Enantioselective Allylation and Halocyclization of Allyl Hydrazides and Allyl Oximes for the Synthesis of Enantioenriched Pyrazolidines and Isoxazolidines

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Abstract

N,N'-Diprotected hydrazides were synthesized and investigated as nucleophiles for monoallylation in a nucleophilic substitution reaction with (*E*)-cinnamyl bromide. The thus obtained monoallylated compounds were subjected to halocyclization conditions. *trans*-Ethyl 4-bromo-3-phenylpyrazolidine-1-carboxylate was obtained in 33% yield.

Diary ketoximes and symmetrically substituted allylic carbonates or acetates were synthesized and subjected to an asymmetric Tsuji-Trost reaction mediated by palladium-catalysis and the chiral hybrid ligand (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane. The obtained allyl oximes were cyclized with bis(2,4,6-trimethylpyridine)bromine(I) hexafluorophosphate in a diastereoselective halocyclization reaction and the resulting isoxazolidines protected with benzoyl chloride. A "one-pot" protocol for this reaction sequence was developed. The *N*-protected trisubstituted isoxazolidines were obtained in overall yields of 38% to 69% for the three-step transformation and enantiomeric excesses up to 95%.

Erklärung gem. § 5 Abs. 1b Promotionsordnung

Ich versichere an Eides Statt, dass die Dissertation von mir selbständig und ohne unzulässige fremde Hilfe unter Beachtung der „Grundsätze zur Sicherung guter wissenschaftlicher Praxis an der Heinrich-Heine-Universität Düsseldorf“ erstellt worden ist.

Düsseldorf, Dezember 2018

(Jana Reineke)

Für Elise und Christa

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Content

Abbreviations

API	active pharmaceutical ingredient
approx.	approximately
BINOL	1,1'-bi-2-naphthol
$Br^+(coll)_2PF_6^-$	bis(2,4,6-collidine)bromine(I) hexafluorophosphate
coll	2,4,6-collidine
conc.	concentrated
DABCO	1,4-diazabicyclo[2.2.2]octane
dba	(1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one (dibenzylideneacetone)
DIPEA	*N*,*N*-diisopropylethylamine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
dr	diastereomeric ratio
ee	enantiomeric excess
e.g.	for example
EI	electron ionization
ESI	electron spray ionization
equiv	equivalent(s)
er	enantiomeric ratio
IR	infrared spectroscopy
max.	maximum
mp	melting point
MS	mass spectrometry
NBA	*N*-bromo acetamide
nd	not determined
NMR	nuclear magnetic resonance
R_f	retention factor

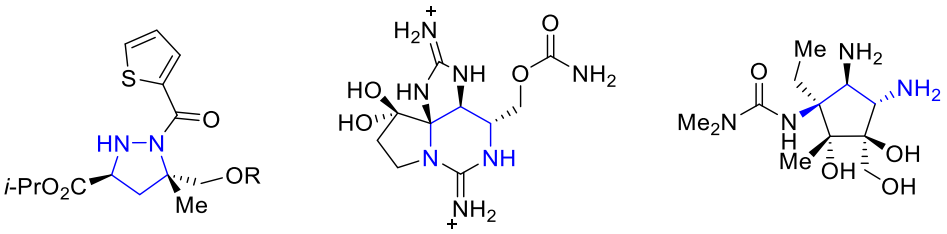
rt	room temperature
TBAF	tetra-*n*-butylammonium fluoride
temp.	temperature
THF	tetrahydrofuran
TLC	thin layer chromatography
t_R	retention time

1 Introduction

Many natural products show interesting biological reactivity and have therefore been a research target as well as an inspiration for organic chemists. Even minor structural variations can turn natural compounds into active pharmaceutical ingredients (API) or have the potential to enhance bioavailability as well as biocompatibility tremendously.[1] Since the possibilities to modify natural products ex post facto are limited, there is an increasing need for flexible synthetic routes that allow for an efficient synthesis of a wide range of derivatives. The vast majority of biological receptors have a unique asymmetrical chiral structure. Therefore, enantiomers most often have distinct physiological activities, requiring new synthetic routes to be highly selective for one of the two enantiomeric structures.[2-4] The development of new stereoselective synthetic strategies, yielding products with excellent selectivity and performance, is in this regard still one of the most important goals in organic chemistry.

1.1 Pyrazolidines

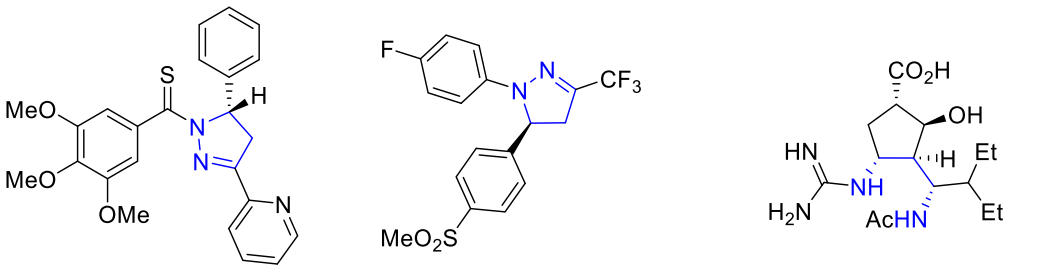
N-Heterocycles are a common structural motif in many natural as well as pharmaceutically active compounds. Pyrazolidines in particular are a prominent and important substructure in medicinal chemistry and accountable for the biological activity of a variety of compounds. In addition they can be oxidized to afford pyrazole as well as pyrazoline rings, which exhibit extraordinary pharmacological activity and have recently also been employed in material science.[5-7] As synthetic intermediates pyrazolidines can also be reductively cleaved into 1,3-diamines, again a widely found motif in natural products (Figure 1). Azaprolines, a term established by Carreira[8] for pyrazolidine- and pyrazoline-derived amino acid analogs, are valuable building blocks for peptidomimetics.[9]



intermediate of Manzacidin C saxitoxin jogyamycin

Figure 1. Examples of Natural Products Containing Pyrazolidine and 1,3-Diamine Structures[10-12]

The benefits of the compounds containing or being derived from pyrazolidine rings range from antibacterial, anti-inflammatory and antiviral to antidepressant, cytostatic, as well as anticonvulsant activities (Figure 2).[13, 14] In contrast to pyrazoles, pyrazoline and pyrazolidine rings contain one to three potential stereocenters. Obviously, this increases the level of difficulty with respect to enantioselective synthesis. Nonetheless, some synthetic routes to enantiomerically-enriched pyrazolidine derivatives have been developed.



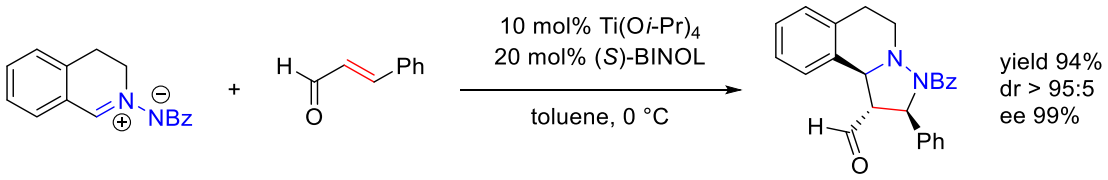
cytostatic activity | anti-inflammatory activity | "Peramivir" anti-influenza drug

Figure 2. Drug Candidates Incorporating Pyrazolidine, Pyrazoline or 1,3-Diamine Moieties[14-16]

1.1.1 Asymmetric Syntheses of Pyrazolidine Derivatives

1.1.1.1 1,3-Dipolar Cycloadditions

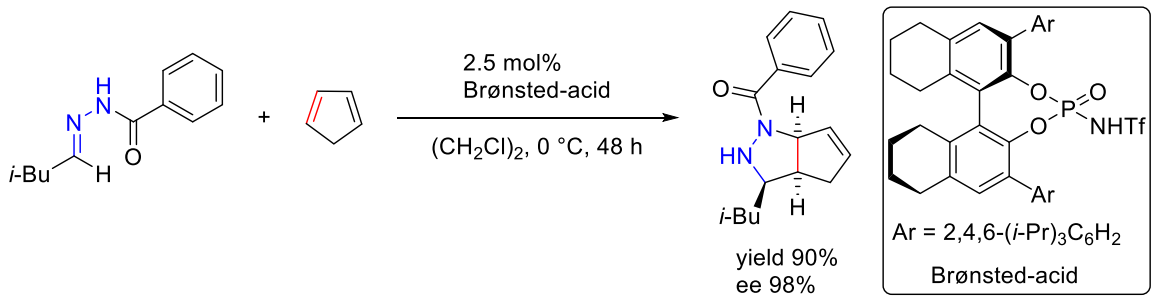
The beginnings of asymmetric pyrazolidine synthesis were dominated by 1,3-dipolar cycloaddition reactions of diazo compounds to alkenes. Diazoalkanes are neither readily available nor easily stored, due to their thermal instability. One of the first asymmetric examples by the Carreira group was the cycloaddition of trimethylsilyl stabilized diazomethane to a range of Oppolzer's chiral sultam derivatives.[8] The enantioselective variations of this route rely foremost on azomethine imines, which are mainly derived from the reaction of pyrazolidine-3-one with aldehydes. Binaphthyldiimine nickel(II) complexes as published by Suga et al.[17] or chiral primary or secondary amines as published by Chen and co-workers[18, 19] are used as catalysts. Examples by Maruoka et al. employ titanium complexes with chiral BINOL ligands as catalysts (Scheme 1).[20, 21]



Scheme 1. Example of an Enantioselective 1,3-Dipolar Cycloaddition of an Azomethine Imine to *trans*-Cinnamaldehyde[20, 21]

1.1.1.2 [3+2]-Cycloadditions

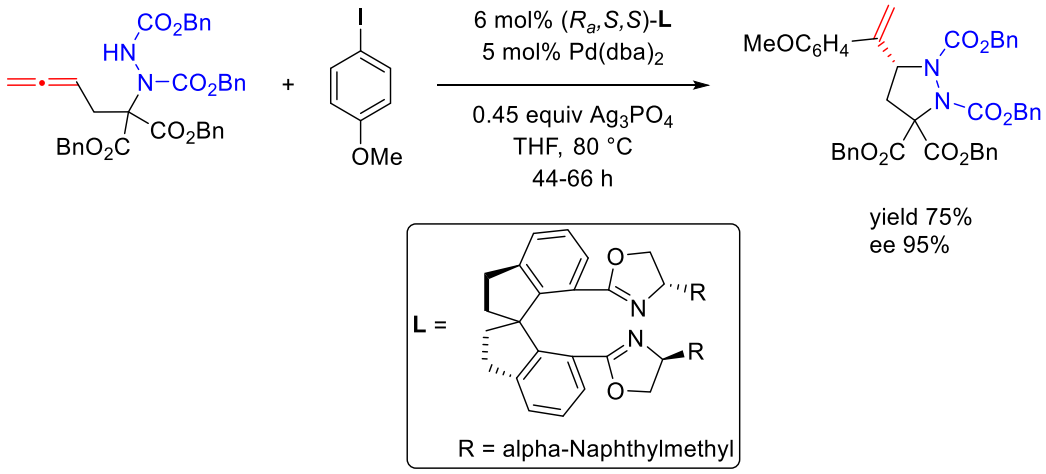
Another cycloaddition route to enantiopure pyrazolidines is the [3+2]-cycloaddition reaction of hydrazones with alkenes. It was first described by the Kobayashi group[22, 23] as reacting hydrazones with ketene dithioacetals or vinyl ethers in the presence of chiral Lewis acidic zirconium-BINOL catalysts. Leighton et al.[24] published a related cycloaddition of acylhydrazones with enol ethers brought about by the addition of 1.5 equivalents of chiral silicone-based Lewis acids. Another approach employing a BINOL-phosphate-derived Lewis acid catalyst was reported by Tsogoeva et al.[25]. An organocatalytic variation, namely a Brønsted-acid catalyzed cycloaddition of *N*-benzoylhydrazones and cyclopentadiene or α-methylstyrenes was recently conducted by Rueping et al.[26] (Scheme 2).



Scheme 2. Example of an Enantioselective [3+2]-Cycloaddition of an *N*-Benzoylhydrazone with Cyclopentadiene[26]

1.1.1.3 Metal-Catalyzed Aminations and Cyclization of Allenes

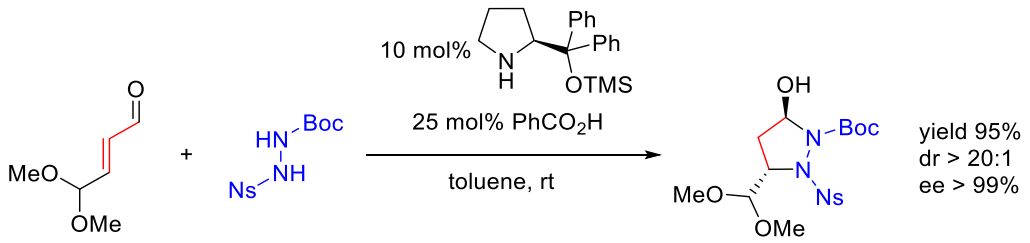
The enantioselective synthesis of pyrazolidines by metal-catalyzed amination and cyclization of allenes was first reported by Ma et al.[27-29] employing copper for the amination and palladium as well as a variety of bisoxazoline ligands for the selective cyclization of the thus generated hydrazine allene compound (Scheme 3). Thereafter, the Toste group[30] applied this strategy to gold(I)-catalysis. In combination with BINAP as ligand they reached up to 98% yield and 99% enantiomeric excess.



Scheme 3. Example of an Enantioselective Synthesis of Pyrazolidine by Palladium-Catalyzed Cyclization[29]

1.1.1.4 Cascade aza-Michael/Hemiaminal Reaction

Since the research field of organocatalysis has been growing rapidly over the past decade, it is not surprising that besides the cycloaddition reactions there is as well an organocatalytic approach towards the synthesis of enantiopure pyrazolidines. It is based on the double addition of disubstituted hydrazides to α,β-unsaturated aldehydes in a cascade aza-Michael/hemiaminal reaction. This setting was almost simultaneously published by Wang et al.[31], Córdova et al.[13] as well as Vicario and co-workers[32]. All employed secondary amines as catalysts, consistently identifying diphenylprolinol trimethyl silyl ether as the most potent derivative (Scheme 4).



Scheme 4. Example of an Enantioselective Cascade aza-Michael/Hemiacetal Reaction[32]

1.2 Isoxazolidines

Isoxazolidines as *N,O*-heterocycles with neighboring nitrogen and oxygen atoms exclusively appear as fused bicyclic ring systems in natural products and are mostly alkaloids originating from marine sponges, plants or fungal metabolites (Figure 3).[33] Zetekitoxin AB as the first isolated isoxazolidine-containing alkaloid obtained from the skin of the Panamanian golden frog is one of the few examples of animal origin.[34] The first structurally described isoxazolidine alkaloid is a slightly more complex analogue of dactylicapnosinine, both isolable from a Chinese medicinal plant.[35]

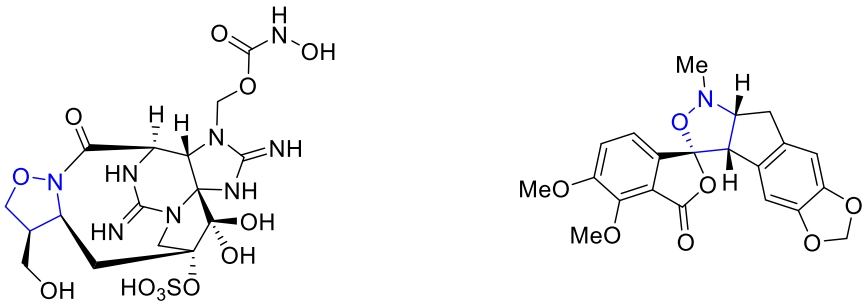


Figure 3. Examples of Natural Products Containing the Isoxazolidine Motif[33]

Isoxazolidines are significant motifs in API development despite the labile nature of the *N-O* bond. The interest in these structures is enhanced by the diversity of biological activities since isoxazolidines mimic a multitude of natural building blocks.[33] Among multiple biological activities exhibited by isoxazolidine derivatives, the most prominent are cytostatic, antiviral, antifungal and anti-inflammatory properties (Figure 4).

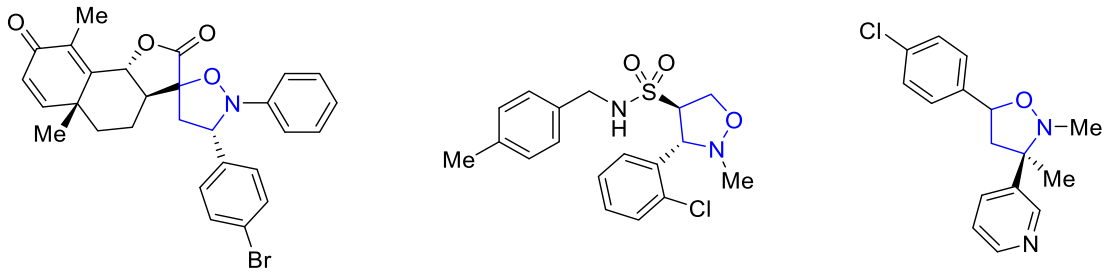
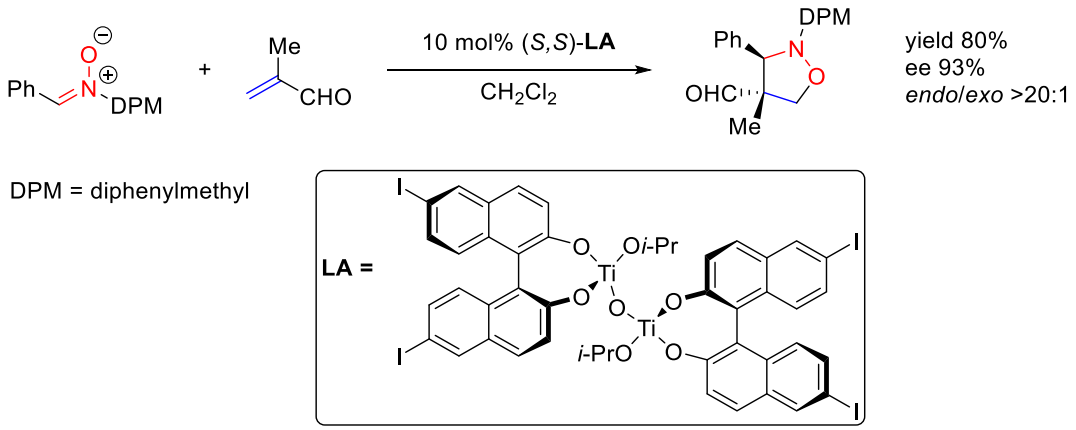


Figure 4. Drug Candidates Incorporating the Isoxazolidine Moiety[33]

1.2.1 Asymmetric Syntheses of Isoxazolidine Derivatives

1.2.1.1 1,3-Dipolar Cycloadditions

Like the pyrazolidine motif the isoxazolidine structure contains three potential stereocenters rendering the preparation of enantiopure compounds challenging. The most developed reaction to synthesize isoxazolidines is by far the 1,3-dipolar cycloaddition reaction of nitrones and alkenes. Asymmetric versions range from vinyl ethers as electron-rich to enons as electron-poor dipolarophiles employing cyclic as well as acyclic structures and all kinds of catalytic systems.[33] "Green protocols" as well as microwave-assisted syntheses and solvent free reaction conditions are well established. Maruoka et al.[36] reacted methacrolein with nitrones catalyzed by a chiral bis-titanium Lewis acid achieving 3,4-*endo* selectivity and high enantiomeric excesses for the resulting all-carbon quaternary stereocenters (Scheme 5).

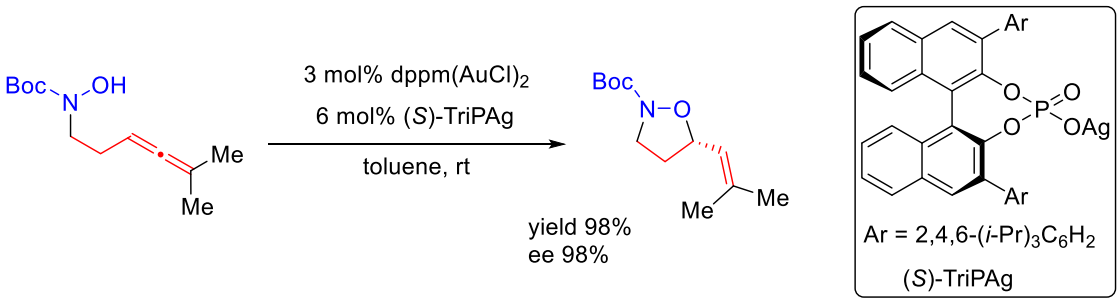


Scheme 5. Asymmetric 1,3-Dipolar Cycloaddition of Methacrolein with (*Z*)-*N*-Benzhydryl-1-phenylmethanimine Oxide by Maruoka et al.[36]

In this case the diphenylmethyl protecting group on nitrogen can be removed quantitatively by treatment with sodium borohydride.[36] This is remarkable since syntheses of isoxazolidines carrying removable *N*-protecting groups in 1,3-dipolar cycloaddition reactions is difficult due to the low stability of the corresponding nitrones. To circumvent this problem other synthetic strategies were developed.

1.2.1.2 Cyclizations of Unsaturated Hydroxylamines

The second important method is the cyclization reaction of unsaturated hydroxylamines, which is emerging as a complementary intramolecular alternative for the synthesis of a wide variety of isoxazolidines.[33, 37] These cyclization reactions can be conducted by electrophilic cyclization[38, 39] or metal catalysis, mainly palladium catalysis[40-43], copper catalysis[37] or a combination of both[44]. Recently Cossy et al.[45] published an iron-catalyzed methodology. These cyclization reactions are mostly diastereoselective. The before-mentioned gold-catalyzed pyrazolidine synthesis developed by Toste et al.[30] is also applicable for the synthesis of isoxazolidines and one of the few enantioselective examples of this approach (Scheme 6).

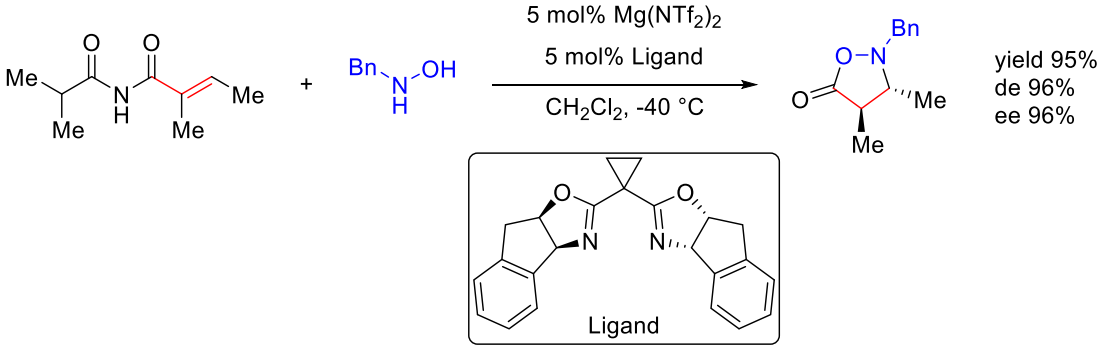


Scheme 6. Gold Catalyzed Cyclization by Intramolecular Addition of a Hydroxylamine to an Allene

1.2.1.3 Catalytic Reactions between *N*-Protected Hydroxylamines and α,β-Unsaturated Carbonyl Compounds

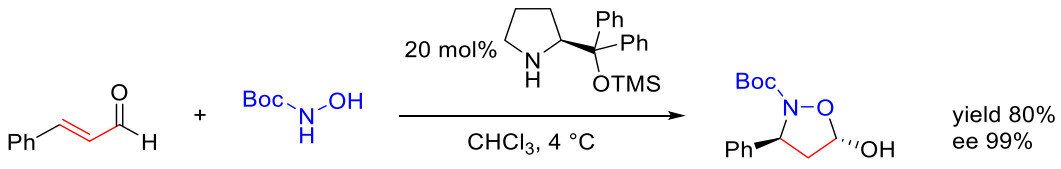
Sibi et al.[46] developed an enantioselective conjugate addition of hydroxyl amines to α,β-unsaturated amides catalyzed by a Lewis acidic Mg-complex (Scheme 7). The resulting 5-isoxazolidinones, which are of great importance as chiral building blocks[47], were obtained with moderate to excellent enantiomeric excess values. Furthermore, they can be easily

converted into the corresponding substituted β-amino acids by simple catalytic hydrogenolysis.



Scheme 7. Chiral Lewis Acid-Mediated Conjugate Amine Addition

As shown for the pyrazolidine synthesis organocatalytic approaches have proven to be of great use in asymmetric transformations. This is also the case for the asymmetric isoxazolidine syntheses. A reaction sequence by MacMillan et al.[48] employs an imidazolidinone catalyst for the enantioselective coupling of α,β-unsaturated aldehydes with *N*-protected *tert*-butyldimethylsilyloxycarbamates. The silyl ether is subsequently deprotected with TBAF leading to cyclization by intramolecular oxy-Michael addition. This procedure affords isoxazolidines in moderate to excellent yields with enantiomeric excesses up to 97%. Córdova and co-workers[49] recently developed a chemo- and enantioselective organocatalytic tandem reaction between *N*-protected hydroxyl amines and α,β-unsaturated aldehydes (Scheme 8). As seen before, diphenylprolinol trimethyl silyl ether turned out to be most useful as a catalyst reaching enantiomeric excesses up to 99%.



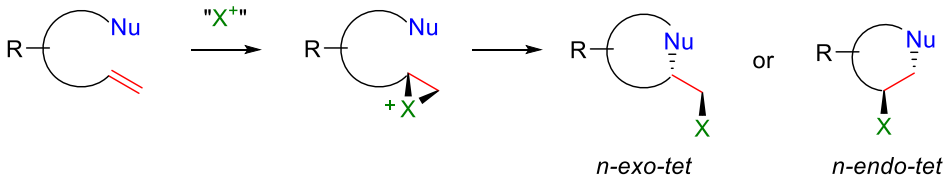
Scheme 8. Organocatalytic Reaction Between an *N*-Protected Hydroxylamine and an α,β-Unsaturated Aldehyde

1.3 Halocyclization

One of the fundamental reactions in organic chemistry is the addition of electrophiles to carbon-carbon multiple bonds. The halocyclization reaction as an electrophilic cyclization reaction is an intramolecular version, namely a halofunctionalization of alkenes or alkynes.

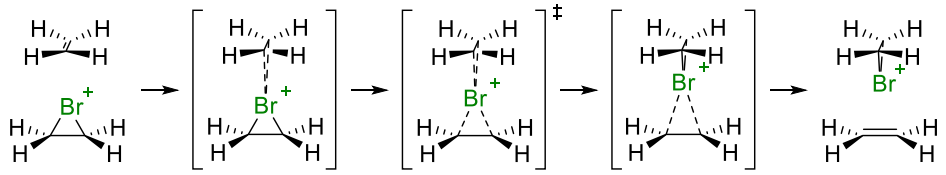
1.3.1 Mechanistic Aspects

The C-C multiple bond is formally activated by a halonium ion ("X^+"), followed in general by the formation of a cyclic haliranium ion or in case of fluorine and some chlorine analogues an acyclic β-halocarbenium ion.[50] The haliranium ion is then opened in a substitution reaction by an internal nucleophile (S_N2 mechanism) leading to cyclization (Scheme 9).



Scheme 9. Mechanism of the Halocyclization of an Alkene[51]

All cases involving a cyclic haliranium ion transition state result in a stereospecific 1,2-*anti* addition product with respect to halogen and nucleophile. Brown and co-workers analyzed an adamantylidene adamantane system and the respective isolable bromiranium as well as iodiranium ions by variable-temperature ^{1}H NMR spectroscopy and found evidence of a rapid, degenerate olefin-to-olefin transfer process (Scheme 10).[52-54] This transfer process is responsible for the challenge posed to enantioselective halofunctionalizations, since nucleophilic capture needs to be faster than the transfer process in order to prevent racemization of the enantiomerically enriched haliranium ions. In this regard, intramolecular halocyclizations are favored due to the spatial proximity.



Scheme 10. Mechanism of the Transfer Process Exemplified by a Bromiranium Ion[50]

1.3.2 Electrophilic Halogenating Agents

Although the first examples of halocyclization reactions were carried out with elementary halogens, this approach is not entirely convenient. Elementary halogens are highly reactive, volatile and, except for iodine, also toxic. Therefore, the invention of electrophilic halogenating agents greatly prompted the utility of halocyclization reactions.[55] The most utilized reagents are succinimides, *N*-iodo- (NIS), *N*-bromo- (NBS) and *N*-chlorosuccinimide (NCS), and the corresponding phthalimides or hydantoin derivatives, like 1,3-dichloro-5,5-dimethylhydantoin (DCDMH) or 1,3-dichloro-5,5-diphenylhydantoin (DCDPH) (Figure 5). For bromocyclizations, *N*-bromoacetamide (NBA) is also frequently employed. Another method for stabilizing cationic bromonium and iodonium ions is the ligation with sterically demanding 2,4,6-collidine in combination with a non-coordinating anion like hexafluorophosphate. For these reagents dissociation of one amine ligand proceeds the electrophilic activation, which is usually the rate determining step.[56]

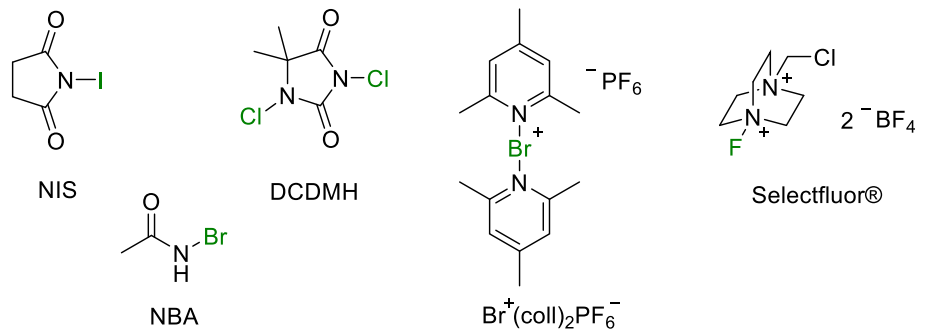
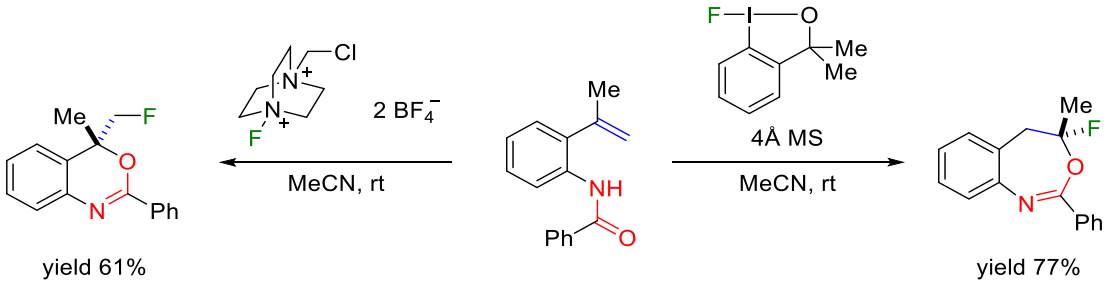


Figure 5. Examples of Common Electrophilic Halogen Sources

Selectfluor®, a DABCO analog first described by Banks et al.[57] is generally used as the electrophilic fluorine source in fluorocyclizations. A more recent approach which is also applicable for fluorocyclizations was developed by Gulder et al.[58, 59] and employs hypervalent (λ^3)-iodine compounds (Scheme 11). This specific fluorocyclization is promoted by a bench-stable, crystalline fluoro benziodoxole which was first synthesized nearly simultaneously by Tongi et al.[60] and Stuart et al.[61].

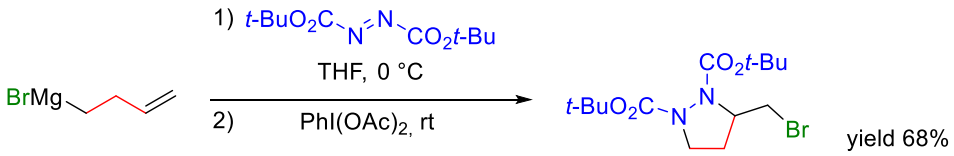


Scheme 11. Comparison of Fluorocyclization with Selectfluor® and a (λ^3)-Hypervalent Iodine Compound

Although the mechanism follows presumably a complex fluorination/1,2-aryl migration/cyclization cascade the product formally represents a 7-*endo* cyclization product where Selectfluor® exhibits 6-*exo* selectivity. In terms of reactivity, iodine is the most reactive towards electrophilic halogenation of alkenes, followed by bromine and chlorine in accordance with their polarizability.[55] The same applies for their reactivity as leaving groups in an S_N2 replacement.

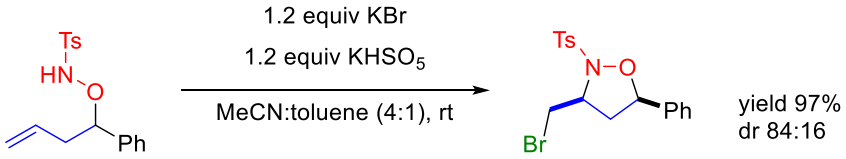
1.3.3 Choice of Nucleophile

The first halocyclization reactions were already established at the beginning of the last century. Bougault[62] and Stobbe[63] developed the transformation reaction of unsaturated carboxylic acids into iodo- and bromolactones, namely halolactonizations which are still the most prominent examples of halocyclizations.[64] The diversity of this reaction was confirmed when other *O*- or *N*-nucleophiles were employed, rendering access to a variety of heterocycles based on the choice of nucleophile. For the development of haloaminocyclizations, the choice of compatible protecting groups on the nucleophilic nitrogen turned out to be crucial. Ester and sulfonyl groups proved to be useful in many cases.[64] In light of the wide variety of halocyclization reactions, surprisingly there are rather few examples where nucleophiles activated by an α-effect, such as oximes[65-67], oxime ethers[68], hydroxylamines[69] and hydrazines[70] have been used in halocyclization reactions yielding oxazoles, isoxazolidines, pyrazoles[71] and pyrazolidines. The α-effect refers to the observation that nucleophiles carrying a neighboring heteroatom often exceed the kinetic reactivity deduced form their Brønsted basicity.[72] The attempts made for halocyclization with these nucleophiles mostly rendered achiral or racemic products. An example employing a hydrazide nucleophile is the one-pot bromocyclization of a Grignard-alkenyl compound with azodicarboxylate yielding a pyrazolidine in a 5-*exo* cyclization by Yamamoto and Tomioka et al.[70] (Scheme 12).



Scheme 12. One-Pot Bromocyclization of a Grignard-Alkenyl Compound with Azodicarboxylate[70]

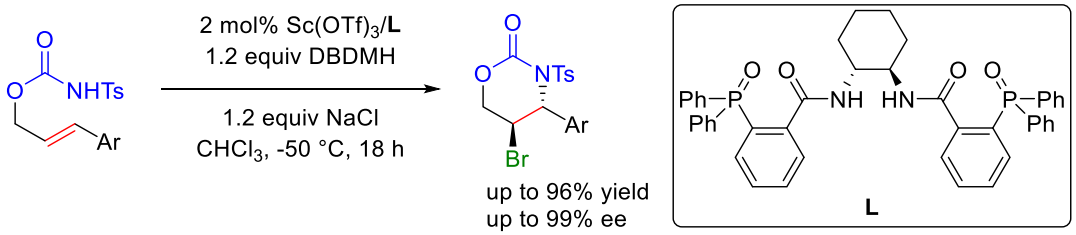
In case of isoxazolidine synthesis two scenarios are possible employing either an *N*- or an *O*-nucleophile. An *N*-nucleophile approach by Togo et al.[73] gives several isoxazolidines in good yields and good diastereoselectivities using the umpolung of alkali metal bromides with Oxone® to generate the bromonium ion (Scheme 13).



Scheme 13. 5-*exo* Cyclization Using the Umpolung of Alkali Metal Bromides with Potassium Peroxymonosulfate for the Isoxazolidine Synthesis

1.3.4 Asymmetric Halocyclization

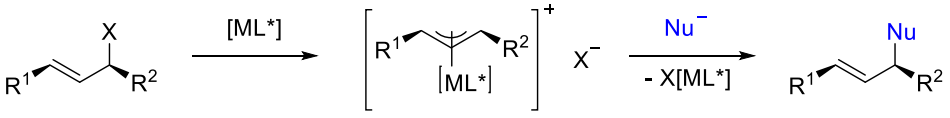
More than 4700 natural products carry halogen atoms, of which about half are bound to a sp^3-configured carbon atom, therefore a potential stereo center.[74] These numbers illustrate the potential of halogenated compounds with respect to the development of APIs, and the increasing emphasis on the development of asymmetric halogenation strategies. Furthermore, halogen-substituted compounds are reactive substrates for substitution as well as cross-coupling reactions. Halocyclization reactions introduce halogen atoms, while simultaneously adding an additional functional group, creating a ring and two new stereocenters. Therefore, these reactions are a useful tool for the preparation of halogenated heterocycles destined to be of use in a pharmaceutical context. Recently, Shi et al.[75] published the highly regio- and enantioselective bromoamidocyclization of (*E*)-cinnamyl tosylcarbamates. They employed a scandium catalyst in combination with a chiral phosphine oxide Trost-type ligand (Scheme 14). This approach based on a *N*-nucleophilic attack of the bromiranium ion results in 5-bromo-1,3-oxazinan-2-ones with two adjacent stereocenters.



Scheme 14. Enantioselective Bromoamidocyclization of (*E*)-Cinnamyl Tosylcarbamates[75]

1.4 Asymmetric Allylic Substitution

Transition metal-catalyzed reactions are greatly utilized in organic chemistry. Especially with respect to the efficient and reliable induction of chirality, they are unrivaled due to the multitude of possibilities of combining a transition metal with a chiral ligand. In this regard the selectivity of an allylic substitution reaction is influenced by several factors, namely the metal ion, the ligands but also the nucleophile, the leaving group and the substituents of the allylic system. Most allylic substitution reactions are either catalyzed by palladium or iridium complexes. The choice of nucleophile has a particular impact on the stereochemical outcome since the employment of a “hard” or “soft” nucleophile influences the reaction mechanism.[76] For “soft” nucleophiles the displacement of the leaving group by the metal catalyst as well as the preceding nucleophilic attack happen in an S_N2 fashion with an overall retention of configuration (Scheme 15).



X = OAc, OCO_2Me, Halides etc.

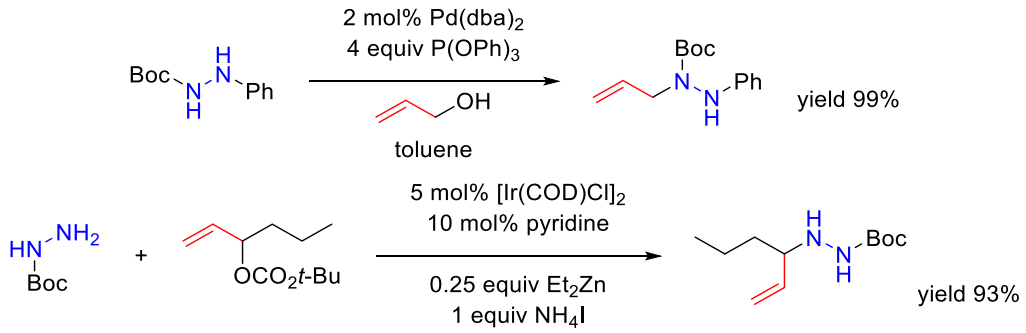
Scheme 15. Allylic Substitution via π-Allyl Complexes for “Soft” Nucleophiles

The metal catalyst and the chiral ligand are therefore separated from the leaving group and nucleophile, rendering enantioselective variations challenging. Regarding the regioselectivity for mono-substituted allyl derivatives, palladium-catalyzed reactions usually result in linear, achiral products while iridium catalysts render branched, chiral products.[77] For unsymmetrically substituted allyl derivatives, reactions were frequently not simultaneously

regio- and enantioselective; however, recent progress in the development of new chiral ligands seems promising.[78] The first enantioselective palladium-catalyzed allylic substitution reaction was reported in 1977 by Trost et al.[79], giving way to the development of a multitude of strategies regarding the enantioselective transition metal catalyzed allylic alkylation. These reactions therefore provide a great tool-box for introducing stereocenters in the perspective of natural and pharmaceutical product synthesis.

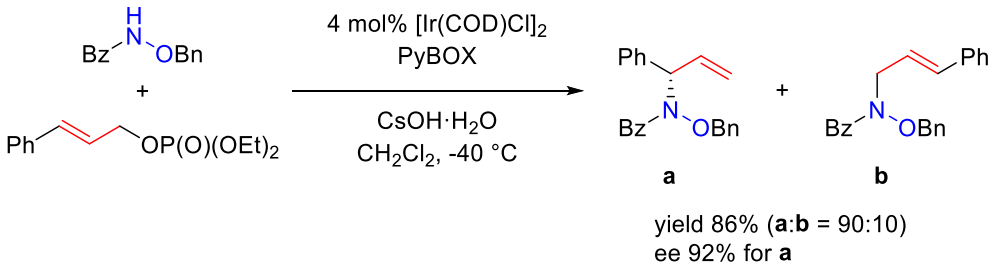
1.4.1 Enantioselective Substrate Synthesis

For an enantioselective route to pyrazolidines and isoxazolidines stereoselective syntheses for chiral allyl hydrazide and allyl hydroxylamine substrates needed to be developed. Hydrazides have been applied as nucleophiles in non-stereoselective palladium-[80] as well as iridium-catalyzed[81] allylation reactions (Scheme 16).



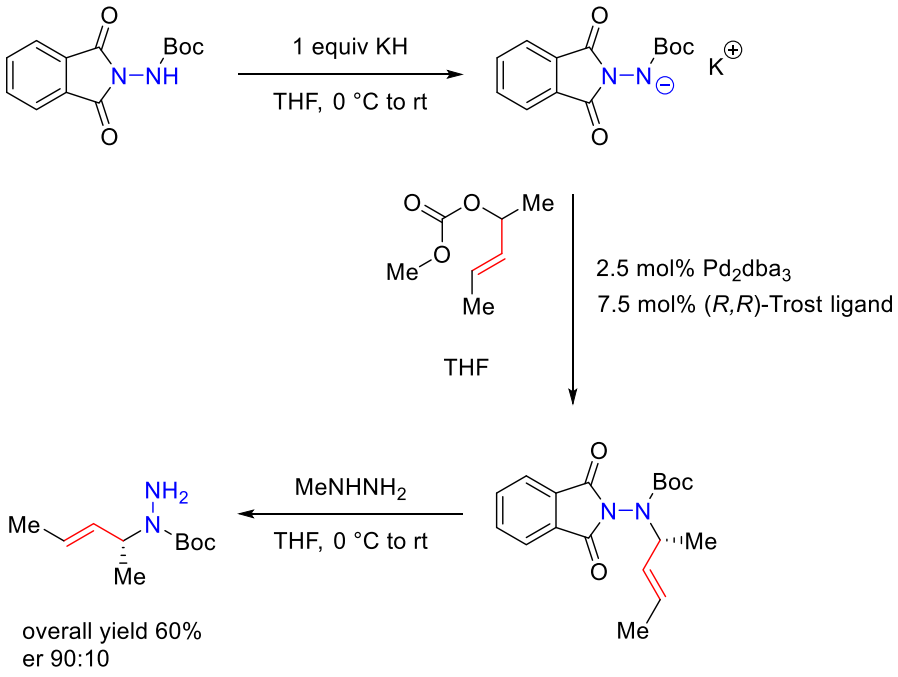
Scheme 16. Examples of Palladium- and Iridium-Catalyzed Allylic Alkylations with Hydrazine Nucleophiles

Since iridium catalysts are known to give branched products in allylic substitution reactions, iridium catalysis opens a route to chiral substrates starting from achiral allylic compounds. Employing a PyBOX ligand, chiral allylic hydroxylamine derivatives have been synthesized by the Takemoto group, with both high regio- and enantioselectivity (Scheme 17).[82]



Scheme 17. Example of Regio- and Enantioselective Iridium Catalysis[82]

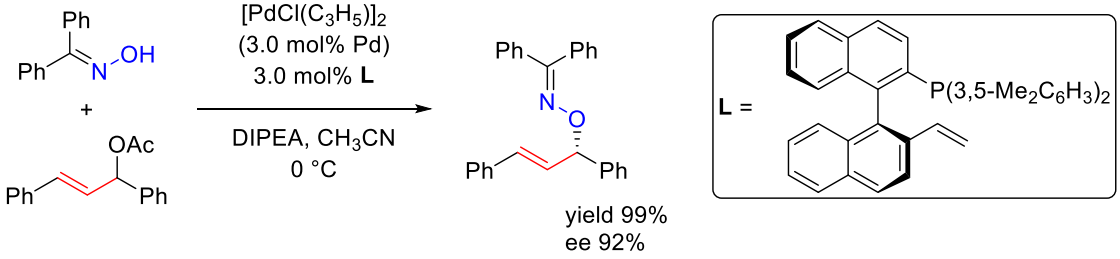
For symmetrically substituted allyl derivatives, an enantioselective allylation is less challenging, as there is no concern about regioselectivity. One of the potential enantioenriched substrates regarding the halocyclization of hydrazines could possibly be obtained by palladium-catalyzed allylation, with Pd_2dba_3 as the palladium(0) source in combination with the (*R,R*)-configured Trost ligand as proposed by Thomson et al.[83] (Scheme 18).



Scheme 18. Synthetic Route to Enantioenriched Allyl Hydrazides[83]

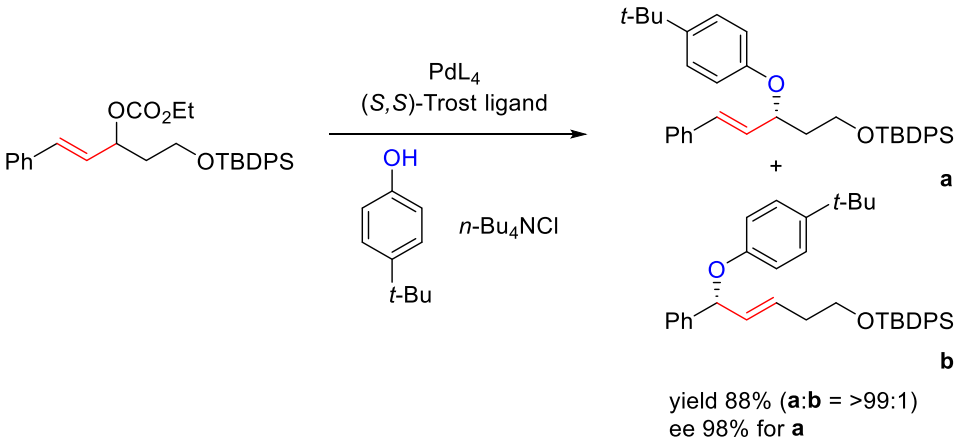
An approach for the desymmetrization of symmetrically phenyl-substituted allyl derivatives is an asymmetric allylic etherization reaction published by Du et al.[84] (Scheme 19). The

palladium-catalyzed reaction employs chiral alkene-phosphine hybrid ligands developed by the group[85] and oximes as nucleophiles.



Scheme 19. Asymmetric Allylic Etherization with Oximes by Du et al.[84]

For the symmetrically substituted allylic substrates, palladium catalysis is typically superior. Carbonates as leaving groups have the advantage of liberating the corresponding alkoxide upon addition of the palladium complex. This alkoxide is able to deprotonate the nucleophilic reaction partner rendering the addition of a supplementary base redundant.



Scheme 20. Example for Regio- and Stereocontrolled Allylation of Unsymmetrically 1,3-Disubstituted Substrates

The enantioselective synthesis of unsymmetrically 1,3-disubstituted chiral substrates for halocyclization constitutes the most challenging variation involving regio- and stereocontrol. A rather successful attempt was made by Hoberg et al.[86] using oxygen nucleophiles (Scheme 20).

Apart from the ligands mentioned thus far, multitudes of other chiral ligands exist, that might be similarly suitable for asymmetric allylation reactions (Figure 6).

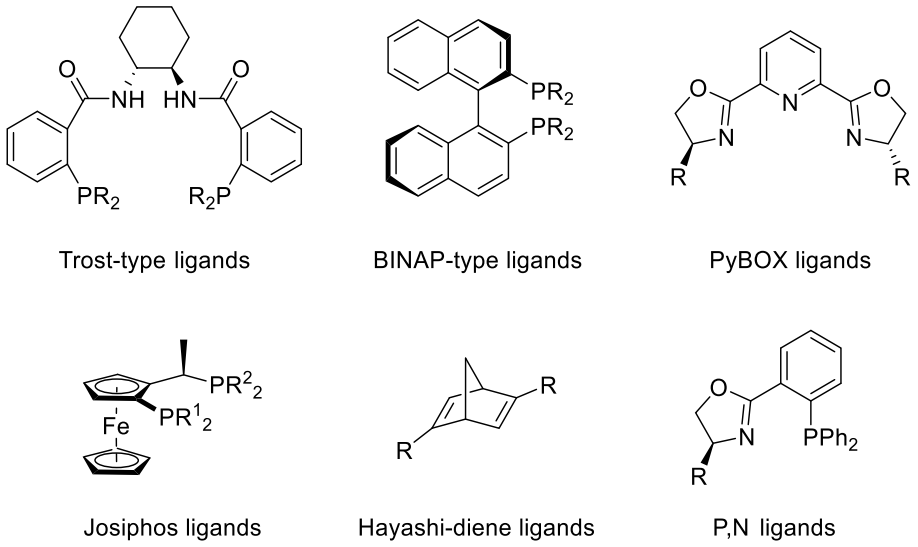
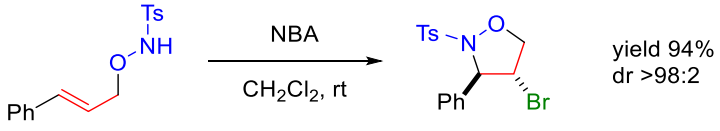


Figure 6. Examples of Chiral Ligands Used in Allylic Alkylation Reactions[76]

1.5 Preliminary Work

1.5.1 Diastereoselective Synthesis of Bromo-Isoxazolidines

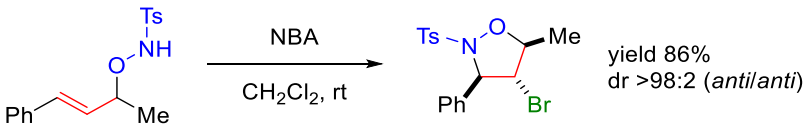
In 2013, Czekelius et al.[87] published the diastereoselective bromocyclization of *O*-allyl-*N*-tosyl-hydroxylamines to afford bromo-isoxazolidines (Scheme 21). It is one of the few examples employing hydroxylamines as an *N*-nucleophile activated by an α-effect in halocyclizations.



Scheme 21. Diastereoselective Synthesis of Bromoisoxazolidines with NBA[87]

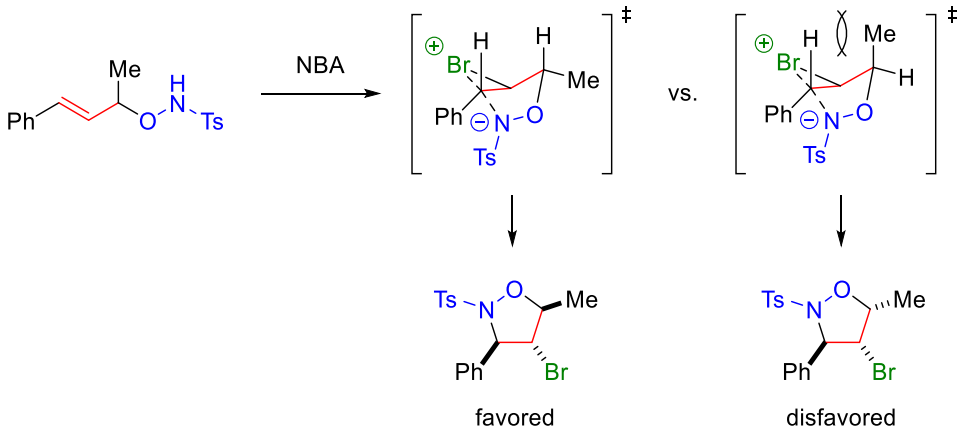
Different electrophile sources and solvents were examined for the cyclization of an achiral *trans*-crotyl-hydroxylamine. The diastereomeric ratio was determined by ^{1}H NMR

spectroscopy as greater than 98:2. The assumed *anti*-addition resulting in a *trans*-configuration of the phenyl- and bromo-substituent was confirmed by X-ray analysis. Regarding the versatility of the reaction, attempts to cyclize several substrates under the determined conditions were made. Electron-rich aromatic systems are readily cyclized, while an electron-deficient *p*-NO_2-phenyl-substituent prevents cyclization, confirming the electrophilic activation of the alkene. *cis*-Styrene derivatives need longer reaction times, allegedly due to an $A^{1,3}$-strain, but still result consistently in *cis*-aryl-bromo-isoxazolidines.



