Conversion of 4-hydroxy-2-cyclopentenone derivatives into valuable fine chemicals

Dissertation

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Besonders bedanken möchte ich mich bei Herrn Prof. Dr. Oliver Reiser für die Aufnahme in seinen Arbeitskreis, die Überlassung des vielseitigen Themas, die anregenden Diskussionen und seine Unterstützung.

Meiner Frau Maria und meinen Eltern

“Ich freue mich, wenn es regnet. Denn wenn ich mich nicht freue, regnet es auch.”

Karl Valentin

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Abbreviations

Ac	acetyl
acac	acetylacetone
AL-PS	Amano lipase from *Burkholderia cepacia*
Ar	aryl
atm	atmosphere
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
BQ	benzoquinone
cat	catalyst or catalytic
CI	chemical ionization
Cy	cyclohexyl
Cyp	cyclopentyl
d	day
dba	dibenzylideneacetone
DCM	dichloromethane
DEPT	distortionless enhancement by polarization transfer
DIPEA	N,N-diisopropylethyldiamine
DMAP	4-dimethylaminopyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
dppf	1,1'-bis (diphenylphosphino)ferrocene
EA	ethyl acetate
EDC	1-ethyl-3-(3-dimethyl-aminopropyl)carbodiimide
ee	enantiomeric excess
EI	electron impact
equiv.	equivalent
er	enantiomeric ratio
ESI	electronspray ionization
Et	ethyl
FVT	flash vacuum thermolysis
GC	gas chromatography
h	hour
HOBt	1-hydroxybenzotriazole
HOMO	highest occupied molecular orbital
HPLC	high-performance liquid chromatography
HRMS	high resolution mass spectrometry
hν	light
i-Pr	*iso*-propyl
IR	infrared spectroscopy
L	undefined ligand
LDA	lithium diisopropylamide
LUMO	lowest unoccupied molecular orbital
M	molar
m-CPBA	*meta*-chloroperoxybenzoic acid
Me	methyl
min	minute
mp	melting point
MS	mass spectrometry or molecular sieves
MW	microwave
m/z	mass-to-charge ratio
n-Bu	*n*-butyl
n-Hept	*n*-heptyl
n-Hex	*n*-hexyl

NMR	nuclear magnetic resonance
n-Pent	*n*-pentyl
n-Pr	*n*-propyl
Nu	nucleophile
OTf	triflate
PE	petroleum ether
Ph	phenyl
pin	pinacolyl
Piv	pivalate
quant.	quantitative
R	arbitrary rest
R_f	retention factor
rt	room temperature
sat.	saturated
TBAB	tetrabutylammonium bromide
TBDMS	*tert*-butyldimethyl silyl
t-Bu	*tert*-butyl
TEMPO	2,2,6,6-tetramethylpiperidine 1-oxyl
TEMPO-OH	4-hydroxy-2,2,6,6-tetramethylpiperidine 1-oxyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Ts	tosyl
vs.	versus

A Introduction

1 The 2-pyrone scaffold - a widespread motif in nature and synthesis

2-Pyrone (**1**) is a six-membered unsaturated cyclic ester with similar reactivity like 1,3-dienes and lactones. The core structure is present in a broad variety of natural products found in various facets of life, e.g., bacteria, microbes, fungi, plants, marine organisms or animals.[1] Additionally, natural products containing the 2-pyrone scaffold are involved in different biological processes and display many biological activities like anti-HIV, antitumor, telomerase inhibition, antimicrobial, antifungal, cardiotonic, pheromonal, cytotoxic, neurotoxic, and phytotoxic effects.[1,2] Some prominent examples of natural products containing the 2-pyrone moiety are depicted in Figure 1.

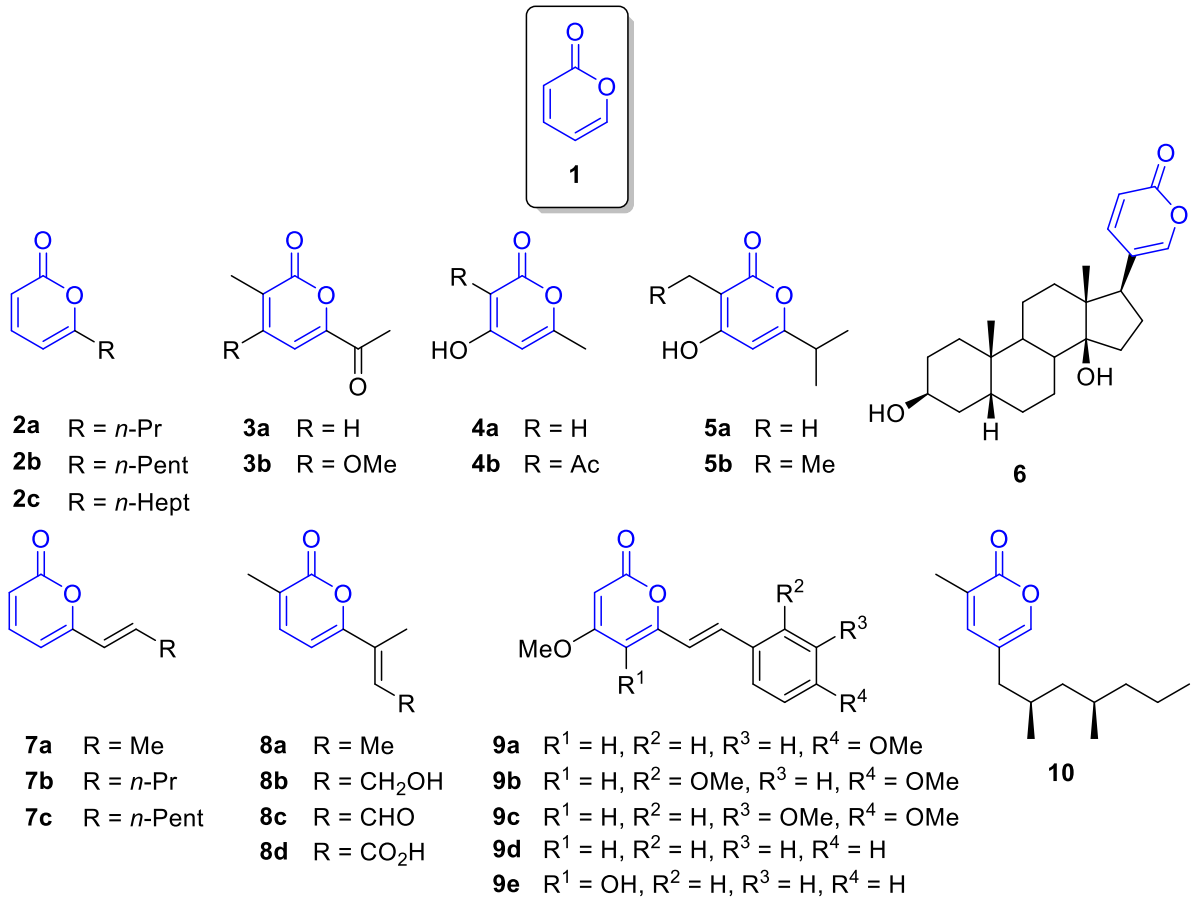


Figure 1. Natural products containing the 2-pyrone moiety.[1,3–5]

Furthermore, the high functional group density of the 2-pyrone moiety displayed over the six-membered cyclic skeleton offers outstanding opportunities for the synthesis of complex molecules due to its versatile reactivity e.g. cycloadditions, ring opening reactions or cross-coupling reactions (Figure 2).

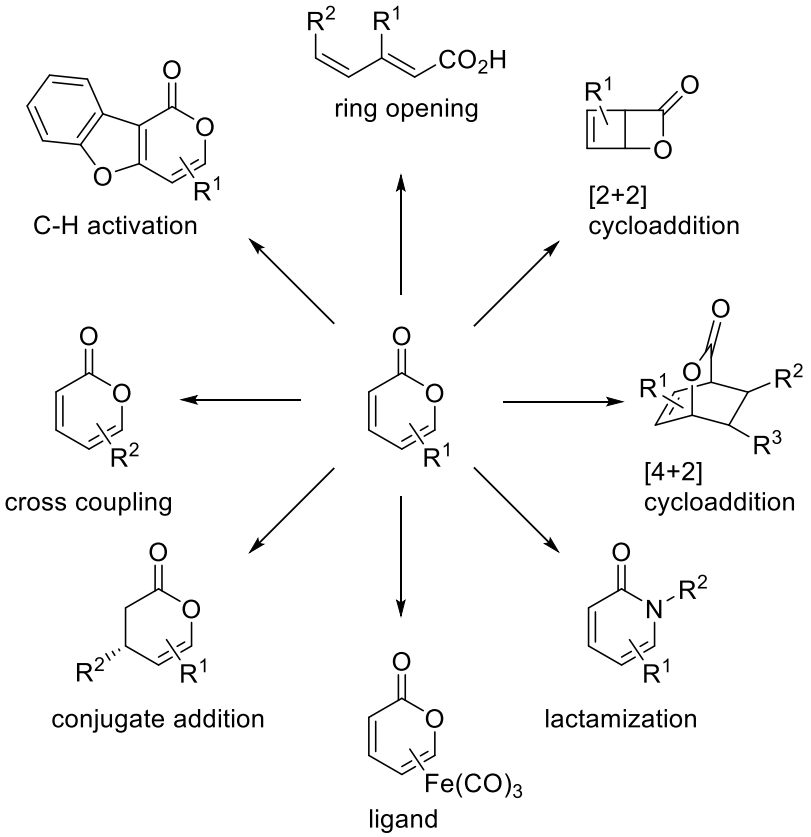


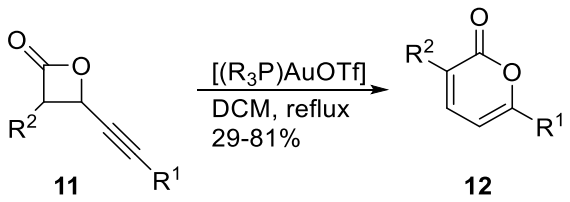
Figure 2. Reactivity of 2-pyrones.

2 Synthesis of 2-pyrones

2.1 Transition-metal-catalyzed synthesis

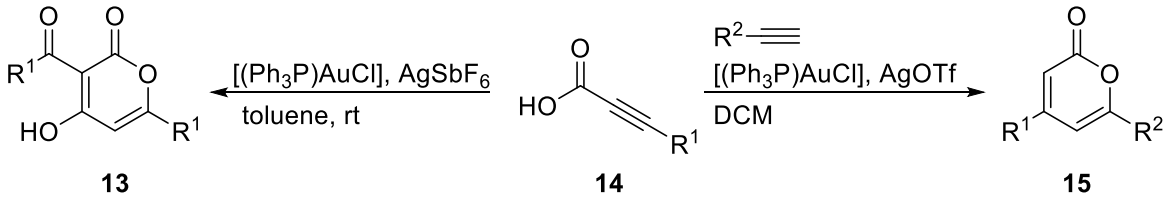
Transition-metal-catalysis provides various elegant pathways for the synthesis of complex molecules including the synthesis of 2-pyrone derivatives. Pale *et al.*[6] described a straightforward gold-catalyzed rearrangement of β-alkynyl propiolactones **11** to substituted

2-pyrones **12** (Scheme 1). The starting materials are prepared by condensation of acyl chlorides to aldehydes, providing diverse 2-pyrone derivatives in two steps.[7]



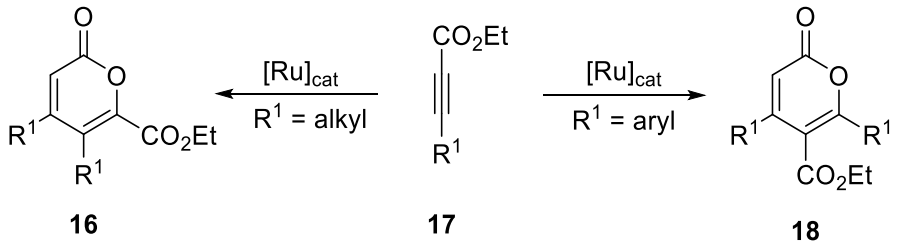
Scheme 1.Gold-catalyzed cycloisomerization to substituted 2-pyrones **12**.[6]

Schreiber *et al.*[8] investigated the gold-catalyzed dimerization of propiolic acids **14** to afford 2-pyrone derivatives **13**. After slightly changing the reactions conditions and the addition of other alkynes it was additionally possible to obtain 2-pyrones of type **15** in good yields (Scheme 2). This strategy offers a simple and efficient route to various multiple substituted 2-pyrone derivatives.



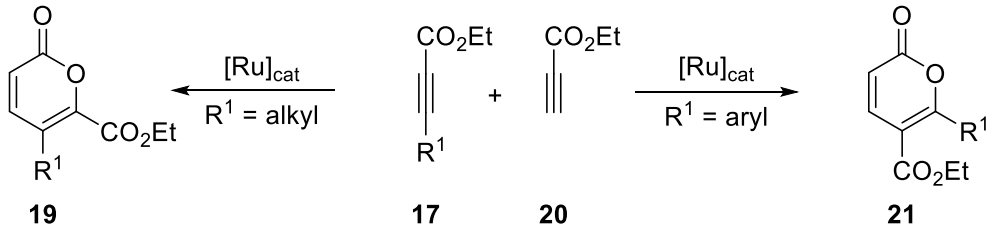
Scheme 2. Syntheses of 2-pyrones using gold-catalyzed coupling reactions.[8]

Propiolates **17** can serve as suitable starting materials for the synthesis of 2-pyrone derivatives as well. Jeganmohan *et al.*[9] presented the ruthenium-catalyzed homodimerization of propiolates **17** giving different types of 2-pyrones depending on the residue of the propiolates **17**: while alkyl substituted ones furnish mainly **16**, aryl substituted propiolates deliver **18** (Scheme 3).



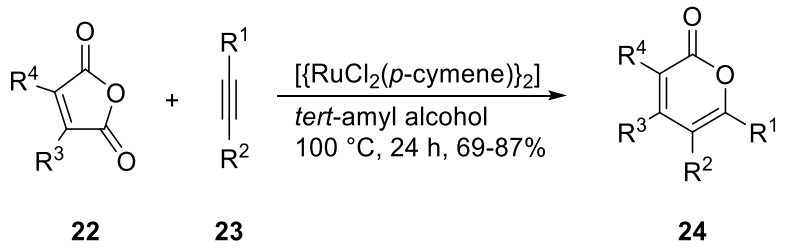
Scheme 3. Homodimerization of substituted propiolates **17**.[9]

Similar behavior was observed after addition of a terminal alkyne **20**, affording 5,6-substituted 2-pyrones of type **19** or **21** depending on the substrates used (Scheme 4).



Scheme 4. Heterodimerization of substituted propiolates **17**.[9]

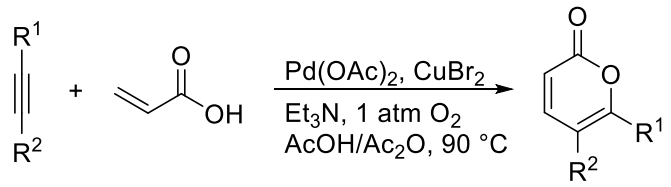
Boruah *et al.*[10] described the ruthenium-catalyzed decarbonylative addition reaction of anhydrides **22** with alkynes **23** to arrive at substituted 2-pyrones **24**. The decarbonylative addition is highly regioselective, a broad substrate scope is covered, and good yields were obtained (Scheme 5).



22 **23** **24**

Scheme 5. Ruthenium-catalyzed decarbonylative addition.[10]

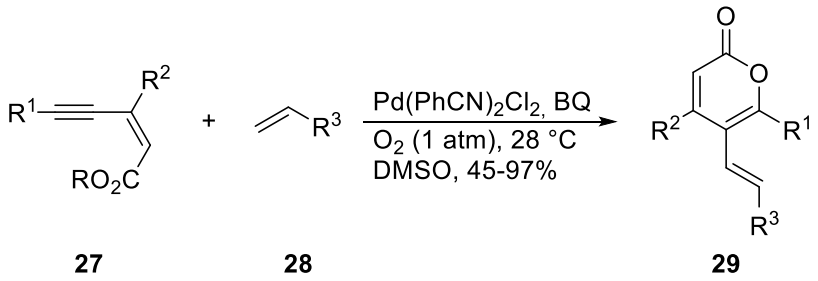
Additionally, palladium-catalysis is widely used for the synthesis of 2-pyrones. Jiang *et al.*[11] used palladium-catalysis for the oxidative annulation of internal alkynes **23** with acrylic acid **25** under mild conditions using O_2 as the oxidant. The process yields 5,6-substituted 2-pyrones **26** with high regioselectivity in good to excellent yields (Scheme 6).



23 **25** **26**

Scheme 6. Palladium-catalyzed oxidative annulation.[11]

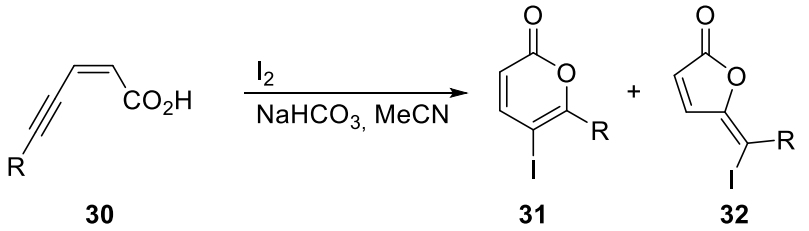
In addition to this, Loh *et al.*[12] reported the palladium-catalyzed difunctionalization of internal alkynes via 6-*endo* cyclization and alkenylation of enynoates **27**. Various enynoates **27** and electron-deficient alkenes **28** were utilized for the syntheses of 2-pyrone derivatives **29**. The reaction is highly regioselective, compatible with many functional groups and good yields were obtained (Scheme 7).



Scheme 7. Highly regioselective 6-*endo* cyclization and alkenylation of enynoates.[12]

2.2 Transition-metal-free synthesis

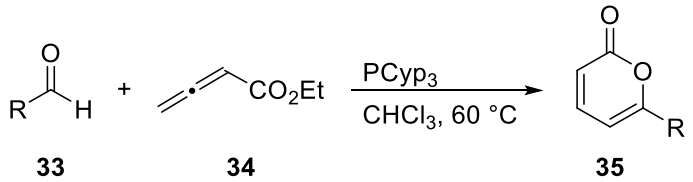
Since its discovery, the iodolactonization has been one of the most efficient ways to synthesize lactones.[13] In 2001, Rossi *et al.*[14] used this strategy for the synthesis of 2-pyrone derivatives **31** starting from acids **30**, which themselves are easily prepared by Sonogashira coupling. Butenolides **32** are observed as byproducts, depending on the reactions conditions 2-pyrones **31** are still the major products (Scheme 8). The halogenated 2-pyrones **31** can be used for further reactions, e.g., cross-coupling reactions or dehalogenation reaction to arrive at 6-substituted 2-pyrones.



Scheme 8. 2-Pyrone synthesis via iodolactonization.[14]

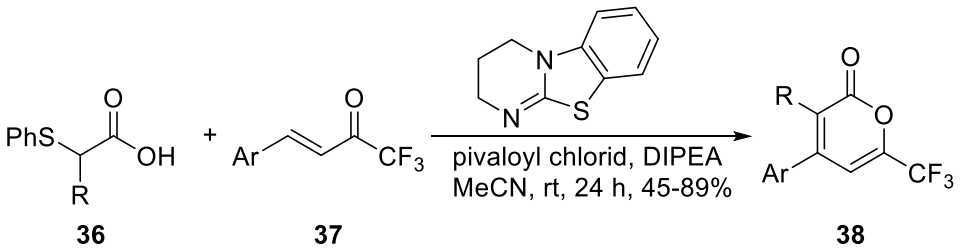
Kwon *et al.*[15] reported a phosphine-catalyzed synthesis of 6-substituted 2-pyrones starting from commercially available aldehydes **33** and ethyl allenoate **34**. Sterically demanding

trialkylphosphines are required to shift the equilibrium toward the *E*-isomeric zwitterion to form 2-pyrones **35**. Various aldehydes such as aromatic or aliphatic ones undergo the transformation in moderate to excellent yield (Scheme 9).



Scheme 9. Phosphine-catalyzed synthesis of 2-pyrones **35**.[15]

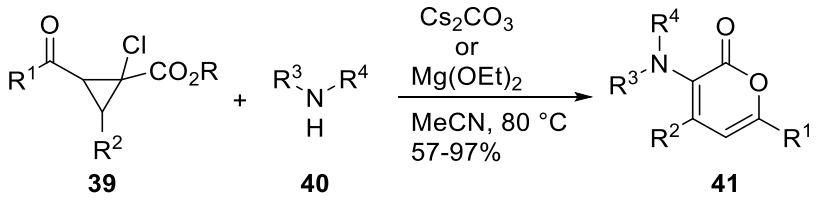
A successful development of an organocatalyzed synthesis was described by Smith *et al.*[16] for the synthesis of substituted 2-pyrone derivatives **38**. A broad variety of di- and trisubstituted 2-pyrones were realized (including biologically relevant compounds) with high selectivity and yield via an isothiourea-mediated Michael addition/lactonization/thiol elimination cascade sequence starting from phenylthio acetic acids **36** and α,β-unsaturated trifluoromethyl ketones **37** (Scheme 10).



Scheme 10. Isothiourea-mediated synthesis of trifluoromethyl substituted 2-pyrones **38**.[16]

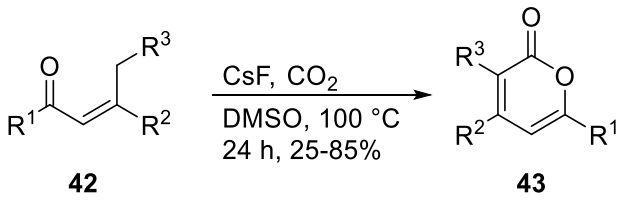
Moreover, cyclopropanes are known as useful synthetic precursors in organic chemistry. Gong *et al.*[17] developed a methodology for the synthesis of 2-pyrone derivatives **41** using cyclopropanes **39** and amines **40** as starting materials. This base-promoted domino reaction

provides a simple strategy for the transition-metal-free construction of the 2-pyrone skeleton in high yields (Scheme 11).



Scheme 11. 2-Pyrone synthesis starting from cyclopropanes **39**.[17]

The carboxylative cyclization of substituted propenyl ketones **42** using carbon dioxide offers an additional facile transition-metal-free variant for the synthesis of 2-pyrones **43** (Scheme 12). Especially, carbon dioxide is non-toxic and easily obtained from renewable resources. Therefore it is a highly interesting reagent in the meanings of green chemistry.



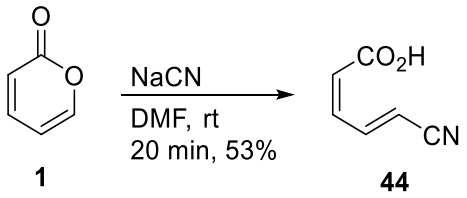
Scheme 12. Carboxylative cyclization of substituted propenyl ketones **42** using CO_2.[18]

3 Reactivity of 2-pyrones

3.1 Ring opening

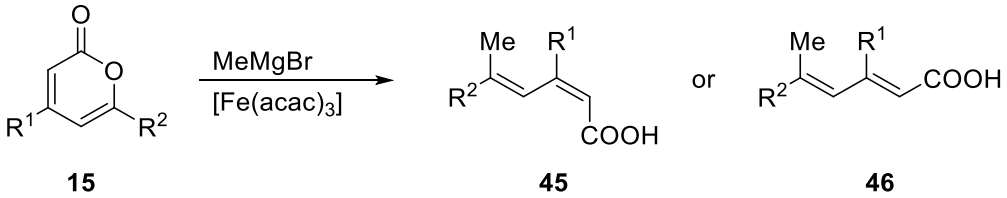
2-Pyrones possess properties of unsaturated lactones, therefore they undergo hydrolysis by aqueous alkali to yield the corresponding ring opening products. In general, nucleophiles are added to the 2-pyrone scaffold either at the carbonyl group (e.g. Grignard reagents) or in a 1,4-

or a 1,6-addition fashion under ring opening.[19] The latter is true for the addition of cyanide to 2-pyrone (**1**), which was already described in 1965 by Vogel *et al.*[20] (Scheme 13).



Scheme 13. Nucleophilic ring opening of 2-pyrone (**1**).[20]

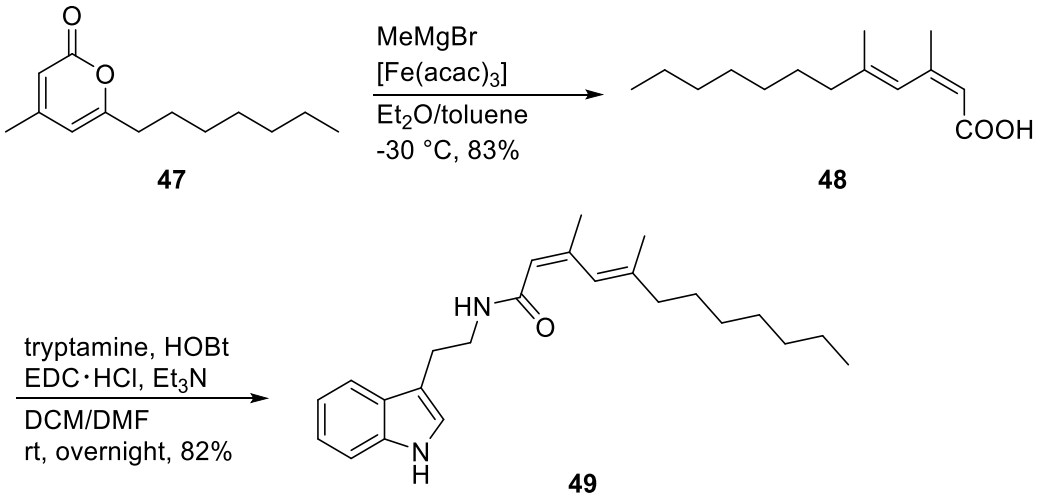
Nowadays, chemists are particularly interested in ring opening reactions of the 2-pyrone moiety since the resulting products are highly valuable compounds for organic synthesis. In 2013, Fürstner *et al*. reported an unusual behavior of Grignard reagents in the reaction with 2-pyrone derivatives under iron catalysis (Scheme 14).[21]



Scheme 14. Iron-catalyzed ring opening reaction.[21]

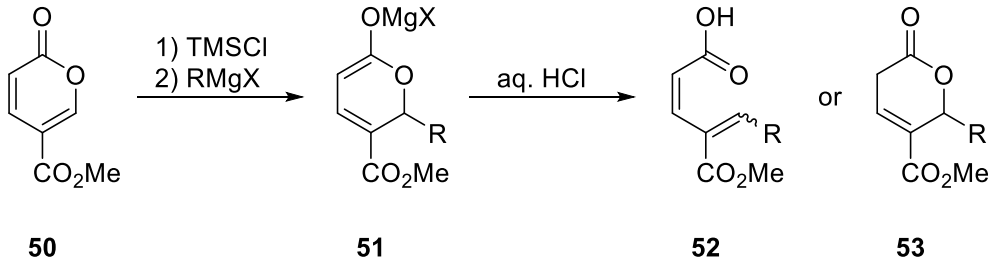
Iron catalysis superseded the conventional reactivity of the Grignard reagent and turned it into a cross-coupling process with the lactone moiety as a nontraditional leaving group. This offers access to di-unsaturated acid derivatives, which are of high importance for the synthesis of many natural products. Additionally, the stereochemistry of the acid derivatives (2*Z*,4*E* vs. 2*E*,4*E*) can be controlled by varying the temperature before work up, and the reaction is compatible with a multitude of functional groups. With this strategy in hand, the synthesis of cytotoxic tryptamine derivative Granulatamide B **49**, isolated from the gorgonian

Eunicella granulate, was accomplished (Scheme 15). Additionally, a Pateamine A analogue with in vivo anticancer activity was developed by the same working group using the iron-catalyzed 2-pyrone ring opening as a key step.[22]



Scheme 15. Synthesis of Granulatamide B **49**.[21]

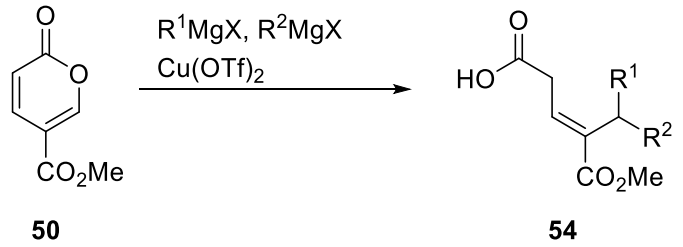
Concomitantly, Dechoux *et al.*[23] demonstrated a highly regio-, chemo- and stereoselective synthesis of conjugated 2*Z*,4*Z* or 2*Z*,4*E* dienoic acids **52**. Herein, the nature of the Grignard reagent is of crucial importance for the outcome of the reaction. With alkenyl, alkynyl and aromatic Grignard reagents mainly dienoic acid **52** formation was observed, while with alkyl Grignard reagents unsaturated lactones **53** were obtained. Furthermore, the stereochemical outcome of the reaction for the dienoic acids was explained by thermodynamic control masking the kinetic torquoselectivity (Scheme 16).



50 **51** **52** **53**

Scheme 16. Stereoselective synthesis of conjugated dienoic acids **52**.[23]

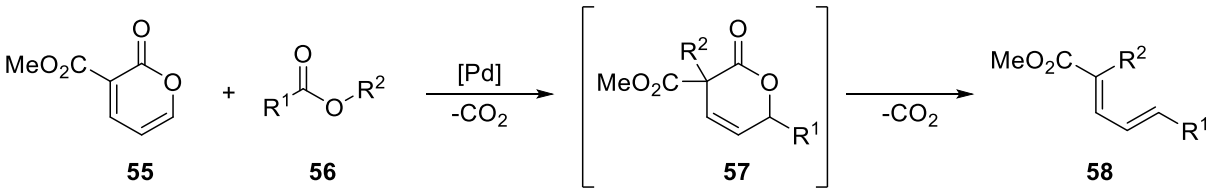
In addition to this, Dechoux *et al.*[24] developed a route for the synthesis of β,γ-unsaturated carboxylic acids **54** with highly regio-, chemo- and stereoselectivity starting from (±)-**50** by employing a one-pot double alkyl-alkyl or alkyl-hydride 1,6-addition (Scheme 17).



50 **54**

Scheme 17. Metal-catalyzed addition of two Grignard reagents to 2-pyrone **54**.[24]

In contrast, the palladium-catalyzed double-decarboxylative addition provides an entirely different strategy for the ring opening reaction of the 2-pyrone scaffold yielding conjugated dienoic esters **58**.[25] Dienoic esters **58** are known as useful compounds for organic synthesis, and the only byproduct of the reaction is carbon dioxide (Scheme 18).

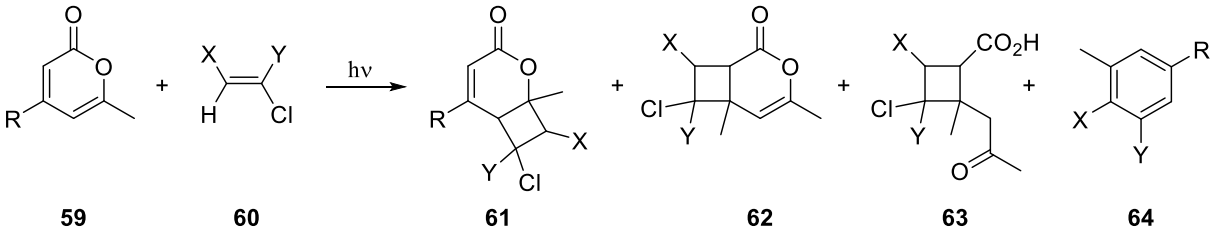


Scheme 18. Double-decarboxylative addition to 2-pyrone **55.**[25]

3.2 [2+2] Cycloaddition

3.2.1 Intermolecular [2+2] cycloaddition

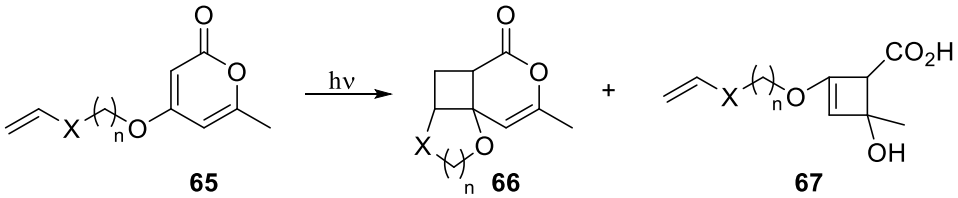
There are some examples for the light-induced intermolecular [2+2] cycloaddition with 2-pyrones known in the literature, but all of them face the same general problems: The low selectivity between the two double bonds of the 2-pyrone moiety and the competing intramolecular [2+2] cycloaddition or [4+2] cycloaddition. Therefore, in most cases, low yields and several byproducts are obtained. All products obtained in the [2+2] cycloaddition of 2-pyrones **59** and alkene **60** by Tanabe *et al.*[26] are depicted in Scheme 19.



Scheme 19. Intermolecular [2+2] cycloaddition.[26]

3.2.2 Intramolecular [2+2] cycloaddition

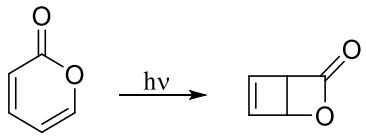
Due to precoordination of the reactants, intramolecular reactions show higher efficiency. The intramolecular [2+2] cycloaddition of **65** gave site- and regiospecific adducts in excellent yields dependent on the length of the side chain (Scheme 20).[27] However, byproduct **67**, arising from a prior intramolecular [2+2] cycloaddition of the 2-pyrone ring and subsequent hydrolysis was obtained.



65 **66** **67**

Scheme 20. Intramolecular [2+2] cycloaddition with the side chain.[27]

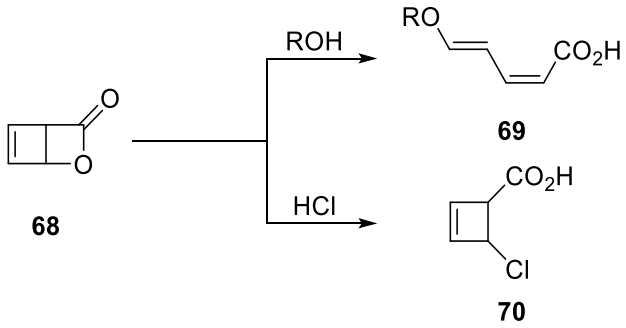
The intramolecular [2+2] cycloaddition of the 2-pyrone scaffold itself offers outstanding possibilities for the synthesis of many different valuable chemicals. Already in 1964, the intramolecular [2+2] cycloaddition of **1**, which provides access to cyclobutadiene derivatives was described by Corey *et al.*[28] (Scheme 21).



1 **68**

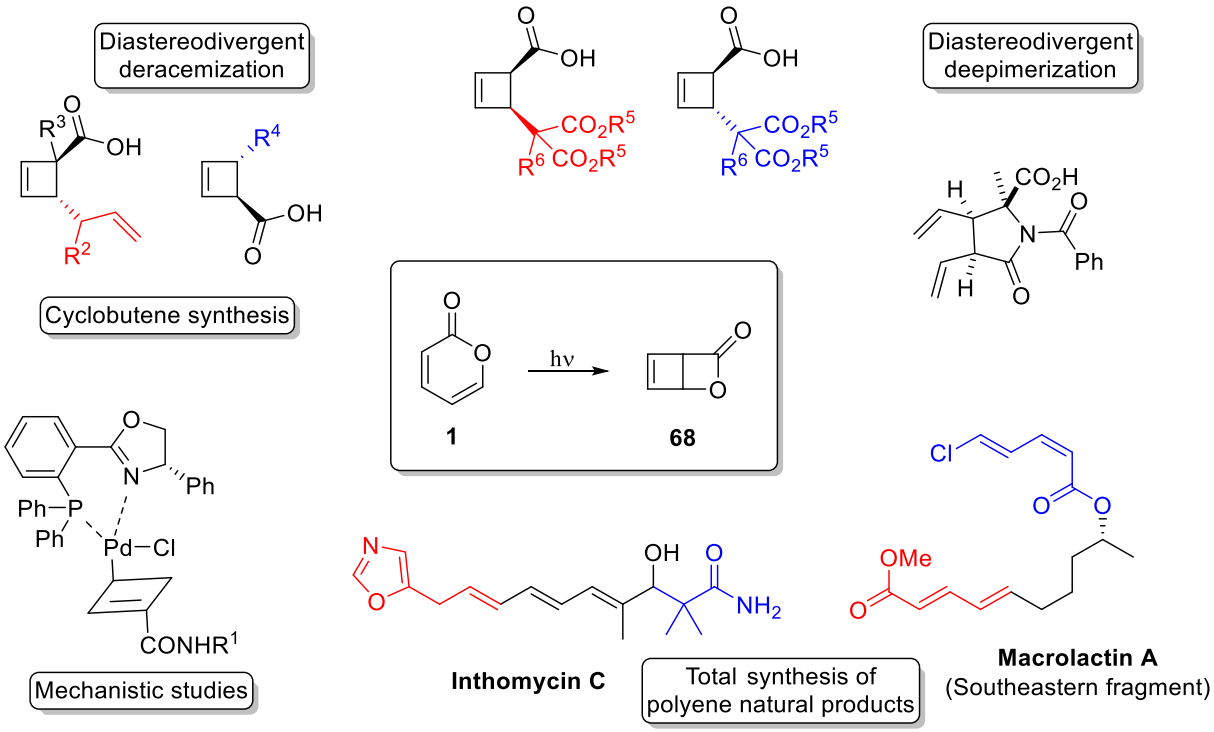
Scheme 21. Intramolecular [2+2] cycloaddition.[28]

The synthetic potential of **68** was used first by McKendry *et al.*[29] in 1969, for the synthesis of (2*Z*,4*E*)-alkoxypentadienoic acids **69** and chlorocyclobutene carboxylic acids **70** (Scheme 22).



Scheme 22. Synthesis of dienoic acid **69** and chlorocyclobutene carboxylic acids **70**.[29]

In the following years, the chemistry of **68** did not attract much attention until 2010, when Maulide *et al*.[30] rediscovered the potential of **68** and since then much fascinating chemistry has been done with it (Scheme 23).[31]



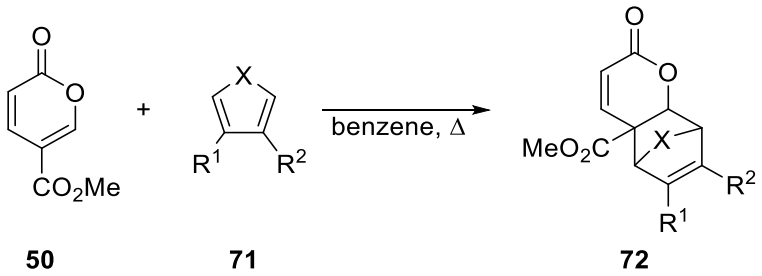
Scheme 23. Versatile chemistry of **68**.[31]

The palladium-catalyzed allylic alkylation of **68** offers access to functionalized cyclobutenes. Several nucleophiles were added such as malonate anions and azlactones.[32] The obtained products are highly functionalized mono- and bicyclic building blocks for the synthesis of complex compounds. Additionally, high levels of diastereoselectivity were achieved, and the transfer of the methodology to an asymmetric version led to the discovery of a family of highly enantioselective, diastereodivergent, catalytic processes. This enables access to each of the four stereoisomeric products starting from a racemic lactone and was rationalized by mechanistic studies. The received cyclobutenes can be opened by electrocyclic ring-opening reactions giving rise to diene and polyene frameworks, which themselves were then used for the synthesis of polyenic natural products.[31]

3.3 [4+2] Cycloaddition

The Diels-Alder reaction offers an atom-economical and straightforward route for the synthesis of complex structures of defined geometry while producing nearly no waste via the reaction of a diene and a dienophile.

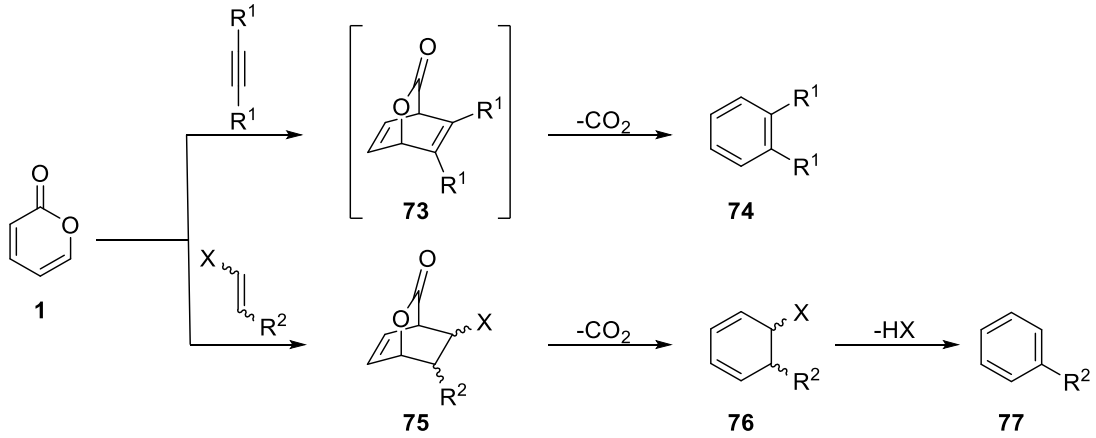
Interestingly, 2-pyrones are known to act as both, diene and dienophile in [4+2] cycloadditions. However, just a few examples of 2-pyrone acting as dienophile are reported in the literature and an electron withdrawing substituent in 5-position is necessary. The first reported [4+2] cycloadditions with a 2-pyrone derivative **50** serving as dienophile is shown in Scheme 24.[33]



50 **71** **72**

Scheme 24. 2-Pyrone **50** as dienophile in a [4+2] cycloaddition.[33]

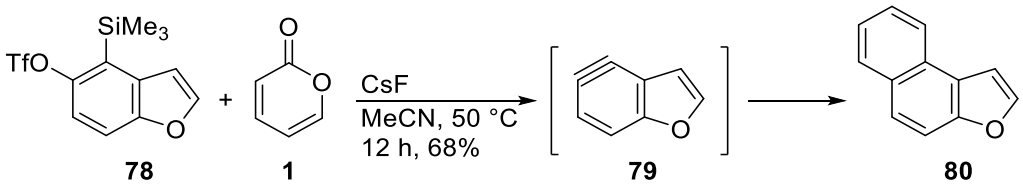
The 2-pyrone scaffold containing a cyclic diene structure is classically known as active diene component in [4+2] cycloadditions, although the 2-pyrones moiety also possesses aromatic character. The [4+2] cycloaddition of 2-pyrone (**1**) with alkynes provides highly strained bicyclooctadiens **73**, which easily form aromatic products **74** after extrusion of CO_2. The cycloadducts **75** generated with alkenes are generally more stable and can be isolated in some cases. These structurally and stereochemically rich compounds can be used as synthetic intermediates. After extrusion of CO_2 dihydrobenzenes **76** are obtained, and additional elimination then leads to aromatic compounds **77** as well (Scheme 25).[34]



Scheme 25. 2-Pyrone (**1**) as diene in [4+2] cycloadditions.[34]

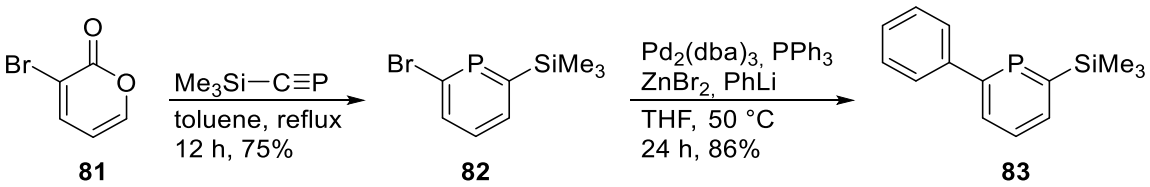
Due to its diverse opportunities for organic synthesis,[34,3] 2-pyrones have frequently been used as dienes in [4+2] cycloadditions, ever since Diels and Alder[35] published that 2-pyrones could act as diene in [4+2] cycloadditions in 1931. The [4+2] cycloadditions of 2-pyrones are mainly used for the synthesis of aromatic and heteroaromatic compounds or natural products. Therefore, one recent example for every mentioned usage is given in the following.

Garg *et al.*[36] developed a methodology that offers access to oxygen-containing strained alkynes **79**, demonstrating their chemical potential (among others) via a [4+2] cycloaddition with 2-pyrone (**1**). With this strategy in hand, it was possible to introduce an additional benzene ring to oxygen-containing strained alkynes (Scheme 26). The same group already used similar strategies for nitrogen-containing strained alkynes before.[37]



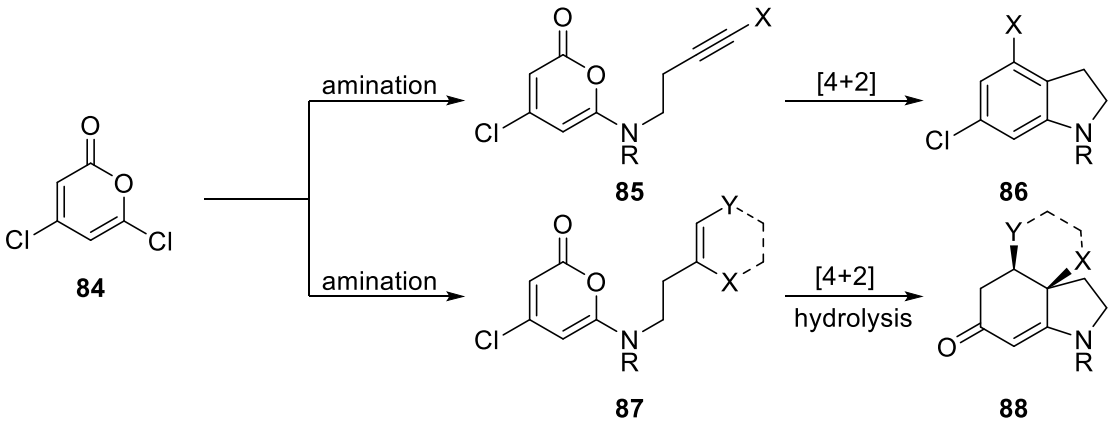
Scheme 26. [4+2] cycloaddition of 4,5-Benzofuranyne **79** with 2-pyrone (**1**).[36]

Additionally, the [4+2] cycloaddition provides a straightforward way for the synthesis of heteroaromatic compounds such as phosphines. Müller *et al.*[38] developed a convenient route to functionalized phosphines via [4+2] cycloaddition of 3-bromo-2-pyrone (**81**) with a phosphaalkyne and using Negishi cross-coupling to introduce a phenyl substituent into the final product **83** (Scheme 27).



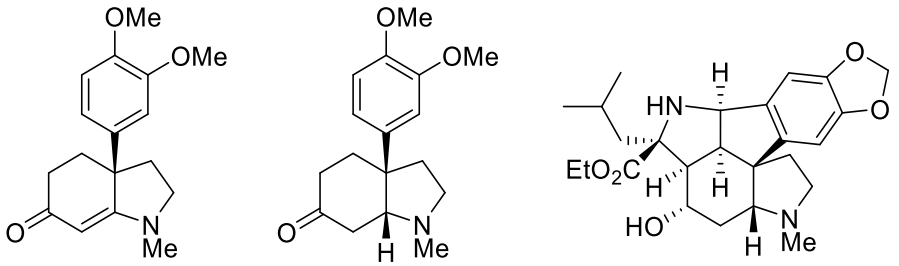
Scheme 27. Synthesis of functionalized phosphinines.[38]

Synder *et al.*[39] utilized the potential of 2-pyrone derivatives for the elegant preparation of indolines and hydroindolines. Starting from 2-pyrone **84**, an amine was introduced containing either an alkyne or an alkene moiety. The following intramolecular [4+2] cycloaddition of **85** or **87** then afforded indolines **86** and hydroindolines after extrusion of CO_2. Additionally, hydroindolines could be hydrolyzed to obtain structure **88**, which is present in a broad variety of natural products (Scheme 28).



Scheme 28. [4+2] cycloaddition routes to indolines and hydroindolines.[39]

Finally, this strategy was employed for the total synthesis or formal total synthesis of three natural products: Δ7-mesembrenone (**89**), mesembrine (**90**) and gracilamine (**91**), depicted in Scheme 29.

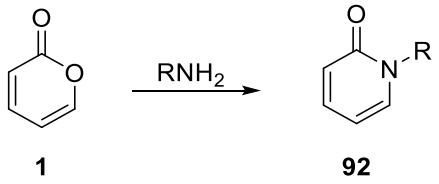


Scheme 29. Natural products Δ7-mesembrenone (**89**), mesembrine (**90**) and gracilamine (**91**).[39]

3.4 Lactamization

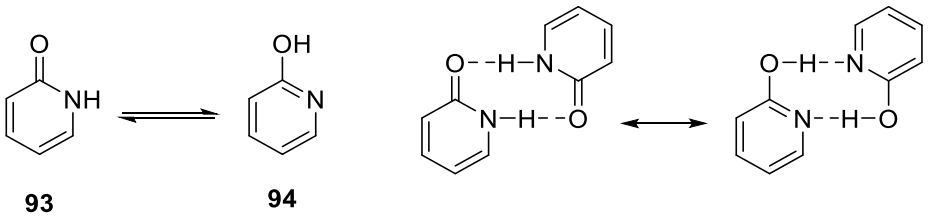
2-Pyridones are a widespread motif in nature, and due to their versatile reactivity, they are useful materials for the synthesis of complex molecules and additionally they are known to act as a ligand in coordination chemistry.[40,41–44]

2-Pyrones are easily converted into the corresponding lactams by reaction with ammonia to arrive at the N-unsubstituted 2-pyridones **93**, while the reaction with primary amines yields N-substituted 2-pyrone derivatives **92** (Scheme 30).[45]



Scheme 30. Lactamization of 2-pyrone (**1**).[45]

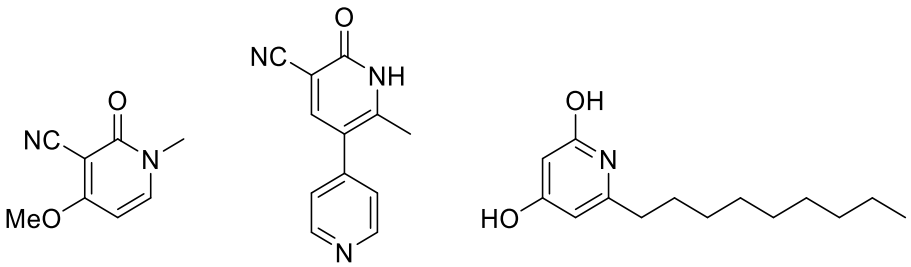
2-Pyridone derivatives are known to act as a diene in [4+2] cycloadditions similar to 2-pyrones.[34] 2-Pyridone exists as two tautomers, which can form dimers similar to the base-pairing in DNA or RNA (Scheme 31).[46]



93 **94**

Scheme 31. Tautomerization and dimerization of 2-pyridone **93**.[46]

As shown before, many procedures for the synthesis of 2-pyrones are available, and due to the facile transformation of the latter into 2-pyridones **92**, these procedures can serve for the synthesis of 2-pyridones **92** as well. The transfer of 2-pyrones in 2-pyridones is frequently used in research, especially in the search for new bioactive substances. In many cases, substances containing the 2-pyridone motif exhibit interesting activities such as antifungal, antibacterial, insecticidal and cytotoxic activity, selected examples are depicted in Scheme 32.[41–44]



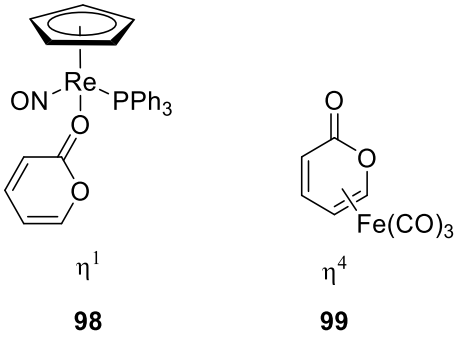
95 **96** **97**

Scheme 32. Bioactive 2-pyridone derivatives.[41–44]

3.5 Ligand

Catalysis is one of the main interests in chemistry, and there is an ongoing search for new strategies and catalysts. As the 2-pyrone scaffold offers versatile opportunities for the complexation of metals it served as ligand in many different complexes with various metals,

e.g., Fe,[47] Os,[48] Co,[49] Re[50] or Mo.[51] In Scheme 33, 2-pyrone is illustrated as a ligand in two different complexes possessing different hapticity: in **98** a η^1-2-pyrone and in **99** a η^4-2-pyrone ligand is shown.



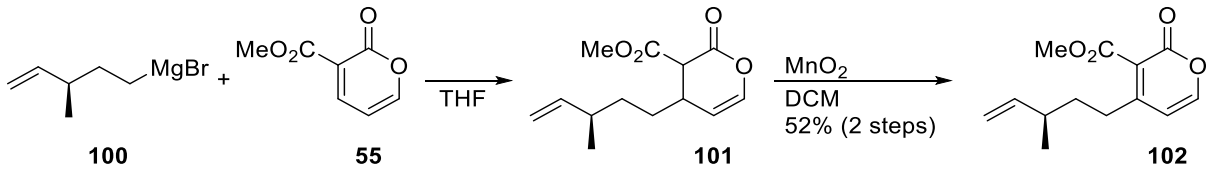
Scheme 33. 2-Pyrone (**1**) as versatile ligand.[47,50]

Furthermore, some complexes containing a 2-pyrone ligand show interesting properties. Complex **99** exhibits excellent CO-releasing properties, its intrinsic stability influences the extent and rate of CO release revealing highly interesting bioactive properties.[52] This behavior can be affected by choice of substituents at the 2-pyrone scaffold.[53]

3.6 Conjugate addition

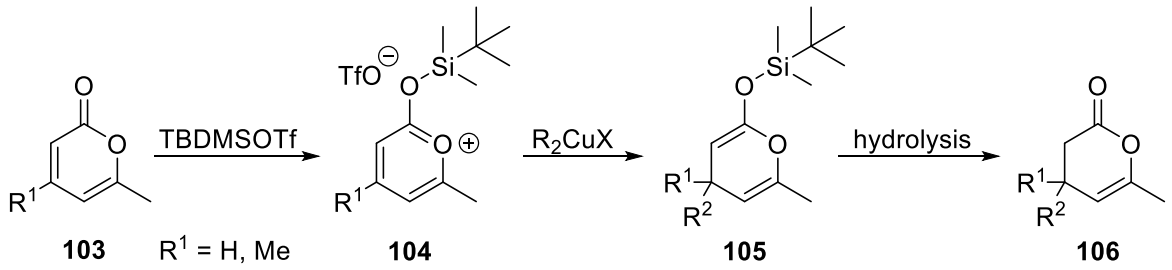
The 2-pyrone moiety contains an α,β-unsaturated carbonyl group, which offers the opportunity for conjugate addition. The resulting 3,4-dihydro 2-pyrones have attracted much interest due to their biological activities and their use in synthesis.[54] Furthermore, the conjugate addition was used for the introduction of substituents into the 2-pyrone ring. During the synthesis of Lasalocid A, Ireland *et al.*[55] investigated the conjugate addition of Grignard reagents in the absence of any copper source. Surprisingly, the conjugate addition of organocuprates failed

before. 2-Pyrone **55** underwent conjugate addition with **100** and after MnO_2 promoted dehydrogenation **102** was obtained in 52% yield over 2 steps (Scheme 34).



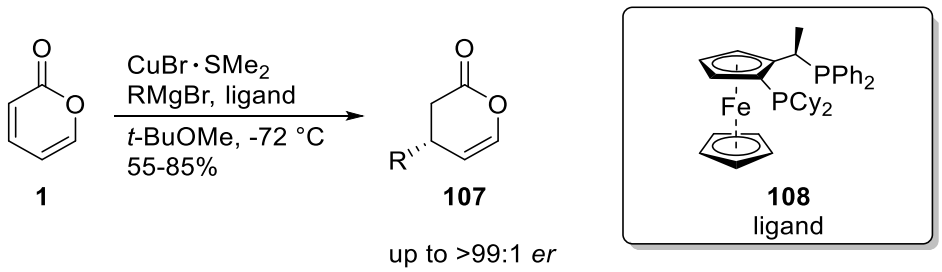
Scheme 34. Conjugate addition of Grignard reagent.[55]

Akiba *et al.*[56] enhanced the reactivity of 2-pyrones towards conjugate addition with organocopper reagents by silylation using *tert*-butyldimethylsilyl triflate to yield the corresponding pyrylium salt **104**. After silylation, several substituents were introduced by conjugate addition. This reaction was affected by the steric hindrance of the organocopper reagents. Finally, the silylated adducts **105** could be hydrolyzed to afford the substituted 3,4-dihydro 2-pyrones **106** (Scheme 35).



Scheme 35. Conjugate addition of organocopper reagents to pyrylium salt **104**.[56]

In 2013, Feringa *et al*. developed the asymmetric conjugate addition of alkyl Grignard reagents to 2-pyrones opening access to chiral 3,4-dihydro 2-pyrones **107**. The conjugate addition is catalyzed by copper using a ferrocenyl-based bisphosphine ligand **108**. The used catalytic system provided excellent enantioselectivity (up to >99:1 *er*) with various Grignard reagents (Scheme 36).

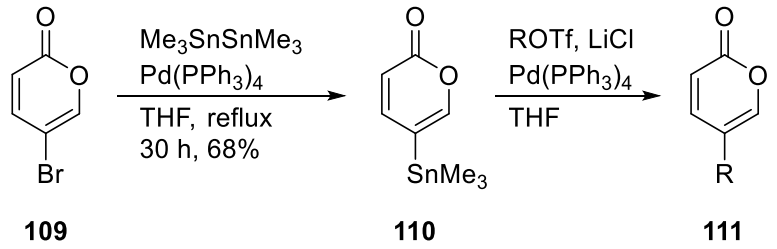


Scheme 36. Asymmetric conjugate addition of alkyl Grignard reagents to 2-pyrones.[54]

3.7 Cross-coupling

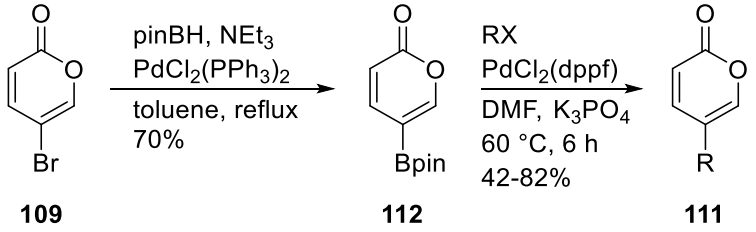
The synthesis of 2-pyrone derivatives is of high interest, and cross-coupling reactions offer an important and routinely applied option for their synthesis. The 2-pyrone moiety exhibits both aromatic and alkenic chemical properties. In cross-coupling reactions, the 2-pyrone scaffold is used as the organometallic nucleophilic component or the halide/pseudohalide electrophilic component.

2-Pyrones are used in combination with various metals, Meinwald *et al.*[57] investigated the synthesis of 5-substituted 2-pyrones **111**. Their studies showed that the synthesis of 5-substituted 2-pyrones gives higher yields when using organotin reagent **110** and coupling it with enol triflates, rather than using bromide **109** and transfer it to the corresponding 5-substituted 2-pyrones via the cross-coupling reaction with organotin compounds (Scheme 37). Additionally, this concept was proven for 3-bromo-2-pyrone giving rise to 3-substituted 2-pyrones in the same study.



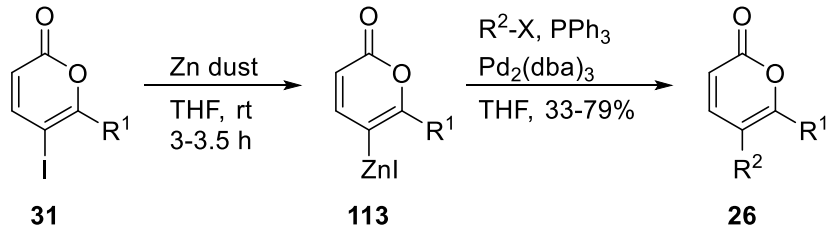
Scheme 37. Reaction of 5-trimethylstannyl-2-pyrone **110**.[57]

In an analogous manner, the 2-pyrone-5-boronate **112** was synthesized by reacting bromide **109** with pinacolborane by Jones *et al*.[58] The Suzuki coupling of **112** with various aryl and heteroaryl halides or triflates provided 5-aryl- or 5-heteroaryl-2-pyrones in good yields (Scheme 38). The same work group also developed a high yielding route to bufadienolide type steroids by using this strategy.[59]



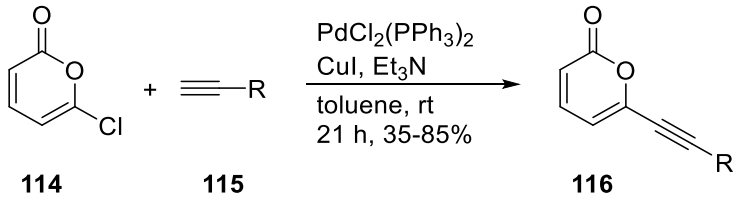
Scheme 38. Suzuki coupling of 2-pyrone **112**.[58]

Rossi *et al.*[60] showed the palladium-catalyzed reaction of 5-iodozinc-2-pyrones **113** with various organic electrophiles. The required iodides **31** are received via iodolactonization as discussed earlier. Afterward, the iodides **31** are transferred into the corresponding organozinc iodides **113** (Scheme 39). Additionally, hydrolysis of the organozinc iodides **113** allows the facile synthesis of 6-substituted 2-pyrones.



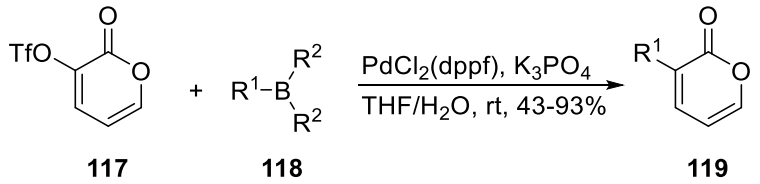
Scheme 39. Reaction of 5-iodozinc-2-pyrones **113**.[60]

Additionally, halides or pseudohalides of different 2-pyrones are frequently used in palladium-catalyzed cross-coupling reactions, offering facile access to valuable substituted 2-pyrones. Rossi *et al.*[61] investigated the Sonogashira coupling of chloride **114** and different alkynes **115** (Scheme 40). Additionally, 4-halogenated 2-pyrones were used under Sonogashira coupling conditions to introduce substituents in the 2-pyrone scaffold.[62]



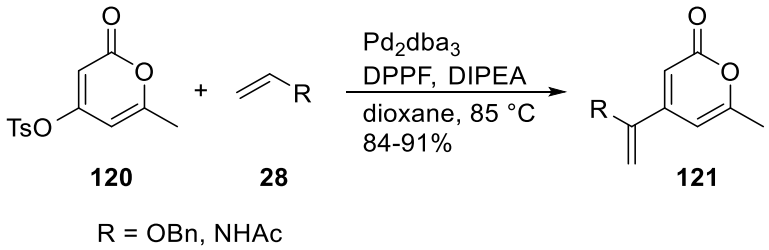
Scheme 40. Sonogashira coupling of 2-pyrone **114**.[61]

Furthermore, Suzuki coupling of 2-pyrone triflate **117** with various boron reagents resulted in the desired 3-substituted-2-pyrones **119**. The strategy developed by Maulide *et al.*[63] offers a facile opportunity for the rapid synthesis of different 3-substituted 2-pyrones on multigram scale (Scheme 41). Similarly, the Suzuki coupling of 4-bromo 2-pyrones with arylboronates proceeds in excellent yields.[64] It was even possible to switch to the more affordable nickel catalysis in the reaction of 4-tosyl 2-pyrones with arylboronates, giving rise to 4-substituted 2-pyrones.[65]



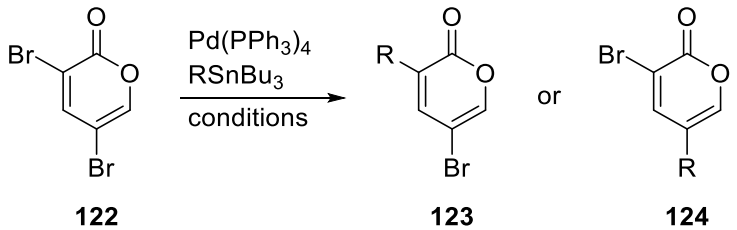
Scheme 41. Suzuki coupling of 2-pyrone (±)-**117**.[63]

Tosylated 2-pyrone **120** also reacted in a Heck coupling with enamides and butyl vinyl ether to yield the expected 2-pyrone **121** in excellent yields (Scheme 42).[66]



Scheme 42. Heck coupling of 2-pyrone **120**.[66]

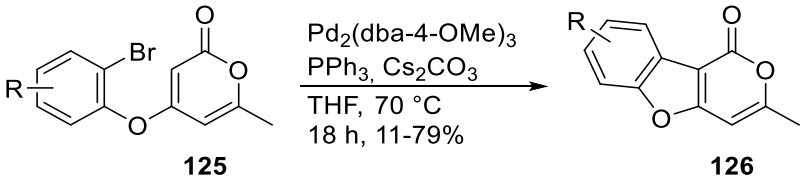
Cho *et al.*[67] developed the regioselective Stille coupling of 3,5-dibromo-2-pyrone **122** with various stannanes. Depending on the reaction conditions, it was possible to form the desired isomer nearly exclusively (Scheme 43).



Scheme 43. Regioselective Stille coupling of 3,5-dibrome-2-pyrone **122**.[67]

3.8 C-H activation

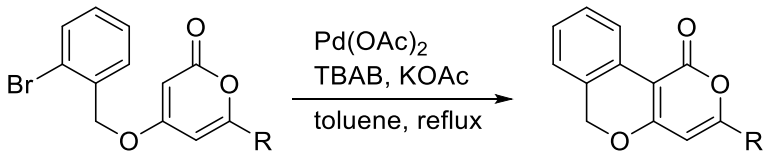
While cross-coupling reactions offer a versatile way for introducing substituents into the 2-pyrone scaffold, they also require suitable prefunctionalization. Therefore, the appropriate C-H activation of less functionalized substrates is an even more efficient strategy. In 2010, Fairlamb *et al.*[68] developed the first synthetic methodology for the catalytic C-H functionalization of 2-pyrones. The intramolecular palladium-catalyzed reaction proceeds regioselectively at the 3-position of the 2-pyrone moiety to yield **126** (Scheme 44).



125 **126**

Scheme 44. Palladium-catalyzed regioselective C–H functionalization of 2-pyrone **125**.[68]

The same work group expanded the scope for the intramolecular reaction by varying the length of the side chain. By changing the reaction conditions, they were also able to improve the system so that no phosphine ligands are necessary anymore (Scheme 45).[69]

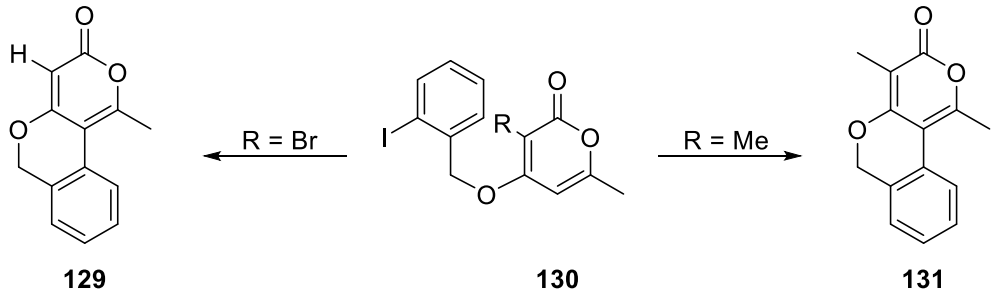


127 **128**

Scheme 45. C–H functionalization of 2-pyrone **127**.[69]

Interestingly, if the 3-position is blocked, e.g., with a methyl group cyclization occurs at the 5-position of the 2-pyrone in excellent yields. Surprisingly, if 3-bromo 2-pyrone is used,

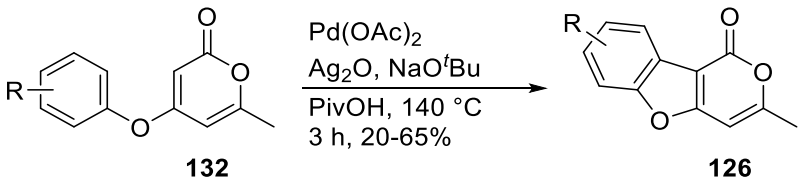
cyclization occurs also at the 5-position, but an additionally hydrodebromination process is observed in 3-position to yield **129** (Scheme 46).



129 **130** **131**

Scheme 46. Reactivity towards different blocking substituents in 3-position.[69]

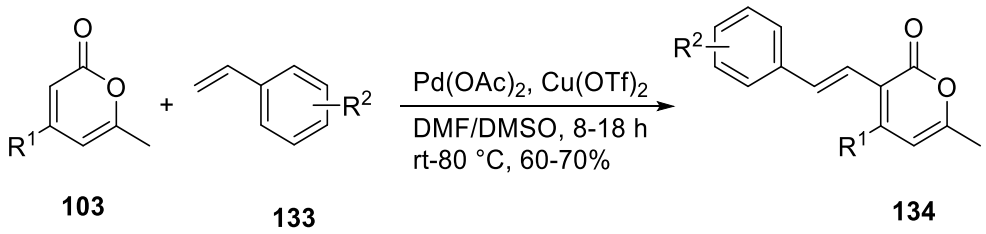
McGlacken *et al.*[70] investigated the double C-H activation of **132** without any activating group. Their developed synthetic route offers simple access to cyclized products of type **126** with excellent regioselectivity (Scheme 47).



132 **126**

Scheme 47. Cyclization of 2-pyrones **132** via a double C-H activation.[70]

In addition to this, Yousuf *et al.*[71] developed an intermolecular approach for the C-H activation of 2-pyrone derivatives in 3-position without using an activating group (Scheme 48).



Scheme 48. C-H activation of 2-pyrone derivatives and intermolecular C-C coupling.[71]

The reaction proceeds with high regioselectivity and broad substrate scope, opening facile access to potentially useful 2-pyrone derivatives **134**.

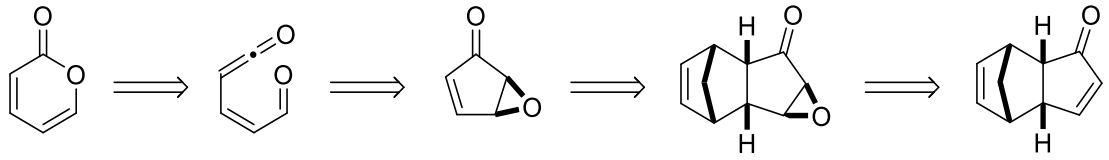
B Main Part

1 Synthesis of 2-pyrones starting from renewable resources

1.1 Introduction

The production pathways in the chemical industry are mainly based on non-renewable resources like natural gas, oil and coal.[72] However, these feedstocks are not infinitely available, and there is a high demand to develop alternative routes based on renewable resources. This is particularly the case, for the synthesis of many fine chemicals like, e.g. 2-pyrones.

The 2-pyrone scaffold is present in a number of natural products, and 2-pyrones have been proven to be useful building blocks for the synthesis of complex molecules and, therefore, they are valuable starting materials for organic chemistry.[30,31,34] The synthesis of substituted 2-pyrones is of broad interest, as a number of elegant methods have been developed over the years to access this class of compounds as discussed earlier. Among these, the thermal rearrangement of cyclopentadienone epoxide (**136**) stands out, as it provides an atom-economical approach to 2-pyrone (**1**),[73] this rearrangement proceeds through a 6π electrocyclic reaction via a vinyl ketene **135** (Scheme 49).[74–76]

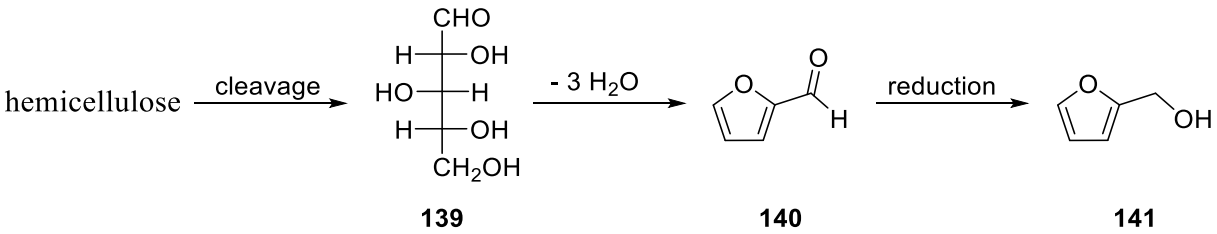


Scheme 49. Synthetic approach toward 2-pyrone (**1**).

Although the mechanism of the reaction is well studied, this rearrangement did not attract much attention for the synthesis of 2-pyrone derivatives. This could be due to difficulties to access

the required starting materials, often requiring harsh reaction conditions resulting in low yields.[74–76] In particular, cyclopentadienone epoxide ((±)-**136**) cannot be synthesized from cyclopentadienone due to the high tendency of the latter to dimerize. As a well-known surrogate for cyclopentadienone,[77] therefore, enone (±)-**138**, a suitable precursor for the synthesis of different 2-pyrones, which can be synthesized from renewable resources, was explored in this work.

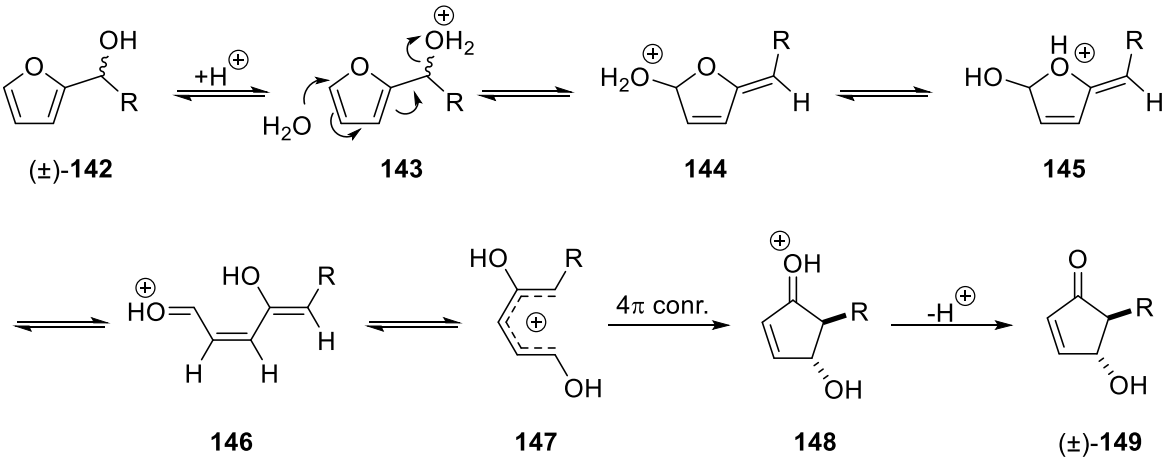
The key compound enone (±)-**138** for the synthesis of the 2-pyrone moiety can be produced via a reaction sequence starting from hemicellulose. Hemicellulose is an inexpensive renewable resource based on non-edible sources like e.g. bagasse and bran. Bagasse is a residue of sugarcane processing, and bran is a byproduct of the rice milling process. Additionally, waste from deciduous and coniferous wood waste, municipal solid wastes and waste from the pulp and paper industry can serve as a source for hemicellulose. Hemicellulose, a polysaccharide, is composed of many different sugar monomers, e.g., Xylose, Arabinose, Glucose, Mannose and Galactose.[78] Xylose (**139**) is the main component in hemicellulose and can be readily accessed through treatment of hemicellulose with acids. Further dehydration of aforementioned Xylose (**139**) gives rise to furfural (**140**).[78] Furfural (**140**) is considered as a platform chemical, having found use in the production of biofuels or solvents (Scheme 50). [79] As it is readily available through the aforementioned process, it is an ideal starting material for the sustainable synthesis of fine chemicals.



139 **140** **141**

Scheme 50. Synthesis of **141** starting from renewable resources.

Furfuryl alcohol (**141**), being produced from furfural (**140**) by catalytic reduction on ton scale, offers particularly attractive opportunities for the production of fine chemicals and drugs due to the versatile skeletal transformations it can undergo, e.g., by the Piancatelli or the Achmatowicz rearrangement.[80,81] The Piancatelli rearrangement is believed to proceed through a sequence that concludes with a 4π conrotatory electrocyclic ring closure of a pentadienyl cation **147** (Scheme 51).[80]



Scheme 51. Proposed mechanism of the rearrangement of furfuryl alcohols by Piancatelli.[80]

4-Hydroxy-2-cyclopentenone ((±)-**150**), is a versatile starting material and available via the Piancatelli rearrangement from renewable resources, hence it can serve as starting material for the sustainable synthesis of the 2-pyrone motif.[82] Recently, Reiser *et al.*[83] reported that the Piancatelli rearrangement of furfuryl alcohol (**141**) to 4-hydroxy-2-cyclopentenone ((±)-**150**) could be conducted on large scale and high yield using a microreactor setup (Figure 3).

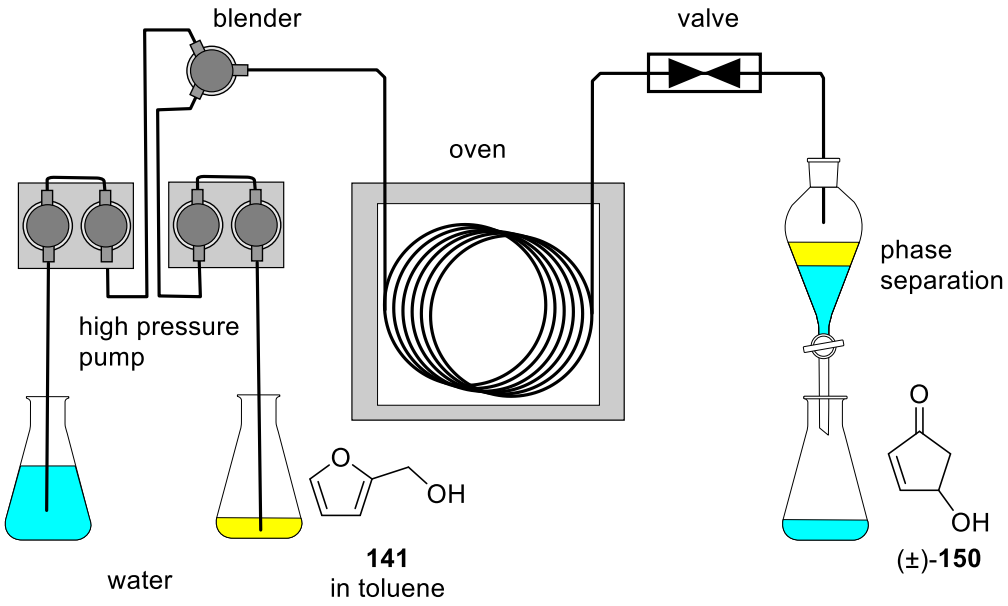


Figure 3. Microreactor for the Piancatelli rearrangement.[83]

Furfuryl alcohol (**141**), dissolved in toluene and water is injected via a high-pressure pump and thoroughly mixed with a blender. The mixture is then heated in an oven and after a contact time of less than 1 min two separate layers are obtained. The aqueous phase contains 4-hydroxy-2-cyclopentenone ((±)-**150**), which is isolated in 87% yield and 97% purity after evaporation of water. With this strategy in hand, 4-hydroxy-2-cyclopentenone ((±)-**150**) can be used as starting material for the synthesis of enone (±)-**138** in multigram scale, which itself serves as a key compound in the aforementioned synthesis of the 2-pyrone scaffold. For the rearrangement to the final 2-pyrone moiety a flash vacuum thermolysis (FVT) setup is used (Figure 4).

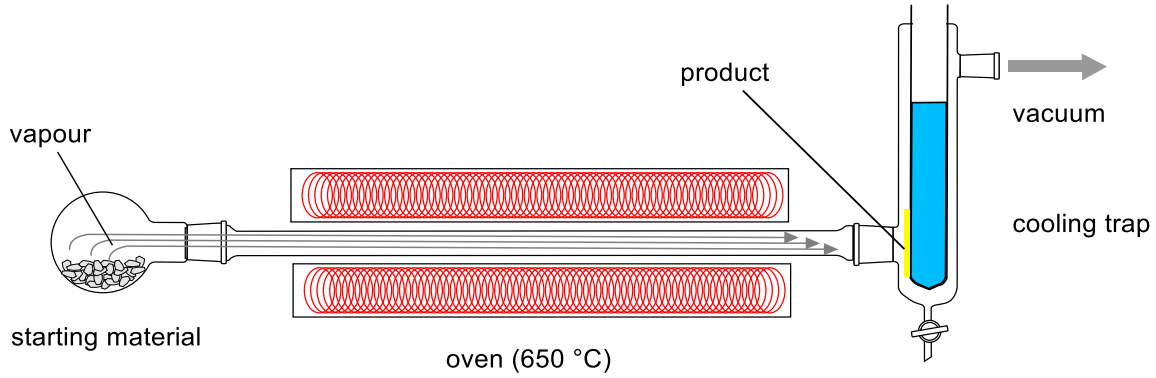
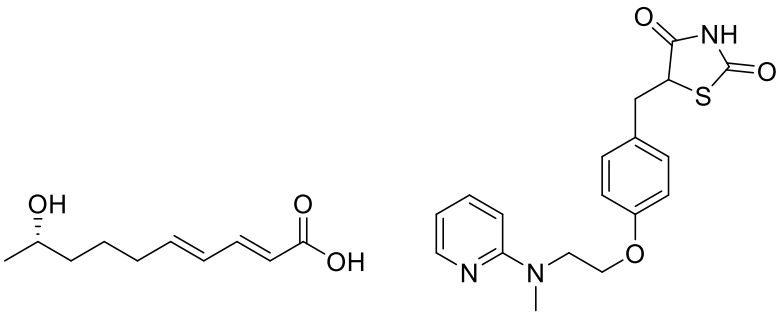


Figure 4. Setup for flash vacuum thermolysis.

FVT is a special application of gas-phase thermolysis, which typically uses temperatures between 400 and 1100 °C. The apparatus consists of a quartz tube containing the starting material on the one end, an oven in the middle and a cooling trap on the other end. The starting material is then evaporated by external heating and sucked through the high-temperature zone of the oven by a vacuum. Because the substrate is sucked very quickly through the heated area, high-temperature exposure periods are only very short (between 10^{-3}-1 s). This allows the use of very high temperatures of up to 650 °C, without destroying the compound, thus enabling access to reactions pathways and compounds which are not accessible by other strategies.[84]

1.2 Synthesis of unsubstituted 2-pyrone

As mentioned in the introduction, the basic structure, unsubstituted 2-pyrone (**1**), is a versatile and valuable starting material for organic chemistry, its aforementioned reactivity offers many different transformations e.g. for the synthesis of (-)-Leodomycin D (**151**) or Rosiglitazone (**152**) (Scheme 52).[85,86]

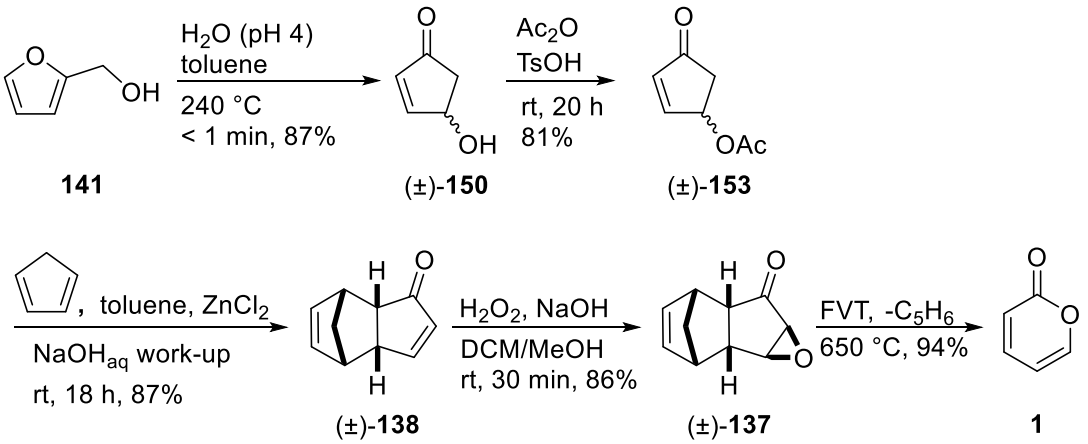


151
(-)-Leodomycin D

152
Rosiglitazone

Scheme 52. Examples of compounds obtained using 2-pyrone (**1**) as starting material.[85,86]

The synthesis of 2-pyrone (**1**) starting from renewable resources like furfuryl alcohol (**141**) offers an inexpensive and sustainable route to this interesting compound. As mentioned before, furfuryl alcohol (**141**) can be rearranged in a continuous flow system with a microreactor setup in 87% yield (Scheme 53). Gaining a better leaving group for the subsequent elimination, (±)-**150** was acetylated to (±)-**153**[87] in good yields using acetic anhydride and catalytic amounts of toluenesulfonic acid. The following [4+2] cycloaddition of acetate (±)-**153** with cyclopentadiene proceeds in the presence of zinc(II)chloride and after basic work up, enone (±)-**138** is obtained in excellent yield.[88] The latter is an interesting starting material for many different syntheses[89,90] itself and readily available by this route in multigram scale. Enone (±)-**138** was epoxidized with hydrogen peroxide to yield 86% of the expected epoxide (±)-**137**.[91] Finally, epoxide (±)-**137** was subjected to FVT, causing a retro-Diels-Alder reaction and the subsequent rearrangement yielded **1** in 94% with a purity of >99% (GC-analysis) without any further purification. Notably, this purity is achieved without any chromatographic work up, (±)-**150**, (±)-**153**, (±)-**138** were distilled, while (±)-**137** was extracted after completion of the reaction.

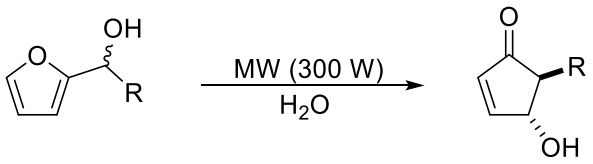


Scheme 53. Synthesis of 2-pyrone (**1**) from furfuryl alcohol (**141**)

1.3 Synthesis of naturally occurring 6-substituted alkyl 2-pyrones

Besides the synthesis of unsubstituted 2-pyrone (**1**), attempts were made to introduce substituents into the final 2-pyrone moiety. One strategy was to start the synthesis with furfuryl alcohol derivatives (±)-**142**. Substituted furfuryl alcohol derivatives are readily available using a Grignard reaction starting from furfural (**140**). This strategy leads to 6-substituted 2-pyrones **2**, which are known e.g. as natural products. Introducing *n*-propyl-, *n*-pentyl- and *n*-heptyl residues yield three naturally occurring 6-substituted 2-pyrones **2**, which were reported as a metabolite from strains of *Trichoderma viride* (Scheme 54).[5,92]

The reaction of furfural (**140**) with the corresponding Grignard reagents yielded the substituted furfuryl alcohol derivatives (±)-**142** in good to excellent yields. The subsequent Piancatelli rearrangement was performed under microwave irradiation, which is perfectly suitable for small-scale reactions. Reiser *et al.*[83] demonstrated the great advance of transferring the Piancatelli rearrangement to a microwave setup in 2010. Using microwave irradiation, the reaction of (±)-**142** to (±)-**149** is achieved within minutes and with improved yields compared to the conventional reflux conditions (Table 1).



(±)-**142** (±)-**149**

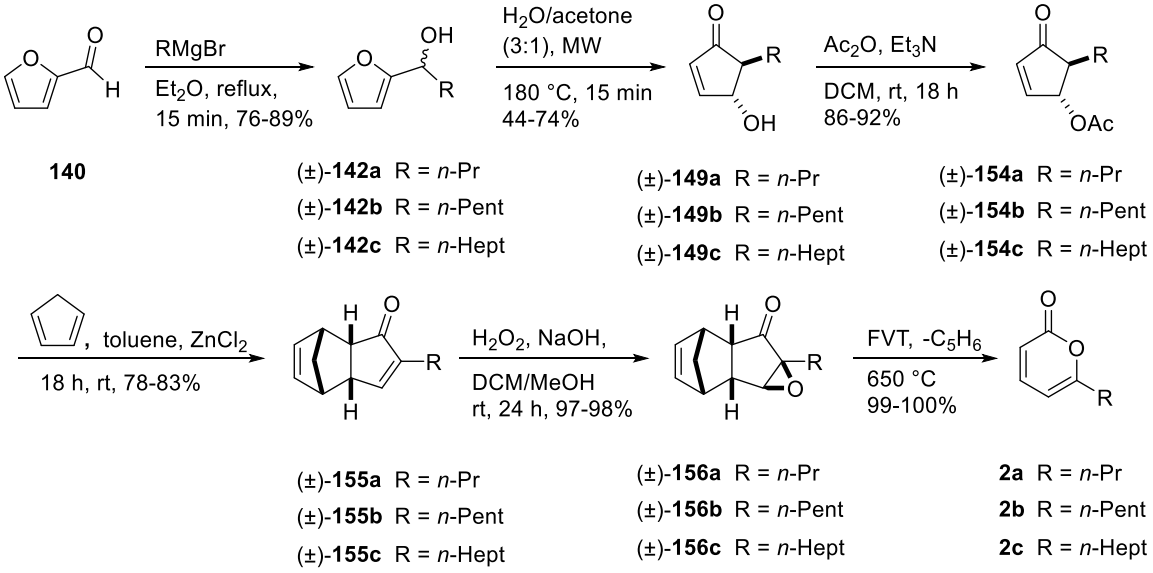
Entry	R	time (min)	dr (cis/trans)	yield (%)
1	Ph	2	1:5	96
2	$CH_2CH=CHMe$	5	1:12	73
3	Et	15	1:7	54
4	*n*-pentyl	15	1:7	65
5	*n*-dodecyl	30	-	0

Conditions: (±)-**142** (1.5 mmol) in H_2O (6 mL), microwave irradiation (300 W) under closed vessel conditions (200-210 °C, 15 bar)

Table 1. Rearrangement of furfuryl alcohol derivatives (±)-**142**.[83]

In this work, a water/acetone mixture was used for reasons of solubility, giving rise to 5-substituted 4-hydroxy-2-cyclopentenones (±)-**149**. Acetylation with acetic anhydride gave the corresponding acetates (±)-**154** in excellent yields. The following Diels-Alder reaction proceeded with zink(II)chloride followed by elimination. Enones (±)-**155** contain two double bonds displaying different reactivity. The double bond next to the electron-withdrawing carbonyl group is much more electron-poor. Therefore, nucleophilic epoxidation should occur at the double bond next to the carbonyl group with nucleophilic reagents, while the electrophilic epoxidation takes place on the other double bond with electrophilic reagents like *m*-CPBA.[93] Such a nucleophilic epoxidation of unsaturated carbonyl compounds can e.g. be performed in the presence of hydrogen peroxide under basic conditions. At the same time, this provides an efficient and environmentally friendly option for the epoxidation of the synthesized enones

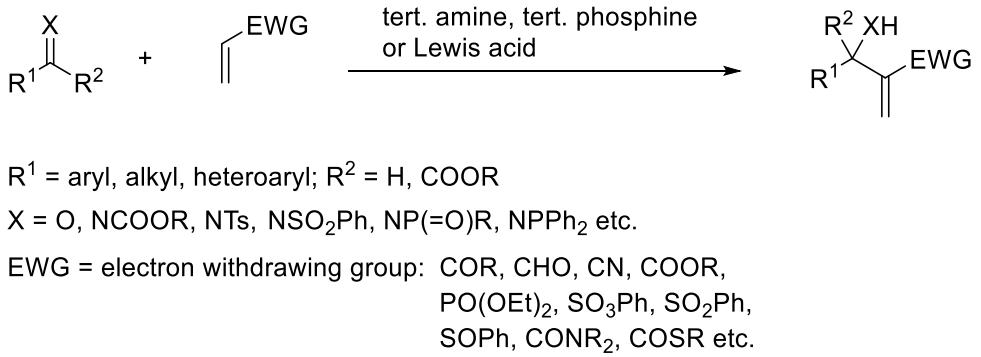
(±)-**155** since no catalyst is needed and the only byproduct formed during the reaction is water. In the last step, the epoxides (±)-**156** were rearranged by flash FVT to afford the three naturally occurring 6-substituted 2-pyrones **2** in quantitative yield (Scheme 54).



Scheme 54. Synthesis of 6-substituted 2-pyrones **2** from furfural (**140**).

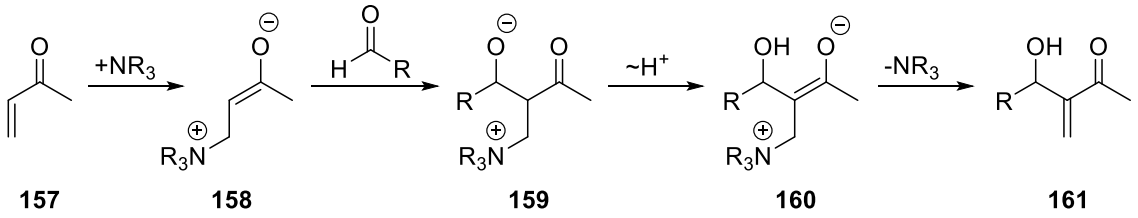
1.4 Synthesis of 6-substituted α-hydroxyalkyl 2-pyrones

Enone (±)-**138** offers the opportunity to introduce substituents into the final 2-pyrone moiety, however, the double bond of the enone (±)-**138** still needs to be available for epoxidation after the substitution. The Baylis-Hillman reaction offers an atom economic and versatile tool for the substitution of enones while retaining the required double bond in the product after the transformation. The Baylis-Hillman reaction requires three essential components: an activated alkene, alkyne or allene, an electrophile and a catalyst. Over the last years, a broad variety of combinations of these three components was investigated and used in organic synthesis. The diversity of the Baylis-Hillman reaction is indicated in Scheme 55.[94–96]



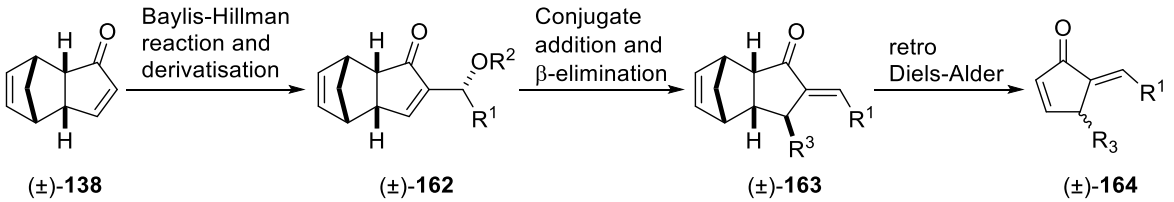
Scheme 55. Overview over the Baylis-Hillman reaction.[95]

The mechanism of the Baylis-Hillman reaction proceeds through a Michael-initiated addition-elimination sequence. An amine-catalyzed reaction mechanism is illustrated in Scheme 56. The tertiary amine attacks the activated alkene **157** via nucleophilic addition, resulting in a zwitterionic enolate **158**. This enolate **158** attacks the aldehyde in an aldol fashion to generate **159**. Subsequent proton migration and release of the catalyst provides the desired product **161**.



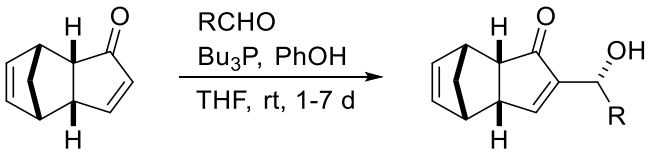
Scheme 56. Mechanism of the Baylis-Hillman reaction.[96]

Eddols *et al.*[89] already used the Baylis-Hillman reaction for the substitution of enone (±)-**138** to obtain β-hydroxy alkylated enones (±)-**162** which were derivatized afterward. An alkylcuprate conjugate addition followed by a spontaneous β-elimination yielded exocyclic alkenes (±)-**163**. Finally, a retro-Diels–Alder reaction released the corresponding cross-conjugated cyclopentadienone (±)-**164** (Scheme 57).



Scheme 57. Preparation of cross-conjugated cyclopentadienones.[89]

The Baylis-Hillman reaction of (±)-**138** and aldehydes (Table 2), precedented by Eddols *et al.*,[89] smoothly gave rise to adducts (±)-**165** that were envisioned to be suitable precursors for the synthesis of 6-substituted 2-pyrones. Expanding the scope previously reported,[89] different aliphatic and aromatic aldehydes with both electron withdrawing and donating groups yielded the target compounds in good yields. Sterically less hindered aliphatic and aromatic aldehydes with electron withdrawing groups proved to be more reactive, resulting in significantly reduced reaction times.



(±)-**138** (±)-**165**

entry	R	(±)-**165**	time (d)	yield (%)
1	Me	**a**	3	84
2	Et	**b**	3	79
3	*i*-Pr	**c**	7	85 (87)[a]
4	*n*-Pr	**d**	3	83
5	*n*-Bu	**e**	3	80
6	*n*-Hex	**f**	3	82
7	Ph	**g**	2	83 (89)[a]
8	4-Cl-Ph	**h**	1	79
9	4-NO_2-Ph	**i**	1	86
10	4-MeO-Ph	**j**	7	85
11	2-Furyl	**k**	3	90

[a] Taken from reference [89]

Table 2. Baylis-Hillman reaction of enone (±)-**138** with various aldehydes.

Theoretically, the outcome of this reaction could lead to the formation of four different stereoisomers (a set of two diastereomers), as illustrated in Figure 5. However, when submitted to NMR analysis, no indication of diastereomeric proton signals was found. Hence, it is plausible to assume that just one pair of enantiomers is formed during the reaction.

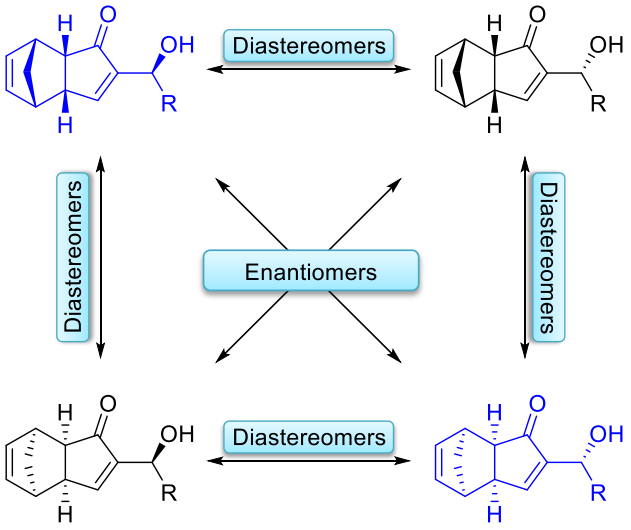
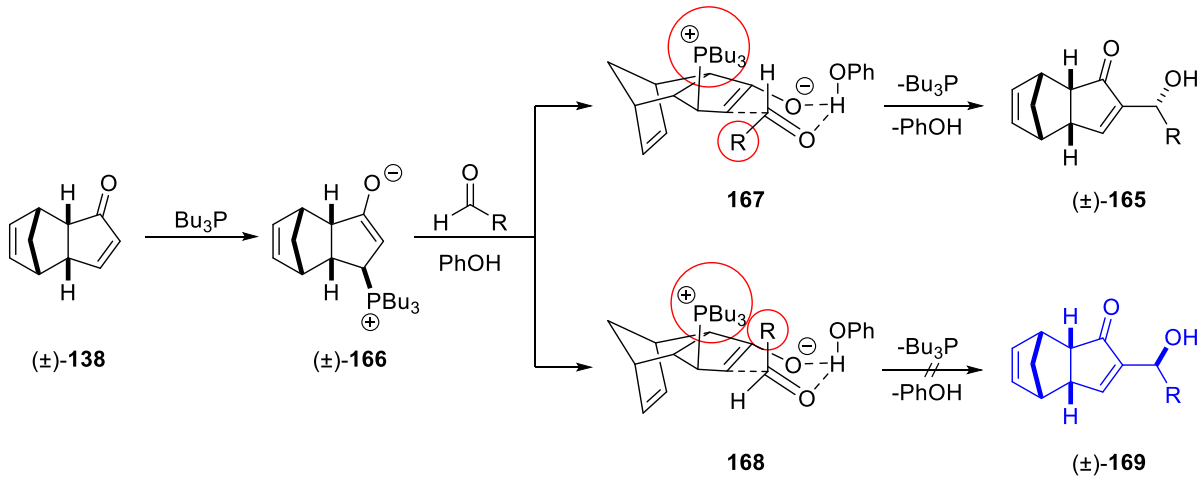


Figure 5. Theoretically possible products of the Baylis-Hillman reaction.

On these grounds, the Baylis-Hillman reaction to (±)-**165** must take place with complete diastereoselectivity. This can be rationalized taking into account that the phosphine catalyst adds to the enone (±)-**138** from its sterically less hindered convex side, followed by an aldol reaction of the resulting (±)-**166** via a Zimmermann-Traxler-type transition state **167**, due to steric hindrance **168** is not formed (Scheme 58).



Scheme 58. Diastereoselective Baylis-Hillman reaction.

The relative stereochemistry could be unambiguously assigned by X-ray crystallography of (±)-**165g** (Figure 6).

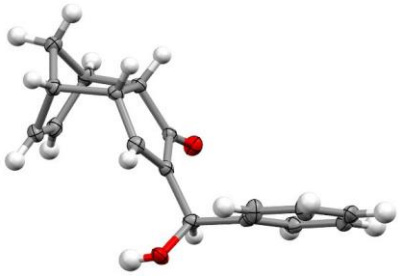
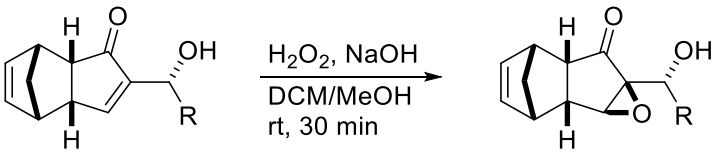


Figure 6. Crystal structure of (±)-**165g**.

With the Baylis-Hillman adducts in hand, the next step was the epoxidation of the double bond of the enone system. The aforementioned system, using hydrogen peroxide under basic conditions, proved to be highly effective for different enones. Applying these conditions to the substituted enones (±)-**165** lead to epoxidized products (±)-**170** within 30 min with excellent yields, chemo- and diastereoselectivity. Furthermore, steric or electronic properties of the substituent did not show any influence on the epoxidation (Table 3).

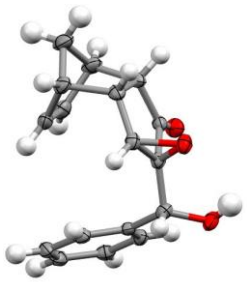


(±)-**165** (±)-**170**

entry	R	(±)-**170**	yield (%)
1	Me	**a**	91
2	Et	**b**	92
3	*i*-Pr	**c**	97
4	*n*-Pr	**d**	95
5	*n*-Bu	**e**	92
6	*n*-Hex	**f**	96
7	Ph	**g**	96
8	4-Cl-Ph	**h**	91
9	4-NO_2-Ph	**i**	89
10	4-MeO-Ph	**j**	92
11	2-Furyl	**k**	97

Table 3. Epoxidation of Baylis-Hillman adducts (±)-**165**.

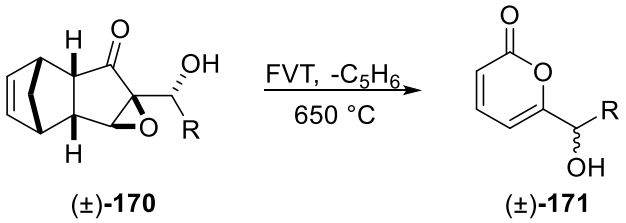
Epoxidation of (±)-**165** occurred exclusively from the convex face of the enone, which was ascertained by X-ray crystallography of (±)-**170g** (Figure 7).



(±)-**170g**

Figure 7. Crystal structure of (±)-**170g**.

These epoxides (±)-**170** could then be subjected to flash vacuum thermolysis, triggering extrusion of cyclopentadiene by a retro-Diels-Alder reaction and the subsequent rearrangement to 2-pyrones (±)-**171** (Table 4). A temperature of 650 °C at 0.02 mbar was found to be necessary, as lower temperatures resulted in the incomplete conversion of the starting materials. High yields (88-98%) and no byproducts or decomposition were generally observed. The only exception was the furyl substituted derivative (±)-**171k**, which was formed in only 62% yield. In this case, significant amounts of polymeric material were formed during the FVT, indicating the thermal lability of 2-pyrone (±)-**171k**.

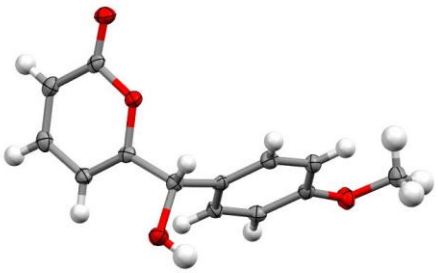


(±)-**170** (±)-**171**

entry	R	(±)-171	yield (%)
1	Me	**a**	98
2	Et	**b**	92
3	*i*-Pr	**c**	96
4	*n*-Pr	**d**	92
5	*n*-Bu	**e**	91
6	*n*-Hex	**f**	90
7	Ph	**g**	98
8	4-Cl-Ph	**h**	97
9	4-NO_2-Ph	**i**	88
10	4-MeO-Ph	**j**	98
11	2-Furyl	**k**	62

Table 4. Rearrangement to 6-substituted α-hydroxyalkyl 2-pyrones (±)-**171**.

As with the previous compounds, the structure of 2-pyrones (±)-**171** were confirmed by X-ray crystallography of (±)-**171j** (Figure 8).

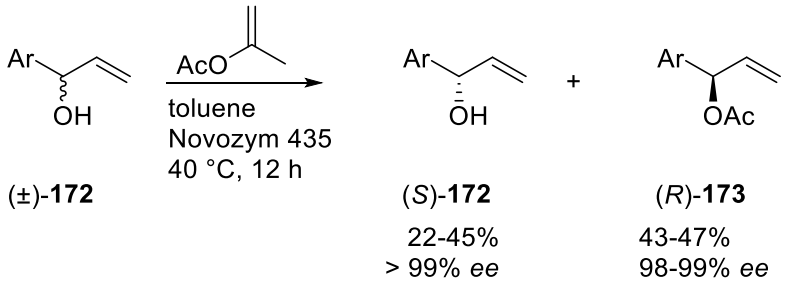


(±)-**171j**

Figure 8. Crystal structure of (±)-**171j**.

1.5 Enzymatic Resolution

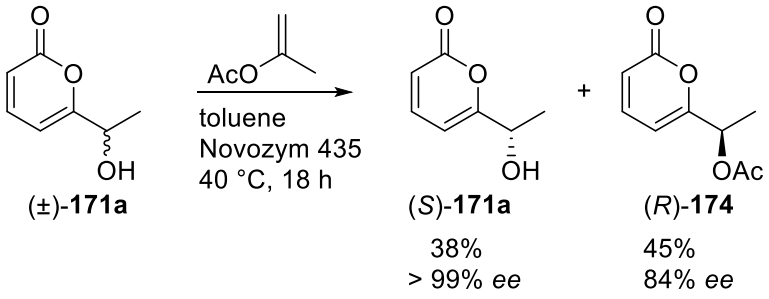
Enzymes are widely used in organic chemistry; especially lipases have excellent abilities in e.g. the kinetic resolution of racemic compounds. The active center of the lipases forms a special environment, which allows distinguishing between the two enantiomers affected by steric effects. Remarkably, lipases tolerate a broad range of unnatural substrates, and they are stable and active in organic solvents without cofactors. Furthermore, they are commercially available in free and immobilized form, which makes lipases even more attractive for organic synthesis.[97] Since 2-pyrones are valuable building blocks in organic chemistry, furthermore the enzymatic resolution of (±)-**171** was investigated to arrive at enantiomerically pure compounds. Novozym 435 (*Candida antarctica* lipase B) is a widely used lipase because of its outstanding stability and activity in hydrophobic organic media.[97] Kocovsky *et al.*[98] used the great abilities Novozym 435 offers for the kinetic resolution of substituted secondary alcohols bearing an allyl and different aryl substituents. Using isopropenyl acetate as acylation agent in toluene gave excellent results (Scheme 59).



Scheme 59. Resolution of racemic alcohols by Novozym 435.[98]

The 6-substituted α-hydroxyalkyl 2-pyrones (±)-**171** synthesized in this work have a similar steric structure compared to (±)-**172**, and therefore the conditions of Kocovsky *et al.*[98] were tested. The difference in size of the two substituents of the secondary alcohol is essential for the resolution. The more difference the two substituents exhibit, the better the resolution proceeds. Therefore, (±)-**171a** having the biggest difference in size of the two substituents at the secondary alcohol, was tested under these conditions first (Scheme 60).

The kinetic resolution of 2-pyrone (±)-**171a** gave (*S*)-**171a** with > 99% *ee* in 38% yield. The stereochemistry was assigned by applying Kazlauskas' rule.[99]



Scheme 60. Resolution of (±)-**171a** by Novozym 435.

Kazlauskas' rule is a stereoselectivity model applicable for lipase-catalyzed reactions of secondary alcohols, offering a way to predict which enantiomer reacts faster (Figure 9). According to Kazlauskas' rule enantiomer **A** reacts faster due to higher matching to the active

site of the lipase, therefore acylation of **A** is faster. Applying this rule the kinetic resolution of (±)-**171a** gives (*S*)-**171a** and (*R*)-**174**.

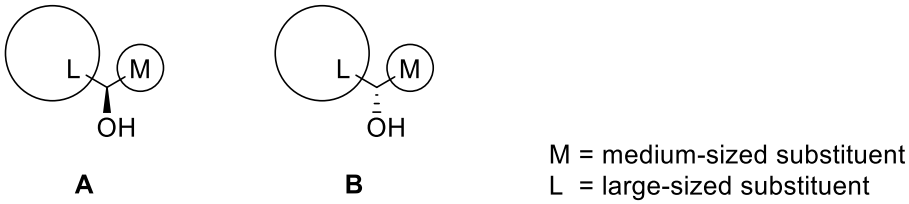
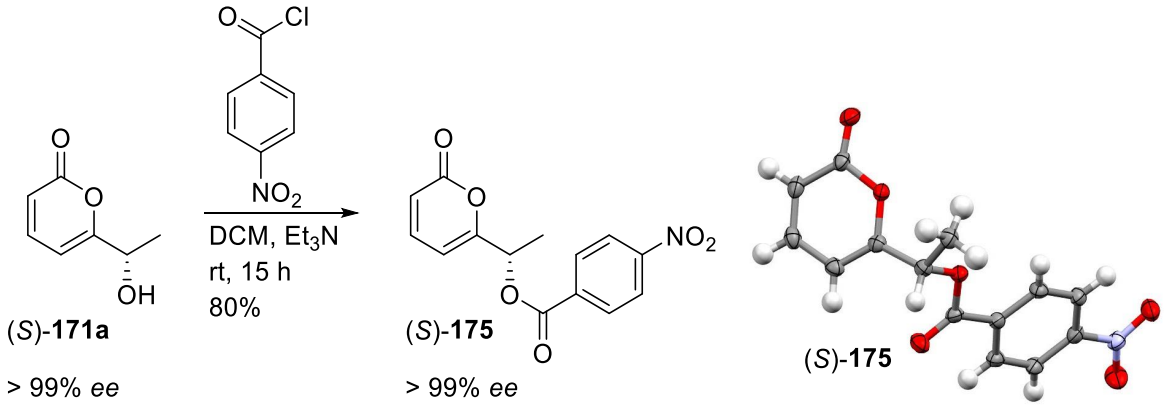


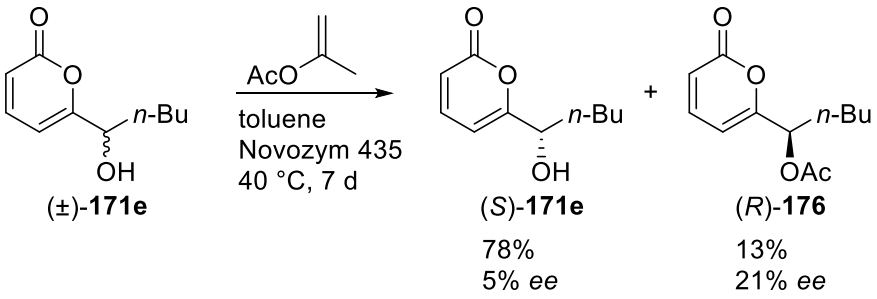
Figure 9. Kazlauskas' rule for secondary alcohols.[99]

This assignment was proven unambiguously by X-ray crystallography after derivatization of (*S*)-**171a** to (*S*)-**175** (Scheme 61).



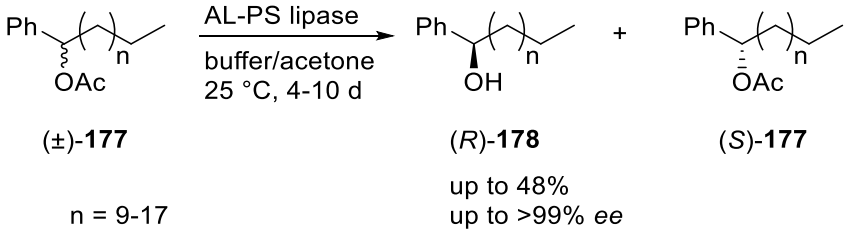
Scheme 61. Derivatization and Crystal structure of (S)-**175**.

Encouraged by the promising results with (±)-**171a**, it was tried to use 2-pyrone (±)-**171e** containing a longer alkyl side chain under the same conditions. However, even after 7 d mainly starting material was recovered, and the isolated 2-pyrones showed poor enantiomeric excess (Scheme 62). Therefore it was concluded, that these conditions are not suitable for 2-pyrone (±)-**171e** containing a longer side chain and a new pathway had to be found.



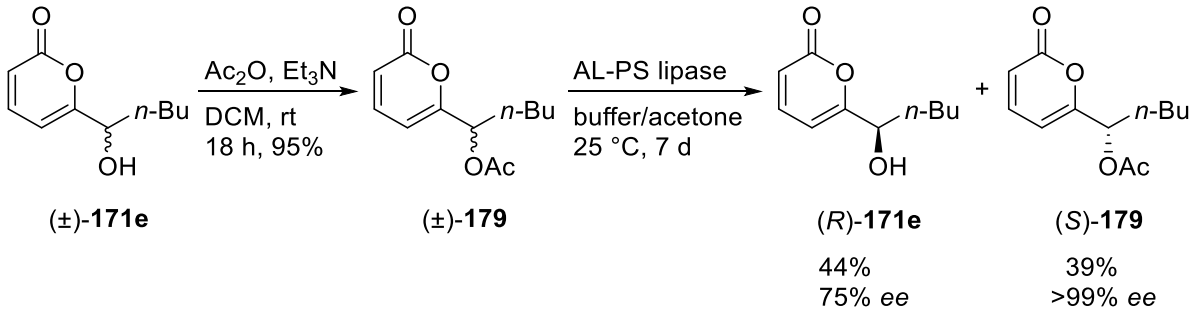
Scheme 62. Resolution of (±)-**171e** by Novozym 435.

The enzymatic hydrolysis of racemic acetates, synthesized from secondary alcohols, is another effective route for the synthesis of enantiomerically pure secondary alcohols. Yusufoğlu *et al.*[100] used Amano lipase from *Burkholderia cepacia* (AL-PS) for the enzymatic hydrolysis of secondary acetates (±)-**177** bearing a phenyl substituent and a side chain of 11-19 carbon atoms (Scheme 63).



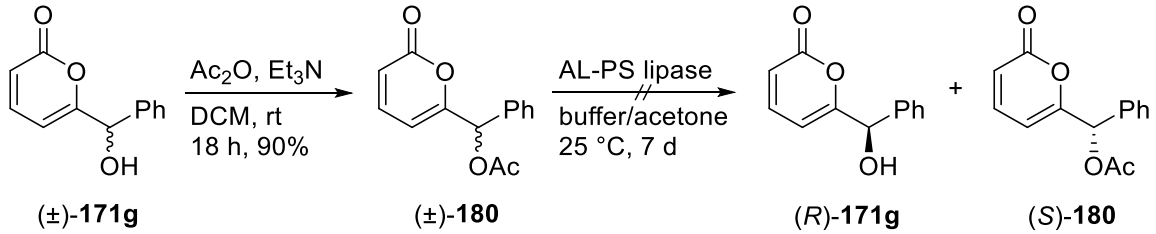
Scheme 63. Enzymatic hydrolysis of the racemic acetates (±)-**177**.[100]

The size of the phenyl substituent is comparable with the one of the 2-pyrone moiety. Hence, the strategy was changed to an enzymatic hydrolysis of the racemic acetate (±)-**179**, which was prepared from (±)-**171e** with acetic anhydride in 95% yield. Hydrolysis of (±)-**179** with AL-PS in a buffer/acetone mixture provided (*S*)-**179** with >99% *ee* in 39% yield (Scheme 64).



Scheme 64. Acetylation of (±)-**171e** and enzymatic hydrolysis of (±)-**179**.

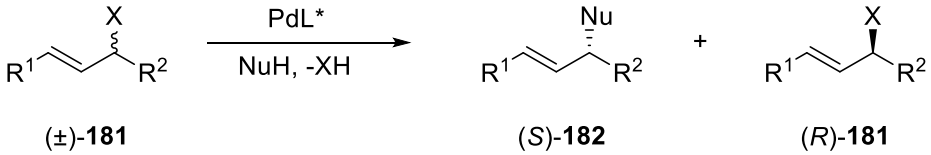
Furthermore, an even more sterically demanding phenyl substituent was chosen for the enzymatic hydrolysis. Therefore 2-pyrone (±)-**171g** was acetylated to (±)-**180** in 90% yield (Scheme 65). However, after 7 d no enzymatic hydrolysis was observed, which leads to the conclusion that a phenyl substituent might be too sterically demanding for the active site of the enzyme.



Scheme 65. Acetylation of (±)-**171g** and attempted enzymatic hydrolysis of (±)-**180**.

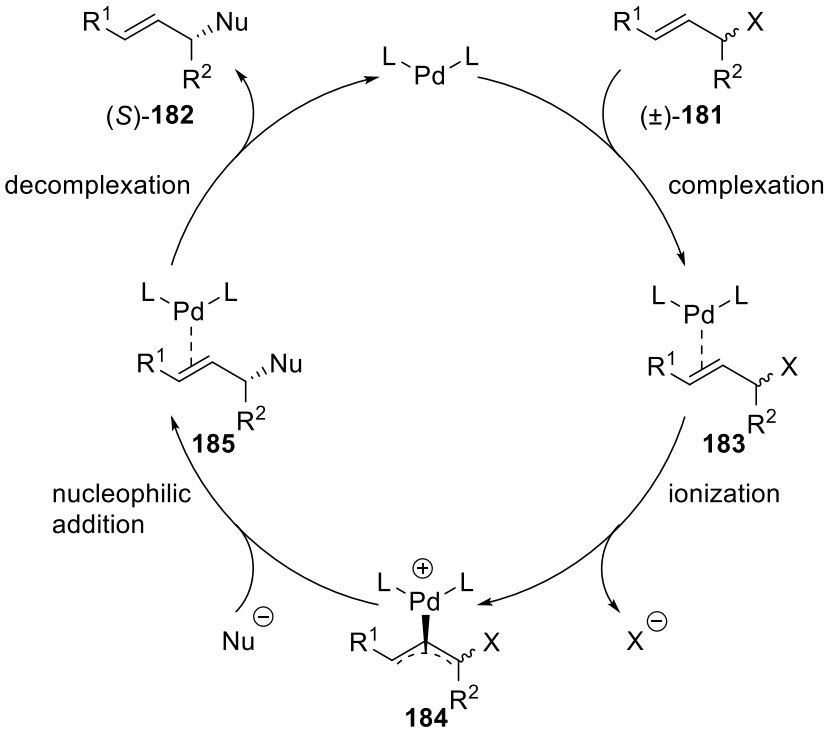
1.6 Tsuji-Trost reaction

The Tsuji-Trost reaction is a metal-catalyzed asymmetric allylic alkylation reaction, which is widely applied in many different syntheses using various types of nucleophiles, leaving groups and metals (Scheme 66).



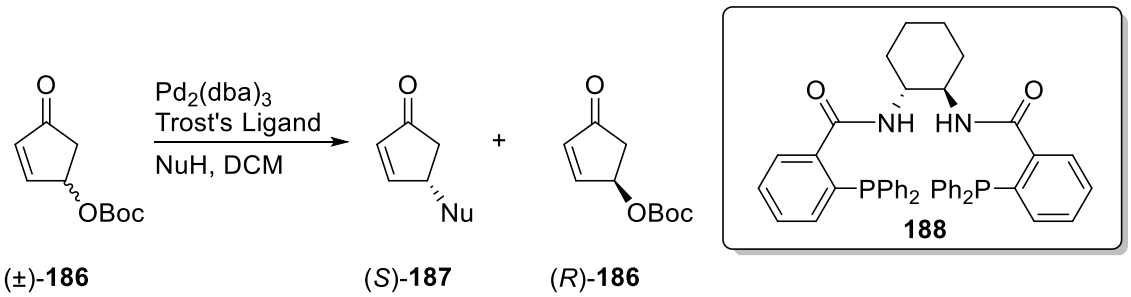
Scheme 66. Tsuji-Trost reaction.

This reaction offers a versatile opportunity for organic syntheses to arrive at enantiomerically pure compounds. The mechanism of the reaction is illustrated in Scheme 67.



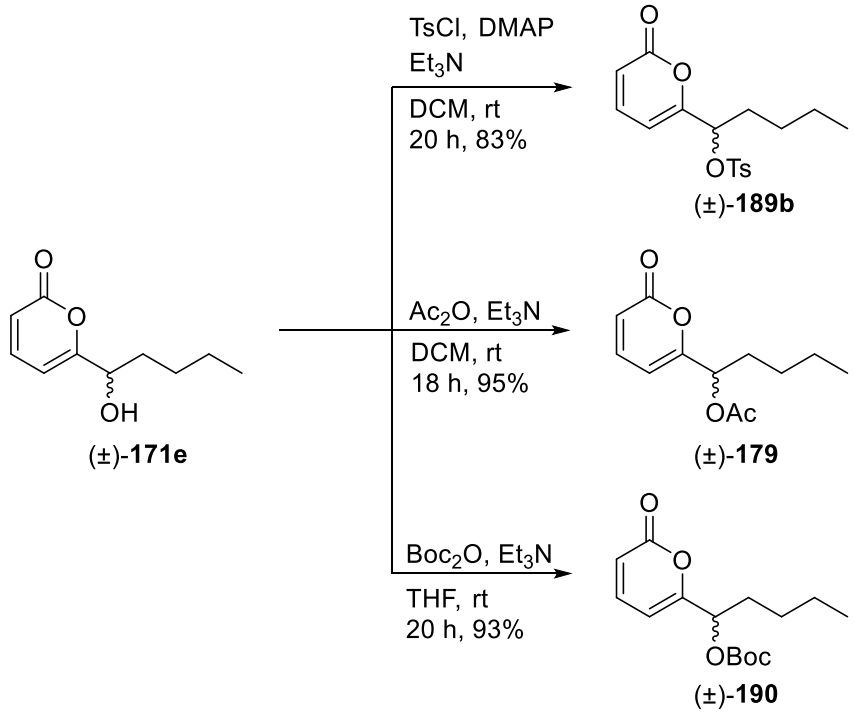
Scheme 67. Mechanism of the Tsuji-Trost reaction.[101]

Reiser *et al.*[102] demonstrated the palladium-catalyzed kinetic resolution of the O-Boc derivative of 4-hydroxy-2-cyclopentenone (±)-**186** with high enantioselectivity as well as its application in synthesis (Scheme 68).



Scheme 68. Palladium-catalyzed allylic substitutions of (±)-**186**.[102]

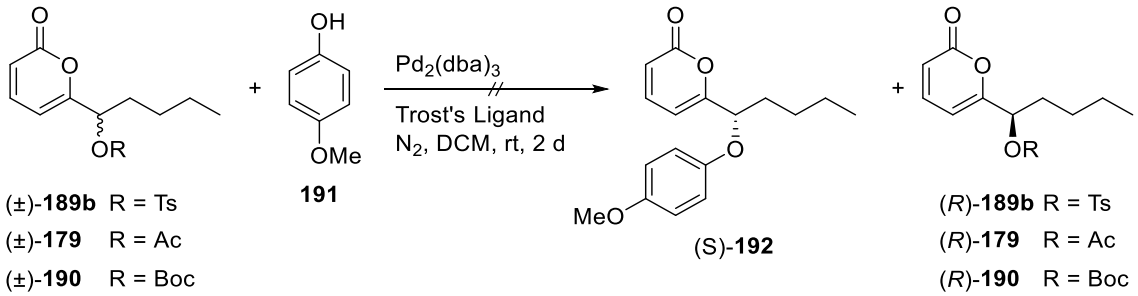
First, the α-hydroxy group of the 6-substituted 2-pyrones was converted into a better leaving group. Therefore, (±)-**171e** was convert into its corresponding tosyl (±)-**189b**, acetate (±)-**179** and O-Boc derivative (±)-**190** in excellent yields (Scheme 69).



Scheme 69. Synthesis of 2-pyrone derivatives containing a good leaving group.

The synthesized substrates for the Tsuji-Trost reaction were tested under the optimized conditions for the kinetic resolution of (±)-**186** with *p*-methoxyphenol as a nucleophile.[103]

Unfortunately, in all cases no conversion was observed even after 2 d of reaction time (Scheme 70).

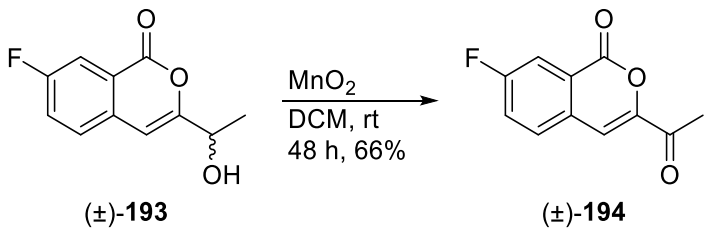


Scheme 70. Attempted palladium-catalyzed allylic substitutions.

This might be due to the aromatic character the 2-pyrone ring exhibits. Therefore the π-allyl complex cannot be formed, and no product formation is observed.

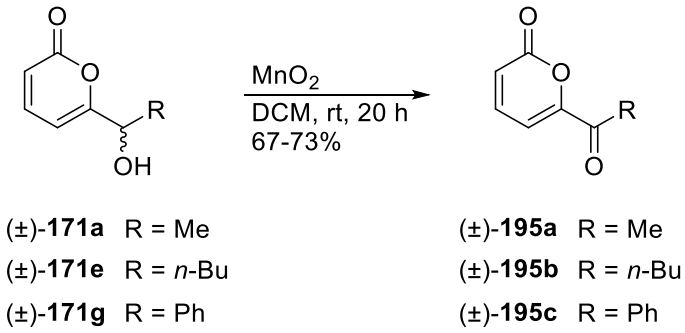
1.7 Oxidation of the α-hydroxy group and total synthesis of Gibepyrone F

A α-ketone functionality is a known structure in natural occurring 6-substituted 2-pyrones (Figure 1).[104] This scaffold is readily accessible by oxidation of the α-hydroxy group of the α-hydroxyalkyl 2-pyrones (±)-**171**. Karp *et al.*[105] showed the oxidation of the α-hydroxy group of substituted isocoumarin (±)-**193** using MnO_2 (Scheme 71).



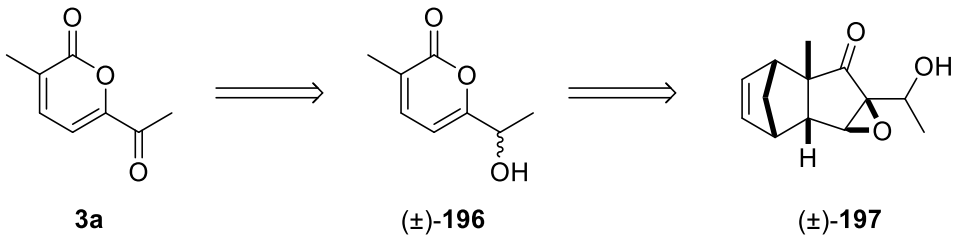
Scheme 71. Oxidation of substituted isocoumarin as reported by Karp *et al.*[105]

This strategy turned out to be suitable also for the oxidation of the α-hydroxy group of 6-substituted 2-pyrones. Therefore, three different 6-subtituted 2-pyrones bearing different substituents were oxidized under these conditions in good yields (Scheme 72). The varying steric hindrance of the side chain of the α-hydroxyalkyl 2-pyrones **171a**, **171e**, **171g** did not display any influence to the reaction, and a carbonyl group was introduced straightforwardly.



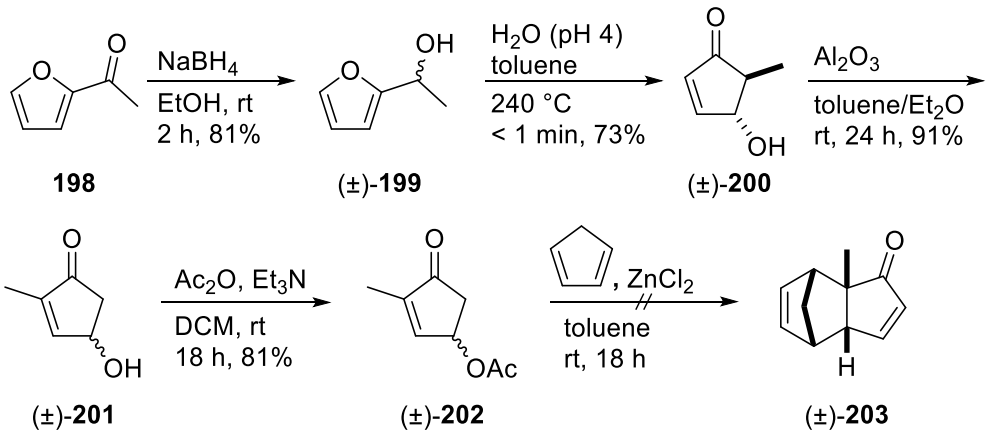
Scheme 72. Oxidation of α-hydroxyalkyl 2-pyrones **171a**, **171e**, **171g**.

Interestingly, by the introduction of a methyl substituent in 3-postion of (±)-**195a** it would be possible to obtain the natural occurring 3,6-substituted 2-pyrone Gibepyrone F **3a**, which was identified in cultures of *Gibberella fujikuroi*.[104] Having a look at the retrosynthesis, an additional methyl substituent has to be introduced in α-position to the carbonyl group, between the 6- and the 5-membered ring in epoxide (±)-**197** (Scheme 73).



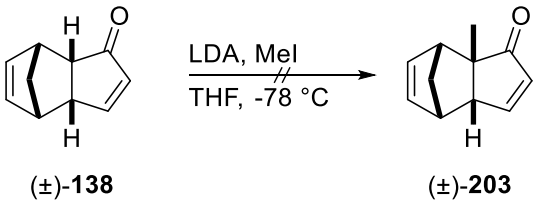
Scheme 73. Retrosynthesis of Gibepyrone F **3a**.

The initial strategy for addition of the additional methyl group to the final compound was starting the synthesis with a methyl substituted furfuryl alcohol derivative (±)-**199**, which was synthesized by reduction of **198** (Scheme 74). In the next step, (±)-**199** was rearranged to (±)-**200** using the above-mentioned microreactor setup in 73% yield. The 5-substituted 4-hydroxy-2-cyclopentenone derivative (±)-**200** was isomerized to the 2-substituted derivative (±)-**201** by adsorption on Al_2O_3.[106] This isomerization gives the methyl substituent in the desired position. Acylation of (±)-**201** with acetic anhydride yielded (±)-**202** in 81%. Unfortunately, the following Diels-Alder reaction did not lead to any conversion. This might be due to the increased steric hindrance at the dienophile.



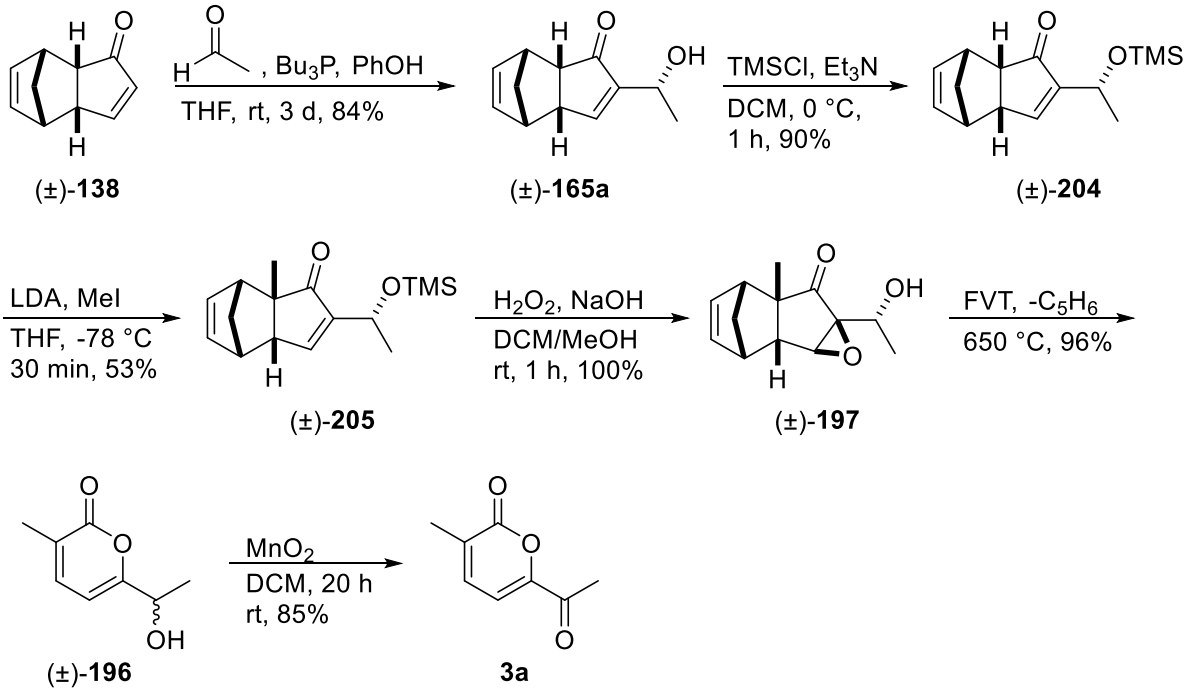
Scheme 74. Attempted synthesis of (±)-**203**.

De *et al.*[107] reported that the methylation of (±)-**138** using various methods gave an inseparable mixture of many different compounds, which probably arose from isomerization of the initially methylated product (Scheme 75).



Schema 75. Attempted methylation of (±)-**138** as reported by De *et al*.[107]

Therefore, the substituent in 6-position was introduced first via a Baylis-Hillman reaction to yield (±)-**165a**. Afterward, the alcohol of (±)-**165a** was protected by a TMS group to afford (±)-**204** in excellent yield. Methylation using LDA and methyl iodide gave (±)-**205**. Epoxidation and deprotection proceeded in one step under basic conditions with hydrogen peroxide to yield quantitatively (±)-**197**. Epoxide (±)-**197** was rearranged to the corresponding 3,6-substituted 2-pyrone (±)-**196**, which was finally oxidized to Gibepyrone F **3a** in good yield (Scheme 76).

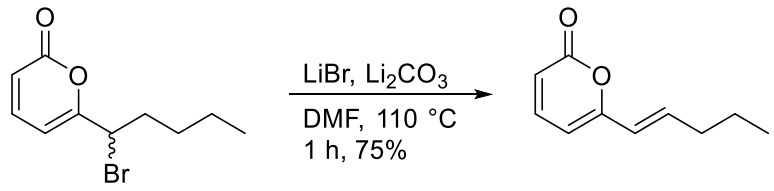


Scheme 76. Total synthesis of Gibepyrone F **3a**.

1.8 Elimination of the α-hydroxy group

Elimination of the α-hydroxy group offers the opportunity to introduce a double bond into the side chain of the synthesized α-hydroxyalkyl 2-pyrones (±)-**171**, which is a known motif in natural products (Figure 1).[5] The 2-pyrones (±)-**171b**, (±)-**171e,** and (±)-**171f** allowed the facile synthesis of Sibirinone (**7a**) and related natural products **7b-c**, which have been found in cultures of fungi. Sibirinone (**7a**) was isolated from *Hypomyces semitranslucens*,[108] **7b** and **7c** were reported as a metabolite from strains of *Trichoderma viride* along with their elegant synthesis starting from propargyl bromide and propiolic acid.[5,92] Additionally, **7c** was found in the marine isolate of fungus *Botrytis* sp,[109] while **7b** is also a component of the queen recognition pheromone of fire ants *Solenopsis invicta*.[110]

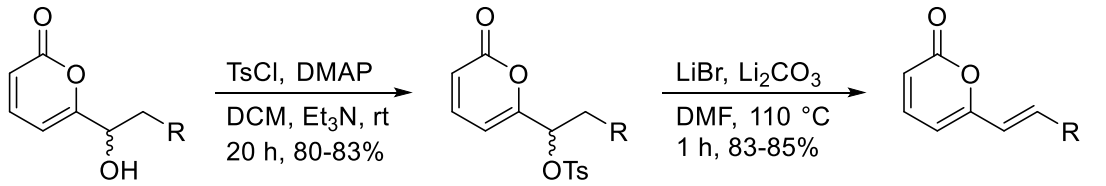
Attempting the direct elimination of water from (±)-**171e** under acidic conditions failed. Daoubi *et al.*[111] showed the elimination of the α-bromide group of 2-pyrone (±)-**206** using basic conditions (Scheme 77).



(±)-**206** **7b**

Scheme 77. Bromine elimination of (±)-**206** by Daoubi *et al*.[111]

Therefore, the α-hydroxy group had to be converted into a better leaving group comparable to the quality of bromide. This was achieved by tosylation of the α-hydroxy group. The tosyl group is an even better leaving group than bromide and elimination under the stated conditions smoothly gave rise to the desired 2-pyrones **7** (Scheme 80). The compounds were exclusively obtained in the naturally occurring (*E*)-configuration in excellent yield and purity (Scheme 78).

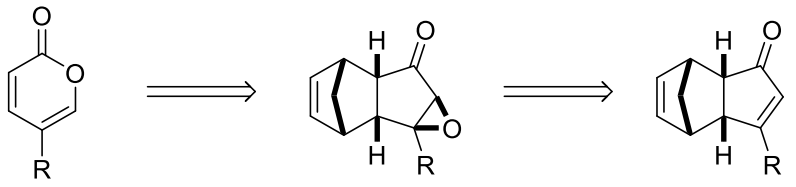


(±)-**171b** R = Me (±)-**189a** R = Me **7a** R = Me
(±)-**171e** R = *n*-Pr (±)-**189b** R = *n*-Pr **7b** R = *n*-Pr
(±)-**171f** R = *n*-Pent (±)-**189c** R = *n*-Pent **7c** R = *n*-Pent

Scheme 78. Synthesis of Sibirinone (**7a**) and related natural products.

1.9 Synthesis of 5-substituted alkyl 2-pyrones

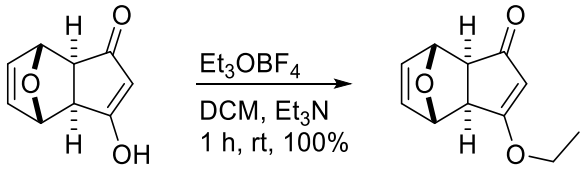
After introducing substituents in 3- and 6-position, it was attempted to further expand the scope of the synthesis of substituted 2-pyrones to other positions. 5-Substituted 2-pyrones represent another interesting class of substituted 2-pyrones displaying a wide range of biological activity, e.g. bufadienolides. Bufadienolides contain a steroid structure, one example **6** is depicted in Figure 1.[1] A retrosynthetic analysis shows that the substituent needs to be inserted at the double bond of the enone moiety in β-position to the carbonyl group (Scheme 79).



111 (±)-**207** (±)-**208**

Scheme 79. Retrosynthesis of 5-substituted 2-pyrones **111**.

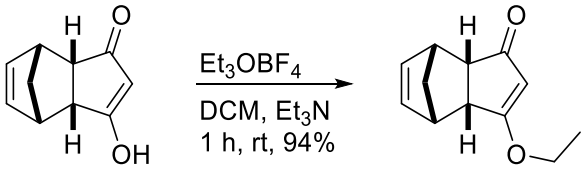
Oda *et al.*[112] demonstrated the facile synthesis of ether (±)-**210** from (±)-**209** using Meerwein's reagent (Scheme 80).



(±)-**209** (±)-**210**

Scheme 80. Synthesis of ether (±)-**210**.[112]

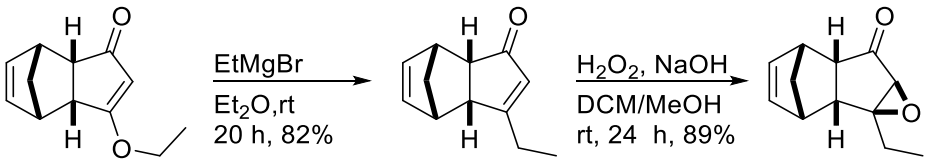
This concept was expanded to the Diels-Alder adduct (±)-**211** yielding (±)-**212**, which was envisioned to be a suitable precursor for the synthesis of 5-substituted 2-pyrones (Scheme 81). The synthesis of Diels-Alder adduct (±)-**211** from 4-hydroxy-2-cyclopentenone ((±)-**150**) is described in the next chapter.



(±)-**211** (±)-**212**

Scheme 81. Synthesis of ether (±)-**212**.

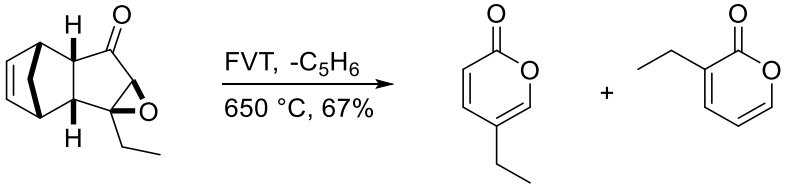
The use of EtMgBr as nucleophile gave rise to the desired product (±)-**213**, which was obtained in 82% yield. Nucleophilic epoxidation of (±)-**213** with hydrogen peroxide proceeded in excellent yield, but extended reaction time was required compared to the substrates used before (Scheme 82). This might be due to higher steric hindrance since the initial step of the nucleophilic epoxidation contains a conjugate addition of the hydroperoxide anion to the enone.



(±)-**212** (±)-**213** (±)-**214**

Scheme 82. Synthesis of epoxide (±)-**214**.

With the epoxide (±)-**214** in hand, FVT was conducted under the previously suitable conditions. The starting material was converted completely, but surprisingly more than one product was observed. The rearrangement yielded two different monosubstituted 2-pyrones a 5-, and a 3-substituted compound in a ratio of 1:2. (Scheme 83).

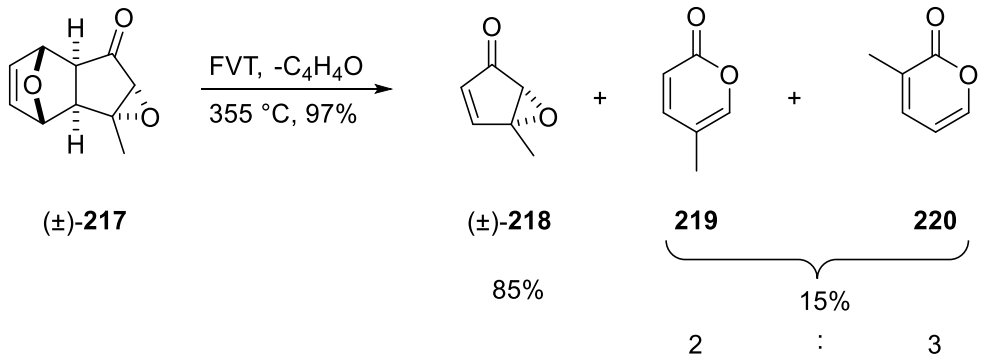


(±)-**214** **215** + **216**

1 : 2

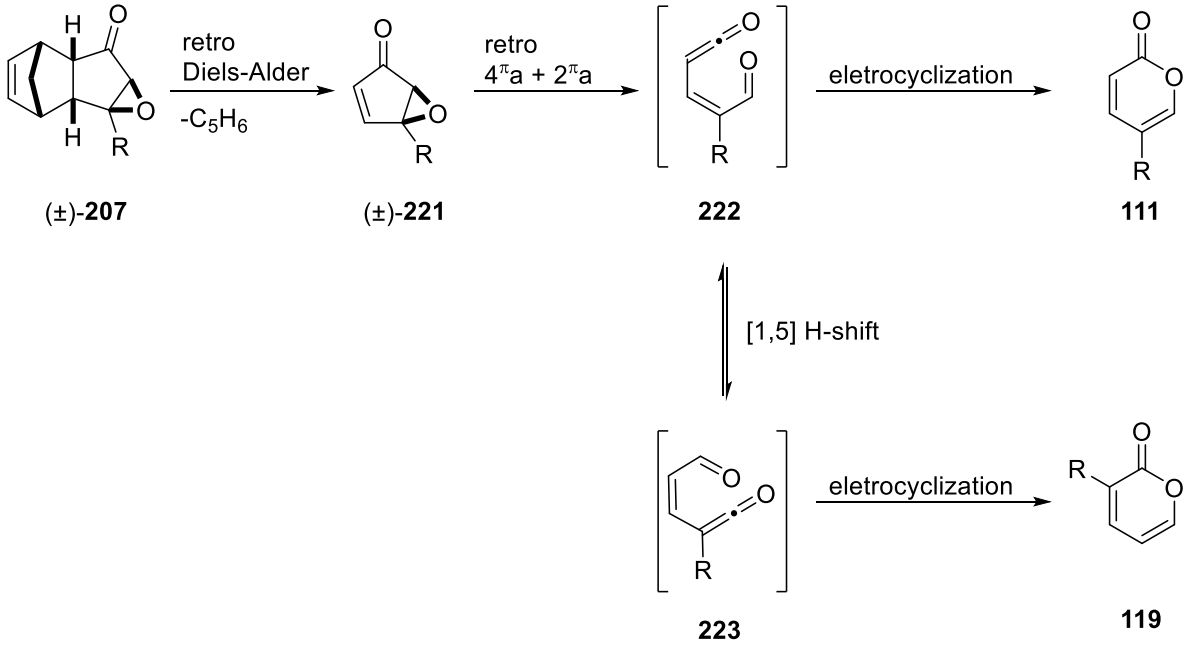
Scheme 83. FVT of epoxide (±)-**214**.

Zwanenburg *et al.*[113] also observed the formation of two different 2-pyrones as byproducts during the synthesis of cyclopentadienone epoxide (±)-**218**. Analogously, the two byproducts emerged to be the corresponding 5-, and 3-substituted 2-pyrones in a ratio of 2:3 (Scheme 84).



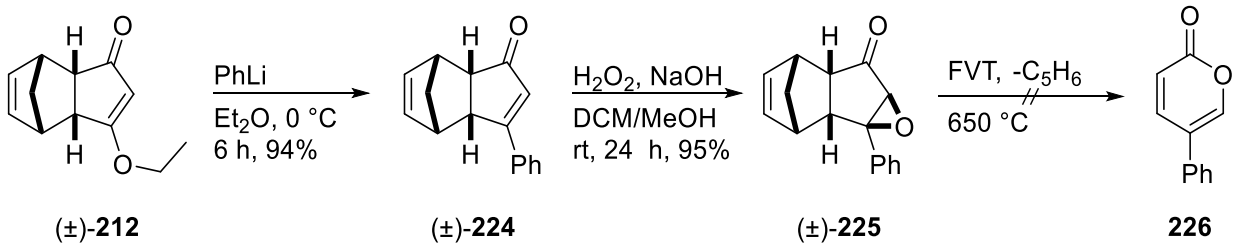
Scheme 84. FVT of epoxide (±)-**217**.[113]

This observation was rationalized by a [1,5] sigmatropic H-shift of ketene **222** to ketene **223**. After electrocyclization of the two different ketene intermediates 5-, and 3-substituted 2-pyrones are obtained (Scheme 85).



Scheme 85. Mechanism and [1,5] sigmatropic H-shift.[113]

Following the previously described methods to obtain 6-substitutedd 2-pyrones, no [1,5] sigmatropic H-shift can occur due to the missing hydrogen atom. Additionally, the reaction was tried with a phenyl substituent (Scheme 86).



(±)-**212** (±)-**224** (±)-**225** **226**

Scheme 86. Synthesis and FVT of epoxide (±)-**225**.

The Grignard reaction of (±)-**212** with PhMgBr resulted only in traces of the desired product. Therefore, the more reactive PhLi was used to introduce a phenyl substituent. Using a modified protocol developed by Ogino *et al.*[114] gave the product (±)-**224** with improved yield of 94%. Epoxidation of (±)-**224** to (±)-**225** proceeded smoothly within 24 h with 95% yield. Surprisingly, FVT of (±)-**225** gave a complex mixture of more than two compounds.

In summary, a high yielding sequence for the synthesis of different 2-pyrone derivatives including unsubstituted 2-pyrone (**1**) in high purity from renewable resources was developed. It was possible to introduce substituents in 3- and 6-postion furnishing different natural products. Synthesized α-hydroxyalkyl 2-pyrones (±)-**171** were enzymatically resolved to arrive at enantiomerically pure compounds. The hydroxy group of the racemic compounds was eliminated and additionally oxidized to receive natural products. During the synthesis of α-hydroxyalkyl 2-pyrones (±)-**171** diastereoselectivity of the performed Baylis-Hillman reaction was observed and explained by a Zimmermann-Traxler transition state.

2 Synthesis of γ-alkylidenebutenolides

2.1 Introduction

The butenolide motif is abundant in nature and compounds containing this motif display a number of biologically, and medically interesting properties. Especially, butenolides containing an exocyclic double bond, called γ-alkylidenebutenolides, exhibit great activities such as cytotoxicity, antibiotic activity or inhibition of cholesterol biosynthesis.[115] A selection of different naturally occurring γ-alkylidenebutenolides is depicted in Figure 10.

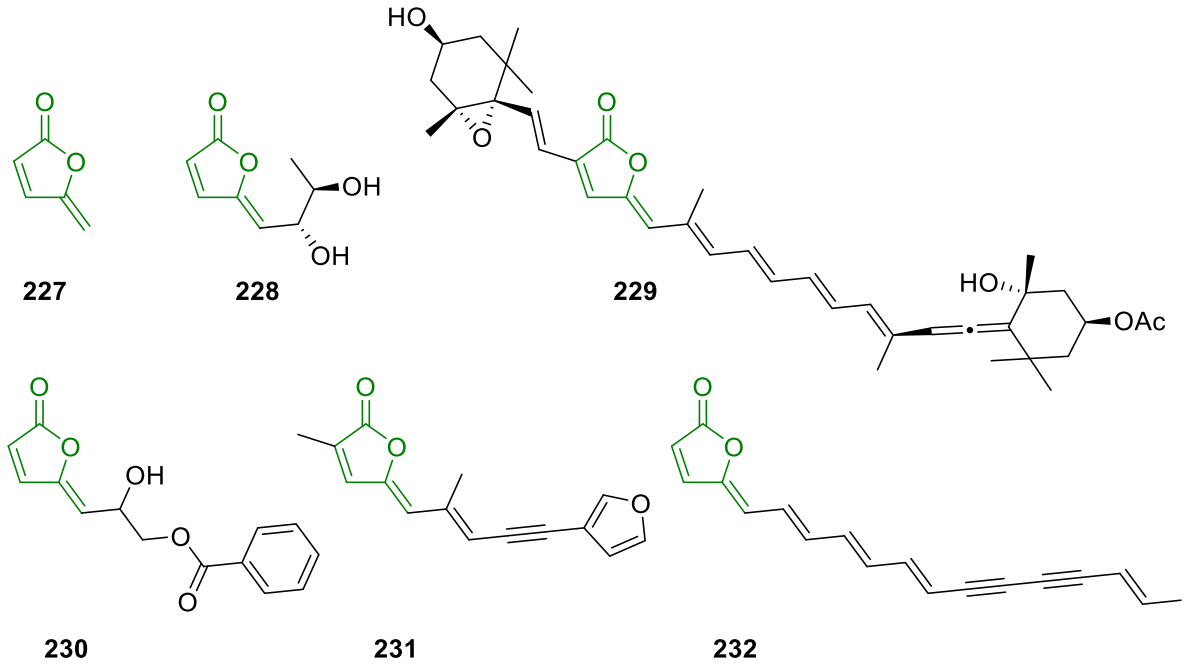
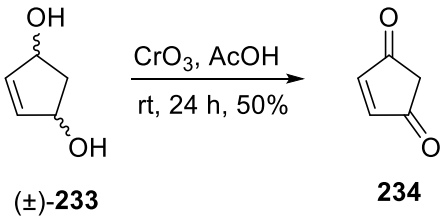


Figure 10. Naturally occurring butenolides containing an exocyclic double bond.[115,116]

Hence, the synthesis of the γ-alkylidenebutenolide scaffold is of tremendous interest especially since there are not many syntheses known in literature until today.[117]

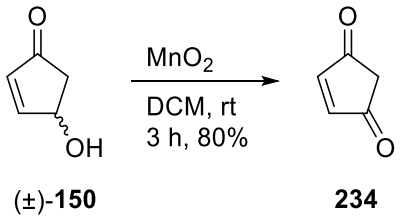
2.2 Oxidation of 4-hydroxy-2-cyclopentenone

Oxidation of 4-hydroxy-2-cyclopentenone ((±)-**150**) furnishes dione **234**, which is known as versatile starting material for many different syntheses and it especially displays exceptional properties as a dienophile in Diels-Alder reactions.[118,119] Therefore, dione **234** was extensively studied by DePuy *et al.*[120] using CrO_3 for the oxidation of diol (±)-**233** (Scheme 87). The oxidant CrO_3 is highly toxic and high amounts are needed for the oxidation of diol (±)-**233**, which is not desirable regarding sustainability.



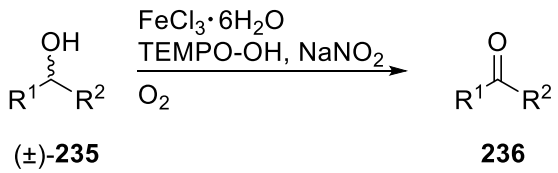
Scheme 87. Synthesis of dione **234** using chromium trioxide.[120]

Another way to synthesize dione **234** is the oxidation of 4-hydroxy-2-cyclopentenone ((±)-**150**), which was achieved using MnO_2 as an oxidant (Scheme 88).[121] MnO_2 is considerable less toxic than CrO_3, but this reaction as well needs highly overstoichiometric amounts of this oxidizing reagent, which produces high amounts of metallic waste.



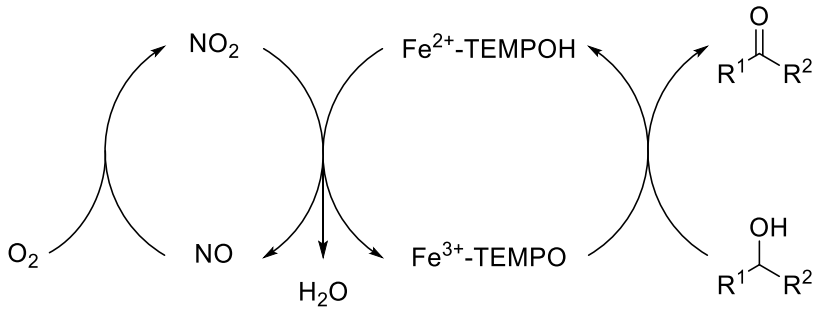
Scheme 88. Oxidation of (±)-**150** by MnO_2.[121]

Producing large amounts of metallic waste does not match with the concept of green chemistry and sustainability.[122] Hence, a sustainable protocol for the oxidation of 4-hydroxy-2-cyclopentenone ((±)-**150**) to dione **234** was searched. Additionally, the used conditions need to be mild, since dione **234** is not stable under basic conditions and decomposes at temperatures above 40 °C rapidly.[120,123] Liang *et al.*[124] demonstrated a mild aerobic oxidation of various alcohols using catalytic amounts of $FeCl_3 \cdot 6H_2O$, TEMPO, and $NaNO_2$ (Scheme 89).



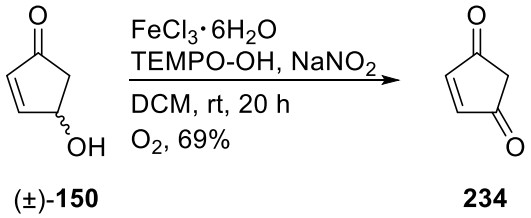
Scheme 89. Aerobic oxidation of various alcohols.[124]

The proposed overall mechanism can be formulated as a cascade of two redox cycles (Scheme 90). The Fe^{3+}-TEMPO species is able to oxidize the alcohol to the corresponding carbonyl compound yielding the reduced form, Fe^{2+}-TEMPOH. The $NaNO_2$ salt acts herein as a source for NO_2, which regenerates the Fe^{3+}-TEMPO species. Finally, the resulting NO is easily reoxidized by O_2 to close the catalytic cycle.[124]



Scheme 90. Mechanism of iron-catalyzed aerobic oxidation.[124]

The aerobic oxidation of 4-hydroxy-2-cyclopentenone ((±)-**150**) would offer a sustainable opportunity for the synthesis of dione **234**. The described oxidation was tested under similar conditions giving rise to 69% of the desired product **234** (Scheme 91).

