Studies towards Molecular Catalysis with Transition Metal-Isonitrile Complexes

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Herrn Prof. Dr. Oliver Reiser möchte ich herzlich für die Überlassung des äußerst interessanten Themas, die anregenden Diskussionen und seine stete Unterstützung während der Durchführung dieser Arbeit danken.

To my beloved family

谨以此论文献给我挚爱的家人

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Abbreviations

Atm.	atmosphere
Bn	benzy
Bph	diphenyl-
CuAAC	Copper(I) catalyzed azide-alkyne cycloaddition
COD	1,5-cyclooctadiene
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DDQ	2,3-Dichloro-5,6-dicyanobenzoquinone
DMF	N,N-dimethylformamide
DMA	N,N-dimethylacetal
dppf	diphenylphosphino ferrocene
GC	gas chromatography
h	hour
IR	infrared spectroscopy
LDA	lithium diisopropylamide
m-	meta
MCR	multicomponent reaction
min.	minute
MS	molecular sieves, mass spectroscopy
*m*CPBA	3-chloroperoxybenzoic acid
MW	microwave
NBS	N-bromosuccinimide
n.d.	not determined
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
n.r.	no reaction

Abbreviations

o-	ortho
p-	para
$POCl_3$	phosphorus oxychloride
quant.	Quantitative
RNC	isonitrile
rt	room temperature
sat.	saturated
temp.	temperature
TOF	turn over frequency
THF	tetrahydrofuran
THP	tetrahydropyran
TBHP	tert-butylhydroperoxide
TCT	cyanuric chloride
TLC	thin layer chromatography
U-4CR	Ugi-four component reaction

A. Introduction

1 Overview

Over the past decade, transition metal catalysis has developed into a new field in organic synthesis and has become the fastest growing area of organic chemistry, enabling numerous synthetic transformations that were previously not feasible.[1] With continuing studies in transition metal catalysis, the discovery and design of new ligands have received much attention, since these ligands assemblies coordinate to transition metals leading to a new class of transition metal-ligand complex catalysts.

Isonitriles are compounds in which the multiple bonded functional groups may be represented in the ground state by the resonance forms **1a** and **1b** (Figure 1). The closest representation of the isonitrile group in the ground state appears to be the canonical form **1a**, and this polar form is supported by data from a wide range of physical measurements.[2] In simple terms, isonitriles were always recognized as **1c**.

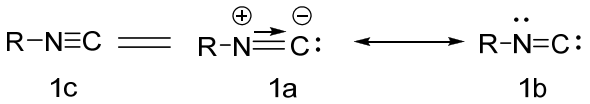


Figure 1. The forms of isonitrile group in the ground state.

Due to the presence of a formally divalent carbon atom, isonitriles occupy a unique position in the field of organic chemistry, and have enjoyed widespread use in organic synthesis,[3] especially in multicomponent transformations.[4] The chemistry of isonitriles is dominated by the nucleophilicity of the isocyano carbon atom as a result of the interaction of the vacant p-π orbital with the lone pair of electrons on the nitrogen atom (Figure 2, a). It should also be noted that isonitriles could serve as an electrophile as well, in which the π^* orbital of the isocyano group accepts an electron from the nucleophile (Figure 2, b).[2]

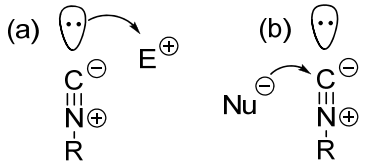


Figure 2. Ambiphilic reactivity of isonitrile serving (a) as nucleophile, (b) as electrophile.

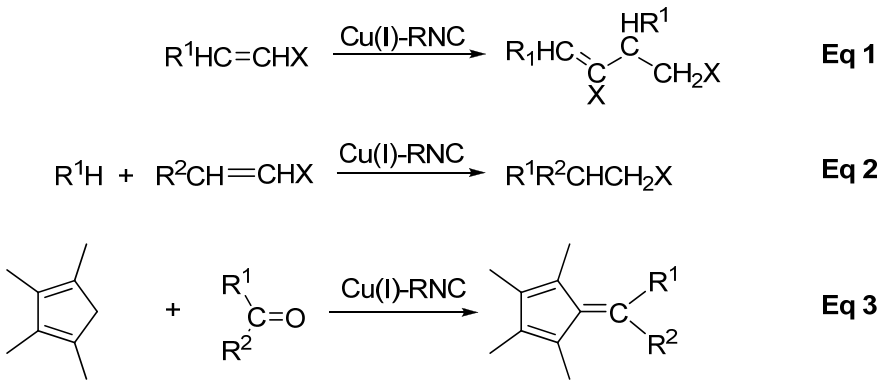
Moreover, isonitriles (C≡NR) are interesting ligands in organometallic chemistry due to their σ-donor and π-acceptor properties and their coordination ability to give very stable complexes with many metals in a high or low valence state.[2,5] Isonitriles (CNR) are similar in their electronic structures to carbon monoxide (CO), but have stronger σ-donor and weaker π-acceptor properties as ligands of transition metal complexes.[6] Since their properties as a ligand depend on the steric and electronic factors of R groups in CNR, the ligand design of metal isonitriles as a key to controlling the catalysis may open an attractive research area in organometallic chemistry. However, high reactivity of CNR to metal-catalyzed self-polymerization[2,7] or insertion between O-H, N-H, and C-H bonds in certain organic molecules prevents studies using metal isonitrile complexes as catalysts for chemical transformation of organic molecules.[8] Molecular catalysis of transition metal-isonitrile complexes has been promoted by appropriate design of the isonitrile ligands. The development in transition metal-isonitrile complex catalyzed reactions is undertaken in the next section.

2 Copper isonitrile complexes

2.1 Catalyzed reactions involving active hydrogen compounds

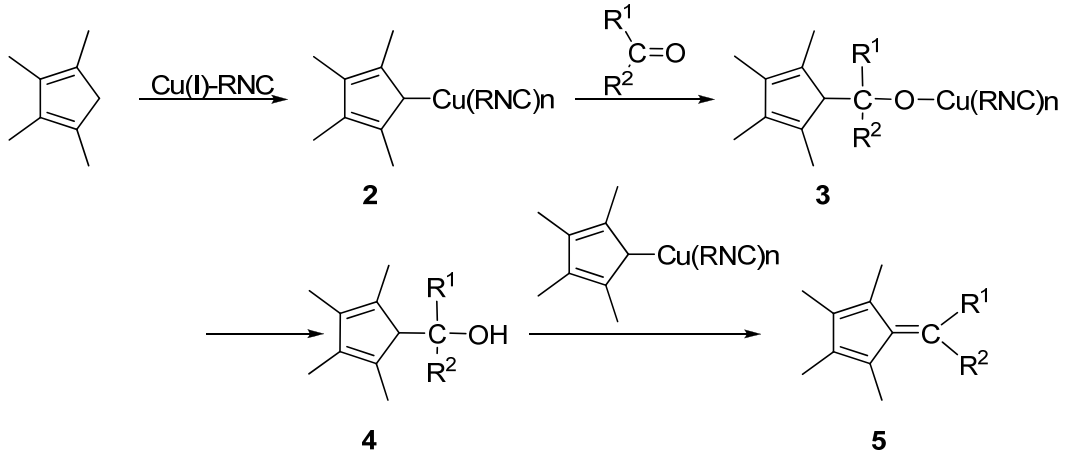
Since 1967，*Saegusa* and co-workers have devoted their studies on the catalytic activity of Cu(I)-alkyl isonitrile complexes.[9-14] They have prepared organocopper(I)-isonitrile complexes derived from Cu_2O, isonitrile and showed that Cu-isonitrile complexes could catalyze a number of reactions. As is shown in Scheme 1, characteristic catalytic activity of

the Cu(I)-isonitrile system has been firstly demonstrated in reactions involving active hydrogen compounds, such as the dimerization of α,ß-unsaturated carbonyl and nitrile compounds (Eq 1),[9,10] Michael-type addition reaction[10] (Eq 2), the reactions of malonate with aldehyde affording the corresponding alkylidene malonate derivatives (Eq 3)[11].



Scheme 1. Cu(I)-alkyl isonitrile complexes catalyzed reactions.

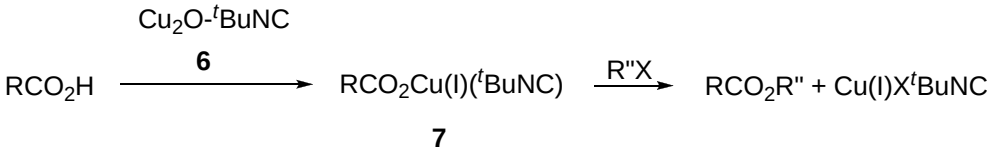
In above mentioned reactions, an organocopper(I)-isonitrile complex may be as an active intermediate. For example in Scheme 2, organocopper complex (**2**) is first formed from Cu_2O, a cyclopentadiene homolog, and an isonitrile; (**2**) in turn reacts with a carbonyl compound to afford a copper alkoxide species (**3**). In the hydrogen abstraction of (**3**) from the second molecule of the cyclopentadiene homolog, a carbinol (**4**) is produced and (**2**) is reproduced. The dehydration of (**5**) gives rise to the ulvene-type product. Isonitrile functions as an essential ligand in a series of copper complexes.



Scheme 2. Proposed mechanism of the Cu-CNR complex catalyzed reaction.

2.2 Esterification of carboxylic acid.

Shortly after, they found that carboxylic acid can be readily esterified with alkyl halide in the presence of Cu_2O-isonitrile complex.[12] Copper(I) carboxylate-isonitrile complex (**7**) was generated from Cu_2O-isonitrile complex (**6**) and carboxylic acid, and then reacted with alkyl halide to produce the corresponding carboxylic ester.

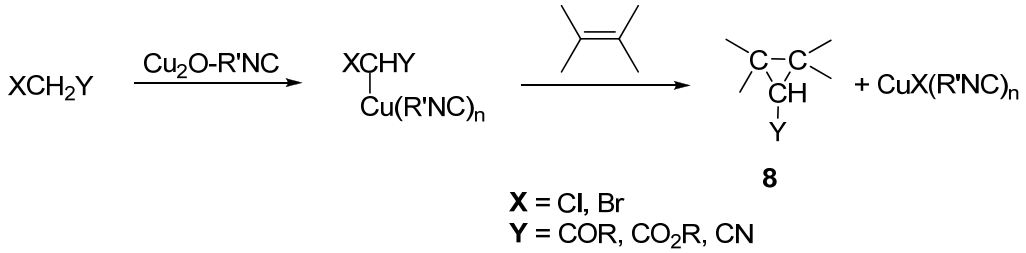


Scheme 3. Esterification of carboxylic acid.

2.3 Cyclopropanation

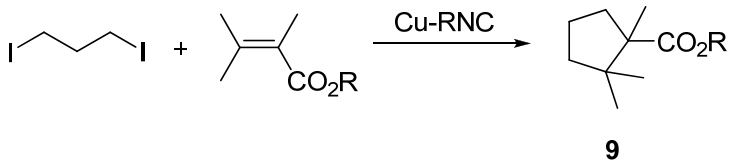
Saegusa and co-workers have also found that an aliphatic halide reacts with metallic copper in the presence of RNC to form the corresponding organocopper(I)-isonitrile complex, which then adds to α,ß-unsaturated carbonyl and nitrile compounds in the manner of a conjugate addition. Moreover, an organocopper-isonitrile complex bearing a halogen atom in the same molecule readily undergoes cyclization by the intramolecular elimination of copper

halide-isonitrile complex. The following cyclopropane syntheses have been based upon this interesting reactivity of organocopper-isonitrile complex.[13] The reaction of α-halocarbonyl or α-halonitrile was performed with α, ß-unsaturated carbonyl or nitrile in the presence of Cu_2O-isonitrile complex to produce cyclopropane derivatives (**8**). The key intermediate assumed in this reaction is formed by the reaction of the cuprous oxide-isonitrile complex with the σ-halo compound, which then reacts with an electron-deficient olefin to give the corresponding cyclopropane derivative.



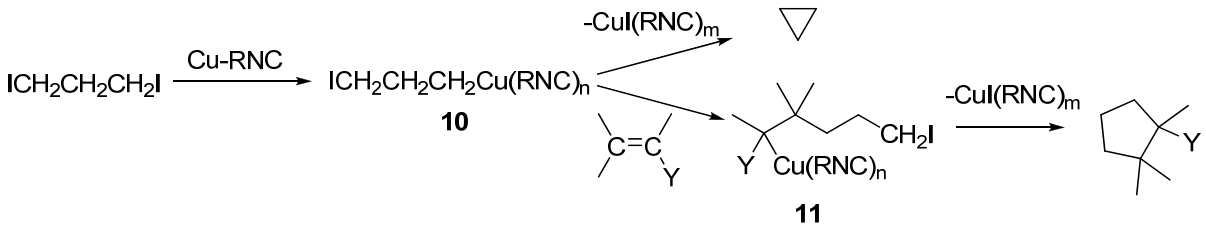
Scheme 4. Cyclopropanation of alkenes using Cu_2O-isonitirle complex.

Cyclopentanecarboxylates (**9**), readily prepared from 1,3-diiodopropane and methylacrylate, was reported by the same group (Scheme 5).[14]



Scheme 5. Cu_2O-isonitirle complex catalyzed preparation of cyclopentanecarboxylic acid methyl ester (**9**).

The cyclization which afforded a five-membered ring may be explained by Scheme 6 involving an intermediate of 3-iodopropylcopper-isonitrile complex (**10)** which is initially formed by the reaction of diiodopropane with Cu-RNC. The addition of **10** to α,ß-unsaturated ester gives the second organocopper species (**11**), which in turn undergoes the cyclization by the intramolecular 1,5-elimination of CuI-RNC complex. Unfortunately, the cyclization would give the byproduct by the intramolecular 1,3-elimination of CuI-RNC complex (**10)**.

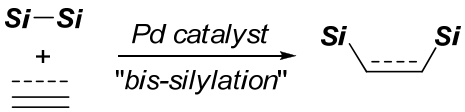


Scheme 6. Proposed mechanism of Cu_2O-isonitirle complex catalyzed cyclopentanation.

3 Palladium isonitrile complexes

3.1 Bissilylation of unsaturated C-C bonds

The transition metal-catalyzed addition of Si-Si bond across C-C multiple bond, i.e. bis-silylation, is attractive transformation in that two Si-C bonds are stereoselectively created at once.[15] In the mid of 1970s, *Kumada* and *Sakurai* groups independently reported the catalytic addition of disilandes to alkynes in the presence of palladium complexes (Scheme 7).[16] These reactions were proposed to involve bis(silyl)-palladium(II) complexes as a key intermediate, which may be formed through interaction of the Si-Si bond with a palladium(0) complex.

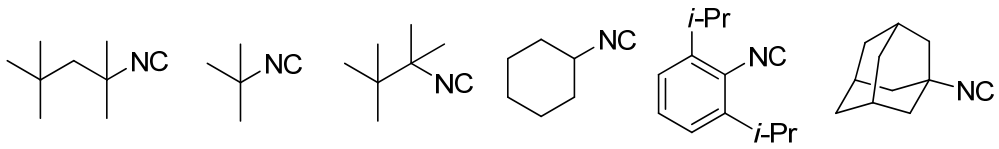


(***Si*** denotes a triorganosilyl group)

Scheme 7. Catalytic addition of disilandes to alkynes in the presence of palladium complexes.

In the initial period, most bis-silylation reactions were carried out in the presence of palladium-phosphine catalysts, requiring the use of 'activated disilane', i.e. disilanes bearing electron-withdrawing substituents and strained cyclic disilanes.[17] In addition, the palladium-phosphine catalytic system cannot involve the intramolecular bis-silylation of unsaturated organic substrates. These drawbacks have strongly hampered the synthetic

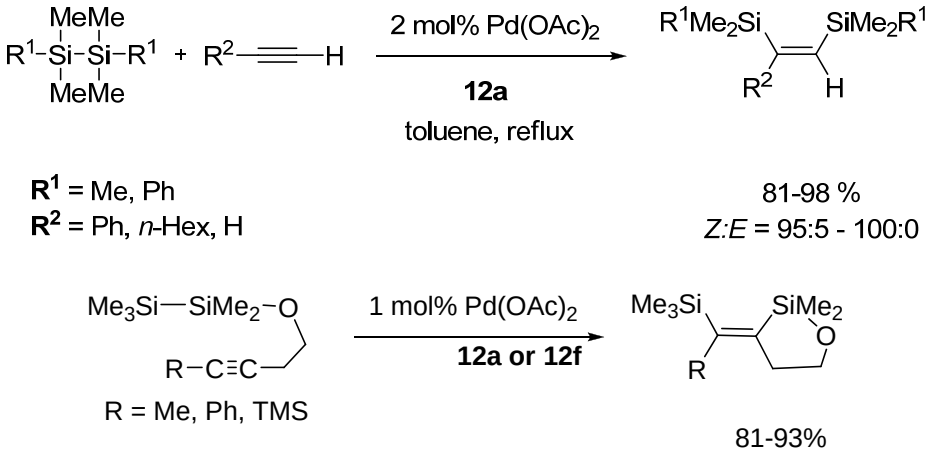
application of the bis-silylation reactions. The breakthrough in this field was the discovery of *tert*-alkyl isonitriles served as highly efficient ligands (Figure 3, **12a**-**12f**) to facilitate the Palladium-catalyzed bis-silylation reactions by *Ito* and co-workers.[18-20]



12a **12b** **12c** **12d** **12e** **12f**

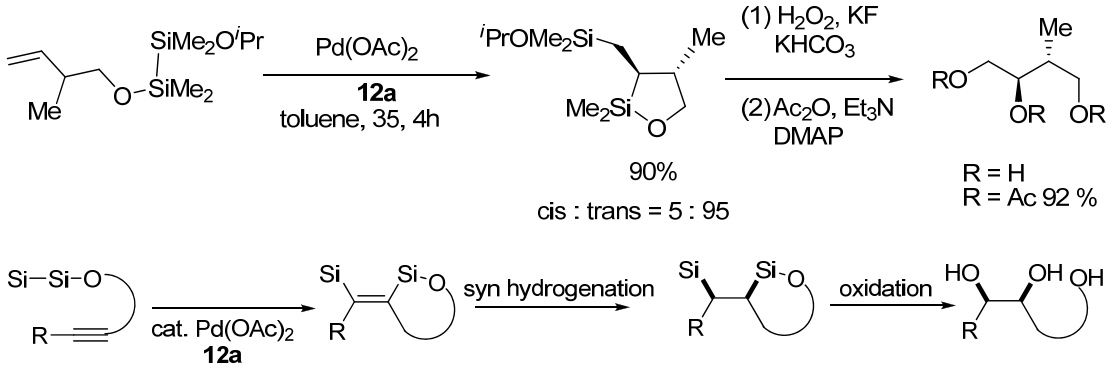
Figure 3. Examples of *tert*-isonitrile ligands.

Palladium(II) acetate-*tert*-alkyl isonitrile is firstly found to be a highly efficient catalyst system for intermolecular and intramolecular bis-silylation of unsaturated triple bonds, with characteristic selectivity (Scheme 8).[18]



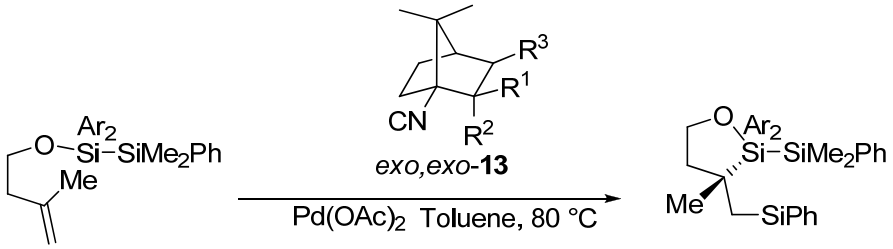
Scheme 8. Palladium(II) acetate-*tert*-alkyl isonitrile catalyzed bis-silylation of triple bonds.

It is worth mentioning that intramolecular bis-silylation of alkynes or alkenes was applied to the stereoselective synthesis of triols and polyols.[19] As is shown in Scheme 9, intramolecular bis-silylation followed by oxidation offers a new entry to stereoselective synthesis of triols and their derivatives.



Scheme 9. The stereoselective synthesis of triols and their derivatives by intramolecular bis-silylation.

Remarkably, for the first time optically active chiral isonitriles were employed by the same group in the enatioseletive intramolecular bissilylation of alkenes (Scheme 10).[20] The best *ee* was achieved by the ligand (**13)** with two exo-siloxy groups (R^1= R^2= $OSiMe_3$, R^3= H, Scheme 10).



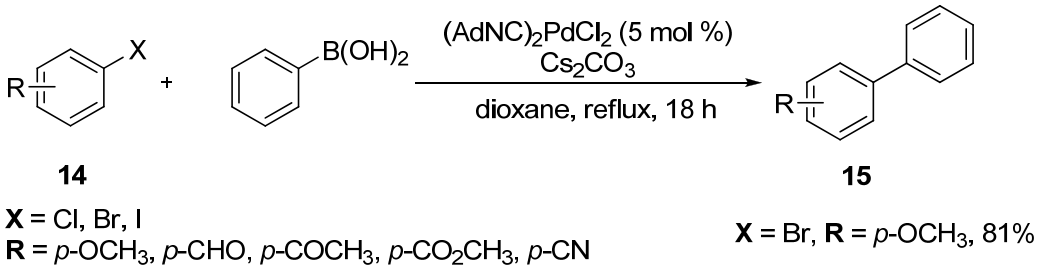
Scheme 10. The enatioseletive intramolecular bissilylation of alkenes.

The active species in the above catalyst system is believed to be '$(RNC)_nPd(0)$', where the coordination number(n) may vary from 2 to 4. As palladium precursors, $Pd(OAc)_2$, $Pd(acac)_2$, and PdCp(π-allyl) have been successfully used. Typically 4–15 equivalents (to Pd) of isonitrile were employed because part of the isonitriles may be consumed for the Pd(II) – Pd(0) reduction. The excess isonitriles do not interfere with the bissilylation reaction. It was explained that $Pd(OAc)_2$ is reduced by isonitriles initially to form Pd(0) species ligated isonitrile. Next the oxidative insertion of Pd(0) species into the Si-Si linkage takes place to give a bis(organisilyl)palladium (II) complex. Insertion of the double bond into Pd-Si bond followed by reductive elimination of the Pd(0) species would complete the catalytic cycle.

Excess of isonitrile was required to hinder the palladium(0) isonitrile complex from decomposing during the reaction course.

3.2 Suzuki miyaura coupling

Villemin and co-workers prepared palladium complexes [$PdCl_2(RNC)_2$] of five hindered isonitriles from *tert*-butylisonitrile (^{t}BuNC, **12b**), 1,1,3,3-tetramethylbutylisonotrile (^{t}OcNC, **12a**), cyclohexylisonitrile (CyNC, **12d**), 2,6-didiopropylphenylisonotrile [(^{i}Pr)$_2$PhNC), **12e**] and adamantylisonitrile (AdNC, **12f**) and tested their activities in Suzuki-Miyaura reaction (Scheme 11).[21] [$PdCl_2(AdNC)_2$] was found to be the most effective catalyst and was used in the phenylation of several chloro and bromoaromatic substrates (**14**). The activity of [$PdCl_2(AdNC)_2$] complex is very close to the best Arduengo's carbene palladium complex, while the isonitrile ligands are isoelectronic with Arduengo's carbene and hence promote the Suzuki-Miyaura reaction.

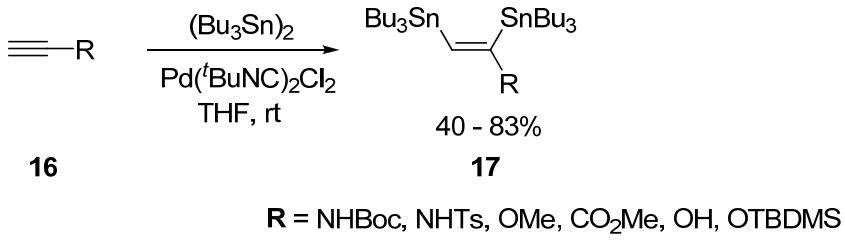


Scheme 11. Suzuki Miyaura coupling employing Pd-isonitrile catalyst.

3.3 Bisstannylation of alkynes

Mancuso and co-workers reported a palladium-isonitrile complex catalyzed bis(stannylation) of terminal alkynes (**16**) using a hexaalkylditin as a stannyl group transfer reagent in an atom-efficient and mild catalytic process (Scheme 12).[22] Generally, modern to good yields (40-83%) were obtained with different types of alkynes, and functional group tolerance is good allowing the presence of amine, carbamate, silyl, ester, and ether moieties. Furthermore,

an activated internal alkyne also underwent bis(stannylation) in moderate yield, allowing access to symmetrical bis(alkenyl)stannanes.

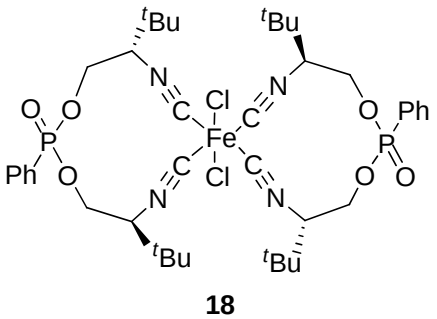


Scheme 12. Bisstannylation of alkynes using Pd-isonitrile complex.

4 Iron isonitrile complexes

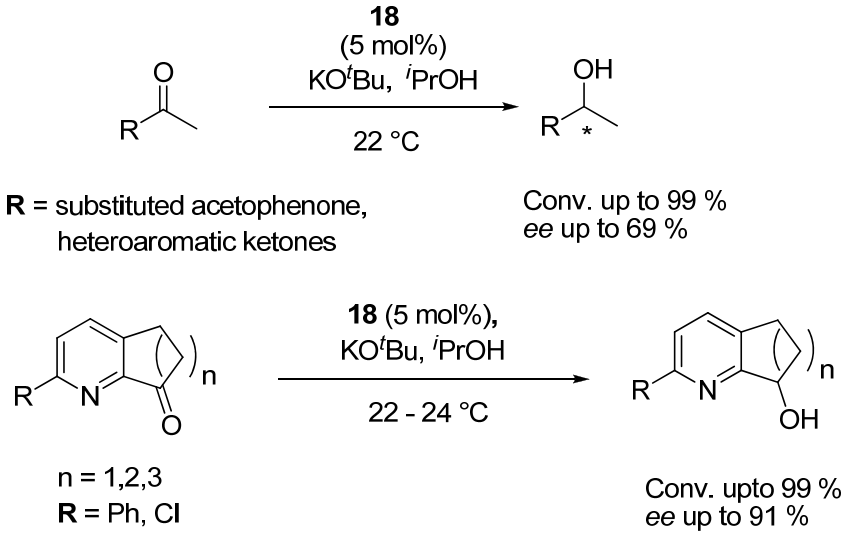
4.1 Transfer hydrogenation

The application of iron in homogeneous catalysis has recently received considerable attention since iron is the most abundant metal on earth. *Reiser* and co-workers have developed a new iron complex of chiral bis(isonitrile) ligand (**18**) (Figure 4), catalyzing asymmetric transfer hydrogenation of aromatic, heteroaromatic and pyridyl ketones under mild conditions (scheme 13).[23] This is the first report that demonstrates the ability of isonitriles to be able to serve as chiral ligands in asymmetric catalysis.



18

Figure 4 A new iron complex of chiral bis(isonitrile) ligand (**18**).



Scheme 13. Transfer Hydrogenation catalyzed by iron complex of chiral bis(isonitrile) ligand.

They propose the hydride transfer mechanism as shown in Figure 5,[24] being different from the reported mechanisms for transfer hydrogenations with ruthenium involving a chiral isonitrile ligands.[25] The proposed mechanism consists of following steps: (a) iron bis(isonitrile) (**18**) was thought to undergo reduction of NC (Figure 5) to imine by basic isopropanol (confirmed by IR), (b) coordination of ketone to iron centre, (c) hydride transfer from imine carbon *via* five-membered transition state to carbonyl group, (d) formation of alcohol by protonation by isopropanol, (e) hydride elimination from isopropoxide generated acetone, (f) regeneration of the active iron species.

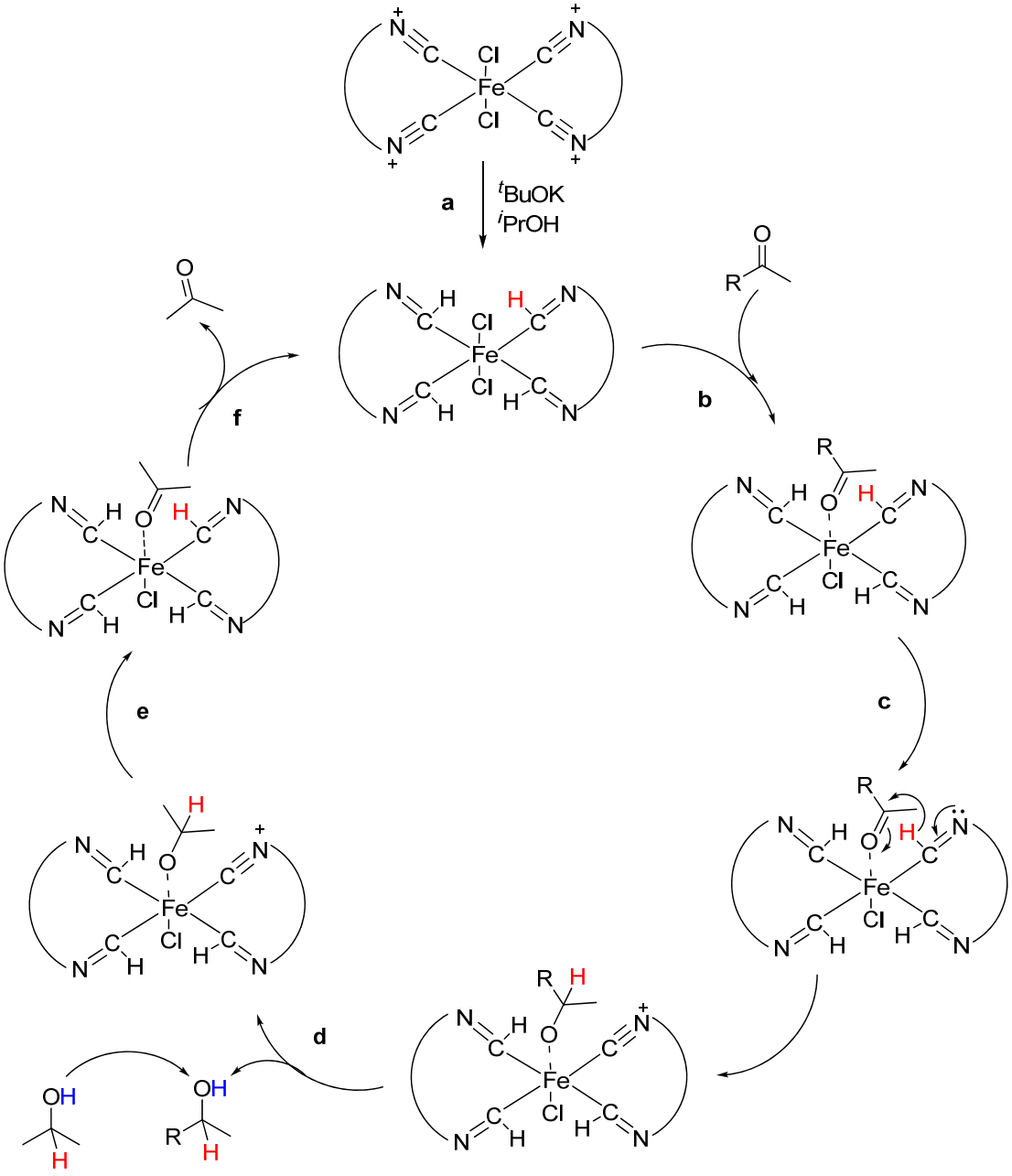


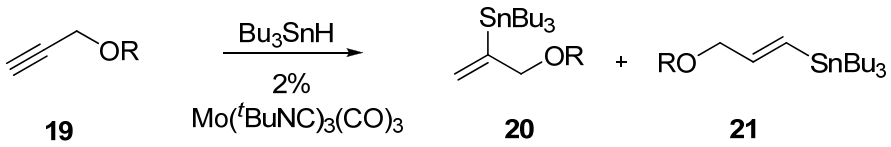
Figure 5. The proposed mechanism for Transfer Hydrogenation catalyzed by **18**.

5 Low valent transition metal isonitrile complexes (M = W, Mo, Ni)

5.1 Hydrostannylation and bisstannylation of alkynes

Hydrometalation is an important category of reactions catalyzed by transition metals such as hydrostannation of alkynes, used for the synthesis of vinylstannanes, which can be further

modified by Stille coupling.[26] *Uki* and co-workers have reported highly regioselective hydrostannations catalyzed by molybdenum isonitrile complexes.[27] Replacing three CO ligands in $Mo(CO)_6$ by isoelectronic isonitrile ligands resulted in $Mo(^{t}BuNC)_3(CO)_3$, which catalyzed hydrostannylation of propargylic alcohol derivative (**19**) with a significant increase of the yield and the selectivity as well afforded α-stannylated allylic alcohol or their derivative (**20**) as a major product (Scheme 14) in comparison to the results obtained with several isonitrile complexes and other commonly used palladium and molybdenum catalysts (Table 1).



Scheme 14. Hydrostannylation of unsymmetric alkynes.

Table 1. Catalytic hydrostannations of the THP-propargylether.

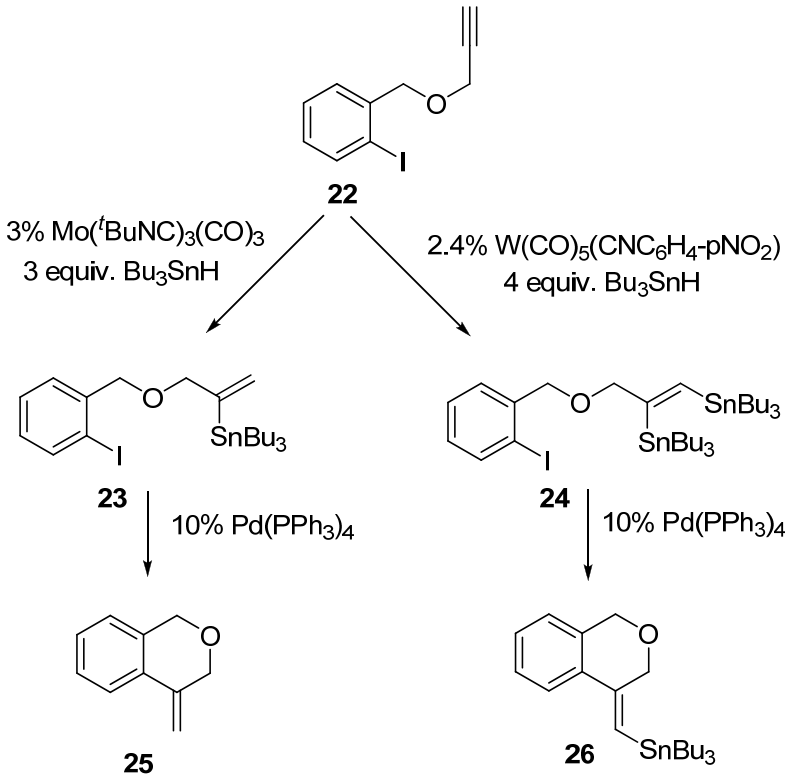
entry	catalyst	Yield (%)	selectivity
1	$PdCl_2(PPh_3)_2$	68	67:33
2	$MoBr(allyl)(CO)_2(MeCN)_2$	nr[a]	64:36
3	$Mo(CO)_6$	35	28:72
4	$Mo(^{t}BuNC)(CO)_5$	64	62:38
5	$Mo(^{t}BuNC)_2(CO)_4$	89	87:13
6	$Mo(^{t}BuNC)_3(CO)_3$	98	98:2
7	$Mo(^{t}BuNC)_4(CO)_3$	85	>95:<5

[a] No reported.

^{t}Butylisonitrile was chosen for steric reasons, with the expectation that the sterically demanding ^{t}Butyl groups may have an influence on the regioselective outcome of the reaction. Isonitriles also have the advantage to stay in solution after dissociation from the metal, resulting in a prolonged lifetime of the catalyst. Because of a weaker π-back donation from

the metal to the isonitrile, in comparison to CO, the isonitriles are weaker bound in the complex. Therefore, they can dissociate easily, opening up free coordination sites on the catalytically active metal. Based on these reasons it can give a strong influence of the number of the isonitrile ligands (Table 1, entries 4-7).

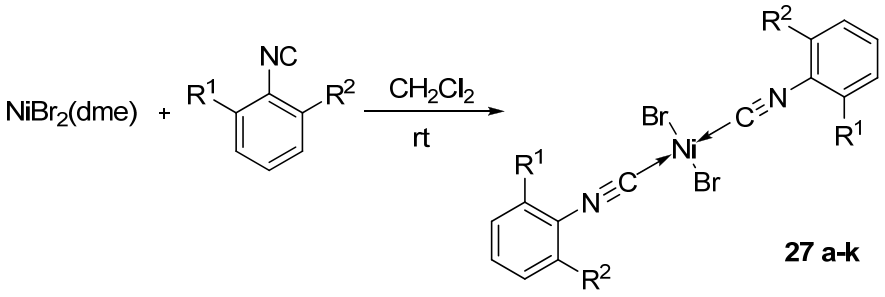
Tungsten based isonitrile complex $W(CO)_5(CNC_6H_4\text{-}pNO_2)$ have been prepared by the same group and can achieve the bisstannylation reaction of terminal alkynes using Bu_3SnH,[28] In contrast, $Mo(^tBuNC)_3(CO)_3$ allows regioselective hydrostannation of the same alkynes with Bu_3SnH_4 (Scheme 15). Both hydrostannylation product (**23**) and bisstannylation product (**24**) further underwent intramolecular Stille coupling to afford compound (**25**) and (**26**), respectively.



Scheme 15. Hydro- and Bisstannylation of propargylic ethers (**22**).

5.2 Polymerization of ethylene

For example, *Nagashima* and co-workers[29] reported that Ni(II) isonitrile complexes, $NiBr(CNAr)_2$ (**27**) (Scheme 16, Table 2), can be active catalysts for polymerization of ethylene in the presence of methylaluminoxane (MAO). The ligand structure, particularly, substituents on the aryl group in the isonitrile ligands of Ni(II) isonitrile complexes, apparently affect the catalytic activity and the molecular weight and number of methyl branches of the formed polymers, since the design of the ligand structure is crucial important for chain polyethylene. The nickel complexes having 2,6-diphenylphenylisonitrile and its analogues are catalysts showing moderate activity and giving high molecular weight polyethylene (M_v >10^6), whereas those bearing 2-phenylphenylisonitrile and its analogues give polyethylene with M_w = 10^3-10^4.



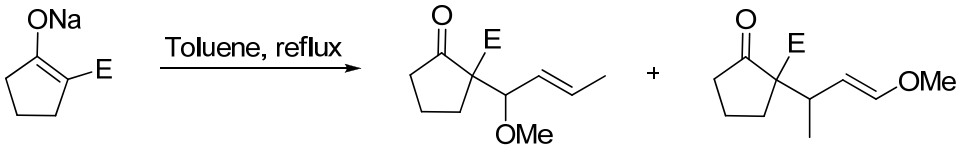
Scheme 16. Synthesis of $NiBr_2(ArNC)_2$ complex (**27**).

Table 2. Substituents on the aryl group in the isonitrile ligands.

complex	R^1	R^2	Yield (%)	complex	R^1	R^2	Yield (%)
27a	Me	Me	85	**27g**	4-*t*-BuC_6H_4	H	77
27b	Et	Et	80	**27h**	4-*t*-BuC_6H_4	4-*t*-BuC_6H_4	98
27c	i-Pr	i-Pr	82	**27i**	2-MeC_6H_4	H	69
27d	i-Pr	H	81	**27j**	2,6-$Me_2C_6H_3$	H	72
27e	Ph	H	85	**27k**	2,6-$Me_2C_6H_3$	2,6-$Me_2C_6H_3$	54
27f	Ph	Ph	83				

5.3 Allylic allylation

Highly reactive Molybdenum-isonitrile complexes were prepared by *Trost* and co-workers for the allylic alkylation reaction (Scheme 17).[30] $Mo(^tBuNC)_4(CO)_2$ was proven to be a superior catalyst in comparison to $Mo(CO)_6$ and also enhanced reactivity as well as chemo-, region-, and stereoselectivity in allyl alkylation reaction. This is the first successful example of molybdenum isonitrile complex catalyzed reactions.



28 **29** **30**

		29 : 30
$Mo(tBuNC)_4(CO)_2$	(40%)	93 : 7
$Mo(CO)_6$	(68%)	60 : 40

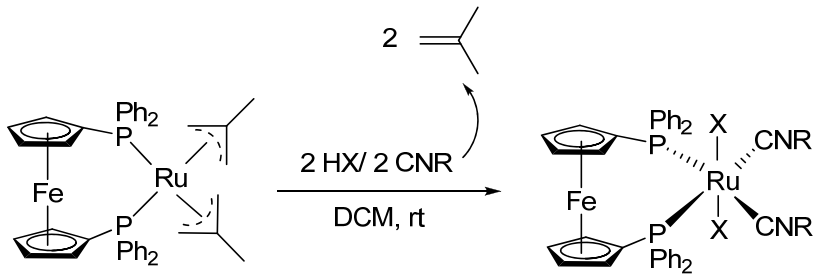
Scheme 17. Allylic allylation catalyzed by $Mo(^tBuNC)_4(CO)_2$ complex.

6 Ruthenium, Rhodium and Rhenium isonitrile complexes

6.1 Transfer hydrogenation using Ru-isonitrile complex

Transfer hydrogenation (TH) of ketones by ruthenium(II) catalysis currently one of the most appealing synthetic routes to alcohols and constitutes a good alternative to the widely used catalytic hydrogenation.[31] The bis(isonitrile)-ruthenium(II) complexes[32] *trans,cis,cis*-$[RuX_2(CNR)_2(dppf)]$ (X = Cl, Br) (**32**) have been prepared by reaction of bis(allyl)-ruthenium(II) derivative $[Ru(\eta^3C_3H_4Me)_2(dppf)]$ (**31**) with the appropriate isonitrile ligand, in dichloromethane at room temperature and in the presence of the corresponding hydrogen halide HX (Scheme 18). Among these bis(isonitrile)-ruthenium(II) complexes, *trans,cis,cis* -$[RuCl_2(CNCH_2Ph)_2(dppf)]$ was found to be the most active catalyst and used as

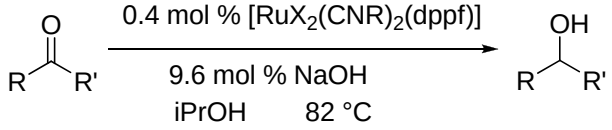
catalyst in the transfer hydrogenation leading to nearly quantitative conversions of a large variety of ketones in basic propan-2-ol (Scheme 19). It has been shown to be particularly efficient in the reduction of dialkyl ketones (TOF up to 1500 h^{-1}) in comparison to aryl alkyl ketones (TOF up to 500 h^{-1}).



31 **32**

X = Cl, Br
R = Bn, Cy, ^{t}Bu, 2,6-$C_6H_3Me_2$, (S)-(-)-C(H)MePh

Scheme 18. Synthesis of *trans,cis,cis*-[$RuX_2(CNR)_2$(dppf)] (**32**).



Scheme 19. Catalytic transfer hydrogenation of acetophenone by the complexes *trans,cis,cis*-[$RuX_2(CNR)_2$(dppf)].

6.2 Hydrogenation with rhodium-isonitrile complex

Efraty group[33] synthesized an insoluble matrix of the type $[RhCl(CO)(1,4\text{-}(CN)_2C_6H_4)]_n$ using $[Rh(CO)_2Cl]_2$ and an equimolar amount of 1,4-diisocyanobenzene. They have investigated its activity with respect to the hydrogenation and isomerization of 1-hexene in the dark as well as under irradiation. The insoluble matrix may exist resulting from either regular or irregular intrachain Rh−Rh interactions (3.2-3.5 Å) of units such as a linear polymer, a non linear polymer, or a tetranuclear cyclic oligomer (Figure 6).

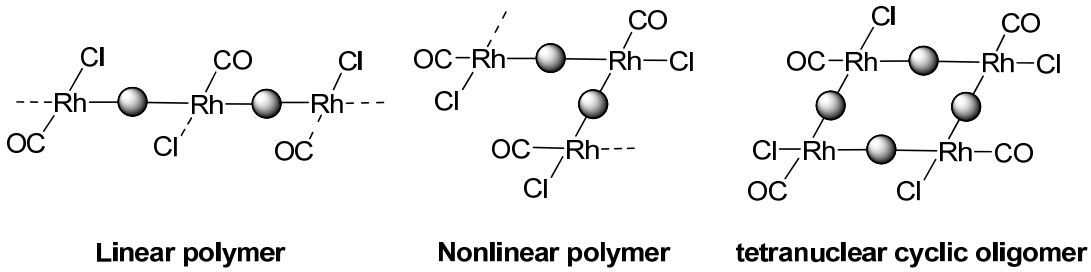


Figure 6. Types of insoluble matrix of $[RhCl(CO)(1,4\text{-}(CN)_2C_6H_4)]_n$.

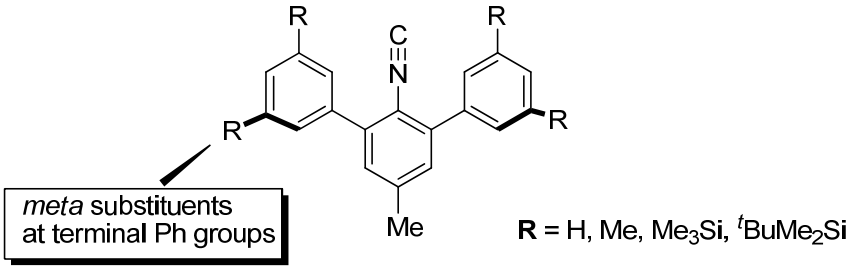
The hydrogenation and isomerization of 1-hexene was carried out in the presence of the insoluble catalyst under a constant positive hydrogen pressure of 0.5 atm at 25 °C. In the dark, hydrogenation of 1-hexene to n-hexane also involves isomerization to *trans*- and *cis*- hexenes which subsequently hydrogenated to n-hexane. While in the presence of UV irradiation, the formation of n-hexane slowed down substantially. Isomerization was observed at a somewhat earlier stage in the presence of light but no hydrogenation of isomers was observed.

6.3 Hydrosilylation with rhodium-isonitrile complex

In 1985 *Nile* group explored Rhodium complexes of sterically hindered 2,6-disubstituted-phenylisonitriles for hydrosilylation reaction.[34] The use of this isonitrile, together with 2,6-dimethylphenylisonitrile, as ligands for complexes of Group VIA metals and rhodium, which were catalysts for the hydrosilylation of a variety of unsaturated species, and for the metathesis of alkynes. The optimum yield of 1-octyltriethylsilane from 1-octene and triethylsilane was obtained at XNC/Rh ratio of 2:1 (Yields = 1:1, 69%; 2:1, 82%; 3:1, 61%; 4:1, 0%), while with the bulky ArNC, the catalyst remained active even at a higher ratio of 10:1. The Rh-isonitrile complexes showed higher reactivity towards alkylsilanes as compared to alkoxysilanes such as the yield of 1-octylsilane at 20 ℃ falls in the order $HSiMe_2Ph$ (81%) > $HSiEt_3$ (66%) > $HSi(OEt)_3$ (40%).

Hydrosilylation of acetophenone with dimethylphenylsilane was also achieved using $PtCl_2(2,6\text{-}Me_2C_6H_3NC)_2$ at room temperature.[35] The catalytic activity of the platinum isonitrile complexes was higher than the phosphines. The rhodium complexes of bulky

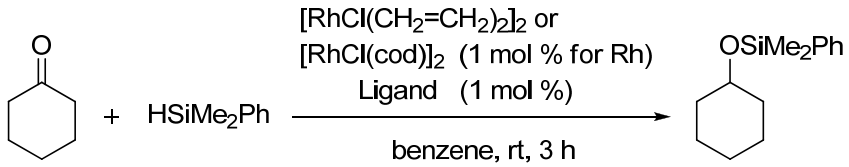
isonitrile ligands with *meta*-terphenyl backbone (Figure 7) were developed by *Sawamura et al*.[36] and their catalytic activity was illustrated by application to hydrosilylation of cyclohexanone with dimethylphenyl silane in benzene at room temperature (Table 3).



33

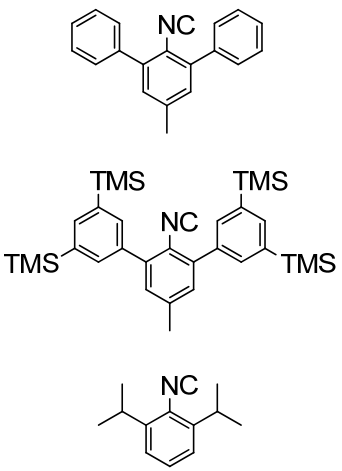
Figure 7. Bulky isonitrile ligands with meta-terphenyl backbone.

Table 3. Hydrosilylation in the presence of neutral Rh-isonitrile complex with various isonitrile and phosphine ligands.



ligands (**R**)	yield %
-	15
H	48
Me_3Si	97
2,6-diisopropylphenylisocyanide	63
PPh_3	24

Ligands 34

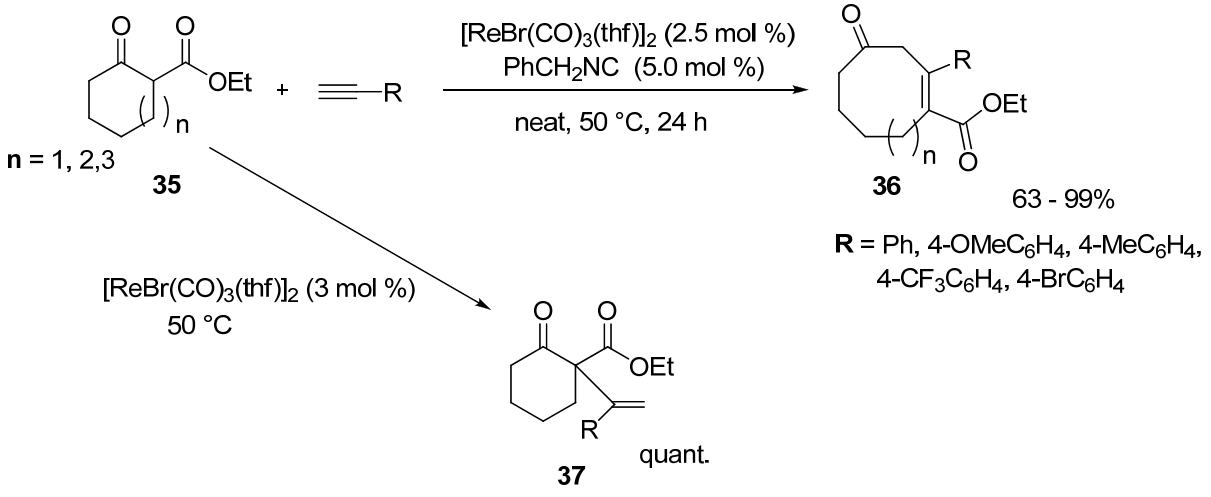


The highest activity was proceeded with Rh/L at a ratio 1:1. The acceleration effect on hydrosilylation reaction which varied with bulkiness of ligands was evaluated with each

ligand. Sterically less demanding isonitriles (**34**) (**R** = H, Me, 2,6-diisopropylphenylisonitrile) exhibited less acceleration effect compared to sterically more demanding ligands (**34**) (**R** = Me_3Si, $^tBuMe_2Si$) due to their concave steric features.

6.4 Insertion using rhenium-isonitrile complex

Recently, the insertion of terminal acetylenes into a Carbon-Carbon single bond next to a carbonyl group of nonstrained cyclic compounds was achieved by *Takai* and co-workers[37] using rhenium-isonitrile complex (Scheme 20). The reaction of cyclohexanone-2-carboxylic acid ethyl ester (**35**) with phenylacetylene in the presence of catalytic amounts of a rhenium complex, $[(ReBr(CO)_3(thf)]_2$[38], and benzyl isonitrile at 40 °C under solvent free conditions gave an eight-membered ring product (**36**). In the absence of isonitrile, the rhenium-catalyzed reaction of a,ß-keto ester with phenylacetylene afforded compound (**37**) in quantitative yield.



Scheme 20. Re-isonitrile complex catalyzed synthesis of eight-membered rings **36**.

7 Objectives

The list of applications of transition metal isonitrile complexes catalyzed reactions shows that isonitriles have been less frequently applied as ligands in metal catalysis. Thus, the effective transition metal isonitrile complexes catalysts in organic transformation are desirable.

In a first project, copper isonitrile complexes as catalysts will be investigated in "click" reaction, Ullmann-type coupling reaction, Sonogashira reaction. The goal of this project is to develop a versatile copper catalytic system which can give high reactivity and selectivity as well. The second project will involve the Pd isonitrile complexes as catalyst for Wacker oxidation. Terminal aliphatic and aromatic alkenes as substrates will be attempted in the reaction. In a third project, iron isonitrile catalyzed transfer hydrogenation will be investigated. The fourth topic will focus on photoluminescence-tuning Pt(II) cyclometallated complexes based isonitrile ligands outside of molecular catalysis of transition metal isonitrile complexes.

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B. Synthesis of isonitrile ligands

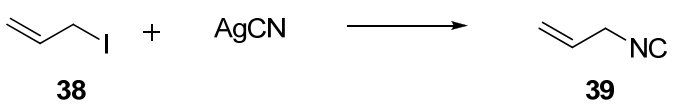
1 Introduction

An isonitrile ligand, having a donor carbon atom of low electronegativity and a potentially vacant orbital, may also act as a π acceptor of electrons with those elements also capable of back-donating electrons.[1] These properties of isonitriles make them act as nucleophiles as well as electrophiles in the course of a reaction. On the other hand, the chemistry of isonitriles is fundamentally different from the rest of organic chemistry, since they are one of the chemical compounds with divalent carbon atoms C^{II}, and all of their chemical reactions correspond to conversions of the divalent carbon atoms C^{II} into the tetravalent carbon atoms C^{IV}. Given the special role of isonitriles in organic and organometallic synthesis,[2,3] catalysis,[3a-c] materials science[4], drug discovery,[5] and diagnostic medicine,[6] it is predictable that isonitriles shall find expanding usage in organic and organometallic synthesis.

However, most of isonitriles are relatively unavailable commercially and can be challenging to prepare. Various types of reactions leading to isonitriles have been reported since 1859. The following methods have made available not only the simple isonitriles, but also difunctional isonitriles.

2 Important methods of isonitrile preparation

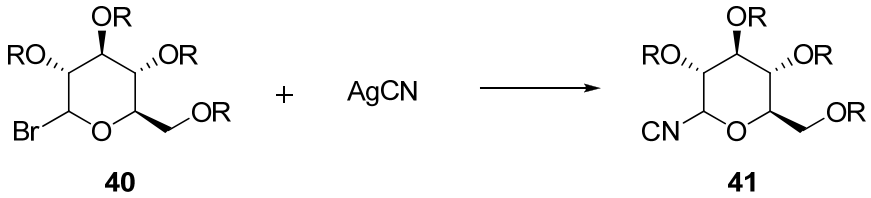
Isonitriles were first synthesized in 1859 by *Lieke*[7] employing a substitution reaction of reactive alkyl halides (**38**) with silver cyanide (Scheme 21).



38 **39**

Scheme 21. The first preparation of isonitriles by alkyl halides with silver cyanide.

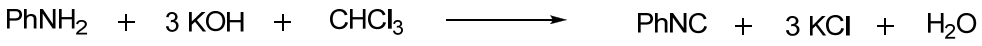
In 1866-1869, *Gautier* and co-worker further developed the preparation of methyl, ethyl, and isopropyl isonitriles by the reaction of silver cyanide with aryl halides (**40**) (Scheme 22).[8] After that, active alkyl or aryl halides, alkyl sulfate, diazomethane, and even organometallic halide have been used as alkylating agents,[9] but the yields of the isonitriles are usually low.



40 **41**

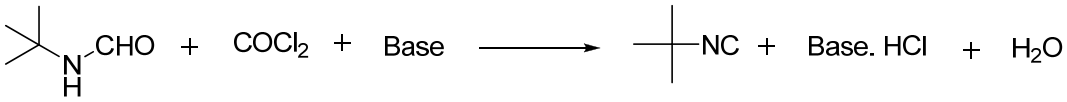
Scheme 22. An example of isonitriles by the reaction of silver cyanide and alkyl halides.

Contemporaneously with *Gautier*'s isonitrile synthesis, *Hofmann* found a new approach towards isonitriles with the reaction of primary amines, potash and chloroform (Scheme 23). During this period, the methods for preparation of isonitriles were facing a number of problems such as their cumbersome preparation, poor substrate tolerance (the availability of appropriate primary amines as starting materials) and relative low yields of products.



Scheme 23. The preparation of isonitriles by the reaction of primary amines, potash and chloroform.

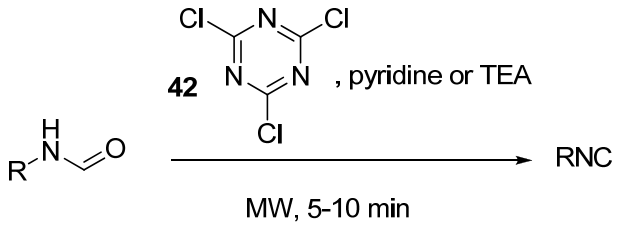
In 1958 *Ugi* and co-workers introduced a new method for synthesis of isonitriles by dehydration of formamides prepared from primary amines (Scheme 24).[11a] The formamides are conveniently prepared in good yields from the corresponding available amines. The reaction of N-formamides with phosgene as the anhydrating agent gives the best results considering cost, yield, and implementation in comparison to the above mentioned methods. *Ugi* and co-workers reported a variety of isonitriles prepared by the reaction of N-formamides with phosgene with phosgene.[11b]



Scheme 24. Dehydration of formamides towards isonitriles.

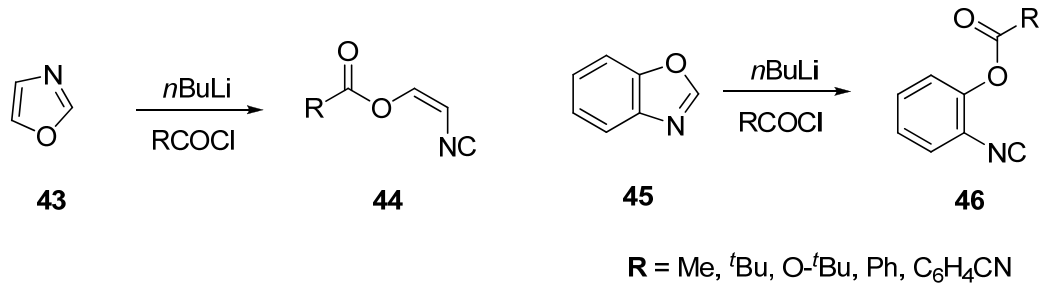
However, the extreme toxicity and cumbersome handling of phosgene prevent *Ugi*'s method becoming a general access to isonitriles. To circumvent the use of phosgene, much attention has been paid to new anhydrating agents of N-formamide. Up to now, dehydration of N-formamides was also achieved using $POCl_3$,[12] chlorodimethylforminium chloride,[13] DABCO,[14] aryl chlorothionformate,[15] supported sulfonyl chlorides under microwave irradiation.[16] Unfortunately, most of these methods have limited utility and applicability due to the low tolerance of substrates and high costs in the availability of the reagents. Sometimes the reagents employed require tedious preparation procedures or workup, and purification of the reaction product can be problematic due to the reactivity of the isonitriles.

A facile conversion of formamides to isonitriles under very mild conditions and microwave irradiation is described by *Porcheddu* and co-workers (Scheme 25). This simple and efficient method has been applied for the synthesis of both aliphatic and aromatic isonitriles in high yields, using 2,4,6-trichloro[1,3,5]triazine (cyanuric chloride, TCT) (**42**) as the anhydrating agent.[17]



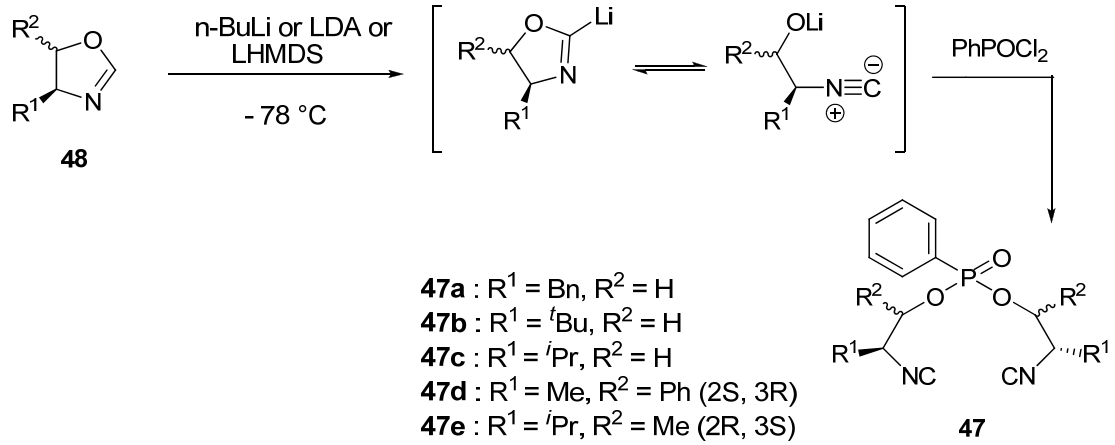
Scheme 25. Conversion of formamides RNHCHO to isonitriles by TCT/base methods.

Recently, *Pirrung* and co-workers[18] developed a new family of fragrant isonitriles by treating oxazole (**43**) or benzoxazole (**44**) with n-butyllithium and various acyl chlorides to generate a series of (Z)-isocyanovinyl esters (**45**) (Scheme 26) and 2-isocyanylphenyl esters (**46**), which smell of mild isonitrile at their worst and like taffy or cherry at their best.



Scheme 26. Synthesis of fragrant isonitriles from oxazoles.

Very recently, *Reiser* and co-workers synthesized a wide variety of sterically and electronically different chiral bis(isonitrile) ligands (**47**) by structural variation of the oxazolines (**48**) and phosphorus chloride (Scheme 27).[19] The chiral bis(isonitrile) ligands (**47a-e**) were prepared in moderate yields via lithiation of 2-oxazolines (**48a-e**) following the procedure of *Meyers* and *Novachek* and subsequent treatment with phenylphosphonic dichloride at low temperature (Scheme 27).[20]



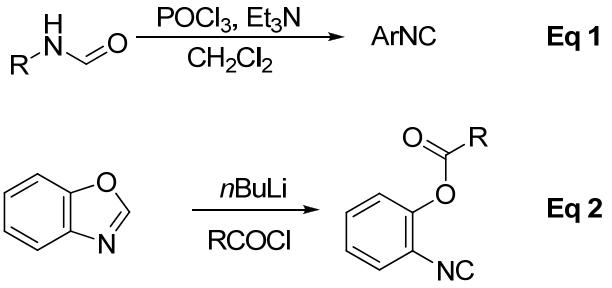
Scheme 27. Synthesis of BINC ligands (**47a-e**).

3 The isonitrile ligands to be investigated in catalysis

Starting from the idea that the presence of isonitrile ligands coordinating the metal center is the most important factor in determining the efficiency of the catalyst system, we initiated a

research program aimed at synthesizing electronically different isonitrile ligands to broaden the application of isonitriles in catalysis.

Based on the above mentioned methods for preparation of isonitriles, a variety of electronically different isonitriles (**49-53**) were prepared by classic methods *i.e*. dehydration of N-formamides using $POCl_3$ (Eq 1, Scheme 28). Following the procedure of *Pirrung*,[17] preparation of the isonitrile ligands (**54-55**) was achieved (Eq 2, Scheme 28).



Scheme 28. Synthesis of different functional ligands (**49-55**).

The isonitrile ligands to be investigated in catalysis are summarized in Figure 8. In order to get good yields one should work up the reaction mixture as quickly as possible and avoid unnecessary heating of the crude isonitrile. If it is to be stored for a long time, it should be kept at minus temperature.

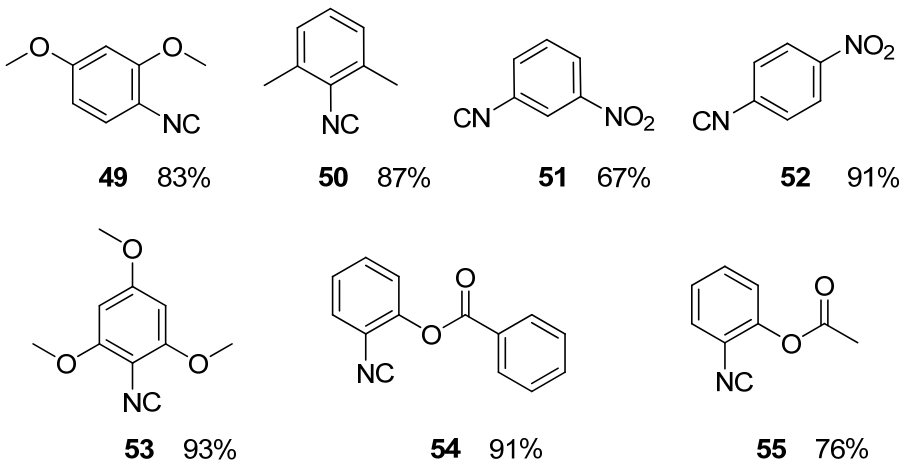


Figure 8. Isonitrile Ligands to be investigated (**49-55**).

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C. Copper(I)-Isonitrile Complexes

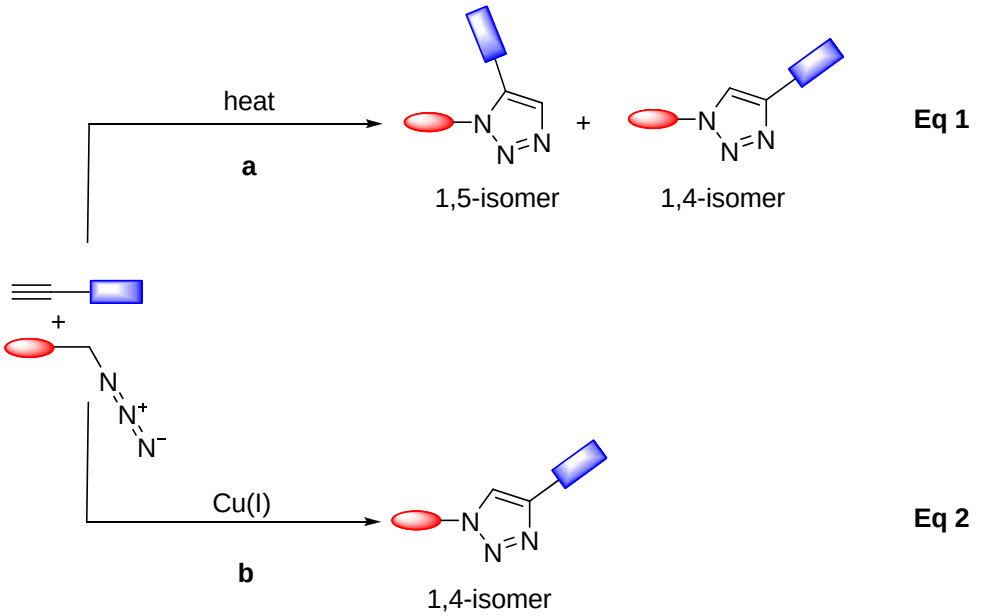
Part I. Click reaction catalyzed by copper(I)-isonitrile complexes

1 Introduction

Click chemistry is a chemical philosophy introduced by *Sharpless* in 2001 and it relies on click reactions which generate substances quickly and reliably by joining small units together.[1] Click reaction would be a set of nearly perfect reactions with respect to reliability, modularity, selectivity, and experimental simplicity. The use of environmentally benign solvents, mild conditions, and readily available reagents are also key criteria to click reactions.[1, 2]

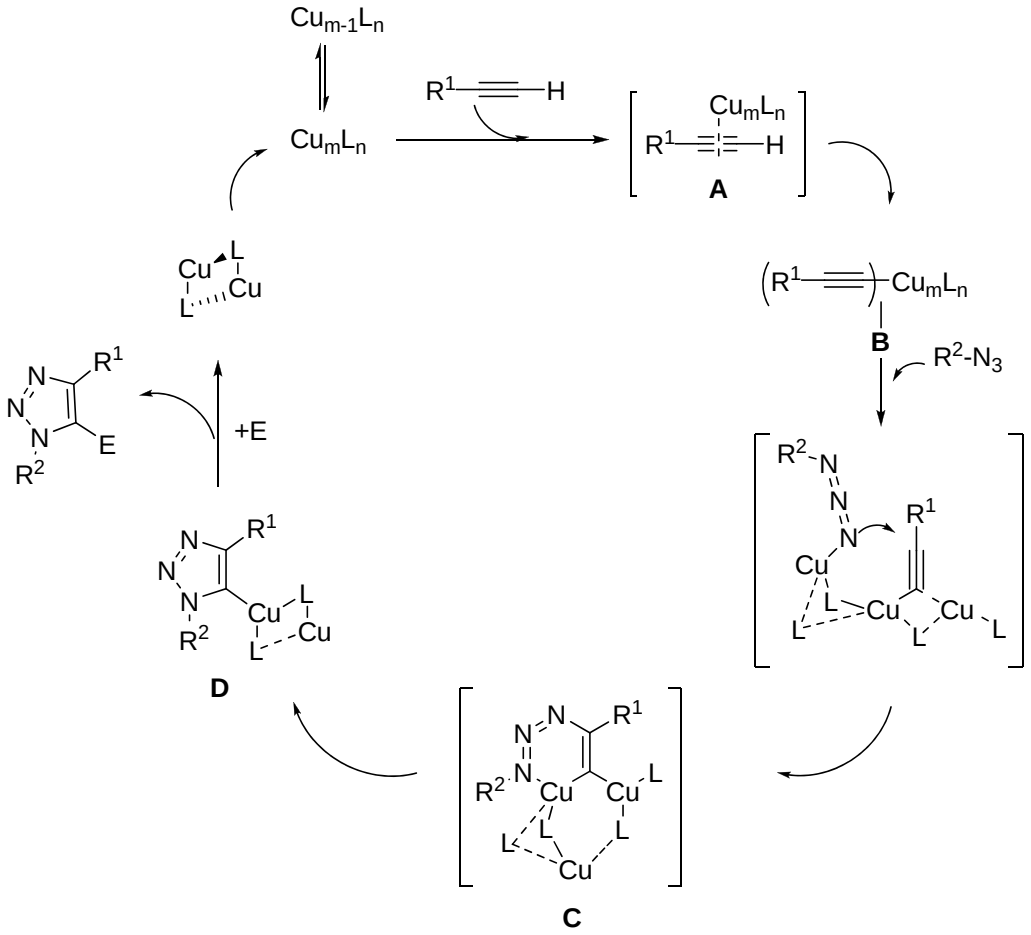
Since *Rolf Huisgen* has made great contributions in cycloaddition reactions and firstly proposed the generalized concept of the 1,3-dipolar cycloaddition, these reactions were named as Huisgen cycloaddition.[3] The reaction between an azide and a terminal alkyne is one of the most popular 1,3-dipolar Huisgen cycloaddition reactions.[4] Under thermal conditions, this reaction usually affords a mixture of 1,4- and 1,5-disubstituted regioisomers (Scheme 29, Eq 1). However, the practical regioselectivity control is very difficult to achieve using steric or electronic influences and regioisomers are often non-trival to separate.

Recently, it was found that the copper(I) catalyzed azide alkyne cycloaddition (CuAAC) gives exclusively a 1,4-regioisomeric triazole, which was discovered independently by the groups of *Meldal* and *Sharpless*.[5] The copper(I)-catalyzed Huisgen [3+2] dipolar cyclo-addition (CuAAC) between alkynes and azides has become an exemplary click reaction (Scheme 29, Eq 2), since it meets with the gold standard of click chemistry. Due to its efficiency and simplicity, this reaction has arguably become the most popular ligation reaction, and has been widely applied in many areas such as polymer and combinatorial organic synthesis, advanced material science, surface science, etc.[6]



Scheme 29. 1,3-Dipolar cycloaddition between an azide and a terminal alkyne.

The mechanism of the CuAAC reaction has been extensively reviewed (Scheme 30).[7] Copper(I) coordinates first with the acetylene π electrons **A**, thereby lowering the pKa of the acetylene proton followed by exothermal formation of copper-acetylide cluster **B**. The Cu^{+} acetylide cluster **B** coordinates to the azide followed by rearrangement of the complex in a stepwise manner *via* a six-membered metallacycle **C** and further to the copper-metallated triazole **D**. Finally, the copper-triazole complex eventually releases the regioselective formation of the 1,4-triazole and $L_nCu(I)$ by protonation or reaction with electrophiles.



Scheme 30. The mechanism of the CuAAC reaction.

Much attention has been paid to the development of copper(I) catalytic systems for CuAAC reactions. Most of the reported copper(I) catalytic species were prepared *in situ* by reduction of Cu(II) salts[8], oxidation of Cu(0) metal[9], or Cu(II)/Cu(0) comproportionation[10]. Copper(I) salts are less used due to their general thermodynamic instability, with copper(I) iodide being a notable exception.[6d,11] The latter, however, requires the employment of amines as additives. However, *Fokin* and co-workers recommended against the use of cuprous iodide because of the ability of iodide anion to act as a bridging ligand for the metal, resulting in the formation of polynuclear acetylide complexes which interfere with the productive catalytic cycle by tying up the catalyst.[12]

To circumvent the drawbacks of copper(I) salts, copper(I) complexes involving ligands have been reported as catalysts for the CuAAC reaction. It has been proven to be accelerated by

Cu(I) species supported by nitrogen[13], sulfur[14], NHC[15], and polydentate ligands[16] (**56**-**59**) since those serve both to protect the copper(I) center from oxidation or dispropotionation and to enhance its catalytic activity (Figure 9). However, most of above mentioned supported copper(I) catalysts are always not easily prepared. Owing to isonitriles' electronic properties, being strong σ-donor ligands comparable to *N*-heterocyclic carbenes (NHCs), the exploration of copper isonitrile complexes as catalysts appears to be promising in CuAAC reaction.

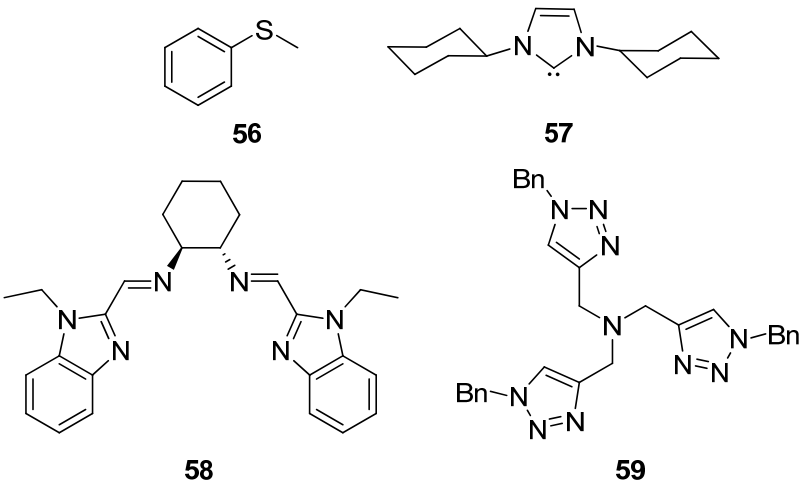


Figure 9. Ligands of copper(I) complexes in CuAAC reactions.

On the other hand, the reusability of heterogeneous copper catalysts for the CuAAC reaction is scarcely studied [17] (Figure 10) because of the generally homogeneous nature of the above ligand-supported catalysts, which renders their recovery and recycling difficult. Considering the virtues of ligands and heterogeneous catalysts, we set out to develop a practical, heterogeneous, ligand-supported copper(I) catalyst without the need of immobilization on a polymeric or an inorganic support.

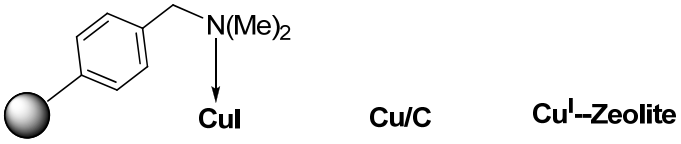
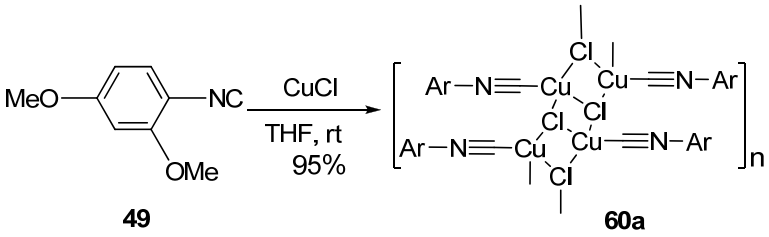


Figure 10. Heterogeneous catalysts in CuAAC reactions.

2 Synthesis of copper-isonitrile complexes

The isonitrile ligand (**49**) was prepared following literature procedures.[18] Upon treatment of 1.05 equiv. (**49**) with 1.0 equiv. CuCl in THF, the off-white complex (**60a**) was obtained in 95% yield that is stable in air or water for several months (Scheme 31). Furthermore, the complex (**60a**) is insoluble in water and common organic solvents such as THF, ethanol, acetone, and ethyl acetate but soluble in acetonitrile and DMF.



49 **60a**

Scheme 31. The synthesis of copper-isonitrile (**60a**).

The complex (**60a**) was characterized by NMR spectroscopy as well as X-ray crystallographic analysis. Suitable single crystals for X-ray diffraction were obtained by slow diffusion of hexane into a concentrated DCM solution of the complex (**60a**). The latter revealed (Figures 11, 12) that each Cu(I) center is coordinated to an isonitrile ligand and possesses three bridging chloride atoms that coordinate to another Cu(I) center of the next molecule. Hence, the [CuLCl] units are linked into an extended one-dimensional chain polymer, contrasting an earlier report on copper($CNAr^{Mes2}$) (Mes = 2,4,6-$Me_3C_6H_2$) (**61-62**) resided as bridging halide complexes rather than as one-dimensional chain structures (Scheme 32).[19]

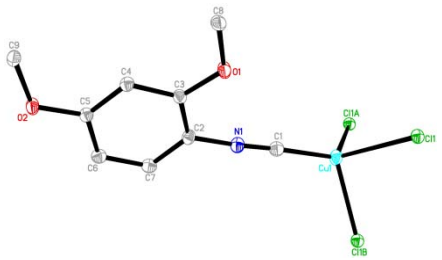


Figure 11. Coordination environment of Cu(I) in $[CuLCl]_n$.

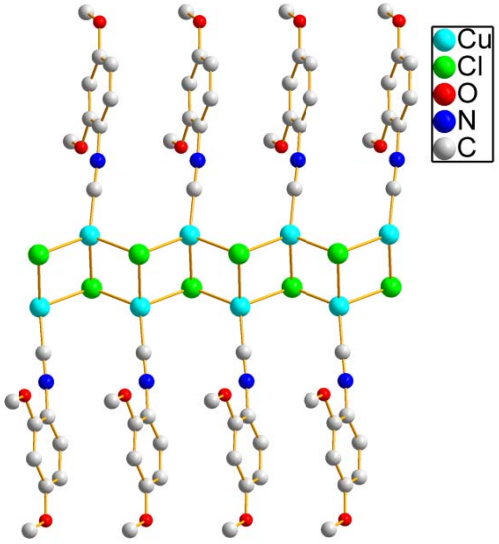
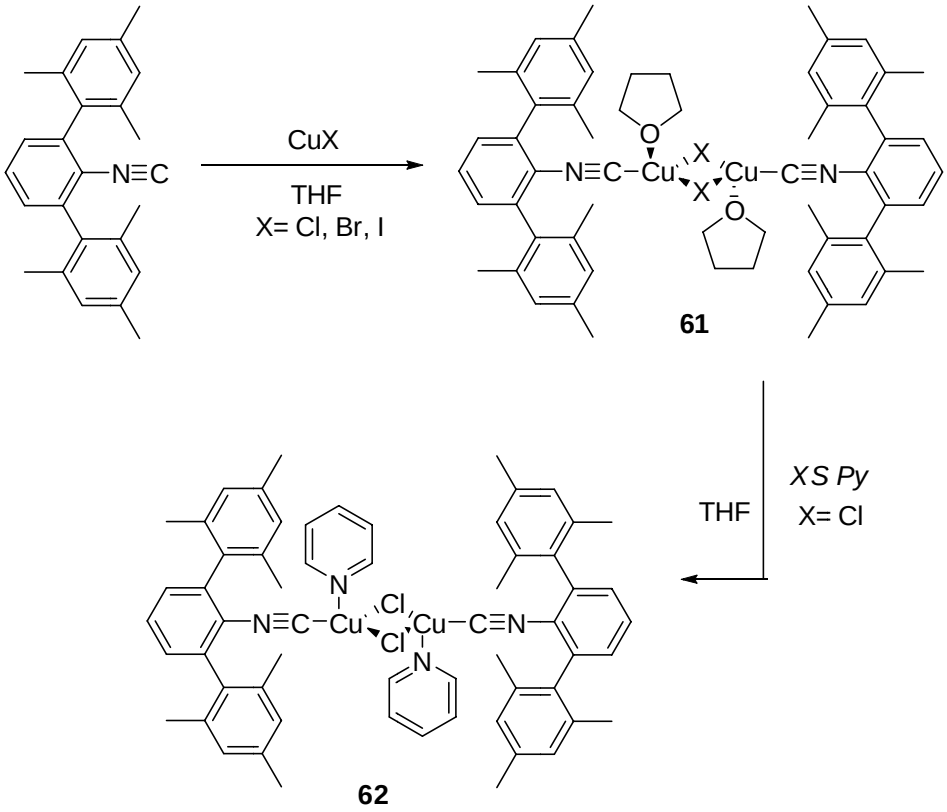


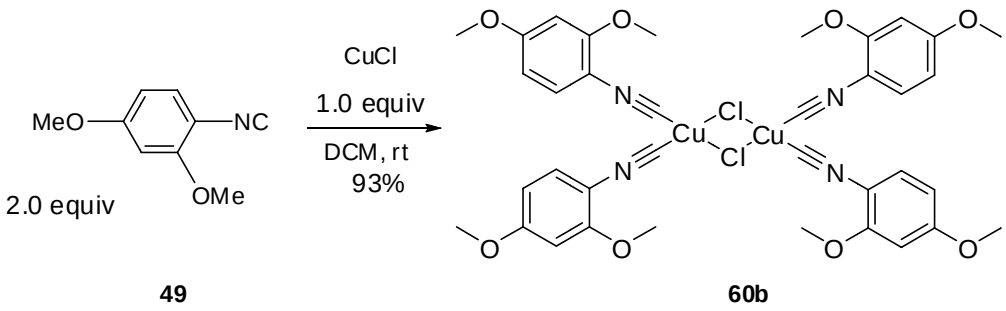
Figure 12. One-dimension chain structure of (**60a**) (color codes: Cu Cyan, Cl green, O red, N blue, C grey).



