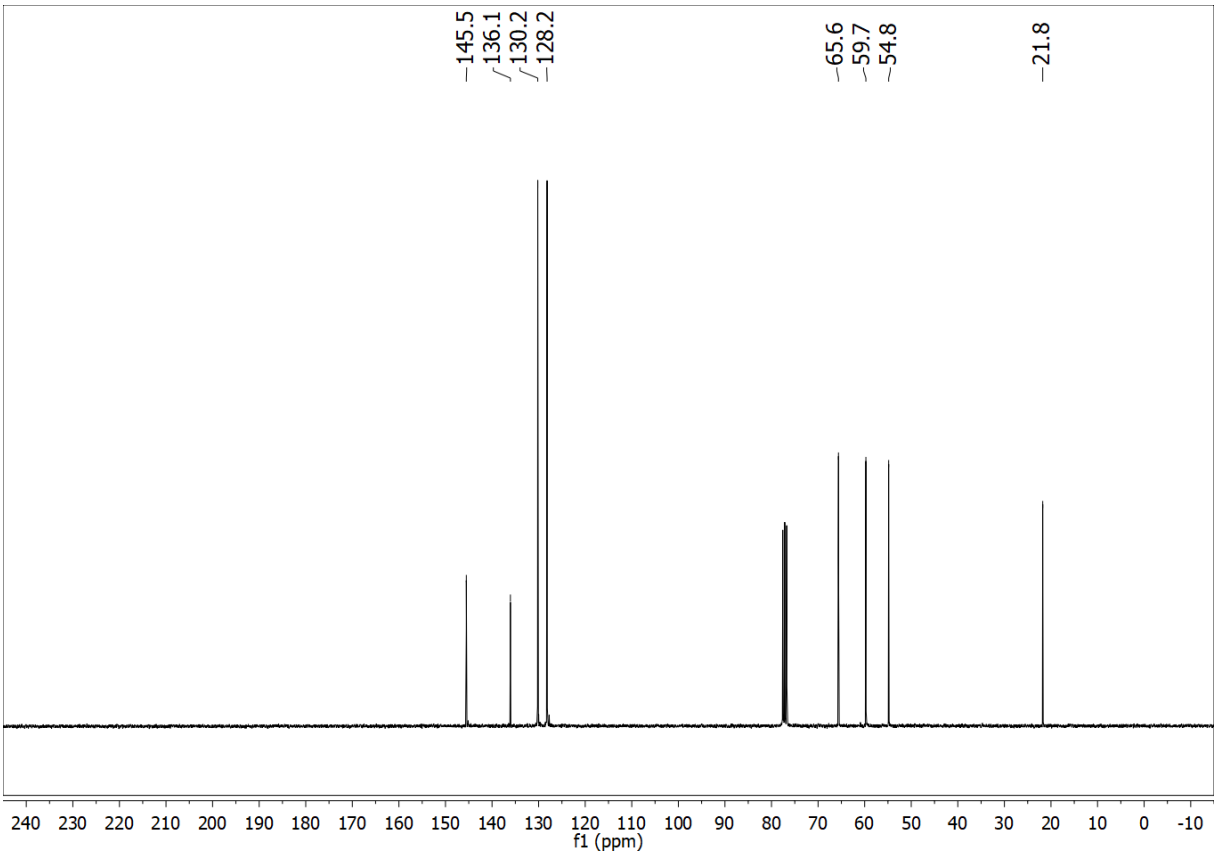




NMR-Solvent: $CDCl_3$

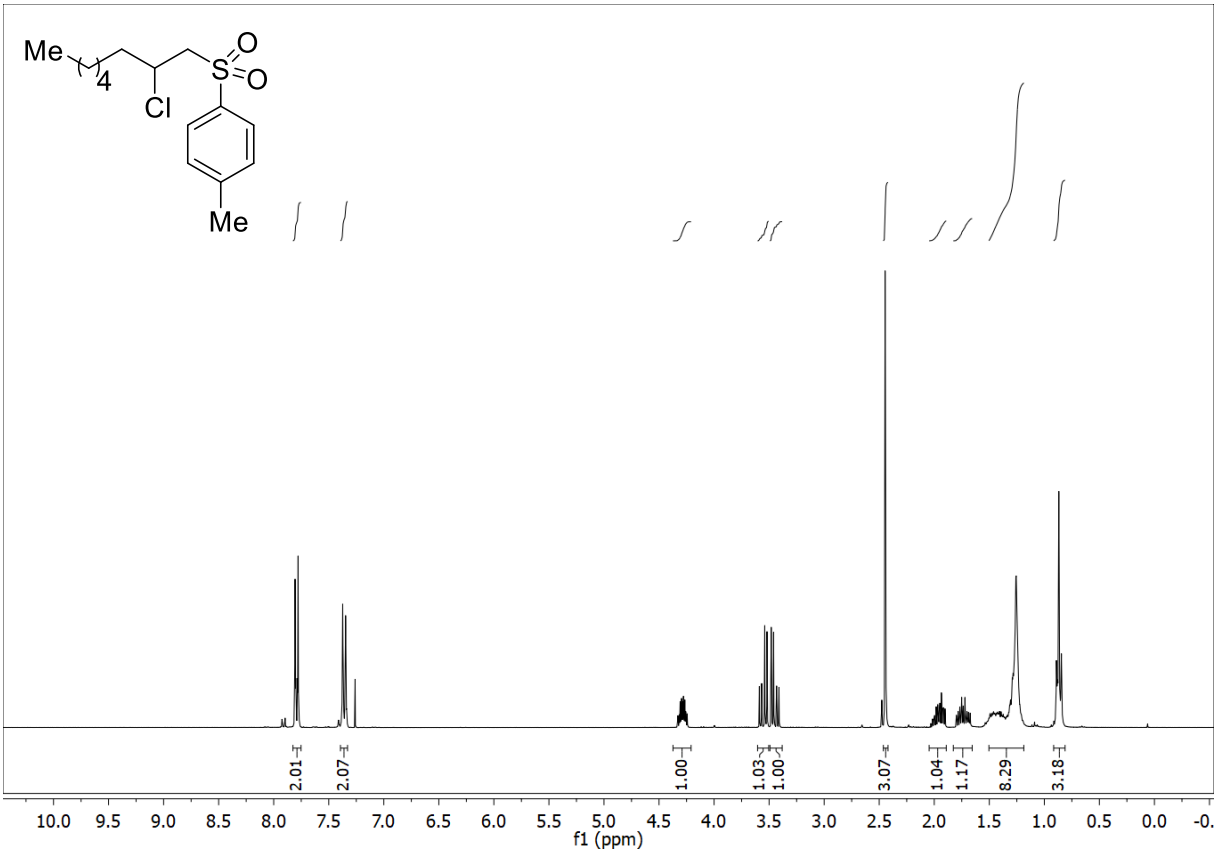
2-Chloro-3-tosylpropan-1-ol (3f)

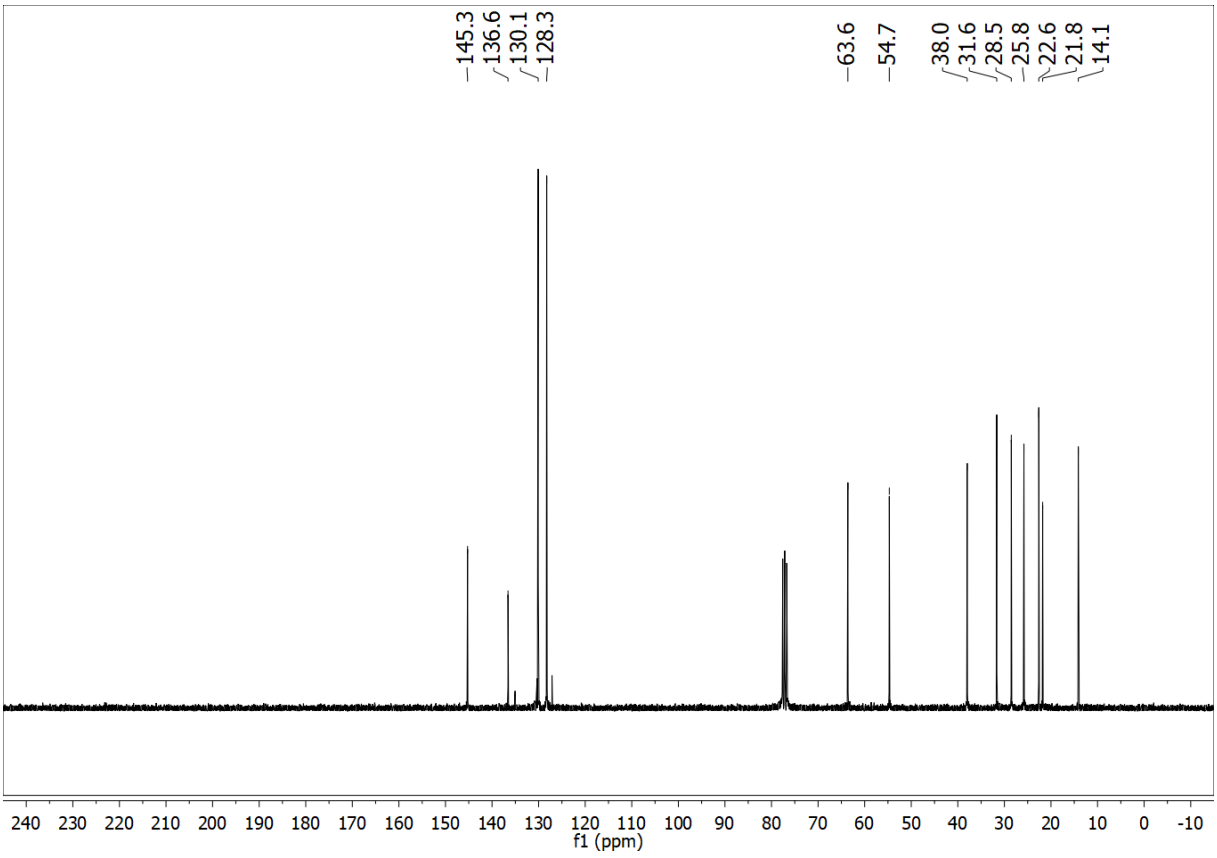




NMR-Solvent: $CDCl_3$

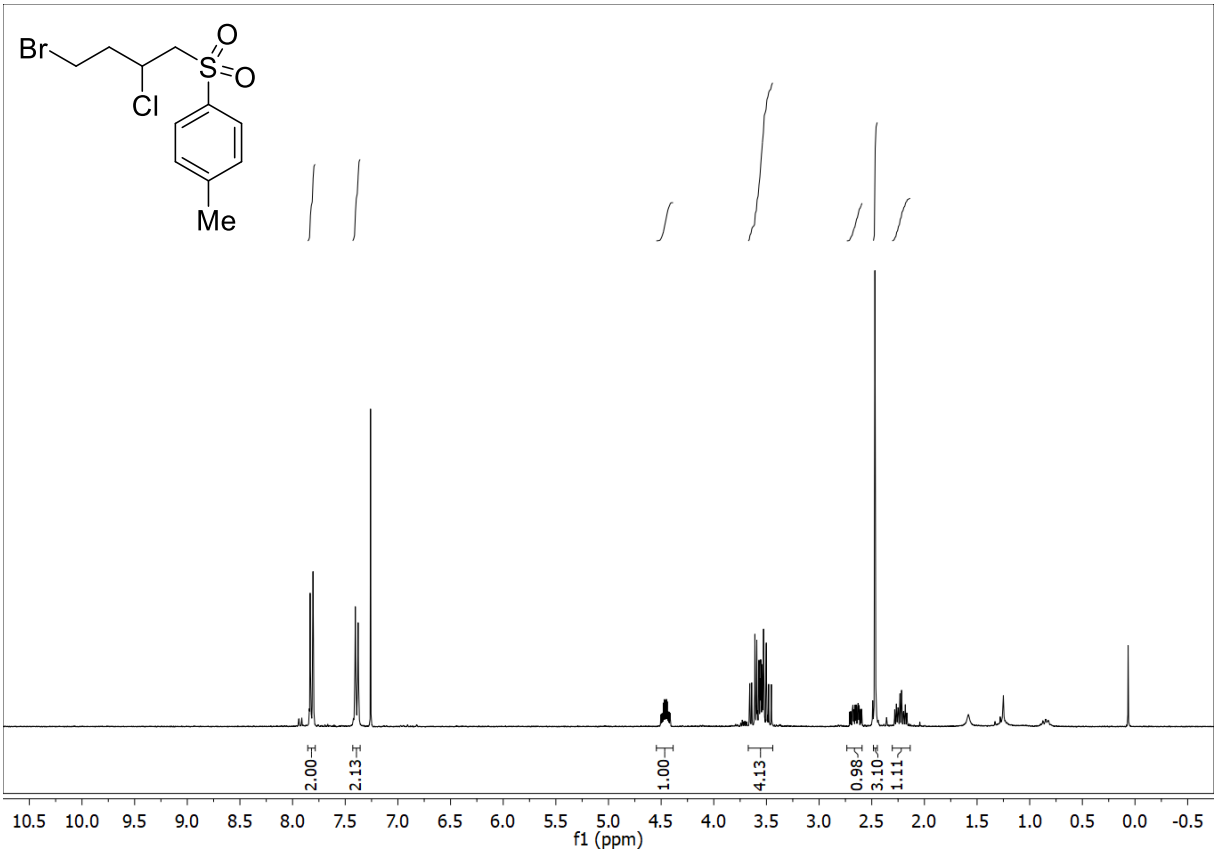
1-((2-Chlorooctyl)sulfonyl)-4-methylbenzene (3g)

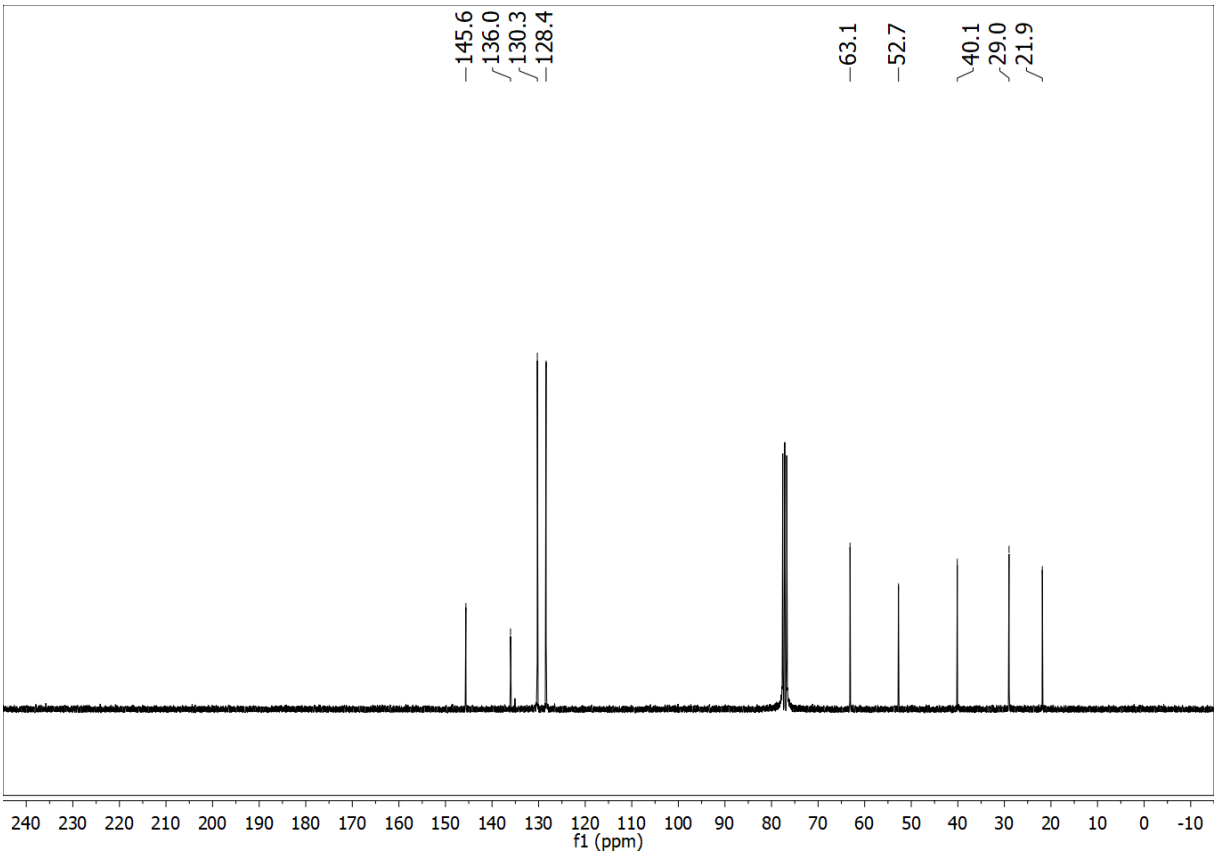




NMR-Solvent: $CDCl_3$

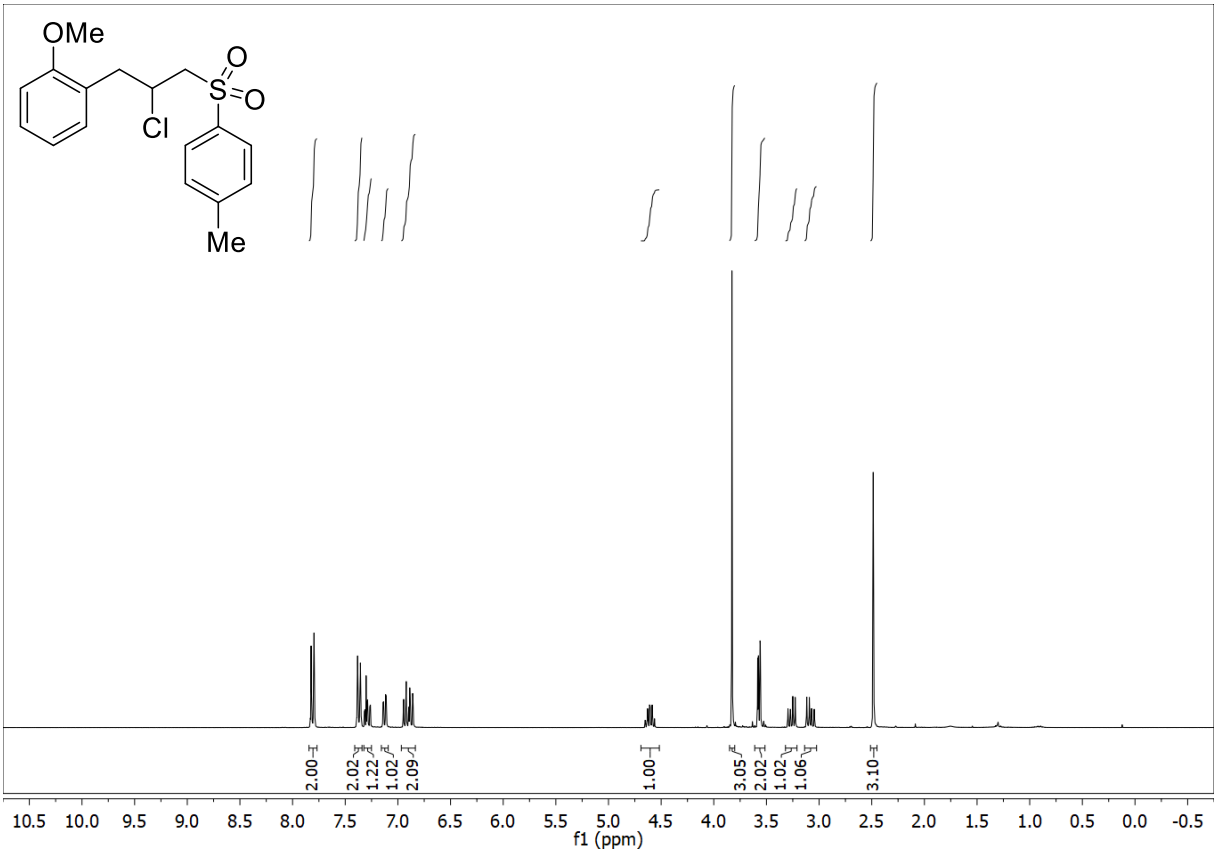
1-((4-Bromo-2-chlorobutyl)sulfonyl)-4-methylbenzene (3h)

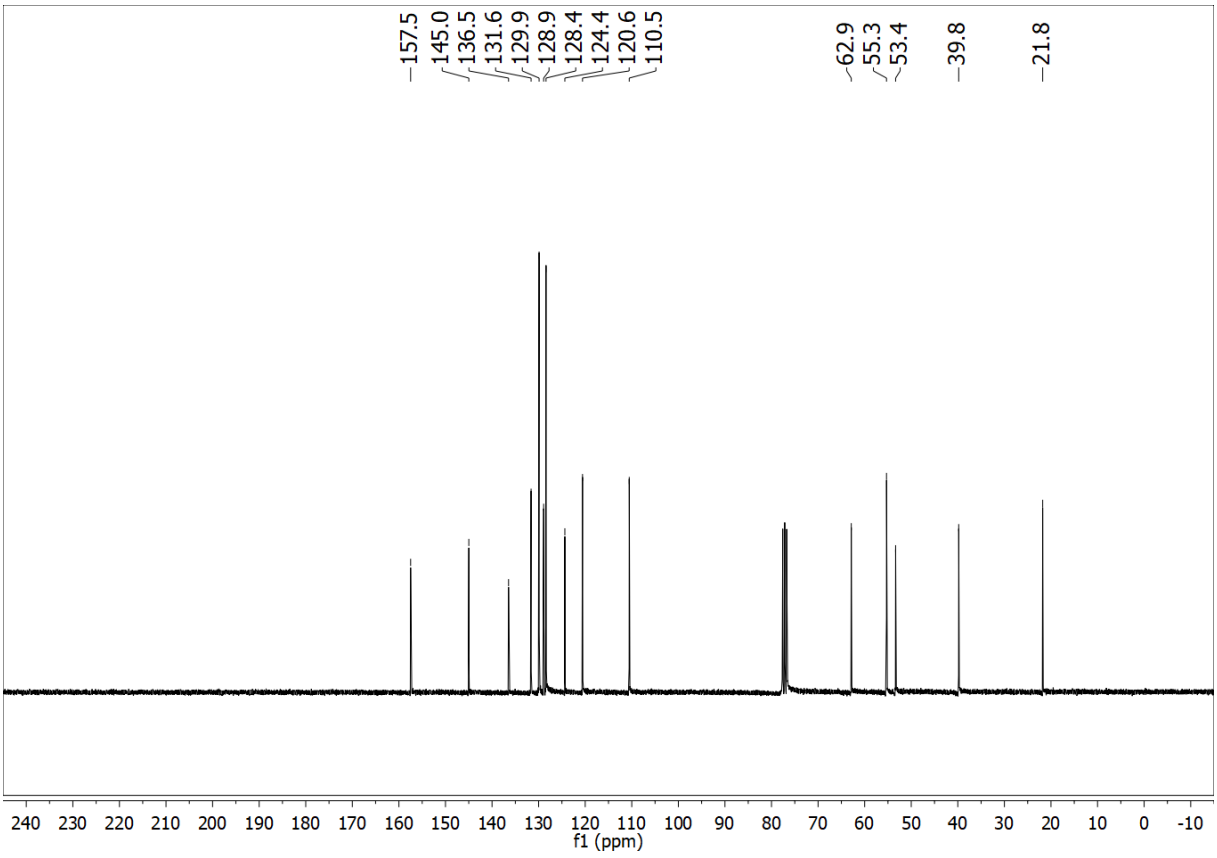




NMR-Solvent: $CDCl_3$

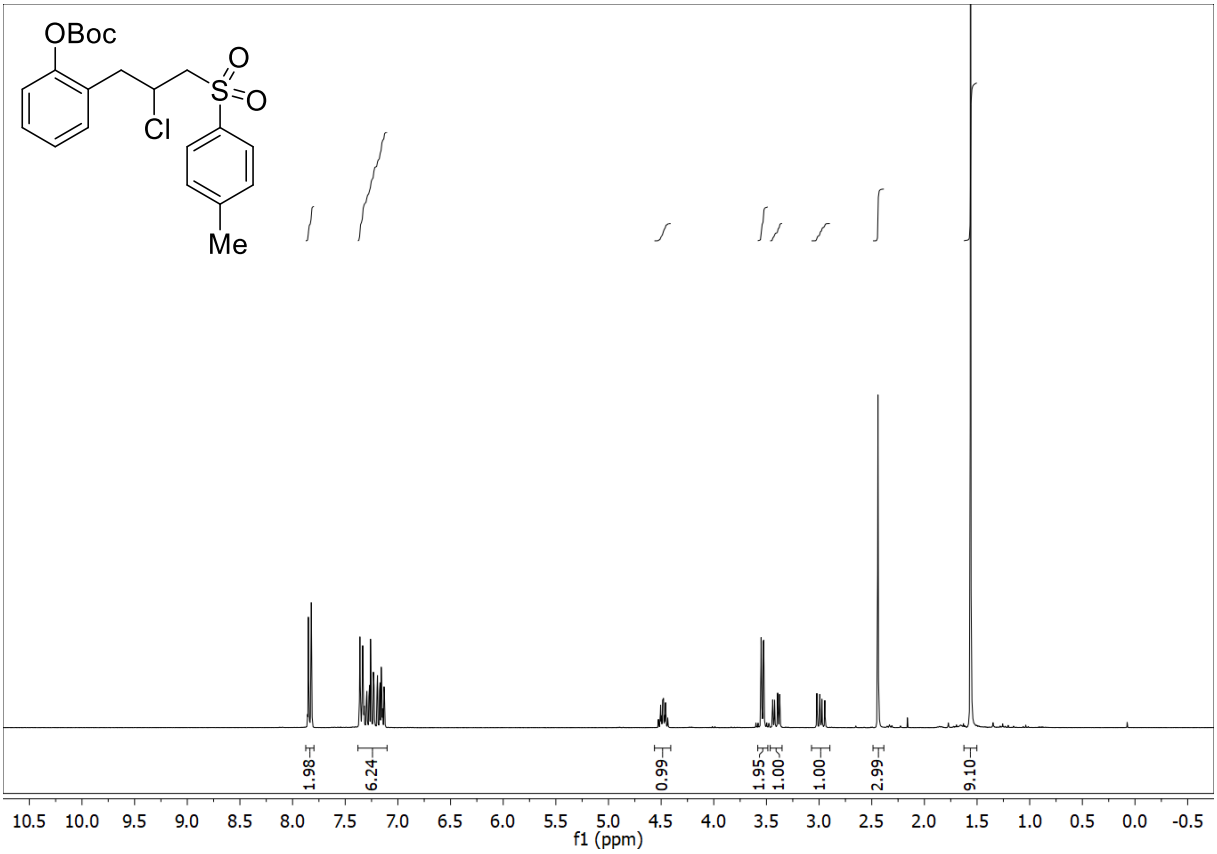
1-(2-Chloro-3-tosylpropyl)-2-methoxybenzene (3j)

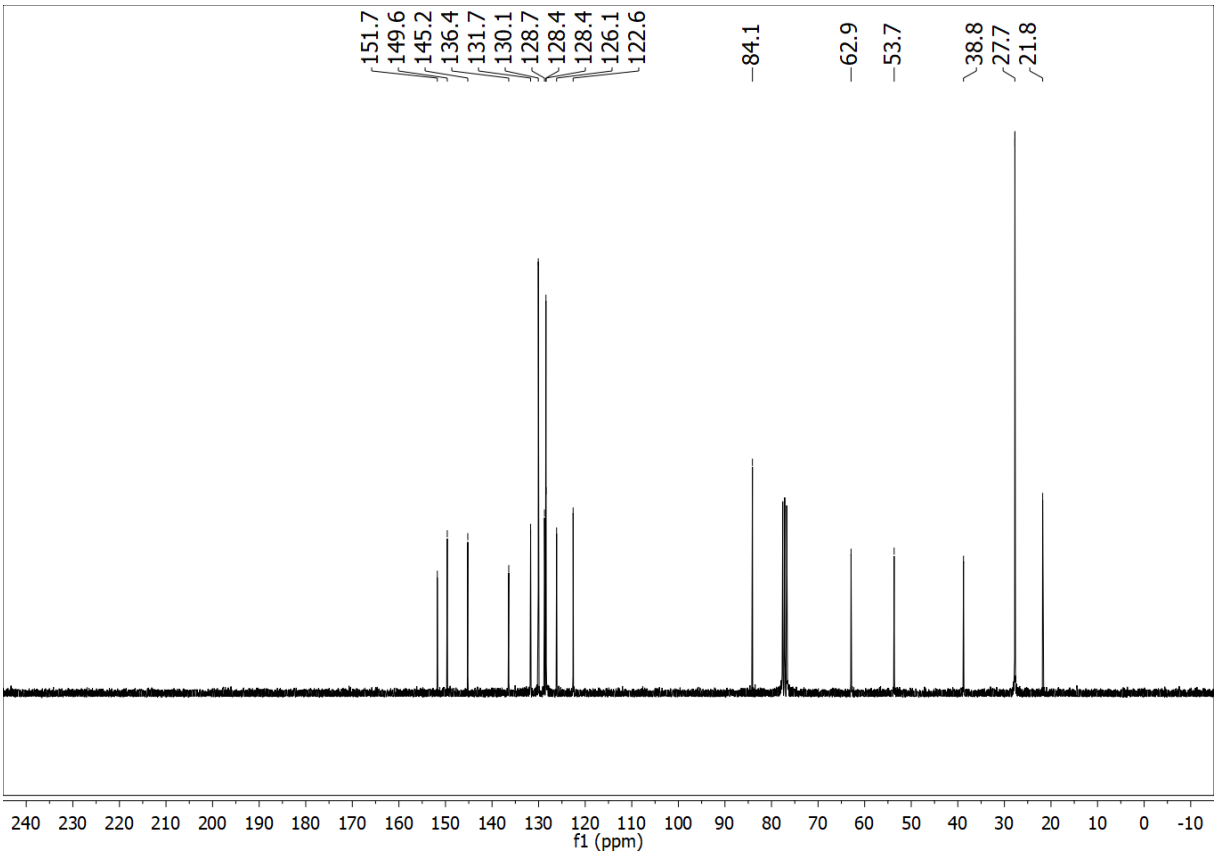




NMR-Solvent: $CDCl_3$

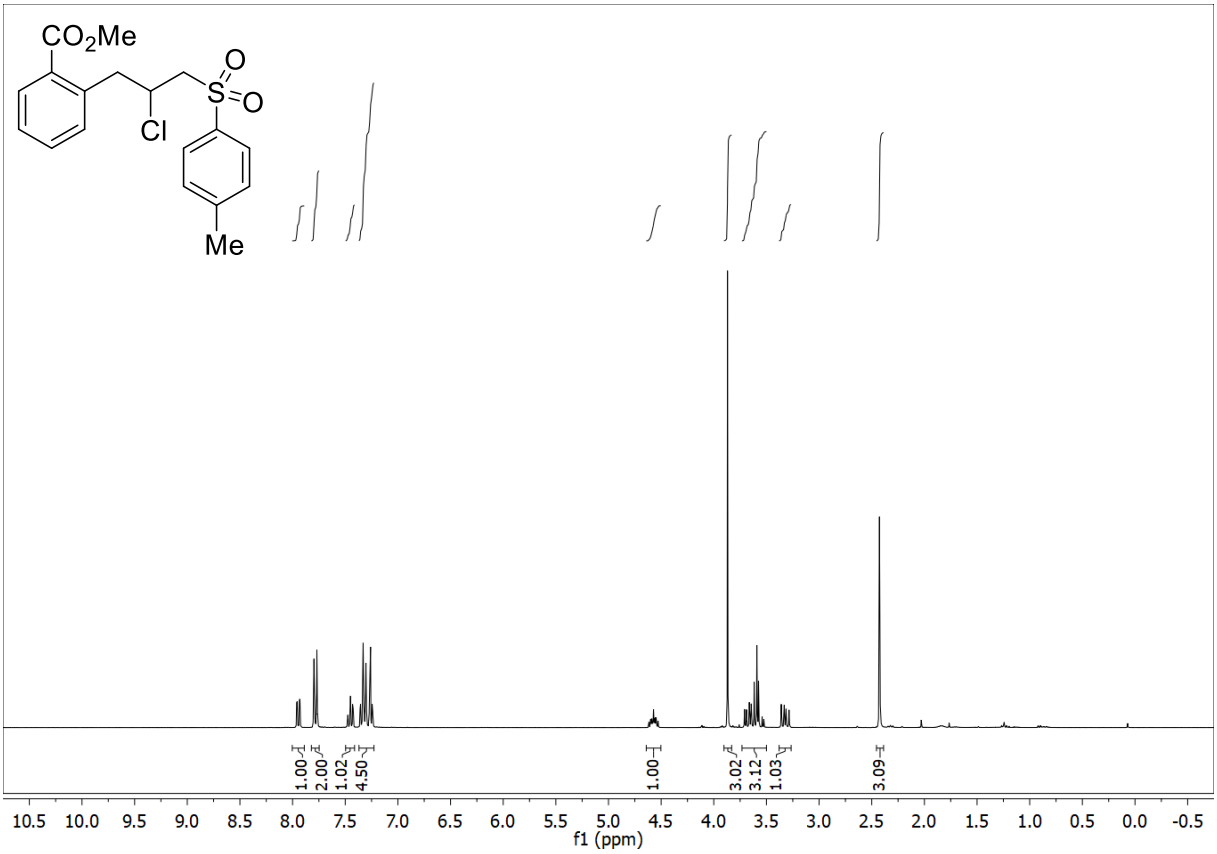
tert-Butyl (2-(2-chloro-3-tosylpropyl)phenyl) carbonate (3k)