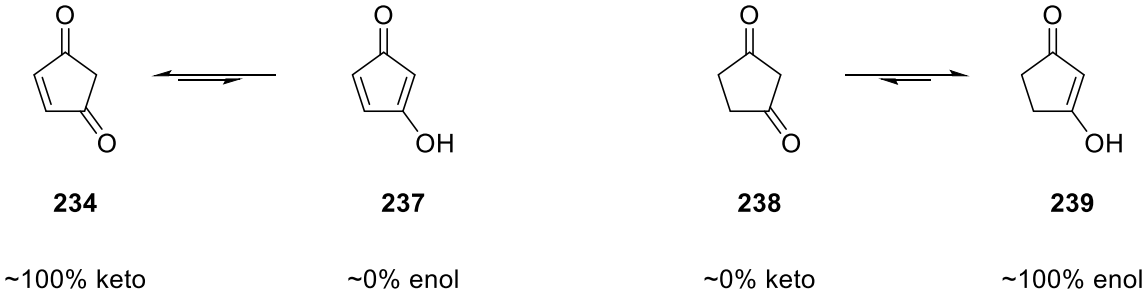


Scheme 91. Iron-catalyzed aerobic oxidation of (±)-**150**.

In conclusion, dione **234** was synthesized in good yield from 4-hydroxy-2-cyclopentenone (±)-**150** using a combination of $FeCl_3 \cdot 6H_2O$ (5mol%), TEMPO-OH (5mol%), $NaNO_2$ (3mol%) and O_2 (1 atm) as the oxidant.

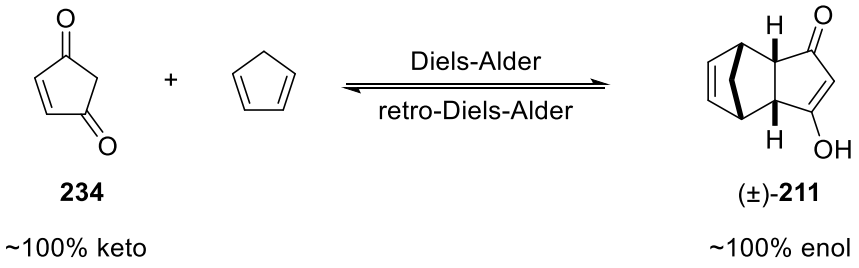
2.3 Keto-enol tautomerism

Besides its broad abilities as starting material for several syntheses, **234** and related compounds exhibit interesting behavior regarding their keto-enol tautomerism (Scheme 92).



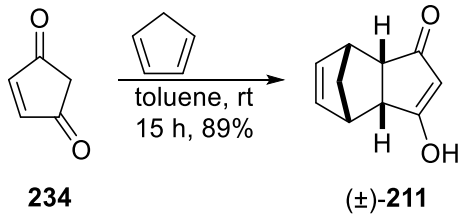
Scheme 92. Keto-enol tautomerism.

Dione **234** appears to about 100% in its keto form and not in its enol form **237**, which is a hydroxy derivative of cyclopentadienone. Unsubstituted cyclopentadienone has a very high tendency to dimerize. Therefore, the enol form **237** might be unfavored for electronic reasons. In contrast, the reduced dihydro derivative **238** is approximately completely in its enol form **239** under similar conditions.[120] The Diels-Alder adduct of (±)-**211** and cyclopentadiene is an interesting compound to investigate this behavior more intensively. Because of its ability to "mask" the double bond and therefore convert the molecule completely into its enol form being reversible by retro-Diels-Alder reaction (Scheme 93).



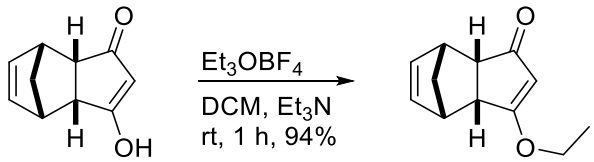
Scheme 93. Diel-Alder and retro-Diels-Alder reaction of dione **234**.

For the synthesis of Diels-Alder adduct (±)-**211** a slightly changed protocol developed by DePuy *et al.*[120] was applied (Scheme 94). Benzene was replaced by toluene due to safety reasons. Furthermore, three equivalents of cyclopentadiene were used instead of equimolar amounts to increase the yield of the adduct (±)-**211**.



Scheme 94. Synthesis of Diels-Alder adduct (±)-**211**.[120]

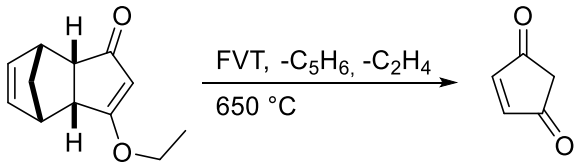
The strategy was to fix the molecule (±)-**211** in its enol form by protecting the hydroxyl group and subsequently performing a retro-Diels-Alder reaction. The transfer of the Diels-Alder adduct (±)-**211** into its enol ether offers an opportunity to keep the molecule in its enol form. Oda *et al.*[112] described the reaction of a Diels-Alder adduct (±)-**209** into the corresponding enol ether (±)-**210** using Meerwein's reagent as mentioned earlier. In this way, compound (±)-**211** was transferred into the corresponding enol ether (±)-**212** in 94% yield (Scheme 95).



(±)-**211** (±)-**212**

Scheme 95. Synthesis of enol ether (±)-**212**.

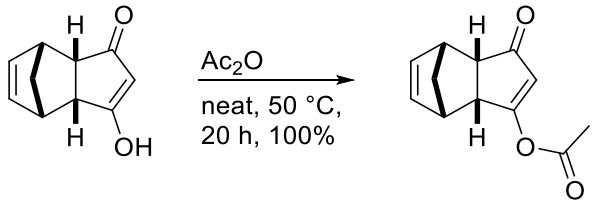
With enol ether (±)-**212** in hand, the FVT was performed to induce the retro-Diels-Alder reaction. However, the only detected product under these conditions was dione **234**; this might be due to the lability of enol ether (±)-**212** (Scheme 96). The retro-Diels-Alder reaction took place, but the ether bond was also cleaved giving rise to dione **234** and ethylene.



(±)-**212** **234**

Scheme 96. Retro-Diels-Alder reaction of enol ether (±)-**212**.

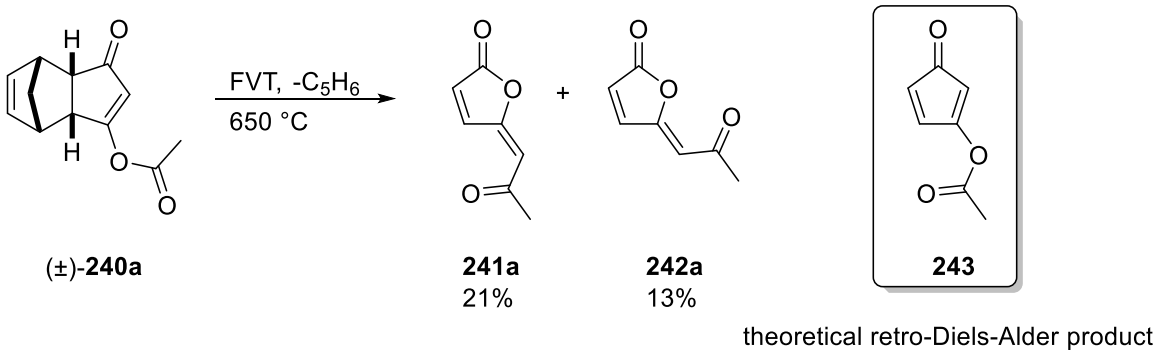
Another option to fix the enol form is to convert the Diels-Alder adduct (±)-**211** into an enol ester. The protocol described by Zwanenburg *et al.*[125] afforded acetyl ester (±)-**240a** in quantitative yield using acetic anhydride (Scheme 97).



(±)-**211** (±)-**240a**

Scheme 97. Synthesis of acetyl ester (±)-**240a**.[125]

Surprisingly, FVT of acetyl ester (±)-**240a** yielded *E*-butenolide **241a** and *Z*-butenolide **242a** (Scheme 98). The γ-alkylidenebutenolides **241a** and **242a** share the same molecular formula with the theoretical retro-Diels-Alder product of **243**.

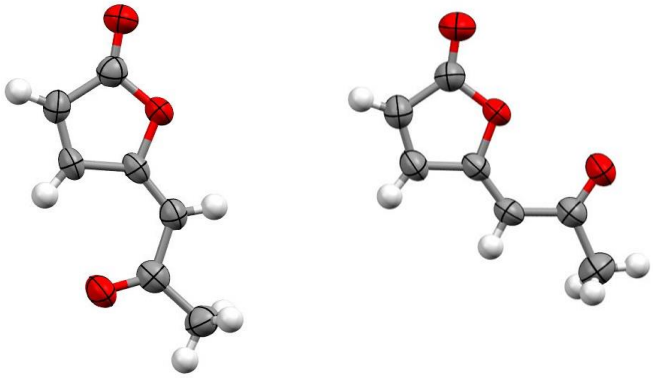


(±)-**240a** **241a** 21% **242a** 13% **243**

theoretical retro-Diels-Alder product

Scheme 98. FVT of acetyl ester (±)-**240a**.

Stereoisomers **241a** and **242a** were easily separable by column chromatography, and their structure was unambiguously assigned by X-ray crystallography (Figure 11).

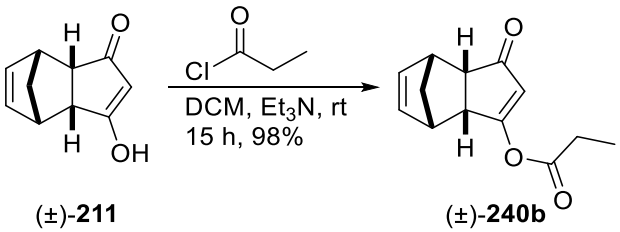


241a **242a**

Figure 11. Crystal structure of γ-alkylidenebutenolides **241a** and **242a**.

2.4 Mechanism

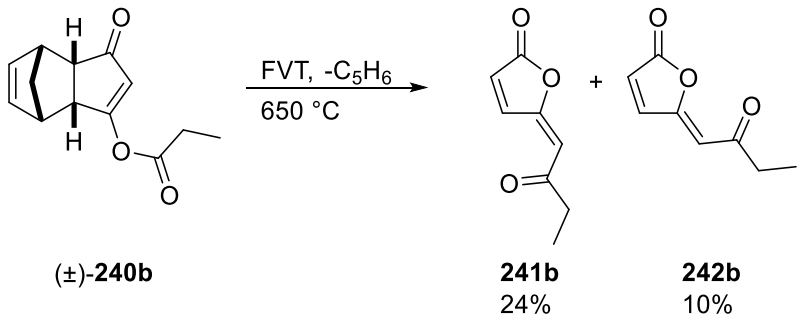
This unusual and interesting reaction behavior have never been observed before. Therefore, the mechanism was studied more in detail. First, another enol ester was synthesized to see if the reaction is still working and giving a hint for the reaction mechanism. Since higher substituted anhydrides are not suitable for the reaction conditions used before first the strategy for the enol ester synthesis had to be changed. An acid chloride mediated esterification using propionyl chloride gave enol ester (±)-**240b** in 98% yield (Scheme 99).



(±)-**211** (±)-**240b**

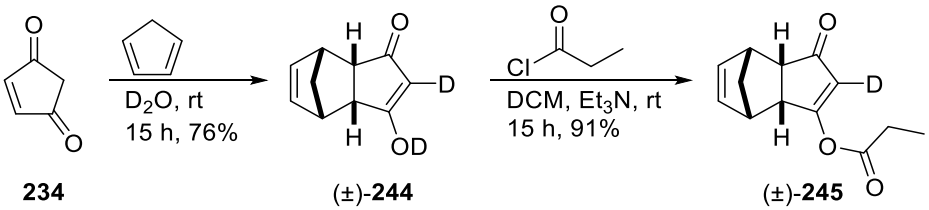
Scheme 99. Esterification of (±)-**211** using propionyl chloride.

With enol ester (±)-**240b** in hand, FVT was performed giving rise to *E*-butenolide **241b** and *Z*-butenolide **242b** (Scheme 100).



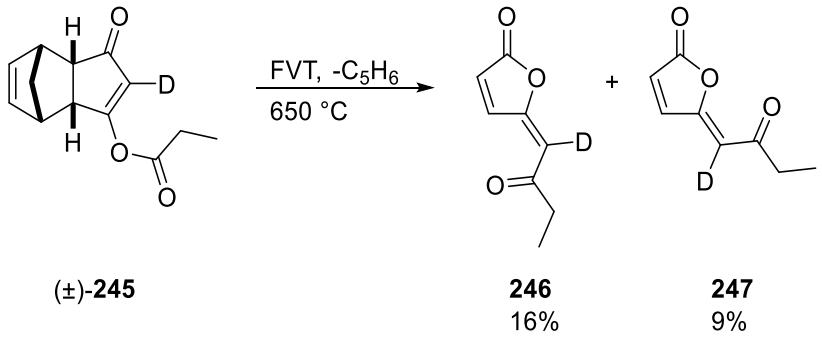
Scheme 100. FVT of propionyl ester (±)-**240b**.

Surprisingly, the additional carbon, in this case, is located outside of the five-membered ring on the side chain. In the next step, dione **234** was deuterated to obtain additional insight into the mechanism of the rearrangement. Dione **234** is easily deuterated in 2-postion by stirring in deuterated water due to the acidic protons located at this position, the addition of cyclopentadiene yielded deuterated Diels-Alder adduct (±)-**244** in 76% yield (Scheme 101).



Scheme 101. Synthesis of deuterated enol ester (±)-**245**.

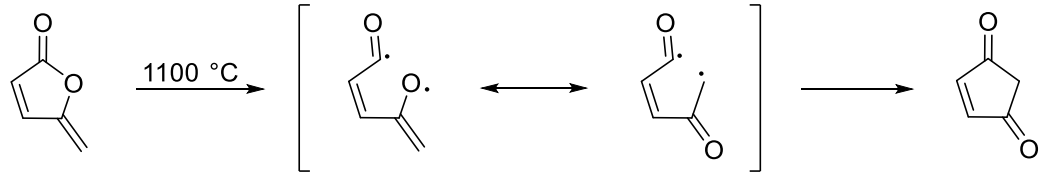
Deuterated compound (±)-**244** was transferred into the corresponding enol ester (±)-**245** using propionyl chloride. Subsequently, the deuterated enol ester (±)-**245** was subjected to FVT to obtain butenolides **246** and **247** having the deuterium on the *exo*-methylene group (Scheme 102).



(±)-**245** **246** 16% **247** 9%

Scheme 102. FVT of deuterated enol ester (±)-**245**.

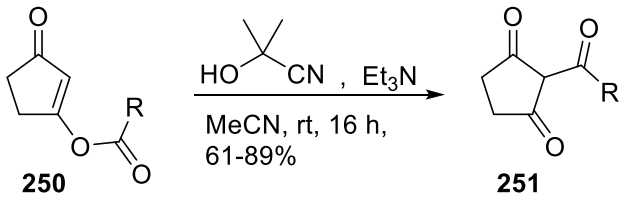
Orvane *et al.*[126] described the thermal rearrangement of butenolide **227** to dione **234**, which would be exactly the inverse reaction assumed for the rearrangement of enol esters to butenolides (Scheme 103). For this mechanism, a biradical **249**, which leads after recombination to dione **234** is proposed. In addition to this, the reaction of diones to butenolides was already observed under photochemical conditions.[127]



227 **248** **249** **234**

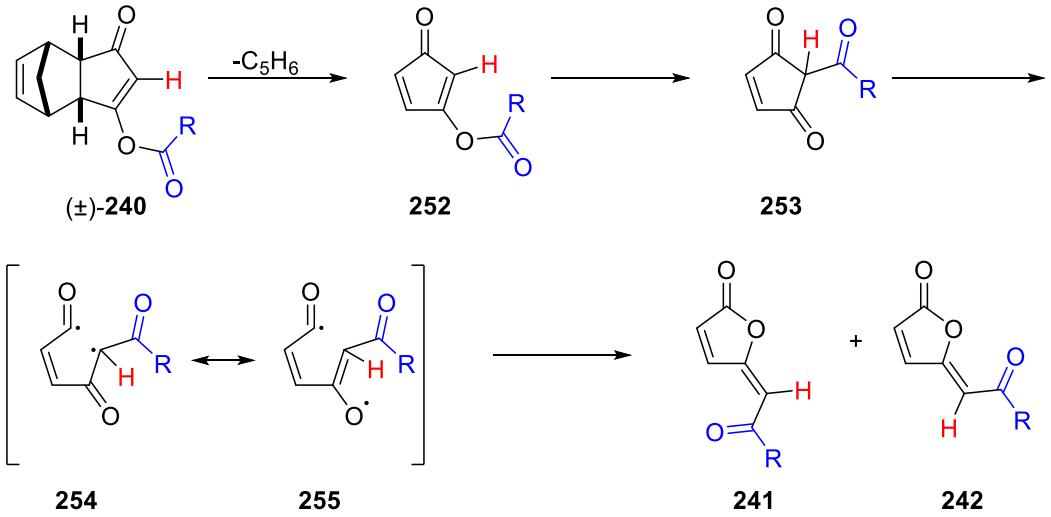
Scheme 103. Rearrangement of butenolide **227** to dione **234**.[126]

Moreover, isomerization of enol esters **250** to triketone **251** was demonstrated by Lakhvich *et al.*,[128] which would describe the observed shift of the additional residue in the rearrangement (Scheme 104).



Scheme 104. Isomerization of enol esters **250** to triketones **251**.[128]

Taking literature evidence and results of the investigation of the rearrangement in account the following mechanism was proposed (Scheme 105). In the first step, (±)-**240** undergoes a retro-Diels-Alder reaction with the loss of cyclopentadiene. The cyclopentadienone derivative **252** rearranges to **253**, which undergoes ring opening giving rise to biradical **254**. Finally, recombination of biradical **255** yields a mixture of *E*-/*Z*-butenolides **241** and **242**.



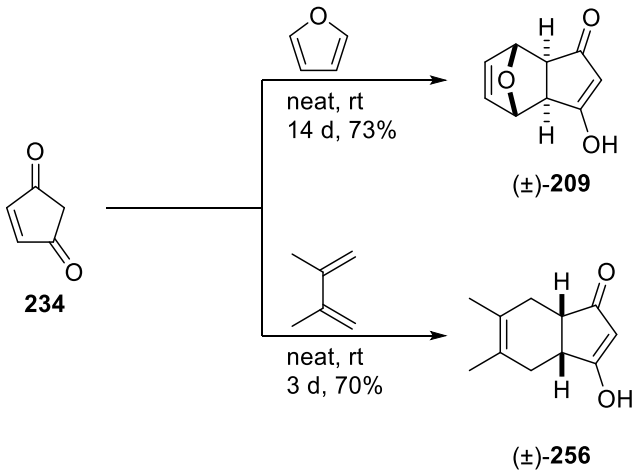
Scheme 105. Proposed mechanism for the rearrangement of enol ester (±)-**240**.

2.5 Variation of the reaction conditions

The Diels-Alder, as well as the retro-Diels-Alder reaction, are highly affected by the HOMO/LUMO ratio of diene and dienophile. Hence, two additional Diels-Alder adducts were

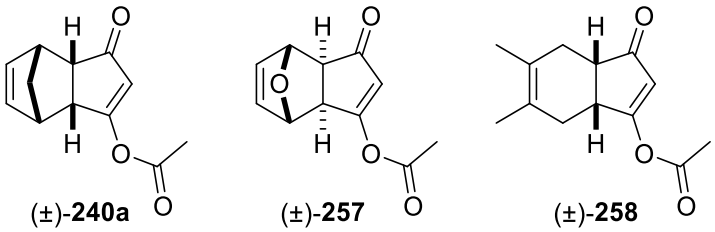
synthesized containing different dienes to investigate the influence of the retro-Diels-Alder reaction, the first proposed step of the mechanism.

Dione **234** reacted with furan to obtain Diels-Alder adduct (±)-**209** in 73% yield and with dimethylbutadiene to obtain (±)-**256** in 70% yield, respectively (Scheme 106).



Scheme 106. Synthesis of Diels-Alder adducts.

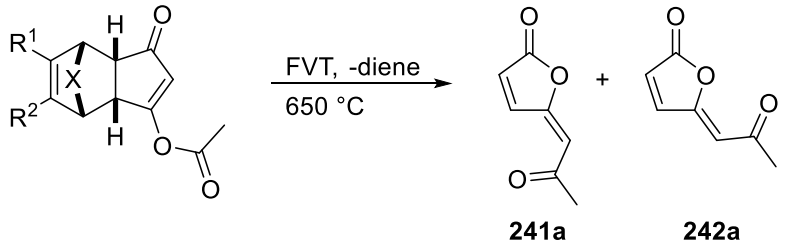
The synthesized Diels-Alder adducts were transferred into the corresponding acetyl ester using acetic anhydride as described before for Diels-Alder adduct (±)-**240a**. The received acetyl esters are depicted in Scheme 107.



Scheme 107. Synthesized acetyl esters.

These acetyl esters were tested in FVT at a constant temperature to compare the influence of the diene for the rearrangement (Table 5). The best results were obtained for the most reactive

diene in this row, the cyclopentadiene adduct (±)-**240a**. The furan adduct (±)-**257** yielded approximately half of the yield of the cyclopentadiene adduct (±)-**240a** and the dimethylbutadiene adduct (±)-**258** only gave traces of the desired products.



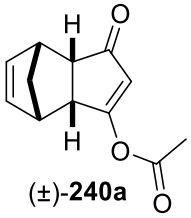
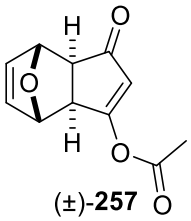
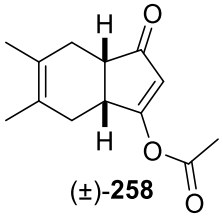
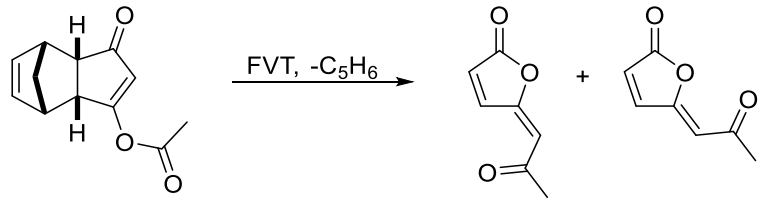
entry	ester	yield (%)	*E*/*Z*
1	 (±)-**240a**	31	61:39
2	 (±)-**257**	16	75:25
3	 (±)-**258**	traces	-

Table 5. FVT of different enol esters.

In the following, the behavior of acetyl ester (±)-**240a** using different temperatures in the FVT was examined (Table 6). At 550 °C, no formation of γ-alkylidenebutenolides was observed. In this case, it seems that the initial retro-Diels-Alder reaction did not take place and therefore no product formation was detected. At higher temperatures than 650 °C lower yields were obtained.

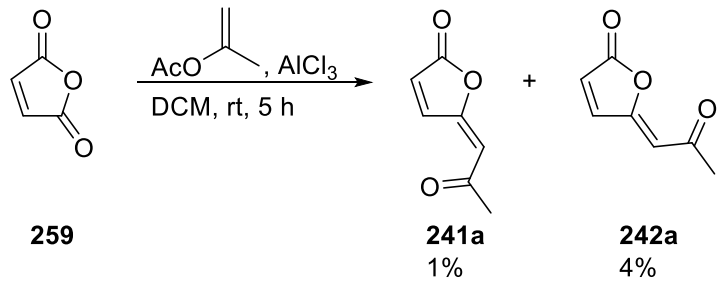


(±)-**240a** **241a** **242a**

entry	temperature (°C)	yield (%)	*E*/*Z*
1	550	0	-
2	650	31	61:39
3	750	16	75:25
4	850	traces	-

Table 6. FVT of (±)-**240a** at different temperatures.

In conclusion, the best reactions conditions found were using cyclopentadiene derived enol esters at 650 °C oven temperature in the FVT. The reaction provided about 30% yield of an *E*/*Z* mixture of γ-alkylidenebutenolides. The starting materials were easily synthesized in high yields, and the obtained butenolides are highly interesting materials, which have never been synthesized before. Except from Seltzer *et al.*[129] who described a very low yielding reaction to receive **241a** and **242a** (Scheme 108).

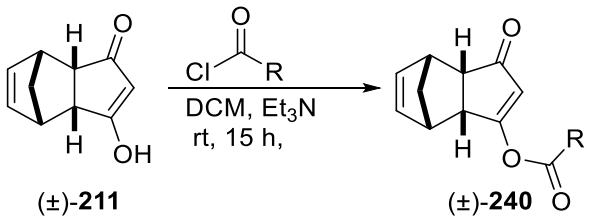


259 **241a** 1% **242a** 4%

Scheme 108. Synthesis of γ-alkylidenebutenolides **241a** and **242a** by Seltzer *et al*.[129]

2.6 Synthesis of enol esters and rearrangement to γ-alkylidenebutenolides

First of all different enol esters were synthesized using the reaction conditions mentioned before (Table 7). Esterification of (±)-**211** gave excellent yields in all cases with various acid chlorides used. Hence, enol esters with different steric hindrance and functional groups were obtained.



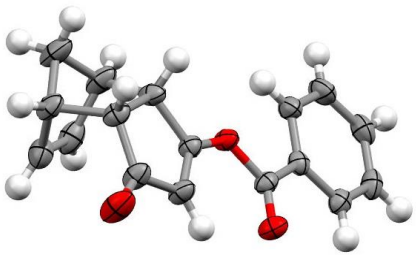
(±)-**211** (±)-**240**

entry	R	(±)-**240**	yield (%)
1	Me[a)]	**a**	100
2	Et	**b**	98
2	*i*-Pr	**c**	100
3	*t*-Bu	**d**	100
4	Allyl	**e**	100
5	*n*-Pent	**f**	94
6	Ph	**g**	91
7	4-OMe-Ph	**h**	96
8	OEt	**i**	100

a) (±)-**240a** was prepared using Ac_2O as described above.

Table 7. Synthesis of various enol esters.

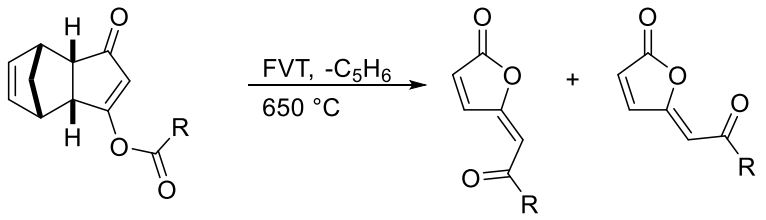
Additionally, the structure of enol esters (±)-**240** was clearly proven by X-ray crystallography of (±)-**240g** (Figure 12).



(±)-**240g**

Figure 12. Crystal structure of (±)-**240g**.

With a broad selection of enol esters in hand, the synthesized derivatives were subjected to FVT (Table 8).



(±)-**240** **241** **242**

entry	R	241 + 242	yield (%)	*E*/*Z*
1	Me	**a**	34	62:38
2	Et	**b**	34	71:29
3	*i*-Pr	**c**	27	70:30
4	*t*-Bu	**d**	35	63:37
5	Allyl	**e**	-	-
6	*n*-Pent	**f**	35	66:34
7	Ph	**g**	31	100:0
8	4-OMe-Ph	**h**	35	100:0
9	OEt	**i**	-	-

Table 8. FVT of various enol esters.

All alkyl substituents tested gave a similar yield of 27-35%. The steric hindrance of the substituents did not affect the *E*/*Z*-ratio. In contrast, aromatic substituents yielded exclusive the corresponding *E*-butenolides in about 30% yield. The reactions with allyl and ethoxy residues did not show any formation of the expected products.

Additionally, it was found that *Z*-butenolides **242** isomerize into the corresponding *E*-butenolides **241** in solution (Figure 13). Therefore, pure *Z*-butenolide **242a** was dissolved in deuterated chloroform, and the amount of *E*- and *Z*-butenolide was monitored via NMR-spectroscopy. After one day, approximately 20% of the Z-butenolide **242a** was

transferred into the *E*-isomer **241a**. With progressing time, the isomerization was becoming slower and after about five days the *E*-isomers **241a** is the major product in solution. After 14 d the *Z*/*E*-ratio was 38:62. The addition of toluenesulfonic acid as an acid catalyst could not accelerate the observed isomerization.

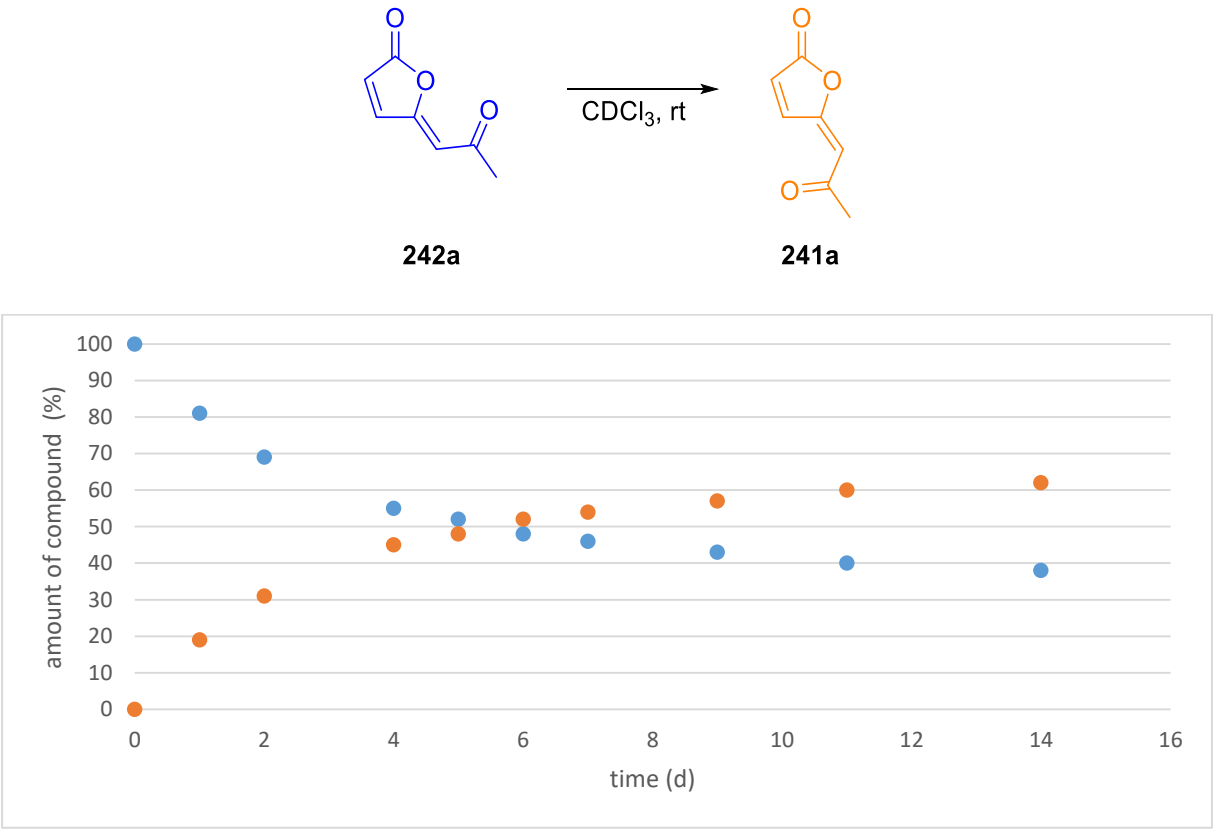


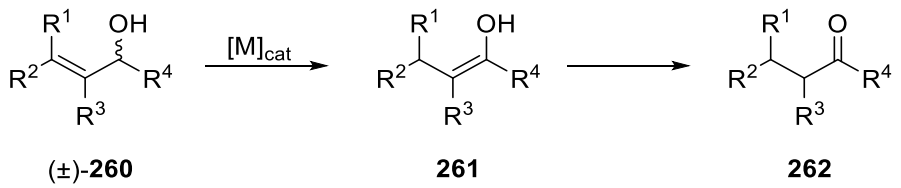
Figure 13. Isomerization of *Z*-Butenolide **242a**.

In summary, a highly interesting rearrangement of enol esters to γ-alkylidenebutenolides was discovered, the reaction was studied, and a mechanism was proposed. The starting materials were straightforwardly synthesized from renewable resources in high yields. Unfortunately, the γ-alkylidenebutenolides were obtained as *E*/*Z* mixtures and in low yields of about 30%, which could not be improved during this studies.

3 Redox isomerization of 4-hydroxy-2-cyclopentenone derivatives

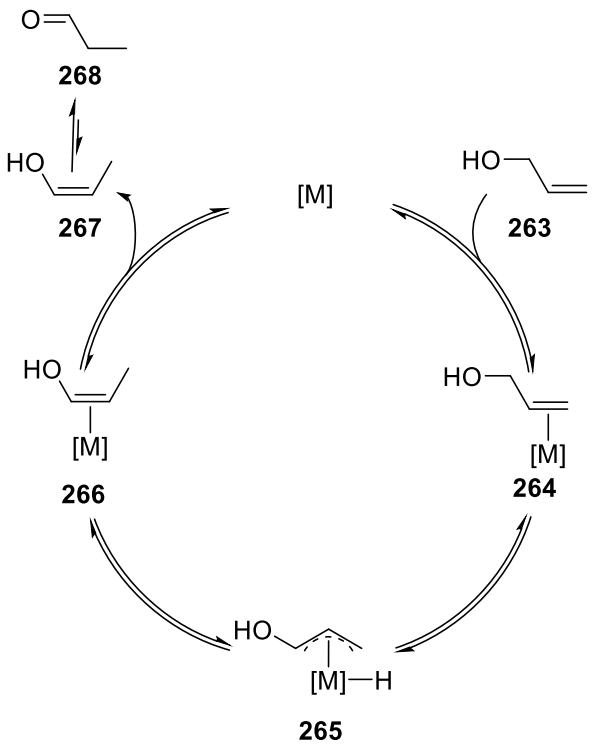
3.1 Introduction

Carbonyl compounds are important substrates in organic synthesis and redox isomerization of readily accessible allylic alcohols (±)-**260** provides an elegant opportunity for their atom economic synthesis. This isomerization reaction, which typically does not generate any byproducts, is grounded on the ability of transition metals to induce the migration of carbon-carbon double bonds to yield the corresponding enolate **261** followed by tautomerization to carbonyl compound **262** (Scheme 109).[130]



Scheme 109. Isomerization of allylic alcohols.[130]

Three different mechanisms for the redox isomerization of allyl alcohols are proposed: an alkyl mechanism, a η^3-allyl-mechanism, and a η^3-oxo-allyl-mechanism. The η^3-allyl-mechanism is depicted in Scheme 110.[131]



Scheme 110. The η^3-allyl-mechanism.[131]

The catalytic cycle starts with coordination of the metal to the double bond of the allyl alcohol **264**. A formal oxidative addition of one of the C-H bonds of the double bond leads to π-allyl metal-hydride intermediate **265**. Reductive elimination furnishes η^2-enol complex **266**. The decoordination to **267** followed by tautomerization of the free enol yields the final carbonyl compound **268** and regenerates the metal to close the catalytic cycle.[131]

The redox isomerization of 4-hydroxy-2-cyclopentenone ((±)-**150**) would furnish 1,3-cyclopentanedione **238**, which is known as valuable starting material for many biologically active substances such as prostaglandins, antibiotics, fragrances or herbicides (Figure 14).[132]

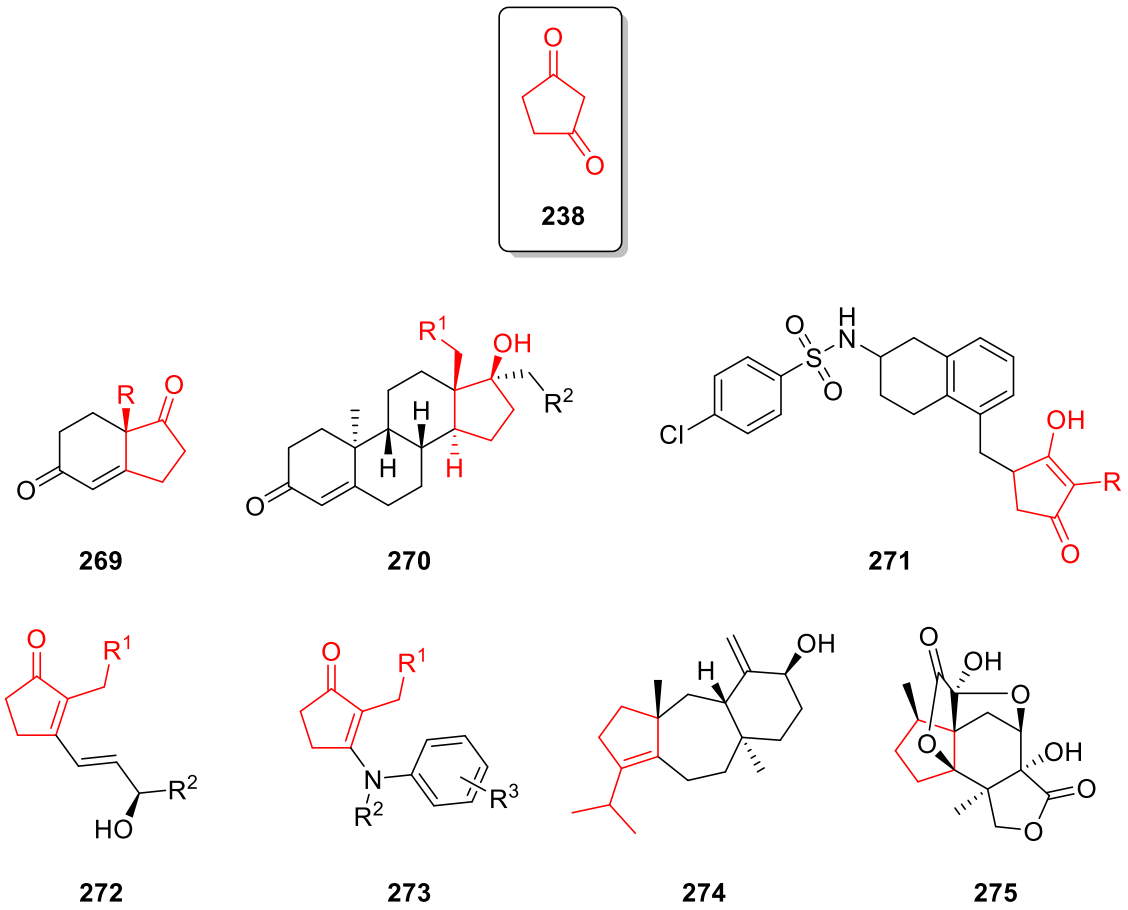


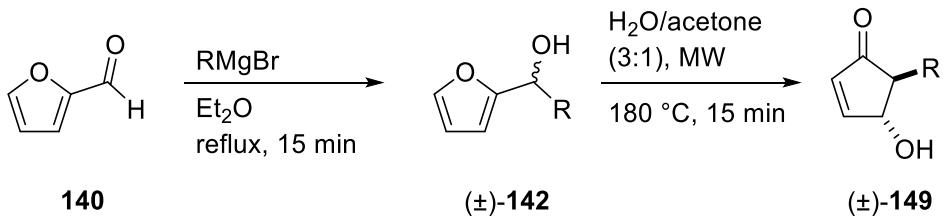
Figure 14. Biological active compounds synthesized from 1,3-cyclopentanedione derivatives.

The redox isomerization of 4-hydroxy-2-cyclopentenone derivatives would open a simple and useful access to substituted 1,3-cyclopentanediones.

3.2 Synthesis of 4-hydroxy-2-cyclopentenone derivatives

Several 4-hydroxy-2-cyclopentenone derivatives were straightforwardly synthesized starting from furfural (**140**) as mentioned earlier. Via a Grignard reaction various substituted furfuryl alcohol derivatives (±)-**142** were accessible and subsequent Piancatelli rearrangement yielded 5-substituted 4-hydroxy-2-cyclopentenones (±)-**149**.[80] The aforementioned Piancatelli rearrangement can be improved by using microwave irradiation. Therefore, furfuryl alcohol

derivatives (±)-**142** were converted into the corresponding 5-substituted 4-hydroxy-2-cyclopentenone (±)-**149** using microwave irradiation in good yields (Table 9).



140 (±)-**142** (±)-**149**

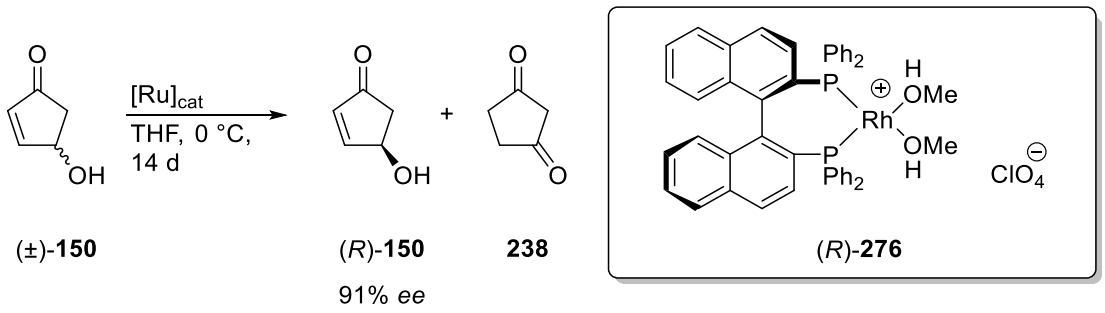
entry	R	(±)-**142** +(±)-**149**	**yield** (±)-**142 (%)**	**yield** (±)-**149 (%)**
1	*n*-Pr	**a**	76	64
2	*n*-Pent	**b**	89	74
3	*n*-Hept	**c**	86	44
4	Et	**d**	62	76
5	*i*-Pr	**e**	55	69
6	Allyl	**f**	61	57

Table 9. Microwave-assisted synthesis of 4-hydroxy-2-cyclopentenone derivatives.

Unsubstituted 4-hydroxy-2-cyclopentenone ((±)-**150**) and the 5-methyl-substituted derivative (±)-**200** were synthesized using the aforementioned microreactor setup. Additionally, a 2-methyl-substituted derivative ((±)-**201** was obtained by isomerization of compound (±)-**200** on Al_2O_3.[106]

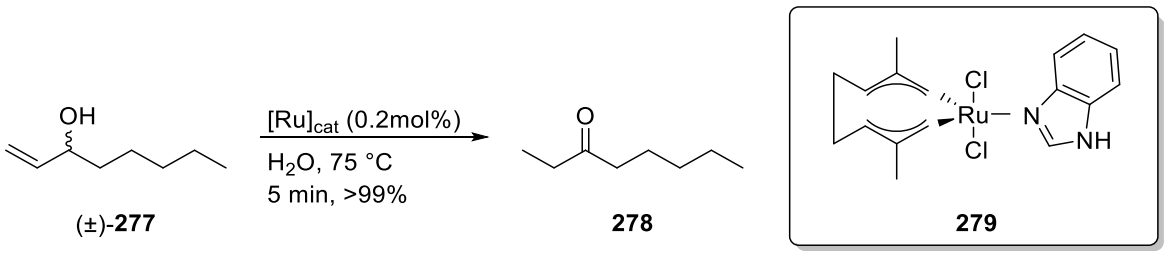
3.3 Redox isomerization

Noyori *et al.*[133] performed the asymmetric redox isomerization of 4-hydroxy-2-cyclopentenone ((±)-**150**) using complex (*R*)-**276** to obtain **238** and the valuable enantiomer (*R*)-**150** with good enantiomeric excess (Scheme 111).



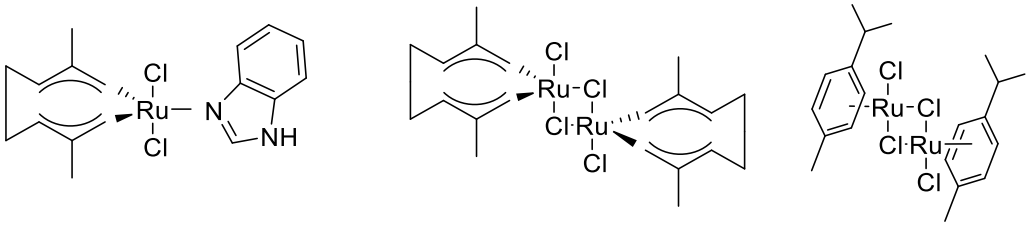
Scheme 111. Kinetic resolution of 4-hydroxy-2-cyclopentenone ((±)-**150**).[133]

Since diketone **238**, and its derivatives are highly valuable materials, it would be interesting to perform the redox isomerization without any enantiomeric discrimination. Preferably, with water as a solvent since the products are hardly soluble in it and the previous Piancatelli rearrangement is also performed in aqueous medium. This would give the opportunity to carry out two reactions in one step. The redox isomerization of allylic alcohols using water as solvent is well known in the literature and some ruthenium-based catalysts show high activity for various substrates.[134] A very active ligand was described by Gimeno *et al.*[135] with a turnover frequency value of about 60 000 h^{-1} (Scheme 112).



Scheme 112. Redox isomerization catalyzed by an imidazole-based ruthenium complex.[135]

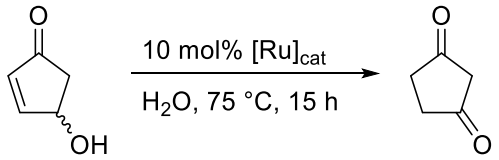
These reactions conditions were adopted for the redox isomerization of 4-hydroxy-2-cyclopentenone ((±)-**150**) and three different catalysts were tested (Scheme 113).



279 **280** **281**

Scheme 113. Ruthenium-based catalysts.

These catalysts have been shown good activities in the redox isomerization of allyl alcohols. As a starting point, 10 mol% of catalyst were used because previous studies showed that higher substituted double bonds require higher catalyst amounts (Table 10).[134,135]

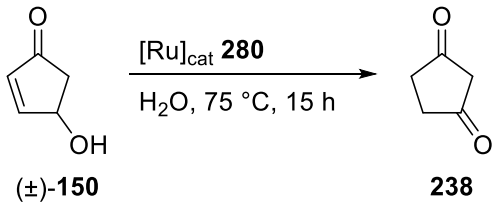


(±)-**150** **238**

entry	complex	yield (%)
1	**279**	57
2	**280**	80
3	**281**	7

Table 10. Redox isomerization of (±)-**150** with different catalysts.

Complex **280** showed the best activity for the chosen substrate (±)-**150** providing 80% of the expected product **238**. In the next step, the amount of catalyst was varied to optimize the reaction conditions (Table 11).

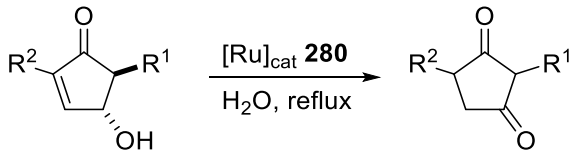


(±)-**150** **238**

entry	280 (mol%)	yield (%)
1	1	17
2	5	73
3	10	75

Table 11. Redox isomerization of (±)-**150** with different catalyst loadings.

The redox isomerization of (±)-**150** gave similar yield with 5 and 10 mol% of catalyst, with 1 mol% an immense drop in yield was observed. Therefore, 5 mol% catalyst were used in the following reactions. Additionally, higher reaction temperatures were identified as beneficial for the reaction, therefore the reaction temperature was raised to reflux. With the optimized reaction conditions in hand, the redox isomerization of various 4-hydroxy-2-cyclopentenone derivatives was investigated (Table 12).



entry	R^1	R^2	alcohol	product	mol% $[Ru]_{cat}$	time (h)	yield (%)
1	H	H	(±)-**150**	**238**	5	8	80
2	Me	H	(±)-**200**	**282a**	5	15	91
3	*n*-Pr	H	(±)-**149a**	**282b**	5	30	81
4	*n*-Pent	H	(±)-**149b**	**282c**	10	15	72
5	*n*-Hept	H	(±)-**149c**	**282d**	10	30	traces
6	Et	H	(±)-**149d**	**282e**	5	15	86
7	*i*-Pr	H	(±)-**149e**	**282f**	10	30	51
8	Allyl	H	(±)-**149f**	**282g**	5	15	decomposition
9	H	Me	(±)-**201**	**282h**	5	15	decomposition

Table 12. Redox isomerization of various 4-hydroxy-2-cyclopentenone derivatives.

The redox isomerization of 4-hydroxy-2-cyclopentenone ((±)-**150**) yielded the expected diketone **238** in 80% yield within 8 h. Afterward, 5-substituted 4-hydroxy-2-cyclopentenone derivatives were tested. The methyl derivative (±)-**200** gave 91% of the desired product by elongation of the reaction time to 15 h. The ethyl derivative was isolated in 86% under the same conditions in entry 6. By elongation of the side chain to the *n*-propyl derivative in entry 3 the reaction time was extended to 30 h giving the product **282b** in 81% yield. The *i*-propyl derivative **282f** having the most steric hindrance was obtained after 30 h with 10 mol% of catalyst in 51% yield. In the case of the *n*-pentyl compound, 72% of **282c** were isolated after 15 h using 10 mol% of the catalyst. However, substrates containing an allyl substituent in 5-position or a substituent in 2-postion showed only decomposition. The *n*-Heptyl derivative was only observed in traces, which might be due to bad solubility in the solvent. All in all the

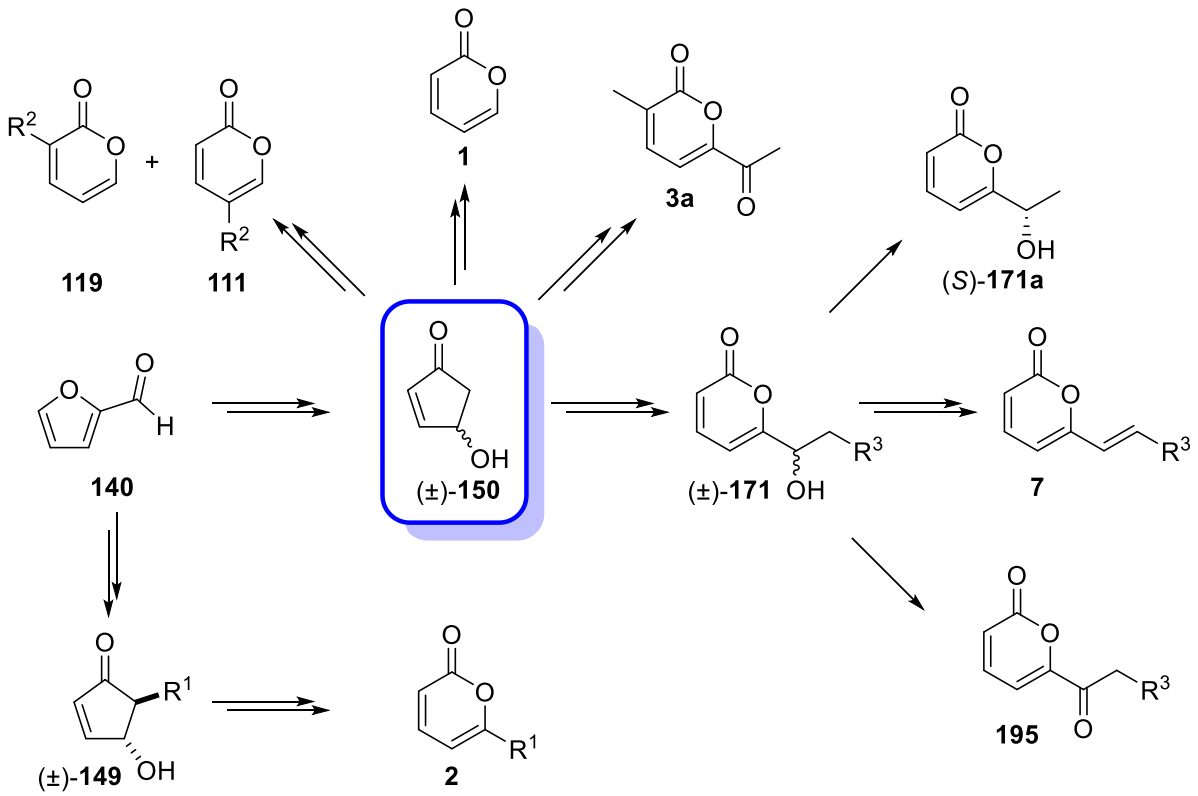
steric hindrance of the used substrates showed high influence on the redox isomerization. The bulkier the chosen substituent, the slower is the reaction rate. As a result, either higher amounts of catalyst or longer reaction times were required by increasing the spatial demand of the substituents.

In conclusion, an efficient way for the synthesis of substituted 1,3-cyclopentanedione derivatives starting from renewable resources was developed. The reaction is dependent on the steric hindrance and the position of the substituents of the 4-hydroxy-2-cyclopentenone derivatives. The best results were obtained with no substituent or small substituents in 5-position of the 4-hydroxy-2-cyclopentenone derivatives.

C Summary

This thesis deals with the synthesis of valuable chemicals starting from renewable resources. All syntheses start from 4-hydroxy-2-cyclopentenone ((±)-**150**) and its derivatives, which can be readily obtained from furfural (**140**), made from agricultural waste like bran or bagasse, via a straightforward reaction sequence. Reduction of furfural (**140**) yields furfuryl alcohol (**141**), which is then efficiently converted to 4-hydroxy-2-cyclopentenone ((±)-**150**) via a Piancatelli rearrangement in a microreactor. Therefore, 4-hydroxy-2-cyclopentenone ((±)-**150**) and its derivatives represent the key building blocks used in this thesis.

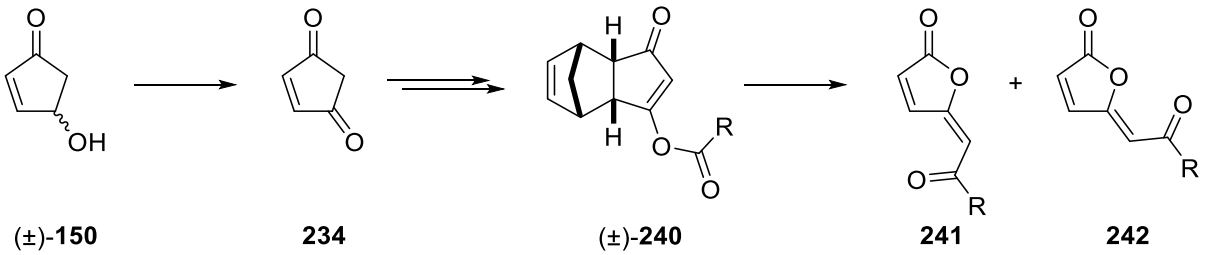
In the first chapter, various substituted 2-pyrones were synthesized from 4-hydroxy-2-cyclopentenone ((±)-**150**) and its derivatives, utilizing the thermal rearrangement of cyclopentadienone epoxides to 2-pyrone as the key step (Scheme 114).



Scheme 114. Overview of the synthesis of 2-pyrones starting from renewable resources.

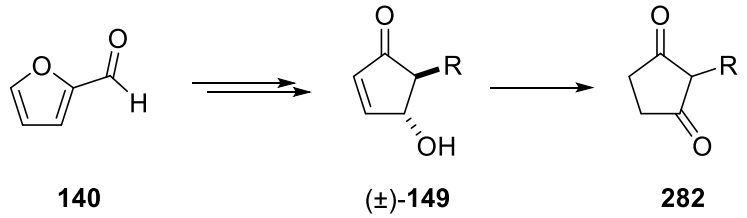
It was possible to obtain unsubstituted 2-pyrone (**1**) via a short reaction sequence in multigram scale with high yield and purity. Using a similar reaction sequence allowed the synthesis of naturally occurring 6-substituted alkyl 2-pyrones **2** in excellent yields. Additionally, 4-hydroxy-2-cyclopentenone ((±)-**150**) could be converted into various 6-substituted α-hydroxyalkyl 2-pyrones (±)-**171** via a Baylis Hillman reaction with different aldehydes. The so obtained compounds bearing a α-hydroxyalkyl side chain allowed a plethora of transformations. The enzymatic resolution provided access to enantiomerically pure 2-pyrones. Alternatively, elimination of the α-hydroxy group gave access to naturally occurring Sibirinone (**7**) and related natural products. Oxidation of the α-hydroxy group yielded the corresponding carbonyl compounds, which was used for the synthesis of naturally occurring Gibepyrone F after introducing a methyl substituent in 3-position. Using a different strategy, the synthesis for 5-substituted 2-pyrones yielded a mixture of 3- and 5-substituted 2-pyrones **119** and **111**, which could be explained by a [1,5] sigmatropic H-shift.

The second chapter deals with the sustainable oxidation of 4-hydroxy-2-cyclopentenone ((±)-**150**) to dione **234**, which was used for the synthesis of enol esters (±)-**240**. Investigation of the reactivity of these enol esters (±)-**240** revealed that they undergo an interesting rearrangement when subjected to FVT. The resulting γ-alkylidenebutenolides are highly interesting new compounds with high functional group density (Scheme 115). After an intensive study of the reaction and its conditions, a plausible mechanism for the rearrangement was proposed. Additionally, a broad scope of esters (±)-**240** was synthesized and rearranged to the corresponding γ-alkylidenebutenolides. The γ-alkylidenebutenolides were obtained in an *E*/*Z* mixture, which was separable by chromatography in about 30% combined yield.



Scheme 115. Synthesis of γ-alkylidenebutenolides.

The final chapter concentrates on the ruthenium-catalyzed redox isomerization of different 4-hydroxy-2-cyclopentenones (±)-**149** to 1,3-cyclopentanedione derivatives **282** in water (Scheme 116). These diketone derivatives **282** are highly valuable compounds for the synthesis of various complex organic molecules and not many protocols are reported for their synthesis. The redox isomerization proved to be suitable for unsubstituted 4-hydroxy-2-cyclopentenone ((±)-**150**) and for derivatives with a substitution in 5-position (±)-**149** giving the corresponding diketones **282** in up to 91% yield. However, the reaction proved to be dependent on the steric bulk of the substituent as smaller substituents gave the best results for the isomerization.



Scheme 116. Redox isomerization of 4-hydroxy-2-cyclopentenone derivatives.

In conclusion, an efficient synthetic strategy for various valuable compounds was developed, namely 2-pyrones, γ-alkylidenebutenolides and 1,3-cyclopentanedione derivatives. All compounds could be obtained from the same starting materials, 4-hydroxy-2-cyclopentenone and its derivatives, which are readily available from renewable resources. This underlines that

C Summary

4-hydroxy-2-cyclopentenones are useful and reliable platform chemicals for fine chemical synthesis.

D Zusammenfassung

Diese Dissertation beschäftigt sich mit der Synthese von wertvollen Chemikalien ausgehend von erneuerbaren Ressourcen. Alle Synthesen beginnen mit 4-Hydroxy-2-cyclopentenon ((±)-**150**) und dessen Derivaten, welche leicht aus Furfural (**140**), das aus landwirtschaftlichen Abfallprodukten wie Kleie und Bagasse gewonnen wird, mit Hilfe einer unkomplizierten Reaktionssequenz erhalten werden kann. Reduktion von Furfural (**140**) ergibt Furfurylalkohol (**141**), welcher mit Hilfe der Piancatelli-Umlagerung in einem Mikroreaktor in 4-Hydroxy-2-cyclopentenon überführt wird. Deshalb stellen 4-Hydroxy-2-cyclopentenon und dessen Derivate einen zentralen Baustein in dieser Dissertation dar.

Im ersten Kapitel wurden verschiedene substituierte 2-Pyrone aus 4-Hydroxy-2-cyclopentenon ((±)-**150**) und dessen Derivaten synthetisiert, wobei die thermische Umlagerung von Cyclopentadienonepoxiden zu 2-Pyronen als Schlüsselschritt genutzt wurde (Abbildung 1).

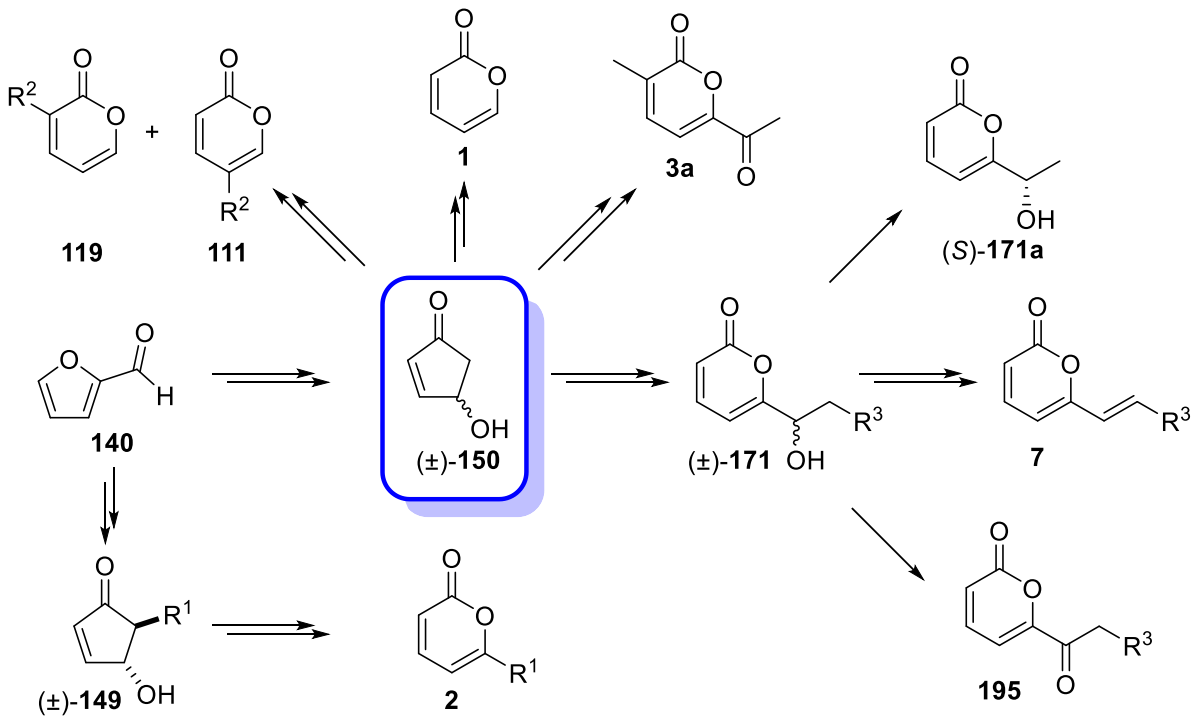


Abbildung 1. Übersicht über die Synthese von 2-Pyronen aus erneuerbaren Ressourcen.

Es war möglich unsubstituiertes 2-Pyron (**1**) mit Hilfe einer kurzen Reaktionssequenz im Multigrammmaßstab mit hoher Ausbeute und Reinheit zu erhalten. Die Verwendung einer ähnlichen Reaktionssequenz ermöglichte die Synthese 6-substituierter Alkyl-2-pyrone in exzellenten Ausbeuten. Zusätzlich konnte 4-Hydroxy-2-cyclopentenon ((±)-**150**) mit Hilfe einer Baylis-Hillman Reaktion und verschiedenen Aldehyden in diverse 6-substituierte α-Hydroxyalkyl-2-pyrone (±)-**171** überführt werden Die so erhaltenen Verbindunngen enthalten eine α-Hydroxyalkylseitenkette, die eine Fülle an Transformationen erlaubt. Racematspaltung lieferte Zugang zu enantiomerenreinen 2-Pyronen. Alternativ lieferte die Eliminierung der α-Hydroxygruppe Zugang zu natürlich vorkommendem Sibirinon (**7a**) und verwandten Naturstoffen. Oxidation der α-Hydroxygruppe ergab die entsprechenden Carbonylverbindungen und dies wurde für die Synthese von natürlich vorkommendem Gibepyron F nach der Einführung eines Methylsubstituenten in 3-Position genutzt. Die Anwendung einer anderen Strategie zur Synthese von 5-substituierten 2-Pyronen ergab ein Gemisch aus 3- und 5-substituierten 2-Pyronen **119** und **111**, was mit einer sigmatropen [1,5] H-Verschiebung erklärt werden konnten.

Das zweite Kapitel beschäftigt sich mit der nachhaltigen Oxidation von 4-Hydroxy-2-cyclopentenon ((±)-**150**) zu Dion **234**, das für die Synthese der Enolester (±)-**240** verwendet wurde. Untersuchungen der Reaktivität dieser Enolester (±)-**240** zeigten, dass sie eine interessante Umlagerung in der FVT eingehen. Die entstandenen γ-Alkylidenebutenolide sind hochinteressante neue Verbindungen mit einer hohen Dichte an funktionellen Gruppen (Abbildung 2). Nach intensiver Untersuchung der Reaktion und ihrer Bedingungen wurde ein plausibler Mechanismus für die Umlagerung vorgeschlagen. Zusätzlich wurde eine breite Auswahl an Estern (±)-**240** synthetisiert und zu den entsprechenden γ-Alkylidenebutenoliden umgelagert. Die γ-Alkylidenebutenolide wurden als *E*/*Z*-Mischung erhalten in einer Gesamtausbeute von ca. 30%, welche chromatographisch getrennt werden konnten.

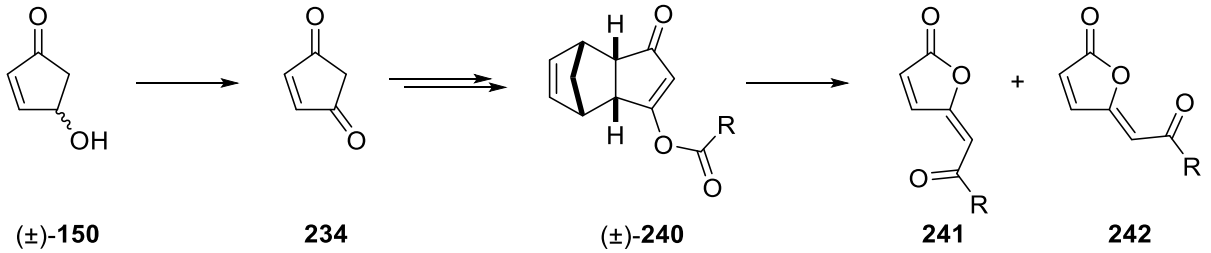


Abbildung 2. Synthese von γ-Alkylidenebutenoliden.

Das letzte Kapitel konzentriert sich auf die Ruthenium katalysierte Redoxisomerisierung von verschiedenen 4-Hydroxy-2-cyclopentenonen (±)-**149** zu 1,3-Cyclopentandionderivaten **282** in Wasser (Abbildung 3). Diese Diketonderivate **282** sind sehr wertvolle Verbindungen für die Synthese von diversen komplexen organischen Molekülen und es sind nicht viele Vorschriften für deren Synthese berichtet. Die Redoxisomerisierung erwies sich als geeignet für unsubstituiertes 4-Hydroxy-2-cyclopentenonen ((±)-**150**) und für Derivate mit Substitution in 5-Position (±)-**149**, welche die entsprechenden Diketone **282** in bis zu 91% Ausbeute lieferte. Jedoch, erwies sich die Reaktion als abhängig von der sterischen Hinderung der Substituenten, da kleinere Substituenten die besten Ergebnisse für die Isomerisierung lieferten.

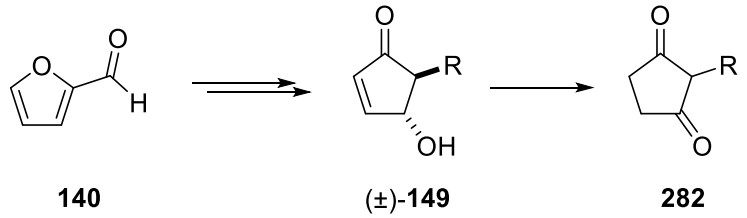


Abbildung 3. Redoxisomerisierung von 4-Hydroxy-2-cyclopentenonderivativen.

Zusammenfassend wurde eine effiziente synthetische Strategie zur Synthese verschiedener wertvoller Verbindungen wie 2-Pyrone, γ-Alkylidenebutenolide und 1,3-Cyclopentandionderivate entwickelt. Alle Verbindungen konnten von denselben Startmaterialien, 4-Hydroxy-2-cyclopentenon und dessen Derivaten, welche leicht aus

erneuerbaren Ressourcen erhalten werden können, gewonnen werden. Dies unterstreicht, dass 4-Hydroxy-2-cyclopentenone nützliche und zuverlässige Plattformchemikalien für die Feinchemikaliensynthese darstellen.

E Experimental

1 General information

Commercially available chemicals were purchased in high quality and used without any further purification. All reactions were carried out in oven-dried glassware under atmospheric conditions unless otherwise stated. DCM, ethyl acetate and hexanes (petroleum ether, PE (60/40)) were distilled prior to use. THF and Et_2O were received from a MB-SPS solvent purification system. Other anhydrous solvents were prepared by established procedures.[136]

^{1}H- and ^{13}C-NMR

NMR spectra were recorded on a BRUKER Avance III 400 Nanobay (400 MHz) and a BRUKER Avance 300 (300 MHz) spectrometer at ambient temperature. Chemical shifts are reported as δ (ppm) relative to the signal of the solvent. Characterization of the signals: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, m = multiplet, bs = broad singlet, dd = doublet of a doublet, dt = doublet of a triplet, dq = doublet of a quartet, ddd = doublet of a doublet of a doublet. Integration is determined as the relative number of atoms, and the coupling constants (*J*) are given in Hertz (Hz). The multiplicity of the carbon atoms is given as (+) = CH_3 or CH (positive DEPT signal), (-) = CH_2 (negative DEPT signal) and (C_q) for quaternary carbon atoms (no DEPT signal).

Column chromatography

Column chromatography was performed using Merck Gerduran 60 silica gel (0.063–0.200 mm) or Merck flash silica gel 60 (0.040–0.063 mm).

Gas chromatography

Gas chromatography was carried out on a Fisons GC 8000 Series with a flame ionization detector (FID). As stationary phase DB1 (100% dimethylpolysiloxane, 30 m, ID 0.25 mm, 0.25 µm Film) was used. GC instrument conditions: Inlet temperature = 250 °C; detector temperature = 300 °C. GC method: starting temperature 80 °C, then temperature ramp (5 °C/min) for 24 min to 200 °C followed by an isothermal period at 200 °C for 5 min

HPLC

HPLC was performed on a Varian 920-LC with a photodiode array (PDA) detector, and a specified chiral stationary phase was used.

IR spectroscopy

ATR-IR spectroscopy was carried out on a Biorad Excalibur FTS 3000 MX, equipped with a Specac Golden Gate Diamond Single Reflection ATR-System or on an Agilent Technologies Cary 630 FTIR . Solid and liquid compounds were measured neatly, and wave numbers are reported in cm^{-1}.

Mass spectrometry

Mass spectrometry was performed in the Central Analytical Department of the University of Regensburg on a Jeol AccuTOF GCX, Agilent Q-TOF 6540 UHD, Finnigan MAT SSQ 710 A or a ThermoQuest Finnigan TSQ 7000.

Melting points

The melting points were measured on a SRS MPA 100 OptiMelt in a silicon oil bath. Values thus obtained were not corrected.

Microwave

Microwave reactions were carried out on an Anton-Paar Monowave 300 microwave using pressure stable sealed 10 mL or 35 mL vessels.

Optical rotation

The optical rotation was determined on an Anton Paar MCP 500 polarimeter at 589 nm wavelength (sodium-d-line) in a 1.0 dm measuring cell.

Thin layer chromatography

Thin layer chromatography was done using Merck silica gel 60 F254 coated with 0.2 mm silica. Visualization was accomplished by UV light (254 nm), and staining was performed with vanillin or potassium permanganate solutions followed by heating.

X-ray-crystallography

X-Ray crystallography was done by the crystallography laboratory of the University of Regensburg.

Synthesis of literature known compounds

The following compounds were synthesized according to literature known procedures:

(±)-**150**,[83] (±)-**138**,[88] (±)-**137**,[91] (±)-**211**,[120] (±)-**209**,[119], **279**,[135] **280**.[137]

2 Synthesis of 2-pyrones starting from renewable resources

General Procedure 1: Flash Vacuum Thermolysis: For flash vacuum thermolysis a high-quality glass tube (length 90 cm, diameter 1 cm) open at both ends was fixed horizontally in a tube furnace connected to a cooling trap and a flask containing the epoxide. The tube furnace was heated to 650 °C and connected to a high-vacuum line at $2 \cdot 10^{-2}$ mbar. The starting material was slowly evaporated through the tube furnace, and the product was collected in a trap cooled with liquid nitrogen. The product was washed off the cooling trap with DCM, the solvent was removed, and the product was dried under reduced pressure to yield the pure compound.

General Procedure 2: Grignard reaction of 140 to (±)-**142:** Magnesium shavings (1.3 equiv) were suspended in dry Et_2O (2.50 M), and a catalytic amount iodine was added. The bromide (1.6 equiv) was dissolved in dry Et_2O (1.25 M) and added dropwise to the suspension. When the suspension stopped boiling it was refluxed for 1 h and afterward cooled down to 0 °C. A solution of furfural (**140**) (1.0 equiv) in dry Et_2O (1.25 M) was slowly dropped into the suspension and stirred for 15 min. The reaction was quenched with water, and the phases were separated. The water phase was extracted with Et_2O (3x), and the combined organic layers were dried over $MgSO_4$. The crude was purified via flash chromatography (silica, PE/EA = 10:1).

General Procedure 3: Piancatelli rearrangement of (±)-**142 to** (±)-**149:** To a solution of furfuryl alcohol (±)-**142** (5.00 mmol) in acetone (5 mL) water (15 mL) was added, and the mixture was heated in the microwave at 180 °C for 15 min. This procedure was repeated as often as necessary, and the combined layers were extracted with DCM (3x). The combined

organic layers were dried over $MgSO_4$, and the crude product was purified via flash chromatography (silica, PE/EA = 2:1).

General Procedure 4: Acetylation: To a solution of 5-substituted 4-hydroxy-2-cyclopentenone (±)-**149** (20.0 mmol) in DCM (120 mL) Et_3N (13.86 mL, 100 mmol), and Ac_2O (9.45 mL, 100 mmol) were added, and the reaction mixture was stirred for 18 h at room temperature. The mixture was quenched with water (100 mL), and the phases were separated. The water phase was extracted with DCM (3x), and the combined organic layers were dried over $MgSO_4$. The crude product was purified via flash chromatography (silica, PE/EA = 10:1).

General Procedure 5: Diels-Alder reaction and Elimination of (±)-**154 to** (±)-**155:** Zink(II)chloride (1.36 g, 10.0 mmol) was suspended in toluene (60 mL), acetate (±)-**154** (10.0 mmol) was added, and the mixture was stirred for 15 min at room temperature. Freshly distilled cyclopentadiene (2.48 mL, 30.0 mmol) was added, and the mixture was stirred for 18 h at room temperature. The solvent was evaporated, and the crude product was dissolved in DCM/MeOH 1:1 (90 mL), 10 M NaOH (15 mL) was added and stirred for 1 h at room temperature. The mixture was washed with brine (1x), and the phases were separated. The water phase was extracted with DCM (3x), and the combined organic layers were dried over $MgSO_4$, and the crude product was purified via flash chromatography (silica, PE/EA = 10:1).

General Procedure 6: Epoxidation: To a solution of the enone (1.0 equiv) in DCM/MeOH 1:1 (5 M) 2 M NaOH (1.2 equiv), and H_2O_2 (30% in water, 5.4 equiv) were added, and the reaction mixture was stirred at room temperature. The reaction mixture was poured into DCM (30 mL) and once washed with brine. The organic layer was dried over $MgSO_4$ and concentrated under vacuum to yield the pure compound.

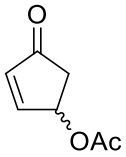
General Procedure 7: Baylis-Hillman reaction of (±)-**138 to** (±)-**165:** Under nitrogen atmosphere enone (±)-**138** (1.0 equiv) and the aldehyde (1.5 equiv) were dissolved in dry, degassed THF (1 M) at room temperature phenol (0.2 equiv), and Bu_3P (0.4 equiv) were added. The progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was evaporated, and the crude product was purified via flash chromatography by an appropriate PE/EA mixture.

General Procedure 8: Oxidation: To a solution of the 2-pyrone (1.0 mmol) in DCM (10 mL) MnO_2 (2.61 g, 30.0 mmol) was added, and the reaction mixture was stirred at room temperature for 20 h. The suspension was filtered through a celite plug, and the solution was concentrated under reduced pressure.

General Procedure 9: Tosylation of (±)-**171 to** (±)-**189:** To a solution of 2-pyrone (±)-**171** (1.0 mmol) in DCM (10 mL) DMAP (12 mg, 0.10 mmol), Et_3N (0.42 mL, 3.00 mmol), and 4-toluenesulfonyl chloride (229 mg, 1.20 mmol) were added, and the reaction mixture was stirred at room temperature. After 20 h saturated $KHSO_4$ solution (20 mL) was added, the water phase was extracted with DCM (3x), and the organic phase was dried over $MgSO_4$. The crude was purified via flash chromatography (silica, PE/EA = 3:1) to yield (±)-**189**.

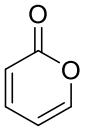
General Procedure 10: Elimination of (±)-**189 to 7:** To a solution of tosylated compound (±)-**189** (0.5 mmol) in DMF (5 mL) LiBr (261 mg, 3.00 mmol), and Li_2CO_3 (222 mg, 3.00 mmol) were added and the reaction mixture was heated for 1 h at 110 °C. After cooling to room temperature H_2O (20 mL) was added, the mixture was extracted with ethyl acetate (3x), and the combined organic layers were dried over $MgSO_4$. The crude product was purified via flash chromatography (silica, PE/EA = 5:1) to yield **7**.

4-Oxocyclopent-2-en-1-yl acetate ((±)-153):[138]



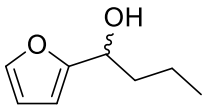
A solution of 4-hydroxycyclopent-2-en-1-one ((±)-**150**) (50.3 g, 513 mmol) in Ac_2O (75 mL, 793 mmol) was cooled to 0 °C and 4-toluenesulfonic acid (100 mg, 0.53 mmol) was added. The reaction mixture was stirred at room temperature for 18 h and the product was purified by distillation under reduced pressure to give 58.5 g (417 mmol, 81%) of a colorless oil which solidified to white crystals: **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H = (dd, *J* = 5.7, 2.4 Hz, 1H), 6.26 (dd, *J* = 5.7, 1.2 Hz, 1H), 5.78 (ddd, *J* = 6.1, 3.5, 2.2 Hz, 1H), 2.75 (dd, *J* = 18.7, 6.4 Hz, 1H), 2.25 (dd, *J* = 18.7, 2.2 Hz, 1H), 2.03 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C = 204.8 (C_q), 170.3 (C_q), 159.0 (+), 136.9 (+), 71.9 (+), 41.0 (-), 20.8 (+).

2*H*-Pyran-2-one (1):[139]



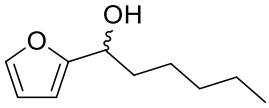
Following general procedure 1 epoxide (±)-**137** (11.35 g, 70.0 mmol) was used to afford a brownish liquid (6.34 g, 66.0 mmol, 94%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.48 (ddd, *J* = 5.1, 2.1, 1.2 Hz, 1H), 7.31 (ddd, *J* = 9.3, 6.4, 2.2 Hz, 1H), 6.32 (dt, *J* = 9.5, 1.0 Hz, 1H), 6.21 (ddd, *J* = 6.3, 5.3, 1.0 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 161.7 (C_q), 152.0 (+), 142.8 (+), 117.0 (+), 106.0 (+).

1-(Furan-2-yl)butan-1-ol ((±)-142a):[140]



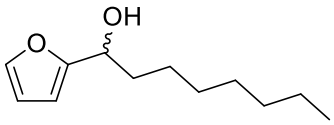
Following general procedure 2 magnesium shavings (2.28 g, 93.6 mmol), 1-bromopropane (10.5 mL, 115.2 mmol) and furfural (**140**) (5.96 mL, 72.0 mmol) to afford (±)-**142a** (7.62 g, 54.37 mmol, 76%) as a yellowish oil: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.39 – 7.34 (m, 1H), 6.32 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.23 (dd, *J* = 3.2, 0.6 Hz, 1H), 4.68 (t, *J* = 6.8 Hz, 1H), 1.93 (bs, 1H), 1.87 – 1.79 (m, 2H), 1.53 – 1.28 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 156.9 (C_q), 141.9 (+), 110.1 (+), 105.8 (+), 67.6 (+), 37.6 (-), 18.8 (-), 13.9 (+).

1-(Furan-2-yl)hexan-1-ol ((±)-142b):[141]



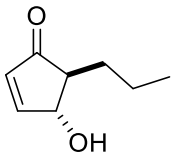
Following general procedure 2 magnesium shavings (2.28 g, 93.6 mmol), 1-bromopentane (14.26 mL, 115.2 mmol) and furfural (**140**) (5.96 mL, 72.0 mmol) to afford (±)-**142b** (10.76 g, 63.98 mmol, 89%) as a yellowish oil: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.37 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.33 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.23 (dt, *J* = 3.3, 0.7 Hz, 1H), 4.67 (t, *J* = 6.8 Hz, 1H), 1.92 – 1.80 (m, 3H), 1.44 – 1.27 (m, 6H), 0.88 (t, *J* = 6.9 Hz, 31H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 156.9 (C_q), 141.9 (+), 110.1 (+), 105.8 (+), 67.9 (+), 35.5 (-), 31.6 (-), 25.2 (-), 22.6 (-), 14.0 (+).

1-(Furan-2-yl)octan-1-ol ((±)-142c):[142]



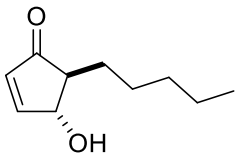
Following general procedure 2 magnesium shavings (2.28 g, 93.6 mmol),1-bromoheptane (18.10 mL, 115.2 mmol) and furfural (**140**) (5.96 mL, 72.0 mmol) to afford (±)-**142c** (12.08 g, 61.56 mmol, 86%) as a yellowish oil: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.37 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.32 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.22 (d, *J* = 3.2 Hz, 1H), 4.66 (t, *J* = 6.8 Hz, 1H), 1.92 (bs, 1H), 1.89 – 1.81 (m, 2H), 1.44 – 1.24 (m, 10H), 0.87 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 156.9 (C_q), 141.9 (+), 110.1 (+), 105.8 (+), 67.9 (+), 35.6 (-), 31.8 (-), 29.4 (-), 29.2 (-), 25.6 (-), 22.7 (-), 14.1 (+).

4-Hydroxy-5-propylcyclopent-2-en-1-one ((±)-149a):



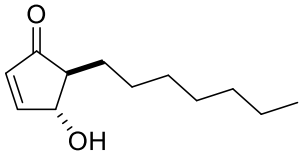
According to general procedure 3 (±)-**142a** (5.61 g, 40.0 mmol) was used to afford a yellowish oil (3.58 g, 25.6 mmol, 64%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.49 (dd, *J* = 5.8, 2.2 Hz, 1H), 6.19 (dd, *J* = 5.7, 1.1 Hz, 1H), 4.80 – 4.61 (m, 1H), 2.27 – 2.22 (m, 1H), 2.08 (bs, 1H), 1.90 – 1.75 (m, 1H), 1.54 – 1.39 (m, 3H), 0.96 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 208.2 (C_q), 161.6 (+), 134.4 (+), 76.9 (+), 55.3 (+), 30.7 (-), 20.6 (-), 14.1 (+).

4-Hydroxy-5-pentylcyclopent-2-en-1-one ((±)-149b):[83]



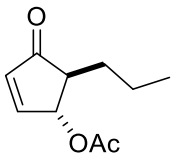
According to the general procedure 3 (±)-**142b** (6.73 g, 40.0 mmol) was used to afford a yellowish oil (4.95 g, 29.4 mmol, 74%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.49 (dd, *J* = 5.8, 2.2 Hz, 1H), 6.20 (dd, *J* = 5.8, 1.2 Hz, 1H), 4.75 – 4.62 (m, 1H), 2.28 – 2.18 (m, 1H), 1.97 (bs, 1H), 1.90 – 1.79 (m, 1H), 1.48 – 1.29 (m, 7H), 0.89 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 208.1 (C_q), 161.5 (+), 134.4 (+), 76.8 (+), 55.5 (+), 31.9 (-), 28.6 (-), 27.0 (-), 22.5 (-), 14.1 (+).

5-Heptyl-4-hydroxycyclopent-2-en-1-one ((±)-149c):[142]



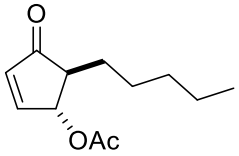
According to general procedure 3 (±)-**142c** (7.85 g, 40.0 mmol) was used to afford a yellowish oil (3.48 g, 17.7 mmol, 44%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.49 (dd, *J* = 5.8, 2.2 Hz, 1H), 6.20 (dd, *J* = 5.8, 1.3 Hz, 1H), 4.71 – 4.67 (m, 1H), 2.27 – 2.18 (m, 1H), 1.92 (s, 1H), 1.89 – 1.81 (m, 1H), 1.52 – 1.41 (m, 3H), 1.34 – 1.23 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 208.0 (C_q), 161.4 (+), 134.5 (+), 76.9 (+), 55.5 (+), 31.8 (-), 29.7 (-), 29.1 (-), 28.6 (-), 27.4 (-), 22.7 (-), 14.1 (+).

4-Oxo-5-propylcyclopent-2-en-1-yl acetate ((±)-154a):



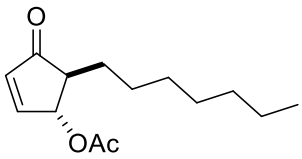
According to general procedure 4 (±)-**149a** (2.80 g, 20.0 mmol) was used to afford a yellowish oil (3.13 g, 17.2 mmol, 86%): $\mathbf{R_f}$ = 0.57 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.49 (dd, *J* = 5.8, 2.3 Hz, 1H), 6.29 (dd, *J* = 5.8, 1.2 Hz, 1H), 5.68 – 5.61 (m, 1H), 2.39 (ddd, *J* = 8.5, 5.0, 2.4 Hz, 1H), 2.10 (s, 3H), 1.85 – 1.73 (m, 1H), 1.56 – 1.34 (m, 3H), 0.92 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.0 (C_q), 170.6 (C_q), 157.8 (+), 136.2 (+), 77.6 (+), 51.4 (+), 30.8 (-), 21.0 (+), 20.1 (-), 14.0 (+); **IR** (ν/cm^{-1}): 2960, 2937, 2874, 1715, 1595, 1485, 1372, 1327, 1230, 1170, 1088, 1025, 954, 924, 895, 857, 798, 734; **HRMS** (APCI) *m/z* calculated for $C_{10}H_{15}O_3$ [MH^+]: 183.1016, found: 183.1026.

4-Oxo-5-pentylcyclopent-2-en-1-yl acetate ((±)-154b):



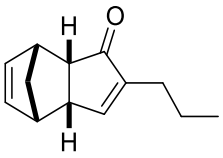
According to general procedure 4 (±)-**149b** (3.37 g, 20.0 mmol) was used to afford a yellowish oil (3.88 g, 18.5 mmol, 92%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.49 (dd, *J* = 5.8, 2.3 Hz, 1H), 6.29 (dd, *J* = 5.8, 1.2 Hz, 1H), 5.67 – 5.61 (m, 1H), 2.38 (ddd, *J* = 8.4, 4.9, 2.4 Hz, 1H), 2.10 (s, 3H), 1.87 – 1.74 (m, 1H), 1.57 – 1.46 (m, 1H), 1.37 – 1.23 (m, 6H), 0.87 (t, *J* = 6.7 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.1 (C_q), 170.6 (C_q), 157.8 (+), 136.2 (+), 77.6 (+), 51.5 (+), 31.7 (-), 28.6 (-), 26.4 (-), 22.4 (-), 21.0 (+), 14.0 (+).

5-Heptyl-4-oxocyclopent-2-en-1-yl acetate ((±)-154c):



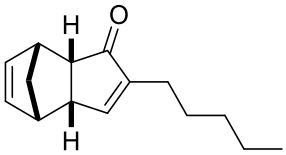
According to general procedure 4 (±)-**149c** (3.93 g, 20.0 mmol) was used to afford a yellowish oil (4.11 g, 12.9 mmol, 86%): $\mathbf{R_f}$ = 0.55 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.49 (dd, *J* = 5.8, 2.3 Hz, 1H), 6.29 (dd, *J* = 5.8, 1.2 Hz, 1H), 5.67 – 5.61 (m, 1H), 2.37 (ddd, *J* = 8.4, 4.9, 2.4 Hz, 1H), 2.10 (s, 3H), 1.88 – 1.75 (m, 1H), 1.57 – 1.46 (m, 1H), 1.37 – 1.21 (m, 10H), 0.86 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.1 (C_q), 170.6 (C_q), 157.8 (+), 136.2 (+), 77.6 (+), 51.5 (+), 31.8 (-), 29.5 (-), 29.1 (-), 28.6 (-), 26.7 (-), 22.6 (-), 21.0 (+), 14.1 (+); **IR** (ν/cm^{-1}): 2926, 2855, 1718, 1595, 1581, 1372, 1230, 1170, 1096, 1021, 976, 906, 794, 723; **HRMS** (APCI) *m/z* calculated for $C_{14}H_{23}O_3$ [MH^+]: 239.1642, found: 239.1641.

2-Propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-155a):



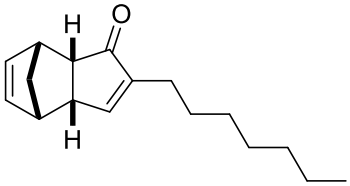
Following general procedure 5 acetate (±)-**154a** (1.82 g, 10.0 mmol) was used to afford a colorless oil (1.53 g, 8.11 mmol, 81%): $\mathbf{R_f}$ = 0.45 (PE/EA = 10:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.04 – 6.90 (m, 1H), 5.86 (dd, *J* = 5.5, 2.9 Hz, 1H), 5.74 (dd, *J* = 5.5, 2.9 Hz, 1H), 3.27 – 3.22 (m, 1H), 3.21 – 3.17 (m, 1H), 2.93 – 2.88 (m, 1H), 2.80 (t, *J* = 5.1 Hz, 1H), 2.08 – 1.92 (m, 2H), 1.72 (dt, *J* = 8.4, 1.7 Hz, 1H), 1.62 – 1.57 (m, 1H), 1.39 (sext, *J* = 7.4 Hz, 2H), 0.85 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.3 (C_q), 157.6 (+), 149.3 (C_q), 132.6 (+) 132.3 (+), 52.6 (-), 50.8 (+), 45.3 (+), 45.1 (+), 44.1 (+), 26.7 (-), 21.1 (-), 13.8 (+); **IR** (ν/cm^{-1}): 3064, 2960, 2933, 2870, 1692, 1625, 1454, 1338, 1230, 1204, 1126, 1074, 828, 738, 712; **HRMS** (EI) *m/z* calculated for $C_{13}H_{16}O$ [$M^{+\cdot}$]: 188.11957, found: 188.12003.

2-Pentyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-155b):[143]



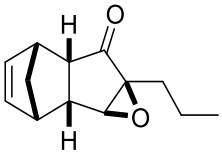
Following general procedure 5 acetate (±)-**154b** (2.10 g, 10.0 mmol) was used to afford a colorless oil (1.69 g, 7.82 mmol, 78%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.06 – 6.90 (m, 1H), 5.86 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.74 (dd, *J* = 5.5, 2.9 Hz, 1H), 3.29 – 3.22 (m, 1H), 3.21 – 3.15 (m, 1H), 2.94 – 2.87 (m, 1H), 2.81 (t, *J* = 5.1 Hz, 1H), 2.09 – 1.93 (m, 2H), 1.72 (dt, *J* = 8.4, 1.7 Hz, 1H), 1.61 – 1.56 (m, 1H), 1.39 – 1.18 (m, 6H), 0.86 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.2 (C_q), 157.5 (+), 149.5 (C_q), 132.6 (+), 132.3 (+), 52.6 (-), 50.8 (+), 45.3 (+), 45.1 (+), 44.1 (+), 31.5 (-), 27.6 (-), 24.6 (-), 22.4 (-), 14.1 (+).

2-Heptyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-155c):



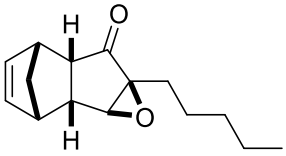
Following general procedure 5 acetate (±)-**154c** (2.38 g, 10.0 mmol) was used to afford a colorless oil (2.02 g, 8.27 mmol, 83%): **R_f** = 0.50 (PE/EA = 10:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.03 – 6.91 (m, 1H), 5.86 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.74 (dd, *J* = 5.5, 2.9 Hz, 1H), 3.28 – 3.22 (m, 1H), 3.22 – 3.17 (m, 1H), 2.94 – 2.88 (m, 1H), 2.81 (t, *J* = 5.1 Hz, 1H), 2.09 – 1.95 (m, 2H), 1.72 (dt, *J* = 8.4, 1.7 Hz, 1H), 1.62 – 1.57 (m, 1H), 1.39 – 1.20 (m, 10H), 0.86 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.3 (C_q), 157.5 (+), 149.5 (C_q), 132.6 (+), 132.3 (+), 52.6 (-), 50.8 (+), 45.3 (+), 45.1 (+), 44.1 (+), 31.8 (-), 29.2 (-), 29.1 (-), 27.9 (-), 24.7 (-), 22.7 (-), 14.1 (+); **IR** (ν/cm^{-1}): 3064, 2926, 2855, 1696, 1625, 1461, 1338, 1293, 1230, 1126, 910, 738, 716; **HRMS** (EI) *m/z* calculated for $C_{17}H_{24}O$ [$M^{+\cdot}$]: 244.18217, found: 244.18158.

6a-Propyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-156a):



According to general procedure 6 (±)-**155a** (753 mg, 4.00 mmol), 2 M NaOH (2.4 mL, 4.80 mmol) and H_2O_2 (2.2 mL, 30% in water, 21.6 mmol) were used and stirred for 24 h to afford a colorless oil (801 mg, 3.92 mmol, 98%): $\mathbf{R_f}$ = 0.47 (PE/EA = 10:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = δ 6.04 (dd, *J* = 5.6, 2.8 Hz, 1H), 5.99 (dd, *J* = 5.6, 2.8 Hz, 1H), 3.46 (d, *J* = 1.6 Hz, 1H), 3.26 – 3.18 (m, 1H), 3.10 – 3.04 (m, 1H), 3.01 – 2.96 (m, 1H), 2.85 – 2.78 (m, 1H), 1.85 – 1.72 (m, 1H), 1.60 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.58 – 1.47 (m, 1H), 1.47 – 1.42 (m, 1H), 1.33 – 1.19 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.5 (C_q), 135.1 (+), 133.7 (+), 66.9 (C_q), 65.5 (+), 51.8 (-), 50.0 (+), 45.8 (+), 43.5 (+), 43.3 (+), 26.9 (-), 17.9 (-), 14.4 (+); **IR** (ν/cm^{-1}): 3064, 2963, 2874, 1733, 1457, 1338, 1200, 1126, 1029, 910, 835, 775, 723; **HRMS** (EI) *m/z* calculated for $C_{13}H_{16}O_2$ [$M^{+\cdot}$]: 204.11448, found: 204.11452.

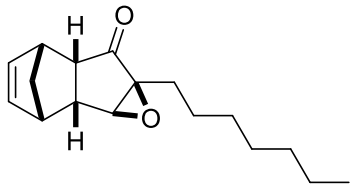
6a-Pentyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-156b):



According to general procedure 6 (±)-**155b** (865 mg, 4.00 mmol), 2 M NaOH (2.4 mL, 4.80 mmol) and H_2O_2 (2.2 mL, 30% in water, 21.6 mmol) were used and stirred for 24 h to afford a colorless oil (897 mg, 3.86 mmol, 97%): $\mathbf{R_f}$ = 0.54 (PE/EA = 10:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.04 (dd, *J* = 5.6, 2.8 Hz, 1H), 5.99 (dd, *J* = 5.6, 2.8 Hz, 1H),

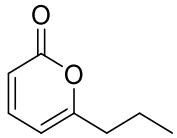
3.46 (d, *J* = 1.6 Hz, 1H), 3.26 – 3.17 (m, 1H), 3.10 – 3.04 (m, 1H), 3.02 – 2.95 (m, 1H), 2.85 – 2.79 (m, 1H), 1.84 – 1.72 (m, 1H), 1.62 – 1.43 (m, 3H), 1.34 – 1.19 (m, 6H), 0.86 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = δ 210.5 (C_q), 135.1 (+), 133.7 (+), 67.0 (C_q), 65.5 (+), 51.8 (-), 50.0 (+), 45.8 (+), 43.5 (+), 43.3 (+), 32.0 (-), 24.7 (-), 24.0 (-), 22.4 (-), 14.0 (+); **IR** (ν/cm^{-1}): 3064, 2933, 2862, 1737, 1461, 1420, 1338, 1252, 1126, 1088, 1044, 910, 842, 775, 723; **HRMS** (EI) *m/z* calculated for $C_{15}H_{20}O_2$ [$M^{+\cdot}$]: 232.14578, found: 232.14517.

6a-Heptyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-156c):



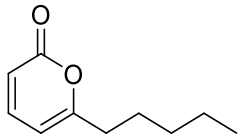
According to general procedure 6 (±)-**155c** (978 mg, 4.00 mmol), 2 M NaOH (2.4 mL, 4.80 mmol) and H_2O_2 (2.2 mL, 30% in water, 21.6 mmol) were used and stirred for 24 h to afford a colorless oil (1.018 g, 3.91 mmol, 98%): **R_f** = 0.54 (PE/EA = 10:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.04 (dd, *J* = 5.6, 2.8 Hz, 1H), 5.99 (dd, *J* = 5.5, 2.8 Hz, 1H), 3.46 (d, *J* = 1.6 Hz, 1H), 3.29 – 3.17 (m, 1H), 3.10 – 3.03 (m, 1H), 3.01 – 2.94 (m, 1H), 2.86 – 2.77 (m, 1H), 1.86 – 1.72 (m, 1H), 1.60 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.58 – 1.47 (m, 1H), 1.47 – 1.43 (m, 1H), 1.24 (m, 10H), 0.87 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.5 (C_q), 135.1 (+), 133.71 (+), 67.0 (C_q), 65.5 (+), 51.8 (-), 50.0 (+), 45.8 (+), 43.5 (+), 43.3 (+) 31.8 (-), 29.8 (-), 29.1 (-), 24.7 (-), 24.4 (-), 22.6 (-), 14.1 (+); **IR** (ν/cm^{-1}): 3064, 2930, 2855, 1737, 1461, 1338, 1200, 1126, 1088, 1044, 910, 842, 775, 723; **HRMS** (EI) *m/z* calculated for $C_{17}H_{24}O_2$ [$M^{+\cdot}$]: 260.17708, found: 260.17650.

6-Propyl-2*H*-pyran-2-one (2a):[5]



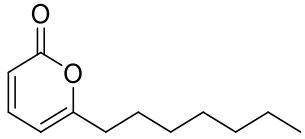
Following general procedure 1 epoxide (±)-**156a** (204 mg, 1.00 mmol) was used to afford a colorless oil (138 mg, 1.00 mmol, 100%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.26 (dd, *J* = 9.4, 6.5 Hz, 1H), 6.15 (d, *J* = 9.4 Hz, 1H), 5.97 (dd, *J* = 6.6, 0.8 Hz, 1H), 2.46 (t, *J* = 7.5 Hz, 2H), 1.69 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 166.5 (C_q), 163.0 (C_q), 143.7 (+), 113.2 (+), 102.8 (+), 35.7 (-), 20.3 (-), 13.5 (+).

6-Pentyl-2*H*-pyran-2-one (2b):[5]



Following general procedure 1 epoxide (±)-**156b** (232 mg, 1.00 mmol) was used to afford a colorless oil (165 mg, 0.99 mmol, 99%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.25 (dd, *J* = 9.4, 6.5 Hz, 1H), 6.14 (d, *J* = 9.4 Hz, 1H), 5.97 (dd, *J* = 6.6, 0.7 Hz, 1H), 2.47 (t, *J* = 7.6 Hz, 2H), 1.69 – 1.60 (m, 2H), 1.36 – 1.27 (m, 4H), 0.89 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 166.8 (C_q), 163.0 (C_q), 143.8 (+), 113.1 (+), 102.6 (+), 33.8 (-), 31.1 (-), 26.6 (-), 22.3 (-), 13.9 (+).

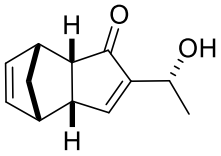
6-Heptyl-2*H*-pyran-2-one (2c):[5]



Following general procedure 1 epoxide (±)-**156c** (260 mg, 1.00 mmol) was used to afford a colorless oil (194 mg, 1.00 mmol, 100%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.25 (dd, *J* = 9.4,

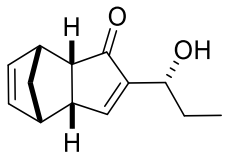
6.6 Hz, 1H), 6.15 (d, *J* = 9.4 Hz, 1H), 5.96 (dd, *J* = 6.6, 0.8 Hz, 1H), 2.47 (t, *J* = 7.5 Hz, 2H), 1.70 – 1.60 (m, 2H), 1.35 – 1.22 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 166.8 (C_q), 163.0 (C_q), 143.8 (+), 113.1 (+), 102.6 (+), 33.9 (-), 31.7 (-), 28.9 (-) 28.9 (-), 26.9 (-), 22.6 (-), 14.1 (+).

2-(1-Hydroxyethyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165a):



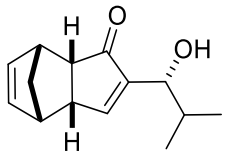
According to general procedure 7 enone (±)-**138** (4.39 g, 30.0 mmol), acetaldehyde (2.53 mL, 45.0 mmol), phenol (0.565 g, 6.0 mmol), and Bu_3P (2.96 mL, 12.0 mmol) were used and the reaction was complete after 3 d. Purification via flash chromatography (silica, PE/EA = 3:1) yielded a colorless oil (4.80 g, 25.6 mmol, 84%): **R_f** = 0.17 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.13 – 7.10 (m, 1H), 5.93 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.79 (dd, *J* = 5.6, 2.9 Hz, 1H), 4.48 (q, *J* = 6.5 Hz, 1H), 3.34 – 3.28 (m, 1H), 3.25 – 3.20 (m, 1H), 2.99 – 2.93 (bs, 1H), 2.87 (t, *J* = 5.0 Hz, 1H), 1.75 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.64 – 1.59 (m, 1H), 1.30 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.6 (C_q), 157.1 (+), 151.6 (C_q), 132.5 (+), 132.3 (+), 63.9 (+), 52.7 (-), 51.6 (+), 45.4 (+), 45.2 (+), 44.1 (+), 22.0 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2971, 2933, 2870, 1742, 1679, 1627, 1453, 1365, 1338, 1118, 1068, 1019, 714; **HRMS** (ESI) *m/z* calculated for $C_{12}H_{15}O_2$ [MH^+]: 191.1067, found: 191.1067.

2-(1-Hydroxypropyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165b):



According to general procedure 7 enone (±)-**138** (4.39 g, 30.0 mmol), propionaldehyde (3.23 mL, 45.0 mmol), phenol (0.565 g, 6.0 mmol), and Bu_3P (2.96 mL, 12.0 mmol) were used and the reaction was complete after 3 d. Purification via flash chromatography (silica, PE/EA = 3:1) yielded a white solid (4.81 g, 23.6 mmol, 79%): **mp** 58.7 – 61.5 °C; $\mathbf{R_f}$ = 0.30 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.04 (d, *J* = 2.6 Hz, 1H), 5.85 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.72 (dd, *J* = 5.6, 3.0 Hz, 1H), 4.13 (t, *J* = 6.5 Hz, 1H), 3.30 – 3.22 (m, 1H), 3.18 – 3.12 (m, 1H), 2.93 – 2.87 (m, 1H), 2.81 (t, *J* = 5.0 Hz, 1H), 1.69 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.60 – 1.49 (m, 3H), 0.82 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.7 (C_q), 158.1 (+), 150.0 (C_q), 132.6 (+), 132.4 (+), 69.8 (+), 52.7 (-), 51.6 (+), 45.5 (+), 45.2 (+), 44.1 (+), 29.2 (-), 9.8 (+); **IR** (ν/cm^{-1}): 3500 – 3300, 2963, 2934, 2870, 1677, 1624, 1451, 1332, 1293, 1251, 1228, 1204, 1086, 1040, 975, 879, 837, 803, 771, 750, 724; **HRMS** (ESI) *m/z* calculated for $C_{13}H_{17}O_2$ [MH^+]: 205.1223, found: 205.1229.

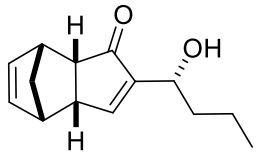
2-(1-Hydroxy-2-methylpropyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165c):[89]



According to general procedure 7 enone (±)-**138** (438 mg, 3.00 mmol), isobutyraldehyde (0.41 mL, 4.50 mmol), phenol (56 mg, 0.6 mmol) and Bu_3P (0.30 mL, 1.20 mmol) were used and the reaction was complete after 7 d. Purification via flash chromatography (silica, PE/EA = 3:1) yielded a white solid (553 mg, 2.53 mmol, 85%): **mp** 76.3 – 78.0 °C;

R_f = 0.69 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.07 (d, *J* = 2.7 Hz, 1H), 5.92 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.79 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.98 (d, *J* = 6.5 Hz, 1H), 3.36 – 3.30 (m, 1H), 3.24 – 3.18 (m, 1H), 3.00 – 2.94 (m, 1H), 2.87 (t, *J* = 5.0 Hz, 1H), 1.90 – 1.78 (m, 1H), 1.75 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.64 – 1.59 (m, 1H), 0.88 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 211.0 (C_q), 159.3 (+), 148.8 (C_q), 132.9 (+), 132.6 (+), 74.5 (+), 52.8 (-), 51.6 (+), 45.8 (+), 45.1 (+), 44.2 (+), 33.2 (+), 18.9 (+), 17.6 (+); **IR** (ν/cm^{-1}): 3600 – 3300, 2966, 2961, 2929, 2867, 1675, 1618, 1466, 1329, 1294, 1250, 1227, 1202, 1131, 1070, 1024, 1008, 949, 923, 908, 889, 840, 802, 773, 750, 724; **HRMS** (ESI) *m/z* calculated for $C_{14}H_{19}O_2$ [MH^+]: 219.1380, found: 219.1377.

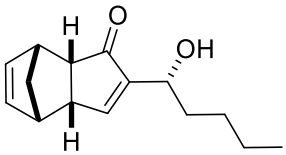
2-(1-Hydroxybutyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165d):



According to general procedure 7 enone (±)-**138** (438 mg, 3.00 mmol), butyraldehyde (0.41 mL, 4.50 mmol), phenol (56 mg, 0.60 mmol) and Bu_3P (0.30 mL, 1.20 mmol) were used and the reaction was complete after 3 d. Purification via flash chromatography (silica, PE/EA = 3:1) yielded a colorless oil (541 mg, 2.48 mmol, 83%): **R_f** = 0.20 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.04 (d, *J* = 2.6 Hz, 1H), 5.85 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.72 (dd, *J* = 5.5, 2.9 Hz, 1H), 4.21 (t, *J* = 6.5 Hz, 1H), 3.28 – 3.22 (m, 1H), 3.18 – 3.12 (m, 1H), 2.92 – 2.87 (m, 1H), 2.80 (t, *J* = 5.0 Hz, 1H), 1.69 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.59 – 1.44 (m, 3H), 1.38 – 1.19 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H), **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.7 (C_q), 157.8 (+), 150.5 (C_q), 132.6 (+), 132.3 (+), 68.1 (+), 52.7 (-), 51.6 (+), 45.5 (+), 45.2 (+), 44.1 (+), 38.3 (-), 18.6 (-), 13.9 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2958, 2933, 2872, 1743, 1678, 1623, 1456, 1337, 1294, 1228, 1122, 1070, 1024,

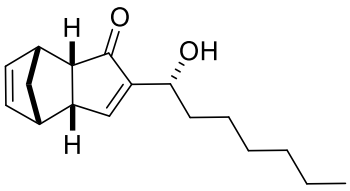
957, 839, 805, 748, 714; **HRMS** (ESI) *m/z* calculated for $C_{14}H_{19}O_2$ [MH^+]: 219.1380, found: 219.1380.

2-(1-Hydroxypentyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165e):



According to general procedure 7 enone (±)-**138** (4.38 g, 30.0 mmol), valeraldehyde (4.79 mL, 45.0 mmol), phenol (0.565 g, 6.0 mmol) and Bu_3P (2.96 mL, 12.0 mmol) were used and the reaction was complete after 3 d. Purification via flash chromatography (silica, PE/EA = 5:1) yielded a colorless oil (5.58 g, 24.03 mmol, 80%): $\mathbf{R_f}$ = 0.32 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.09 (d, *J* = 2.6 Hz, 1H), 5.92 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.78 (dd, *J* = 5.6, 2.9 Hz, 1H), 4.25 (t, *J* = 6.6 Hz, 1H), 3.35 – 3.28 (m, 1H), 3.25 – 3.18 (m, 1H), 2.99 – 2.93 (m, 1H), 2.87 (t, *J* = 5.0 Hz, 1H), 2.47 – 2.25 (bs, 1H), 1.75 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.66 – 1.51 (m, 3H), 1.42 – 1.19 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.8 (C_q), 157.9 (+), 150.3 (C_q), 132.6 (+), 132.4 (+), 68.5 (+), 52.7 (-), 51.6 (+), 45.5 (+), 45.2 (+), 44.1 (+), 35.9 (-), 27.6 (-), 22.5 (-), 14.1 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2957, 2929, 2870, 1682, 1458, 1337, 1258, 1205, 1124, 1072, 1043, 1015, 795, 714; **HRMS** (ESI) *m/z* calculated for $C_{15}H_{21}O_2$ [MH^+]: 233.1536, found: 233.1540.

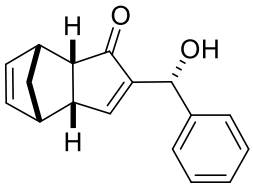
2-(1-Hydroxyheptyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165f):



According to general procedure 7 enone (±)-**138** (4.39 g, 30.0 mmol), *n*-heptanal (6.27 mL, 45.0 mmol), phenol (0.565 g, 6.0 mmol) and Bu_3P (2.96 mL, 12.0 mmol) were used and the

reaction was complete after 3 d. Purification via flash chromatography (silica, PE/EA = 5:1) yielded a colorless oil (6.44 g, 24.72 mmol, 82%): **R_f** = 0.53 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.08 (d, *J* = 2.6 Hz, 1H), 5.89 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.76 (dd, *J* = 5.6, 2.9 Hz, 1H), 4.23 (t, *J* = 6.6 Hz, 1H), 3.33 – 3.26 (m, 1H), 3.22 – 3.16 (m, 1H), 2.97 – 2.91 (m, 1H), 2.84 (t, *J* = 5.0 Hz, 1H), 2.81 – 2.75 (bs, 1H), 1.73 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.63 – 1.48 (m, 3H), 1.37 – 1.15 (m, 8H), 0.84 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.7 (C_q), 157.9 (+), 150.4 (C_q), 132.6 (+), 132.3 (+), 68.4 (+), 52.7 (-), 51.6 (+), 45.5 (+), 45.2 (+), 44.1 (-), 36.2 (-), 31.8 (-), 29.1 (-), 25.4 (-), 22.6 (-), 14.1 (+); **IR** (ν/cm^{-1}): 3600 – 3200, 3064, 2930, 2859, 1681, 1625, 1457, 1379, 1338, 1293, 1204, 1126, 1066, 1040, 913, 876, 805, 749, 716; **HRMS** (ESI) *m/z* calculated for $C_{17}H_{25}O_2$ [MH^+]: 261.1849, found: 261.1850.

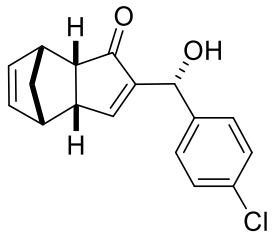
2-(Hydroxy(phenyl)methyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165g):[89]



According to general procedure 7 enone (±)-**138** (4.39 g, 30.0 mmol), benzaldehyde (4.55 mL, 45.0 mmol), phenol (0.565 g, 6.0 mmol) and Bu_3P (2.96 mL, 12.0 mmol) were used and the reaction was complete after 2 d. Purification via flash chromatography (silica, PE/EA = 3:1) yielded a white solid (6.28 g, 24.91 mmol, 83%): **mp** 108.7 – 110.0 °C; **R_f** = 0.25 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.36 – 7.26 (m, 5H), 6.96 – 6.92 (m, 1H), 5.90 (dd, *J* = 5.5, 2.9 Hz, 1H), 5.76 (dd, *J* = 5.5, 2.9 Hz, 1H), 5.43 – 5.40 (m, 1H), 3.32 – 3.26 (m, 1H), 3.24 – 3.19 (m, 1H), 2.95 – 2.91 (m, 1H), 2.89 (t, *J* = 5.0 Hz, 1H), 1.74 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.64 – 1.57 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.2 (C_q), 159.3 (+), 150.4

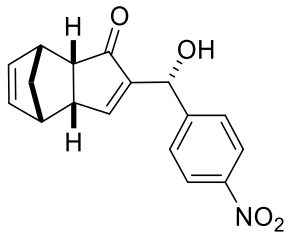
(C_q), 141.5 (C_q), 132.6 (+), 132.5 (+) 128.4 (+), 127.7 (+), 126.4 (+), 70.2 (+), 52.7 (-), 51.7 (+), 45.6 (+), 45.2 (+), 44.2 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 3065, 3027, 2975, 2937, 2886, 2871, 1739, 1670, 1618, 1492, 1456, 1411, 1356, 1301, 1252, 1210, 1125, 1090, 1075, 1034, 1007, 941, 907, 871, 847, 802, 768; **HRMS** (ESI) *m/z* calculated for $C_{17}H_{16}NaO_2$ [MH$^+$]: 275.1043, found: 275.1042.

2-((4-Chlorophenyl)(hydroxy)methyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165h):



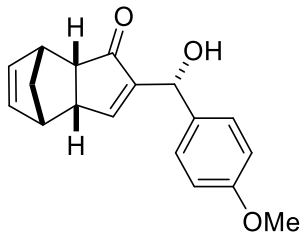
According to general procedure 7 enone (±)-**138** (438 mg, 3.00 mmol), 4-chlorobenzaldehyde (633 mg, 4.50 mmol), phenol (56 mg, 0.60 mmol) and Bu_3P (0.30 mL, 1.20 mmol) were used and the reaction was complete after 1 d. Purification via flash chromatography (silica, PE/EA = 5:1) yielded a white solid (675 mg, 2.35 mmol, 79%): **mp** 114.6 – 116.3 °C; **R_f** = 0.29 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.33 – 7.23 (m, 4H), 6.94 (d, *J* = 2.1 Hz, 1H), 5.89 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.74 (dd, *J* = 5.6, 3.0 Hz, 1H), 5.39 (s, 1H), 3.59 – 3.35 (bs, 1H), 3.32 – 3.27 (m, 1H), 3.24 – 3.19 (m, 1H), 2.96 – 2.91 (m, 1H), 2.89 (t, *J* = 5.0 Hz, 1H), 1.75 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.63 – 1.58 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.2 (C_q), 159.4 (+), 150.0 (C_q), 140.1 (C_q), 133.5 (C_q), 132.6 (+), 132.5 (+), 128.5 (+), 127.8 (+), 69.6 (+), 52.8 (-), 51.7 (+), 45.6 (+), 45.3 (+), 44.2 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 3067, 2989, 2968, 2940, 2918, 2899, 2870, 1668, 1616, 1483, 1341, 1330, 1291, 1248, 1225, 1187, 1122, 1084, 1027, 1003, 847, 821, 800, 711; **HRMS** (ESI) *m/z* calculated for $C_{17}H_{15}ClNaO_2$ [MNa$^+$]: 309.0653, found: 309.0657.

2-(Hydroxy(4-nitrophenyl)methyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165i):



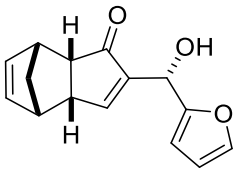
According to general procedure 7 enone (±)-**138** (438 mg, 3.00 mmol), 4-nitrobenzaldehyde (680 mg, 4.50 mmol), phenol (56 mg, 0.60 mmol) and Bu_3P (0.30 mL, 1.20 mmol) were used and the reaction was complete after 1 d. Purification via flash chromatography (silica, PE/EA = 3:1) yielded a yellow solid (763 mg, 2.57 mmol, 86%): **mp** 138.6 – 140.5 °C; $\mathbf{R_f}$ = 0.38 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.23 – 8.16 (m, 2H), 7.55 – 7.48 (m, 2H), 6.99 (d, *J* = 2.3 Hz, 1H), 5.86 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.74 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.52 (s, 1H), 3.69 – 3.45 (bs, 1H), 3.37 – 3.31 (m, 1H), 3.26 – 3.20 (m, 1H), 2.99 – 2.94 (m, 1H), 2.92 (t, *J* = 5.0 Hz, 1H), 1.76 (dt, *J* = 8.6, 1.7 Hz, 1H), 1.65 – 1.59 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.0 (C_q), 160.0 (+), 149.2 (C_q), 148.9 (C_q), 147.3 (C_q), 132.6 (+) 132.5 (+), 127.1 (+), 123.6 (+), 69.2 (+), 52.8 (-), 51.6 (+), 45.8 (+), 45.3 (+), 44.2 (+); **IR** (ν/cm^{-1}): 3500 – 3300, 3065, 2985, 2941, 2913, 2875, 1666, 1619, 1606, 1515, 1345, 1293, 1250, 1226, 1187, 1124, 1109, 1079, 1029, 1005, 839, 803, 751, 718; **HRMS** (ESI) *m/z* calculated for $C_{17}H_{16}NO_4$ [MH^+]: 298.1074, found: 298.1069.

2-(Hydroxy(4-methoxyphenyl)methyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165j):



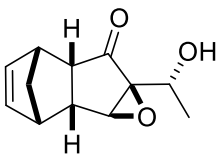
According to general procedure 7 enone (±)-**138** (438 mg, 3.00 mmol), 4-methoxybenzaldehyde (0.55 mL, 4.50 mmol), phenol (56 mg, 0.60 mmol) and Bu_3P (0.30 mL, 1.20 mmol) were used and the reaction was complete after 7 d. Purification via flash chromatography (silica, PE/EA = 3:1) yielded a colorless oil (716 mg, 2.54 mmol, 85%): **R_f** = 0.24 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.25 – 7.20 (m, 2H), 6.97 – 6.93 (m, 1H), 6.89 – 6.82 (m, 2H), 5.92 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.77 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.36 (s, 1H), 3.79 (s, 3H), 3.32 – 3.25 (m, 1H), 3.24 – 3.19 (m, 1H), 2.95 – 2.91 (m, 1H), 2.88 (t, *J* = 5.0 Hz, 1H), 1.74 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.63 – 1.58 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.2 (C_q), 159.1 (C_q), 159.1 (+), 150.7 (C_q), 133.8 (C_q), 132.6 (+), 132.5 (+), 127.7 (+), 113.7 (+), 69.7 (+), 55.3 (+), 52.7 (-), 51.7 (+), 45.5 (+), 45.2 (+), 44.1 (+); **IR** (ν/cm^{-1}): 3500 – 3300, 3063, 2973, 2868, 2836, 1686, 1610, 1510, 1462, 1337, 1302, 1246, 1173, 1125, 1078, 1030, 1000, 830, 804, 749, 710; **HRMS** (ESI) *m/z* calculated for $C_{18}H_{19}O_3$ [MH^+]: 283.1329, found: 283.1329.

2-(Furan-2-yl(hydroxy)methyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165k):



According to general procedure 7 enone (±)-**138** (438 mg, 3.00 mmol), furfural (0.37 mL, 4.50 mmol), phenol (56 mg, 0.60 mmol) and Bu_3P (0.30 mL, 1.20 mmol) were used and the reaction was complete after 3 d. Purification via flash chromatography (silica, PE/EA = 3:1) yielded a yellow solid (653 mg, 2.70 mmol, 90%): **mp** 89.8 – 91.4 °C; $\mathbf{R_f}$ = 0.34 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.36 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.22 – 7.19 (m, 1H), 6.31 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.22 (dt, *J* = 3.3, 0.7 Hz, 1H), 5.94 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.80 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.43 (s, 1H), 3.40 – 3.33 (m, 1H), 3.27 – 3.21 (m, 1H), 3.01 – 2.96 (m, 1H), 2.92 (t, *J* = 4.9 Hz, 1H), 1.76 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.66 – 1.60 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 209.8 (C_q), 159.9 (+), 154.0 (C_q), 147.2 (C_q), 142.3 (+), 132.6 (+), 132.5 (+), 110.3 (+), 107.1 (+), 64.2 (+), 52.7 (-), 51.5 (+), 45.8 (+), 45.2 (+), 44.2 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2977, 2937, 2870, 1685, 1626, 1501, 1338, 1293, 1228, 1201, 1145, 1081, 1011, 742; **HRMS** (ESI) *m/z* calculated for $C_{15}H_{15}O_3$ [MH^+]: 243.1016, found: 243.1011.

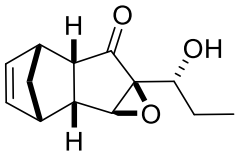
6a-(1-Hydroxyethyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170a):



According to general procedure 6 (±)-**165a** (3.81 g, 20.0 mmol), 2 M NaOH (12.0 mL, 24.0 mmol) and H_2O_2 (11.0 mL, 30% in water, 108 mmol) were used and stirred for 30 min to afford a colorless oil (3.75 g, 18.2 mmol, 91%): $\mathbf{R_f}$ = 0.47 (PE/EA = 2:1);

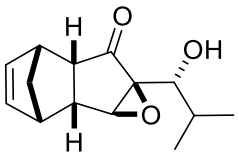
^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 6.08 (dd, *J* = 5.5, 2.8 Hz, 1H), 6.04 (dd, *J* = 5.6, 2.8 Hz, 1H), 4.03 – 3.91 (m, 1H), 3.64 (d, *J* = 1.7 Hz, 1H), 3.29 – 3.22 (m, 1H), 3.12 – 3.07 (m, 1H), 3.05 – 2.99 (m, 1H), 2.90 – 2.84 (m, 1H), 2.09 (d, *J* = 8.0 Hz, 1H), 1.65 – 1.62 (dt, *J* = 8.6, 1.8 Hz, 1H), 1.49 – 1.43 (m, 1H), 1.26 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.9 (C_q), 135.1 (+), 133.7 (+), 68.5 (C_q), 64.9 (+), 63.9 (+), 51.8 (-), 50.9 (+), 45.9 (+), 43.5 (+), 43.0 (+), 19.2 (+); **IR** (ν/cm^{-1}): 3600 – 3300, 2978, 2940, 2870, 1730, 1454, 1417, 1121, 1041, 724, 633; **HRMS** (ESI) *m/z* calculated for $C_{12}H_{15}O_3$ [MH^+]: 207.1016, found: 207.1017.

6a-(1-Hydroxypropyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170b):



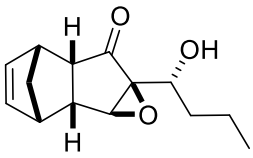
According to general procedure 6 (±)-**165b** (4.09 g, 20.0 mmol), 2 M NaOH (12.0 mL, 24.0 mmol) and H_2O_2 (11.0 mL, 30% in water, 108 mmol) were used and stirred for 30 min to afford a colorless oil (4.04 g, 18.3 mmol, 92%): **R_f** = 0.50 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.02 (dd, *J* = 5.6, 2.8 Hz, 1H), 5.97 (dd, *J* = 5.6, 2.8 Hz, 1H), 3.61 (dd, *J* = 9.8, 3.3 Hz, 1H), 3.56 (d, *J* = 1.6 Hz, 1H), 3.21 – 3.15 (m, 1H), 3.06 – 3.00 (m, 1H), 2.98 – 2.92 (m, 1H), 2.83 – 2.77 (m, 1H), 2.17 – 2.08 (bs, 1H), 1.65 – 1.52 (m, 2H), 1.43 – 1.33 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 211.0 (C_q), 135.1 (+), 133.8 (+), 69.3 (+), 68.0 (C_q), 64.7 (+), 51.9 (-), 50.9 (+), 45.9 (+), 43.5 (+), 43.1 (+), 26.1 (-), 10.2 (+); **IR** (ν/cm^{-1}): 3600 – 3300, 2970, 2937, 2876, 1730, 1457, 1336, 1235, 1122, 1038, 975, 766, 728, 633; **HRMS** (ESI) *m/z* calculated for $C_{13}H_{17}O_3$ [MH^+]: 221.1172, found: 221.1171.

6a-(1-Hydroxy-2-methylpropyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170c):



According to general procedure 6 (±)-**165c** (218 mg, 1.00 mmol), 2 M NaOH (0.6 mL, 1.20 mmol) and H_2O_2 (0.55 mL, 30% in water, 5.40 mmol) were used and stirred for 30 min to afford a white solid (227 mg, 0.97 mmol, 97%): **mp** 54.1 – 56.8 °C; $\mathbf{R_f}$ = 0.82 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.05 (dd, *J* = 5.7, 2.9 Hz, 1H), 5.99 (dd, *J* = 5.7, 2.8 Hz, 1H), 3.59 (d, *J* = 1.7 Hz, 1H), 3.56 (d, *J* = 4.9 Hz, 1H), 3.22 – 3.16 (m, 1H), 3.07 – 3.02 (m, 1H), 2.98 – 2.92 (m, 1H), 2.86 – 2.79 (m, 1H), 2.20 – 2.03 (m, 1H), 1.98 – 1.82 (bs, 1H), 1.57 (dt, *J* = 8.6, 1.7 Hz, 1H), 1.45 – 1.37 (m, 1H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.6 (C_q), 135.1 (+), 134.0 (+), 71.6 (+), 67.7 (C_q), 64.3 (+), 51.9 (-), 50.9 (+), 45.8 (+), 43.5 (+), 43.0 (+), 29.9 (+), 20.0 (+), 16.5 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2981, 2961, 2933, 2863, 1736, 1467, 1414, 1386, 1335, 1246, 1227, 1139, 1061, 1020, 928, 739, 719, 702; **HRMS** (ESI) *m/z* calculated for $C_{14}H_{19}O_3$ [MH^+]: 235.1329, found: 235.1326.

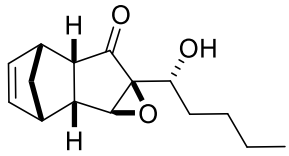
6a-(1-Hydroxybutyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170d):



According to general procedure 6 (±)-**165d** (218 mg, 1.00 mmol), 2 M NaOH (0.6 mL, 1.20 mmol) and H_2O_2 (0.55 mL, 30% in water, 5.40 mmol) were used and stirred for 30 min to afford a colorless oil (222 mg, 0.95 mmol, 95%): $\mathbf{R_f}$ = 0.59 (PE/EA = 2:1);

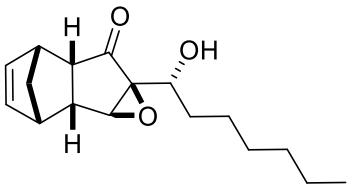
^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 6.01 (dd, *J* = 5.7, 2.9 Hz, 1H), 5.97 (dd, *J* = 5.6, 2.8 Hz, 1H), 3.72 (d, *J* = 9.1 Hz, 1H), 3.56 (d, *J* = 1.6 Hz, 1H), 3.20 – 3.16 (m, 1H), 3.05 – 3.00 (m, 1H), 2.97 – 2.92 (m, 1H), 2.82 – 2.77 (m, 1H), 2.12 – 2.06 (bs, 1H), 1.55 (dt, *J* = 8.6, 1.8 Hz, 1H), 1.53 – 1.45 (m, 2H), 1.42 – 1.38 (m, 1H), 1.37 – 1.24 (m, 2H), 0.85 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 211.0 (C_q), 135.1 (+), 133.8 (+), 68.2 (C_q), 67.5 (+), 64.7 (+), 51.8 (-), 50.9 (+), 45.9 (+), 43.5 (+), 43.1 (+), 34.9 (-), 18.7 (-), 13.8 (+); **IR** (ν/cm^{-1}): 3600 – 3300, 2959, 2938, 2872, 1730, 1458, 1414, 133, 1123, 1075, 1033, 952, 911, 845, 776, 715; **HRMS** (ESI) *m/z* calculated for $C_{14}H_{19}O_3$ [MH^+]: 235.1329, found: 235.1328.

6a-(1-Hydroxypentyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170e):



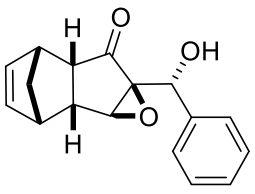
According to general procedure 6 (±)-**165e** (4.65 g, 20.0 mmol), 2 M NaOH (12.0 mL, 24.0 mmol) and H_2O_2 (11.0 mL, 30% in water, 108 mmol) were used and stirred for 30 min to afford a colorless oil (4.58 g, 18.4 mmol, 92%): **R_f** = 0.76 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.08 (dd, *J* = 5.5, 2.8 Hz, 1H), 6.04 (dd, *J* = 5.6, 2.7 Hz, 1H), 3.77 (dd, *J* = 9.4, 3.0 Hz, 1H), 3.63 (d, *J* = 1.5 Hz, 1H), 3.28 – 3.22 (m, 1H), 3.12 – 3.07 (m, 1H), 3.04 – 2.98 (m, 1H), 2.89 – 2.832 (m, 1H), 1.93 – 1.82 (bs, 1H), 1.63 – 1.25 (m, 8H), 0.89 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 211.1 (C_q), 135.1 (+), 133.8 (+), 68.1 (C_q), 67.9 (+), 64.8 (+), 51.9 (-), 50.9 (+), 45.9 (+), 43.5 (+), 43.1 (+), 32.6 (-), 27.7 (-), 22.5 (-), 14.0 (+); **IR** (ν/cm^{-1}): 3600 – 3300, 2934, 2871, 1731, 1457, 1336, 1125, 1039, 717; **HRMS** (ESI) *m/z* calculated for $C_{15}H_{21}O_3$ [MH^+]: 249.1485, found: 249.1488.

6a-(1-Hydroxyheptyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170f):



According to general procedure 6 (±)-**165f** (5.21 g, 20.0 mmol), 2 M NaOH (12.0 mL, 24.0 mmol) and H_2O_2 (11.0 mL, 30% in water, 108 mmol) were used and stirred for 30 min to afford a colorless oil (5.33 g, 19.3 mmol, 96%): $\mathbf{R_f}$ = 0.79 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.07 (dd, *J* = 5.6, 2.8 Hz, 1H), 6.03 (dd, *J* = 5.6, 2.7 Hz, 1H), 3.76 (dd, *J* = 9.5, 2.9 Hz, 1H), 3.62 (d, *J* = 1.6 Hz, 1H), 3.27 – 3.21 (m, 1H), 3.12 – 3.06 (m, 1H), 3.04 – 2.97 (m, 1H), 2.90 – 2.82 (m, 1H), 2.10 – 1.97 (bs, 1H), 1.67 – 1.18 (m, 12H), 0.87 (t, *J* = 6.7 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 211.1 (C_q), 135.1 (+), 133.8 (+), 68.1 (C_q), 67.9 (+), 64.8 (+), 51.9 (-), 50.9 (+), 45.9 (+), 43.5 (+), 43.1 (+), 33.0 (-), 31.8 (-), 29.1 (-), 25.5 (-), 22.6 (-), 14.1 (+); **IR** (ν/cm^{-1}): 3600 – 3300, 2930, 2859, 1733, 1461, 1416, 1338, 1234, 1200, 1126, 1085, 1029, 913, 865, 775, 716; **HRMS** (EI) *m/z* calculated for $C_{17}H_{25}O_3$ [MH^+]: 277.1798, found: 277.1803.

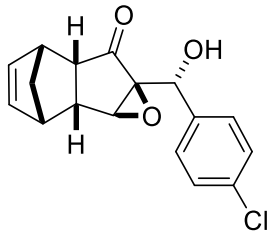
6a-(Hydroxy(phenyl)methyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170g):



According to general procedure 6 (±)-**165g** (5.05 g, 20.0 mmol), 2 M NaOH (12.0 mL, 24.0 mmol) and H_2O_2 (11.0 mL, 30% in water, 108 mmol) were used and stirred for 30 min to afford a white solid (5.14 g, 19.2 mmol, 96%): **mp** 121.5 – 123.0 °C; $\mathbf{R_f}$ = 0.63 (PE/EA = 2:1);

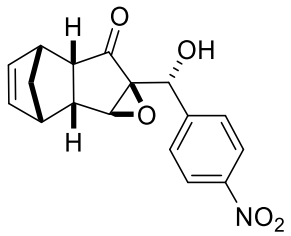
^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.36 – 7.26 (m, 5H), 5.74 (dd, *J* = 5.7, 2.8 Hz, 1H), 5.68 (dd, *J* = 5.7, 2.8 Hz, 1H), 4.94 (s, 1H), 3.39 (d, *J* = 1.6 Hz, 1H), 3.20 – 3.15 (m, 1H), 3.02 – 2.97 (m, 1H), 2.96 – 2.91 (m, 1H), 2.87 – 2.81 (m, 1H), 1.54 (dt, *J* = 8.6, 1.7 Hz, 1H), 1.41 – 1.36 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 211.2 (C_q), 138.5 (C_q), 134.6 (+), 133.5 (+), 128.2 (+), 128.1 (+) 126.9 (+), 70.7 (+), 67.7 (C_q), 64.9 (+), 51.7 (-), 50.9 (+), 45.9 (+), 43.4 (+), 43.0 (+); **IR** (ν/cm^{-1}): 3600 – 3400, 2979, 2941, 2868, 1739, 1495, 1451, 1407, 1339, 1307, 1197, 1036, 912, 866, 843, 757, 725, 704; **HRMS** (ESI) *m/z* calculated for $C_{17}H_{17}O_3$ [MH$^+$]: 269.1172, found: 269.1175.

6a-((4-Chlorophenyl)(hydroxy)methyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170h):



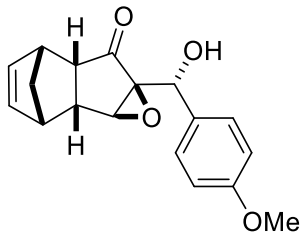
According to general procedure 6 (±)-**165h** (287 mg, 1.00 mmol), 2 M NaOH (0.6 mL, 1.20 mmol) and H_2O_2 (0.55 mL, 30% in water, 5.40 mmol) were used and stirred for 30 min to afford a white solid (274 mg, 0.91 mmol, 91%): **mp** 128.8 – 130.9 °C; **R_f** = 0.32 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.34 – 7.28 (m, 2H), 7.26 – 7.21 (m, 2H), 5.82 (dd, *J* = 5.6, 2.8 Hz, 1H), 5.77 (dd, *J* = 5.6, 2.8 Hz, 1H), 4.97 (s, 1H), 3.35 (d, *J* = 1.6 Hz, 1H), 3.23 – 3.18 (m, 1H), 3.05 – 2.99 (m, 1H), 2.98 – 2.93 (m, 1H), 2.89 – 2.83 (m, 1H), 1.57 (dt, *J* = 8.6, 1.7 Hz, 1H), 1.44 – 1.38 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 211.1 (C_q), 136.9 (C_q), 134.8 (+), 133.9 (C_q), 133.6 (+), 128.3 (+), 128.2 (+), 69.6 (+), 67.6 (C_q), 64.8 (+), 51.8 (-), 50.9 (+), 45.9 (+), 43.4 (+), 42.9 (+); **IR** (ν/cm^{-1}): 3600 – 3400, 2984, 2929, 2872, 1723, 1489, 1404, 1334, 1275, 1258, 1213, 1198, 1089, 1060, 1033, 1016, 939, 898, 850, 820, 745, 723; **HRMS** (ESI) *m/z* calculated for $C_{17}H_{16}ClO_3$ [MH$^+$]: 303.0782, found: 303.0791.

6a-(Hydroxy(4-nitrophenyl)methyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170i):



According to general procedure 6 (±)-**165i** (297 mg, 1.00 mmol), 2 M NaOH (0.6 mL, 1.20 mmol) and H_2O_2 (0.55 mL, 30% in water, 5.40 mmol) were used and stirred for 30 min to afford a yellow solid (279 mg, 0.89 mmol, 89%): **mp** 141.6 – 143.4 °C; $\mathbf{R_f}$ = 0.56 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.23 – 8.17 (m, 2H), 7.54 – 7.47 (m, 2H), 5.88 (dd, *J* = 5.6, 2.8 Hz, 1H), 5.82 (dd, *J* = 5.7, 2.8 Hz, 1H), 5.16 (s, 1H), 3.33 (d, *J* = 1.6 Hz, 1H), 3.25 – 3.20 (m, 1H), 3.06 – 3.01 (m, 1H), 3.00 – 2.95 (m, 1H), 2.91 – 2.85 (m, 1H), 1.60 (dt, *J* = 8.7, 1.7 Hz, 1H), 1.46 – 1.40 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.7 (C_q), 147.7 (C_q), 145.4 (C_q), 135.0 (+), 133.6 (+), 127.8 (+), 123.3 (+), 68.9 (+), 67.4 (C_q), 64.7 (+), 51.8 (-), 50.8 (+), 45.9 (+), 43.4 (+), 42.8 (+); **IR** (ν/cm^{-1}): 3600 – 3400, 2962, 2937, 2872, 1725, 1602, 1509, 1397, 1346, 1260, 1235, 1193, 1106, 1064, 1034, 899, 834, 806, 754, 718; **HRMS** (ESI) *m/z* calculated for $C_{17}H_{16}NO_5$ [MH^+]: 314.1023, found: 314.1026.

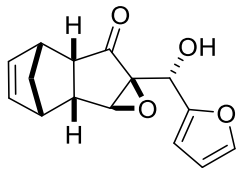
6a-(Hydroxy(4-methoxyphenyl)methyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170j):



According to general procedure 6 (±)-**165j** (282 mg, 1.00 mmol), 2 M NaOH (0.6 mL, 1.20 mmol) and H_2O_2 (0.55 mL, 30% in water, 5.40 mmol) were used and stirred for 30 min to

afford a colorless oil (273 mg, 0.92 mmol, 92%): $\mathbf{R_f}$ = 0.64 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.25 – 7.19 (m, 2H), 6.90 – 6.83 (m, 2H), 5.80 (dd, *J* = 5.6, 2.8 Hz, 1H), 5.75 (dd, *J* = 5.6, 2.8 Hz, 1H), 4.91 (s, 1H), 3.80 (s, 3H), 3.39 (d, *J* = 1.6 Hz, 1H), 3.22 – 3.16 (m, 1H), 3.04 – 2.99 (m, 1H), 2.98 – 2.92 (m, 1H), 2.88 – 2.82 (m, 1H), 1.55 (dt, *J* = 8.6, 1.7 Hz, 1H), 1.43 – 1.37 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 211.25 (C_q), 159.4 (C_q), 134.7 (+), 133.5 (+), 130.7 (C_q), 128.1 (+), 113.6 (+), 70.1 (+), 67.9 (C_q), 64.9 (+), 55.3 (+), 51.7 (-), 50.9 (+), 45.9 (+), 43.4 (+), 42.9 (+); **IR** (ν/cm^{-1}): 3600 – 3400, 2984, 2938, 2867, 1720, 1613, 1587, 1511, 1462, 1416, 1335, 1306, 1245, 1200, 1170, 1126, 1062, 1034, 939, 898, 866, 827, 712; **HRMS** (ESI) *m/z* calculated for $C_{18}H_{18}NaO_4$ [MNa$^+$]: 321.1097, found: 321.1093.

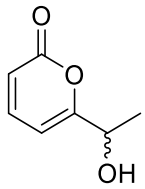
6a-(furan-2-yl(hydroxy)methyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170k):



According to general procedure 6 (±)-**165k** (242 mg, 1.00 mmol), 2 M NaOH (0.6 mL, 1.20 mmol) and H_2O_2 (0.55 mL, 30% in water, 5.40 mmol) were used and stirred for 30 min to afford a yellowish oil (251 mg, 0.97 mmol, 97%): $\mathbf{R_f}$ = 0.50 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.38 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.36 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.34 – 6.31 (m, 1H), 5.85 (dd, *J* = 5.7, 2.8 Hz, 1H), 5.74 (dd, *J* = 5.7, 2.8 Hz, 1H), 4.83 (s, 1H), 3.68 (d, *J* = 1.6 Hz, 1H), 3.22 – 3.17 (m, 1H), 3.09 – 3.04 (m, 1H), 3.04 – 2.99 (m, 1H), 2.89 – 2.83 (m, 1H), 1.57 (dt, *J* = 8.6, 1.7 Hz, 1H), 1.45 – 1.40 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.5 (C_q), 151.9 (C_q), 142.1 (+), 134.5 (+), 133.2 (+), 110.6 (+), 108.0 (+), 66.5 (C_q), 65.7 (+), 64.9 (+), 51.7 (-), 50.9 (+), 45.8 (+), 43.5 (+), 43.3 (+); **IR** (ν/cm^{-1}): 3600 – 3300,

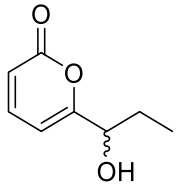
2970, 2937, 2870, 1734, 1502, 1421, 1374, 1338, 1230, 1145, 1126, 1011, 912, 831, 729, 715; **HRMS** (ESI) *m/z* calculated for $C_{15}H_{15}O_4$ [MH^+]: 259.0965, found: 259.0962.

6-(1-Hydroxyethyl)-2*H*-pyran-2-one ((±)-171a):



Following general procedure 1 (±)-**170a** (1.65 g, 8.00 mmol) was used to give rise to a brownish oil (1.10 g, 7.84 mmol, 98%): $\mathbf{R_f}$ = 0.29 (PE/EA = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.34 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.29 (dt, *J* = 6.6, 0.9 Hz, 1H), 6.21 (d, *J* = 9.4 Hz, 1H), 4.60 (q, *J* = 6.6 Hz, 1H), 2.46 – 2.29 (bs, 1H), 1.51 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 167.7 (C_q), 162.3 (C_q), 144.0 (+), 114.2 (+), 100.6 (+), 66.7 (+), 21.4 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2982, 2932, 1698, 1630, 1558, 1453, 1409, 1366, 1309, 1214, 1093, 1015, 976, 906, 858, 804; **HRMS** (EI) *m/z* calculated for $C_7H_9O_3$ [MH^+]: 141.0546, found: 141.0547.

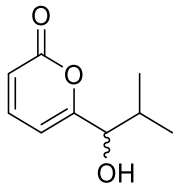
6-(1-Hydroxypropyl)-2*H*-pyran-2-one ((±)-171b):



Following general procedure 1 (±)-**170b** (1.76 g, 8.00 mmol) was used to give rise to a brownish oil (1.13 g, 7.36 mmol, 92%): $\mathbf{R_f}$ = 0.39 (PE/EA = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.34 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.28 (d, *J* = 6.6 Hz, 1H), 6.21 (d, *J* = 9.4 Hz, 1H), 4.37 (dd, *J* = 7.3, 5.1 Hz, 1H), 2.29 – 2.15 (bs, 1H), 1.98 – 1.69 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 166.8 (C_q), 162.4 (C_q), 143.9 (+), 114.1 (+), 101.6 (+), 71.9 (+), 28.3 (-), 9.4 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2968, 2934, 2878, 1707, 1631, 1557, 1462,

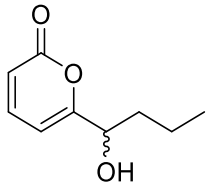
1412, 1313, 1210, 1094, 1050, 995, 808, 633; **HRMS** (EI) *m/z* calculated for $C_8H_{11}O_3$ [MH^+]: 155.0703, found: 155.0704.

6-(1-Hydroxy-2-methylpropyl)-2*H*-pyran-2-one ((±)-171c):



Following general procedure 1 (±)-**170c** (117 mg, 0.50 mmol) was used to give rise to a brownish oil (81 mg, 0.48 mmol, 96%): $\mathbf{R_f}$ = 0.44 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.33 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.27 (dt, *J* = 6.6, 0.8 Hz, 1H), 6.19 (dd, *J* = 9.4, 0.5 Hz, 1H), 4.18 (d, *J* = 5.4 Hz, 1H), 2.54 – 2.38 (bs, 1H), 2.22 – 2.06 (m, 1H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 166.3 (C_q), 162.1 (C_q), 143.6 (+), 114.1 (+), 102.3 (+), 75.8 (+), 32.3 (+), 19.0 (+), 16.6 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2963, 2930, 2875, 1708, 1629, 1557, 1467, 1410, 1386, 1368, 1259, 1212, 1177, 1095, 1027, 937, 900, 869, 804; **HRMS** (ESI) *m/z* calculated for $C_9H_{13}O_3$ [MH^+]: 169.0859, found: 169.0859.

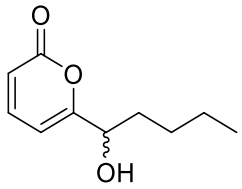
6-(1-Hydroxybutyl)-2*H*-pyran-2-one ((±)-171d):



Following general procedure 1 (±)-**170d** (117 mg, 0.50 mmol) was used to give rise to a brownish oil (77 mg, 0.49 mmol, 92%): $\mathbf{R_f}$ = 0.27 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.33 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.28 (d, *J* = 6.6 Hz, 1H), 6.19 (d, *J* = 9.3 Hz, 1H), 4.41 (dd, *J* = 8.0, 4.8 Hz, 1H), 2.83 – 2.50 (bs, 1H), 1.86 – 1.65 (m, 2H), 1.53 – 1.34 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 167.1 (C_q), 162.2 (C_q), 143.7 (+), 114.2 (+),

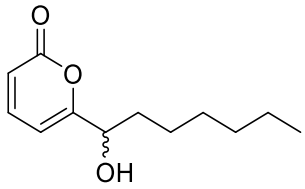
101.3 (+), 70.7 (+), 37.4 (-), 18.4 (-), 13.8 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2961, 2935, 2873, 1704, 1630, 1556, 1465, 1413, 1380, 1315, 1259, 1209, 1094, 1035, 864, 806; **HRMS** (EI) *m/z* calculated for $C_9H_{13}O_3$ [MH$^+$]: 169.0859, found: 169.0858.

6-(1-Hydroxypentyl)-2*H*-pyran-2-one ((±)-171e):



Following general procedure 1 (±)-**170e** (1.99 g, 8.00 mmol) was used to give rise to a brownish oil (1.33 g, 7.28 mmol, 91%): **R$_f$** = 0.35 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.34 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.27 (d, *J* = 6.6 Hz, 1H), 6.21 (d, *J* = 9.3 Hz, 1H), 4.41 (dd, *J* = 7.9, 4.8 Hz, 1H), 2.19 – 2.06 (bs, 1H), 1.93 – 1.66 (m, 2H), 1.47 – 1.30 (m, 4H), 0.91 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 167.0 (C_q), 162.2 (C_q), 143.8 (+), 114.2 (+), 101.3 (+), 70.9 (+), 35.0 (-), 27.3 (-), 22.4 (-), 14.0 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2960, 2936, 2863, 1703, 1633, 1558, 1461, 1409, 1316, 1264, 1208, 1092, 1044, 865, 805; **HRMS** (EI) *m/z* calculated for $C_{10}H_{15}O_3$ [MH$^+$]: 183.1016, found: 183.1019.

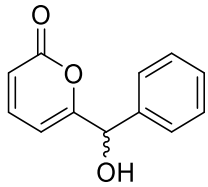
6-(1-Hydroxyheptyl)-2*H*-pyran-2-one ((±)-171f):



Following general procedure 1 (±)-**170f** (2.21 g, 8.00 mmol) was used to give rise to a brownish oil (1.51 g, 7.19 mmol, 90%): **R$_f$** = 0.47 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.33 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.27 (d, *J* = 6.6 Hz, 1H), 6.19 (d, *J* = 9.4, 1H), 4.40 (dd, *J* = 7.9, 4.8 Hz, 1H), 2.94 – 2.72 (s, 1H), 1.91 – 1.63 (m, 2H), 1.42 – 1.21 (m, 8H), 0.86 (t, *J* = 6.7 Hz, 3H);

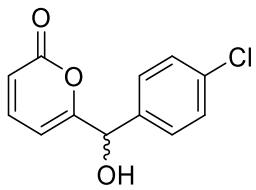
^{13}C NMR (75 MHz, $CDCl_3$) δ_C = 167.0 (C_q), 162.2 (C_q), 143.8 (+), 114.2 (+), 101.3 (+), 70.9 (+), 35.3 (-), 31.7 (-), 29.0 (-), 25.1 (-), 22.6 (-), 14.1 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 2926, 2859, 1703, 1633, 1558, 1461, 1409, 1316, 1211, 1092, 1047, 913, 865, 805; **HRMS** (ESI) *m/z* calculated for $C_{12}H_{19}O_3$ [MH^+]: 211.1329, found: 211.1334.

6-(Hydroxy(phenyl)methyl)-2*H*-pyran-2-one ((±)-171g):



Following general procedure 1 (±)-**170g** (2.15 g, 8.00 mmol) was used to give rise to an orange solid (1.59 g, 7.85 mmol, 98%): **mp** 78.4 – 79.8 °C; **R_f** = 0.19 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.47 – 7.30 (m, 6H), 6.33 (dt, *J* = 6.6, 1.0 Hz, 1H), 6.23 – 6.15 (m, 1H), 5.50 (s, 1H), 2.65 – 2.45 (bs, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 165.5 (C_q), 161.8 (C_q), 143.5 (+), 139.1 (C_q), 128.9 (+), 126.9 (+), 114.5 (+), 101.7 (+), 73.0 (+); **IR** (ν/cm^{-1}): 3400 – 3200, 1687, 1630, 1557, 1491, 1454, 1423, 1329, 1258, 1213, 1099, 1033, 903, 796, 750, 707; **HRMS** (EI) *m/z* calculated for $C_{12}H_{11}O_3$ [MH^+]: 203.0703, found: 203.0700.

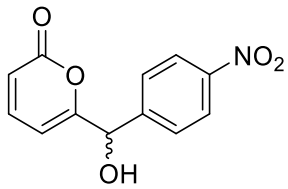
6-((4-Chlorophenyl)(hydroxy)methyl)-2*H*-pyran-2-one ((±)-171h):



Following general procedure 1 (±)-**170h** (151 mg, 0.50 mmol) was used to give rise to an orange solid (114 mg, 0.48 mmol, 97%): **mp** 98.6 – 101.7 °C; **R_f** = 0.39 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.33 – 7.24 (m, 5H), 6.26 (dt, *J* = 6.6, 0.9 Hz, 1H), 6.18 – 6.12

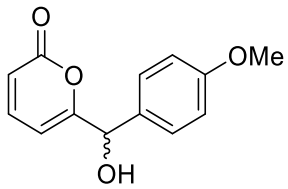
(m, 1H), 5.43 (s, 1H), 3.24 – 2.54 (bs, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 165.0 (C_q), 161.7 (C_q), 143.6 (+), 137.5 (C_q), 134.7 (C_q), 129.0 (+), 128.2 (+), 114.7 (+), 101.8 (+), 72.2 (+); **IR** (ν/cm^{-1}): 3400 – 3200, 2865, 1695, 1625, 1554, 1483, 1408, 1271, 1237, 1191, 1086, 1013, 885, 868, 846, 798, 782; **HRMS** (ESI) *m/z* calculated for $C_{12}H_{10}ClO_3$ [MH^+]: 237.0313, found: 237.0313.

6-(Hydroxy(4-nitrophenyl)methyl)-2*H*-pyran-2-one ((±)-171i):



Following general procedure 1 (±)-**170i** (157 mg, 0.50 mmol) was used to give rise to an orange solid (109 mg, 0.43 mmol, 88%): **mp** 118.4 – 120.7 °C; **R_f** = 0.33 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.27 – 8.21 (m, 2H), 7.69 – 7.62 (m, 2H), 7.34 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.33 (dt, *J* = 6.6, 0.8 Hz, 1H), 6.22 (d, *J* = 9.4 Hz, 1H), 5.62 (s, 1H), 3.22 – 2.72 (bs, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 163.9 (C_q), 161.3 (C_q), 148.1 (C_q), 145.8 (C_q), 143.4 (+), 127.7 (+), 124.0 (+), 115.3 (+), 102.0 (+), 72.0 (+); **IR** (ν/cm^{-1}): 3500 – 3300, 3107, 3076, 1716, 1632, 1600, 1556, 1515, 1409, 1344, 1289, 1232, 1213, 1197, 1097, 1064, 1037, 986, 907, 856, 821, 801, 740; **HRMS** (ESI) *m/z* calculated for $C_{12}H_{10}NO_5$ [MH^+]: 248.0553, found: 248.0556.

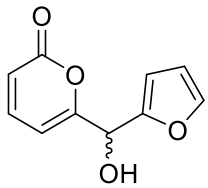
6-(Hydroxy(4-methoxyphenyl)methyl)-2*H*-pyran-2-one ((±)-171j):



Following general procedure 1 (±)-**170j** (149 mg, 0.50 mmol) was used to give rise to an orange solid (114 mg, 0.49 mmol, 98%): **mp** 109.6 – 111.4 °C; **R_f** = 0.31 (PE/EA = 1:1);

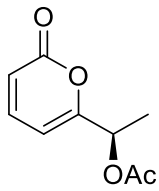
^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 7.37 – 7.30 (m, 3H), 6.94 – 6.87 (m, 2H), 6.33 (dt, *J* = 6.6, 0.9 Hz, 1H), 6.19 (d, *J* = 9.3 Hz, 1H), 5.45 (s, 1H), 3.81 (s, 3H), 2.05 – 1.69 (bs, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 165.7 (C_q), 161.8 (C_q), 160.0 (C_q), 143.5 (+), 131.3 (C_q), 128.3 (+), 114.4 (+), 114.3 (+), 101.4 (+), 72.6 (+), 55.4 (+); **IR** (ν/cm^{-1}): 3500 – 3300, 3080, 2963, 1690, 1626, 1553, 1509, 1410, 1306, 1287, 1249, 1228, 1173, 1098, 1066, 1022, 876, 839, 792; **HRMS** (ESI) *m/z* calculated for $C_{13}H_{13}O_4$ [MH^+]: 233.0808, found: 233.0808.

6-(Furan-2-yl(hydroxy)methyl)-2*H*-pyran-2-one ((±)-171k):

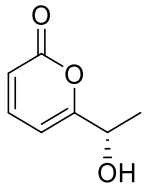


Following general procedure 1 (±)-**170k** (129 mg, 0.50 mmol) was used to give rise to a yellow oil (59 mg, 0.31 mmol, 62%) after purification via flash chromatography (silica, PE/EA = 2:1): **R_f** = 0.21 (PE/EA = 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H = 7.42 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.36 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.43 – 6.37 (m, 3H), 6.25 (d, *J* = 9.4 Hz, 1H), 5.53 (s, 1H), 2.03 – 1.64 (bs, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C = 162.6 (C_q), 161.4 (C_q), 151.2 (C_q), 143.4 (+), 143.3 (+), 115.2 (+), 110.8 (+), 109.1 (+), 102.3 (+), 67.0 (+); **IR** (ν/cm^{-1}): 3500 – 3200, 1700, 1633, 1558, 1521, 1409, 1208, 1148, 1092, 1062, 883, 809, 738; **HRMS** (ESI) *m/z* calculated for $C_{10}H_9O_4$ [MH^+]: 193.0495, found: 193.0496.

(*R*)-1-(2-Oxo-2*H*-pyran-6-yl)ethyl acetate (174):



(*S*)-6-(1-Hydroxyethyl)-2*H*-pyran-2-one (171a):

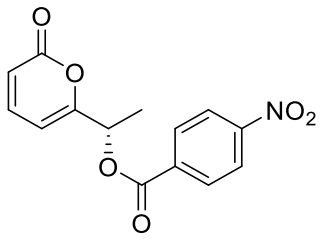


To a solution of (±)-**171a** (140 mg, 1.0 mmol) in abs. toluene (8 mL) Novozym 435 (200 mg, immobilized on acrylic resin), molecular sieves 4 Å (1.00 g), and isopropenyl acetate (0.44 mL, 4.0 mmol) were added. The reaction mixture was stirred at 40 °C for 18 h. After filtration and evaporation of the solvent the products were separated via flash chromatography (silica, PE/EA = 1:1) to yield (*R*)-**174** (81 mg, 0.45 mmol, 45%) as a colorless oil and (*S*)-**171a** (53 mg, 0.38 mmol, 38%) as a brownish oil:

(*R*)-**174**: $\mathbf{R_f}$ = 0.50 (PE/EA = 1:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.29 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.23 (d, *J* = 9.0 Hz, 1H), 6.20 – 6.16 (m, 1H), 5.55 (q, *J* = 6.7 Hz, 1H), 2.09 (s, 3H), 1.52 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 169.8 (C_q), 162.7 (C_q), 161.5 (C_q), 143.2 (+), 115.4 (+), 102.2 (+), 68.2 (+), 21.0 (+), 18.3 (+); **IR** (ν/cm^{-1}): 3092, 2993, 2940, 1727, 1640, 1561, 1370, 1321, 1227, 1085, 1066, 1043, 943, 868, 801, 726, 610, 542, 442; **HRMS** (APCI) *m/z* calculated for $C_9H_{11}O_4$ [MH^+]: 183.0652, found: 183.0656; **Chiral HPLC** 84% *ee* (t_R major, minor = 42.1, 69.5 min, Chiralpak AS-H 4.6 x 250 mm 10 µm, *n*-heptane:*i*-PrOH 90:10, 0.5 mL/min); $[\alpha]_D^{25}$ = -142.1 (c = 1.0, $CHCl_3$).

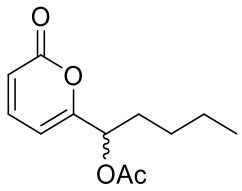
(*S*)-**171a**: **Chiral HPLC** >99% *ee* (t_R major, minor = 46.9, 52.0 min, Chiralpak AS-H 4.6 x 250 mm 10 µm, *n*-heptane:*i*-PrOH 90:10, 0.5 mL/min); $[\alpha]_D^{25}$ = +52.6 (c = 1.0, $CHCl_3$).