Scheme 32. copper($CNAr^{Mes2}$) (Mes = 2,4,6-$Me_3C_6H_2$) resided as bridging halide complexes.

Upon treatment of 2.0 equiv. (**49**) with 1.0 equiv. CuCl in DCM, the white complex (**60b**) was obtained in 93% yield that is stable in air or water for several months (Scheme 33). In

remarkable contrast, the complex (**60b**) is soluble in common organic solvents such as THF, ethanol, acetone, ethyl acetate, acetonitrile and DMF.



49 **60b**

Scheme 33. The synthesis of copper isonitrile (**60b**).

The complex (**60b**) was also characterized by NMR spectroscopy as well as X-ray crystallographic analysis. The latter revealed (Figure 13) that each Cu(I) center is coordinated to two isonitrile ligands and possesses two bridging chloride atoms that coordinate to another Cu(I) center of the next molecule. Hence the $[CuL_2Cl]$ units are linked into bridging halide complexes, contrasting an earlier report on the structure of $ClCu(CN\text{-}t\text{-}Bu)_2$ as a structurally characterized monomeric, $XCu(CNR)_2$ ((X) halide) species rather than as bridging halide complexes.[19]

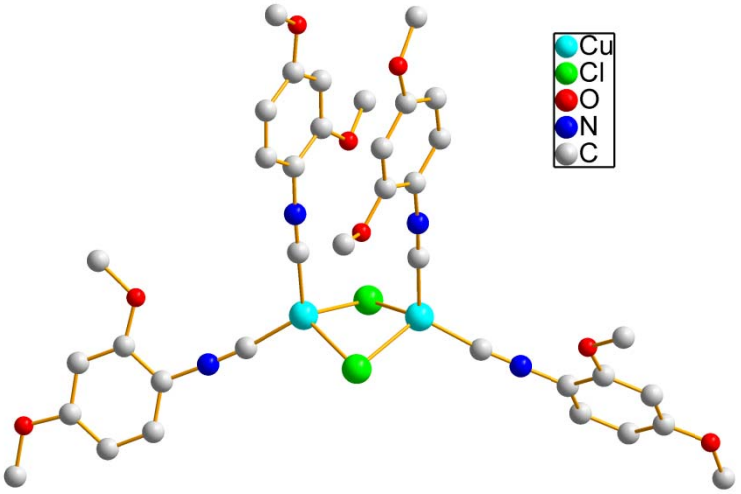
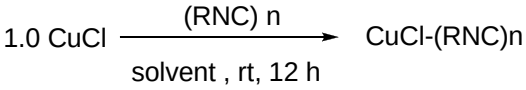
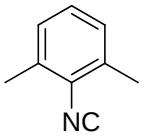
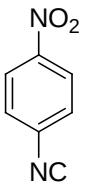
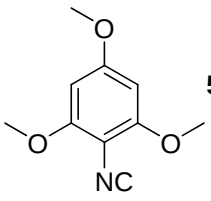
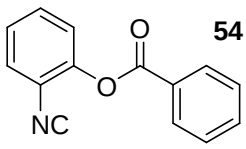


Figure 13. The molecular structure of (**60b**) (color codes: Cu Cyan, Cl green, O red, N blue, C grey).

In comparison, we prepared other copper(I) complexes [CuCl(RNC)$_{1-2}$] of electronically different isonitriles: from 1,3-dimethylphenylisonitrile (**50**), from 4-nitrobenzeneisonitrile (**52**), from 2-isocyano-1,3,5-trimethoxybenzene (**53**) and from 2-isocyanophenylbenzoate (**54**). Complexation of (**50, 52, 53, 54**) with CuCl in dichloromethane or tetrahydrofuran at room temperature gave rise to the corresponding [CuCl(RNC)$_{1-2}$] complexes (**63-66**) in good yields (Table 4), which were characterized by ^{1}H NMR and IR spectroscopy as well as HR-Mass analysis.

Table 4. Copper(I) complexes [CuCl(RNC)$_{1-2}$] of different functional isonitriles.

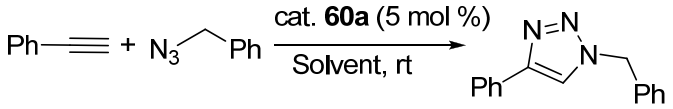


entry	isonitrile ligand	addition/ solvent	complex	yield (%)
1	 **50**	1.05 equiv/ THF	**CuCl-L$_1$ 63a**	89
2		2.1 equiv/ DCM	**CuCl-L$_2$ 63b**	75
3	 **52**	1.05 equiv/ THF	**CuCl-L$_1$ 64a**	71
4		2.1 equiv/ DCM	**CuCl-L$_2$ 64b**	59
5	 **53**	1.05 equiv/ THF	**CuCl-L$_1$ 65a**	82
6		2.1 equiv/ DCM	**CuCl-L$_2$ 65b**	87
7	 **54**	1.05 equiv/ THF	**CuCl-L$_1$ 66a**	79
8		2.1 equiv/ DCM	**CuCl-L$_2$ 66b**	71

3 Results and discussion

The activity of CuCl(RNC) complex (**60a**) was investigated in the Huisgen cycloaddition with benzyl azide (**67a**) and phenylacetylene (**68a**) as model substrates. The amount of copper catalyst (5 mol %) and the reaction time (1 h) were the same for the evaluation. Firstly, we evaluated the solvent effect in the cycloaddition reaction. As evident from Table 5, entries 1-7, the reaction works in different organic solvents (48-85%) in the presence of 5 mol % of the catalyst (**60a**). To our delight, treatment of two components with (**60a**) in water afforded the corresponding triazole (**67a**) smoothly in 98% yield after stirring at room temperature. In fact, the cycloaddition reached completion within 5 min (entry 9, Table 5). Moreover, no other additive was needed for this reaction. The reaction was found to proceed smoothly in 78% yield under neat conditions. No precautions to exclude oxygen or moisture were undertaken during the screenings of organic solvents. Neither copper disproportionation with the precipitation of metallic copper nor copper oxidation was observed under the optimized reaction conditions even in water, which indicates the high ability of isonitrile to stabilize copper(I) species. It is similar with the NHCs which can stabilize copper(I) species in CuAAC reaction. Since water is a green solvent, we chose it as the solvent for further optimization.

Table 5. Solvent optimization studies.[a]



67a **68a** **69a**

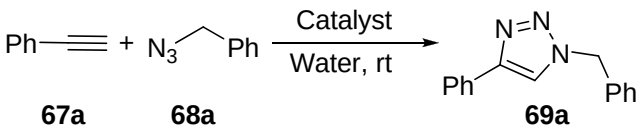
entry	catalyst	solvent	yield (%)[b]
1	**60a**	THF	85
2	**60a**	H_2O-*t*-BuOH	94
3	**60a**	*i*-PrOH	34
4	**60a**	MeOH	42

5	**60a**	DMF	61
6	**60a**	Acetone	59
7	**60a**	DMSO	48
8	**60a**	Neat	78
9[c]	**60a**	H_2O	98

[a]Reagents and reaction conditions: **67a** (1.05 mmol), **68a** (1.0 mmol), and catalyst **60a** (5 mol %) in the given solvent was stirred at room temperature for 1 h unless otherwise stated. [b]Isolated yields as an average of at least two independent experiments. [c]Reaction time (10 min).

We then used water as the reaction solvent to test other copper catalysts. As expected, in the presence of 5 mol % common copper catalysts (CuI, CuCl, CuBr, CuCN) in water, the reaction did not perform well to give (**69a**) in 4-32% yield (Table 6, entries 1, 3, 5, 7). Even when the reaction was treated with 50 mol % CuI, CuCl, CuBr, CuCN, only low to modern yields were obtained. It was indicated that common copper salt could also catalyze the cycloaddition reaction, however, it always required a large amount of catalyst and extended reaction time with the exception of $[(CuOAc)_2]_n$ (Table 6, entry 8) which was recently reported to be a highly efficient catalyst for this reaction.[20] Finally, compared to the previous reported CuCl system, which required higher temperature, this new copper complex (**60a**) was found to be a promising and effective catalyst for the Huisgen cycloaddition in water under mild conditions.

Table 6. Catalyst optimization studies.[a]



67a **68a** **69a**

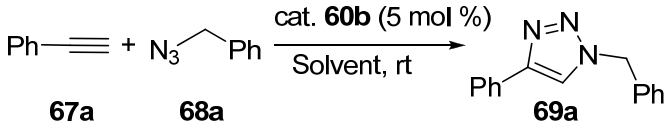
entry	catalyst	time (min)	yield (%)[b]	cat (mol %)
1	CuCl	60	32	5
2	CuCl	60	59	50
3	CuI	60	4	5
4	CuI	60	62	50

5	CuBr	60	15	5
6	CuBr	60	66	50
7	CuCN	60	6	5
7	CuCN	60	22	50
8	CuOAc	10	98	5
9	**60a**	60 (5)	98	5

[a]Reagents and reaction conditions: **67a** (1.05 mmol), **68a** (1.0 mmol), and catalyst (5 mol %) in the given solvent was stirred at room temperature for 1 h unless otherwise stated. [b]Isolated yields as an average of at least two independent experiments.

In contrast, the activity of $CuCl(RNC)_2$ complex (**60b**) was investigated in the Huisgen cycloaddition with benzyl azide and phenylacetylene as model substrates. The amount of copper catalyst (5 mol %) and the reaction time (1 h) were the same for the evaluation. Unfortunately, treatment of two components with (**60b**) afforded the corresponding triazole (**69a**) in lower 81% yields with longer reaction time in different solvents even in homogeneous cases in comparison with the obtained results of (**60a**) (Table 7).

Table 7. Azide-alkyne cycloaddition catalyzed with (**60b**).[a]



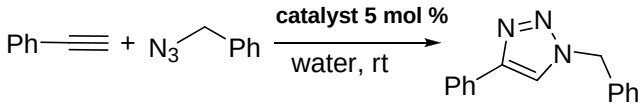
67a **68a** **69a**

entry	catalyst	solvent	Time(min)	yield (%)[b]
1	**60b**	THF	3600	32
2	**60b**	H_2O-^{t}BuOH	45	73
3	**60b**	MeOH	3600	36
4	**60b**	H_2O	30	81
5	**60b**	acetonitrile	180	68

[a]Reagents and reaction conditions: **67a** (1.05 mmol), **68a** (1.0 mmol), and catalyst **60b** (5 mol %) in the given solvent was stirred at room temperature. [b]Isolated yields as an average of at least two independent experiments.

Next, all of the other Cu(I)-isonitrile complexes were examined for their catalytic activities in CuAAC of phenylacetylen (**67a**) with benzyl azide (**68a**) in comparison of the two structurally well-defined complexes (**60a**) and (**60b**) under the above optimum conditions. Results were summarized in Table 8. Excellent yields obtained strongly suggest that [CuCl(RNC)$_{1\text{-}2}$] with various functional isonitriles can promote CuAAC reaction under short reaction time. The reason for the high activity that is conferred by the isonitrile ligands for the CuAAC might be that these ligands are similar in their electronic properties like nucleophilic carbenes that have shown to give excellent results for the CuAAC reaction.[15] The structurally well-defined complex (**60a**) was the more efficient of [CuCl(RNC)$_{1\text{-}2}$] complexes as catalyst in the CuAAC reaction.

Table 8. CuAAC in the presence of various Cu(I)-isonitrile complexes.[a]



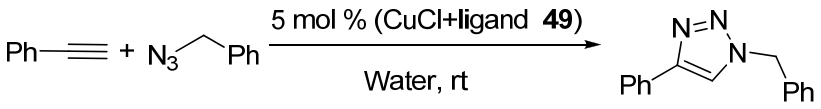
67a **68a** **69a**

entry	catalyst	reaction time (min)	yield (%)
1	**63a**	30	96
2	**63b**	30	83
3	**64a**	30	81
4	**64b**	30	89
5	**65a**	30	72
6	**65b**	30	85
7	**66a**	30	89
8	**66b**	30	94
9	**60a**	30	98
10	**60b**	30	81

[a]Reagents and reaction conditions: **67a** (1.05 mmol), **68a** (1.0 mmol), and catalyst (5 mol %) in the given solvent was stirred at room temperature. [b]Isolated yields as an average of at least two independent experiments.

Copper(I) complexes formed *in situ* with the isonitrile ligand (**49**) were tested for CuAAC reaction of phenylacetylen (**67a**) with benzyl azide (**68a**) in water. As is evident in Table 9, the reaction gave the corresponding triazole (**69a**) in 85% yield with 45 min at a ratio (1:1) of CuCl:RNC. At a ratio (1:2) of CuCl:RNC, it afforded the corresponding triazole (**69a**) in lower 73% yields with longer reaction time. The fact suggests that the *in situ* copper complexes have less effectivity than copper isonitrile complex (**60a**).

Table 9. Catalyst optimization studies.[a]



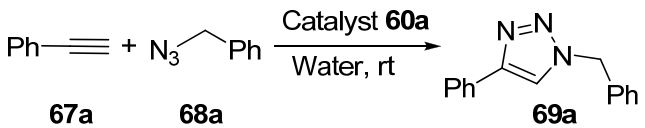
67a **68a** **69a**

Entry	CuCl:ArCN	time (min)	yield (%)[b]	cat. (mol %)
1	1:1	45	85	5
2	1:2	120	76	5

[a]Reagents and reaction conditions: **67a** (1.05 mmol), **68a** (1.0 mmol), and catalyst (CuCl+ Ligand **49**) (5 mol %) in the given solvent was stirred at room temperature for 1 h unless otherwise stated. [b]Isolated yields as an average of at least two independent experiments.

Having identified water as the best solvent and the complex (**60a**) as the best catalyst for the reaction, we next investigated catalyst loading and recyclability for the title reaction (Table 10). Gratifyingly, upon lowering the catalyst concentration to 0.5 mol % the reaction still proceeded within 30 min in 91% yield (Table 10, entry 2). A catalyst loading of 2 mol % appeared to be optimal with respect to yield and short reaction times (Table 10, entries 3, 4).

Table 10. CuAAC with different loading of catalyst **60a**.[a]



67a **68a** **69a**

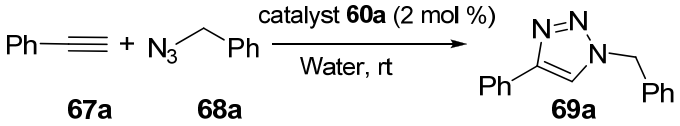
entry	catalyst (mol %)	time (min)	yield (%)[b]
1	5	10	98

2	2	10	96
3	0.5	30	91
4	2	5	94

[a]Reagents and reaction conditions: **67a** (1.05 mmol), **68a** (1.0 mmol), and catalyst **60a** (0.5-5 mol %), water. [b]Isolated yields after complete conversion of the starting materials as an average of at least two independent experiments.

Starting with catalyst loading of 2 mol %, the reaction was performed through 5 cycles on a 15.0 mmol scale each (Table 11). After each cycle the heterogeneous catalyst was recovered by simple filtration and reused without further purification. High yields (93-98%) were achieved at every run, and after five runs 50% of the initial amount of (**60a**) was still recovered. We attribute the overall loss of the catalyst to transfer operations between the filter and the reaction flask.

Table 11. Recyclability experiments.[a]



67a **68a** **69a**

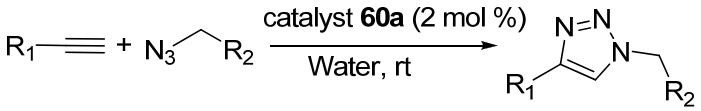
entry	run	time (min)	yield (%)[b]	recovery of catalyst based on the initial amount (%)
1	1	10	98	92
2	2	10	96	83
3	3	10	96	72
4	4	10	97	62
5	5	10	93	50

[a]Reagents and reaction conditions: **67a** (15.75 mmol), **68a** (15.0 mmol), and catalyst **60a** (78 mg, 0.30 mmol, 2 mol %). [b]Isolated yields.

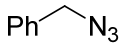
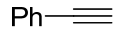
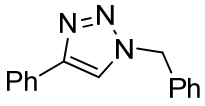
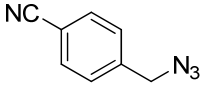
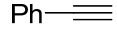
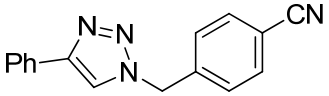
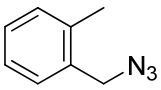
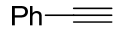
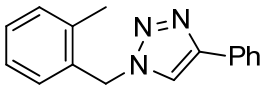
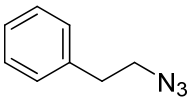
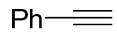
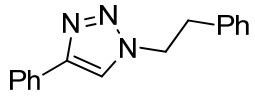
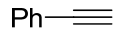
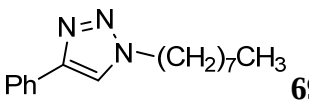
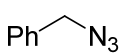
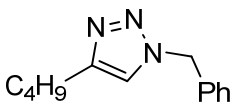
Having optimized the reaction conditions, the catalyst (**60a**) was applied to the cycloaddition reaction of electron-rich, electron-poor, hindered and dialkynes at room temperature in water to give the corresponding triazoles (**69a-69q**) in high yields (Table 12, entries 1-17). A broad

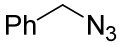
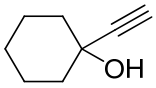
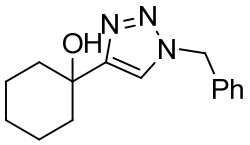
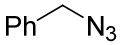
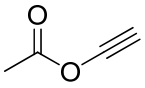
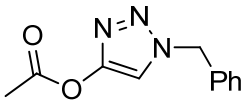
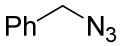
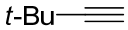
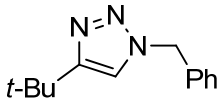
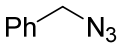
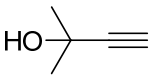
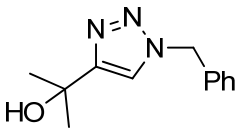
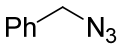
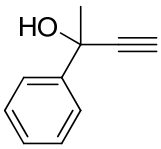
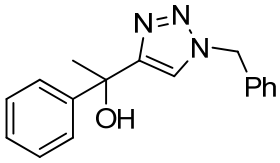
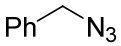
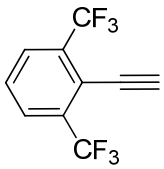
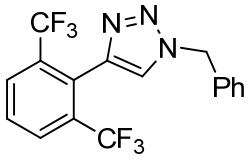
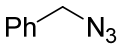
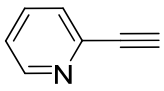
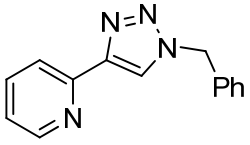
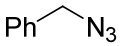
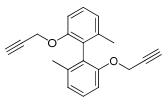
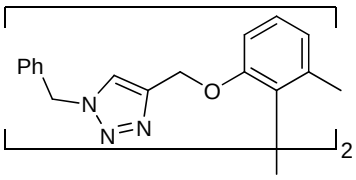
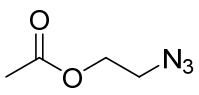
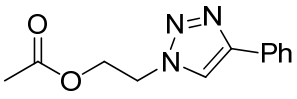
variety of azides equipped with various functional moieties such as alcohol, ketone, pyridine, nitrile, and fluoride was successfully employed. The methodology can be extended to dialkyne (**67n**) to afford the targeted triazole (**69n**) (Table 12, entry 14), which suggests that the catalyst (**60a**) has a high potential application in the synthesis of bidentate ligands. However, an internal alkyne was unsuccessfully used in this copper-catalyzed cycloaddition reaction (Table 12, entry 18).

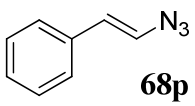
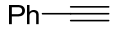
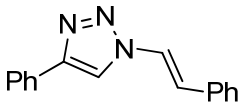
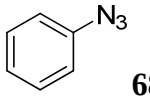
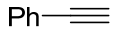
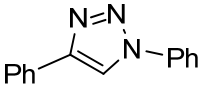
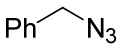
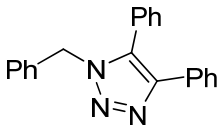
Table 12. Azide-alkyne cycloaddition catalyzed with (**60a**).[a]



67 **68** **69**

entry	azide (**68**)	alkyne (**67**)	time (min)	triazole (**69**)	yield (%)[b]
1	 **68a**	 **67a**	5	 **69a**	94
2	 **68b**		10	 **69b**	91
3	 **68c**		50	 **69c**	92
4	 **68d**		30	 **69d**	89
5	CH_3-$(CH_2)_7$-N_3 **68e**		10	 **69e**	96
6		C_4H_9— **67f**	30	 **69f**	93

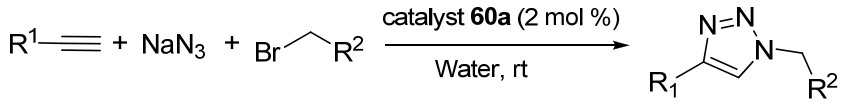
7		 **67g**	30	 **69g**	89
8		 **67h**	90	 **69h**	98
9		 **67i**	240	 **69i**	85
10		 **67j**	45	 **69j**	92
11		 **67k**	360	 **69k**	89
12		 **67l**	45	 **69l**	92
13		 **67m**	180	 **69m**	87
14		 **67n**	180	 **69n**	76
15	 **68o**		45	 **69o**	93

16	 **68p**		60	 **69p**	95
17	 **68q**		30	 **69q**	85
18[c]		 **67r**	560	 **69r**	21

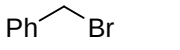
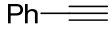
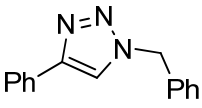
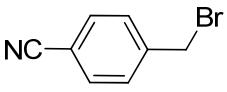
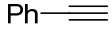
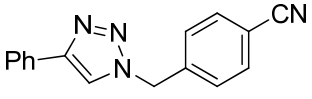
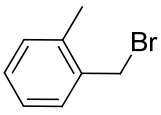
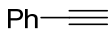
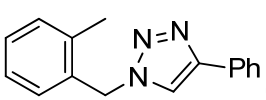
[a]Reagents and reaction conditions: **67** (1.05 mmol), **68** (1.0 mmol), and catalyst **60a** (5 mg, 2 mol %), water. [b]Isolated yields as an average of at least two independent experiments. [c]The reaction was run at 70 ℃.

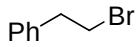
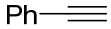
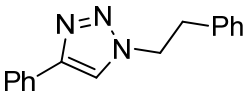
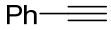
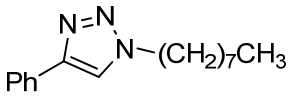
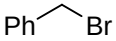
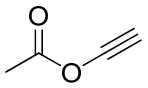
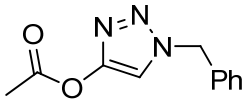
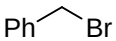
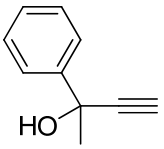
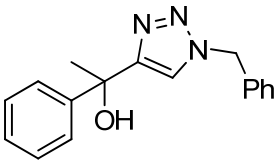
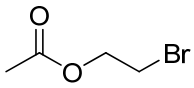
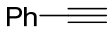
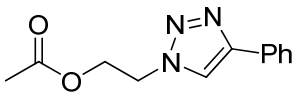
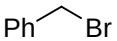
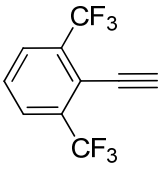
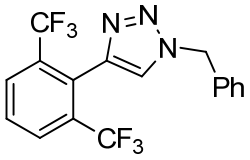
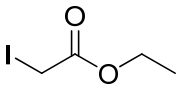
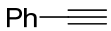
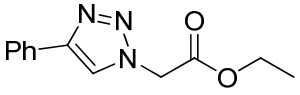
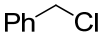
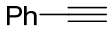
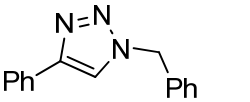
The performance of (**60a**) as an excellent catalyst was witnessed in two-component azide-alkyne click reaction in water as shown in Table 12. Inspired by recent work of *Hor* group, we turned our attention towards the three-component (alkyl halide, sodium azide, and alkyne) azide-alkyne cycloaddition reaction. As evident from Table 13, the catalyst (**60a**) can function in pure water to give the desired products (Table 13, entries 1-11) in isolated yields (84-97%), and a number of functional groups were tolerated.

Table 13. Azide-alkyne cycloaddition catalyzed with **60a**.[a]



67 **70** **69**

entry	alkyl halide (**70**)	alkyne (**67**)	time (h)	triazole (**69**)	yield (%)
1	 **70a**		2	 **69a**	95
2	 **70b**		1	 **69b**	93
3	 **70c**		3	 **69c**	84

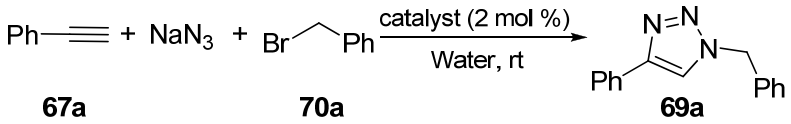
4	 **70d**		5	 **69d**	88
5	CH_3-$(CH_2)_7$-Br **70e**		3	 **69e**	94
6		 **67h**	8	 **69h**	95
7		 **67k**	1	 **69k**	92
8	 **70o**		7	 **69o**	91
9		 **67l**	1	 **69l**	90
10	 **70s**		3	 **69s**	91
11	 **70t**		1	 **69a**	97

[a]Reagents and reaction conditions: **67** (1.05 mmol), NaN_3 (1.05 mmol), alkyl halide **70** (1.0 mmol) and catalyst **60a** (5 mg, 2 mol %). [b] Isolated yields as an average of at least two independent experiments. [c] alkyl halide = ethyl 2-iodoethanoate. [d] alkyl halide = benzylchloride.

As a rule, the copper complexes formed *in situ* with ligands as catalyst will be easily prepared if the heterogeneous catalysis will not be considered any more. Thus, the two copper complexes formed *in situ* with ligands as catalyst were studied (Table 14). Though CuI has often been selected as the copper source, anhydrous conditions were required. However, the

CuI complex is more effective in water. The results further indicate the high ability of isonitrile to stabilize copper(I) species in water.

Table 14. Catalyst optimization studies.[a]



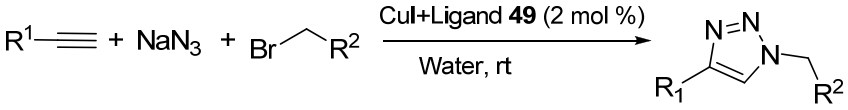
67a **70a** **69a**

entry	catalyst	time (h)	yield (%)[b]
1	2 mol % CuCl+RNC	2	85
2	2 mol % CuI+RNC	1.5	94

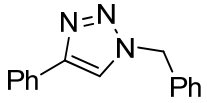
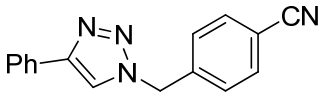
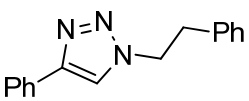
[a]Reagents and reaction conditions: **67a** (1.05 mmol), **70a** (1.0 mmol), and catalyst (2 mol %), water. [b]Isolated yields as an average of at least two independent experiments.

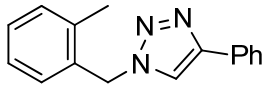
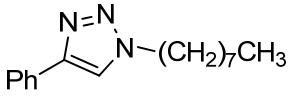
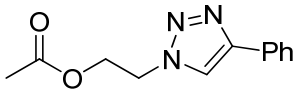
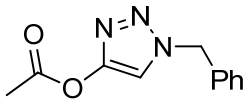
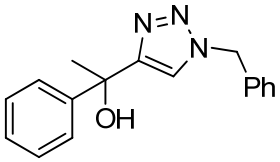
Finally, we explored the three-component (alkyl halide, sodium azide, and alkyne) azide-alkyne cycloaddition reaction with CuI complex formed *in situ* with the isonitrile ligand (**49**). As evident from Table 15, this catalytic system can function in pure water to give the desired products (Table 15, entries 1-8) in excellent yields (85-97%), and a number of functional groups were tolerated.

Table 15. Azide-alkyne cycloaddition catalyzed with CuI complex.[a]



67 **70** **69**

entry	triazole (**69**)	time (h)	Yield (%)
1	 **69a**	1.5	94
2	 **69b**	3	97
3	 **69d**	3	89

4	 **69c**	2.5	85
5	 **69e**	4	94
6	 **69o**	6	95
7	 **69h**	6	97
8	 **69k**	1	91

[a]Reagents and reaction conditions: **67** (1.05 mmol), NaN_3 (1.05 mmol), alkyl halide **70** (1.0 mmol) and catalyst (CuI+Ligand **49**) (5 mg, 2 mol %). [b] Isolated yields as an average of at least two independent experiments.

4 The role of ligands in CuAAC reaction

Since problems can arise from copper(I)'s vulnerability towards oxidation and disproportation and the formation of undesired alkyne-alkyne coupling products sometimes observed in their presence, copper(I) salts have been less used in CuAAC reaction. Active copper(I) catalytic species in CuAAC reaction can be prepared *in situ* by reduction of copper(II) salts, oxidation of copper(0) metal, or copper(II)/copper(0) comproportionation. To circumvent the limitation of copper(I) salts, the ligands have been proven to protect the metal center from oxidation and disproportionation, while enhancing its catalytic activity.

5 Summary

In conclusion, the structurally well-defined copper(I) isonitrile complex (**60a**) was successfully synthesized and developed as a heterogeneous catalyst for the copper catalyzed

azide-alkyne cycloaddition under mild conditions in water. This catalyst shows considerable synthetic advantages in terms of facile and sustainable reaction set-up (aerobic conditions in water, no additives are necessary), wide scope, and high reactivity. The catalyst (**60a**) is also efficient in the three-component (alkyl halide, sodium azide, and alkyne) azide-alkyne cycloaddition. Furthermore, it can be readily recovered by filtration and be recycled for at least five runs without significant loss of activity.

6 References

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Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed*. **2002**, *41*, 2596. (c) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057.

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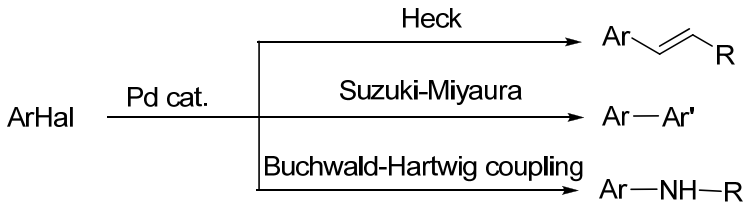
C. Copper(I)-Isonitrile Complexes

Part Ⅱ. Ullmann-type coupling reaction catalyzed by copper isonitrile complex

1 Introduction

Transition metal-catalyzed carbon-carbon and carbon-heteroatom cross-coupling are now among the most prominent synthetic methods for the formation of carbon-carbon, carbon-nitrogen, carbon-oxygen and carbon-sulfur bonds in the preparation of numerous important products that are of biological, pharmaceutical, and materials interest.[1] Most noteworthy among them are the palladium-catalyzed Heck reaction[2], the Suzuki-Miyaura reaction[3], and the C-N coupling of organic halides with nitrogen-containing compounds (Buchwald-Hartwig coupling[4]) (Scheme 34).

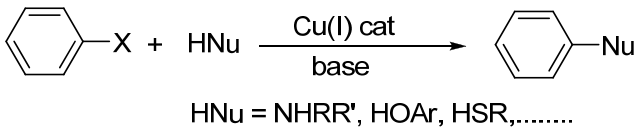


Scheme 34. Pd catalyst in organic transformation.

Although these methods are highly effective, there is still much room for improvement, for example, these methods usually require long reaction times and high reaction temperatures, bear with the cost of the metal catalyst (though in extremely low amount in some cases) and air sensitivity of Pd catalyst systems. Moreover, some of them suffer from a relatively narrow scope of substrates. For example, the palladium-catalyzed amidation of electron-rich or ortho-substituted aryl halides is difficult.[5] These drawbacks limit their application to large

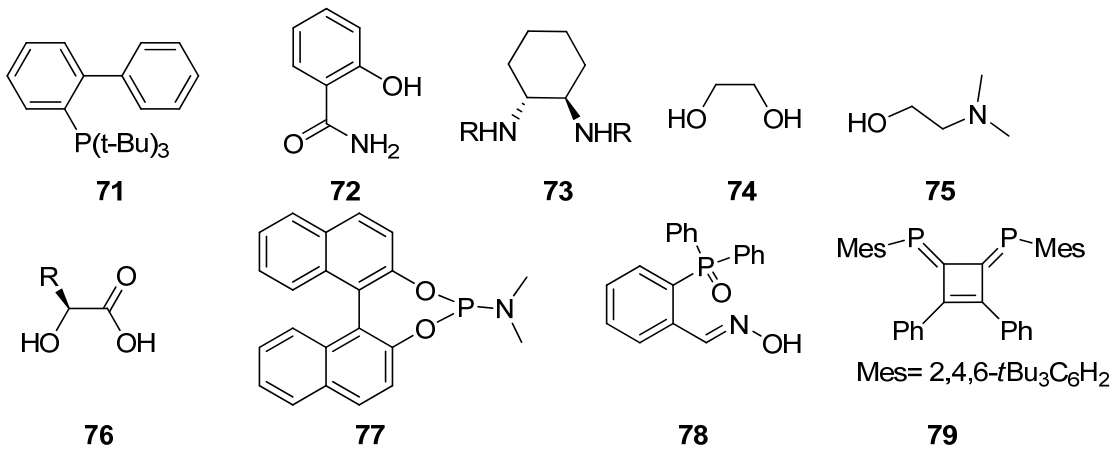
and industrial scale synthesis. To circumvent these limitations, inexpensive and efficient catalytic systems made of non-noble metals such as nickel, copper have been developed.[6] The low cost of copper-based catalytic systems make them particularly attractive for large-scale industrial applications and have undoubtedly taken the lead.

Ullmann and *Goldberg* discovered at the beginning of the last century,[7] the reactions later named after them, namely the C-N coupling of aryl halides with amines or amides. The scope of these reactions was later extended to include the formation of a C-N, C-O，C-S bonds (Scheme 35).[8] Copper-mediated Ullmann-type coupling reaction is an alternative for the palladium-catalyzed reactions for the formation of carbon-heteroatom bonds.[9]



Scheme 35. The copper-mediated Ullmann-type coupling reaction.

However, harsh reaction conditions such as high temperatures (125-220 ℃), the usual requirement of stoichiometric quantities of the copper catalyst, and the low to moderate yields have greatly limited the utility of this reaction.[8-9] A remarkable approach is that the deliberate use of additional ligands to facilitate copper-catalyzed Ullmann-type N-arylation of amines/amides, O-arylation of phenols, and S-arylation of thiols with aryl halides. The additional mono- and bidentate ligands, such as phosphines (**71**),[10] salicylamides (**72**),[11] diamines (**73**),[12] diols (**74**),[13] amino alcohols (**75**),[14] amino acids (**76**),[15] phosphoramidites (**77**),[16] oximephosphine oxides (**78**),[17] and phosphinidenes (**79**),[18] have been shown to significantly improve the yields and generality of this reaction (Figure 14). In some cases, it can make the reaction work well at the relative low temperature. These ligands are thought to increase catalyst solubility, stability, and/or to prevent aggregation of the metal. This approach has been regarded as a synthetic strategy to prepare the corresponding coupled products, given the low cost, air-stable system, tolerant to functional groups and wide availability of the aryl halide substrates and functionalized halide substrates.

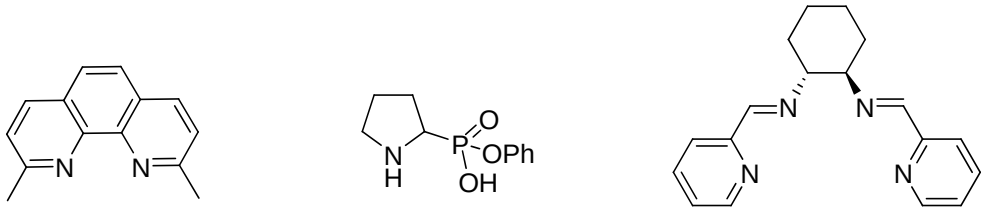


71 **72** **73** **74** **75**

76 **77** **78** **79**

Figure 14. The ligands in Ullmann-type reactions.

Notably, only few examples have been reported to demonstrate the versatility of the same ligands without any additional modification or other additive can be effectively used in three or more kinds of copper-catalyzed cross-coupling reactions for the formation of C-N, C-O, C-S bonds, such as neocuproine (**80**)[19] (2,9-dimethyl-1,10-phenanthroline; a bidentate ligand with N,N-chelators for Ar-N, Ar-O, and Ar-S bond formations), pyrrolidine-2-phosphonic acid phenyl monoester (**81**)[20] (a bidentate ligand with N,O-chelators for Ar-N, Ar-O, and Ar-P bond formations), and Chxn-Py-Al (**82**)[21] (a tetradentate ligand with N,N,N,N-chelators for Ar-N, Ar-O, and Ar-C bond formations) (Figure 15).

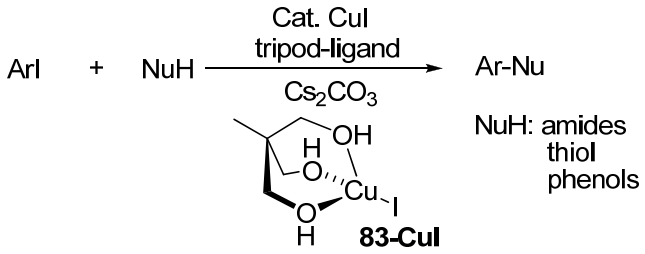


80 **81** **82**

Figure 15. The versatile ligands in Ullmann-type reactions.

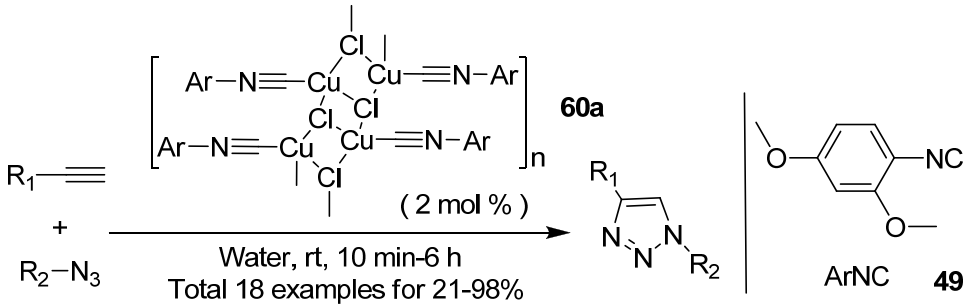
However, the high cost and/or the complicated preparation procedure of the ligands used in these important protocols were drawbacks. To search other new, less expensive, and versatile ligands for this copper-catalyzed protocol, a pioneering work has been given by *Chen* group[22] (Scheme 36). They have successfully demonstrated that 1,1,1- tris(hydroxymethyl)ethane (**83**)

can be used as a new, efficient, and versatile tridentate ligand in the copper catalyzed formation of C-N, C-S, and C-O bonds. Thus, the need for cheaper and more versatile ligands in three or more kinds of copper-catalyzed cross-coupling reactions is highly desirable.



Scheme 36. A simple versatile ligand in Ullmann-type reactions.

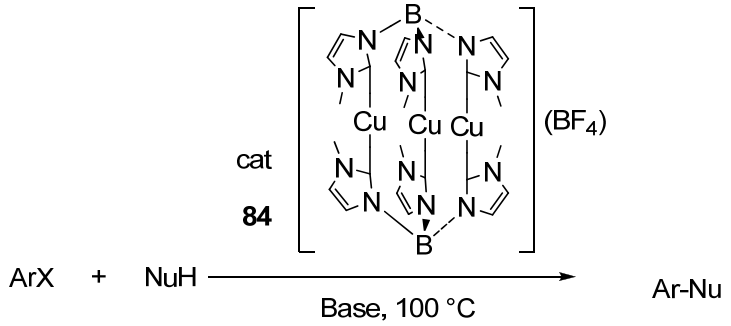
We have described a readily prepared and structually well-defined copper isonitrile complex (**60a**) (Scheme 37), which exhibits excellent activity to CuAAC reaction under mild reaction conditions in water.[23] Owing to isonitriles' electronic properties, being strong σ-donor ligands comparable to *N*-heterocyclic carbenes, copper isonitrile complexes will be good candidates for many transformation which is similar with copper *N*-heterocyclic carbenes complex.



Scheme 37. Copper isonitrile complex in CuAAC reaction.

Biffis group has developed a trinuclear copper(I) carbene complex (**84**) that displays good catalytic efficiency in the Ullmann-type arylation reaction of azoles and phenols (Scheme 38).[24] The catalyst is capable of converting aryl iodides, bromides or even activated chlorides at a

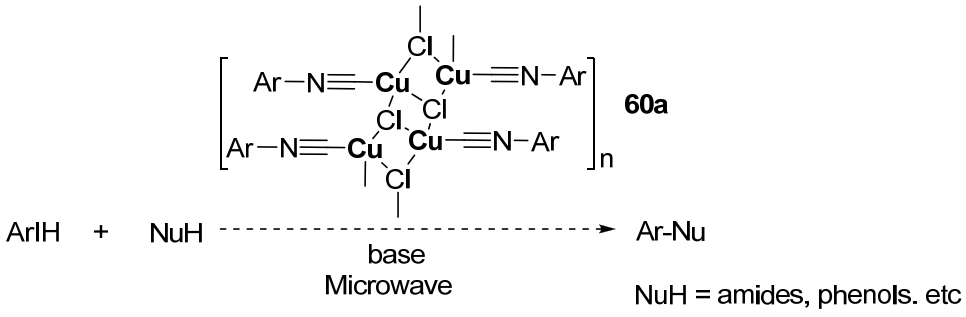
comparatively low reaction temperature (100 ℃). Furthermore, different azoles such as pyrazole, imidazole or 1,2,4-triazole are converted with comparable efficiency.



Scheme 38. Copper carbene complex in Ullmann-type reactions.

On one hand, encouraged by *Biffis*'s work, we turned our attention towards Ullmann-type reactions catalyzed by our copper isonitrile complex (**60a**). On the other hand, microwave (MW)-assisted organic reactions have been demonstrated as a powerful means which require short reaction times and low relatively reaction temperatures, and a relatively broaden scope of substrates.[25]

Thus, not only to broaden the application of copper isonitrile complex, but also we wish to develop an easily-prepared, efficient and versatile catalytic system for Ullmann-type reaction using MW technique (Scheme 39).



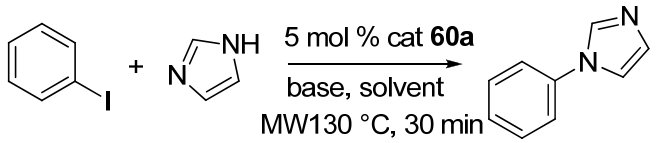
Scheme 39. The proposal of this part.

2 Synthesis of copper(I)-isonitrile complexes

See chapter **C. Part I-2**.

3 Results and discussions

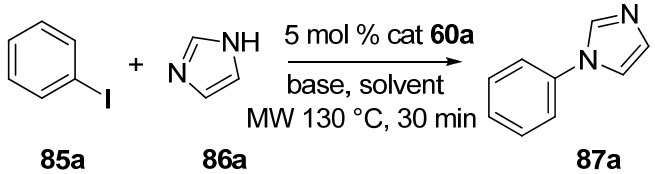
While optimizing the reaction conditions for the C-N cross-coupling reaction using the complex (**60a**), the amount of copper catalyst (5 mol %) and the reaction time (30 min) were the same for all experiments and were not further optimized at first (Scheme 40). The reaction temperature (130 ℃) was also set constant for all reaction tests. We took the N-arylation of iodobenzene with imidazole as a standard test reaction.



Scheme 40. C-N cross-coupling of iodobenzene with imidazole.

In previous study in the literature,[25] the superiority of dimethylsulfoxide (DMSO) and N,N-dimethylformamide (DMF) as reaction solvents for this reaction is witnessed. Thus, we just investigated DMSO and DMF as reaction solvents. In order to screen for the best base, we firstly examined the effect of different bases such as KO^{t}Bu, K_3PO_4, Cs_2CO_3, DBU and K_2CO_3 in DMSO and DMF. It was found that the combination of KO^{t}Bu and DMF provided the N-arylated product in good yield (Table 16, entry 4), whereas other bases in DMF or DMSO were less effective as shown in Table 16.

Table 16. N-Arylation of iodobenzene with imidazole: influence of the base.[a]

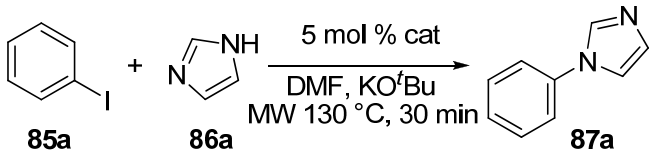


entry	solvent	base	Yield (%)[b]
1	DMF	K_2CO_3	68
2	DMF	$CsCO_3$	73
3	DMF	K_3PO_4	69
4	DMF	KO^tBu	90
5	DMF	DBU	23
6	DMF	KOH	49
7	DMSO	K_2CO_3	45
8	DMSO	$CsCO_3$	56
9	DMSO	K_3PO_4	63
10	DMSO	KO^tBu	73
11	DMSO	DBU	31
12	DMSO	KOH	51

[a]Reagents and reaction conditions: imidazole **86a** (2.0 mmol), iodobenzene **85a** (1.0 mmol), catalyst **60a** (5 mol %), base (3.0 equiv.), solvent (2.0 mL), 130 ℃, 30 min. [b]Isolated yield of the product after column chromatography.

For comparison with the complex (**60a**), copper(I) salt was studied with 10 mol % catalyst loading in DMF as a catalyst for this reaction. As is shown in Table 17, CuCl was less effective, even though increasing the catalyst loading form 5 mol % to 50 mol %. The similar results are for CuI. These results demonstrated that the choice of copper salts appeared not to be very critical for the present reaction. In addition, when the reaction was performed with 5 mol % of Cu(I) complex (**60b**) in the presence of KO^tBu as a base in DMF at 130 ℃ for 30 min (entry 6, Table 17), the expected coupling product was obtained in 67 % yield. The reactivity of Cu(I) complex (**60b**) is parallel with that of CuAAC reaction. On the basis of results, it is plausible to propose the complex (**60a**) as a suitable catalyst that can be used in copper-catalyzed cross-coupling reactions.

Table 17. The Screening of catalysts for C-N cross coupling of iodobenzene with imidazole.[a]



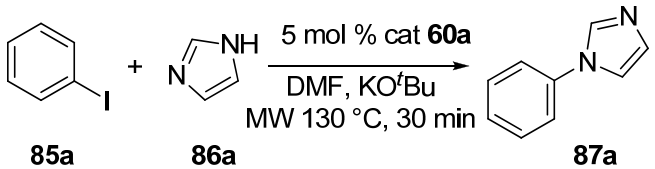
85a **86a** **87a**

entry	solvent	catalyst	yield (%)[b]
1	DMF	**60a**	90
2	DMF	50 mol %CuCl	76
3	DMF	5mol % CuCl	51
4	DMF	50 mol % CuI	73
5	DMF	5 mol % CuI	69
6	DMF	**60b**	67

[a]Reagents and reaction conditions: catalyst (5 mol %), imidazole **86a** (2.0 mmol), iodobenzene **85a** (1.0 mmol), KO^{t}Bu (3.0 equiv.), DMF (2.0 mL), 130 ℃, 30 min. [b]Isolated yield of the product after column chromatography.

For further optimization of the reaction conditions, the effect of the ratio of iodobenzene to imidazole was studied in Table 18. Increasing yields of the coupling product were observed by simply changing the ratio of iodobenzene (**85a**) to imidazole (**86a**) from 1:2 to 2:1. The 1:2 ratio of iodobenzene (**85a**) to imidazole (**86a**) is found to be the best condition. When comparing microwave reactions with conventional pre-heated oil bath reactions, we observed a decrease in yield (65%) under conventional thermal condition (Table 18, entry 7).

Table 18. The effect of the ratio of iodobenzene to imidazole for C-N cross coupling.[a]



85a **86a** **87a**

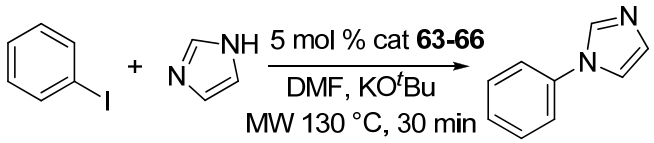
entry	the ratio of iodobenzene to imidazole (**85a:86a**)	yield (%)
1	1:3	85

2	1:2	90
3	1:1.5	71
4	1:1	68
5	2:1	65
6	3:1	69
7[c]	2:1	65

[a]Reagents and reaction conditions: catalyst **60a** (5 mol %), KO^{t}Bu (3.0 equiv.), DMF (2.0 mL), 130 ℃, 30 min. [b]Isolated yield of the product after column chromatography. [c]Under conventional thermal condition.

In addition, all of the other Cu(I)-isonitrile complexes were examined for their catalytic activities in Ullmann reaction of iodobenzene (**85a**) with imidazole (**86a**) for comparison with the structurally well-defined complexes (**60a**) and (**60b**) under the above optimum conditions. Results were summarized in Table 19. These yields obtained strongly suggest that [CuCl(RNC)$_{1\text{-}2}$] with various functional groups of isonitriles can promote Ullmann reaction under microwave irradiation. The structurally well-defined complex (**60a**) was the more efficient of [CuCl(RNC)$_{1\text{-}2}$] complexes as catalyst in the Ullmann reaction.

Table 19. Ullmann in the presence of various Cu(I)-isonitrile complexes.



85a **86a** **87a**

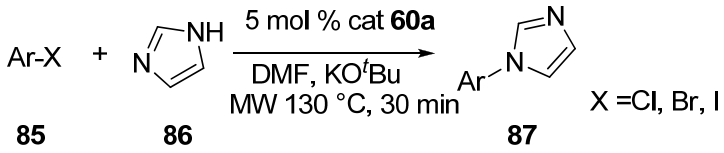
entry	catalyst	reaction time (min)	yield (%)
1	**63a**	30	74
2	**63b**	30	66
3	**64a**	30	80
4	**64b**	30	67
5	**65a**	30	71
6	**65b**	30	67
7	**66a**	30	69

8	**66b**	30	63
9	**60a**	30	90
10	**60b**	30	67

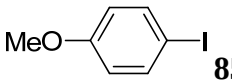
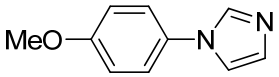
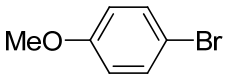
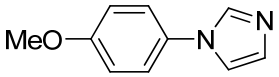
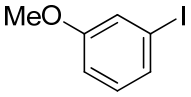
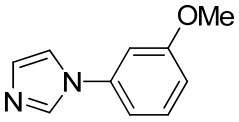
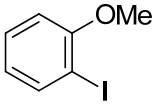
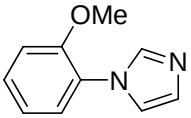
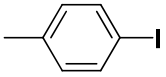
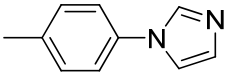
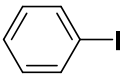
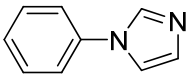
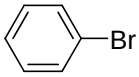
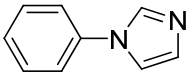
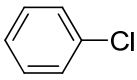
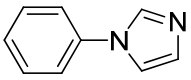
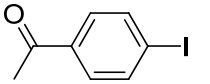
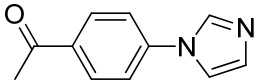
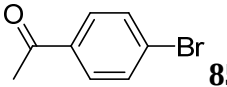
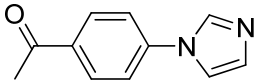
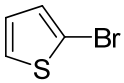
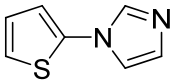
[a]Reagents and reaction conditions: imidazole **86a** (2.0 mmol), iodobenzene **85a** (1.0 mmol), KO^{t}Bu (3.0 equiv.), catalyst (5 mol %), DMF (2.0 mL), 130 ℃, 30 min. [b]Isolated yield of the product after column chromatography.

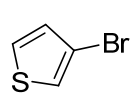
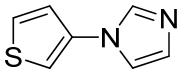
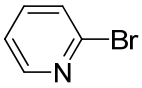
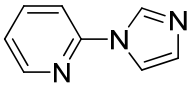
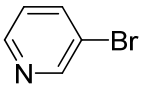
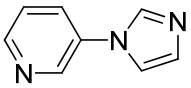
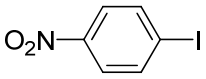
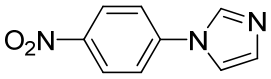
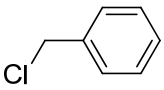
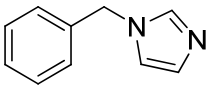
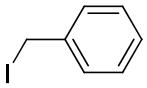
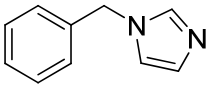
Thus, the optimized reaction conditions utilized 5 mol % of **60a**, and KO^{t}Bu in DMF as a solvent at 130 ℃. In the first part, these reaction conditions were applied to the coupling reaction with a vast array of aryl halides containing electron-donating and -withdrawing substituents and imidazole. The representative results are tabulated in Table 20. The corresponding N-arylation products were obtained in moderate to excellent yields (42-96%). Electronic effects on the reactions were limited. An electron-donating group or an electron-withdrawing group on the iodobenzenes and nitrogen nucleophiles has no significant effect on the yield of the C-N cross-coupled product (entries 1, 5, 9 and 15, Table 20). However, steric effect is significant. Reactions of meta-substituted aryl halides proceeded in high yields (entries 1 and 2, Table 20), while steric para- and ortho-substituted ones were not effective (entries 3 and 4, Table 20). We also investigated the coupling reaction of different heterocyclic halides with imidazole. It was found that pyridyl halides worked well, affording the corresponding product in good yields (entries 13 and 14, Table 20). The less-reactive thienyl halides gave rise to moderate yields (entries 11 and 12, Table 20). Encouraged by these results, we further investigated the coupling reaction of (iodomethyl)benzene with imidazole (entries 17, Table 20). The corresponding N-arylation products were obtained in good yield (79%). To our surprise, this catalytic system can activate chlorobenzene and (chloromethyl)benzene, they can give the desired products (**87**) in 42-53% yields. To our knowledge, the reactivity of the catalyst (**60a**) can compare to the other copper catalytic systems, which actives the coupling of aryl chlorides with imidazole. The chloride showed lower reactivity compared to the bromides and iodides derivatives. The results indicate the reactivity order of aryl halides: iodides >bromides > chlorides (entries 6, 7 and 8, Table 20).

Table 20. C-N cross-coupling of various aryl halides with imidazole.[a]



85 **86** **87**

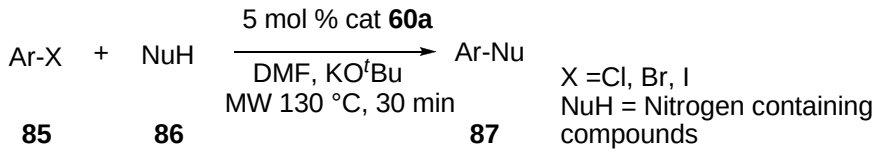
entry	aryl halide (**85**)	product (**87**)	yield (%)[b]
1	 **85b**	 **87b**	85
2	 **85c**	 **87b**	81
3	 **85q**	 **87c**	46
4	 **85r**	 **87v**	23
5	 **85d**	 **87d**	83
6	 **85a**	 **87a**	90
7	 **85e**	 **87a**	84
8	 **85f**	 **87a**	42
9	 **85g**	 **87e**	89
10	 **85h**	 **87e**	71
11	 **85i**	 **87f**	73

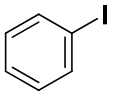
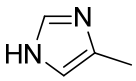
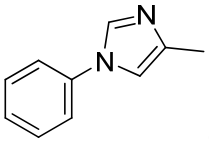
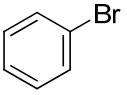
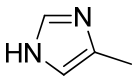
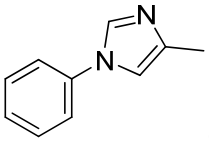
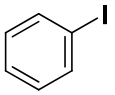
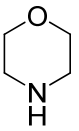
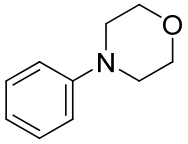
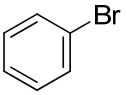
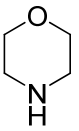
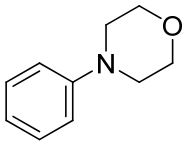
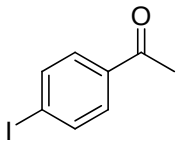
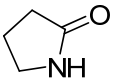
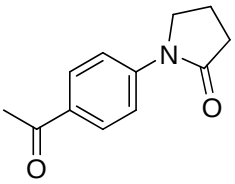
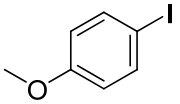
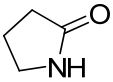
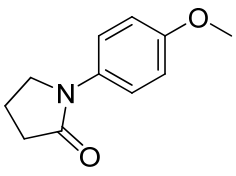
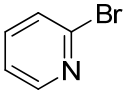
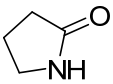
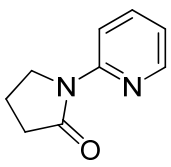
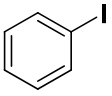
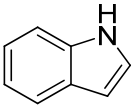
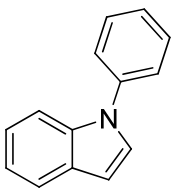
12		**85j**		**87g**	80
13		**85k**		**87h**	96
14		**85l**		**87i**	93
15		**85m**		**87j**	79
16		**85n**		**87k**	53
17		**85o**		**87k**	79

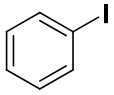
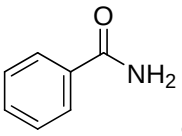
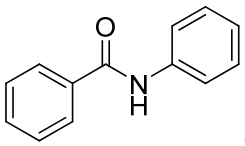
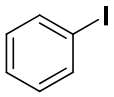
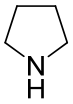
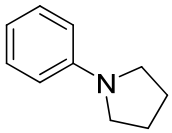
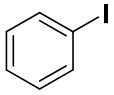
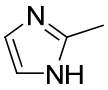
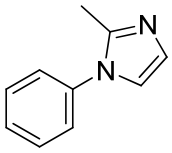
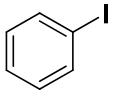
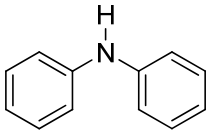
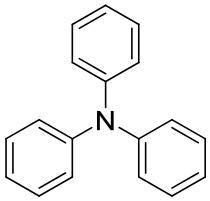
[a]Reagents and reaction conditions: imidazole **86** (2.0 mmol), aryl halides **85** (1.0 mmol), KO^{t}Bu (3.0 equiv.), DMF (2.0 mL), 130 ℃, 30 min. [b]Isolated yield of the product after column chromatography.

With a view to understand the scope of nitrogen nucleophiles, we carried out the coupling with a variety of nitrogen containing compounds (Table 21), including methyl midazole, pyrrole, benzamide, pyrrolidin-2-one, pyrrolidine, morpholine with iodo- or bromobenzene. It was found that all amines worked well, affording the corresponding coupling product in good yields. Furthermore, the present catalytic system also worked well for the coupling of arylamides with aryl halides. The other desired amination products were obtained in moderate to excellent yields. These results show that our copper catalytic system is highly tolerant to functional nitrogen containing groups.

Table 21. C-N cross-coupling of aryl halides with various nitrogen nucleophiles.[a]



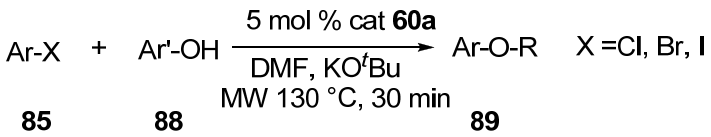
entry	aryl halide (**85**)	nitrogen nucleophiles (**86**)	product (**87**)	yield(%)[b]
1	 **85a**	 **86b**	 **87l**	83
2	 **85e**	 **86b**	 **87l**	81
3	 **85a**	 **86c**	 **87m**	78
4	 **85e**	 **86c**	 **87m**	73
5	 **85g**	 **86d**	 **87n**	85
6	 **85b**	 **86d**	 **87o**	92
7	 **85k**	 **86d**	 **87p**	96
8	 **85a**	 **86e**	 **87q**	85

9		**85a**		**86f**	 **87r**	83
10		**85a**		**86g**	 **87s**	54
11		**85a**		**86h**	 **87t**	63
12		**85a**		**86i**	 **87u**	73

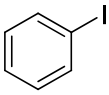
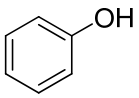
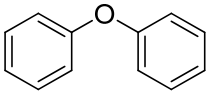
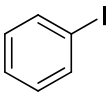
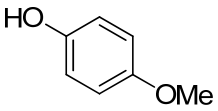
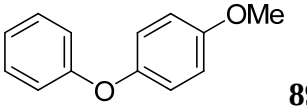
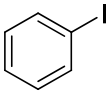
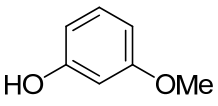
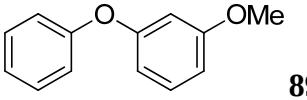
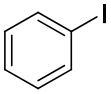
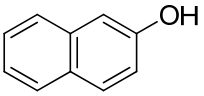
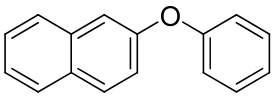
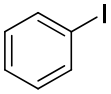
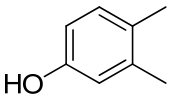
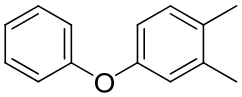
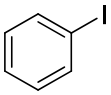
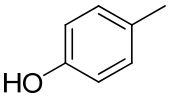
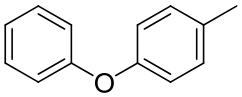
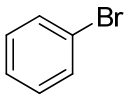
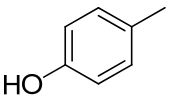
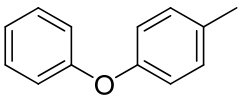
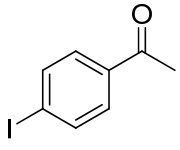
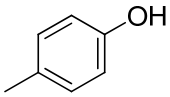
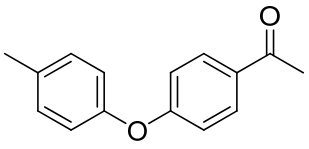
[a]Reagents and reaction conditions: imidazole **86** (2.0 mmol), aryl halides **85** (1.0 mmol), KO^{t}Bu (3.0 equiv.), DMF (2.0 mL), 130 ℃, 30 min. [b]Isolated yield of the product after column chromatography.

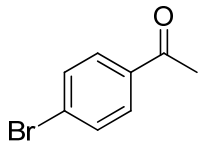
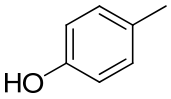
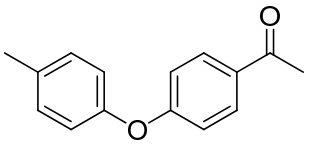
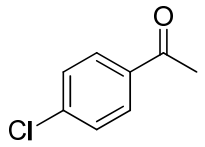
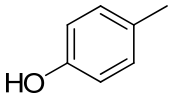
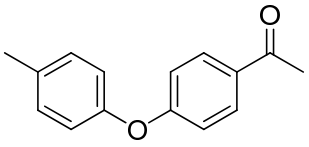
Using the above optimized conditions, we initiated our investigations into the coupling with aryl halides with phenols. The results are shown in Table 22. It was found that aryl iodide worked well, affording the corresponding products in good yields. Thus, the reactivity of phenols with the catalyst (**60a**) appears to be comparable with that of imidazole. We noted that aryl bromides also reacted with phenols to provide the corresponding diaryl ethers. It is very important to mention that in general, aryl bromides are less reactive than aryl iodides and require much more drastic reaction conditions for arylation. However in the presence of our catalyst system even aryl bromides reacted with phenols to give good yields of the expected diaryl ethers without increasing the reaction temperature and time. Moreover, this catalytic system can activate chlorobenzene and give the desired products in 39% yield. The results indicate the reactivity order of aryl halides: iodides > bromides > chlorides.

Table 22. C-N cross-coupling of aryl halides with various phenols.[a]



85 **88** **89**

entry	aryl halide (**85**)	phenol (**88**)	product (**89**)	yield(%)
1	 **85a**	 **88a**	 **89a**	98
2		 **88b**	 **89b**	85
3		 **88c**	 **89c**	79
4		 **88d**	 **89d**	82
5		 **88e**	 **89e**	92
6		 **88f**	 **89f**	77
7	 **85e**	 **88f**	 **89f**	62
8	 **85g**	 **88f**	 **89g**	81

9	 **85h**	 **88f**	 **89g**	58
10	 **85p**	 **88f**	 **89g**	39

[a]Reagents and reaction conditions: phenol **88** (1.5 mmol), aryl halides **85** (1.0 mmol), KO^{t}Bu (3.0 equiv.), DMF (2.0 mL), 130 ℃, 30 min. [b]Isolated yield of the product after column chromatography.

4 Proposed mechanism[21]

Ullmann-type reactions proceed through a catalytic cycle (Figure 16), and in proposed mechanism the copper is postulated to undergo oxidation to Cu(III).[26] This mechanism involves the three following elementary steps: oxidative addition of the aryl halide to copper(I) generating a transient Cu^{III} species, nucleophilic substitution of copper-bound halide by nucleophilic anion (*in-situ* generation from amines/amides, phenol, etc.), and reductive elimination of the coupling product, thereby regenerating the active catalyst. Uncertainty remains as to whether nucleophilic substitution step proceeds or follows the oxidative addition step. Both possibilities are depicted on Figure 16.

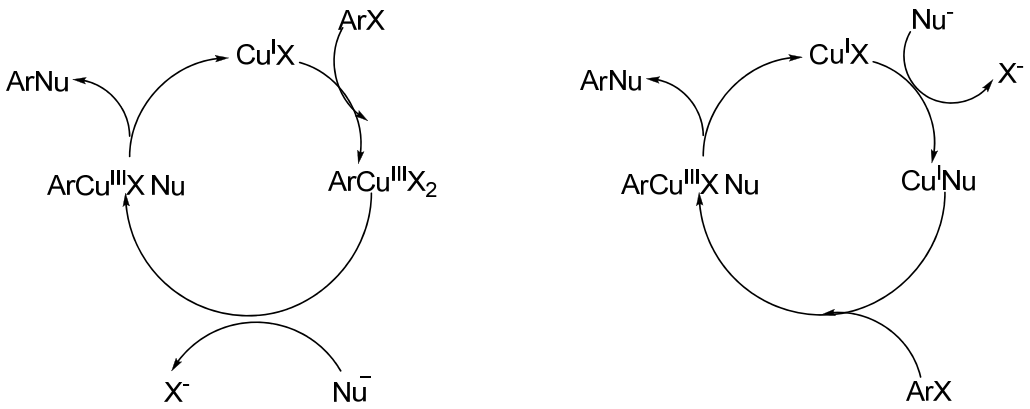
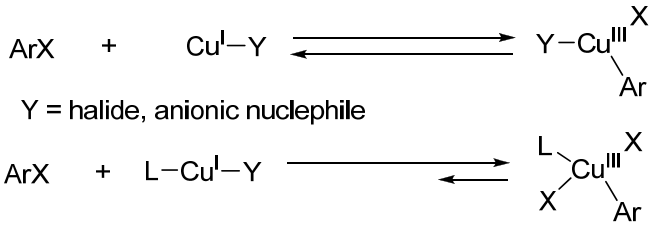


Figure 16. The two alternative oxidative addition/reductive elimination mechanistic pathways for copper-catalyzed nucleophilic aromatic substitutions with aryl halides.

A possible role played by the isonitrile ligand in the present Ullmann-type coupling is being able to promote oxidative addition to the CuI complex. Indeed, oxidative addition of cuprous halides to aryl halides would be a reversible process according to the literature.[26a] The well-documented copper catalyzed halogen exchange in aryl halides is a further indication of this reversibility, [26a, 27] seeing that the reverse reaction is equivalent to reductive elimination of aryl halide from Cu^{III}. Our isonitrile ligand is a hard donor ligand (Lewis base), which may display a higher affinity toward hard copper(III) than soft copper(I).[28] Due to their suitable properties, they might exhibit a superior ability to stabilize the oxidative addition product, thus shifting to the right position of the equilibrium in Scheme 41.



Scheme 41. Hypothesis of stabilization of the Cu^{III} oxidative addition product by the use of an appropriate supporting ligand L.

5 Summary

We have developed an easily-prepared, practical and versatile catalytic system for Ullmann-type reaction under MW irradiation. A variety of aryl idodides, aryl bromides with nitrogen containing compounds, and phenols participate in the process with good to excellent yields. Furthermore, this catalytic system can active aryl chlorides and give the desired products in moderate yields. The short reaction time and simple reaction conditions, tolerance of a broad substrate scope, make this method particularly attractive for the application in

biologically and medicinally interesting molecules, and the versatility of this methodology is suitable for library synthesis in drug screening.

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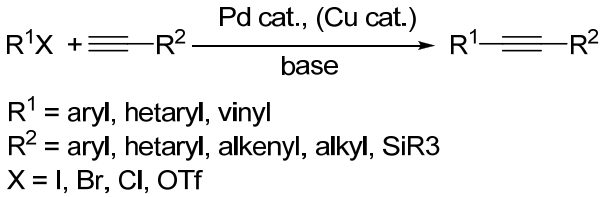
C. Copper(I)-Isonitrile Complexes

Part Ⅲ. Sonogashira coupling reaction catalyzed by copper isonitrile complex

1 Introduction

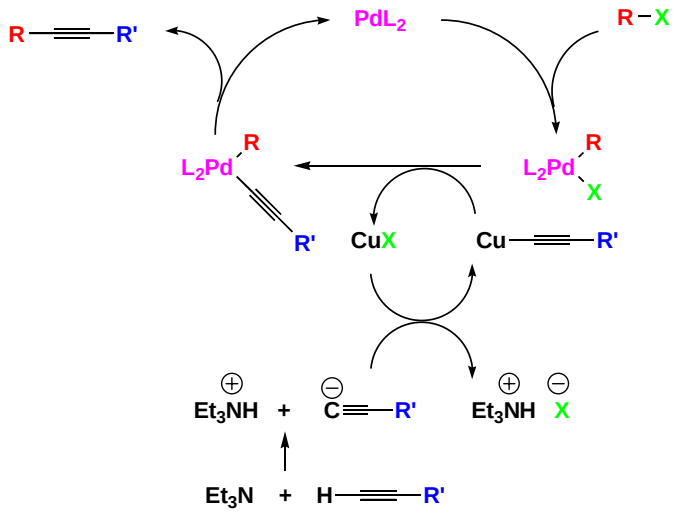
Transition metal-catalyzed carbon-carbon cross-coupling reactions have become an important corner-stone of modern organic synthetic chemistry.[1] Noteworthy among them, the palladium-catalyzed sp^2-sp coupling reaction between aryl or alkenyl halides or triflates and terminal alkynes, in the presence of a copper(I) co-catalyst, otherwise known as the Sonogashira reaction[2], this reaction has become an extremely important method to prepare aryl alkynes and conjugated enynes, which are important precursors for natural products, pharmaceuticals, and molecular organic materials (Scheme 42).[3]



Scheme 42. Sonogashira reaction.

The copper co-catalyzed Sonogashira reaction is believed to take place through two independent catalytic cycles which requires the use of a palladium(0) complex, in the presence of base and copper(I) iodide as a co-catalyst (Scheme 43).[1-3] Oxidative addition of the organic halide gives a Pd(II) intermediate that undergoes transmetallation with the alkynyl copper (generated from the terminal alkyne, base, and copper iodide). Reductive elimination followed by coupling of the two organic ligands gives the product and regenerates the Pd(0) catalyst. The base (generally an amine) abstracts the acetylenic proton

of the terminal alkyne, thus forming a copper acetylide in the presence of copper(I) salt. It should be pointed out that the amines generally employed are usually not basic enough to deprotonate the alkyne in order to generate the anionic nucleophile that should form the copper acetylide. Therefore, an alkyne-Cu complex as shown in Scheme 2 could be involved in the cycle. However, the copper intermediate has never been proven, leaving the Cu cycle still poorly understood.[3]



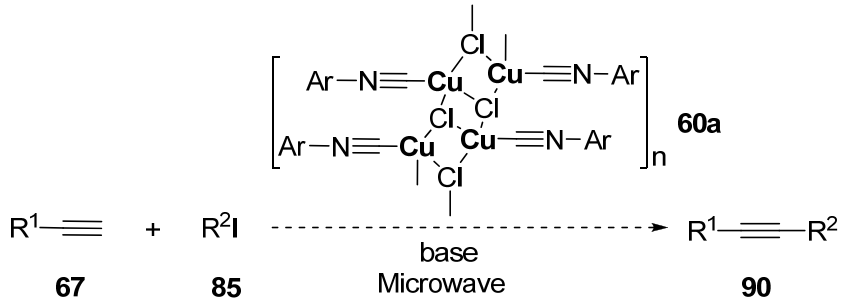
Scheme 43. The two catalytic cycles of Sonogashira reaction.

The copper co-catalysts in the Sonogashira cross-coupling reactions have some drawbacks, because the *in situ* generation of copper acetylides under the reaction conditions often generates homocoupling products of the terminal alkyne (the so-called Glaser coupling). This side reaction is especially problematic when the terminal acetylene is difficult to obtain or expensive, although it has been shown that the presence of a reductive atmosphere formed by difficult-to-handle hydrogen can diminish homocoupling, as well as the slow addition of the acetylene. Thus, the development of methods which eliminate the side reaction, under copper-free Sonogashira cross-coupling has been pursued in the past few years.[4] The copper-free Sonogashira reaction has been performed using palladium complexes as catalyst in the presence of a catalytic amount of a copper(I) salt and an amine (as a solvent or in large excess) under homogeneous conditions. Although these methods of copper-free Sonogashira

reaction are highly effective, there is still much room for improvement, for example, these methods usually bear with the cost of the metal catalyst (though in extremely low amount in some cases) and air sensitivity of Pd catalyst systems. To circumvent these limitations, inexpensive and efficient catalytic Pd-free systems made of non-noble metals such as nickel and copper have been developed.[5]

We summarized some examples of copper-catalyzed Sonogashira reaction. The catalytic system copper(I) iodide/triphenylphosphine in the presence of potassium carbonate in DMF or DMSO at 120 ℃ has allowed the cross-coupling reaction of aryl and vinyl iodides and terminal alkynes,[5d,5e] with the reaction being performed faster under microwave heating, whereas a copper(I) bromide complex of triphenylphosphine and 1,3-phenanthroline has been used as catalyst in the reaction of aryl iodides and phenylacetylene, using potassium carbonate as base in refluxing toluene.[5g]

Copper(I) iodide has also been shown to catalyze the coupling of aryl iodides or bromides and terminal alkynes when *N*,*N*-dimethylglycine was used as additive, using potassium carbonate as base in DMF at 100 ℃. Inspired by the above work and as an extension of our interest in cross coupling with copper-isonitrile complex as catalyst, we turned our attention to copper-catalyzed Sonogashira coupling reaction using a MW technique (Scheme 44).



Scheme 44. The proposal of this part.

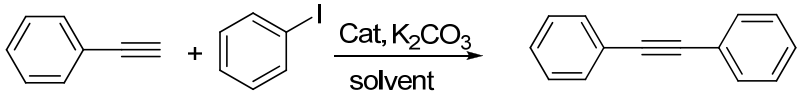
2 Synthesis of copper(I)-isonitrile complexes

See chapter **C. Part I-2**.

3 Results and discussion

A series of experiments were performed to find an optimum condition for the coupling of phenylacetylene with iodobenzene using potassium carbonate as base. Of the catalysts tested, copper isonitrile complex was the best choice in DMF using MW technique. Copper(I)-isonitrile complex (**60a**) can be used as catalysts for coupling of aryl iodides with aryl acetylenes using K_2CO_3 as the base in DMF at 130 °C. Other bases such as triethylamine and KO^{t}Bu were not effective in this reaction.[6] No reaction was observed with the catalyst (**60a**) in THF (Table 23, entries 1-2). Moreover, no reaction occurred under microwave heating with the catalyst (**60a**) in THF (Table 23, entry 3). This is probably because the heterogeneous nature of the catalyst (**60a**) (insolubility in THF) render it inactive. With CuI and CuCl, they gave rather low yields under microwave heating. As the solvent, DMF was found to be suitable for this reaction (Table 23, entry 5).

Table 23. Experiments to find an optimum condition.[a]



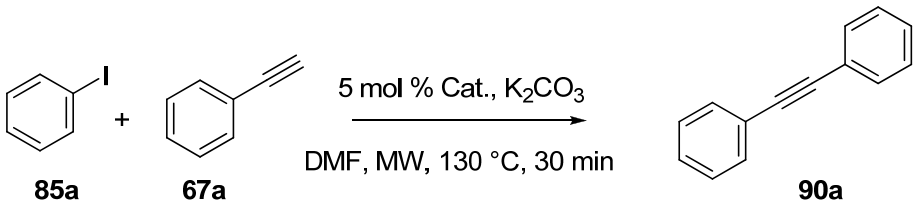
67a **85a** **90a**

entry	catalyst	conditions	slovents	yield (%)[b]
1	**60a**	rt, 24 h	THF	n.r
2	**60a**	Reflux, 24 h	THF	n.r
3	**60a**	MW, 90℃ 30min	THF	n.r
4	**60a**	MW,130℃ 30 min	DMF	85
5	CuCl	MW, 130℃ 30min	DMF	39
6	CuI	MW, 130℃ 30min	DMF	23

[a]Reagents and reaction conditions: phenylacetylene **67a** (1.2 mmol), iodobenzene **85a** (1.0 mmol), K_2CO_3 (3.0 equiv.), solvent (2.0 mL). [b]Isolated yield of the product after column chromatography.

All of the other Cu(I)-isonitrile complexes were examined for their catalytic activities in Sonogashira of iodobenzene (**85a**) with phenylacetylene (**67a**) in comparison with the structurally well-defined complexes (**60a**) and (**60b**) under the above optimum conditions. Results were summarized in Table 24. The lower yields obtained from other Cu(I)-isonitrile complexes strongly suggest that the structurally well-defined complex (**60a**) was the more efficient of [$CuCl(RNC)_{1-2}$] complexes as catalyst in the Sonogashira reaction.

Table 24. Sonogashira in the presence of various Cu(I)-isocyanide complexes.



85a **67a** **90a**

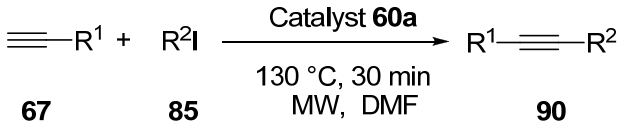
entry	catalyst	reaction time (min)	yield (%)
1	**63a**	30	31
2	**63b**	30	34
3	**64a**	30	42
4	**64b**	30	49
5	**65a**	30	34
6	**65b**	30	47
7	**66a**	30	56
8	**66b**	30	49
9	**60a**	30	85
10	**60b**	30	69

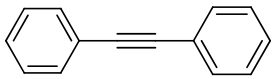
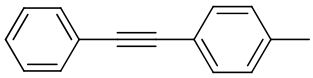
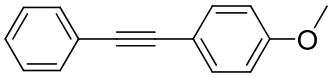
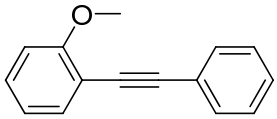
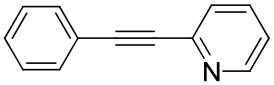
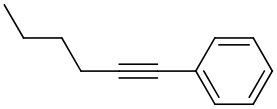
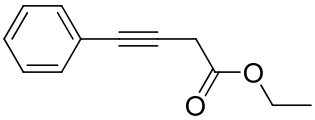
[a]Reagents and reaction conditions: phenylacetylene **67a** (1.2 mmol), iodobenzene **85a** (1.0 mmol), K_2CO_3 (3.0 equiv.), solvent (2.0 mL). [b]Isolated yield of the product after column chromatography.

The results of the CuI-catalyzed cross-coupling reaction of terminal alkynes with iodides are summarized in Table 25. The catalyst (**60a**) was applied to cross-coupling reaction of ethynylbenzene with iodides to give the corresponding products in good yields (Table 25, entries 1-4). It was found that pyridyl alkyne and 1-hexyne worked well, affording the

corresponding products in good yield (Table 25, entries 5 and 6). No homocoupling products were detected under optimum conditions. However, this copper-catalyzed cross-coupling method cannot be extended to electron-deficient alkynes (Table 25, entry 7).

Table 25. Cu-Catalyzed Cross-Coupling of Terminal Alkynes with iodides.[a]



entry	(**67**) R^1	iodides (R^2I) (**85**)	product (**90**)	yield (%)[b]
1	Ph	PhI	 **90a**	85
2	Ph	*p*-CH_3-PhI	 **90b**	65
3	Ph	*p*-OCH_3-PhI	 **90c**	89
4	Ph	*o*-OCH_3-PhI	 **90d**	72
5	2-Py	PhI	 **90e**	56
6	*n*-Bu	PhI	 **90f**	63
7	Ph	$EtOCOCH_2I$	 **90g**	n.r

[a]Reagents and reaction conditions: alkyne **67** (1.2 mmol), iodide **85** (1.0 mmol), K_2CO_3 (3.0 equiv.), DMF (2.0 mL), 130 ℃, 30 min. [b]Isolated yield of the product after column chromatography.

4 Summary

In conclusion we have developed a copper(I)-isonitrile complex that displays good catalytic efficiency in the Sonogashira coupling reaction. However, the relatively narrow scope in this study of substrates might limit its application in organic synthesis.

5 References

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Miura, M.; Nomura, M. *J. Org. Chem.* **1993**, *58*, 4716. (f) Wang, J.-X.; Liu, Z.; Hu, Y.; Wei, B.; Kang, L. *Synth. Commun.* **2002**, *32*, 1937. (g) Kang, S.-K.; Yoon, S.-K.; Kim, Y.-M. *Org. Lett.* **2001**, *3*, 2697. (h) Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315. (i) Ma, D.; Liu, F. *Chem. Commun.* **2004**, 1934. (j) Thathagar, M. B.; Beckers, J.; Rothenberg, G. *Green Chem.* **2004**, *6*, 215. (k) Zhang, L.; Li, P.; Wang, L. *Lett. Org. Chem.* **2006**, *3*, 282.