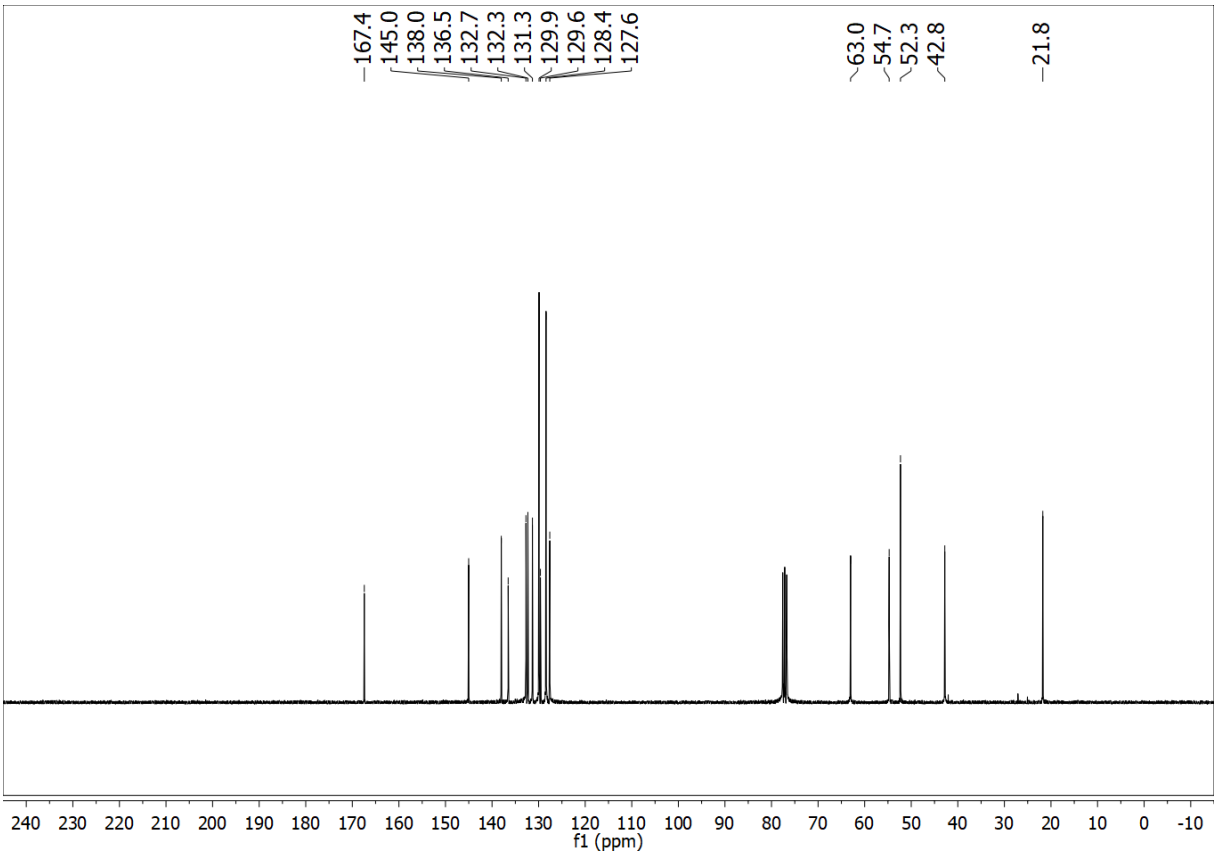




NMR-Solvent: $CDCl_3$

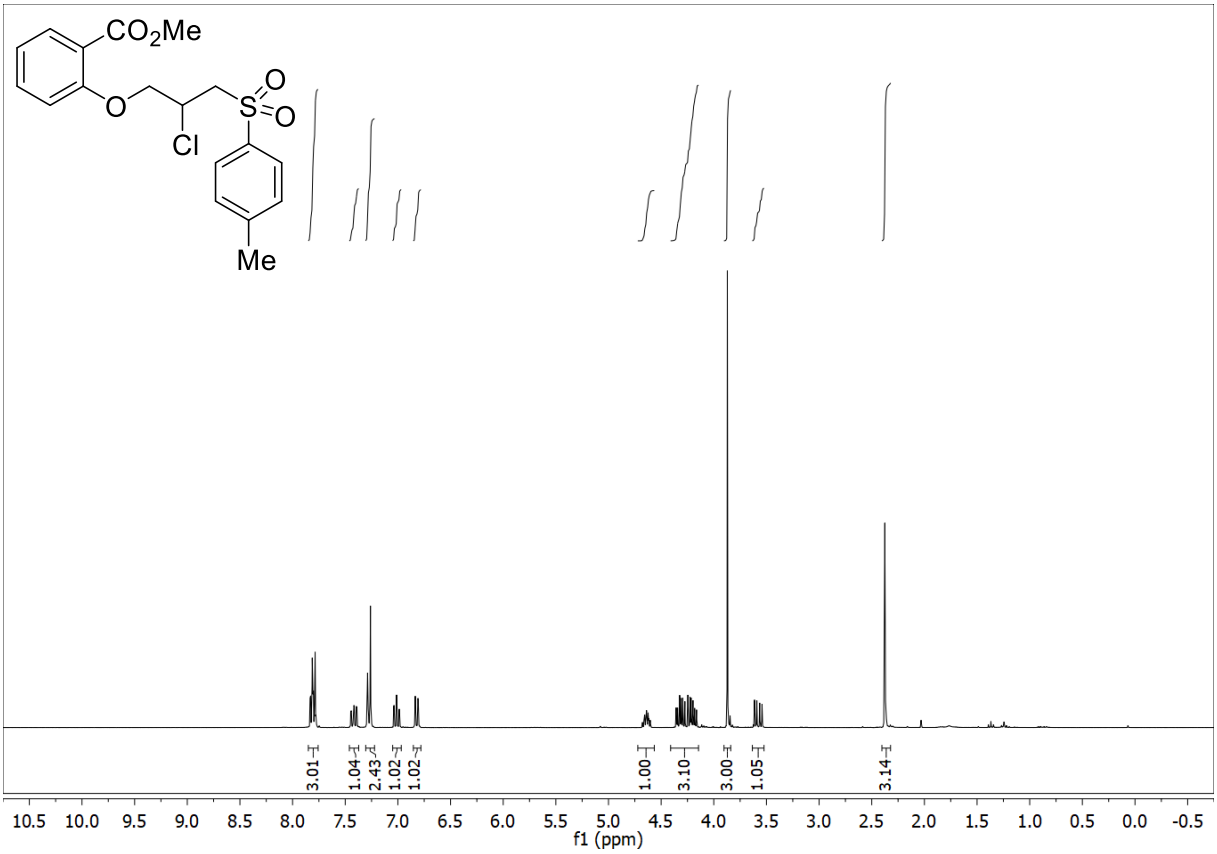
Methyl 2-(2-chloro-3-tosylpropyl)benzoate (3l)

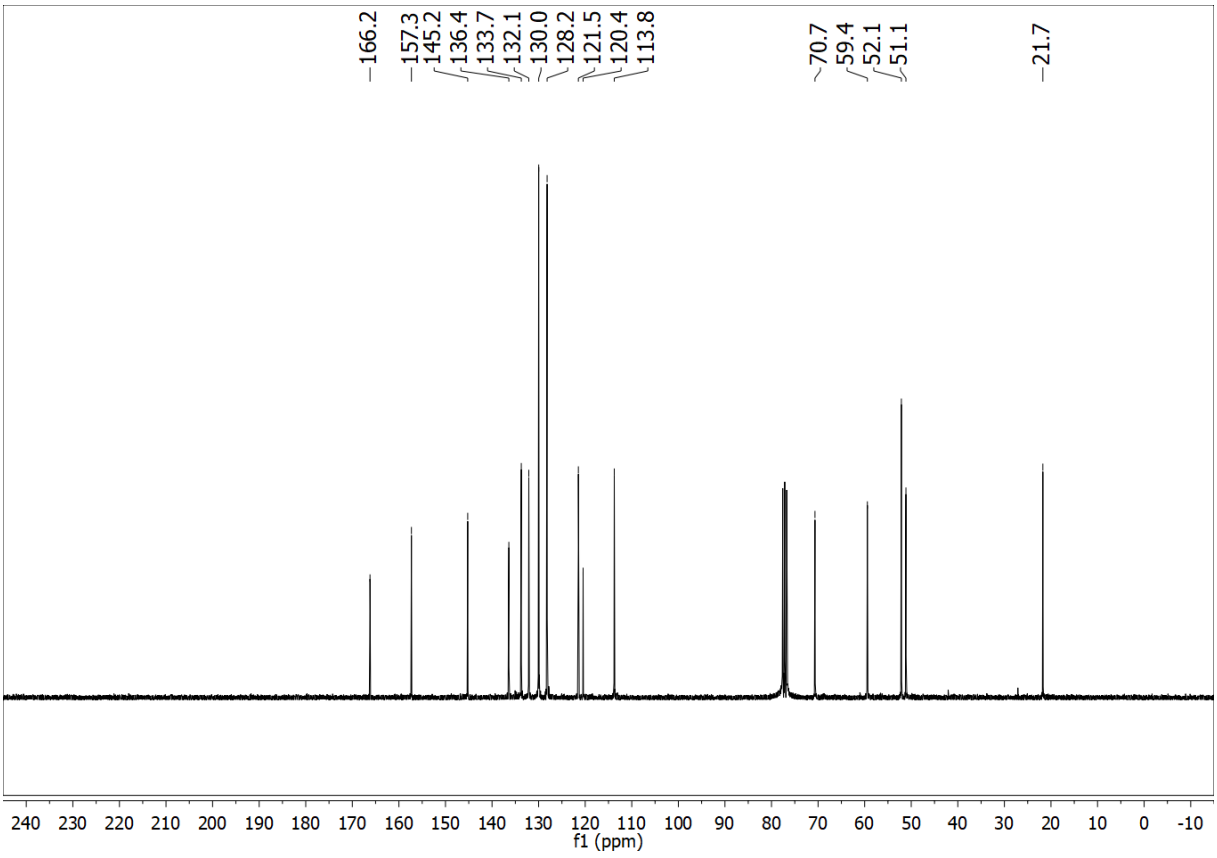




NMR-Solvent: $CDCl_3$

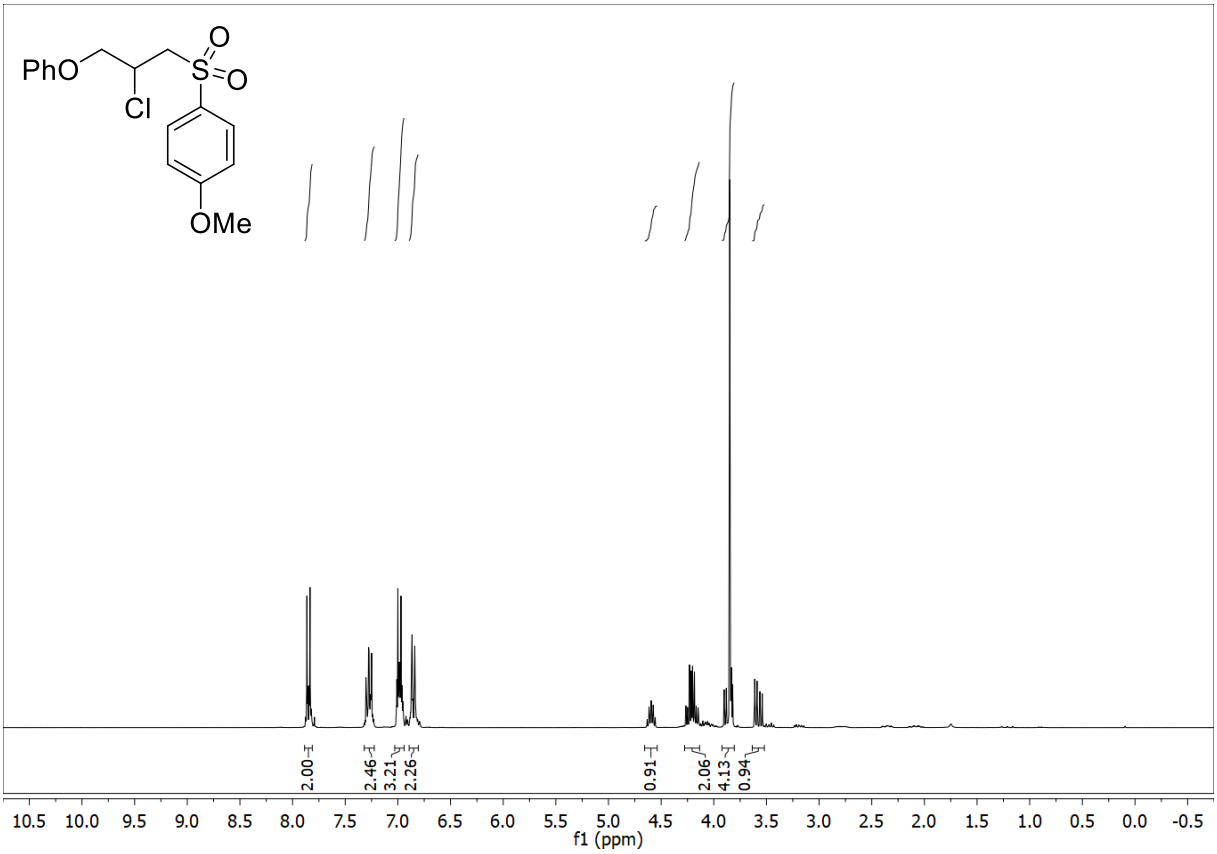
Methyl 2-(2-chloro-3-tosylpropoxy)benzoate (3m)

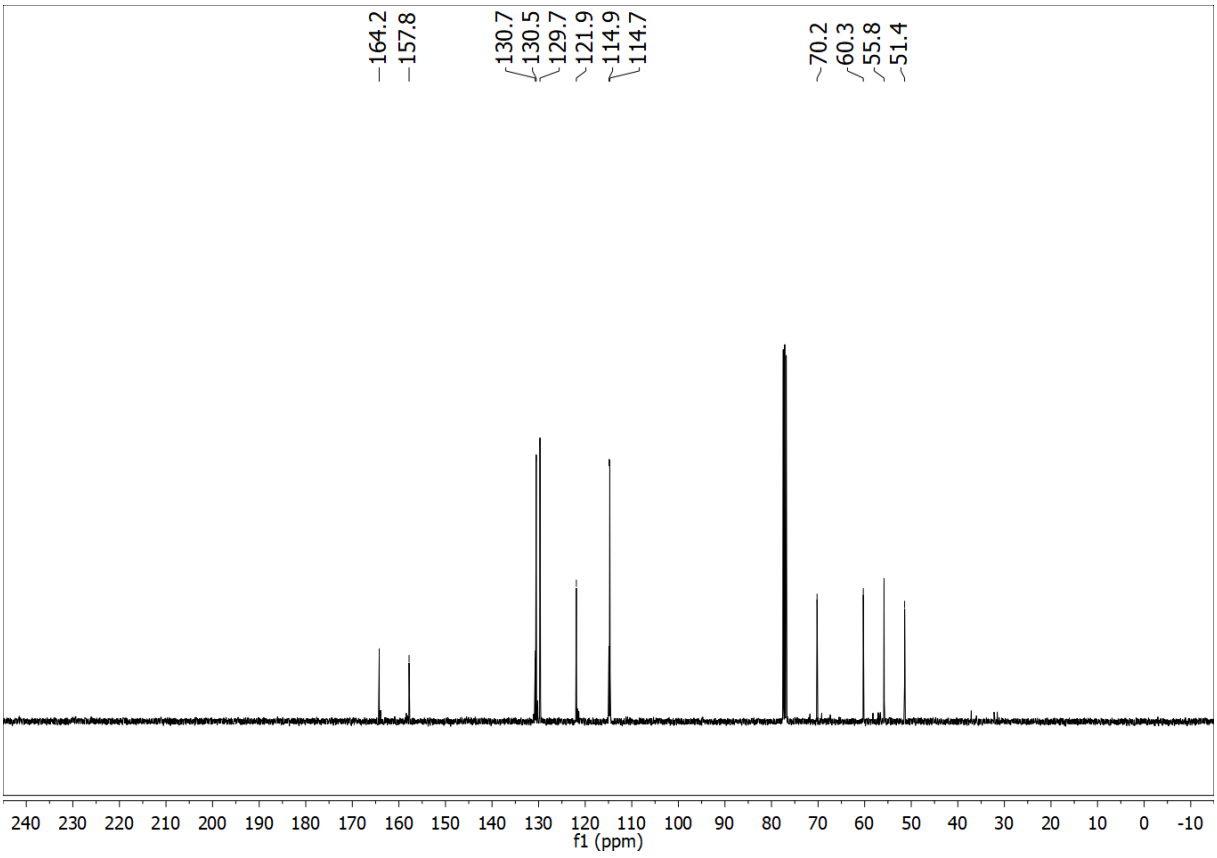




NMR-Solvent: $CDCl_3$

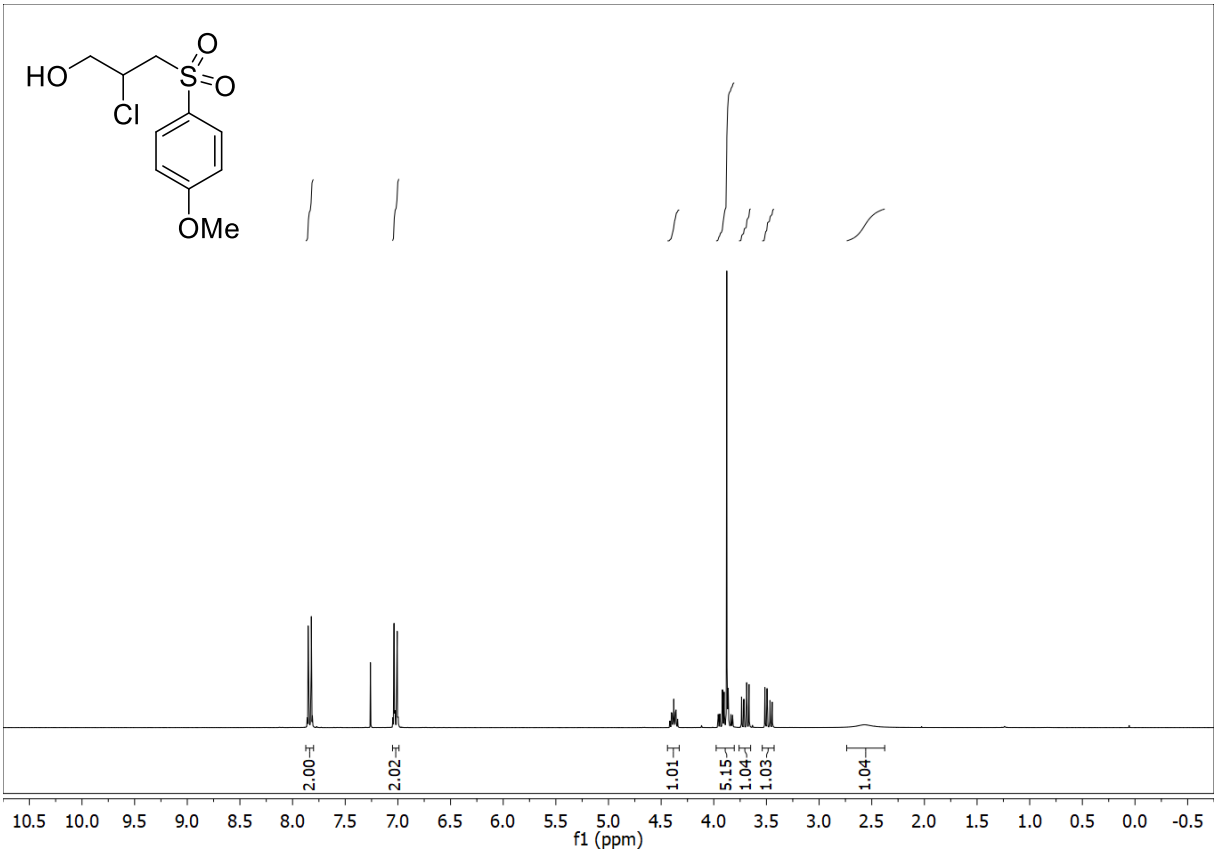
1-((2-Chloro-3-phenoxypropyl)sulfonyl)-4-methoxybenzene (15b)

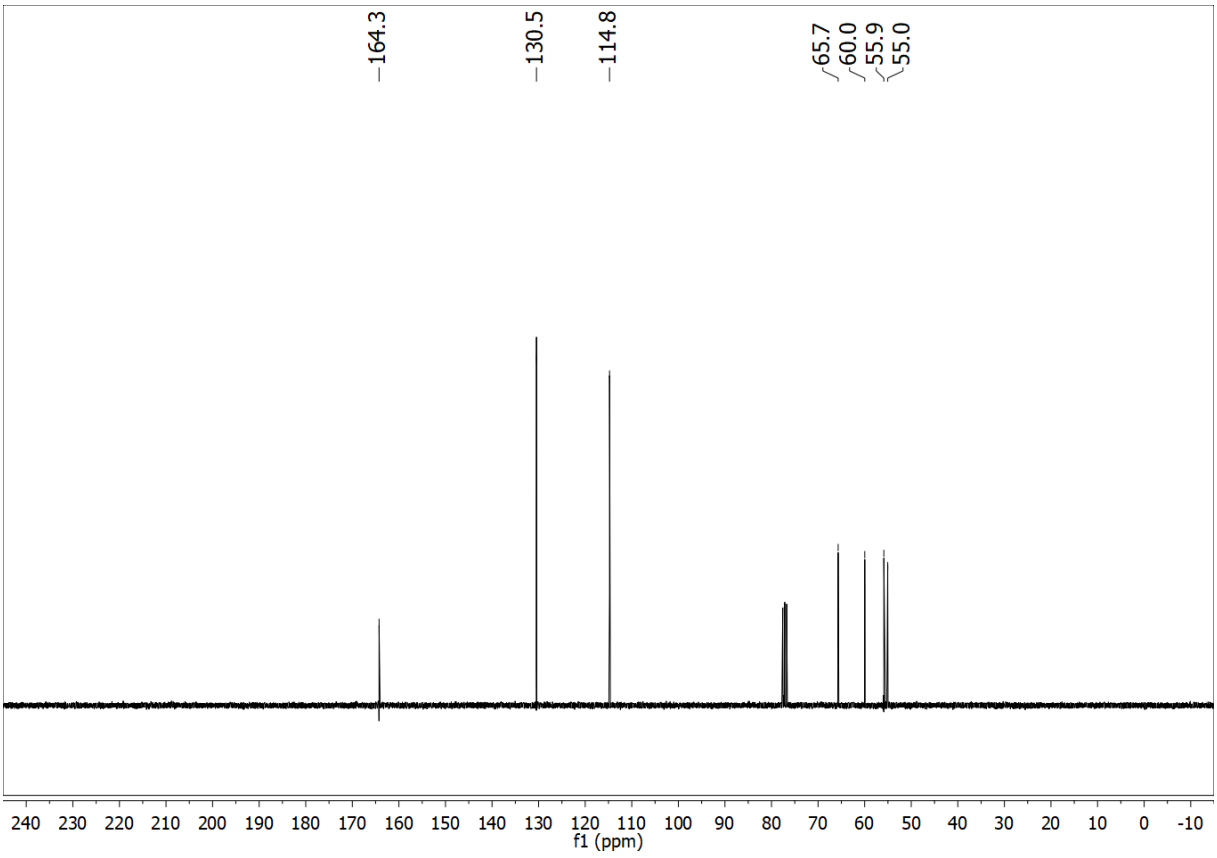




NMR-Solvent: $CDCl_3$

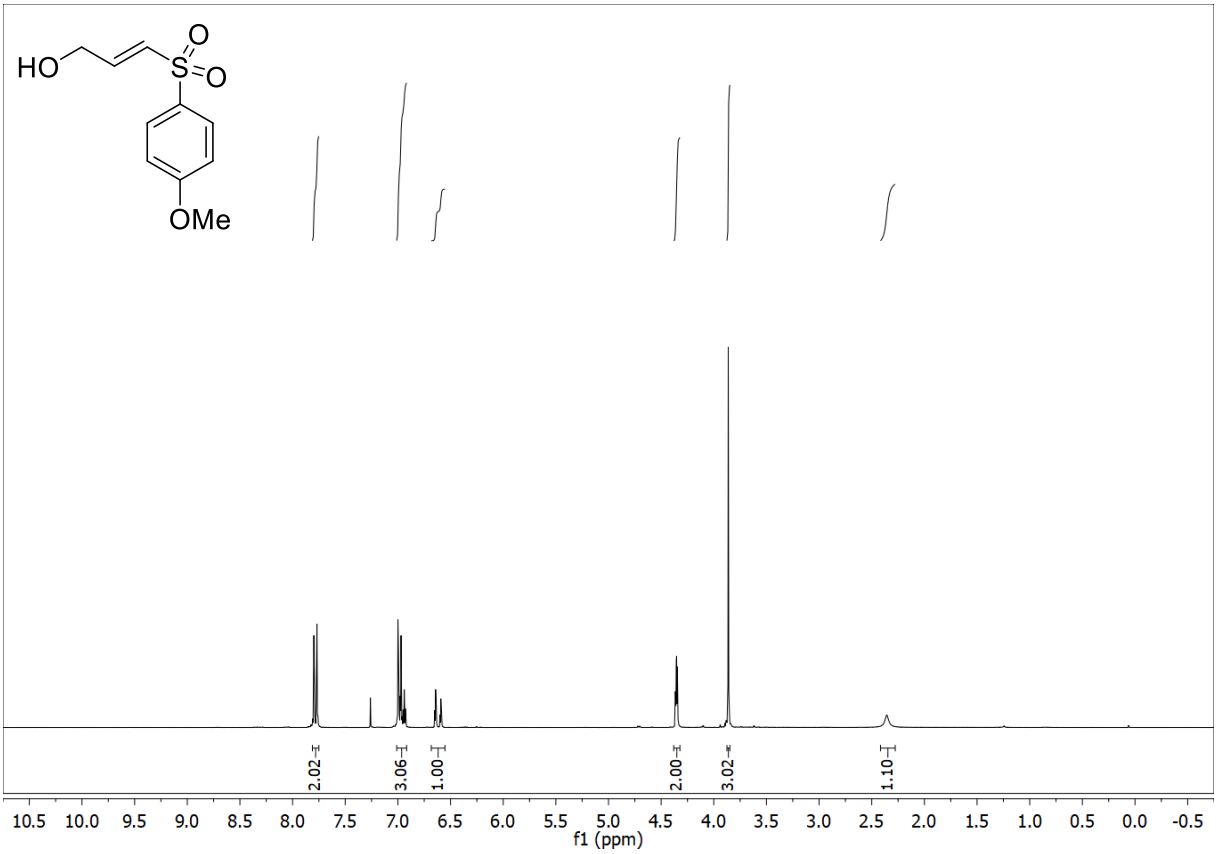
2-Chloro-3-((4-methoxyphenyl)sulfonyl)propan-1-ol (15b´)

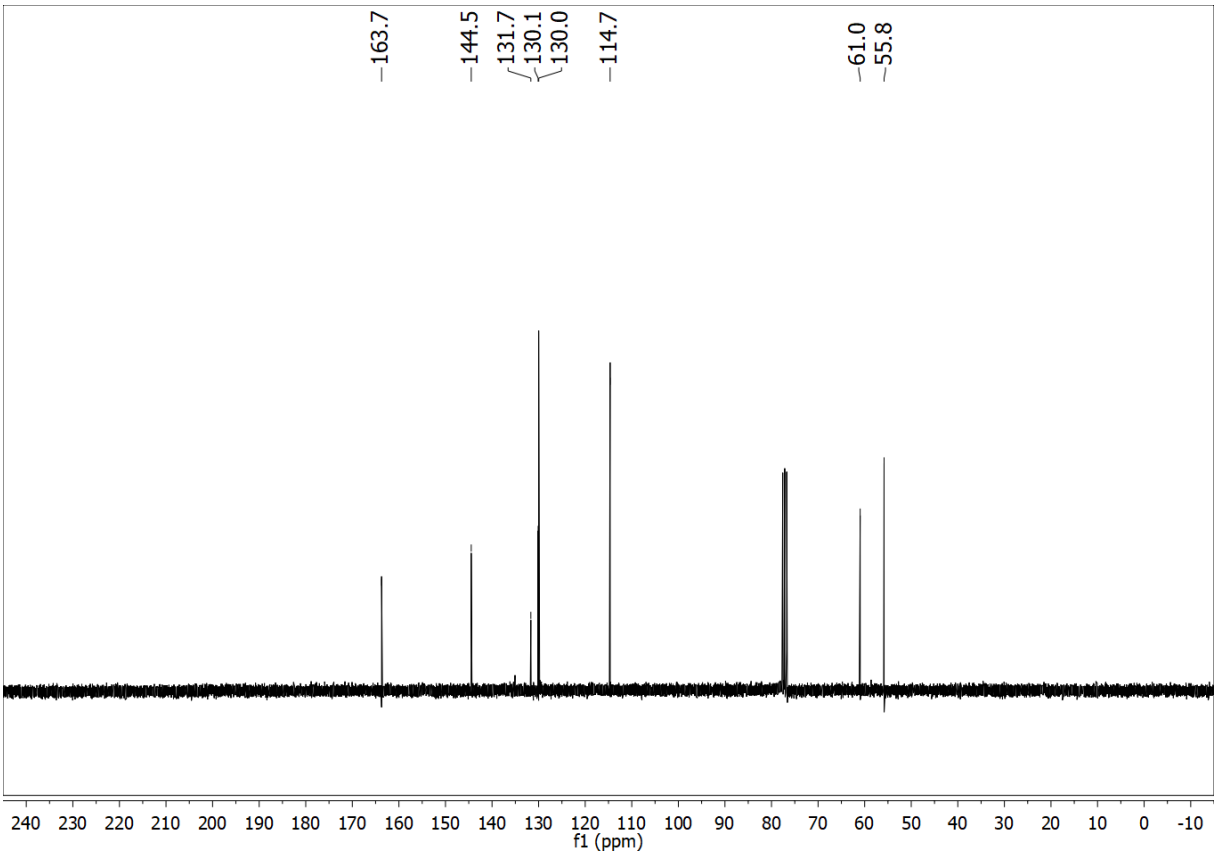




NMR-Solvent: $CDCl_3$

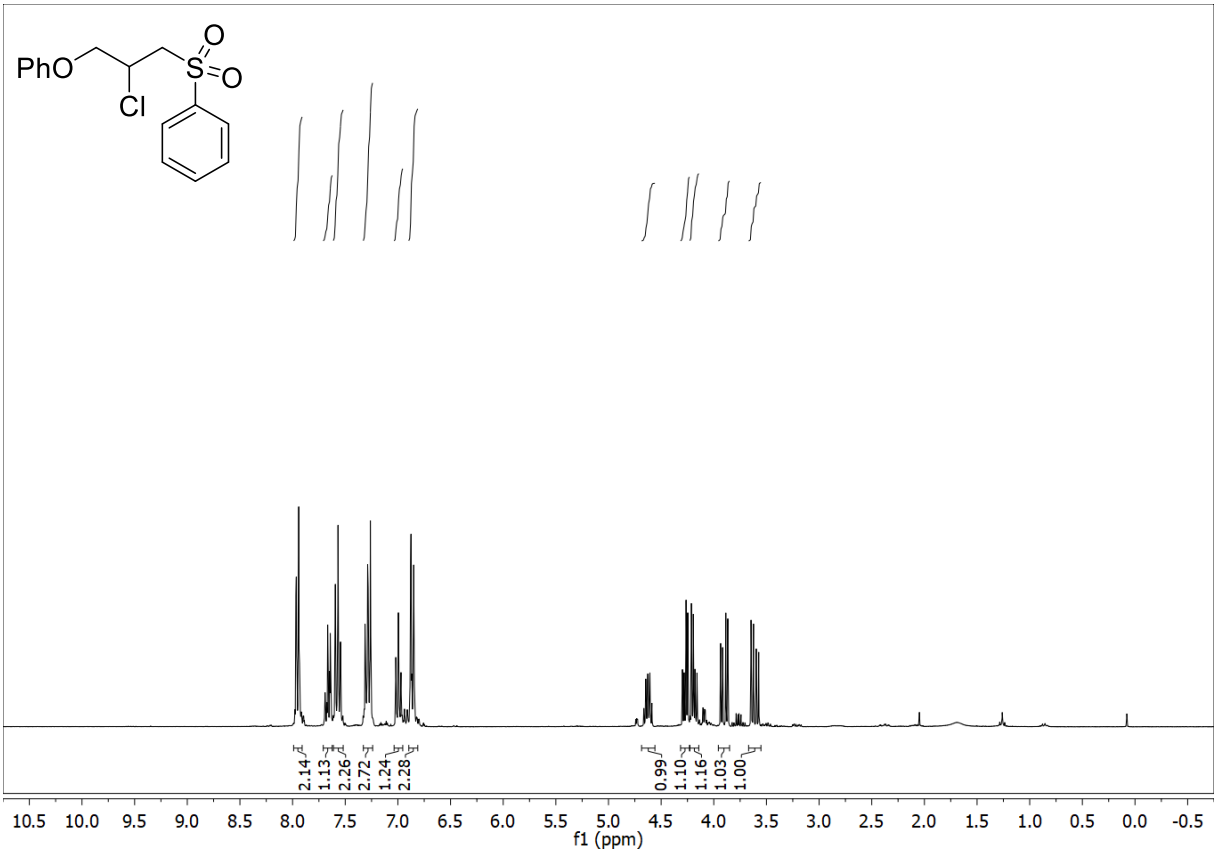
(*E*)-3-((4-Methoxyphenyl)-sulfonyl)prop-2-en-1-ol (16b´)

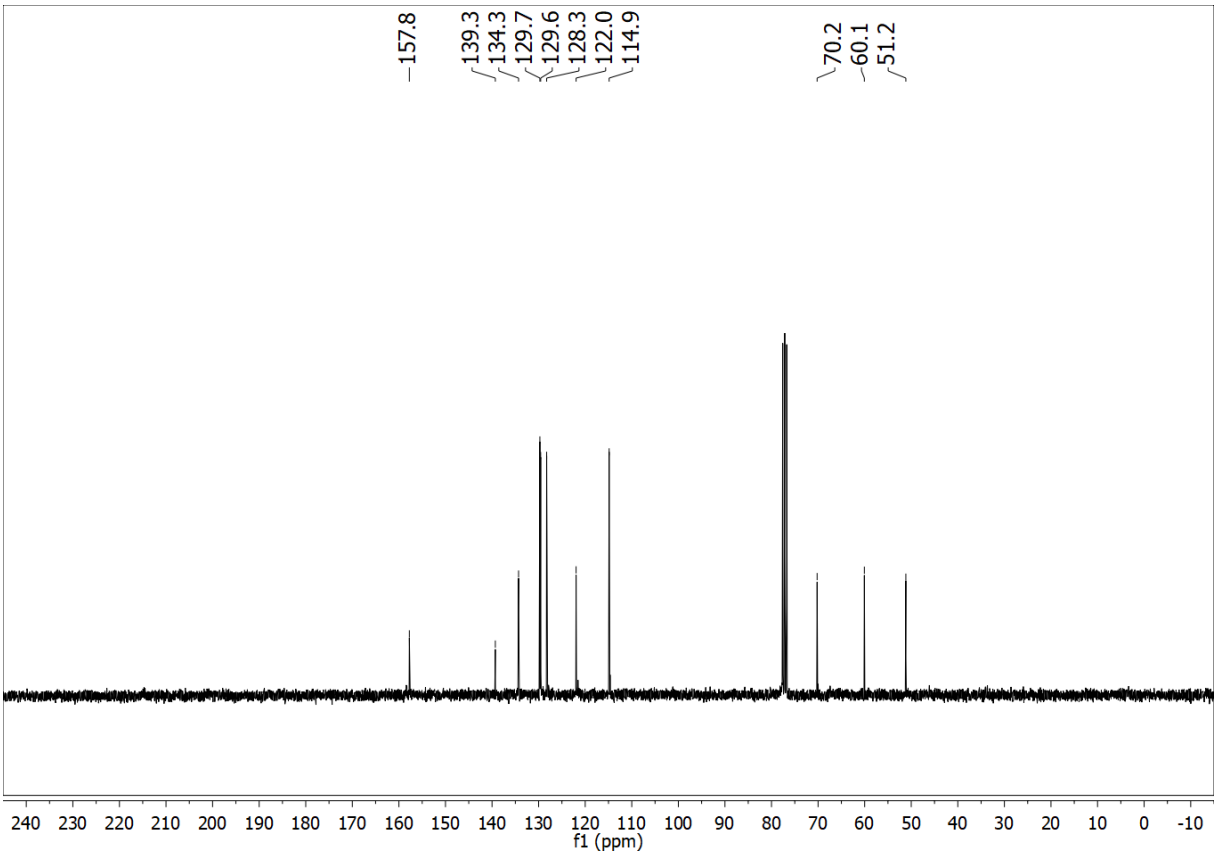




NMR-Solvent: $CDCl_3$

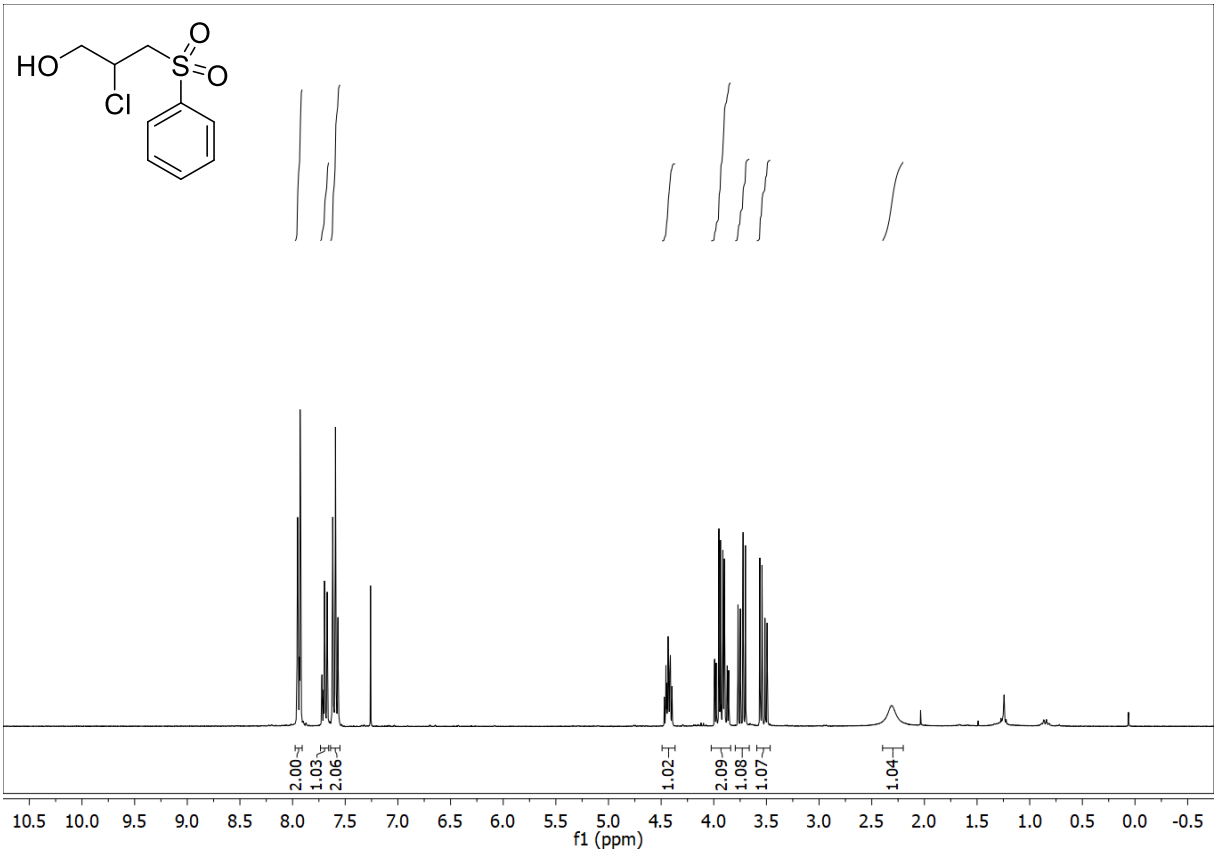
(2-Chloro-3-(phenylsulfonyl)propoxy)benzene (15c)