(*S*)-1-(2-Oxo-2*H*-pyran-6-yl)ethyl 4-nitrobenzoate (175):



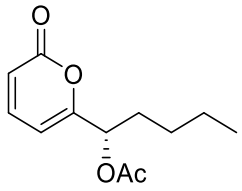
To a solution of (*S*)-**171a** >99% *ee* (70 mg, 0.50 mmol) and Et_3N (0.1 mL, 0.7 mmol) in DCM (2 mL) a solution of 4-nitrobenzoyl chloride (111 mg, 0.60 mmol) in DCM (2 mL) was added. The reaction mixture was stirred at room temperature for 15 h and the product was purified via flash chromatography (silica, PE/EA = 2:1) to yield (*S*)-**175** (116 mg, 0.40 mmol, 80%) as a white solid: **mp** 162.3 – 164.1 °C; $\mathbf{R_f}$ = 0.40 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.34 – 8.28 (m, 2H), 8.28 – 8.19 (m, 2H), 7.33 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.33 – 6.30 (m, 1H), 6.30 – 6.26 (m, 1H), 5.86 (q, *J* = 6.7 Hz, 1H), 1.72 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 163.6 (C_q), 161.6 (C_q), 161.3 (C_q), 150.8 (C_q), 143.0 (+), 134.8 (C_q), 131.0 (+), 123.7 (+), 116.0 (+), 102.9 (+), 69.8 (+), 18.2 (+); **IR** (ν/cm^{-1}): 3116, 2986, 2941, 2863, 1715, 1636, 1607, 1558, 1525, 1346, 1312, 1267, 1103, 1015, 891, 839, 805, 716; **HRMS** (CI) *m/z* calculated for $C_{14}H_{12}NO_6$ [MH^+]: 290.06591, found: 290.06596; **Chiral HPLC** >99% *ee* (t_R major, minor = 29.0, 36.4 min, Chiralpak AS-H 4.6 x 250 mm 10 µm, *n*-heptane:*i*-PrOH 50:50, 0.5 mL/min); $[\alpha]_D^{25}$ = -65.9 (c = 1.0, $CHCl_3$).

1-(2-Oxo-2*H*-pyran-6-yl)pentyl acetate ((±)-179):

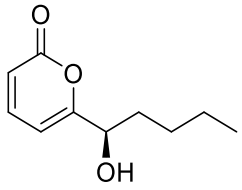


To a solution of (±)-**171e** (1.09 g, 6.00 mmol) in DCM (40 mL) Et_3N (4.2 mL, 30.0 mmol), and Ac_2O (2.8 mL, 30.0 mmol) were added. The reaction mixture was stirred at room temperature for 18 h. The solvent was evaporated and the product was purified via flash chromatography (silica, PE/EA = 3:1) to yield (±)-**179** (1.28 g, 5.70 mmol, 95%) as a yellowish oil: $\mathbf{R_f}$ = 0.62 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.24 (dd, *J* = 9.4, 6.5 Hz, 1H), 6.17 (dd, *J* = 9.4, 0.9 Hz, 1H), 6.11 (d, *J* = 6.5 Hz, 1H), 5.41 – 5.34 (m, 1H), 2.05 (s, 3H), 1.89 – 1.74 (m, 2H), 1.35 – 1.15 (m, 4H), 0.83 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 170.0 (C_q), 162.1 (C_q), 161.6 (C_q), 143.1 (+), 115.3 (+), 102.9 (+), 71.9 (+), 31.9 (-), 27.1 (-), 22.3 (-), 20.9 (+), 13.9 (+); **IR** (ν/cm^{-1}): 2958, 2934, 2873, 1730, 1639, 1561, 1371, 1221, 1092, 1022, 803; **HRMS** (ESI) *m/z* calculated for $C_{12}H_{17}O_4$ [MH^+]: 225.1121, found: 225.1116.

(*S*)-1-(2-Oxo-2*H*-pyran-6-yl)pentyl acetate (179):



(*R*)-6-(1-Hydroxypentyl)-2*H*-pyran-2-one (171e):



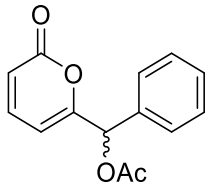
To a solution of (±)-**179** (224 mg, 1.0 mmol) in acetone (5 mL), phosphate buffer (25 mL, 50 mM, pH 8), and Amano lipase from *Burkholderia cepacia* (200 mg) were added and the

reaction mixture was stirred at 25 °C for 7 d. After filtration, the mixture was extracted with DCM (3x) and dried over $MgSO_4$. The products were separated via flash chromatography (silica, PE/EA = 2:1) to yield (*S*)-**179** (87 mg, 0.39 mmol, 39%) as a yellowish oil and (*R*)-**171e** (80 mg, 0.44 mmol, 44%) as a brownish oil:

(*S*)-**179**: **Chiral HPLC** >99% *ee* (t_R major, minor = 28.9, 37.1 min, Chiralpak AS-H 4.6 x 250 mm 10 µm, *n*-heptane:*i*-PrOH 90:10, 0.5 mL/min); $[\alpha]_D^{25}$ +127.3 (c = 1.0, $CHCl_3$).

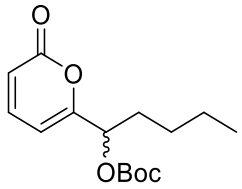
(*R*)-**171e**: **Chiral HPLC** 75% *ee* (t_R major, minor = 33.4, 40.2 min, Chiralpak AS-H 4.6 x 250 mm 10 µm, *n*-heptane:*i*-PrOH 90:10, 0.5 mL/min); $[\alpha]_D^{25}$ –62.2 (c = 1.0, $CHCl_3$).

(2-Oxo-2*H*-pyran-6-yl)(phenyl)methyl acetate ((±)-180):



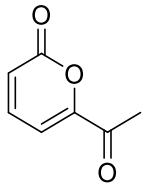
To a solution of (±)-**171g** (404 mg, 2.00 mmol) in DCM (12 mL) Et_3N (1.4 mL, 10.0 mmol), and Ac_2O (1.0 mL, 10.0 mmol) were added. The reaction mixture was stirred at room temperature for 18 h. The solvent was evaporated and the product was purified via flash chromatography (silica, PE/EA = 2:1) to yield (±)-**180** (441 mg, 1.81 mmol, 90%) as a brownish oil: $\mathbf{R_f}$ = 0.45 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.48 – 7.36 (m, 5H), 7.29 (dd, *J* = 9.3, 6.6 Hz, 1H), 6.48 (s, 1H), 6.25 – 6.19 (m, 2H), 2.18 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 169.4 (C_q), 161.6 (C_q), 161.3 (C_q), 142.9 (+), 135.4 (C_q), 129.2 (+), 128.9 (+), 127.5 (+), 115.5 (+), 103.0 (+), 73.3 (+), 21.0 (+); **IR** (ν/cm^{-1}): 3090, 3035, 1726, 1638, 1558, 1496, 1455, 1371, 1218, 1094, 1024, 800, 744, 698, 604, 581, 527; **HRMS** (APCI) *m/z* calculated for $C_{14}H_{13}O_4$ [MH^+]: 245.0808, found: 245.0808.

tert-Butyl (1-(2-oxo-2*H*-pyran-6-yl)pentyl) carbonate ((±)-190)



Under nitrogen atmosphere (±)-**171e** (547 mg, 3.00 mmol) was dissolved in dry THF and Boc_2O (786 mg, 3.60 mmol), Et_3N (0.5 mL, 3.60 mmol) and DMAP (6 mg, 0.05 mmol) were added. The reaction mixture was stirred for 20 h at room temperature, the solvent was evaporated and the crude product was purified via flash chromatography (silica, PE/EA = 5:1) to yield (±)-**190** (784 mg, 2.78 mmol, 93%) as a yellowish oil: $\mathbf{R_f}$ = 0.40 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.30 (dd, *J* = 9.4, 6.6 Hz, 1H), 6.28 – 6.15 (m, 2H), 5.25 (dd, *J* = 7.6, 5.6 Hz, 1H), 1.99 – 1.80 (m, 2H), 1.49 (s, 9H), 1.38 – 1.27 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 162.7 (C_q), 161.5 (C_q), 152.6 (C_q), 143.1 (+), 115.1 (+), 102.2 (+), 83.2 (C_q), 74.6 (+), 32.3 (-), 27.7 (+), 27.0 (-), 22.3 (-), 13.9 (+); **IR** (ν/cm^{-1}): 2960, 2934, 2873, 1733, 1640, 1560, 1459, 1370, 1272, 1253, 1158, 1089, 863, 803, 539; **HRMS** (APCI) *m/z* calculated for $C_{15}H_{23}O_5$ [MH^+]: 283.1540, found: 283.1540.

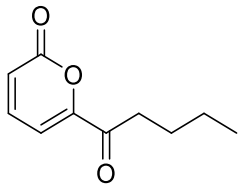
6-Acetyl-*2H*-pyran-2-one ((±)-195a)



Following general procedure 8 (±)-**171a** (114 mg, 1.0 mmol) was used to give rise to a white solid (96 mg, 0.70 mmol, 70%): **mp** 107.5 – 108.3 °C; $\mathbf{R_f}$ = 0.27 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.46 (dd, *J* = 9.4, 6.6 Hz, 1H), 7.01 (dd, *J* = 6.6, 1.0 Hz, 1H), 6.57 (dd, *J* = 9.4, 1.0 Hz, 1H), 2.54 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 191.5 (C_q), 159.8 (C_q), 155.1 (C_q), 142.2 (+), 121.2 (+), 106.4 (+), 25.9 (+);**IR** (ν/cm^{-1}): 3078, 3059, 2942,

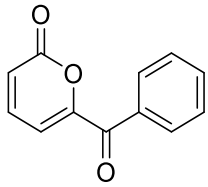
1720, 1682, 1628, 1368, 1343, 1257, 1096, 1038, 988, 954, 818, 693, 597, 556, 503, 439; **HRMS** (APCI) *m/z* calculated for $C_7H_7O_3$ [MH^+]: 139.0390, found: 139.0394.

6-Pentanoyl-2*H*-pyran-2-one ((±)-195b)



Following general procedure 8 (±)-**171e** (182 mg, 1.0 mmol) was used to give rise to a white solid (121 mg, 0.67 mmol, 67%): **mp** 70.5 – 70.8 °C; $\mathbf{R_f}$ = 0.56 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.45 (dd, *J* = 9.4, 6.6 Hz, 1H), 7.00 (dd, *J* = 6.6, 1.0 Hz, 1H), 6.56 (dd, *J* = 9.4, 1.0 Hz, 1H), 2.91 (t, *J* = 7.3 Hz, 2H), 1.71 – 1.61 (m, 2H), 1.44 – 1.33 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 194.0 (C_q), 159.9 (C_q), 155.3 (C_q), 142.3 (+), 121.0 (+), 106.2 (+), 37.8 (-), 25.2 (-), 22.2 (-), 13.9 (+); **IR** (ν/cm^{-1}): 3114, 3080, 3060, 2953, 2932, 2873, 1719, 1689, 1631, 1404, 1383, 1337, 1273, 1218, 1108, 1055, 1009, 953, 846, 820, 799, 732, 644, 573, 505, 459; **HRMS** (APCI) *m/z* calculated for $C_{10}H_{13}O_3$ [MH^+]: 181.0859, found: 181.0861.

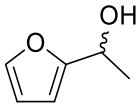
6-Benzoyl-2*H*-pyran-2-one ((±)-195c)



Following general procedure 8 (±)-**171g** (202 mg, 1.0 mmol) was used to give rise to a white solid (147 mg, 0.73 mmol, 73%): **mp** 113.1 – 115.4 °C; $\mathbf{R_f}$ = 0.40 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.04 – 7.93 (m, 2H), 7.67 – 7.59 (m, 1H), 7.55 – 7.47 (m, 3H), 7.04 (dd, *J* = 6.6, 1.0 Hz, 1H), 6.59 (dd, *J* = 9.4, 1.0 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$)

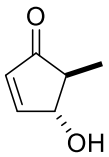
δ_C = 185.7 (C_q), 159.7 (C_q), 156.3 (C_q), 142.3 (+), 134.8 (C_q), 133.9 (+), 130.1 (+), 128.7 (+), 120.5 (+), 109.9 (+); **IR** (ν/cm^{-1}): 3120, 3088, 3063, 1729, 1649, 1596, 1577, 1448, 1344, 1325, 1273, 1185, 1100, 1003, 934, 812, 726, 699, 685, 596, 549; **HRMS** (APCI) *m/z* calculated for $C_{12}H_9O_3$ [MH^+]: 201.0546, found: 201.0549.

1-(Furan-2-yl)ethan-1-ol ((±)-199):[144]



To a solution of **198** (50.0 g, 454 mmol) in ethanol (400 mL) $NaBH_4$ (8.6 g, 227 mmol) was added over a period of 1 h and stirred for 2 h at room temperature. Acetone (75 mL) was slowly added, and the mixture was stirred for additional 30 min. Subsequently, water (200 mL) was added to the solution, and the organic solvent was evaporated under reduced pressure. The remaining aqueous phase was extracted with ethyl acetate (5x), and the combined organic layers were washed with brine (1x) and dried over Na_2SO_4. The crude was distilled under reduced pressure to afford a yellowish oil (41.1 g, 366 mmol, 81%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.36 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.32 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.24 – 6.19 (m, 1H), 4.86 (q, *J* = 6.6 Hz, 1H), 2.30 – 2.10 (bs, 1H), 1.53 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 157.6 (C_q), 141.9 (+), 110.1 (+), 105.1 (+), 63.6 (+), 21.3 (+).

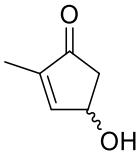
4-Hydroxy-5-methylcyclopent-2-en-1-one ((±)-200):[145]



A solution of (±)-**199** (16.8 g, 150 mmol) in toluene (45 mL, flowrate: 0.3 mL/min) was mixed with acidulated water pH 4 (630 mL, flowrate: 3.5 mL/min) in a microreactor setup (stainless steel capillary tube, heated zone: 10 m x 1.0 mm) at 240 °C. The solvent was evaporated and

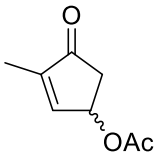
the crude product was distilled under reduced pressure to afford a yellowish oil (12.2 g, 109 mmol, 71%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.50 (dd, *J* = 5.8, 2.1 Hz, 1H), 6.22 (dd, *J* = 5.8, 1.2 Hz, 1H), 4.60 – 4.55 (m, 1H), 2.27 (qd, *J* = 7.5, 2.6 Hz, 1H), 2.13 – 1.92 (bs, 1H), 1.26 (d, *J* = 7.5 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 208.0 (C_q), 161.3 (+), 134.1 (+), 78.4 (+), 50.5 (+), 12.6 (+).

4-Hydroxy-2-methylcyclopent-2-en-1-one ((±)-201):[145]



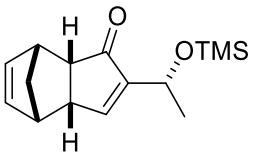
Adsorption of (±)-**200** (5.61 g, 50.0 mmol) on alumina (200 g, Brockman grade III) for 24 h and elution with benzene/diethyl ether 4:1 yielded pure (±)-**201** (5.10 g, 45.5 mmol) as a yellowish oil: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.17 – 7.12 (m, 1H), 4.94 – 4.81 (m, 1H), 2.73 (dd, *J* = 18.6, 6.0 Hz, 1H), 2.64 – 2.50 (bs, 1H), 2.23 (dd, *J* = 18.6, 1.9 Hz, 1H), 1.73 (t, *J* = 1.5 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 206.9 (C_q), 157.1 (+), 143.6 (C_q), 68.4 (+), 44.5 (-), 10.0 (+).

3-Methyl-4-oxocyclopent-2-en-1-yl acetate ((±)-202):[145]



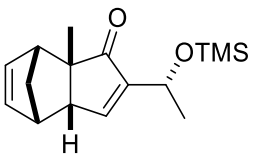
According to general procedure 4 (±)-**201** (2.24 g, 20.0 mmol) was used to afford a yellowish oil (2.48 g, 16.1 mmol, 81%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.17 – 7.05 (m, 1H), 5.74 – 5.56 (m, 1H), 2.82 – 2.71 (m, 1H), 2.30 – 2.21 (m, 1H), 2.02 – 1.97 (m, 3H), 1.77 – 1.72 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 205.0 (C_q), 170.5 (C_q), 152.5 (+), 145.5 (C_q), 70.3 (+), 41.1 (-), 20.9 (+), 10.0 (+).

2-(1-((Trimethylsilyl)oxy)ethyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-204):



Under nitrogen atmosphere (±)-**165a** (4.76 g, 25.0 mmol) was dissolved in DCM (100 mL) TMSCl (4.13 mL, 32.5 mmol) and Et_3N (4.51 mL, 32.5 mmol) were added at 0 °C. The reaction mixture was stirred for 1 h at the same temperature and quenched with water (25 mL). The water phase was extracted with DCM (3x) and the organic phase was dried over $MgSO_4$. The crude product was purified via flash chromatography (silica, PE/EA = 20:1) yielding a colorless oil (5.88 g, 22.4 mmol, 90%): $\mathbf{R_f}$ = 0.42 (PE/EA = 20:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.25 – 7.13 (m, 1H), 5.88 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.74 (dd, *J* = 5.6, 3.0 Hz, 1H), 4.39 (qt, *J* = 6.4, 1.3 Hz, 1H), 3.30 – 3.23 (m, 1H), 3.23 – 3.17 (m, 1H), 2.98 – 2.92 (m, 1H), 2.86 (t, *J* = 5.1 Hz, 1H), 1.74 (dt, *J* = 8.4, 1.7 Hz, 1H), 1.63 – 1.58 (m, 1H), 1.22 (d, *J* = 6.5 Hz, 3H), 0.07 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 208.8 (C_q), 157.5 (+), 154.0 (C_q), 132.9 (+), 132.4 (+), 63.9 (+), 52.9 (-), 52.2 (+), 45.4 (+), 45.1 (+), 44.2 (+), 23.8 (+), 0.0 (+); **IR** (ν/cm^{-1}): 3064, 2960, 2870, 1696, 1629, 1450, 1372, 1338, 1252, 1204, 1100, 1051, 985, 910, 835, 738; **HRMS** (CI) *m/z* calculated for $C_{15}H_{23}O_2Si$ [MH^+]: 263.14618, found: 263.14658.

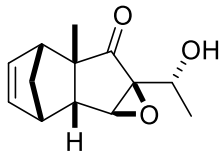
7a-Methyl-2-(1-((trimethylsilyl)oxy)ethyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-205):



Under nitrogen atmosphere diisopropylamine (3.16 mL, 22.5 mmol) was dissolved in dry THF (30 mL) at -78 °C *n*-BuLi (10.9 mL, 2.7 M in toluene, 21.0 mmol) was added and the mixture

was stirred for 10 min. To the solution (±)-**204** (3.94 g, 15.0 mmol) in dry THF (30 mL) was added slowly and stirred for 45 min. Then MeI (4.67 mL, 75.0 mmol) was added and stirred for 30 min. The reaction was quenched slowly with 1 M HCl (25 mL). The water phase was extracted with ethyl acetate (3x), the organic phase was washed with brine (1x) and dried over $MgSO_4$. The crude was purified via flash chromatography (silica, PE/EA = 20:1) yielding a colorless oil (2.22 g, 8.02 mmol, 53%): $\mathbf{R_f}$ = 0.40 (PE/EA = 20:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.14 (dd, *J* = 2.7, 1.5 Hz, 1H), 5.96 (dd, *J* = 5.6, 3.0 Hz, 1H), 5.68 (dd, *J* = 5.6, 2.9 Hz, 1H), 4.42 (qt, *J* = 6.4, 1.3 Hz, 1H), 2.97 – 2.92 (m, 1H), 2.87 – 2.82 (m, 1H), 2.68 (s, 1H), 1.89 – 1.83 (m, 1H), 1.75 (dt, *J* = 8.7, 1.7 Hz, 1H), 1.28 (s, 3H), 1.22 (d, *J* = 6.5 Hz, 3H), 0.07 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 211.3 (C_q), 155.9 (+), 152.0 (C_q), 134.7 (+), 133.0 (+), 63.8 (+), 56.1 (C_q), 53.6 (+), 51.1 (-), 50.3 (+), 45.2 (+), 23.6 (+), 21.0 (+), 0.0 (+); **IR** (ν/cm^{-1}): 3064, 2960, 2900, 2870, 1700, 1633, 1454, 1372, 1252, 1185, 1159, 1100, 1044, 947, 835, 731, 671; **HRMS** (CI) *m/z* calculated for $C_{16}H_{25}O_2Si$ [MH^+]: 277.16183, found: 277.16124.

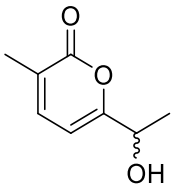
6a-(1-Hydroxyethyl)-5a-methyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-197):



To a solution of (±)-**205** (1.11 g, 4.00 mmol) in DCM/MeOH 1:1 (20 mL) 2 M NaOH (2.4 mL, 4.80 mmol), and H_2O_2 (30% in water, 2.2 mL, 21.6 mmol) were added and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was poured into DCM (120 mL) and washed with brine (1x). The organic layer was dried over $MgSO_4$ and concentrated under vacuum to yield pure (±)-**197** (876 mg, 3.98 mmol 100%) as a colorless oil: $\mathbf{R_f}$ = 0.35 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.02 (dd, *J* = 5.4, 2.8 Hz, 1H), 5.99 (dd,

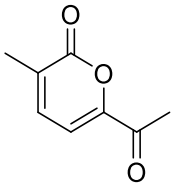
J = 5.2, 2.8 Hz, 1H), 4.06 – 3.74 (m, 1H), 3.57 (s, 1H), 3.01 – 2.93 (m, 1H), 2.77 – 2.66 (m, 1H), 2.51 (d, *J* = 4.0 Hz, 1H), 2.06 (d, *J* = 8.0 Hz, 1H), 1.67 – 1.61 (m, 1H), 1.60 – 1.57 (m, 1H), 1.25 (s, 3H), 1.23 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 213.6 (C_q), 135.8 (+), 133.7 (+), 77.2 (C_q), 68.7 (C_q), 64.3 (+), 64.1 (+), 56.0 (C_q), 52.0 (+), 50.0 (-), 44.2 (+), 23.6 (+), 19.2 (+); **IR** (ν/cm^{-1}): 3700 – 3300, 3064, 2971, 2874, 1730, 1454, 1416, 1372, 1334, 1297, 1249, 1118, 1033, 958, 887, 753, 716; **HRMS** (ESI) *m/z* calculated for $C_{13}H_{16}O_3$ [MH^+]: 221.1172, found: 221.1179.

6-(1-Hydroxyethyl)-3-methyl-2*H*-pyran-2-one ((±)-196):



Following general procedure 1 (±)-**197** (661 mg, 3.00 mmol) was used to afford a colorless oil (445 mg, 2.89 mmol, 96%): **R_f** = 0.29 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.13 (dq, *J* = 6.6, 1.2 Hz, 1H), 6.18 (d, *J* = 6.7 Hz, 1H), 4.58 (q, *J* = 6.6 Hz, 1H), 2.57 – 2.11 (bs, 1H), 2.08 (s, 3H), 1.49 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 164.3 (C_q), 163.4 (C_q), 139.6 (+), 124.1 (C_q), 100.7 (+), 66.7 (+), 21.3 (+), 16.7 (+); **IR** (ν/cm^{-1}): 3600 – 3200, 2982, 2930, 1689, 1640, 1580, 1454, 1364, 1308, 1163, 1103, 1025, 995, 947, 891, 828, 760, 727; **HRMS** (CI) *m/z* calculated for $C_8H_{11}O_3$ [MH^+]: 155.07027, found: 155.07042.

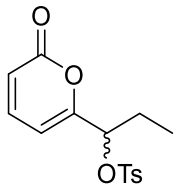
6-Acetyl-3-methyl-2*H*-pyran-2-one (3a):[104]



Following general procedure 8 (±)-**196** (154 mg, 1.0 mmol) was used to give rise to a yellowish solid (129 mg, 0.85 mmol, 85%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.20 (dq, *J* = 6.7, 1.3 Hz,

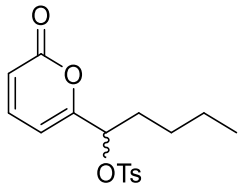
1H), 6.91 (d, *J* = 6.7 Hz, 1H), 2.47 (s, 3H), 2.14 (d, *J* = 1.3 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 191.4 (C_q), 161.3 (C_q), 153.3 (C_q), 138.0 (+), 132.0 (C_q), 107.2 (+), 25.9 (+), 17.5 (+).

1-(2-Oxo-2*H*-pyran-6-yl)propyl 4-methylbenzenesulfonate ((±)-189a):



Following general procedure 9 (±)-**171b** (154 mg, 1.0 mmol) was used to give rise to a white solid (249 mg, 0.81 mmol, 81%): **mp** 69.7 – 71.1 °C; **R_f** = 0.43 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.77 – 7.69 (m, 2H), 7.34 – 7.27 (m, 2H), 7.21 (dd, *J* = 9.3, 6.7 Hz, 1H), 6.23 – 6.11 (m, 2H), 5.00 (t, *J* = 6.5 Hz, 1H), 2.41 (s, 3H), 1.90 (qui, *J* = 7.3 Hz, 2H), 0.84 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 160.93 (C_q), 160.0 (C_q), 145.3 (C_q), 142.8 (+), 133.3 (C_q), 129.9 (+), 127.9 (+), 115.6 (+), 104.0 (+), 79.9 (+), 26.3 (-), 21.7 (+), 9.0 (+); **IR** (ν/cm^{-1}): 3097, 2974, 2937, 2881, 1730, 1640, 1595, 1562, 1461, 1409, 1361, 1215, 1174, 1096, 890, 850; **HRMS** (ESI) *m/z* calculated for $C_{15}H_{17}O_5S$ [MH^+]: 309.0791, found: 309.0792.

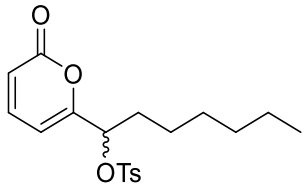
1-(2-Oxo-2*H*-pyran-6-yl)pentyl 4-methylbenzenesulfonate ((±)-189b):



Following general procedure 9 (±)-**171e** (182 mg, 1.0 mmol) was used to give rise to a white solid (278 mg, 0.83 mmol, 83%): **mp** 63.4 – 65.1 °C; **R_f** = 0.48 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.77 – 7.71 (m, 2H), 7.34 – 7.27 (m, 2H), 7.20 (dd, *J* = 9.2, 6.8 Hz, 1H), 6.17 – 6.13 (m, 2H), 5.05 (t, *J* = 6.2 Hz, 1H), 2.43 (s, 3H), 1.92 – 1.80 (m, 2H), 1.31 – 1.12 (m, 4H), 0.82 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 160.8 (C_q),

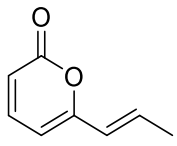
160.3 (C_q), 145.2 (C_q), 142.7 (+), 133.4 (C_q), 129.8 (+), 127.9 (+), 115.6 (+), 103.7 (+), 78.8 (+), 32.8 (-), 26.6 (-), 22.0 (-), 21.7 (+), 13.8 (+); **IR** (ν/cm^{-1}): 2960, 2933, 2870, 1737, 1640, 1599, 1558, 1461, 1405, 1364, 1174, 1092, 1036, 992, 805; **HRMS** (ESI) *m/z* calculated for $C_{17}H_{21}O_5S$ [MH^+]: 337.1104, found: 337.1106.

1-(2-Oxo-2*H*-pyran-6-yl)heptyl 4-methylbenzenesulfonate ((±)-189c):



Following general procedure 9 (±)-**171f** (210 mg, 1.0 mmol) was used to give rise to a colorless oil (291 mg, 0.80 mmol, 80%): $\mathbf{R_f}$ = 0.46 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.77 – 7.71 (m, 2H), 7.34 – 7.28 (m, 2H), 7.21 (dd, *J* = 9.3, 6.6 Hz, 1H), 6.20 – 6.13 (m, 2H), 5.04 (t, *J* = 7.2 Hz, 1H), 2.42 (s, 3H), 1.93 – 1.78 (m, 2H), 1.33 – 1.06 (m, 8H), 0.84 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 161.0 (C_q), 160.4 (C_q), 145.3 (C_q), 142.9 (+), 133.3 (C_q), 129.8 (+), 127.9 (+), 115.6 (+), 103.8 (+), 78.8 (+), 33.1 (-), 31.5 (-), 28.5 (-), 24.5 (-), 22.4 (-), 21.7 (+), 14.0 (+); **IR** (ν/cm^{-1}): 2930, 2859, 1737, 1640, 1599, 1558, 1461, 1364, 1174, 1096, 1006, 887, 805; **HRMS** (ESI) *m/z* calculated for $C_{19}H_{25}O_5S$ [MH^+]: 365.1417, found: 365.1411.

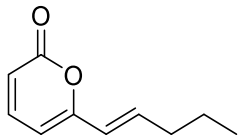
(E)-6-(prop-1-en-1-yl)-2*H*-pyran-2-one (7a):[146]



Following general procedure 10 (±)-**189a** (154 mg, 0.50 mmol) was used to give rise to a white solid (58 mg, 0.43 mmol, 85%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.22 (dd, *J* = 9.3, 6.7 Hz, 1H), 6.62 (dq, *J* = 14.0, 7.0 Hz, 1H), 6.08 (d, *J* = 9.3 Hz, 1H), 5.98 – 5.91 (m, 1H), 5.89 (d,

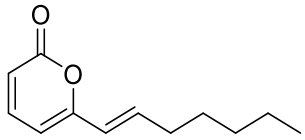
J = 6.7 Hz, 1H), 1.83 (dd, *J* = 7.0, 1.5 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 162.1 (C_q), 159.7 (C_q), 143.9 (+), 134.7 (+), 122.9 (+), 113.7 (+), 102.9 (+), 18.5 (+).

(E)-6-(Pent-1-en-1-yl)-2*H*-pyran-2-one (7b):[5]



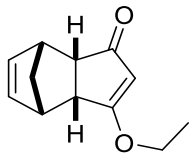
Following general procedure 10 (±)-**189b** (168 mg, 0.50 mmol) was used to give rise to a colorless oil (68 mg, 0.41 mmol, 83%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.23 (dd, *J* = 9.3, 6.7 Hz, 1H), 6.63 (dt, *J* = 15.6, 7.2 Hz, 1H), 6.09 (d, *J* = 9.2 Hz, 1H), 5.96 – 5.88 (m, 2H), 2.13 (dq, *J* = 7.3, 1.5 Hz, 2H), 1.42 (sext, *J* = 7.4 Hz, 2H), 0.87 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 162.1 (C_q), 159.7 (C_q), 143.9 (+), 139.7 (+), 121.7 (+), 113.7 (+), 103.1 (+), 34.9 (-), 21.9 (-), 13.7 (+).

(E)-6-(Hept-1-en-1-yl)-2*H*-pyran-2-one (7c):[5]



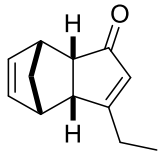
Following general procedure 10 (±)-**189c** (182 mg, 0.50 mmol) was used to give rise to a colorless oil (81 mg, 0.42 mmol, 84%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.22 (dd, *J* = 9.3, 6.7 Hz, 1H), 6.63 (dt, *J* = 15.6, 7.2 Hz, 1H), 6.09 (d, *J* = 9.2 Hz, 1H), 5.96 – 5.87 (m, 2H), 2.14 (dq, *J* = 7.3, 1.4 Hz, 2H), 1.44 – 1.33 (m, 2H), 1.31 – 1.15 (m, 4H), 0.82 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 162.1 (C_q), 159.7 (C_q), 143.9 (+), 139.9 (+), 121.5 (+), 113.6 (+), 103.1 (+), 32.8 (-), 31.3 (-), 28.3 (-), 22.5 (-), 14.0 (+).

3-Ethoxy-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-212):



To a solution of (±)-**211** (7.00 g, 43.2 mmol) in DCM (70 mL) Et_3N (7.80 mL, 56.3 mmol), and Et_3OBF_4 (9.84 g, 51.8 mmol) were added and stirred for 1 h at room temperature. The mixture was washed with water (5x), dried over $MgSO_4$ and concentrated under reduced pressure to yield pure (±)-**212** (7.74 g, 40.7 mmol, 94%) as a yellow solid: **mp** 63.3 – 64.7 °C; $\mathbf{R_f}$ = 0.45 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 5.98 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.81 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.00 (s, 1H), 3.96 – 3.80 (m, 2H), 3.19 – 3.11 (m, 2H), 3.05 – 2.96 (m, 1H), 2.89 (dd, *J* = 6.2, 4.6 Hz, 1H), 1.69 (dt, *J* = 8.5, 1.6 Hz, 1H), 1.50 – 1.45 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 206.4 (C_q), 189.8 (C_q), 133.9 (+), 131.9 (+), 107.0 (+), 67.4 (-), 52.1 (-), 50.9 (+), 46.6 (+), 43.8 (+), 43.5 (+), 14.1 (+); **IR** (ν/cm^{-1}): 3078, 3060, 2984, 2952, 2929, 2879, 1663, 1588, 1490, 1443, 1390, 1372, 1339, 1289, 1237, 1222, 1189, 1130, 1088, 1056, 1021, 985, 834, 779, 732, 655, 600; **HRMS** (APCI) *m/z* calculated for $C_{12}H_{15}O_2$ [MH^+]: 191.1067, found: 191.1070.

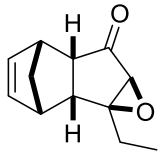
3-Ethyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-213):



Magnesium shavings (194 mg, 8.00 mmol) were suspended in dry Et_2O (15 mL) and a catalytic amount iodine was added. Bromoethane (0.72 mL; 9.60 mmol) was dissolved in dry Et_2O (10 mL) and added dropwise to the suspension. When the suspension stopped boiling it was refluxed for 1 h and afterwards cooled down to 0 °C. A solution of (±)-**212** (4 mmol) in dry Et_2O (25 mL) was slowly dropped into the suspension and stirred for 20 h at room temperature.

The reaction was quenched with HCl solution (25 mL, 1 M) and the phases were separated. The water phase was extracted with Et_2O (3x) and the combined organic layers were washed successively with sat. $NaHCO_3$ solution, brine and water and dried over $MgSO_4$. The crude product was purified via flash chromatography (silica, PE/EA = 10:1) yielding a yellowish oil (569 mg, 3.27 mmol, 82%): **R_f** = 0.24 (PE/EA = 10:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 5.97 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.75 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.73 – 5.64 (m, 1H), 3.25 (t, *J* = 4.9 Hz, 1H), 3.20 – 3.14 (m, 1H), 3.01 – 2.96 (m, 1H), 2.84 (t, *J* = 5.2 Hz, 1H), 2.27 (q, *J* = 7.5 Hz, 2H), 1.74 (dt, *J* = 8.4, 1.7 Hz, 1H), 1.59 – 1.55 (m, 1H), 1.12 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.1 (C_q), 184.0 (C_q), 133.5 (+), 131.7 (+), 131.0 (+), 52.4 (-), 51.4 (+), 50.0 (+), 44.2 (+), 43.6 (+), 25.6 (-), 11.3 (+); **IR** (ν/cm^{-1}): 3064, 2971, 2940, 2878, 1685, 1607, 1461, 1420, 1372, 1338, 1297, 1178, 1122, 1092, 910, 869, 783, 731; **HRMS** (EI) *m/z* calculated for $C_{12}H_{14}O$ [$M^{+\cdot}$]: 174.10392, found: 174.103660.

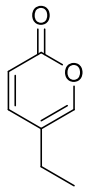
1a-Ethyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-214):



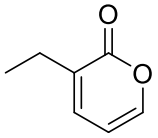
According to general procedure 6 (±)-**213** (348 mg, 2.00 mmol), 2 M NaOH (1.2 mL, 2.4 mmol) and H_2O_2 (1.1 mL, 30% in water, 10.8 mmol) were used and stirred for 24 h to afford a yellowish oil (374 mg, 1.97 mmol, 98%): **R_f** = 0.62 (PE/EA = 10:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.15 – 5.97 (m, 2H), 3.23 – 3.16 (m, 1H), 3.11 – 2.98 (m, 3H), 2.85 (dd, *J* = 6.7, 4.9 Hz, 1H), 2.10 – 1.96 (m, 1H), 1.69 – 1.55 (m, 2H), 1.49 – 1.42 (m, 1H), 1.01 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 210.6 (C_q), 136.4 (+), 133.1 (+), 71.7 (C_q), 63.4 (+), 51.7 (-), 50.4 (+), 46.1 (+), 45.4 (+), 43.5 (+), 23.0 (-), 8.9 (+); **IR** (ν/cm^{-1}): 3064, 2974, 2941, 2870, 1737, 1461, 1398, 1338, 1282, 1234, 1182, 1126, 1092,

999, 939, 910, 857, 775, 712, 678; **HRMS** (EI) *m/z* calculated for $C_{12}H_{14}O_2$ [$M^{+\cdot}$]: 190.9883, found: 190.09964.

5-Ethyl-2H-pyran-2-one (215):[147]



3-Ethyl-2H-pyran-2-one (216):[63]

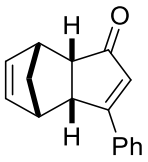


Following general procedure 1 (±)-**214** (190 mg, 1.0 mmol) was used. Purification of the crude product via flash chromatography (silica, PE/EA = 5:1) gave rise to **215** (26 mg, 0.21 mmol, 21%) and **216** (57 mg, 0.46 mmol, 46%) as colorless oils:

215: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.27 – 7.21 (m, 2H), 6.31 (dd, *J* = 8.8, 2.0 Hz, 1H), 2.33 (q, *J* = 7.5 Hz, 2H), 1.15 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 162.1 (C_q), 147.4 (+), 145.3 (+), 120.7 (C_q), 116.4 (+), 22.6 (-), 13.8 (+).

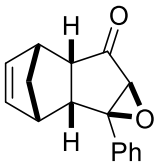
216: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.36 – 7.30 (m, 1H), 7.07 – 7.01 (m, 1H), 6.12 (dd, *J* = 6.5, 5.2 Hz, 1H), 2.44 (q, *J* = 7.4 Hz, 2H), 1.13 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 163.0 (C_q), 149.1 (+), 136.9 (+), 131.9 (C_q), 106.2 (+), 23.7 (-), 12.1 (+).

3-Phenyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-224):[114]



Under nitrogen atmosphere (±)-**212** (2.09 g, 11.0 mmol) was dissolved in dry Et_2O (30 mL). The reaction mixture was cooled to 0 °C, PhLi (12.2 mL, 1.8 M in dibutyl ether, 22.0 mmol) was added dropwise and stirred for 6 h at room temperature. An ice-cold sulphuric acid solution (20 mL, 10%) was added and the mixture was stirred vigorously for 1 h. The aqueous layer was extracted with DCM (3x) and the combined organic layers were washed successively with sat. $NaHCO_3$ solution, brine and water and were dried over $MgSO_4$. The crude product was purified via flash chromatography (silica, PE/EA = 5:1) yielding a yellowish solid (2.29 g, 10.3 mmol, 94%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.69 – 7.62 (m, 2H), 7.51 – 7.40 (m, 3H), 6.32 (s, 1H), 6.03 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.64 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.88 – 3.82 (m, 1H), 3.32 – 3.24 (m, 1H), 3.21 – 3.15 (m, 1H), 3.05 (t, *J* = 5.2 Hz, 1H), 1.79 (dt, *J* = 8.4, 1.5 Hz, 1H), 1.71 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 209.5 (C_q), 173.9 (C_q), 133.7 (C_q), 133.5 (+), 132.1 (+), 131.1 (+), 129.8 (+), 128.9 (+), 127.1 (+), 52.2 (-), 52.0 (+), 47.5 (+), 44.8 (+), 44.3 (+).

1a-Phenyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-225):



According to general procedure 6 (±)-**224** (445 mg, 2.00 mmol), 2 M NaOH (1.2 mL, 2.40 mmol) and H_2O_2 (1.1 mL, 30% in water, 10.8 mmol) were used and stirred for 24 h to afford a yellow oil (451 mg, 1.89 mmol, 95%): $\mathbf{R_f}$ = 0.67 (PE/EA = 5:1): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.46 – 7.37 (m, 5H), 6.09 (dd, *J* = 5.7, 2.9 Hz, 1H), 5.89 (dd,

J = 5.7, 2.9 Hz, 1H), 3.68 (d, *J* = 1.0 Hz, 1H), 3.54 (ddd, *J* = 7.1, 4.0, 0.9 Hz, 1H), 3.33 – 3.21 (m, 1H), 3.02 (dd, *J* = 7.1, 4.9 Hz, 1H), 2.96 – 2.84 (m, 1H), 1.61 (dt, *J* = 1.8, 8.6 Hz, 1H), 1.54 – 1.48 (m, *J* = 8.6 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 209.6 (C_q), 135.8 (+), 133.8 (C_q), 133.6 (+) 129.3 (+), 128.8 (+), 128.2 (+), 71.7 (C_q), 63.5 (+), 51.7 (-), 50.9 (+), 47.5 (+), 45.8 (+), 44.3 (+); **IR** (ν/cm^{-1}): 3064, 2982, 2941, 2870, 1737, 1498, 1450, 1398, 1339, 1256, 1230, 1178, 1074, 1029, 969, 936, 861, 768, 697; **HRMS** (EI) *m/z* calculated for $C_{16}H_{14}O_2$ [$M^{+\cdot}$]: 238.09883, found: 238.09871.

3 Synthesis of γ-alkylidenebutenolides

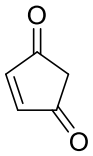
General Procedure 1: Flash Vacuum Thermolysis: For flash vacuum thermolysis a high-quality glass tube (length 90 cm, diameter 1 cm) open at both ends was fixed horizontally in a tube furnace connected to a cooling trap and a flask containing the epoxide. The tube furnace was heated to 650 °C and connected to a high-vacuum line at $2 \cdot 10^{-2}$ mbar. The starting material was slowly evaporated through the tube furnace, and the product was collected in a trap cooled with liquid nitrogen. The product was washed off the cooling trap with DCM, the solvent was removed, and the product was dried under reduced pressure. The crude product was purified via flash chromatography by an appropriate PE/EA mixture.

General Procedure 2: Esterification using acetic anhydride: The Diels-Alder adduct (1.0 equiv) was dissolved in Ac_2O (2.5 M) and stirred for 20 h at 50 °C. The reaction mixture was dried under reduced pressure to yield the pure product.

General Procedure 3: Esterification of (±)-**211 to** (±)-**240:** To a solution of (±)-**211** (4.0 mmol) in DCM (16 mL) Et_3N (0.8 mL, 5.8 mmol), and a solution of the acyl chloride (4.8 mmol) in DCM (16 mL) was added dropwise. The reaction mixture was stirred for 15 h at

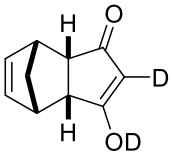
room temperature. The reaction was diluted with DCM (40 mL) and washed (1x) with sat. $KHSO_4$ solution (100 mL). The organic phase was dried over $MgSO_4$.

Cyclopent-4-ene-1,3-dione (234):[120]



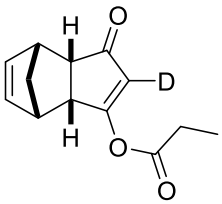
To a solution of (±)-**150** (9.81 g, 0.10 mol) in DCM (100 mL) TEMPO-OH (861 mg, 5.00 mmol), $FeCl_3 \cdot 6H_2O$ (1.35 g, 5.0 mmol), and $NaNO_2$ (207 mg, 3.0 mmol) were added and stirred for 24 h at room temperature under oxygen atmosphere (1 atm). The reaction mixture was washed with water, and the aqueous phase was extracted with DCM (3x). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure to yield pure **234** (6.64 g, 69 mmol, 69%) as a yellow solid: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.30 (s, 2H), 2.89 (s, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 200.71 (C_q), 150.55 (+), 41.54 (-).

3-(Hydroxy-d)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one-2-d ((±)-244):



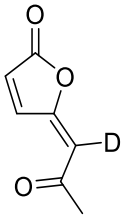
A solution of dione **234** (480 mg, 5.00 mmol) in D_2O (5 mL) was stirred at room temperature. After 4 h cyclopentadiene (4.13 mL, 50.0 mmol) was added and the reaction mixture was stirred for additional 15 h at room temperature. The formed precipitate was filtered off and was with Et_2O to obtain (±)-**244** as a white solid (617 mg, 3.78 mmol, 76%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 5.96 (s, 2H), 3.16 (s, 4H), 1.80 (d, J = 8.5 Hz, 1H), 1.59 (d, J = 8.6 Hz, 1H).

1-Oxo-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-3-yl-2-d propionate ((±)-245):

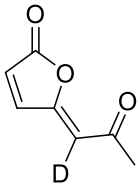


To a solution of (±)-**244** (326 mg, 2.00 mmol) in DCM (8 mL) Et_3N (0.40 mL, 2.89 mmol), and a solution of propionyl chloride (0.21 mL, 2.40 mmol) in DCM (8 mL) was added dropwise. The reaction mixture was stirred for 15 h at room temperature. The reaction was diluted with DCM (40 mL) and washed (1x) with sat. $KHSO_4$ solution (100 mL). The organic phase was dried over $MgSO_4$ to afford a brownish oil (397 mg, 1.81 mmol, 91%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.05 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.87 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.40 (dd, *J* = 6.0, 4.3 Hz, 1H), 3.25 – 3.19 (m, 1H), 3.07 – 3.01 (m, 1H), 2.92 (dd, *J* = 5.9, 4.8 Hz, 1H), 2.55 (q, *J* = 7.5 Hz, 2H), 1.78 (dt, *J* = 8.5, 1.7 Hz, 1H), 1.59 – 1.55 (m, 1H), 1.22 (t, *J* = 7.5 Hz, 3H).

(*E*)-5-(2-Oxopropylidene-1-d)furan-2(5H)-one (246):



(*Z*)-5-(2-Oxopropylidene-1-d)furan-2(5H)-one (247):



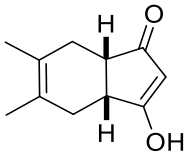
Following general procedure 1 (±)-**245** (219 mg, 1.00 mmol) was used. Purification of the crude product via flash chromatography (silica, PE/EA = 2:1) gave rise to *E* isomer **246**

(24 mg, 0.16 mmol, 16%) and *Z* isomer **247** (13 mg, 0.09 mmol, 9%) as yellow solid compounds:

E isomer **246**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.37 (d, J = 5.6 Hz, 1H), 6.51 (d, J = 5.6 Hz, 1H), 2.67 (q, J = 7.3 Hz, 2H), 1.18 (t, J = 7.3 Hz, 3H).

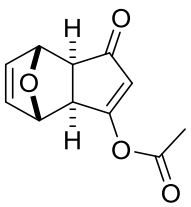
Z isomer **247**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.54 (d, *J* = 5.5 Hz, 1H), 6.48 (d, *J* = 5.5 Hz, 1H), 2.99 (q, *J* = 7.2 Hz, 2H), 1.18 (t, *J* = 7.2 Hz, 3H).

3-Hydroxy-5,6-dimethyl-3a,4,7,7a-tetrahydro-1*H*-inden-1-one ((±)-256):



Dione **234** (288 mg, 3.00 mmol) was dissolved in 2,3-Dimethyl-1,3-butadiene (3.00 mL, 26.4 mmol) and stirred for 3 d at room temperature. The formed precipitated was filtered off and washed with Et_2O (3x) to yield (±)-**256** (372 mg, 2.09 mmol, 70%) as a white solid: **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H = 12.57 – 12.30 (bs, 1H), 5.20 (s, 1H), 2.85 (s, 2H), 2.29 – 2.14 (m, 4H), 1.63 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ_C = 204.3 (C_q), 126.1 (C_q), 106.5 (+), 43.2 (+), 31.2 (-), 19.2 (+).

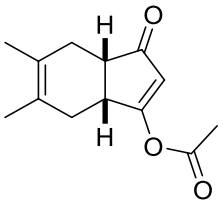
1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-epoxyinden-3-yl acetate ((±)-257):



Following general procedure 2 (±)-**209** (1.31 g, 8.00 mmol) was used to give a brown solid (1.56 g, 7.56 mmol, 95%): **mp** 132.1 – 132.6 °C; **R_f** = 0.25 (PE/EA = 2:1);

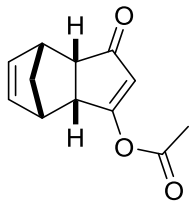
^{1}H NMR (300 MHz, $CDCl_3$) δ_H = 6.49 (dd, *J* = 5.8, 1.6 Hz, 1H), 6.46 (dd, *J* = 5.8, 1.5 Hz, 1H), 6.26 (d, *J* = 0.7 Hz, 1H), 5.05 (d, *J* = 1.1 Hz, 1H), 4.95 (d, *J* = 1.1 Hz, 1H), 2.97 (dd, *J* = 5.3, 0.6 Hz, 1H), 2.51 (d, *J* = 5.3 Hz, 1H), 2.31 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 204.5 (C_q), 177.2 (C_q), 166.1 (C_q), 136.5 (+), 136.3 (+), 119.3 (+), 80.1 (+), 77.9 (+), 50.7 (+), 48.8 (+), 21.5 (+); **IR** (ν/cm^{-1}): 3101, 3002, 1784, 1691, 1592, 1425, 1381, 1339, 1301, 1283, 1197, 1183, 1154, 1089, 1048, 1012, 960, 933, 907, 885, 860, 830, 813, 719, 683, 585; **HRMS** (APCI) *m/z* calculated for $C_{11}H_{11}O_4$ [MH^+]: 207.0652, found: 207.0653.

5,6-Dimethyl-1-oxo-3a,4,7,7a-tetrahydro-1*H*-inden-3-yl acetate ((±)-258):



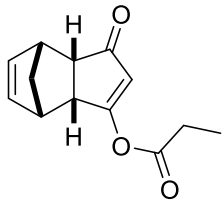
Following general procedure 2 (±)-**256** (357 mg, 2.00 mmol) was used to give an brownish oil (440 mg, 2.00 mmol, 100%): **R_f** = 0.64 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.21 (d, *J* = 1.2 Hz, 1H), 3.20 – 3.13 (m, 1H), 2.65 – 2.58 (m, 1H), 2.29 (s, 3H), 2.28 – 2.07 (m, 4H), 1.64 (d, *J* = 0.7 Hz, 3H), 1.61 (d, *J* = 0.7 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 209.1 (C_q), 179.9 (C_q), 166.4 (C_q), 127.4 (C_q), 124.8 (C_q), 117.4 (+), 44.1 (+), 40.9 (+), 31.3 (-), 30.9 (-), 21.4 (+), 19.29 (+), 19.26 (+); **IR** (ν/cm^{-1}): 2978, 2938, 2858, 1789, 1744, 1699, 1589, 1436, 1370, 1352, 1300, 1183, 1138, 1074, 1007, 843, 701, 609, 579, 558, 451; **HRMS** (APCI) *m/z* calculated for $C_{13}H_{17}O_3$ [MH^+]: 221.1172, found: 221.1172.

1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl acetate ((±)-240a):[125]



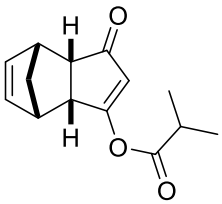
Following general procedure 2 (±)-**211** (1.30 g, 8.00 mmol) was used to give an orange solid (1.63 g, 7.97 mmol, 100%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.05 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.97 (s, 1H), 5.87 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.43 – 3.37 (m, 1H), 3.25 – 3.19 (m, 1H), 3.07 – 3.02 (m, 1H), 2.92 (dd, *J* = 6.0, 4.7 Hz, 1H), 2.26 (s, 3H), 1.78 (dt, *J* = 8.5, 1.6 Hz, 1H), 1.60 – 1.55 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.1 (C_q), 179.1 (C_q), 166.3 (C_q), 134.0 (+), 131.9 (+), 118.7 (+), 52.3 (-), 50.0 (+), 47.0 (+), 44.1 (+), 43.5 (+), 21.5 (+).

1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl propionate ((±)-240b):



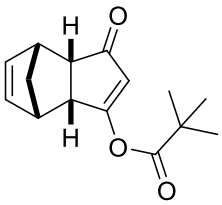
According to general procedure 3 propionyl chloride (0.42 mL, 4.80 mmol) was used to afford a yellowish oil (854 mg, 3.91 mmol, 98%): **R_f** = 0.48 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.04 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.97 (s, 1H), 5.86 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.43 – 3.37 (m, 1H), 3.24 – 3.18 (m, 1H), 3.06 – 3.00 (m, 1H), 2.91 (dd, *J* = 6.0, 4.7 Hz, 1H), 2.54 (q, *J* = 7.5 Hz, 2H), 1.77 (dt, *J* = 8.5, 1.6 Hz, 1H), 1.59 – 1.54 (m, 1H), 1.21 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.2 (C_q), 179.3 (C_q), 170.0 (C_q), 134.0 (+), 131.9 (+), 118.5 (+), 52.3 (-), 49.9 (+), 47.0 (+), 44.1 (+), 43.5 (+), 28.0 (+), 8.6 (+); **IR** (ν/cm^{-1}): 2985, 2943, 2883, 1781, 1735, 1696, 1586, 1462, 1418, 1333, 1282, 1190, 1146, 1099, 1068, 1007, 971, 951, 857, 830, 778, 733; **HRMS** (APCI) *m/z* calculated for $C_{13}H_{15}O_3$ [MH^+]: 219.1016, found: 219.1017.

1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl isobutyrate ((±)-240c):



According to general procedure 3 isobutyryl chloride (0.51 mL, 4.80 mmol) was used to afford a brownish oil (926 mg, 3.99 mmol, 100%): $\mathbf{R_f}$ = 0.76 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.02 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.94 (s, 1H), 5.84 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.44 – 3.38 (m, 1H), 3.23 – 3.17 (m, 1H), 3.04 – 2.99 (m, 1H), 2.90 (dd, *J* = 6.0, 4.7 Hz, 1H), 2.72 (hept, *J* = 7.0 Hz, 1H), 1.75 (dt, *J* = 8.5, 1.5 Hz, 1H), 1.60 – 1.51 (m, 1H), 1.24 (d, *J* = 7.0 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.3 (C_q), 179.6 (C_q), 172.5 (C_q), 133.9 (+), 131.9 (+), 118.4 (+), 52.3 (-), 49.9 (+), 47.0 (+), 44.1 (+), 43.4 (+), 34.5 (+), 18.60 (+), 18.55 (+); **IR** (ν/cm^{-1}): 2979, 2940, 2878, 1775, 1696, 1591, 1469, 1389, 1332, 1281, 1191, 1148, 1124, 1063, 898, 862, 816, 777, 731, 660; **HRMS** (APCI) *m/z* calculated for $C_{14}H_{17}O_3$ [MH^+]: 233.1172, found: 233.1173.

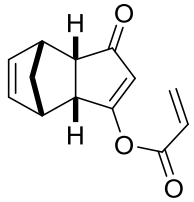
1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl pivalate ((±)-240d):



According to general procedure 3 pivaloyl chloride (0.59 mL, 4.80 mmol) was used to afford a brownish oil (984 mg, 3.99 mmol, 100%): $\mathbf{R_f}$ = 0.65 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 5.98 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.89 (s, 1H), 5.79 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.43 – 3.35 (m, 1H), 3.20 – 3.12 (m, 1H), 3.02 – 2.93 (m, 1H), 2.86 (dd, *J* = 6.0, 4.7 Hz, 1H), 1.72 (dt, *J* = 8.5, 1.6 Hz, 1H), 1.55 – 1.49 (m, 1H), 1.23 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.1 (C_q), 179.7 (C_q), 173.9 (C_q), 134.0 (+), 131.9 (+), 118.4

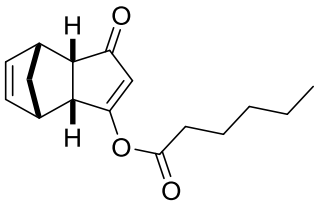
(+), 52.3 (-), 49.9 (+), 46.9 (+), 44.1 (+), 43.4 (+), 39.7 (C_q), 26.8 (+); **IR** (ν/cm^{-1}): 2977, 2938, 2874, 1771, 1699, 1591, 1480, 1462, 1399, 1334, 1269, 1150, 1125, 1069, 1026, 861, 777, 731, 667; **HRMS** (APCI) *m/z* calculated for $C_{15}H_{19}O_3$ [MH$^+$]: 247.1329, found: 247.1324.

1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl acrylate ((±)-240e):



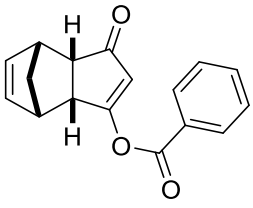
According to general procedure 3 acryloyl chloride (0.39 mL, 4.80 mmol) was used. Further purification via flash chromatography (silica, PE/EA = 3:1) yielded a yellowish solid (862 mg, 3.99 mmol, 100%): **mp** 54.1 – 55.3 °C; **R*f*** = 0.43 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.60 (dd, *J* = 17.1, 1.2 Hz, 1H), 6.28 – 6.17 (m, 1H), 6.13 – 5.99 (m, 3H), 5.88 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.50 – 3.43 (m, 1H), 3.26 – 3.21 (m, 1H), 3.10 – 3.04 (m, 1H), 2.95 (dd, *J* = 6.0, 4.7 Hz, 1H), 1.79 (dt, *J* = 8.6, 1.6 Hz, 1H), 1.61 – 1.56 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.1 (C_q), 179.1 (C_q), 161.4 (C_q), 134.6 (-), 134.0 (+), 131.9 (+), 126.9 (+), 118.8 (+), 52.3 (-), 50.0 (+), 47.0 (+), 44.1 (+), 43.5 (+); **IR** (ν/cm^{-1}): 3107, 3060, 2978, 2949, 2876, 1758, 1683, 1576, 1409, 1348, 1334, 1300, 1284, 1216, 1194, 1152, 1106, 1065, 1014, 983, 869, 819, 802, 775, 733, 663; **HRMS** (APCI) *m/z* calculated for $C_{13}H_{13}O_3$ [MH$^+$]: 217.0859, found: 217.0859.

1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl hexanoate ((±)-240f):



According to general procedure 3 hexanoyl chloride (0.67 mL, 4.80 mmol) was used. Further purification via flash chromatography (silica, PE/EA = 3:1) yielded a yellowish oil (979 mg, 3.76 mmol, 94%): $\mathbf{R_f}$ = 0.59 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 6.05 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.97 (s, 1H), 5.86 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.44 – 3.37 (m, 1H), 3.25 – 3.19 (m, 1H), 3.06 – 3.00 (m, 1H), 2.92 (dd, *J* = 6.0, 4.7 Hz, 1H), 2.50 (t, *J* = 7.4 Hz, 2H), 1.77 (dt, *J* = 8.5, 1.6 Hz, 1H), 1.72 – 1.64 (m, 2H), 1.59 – 1.54 (m, 1H), 1.37 – 1.30 (m, 4H), 0.92 (t, *J* = 6.7 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.2 (C_q), 179.3 (C_q), 169.3 (C_q), 134.0 (+), 131.9 (+), 118.6 (+), 52.3 (-), 49.9 (+), 47.0 (+), 44.1 (+), 43.5 (+), 34.6 (-), 31.1 (-), 24.2 (-), 22.3 (-), 13.9 (+); **IR** (ν/cm^{-1}): 2958, 2935, 2872, 1781, 1698, 1591, 1459, 1414, 1334, 1281, 1246, 1191, 1145, 1124, 1078, 861, 778, 731, 662; **HRMS** (APCI) *m/z* calculated for $C_{16}H_{21}O_3$ [MH^+]: 261.1485, found: 261.1486.

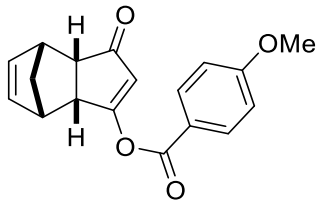
1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl benzoate ((±)-240g):



According to general procedure 3 benzoyl chloride (0.55 mL, 4.80 mmol) was used. Further purification via flash chromatography (silica, PE/EA = 3:1) yielded a white solid (967 mg, 3.63 mmol, 91%): **mp** 107.2 – 108.9 °C; $\mathbf{R_f}$ = 0.35 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.17 – 8.07 (m, 2H), 7.73 – 7.62 (m, 1H), 7.58 – 7.48 (m, 2H), 6.14 (s, 1H), 6.09 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.93 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.66 – 3.54 (m, 1H), 3.33 – 3.22 (m, 1H),

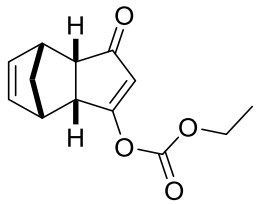
3.20 – 3.11 (m, 1H), 3.00 (dd, *J* = 5.9, 4.7 Hz, 1H), 1.86 – 1.77 (m, 1H), 1.68 – 1.59 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.1 (C_q), 179.4 (C_q), 162.1 (C_q), 134.5 (+), 134.0 (+), 132.0 (+), 130.4 (+), 128.9 (+), 128.3 (C_q), 118.8 (+), 52.4 (-), 50.1 (+), 47.1 (+), 44.2 (+), 43.6 (+); **IR** (ν/cm^{-1}): 3060, 2987, 2947, 1759, 1679, 1582, 1452, 1340, 1233, 1143, 1054, 1040, 1019, 969, 861, 846, 819, 778, 737, 700, 666; **HRMS** (APCI) *m/z* calculated for $C_{17}H_{15}O_3$ [MH$^+$]: 267.1016, found: 267.1017.

1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl 4-methoxybenzoate ((±)-240h):



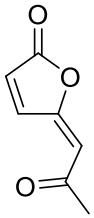
According to general procedure 3 4-methoxybenzoyl chloride (0.82 mL, 4.80 mmol) was used. Further purification via flash chromatography (silica, PE/EA = 2:1) yielded a white solid (1.13 g, 3.82 mmol, 96%): **mp** 136.7 – 138.0 °C; **R_f** = 0.66 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.09 – 8.03 (m, 2H), 7.01 – 6.96 (m, 2H), 6.11 (s, 1H), 6.08 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.92 (dd, *J* = 5.6, 2.9 Hz, 1H), 3.90 (s, 3H), 3.60 – 3.54 (m, 1H), 3.29 – 3.23 (m, 1H), 3.16 – 3.11 (m, 1H), 2.98 (dd, *J* = 5.8, 4.8 Hz, 1H), 1.84 – 1.77 (m, 1H), 1.64 – 1.61 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.2 (C_q), 179.7 (C_q), 164.6 (C_q), 161.8 (C_q), 134.0 (+), 132.6 (+), 132.0 (+), 120.4 (C_q), 118.5 (+), 114.2 (+), 55.7 (+), 52.4 (-), 50.1 (+), 47.2 (+), 44.2 (+), 43.6 (+); **IR** (ν/cm^{-1}): 2981, 2940, 2845, 1743, 1677, 1605, 1585, 1510, 1466, 1452, 1345, 1318, 1241, 1190, 1166, 1142, 1103, 1040, 1020, 971, 932, 907, 844, 761, 734, 693, 661; **HRMS** (ESI) *m/z* calculated for $C_{18}H_{17}O_4$ [MH$^+$]: 297.1121, found: 297.1126.

Ethyl (1-oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl) carbonate ((±)-240i):

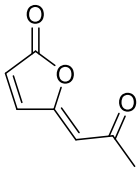


To a solution of (±)-**211** (324 mg, 2.00 mmol) in DCM (8 mL) Et_3N (0.40 mL, 2.89 mmol), and a solution of ethyl chloroformate (0.23 mL, 2.40 mmol) in DCM (8 mL) was added dropwise. The reaction mixture was stirred for 15 h at room temperature. The reaction was diluted with DCM (20 mL) and washed (1x) with sat. $KHSO_4$ solution (50 mL). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to yield (±)-**240i** (466 mg, 1.99 mmol, 100%) as a yellowish oil: $\mathbf{R_f}$ = 0.45 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 5.99 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.91 (s, 1H), 5.85 (dd, *J* = 5.6, 2.9 Hz, 1H), 4.26 (qd, *J* = 7.1, 0.6 Hz, 2H), 3.39 – 3.32 (m, 1H), 3.19 – 3.13 (m, 1H), 3.05 – 3.00 (m, 1H), 2.89 (dd, *J* = 6.0, 4.7 Hz, 1H), 1.72 (dt, *J* = 8.5, 1.5 Hz, 1H), 1.54 – 1.48 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 206.5 (C_q), 179.6 (C_q), 150.3 (C_q), 133.9 (+), 132.0 (+), 117.6 (+), 65.7 (-), 52.3 (-), 50.4 (+), 46.6 (+), 44.1 (+), 43.5 (+), 14.0 (+); **IR** (ν/cm^{-1}): 2984, 2942, 2872, 1775, 1698, 1599, 1337, 1209, 1153, 1124, 1094, 1043, 994, 951, 885, 861, 829, 778, 732, 654; **HRMS** (APCI) *m/z* calculated for $C_{13}H_{15}O_4$ [MH^+]: 235.0965, found: 235.0970.

(*E*)-5-(2-Oxopropylidene)furan-2(5*H*)-one (241a):[129]



(*Z*)-5-(2-Oxopropylidene)furan-2(5*H*)-one (242a):[129]

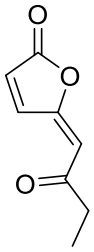


Following general procedure 1 (±)-**240a** (817 mg, 4.00 mmol) was used. Purification of the crude via flash chromatography (silica, PE/EA = 2:1) gave rise to *E* isomer **241a** (118 mg, 0.85 mmol, 21%) and *Z* isomer **242a** (71 mg, 0.51 mmol, 13%) as yellow solid compounds:

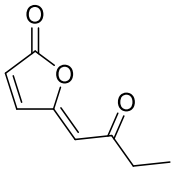
E isomer **241a**: **mp** 90.3 – 92.8 °C; $\mathbf{R_f}$ = 0.60 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.30 (dd, *J* = 5.6, 0.6 Hz, 1H), 6.48 (dd, *J* = 5.6, 1.8 Hz, 1H), 6.25 (d, *J* = 1.5 Hz, 1H), 2.35 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 197.1 (C_q), 168.0 (C_q), 158.7 (C_q), 142.8 (+), 125.3 (+), 108.0 (+), 32.3 (+); **IR** (ν/cm^{-1}): 3151, 3122, 3077, 3051, 1787, 1770, 1683, 1611, 1550, 1484, 1422, 1385, 1356, 1300, 1242, 1172, 1093, 1057, 1020, 952, 892, 839, 742, 710, 575; **HRMS** (APCI) *m/z* calculated for $C_7H_7O_3$ [MH^+]: 139.0390, found: 139.0393.

Z isomer **242a**: **mp** 75.9 – 78.6 °C; $\mathbf{R_f}$ = 0.33 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.50 (d, *J* = 5.5 Hz, 1H), 6.46 (dd, *J* = 5.5, 0.7 Hz, 1H), 5.56 (s, 1H), 2.57 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 196.5 (C_q), 167.7 (C_q), 155.1 (C_q), 145.6 (+), 123.5 (+), 110.9 (+), 31.3 (+); **IR** (ν/cm^{-1}): 3142, 3016, 3083, 3007, 1770, 1696, 1632, 1561, 1425, 1374, 1355, 1236, 1175, 1097, 1074, 1020, 990, 929, 908, 861, 837, 763, 740, 684, 571; **HRMS** (APCI) *m/z* calculated for $C_7H_7O_3$ [MH^+]: 139.0390, found: 139.0394.

(*E*)-5-(2-Oxobutylidene)furan-2(5*H*)-one (241b):



(*Z*)-5-(2-Oxobutylidene)furan-2(5*H*)-one (242b):



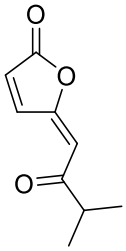
Following general procedure 1 (±)-**240b** (218 mg, 1.00 mmol) was used. Purification of the crude via flash chromatography (silica, PE/EA = 2:1) gave rise to *E* isomer **241b** (36 mg, 0.24 mmol, 24%) and *Z* isomer **242b** (15 mg, 0.10 mmol, 10%) as yellow solid compounds:

E isomer **241b**: **mp** 112.2 – 114.6 °C; $\mathbf{R_f}$ = 0.72 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.31 (dd, *J* = 5.6, 0.7 Hz, 1H), 6.46 (dd, *J* = 5.6, 1.8 Hz, 1H), 6.23 (dd, *J* = 1.7, 0.7 Hz, 1H), 2.62 (q, *J* = 7.3 Hz, 2H), 1.12 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 200.1 (C_q), 168.1 (C_q), 158.5 (C_q), 142.8 (+), 125.1 (+), 107.6 (+), 38.4 (-), 7.8 (+); **IR** (ν/cm^{-1}): 3113, 2981, 2942, 2883, 1828, 1766, 1713, 1624, 1600, 1459, 1407, 1368, 1245, 1201, 1149, 1118, 1090, 1032, 1015, 915, 888, 842, 813; **HRMS** (APCI) *m/z* calculated for $C_8H_9O_3$ [MH^+]: 153.0546, found: 153.0549.

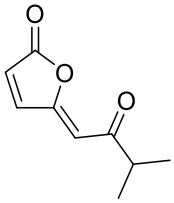
Z isomer **242b**: **mp** 77.0 – 78.6 °C; $\mathbf{R_f}$ = 0.41 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.53 (d, *J* = 5.5 Hz, 1H), 6.49 (dd, *J* = 5.5, 0.8 Hz, 1H), 5.62 (s, 1H), 2.99 (q, *J* = 7.2 Hz, 2H), 1.18 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 199.4 (C_q), 167.9 (C_q), 154.5 (C_q), 145.8 (+), 123.3 (+), 110.5 (+), 36.9 (-), 7.8 (+); **IR** (ν/cm^{-1}): 3143, 3111, 2982, 2943,

2894, 1818, 1773, 1721, 1698, 1632, 1562, 1459, 1409, 1369, 1341, 1260, 1160, 1127, 1096, 1051, 1014, 939, 869, 857, 828; **HRMS** (APCI) *m/z* calculated for $C_8H_9O_3$ [MH^+]: 153.0546, found: 153.0546.

(*E*)-5-(3-Methyl-2-oxobutylidene)furan-2(5*H*)-one (241c):



(*Z*)-5-(3-Methyl-2-oxobutylidene)furan-2(5*H*)-one (242c):

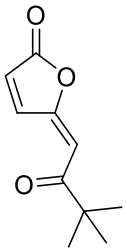


Following general procedure 1 (±)-**240c** (465 mg, 2.00 mmol) was used. Purification of the crude via flash chromatography (silica, PE/EA = 3:1) gave rise to *E* isomer **241c** (62 mg, 0.37 mmol, 19%) and *Z* isomer **242c** (27 mg, 0.16 mmol, 8%) as yellow solid compounds:

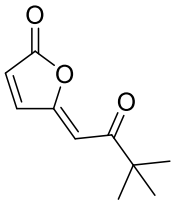
E isomer **241c**: **mp** 170.4 – 172.7 °C; $\mathbf{R_f}$ = 0.80 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.32 (dd, *J* = 5.6, 0.7 Hz, 1H), 6.47 (dd, *J* = 5.6, 1.8 Hz, 1H), 6.31 (dd, *J* = 1.7, 0.7 Hz, 1H), 2.73 (hept, *J* = 6.9 Hz, 1H), 1.16 (d, *J* = 6.9 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 203.4 (C_q), 168.1 (C_q), 159.2 (C_q), 142.9 (+), 125.0 (+), 106.8 (+), 42.5 (+), 17.9 (+); **IR** (ν/cm^{-1}): 3134, 2974, 2936, 2875, 1810, 1770, 1687, 1625, 1465, 1384, 1364, 1283, 1157, 1112, 1045, 948, 853, 828, 633; **HRMS** (APCI) *m/z* calculated for $C_9H_{11}O_3$ [MH^+]: 167.0703, found: 167.0703.

Z isomer **242c**: **mp** 107.1 – 108.9 °C; **R_f** = 0.32 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.48 (d, *J* = 5.5 Hz, 1H), 6.45 (dd, *J* = 5.5, 0.8 Hz, 1H), 5.59 (s, 1H), 3.32 (hept, *J* = 6.8 Hz, 1H), 1.16 (d, *J* = 6.9 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 202.7 (C_q), 168.1 (C_q), 153.9 (C_q), 145.8 (+), 123.3 (+), 109.4 (+), 40.3 (+), 18.3 (+); **IR** (ν/cm^{-1}): 3144, 3111, 3089, 2969, 2933, 2876, 1776, 1689, 1627, 1562, 1466, 1385, 1366, 1094, 1066, 1050, 940, 873, 835; **HRMS** (APCI) *m/z* calculated for $C_9H_{11}O_3$ [MH^+]: 167.0703, found: 167.0701.

(*E*)-5-(3,3-Dimethyl-2-oxobutylidene)furan-2(5*H*)-one (241d):



(*Z*)-5-(3,3-Dimethyl-2-oxobutylidene)furan-2(5*H*)-one (242d):



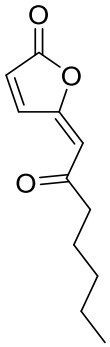
Following general procedure 1 (±)-**240d** (493 mg, 2.00 mmol) was used. Purification of the crude via flash chromatography (silica, PE/EA = 3:1) gave rise to *E* isomer **241d** (78 mg, 0.43 mmol, 22%) and *Z* isomer **242d** (46 mg, 0.26 mmol, 13%) as yellow solid compounds:

E isomer **241d**: **mp** 151.4 – 153.2 °C; **R_f** = 0.87 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.31 (dd, *J* = 5.6, 0.7 Hz, 1H), 6.51 (dd, *J* = 1.7, 0.7 Hz, 1H), 6.46 (dd, *J* = 5.6, 1.8 Hz, 1H), 1.20 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 204.8 (C_q), 168.1 (C_q), 159.7 (C_q), 142.9 (+), 125.0 (+), 104.8 (+), 44.6 (C_q), 26.1 (+); **IR** (ν/cm^{-1}): 2975, 2937, 2873, 1829, 1769, 1699,

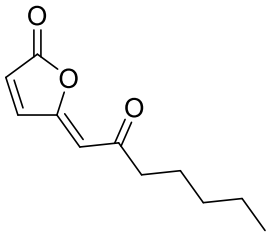
1615, 1476, 1369, 1282, 1249, 1154, 1122, 1095, 1061, 1010, 916, 852, 814, 793, 675; **HRMS** (APCI) *m/z* calculated for $C_{10}H_{13}O_3$ [MH^+]: 181.0859, found: 181.0861.

Z isomer **242d**: **mp** 192.8 – 194.6 °C; $\mathbf{R_f}$ = 0.40 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.44 (d, *J* = 5.5 Hz, 1H), 6.45 (dd, *J* = 5.5, 0.7 Hz, 1H), 6.00 (s, 1H), 1.20 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 202.4 (C_q), 168.8 (C_q), 155.0 (C_q), 145.2 (+), 123.9 (+), 104.6 (+), 44.4 (C_q), 26.1 (+); **IR** (ν/cm^{-1}): 2974, 2935, 2909, 2873, 1821, 1786, 1768, 1687, 1615, 1475, 1367, 1163, 1140, 1084, 1057, 1010, 953, 917, 857, 815, 658, 629; **HRMS** (APCI) *m/z* calculated for $C_{10}H_{13}O_3$ [MH^+]: 181.0859, found: 181.0861.

(*E*)-5-(2-Oxoheptylidene)furan-2(5*H*)-one (241f):



(*Z*)-5-(2-Oxoheptylidene)furan-2(5*H*)-one (242f):

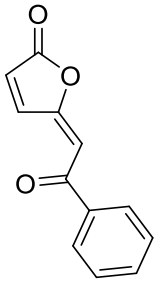


Following general procedure 1 (±)-**240f** (521 mg, 2.00 mmol) was used. Purification of the crude via flash chromatography (silica, PE/EA = 3:1) gave rise to *E* isomer **241f** (90 mg, 0.46 mmol, 23%) and Z isomer **242f** (45 mg, 0.23 mmol, 12%) as yellow solid compounds:

E isomer **241f**: **mp** 72.1 – 73.6 °C; $\mathbf{R_f}$ = 0.78 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.32 (dd, *J* = 5.6, 0.6 Hz, 1H), 6.47 (dd, *J* = 5.6, 1.7 Hz, 1H), 6.24 (d, *J* = 1.1 Hz, 1H), 2.58 (t, *J* = 7.4 Hz, 2H), 1.67 – 1.61 (m, 2H), 1.35 – 1.28 (m, 4H), 0.90 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 199.9 (C_q), 168.1 (C_q), 158.6 (C_q), 142.9 (+), 125.1 (+), 107.8 (+), 45.2 (-), 31.3 (-), 23.6 (-), 22.5 (-), 13.9 (+); **IR** (ν/cm^{-1}): 3152, 3123, 3081, 2956, 2932, 2862, 1776, 1680, 1612, 1553, 1467, 1389, 1317, 1303, 1249, 1223, 1134, 1109, 1063, 950, 892, 878, 847, 833, 745, 721, 666; **HRMS** (APCI) *m/z* calculated for $C_{11}H_{15}O_3$ [MH^+]: 195.1016, found: 195.1015.

Z isomer **242f**: **mp** 80.2 – 82.8 °C; $\mathbf{R_f}$ = 0.38 (PE/EA = 3:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.49 (d, *J* = 5.5 Hz, 1H), 6.44 (dd, *J* = 5.5, 0.7 Hz, 1H), 5.56 (s, 1H), 2.89 (t, *J* = 7.3 Hz, 2H), 1.70 – 1.58 (m, 2H), 1.37 – 1.25 (m, 4H), 0.89 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 199.1 (C_q), 167.9 (C_q), 154.3 (C_q), 145.8 (+), 123.3 (+), 110.6 (+), 43.5 (-), 31.3 (-), 23.5 (-), 22.5 (-), 14.0 (+); **IR** (ν/cm^{-1}): 3147, 3188, 3090, 2954, 2936, 2874, 1780, 1687, 1623, 1563, 1468, 1406, 1354, 1314, 1248, 1214, 1132, 1089, 936, 866, 844, 823, 765, 725, 650; **HRMS** (APCI) *m/z* calculated for $C_{11}H_{15}O_3$ [MH^+]: 195.1016, found: 195.1014.

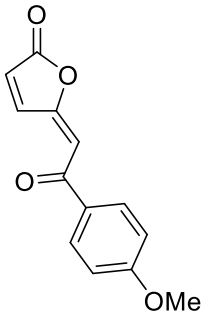
(*E*)-5-(2-Oxo-2-phenylethylidene)furan-2(5*H*)-one (241g):



Following general procedure 1 (±)-**240g** (266 mg, 1.00 mmol) was used. Purification of the crude via flash chromatography (silica, PE/EA = 5:1) gave rise to *E* isomer **241g**

(61 mg, 0.31 mmol, 31%) as a yellow solid: **mp** 157.6 – 159.3 °C; **R_f** = 0.44 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.43 (dd, *J* = 5.6, 0.7 Hz, 1H), 7.99 – 7.94 (m, 2H), 7.68 – 7.59 (m, 1H), 7.56 – 7.49 (m, 2H), 7.03 (dd, *J* = 1.7, 0.7 Hz, 1H), 6.54 (dd, *J* = 5.6, 1.7 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 189.3 (C_q), 168.9 (C_q), 160.4 (C_q), 143.1 (+), 137.9 (C_q), 133.8 (+), 128.9 (+), 128.3 (+), 125.3 (+), 105.6 (+); **IR** (ν/cm^{-1}): 3154, 3123, 3083, 3040, 1789, 1769, 1660, 1605, 1578, 1555, 1448, 1390, 1300, 1264, 1199, 1096, 1063, 1038, 1025, 1000, 909, 889, 852, 828, 781, 734, 694, 646; **HRMS** (APCI) *m/z* calculated for $C_{12}H_9O_3$ [MH^+]: 201.0546, found: 201.0551.

(*E*)-5-(2-(4-Methoxyphenyl)-2-oxoethylidene)furan-2(5*H*)-one (241h):



Following general procedure 1 (±)-**240h** (593 mg, 2.00 mmol) was used. Purification of the crude via flash chromatography (silica, PE/EA = 3:1) gave rise to *E* isomer **241h** (164 mg, 0.70 mmol, 35%) as a yellow solid: **mp** 180.7 – 182.4 °C; **R_f** = 0.71 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 8.43 (dd, *J* = 5.6, 0.7 Hz, 1H), 7.99 – 7.94 (m, 2H), 7.01 – 6.96 (m, 3H), 6.51 (dd, *J* = 5.6, 1.7 Hz, 1H), 3.90 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 187.5 (C_q), 168.1 (C_q), 164.1 (C_q), 159.9 (C_q), 143.2 (+), 131.0 (C_q), 130.8 (+) 124.9 (+), 114.1 (+), 105.8 (+), 55.6 (+); **IR** (ν/cm^{-1}): 3146, 3121, 3077, 2984, 2942, 2847, 1790, 1767, 1661, 1607, 1571, 1549, 1422, 1389, 1300, 1253, 1193, 1175, 1102, 1062, 1040, 1016, 912, 892, 831, 816, 732, 682, 607; **HRMS** (APCI) *m/z* calculated for $C_{13}H_{11}O_4$ [MH^+]: 231.0652, found: 231.0654.

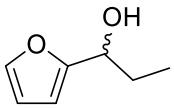
4 Redox isomerization of 4-hydroxy-2-cyclopentenone derivatives

General Procedure 1: Grignard reaction of 140 to (±)-**142:** Magnesium shavings (1.3 equiv) were suspended in dry Et_2O (2.50 M), and a catalytic amount iodine was added. The bromide (1.6 equiv) was dissolved in dry Et_2O (1.25 M) and added dropwise to the suspension. When the suspension stopped boiling it was refluxed for 1 h and afterward cooled down to 0 °C. A solution of furfural (**140**) (1.0 equiv) in dry Et_2O (1.25 M) was slowly dropped into the suspension and stirred for 15 min. The reaction was quenched with water, and the phases were separated. The water phase was extracted with Et_2O (3x), and the combined organic layers were dried over $MgSO_4$. The crude was purified via flash chromatography (silica, PE/EA = 5:1).

General Procedure 2: Piancatelli rearrangement of (±)-**142 to** (±)-**149:** To a solution of furfuryl alcohol (±)-**142** (5.00 mmol) in acetone (5 mL) water (15 mL) was added, and the mixture was heated in the microwave at 180 °C for 15 min. This procedure was repeated as often as necessary, and the combined layers were extracted with DCM (3x). The combined organic layers were dried over $MgSO_4$, and the crude product was purified via flash chromatography (silica, PE/EA = 2:1).

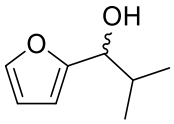
General Procedure 3: Redox isomerization: Under a nitrogen atmosphere, the 4-hydroxy-2-cyclopentenone derivative (1.0 mmol) was dissolved in water (5 mL). After adding catalyst **280** and the reaction mixture was heated to reflux. The progress of the reaction was monitored by TLC. After completion of the reaction, most of the solvent was evaporated, and the residue was cooled down forming a precipitate, which was filtrated and washed with cold water (3x) to obtain the pure product.

1-(Furan-2-yl)propan-1-ol ((±)-142d):[140]



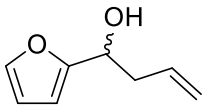
Following general procedure 1 magnesium shavings (1.51 g, 62.4 mmol), bromoethane (5.73 mL, 76.8 mmol) and furfural (**140**) (3.98 mL, 48.0 mmol) were used to yield (±)-**142d** (3.78 g, 29.9 mmol, 62%) as a yellowish oil: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.37 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.33 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.25 – 6.20 (dt, *J* = 3.2, 0.7 Hz, 1H), 4.60 (t, *J* = 6.8 Hz, 1H), 1.96 – 1.80 (m, 3H), 0.95 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 156.7 (C_q), 141.9 (+), 110.1 (+), 105.9 (+), 69.2 (+), 28.6 (-), 10.0 (+).

1-(Furan-2-yl)-2-methylpropan-1-ol ((±)-142e):[140]



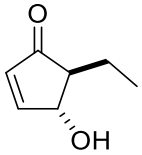
Following general procedure 1 magnesium shavings (1.51 g, 62.4 mmol), 2-bromopropane (5.73 mL, 76.8 mmol) and furfural (**140**) (3.98 mL, 48.0 mmol) were used to yield (±)-**142e** (3.73 g, 26.6 mmol, 55%) as a yellowish oil: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.36 (dd, *J* = 1.8, 0.9 Hz, 1H), 6.33 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.25 – 6.19 (dt, *J* = 3.2, 0.7 Hz, 1H), 4.37 (d, *J* = 7.1 Hz, 1H), 2.19 – 2.02 (m, 1H), 1.98 – 1.81 (bs, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 156.2 (C_q), 141.7 (+), 110.1 (+), 106.5 (+), 73.5 (+), 33.4 (+), 18.7 (+), 18.3 (+).

1-(Furan-2-yl)but-3-en-1-ol ((±)-142f):[148]



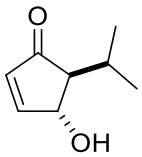
Following general procedure 1 magnesium shavings (1.51 g, 62.4 mmol), allyl bromide (6.64 mL, 76.8 mmol) and furfural (**140**) (3.98 mL, 48.0 mmol) were used to yield (±)-**142f** (4.05 g, 29.3 mmol, 61%) as a yellowish oil: **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.38 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.34 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.26 (dt, *J* = 3.2, 0.7 Hz, 1H), 5.89 – 5.74 (m, 1H), 5.23 – 5.12 (m, 2H), 4.76 (t, *J* = 6.5 Hz, 1H), 2.67 – 2.59 (m, 2H), 2.21 – 1.90 (bs, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 156.0 (C_q), 142.0 (+), 133.7 (+), 118.7 (-), 110.2 (+), 106.1 (+), 66.9 (+), 40.1 (-).

5-Ethyl-4-hydroxycyclopent-2-en-1-one ((±)-149d):[83]



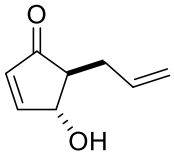
According to general procedure 2 (±)-**142d** (2.52 g, 20.0 mmol) was used to afford a yellowish oil (1.91 g, 15.1 mmol, 76%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.51 (dd, *J* = 5.8, 2.2 Hz, 1H), 6.18 (dd, *J* = 5.8, 0.7 Hz, 1H), 4.72 – 4.65 (m, 1H), 2.70 – 2.49 (bs, 1H), 2.19 (ddd, *J* = 8.6, 4.7, 2.4 Hz, 1H), 1.96 – 1.79 (m, 1H), 1.61 – 1.45 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 208.4 (C_q), 162.1 (+), 134.4 (+), 76.2 (+), 56.6 (+), 21.4 (-), 11.5 (+).

4-Hydroxy-5-isopropylcyclopent-2-en-1-one ((±)-149e):[149]



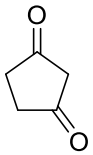
According to general procedure 2 (±)-**142e** (2.80 g, 20.0 mmol) was used to afford a yellowish oil (1.93 g, 13.8 mmol, 69%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.51 (dd, *J* = 5.8, 2.3 Hz, 1H), 6.21 – 6.11 (m, 1H), 4.80 (s, 1H), 2.72 – 2.34 (bs, 1H), 2.33 – 2.24 (m, 1H), 2.23 – 2.18 (m, 1H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 208.4 (C_q), 162.4 (+), 134.9 (+), 72.8 (+), 60.8 (+), 27.1 (+), 20.7 (+), 18.2 (+).

5-Allyl-4-hydroxycyclopent-2-en-1-one ((±)-149f):[149]



According to general procedure 2 (±)-**142f** (2.76 g, 20.0 mmol) was used to afford a yellowish oil (1.57 g, 11.4 mmol, 57%): **^{1}H NMR** (300 MHz, $CDCl_3$) δ_H = 7.51 (dd, *J* = 5.8, 2.2 Hz, 1H), 6.20 (d, *J* = 5.8 Hz, 1H), 5.89 – 5.71 (m, 1H), 5.19 – 5.05 (m, 2H), 4.77 – 4.62 (m, 1H), 2.69 – 2.59 (m, 1H), 2.40 – 2.17 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ_C = 207.2 (C_q), 162.0 (+), 135.2 (+), 134.2 (+), 117.5 (-), 75.7 (+), 54.8 (+), 32.6 (-).

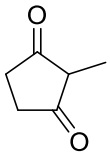
Cyclopentane-1,3-dione (238):[132,132]



Following general procedure 3 (±)-**150** (98 mg, 1.00 mmol) and catalyst **280** (30.8 mg, 0.05 mmol) were used. After 8 h, the reaction was complete and **238** (78 mg, 0.80 mmol, 80%) was obtained after recrystallization from MeOH/PE as a white solid:

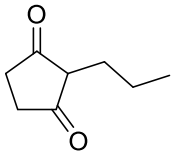
^{1}H NMR (300 MHz, DMSO) δ_H = 13.33 – 10.33 (bs, 1H), 5.08 (s, 1H), 2.37 (s, 4H); **^{13}C NMR** (75 MHz, DMSO) δ_C = 197.6 (C_q), 104.9 (+), 31.2 (-).

2-Methylcyclopentane-1,3-dione (282a):[150]



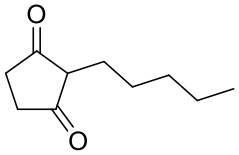
Following general procedure 3 (±)-**200** (112 mg, 1.00 mmol) and catalyst **280** (30.8 mg, 0.05 mmol) were used. After 15 h, the reaction was complete and **282a** (102 mg, 0.91 mmol, 91%) was obtained as a brownish solid: **^{1}H NMR** (300 MHz, DMSO) δ_H = 12.01 – 10.07 (bs, 1H), 2.33 (s, 4H), 1.45 (s, 3H); **^{13}C NMR** (75 MHz, DMSO) δ_C = 194.2 (C_q) 111.5 (C_q), 29.98 (-), 5.66 (+).

2-Propylcyclopentane-1,3-dione (282b):[151]



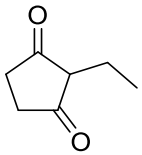
Following general procedure 3 (±)-**149a** (140 mg, 1.00 mmol) and catalyst **280** (30.8 mg, 0.05 mmol) were used. After 30 h, the reaction was complete and **282b** (113 mg, 0.81 mmol, 81%) was obtained as a white solid: **^{1}H NMR** (300 MHz, DMSO) δ_H = 11.58 – 11.24 (bs, 1H), 2.33 (s, 4H), 1.95 (t, *J* = 7.2 Hz, 2H), 1.37 – 1.25 (sext, *J* = 7.5 Hz, 3H), 0.80 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, DMSO) δ_C =197.6 (C_q), 116.1 (C_q), 29.9 (-), 22.7 (-), 20.8 (-), 13.9 (+).

2-Pentylcyclopentane-1,3-dione (282c):[151]



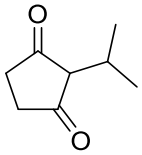
Following general procedure 3 (±)-**149b** (168 mg, 1.00 mmol) and catalyst **280** (61.6 mg, 0.1 mmol) were used. After 15 h, the reaction was complete and **282c** (121 mg, 0.72 mmol, 72%) was obtained as a white solid: **^{1}H NMR** (400 MHz, DMSO) δ_H = 11.67 – 10.95 (bs, 1H), 2.31 (s, 4H), 1.96 (t, *J* = 7.4 Hz, 2H), 1.32 – 1.14 (m, 6H), 0.82 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, DMSO) δ_C =193.3 (C_q), 116.3 (C_q), 31.2 (-), 30.1 (-), 27.2 (-), 21.9 (-), 20.5 (-), 13.9 (+).

2-Ethylcyclopentane-1,3-dione (282e):[151]



Following general procedure 3 (±)-**149d** (126 mg, 1.00 mmol) and catalyst **280** (30.8 mg, 0.05 mmol) were used. After 15 h, the reaction was complete and **282e** (109 mg, 0.86 mmol, 86%) was obtained as a brownish solid: **^{1}H NMR** (300 MHz, DMSO) δ_H = 12.43 – 10.36 (bs, 1H), 2.32 (s, 4H), 1.99 (q, *J* = 7.5 Hz, 2H), 0.88 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (75 MHz, DMSO) δ_C = 193.7 (C_q), 117.6 (C_q), 30.0 (-), 13.9 (-), 12.7 (+).

2-Isopropylcyclopentane-1,3-dione (282f):[151]



Following general procedure 3 (±)-**149e** (140 mg, 1.00 mmol) and catalyst **280** (61.6 mg, 0.1 mmol) were used. After 30 h, the reaction was complete and **282f** (72 mg, 0.51 mmol, 51%) was obtained as a white solid: **^{1}H NMR** (300 MHz, DMSO) δ_H = 11.84 – 10.81 (bs, 1H), 2.69 – 2.54 (m, 1H), 2.30 (s, 4H), 1.05 (d, *J* = 7.0 Hz, 6H); **^{13}C NMR** (75 MHz, DMSO) δ_C = 192.6 (C_q), 120.9 (C_q), 30.0 (-), 22.2 (+), 20.3 (+).

F Appendix

1 NMR-spectra

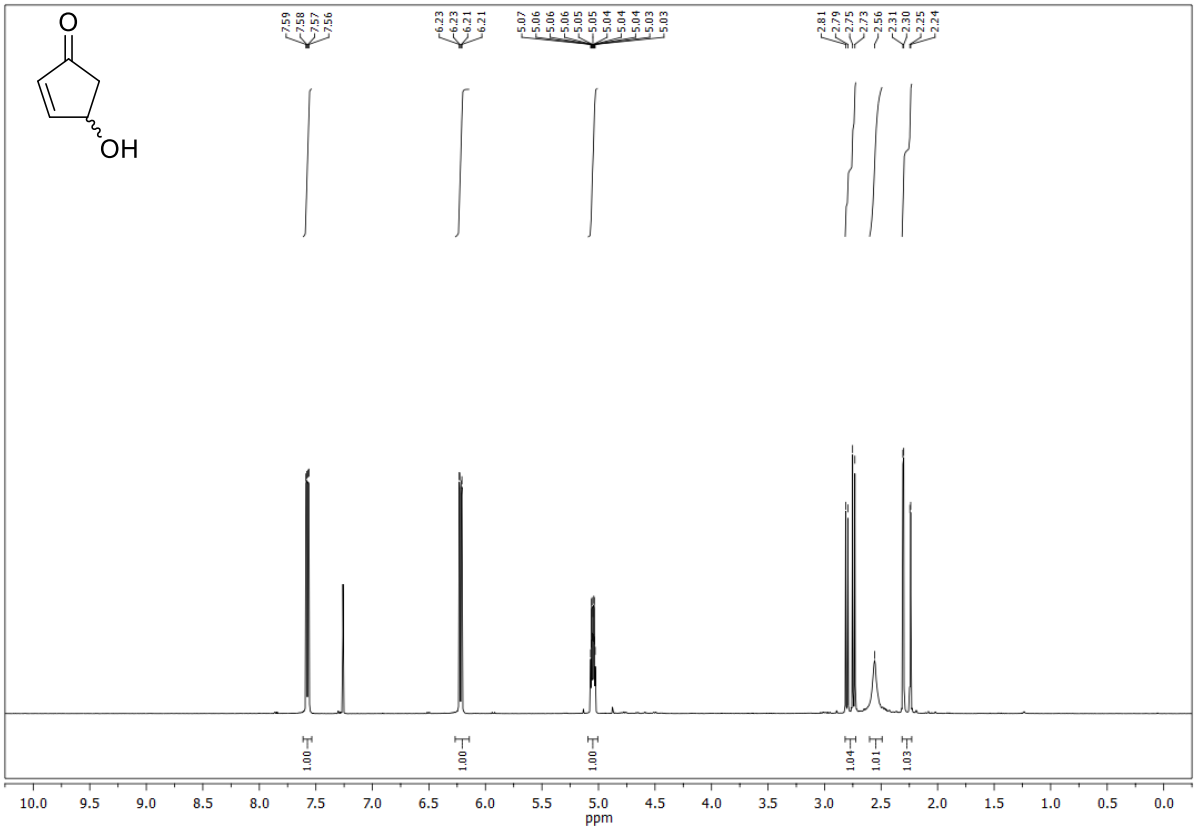
^{1}H NMR spectra upper image

^{13}C NMR spectra lower image

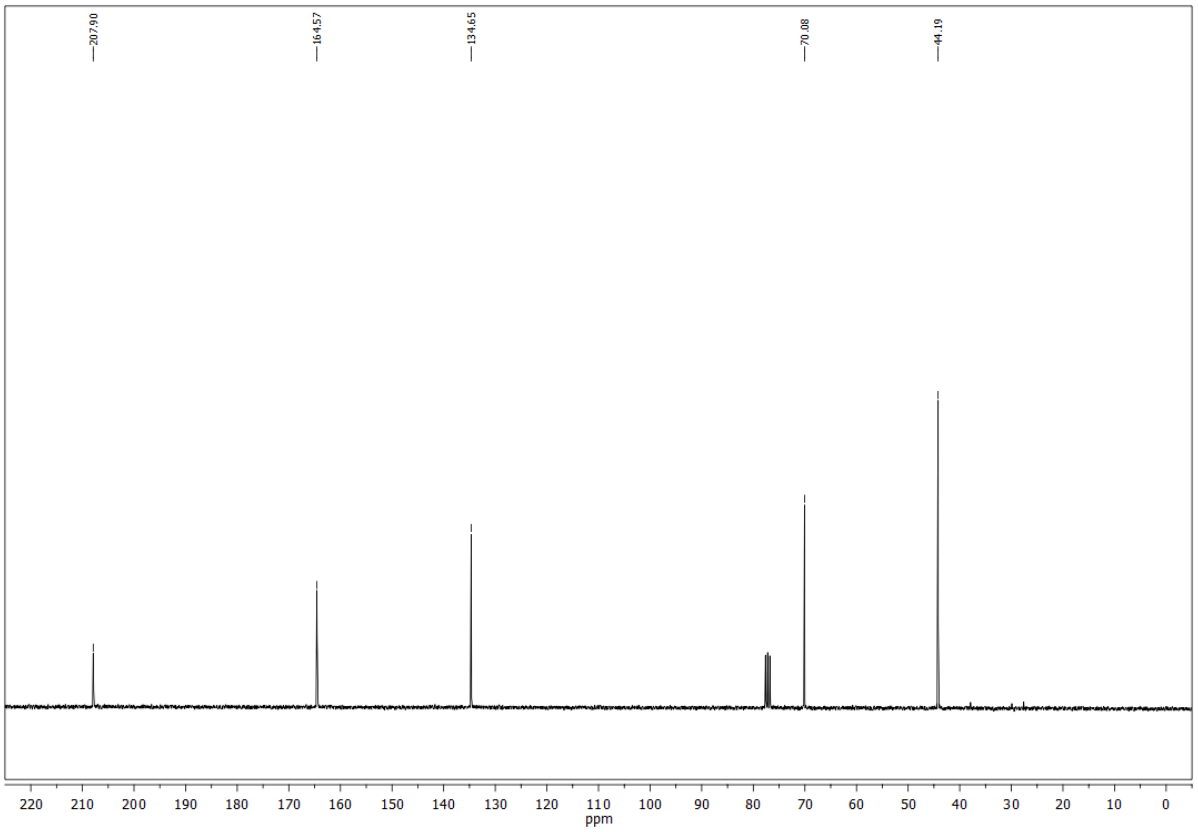
Solvent and frequency are given at the spectra.

4-Hydroxycyclopent-2-en-1-one ((±)-150)

^{1}H NMR (300 MHz, $CDCl_3$)

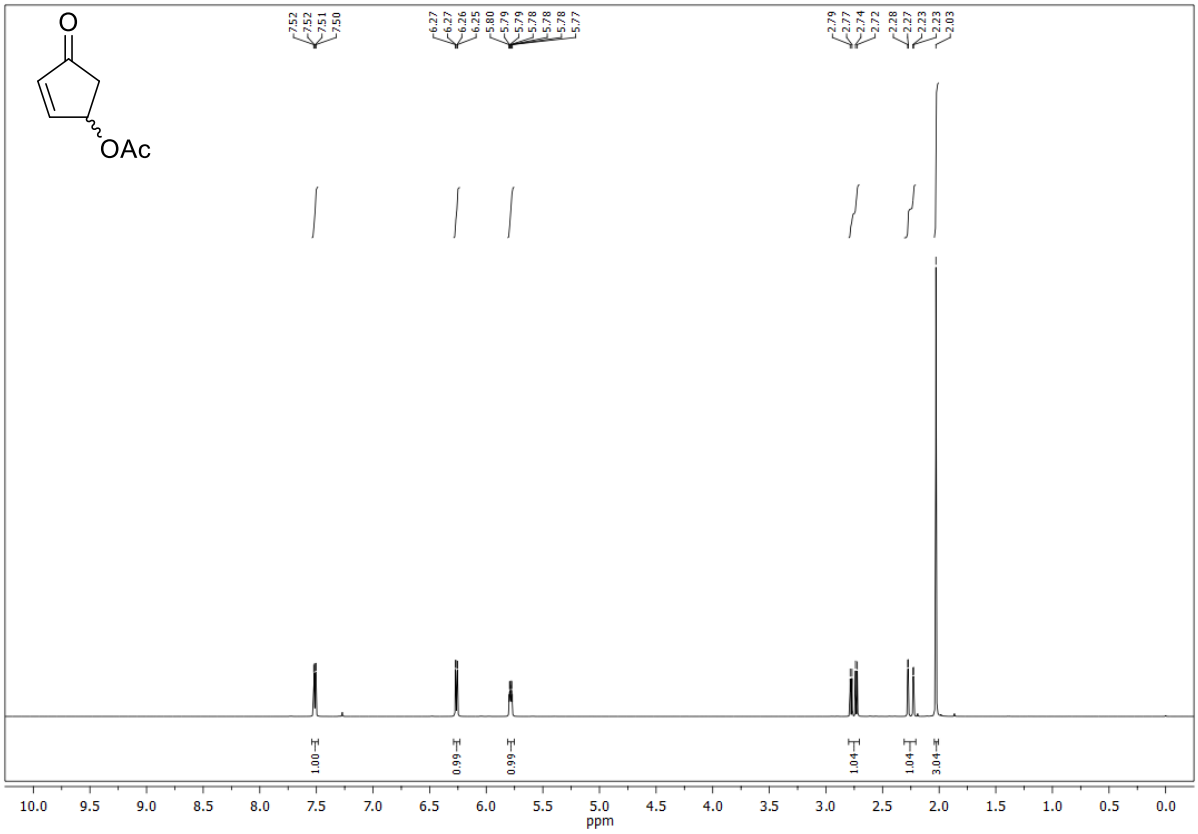


^{13}C NMR (75 MHz, $CDCl_3$)

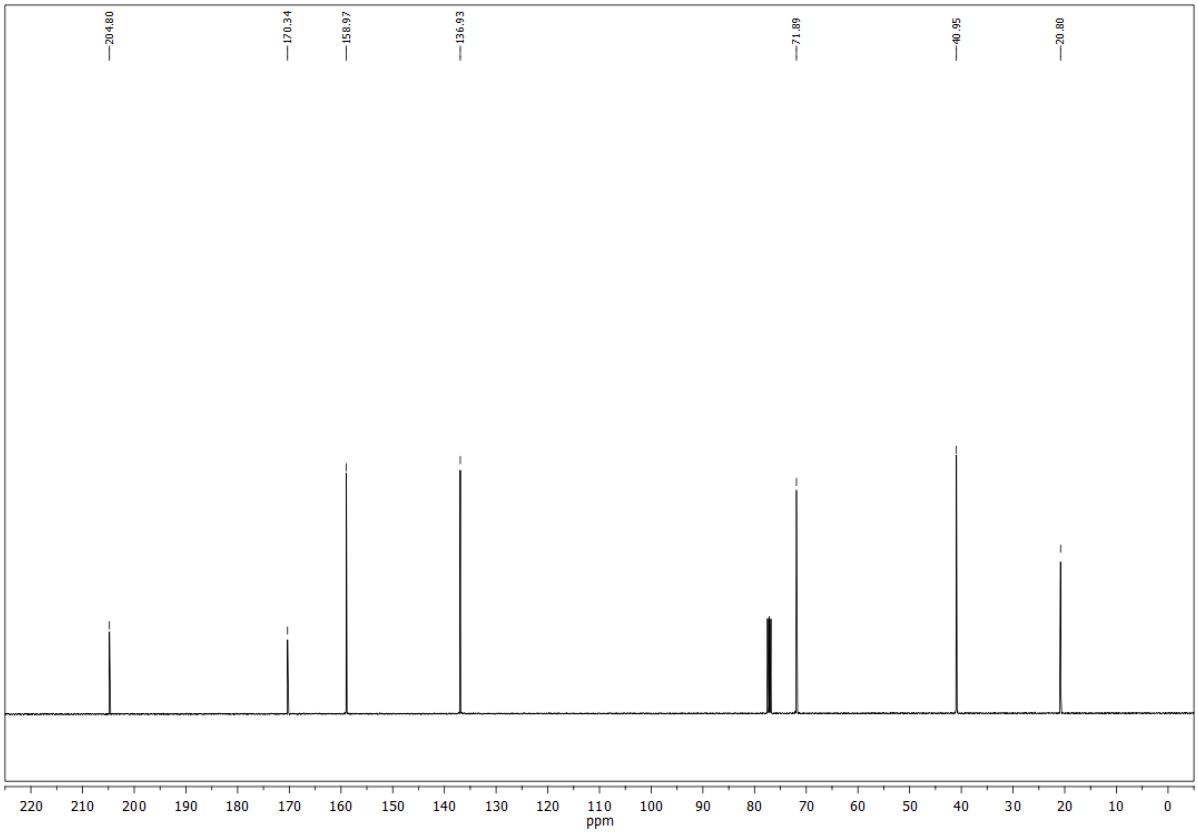


4-Oxocyclopent-2-en-1-yl acetate ((±)-153)

^{1}H NMR (400 MHz, $CDCl_3$)

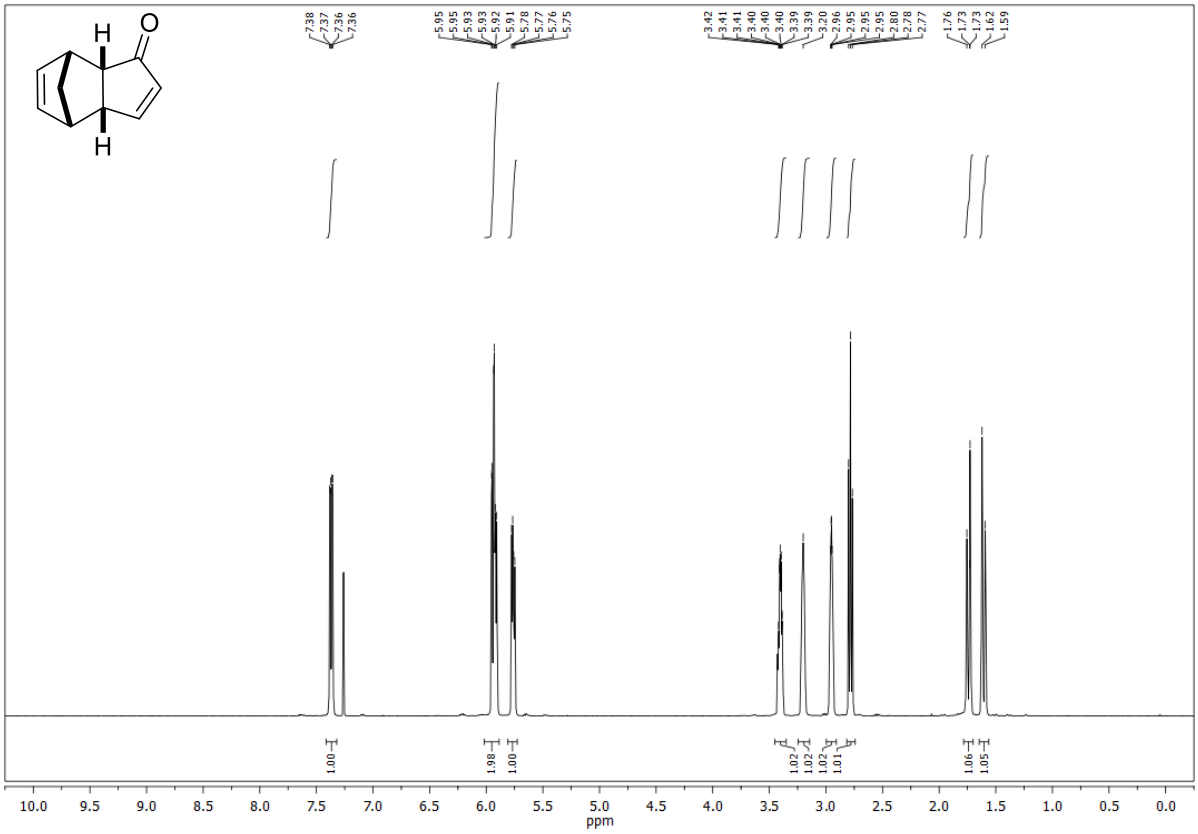


^{13}C NMR (101 MHz, $CDCl_3$)

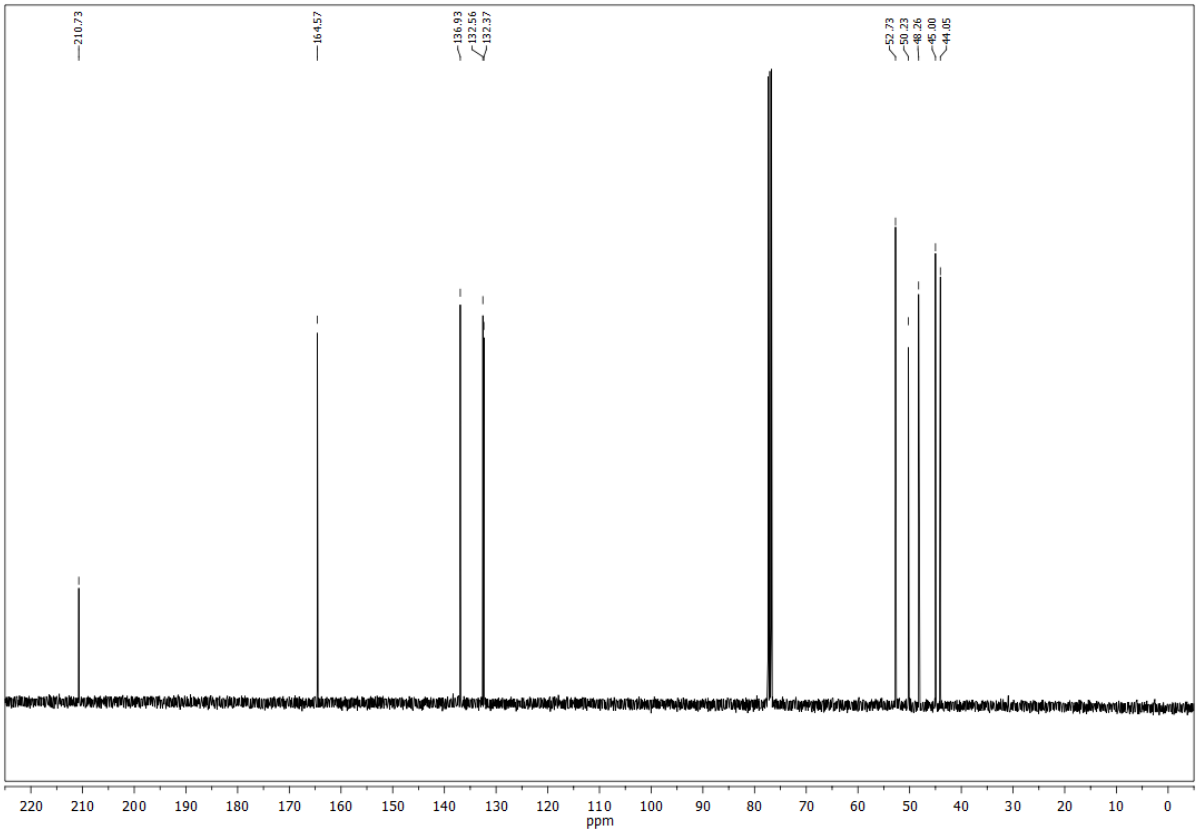


3a,4,7,7a-Tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-138)

^{1}H NMR (300 MHz, $CDCl_3$)

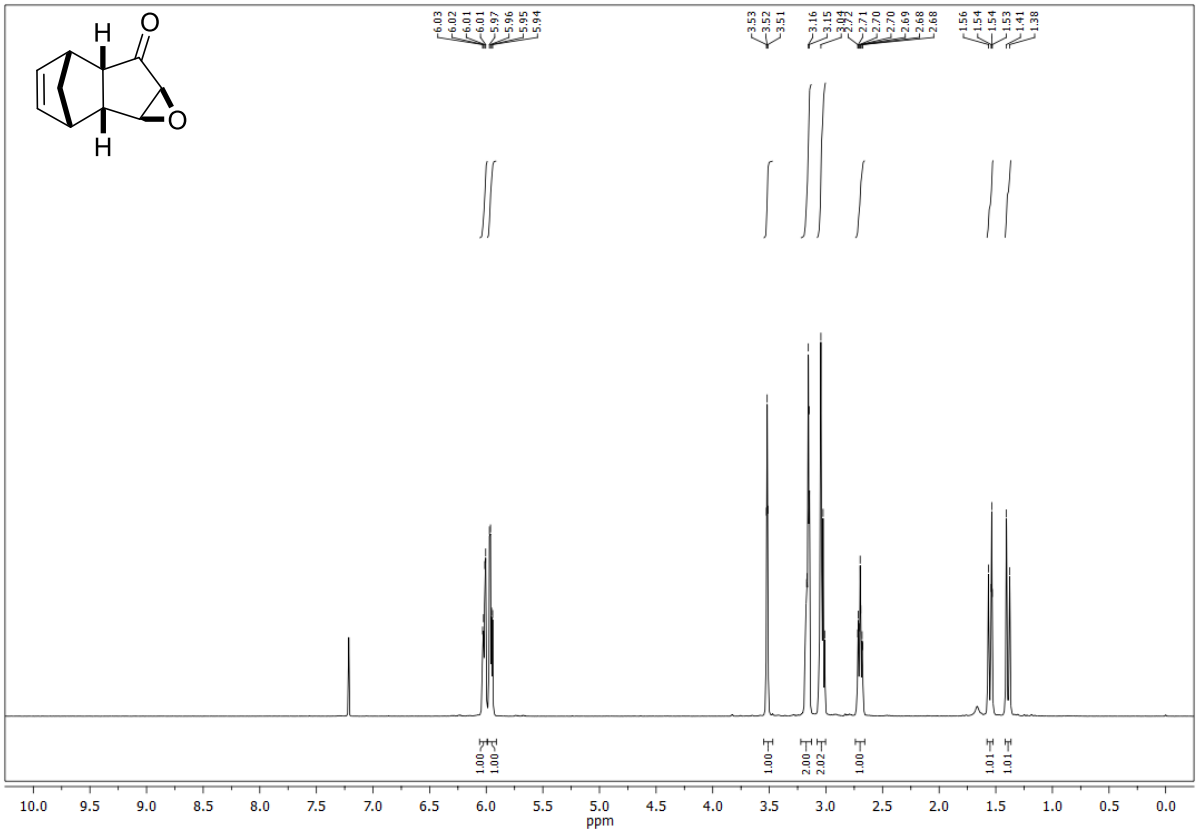


^{13}C NMR (75 MHz, $CDCl_3$)

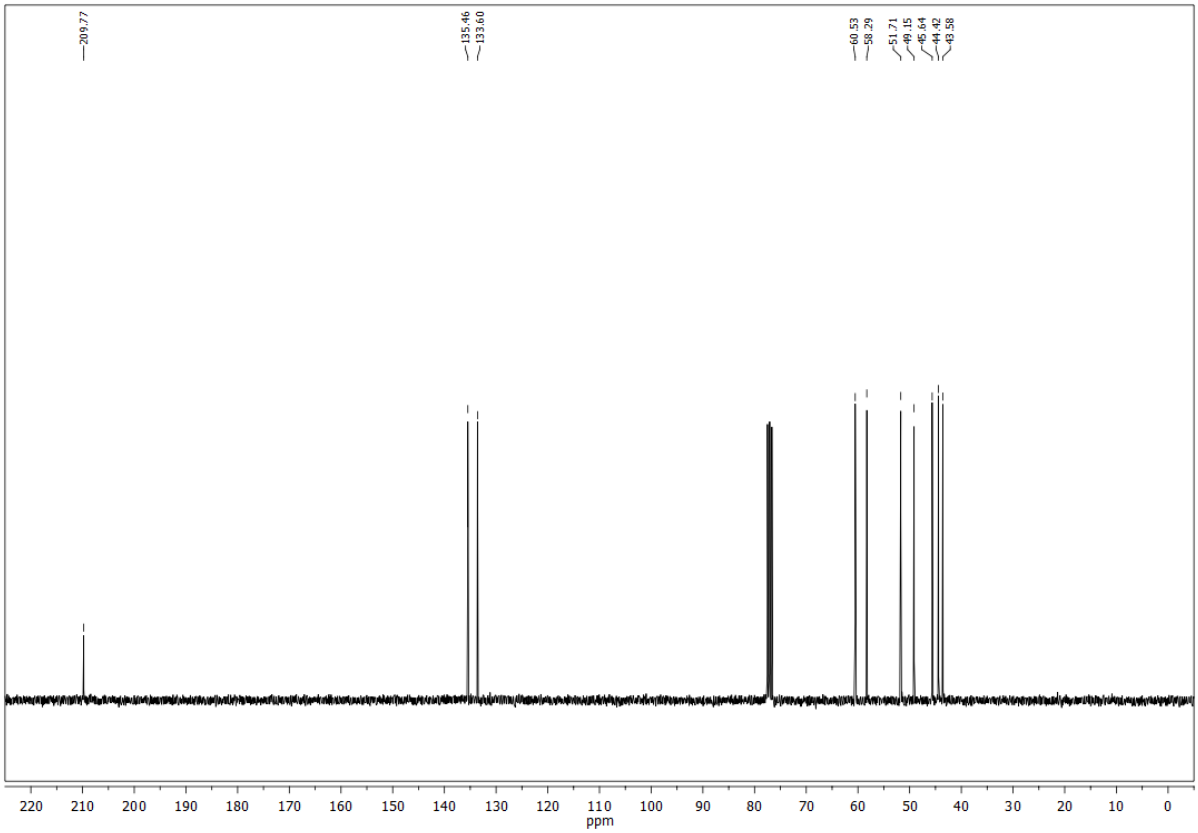


a,1b,2,5,5a,6a-Hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-137)

^{1}H NMR (300 MHz, $CDCl_3$)

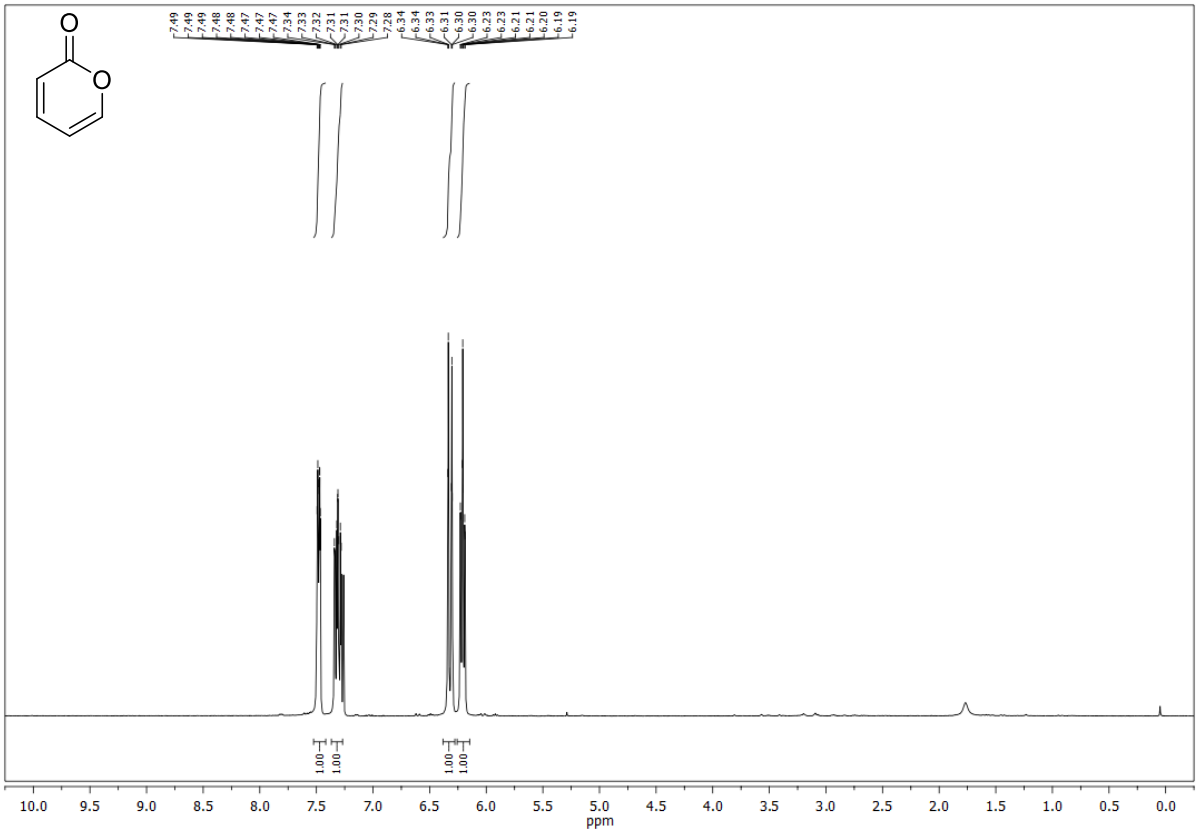


^{13}C NMR (75 MHz, $CDCl_3$)

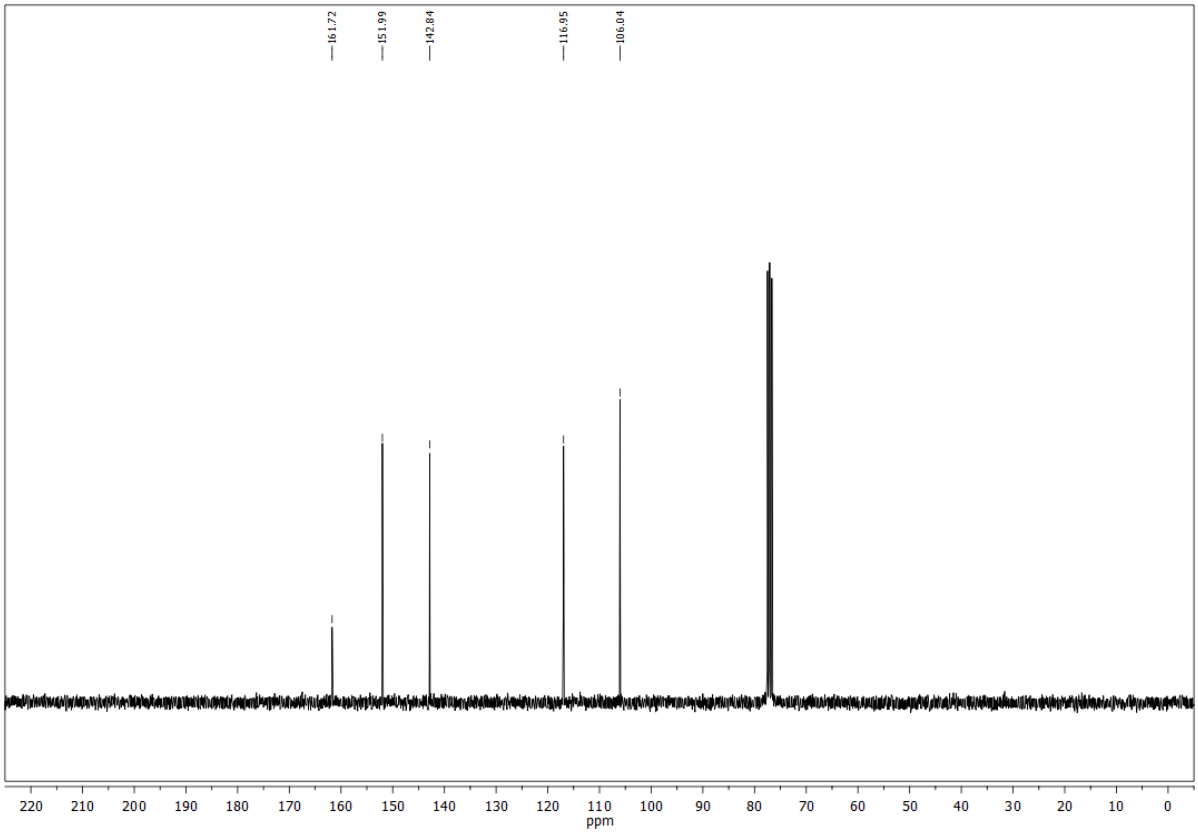


2*H*-Pyran-2-one (1)

^{1}H NMR (300 MHz, $CDCl_3$)

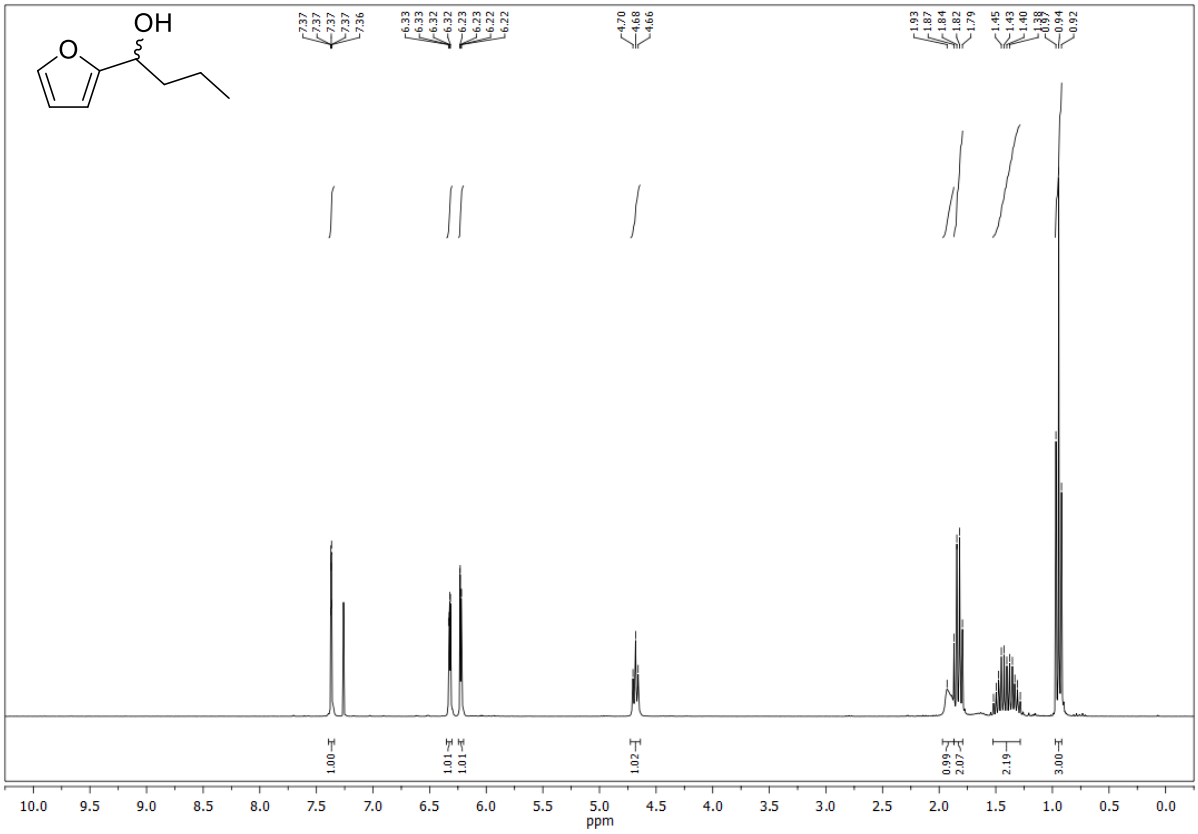


^{13}C NMR (75 MHz, $CDCl_3$)

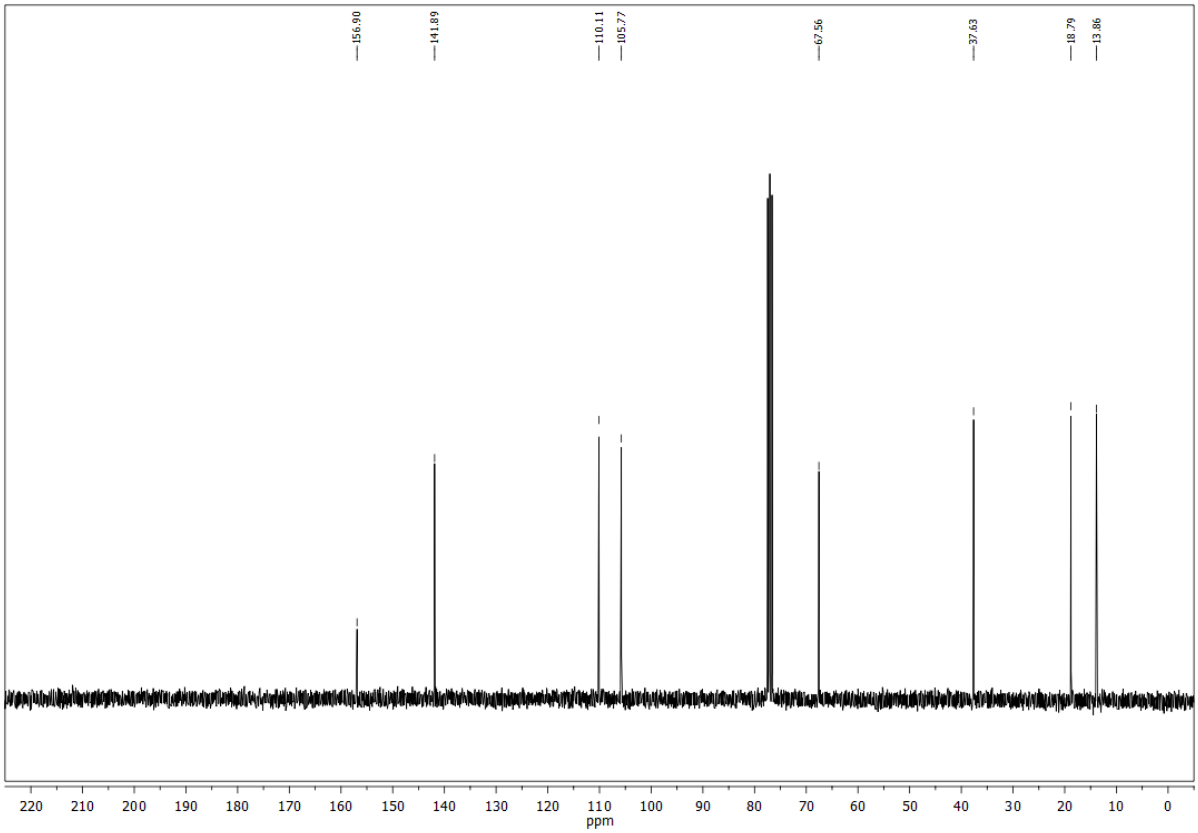


1-(Furan-2-yl)butan-1-ol ((±)-142a)

^{1}H NMR (300 MHz, $CDCl_3$)

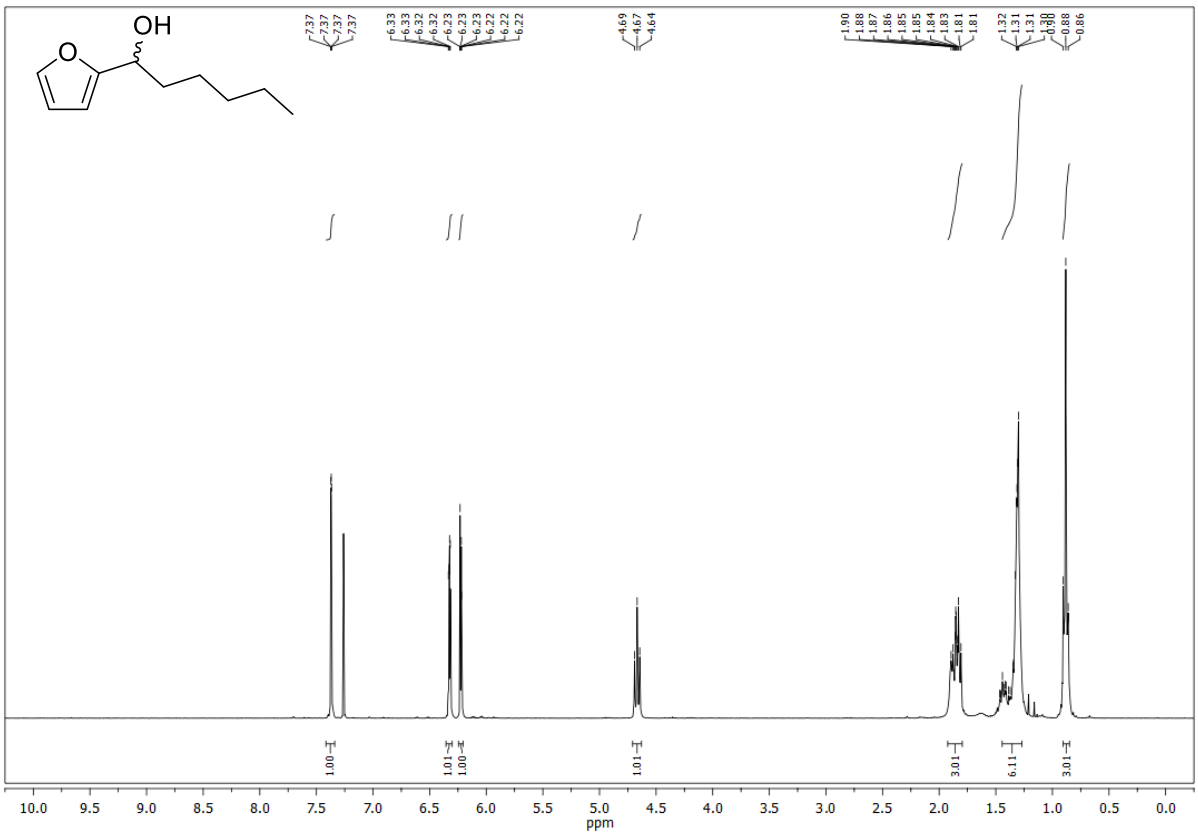


^{13}C NMR (75 MHz, $CDCl_3$)

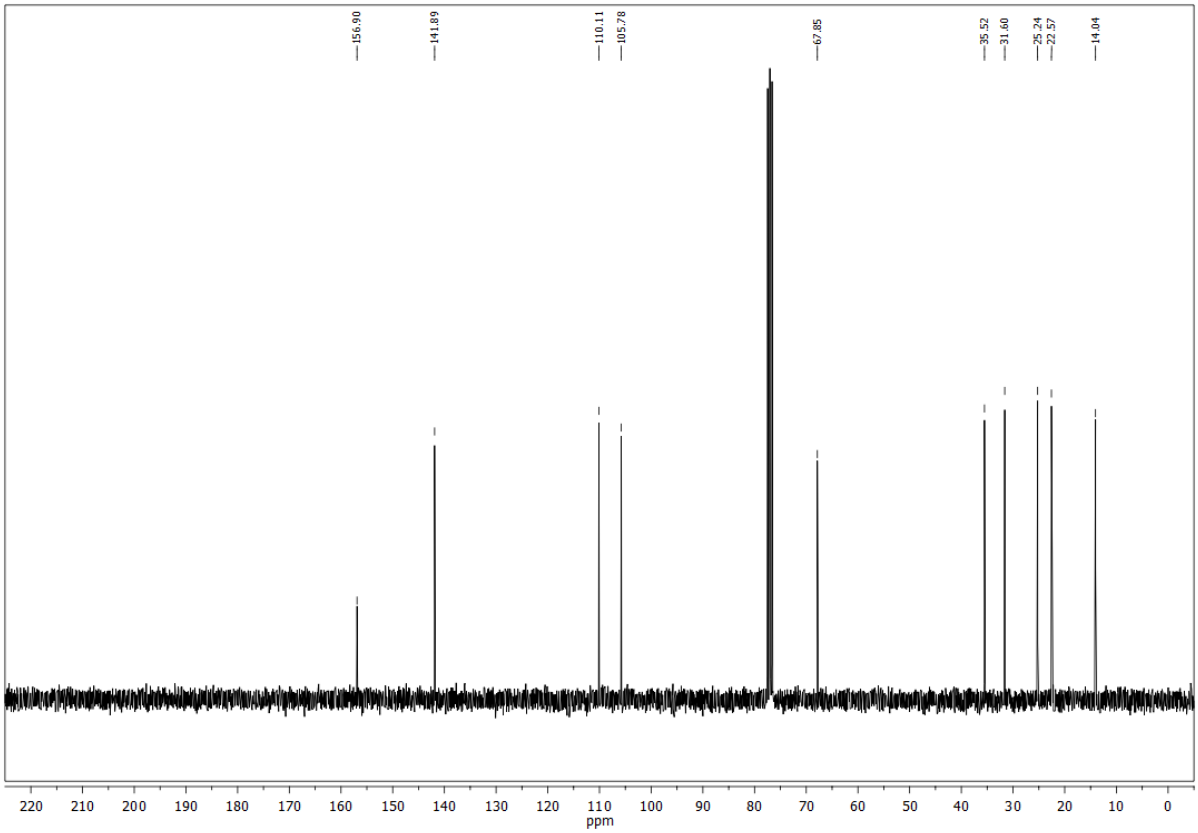


1-(Furan-2-yl)hexan-1-ol ((±)-142b)

^{1}H NMR (300 MHz, $CDCl_3$)

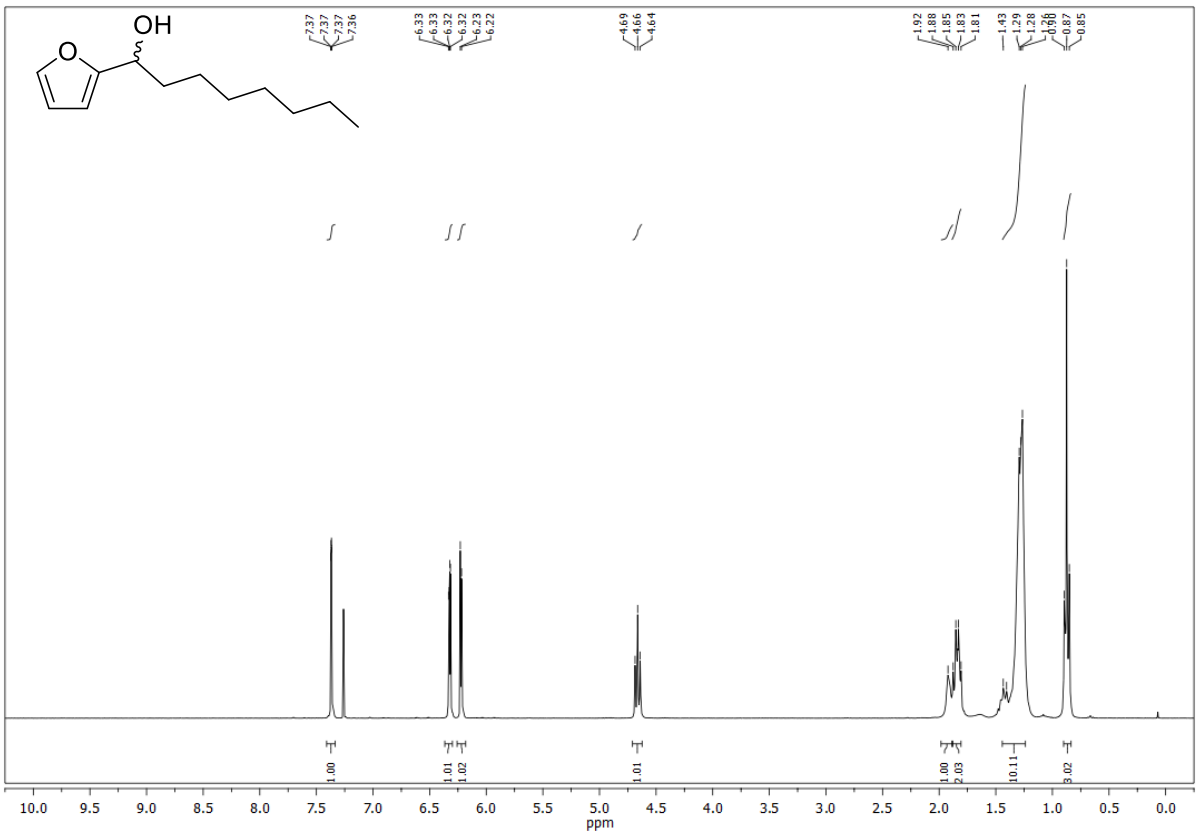


^{13}C NMR (75 MHz, $CDCl_3$)

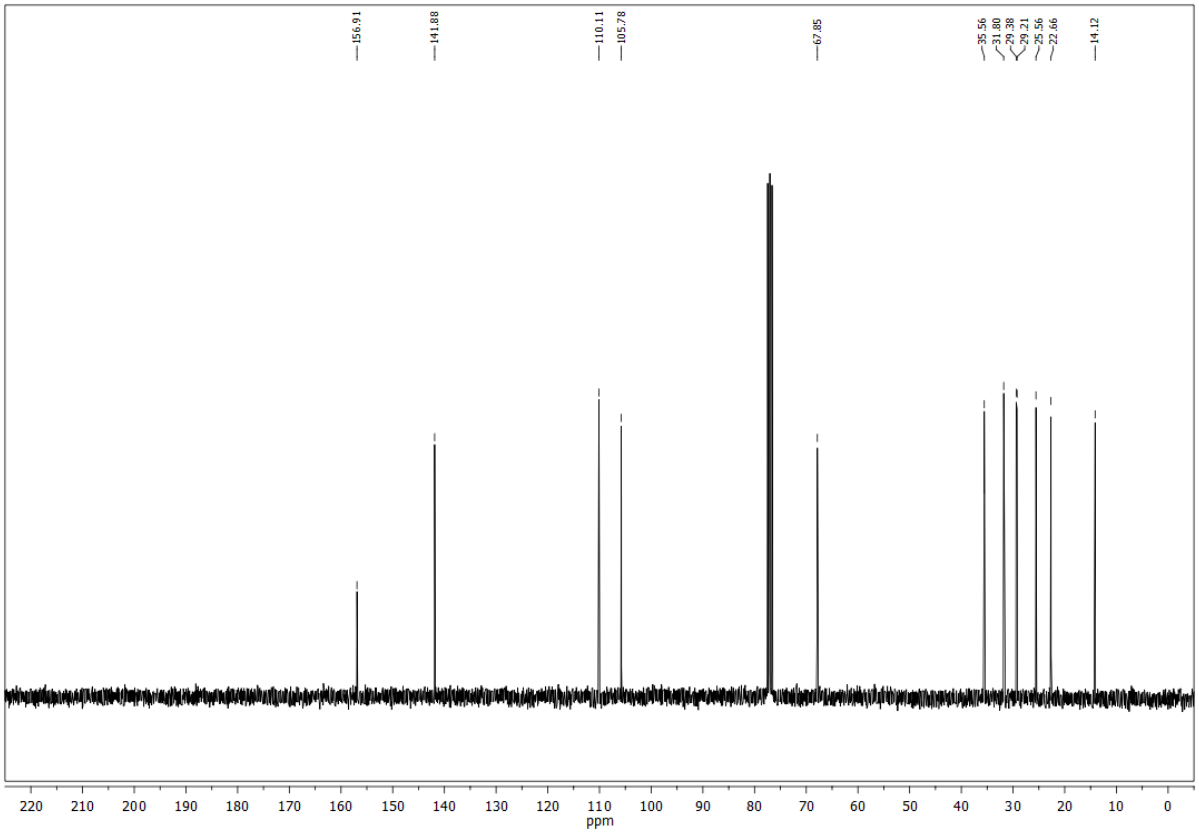


1-(Furan-2-yl)octan-1-ol ((±)-142c)

^{1}H NMR (300 MHz, $CDCl_3$)

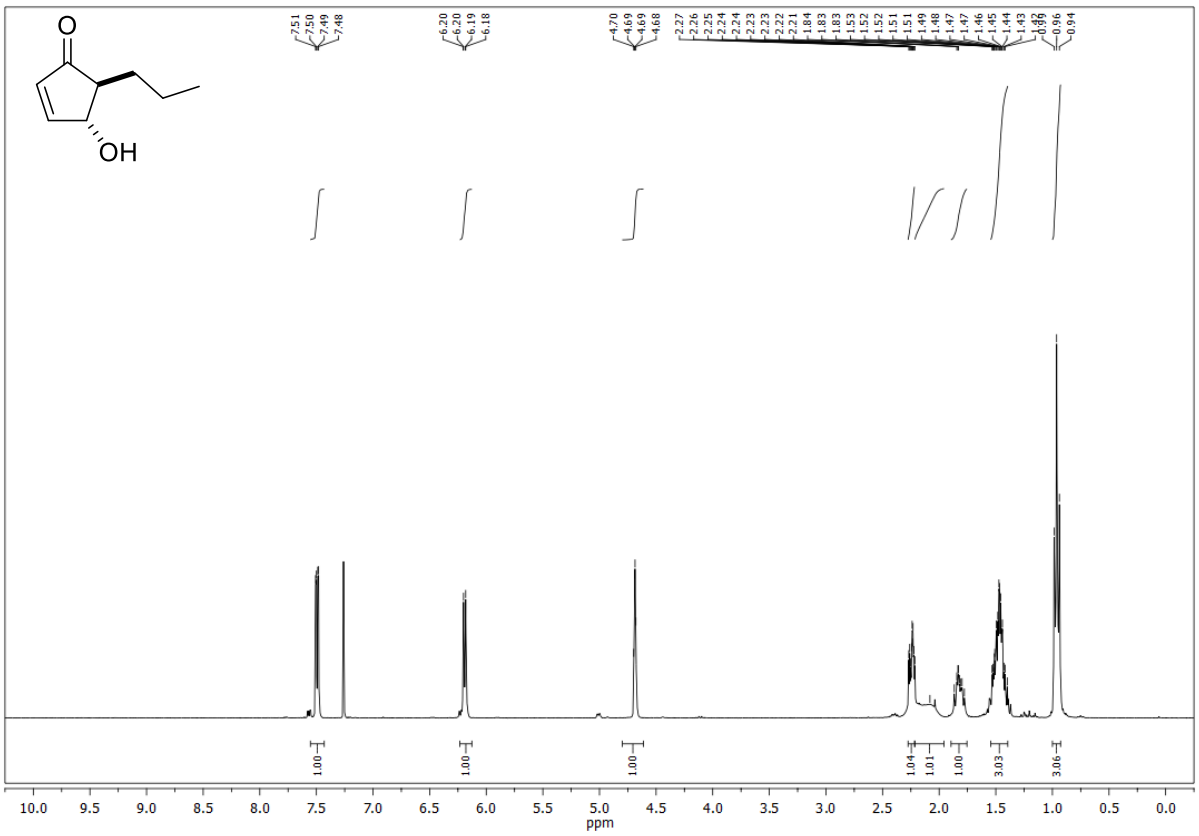


^{13}C NMR (75 MHz, $CDCl_3$)

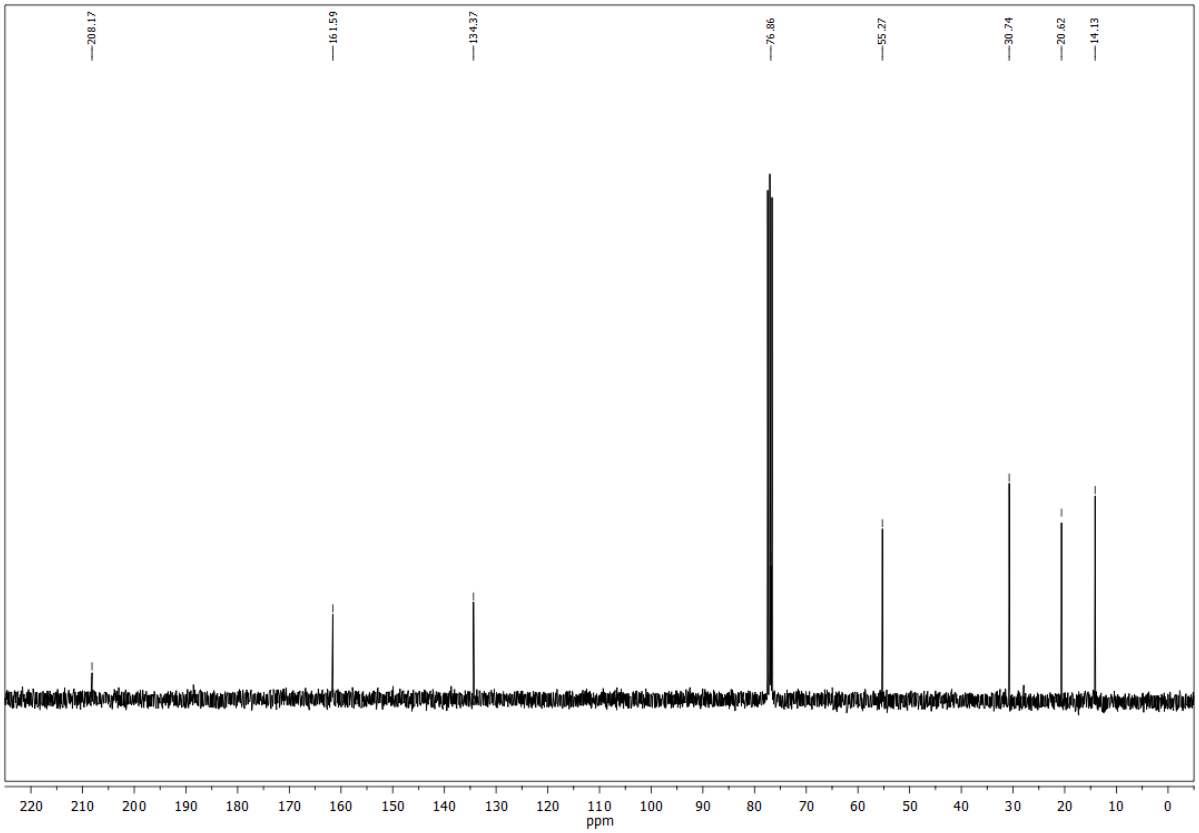


4-Hydroxy-5-propylcyclopent-2-en-1-one ((±)-149a)

^{1}H NMR (300 MHz, $CDCl_3$)

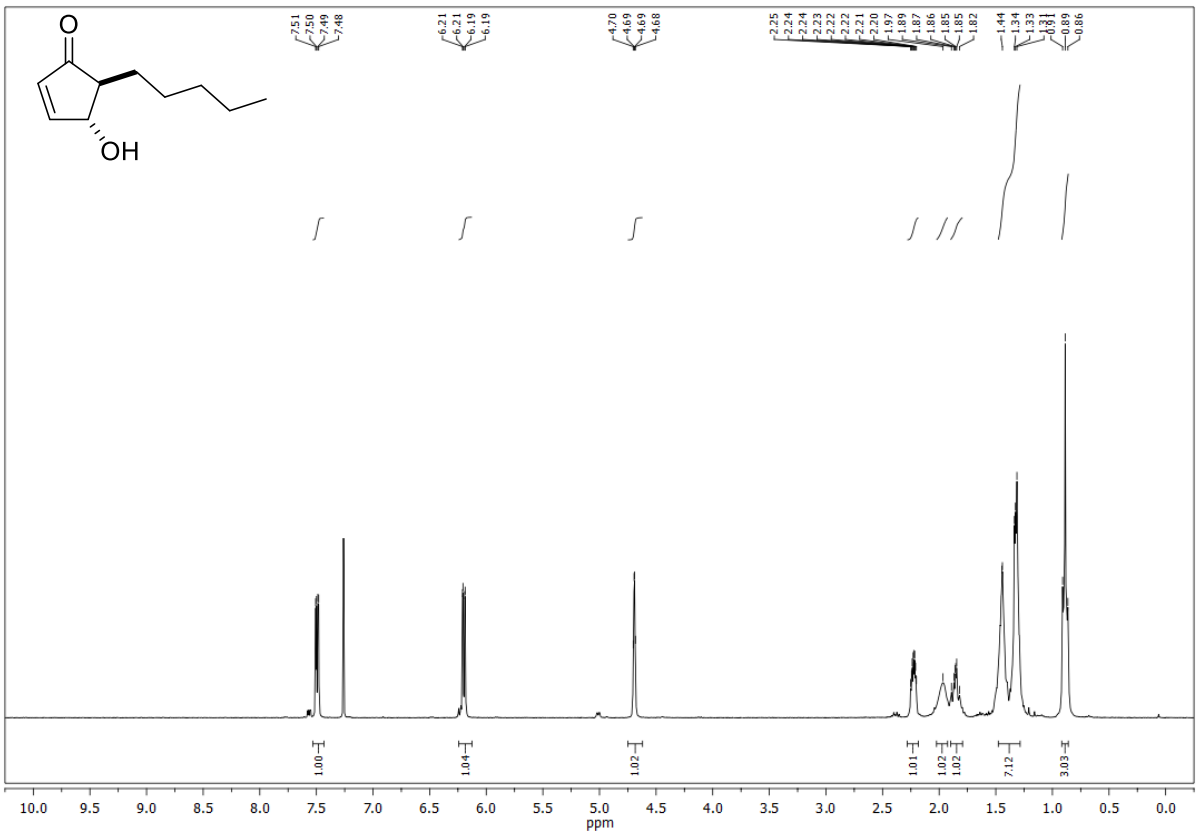


^{13}C NMR (75 MHz, $CDCl_3$)

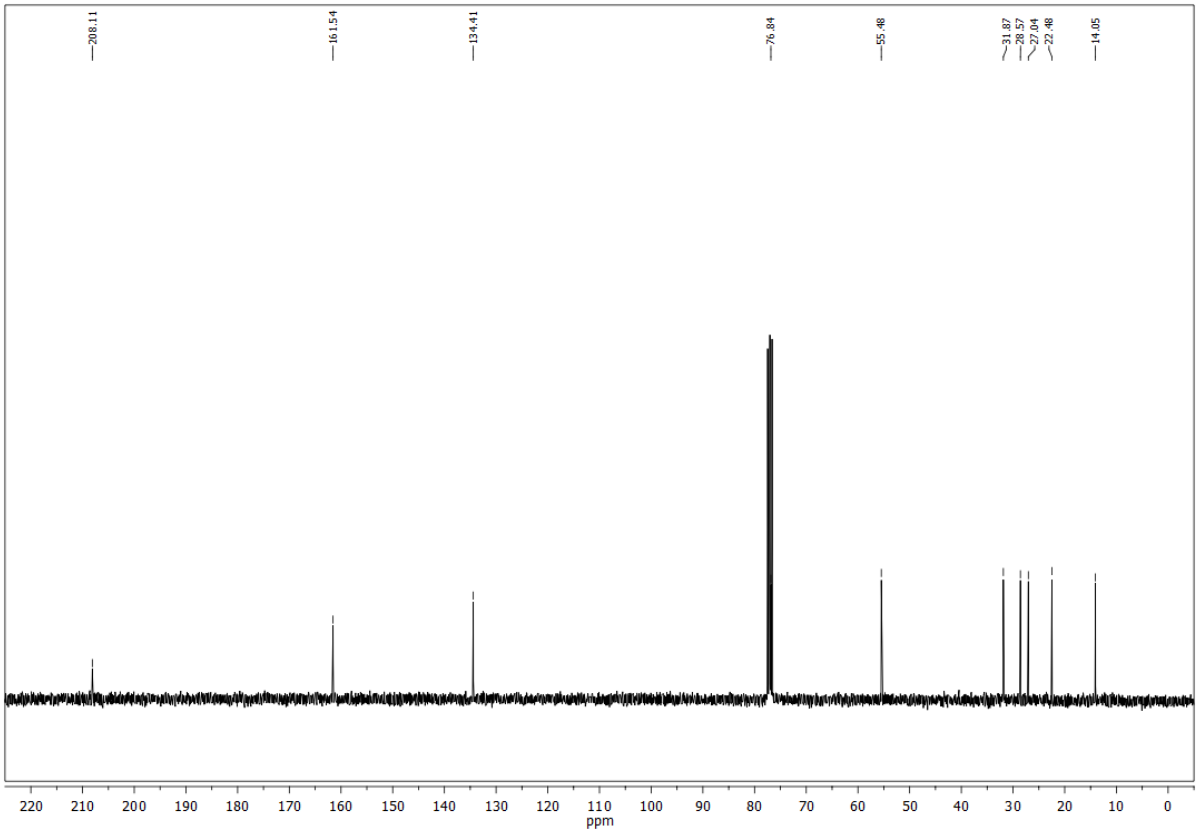


4-Hydroxy-5-pentylcyclopent-2-en-1-one ((±)-149b)

^{1}H NMR (300 MHz, $CDCl_3$)

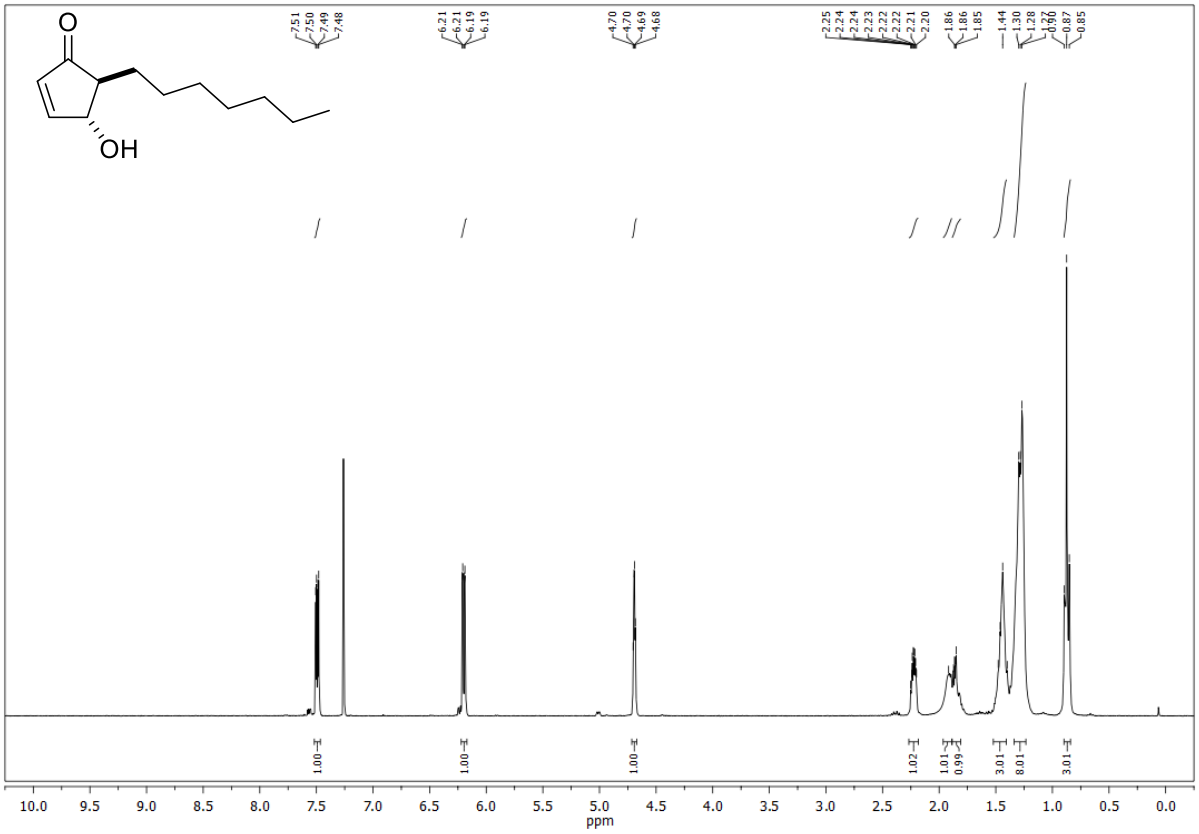


^{13}C NMR (75 MHz, $CDCl_3$)