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D. Palladium(II)-Isonitrile Complex Catalyzed Wacker Oxidation

1 Introduction

The Pd-catalyzed oxidation of alkenes to methyl ketones, otherwise known as the Wacker oxidation, has been paid much attention because of useful protocols for direct oxyfunctionalization.[1] The important advantage of these reactions is the use of molecular oxygen (O_2) as a final oxidant, which is usually achieved by the re-oxidation of reduced palladium species with reversible co-oxidants, $CuCl_2$ being the most convenient one (Wacker catalyst, Figure 17).[2]

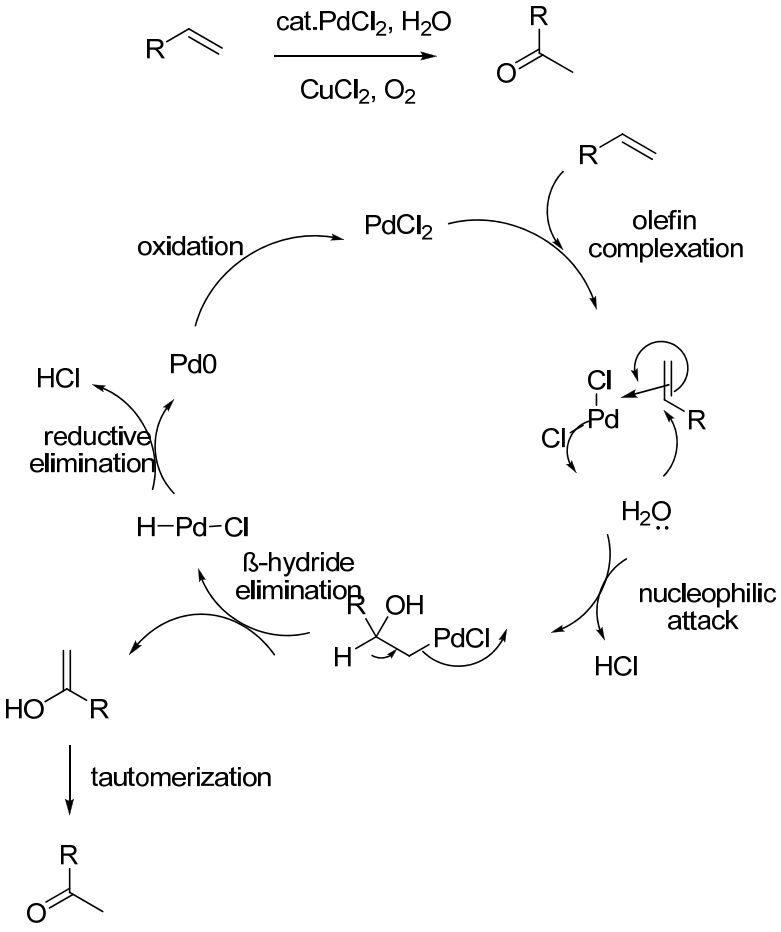
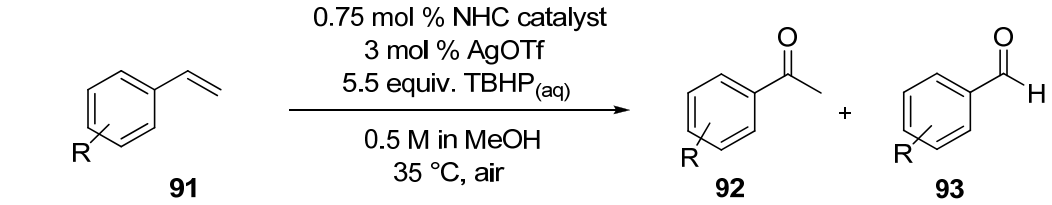


Figure 17. General catalytic cycle of Wacker oxidation.

However, these processes require large amounts of co-catalysts, or reducing agents to maintain the catalytic cycle and prevent its precipitation into inactive metals. To overcome these problems, much attention has been paid to the development of palladium catalysts modulated by special ligands.[3] In these systems, ligands are used to stabilize reduced palladium and promote its regeneration directly by molecular oxygen without the need for additional co-catalysts.

Sigman and *Cornell* reported the direct palladium-catalyzed Wacker oxidation of terminal alkenes without the need for employing copper co-catalysts.[3f] Palladium [(-)-sparteine] dichloride (1 mol %) with 0.2 M substrate in a 4:1 DMA/H_2O solvent system proved to be efficient for the conversion of aliphatic alkenes to methyl ketones using molecular oxygen as the terminal oxidant. The same authors observed that an N-heterocyclic carbene/Pd(II) complex converted styrene (**91**) to acetophenone (**92**) under aerobic conditions using TBHP as the terminal oxidant and catalytic amounts of AgOTf as co-catalyst (Scheme 45).[3g] Moreover, *Kaneda* and co-workers disclosed that $PdCl_2$ is a Wacker catalyst that can be used under 6 atm oxygen pressure. They discovered that DMA serves to stabilize a palladium catalyst preventing its precipitation into inactive metal.[4]



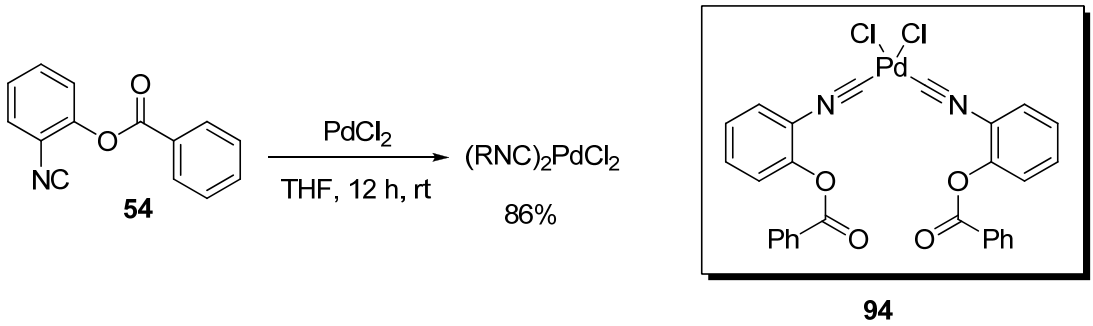
Scheme 45. NHC catalyzed Wacker oxidation of styrenes derivatives reported by *Sigman* and co-workers.

Pd-isonitrile complexes were widely used as catalyst precursors by *Ito* and co-workers in intra- and intermolecular bissilylation of alkynes and alkenes (Chapter A.2.1). *Villemin* and co-workers also reported palladium-isonitrile complexes and their use in Suzuki Miyaura coupling (see Chapter A.2.2). Owing to isonitriles' electronic properties, being strong

σ-donor ligands like N-heterocyclic carbenes (NHC), the palladium isonitrile complexes are also good candidates for aerobic Wacker oxidations.

2 Synthesis of palladium(II)-isonitrile complexes

Palladium isonitrile complex was prepared to study its catalytic activity in aerobic Wacker oxidation. Complexation of the isonitrile (**54)** with $PdCl_2$ in THF at room temperature gave rise to Pd^{II} complex (**94)** in good yield, which was characterized by NMR and IR spectroscopy (Scheme 46). However, we cannot further confirm its structure with X-ray determination. Since similar structures have already been reported in the literature for palladium complexes with isonitrile ligand,[5] we assumed the structure of the complex (**94**) as $(RNC)_2PdCl_2$.



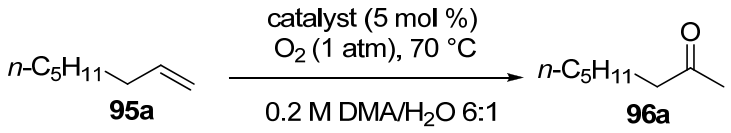
Scheme 46. Synthesis of palladium complex (**94**).

3 Results and discussion

The Complex (**94**) demonstrated its efficiency in the oxidation of 1-octene (**95a**) in the absence of any further co-catalysts using molecular oxygen at ambient pressure. However, around 3% of oxidation products stemming from alkene isomerizations were found through careful GC analysis. As a control experiment, we performed the oxidation of 1-octene with palladium chloride alone (Table 26), which proceeded well with no isomerization according

to the $PdCl_2$-DMA system of *Kaneda*'s work.[3g] These results show that the activity for the catalyst **94** is superior to those reported for the $PdCl_2$-DMA system, but the regioselectivity for the catalyst **94** is inferior to that of the $PdCl_2$-DMA system.

Table 26. Wacker oxidation of aliphatic alkenes.[a]

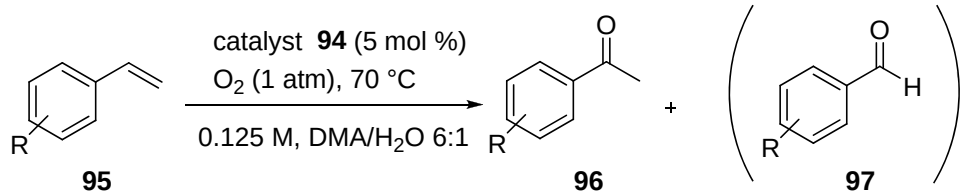


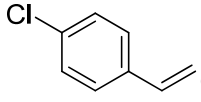
entry	catalyst	reaction time (h)	conversion (%)[b]
1	$PdCl_2$	3	82
2	**94**	24	99

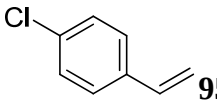
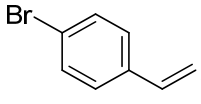
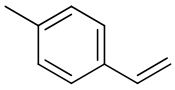
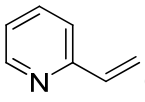
[a]Reaction conditions: 5 mol % catalyst, 4 mL of a 6:1 (v/v) solution of DMA:H_2O, at 70 °C. [b]Determined by GC using decane as internal standard; isolated yields in parentheses.

We turned our attention to the more challenging styrenes because of their propensity for C=C bond cleavage under oxidative conditions. It was found that with 1-chloro-4-vinylbenzene, the catalyst (**94**) showed more selectivity than $PdCl_2$-DMA system at ambient oxygen pressure in the absence of any further co-catalyst (Table 27, entries 1-2). A reaction temperature of 70 °C and a DMA/water mixture of 6:1 were set to perform other substrates. Good yields and selectivities could be obtained for the $PdCl_2$-isonitrile system.

Table 27. Wacker oxidation of aromatic alkenes.

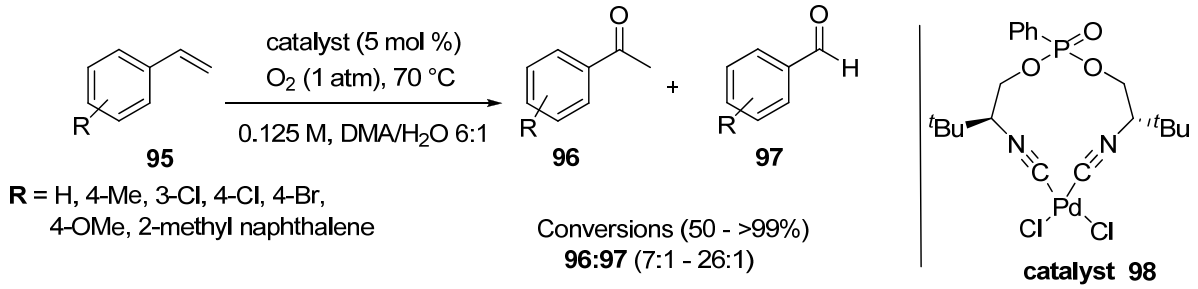


entry	catalyst	substrate (**95**)	reaction time (h)	conversion (%)	ketone/aldehyde (**96:97**)
1	$PdCl_2$	 **95b**	70	>99	4:1

2	**94**	 **95b**	70	>99	6:1
3	**94**	 **95c**	96	58	15:1
4	**94**	 **95d**	48	98	23:1
5	**94**	 **95e**	96	90	10:1

[a]Reaction conditions: 5 mol % catalyst, 4 mL of a 6:1 (v/v) solution of DMA:H_2O, at 70 °C. [b]Determined by GC using decane as internal standard; isolated yields in parentheses.

The Pd-bis(isonitrile) complex is clearly superior to the catalyst (**98**) with monodentate isonitrile ligand (Scheme 47).[6]



Scheme 47. Wacker oxidation of aliphatic alkenes by using Pd-bis(isonitrile) complex (**98**).

4 Conclusion

Palladium isonitrile complex (**94**) was synthesized and characterized by NMR, MS and IR spectroscopy. The Wacker oxidation of terminal aliphatic and aromatic alkenes catalyzed by the complex (**94**) proceeded in good yields and in the absence of other co-catalysts at ambient oxygen pressure, but the selectivities were inferior to Pd-bis(isonitrile) complex systems.

5 References

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5. (a) Takahashi, H.; Tsuji, *J. Bull. Chem. Soc. Jpn.* **1981**, *54*, 2672. (b) Suginome, M.; Oike, H.; Shuff, P. H.; Ito, Y. *J. Organomet. Chem.* **1996**, *521*, 405.
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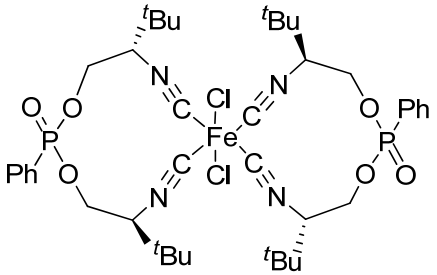
E. Iron(II)-Isonitrile Complex

1 Introduction

Transfer hydrogenation of ketones is one of the most appealing and interesting synthetic routes to enantiopure alcohols and constitutes a good alternative to the widely used catalytic hydrogenation. However, these processes are mainly catalyzed by Ru, Rh or Ir bearing catalysts, which limits their industrial application because of their toxicity, low accessibility and high costs.[1] Therefore, the use of iron catalysts is highly desirable in this regard because of its low toxicity and low price.[2]

2 Transfer hydrogenation

Reiser and co-workers successfully prepared an iron complex of chiral bis(isonitrile) ligand (**18**) (Figure 18), which can catalyze asymmetric transfer hydrogenation of aromatic, heteroaromatic and pyridyl ketones under mild conditions.[3]

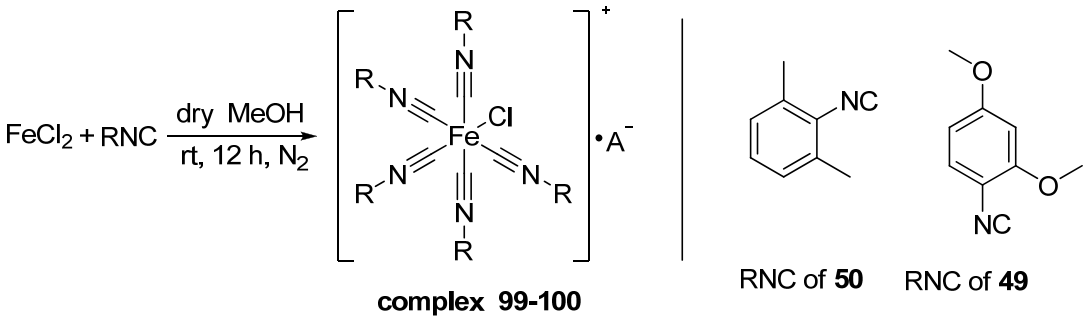


18

Figure 18. Iron complex **18** of chiral bis(isonitrile) ligand

Inspired by the work, we turned our attention to iron catalysts using monodentate isonitrile as ligands in transfer hydrogenation of ketones. The reaction of $FeCl_2$ and xylyl isonitrile (2,6-$Me_2C_6H_3NC$) (**50**) cannot give the expected iron complex [$FeCl_2(RNC)_4$], but the IR and

MS spectra of the complex show the formation of $[FeCl(RNC)_5]^+$. We cannot further determine the anion of iron complex (**99**) since attempts to grow X-ray quality crystals of the complex (**99**) from several solvents failed. Similar results for 2,6-dimethoxy benzenisonitrile (2,6-$MeO_2C_6H_3NC$) (**49**) were also afforded. Further salification of **99** or **100** can't give their desired complexes. Thus, we have to set the anion as A^- and assumed the structure of iron complex (**100**). (Scheme 48, Figure 19)



Scheme 48. Synthesis of Iron-isonitrile complexes (**99-100**).

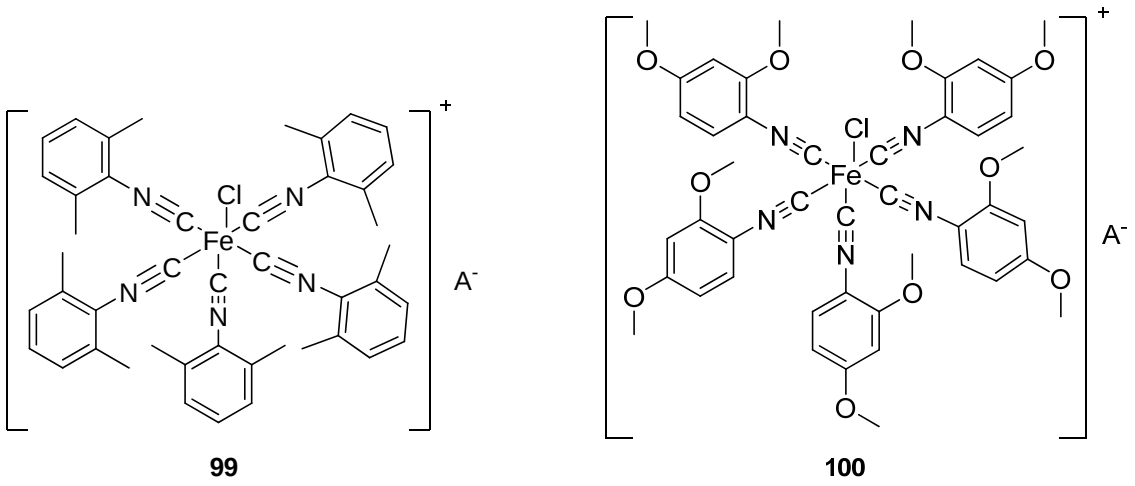
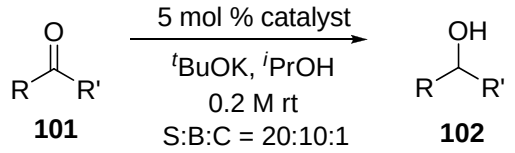


Figure 19. Iron-isonitrile complexes (**99-100**).

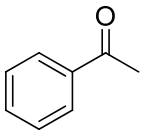
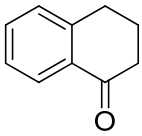
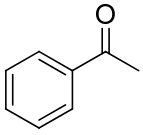
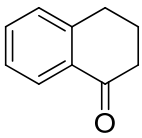
In order to test the activity of the complexes (**99-100**) in transfer hydrogenation, we have chosen transfer hydrogenation of acetophenone to 1-phenylethanol in basic isopropanol and the results are summarized in Table 28. The complexes (**99-100**) were found to be inactive

catalysts either at room temperature or at high temperature (Table 28, entries 2-4) and showed bad activity with no conversion or rather low yield. Based on these results it was concluded that (**99-100**) cannot function well under transfer hydrogenation conditions. The low activity of the complexes (**99-100**) for transfer hydrogenation was understood according to the proposed mechanism for transfer hydrogenation catalyzed by the complex (**18**). The coordination of five isonitrile ligands to the iron center makes coordination of ketone to iron centre difficult.[3]

Table 28. Transfer Hydrogenation of Acetophenone Catalyzed by Complexes (**99**) and (**100**).[a]



101 **102**

entry	catalyst	substrate	time (h)	yield (%)
1	**99**	 **102a**	24	25
2	**99**	 **102b**	24	11
3	**100**	 **102a**	24	18
4	**100**	 **102b**	24	10

[a]Reaction conditions: catalyst (5 mol %), 0.2 M concentration of substrate, KO^{t}Bu (10.0 equiv.).
[b]Isolated yield.

3 Summary

In conclusion, iron complexes (**99-100**) showed lower activity in transfer hydrogenations of ketones. Therefore, no further exploration regarding these transformation reactions were undertaken.

4 References

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F. Platinum(II)-Isonitrile Complex

1 Introduction

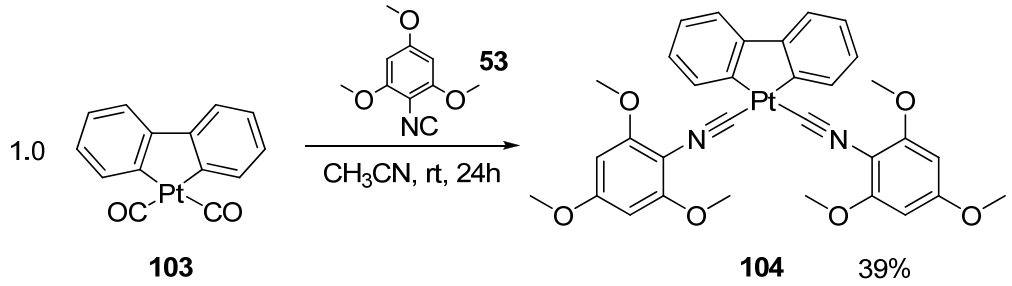
Significant research efforts are currently focused on the study of platinum cyclometallated complexes because of their interesting photochemical and photophysical properties such as good stability, high photoluminescence quantum yields, short tripletstate lifetimes (several microseconds), and ease of spectral tuning.[1] Many of these complexes have attracted much attention due to their applicability as emitters in highly efficient light emitting diodes (OLEDs).[2]

Photoluminescence-tuning Pt(II) cyclometallated complexes from near-UV to IR have been reported. There are two alternatives for tuning emission in isolated complexes: modification of the cyclometallating ring system[2] or variation of the ancillary ligands[3]. We turned our attention to the latter methodology. Isonitrile ligands are unique in their ability to coordinate to transition metals encompassing the various oxidation states.[4] Isonitriles stabilize not only low-valent complexes by participating as σ-acceptor ligands, but also coordinate to high-valent transition metals as strong σ donors. In recent years, several platinum(II) cyclometalated complexes based isonitrile ligands have attracted a great deal of interest as components in luminescent chromophores.[5]

Inspired by these results, we sought platinum cyclometalated complexes which were not modified by isonitrile ligands and paid our attention to Pt(bph)$(CO)_2$ (**103**) (Scheme 50). Pt(bph)$(CO)_2$ (**103**) has been isolated and was found to exhibit a number of unique properties related to its structure in solid state and in solution.[6] The two carbonyl ligands of Pt(bph)$(CO)_2$ (**103**) would be replaced by isonitrile ligands. However, no efforts are currently focused on isonitrile ligands for tuning emission in Pt(bph)$(CO)_2$ (**103**).

2 Results and Discussion

$Pt(bph)(CO)_2$ (**103**) is prepared from $[Pt(bph)((C_2H_5)_2S)]_2$. Upon treatment of 2,4,6-trimethoxy benzenisonitrile (2,4,6-$MeO_3C_6H_2NC$) (**53**) with 1.0 equiv $Pt(bph)(CO)_2$ (**103**) in CH_3CN, the light yellow complex (**104**) was obtained in 39% yield (Scheme 49), which was characterized by IR spectroscopy as well as X-ray crystallographic analysis. However, the corresponding elemental analysis data of (**104**) couldn't be obtained and this failure prevents further studying of its photophysical properties.



Scheme 49. Synthesis of Pt(II)-isonitrile complex (**104**).

Figure 19 shows the structure of the complex Pt(bph)(2,4,6-$MeO_3C_6H_2NC)_2$ (**104**). Selected bond distances and angles are listed in Table 29. The molecule has a slightly distorted square planar geometry. The two carbons of isonitrile moiety in the complex are bonded to the Pt center with bond distances of 1.995(10) Å (C13) and 1.992(10) Å (C23), respectively. The Pt-C-N angle is nearly linear at 177.5(9)° (Pt(1)-C(23)-N(2)) or 175.6(9)° (Pt(1)-C(13)-N(1)). The C-Pt-C angle involving the coordinated carbon atoms of the biphenyl ligand is 92.8(4)° or 92.9(4)°. The small bite size of the biphenyl dianion is responsible for the deviation from ideal square planar geometry.[6]

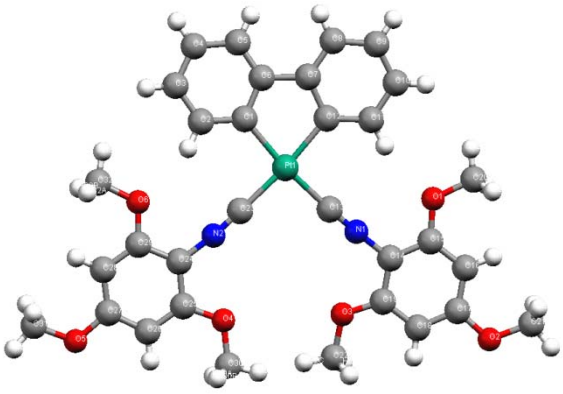


Figure 19. The molecular structure of complex (**104**).

Table 29. Bond lengths (A°) and angles (°) for complex (**104**).

Bond lengths [A°]		Bond angles [°]	
Pt(1)-C(1)	2.052(9)	C(1)-Pt(1)-C(12)	80.2(4)
Pt(1)-C(12)	2.046(10)	C(1)-Pt(1)-C(13)	171.9(4)
Pt(1)-C(13)	1.995(10)	C(1)-Pt(1)-C(23)	92.8(4)
Pt(1)-C(23)	1.992(10)	C(12)-Pt(1)-C(13)	92.9(4)
C(1)-C(2)	1.403(13)	C(12)-Pt(1)-C(23)	172.3(4)
C(11)-C(12)	1.421(14)	C(13)-Pt(1)-C(23)	94.4(4)
C(1)-C(6)	1.417(12)	Pt(1)-C(1)-C(2)	127.1(7)
C(7)-C(12)	1.461(14)	Pt(1)-C(1)-C(6)	117.0(7)
N(1)-C(13)	1.160(12)	Pt(1)-C(12)-C(7)	115.2(7)
N(1)-C(14)	1.400(12)	Pt(1)-C(12)-C(11)	128.1(8)
N(2)-C(23)	1.163(12)	N(1)-C(14)-C(15)	119.2(8)
N(2)-C(24)	1.372(12)	N(2)-C(24)-C(25)	121.1(8)
C(1)-C(2)	1.403(13)	Pt(1)-C(23)-N(2)	177.5(9)
C(7)-C(8)	1.391(14)	Pt(1)-C(13)-N(1)	175.6(9)

3 Summary

The reaction of Pt(bph)$(CO)_2$ (**103**) with 2,4,6-$MeO_3C_6H_2NC$ (**53**) in CH_3CN resulted in the formation of Pt(bph)(2,4,6-$MeO_3C_6H_2NC)_2$ (**104**), which has been structurally characterized by X-ray crystallography. However, the failure in obtaining the corresponding elemental analysis data prevents us further studying its photophysical properties.

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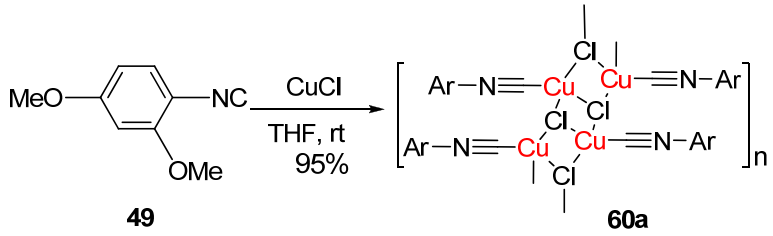
G. Summary

Synthesis of transition metal-isonitrile complexes

This thesis describes new molecular catalysis of transition-metal isonitrile complexes. The investigated ligands are capable of forming very stable complexes with various transition metals such as Cu, Pd, Fe, Pt.

Specifically, a novel, well defined polymeric Cu(I)-isonitrile complex (**60a**) has been successfully synthesized (Scheme 50). Upon treatment of (**49**) with CuCl in THF, the off-white complex (**60a**) was obtained in 95% yield, being stable in air or water for several months. The X-ray crystallographic analysis of **60a** revealed that each Cu(I) center is coordinated to an isonitrile ligand and possesses three bridging chloride atoms that coordinate to another Cu(I) center of the next entity. Hence the [CuLCl] units are linked into an extended one-dimensional chain polymer.



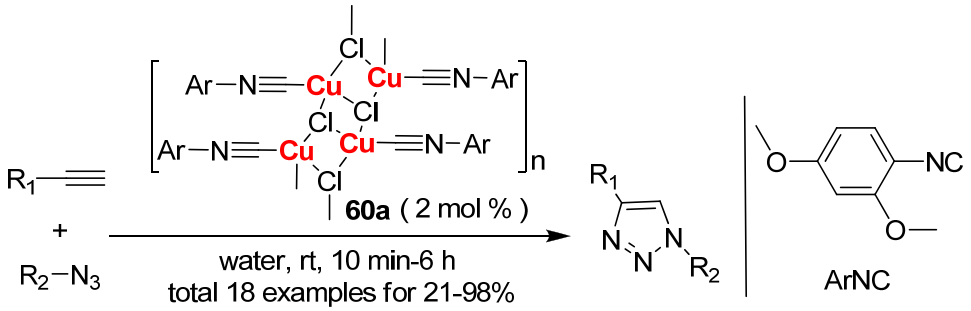
49 **60a**

Scheme 50. The synthesis of copper isonitrile (**60a**).

Copper(I)-isonitrile complex as a heterogeneous catalyst for azide-alkyne cycloaddition in water

The structurally well-defined copper(I)-isonitrile complex (**60a**) was successfully developed as a heterogeneous catalyst for the copper catalyzed azide-alkyne cycloaddition under mild conditions in water (Scheme 51). This catalyst shows considerable synthetic advantages in

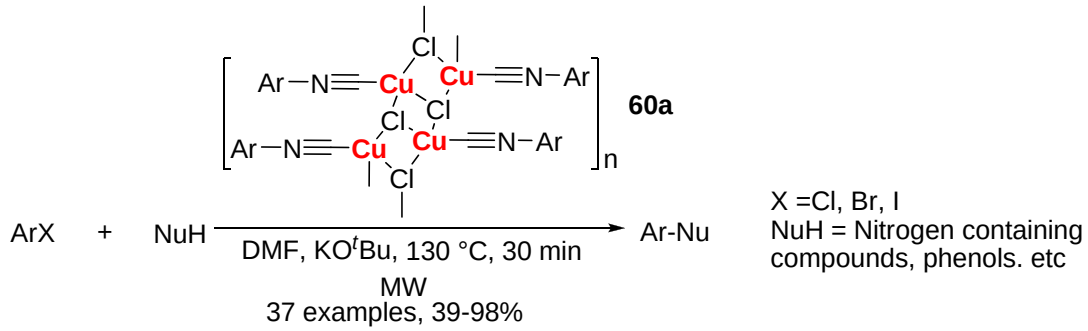
terms of facile and sustainable reaction set-up (aerobic conditions in water, no additives are necessary), wide scope, and high reactivity. The catalyst (**60a**) is also efficient in the three-component (alkyl halide, sodium azide and alkyne) azide-alkyne cycloaddition. Furthermore, it can be readily recovered by filtration and be recycled for at least five runs without significant loss of activity.



Scheme 51. Copper(I)-isonitrile complex (**60a**) as a heterogeneous catalyst for azide-alkyne cycloaddition in water

Ullmann-type coupling reaction catalyzed by copper-isonitrile complex

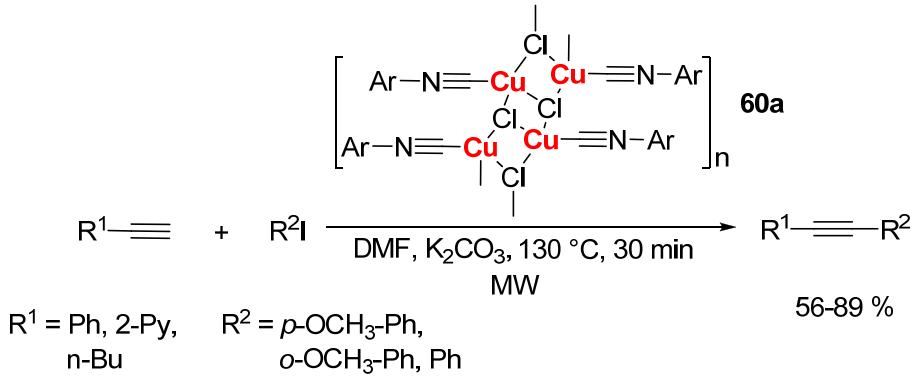
The copper(I)-isonitrile complex (**60a**) was found to be a practical and versatile catalytic system for Ullmann-type coupling reactions under MW irradiation (Scheme 52). A variety of aryl idodides, aryl bromides with nitrogen containing compounds, and phenols participate in the process with good to excellent yields. Furthermore, this catalytic system can active aryl chlorides and give the desired products in moderate yields. The short reaction time and simple reaction conditions, tolerance of a broad substrate scope, make this method particularly attractive for the application in biologically and medicinally interesting molecules.



Scheme 52. Ullmann-type coupling reaction catalyzed by copper-isonitrile complex (**60a**).

Sonogashira coupling reaction catalyzed by copper-isonitrile complex

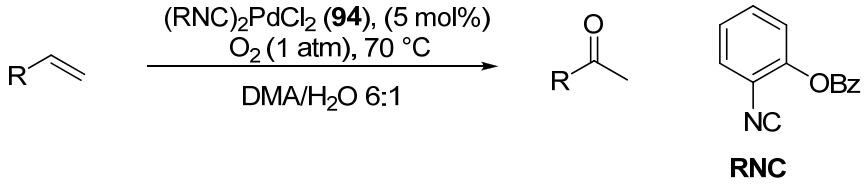
The copper(I)-isonitrile complex (**60a**) displays good catalytic efficiency in the Sonogashira coupling reaction (Scheme 53). However, the relatively narrow scope in this study of substrates may limit its application in organic synthesis.



Scheme 53. Sonogashira coupling reaction catalyzed by copper-isonitrile complex (**60a**).

Palladium(II)-isonitrile complex catalyzed Wacker oxidation

Palladium isonitrile complex (**94**) was synthesized and characterized by NMR, MS and IR spectroscopy. The Wacker oxidation of terminal aliphatic and aromatic alkenes catalyzed by the complex (**94**) proceeded in good yields and selectivities in the absence of other co-catalysts at ambient oxygen pressure (Scheme 54).



Scheme 54. Wacker oxidation of aliphatic and aromatic alkenes using palladium-isonitrile complex (**94**).

From our study, the molecular catalysis with transition metal isonitrile complex is not only promoted, but aslo it has already resulted in the formation of highly effective catalysts that outperformed their former reports. Clearly, there is a bright future for molecular catalysis with transition metal isonitrile complex.

H. Experimental

General

^{1}H NMR-Spectra were recorded on Bruker Avance 300, Bruker Avance 400, Bruker Avance 600, Varian Inova 600, Bruker DRX-400 with a H/C/P/F QNP gradient probe and Bruker Avance 500 with a dual carbon/proton CPDUL cryoprobe. The chemical shift δ is given in [ppm], calibration was set on chloroform-d_1 (7.26 ppm) or tetramethylsilane (0.00 ppm) as internal standard. The spectra were evaluated in 1st order and the coupling constants are given in Hertz [Hz]. The following abbreviations for the spin multiplicity were used: s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, m = multiplet, dt = doublet of a triplet, dd = double doublet, ddd = doublet of a double doublet, sept = septet. The used deuterated solvents are given separately.

^{13}C NMR-Spectra were recorded on Bruker Avance 300, Bruker Avance 400, Bruker Avance 600, Varian Inova, Bruker DRX-400 with a H/C/P/F QNP gradient probe and Bruker Avance 500 with a dual carbon/proton CPDUL cryoprobe. The chemical shift δ is given in [ppm], calibration was set on chloroform-d_1 (77.16 ppm), or tetramethylsilane (0.00 ppm) as internal standard.

Melting points were measured on a Büchi SMP 20 in a silicon oil bath. The melting points are uncorrected.

Infrared-Spectra were recorded on a Bio-Rad Excalibur FTS 3000 spectrometer, equipped with a Specac Golden Gate Diamond Single Reflection ATR-System. The wave numbers are given in [cm^{-1}].

Masspectrometry was performed on Varian MAT 311A, Finnigan MAT 95, Thermoquest Finnigan TSQ 7000, Nermag quadrupoles, VG ZAB high-resolution double-focusing and VG Autospec-Q tandem hybrid with EBEqQ configuration. The percentage set in brackets gives the peak intensity related to the basic peak (I = 100%). High resolution mass spectrometry (HRMS): The molecular formula was proven by the calculated precise mass.

Elemental analysis was prepared by the micro analytic section of the University of Regensburg using a Vario EL III or Mikro-Rapid CHN (Heroes).

X-ray analysis was performed by the crystallography laboratory of the University of Regensburg (STOE-IPDS, Stoe & Cie GmbH).

Gaschromatography (GC) was measured in the analytic department of the University of Regensburg or on Fisons Instruments GC 8000 series (Data Jet Integrator, CP-chiralsil-DEX-CP column).

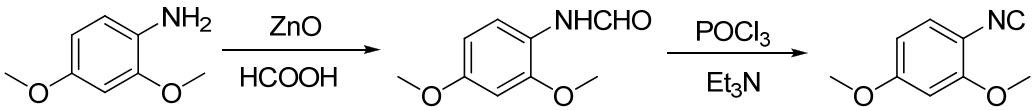
Thin layer chromatography (TLC) was prepared on TLC-aluminium sheets (Merck, silica gel 60 F_{254}, 0.2 mm). Detection in UV-light λ = 254 nm, staining with I_2, Mostain, molybdatophosphoric-acid (5% in ethanol), $KMnO_4$ solution or vanillin-sulfuric acid. GC conversions for the reactions were determined relative to decane as an internal standard

Column chromatography was performed in glass columns (G2 or G3). As a stationary phase silica gel Merck-Geduran 60 (0.063-0.200 mm) or flash silica gel Merck 60 (0.040-0.063 mm) was used.

Solvents: Absolute solvents were prepared according to usual lab procedures or taken from the MB-SPS solvent purification system. Ethylacetate, hexanes (40-60 °C) and dichloromethane were purified by distillation before use. Further solvents and reagents were of p.a. quality. THF, diethyl ether and toluene were distilled over sodium/benzophenone.

Isopropanol was dried over sodium. DMF was distilled from CaH_2 and was stored on 4 Å activated molecular sieves under a nitrogen atmosphere. All of the reagents were stored in the presence of $CaCl_2$ in a desiccator under vacuum at room temperature and protected from light. Reactions with oxygen- and moisture sensitive reactants were performed in oven dried and in vacuo heated reaction flasks under a pre-dried inert gas (nitrogen or argon) atmosphere. For cooling to temperatures < -40 °C a cryostat Haake EK 90 or dry ice/*iso*-propanol mixture was used.

Synthesis of Isonitrile Ligands (49-53)

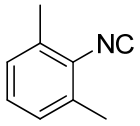


2,4-dimethoxyphenyl isonitrile (49)

To a mixture of HCOOH (150 mmol, 5.5 mL) and ZnO (25 mmol, 2.0 g), 2,4-dimethoxy aniline (50 mmol, 7.6 g) was added and then the reaction mixture was heated in an oil bath at 70 ℃ and stirred with a magnetic stirrer. The progress of the reaction was monitored by TLC. After the reaction was complete, EtOAc was added to the reaction mixture and ZnO was removed by filtration. The organic solvent was then washed with H_2O (2x10 mL), saturated solution of $NaHCO_3$, and dried over anhydrous Na_2SO_4. After removal of the solvent, further purify by recrystallization with suitable solvent (ether or $CHCl_3$), the pure product of N-(2,4-dimethoxyphenyl)-formamide was obtained as a purple solid (7.91 g, 87%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 3.77 (s, 3H), 3.83(s, 3H), 6.41-6.50 (m, 2H), 7.70 (s, 1H), 8.21 (d, *J* = 9.0 Hz, 1H), 8.38 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.45, 55.64, 98.55, 103.63, 119.30, 121.17, 149.14, 156.65, 162.17. MS (EI-MS, m/z): 181.1 ($M^{+\cdot}$).

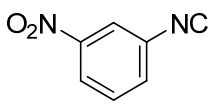
The required formamide (43 mmol) was dissolved in dichloromethane (80 mL) and 17.9 mL (130 mmol) of triethylamine added. The mixture was cooled in an ice bath and a solution of 4.80 mL (51.6 mmol) of Phosphorus oxychloride added dropwise under vigorous stirring.

When the addition was finished, the reaction mixture was continued to stir for 2 h; when the formamide had been consumed, sodium carbonate in distilled water (75 mL) was added at room temperature in a rate so that the temperature was maintained at 25-35 ℃.The organic layer separated and dried over anhydrous $MgSO_4$. The residue from evaporation of the solvent was chromatographed through a silica gel column (R_f= 0.5, petroleum ether/EtOAc = 1:1) as the eluent or recrystallised from dichloromethane–petroleum ether (40–60 ℃). 2,4-dimethoxyphenyl isonitrile (**49**) was observed as a pink needle solid (5.89 g, 83%).
^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 3.74 (s, 3H), 3.81 (s, 3H), 6.34 (dd, *J* = 8.7 Hz, 1H), 6.38 (d, *J* = 2.4 Hz, 1H), 7.16 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.44, 55.76, 98.70, 104.40, 109.09, 128.04, 155.82, 160.96, 165.72 (NC). mp 70–71 ℃. IR (neat): υ = 2127, 1600, 1505, 1475, 1434 cm^{-1}. MS (EI-MS, m/z): 163.1 ($M^{+\cdot}$). Anal. Found: C, 66.2; H, 5.7; N, 8.6.Calc. for $C_9H_9NO_2$: C, 66.2; H, 5.6; N, 8.6%.



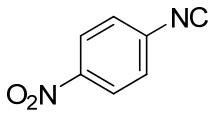
2-isocyano-1,3-dimethylbenzene (50)

Using the general procedure from 2,6-dimethyl-anilin (1.2 mL, 10.0 mmol) after 8 h of reaction, the compound of N-(2,6-dimethylphenyl)formamide were isolated as pale crystals (1.25 g, 83%). Then using the general procedure from formamide (1.25 g, 8.3mmol) after 3 h at 0 ℃, the corresponding isonitrile compound of (**50**) were isolated as a white needle crystals (0.95 g, 87%). ^{1}H NMR (300MHz, $CDCl_3$): δ = 2.34 (s, 6H), 7.00 (s, 1H), 7.03 (s, 1H), 7.08-7.18 (M, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.86, 127.71, 128.61, 134.86, 167.56.



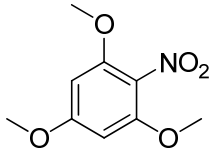
1-isocyano-3-nitrobenzene (51)

Using the general procedure from 3-nitroaniline (1.38 g, 10.0 mmol) after 10 h of reaction, the compound of N-(3-nitrophenyl)formamide were isolated as light yellow solid (1.26 g, 76%). Then using the general procedure from formamide (1.25 g, 7.5 mmol) after 3 h at 0 ℃, the corresponding isonitrile compound of (**51**) were isolated as a yellow solid (0.75 g, 67%). ^{1}H NMR (300MHz, $CDCl_3$): δ = 7.58-7.63 (m, 1H), 7.67-7.71 (m, 1H), 8.21-8.27 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 121.01, 124.24, 130.68, 132.09, 148.12, 167.99.



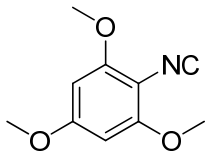
1-isocyano-4-nitrobenzene (52)

Using the general procedure from 4-nitroaniline (1.38 g, 10.0 mmol) after 6 h of reaction, the compound of N-(4-nitrophenyl)formamide were isolated as light yellow solid (1.44 g, 87%). Then using the general procedure from formamide (1.40 g, 8.6 mmol) after 3 h at 0 ℃, the corresponding isonitrile compound of (**52**) were isolated as an orange solid (1.16 g, 91%). ^{1}H NMR (300MHz, $CDCl_3$): δ = 7.55 (d, *J* = 3.0 Hz, 2H), 8.25 (d, *J* = 3.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 124.99, 127.47, 131.16, 147.44, 169.53.



1,3,5-trimethoxy-2-nitrobenzene

1,3,5-trimethoxybenzol (1.68 g, 10.0 mmol) in HCOOH (15 mL) was treated with concd. H_2SO_4, and then the solution were stirred dropwise with 20.0 ml concd.HNO_3 at 0 ℃. After 1 h the title product was filtered off to obtain the product as bright yellow solid powder (1.91 g, 89%). ^{1}H NMR (300MHz, $CDCl_3$): δ = 3.77 (s, 3H), 3.79 (s, 6H), 6.05 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 55.46, 56.30, 90.62, 126.32 (C-NO_2), 153.22, 162.11.

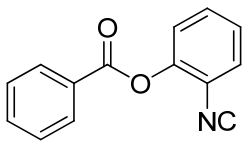


2-isocyano-1,3,5-trimethoxybenzene (53)

Using the general procedure from 2,4,6-trimethoxyaniline (1.45 g, 7.9 mmol) after 8 h of reaction, the compound of N-(2,4,6-trimethoxyphenyl)formamide were isolated as deep pale powder (1.38 g, 83%). Then using the general procedure from formamide (1.3 g, 6.2 mmol) after 2 h at 0 ℃, the corresponding isonitrile compound of (**53**) were isolated as a light yellow solid (1.13 g, 93%). ^{1}H NMR (300MHz, $CDCl_3$): δ = 3.75 (s, 3H), 3.82 (s, 6H), 6.01 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.58, 56.14, 90.33, 157.06, 161.22, 169.11 (NC). IR (neat): υ = 2122, 1945, 1599, 1498, 1468, 1417.

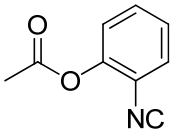
General procedure for isonitrile (54-55) formation

A 50 mL round-bottom flask equipped with a magnetic stir bar and charged with benzoxazole (0.90 g, 7.56 mmol) and THF (18 mL) are allowed to cool to -78 °C for five min prior to addition of *n*-BuLi (1.6 M solution in hexanes, 4.96 mL, 7.94 mmol). The reaction mixture was allowed to stir at the same temperature for 1.5 h. The acid chloride (7.94 mmol) was added dropwise to the solution. The solution was allowed to warm to room temperature and stirred for 2 h. The reaction mixture was poured onto a mixture of ether (100 mL) and saturated aqueous $NaHCO_3$ (50 mL). The organic layer was washed with water (2 x 50 mL), dried, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash column chromatography (solvent noted) and the organics concentrated *in vacuo* to provide the title compounds (**54-55**).



2-isocyanophenyl benzoate (54)

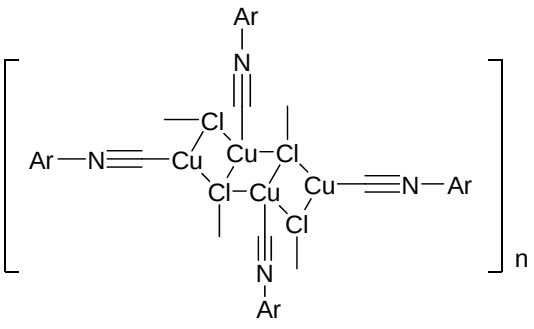
Eluting with hexanes to 10:1 hexanes/ethyl acetate gradient to provide the title compound (**54**) as a white solid (91%). ^{1}H NMR (300MHz, $CDCl_3$): δ = 7.17-7.24 (m, 1H), 7.28-7.32 (m, 1H), 7.36-7.47 (m, 4H), 7.56-7.61 (m, 1H), 8.15-8.18 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 120.23, 123.51, 126.47, 127.55, 128.32, 128.70, 130.26, 130.38, 134.12, 146.50, 163.81, 169. IR (neat): υ = 2131, 1940, 1731, 1693, 1662, 1601, 1528, 1494, 1448.



2-isocyanophenyl acetate (55)

Eluting with hexanes to 49:1 hexanes/ethyl acetate gradient to provide the title compound (**55**) as a liquid (76%). ^{1}H NMR (300MHz, $CDCl_3$): δ = 2.35 (s, 3H), 7.12-7.28 (m, 2H), 7.35-7.46 (m, 2H).

Synthesis of transition metal-isonitrile complexes

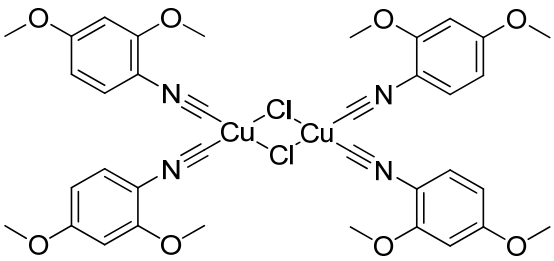


Ar=2,4-dimethoxyphenyl

Cu(I)Cl-(2,4-dimethoxyphenylisonitrile) complex (60a)

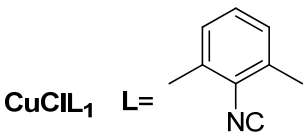
A round-bottom flask was charged with copper (I) chloride (2.0 mmol, 1.0 equiv) and THF (25 mL). A solution of 2,4-dimethoxyphenyl isonitrile (2.1 mmol, 1.05 equiv) in THF (15 mL) was added dropwise over 10 minute, and the solution was stirred under nitrogen for 6 h. The

precipitate was filtered off, washed with EtOAc to remove any unreacted isonitrile, and then dried in vacuum to afford 0.495 g (95%) of the title complex (**60a**) as an off-white solid. Crystals suitable for X-ray structure analysis were obtained by recrystallization from solvent (acetonitrile and $CHCl_3$) as white needle crystals. ^1H NMR (300 MHz, CD_3CN, ppm): δ = 3.83 (s, 3H), 3.94 (s, 3H), 6.56 (dd, *J* = 8.7 Hz, 1H), 6.66 (d, *J* = 2.4 Hz, 1H), 7.44 (d, *J* = 9.0 Hz, 1H). IR (neat): υ = 2158, 1601, 1588, 1504, 1478 cm^{-1}. MS (EI-MS, m/z): 260.9 ($M^{+\cdot}$). HRMS: calcd. for $C_9H_9CuNO_2Cl$ [$M^{+\cdot}$]: 260.9618, found: 260.9614.



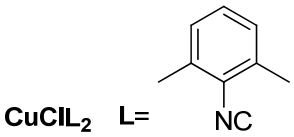
Complex (60b)

Upon treatment of 2.0 equiv (**49**) with 1.0 equiv CuCl in DCM, the white complex (**60b**) was obtained in 93% yield that is stable in air or water for several months. ^1H NMR (300 MHz, $CDCl_3$, ppm): δ = 3.78 (s, 6H), 3.83 (s, 6H), 6.37 (d, *J* = 2.7 Hz, 1H), 6.40-6.42 (m, 3H), 7.24 (s, 1H), 7.26 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.72, 56.01, 98.87, 104.94 108.44 (NC), 128.52, 148.49, 156.39, 161.84. IR (neat): υ = 2170, 2135, 1606, 1583, 1453 cm^{-1}. MS (EI-MS, m/z): 391.1 (M-$Cl^{+\cdot}$). HRMS (LSI-MS): calcd. for $C_{18}H_{18}{}^{63}CuN_2O_4[Cu^{+\cdot}L_2]$: 391.1006, found: 391.1012.

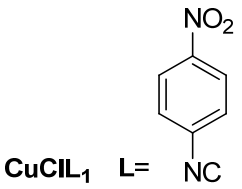


Complex (63a) ^1H NMR (300MHz, DMSO, ppm): δ = 2.39 (s, 6H), 7.29-7.37 (m, 3H). IR (neat): υ = 2140, 1987, 1470, 1384, 1090, 1036, 763 cm^{-1}. MS (EI-MS, m/z): 234.8

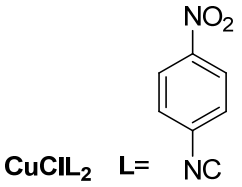
(M-Cl+MeCN$^{+\cdot}$). HRMS (LSI-MS): calcd. for $C_9H_9{}^{63}CuN$ [$Cu^{+\cdot}L_1$]: 194.0031, found: 194.0025.



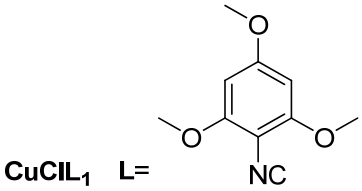
Complex (63b) ^{1}H NMR (300MHz, DMSO, ppm): δ = 2.44 (s, 12H), 7.31-7.33 (m, 4H), 7.38-7.43 (m, 2H). IR (neat): υ = 2153, 2128, 1464, 1381, 1260, 1167 cm^{-1}. MS (EI-MS, m/z): 324.9 (M-Cl$^{+\cdot}$). HRMS (LSI-MS): calcd. for $C_{18}H_{18}{}^{63}CuN_2$ [$Cu^{+\cdot}L_2$]: 325.0766, found: 325.0774.



Complex (64a) ^{1}H NMR (300MHz, DMSO, ppm): δ = 7.98 (d, *J* = 6.9 Hz, 2H), 8.39 (d, *J* = 7.2 Hz, 2H). IR (neat): υ = 2146, 1985, 1609, 1589, 1524, 1485, 1429, 1345, 1312, 1296, 1254, 1202 cm^{-1}. MS (EI-MS, m/z): 251.8 (M-Cl+MeCN$^{+\cdot}$).

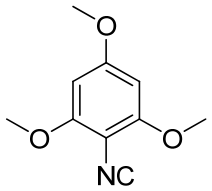


Complex (64b) ^{1}H NMR (300MHz, DMSO, ppm): δ = 7.98 (s, 2H), 8.02 (s, 2H), 8.39 (s, 2H), 8.42 (s, 2H). IR (neat): υ = 2157, 2133, 1609, 1590, 1524, 1483, 1412, 1343, 1309 cm^{-1}. MS (EI-MS, m/z): 395.2 (M-Cl+MeCN$^{+\cdot}$).



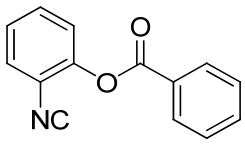
Complex (65a) ^{1}H NMR (300MHz, DMSO, ppm): δ = 3.89 (s, 9H), 6.37 (s, 2H). IR (neat): υ = 2147, 1984, 1733, 1591, 1498, 1473, 1418, 1350, 1233, 1206 cm^{-1}. MS (EI-MS, m/z): 296.9 (M-Cl+MeCN$^{+\cdot}$). HRMS (LSI-MS): calcd. for $C_{10}H_{11}{}^{63}CuNO_3$ [$Cu^{+\cdot}L_1$]: 256.1023, found: 256.1036.

$CuClL_2$ L=



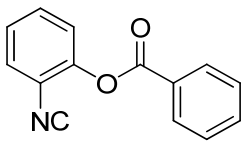
Complex (65b) IR (neat): υ = 2174, 1589, 1498, 1473, 1419, 1352, 1237 cm^{-1}. MS (EI-MS, m/z): 448.9 (M-Cl$^{+\cdot}$). HRMS (LSI-MS): calcd. for $C_{20}H_{22}{}^{63}CuN_2O_6$ [$Cu^{+\cdot}L_2$]: 449.0774, found: 449.0768.

$CuClL_1$ L=

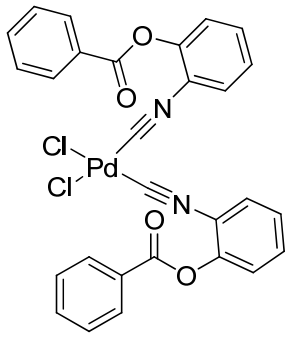


Complex (66a) ^{1}H NMR (300MHz, DMSO, ppm): δ = 7.55-7.84 (m, 7H), 8.21 (s, 2H). IR (neat): υ = 2147, 1749, 1601, 1488, 1449, 1317, 1296 cm^{-1}. MS (EI-MS, m/z): 285.8 (M-Cl$^{+\cdot}$). HRMS (LSI-MS): calcd. for $C_{14}H_9{}^{63}CuNO_2$ [$Cu^{+\cdot}L_1$]: 285.9929, found: 285.9922.

$CuClL_2$ L=

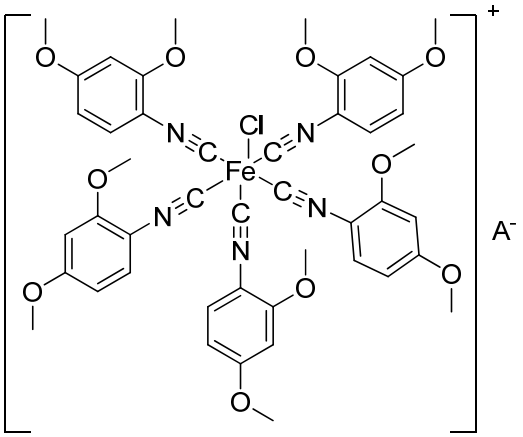


Complex (66b) ^{1}H NMR (300MHz, DMSO, ppm): δ = 7.57-7.71 (m, 14H), 8.18 (s, 4H). IR (neat): υ = 2137, 1749, 1730, 1600, 1540, 1488, 1450, 1316, 1296, 1256, 1229 cm^{-1}. MS (EI-MS, m/z): 509.0 (M-Cl $^{+\cdot}$). HRMS (LSI-MS): calcd. for $C_{28}H_{18}{}^{63}CuN_2O_4$ [$Cu^{+\cdot}L_2$]: 509.0563, found: 509.0563.



[$PdCl_2$(RNC)] (94)

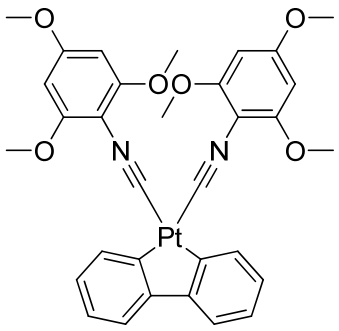
A mixture of the isonitrile ligand (**54**, 30 mg, 0.133 mmol) and $PdCl_2$ (50 mg, 0.131 mmol) in dichloromethane (2.0 mL) was stirred at room temperature for 16 h. The mixture was filtered through a small pad of celite and washed with dichloromethane. The filtrate was concentrated to a volume of approx. 0.5 ml. The crude product was precipitated by addition of 1 mL of hexane and solvent was decanted after stirring for 10 min. This procedure was repeated thrice. The resulting solid was washed with diethyl ether (3 x 1 mL) to give **94** (68 mg, 86% yield) as an off white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.23-7.58 (m, 14H), 8.03 (s, 2H), 8.06 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 118.19, 123.50, 126.51, 127.20, 127.94, 128.06, 128.54, 130.19, 130.65, 132.56, 134.31, 146.85, 163.06. IR (neat): υ = 2212, 1730, 1599, 1485, 1450, 1316, 1258. MS (ES-MS, m/z): 604.1(MNH_4^+-Cl^-).



100 $Fe^{2+}Cl^-L_5$

Typical procedure for synthesis of iron-isonitrile complex (100)

To $FeCl_2.4H_2O$ (1.0 equiv.) in dry MeOH was added a solution of the isonitrile ligand (**49**, 2.05 equiv.) dissolved in minimum amount of dichloromethane. The reddish solution was obtained which was stirred for 12 h at room temperature after which no isonitrile was seen by TLC. The solvent was removed under pressure and residue was washed with hexane thrice. Yellowish orange colored solid (**100**) was obtained after drying under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.65-3.79 (m, 36H), 6.05 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.78, 56.11, 90.33, 100.26, 157.29, 161.63, 164.23. IR (neat): υ = 2945, 2840, 2292, 2151, 2050, 1993, 1503, 1456. MS (LSI-MS, m/z): 906.4 ($M^{+\cdot}$).



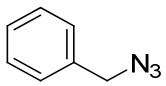
[Pt(RNC)$_2$(CO)$_2$] Complex (104)

General procedure: A round-bottom flask was charged with Pt(bph)(CO)$_2$ (**103**) (40 mg, 0.1 mmol, 1.0 equiv) and acetonitrile (5 mL). A solution of isonitrile (**53**) (40 mg, 0.21 mmol, 2.05 equiv) in acetonitrile (3 mL) was added dropwise and the solution stirred for 12 h. The solvent was removed under vacuum, and the resulting residue was washed with Et_2O and hexane. The precipitate was dried in vacuum and dissolved in only methanol and ethanol. The title complex (**104**) was obtained as a yellow solid (61 mg, 83%), which has been structurally characterized by X-ray crystallography (see X-ray diffraction structure of **104**). MS (LSI-MS, m/z): 734.3 ($MH^{+\cdot}$).

Synthesis for Click reaction

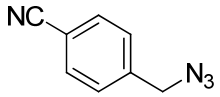
Synthesis of Azides (68)

All azides were synthesized from the corresponding bromides or chlorides by nucleophilic substitution with sodium azide in DMSO at room temperature, for this a stock solution of 0.5 M NaN_3 in DMSO was prepared. To a 100 mL round-bottom flask equipped with a magnetic stirring bar was added NaN_3 (0.715 g, 11.0 mmol) in DMSO (22 mL) at 25 ℃. To this solution was added the alkyl halide (10.0 mmol), and the mixture was stirred until all the starting material had been consumed as observed by TLC. The reaction was quenched with water and stirred until it cooled to RT. The mixture was extracted with ether. The organic layer was washed with brine, dried ($MgSO_4$), filtered, and the solvent removed in vacuum to give the corresponding azide.



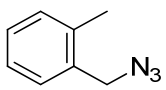
Benzylazide (68a)

From benzyl bromide **70a** (3.6 mL, 30.0 mmol), the title compound (**68a**) was isolated as a colorless oil (3.77 g, 94%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 4.23 (S, 2H), 7.19-7.22 (m, 4H), 7.33-7.35 (m, 1H).



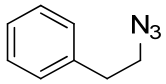
4-(Azidomethyl)benzonitrile (68b)

From 4-(bromomethyl)benzonitrile (**70b**) (1.96 g, 10.0 mmol), the title compound (**68b**) was isolated as a light yellow oil (1.48 g, 94%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 4.38 (s, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H).



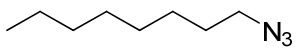
1-(Azidomethyl)-2-methylbenzene (68c)

From 3-methyl-benzylbromid **70d** (4.0 mL, 30.0 mmol), the title compound (**68c**) was isolated as a light yellow oil (3.74 g, 85%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 2.41 (s, 3H), 4.33 (s, 2H), 7.14-7.21 (m, 3H), 7.29-7.34 (m, 1H).



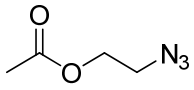
(2-Azidomethyl)benzene (68d)

From (2-bromoethyl)benzene **70e** (4.0 mL, 30.0 mmol), the title compound (**68d**) was isolated as a light yellow oil (4.14 g, 83%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 2.80-2.85 (m, 2H), 3.41-3.46 (m, 2H), 7.13-7.20 (m, 3H), 7.23-7.25 (m, 2H).



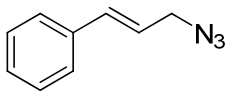
Azidoheptane (68e)

From 1-bromoheptane **70f** (4.7 mL, 30.0 mmol), the title compound (**68e**) was isolated as a light yellow oil (3.71 g, 88%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 0.88 (t, *J* = 6.6 Hz, 3H), 1.28-1.36 (m, 8H), 1.57-1.62 (m, 2H), 3.24 (t, *J* = 7.0 Hz, 2H).



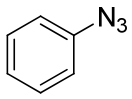
2-Azidoethyl acetate (68o)

From 2-bromethylacetat **70i** (3.3 mL, 30.0 mmol), the title compound (**68o**) was isolated as a light yellow oil (3.61 g, 93%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 1.97 (s, 3H), 3.35 (t, *J* = 4.8 Hz, 2H), 4.09-4.13 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.43, 49.42, 62.71, 170.53. MS (EI-MS, m/z): 147.1 ($MNH_4^{+\cdot}$).



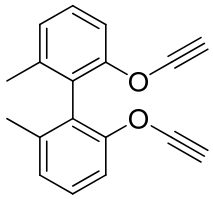
(3-Azidoprop-1-enyl)benzene (68p)

From 3-phenyl-allylbromid (5.49 g, 30.0 mmol), the title compound (**68p**) was isolated as a light yellow oil. (4.01 g, 92%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 3.22 (dd, *J* = 1.2 Hz, 2H), 6.00-6.10 (m, 1H), 6.46 (d, *J* = 15.3 Hz, 1H), 7.08-7.26 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.70, 122.19, 126.43, 127.94, 128.44, 134.19, 135.78.



Phenyl azide (68q)

General procedure: To a suspension of $CuSO_4 \cdot 5H_2O$ (1.25 g, 0.5 equiv) and NaN_3 (0.78 g, 1.2 equiv) in MeOH (30.0 mL) was added the corresponding benzolboronic acid (1.22 g, 1.0 equiv) in one portion. The suspension was stirred vigorously in an open flask for 1 day. The MeOH was evaporated and the residue was extracted with hexanes. The combined hexanes were evaporated and the mixture was then concentrated under vacuum, and the crude product was purified by silica gel chromatography (hexane, R_f = 0.4) to give phenyl azide (**68q**) as a pale yellow oil (0.39 g, 32 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.88-6.91 (m, 2H), 6.98-7.03 (m, 1H), 7.19-7.24 (m, 2H).

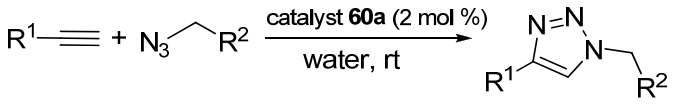


Synthesis of 2,2'-dimethyl-6,6'-bis(prop-2-ynyloxy)biphenyl (67n)

To a 250 mL two-neck round-bottom flask equipped with a condenser was added 6,6'-dimethylbiphenyl-2,2'-diol (2.14 g, 10.0 mmol), propargyl bromide (0.36 mL, 40.0 mmol), potassium carbonate (5.6 g, 40.0 mmol), and acetone (100 mL) under nitrogen atmosphere, and the suspension was refluxed with stirring for 16h. The mixture was filtrated and the filtrate was concentrated under reduced pressure. The product (**67n**) was obtained as a bright yellow liquid after purification on silica (R_f = 0.5, hexanes/ EtOAc = 1:1) in 95% yield (2.49 g). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 1.84 (s, 6H), 2.18 (t, *J* = 2.4 Hz, 2H), 4.35 (d, *J* = 2.4 Hz, 4H), 6.81 (d, *J* = 2.7 Hz, 2H), 6.79 (d, *J* = 3.3 Hz, 2H), 7.06-7.11 (t, *J* = 7.8Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.48, 55.55, 74.95, 79.00, 110.04, 123.00, 126.37, 127.65, 138.25, 154.47. MS (EI-MS, m/z): 290.1($M^{+\cdot}$). HRMS: calcd. for $C_{20}H_{18}O_2$l[$M^{+\cdot}$]: 290.1307, found: 290.1305.

Synthesis of 1,2,3-Triazoles (69)

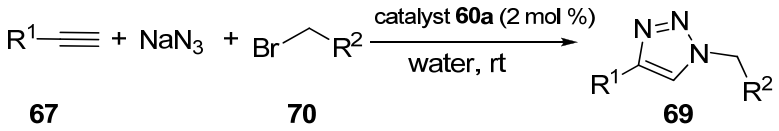
General procedure for the [3+2] cycloaddition of azides and terminal Alkynes (GPA)



67 **68** **69**

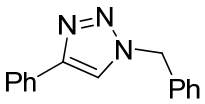
Into a vial fitted with a screw cap, azide (**68**, 1.0 mmol), alkyne (**67**, 1.05 mmol) and complex **60a** (5 mg) in water (1 mL) was given. The reaction was allowed to proceed at room temperature and monitored by TLC. After total consumption of the starting azide, the solid product was collected by filtration and washed with water and pentane. When the corresponding triazole was an oil or a low-melting point solid, the reaction mixture was poured into an aqueous NH_4Cl/diethyl ether mixture. After extraction of the aqueous phase with diethyl ether, the combined organic layers were washed with brine, dried over magnesium sulfate, filtered and evaporated. The residue was finally purified on silica gel (hexane/ethyl acetate). Reported yields are an average of at least two runs.

General procedure for three-component azide-alkyne cycloaddtion (GPB)



67 **70** **69**

The procedure described above was followed using an alkyl halide (**70**) (1.0 mmol), NaN_3 (68 mg, 1.05 mmol) and an alkyne (**67**) (1.05 mmol) in water (1.0 mL).

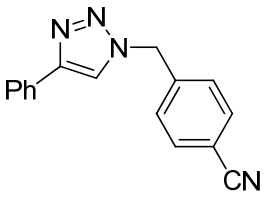


1-Benzyl-4-phenyl-1*H*-1,2,3-triazole (69a)

Using **GPA** benzyl azide **68a** (0.12 mL, 1.0 mmol) and phenylacetylene **67a** (0.12 mL, 1.05 mmol) were reacted for 5 min, **69a** was isolated (R_f= 0.3, hexanes/EtOAc = 2:1) as a white solid (0.221 g, 94% yield).

Using **GPB 67a** (0.12 mL, 1.0 mmol) and **70a** (0.12 mL, 1.05 mmol) were reacted for 2 h, **69a** was isolated (R_f= 0.3, hexanes/ EtOAc = 2:1) as a white solid (0.223 g, 95% yield).

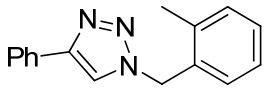
Using **GPB** Benzyl chloride (0.12 mL, 1.0 mmol) and **67a** (0.12 mL, 1.05 mmol) were reacted for 1 h, **69a** was isolated (R_f= 0.3, hexanes/ EtOAc = 2:1) as a white solid (0.229 g, 97% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 5.46 (s, 2H), 7.17-7.33 (m, 8H), 7.58 (s, 1H), 7.66-7.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 54.15, 119.46, 125.64, 127.99, 128.10, 128.72, 128.75 , 129.09, 130.48, 134.65, 148.15. MS (EI-MS, m/z): 235.1 ($M^{+\cdot}$). HRMS: calcd. for $C_{15}H_{13}N_3$ [$M^{+\cdot}$]: 235.1109, found: 235.1112.



4-[(4-Phenyl-1*H*-1,2,3-triazol-1-yl)methyl]benzonitrile (69b)

Using **GPA** 4-(azidomethyl)benzonitrile **68b** (0.158 g, 1.0 mmol) and phenylacetylene **67a** (0.12 mL, 1.05 mmol) were reacted for 10 min, **69b** was isolated (R_f = 0.4, hexanes/EtOAc = 2:1) as a white solid (0.238 g, 91% yield).

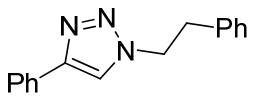
Using **GPB 70b** (0.196 g, 1.0 mmol) and **67a** (0.12 mL, 1.05 mmol) were reacted for 1 h, **69b** was isolated (R_f = 0.4, hexanes/EtOAc = 2:1) as a white solid (0.242 g, 93% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 5.52 (s, 2H), 7.22-7.36 (m, 5H), 7.51 (s, 1H), 7.53 (s, 1H), 7.68 (d, *J* = 5.1 Hz, 2H), 7.71 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.19, 112.41, 118.05, 119.81, 125.54, 128.22, 128.27, 128.74, 130.02, 132.67, 139.84, 148.32. MS (EI-MS, m/z): 260.2 (M^+). HRMS: calcd. for $C_{16}H_{12}N_4$ [$M^{+\cdot}$]: 260.1062, found: 260.1059.



1-(4-Methylbenzyl)-4-phenyl-1*H*-1,2,3-triazole (69c)

Using **GPA 68c** (0.147 g, 1.0 mmol) and phenylacetylene **67a** (0.12 mL, 1.05 mmol) were reacted for 50 min, **69c** was isolated (R_f = 0.5, hexanes/EtOAc = 1:1) as a white solid (0.229 g, 92% yield).

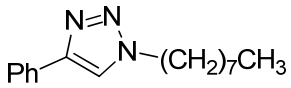
Using **GPB 70c** (0.13 mL, 1.0 mmol) and **67a** (0.12 mL, 1.05 mmol) were reacted for 3 h, **69c** was isolated (R_f = 0.5, hexanes/EtOAc = 1:1) as a white solid (0.209 g, 84% yield). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.19 (s, 3H), 5.35 (s, 2H), 6.94-7.27(m, 7H), 7.56 (s, 1H), 7.66-7.69 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.08, 53.87, 119.51, 124.87, 125.43, 127.88, 128.49, 128.57, 128.75, 129.23, 130.42, 134.47, 138.69, 147.84. MS (EI-MS, m/z): 249.1 ($M^{+\cdot}$). HRMS: calcd. for $C_{16}H_{15}N_3$ [$M^{+\cdot}$]: 249.1278, found: 249.1274.



4-Phenyl-1-(2-phenylethyl)-1*H*-1,2,3-triazole (69d)

Using **GPA 68d** (0.147 g, 1.0 mmol) and phenylacetylene **67a** (0.12 mL, 1.05 mmol) were reacted for 30 min, **69d** was isolated (R_f= 0.5, hexanes/EtOAc = 2:1) as a white solid (0.222 g, 89% yield).

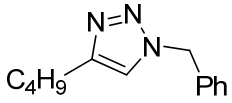
Using **GPB 70d** (0.14 mL, 1.0 mmol) and **67a** (0.12 mL, 1.05 mmol) were reacted for 5 h, **69d** was isolated (R_f= 0.5, hexanes/EtOAc = 1:1) as a white solid (0.219 g, 88% yield). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 3.11 (t, 2H, *J* = 7.4 Hz), 4.48 (t, 2H, *J* = 7.4 Hz), 6.99-7.31 (m, 8H), 7.38 (s, 1H), 7.65-7.68 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 36.64, 51.58, 119.88, 125.57, 127.00, 127.96, 128.63, 128.70, 128.72 , 130.57, 136.97, 147.32. MS (EI-MS, m/z): 249.1 ($M^{+\cdot}$). HRMS: calcd. for $C_{16}H_{15}N_3$ [$M^{+\cdot}$]: 249.1266, found: 249.1268.



1-Octyl-4-phenyl-1H-1,2,3-triazole (69e)

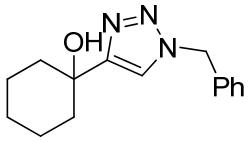
Using **GPA 68e** (0.155 g, 1.0 mmol) and phenylacetylene **67a** (0.12 mL, 1.05 mmol) were reacted for 10 min, **69e** was isolated (R_f= 0.5, hexanes/EtOAc = 1:1) as a light yellow solid (0.246 g, 96% yield).

Using **GPB 70e** (0.17 mL, 1.0 mmol) and **67a** (0.12 mL, 1.05 mmol) were reacted for 3 h, **69e** was isolated (R_f= 0.5, hexanes/EtOAc = 1:1) as a light yellow solid (0.241g, 94% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 0.82-0.87 (m, 3H), 1.23-1.29 (m, 10H), 1.89 (t, *J* = 6.9 Hz, 2H), 4.33 (t, *J* = 7.5 Hz, 2H), 7.28-7.41 (m, 3H), 7.74 (s, 1H), 7.79-7.83 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.94, 22.49, 26.38, 28.86, 28.94, 30.42, 31.60, 50.30, 119.36, 125.56, 127.40, 127.93, 128.70, 130.19, 130.68, 147.56. MS (EI-MS, m/z): 257.2 (M^+). HRMS: calcd. for $C_{16}H_{23}N_3$ [M^+]: 257.1894, found: 257.1898.



Benzyl- 4-butyl-1H-1,2,3-triazole (69f)

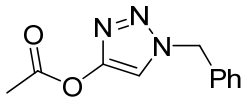
Using **GPA** benzyl azide **68a** (0.12 mL, 1.0 mmol) and hex-1-yne **67f** (0.12 mL, 1.05 mmol) were reacted for 30 min, **69f** was isolated (R_f= 0.5, hexanes/EtOAc = 2:1) as a white solid (0.202 g, 93% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 0.81 (t, *J* = 7.5 Hz, 3H), 1.23-1.30 (m, 2H), 1.53 (q, *J* = 7.8 Hz, 2H), 2.59 (t, *J* = 7.2 Hz, 2H), 5.38 (s, 2H), 7.13-7.16 (m, 3H), 7.22-7.28 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.57, 22.08, 25.18, 31.27, 53.68, 120.39, 127.70, 128.32, 128.59, 128.78, 134.86, 148.67. MS (EI-MS, m/z): 215.1 (M^+). HRMS: calcd. for $C_{13}H_{17}N_3$ [$M^{+\cdot}$]: 215.1422, found: 215.1418.



1-(1-Benzyl-1H-1,2,3-triazol-4-yl)cyclohexanol (69g)

Using **GPA** benzyl azide **68a** (0.12 mL, 1.0 mmol) and 1-ethynylcyclohexanol **67g** (0.14 mL, 1.05 mmol) were reacted for 30 min, **69g** was isolated (R_f= 0.5, hexanes/EtOAc = 3:1) as a white solid (0.191 g, 89% yield).

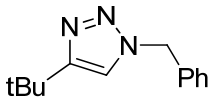
Using **GPB 70a** (0.12 mL, 1.0 mmol) and 1-ethynylcyclohexanol **67g** (0.14 mL, 1.05 mmol) were reacted for 1 h, **69g** was isolated (R_f= 0.5, hexanes/EtOAc = 3:1) as a white solid (0.198 g, 92% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 1.18-1.86 (m, 12H), 2.96 (s, 1H), 5.37 (s, 2H), 7.14-7.17 (m, 2H), 7.24-7.26 (m, 3H), 7.31 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.76, 25.20, 37.88, 53.85, 69.31, 115.81, 119.51, 127.89, 128.47, 128.88, 134.59, 156.00. MS (EI-MS, m/z): 215.1 ($M^{+\cdot}$). HRMS: calcd. for $C_{13}H_{17}N_3$ [$M^{+\cdot}$]: 215.1422, found: 215.1423.



Methyl 1-benzyl-1*H*-1,2,3-triazole-carboxylate (69h)

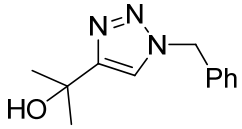
Using **GPA** benzyl azide **68a** (0.12 mL, 1.0 mmol) and methyl-propiolat **67h** (0.09 mL, 1.05 mmol) were reacted for 90 min, **69h** was isolated (R_f= 0.5, hexanes/EtOAc = 2:1) as a white solid (0.213 g, 98% yield).

Using **GPB 70a** (0.12 mL, 1.0 mmol) and methyl-propiolat **67h** (0.09 mL, 1.05 mmol) were reacted for 8 h, **69h** was isolated *(*R_f= 0.5, hexanes/EtOAc = 2:1) as a white solid (0.206 g, 95% yield). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 3.77 (s, 3H), 5.49 (s, 2H), 7.16-7.19 (m, 2H), 7.23-7.26 (m, 3H), 8.01 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 51.70, 53.96, 127.34, 127.85, 128.61, 128.82, 133.61, 139.70, 160.68. MS (EI-MS, m/z): 217.1 ($M^{+\cdot}$). HRMS: calcd. for $C_{11}H_{11}N_3O_2$ [$M^{+\cdot}$]: 217.0851, found: 217.0851. mp: 105-107 ℃.



1-Benzyl-4-tert-butyl-1H-1,2,3-triazole (69i)

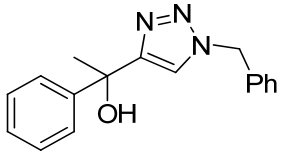
Using **GPA** benzyl azide **68a** (0.12 mL, 1.0 mmol) and tert-butylacetylen **67i** (0.13 mL, 1.05 mmol) were reacted for 4 h, **69i** was isolated (R_f= 0.5, hexanes/EtOAc = 3:1) as a white solid (0.183 g, 85% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 1.23 (s, 9H), 5.37 (s, 2H), 7.11-7.18 (m, 2H), 7.25-7.27 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.17, 30.57, 53.69, 118.30, 127.82, 128.34, 128.83, 134.92, 157.91. MS (EI-MS, m/z): 215.1 ($M^{+\cdot}$). HRMS: calcd. for $C_{13}H_{17}N_3$ [$M^{+\cdot}$]: 215.1422, found: 215.1423.



2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-ol (69j)

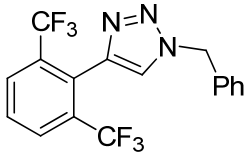
Using **GPA** benzyl azide **68a** (0.12 mL, 1.0 mmol) and 3-methyl-butyne-3-ol **67j** (0.10 mL, 1.05 mmol) were reacted for 45 min, **69j** was isolated (R_f= 0.5, hexanes/EtOAc = 3:1) as a white solid (0.201 g, 92% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 1.49 (s, 6H), 3.58 (s,

1H), 5.35(s, 2H), 7.13-7.20 (m, 2H), 7.21– 7.26 (m, 2H), 7.32 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.24, 53.81, 68.20, 119.16, 127.90, 128.45, 128.85, 134.49, 156.00. EI - MS [M+]: 216 (100%). MS (EI-MS, m/z): 217.1 ($M^{+\cdot}$). HRMS: calcd. for $C_{12}H_{15}N_3O$ [$M^{+\cdot}$]: 217.1215, found: 217.1210.



1-(1-Benzyl-1H-1,2,3-triazol-4-yl)-1-phenylethanol (69k)

Using **GPA** benzyl azide **68a** (0.12 mL, 1.0 mmol) and 2-phenyl-3-butin-2-ol **67k** (0.153 g, 1.05 mmol) were reacted for 6 h, **69k** was isolated (R_f = 0.5, hexanes/EtOAc = 3:1) as a white solid (0.240 g, 86% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 1.85 (s, 3H), 3.33 (s, 1H), 5.35(s, 2H), 7.21-7.28 (m, 9H), 7.35-7.39 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.63, 54.02, 72.03, 120.39, 125.14, 127.04, 127.98, 128.09, 128.62, 129.00, 134.48, 146.48, 155.30. MS (EI-MS, m/z): 279.1 ($M^{+\cdot}$). HRMS: calcd. for $C_{17}H_{17}N_3O$ [$M^{+\cdot}$]: 279.1372, found: 279.1372.

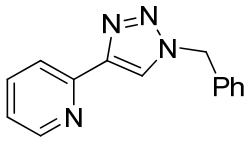


1-Benzyl-4-(2,6-bis(trifluoromethyl)phenyl)-1H-1,2,3-triazole (69l)

Using **GPA** benzyl azide **68a** (0.12 mL, 1.0 mmol) and 1-ethinyl-3,5-bis-(trifluormethyl)-benzol **67l** (0.19 mL, 1.05 mmol) were reacted for 45 min, **69l** was isolated (R_f = 0.5, hexanes /EtOAc = 3:1) as a white solid (0.342 g, 92% yield).

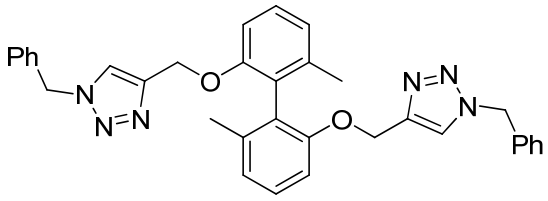
Using **GPB 70a** (0.12 mL, 1.0 mmol) and **67l** (0.19 mL, 1.05 mol) were reacted for 1 h, **69l** was isolated (R_f = 0.5, hexanes/EtOAc = 3:1) as a white solid (0.334 g, 90% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 5.45 (s, 2H), 7.18-7.26 (m, 5H), 7.65 (s, 1H), 7.81 (s, 1H), 8.12

(s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 54.35, 117.69, 120.72, 121.31, 121.38, 124.92, 125.43, 125.46, 128.01, 128.89, 129.14, 131.37, 131.82, 132.25, 132.68, 134.11, 145.36. ^{19}F NMR (282 MHz, $CDCl_3$): δ = -63.61. MS (EI-MS, m/z): 371.2 ($M^{+\cdot}$). HRMS: calcd. for $C_{17}H_{11}N_3F_6$ [$M^{+\cdot}$]: 371.0857, found: 371.0862. mp: 104-106 ℃.