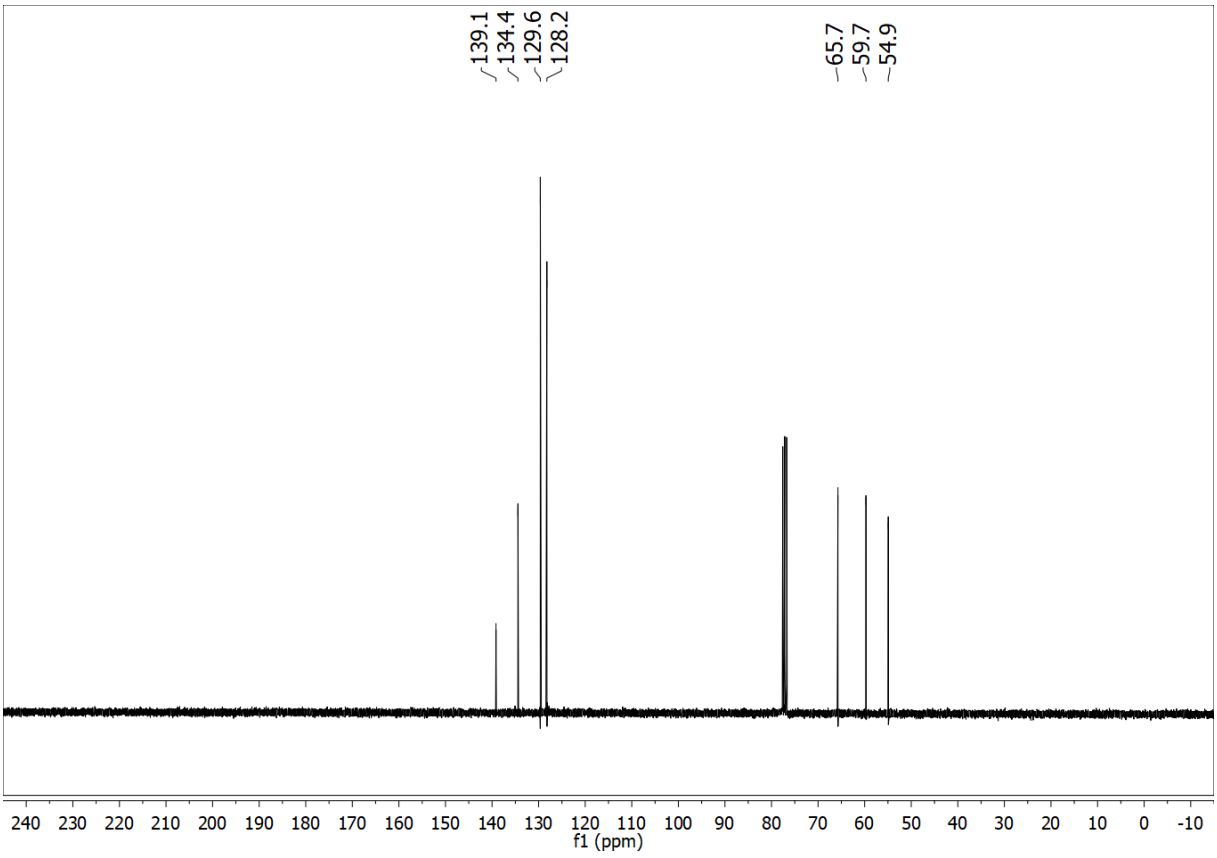




NMR-Solvent: $CDCl_3$

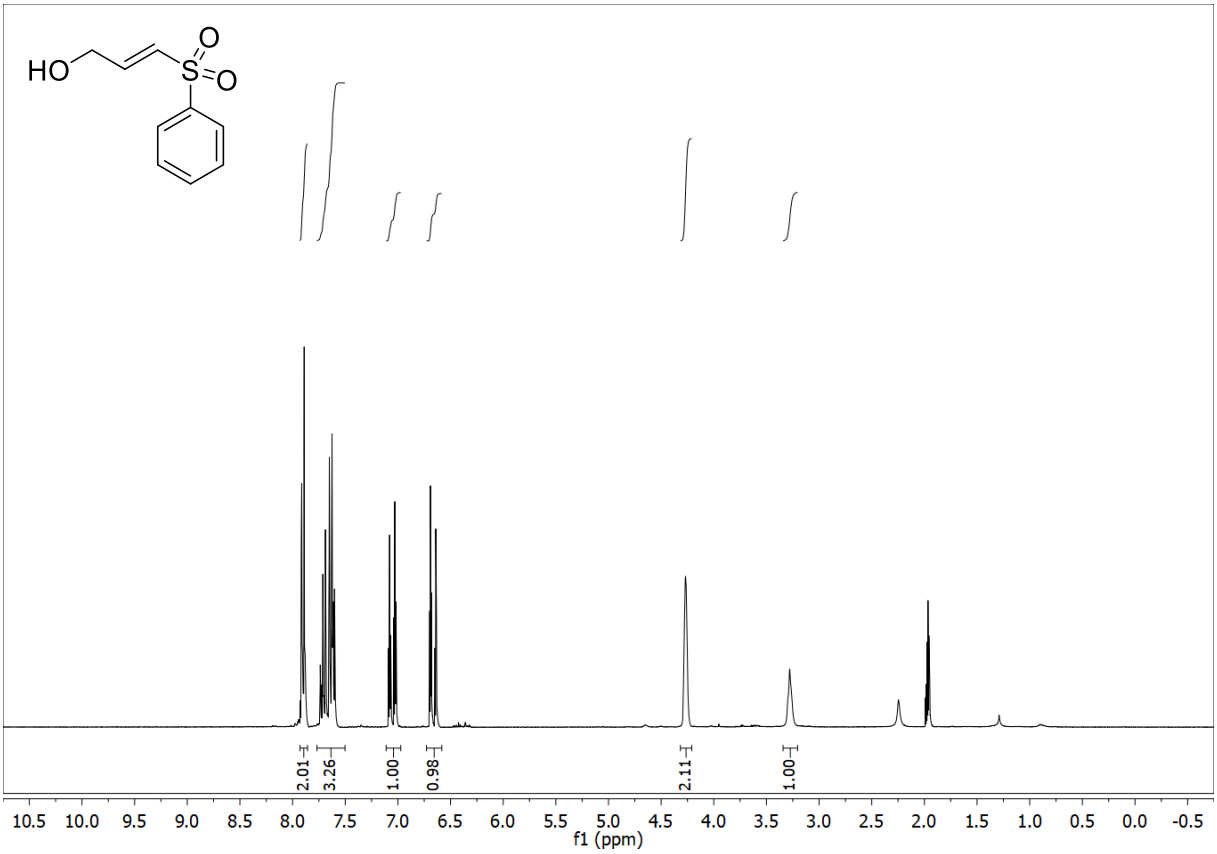
2-Chloro-3-(phenylsulfonyl)propan-1-ol (15c´)

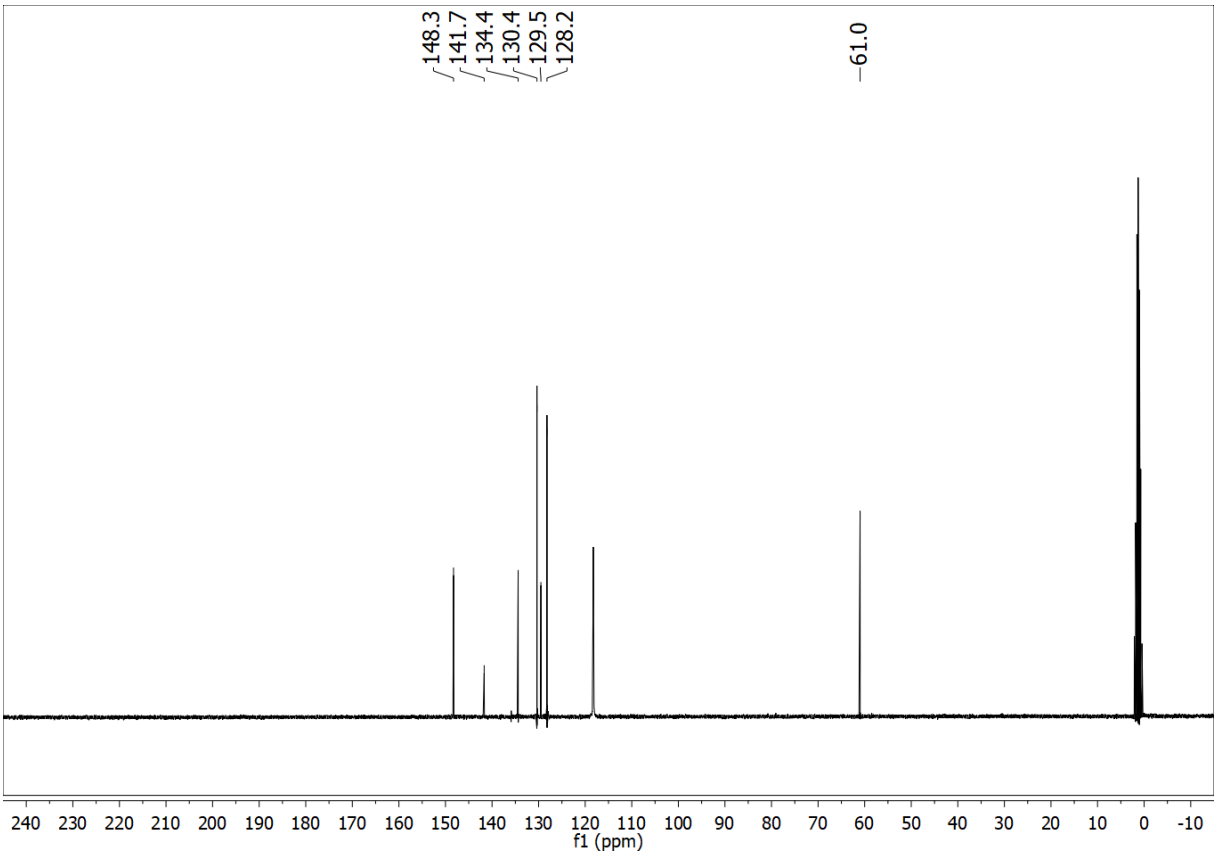




NMR-Solvent: $CDCl_3$

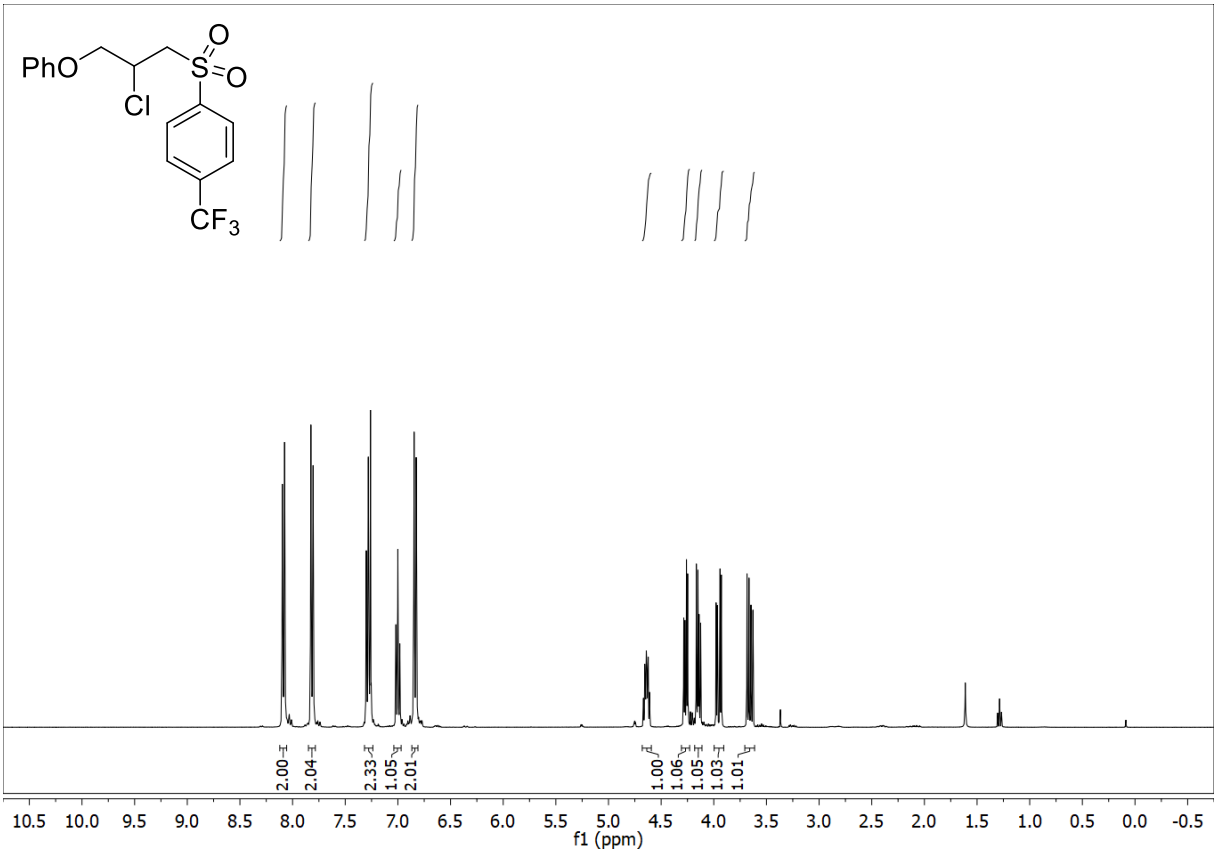
(*E*)-3-(Phenylsulfonyl)prop-2-en-1-ol (16c´)

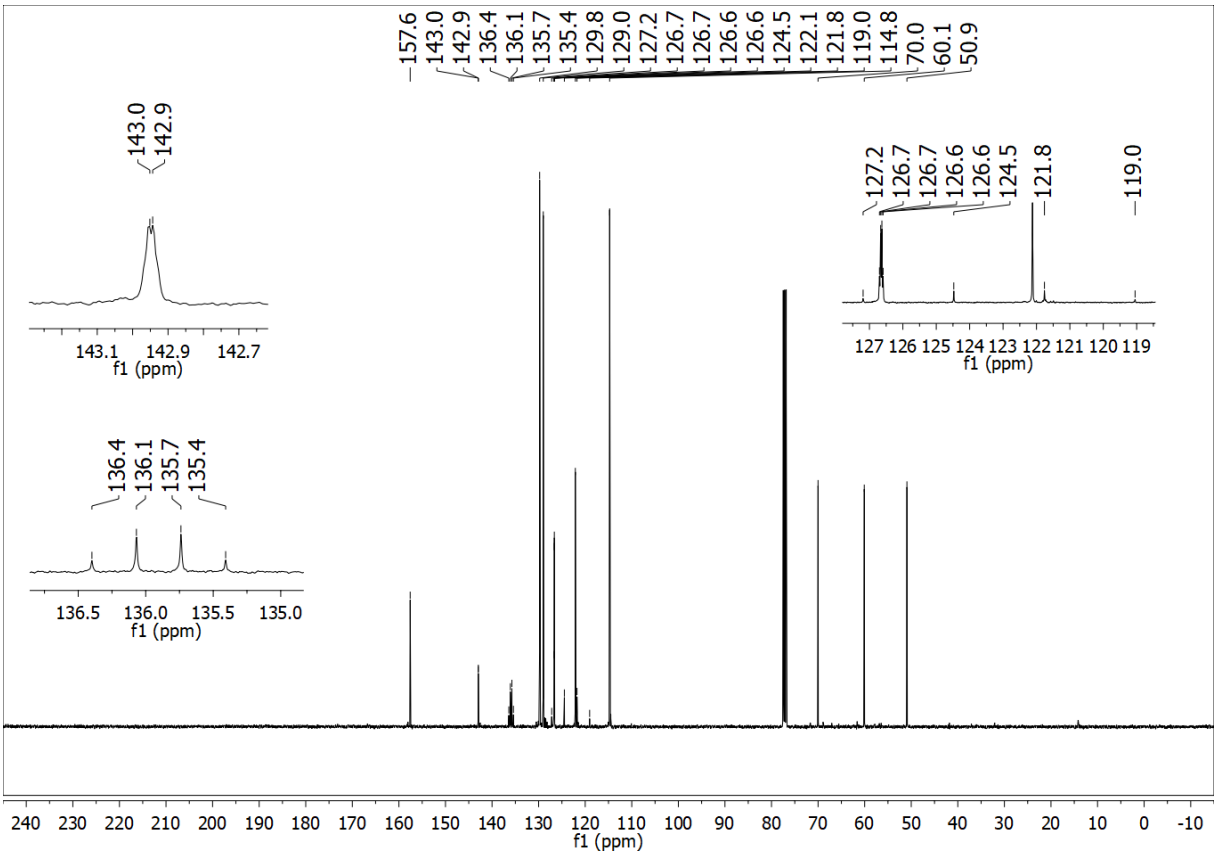


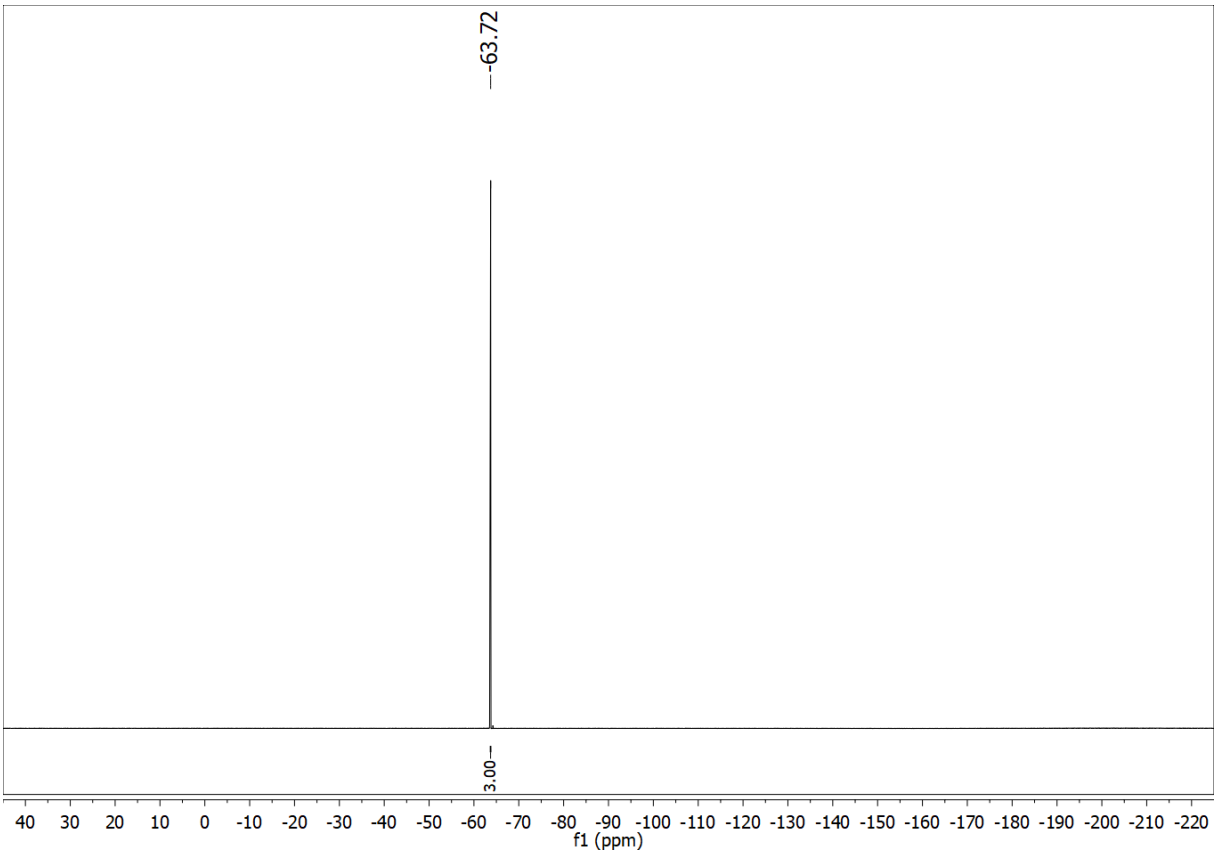


NMR-Solvent: CD_3CN

1-((2-Chloro-3-phenoxypropyl)sulfonyl)-4-(trifluoromethyl)benzene (15d)

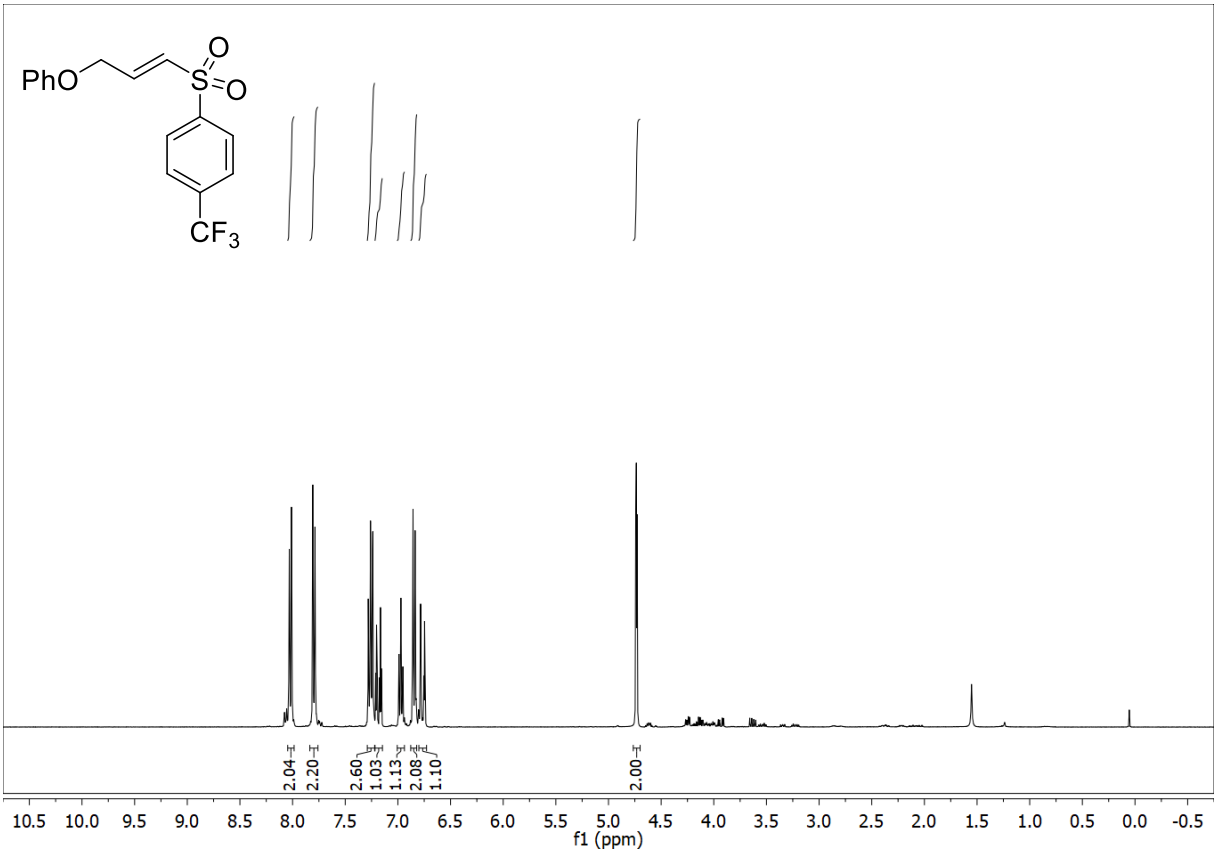


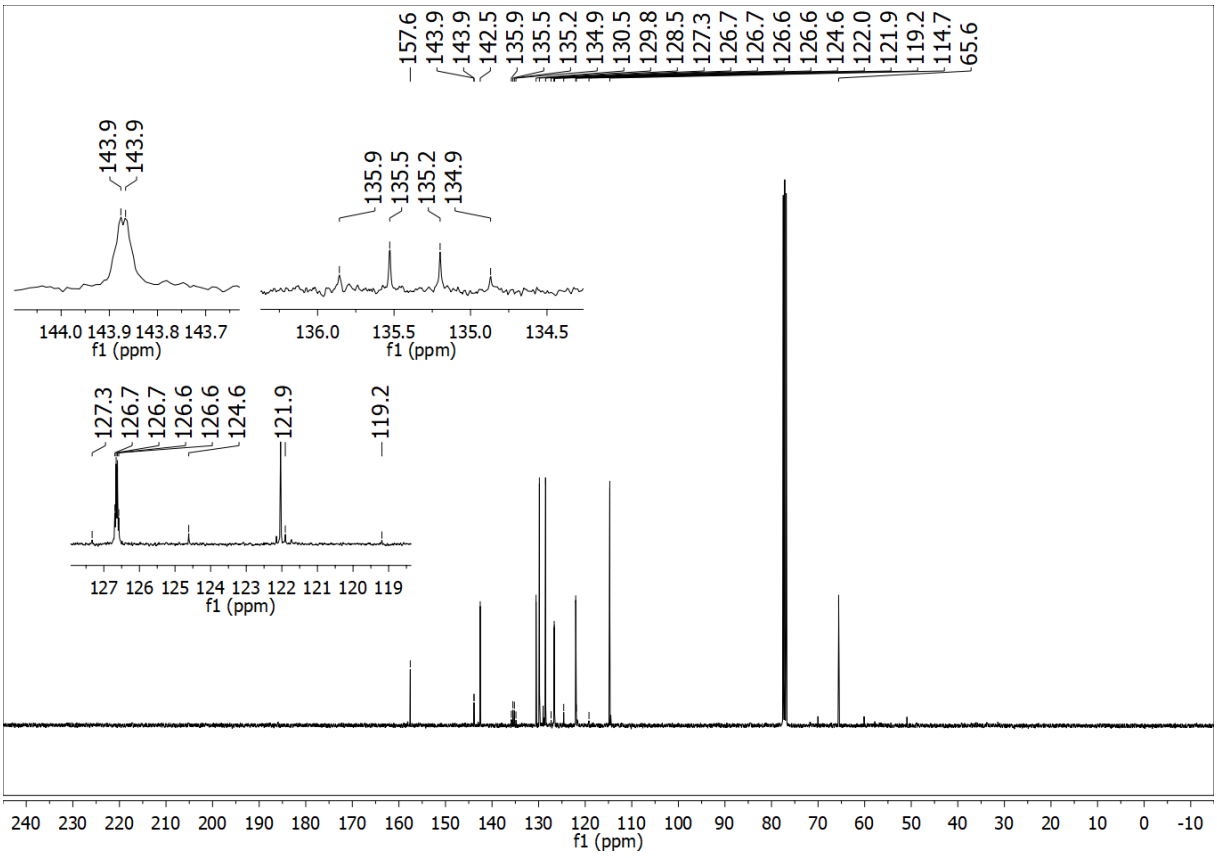


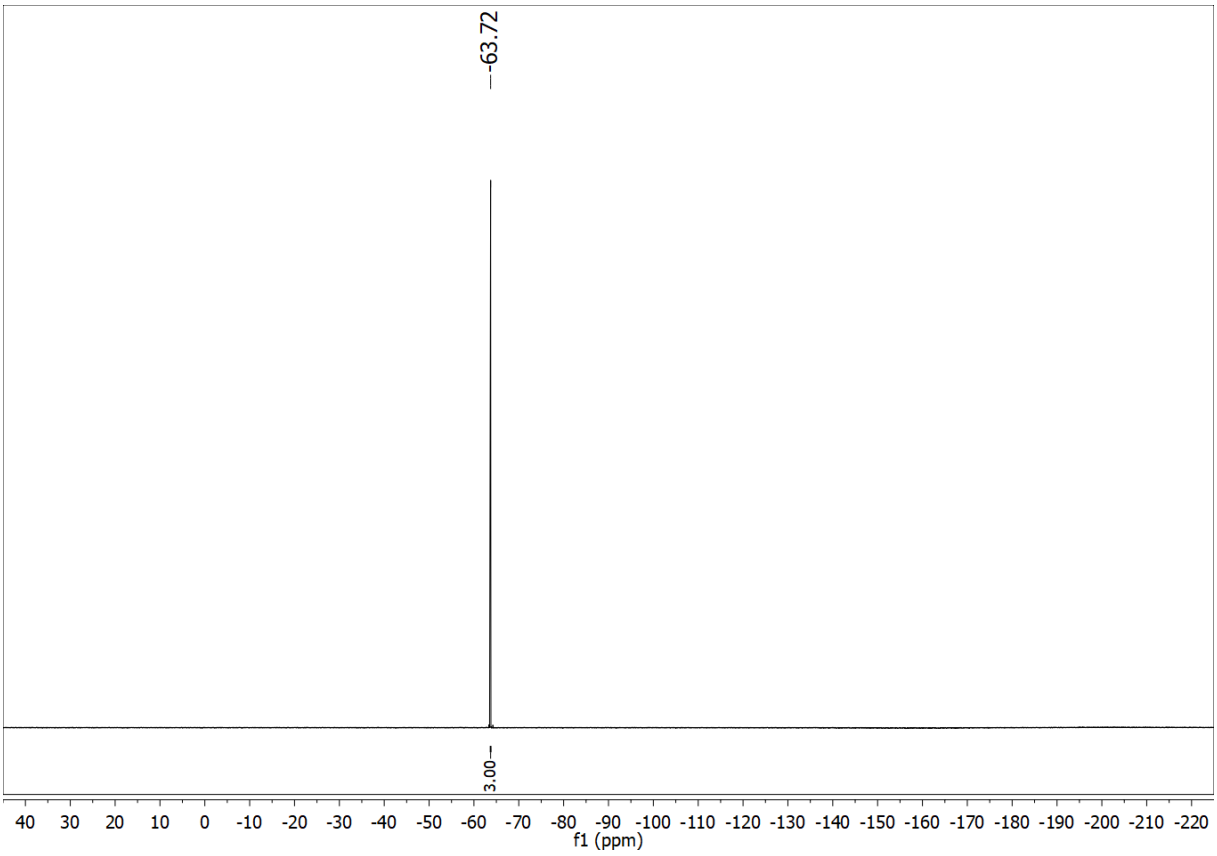


NMR-Solvent: $CDCl_3$

(*E*)-1-((3-Phenoxyprop-1-en-1-yl)sulfonyl)-4-(trifluoromethyl)benzene (16d)

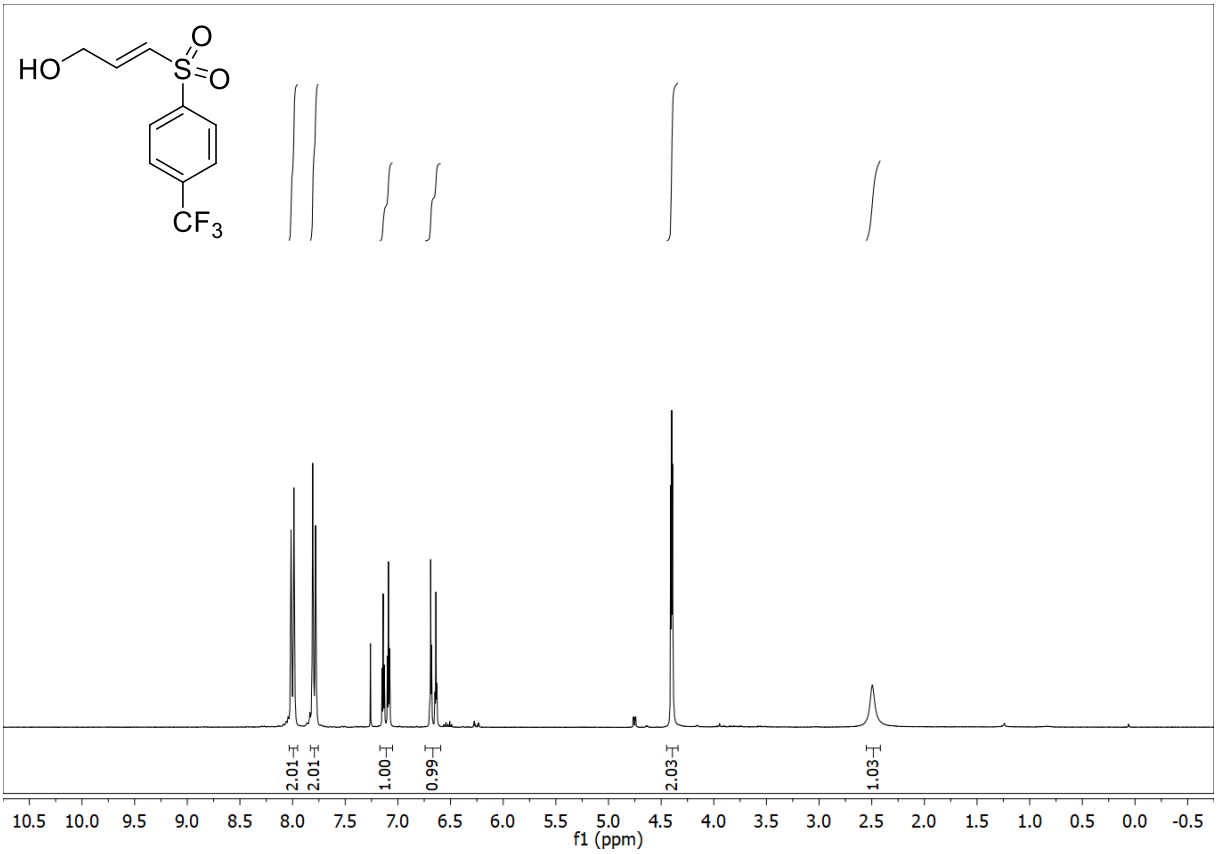


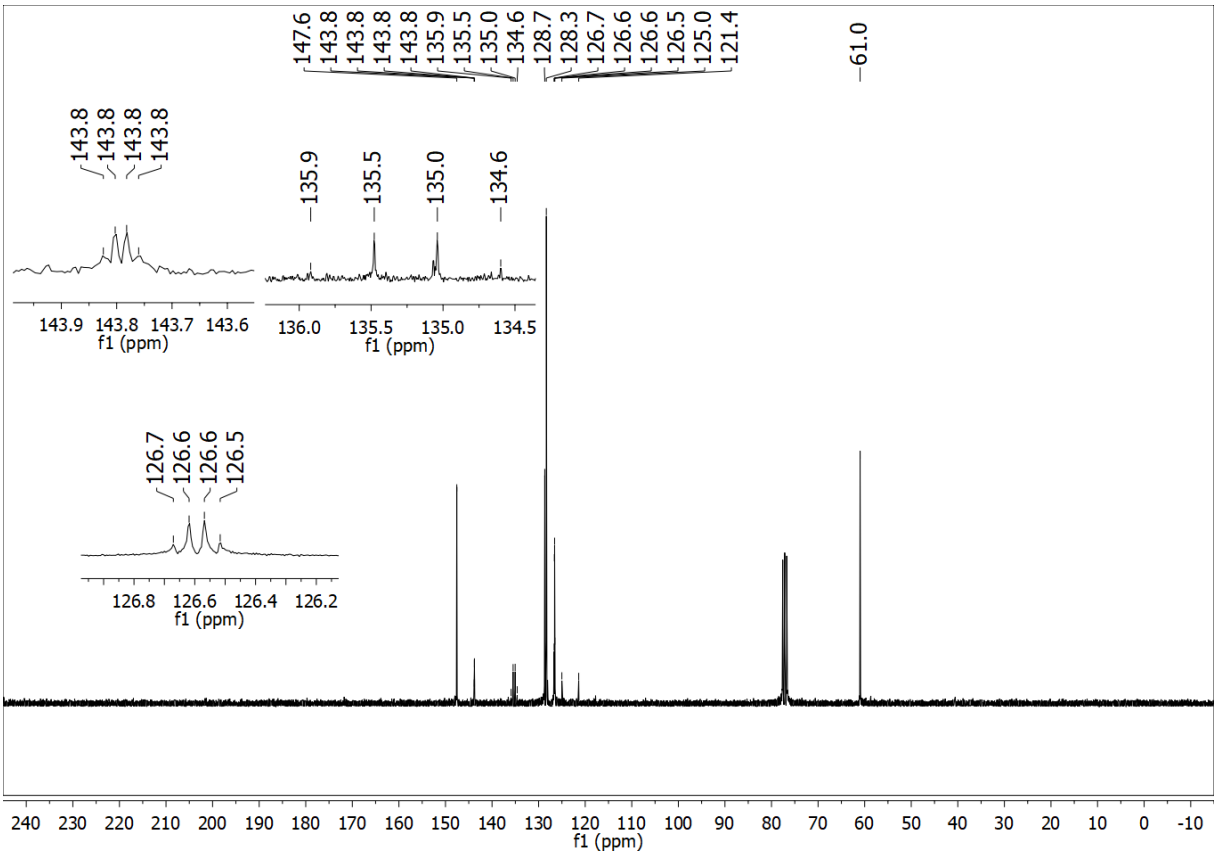


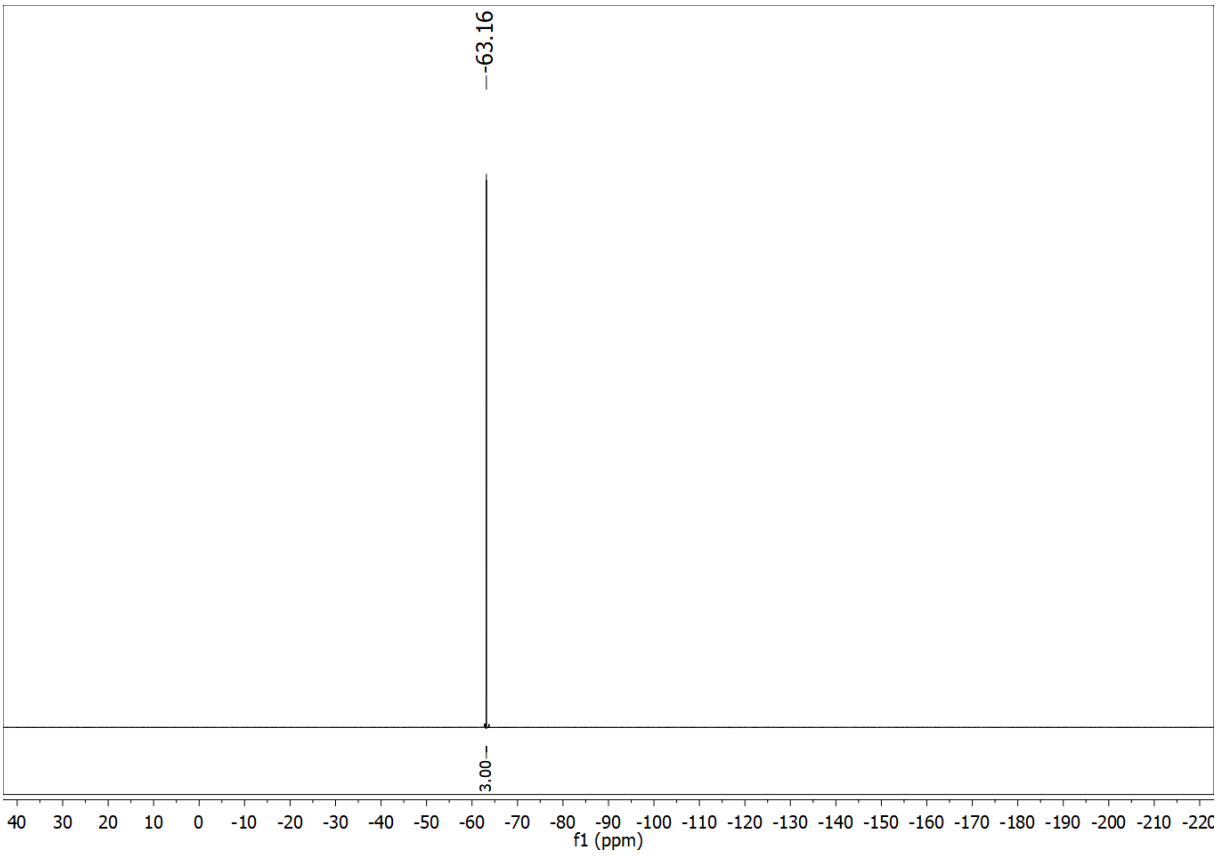


NMR-Solvent: $CDCl_3$

(*E*)-3-((4-(Trifluoromethyl)phenyl)sulfonyl)prop-2-en-1-ol (16d´)