Scheme 22. Influence of an Existing Stereocenter on the Stereochemical Outcome[87]

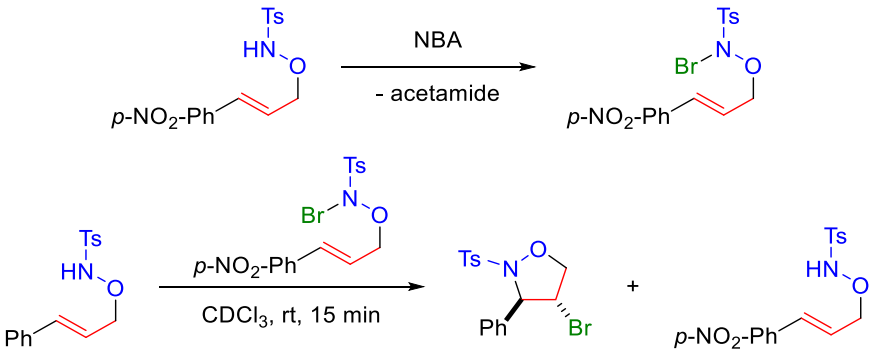
In all cases, a single diastereomer was formed, proving the underlying concept of a *trans*-addition by S_N2-attack of a cyclic bromiranium intermediate. Further evidence of a highly diastereoselective reaction was derived from the cyclization of a chiral substrate resulting in a single diastereomer (Scheme 22). This outcome is supposedly the result of a steric disadvantage of one of the two transition states (Scheme 23).



Scheme 23. Rationale for the Stereochemical Outcome of the Cyclization of Chiral Substrates[87]

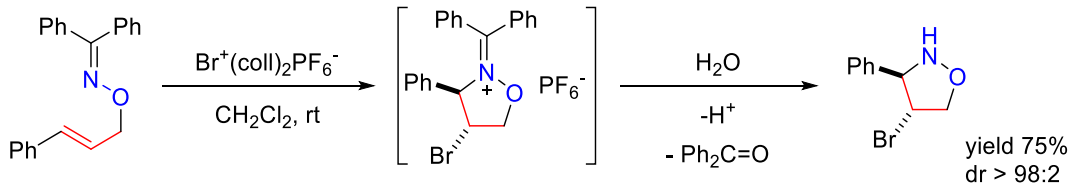
The mechanism of the bromocyclization was analyzed by ^1H NMR spectroscopy of the achiral *trans*-*p*-NO_2-phenyl-substituted substrate (Scheme 24). Upon addition of 1.0 equivalents of NBA a *N*-brominated hydroxylamine derivative is formed, which does not

undergo cyclization and can be isolated. The reaction of this intermediate with *trans*-crotyl-hydroxylamine leads within 15 minutes to the formation of the corresponding phenyl-substituted isoxazolidine with simultaneous back formation of the *trans*-*p*-NO_2-phenyl-alkene. These observations suggest that the acidic amide-proton is replaced by the electrophilic bromine, forming a *N*-bromo-species first. Secondly, this species undergoes either intra- or intermolecular bromination of the alkene, resulting in a bromonium intermediate which renders the final product by nucleophilic ring-opening.



Scheme 24. Intermolecular Bromination by Bromonium Transfer from an *N*-Bromo-hydroxylamine[87]

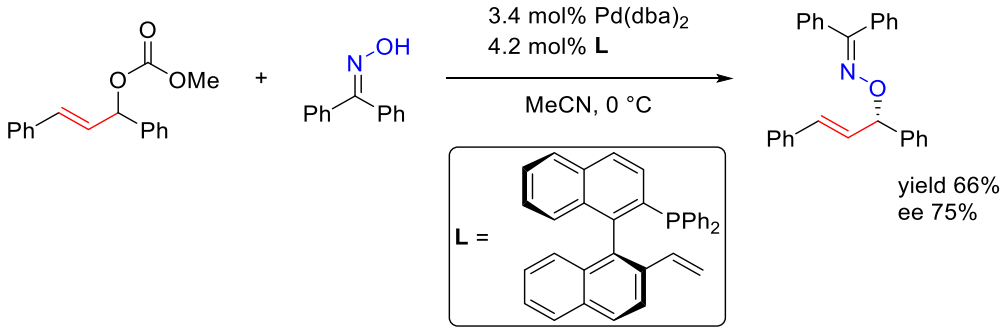
An unprotected isoxazolidine derivative was further obtained by cyclization of an *O*-allylic ketoxime with $Br^+(coll)_2PF_6^-$ as brominating reagent and subsequent hydrolysis of the formed isoxazolidinium salt intermediate (Scheme 25).[88] Two further ketoximes and halogenating agents were tested, but the cyclization of a benzophenone oxime substrate in combination with $Br^+(coll)_2PF_6^-$ gave the best result. *O*-Allylic aldoximes were also tested, affording dihydro-4*H*-1,3-dioxazine in excellent yields.



Scheme 25. Synthesis of an Unprotected Isoxazolidine by Bromocyclization of an *O*-Allylic Ketoxime

1.5.2 Stereoselective Allylation of Hydroxylamine Derivatives

F. Severin[89] investigated the stereoselective allylation of hydroxylamine derivatives in the context of a master thesis. Several allyl carbonates were synthesized as substrates for a palladium-catalyzed Tsuji-Trost allylation. Since *N*-tosyl-*N*-boc-hydroxylamine turned out to be too susceptible to decomposition, benzophenone oxime was sought out as the nucleophilic reaction partner. An enantioselective transformation according to Du et al.[84] was attempted employing a hybrid alkene-phosphine ligand. In case of an symmetrically substituted allyl carbonate an enantiomeric excess of 75% could be obtained (Scheme 26), which turned out to be inferior to the enantiomeric excess reached by Du and co-workers[84]. Unsymmetrically substituted allyl systems were subjected to the reaction conditions as well but regioselectivity turned out to be a great challenge especially concerning separation of the formed regioisomers.

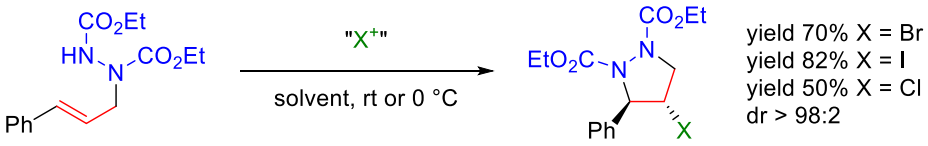


Scheme 26. Enantioselective Palladium-Catalyzed Allylation of Benzophenone Oxime Employing a Symmetrically Substituted Allyl Carbonate[89]

1.5.3 Synthesis of Pyrazolidines by Halocyclization

In the context of a master thesis by Mechsner[90] in our group, the halocyclization of *trans*-cinnamylhydrazides was investigated (Scheme 27). As mentioned above, the protection group can have a significant impact on haloamination reactions. While tosyl-protected *trans*-cinnamylhydrazide gave no cyclization product after three days in several solvents, the ethoxycarbonyl hydrazide analogs readily cyclized under most reaction conditions. Several solvents as well as electrophilic halogenating agents were tested. While acetone turned out to be the best solvent for the bromocyclization in combination with NBA and for the iodocyclization in combination with $I^+(coll)_2PF_6^-$, acetonitrile was favored in the

case of chlorocyclizations brought about by DCDMH. Selectfluor® was also tested, but its application did not result in formation of the desired fluorinated cyclization product.



Scheme 27. Diastereoselective Halocyclization of an Allyl Hydrazide[90]

The 5-*endo* products were isolated in medium to good yields. The diastereomeric ratio was determined by ^{1}H NMR spectroscopy, showing excellent selectivity. The dominating diastereomeric outcome, the *trans*-product, was predicted by assumption of an *anti*-addition mechanism considering formerly published results from our group on the diastereoselective synthesis of isoxazolidines.

1.6 Research Questions and Methodology

Introducing the halocyclization of allyl hydroxylamines, allyl oximes and one allyl hydrazide derivative were the first steps towards a more thorough investigation of these halocyclization reactions as a source of pharmaceutically active isoxazolidine and pyrazolidine derivatives. Based on these results, an enantioselective version of these methods shall be investigated, providing a new tool for the selective preparation of these compounds. Combining the approach of a stereoselective allylation, generating enantiopure allyl oximes, and a diastereoselective halocyclization of the thus obtained allyl oximes shall render a broad and generally applicable approach towards enantioselective isoxazolidine and pyrazolidine synthesis, resulting in up to three adjacent stereocenters.

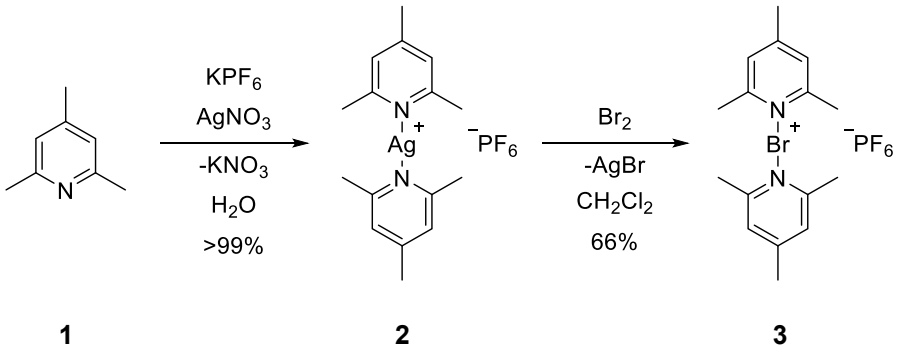
2 Results and Discussion

2.1 Brominating Reagents and Ligands

2.1.1. Bis(2,4,6-trimethylpyridine)bromine(I) Hexafluorophosphate

B. Egart[88] showed that $Br^+(coll)_2PF_6^-$ is most useful in halocyclization reactions of allyl oximes (Scheme 25). Advantages of this reagent are especially the ease of use, low hygroscopicity and toxicity.[91] Furthermore, it has proven to be an effective reagent even for reactions that are difficult or impossible to achieve with other known halogenating agents.[3]

Synthesis of this versatile reagent is accomplished in two steps according to Rousseau et al.[91] (Scheme 28). In the first step the silver complex **2** is generated by slow addition of 2,4,6-collidine (**1**) to a solution of silver(I) nitrate and potassium hexafluorophosphate in water. Since silver compounds are very sensitive to light, exposure should be kept to a minimum. Upon addition of bromine the silver(I) cation is then substituted by a bromonium ion. Driving force for this substitution reaction is the simultaneous silver(I) bromide salt formation.



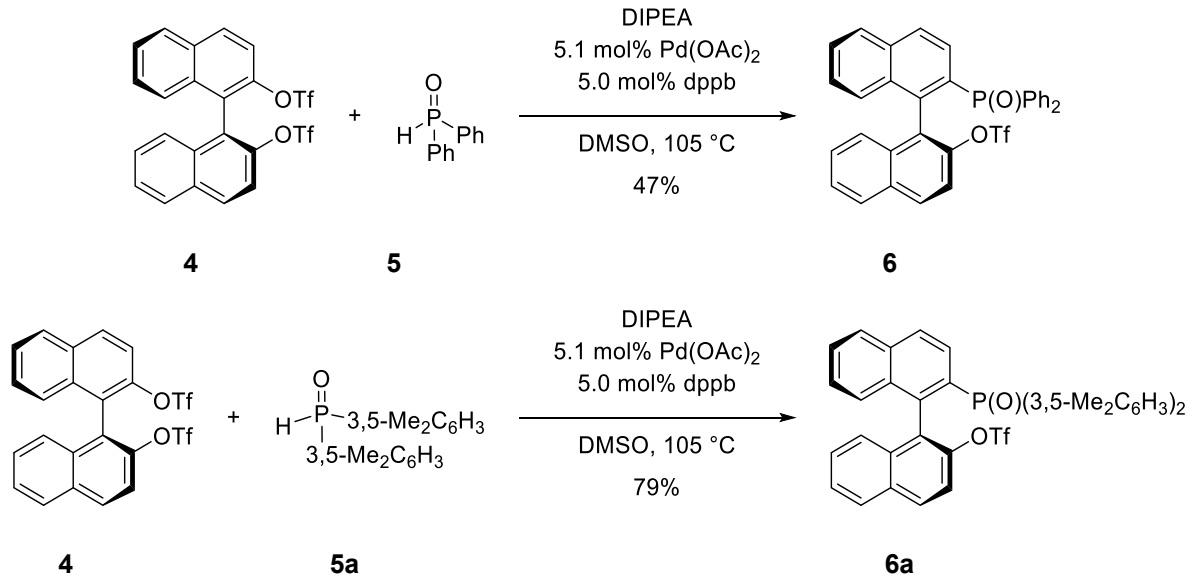
Scheme 28. Synthesis of Bis(2,4,6-trimethylpyridine)bromine(I) Hexafluorophosphate (**3**)

2.1.2. Chiral Hybrid Alkene-Phosphine Ligand

One of the great challenges in enantioselective catalysis is the identification of suitable chiral ligands. Du et al.[85, 92] developed alkene-phosphine hybrid ligands exhibiting high activity and also selectivity in palladium-catalyzed asymmetric allylic substitution reactions. Especially the BINOL-derived ligands (*R*)-diphenyl(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (**8**) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (**8a**) showed great applicability for the palladium-catalyzed allylic substitution on (*E*)-1,3-diphenylallyl acetate

(**148**) with various ketoximes and aldoximes as nucleophiles.[84] Starting from the bis(trifluoromethanesulfonate) BINOL derivative **4** which is generally obtained by treating (*S*)-BINOL with trifluoromethanesulfonic anhydride and triethylamine these ligands can obtained in a three step synthesis published by Du et al.[85].

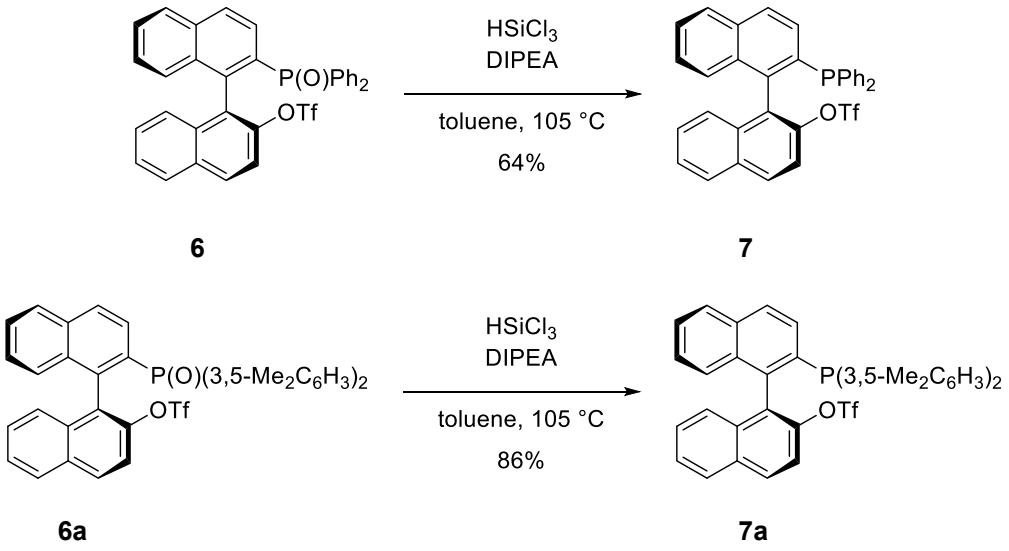
The first step is a palladium-catalyzed cross-coupling reaction in which one of the triflate groups is replaced by a diphenylphosphoryl or diarylphosphoryl group, respectively (Scheme 29). The first account on palladium-catalyzed cross-coupling reactions employing phosphonate as a heteroatom nucleophile dates back to 1980[93] although Buchwald and Hartwig did not establish this kind of chemistry until more than ten years later[94]. The concept was expanded for aryl triflates like the BINOL derivative **4** by Lu et al.[95] and for phosphine oxides like diphenylphosphine oxide (**5**) and the 3,5-dimethylphenyl derivative **5a** by Xu et al.[96]. The transformation with palladium acetate as pre-catalyst, 1,4-bis(phenylphosphino)butane as ligand and DIPEA as base yielded 47% of the mono-substituted BINOL derivative **6**. Employing dry, degassed DIPEA the yield could be increased to 74% for the 3,5-dimethylphenyl variation **6a**.



Scheme 29. Palladium-Catalyzed *C-P* Cross-Coupling Reaction with Phosphine Oxides **5** and **5**a

The deoxygenation of phosphine oxides with trichlorosilane is a common procedure for the synthesis of phosphine ligands (Scheme 30), a method first reported by Fritzsche et al.[97]. In combination with DIPEA the reduction of phosphine oxide **6** afforded a yield of 64%. Again, using dry degassed DIPEA for the reduction of phosphine oxide **6a** led to an increased yield of 86% for the 3,5-dimethylphenyl derivative **7a**. The resulting (*S*)-2'-(diphenylphosphanyl)-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate (**7**) as well as its derivative **7a** are not

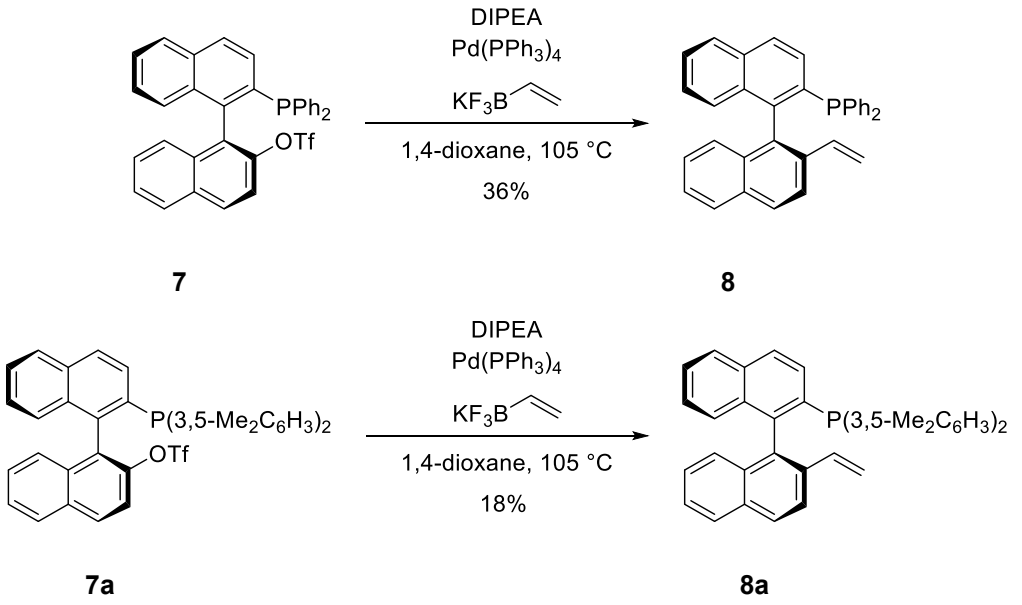
easily storable. According to F. Severin[89] (*S*)-2'-(diphenylphosphanyl)-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate (**7**) decomposes and reoxidizes when kept at ambient conditions. Stored under nitrogen for several days the compound turned yellow as observed by F. Severin but showed no further signs of decomposition or reoxidization and was transformed readily in the third reaction step.



Scheme 30. Trichlorosilane Reduction of the Phosphine Oxides

The third and last is definitely the key step in this hybrid ligand synthesis. The terminal alkene moiety is introduced by a Suzuki-Miyaura coupling reaction (Scheme 31).[85] The palladium-catalyzed cross-coupling of organoboranes with aryl halides or triflates established by Suzuki and Miyaura in 1979[98, 99] developed into one of the most useful tools in organic synthesis and was awarded a Nobel Prize in 2010. Potassium vinyltrifluoroborate was first introduced in 1998, more than 20 years later, as a stable and efficient vinylating agent in coupling reactions by Genêt et al.[100]. The application as a reagent in Suzuki-Miyaura cross-coupling reactions in combination with aryl bromides and triflates was later reported by Molander and co-workers[101, 102].

Du et al.[85] identified tetrakis(triphenylphosphine) palladium(0) as the most suitable palladium catalyst in combination with DIPEA as the required base for the specific transformation into the desired ligand. This setting afforded the hybrid ligand **8** in 36% yield and the derivative **8a**, although in this case dry, degassed DIPEA was used in only 18% yield. Insufficiently dried 1,4-dioxane was made out as a potential reason for the low yields in this third and final step. Therefore, the solvent was dried over sodium with benzophenone as indicator directly prior to the application in a consecutive attempt which albeit did not result in a distinctly increased yield.



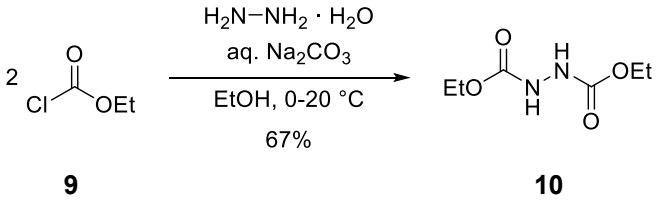
Scheme 31. Suzuki-Miyaura Coupling Reaction with Potassium Vinyltrifluoroborate

2.2 Pyrazolidines

The synthesis of enantiopure pyrazolidines by enantioselective allylation followed by diastereoselective halocyclization was targeted first. All prior research into this field in our group was deducted in the context of a master thesis by B. Mechsner[90] which resulted in the successful iodo-, bromo- and chlorocyclization of diethyl 1-cinnamylhydrazide-1,2-dicarboxylate (**28**). Since the obtained cyclization products consisted of rotamers with regard to the ethylcarboxylate protecting groups the investigation of a different protection strategy had priority.

2.2.1. Hydrazides as Protected *N*-Nucleophiles

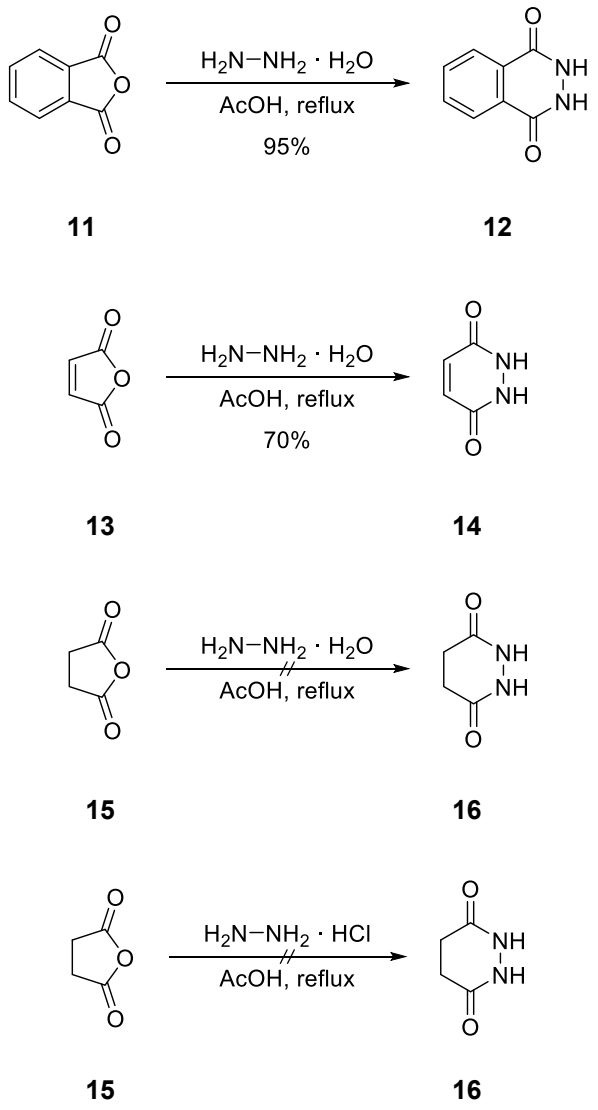
As mentioned before preliminary work by B. Mechsner[90] showed that tosyl-protected *trans*-cinnamylhydrazide gave no cyclization products while the ethoxycarbonylhydrazide analogs readily cyclized in most of the solvents tested. To verify the results by B. Mechsner diethyl hydrazine-1,2-dicarboxylate (**10**) was synthesized as the first hydrazide nucleophile. Hydrazine monohydrate was reacted with two equivalents of ethyl chloroformate (**9**) and sodium carbonate as base (Scheme 32) according to Rabjohn[103] giving the desired hydrazide in 67% yield.



9 **10**

Scheme 32. Synthesis of Diethyl Hydrazine-1,2-dicarboxylate (**10**)

To eliminate free rotation of the protective groups on nitrogen and therefore prevent rotamers, cyclic hydrazides were taken into consideration. Phthalic hydrazide (**12**) as well as maleic hydrazide (**14**) were prepared according to Zhang and Liu et al.[104] and Khoraamabadi-zad et al.[105], respectively by the reaction of the corresponding anhydrides with hydrazine monohydrate under acidic conditions (Scheme 33).



Scheme 33. Reaction of Phthalic Anhydride (**11**), Maleic Anhydride (**13**) and Succinic Anhydride (**15**) with Hydrazine Monohydrate or Hydrazine Hydrochloride

While the ^{1}H NMR spectrum of phthalic hydrazide (**12**) showed the expected signals, the ^{1}H NMR spectrum of maleic hydrazide (**14**) measured at 298 K showed two broad singlets at 11.80 ppm and 11.00 ppm which together account for two protons. Accountable for this phenomenon are most likely tautomeric forms of the maleic hydrazide (**14**) as exhibited by nucleobases.[106, 107] The NMR spectrum measured at 319.4 K led to coalescence of the two signals (Figure 7).

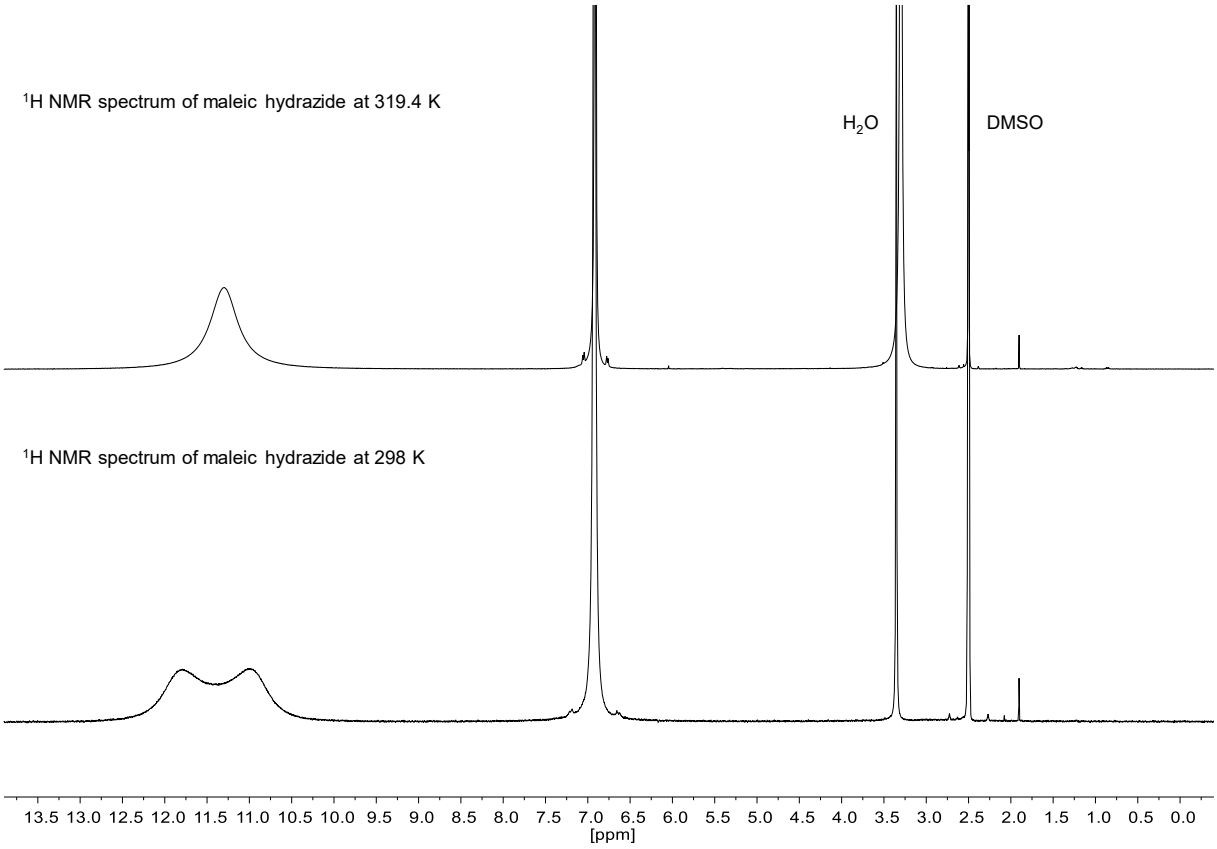
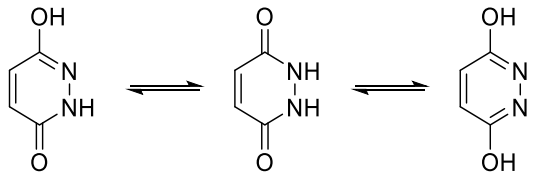


Figure 7. ^{1}H NMR Spectra of Maleic Hydrazide (**14**) at 319.4 K and 298 K

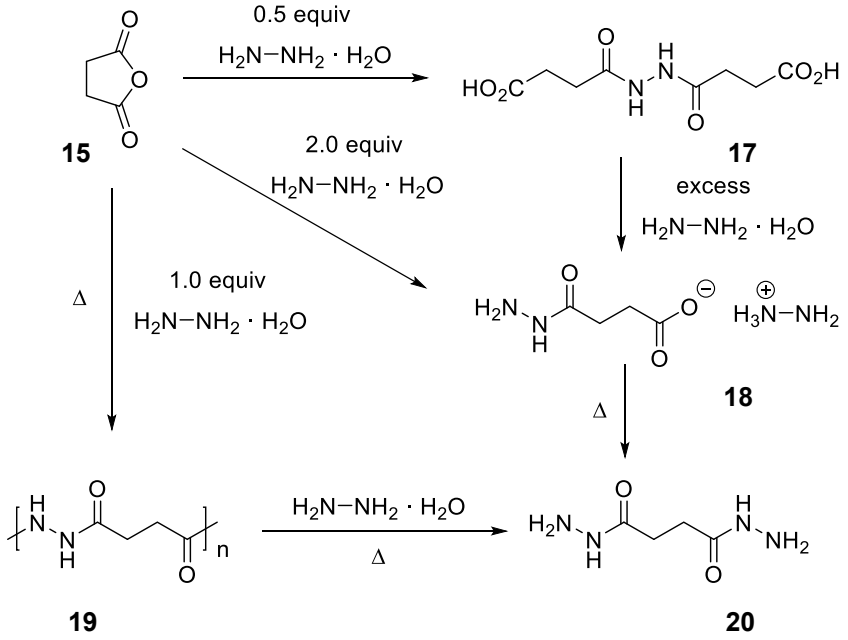
Three different tautomeric forms are theoretically possible not considering the spatial orientation of the hydroxyl proton (Scheme 34). Hofmann et al.[108] conducted quantum chemical calculations providing theoretical support for experimental studies[109] indicating the predominance of the monohydroxy-monoketo tautomer **14a** in the solid state and in solution. Consecutively, the monohydroxy-monoketo tautomer **14a** and the diketo tautomer **14b** were identified as the most stable isomers in gas phase and in solution. Compared to its regio isomer uracil, which favors the planar diketo form, the diketo form of maleic hydrazide **14b** exhibits a distinct non-planar structure. This deviation can be explained by the interaction of the lone pairs on the neighboring nitrogens. The most stable tautomer **14a** allows for an almost perpendicular arrangement, which is favorable as can be seen in non-cyclic hydrazines. The diketo tautomer **14b** already shows considerable deviation from the optimum conformation, resulting in non-planarity while the repulsive lone pair orientation is maximized for the supposedly aromatic dihydroxy tautomer **14c**.



14a **14b** **14c**

Scheme 34. Tautomeric Forms of Maleic Hydrazide (**14**)

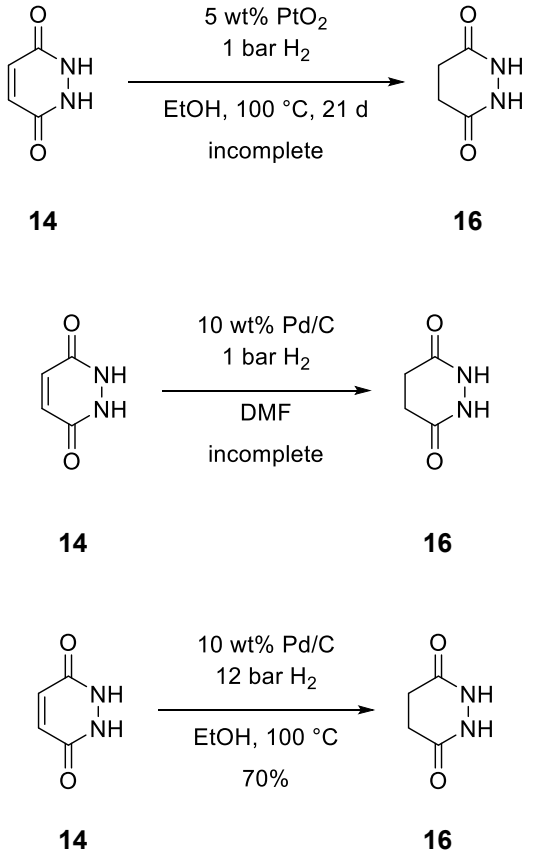
Although phthalic anhydride (**11**) and maleic anhydride (**13**) reacted readily with hydrazine monohydrate to afford the corresponding cyclic hydrazides, the same conditions were not applied successfully for the synthesis of succinic hydrazide (**16**) (Scheme 33), despite being postulated by Kermani et al.[110] as an intermediate under the same conditions in a one-pot synthesis of 6,7-dihydro-1*H*-pyrazolo[1,2-a]pyridazine-5,8-diones. Neither the reaction with hydrazine monohydrate nor with hydrazine hydrochloride resulted in formation of the desired product. White et al.[111] identified the products formed in the reaction of succinic anhydride (**15**) with hydrazine monohydrate as a mixture of disuccinhydrazide diacid (**17**), succinic dihydrazide (**18** or **20**) and a polymeric form assigned the name polysuccinhydrazide (**19**) (Scheme 35). The reason for the formation of these non-cyclic forms in contrast to the reaction with phthalic anhydride (**11**) or maleic anhydride (**13**) is supposedly the pre-determined *cis*-conformation of the latter creating a spatial proximity which favors the cyclization reaction.



15 **17** **18** **19** **20**

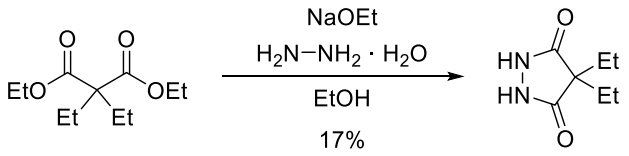
Scheme 35. Product Diversity for the Reaction of Succinic Anhydride (**15**) with Hydrazine Monohydrate

White et al.[111] proposed the reduction of maleic hydrazide (**14**) with Adams Catalyst for the synthesis of cyclic succinic hydrazide (**16**). A slightly modified procedure was executed with 1 bar hydrogen pressure and 5 wt% platinum(IV)oxide as pre-catalyst (Scheme 36). Platinum(IV)oxide is reduced to black platinum(0) in the process and serves as the actual catalyst.[112] Although the reduction was successful to some extend the ^{1}H NMR spectrum still showed substrate signals even after 23 days. Based on a procedure postulated by Basak et al.[113] hydrogenation was attempted with 10 wt% palladium on carbon in dry DMF under atmospheric hydrogen pressure, leading again to incomplete conversion (Scheme 36). A combination of both approaches finally resulted in quantitative transformation into the desired product **16** with an isolated yield of 70%, employing 10 wt% palladium on carbon in ethanol under approximately 12 bar hydrogen pressure in an autoclave (Scheme 36).



Scheme 36. Synthesis of Cyclic Succinic Hydrazide (**16**) by Hydrogenation of Cyclic Maleic Hydrazide (**14**)

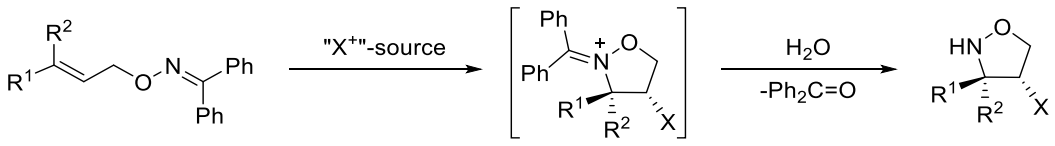
Another approach towards cyclic *N,N'*-diprotected hydrazides are cyclic malonate derivatives. To eliminate C-H acidity the 2,2-diethyl derivative **22** was targeted. Therefore, the diethyl 2,2-diethylmalonate (**21**) was cyclized with hydrazine monohydrate under basic conditions in the presence of sodium ethoxide as published by Ruhkopf[114] which resulted in a rather low yield of 17% (Scheme 37).



21 **22**

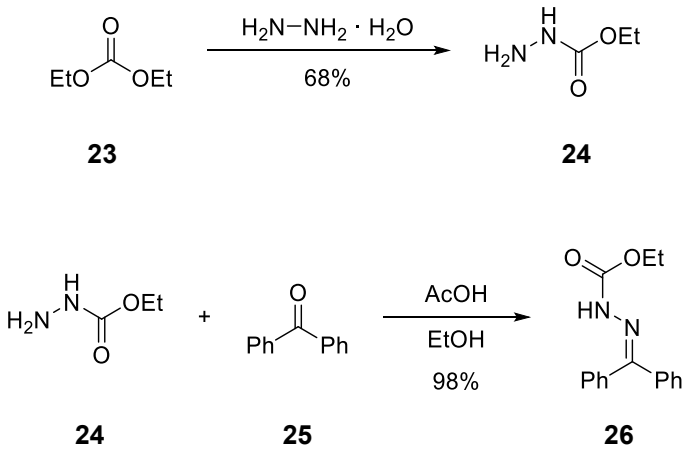
Scheme 37. Cyclization of Diethyl 2,2-Diethylmalonate (**21**) with Hydrazine Monohydrate

An attempt by B. Egart[88] regarding the isoxazolidine synthesis to replace the tosyl protection group on nitrogen with a more easily cleavable alternative led to the development of halocyclization of *O*-allylic benzophenone oximes yielding unprotected isoxazolidines (Scheme 38). These *O*-allylic oximes were considered with regard to an organoselenium mediated access to isoxazolidines developed by Tiecco and co-workers[115, 116].



Scheme 38. Halocyclization of *O*-Allylic Oximes

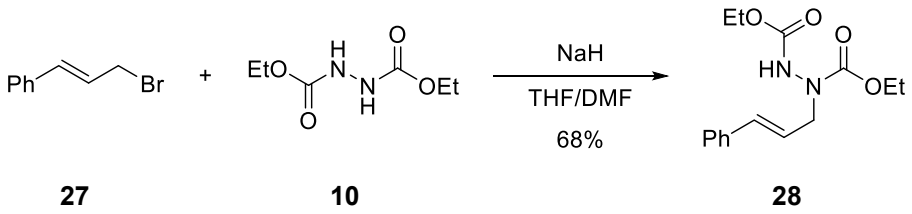
According to these results for the pyrazolidine synthesis, the hydrazone derivative ethyl 2-(diphenylmethylene)hydrazine-1-carboxylate (**26**) was targeted. Ethyl hydrazine carboxylate (**24**) was synthesized by reaction of hydrazine monohydrate with diethyl carbonate (**23**) (Scheme 39). Resulting water, ethanol and unreacted diethyl carbonate were distilled off to afford the pure product as suggested by Wu et al.[117] in 68% yield. The hydrazone **26** was then synthesized according to Cranwell et al.[118] from the hydrazide **24** and benzophenone (**25**) eliminating water in the process (Scheme 39).



Scheme 39. Two Step Synthesis of Ethyl 2-(Diphenylmethylene)hydrazine-1-carboxylate (**26**)

2.2.2. Allylation of Hydrazides

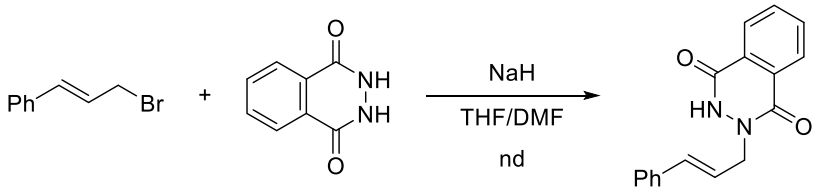
The prepared hydrazides were subjected to *N*-allylation in order to generate the substrates for the halocyclization reaction. To estimate reactivity a non-selective allylation reaction was applied first. *trans*-Cinnamyl bromide (**27**) was chosen, since its hydroxylamine derivative gave the best results for the corresponding halocyclization published by Czekelius et al.[87]. It was also employed for the first halocyclization of hydrazides by B. Mechsner[90] and is commercially available. To enhance nucleophilicity the hydrazides were deprotonated with sodium hydride prior to nucleophilic substitution of the bromide (S_N2).



Scheme 40. Synthesis of Diethyl 1-Cinnamylhydrazide-1,2-dicarboxylate (**28**) by S_N2 Reaction

Interestingly, although diethyl hydrazine-1,2-dicarboxylate (**10**) showed excellent solubility in THF an approach applying only THF as solvent for the substitution reaction was not successful. Therefore in a second attempt DMF was added as proposed by Hsung et al.[119]. This procedure gave the diethyl 1-cinnamylhydrazide-1,2-dicarboxylate (**28**) in 68% yield (Scheme 40).

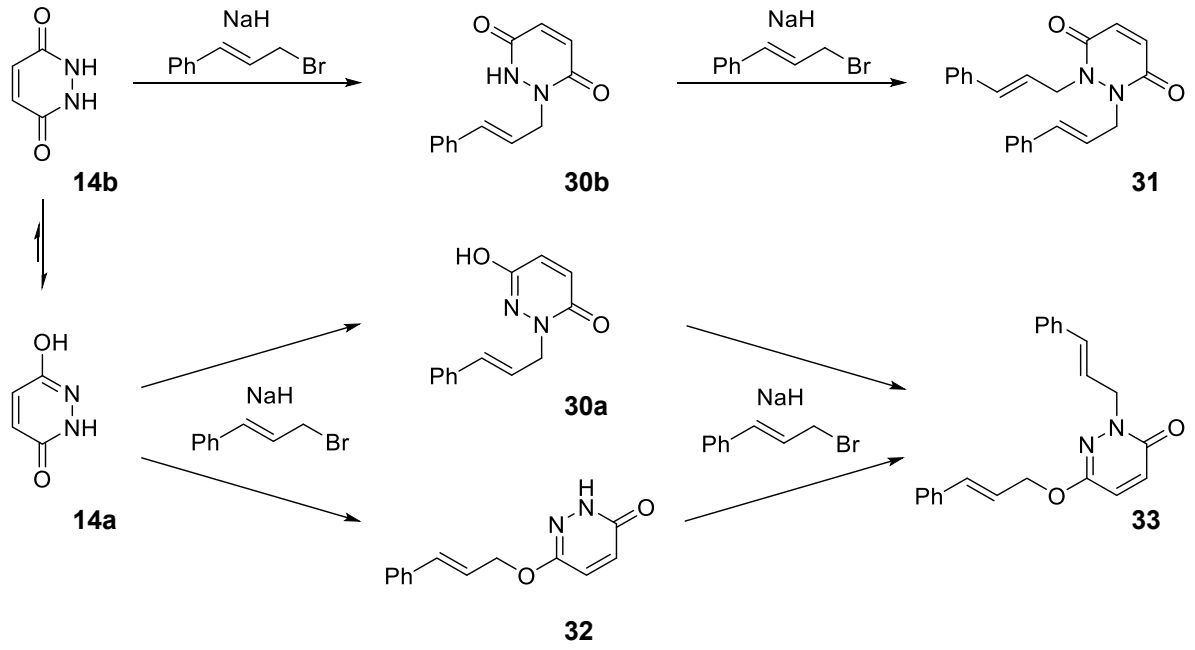
Due to low solubility of phthalic hydrazide (**12**), maleic hydrazide (**14**) as well as 4,4-diethylpyrazolidine-3,5-dione (**22**) in THF the ratio of DMF was increased for these allylation reactions. Although the ^{1}H NMR spectrum of the raw material from the reaction of phthalic hydrazide (**12**) with cinnamyl bromide (**27**) (Scheme 41) looked promising, purification proved to be difficult. Due to low solubility purification by column chromatography was not possible, leaving recrystallization as the only option. Attempts to recrystallize the obtained solid from *n*-hexane/ethyl acetate, *n*-hexane/toluene or *n*-hexane/toluene/ethanol remained unsuccessful.



27 **12** **29**

Scheme 41. Synthesis of 2-Cinnamyl-2,3-dihydrophthalazine-1,4-dione (**29**) by S_N2 Reaction

The reaction of maleic hydrazide (**14**) with cinnamyl bromide (**27**) yielded two main products. Their ^{1}H NMR spectra implied one monoallylated and one diallylated species. With regard to the stability of the maleic hydrazide tautomers (**14a-c**) discussed before in section 2.3.1 it was in question whether the desired *N*-allylated isomer **30** is actually preferred over the *O*-allylated isomer **32**. In fact, two *N*-allyl tautomers **30a-b** and one *O*-allyl regioisomer **32** would be plausible for the monoallylated species, leading to two possible regioisomers, the *N,N'*-diallylated species **31** and the *N,O*-allylated species **33** for the diallylated compound (Scheme 42).



Scheme 42. Plausible Isomers Regarding the Allylation of Maleic Hydrazide (**14**)

DMF as part of the reaction medium favors the keto-hydroxyl tautomer **14a** as observed by Fritz et al.[120] due to the formation of intermolecular H-bonds. The compound $[Na(HMh)(H_2O)_2]_n \cdot H_2O$ (H_2Mh = maleic hydrazide) was synthesized by Morzyk-Ociepa[121] from an alkaline solution of cyclic maleic hydrazide (**14**) and analyzed by X-ray crystallography. Interestingly, the crystal structure reveals that the sodium cation coordinates the carbonyl oxygen of the keto-hydroxy tautomer **14a** and is not bound to the deprotonated hydroxy oxygen (Figure 8). Due to this coordination mode the negative charge on the nitrogen N(2) decreases with regard to the sodium complex as opposed to the free keto-hydroxy tautomer **14a**.

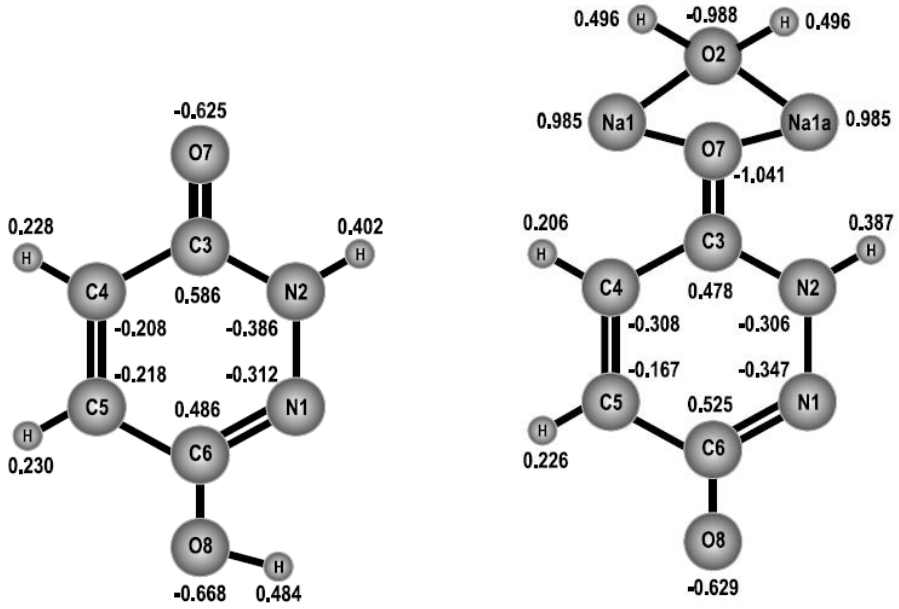
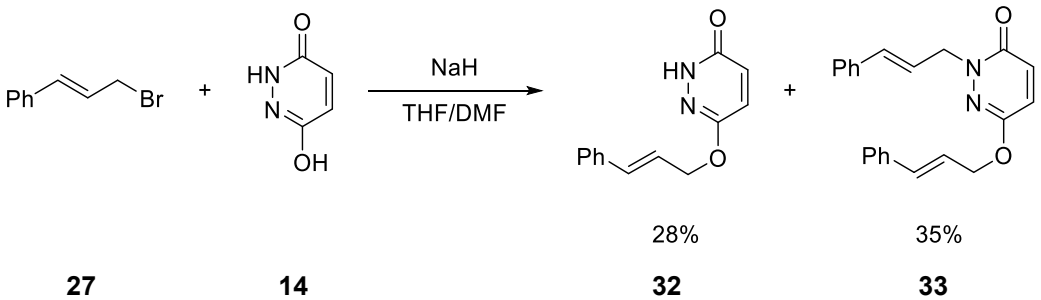


Figure 8. Atom Numbering and Natural Atomic Charges Calculated by NBO Method for the Keto-Hydroxy Form and the Theoretical Model of $[Na(HMh)(H_2O)_2]_n \cdot H_2O$ from Morzyk-Ociepa[121]

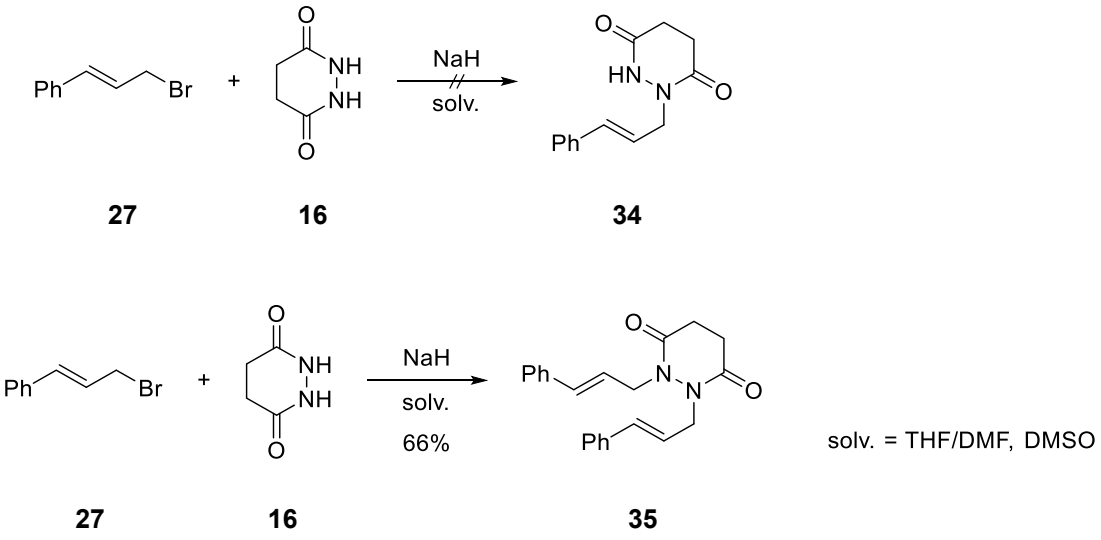
Since the nucleophilic anion for the substitution reaction on cinnamyl bromide (**27**) is generated by deprotonation with sodium hydride, a similar coordination mode as seen for the crystal structure is highly probable. The generation of the *N*-allylated species **30a** is therefore highly unlikely, as coordination of the sodium cation leads to decreased electron density on the supposedly nucleophilic nitrogen atom. On the contrary, deprotonation with sodium hydride leads most likely to an oxygen nucleophile, rendering the *O*-allylated compound **32** (Scheme 43). The thus determined reaction pathway is further supported by analysis of the ^{1}H NMR spectrum of the diallylated compound, which suggests an asymmetric substitution pattern, as exhibited by the *N,O*-diallylated compound **33**, as the signals are mostly multiplets, presumably resulting from two overlapping sets of signals with only slightly differing chemical shifts.