2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl) pyridine (69m)

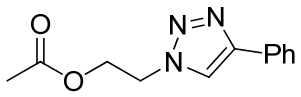
Using **GPA** benzyl azide **68a** (0.12 mL, 1.0 mmol) and 2-ethynylpyridine **67m** (0.12 mL, 1.05 mmol) were reacted for 3h, **69m** was isolated (R_f = 0.5, hexanes/EtOAc = 2:1) as a white solid (0.205 g, 87% yield). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 5.45 (s, 2H), 7.03-7.30（m, 7H）, 7.60 (s, 1H), 7.70-7.73 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 54.01, 119.51, 125.55, 127.90, 128.01, 128.60, 128.68, 128.99, 130.41, 134.60, 148.02. MS (EI-MS, m/z): 235.1 ($M^{+\cdot}$). HRMS: calcd. for $C_{14}H_{12}N_4$ [$M^{+\cdot}$]: 235.1109, found: 235.1102.



4,4'-(6,6'-Dimethylbiphenyl-2,2'-diyl)bis(oxy)bis(methylene)bis(1-benzyl-1H-1,2,3-triazole) (69n)

Using **GPA** benzyl azide **68a** (0.25 mL, 2.0 mmol) and 2,2'-bis(ethynyloxy)-6,6'-dimethylbiphenyl **67n** (0.29 g, 1.05 mmol) were reacted for 6 h, **69n** was isolated (R_f = 0.5, hexanes/EtOAc = 1:1) as a light yellow liquid (0.423 g, 76% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 1.75 (s, 6H), 4.80 (s, 4H), 5.0 (q, *J* = 24.9 Hz, 4H), 6.65 (d, *J* = 3.3 Hz, 2H), 6.68 (d, *J* = 3.0 Hz, 2H), 6.70 (s, 2H), 6.95-7.00 (m, 6H), 7.13-7.18 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.17, 53.38, 62.62, 109.95, 121.85, 122.47, 126.54, 127.50, 127.60,

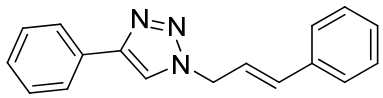
128.17, 128.56, 134.28, 137.89, 144.87, 155.04. MS (EI-MS, m/z): 556.2 ($M^{+\cdot}$). HRMS: calcd. for $C_{34}H_{32}N_6O_2$ [$M^{+\cdot}$]: 556.2587, found: 556.2580.



2-(4-Phenyl-1H-1,2,3-triazol-1-yl) ethyl acetate (69o)

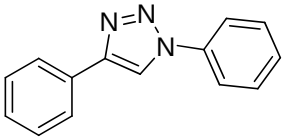
Using **GPA 68o** (0.129 g, 1.0 mmol) and phenylacetylene **67a** (0.12 mL, 1.05 mmol) were reacted for 45 min, **69o** was isolated (R_f= 0.5, hexanes/EtOAc = 3:1) as a white solid (0.215 g, 93% yield).

Using **GPB 70o** (0.11 mL, 1.0 mmol) and **67a** (0.12 mL, 1.05 mmol) were reacted for 7 h, **69o** was isolated (R_f= 0.5, hexanes/EtOAc = 3:1) as a white solid (0.210 g, 91% yield). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 1.96 (s, 3H), 4.40 (t, *J* = 4.8 Hz, 2H), 4.55 (t, *J* = 5.4 Hz, 2H), 7.24-7.35 (m, 3H), 7.72-7.76 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.55, 48.93, 62.25, 120.11, 125.57, 128.09, 128.72, 130.31, 147.81, 170.27. MS (EI-MS, m/z): 231.1 (M^+). HRMS: calcd. for $C_{12}H_{13}N_3O_2$ [M^+]: 231.1008, found: 231.1006. mp: 123-124 ℃.



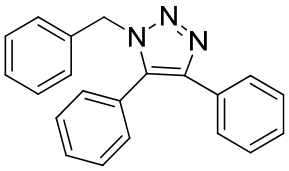
1-(3-Phenyl-2-propenyl)-4-phenyl-1,2,3-triazole (69p)

Using **GPA** (3-azidoprop-1-enyl)benzene **68p** (0.145 g, 1.0 mmol) and phenylacetylene **67a** (0.12 mL, 1.05 mmol) were reacted for 60 min, **69p** was isolated (R_f= 0.4, hexanes/EtOAc = 1:1) as a slightly yellow solid (0.248 g, 95% yield). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 5.02 (d, *J* = 6.3 Hz, 2H), 6.20-6.30 (m, 1H), 6.57 (d, *J* = 15.9 Hz, 1H), 7.18-7.34 (m, 6H), 7.71-7.76 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.20, 119.34, 121.83, 125.56, 126.58, 128.00, 128.40, 128.59, 128.70, 130.50, 135.17, 135.36, 147.87. MS (EI-MS, m/z): 261.2 ($M^{+\cdot}$). HRMS: calcd. for $C_{17}H_{15}N_3$ [$M^{+\cdot}$]: 261.1278, found: 261.1271.



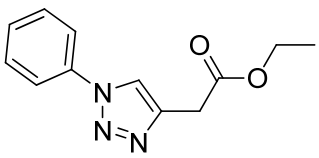
1,4-Diphenyl-1H-1,2,3-triazole (69q)

Using **GPA** phenyl azide **68q** (0.11 mL, 1.0 mmol) and phenylacetylene **67a** (0.12 mL, 1.05 mmol) were reacted for 30 min, **69q** was isolated (R_f = 0.4, petroleum ether/ EtOAc = 3:1) as a white solid (0.186 g, 85% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 7.35-7.40 (m, 1H), 7.43-7.49 (m, 3H), 7.52-7.58 (m, 2H), 7.77-7.81 (m, 2H), 7.90-7.94 (m, 2H), 8.20 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 117.58, 120.50, 125.83, 128.41, 128.76, 128.90, 129.76, 130.22, 137.03, 148.39.



1-benzyl-4,5-diphenyl-1H-1,2,3-triazole (69r)

Using the general procedure from 0.12 mL (1.0 equiv) of Benzylazide **68a** and 0.198 g (1.1 equiv) of 1,2-diphenylethyne **67r** after 48 h at 70℃ in THF, the title compound **69r** was isolated as a white solid after purification by chromatography (21 % yield). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 5.41 (s, 2H), 7.02-7.05 (m, 2H), 7.13-7.16 (m, 2H), 7.24-7.29 (m, 6H), 7.38-7.50 (m, 3H), 7.56-7.59 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 51.93, 126.60, 127.40, 127.60, 127.75, 128.04, 128.35, 128.60, 129.07, 129.60, 129.99, 130.84, 133.80, 135.28, 144.41. MS (EI-MS, m/z): 311.1($M^{+\cdot}$). HRMS: calcd. for $C_{21}H_{17}N_3$ [$M^{+\cdot}$]: 311.1422, found: 311.1423.



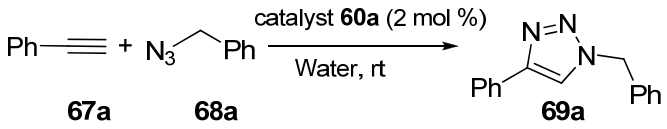
2-ethyl -(1-phenyl-1H-1,2,3-triazol-4-yl) acetate (69s)

Using **GPB** 2-bromethylacetat **70s** (0.12 mL, 1.05 mmol) and **67a** (0.12 mL, 1.0 mmol) were reacted for 3 h, **69s** was isolated (R_f = 0.5, hexanes/EtOAc = 2:1) as a white solid (0.211 g, 91% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 1.19 (t, *J* = 5.9 Hz, 3H), 4.16 (q, *J* = 13.9 Hz, 2H), 5.12 (s, 2H), 7.26-7.37 (m, 3H), 7.77 (d, *J* = 7.2 Hz, 2H), 7.91 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.73, 50.59, 62.06, 121.13, 125.43, 127.93, 128.55, 130.13, 147.70, 166.15. MS (EI-MS, m/z): 231.1($M^{+\cdot}$). HRMS: calcd. for $C_{12}H_{13}N_3O_2$ [$M^{+\cdot}$]: 231.1007, found: 231.10002.

Copper(I)-catalyzed Huisgen [3+2] dipolar cycloaddition (CuAAC) by catalyst 60a; recycling experiments

Using **GPA** benzyl azide **68a** (1.80 mL, 15.0 mmol), phenylacetylene **67a** (1.70 mL, 15.7 mmol) and **60a** (78 mg, 0.30 mmol, 2 mol %) were reacted for 10 min in water (10.0 ml). After completion, the reaction mixture was filtered to recover the catalysts **60a**, which was washed with THF (3×10 mL) and ethyl acetat (3×10 mL). The combined organic layers were washed with water (3×10 mL), dried over Na_2SO_4 and concentrated under vacuum to afford **69a** as a white solid (3.46 g, 98% yield). Catalyst **60a** was reused without further purification for next run. Starting with this catalyst loading, the reaction was performed through 5 cycles on a 15.0 mmol scale each. Fresh portions of **68a** (1.80 mL, 15.0 mmol) and **67a** (1.70 mL, 15.7 mmol) were added to each run. After each cycle the heterogeneous catalyst was recovered by simple filtration and reused without further purification. The detailed yield and the recovery yield of catalyst **60a** at every run are given in Table 11 in the main thesis (see also below).

Table 11. Results of recyclability experiments.[a]

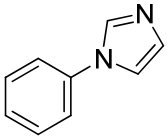


entry	run	time (min)	yield (%)[b]	recovery of catalyst based on the initial amount (%)
1	1	10	98	92
2	2	10	96	83
3	3	10	96	72
4	4	10	97	62
5	5	10	93	50

Synthesis for Ullmann reaction

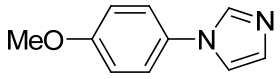
General Procedure for the Coupling Reaction

A mixture of nucleophile **86** or **88** (2.0 eq. or 1.5 eq.) and complex **60a** (5 mol %) was dissolved in dry DMF (2.0 mL). Aryl Halide **85** (1.0 eq.) and KO^{t}Bu or K_2CO_3 (3.0 eq.) was added under nitrogen subsequently. The vial was sealed and this mixture was then irradiated for 30 min at 130 °C. After the reaction was cooled to ambient temperature, the crude reaction mixture was diluted with water, ethyl acetate and then filtered through celite. The filtrate was washed three times with water and brine respectively, and the combined aqueous phase was extracted three times with ethyl acetate (three times). The combined organic layers were dried with Na_2SO_4, concentrated and purified by flash column chromatography (petroleum ether/ethyl acetate) to give the expected product.



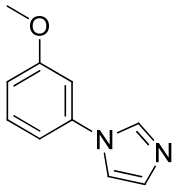
1-phenyl-1H-imidazole (87a)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87a** (0.130 g, 90%). (from bromobenzene **85e**: 0.121 g, yield 84%; from chlorobenzene **85f**: 0.061 g, yield 42%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 7.13 (s, 1H), 7.20 (s, 1H), 7.26-7.32 (m, 3H), 7.36-7.42 (m, 2H), 7.77 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 118.06, 121.28, 127.31, 129.70, 130.25, 135.41, 137.18. MS (EI-MS, m/z): 144.0 ($M^{+\cdot}$).



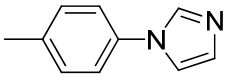
1-(4-methoxyphenyl)-1H-imidazole (87b)

The title compound was prepared according to the general procedure from 4-iodanisol **85b** (0.234 g, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87b** (0.148 g, 85%). (from 4-bromanisol **85c**: 0.141 g, yield 81%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 3.73 (s, 3H), 6.73-6.89 (m, 2H), 7.08 (d, *J* = 6.6 Hz, 2H), 7.15-7.23 (m, 2H), 7.65 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.31, 114.61, 118.47, 122.85, 129.79, 130.40, 135.55, 158.62.



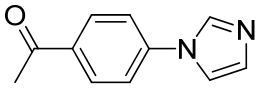
1-(3-methoxyphenyl)-1H-imidazole (87c)

The title compound was prepared according to the general procedure from 3-iodanisol **85q** (0.13 mL, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87c** (0.081 g, yield 46%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 3.78 (s, 3H), 6.82-6.92 (m, 4H), 7.21-7.33 (m, 3H).



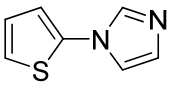
1-p-tolyl-1H-imidazole (87d)

The title compound was prepared according to the general procedure from 4-iodtoluol **85d** (0.218 g, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87d** (0.131g, 83%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 2.28 (s, 3H), 7.15 (s, 6H), 7.71 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.67, 118.06, 121.08, 129.93, 130.08, 134.70, 135.31, 137.13.



1-(4-(1H-imidazol-1-yl)phenyl)ethanone (87e)

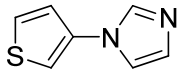
The title compound was prepared according to the general procedure from 4-iodacetophenon **85g** (0.246 g, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87e** (0.166 g, 89%). (from 4-bromoacetophenon **85h**: 0.132 g, yield 71%; from 4-chloroacetophenon: 0.052 g, yield 28%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 2.58 (s, 3H), 7.18 (s, 1H), 7.30 (s, 1H), 7.43-7.46 (m, 2H), 7.90 (s, 1H), 8.01-8.04 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.57, 117.67, 120.65, 130.28, 131.08, 135.71, 140.66, 196.49.



1-(thiophen-2-yl)-1H-imidazole (87f)

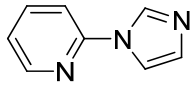
The title compound was prepared according to the general procedure from 2-bromthiophen **85i** (97 μL, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87f** (0.111 g, 73%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ =

6.86-6.89 (m, 2H), 7.03 (q, *J* = 2.1 Hz, 1H), 7.06 (s, 1H), 7.09 (t, *J* = 1.5 Hz, 1H), 7.65 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 118.57, 119.90, 121.42, 126.01, 129.84, 136.61, 138.63.



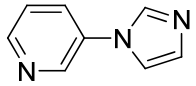
1-(thiophen-3-yl)-1H-imidazole (87g)

The title compound was prepared according to the general procedure from 3-bromthiophen **85j** (94 μL, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatog –raphy to yield **87g** (0.120 g, 80%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 7.08-7.10 (m, 2H), 7.11-7.13 (m, 1H), 7.16 (s, 1H), 7.34 (q, *J* = 5.4 Hz, 1H), 7.73 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 113.04, 118.40, 121.27, 127.04, 129.86, 135.67, 136.05.



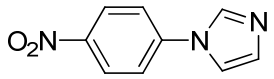
2-(1H-imidazol-1-yl)pyridine (87h)

The title compound was prepared according to the general procedure from 2-brompyridin **85k** (95 μL, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87h** (0.139 g, 96%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 7.09-7.13 (m, 2H), 7.22-7.26 (m, 1H), 7.54 (t, *J* = 1.2 Hz, 1H), 7.66-7.72 (m, 1H), 8.26 (s, 1H), 8.33-8.36 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 111.94, 115.79, 121.67, 130.28, 134.59, 138.69, 148.73.



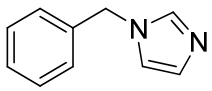
3-(1H-imidazol-1-yl)pyridine (87i)

The title compound was prepared according to the general procedure from 3-brompyridin **85l** (96 µL, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87i** (0.135 g, 93%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 7.18 (s, 1H), 7.25 (s, 1H), 7.36-7.40 (m, 1H), 7.65-7.69 (m, 1H), 7.82 (s, 1H), 7.55 (d, *J* = 4.5 Hz, 1H), 8.68 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 117.92, 124.18, 128.61, 130.86, 133.67, 135.29, 142.74, 148.62.



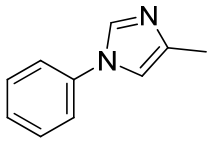
1-(4-nitrophenyl)-1H-imidazole (87j)

The title compound was prepared according to the general procedure from 4-iodnitrobenzol **85m** (0.249 g, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87j** (0.149 g, 79%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 7.21 (s, 1H), 7.34 (t, *J* = 1.5 Hz, 1H), 7.52-7.56 (m, 2H), 7.94 (s, 1H), 8.29-8.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 117.58, 120.94, 125.65, 131.50, 135.29, 141.82, 146.11. MS (LSI-MS, m/z): 189.1($M^{+\cdot}$). HRMS: calcd. for $C_9H_7N_3O_2$ [$M^{+\cdot}$]: 189.0538, found: 189.0539.



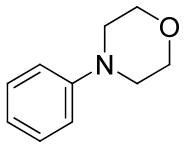
1-benzyl-1H-imidazole (87k)

The title compound was prepared according to the general procedure from benzyliodide **85o** (0.11 mL, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87k** (0.125 g, 79%). (from benzylchlorid **85m**: 0.084 g, yield 53%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 5.00 (s, 2H), 6.80 (s, 1H), 6.99 (s, 1H), 7.03-7.06 (m, 2H), 7.21-7.28 (m, 3H), 7.45 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 50.58, 119.28, 127.09, 128.05, 128.78, 129.52, 136.00, 137.26.



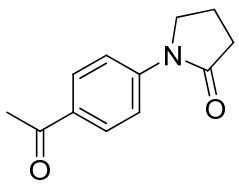
4-methyl-1-phenyl-1H-imidazole (87l)

The title compound was prepared according to the general procedure from iodbenzene **85a** (0.11 mL, 1.0 mmol) and 4(5)-methyl-imidazole **86b** (0.164 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87l** (0.131 g, 83%). (from brombenzene **85e**: 0.128 g, yield 81%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 2.21(s, 3H), 6.92 (s, 1H), 7.17-7.43 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.54, 114.46, 121.03, 125.47, 126.96, 129.77, 134.46, 139.40.



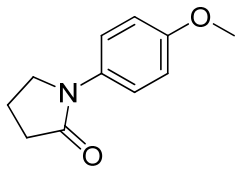
4-phenylmorpholine (87m)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and morpholin **86c** (0.18 mL, 2.0 mmol). The crude product was purified by flash chromatography to yield **87m** (0.127 g, 78%). (from bromobenzene **85e**: 0.119 g, yield 73%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 3.07-3.10 (m, 4H), 3.77-3.80 (m, 4H), 6.74-6.86 (m, 3H), 7.17-7.24 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.33, 66.91, 115.68, 120.02, 129.15, 151.25.



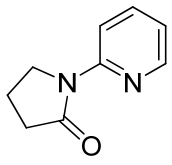
1-(4-acetylphenyl)pyrrolidin-2-one (87n)

The title compound was prepared according to the general procedure from 4-iodacetophenon **85g** (0.246 g, 1.0 mmol) and 2-pyrrolidon **86d** (0.15 mL, 2.0 mmol). The crude product was purified by flash chromatography to yield **87n** (0.173 g, 85%). (from 4-bromacetophenon: 0.026 g, yield 13%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 2.08-2.18 (m, 2H), 2.52 (s, 3H), 2.58 (t, *J* = 8.4 Hz, 2H), 3.84 (t, *J* = 6.9 Hz, 2H), 7.55-7.71 (m, 2H), 7.88-7.93 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.84, 26.45, 32.85, 48.43, 53.97, 118.68, 129.35, 132.68, 143.47, 174.69, 197.02.



1-(4-methoxyphenyl)pyrrolidin-2-one (87o)

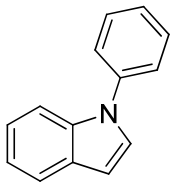
The title compound was prepared according to the general procedure from 1-iodo-4-methoxybenzene **85b** (0.234 g, 1.0 mmol) and 2-pyrrolidon **86d** (0.15 mL, 2.0 mmol). The crude product was purified by flash chromatography to yield **87o** (0.176 g, 92%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 2.04-2.09 (m, 2H), 2.51 (t, *J* = 8.1 Hz, 2H), 3.72-3.77 (m, 5H), 6.82 (d, *J* = 9.0 Hz, 2H), 7.42 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.92, 32.39, 49.11, 55.36, 113.93, 127.74, 132.53, 156.46, 173.86.



1-(pyridin-2-yl)pyrrolidin-2-one (87p)

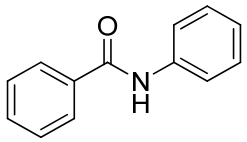
The title compound was prepared according to the general procedure from 2-bromopyridine **85k** (0.10 mL, 1.0 mmol) and 2-pyrrolidon **86d** (0.15 mL, 2.0 mmol). The crude product was purified by flash chromatography to yield **87p** (0.156 g, 96%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 1.98-2.08 (m, 2H), 2.56 (t, *J* = 8.7 Hz, 2H), 4.00 (t, *J* = 6.9 Hz, 2H), 6.90-6.95 (m,

1H), 7.55-7.61 (m, 1H), 8.24-8.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.46, 33.49, 47.13, 114.42, 119.17, 137.30, 147.27, 151.72, 174.76.



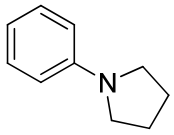
1-phenyl-1H-indole (87q)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and 1H-indol **86e** (0.234 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87q** (0.164 g, 85%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 6.57 (dd, *J* = 0.6 Hz, 1H), 7.04-7.14 (m, 2H), 7.19-7.26 (m, 2H), 7.38 (d, *J* = 3.9 Hz, 4H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.57-7.60 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 103.53, 110.47, 120.32, 121.10, 122.32, 124.30, 126.37, 127.89, 129.29, 129.55, 135.78, 139.77.



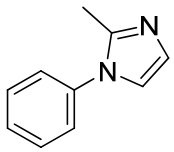
N-phenylbenzamide (87r)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and benzamid **86f** (0.242 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87r** (0.164 g, 83%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 7.03-7.08 (m, 1H), 7.17-7.27 (m, 2H), 7.29-7.38 (m, 2H), 7.42-7.48 (m, 1H), 7.54-7.58 (m, 2H), 7.75-7.79 (m, 2H), 7.92 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 120.25, 124.52, 127.02, 128.71, 129.03, 131.78, 134.93, 137.91, 165.84.



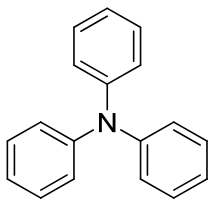
1-phenylpyrrolidine (87s)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and pyrrolidin **86g** (0.17 mL, 2.0 mmol). The crude product was purified by flash chromatography to yield **87s** (0.125 g, 85%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 1.91-1.95 (m, 4H), 3.19-3.25 (m, 4H), 6.49-6.62 (m, 2H), 6.94-6.97 (m, 1H), 7.13-7.16 (m, 2H).



2-methyl-1-phenyl-1H-imidazole (87t)

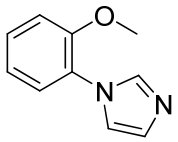
The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and 2-methyl-imidazole **86h** (0.164 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87t** (85 mg, 54%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 2.36 (s, 3H), 7.00 (d, *J* = 5.3 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.50-7.38 (m, 3H).



Triphenylamine (87u)

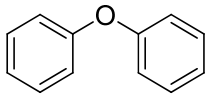
The title compound was prepared according to the general procedure from iodbenzol **85a** (0.11 mL, 1.0 mmol) and diphenylamine **86i** (0.340 g, 2.0 mmol). The crude product was

purified by flash chromatography to yield **87u** (0.180 g, 73%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 6.84-6.90 (m, 3H), 6.96-6.99 (m, 6H), 7.05-7.14 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 122.62, 124.11, 129.16, 147.81.



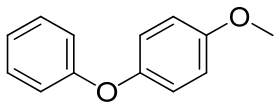
1-(2-methoxyphenyl)-1H-imidazole (87v)

The title compound was prepared according to the general procedure from 2-iodanisol **85r** (0.13 mL, 1.0 mmol) and imidazol **86a** (0.14 g, 2.0 mmol). The crude product was purified by flash chromatography to yield **87v** (0.041 g, 23%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 3.77 (s, 3H), 6.81-7.14 (m, 4H), 7.20-7.33 (m, 2H), 7.63-7.78 (m, 1H).



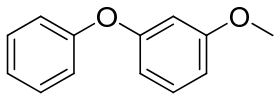
Oxydibenzene (89a)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and phenol **88a** (0.13 mL, 1.5 mmol). The crude product was purified by flash chromatography to yield **89a** (0.167 g, 98%). (from chlorobenzene: 5.1 mg, yield 3%; from iodobenzene catalyzed by complex **60b/CuClL$_2$** : 0. 049 g, yield 29%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 6.85-6.89 (m, 4H), 6.95-6.98 (m, 2H), 7.14-7.21 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 118.83, 123.15, 129.68, 157.20.



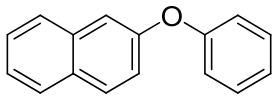
1-methoxy-4-phenoxybenzene (89b)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and 4-methoxy-phenol **88b** (0.186 g, 1.5 mmol). The crude product was purified by flash chromatography to yield **89b** (0.170 g, 85%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 3.67 (s, 3H), 6.74-6.95 (m, 7H), 7.14-7.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.53, 114.79, 117.51, 120.78, 122.36, 129.56, 150.04, 155.84, 158.47.



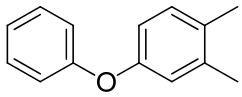
1-methoxy-3-phenoxybenzene (89c)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and 3-methoxy-phenol **88c** (0.17 mL, 1.5 mmol). The crude product was purified by flash chromatography to yield **89c** (0.158 g, 79%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 3.64 (s, 3H), 6.35-6.56 (m, 3H), 6.89-7.13 (m, 3H), 7.18- 7.22 (m, 1H), 7.24-7.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.30, 104.81, 108.82, 110.90, 119.05, 123.34, 129.70, 130.09, 156.94, 158.47, 160.92.



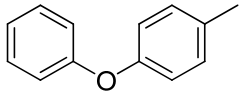
2-phenoxynaphthalene (89d)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and 2-naphthol **88d** (0.216 g, 1.5 mmol). The crude product was purified by flash chromatography to yield **89d** (0.180 g, 82%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 6.83-6.89 (m, 1H), 6.92-6.97 (m, 2H), 7.09 (dd, J_1 = 2.4 Hz, J_2 = 2.1 Hz, 1H), 7.11-7.27 (m, 5H), 7.47-7.50 (m, 1H), 7.60 (s, 1H), 7.63 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 114.04, 119.04, 119.92, 123.36, 124.62, 126.44, 127.05, 127.67, 129.76, 129.81, 130.09, 134.27, 155.00, 157.13.



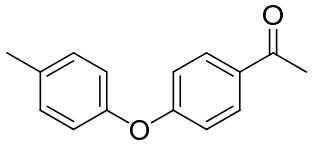
1,2-dimethyl-4-phenoxybenzene (89e)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and 3,4-dimethylphenol **88e** (0.183 g, 1.5 mmol). The crude product was purified by flash chromatography to yield **89e** (0.182 g, 92%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 2.12 (s, 6H), 6.65 (dd, J_1 = 3.0 Hz, J_2 = 2.7 Hz, 1H), 6.72 (d, J = 2.4 Hz, 1H), 6.85-6.98 (m, 4H), 7.15-7.24 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.99, 19.88, 116.43, 118.28, 120.46, 122.64, 129.57, 130.57, 131.53, 138.13, 154.83, 157.86.



1-methyl-4-phenoxybenzene (89f)

The title compound was prepared according to the general procedure from iodobenzene **85a** (0.11 mL, 1.0 mmol) and **88f** (0.183 g, 1.5 mmol). The crude product was purified by flash chromatography to yield **89f** (0.142 g, 77%). (from bromobenzene **85e**: 0.114 g, yield 62%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 2.15 (s, 3H), 6.78-7.03 (m, 7H), 7.14-7.21 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.65, 118.28, 119.09, 122.73, 129.60, 130.19, 132.80, 154.68, 157.78. MS (LSI-MS, m/z): 184.1($M^{+\cdot}$).



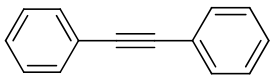
1-(4-(p-tolyloxy)phenyl)ethanone (89g)

The title compound was prepared according to the general procedure from 4-iodacetophenon **85g** (0.246 g, 1.0 mmol) and 4-methyl-phenol **88f** (0.183 g, 1.5 mmol). The crude product

was purified by flash chromatography to yield **89g** (0.184 g, 81%). (from 4-bromoacetophenon **85h**: 0.131 g, yield 58%; from 4-chloroacetophenon **85p**: 88 mg, 39%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 2.14 (s, 3H), 2.46 (s, 3H), 6.65 (d, *J* = 8.7 Hz, 2H), 6.84-6.91 (m, 4H), 7.81(d, *J* = 9.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.36, 26.29, 115.13, 116.76, 120.21, 129.66, 129.97, 130.53, 130.84, 131.00, 153.29, 162.85, 198.76.

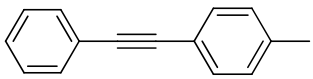
Synthesis for Sonogashira of phenylacetylene with aryl halides

General Procedure: The similar procedure was used except for potassium carbonate (3.0 equiv.) instead of potassium tert-butylate. The reaction was mixture was then cooled to room temperature and filtered to remove any insoluble residues. The filtrate was reduced in vacuo and the residue was purified by flash column chromatography on silica gel to obtain the analytically pure product.



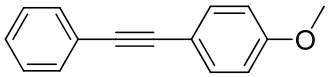
1,2-diphenylethyne (90a)

The title compound was prepared according to the general procedure from iodbenzol **85a** (0.11 mL, 1.0 mmol) and ethynylbenzene **67a** (0.14 mL, 1.2 mmol). The crude product was purified by flash chromatography to yield **90a** (0.151 g, 85%). (from brombenzol: 0.080 g, yield 45%; from chlorbenzol: 0.050 g, yield 28%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 7.21-7.27 (m, 6H), 7.42-7.47 (m, 4H).



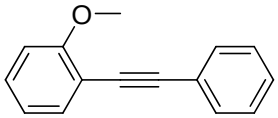
1-methyl-4-(phenylethynyl)benzene (90b)

The title compound was prepared according to the general procedure from 4-iotoluol (0.22 g, 1.0 mmol) and ethynylbenzene (0.14 mL, 1.2 mmol). The crude product was purified by flash chromatography to yield **90b** (0.125 g, 65%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 2.31 (s, 3H), 7.10 (d, *J* = 7.5 Hz, 2H), 7.26-7.28 (m, 3H), 7.36-7.38 (m, 2H), 7.45-7.48 (m, 2H).



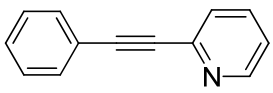
1-methoxy-4-(phenylethynyl)benzene (90c)

The title compound was prepared according to the general procedure from 4-iodanisol (0.234 g, 1.0 mmol) and ethynylbenzene (0.14 mL, 1.2 mmol). The crude product was purified by flash chromatography to yield **90c** (0.185 g, 89%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 3.78 (s, 3H), 6.80-6.85 (m, 2H), 7.24-7.32 (m, 3H), 7.39-7.49 (m, 4H).



1-methoxy-2-(phenylethynyl)benzene (90d)

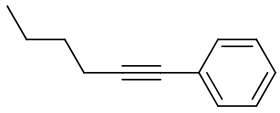
The title compound was prepared according to the general procedure from 2-iodanisol (0.13 mL, 1.0 mmol) and ethynylbenzene (0.14 mL, 1.2 mmol). The crude product was purified by flash chromatography to yield **90d** (0.150 g, 72%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 3.83 (s, 3H), 6.80-6.88 (m, 2H), 7.19-7.29 (m, 4H), 7.41-7.50 (m, 3H).



2-(phenylethynyl)pyridine (90e)

The title compound was prepared according to the general procedure from iodbenzol (0.11 mL, 1.0 mmol) and 2-ethinylpyridin (0.12 mL, 1.2 mmol). The crude product was purified by

flash chromatography to yield **90e** (0.101 g, 56%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 7.16-7.21 (m, 1H), 7.28-7.33 (m, 3H), 7.46-7.65 (m, 4H), 8.56 (s, 1H).



hex-1-ynylbenzene (90f)

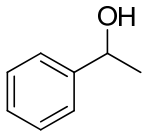
The title compound was prepared according to the general procedure from iodbenzol (0.11 mL, 1.0 mmol) and 1-hexin (0.14 mL, 1.2 mmol). The crude product was purified by flash chromatography to yield **90f** (0.099 g, 63%). ^{1}H NMR (300MHz, $CDCl_3$, ppm): δ = 0.88 (t, *J* = 7.2 Hz, 3H), 1.37-1.55 (m, 4H), 2.34 (t, *J* = 7.5 Hz, 2H), 7.17-7.24 (m, 3H), 7.29-7.35 (m, 2H).

Synthesis for the Wacker oxidation of alkenes

In a flame dried 10 ml schleck tube equipped with a sidearm and stir bar, a mixture of [$PdCl_2$(RNC)] (**94**, 15 mg, 5 mol %) and 4 mL of a 6:1 (v/v) solution of DMA:H_2O mixture were heated at 70 °C for 10 min to assure complete solubility of the catalyst. The tube was allowed to cool to room temperature and connected with a condenser and a one way joint with a balloon of O_2. The tube was evacuated (50 mbar) and refilled with O_2 three times. The reaction mixture was stirred vigorously for 10 min upon which the alkene **95** (0.5 mmol) was added. For the indicated reaction time the mixture was then heated at 70 °C. After cooling to room temperature, the reaction mixture was analyzed by GC using decane as internal standard. For product isolation the reaction mixture diethylether was added and washed twice with 1M HCl. The aqueous layers were combined and extracted thrice with diethylether. The organic layers were combined and washed with brine, dried over Na_2SO_4 and filtered. The product **96** was purified by flash silica chromatography.

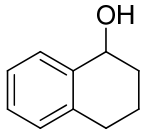
Synthesis for the iron catalyzed transfer hydrogenation

In a 10 mL schlenk tube, the iron complex (**99 or 100** 5 mol %, 15 mg, 0.0169 mmol), KO^{t}Bu (10 equiv., 19 mg, 0.169 mmol) and 2-propanol (1.7 mL, for 0.2 M concentration of substrate) were stirred under nitrogen at room temperature for 5 min. The substrate (20 equiv.) was added to this mixture and stirred for the time period mentioned in the table. The conversion and enantiomeric excess of the products were determined by GC using decane as internal standard. The products were also identified by ^{1}H NMR and ^{13}C NMR spectroscopy and the data obtained matches with literature values.



1-phenylethanol (102a, Table 28, entries 1 and 3)

The title compound **102a** was prepared according to the general procedure as described above in 25% (entry 1) and 18% (entry 3) conversion. ^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.20-7.4 (m, 5H), 4.86 (q, *J* = 6.6, 12.8 Hz, 1H), 2.29 (s, 1H), 1.48 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.17, 70.36, 125.44, 127.46, 128.24, 145.88.



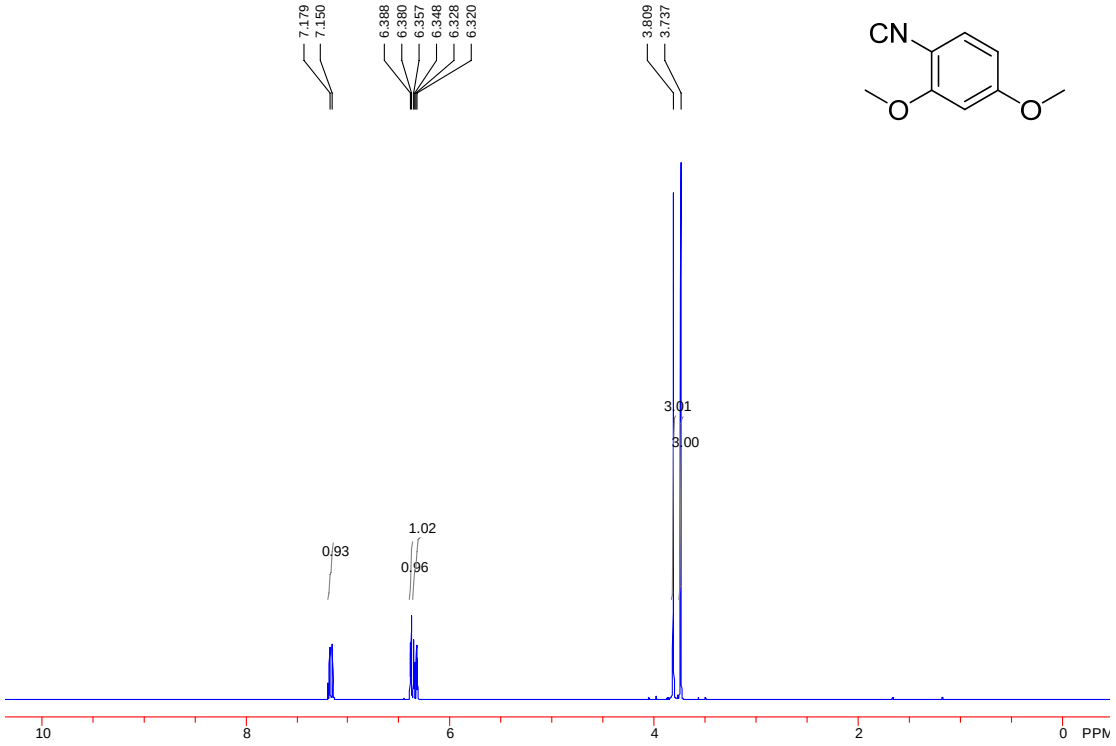
1,2,3,4-tetrahydronaphthalen-1-ol (102b,Table 28, entries 2 and 4)

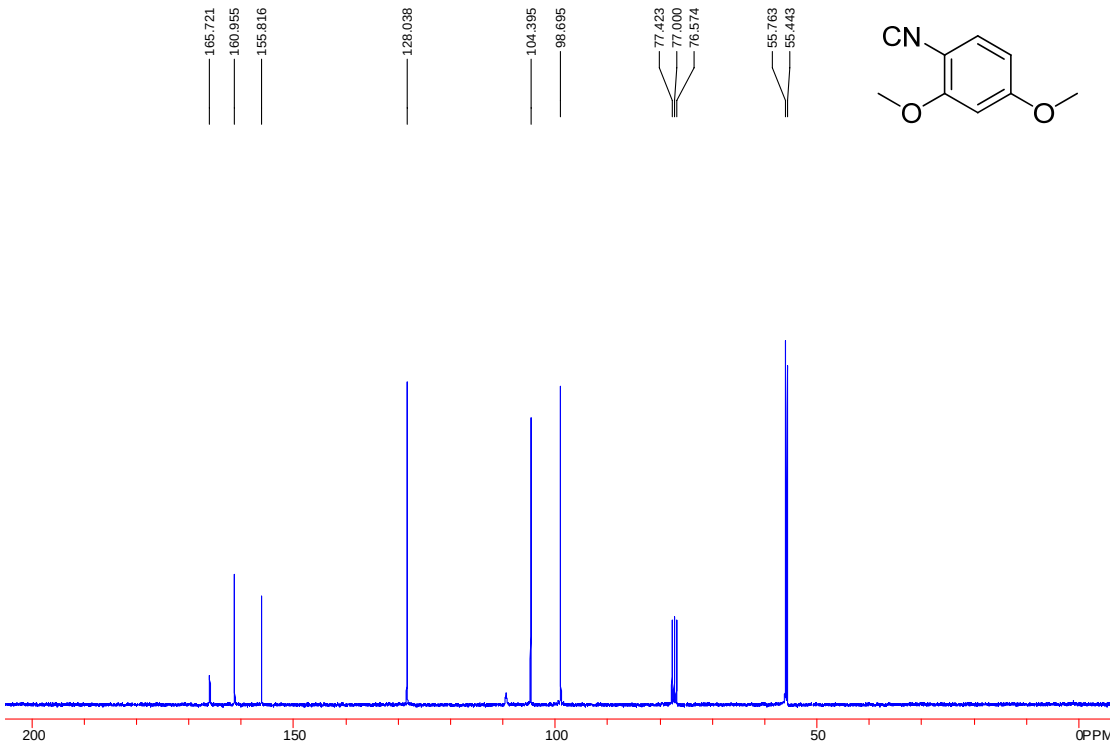
The title compound was prepared according to the general procedure as described above in 11% (entry 2) and 10% (entry 4) conversion. ^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.41-7.46 (m, 1H), 7.18-7.24 (m, 2H), 7.08-7.15 (m, 1H), 4.77 (t, *J* = 5.2 Hz, 1H), 2.65-2.9 (m, 2H), 1.7-2.09 (m,

5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.83, 29.27, 32.28, 68.15, 126.19, 127.59, 128.69, 129.03, 137.14, 138.82.

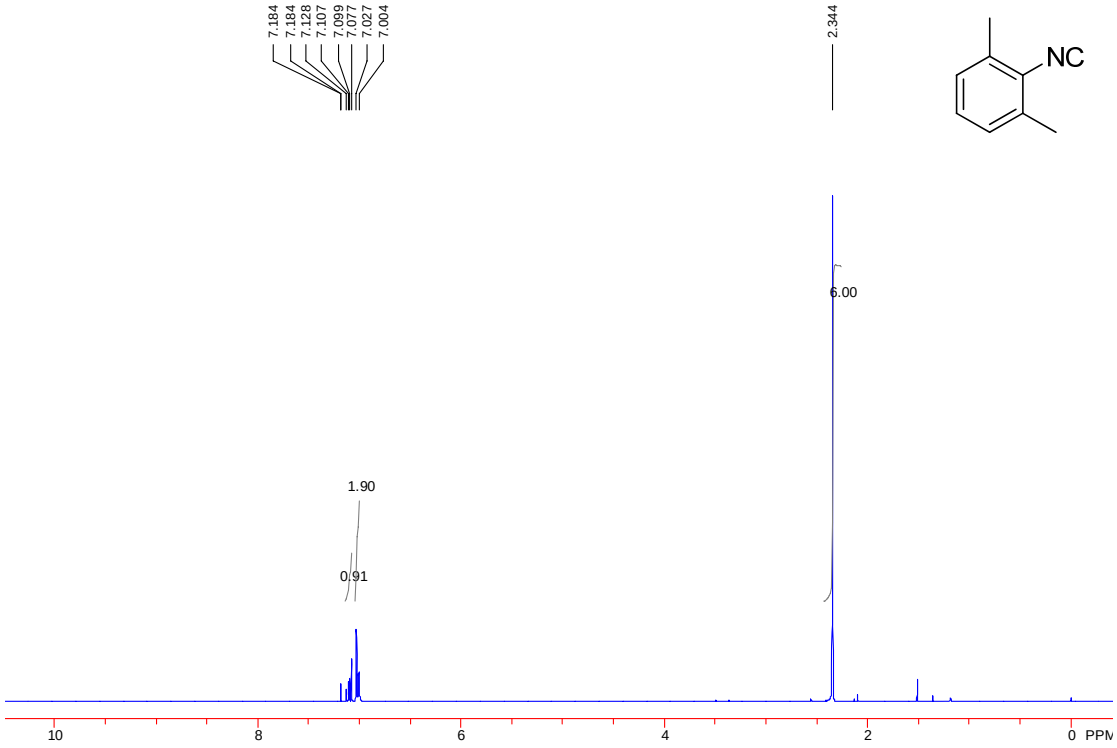
I. Appendix

^{1}H and ^{13}C NMR spectra (49)





(50)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7.184
7.128
7.107
7.099
7.077
7.027
7.004
2.344
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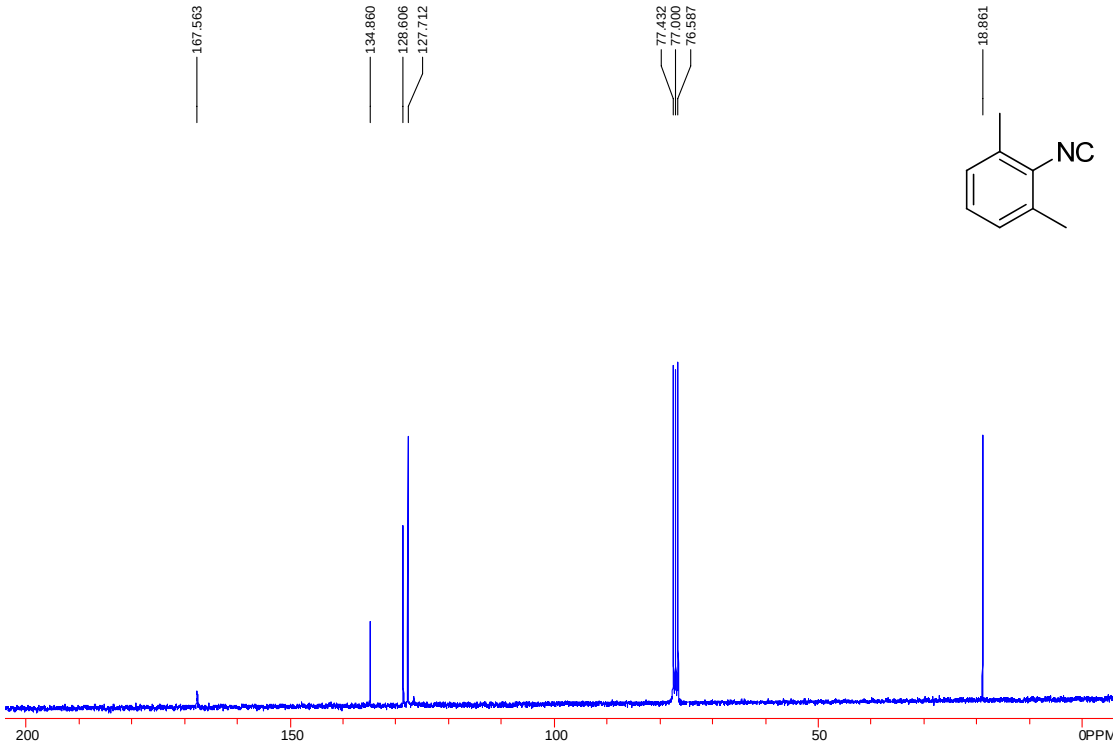
6.00
1.90
0.91
10
8
6
4
2
0 PPM


167.563
134.860
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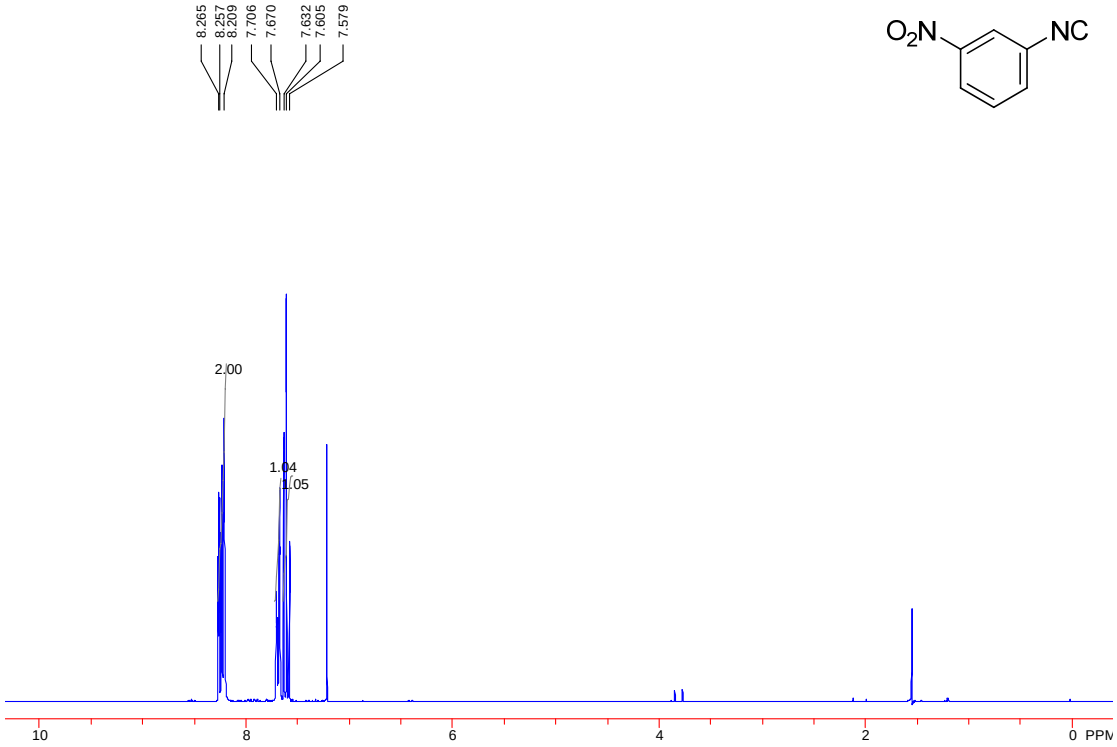
127.712
77.432
77.000
76.587
18.861
NC
200
150
100
50
0PPM

(51)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8.257
8.209
7.706
7.670
7.632
7.605
7.579
O2N
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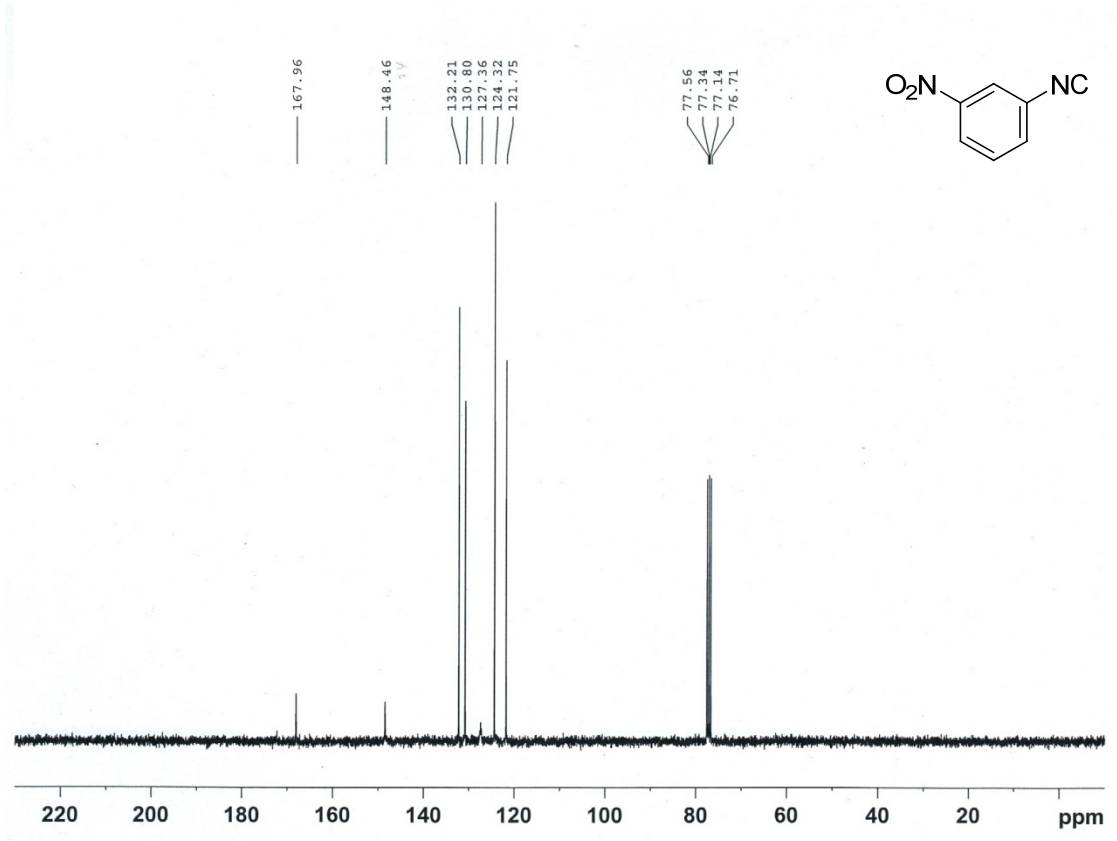
2.00
1.04
1.05
10
8
6
4
2
0 PPM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148.46
132.21
130.80
127.36
124.32
121.75
77.56
77.34
77.14
76.71
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NC
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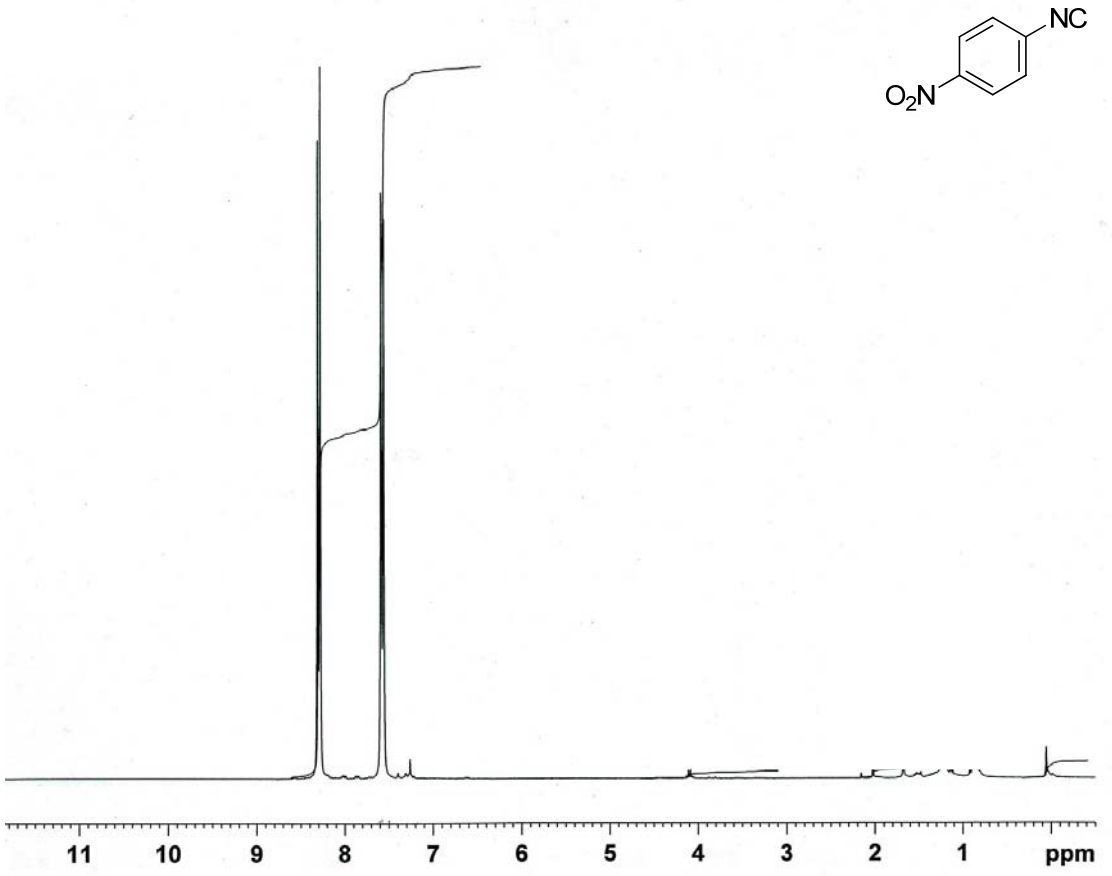
200
180
160
140
120
100
80
60
40
20
ppm

(52)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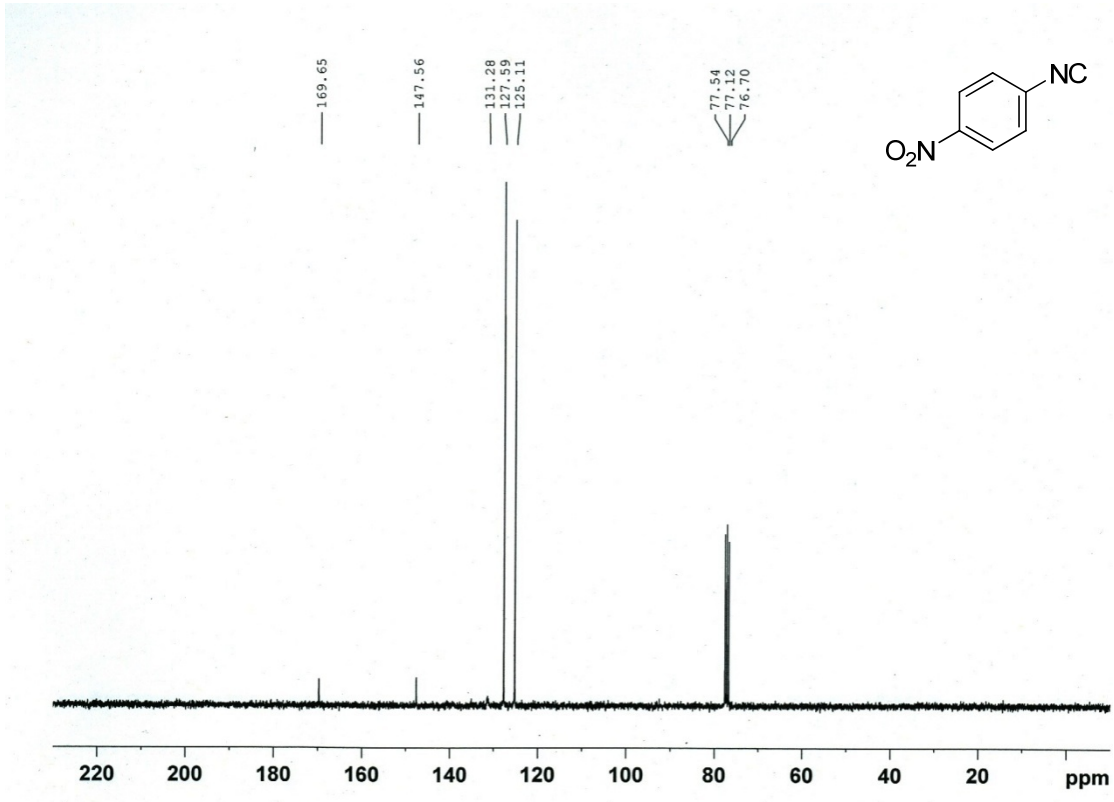
O2N
11
10
9
8
7
6
5
4
3
2
1
ppm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127.59
125.11
77.54
77.12
76.70
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O2N
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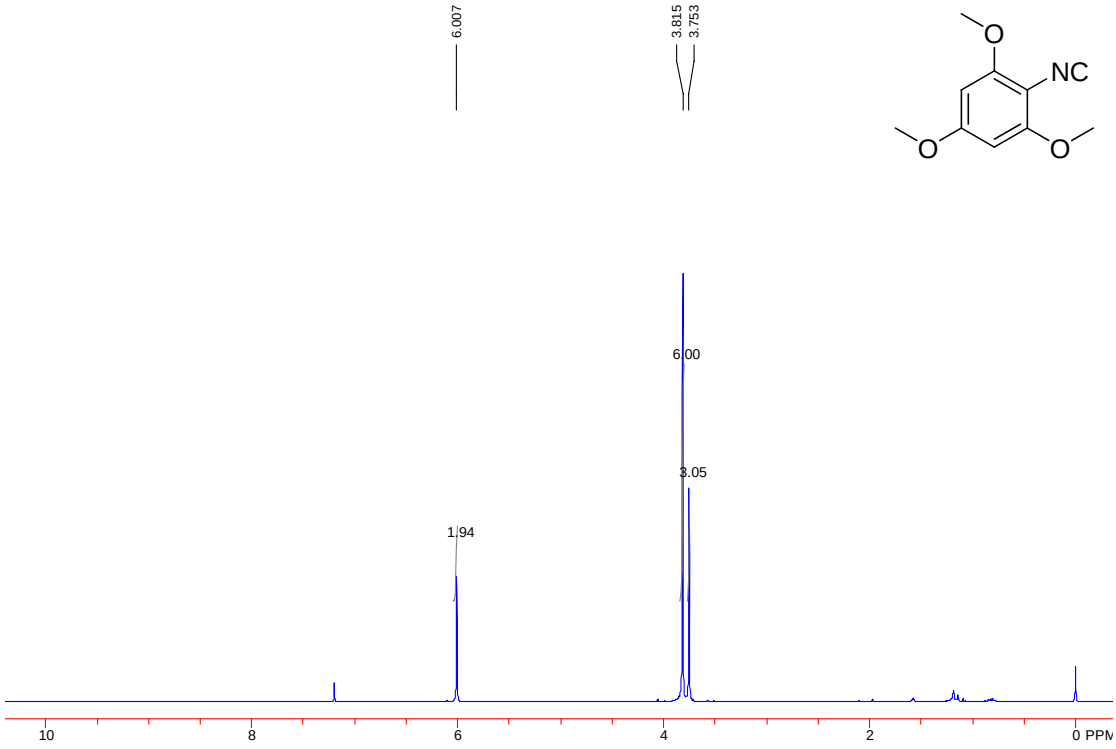
200
180
160
140
120
100
80
60
40
20
ppm

(53)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O
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1.94
10
8
6
4
2
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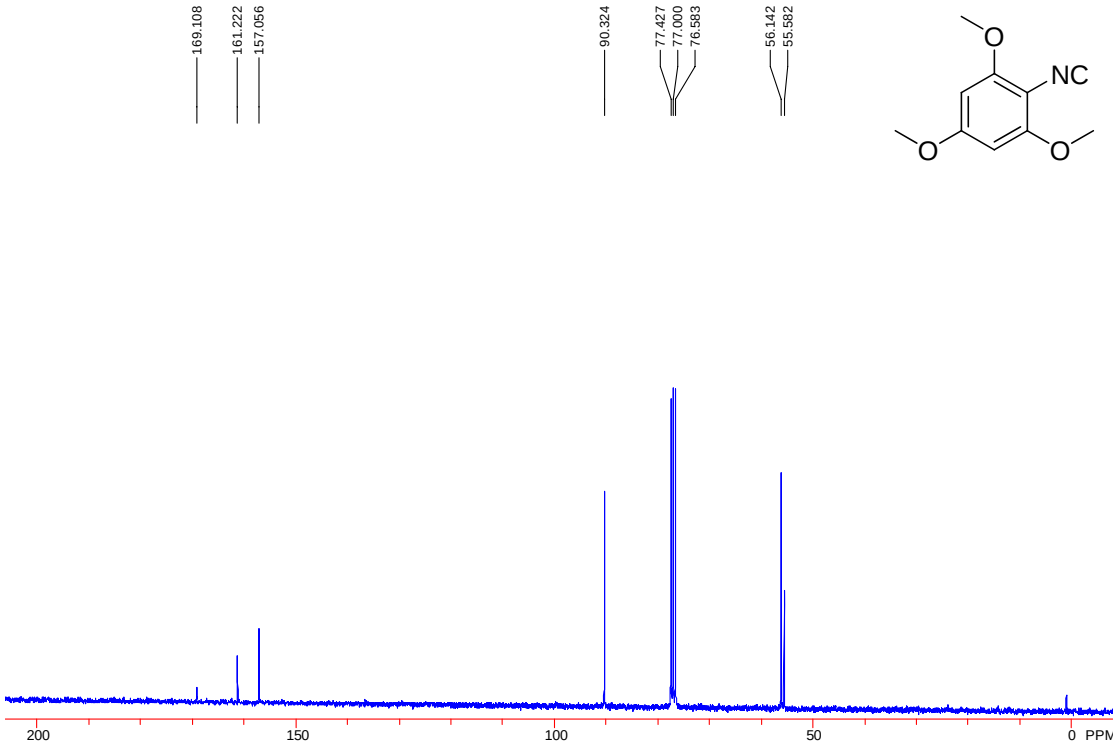
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77.000
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O
O
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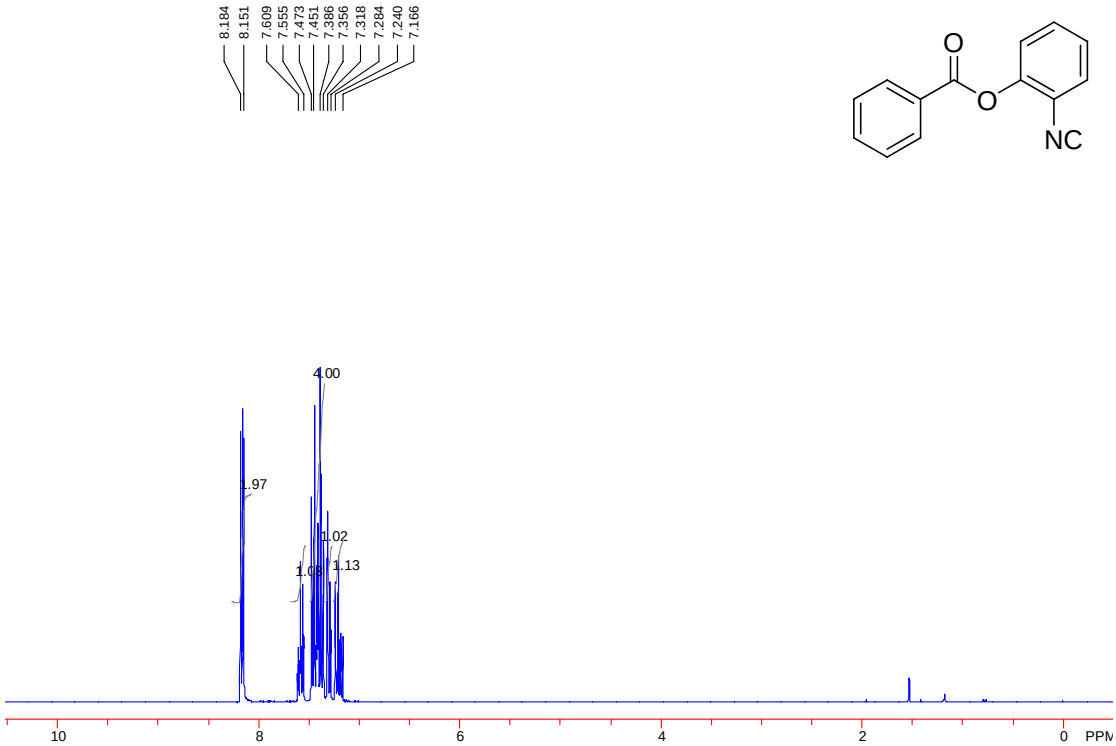
100
50
0 PPM

(54)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7.356
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7.284
7.240
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O
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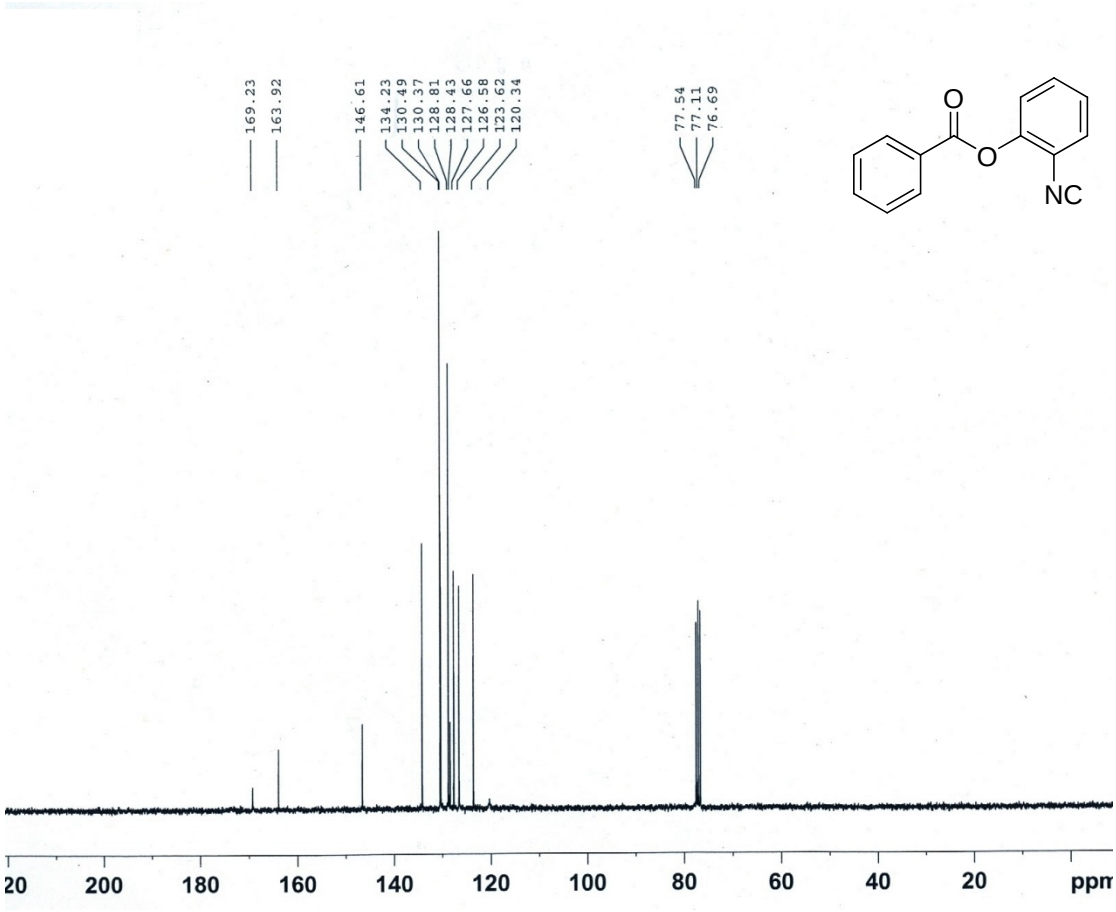
1.03
1.13
10
8
6
4
2
0
PPM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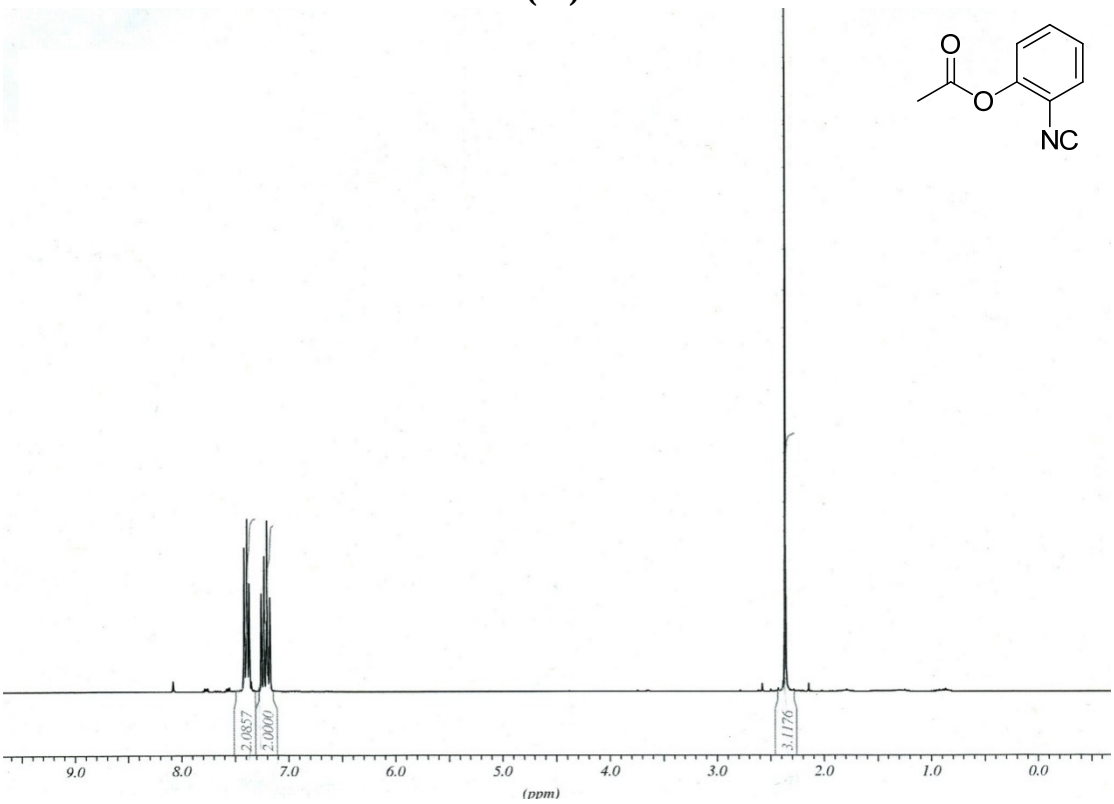
163.92
146.61
134.23
130.49
130.37
128.81
128.43
127.66
126.58
123.62
120.34
77.54
77.11
76.69
O
O
NC
200
180
160
140
120
100
80
60
40
20
ppm

(55)


O
O
NC
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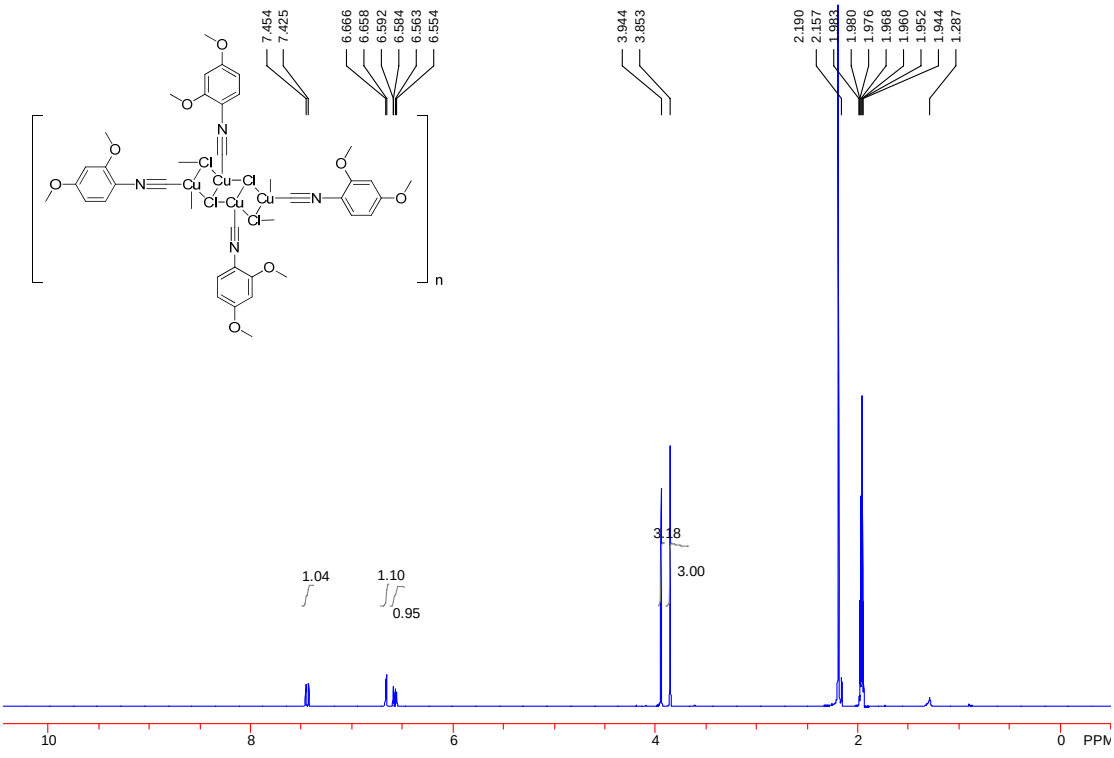
2.0000
3.1176
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

(60a)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6.658
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6.584
6.563
6.554
3.944
3.853
2.190
2.157
1.983
1.980
1.976
1.968
1.960
1.952
1.944
1.287
Cl
Cu
N
O
n
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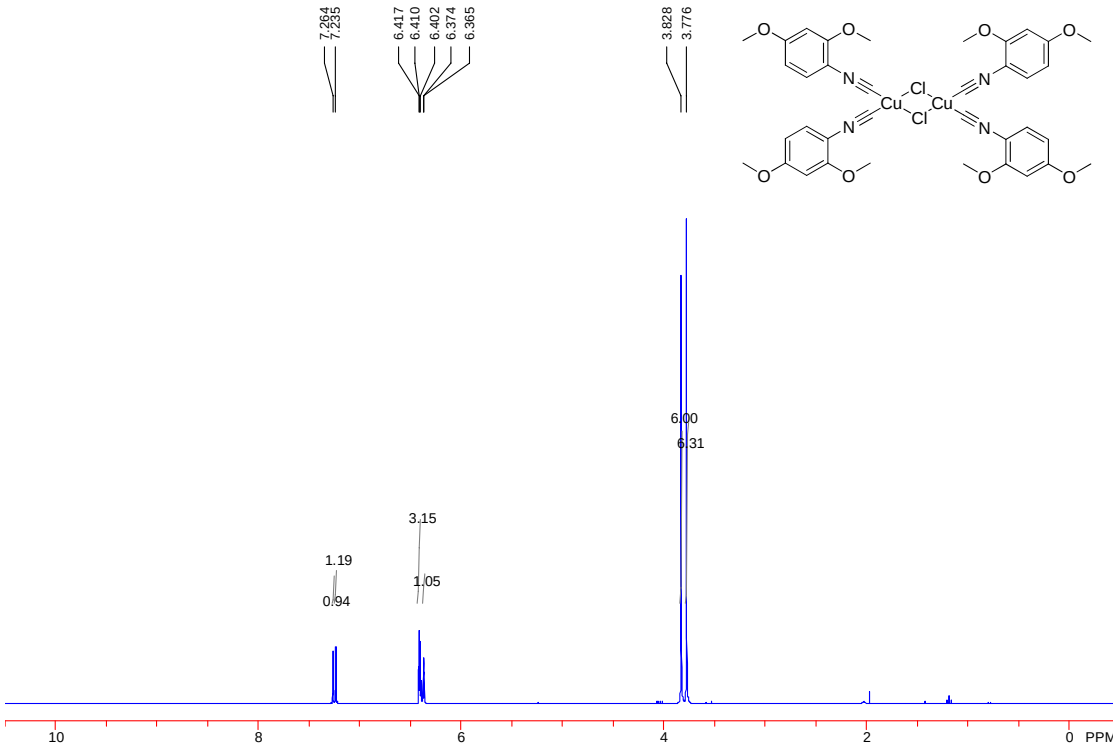
1.10
0.95
3.18
3.00
10
8
6
4
2
0
PPM

(60b)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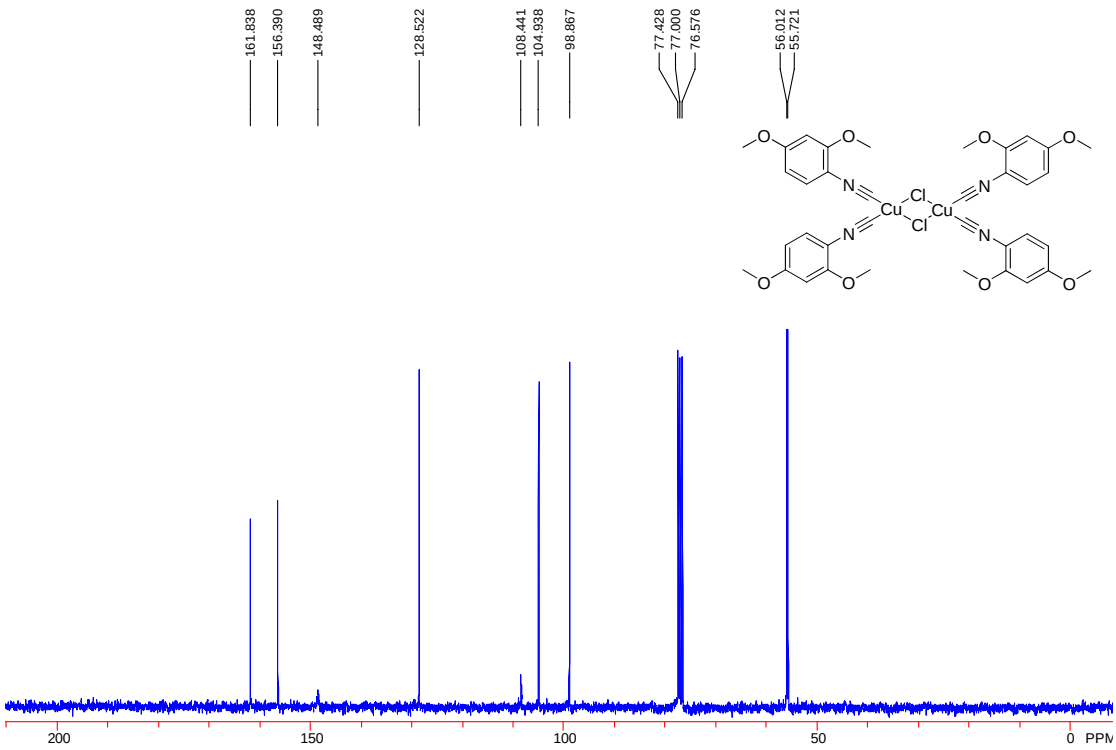
1.19
1.05
0.94
10
8
6
4
2
0 PPM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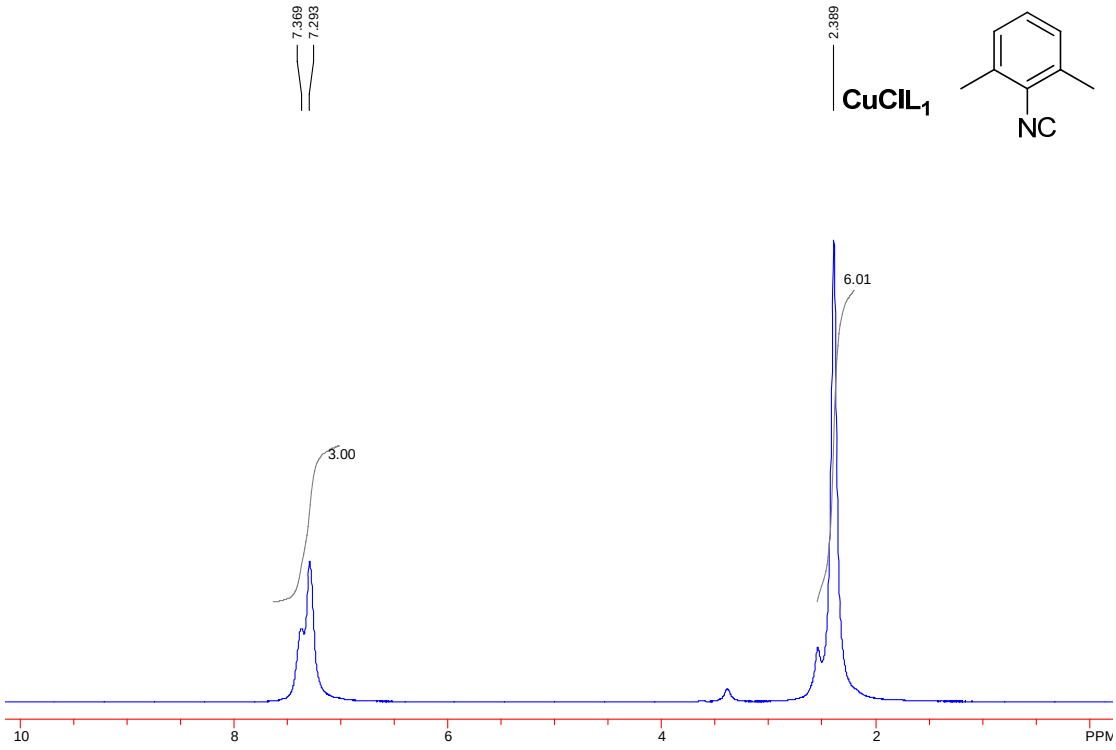
50
0 PPM