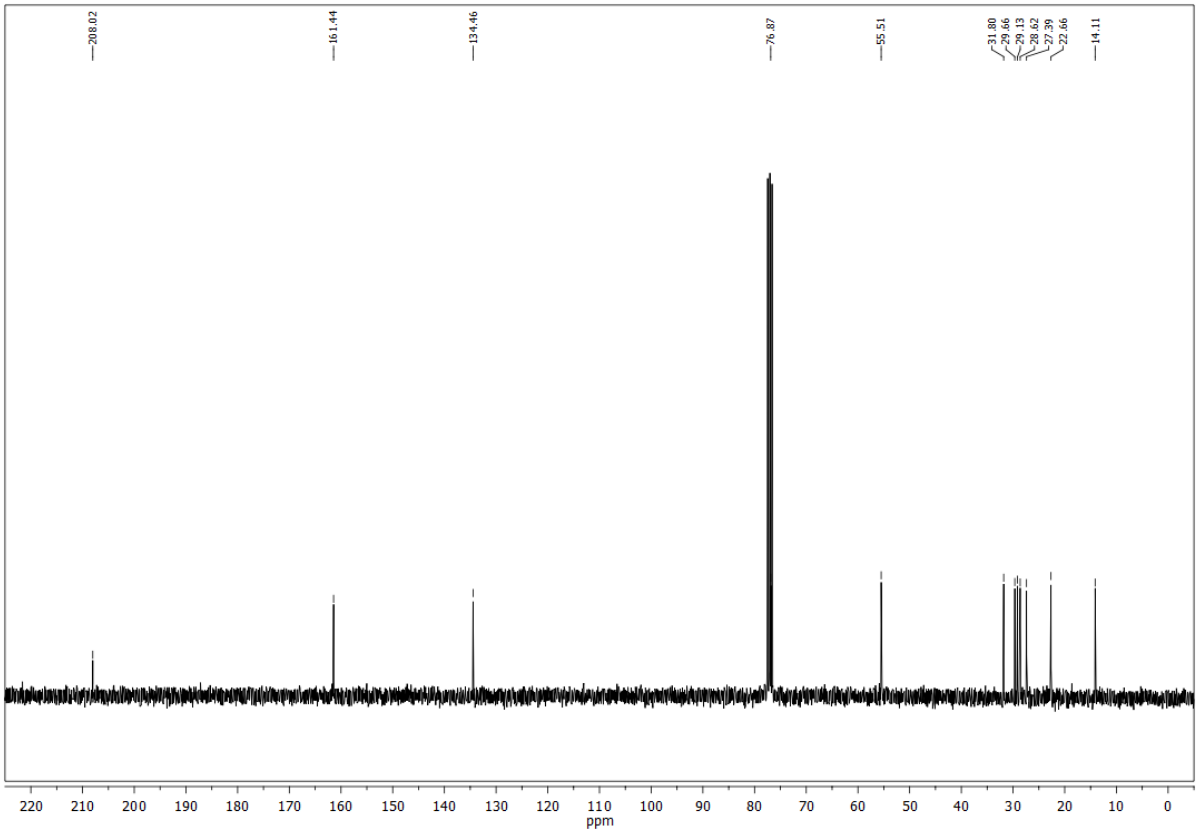


5-Heptyl-4-hydroxycyclopent-2-en-1-one ((±)-149c)

^{1}H NMR (300 MHz, $CDCl_3$)

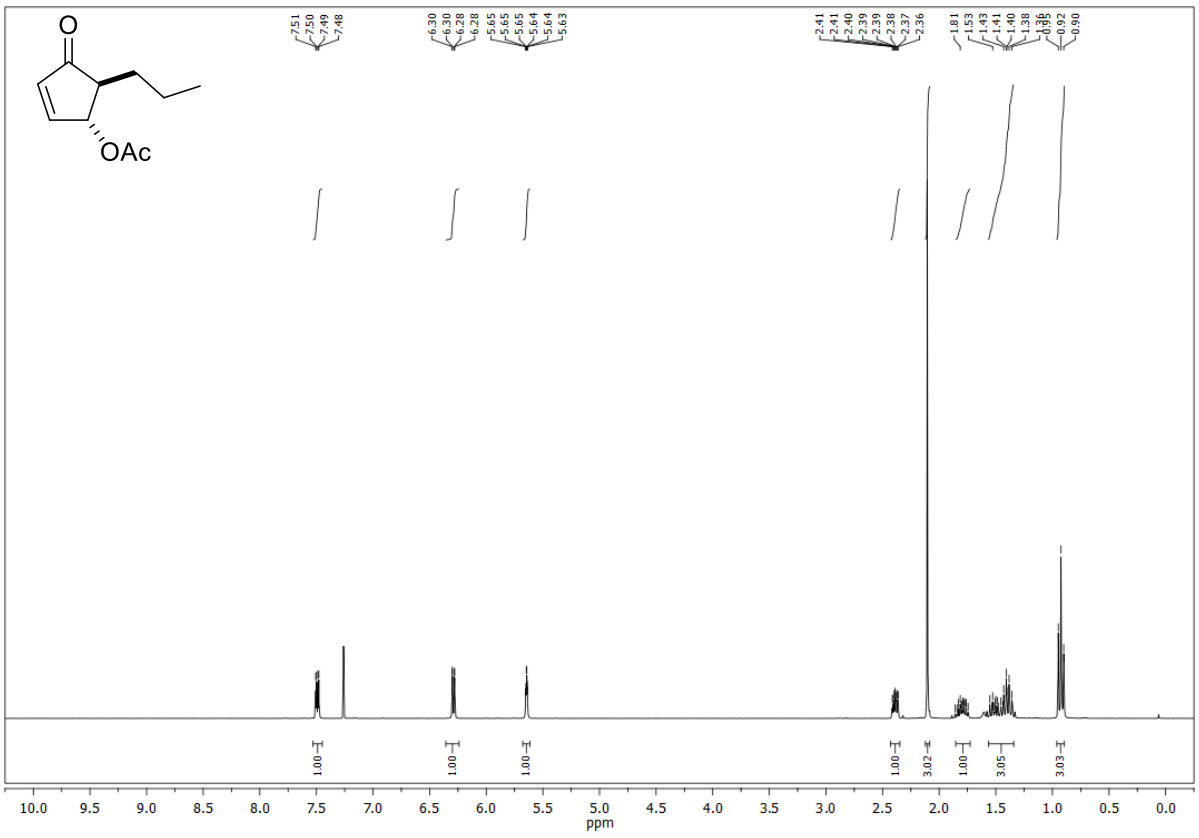


^{13}C NMR (75 MHz, $CDCl_3$)

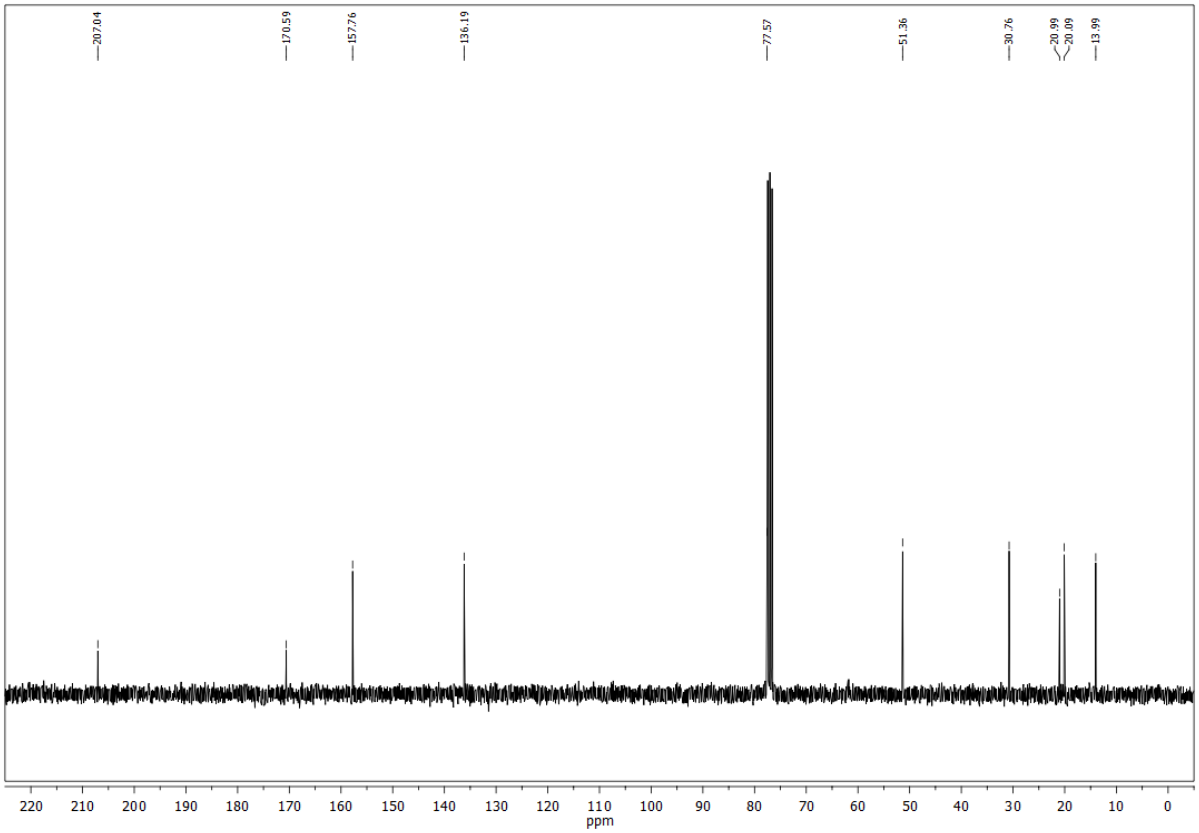


4-Oxo-5-propylcyclopent-2-en-1-yl acetate ((±)-154a)

^{1}H NMR (300 MHz, $CDCl_3$)

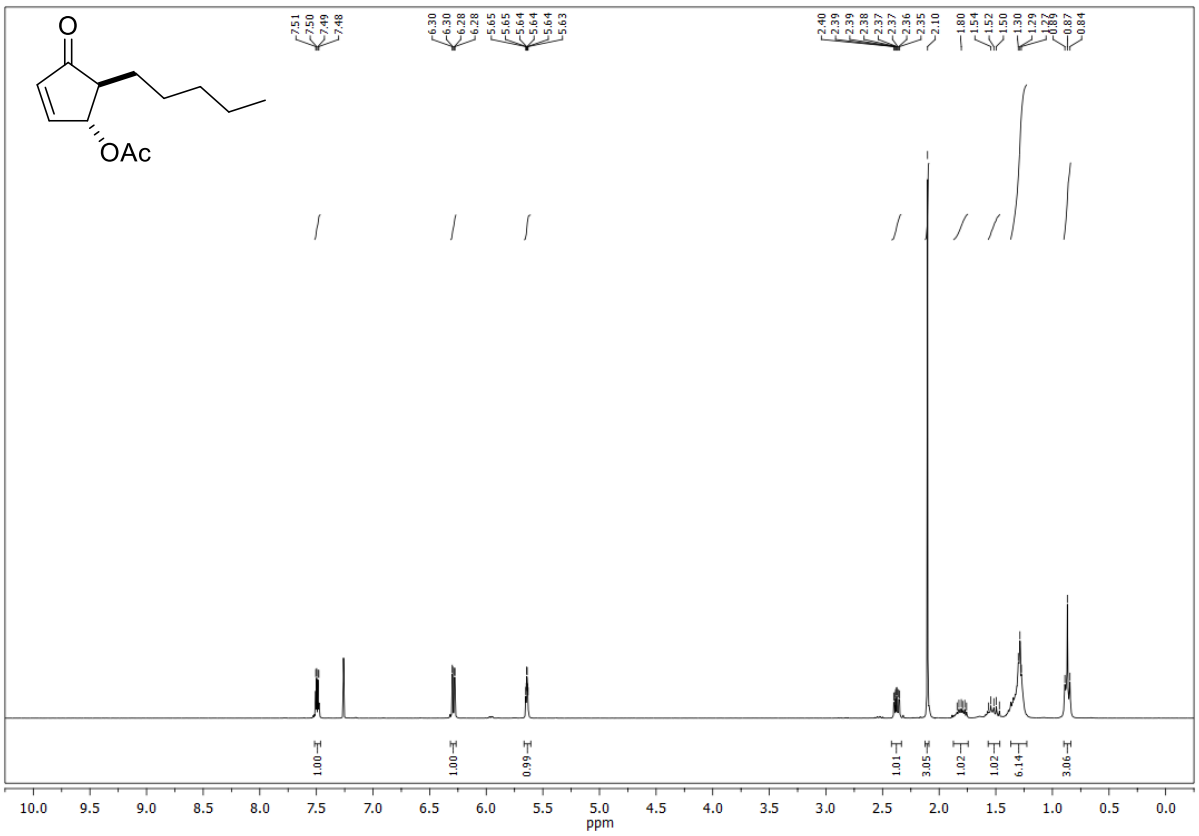


^{13}C NMR (75 MHz, $CDCl_3$)

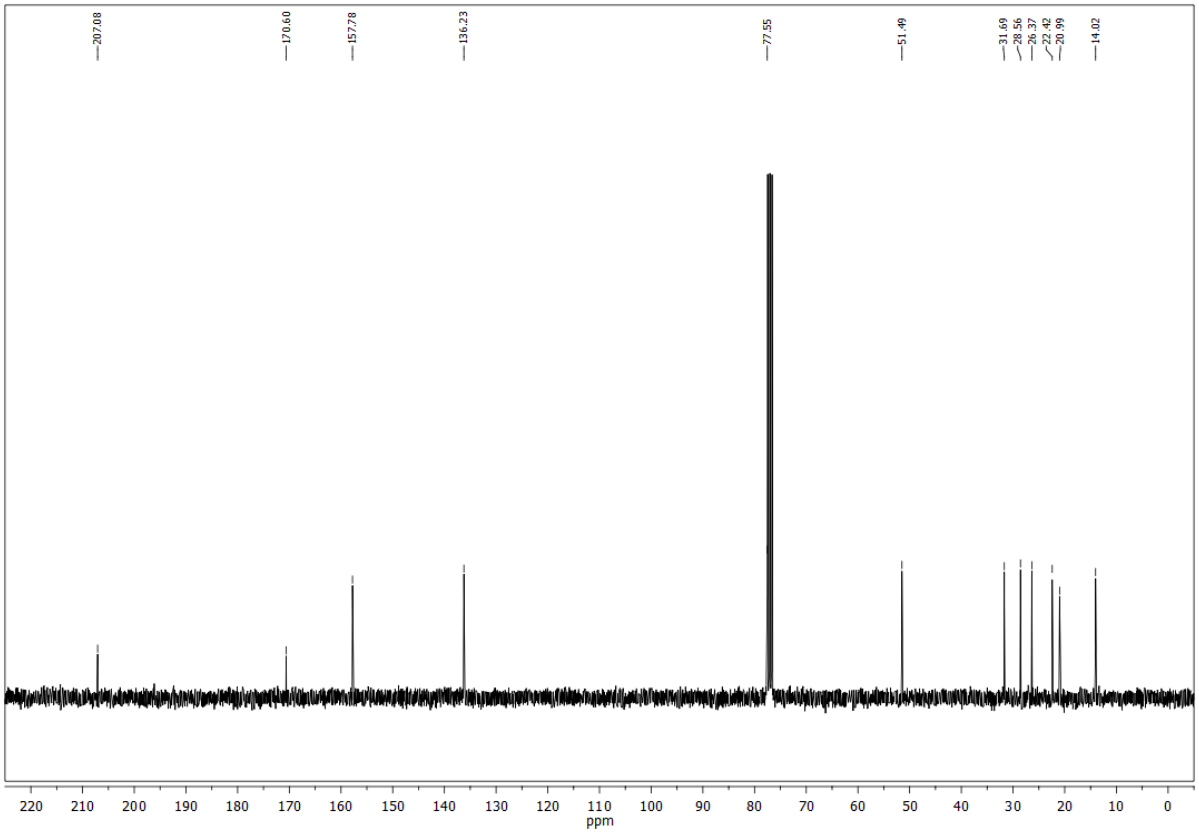


4-Oxo-5-pentylcyclopent-2-en-1-yl acetate ((±)-154b)

^{1}H NMR (300 MHz, $CDCl_3$)

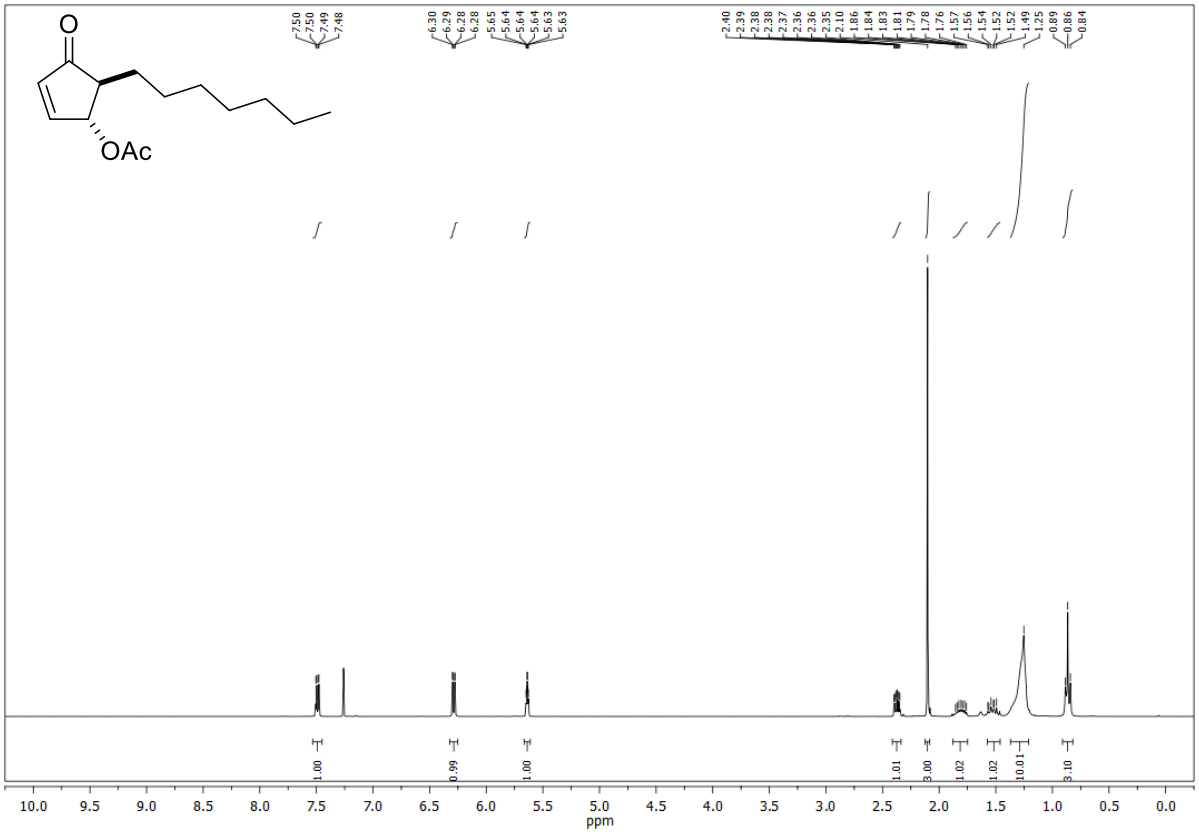


^{13}C NMR (75 MHz, $CDCl_3$)

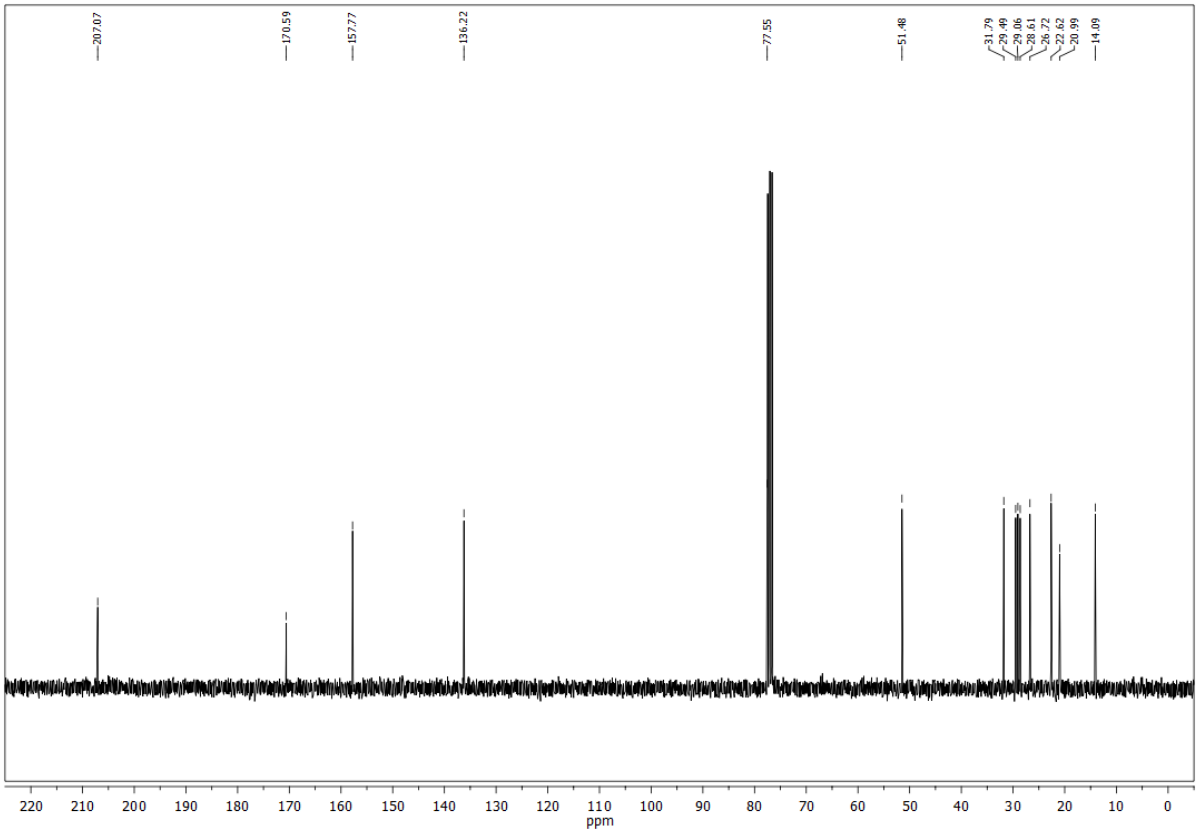


5-Heptyl-4-oxocyclopent-2-en-1-yl acetate ((±)-154c)

^{1}H NMR (300 MHz, $CDCl_3$)

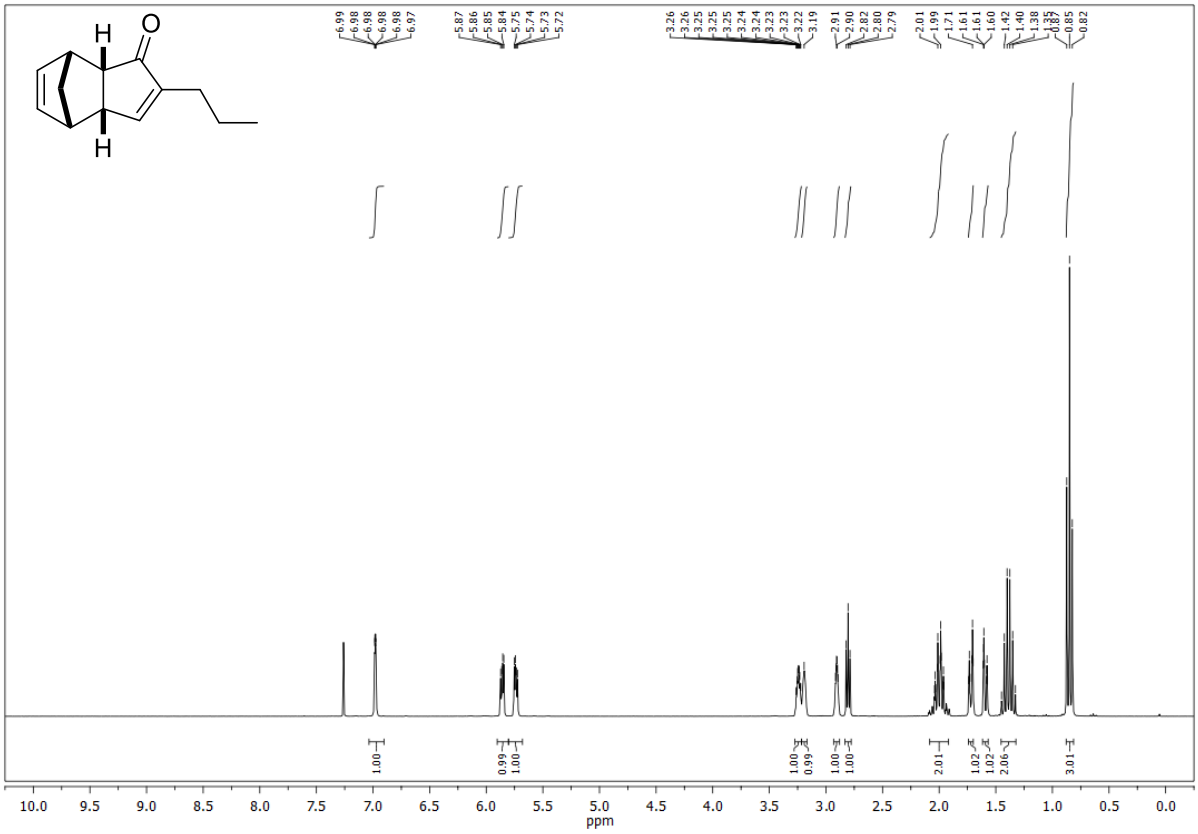


^{13}C NMR (75 MHz, $CDCl_3$)

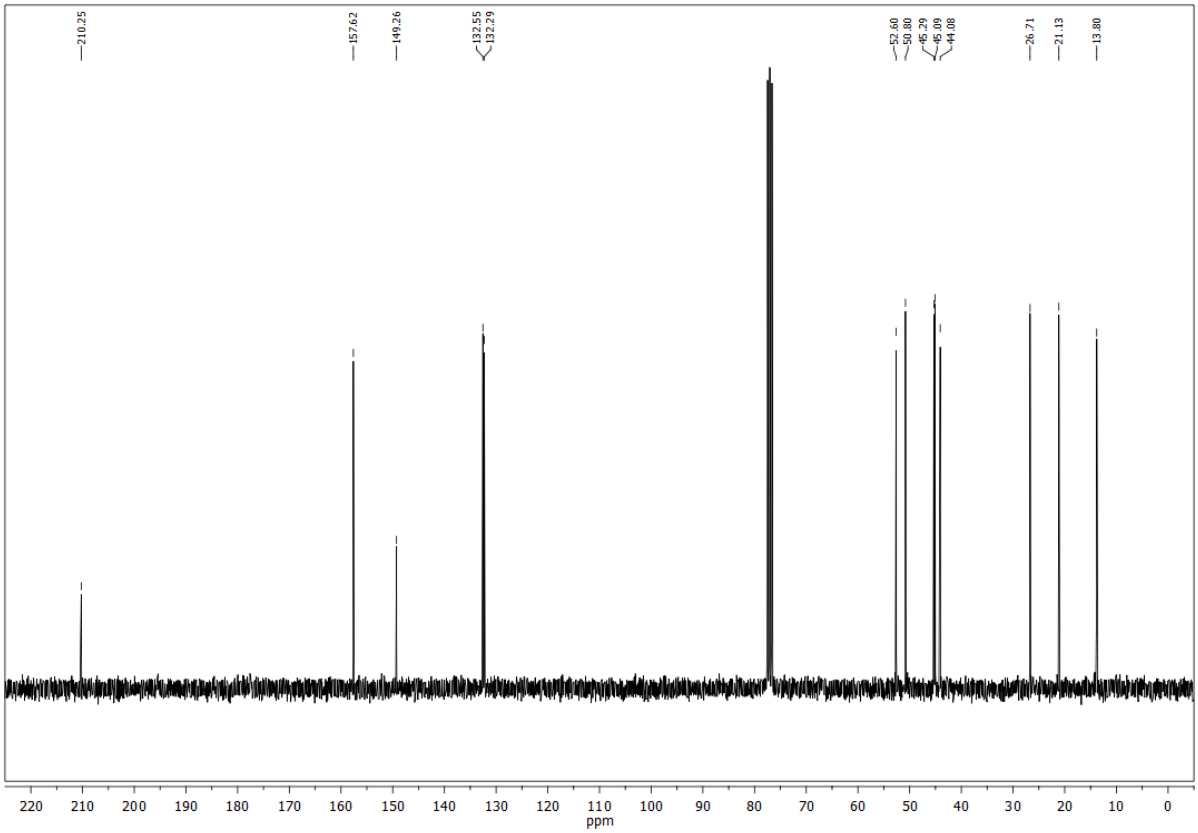


2-Propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-155a)

^{1}H NMR (300 MHz, $CDCl_3$)

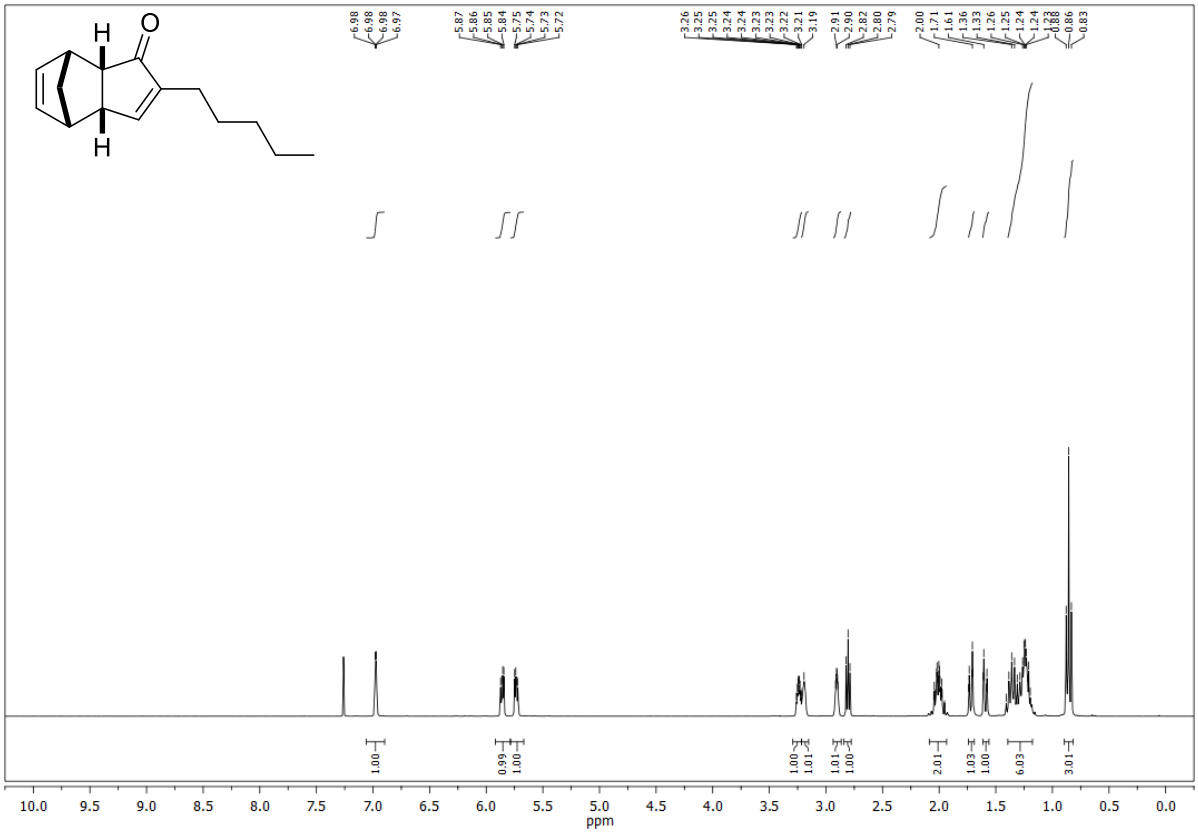


^{13}C NMR (75 MHz, $CDCl_3$)

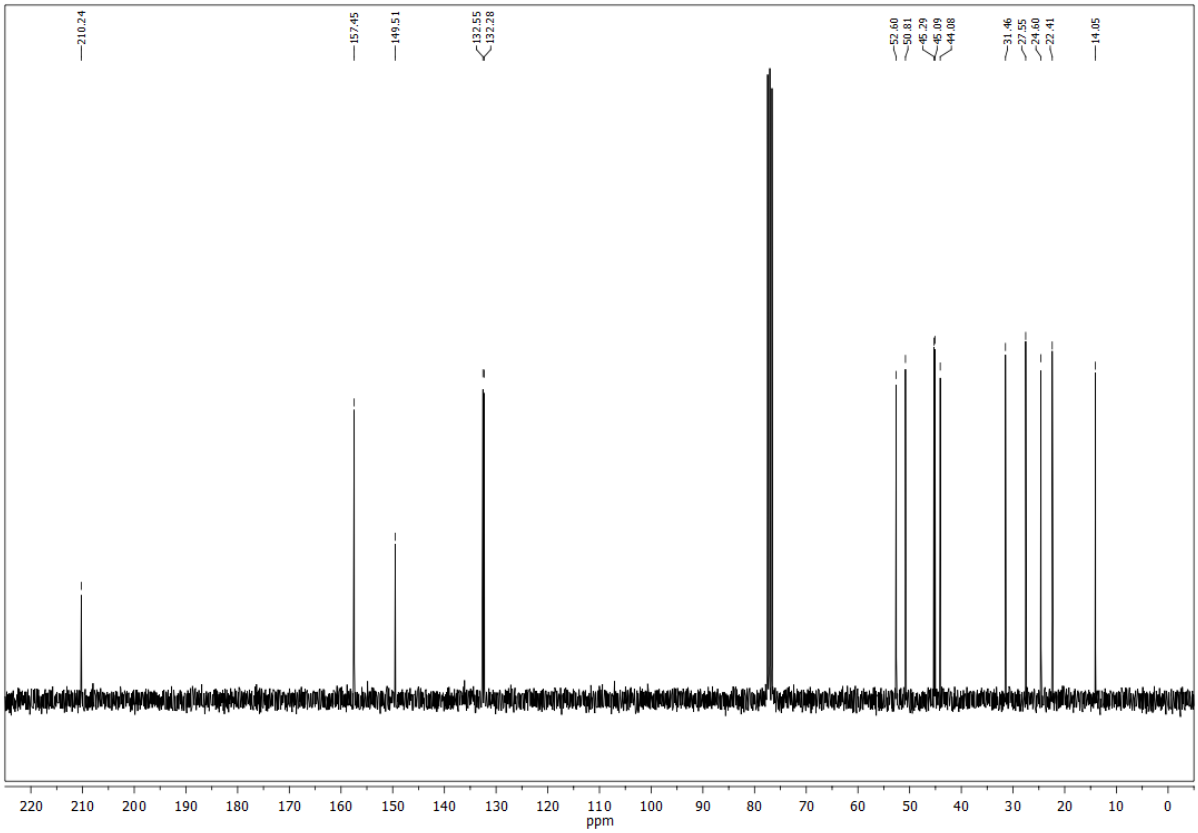


2-Pentyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-155b)

^{1}H NMR (300 MHz, $CDCl_3$)

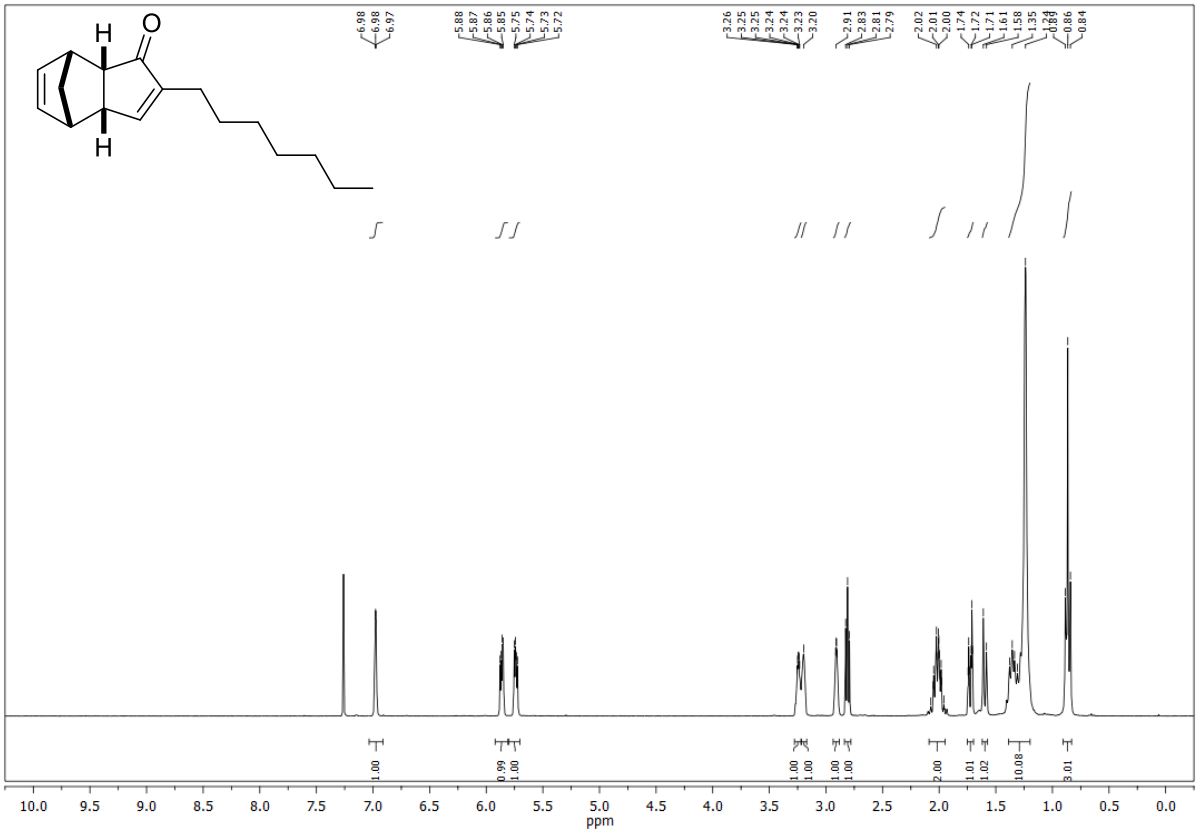


^{13}C NMR (75 MHz, $CDCl_3$)

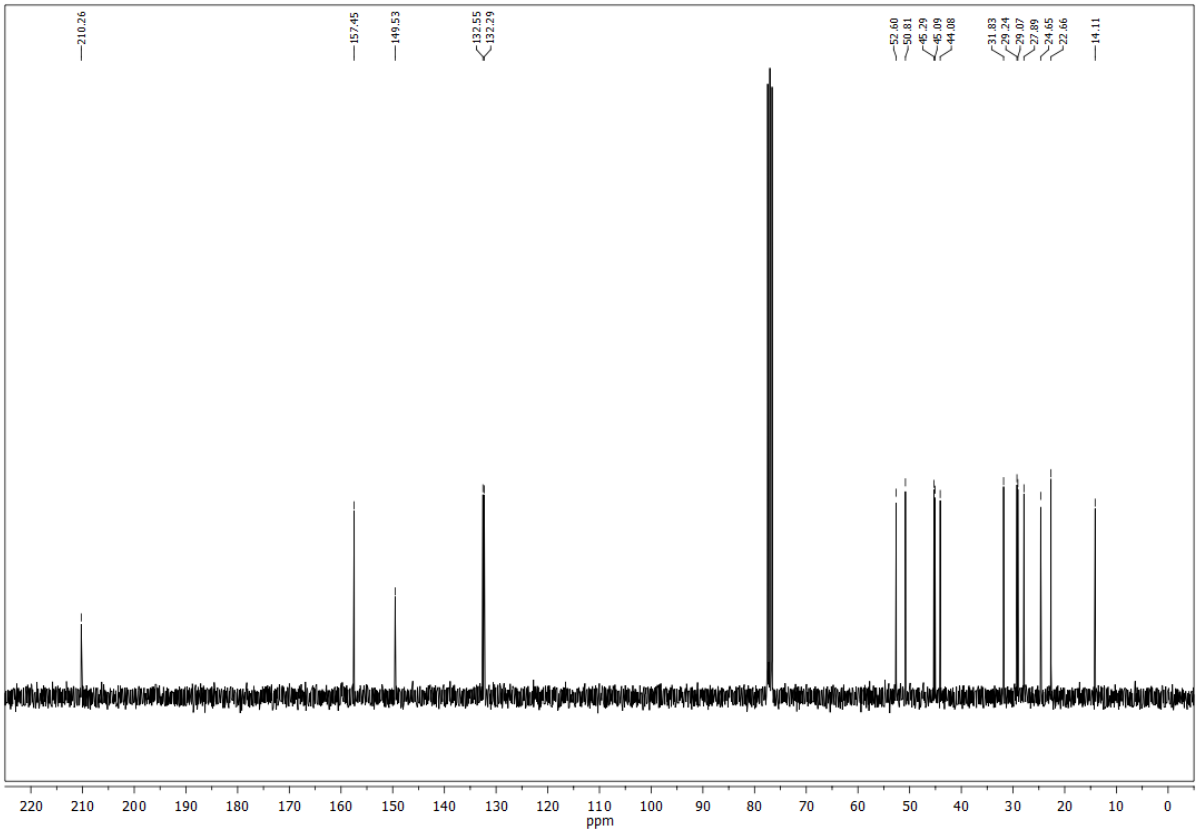


2-Heptyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-155c)

^{1}H NMR (300 MHz, $CDCl_3$)



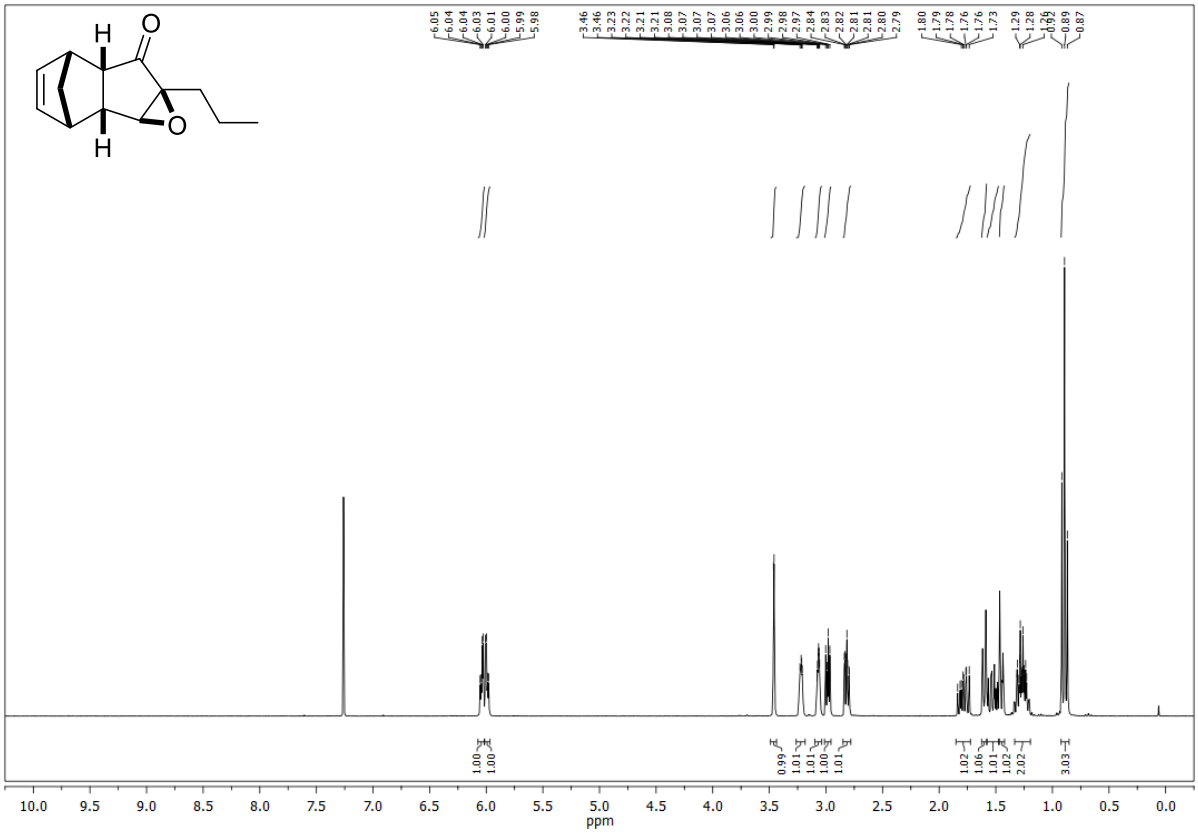
^{13}C NMR (75 MHz, $CDCl_3$)



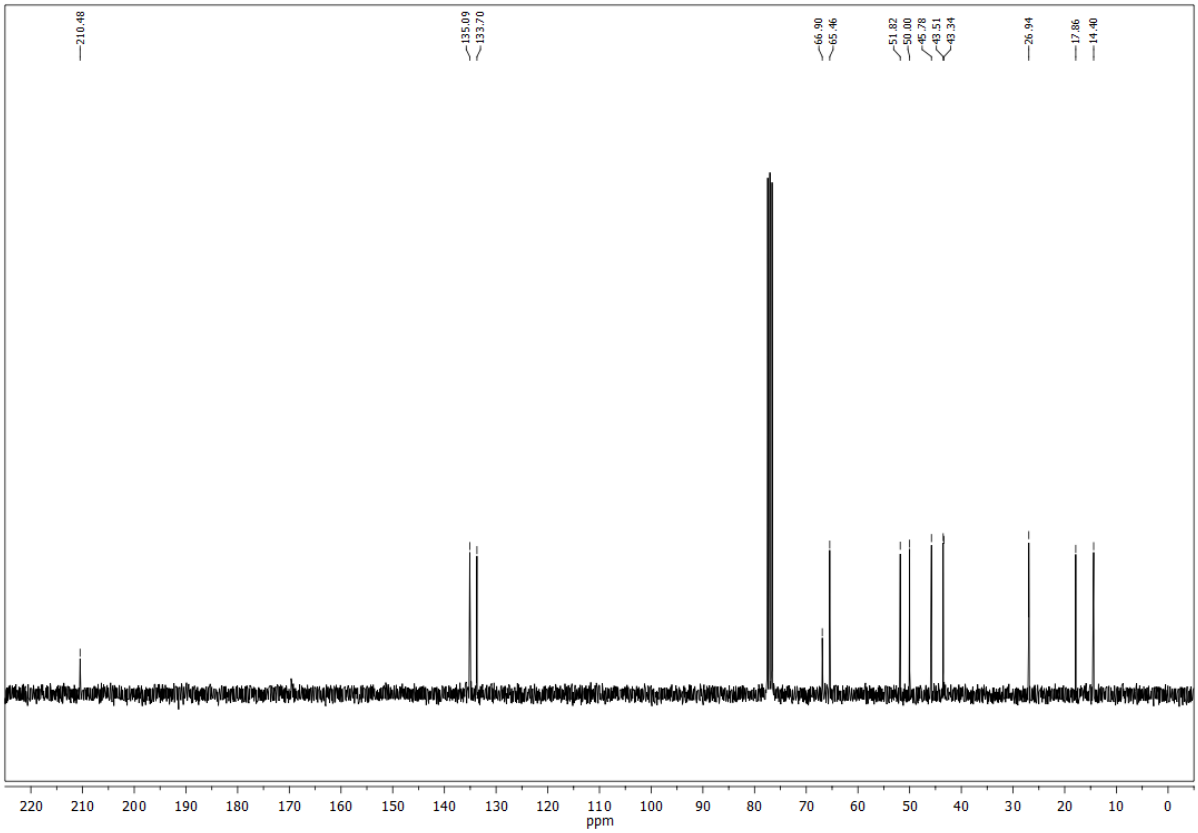
6a-Propyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one

((±)-156a)

^{1}H NMR (300 MHz, $CDCl_3$)

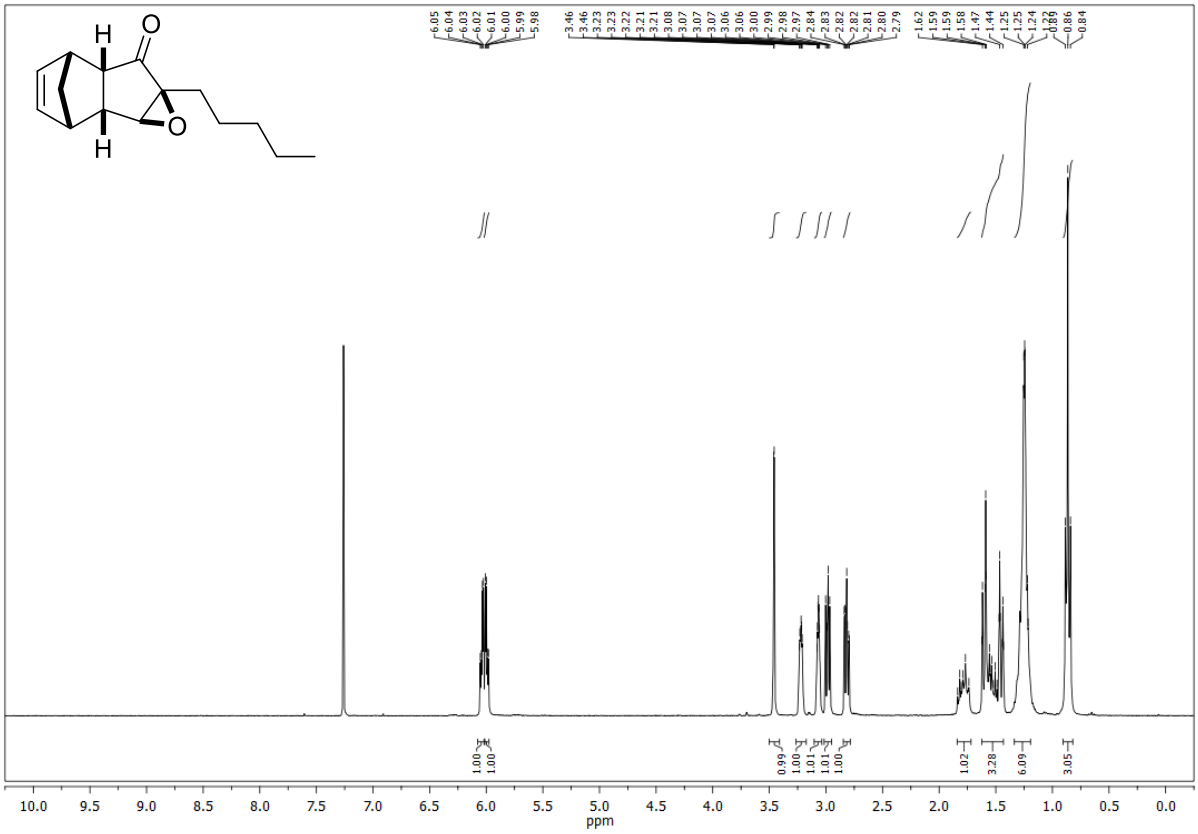


^{13}C NMR (75 MHz, $CDCl_3$)

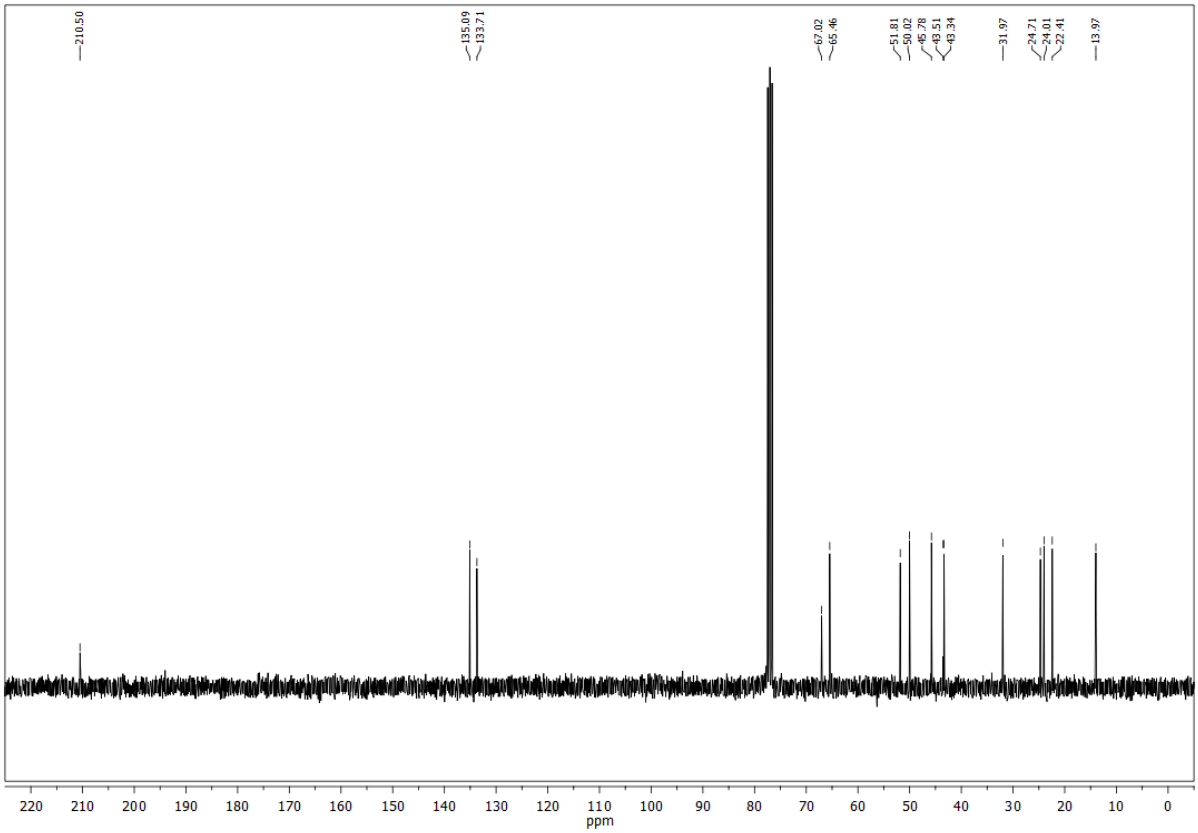


6a-Pentyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one

((±)-156b) **^{1}H NMR** (300 MHz, $CDCl_3$)



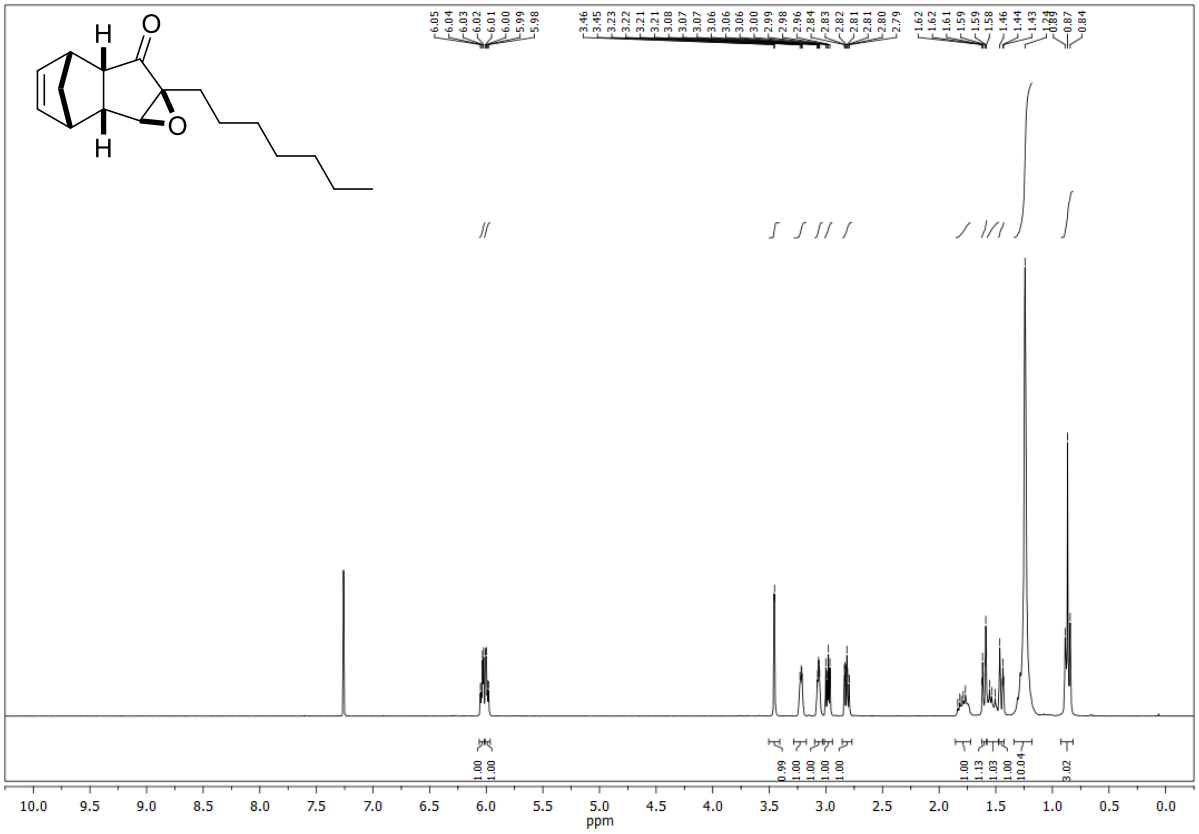
^{13}C NMR (75 MHz, $CDCl_3$)



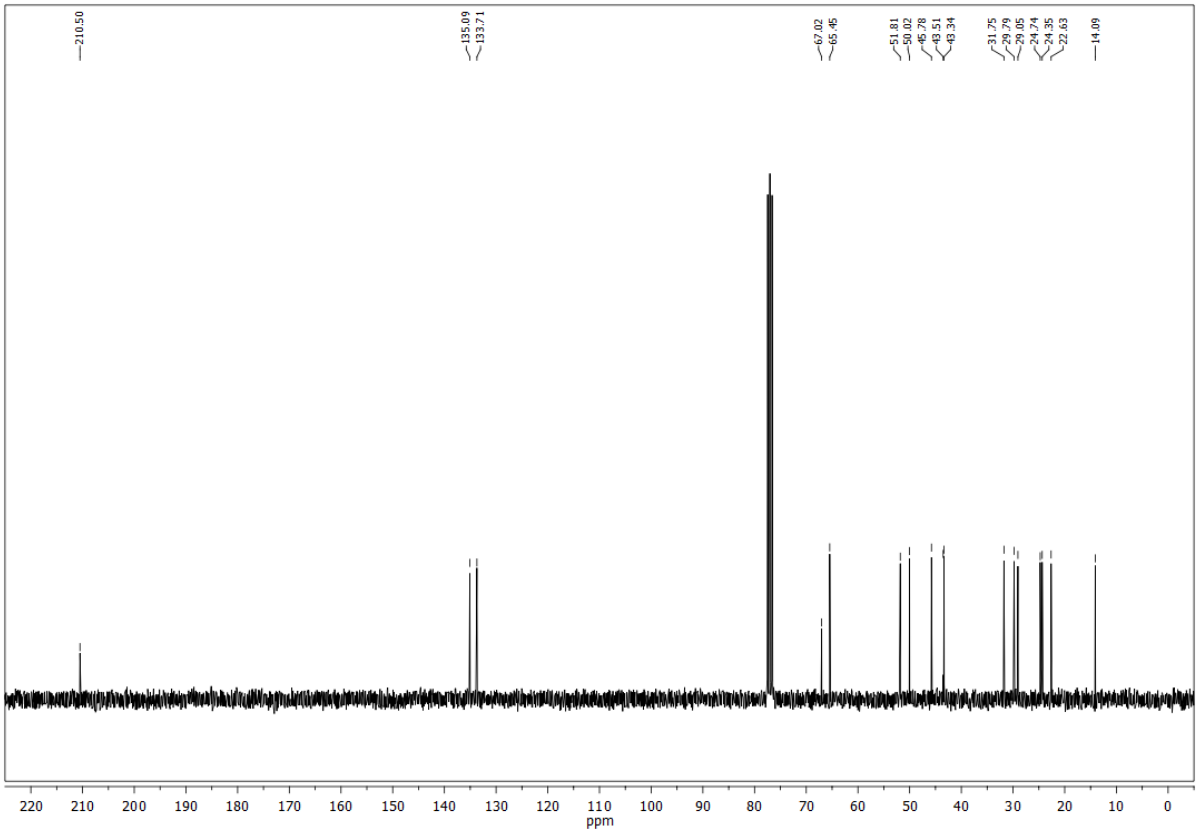
6a-Heptyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one

((±)-156c)

^{1}H NMR (300 MHz, $CDCl_3$)

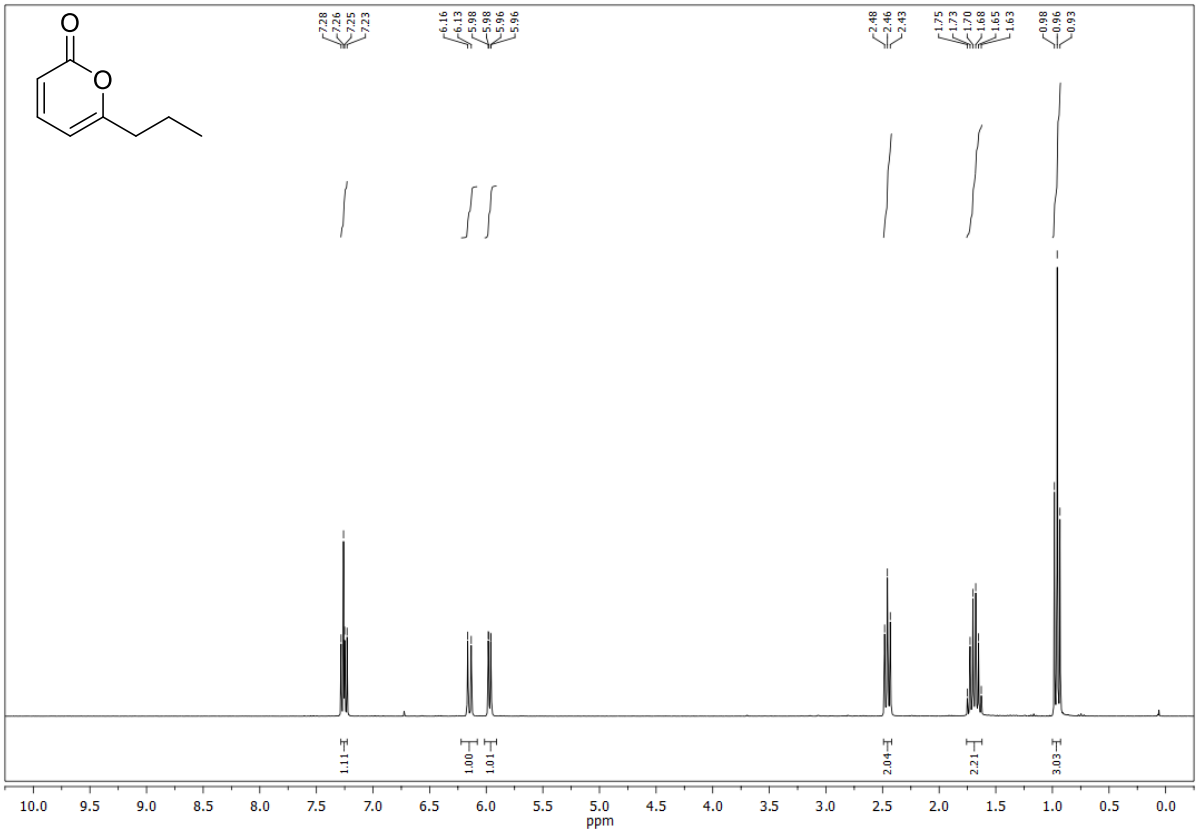


^{13}C NMR (75 MHz, $CDCl_3$)

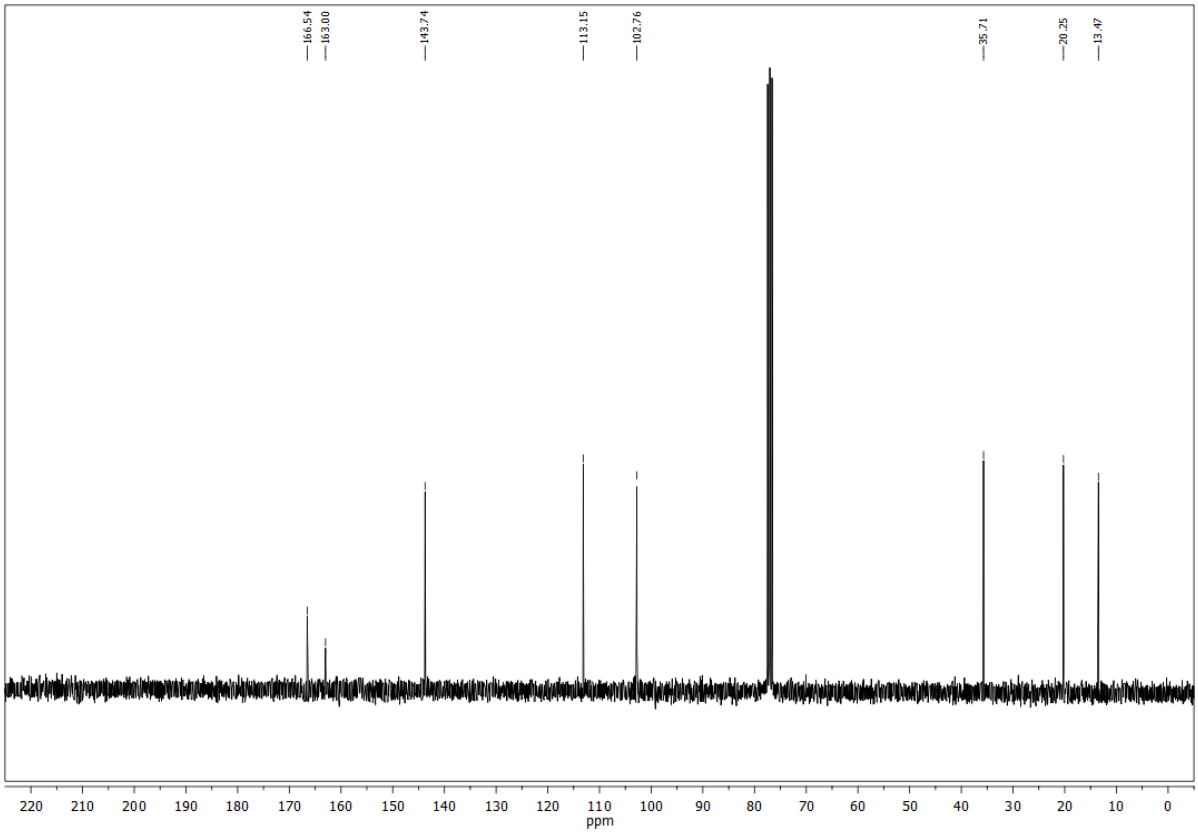


6-Propyl-2*H*-pyran-2-one (2a)

^{1}H NMR (300 MHz, $CDCl_3$)

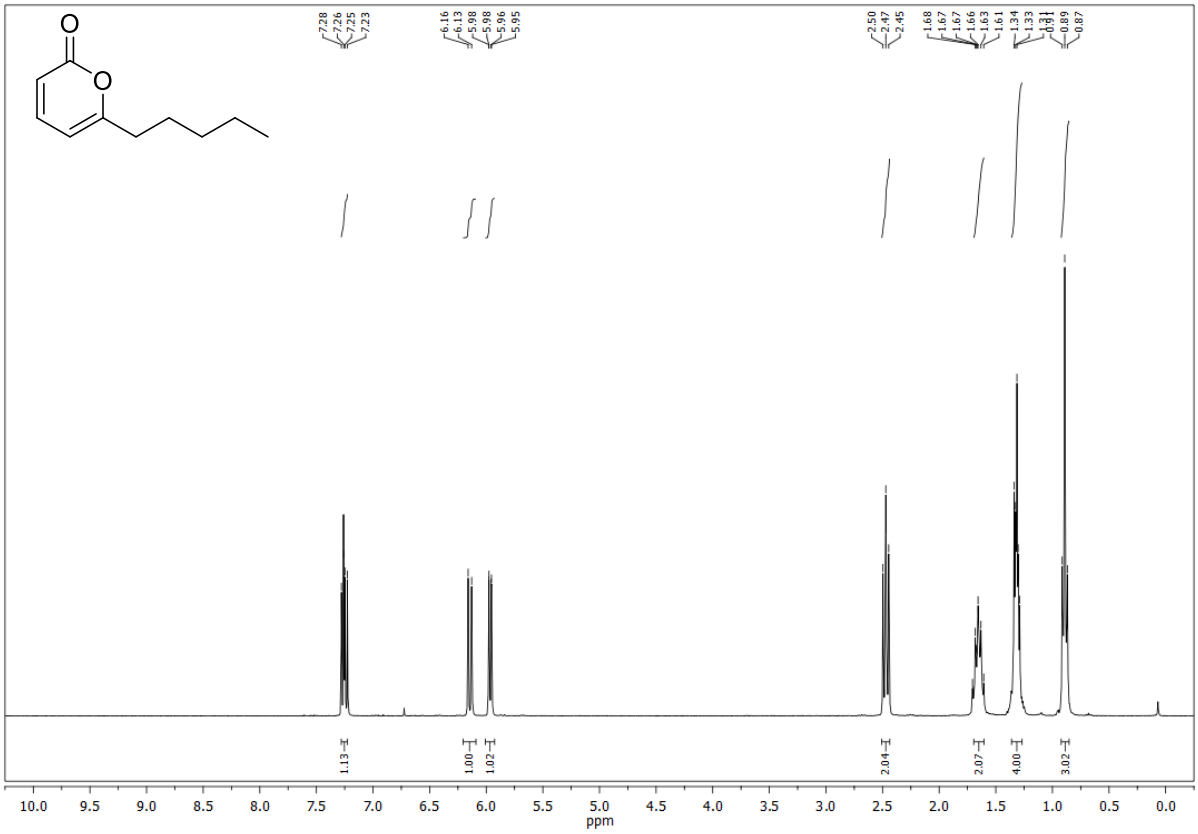


^{13}C NMR (75 MHz, $CDCl_3$)

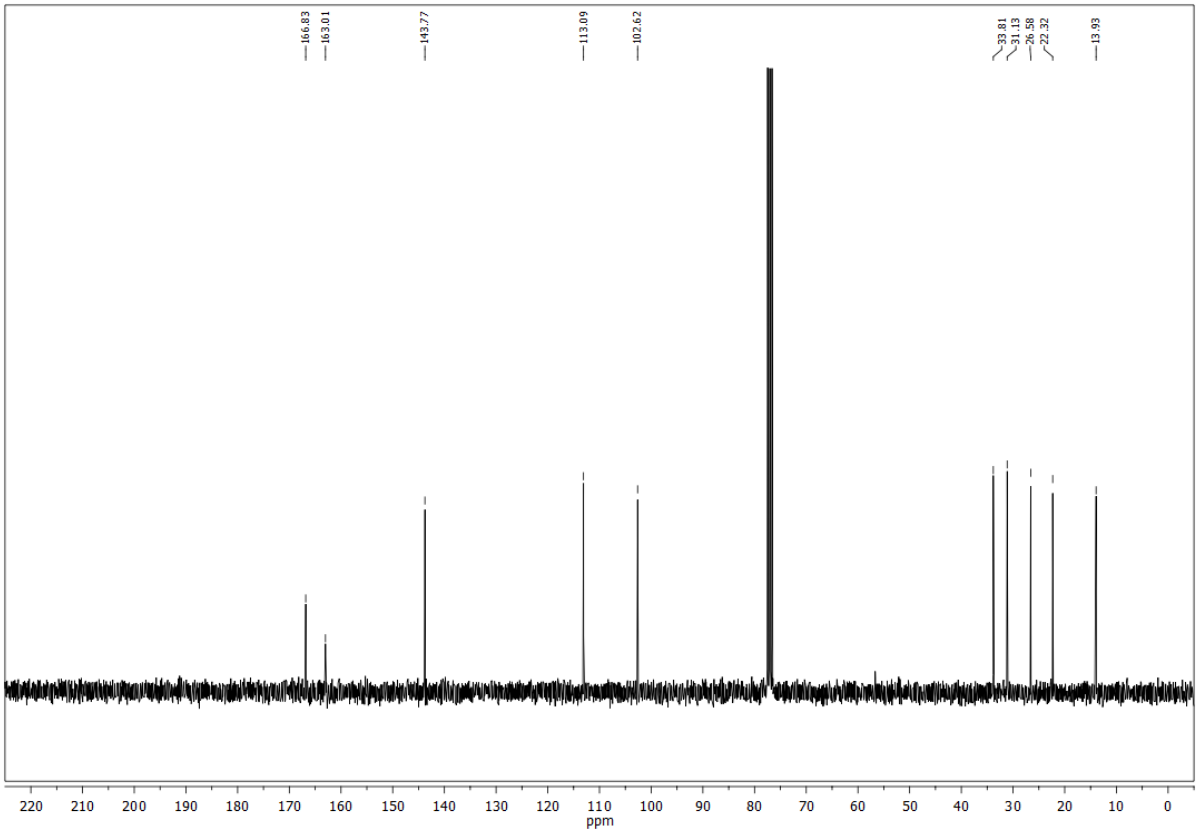


6-Pentyl-2*H*-pyran-2-one (2b)

^{1}H NMR (300 MHz, $CDCl_3$)

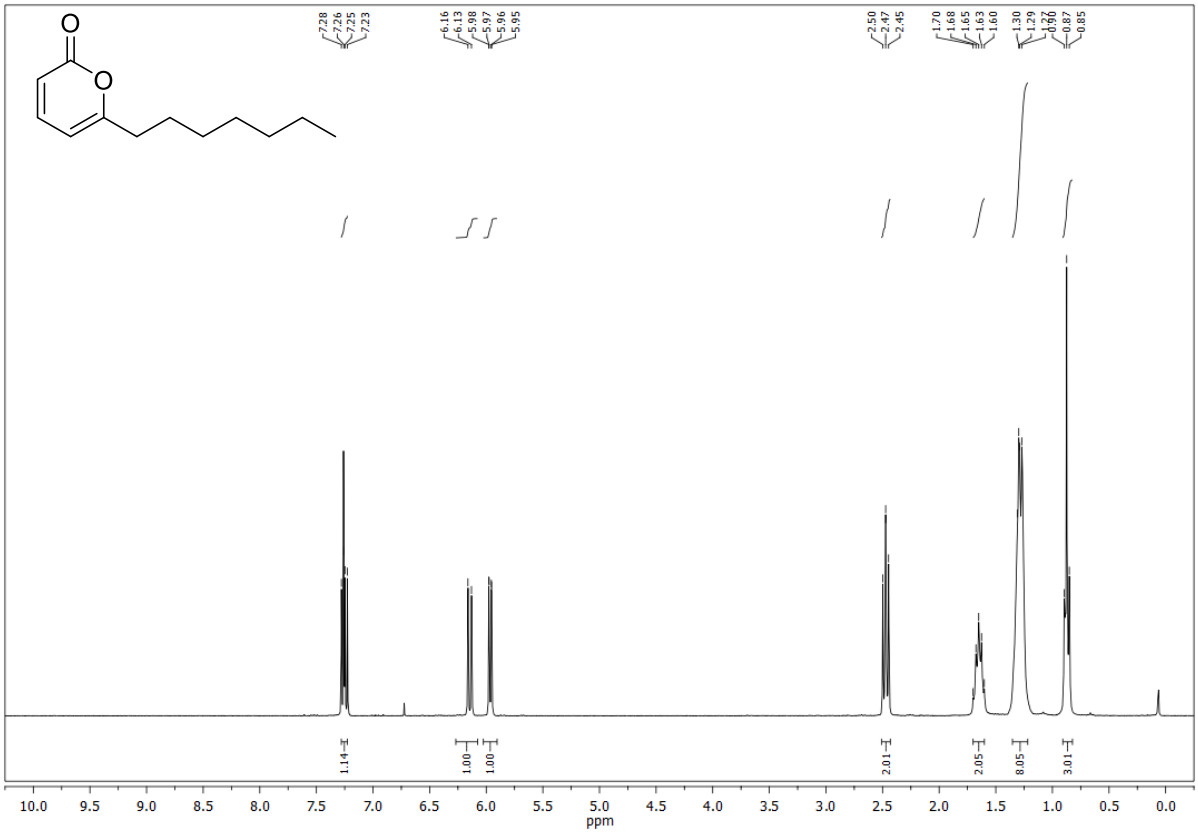


^{13}C NMR (75 MHz, $CDCl_3$)

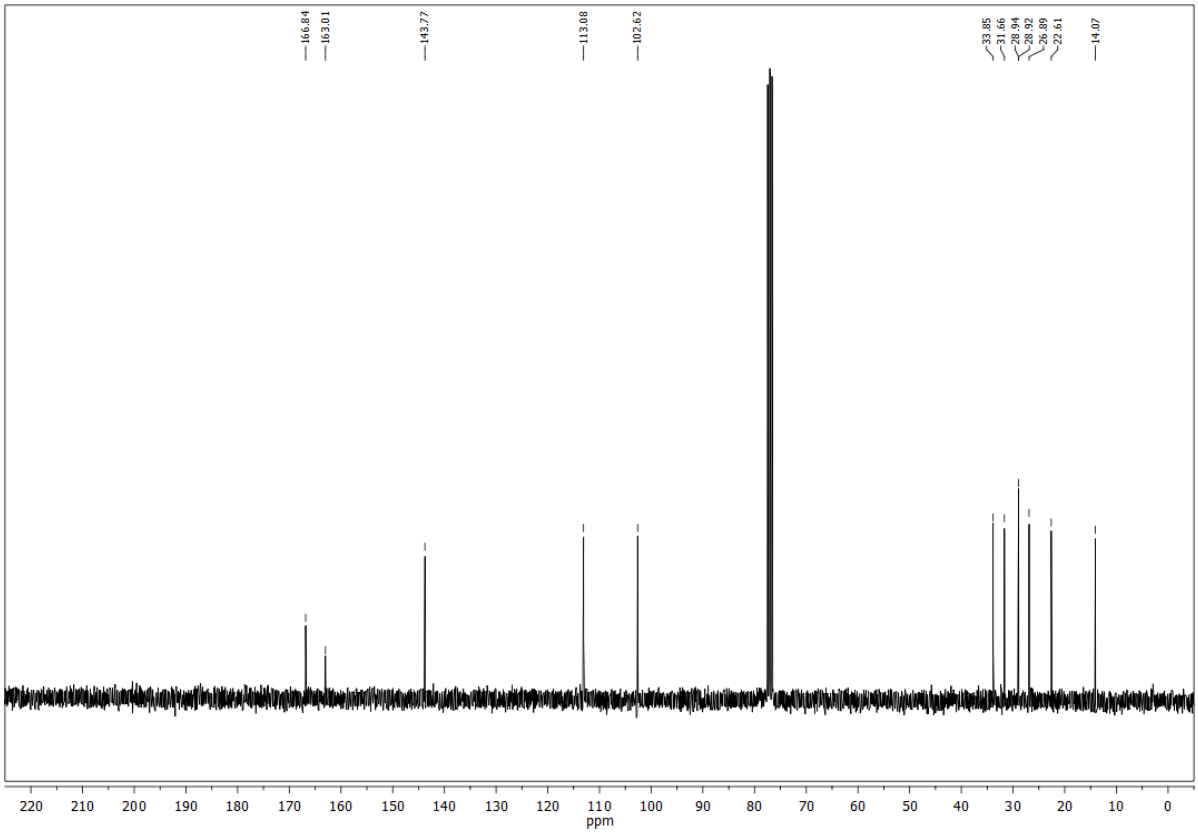


6-Heptyl-2*H*-pyran-2-one (2c)

^{1}H NMR (300 MHz, $CDCl_3$)

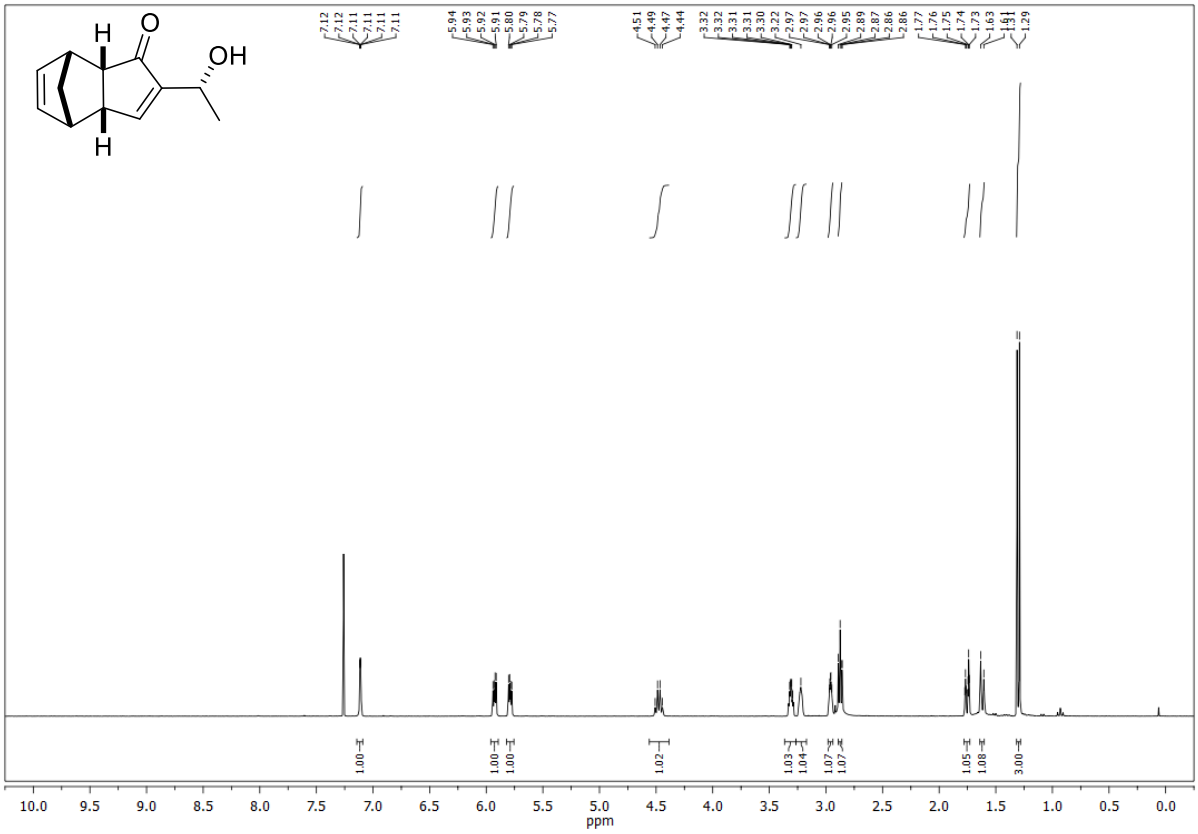


^{13}C NMR (75 MHz, $CDCl_3$)

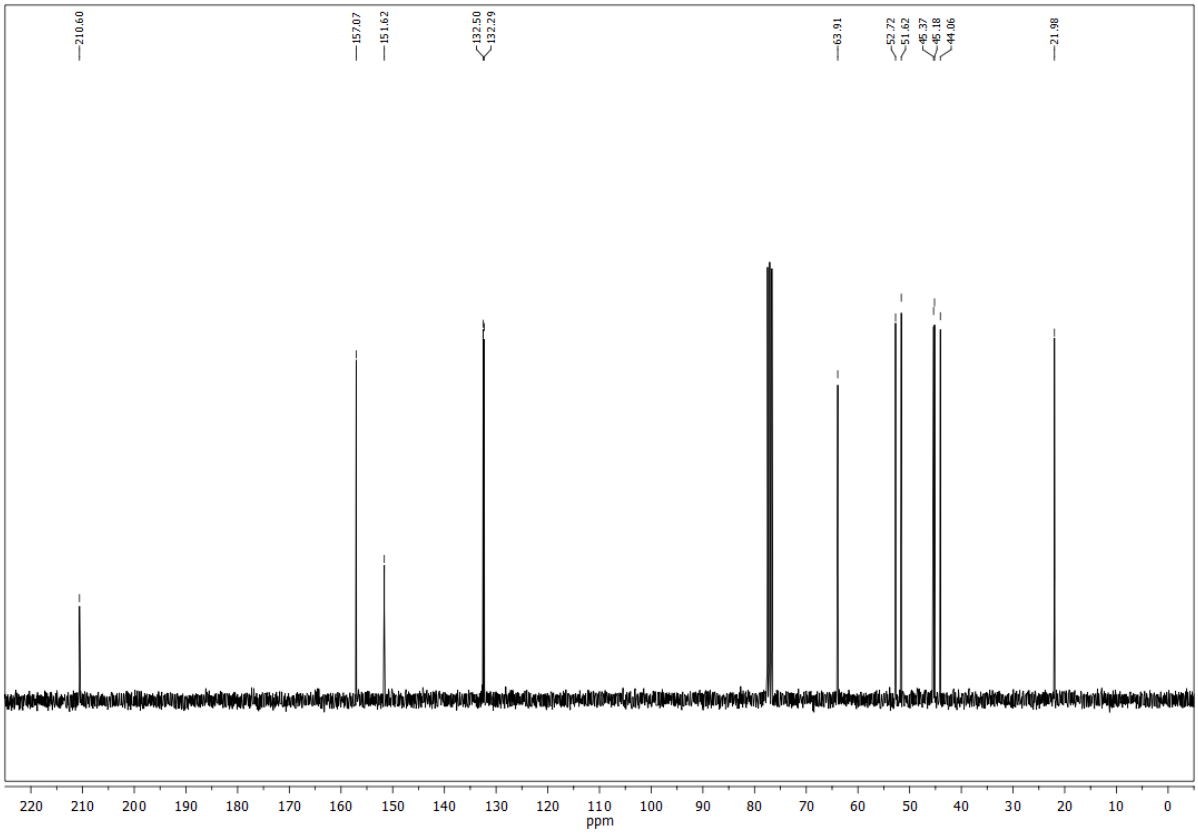


2-(1-Hydroxyethyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165a)

^{1}H NMR (300 MHz, $CDCl_3$)

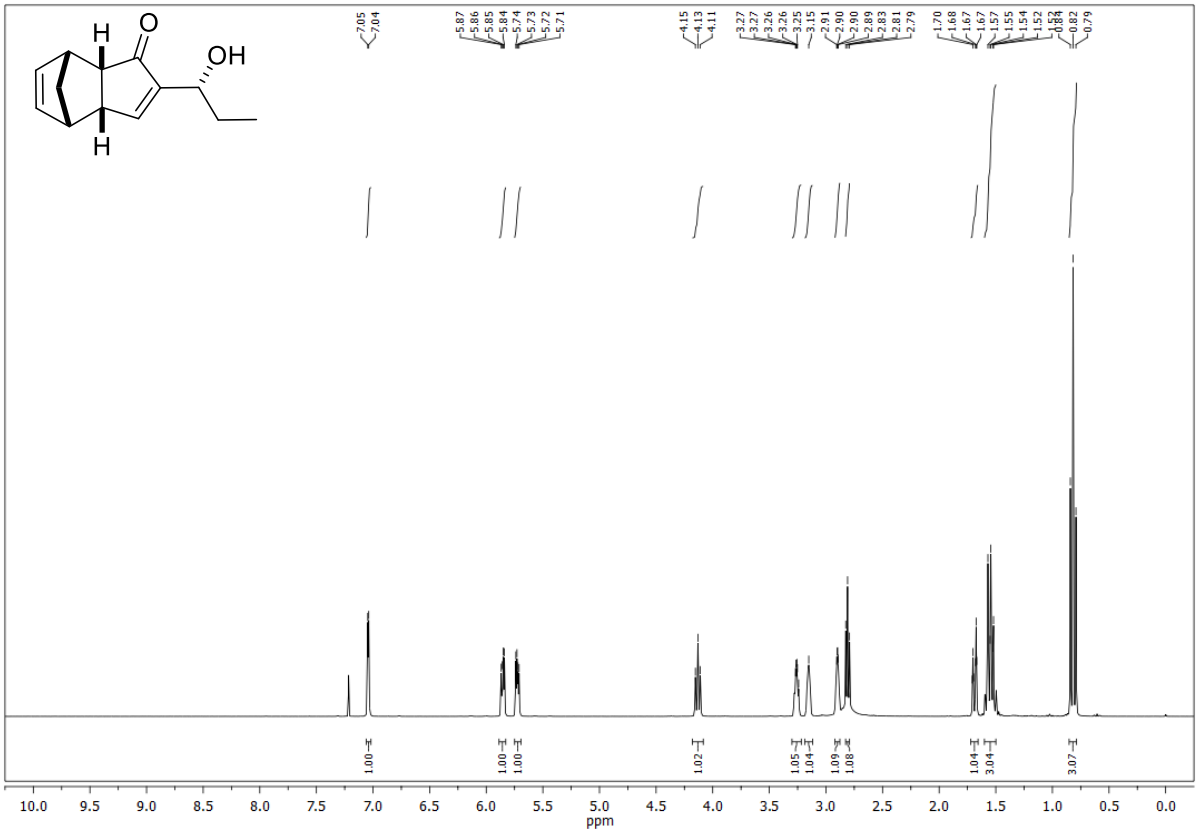


^{13}C NMR (75 MHz, $CDCl_3$)

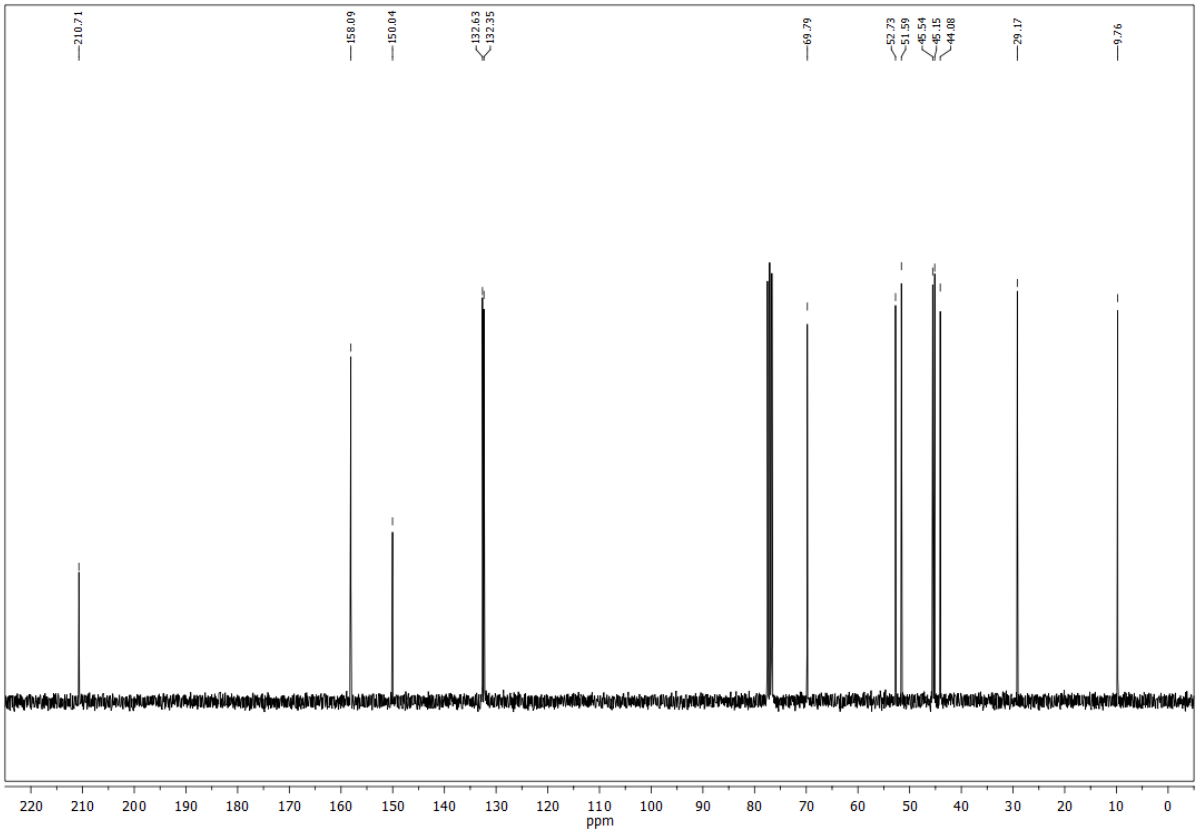


2-(1-Hydroxypropyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165b)

^{1}H NMR (300 MHz, $CDCl_3$)

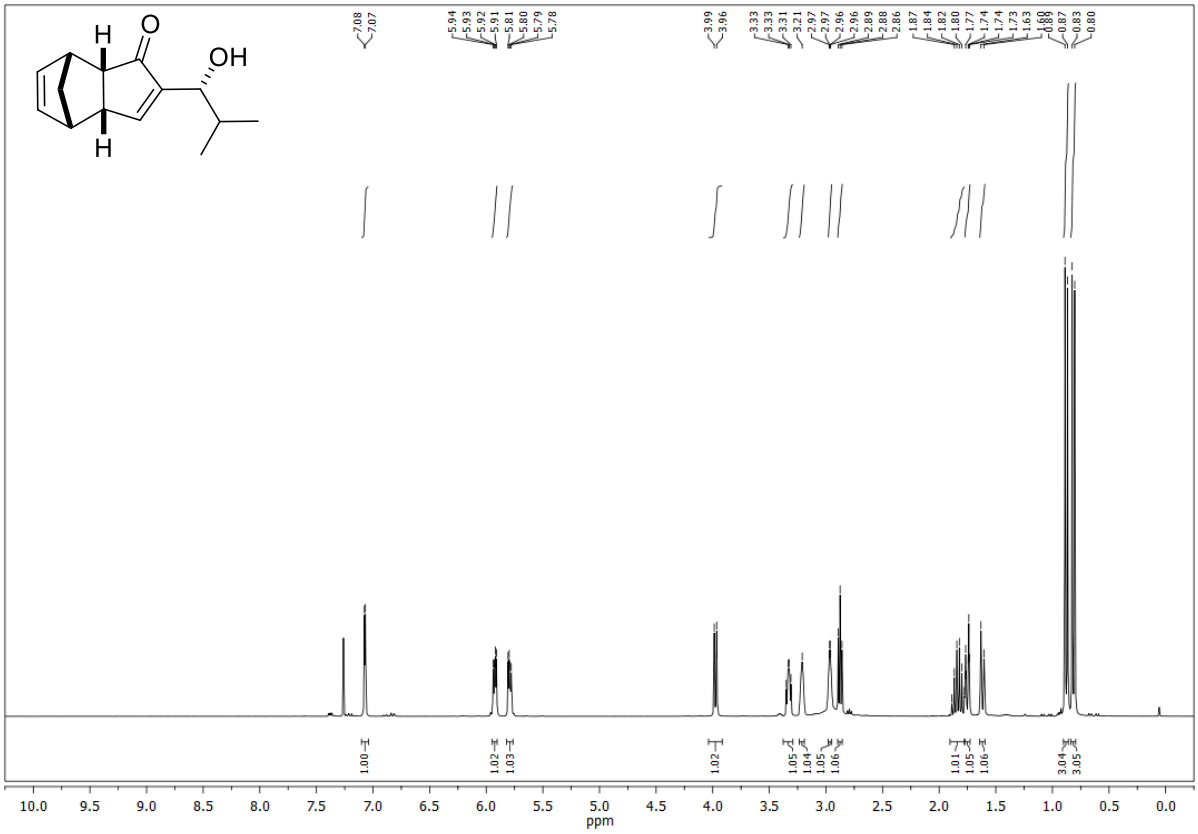


^{13}C NMR (75 MHz, $CDCl_3$)

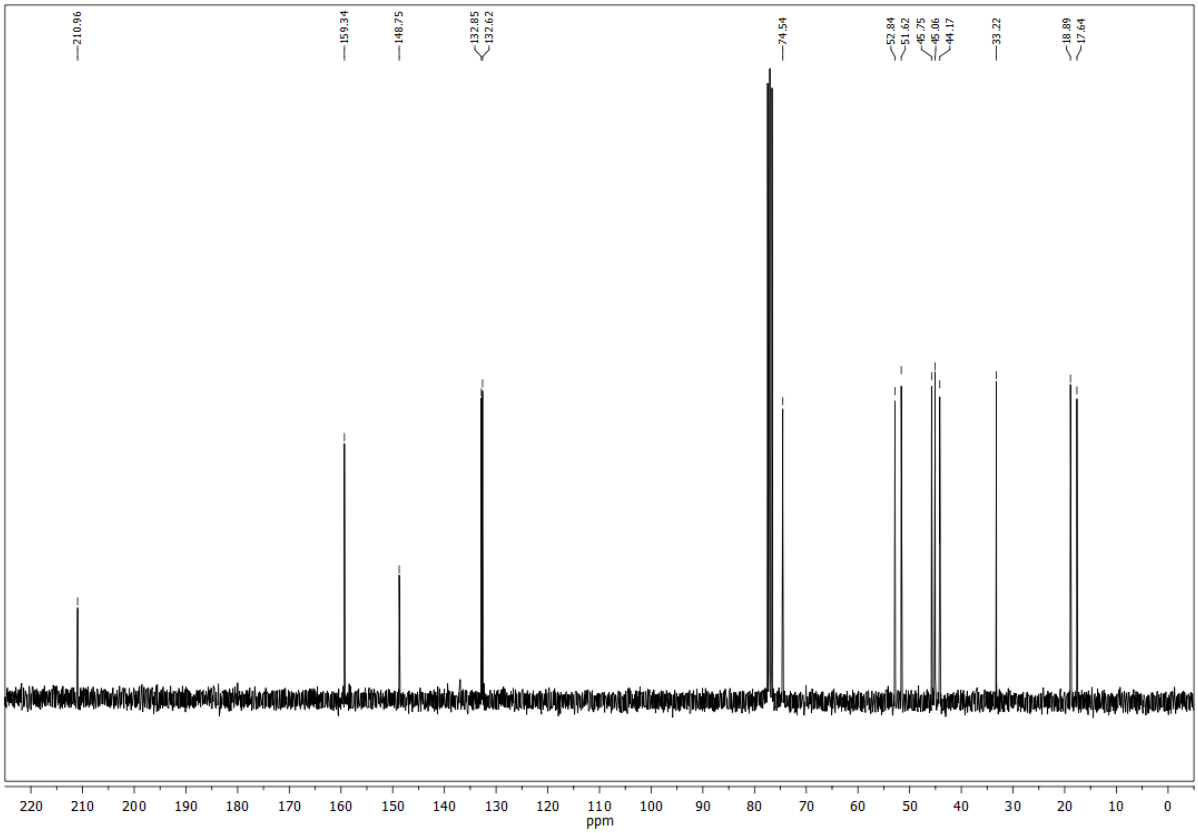


2-(1-Hydroxy-2-methylpropyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one

((±)-165c) **^{1}H NMR** (300 MHz, $CDCl_3$)

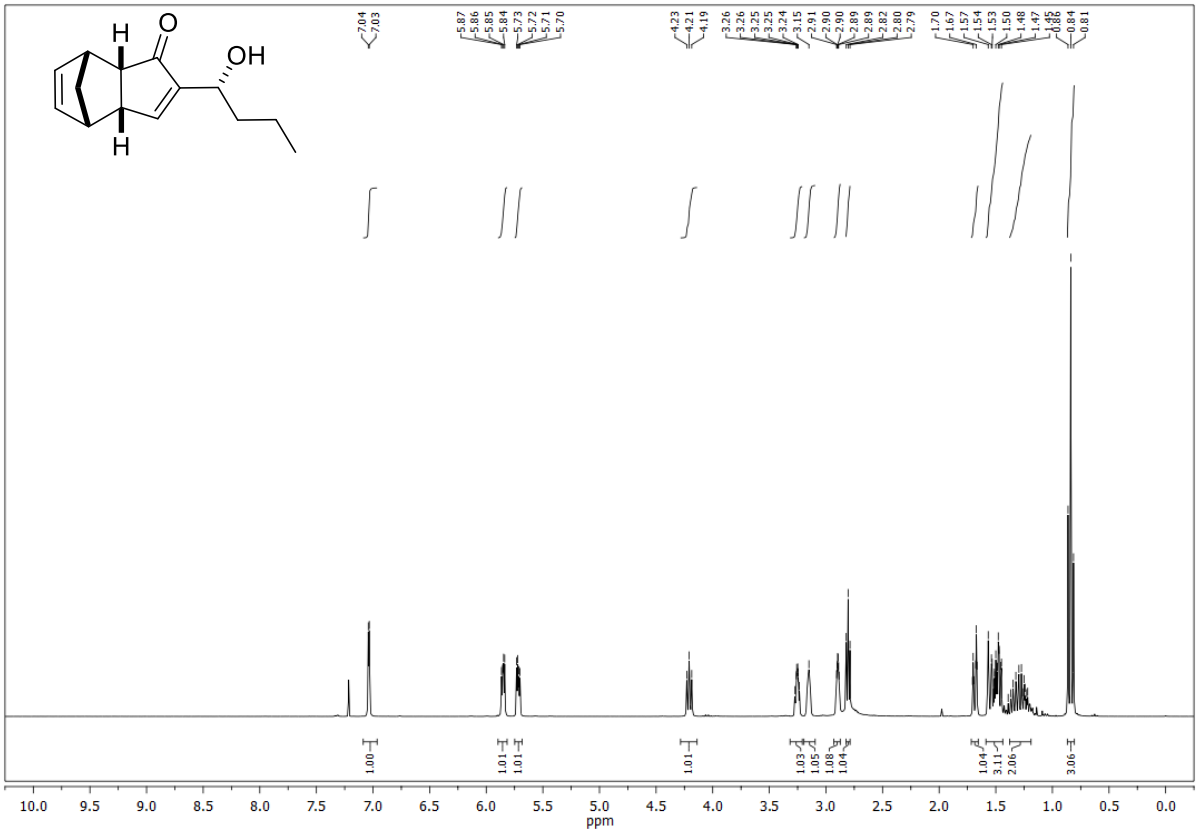


^{13}C NMR (75 MHz, $CDCl_3$)

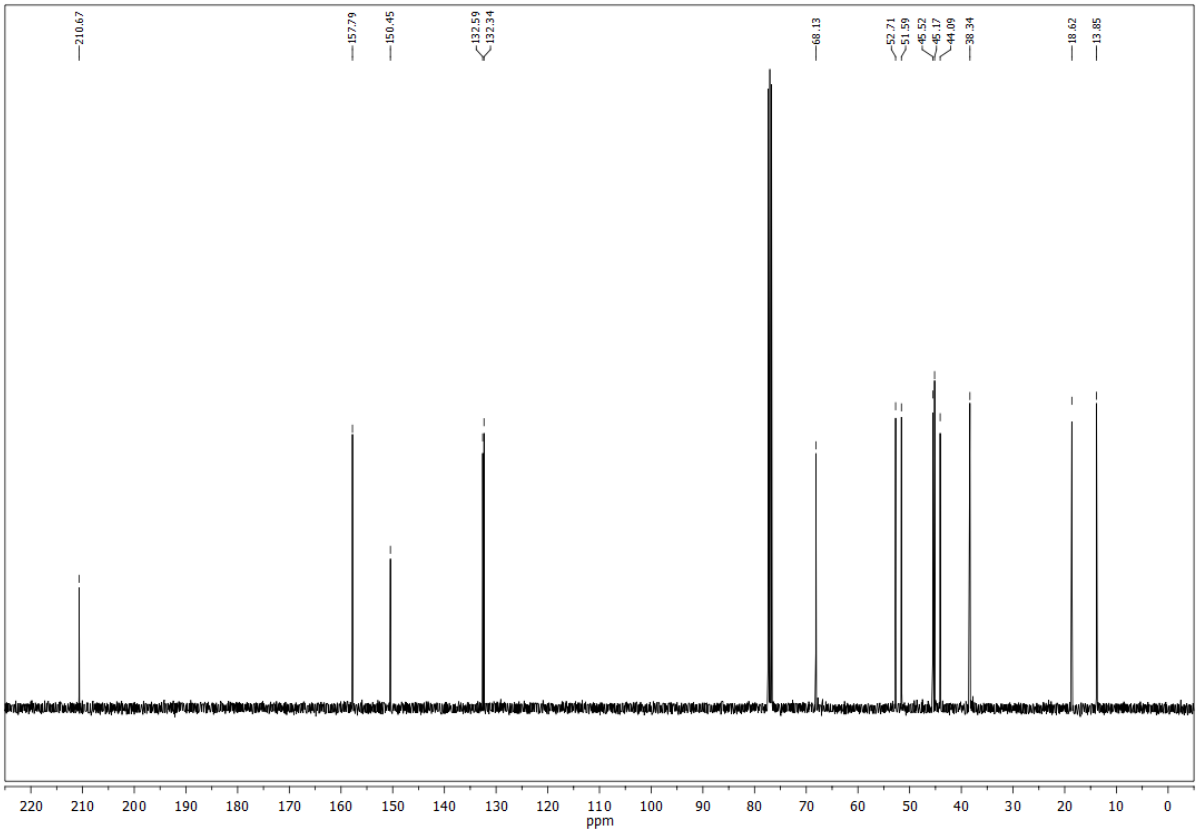


2-(1-Hydroxybutyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165d)

^{1}H NMR (300 MHz, $CDCl_3$)

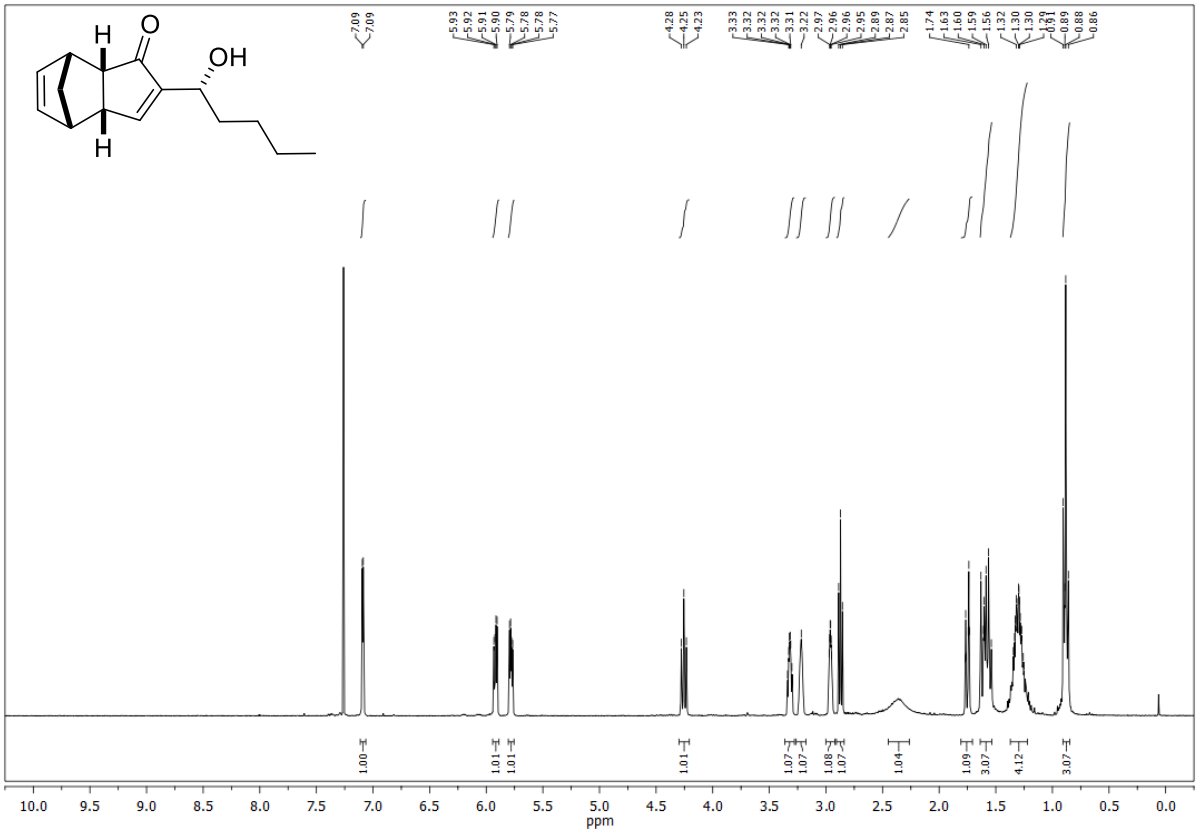


^{13}C NMR (75 MHz, $CDCl_3$)

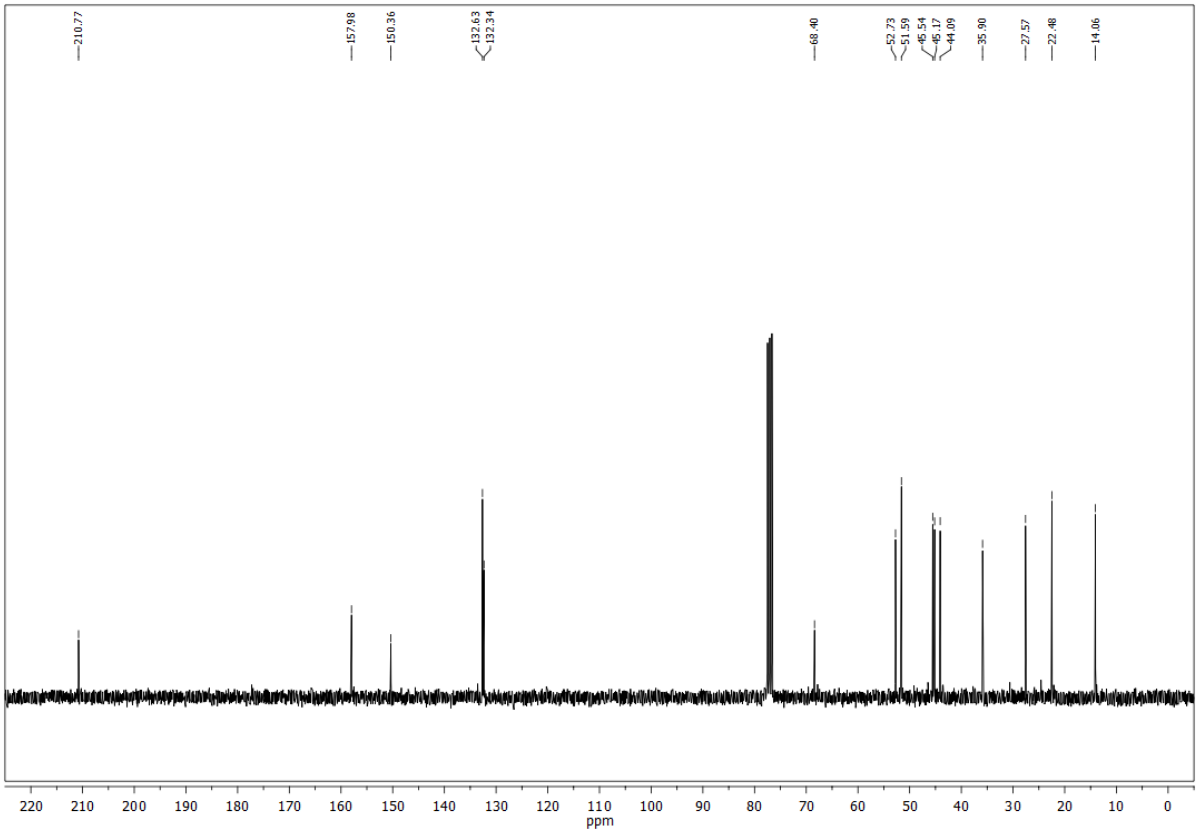


2-(1-Hydroxypentyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165e)

^{1}H NMR (300 MHz, $CDCl_3$)

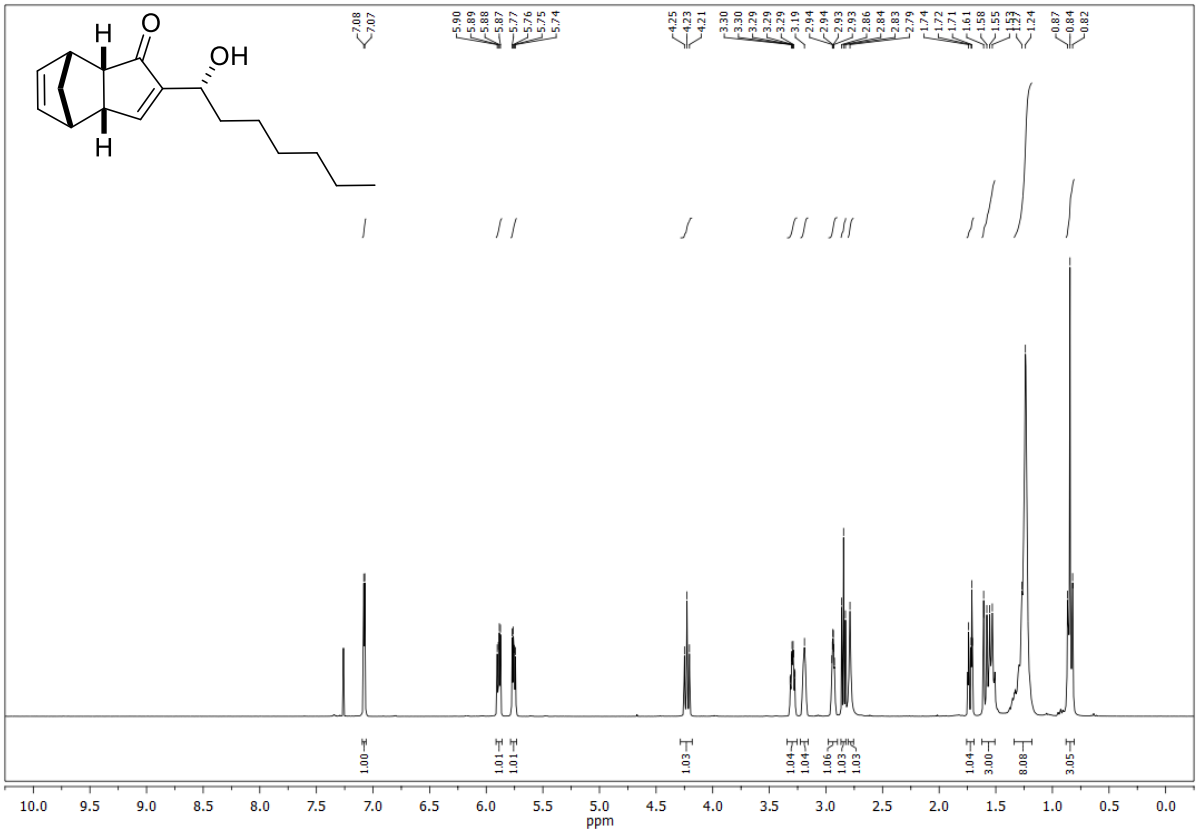


^{13}C NMR (75 MHz, $CDCl_3$)

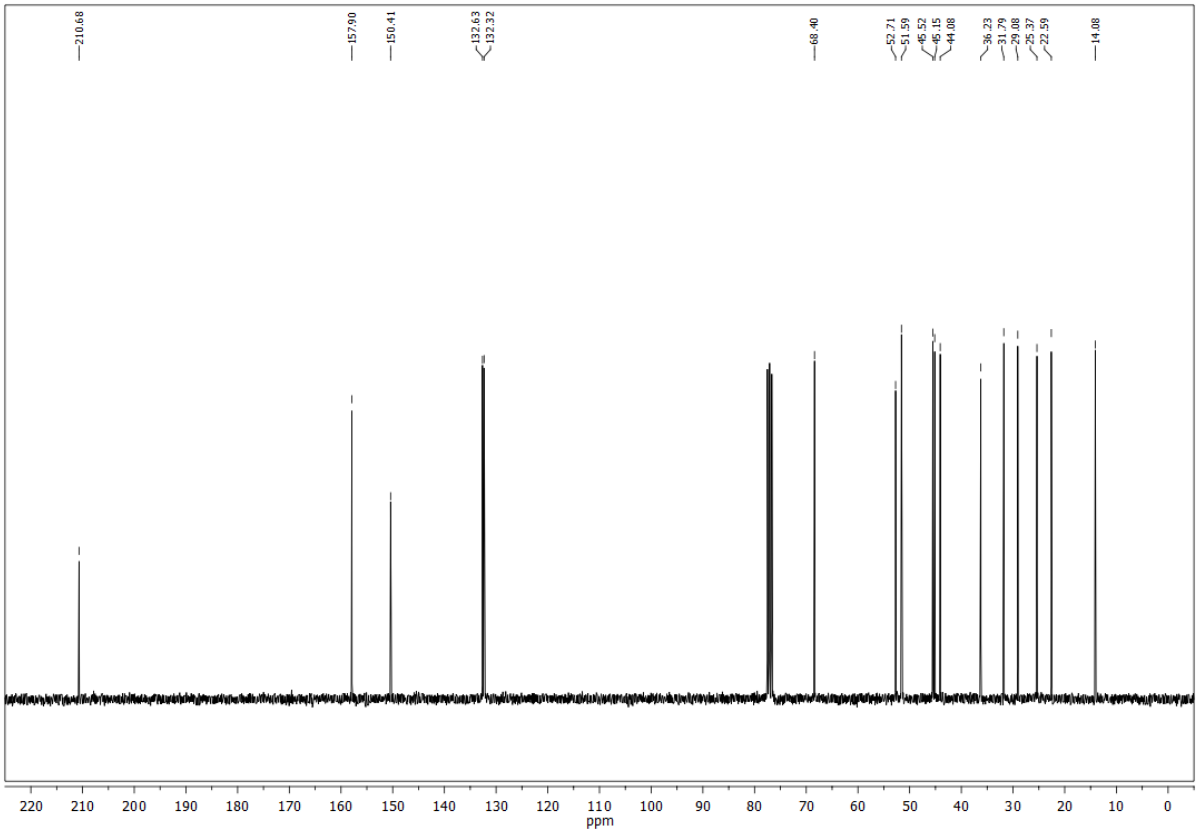


2-(1-Hydroxyheptyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165f)

^{1}H NMR (300 MHz, $CDCl_3$)



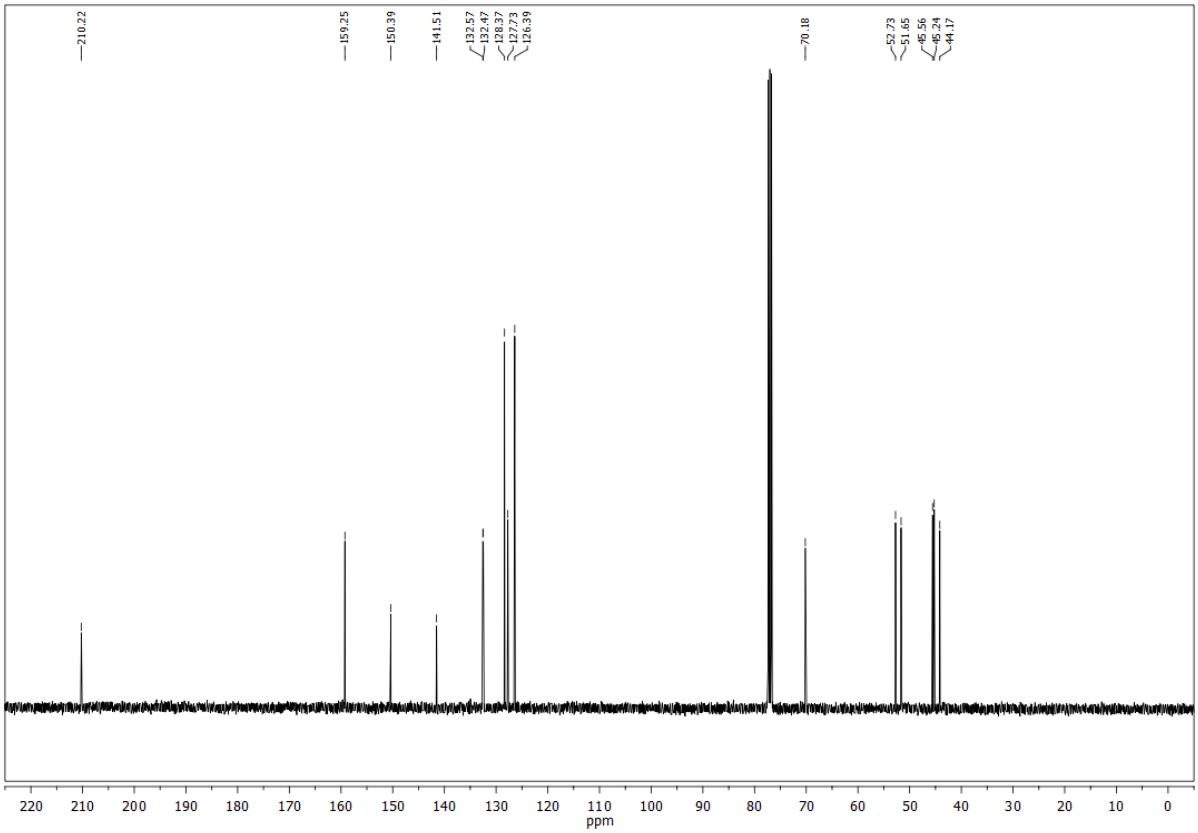
^{13}C NMR (75 MHz, $CDCl_3$)



2-(Hydroxy(phenyl)methyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165g)

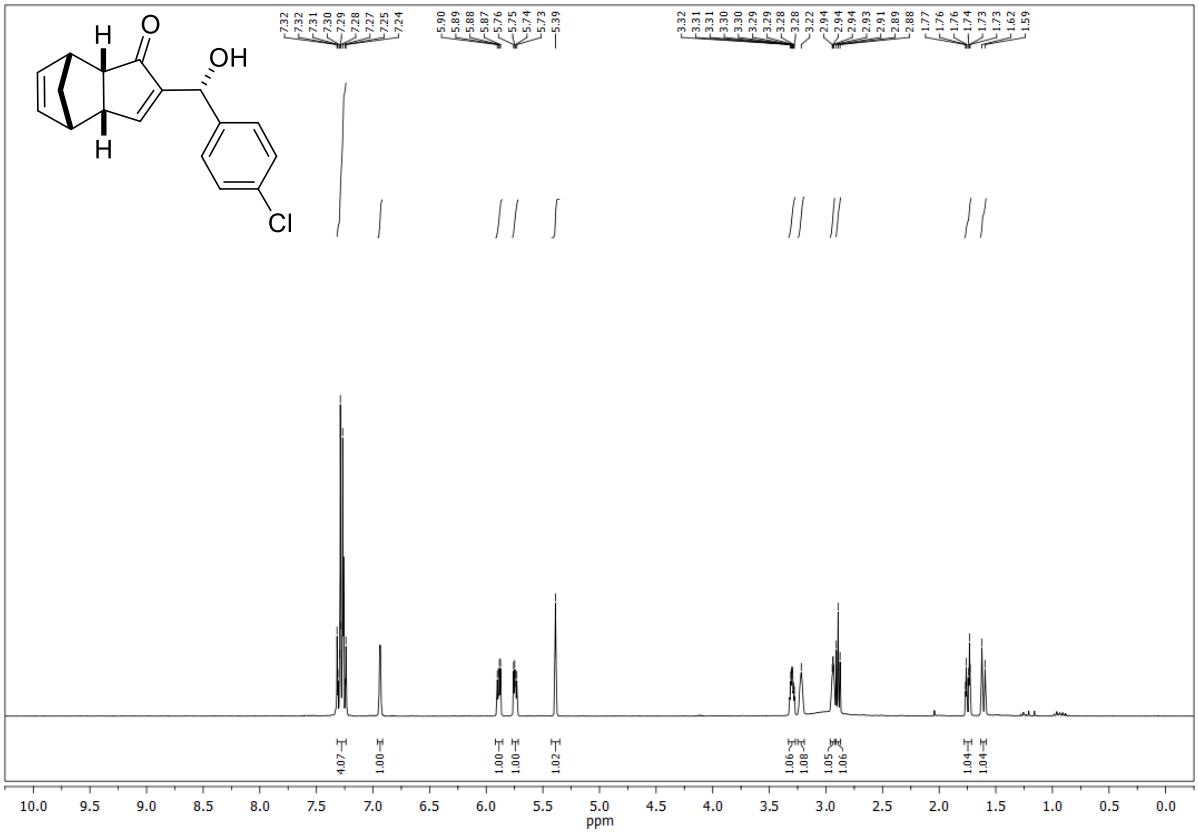
^{1}H NMR (300 MHz, $CDCl_3$)

^{13}C NMR (75 MHz, $CDCl_3$)

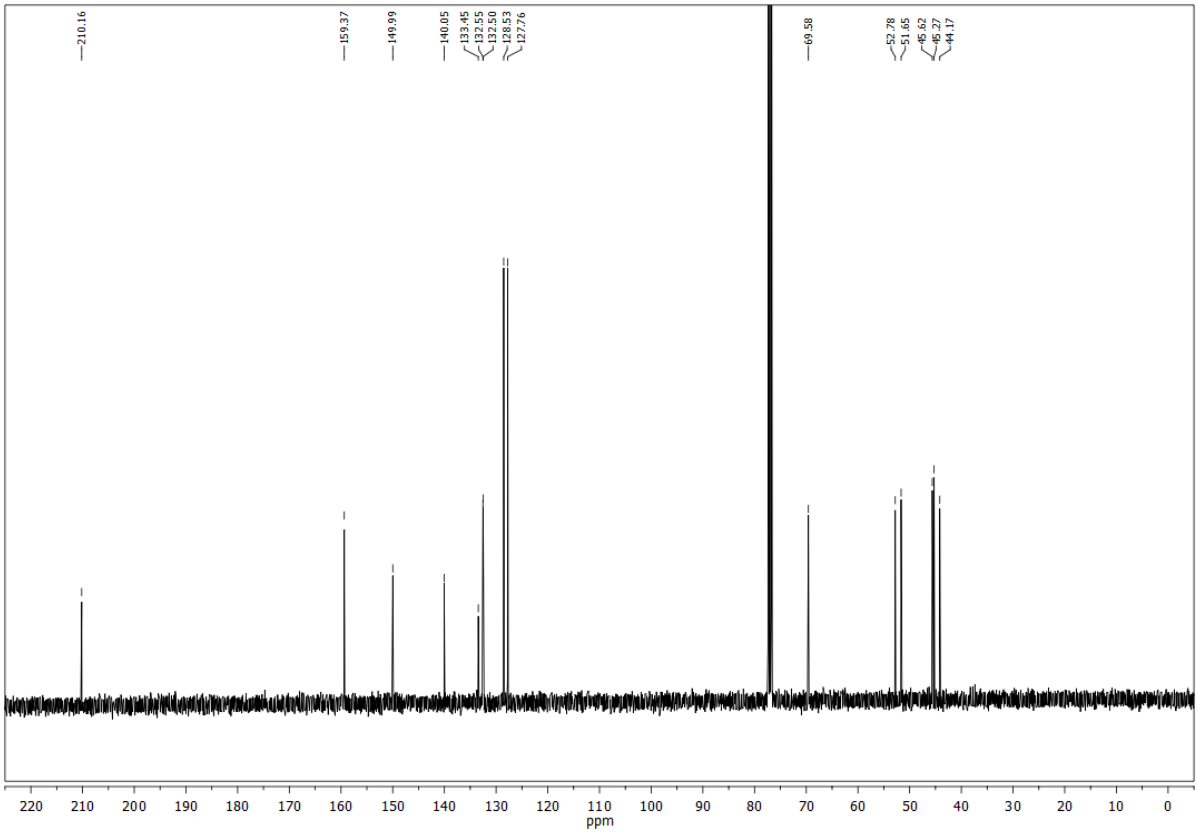


2-((4-Chlorophenyl)(hydroxy)methyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165h)

^{1}H NMR (300 MHz, $CDCl_3$)

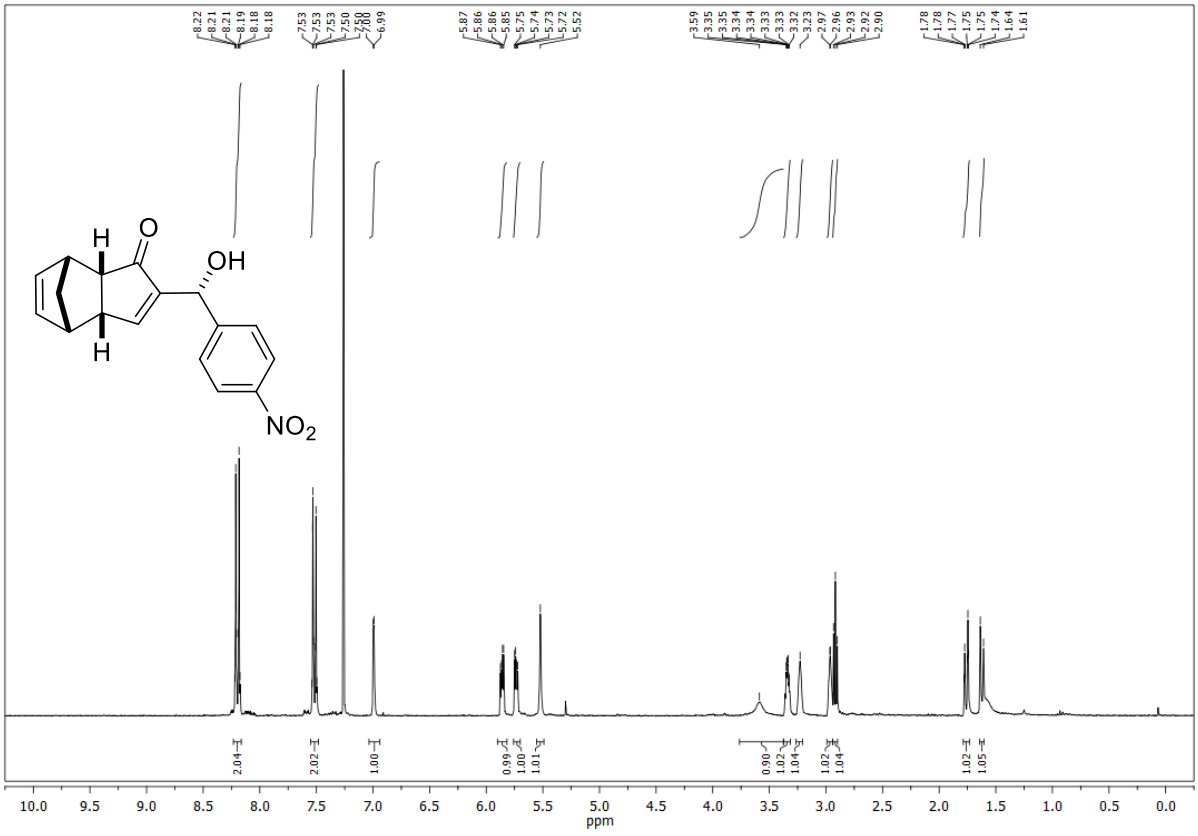


^{13}C NMR (75 MHz, $CDCl_3$)

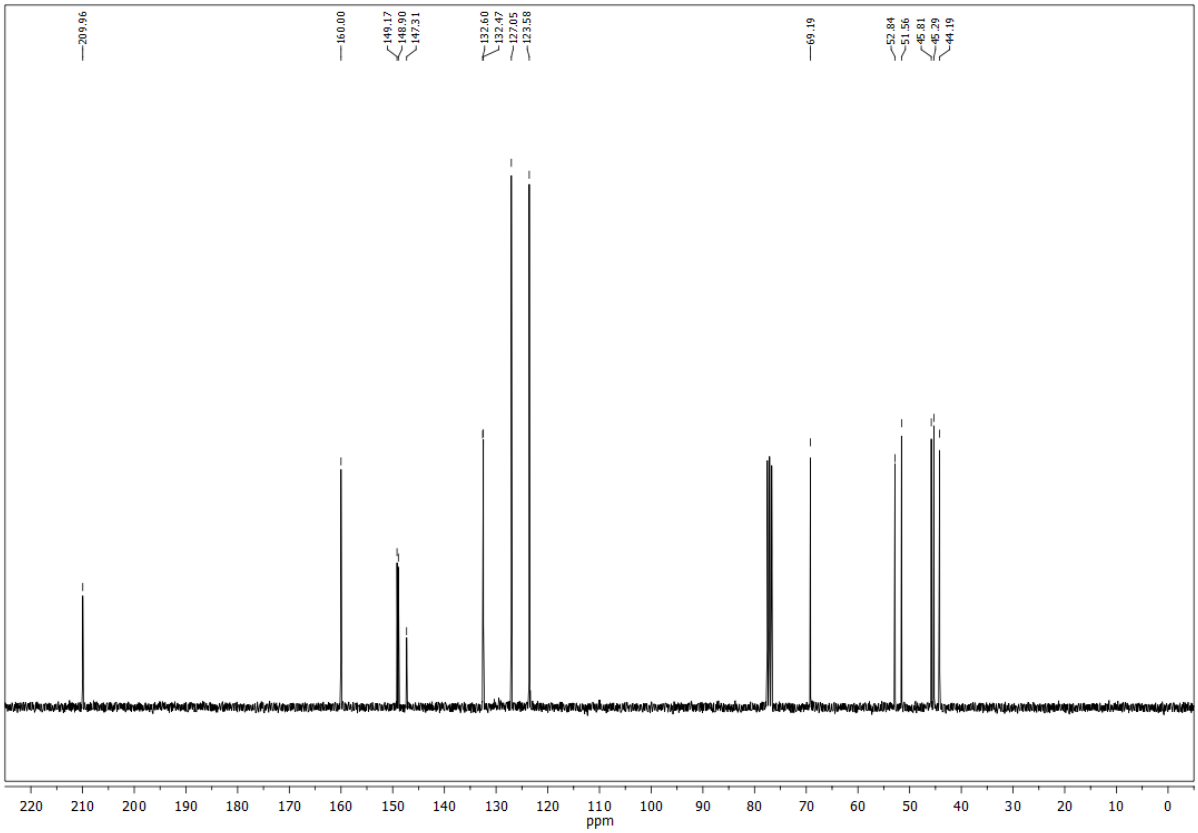


2-(Hydroxy(4-nitrophenyl)methyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165i)

^{1}H NMR (300 MHz, $CDCl_3$)



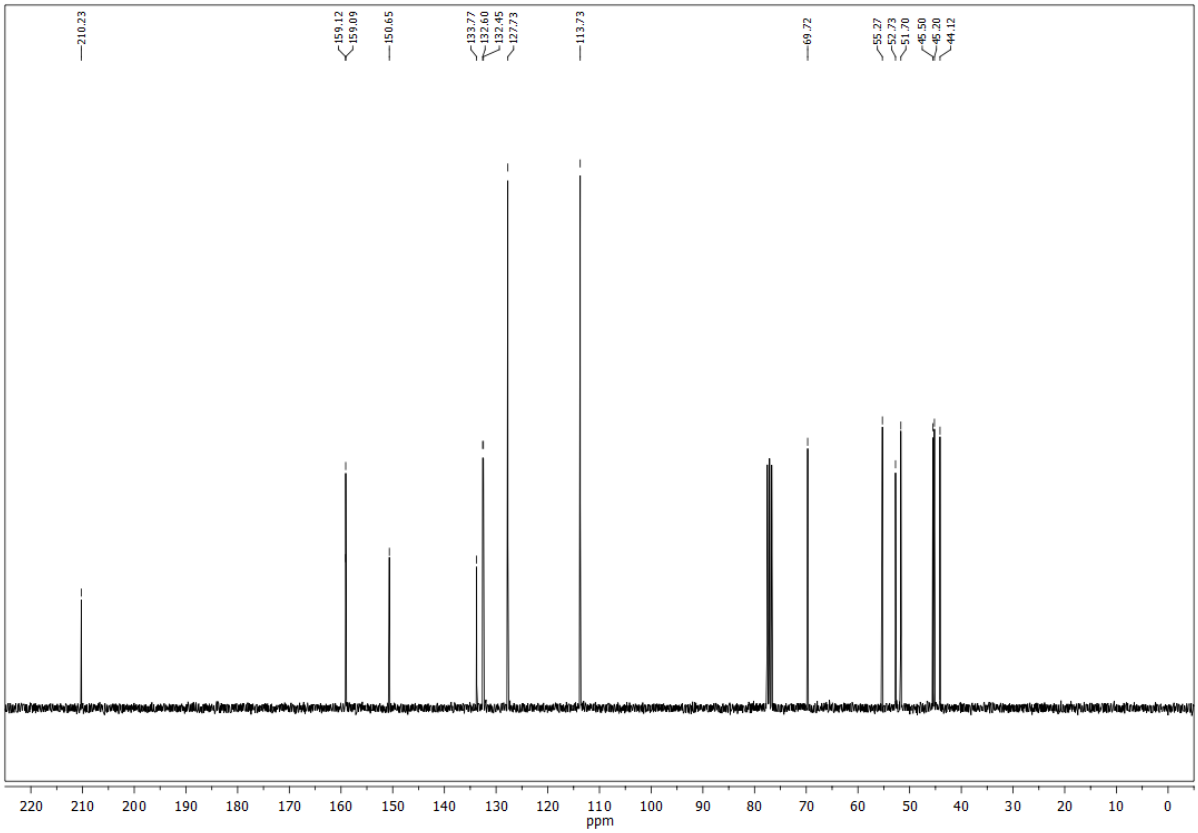
^{13}C NMR (75 MHz, $CDCl_3$)



2-(Hydroxy(4-methoxyphenyl)methyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165j)

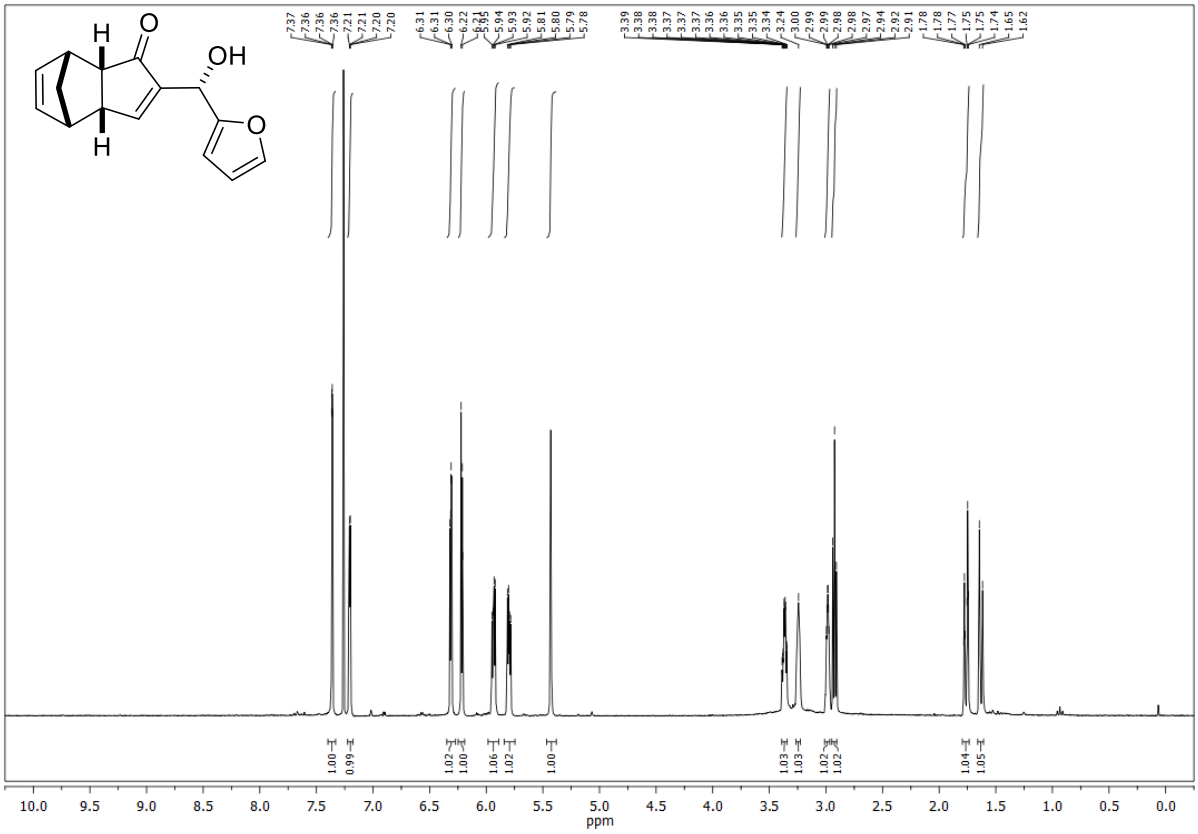
^{1}H NMR (300 MHz, $CDCl_3$)

^{13}C NMR (75 MHz, $CDCl_3$)

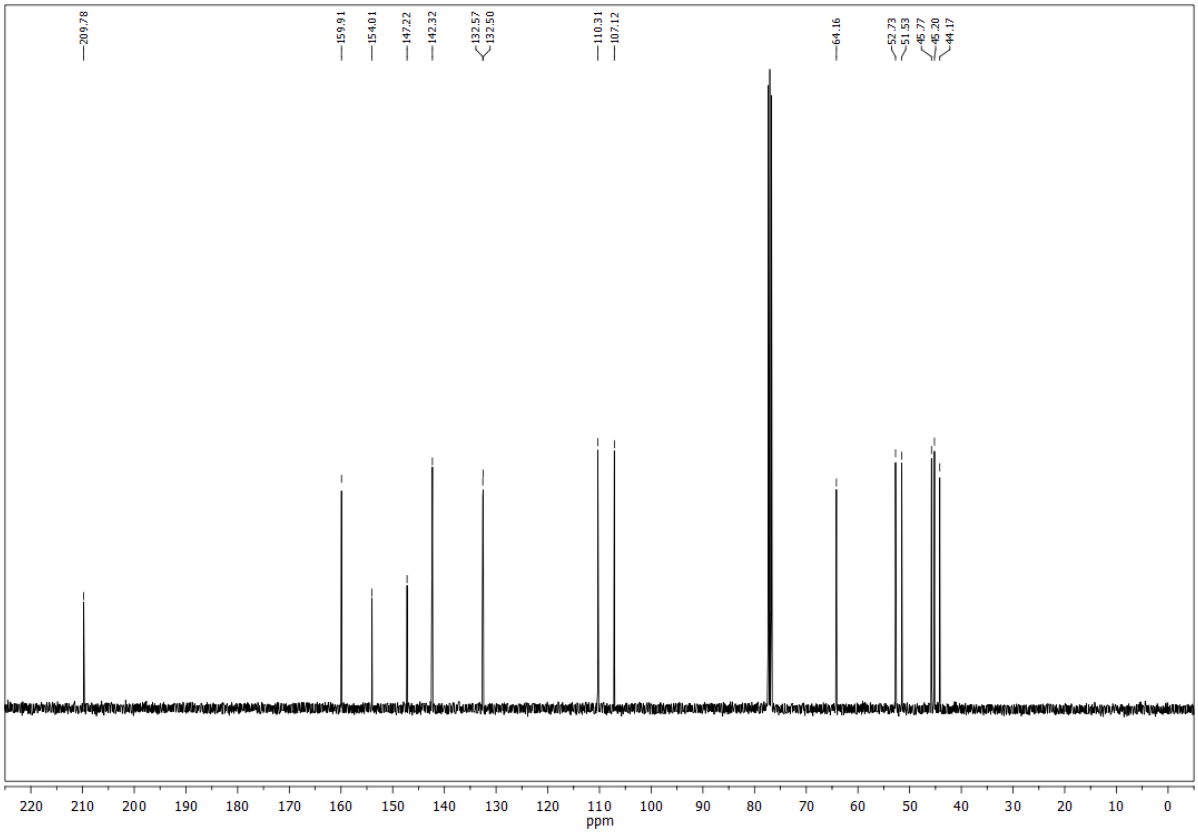


2-(Furan-2-yl(hydroxy)methyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-165k)

^{1}H NMR (300 MHz, $CDCl_3$)

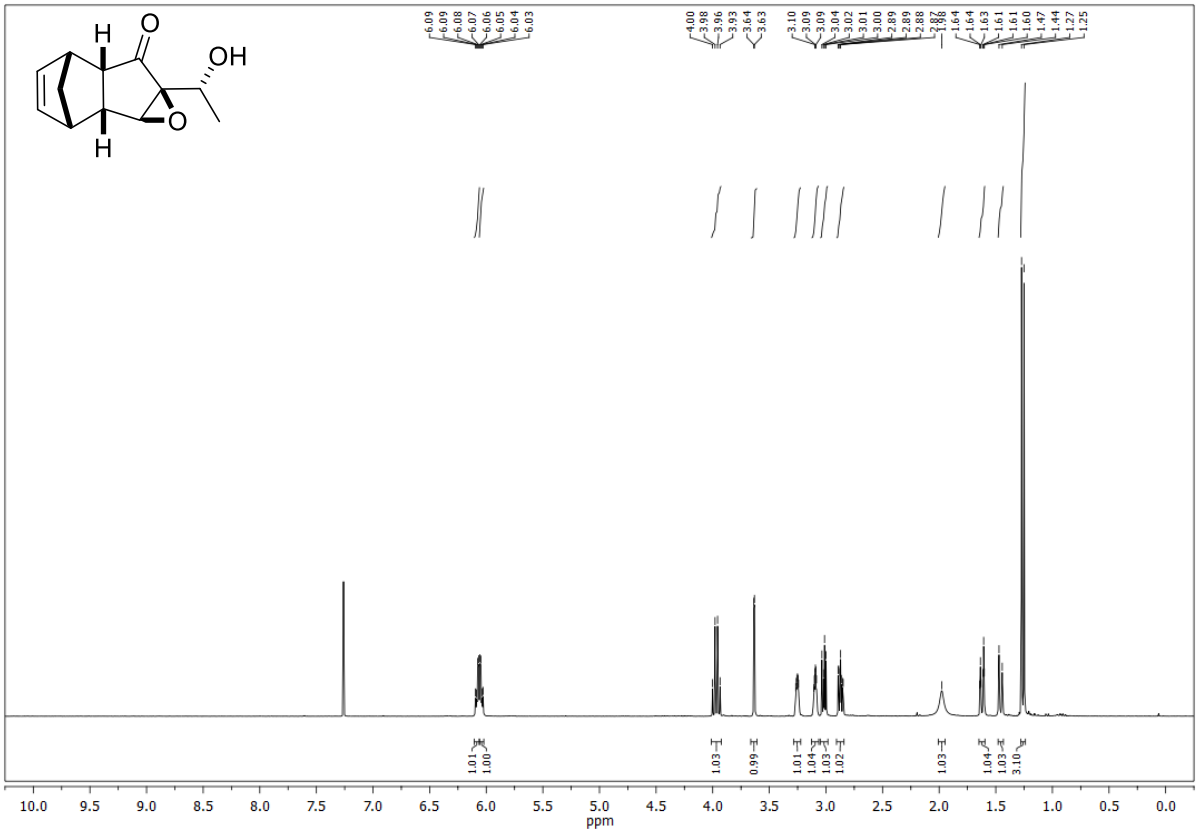


^{13}C NMR (75 MHz, $CDCl_3$)

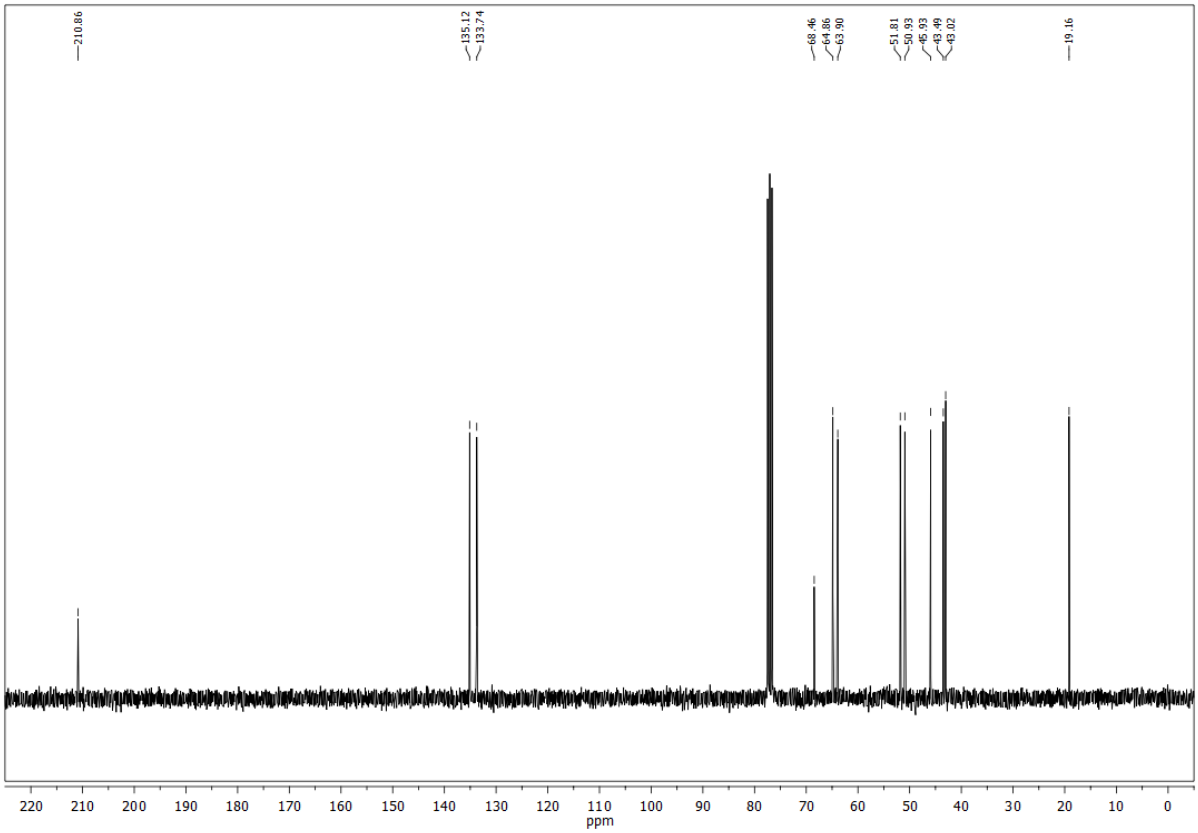


6a-(1-Hydroxyethyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170a)

^{1}H NMR (300 MHz, $CDCl_3$)

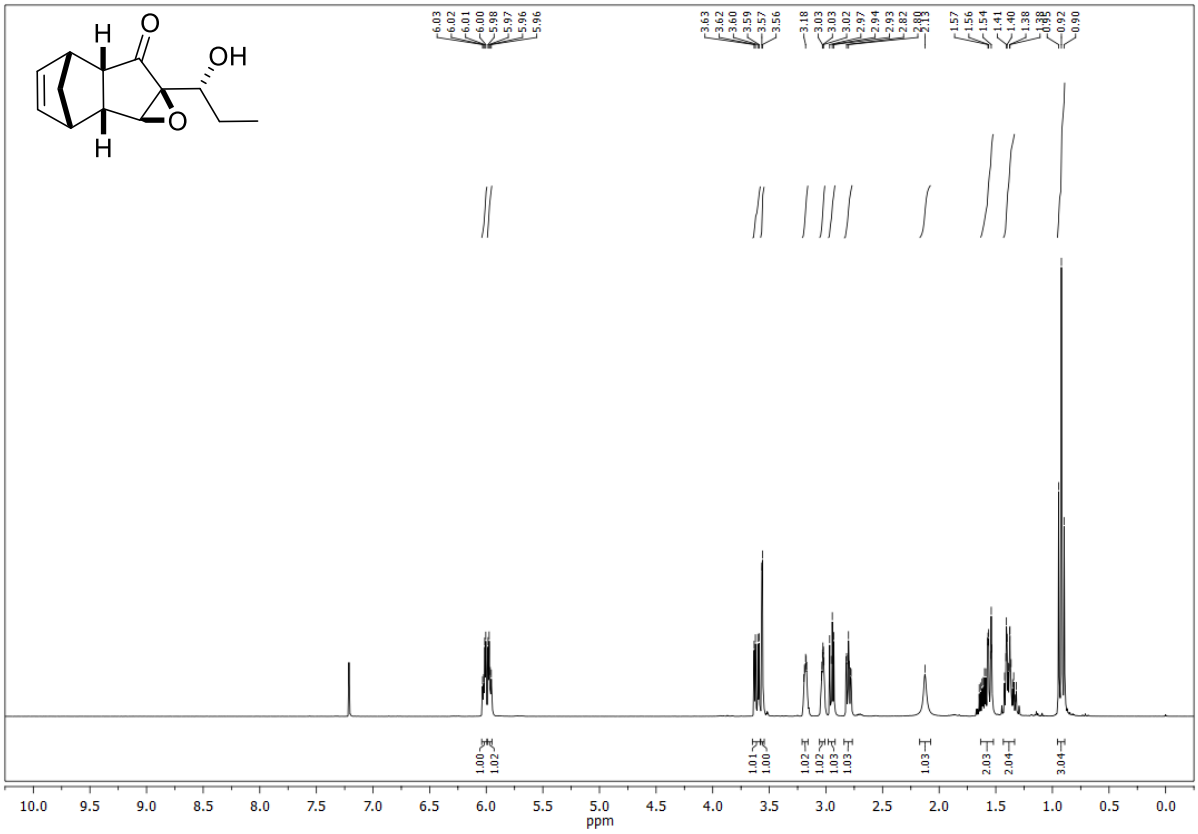


^{13}C NMR (75 MHz, $CDCl_3$)

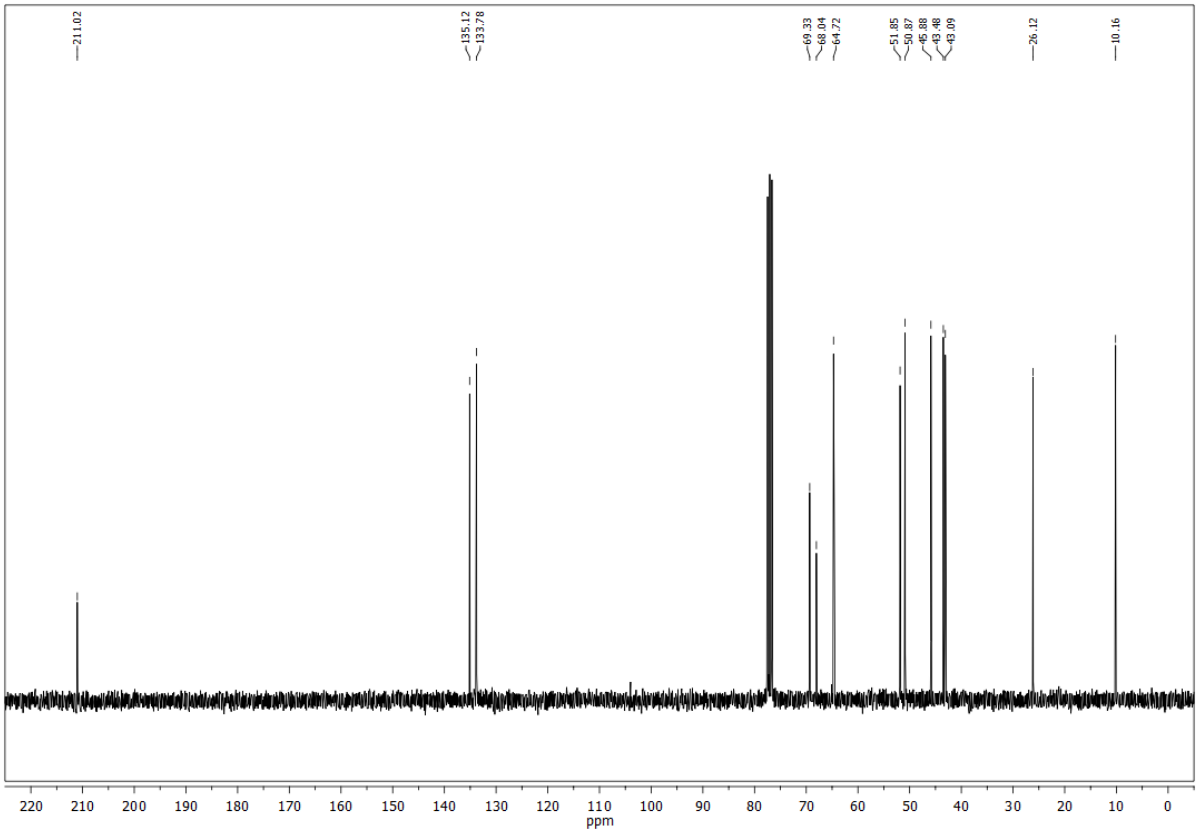


6a-(1-Hydroxypropyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170b)

^{1}H NMR (300 MHz, $CDCl_3$)