Scheme 43. Allylation Reaction of Maleic Hydrazide (**14a**) with Cinnamyl Bromide (**27**) by S_N2 Reaction

The *N*-allylated compound **30a** might be obtainable if a protective group, e.g. a silyl group on the hydroxy moiety is introduced first.

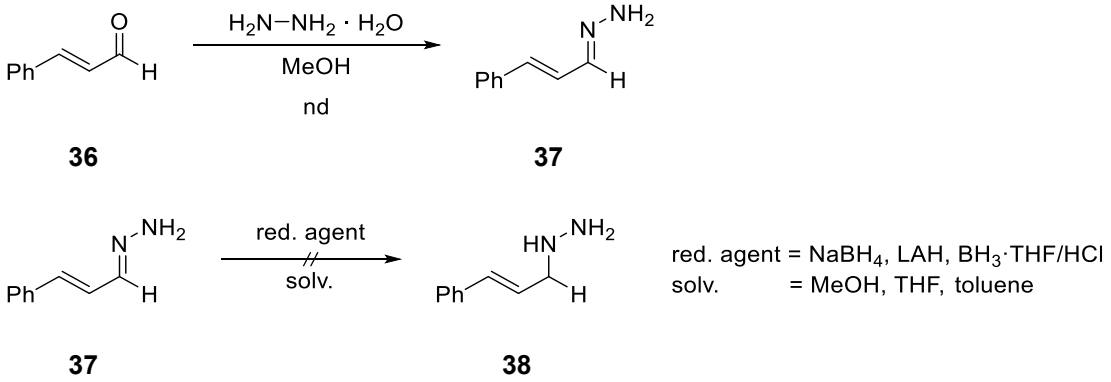
Several attempts to synthesize the monoallylated succinic hydrazide derivative 1-cinnamyltetrahydropyridazine-3,6-dione (**34**) by nucleophilic substitution on cinnamyl bromide (**27**) in different THF/DMF combinations as well as in DMSO led to exclusive formation of the diallylated product **35** (Scheme 44). The crystal structure for cyclic succinic hydrazide (**16**) by Ottersen[122] proved the diketo form **16** to be the prevalent tautomer in solid state. Since the ^{1}H NMR of the diallylated compound exhibits great symmetry, the *N,N'*-diallylated compound **35** is presumed as the single reaction product. The reason for the exclusive diallylation is most likely an increased solubility of the monoallylated compound **34** compared to succinic hydrazide (**16**), which exhibits low solubility in THF. An increase in nucleophilicity after the first allylation reaction is also assumable. Additionally, sodium hydride is a strong non-nucleophilic base with a pK_a > 35[123]. Since the reaction is irreversible, generating hydrogen gas, it generally provides quantitative deprotonation. The pK_a values of maleic hydrazide (**14**) are pK_{a1} = 5.65[124] and pK_{a2} = 12.5–13[125], which can be even lowered by metal coordination (in case of platinum up to a value of 7.3[125]). Although the pK_a values for succinic hydrazide (**16**) surely vary from those of maleic hydrazide (**14**), predominance of the diallylated products for both allylation reactions is plausible.



Scheme 44. Allylation Reaction of Succinic Hydrazide (**16**) with Cinnamyl Bromide (**27**) by S$_N$2 Reaction

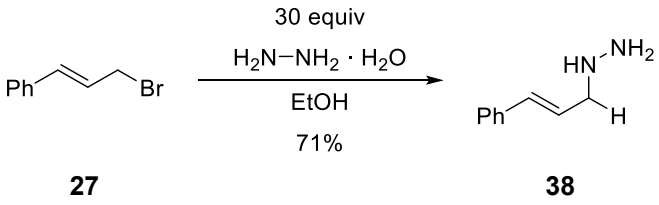
Since the allylation of succinic hydrazide (**16**) did not seem promising, a second approach was pursued starting from (*E*)-cinnamaldehyde (**36**). The first idea was the preparation of the corresponding hydrazone **37** with hydrazine monohydrate followed by reduction resulting in formation of (*E*)-cinnamyl hydrazine (**38**) (Scheme 45). Reduction of allylic imines can be

achieved with sodium borohydride as published by Mathela et al.[126]. In the case of allylic hydrazone **37** no reduction took place and also lithium aluminum hydride as a stronger reducing agent did not show the desired results. The reduction might be inhibited by the deprotonation of the hydrazone **37**, therefore employing stronger reducing agents were discarded. Additionally, stronger reducing agents might have the adverse effect of also reducing the double bond. Perdicchia et al.[127] developed a method applying a borane trimethylamine complex and hydrogen chloride gas to reduce hydrazones like (*E*)-(1-phenylethylidene)hydrazine (**37**) in excellent yields. This procedure was also applied employing a borane THF complex and although TLC showed a multitude of reaction products the desired allyl hydrazine **38** was again not obtained.



Scheme 45. Hydrazone Formation and Attempted Reduction of ((*E*)-3-Phenylallylidene)hydrazine (**37**)

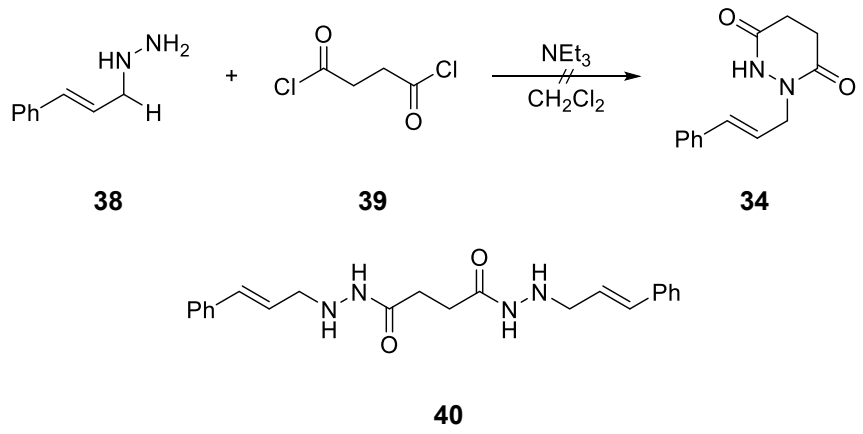
Consequently, a substitution reaction with hydrazine monohydrate on cinnamyl bromide **27** according to Tiecco et al.[128] was considered (Scheme 46). In order to prevent the formation of disubstituted hydrazines an excess of 30 equivalents of hydrazine monohydrate was applied. This setting gave the desired cinnamyl hydrazine (**38**) which was used in the next step without further purification.



Scheme 46. Synthesis of Cinnamyl Hydrazine (**38**) According to Tiecco et al.[128]

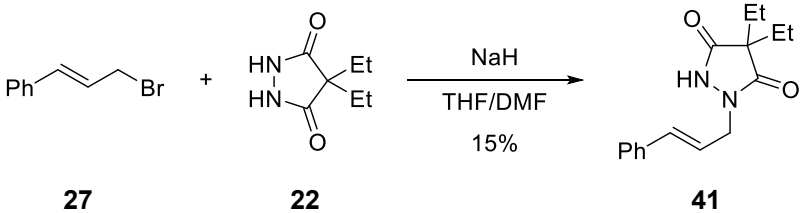
According to Rafeeq et al.[129] allyl hydrazine 2-hydrazinylquinazolin-4(3*H*)-one reacts with succinic anhydride by formation of an amide which undergoes cyclization by elimination of

water at 100 °C. As observed for the hydrazide synthesis discussed in section 2.2.1 this procedure is presumably not applicable for the hydrazine **38** since cyclization of succinic anhydride (**15**) with hydrazine monohydrate did not occur (Scheme 35). A publication by Hassan[130] promotes the cyclization with succinyl chloride (**39**) and triethylamine as base. Although TLC seemed promising showing two main products, isolation proved none of them to be the desired monoallylated succinic hydrazide **34**. Mass spectrometry instead hinted at the formation of linear products like **40** (Scheme 47).



Scheme 47. Synthesis of 1-Cinnamyltetrahydropyridazine-3,6-dione (**34**) as Postulated by Publications by Rafeeq et al.[129] and Hassan[130]

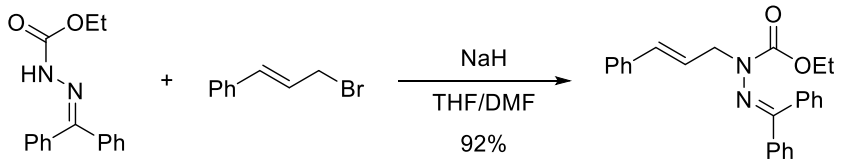
As all these approaches did not give any enlightening results, the synthesis of 1-cinnamyltetrahydropyridazine-3,6-dione (**34**) did not seem genuinely realizable the attention was shifted to more promising hydrazides. The reaction of the 4,4-diethylpyrazolidine-3,5-dione nucleophile (**22**) with cinnamyl bromide (**27**) did result in the formation of the desired monoallylated compound **41** but in a low yield of 15% (Scheme 48). Surprisingly the corresponding diallylated species was not isolated in this case.



Scheme 48. Synthesis of 1-Cinnamyl-4,4-diethylpyrazolidine-3,5-dione (**41**) by S_N2 Reaction on Cinnamyl Bromide (**27**)

The most promising result was obtained by allylation of the hydrazone nucleophile **26**. The reaction with cinnamyl bromide (**27**) resulted in the desired *N*-monoallylated product **42** in

excellent yield of 92% (Scheme 49). Due to the hydrazone structure a diallylated species is not obtained. Despite the non-cyclic structure, the ^{1}H NMR spectrum clearly did not show rotamers.

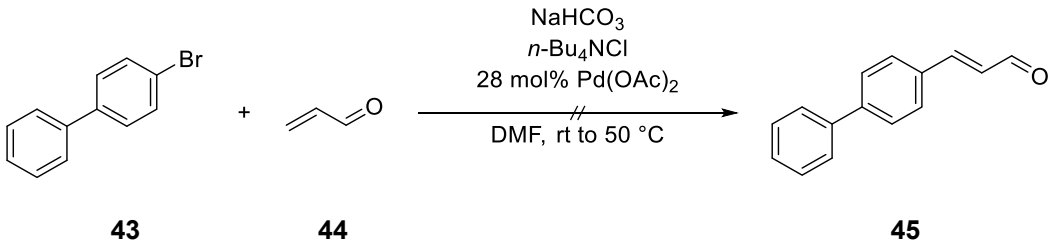


26 **27** **42**

Scheme 49. Synthesis of Ethyl 1-Cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**42**) by S_N2 Reaction on Cinnamyl Bromide (**27**)

As will be discussed in section 2.2.3 the cyclization product of **42** turned out to be almost non-detectable by TLC especially in lower concentrations. Therefore, the synthesis of a more UV active substrate, a biphenyl derivative, was targeted. According to Reinhardt et al.[131] (*E*)-4-(3-bromoprop-1-en-1-yl)-[1,1'-biphenyl] (**189**) can be obtained in a three step synthesis. The first step is a palladium-catalyzed Heck cross-coupling reaction of 4-iodobiphenyl (**46**) with acrolein (**44**), followed by reduction with sodium borohydride resulting in the corresponding alcohol and finally transformation with phosphorus tribromide, a standard procedure for turning alcohols into the respective bromides. The overall yield according to Reinhardt et al.[131] adds up to 31% with the Heck coupling reaction as the key step.

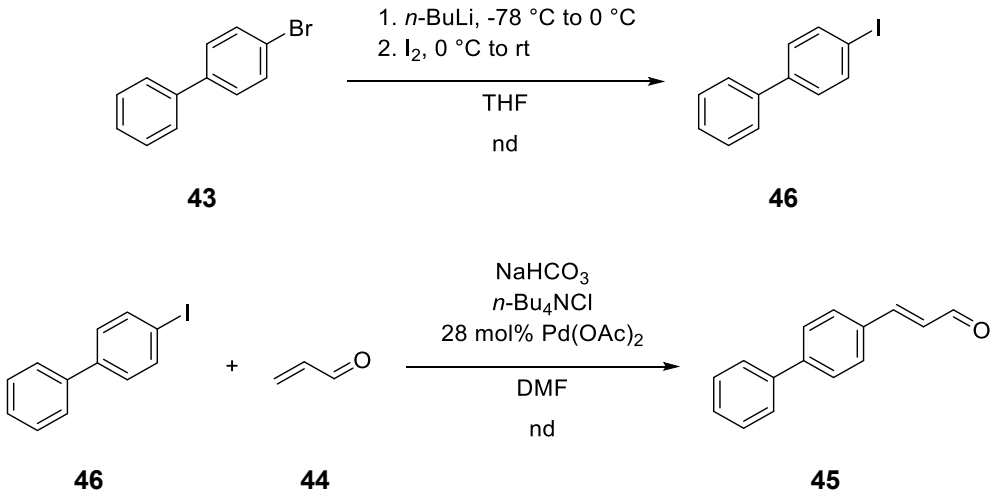
The Heck reaction is a palladium-catalyzed cross-coupling reaction.[132] Herein, a vinylic hydrogen atom is substituted while the double bond is preserved. Stoichiometric amounts of base are necessary for a successful transformation. Regarding the catalytic cycle strong σ-binding ligands are not essential for the transformation. Hence, Jeffery[133] developed a ligand-free variation employing palladium(II) acetate as the pre-catalyst, quaternary ammonium salts as phase transfer agents and sodium hydrogen carbonate or potassium acetate as base. Heck transformations under these conditions are mostly more efficient and can be conducted at lower temperatures. While in the presence of phosphine ligands acceleration of the Heck reaction is achieved by the quarternary ammonium moiety, for ligand free reactions acceleration depends as well on the nature of the counter anion. Accountable for this effect might be the stabilization of the low-ligated palladium(0) complex through halide ion coordination leading to less decomposition of the catalyst complex.[134]



43 **44** **45**

Scheme 50. Attempted Heck Reaction under Jeffery Conditions with 4-Bromobiphenyl (**43**)

For the Heck coupling reaction with acrolein Jeffery conditions were applied accounting for the volatility and polymerization tendency of acrolein. The first attempt was carried out with 4-bromobiphenyl (**43**) (Scheme 50). TLC showed no transformation after 40 hours, therefore triphenylphosphine was added and the reaction was heated to 50 °C but still no transformation was observed. Since iodine is a better leaving group 4-bromobiphenyl (**43**) was retrieved from the unsuccessful attempt and transformed into 4-iodobiphenyl (**46**) by halogen-metal exchange with *n*-butyl lithium and successive addition of iodine and the transformation attempted a second time (Scheme 51).



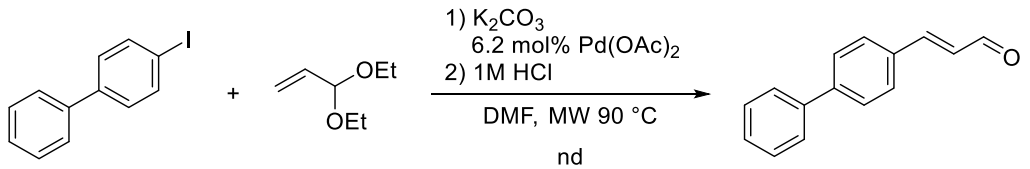
43 **46**

46 **44** **45**

Scheme 51. Bromine-Iodine-Substitution and Heck Reaction with 4-Iodobiphenyl (**46**)

Although partial conversion was observed, the ^{1}H NMR spectrum of the raw material accounted for only marginal product formation not nearly reproducing the 40% yield claimed by Reinhardt et al.[131]. A publication by Cacchi et al.[135] promotes the use of acrolein diethyl acetal (**47**) allegedly prohibiting polymerization which usually occurs as a side reaction under basic Heck conditions.[136] Botta et al.[137] professed an improved efficiency of the reaction when transferred into a microwave reaction. The reaction was conducted as proposed by Botta et al.[137] in two sequential irradiation cycles, lasting 20 minutes each at approximately

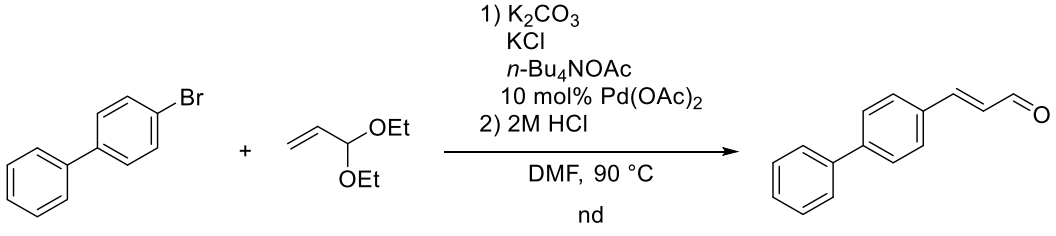
25 W (Scheme 52). After the first cycle TLC showed only partial conversion which did not change after a second cycle of irradiation. Further heating under conventional conditions did not alter the result either.



46 **47** **45**

Scheme 52. Microwave Heck Reaction of 4-Iodobiphenyl (**46**) with Acrolein Diethyl Acetal (**47**)

While an oxidative Heck coupling reaction with diphenylboronic acid and acrolein (**44**) as developed by Larhead et al.[138] was considered one last attempt was made carrying out the reaction as proposed by Cacchi et al.[135] under Jeffrey conditions with 4-bromobiphenyl (**43**) and acrolein diethyl acetal (**47**) as substrates and slightly increased catalyst loading compared to the microwave reaction (Scheme 53). Potassium carbonate as base and potassium chloride as additive supposedly increase the selectivity of β-hydride elimination towards yielding the desired cinnamaldehyde derivative **45** instead of a propanoate ester derivative which is accessible through β-hydride elimination of the second available β-hydrogen.



43 **47** **45**

Scheme 53. Heck Reaction with 4-Bromobiphenyl (**43**) and Acrolein Diethyl Acetal (**47**) as Proposed by Cacchi et al.[135]

Figure 9 shows the ^{1}H NMR spectra of the raw materials isolated from the three different attempts at (*E*)-3-([1,1'-biphenyl]-4-yl)acrylaldehyde (**45**) synthesis by Heck cross-coupling reaction. Especially the aldehyde proton and the neighboring proton show distinct signals at 9.73 ppm and 6.77 ppm respectively. The remaining ten protons of this compound account for nine aromatic signals and one allylic signal. Reduction to the corresponding alcohol and

subsequent transformation into the respective bromide **189** were not attempted. The resulting bromide **189** could supposedly be reacted with the hydrazone **26** rendering the more UV active biphenyl substrate **190** for additional investigation of the halocyclization reaction.

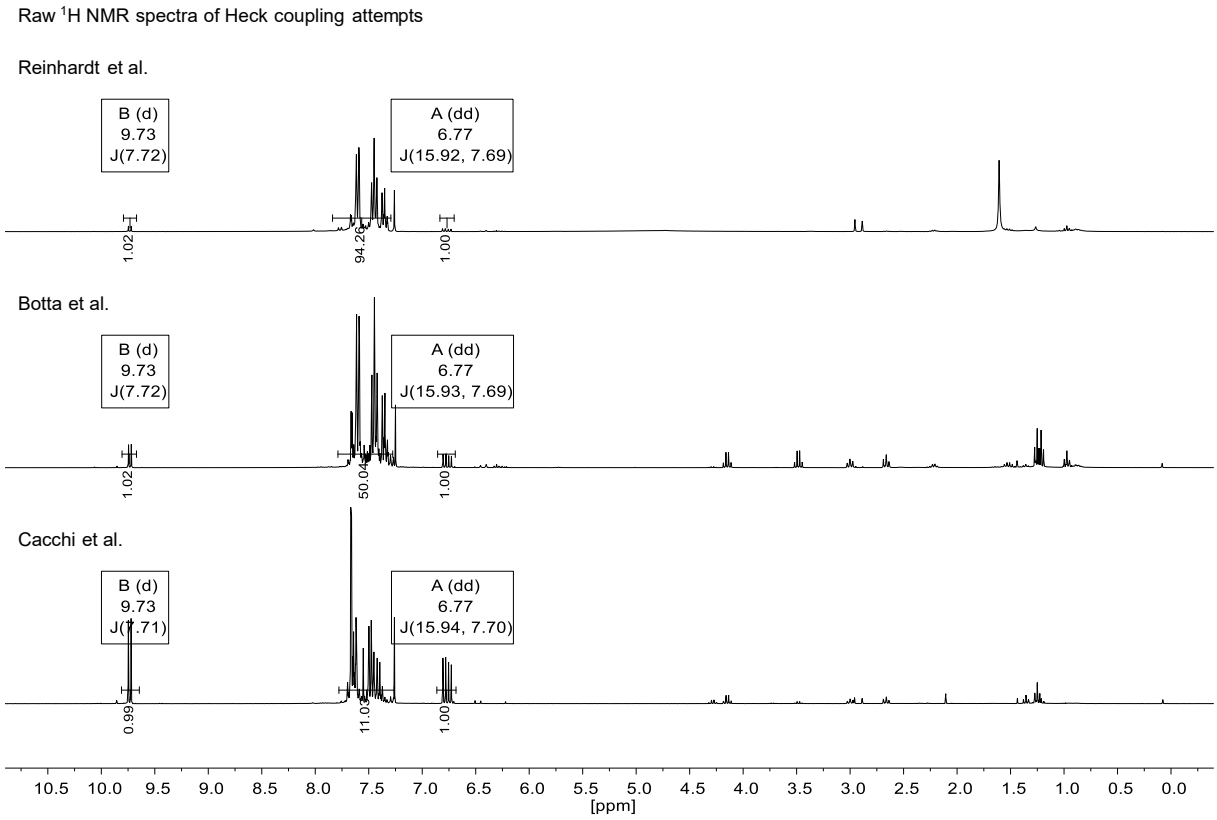
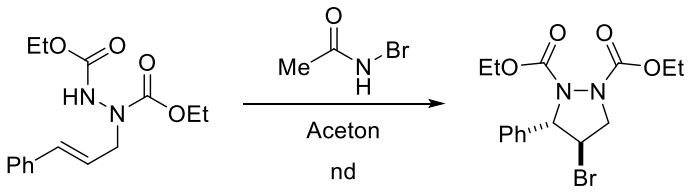


Figure 9. ^{1}H NMR Spectra of the Raw Materials Isolated from Three Different Attempts to Synthesize (*E*)-3-([1,1'-Biphenyl]-4-yl)acrylaldehyde (**45**)

2.2.3. Halocyclization of Allyl Hydrazides

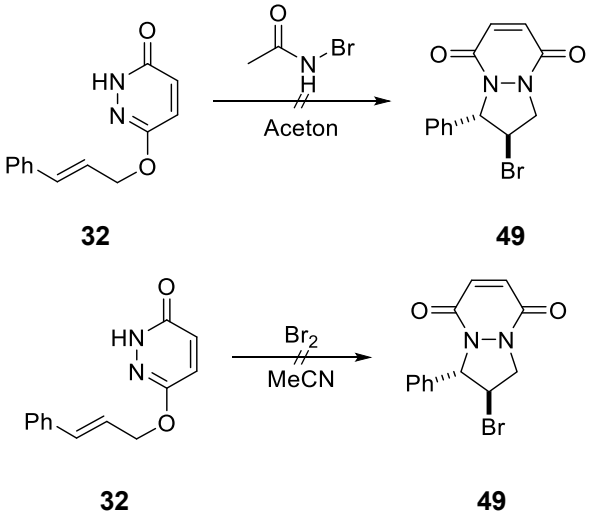
To verify the results concerning the halocyclization by B. Mechsner[90] diethyl 1-cinnamylhydrazide-1,2-dicarboxylate (**28**) was cyclized with NBA in acetone resulting in formation of *trans*-diethyl 4-bromo-3-phenylpyrazolidine-1,2-dicarboxylate (**48**) (Scheme 54). The reaction took longer than indicated by B. Mechsner but successfully gave the desired cyclization product, which could already be deducted from the ^{1}H NMR spectrum of the raw material. The diastereoselectivity of the reaction can be determined by ^{1}H NMR spectroscopy.



28 **48**

Scheme 54. Halocyclization of Diethyl 1-Cinnamylhydrazide-1,2-dicarboxylate (**28**)

Due to the discussed highly likely *O*-allylation of maleic hydrazide tautomer **14a** attempts to cyclize the allylation product 6-(cinnamyloxy)pyridazine-3(2H)-one (**32**) were not successful, neither with NBA nor with bromine (Scheme 55). This is not surprising since the cyclization would lead to a highly strained bridged bicyclic system. It is likely that other reactions took place, like the bromination of the cinnamyl double bond, which were not further investigated.

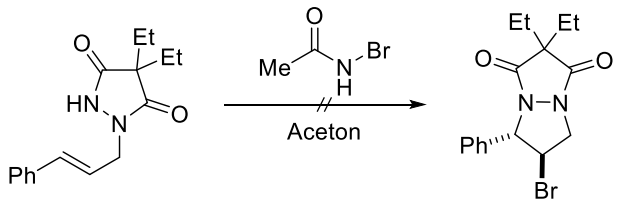


32 **49**

32 **49**

Scheme 55. Attempts on Halocyclization of 6-(Cinnamyloxy)pyridazine-3(2*H*)-one (**32**)

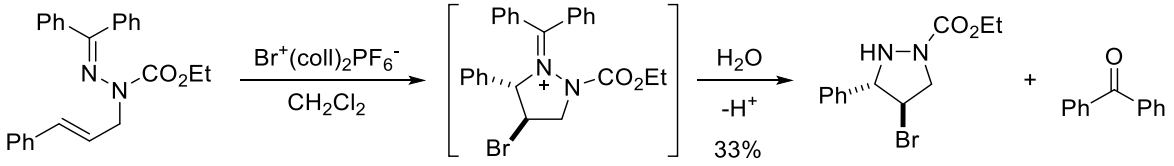
An attempt to cyclize 1-cinnamyl-4,4-diethylpyrazolidine-3,5-dione (**41**) with NBA leading to the pyrazolopyrazole derivative **50** was carried out as well (Scheme 56). Since the substrate was still detectable by TLC after 20 hours additional NBA was submitted adding up to a total of 2.4 equivalents. Purification by column chromatography of the resulting raw material did not afford the desired product.



41 **50**

Scheme 56. Attempted Halocyclization of 1-Cinnamyl-4,4-diethylpyrazolidine-3,5-dione (**41**)

The cyclization of ethyl 1-cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**42**) was attempted several times under varying conditions. Since B. Egart[88] employed bis(2,4,6-trimethylpyridine)bromine(I) hexafluorophosphate ($Br^+(coll)_2PF_6^-$) (**3**) successfully to the halocyclization reactions of oxime allyl compounds this complex seemed to be the brominating reagent of choice. Compared to the afore-mentioned halocyclization reactions this cyclization results in a cationic iminium intermediate **51** which is supposed to liberate the *trans*-ethyl 4-bromo-3-phenylpyrazolidine-1-carboxylate (**52**) and benzophenone (**25**) by subsequent hydrolysis.



42 **51** **52** **25**

Scheme 57. Halocyclization of Ethyl 1-Cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**42**) with $Br^+(coll)_2PF_6^-$ (**3**) Stored at Room Temperature

The first attempt was carried out with $Br^+(coll)_2PF_6^-$ (**3**) which had been stored at room temperature for a longer period. TLC only showed formation of the by-product benzophenone (**25**) and unreacted allyl hydrazone **42**. The reaction was quenched after 3.5 hours yielding 33% of pyrazolidine **52**. 30% of substrate **42** were retrieved (Scheme 57).

Since $Br^+(coll)_2PF_6^-$ (**3**) is only stable at room temperature for several months[91] the incomplete conversion was attributed to partial decomposition of the halogenating agent. Storage of pyrazolidine **52** at room temperature resulted in partial decomposition and oxidation to the corresponding pyrazole **54** which could be observed by TLC and ^1H NMR spectroscopy (Figure 10).

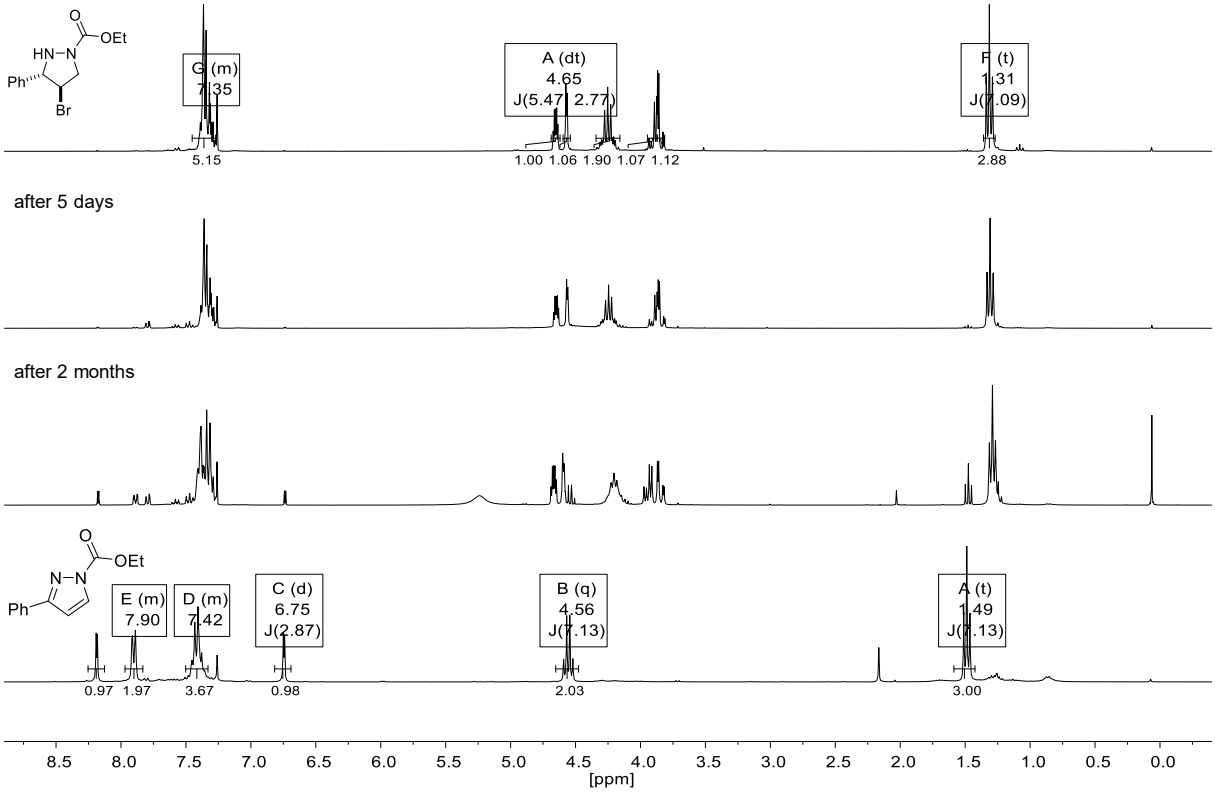


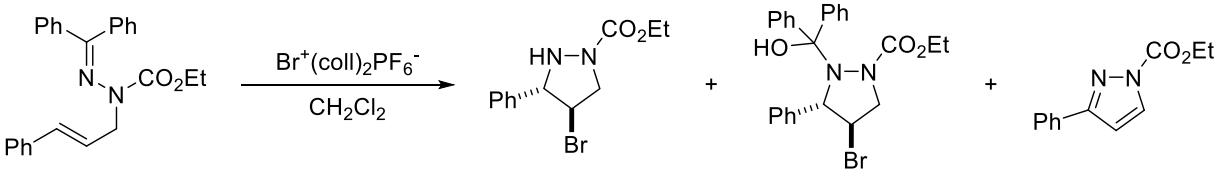
Figure 10. Decomposition and Oxidation of Pyrazolidine **52**

A second attempt with freshly synthesized $Br^{+}(coll)_2PF_6^{-}$ (**3**) resulted in full consumption of the allyl hydrazone substrate **42** within 3.5 hours according to TLC. An identical workup procedure and purification by column chromatography did afford the desired pyrazolidine **52** albeit not in a pure form as revealed by ^{1}H NMR spectroscopy. At first this was attributed to difficulties identifying ethyl 4-bromo-3-phenylpyrazolidine-1-carboxylate (**52**) by TLC, since it is only clearly visible as well as stainable in higher concentrations. Later it was argued whether incomplete hydrolysis, partial decomposition or oxidation of the product as observed upon storage could lead to the observed impurities. The ^{1}H NMR spectrum especially showed more aromatic signals than expected, leading to the assumption, that the iminium intermediate **51** was not fully hydrolyzed but partially converted into the corresponding hemiaminal **53**, although treating the isolated material with 0.1 M hydrochloric acid did not improve the result.

Stirring of the reaction solution with 1 M hydrochloric acid over night before workup in another attempt did yield 89% of benzophenone (**25**) but the ^{1}H NMR spectrum of the hypothetical product revealed the heterogeneity of the isolated substance therefore accounting for less than 38% product yield. Traces of a by-product, with a retention factor regarding TLC approximately the same as that of substrate **42** were isolated for the first time. Upon analysis

of the ^{1}H NMR spectrum this by-product was assumed to be the respective pyrazole derivative **54** which was verified by ESI mass spectrometry (Scheme 58).

Stirring with 10 wt% $NaHSO_3$ solution overnight as opposed to only for approximately one hour before workup did result in roughly 46% yield which albeit already contained a larger amount of the pyrazole by-product **54**.



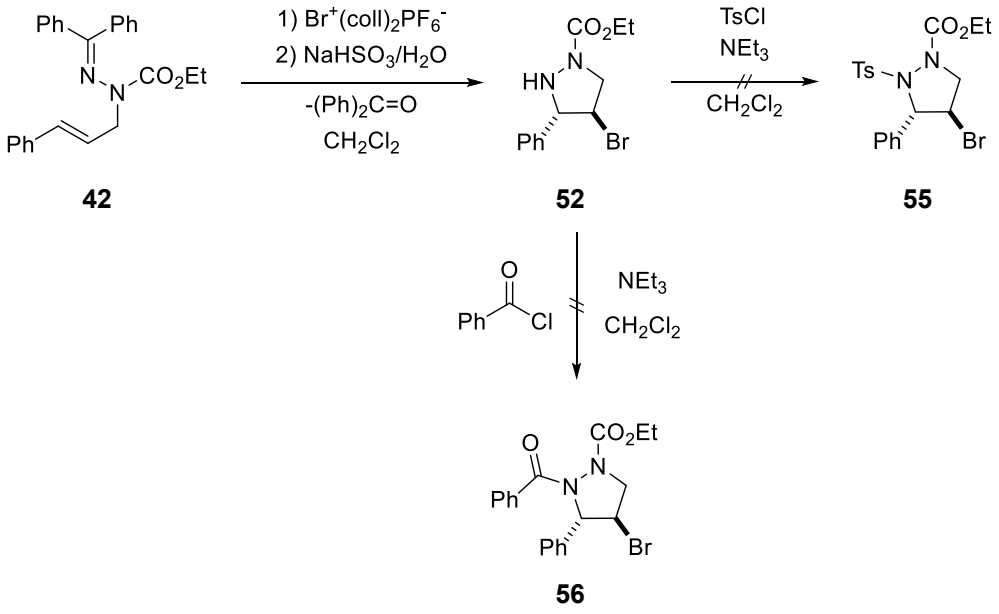
42 **52** **53** **54**

Scheme 58. Isolated Products in Halocyclization Attempts of Ethyl 1-Cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**42**)

Quenching with water resulted in only 59% yield of benzophenone (**25**), 8.4% of the pyrazolidine **52**, 11% of the hemiaminal **53** and 20% of the pyrazole **54**. This led to the conclusion that the slightly acidic pH of the sodium bisulfite solution is necessary as it accelerates the cleavage of the hemiaminal.

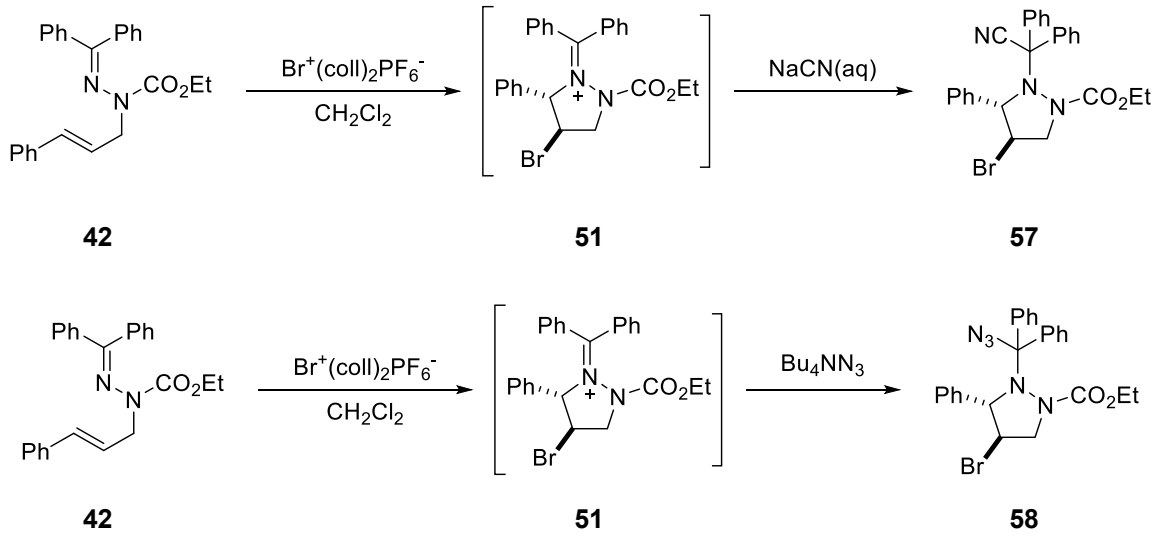
Degassing of the sodium hydrogen sulfite solution did not improve the reaction yield further, although the ^{1}H NMR spectrum of the isolated 38% of pyrazolidine **52** showed the highest purity since the first cyclization attempt.

Switching to NBA as halogenating agent did result in incomplete cyclization of substrate **42** as observed by TLC and ^{1}H NMR spectroscopy.



Scheme 59. Halocyclization of Ethyl 1-Cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**42**) with Subsequent Attempted Tosylation or Benzoylation

Since isolation of the desired pyrazolidine **52** proved difficult, direct tosylation or benzoylation of the raw material were attempted (Scheme 59). Treatment of the raw material with tosyl chloride and triethylamine as base did not result in the tosylated pyrazolidine **55**, neither did the treatment with benzoyl chloride result in the benzoylated pyrazolidine **56**. Since the hemiaminal form **53** is stable enough to be at least partially isolated another approach was to quench the iminium intermediate **51** with a nucleophile other than water like cyanide or azide (Scheme 60). Attempted purification of the raw materials did not result in the pure pyrazolidine compounds **57** or **58**.



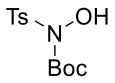
Scheme 60. Halocyclization of Ethyl 1-Cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**42**) and Subsequent Quenching with Cyanide or Azide Anions

2.3 Isoxazolidines

The synthesis of enantiopure isoxazolidines by enantioselective allylation followed by diastereoselective halocyclization was addressed secondly. Prior research into this field in the Czekelius group was conducted mainly by B. Egart[87, 88] which resulted in a methodology for the diastereoselective bromocyclization of *O*-allyl-*N*-tosylhydroxylamines and the successful diastereoselective bromocyclization of an *O*-allylic ketoxime with $Br^+(coll)_2PF_6^-$ resulting in the unprotected *trans*-4-bromo-3-phenylisoxazolidine (**167**). Regarding the enantioselective allylation reaction the investigation was based on prior work by Du et al.[84] employing the hybrid ligands **8** and **8a** in the asymmetric palladium-catalyzed etherization of mainly (*E*)-1,3-diphenylallyl acetate (**148**) with different oximes. First advances into this field in the Czekelius group were attempted in the context of a master thesis by F. Severin[89] resulting in a moderate enantiomeric excess of 75% for the (*S*,*E*)-diphenylmethanone *O*-(1,3-diphenylallyl) oxime ((*S*)-**143**).

2.3.1. Ketoximes as *N*-Protected *O*-Nucleophiles

For the enantioselective *O*-allylation of hydroxylamine a *N,N*-diprotected hydroxylamine derivative is required. Herein, orthogonality of the two protection groups seems necessary, as for the successive halocyclization one protection group has to be removed. Therefore, *tert*-butyl hydroxy(tosyl)carbamate (**59**) was targeted by F. Severin[89] but several attempted syntheses remained unsuccessful (Figure 11). Although once isolated in 10% yield almost immediate decomposition proved the compound unfit for further studies.



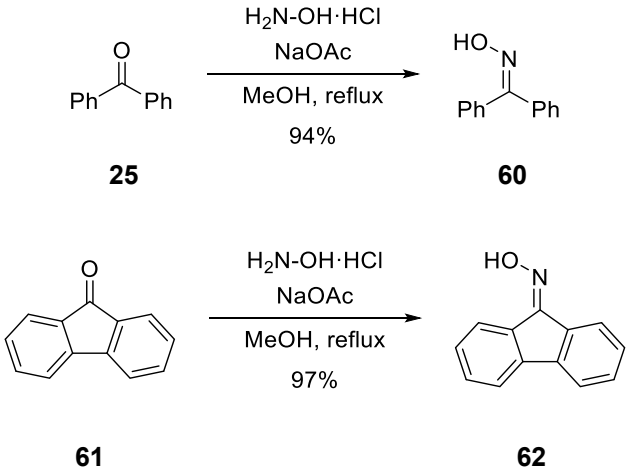
59

Figure 11. *tert*-Butyl Hydroxy(tosyl)carbamate (**59**)

Since B. Egart[88] showed the utility of oximes concerning halocyclization reactions leading to unprotected isoxazolidines, these were taken into consideration. Diphenylmethanone oxime (**60**) as applied by B. Egart[88] as well as Du et al.[84] was synthesized from benzophenone (**25**) and hydroxylamine hydrochloride with sodium acetate as base in 94% yield according to Park et al.[139] (Scheme 61).

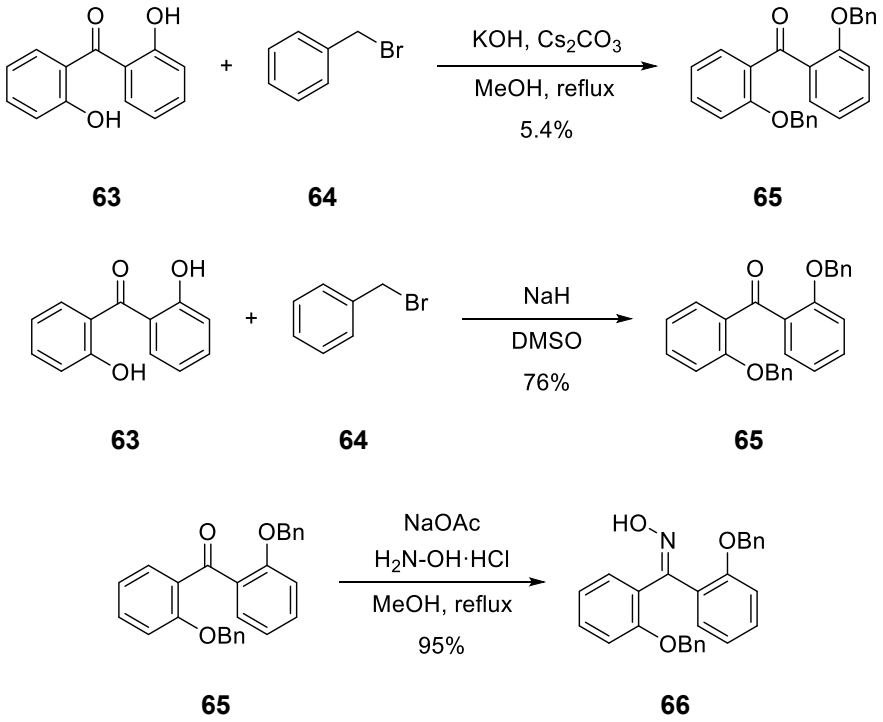
Although Du et al.[84] reported an enantiomeric excess of 92% for the allylic substitution on (*E*)-1,3-diphenylallyl acetate (**148**) with diphenylmethanone oxime (**60**) employing hybrid

ligand **8a**, F. Severin[89] obtained a distinctly lower enantiomeric excess of 75% for the substitution reaction on (*E*)-1,3-diphenylallyl methyl carbonate (**77**) with diphenylmethanone oxime (**60**) employing ligand **8** and $Pd_2(dba)_3$ as pre-catalyst under the otherwise same reaction conditions. The different substrate and ligand were made out to be accountable for the decrease in enantiomeric excess. Nonetheless, strategies to improve the enantiomeric excess for this reaction were investigated.



Scheme 61. Synthesis of Benzophenone Oxime (**60**) and 9*H*-Fluoren-9-one Oxime (**62**)

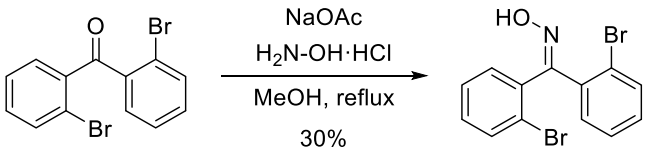
One approach was the substitution of the benzophenone oxime (**60**) with other nucleophiles. 9*H*-Fluoren-9-one oxime (**62**) was identified as one option (Scheme 61), although more sterically demanding nucleophiles seemed more promising. Since the η^3-allyl palladium complexes of the targeted symmetrically substituted allylic substrates (section 2.3.2) are C_{2h}-symmetric the allylic termini of this complex are enantiotopic.[140] Differentiation between these two enantiotopic ends by the incoming nucleophile leads to the desired selectivity which is caused by steric shielding of one end by the chiral ligand. Therefore, 2,2'-disubstituted diphenylmethanone oxime derivatives were considered with regard to investigation of the influence of increased steric hindrance of the nucleophile.



Scheme 62. Introduction of Benzyl Protection Groups in 2,2'-Dihydroxybenzophenone (**63**) and Subsequent Oxime Formation

According to Wagner et al.[141] 2,2'-dihydroxybenzophnenone (**63**) can be transferred into 2,2'-bis(benzyloxy)benzophenone (**65**) with benzyl bromide (**64**) and potassium hydroxide as base in dry methanol. Cesium carbonate was additionally added since TLC did not show sufficient transformation, but the yield still turned out to be low with isolation of only 5.4% of the *O*,*O*'-dibenzylated product **65**. Cesium carbonate is often the base of choice for *O*-alkylations, especially in case of phenols, since it supposedly produces the "naked" phenolate anion in non-aqueous solvents.[142] In a second attempt 2,2'-dihydroxybenzophenone (**63**) was reacted with benzyl bromide (**64**) in dry DMSO with sodium hydride as base yielding 76% of the desired product (**65**) (Scheme 62). Transformation into the corresponding oxime **66** was again carried out according to Park et al.[139] with a yield of 95% (Scheme 62).

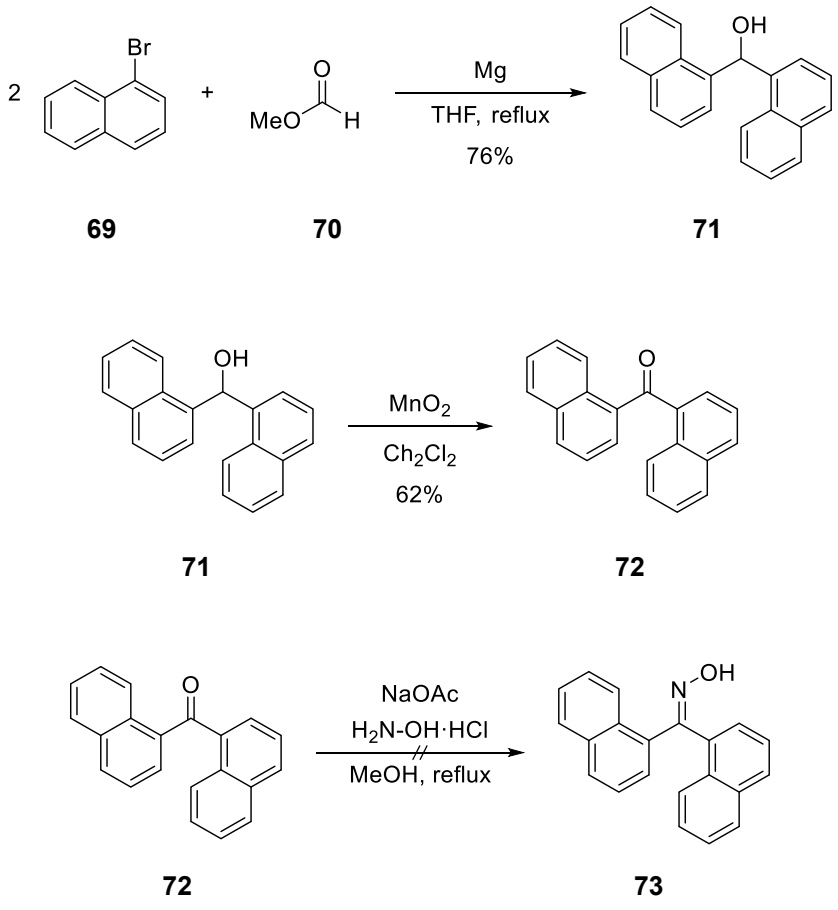
The synthesis of bis(2-bromophenyl)methanone oxime (**68**) was attempted according to the same procedure starting from 2,2'-dibromobenzophenone (**67**). Although sodium acetate and hydroxylamine hydrochloride were repeatedly provided in great excess, after seven days TLC still accounted for incomplete transformation. Additionally, oxime **68** did not precipitate therefore demanding liquid-liquid extraction resulting in only 30% yield (Scheme 63).



67 **68**

Scheme 63. Synthesis of Bis(2-bromophenyl)methanone Oxime (**68**)

Introducing steric hindrance without adding functional groups would be possible by substitution of the phenyl groups with the larger naphthyl moieties. For the synthesis of di(naphthalen-1-yl)methanone oxime (**73**), 1-bromonaphthalene (**69**) was reacted with magnesium forming the corresponding Grignard reagent. The procedure reported by Koskinen et al.[143] was slightly modified by employing methyl formate (**70**) instead of the ethyl derivative but afforded bis(1-naphthyl)methanol (**71**) in an identical yield of 76% (Scheme 64). The oxidation resulting in the corresponding dinaphthyl ketone **72** in 62% yield was carried out employing manganese(IV) dioxide as proposed by Fletcher et al.[144] (Scheme 64).



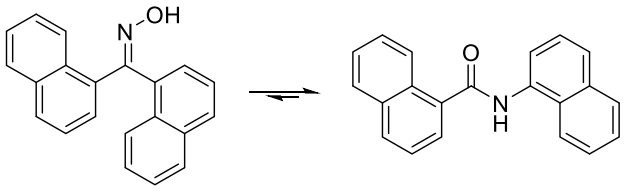
69 **70** **71**

71 **72**

72 **73**

Scheme 64. Attempted Synthesis of Di(naphthalen-1-yl)methanone Oxime (**73**)

For the oxime formation TLC showed barely any transformation into the desired oxime **73** after two days (Scheme 64). According to a report by Beckmann, Liesche and Correns[145] this is not surprising, since the α-naphthyl-α-naphthyl-ketoxime (**73**) is merely accessible in acidic solution, and even then very susceptible to the Beckmann rearrangement reaction resulting in formation of the amide **74** (Scheme 65). An unsuccessful attempt to employ the solid obtained from the oxime formation reaction in an allylation reaction supports this claim.