(63a)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CuClL1
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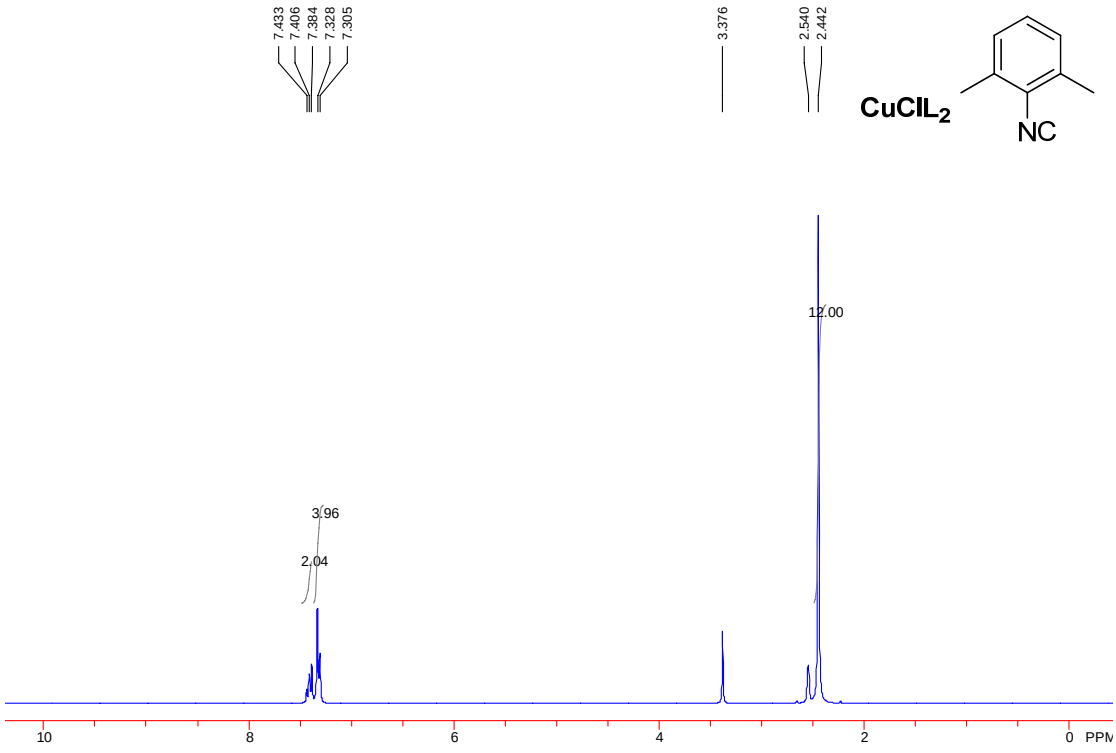
3.00
10
8
6
4
2
PPM

(63b)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3.376
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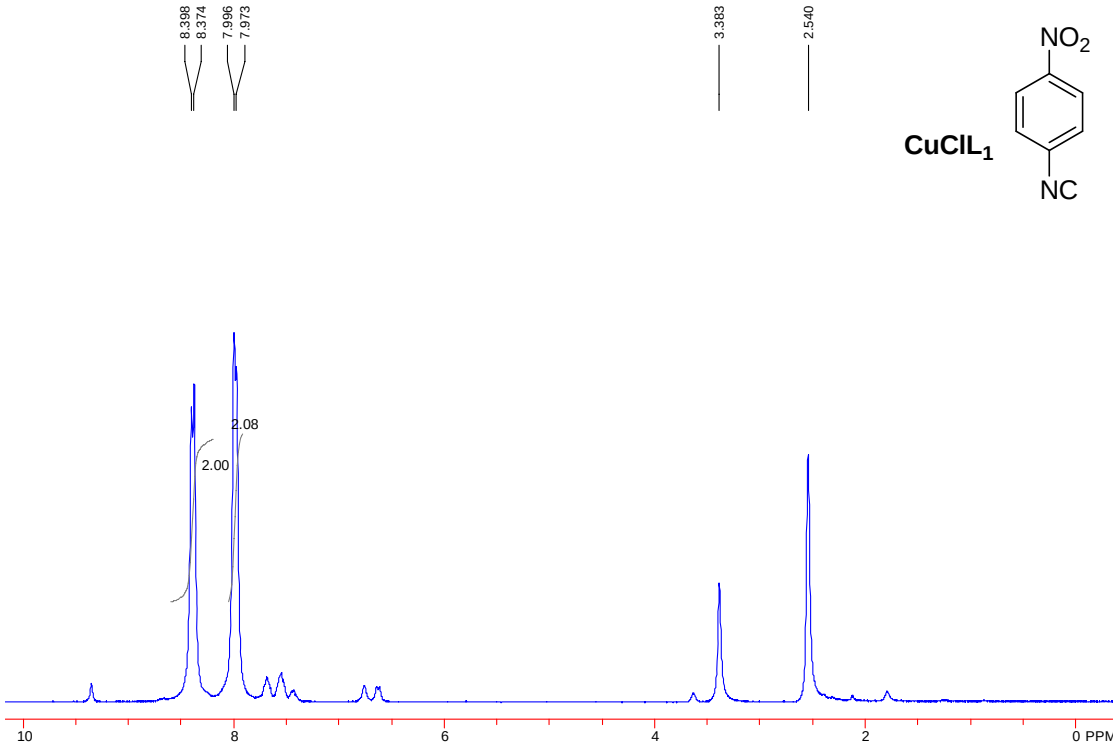
10
8
6
4
2
0
PPM

(64a)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NO2
CuClL1
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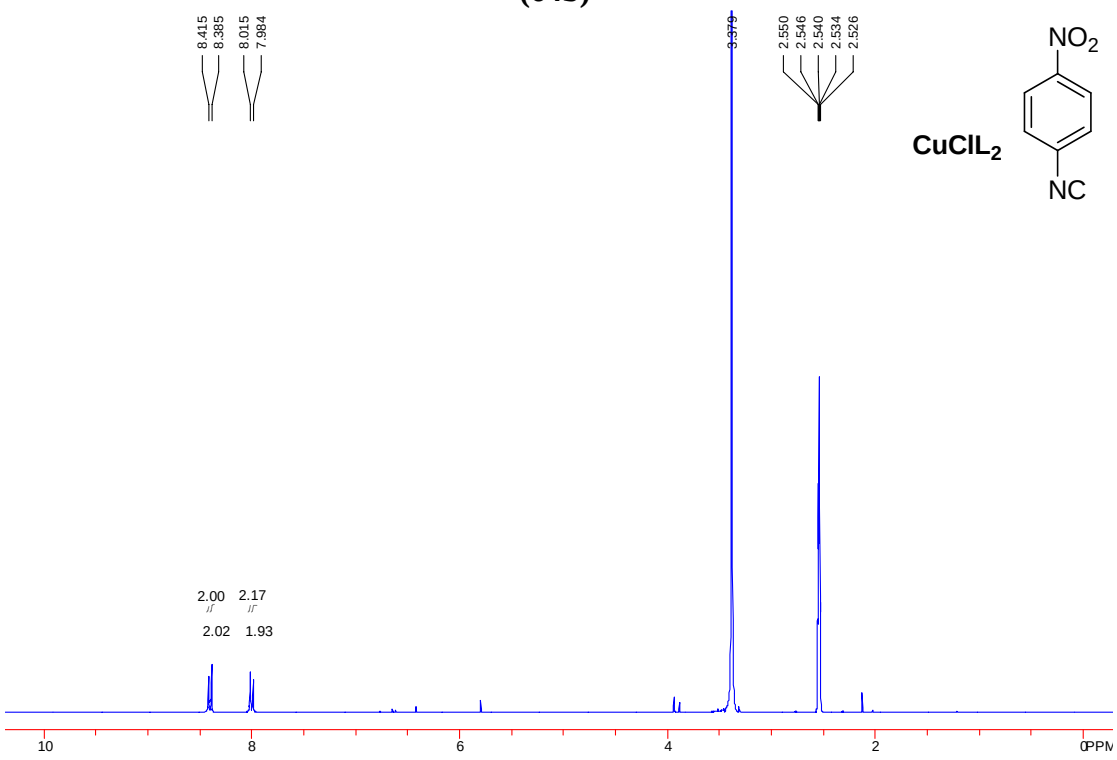
10
8
6
4
2
0 PPM

(64b)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2.540
2.534
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CuClL2
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10
8
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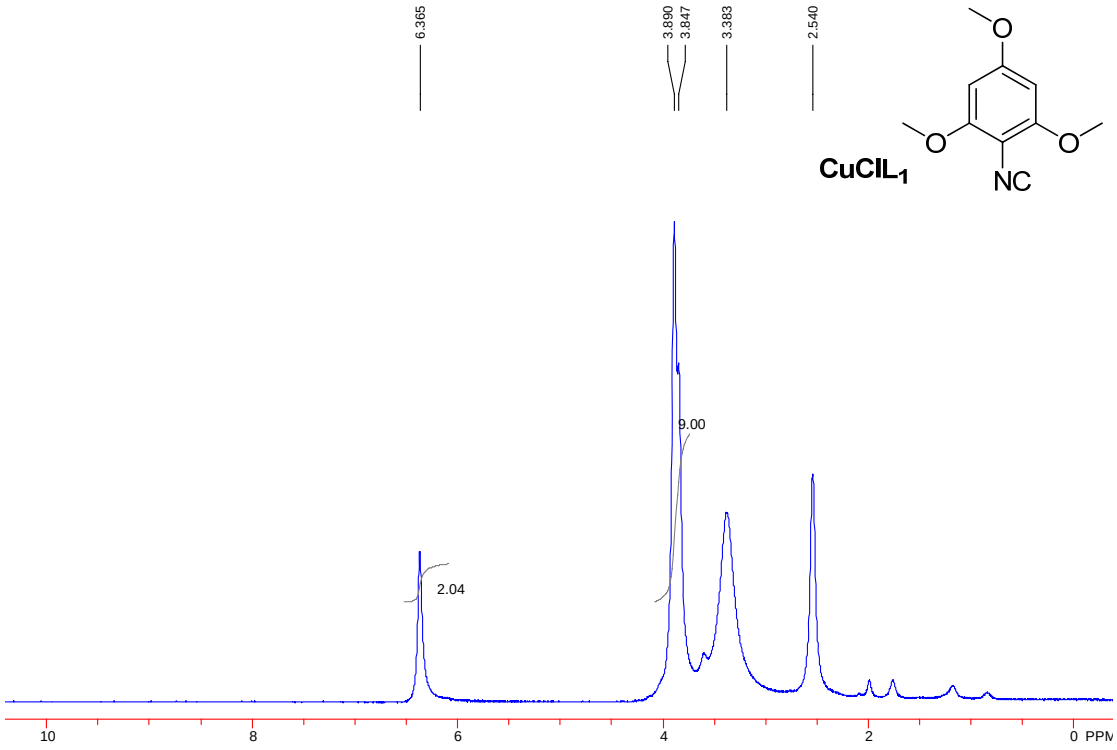
4
2
0PPM

(65a)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10
8
6
4
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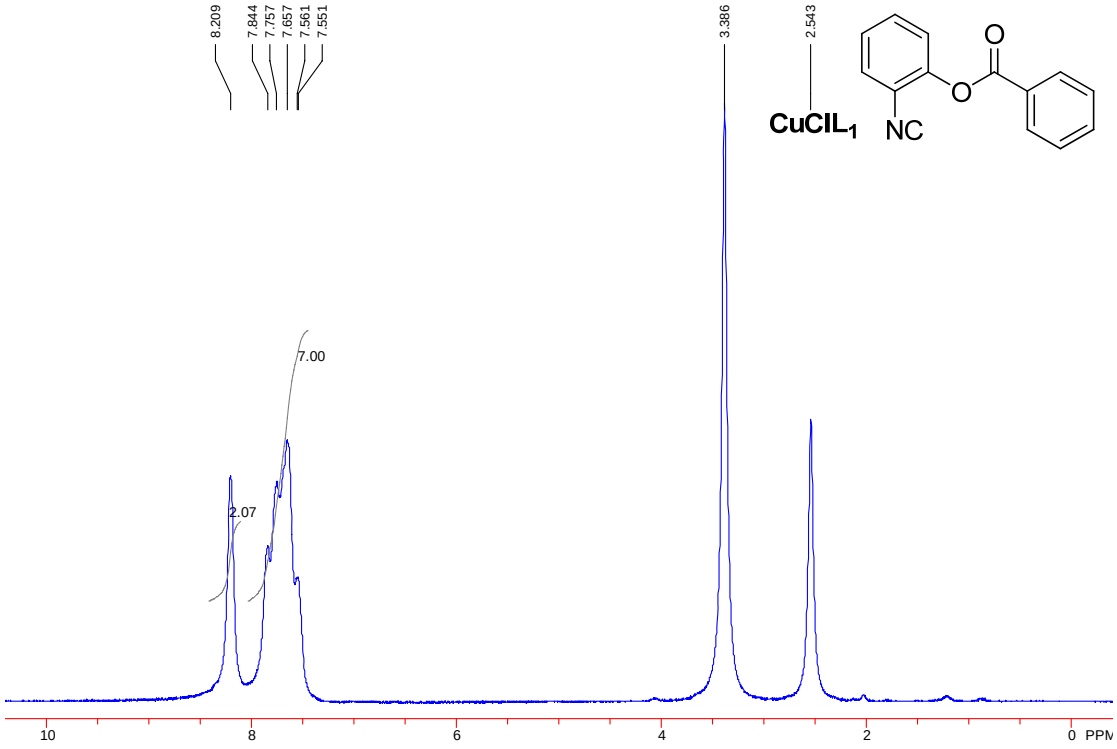
(66a)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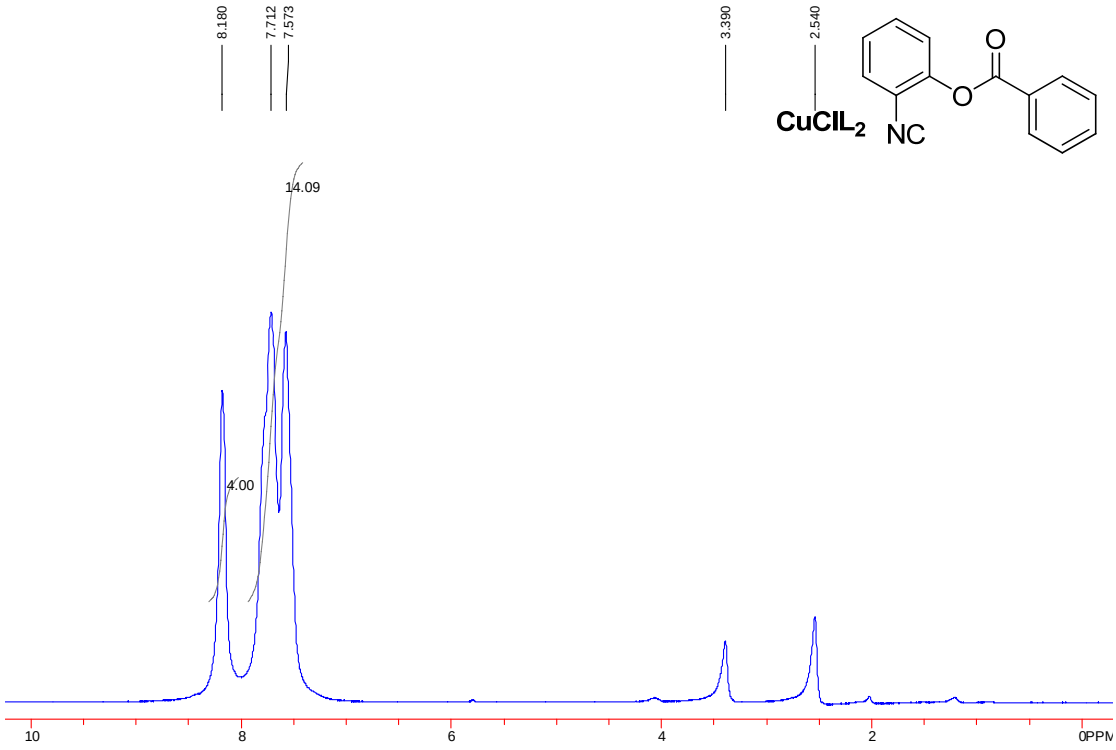
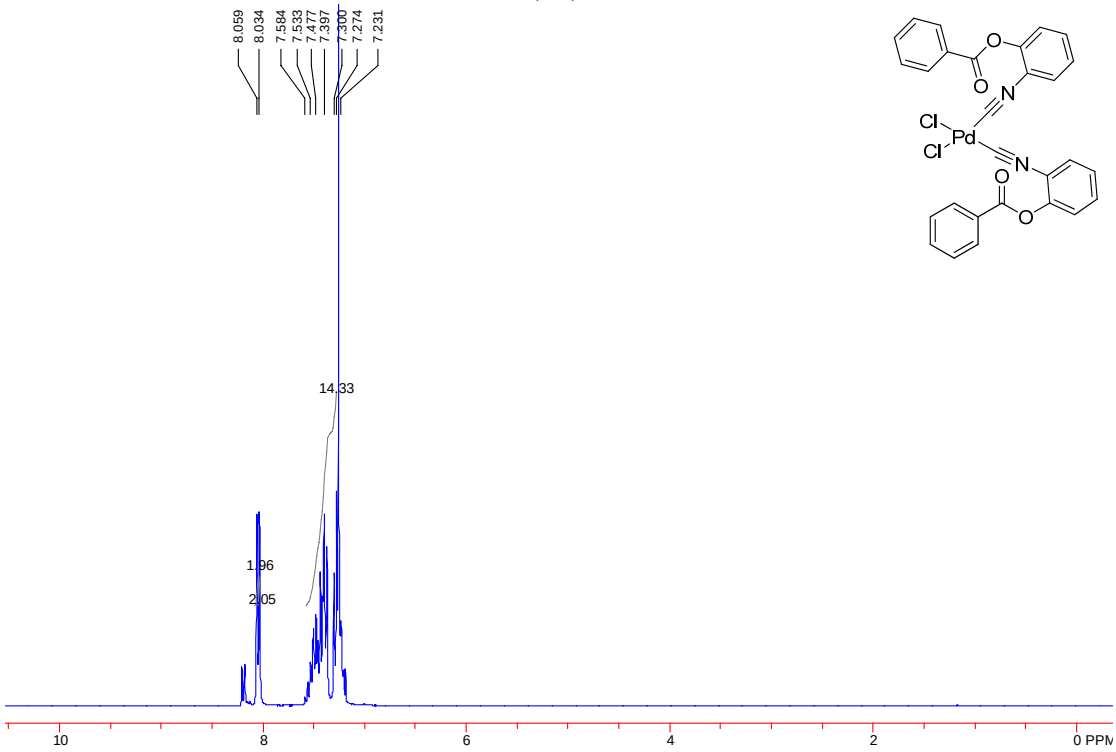
10
8
6
4
2
0 PPM

(66b)



(94)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10
8
6
4
2
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O
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Cl
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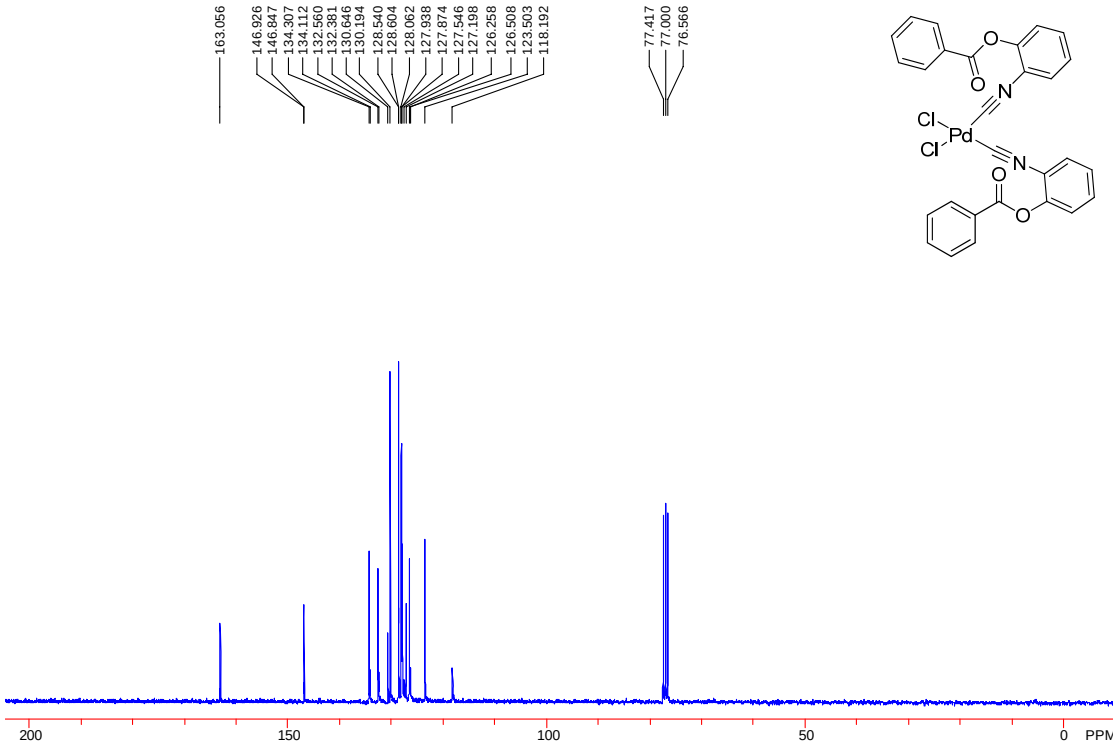
Cl
N
O
O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118.192
77.417
77.000
76.566
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150
100
50
0 PPM
O
O
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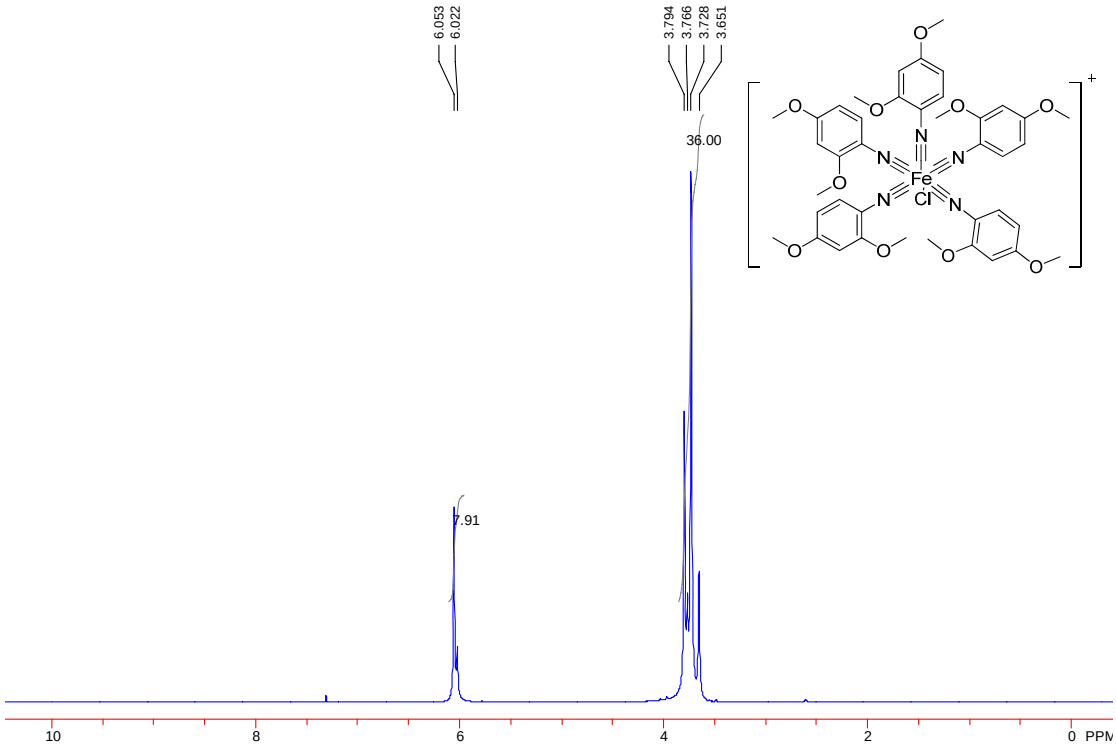
Cl
Pd
Cl
N
O
O

(100)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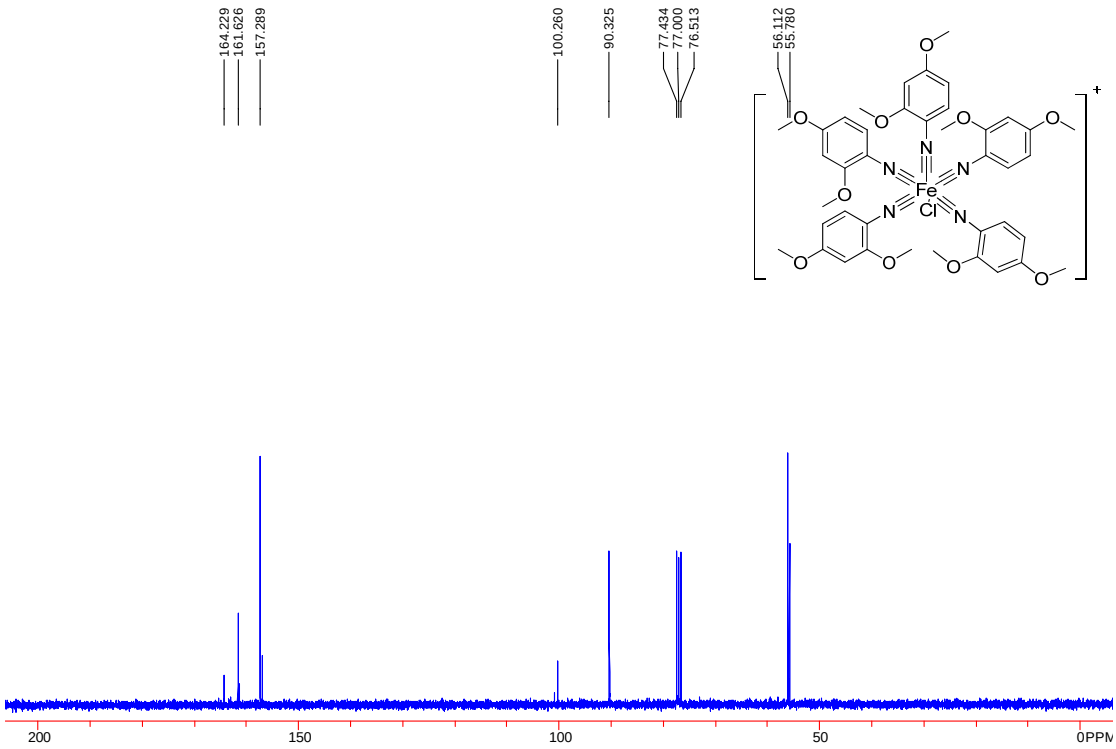
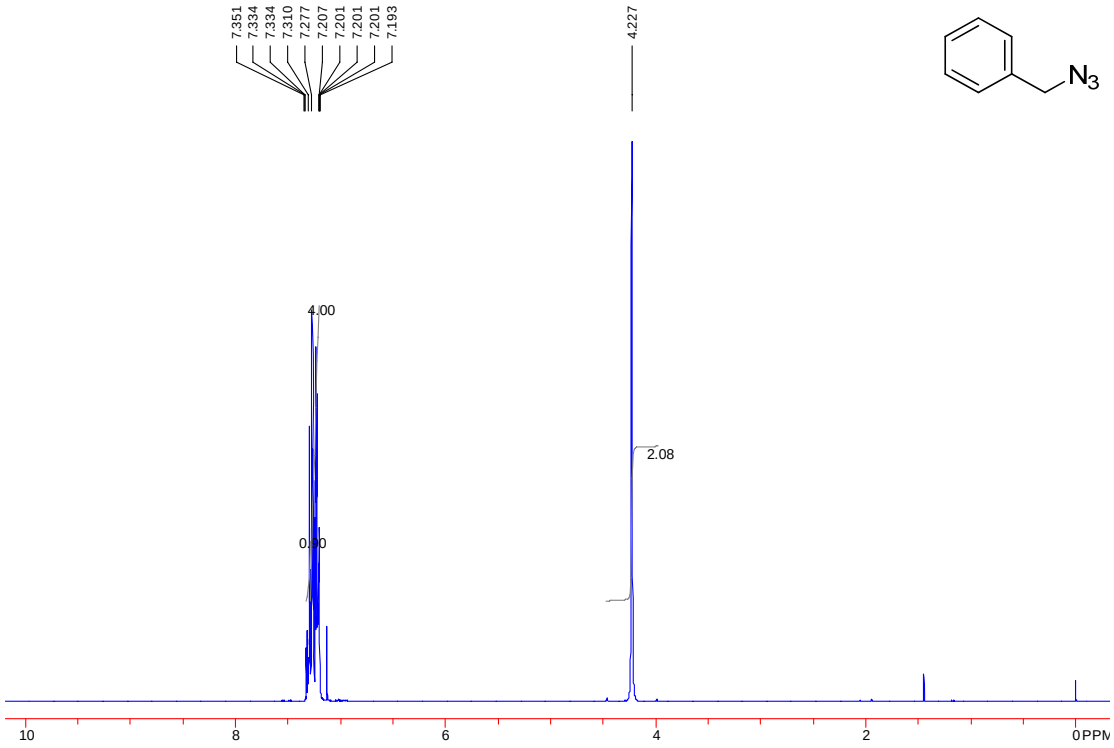
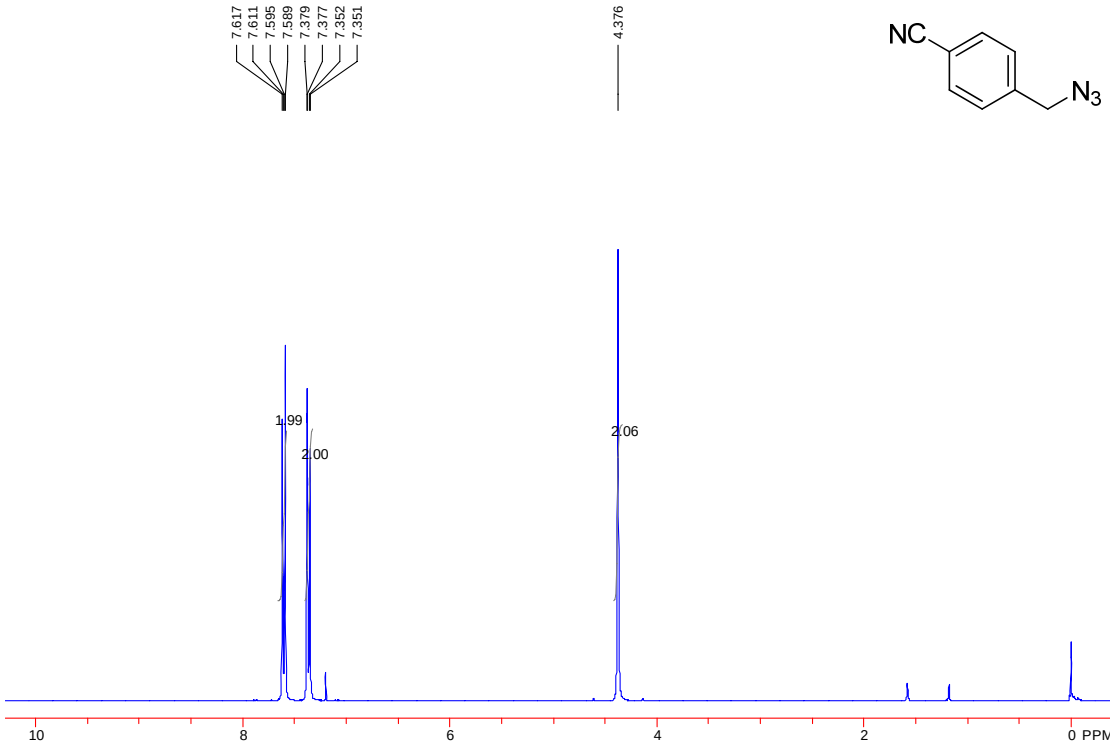
3.728
3.651
36.00
7.91
10
8
6
4
2
0 PPM


164.229
161.626
157.289
100.260
90.325
77.434
77.000
76.513
56.112
55.780
200
150
100
50
0PPM

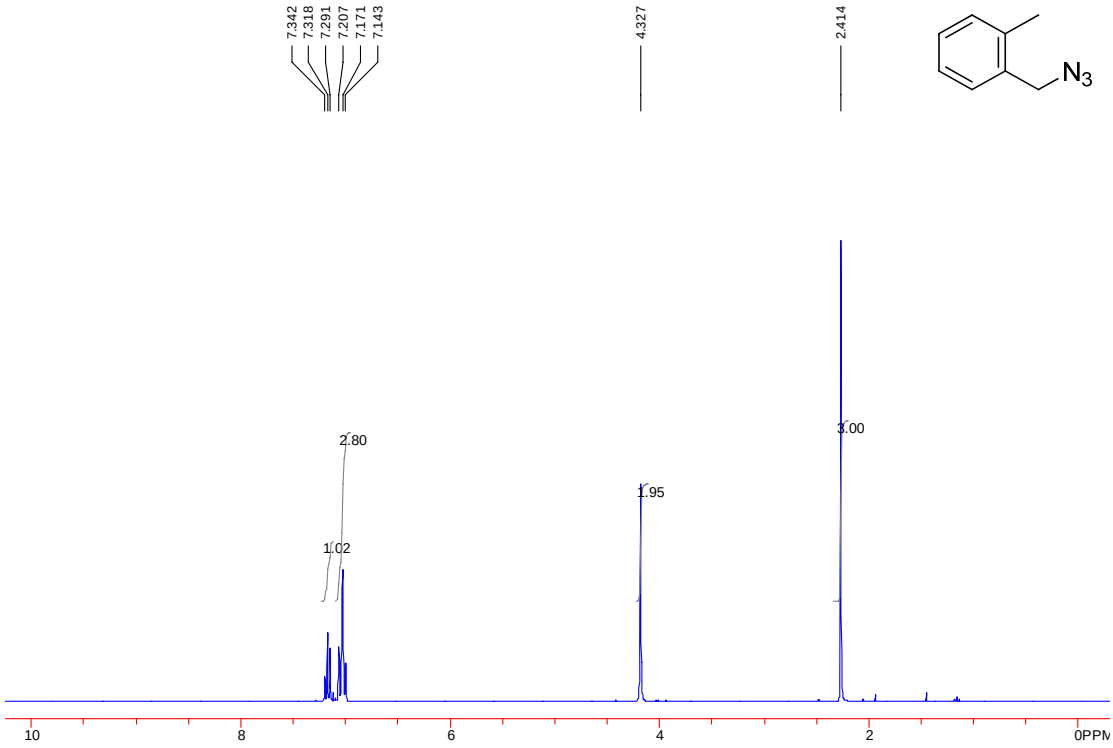
(68a)


7.351
7.334
7.334
7.310
7.277
7.207
7.201
7.201
7.201
7.193
4.227
N3
4.00
2.08
0.90
10
8
6
4
2
0 PPM

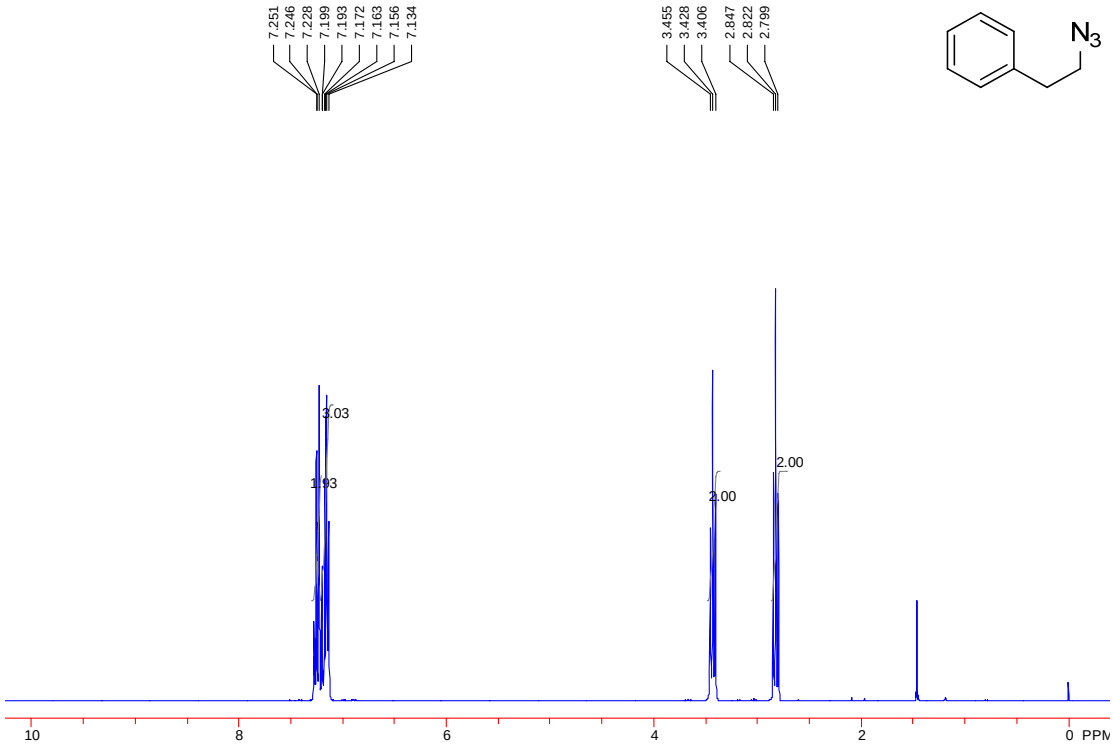
(68b)


7.617
7.611
7.595
7.589
7.379
7.377
7.352
7.351
4.376
NC
N3
1.99
2.00
2.06
10
8
6
4
2
0 PPM

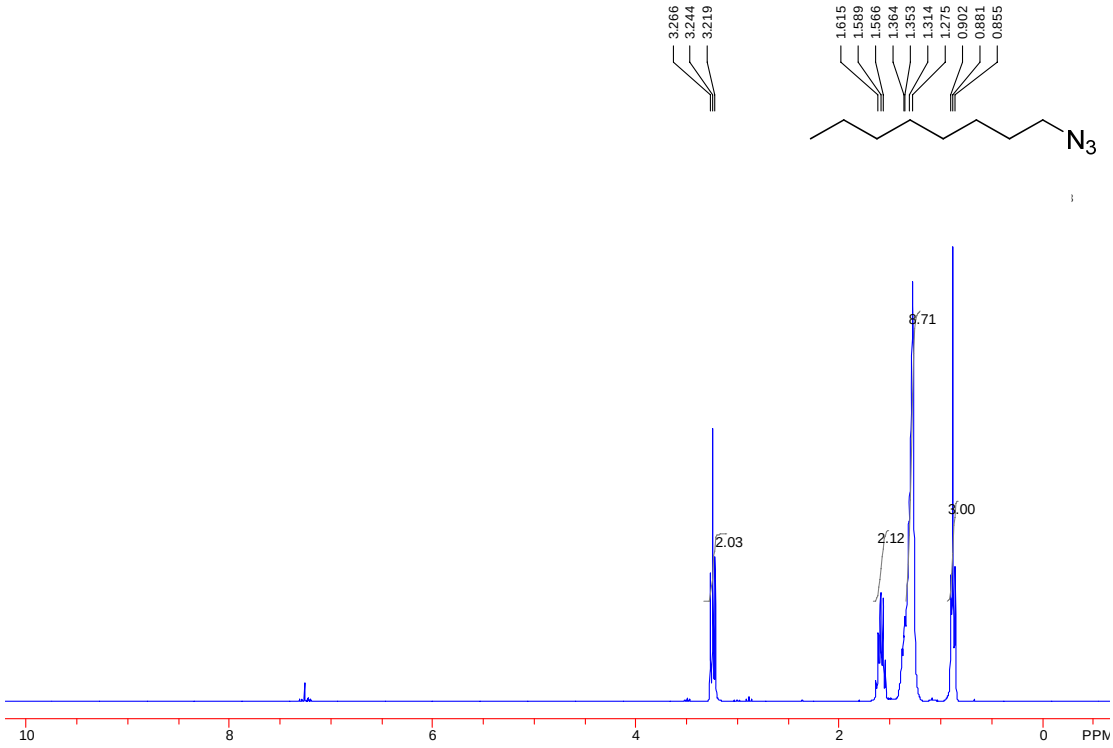
(68c)


7.342
7.318
7.291
7.207
7.171
7.143
4.327
2.414
N3
2.80
1.02
1.95
3.00
10
8
6
4
2
0PPM

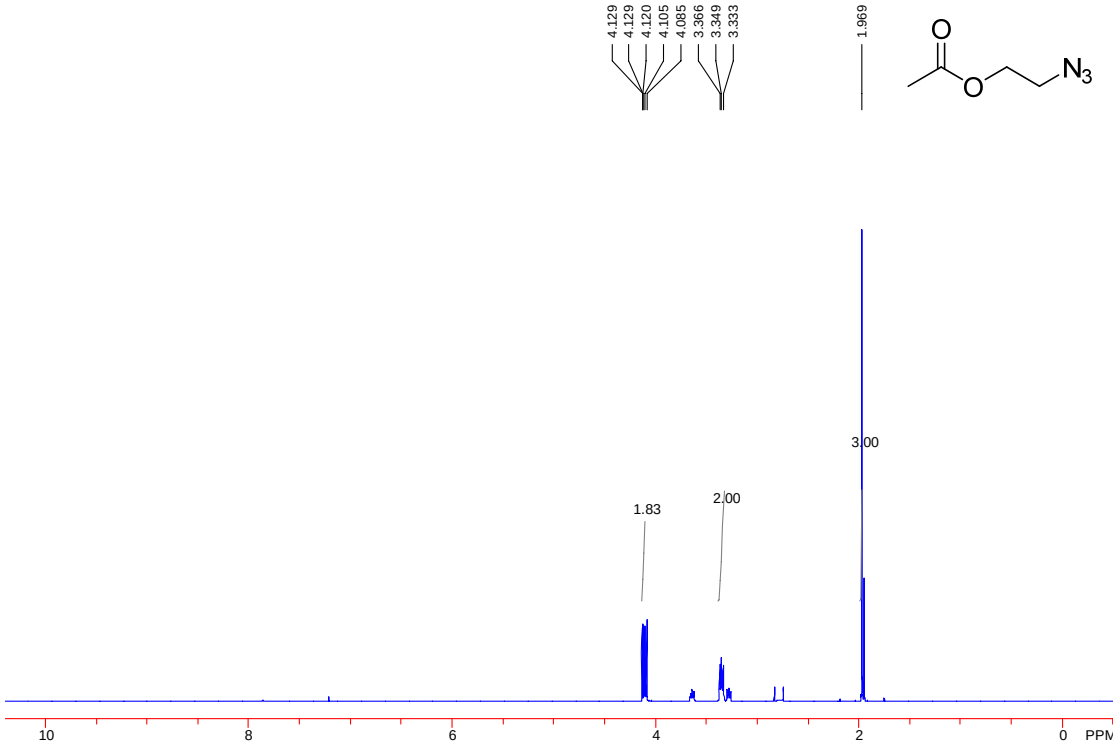
(68d)


7.251
7.246
7.228
7.199
7.193
7.172
7.163
7.156
7.134
3.455
3.428
3.406
2.847
2.822
2.799
N3
3.03
1.93
2.00
2.00
10
8
6
4
2
0 PPM

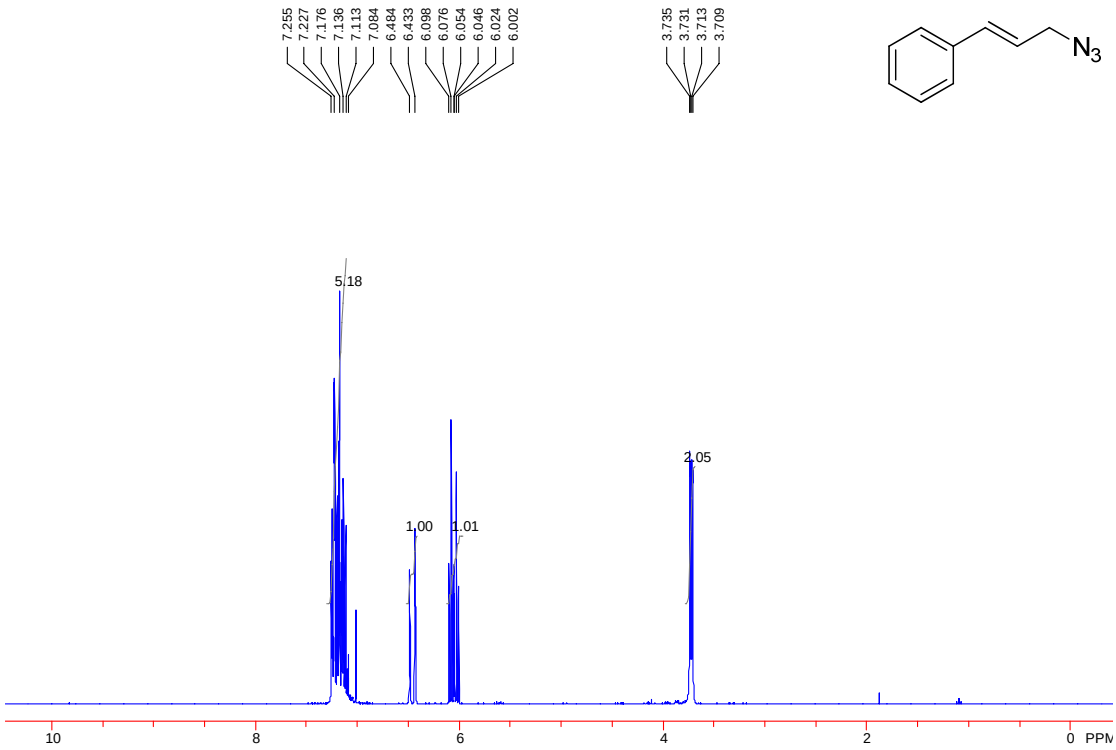
(68e)

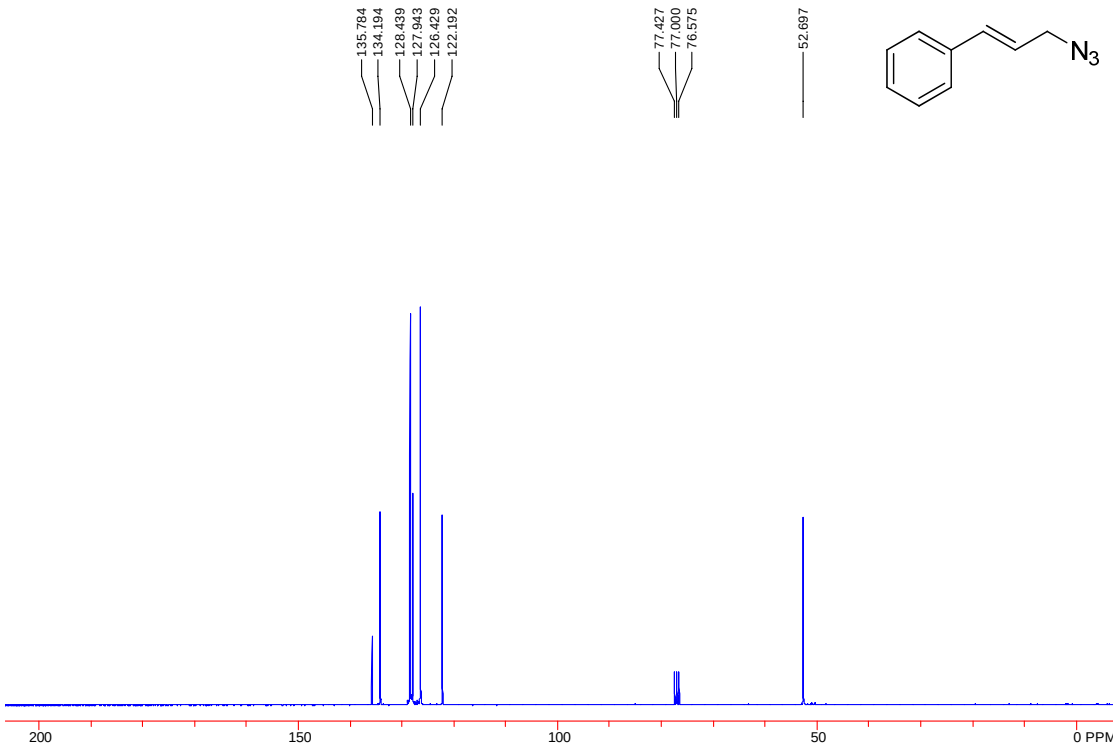

3.266
3.244
3.219
1.615
1.589
1.566
1.364
1.353
1.314
1.275
0.902
0.881
0.855
N3
8.71
3.00
2.12
2.03
10
8
6
4
2
0
PPM

(68o)

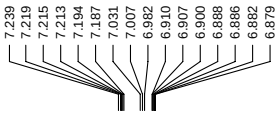

4.129
4.129
4.120
4.105
4.085
3.366
3.349
3.333
1.969
O
O
N3
3.00
1.83
2.00
10
8
6
4
2
0
PPM

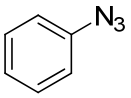
(68p)

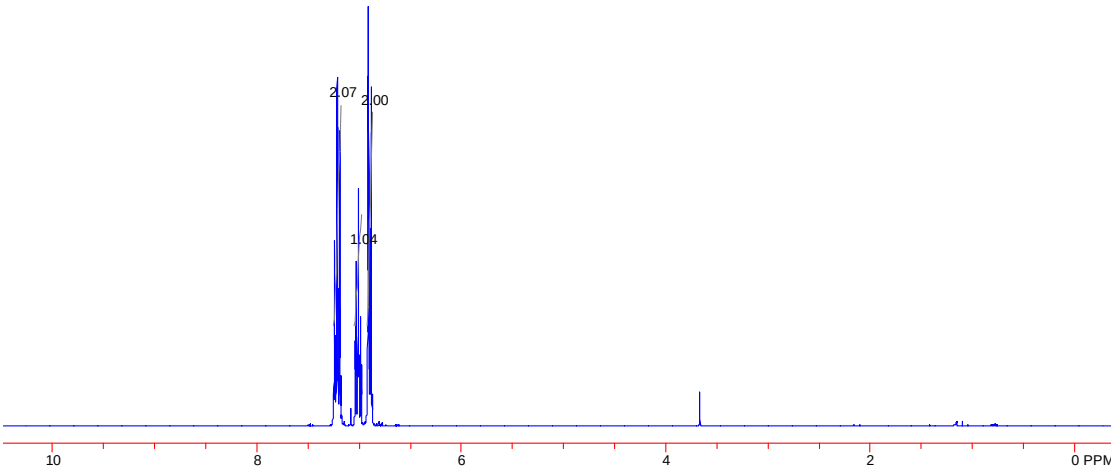

7.255
7.227
7.176
7.136
7.113
7.084
6.484
6.433
6.098
6.076
6.054
6.046
6.024
6.002
3.735
3.731
3.713
3.709
N3
5.18
1.00
1.01
2.05
10
8
6
4
2
0 PPM


135.784
134.194
128.439
127.943
126.429
122.192
77.427
77.000
76.575
52.697
N3
200
150
100
50
0 PPM

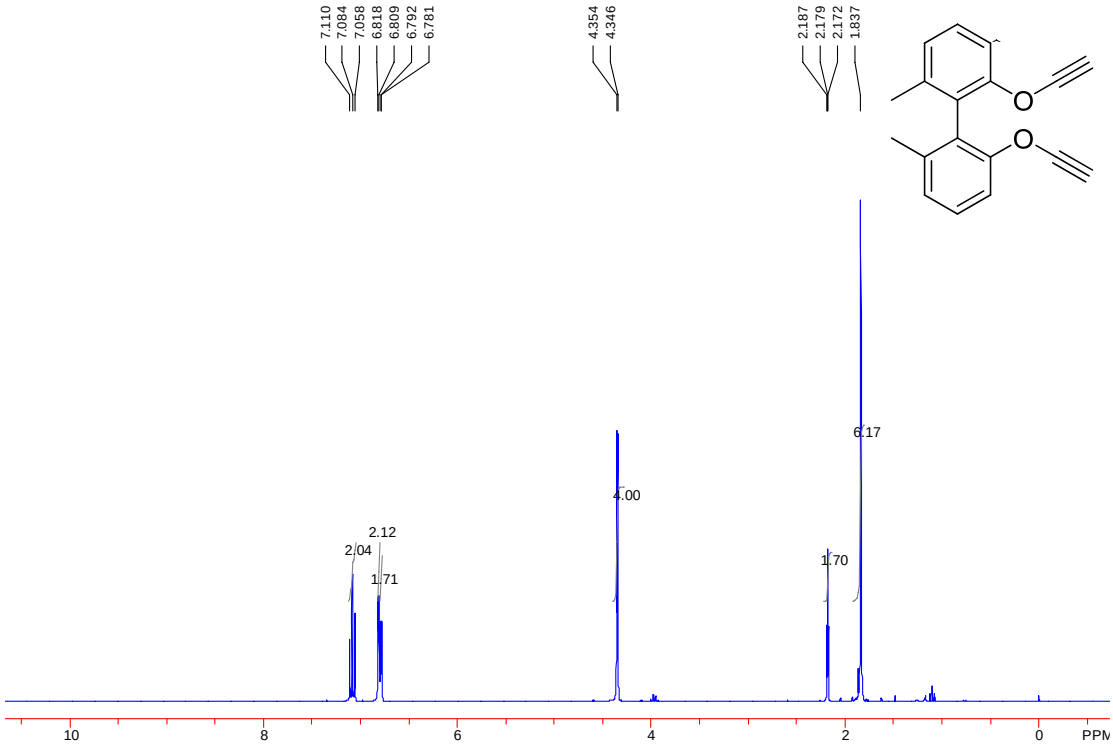
(68q)

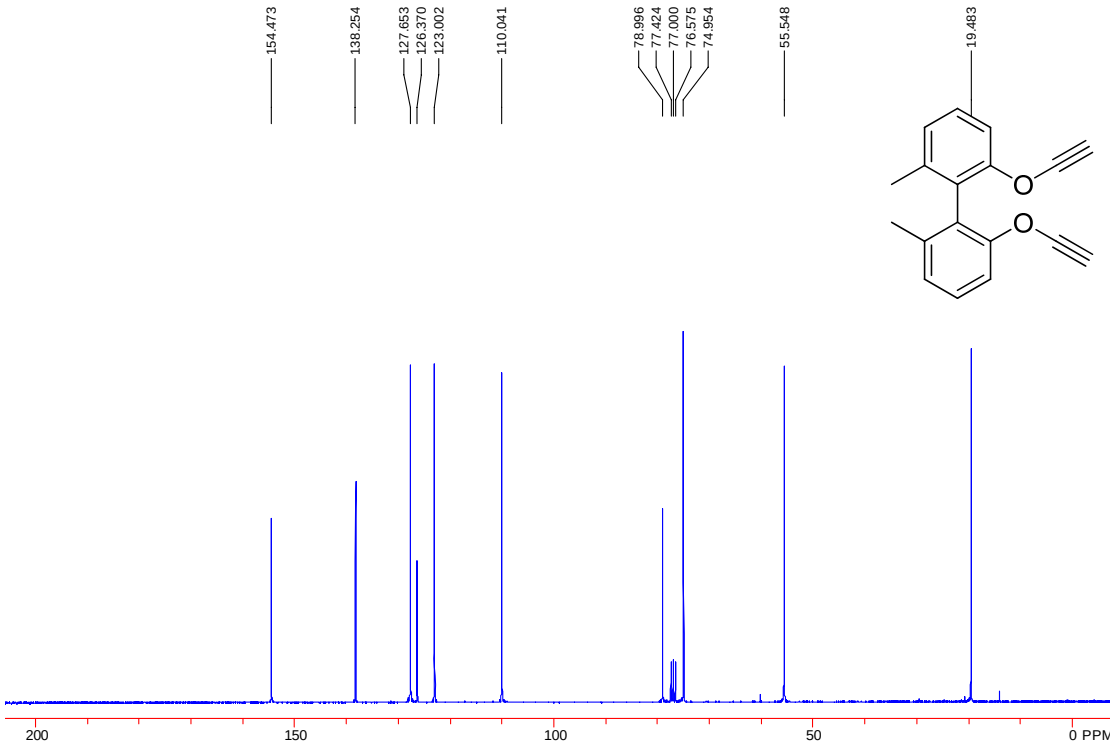

7.239
7.219
7.215
7.213
7.194
7.187
7.031
7.007
6.982
6.910
6.907
6.900
6.888
6.886
6.882
6.879


N3

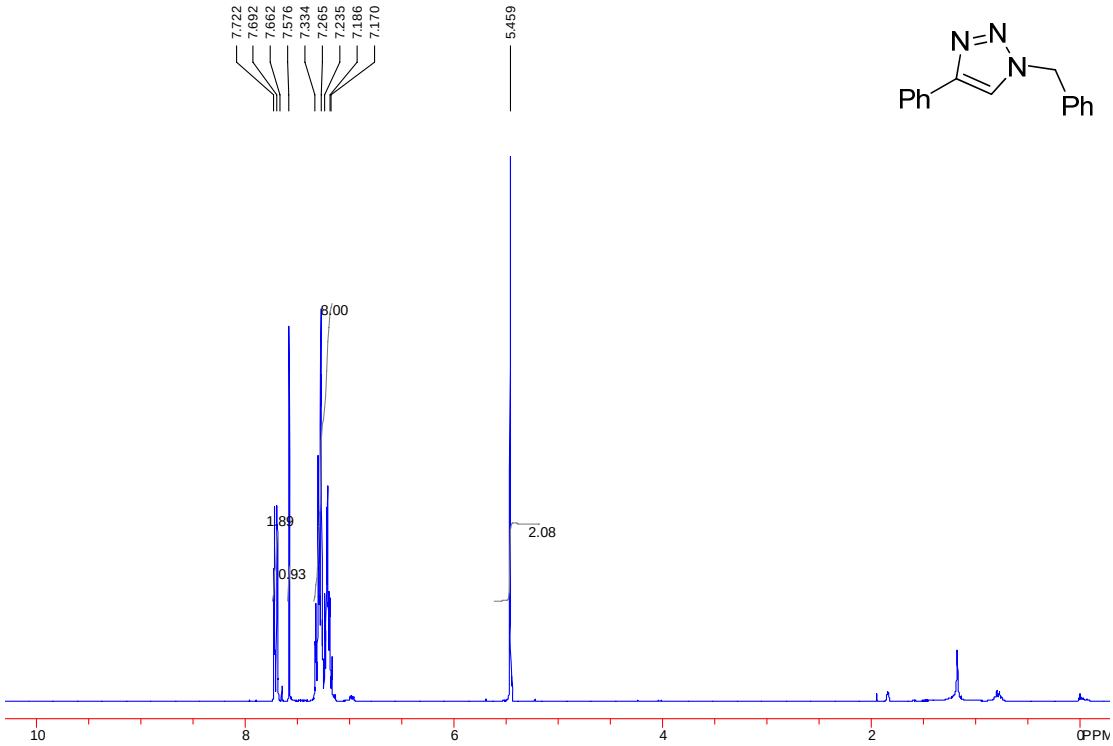

2.07
2.00
1.04
10
8
6
4
2
0 PPM

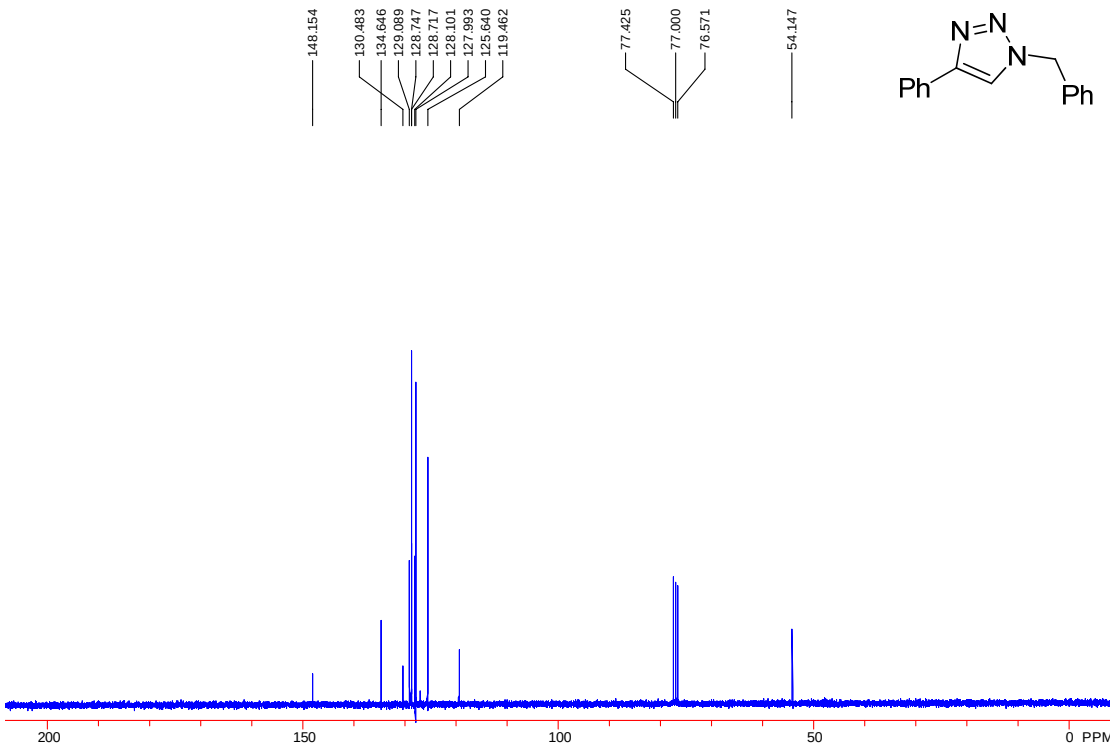
(67n)


7.110
7.084
7.058
6.818
6.809
6.792
6.781
4.354
4.346
2.187
2.179
2.172
1.837
O
O
6.17
4.00
2.12
2.04
1.71
1.70
10
8
6
4
2
0
PPM

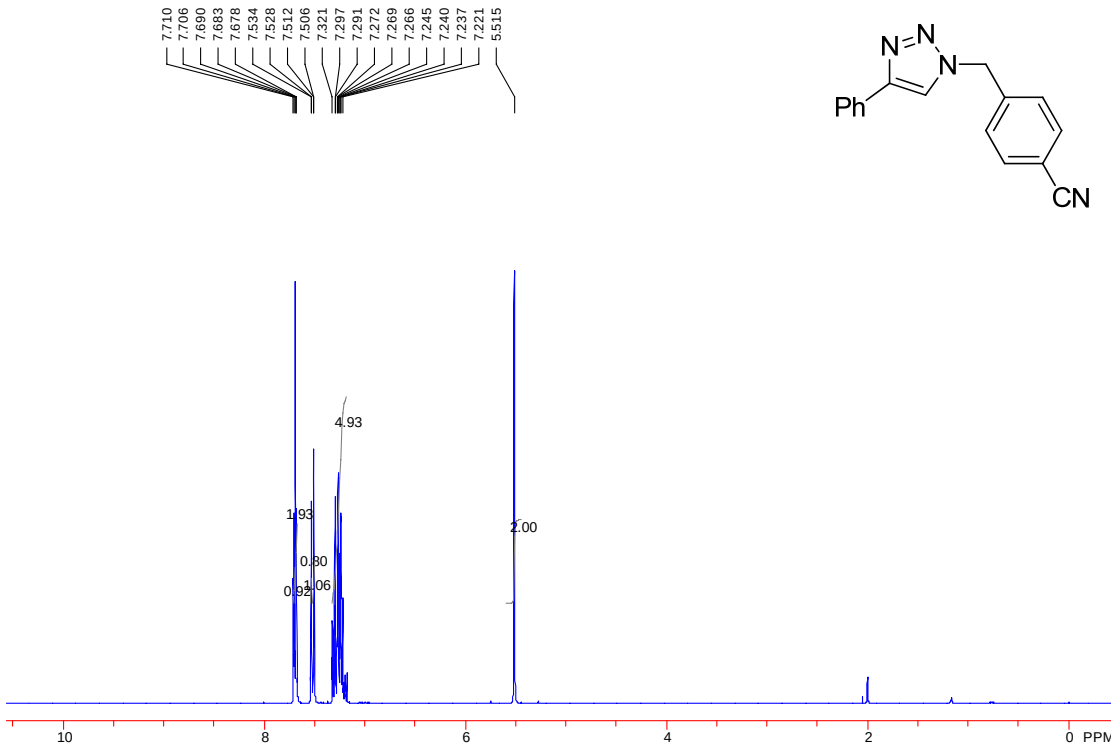

154.473
138.254
127.653
126.370
123.002
110.041
78.996
77.424
77.000
76.575
74.954
55.548
19.483
O
O
200
150
100
50
0 PPM

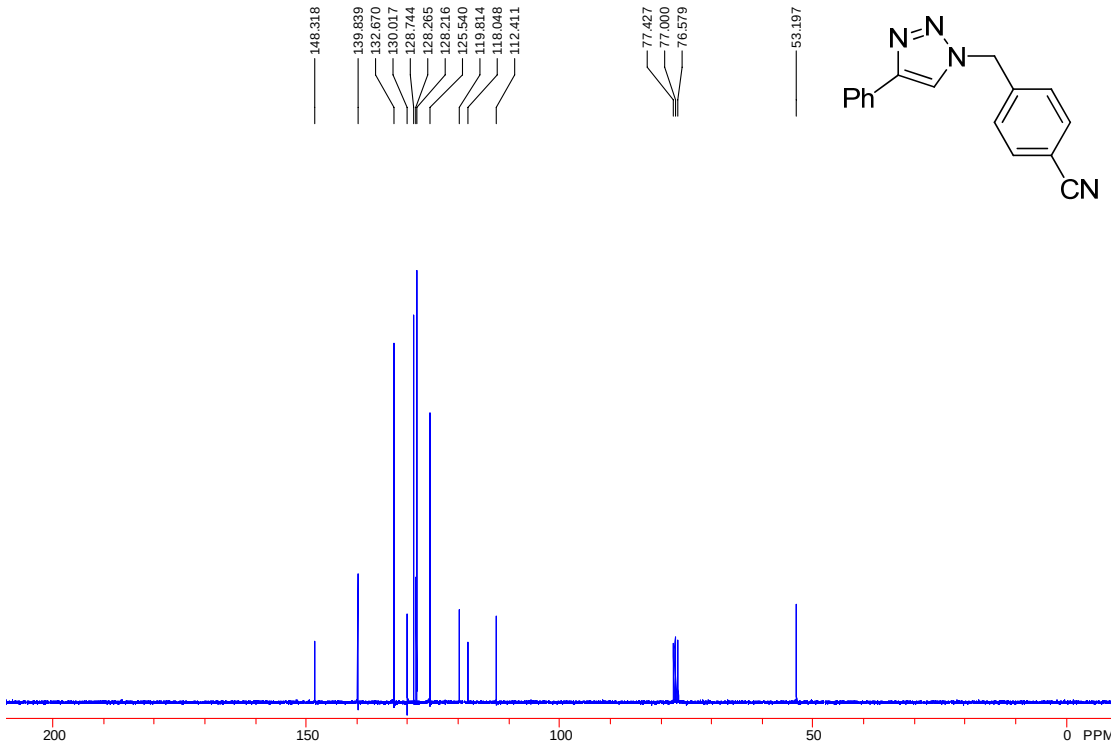
(69a)


7.722
7.692
7.662
7.576
7.334
7.265
7.235
7.186
7.170
5.459
N=N
N
Ph
Ph
8.00
1.89
0.93
2.08
10
8
6
4
2
0
PPM

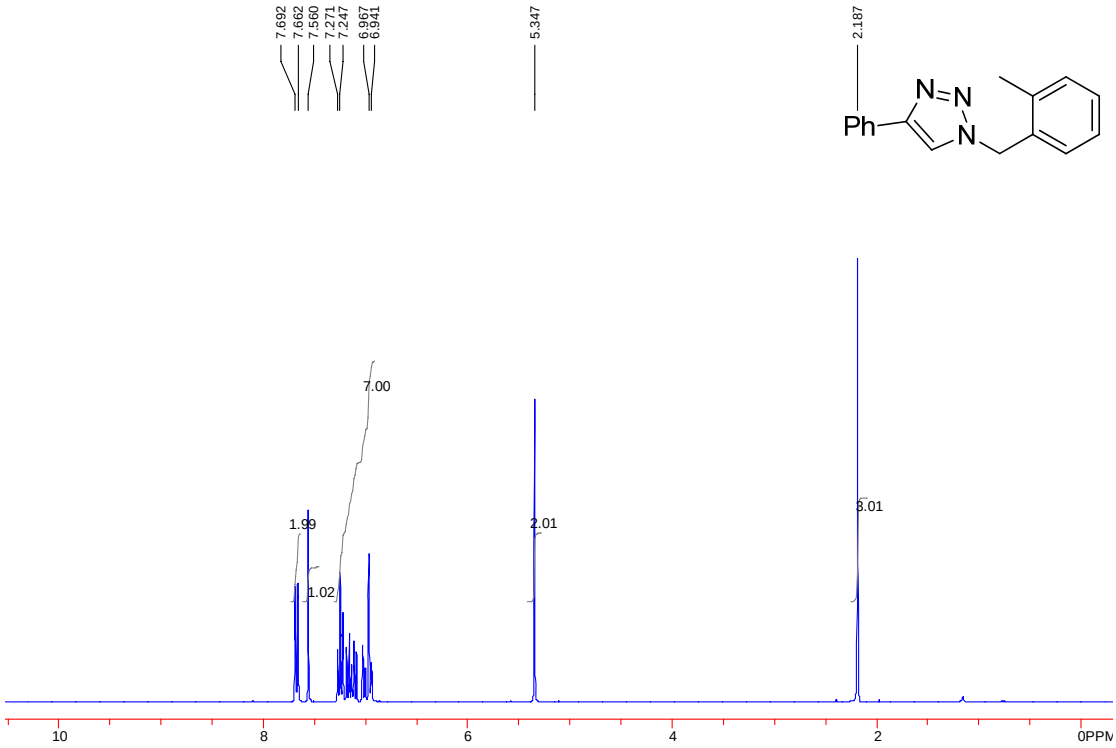

148.154
130.483
134.646
129.089
128.747
128.717
128.101
127.993
125.640
119.462
77.425
77.000
76.571
54.147
N=N
N
Ph
Ph
200
150
100
50
0
PPM

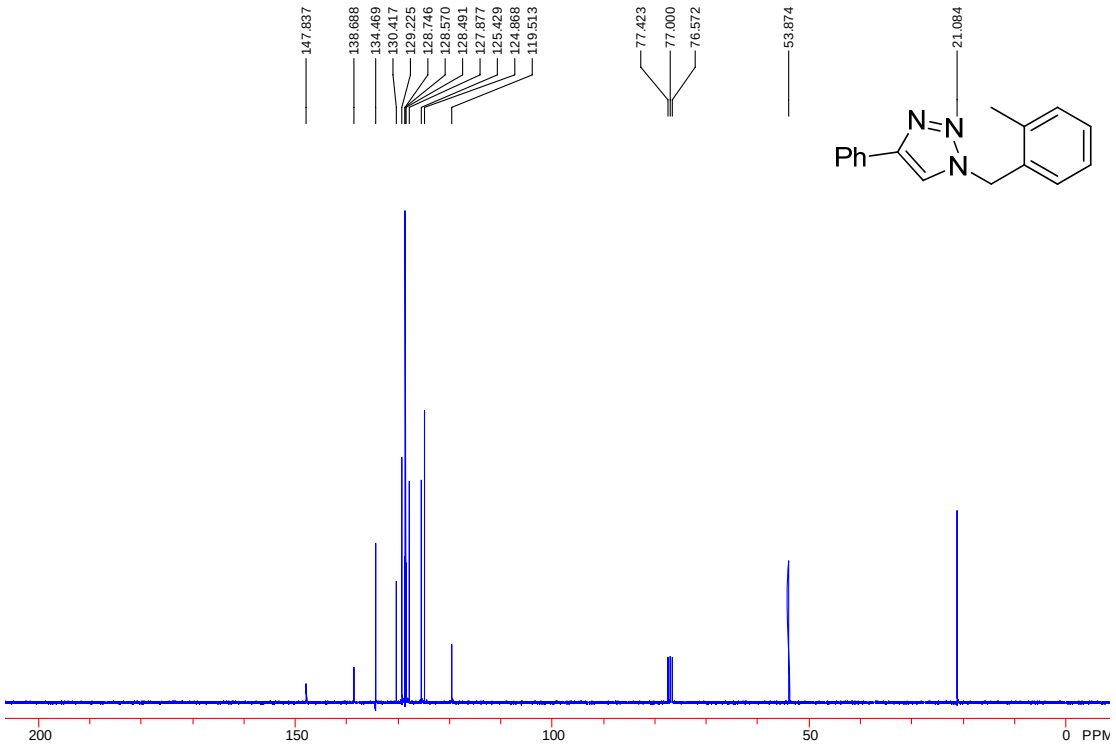
(69b)


7.710
7.706
7.690
7.683
7.678
7.534
7.528
7.512
7.506
7.321
7.297
7.291
7.272
7.269
7.266
7.245
7.240
7.237
7.221
5.515
N
N
N
Ph
CN
4.93
1.93
0.80
1.06
0.92
2.00
10
8
6
4
2
0 PPM

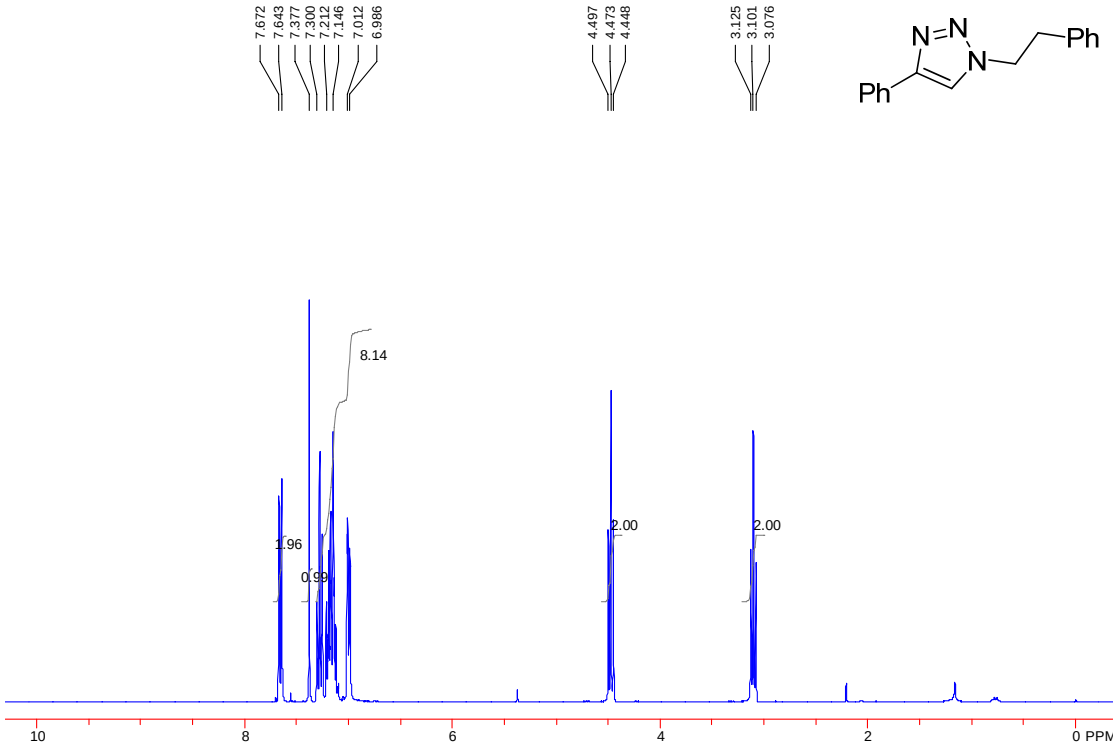

148.318
139.839
132.670
130.017
128.744
128.265
128.216
125.540
119.814
118.048
112.411
77.427
77.000
76.579
53.197
N
N
N
Ph
CN
200
150
100
50
0 PPM

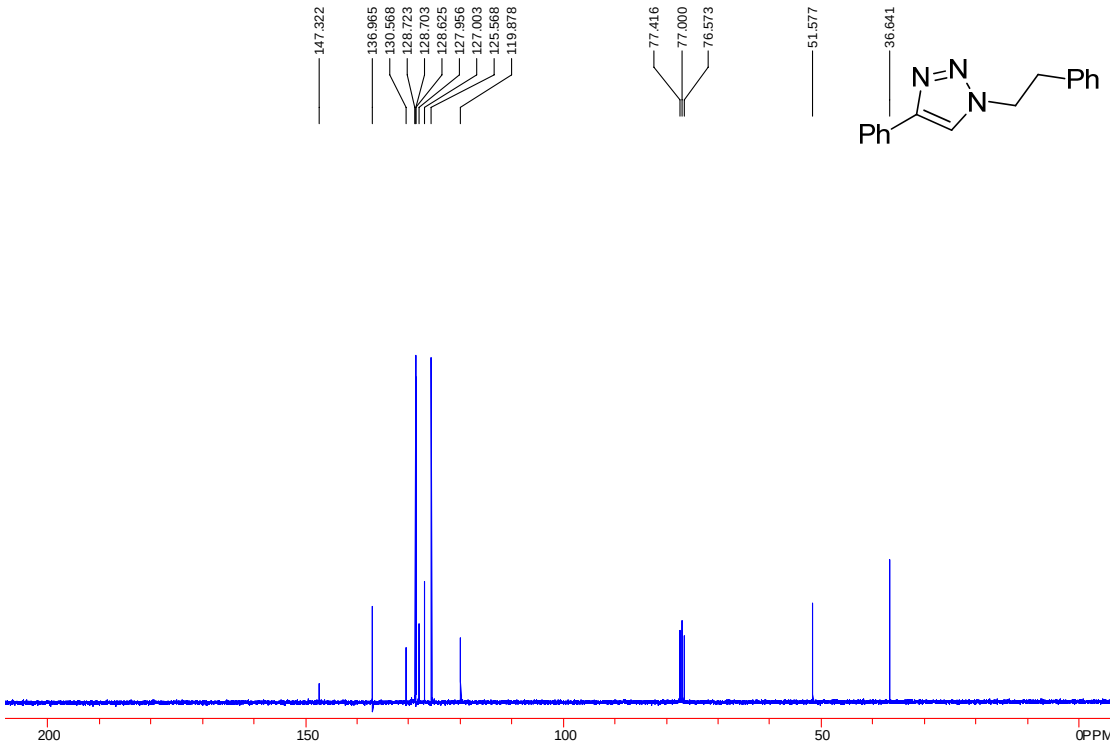
(69c)


7.692
7.662
7.560
7.271
7.247
6.967
6.941
5.347
2.187
Ph
N
N
N
7.00
1.99
1.02
2.01
3.01
10
8
6
4
2
0PPM

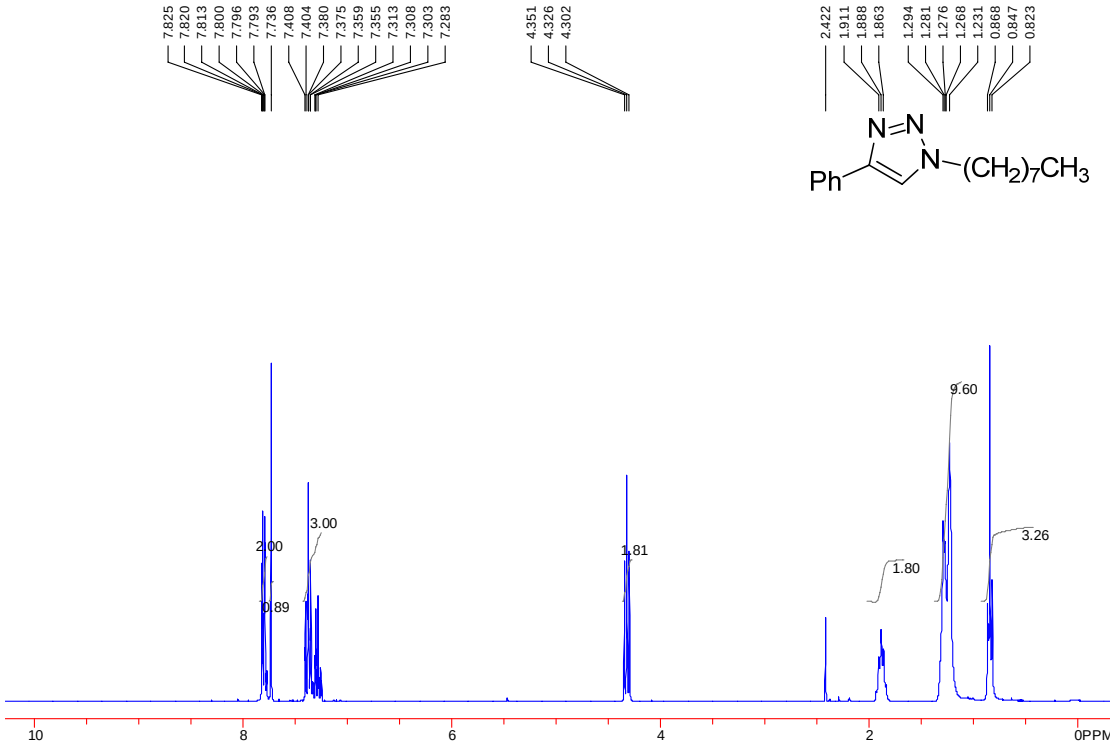

147.837
138.688
134.469
130.417
129.225
128.746
128.570
128.491
127.877
125.429
124.868
119.513
77.423
77.000
76.572
53.874
21.084
Ph
N
N
N
200
150
100
50
0 PPM

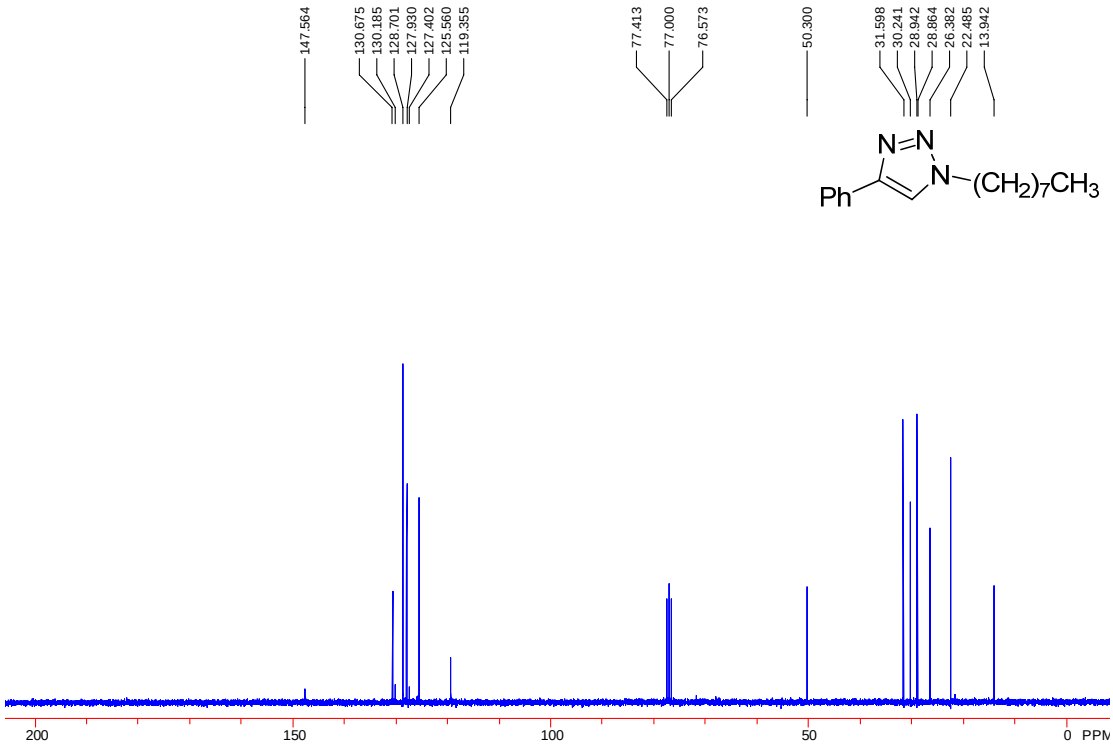
(69d)