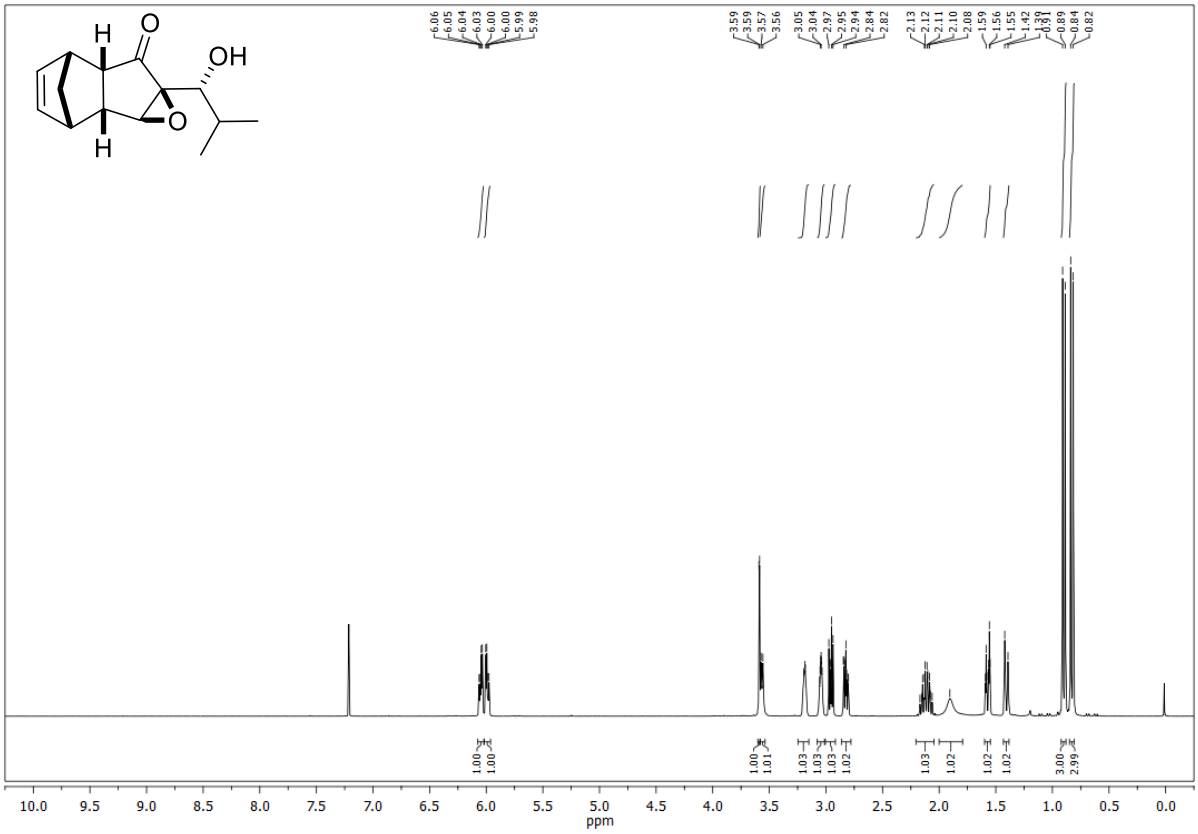


^{13}C NMR (75 MHz, $CDCl_3$)

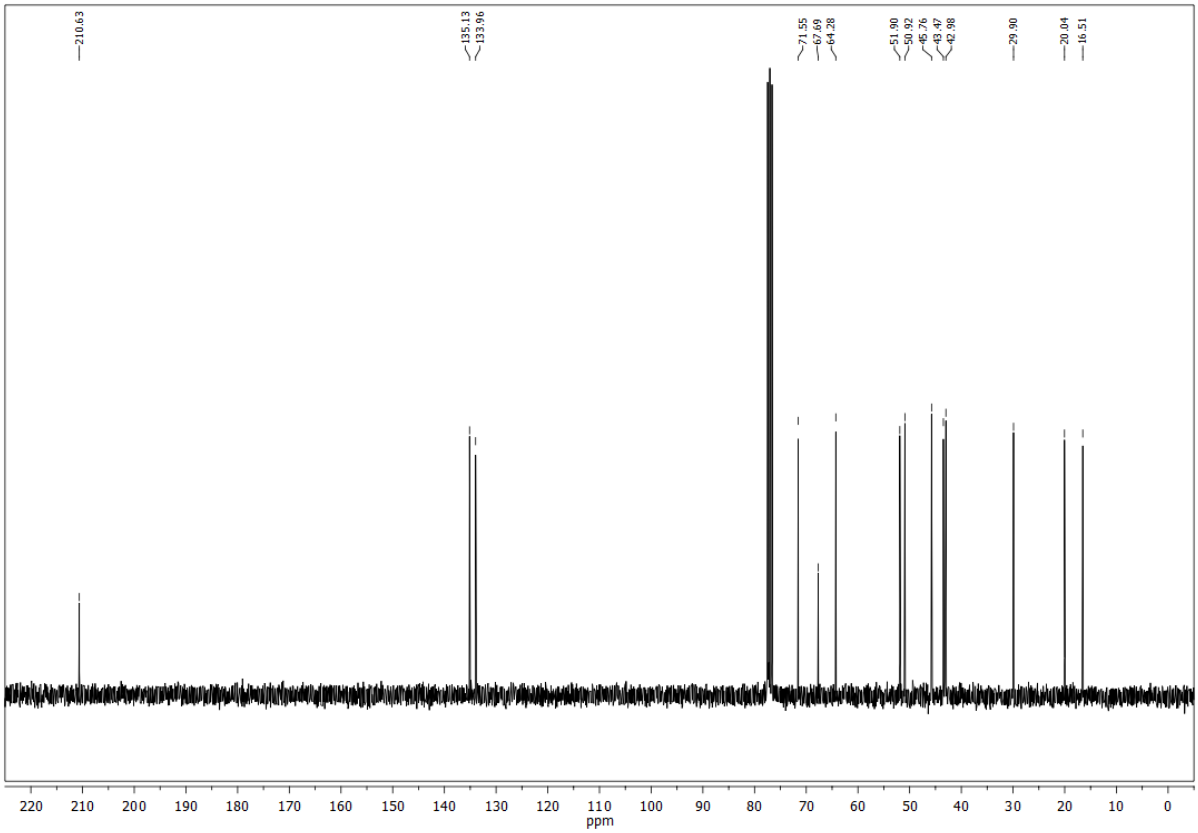


6a-(1-Hydroxy-2-methylpropyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170c)

^{1}H NMR (300 MHz, $CDCl_3$)

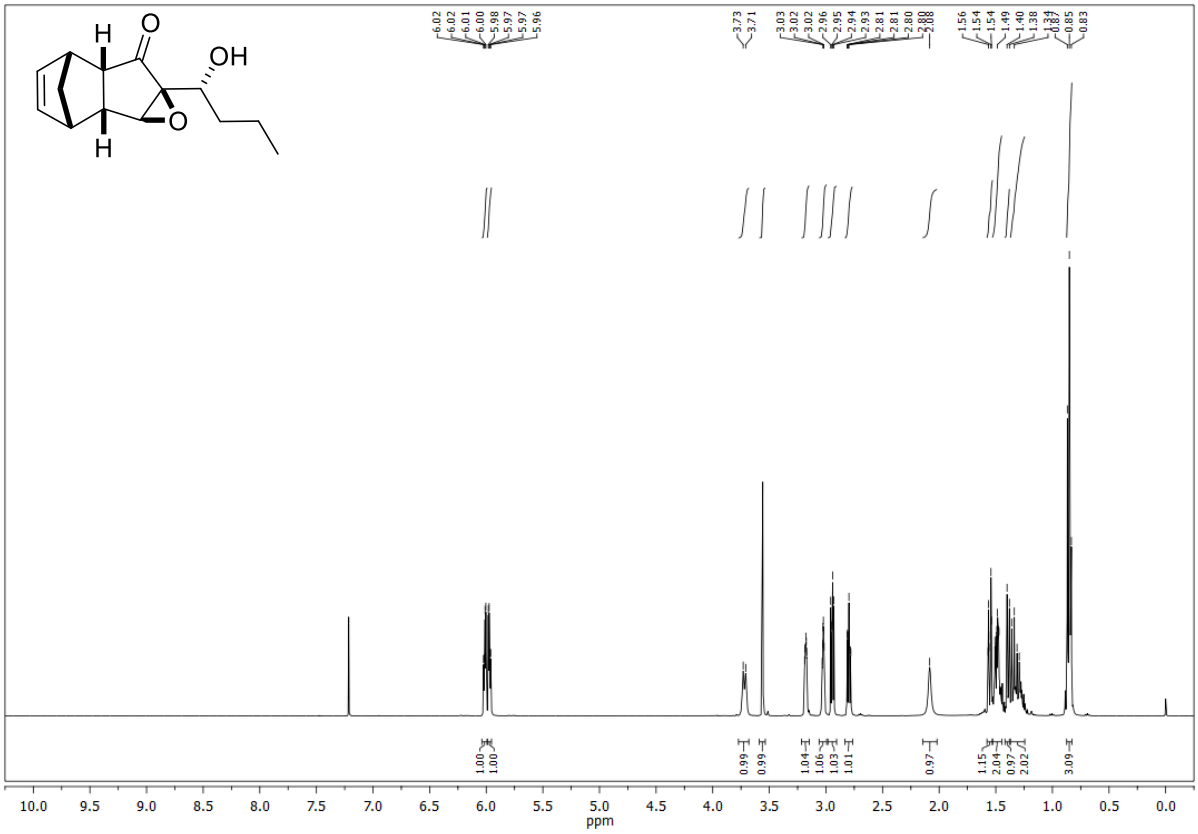


^{13}C NMR (75 MHz, $CDCl_3$)

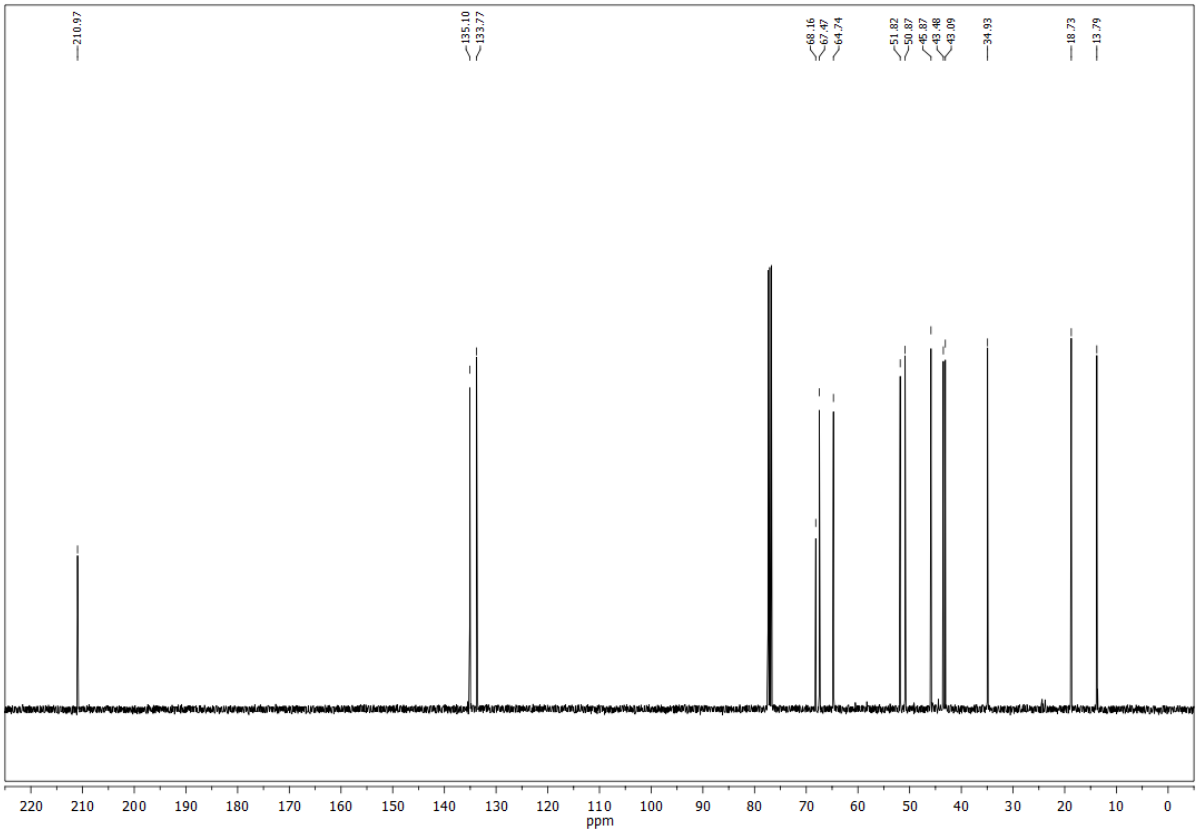


6a-(1-Hydroxybutyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170d)

^{1}H NMR (300 MHz, $CDCl_3$)

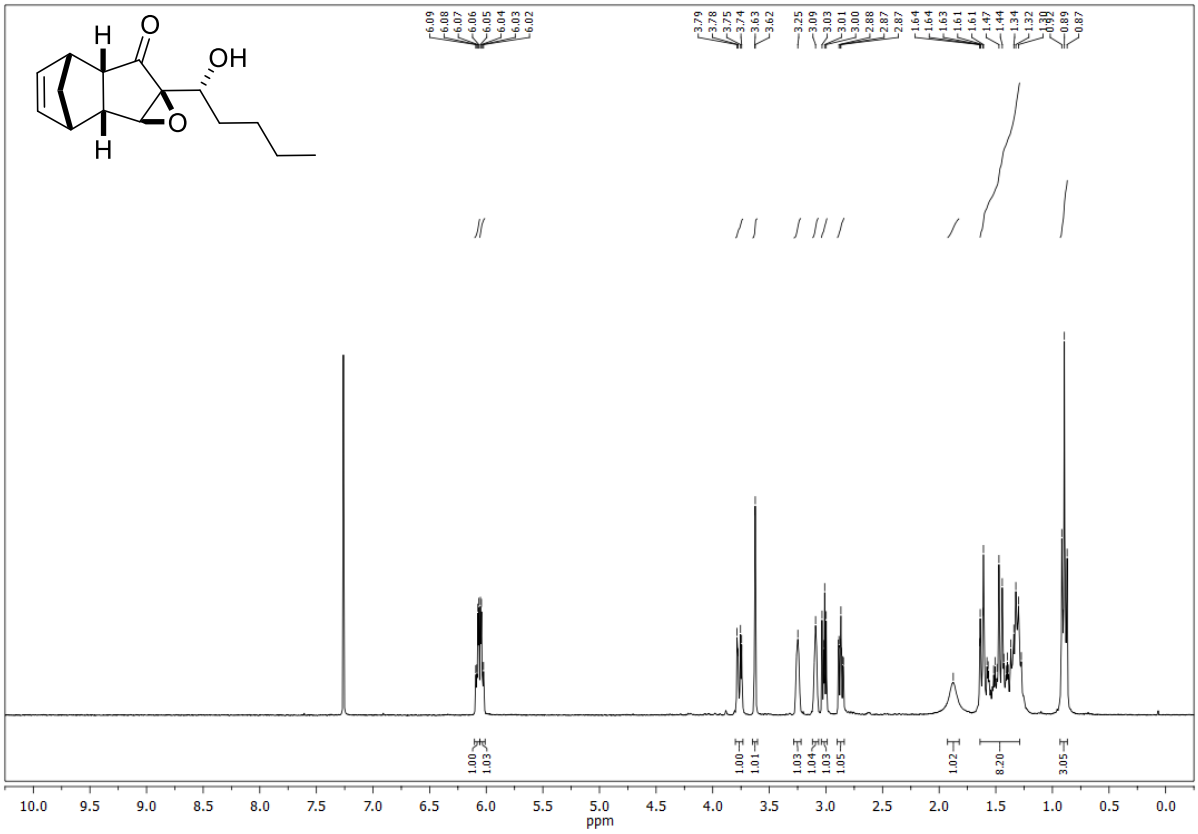


^{13}C NMR (75 MHz, $CDCl_3$)

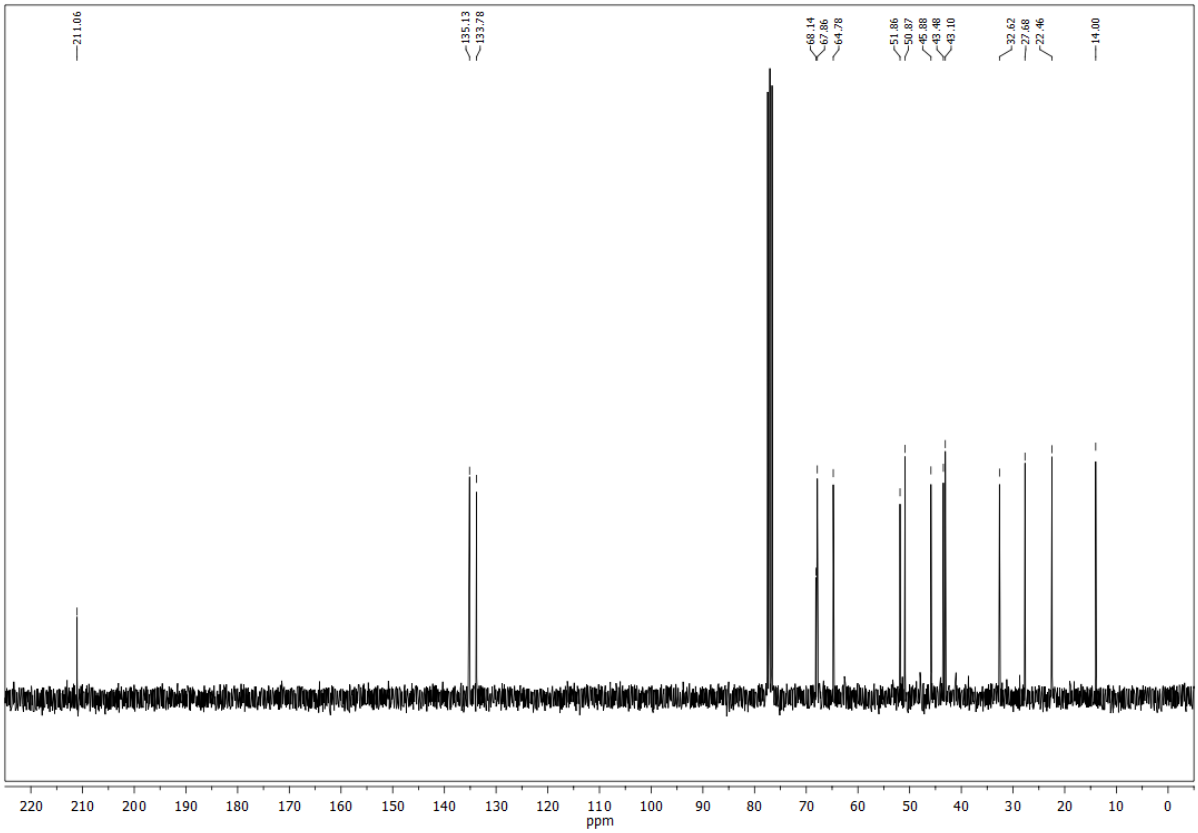


6a-(1-Hydroxypentyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170e)

^{1}H NMR (300 MHz, $CDCl_3$)

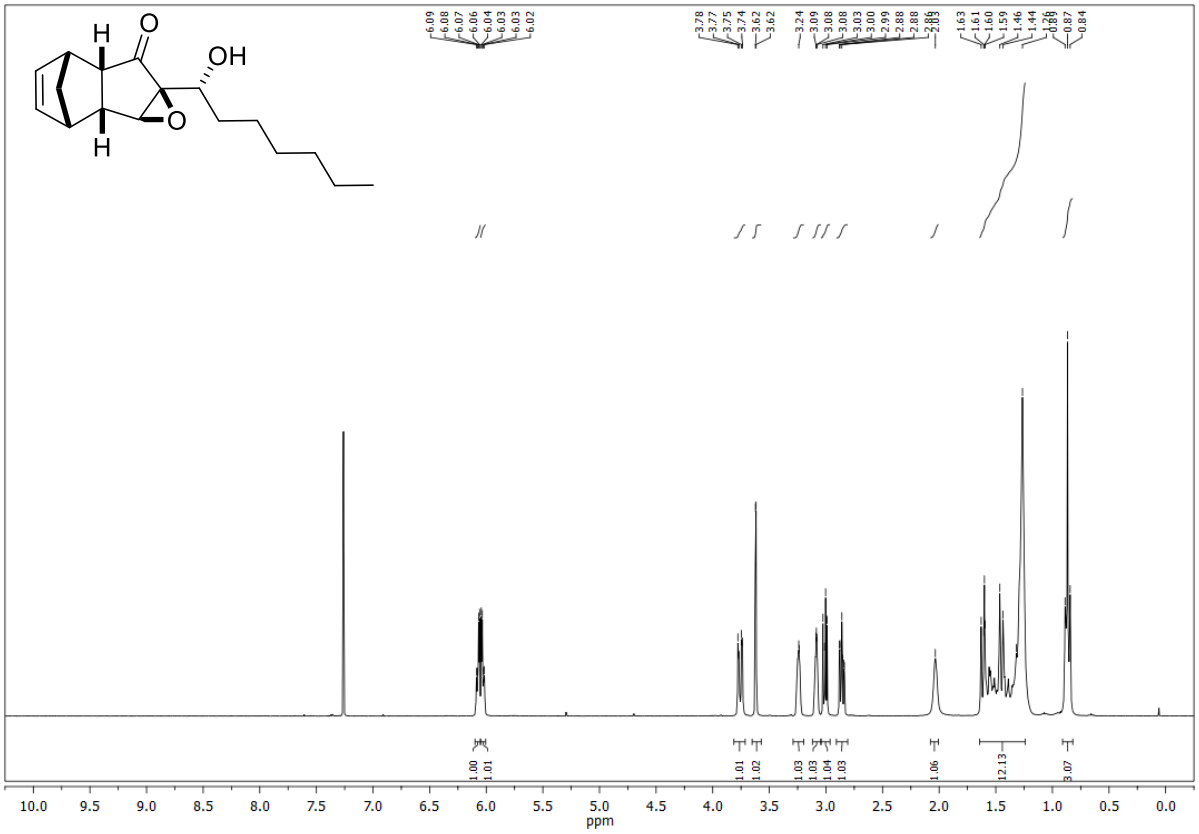


^{13}C NMR (75 MHz, $CDCl_3$)

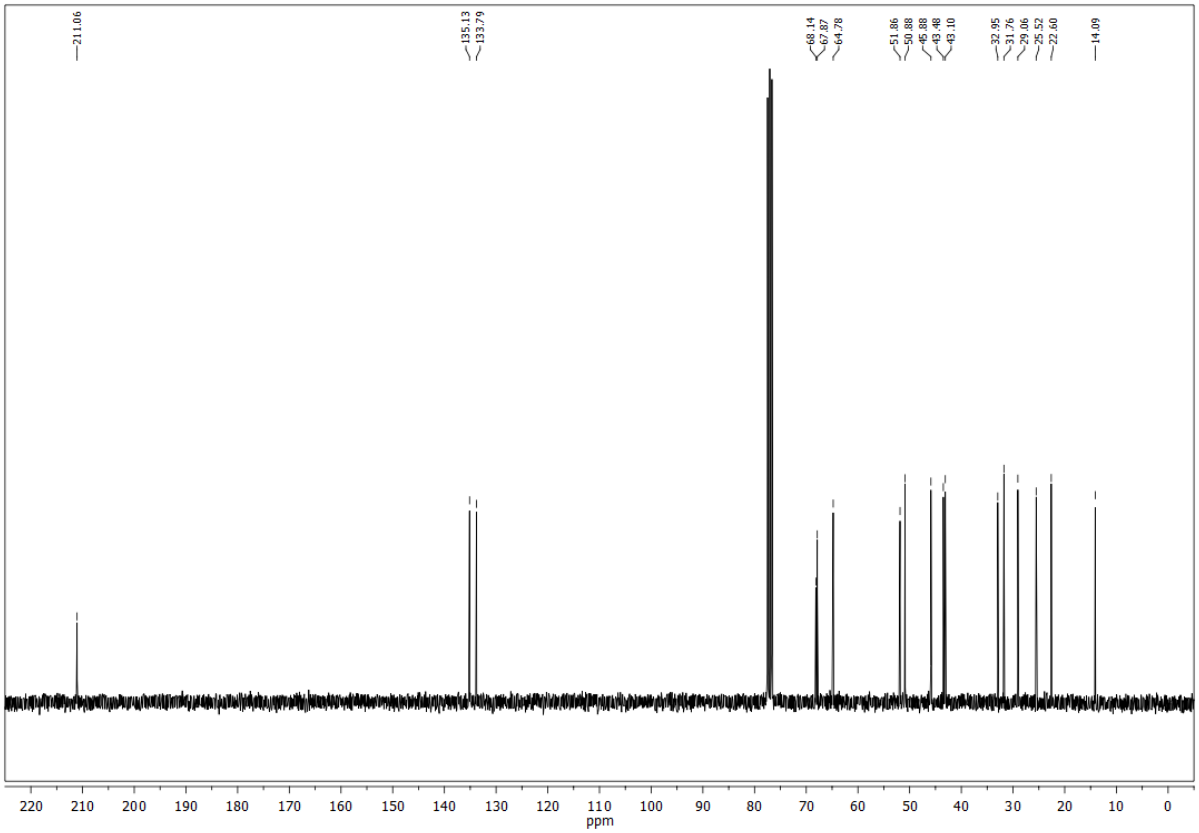


6a-(1-Hydroxyheptyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170f)

^{1}H NMR (300 MHz, $CDCl_3$)

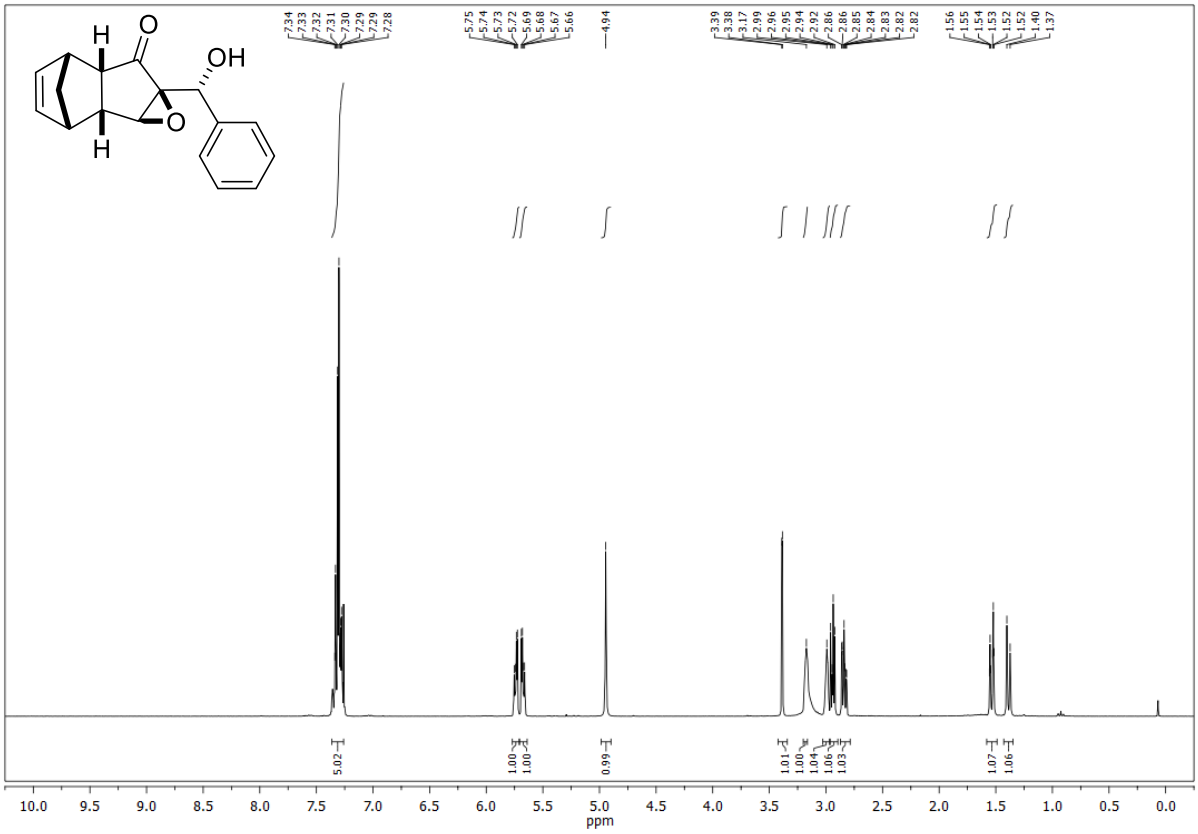


^{13}C NMR (75 MHz, $CDCl_3$)

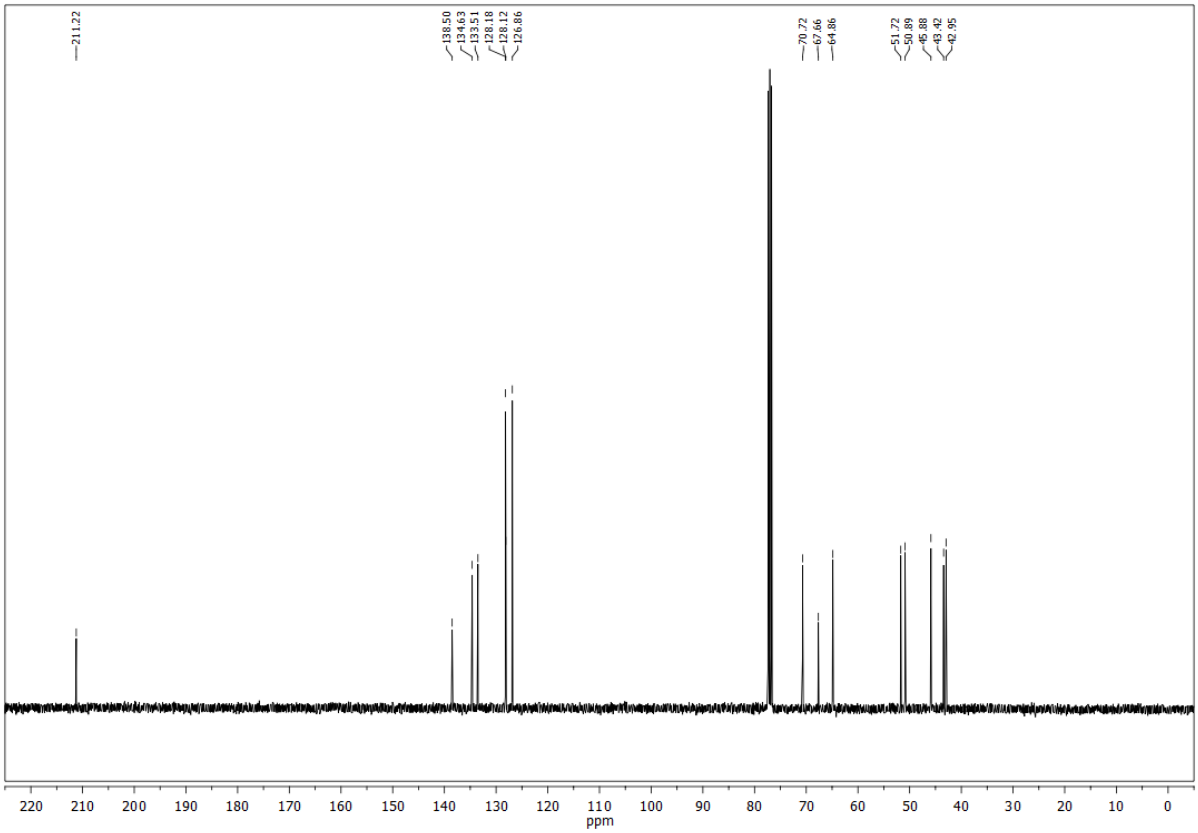


6a-(Hydroxy(phenyl)methyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170g)

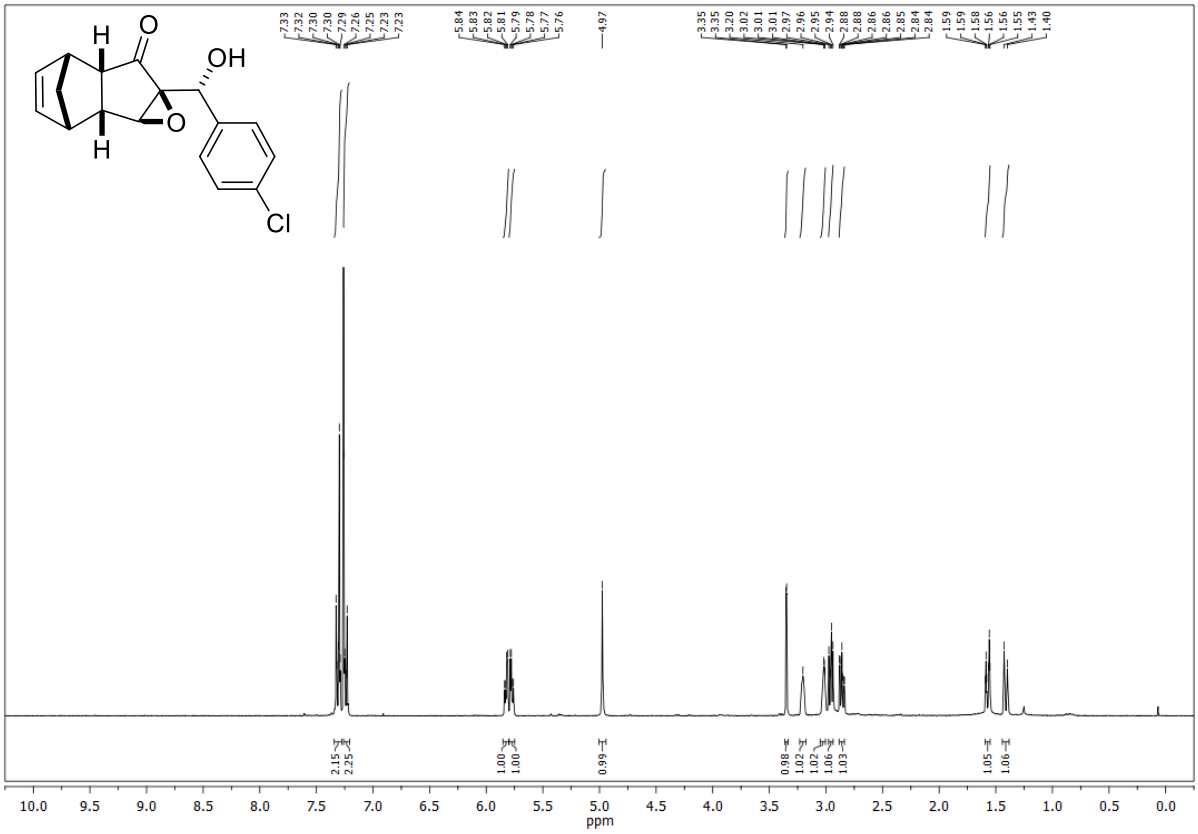
^{1}H NMR (300 MHz, $CDCl_3$)



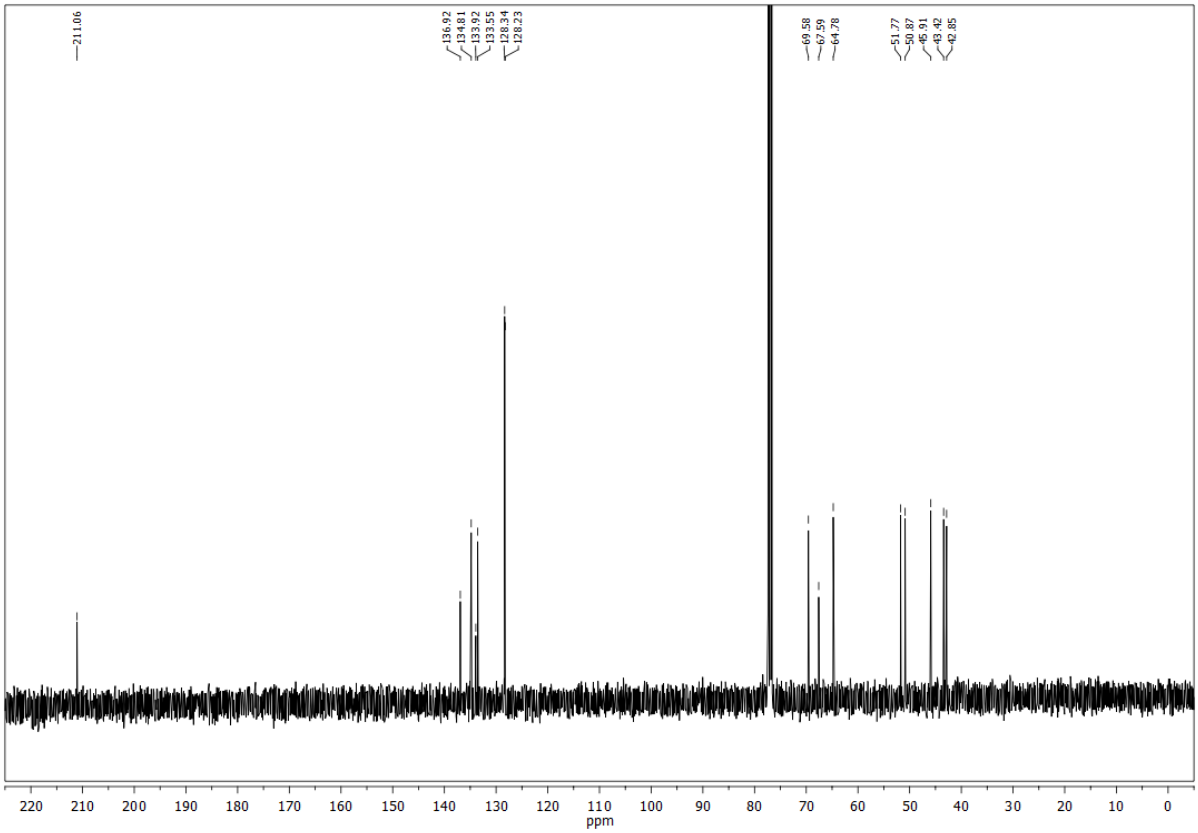
^{13}C NMR (75 MHz, $CDCl_3$)



6a-((4-Chlorophenyl)(hydroxy)methyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170h) **^{1}H NMR** (300 MHz, $CDCl_3$)

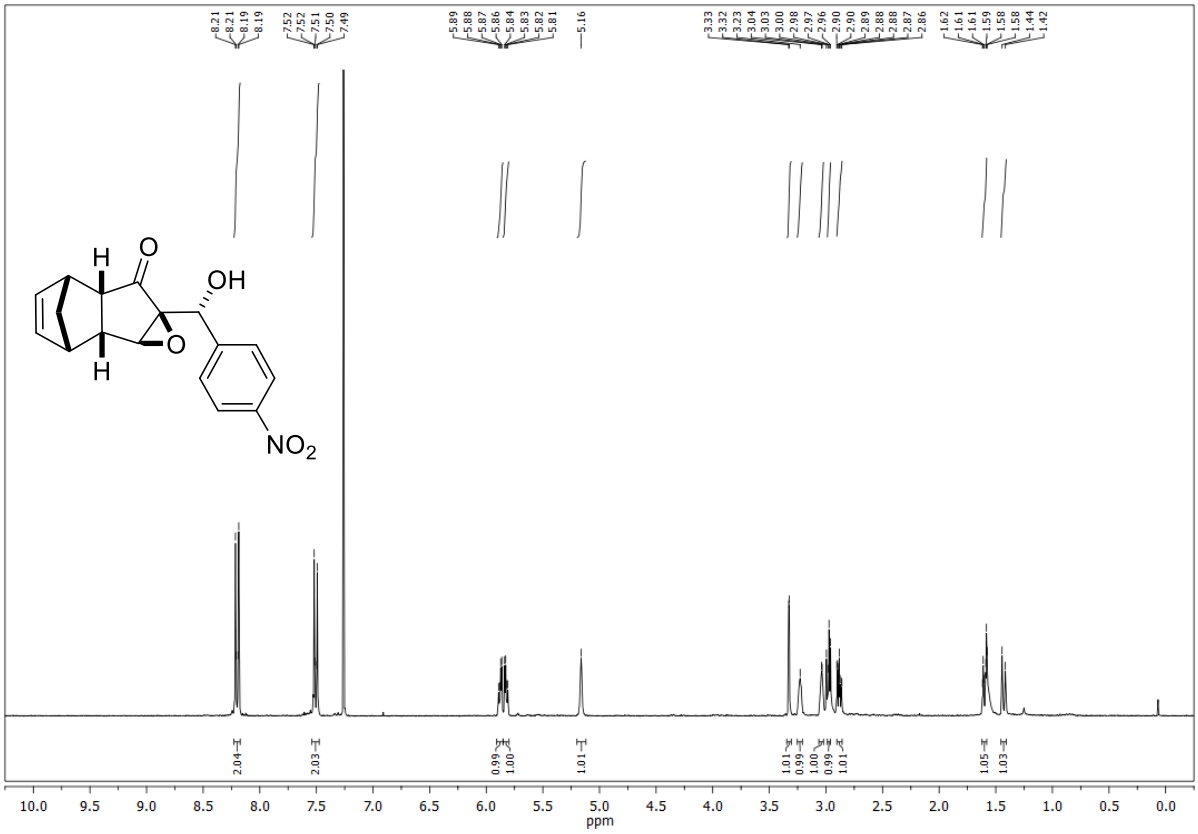


^{13}C NMR (75 MHz, $CDCl_3$)

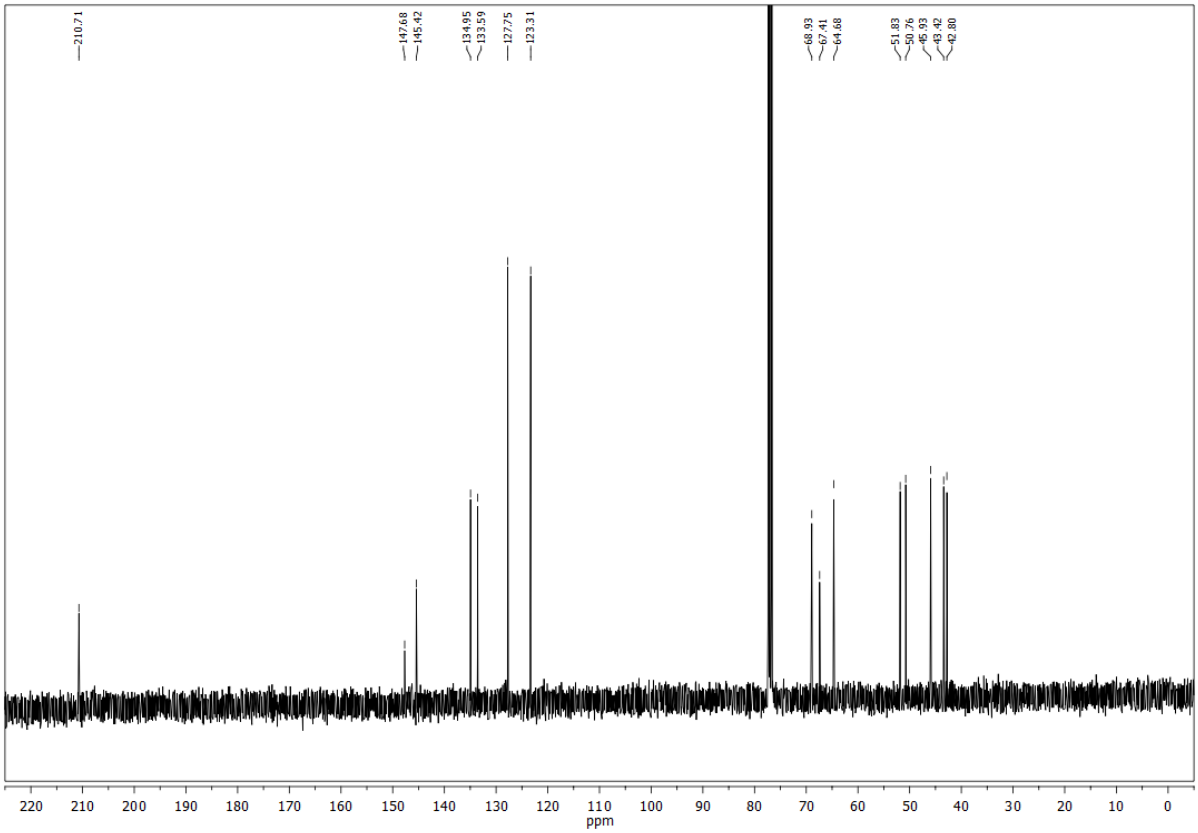


6a-(Hydroxy(4-nitrophenyl)methyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170i)

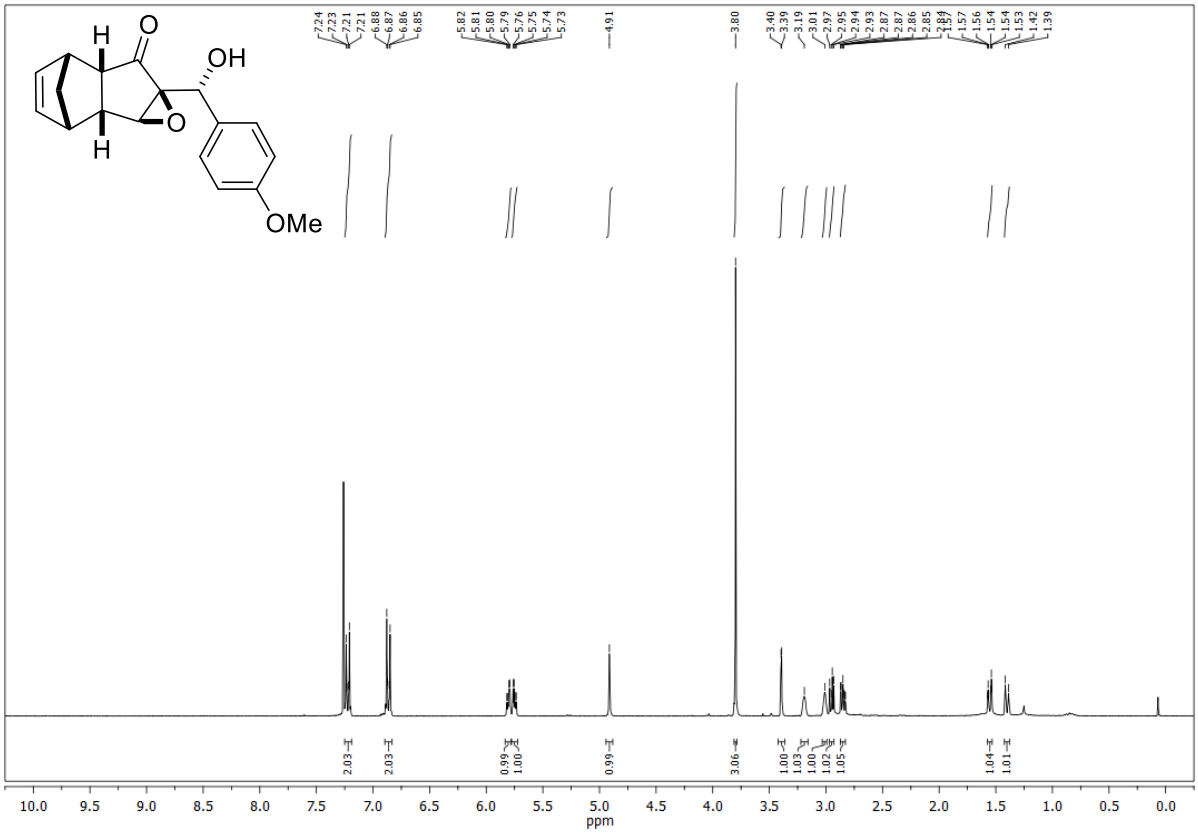
^{1}H NMR (300 MHz, $CDCl_3$)



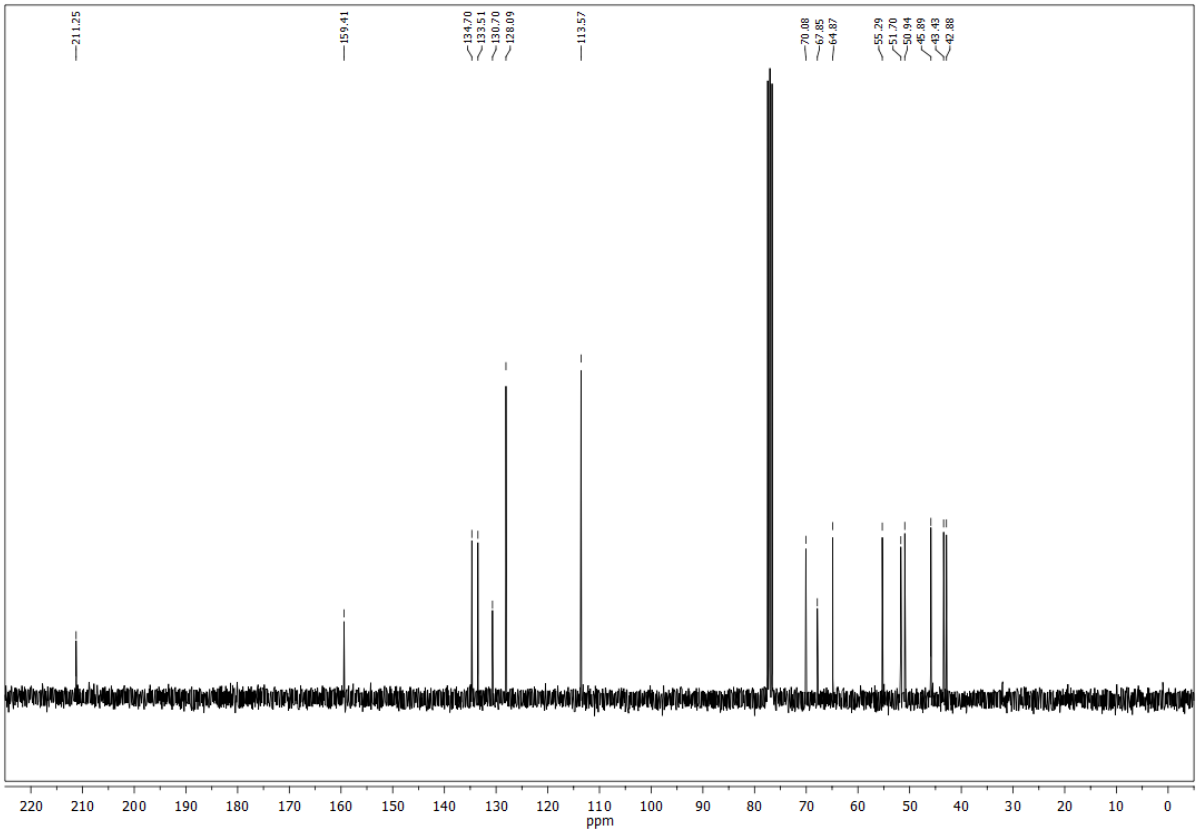
^{13}C NMR (75 MHz, $CDCl_3$)



6a-(Hydroxy(4-methoxyphenyl)methyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170j) **^{1}H NMR** (300 MHz, $CDCl_3$)

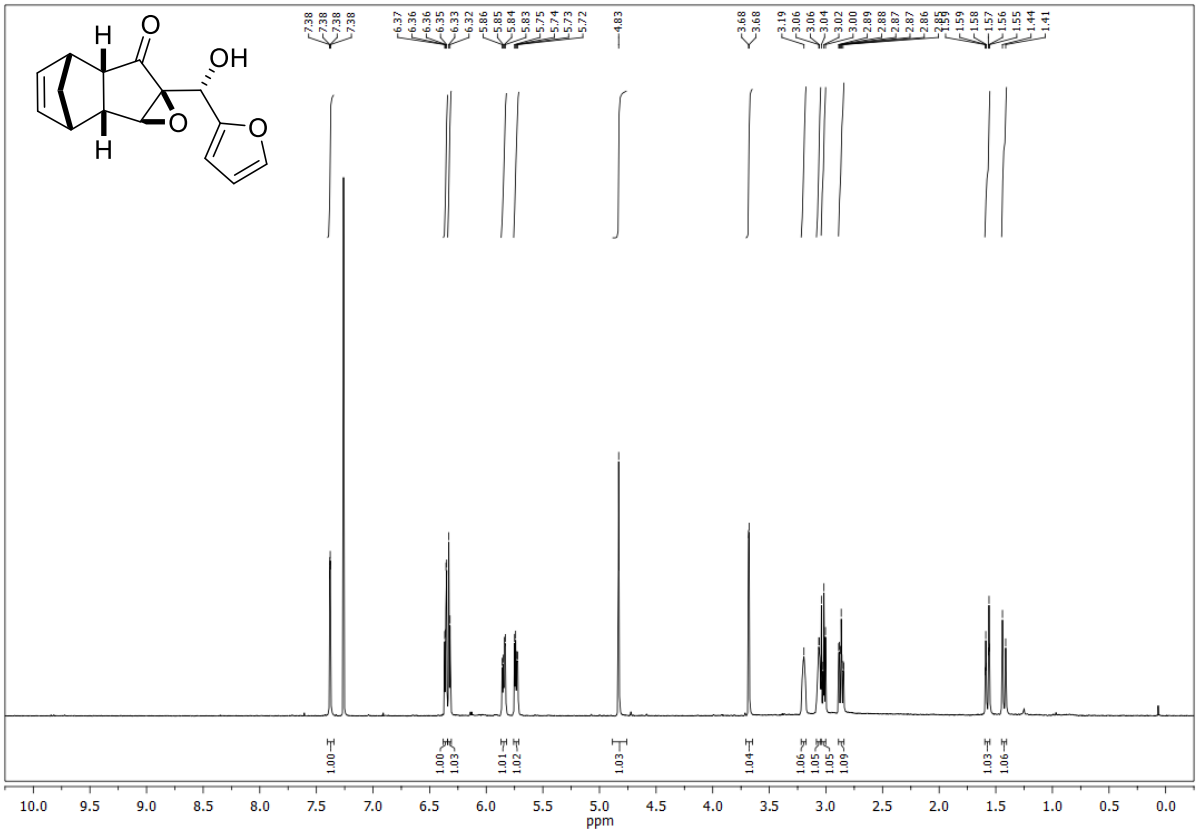


^{13}C NMR (75 MHz, $CDCl_3$)

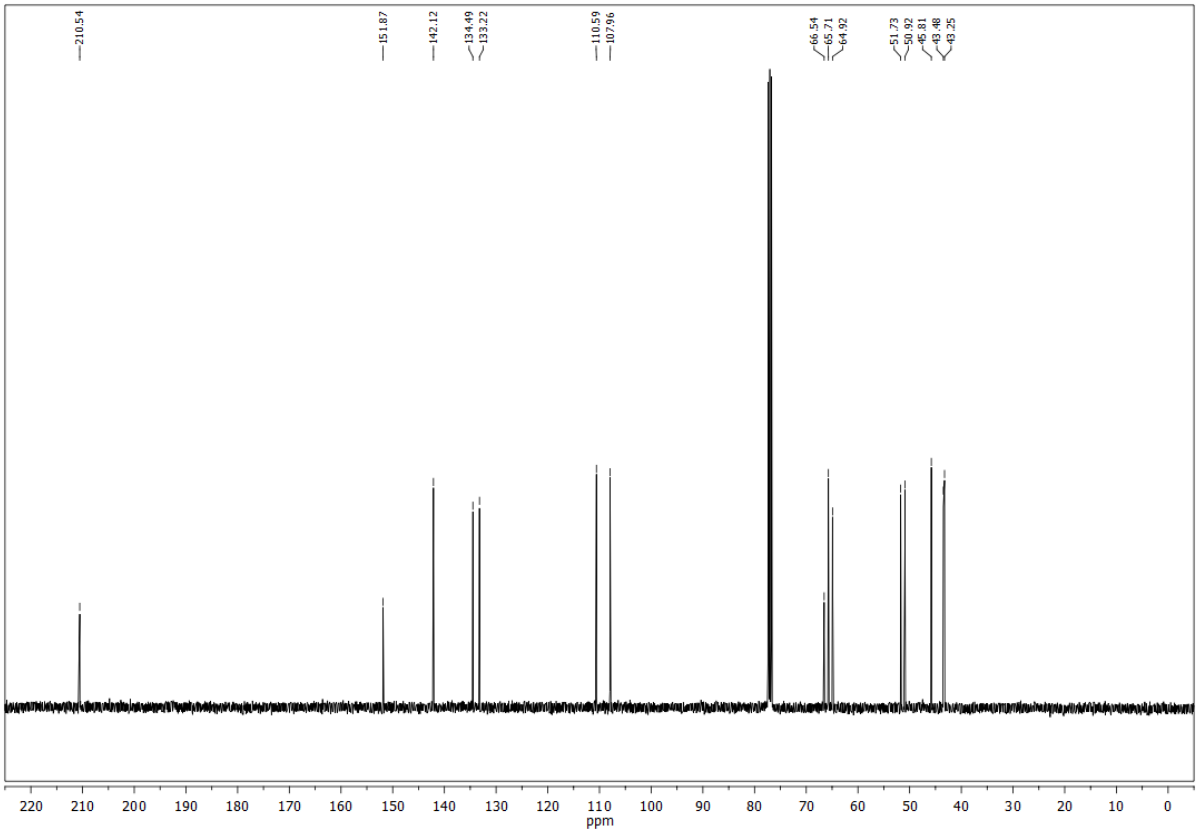


6a-(furan-2-yl(hydroxy)methyl)-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-170k)

^{1}H NMR (300 MHz, $CDCl_3$)

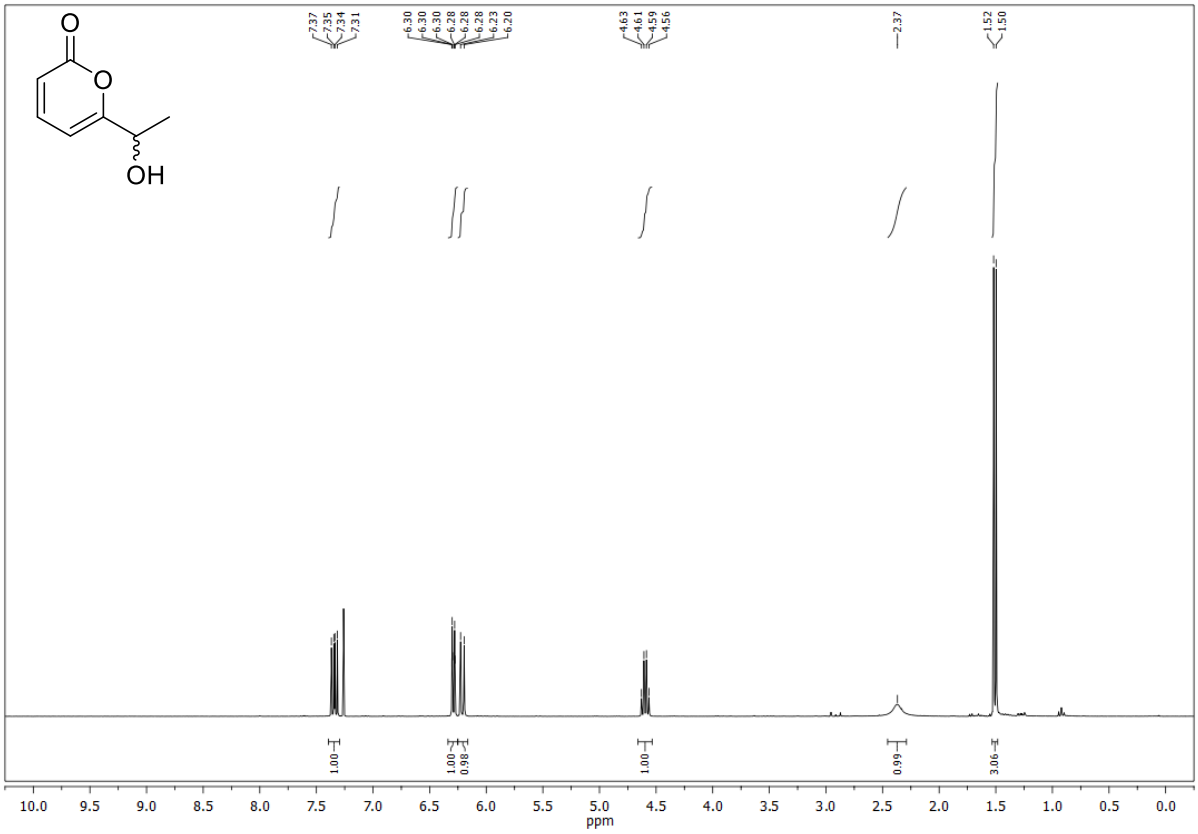


^{13}C NMR (75 MHz, $CDCl_3$)

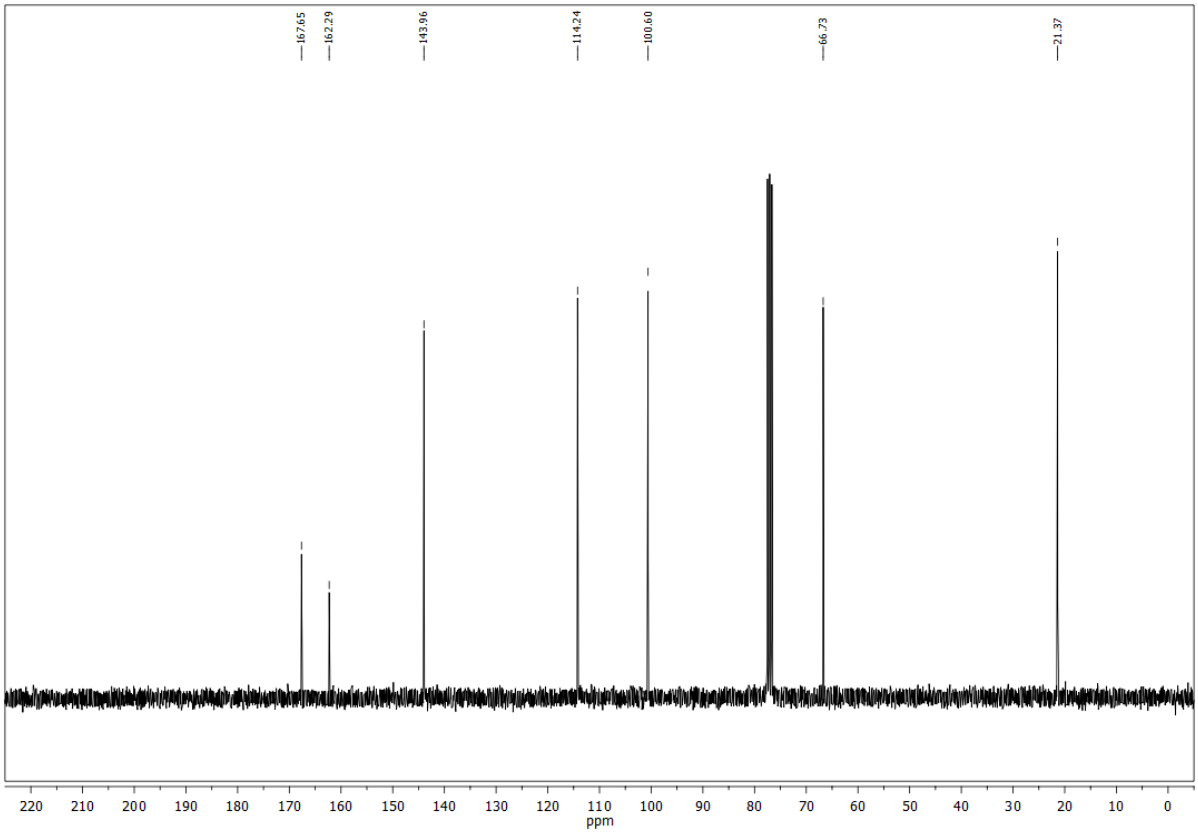


6-(1-Hydroxyethyl)-2*H*-pyran-2-one ((±)-171a)

^{1}H NMR (300 MHz, $CDCl_3$)

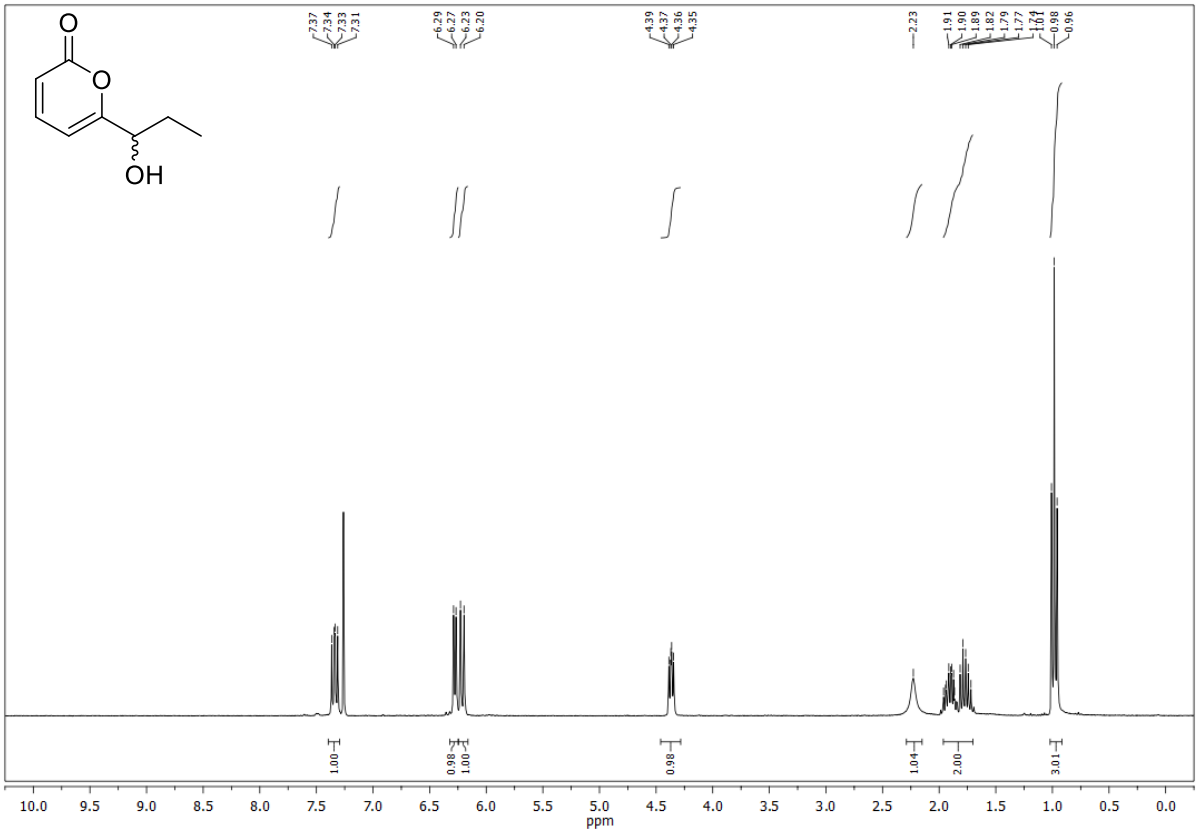


^{13}C NMR (75 MHz, $CDCl_3$)

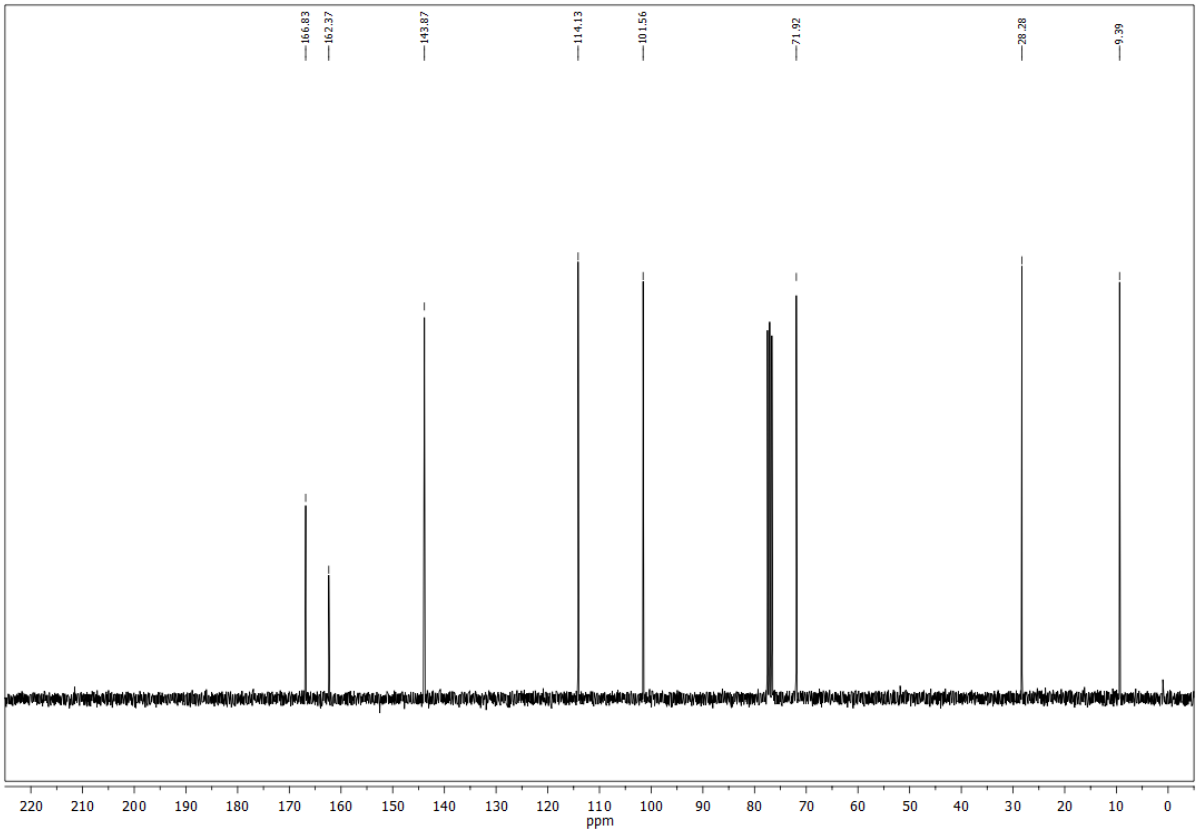


6-(1-Hydroxypropyl)-2*H*-pyran-2-one ((±)-171b)

^{1}H NMR (300 MHz, $CDCl_3$)

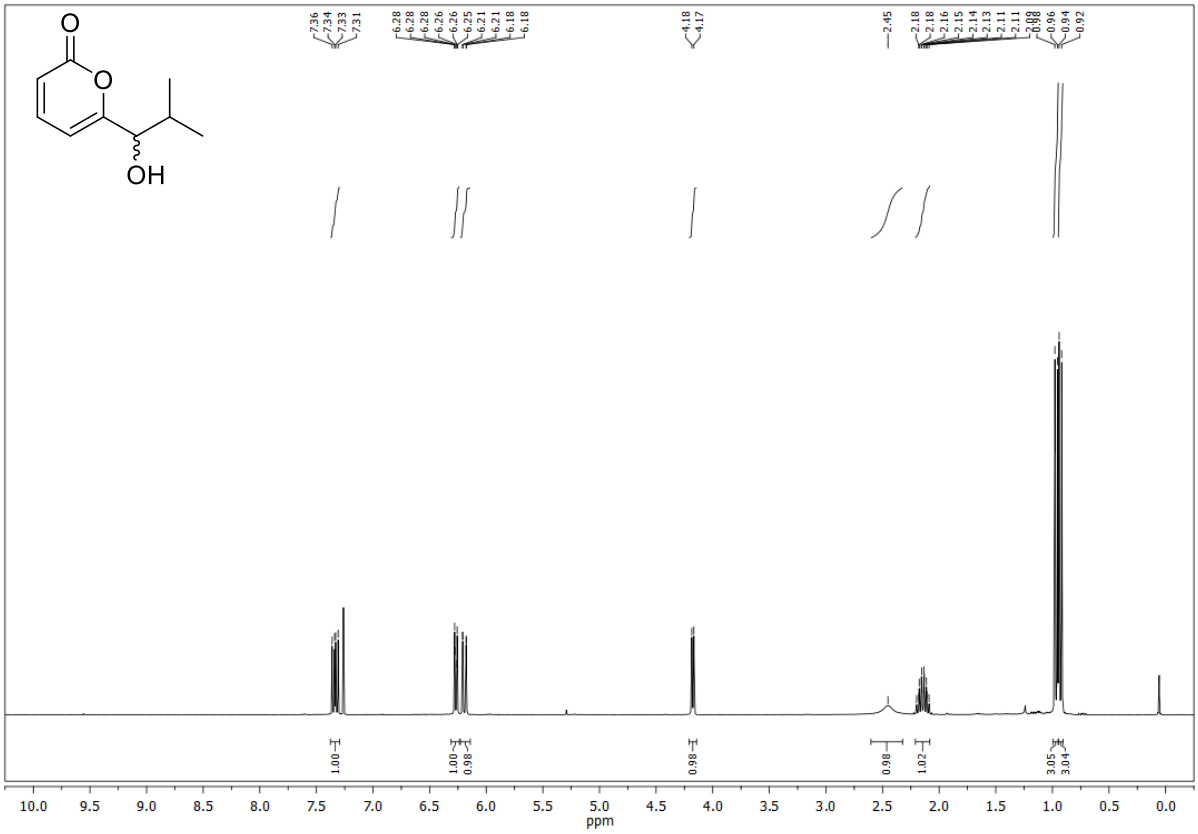


^{13}C NMR (75 MHz, $CDCl_3$)

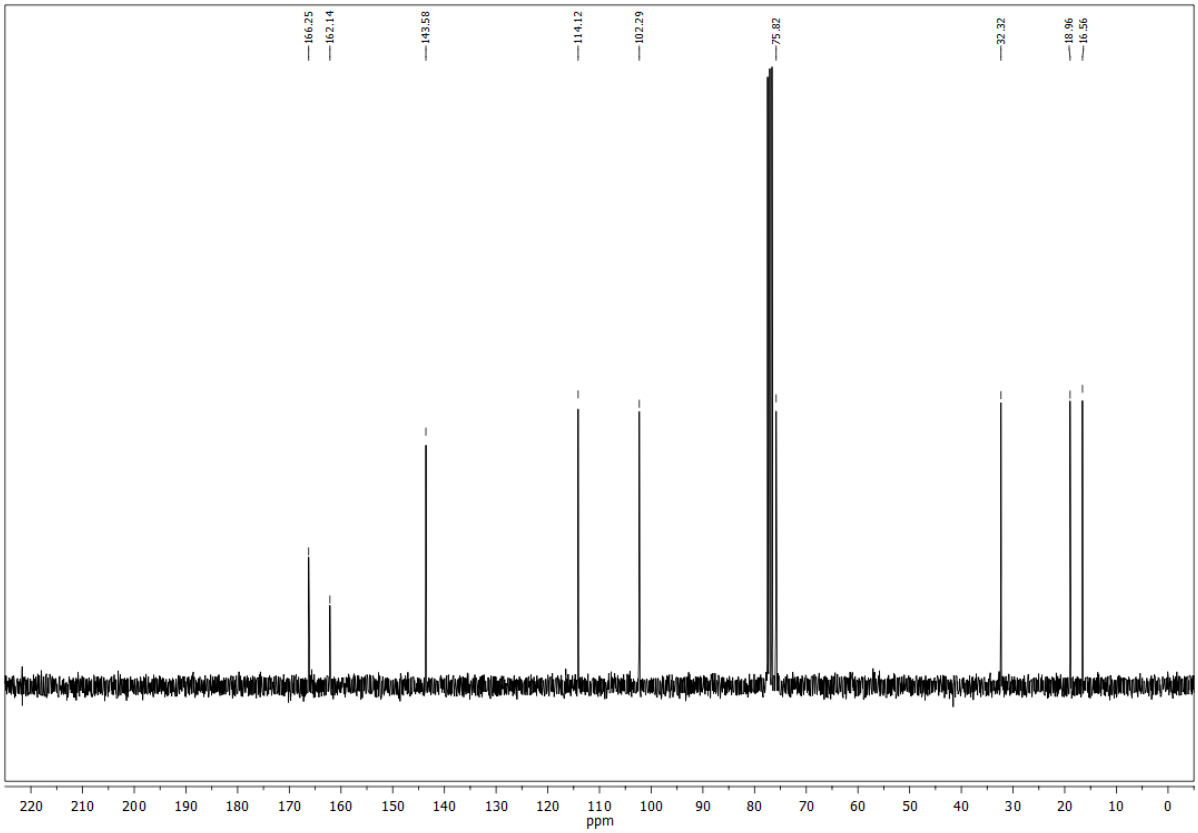


6-(1-Hydroxy-2-methylpropyl)-2*H*-pyran-2-one ((±)-171c)

^{1}H NMR (300 MHz, $CDCl_3$)

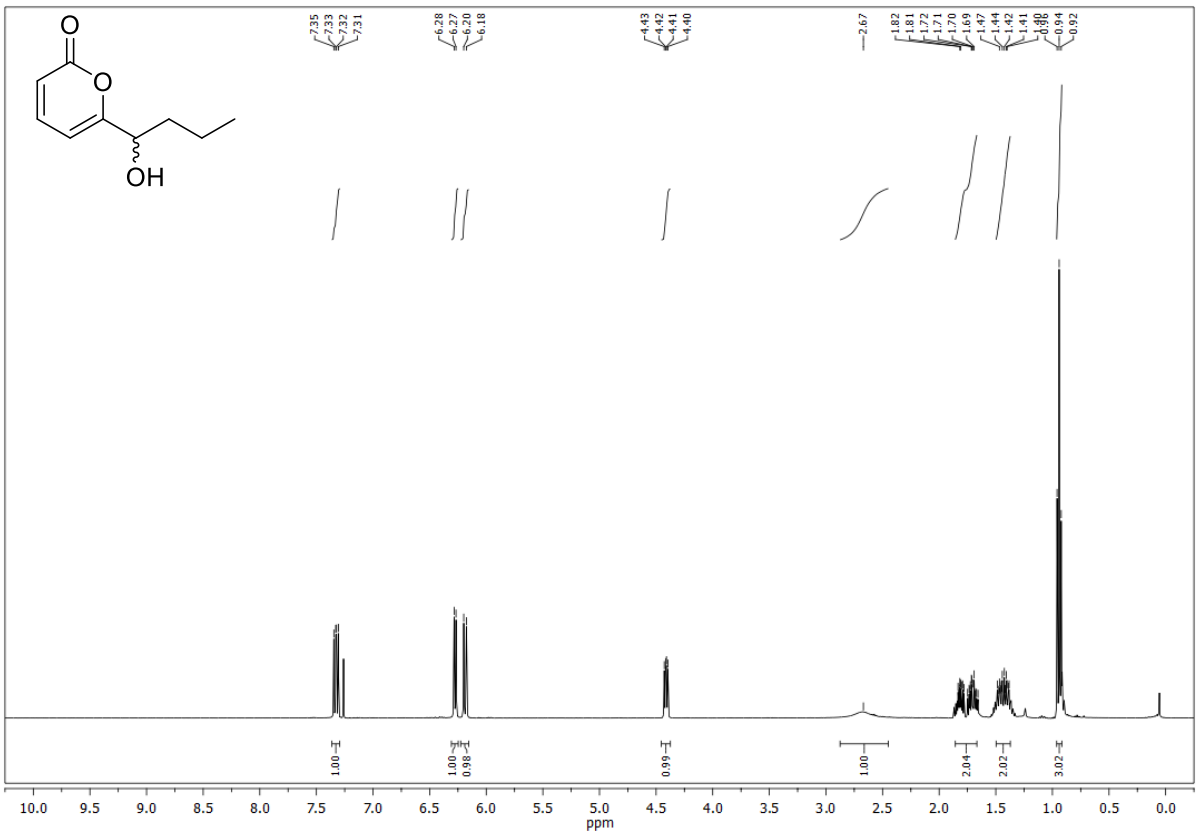


^{13}C NMR (75 MHz, $CDCl_3$)

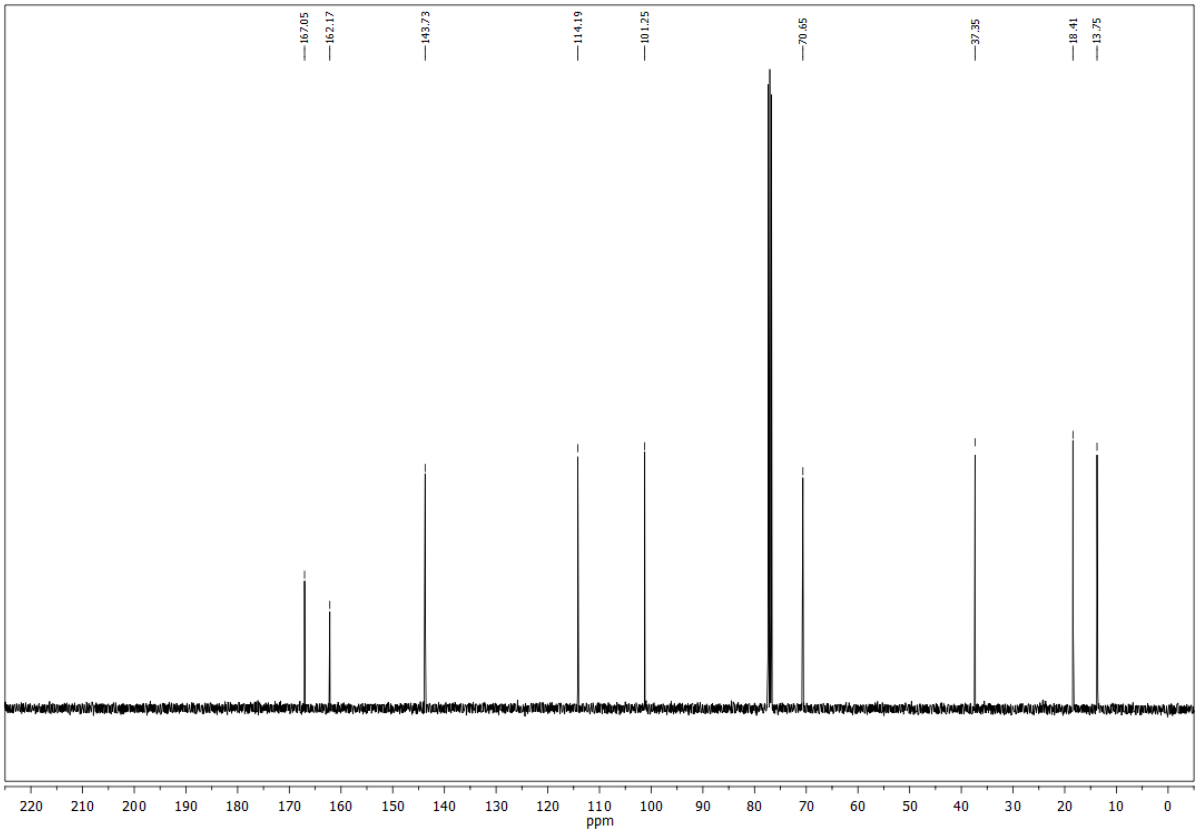


6-(1-Hydroxybutyl)-2*H*-pyran-2-one ((±)-171d)

^{1}H NMR (300 MHz, $CDCl_3$)

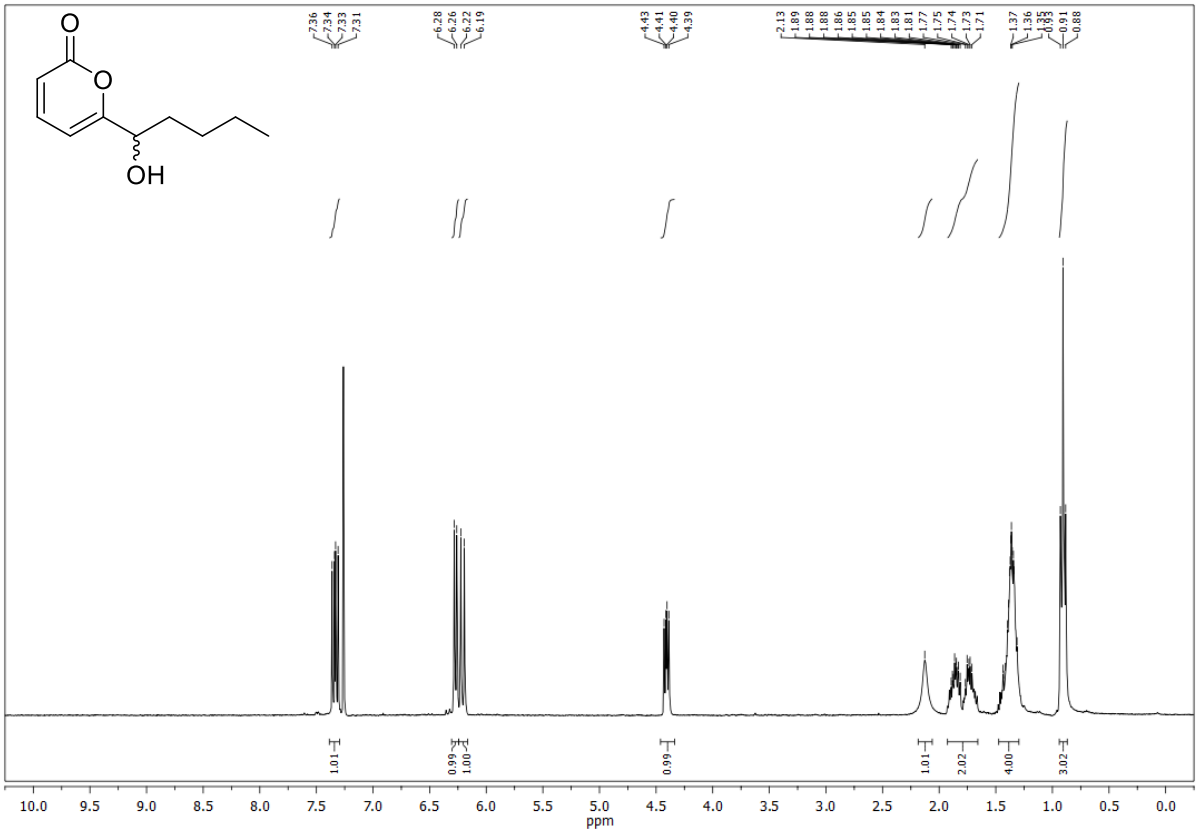


^{13}C NMR (75 MHz, $CDCl_3$)

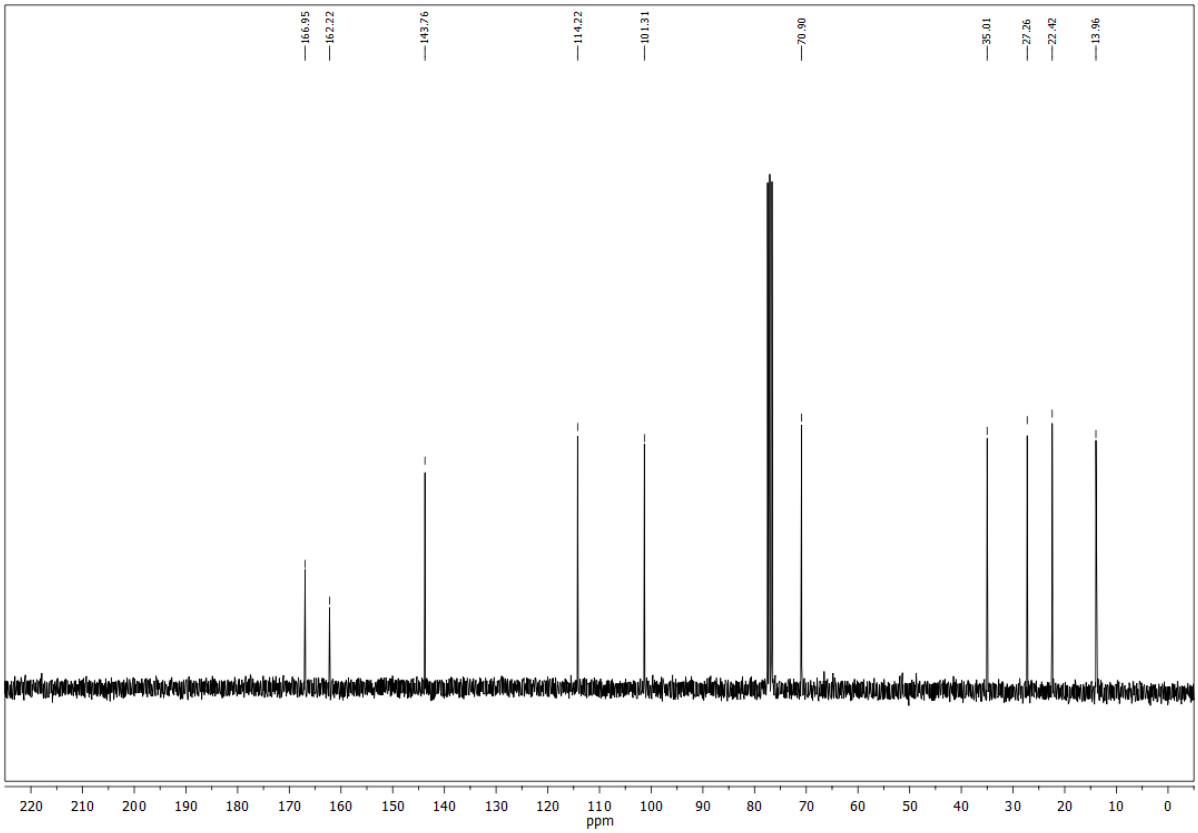


6-(1-Hydroxypentyl)-2*H*-pyran-2-one ((±)-171e)

^{1}H NMR (300 MHz, $CDCl_3$)

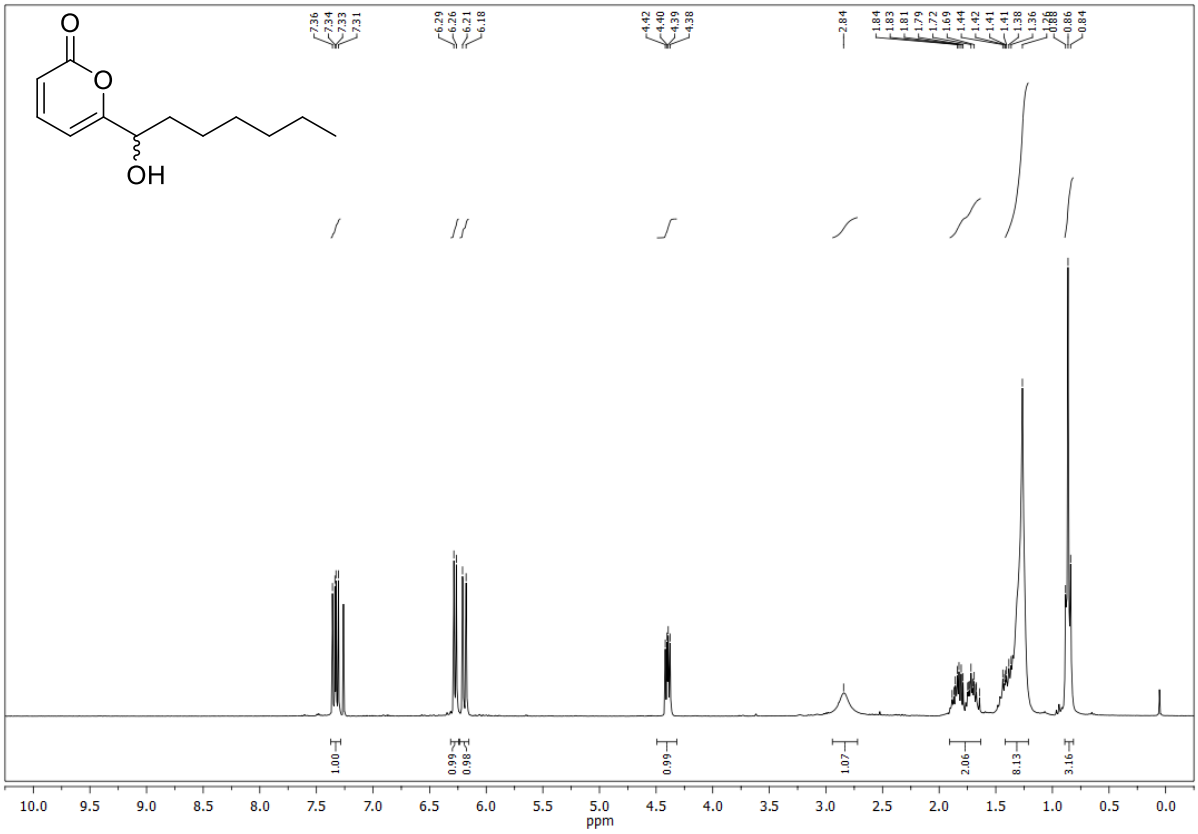


^{13}C NMR (75 MHz, $CDCl_3$)

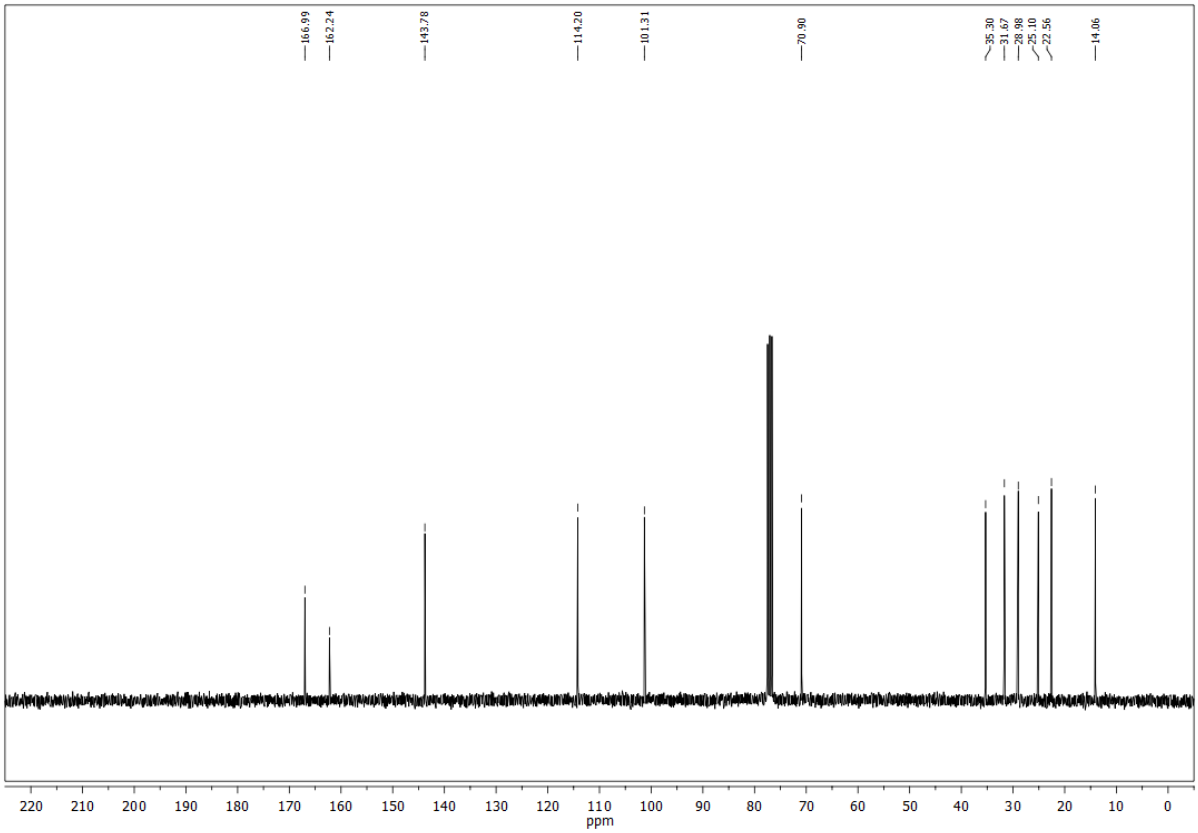


6-(1-Hydroxyheptyl)-2*H*-pyran-2-one ((±)-171f)

^{1}H NMR (300 MHz, $CDCl_3$)

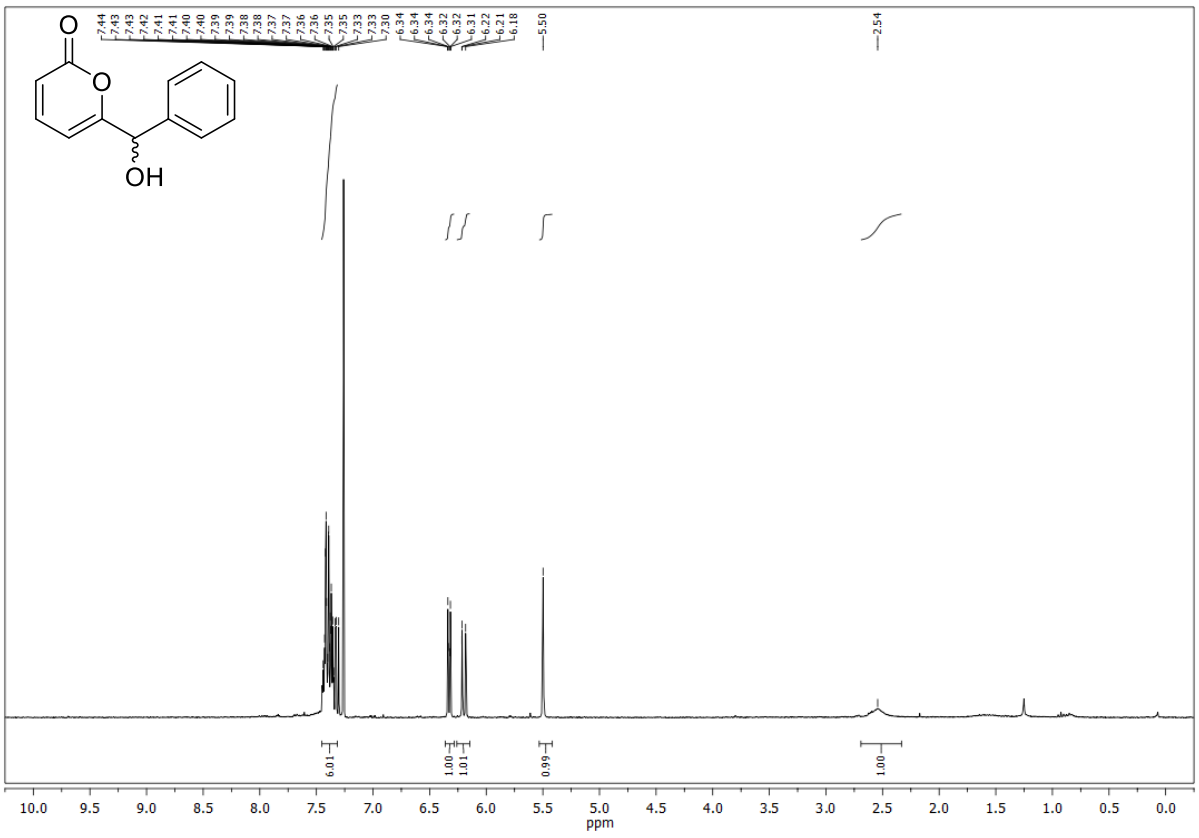


^{13}C NMR (75 MHz, $CDCl_3$)

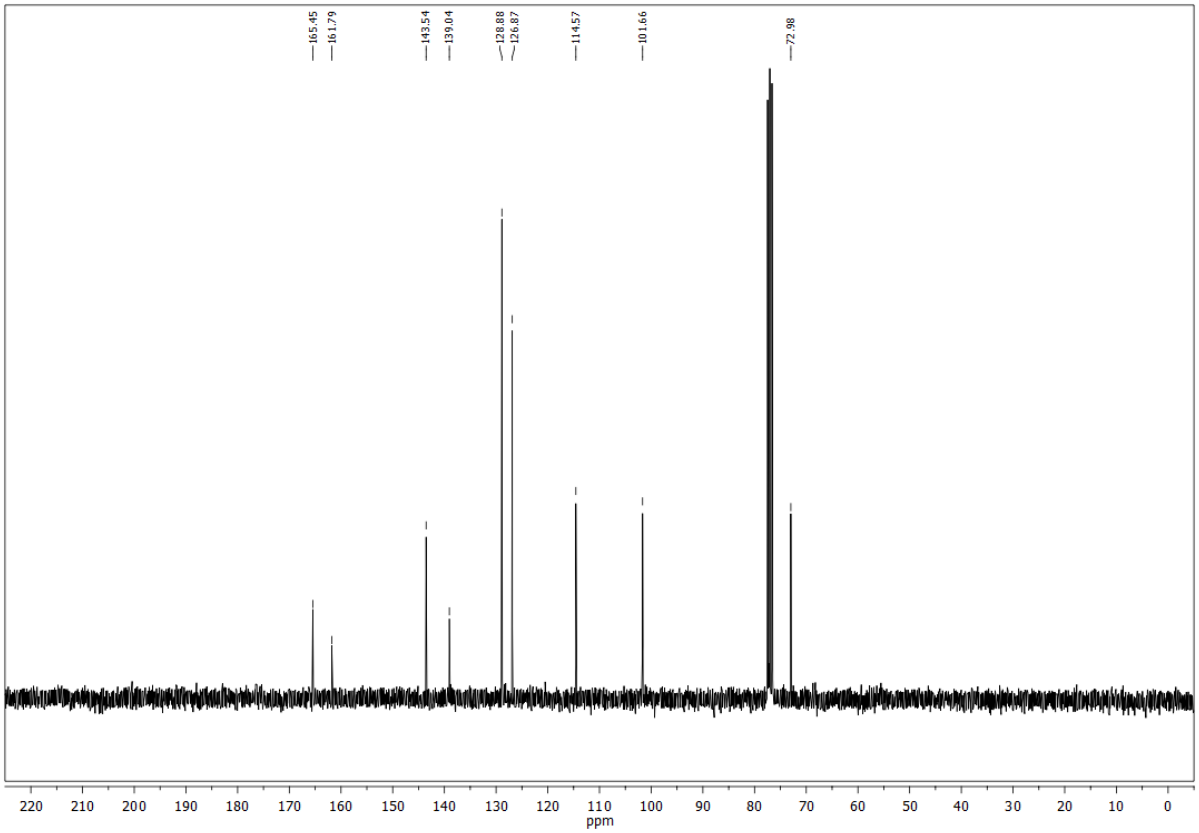


6-(Hydroxy(phenyl)methyl)-2*H*-pyran-2-one ((±)-171g)

^{1}H NMR (300 MHz, $CDCl_3$)

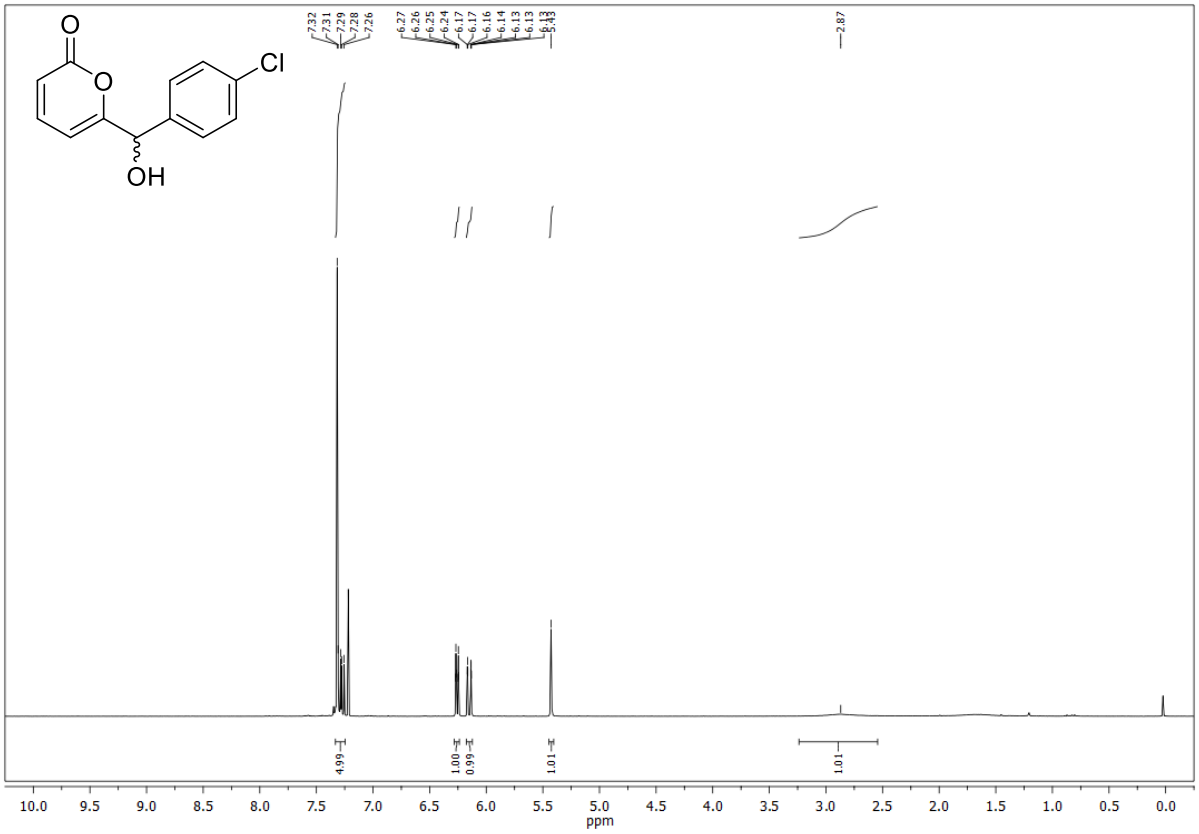


^{13}C NMR (75 MHz, $CDCl_3$)

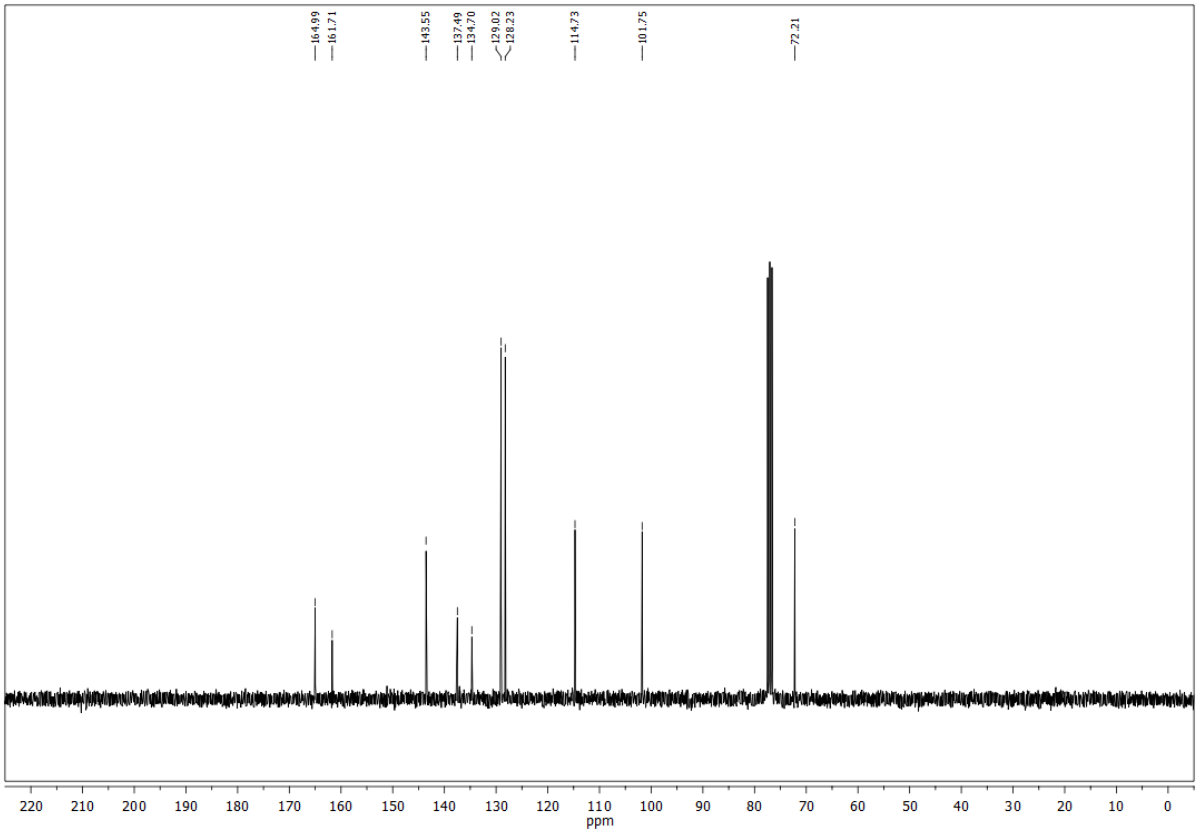


6-((4-Chlorophenyl)(hydroxy)methyl)-2*H*-pyran-2-one ((±)-171h)

^{1}H NMR (300 MHz, $CDCl_3$)

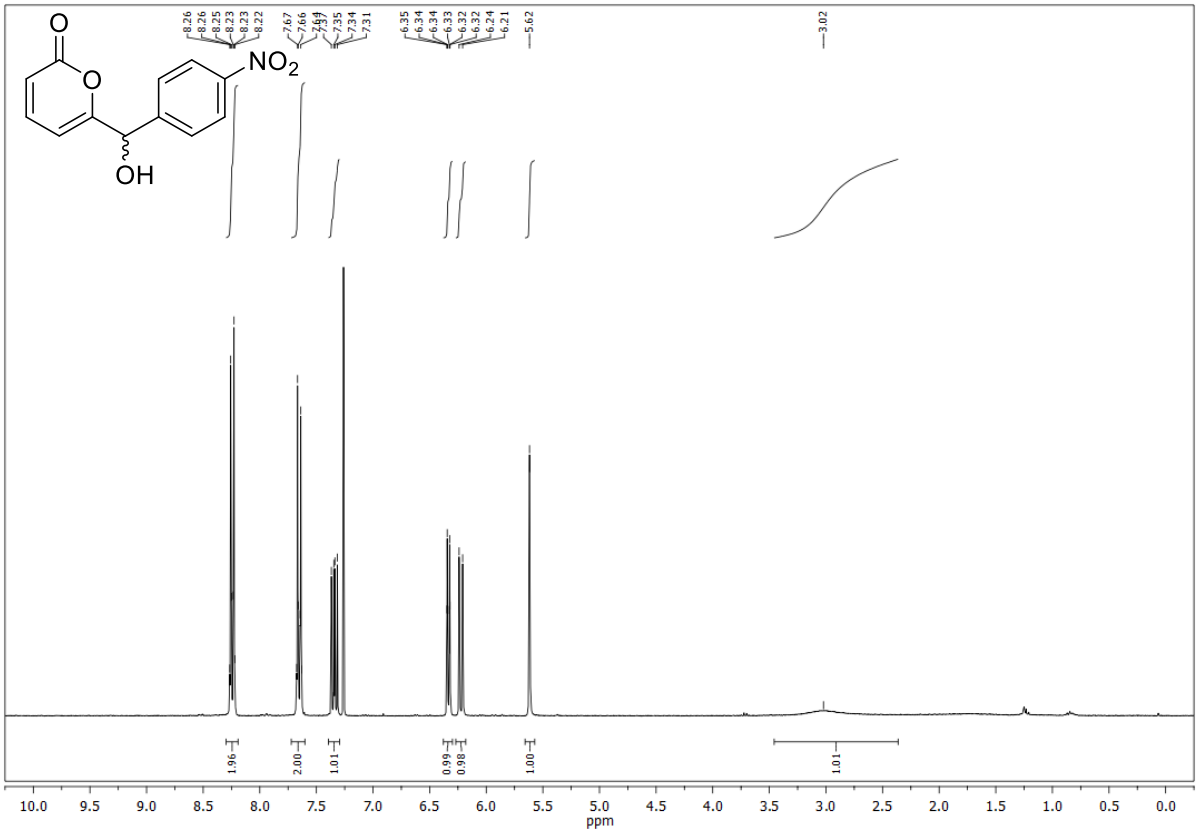


^{13}C NMR (75 MHz, $CDCl_3$)

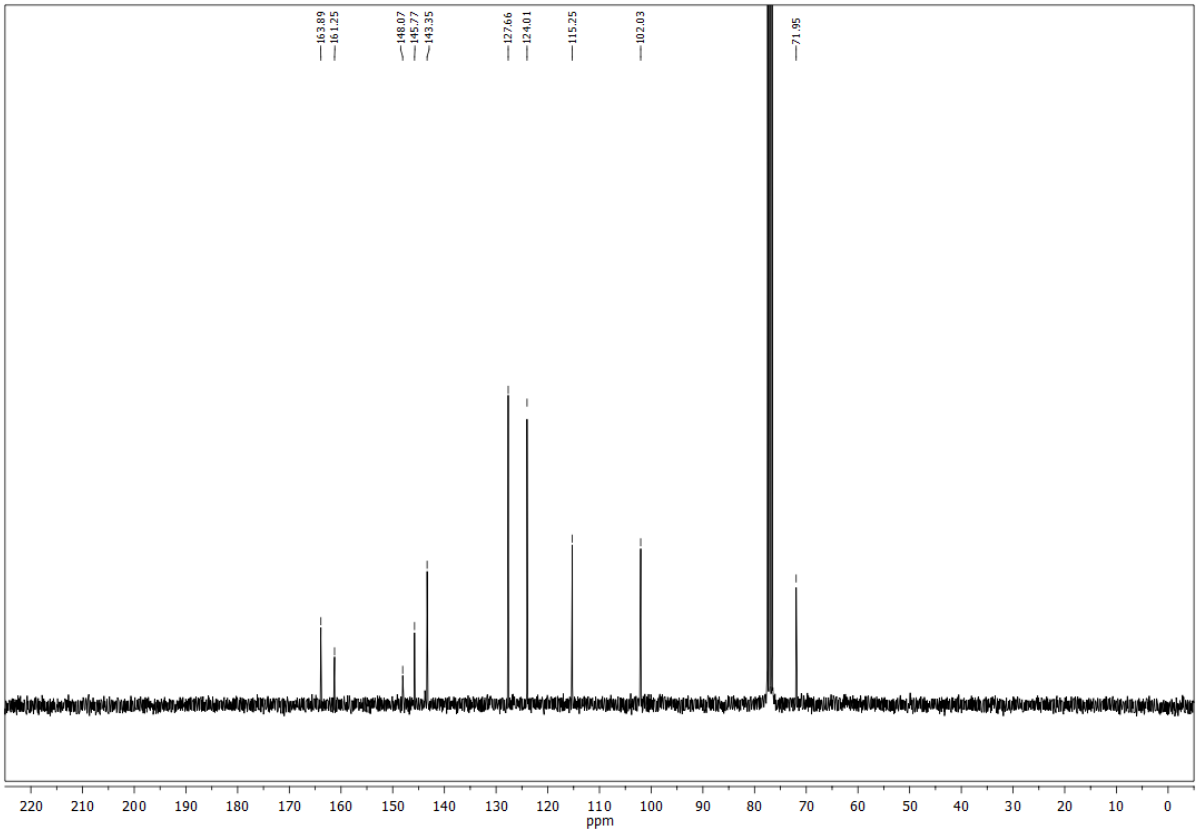


6-(Hydroxy(4-nitrophenyl)methyl)-2*H*-pyran-2-one ((±)-171i)

^{1}H NMR (300 MHz, $CDCl_3$)

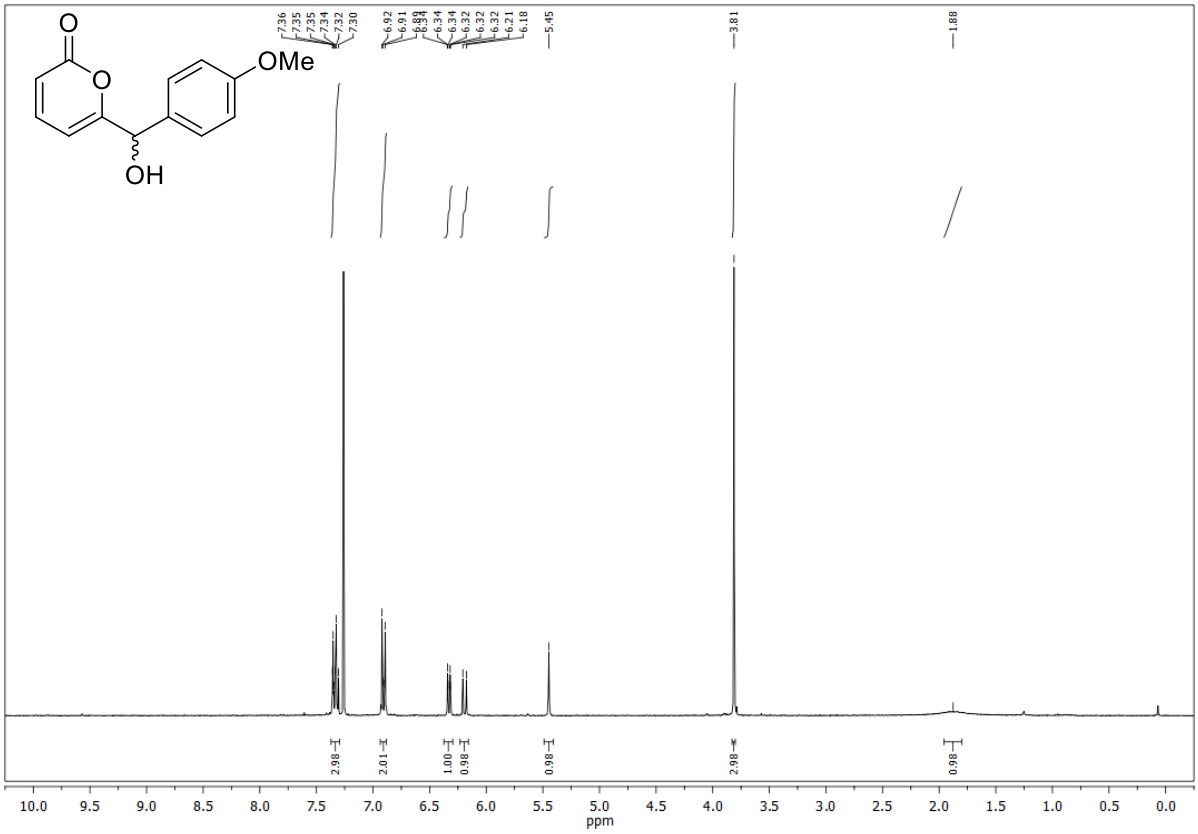


^{13}C NMR (75 MHz, $CDCl_3$)

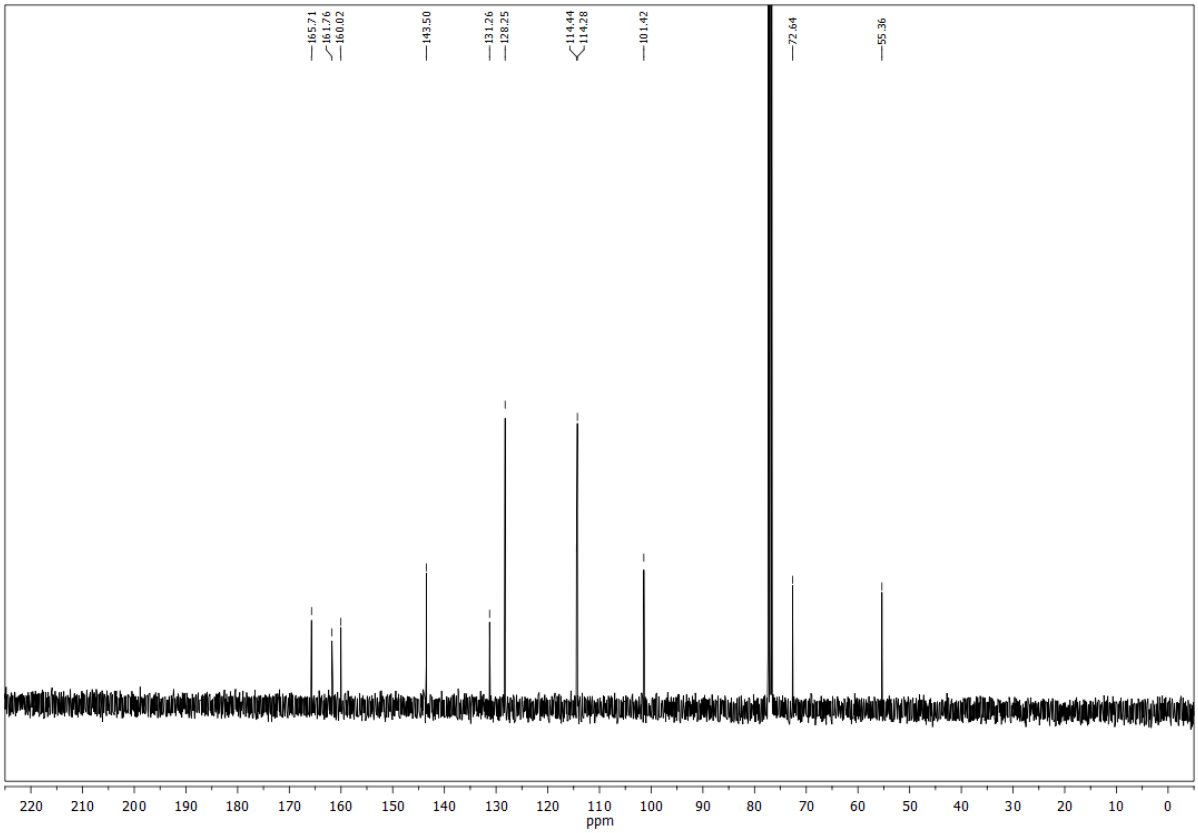


6-(Hydroxy(4-methoxyphenyl)methyl)-2*H*-pyran-2-one ((±)-171j)

^{1}H NMR (300 MHz, $CDCl_3$)

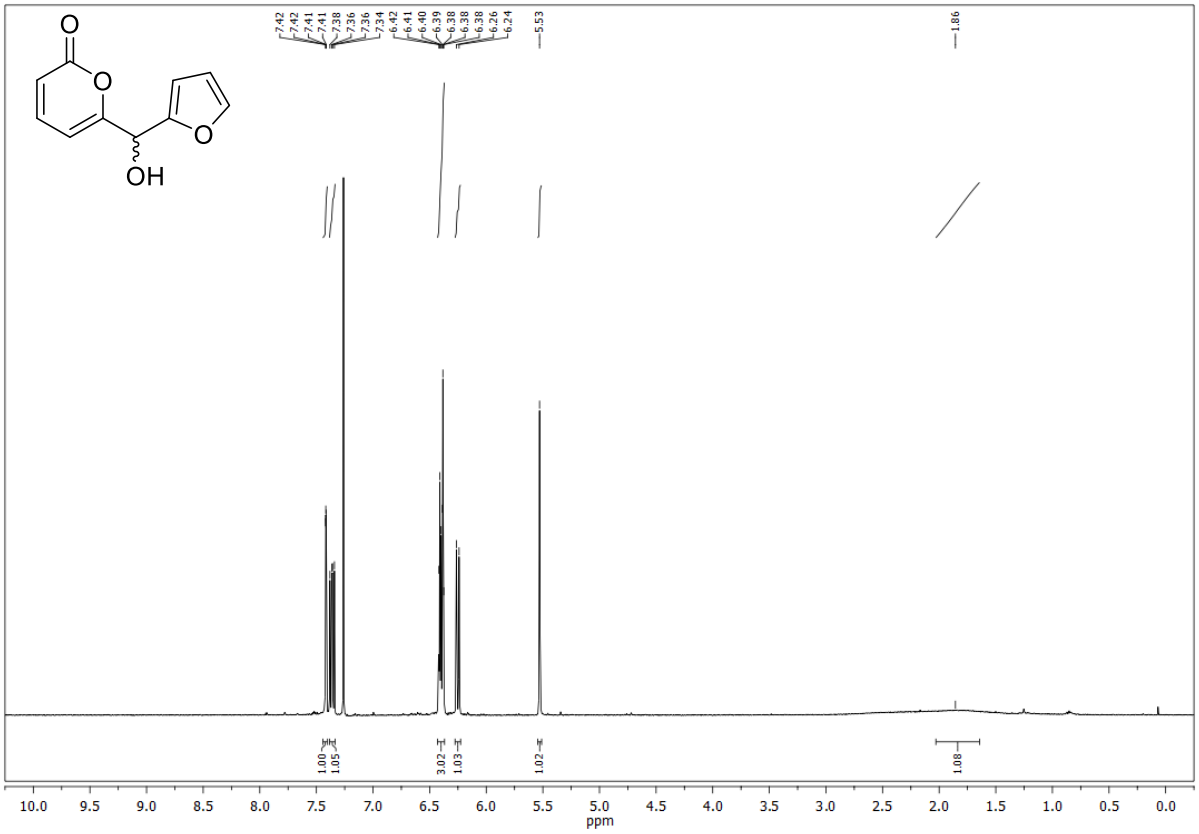


^{13}C NMR (75 MHz, $CDCl_3$)

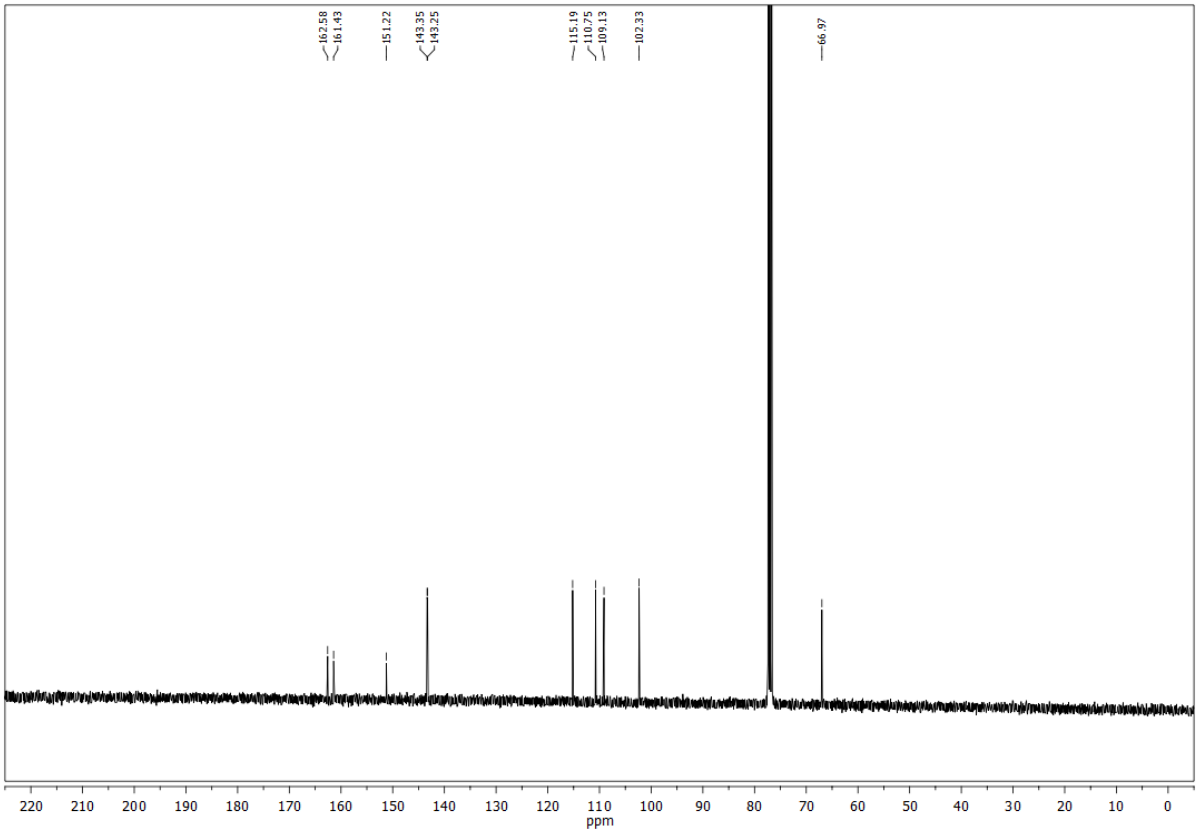


6-(Furan-2-yl(hydroxy)methyl)-2*H*-pyran-2-one ((±)-171k)

^{1}H NMR (400 MHz, $CDCl_3$)

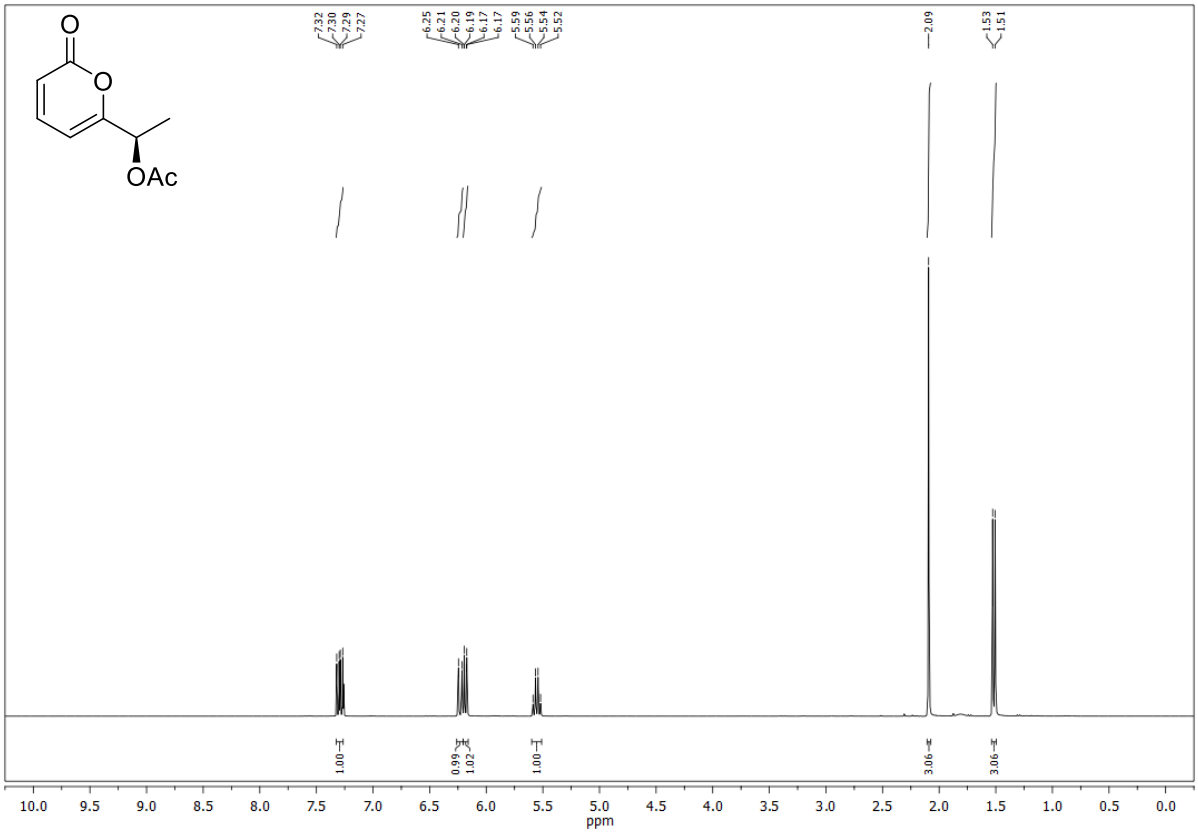


^{13}C NMR (101 MHz, $CDCl_3$)

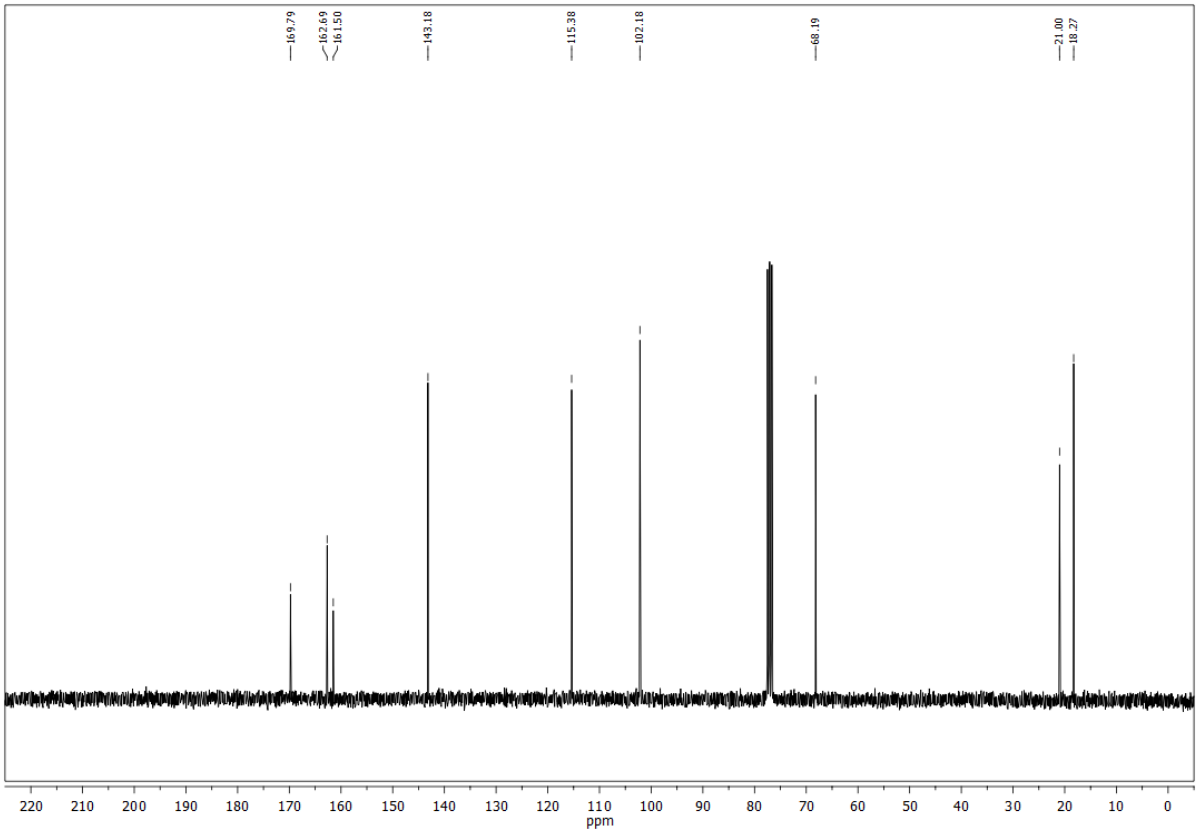


(*R*)-1-(2-Oxo-2*H*-pyran-6-yl)ethyl acetate (174)

^{1}H NMR (300 MHz, $CDCl_3$)

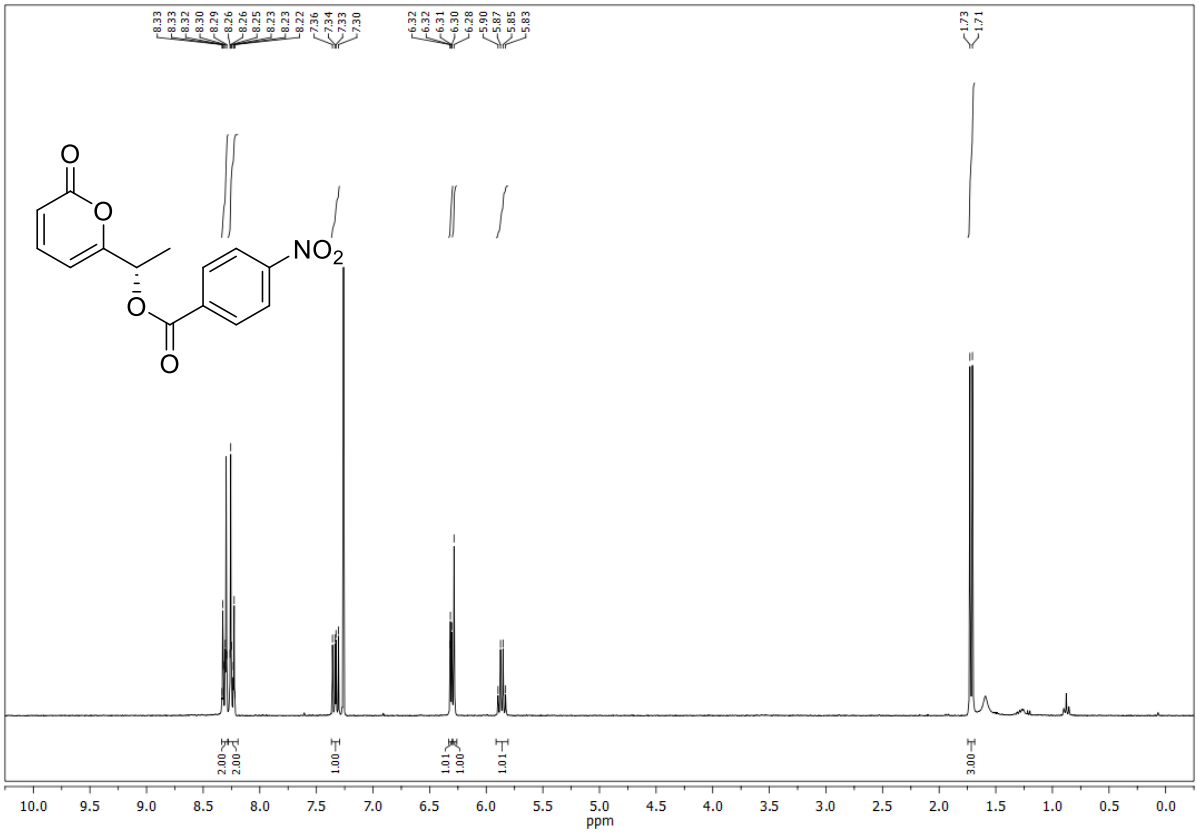


^{13}C NMR (75 MHz, $CDCl_3$)

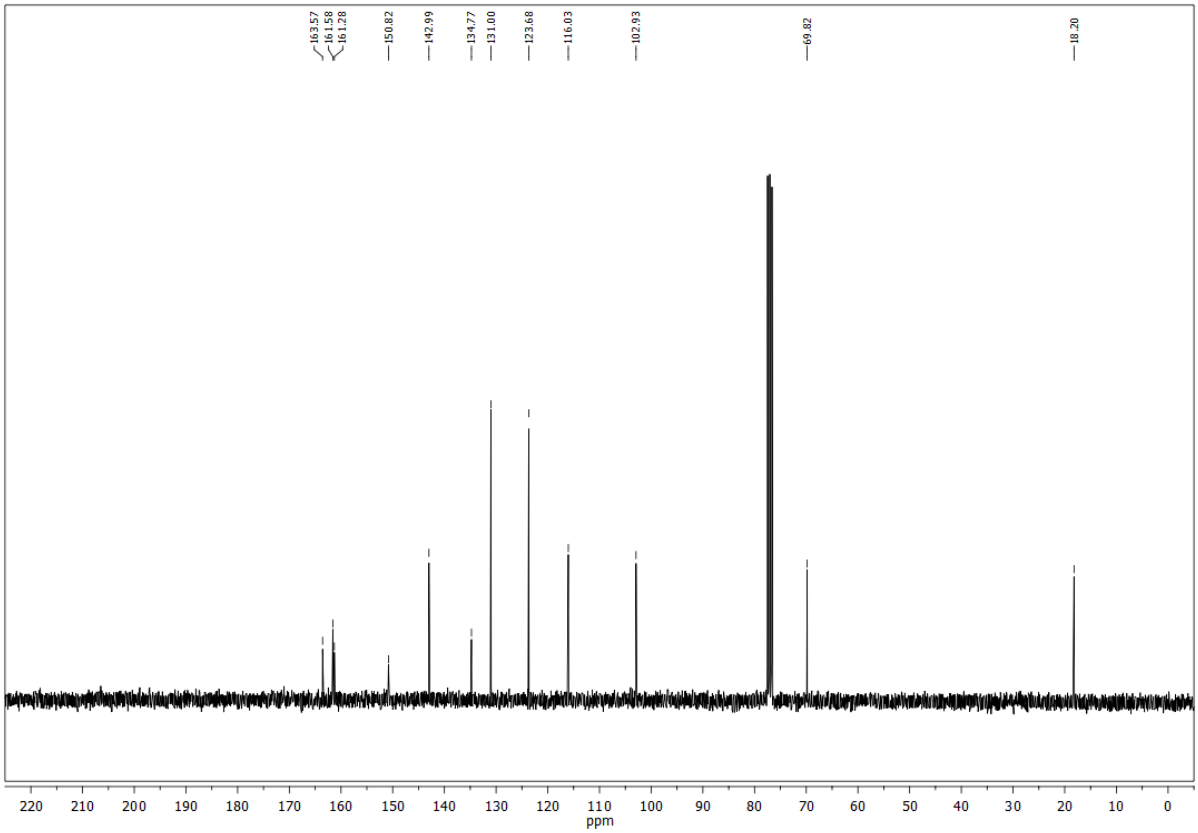


(*S*)-1-(2-Oxo-2*H*-pyran-6-yl)ethyl 4-nitrobenzoate (175)

^{1}H NMR (300 MHz, $CDCl_3$)

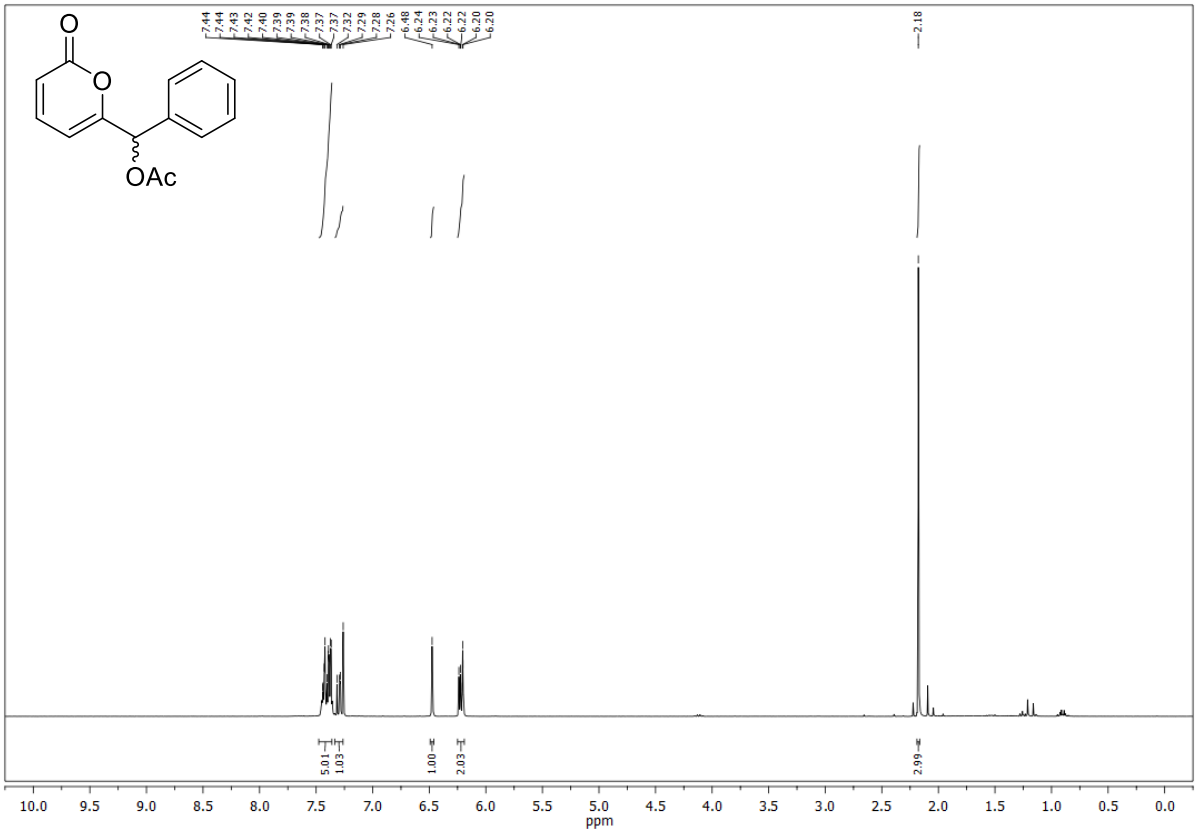


^{13}C NMR (75 MHz, $CDCl_3$)

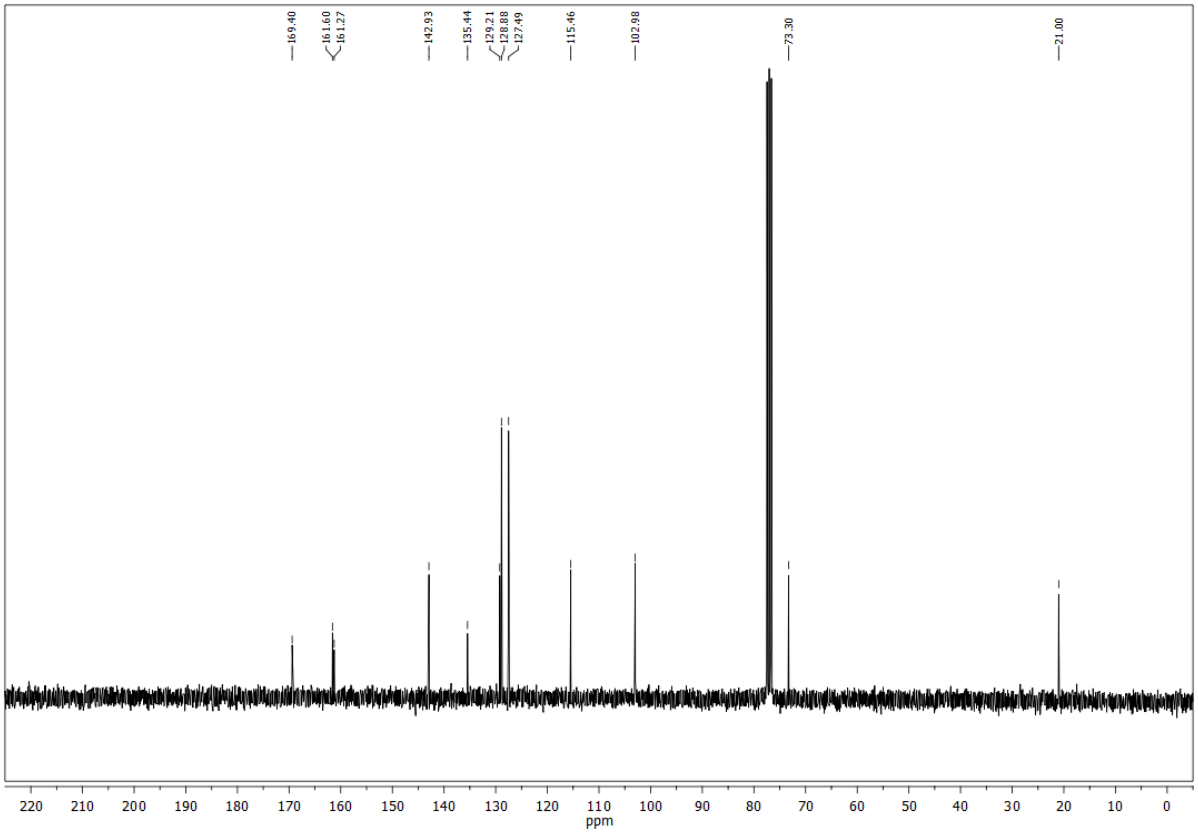


(2-Oxo-2*H*-pyran-6-yl)(phenyl)methyl acetate ((±)-180)

^{1}H NMR (300 MHz, $CDCl_3$)

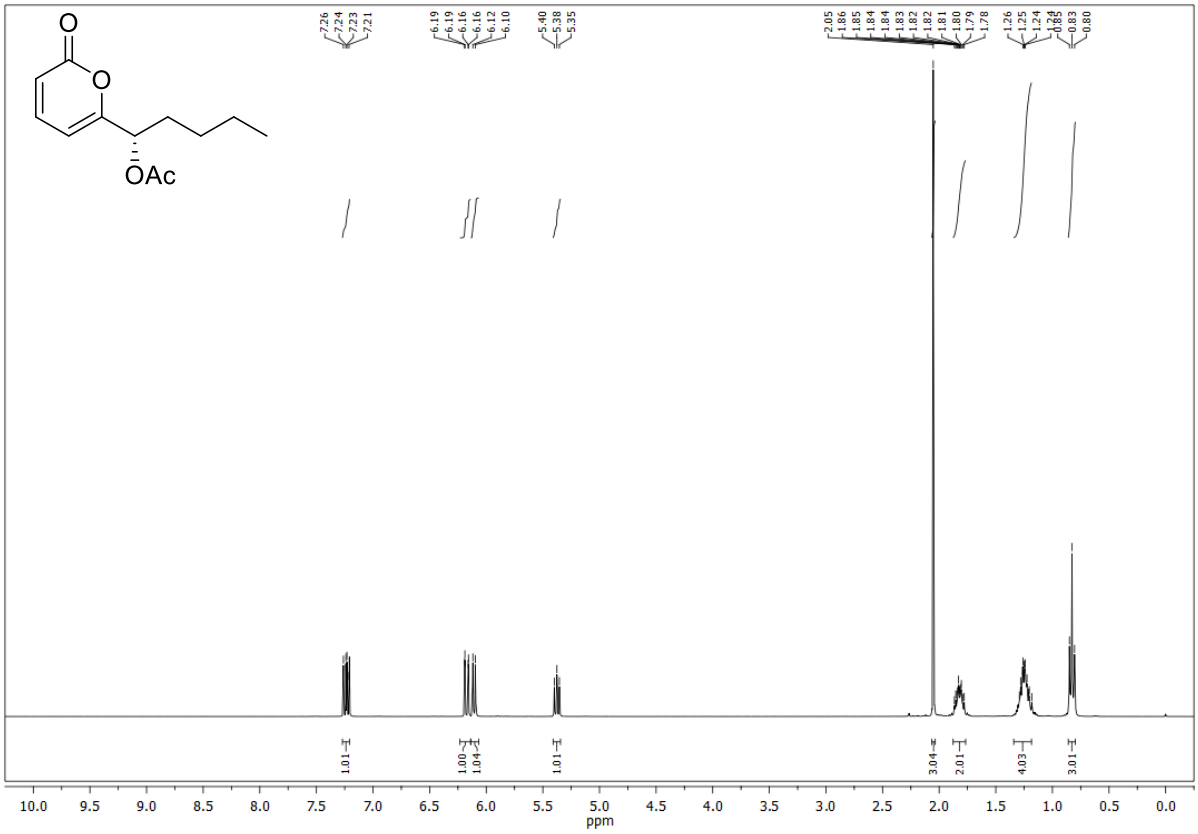


^{13}C NMR (75 MHz, $CDCl_3$)

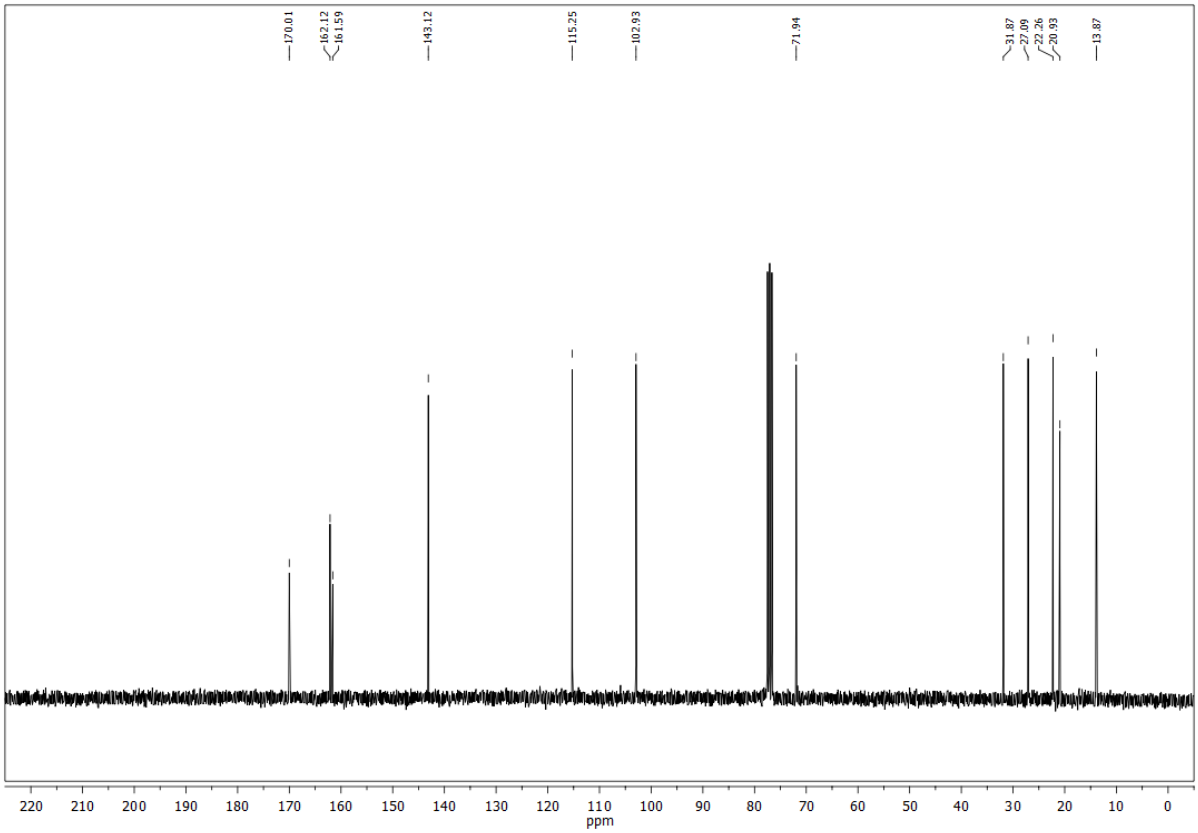


(*S*)-1-(2-Oxo-2*H*-pyran-6-yl)pentyl acetate (179)

^{1}H NMR (300 MHz, $CDCl_3$)

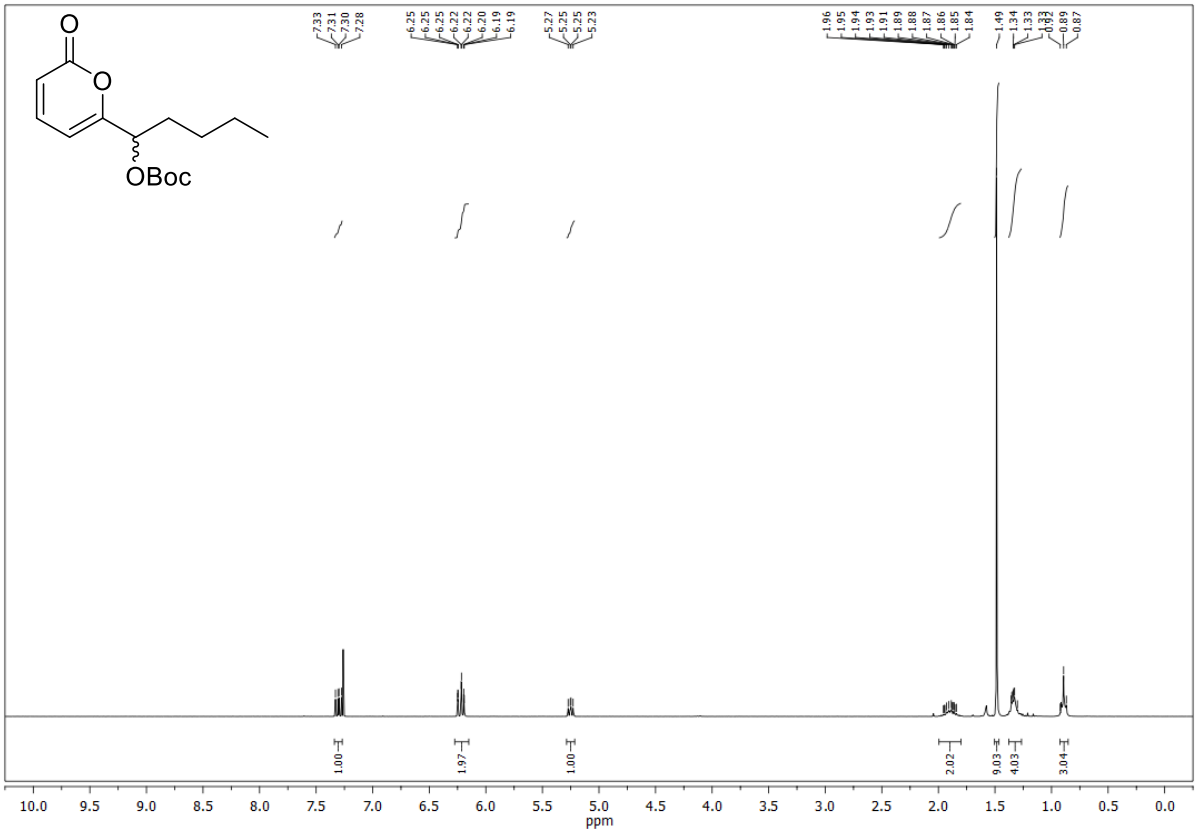


^{13}C NMR (75 MHz, $CDCl_3$)

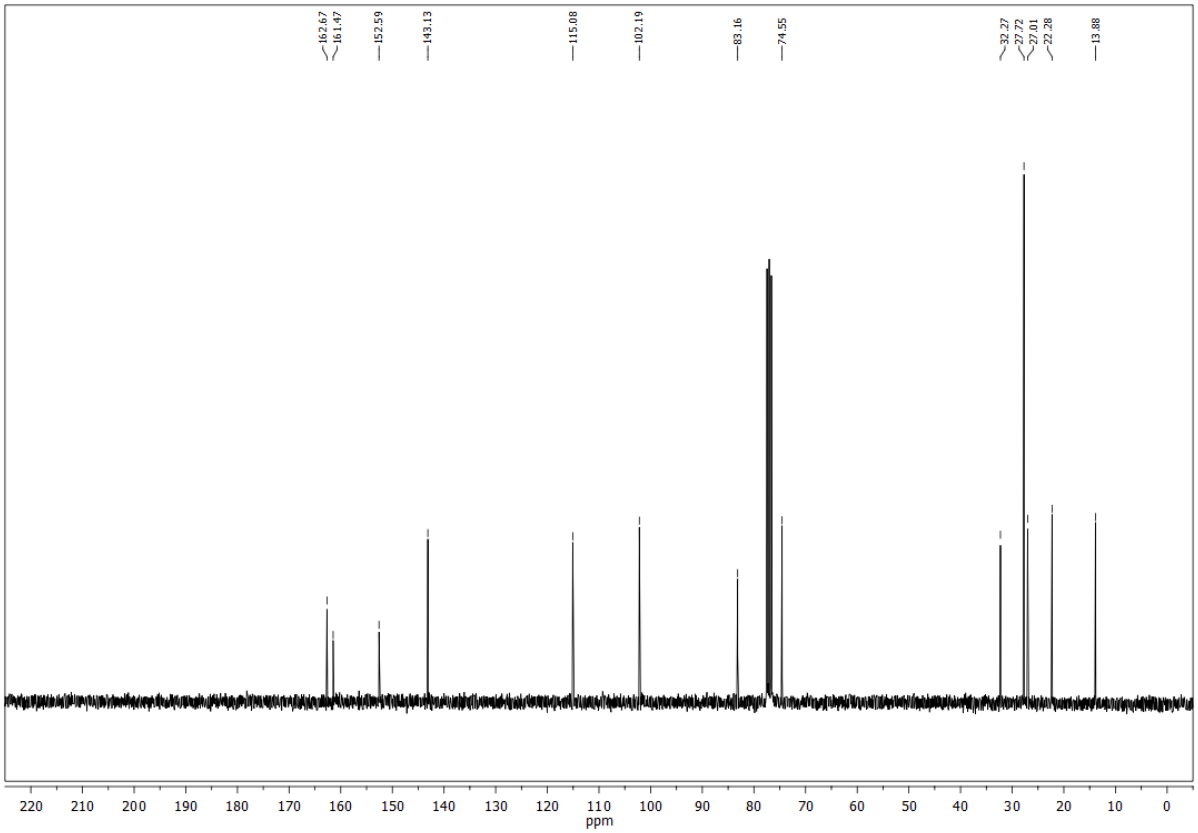


tert-Butyl (1-(2-oxo-2*H*-pyran-6-yl)pentyl) carbonate ((±)-190)