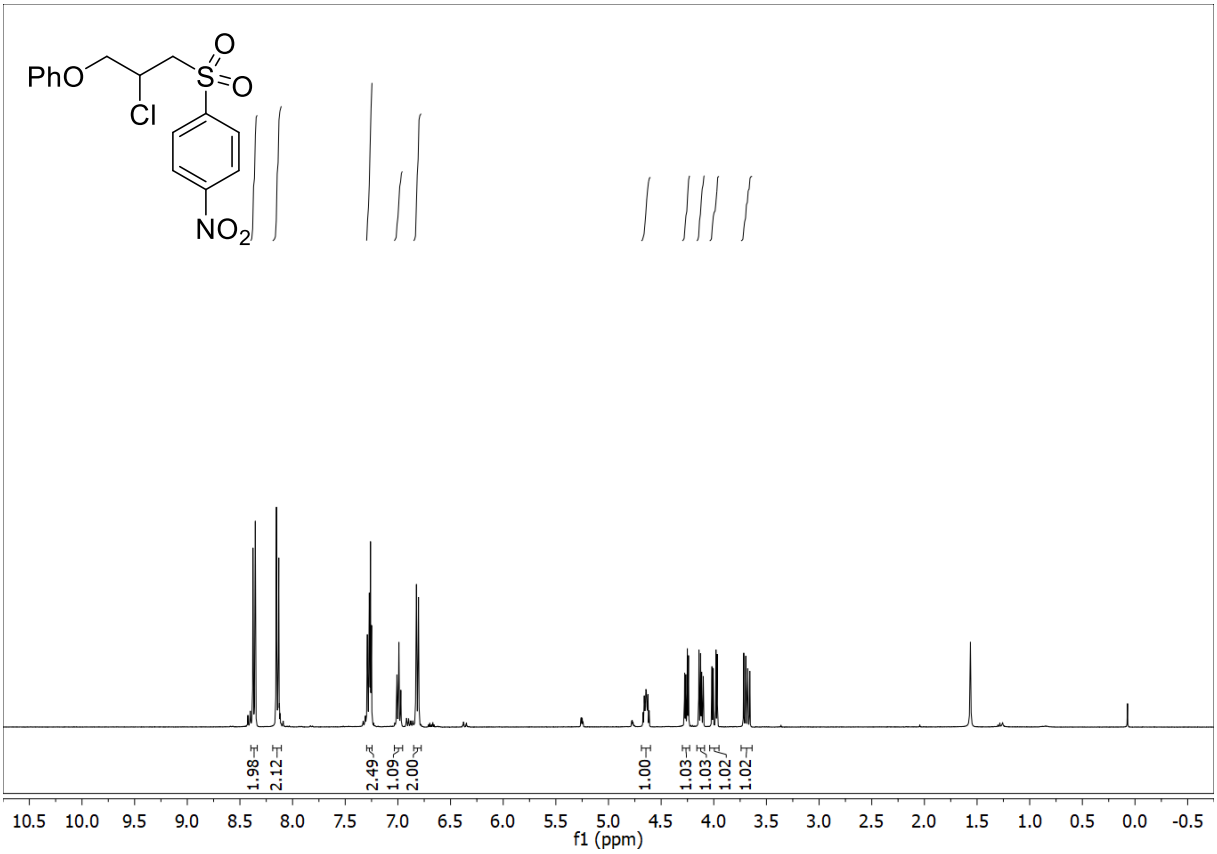


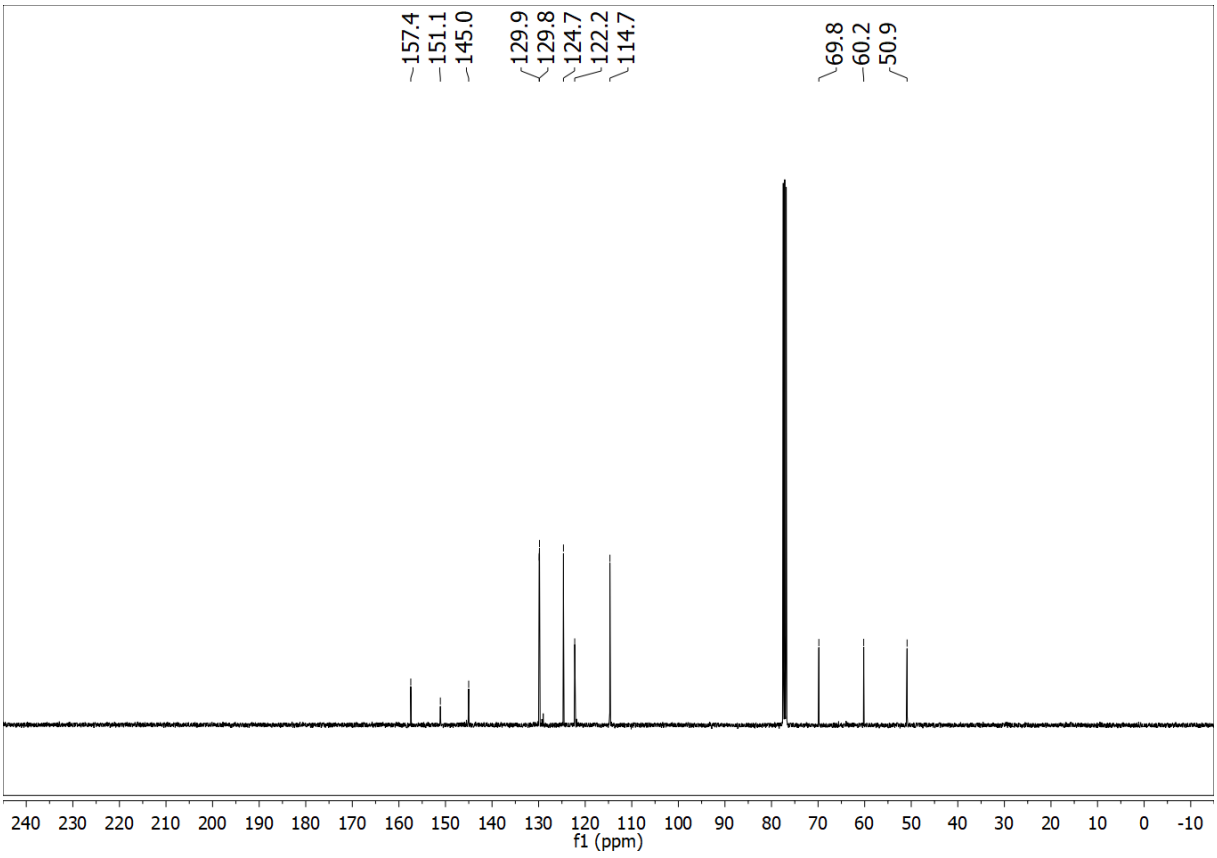




NMR-Solvent: $CDCl_3$

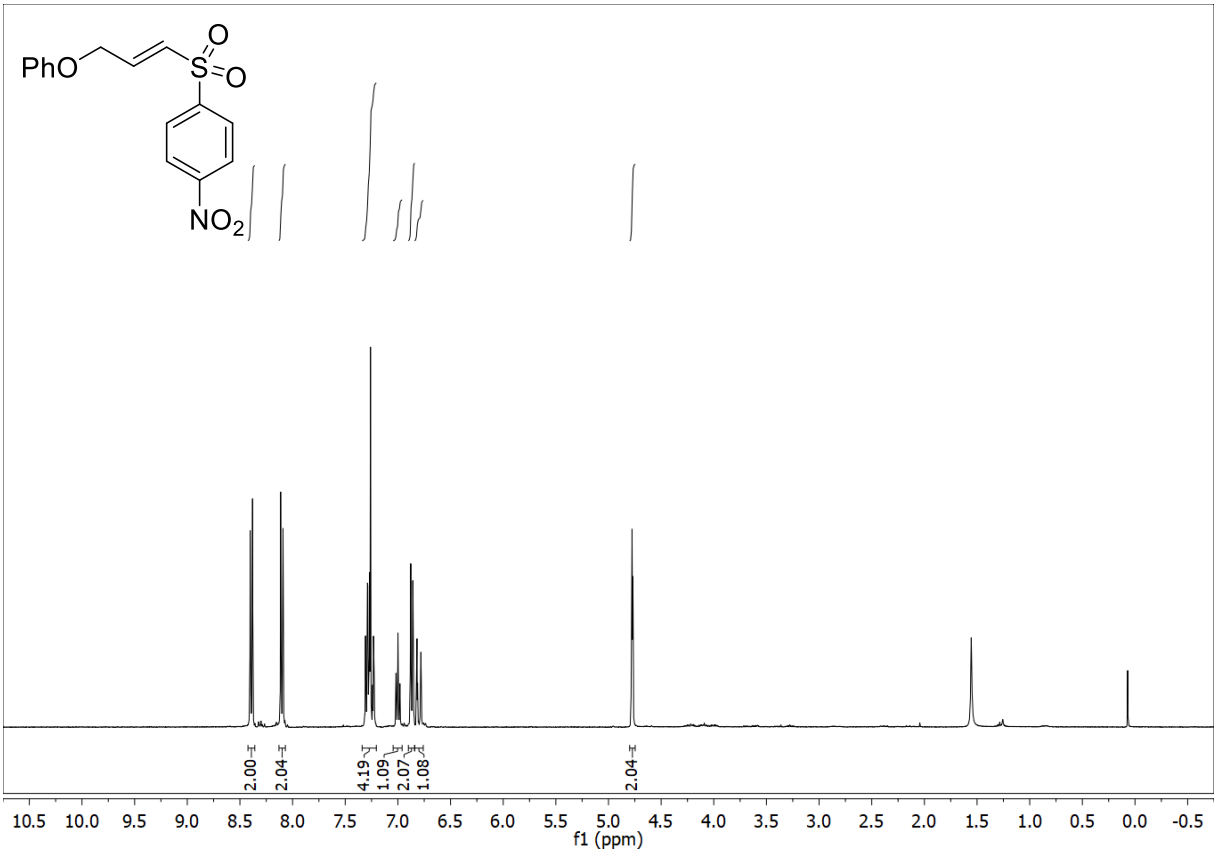
1-((2-Chloro-3-phenoxypropyl)sulfonyl)-4-nitrobenzene (15e)

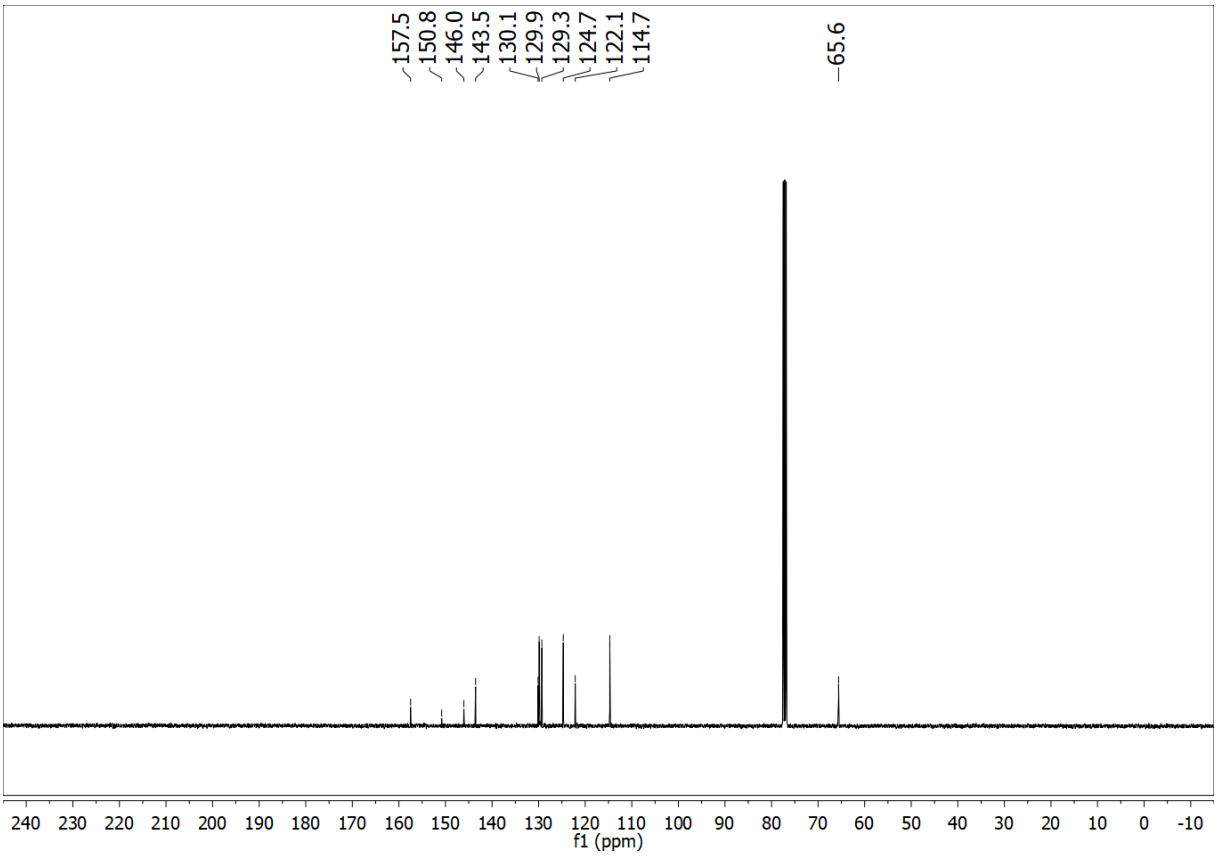




NMR-Solvent: $CDCl_3$

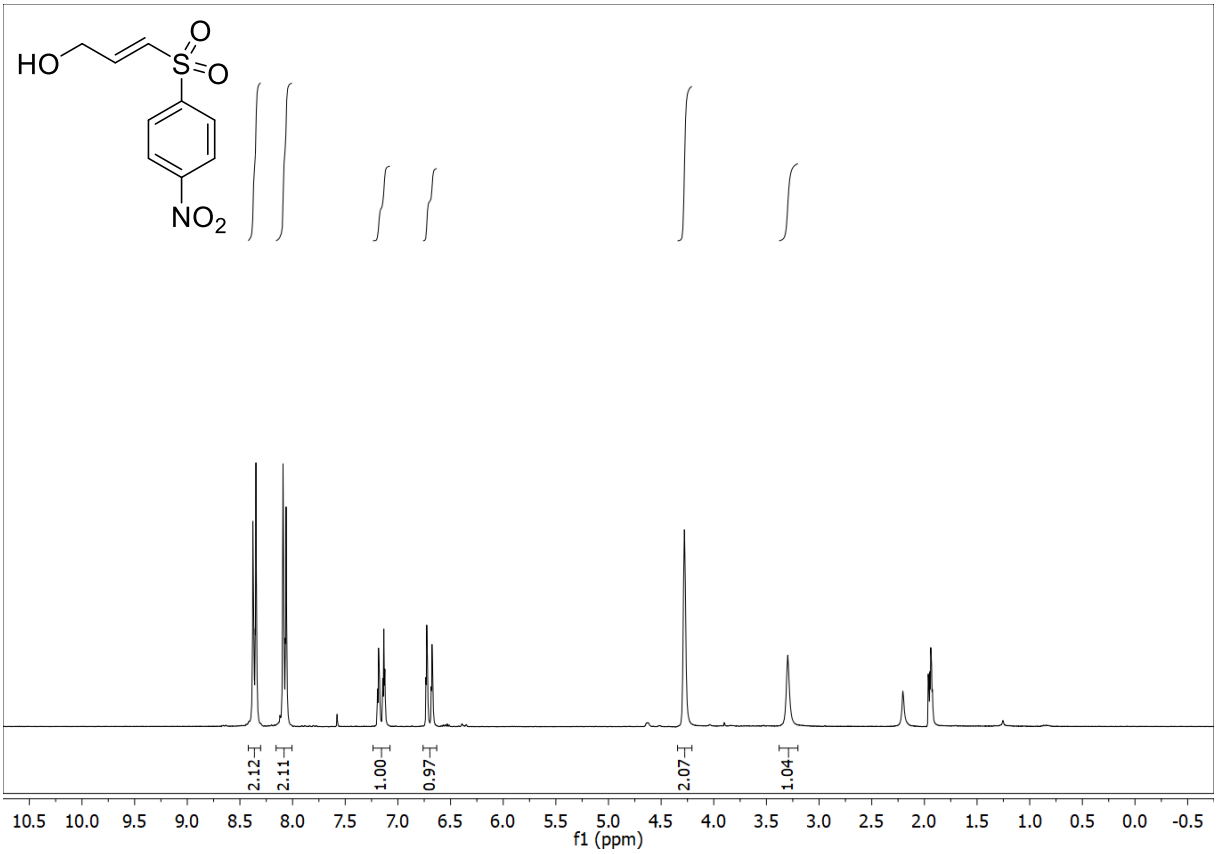
(*E*)-1-Nitro-4-((3-phenoxyprop-1-en-1-yl)sulfonyl)benzene (16e)

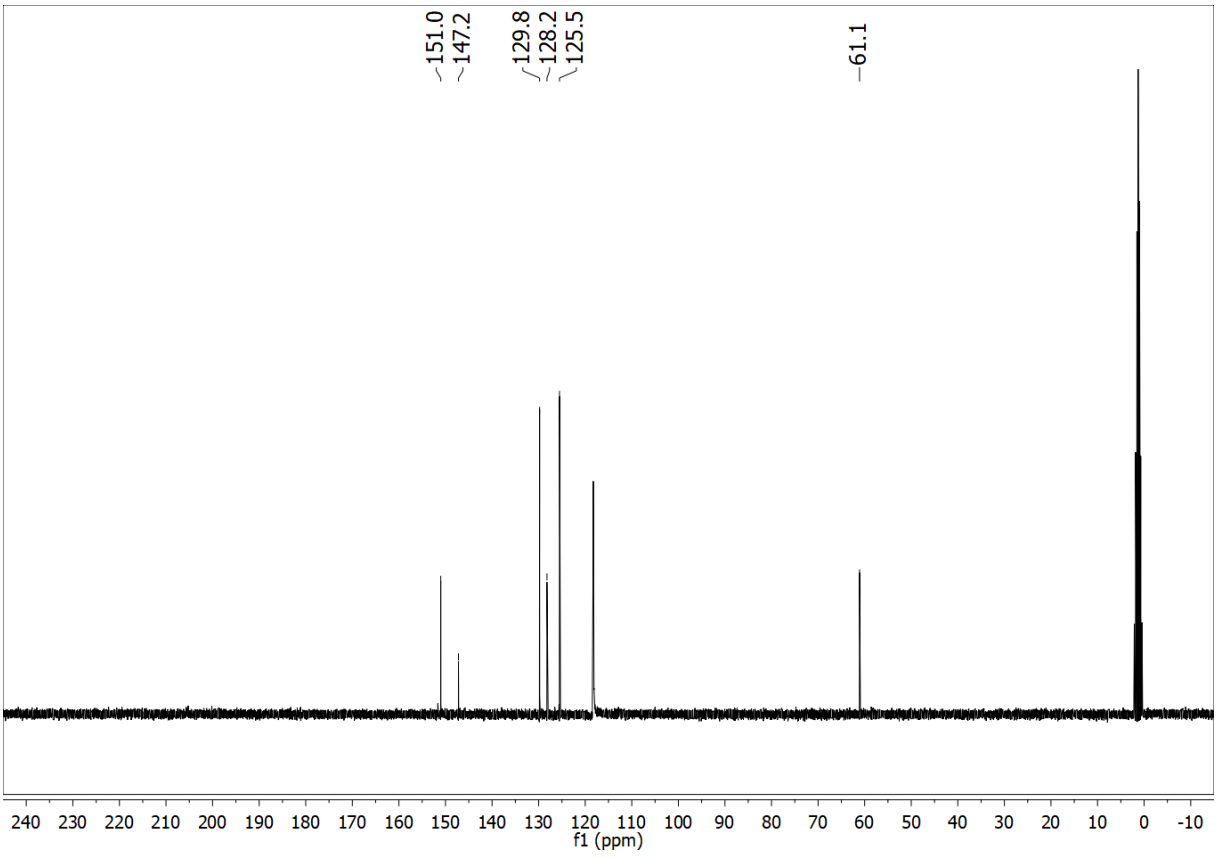




NMR-Solvent: $CDCl_3$

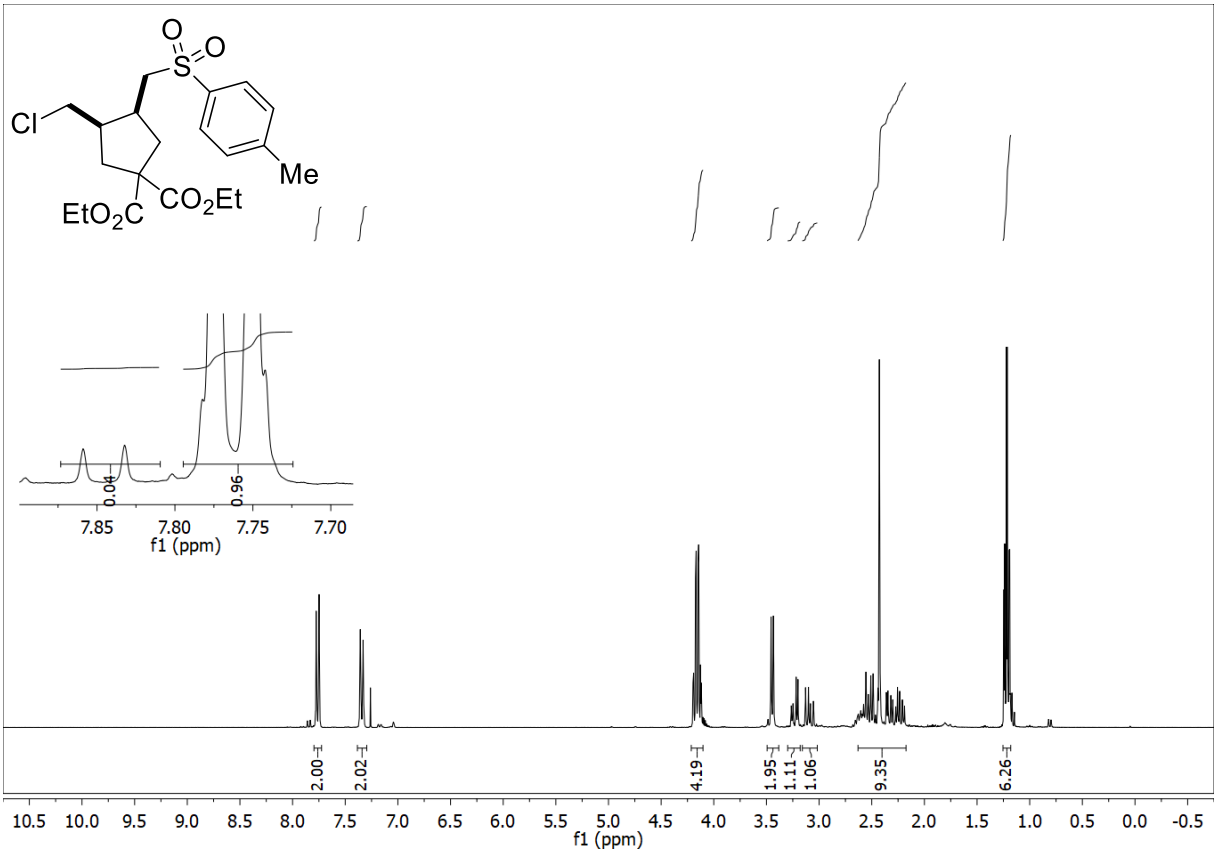
(*E*)-3-((4-Nitrophenyl)sulfonyl)prop-2-en-1-ol (16e´)

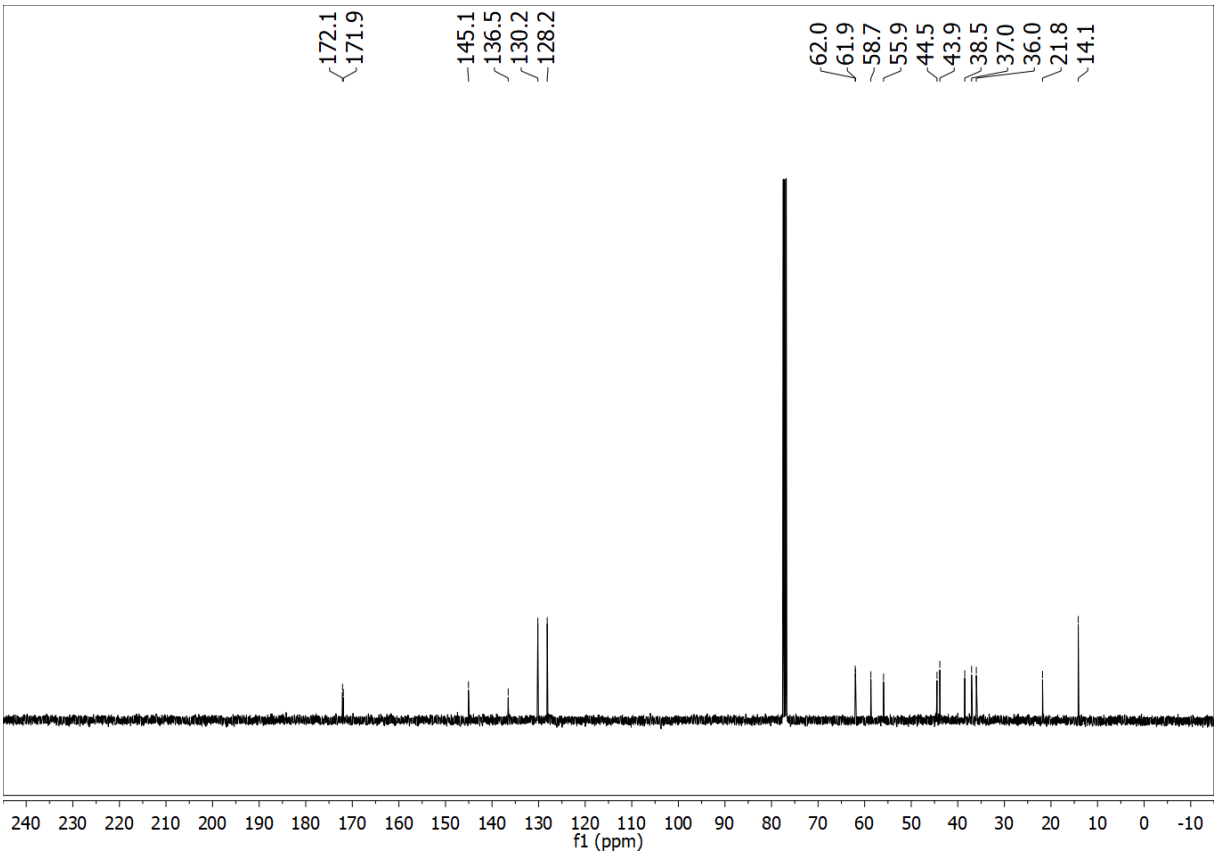




NMR-Solvent: CD_3CN

rac. Diethyl 3-(chloromethyl)-4-(tosylmethyl)cyclopentane-1,1-dicarboxylate (21)





NMR-Solvent: $CDCl_3$

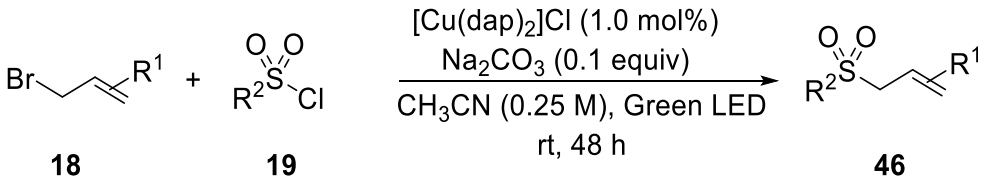
5. Chapter E: Copper Mediated Light Promoted Synthesis of Allylsulfones

5.1. Synthesis of Literature Known Compounds and Reagents

The following compounds were synthesized according to the reported literature procedures. The spectral data were in agreement with the data reported: *fac*-Ir(ppy)$_3$[3], 3-bromocyclohex-1-ene (**18f**)[28].

5.2. Compound Characterization

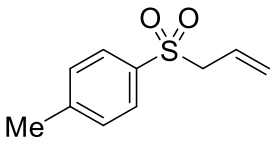
General Procedure for the Formation of Allylsulfones (GP-1):



18 **19** **46**

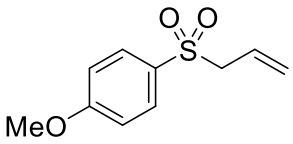
A Schlenk tube equipped with a magnetic stir bar was charged with sulfonyl chloride derivative **19** (0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 50 µmol, 0.1 equiv) and $[Cu(dap)_2]Cl$ (5.0 µmol, 1.0 mol%) in anh. MeCN (2.0 mL). The reaction mixture was degassed by three freeze-pump-thaw cycles and placed under N_2-atmosphere. Allyl bromide **18** (3.0 mmol, 6.0 equiv) was added and the reaction mixture was irradiated with a green LED (λ_{max} = 530 nm) at room temperature. After completion of the reaction (judged by TLC, usually 48 h), the reaction mixture was filtered through a short plug of silica, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel to yield pure product **46**. The results for reactions with *fac*-$Ir(ppy)_3$ and with no catalyst were obtained by crude NMR-analysis after filtration through a short plug of silica. For Ir-catalysis no Na_2CO_3 was used.

1-(Allylsulfonyl)-4-methylbenzene (20a)



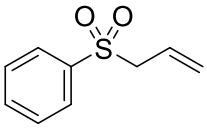
Cu(I)-catalysis: Following general procedure GP-1, using 4-methylbenzenesulfonyl chloride (**19a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 91 mg (464 µmol, 93%) of 1-(allylsulfonyl)-4-methylbenzene (**20a**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc) = 0.38. Staining: $KMnO_4$ (UV active). ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.28 (m, 2H), 5.75 (ddt, *J* = 17.5, 10.2, 7.4 Hz, 1H), 5.29 (dq, *J* = 10.1, 0.9 Hz, 1H), 5.12 (dq, *J* = 17.1, 1.2 Hz, 1H), 3.76 (dt, *J* = 7.4, 1.0 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.8, 135.3, 129.7, 128.5, 124.8, 124.6, 60.9, 21.7. IR (neat): 3030, 2974, 2922, 1640, 1595, 1495, 1454, 1316, 1241, 1197, 1141, 1085, 1044, 992, 936, 872, 816, 775, 708 cm^{-1}. HRMS (ESI) m/z calculated for $C_{10}H_{13}O_2S$ ($[M+H]^+$) 197.0631, found 197.0630.

1-(Allylsulfonyl)-4-methoxybenzene (20b)



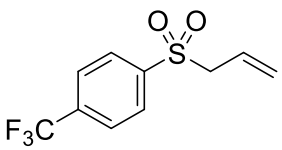
Cu(I)-catalysis: Following general procedure GP-1, using 4-methoxybenzenesulfonyl chloride (**19b**) (103 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 88 mg (415 µmol, 83%) of 1-(allylsulfonyl)-4-methoxybenzene (**20b**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 3:1). R_f (hexanes / EtOAc 4:1) = 0.21. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.9 Hz, 2H), 6.99 (d, *J* = 8.9 Hz, 2H), 5.78 (ddt, *J* = 17.5, 10.2, 7.4 Hz, 1H), 5.31 (dq, *J* = 10.2, 0.9 Hz, 1H), 5.13 (dq, *J* = 17.1, 1.2 Hz, 1H), 3.87 (s, 3H), 3.77 (dt, *J* = 7.4, 1.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.9, 130.8, 130.0, 125.1, 124.6, 114.3, 61.3, 55.8. IR (neat): 3079, 2974, 2844, 1640, 1595, 1498, 1461, 1416, 1293, 1260, 1182, 1133, 1088, 1021, 936, 872, 835, 716, 682 cm^{-1}. HRMS (ESI) m/z calculated for $C_{10}H_{13}O_3S$ ($[M+H]^+$) 213.0580, found 213.0583.

(Allylsulfonyl)benzene (20c)



Cu(I)-catalysis: Following general procedure GP-1, using benzenesulfonyl chloride (**19c**) (88 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 57 mg (313 µmol, 63%) of (allylsulfonyl)benzene (**20c**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 3:1). R_f (hexanes / EtOAc 4:1) = 0.33. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 – 7.83 (m, 2H), 7.68 – 7.60 (m, 1H), 7.59 – 7.49 (m, 2H), 5.78 (ddt, *J* = 17.5, 10.2, 7.4 Hz, 1H), 5.32 (dq, *J* = 10.2, 0.9 Hz, 1H), 5.14 (dq, *J* = 17.0, 1.2 Hz, 1H), 3.80 (dt, *J* = 7.4, 1.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 133.9, 129.2, 128.6, 124.8, 124.7, 61.0. IR (neat): 3064, 2974, 2919, 1640, 1588, 1480, 1446, 1398, 1308, 1241, 1197, 1144, 1085, 1025, 992, 936, 872, 790, 753, 727, 690 cm^{-1}. HRMS (ESI) m/z calculated for $C_9H_{11}O_2S$ ($[M+H]^+$) 183.0474, found 183.0473.