7.672
7.643
7.377
7.300
7.212
7.146
7.012
6.986
4.497
4.473
4.448
3.125
3.101
3.076
N
N
N
Ph
Ph
8.14
1.96
0.99
2.00
2.00
10
8
6
4
2
0 PPM

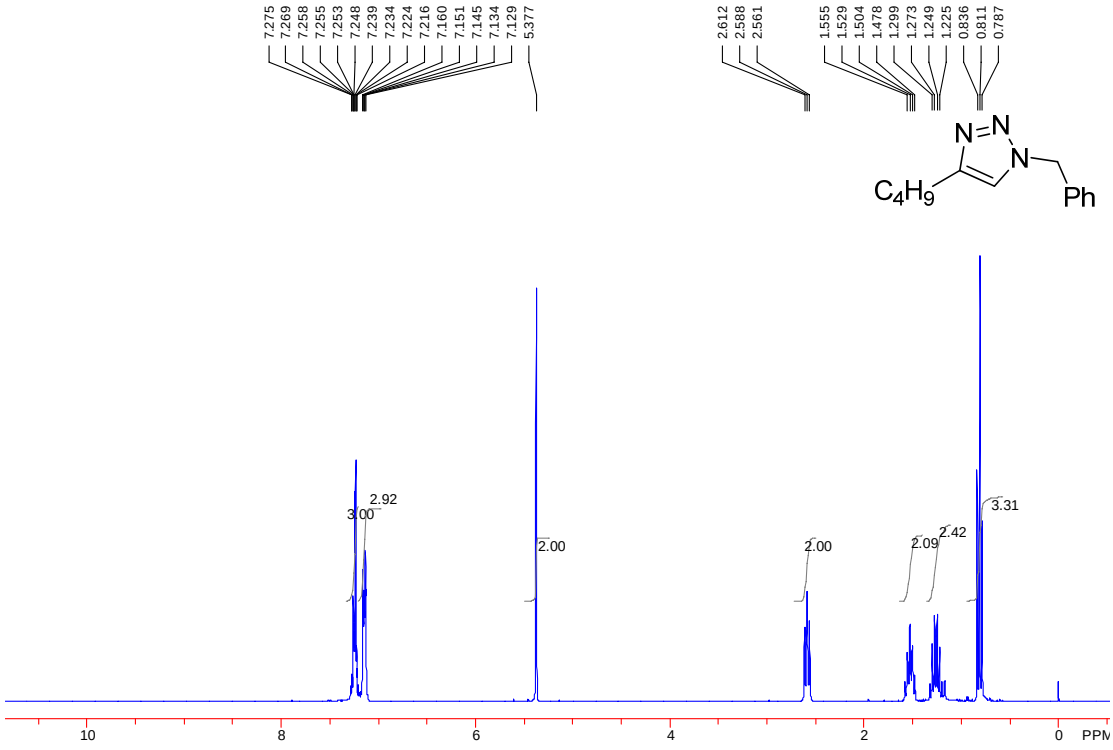

147.322
136.965
130.568
128.723
128.703
128.625
127.956
127.003
125.568
119.878
77.416
77.000
76.573
51.577
36.641
N
N
N
Ph
Ph
200
150
100
50
0PPM

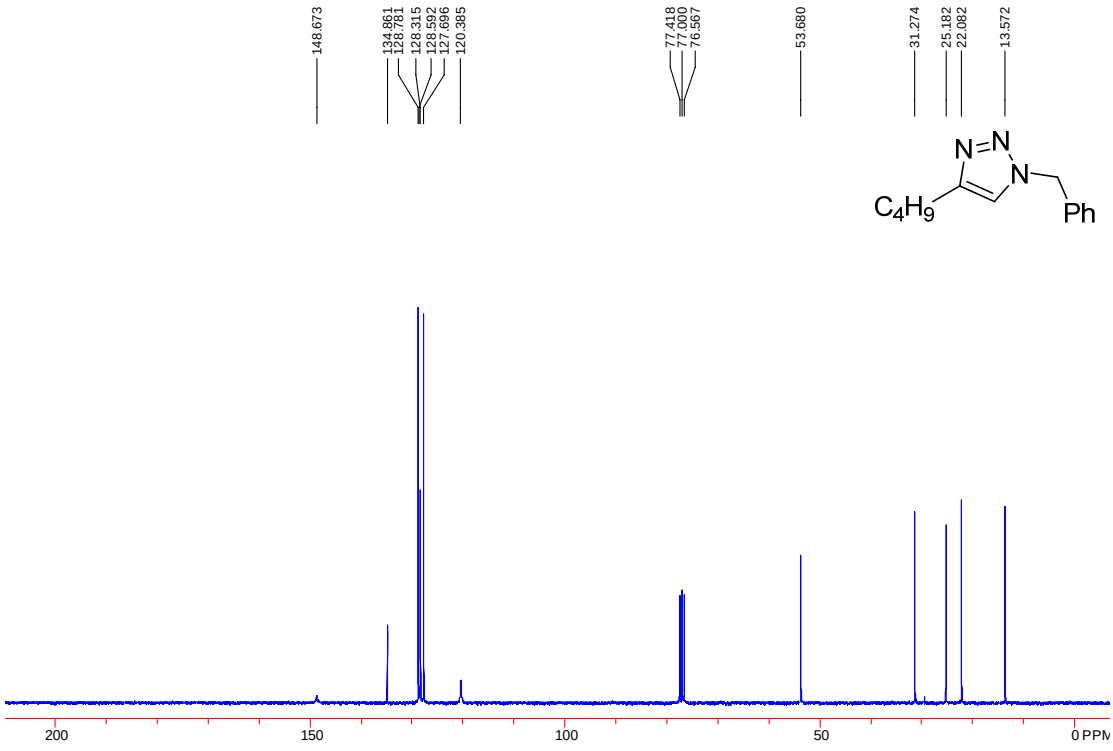
(69e)


7.825
7.820
7.813
7.800
7.796
7.793
7.736
7.408
7.404
7.380
7.375
7.359
7.355
7.313
7.308
7.303
7.283
4.351
4.326
4.302
2.422
1.911
1.888
1.863
1.294
1.281
1.276
1.268
1.231
0.868
0.847
0.823
N=N
N
(CH2)7CH3
Ph
2.00
3.00
0.89
1.81
1.80
9.60
3.26
10
8
6
4
2
0PPM

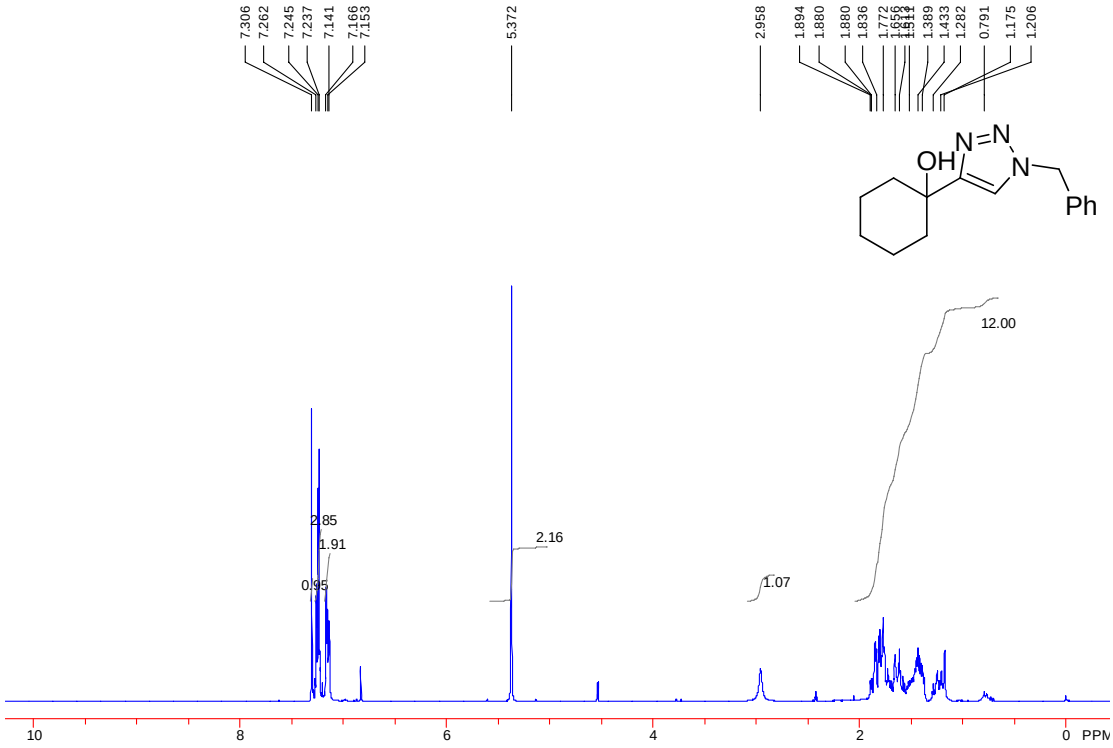

147.564
130.675
130.185
128.701
127.930
127.402
125.560
119.355
77.413
77.000
76.573
50.300
31.598
30.241
28.942
28.864
26.382
22.485
13.942
N=N
N
(CH2)7CH3
Ph
200
150
100
50
0 PPM

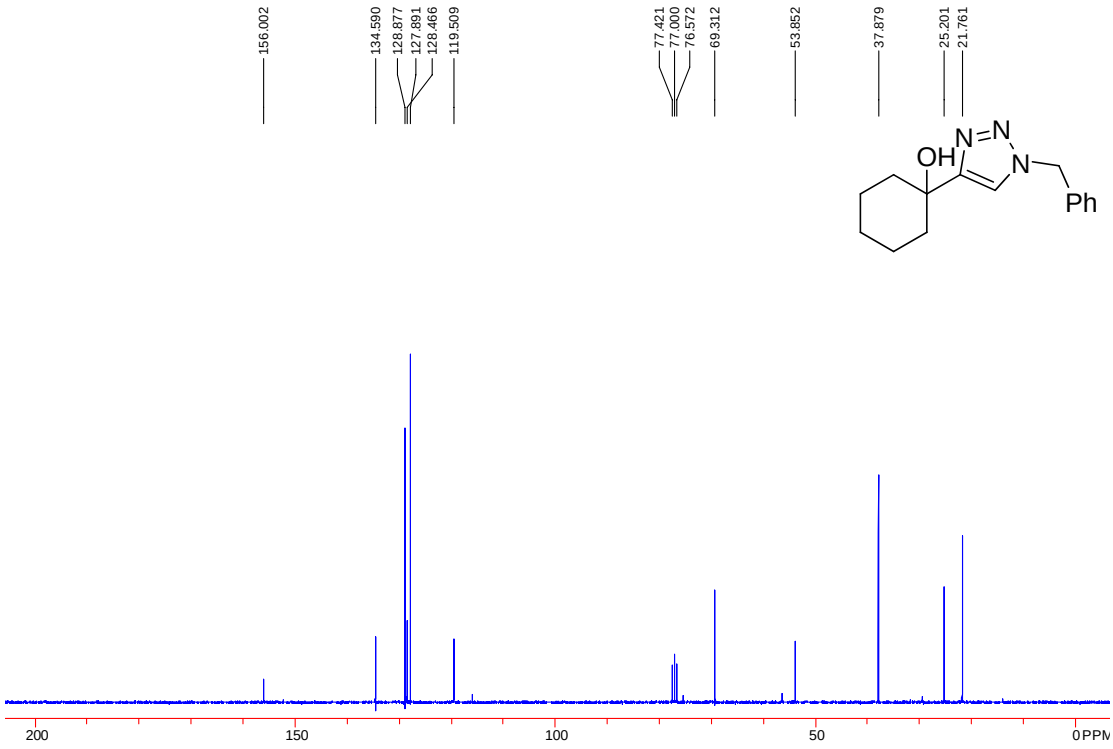
(69f)


7.275
7.269
7.258
7.255
7.253
7.248
7.239
7.234
7.224
7.216
7.160
7.151
7.145
7.134
7.129
5.377
2.612
2.588
2.561
1.555
1.529
1.504
1.478
1.299
1.273
1.249
1.225
0.836
0.811
0.787
N=N
N
C4H9
Ph
3.00
2.92
2.00
2.00
2.09
2.42
3.31
10
8
6
4
2
0
PPM

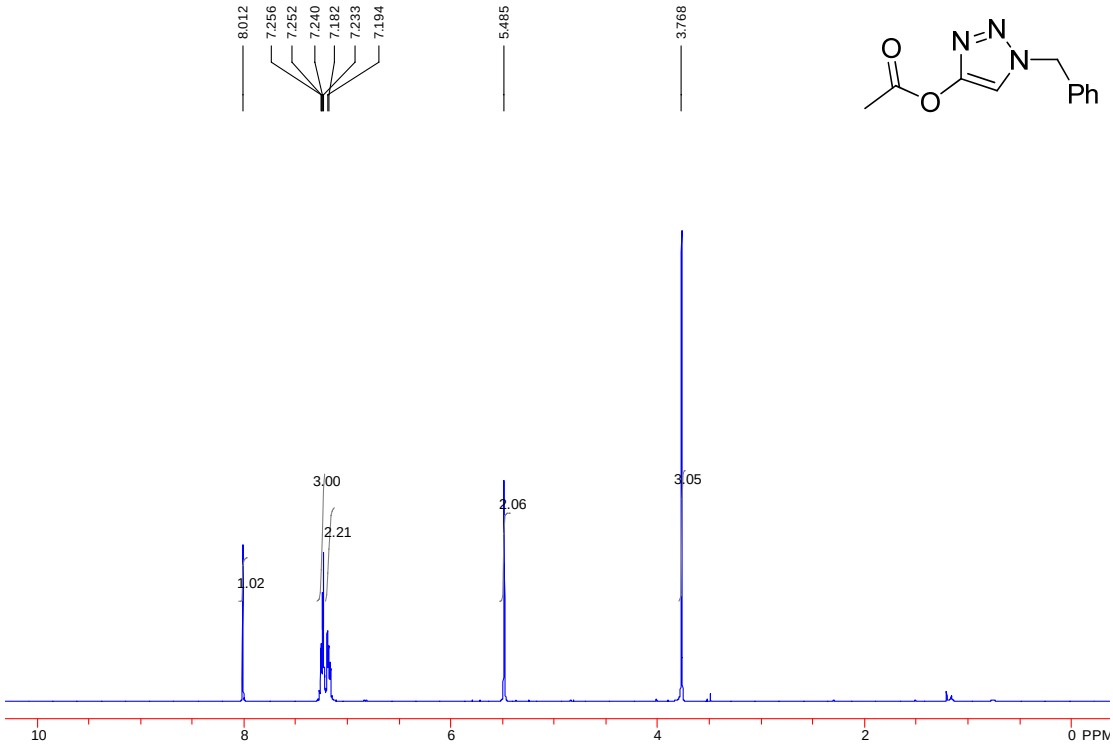

148.673
134.861
128.781
128.315
128.592
127.696
120.385
77.418
77.000
76.567
53.680
31.274
25.182
22.082
13.572
N=N
N
C4H9
Ph
200
150
100
50
0 PPM

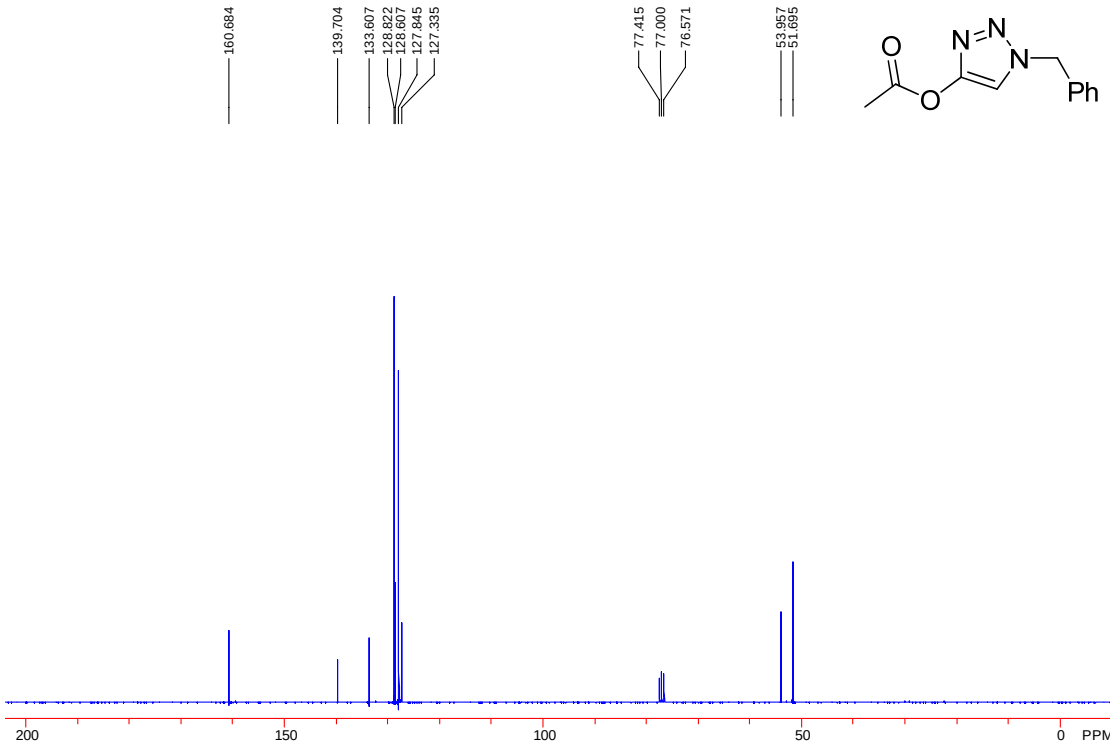
(69g)


7.306
7.262
7.245
7.237
7.141
7.166
7.153
5.372
2.958
1.894
1.880
1.880
1.836
1.772
1.433
1.282
0.791
1.175
1.206
OH
N=N
N
Ph
12.00
2.85
1.91
0.95
2.16
1.07
10
8
6
4
2
0 PPM

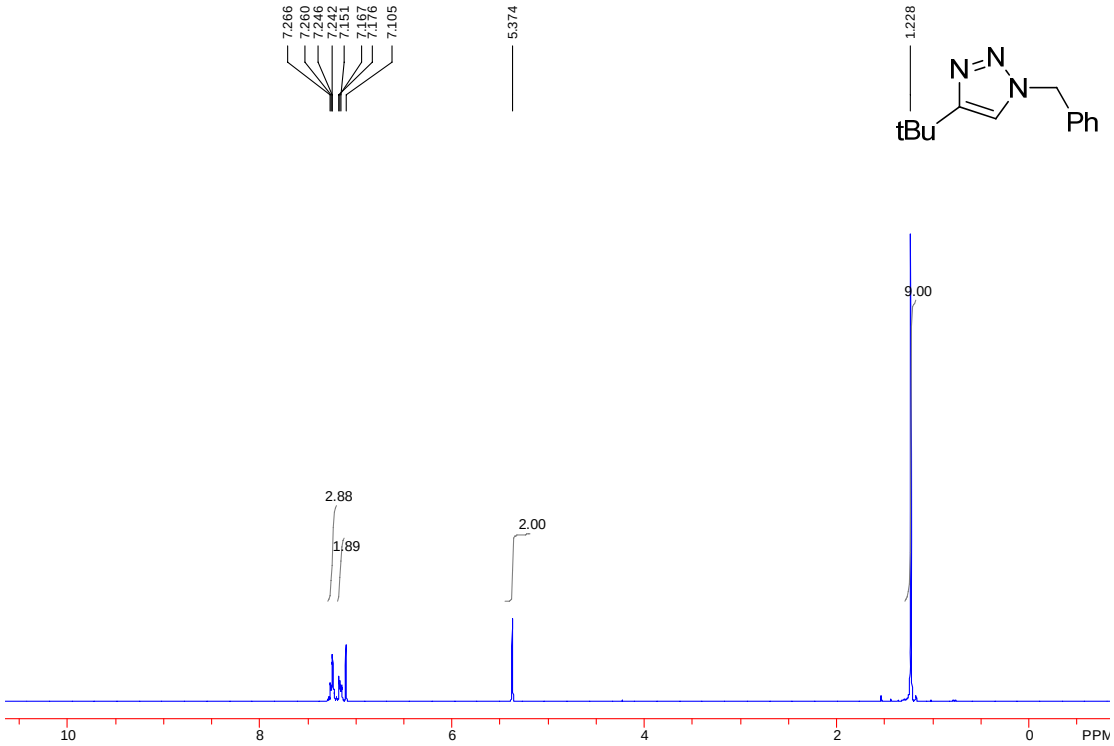

156.002
134.590
128.877
127.891
128.466
119.509
77.421
77.000
76.572
69.312
53.852
37.879
25.201
21.761
OH
N=N
N
Ph
200
150
100
50
0 PPM

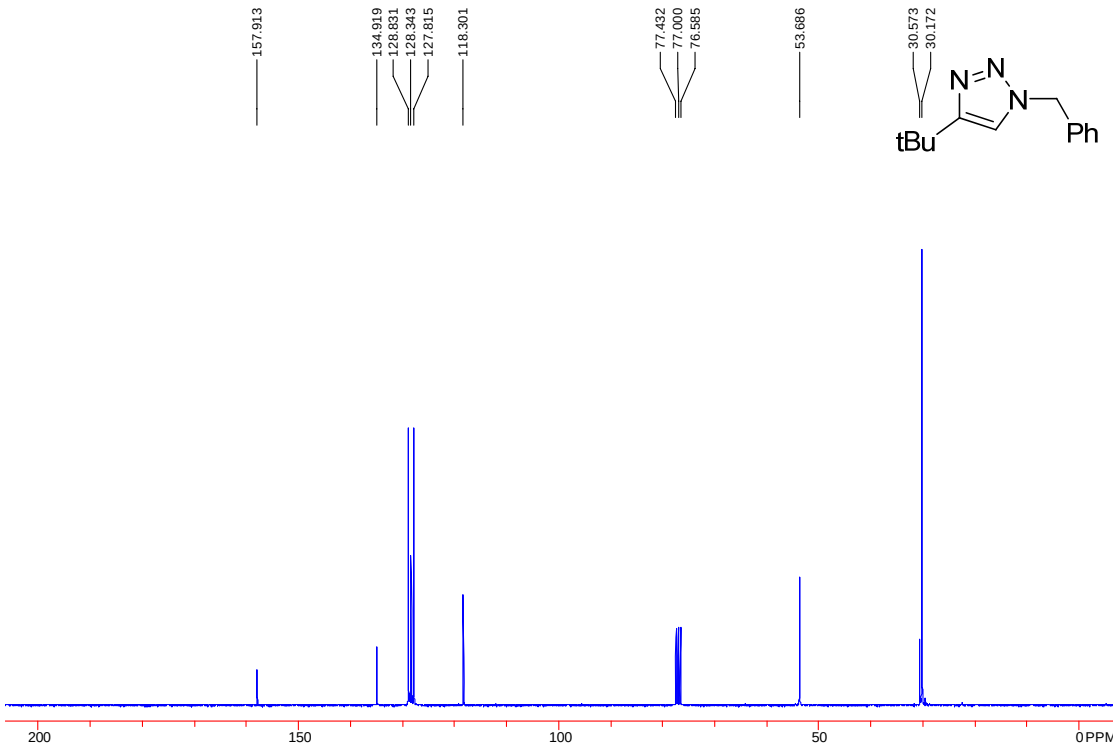
(69h)


8.012
7.256
7.252
7.240
7.182
7.233
7.194
5.485
3.768
O
N
N
O
Ph
3.00
2.21
1.02
2.06
3.05
10
8
6
4
2
0 PPM

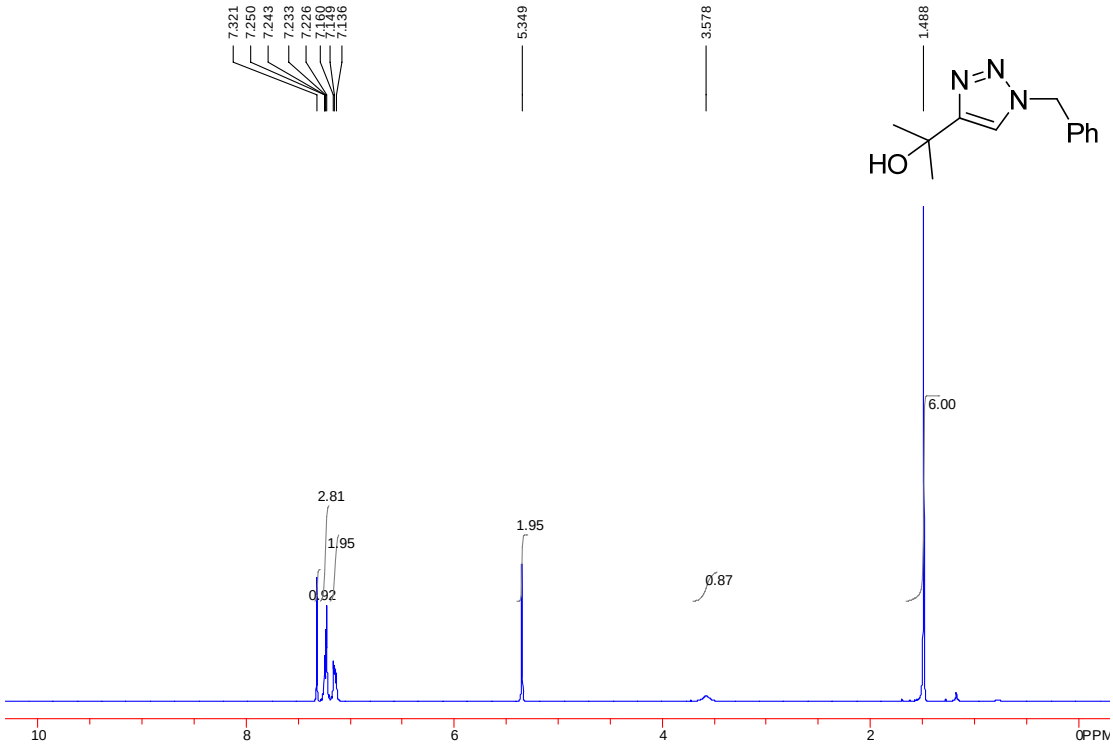

160.684
139.704
133.607
128.822
128.607
127.845
127.335
77.415
77.000
76.571
53.957
51.695
O
N
N
O
Ph
200
150
100
50
0 PPM

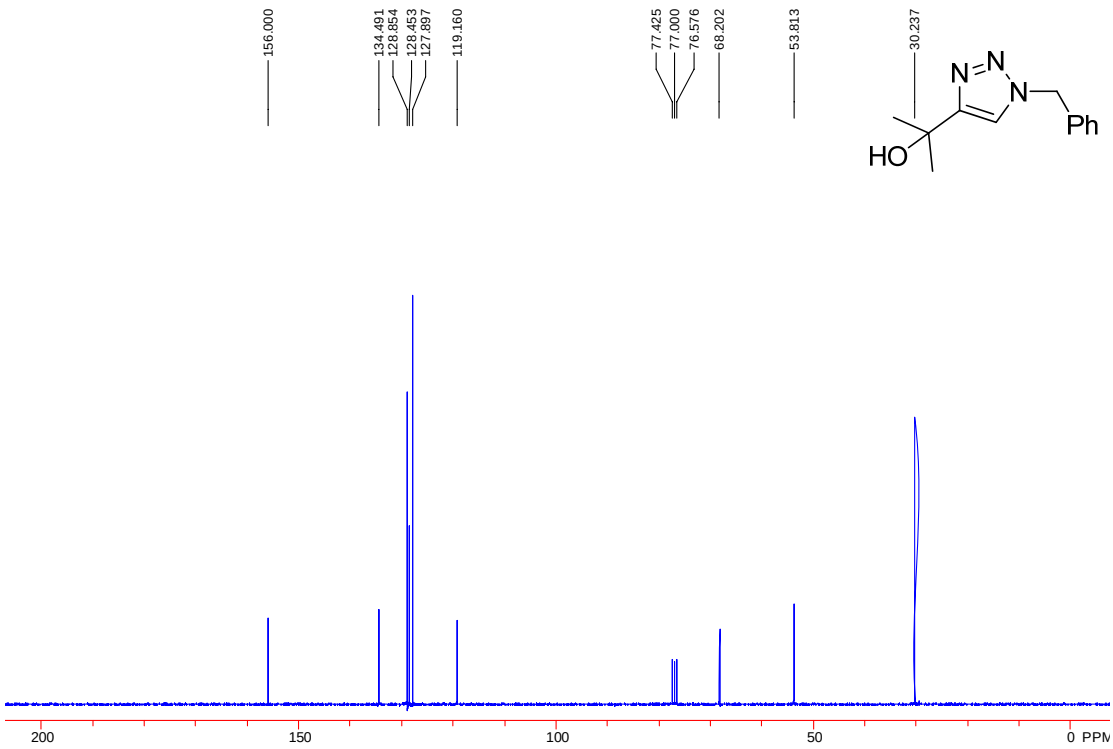
(69i)


7.266
7.260
7.246
7.242
7.151
7.167
7.176
7.105
5.374
1.228
tBu
Ph
9.00
2.88
1.89
2.00
10
8
6
4
2
0
PPM

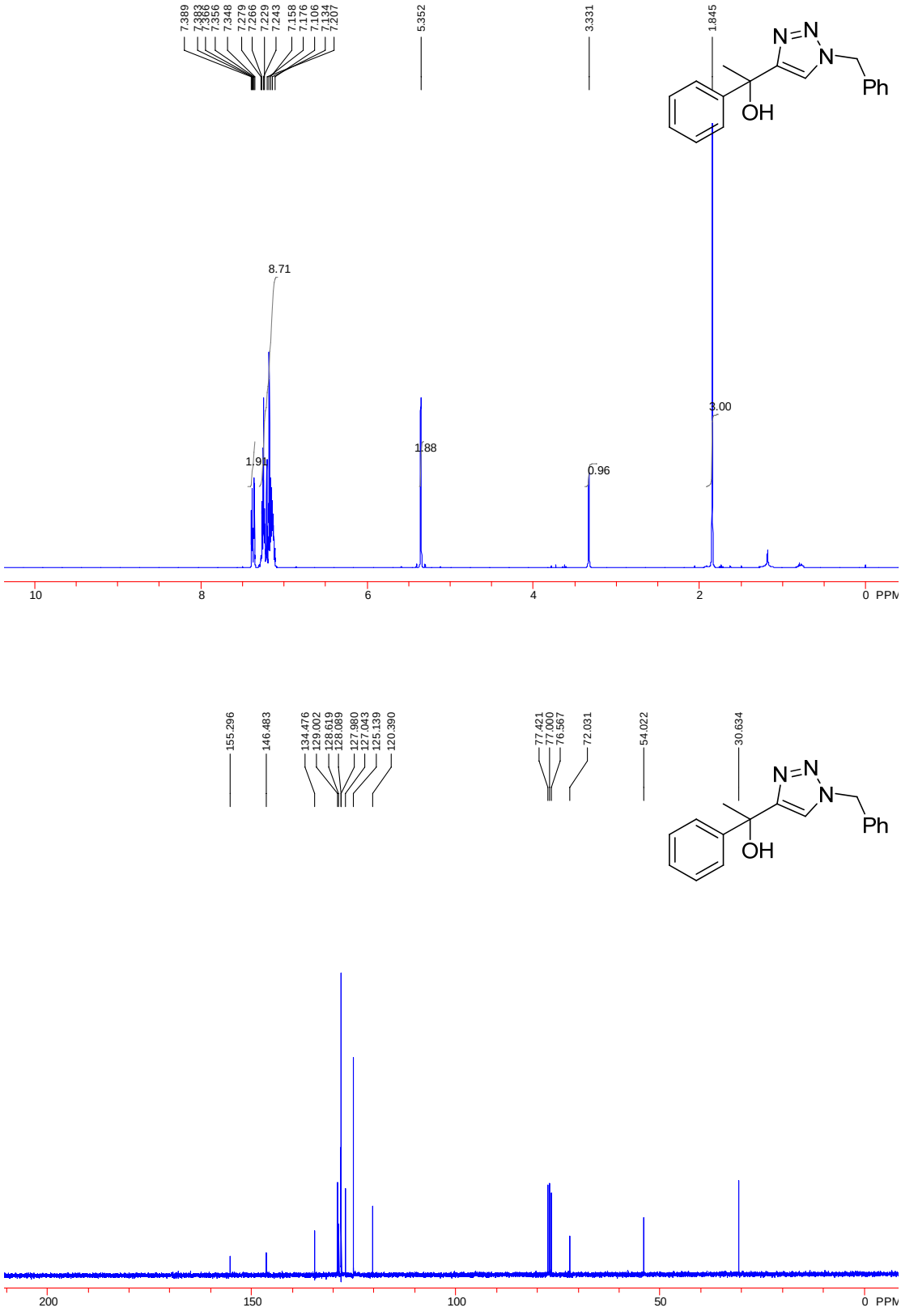

157.913
134.919
128.831
128.343
127.815
118.301
77.432
77.000
76.585
53.686
30.573
30.172
tBu
Ph
200
150
100
50
0 PPM

(69j)

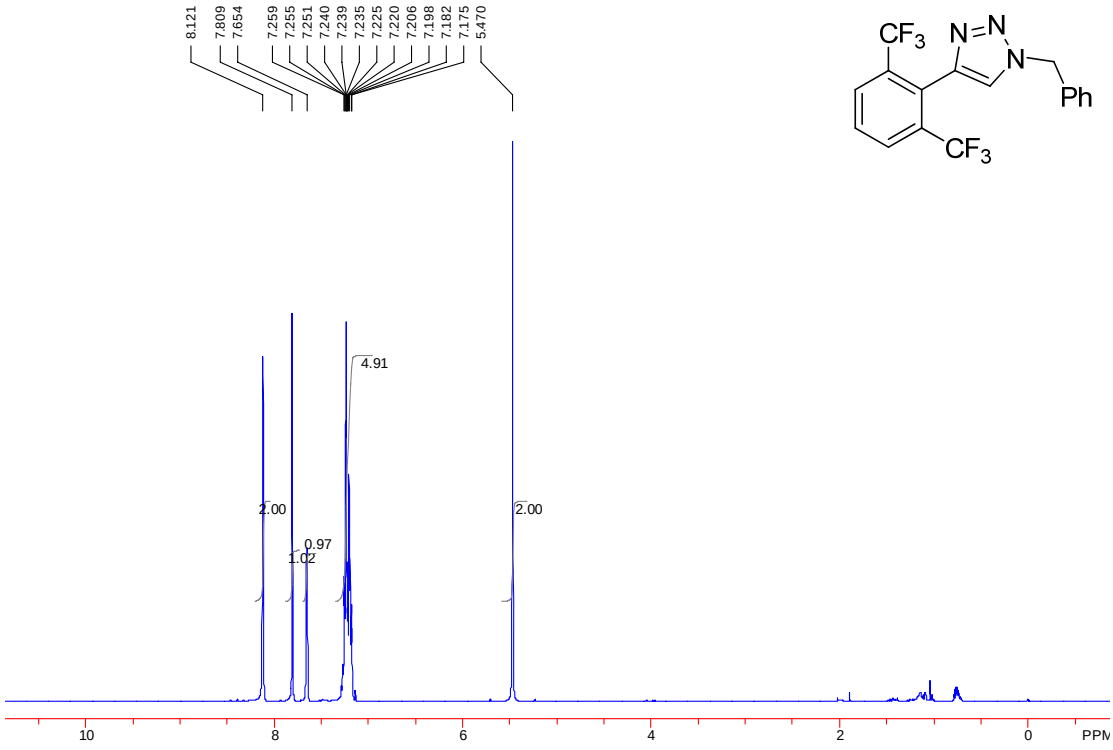

7.321
7.250
7.243
7.233
7.226
7.160
7.149
7.136
5.349
3.578
1.488
N
N
N
Ph
HO
6.00
2.81
1.95
1.95
0.92
0.87
10
8
6
4
2
0PPM

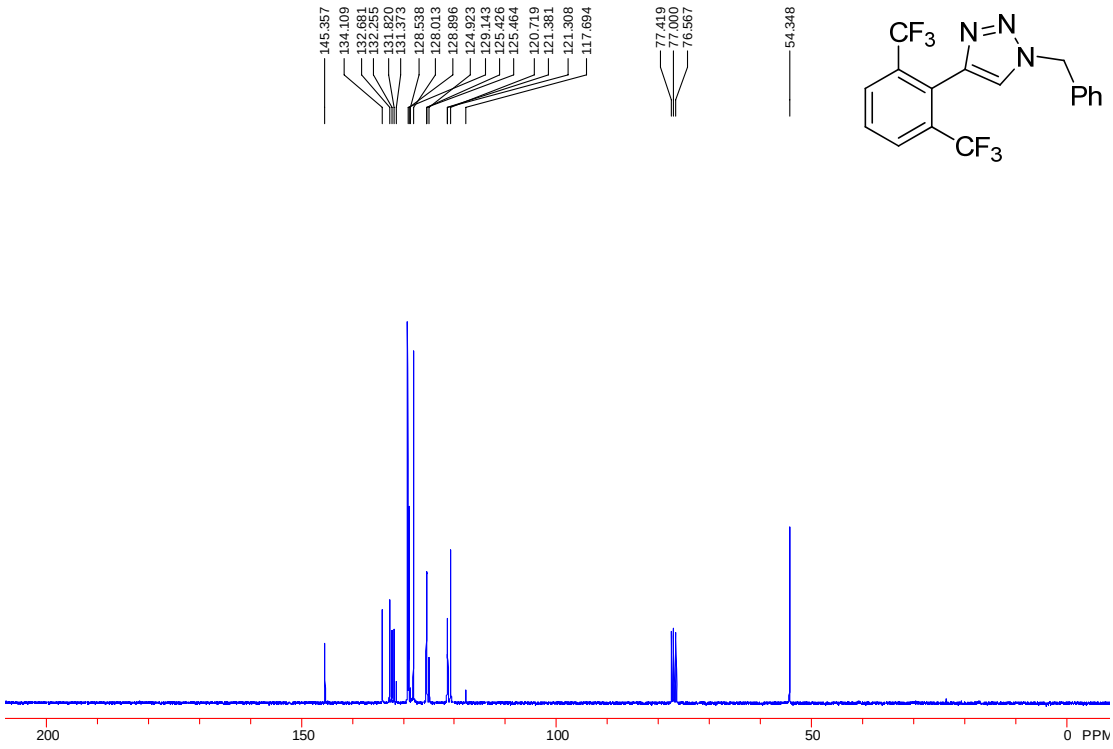

156.000
134.491
128.854
128.453
127.897
119.160
77.425
77.000
76.576
68.202
53.813
30.237
N
N
N
Ph
HO
200
150
100
50
0 PPM

(69k)

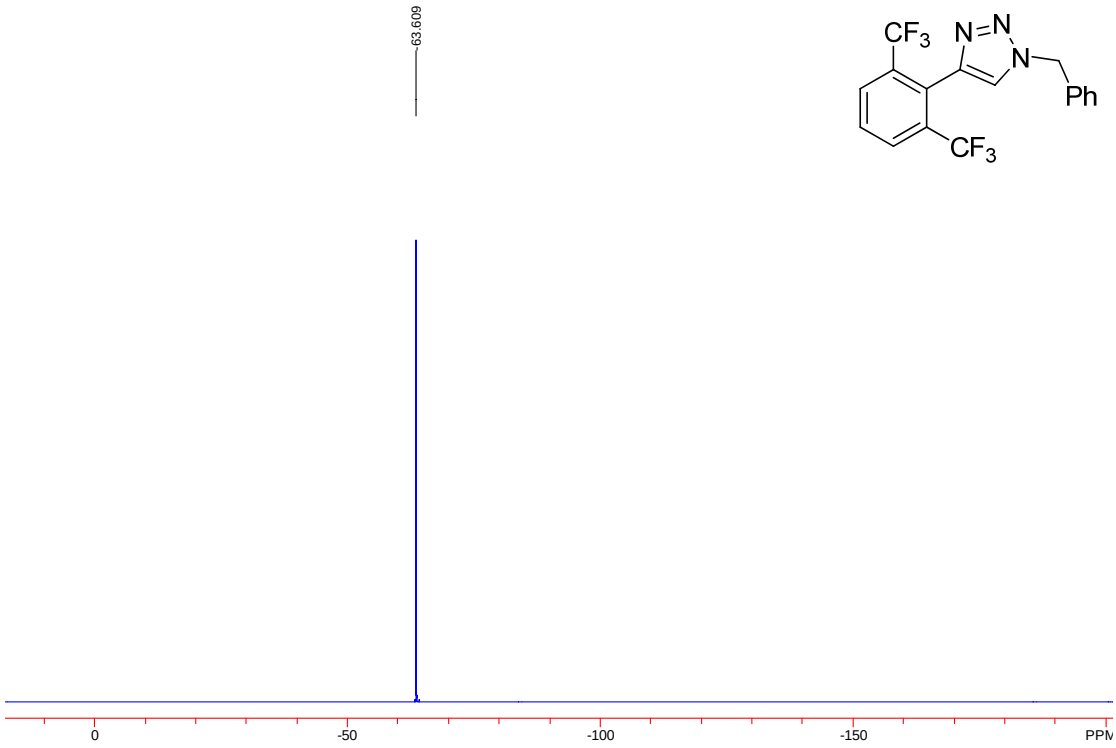

7.389
7.383
7.366
7.356
7.348
7.279
7.266
7.229
7.243
7.158
7.176
7.106
7.134
7.207
5.352
3.331
1.845
N=N
N
Ph
OH
8.71
1.91
1.88
0.96
3.00
10
8
6
4
2
0 PPM
155.296
146.483
134.476
129.002
128.619
128.089
127.980
127.043
125.139
120.390
77.421
77.000
76.567
72.031
54.022
30.634
N=N
N
Ph
OH
200
150
100
50
0 PPM

(69l)

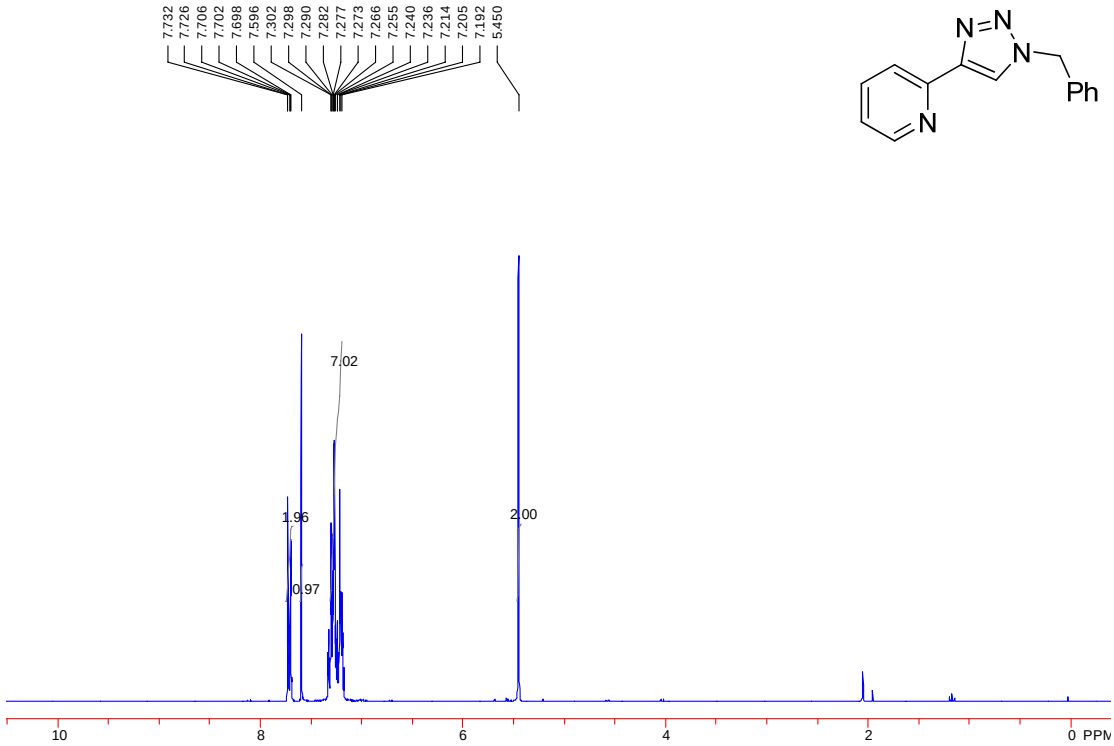

8.121
7.809
7.654
7.259
7.255
7.251
7.240
7.239
7.235
7.225
7.220
7.206
7.198
7.182
7.175
5.470
CF3
N=N
N
Ph
CF3
4.91
2.00
0.97
1.02
2.00
10
8
6
4
2
0
PPM

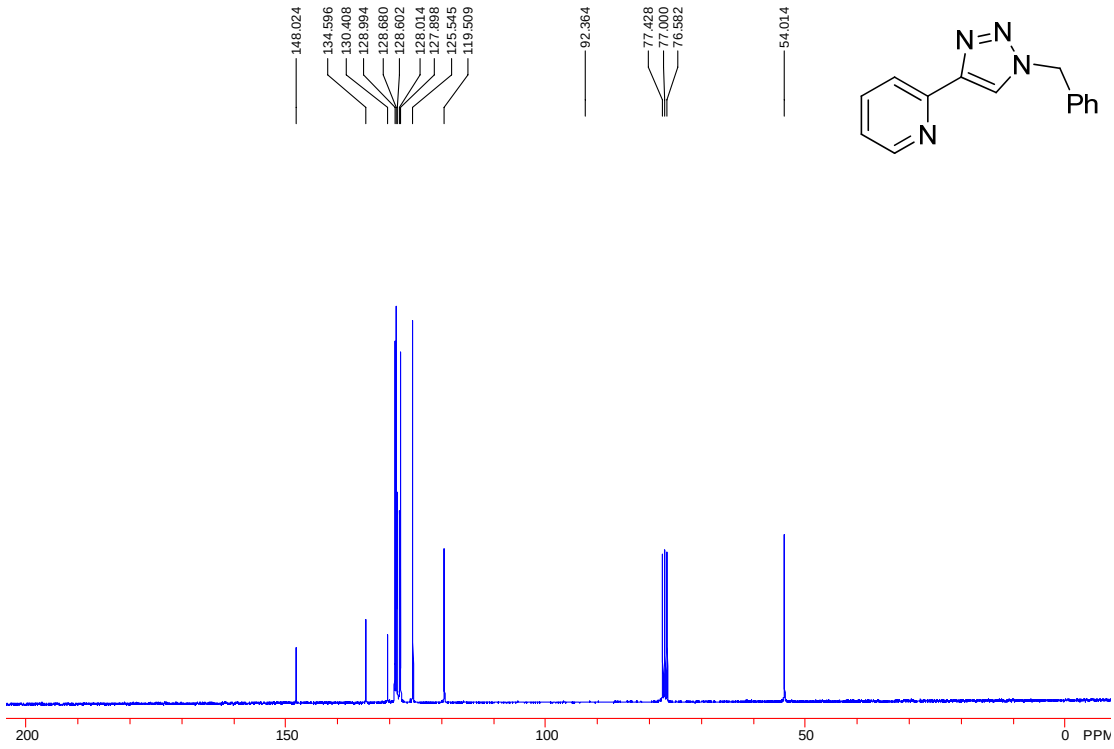

145.357
134.109
132.681
132.255
131.820
131.373
128.538
128.013
128.896
124.923
129.143
125.426
125.464
120.719
121.381
121.308
117.694
77.419
77.000
76.567
54.348
CF3
N=N
N
Ph
CF3
200
150
100
50
0
PPM

(69l)

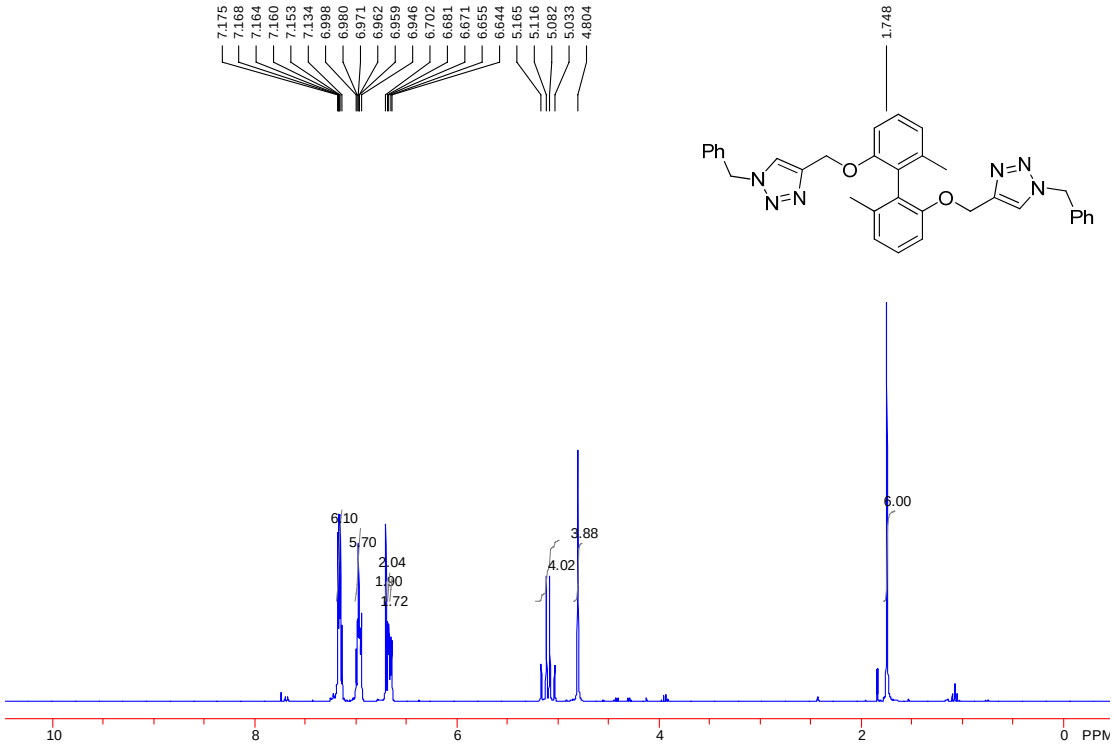


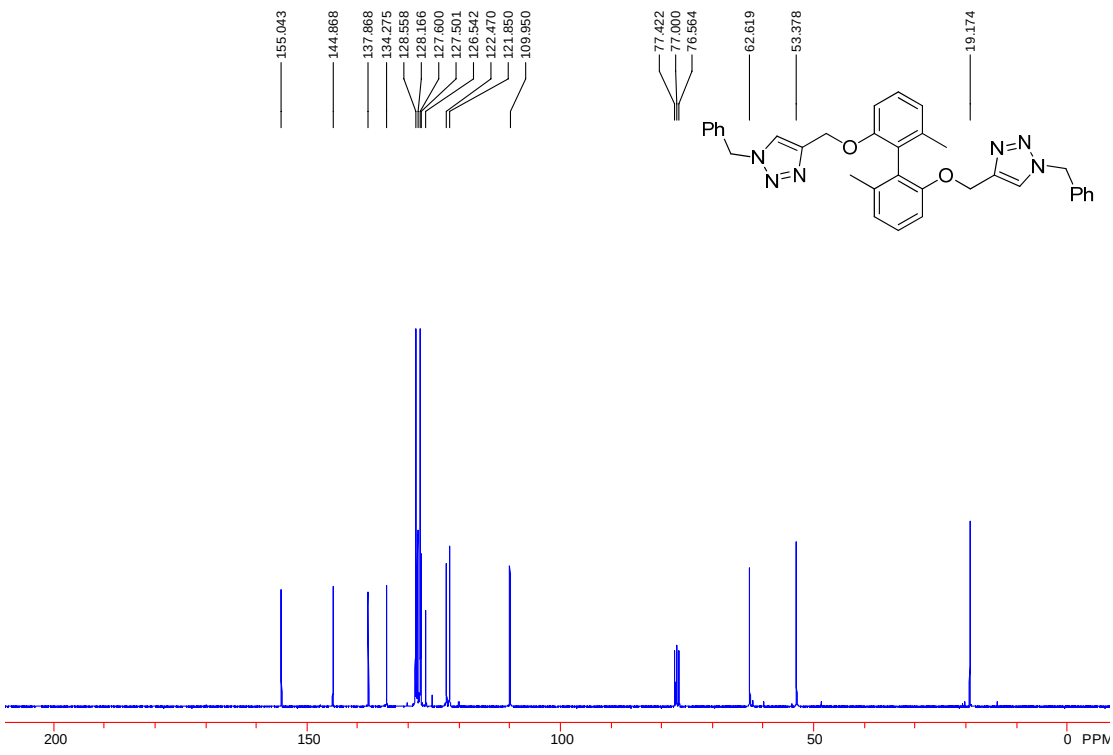
(69m)


7.732
7.726
7.706
7.702
7.698
7.596
7.302
7.298
7.290
7.282
7.277
7.273
7.266
7.255
7.240
7.236
7.214
7.205
7.192
5.450
N
N
N
Ph
7.02
1.96
0.97
2.00
10
8
6
4
2
0 PPM

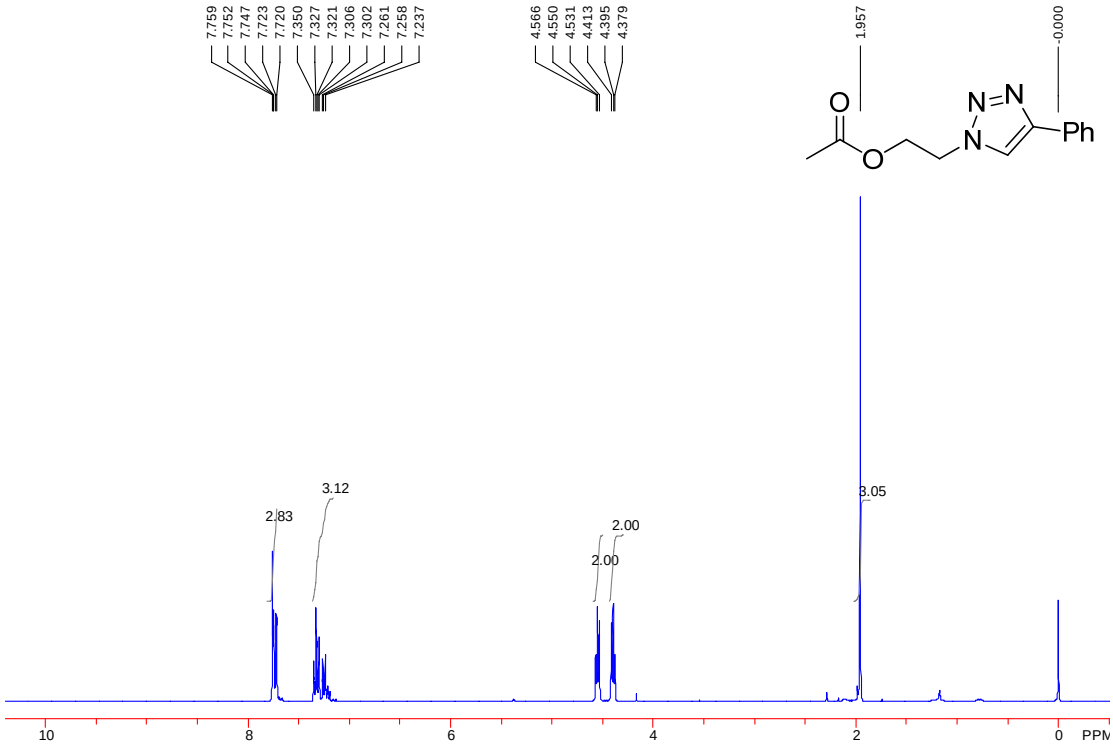

148.024
134.596
130.408
128.994
128.680
128.602
128.014
127.898
125.545
119.509
92.364
77.428
77.000
76.582
54.014
N
N
N
Ph
200
150
100
50
0 PPM

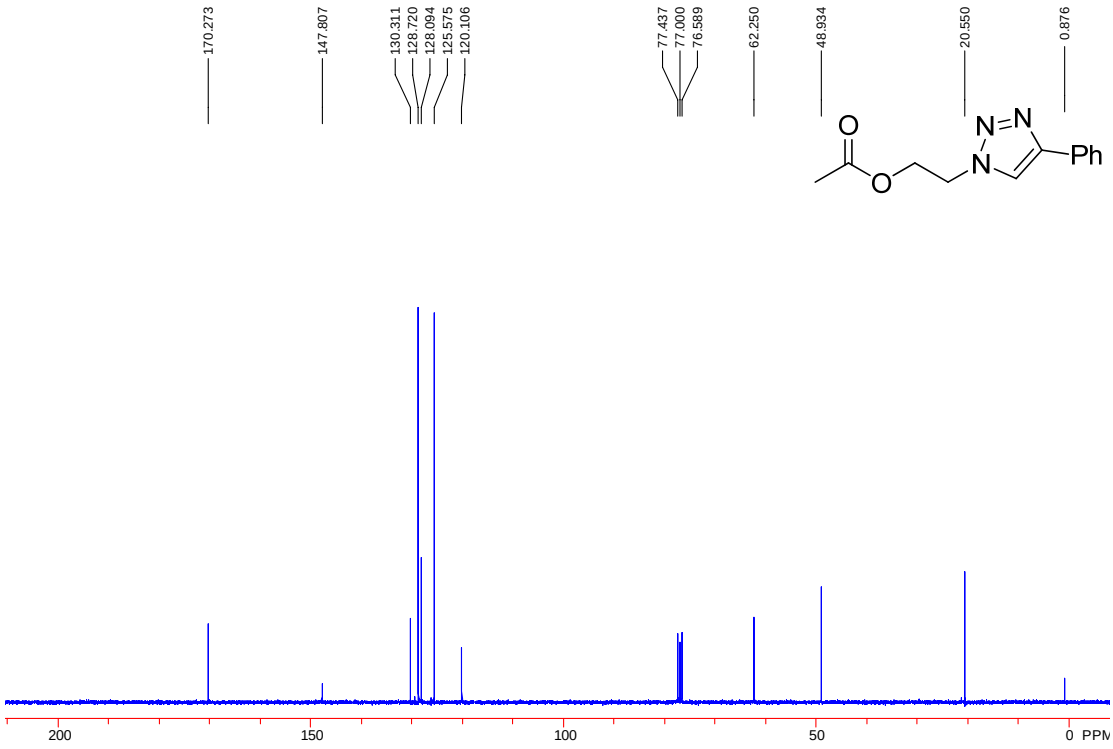
(69n)


7.175
7.168
7.164
7.160
7.153
7.134
6.998
6.980
6.971
6.962
6.959
6.946
6.702
6.681
6.671
6.655
6.644
5.165
5.116
5.082
5.033
4.804
1.748
Ph
N
N=N
O
O
N=N
N
Ph
6.10
5.70
2.04
1.90
1.72
3.88
4.02
6.00
10
8
6
4
2
0
PPM

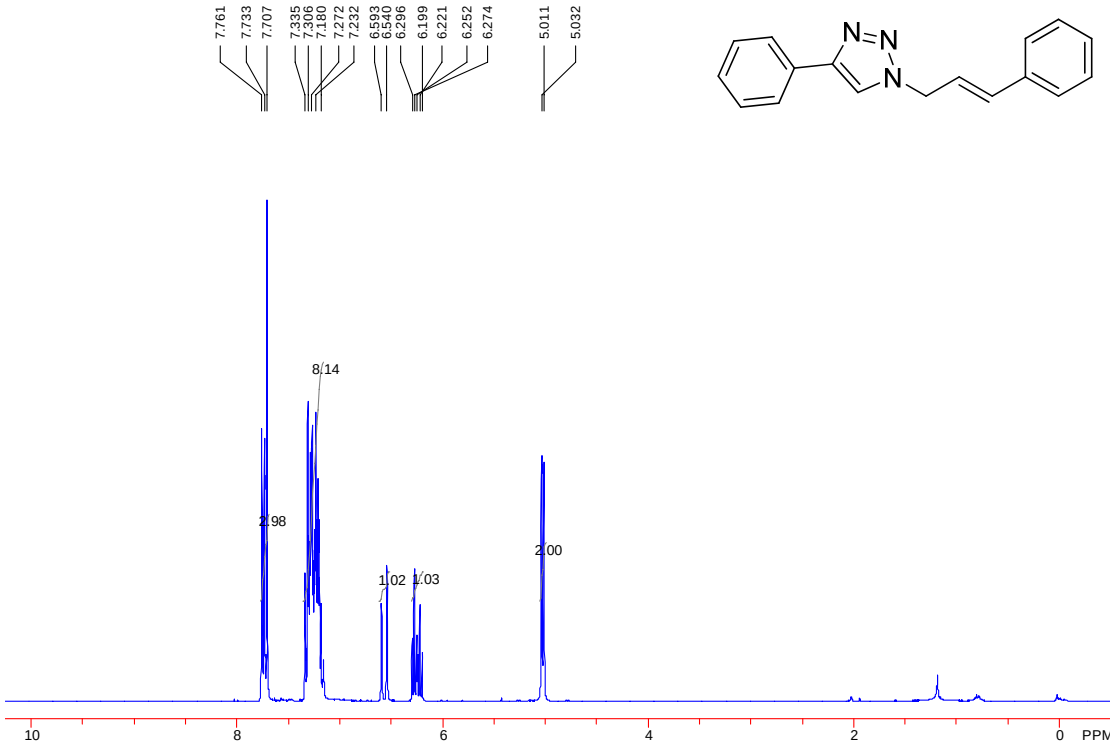

155.043
144.868
137.868
134.275
128.558
128.166
127.600
127.501
126.542
122.470
121.850
109.950
77.422
77.000
76.564
62.619
53.378
19.174
Ph
N
N=N
O
O
N=N
N
Ph
200
150
100
50
0
PPM

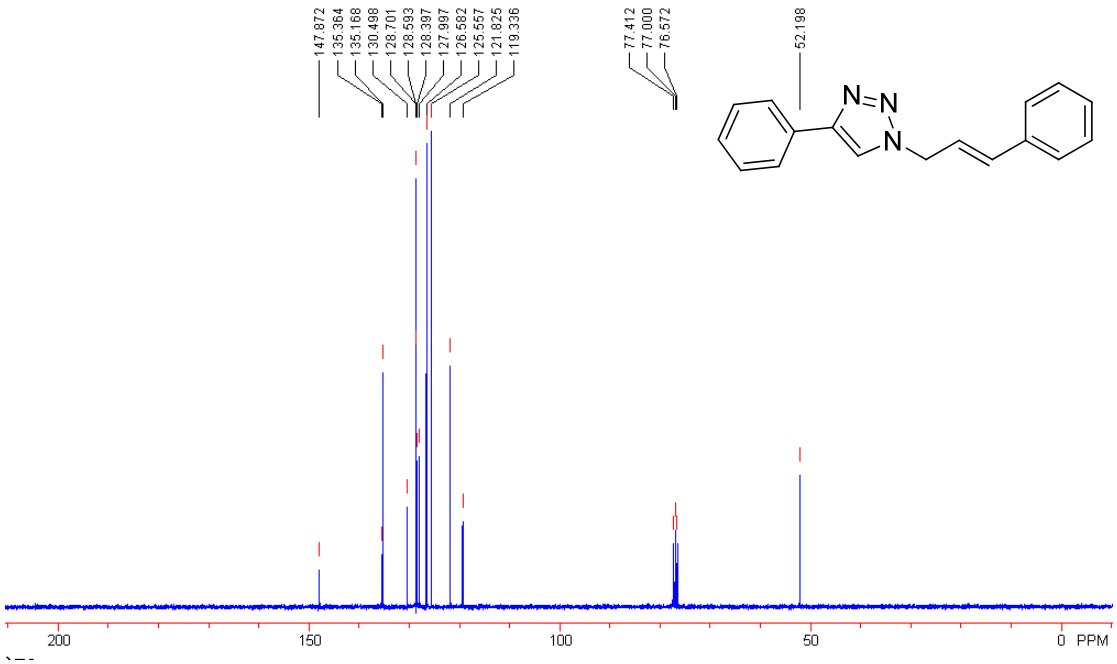
(69o)


7.759
7.752
7.747
7.723
7.720
7.350
7.327
7.321
7.306
7.302
7.261
7.258
7.237
4.566
4.550
4.531
4.413
4.395
4.379
1.957
-0.000
O
O
N=N
N
Ph
2.83
3.12
2.00
2.00
3.05
10
8
6
4
2
0
PPM

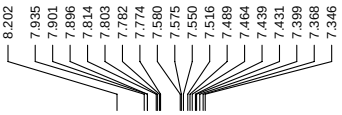

170.273
147.807
130.311
128.720
128.094
125.575
120.106
77.437
77.000
76.589
62.250
48.934
20.550
0.876
O
O
N=N
N
Ph
200
150
100
50
0
PPM

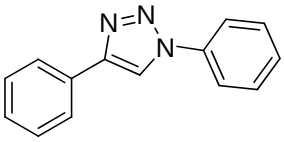
(69p)

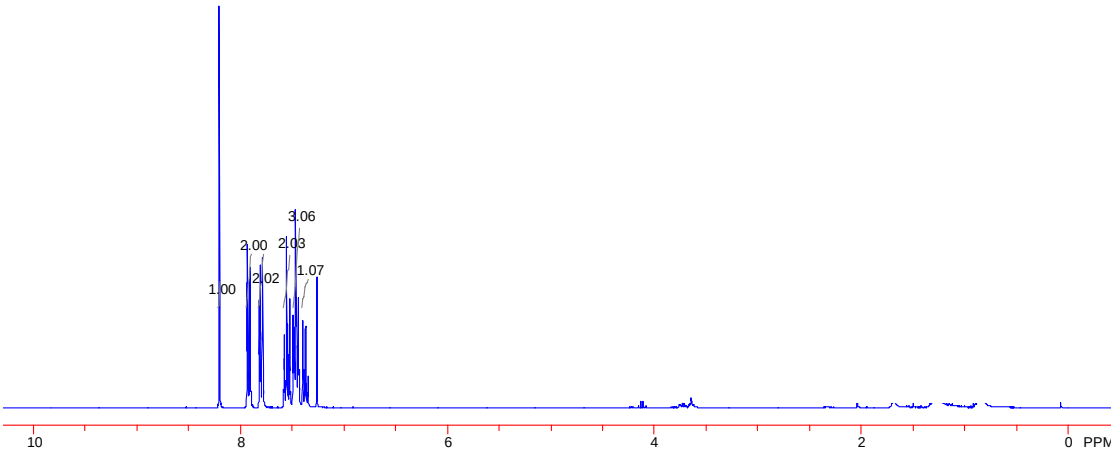

7.761
7.733
7.707
7.335
7.306
7.180
7.272
7.232
6.593
6.540
6.296
6.199
6.221
6.252
6.274
5.011
5.032
N
N
N
8.14
2.98
2.00
1.02
1.03
10
8
6
4
2
0
PPM

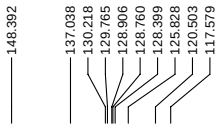

147.872
135.364
135.168
130.498
128.701
128.593
128.397
127.997
126.582
125.557
121.825
119.336
77.412
77.000
76.572
52.198
N
N
N
200
150
100
50
0
PPM

(69q)

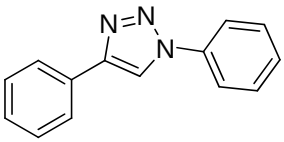

8.202
7.935
7.901
7.896
7.814
7.803
7.782
7.774
7.580
7.575
7.550
7.516
7.489
7.464
7.439
7.431
7.399
7.368
7.346

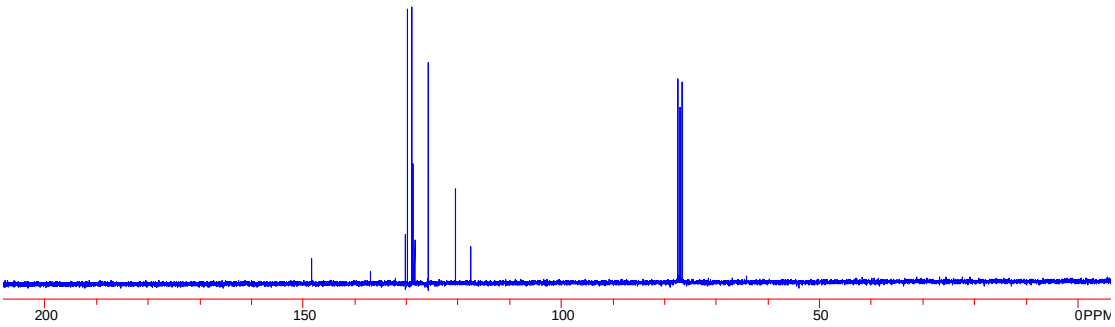

N
N
N


3.06
2.00
2.03
1.07
2.02
1.00
10
8
6
4
2
0 PPM

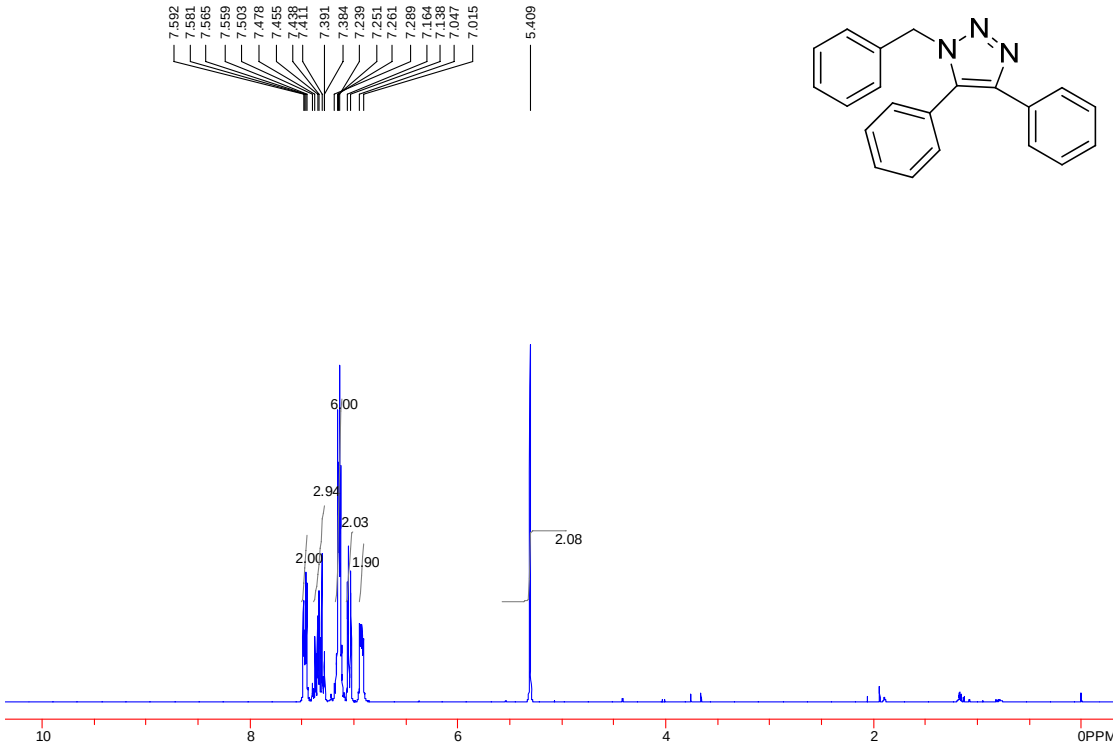

148.392
137.038
130.218
129.765
128.906
128.760
128.399
125.828
120.503
117.579

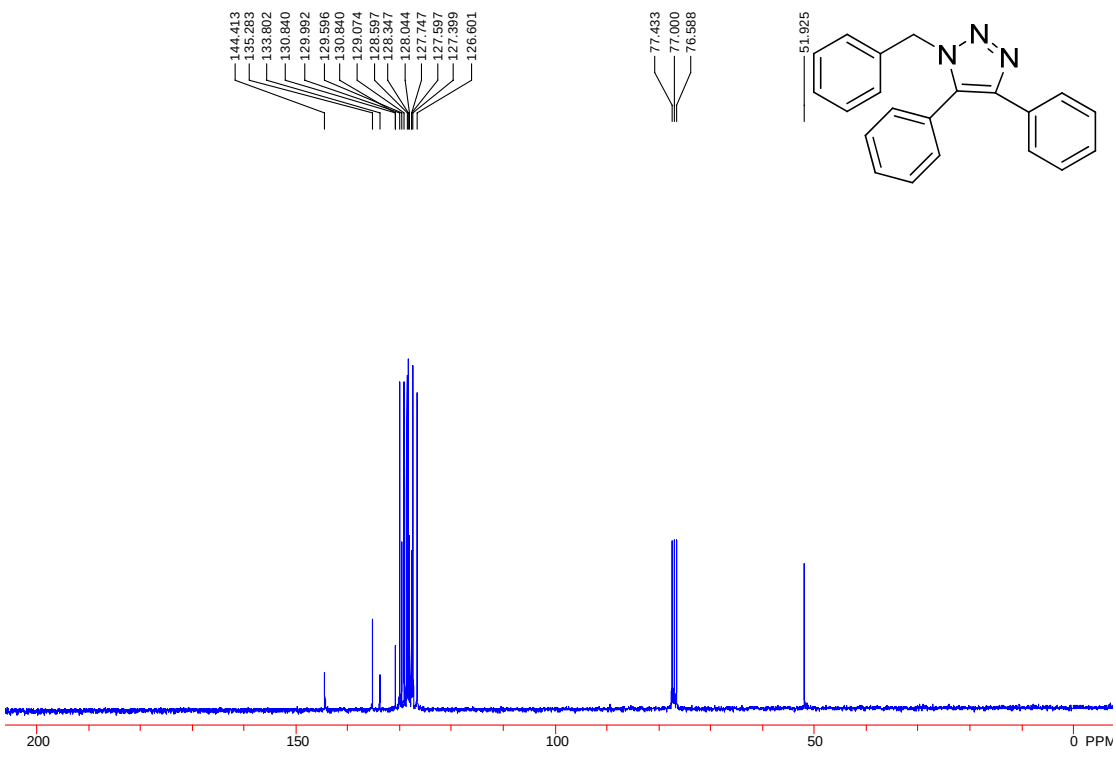

77.426
77.000
76.577


N
N
N

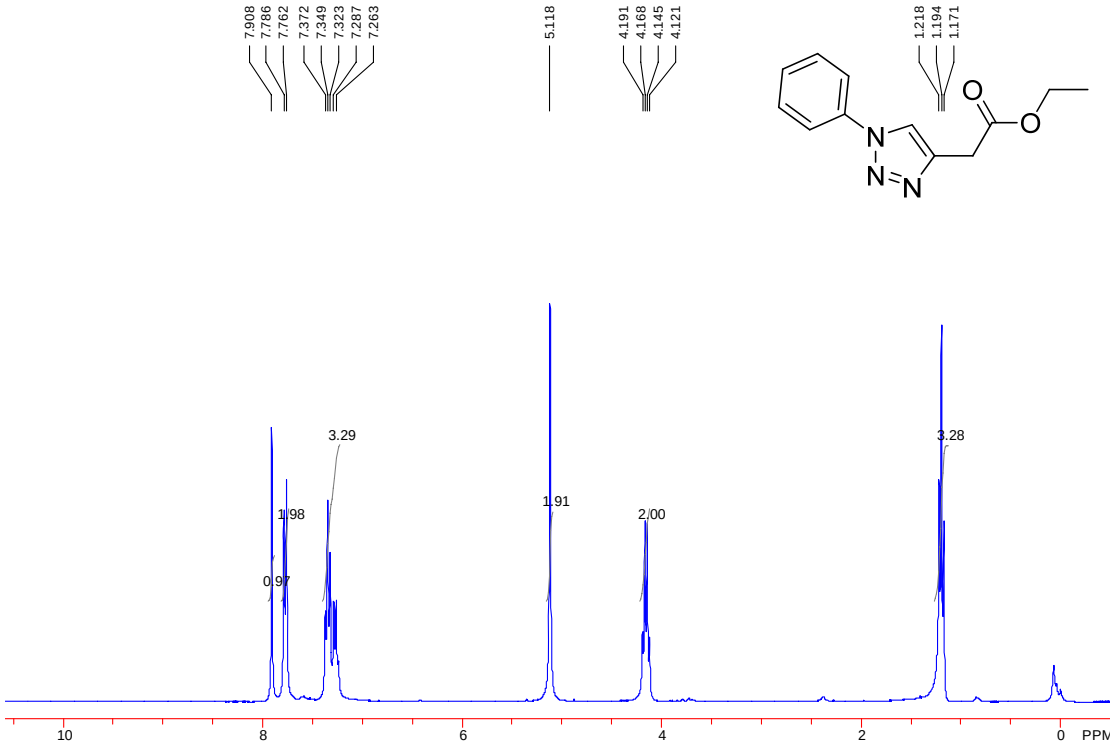

200
150
100
50
0PPM

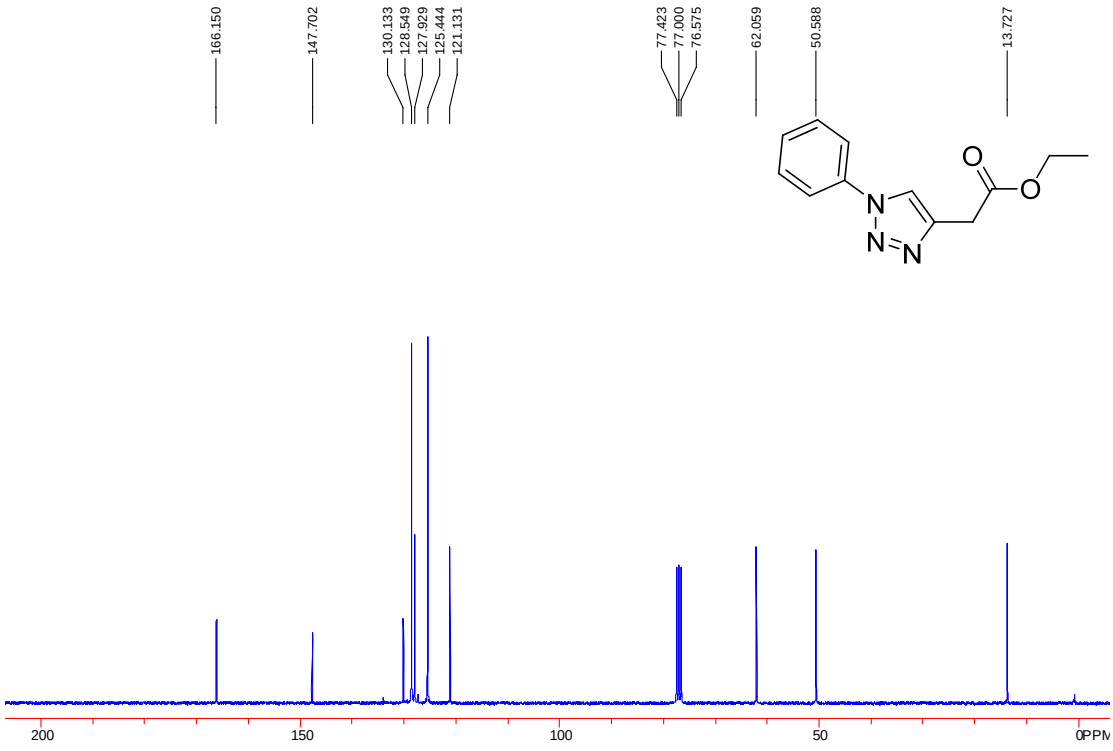
(69r)


7.592
7.581
7.565
7.559
7.503
7.478
7.455
7.438
7.411
7.391
7.384
7.239
7.251
7.261
7.289
7.164
7.138
7.047
7.015
5.409
N
N
N
6.00
2.94
2.03
2.00
1.90
2.08
10
8
6
4
2
0PPM

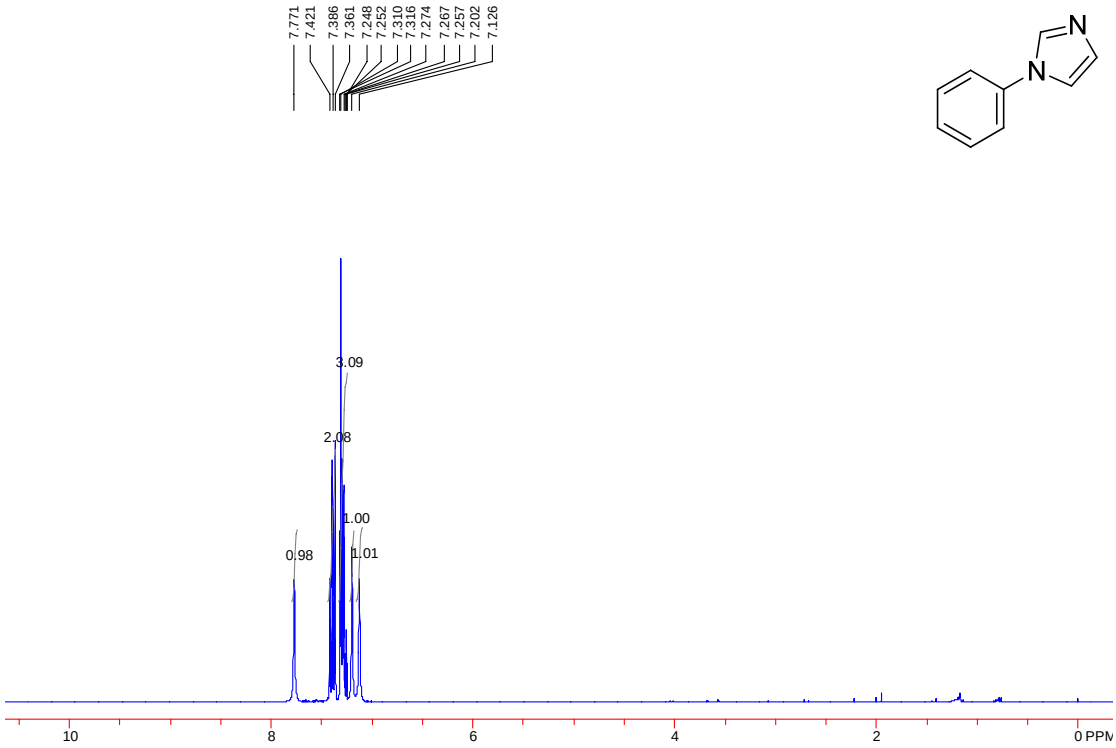

144.413
135.283
133.802
130.840
129.992
129.596
130.840
129.074
128.597
128.347
128.044
127.747
127.597
127.399
126.601
77.433
77.000
76.588
51.925
N
N
N
200
150
100
50
0 PPM