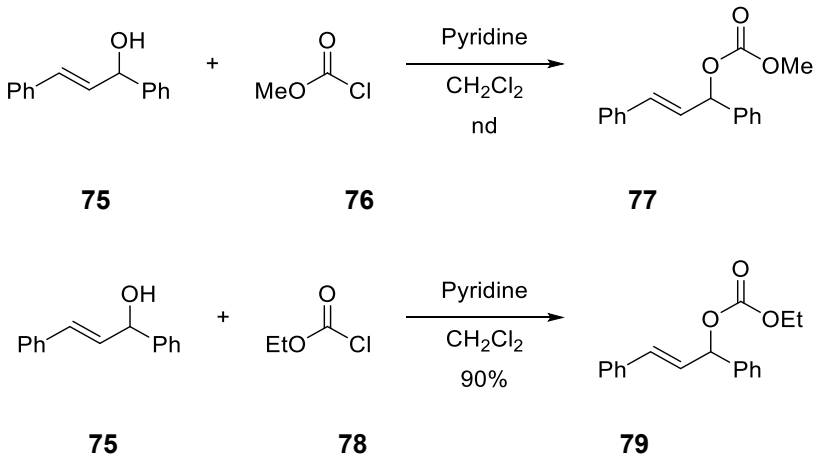


73 **74**

Scheme 65. Beckmann Rearrangement of Di(naphthalen-1-yl)methanone Oxime (**73**) Resulting in the Corresponding Amide **74**

2.3.2. Allyl Carbonates and Allyl Acetates as Substrates for Allylic Substitution

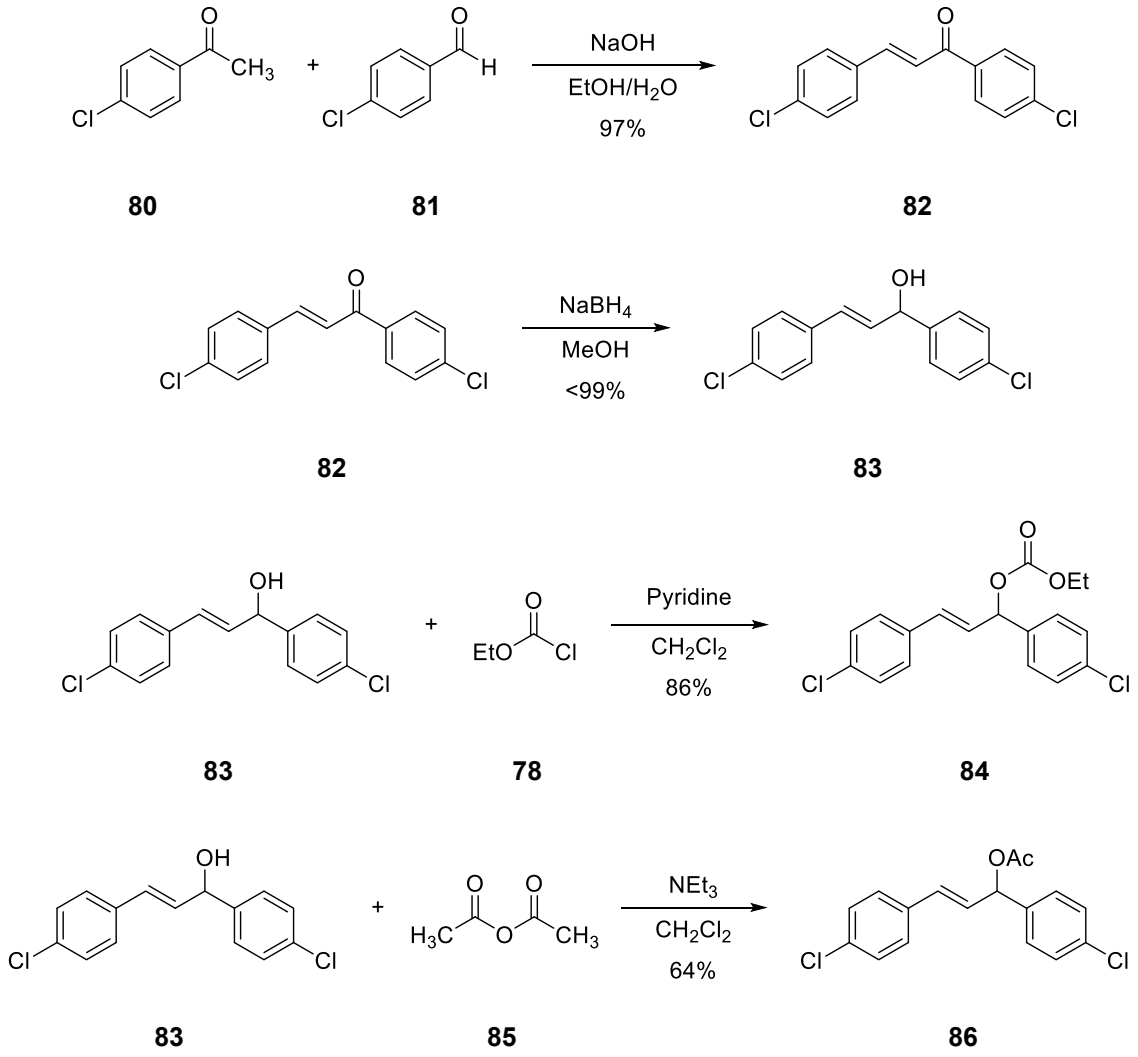
As mentioned above Du et al.[84] employed allylic acetates for asymmetric allylic etherification with oximes. Carbonates however offer the advantage that upon substitution of the leaving group by palladium the carbonate leaving group degrades into carbon dioxide and the corresponding alkoxide anion. This alkoxide anion serves as the base required for deprotonation of the oxime therefore addition of supplementary base is expendable. Nonetheless, carbonate is generally a better leaving group than acetate, therefore changing the kinetics of the palladium catalyzed reaction[146] and presumably resulting in a change of selectivity as observed by F. Severin[89]. To verify the obtained results and further investigate the application of carbonates as substrates allylic carbonates as well as allylic acetates were targeted as substrates for the enantioselective allylic substitution reaction. To further eliminate complications posed by regioselectivity the attention was focused on allylic substrates that are symmetrically substituted as their corresponding η^3-allyl palladium complexes exhibit C_{2h} symmetry while later three unsymmetrically substituted substrates were added.



Scheme 66. Synthesis of (*E*)-1,3-Diphenylallyl Methyl Carbonate (**77**) and (*E*)-1,3-Diphenylally Ethyl Carbonate (**79**)

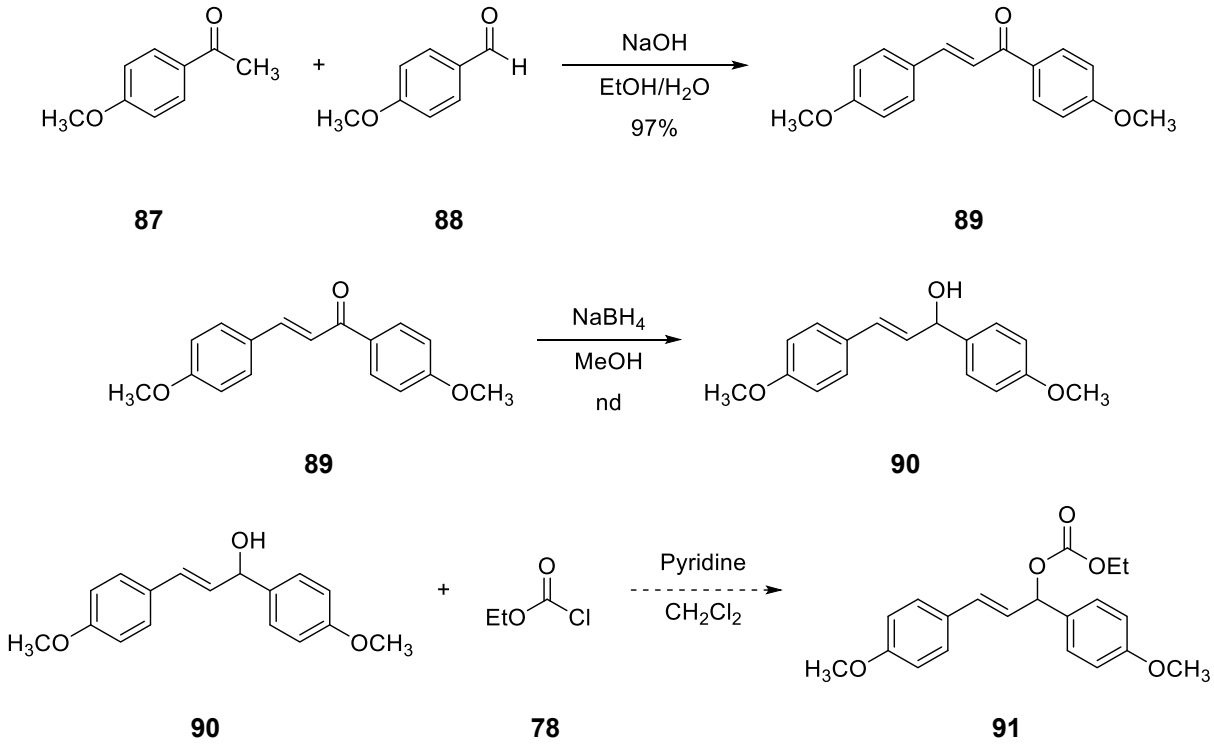
The carbonates were synthesized from the corresponding alcohols by reaction with the appropriate chloroformate and pyridine as base according to a procedure by Kobayashi et al.[147]. While the reaction of (*E*)-1,3-diphenylprop-2-en-1-ol (**75**) with methyl chloroformate (**76**) did not result in complete transformation into carbonate **77**, the formation of (*E*)-1,3-diphenylallyl ethyl carbonate (**79**) proceeded smoothly employing ethyl chloroformate (**78**) (Scheme 66).

The *para*-chloro derivative **84** required two additional steps starting with the formation of the respective chalcone **82** followed by a reduction of the carbonyl group (Scheme 67). 4-Chloroacetophenon (**80**) was reacted with 4-chlorobenzaldehyde (**81**) in an aldol condensation reaction with sodium hydroxide as base, affording (*E*)-1,3-bis(4-chlorophenyl)prop-2-en-1-one (**82**) in 97% yield. Reduction with sodium borohydride resulted in formation of the corresponding allylic alcohol **83** in over 99% yield. Both reactions were run according to a protocol by Mayr et al.[148]. Conversion into the carbonate **84** was carried out as described before with ethyl chloroformate (**78**) and pyridine in 86% yield. Secondly, the corresponding allylic acetate **86** was obtained in 64% yield by transformation of the allylic alcohol **83** with acetic anhydride (**85**) and triethylamine as base as proposed by Yudin et al.[149] for the synthesis of (*E*)-1,3-diphenylallyl acetate (**148**).



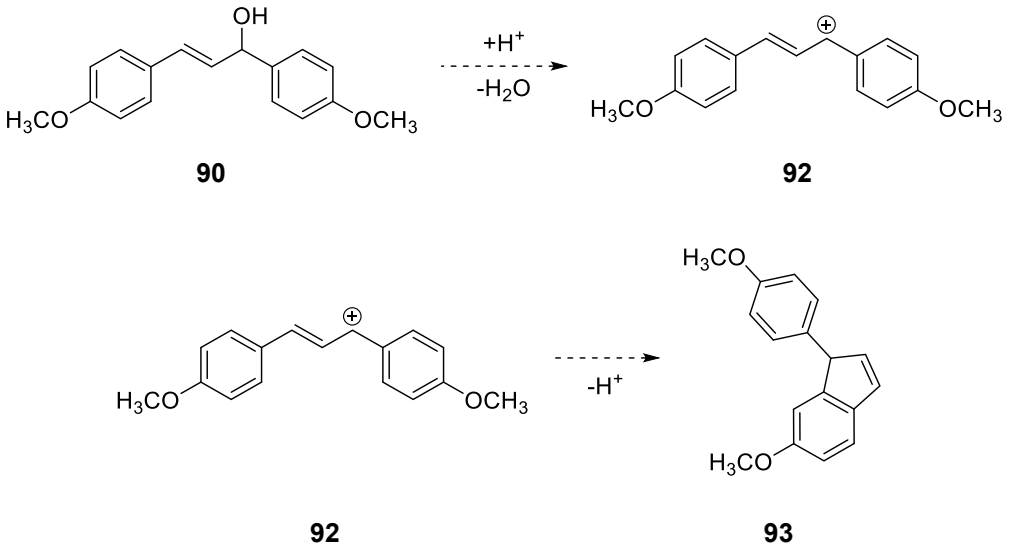
Scheme 67. Synthesis of (*E*)-1,3-Bis(4-chlorophenyl)allyl Ethyl Carbonate (**84**) and Acetate (**86**)

Attempts to synthesize a *para*-methoxy derivative **91** turned out to be more challenging. The corresponding chalcone **89** was obtained readily in 97% yield following the aldol condensation reaction of 4'-methoxyacetophenone (**87**) and *p*-anisaldehyde (**88**) (Scheme 68). The subsequent reduction with sodium borohydride did afford allylic alcohol **90**. However, TLC and ^{1}H NMR spectroscopy showed rapid decomposition of the isolated material even if stored at 4 °C. The allylic alcohol **90** might be less stable than the *para*-chloro derivative **83** due to the +M-effect of the methoxy groups.



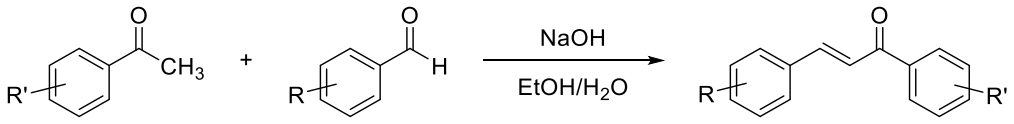
Scheme 68. Attempted Synthesis of (*E*)-1,3-Bis(4-methoxyphenyl)prop-2-en-1-ol (**90**)

Protonation of the hydroxy group and subsequent abstraction of water might lead to formation of carbocation **92** (Scheme 69). This cation is generally well stabilized, even regarding the unsubstituted 1,3-diphenyl system, as the positive charge is located in an allylic as well as benzylic position rendering the allylic alcohols highly reactive. In case of the methoxy substituents the cation is additionally activated concerning electrophilic aromatic substitution. This reactivity might account for the formation of a hypothetically less polar by-product like **93**, observed by TLC. Further conversion into the corresponding carbonate was not attempted since this motive might even increase the instability.



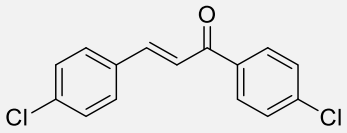
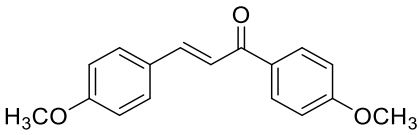
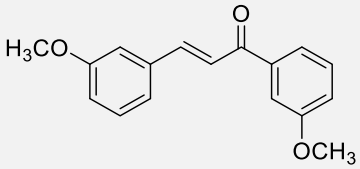
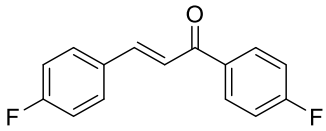
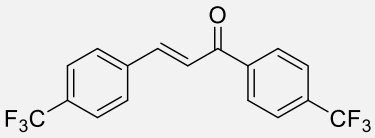
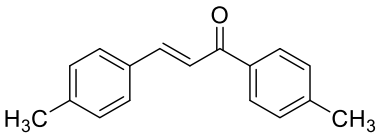
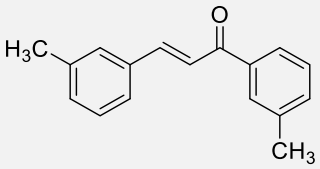
Scheme 69. Potential Reactivity of Diphenylchalcone-Derived Alcohols Illustrated by the *para*-Methoxy Derivative **90**

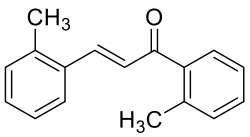
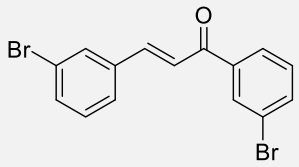
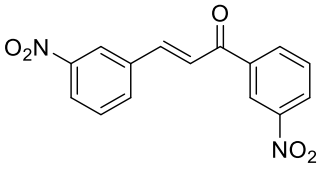
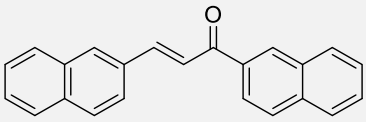
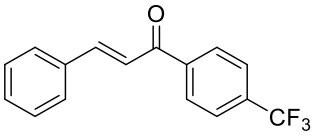
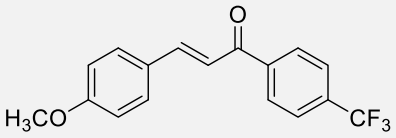
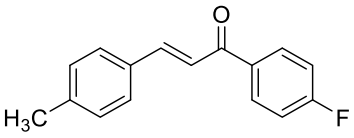
Further chalcone derivatives were synthesized by aldol condensation reactions of the corresponding aldehydes and ketones (Scheme 70) with the corresponding yields summarized in Table 1. While the *para*-substituted chalcones as well as the *meta*-bromo derivative **100** were isolable by precipitation from the reaction mixture the *meta*-tolyl **98**, *ortho*-tolyl **99** and *meta*-methoxy **94** derivatives were obtained by liquid-liquid extraction. (*E*)-1,3-bis(3-bromophenyl)prop-2-en-1-one (**100**) and (*E*)-1,3-bis(4-(trifluoromethyl)phenyl) prop-2-en-1-one (**96**) needed to be purified by column chromatography resulting in lower yields of 72% and 43%, respectively. The *m*-nitro derivative **101** could not be obtained under these conditions. With compounds **103** through **105** asymmetric chalcones were synthesized as well.



Scheme 70. Syntheses of Further Chalcone Derivatives

Table 1. Yields of Synthesized Chalcones

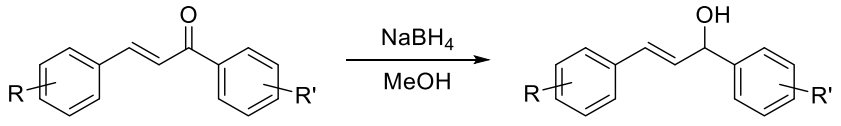
R, R’	Compound	Yield
p-Cl	 **82**	97%
p-OCH_3	 **89**	97%
m-OCH_3	 **94**	94%
p-F	 **95**	99%
p-CF_3	 **96**	62%[a)]
p-CH_3	 **97**	90%
m-CH_3	 **98**	99%

o-CH_3	 **99**	98%
m-Br	 **100**	72%[a)]
m-NO_2	 **101**	-
Ph	 **102**	86%[150]
H, *p*-CF_3	 **103**	96%
p-OCH_3, *p*-CF_3	 **104**	96%
p-CH_3, *p*-F	 **105**	99%

[a)] Purification by column chromatography

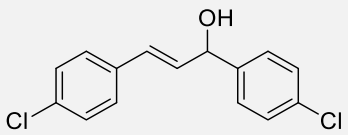
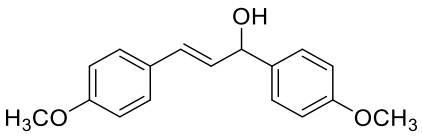
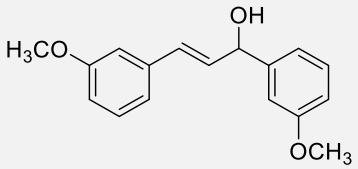
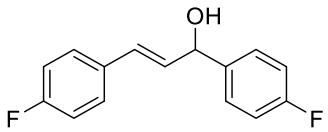
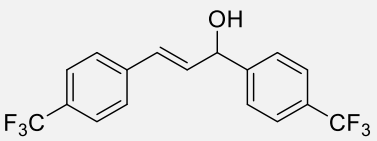
These chalcones were subsequently transformed into the corresponding alcohols by reduction with sodium borohydride (Scheme 71). As priorly discussed for (*E*)-1,3-bis(4-methoxyphenyl)prop-2-en-1-ol (**90**), the allyl benzyl alcohols exhibit great fragility, especially under acidic conditions (Scheme 69). Therefore, the alcohols were not

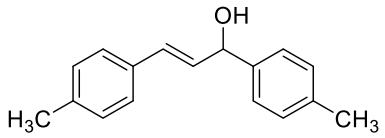
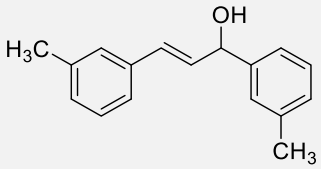
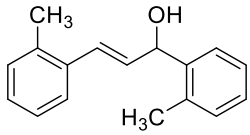
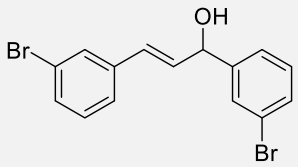
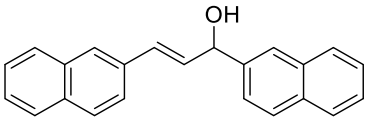
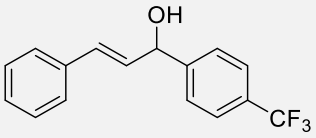
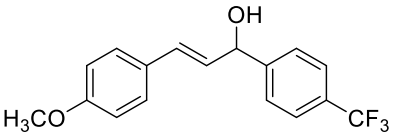
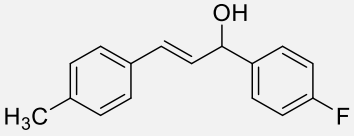
subjected to chromatographic purification but rather transformed directly into the respective allyl acetates (Scheme 72). If isolated the respective yields are given in Table 2.



Scheme 71. Reduction of Chalcones with $NaBH_4$

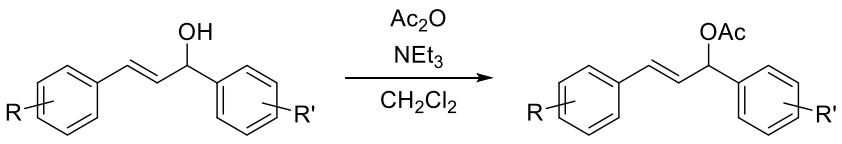
Table 2. Yields of Allylic Alcohols, if Isolated

R, R’	Compound	Yield
p-Cl	 **83**	>99%
p-OCH_3	 **90**	nd[a)]
m-OCH_3	 **106**	nd[a)]
p-F	 **107**	95%
p-CF_3	 **108**	99%

p-CH_3	 **109**	nd[a)]
m-CH_3	 **110**	nd[a)]
o-CH_3	 **111**	96%
m-Br	 **112**	nd[a)]
Ph	 **113**	nd[a)]
H, *p*-CF_3	 **114**	nd[a)]
p-OCH_3, *p*-CF_3	 **115**	nd[a)]
p-CH_3, *p*-F	 **116**	nd[a)]

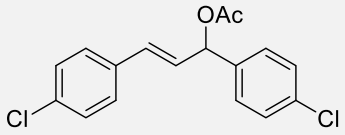
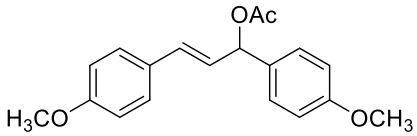
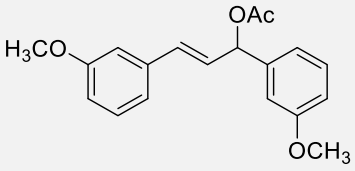
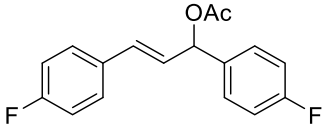
[a)] Yield of the allylic alcohol was not determined but instead directly transferred into the allylic acetate

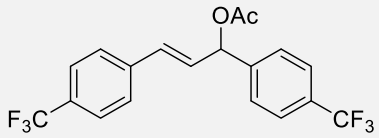
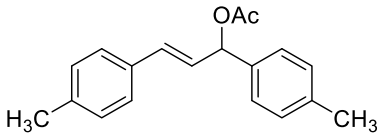
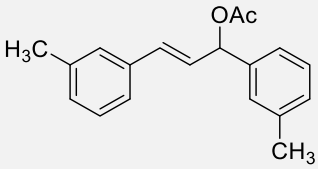
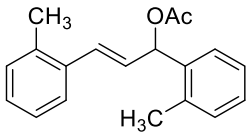
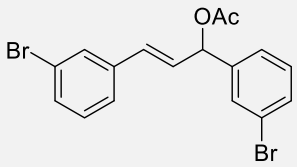
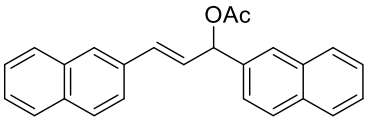
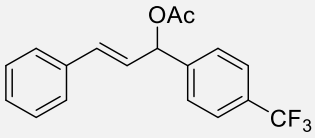
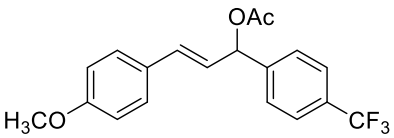
The allylic alcohols were acylated employing acetic anhydride and triethylamine as base (Scheme 72). The allyl acetates exhibit a slightly greater stability than the corresponding alcohols and are therefore more easily purified by column chromatography, if necessary and are as well more stable than the allylic carbonates. They could be obtained in sufficient to good yields ranging from 64% to 90% (Table 3).

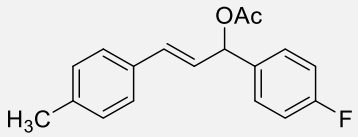


Scheme 72. Synthesis of Allylic Acetates by Acylation of Allylic Alcohols

Table 3. Yields of Allylic Acetates

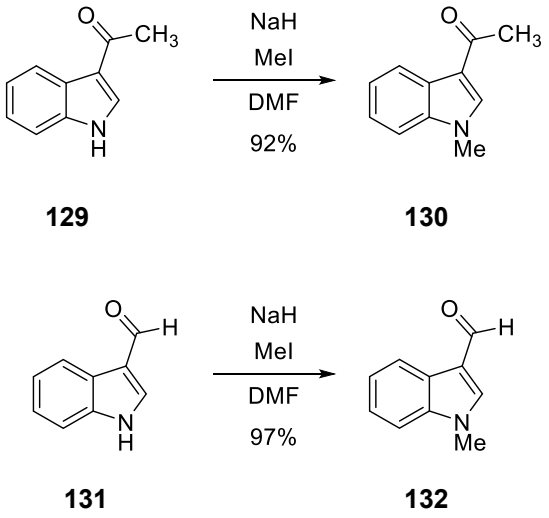
R, R’	Compound	Yield
p-Cl	 **86**	64%
p-OCH_3	 **117**	89%[a)]
m-OCH_3	 **118**	89%[a)]
p-F	 **119**	78%

p-CF_3	 **120**	67%
p-CH_3	 **121**	89%[a)]
m-CH_3	 **122**	89%[a)]
o-CH_3	 **123**	82%
m-Br	 **124**	90%[a)]
Ph	 **125**	67%[a)][150]
H, *p*-CF_3	 **126**	90%[a)]
p-OCH_3, *p*-CF_3	 **127**	87%[a)]

p-CH_3, *p*-F	 **128**	88%[a)]

[a)] Regarding the two-step transformation starting from the corresponding chalcone

For the synthesis of an indole chalcone derivative the corresponding ketone **129** and aldehyde **131** were subjected to methylation first (Scheme 73). 3-Acetyl-1-methylindole (**130**) was obtained in 92% yield and 1-methylindole-3-carboxaldehyde (**132**) in 97% yield according to a procedure employing methyl iodide and sodium hydride as base as published by Nakao and Hiyama et al.[151].

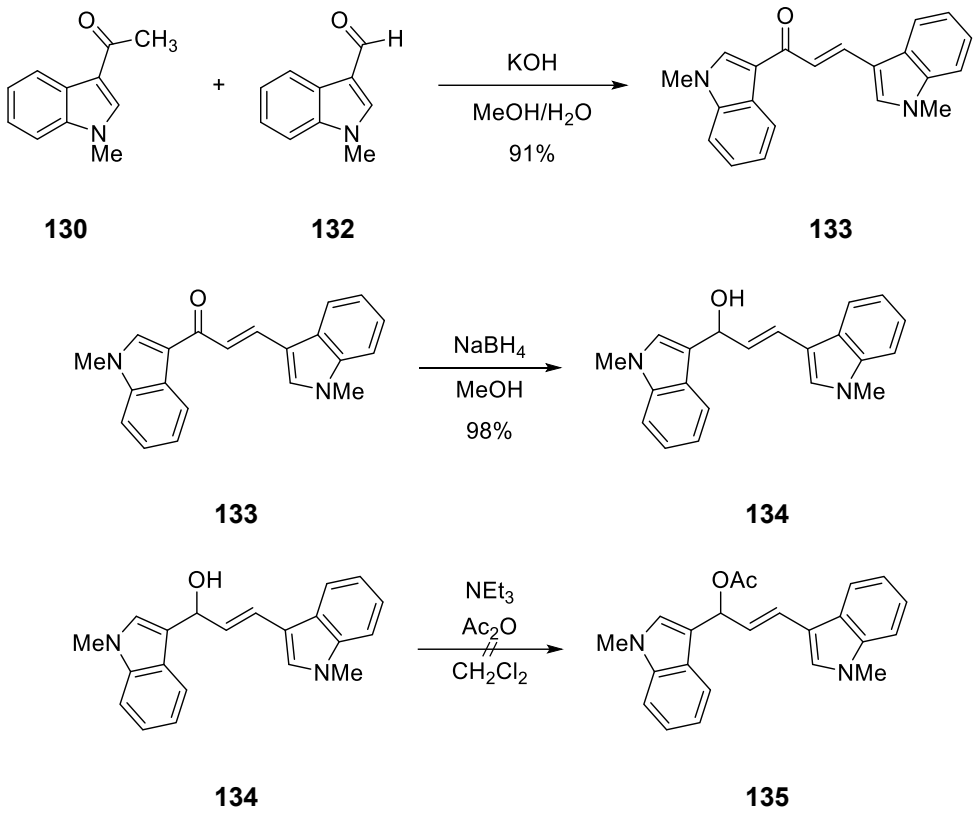


129 **130**

131 **132**

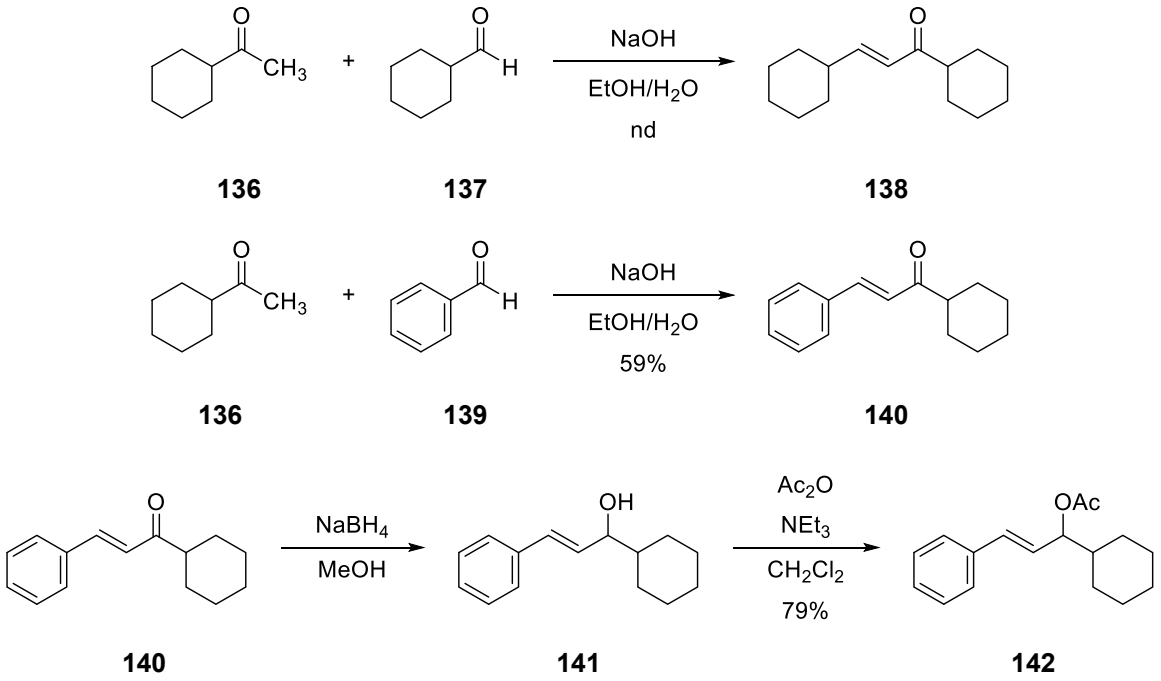
Scheme 73. Methylation of Indole Derivatives

These methylated indole derivatives were then reacted to afford chalcone **133** in 91% yield (Scheme 74). Contrary to the former reported reaction conditions potassium hydroxide in methanol/water was applied in this case as published by Martel-Frachet et al.[152] since an attempt with sodium hydroxide in water/ethanol did not result in the desired aldol condensation reaction. Reduction with sodium borohydride gave the allyl alcohol **134** in 98% yield, although the reaction could not be monitored by TLC. Consecutive acetylation was not successful, presumably due to high instability of the allyl acetate **135**. The ^{1}H NMR spectrum of the obtained solid revealed that merely the substrate **134** was retrieved.



Scheme 74. Attempted Synthesis of a Symmetric 3-Indol Substrate **135**

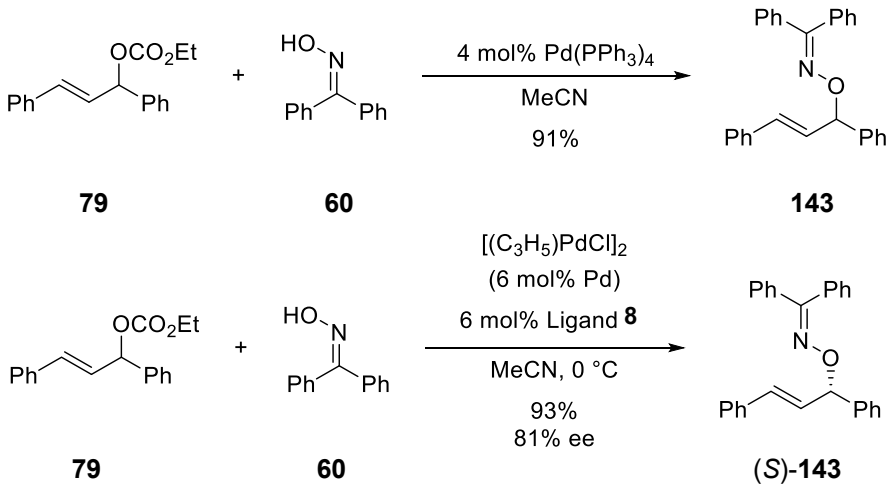
Additionally, the synthesis of an aliphatically substituted chalcone was considered. The pertinent reaction conditions were applied to cyclohexyl methyl ketone (**136**) and cyclohexanecarboxaldehyde (**137**) (Scheme 75). Attempted purification of the raw material did however not afford the desired dicyclohexyl chalcone **138** in pure form. Since D. Scholz[150] showed in his bachelor thesis, that a phenyl methyl substituted substrate could be transformed into the corresponding racemic isoxazolidine, the phenyl cyclohexyl substituted substrate **142** as an asymmetrical substrate with a substantially larger aliphatic residue was targeted (Scheme 75). The chalcone **138** was obtained in 59% yield according to Kerr et al.[153] and the allylic acetate **142** in the two consecutive steps in an overall yield of 79%.



Scheme 75. Synthesis of a Cyclohexyl Derivative

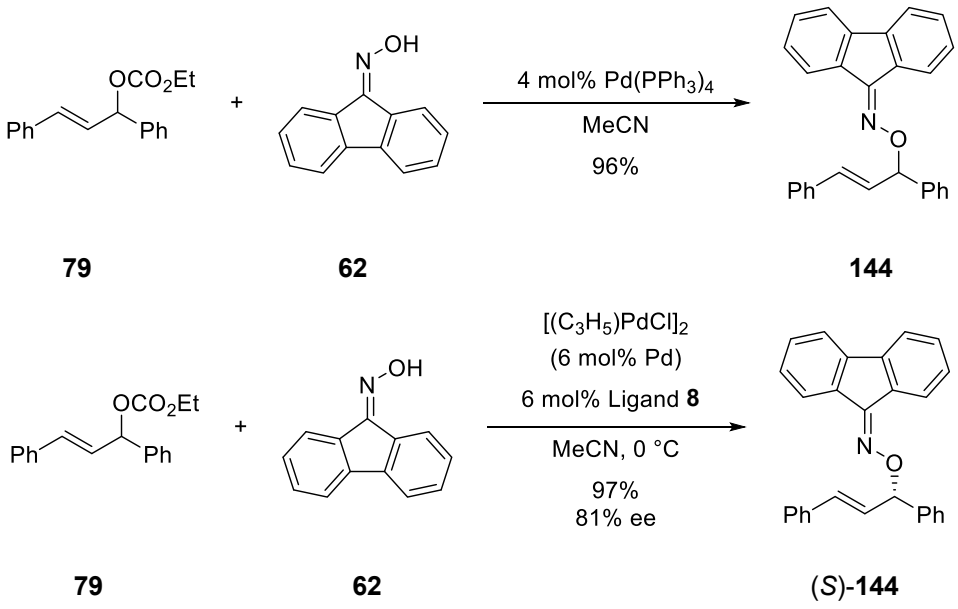
2.3.3. Tsuji-Trost Allylation with Ketoximes

The first attempts regarding the Tsuji-Trost allylation reaction were carried out employing benzophenone oxime (**60**) and allylic ethyl carbonate **79** (Scheme 76). The unselective transformation was catalyzed by tetrakis(triphenylphosphine) palladium(0) and yielded 91% of the desired racemic allyl oxime **143**. For the enantioselective transformation the method developed by Du et al.[84], employing allylpalladium(II) chloride dimer as pre-catalyst and the hybrid ligand (*R*)-diphenyl(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (**8**) at 0 °C, was applied and adapted in terms of omitting the additional base, since the alkoxide derived from the carbonate leaving group serves as base. This procedure resulted in nearly quantitative isolated yield of the desired (*S*)-allyl oxime (*S*)-**143** in four hours with an enantiomeric excess of 81%.



Scheme 76. First Attempted Enantioselective Allylation with Benzophenone Oxime (**60**) and Allyl Carbonate **79**

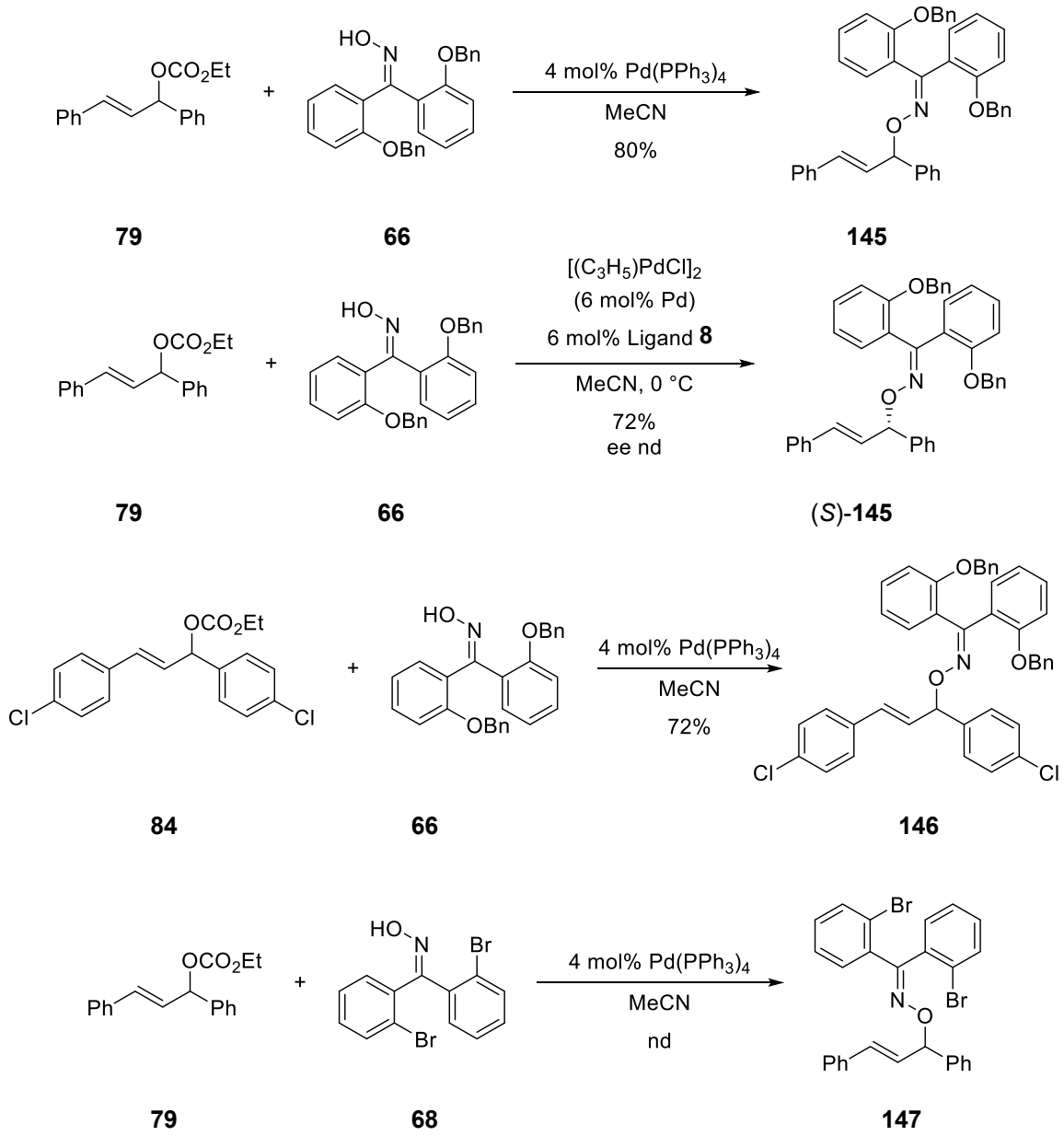
Although the enantiomeric excess was improved slightly compared to the 75% obtained employing $Pd(dba)_2$ as pre-catalyst by F. Severin[89] the selectivity observed by Du et al.[84] of 92% was not achieved. To determine the influence of the oxime nucleophile, benzophenone oxime (**60**) was substituted in a second attempt by 9*H*-fluoren-9-one oxime (**62**) (Scheme 77). Both yields increased slightly to 96% and 97%, respectively, but had no influence on the enantiomeric excess of the resulting allyl oxime **144**, which again amounted to 81%.



Scheme 77. Enantioselective Allylation with 9*H*-Fluoren-9-one Oxime (**62**) and Allyl Carbonate **79**

As discussed previously in section 2.3.1 the application of 2,2'-disubstituted diphenylmethanone oximes seemed more promising concerning an increase in selectivity.

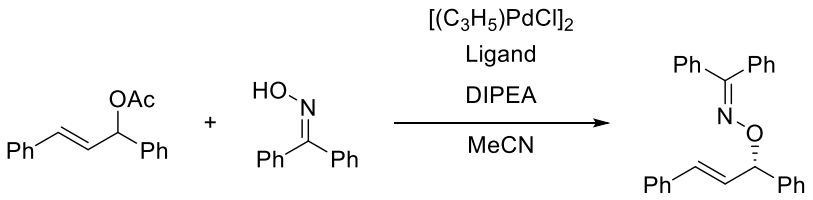
For bis(2-(benzyloxy)phenyl)methanone oxime (**66**), racemic allyl oxime **145** and (*S*)-enantiomer (*S*)-**145** were synthesized under the respective previously described reaction conditions (Scheme 78). The yield turned out lower than for the non-hindered oximes which is not surprising in light of the increased steric hindrance of the oxime **66** compared to benzophenone oxime (**60**). The exact enantiomeric excess could not be determined, due to insufficient separation by chiral HPLC. Although separation was sufficient to indicated that at least the enantiomeric excess did not show dramatic improvement. In hope for better separation the racemic *para*-chloro derivative **146** was synthesized but showed as well poor separation of the two enantiomers concerning the HPLC chromatogram (Scheme 78). Since the racemic (*E*)-bis(2-bromophenyl)methanone *O*-(1,3-diphenylallyl) oxime (**147**) could not be isolated in sufficient purity and additionally the isomers could not be separated by chiral HPLC either, it was refrained from selective transformation of (*E*)-1,3-diphenylallyl ethyl carbonate (**79**) with bis(2-bromophenyl)methanone oxime (**68**) (Scheme 78).



Scheme 78. Allylation Reaction of Sterically Hindered 2,2'-Disubstituted Diphenylmethanone Oximes **66** and **68**

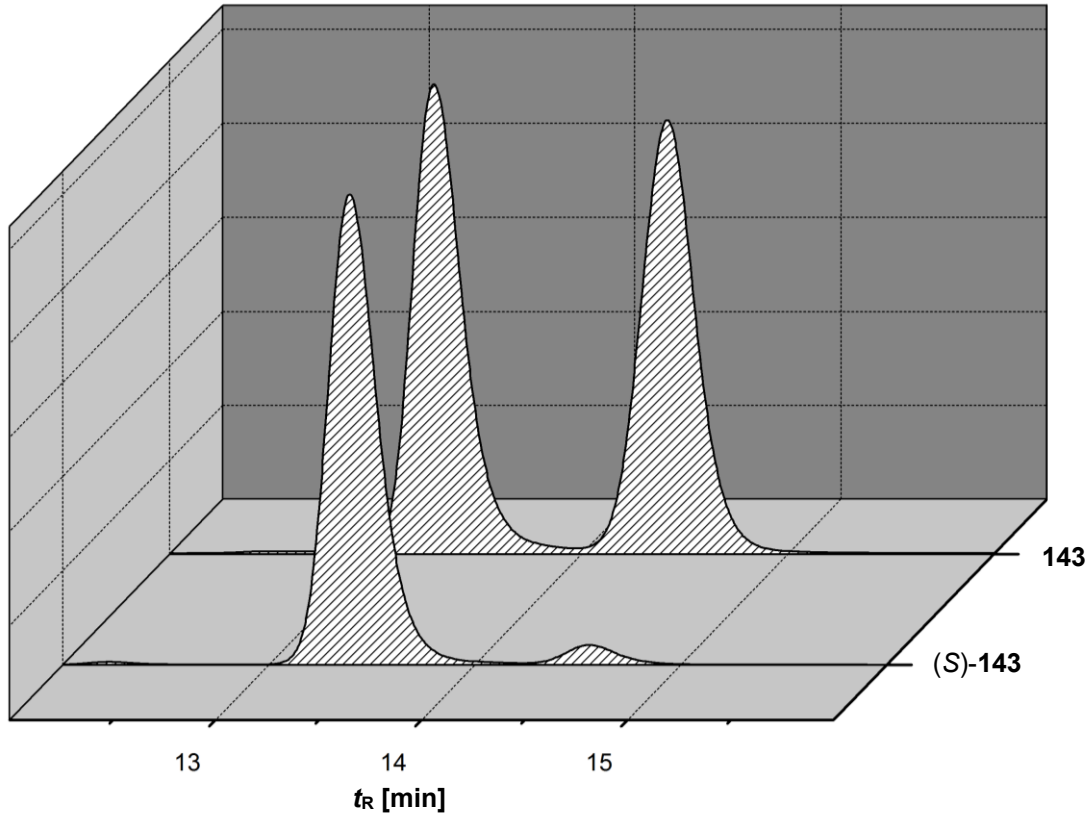
To verify the results obtained by Du et al.[84] the attention was shifted towards allyl acetate **148**. It was consequently reacted with the benzophenone oxime (**60**) to obtain the enantioenriched allyl oxime (*S*)-**143** several times under varying conditions (Scheme 79). While the hybrid ligand **8** did result in 88% enantiomeric excess the 3,5-dimethylphenyl derivative **8a** resulted in up to 92% enantiomeric excess although accompanied by slightly lower yields and longer reaction times. Contradictory to the reaction time of two hours reported by Du et al.[84] the reaction solution had to be stirred for two or three days until TLC showed sufficient conversion of the substrate **148**. Furthermore, additional benzophenone oxime (**60**) had to be submitted to the reaction after approximately 24 hours or an excess of had to be applied from the beginning in order to achieve thorough transformation. Although

an increase in catalyst loading to 5.0 mol% rendered this requirement avoidable. Moreover, it might be assumed that an addition of more than two equivalents of base is not favorable since in this case completion of the reaction took an additional day.



148 **60** (*S*)-**143**

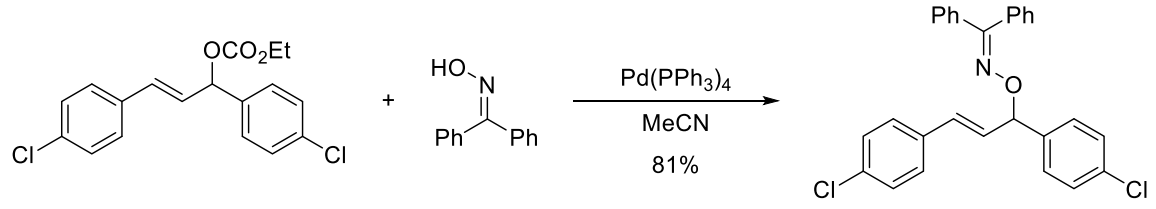
Allyl acetate [mmol]	Oxime [equiv]	Catalyst [mol%]	Ligand	DIPEA [equiv]	T [°C]	Reaction time	Yield	ee
0.480	1.0 + 0.2	4.1	**8**	2.0	ice	1d	80%	88%
0.484	1.0 + 0.6	3.4	**8a**	1.8	ice	2d	78%	90%
0.416	3.9	3.9	**8a**	3.9	ice	3d	76%	92%
0.400	1.0	5.0	**8a**	2.0	0	2d	78%	91%



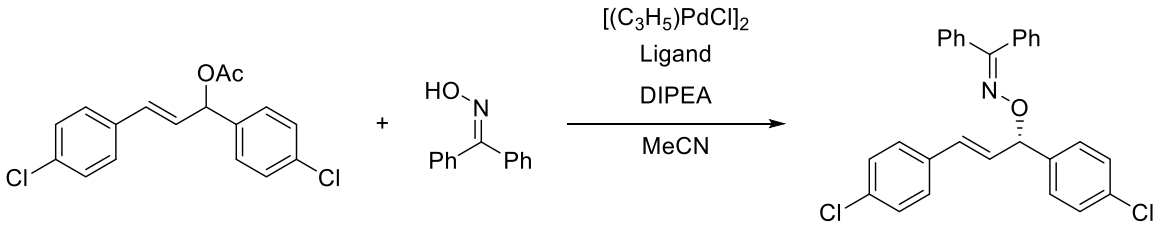
Scheme 79. Enantioselective Allylation Affording Allyl Oxime (*S*)-**143** According to Du et al.[84]

The reaction time compared to carbonate **79** is significantly longer while affording a notably higher enantiomeric excess up to 92%, indicating that the distinctly higher reactivity of carbonate **79** resulting in an increased reaction rate has a negative effect on the selectivity of the reaction.

The reaction conditions were in turn applied to (*E*)-1,3-bis(4-chlorophenyl)allyl acetate (**86**), affording the corresponding allyl oxime (*S*)-**149** with up to 86% enantiomeric excess (Scheme 80). The racemic allyl oxime **149** was isolated in 81% yield from the reaction of carbonate **84**, which was employed due to expectation of a shorter reaction time.



84 **60** **149**



86 **60** (*S*)-**149**

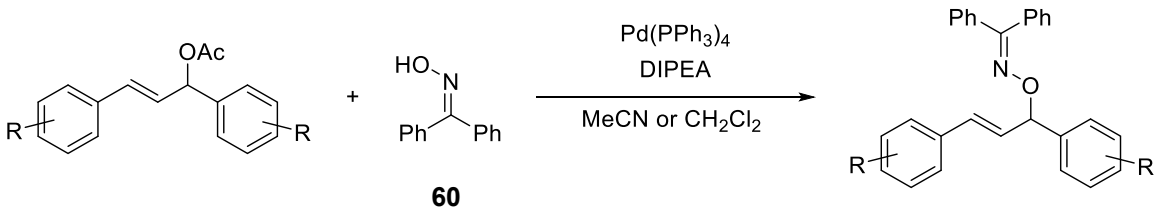
Allyl acetate [mmol]	Oxime [equiv]	Catalyst [mol%]	Ligand	DIPEA [equiv]	T [°C]	Reaction time	Yield	ee
0.405	1.6	4.0	**8a**	4.1	ice	2d	90%	86%
0.395	4.0	5.1	**8a**	4.1	ice	1d	92%	84%
0.436	1.0	4.6	**8a**	1.8	0	1d	83%	84%
0.402	1.0	>5.0 [a)]	**8a**	2.0	-16	1d	83%	66%

[a)] could not be determined exactly due to vibration of the scale

Scheme 80. Enantioselective Allylation with (*E*)-1,3-Bis(4-chlorophenyl)allyl Acetate (**86**)

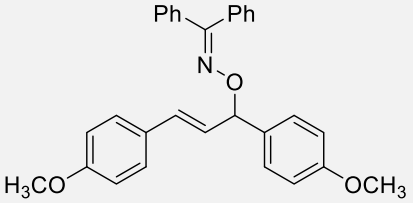
The reaction proceeded smoothly in one day after the catalyst loading was increased to approximately 5% although accompanied by a slight decrease in enantiomeric excess. Lowering the reaction temperature did not improve the enantiomeric excess rather on the contrary led to a huge drop to 66% enantiomeric excess. This was later attributed to an even further increase in catalyst loading, which could not be determined exactly due to vibration of the scale. The allyl oxime (*S*)-**149** eventually showed a decrease in enantiomeric excess upon storage at room temperature. Exposure to *n*-hexane, silica gel or Al_2O_3 (neutral, III) did not result in racemization after a period of three days. However, after another five days a decrease of 3% (84% ee $\rightarrow$ 81% ee) was recorded, for storage in *n*-hexane solution. Treating the respective solution with NH_4Cl solution did not lead to further racemization, whereas washing with citric acid solution caused the enantiomeric excess to drop to 70%.