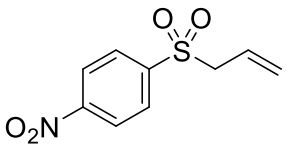
1-(Allylsulfonyl)-4-(trifluoromethyl)benzene (20d)



Cu(I)-catalysis: Following general procedure GP-1, using 4-(trifluoromethyl)benzenesulfonyl chloride (**19d**) (122 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 87 mg (348 µmol, 70%) of 1-(allylsulfonyl)-4-(trifluoromethyl)benzene (**20d**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 3:1). R_f (hexanes / EtOAc 4:1) = 0.39. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.3 Hz, 2H), 5.79 (ddt, *J* = 17.4, 10.1,

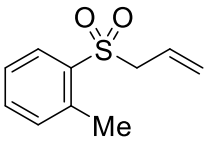
7.4 Hz, 1H), 5.38 – 5.33 (m, 1H), 5.16 (dq, *J* = 17.0, 1.2 Hz, 1H), 3.84 (dt, *J* = 7.4, 1.0 Hz, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.75 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.8, 135.6 (q, *J* = 33.2 Hz), 129.3, 126.3 (q, *J* = 3.6 Hz), 125.5, 124.3, 123.2 (q, *J* = 273.1 Hz), 60.9. IR (neat): 3109, 2974, 2930, 1402, 1316, 1185, 1129, 1059, 947, 839, 794, 716 cm^{-1}. HRMS (ESI) m/z calculated for $C_{10}H_{10}F_3O_2S$ ([M+H]$^+$) 251.0348, found 251.0355.

1-(Allylsulfonyl)-4-nitrobenzene (20e)



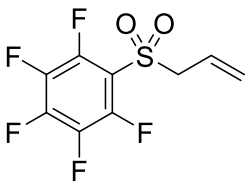
Cu(I)-catalysis: Following general procedure GP-1, using 4-nitrobenzenesulfonyl chloride (**19e**) (110 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 78 mg (343 µmol, 69%) of 1-(allylsulfonyl)-4-nitrobenzene (**20e**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 2:1). R_f (hexanes / EtOAc 4:1) = 0.23. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.8 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 5.80 (ddt, *J* = 17.4, 10.2, 7.4 Hz, 1H), 5.37 (dq, *J* = 10.1, 0.8 Hz, 1H), 5.15 (dq, *J* = 17.1, 1.2 Hz, 1H), 3.87 (dt, *J* = 7.4, 1.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 143.8, 130.2, 125.8, 124.4, 124.1, 60.9. IR (neat): 3101, 3038, 2967, 2919, 2870, 1607, 1528, 1424, 1402, 1349, 1297, 1241, 1200, 1144, 1085, 1006, 951, 876, 828, 790, 727, 682 cm^{-1}. HRMS (ESI) m/z calculated for $C_9H_{10}NO_4S$ ([M+H]$^+$) 228.0325, found 228.0331.

1-(Allylsulfonyl)-2-methylbenzene (20h)



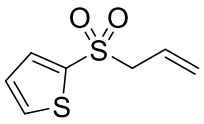
Cu(I)-catalysis: Following general procedure GP-1, using 2-methylbenzenesulfonyl chloride (**19h**) (72 µL, 95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 41 mg (209 µmol, 42% (brsm 79%)) of 1-(allylsulfonyl)-2-methylbenzene (**20h**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc 4:1) = 0.38. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.51 (td, *J* = 7.5, 1.5 Hz, 1H), 7.39 – 7.30 (m, 2H), 5.85 – 5.67 (m, 1H), 5.30 (dq, *J* = 10.1, 0.9 Hz, 1H), 5.17 (dq, *J* = 17.0, 1.2 Hz, 1H), 3.85 (dt, *J* = 7.4, 1.1 Hz, 2H), 2.70 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2, 136.6, 133.9, 132.7, 130.9, 126.6, 124.7, 124.6, 60.2, 20.7. IR (neat): 3064, 3023, 2982, 2926, 1640, 1595, 1569, 1454, 1398, 1312, 1238, 1197, 1148, 1082, 992, 936, 872, 805, 760, 708, 678 cm^{-1}. HRMS (APCI) m/z calculated for $C_{10}H_{16}NO_2S$ ([M+NH_4]$^+$) 214.0896, found 214.0899.

1-(Allylsulfonyl)-2,3,4,5,6-pentafluorobenzene (20i)



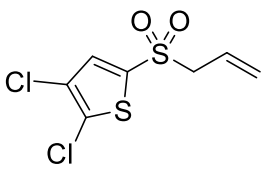
Cu(I)-catalysis: Following general procedure GP-1, using 2,3,4,5,6-pentafluorobenzenesulfonyl chloride (**19i**) (74 µL, 133 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 95 mg (349 µmol, 70%) of 1-(allylsulfonyl)-2,3,4,5,6-pentafluorobenzene (**20i**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc 4:1) = 0.50. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.01 – 5.81 (m, 1H), 5.45 (dq, *J* = 10.1, 0.8 Hz, 1H), 5.32 (dq, *J* = 17.1, 1.2 Hz, 1H), 4.04 (ddd, *J* = 7.4, 1.3, 0.7 Hz, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -135.40 – -135.78 (m, 2F), -143.14 (tt, *J* = 20.9, 7.4 Hz, 1F), -158.08 – -158.47 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1 – 135.5 (m), 126.5, 123.5, 62.3. IR (neat): 2978, 2922, 1640, 1543, 1495, 1398, 1353, 1293, 1244, 1204, 1148, 1092, 992, 951, 883, 842, 779, 727 cm^{-1}. HRMS (APCI) m/z calculated for $C_9H_9F_5NO_2S$ ($[M+NH_4]^+$) 290.0269, found 290.0271.

2-(Allylsulfonyl)thiophene (20j)



Cu(I)-catalysis: Following general procedure GP-1, using thiophene-2-sulfonyl chloride (**19j**) (91 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 86 mg (457 µmol, 91%) of 2-(allylsulfonyl)thiophene (**20j**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 2:1). R_f (hexanes / EtOAc 4:1) = 0.23. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.63 (dd, *J* = 3.8, 1.4 Hz, 1H), 7.13 (dd, *J* = 5.0, 3.8 Hz, 1H), 5.82 (ddt, *J* = 17.0, 10.1, 7.4 Hz, 1H), 5.36 (dq, *J* = 10.1, 0.9 Hz, 1H), 5.20 (dq, *J* = 17.0, 1.2 Hz, 1H), 3.88 (ddd, *J* = 7.3, 1.3, 0.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 134.7, 134.3, 127.9, 125.1, 124.6, 62.1. IR (neat): 3094, 2974, 2919, 1640, 1506, 1402, 1316, 1226, 1197, 1137, 1088, 1014, 936, 853, 779, 723, 678 cm^{-1}. HRMS (APCI) m/z calculated for $C_7H_{12}NO_2S_2$ ($[M+NH_4]^+$) 206.0304, found 206.0306.

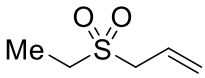
5-(Allylsulfonyl)-2,3-dichlorothiophene (20k)



Cu(I)-catalysis: Following general procedure GP-1, using 4,5-dichlorothiophene-2-sulfonyl chloride (**19k**) (126 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 107 mg (416 µmol, 83%) of 5-(allylsulfonyl)-2,3-dichlorothiophene (**20k**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 3:1). R_f (hexanes / EtOAc 4:1) = 0.50. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (s, 1H),

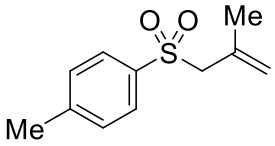
5.84 (ddt, *J* = 17.0, 10.1, 7.4 Hz, 1H), 5.46 (dq, *J* = 10.1, 0.9 Hz, 1H), 5.30 (dq, *J* = 17.0, 1.2 Hz, 1H), 3.89 (dt, *J* = 7.4, 1.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.4, 134.1, 133.6, 126.0, 125.6, 124.2, 62.0. IR (neat): 3094, 3023, 2974, 2915, 1640, 1513, 1402, 1323, 1241, 1193, 1133, 1081, 1021, 939, 865, 779, 705 cm^{-1}. HRMS (APCI) m/z calculated for $C_7H_{10}Cl_2NO_2S_2$ ($[M+NH_4]^+$) 273.9525, found 273.9528.

3-(Ethylsulfonyl)prop-1-ene (20l)



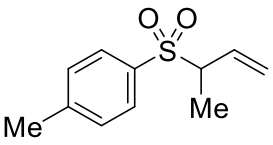
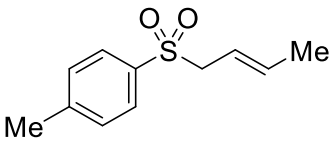
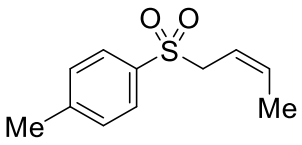
Cu(I)-catalysis: Following general procedure GP-1, using ethanesulfonyl chloride (**19l**) (47 µL, 64 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 47 mg (350 µmol, 70%) of 3-(ethylsulfonyl)prop-1-ene (**20l**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 1:1). R_f (hexanes / EtOAc 4:1) = 0.10. Staining: $KMnO_4$ (UV inactive). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.95 (ddt, *J* = 17.0, 10.2, 7.4 Hz, 1H), 5.56 – 5.40 (m, 2H), 3.70 (dq, *J* = 7.5, 1.0 Hz, 2H), 2.99 (q, *J* = 7.5 Hz, 2H), 1.39 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 125.3, 124.6, 57.0, 45.7, 6.6. IR (neat): 3090, 2982, 2945, 1640, 1457, 1423, 1308, 1241, 1126, 1085, 1044, 992, 939, 880, 801, 723, 675 cm^{-1}. HRMS (APCI) m/z calculated for $C_5H_{14}NO_2S$ ($[M+NH_4]^+$) 152.0740, found 152.0739.

1-Methyl-4-((2-methylallyl)sulfonyl)benzene (23c)



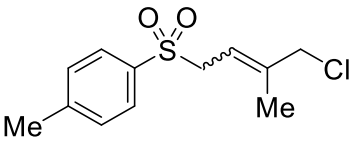
Cu(I)-catalysis: Following general procedure GP-1, using 4-methylbenzenesulfonyl chloride (**19a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromo-2-methylprop-1-ene (**18c**) (302 µL, 405 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 97 mg (461 µmol, 92%) of 1-methyl-4-((2-methylallyl)sulfonyl)benzene (**23c**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc) = 0.43. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.01 (p, *J* = 1.5 Hz, 1H), 4.68 (p, *J* = 1.0 Hz, 1H), 3.73 (s, 2H), 2.43 (s, 3H), 1.87 – 1.82 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 135.6, 133.6, 129.7, 128.6, 120.7, 64.6, 22.8, 21.7. IR (neat): 3068, 3031, 2974, 2915, 1774, 1644, 1595, 1491, 1454, 1308, 1241, 1159, 1126, 1088, 1018, 910, 835, 809, 783, 708, 686 cm^{-1}. HRMS (ESI) m/z calculated for $C_{11}H_{18}NO_2S$ ($[M+NH_4]^+$) 228.1053, found 228.1056.

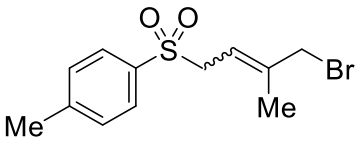
1-(But-3-en-2-ylsulfonyl)-4-methylbenzene (23d´), (*E*)-1-(but-2-en-1-ylsulfonyl)-4-methylbenzene (*E*-23d) and (*Z*)-1-(but-2-en-1-ylsulfonyl)-4-methylbenzene (*Z*-23d)

Cu(I)-catalysis: Following general procedure GP-1, using 4-methylbenzenesulfonyl chloride (**19a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), (*E*)-1-bromobut-2-ene (**18d**) (364 µL, 405 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 53 mg (250 µmol, 50%) of 1-(but-3-en-2-ylsulfonyl)-4-methylbenzene (**23d´**) and a *E*/*Z* mixture with 24 mg (114 µmol, 23%) of (*E*)-1-(but-2-en-1-ylsulfonyl)-4-methylbenzene (***E*-23d**) and 8 mg (39 µmol, 8%) of (*Z*)-1-(but-2-en-1-ylsulfonyl)-4-methylbenzene (***Z*-23d**) as colorless oils after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (**23d´**, hexanes / EtOAc 4:1) = 0.42. Staining: $KMnO_4$ (UV active). R_f (***E*-23d**, hexanes / EtOAc 4:1) = 0.38. Staining: $KMnO_4$ (UV active). R_f (***Z*-23d**, hexanes / EtOAc 4:1) = 0.38. Staining: $KMnO_4$ (UV active). ^{1}H NMR (**23d´**, 400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.82 (ddd, *J* = 17.2, 10.3, 7.8 Hz, 1H), 5.26 (dt, *J* = 10.3, 0.9 Hz, 1H), 5.09 (dt, *J* = 17.2, 1.0 Hz, 1H), 3.74 – 3.64 (m, 1H), 2.44 (s, 3H), 1.42 (d, *J* = 7.0 Hz, 3H). ^{1}H NMR (*E*/*Z* mixture **23d**, 400 MHz, $CDCl_3$) δ 7.75 (*Z*-isomer, d, *J* = 8.3 Hz, 2H), 7.73 (*E*-isomer d, *J* = 8.3 Hz, 2H), 7.33 (*E*/*Z*-isomer d, *J* = 8.0 Hz, 2H), 5.87 – 5.76 (*Z*-isomer, m, 1H), 5.56 (*E*-isomer, dqt, *J* = 14.9, 6.3, 1.0 Hz, 1H), 5.41 (*E*/*Z*-isomer, dtq, *J* = 12.9, 7.3, 1.6 Hz, 1H), 3.83 (*Z*-isomer, dt, *J* = 7.9, 0.9 Hz, 2H), 3.70 (*E*-isomer, dt, *J* = 7.3, 1.1 Hz, 2H), 2.44 (*E*/*Z*-isomer, s, 3H), 1.67 (*E*-isomer, dd, *J* = 6.2, 1.2 Hz, 3H), 1.36 (*Z*-isomer, dd, *J* = 7.0, 1.8 Hz, 3H). ^{13}C NMR (**23d´**, 101 MHz, $CDCl_3$) δ 144.7, 134.0, 131.5, 129.6, 129.5, 121.8, 64.3, 21.8, 13.2. ^{13}C NMR (*E*/*Z* mixture **23d**, 101 MHz, $CDCl_3$) δ 144.7 (*E*-isomer), 144.7 (*Z*-isomer), 136.5 (*E*/*Z*-isomer), 135.8 (*E*-isomer), 135.8 (*Z*-isomer), 133.9 (*Z*-isomer), 129.8 (*Z*-isomer), 129.7 (*E*-isomer), 128.6 (*Z*-isomer), 128.6 (*E*-isomer), 117.3 (*E*-isomer), 116.5 (*Z*-isomer), 60.3 (*E*-isomer), 55.0 (*Z*-isomer), 21.8 (*E*/*Z*-isomer), 18.3 (*E*-isomer), 12.9 (*Z*-isomer). IR (**23d´**, neat): 3064, 3030, 2986, 2937, 2878, 1640, 1595, 1495, 1454, 1312, 1230, 1144, 1021, 932, 865, 816, 749, 667 cm^{-1}. IR (*E*/*Z*-mixture **23d**, neat): 3034, 2971, 2922, 1670, 1595, 1495, 1446, 1402, 1290, 1238, 1170, 1141, 1088, 1044, 965, 932, 869, 816, 727, 686 cm^{-1}. HRMS (**23d´**, ESI) m/z calculated for $C_{11}H_{18}NO_2S$ ($[M+NH_4]^+$) 228.1053, found 228.1054. HRMS (***E*-23d**, ESI) m/z calculated for $C_{11}H_{18}NO_2S$ ($[M+NH_4]^+$) 228.1053, found 228.1052. HRMS (***Z*-23d**, ESI) m/z calculated for $C_{11}H_{18}NO_2S$ ($[M+NH_4]^+$) 228.1053, found 228.1053.

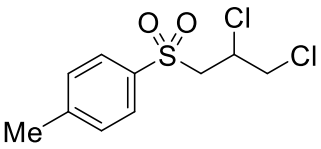
(*E*/*Z*)-1-((4-chloro-3-methylbut-2-en-1-yl)sulfonyl)-4-methylbenzene (23e) and (*E*/*Z*)-1-((4-bromo-3-methylbut-2-en-1-yl)sulfonyl)-4-methylbenzene (23e´)





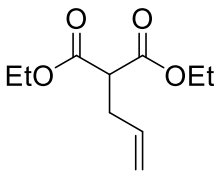
Cu(I)-catalysis: Following general procedure GP-1, using 4-methylbenzenesulfonyl chloride (**19a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 1-bromo-3-methylbut-2-ene (**18e**) (365 µL, 447 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 59 mg (195-228 µmol, 39-46%) of an inseparable mixture of (*E*/*Z*)-1-((4-chloro-3-methylbut-2-en-1-yl)sulfonyl)-4-methylbenzene (**23e**) and (*E*/*Z*)-1-((4-bromo-3-methylbut-2-en-1-yl)sulfonyl)-4-methylbenzene (**23e´**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc 4:1) = 0.30. Staining: $KMnO_4$ (UV active). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 – 7.69 (*E*/*Z*-isomers, m, 2H), 7.36 – 7.31 (*E*/*Z*-isomers, m, 2H), 5.65 – 5.55 (*Z*-isomers, m, 1H), 5.44 – 5.35 (*E*-isomers, m, 1H), 3.88 (*Z*-isomers, s, 2H), 3.87 (*E*-isomers, s, 1H), 3.84 (*E*-isomers, s, 1H), 3.79 (*Z*-isomers, d, *J* = 8.0 Hz, 2H), 3.74 (*E*-isomers, s, 2H), 2.44 (*E*/*Z*-isomers, s, 3H), 1.84 (*E*-isomers, d, *J* = 1.5 Hz, 3H), 1.47 – 1.43 (*Z*-isomers, m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 141.6, 135.3, 130.5, 130.4, 130.0, 129.9, 128.6, 128.6, 116.6, 65.8, 56.2, 39.0, 27.0, 21.8, 16.9, 15.0. IR (neat): 3060, 3023, 2986, 2937, 1651, 1595, 1491, 1446, 1409, 1286, 1204, 1148, 1085, 1036, 902, 820, 731, 671 cm^{-1}. HRMS (Cl-Product, APCI) m/z calculated for $C_{12}H_{19}ClNO_2S$ ($[M+NH_4]^+$) 276.0820, found 276.0824. HRMS (*E*-isomer Br-Product, APCI) m/z calculated for $C_{12}H_{19}BrNO_2S$ ($[M+NH_4]^+$) 320.0314, found 320.0320. HRMS (*Z*-isomer Br-Product, APCI) m/z calculated for $C_{12}H_{19}BrNO_2S$ ($[M+NH_4]^+$) 320.0314, found 320.0317.

1-((2,3-Dichloropropyl)sulfonyl)-4-methylbenzene (24)



Cu(I)-catalysis: Following general procedure GP-1, using 4-methylbenzenesulfonyl chloride (**19a**) (95 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-chloroprop-1-ene (**18a**) (246 µL, 230 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 17 mg (86 µmol, 17%) of 1-(allylsulfonyl)-4-methylbenzene (**20a**) and 75 mg (282 µmol, 56%) of 1-((2,3-dichloropropyl)sulfonyl)-4-methylbenzene (**24**) as colorless oils after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc 9:1) = 0.40. Staining: $KMnO_4$ (UV active). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 4.53 (qd, *J* = 6.2, 4.6 Hz, 1H), 3.95 (dd, *J* = 11.9, 4.6 Hz, 1H), 3.86 – 3.74 (m, 2H), 3.49 (dd, *J* = 14.7, 6.4 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.7, 136.2, 130.3, 128.3, 60.3, 52.8, 47.9, 21.8. IR (neat): 3015, 2978, 2922, 1595, 1495, 1431, 1394, 1349, 1282, 1238, 1189, 1137, 1036, 977, 924, 861, 813, 708 cm^{-1}. HRMS (APCI) m/z calculated for $C_{10}H_{16}Cl_2NO_2S$ ($[M+NH_4]^+$) 284.0273, found 284.0278.

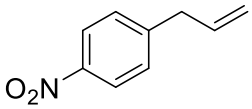
Diethyl 2-allylmalonate (40)



Cu(I)-catalysis: Following general procedure GP-1, using diethyl 2-bromomalonate (**38**) (120 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 105 mg (376 µmol, 75%) of diethyl 2-allyl-2-bromomalonate (**39**)[29] and 11 mg (55 µmol, 11%) of diethyl 2-allylmalonate (**40**) as colorless oils after flash column purification (hexanes / EtOAc 9:1 to 4:1).

Ir(III)-catalysis: Following general procedure GP-1, using diethyl 2-bromomalonate (**38**) (120 mg, 0.5 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and *fac*-$Ir(ppy)_3$ (3.3 mg, 5.0 µmol, 1.0 mol%) gave 84 mg (420 µmol, 84%) of diethyl 2-allylmalonate (**40**) as a colorless oil after flash column purification (hexanes / EtOAc 9:1 to 4:1). The ^1H NMR spectra was in accordance with the reported literature[30]. ^1H NMR (300 MHz, $CDCl_3$) δ 5.77 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.18 – 5.01 (m, 2H), 4.19 (qd, *J* = 7.2, 1.0 Hz, 4H), 3.41 (t, *J* = 7.6 Hz, 1H), 2.63 (ddt, *J* = 7.6, 6.8, 1.3 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 134.2, 117.6, 61.5, 51.8, 33.0, 14.2.

1-Allyl-4-nitrobenzene (44)



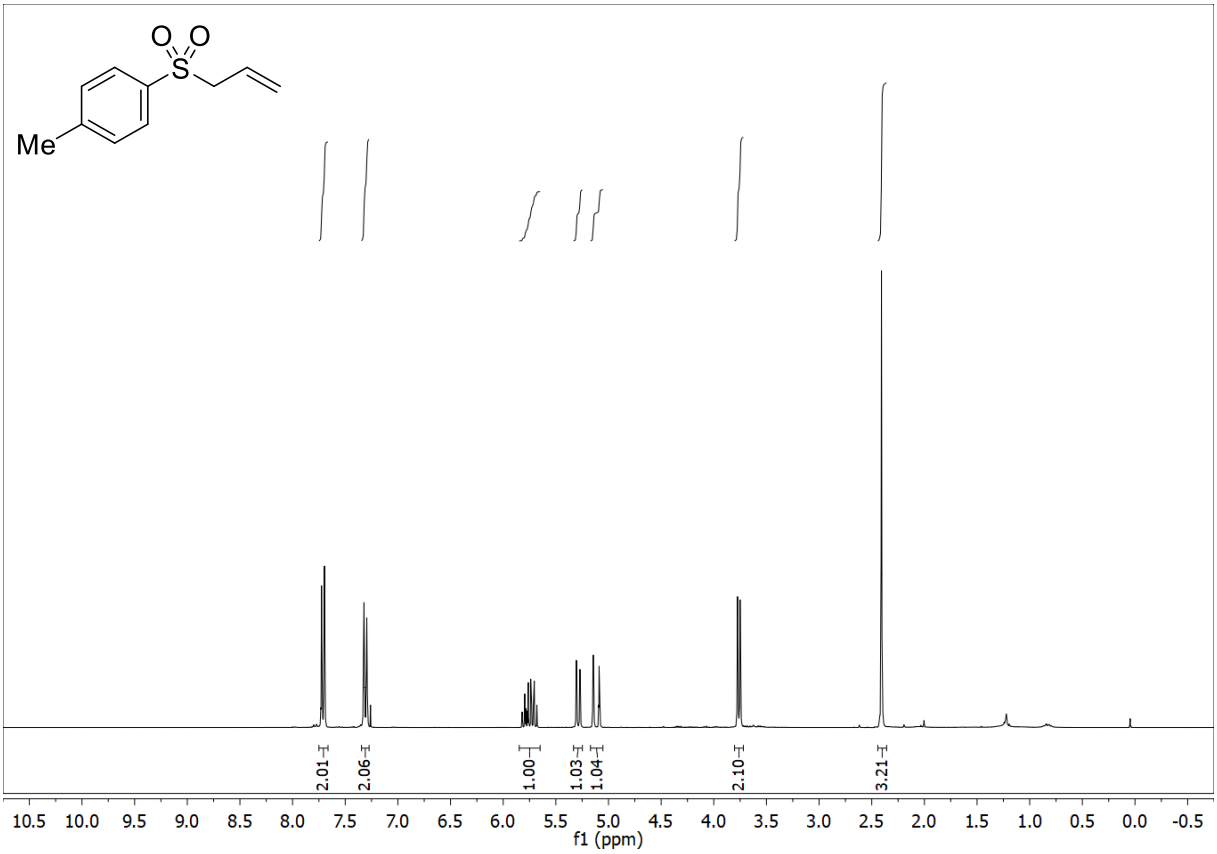
Cu(I)-catalysis: Following general procedure GP-1, using 4-nitrobenzenediazonium tetrafluoroborate (**43**) (119 mg, 0.5 mmol, 1.0 equiv), Na_2CO_3 (5.3 mg, 0.1 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and $[Cu(dap)_2]Cl$ (4.4 mg, 5.0 µmol, 1.0 mol%) gave 23 mg (141 µmol, 28%) of 1-allyl-4-nitrobenzene (**44**) as a white solid after flash column purification (hexanes / EtOAc 9:1 to 4:1).

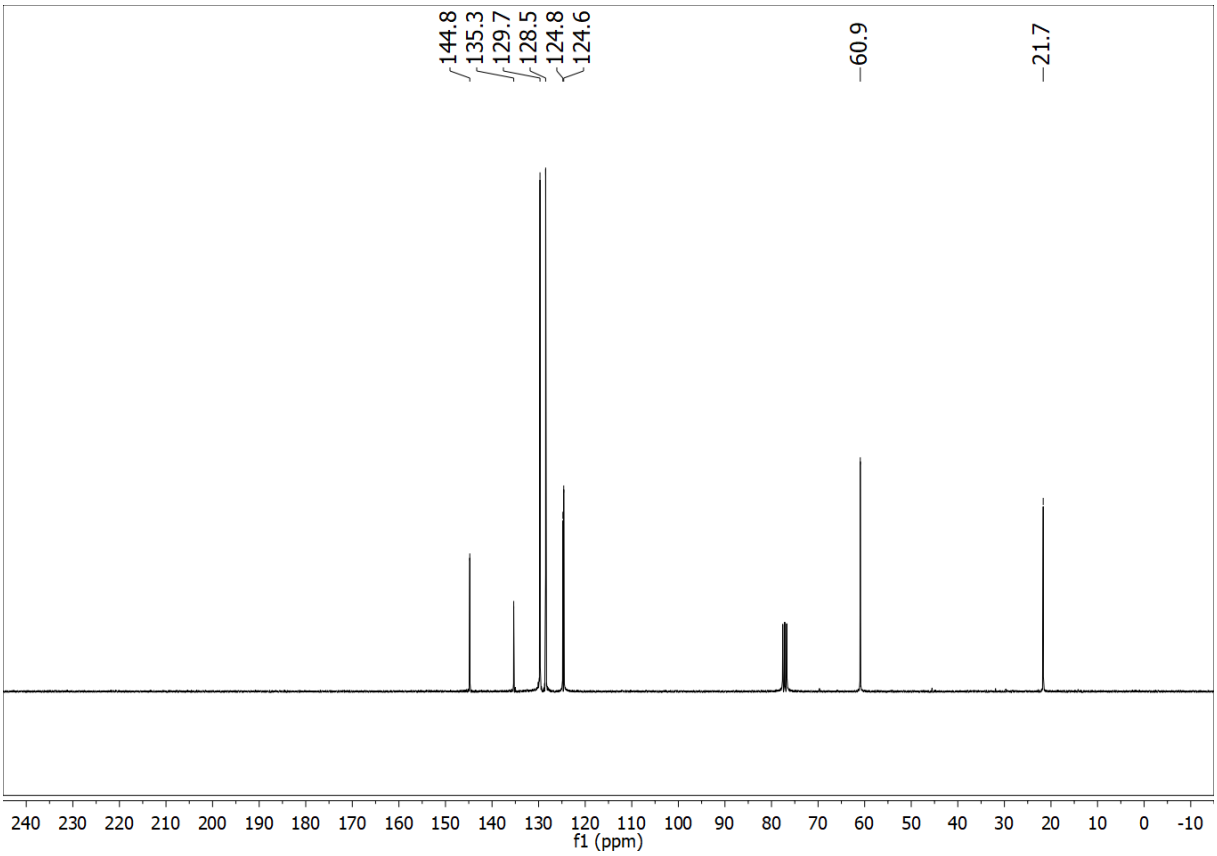
Ir(III)-catalysis: Following general procedure GP-1, using 4-nitrobenzenediazonium tetrafluoroborate (**43**) (119 mg, 0.5 mmol, 1.0 equiv), 3-bromoprop-1-ene (**18a**) (259 µL, 363 mg, 3.0 mmol, 6.0 equiv) and *fac*-$Ir(ppy)_3$ (3.3 mg, 5.0 µmol, 1.0 mol%) gave 36 mg (221 µmol, 44%) of 1-allyl-4-nitrobenzene (**44**) as a white solid after flash column purification (hexanes / EtOAc 9:1 to 4:1). R_f (hexanes / EtOAc 4:1) = 0.69. Staining: $KMnO_4$ (UV active). The ^1H NMR spectra was in accordance with the reported literature[31]. ^1H NMR (300 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.7 Hz, 2H), 7.35 (dt, *J* = 8.9, 0.7 Hz, 2H), 5.94 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.22 – 5.06 (m, 2H), 3.49 (d, *J* = 6.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.9, 135.6, 129.5, 123.8, 117.6, 40.1.

5.3. NMR Spectra

^{1}H NMR	first image
^{13}C NMR	second image
^{19}F NMR	third image

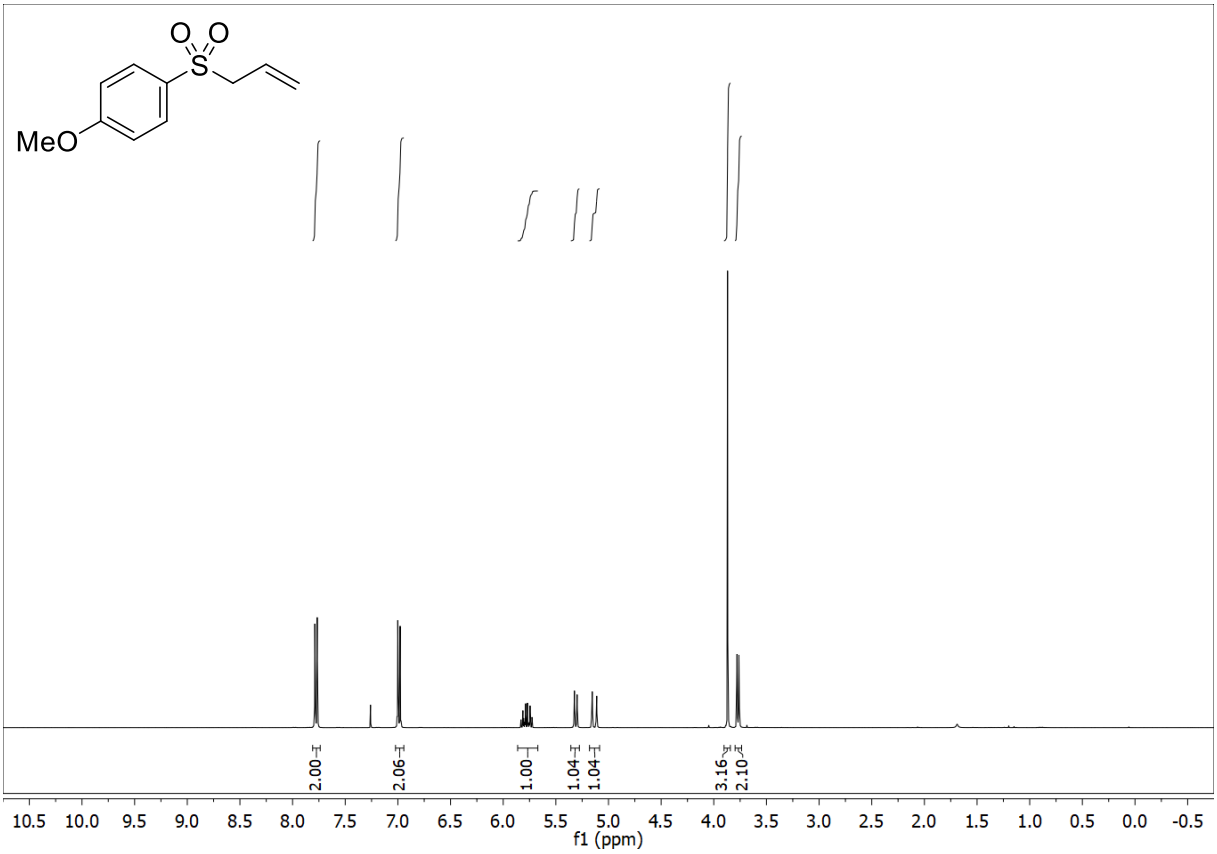
1-(Allylsulfonyl)-4-methylbenzene (20a)