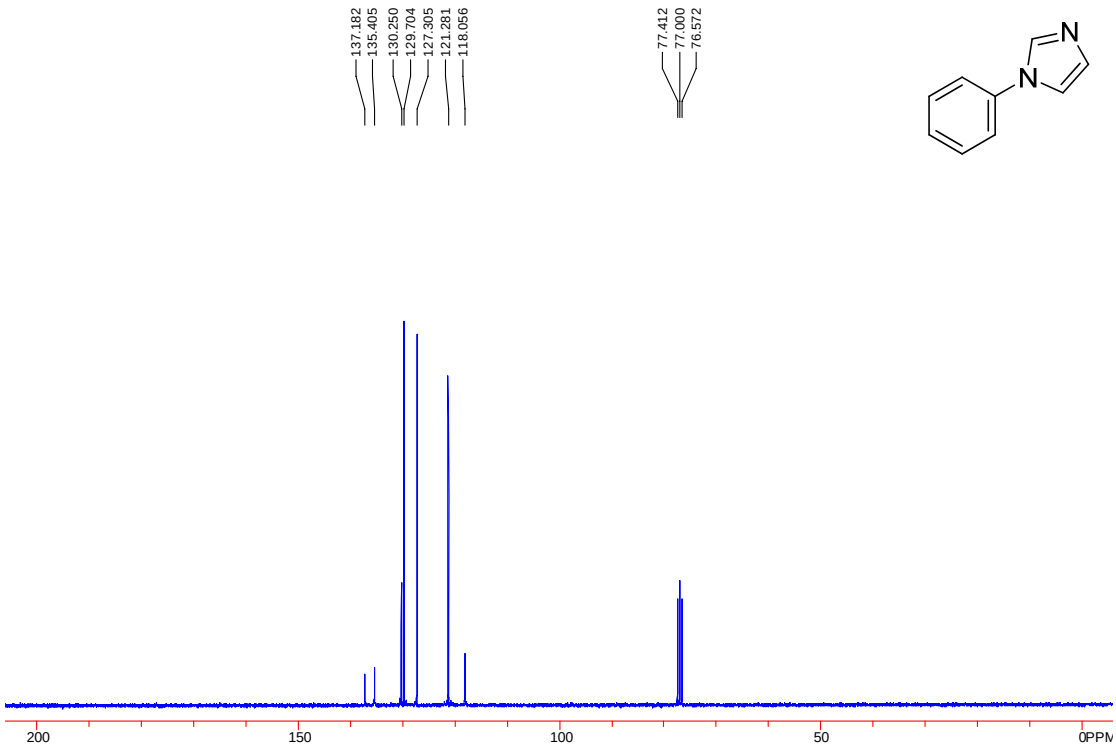
(69s)


7.908
7.786
7.762
7.372
7.349
7.323
7.287
7.263
5.118
4.191
4.168
4.145
4.121
1.218
1.194
1.171
O
O
N
N
N
3.29
3.28
1.98
1.91
2.00
0.97
10
8
6
4
2
0
PPM

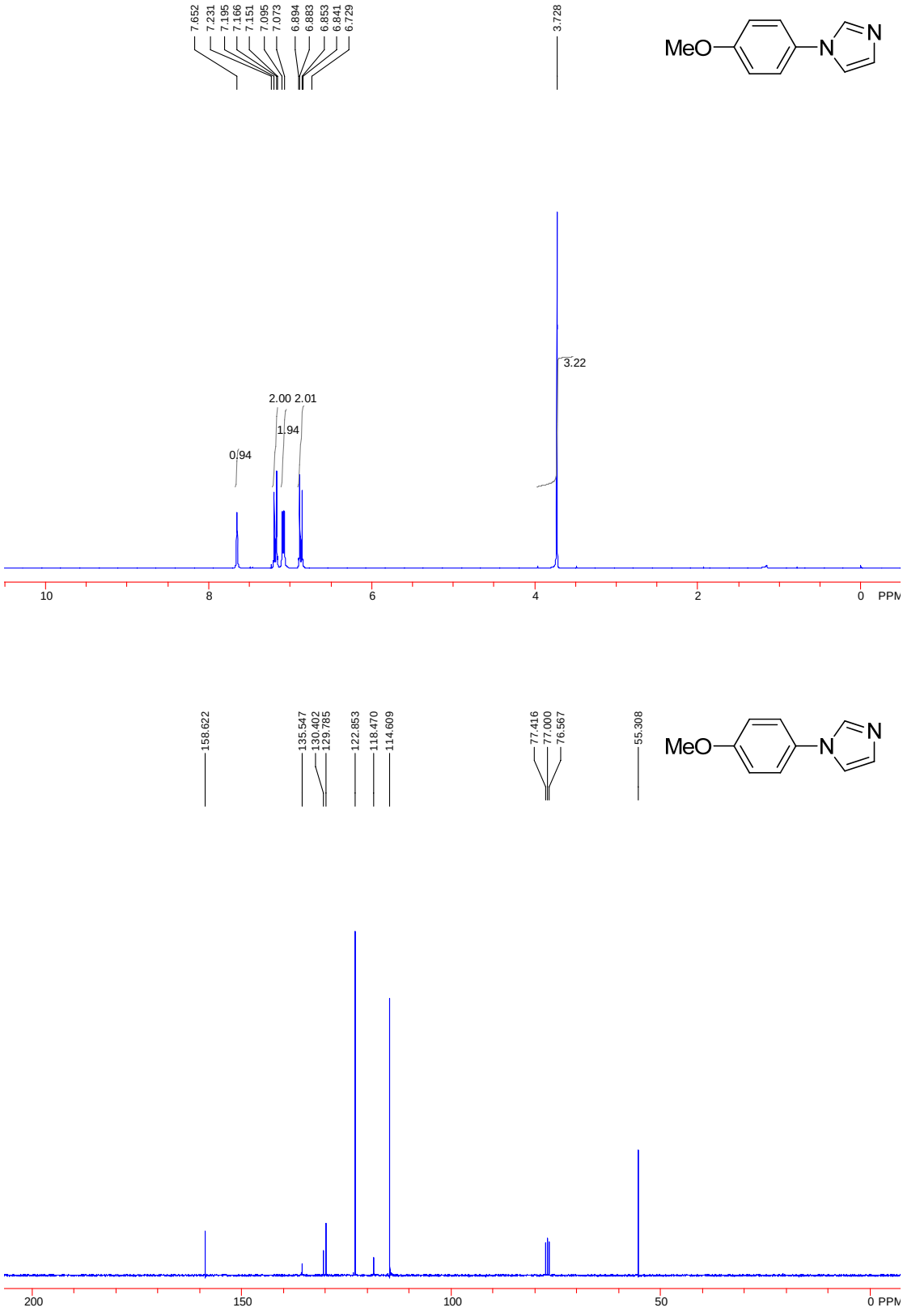

166.150
147.702
130.133
128.549
127.929
125.444
121.131
77.423
77.000
76.575
62.059
50.588
13.727
O
O
N
N
N
200
150
100
50
0
PPM

(87a)

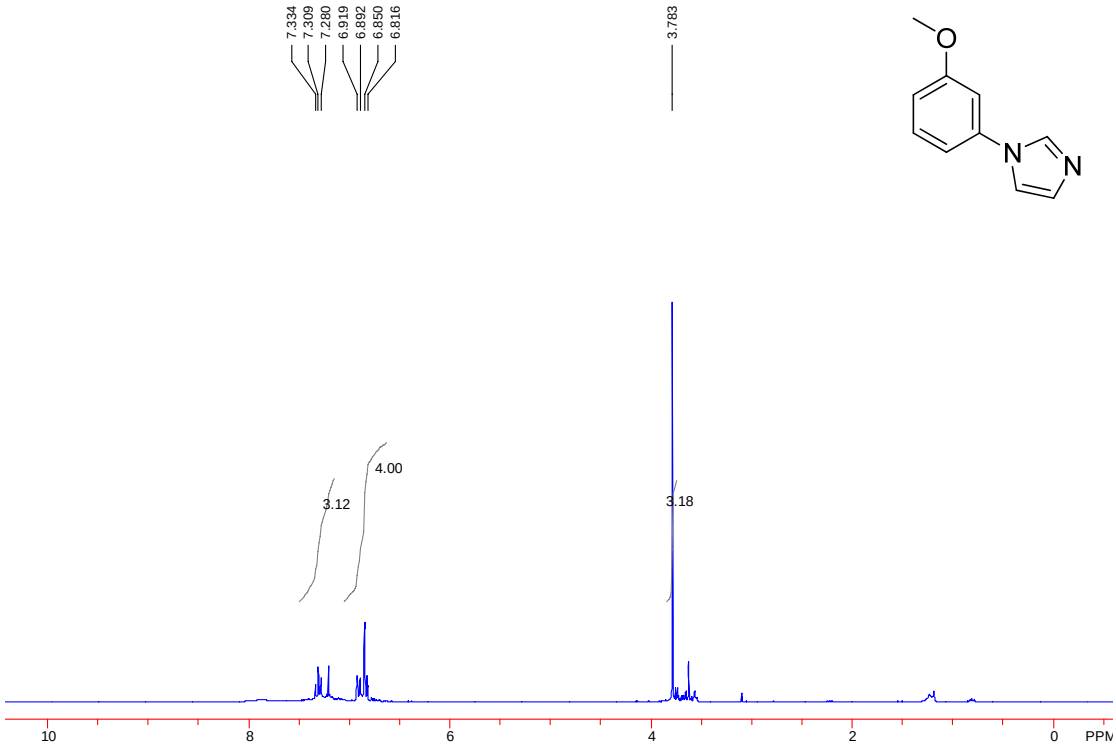

7.771
7.421
7.386
7.361
7.248
7.252
7.310
7.316
7.274
7.267
7.257
7.202
7.126
N
N
3.09
2.08
1.00
0.98
1.01
10
8
6
4
2
0 PPM


137.182
135.405
130.250
129.704
127.305
121.281
118.056
77.412
77.000
76.572
N
N
200
150
100
50
0PPM

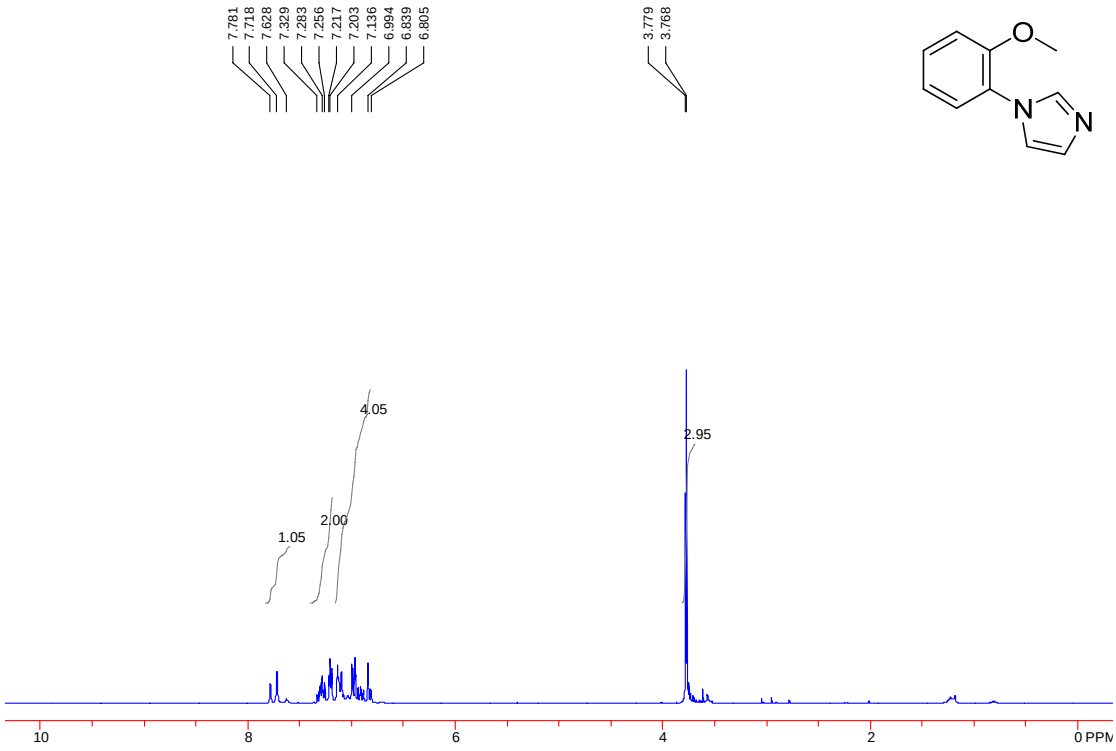
(87b)


7.652
7.231
7.195
7.166
7.151
7.095
7.073
6.894
6.883
6.853
6.841
6.729
3.728
MeO
N
N
3.22
2.00 2.01
1.94
0.94
10
8
6
4
2
0 PPM
158.622
135.547
130.402
129.785
122.853
118.470
114.609
77.416
77.000
76.567
55.308
MeO
N
N
200
150
100
50
0 PPM

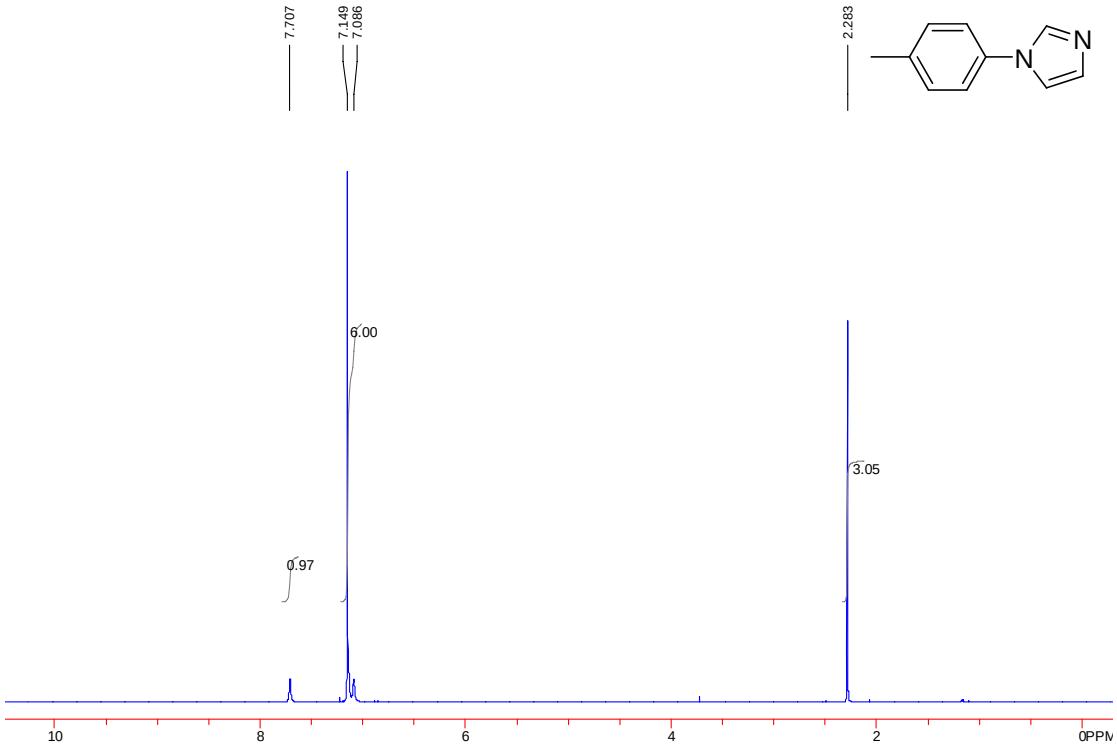
(87c)

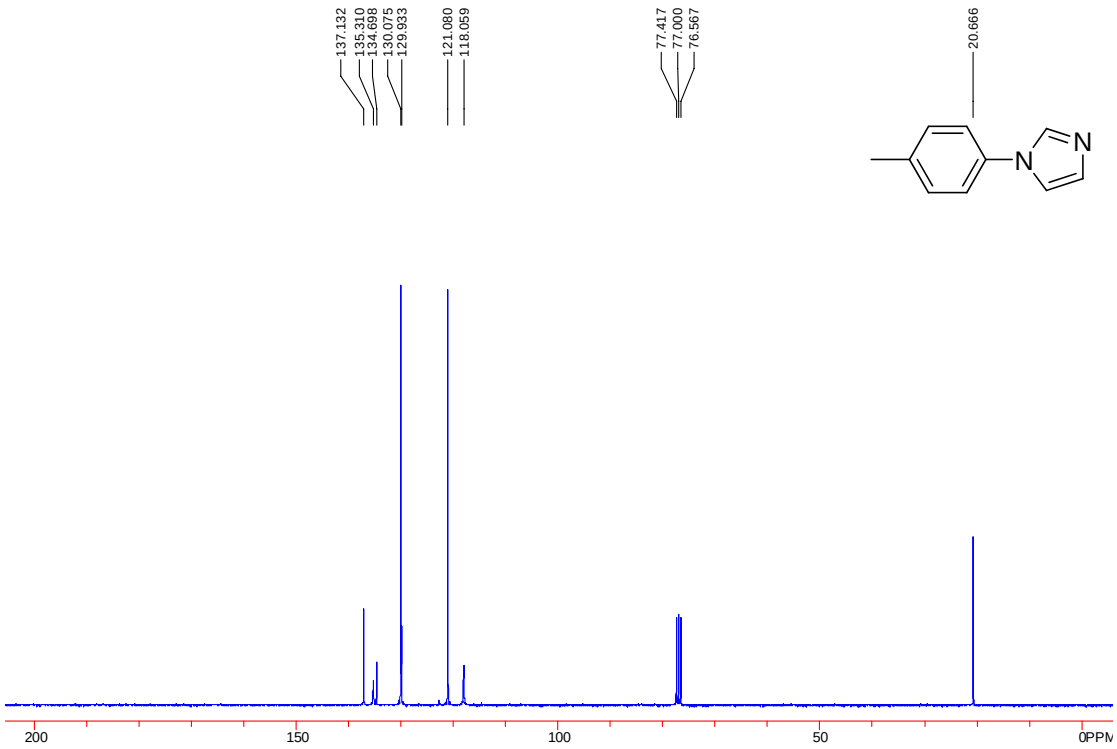

7.334
7.309
7.280
6.919
6.892
6.850
6.816
3.783
O
N
N
4.00
3.12
3.18
10
8
6
4
2
0
PPM

(87v)

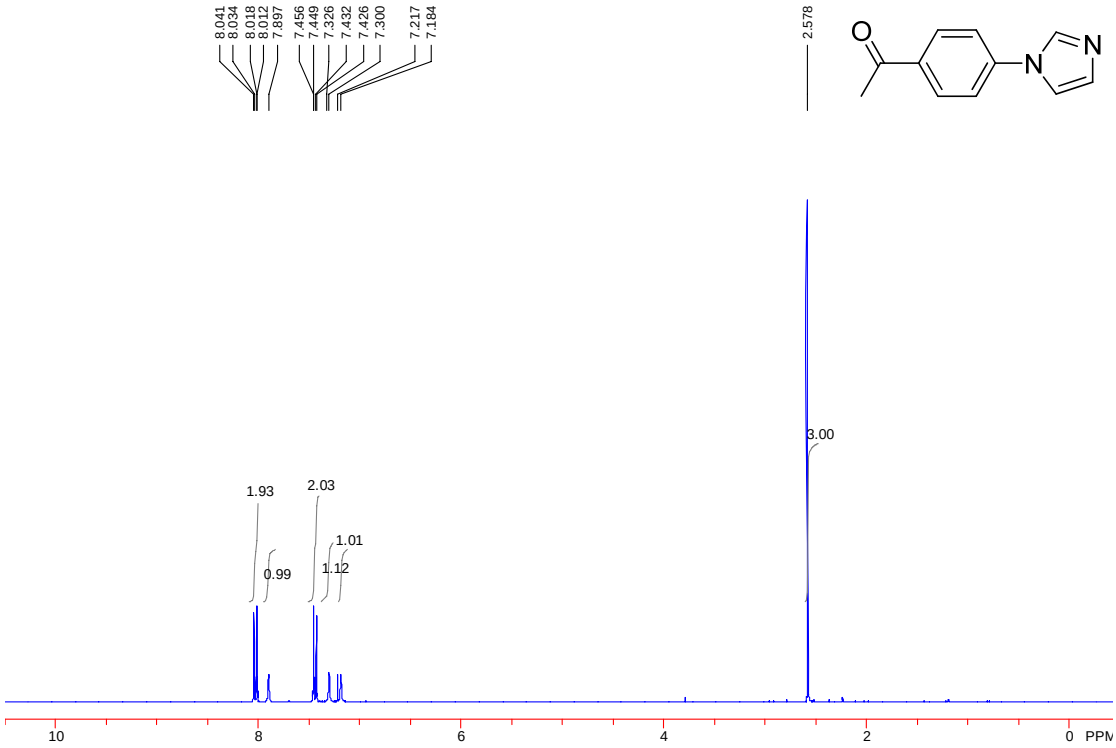

7.781
7.718
7.628
7.329
7.283
7.256
7.217
7.203
7.136
6.994
6.839
6.805
3.779
3.768
O
N
N
4.05
2.95
2.00
1.05
10
8
6
4
2
0 PPM

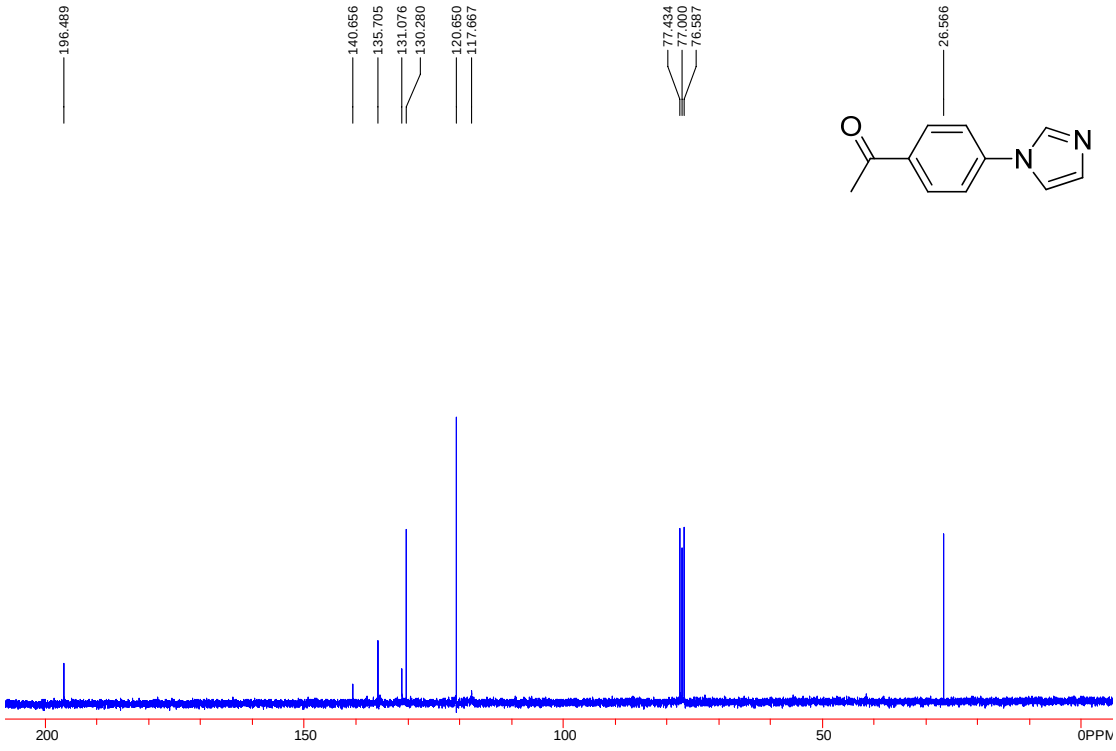
(87d)


7.707
7.149
7.086
2.283
N
N
6.00
3.05
0.97
10
8
6
4
2
0PPM


137.132
135.310
134.698
130.075
129.933
121.080
118.059
77.417
77.000
76.567
20.666
N
N
200
150
100
50
0PPM

(87e)


8.041
8.034
8.018
8.012
7.897
7.456
7.449
7.326
7.432
7.426
7.300
7.217
7.184
2.578
O
N
N
3.00
1.93
2.03
1.01
0.99
1.12
10
8
6
4
2
0
PPM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140.656
135.705
131.076
130.280
120.650
117.667
77.434
77.000
76.587
26.566
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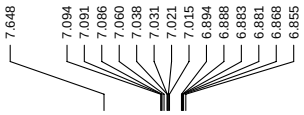
N
N
200
150
100
50
0
PPM

(87f)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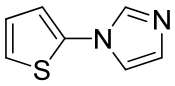
7.094
7.091
7.086
7.060
7.038
7.031
7.021
7.015
6.894
6.888
6.883
6.881
6.868
6.855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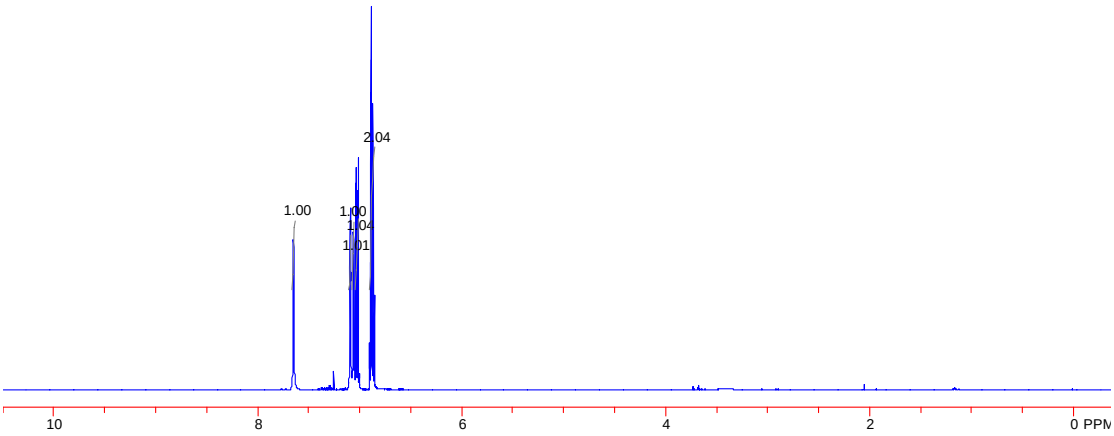
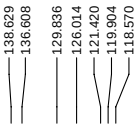
N
S


2.04
1.00
1.00
1.04
1.01
10
8
6
4
2
0 PPM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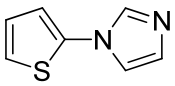
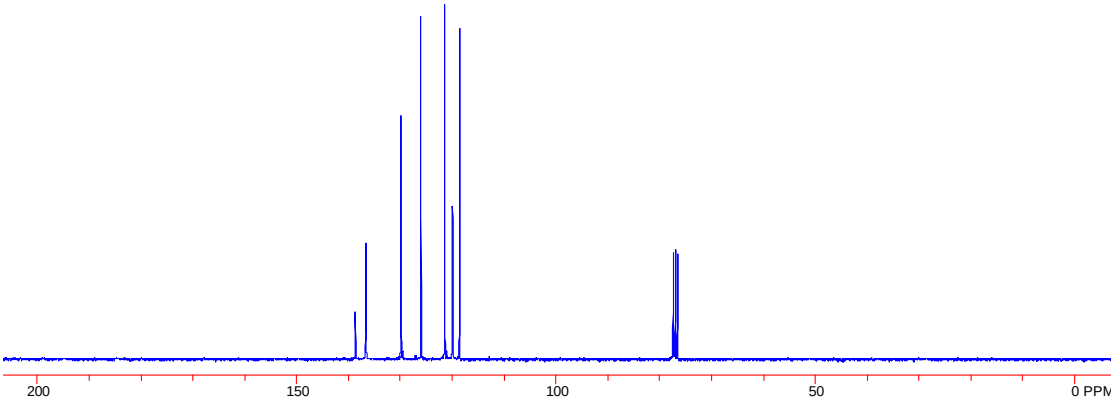
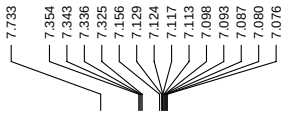
129.836
126.014
121.420
119.904
118.570


77.416
77.000
76.567


N
N
S


200
150
100
50
0 PPM

(87g)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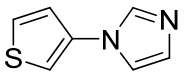
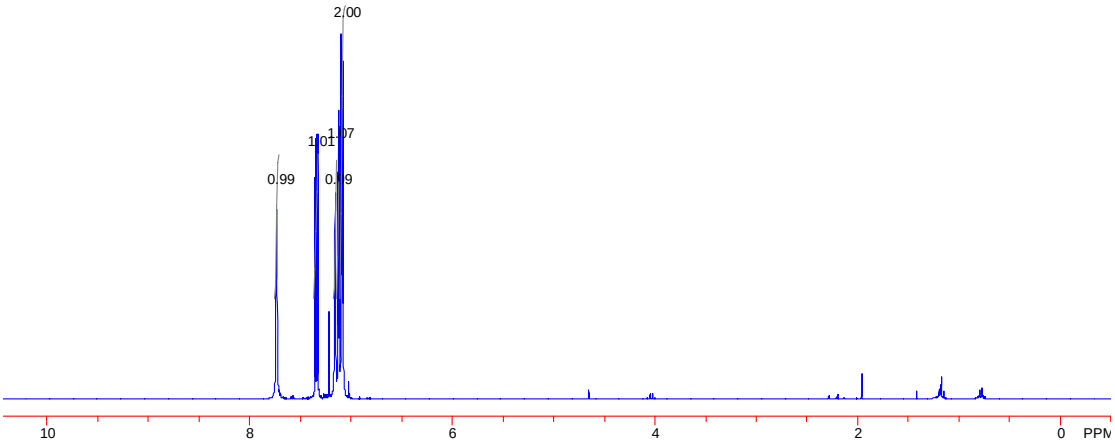
7.354
7.343
7.336
7.325
7.156
7.129
7.124
7.117
7.113
7.098
7.093
7.087
7.080
7.076


S
N
N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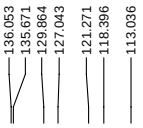
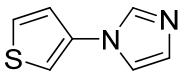
1.01
1.07
0.99
0.99
10
8
6
4
2
0
PPM


136.053
135.671
129.864
127.043
121.271
118.396
113.036


77.424
77.000
76.577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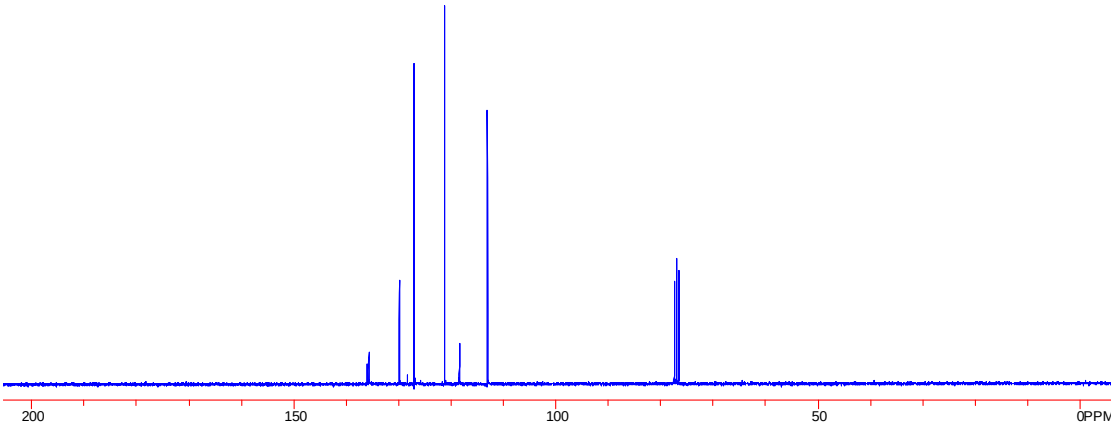
N
N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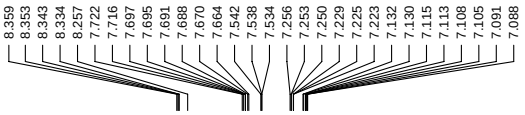
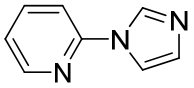
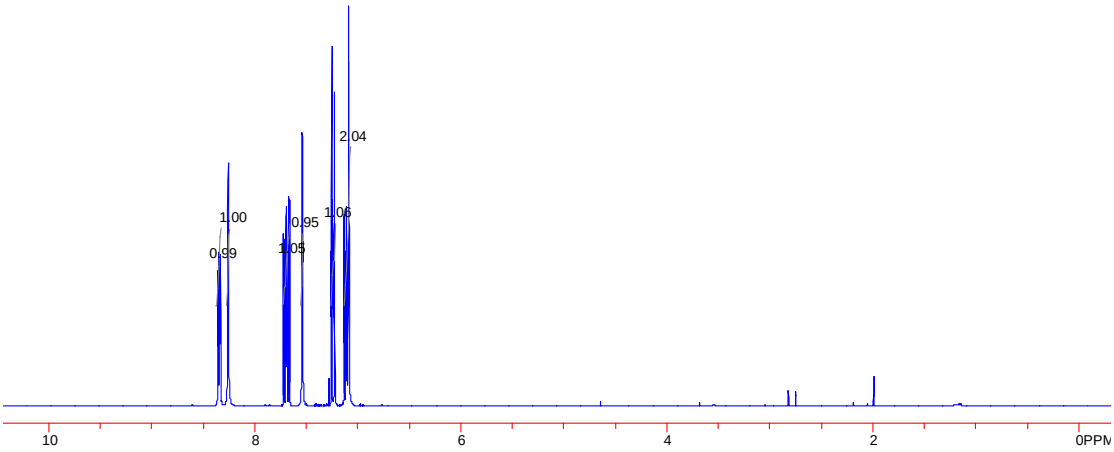
150
100
50
0PPM

(87h)


8.359
8.353
8.343
8.334
8.257
7.722
7.716
7.697
7.695
7.691
7.688
7.670
7.664
7.542
7.538
7.534
7.256
7.253
7.250
7.229
7.225
7.223
7.132
7.130
7.115
7.113
7.108
7.105
7.091
7.088

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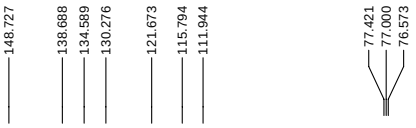
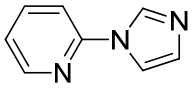
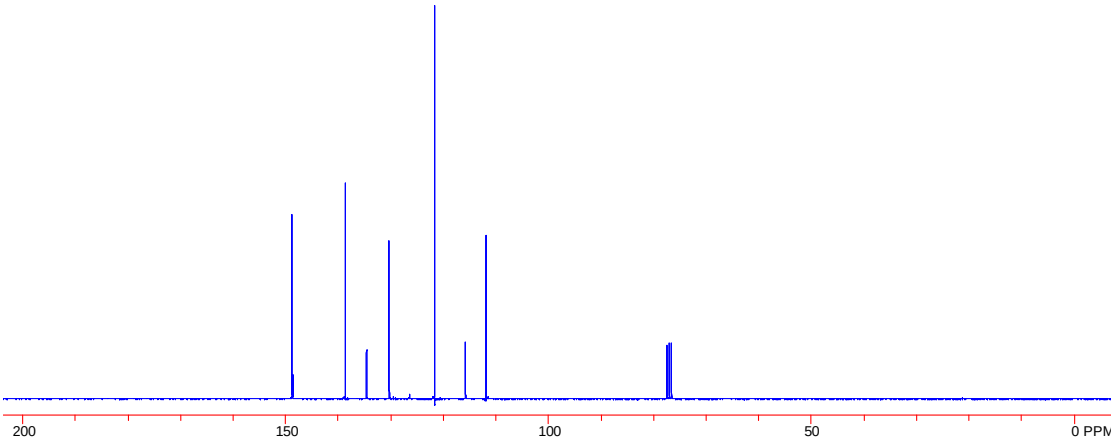
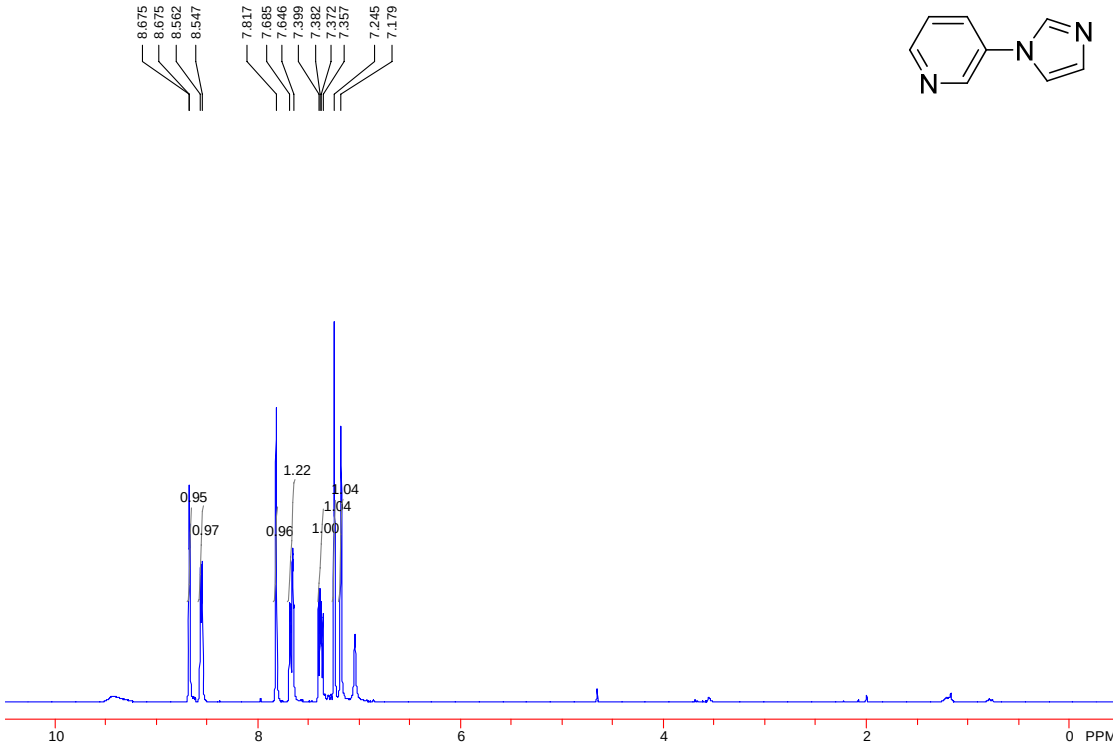
0.99
0.95
1.05
1.06
2.04
10
8
6
4
2
0PPM

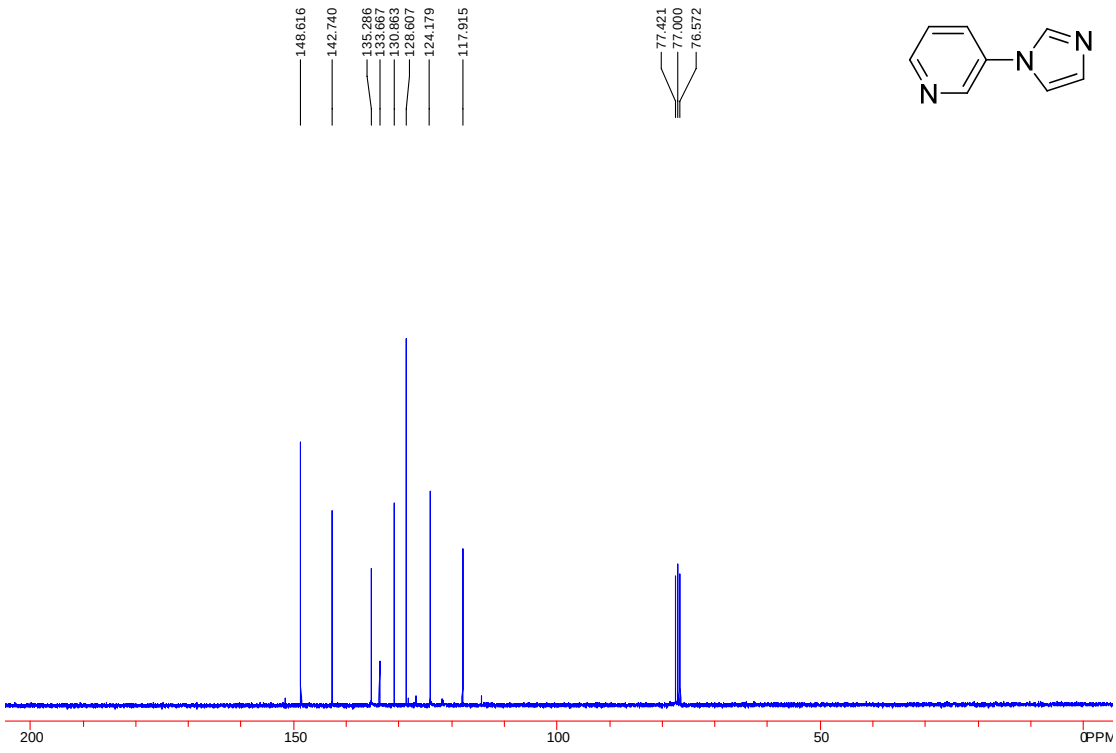

148.727
138.688
134.589
130.276
121.673
115.794
111.944
77.421
77.000
76.573




200
150
100
50
0 PPM

(87i)


8.675
8.675
8.562
8.547
7.817
7.685
7.646
7.399
7.382
7.372
7.357
7.245
7.179
N
N
N
0.95
0.97
0.96
1.22
1.00
1.04
1.04
10
8
6
4
2
0 PPM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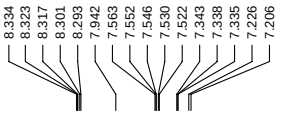
142.740
135.286
133.667
130.863
128.607
124.179
117.915
77.421
77.000
76.572
N
N
N
200
150
100
50
0PPM

(87j)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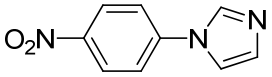
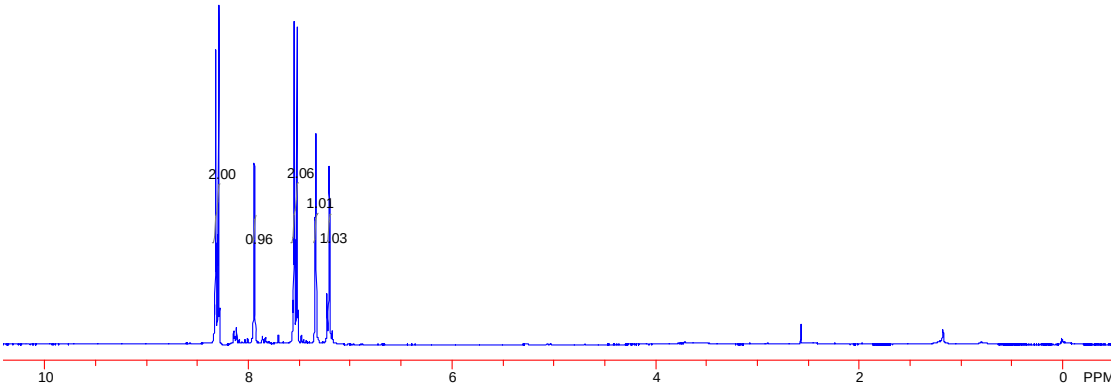
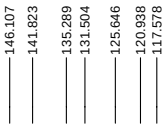
8.317
8.301
8.293
7.942
7.563
7.552
7.546
7.530
7.522
7.343
7.338
7.335
7.226
7.206


O2N
N
N


2.00
2.06
1.01
0.96
1.03
10
8
6
4
2
0
PPM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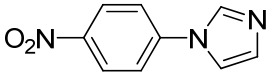
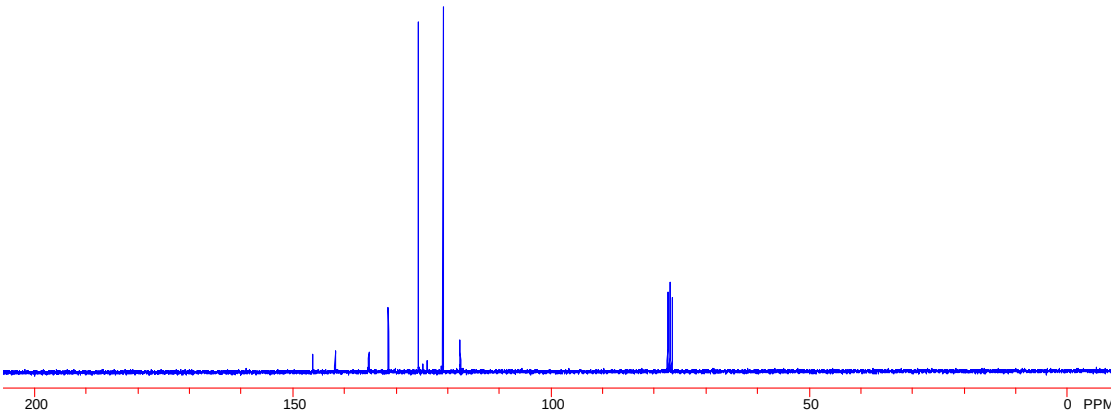
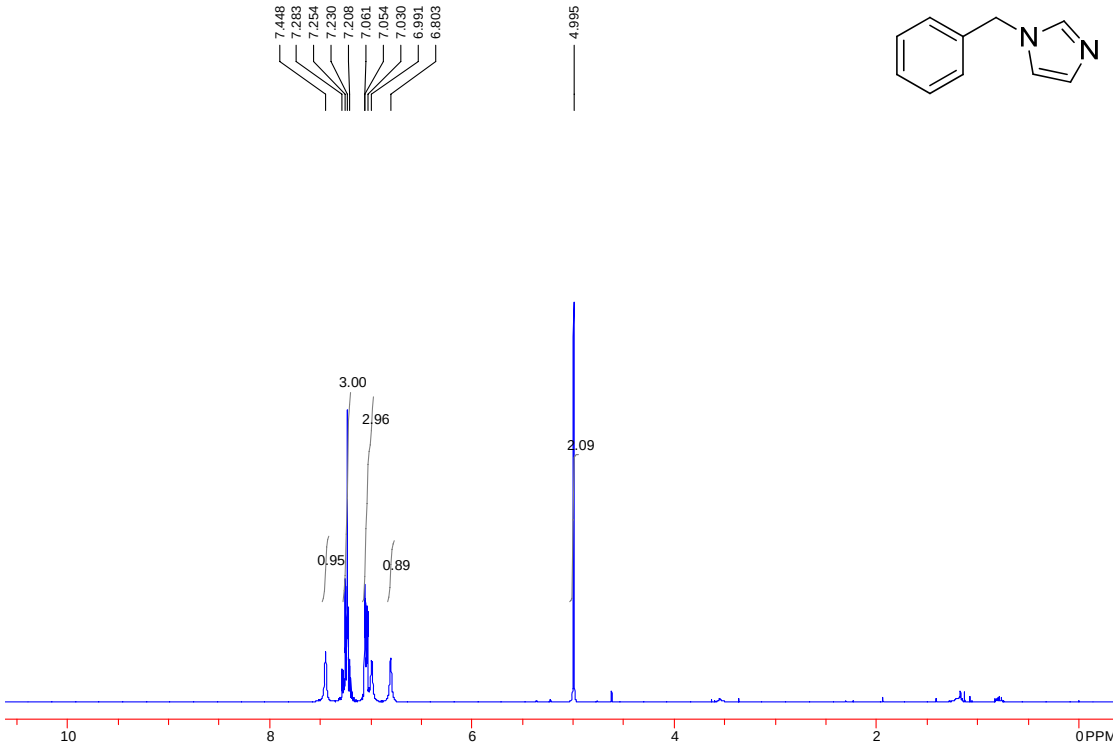
141.823
135.289
131.504
125.646
120.938
117.578


77.415
77.000
76.563


O2N
N
N


200
150
100
50
0
PPM

(87k)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7.254
7.230
7.208
7.061
7.054
7.030
6.991
6.803
4.995
N
N
3.00
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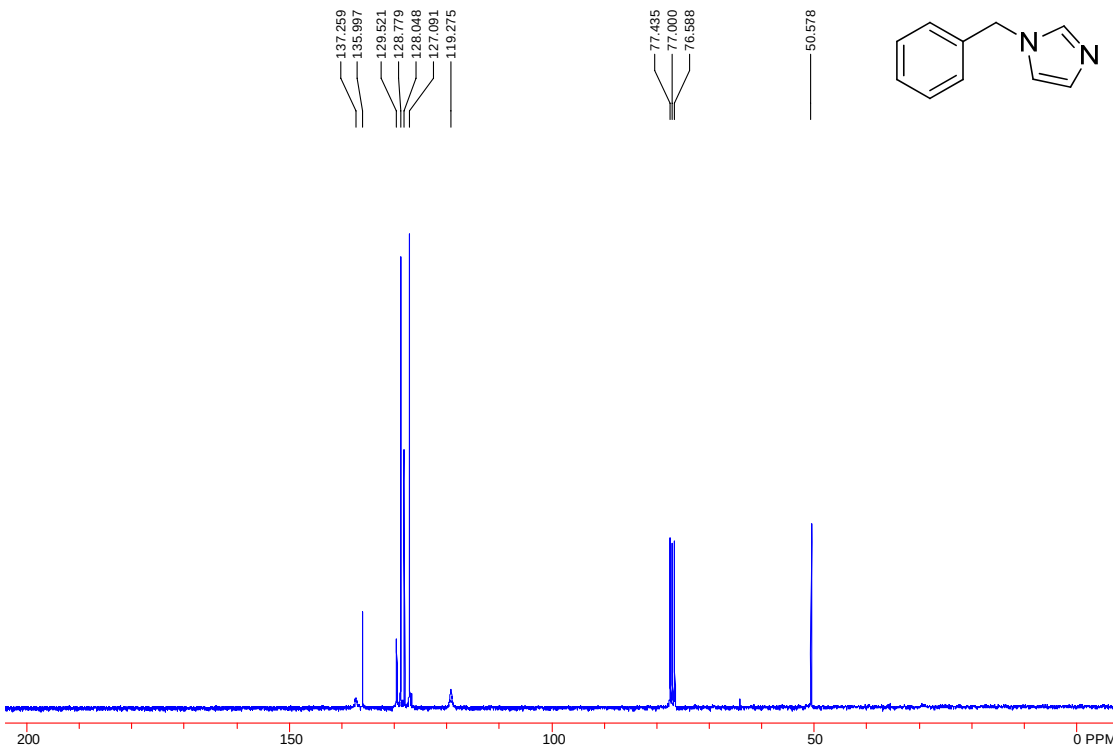
2.09
0.95
0.89
10
8
6
4
2
0 PPM


137.259
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129.521
128.779
128.048
127.091
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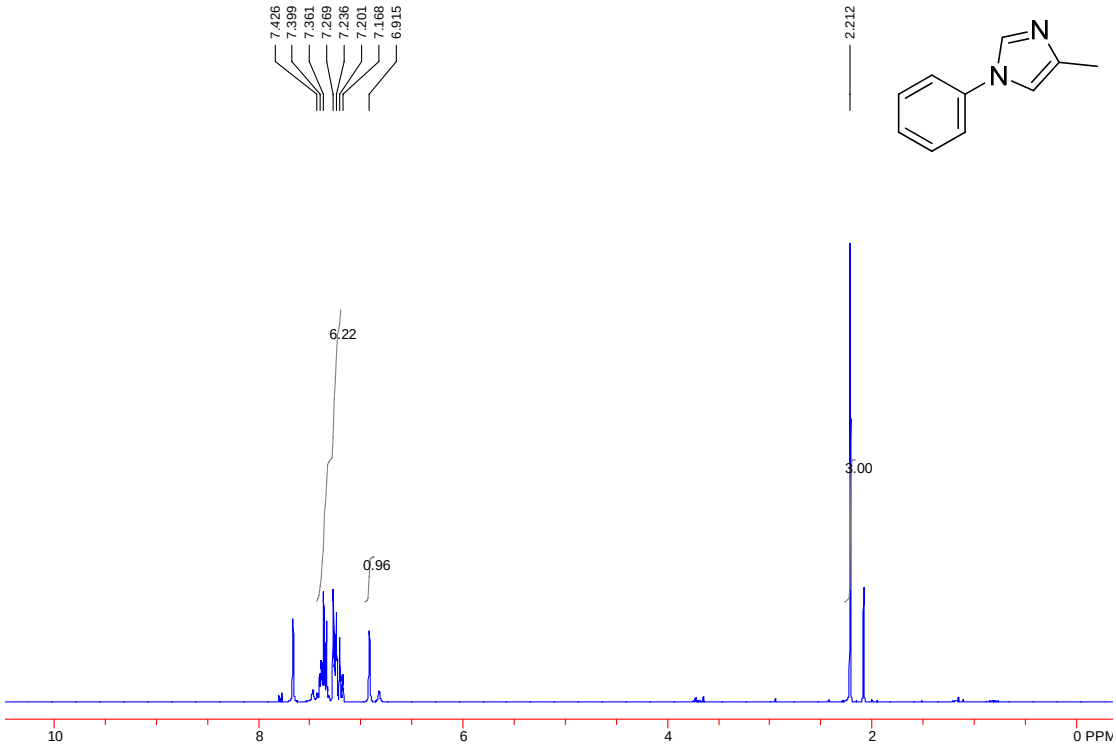
77.435
77.000
76.588
50.578
N
N
200
150
100
50
0 PPM

(87l)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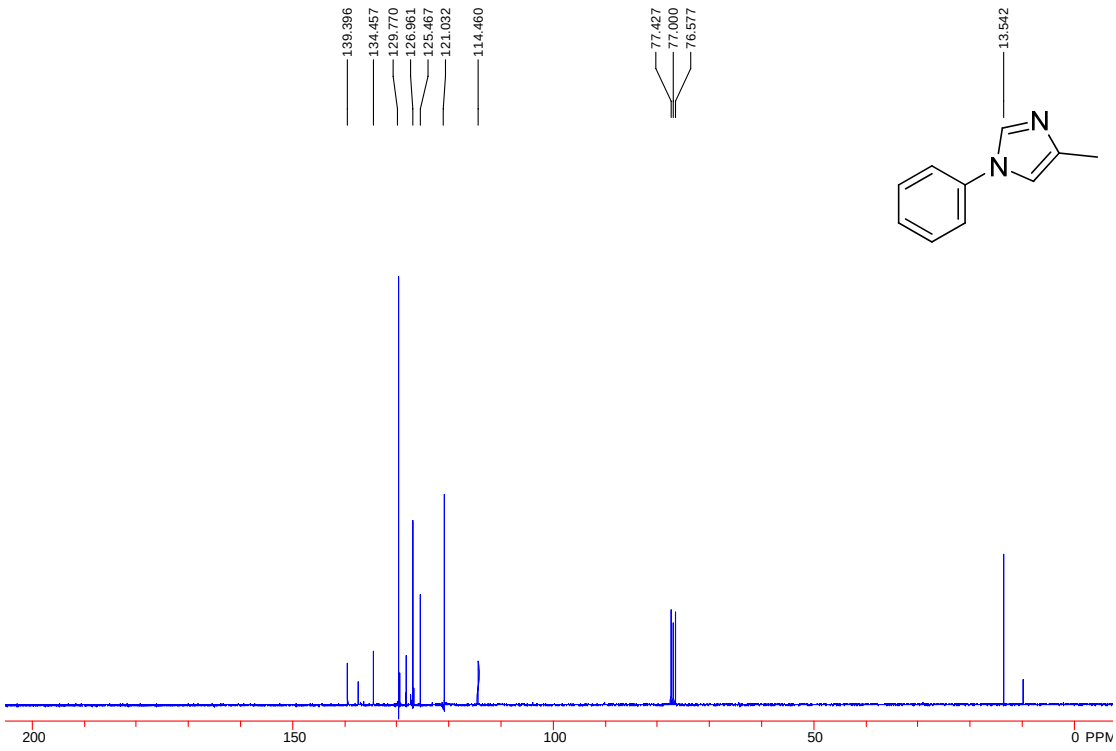
7.361
7.269
7.236
7.201
7.168
6.915
2.212
N
N
6.22
3.00
0.96
10
8
6
4
2
0 PPM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134.457
129.770
126.961
125.467
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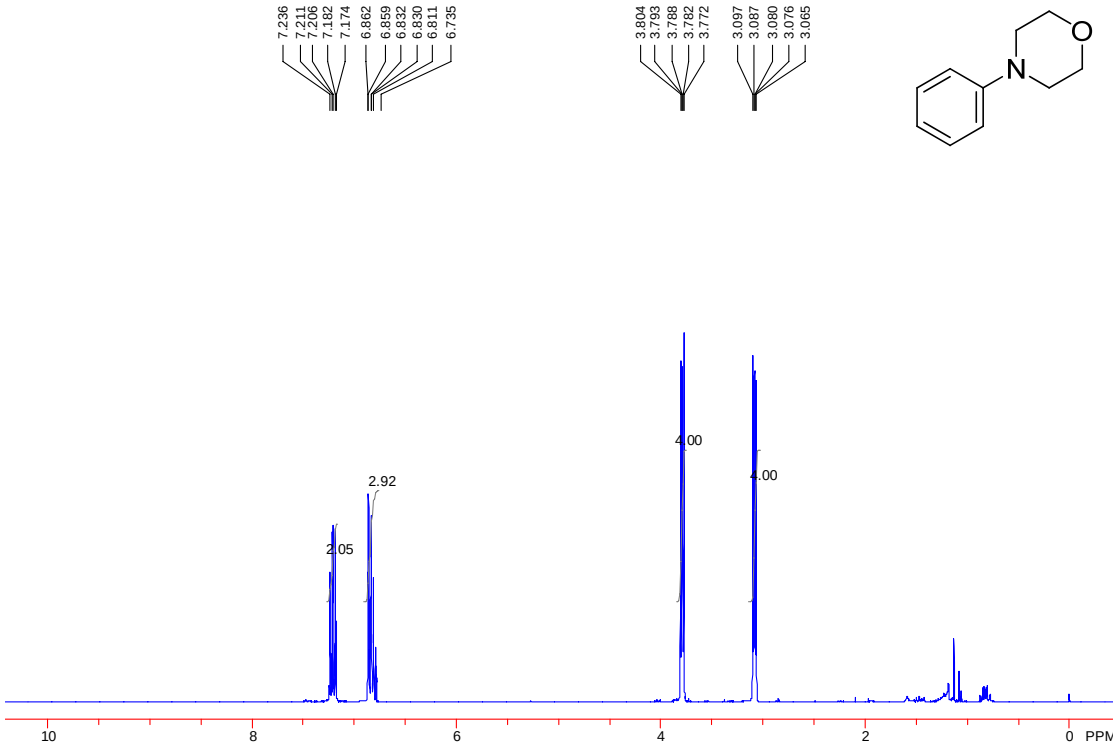
77.427
77.000
76.577
13.542
N
N
200
150
100
50
0 PPM

(87m)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7.206
7.182
7.174
6.862
6.859
6.832
6.830
6.811
6.735
3.804
3.793
3.788
3.782
3.772
3.097
3.087
3.080
3.076
3.065
O
N
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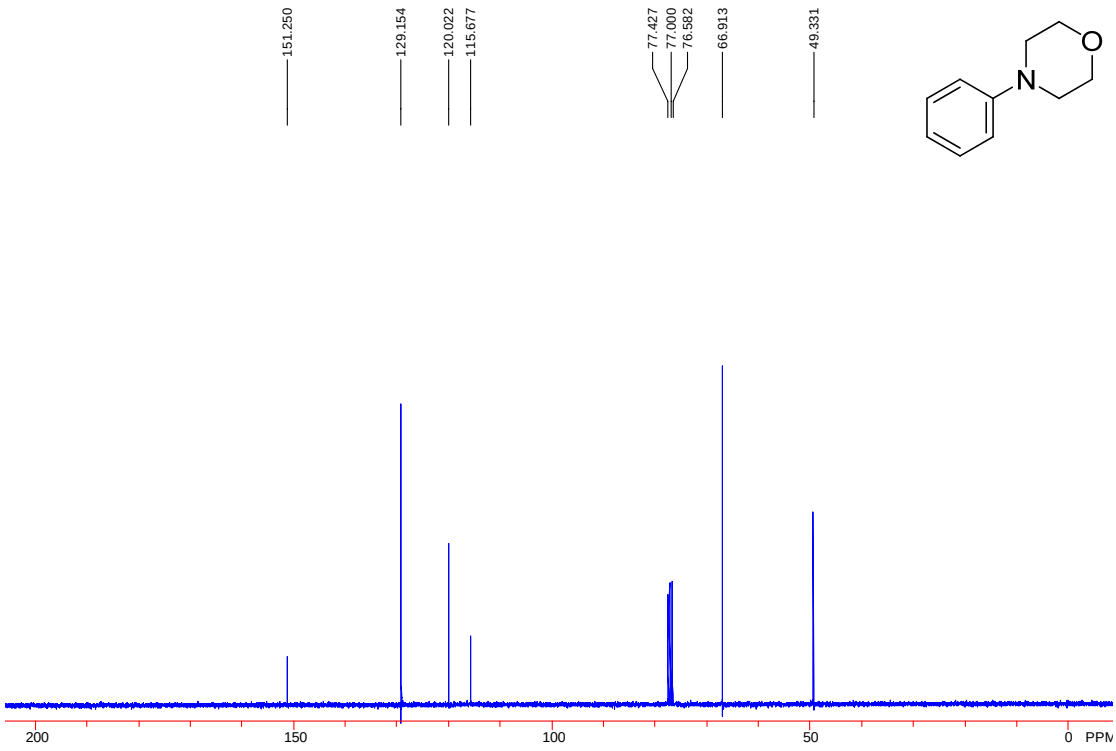
2.92
4.00
4.00
10
8
6
4
2
0
PPM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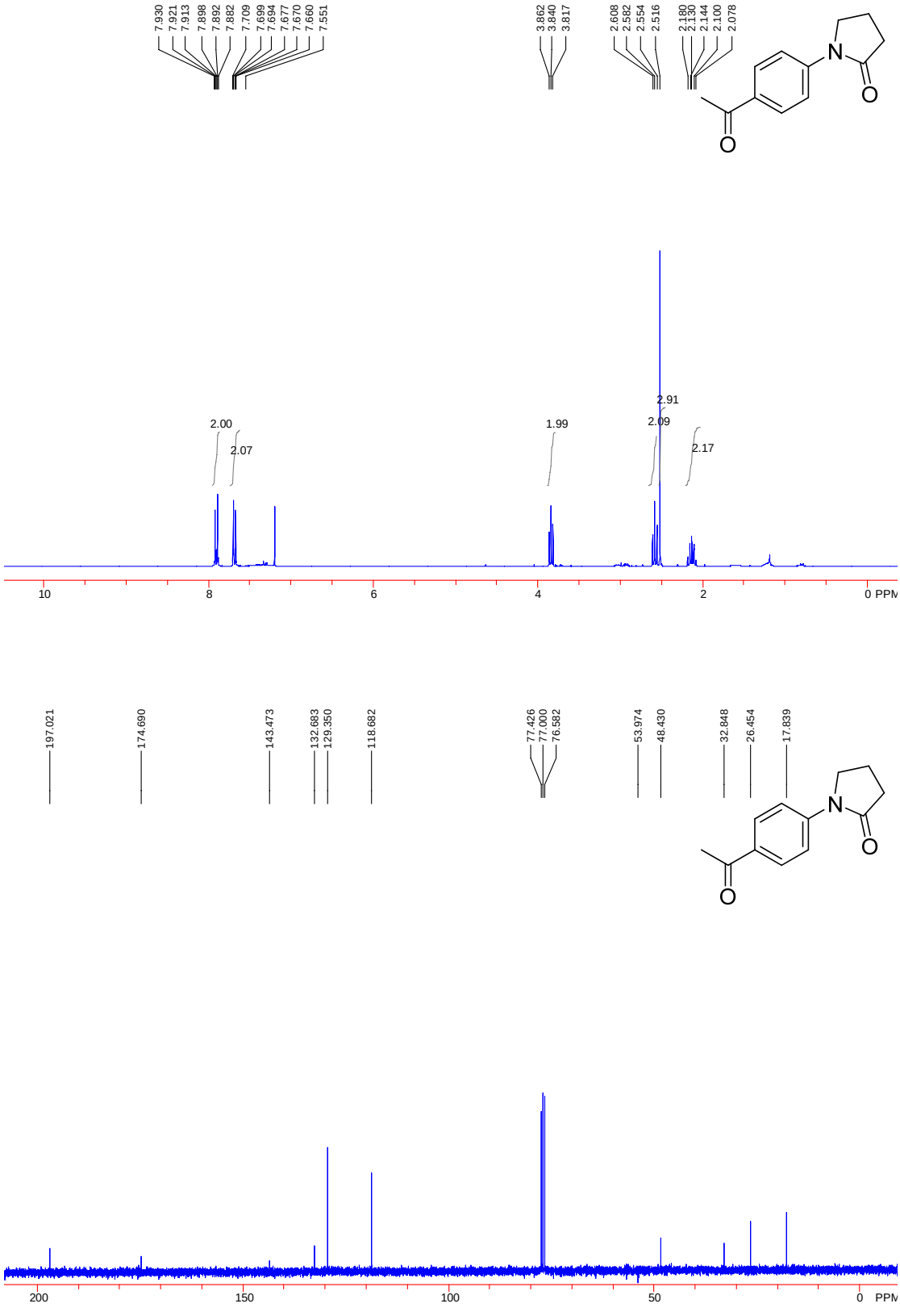
129.154
120.022
115.677
77.427
77.000
76.582
66.913
49.331
O
N
200
150
100
50
0
PPM

(87n)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7.913
7.898
7.892
7.882
7.709
7.699
7.694
7.677
7.670
7.660
7.551
3.862
3.840
3.817
2.608
2.582
2.554
2.516
2.180
2.130
2.144
2.100
2.078
N
O
O
2.00
2.07
1.99
2.91
2.09
2.17
10
8
6
4
2
0 PPM
197.021
174.690
143.473
132.683
129.350
118.682
77.426
77.000
76.582
53.974
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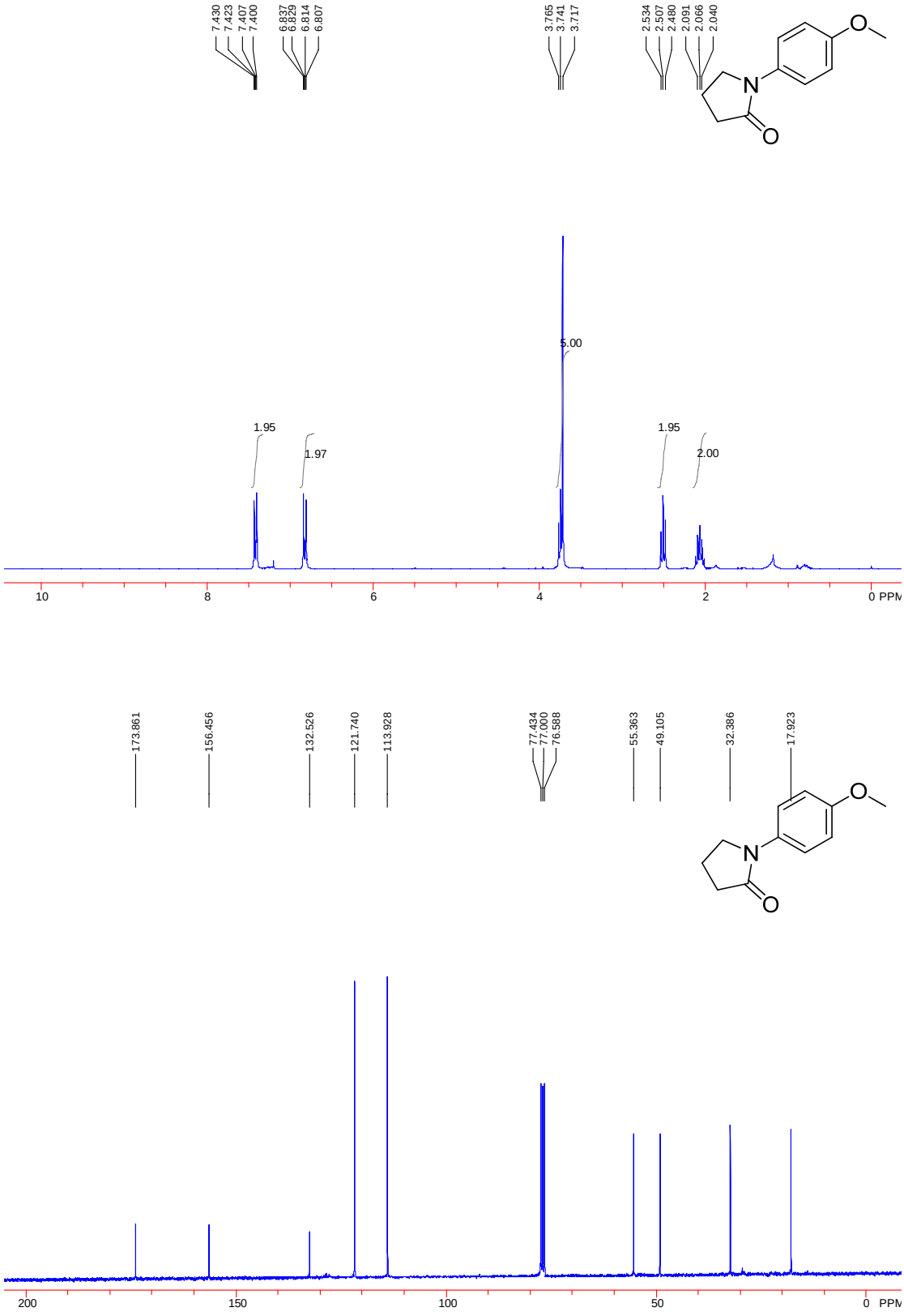
32.848
26.454
17.839
N
O
O
200
150
100
50
0 PPM

(87o)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7.423
7.407
7.400
6.837
6.829
6.814
6.807
3.765
3.741
3.717
2.534
2.507
2.480
2.091
2.066
2.040
O
N
O
5.00
1.95
1.97
1.95
2.00
10
8
6
4
2
0 PPM
173.861
156.456
132.526
121.740
113.928
77.434
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76.588
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49.105
32.386
17.923
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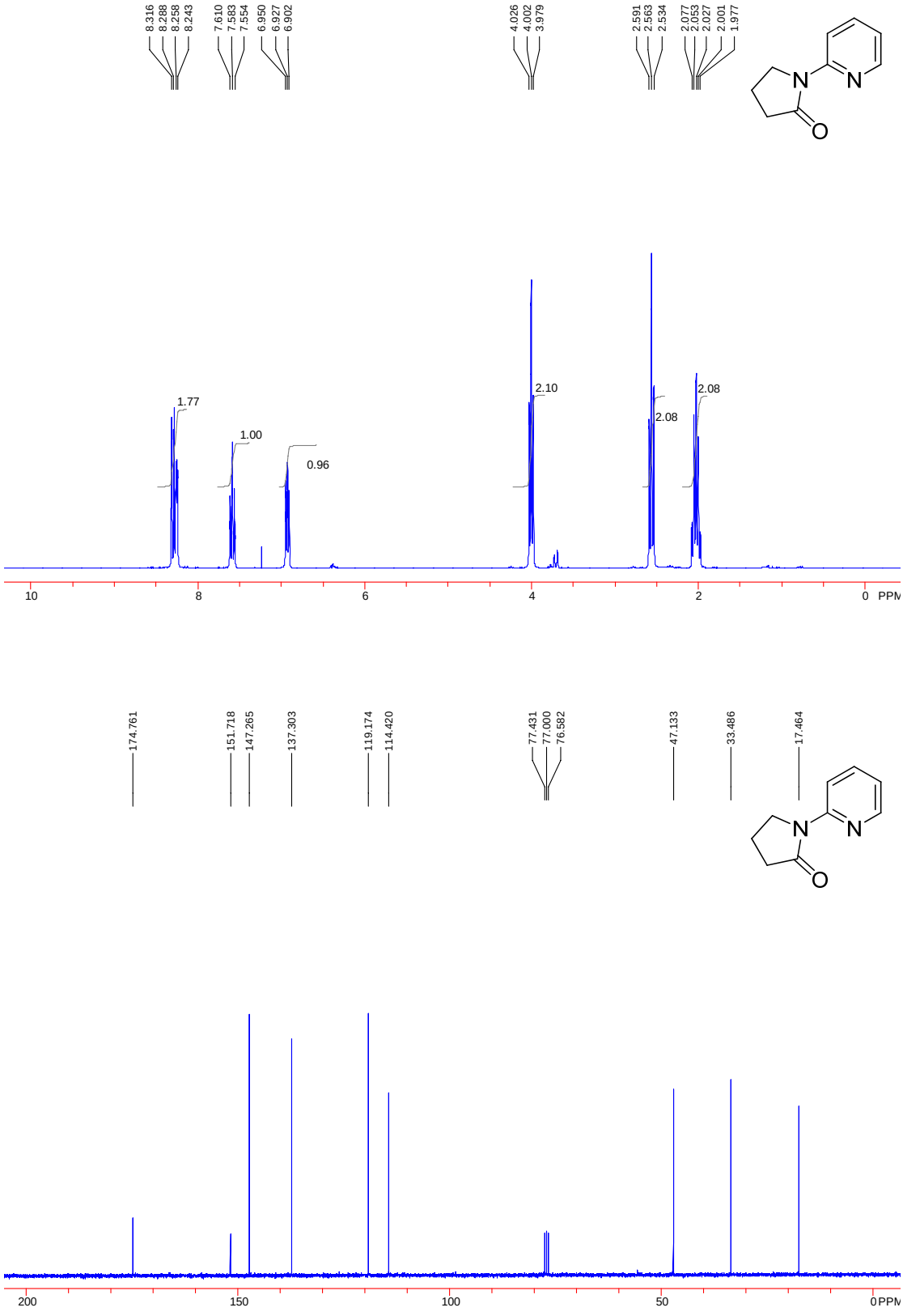
N
O
200
150
100
50
0 PPM

(87p)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8.243
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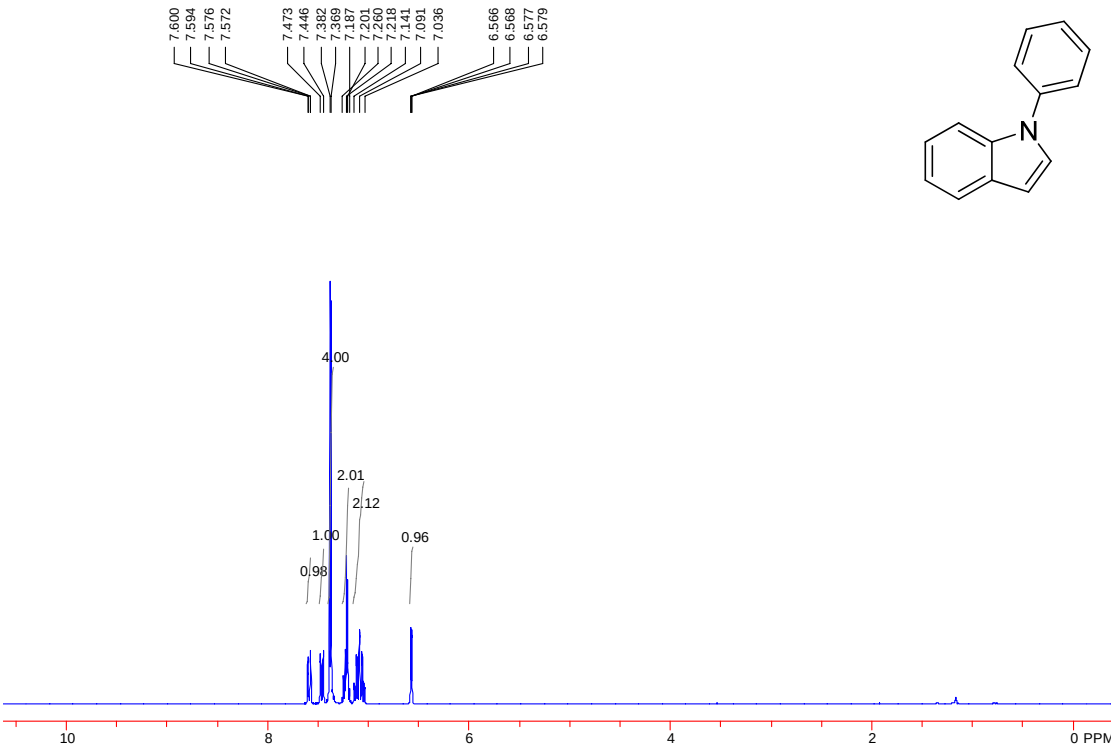
7.583
7.554
6.950
6.927
6.902
4.026
4.002
3.979
2.591
2.563
2.534
2.077
2.053
2.027
2.001
1.977
N
N
O
1.77
1.00
0.96
2.10
2.08
2.08
10
8
6
4
2
0 PPM
174.761
151.718
147.265
137.303
119.174
114.420
77.431
77.000
76.582
47.133
33.486
17.464
N
N
O
200
150
100
50
0 PPM

(87q)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7.446
7.382
7.369
7.187
7.201
7.260
7.218
7.141
7.091
7.036
6.566
6.568
6.577
6.579
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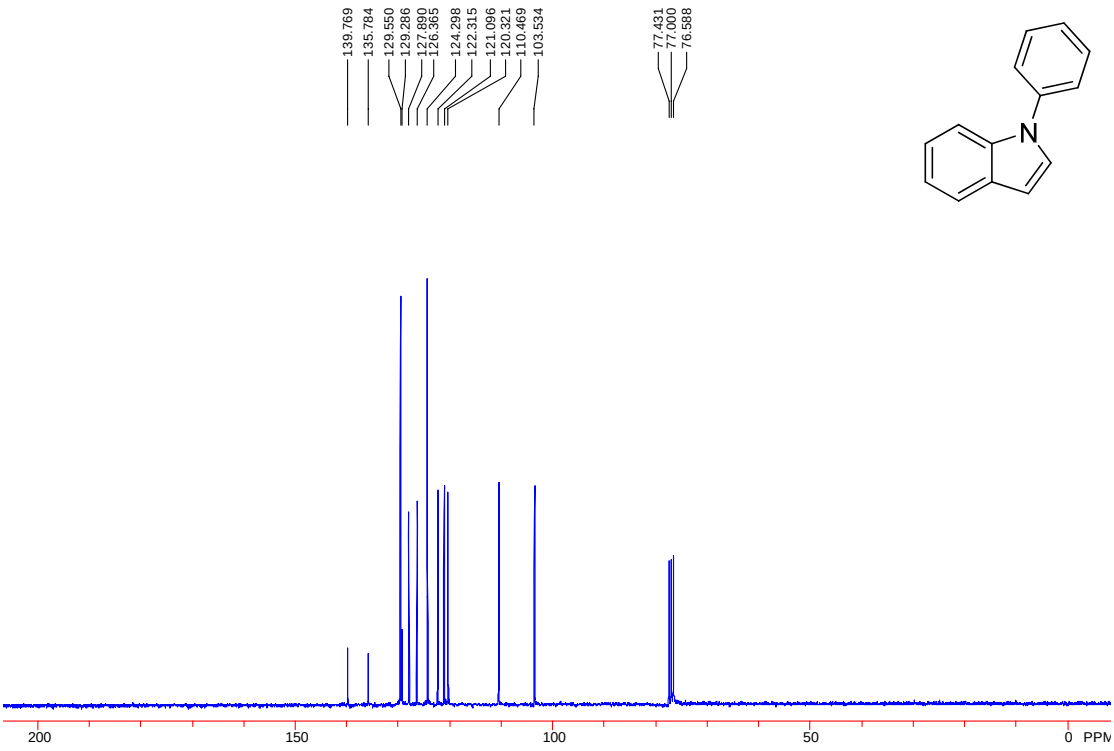
2.01
2.12
1.00
0.98
0.96
10
8
6
4
2
0 PPM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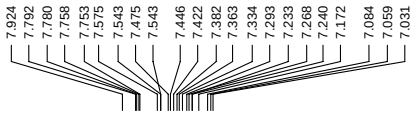
129.286
127.890
126.365
124.298
122.315
121.096
120.321
110.469
103.534
77.431
77.000
76.588
N
200
150
100
50
0 PPM

(87r)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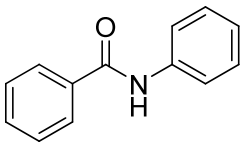
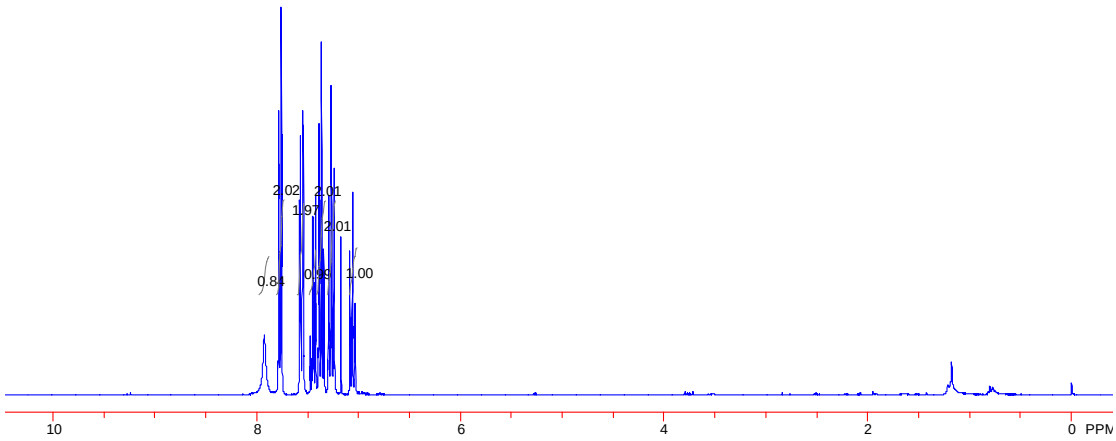
7.792
7.780
7.758
7.753
7.575
7.543
7.475
7.543
7.446
7.422
7.382
7.363
7.334
7.293
7.233
7.268
7.240
7.172
7.084
7.059
7.031