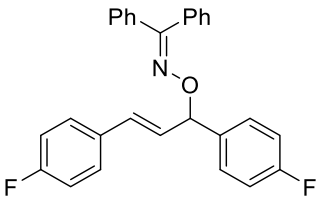
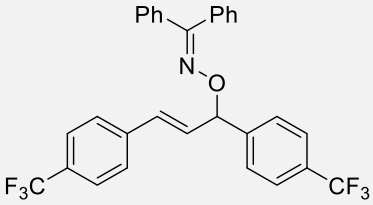
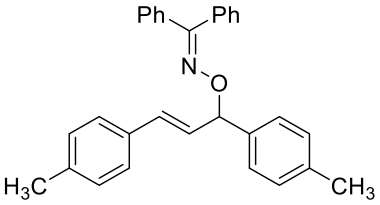
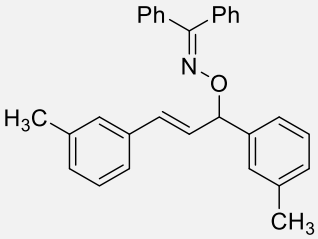
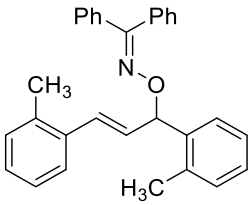
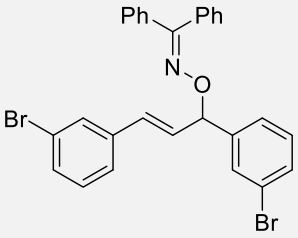
Further racemic allyl oximes **150** through **157** were obtained from the respective allyl acetates **117** and **119** through **125**, respectively (Table 4), employing $Pd(PPh)_3$ and DIPEA as base in an allylic substitution reaction (Scheme 81). While the yields in acetonitrile remained rather low between 40% to 76%, employing CH_2Cl_2 as solvent led to yields up to 86%.

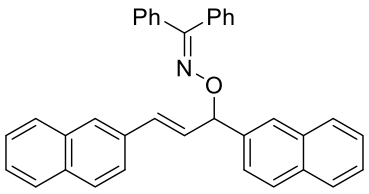


Scheme 81. Synthesis of Further Racemic Allyl Oximes from Allyl Acetates

Table 4. Yields of Racemic Symmetrically Substituted Allyl Oximes

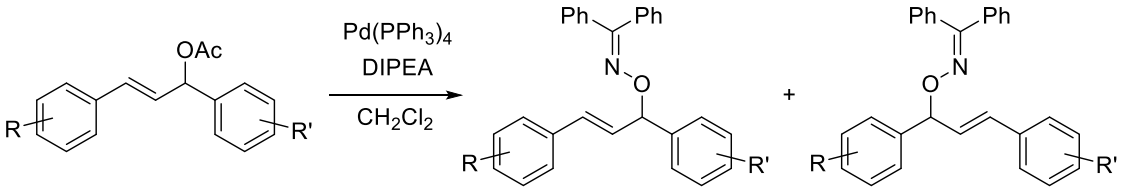
R	Compound	Yield
p-OCH_3	 **150**	84% [a)]

p-F	 **151**	50%
p-CF_3	 **152**	76%
p-CH_3	 **153**	40%
m-CH_3	 **154**	67% [a)]
o-CH_3	 **155**	50%
m-Br	 **156**	86% [a)]

Ph	 **157**	48% [a)][150]

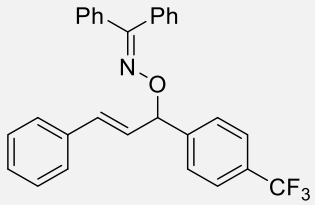
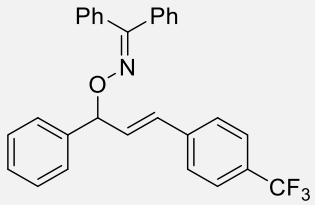
[a)] CH_2Cl_2 was used as solvent

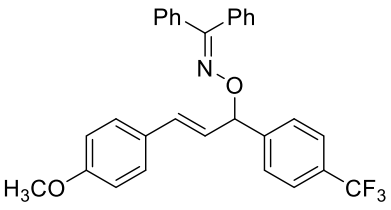
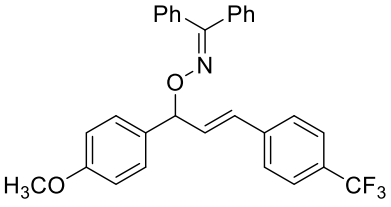
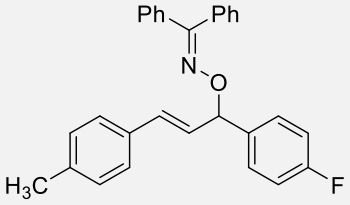
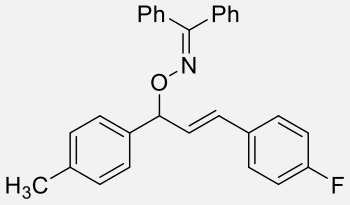
For the allylation reaction employing the unsymmetrically substituted allyl acetates **126** through **128**, two products need to be considered for each case (Scheme 82). Due to the high structural similarity of the two products they are merely adequately separable by column chromatography. The individual yields were determined by ^1H and ^{19}F NMR spectroscopy of the obtained mixtures (Table 5).



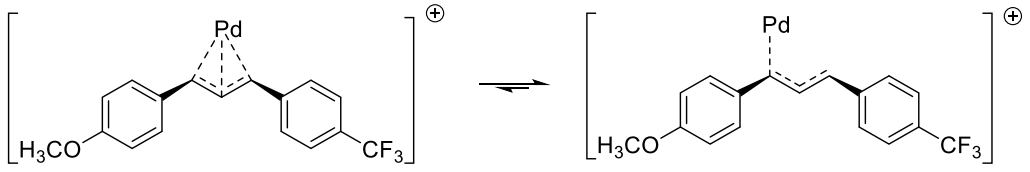
Scheme 82. Synthesis of Unsymmetrically Substituted Racemic Allyl Oximes from Allyl Acetates

Table 5. Yields of Racemic Unsymmetrically Substituted Allyl Oximes

R, R’	Compound	Yield
H, *p*-CF_3	 **158**	73% **158**:**159** 0.9:1.0
H, *p*-CF_3	 **159**	

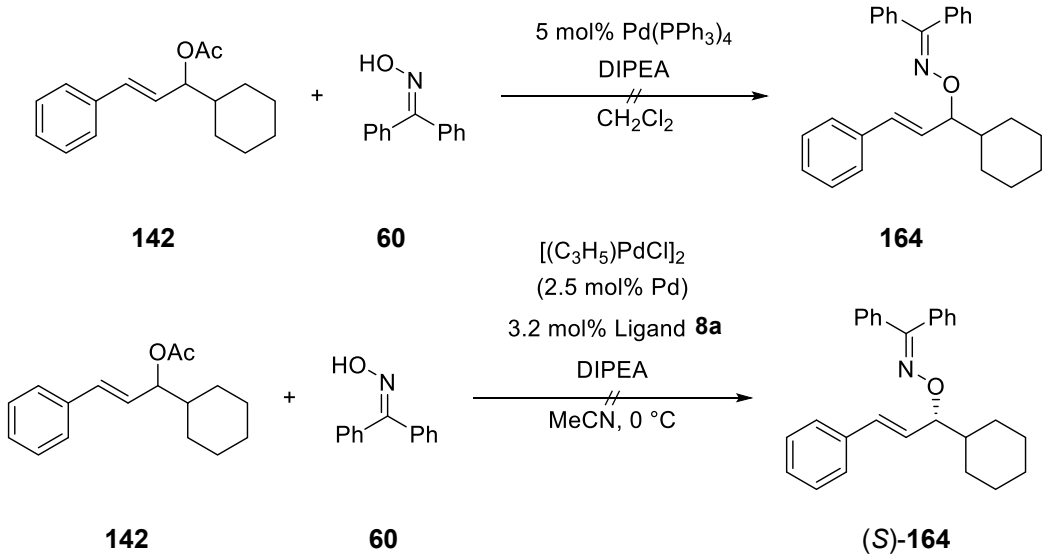
p-OCH_3, *p*-CF_3	 **160**	
p-OCH_3, *p*-CF_3	 **161**	60% **160**:**161** 0.1:1.0
p-CH_3, *p*-F	 **162**	
p-CH_3, *p*-F	 **163**	70% **162**:**163** 0.9:1.0

While the allylation reaction with the phenyl/*para*-(trifluoromethyl)phenyl derivative **126** and the *para*-tolyl/*para*-fluorophenyl derivative **128** showed nearly no selectivity yielding the allyl oximes **158**/**159** and **162**/**163** respectively both in a ratio of almost 1:1, the allyl oximes **160**/**161** obtained from allylation of the corresponding *para*-methoxy/*para*-(trifluoromethyl) phenyl derivative **127** showed much greater selectivity with almost 90% product share of the allyl oxime **161**. This result might be attributed to the substituent effects which are the most complementary in the allyl acetate **127**, as the methoxy substituent exhibits a strong +M-effect while the trifluoromethyl group pulls electron density due to the high electronegativity of the fluoro substituents adding up to a strong -I-effect on the other side of the molecule. This will most certainly lead to a severely asymmetric η^3 palladium-complex where the equilibrium might even be distinctly favoring a η^1 coordination (Scheme 83).



Scheme 83. η^3 vs. η^1 Coordination in the Palladium Allyl Complex

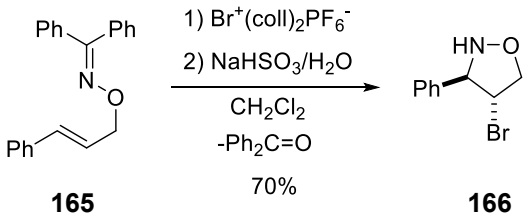
The allylation reaction employing the phenyl cyclohexyl allyl acetate **142** was not successful neither under racemic nor under enantioselective conditions yielding the desired allyl oxime **164** (Scheme 84).



Scheme 84. Attempted Synthesis of Phenyl Cyclohexyl Allyl Oxime **164**

2.3.4. Halocyclization of Allyl Ketoximes

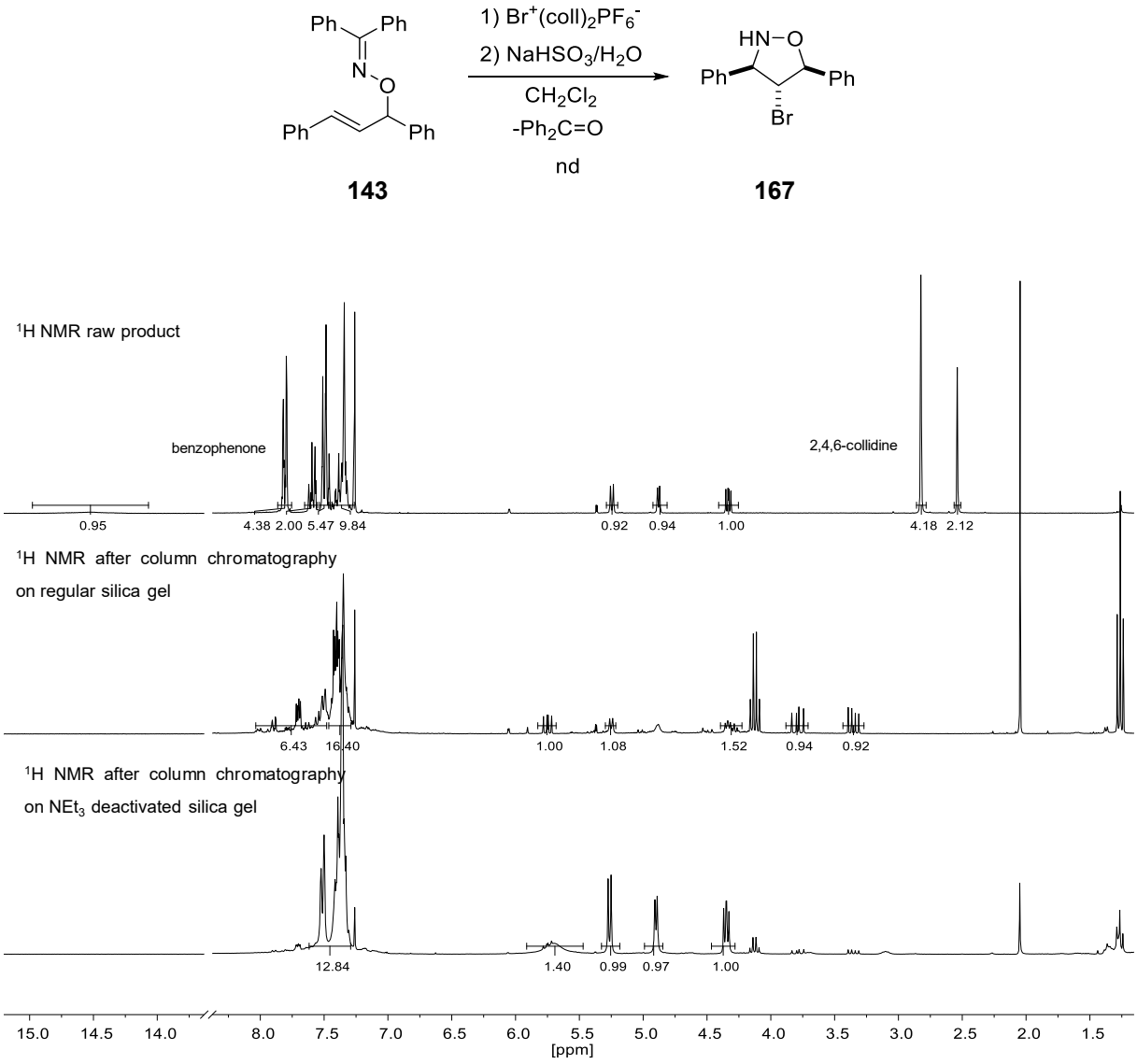
The first cyclization reaction conducted was the halocyclization of (*E*)-diphenylmethanone *O*-cinnamyl oxime (**165**) already examined by B. Egart[88] (Scheme 85). The reaction proceeded smoothly in a short reaction time as previously observed. The isolated yield of 70% for the *trans*-4-bromo-3-phenylisoxazolidine (**166**) complies with the yield observed by B. Egart as well, verifying the afore-obtained results.



165 **166**

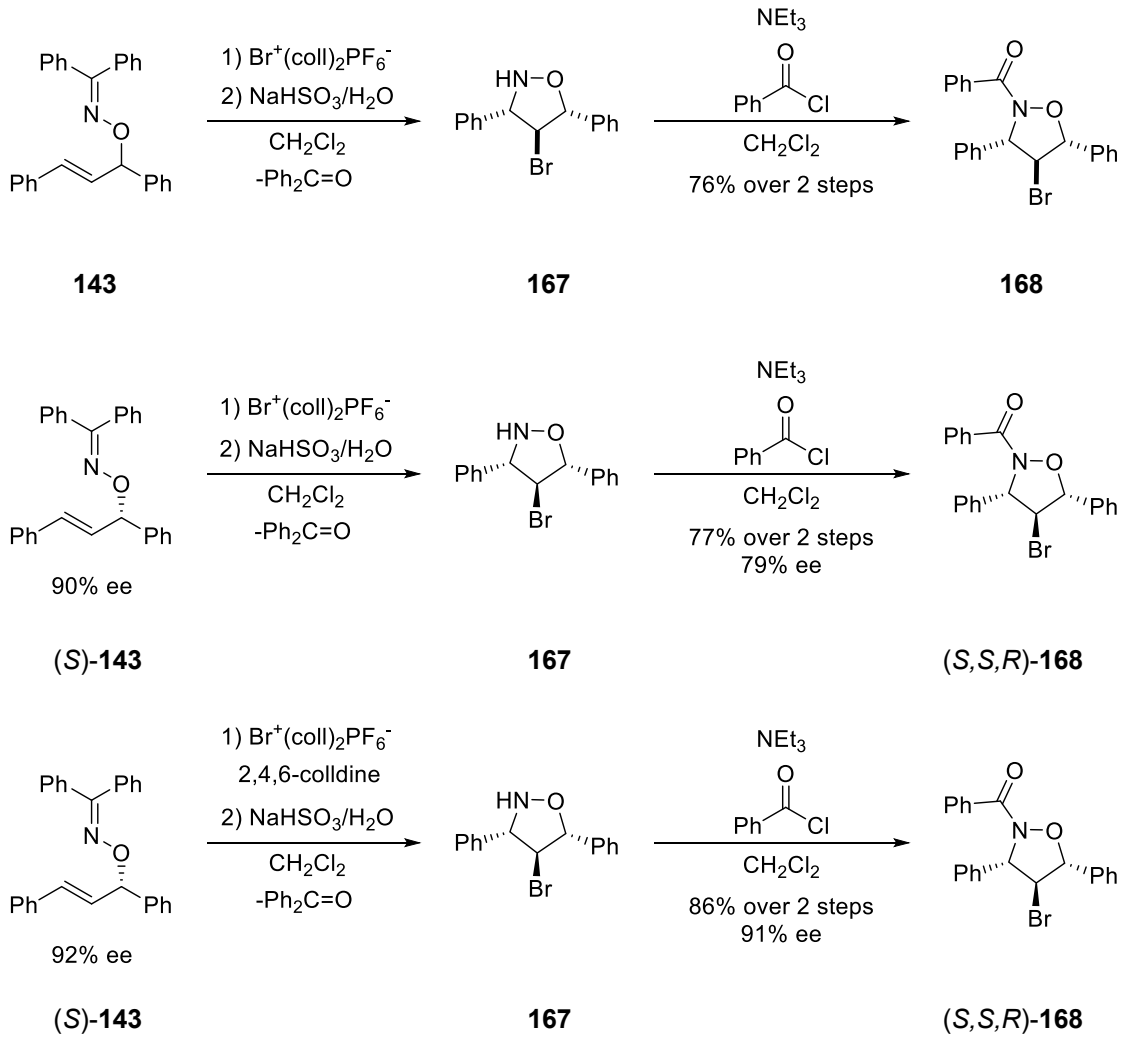
Scheme 85. Halocyclization of (*E*)-Diphenylmethanone *O*-Cinnamyl Oxime (**165**)

Application of the same reaction conditions and purification method to (*E*)-diphenylmethanone *O*-(1,3-diphenylallyl) oxime (**143**) did albeit not afford the desired isoxazolidine **167** in pure form although the ^{1}H NMR spectrum of the raw product shows solely signals of the desired isoxazolidine **167** and of the expected by-products benzophenone (**25**) and 2,4,6-collidine (**1**) (Scheme 86). After attempted purification by column chromatography the ^{1}H NMR spectrum revealed that the desired product **167** was not exclusively isolated but as a mixture with at least one new impurity which might be accounted for by partial decomposition. Deactivation of the applied silica gel with triethylamine prior to column chromatographic purification improved the product-impurity-ratio but still did not afford the pure isoxazolidine **167**.



Scheme 86. Halocyclization of (*E*)-Diphenylmethanone *O*-(1,3-Diphenylallyl) Oxime (**143**)

The acidity of the used silica gel could be accountable for the occurrence of undesired decomposition during column chromatography. The most vulnerable position in the isoxazolidine **167** is presumably the unprotected nitrogen atom. The pursued solution was the transformation of the obtained raw product with benzoyl chloride and triethylamine as base, introducing the benzoyl moiety as a protection group on the nitrogen atom. Thus, the *trans*,*trans*-isoxazolidine **168** was obtained in 76% yield over the two step transformation starting from the allyl oxime **143** (Scheme 87).



Scheme 87. Halocyclization of (*E*)-Diphenylmethanone *O*-(1,3-Diphenylallyl) Oxime (**143**) and Subsequent Transformation with Benzoyl Chloride

An attempt to cyclize the enantiomerically enriched allyl oxime (*S*)-**143** yielded the desired isoxazolidine (*S,S,R*)-**168** in 77% yield. The following chiral HPLC measurement revealed that the enantiomeric excess of the starting material (*S*)-**143** of 90% was reduced to only 79% for the obtained cyclization product (*S,S,R*)-**168**. Since the ^{1}H NMR spectrum did not show diastereomers it was assumed, that the loss in enantiomeric excess must result from racemization of the starting material (*S*)-**143** prior to the cyclization reaction. Since the allyl oximes are prone to racemization, especially if subjected to acidic conditions one equivalent of the base 2,4,6-collidine (**1**) was added immediately after addition of the solvent and prior to the exposure to the cyclization agent $Br^{+}(coll)_2PF_6^{-}$ (**3**). These conditions led to formation of isoxazolidine (*S,S,R*)-**168** with an increased yield of 86% and more importantly a roughly maintained enantiomeric excess of 91% as revealed by chiral HPLC (Figure 12).

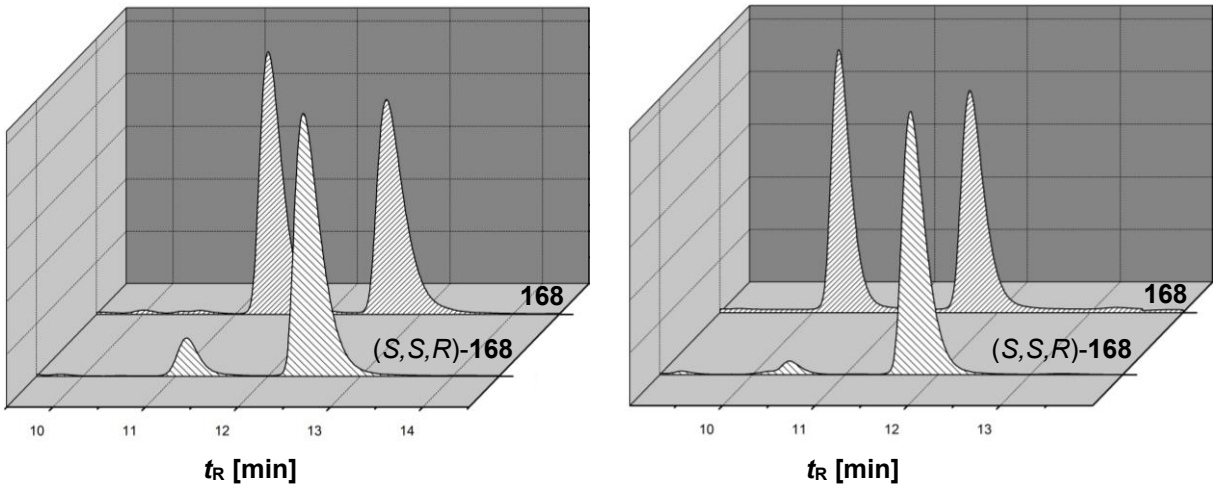
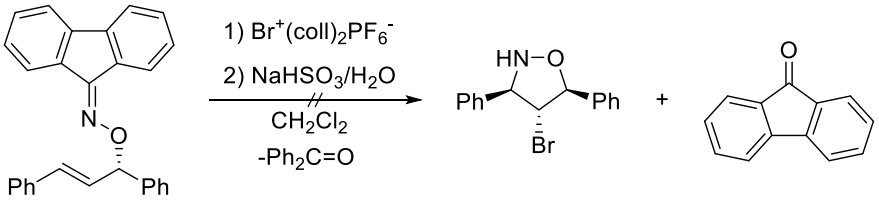


Figure 12. Chiral HPLC Chromatograms of the Isolated Isoxazolidine **(*S,S,R*)-168** with and without Addition of 2,4,6-Collidine (**1**) During Cyclization

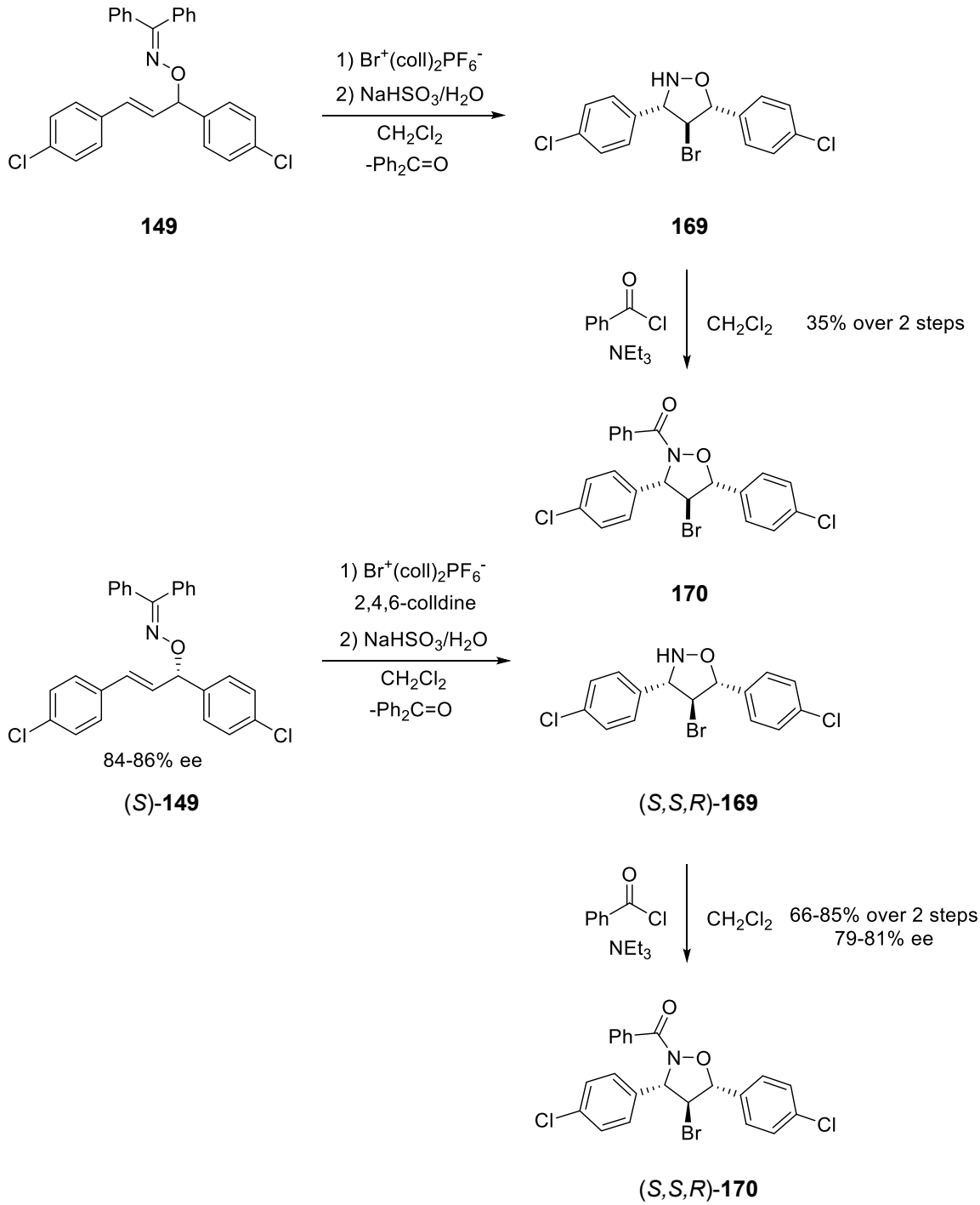
(*S*,*E*)-9*H*-Fluoren-9-one *O*-(1,3-diphenylallyl) oxime ((*S*)-**144**) was subjected as well to these reaction conditions but TLC showed no transformation into the desired isoxazolidine **167** (Scheme 88). The consecutive reaction with benzoyl chloride was attempted since isoxazolidine **167** is not easily detectable by TLC but did not result in formation of the protected isoxazolidine **168** as confirmed by TLC as well as ^{1}H NMR spectroscopy. This resistance to cyclization might be due to the rigidity of the fluorenone moiety compared to the two separate phenyl rings in the benzophenone allyl oxime **143**. A certain flexibility might be necessary for the aromatic system to be arranged in a favorable position concerning cyclization.



(*S*)-**144** **167** **61**

Scheme 88. Attempted Halocyclization of (*S*,*E*)-9H-Fluoren-9-one *O*-(1,3-Diphenylallyl) Oxime ((*S*)-**144**)

The identified reaction conditions were then applied for the halocyclization of the *para*-chlorophenyl allyl oxime derivative **149** and the corresponding (*S*,*E*)-Diphenylmethanone *O*-(1,3-bis(4-chlorophenyl)allyl) oxime ((*S*)-**149**) respectively (Scheme 89). The racemic *para*-chlorophenyl isoxazolidine derivative **170** was obtained in a rather low yield of 35% over two steps.

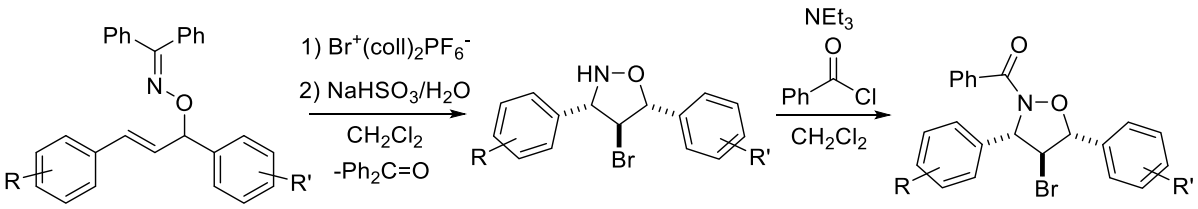


Scheme 89. Halocyclization of (*E*)-Diphenylmethanone *O*-(1,3-Bis(4-chlorophenyl)allyl) Oxime (**149**) and the Corresponding (*S*)-Enantiomer (*S*)-**149**

Transformation of the enantioenriched allyl oxime (*S*)-**149** into the corresponding isoxazolidine (*S,S,R*)-**170** gave higher yields of 66% and 85% in two separate attempts with enantiomeric excesses of 79% and 81%, respectively. Although the enantiomeric excesses of the substrates were initially determined to be 84% and 86% for allyl oxime (*S*)-**149**, the decrease can be attributed to racemization prior to the halocyclization reaction, as racemization was observed upon storage as described in section 2.3.3. In further attempts

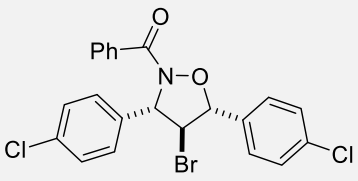
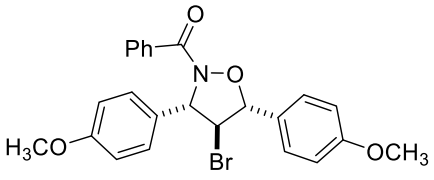
higher enantiomeric excesses might be obtained by reducing the storage time of the allyl oxime (*S*)-**149**. This led to the conclusion that storage of the enantioenriched allyl oximes should be reduced to a minimum before halocyclization in order to maintain the enantiomeric excess and prevent substantial racemization.

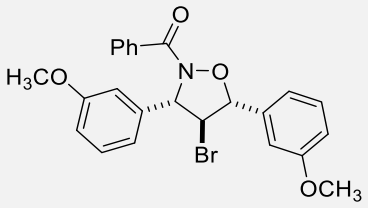
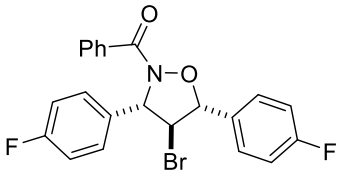
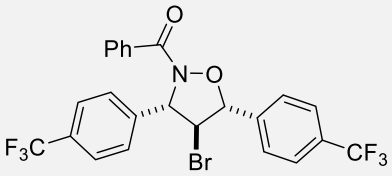
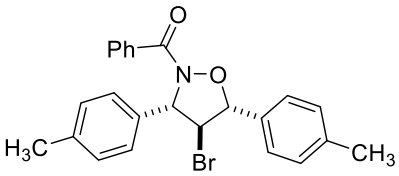
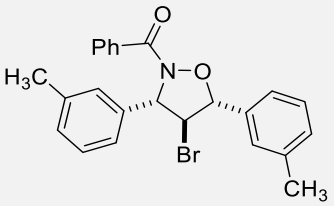
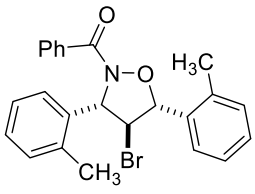
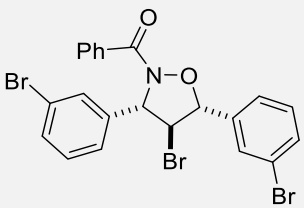
Further racemic isoxazolidine derivatives **171** through **185** were synthesized starting from the respective allyl oximes **150** through **163** in a two-step synthesis under the identified conditions or from allyl acetates **118** and **124** in three steps without purification of the allyl oxime intermediate (Scheme 90). The yields varied to a great extend as depicted in Table 6. The yields of the individual unsymmetrically substituted isoxazolidines **180** through **185** were again determined from the ^{1}H and ^{19}F NMR spectra of the obtained mixtures.

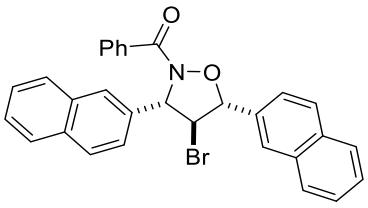
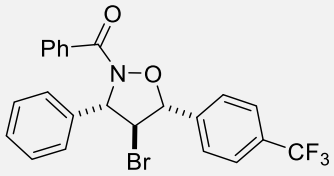
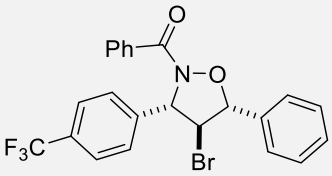
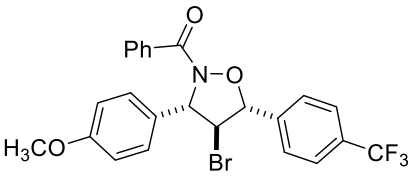
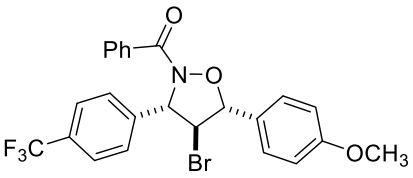
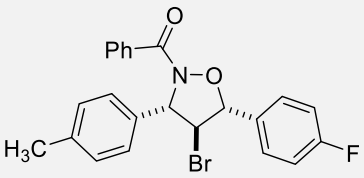
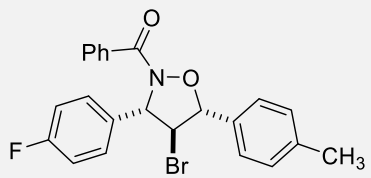


Scheme 90. Synthesis of Racemic Isoxazolidines from the Corresponding Racemic Allyl Oximes

Table 6. Yields of Racemic Isoxazolidines

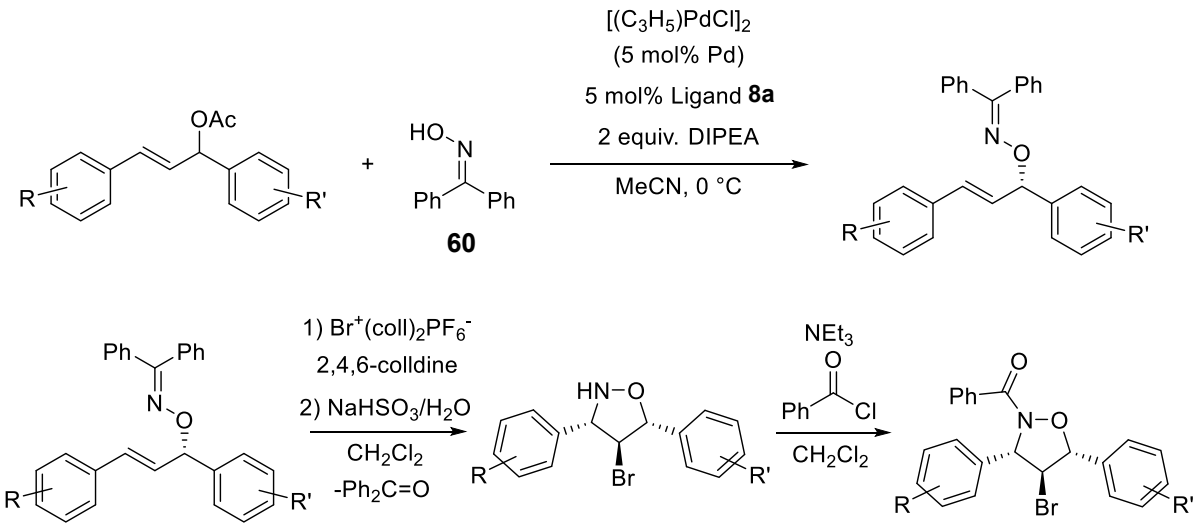
R, R’	Compound	Yield
p-Cl	 **170**	35%
p-OCH_3	 **171**	37%

m-OCH_3	 **172**	14%[a)]
p-F	 **173**	62%
p-CF_3	 **174**	16%[b)]
p-CH_3	 **175**	78%
m-CH_3	 **176**	35%
o-CH_3	 **177**	79%
m-Br	 **178**	41%[a)]

Ph	 **179**	42%[150]
H, *p*-CF_3	 **180**	
p-CF_3, H	 **181**	46% **180**:**181** 0.8:1.0
p-OCH_3, *p*-CF_3	 **182**	
p-CF_3, *p*-OCH_3	 **183**	66% **182**:**183** 0.1:1.0
p-CH_3, *p*-F	 **184**	
p-F, *p*-CH_3	 **185**	66% **184**:**185** 1.0:1.0

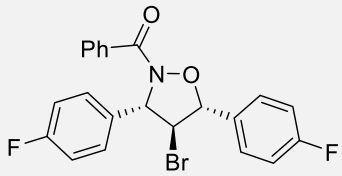
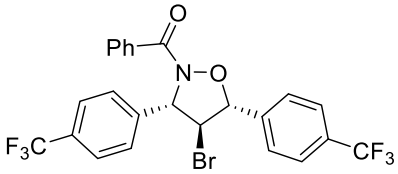
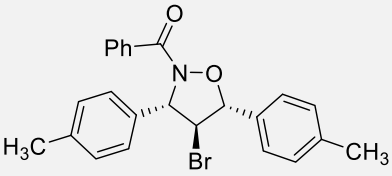
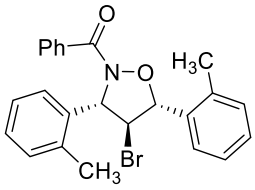
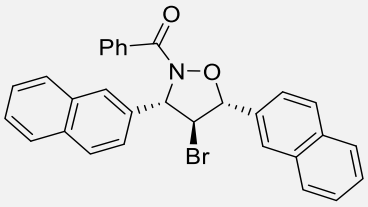
[a] No purification of the allyl oxime, “one-pot” synthesis; [b] Leakage of chromatography column

For the selective transformations of the allyl acetates into the respective isoxazolidine derivatives the enantioenriched allyl oximes obtained from the asymmetric allylation reaction with approximately 5 mol% of catalyst and hybrid ligand **8a** were isolated by column chromatography. Since the same instability considerations apply as discussed for the *para*-chlorophenyl derivative (*S*)-**149** in section 2.3.3, the isolated allyl oximes were directly transferred into the corresponding isoxazolidines (Scheme 91). Enantiomeric excess values as well as reaction yields were determined for the isoxazolidine products after the three-step conversion (Table 7). The obtained yields turned out satisfactory for a three-step process ranging from 47% to 65%. The *para*-(trifluoromethyl)phenyl derivative (*S,S,R*)-**174** gave a lower yield of 24% which is not surprising since the halocyclization reaction depends on the electrophilicity of the double bond which decreases in the presence of electron-withdrawing substituents. This can be already observed during the cyclization process, while other derivative are readily cyclized by one equivalent of $Br^+(coll)_2PF_6^-$ (**3**), the trifluorophenyl derivative (*S,S,R*)-**174** needs additional two equivalents of the cyclization agent **3** for TLC to account for complete consumption of the substrate (*S*)-**152**. The enantiomeric excess of the *ortho*-tolyl derivate (*S,S,R*)-**177** is low with only 30%, which could be explained by steric interference of the *ortho*-substituents. The remaining enantiomeric excesses were acceptable ranging from 81% to 89% with exception of the *para*-tolyl derivative (*S,S,R*)-**175** exhibiting a moderate value of 55%. As this was unexpectedly low, racemization of the corresponding allyl oxime (*S*)-**152** upon storage and therefore the utility of a “one-pot” approach was reconsidered.



Scheme 91. Synthesis of Enantioenriched Isoxazolidine Derivatives

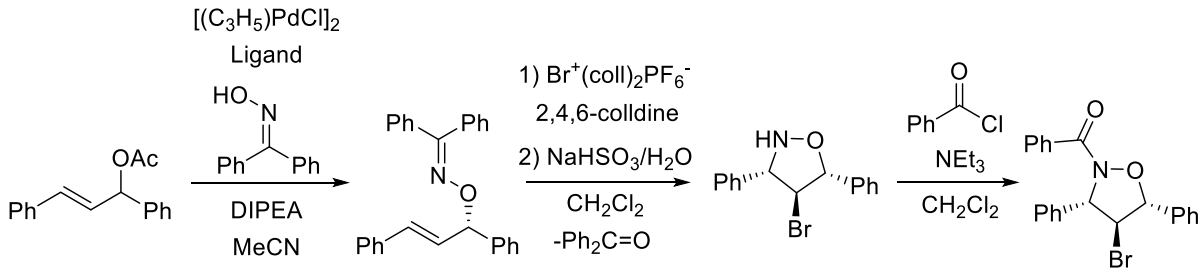
Table 7. Yields and Enantiomeric Excesses of Enantioenriched Isoxazolidines

R	Compound	Yield (ee)
p-F	 (*S,S,R*)-**173**	60% (87% ee)
p-CF_3	 (*S,S,R*)-**174**	24% (81% ee)
p-CH_3	 (*S,S,R*)-**175**	47% (55% ee)
o-CH_3	 (*S,S,R*)-**177**	65% (30% ee)
Ph	 (*S,S,R*)-**179**	49% (89%ee)[150]

2.3.5. One-Pot Strategy

Since the allyl oximes are prone to racemization upon storage at room temperature as well as 0 °C as discussed in sections 2.3.3 and 2.3.4, a “one-pot” strategy was considered. In a first attempt employing (*E*)-1,3-diphenyl allyl acetate (**148**) and benzophenone oxime (**60**) as substrates acetonitrile was removed after the allylation reaction and subsequently dichloromethane as well as the cyclization agent $Br^+(coll)_2PF_6^-$ (**3**) were added. This setting did not result in the desired cyclization reaction, presumably due to the consumption of the cyclization reagent $Br^+(coll)_2PF_6^-$ (**3**) by oxidation of DIPEA, although additionally added $Br^+(coll)_2PF_6^-$ (**3**) did not lead to the desired cyclization either. Another idea to conduct the asymmetric allylation reaction in dichloromethane with 2,4,6-collidine (**1**) as base, which however did not result in the desired allyl oxime (*S*)-**143**.

Consequently, DIPEA needed to be removed before attempting the cyclization reaction. DIPEA as a base is most easily removed by protonation under acidic conditions. However, since the allyl oximes are acid-sensitive an attempt was made employing saturated ammonium chloride solution for the extraction of the undesired base from the reaction solution. Prior investigations discussed in section 2.3.3 had shown that saturated ammonium chloride solution with a pH between 4.6 to 6 was most likely to leave the fragile allyl oxime bond intact while still protonating DIPEA with a pK_a of 10.75[154] of the conjugated acid. Extraction of DIPEA with saturated ammonium chloride solution from the reaction solution turned out as key step for a successful consecutive cyclization reaction. The desired isoxazolidine (*S,S,R*)-**168** was obtained in 62% yield with an enantiomeric excess of 82% employing ligand **8** in a first attempt and with 50% yield at -20 °C and 56% yield at 0 °C with a consistent enantiomeric excess of 88% employing ligand **8a** (Scheme 92). Incidentally, this led to the conclusion, that a decrease in reaction temperature solely led to a decrease in yield while no improvement of the obtained enantiomeric excess was observed.

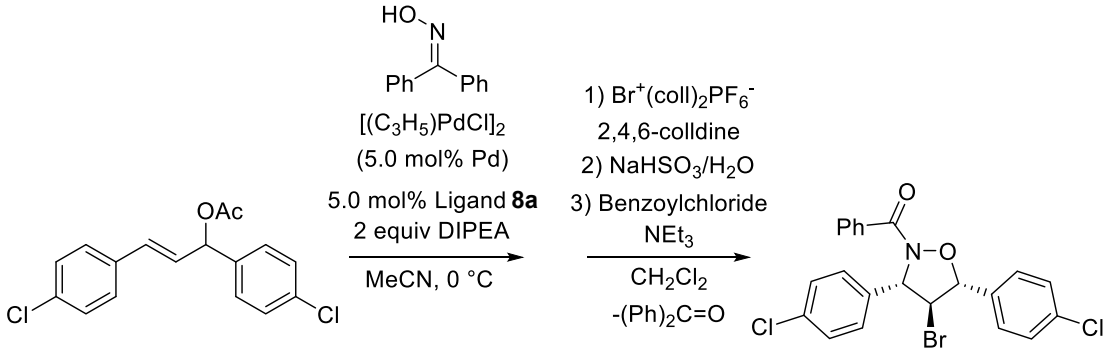


148 (*S*)-**143** (*S,S,R*)-**167** (*S,S,R*)-**168**

Allyl acetate [mmol]	Oxime [equiv]	Catalyst [mol%]	Ligand	DIPEA [equiv]	T [°C]	Reaction Time	Yield	ee
0.404	1.0	5.0	**8**	2.1	-20	2d	62%	82%
0.408	1.0	4.4	**8a**	1.9	-20	8d	50%	88%
0.400	1.0	5.0	**8a**	2.0	0	1d	56%	88%

Scheme 92. "One-Pot" Synthesis of (3*R*,4*R*,5*S*)-Bromo-3,5-diphenyloxazolidin-2-yl-(phenyl)methanone ((*S,S,R*)-**168**)

The same "one-pot" procedure was applied for the synthesis of the *para*-chlorophenyl derivative (*S,S,R*)-**170** starting from the respective allyl acetate **86** with a similar result (Scheme 93). The obtained yield of 47% is slightly lower than the combined yields of the reactions carried out individually. The enantiomeric excess of 79% resulting from the application of 5.0 mol% catalyst with the hybrid ligand **8a** is comparable as well.

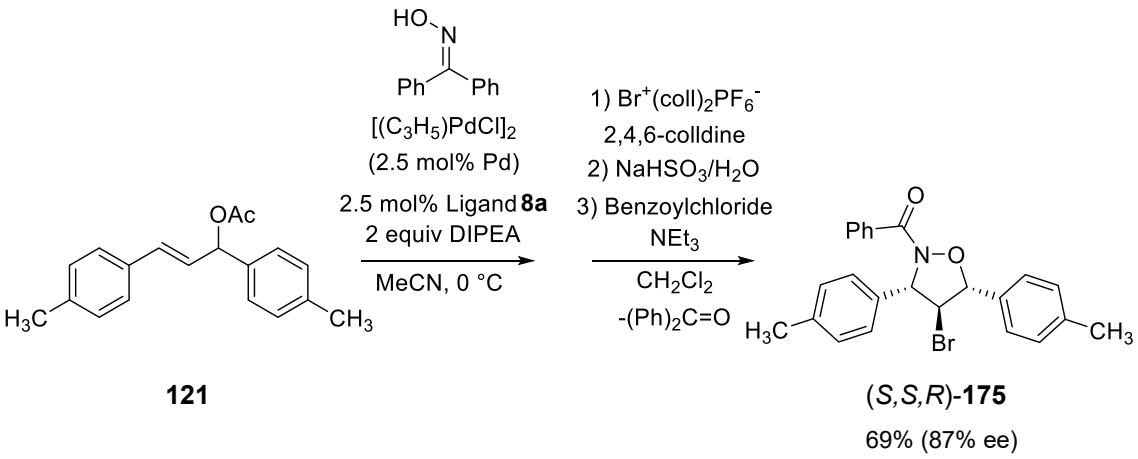


86 (*S,S,R*)-**170**

47% (79% ee)

Scheme 93. "One-Pot" Synthesis of *para*-Chlorophenyl Derivative (*S,S,R*)-**170**

At this point the “one-pot” approach was deferred since the individual reaction scheme led to slightly higher overall yields and comparable enantiomeric excess values. It was reconsidered since *para*-tolyl derivative (*S,S,R*)-**175** exhibited a rather poor enantiomeric excess of 55% for the individual reaction approach. Furthermore, the enantiomeric excess values of 79% to 81% for *para*-chlorophenyl derivative (*S,S,R*)-**170** were not reproducible with catalyst loadings slightly higher than 5 mol%. For the attempted “one-pot” synthesis of ((3*S*,4*S*,5*R*)-4-bromo-3,5-di-*p*-tolylisoxazolidin-2-yl)(phenyl)methanone ((*S,S,R*)-**175**) the catalyst loading was reduced to 2.5 mol% and a slightly varied protocol was applied where the reaction solution was not only extracted with NH_4Cl solution but washed directly afterwards with $NaHCO_3$ solution to restore a slightly bacic pH. Surprisingly under these conditions the enantiomeric excess increased from 55% to 87% (Scheme 94). This increase in enantiomeric excess was additionally accompanied by an increased yield of 69% compared to 47% as the combined yield of the individual reactions.