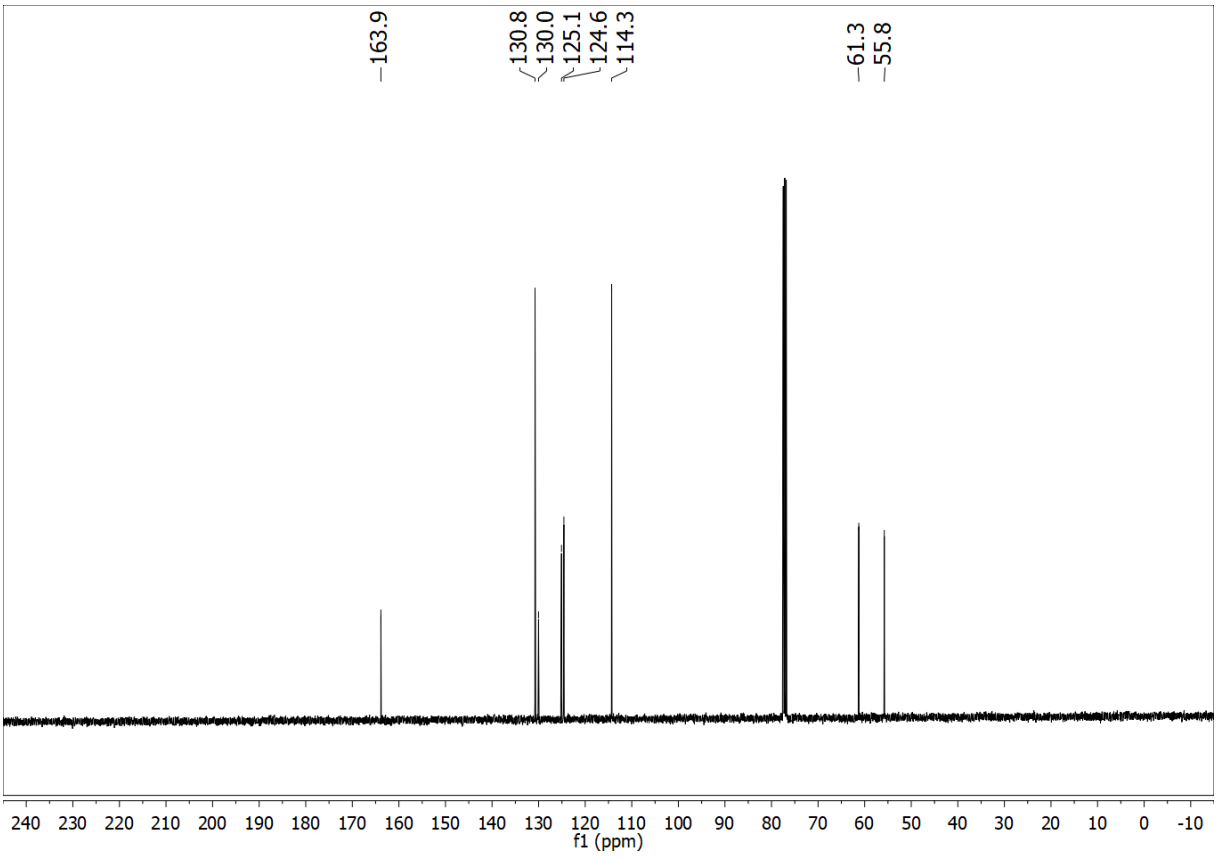




NMR-Solvent: $CDCl_3$

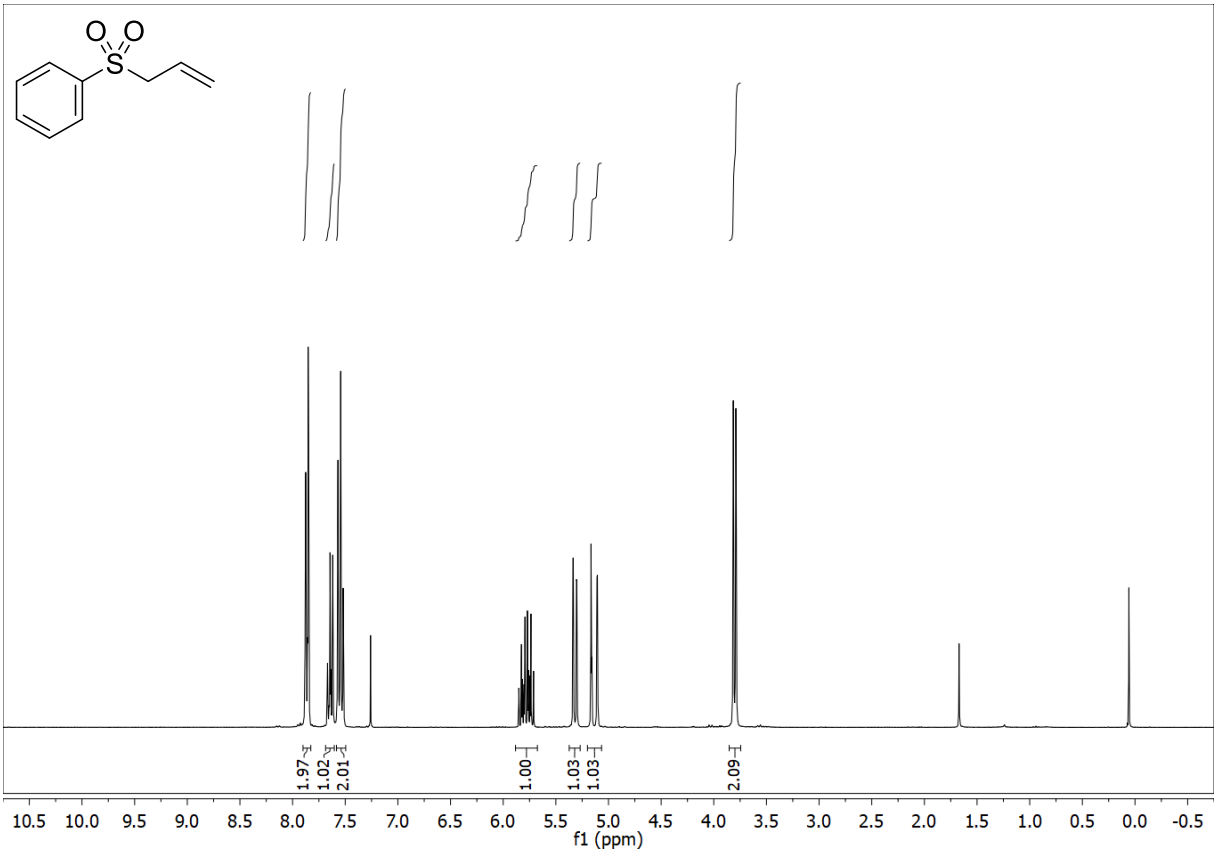
1-(Allylsulfonyl)-4-methoxybenzene (20b)

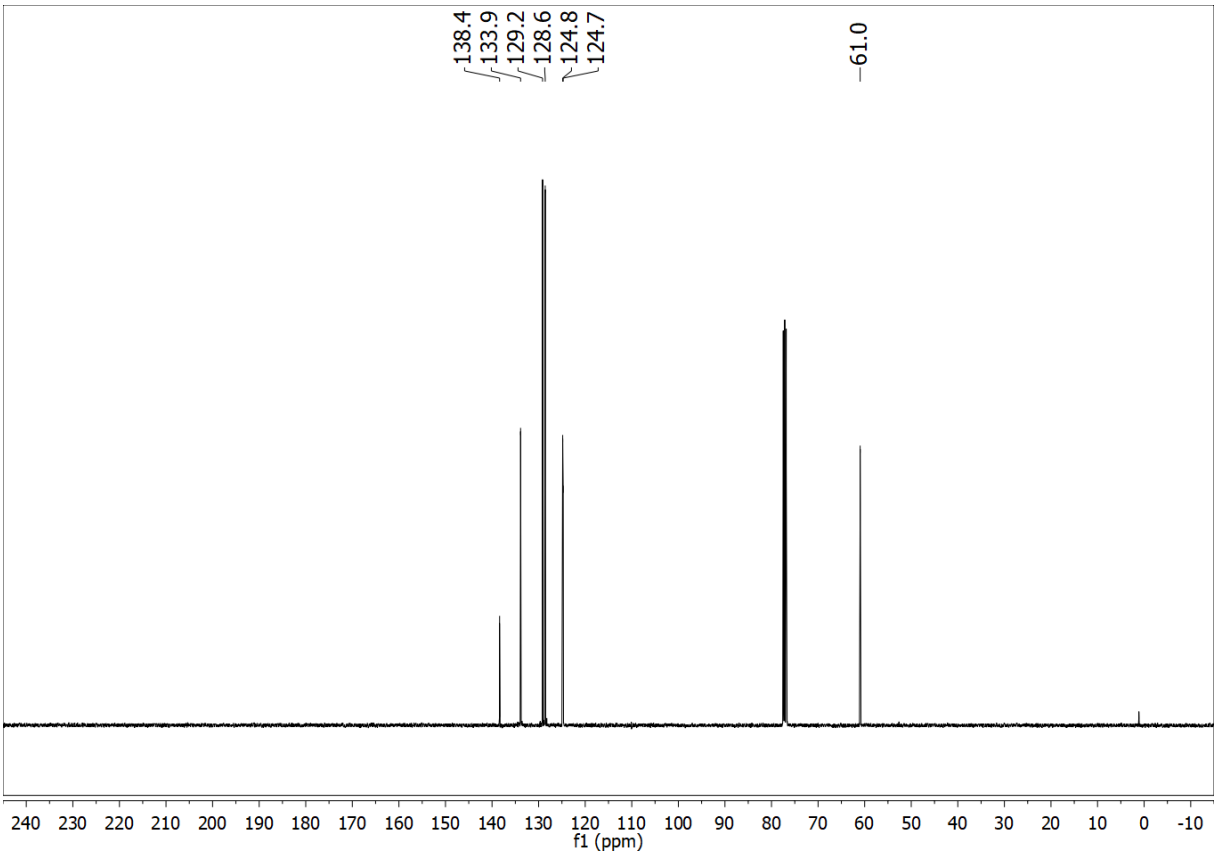




NMR-Solvent: $CDCl_3$

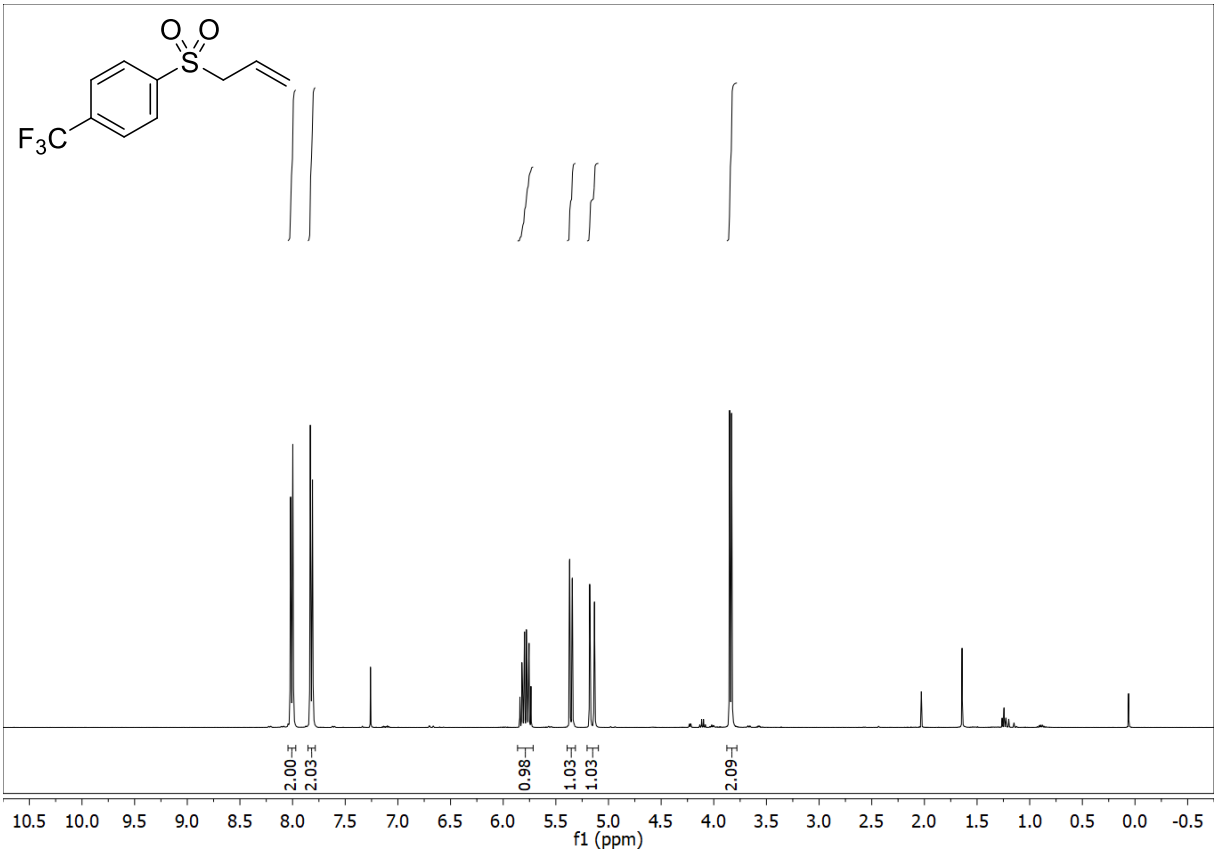
(Allylsulfonyl)benzene (20c)

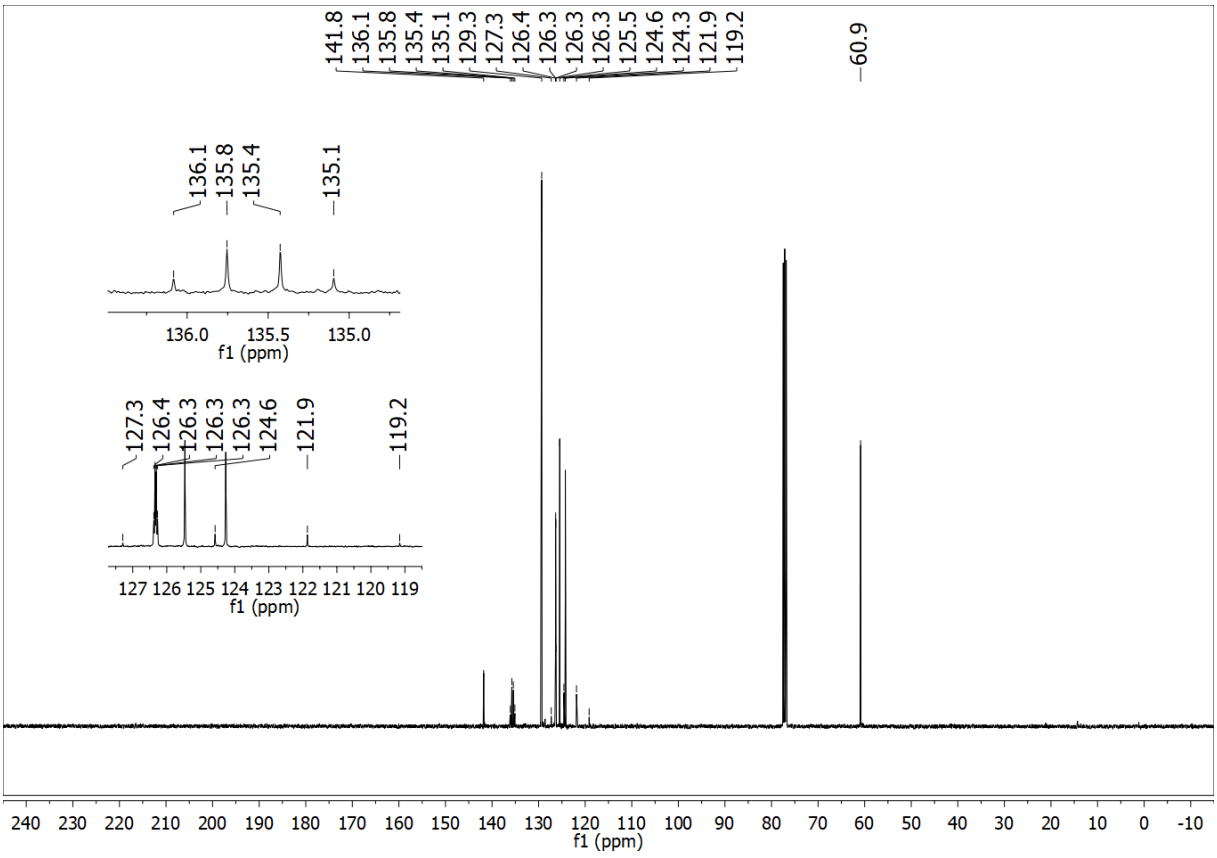


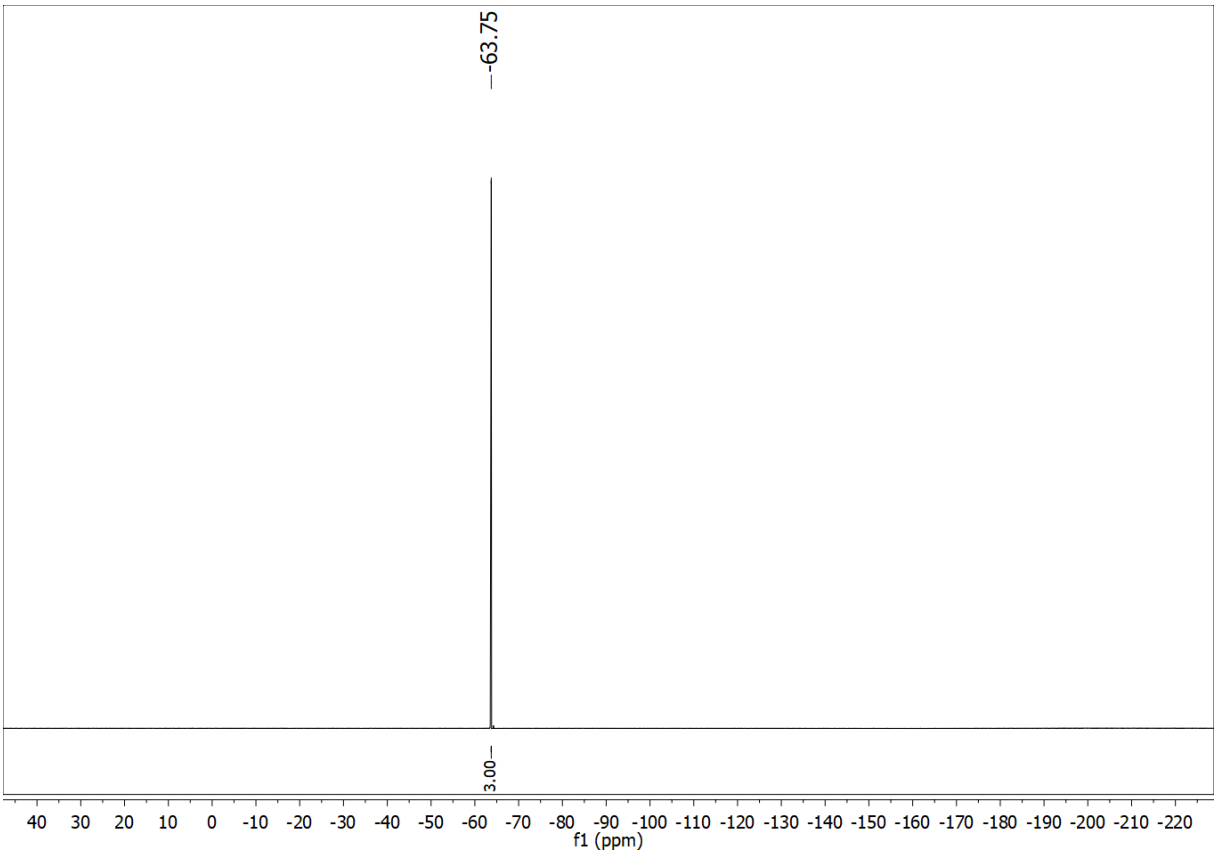


NMR-Solvent: $CDCl_3$

1-(Allylsulfonyl)-4-(trifluoromethyl)benzene (20d)

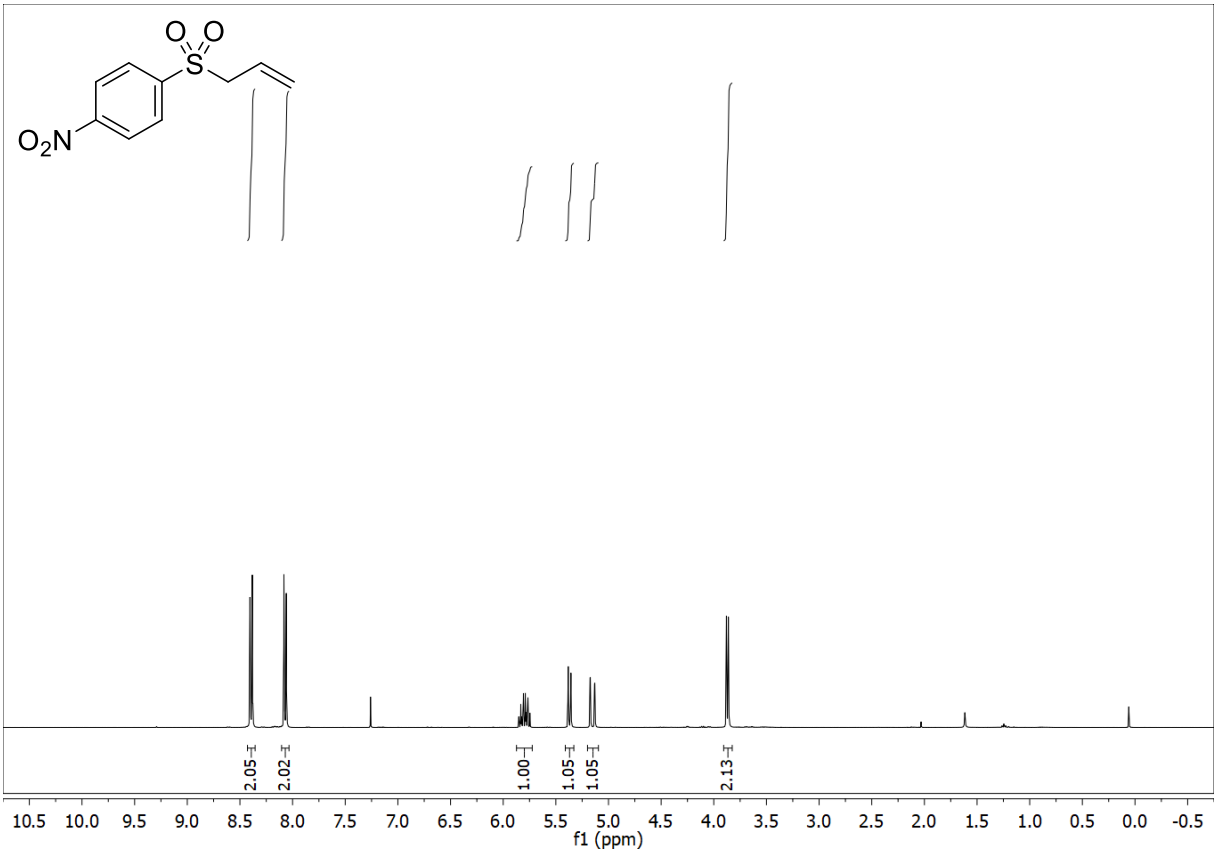


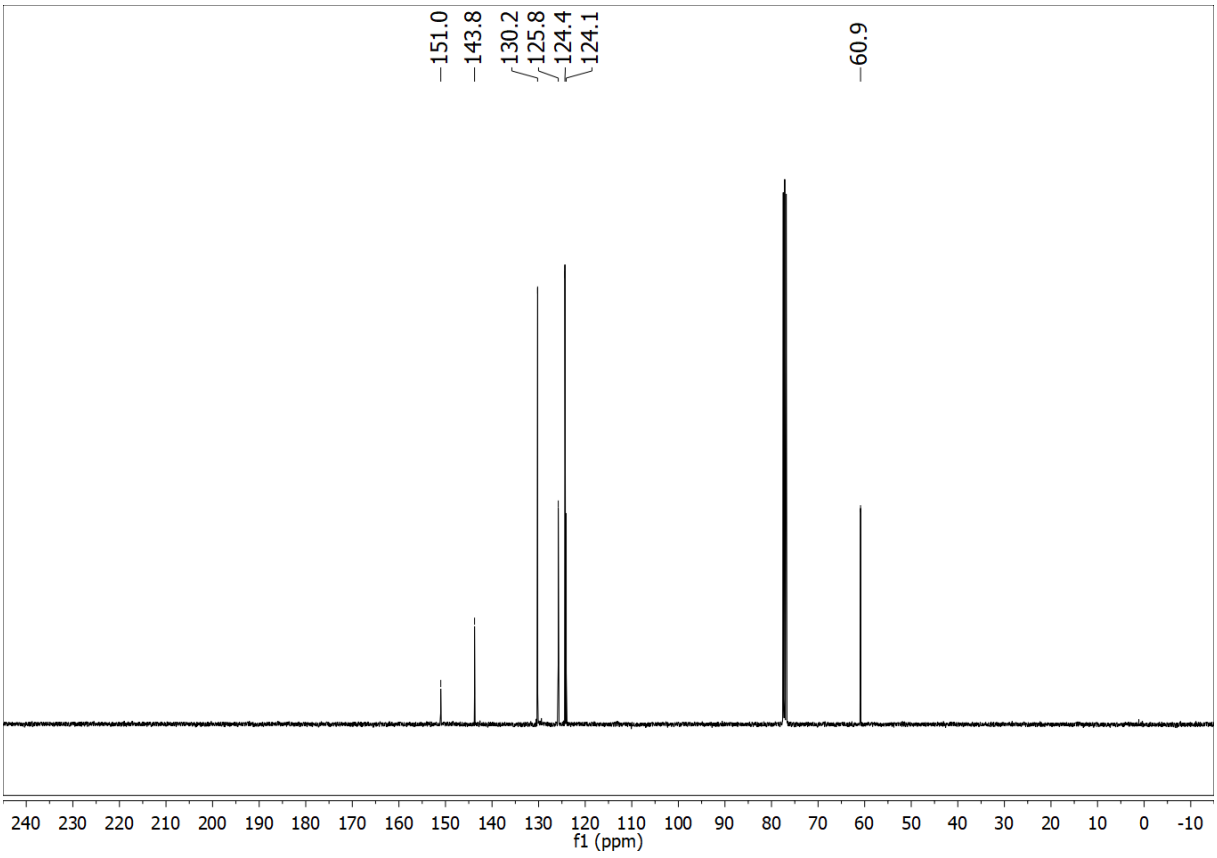




NMR-Solvent: $CDCl_3$

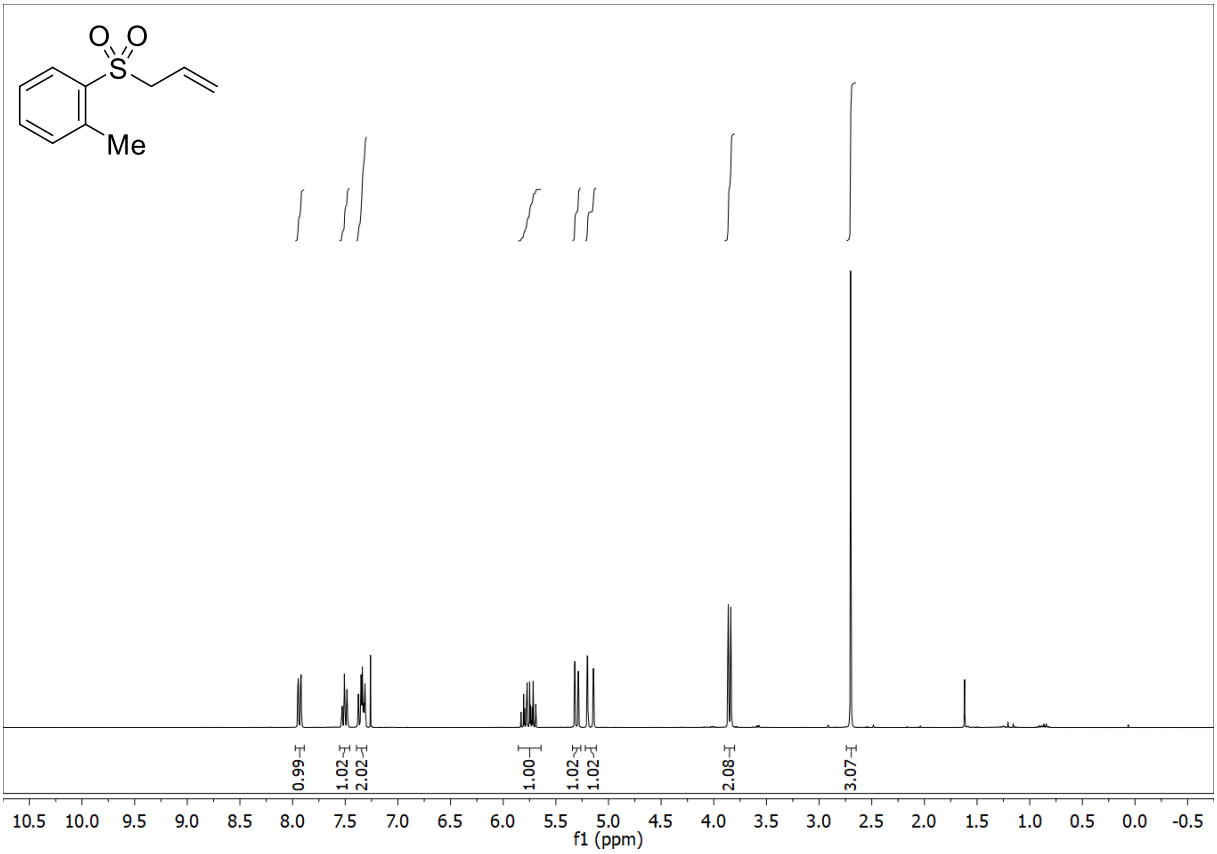
1-(Allylsulfonyl)-4-nitrobenzene (20e)

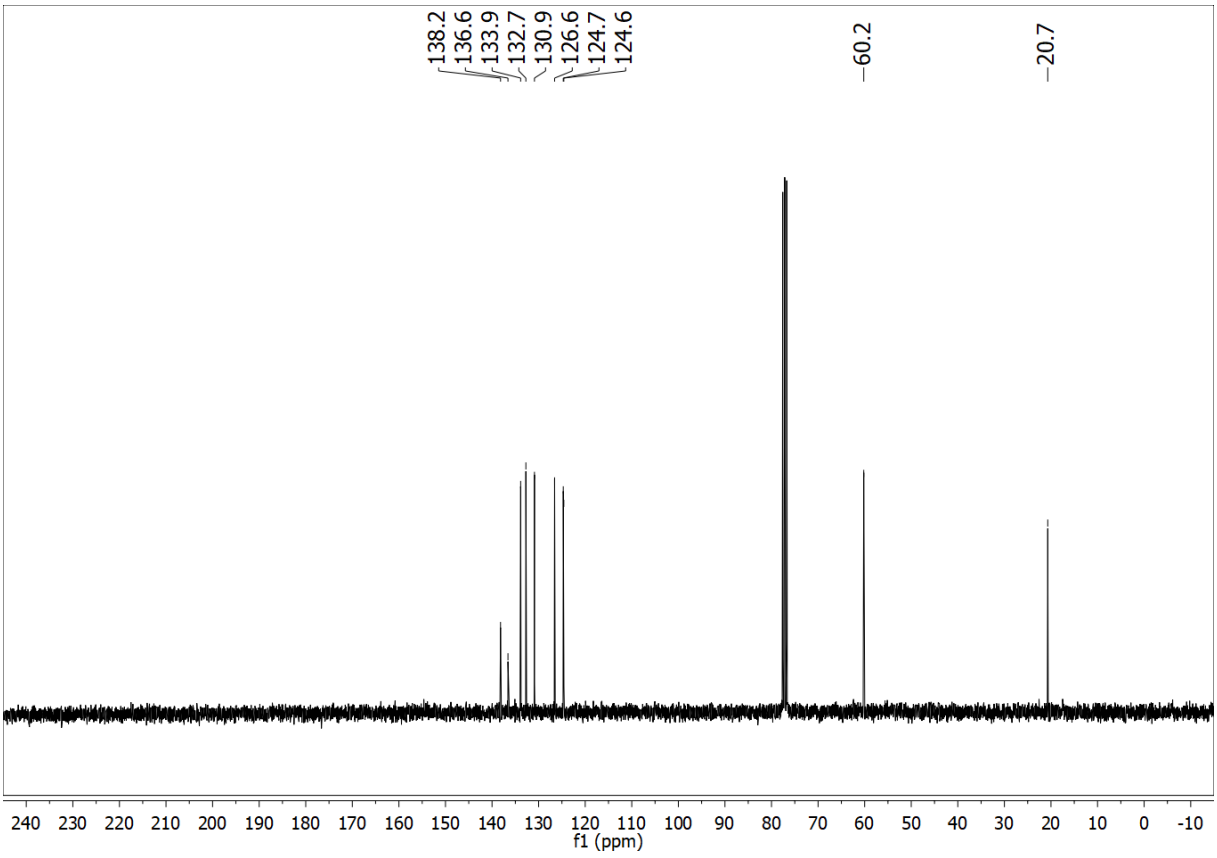




NMR-Solvent: $CDCl_3$

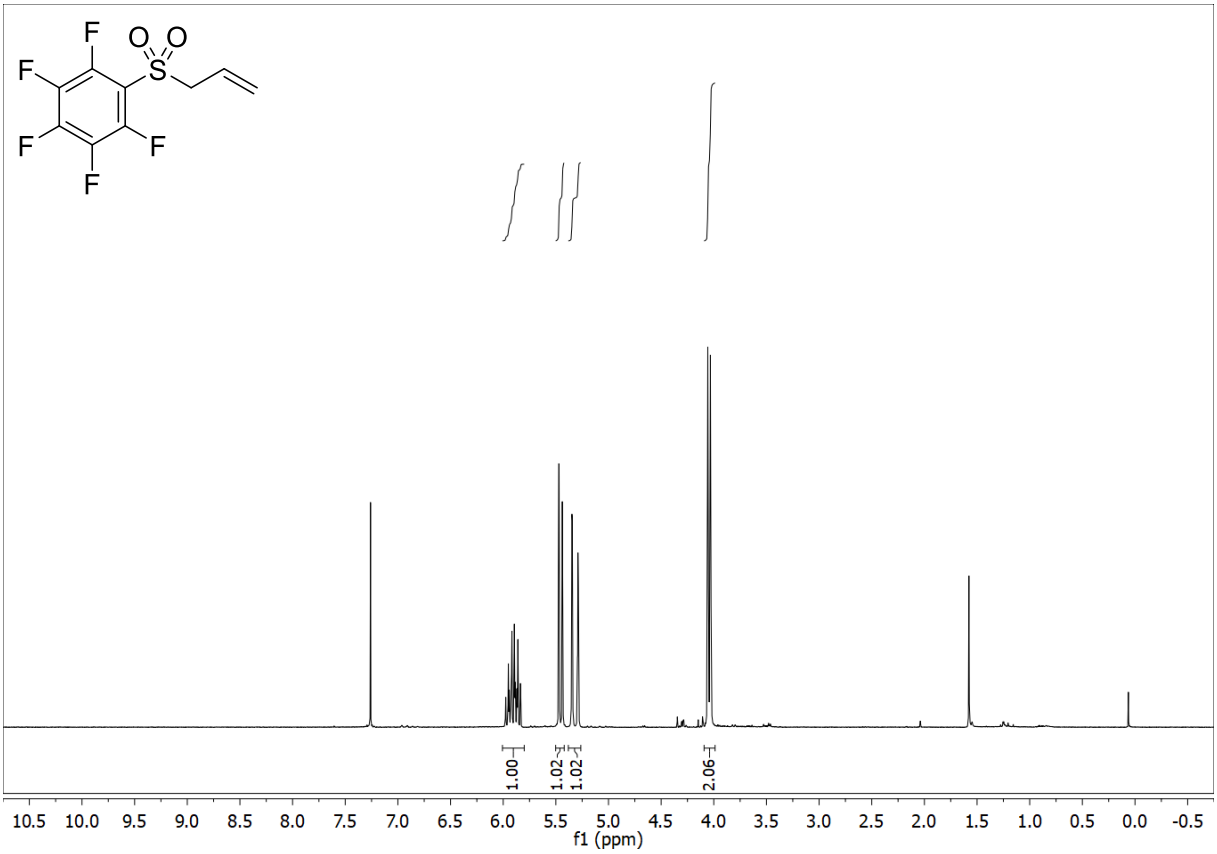
1-(Allylsulfonyl)-2-methylbenzene (20h)