^{1}H NMR (300 MHz, $CDCl_3$)

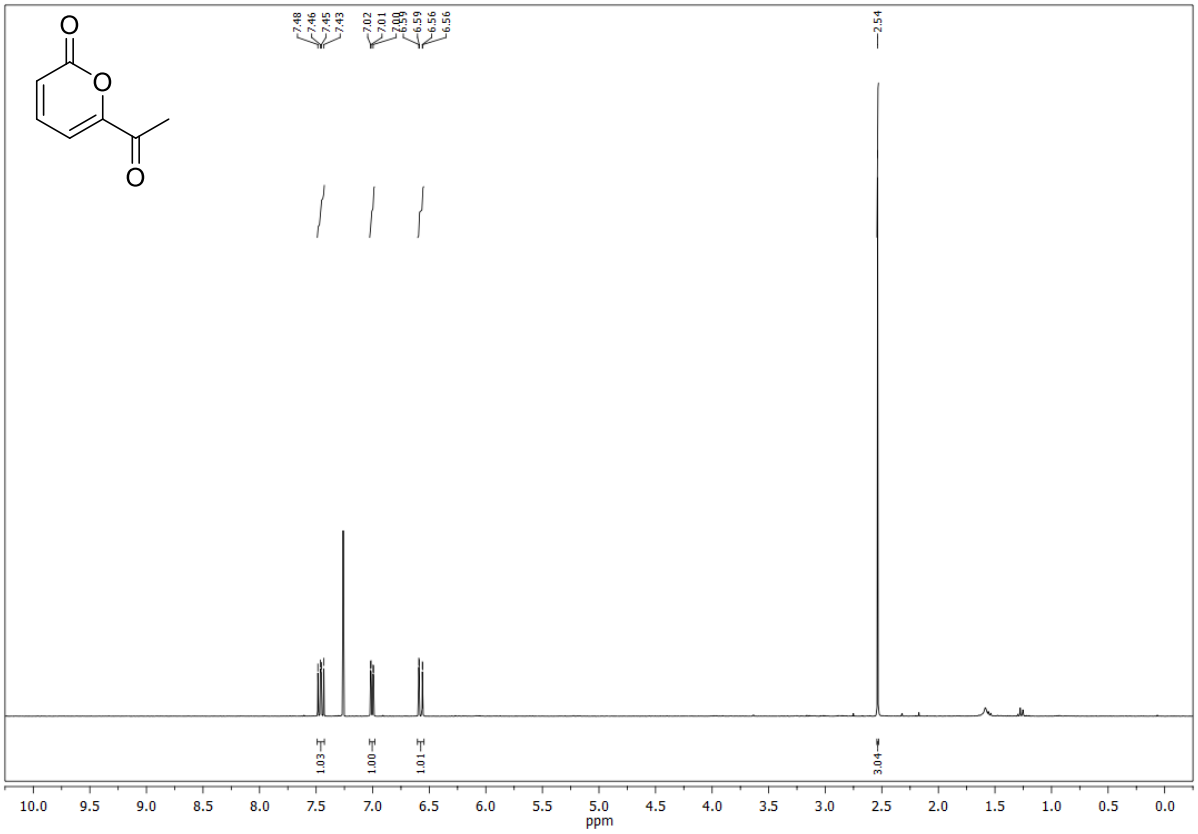


^{13}C NMR (75 MHz, $CDCl_3$)

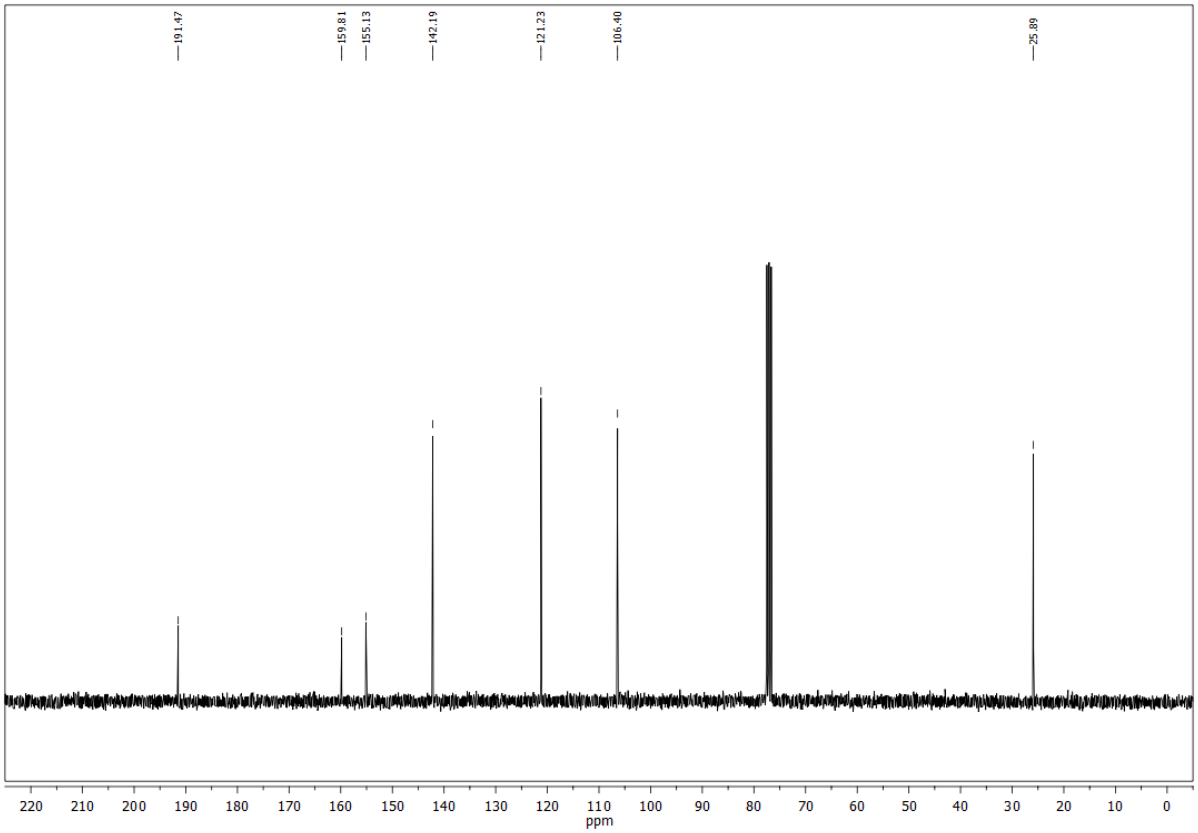


6-Acetyl-*2H*-pyran-2-one (195a)

^{1}H NMR (300 MHz, $CDCl_3$)

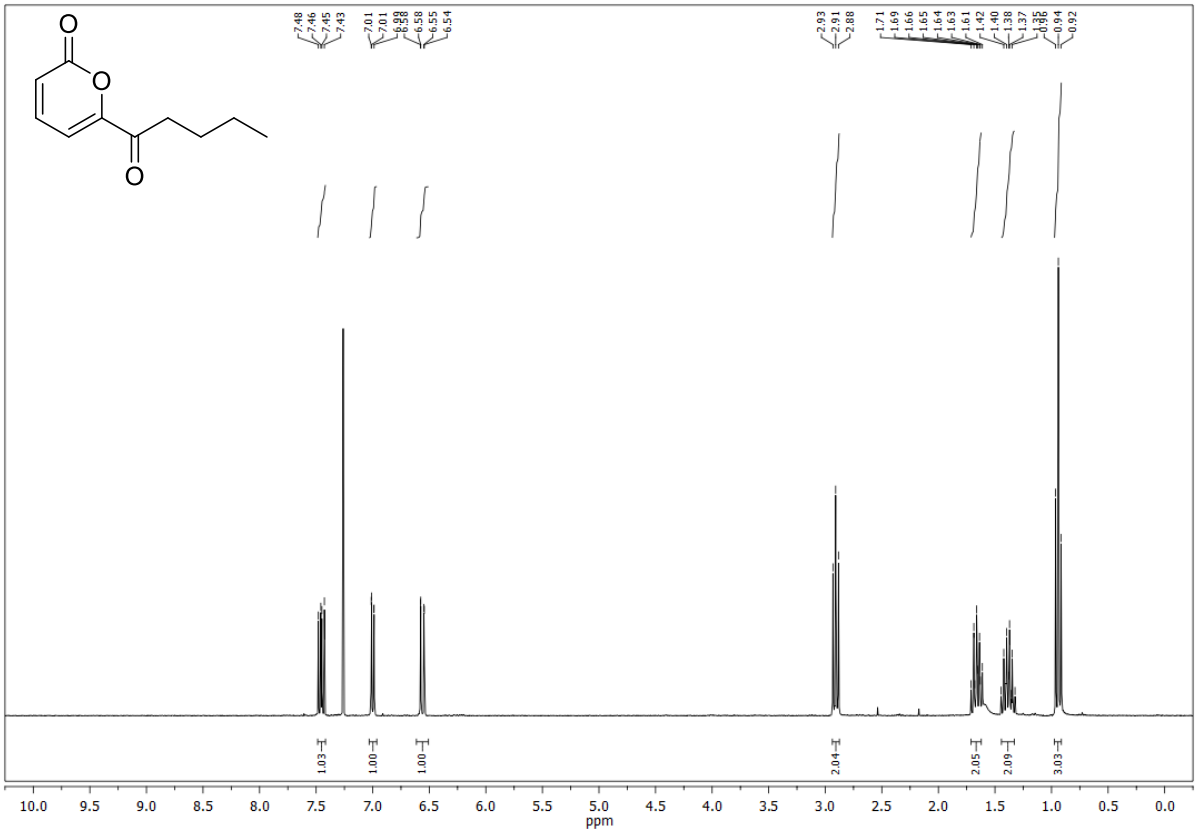


^{13}C NMR (75 MHz, $CDCl_3$)

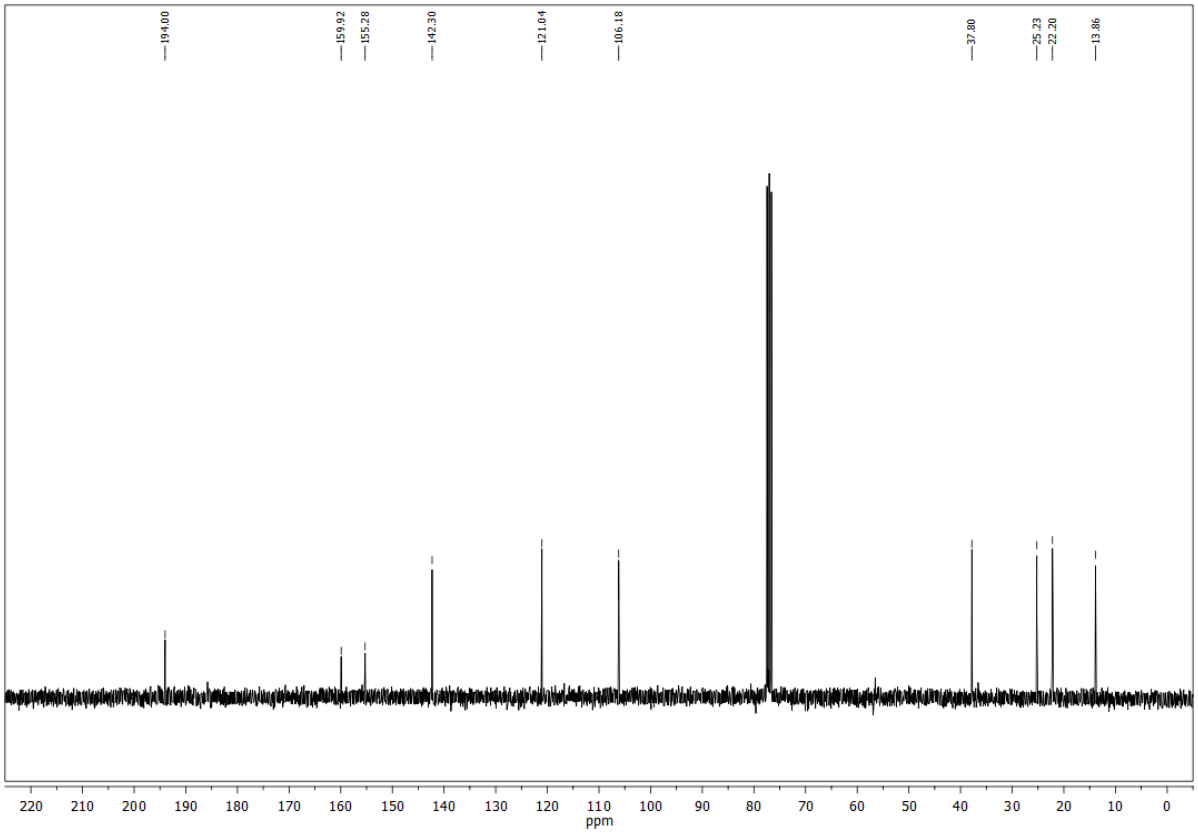


6-Pentanoyl-2*H*-pyran-2-one (195b)

^{1}H NMR (300 MHz, $CDCl_3$)

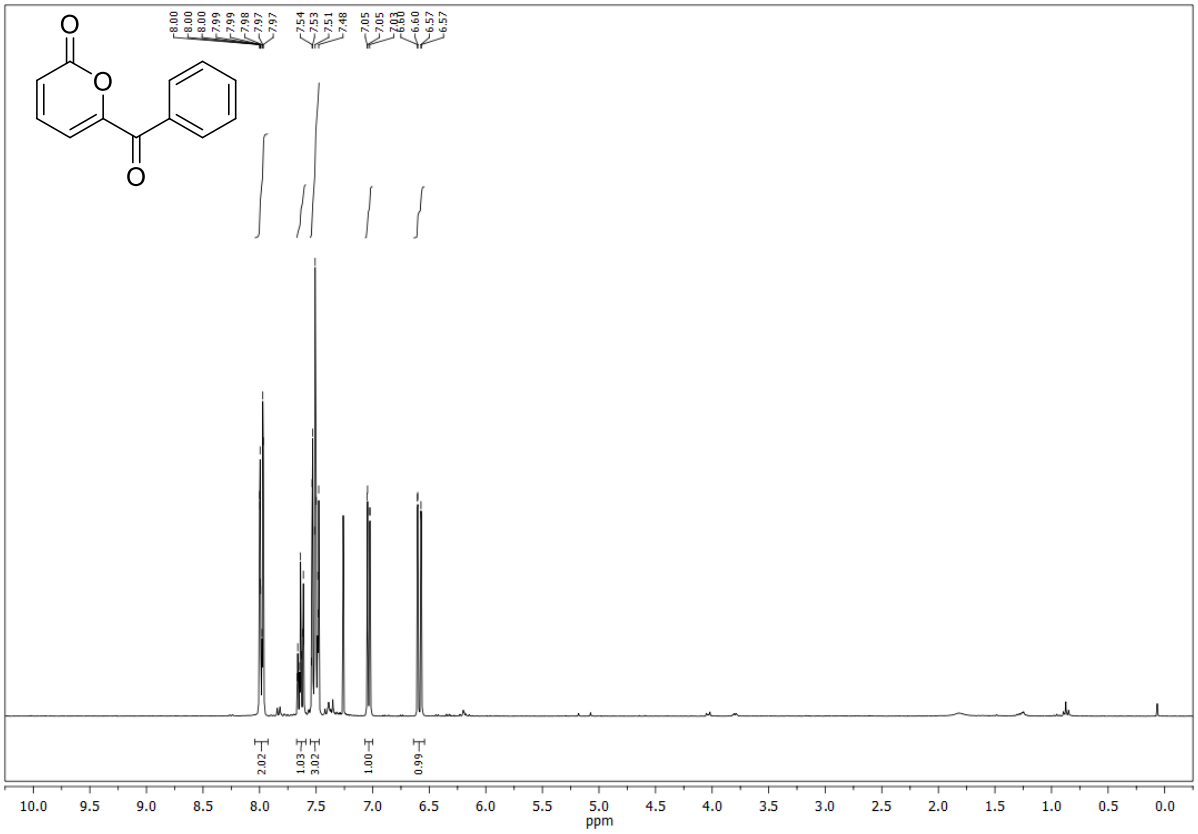


^{13}C NMR (75 MHz, $CDCl_3$)

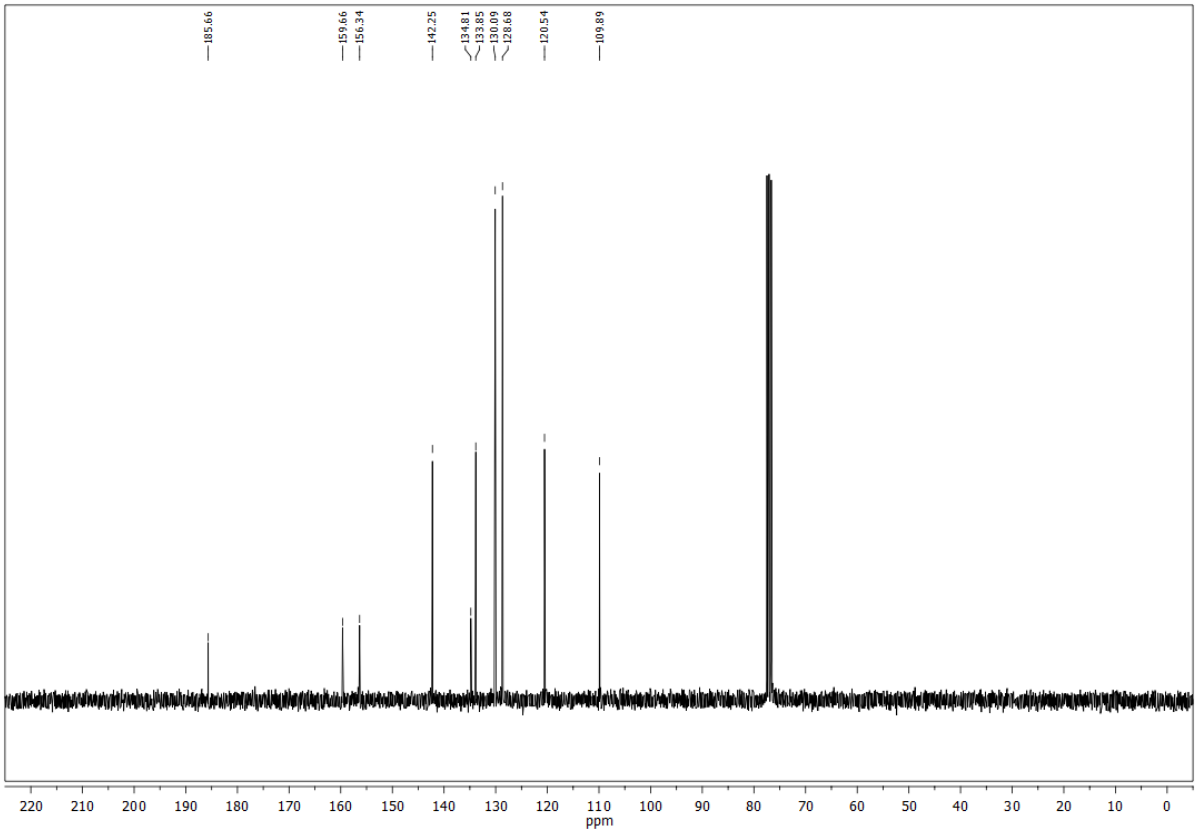


6-Benzoyl-2*H*-pyran-2-one (195c)

^{1}H NMR (300 MHz, $CDCl_3$)

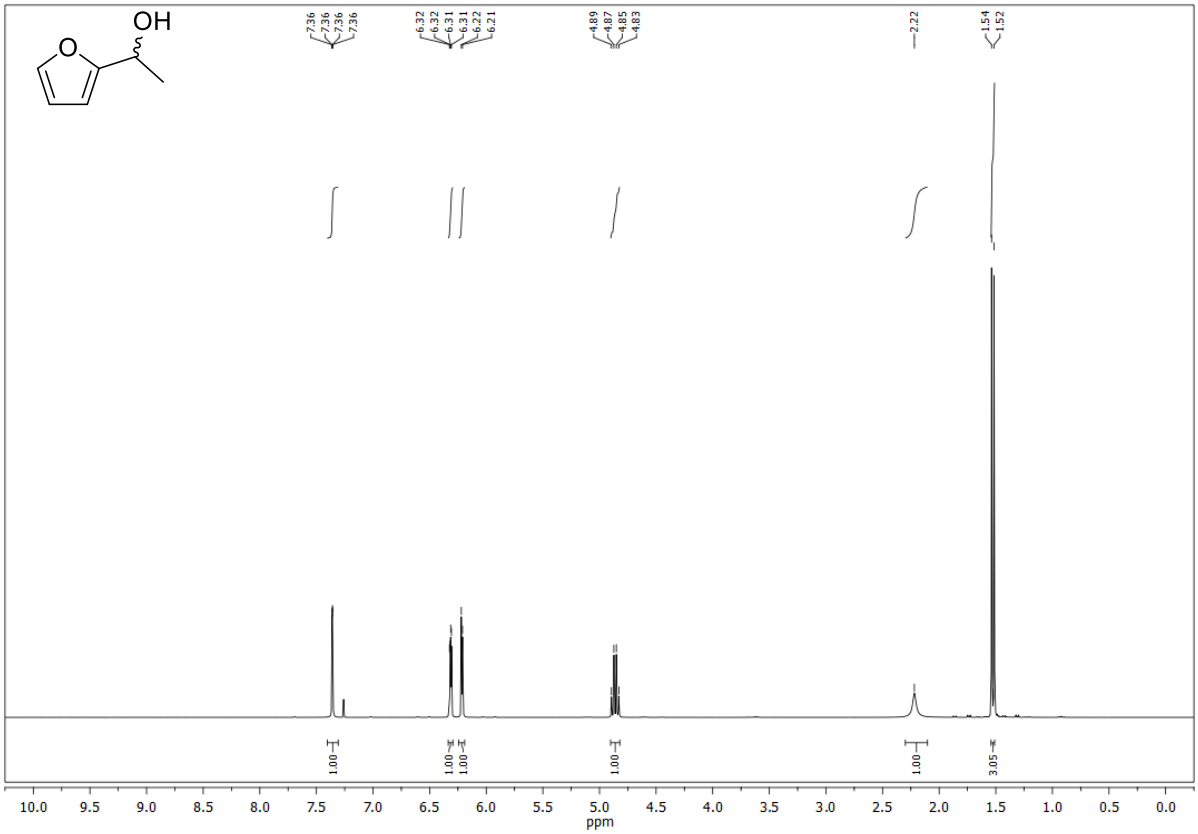


^{13}C NMR (75 MHz, $CDCl_3$)

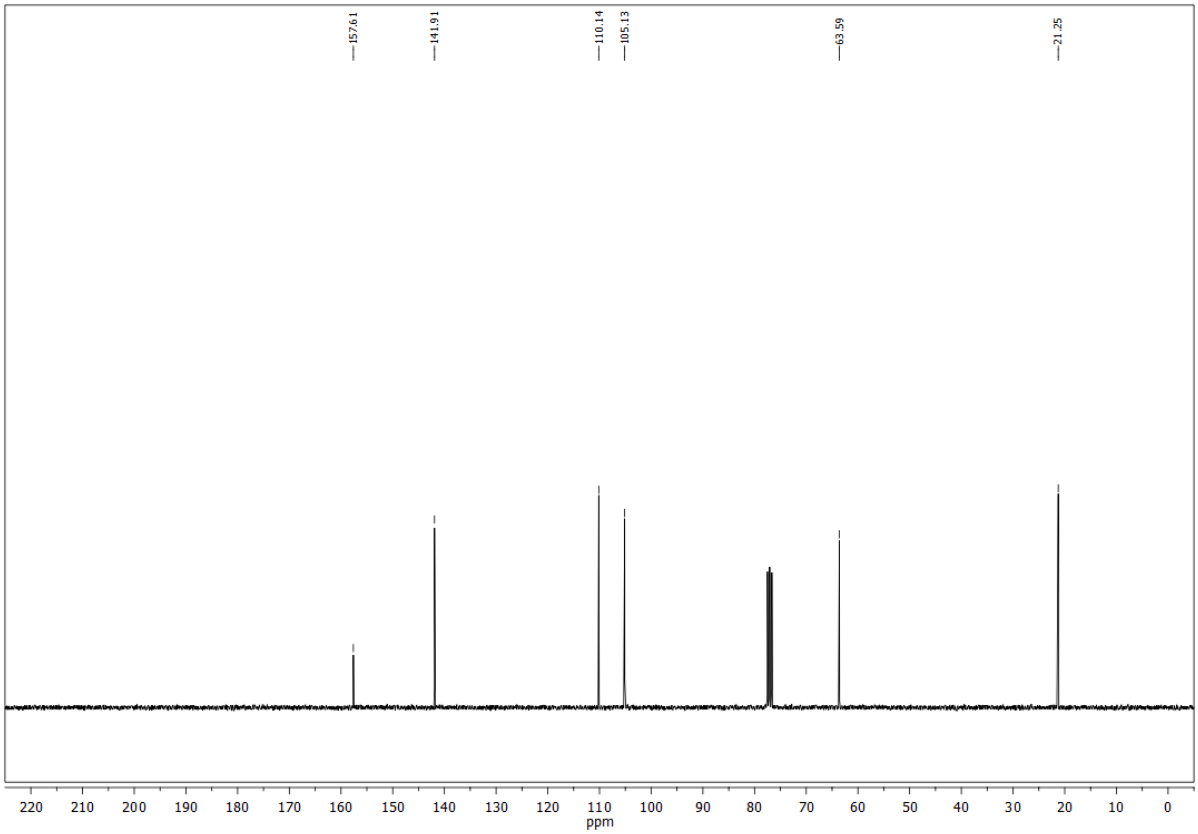


1-(Furan-2-yl)ethan-1-ol ((±)-199)

^{1}H NMR (300 MHz, $CDCl_3$)

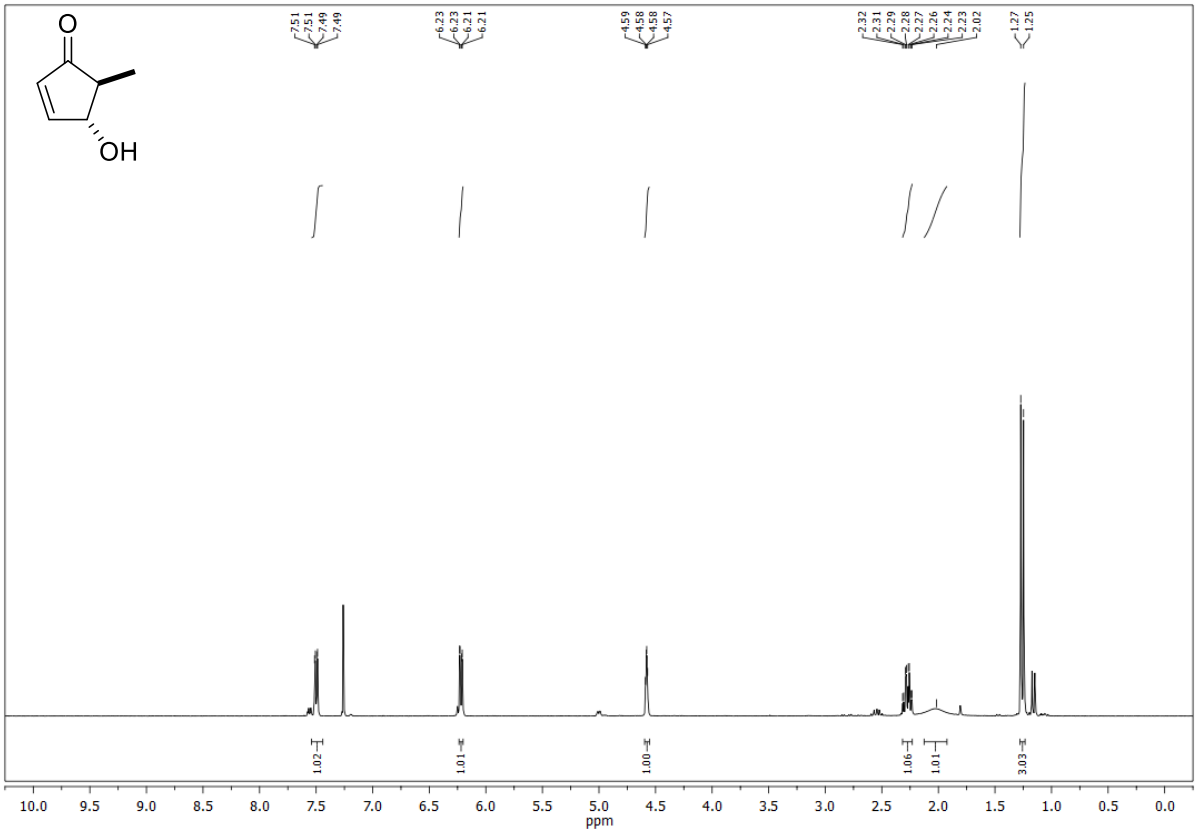


^{13}C NMR (75 MHz, $CDCl_3$)

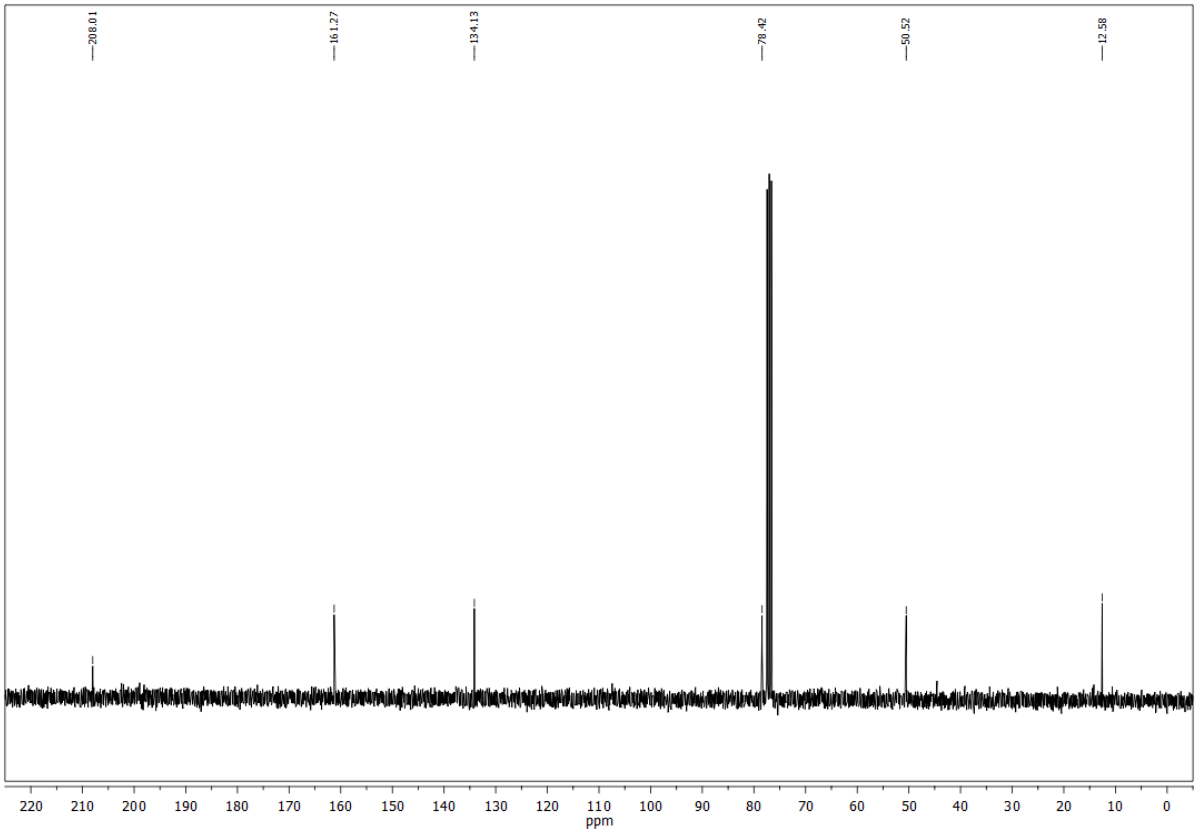


4-Hydroxy-5-methylcyclopent-2-en-1-one ((±)-200)

^{1}H NMR (300 MHz, $CDCl_3$)

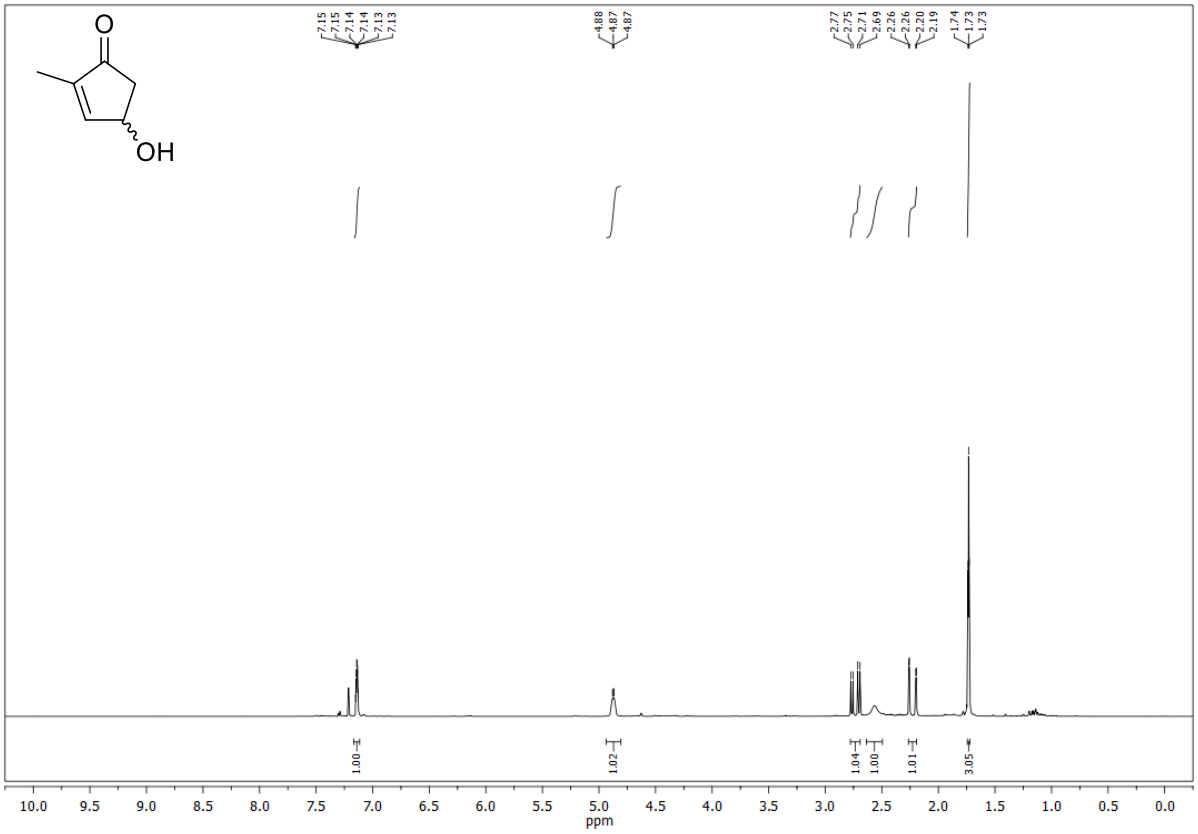


^{13}C NMR (75 MHz, $CDCl_3$)

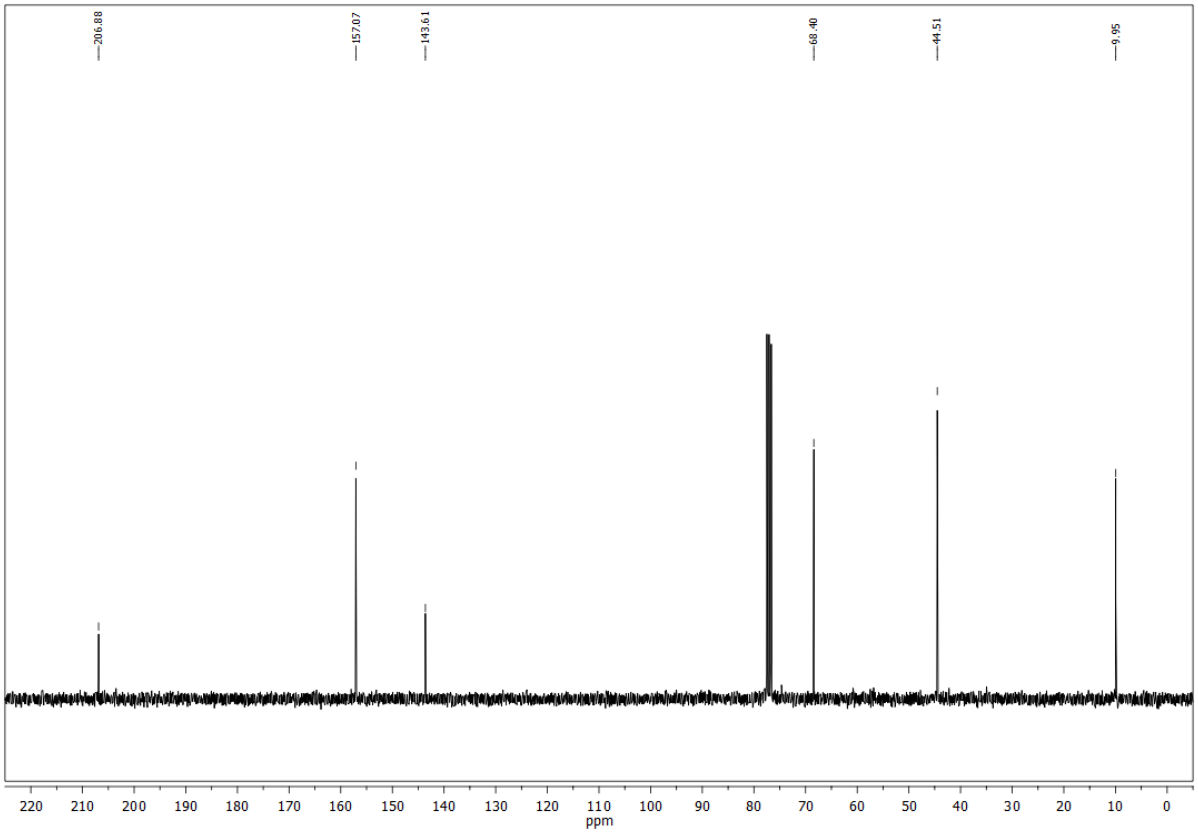


4-Hydroxy-2-methylcyclopent-2-en-1-one ((±)-201)

^{1}H NMR (300 MHz, $CDCl_3$)

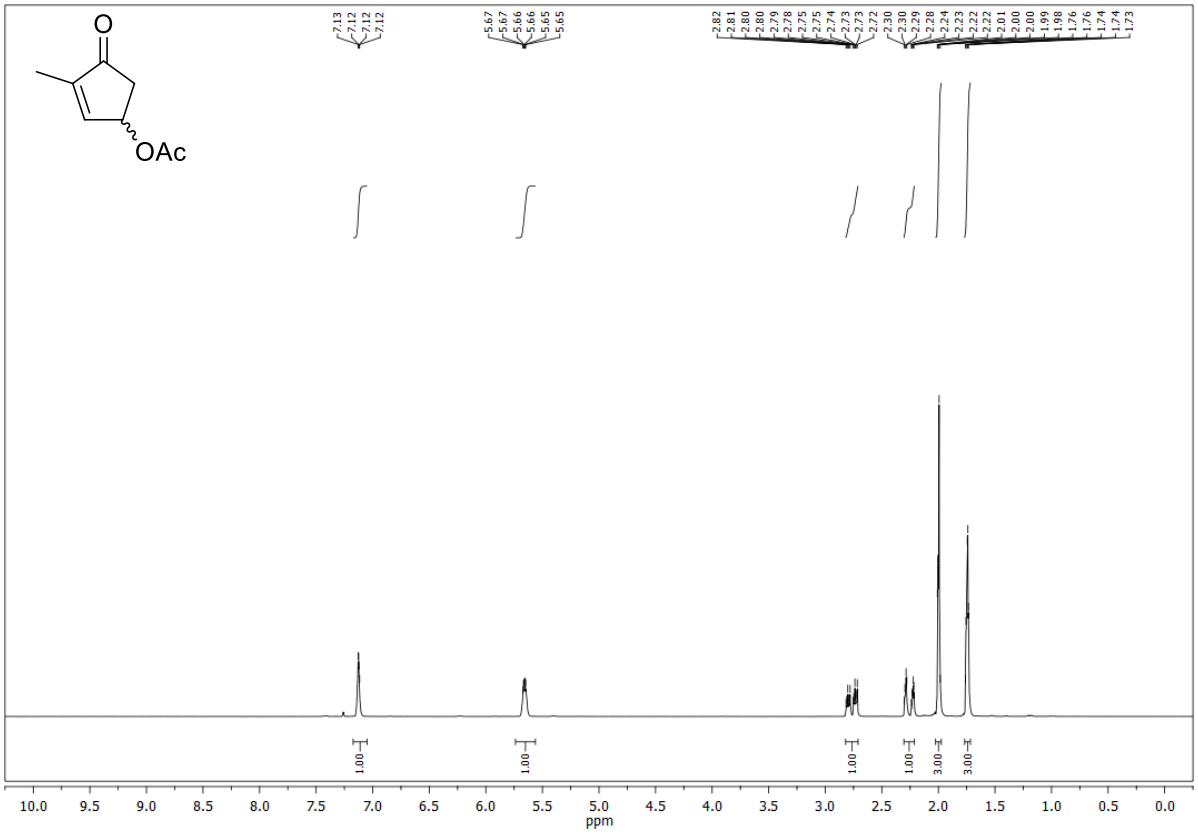


^{13}C NMR (75 MHz, $CDCl_3$)

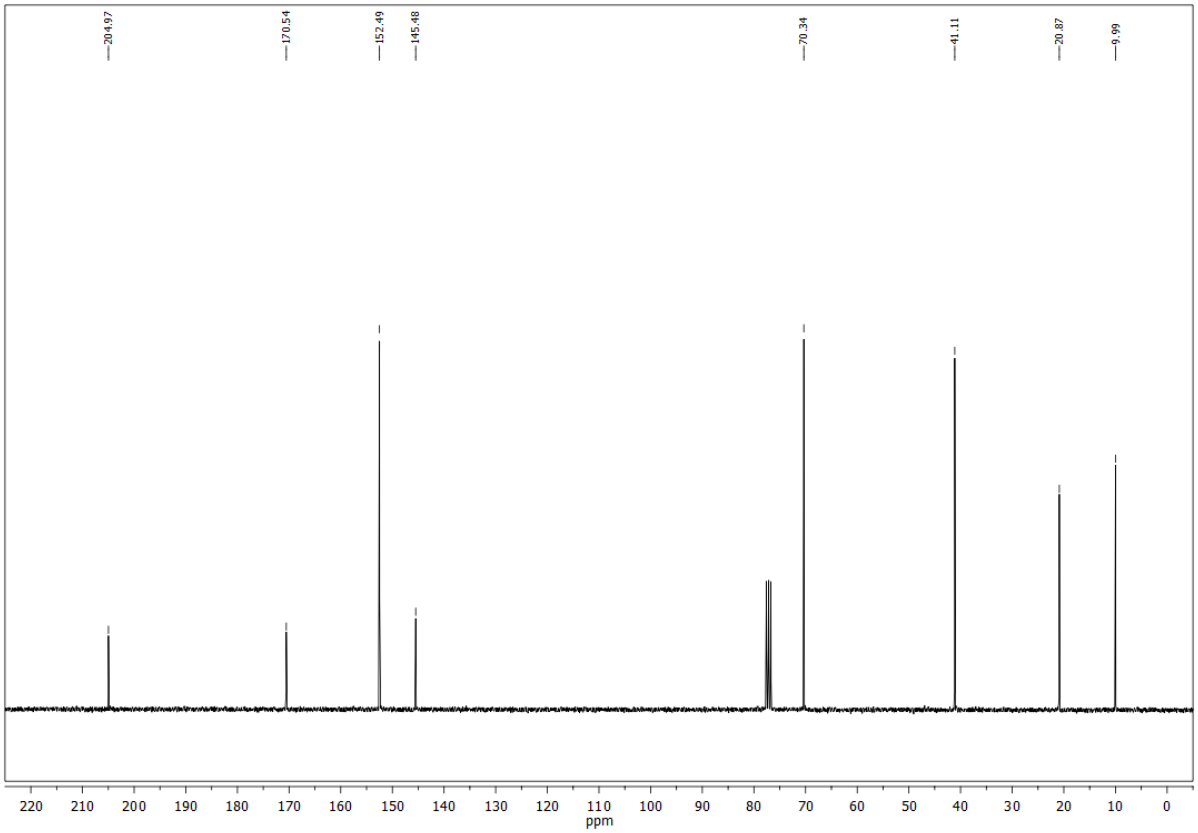


3-Methyl-4-oxocyclopent-2-en-1-yl acetate ((±)-202)

^{1}H NMR (300 MHz, $CDCl_3$)

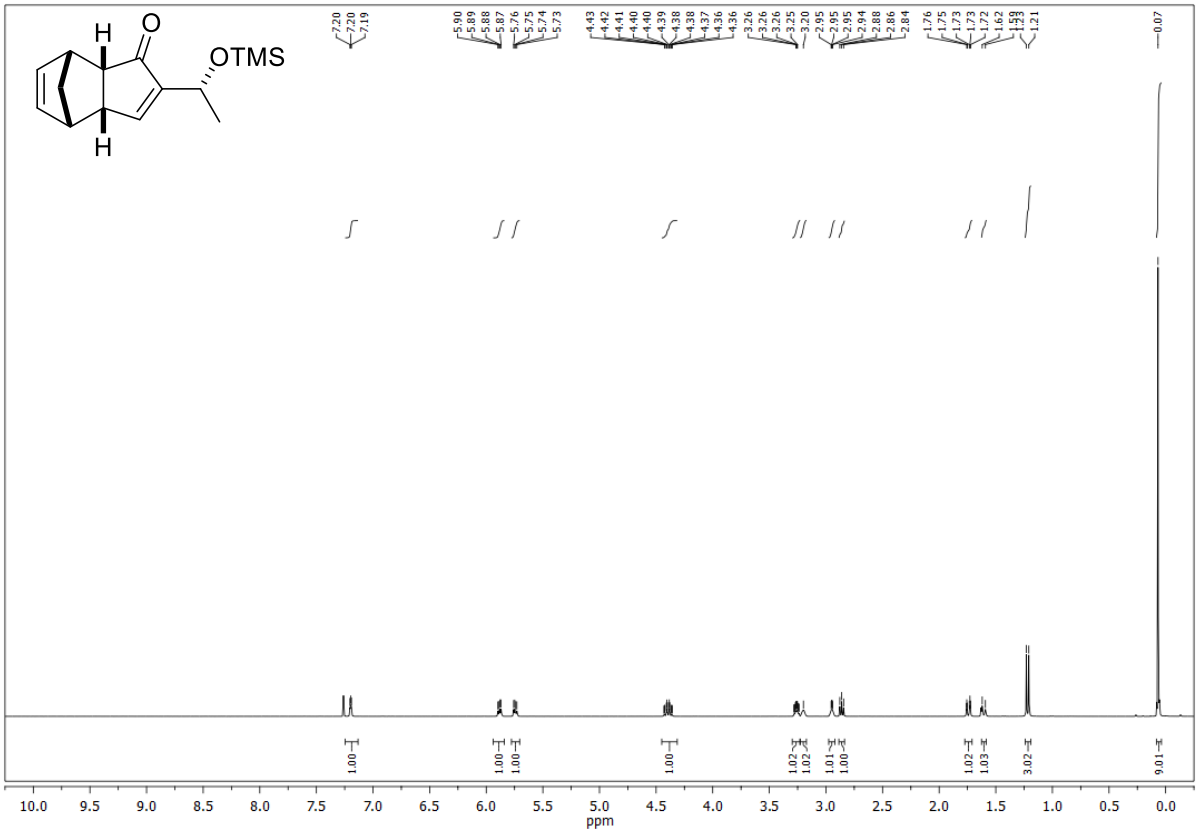


^{13}C NMR (75 MHz, $CDCl_3$)

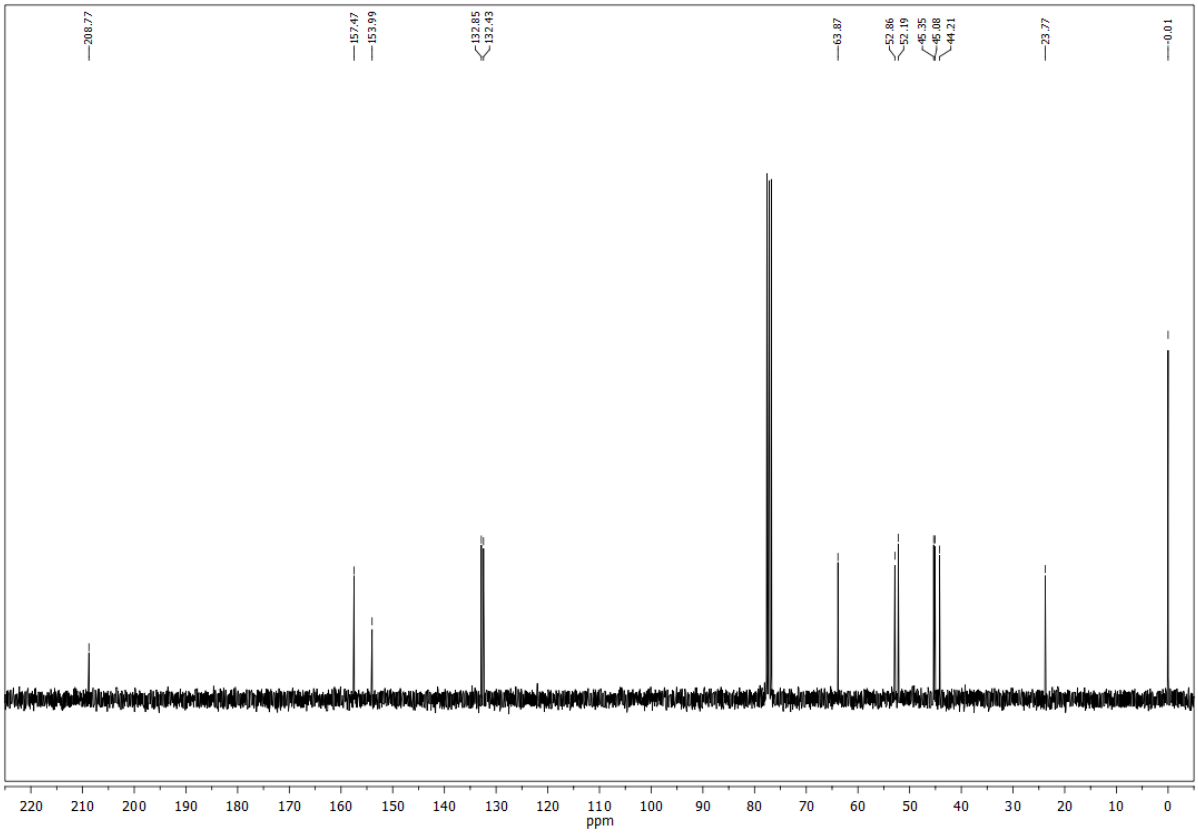


2-(1-((Trimethylsilyl)oxy)ethyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-204)

^{1}H NMR (300 MHz, $CDCl_3$)

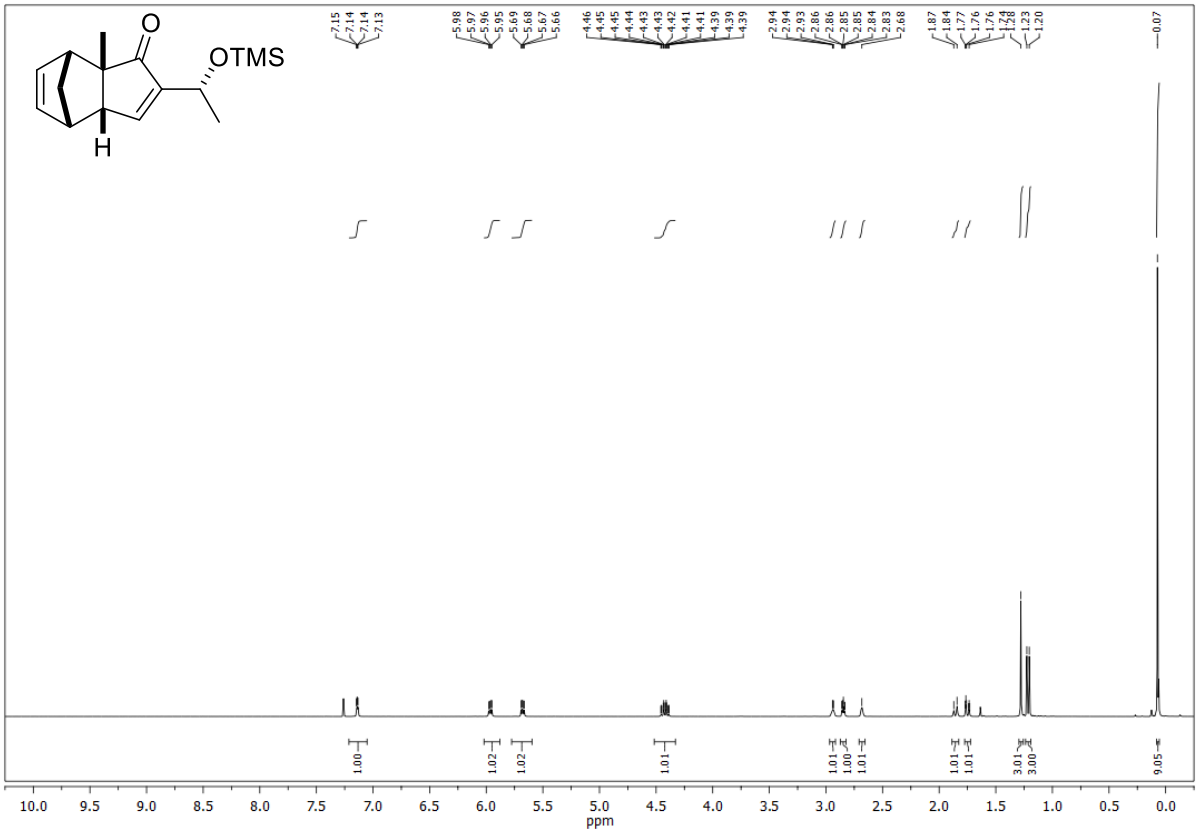


^{13}C NMR (75 MHz, $CDCl_3$)

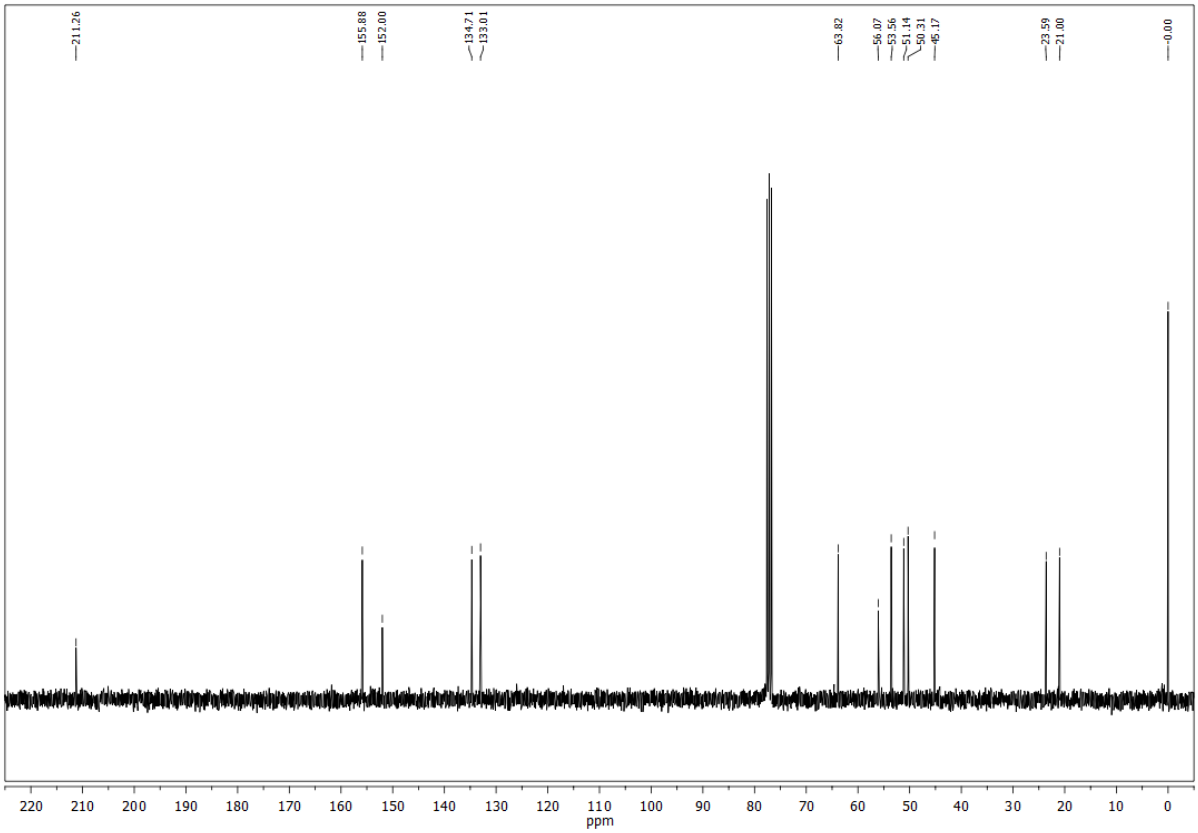


7a-Methyl-2-(1-((trimethylsilyl)oxy)ethyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-205)

^{1}H NMR (300 MHz, $CDCl_3$)

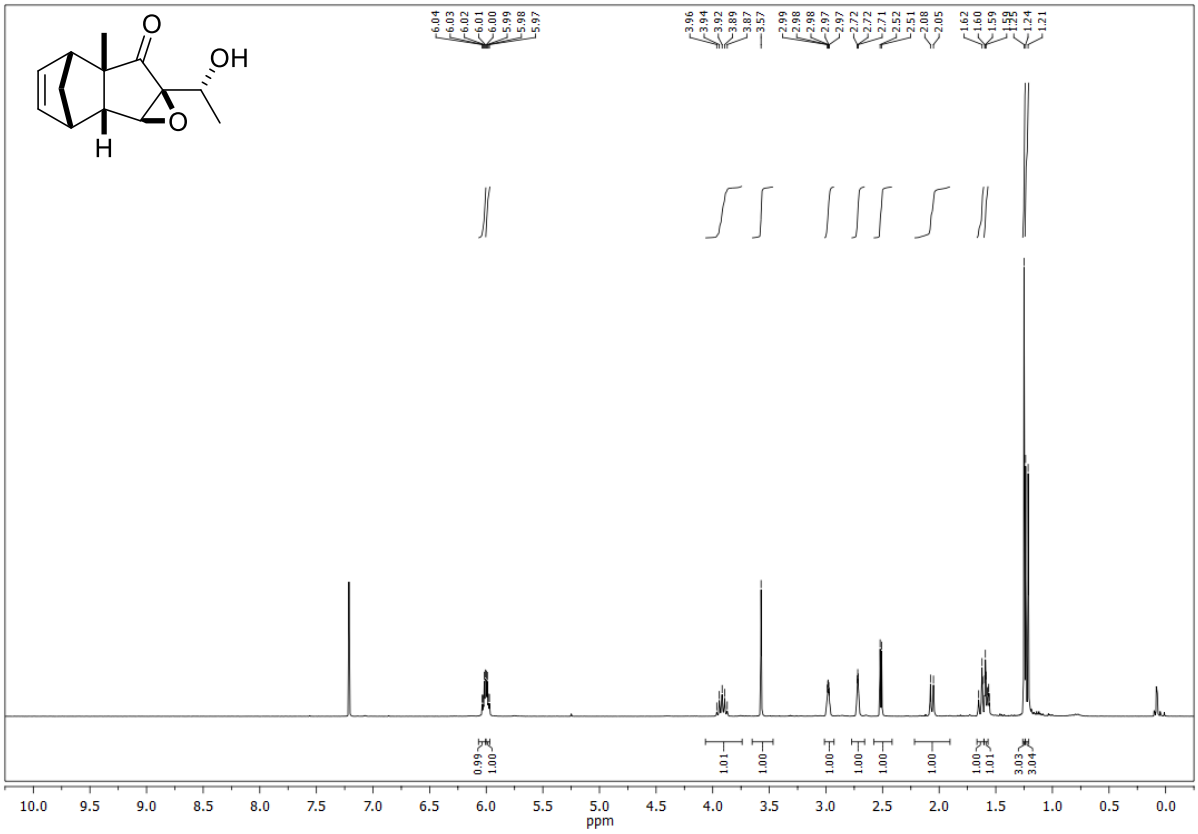


^{13}C NMR (75 MHz, $CDCl_3$)

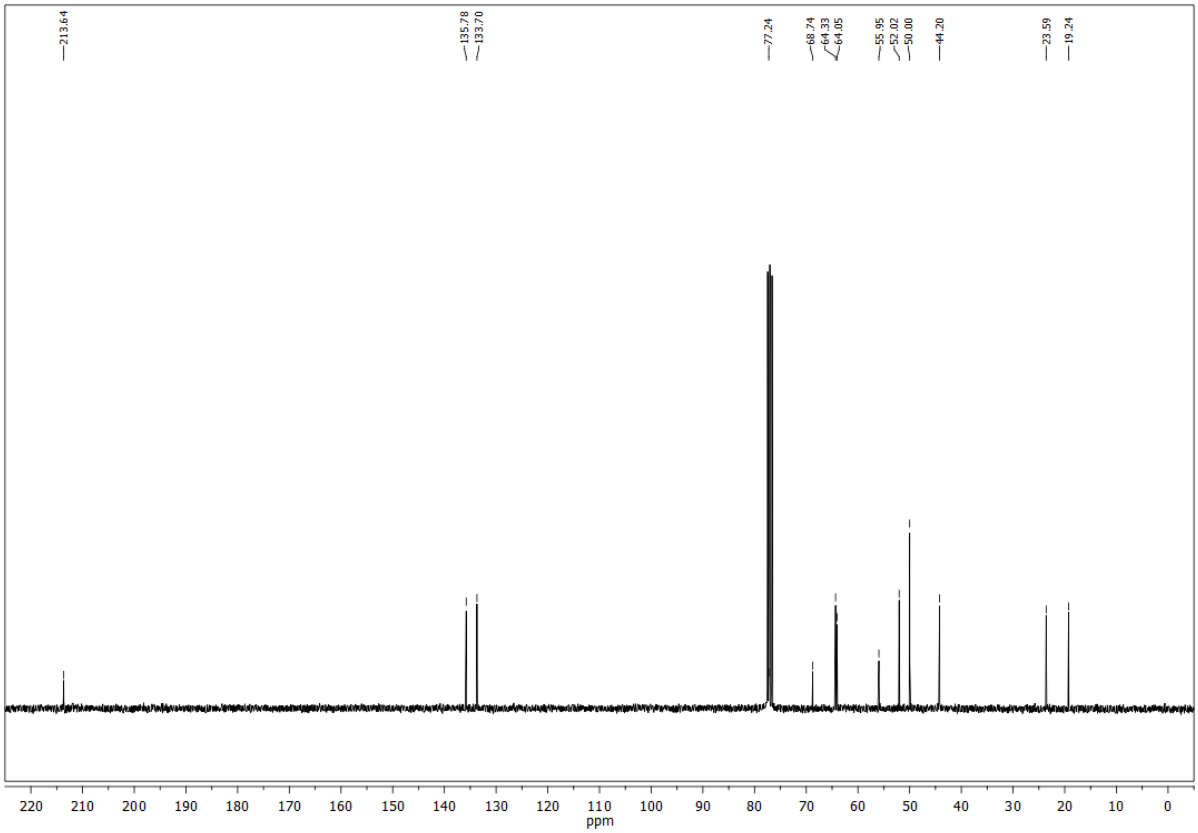


6a-(1-Hydroxyethyl)-5a-methyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-197)

^{1}H NMR (300 MHz, $CDCl_3$)

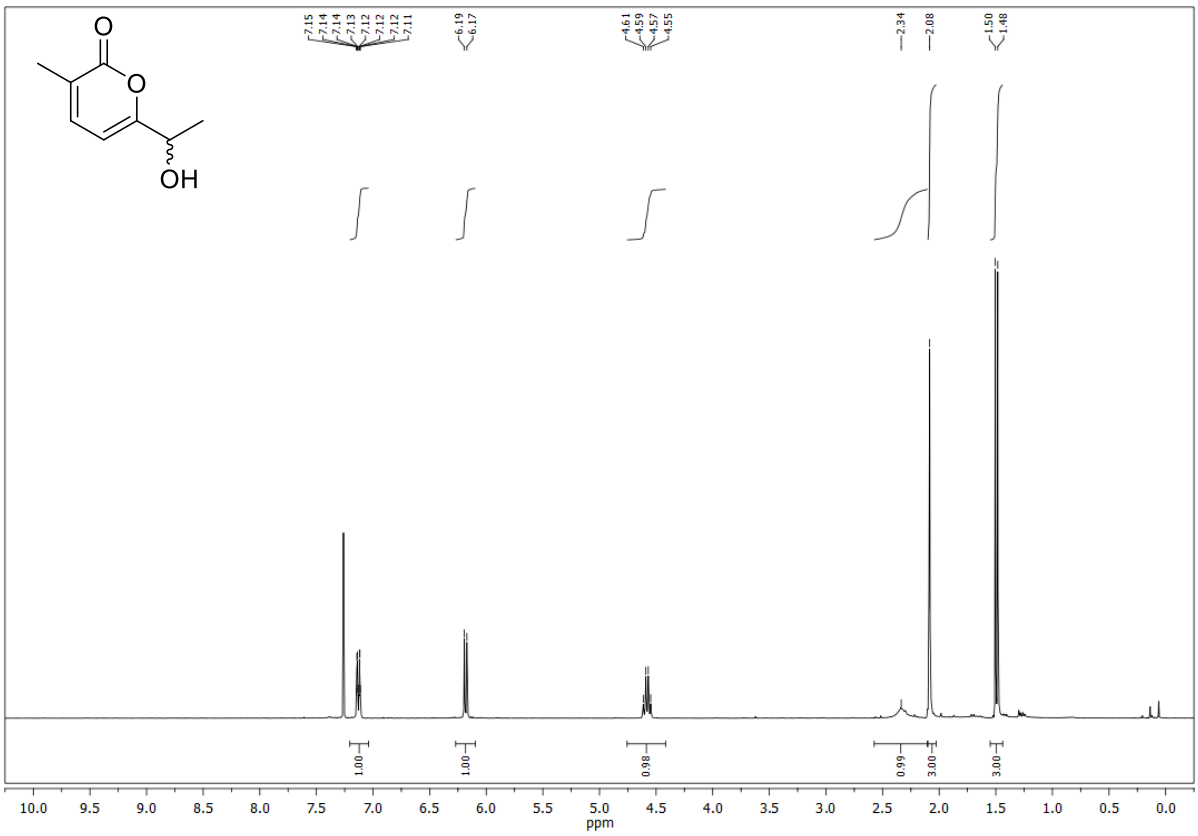


^{13}C NMR (75 MHz, $CDCl_3$)

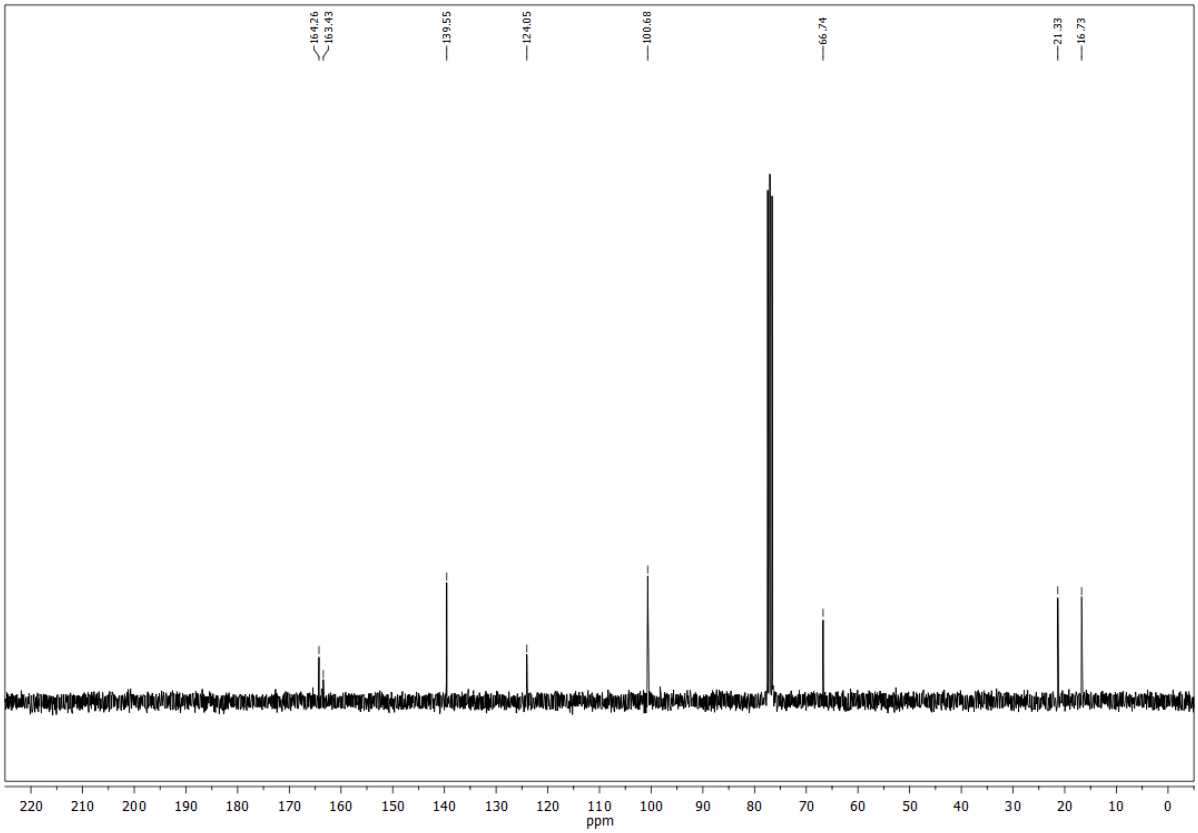


6-(1-Hydroxyethyl)-3-methyl-2*H*-pyran-2-one ((±)-196)

^{1}H NMR (300 MHz, $CDCl_3$)

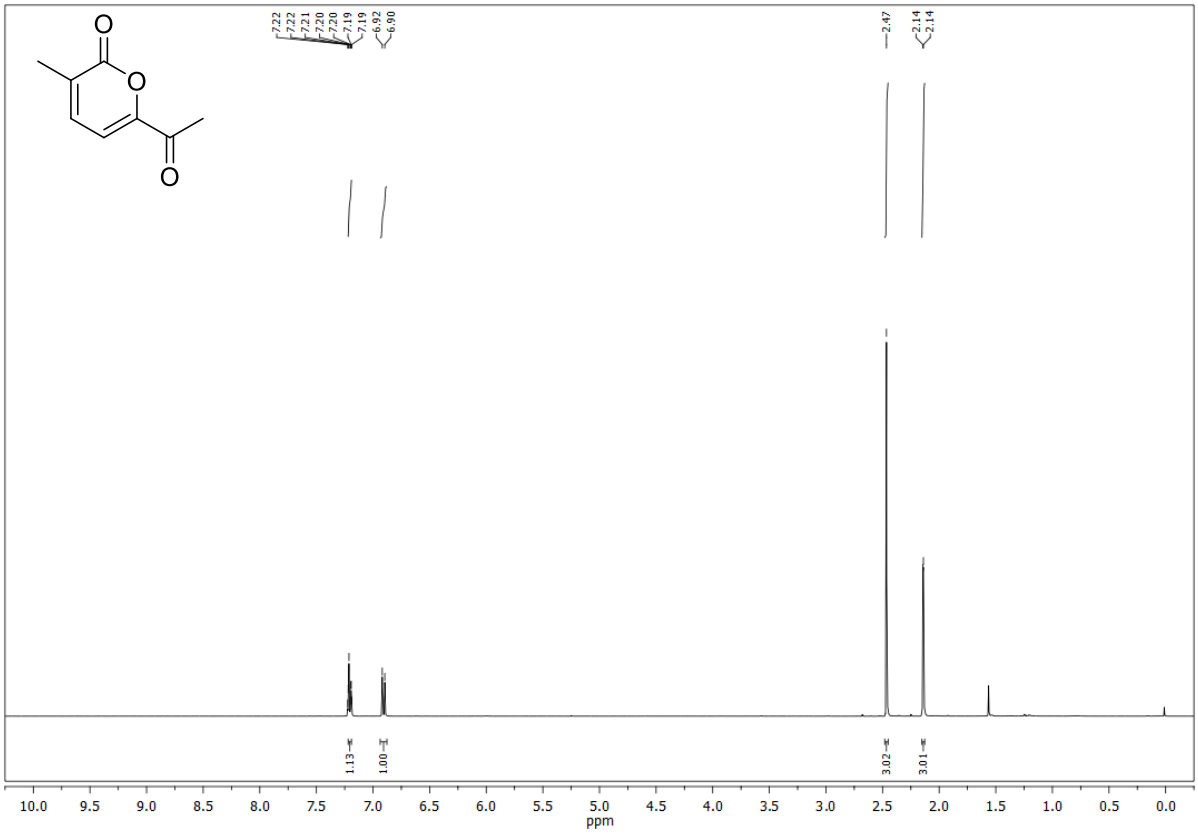


^{13}C NMR (75 MHz, $CDCl_3$)

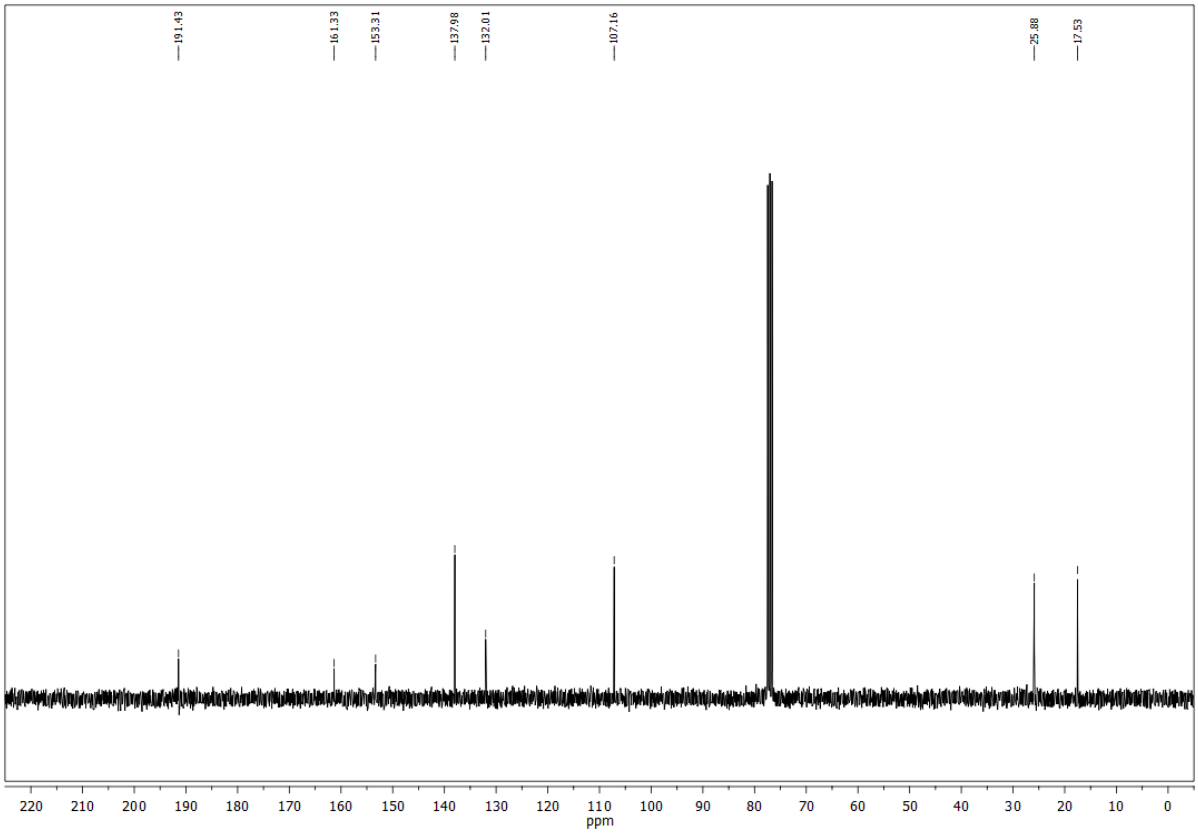


6-Acetyl-3-methyl-2*H*-pyran-2-one (3a)

^{1}H NMR (300 MHz, $CDCl_3$)

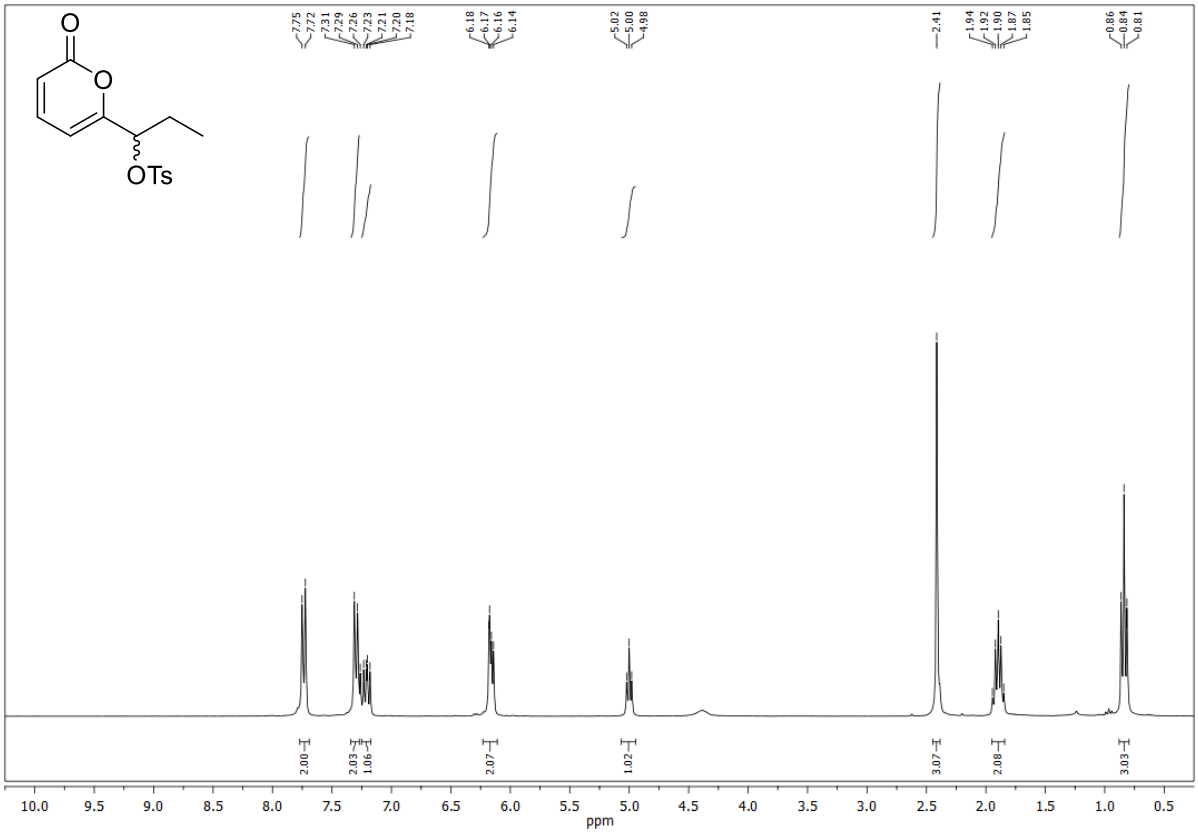


^{13}C NMR (75 MHz, $CDCl_3$)

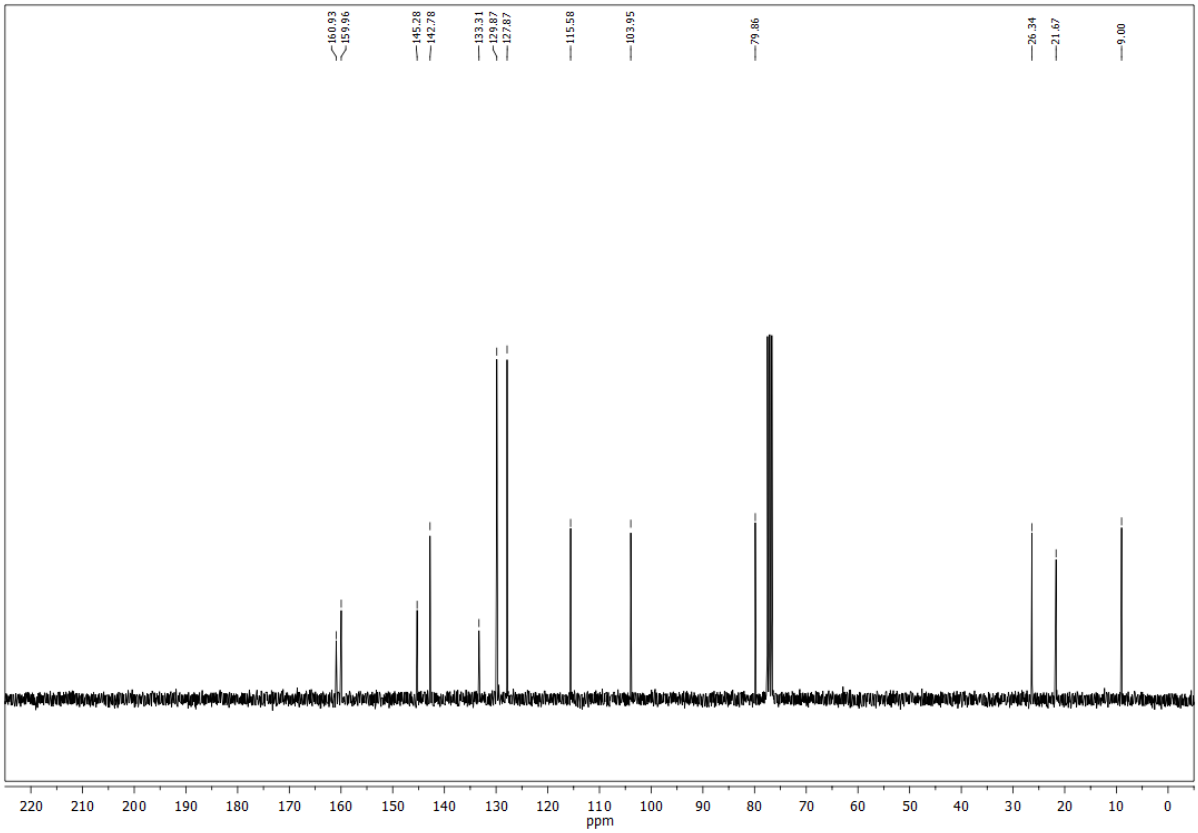


1-(2-Oxo-2*H*-pyran-6-yl)propyl 4-methylbenzenesulfonate ((±)-189a)

^{1}H NMR (300 MHz, $CDCl_3$)

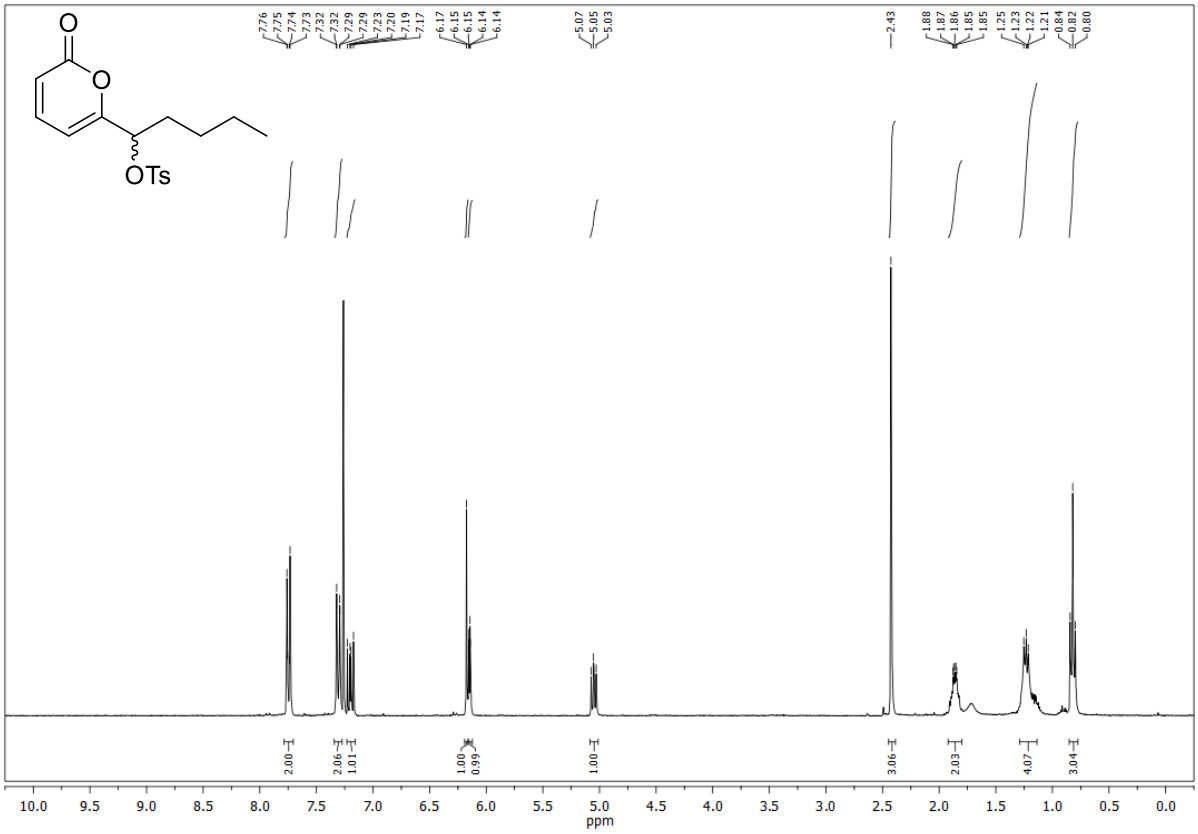


^{13}C NMR (75 MHz, $CDCl_3$)

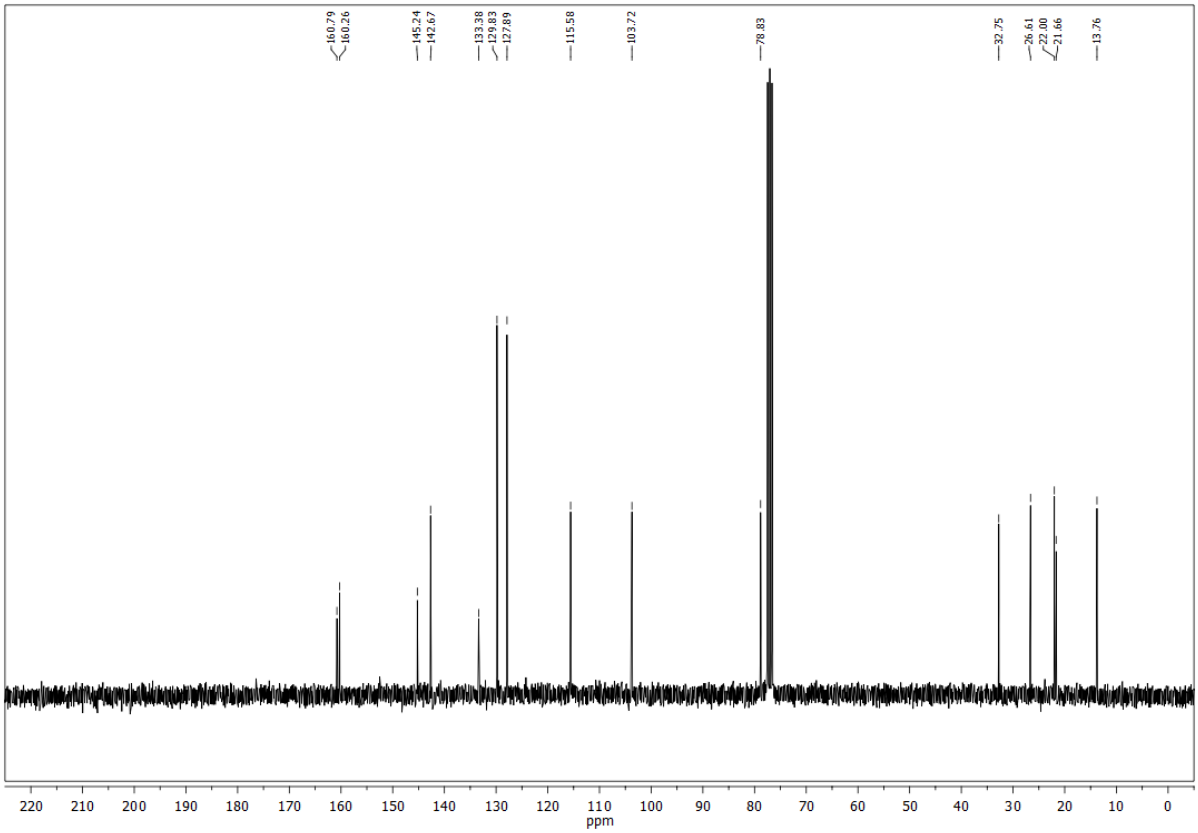


1-(2-Oxo-2*H*-pyran-6-yl)pentyl 4-methylbenzenesulfonate ((±)-189b)

^{1}H NMR (300 MHz, $CDCl_3$)

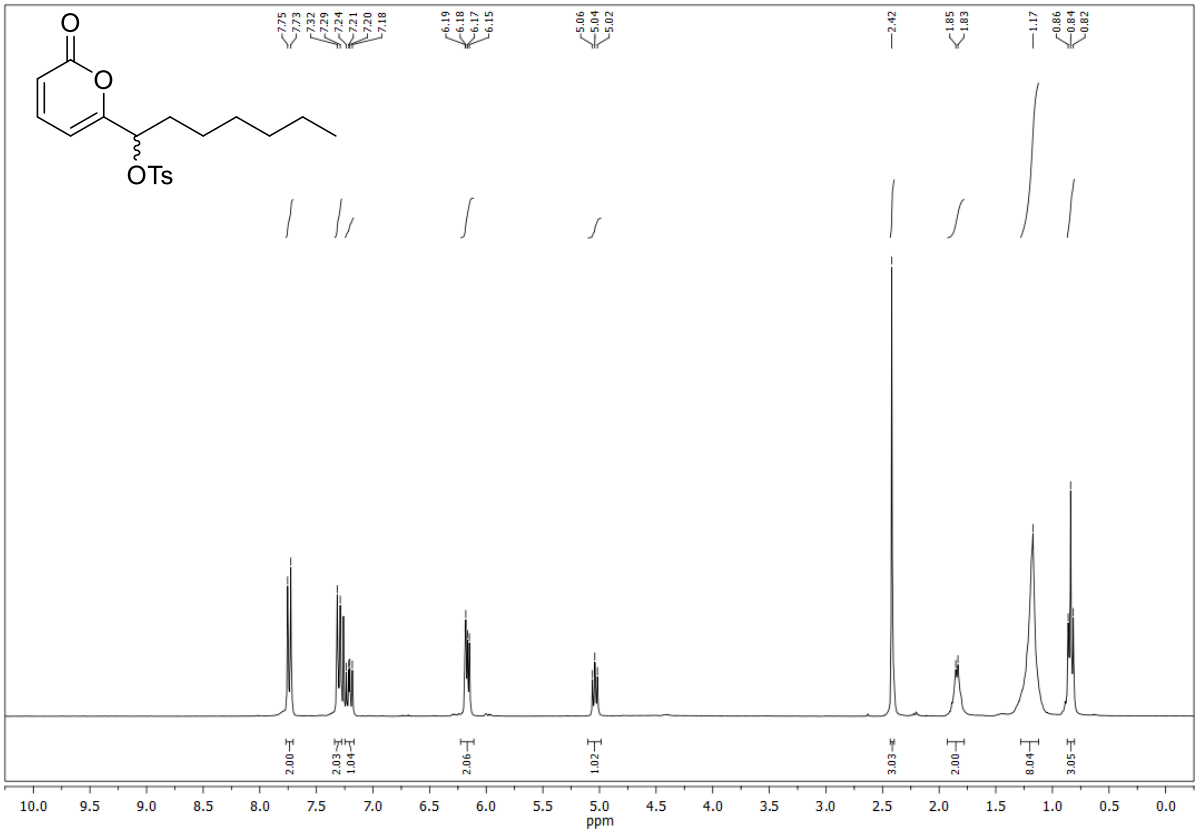


^{13}C NMR (75 MHz, $CDCl_3$)

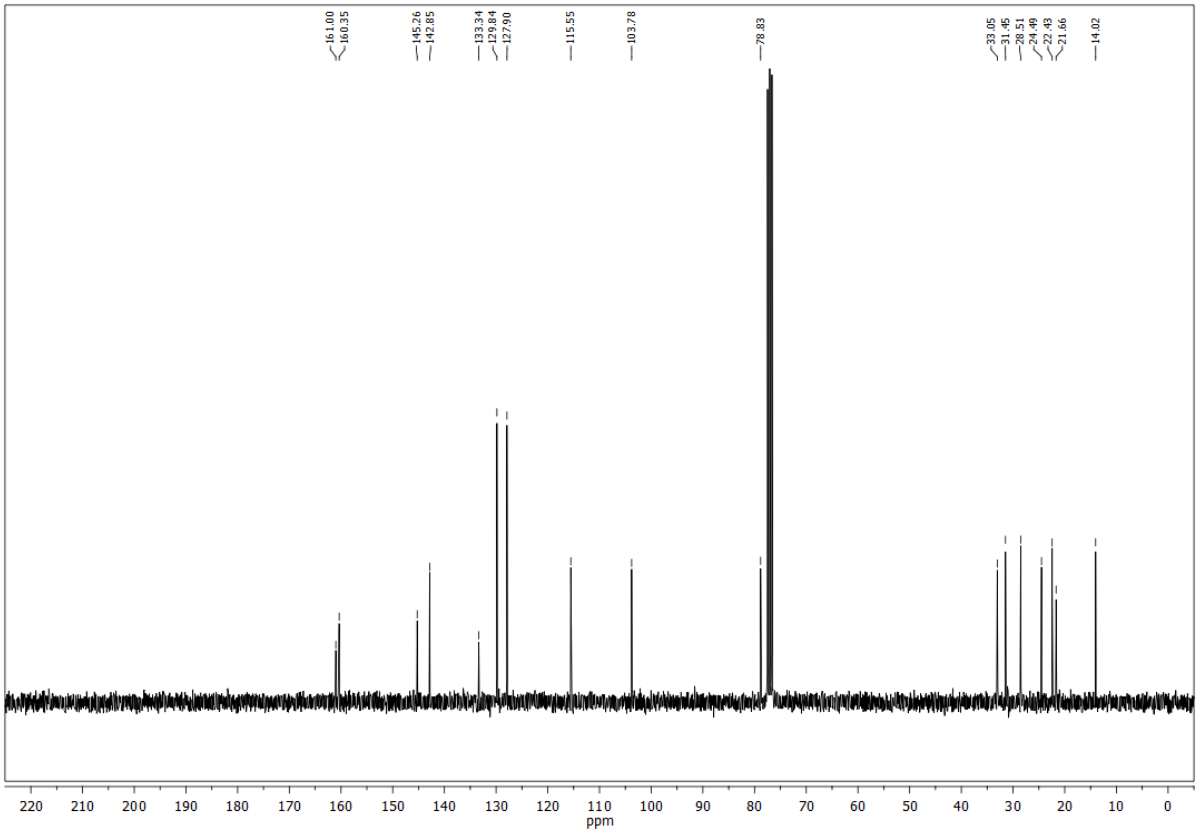


1-(2-Oxo-2*H*-pyran-6-yl)heptyl 4-methylbenzenesulfonate ((±)-189c)

^{1}H NMR (300 MHz, $CDCl_3$)

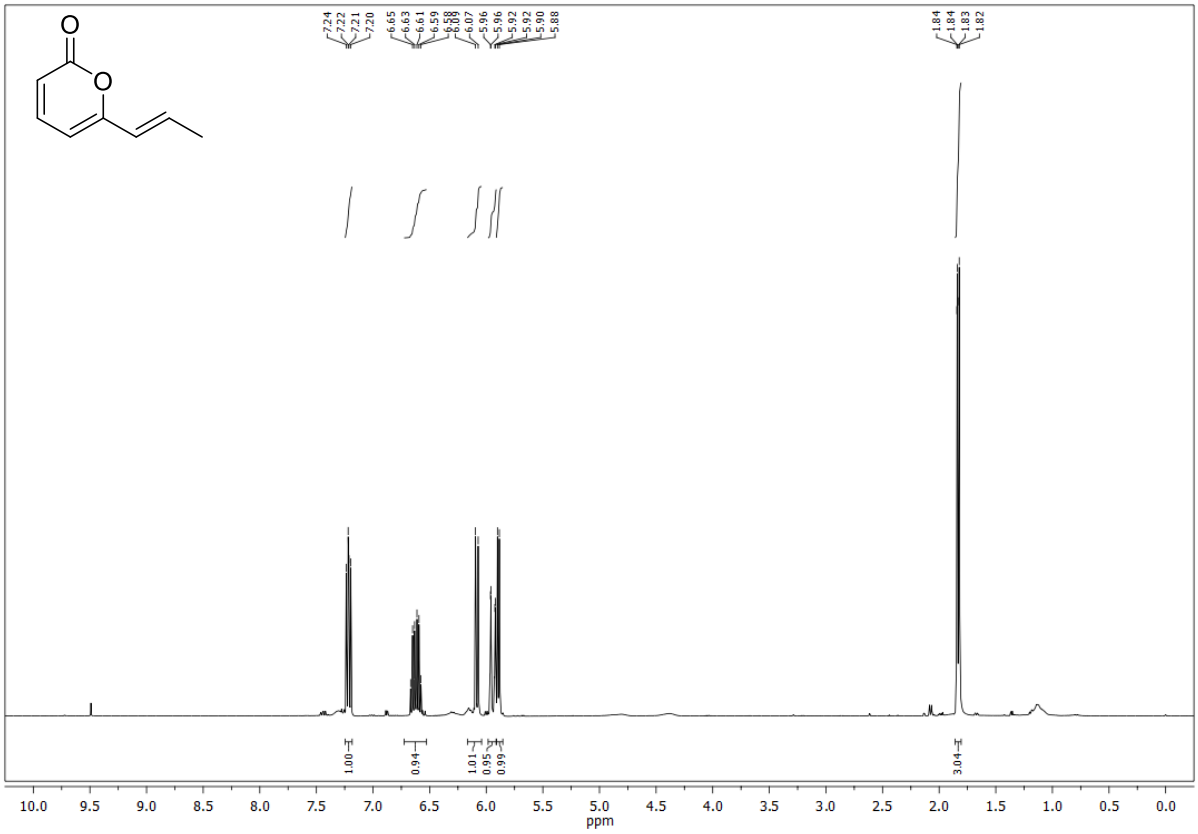


^{13}C NMR (75 MHz, $CDCl_3$)

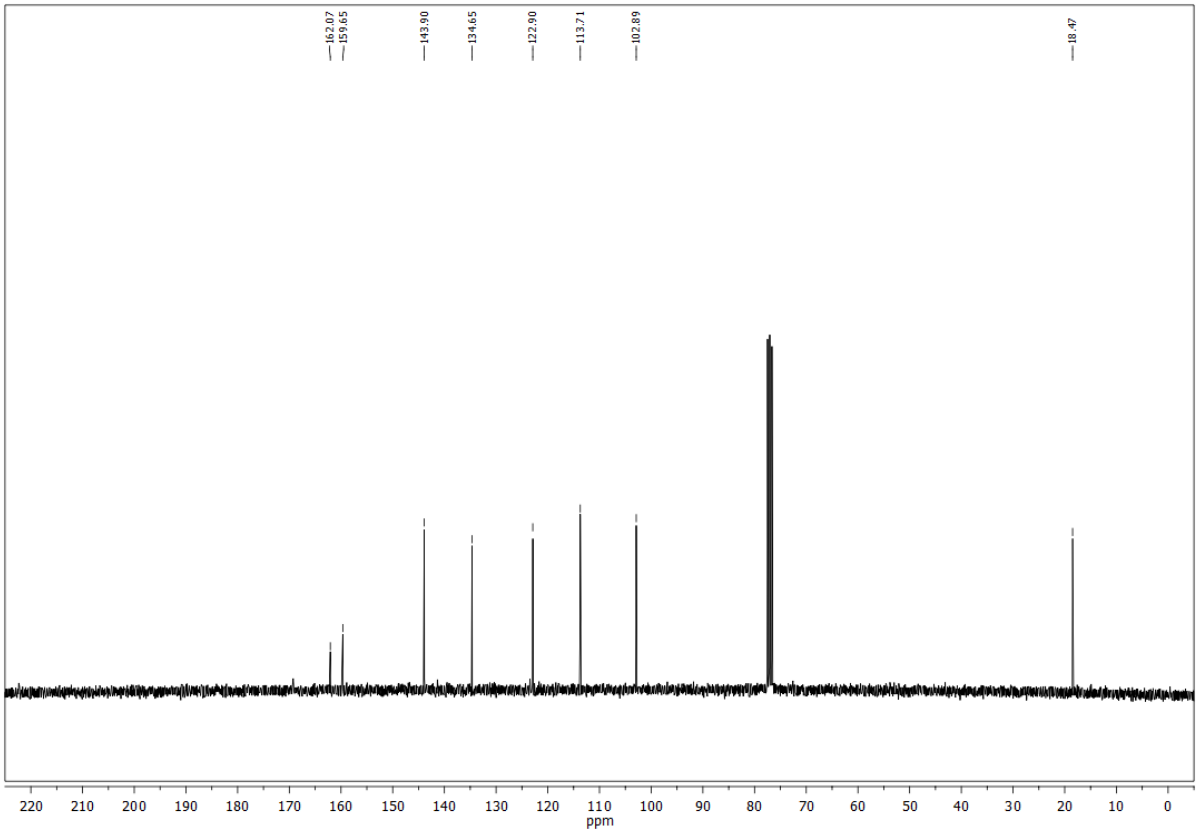


(*E*)-6-(prop-1-en-1-yl)-2*H*-pyran-2-one (7a)

^{1}H NMR (300 MHz, $CDCl_3$)

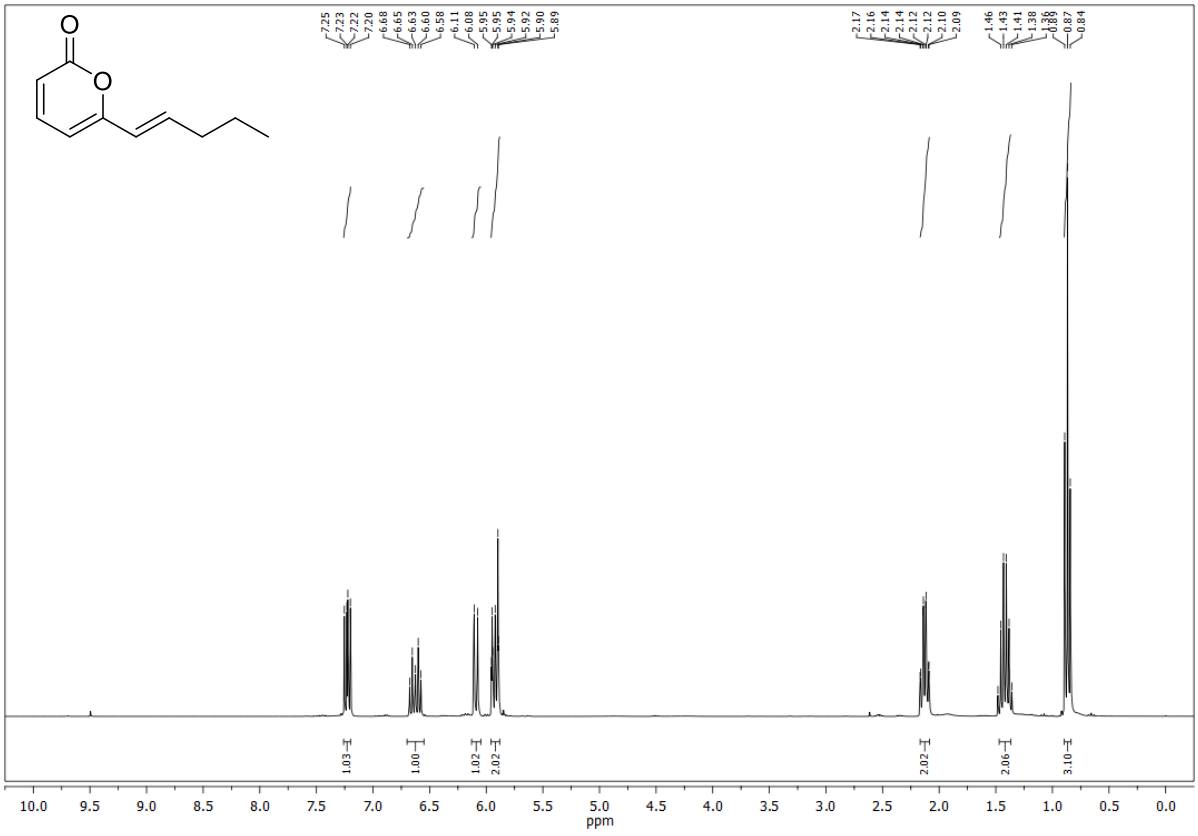


^{13}C NMR (75 MHz, $CDCl_3$)

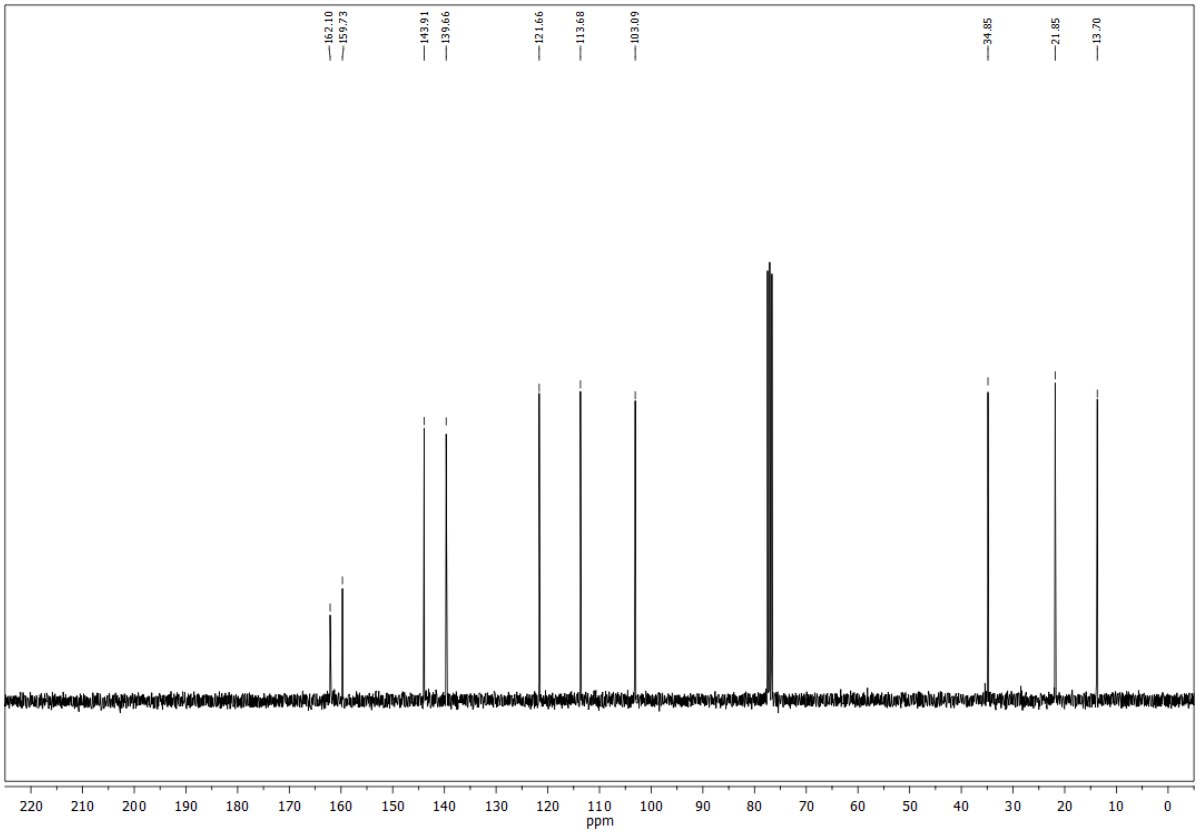


(*E*)-6-(Pent-1-en-1-yl)-2*H*-pyran-2-one (7b)

^{1}H NMR (300 MHz, $CDCl_3$)

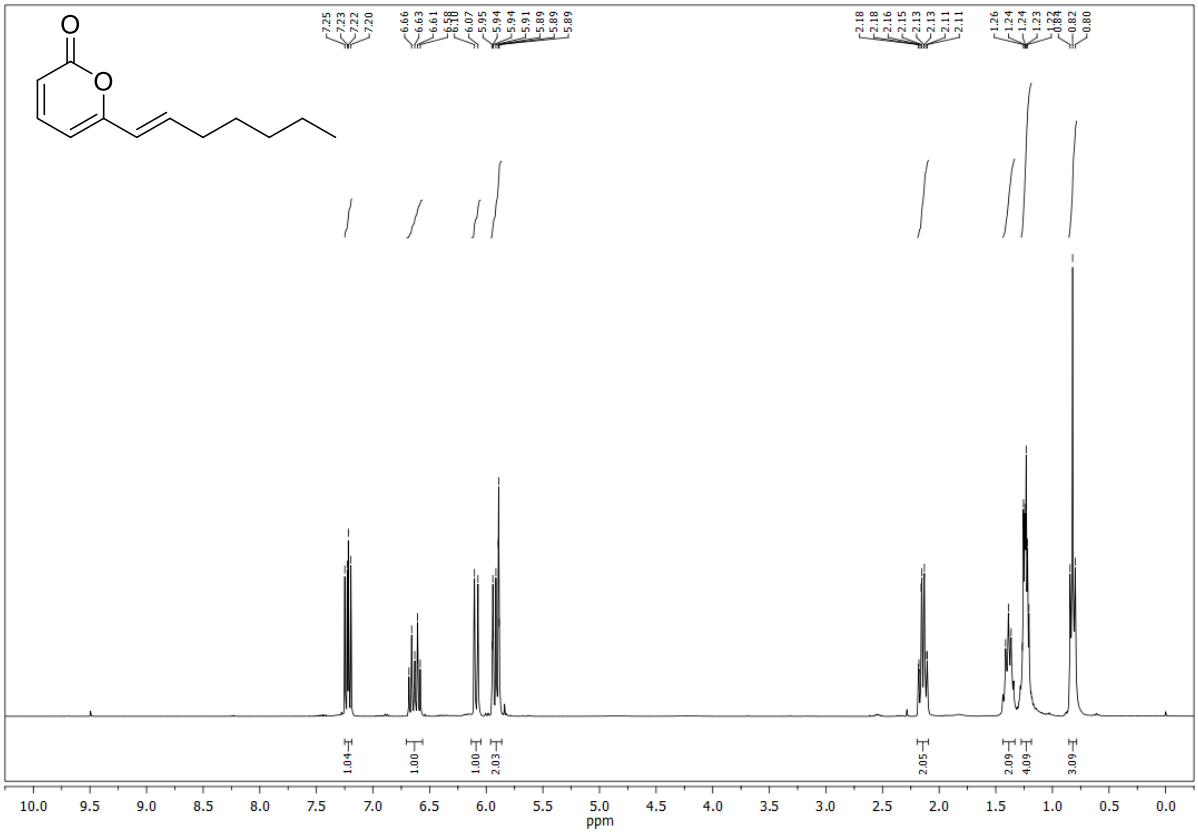


^{13}C NMR (75 MHz, $CDCl_3$)

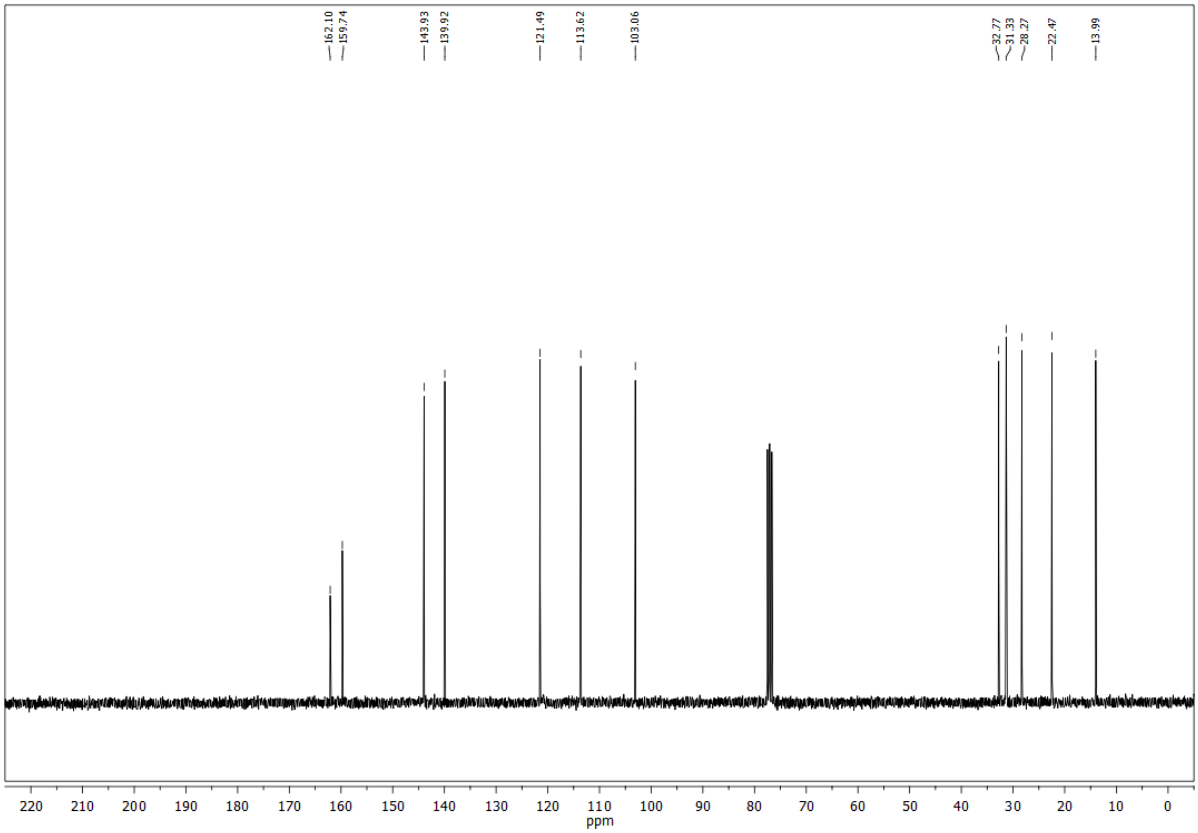


(*E*)-6-(Hept-1-en-1-yl)-2*H*-pyran-2-one (7c)

^{1}H NMR (300 MHz, $CDCl_3$)

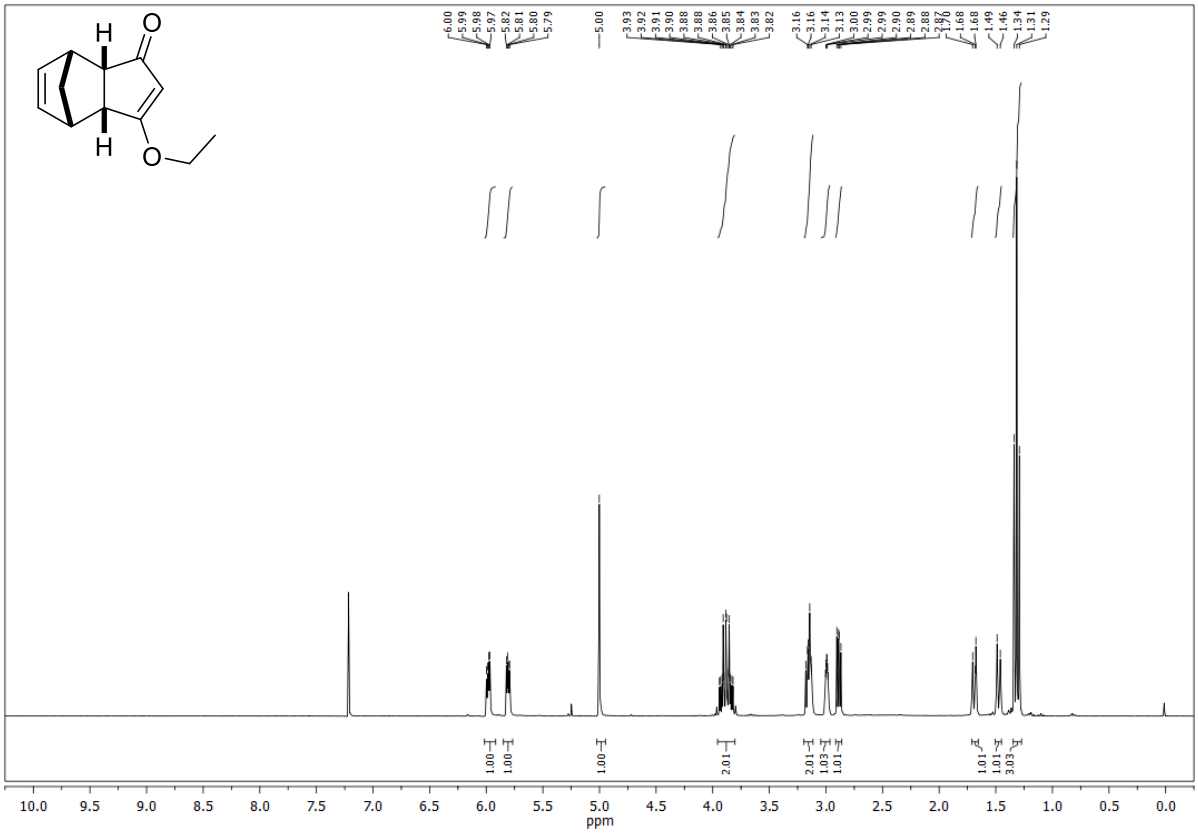


^{13}C NMR (75 MHz, $CDCl_3$)

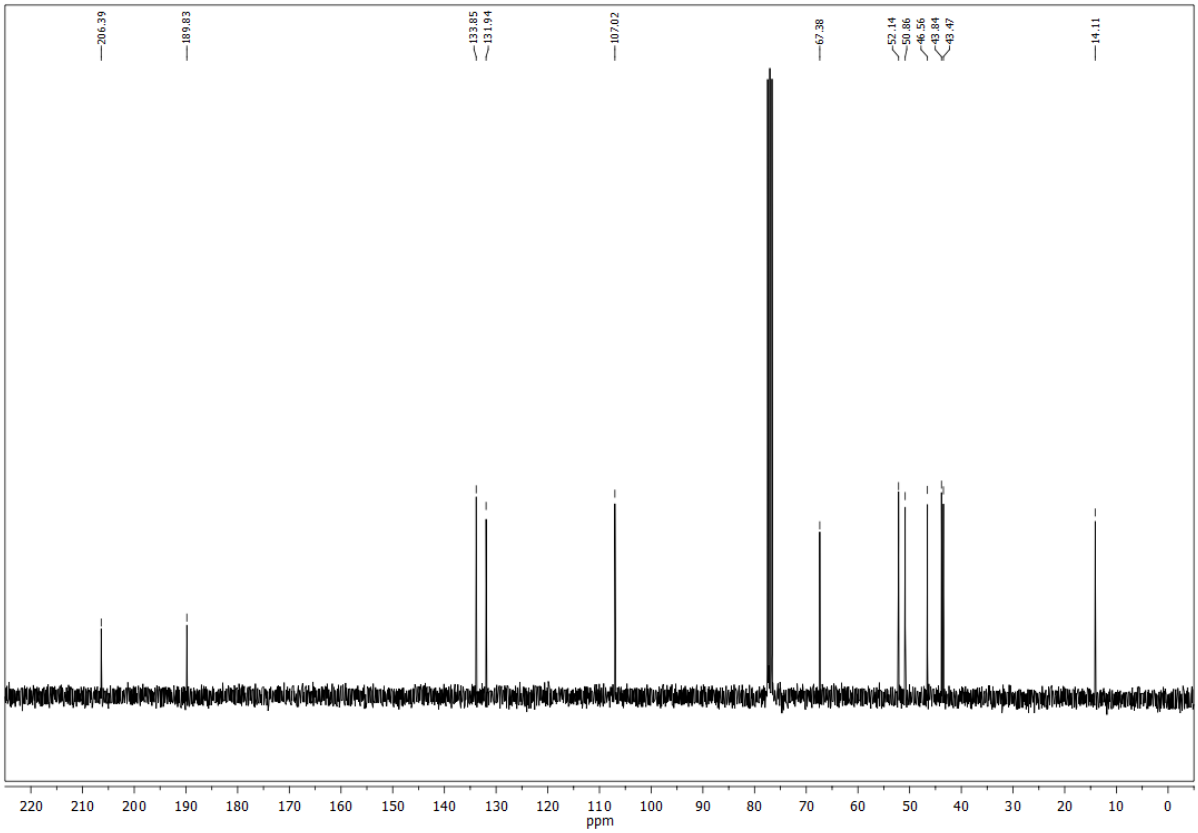


3-Ethoxy-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-212)

^{1}H NMR (300 MHz, $CDCl_3$)

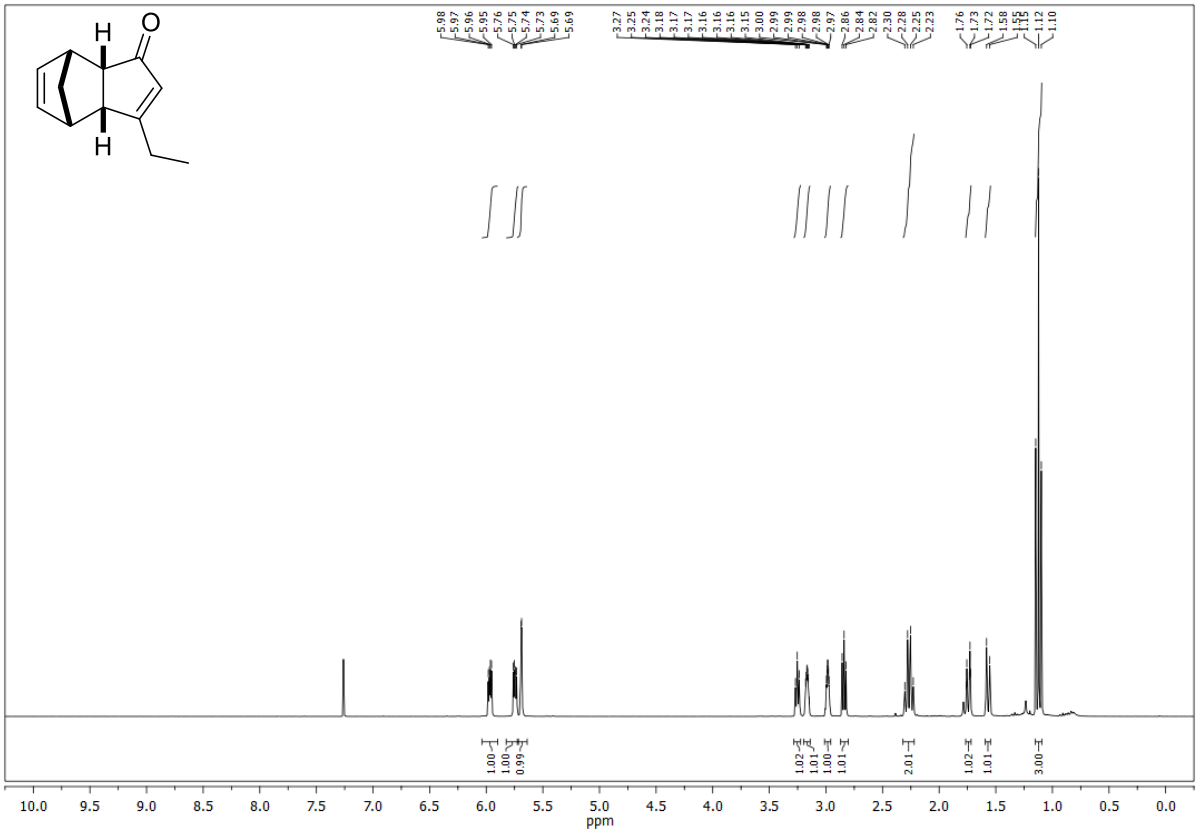


^{13}C NMR (75 MHz, $CDCl_3$)

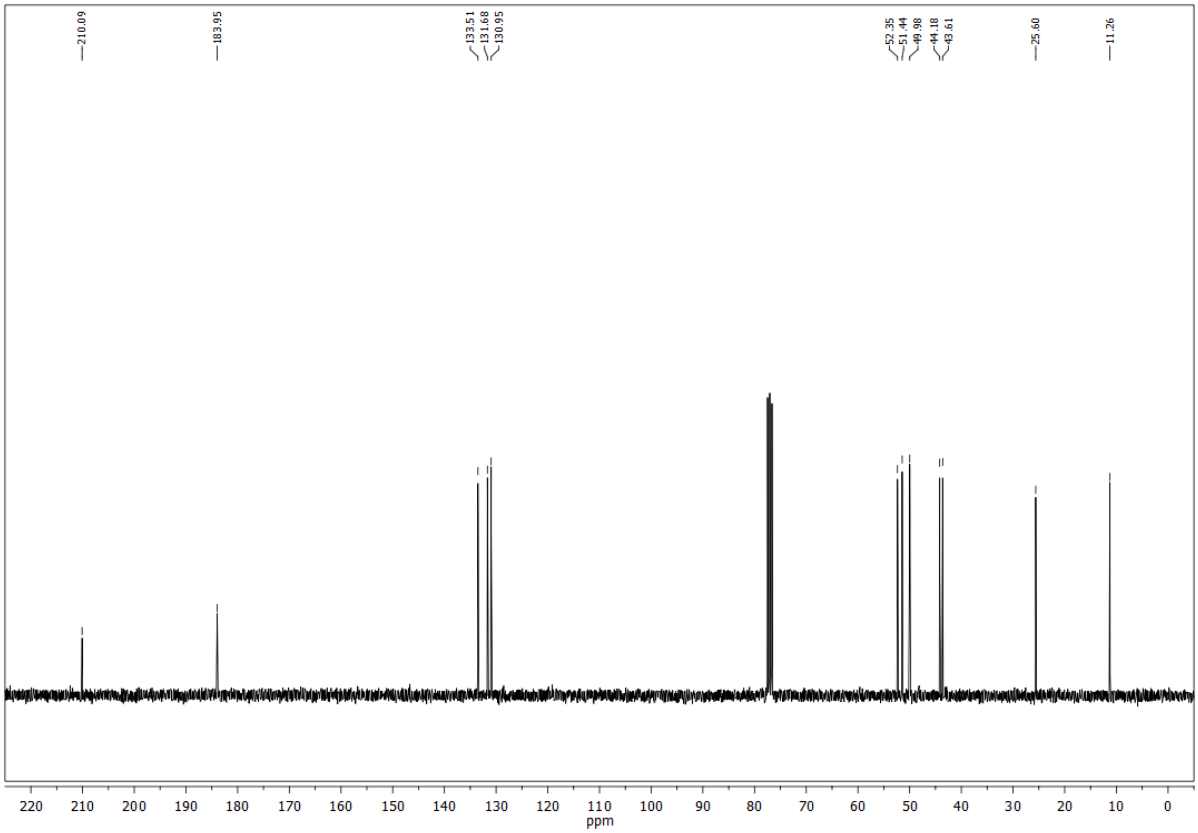


3-Ethyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-213)

^{1}H NMR (300 MHz, $CDCl_3$)

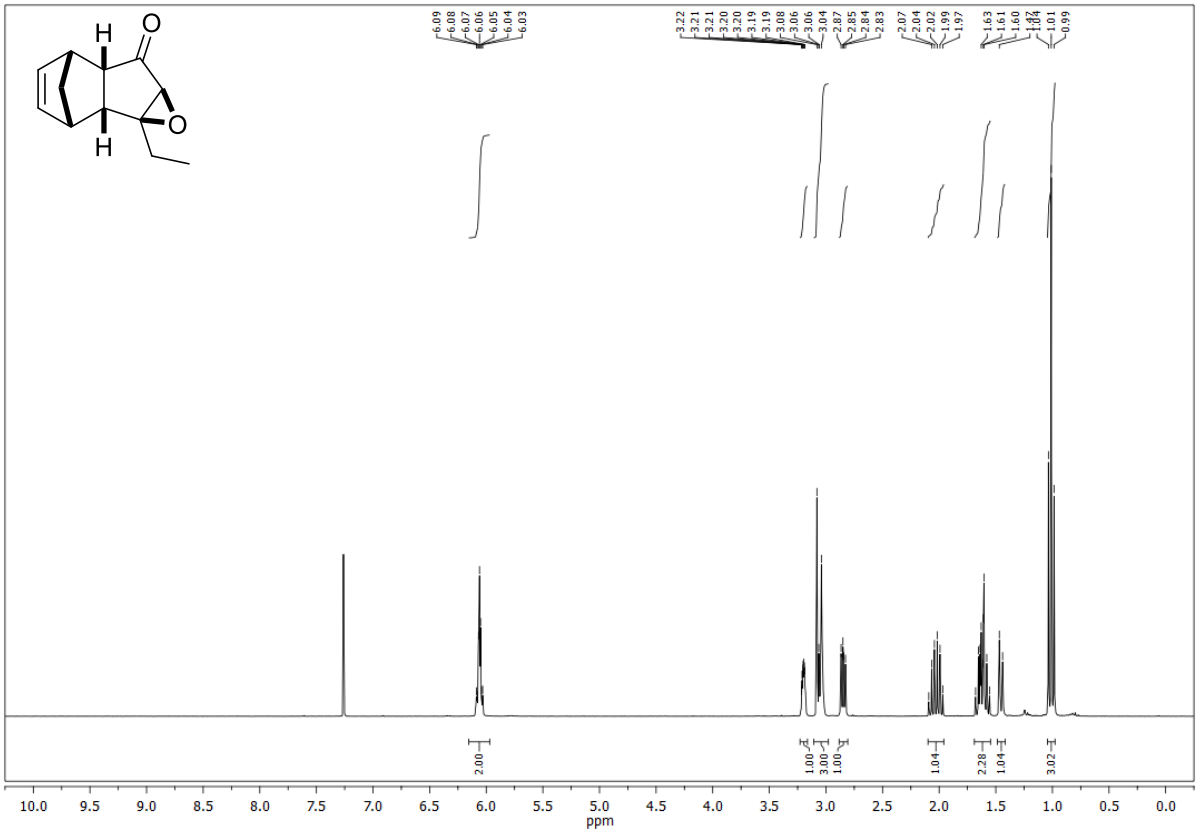


^{13}C NMR (75 MHz, $CDCl_3$)

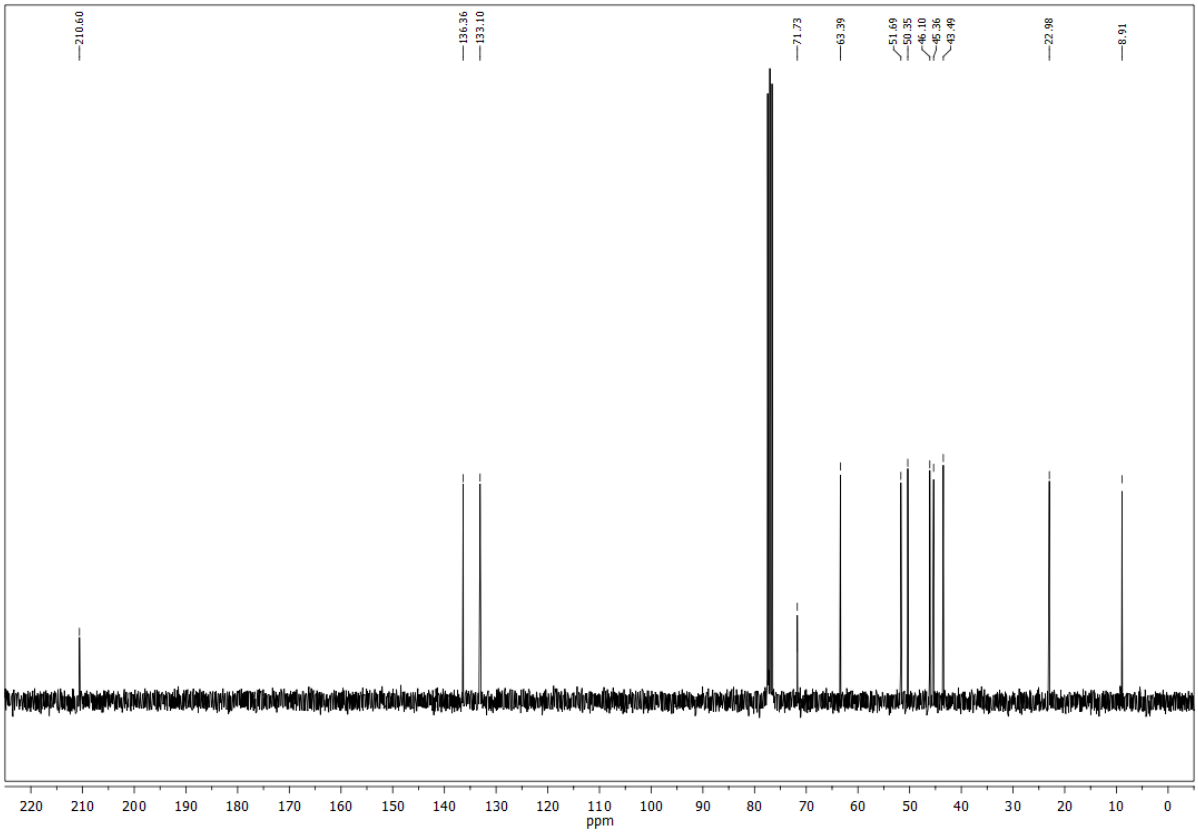


1a-Ethyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one ((±)-214)

^{1}H NMR (300 MHz, $CDCl_3$)

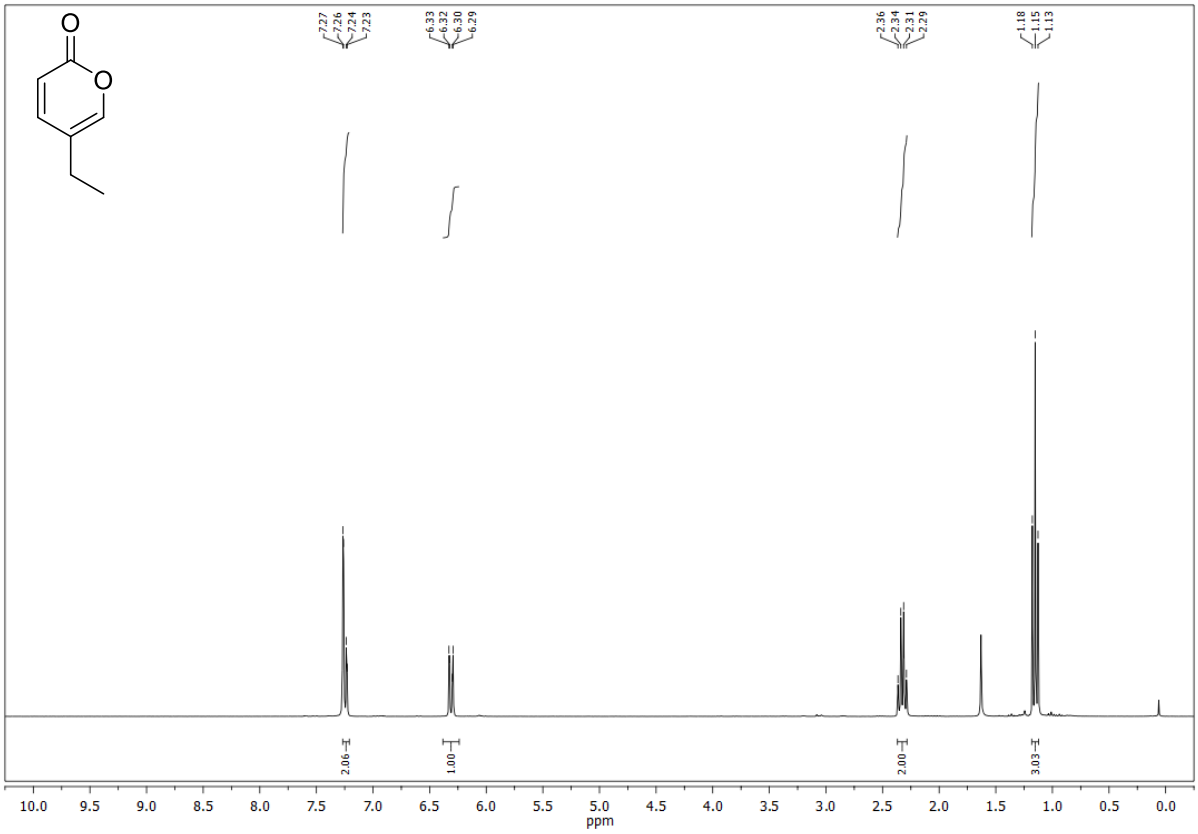


^{13}C NMR (75 MHz, $CDCl_3$)

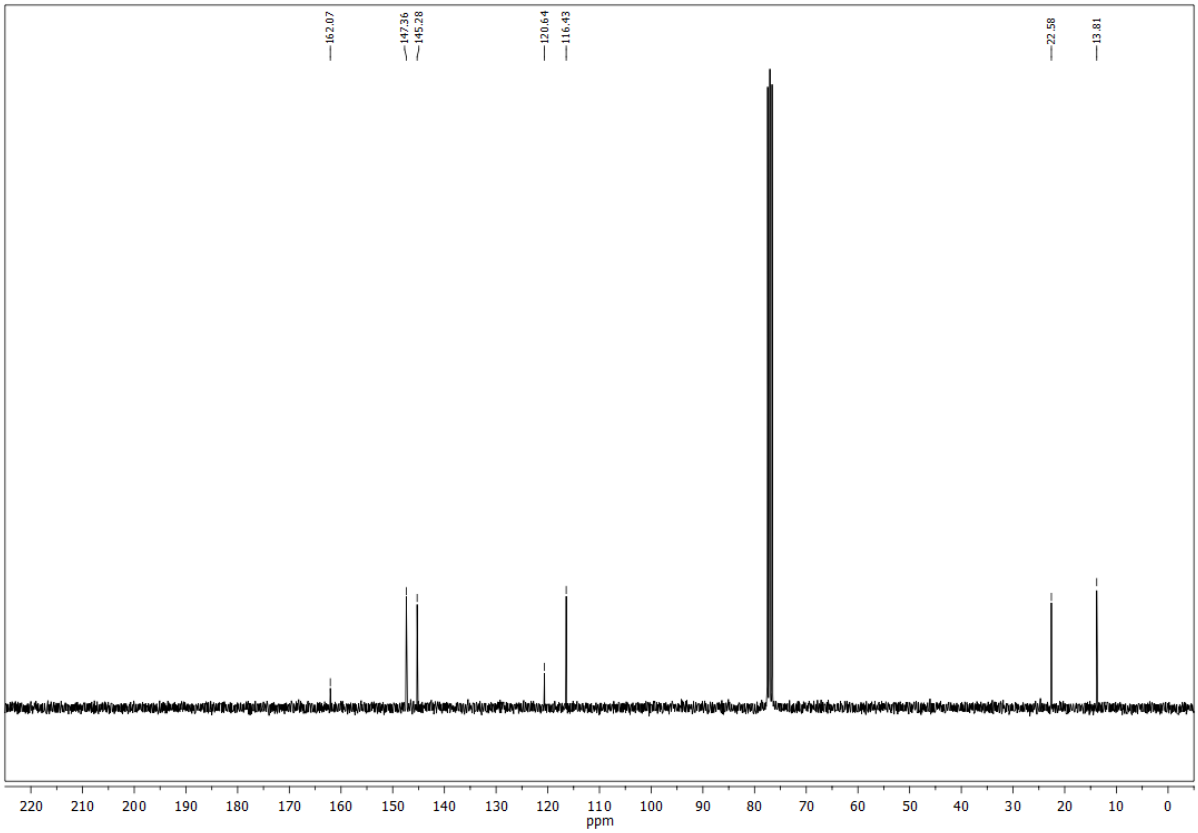


5-Ethyl-2H-pyran-2-one (215)

^{1}H NMR (300 MHz, $CDCl_3$)

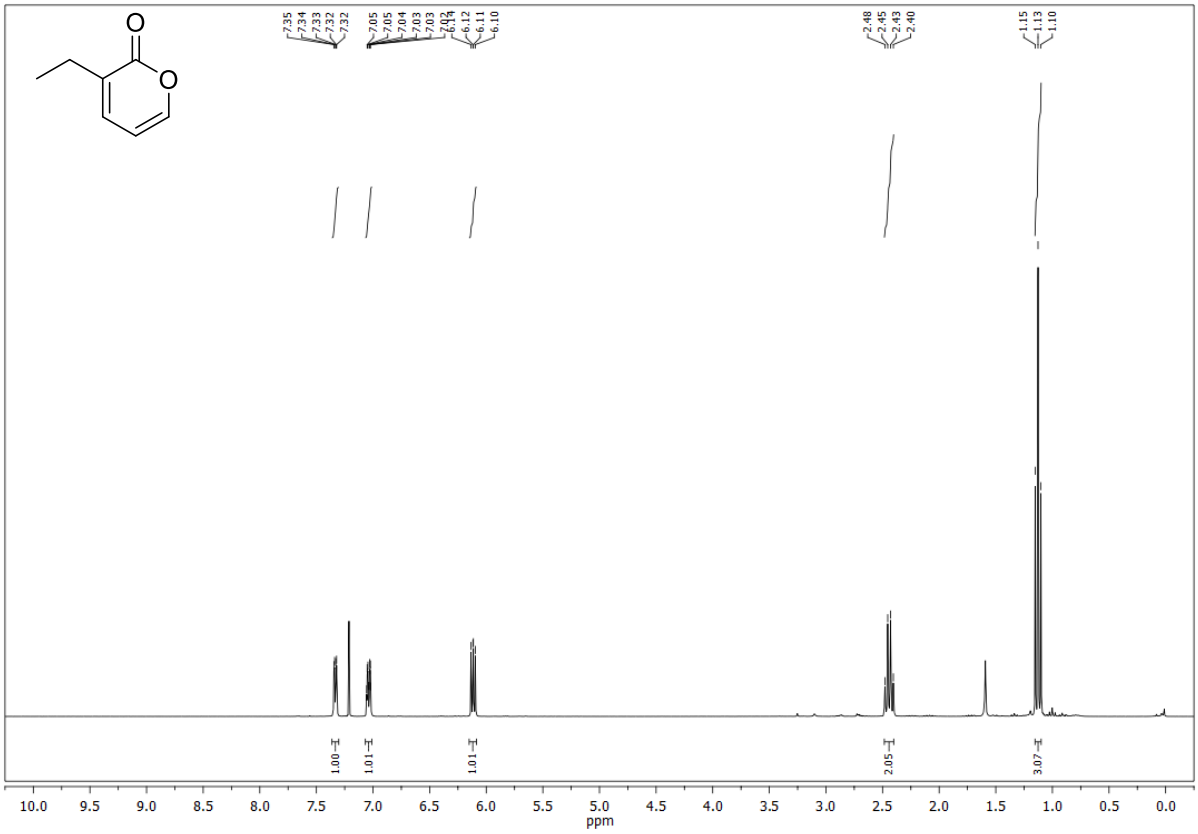


^{13}C NMR (75 MHz, $CDCl_3$)

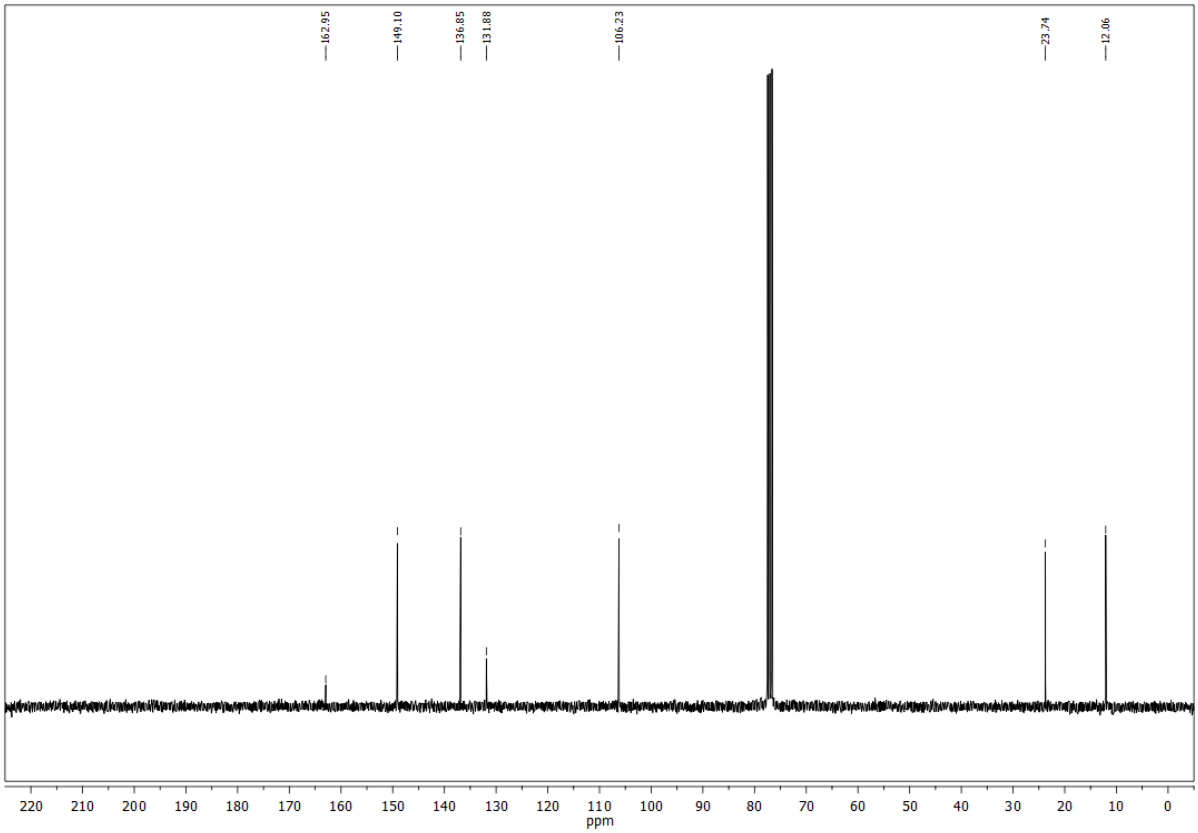


3-Ethyl-2H-pyran-2-one: (216)

^{1}H NMR (300 MHz, $CDCl_3$)

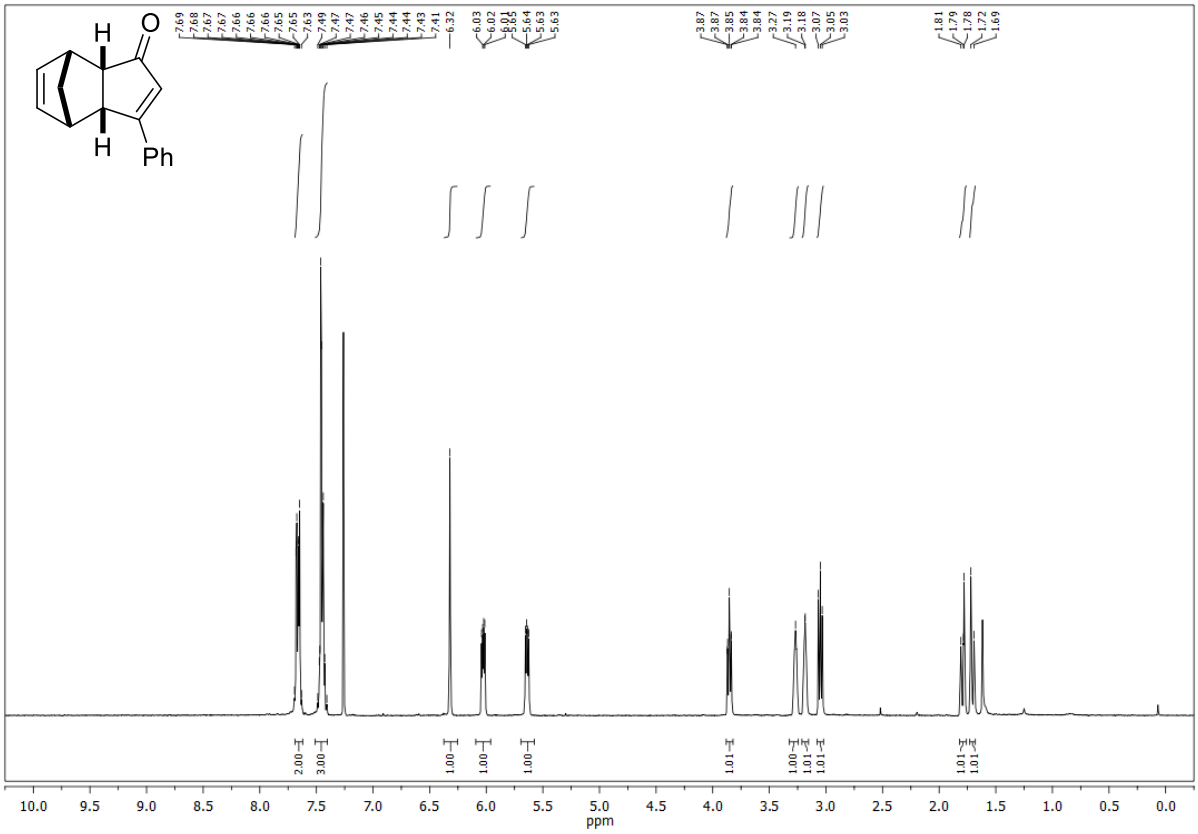


^{13}C NMR (75 MHz, $CDCl_3$)

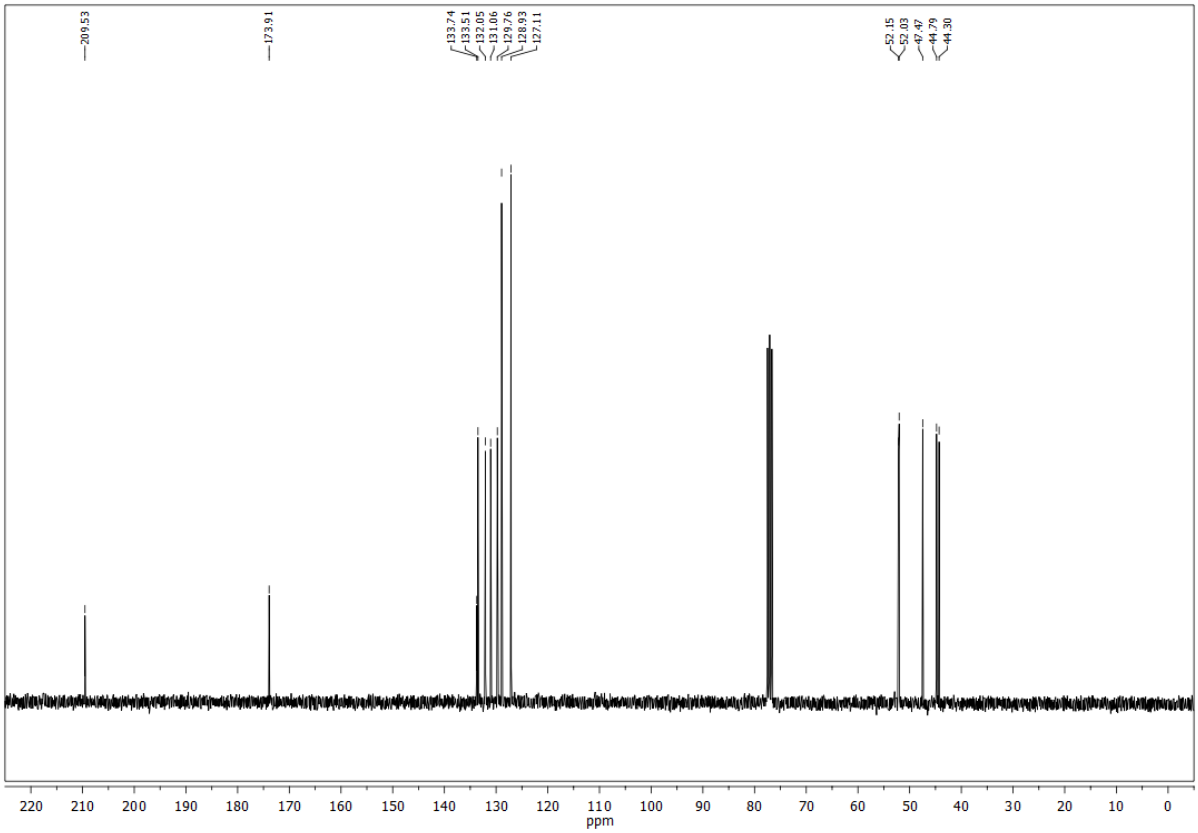


3-Phenyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-224)

^{1}H NMR (300 MHz, $CDCl_3$)

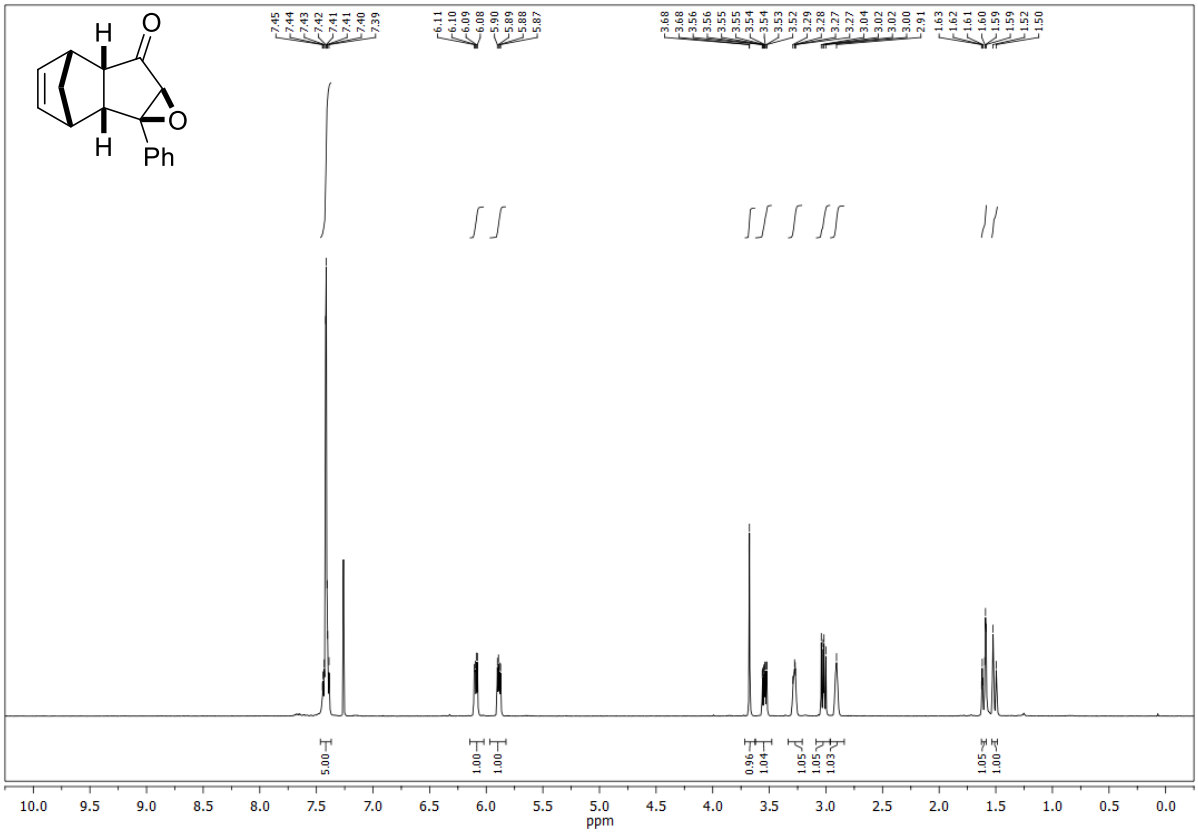


^{13}C NMR (75 MHz, $CDCl_3$)