O
N
H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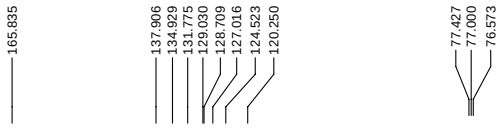
2.01
1.97
2.01
0.84
1.00
10
8
6
4
2
0
PPM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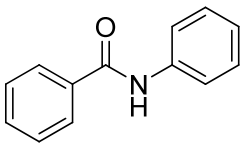
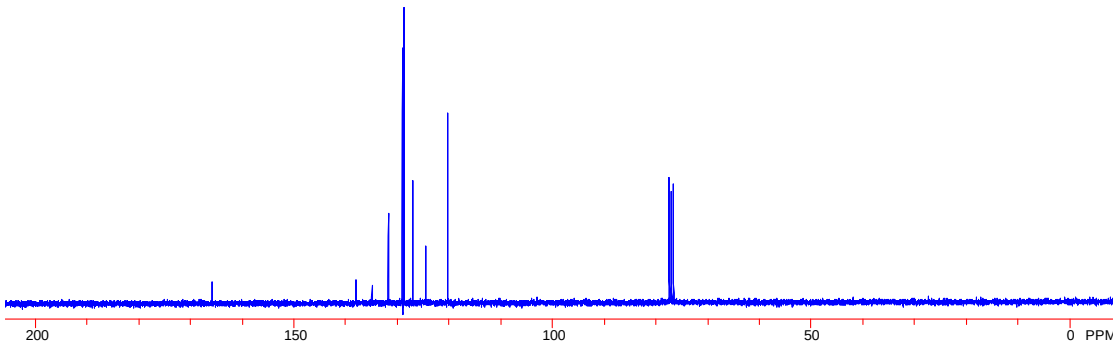
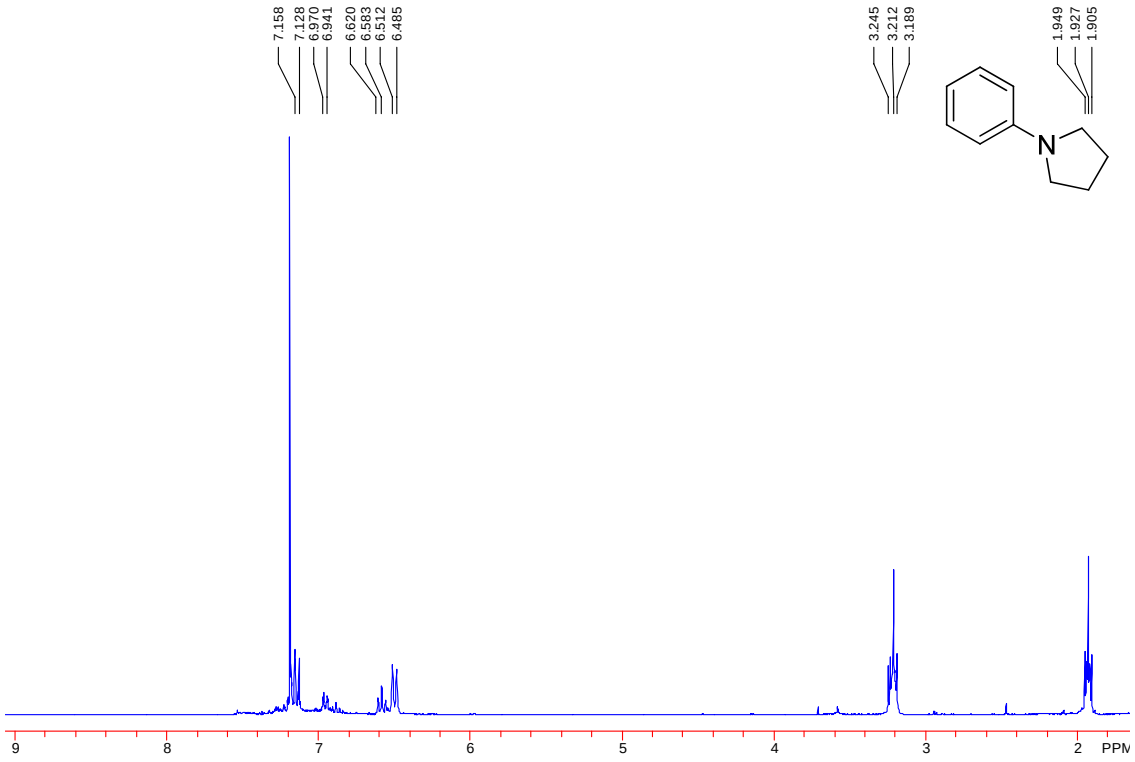
134.929
131.775
129.030
128.709
127.016
124.523
120.250
77.427
77.000
76.573

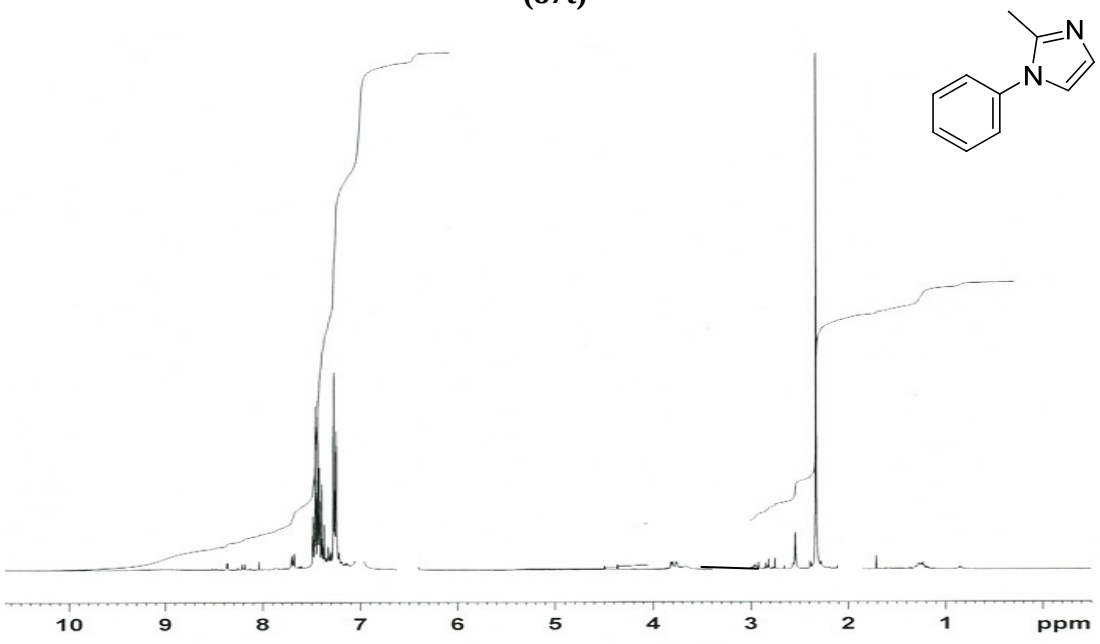

O
N
H


200
150
100
50
0
PPM

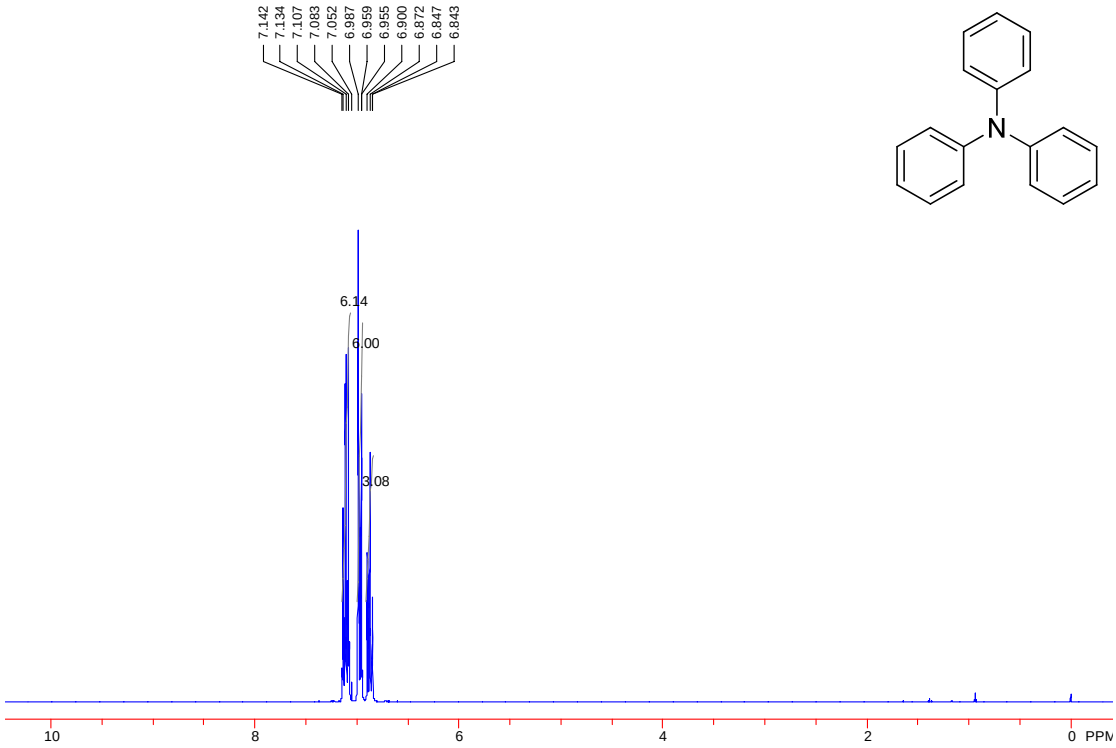
(87s)


7.158
7.128
6.970
6.941
6.620
6.583
6.512
6.485
3.245
3.212
3.189
1.949
1.927
1.905
N
9
8
7
6
5
4
3
2
PPM

(87t)


N
N
10
9
8
7
6
5
4
3
2
1
ppm

(87u)


7.142
7.134
7.107
7.083
7.052
6.987
6.959
6.955
6.900
6.872
6.847
6.843
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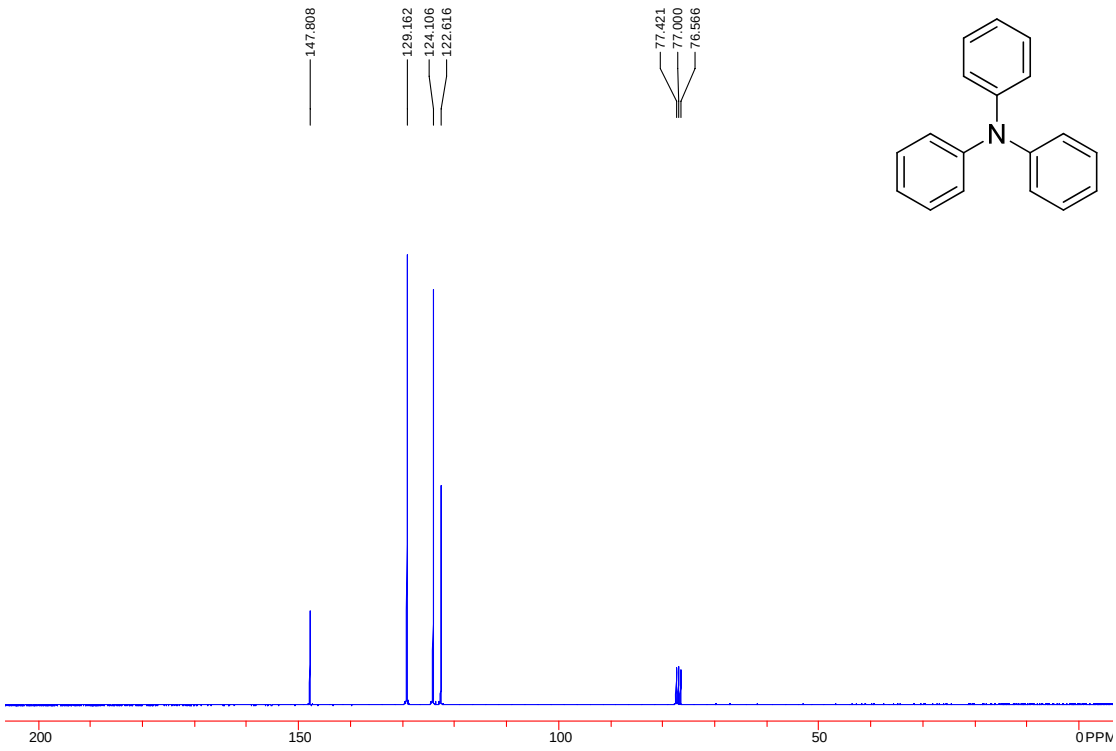
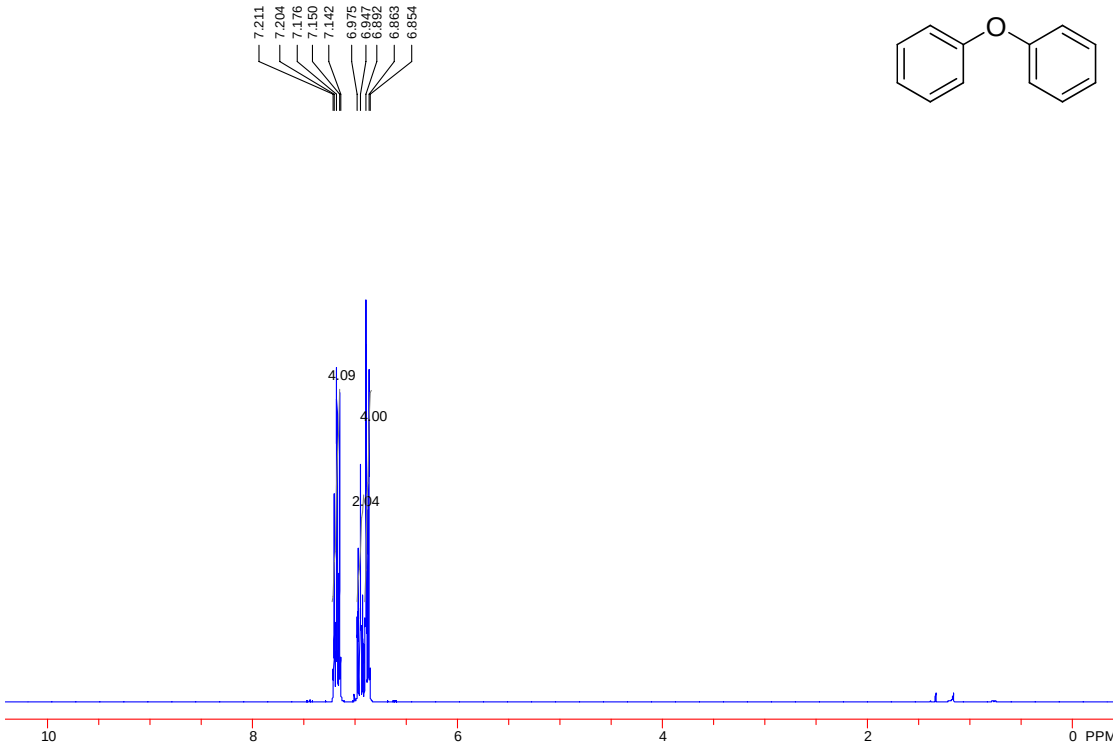
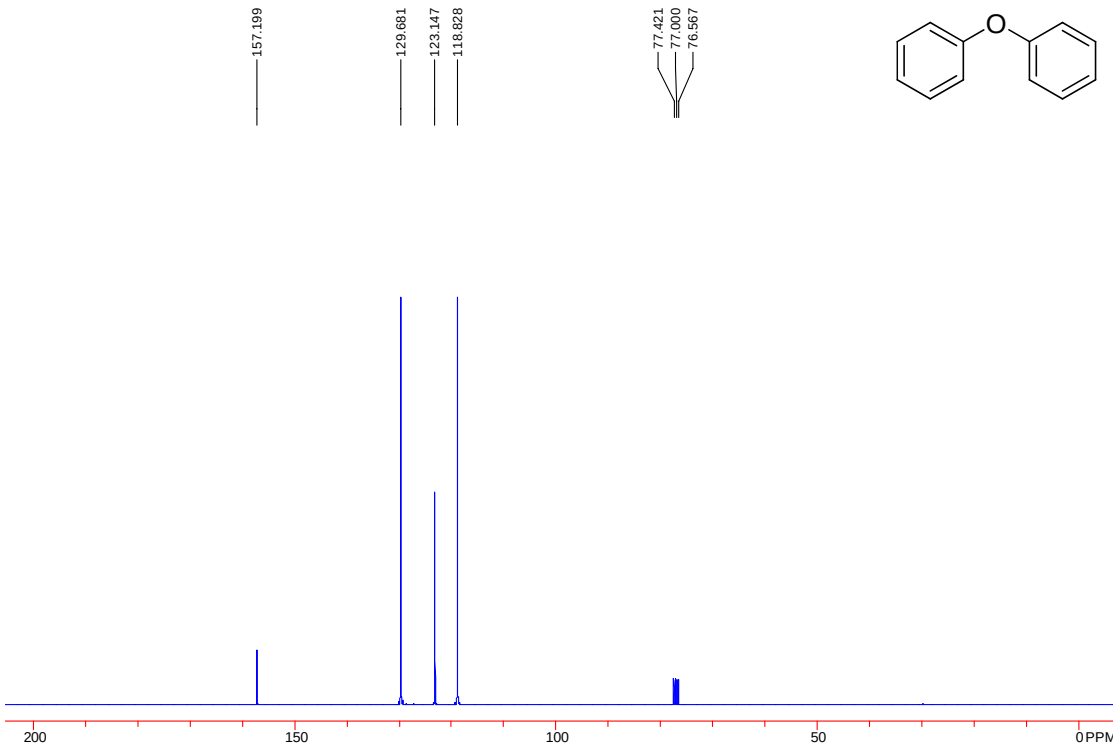
6.00
3.08
10
8
6
4
2
0 PPM

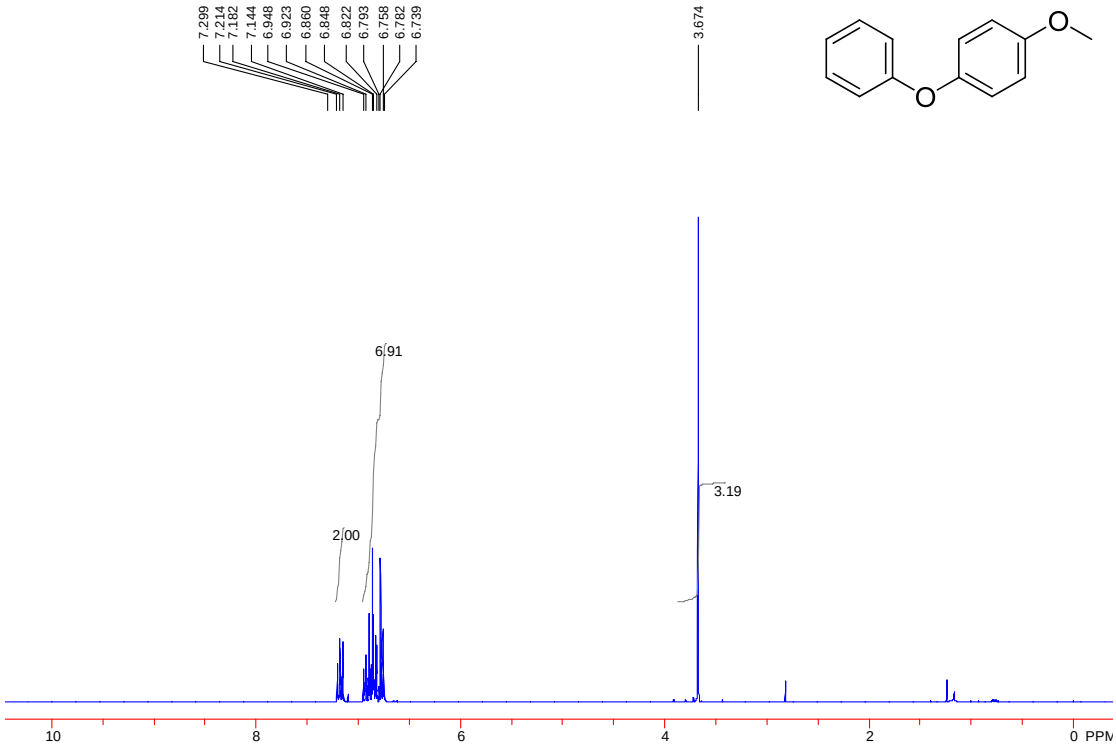

147.808
129.162
124.106
122.616
77.421
77.000
76.566
N
200
150
100
50
0 PPM

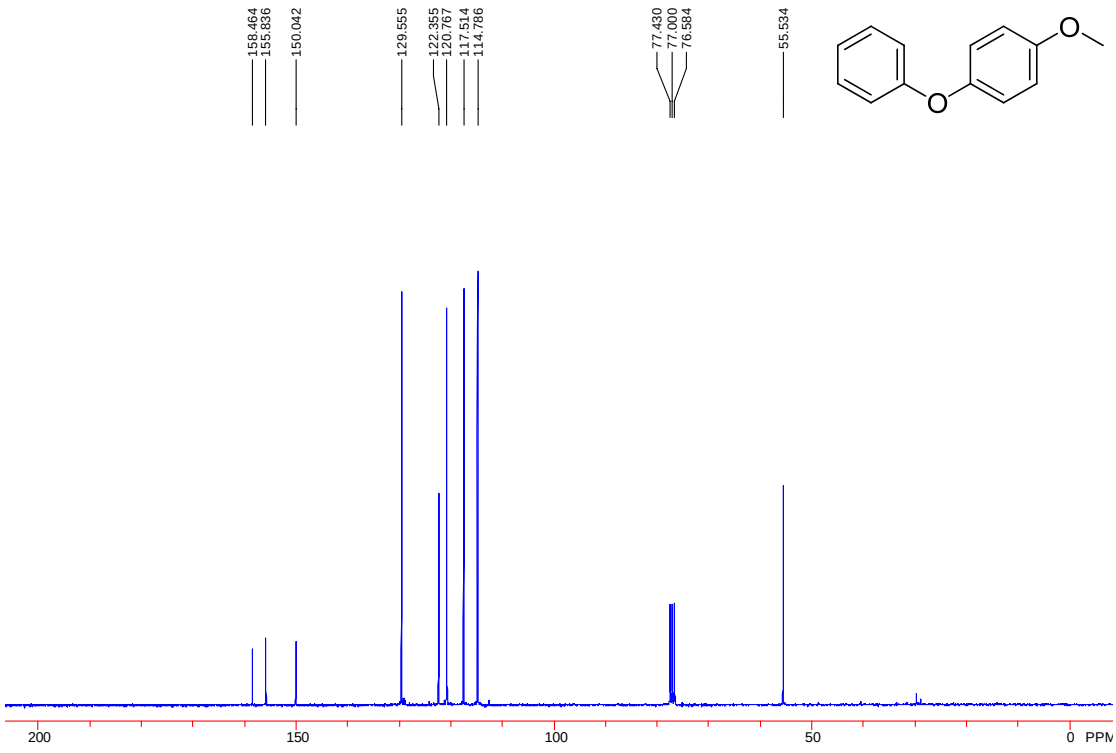
(89a)


7.211
7.204
7.176
7.150
7.142
6.975
6.947
6.892
6.863
6.854
O
4.09
4.00
2.04
10
8
6
4
2
0 PPM

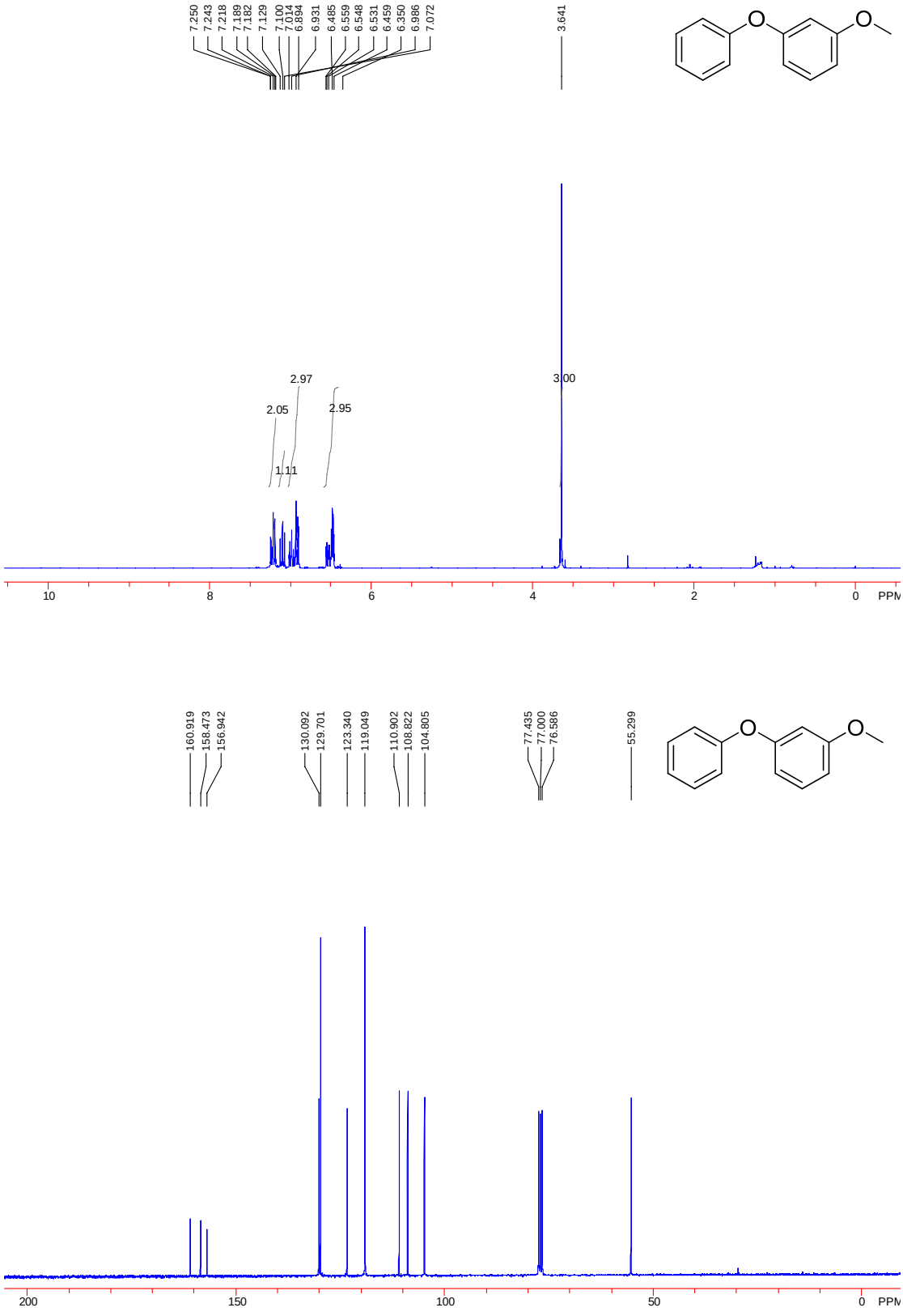

157.199
129.681
123.147
118.828
77.421
77.000
76.567
O
200
150
100
50
0 PPM

(89b)


7.299
7.214
7.182
7.144
6.948
6.923
6.860
6.848
6.822
6.793
6.758
6.782
6.739
3.674
6.91
3.19
2.00
10
8
6
4
2
0 PPM


158.464
155.836
150.042
129.555
122.355
120.767
117.514
114.786
77.430
77.000
76.584
55.534
200
150
100
50
0 PPM

(89c)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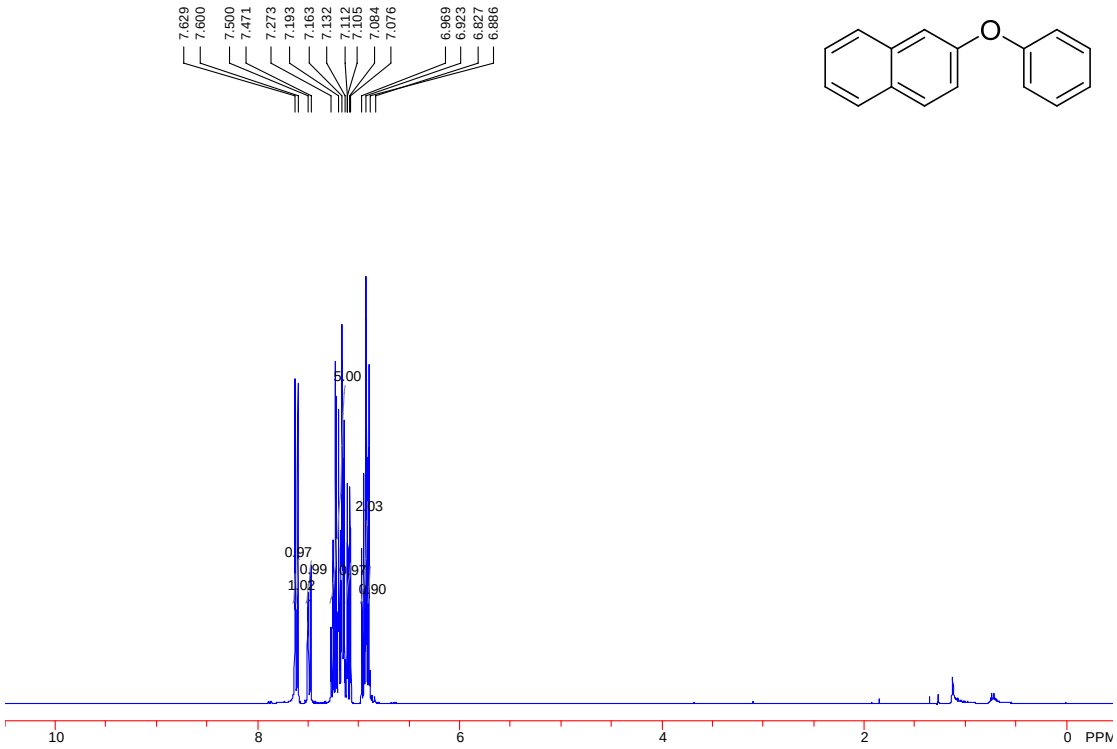
7.243
7.218
7.189
7.182
7.129
7.100
7.014
6.894
6.931
6.485
6.559
6.548
6.531
6.459
6.350
6.986
7.072
3.641
2.97
2.05
2.95
1.11
3.00
10
8
6
4
2
0
PPM
160.919
158.473
156.942
130.092
129.701
123.340
119.049
110.902
108.822
104.805
77.435
77.000
76.586
55.299
200
150
100
50
0
PPM

(89d)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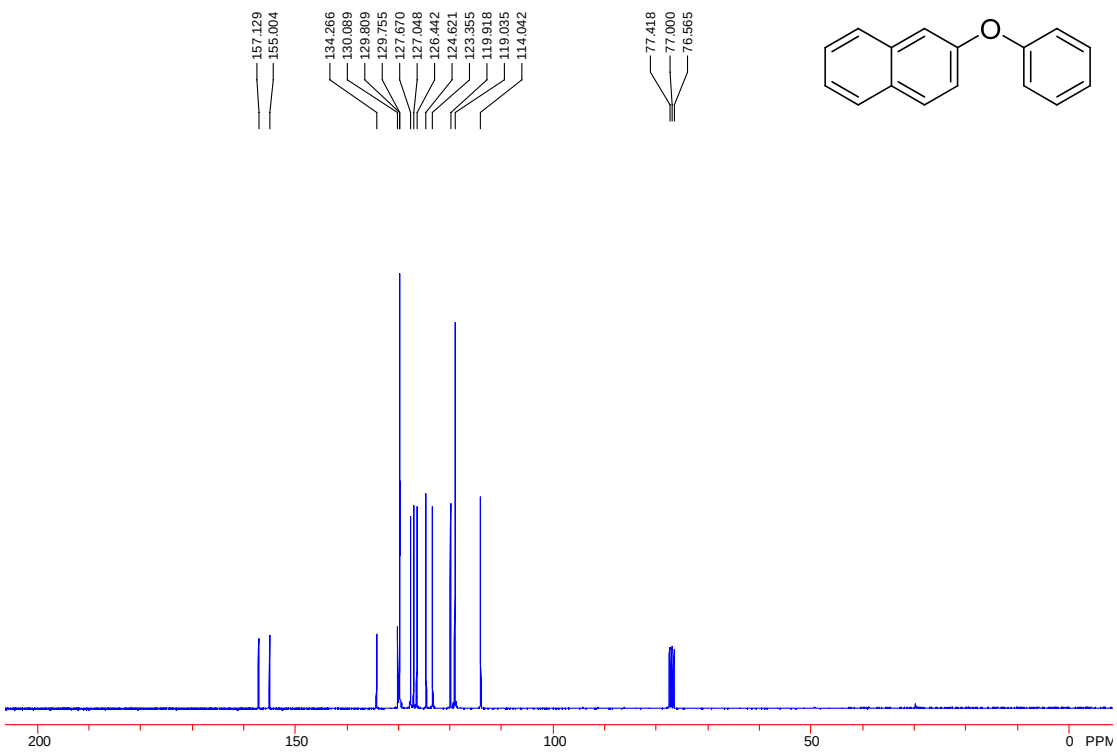
7.600
7.500
7.471
7.273
7.193
7.163
7.132
7.112
7.105
7.084
7.076
6.969
6.923
6.827
6.886
O
5.00
2.03
0.97
0.99
0.97
1.02
0.90
10
8
6
4
2
0
PPM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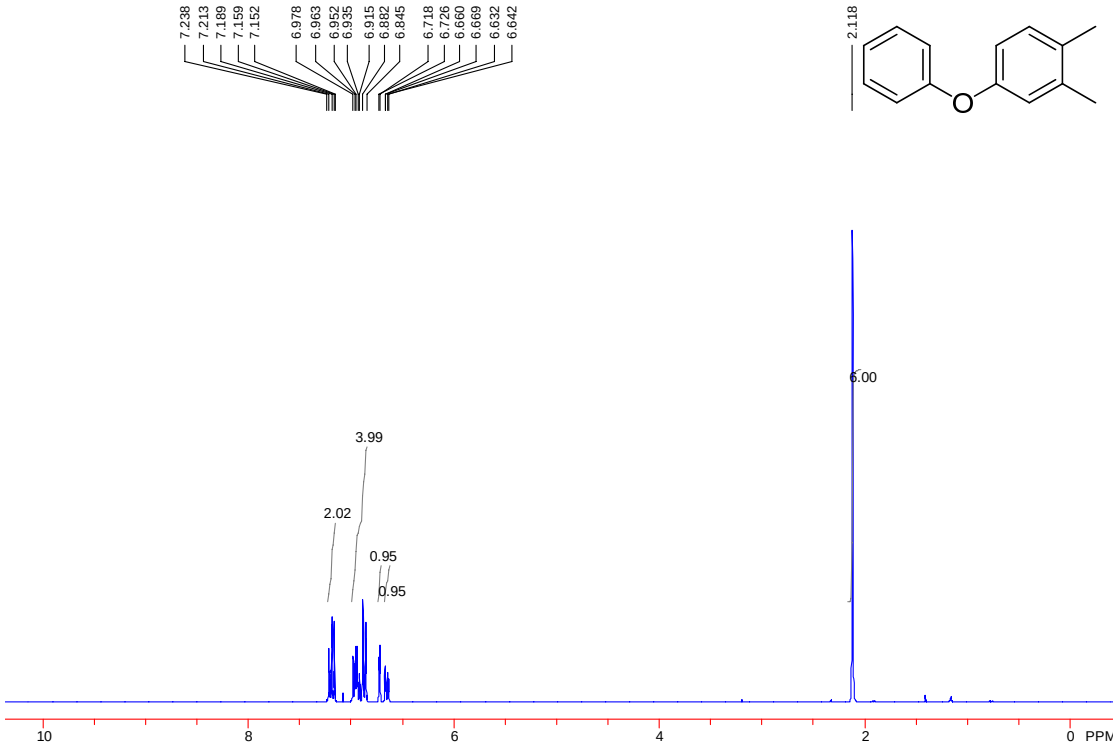
155.004
134.266
130.089
129.809
129.755
127.670
127.048
126.442
124.621
123.355
119.918
119.035
114.042
77.418
77.000
76.565
O
200
150
100
50
0
PPM

(89e)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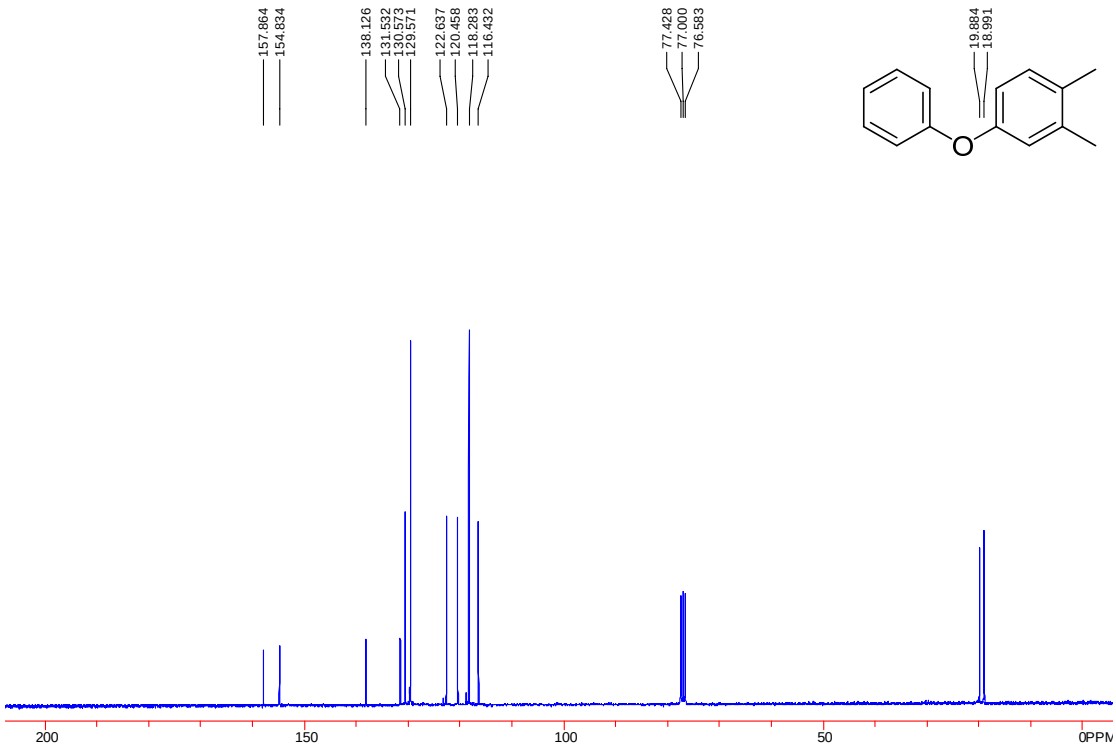
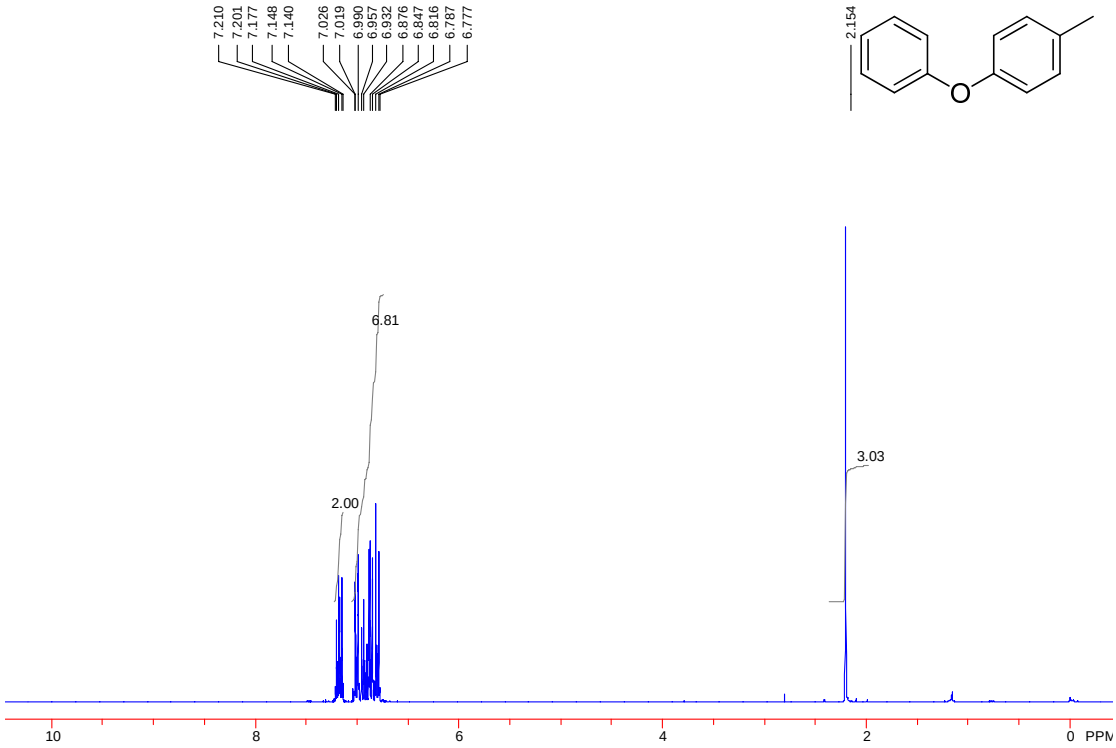
7.213
7.189
7.159
7.152
6.978
6.963
6.952
6.935
6.915
6.882
6.845
6.718
6.726
6.660
6.669
6.632
6.642
2.118
O
6.00
3.99
2.02
0.95
0.95
10
8
6
4
2
0 PPM


157.864
154.834
138.126
131.532
130.573
129.571
122.637
120.458
118.283
116.432
77.428
77.000
76.583
19.884
18.991
O
200
150
100
50
0PPM

(89f)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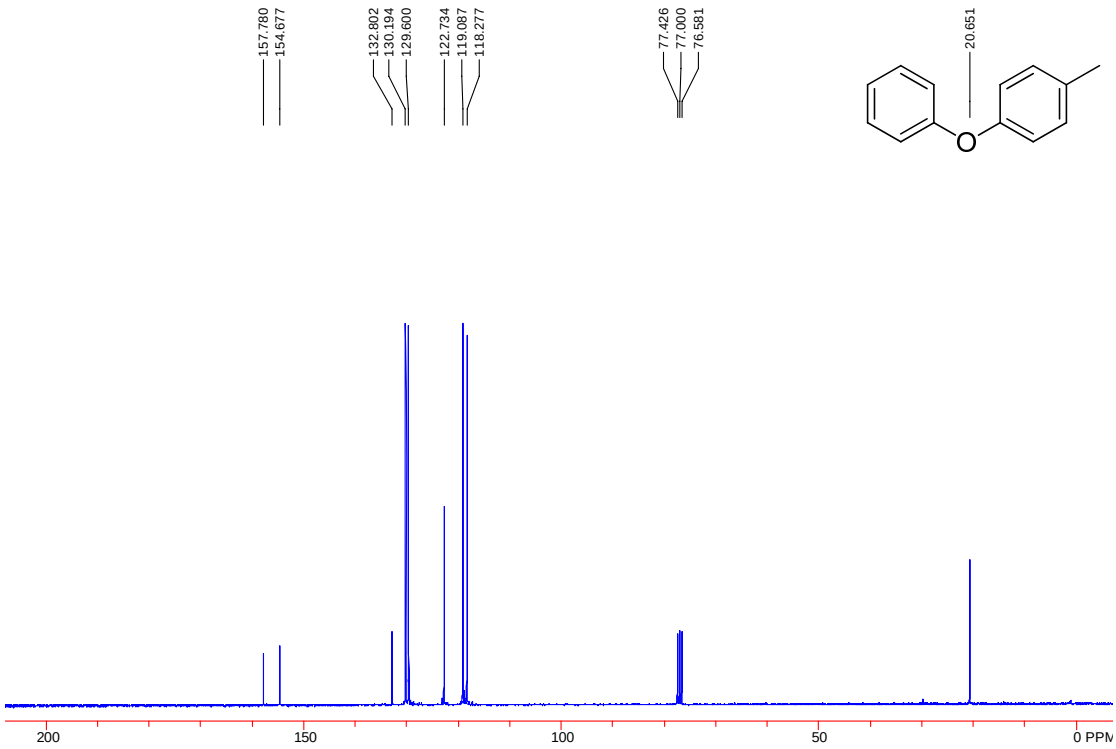
7.201
7.177
7.148
7.140
7.026
7.019
6.990
6.957
6.932
6.876
6.847
6.816
6.787
6.777
2.154
O
6.81
3.03
2.00
10
8
6
4
2
0 PPM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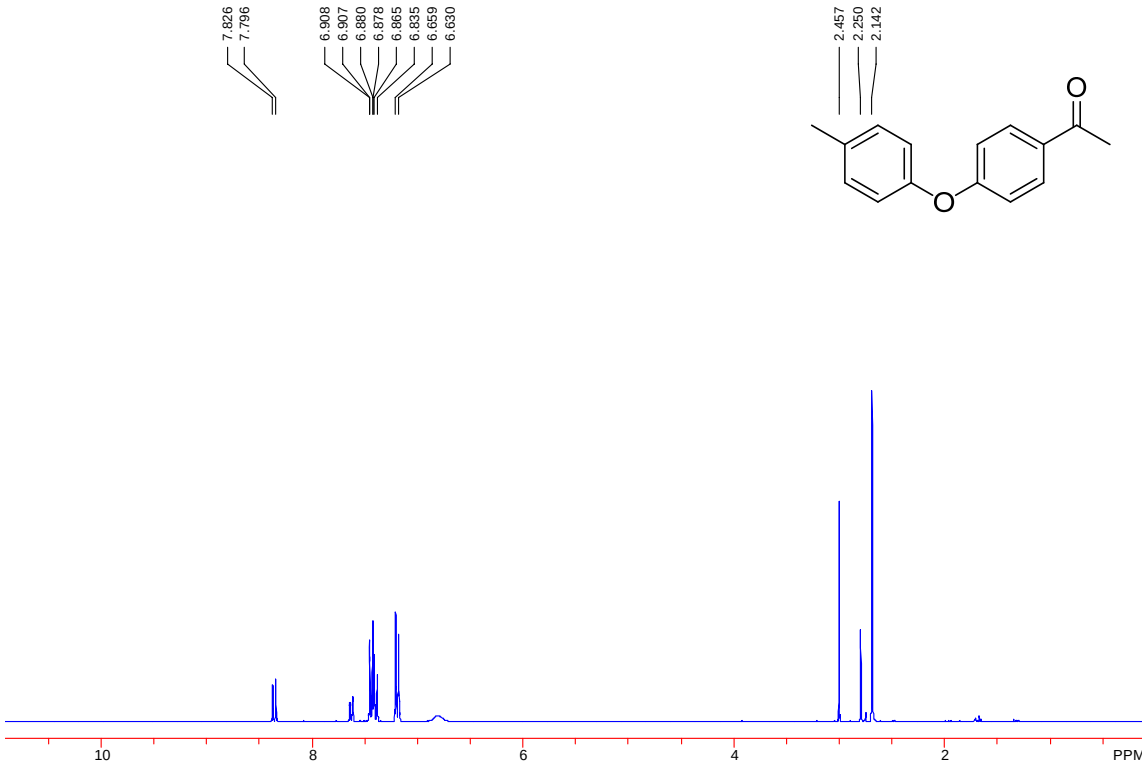
154.677
132.802
130.194
129.600
122.734
119.087
118.277
77.426
77.000
76.581
20.651
O
200
150
100
50
0 PPM

(89g)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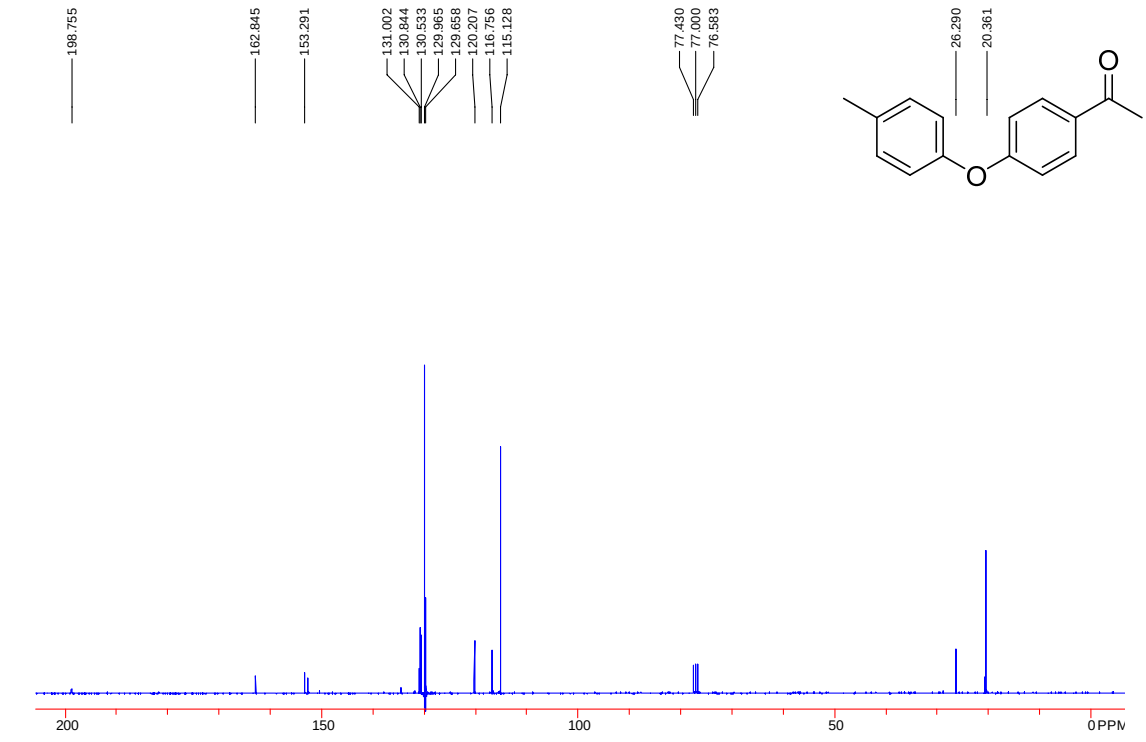
7.796
6.908
6.907
6.880
6.878
6.865
6.835
6.659
6.630
2.457
2.250
2.142
O
O
10
8
6
4
2
PPM


198.755
162.845
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131.002
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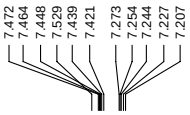
130.533
129.965
129.658
120.207
116.756
115.128
77.430
77.000
76.583
26.290
20.361
O
O
200
150
100
50
0 PPM

(90a)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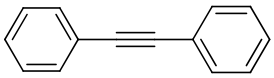
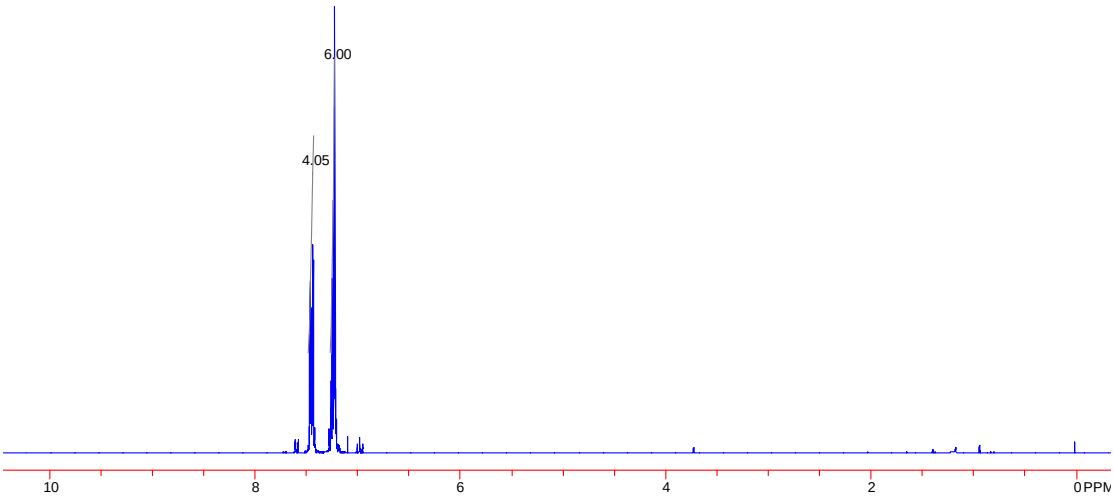
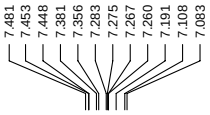
7.529
7.439
7.421
7.273
7.254
7.244
7.227
7.207




6.00
4.05
10
8
6
4
2
0 PPM

(90b)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7.267
7.260
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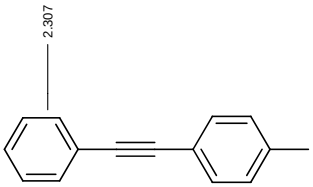
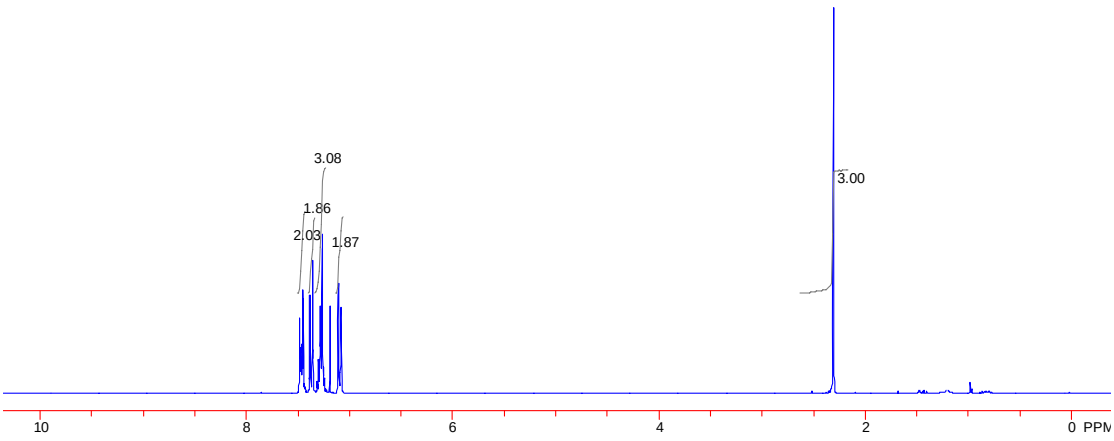
7.108
7.083


2.307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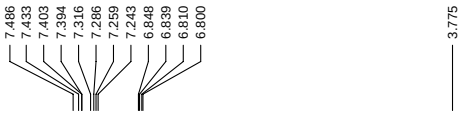
1.86
2.03
1.87
3.00
10
8
6
4
2
0 PPM

(90c)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7.316
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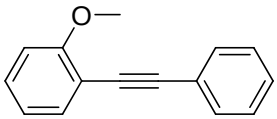
7.259
7.243
6.848
6.839
6.810
6.800

3.775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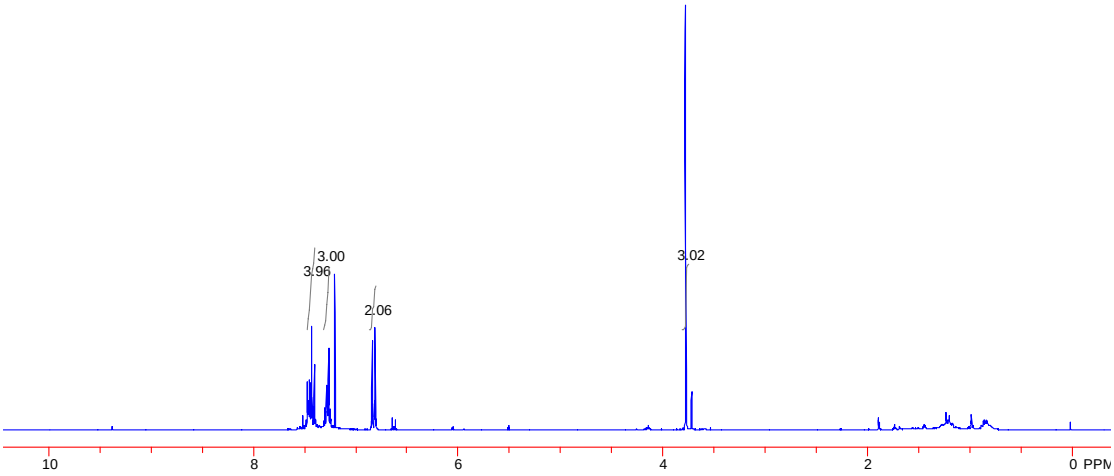
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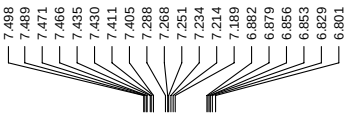
3.96
2.06
3.02
10
8
6
4
2
0 PPM

(90d)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7.466
7.435
7.430
7.411
7.405
7.288
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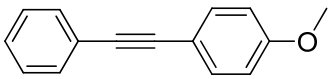
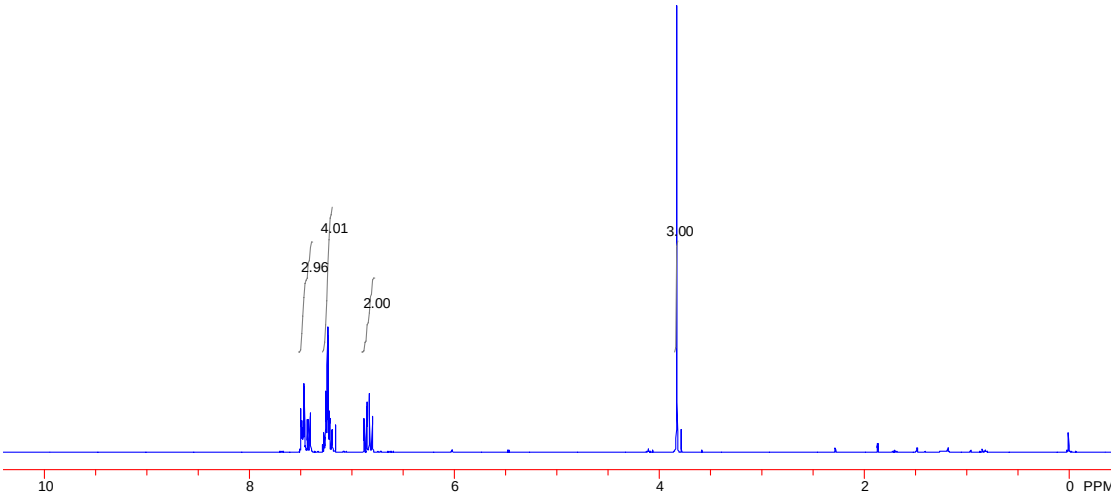
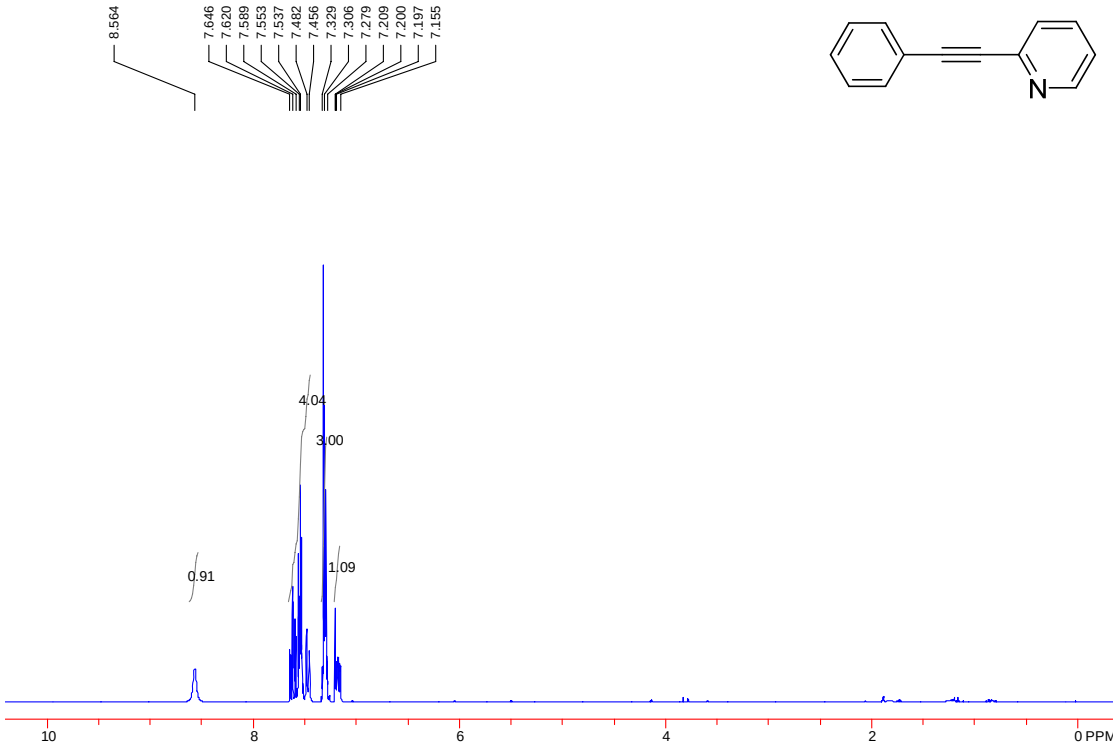
7.214
7.189
6.882
6.879
6.856
6.853
6.829
6.801


3.825


O


4.01
2.96
2.00
3.00
10
8
6
4
2
0 PPM

(90e)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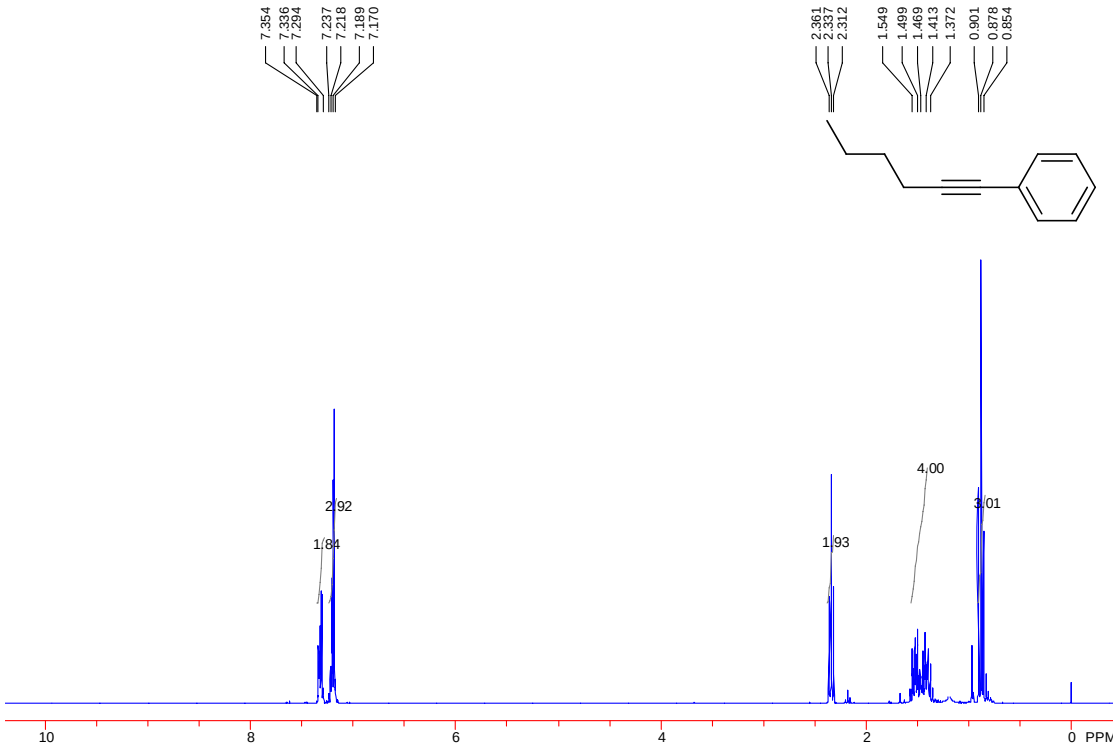
7.537
7.482
7.456
7.329
7.306
7.279
7.209
7.200
7.197
7.155
N
4.04
3.00
1.09
0.91
10
8
6
4
2
0 PPM

(90f)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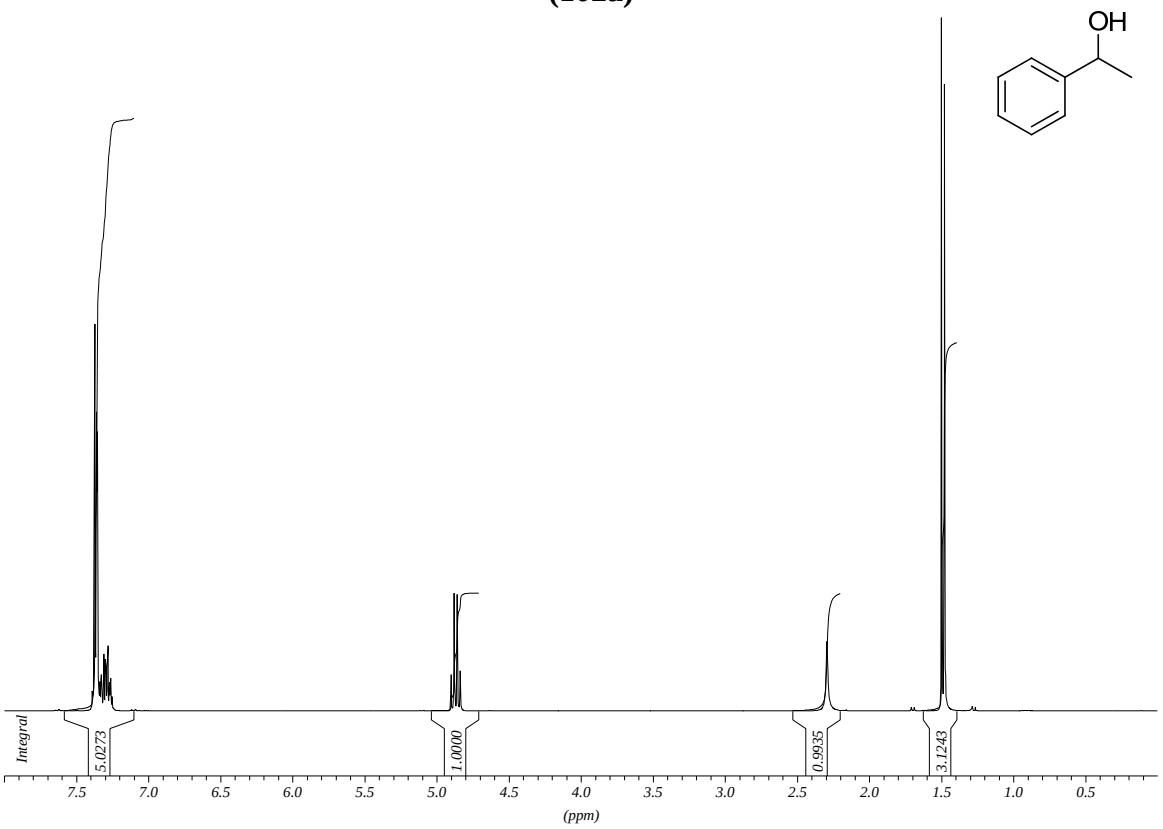
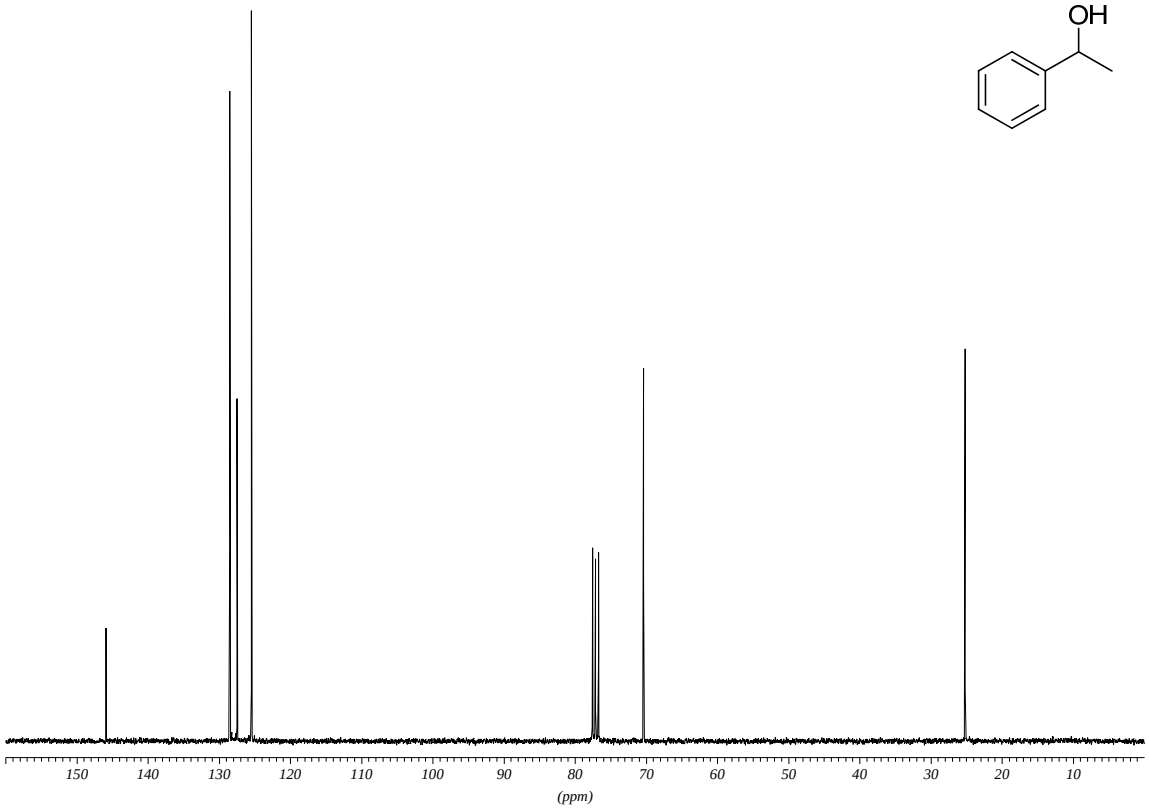
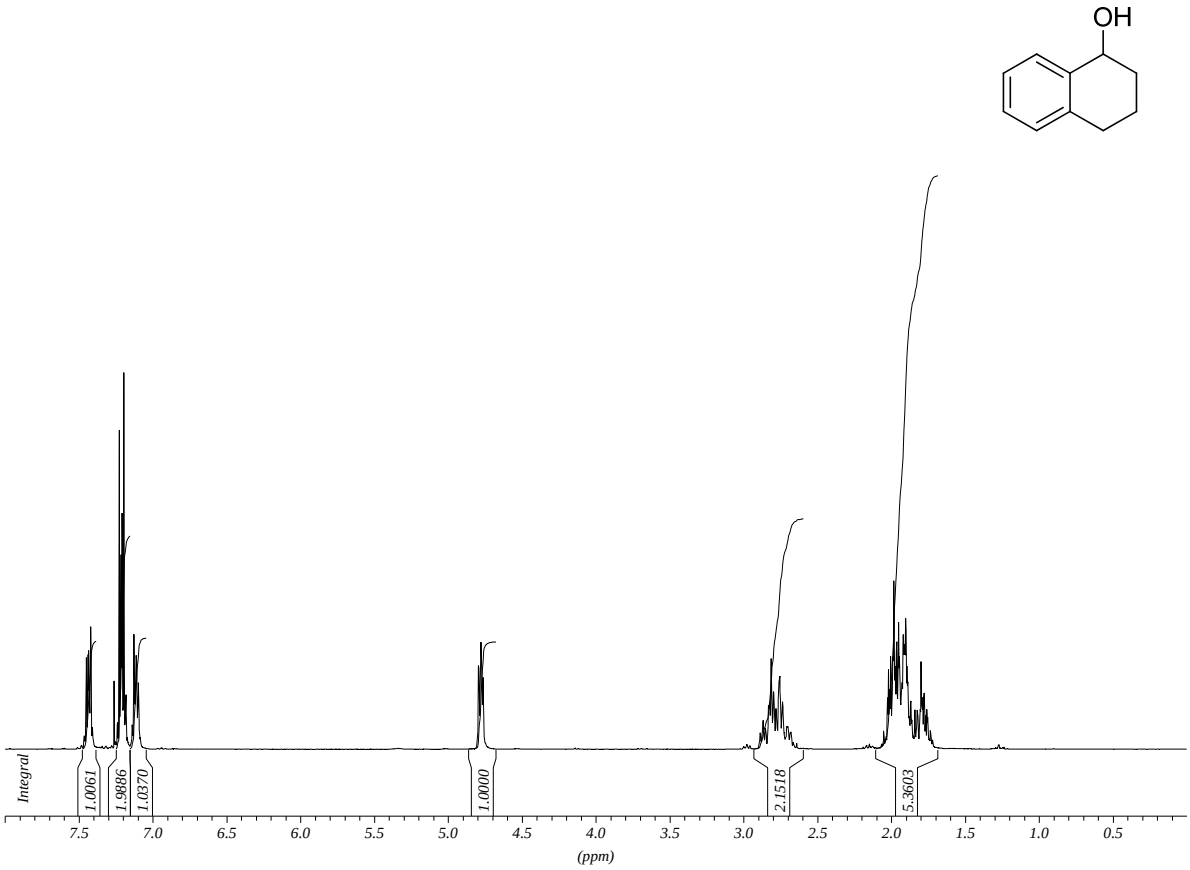
7.294
7.237
7.218
7.189
7.170
2.361
2.337
2.312
1.549
1.499
1.469
1.413
1.372
0.901
0.878
0.854
2.92
1.84
1.93
4.00
3.01
10
8
6
4
2
0 PPM

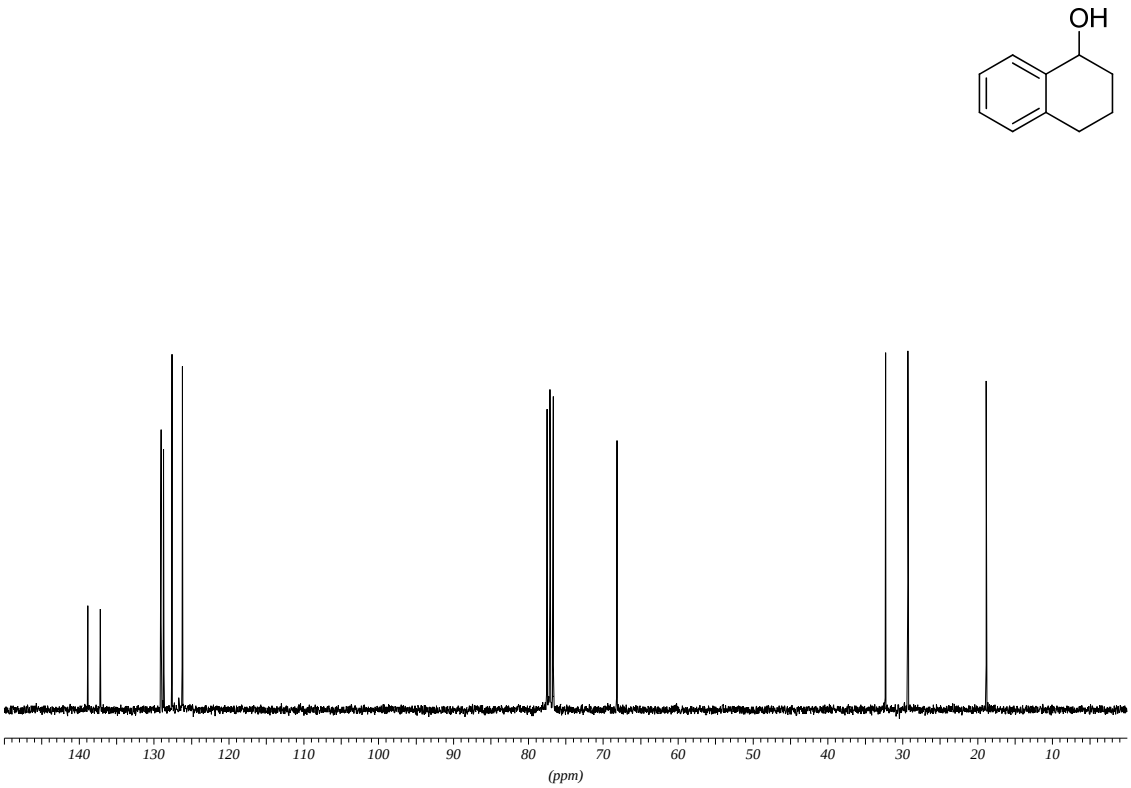
(102a)


OH
Integral
5.0273
1.0000
0.9935
3.1243
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
(ppm)

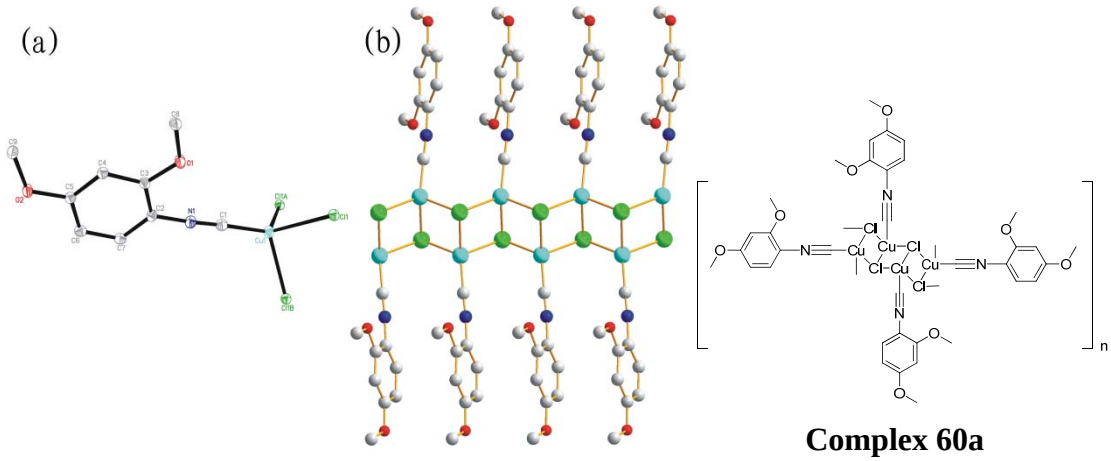

OH
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

(102b)


OH
Integral
1.0061
1.9886
1.0370
1.0000
2.1518
5.3603
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
(ppm)


OH
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

X-ray diffraction structure



Complex 60a

Table 1. Crystal data and structure refinement for **60a**.

(a) Coordination environment of Cu(I) in $[CuLCl]_n$.

(b) one-dimension chain structure of **60a** (color codes: Cu Cyan, Cl green, O red, N blue, C grey).

Crystal data

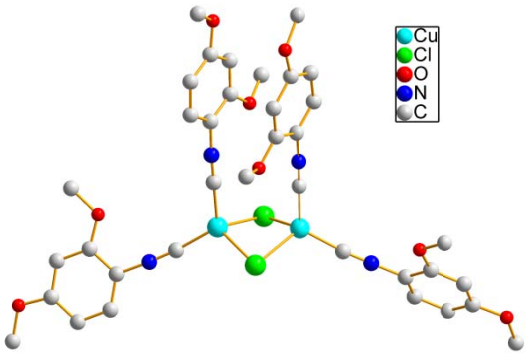
Empirical formula	$C_9H_9ClCuNO_2$	
Formula weight	262.17	
Temperature	123 K	
Wavelength	1.54184 Å	
Crystal system	Orthorhombic	
Space group	P n a 21	
Unit cell dimensions	a = 16.5494(2) Å	α = 90°
	b = 16.2055(2) Å	β = 90°
	c = 3.78028(4) Å	γ = 90°
Volume	1013.84(2) $Å^3$	
Z	4	
Density (calculated)	1.718 Mg/m^3	
Absorption coefficient	5.250 mm^{-1}	
F(000)	528	

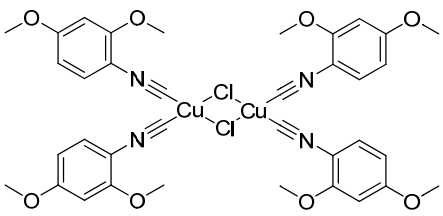
Data collection

Crystal size	0.6446 × 0.0524 × 0.0232 mm
Theta range for data collection	3.82° to 69.05°
Index ranges	-20 <= *h* <= 19, -19 <= *k* <= 19, -4 <= l <= 4
Reflections collected	34516
Absorption correction	Analytical
Max. and min. transmission	0.887 and 0.271

Refinement

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1893 / 1 / 129
Goodness-of-fit on F^2	1.024
Final R indices [I＞σ(Ⅰ)]	R1 = 0.0274, wR2 = 0.0723
R indices (all data)	R1 = 0.0301, wR2 = 0.0742
Absolute structure parameter	0.08(2)
Largest diff. peak and hole	0.310 and -0.483 e. $Å^{-3}$





Complex 60b

Table 2. Crystal data and structure refinement for **60b**.

Crystal data

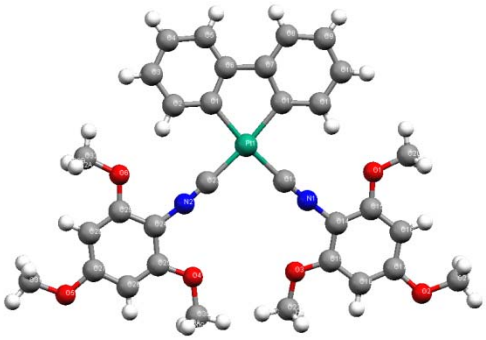
Empirical formula	$C_{36}H_{36}C_{l2}Cu_2\ N_4O_8$	
Formula weight	850.69	
Temperature	123 K	
Wavelength	1.54184 Å	
Crystal system	Orthorhombic	
Space group	C 2/c	
Unit cell dimensions	a = 22.9000(5) Å	α = 90°
	b = 14.1916(2) Å	β = 116.311°
	c = 12.7953(3) Å	γ = 90°
Volume	3727.52(16) $Å^3$	
Z	4	
Density (calculated)	1.516 Mg/m^3	
Absorption coefficient	3.198 mm^{-1}	
F(000)	1744	

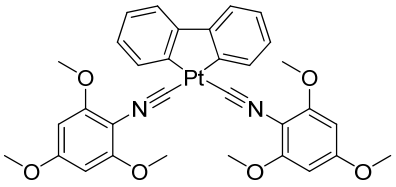
Data collection

Crystal size	0.5287 x 0.2716 x 0.2272 mm
Theta range for data collection	3.79° to 66.69°
Index ranges	-26<=h<=27, -16<=k<=16, -14<=l<=15
Reflections collected	9047
Absorption correction	Analytical
Max. and min. transmission	0.619 and 0.347

Refinement

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3235 / 0 / 235
Goodness-of-fit on F^2	1.032
Final R indices [I＞σ(Ⅰ)]	R1 = 0.0399, wR2 = 0.1060
R indices (all data)	R1 = 0.0426, wR2 = 0.1090
Absolute structure parameter	--
Largest diff. peak and hole	0.620 and -0.590 e. $Å^{-3}$





Complex 104

Table 3. Crystal data and structure refinement for **104**.

Crystal data

Empirical formula	$C_{32}H_{30}N_2O_6Pt$
Formula weight	733.66
Temperature	123 K
Wavelength	1.54184 Å
Crystal system	Orthorhombic
Space group	P -1
Unit cell dimensions	a = 9.8822(12) Å α = 101.384°
	b = 10.9367(15) Å β = 101.824(14)°
	c = 13.3860(16) Å γ = 92.215(15)°
Volume	1383.5(3) $Å^3$
Z	2
Density (calculated)	1.761 Mg/m^3
Absorption coefficient	5.120 mm^{-1}
F(000)	724

Data collection

Crystal size	0.350 x 0.270 x 0.010 mm
Theta range for data collection	2.11° to 27.00°
Index ranges	-12<=h<=12, -13<=k<=13, -8<=l<=17
Reflections collected	5519
Absorption correction	Analytical
Max. and min. transmission	0.8885 and 0.1675

Refinement

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5519 / 0 / 371
Goodness-of-fit on F^2	1.169
Final R indices [I＞σ(Ⅰ)]	R1 = 0.0525, wR2 = 0.1335
R indices (all data)	R1 = 0.0554, wR2 = 0.1374
Absolute structure parameter	--
Largest diff. peak and hole	2.615 and -1.348 e. $Å^{-3}$

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August 2003- June 2006	M. Sc	Master of Science in Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences & Hebei Normal Universiy, China (Supervisor: **Prof. Dr.Yuanhong Liu**) Title of the dissertation: Study on highly selective cyclodimerization of alkynes and construction of 3(*2H*)-furanones by gold-catalyst
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REPRESENTATIVE PUBLICATIONS

1 Highly Regio- and Stereoselective Synthesis of Tetrasubstituted Cyclobutenes via

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