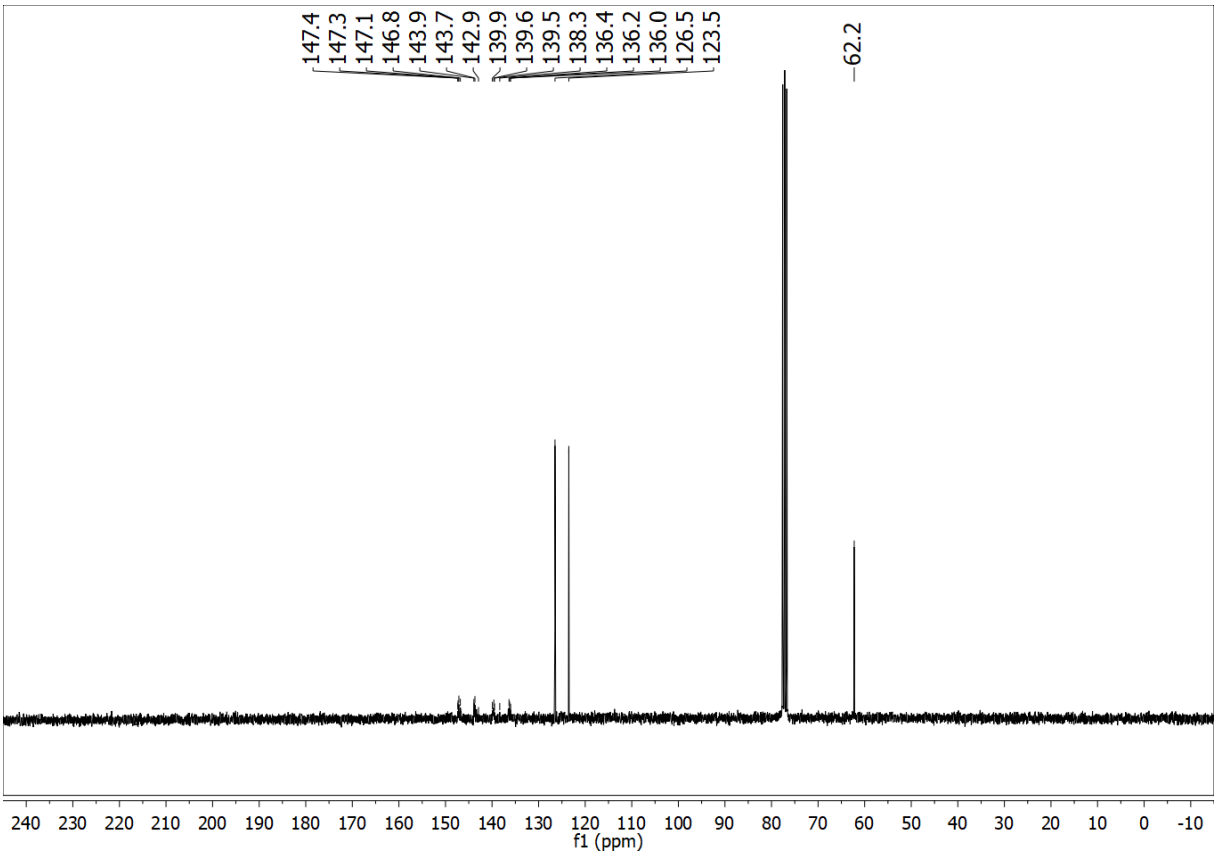


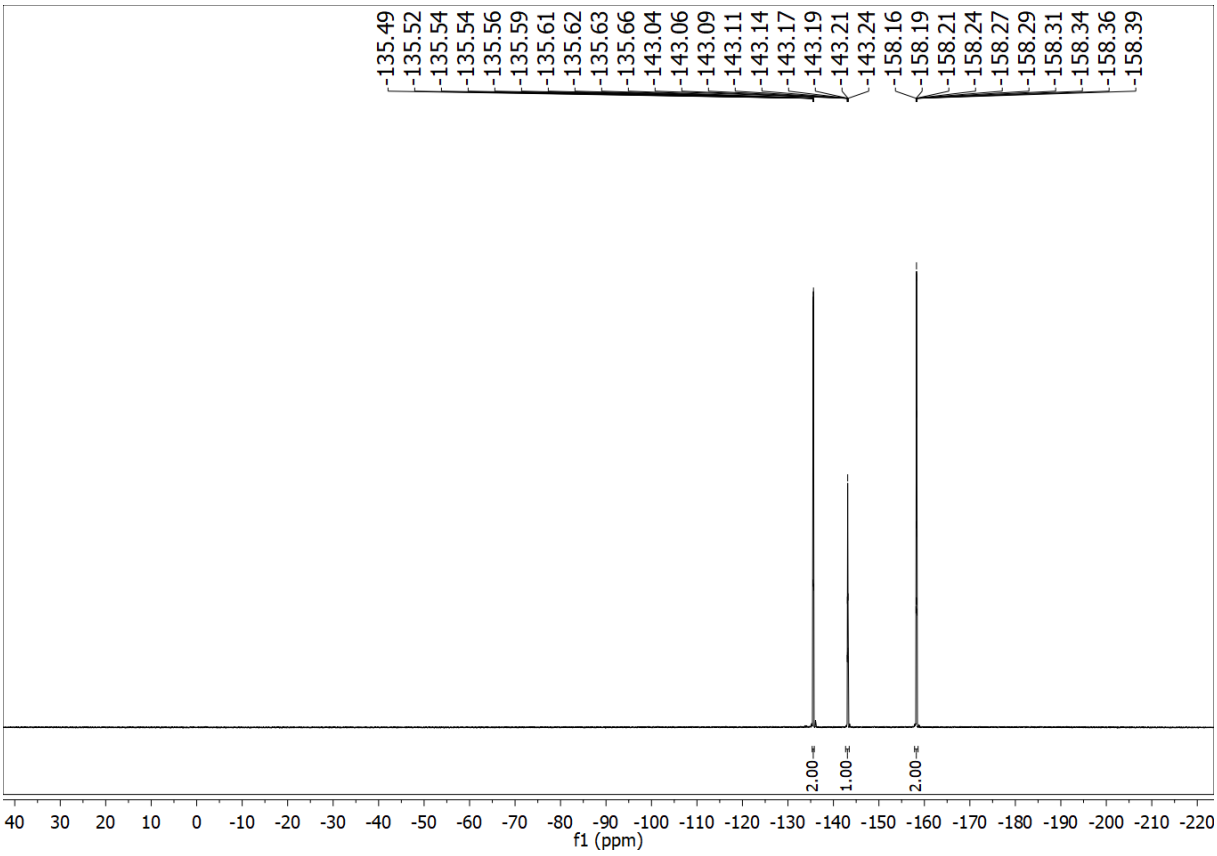


NMR-Solvent: $CDCl_3$

1-(Allylsulfonyl)-2,3,4,5,6-pentafluorobenzene (20i)

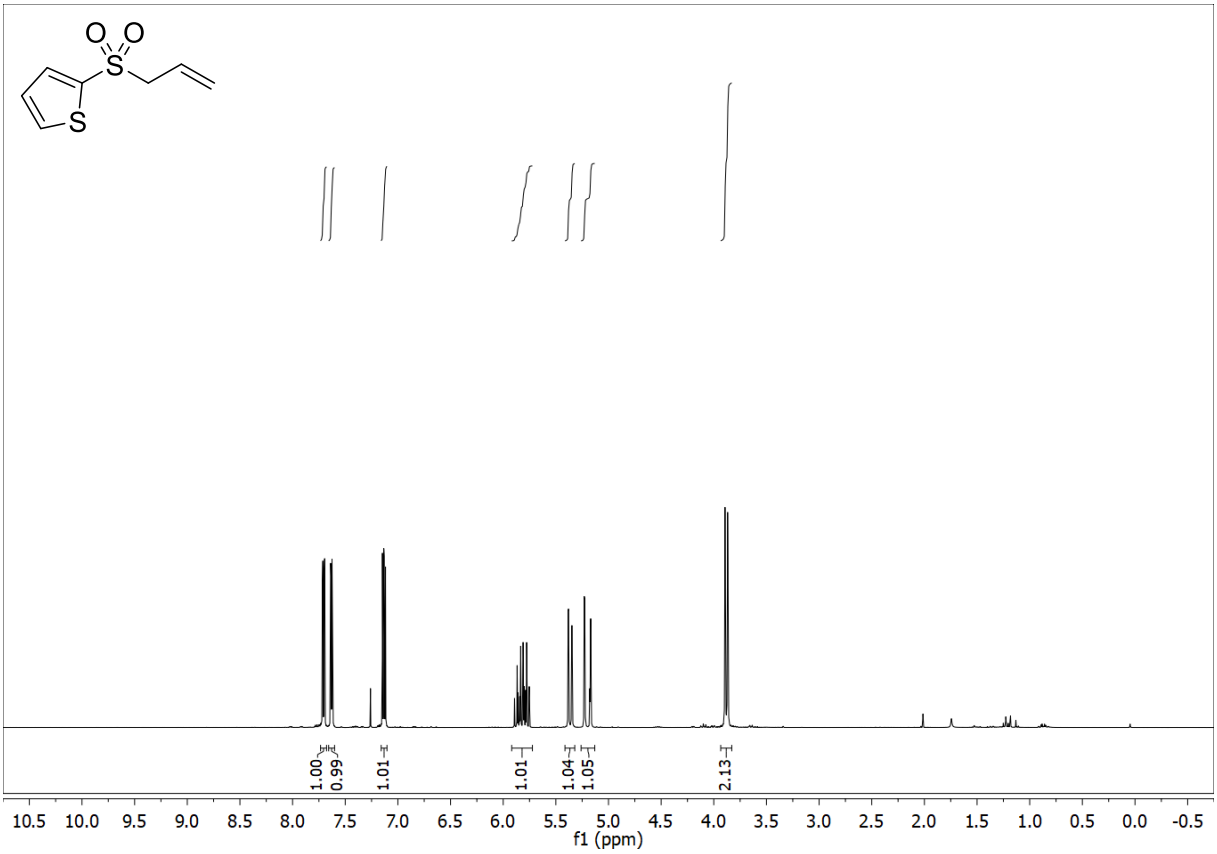


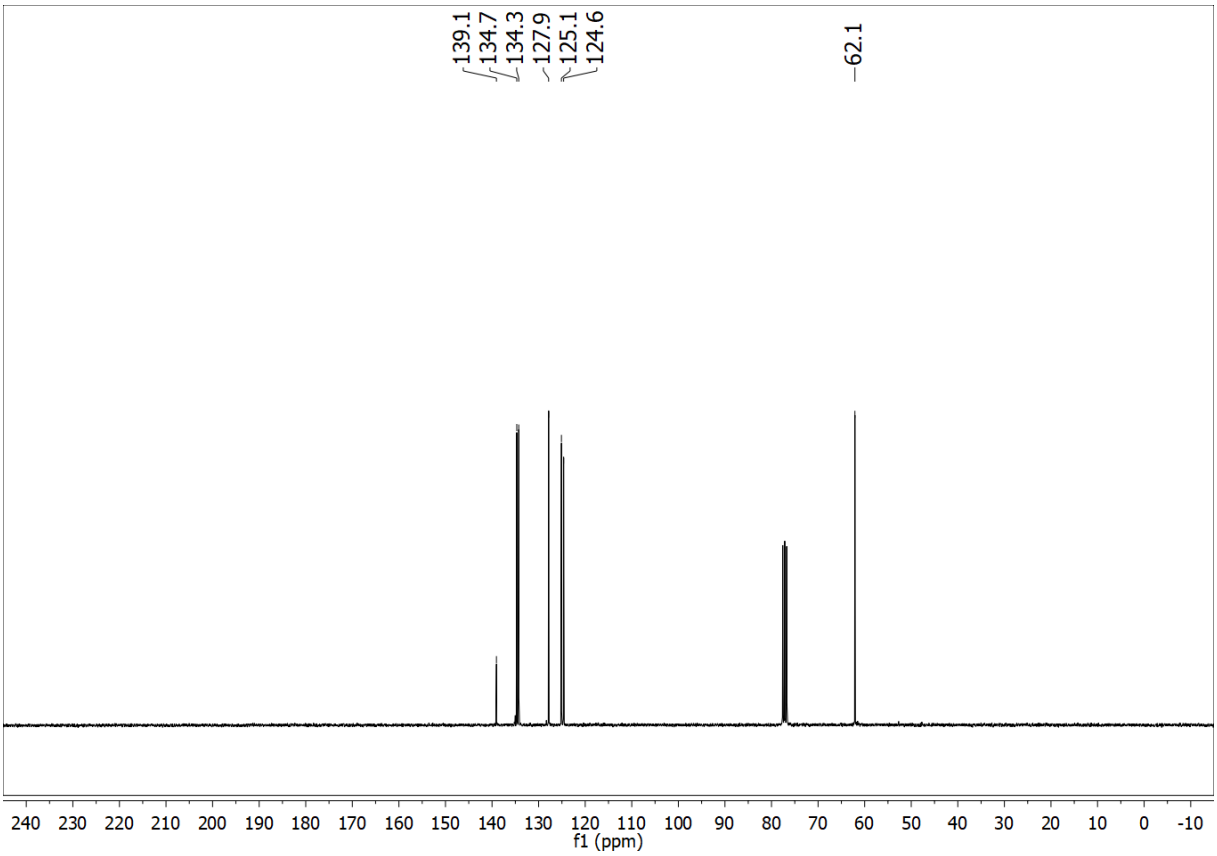




NMR-Solvent: $CDCl_3$

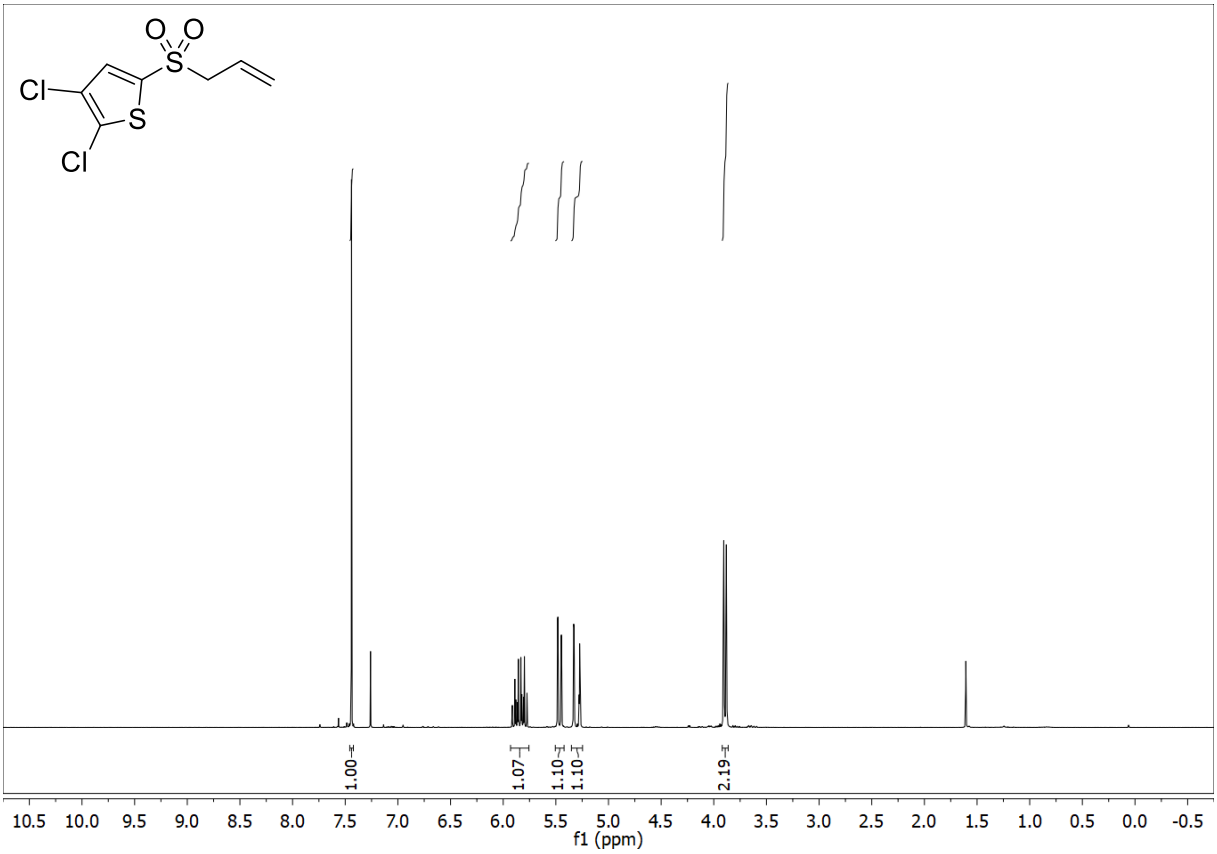
2-(Allylsulfonyl)thiophene (20j)

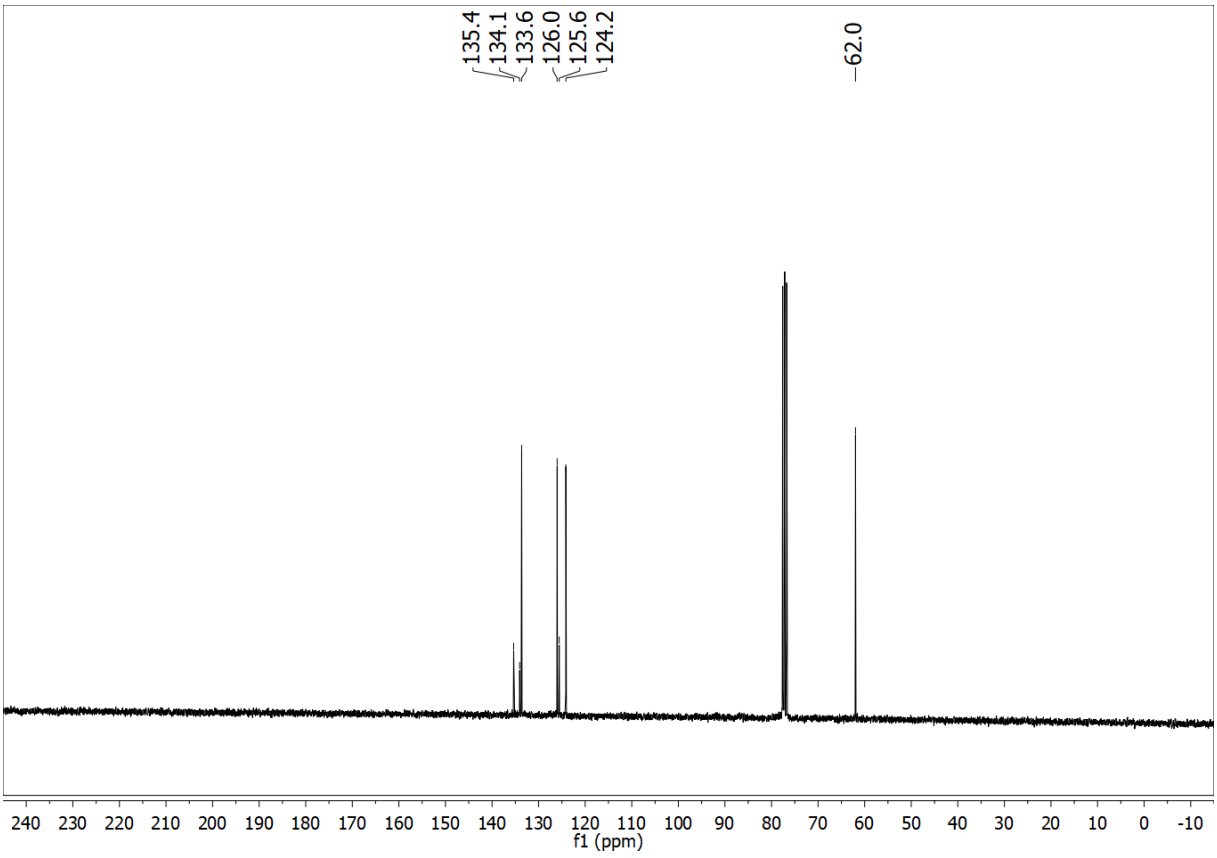




NMR-Solvent: $CDCl_3$

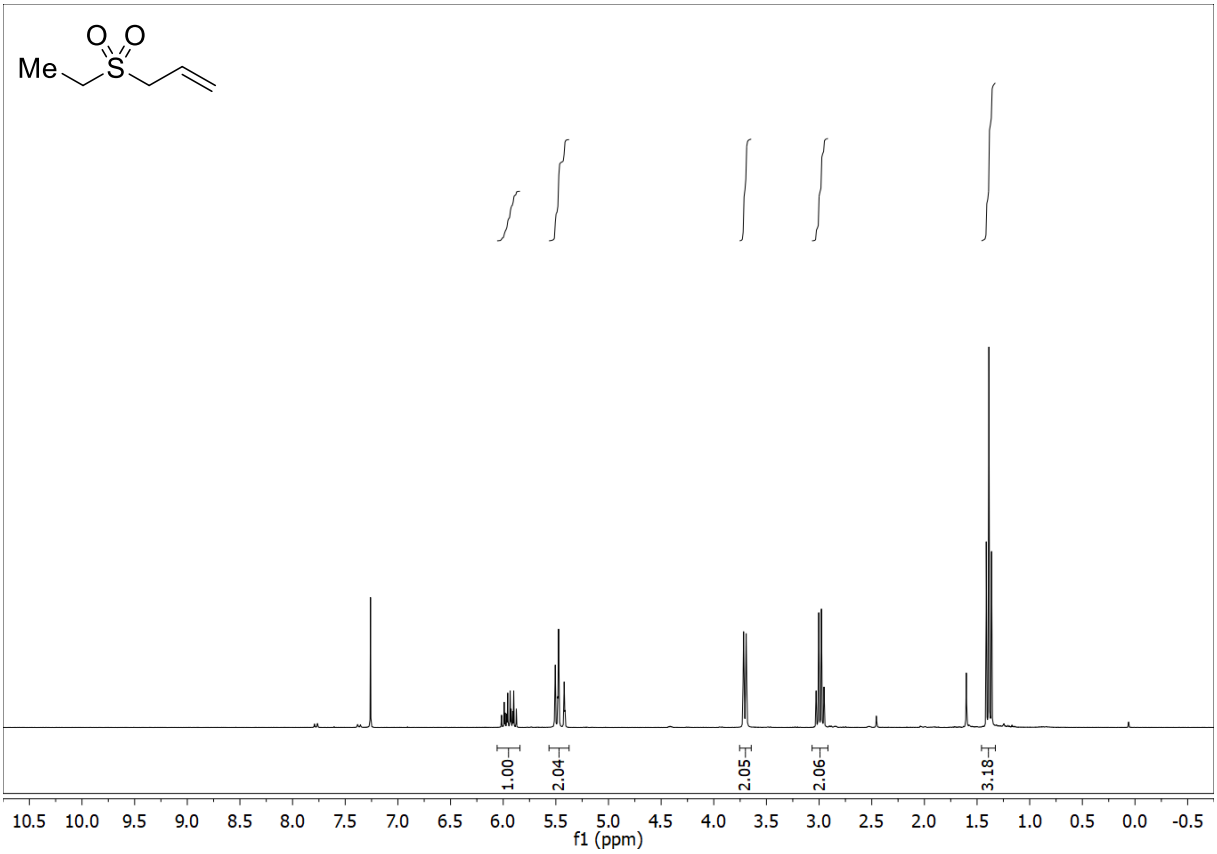
5-(Allylsulfonyl)-2,3-dichlorothiophene (20k)

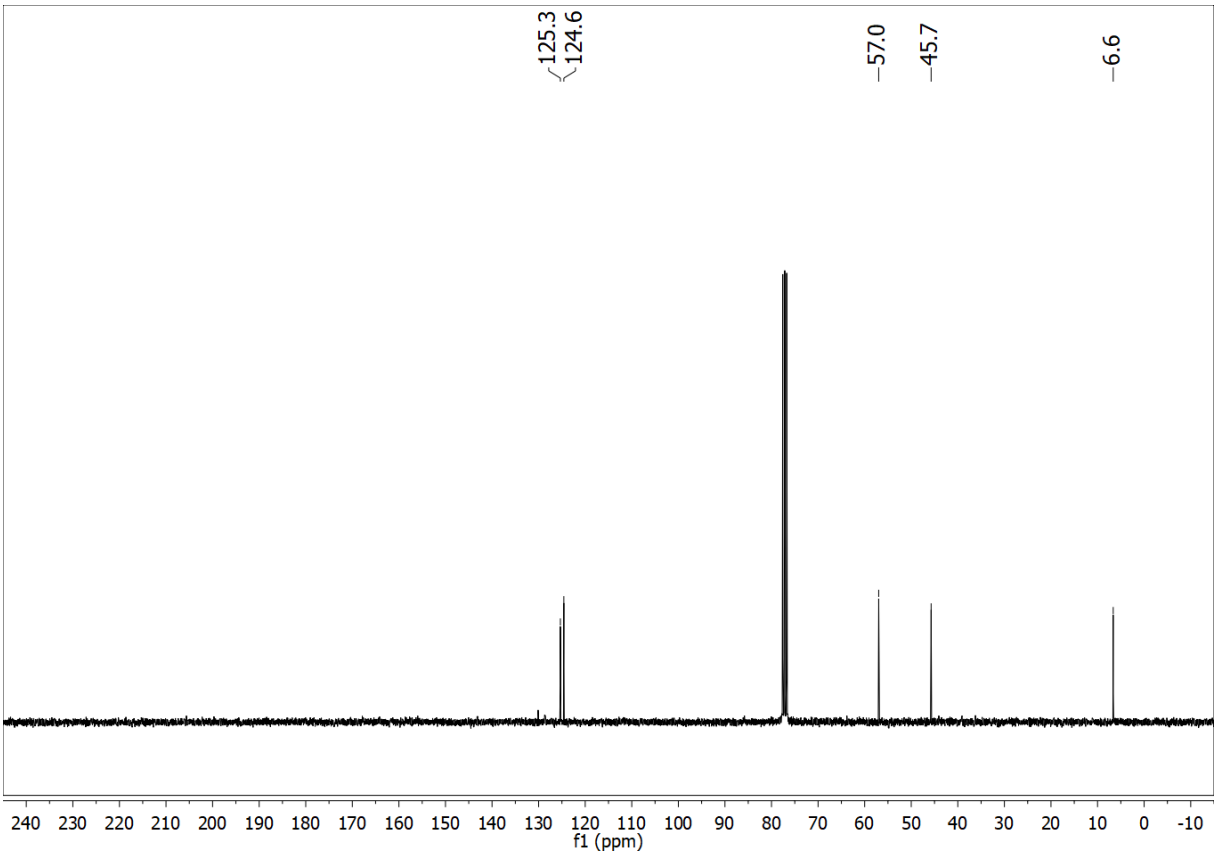




NMR-Solvent: $CDCl_3$

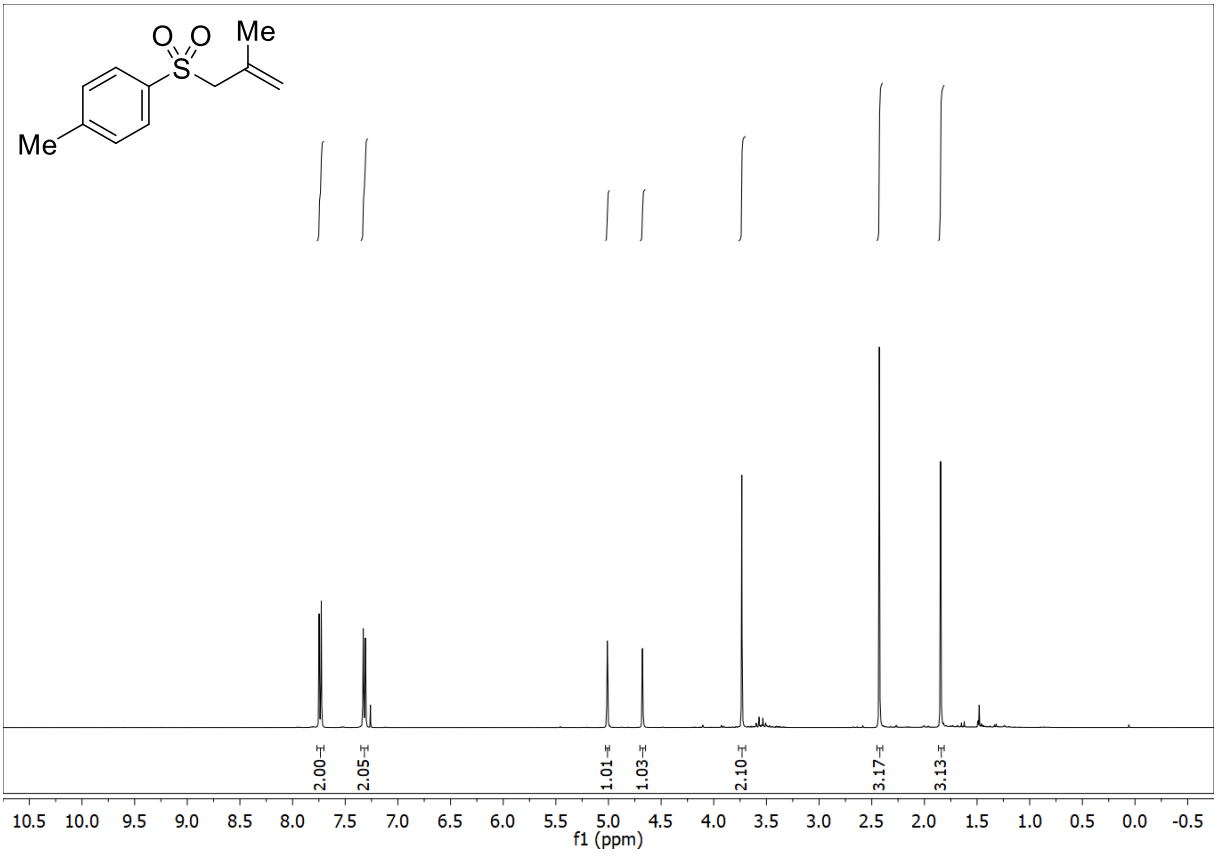
3-(Ethylsulfonyl)prop-1-ene (20l)

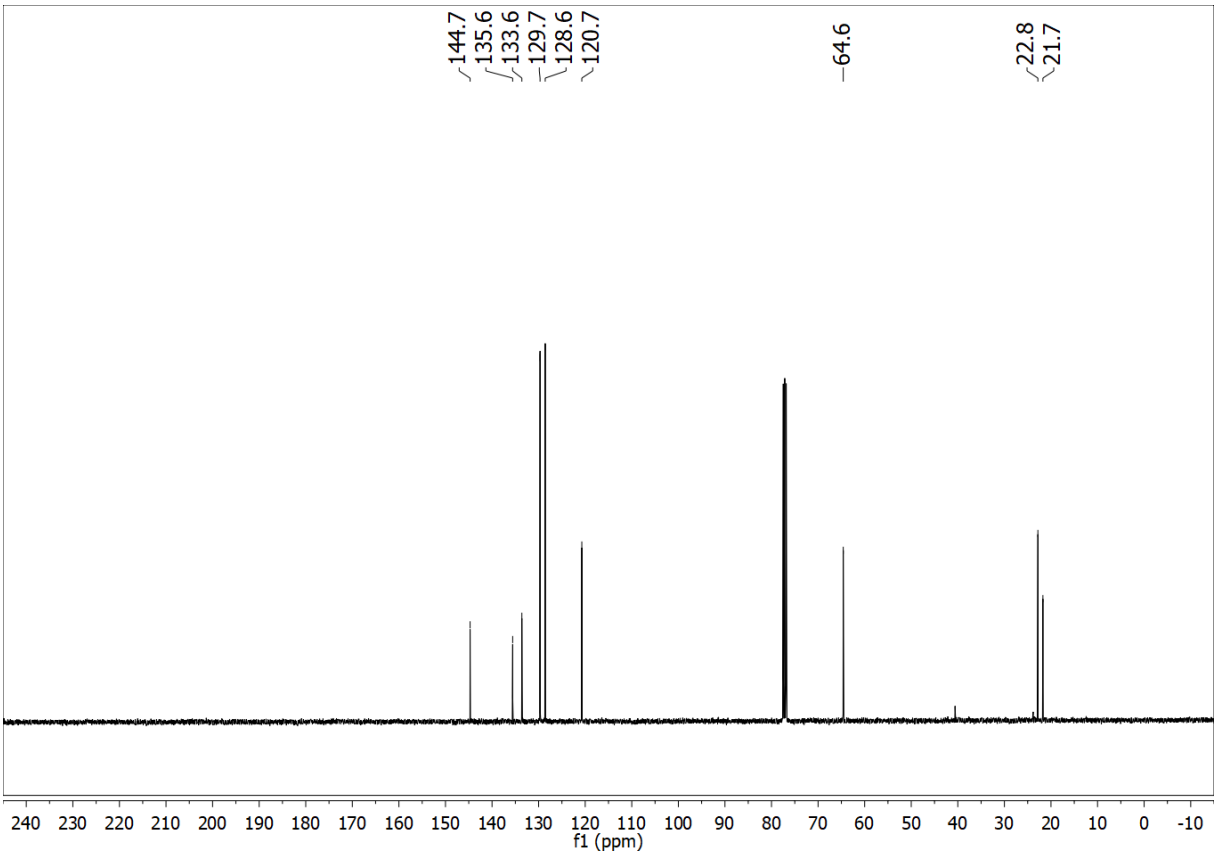




NMR-Solvent: $CDCl_3$

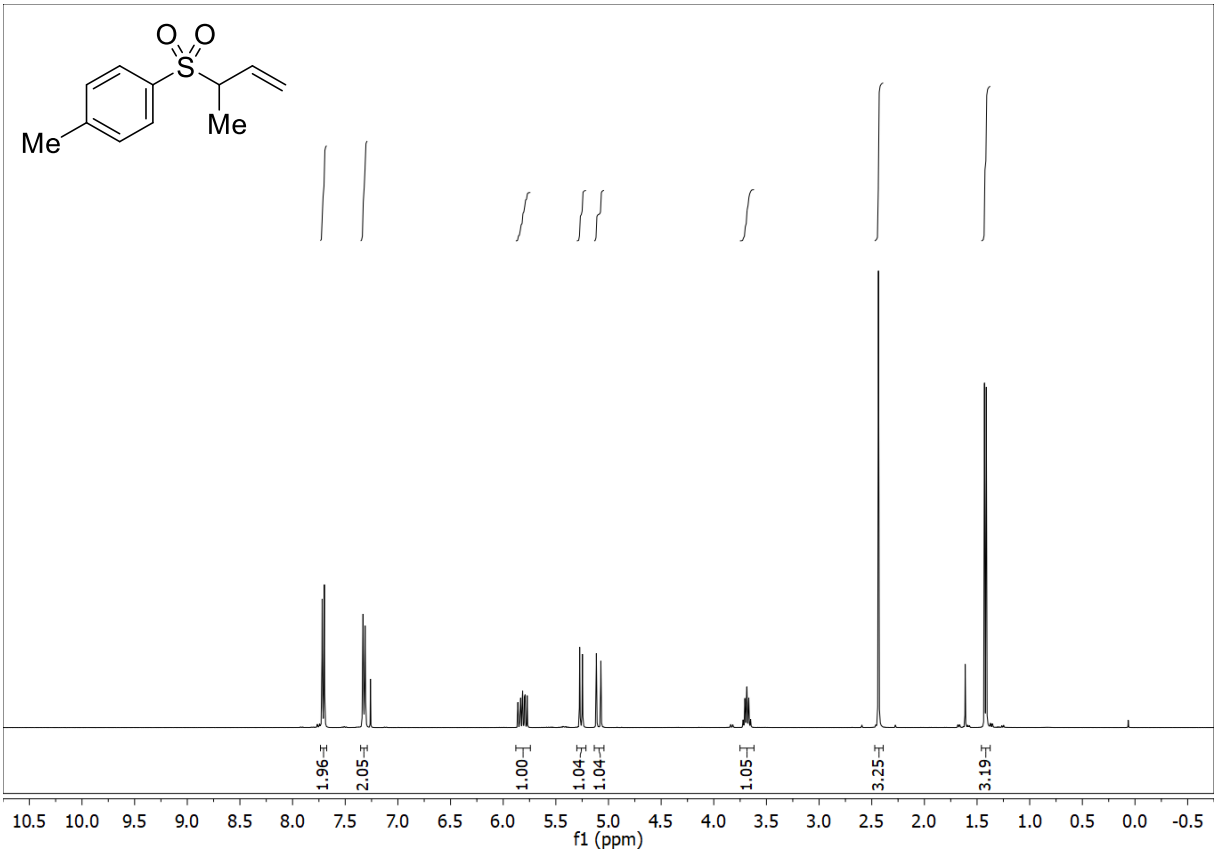
1-Methyl-4-((2-methylallyl)sulfonyl)benzene (23c)