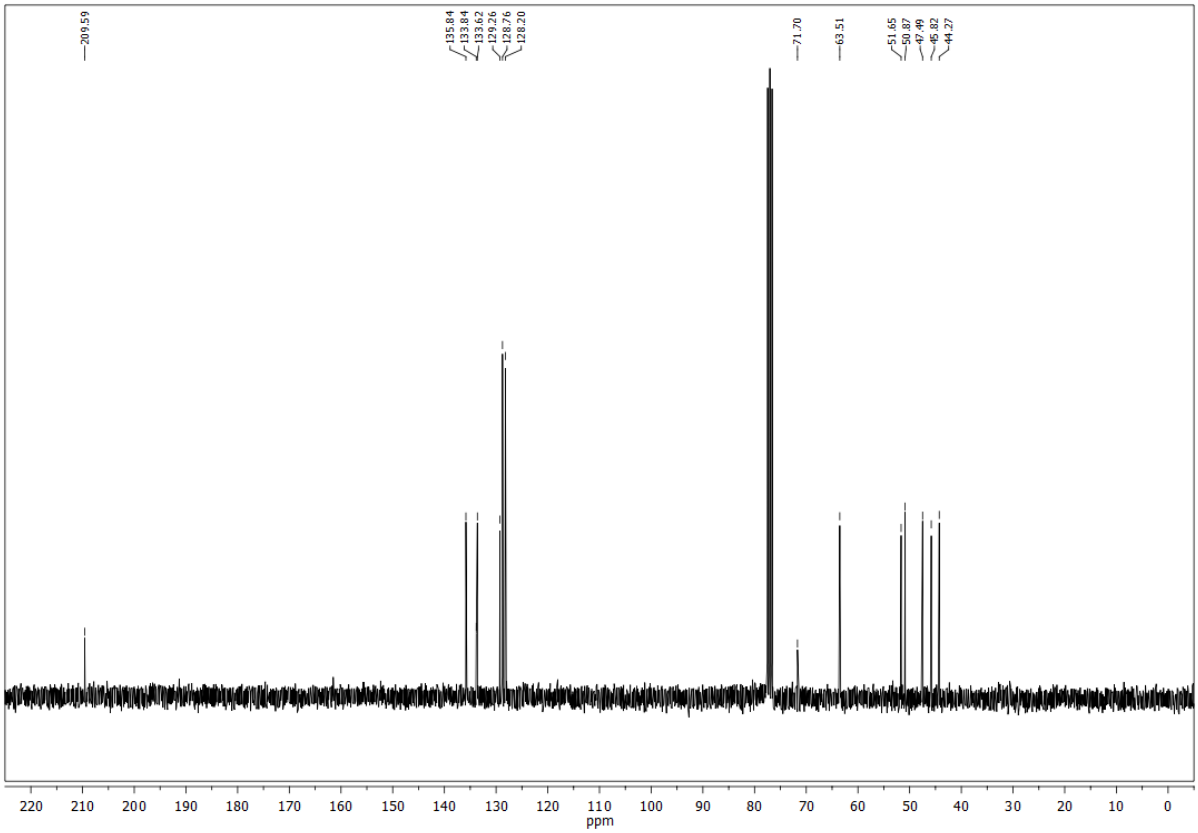


1a-Phenyl-1a,1b,2,5,5a,6a-hexahydro-6*H*-2,5-methanoindeno[1,2-*b*]oxiren-6-one

((±)-225) **^{1}H NMR** (300 MHz, $CDCl_3$)

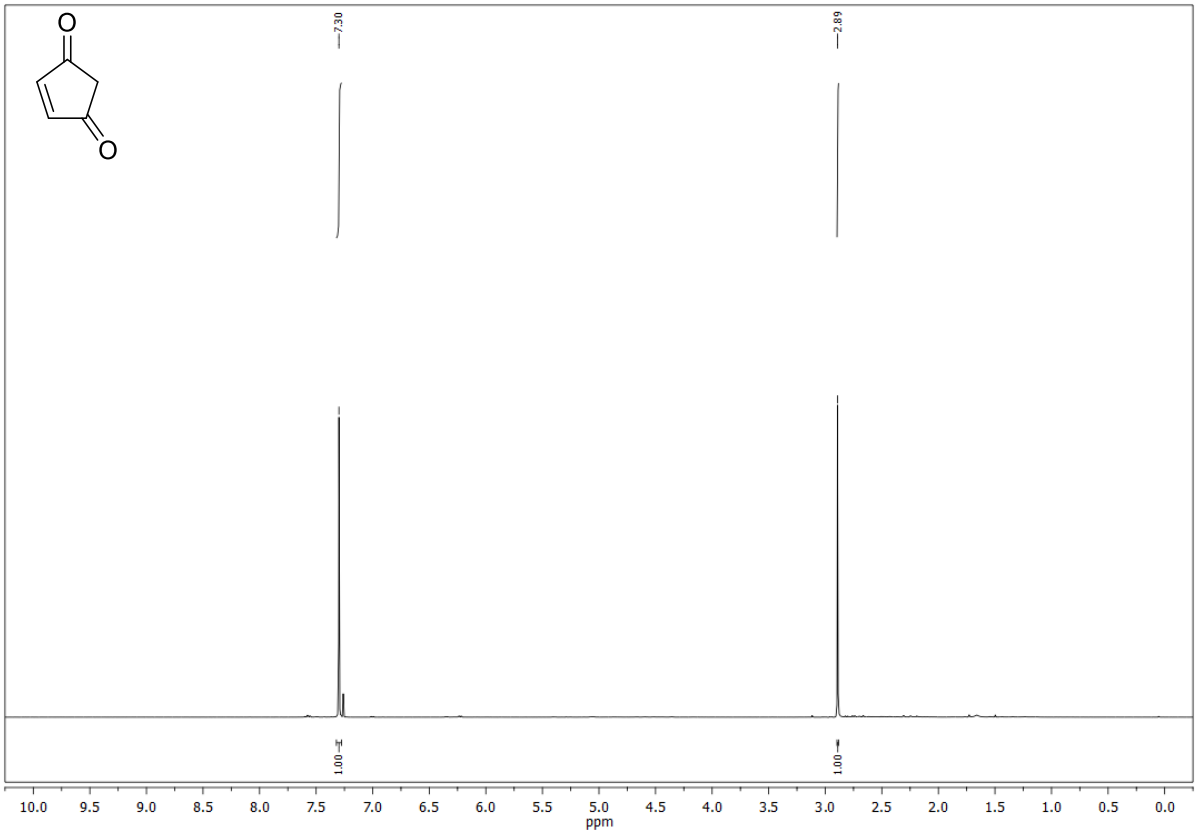


^{13}C NMR (75 MHz, $CDCl_3$)

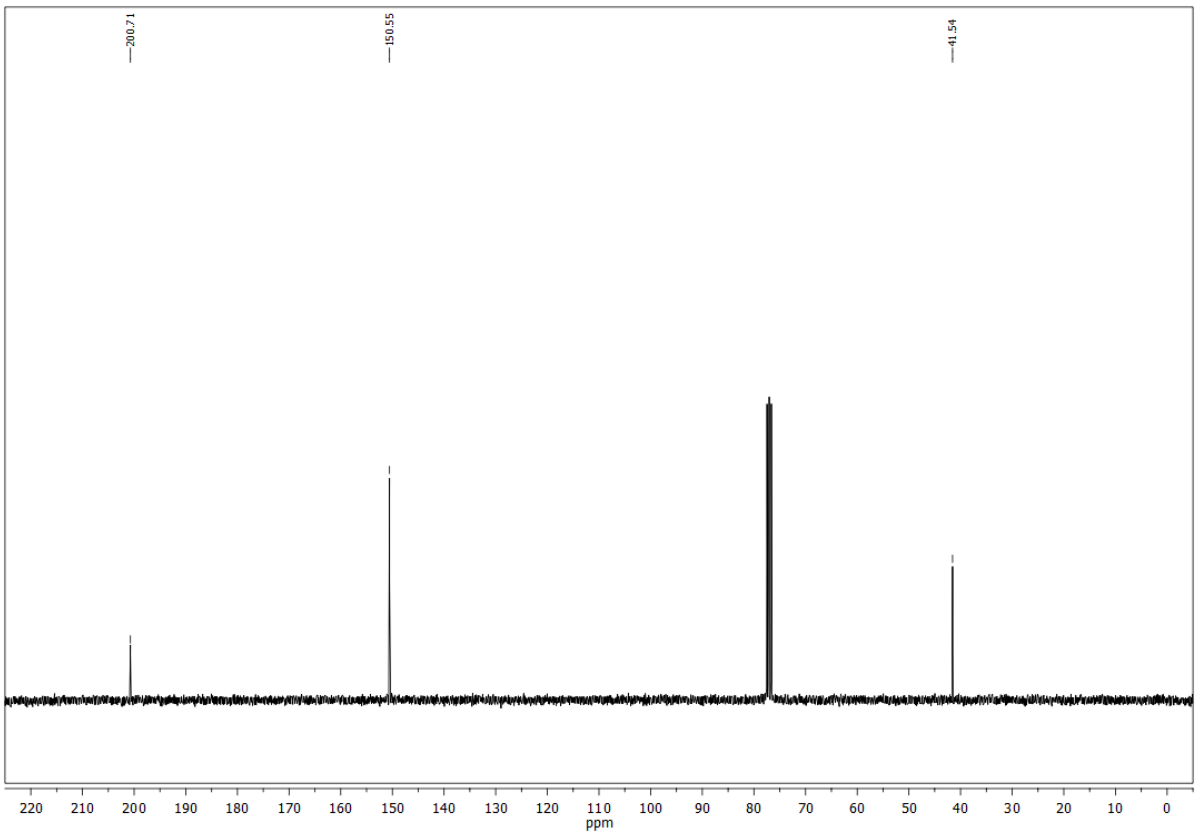


Cyclopent-4-ene-1,3-dione (234)

^{1}H NMR (300 MHz, $CDCl_3$)

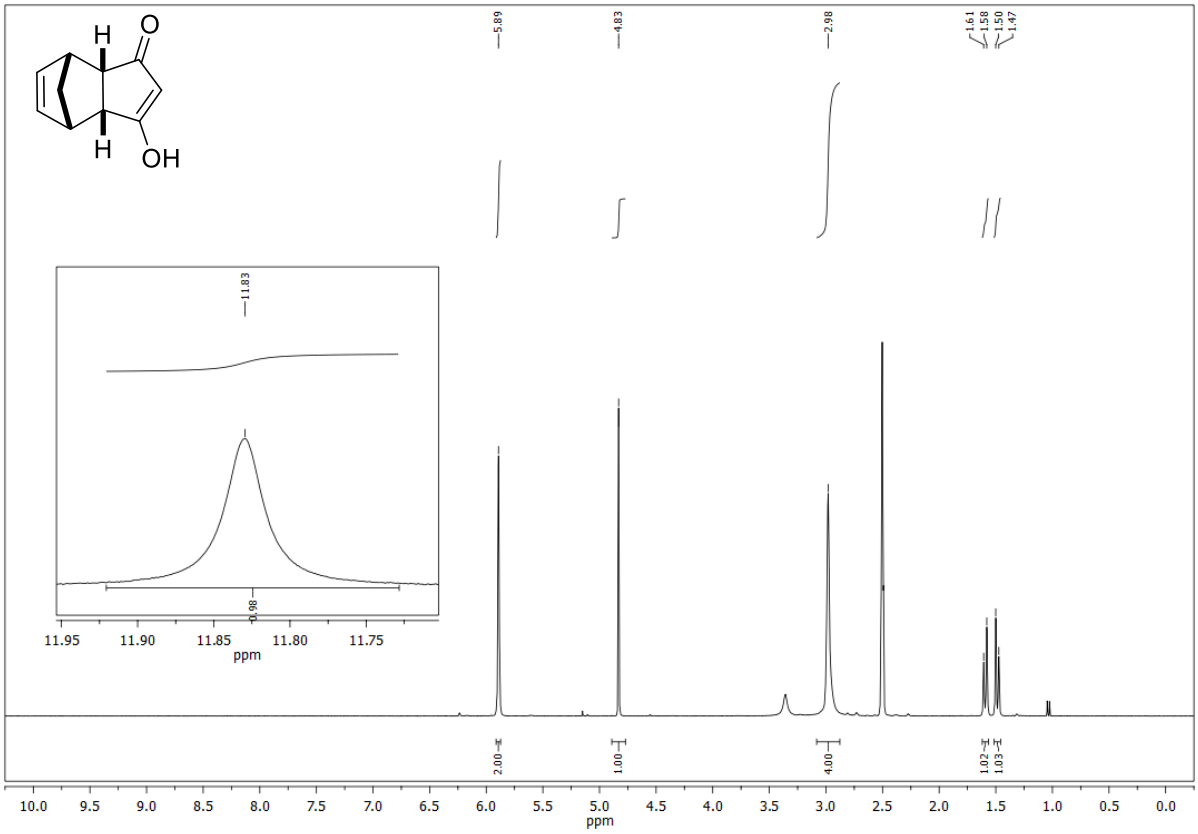


^{13}C NMR (75 MHz, $CDCl_3$)

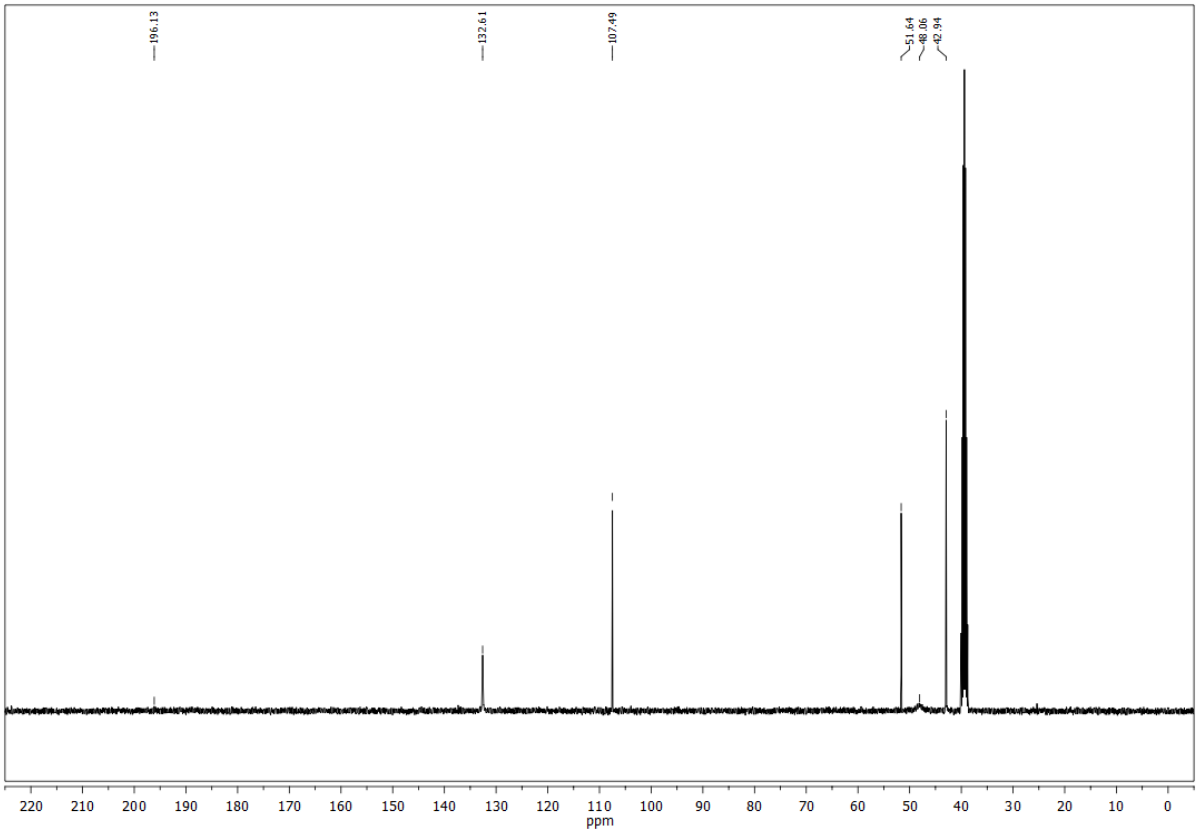


3-Hydroxy-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ((±)-211)

^{1}H NMR (300 MHz, DMSO)

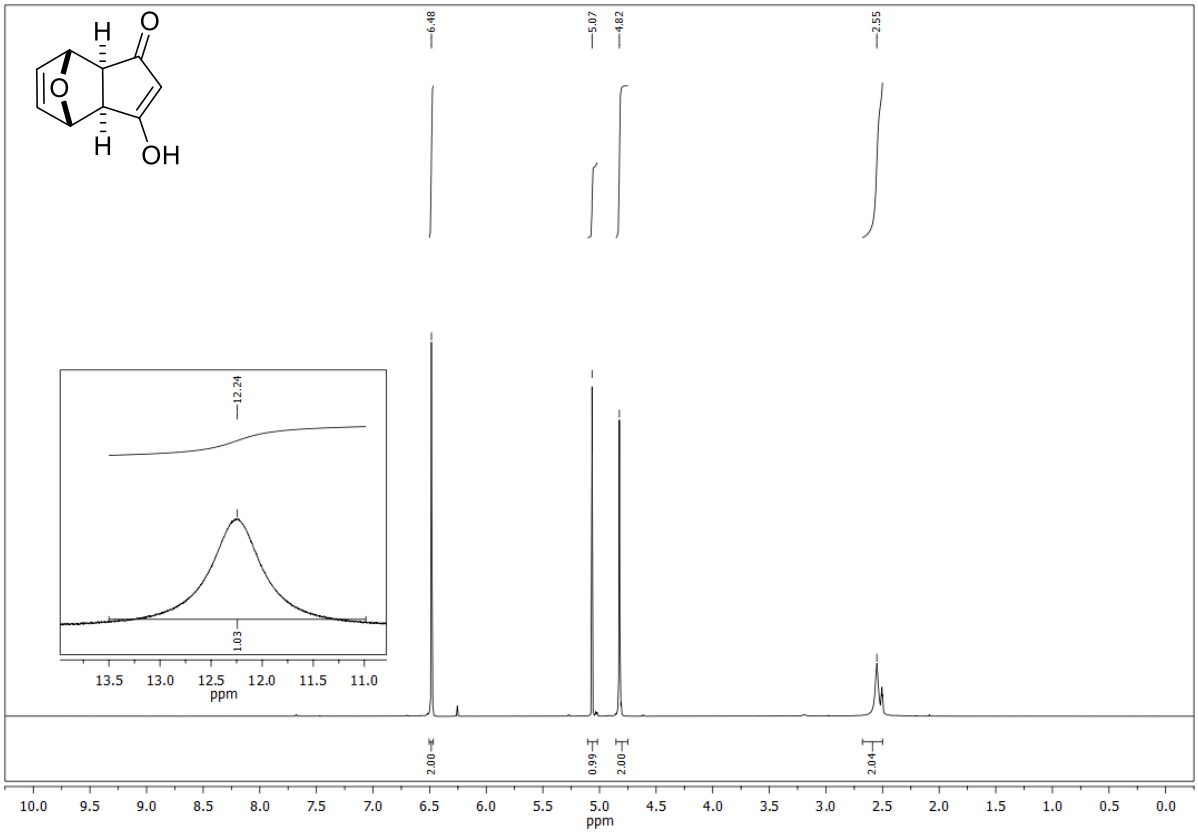


^{13}C NMR (75 MHz, DMSO)

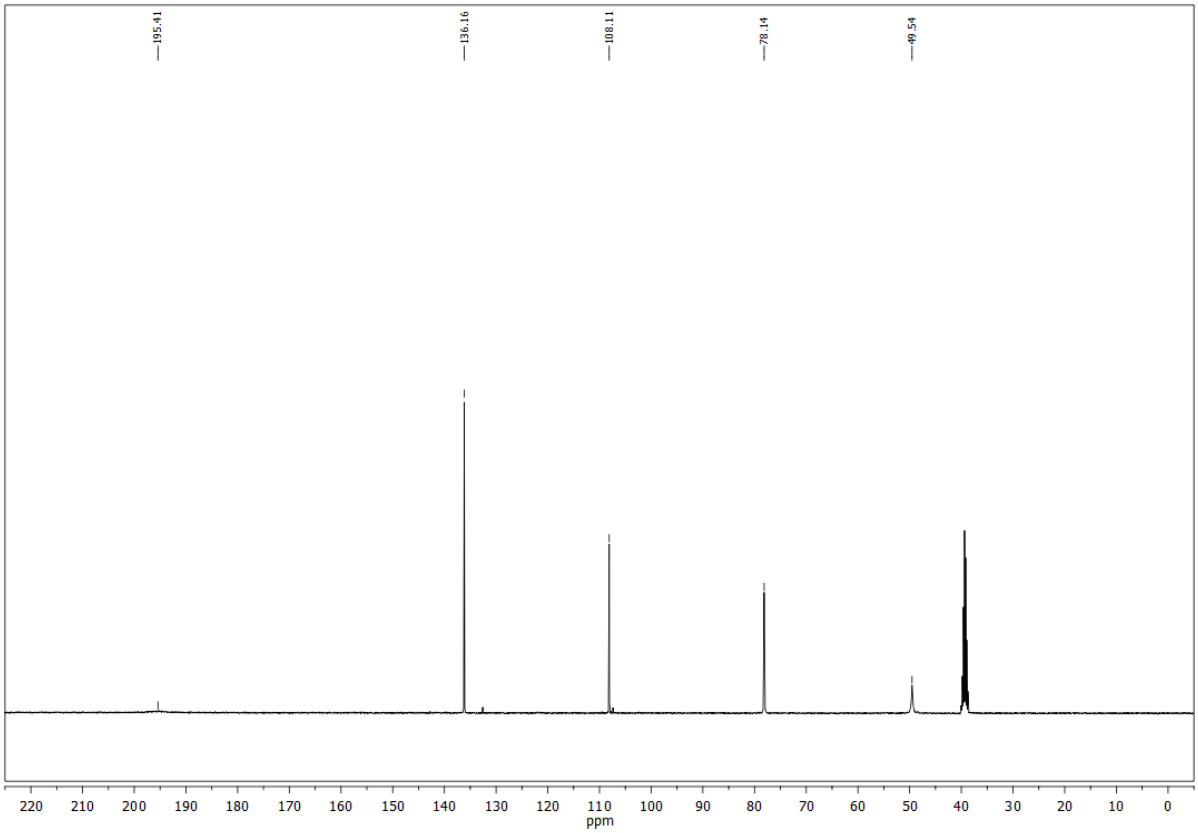


3-Hydroxy-3a,4,7,7a-tetrahydro-1*H*-4,7-epoxyinden-1-one ((±)-209)

^{1}H NMR (300 MHz, DMSO)

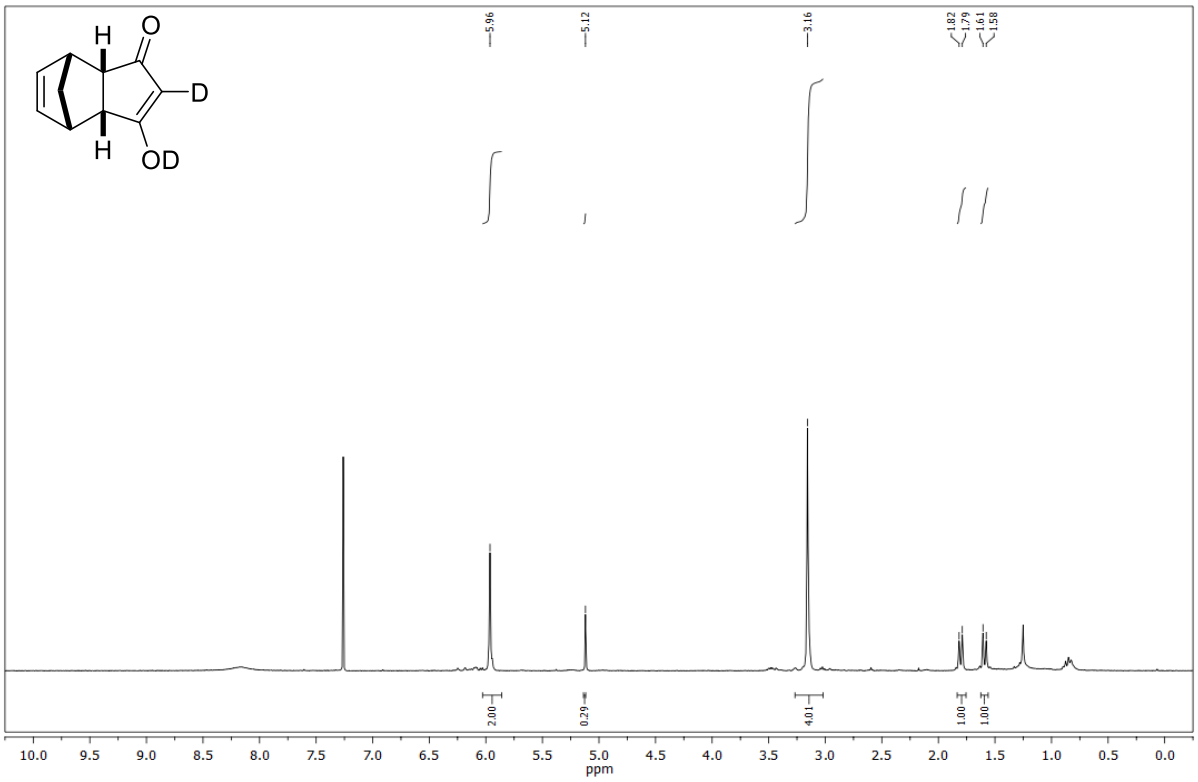


^{13}C NMR (75 MHz, DMSO)



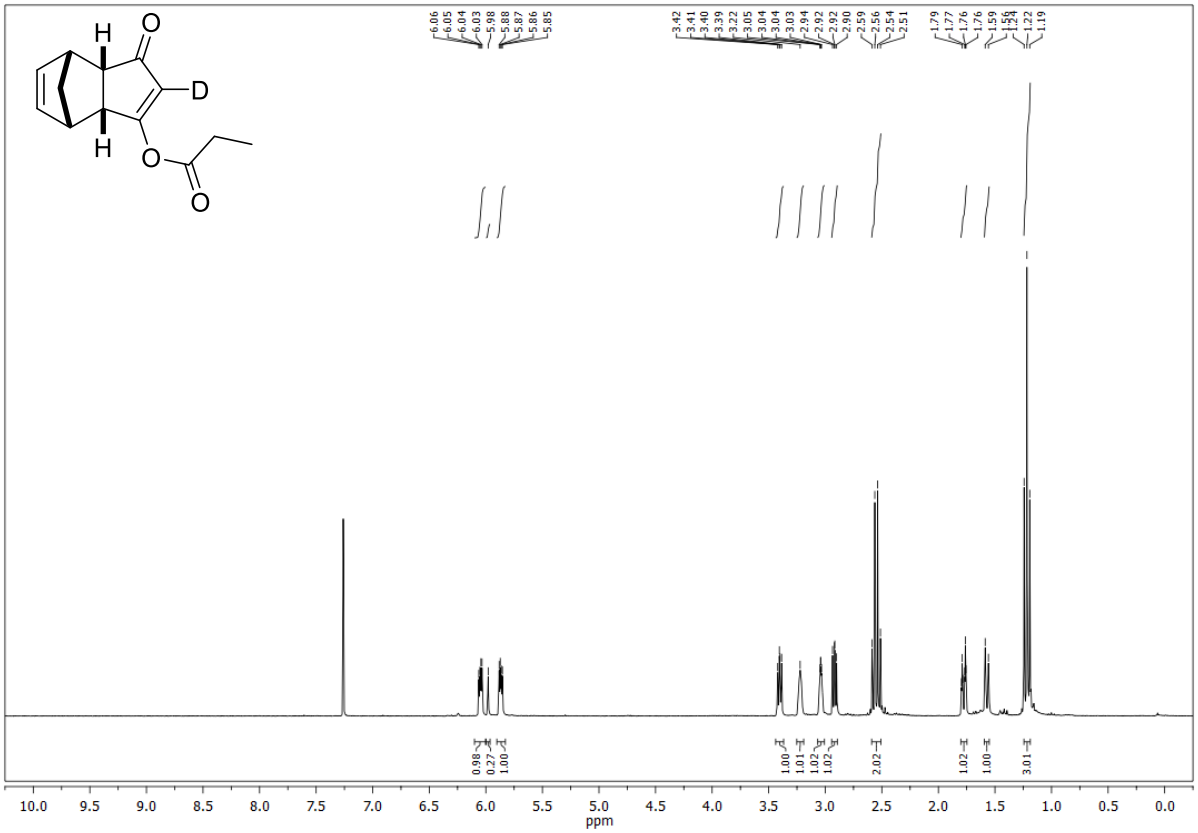
3-(Hydroxy-d)-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-1-one-2-d ((±)-244)

^{1}H NMR (300 MHz, $CDCl_3$)



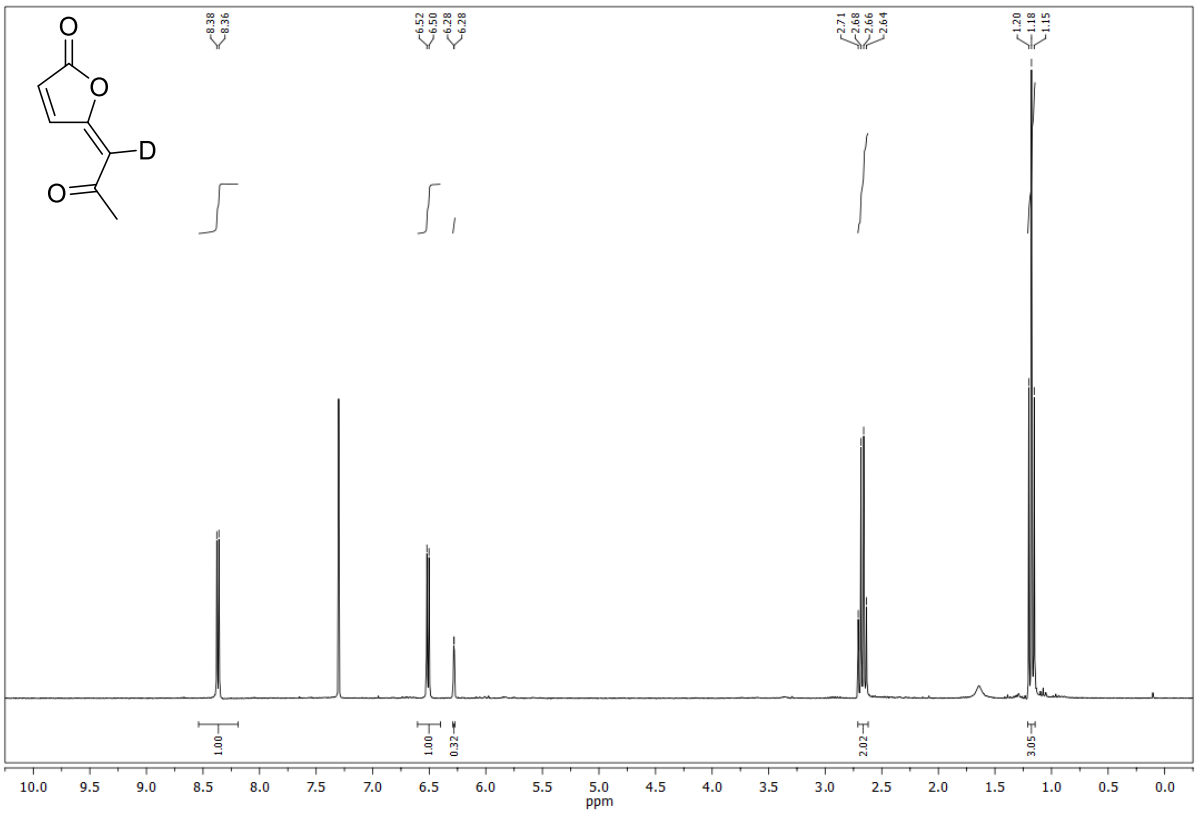
1-Oxo-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-3-yl-2-d propionate ((±)-245)

^{1}H NMR (300 MHz, $CDCl_3$)



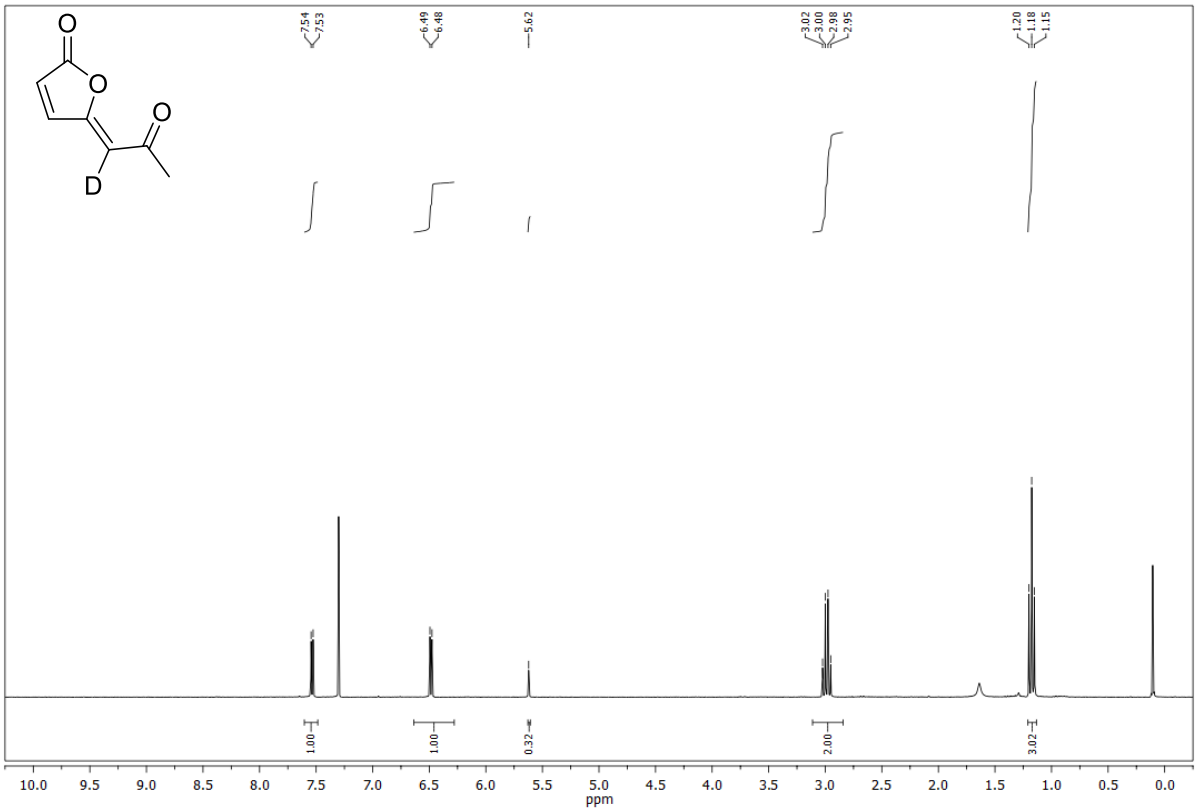
(*E*)-5-(2-Oxopropylidene-1-d)furan-2(5H)-one (246)

^{1}H NMR (300 MHz, $CDCl_3$)



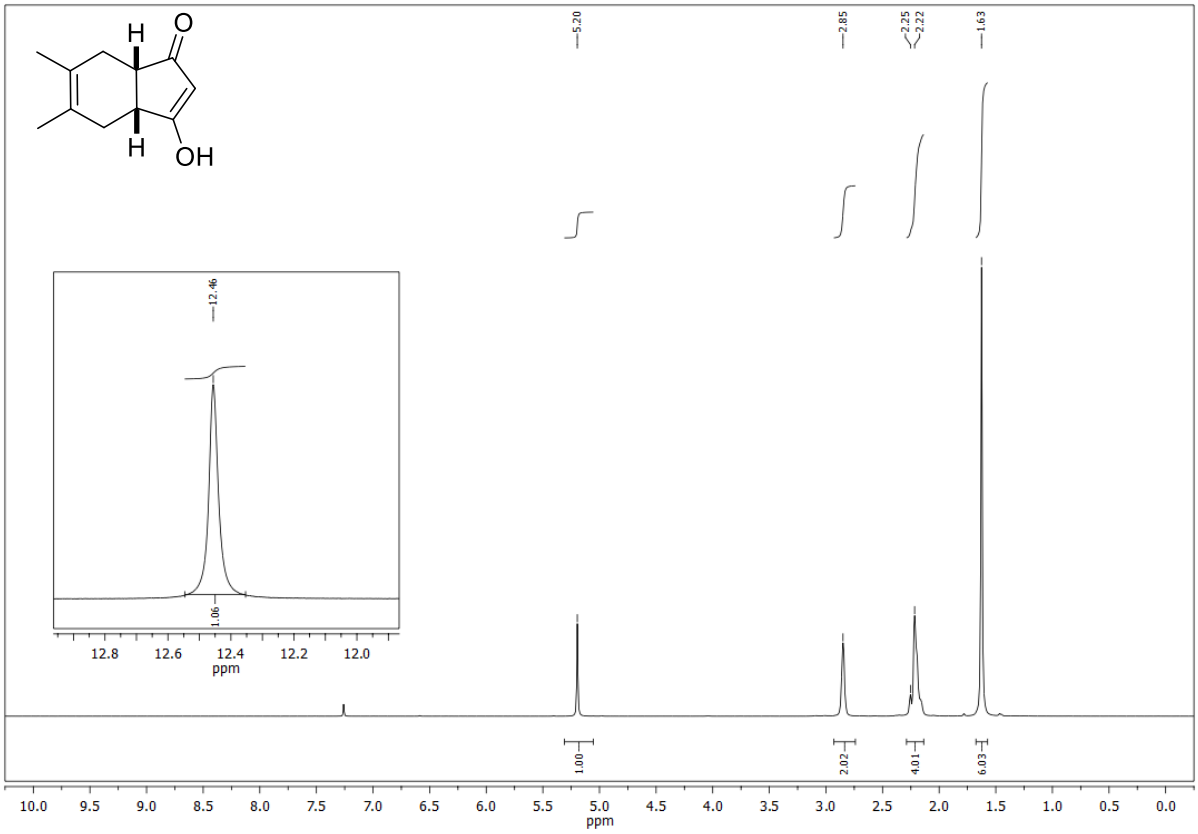
(*Z*)-5-(2-Oxopropylidene-1-d)furan-2(5H)-one (247)

^{1}H NMR (300 MHz, $CDCl_3$)

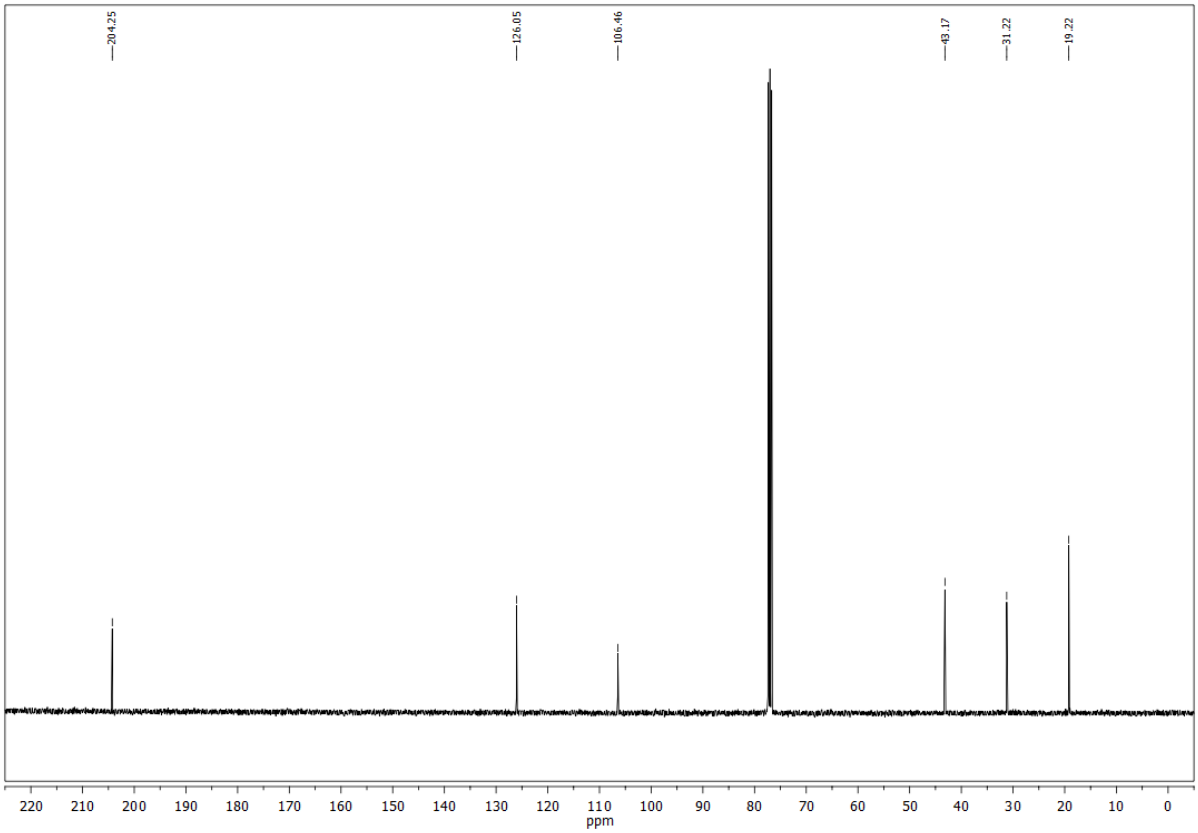


3-Hydroxy-5,6-dimethyl-3a,4,7,7a-tetrahydro-1*H*-inden-1-one ((±)-256)

^{1}H NMR (400 MHz, $CDCl_3$)

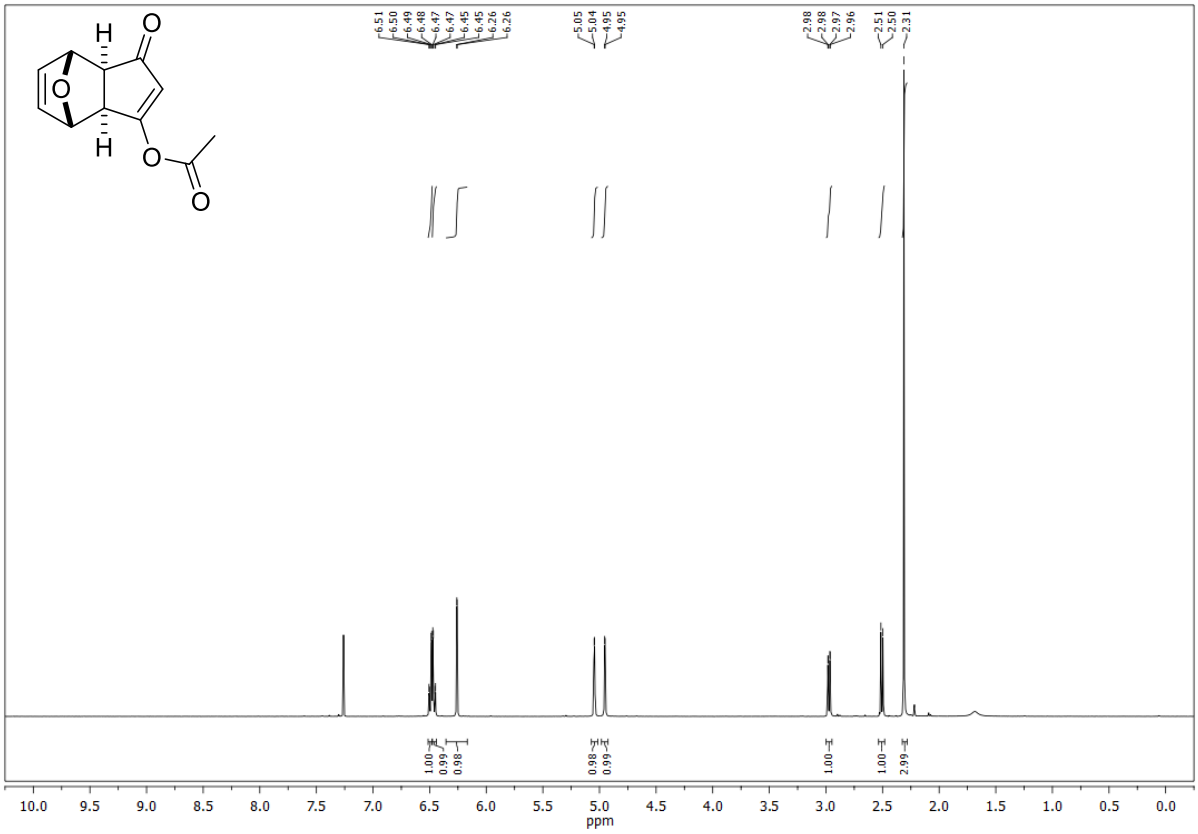


^{13}C NMR (101 MHz, $CDCl_3$)

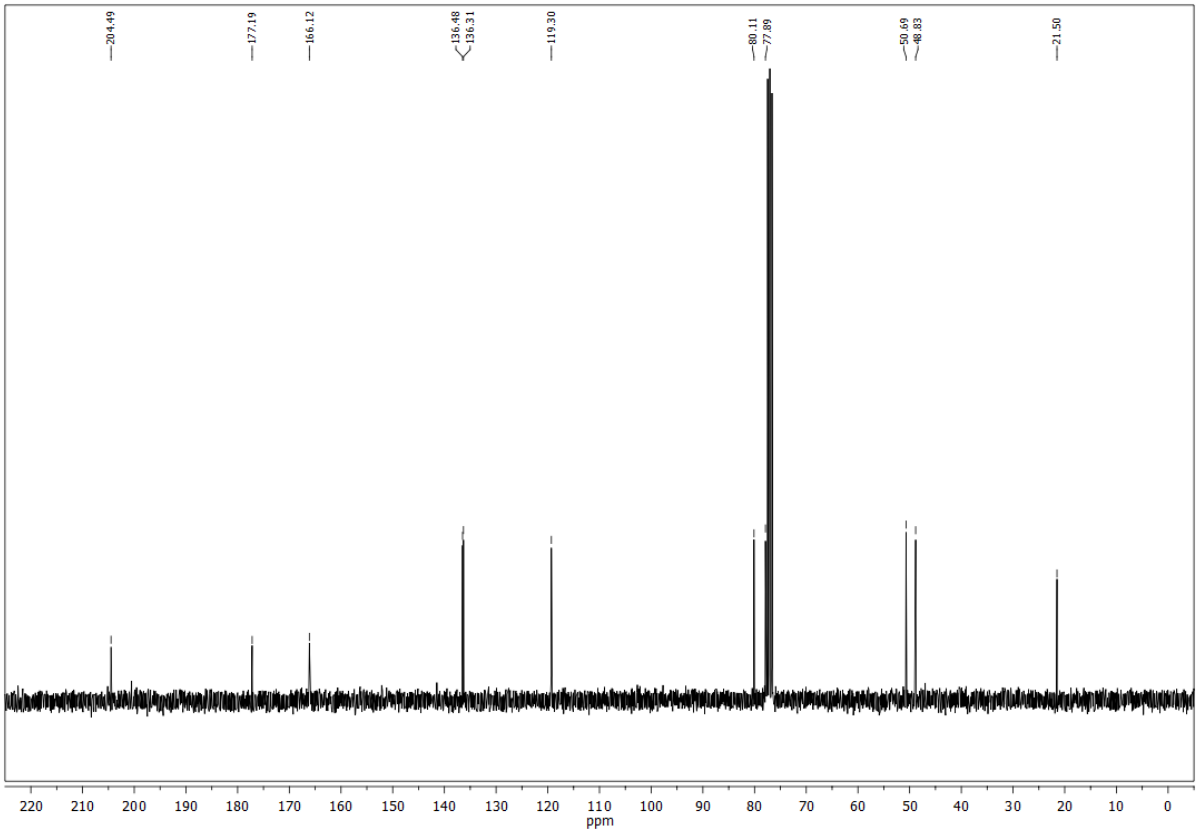


1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-epoxyinden-3-yl acetate ((±)-257)

^{1}H NMR (300 MHz, $CDCl_3$)

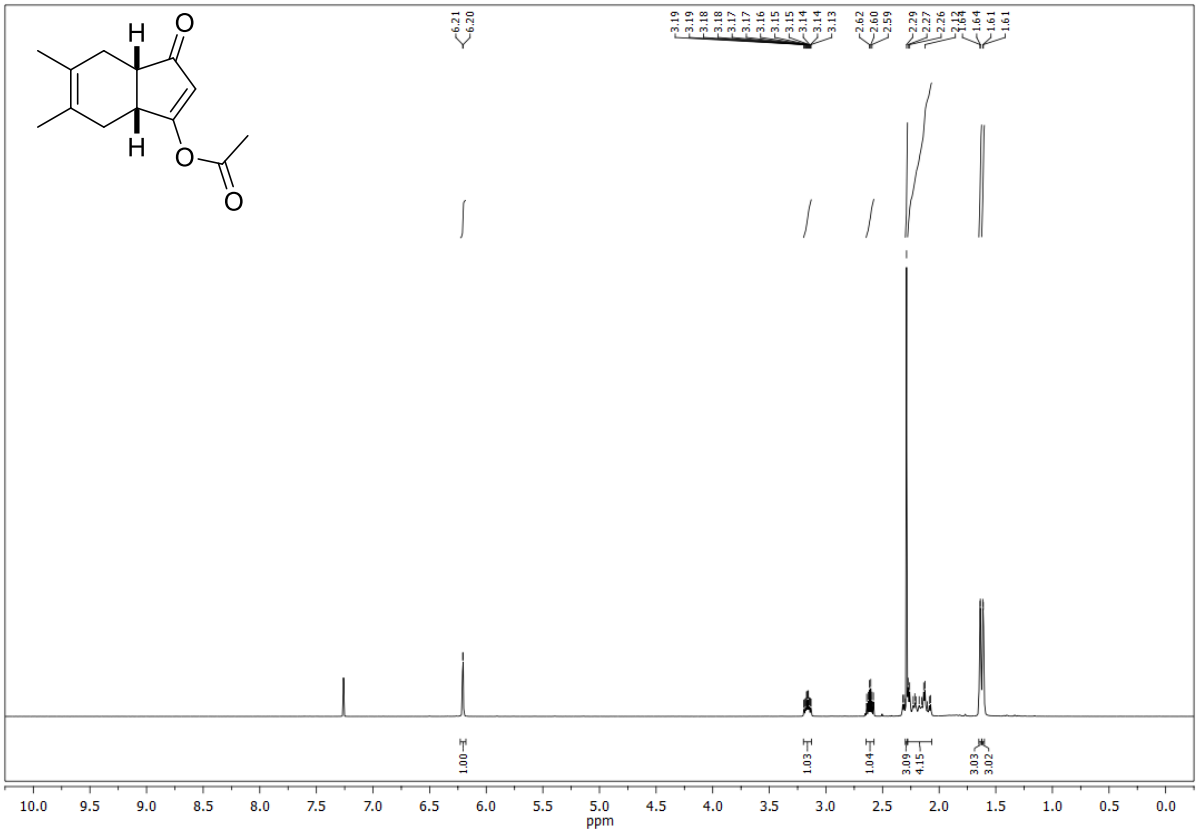


^{13}C NMR (75 MHz, $CDCl_3$)

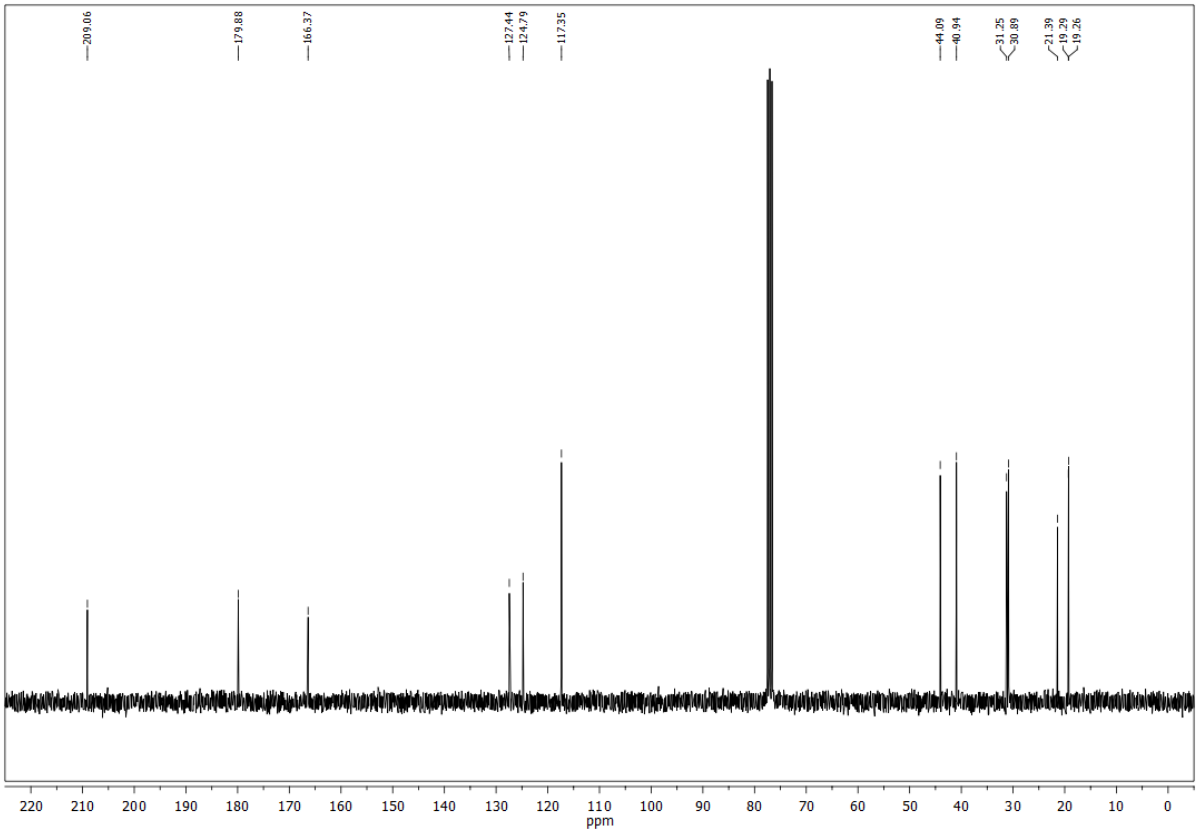


5,6-Dimethyl-1-oxo-3a,4,7,7a-tetrahydro-1*H*-inden-3-yl acetate ((±)-258)

^{1}H NMR (300 MHz, $CDCl_3$)

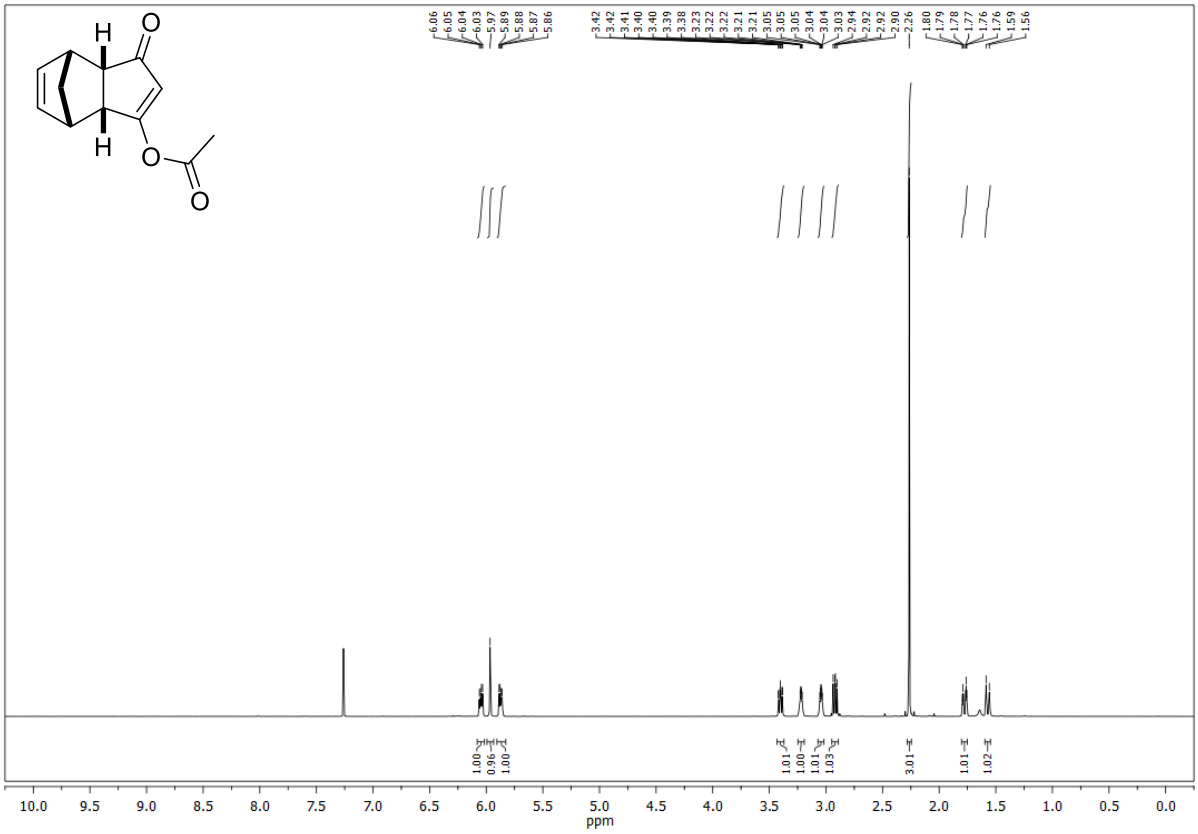


^{13}C NMR (75 MHz, $CDCl_3$)

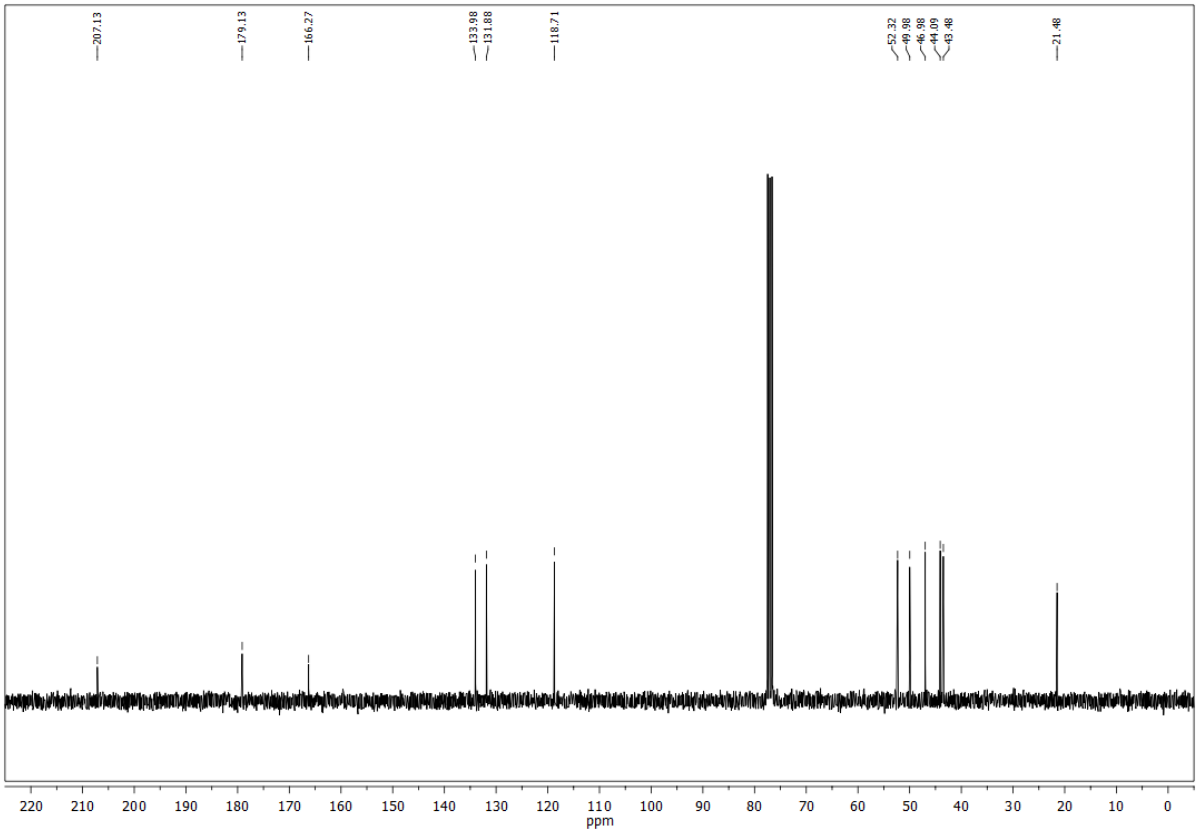


1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl acetate ((±)-240a)

^{1}H NMR (300 MHz, $CDCl_3$)

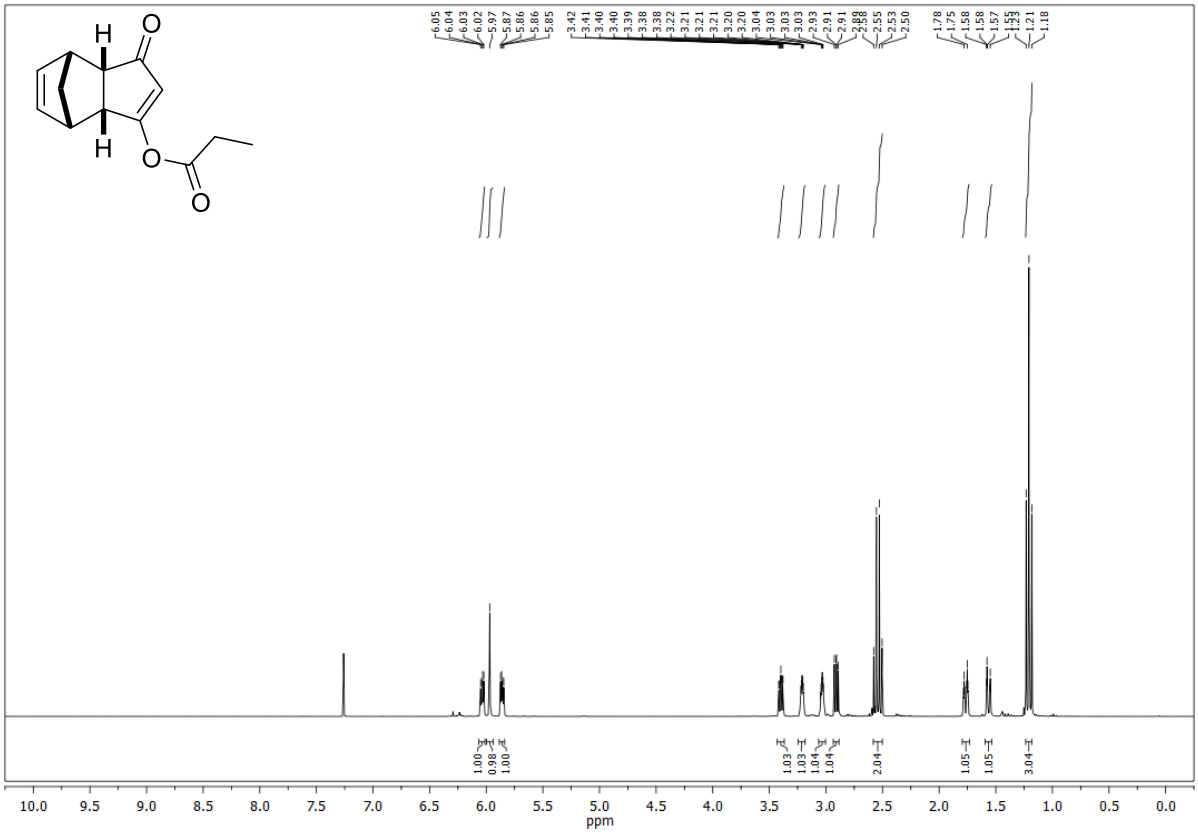


^{13}C NMR (75 MHz, $CDCl_3$)

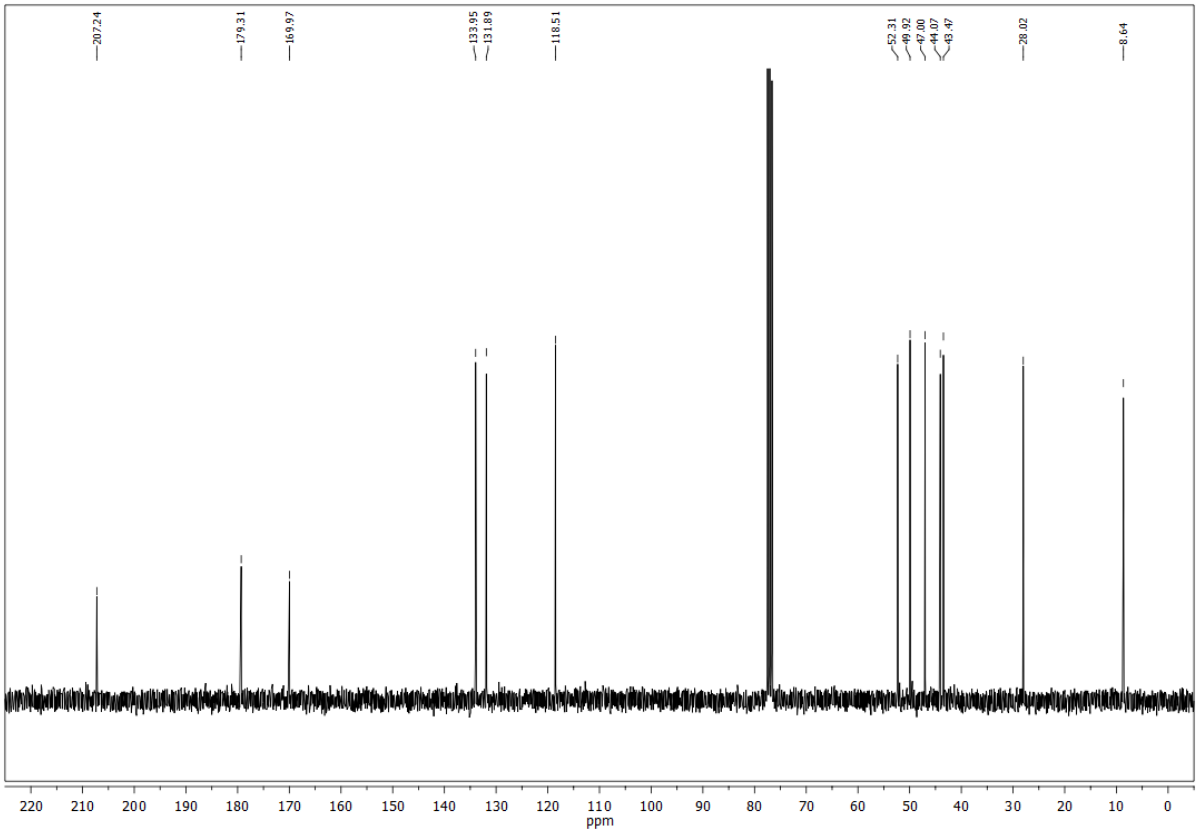


1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl propionate ((±)-240b)

^{1}H NMR (300 MHz, $CDCl_3$)

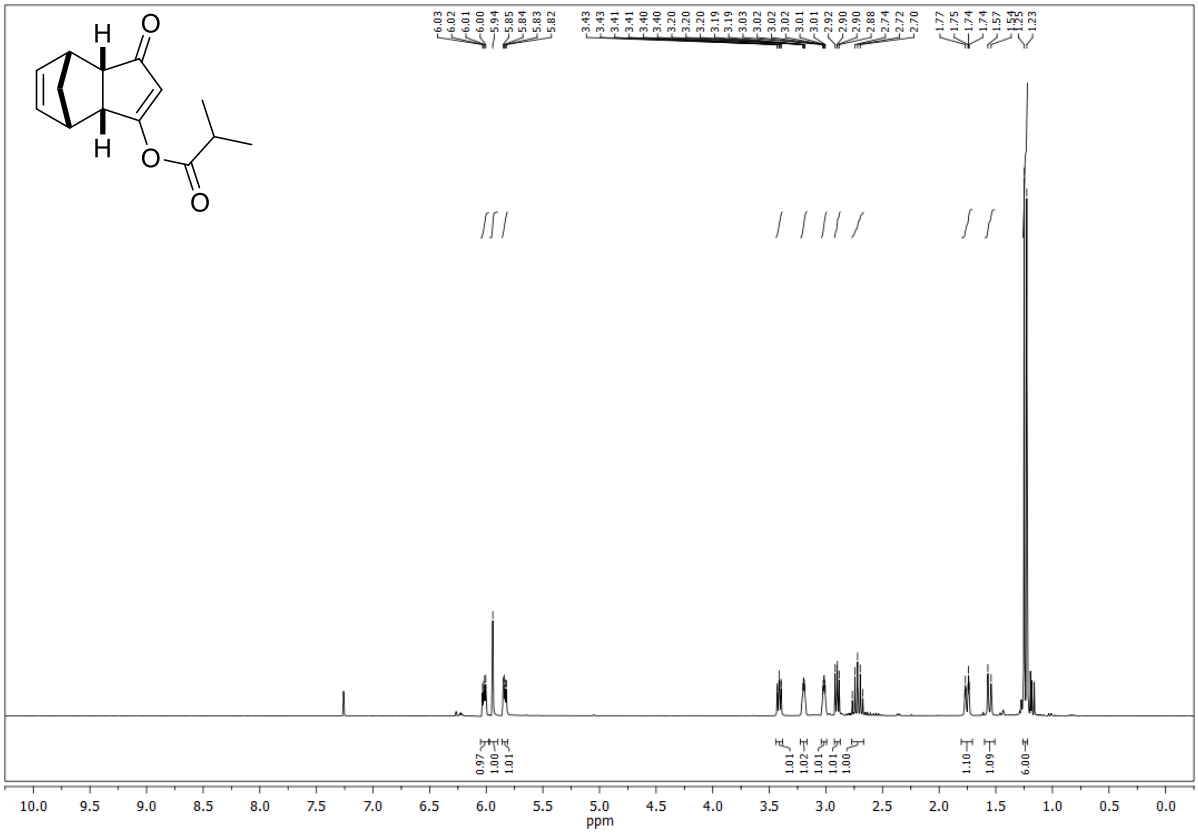


^{13}C NMR (75 MHz, $CDCl_3$)

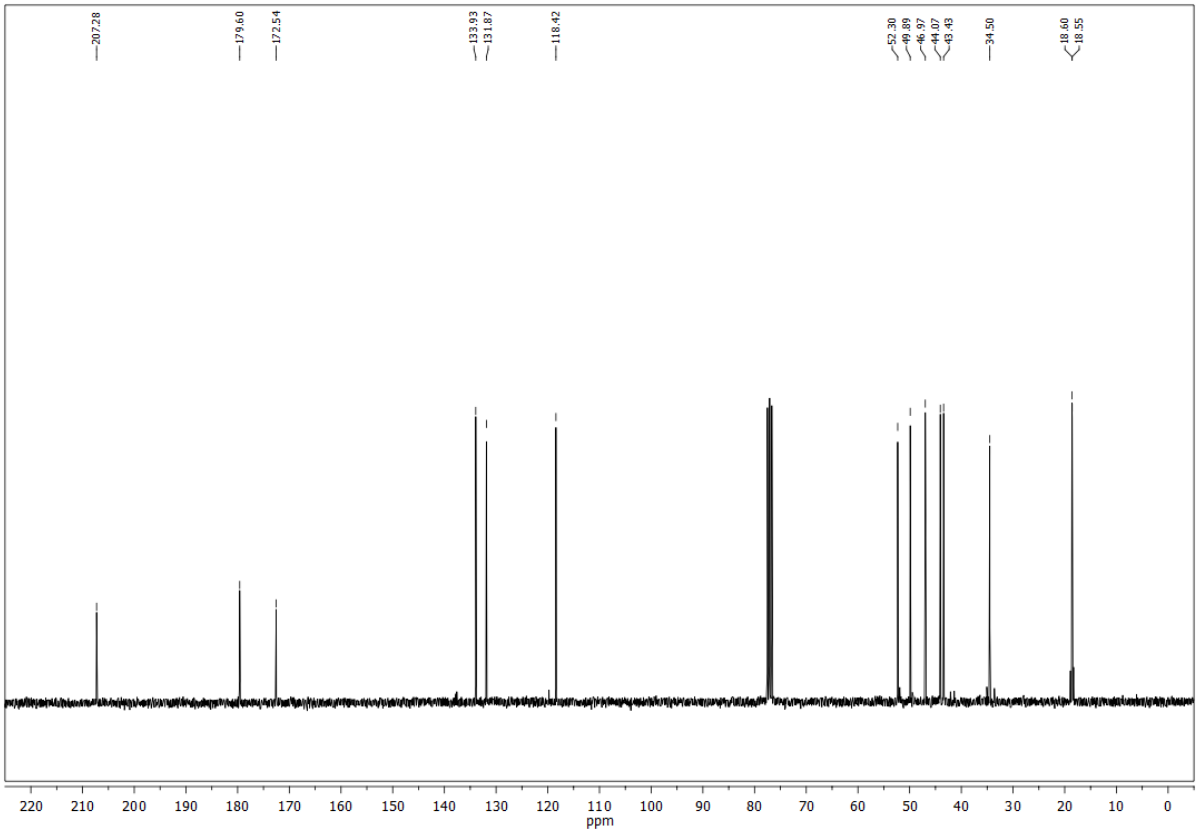


1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl isobutyrate ((±)-240c)

^{1}H NMR (300 MHz, $CDCl_3$)

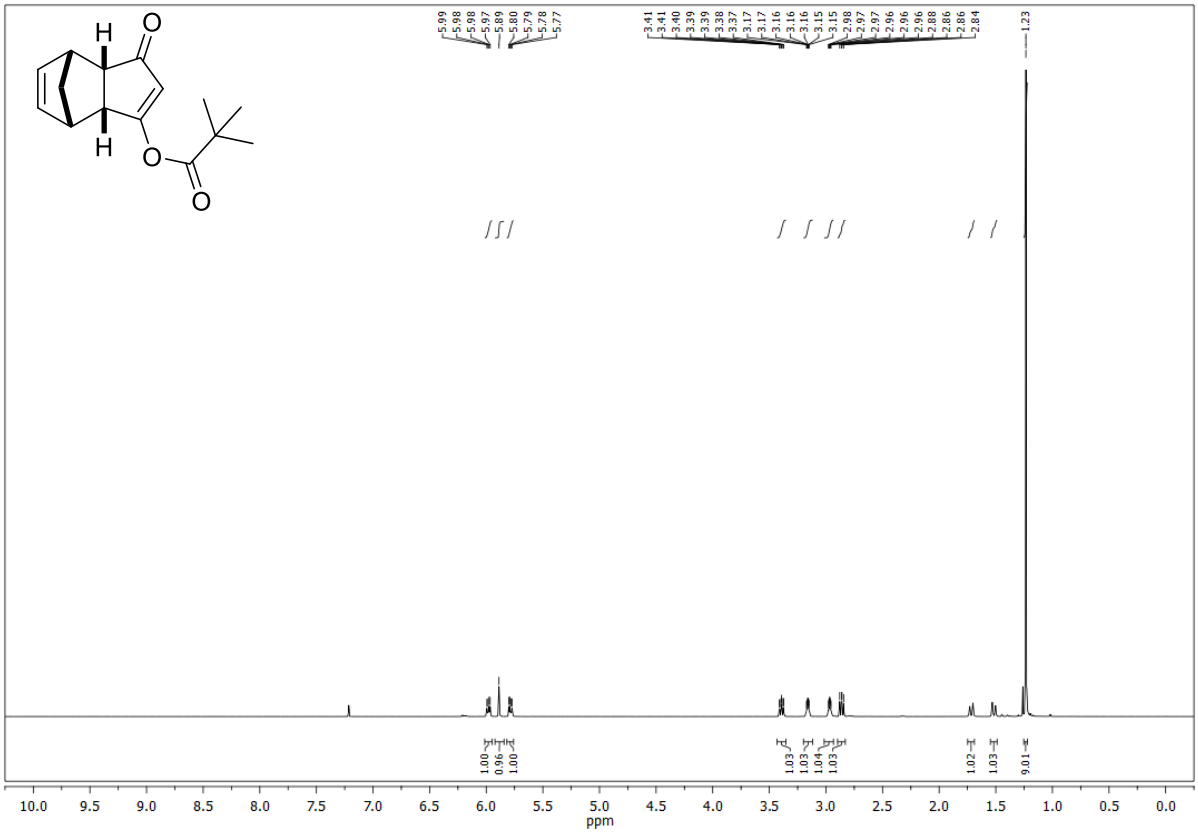


^{13}C NMR (75 MHz, $CDCl_3$)

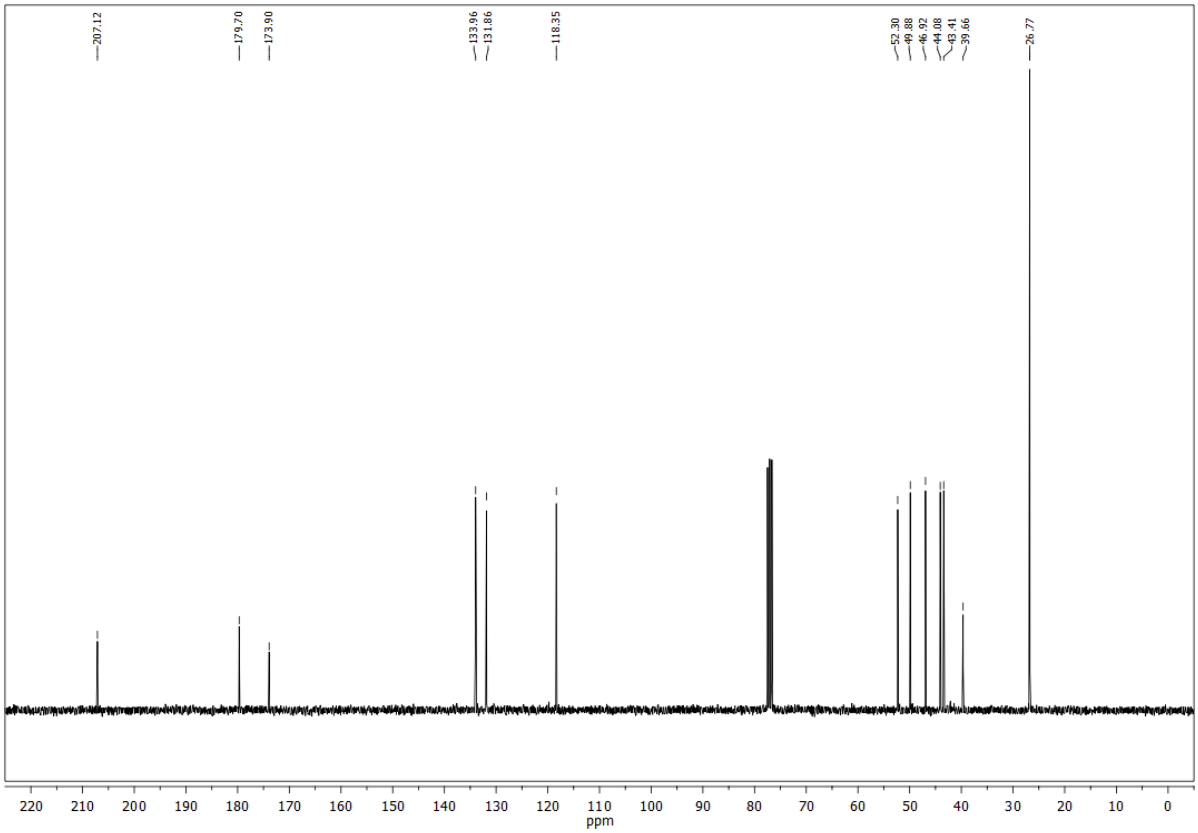


1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl pivalate ((±)-240d)

^{1}H NMR (300 MHz, $CDCl_3$)

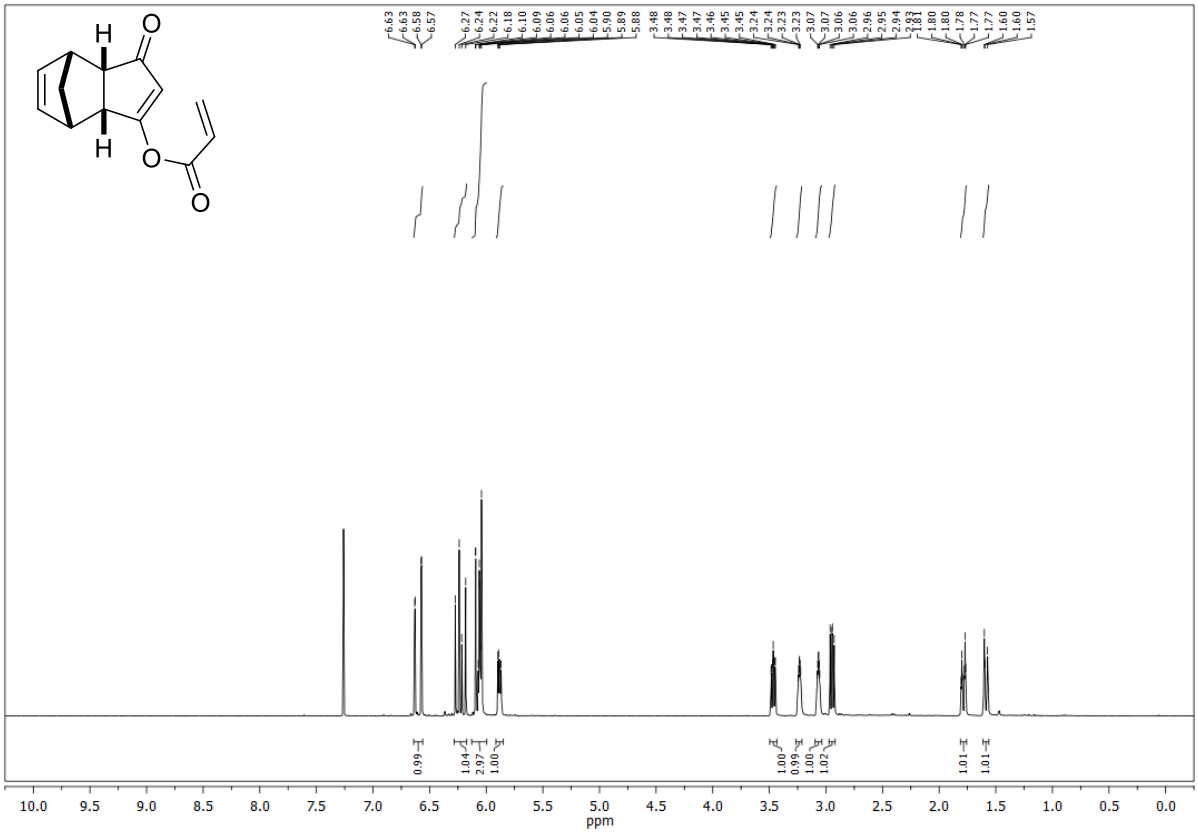


^{13}C NMR (75 MHz, $CDCl_3$)

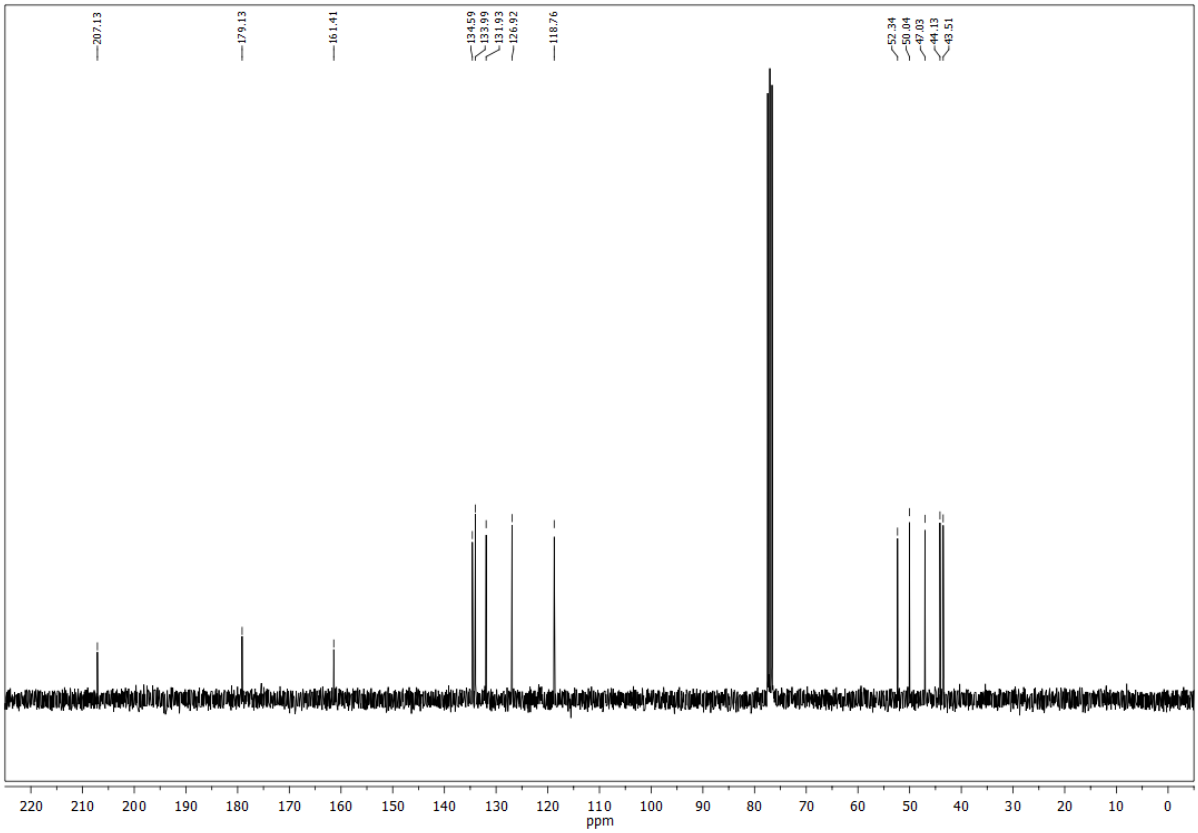


1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl acrylate ((±)-240e)

^{1}H NMR (300 MHz, $CDCl_3$)

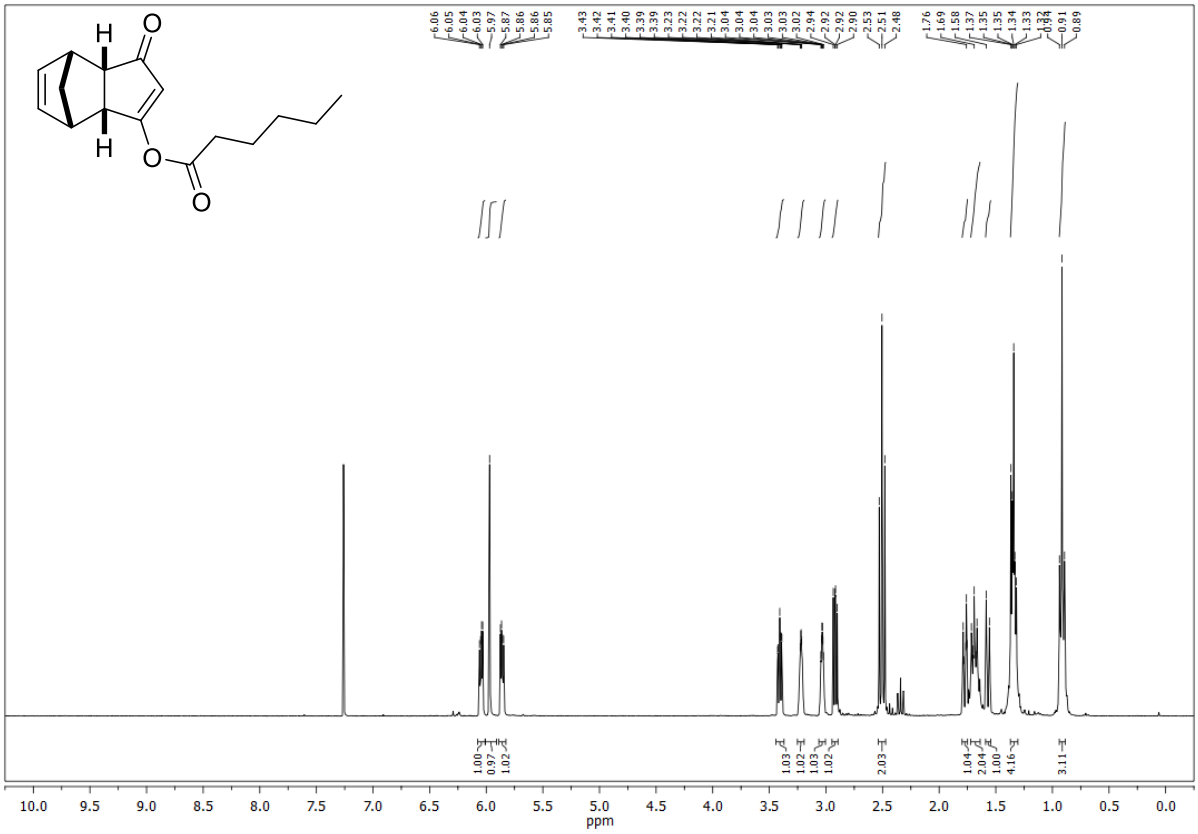


^{13}C NMR (75 MHz, $CDCl_3$)

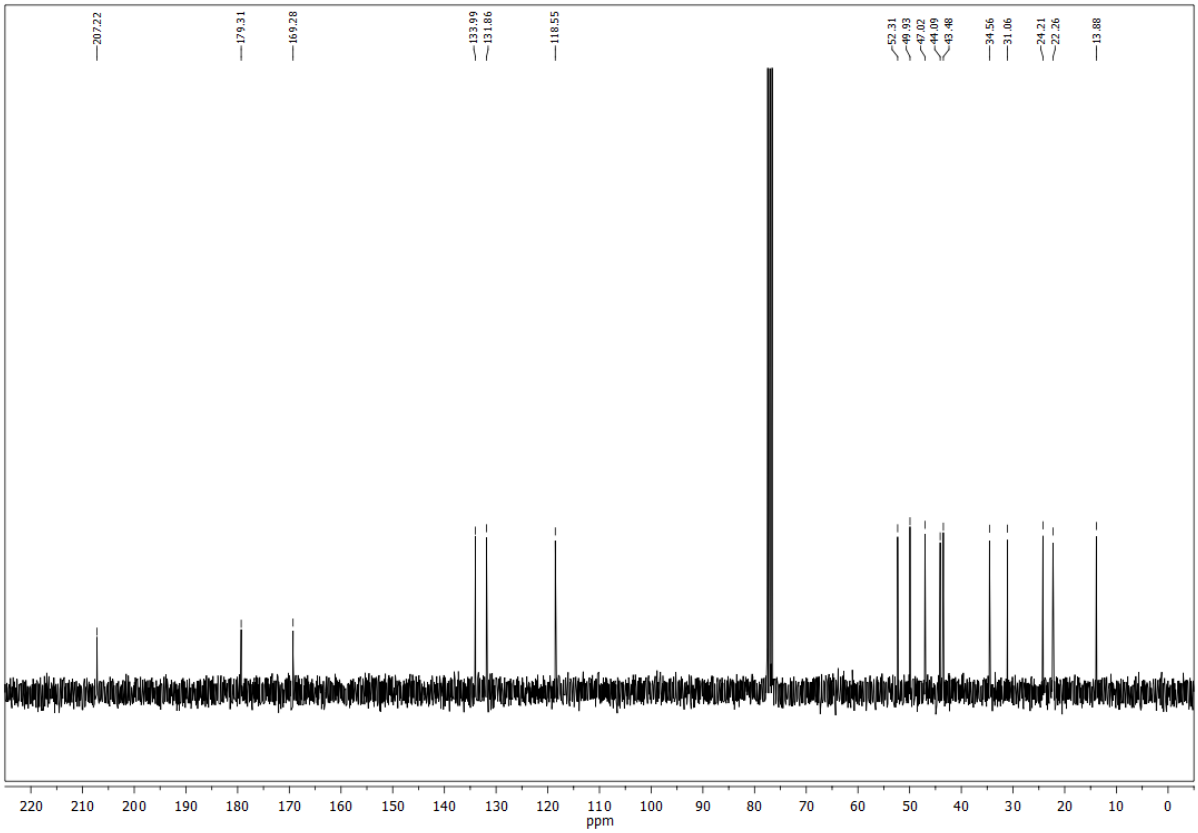


1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl hexanoate ((±)-240f)

^{1}H NMR (300 MHz, $CDCl_3$)

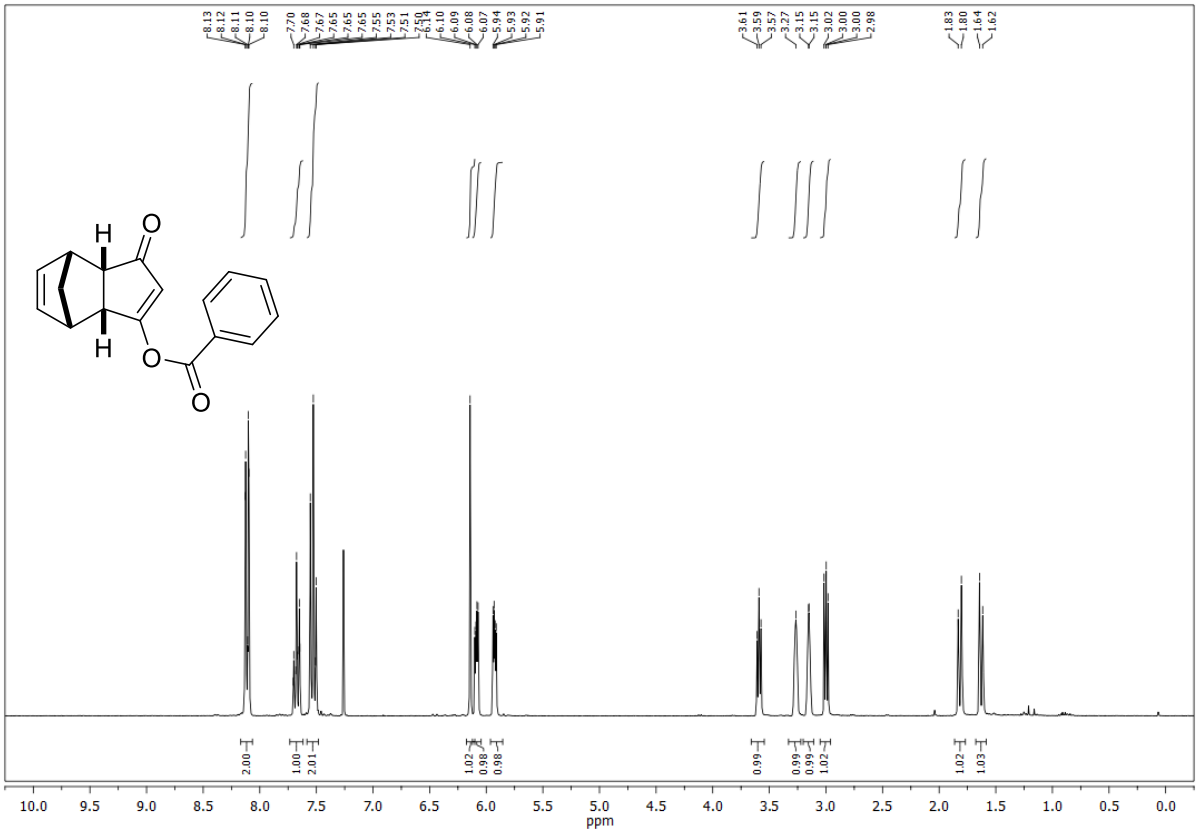


^{13}C NMR (75 MHz, $CDCl_3$)

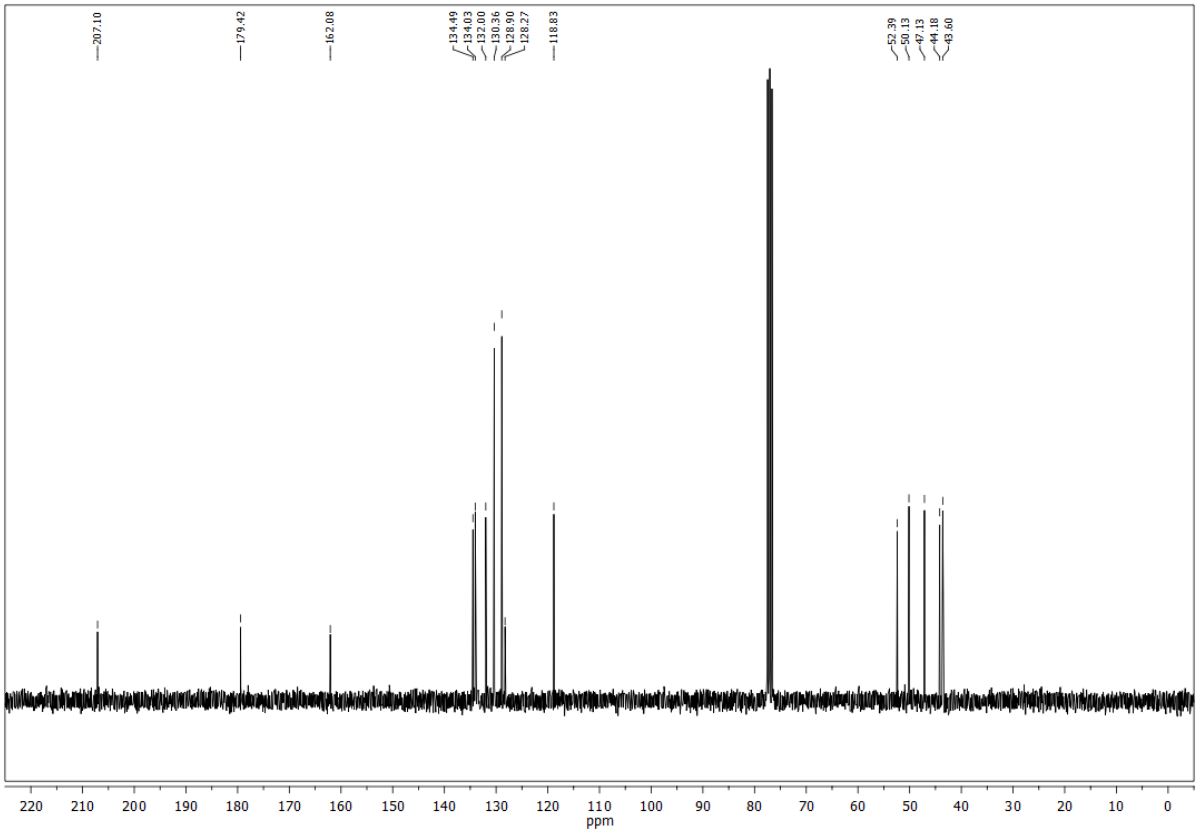


1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl benzoate ((±)-240g)

^{1}H NMR (300 MHz, $CDCl_3$)

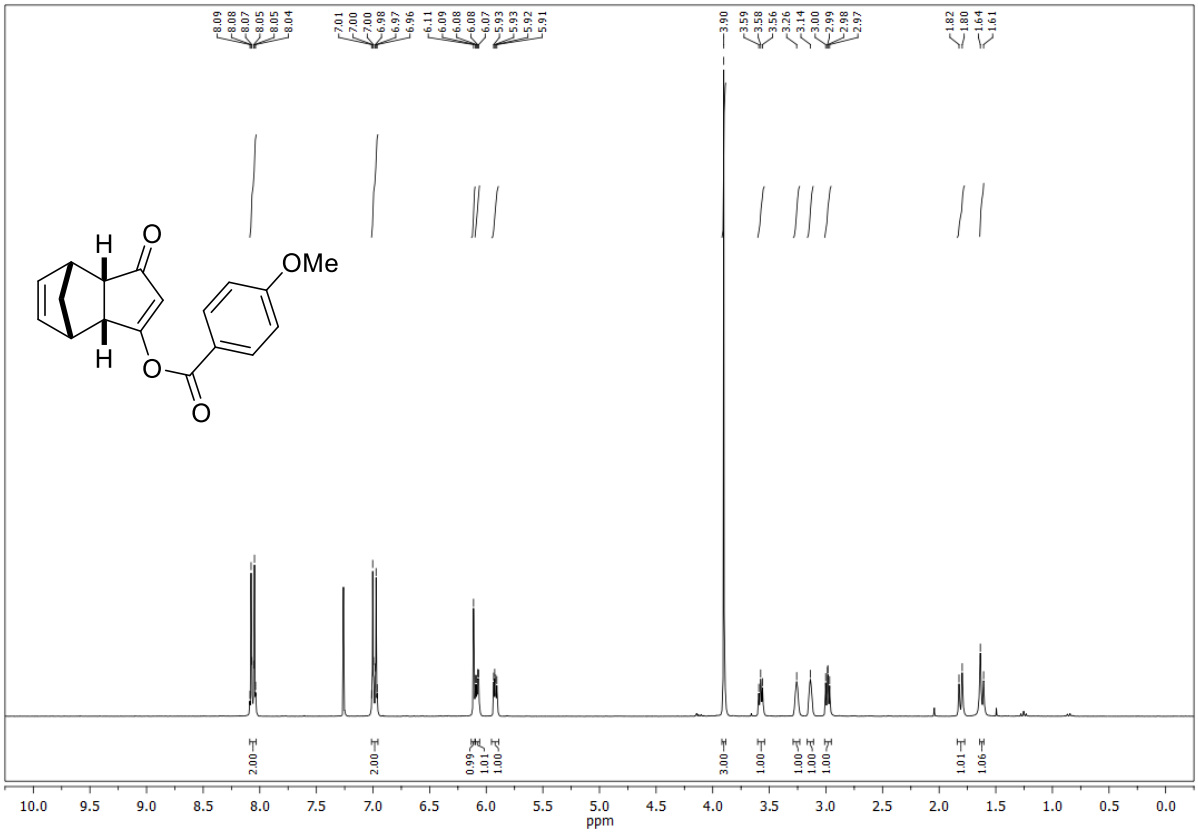


^{13}C NMR (75 MHz, $CDCl_3$)

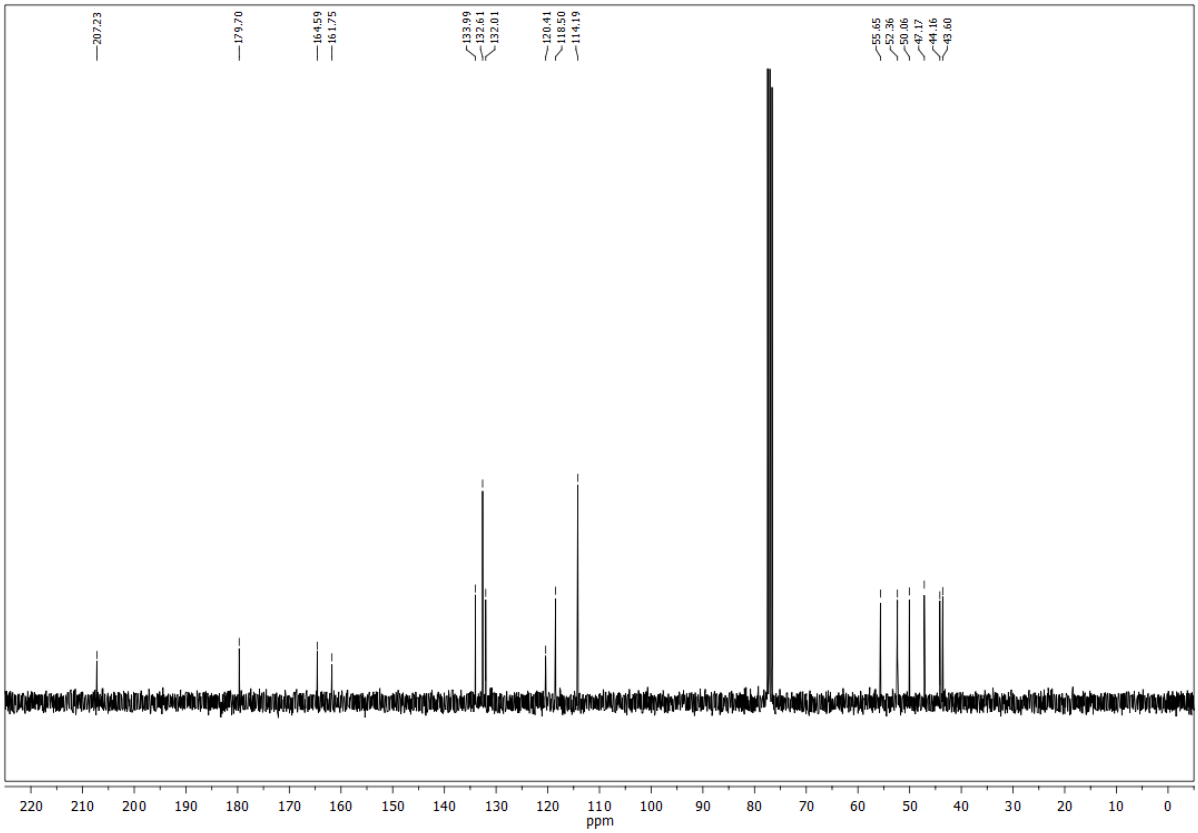


1-Oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl 4-methoxybenzoate ((±)-240h)

^{1}H NMR (300 MHz, $CDCl_3$)

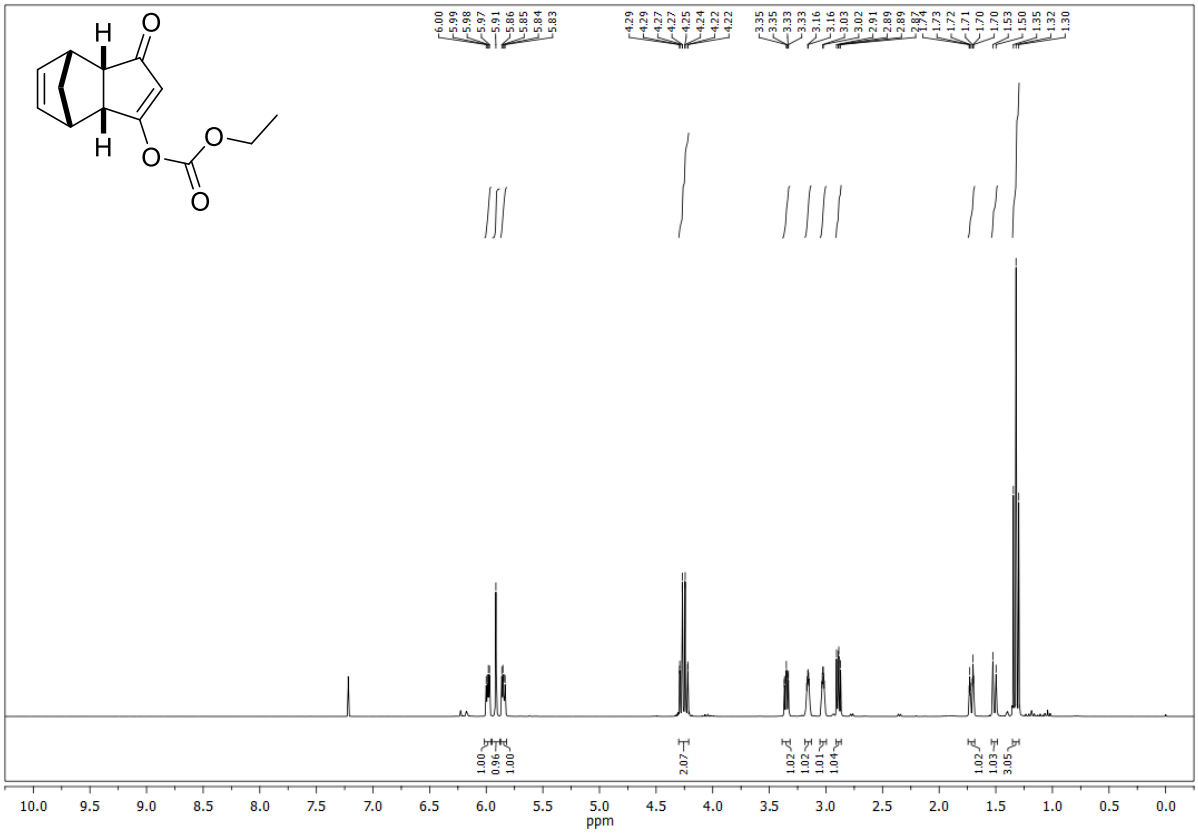


^{13}C NMR (75 MHz, $CDCl_3$)

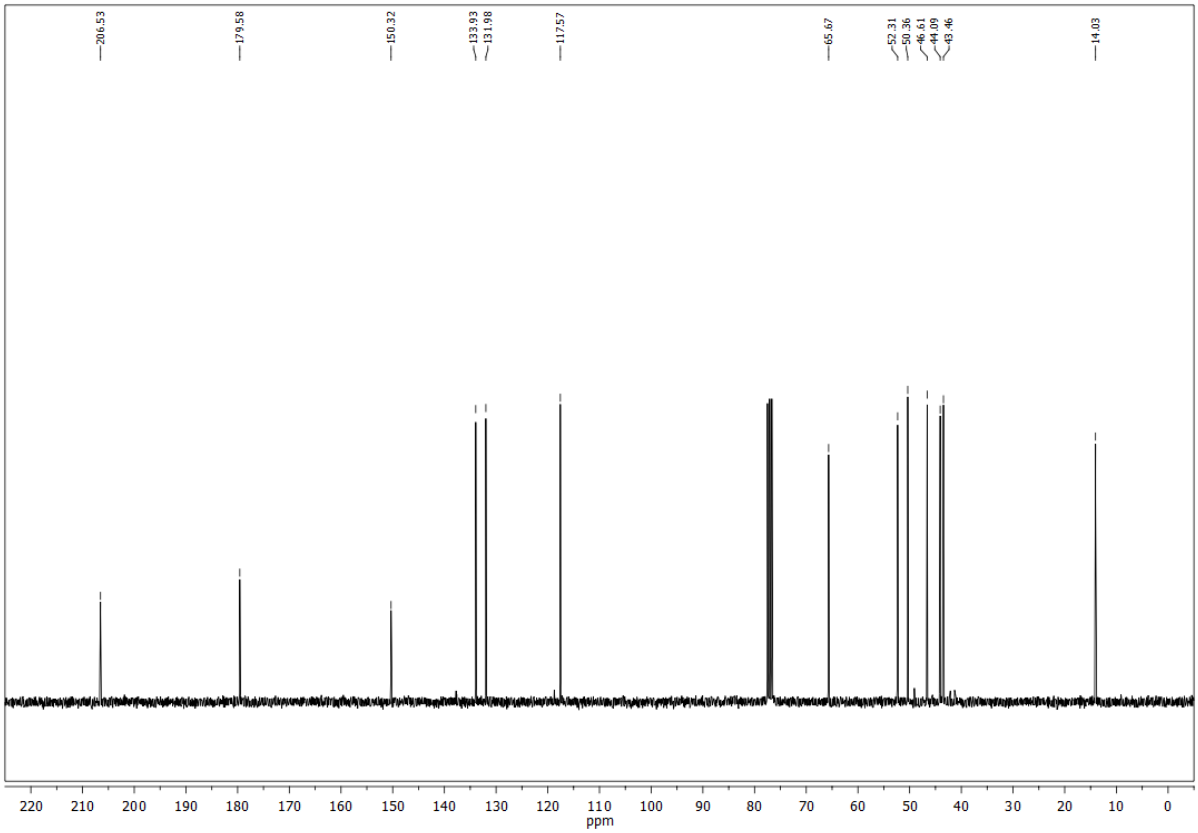


Ethyl (1-oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl) carbonate ((±)-240i)

^{1}H NMR (300 MHz, $CDCl_3$)

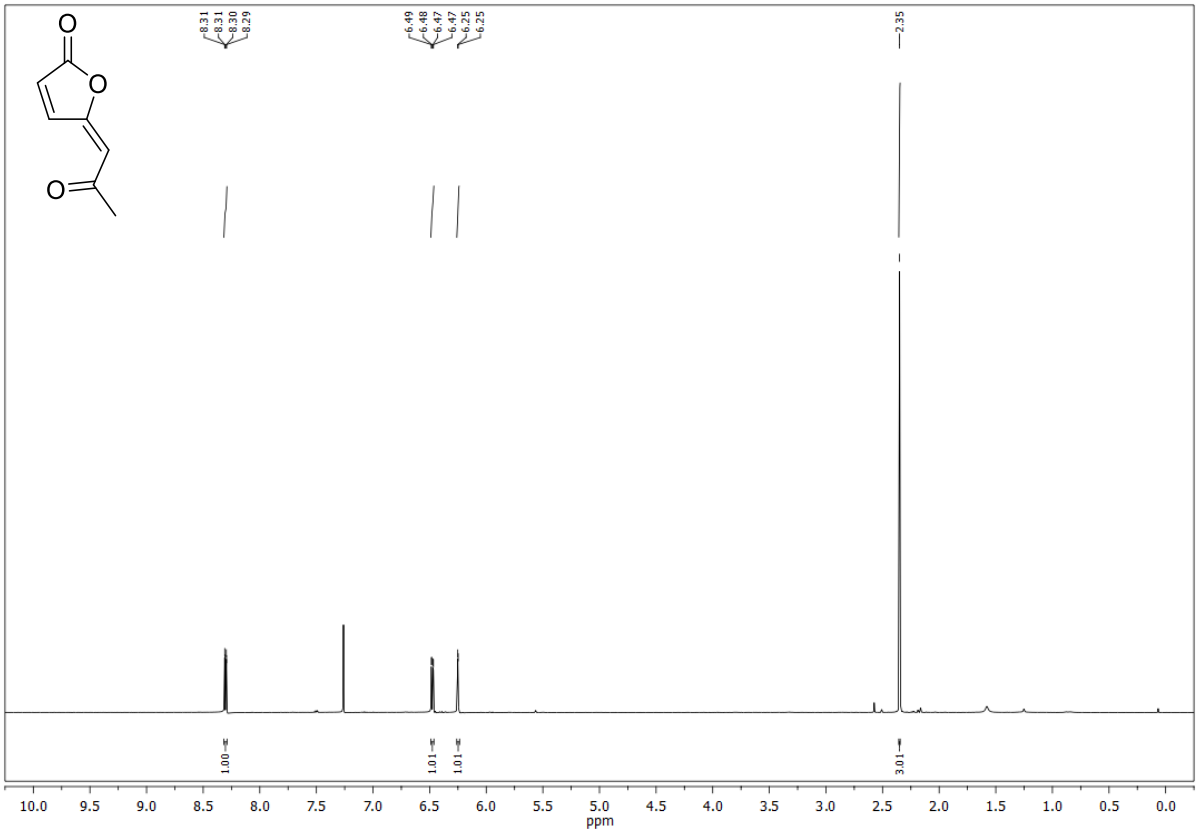


^{13}C NMR (75 MHz, $CDCl_3$)

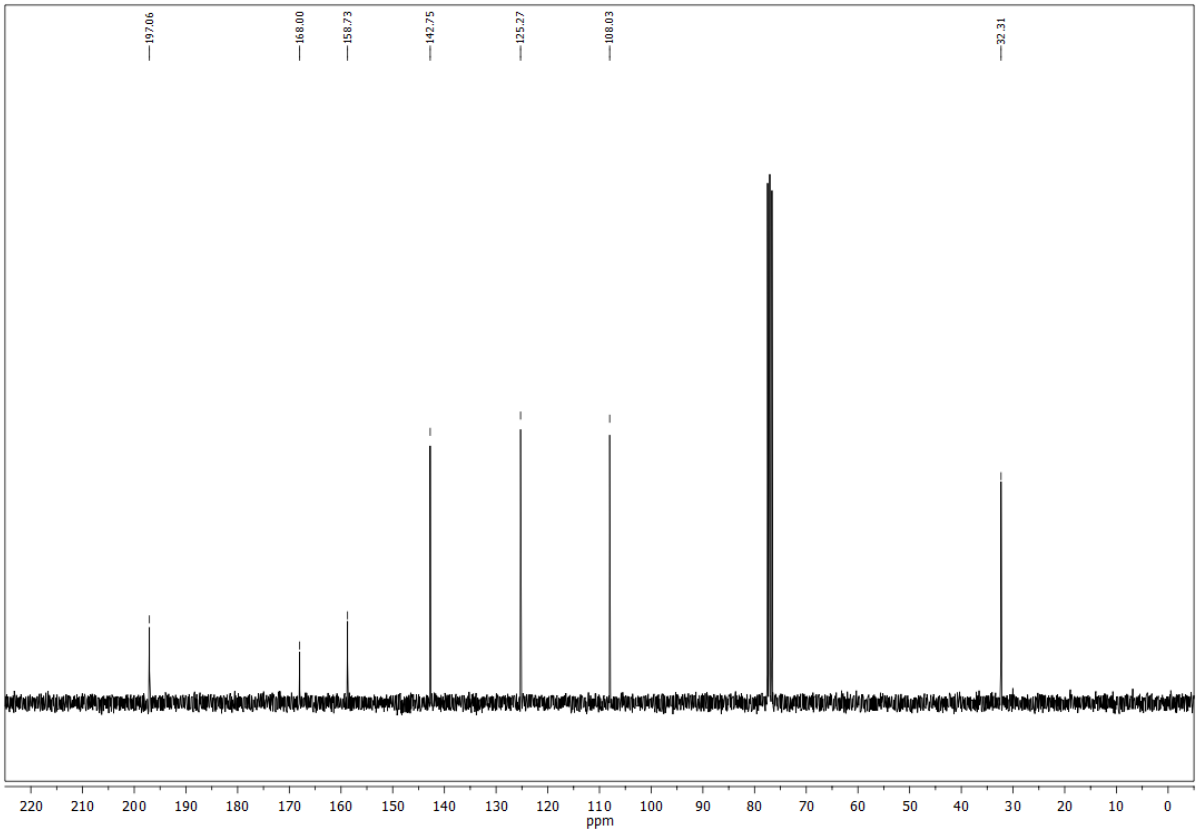


(*E*)-5-(2-Oxopropylidene)furan-2(5*H*)-one (241a)

^{1}H NMR (300 MHz, $CDCl_3$)

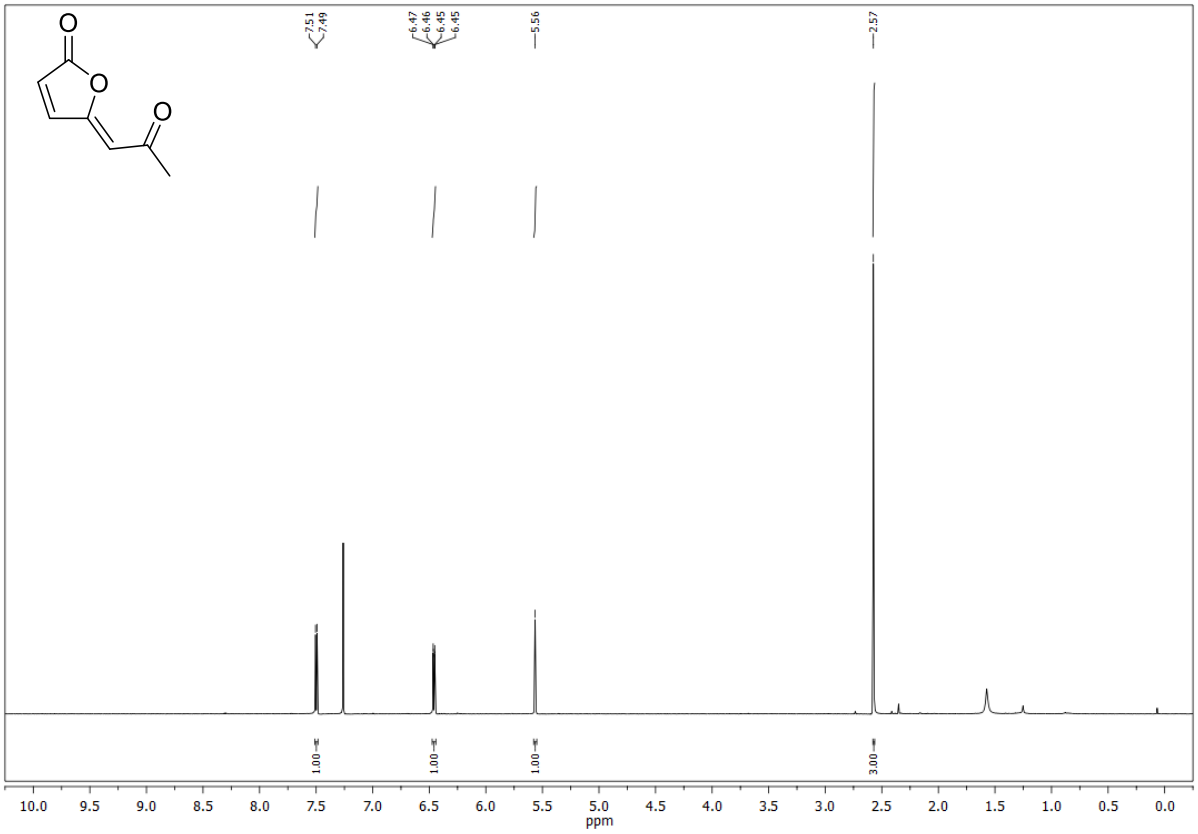


^{13}C NMR (75 MHz, $CDCl_3$)

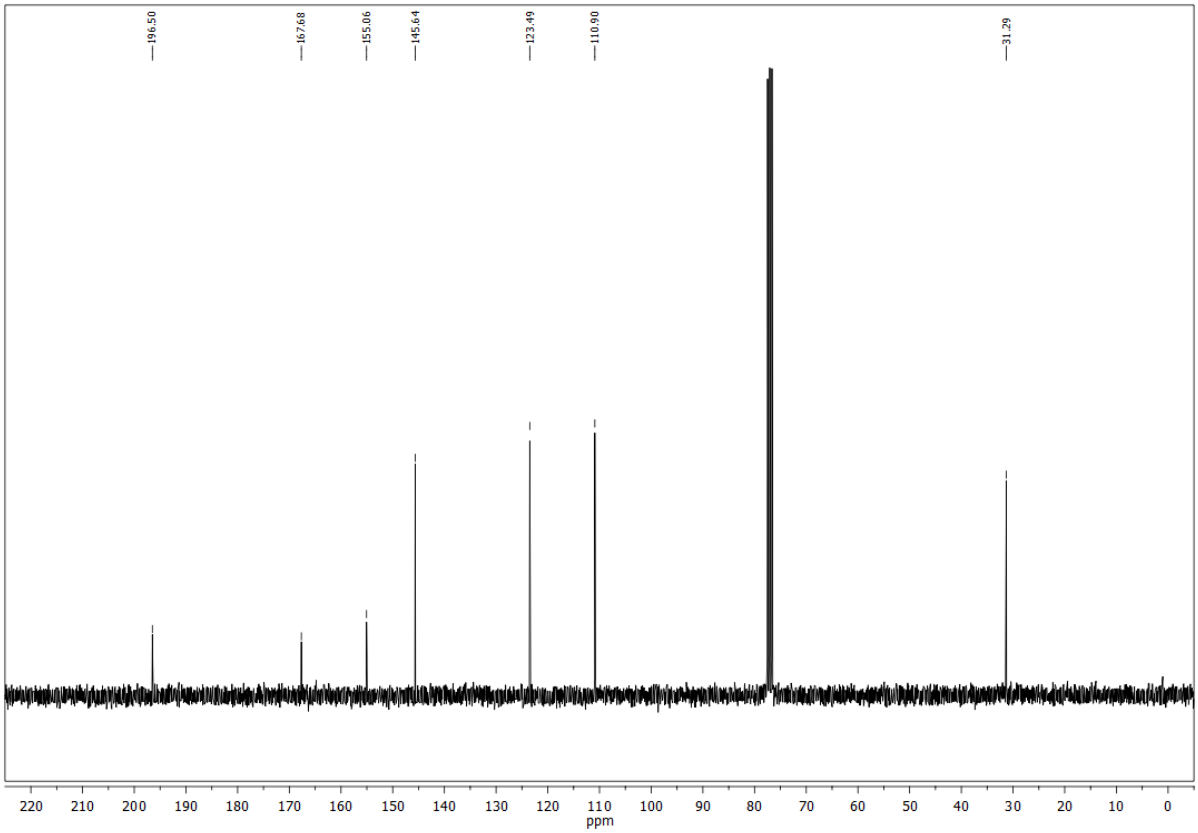


(*Z*)-5-(2-Oxopropylidene)furan-2(5*H*)-one (242a)

^{1}H NMR (300 MHz, $CDCl_3$)

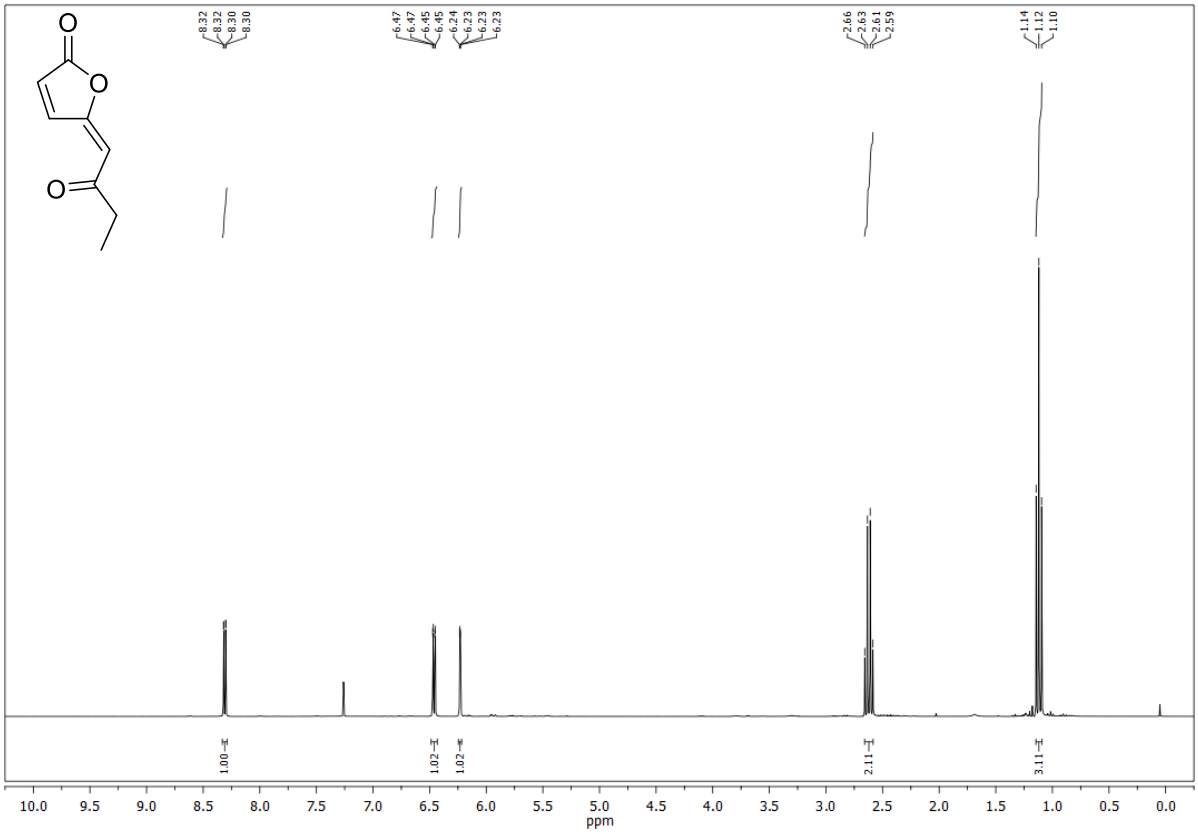


^{13}C NMR (75 MHz, $CDCl_3$)

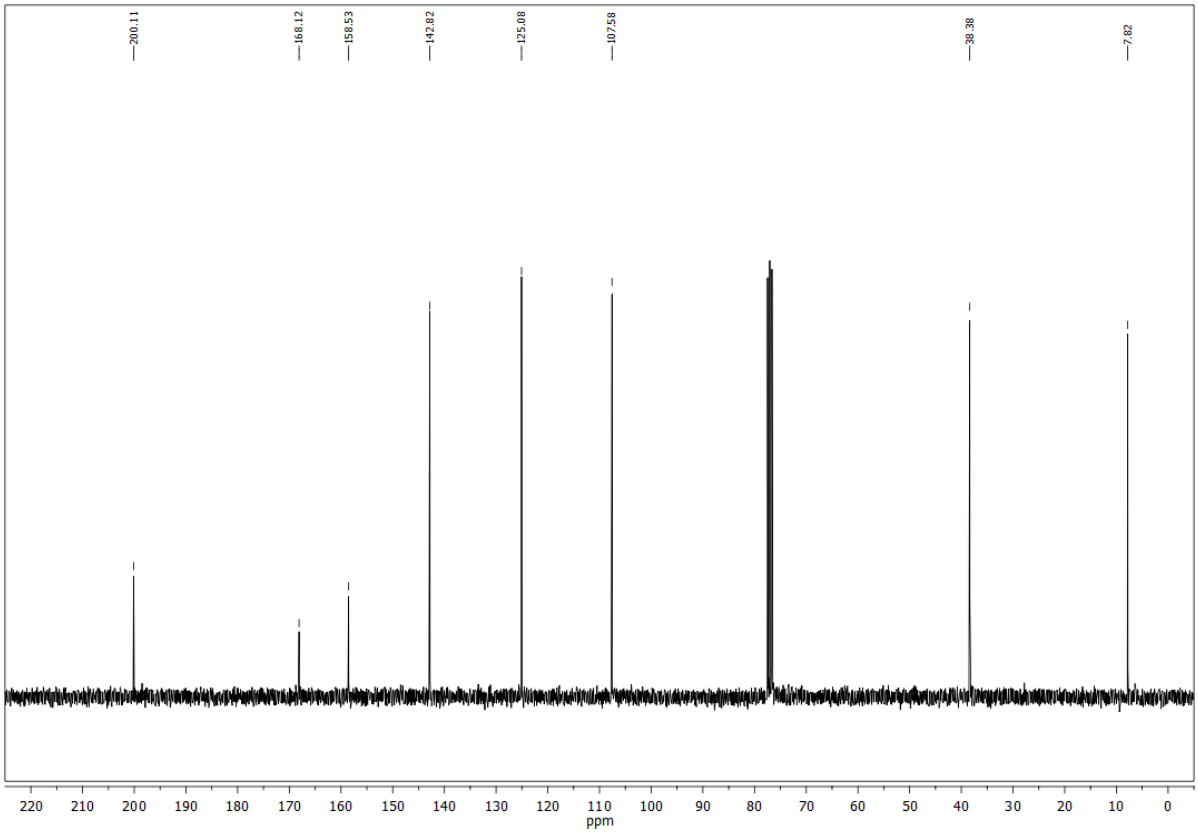


(*E*)-5-(2-Oxobutylidene)furan-2(5*H*)-one (241b)

^{1}H NMR (300 MHz, $CDCl_3$)

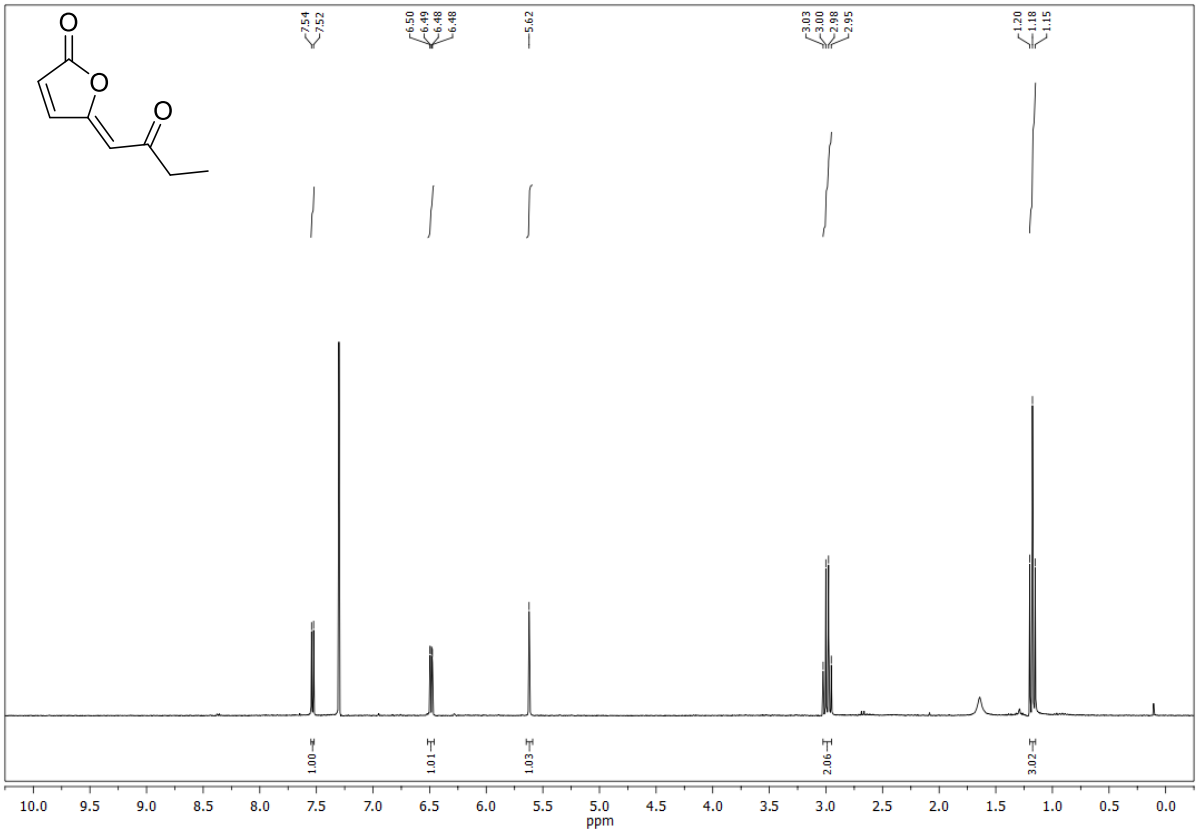


^{13}C NMR (75 MHz, $CDCl_3$)

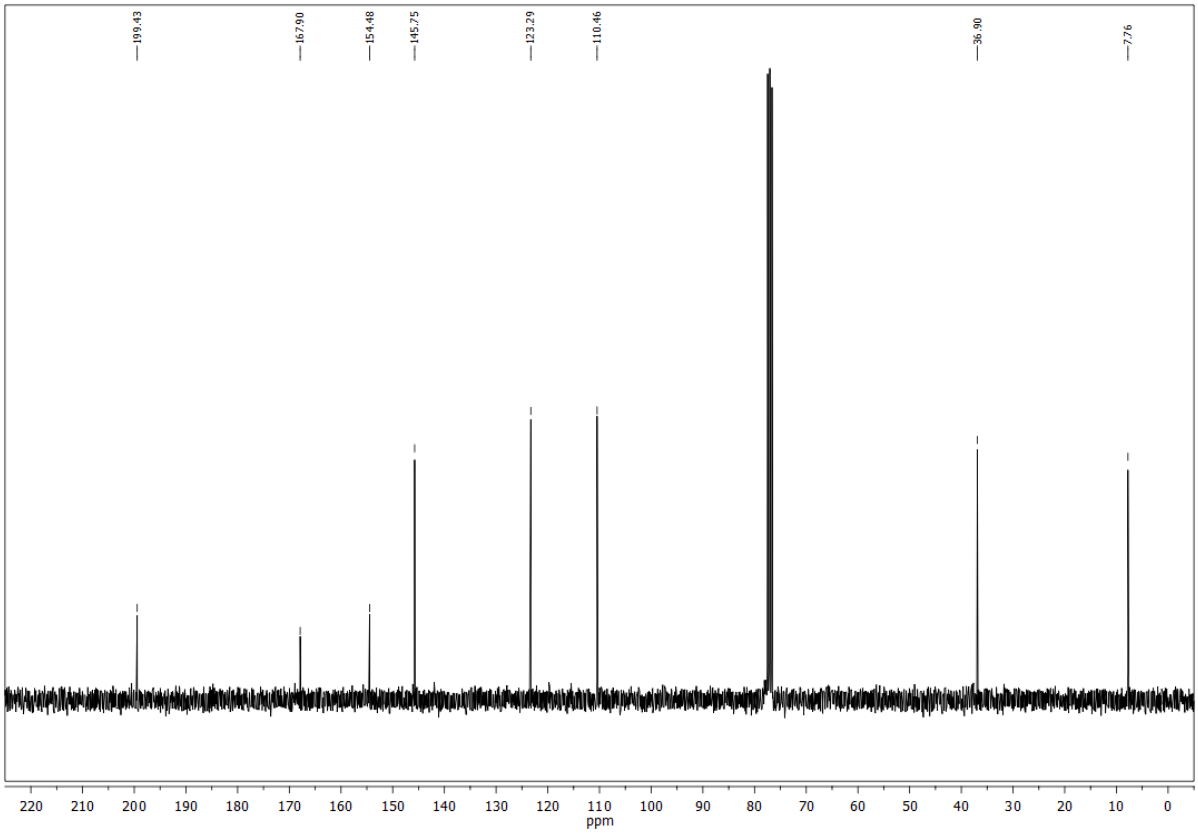


(*Z*)-5-(2-Oxobutylidene)furan-2(5*H*)-one (242b)

^{1}H NMR (300 MHz, $CDCl_3$)

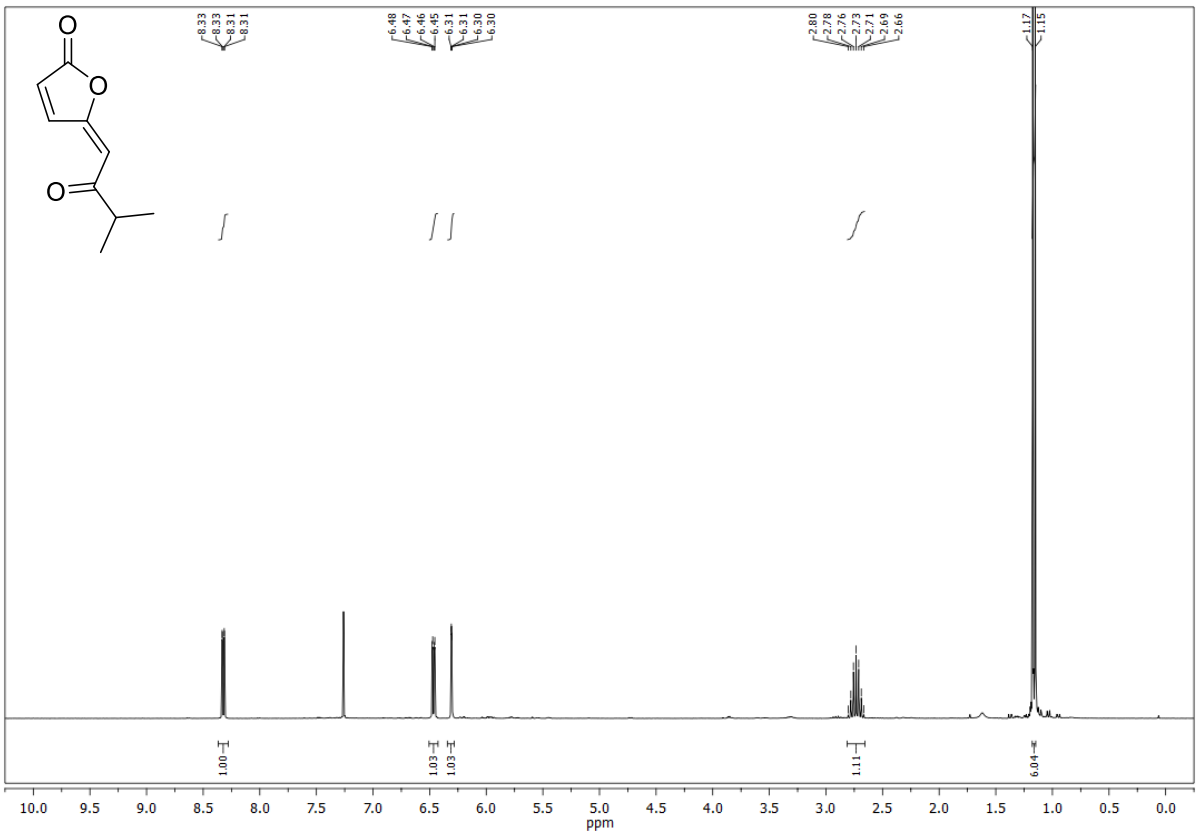


^{13}C NMR (75 MHz, $CDCl_3$)

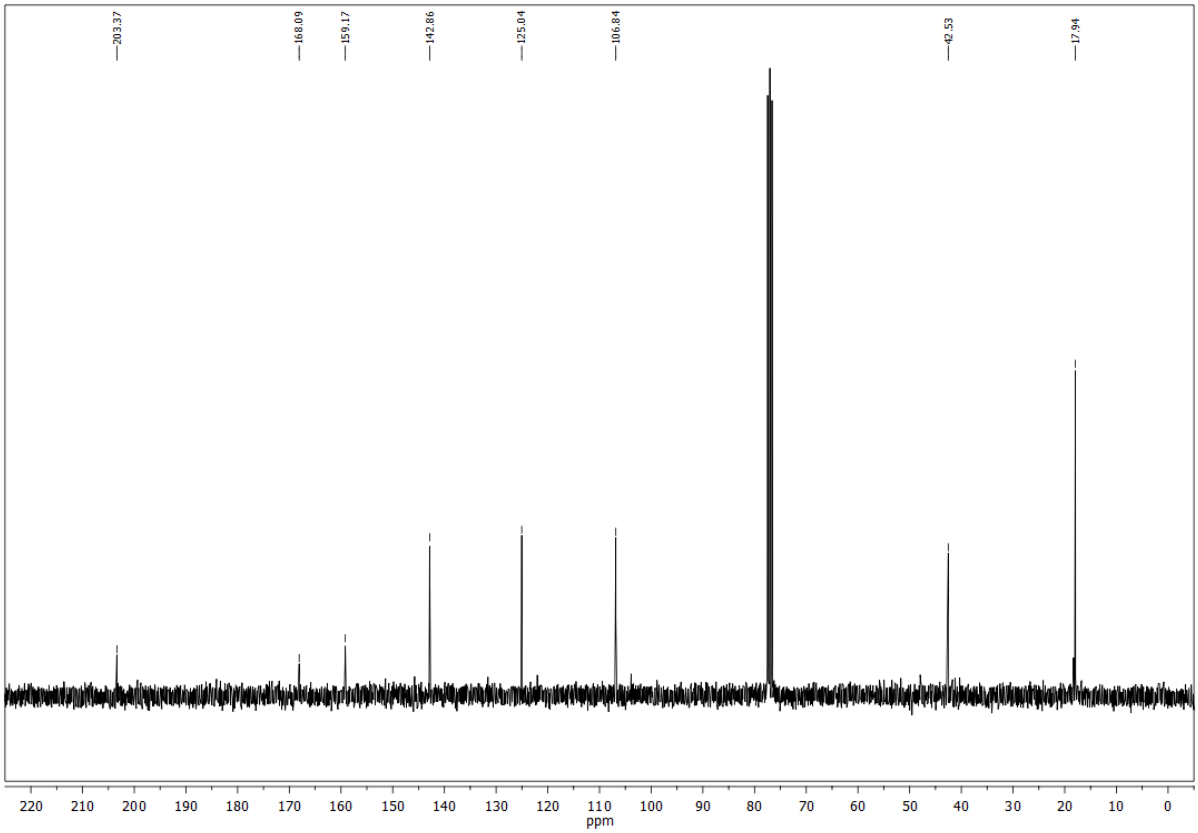


(*E*)-5-(3-Methyl-2-oxobutylidene)furan-2(5*H*)-one (241c)

^{1}H NMR (300 MHz, $CDCl_3$)

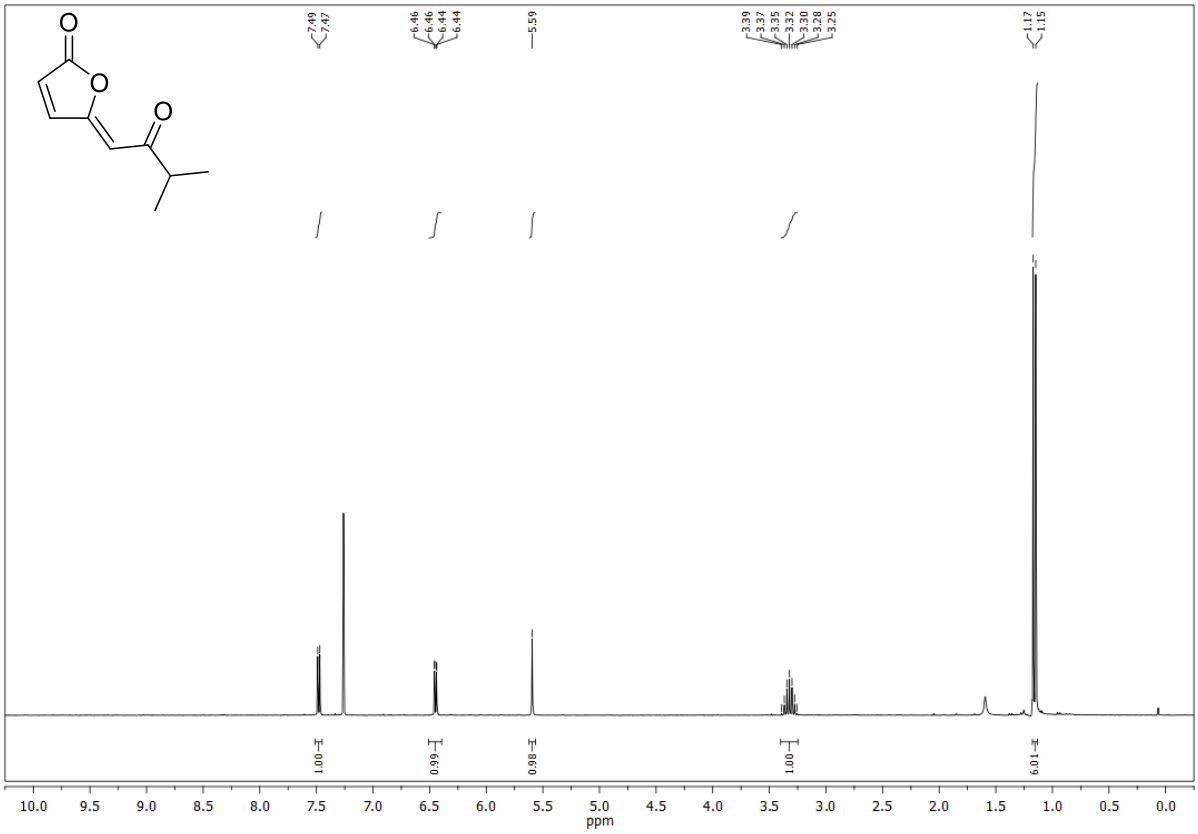


^{13}C NMR (75 MHz, $CDCl_3$)

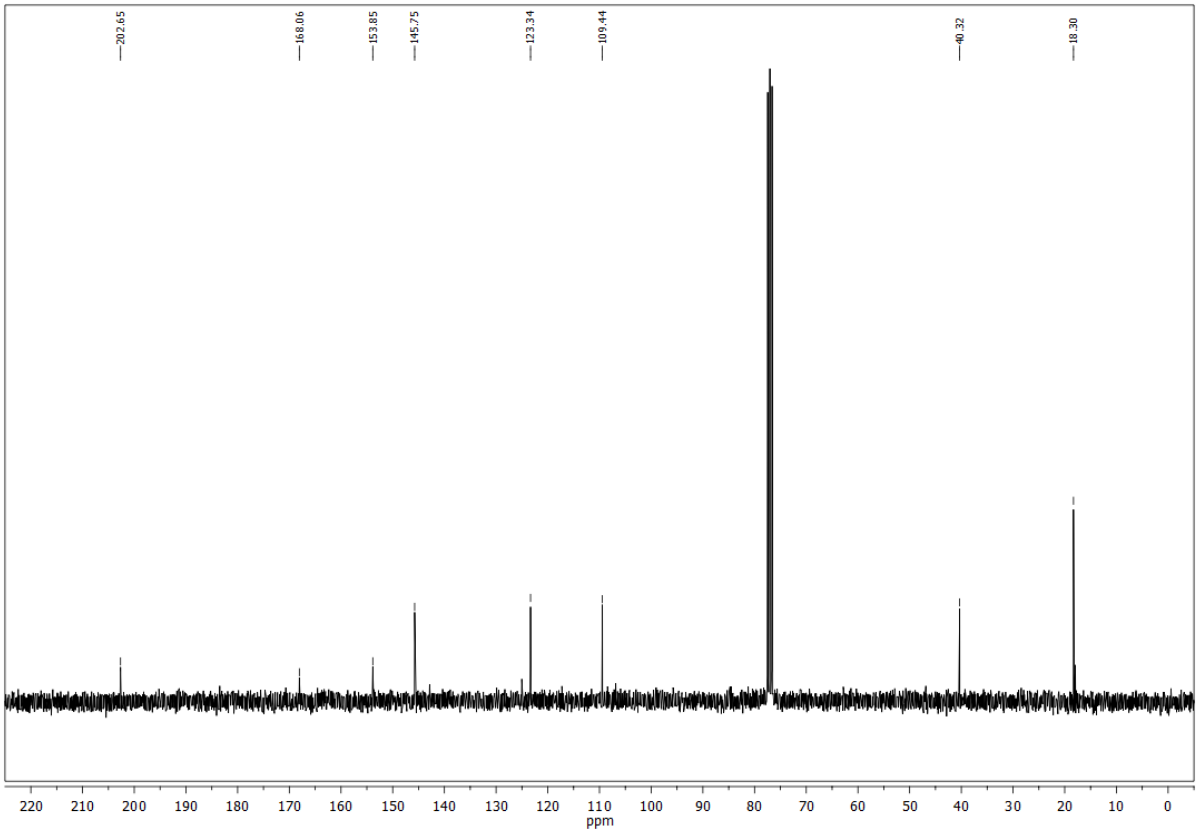


(*Z*)-5-(3-Methyl-2-oxobutylidene)furan-2(5*H*)-one (242c)

^{1}H NMR (300 MHz, $CDCl_3$)

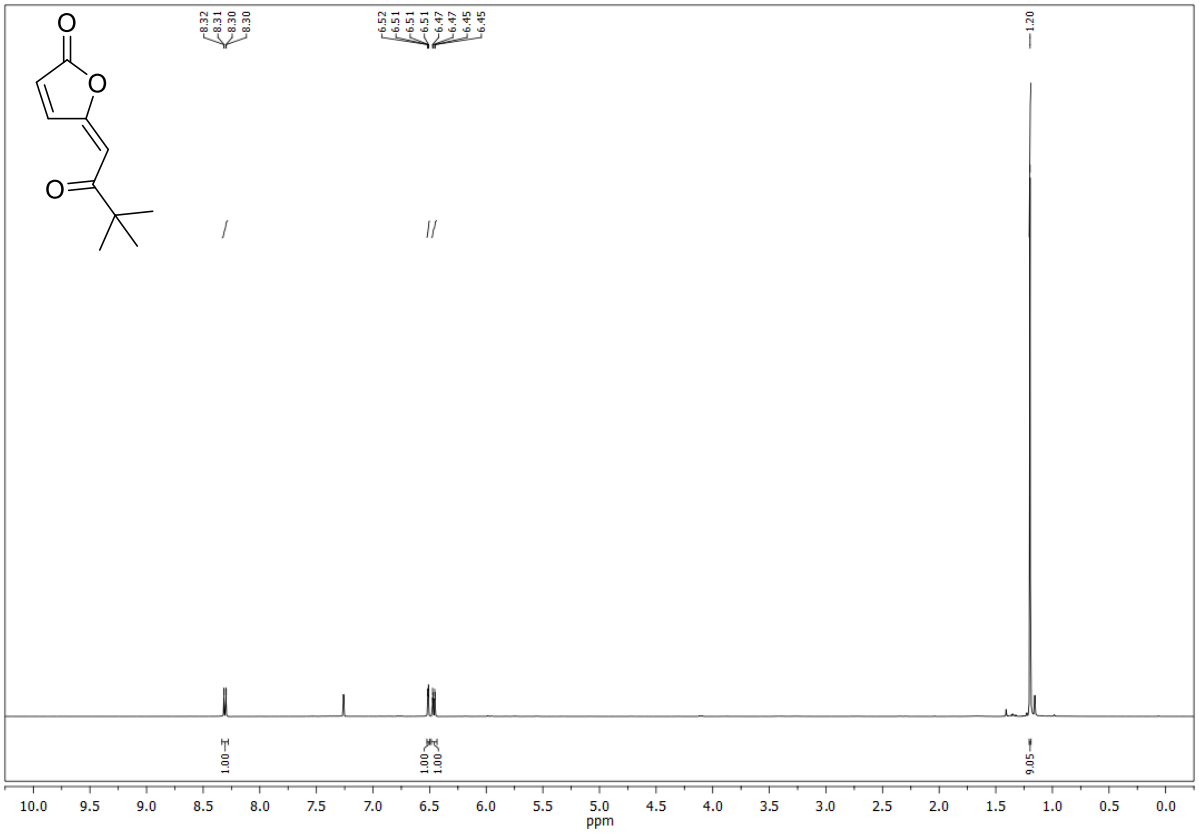


^{13}C NMR (75 MHz, $CDCl_3$)

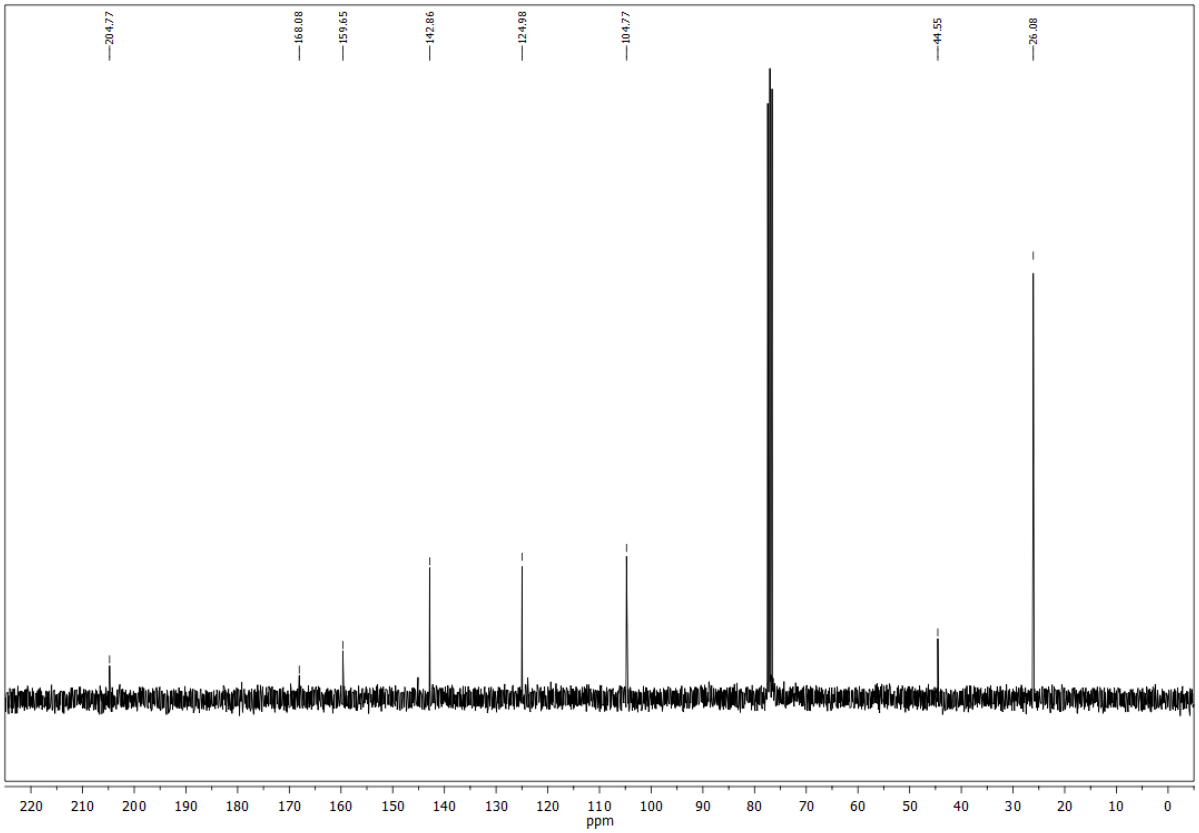


(*E*)-5-(3,3-Dimethyl-2-oxobutylidene)furan-2(5*H*)-one (241d)

^{1}H NMR (300 MHz, $CDCl_3$)