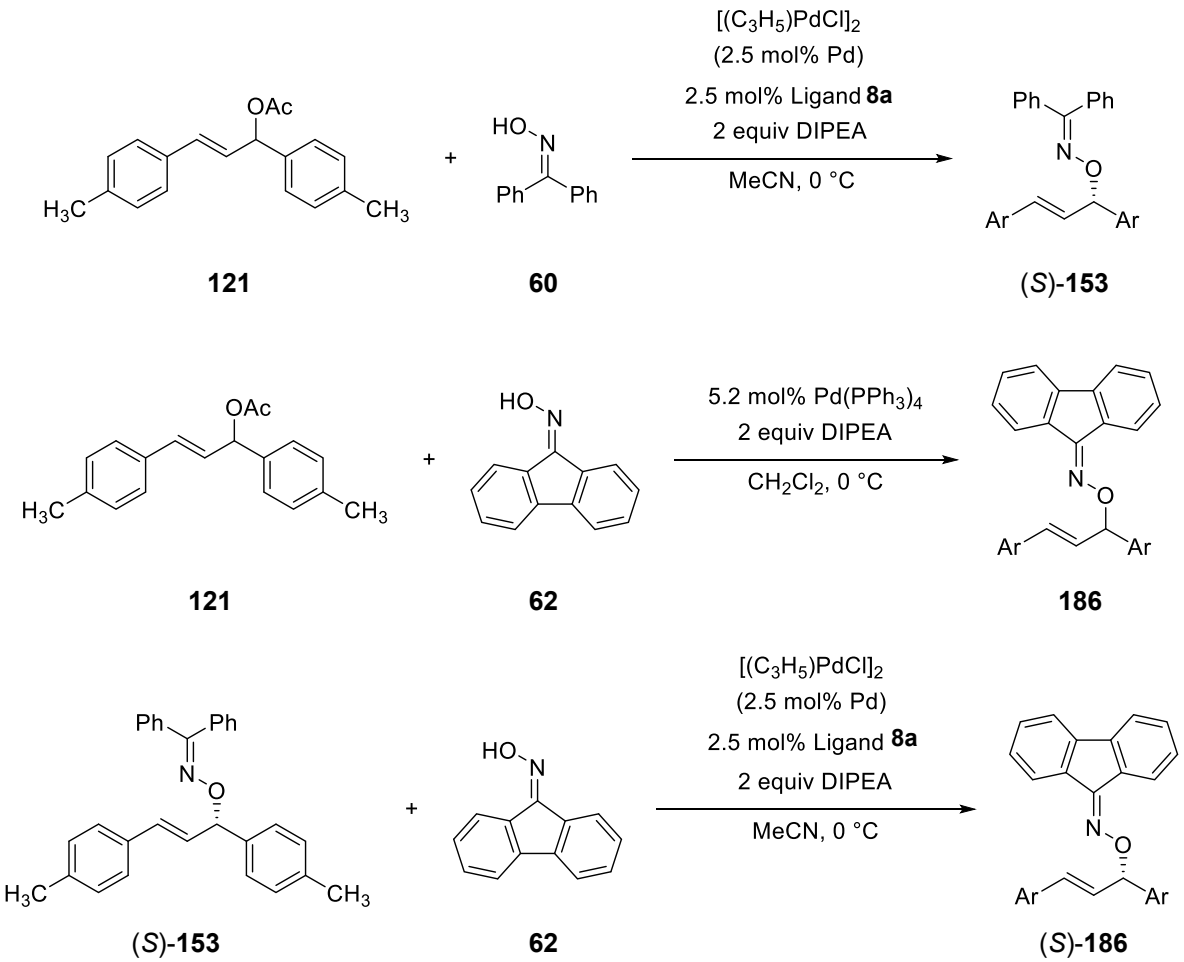
121 (*S,S,R*)-**175**
69% (87% ee)

Scheme 94. “One-Pot” Synthesis of *para*-Tolyl Derivative (*S*,*S*,*R*)-**175**

The idea to reduce catalyst loadings was deduced from a publication by Berkessel and Gröger et al.[155] investigating the influence of catalyst loadings on an organocatalytic aldol reaction. Catalyst loadings were varied between 0.5 to 10 mol% resulting in decreasing enantiomeric excess for the β-hydroxy ketone, the higher the amount of catalyst employed. By investigation of the reaction rates and the change in enantiomeric excess with respect to the reaction time Berkessel and Gröger et al. concluded that the decrease in enantiomeric excess was caused by switching from a kinetically controlled to a thermodynamically controlled catalytic aldol reaction if higher amounts of catalyst were employed. Although this concept is well known for drastically increased amounts of catalyst, it had so far not been observed in such a significant fashion for such small amounts of catalyst. This phenomenon was observed again later by Gröger and Berkessel et al.[156] for an organocatalytic

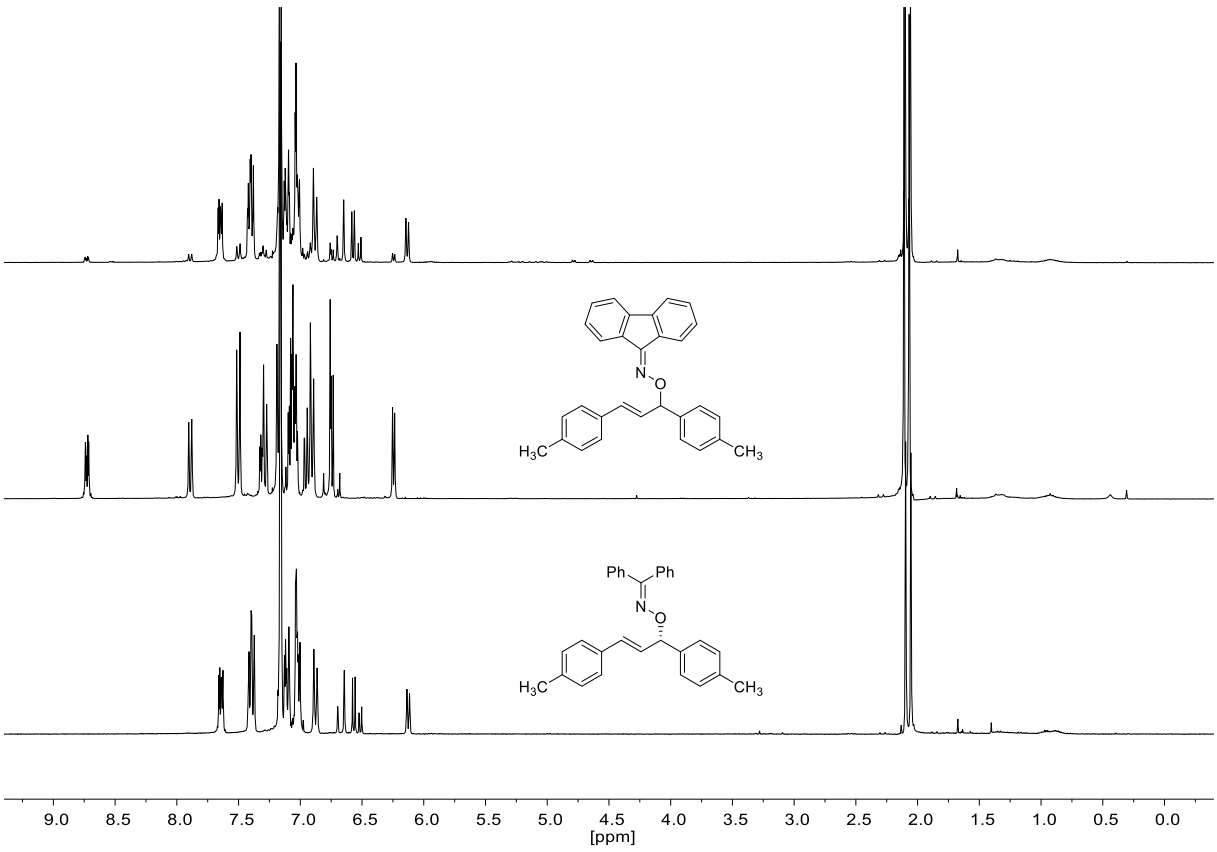
trifluoromethyl carbinol synthesis while a related observation was already made by Blackmond et al.[157] in 2006 regarding the thermodynamic control of the asymmetric amplification in proline-catalysis.

Since enantioselective catalytic allylation reactions are expected to proceed under kinetic control for small amounts of catalyst the variation in the amount of catalyst applied is a widely utilized tool for rate optimization. Furthermore, the organocatalytic aldol addition reaction investigated by Berkessel and Gröger et al. is reversible, therefore thermodynamic control seems plausible whereas this explanation seems farfetched for the potentially irreversible Tsuji-Trost allylation of allyl acetates with oximes. Nonetheless, to clarify the circumstances it was investigated whether the allylation reaction could potentially be reversible. 1,3-Di-*p*-tolyl allyl acetate (**121**) was again transformed under the priorly defined reaction conditions with a reduced catalyst loading of 2.5 mol% and the resulting allyl oxime (*S*)-**153** isolated by column chromatography. The obtained allyl oxime (*S*)-**153** was in turn not cyclized by addition of $Br^+(coll)_2PF_6^-$ (**3**) but instead was subjected again to the allylation reaction conditions in the presence of 9*H*-fluoren-9-one oxime (**62**) (Scheme 95).



Scheme 95. Investigation of Reversibility of the Allylation Reaction (Ar = 4-CH_3-C_6H_4)

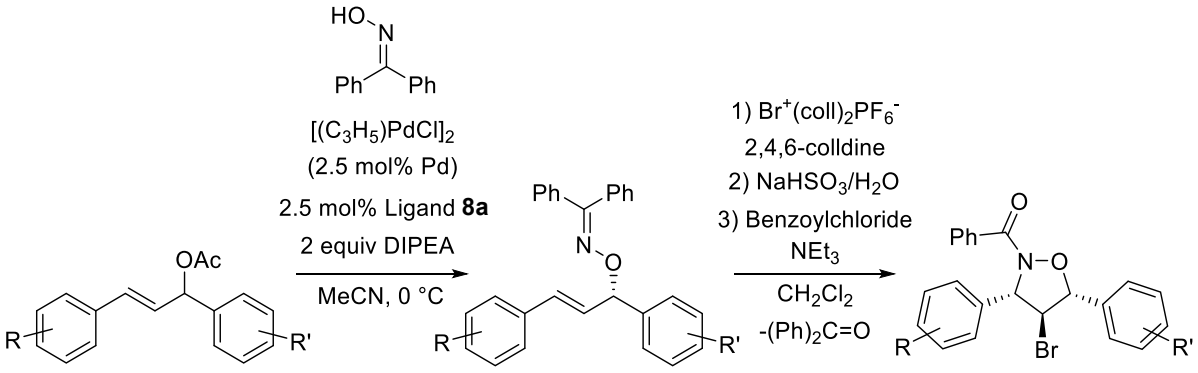
The ^{1}H NMR spectrum of the isolated oil showed the presence of the substrate and a second compound. Since this compound could not be identified unambiguously, the expected (*E*)-9*H*-fluoren-9-one *O*-(1,3-di-p-tolylallyl) oxime (**186**) was synthesized separately. Comparison of the ^{1}H NMR spectra proved the oxime substitution and therefore the reversibility of the allylation reaction (Scheme 96). This led to the conclusion that the benzophenone oxime anion can act as a leaving group in the palladium-catalyzed Tsuji-Trost reaction. With a pK_a of 11.3 for benzophenone oxime (**60**) as the conjugated acid the reactivity is notably reduced compared to acetate (pK_a of 4.76 acetic acid) as the leaving group, explaining the obtained small share of the substitution product (*S*)-**186**.[158]



Scheme 96. Comparison of the ^{1}H NMR Spectrum of the Product of the Oxime Substitution Reaction with the Spectra of the Isolated Allyl Oximes **186** and (*S*)-**153**

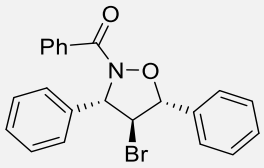
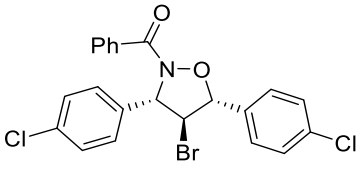
Since these reaction conditions proved to be exceptionally successful they were applied to the allyl acetate substrates **86**, **119**, **120**, **122** through **128** and **148** (Scheme 97). All yields were increased ranging from 61% to 69% for the symmetrically substituted isoxazolidines with the exception of trifluorophenyl derivative (*S,S,R*)-**174** for which the yield was increased as well but still falling way behind the other yields with 38% (Table 8). The alleged reason lies with the electron-withdrawing effect of the trifluoromethyl substituents which was already

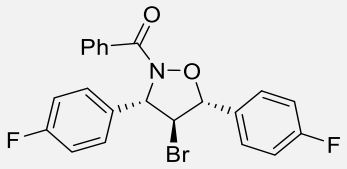
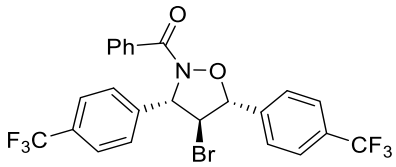
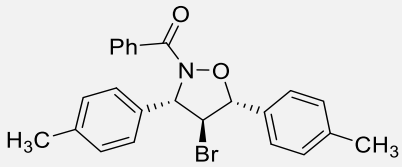
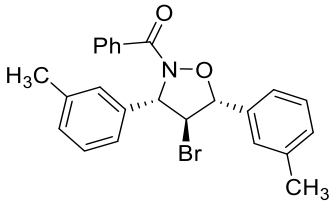
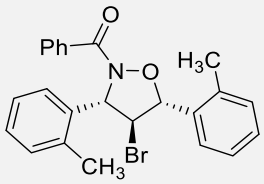
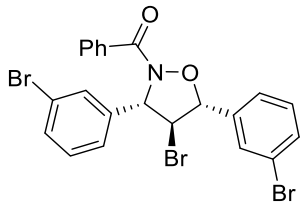
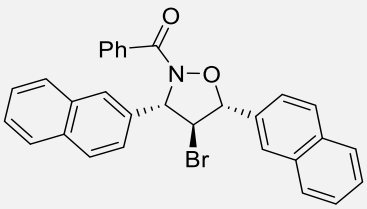
discussed in section 2.3.4. Moreover, most of the enantiomeric excesses were increased ranging from 87% to 93% for the symmetrically substituted isoxazolidines. One exception was made by ((3*S*,4*S*,5*R*)-4-Bromo-3,5-di-*o*-tolylisoxazolidin-2-yl)(phenyl)methanone ((*S,S,R*)-**177**). While the yield increased as observed for the other isoxazolidines the enantiomeric excess remained unchanged at 30%. This observation can be attributed to the steric hindrance in case of an *ortho*-substitution as already mentioned in section 2.3.4.

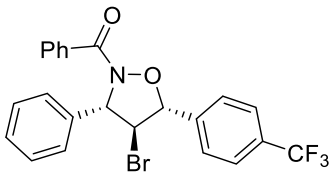
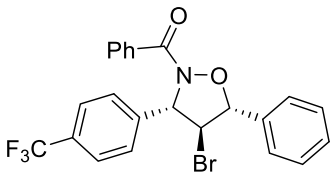
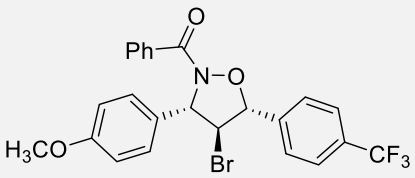
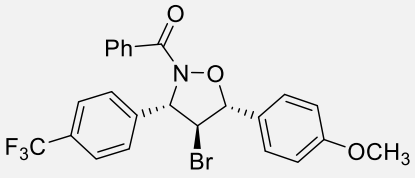
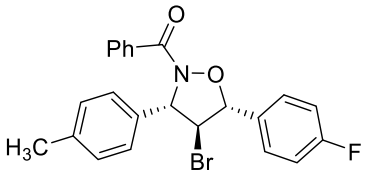
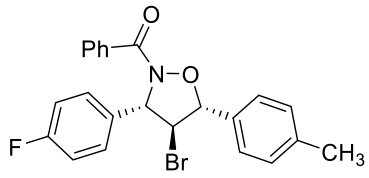


Scheme 97. "One-pot" Synthesis of Enantioenriched Isoxazolidine Derivatives

Table 8. Yields and Enantiomeric Excesses of Enantioenriched Isoxazolidines in the "One-Pot" Synthesis

R	Compound	Yield (ee)
H	 (*S,S,R*)-**168**	65% (92% ee)
p-Cl	 (*S,S,R*)-**170**	64% (91% ee)

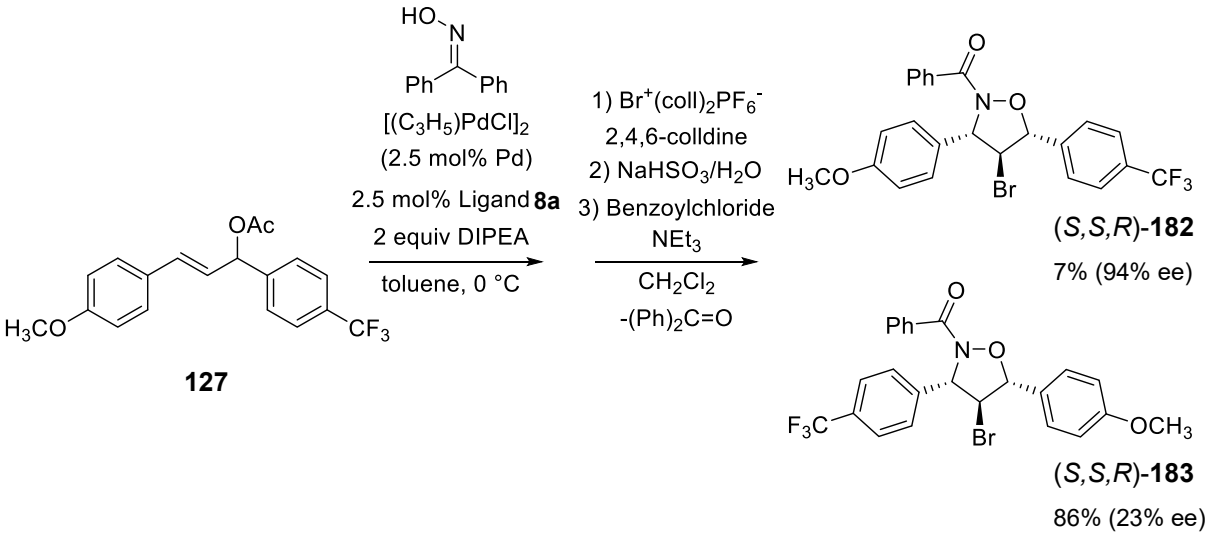
p-F	 (*S,S,R*)-**173**	61% (92% ee)
p-CF_3	 (*S,S,R*)-**174**	38% (91% ee)
p-CH_3	 (*S,S,R*)-**175**	69% (87% ee)
m-CH_3	 (*S,S,R*)-**176**	68% (92% ee)
o-CH_3	 (*S,S,R*)-**177**	65% (30% ee)
m-Br	 (*S,S,R*)-**178**	69% (93% ee)
Ph	 (*S,S,R*)-**179**	66% (93% ee)

H, *p*-CF_3	 (*S,S,R*)-**180**	
p-CF_3, H	 (*S,S,R*)-**181**	46% **180**:**181** 1.0:1.0 (95% ee/75% ee)
p-OCH_3, *p*-CF_3	 (*S,S,R*)-**182**	
p-CF_3, *p*-OCH_3	 (*S,S,R*)-**183**	44% **182**:**183** 0.3:1.0 (94% ee/45% ee)
p-CH_3, *p*-F	 (*S,S,R*)-**184**	
p-F, *p*-CH_3	 (*S,S,R*)-**185**	63% **184**:**185** 0.7:1.0 (93% ee/86% ee)

The asymmetric isoxazolidine mixture of (*S,S,R*)-**184** and (*S,S,R*)-**185** gave a combined yield of 63% while the combined yields of the mixtures (*S,S,R*)-**180**/(*S,S,R*)-**181** and (*S,S,R*)-**182**/(*S,S,R*)-**183** turned out slightly lower with 46% and 44%, respectively. As priorly discussed, this can be attributed to the presence of the trifluoromethyl group in both derivatives. As a rule of thumb one additional equivalent of $Br^+(coll)_2PF_6^-$ (**3**) needed to be

submitted to the reaction solution per trifluoromethyl group present in the allyl oxime substrate, resulting in proportionally lower yields. The product ratios as well as the obtained enantiomeric excesses varied greatly. The best regioselectivity was observed for the combination (*S,S,R*)-**182**/(*S,S,R*)-**183** with a ratio of 23% to 77%, while the NMR spectra of the other products revealed nearly 50:50 mixtures. Supposedly, this might be a result of the before-mentioned complementary substituent effects of the methoxy and the trifluoromethyl group. Concerning the enantioselectivity the minor isomer generally was obtained with superior selectivity, with values of 93% enantiomeric excess for (*S,S,R*)-**184**, 94% for (*S,S,R*)-**182** and 95% for (*S,S,R*)-**180** matching or even exceeding the best selectivities observed for the symmetrically substituted isoxazolidines. The enantiomeric excesses for the major isomers (*S,S,R*)-**181** and (*S,S,R*)-**185** were acceptable with 75% and 86%, respectively, while the enantiomeric excess dropped to 45% for the major isomer of the most regioselective reaction (*S,S,R*)-**183**. It was concluded, that in this case the allyl oxime (*S*)-**161** is especially fragile since the resulting cation in case of cleavage of this bond is additionally stabilized by the methoxy substituent leading to a drastic decrease in enantiomeric excess.

Attempting to improve this result the solvent for the allylation reaction was switched to toluene. Toluene as a less polar solvent might minimize the dissociation of the ions leading to diminished racemization. Although the reaction yield was slightly increased to 50% and the regioselectivity of the allylation reaction was enhanced to a ratio of 14% to 85% the enantiomeric excess of the major isomer turned out to be approximately half of the value reached before with only 23% while the enantiomeric excess of the minor isomer remained at 94% (Scheme 98).



Scheme 98. "One-Pot" Transformation of (*E*)-1-(4-(Trifluoromethyl)phenyl)-3-(4-methoxyphenyl)allyl Acetate (**127**) with Toluene as Solvent for the Allylation Reaction

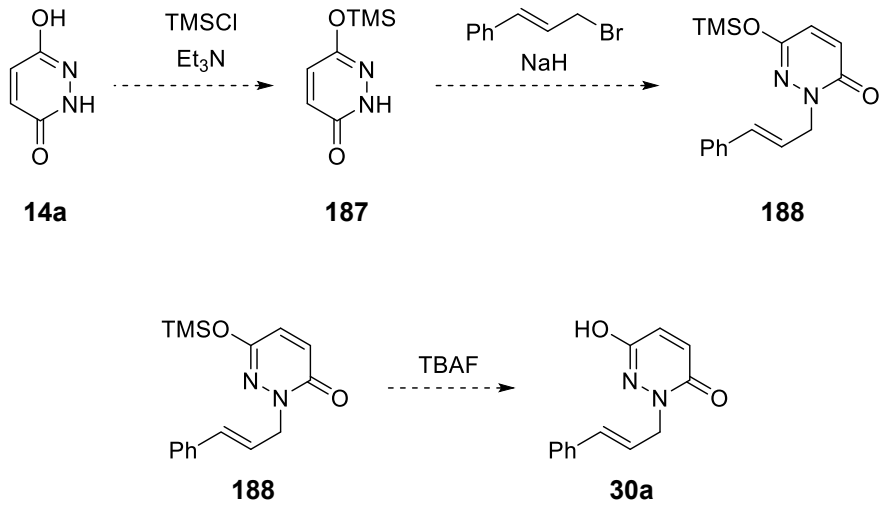
3 Conclusion and Outlook

Bis(2,4,6-trimethylpyridine)bromine(I) hexafluorophosphate (**3**) was synthesized from the corresponding silver complex **2** which was obtained from the reaction of 2,4,6-collidine (**1**) with silver(I) nitrate and potassium hexafluorophosphate. (*R*)-Diphenyl(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (**8**) and its derivative (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (**8a**) were obtained in three step syntheses starting from (*S*)-[1,1'-binaphthalene]-2,2'-diyl bis(trifluoromethane sulfonate) (**4**). These BINOL derivatives carrying a terminal alkene as well as a phosphane moiety serve as hybrid ligands for the asymmetric allylic substitution reaction.

Diethyl hydrazine-1,2-dicarboxylate (**10**) and ethyl 2-(diphenylmethylene)hydrazine-1-carboxylate (**26**) as well as the cyclic structures of phthalic hydrazide (**12**), maleic hydrazide (**14**), succinic hydrazide (**16**) as well as 4,4-diethylpyrazolidine-3,5-dione (**22**) were synthesized as *N,N'*-diprotected hydrazide nucleophiles.

Allylation was attempted for all of these hydrazides by nucleophilic substitution on cinnamyl bromide (**27**). In the cases of the two acyclic structures this allylation was particularly successful, providing diethyl 1-cinnamylhydrazine-1,2-dicarboxylate (**28**) and ethyl 1-cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**42**) in excellent yields. The allylation product of phthalic hydrazide (**29**) could not be obtained in pure form, due to low solubility and inherent purification difficulties. For the allylation of maleic hydrazide (**14**) and 4,4-diethylpyrazolidine-3,5-dione (**22**) the monoallylated species were obtained albeit in low yields. In the case of 4,4-diethylpyrazolidine-3,5-dione (**22**) this allylation product turned out to be the desired *N*-allylated 1-cinnamyl-4,4-diethylpyrazolidine-3,5-dione (**41**) while for maleic hydrazide (**14**) the *O*-allylated product 6-(cinnamyloxy)pyridazine-3(2*H*)-one (**32**) was most likely formed, since the keto-hydroxy form of succinic hydrazide (**14a**) turned out to be the most stable tautomer.

In pursuit of the *N*-allylated derivative **30a** maleic hydrazide (**14**) could be reacted with trimethylsilyl chloride presumably resulting in the silyl ether **187** which could be allylated in a consecutive step most likely affording the *N*-allylated *O*-protected compound **188** (Scheme 99). Deprotection with TBAF should render the *N*-allylated compound **30a**.[159]



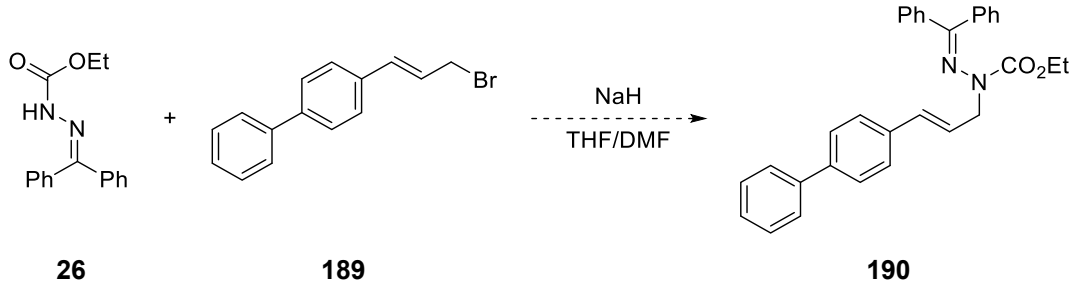
Scheme 99. Potential Synthesis of 2-Cinnamyl-6-hydroxypyridazine-3(2*H*)-one (**30a**)

Especially for maleic hydrazide the low yield resulted from the predominance of the diallylated by-product 2-cinnamyl-6-(cinnamyloxy)pyridazine-3(2*H*)-one (**33**). In case of succinic hydrazide (**16**) the diallylated species 1,2-dicinnamyltetrahydropyridazine-3,6-dione (**35**) was the solitary product. Consequently, a different strategy was pursued regarding the monoallylated 1-cinnamyltetrahydropyridazine-3,6-dione (**34**). Cinnamaldehyde (**36**) was transformed into the corresponding hydrazone ((*E*)-3-phenylallylidene)hydrazine (**37**). Reduction to cinnamyl hydrazine (**38**) under varying conditions was not successful but S_N2 reaction on cinnamyl bromide (**27**) with a large excess of hydrazine monohydride yielded the desired cinnamyl hydrazine (**38**). Cyclization with succinyl chloride (**39**) did albeit not afford the monoallylated 1-cinnamyltetrahydropyridazine-3,6-dione (**34**).

1-Cinnamylhydrazine-1,2-dicarboxylate (**28**) was successfully cyclized by halocyclization with NBA in a diastereoselective manner, as postulated by B. Mechsner[90]. The cyclization of 6-(cinnamyloxy)pyridazine-3(2*H*)-one (**32**) with NBA or bromine was not successful, which is plausible with regard to the *O*-allylation. Cyclization of 1-cinnamyl-4,4-diethylpyrazolidine-3,5-dione (**41**) was attempted with excess NBA but the desired cyclization product was not obtained.

The halocyclization of ethyl 1-cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**42**) with $Br^+(coll)_2PF_6^-$ (**3**), as observed by B. Egart[88] for (*E*)-diphenylmethanone *O*-cinnamyl oxime (**165**), was investigated. Although allowing for complete transformation of the reactant the reaction did not afford the desired pyrazolidine **52** in satisfying yields (Scheme 57). Several workup variations were tried but did not improve the results. The by-products were analyzed and identified as hemiaminal derivative **53** and pyrazole derivative **54** (Scheme 58). Low visibility of pyrazolidine **52** on TLC, especially in low concentrations, rendered monitoring of the cyclization process difficult. Therefore, a supposedly more UV active

biphenyl substrate **190** was targeted. After several attempts (*E*)-3-([1,1'-biphenyl]-4-yl)acrylaldehyde (**45**) could finally be obtained in satisfying yield from 4-bromobiphenyl (**43**) and acrolein diethyl acetal (**47**) in a Heck cross coupling reaction. Provided the thus obtained (*E*)-3-([1,1'-biphenyl]-4-yl)acrylaldehyde (**45**) can be transferred into the corresponding bromide **189**. Nucleophilic substitution with hydrazone **26** should give the allyl hydrazone **190** (Scheme 100), yielding a more UV active halocyclization substrate. This might lead to an improved ability to observe the cyclization reaction by TLC and therefore a better understanding of the cyclization reaction and simultaneous or subsequent formation of side products.

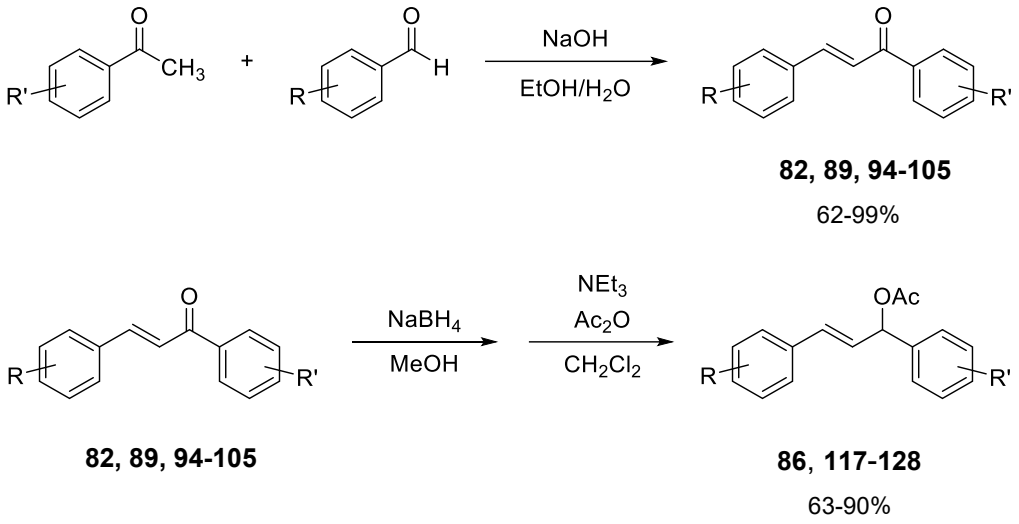


26 **189** **190**

Scheme 100. Allylation of Hydrazone **26** with (*E*)-4-(3-Bromoprop-1-en-1-yl)-1,1'-biphenyl (**189**)

Concerning a methodology towards asymmetric isoxazolidines diphenylmethanone oxime (**60**) and 9*H*-fluoren-9-one oxime (**62**) were synthesized as *N*-protected *O*-nucleophiles. As sterically more demanding nucleophiles bis(2-(benzyloxy)phenyl)methanone oxime (**66**) was generated in two steps from 2,2'-dihydroxybenzophenone (**63**) and bis(2-bromophenyl)methanone oxime (**68**) by oxime formation from 2,2'-dibromobenzophenone (**67**). An attempt to synthesize di(naphthalen-1-yl)methanone oxime (**73**) in three steps from 1-bromonaphthalene (**69**) was not successful, since the desired oxime is only accessible under acetic conditions which in turn lead to high susceptibility to Beckmann rearrangement.[145]

Regarding the electrophilic component for the allylation reaction the allylic carbonates (*E*)-1,3-diphenylallyl ethyl carbonate (**79**) and (*E*)-1,3-bis(4-chlorophenyl)allyl ethyl carbonate (**84**) were prepared. An attempt to synthesize (*E*)-1,3-bis(4-methoxyphenyl)allyl ethyl carbonate (**91**) was challenged by the instability of the corresponding alcohol (*E*)-1,3-bis(4-methoxyphenyl)-prop-2-en-1-ol (**90**) and was not pursued further. Since the carbonates reacted faster but led to lower enantiomeric excess for the generated allyl oximes than acetate **148** employed by Du et al.[84] attention was shifted to the allylic acetates. Therefore, a library of allylic acetates was synthesized, starting with aldol condensation followed by reduction and subsequent acetylation in moderate to excellent yields (Scheme 101).



Scheme 101. Reaction Scheme for the Allylic Acetate Substrate Library Synthesis

The indole derivative (*E*)-1,3-bis(1-methyl-1*H*-indol-3-yl)allyl acetate (**135**) could not be obtained from 3-acetyl-1-methylindole (**130**) and 1-methylindole-3-carboxaldehyde (**132**), since acetylation resulted in no transformation of the obtained alcohol **134**. As an aliphatic derivative (*E*)-1-cyclohexyl-3-phenylallyl acetate (**142**) was successfully synthesized with an overall yield of 47%.

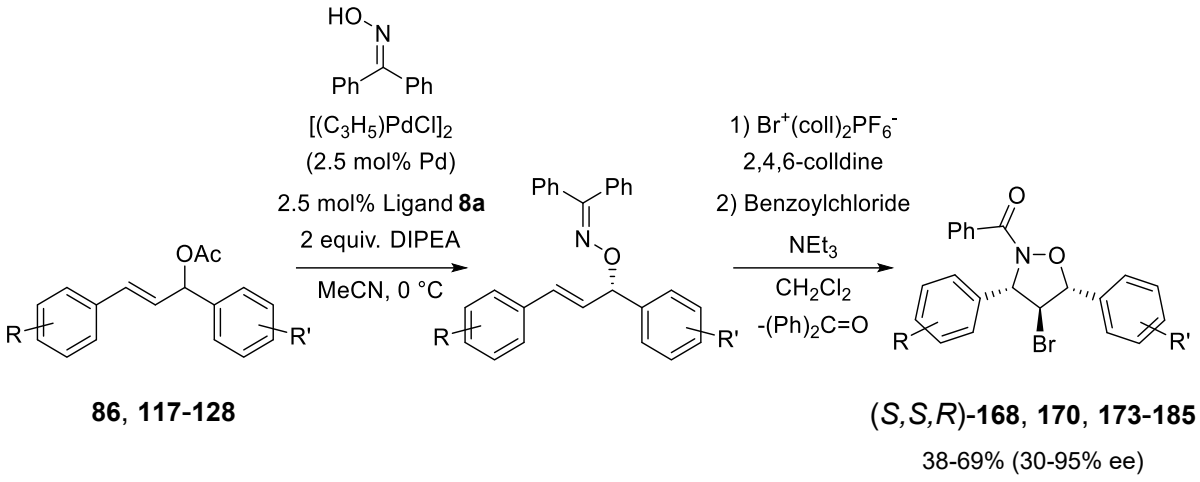
Racemic and enantioselective allylation proceeded smoothly employing diphenylmethanone oxime (**60**) and 9*H*-Fluoren-9-one oxime (**62**) as well as the more sterically demanding bis(2-(benzyloxy)phenyl)methanone oxime (**66**) and bis(2-bromophenyl)methanone oxime (**68**) in combination with allylic carbonates **79** and **84**. The best results however were obtained in the reaction of diphenylmethanone oxime (**60**) with (*E*)-1,3-diphenylallyl acetate (**148**) employing hybrid ligand **8a**, resulting in allyl oxime (*S*)-**143** in 92% enantiomeric excess (Scheme 79). (*S*,*E*)-Diphenylmethanone *O*-(1,3-bis(4-chlorophenyl)allyl) oxime ((*S*)-**149**) was synthesized from the corresponding acetate **86** under the same conditions with 86% enantiomeric excess. Upon storage the obtained allyl oxime (*S*)-**149** showed decrease in enantiomeric excess. Racemic allyl oximes were successfully obtained by Tsuji-Trost allylation employing the allylic acetates in combination with diphenylmethanone oxime (**60**) in the presence of tetrakis(triphenylphosphine) palladium(0) as catalyst and DIPEA as base. Dichloromethane as solvent gave mostly better yields than acetonitrile. (*E*)-1-Cyclohexyl-3-phenylallyl acetate (**142**) turned out as an exception which was neither readily transformed under racemic nor under enantioselective conditions.

The cyclization of the thus obtained allyl oximes was carried out with $Br^{+}(coll)_2PF_6^{-}$ (**3**). Isolation of the unprotected isoxazolidine **167** proved difficult. Therefore the raw product **167** was reacted with benzoyl chloride in the presence of triethylamine as base, rendering the *N*-protected isoxazolidine **168**, which was easily purified by column chromatography.

Racemization of allyl oxime (*S*)-**143** during cyclization was successfully suppressed by addition of one equivalent of 2,4,6-collidine (**1**) prior to the addition of $Br^{+}(coll)_2PF_6^{-}$ (**3**) yielding ((3*S*,4*S*,5*R*)-4-Bromo-3,5-diphenylisoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**168**) with 91% enantiomeric excess. (*S*,*E*)-9*H*-Fluoren-9-one *O*-(1,3-diphenylallyl) oxime ((*S*)-**144**) could not be cyclized under these conditions, which might be attributed to the rigidity of the fluorenone moiety.

Since decrease in enantiomeric excess was observed upon storage of the allyl oximes the allyl acetates were transformed in the enantioselective allylation reaction with diphenylmethanone oxime (**60**) and the resulting allyl oximes purified by column chromatography and subjected to cyclization within 24 hours. After *N*-protection the isoxazolidines were obtained in moderate to good yields regarding the three-step synthesis with enantiomeric excess ranging from 81% to 91%. An exception was the *ortho*-substituted ((3*S*,4*S*,5*R*)-4-bromo-3,5-di-*o*-tolylisoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**177**) with only 30% enantiomeric excess which can be attributed to steric interaction. More surprisingly the corresponding *para*-substituted ((3*S*,4*S*,5*R*)-4-bromo-3,5-di-*p*-tolylisoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**175**) was also obtained with a rather low enantiomeric excess of 55%.

Consequently, a one-pot synthesis for the isoxazolidine ((3*S*,4*S*,5*R*)-4-Bromo-3,5-diphenylisoxazolidin-2-yl)(phenyl)methanone ((*S,S,R*)-**168**) was developed. A key aspect of this protocol was the removal of DIPEA with saturated ammonium chloride solution after the allylation step. The decrease in catalyst loading from 5 mol% to 2.5 mol% proved especially successful increasing the enantiomeric excess for ((3*S*,4*S*,5*R*)-4-Bromo-3,5-di-*p*-tolylisoxazolidin-2-yl)(phenyl)methanone ((*S,S,R*)-**175**) instantly from 55% to 86% while the yield was simultaneously increased from 47% to 69% for the three step conversion. These conditions were applied to the allylic acetates resulting in yields between 38% and 69% with increased enantiomeric excess up to 95% (Scheme 102). ((3*S*,4*S*,5*R*)-4-bromo-3,5-di-*o*-tolylisoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**177**) remained as an exception with no increase in enantiomeric excess as well as ((3*S*,4*S*,5*R*)-4-bromo-5-(4-methoxyphenyl)-3-(4-(trifluoromethyl)phenyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**183**) with an enantiomeric excess of 45% which can be attributed to the increased instability of the allyl oxime bond with regard to the para-methoxy substituent.



86, **117-128**

(*S,S,R*)-**168**, **170**, **173-185**

38-69% (30-95% ee)

Scheme 102. “One-Pot” Protocol for the Synthesis of Enantioenriched Isoxazolidines

4 Experimental Section

4.1 Materials

All chemicals used were purchased from specialized suppliers like Sigma-Aldrich Co. LLC, Acros Organics, Merck KGaA etc. and unless stated otherwise applied without further purification.

4.2 Equipment

The following equipment was used for the synthesis and analysis of all compounds:

^{1}H NMR spectra:	Bruker Avance III – 300, Bruker Avance III – 600	
^{13}C NMR spectra:	Bruker Avance III – 300, Bruker Avance III – 600	
Mass spectrometry:	ESI:	Bruker Daltonics UHR-QTOF maXis 4G
	EI:	Thermo Electron Corp. Finnigan Trace DSQ with Finnigan Trace GC Ultra
IR:	JASCO FT/IR-6200	
TLC:	ALUGRAM® Xtra SIL G/UV254; Silica gel 60 with Fluorescence-Indicator UV254 (Macherey-Nagel)	
Column chromatography:	Silica gel 60, 0.04 – 0.063 mm (Macherey-Nagel)	
Rotary vane pump:	VACUUBRAND RZ 6	
Rotary evaporator:	BÜCHI Rotavapor R-210	
HPLC:	VWR HITACHI – ELITE LaChrom	
Chrial Columns:	CHIRALPAK IB, IC (0.46x25cm)	

4.3 Drying and Storage of Solvents

Solvents in technical grade were purified by distillation with a rotary evaporator. Unless stated otherwise, dry solvents were used as provided by the Solvent Purification System MB-SPS-800 manufactured by M. BRAUN INERTGAS-SYSTEME GmbH.

4.4 Working under N_2 Atmosphere

Syntheses under exclusion of air and humidity were carried out using Schlenk technique. Reaction flasks were evacuated using a rotary vane pump generating a high vacuum and in turn flushed with nitrogen. This process was operated by a nitrogen-vacuum line and repeated at least three times. Solids were submitted beforehand or added under nitrogen countercurrent. Liquids were added with a nitrogen flushed syringe through a septum. Larger volumes were transferred by nitrogen flushed double cannula. The nitrogen used was dried over molecular sieve and channeled through a bubble counter charged with silicon oil, to ensure that no ambient air enters the line. A condensation trap was used to separate the vacuum pump from evaporating chemicals and solvents. This condensation trap was cooled with liquid nitrogen.

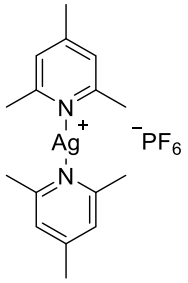
4.5 Preparation of Cooling Baths

Cooling baths were prepared in Dewar flasks to ensure better insulation and therefore constant reaction conditions. To reach temperatures down to 0 °C an ice bath or more regularly a cryostat was employed. Temperatures down to -21 °C were obtained with an ice/salt bath and down to -78 °C with an acetone-dry ice combination.

4.6 Experiments

I. Brominating Reagent and Ligands

4.6.1 Bis(2,4,6-trimethylpyridine)silver(I) hexafluorophosphate (**2**)[91]



$C_{16}H_{22}AgF_6N_2P$

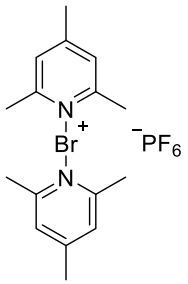
[495.20]

Silver nitrate (10.0 g, 58.9 mmol, 1.0 equiv) and potassium hexafluorophosphate (10.9 g, 59.2 mmol, 1.0 equiv) were dispersed in H_2O (100 mL). 2,4,6-Collidine (22.1 mL, 167 mmol, 2.0 equiv) was added dropwise over a 10-minute period resulting in the formation of a white precipitate. The mixture was stirred at rt for 1 hour before it was suction-filtered. The obtained solid was dried over P_4O_{10} in a desiccator under exclusion of light for one week to afford a white-grey solid (29.1 g, 58.8 mmol, <99%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (s, 4H, Ar H); 2.76 (s, 12H, *o*-CH_3); 2.38 (s, 6H, *p*-CH_3).

mp 222-229 °C (lit.[91] 210 °C)

4.6.2 Bis(2,4,6-trimethylpyridine)bromine(I) hexafluorophosphate (**3**)[91]



$C_{16}H_{22}BrF_6N_2P$

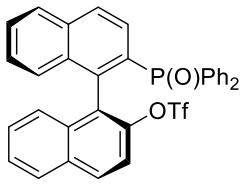
[467.23]

Bis(2,4,6-trimethylpyridine)silver(I) hexafluorophosphate (29.0 g, 58.6 mmol, 1.0 equiv) was largely dissolved in dry CH_2Cl_2 (175 mL) under exclusion of light and Br_2 (2.90 mL, 56.8 mmol, 1.0 equiv) was added dropwise over a 10-minute period. The mixture was stirred at rt for 1 hour before the formed yellow AgBr was removed by suction filtration and washed with dry CH_2Cl_2. The solvent of the filtrate was removed in vacuo (bath temp. 30 °C). The obtained white solid was recrystallized from dry CH_2Cl_2 at rt (17.5 g, 37.5 mmol, 66%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (s, 4H, Ar H); 2.81 (s, 12H, *o*-CH_3); 2.43 (s, 6H, *p*-CH_3).

mp 126-130 °C (lit.[91] 127-128 °C)

4.6.3 (*S*)-2'-(Diphenylphosphoryl)-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate (**6**)[85]



$C_{33}H_{22}F_3O_4PS$

[602.56]

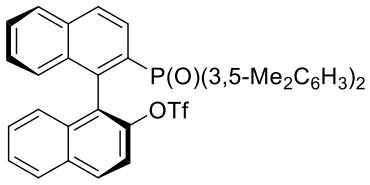
(*S*)-[1,1'-Binaphthalene]-2,2'-diyl bis(trifluoromethane sulfonate) (1.10 g, 2.00 mmol, 1.0 equiv), diphenylphosphine oxide (809 mg, 4.00 mmol, 2.0 equiv) and 1,4-bis(diphenylphosphino)butane (43.0 mg, 0.101 mmol, 5.0 mol%) were dissolved in dry, degassed DMSO (9.0 mL). $Pd(OAc)_2$ (23.0 mg, 0.102 mmol, 5.1 mol%) and DIPEA (1.40 mL, 8.04 mmol, 4.0 equiv) were added and the resulting brown solution heated to 105 °C bath temp. After 34 hours diphenylphosphine oxide (202 mg, 0.999 mmol, 0.5 equiv) was added again, since TLC showed incomplete transformation. After another 2 days TLC remained unchanged. The reaction was allowed to cool to rt and diluted with EtOAc. The organic phase was washed three times with H_2O and once with brine, dried over Na_2SO_4 and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 1:1, R_f = 0.29) afforded a white solid (570 mg, 0.946 mmol, 47%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (ddd, *J* = 8.7, 2.4, 0.8 Hz, 1H), 7.95 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.90 (d, *J* = 9.1 Hz, 1H), 7.84 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.66 (dd, *J* = 11.5, 8.6 Hz, 1H), 7.58 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.53 – 7.22 (m, 13H), 7.21 – 7.12 (m, 2H), 7.00 (dq, *J* = 8.5, 0.9 Hz, 1H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -74.98.

^{31}P(^{1}H) NMR (121 MHz, $CDCl_3$) δ 28.07.

4.6.4 (*S*)-2'-(Bis(3,5-dimethylphenyl)phosphoryl)-[1,1'-binaphthalen]-2-yl trifluoromethane sulfonate (**6a**)[85]



$C_{37}H_{30}F_3O_4PS$

[658.67]

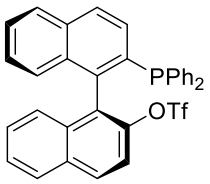
(*S*)-[1,1'-Binaphthalene]-2,2'-diyl bis(trifluoromethane sulfonate) (2.20 g, 4.00 mmol, 1.0 equiv), bis(3,5-dimethylphenyl)phosphine oxide (2.07 g, 8.00 mmol, 2.0 equiv) and 1,4-bis(diphenylphosphino)butane (85.3 mg, 0.200 mmol, 5.0 mol%) were dissolved in dry, degassed DMSO (18 mL). $Pd(OAc)_2$ (44.9 mg, 0.200 mmol, 5.0 mol%) and dry, degassed DIPEA (2.80 mL, 16.0 mmol, 4.0 equiv) were added and the resulting brown solution heated to 105 °C bath temp. After 22 hours the reaction was allowed to cool to rt and diluted with EtOAc (100 mL). The organic phase was washed three times with H_2O (3x40 mL) and once with brine (40 mL), dried over Na_2SO_4 and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 3:2, R_f = 0.14) afforded a slightly yellowish solid (2.07 g, 3.14 mmol, 79%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (ddd, *J* = 8.7, 2.3, 0.8 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.85 (dd, *J* = 8.6, 6.0 Hz, 2H), 7.76 (dd, *J* = 11.4, 8.6 Hz, 1H), 7.56 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.43 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.36 – 7.17 (m, 3H), 7.14 – 7.00 (m, 6H), 6.96 (d, *J* = 10.2 Hz, 2H), 2.18 (s, 6H), 2.16 (s, 6H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -74.92.

^{31}P(^{1}H) NMR (121 MHz, $CDCl_3$) δ 28.83.

4.6.5 (*S*)-2'-(Diphenylphosphanyl)-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate (**7**)[85]



$C_{33}H_{22}F_3O_3PS$

[586.56]

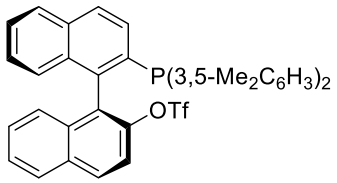
(*S*)-2'-(Diphenylphosphoryl)-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate (565 mg, 0.938, 1.0 equiv) was dissolved in dry, degassed toluene (5 mL) and transferred into an overpressure flask. The original flask was rinsed with toluene (2x5 mL) and additional toluene (10 mL) was added. The solution was cooled with an ice bath and DIPEA (0.96 mL, 5.5 mmol, 5.9 equiv) and $HSiCl_3$ (0.47 mL, 4.7 mmol, 5.0 equiv) were added. The flask was sealed, the ice bath removed, and the solution heated to 105 °C bath temp. After 21 hours the solution was again cooled with an ice bath, Et_2O and saturated Na_2CO_3 solution added, the resulting mixture stirred for 1 hour and then filtered through a celite plug. The organic layer was dried over Na_2SO_4 and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.32) yielded a white solid (350 mg, 0.597 mmol, 64%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, *J* = 9.0 Hz, 1H), 7.98 – 7.87 (m, 3H), 7.58 – 7.40 (m, 4H), 7.34 – 7.22 (m, 5H), 7.21 – 7.07 (m, 4H), 7.07 – 6.98 (m, 2H), 6.94 (dq, *J* = 8.5, 0.9 Hz, 1H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -74.87.

^{31}P(^{1}H) NMR (121 MHz, $CDCl_3$) δ -13.17.

4.6.6 (*S*)-2'-(Bis(3,5-dimethylphenyl)phosphanyl)-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate (**7a**)[85]



$C_{37}H_{30}F_3O_3PS$

[642.67]

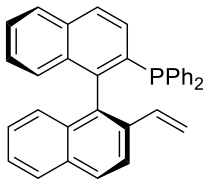
(*S*)-2'-(Bis(3,5-dimethylphenyl)phosphoryl)-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate (1.95 g, 2.96 mmol, 1.0 equiv) was dissolved in dry, degassed toluene (10 mL) and transferred into an overpressure flask. The original flask was rinsed with toluene (2x10 mL) and additional toluene (50 mL) was added. The solution was cooled with an ice bath and dry, degassed DIPEA (3.0 mL, 17 mmol, 5.8 equiv) and $HSiCl_3$ (1.5 mL, 15 mmol, 5.0 equiv) were added. The flask was sealed, the ice bath removed, and the solution heated to 105 °C bath temp. After 22 hours the solution was again cooled with an ice bath, Et_2O (35 mL) and saturated Na_2CO_3 solution (10 mL) were added, the resulting mixture stirred for 1 hour and then filtered through a celite plug. The organic layer was dried over Na_2SO_4 and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.31) yielded a white solid (1.64 g, 2.55 mmol, 86%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 9.1 Hz, 1H), 7.98 – 7.85 (m, 3H), 7.58 – 7.42 (m, 4H), 7.32 – 7.23 (m, 1H), 7.20 – 7.09 (m, 2H), 6.97 – 6.87 (m, 4H), 6.80 – 6.74 (m, 1H), 6.61 (dt, *J* = 8.2, 1.0 Hz, 2H), 2.24 (s, 6H), 2.09 (s, 6H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -74.91.

^{31}P(^{1}H) NMR (121 MHz, $CDCl_3$) δ -12.26.

4.6.7 (*R*)-Diphenyl(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (**8**)[85]



$C_{34}H_{25}P$

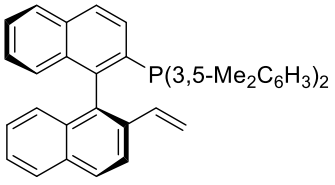
[464.55]

(*S*)-2'-(Diphenylphosphanyl)-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate (325 mg, 0.554 mmol, 1.0 equiv), potassium vinyltrifluoroborate (89.4 mg, 0.667 mmol, 1.2 equiv) and $Pd(PPh_3)_4$ (25.4 mg, 0.0220 mmol, 4.0 mol%) were dissolved in dry, degassed 1,4-dioxane (10 mL). DIPEA (0.15 mL, 0.89 mmol, 1.6 equiv) was added and the reaction heated to 105 °C bath temp. The reaction was monitored by TLC and after 5 hours allowed to cool to rt and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/Et_2O 50:1, R_f = 0.39) afforded a white solid (93.3 mg, 0.201 mmol, 36%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 – 7.82 (m, 5H), 7.52 – 7.44 (m, 2H), 7.33 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H), 7.29 – 7.11 (m, 8H), 7.10 – 6.98 (m, 3H), 6.92 – 6.85 (m, 1H), 6.15 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.64 (dd, *J* = 17.5, 1.1 Hz, 1H), 4.88 (dd, *J* = 11.0, 1.0 Hz, 1H).

^{31}P(^{1}H) NMR (121 MHz, $CDCl_3$) δ -14.59.