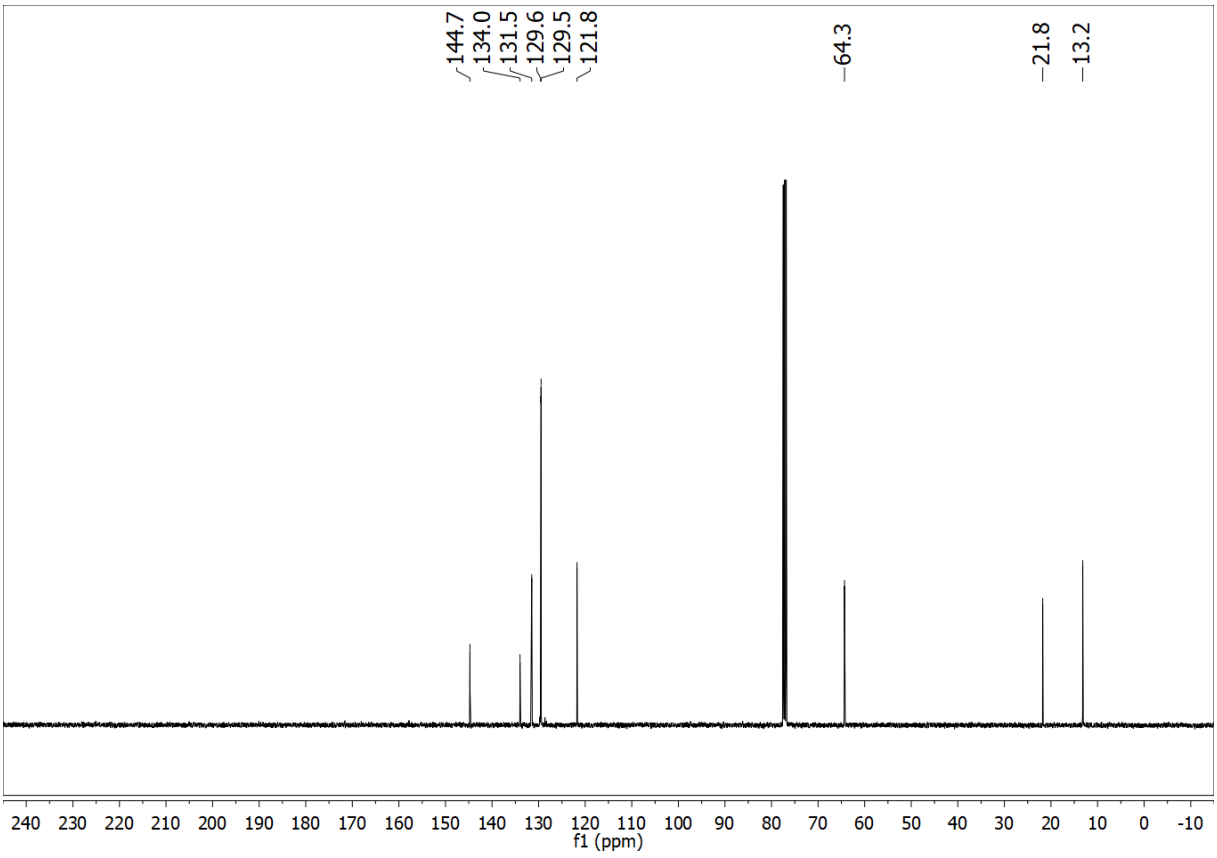




NMR-Solvent: $CDCl_3$

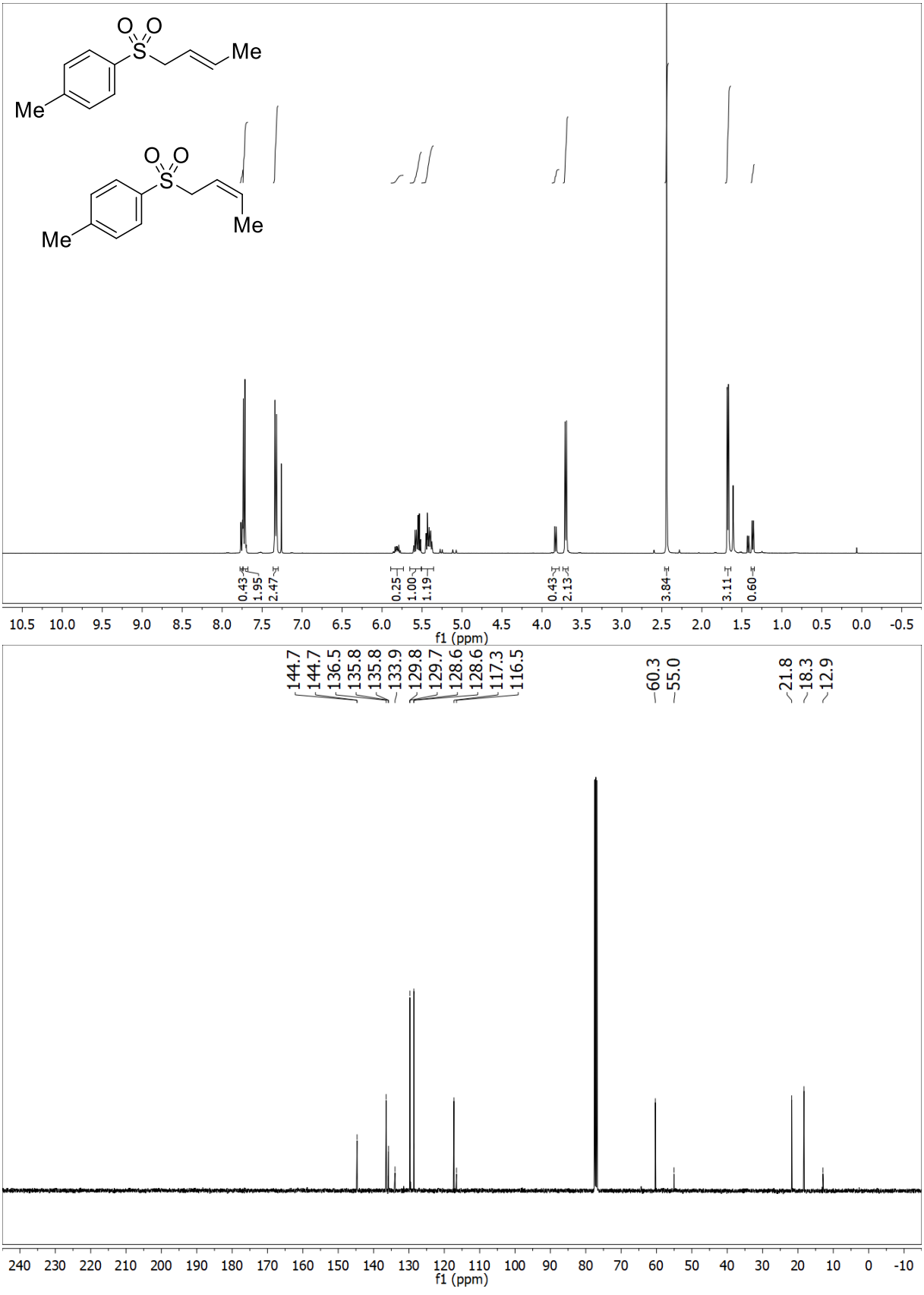
1-(But-3-en-2-ylsulfonyl)-4-methylbenzene (23d´)





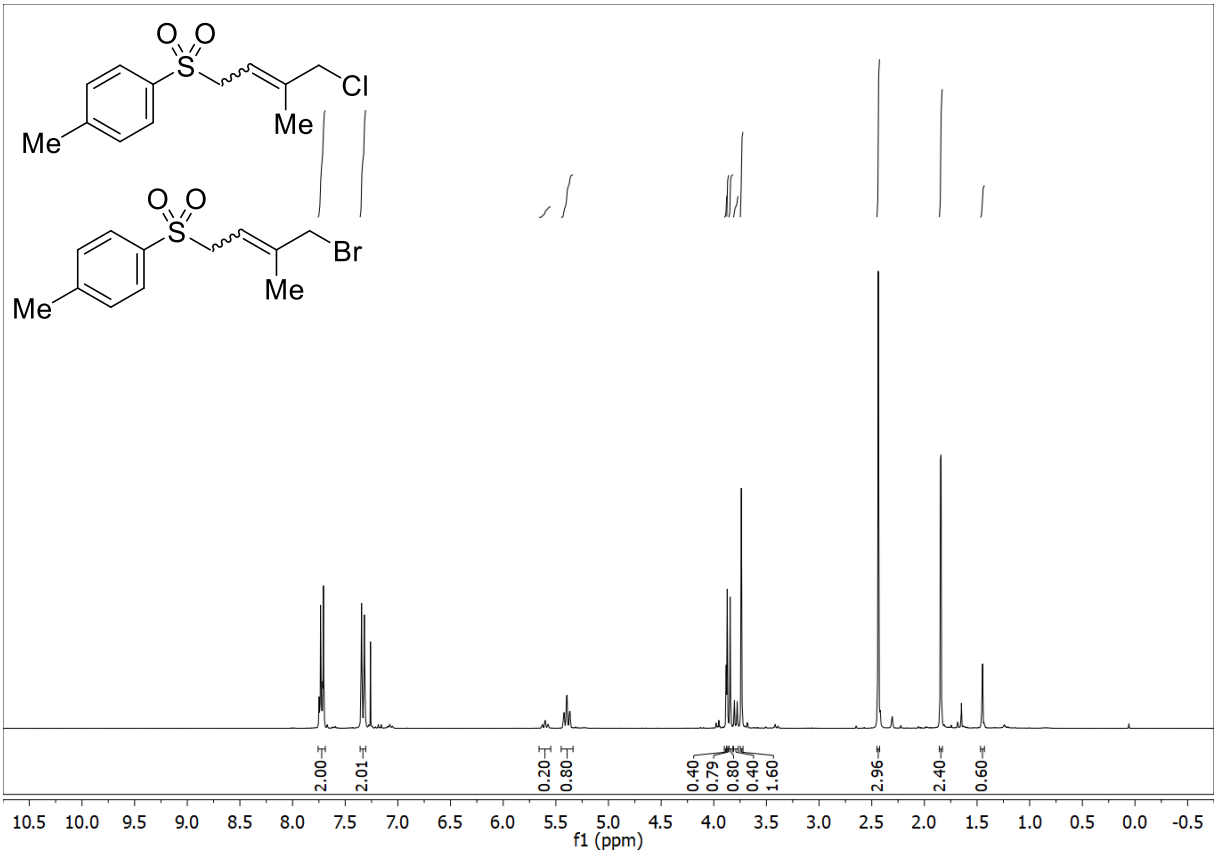
NMR-Solvent: $CDCl_3$

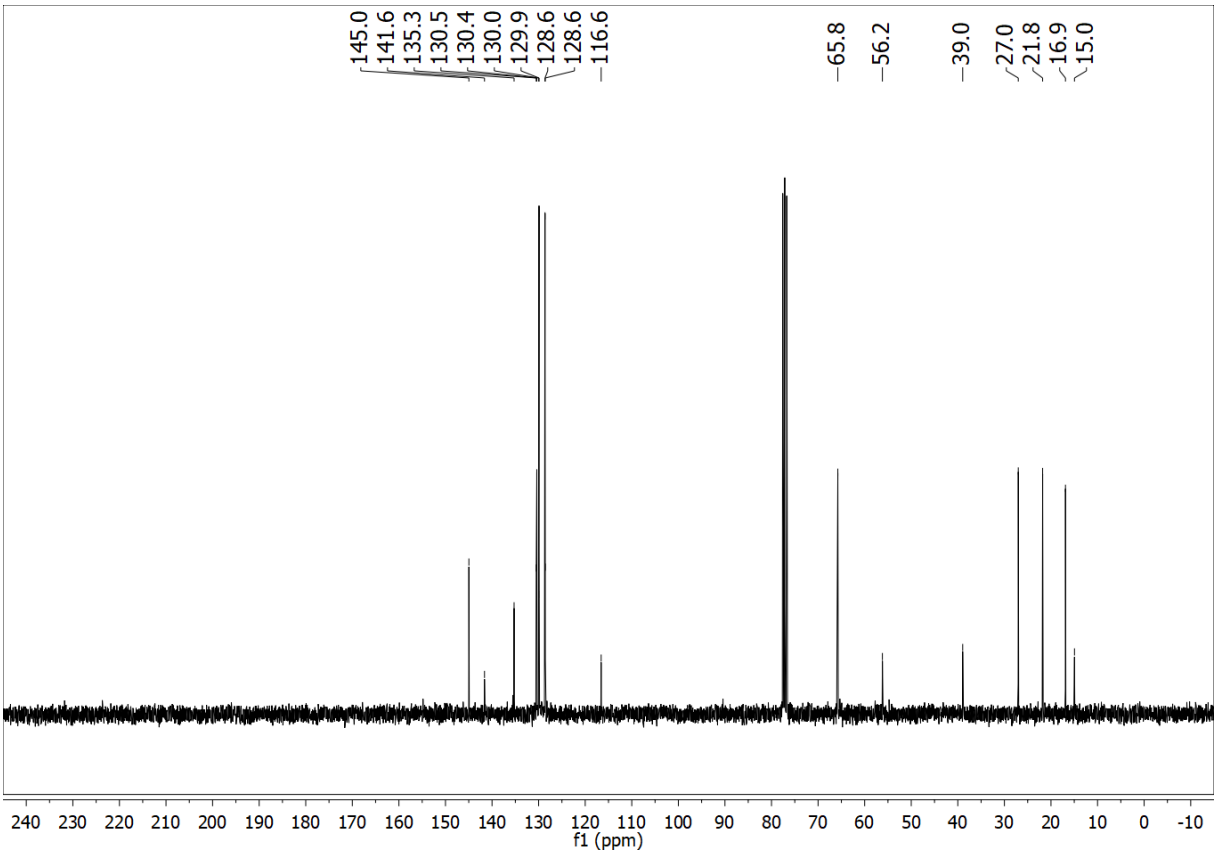
(*E*)-1-(But-2-en-1-ylsulfonyl)-4-methylbenzene (*E*-23d) and (*Z*)-1-(But-2-en-1-ylsulfonyl)-4-methylbenzene (*Z*-23d)



NMR-Solvent: $CDCl_3$

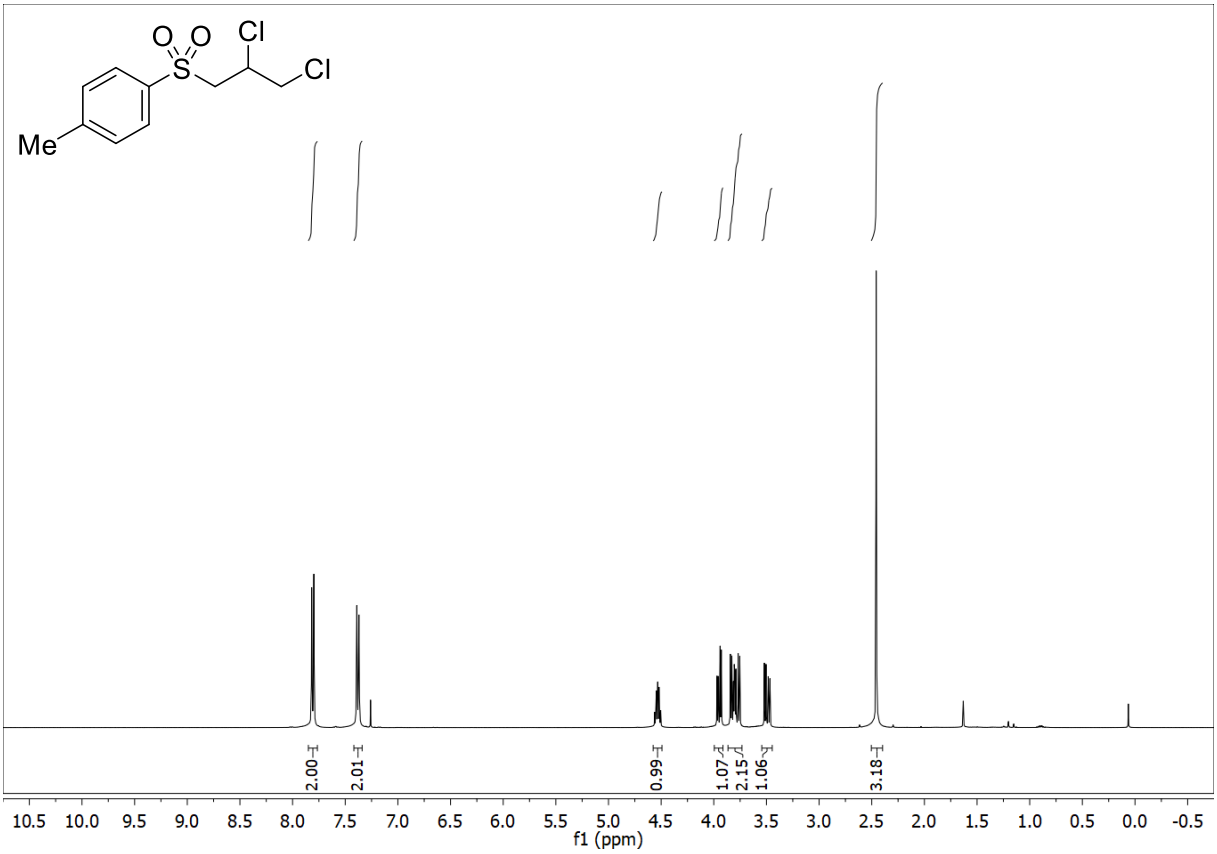
(*E*/*Z*)-1-((4-Chloro-3-methylbut-2-en-1-yl)sulfonyl)-4-methylbenzene (23e) and (*E*/*Z*)-1-((4-Bromo-3-methylbut-2-en-1-yl)sulfonyl)-4-methylbenzene (23e´)

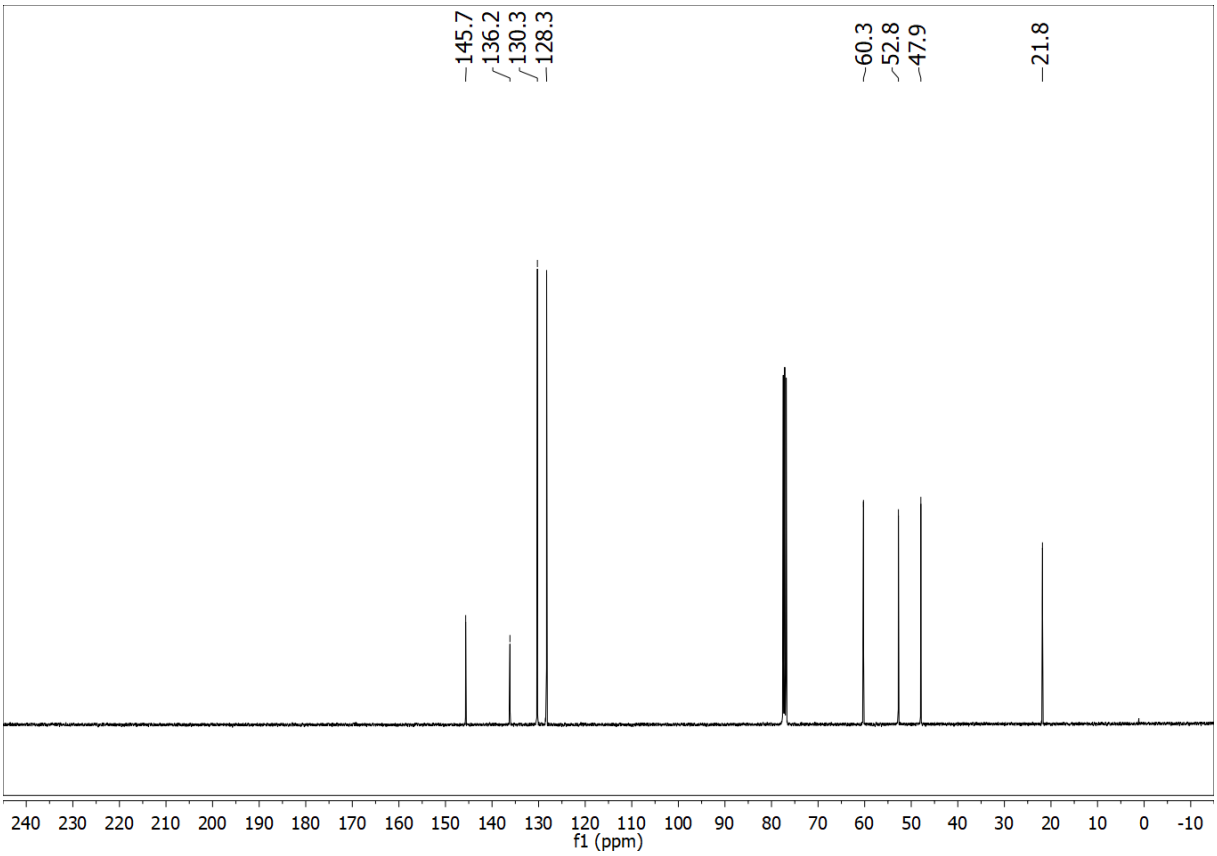




NMR-Solvent: $CDCl_3$

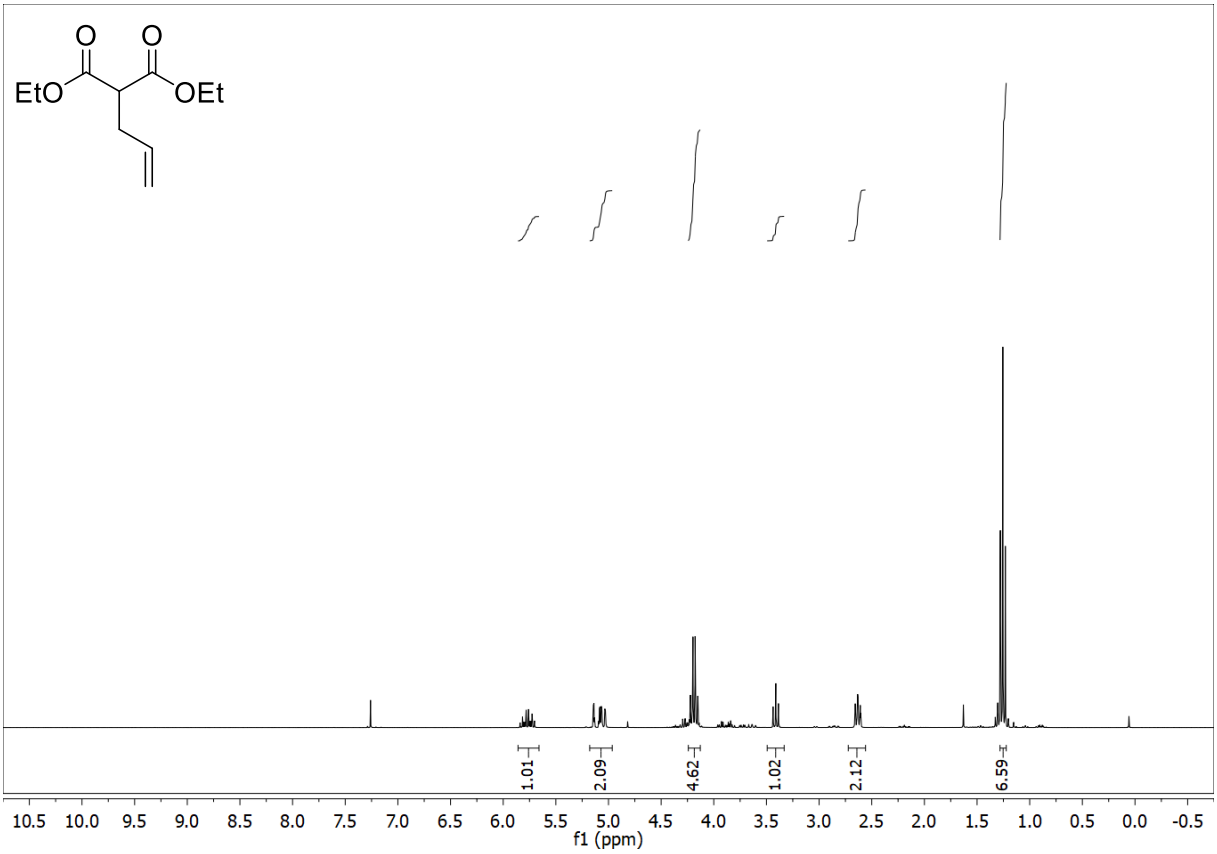
1-((2,3-Dichloropropyl)sulfonyl)-4-methylbenzene (24)

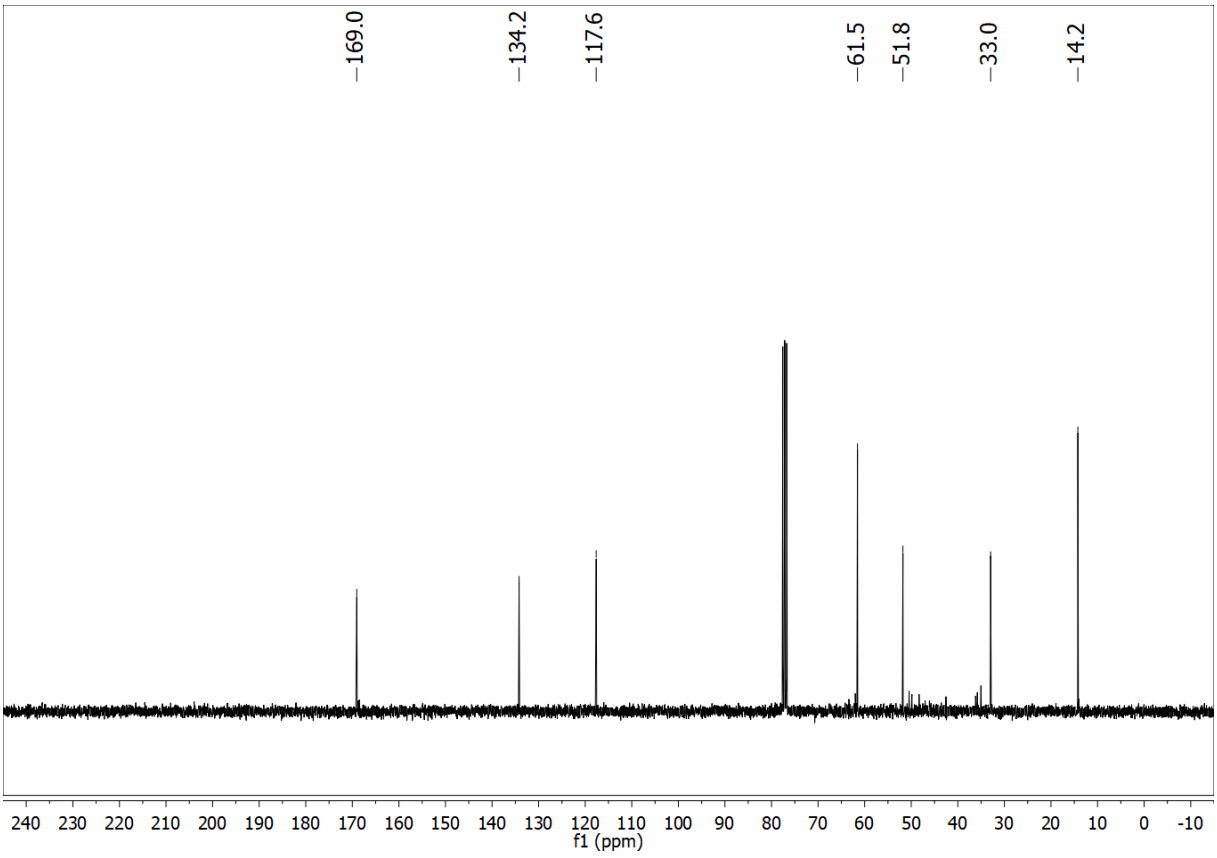




NMR-Solvent: $CDCl_3$

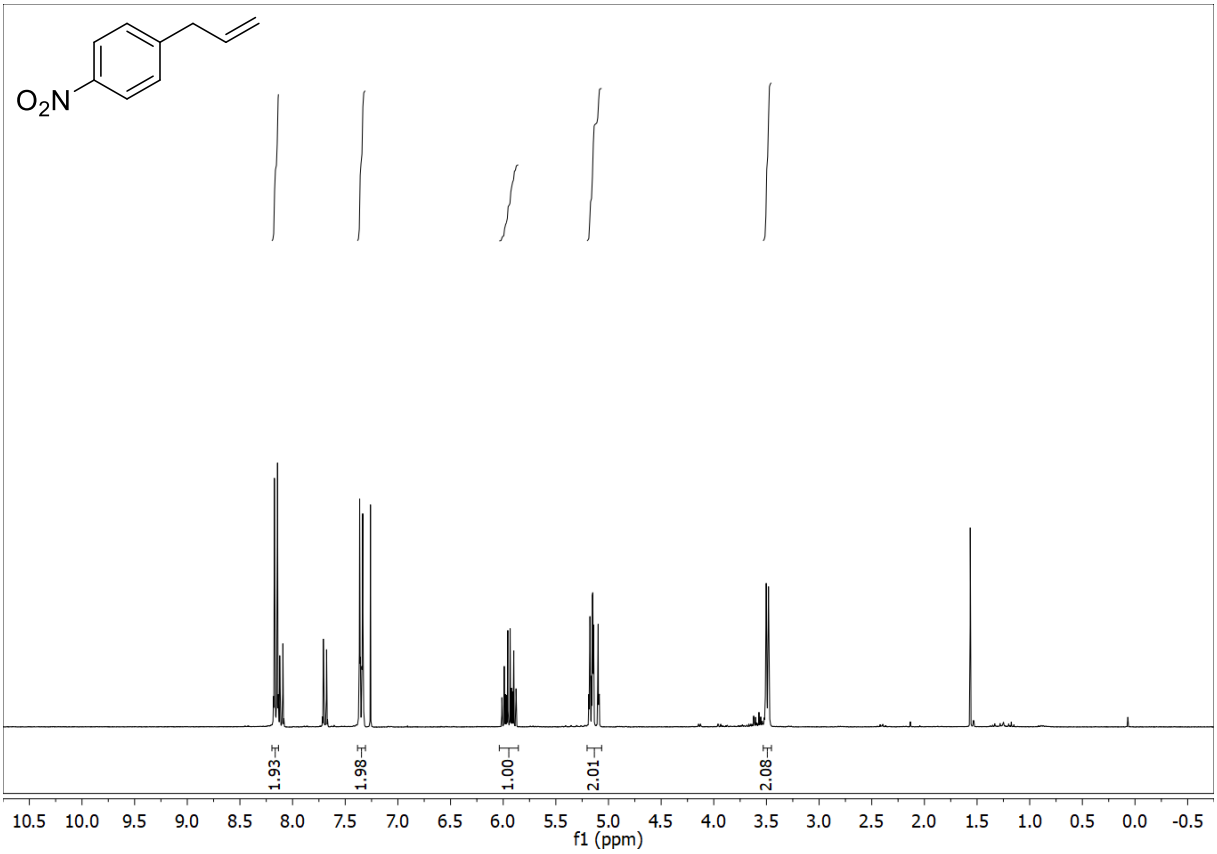
Diethyl 2-allylmalonate (40)

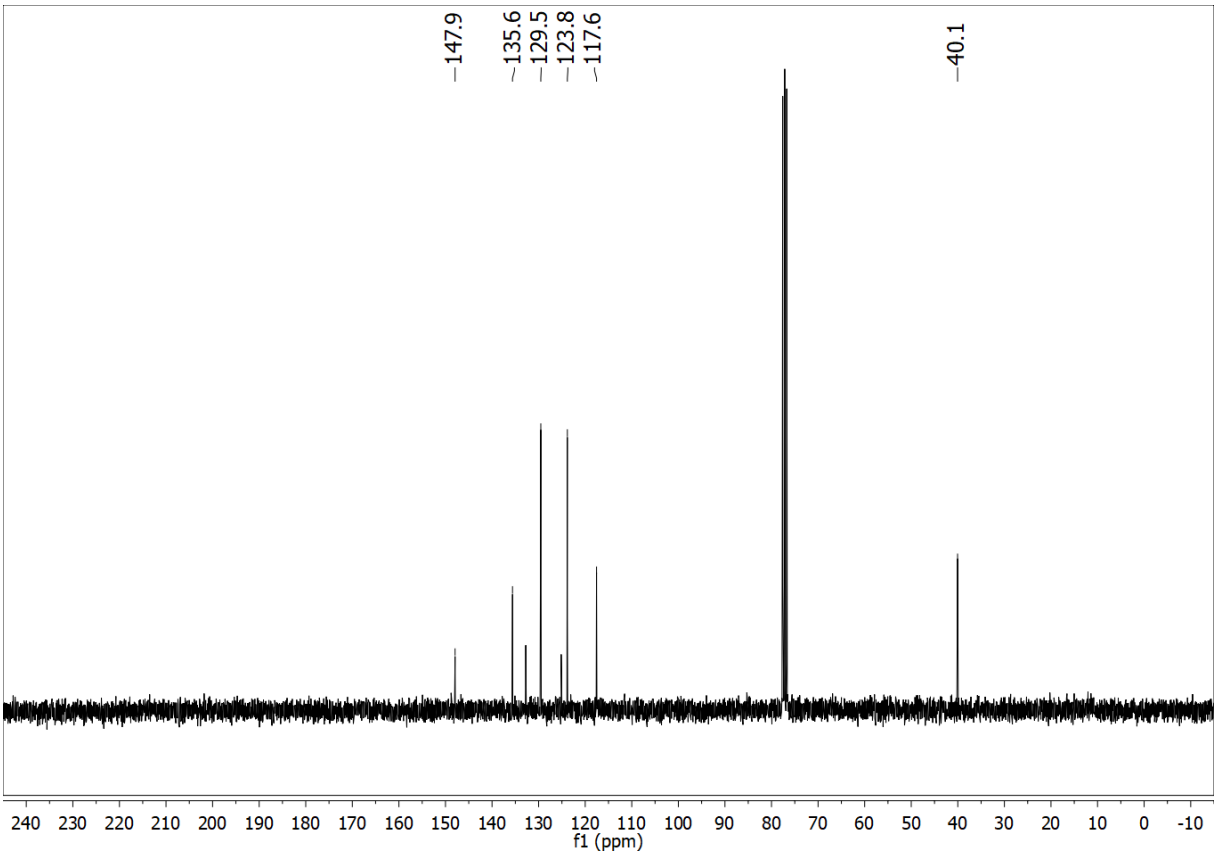




NMR-Solvent: $CDCl_3$

1-Allyl-4-nitrobenzene (44)





NMR-Solvent: $CDCl_3$

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H. Appendix

1. Curriculum Vitae

Personal Data

Name	Eugen Lutsker
Date and place of birth	12.03.1989 in Ushgorod, Ukraine
Nationality	German
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Education

10/2015 - 06/2019	**PhD Thesis** at the University of Regensburg under supervision of Prof. Dr. Oliver Reiser "*The Different Behaviors of Photoredox Catalysts in Visible Light Promoted Organic Transformations*"
10/2013 - 09/2015	**Studies in Chemistry (M. Sc.)**, University of Regensburg, Germany **Master Thesis** at the University of Regensburg under supervision of Prof. Dr. Oliver Reiser *"Visible light photoredox catalyzed synthesis of substituted tetrahydrofuranes & pyrrolidines"* (1.0) **Graduation**: Master of Science (1.1)
10/2010 - 09/2013	**Studies in Chemistry (B. Sc.)**, University of Regensburg, Germany **Bachelor Thesis** at the University of Regensburg under supervision of Prof. Dr. Oliver Reiser „Synthese zweizähniger Isonitril/Carben-Palladium-Komplexe und ihre Anwendung in der Katalyse*"* (1.0) **Graduation**: Bachelor of Science (1.3)
09/2001 - 06/2010	**Abitur**, Ludwigsgymnasium, Straubing, Germany **Graduation**: general qualification for university entrance (1.6)

09/1996 - 05/2001 **Primary School**, Ushgorod, Ukraine

Languages

German (native)

Russian (native)

English (fluently)

French (basics)

Professional References

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2. Congresses and Scientific Meetings

[1] 26. Lecture Conference on Photochemistry, Garching/Munich, Germany, **2018**
"*Copper Based Photocatalysts for Visible Light Mediated Organic Transformations*"
Eugen Lutsker, Thomas Rawner, Christian Kaiser, Asik Hossain, Matthias Knorn, Santosh K. Pagire, Michael Pirtsch, Dattatraya B. Bagal and Oliver Reiser

[2] 26. Lecture Conference on Photochemistry, Garching/Munich, Germany, **2018**
"*Copper Mediated Photoredox Catalyzed Iodoperfluoroalkylation of Alkenes and Alkynes*"
Eugen Lutsker, Sebastian Engl, Christian Kaiser, Thomas Rawner and Oliver Reiser

[3] 7. EuCheMS Chemistry Congress in Liverpool, Great Britain, **2018**
"*Visible Light Mediated Copper Catalyzed Atom Transfer Radical Addition (ATRA) Reactions of Perfluoroalkyliodides with Styrenes and Phenylacetylenes*"
Eugen Lutsker, Christian Kaiser, Thomas Rawner and Oliver Reiser

[4] GDCh-Wissenschaftsforum Chemie in Berlin, Germany, **2017**
„*Visible Light Mediated Deoxygenation as Key Step for the Construction of Polysubstituted N-Heterocycles*"
Eugen Lutsker and Oliver Reiser

[5] 26. ISHC Congress in Regensburg, Germany, **2017**
"*Visible Light Mediated Synthesis of Polysubstituted N-Heterocycles via Deoxygenative Radical Formation*"
Eugen Lutsker and Oliver Reiser

[6] Tag der Chemie in Regensburg, Germany, **2017**
"*Synthesis of substituted pyrrolidine derivatives via visible light mediated deoxygenation* "
Eugen Lutsker and Oliver Reiser

[7] J-NOST Conference for Research Scholars in Lucknow, India, **2016**
"Visible-Light Photoredox Catalyzed Synthesis of Substituted N-Heterocycles"
Eugen Lutsker and Oliver Reiser

[8] 6. EuCheMS Chemistry Congress in Sevilla, Spain, **2016**
"*Visible light photoredox catalyzed synthesis of substituted N-heterocycles*"
Eugen Lutsker and Oliver Reiser

3. List of Publications

[1] Hossain, A.; Engl, S.; Lutsker, E.; Reiser, O., Visible-Light-Mediated Regioselective Chlorosulfonylation of Alkenes and Alkynes: Introducing the Cu(II) Complex [Cu(dap)Cl_2] to Photochemical ATRA Reactions. *ACS Catal.* **2018**, 1103-1109.

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[3] Rackl, D.; Kais, V.; Lutsker, E.; Reiser; O., Synthesis of Chiral Tetrahydrofurans and Pyrrolidines by Visible-Light-Mediated Deoxygenation. *Eur. J. Org. Chem.* **2017,** *2017* (15), 2130-2138. (Front Cover: *Eur. J. Org. Chem.* **2017,** *2017* (15), 1978-1978. Highlighted in *Synfacts* **2017,** *13* (07), 0691).

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[5] Knorn, M.; Lutsker, E.; Reiser, O., Synthesis of New Chiral Bidentate Isonitrile–Acyclic Diaminocarbene Palladium(II) Compounds and Their Catalytic Activity. *Organometallics* **2015,** *34* (18), 4515-4520.

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J. Declaration

Herewith I declare that this present PhD thesis is a presentation of my original work prepared single-handed. Wherever contributions from others are involved, all of them are marked clearly, with reference to the literature, license and acknowledgement of collaborative research.

Regensburg, 29.04.2019

Eugen Lutsker