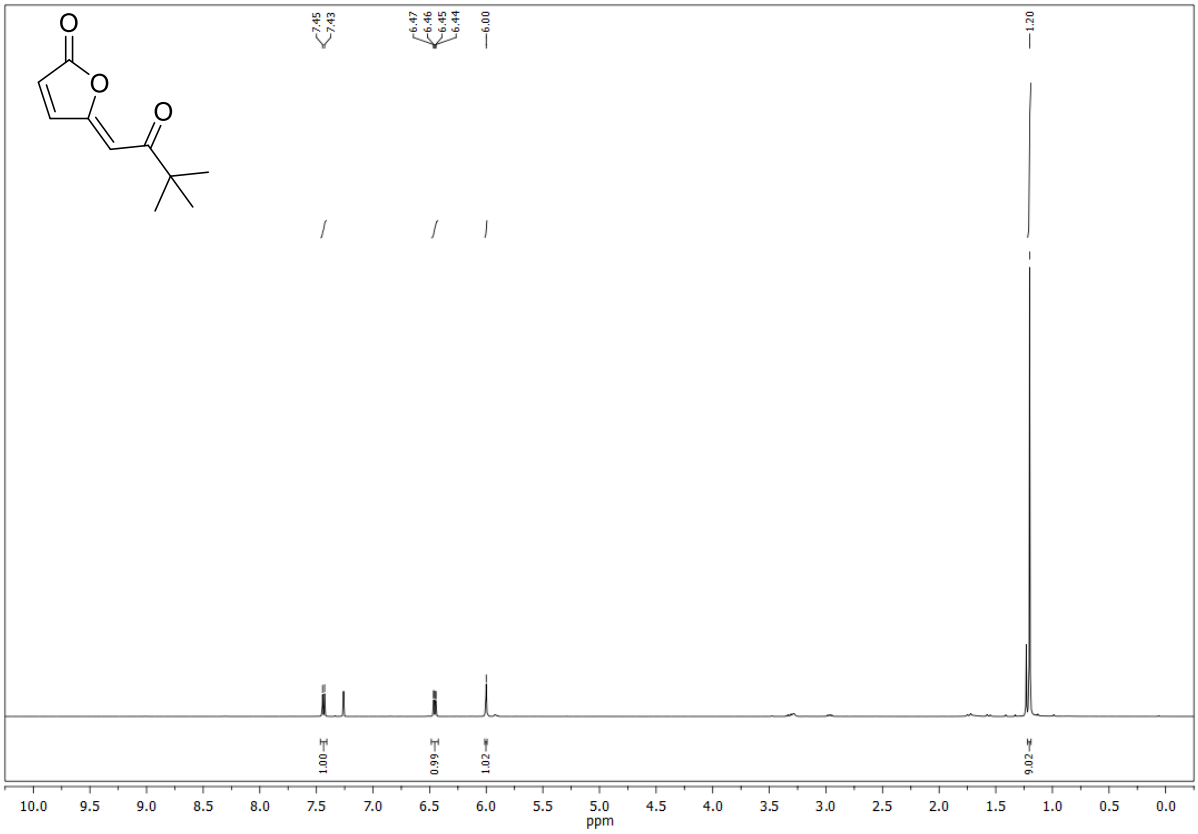


^{13}C NMR (75 MHz, $CDCl_3$)

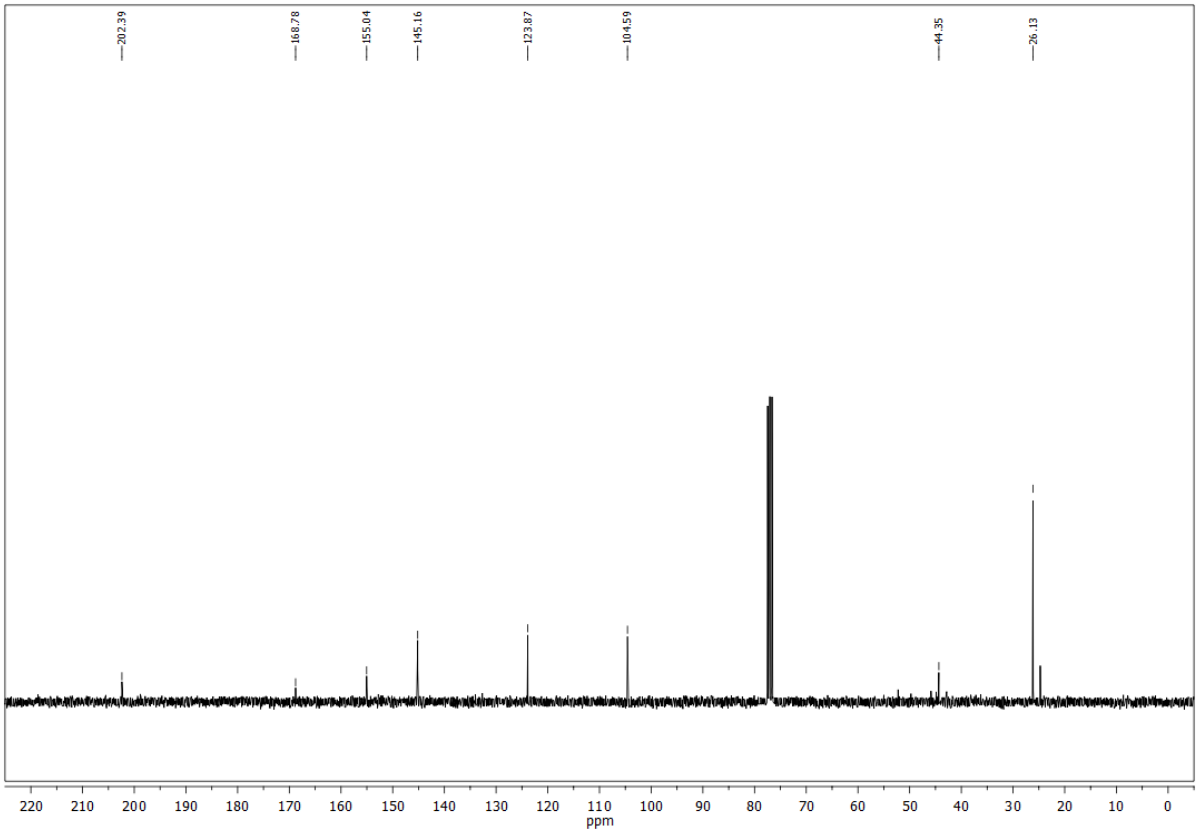


(*Z*)-5-(3,3-Dimethyl-2-oxobutylidene)furan-2(5*H*)-one (242d)

^{1}H NMR (300 MHz, $CDCl_3$)

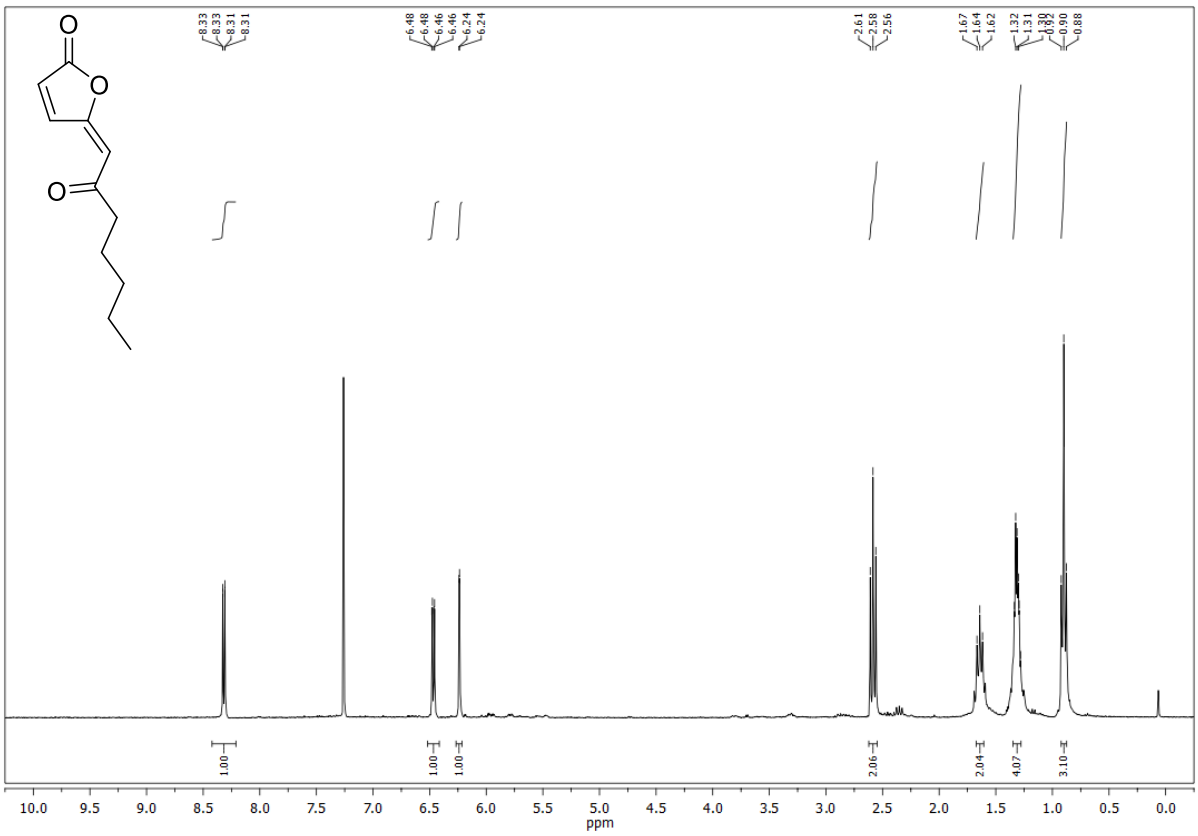


^{13}C NMR (75 MHz, $CDCl_3$)

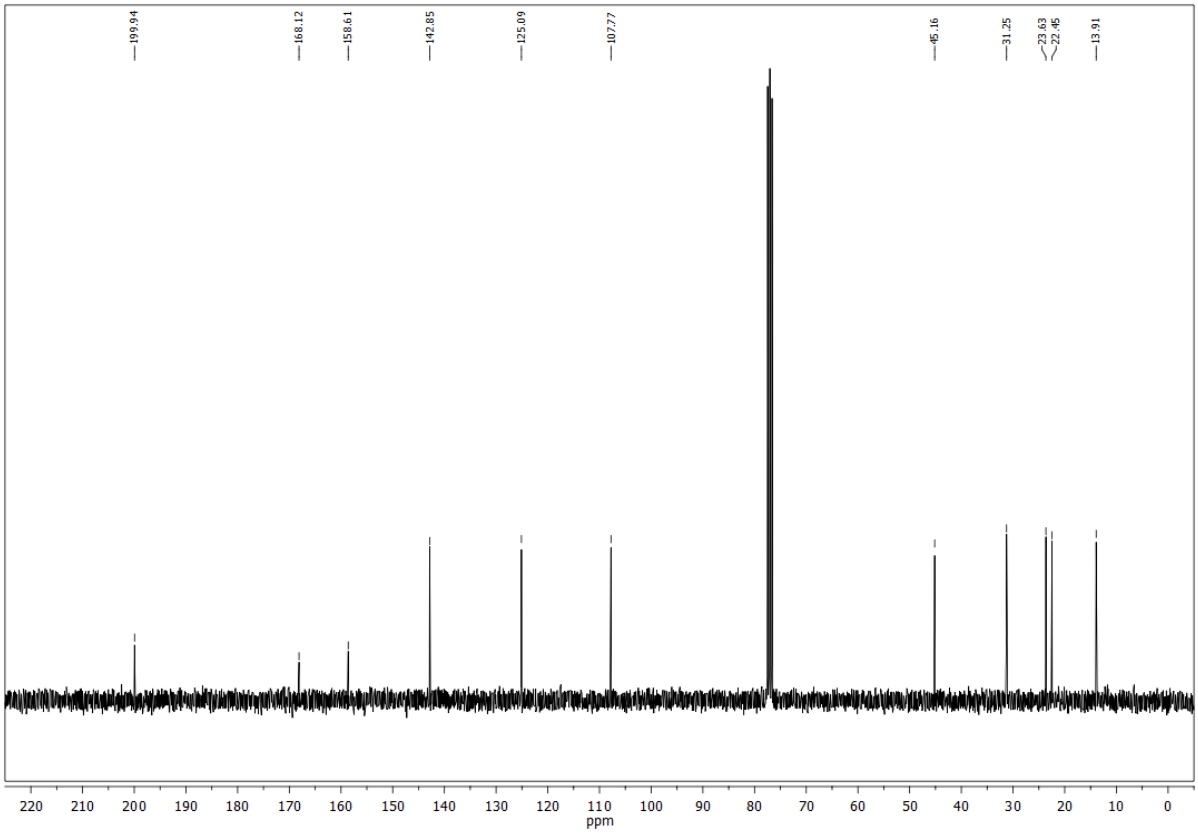


(*E*)-5-(2-Oxoheptylidene)furan-2(5*H*)-one (241f)

^{1}H NMR (300 MHz, $CDCl_3$)

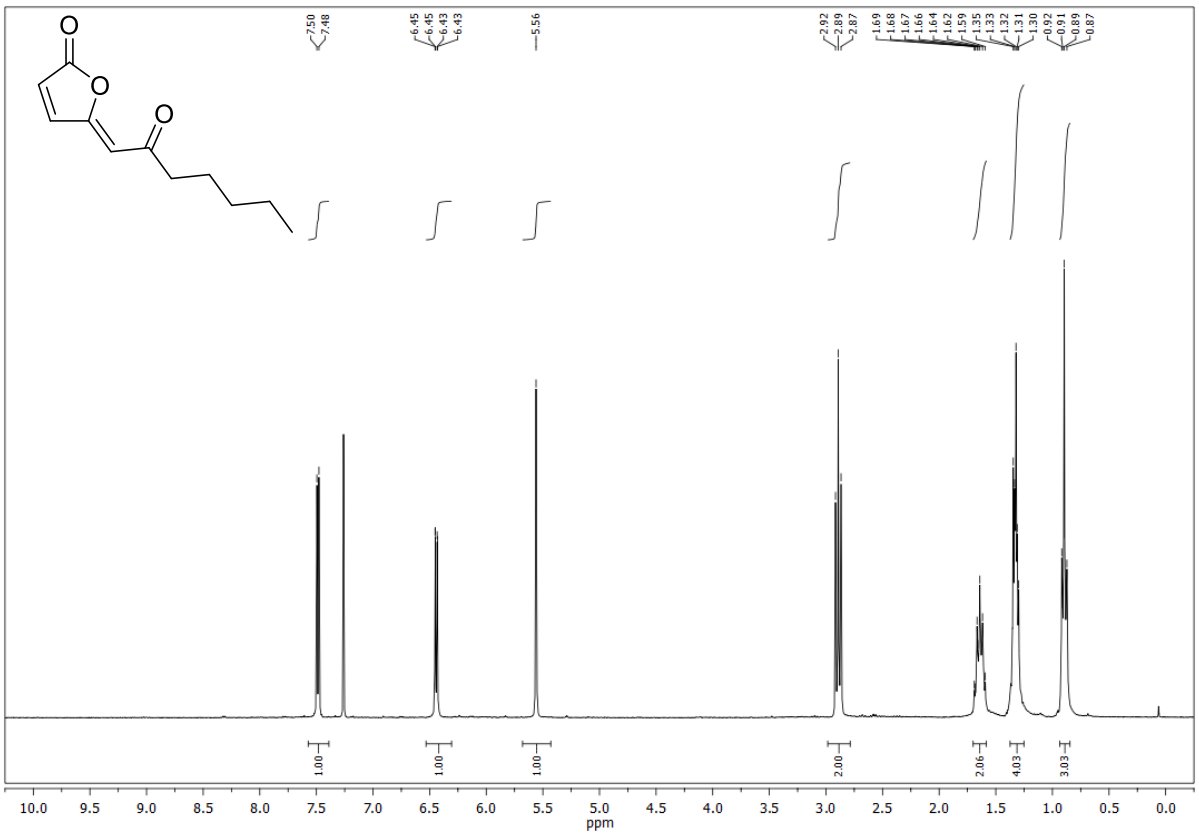


^{13}C NMR (75 MHz, $CDCl_3$)

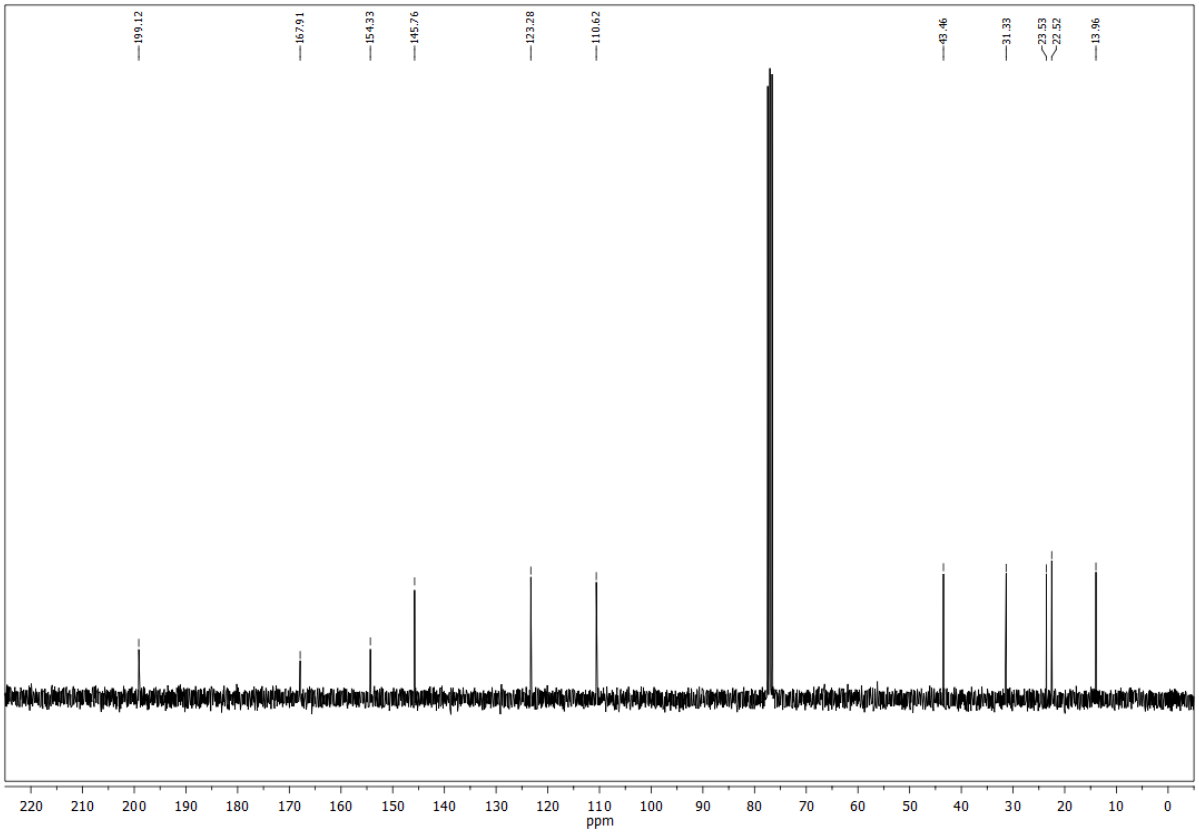


(*Z*)-5-(2-Oxoheptylidene)furan-2(5*H*)-one (242f)

^{1}H NMR (300 MHz, $CDCl_3$)

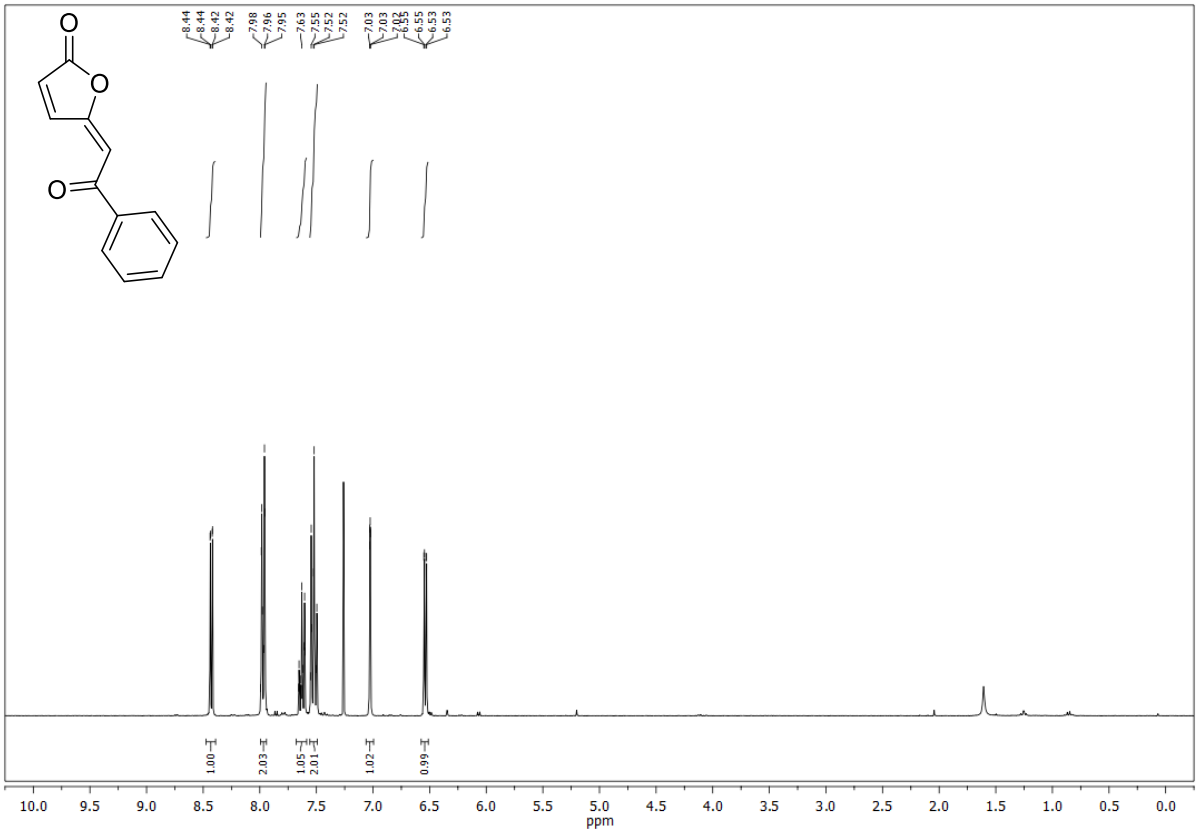


^{13}C NMR (75 MHz, $CDCl_3$)

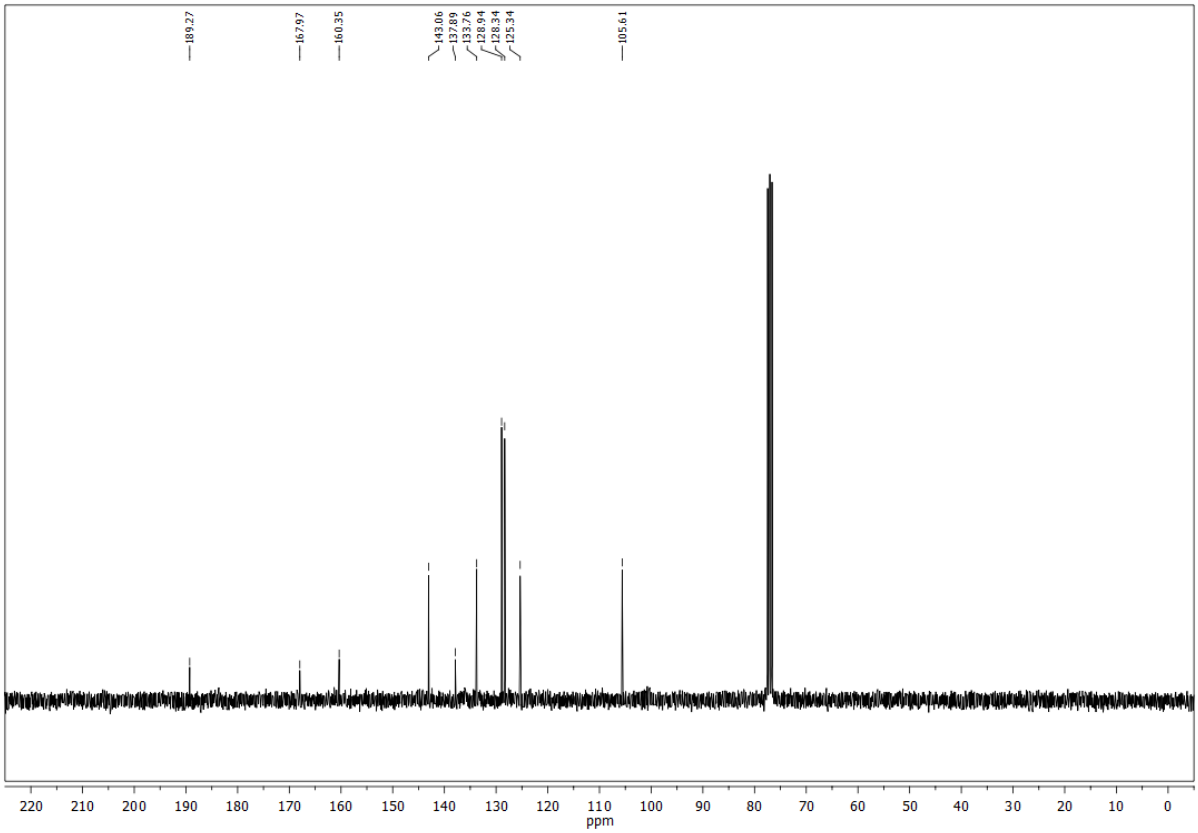


(*E*)-5-(2-Oxo-2-phenylethylidene)furan-2(5*H*)-one (241g)

^{1}H NMR (300 MHz, $CDCl_3$)

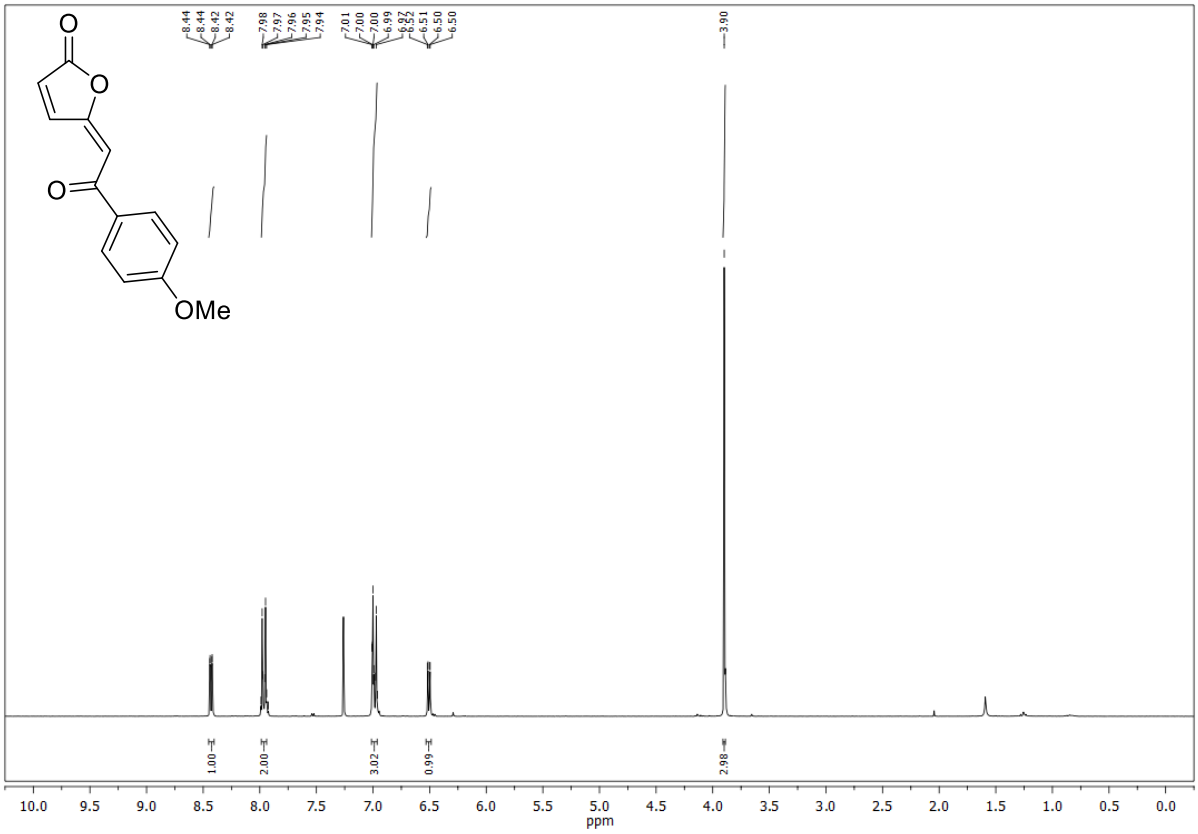


^{13}C NMR (75 MHz, $CDCl_3$)

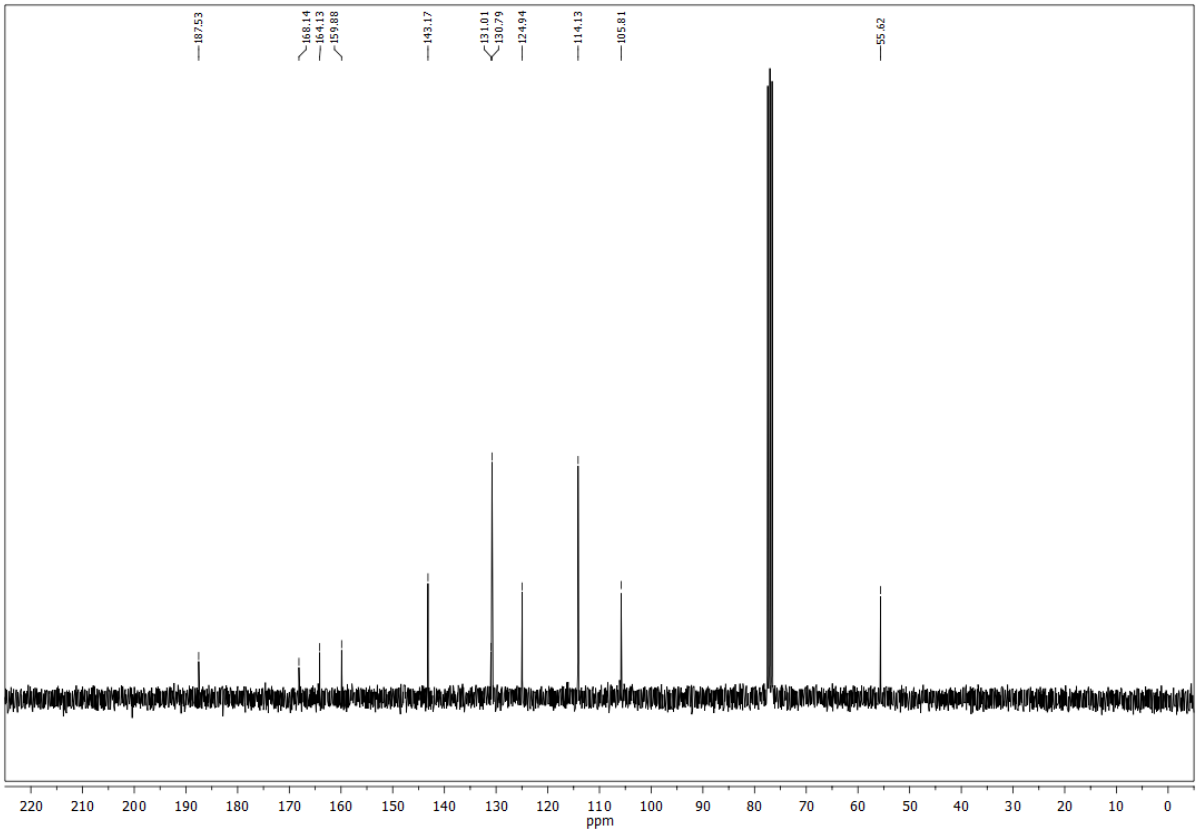


(*E*)-5-(2-(4-Methoxyphenyl)-2-oxoethylidene)furan-2(5*H*)-one (241h)

^{1}H NMR (300 MHz, $CDCl_3$)

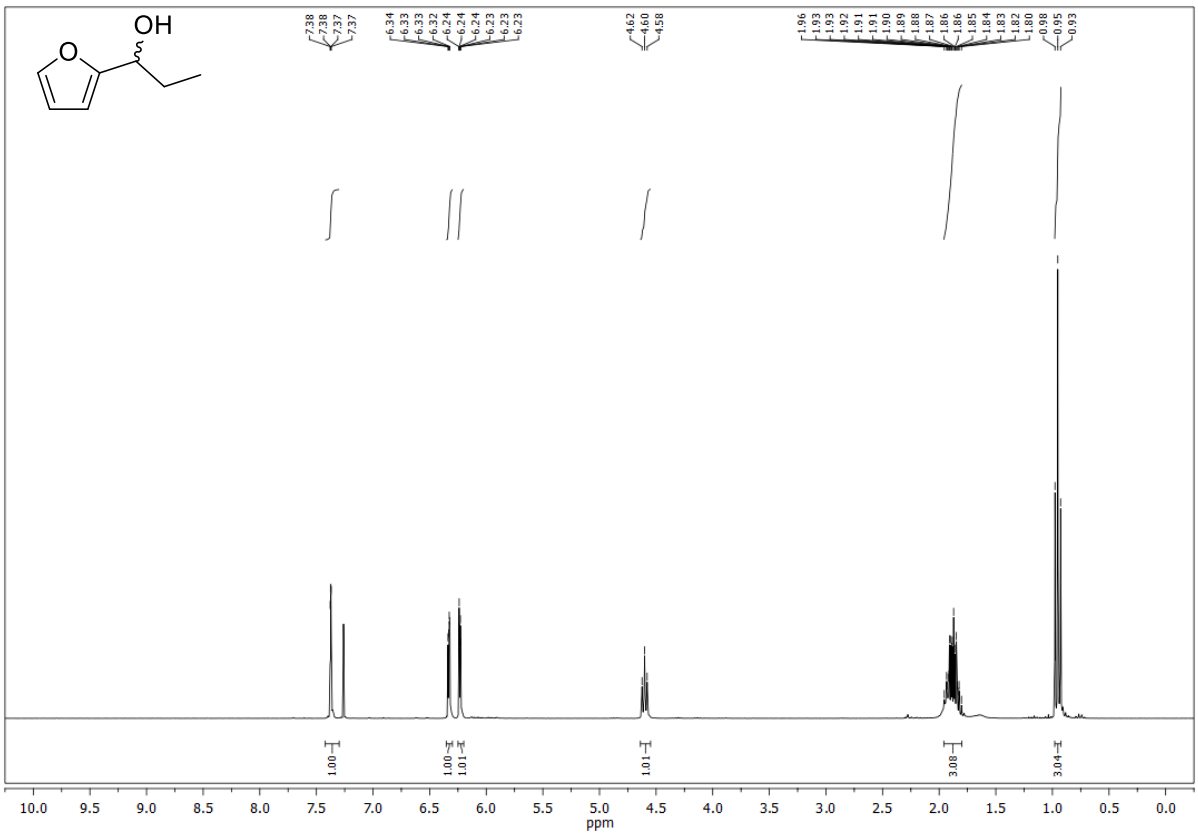


^{13}C NMR (75 MHz, $CDCl_3$)

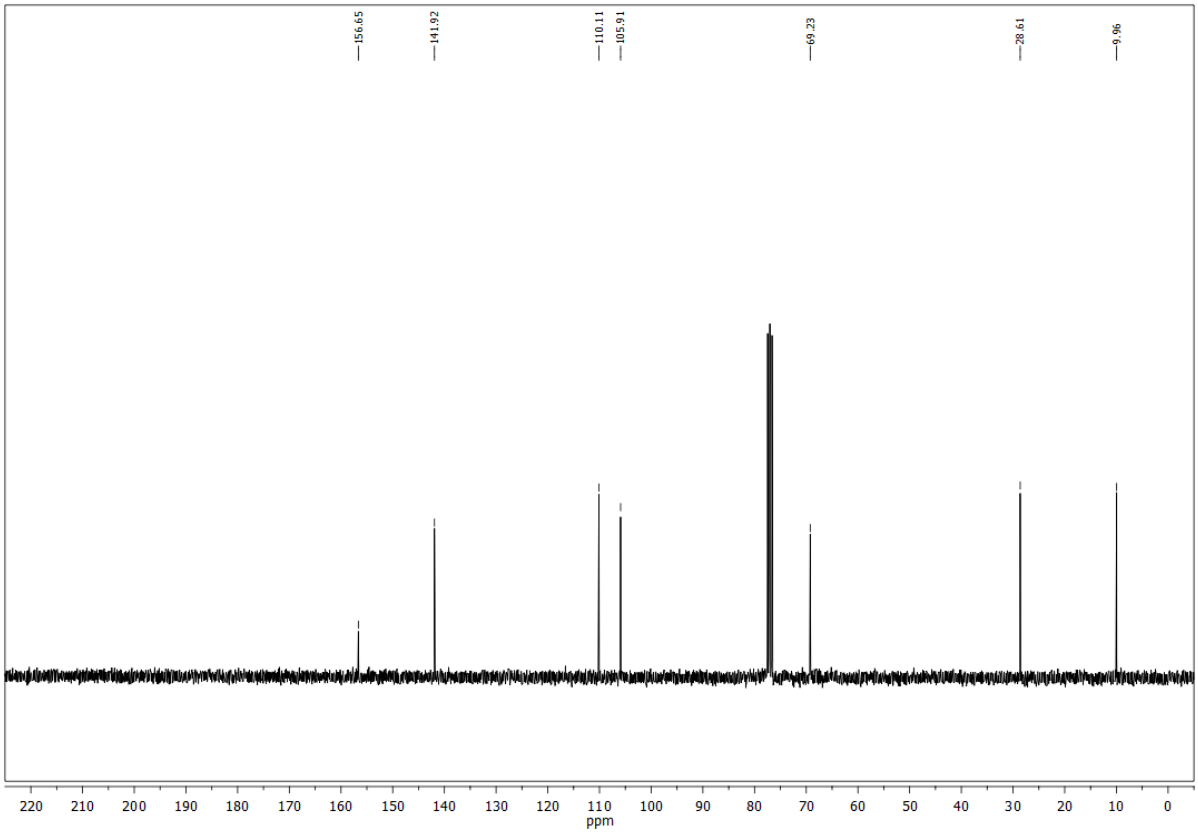


1-(Furan-2-yl)propan-1-ol ((±)-142d)

^{1}H NMR (300 MHz, $CDCl_3$)

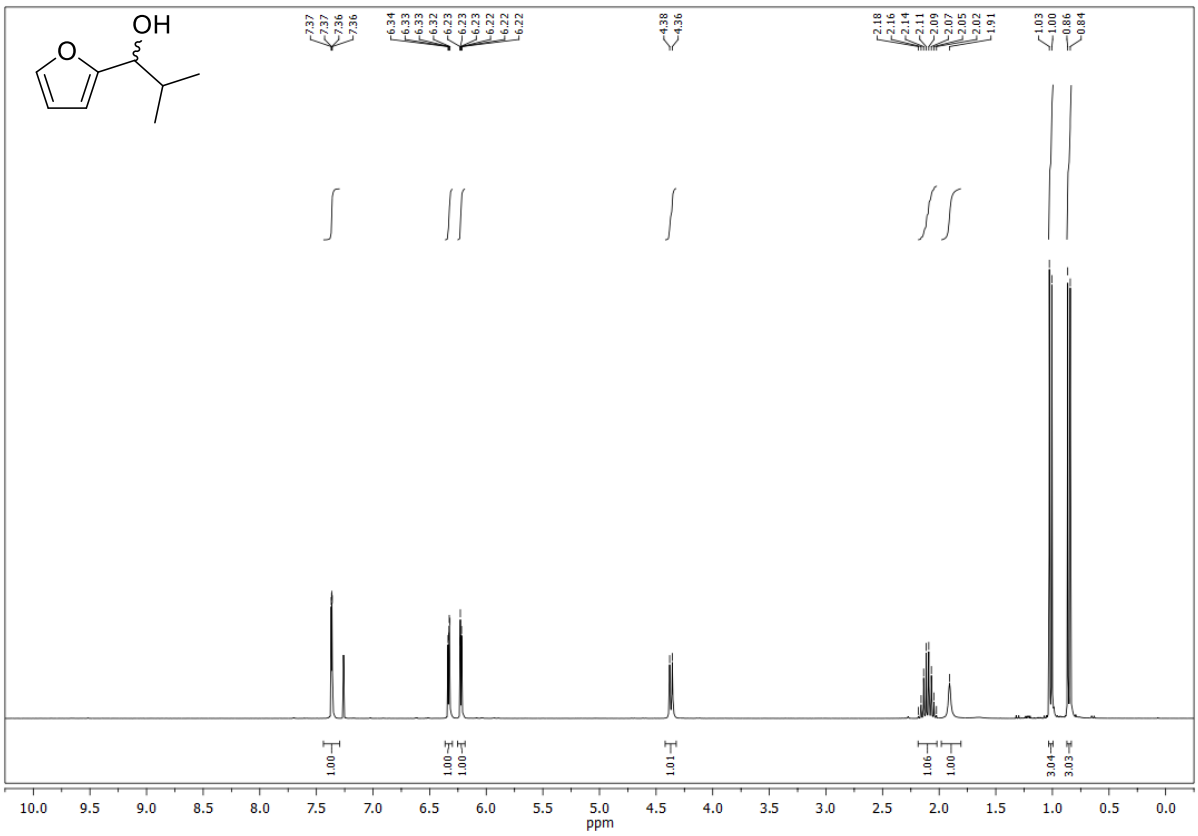


^{13}C NMR (75 MHz, $CDCl_3$)

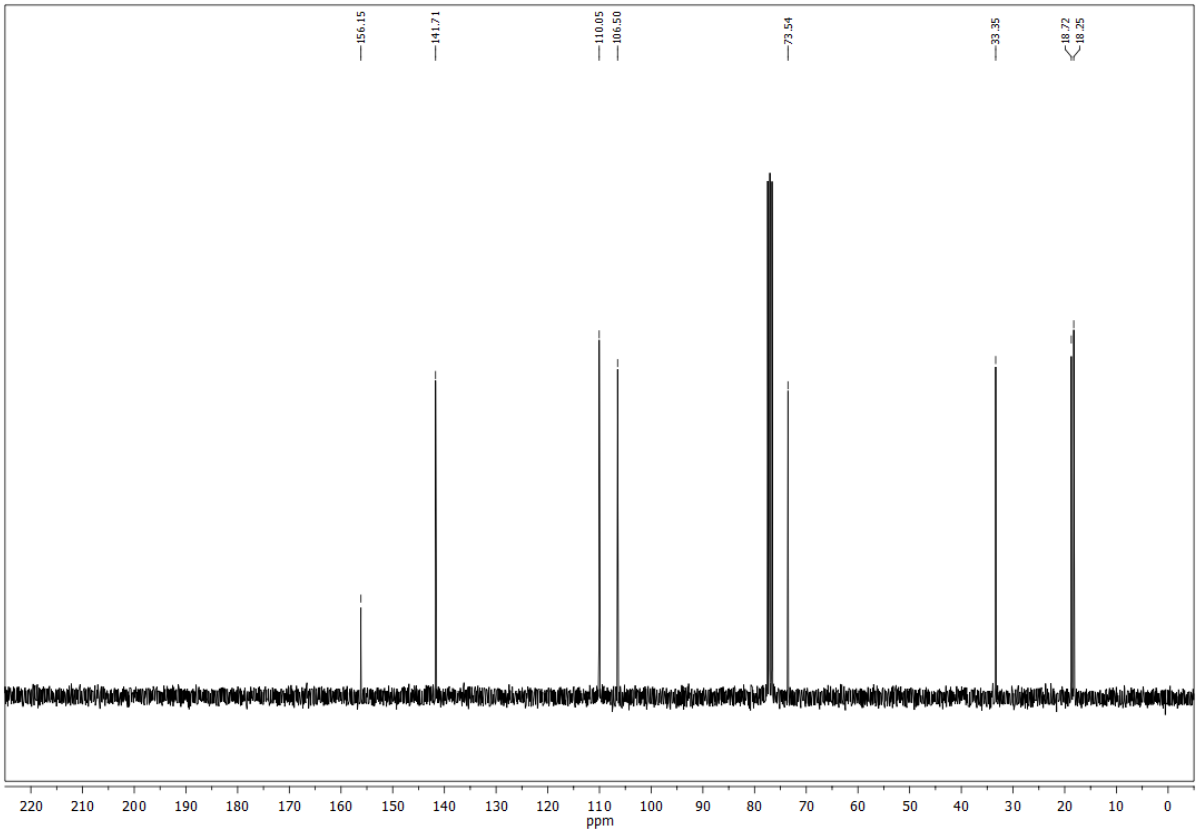


1-(Furan-2-yl)-2-methylpropan-1-ol ((±)-142e)

^{1}H NMR (400 MHz, $CDCl_3$)

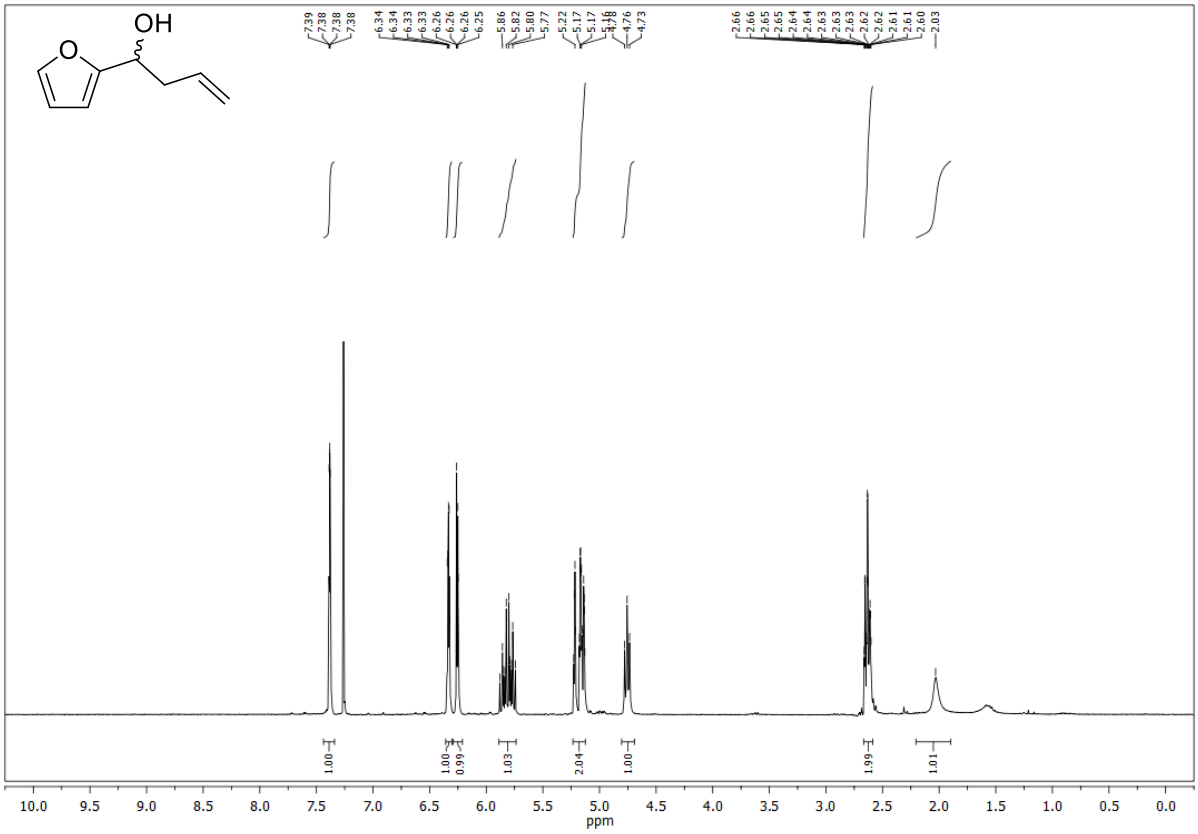


^{13}C NMR (101 MHz, $CDCl_3$)

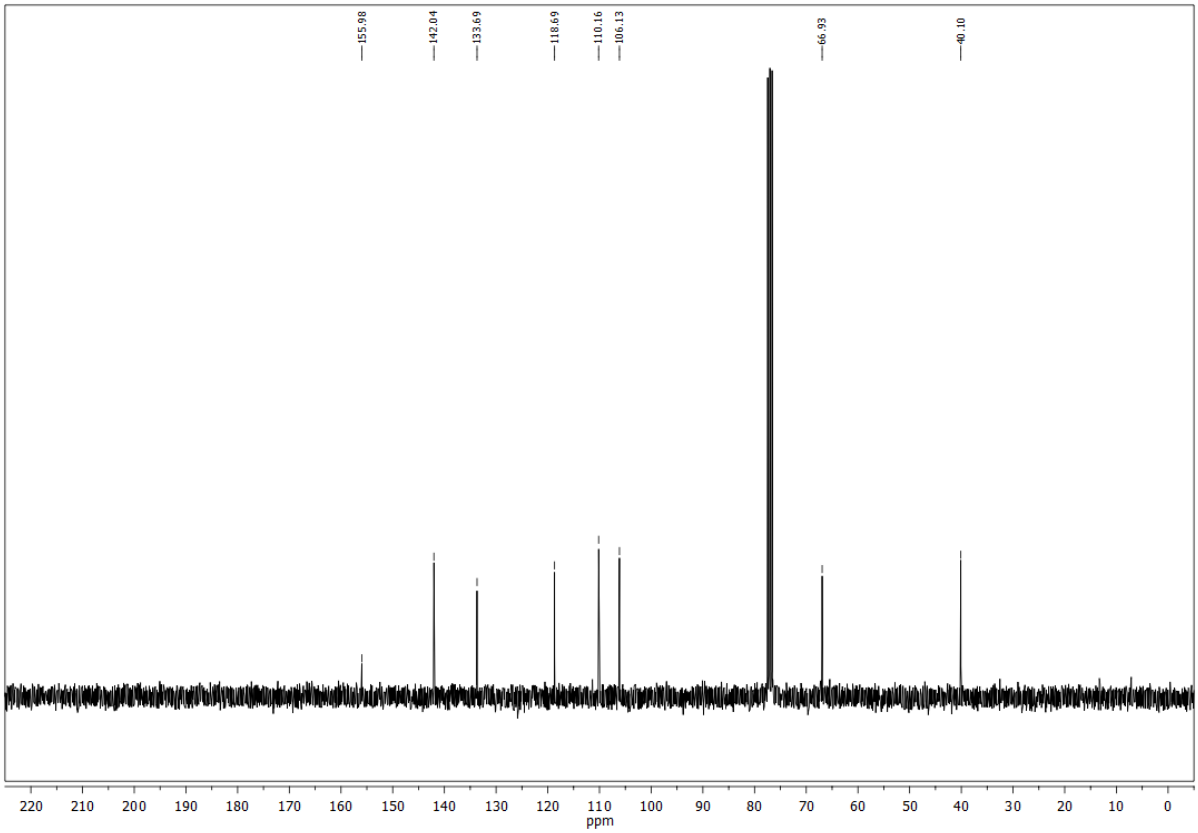


1-(Furan-2-yl)but-3-en-1-ol ((±)-142f)

^{1}H NMR (300 MHz, $CDCl_3$)

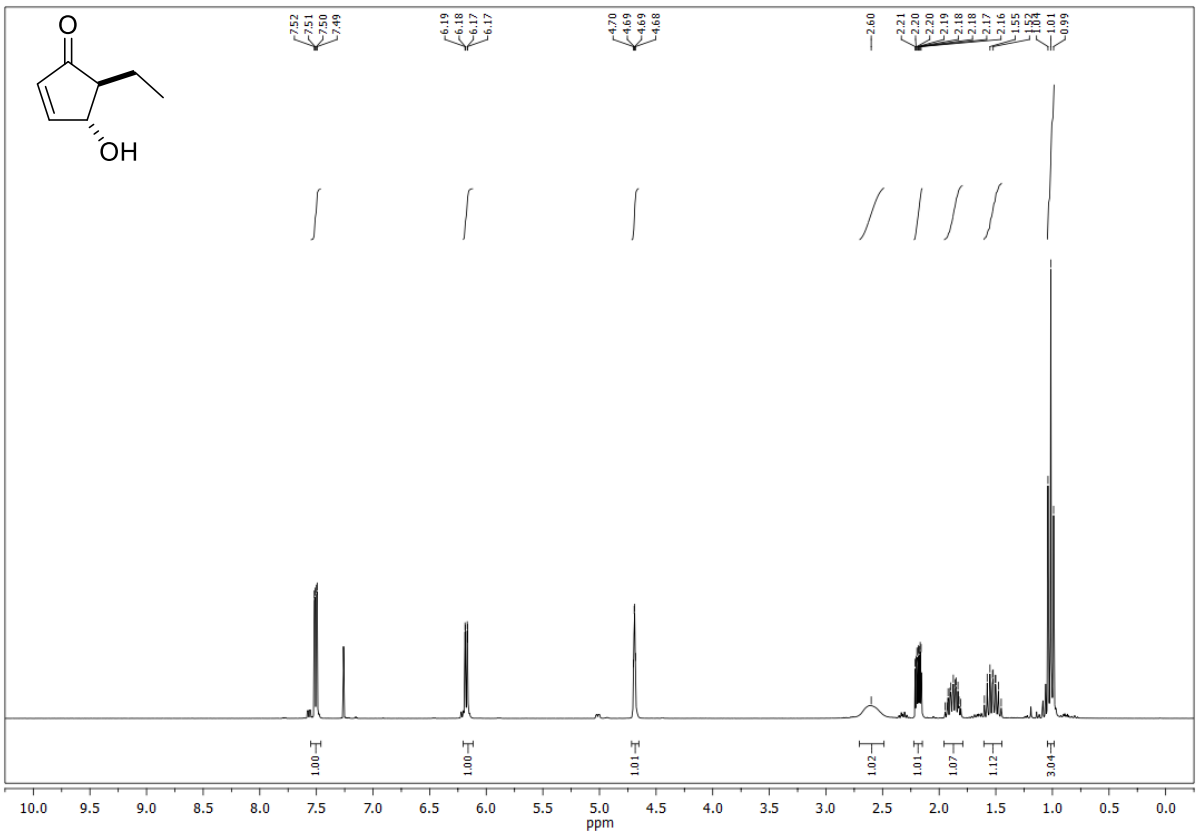


^{13}C NMR (75 MHz, $CDCl_3$)

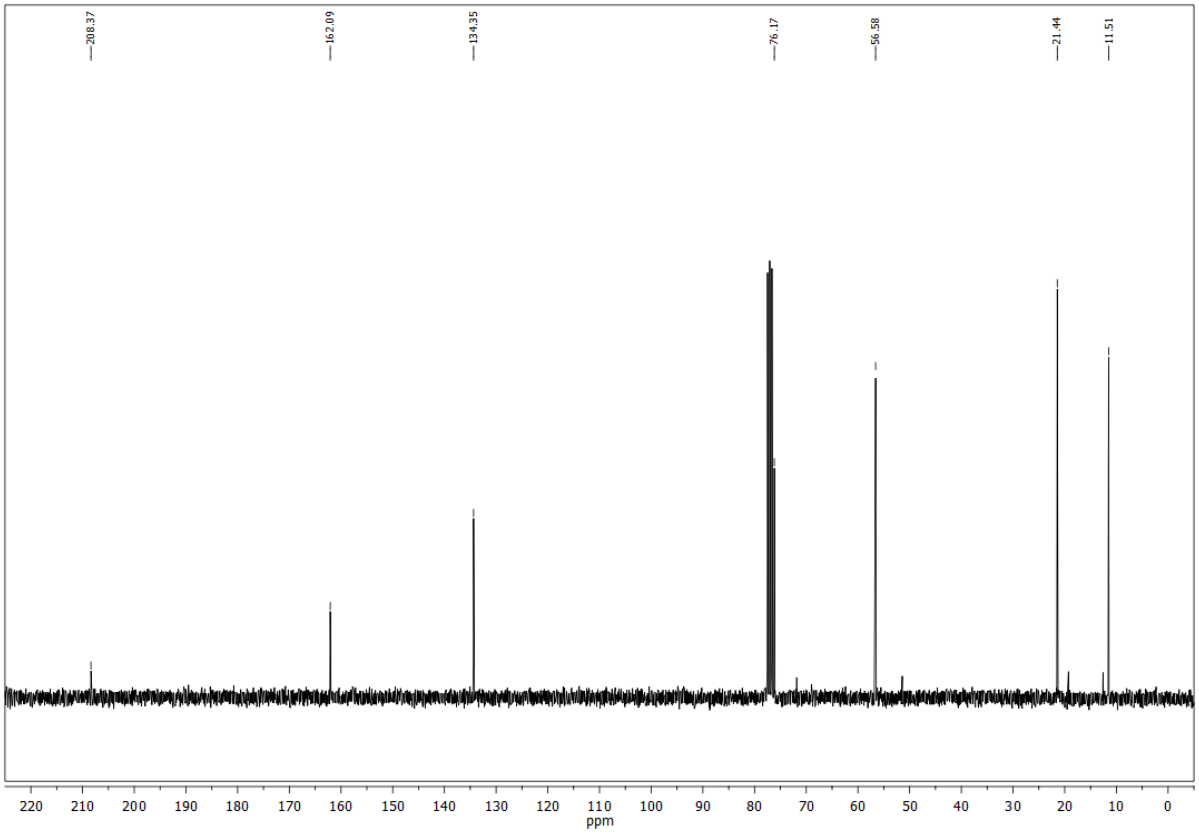


5-Ethyl-4-hydroxycyclopent-2-en-1-one ((±)-149d)

^{1}H NMR (300 MHz, $CDCl_3$)

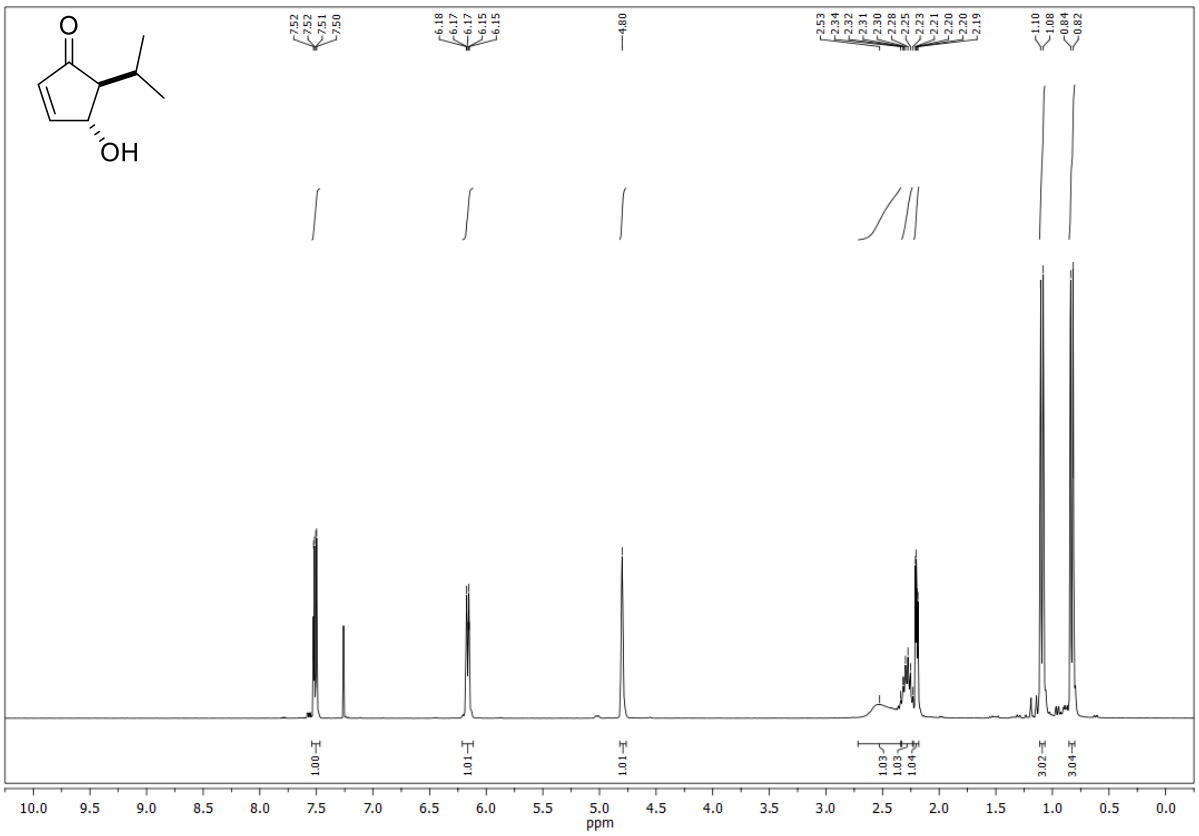


^{13}C NMR (75 MHz, $CDCl_3$)

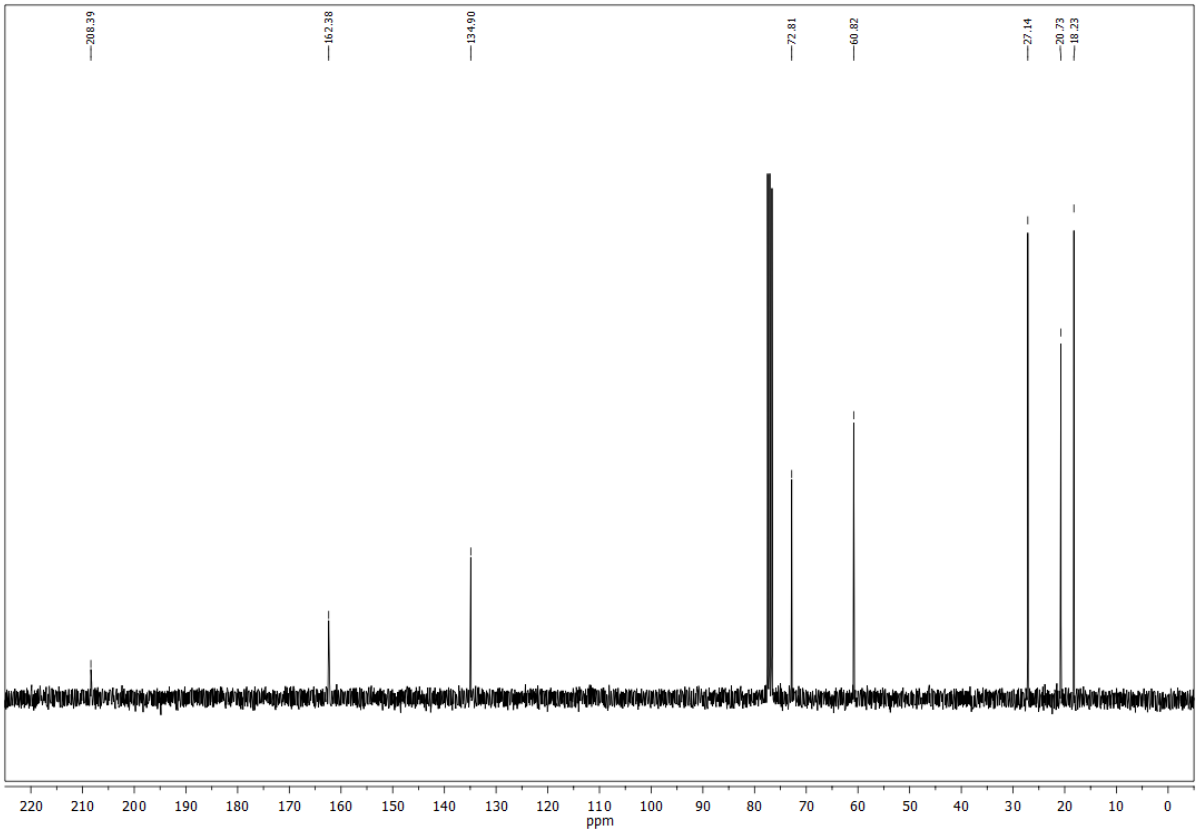


4-Hydroxy-5-isopropylcyclopent-2-en-1-one ((±)-149e)

^{1}H NMR (300 MHz, $CDCl_3$)

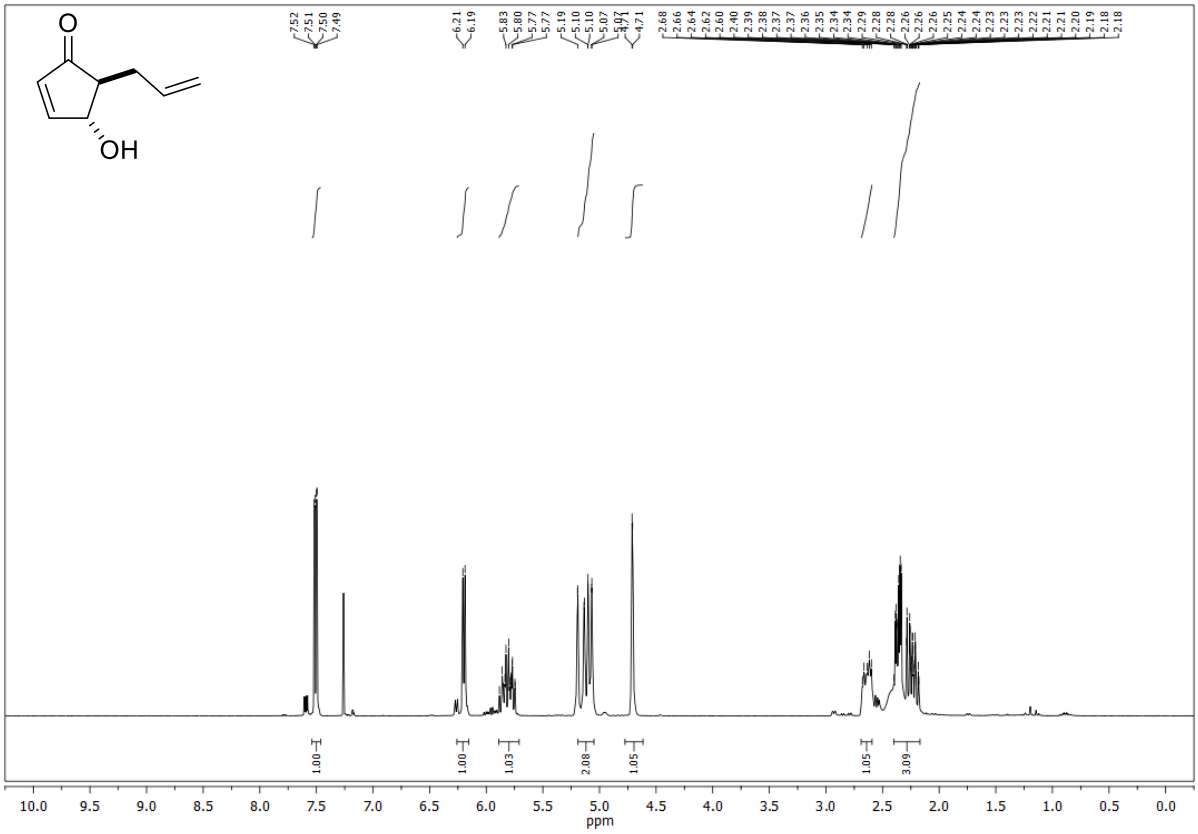


^{13}C NMR (75 MHz, $CDCl_3$)

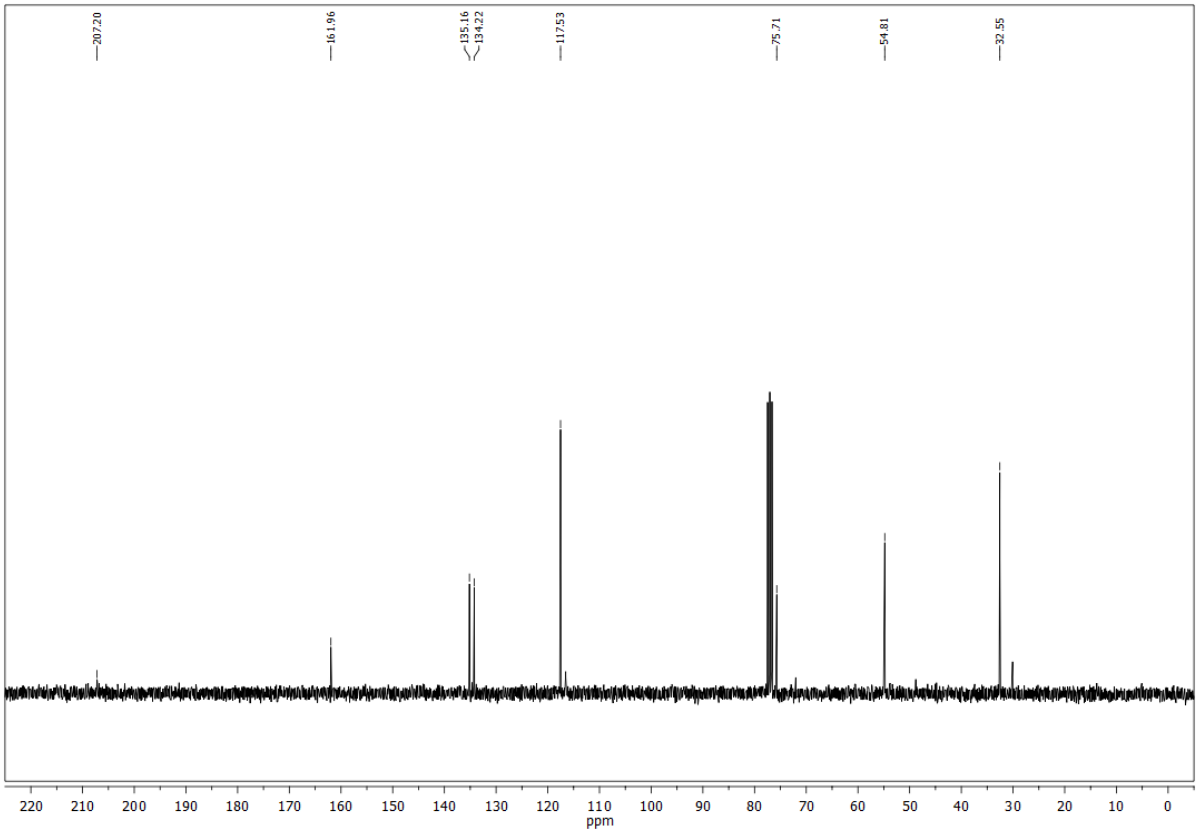


5-Allyl-4-hydroxycyclopent-2-en-1-one ((±)-149f)

^{1}H NMR (300 MHz, $CDCl_3$)

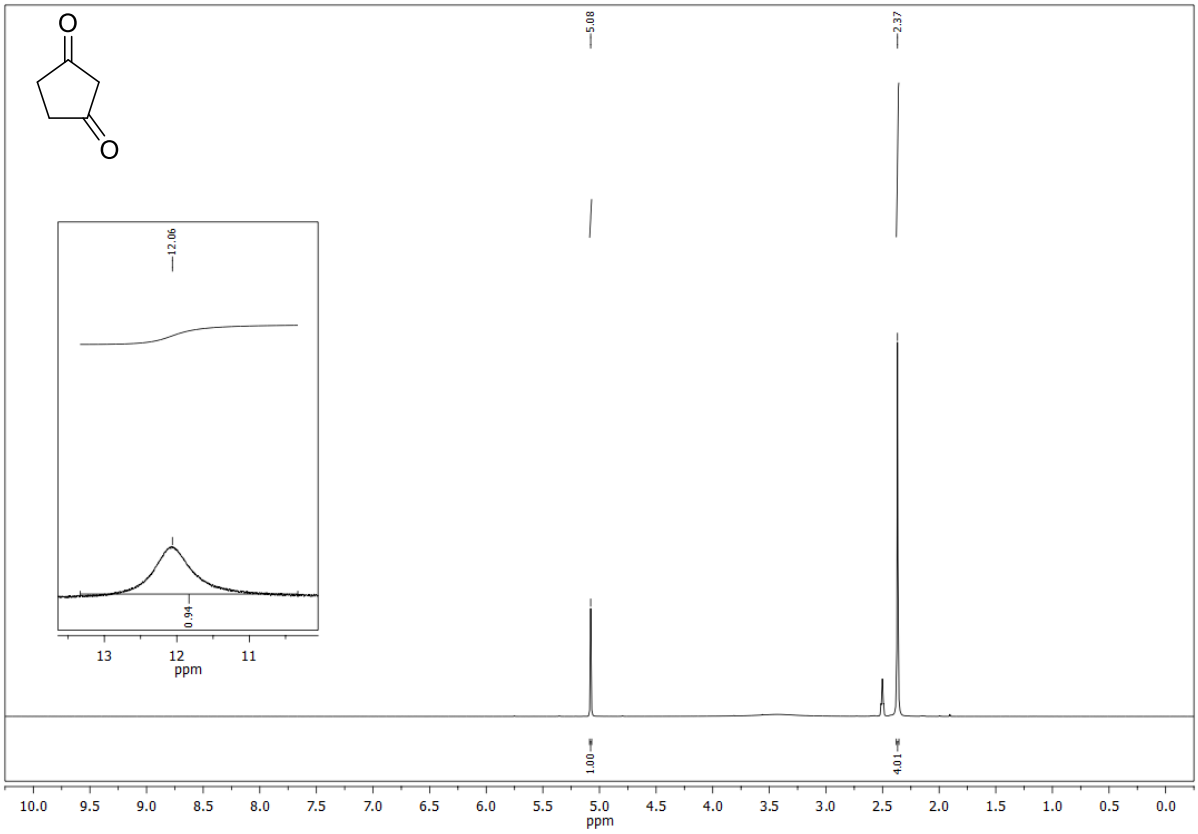


^{13}C NMR (75 MHz, $CDCl_3$)

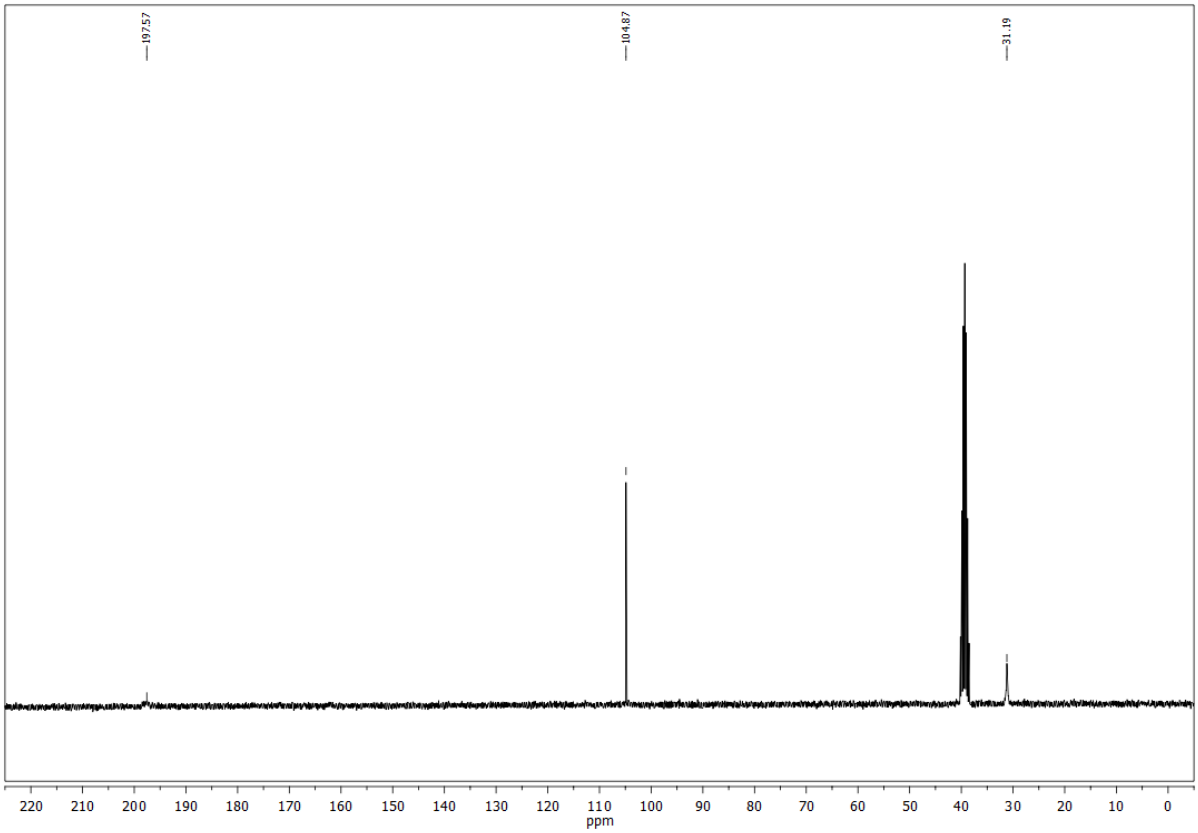


Cyclopentane-1,3-dione (238)

^{1}H NMR (300 MHz, DMSO)

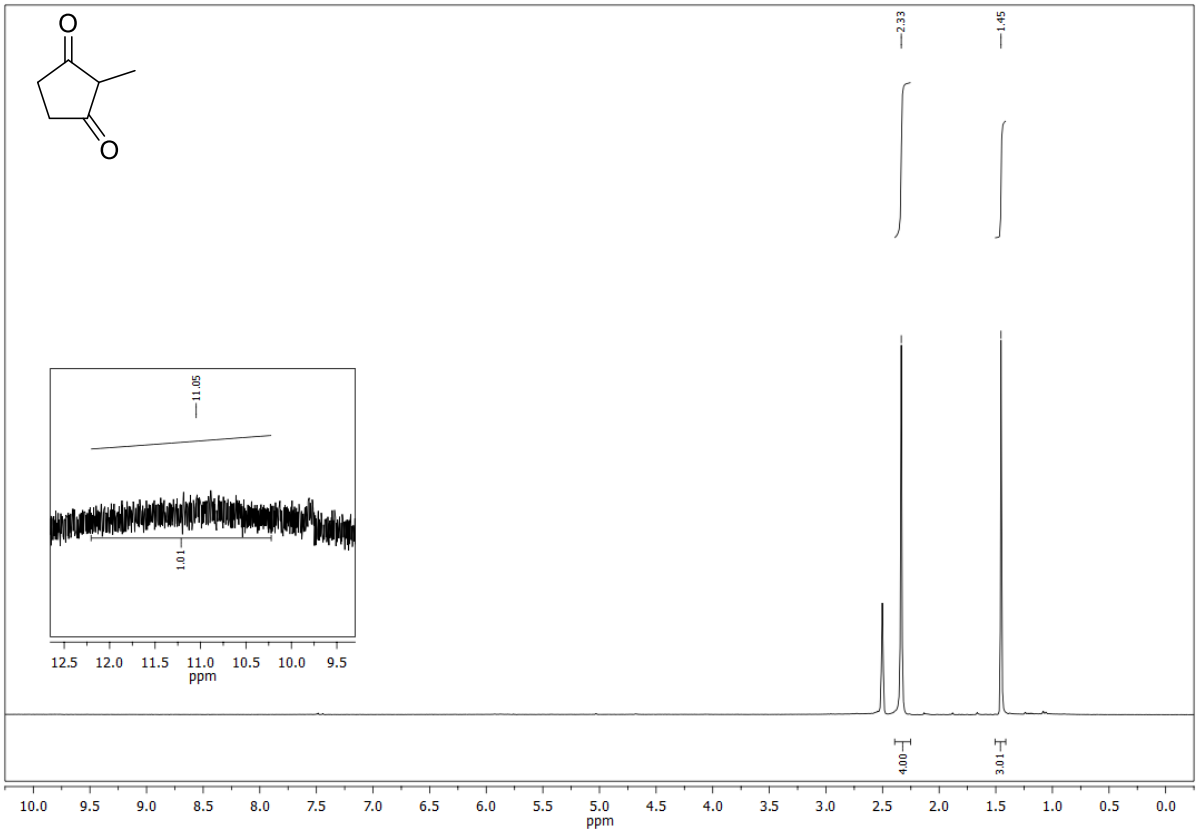


^{13}C NMR (75 MHz, DMSO)

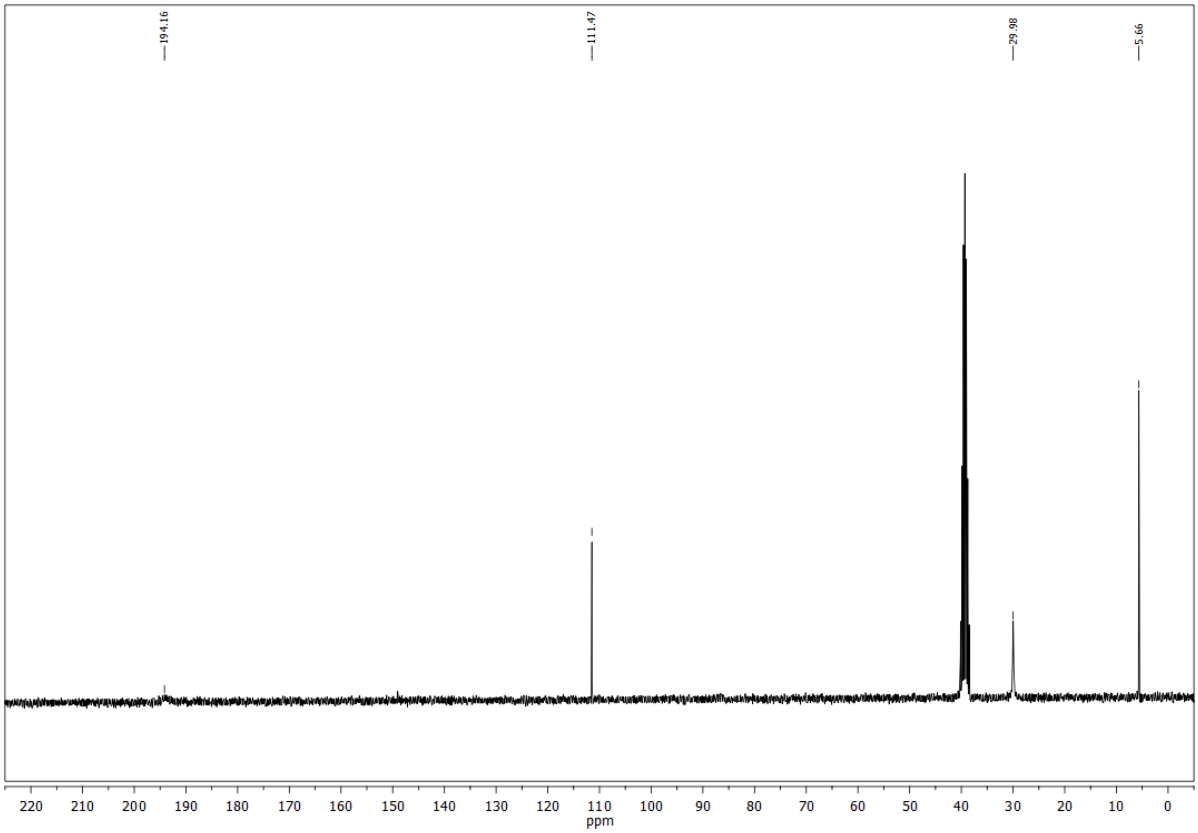


2-Methylcyclopentane-1,3-dione (282a)

^{1}H NMR (300 MHz, DMSO)

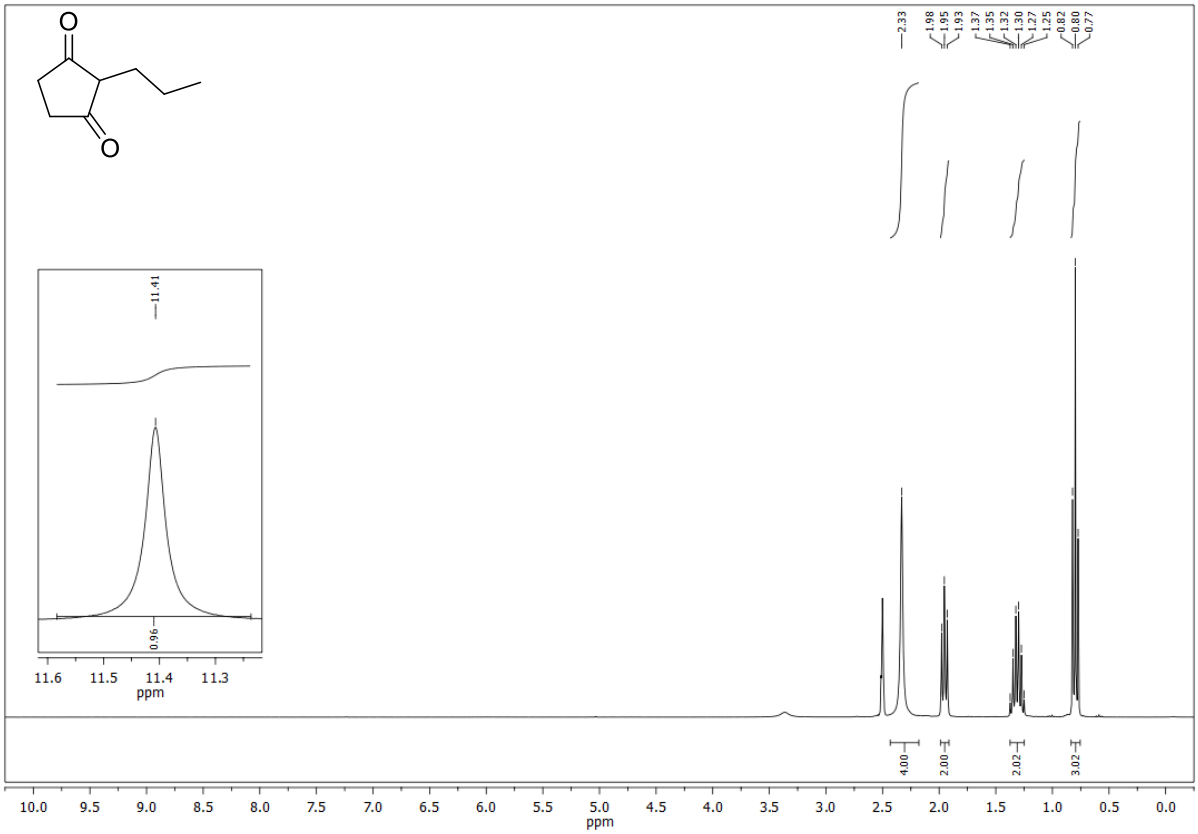


^{13}C NMR (75 MHz, DMSO)

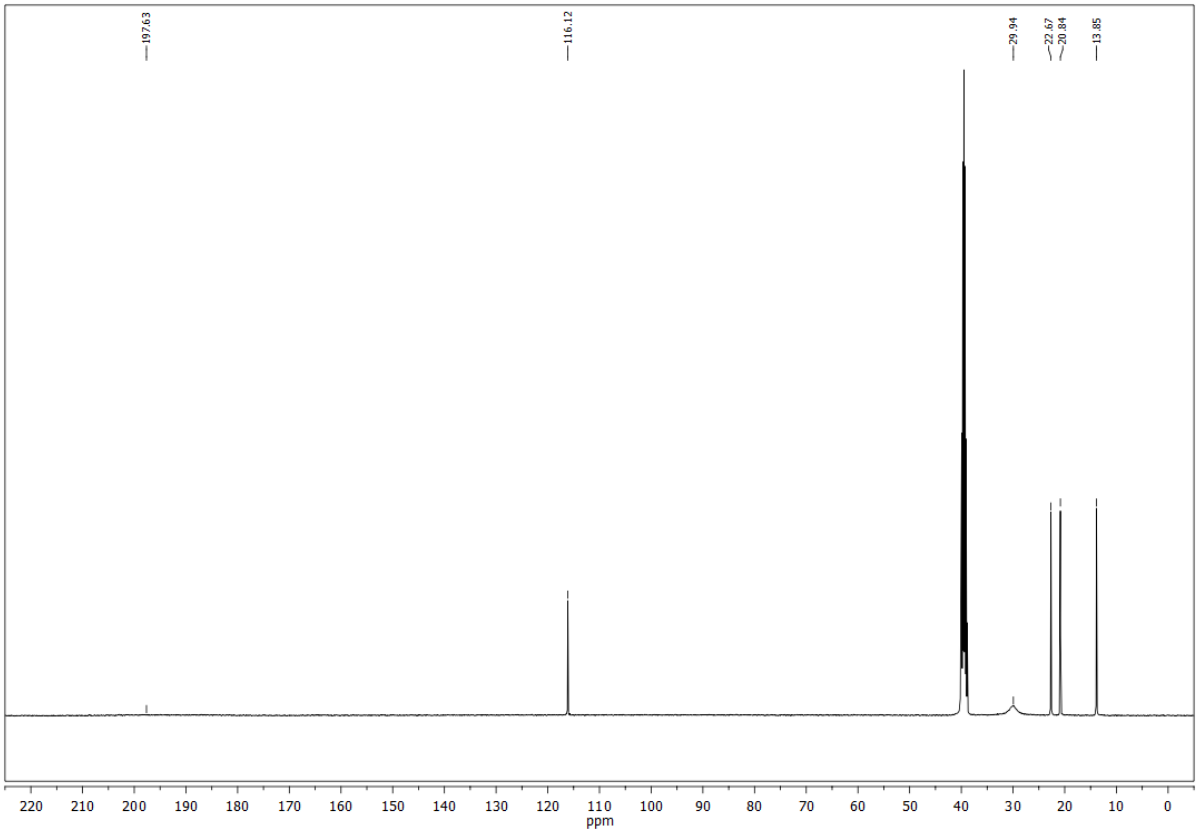


2-Propylcyclopentane-1,3-dione (282b)

^{1}H NMR (300 MHz, DMSO)

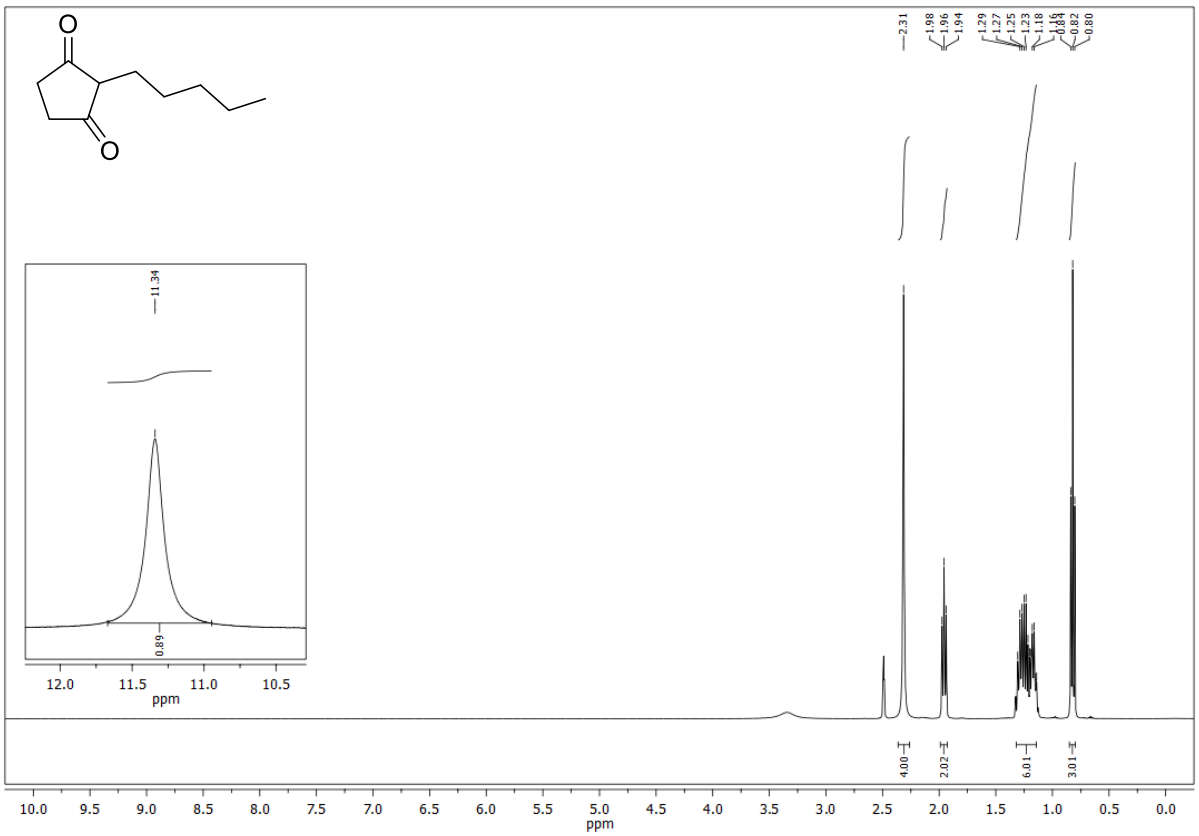


^{13}C NMR (75 MHz, DMSO)

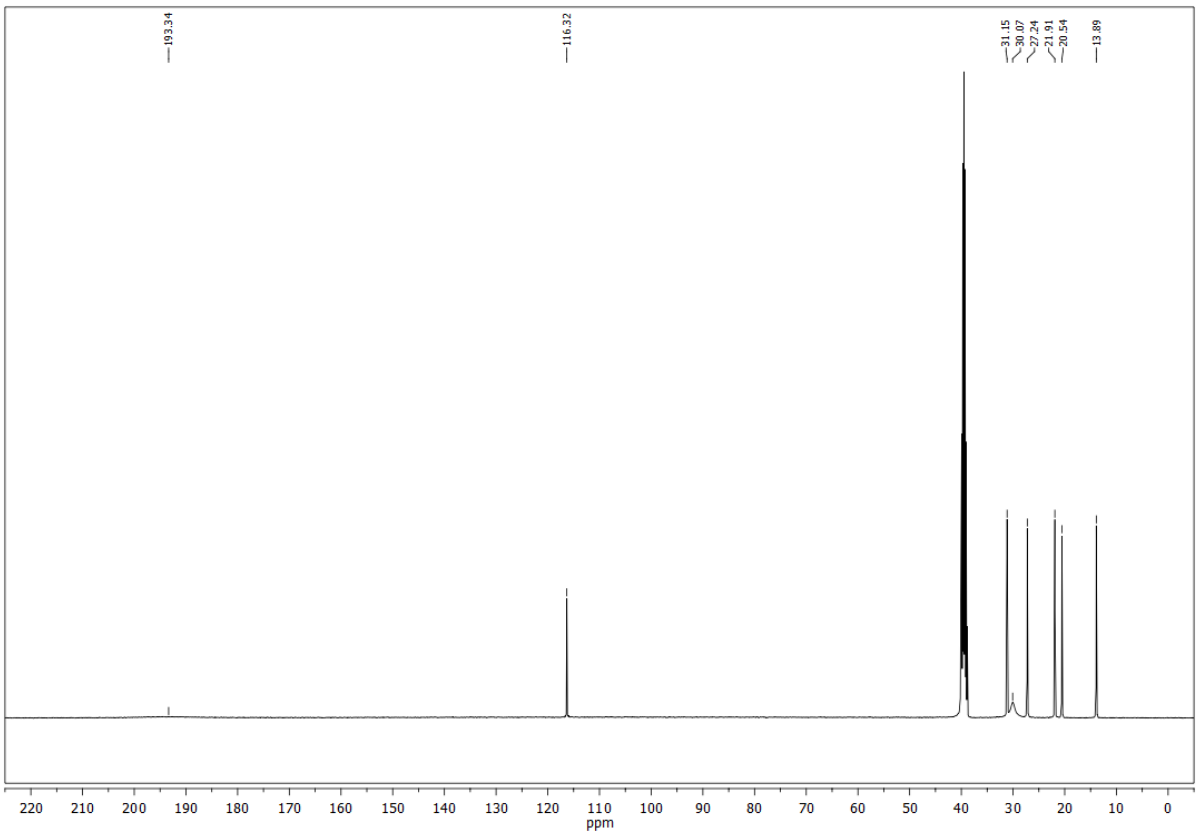


2-Pentylcyclopentane-1,3-dione (282c)

^{1}H NMR (300 MHz, DMSO)

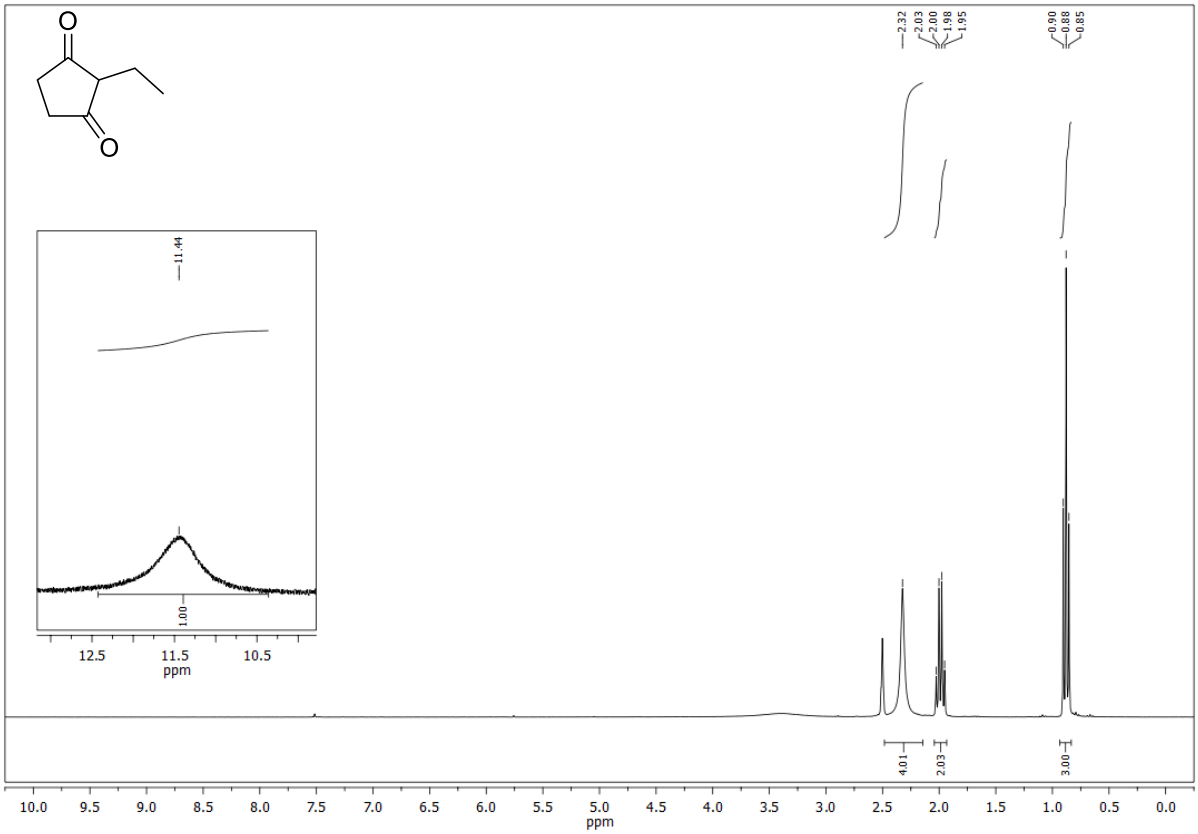


^{13}C NMR (75 MHz, DMSO)

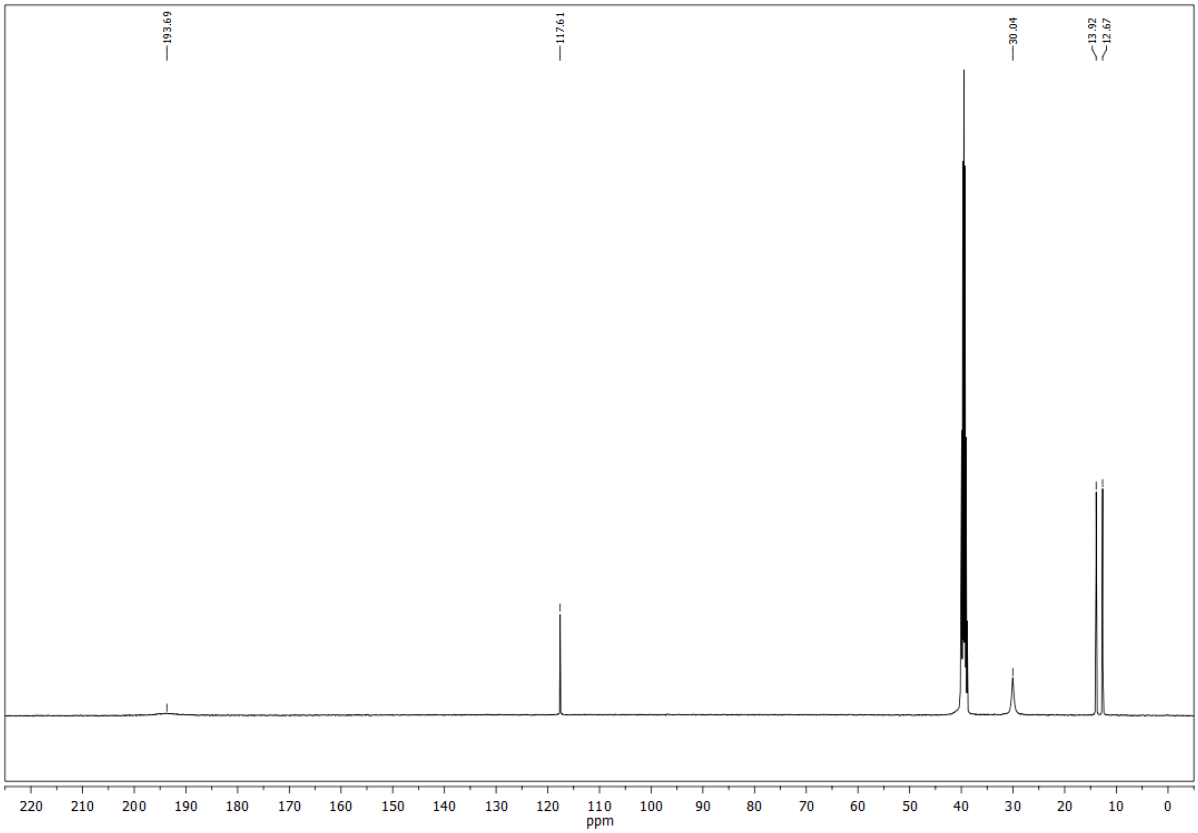


2-Ethylcyclopentane-1,3-dione (282e)

^{1}H NMR (300 MHz, DMSO)

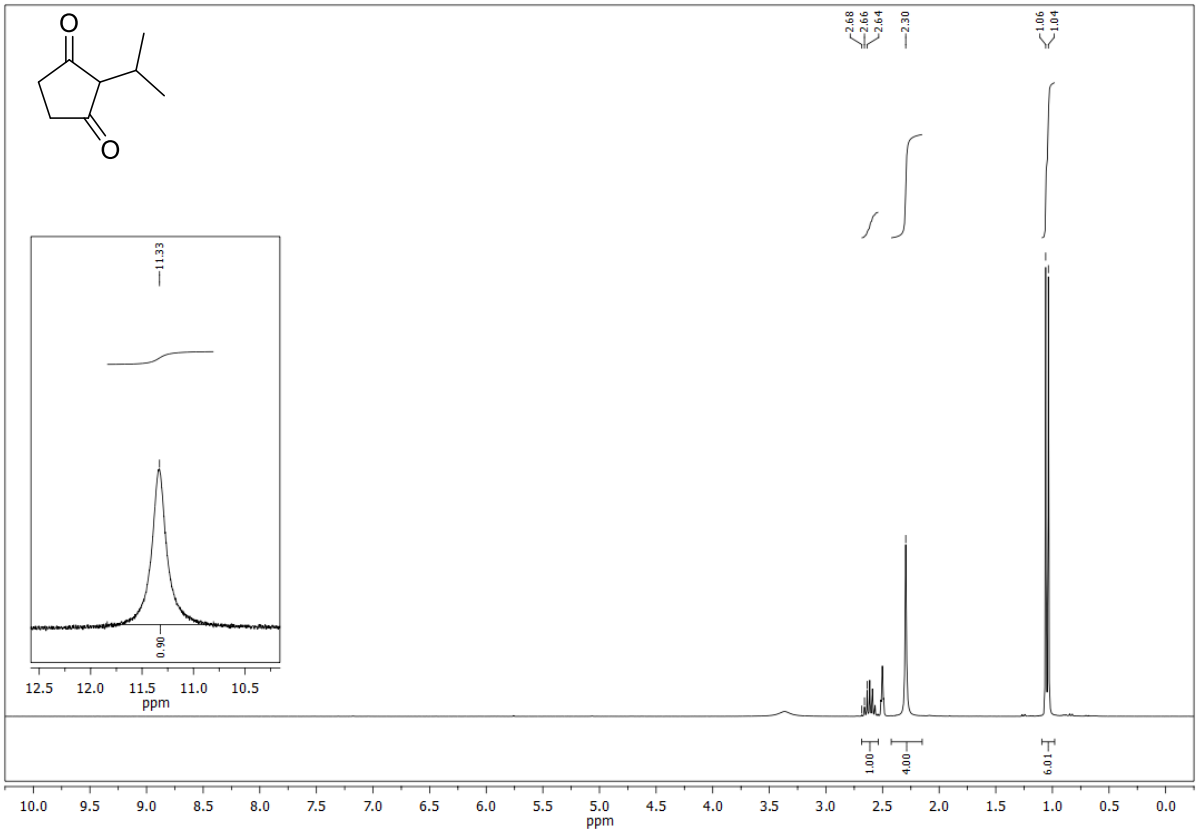


^{13}C NMR (75 MHz, DMSO)

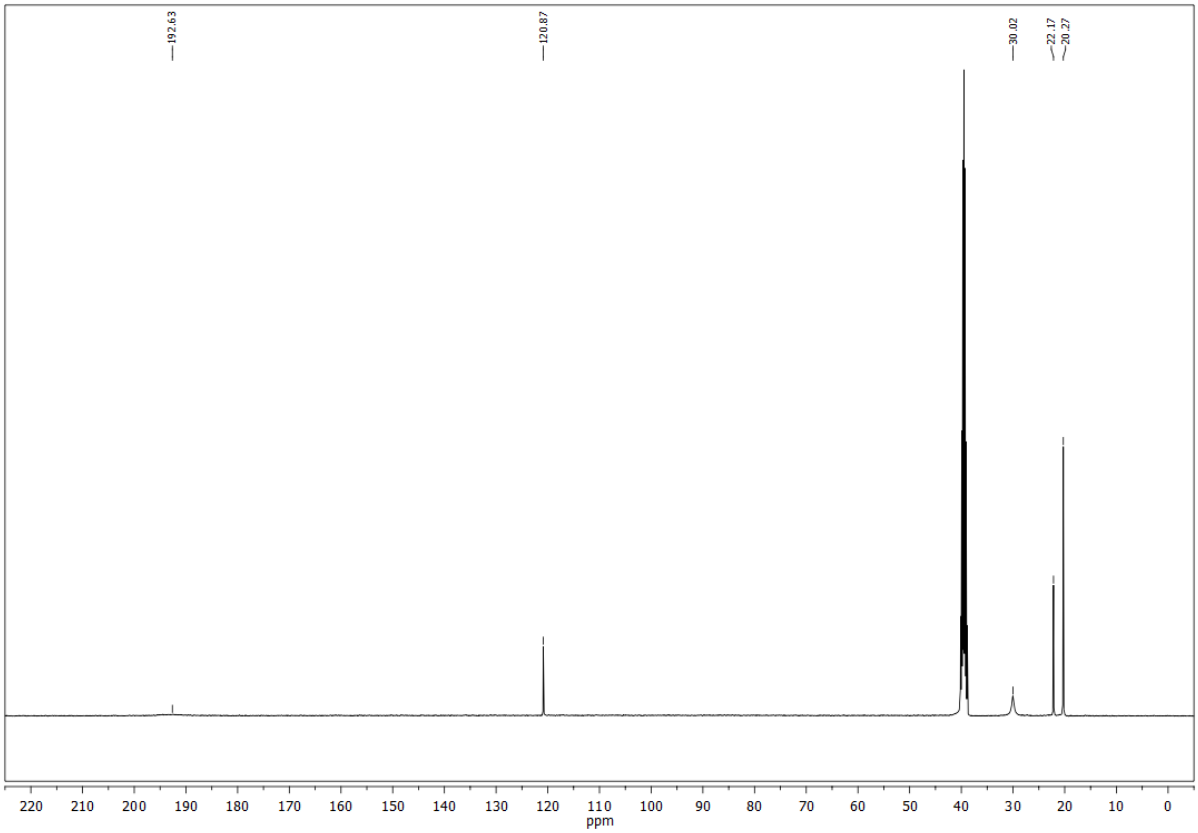


2-Isopropylcyclopentane-1,3-dione (282f)

^{1}H NMR (300 MHz, DMSO)

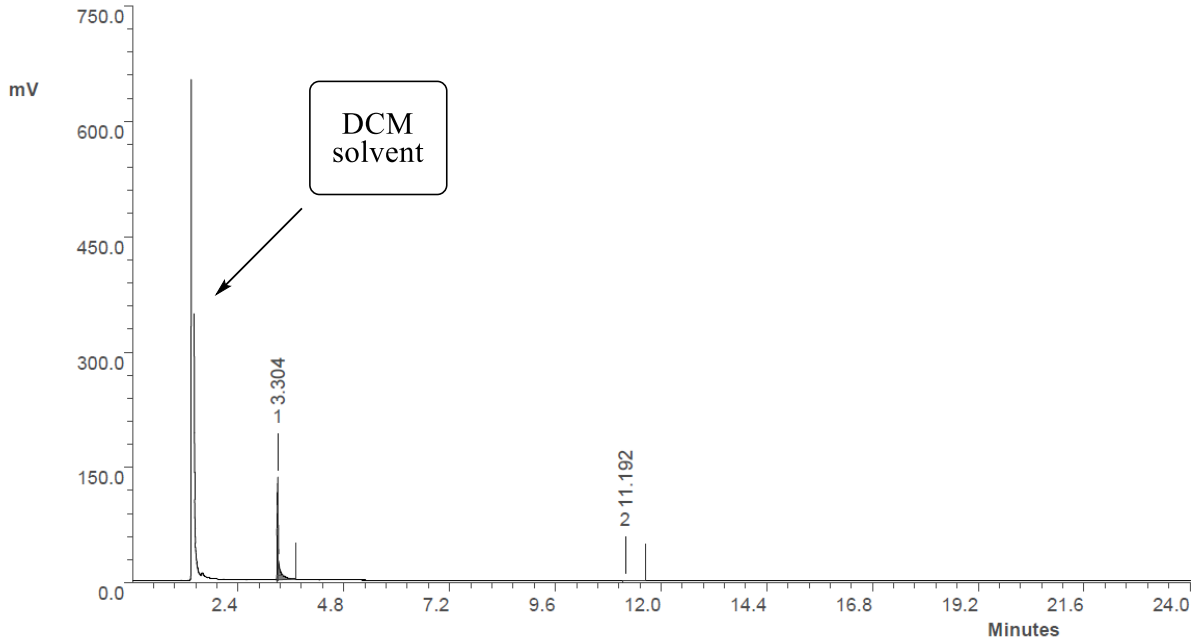


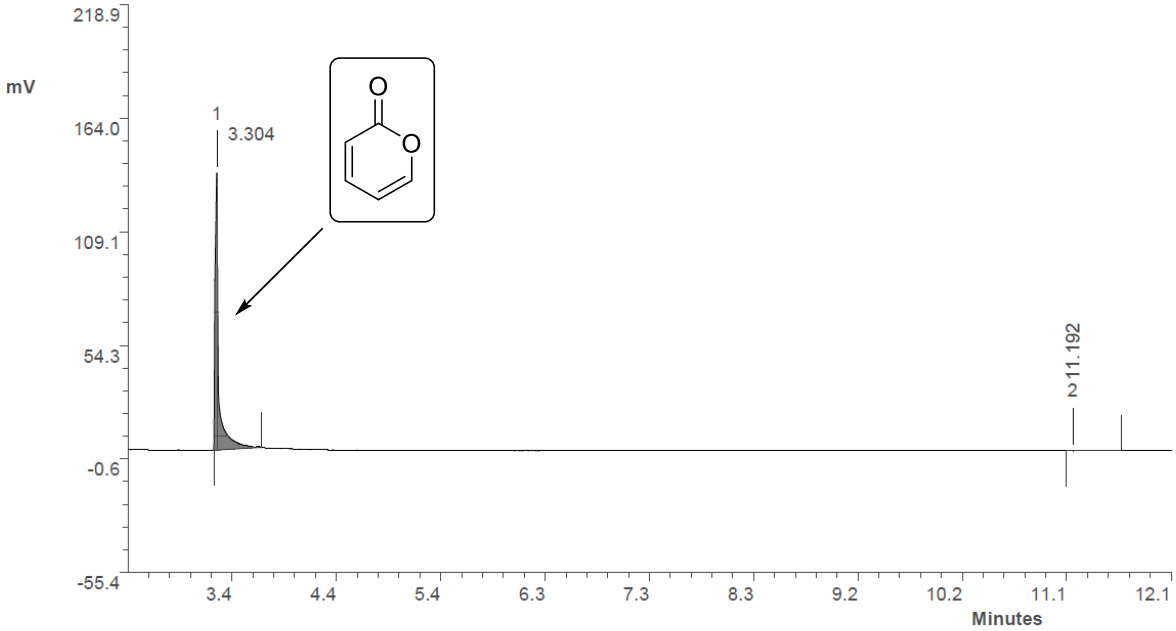
^{13}C NMR (75 MHz, DMSO)



2 GC-spectra

2*H*-Pyran-2-one (1)



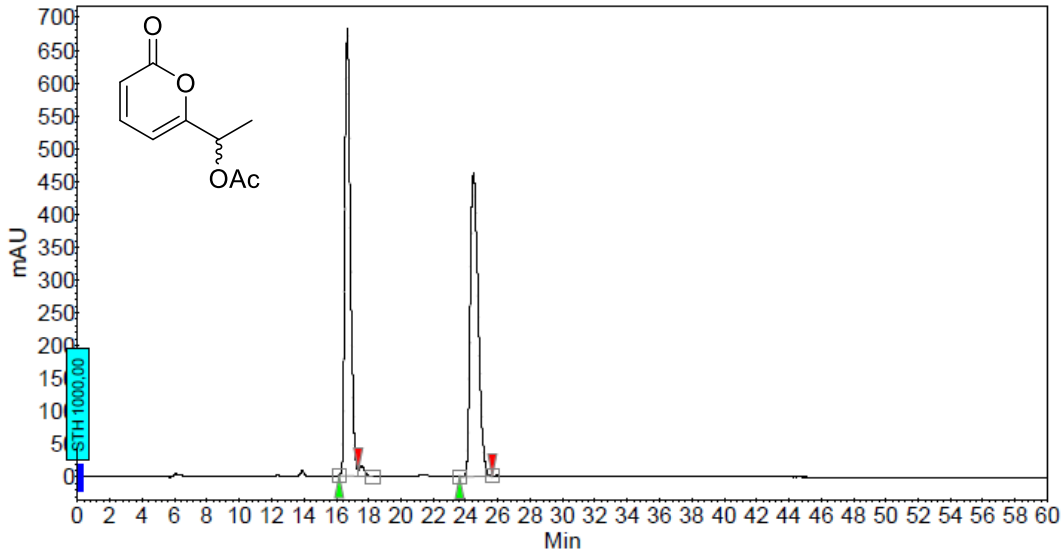


Peak	RT	Area	%Ar	Height
1	3.304	311.528	99.63	133.688
2	11.192	1.157	0.37	0.118

GC-Analysis: purity >99%, RT = 3.304

3 Chiral HPLC data

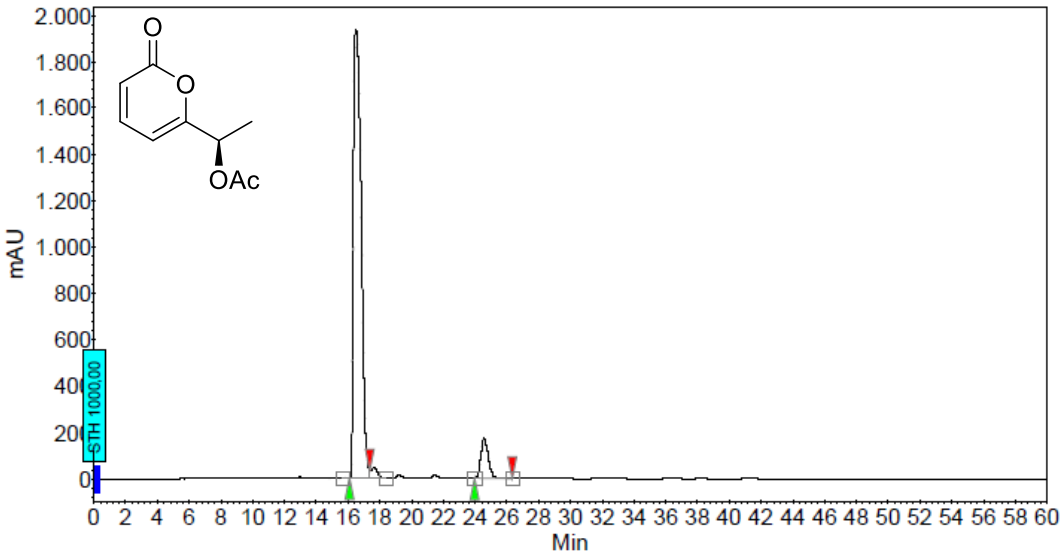
1-(2-Oxo-2*H*-pyran-6-yl)ethyl acetate



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	16,67	50,85	681,4	272,5	50,845
2	UNKNOWN	24,49	49,15	463,4	263,5	49,155
Total			100,00	1144,8	536,0	100,000

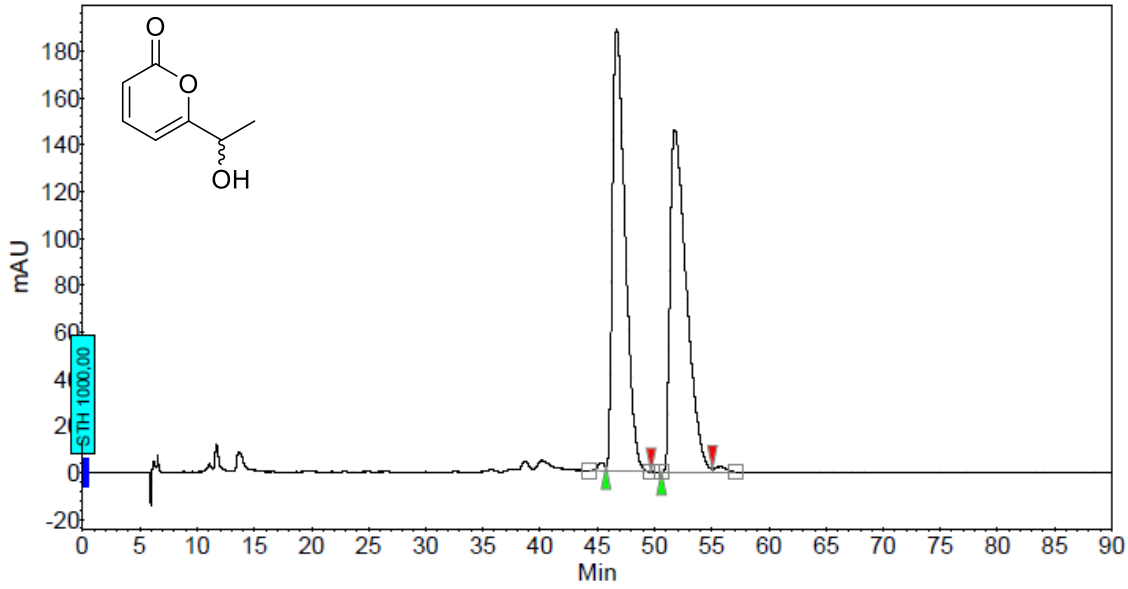
(*R*)-1-(2-Oxo-2*H*-pyran-6-yl)ethyl acetate (174)



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
2	UNKNOWN	16,50	92,13	1936,0	1089,6	92,128
1	UNKNOWN	24,57	7,87	173,8	93,1	7,872
Total			100,00	2109,8	1182,7	100,000

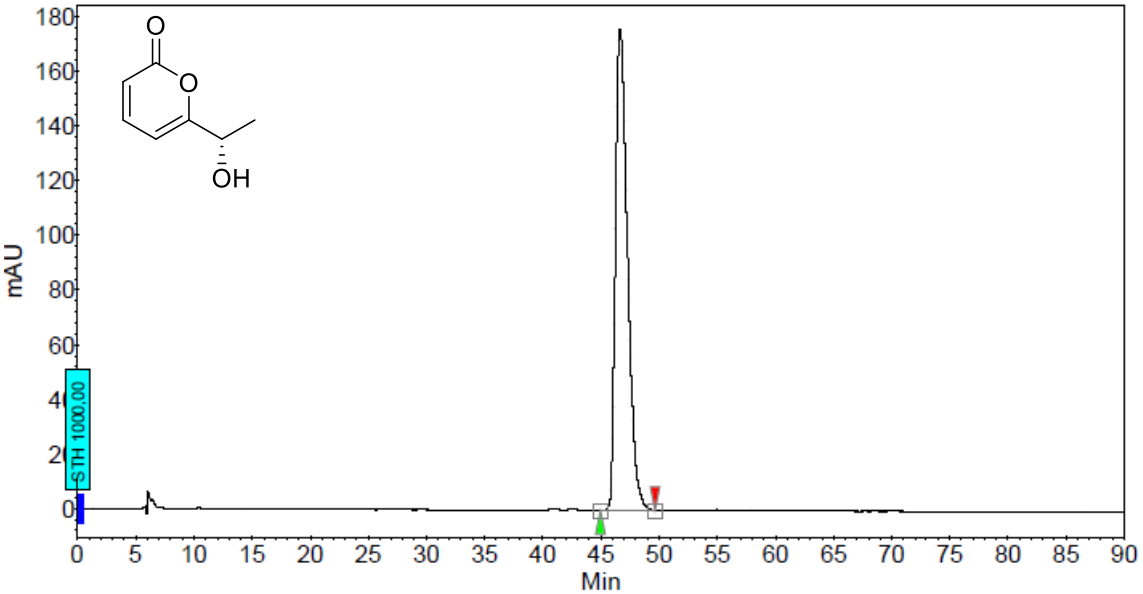
6-(1-Hydroxyethyl)-2*H*-pyran-2-one ((±)-171a)



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	46,69	50,09	188,8	243,9	50,086
2	UNKNOWN	51,80	49,91	146,2	243,1	49,914
Total			100,00	335,0	487,0	100,000

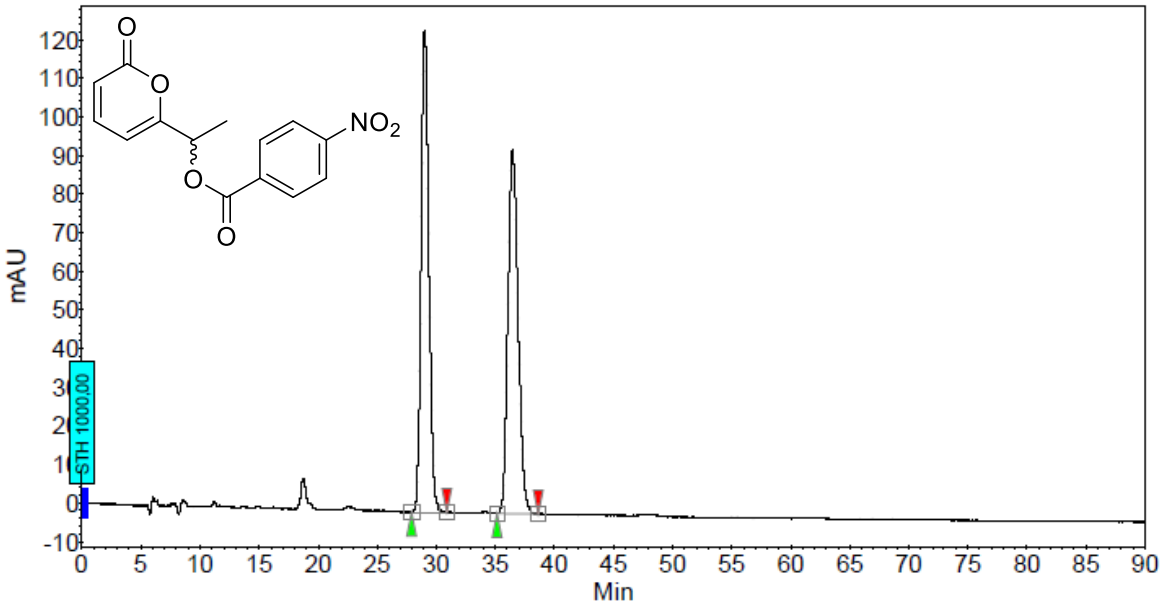
(*S*)-6-(1-Hydroxyethyl)-2*H*-pyran-2-one (171a)



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	46,64	100,00	175,9	212,8	100,000
Total			100,00	175,9	212,8	100,000

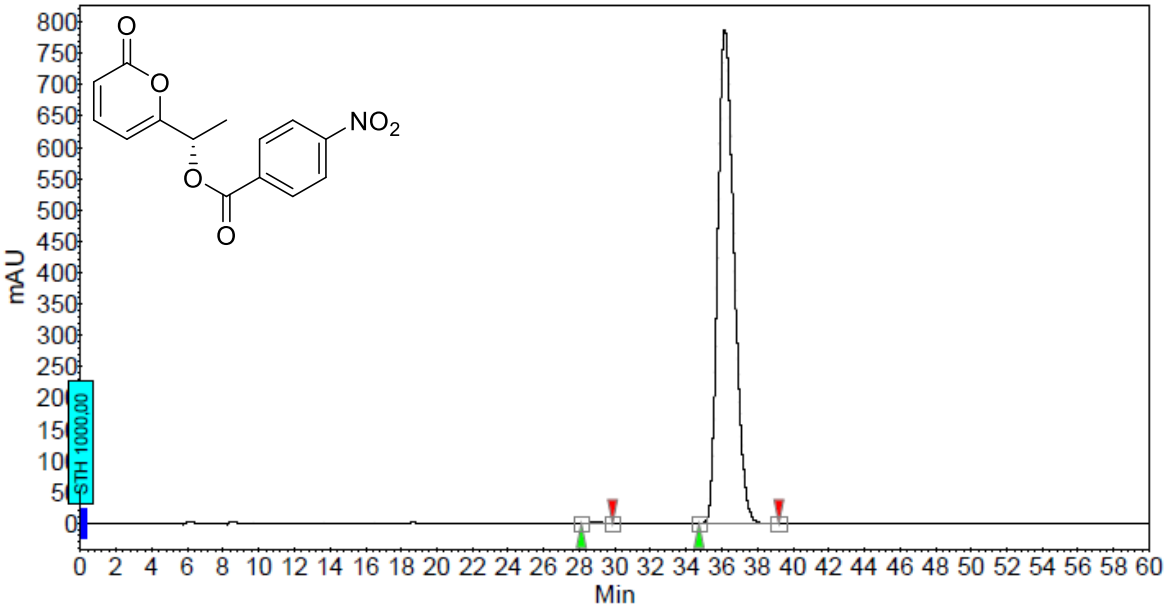
1-(2-Oxo-2*H*-pyran-6-yl)ethyl 4-nitrobenzoate



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	29,02	49,92	124,6	94,2	49,916
2	UNKNOWN	36,46	50,08	94,2	94,5	50,084
Total			100,00	218,9	188,6	100,000

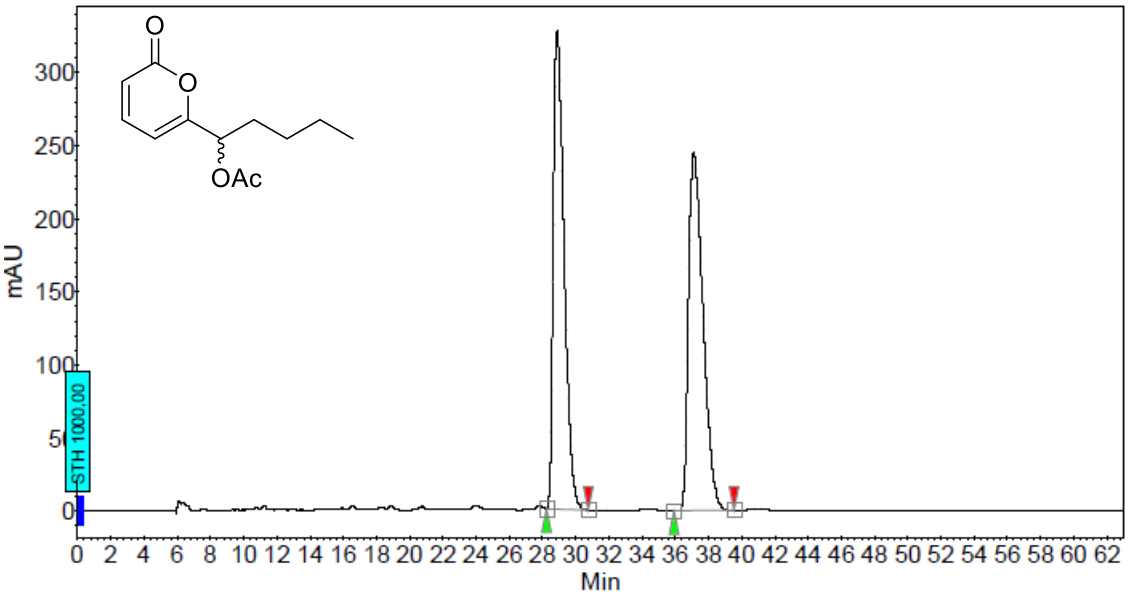
(*S*)-1-(2-Oxo-2*H*-pyran-6-yl)ethyl 4-nitrobenzoate (175)



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	28,94	0,22	2,5	1,8	0,216
2	UNKNOWN	36,17	99,78	787,3	841,5	99,784
Total			100,00	789,8	843,3	100,000

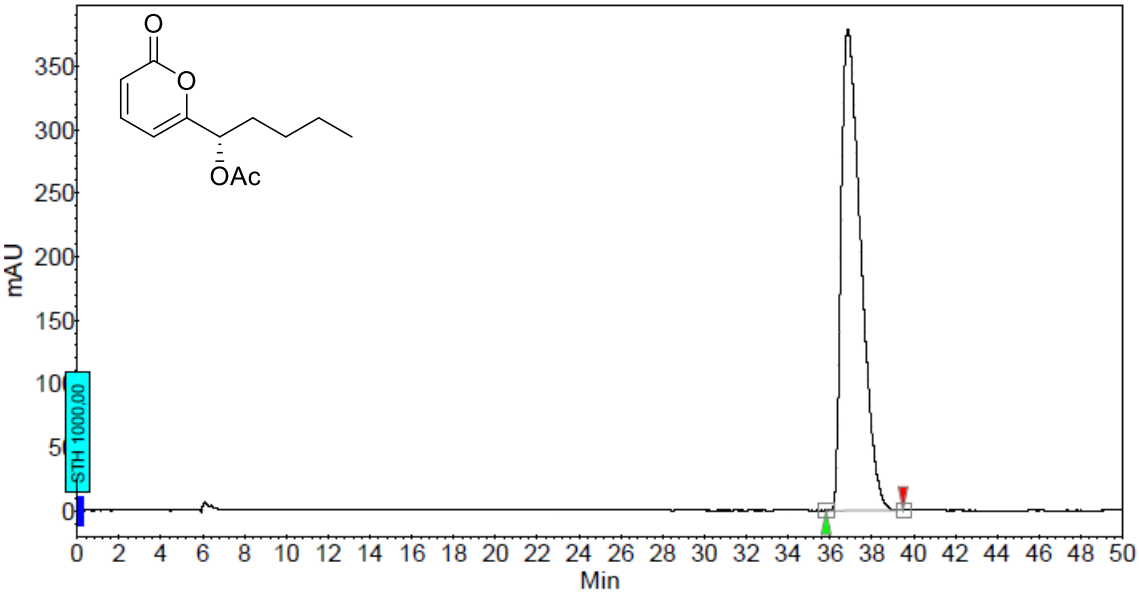
1-(2-Oxo-2*H*-pyran-6-yl)pentyl acetate ((±)-179)



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	28,89	49,78	327,9	247,3	49,784
2	UNKNOWN	37,11	50,22	245,7	249,5	50,216
Total			100,00	573,6	496,8	100,000

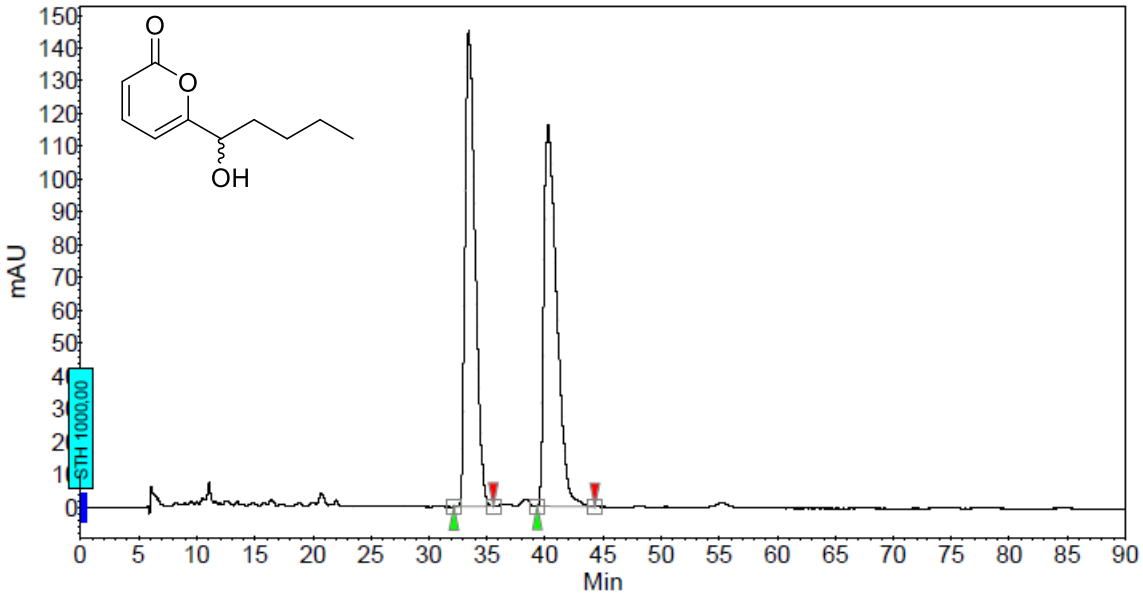
(*S*)-1-(2-Oxo-2*H*-pyran-6-yl)pentyl acetate (179)



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	36,85	100,00	378,8	412,6	100,000
Total			100,00	378,8	412,6	100,000

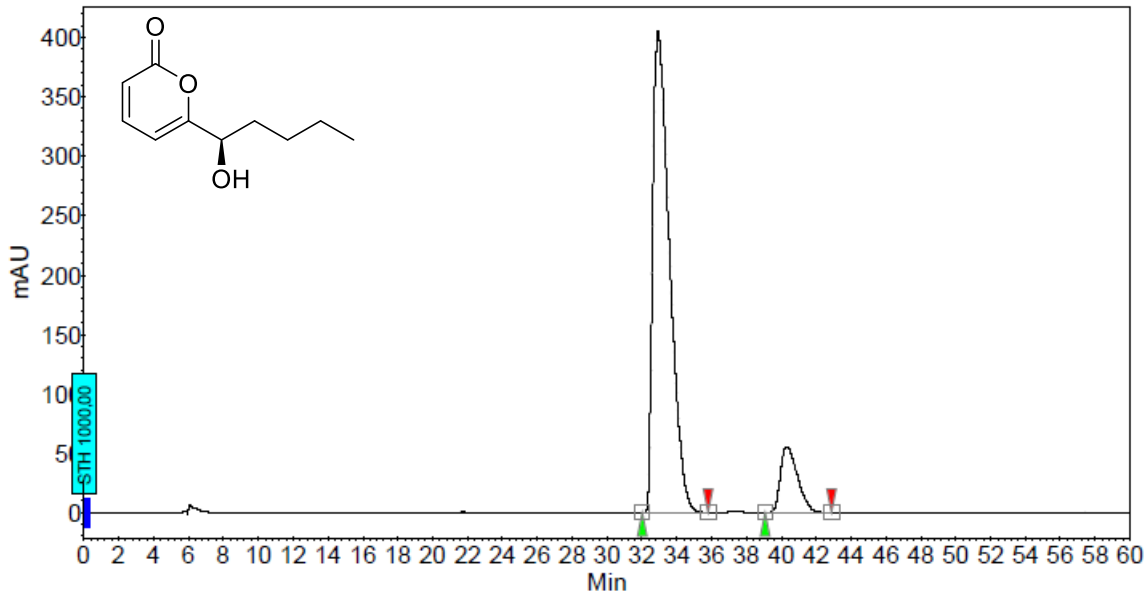
6-(1-Hydroxypentyl)-2*H*-pyran-2-one ((±)-171e)



Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	33,44	49,44	145,1	145,9	49,439
2	UNKNOWN	40,26	50,56	116,0	149,3	50,561
Total			100,00	261,1	295,2	100,000

(*R*)-6-(1-Hydroxypentyl)-2*H*-pyran-2-one (171e)

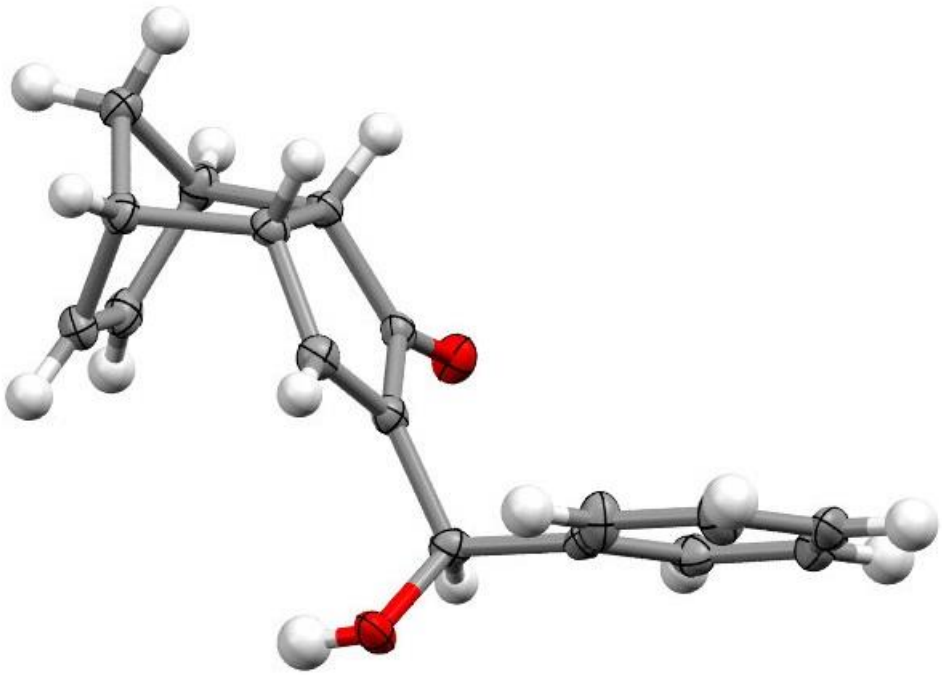


Peak Results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	32,93	87,72	405,3	452,2	87,716
2	UNKNOWN	40,31	12,28	55,4	63,3	12,284
Total			100,00	460,6	515,5	100,000

4 X-ray data

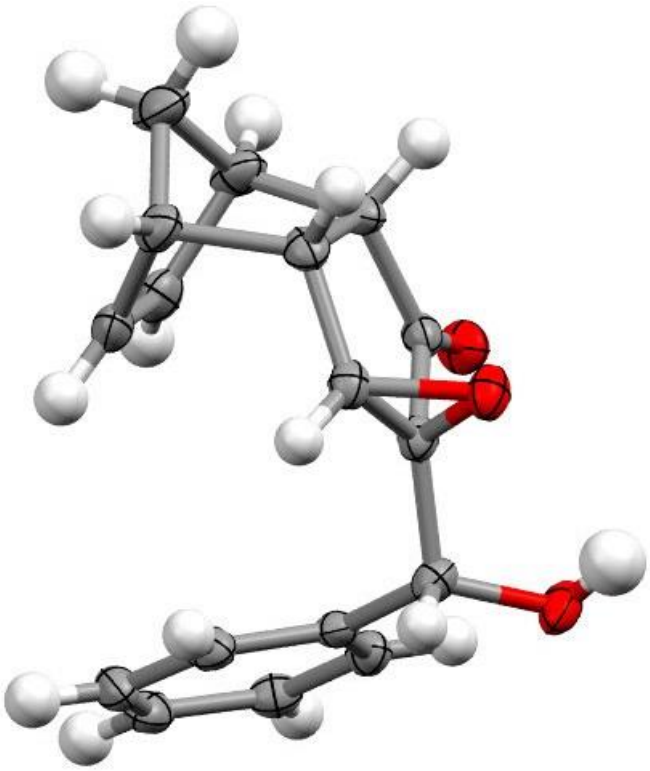
X-ray crystallography structure of (±)-**165g** (the ellipsoid contour percent probability level is 50%)



F Appendix

Formula	$C_{17}H_{16}O_2$
$D_{calc.}$/ g cm^{-3}	1.307
μ/mm^{-1}	0.670
Formula Weight	252.30
Colour	clear colourless
Shape	plate
Max Size/mm	0.11
Mid Size/mm	0.08
Min Size/mm	0.04
T/K	123.00(10)
Crystal System	monoclinic
Space Group	$P2_1/c$
a/Å	11.2968(4)
b/Å	10.0528(3)
c/Å	11.7838(4)
α/°	90
β/°	106.701(4)
γ/°	90
V/Å^3	1281.77(8)
Z	4
Z'	1
Θ_{min}/°	4.086
Θ_{max}/°	73.509
Measured Refl.	11218
Independent Refl.	2541
Reflections Used	2172
R_{int}	0.0317
Parameters	173
Restraints	0
Largest Peak	0.254
Deepest Hole	-0.208
GooF	1.052
wR_2 (all data)	0.0909
wR_2	0.0852
R_1 (all data)	0.0437
R_1	0.0358

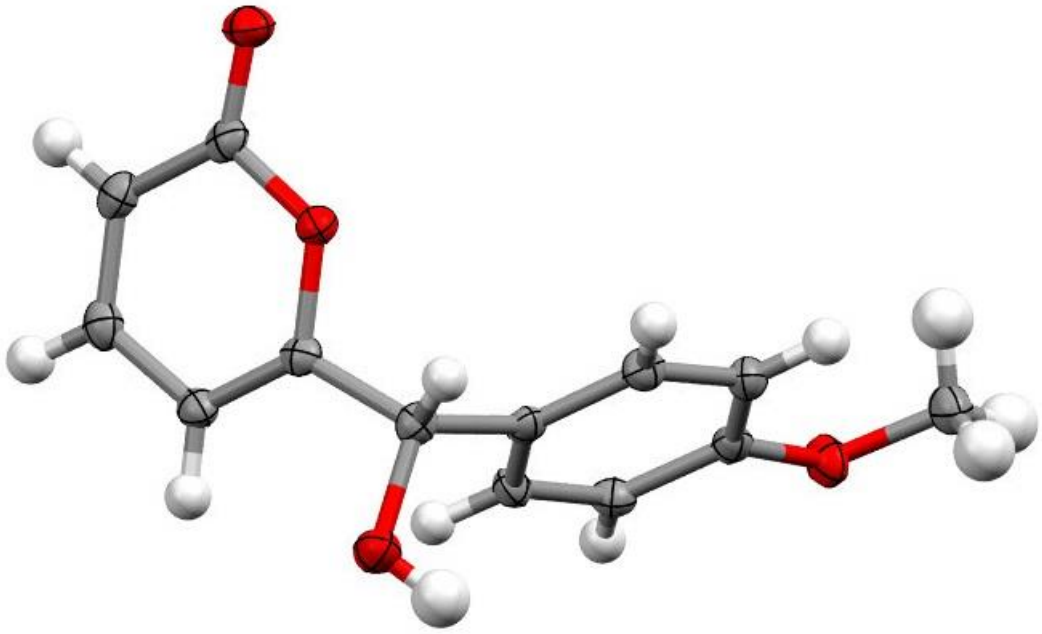
X-ray crystallography structure of **(±)-170g** (the ellipsoid contour percent probability level is 50%)



F Appendix

Formula	$C_{17}H_{16}O_3$
$D_{calc.}$/ g cm^{-3}	1.3473
μ/mm^{-1}	0.741
Formula Weight	268.31
Colour	colourless
Shape	irregular
Max Size/mm	0.24
Mid Size/mm	0.15
Min Size/mm	0.10
T/K	123.01(10)
Crystal System	monoclinic
Space Group	$P2_1/n$
a/Å	9.9767(2)
b/Å	11.8794(2)
c/Å	11.9166(3)
α/°	90
β/°	110.522(3)
γ/°	90
V/Å^3	1322.70(6)
Z	4
Z'	1
Θ_{min}/°	5.00
Θ_{max}/°	73.41
Measured Refl.	12773
Independent Refl.	2633
Reflections Used	2262
R_{int}	0.0286
Parameters	181
Restraints	0
Largest Peak	0.2605
Deepest Hole	-0.2237
GooF	1.0660
wR_2 (all data)	0.0959
wR_2	0.0910
R_1 (all data)	0.0420
R_1	0.0357

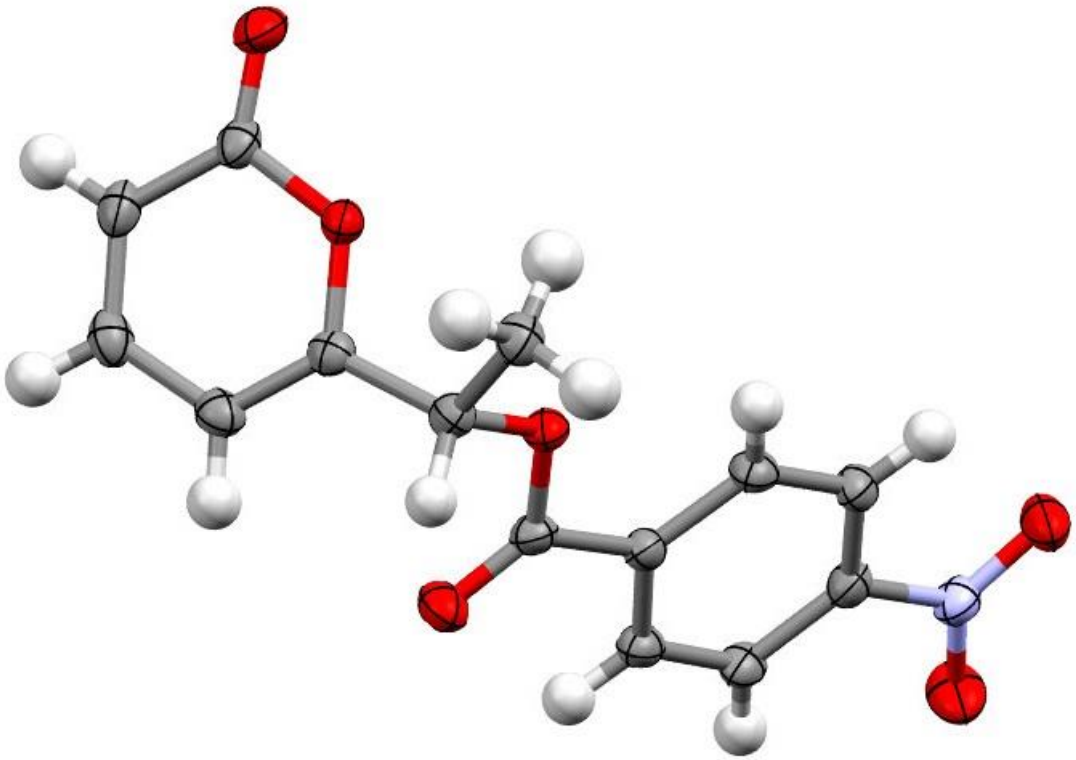
X-ray crystallography structure of **(±)-171j** (the ellipsoid contour percent probability level is 50%)



F Appendix

Formula	$C_{13}H_{12}O_4$
$D_{calc.}$/ g cm^{-3}	1.443
μ/mm^{-1}	0.895
Formula Weight	232.23
Colour	clear colourless
Shape	needle
Max Size/mm	0.13
Mid Size/mm	0.03
Min Size/mm	0.02
T/K	123.00(10)
Crystal System	orthorhombic
Flack Parameter	0.15(12)
Hooft Parameter	0.12(12)
Space Group	$P2_12_12_1$
a/Å	6.4205(3)
b/Å	11.7811(6)
c/Å	14.1339(6)
α/°	90
β/°	90
γ/°	90
V/Å^3	1069.10(8)
Z	4
Z'	1
Θ_{min}/°	4.887
Θ_{max}/°	66.606
Measured Refl.	4585
Independent Refl.	1836
Reflections Used	1732
R_{int}	0.0275
Parameters	156
Restraints	0
Largest Peak	0.352
Deepest Hole	-0.154
GooF	1.054
wR_2 (all data)	0.0791
wR_2	0.0767
R_1 (all data)	0.0335
R_1	0.0305

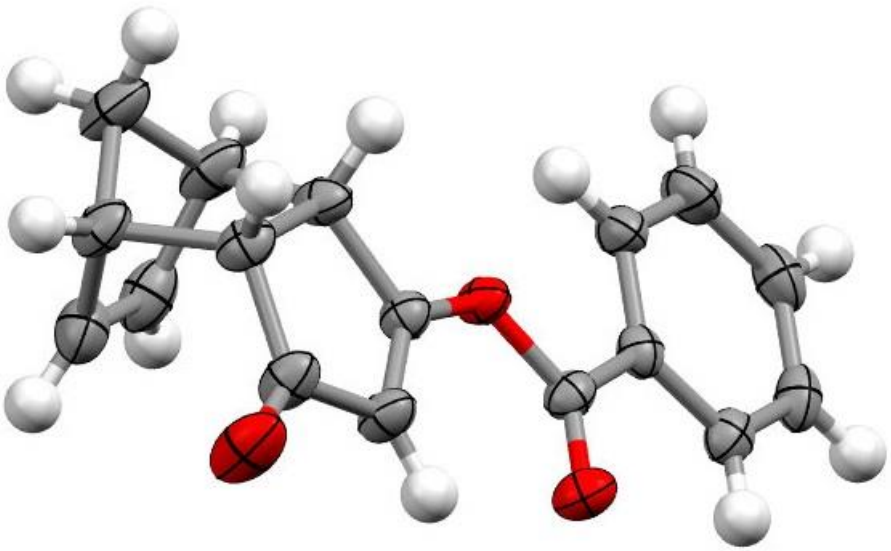
X-ray crystallography structure of **(*S*)-175** (the ellipsoid contour percent probability level is 50%)



F Appendix

Formula	$C_{14}H_{11}NO_6$
$D_{calc.}$/ g cm^{-3}	1.497
μ/mm^{-1}	1.017
Formula Weight	289.24
Colour	clear colourless
Shape	irregular
Size/mm^3	0.22×0.09×0.05
T/K	123.01(10)
Crystal System	monoclinic
Flack Parameter	0.02(7)
Hooft Parameter	0.05(6)
Space Group	$P2_1$
a/Å	4.25027(12)
b/Å	29.6140(5)
c/Å	10.3858(2)
α/°	90
β/°	100.939(3)
γ/°	90
V/Å^3	1283.49(5)
Z	4
Z'	2
Wavelength/Å	1.54184
Radiation type	CuK$_\alpha$
Θ_{min}/°	4.336
Θ_{max}/°	73.606
Measured Refl.	16728
Independent Refl.	4990
Reflections Used	4811
R_{int}	0.0322
Parameters	381
Restraints	1
Largest Peak	0.216
Deepest Hole	-0.213
GooF	1.065
wR_2 (all data)	0.0983
wR_2	0.0966
R_1 (all data)	0.0376
R_1	0.0361

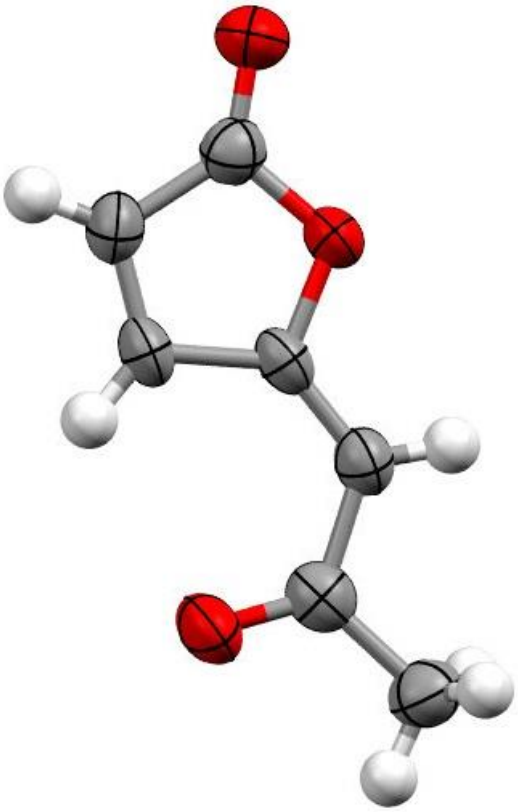
X-ray crystallography structure of **(±)-240g** (the ellipsoid contour percent probability level is 50%)



F Appendix

Formula	$C_{17}H_{14}O_3$
$D_{calc.}$/ g cm^{-3}	1.323
μ/mm^{-1}	0.733
Formula Weight	266.28
Colour	colourless
Shape	plate
Max Size/mm	0.19
Mid Size/mm	0.15
Min Size/mm	0.02
T/K	123.02(16)
Crystal System	monoclinic
Space Group	$P2_1/c$
a/Å	18.1617(4)
b/Å	6.28851(16)
c/Å	11.7251(3)
α/°	90
β/°	92.979(2)
γ/°	90
V/Å^3	1337.32(6)
Z	4
Z'	1
Θ_{min}/°	2.436
Θ_{max}/°	74.115
Measured Refl.	22420
Independent Refl.	2718
Reflections Used	2377
R_{int}	0.0490
Parameters	263
Restraints	156
Largest Peak	0.285
Deepest Hole	-0.168
GooF	1.080
wR_2 (all data)	0.1272
wR_2	0.1215
R_1 (all data)	0.0505
R_1	0.0440

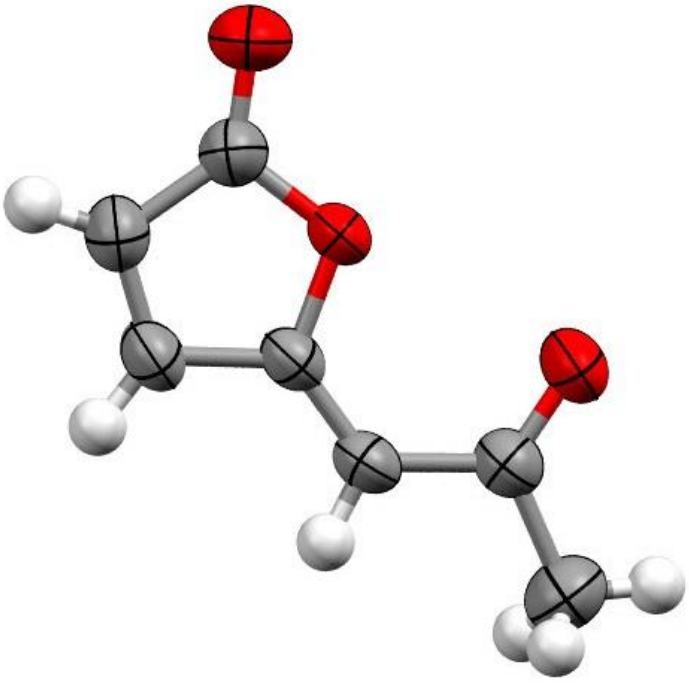
X-ray crystallography structure of **241a** (the ellipsoid contour percent probability level is 80%)



F Appendix

Formula	$C_7H_6O_3$
$D_{calc.}$/ g cm^{-3}	1.414
μ/mm^{-1}	0.953
Formula Weight	138.12
Colour	clear colourless
Shape	needle
Max Size/mm	0.23
Mid Size/mm	0.06
Min Size/mm	0.04
T/K	122.9(2)
Crystal System	monoclinic
Flack Parameter	0.11(11)
Space Group	$P2_1$
a/Å	6.4211(2)
b/Å	5.5763(2)
c/Å	9.0881(3)
α/°	90
β/°	94.595(3)
γ/°	90
V/Å^3	324.362(19)
Z	2
Z'	1
Θ_{min}/°	4.882
Θ_{max}/°	66.588
Measured Refl.	3661
Independent Refl.	1142
Reflections Used	1107
R_{int}	0.0251
Parameters	92
Restraints	1
Largest Peak	0.111
Deepest Hole	-0.140
GooF	1.060
wR_2 (all data)	0.0587
wR_2	0.0580
R_1 (all data)	0.0250
R_1	0.0238

X-ray crystallography structure of **242a** (the ellipsoid contour percent probability level is 50%)



F Appendix

Formula	$C_7H_6O_3$
$D_{calc.}$/ g cm^{-3}	1.342
μ/mm^{-1}	0.904
Formula Weight	138.12
Colour	clear colourless
Shape	plate
Max Size/mm	0.56
Mid Size/mm	0.20
Min Size/mm	0.03
T/K	293(1)
Crystal System	monoclinic
Space Group	$P2_1/c$
a/Å	6.7141(6)
b/Å	5.6388(3)
c/Å	18.1251(12)
α/°	90
β/°	94.998(7)
γ/°	90
V/Å^3	683.59(9)
Z	4
Z'	1
Θ_{min}/°	4.899
Θ_{max}/°	66.647
Measured Refl.	4120
Independent Refl.	1181
Reflections Used	929
R_{int}	0.0485
Parameters	92
Restraints	0
Largest Peak	0.194
Deepest Hole	-0.202
GooF	1.063
wR_2 (all data)	0.1507
wR_2	0.1399
R_1 (all data)	0.0672
R_1	0.0550

5 Curriculum Vitae

Personal data

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Education

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10/2011-09/2013	Advanced studies in chemistry, University of Regensburg, Germany
09/2011	Bachelor of Science in chemistry
10/2008 – 09/2011	Studies in chemistry, University of Regensburg, Germany
09/1997 – 06/2007	Abitur (A-levels), Hertzhaimer-Gymnasium (secondary school), Trostberg, Germany

Publications

Dobler, D.; Reiser, O. *J. Org. Chem.* **2016**, 81, 10357–10365.

"Synthesis of 6-Substituted 2-Pyrones Starting from Renewable Resources: Total Synthesis of Sibirinone, (E)-6-(Pent-1-en-1-yl)-2H-pyran-2-one, and (E)-6-(Hept-1-en-1-yl)-2H-pyran-2-one"

Kastl, B.; **Dobler, D**.; Reiser, O. Manuscript in preparation.

"Stabilized Pd(0) on functionalized magnetic Co/C nanoparticles as an efficient and stable catalyst for hydrogenation of olefins in water"

Dobler, D.; Urlep, M.; Reiser, O. Manuscript in preparation.

"Synthesis of 2H-Pyran-2-one Starting from Renewable Resources"

Conferences

[1] GDCh Wissenschaftsforum, Dresden, Germany, August 30-September 02, 2015

Poster contribution: "Synthesis of 6-substituted 2-pyrones starting from renewable resources"

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I Declaration

Herewith I declare that this present thesis is a presentation of my original work prepared single-handed. Wherever contributions from others are involved, all of them are marked clearly, with reference to the literature, license, and acknowledgment of collaborative research.

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Daniel Dobler