4.6.8 (*R*)-Bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (**8a**)[85]



$C_{38}H_{33}P$

[520.66]

(*S*)-2'-(Bis(3,5-dimethylphenyl)phosphanyl)-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate (1.64 g, 2.55 mmol, 1.0 equiv), potassium vinyltrifluoroborate (412 mg, 3.08 mmol, 1.2 equiv) and $Pd(PPh_3)_4$ (120 mg, 0.104 mmol, 4.0 mol%) were dissolved in dry, degassed 1,4-dioxane (50 mL). Dry, degassed DIPEA (0.71 mL, 4.08 mmol, 1.6 equiv) was added and the reaction heated to 105 °C bath temp. The reaction was monitored by TLC and after 5 hours allowed to cool to rt and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/Et_2O 50:1, R_f = 0.31) afforded a white solid (242 mg, 0.465 mmol, 18%).

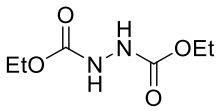
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 – 7.81 (m, 5H), 7.54 (dd, *J* = 8.5, 2.8 Hz, 1H), 7.47 (ddd, *J* = 8.1, 6.7, 1.4 Hz, 1H), 7.33 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.25 – 7.20 (m, 1H), 7.18 – 7.12 (m, 1H), 7.01 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 6.90 – 6.78 (m, 5H), 6.71 – 6.64 (m, 2H), 6.22 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.68 (dd, *J* = 17.6, 1.1 Hz, 1H), 4.94 (dd, *J* = 11.0, 1.1 Hz, 1H), 2.21 (s, 6H), 2.13 (s, 6H).

^{31}P(^{1}H) NMR (121 MHz, $CDCl_3$) δ -13.49.

II. Pyrazolidine Syntheses

i. Hydrazides

4.6.9 Diethyl hydrazine-1,2-dicarboxylate (**10**)[103]



$C_6H_{12}N_2O_4$

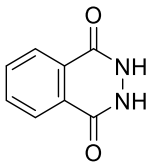
[176.17]

A solution of hydrazine monohydrate (4.90 mL, 101 mmol, 1.0 equiv) in EtOH (50 mL) was cooled with an ice bath. Ethyl chloroformate (19.1 mL, 200 mmol, 2.0 equiv) was added dropwise, so that the temp. of the solution did not exceed 20 °C. After approx. half of the ethyl chloroformate was added, a solution of Na_2CO_3 (10.6 g, 100 mmol, 1.0 equiv) in H_2O (50 mL) was added simultaneously. The addition was regulated, so that the reaction temp. did not exceed 20 °C and the addition of the ethyl chloroformate was finished slightly in advance of the Na_2CO_3 solution. The mixture was stirred for another 45 minutes. The white

precipitate was suction-filtered, washed with H_2O (approx. 200 mL) and dried in a vacuum oven at 65 °C yielding a white solid (12.0 g, 68.1 mmol, 67%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.54 (s, 2H), 4.20 (q, *J* = 7.1 Hz, 4H), 1.27 (t, *J* = 7.1 Hz, 6H).

4.6.10 2,3-Dihydrophthalazine-1,4-dione (**12**)[104]



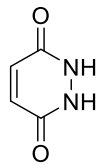
$C_8H_6N_2O_2$

[176.17]

Phthalic anhydride (7.41 g, 50.0 mmol, 1.0 equiv) was dispersed in AcOH (50 mL) and hydrazine monohydrate (2.90 mL, 59.7 mmol, 1.2 equiv) was added slowly. The slightly yellow suspension was refluxed for 4.5 hours. It was allowed to cool to rt and white precipitate suction-filtered, washed with H_2O and *n*-hexane and dried in a vacuum oven at 65 °C yielding a white solid (7.67 g, 47.3 mmol, 95%).

^{1}H NMR (300 MHz, DMSO-*d*^{6}) δ 11.53 (s, 2H), 8.07 (dd, *J* = 5.9, 3.3 Hz, 2H), 7.88 (dd, *J* = 5.9, 3.3 Hz, 2H).

4.6.11 1,2-Dihydropyridazine-3,6-dione (**14**)[105]



$C_4H_4N_2O_2$

[176.17]

Maleic anhydride (4.92 g, 50.2 mmol, 1.0 equiv) was dissolved in AcOH (30 mL). The solution was cooled with an ice bath and hydrazine monohydrate (2.90 mL, 59.7 mmol, 1.2 equiv) was added. The yellow dispersion was refluxed for 4 hours. The dark yellow-orange dispersion was suction-filtered affording an off-white solid. The obtained solid was washed with H_2O and 50 vol.% EtOH solution and dried in a vacuum oven at 65 °C yielding an off-white solid (3.96 g, 35.3 mmol, 70%).

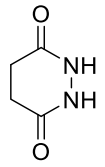
^{1}H NMR (300 MHz, DMSO-*d*^{6}) δ 11.39 (br d, *J* = 227.2 Hz, 2H), 6.92 (s, 2H).

^{1}H NMR (600 MHz, DMSO-*d*^{6}, 50 °C) δ 11.30 (br s, 2H), 6.91 (s, 2H).

^{13}C NMR (75 MHz, DMSO-*d*^{6}) δ 156.24, 130.44.

MS-EI (*m/z*) 112 (100%, $M^{+\bullet}$); 82 (58%, $M^{+\bullet} - N_2H_2$); 55 (26%, $M^{+\bullet}$ – NH-C=O); 54 (16%, $M^{+\bullet}$ – NH-NH-C=O).

4.6.12 Tetrahydropyridazine-3,6-dione (**16**)



$C_4H_6N_2O_2$

[114.10]

Version 1:[104]

Succinic anhydride (3.53 g, 35.3 mmol, 1.0 equiv) was dispersed in AcOH (20 mL) and hydrazine monohydrate (1.90 mL, 39.1 mmol, 1.1 equiv) was added slowly. The resulting suspension was refluxed for 4.5 hours. Upon cooling no precipitate had formed. The solution was diluted with ice water and neutralized with $NaHCO_3$ solution (pH 6) still forming no precipitate. Extraction of the aqueous solution was also not successful.

In a second attempt succinic anhydride (1.00 g, 9.99 mmol, 1.0 equiv) was dispersed in AcOH (15 mL) and hydrazine monohydrate (0.55 mL, 11 mmol, 1.1 equiv) was added. The resulting suspension was refluxed for 16 hours. Upon cooling no precipitate had formed. AcOH was largely removed in vacuo and the resulting colorless oil dried in vacuo. The ^{1}H NMR spectrum of the resulting highly viscous oil did neither show substrate nor product signals.

Version 2:

Succinic anhydride (1.00 g, 9.99 mmol, 1.0 equiv) was dispersed in AcOH (15 mL) and hydrazine hydrochloride (753 mg, 11.0 mmol, 1.1 equiv) was added. The resulting suspension was refluxed for 4 hours. The white precipitate was suction-filtered, washed with H_2O and dried in a vacuum oven overnight at 60 °C. The resulting white solid was identified as mostly starting material.

Version 3:[113]

1,2-Dihydropyridazine-3,6-dione (1.00 g, 8.92 mmol, 1.0 equiv) was dissolved in dry DMF (60 mL). Pd/C (10 wt%) (100 mg, 94.0 µmol, 10.5 mol%) was added, the reaction flask flushed with H_2 and the mixture reacted under balloon pressure. 10 mL of this solution were withdrawn with a syringe after 19.5 hours and the catalyst removed by plug filtration. The solvent was largely removed in vacuo and the resulting solid dried in a vacuum oven overnight at 100 °C. The ^{1}H NMR spectrum of the resulting white solid still showed mostly signals of the starting material. This withdrawal procedure was repeated after 3 days leading to the same result.

Version 4:[111]

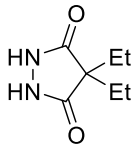
1,2-Dihydropyridazine-3,6-dione (1.00 g, 8.92 mmol, 1.0 equiv) was dispersed in dry EtOH (150 mL). PtO_2 (50 mg, 0.22 mmol, 2.5 mol%) was added, the flask flushed with H_2 and the mixture reacted under balloon pressure and refluxed for 3 days. 20 mL of this solution were withdrawn with a syringe, the catalyst removed by plug filtration and the solvent removed in vacuo. The ^{1}H NMR spectrum of the resulting white solid still showed starting material signals. After another 7 days the withdrawal procedure was repeated affording the same result. After another 14 days the remaining reaction solution was subjected to this procedure. The ^{1}H NMR spectrum of the resulting white solid still showed starting material signals.

Version 5:[111, 113]

1,2-Dihydropyridazine-3,6-dione (503 mg, 4.49 mmol, 1.0 equiv), Pd/C (10 wt%) (49.7 mg, 46.7 µmol, 10.4 mol%) were dispersed in EtOH (75 mL) in an autoclave. The autoclave was flushed with N_2 and three times with H_2 afterwards. The mixture was reacted at 12 bar H_2 pressure and 100 °C bath temp. for 24 hours. The catalyst was removed by plug filtration and the solvent removed in vacuo yielding a white solid (360 mg, 3.16 mmol, 70%).

^{1}H NMR (300 MHz, DMSO-*d*^{6}) δ 10.05 (s, 2H), 2.41 (s, 4H).

4.6.13 4,4-Diethylpyrazolidine-3,5-dione (**22**)[114]



$C_7H_{12}N_2O_2$

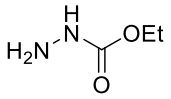
[156.19]

Na (486 mg, 21.1 mmol, 1.0 equiv) was added in small pieces to EtOH p.a. (10 mL) from a freshly opened bottle. After the Na had dissolved, diethyl 2,2-diethylmalonate (4.40 mL, 20.1 mmol, 1.0 equiv) and hydrazine monohydrate (1.95 mL, 40.1 mmol, 2.0 equiv) were added and the EtOH was distilled off. After cooling the white residue was dissolved in H_2O, unreacted ester extracted with EtOAc and then acidified with conc. HCl (pH 3). The solvent was removed in vacuo to afford a yellow solid, which was recrystallized from Et_2O/EtOH. The white precipitate was suction-filtered, washed with Et_2O and EtOH and dried in vacuo yielding a white solid (546 mg, 3.50 mmol, 17%).

^{1}H NMR (300 MHz, DMSO-*d*^{6}) δ 10.51 (s, 2H), 1.54 (q, *J* = 7.4 Hz, 4H), 0.73 (t, *J* = 7.4 Hz, 6H).

MS-ESI (*m/z*) 156 (18%, $M^{+\bullet}$); 128 (26%, $M^{+\bullet}$ – Et); 113 (13%, $M^{+\bullet}$ – NH-C=O); 83 (13%); 38 (32%); 36 (100%, HCl).

4.6.14 Ethyl hydrazine carboxylate (**24**)[117]



$C_3H_8N_2O_2$

[104.11]

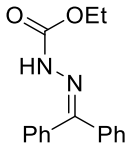
Diethyl carbonate (25.0 mL, 0.207 mol, 1.1 equiv) and hydrazine monohydrate (9.50 mL, 0.196 mol, 1.0 equiv) were heated at 60 °C bath temp. for 60 minutes and stirred overnight at rt. Excess diethyl carbonate and EtOH were distilled of under reduced pressure up to a head temp. of 60 °C (28 mbar, oil bath temp. 90 °C). The residue was dried in vacuo yielding a colorless oil (16.5 g, 0.158 mol, 81%).

^{1}H NMR (300 MHz, DMSO-d^6) δ 8.06 (br s, 1H), 4.00 (br s, 2H), 3.99 (q, *J* = 7.1 Hz, 2H), 1.15 (t, *J* = 7.1 Hz, 3H).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.11 (br s, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.74 (br s, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

MS-ESI (*m/z*) 105 (100%, $[M + H]^+$); 77 (34%, $[M - Et]^+$).

4.6.15 Ethyl 2-(diphenylmethylene)hydrazine-1-carboxylate (**26**)[118]



$C_{16}H_{16}N_2O_2$

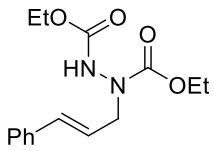
[268.32]

Benzophenone (1.02 g, 5.60 mmol, 1.0 equiv) was dissolved in EtOH (10 mL). Ethyl hydrazine carboxylate (745 mg, 7.16 mmol, 1.3 equiv) and AcOH (5 drops) were added and the solution heated to 80-90 °C bath temp. The reaction was monitored by TLC and after 25 hours additional ethyl hydrazine carboxylate (745 mg, 7.16 mmol, 1.3 equiv) and AcOH (5 drops) were added. After another 24 hours the solution was allowed to cool to rt and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 4:1, R_f = 0.28) yielded a white solid (1.48 g, 5.52 mmol, 98%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.67 – 7.48 (m, 5H), 7.31 (ddd, *J* = 16.8, 5.4, 3.1 Hz, 5H), 4.28 (q, *J* = 7.2 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H).

ii. Allyl Hydrazides

4.6.16 Diethyl 1-cinnamylhydrazine-1,2-dicarboxylate (**28**)



$C_{15}H_{20}N_2O_4$

[292.34]

Version 1:[90]

Diethyl hydrazine-1,2-dicarboxylate (883 mg, 5.01 mmol, 1.0 equiv) was dissolved in dry THF (20 mL). Cinnamyl bromide (986 mg, 5.00 mmol, 1.0 equiv) and a 60% dispersion of NaH in mineral oil (200 mg, 5.00 mmol, 1.0 equiv) were added. The resulting dispersion was stirred at rt and the reaction monitored by TLC. After 3 hours the reaction was quenched with saturated NH_4Cl solution. EtOAc and H_2O were added until the formed precipitate was fully dissolved. The aqueous layer was extracted twice with EtOAc. The combined organic layers were washed twice with H_2O and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. The ^{1}H NMR spectrum of this material did not show any product signals.

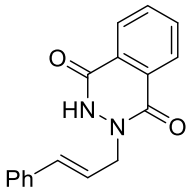
Version 2:[119]

Diethyl hydrazine-1,2-dicarboxylate (350 mg, 1.99 mmol, 1.0 equiv) was dissolved in a mixture of dry THF (8 mL) and dry DMF (0.7 mL). The solution was cooled with an ice bath, a dispersion of 60% NaH in mineral oil (81.0 mg, 2.03 mmol, 1.0 equiv) was added and the resulting suspension stirred for 40 minutes. Cinnamyl bromide (394 mg, 2.00 mmol, 1.0 equiv) was added, the ice bath removed, and the suspension stirred for 24 hours at rt. The reaction was quenched with saturated NH_4Cl solution. EtOAc and H_2O were added until the formed precipitate was fully dissolved. The aqueous layer was extracted twice with EtOAc. The combined organic layers were washed twice with H_2O and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 4:1, R_f = 0.10) yielded a colorless oil (400 mg, 1.37 mmol, 68%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.18 (m, 5H), 6.53 (dt, *J* = 15.8, 1.3 Hz, 1H), 6.21 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.27 (br d, *J* = 7.1 Hz, 2H), 4.19 (q, *J* = 7.1 Hz, 4H), 1.27 (t, *J* = 7.1 Hz, 6H).

Major peaks reported, minor peaks due to rotamers.

4.6.17 2-Cinnamyl-2,3-dihydrophthalazine-1,4-dione (**29**)[119]



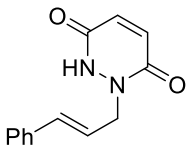
$C_{17}H_{14}N_2O_2$

[278.31]

2,3-Dihydrophthalazine-1,4-dione (324 mg, 2.00 mmol, 1.0 equiv) was dispersed in a mixture of dry THF (8 mL) and dry DMF (8 mL). A dispersion of 60% NaH in mineral oil (80.5 mg, 2.01 mmol, 1.0 equiv) was added and the resulting suspension stirred at rt for 30 minutes. Cinnamyl bromide (393 mg, 1.99 mmol, 1.0 equiv) was added and the suspension stirred for another 4 days. The reaction was quenched by addition of a saturated NH_4Cl solution. H_2O and EtOAc were added until the formed precipitate was fully dissolved. The aqueous layer was extracted twice with EtOAc. The combined organic layers were washed twice with H_2O

and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. Recrystallization from *n*-hexane/EtOAc, *n*-hexane/toluene or *n*-hexane/toluene/EtOH remained unsuccessful.

4.6.18 1-Cinnamyl-1,2-dihydropyridazine-3,6-dione (**30b**) [119]

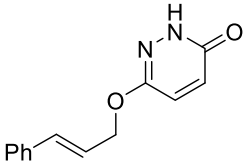


$C_{13}H_{12}N_2O_2$

[228.25]

1,2-Dihydropyridazine-3,6-dione (224 mg, 2.00 mmol, 1.0 equiv) was dispersed in a mixture of dry THF (8 mL) and dry DMF (8 mL). A dispersion of 60% NaH in mineral oil (83.3 mg, 2.08 mmol, 1.0 equiv) was added and the resulting suspension stirred at rt for 40 minutes. Cinnamyl bromide (394 mg, 2.00 mmol, 1.0 equiv) was added and the suspension stirred for another 4 days. The reaction was quenched by addition of a saturated NH_4Cl solution. H_2O and EtOAc were added until the formed precipitate was fully dissolved. The aqueous layer was extracted twice with EtOAc. The combined organic layers were washed twice with H_2O and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. This solid was purified by column chromatography (*n*-hexane/EtOAc 2:1 (R_f = 0.07) to 3:2 to 1:1; *n*-hexane/EtOH 9:1 (R_f = 0.21) to 4:1) to afford the *O*-allylated species as a white solid (126 mg, 0.552 mmol, 28%). The diallylated 1,2-dihydropyridazine-3,6-dione was isolated as a by-product as a white solid (124 mg, 0.360 mmol, 35%).

Monoallylated 1,2-dihydropyridazine-3,6-dione (**32**):

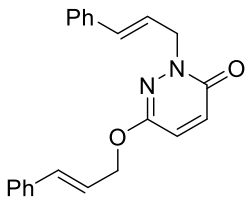


$C_{13}H_{12}N_2O_2$

[228.25]

^{1}H NMR (300 MHz, $CDCl_3$) δ 11.78 (br s, 1H), 7.45 – 7.22 (m, 5H), 7.04 (d, *J* = 9.9 Hz, 1H), 6.96 (d, *J* = 9.8 Hz, 1H), 6.72 (dt, *J* = 15.9, 1.3 Hz, 1H), 6.39 (dt, *J* = 15.9, 6.3 Hz, 1H), 4.82 (dd, *J* = 6.3, 1.3 Hz, 2H).

Diallylated 1,2-dihydropyridazine-3,6-dione (**33**):

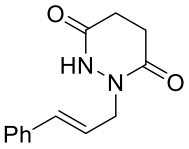


$C_{22}H_{20}N_2O_2$

[344.41]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.17 (m, 10H), 7.01 – 6.87 (m, 2H), 6.81 – 6.58 (m, 2H), 6.47 – 6.28 (m, 2H), 4.91 – 4.71 (m, 4H).

4.6.19 1-Cinnamyltetrahydropyridazine-3,6-dione (**34**)



$C_{13}H_{14}N_2O_2$

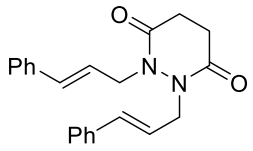
[230.27]

Version 1:[119]

Tetrahydropyridazine-3,6-dione (330 mg, 2.89 mmol, 1.0 equiv) was dissolved in a mixture of dry THF (10 mL) and dry DMF (30 mL). The solution was cooled with an ice bath and a dispersion of 60% NaH in mineral oil (127 mg, 3.18 mmol, 1.1 equiv) was added and the resulting suspension stirred at rt for 55 minutes. Cinnamyl bromide (570 mg, 2.89 mmol, 1.0 equiv) was added and the suspension stirred for 18 hours. The reaction was quenched with saturated NH_4Cl solution. H_2O and EtOAc were added until the formed precipitate was

fully dissolved. The aqueous layer was extracted twice with EtOAc. The combined organic layers were washed twice with H_2O and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. The obtained solid was washed with *n*-hexane/EtOH 1:1 (6 mL) to afford a white solid, which was identified as the diallylated tetrahydropyridazine-3,6-dione (330 mg, 0.953 mmol, 66%) by ^{1}H NMR spectroscopy.

Diallylated tetrahydropyridazine-3,6-dione (**35**):



$C_{22}H_{22}N_2O_2$

[346.43]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.22 (m, 10H), 6.62 (dt, *J* = 15.9, 1.3 Hz, 2H), 6.12 (dt, *J* = 15.9, 6.7 Hz, 2H), 4.48 (dd, *J* = 6.7, 1.3 Hz, 4H), 2.62 (s, 4H).

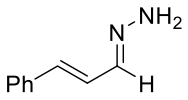
In a second attempt tetrahydropyridazine-3,6-dione (200 mg, 1.75 mmol, 1.0 equiv) was dispersed in a mixture of dry THF (8 mL) and dry DMF (8 mL) and a 60% NaH dispersion in mineral oil (70.0 mg, 1.75 mmol, 1.0 equiv) was added. The resulting suspension was stirred for 30 minutes before cinnamyl bromide (345 mg, 1.75 mmol, 1.0 equiv) was added. TLC and the ^{1}H NMR spectrum did again only show the diallylated product.

In a third attempt a 60% NaH dispersion in mineral oil (175 mg, 4.38 mmol, 1.0 equiv) was dispersed in dry DMSO (25 mL), cooled with an ice bath and stirred for 45 minutes. Tetrahydropyridazine-3,6-dione (500 mg, 4.38 mmol, 1.0 equiv) was added and the resulting suspension stirred for 40 minutes before cinnamyl bromide (864 mg, 4.38 mmol, 1.0 equiv) was added. After 20 hours the reaction was quenched with saturated NH_4Cl solution and H_2O and Et_2O were added. The aqueous phase extracted twice with EtO_2. The combined organic layers were washed twice with H_2O and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo. TLC and the ^{1}H NMR spectrum of the resulting yellow solid did again only show the diallylated product.

Version 2:[130]

Cinnamyl hydrazine (1.05 g, 7.08 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (70 mL) and NEt_3 (1 mL) was added. Succinyl chloride (0.80 mL, 7.2 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (15 mL) and added dropwise to the cinnamyl hydrazine solution. The reaction was monitored by TLC. After 5 hours the reaction solution was washed three times with H_2O, dried over Na_2SO_4 and the solvent removed in vacuo to afford a brown oil (1.38 g). Recrystallization was not successful. Purification by column chromatography did not afford the desired compound.

4.6.20 ((*E*)-3-Phenylallylidene)hydrazine (**37**)[160]



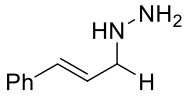
$C_9H_{10}N_2$

[146.19]

trans-Cinnamaldehyde (5.30 mL, 42.1 mmol, 1.0 equiv) was dissolved in MeOH (50 mL) and hydrazine monohydrate (2.60 mL, 53.5 mmol, 1.3 equiv) was added. The resulting solution was stirred at rt and monitored by TLC. After 1.5 hours the solvent was removed in vacuo to afford a waxy yellow solid (6.22 g). Column chromatography was not possible due to low solubility. Recrystallization from *n*-hexane/EtOAc was not successful even leading to increasing amount of impurities in the ^{1}H NMR spectrum.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 9.0, 0.5 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.38 – 7.21 (m, 3H), 6.86 (dd, *J* = 16.0, 9.0 Hz, 1H), 6.65 (d, *J* = 16.0 Hz, 1H), 5.48 (s, 2H).

4.6.21 Cinnamyl hydrazine (**38**)



$C_9H_{12}N_2$

[148.21]

Version 1:[126]

((*E*)-3-Phenylallylidene)hydrazine (1.00 g, 6.84 mmol, 1.0 equiv) was dissolved in dry MeOH (35 mL). $NaBH_4$ (261 mg, 6.90 mmol, 1.0 equiv) was added and the reaction monitored by TLC. After 21 hours the reaction was quenched with H_2O and CH_2Cl_2 was added. The aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo. A yellow solid was obtained (893 mg). The ^1H NMR spectrum of this solid matched that of the substrate.

Version 2:

((*E*)-3-Phenylallylidene)hydrazine (893 mg, 6.11 mmol, 1.0 equiv) was dissolved in MeOH (40 mL). $LiAlH_4$ (256 mg, 6.75 mmol, 1.1 equiv) was added and the reaction monitored by TLC. After 23 hours TLC did not show any progress for the reaction. After 11 days the reaction mixture was cooled with an ice bath and quenched by careful addition of H_2O and 1M NaOH solution. The resulting solution was extracted three times with EtOAc. The combined organic layers were washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid (790 mg). The ^1H NMR spectrum of this solid matched that of the substrate.

Substitution of methanol with THF as solvent did not result in the desired transformation either.

Version 3:[127]

((*E*)-3-Phenylallylidene)hydrazine (460 mg, 3.15 mmol, 1.0 equiv) was dissolved in dry toluene (20 mL) in a 50 ml two-necked flask with gas inlet tube and a 1M BH_3 solution in THF (3.15 mL, 3.15 mmol, 1.0 equiv) was added. HCl gas was produced by dropwise addition of H_2SO_4 to NaCl in a 500 ml three-necked flask and introduced to the reaction vessel through the gas inlet tube resulting in precipitation and darkening of the solution. After 30 minutes the

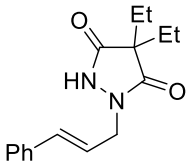
addition of HCl gas to the red-brown solution was terminated and saturated $NaHCO_3$ solution was added carefully. The aqueous phase was extracted with Et_2O three times before it was brought to a basic pH by addition of saturated $NaHCO_3$ solution and then extracted with EtOAc three times. The combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. The ^1H NMR spectrum of the obtained material did not match the desired product.

Version 4:[128]

trans-Cinnamyl bromide (1.97 g, 10.0 mmol, 1.0 equiv) was dissolved in EtOH (50 mL). Hydrazine monohydrate was added (14.6 mL, 300 mmol, 30 equiv) and the reaction monitored by TLC. After 1.5 hours EtOH was removed in vacuo and the residue dissolved in CH_2Cl_2 and H_2O. The organic phase was washed with brine, dried over Na_2SO_4 and the solvent removed in vacuo to afford a yellow oil (1.05 g, 7.08 mmol, 71%).

^1H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.07 (m, 5H), 6.53 (dt, *J* = 15.9, 1.4 Hz, 1H), 6.15 (dt, *J* = 15.9, 6.7 Hz, 1H), 3.50 (dd, *J* = 6.7, 1.3 Hz, 2H), 3.06 (br s, 3H).

4.6.22 1-Cinnamyl-4,4-diethylpyrazolidine-3,5-dione (**41**)[119]



$C_{16}H_{20}N_2O_2$

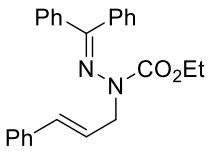
[272.35]

4,4-Diethylpyrazolidine-3,5-dione (250 mg, 1.60 mmol, 1.0 equiv) was dispersed in a mixture of dry THF (7 mL) and dry DMF (21 mL). A dispersion of 60% NaH in mineral oil (70.2 mg, 1.76 mmol, 1.1 equiv) was added and the resulting suspension stirred at rt for 2 hours. Cinnamyl bromide (314 mg, 1.59 mmol, 1.0 equiv) was added and the suspension stirred for another 18 hours. The reaction was quenched by addition of saturated NH_4Cl solution. H_2O and EtOAc were added until the formed precipitate was fully dissolved. The aqueous layer was extracted twice with EtOAc. The combined organic layers were washed twice with H_2O

and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo. The obtained yellow oil was purified by column chromatography (*n*-hexane/EtOAc 1:1; R_f = 0.19) yielding a slightly yellowish highly viscous oil (66 mg, 0.242 mmol, 15%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 6.69 (dt, *J* = 15.8, 1.3 Hz, 1H), 6.12 (dt, *J* = 15.8, 6.8 Hz, 1H), 4.37 (dd, *J* = 6.8, 1.3 Hz, 2H), 1.86 – 1.63 (m, 4H), 0.83 (t, *J* = 7.4 Hz, 6H).

4.6.23 Ethyl 1-cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**42**)[119]



$C_{25}H_{24}N_2O_2$

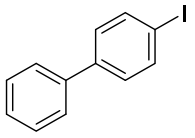
[384.48]

Ethyl 2-(diphenylmethylene)hydrazine-1-carboxylate (501 mg, 1.87 mmol, 1.0 equiv) was dissolved in a mixture of dry THF (8 mL) and dry DMF (0.6 mL). A 60% dispersion of NaH in mineral oil (74.0 mg, 1.85 mmol, 1.0 equiv) was added and the resulting suspension stirred for 30 minutes. Cinnamyl bromide (367 mg, 1.86 mmol, 1.0 equiv) was added and the reaction monitored by TLC. After 16 hours the reaction was quenched with saturated NH_4Cl solution. EtOAc and H_2O were added until the formed precipitate was fully dissolved. The aqueous layer was extracted twice with EtOAc. The combined organic layers were washed twice with H_2O and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 5:1, R_f = 0.25) yielded a slightly yellowish oil (660 mg, 1.72 mmol, 92%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 – 7.56 (m, 2H), 7.50 – 7.17 (m, 13H), 6.47 (dt, *J* = 15.9, 1.3 Hz, 1H), 6.14 (dt, *J* = 15.9, 6.6 Hz, 1H), 4.23 (dd, *J* = 6.6, 1.3 Hz, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 1.19 (t, *J* = 7.1 Hz, 3H).

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3512, 3058, 3026, 2979, 1698 (s, C=O), 1562, 1492, 1377, 1222, 1112, 1030, 967, 749, 695 (s).

4.6.24 4-Iodobiphenyl (**43**)



$C_{12}H_9I$

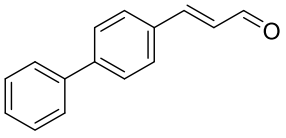
[280.11]

4-Bromobiphenyl (7.93 g, 34.0 mmol) was dissolved in dry THF (80 mL) and cooled to -78 °C. *n*-BuLi 1.6M in *n*-hexane (20.0 mL, 32.0 mmol) was added dropwise and the solution allowed to warm to 0 °C. The solution was stirred for 4 hours before a solution of iodine (8.12 g, 32.0 mmol) in dry THF (15 mL) was added dropwise. Since TLC showed no transformation the reaction was stirred at rt overnight and then quenched by addition of a 10 wt% $NaHSO_3$ solution (200 mL). Upon discoloration the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layers were washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo to afford a brown oil. This oil was purified by column chromatography (*n*-hexane, R_f = 0.71) resulting in a white solid (2.30 g, 8.21 mmol, 24%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 – 7.83 (m, 9H).

MS-ESI (*m/z*) 280 (100%, $[M]^{\bullet+}$); 193 (24%); 152 (52%).

4.6.25 (*E*)-3-([1,1'-Biphenyl]-4-yl)acrylaldehyde (**45**)



$C_{15}H_{12}O$

[208.26]

Version 1:[131]

4-Bromophenyl (5.01 g, 21.5 mmol, 1.0 equiv), $NaHCO_3$ (4.53, 53.9 mmol, 2.5 equiv) and *n*-Bu_4NCl (6.98 g, 25.1 mmol, 1.2 equiv) were dissolved in dry, degassed DMF (60 mL). Acrolein (2.90 mL, 43.3 mmol, 2.0 equiv) and $Pd(OAc)_2$ (1.35 g, 6.02 mmol, 28 mol%) were added. The reaction was monitored by TLC and showed no conversion after 24 hours. After 40 hours PPh_3 (6.32 g, 24.1 mmol, 1.1 equiv) was added. After another 3 hours TLC still showed no conversion. The reaction mixture was heated to 50 °C bath temp. for 5 hours and stirred at rt overnight. Since TLC still showed no conversion the reaction mixture was poured into H_2O resulting in precipitation. This suspension was extracted with *n*-hexane and toluene. Combined organic layers were washed with H_2O, dried over $MgSO_4$ and the solvent removed in vacuo. After plug filtration a brown solid (8.59 g) was obtained. The ^1H NMR spectrum matched that of 4-bromophenyl.

4-Iodophenyl (282 mg, 1.01 mmol, 1.0 equiv), $NaHCO_3$ (226 mg, 2.69 mmol, 2.7 equiv) and *n*-Bu_4NCl (334 mg, 1.20 mmol, 1.2 equiv) were dissolved in dry, degassed DMF (5 mL). Acrolein (0.15 mL, 2.2 mmol, 2.2 equiv) and $Pd(OAc)_2$ (63.0 g, 0.281 mmol, 28 mol%) were added. The reaction was monitored by TLC. After 22 hours additional acrolein (0.20 mL, 2.99 mmol, 3.0 equiv) was added. Since TLC remained unchanged after another 3.5 hours additional $NaHCO_3$ (210 mg, 2.50 mmol, 2.5 equiv), *n*-Bu_4NCl (336 mg, 1.21 mmol, 1.2 equiv) and $Pd(OAc)_2$ (63.0 g, 0.281 mmol, 28 mol%) were added. After another 20 hours TLC still remained unchanged. The reaction mixture was poured into H_2O (35 mL) resulting in precipitation. The resulting brown solid was suction-filtered and washed with H_2O. Although TLC showed partial conversion, the ^1H NMR spectrum of the raw material accounted for at most marginal product formation.

Version 2:[137]

4-Iodobiphenyl (100 mg, 0.357 mmol, 1.0 equiv) and K_2CO_3 (74.3 mg, 0.538 mmol, 1.5 equiv) were dissolved in dry, degassed DMF (2.0 mL) in a microwave tube. Acrolein diethyl acetal (0.16 mL, 1.0 mmol, 2.9 equiv) and $Pd(OAc)_2$ (5.0 mg, 0.022 mmol, 6.2 mol%) were added and the tube subjected to microwave irradiation in two cycles (20 minutes, 90 °C, approx. 25 W). Since TLC showed only partial conversion after the first cycle and did not change after the second cycle the tube was conventionally heated to 105 °C bath temp. for 18 hours. TLC remained unchanged and the reaction solution was poured into 1M HCl and stirred at rt for 15 minutes resulting in precipitation of a white solid which was resolved after 15 additional minutes of stirring. The aqueous solution was extracted with Et_2O three times and the combined organic layers were dried over $MgSO_4$ and the solvent removed in

vacuo to afford a brown oil (69.5 mg). The ^{1}H NMR of the raw material showed improvement in product formation compared to version 1 but still did not show nearly quantitative transformation.

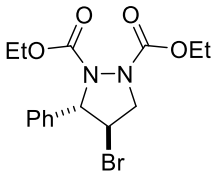
Version 3:[135]

4-Bromobiphenyl (119 mg, 0.510 mmol, 1.0 equiv), K_2CO_3 (106 mg, 0.767 mmol, 1.5 equiv), KCl (37.3 mg, 0.500 mmol, 1.0 equiv.) and *n*-Bu_4NOAc (~300 mg, 0.995 mmol, 2.0 equiv) were dissolved in dry, degassed DMF (2.0 mL). Acrolein diethyl acetal (0.23 mL, 1.5 mmol, 2.9 equiv) and $Pd(OAc)_2$ (12.0 mg, 0.0535 mmol, 10 mol%) were added and the resulting dispersion heated to 90 °C bath temp. The reaction was monitored by TLC and after 23 hours allowed to cool to rt. 2M HCl (~4 mL) was added and the resulting mixture stirred for 15 minutes. The aqueous dispersion was extracted with Et_2O and the organic layer washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a slightly brownish solid (98.0 mg, 0.471 mmol, 61%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.73 (d, *J* = 7.7 Hz, 1H), 7.71 – 7.57 (m, 6H), 7.52 (d, *J* = 15.9 Hz, 2H), 7.49 – 7.35 (m, 3H), 6.77 (dd, *J* = 15.9, 7.7 Hz, 1H).

iii. Pyrazolidines

4.6.26 *trans*-Diethyl 4-bromo-3-phenylpyrazolidine-1,2-dicarboxylate (**48**)



$C_{15}H_{19}BrN_2O_4$

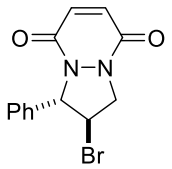
[371.21]

Diethyl 1-cinnamylhydrazine-1,2-dicarboxylate (100 mg, 0.342 mmol, 1.0 equiv) was dissolved in dry acetone (7 mL). *N*-Bromoacetamide (52.1 mg, 0.378 mmol, 1.1 equiv) was added under exclusion of light. The reaction was monitored by TLC and after 22 hours the reaction was quenched with 10 wt% $Na_2S_2O_3$ solution. The aqueous phase was extracted with CH_2Cl_2 three times. The combined organic layers were washed with brine, dried over

Na_2SO_4 and the solvent removed in vacuo to afford a yellow oil. The ^1H NMR spectra of the raw material showed the successful product formation.

^1H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 5H), 5.53 (d, *J* = 3.5 Hz, 1H), 4.48 – 4.40 (m, 1H), 4.32 – 4.17 (m, 5H), 3.76 (s, 1H), 1.29 (td, *J* = 7.4, 2.7 Hz, 6H).

4.6.27 *trans*-2-Bromo-1-phenyl-2,3-dihydro-1*H*-pyrazolo[1,2-a]pyridazine-5,8-dione (**49**)



$C_{13}H_{11}BrN_2O_2$

[307.15]

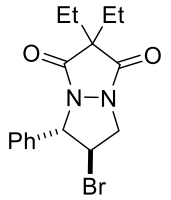
Version 1:[90]

6-(Cinnamyloxy)pyridazine-3(2*H*)-one (50.0 mg, 0.219 mmol, 1.0 equiv) was dissolved in dry acetone (7 mL). *N*-Bromoacetamide (36.0 mg, 0.261 mmol, 1.2 equiv) was added under exclusion of light. After 4 hours the reaction was quenched with 10 wt% $Na_2S_2O_3$ solution. The aqueous phase was extracted with CH_2Cl_2 three times. The combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. The ^1H NMR of this raw material showed mostly signals of the substrate.

Version 2:

Br_2 (0.25 mL, 4.88 mmol) was dissolved in dry acetonitrile (102 mL) under exclusion of light and 7 mL of this 54 mM solution were added to 6-(cinnamyloxy)pyridazine-3(2*H*)-one (70.0 mg, 0.307 mmol, 1.0 equiv) under exclusion of light. The resulting solution was stirred at rt and the reaction monitored by TLC. After two days the reaction was quenched with 10 wt% $Na_2S_2O_3$ solution. The aqueous phase was extracted with CH_2Cl_2 three times. The combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. The ^1H NMR of this raw material did not show signals of the desired compound.

4.6.28 *trans*-6-Bromo-2,2-diethyl-5-phenyldihydro-1*H*,5*H*-pyrazolo[1,2-a]pyrazole-1,3(2*H*)-dione (**50**)

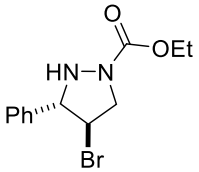


$C_{16}H_{19}BrN_2O_2$

[351.24]

1-Cinnamyl-4,4-diethylpyrazolidine-3,5-dione (66.0 mg, 0.242 mmol, 1.0 equiv) was dissolved in dry acetone (5 mL). *N*-Bromoacetamide (36.8 mg, 0.267 mmol, 1.1 equiv) was added under exclusion of light. The reaction was monitored by TLC and after 20 hours additional *N*-bromoacetamide (42.0 mg, 0.304 mmol, 1.3 equiv) was added. After another 4.5 hours the reaction was quenched with 10 wt% $Na_2S_2O_3$ solution. The aqueous phase was extracted with CH_2Cl_2 four times. The combined organic layers were washed with H_2O and brine, dried over Na_2SO_4 and the solvent was removed in vacuo to afford a yellow oil (80.2 mg). Purification by column chromatography did not afford the desired product in pure form.

4.6.29 *trans*-Ethyl 4-bromo-3-phenylpyrazolidine-1-carboxylate (**52**)



$C_{12}H_{15}BrN_2O_2$

[299.17]

Version 1:

Ethyl 1-cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (286 mg, 0.744 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (15 mL). Under exclusion of light $Br^+(coll)_2PF_6^-$

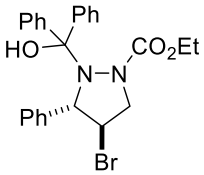
(383 mg, 0.818 mmol, 1.1 equiv) was added. The reaction was monitored by TLC and after 3.5 hours quenched with 10 wt% $Na_2S_2O_5$ solution. The aqueous phase was extracted with CH_2Cl_2 twice and the combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (CH_2Cl_2 to *n*-hexane/EtOAc 4:1, R_f = 0.26) afforded a slightly yellow oil (74.0 mg, 0.247 mmol, 33%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.27 (m, 5H), 4.65 (dt, *J* = 5.5, 2.8 Hz, 1H), 4.57 (d, *J* = 2.7 Hz, 1H), 4.34 – 4.16 (m, 2H), 3.90 (dd, *J* = 12.6, 5.3 Hz, 1H), 3.84 (dd, *J* = 12.6, 2.9 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.92, 136.46, 129.05, 128.40, 126.32, 70.54, 62.19, 54.82, 52.65, 14.88.

MS-ESI (*m/z*) 299 (93%, $[M + H]^+$); 301 (100%).

Hemiaminal by-product (**53**):



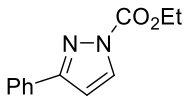
$C_{25}H_{25}BrN_2O_3$

[481.39]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 – 7.54 (m, 2H), 7.52 – 7.45 (m, 1H), 7.44 – 7.27 (m, 12H), 4.97 (d, *J* = 6.7 Hz, 1H), 4.66 – 4.52 (m, 1H), 4.36 (dd, *J* = 15.3, 5.7 Hz, 1H), 3.95 (qq, *J* = 7.5, 3.6 Hz, 2H), 3.81 (dd, *J* = 15.3, 5.3 Hz, 1H), 1.09 (t, *J* = 7.1 Hz, 3H).

MS-ESI (*m/z*) 481 (95%, $[M + H]^+$); 483 (100%).

Pyrazole by-product (**54**):



$C_{12}H_{12}N_2O_2$

[216.24]

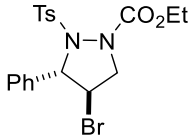
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, *J* = 2.9 Hz, 1H), 7.97 – 7.83 (m, 2H), 7.50 – 7.33 (m, 4H), 6.75 (d, *J* = 2.9 Hz, 1H), 4.56 (q, *J* = 7.1 Hz, 2H), 1.49 (t, *J* = 7.1 Hz, 3H).

MS-ESI (*m/z*) 217 (100%, $[M + H]^+$).

Version 2:

Ethyl 1-cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (180 mg, 0.468 mmol, 1.0 equiv) was dissolved in dry acetone (10 mL). Under exclusion of light NBA (71.5 mg, 0.518 mmol, 1.1 equiv) was added. The reaction was monitored by TLC and after 19 hours quenched with 10 wt% $Na_2S_2O_5$ solution. The aqueous phase was extracted with CH_2Cl_2 twice and the combined organic layers were washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo. TLC as well as ^{1}H NMR of the raw material showed incomplete transformation of the substrate.

4.6.30 *trans*-Ethyl 4-bromo-3-phenyl-2-tosylpyrazolidine-1-carboxylate (**55**)



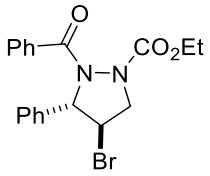
$C_{19}H_{21}BrN_2O_4S$

[453.35]

Ethyl 1-cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (209 mg, 0.544 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (15 mL). Under exclusion of light $Br^+(coll)_2PF_6^-$ (281 mg, 0.601 mmol, 1.1 equiv) was added. The reaction was monitored by TLC and after

3.5 hours quenched with 10 wt% $Na_2S_2O_5$ solution. The aqueous phase was extracted with CH_2Cl_2 three times and the combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. This raw material was dissolved in dry CH_2Cl_2 (15 mL) and the solution cooled with an ice bath. NEt_3 (0.10 mL, 0.721 mmol, 1.3 equiv) and tosyl chloride (116 mg, 0.608 mmol, 1.1 equiv) were added, the ice bath removed, and the reaction monitored by TLC. After 5 days TLC showed no transformation and the reaction was quenched with saturated $NaHCO_3$ solution. The aqueous phase was extracted with CH_2Cl_2 twice and the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown oil. Since TLC did not show any conversion purification of the raw material was not attempted.

4.6.31 *trans*-Ethyl 2-benzoyl-4-bromo-3-phenylpyrazolidine-1-carboxylate (**56**)

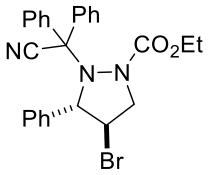


$C_{19}H_{19}BrN_2O_3$

[403.28]

Ethyl 1-cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (130 mg, 0.338 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (7 mL) and 2,4,6-collidine (0.050 mL, 0.38 mmol, 1.1 equiv.) was added. Under exclusion of light $Br^+(coll)_2PF_6^-$ (176 mg, 0.377 mmol, 1.1 equiv) was added and the reaction monitored by TLC. After 2 hours the reaction was quenched with 10 wt% $Na_2S_2O_5$ solution. The aqueous phase was extracted with CH_2Cl_2 three times and the combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. This raw material was dissolved in dry CH_2Cl_2 (7 mL). NEt_3 (0.080 mL, 0.57 mmol, 1.7 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.8 equiv) were added. The reaction was monitored by TLC, showing no transformation. After 24 hours the reaction was quenched with conc. NH_3 and H_2O was added. The aqueous phase was extracted with CH_2Cl_2 three times and the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown oil. Since the ^1H NMR spectrum of the raw material did not show conversion into the desired product the raw material was not purified.

4.6.32 *trans*-Ethyl 4-bromo-2-(cyanodiphenylmethyl)-3-phenyl-pyrazolidine-1-carboxylate (**57**)

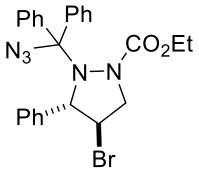


$C_{26}H_{24}BrN_3O_2$

[490.40]

Ethyl 1-cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**43**) (100 mg, 0.260 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (10 mL). Under exclusion of light $Br^+(coll)_2PF_6^-$ (135 mg, 0.288 mmol, 1.1 equiv) was added. The reaction was monitored by TLC and quenched with a 12M solution of NaCN in H_2O (0.50 mL, 6.0 mmol, 23 equiv). After 3.5 days H_2O was added. The aqueous phase was extracted with CH_2Cl_2 three times and the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown oil. Attempted purification did not afford the desired compound in pure form.

4.6.33 *trans*-Ethyl 4-bromo-2-(azidodiphenylmethyl)-3-phenyl-pyrazolidine-1-carboxylate (**58**)



$C_{25}H_{24}BrN_5O_2$

[506.40]

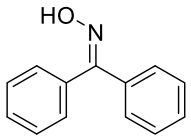
Ethyl 1-cinnamyl-2-(diphenylmethylene)hydrazine-1-carboxylate (**43**) (100 mg, 0.260 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (10 mL). Under exclusion of light $Br^+(coll)_2PF_6^-$ (135 mg, 0.288 mmol, 1.1 equiv) was added. The reaction was monitored by TLC and quenched by addition of *n*-Bu_4NN_3 (83.0 mg, 0.292 mmol, 1.1 equiv). After 3.5 days H_2O was

added. The aqueous phase was extracted with CH_2Cl_2 three times and the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. Attempted purification did not afford the desired compound in pure form.

III. Isoxazolidine Syntheses

i. Oximes

4.6.34 Diphenylmethanone oxime (**60**)



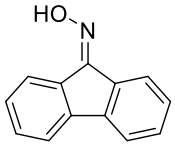
$C_{13}H_{11}NO$

[197.24]

Benzophenone (1.02 g, 5.60 mmol, 1.0 equiv) was dissolved in MeOH (20 mL) and hydroxylamine HCl (877 mg, 12.6 mmol, 2.3 equiv) and NaOAc (1.13 g, 13.7 mmol, 2.5 equiv) were added. The mixture was refluxed and the reaction monitored by TLC. After 25 hours the reaction was allowed to cool to rt and H_2O was added. The resulting precipitate was suction-filtered, washed with H_2O and dried in a desiccator to afford a white solid (1.04 g, 5.27 mmol, 94%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.75 (br s, 1H), 7.54 – 7.40 (m, 7H), 7.39 – 7.29 (m, 3H).

4.6.35 9*H*-Fluoren-9-one oxime (**62**)



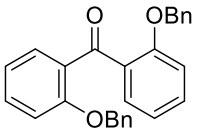
$C_{13}H_9NO$

[195.22]

9-Fluorenone (1.00 g, 5.55 mmol, 1.0 equiv) was dissolved in MeOH (20 mL) and hydroxylamine HCl (889 mg, 12.8 mmol, 2.3 equiv) and NaOAc (1.15 g, 14.0 mmol, 2.5 equiv) were added. The mixture was refluxed and the reaction monitored by TLC. After 24 hours the reaction was allowed to cool to rt and H_2O was added. The resulting precipitate was suction-filtered, washed with H_2O and dried in a desiccator to afford a yellow solid (1.05 g, 5.38 mmol, 97%).

^{1}H NMR (300 MHz, DMSO-*d*^{6}) δ 12.53 (s, 1H), 8.34 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.86 (ddt, *J* = 12.9, 7.6, 0.9 Hz, 2H), 7.70 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.50 (td, *J* = 7.5, 1.2 Hz, 1H), 7.47 – 7.29 (m, 3H).

4.6.36 2,2'-Bis(benzoyloxy)benzophenone (**65**)



$C_{27}H_{22}O_3$

[394.47]

Version 1:[141]

2,2'-Dihydroxybenzophenone (1.00 g, 4.67 mmol, 1.0 equiv) was dissolved in dry MeOH (15 mL). KOH (785 mg, 14.0 mmol, 3.0 equiv) and after 80 minutes benzyl bromide (1.20 mL, 10.1 mmol, 2.2 equiv) were added and the solution refluxed and the reaction monitored by TLC. After 21 hours additional benzyl bromide (1.10 mL, 9.25 mmol, 2.0 equiv) and after another 2.5 hours Cs_2CO_3 (3.00 g, 9.21 mmol, 2.0 equiv) were added. After another 22 hours additional benzyl bromide (2.20 mL, 18.5 mmol, 4.0 equiv) was added again. After another two days the solvent was removed in vacuo and the residue dissolved in EtOAc and H_2O. The aqueous phase was extracted with EtOAc and the combined organic layers washed with saturated NH_4Cl solution, H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.26) yielded a white solid (100 mg, 0.254 mmol, 5.4%).

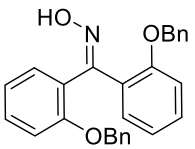
Version 2:

2,2'-Dihydroxybenzophenone (250 mg, 1.17 mmol, 1.0 equiv) was dissolved in dry DMSO (5.0 mL). Benzyl bromide (0.30 mL, 2.5 mmol, 2.1 equiv) and a 60% dispersion of NaH in mineral oil (95.0 mg, 2.38 mmol, 2.0 equiv) were added resulting in an orange suspension. The reaction was monitored by TLC and after 24 hours additional benzyl bromide (0.30 mL, 2.5 mmol, 2.1 equiv) as well as a 60% dispersion of NaH in mineral oil (100 mg, 2.50 mmol, 2.1 equiv) were added. After another 4 days the solution was with H_2O and CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 and the combined organic layers washed three times with H_2O and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.26) yielded a white solid (353 mg, 0.895 mmol, 76%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.6, 1.8 Hz, 2H), 7.38 (ddd, *J* = 8.3, 7.4, 1.8 Hz, 2H), 7.23 – 7.11 (m, 6H), 7.02 (td, *J* = 7.5, 1.0 Hz, 2H), 6.94 – 6.83 (m, 6H), 4.88 (s, 4H).

2,2'-Dihydroxybenzophenone (1.00 g, 4.67 mmol, 1.0 equiv) was dissolved in dry DMSO (10 mL). Benzyl bromide (1.70 mL, 14.3 mmol, 3.1 equiv) and a 60% dispersion of NaH in mineral oil (560 mg, 14.0 mmol, 3.0 equiv) were added resulting in an orange suspension. The reaction was cooled with an ice bath and additional dry DMSO (10 mL) was added. The reaction was monitored by TLC and after 22 hours the solution was diluted with H_2O and CH_2Cl_2. The aqueous phase was extracted twice with CH_2Cl_2 and the combined organic layers were washed three times with H_2O and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. Purification by column chromatography (*n*-hexane/EtOAc 9:1 to 8:2, R_f = 0.26) yielded a white solid (1.69 g, 4.28 mmol, 92%).

4.6.37 Bis(2-(benzyloxy)phenyl)methanone oxime (**66**)[139]



$C_{27}H_{23}NO_3$

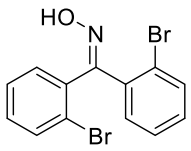
[409.49]

2,2'-Bis(benzoyloxy)benzophenone (350 mg, 0.887 mmol, 1.0 equiv) was dissolved in hot MeOH (20 mL). Hydroxylamine HCl (148 mg, 2.13 mmol, 2.4 equiv) and NaOAc (184 mg, 2.24 mmol, 2.5 equiv) were added and the resulting suspension refluxed. The reaction was monitored by TLC and after 22 hours additional hydroxylamine HCl (146 mg, 2.10 mmol, 2.4 equiv) and NaOAc (183 mg, 2.23 mmol, 2.5 equiv) were added. The reaction was refluxed for another 27 hours before H_2O was added. CH_2Cl_2 was added, the aqueous phase extracted twice with CH_2Cl_2. The combined organic layers were washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a slightly reddish solid (363 mg, 0.886 mmol, 99%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (br s, 1H), 7.45 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.33 – 7.19 (m, 9H), 7.14 (dd, *J* = 6.8, 2.9 Hz, 2H), 7.05 – 6.99 (m, 2H), 6.96 – 6.84 (m, 4H), 4.84 (d, *J* = 2.2 Hz, 4H).

2,2'-Bis(benzoyloxy)benzophenone (1.66 g, 4.21 mmol, 1.0 equiv) was dispersed in MeOH (20 mL). Hydroxylamine HCl (673 mg, 9.68 mmol, 2.3 equiv) and NaOAc (868 mg, 10.6 mmol, 2.5 equiv) were added and the resulting suspension refluxed. The reaction was monitored by TLC and after 23 hours additional hydroxylamine HCl (680 mg, 9.79 mmol, 2.3 equiv) and NaOAc (870 mg, 10.6 mmol, 2.5 equiv) were added. The reaction was refluxed for another 24 hours before H_2O was added. The resulting precipitate was suction-filtered, washed with H_2O and dried in a desiccator to afford a white solid (1.63 g, 3.98 mmol, 95%).

4.6.38 Bis(2-bromophenyl)methanone oxime (**68**)



$C_{13}H_9Br_2NO$

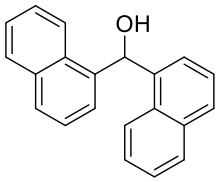
[355.03]

2,2'-Dibromobenzophenone (500 mg, 1.47 mmol, 1.0 equiv) was dispersed in MeOH (10 mL). Hydroxylamine HCl (237 mg, 3.41 mmol, 2.3 equiv) and NaOAc (303 mg,

3.69 mmol, 2.5 equiv) were added and the resulting suspension refluxed. The reaction was monitored by TLC and after 24 hours additional hydroxylamine HCl (250 mg, 3.60 mmol, 2.4 equiv) and NaOAc (350 mg, 4.27 mmol, 2.9 equiv) were added, and again after another 26 hours additional hydroxylamine HCl (470 mg, 6.76 mmol, 4.6 equiv), NaOAc (604 mg, 7.36 mmol, 5.0 equiv) and additional MeOH (5 mL) were added. The reaction was refluxed for another 21 hours before H_2O was added and the dispersion cooled with an ice bath. The resulting precipitate could not be suction-filtered. The solution was decanted and the precipitate washed with H_2O. It was dissolved in acetone, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 9:1 to 8:2, R_f = 0.19, 0.34) yielded a yellow solid (155 mg, 0.437 mmol, 30%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (br s, 1H), 7.63 (td, *J* = 7.6, 1.1 Hz, 2H), 7.44 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.31 – 7.17 (m, 3H).

4.6.39 Bis(1-naphthyl)methanol (**71**)[143, 161]



$C_{21}H_{16}O$

[284.36]

Version 1:

Mg turnings (860 mg, 35.4 mmol, 4.0 equiv) were activated and dispersed in dry THF (2 mL). The reaction was started by addition of 1,2-dibromoethane (0.10 mL, 1.2 mmol, 13 mol%) before a solution of 1-bromonaphthalene (2.50 mL, 17.9 mmol, 2.0 equiv) in THF (8 mL) was added over a period of 10 minutes. The dropping funnel was rinsed with dry THF (1 mL) resulting in precipitation of a white solid. After 2 hours a solution of methyl formate (0.54 mL, 8.8 mmol, 1.0 equiv) in THF (2 mL) was added over a period of 10 minutes resulting in warming of the reaction mixture and solvation of the precipitate. The reaction was monitored by TLC and after 24 hours the solution poured onto 2M HCl/ice. The aqueous phase was extracted three times with Et_2O and the combined organic layers washed with brine, dried

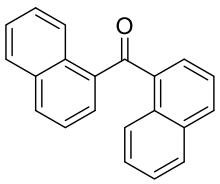
over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography was not successful due to a broad variety of reaction products.

Version 2:

Mg turnings (584 mg, 24.0 mmol, 2.4 equiv) were activated and dispersed in dry THF (10 mL). The reaction was started by addition of 1,2-dibromoethane (0.05 mL, 0.6 mmol, 2.5 mol%) before a solution of 1-bromonaphthalene (2.80 mL, 20.0 mmol, 2.0 equiv) in THF (10 mL) was added over a period of 10 minutes. The resulting green solution was refluxed for 4 hours before a solution of methyl formate (0.61 mL, 10 mmol, 1.0 equiv) in THF (2.5 mL) was added over a period of 10 minutes. The reaction was monitored by TLC and refluxed for another 2 hours before the solvent was removed in vacuo. The residue was dissolved in Et_2O and 1M HCl. The organic phase was washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. The solid was recrystallized from *n*-hexane, the resulting white precipitate suction-filtered and dried in a desiccator yielding a white solid (2.17 g, 7.63 mmol, 76%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 – 8.01 (m, 2H), 7.96 – 7.89 (m, 2H), 7.84 (dt, *J* = 7.9, 1.1 Hz, 2H), 7.56 – 7.37 (m, 8H), 7.30 (d, *J* = 4.9 Hz, 1H), 2.46 (d, *J* = 5.0 Hz, 1H).

4.6.40 Di(naphthalen-1-yl)methanone (**72**)[144]



$C_{21}H_{14}O$

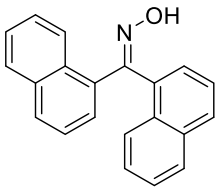
[282.34]

Bis(1-naphthyl)methanol (2.17 g, 7.63 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (15 mL) and MnO_4 (6.65 g, 76.5 mmol, 10 equiv) was added. The reaction was monitored by TLC and after 22 hours additional CH_2Cl_2 (10 mL) was added. After another 20 hours the dispersion was filtered through a celite plug, washed with CH_2Cl_2 and the solvent removed in vacuo to

afford a highly viscous yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.4) yielded a slightly yellow oil (1.34 g, 4.75 mmol, 62%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 – 8.50 (m, 2H), 8.03 (dt, *J* = 8.2, 1.1 Hz, 2H), 8.00 – 7.91 (m, 2H), 7.64 – 7.53 (m, 6H), 7.44 (dd, *J* = 8.2, 7.2 Hz, 2H).

4.6.41 Di(naphthalen-1-yl)methanone oxime (**73**)



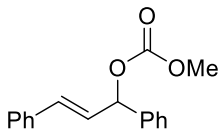
$C_{21}H_{15}NO$

[297.36]

Di(naphthalen-1-yl)methanone (1.34 g, 4.75 mmol, 1.0 equiv) was dissolved in MeOH (17 mL) and hydroxylamine HCl (760 mg, 10.9 mmol, 2.3 equiv) and NaOAc (974 mg, 11.9 mmol, 2.5 equiv) were added. The mixture was refluxed and the reaction monitored by TLC. After 22 hours additional hydroxylamine HCl (759 mg, 10.9 mmol, 2.3 equiv) and NaOAc (970 mg, 11.8 mmol, 2.5 equiv) were added. After another 24 hours the reaction was allowed to cool to rt and H_2O was added. The resulting precipitate could not be suction-filtered. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent was removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 8:2, R_f = 0.29) yielded a slightly yellow solid. The ^{1}H NMR spectrum did not correspond to the desired product.

ii. Allyl Carbonates and Allyl Acetates

4.6.42 (*E*)-1,3-Diphenylallyl methyl carbonate (**77**)[147]



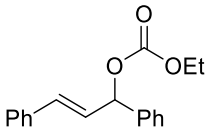
$C_{17}H_{16}O_3$

[268.31]

(*E*)-1,3-Diphenylprop-2-en-1-ol (211 mg, 1.00 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (10 mL) and the solution cooled with an ice bath. Pyridine (0.35 mL, 4.3 mmol, 4.3 equiv) and methyl chloroformate (0.16 mL, 2.1 mmol, 2.1 equiv) were added and the ice bath removed. The reaction was monitored by TLC. After 4 days TLC still showed insufficient transformation.

In a second attempt additional methyl chloroformate (0.32 mL, 4.2 mmol, 4.2 equiv) was added after 2.5 hours and again additional methyl chloroformate (0.16 mL, 2.1 mmol, 2.1 equiv) was added after another 2 hours. The solution was cooled with an ice bath during each addition. The result remained unchanged.

4.6.43 (*E*)-1,3-Diphenylallyl ethyl carbonate (**79**)[147]



$C_{18}H_{18}O_3$

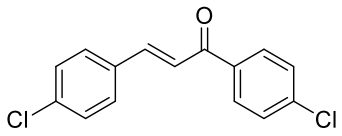
[282.34]

(*E*)-1,3-Diphenylprop-2-en-1-ol (1.07 g, 5.09 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (20 mL) and the solution was cooled with an ice bath. Pyridine (1.65 mL, 20.3 mmol, 4.0 equiv) and ethyl chloroformate (1.50 mL, 15.7 mmol, 3.1 equiv) were added and the ice bath removed. The reaction was monitored by TLC and after 3 hours saturated $NaHCO_3$ solution was added. The aqueous phase was extracted three times with CH_2Cl_2 and the

combined organic layers were washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a slightly yellow oil (1.30 g, 4.60 mmol, 90%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 – 7.21 (m, 10H), 6.70 (d, *J* = 15.7 Hz, 1H), 6.38 (dd, *J* = 15.7, 6.9 Hz, 1H), 6.27 (dd, *J* = 6.9, 0.9 Hz, 1H), 4.22 (qd, *J* = 7.1, 2.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).

4.6.44 (*E*)-1,3-Bis(4-chlorophenyl)prop-2-en-1-one (**82**)[148, 162]



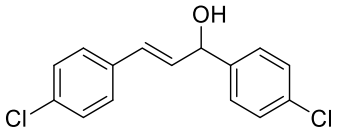
$C_{15}H_{10}Cl_2O$

[277.14]

4-Chloroacetophenon (1.00 mL, 7.70 mmol, 1.0 equiv) was dissolved in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.4 equiv) was added. The resulting solution was cooled with an ice bath, 4-chlorobenzaldehyde (1.08 g, 7.70 mmol, 1.0 equiv) was added and the ice bath removed. After 24 hours the formed solid was suction-filtered and washed with water until the filtrate reached a neutral pH. The resulting slightly yellow solid was dried in a desiccator to afford a white solid (2.07 g, 7.47 mmol, 97%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 – 7.92 (m, 2H), 7.76 (d, *J* = 15.7 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.52 – 7.42 (m, 2H), 7.45 (d, *J* = 15.7 Hz, 1H), 7.42 – 7.37 (m, 2H).

4.6.45 (*E*)-1,3-Bis(4-chlorophenyl)prop-2-en-1-ol (**83**)



$C_{15}H_{12}Cl_2O$

[279.16]

Version 1:[162]

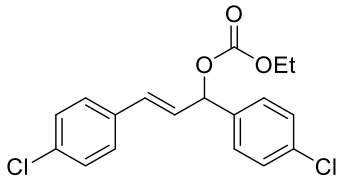
(*E*)-1,3-Bis(4-chlorophenyl)prop-2-en-1-one (2.00 g, 7.22 mmol, 1.0 equiv) was dispersed in dry MeOH (90 mL) and heated to 50 °C bath temp. Since the chalcone did not dissolve the dispersion was refluxed and additional MeOH (30 mL) was added. Still no homogeneous solution was obtained. The dispersion was cooled to rt and $NaBH_4$ (264 mg, 6.98 mmol, 0.96 equiv) was added. The reaction was monitored by TLC. After 2 hours a slightly opaque solution was obtained and additional $NaBH_4$ (20.0 mg, 0.529 mmol, 7.3 mol%) was added. After another hour MeOH was removed in vacuo and the residue dissolved in EtOAc. The resulting solution was washed twice with H_2O, once with 1M HCl and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 4:1, R_f = 0.36) afforded a colorless oil (385 mg, 1.38 mmol, 19%).

Version 2:[148]

(*E*)-1,3-Bis(4-chlorophenyl)prop-2-en-1-one (280 mg, 1.01 mmol, 1.0 equiv) was dispersed in dry MeOH (10 mL) and $NaBH_4$ (46.0 mg, 1.22 mmol, 1.2 equiv) was added. The reaction was monitored by TLC and after 2 hours additional $NaBH_4$ (33.5 mg, 0.886 mmol, 0.88 equiv) was added. After another 4 hours MeOH was removed in vacuo and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a slightly yellowish oil (283 mg, 1.01 mmol, 99%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 8H), 6.62 (dd, *J* = 15.9, 1.2 Hz, 1H), 6.30 (dd, *J* = 15.8, 6.4 Hz, 1H), 5.36 (dd, *J* = 6.4, 2.4 Hz, 1H), 2.09 (d, *J* = 3.0 Hz, 1H).

4.6.46 (*E*)-1,3-Bis(4-chlorophenyl)allyl ethyl carbonate (**84**)[147]



$C_{18}H_{16}Cl_2O_3$

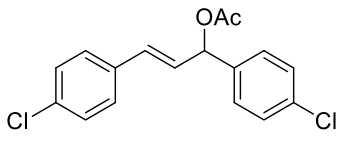
[351.22]

(*E*)-1,3-Bis(4-chlorophenyl)prop-2-en-1-ol (258 mg, 0.924 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (5.0 mL) and the solution cooled with an ice bath. Pyridine (0.30 mL, 3.7 mmol, 4.0 equiv) and ethyl chloroformate (0.30 mL, 3.1 mmol, 3.4 equiv) were added and the ice bath removed. The reaction was monitored by TLC and after 3 hours saturated $NaHCO_3$ solution was added. The aqueous phase was extracted three times with CH_2Cl_2 and the combined organic layers washed twice with H_2O and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a slightly yellow oil (278 mg, 0.792 mmol, 86%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 8H), 6.61 (dd, *J* = 15.6, 0.9 Hz, 1H), 6.29 (dd, *J* = 15.6, 6.7 Hz, 1H), 6.20 (dd, *J* = 6.7, 0.9 Hz, 1H), 4.21 (qd, *J* = 7.1, 1.8 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3033 (w), 2983, 1764 (s, C=O), 1595, 1491, 1371, 1256 (s), 1091, 1013, 965, 830, 789, 508.

4.6.47 (*E*)-1,3-Bis(4-chlorophenyl)allyl acetate (**86**)[149]



$C_{17}H_{14}Cl_2O_2$

[321.20]

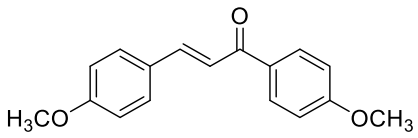
(*E*)-1,3-Bis(4-chlorophenyl)prop-2-en-1-ol (1.51 g, 5.41 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (12 mL). The solution was cooled with an ice bath and Et_3N (1.5 mL, 11 mmol, 2.0 equiv) and acetic anhydride (1.0 mL, 11 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 5 days saturated $NaHCO_3$ solution was added. The organic phase was washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo affording a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.20) yielded a colorless oil (1.12 g, 3.49, 64%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.22 (m, 8H), 6.57 (dd, *J* = 15.8, 1.0 Hz, 1H), 6.39 (dd, *J* = 6.6, 1.1 Hz, 1H), 6.28 (dd, *J* = 15.8, 6.6 Hz, 1H), 2.14 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.99, 137.64, 134.58, 134.24, 134.02, 131.77, 128.99, 128.92, 128.56, 128.03, 127.79, 75.37, 21.39.

IR (thin film) $\tilde{\nu}_{max}$ cm^{-1} 3033 (w), 2934 (w), 1739 (s, C=O), 1491, 1406.82 88.5175, 1370, 1231 (s), 1091, 1066, 1013, 965, 829, 796.

4.6.48 (*E*)-1,3-Bis(4-methoxyphenyl)prop-2-en-1-one (**89**)[148, 162]



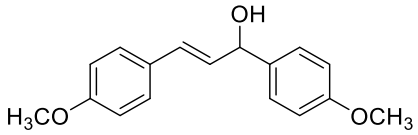
$C_{17}H_{16}O_3$

[268.31]

4'-Methoxyacetophenone (1.25 g, 8.33 mmol, 1.0 equiv) was dissolved in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.4 equiv) added. The resulting solution was cooled with an ice bath, *p*-anisaldehyde (1.0 mL, 8.3 mmol, 1.0 equiv) was added and the ice bath removed. After 2 days the formed yellow solid was suction-filtered and washed with H_2O until the filtrate reached a neutral pH. The resulting solid was dried in a desiccator to afford a yellow solid (2.15 g, 8.02 mmol, 97%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 – 7.99 (m, 2H), 7.78 (d, *J* = 15.6 Hz, 1H), 7.65 – 7.56 (m, 2H), 7.43 (d, *J* = 15.6 Hz, 1H), 7.03 – 6.88 (m, 4H), 3.89 (s, 3H), 3.85 (s, 3H).

4.6.49 (*E*)-1,3-Bis(4-methoxyphenyl)prop-2-en-1-ol (**90**)



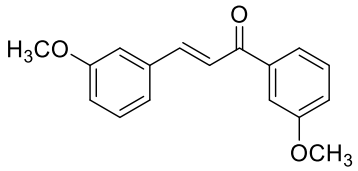
$C_{17}H_{18}O_3$

[270.33]

(*E*)-1,3-Bis(4-methoxyphenyl)prop-2-en-1-one (2.14 g, 7.98 mmol, 1.0 equiv) was dispersed in dry MeOH (100 mL) and $NaBH_4$ (316 mg, 8.35 mmol, 1.0 equiv) added. The reaction was monitored by TLC and after 1 hour additional $NaBH_4$ (77.0 mg, 2.04 mmol, 0.26 equiv) was added. After another 2.5 hours MeOH was removed in vacuo and the residue dissolved in EtOAc. The resulting solution was washed twice with H_2O and once with brine, dried over Na_2SO_4 and the solvent removed in vacuo to afford a yellow oil (2.24 g). Although TLC only showed one product spot after the work-up the ^{1}H NMR spectrum of the raw material showed signals indicating more than one compound. After 24 hours TLC of the raw material showed as well several products and two main components.

In a second attempt, the work-up consisted of washing with saturated $NaHCO_3$ solution, H_2O and brine and drying over $MgSO_4$. After work-up TLC again showed only one product. The $CDCl_3$ used for ^{1}H NMR spectroscopy was filtered through basic aluminum oxide and the raw material stored at 4 °C. Still TLC as well as the ^{1}H NMR spectrum showed rapid decomposition of the product.

4.6.50 (*E*)-1,3-Bis(3-methoxyphenyl)prop-2-en-1-one (**94**)[148, 162][148, 162]



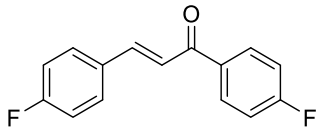
$C_{17}H_{16}O_3$

[268.31]

3'-Methoxyacetophenone (1.23 g, 8.21 mmol, 1.0 equiv) was dissolved in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.4 equiv) and 3-methoxybenzaldehyde (1.0 mL, 8.2 mmol, 1.0 equiv) were added. After 6 days H_2O as well as CH_2Cl_2 were added to the brown solution. The aqueous phase was extracted twice with CH_2Cl_2, the combined organic layers washed with H_2O, saturated NH_4Cl solution and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown oil (2.06 g, 7.68 mmol, 94%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.60 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.54 (dd, *J* = 2.7, 1.6 Hz, 1H), 7.48 (d, *J* = 15.7 Hz, 1H), 7.42 (t, *J* = 7.9 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.17 – 7.11 (m, 2H), 6.97 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 3.89 (s, 3H), 3.86 (s, 3H).

4.6.51 (*E*)-1,3-Bis(4-fluorophenyl)prop-2-en-1-one (**95**)



$C_{15}H_{10}F_2O$

[244.24]

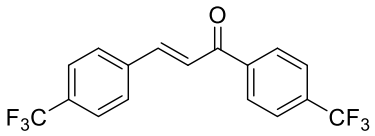
4'-Fluoroacetophenone (0.90 mL, 7.5 mmol, 1.0 equiv) was dissolved in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.5 equiv) was added. The solution was cooled with an ice bath, 4-fluorobenzaldehyde (0.80 mL, 7.5 mmol, 1.0 equiv) was added and the

ice bath removed. After 2 days the formed yellow solid was suction-filtered and washed with H_2O until the filtrate reached a neutral pH. The resulting solid was dried in a desiccator over orange gel affording a white solid (1.82 g, 7.45 mmol, 99%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 – 7.99 (m, 2H), 7.78 (d, *J* = 15.7 Hz, 1H), 7.69 – 7.59 (m, 2H), 7.43 (dd, *J* = 15.6, 0.6 Hz, 1H), 7.24 – 7.06 (m, 4H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -105.44, -108.84.

4.6.52 (*E*)-1,3-Bis(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**96**)



$C_{17}H_{10}F_6O$

[344.26]

Version 1:[163]

NaOH (515 mg, 12.9 mmol, 1.3 equiv) was dissolved in H_2O (2 mL) and EtOH (2 mL). 4'-(Trifluoromethyl)acetophenone (1.89 g, 10.0 mmol, 1.0 equiv) and 4-(trifluoromethyl) benzaldehyde (1.77 g, 10.2 mmol, 1.0 equiv) were added. After 2 hours the resulting solid could not be suction-filtered and the ^{1}H NMR spectrum of this solid did not correspond to the desired product.

Version 2:

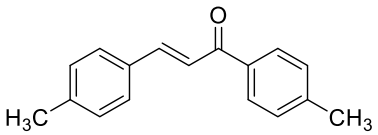
4'-(Trifluoromethyl)acetophenone (1.38 g, 7.35 mmol, 1.0 equiv) was dissolved in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.4 equiv) was added. The resulting solution was cooled with an ice bath, 4-(trifluoromethyl)benzaldehyde (1.0 mL, 7.4 mmol, 1.0 equiv) was added and the ice bath removed. After 2 days the formed yellow solid was suction-filtered and washed with water until the filtrate reached a neutral pH. The resulting solid was dried in a desiccator affording a yellow solid (2.38 g). Purification by

column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.53) yielded a slightly yellow solid (1.58 g, 4.59 mmol, 62%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (dp, *J* = 7.7, 0.9 Hz, 2H), 7.84 (d, *J* = 15.8 Hz, 1H), 7.81 – 7.67 (m, 6H), 7.55 (d, *J* = 15.8 Hz, 1H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -62.92, -63.09.

4.6.53 (*E*)-1,3-Di-*p*-tolylprop-2-en-1-one (**97**)



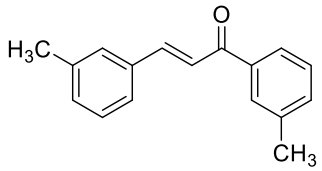
$C_{17}H_{16}O$

[236.31]

p-Methylacetophenone (1.0 mL, 7.5 mmol, 1.0 equiv) was dissolved in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.5 equiv) and 4-methylbenzaldehyde (0.88 mL, 7.5 mmol, 1.0 equiv) were added. After 3 days the formed yellow solid was suction-filtered and washed with H_2O until the filtrate reached a neutral pH. The resulting solid was dried in a desiccator to afford a slightly yellow solid (1.58 g, 6.69 mmol, 90%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 – 7.90 (m, 2H), 7.79 (d, *J* = 15.7 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.50 (d, *J* = 15.7 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 2.44 (s, 3H), 2.40 (s, 3H).

4.6.54 (*E*)-1,3-Di-*m*-tolylprop-2-en-1-one (**98**)



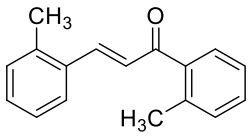
$C_{17}H_{16}O$

[236.31]

3'-Methylacetophenone (1.0 mL, 7.5 mmol, 1.0 equiv) was dissolved in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.5 equiv) and 3-methylbenzaldehyde (0.89 mL, 7.5 mmol, 1.0 equiv) were added. The reaction was monitored by TLC and after 24 hours saturated $NaHCO_3$ solution and CH_2Cl_2 were added. The aqueous phase was extracted with CH_2Cl_2 and the combined organic layers washed with saturated NH_4Cl solution, H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil (1.77 g, 7.49 mmol, 99%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 – 7.82 (m, 2H), 7.79 (d, *J* = 15.7 Hz, 1H), 7.51 (d, *J* = 15.7 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.43 – 7.36 (m, 2H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.25 – 7.20 (m, 1H), 2.45 (s, 3H), 2.41 (s, 3H).

4.6.55 (*E*)-1,3-Di-*o*-tolylprop-2-en-1-one (**99**)



$C_{17}H_{16}O$

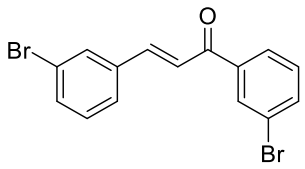
[236.31]

2'-Methylacetophenone (1.0 mL, 7.7 mmol, 1.0 equiv) was dissolved in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.4 equiv) and 2-methylbenzaldehyde (0.90 mL, 7.8 mmol, 1.0 equiv) were added. The reaction was monitored by TLC and after 5 days H_2O

and CH_2Cl_2 were added. The aqueous phase was extracted with CH_2Cl_2 twice and the combined organic layers washed with H_2O, saturated NH_4Cl solution and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil (1.77 g, 7.49 mmol, 98%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, *J* = 15.9 Hz, 1H), 7.64 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.53 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.43 – 7.35 (m, 1H), 7.34 – 7.18 (m, 5H), 7.08 (d, *J* = 15.9 Hz, 1H), 2.48 (s, 3H), 2.39 (s, 3H).

4.6.56 (*E*)-1,3-Bis(3-bromophenyl)prop-2-en-1-one (**100**)



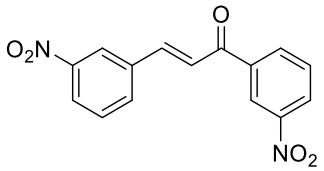
$C_{15}H_{10}Br_2O$

[366.05]

3'-Bromoacetophenone (1.0 mL, 7.6 mmol, 1.0 equiv) was dissolved in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.4 equiv) and 3-bromobenzaldehyde (1.4 g, 7.6 mmol, 1.0 equiv) were added. After 22 hours the formed yellow solid was suction-filtered and washed with H_2O until the filtrate reached a neutral pH. The resulting solid was dried in a desiccator. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.33) yielded a yellow solid (2.00 g, 5.46 mmol, 72%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (t, *J* = 1.8 Hz, 1H), 7.94 (ddd, *J* = 7.8, 1.7, 1.1 Hz, 1H), 7.80 (t, *J* = 1.8 Hz, 1H), 7.74 (d, *J* = 15.6 Hz, 1H), 7.75 – 7.71 (m, 1H), 7.55 (dd, *J* = 7.9, 1.8 Hz, 2H), 7.45 (d, *J* = 15.6 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 1H), 7.31 (dd, *J* = 8.3, 7.5 Hz, 1H).

4.6.57 (*E*)-1,3-Bis(3-nitrophenyl)prop-2-en-1-one (**101**)[164]

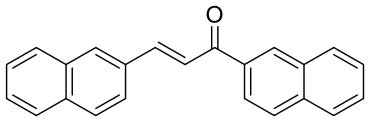


$C_{15}H_{10}N_2O_5$

[298.25]

3'-Nitroacetophenone (2.23 g, 13.5 mmol, 1.0 equiv) and 3-nitrobenzaldehyde (2.04 g, 13.5 mmol, 1.0 equiv) were dissolved in MeOH (30 mL) and NaOH (1.30 g, 32.5 mmol, 2.4 equiv) was added. The reaction was monitored by TLC and after 20 hours the solvent was removed in vacuo. The residue was partially dissolved in CH_2Cl_2 and H_2O and the remaining solid separated by filtration. The aqueous phase was extracted with CH_2Cl_2 twice and the combined organic layers washed with H_2O, saturated NH_4Cl solution and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford brown solid. The ^1H NMR spectrum of this solid did not correspond to the desired product.

4.6.58 (*E*)-1,3-Di(naphthalen-2-yl)prop-2-en-1-one (**102**)[150]



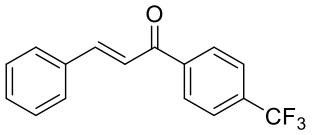
$C_{23}H_{16}O$

[308.38]

2-Acetonaphthone (363 mg, 2.13 mmol, 1.0 equiv) and 2-naphthaldehyde (334 mg, 2.14 mmol, 1.0 equiv) were dissolved in EtOH (4 mL) and a 3M NaOH solution (2.0 mL, 6.0 mmol, 2.8 equiv) was added. After 18 hours the formed white solid was suction-filtered and washed with H_2O until the filtrate reached a neutral pH. The resulting solid was dried in a desiccator affording a white solid (567 mg, 1.84 mmol, 86%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 – 8.57 (m, 1H), 8.15 (dd, *J* = 8.6, 1.7 Hz, 1H), 8.06 (d, *J* = 15.7 Hz, 1H), 8.02 – 7.85 (m, 8H), 7.82 (d, *J* = 15.7 Hz, 1H), 7.68 – 7.49 (m, 4H).

4.6.59 (*E*)-3-Phenyl-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**103**)



$C_{16}H_{11}F_3O$

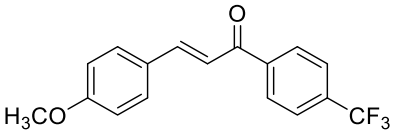
[276.26]

4'-(Trifluoromethyl)acetophenone (1.48 g, 7.87 mmol, 1.0 equiv) was dissolved in EtOH (2 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.4 equiv) and benzaldehyde (0.80 mL, 7.9 mmol, 1.0 equiv) were added. After 3 days the formed yellow solid was suction-filtered and washed with H_2O until the filtrate reached a neutral pH. The resulting solid was dried in a desiccator to afford a slightly yellow solid (2.08 g, 7.53 mmol, 96%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (dq, *J* = 7.7, 0.9 Hz, 2H), 7.84 (d, *J* = 15.8 Hz, 1H), 7.80 – 7.74 (m, 2H), 7.69 – 7.61 (m, 2H), 7.49 (d, *J* = 15.8 Hz, 1H), 7.46 – 7.40 (m, 3H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -63.03.

4.6.60 (*E*)-3-(4-Methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**104**)



$C_{17}H_{13}F_3O_2$

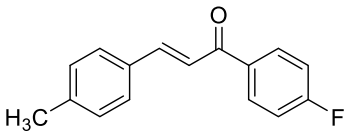
[306.28]

4'-(Trifluoromethyl)acetophenone (1.55 g, 8.23 mmol, 1.0 equiv) was dissolved in EtOH (2 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.3 equiv) and *p*-anisaldehyde (1.00 mL, 8.23 mmol, 1.0 equiv) were added. After 3 days the formed yellow solid was suction-filtered and washed with H_2O until the filtrate reached a neutral pH. The resulting solid was dried in a desiccator to afford a slightly yellow solid (2.41 g, 7.87 mmol, 96%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.1 Hz, 2H), 7.85 – 7.72 (m, 3H), 7.66 – 7.57 (m, 2H), 7.36 (d, *J* = 15.7 Hz, 1H), 7.00 – 6.91 (m, 2H), 3.87 (s, 3H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -62.99.

4.6.61 (*E*)-1-(4-Fluorophenyl)-3-(*p*-tolyl)prop-2-en-1-one (**105**)



$C_{16}H_{13}FO$

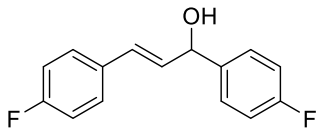
[240.28]

4'-Fluoroacetophenone (1.0 mL, 8.2 mmol, 1.0 equiv) was dissolved in EtOH (2 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.3 equiv) and 4-methylbenzaldehyde (0.97 mL, 8.2 mmol, 1.0 equiv) were added. After 4 days the formed yellow solid was suction-filtered and washed with H_2O until the filtrate reached a neutral pH. The resulting solid was dried in a desiccator to afford a slightly yellow solid (1.97 g, 8.20 mmol, 99%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 – 8.01 (m, 2H), 7.80 (d, *J* = 15.6 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 15.7 Hz, 1H), 7.26 – 7.13 (m, 4H), 2.40 (s, 3H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -105.85.

4.6.62 (*E*)-1,3-Bis(4-fluorophenyl)prop-2-en-1-ol (**107**)



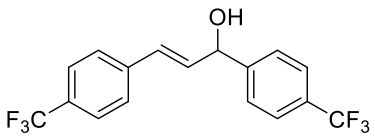
$C_{15}H_{12}F_2O$

[246.26]

(*E*)-1,3-Bis(4-fluorophenyl)prop-2-en-1-one (1.82 g, 7.45 mmol, 1.0 equiv) was dispersed in dry MeOH (70 mL). $NaBH_4$ (430 mg, 11.4 mmol, 1.5 equiv) was added and the reaction monitored by TLC. After 4.5 hours MeOH was removed in vacuo and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a slightly yellowish oil (1.74 g, 7.07 mmol, 95%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.31 (m, 4H), 7.10 – 6.96 (m, 4H), 6.64 (d, *J* = 15.8 Hz, 1H), 6.26 (ddd, *J* = 15.8, 6.5, 0.5 Hz, 1H), 5.36 (d, *J* = 6.5 Hz, 1H), 2.09 (s, 1H).

4.6.63 (*E*)-1,3-Bis(4-(trifluoromethyl)phenyl)prop-2-en-1-ol (**108**)



$C_{17}H_{12}F_6O$

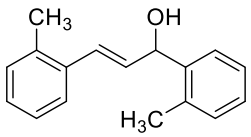
[346.27]

(*E*)-1,3-Bis(4-(trifluoromethyl)phenyl)prop-2-en-1-one (1.10 g, 3.20 mmol, 1.0 equiv) was dispersed in dry MeOH (30 mL). $NaBH_4$ (185 mg, 4.89 mmol, 1.5 equiv) was added and the reaction monitored by TLC. After 4.5 hours MeOH was removed in vacuo and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a slightly yellowish oil (1.10 g, 3.18 mmol, 99%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.56 (q, *J* = 4.2 Hz, 4H), 7.48 (d, *J* = 8.3 Hz, 2H), 6.76 (dd, *J* = 15.9, 1.2 Hz, 1H), 6.43 (dd, *J* = 15.9, 6.4 Hz, 1H), 5.48 (dd, *J* = 6.4, 2.5 Hz, 1H), 2.16 (d, *J* = 3.5 Hz, 1H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -62.55, -62.60.

4.6.64 (*E*)-1,3-Di-*o*-tolylprop-2-en-1-ol (**112**)



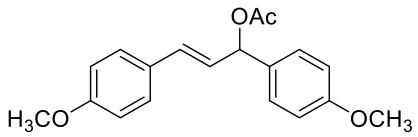
$C_{17}H_{18}O$

[238.33]

(*E*)-1,3-Di-*o*-tolylprop-2-en-1-one (1.75 g, 7.41 mmol, 1.0 equiv) was dispersed in dry MeOH (70 mL). $NaBH_4$ (430 mg, 11.4 mmol, 1.5 equiv) was added and the reaction monitored by TLC. After 4.5 hours MeOH was removed in vacuo and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a slightly yellowish oil (1.70 g, 7.13 mmol, 96%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 – 7.39 (m, 2H), 7.31 – 7.09 (m, 6H), 6.89 (dd, *J* = 15.7, 1.2 Hz, 1H), 6.24 (ddd, *J* = 15.7, 6.3, 0.9 Hz, 1H), 5.61 (dd, *J* = 6.3, 2.8 Hz, 1H), 2.42 (s, 3H), 2.35 (s, 3H).

4.6.65 (*E*)-1,3-Bis(4-methoxyphenyl)allyl acetate (**117**)



$C_{19}H_{20}O_4$

[312.37]

(*E*)-1,3-Bis(4-methoxyphenyl)prop-2-en-1-one (1.79 g, 6.67 mmol, 1.0 equiv) was dispersed in dry MeOH (60 mL). $NaBH_4$ (280 mg, 7.40 mmol, 1.1 equiv) was added and the reaction monitored by TLC. After 2.5 hours additional $NaBH_4$ (140 mg, 3.70 mmol, 0.55 equiv) was added. After another hour MeOH was removed in vacuo (bath temp. 40 °C) and the residue dissolved in EtOAc. This organic solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) to afford a yellow oil.

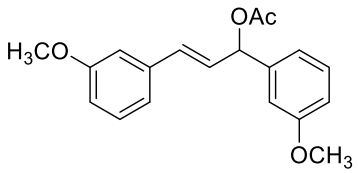
This oil was dissolved in dry CH_2Cl_2 (20 mL) and Et_3N (1.8 mL, 13 mmol, 1.9 equiv) and acetic anhydride (1.3 mL, 14 mmol, 2.1 equiv) were added. The reaction was monitored by TLC and after 5 days saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, the combined organic layers washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo affording a yellow oil (2.10 g). Purification by plug filtration (Al_2O_3, III, *n*-hexane/EtOAc 1:1) gave a yellow oil (1.85 g, 5.92 mmol, 89%). The ^{1}H NMR spectrum showed that the attempted purification led to more impurities.

^{1}H NMR (300 MHz, C_6D_6) δ 7.41 – 7.34 (m, 2H), 7.18 – 7.11 (m, 3H), 6.84 – 6.76 (m, 2H), 6.67 (dd, *J* = 14.4, 8.8 Hz, 3H), 6.40 – 6.23 (m, 1H), 3.29 (s, 3H), 3.26 (s, 3H), 1.74 (s, 3H).

^{13}C NMR (75 MHz, C_6D_6) δ 169.45, 160.11, 160.05, 132.41, 132.35, 129.53, 129.07, 126.28, 114.36, 114.34, 76.26, 54.86, 54.80, 20.96, 20.93.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3003 (w), 2956 (w), 2935 (w), 2836 (w), 1736 (s, C=O), 1608 (s), 1512 (s), 1464, 1442, 1370, 1301, 1249 (s), 1174, 1033, 966, 831, 536.

4.6.66 (*E*)-1,3-Bis(3-methoxyphenyl)allyl acetate (**118**)



$C_{19}H_{20}O_4$

[312.37]

(*E*)-1,3-Bis(3-methoxyphenyl)prop-2-en-1-one (961 mg, 3.58 mmol, 1.0 equiv) was dispersed in dry MeOH (30 mL). $NaBH_4$ (136 mg, 3.58 mmol, 1.0 equiv) was added and the reaction monitored by TLC. After 2 hours MeOH was removed in vacuo (bath temp. 40 °C) and the residue dissolved in EtOAc. This solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) to afford a yellow oil.

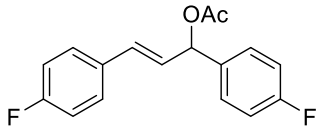
This oil was dissolved in dry CH_2Cl_2 (10 mL) and Et_3N (1.0 mL, 7.2 mmol, 2.0 equiv) and acetic anhydride (0.70 mL, 7.4 mmol, 2.1 equiv) were added. The reaction was monitored by TLC and after 4 days saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, the combined organic layers washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo affording a brownish oil (998 mg, 3.19 mmol, 89%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.13 – 7.09 (m, 1H), 7.07 – 7.03 (m, 1H), 7.00 (d, *J* = 7.9 Hz, 1H), 6.89 – 6.82 (m, 2H), 6.75 – 6.67 (m, 3H), 6.67 – 6.63 (m, 2H), 6.40 (dd, *J* = 15.9, 6.7 Hz, 1H), 3.30 (s, 3H), 3.25 (s, 3H), 1.71 (s, 3H).

^{13}C NMR (75 MHz, C_6D_6) δ 169.27, 160.53, 160.46, 141.69, 138.15, 132.96, 130.02, 129.84, 119.73, 119.68, 114.41, 113.82, 113.31, 112.31, 76.20, 54.80, 54.71, 20.79, 20.77.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3002 (w), 2940 (w), 2836 (w), 1737 (s, C=O), 1600, 1586, 1490, 1455, 1435, 1370, 1318 (w), 1288, 1265, 1232 (s), 1157, 1045, 1021, 967, 913 (w), 871 (w), 782, 743, 700.

4.6.67 (*E*)-1,3-Bis(4-fluorophenyl)allyl acetate (**119**)



$C_{17}H_{14}F_2O_2$

[288.29]

(*E*)-1,3-Bis(4-fluorophenyl)prop-2-en-1-ol (1.74 g, 7.07 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (15 mL) and Et_3N (2.0 mL, 14 mmol, 2.0 equiv) and acetic anhydride (1.3 mL, 14 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 9 days saturated $NaHCO_3$ solution was added. The organic phase was washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo affording a yellow oil (2.08 g). Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.43) yielded a colorless oil (1.58 g, 5.48, 78%).

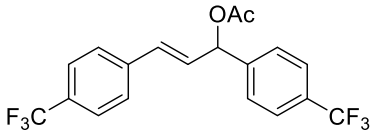
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.29 (m, 4H), 7.13 – 6.94 (m, 4H), 6.57 (d, *J* = 15.8 Hz, 1H), 6.40 (d, *J* = 6.7 Hz, 1H), 6.23 (ddd, *J* = 15.8, 6.7, 0.6 Hz, 1H), 2.13 (s, 3H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -113.49, -113.71.

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.05, 162.73 (d, *J* = 247.7 Hz), 162.63 (d, *J* = 246.8 Hz), 135.12 (d, *J* = 3.3 Hz), 132.31 (d, *J* = 3.3 Hz), 131.66, 129.00 (d, *J* = 8.3 Hz), 128.39 (d, *J* = 8.0 Hz), 127.17, 115.67 (d, *J* = 21.7 Hz), 75.48, 21.40.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3042 (w), 1739 (s, C=O), 1603, 1508 (s), 1415, 1371, 1298, 1227 (s), 1158, 1014, 964, 835, 756, 607, 543, 519.

4.6.68 (*E*)-1,3-Bis(4-(trifluoromethyl)phenyl)allyl acetate (**120**)



$C_{19}H_{14}F_6O_2$

[388.31]

(*E*)-1,3-Bis(4-(trifluoromethyl)phenyl)prop-2-en-1-ol (1.10 g, 3.18 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (7 mL) and Et_3N (0.60 mL, 4.3 mmol, 1.4 equiv) and acetic anhydride (0.88 mL, 9.30 mmol, 2.9 equiv) were added. The reaction was monitored by TLC and after 4 days saturated $NaHCO_3$ solution was added. The organic phase was washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo affording a yellow oil (1.43 g). Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.14) yielded a colorless oil (823 mg, 2.12, 67%).

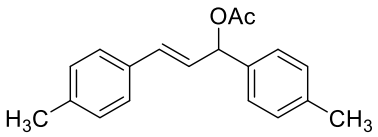
^{1}H NMR (300 MHz, C_6D_6) δ 7.38 (dt, *J* = 7.9, 0.9 Hz, 2H), 7.31 – 7.24 (m, 2H), 7.18 – 7.11 (m, 2H), 6.89 (d, *J* = 8.1 Hz, 2H), 6.42 – 6.33 (m, 2H), 6.05 (dd, *J* = 15.7, 6.9 Hz, 1H), 1.72 (s, 3H).

^{19}F NMR (282 MHz, C_6D_6) δ -62.30, -62.36.

^{13}C NMR (75 MHz, C_6D_6) δ 169.03 (C=O), 143.35 (q, *J* = 1.2 Hz), 139.66 (q, *J* = 1.3 Hz), 131.78, 130.61 (q, *J* = 32.5 Hz), 130.16 (q, *J* = 32.5 Hz), 129.79, 127.64, 127.18, 125.90 (q, *J* = 3.8 Hz), 125.77 (q, *J* = 3.9 Hz), 124.87 (q, *J* = 271.4 Hz, CF_3), 124.75 (q, *J* = 272.1 Hz, CF_3), 75.04, 20.56 (CH_3).

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 2939 (w), 1743 (s, C=O), 1618, 1417, 1373, 1326 (s), 1231, 1166, 1124, 1067, 1017, 969, 841, 754, 606.

4.6.69 (*E*)-1,3-Di-*p*-tolylallyl acetate (**121**)



$C_{19}H_{20}O_2$

[280.37]

(*E*)-1,3-Di-*p*-tolylprop-2-en-1-one (1.00 g, 4.23 mmol, 1.0 equiv) was dispersed in dry MeOH (35 mL). $NaBH_4$ (325 mg, 8.59 mmol, 2.0 equiv) was added and the reaction monitored by TLC. After 2 hours additional $NaBH_4$ (100 mg, 2.64 mmol, 0.62 equiv) was added. After another 2 hours MeOH was removed in vacuo and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo to afford a slightly yellowish oil.

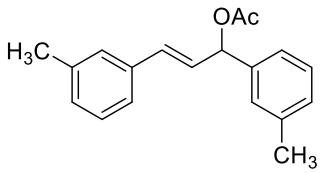
This oil was dissolved in dry CH_2Cl_2 (10 mL) and Et_3N (1.20 mL, 8.66 mmol, 2.1 equiv) and acetic anhydride (0.80 mL, 8.46 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 2 days saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, the combined organic layers washed twice with H_2O and once with brine, dried over Na_2SO_4 and the solvent removed in vacuo affording a slightly yellowish oil (1.05 g, 3.75 mmol, 89%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.38 – 7.32 (m, 2H), 7.15 – 7.10 (m, 2H), 7.04 – 6.99 (m, 2H), 6.93 – 6.87 (m, 2H), 6.71 – 6.68 (m, 1H), 6.67 – 6.63 (m, 1H), 6.38 (dd, *J* = 16.1, 6.4 Hz, 1H), 2.09 (s, 3H), 2.06 (s, 3H), 1.71 (s, 3H).

^{13}C NMR (75 MHz, C_6D_6) δ 169.34, 137.84, 137.35, 134.12, 132.77, 129.55, 127.64, 127.46, 127.08, 76.32, 21.18, 21.11, 20.87.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3025, 2922, 2863 (w), 1739 (s, C=O), 1514, 1449, 1369, 1300, 1234 (s), 1181, 1111, 1017, 965, 816, 800, 513.

4.6.70 (*E*)-1,3-Di-*m*-tolylallyl acetate (**122**)



$C_{19}H_{20}O_2$

[280.37]

(*E*)-1,3-Di-*m*-tolylprop-2-en-1-one (727 mg, 3.08 mmol, 1.0 equiv) was dissolved in dry MeOH (20 mL). $NaBH_4$ (125 mg, 3.30 mmol, 1.1 equiv) was added and the reaction monitored by TLC. After 2 hours the solvent was removed in vacuo (bath temp. 40 °C) and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) to afford a yellowish oil.

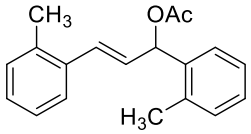
This oil was dissolved in dry CH_2Cl_2 (10 mL) and Et_3N (1.0 mL, 7.2 mmol, 2.3 equiv) and acetic anhydride (0.70 mL, 7.4 mmol, 2.4 equiv) were added. The reaction was monitored by TLC and after 2 days additional Et_3N (1.0 mL, 7.2 mmol, 2.3 equiv) and acetic anhydride (0.70 mL, 7.4 mmol, 2.4 equiv) were added. After another 4 hours saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, the combined organic layers washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) affording a slightly yellowish oil (771 mg, 2.75 mmol, 89%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.33 – 7.25 (m, 2H), 7.14 – 6.83 (m, 6H), 6.72 – 6.67 (m, 1H), 6.65 (s, 1H), 6.40 (dd, *J* = 15.9, 6.5 Hz, 1H), 2.10 (s, 3H), 2.05 (s, 3H), 1.73 (s, 3H).

^{13}C NMR (75 MHz, C_6D_6) δ 169.31, 140.18, 138.42, 138.14, 136.72, 132.97, 129.10, 129.02, 128.88, 128.75, 128.30, 128.18, 127.87, 124.70, 124.38, 76.44, 21.40, 21.29, 20.85.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3027 (w), 2922 (w), 1737 (s, C=O), 1607 (w), 1489 (w), 1457 (w), 1369, 1232 (s), 1019, 963, 783, 704, 693.

4.6.71 (*E*)-1,3-Di-*o*-tolylallyl acetate (**123**)



$C_{19}H_{20}O_2$

[280.37]

(*E*)-1,3-Di-*o*-tolylprop-2-en-1-ol (1.70 g, 7.13 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (15 mL) and Et_3N (2.0 mL, 14 mmol, 2.0 equiv) and acetic anhydride (1.4 mL, 14 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 9 days saturated $NaHCO_3$ solution was added. The organic phase was washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo affording a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.49) yielded a slightly yellowish oil (1.63 g, 5.81 mmol, 82%).

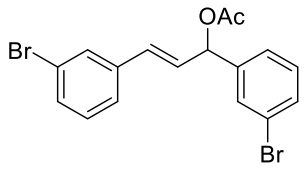
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 – 7.34 (m, 2H), 7.26 – 7.10 (m, 6H), 6.79 (dd, *J* = 15.8, 1.2 Hz, 1H), 6.62 (dd, *J* = 6.7, 1.2 Hz, 1H), 6.20 (dd, *J* = 15.7, 6.7 Hz, 1H), 2.43 (s, 3H), 2.30 (s, 3H), 2.14 (s, 3H).

^{1}H NMR (300 MHz, C_6D_6) δ 7.59 – 7.52 (m, 1H), 7.30 – 7.22 (m, 1H), 7.14 – 6.87 (m, 6H), 6.85 – 6.80 (m, 2H), 6.21 (dd, *J* = 15.7, 6.7 Hz, 1H), 2.30 (s, 3H), 2.05 (s, 3H), 1.71 (s, 3H).

^{13}C NMR (75 MHz, C_6D_6) δ 169.28, 138.33, 135.92, 135.89, 130.98, 130.92, 130.53, 129.05, 128.24, 128.17, 127.14, 126.64, 126.47, 126.31, 73.75, 20.79, 20.77, 19.59, 19.37.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3022 (w), 1736 (s, C=O), 1488, 1460, 1369, 1231 (s), 1015, 961, 745, 564.

4.6.72 (*E*)-1,3-Bis(3-bromophenyl)allyl acetate (**124**)



$C_{17}H_{14}Br_2O_2$

[410.11]

(*E*)-1,3-Bis(3-Bromophenyl)prop-2-en-1-one (1.13 g, 3.09 mmol, 1.0 equiv) was dissolved in dry MeOH (20 mL). $NaBH_4$ (117 mg, 3.09 mmol, 1.0 equiv) was added and the reaction monitored by TLC. After 1 hour the solvent was removed in vacuo (bath temp. 40 °C) and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) to afford a yellowish oil.

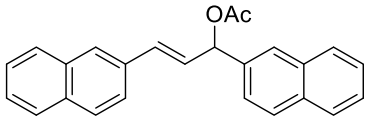
This oil was dissolved in dry CH_2Cl_2 (10 mL) and Et_3N (1.0 mL, 7.2 mmol, 2.3 equiv) and acetic anhydride (0.70 mL, 7.4 mmol, 2.4 equiv) were added. The reaction was monitored by TLC and after 2 days saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, the combined organic layers washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) affording a slightly yellowish oil (1.14 g, 2.78 mmol, 90%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.61 (t, *J* = 1.8 Hz, 1H), 7.29 (t, *J* = 1.8 Hz, 1H), 7.21 (ddd, *J* = 8.0, 2.1, 1.1 Hz, 1H), 7.15 – 7.11 (m, 1H), 7.07 – 7.01 (m, 1H), 6.80 – 6.72 (m, 2H), 6.63 (t, *J* = 7.8 Hz, 1H), 6.33 (dd, *J* = 6.8, 1.2 Hz, 1H), 6.28 (dd, *J* = 15.8, 1.2 Hz, 1H), 5.92 (dd, *J* = 15.8, 6.8 Hz, 1H), 1.63 (s, 3H).

^{13}C NMR (75 MHz, C_6D_6) δ 168.99, 142.06, 138.49, 131.58, 131.54, 131.20, 130.49, 130.35, 130.24, 129.94, 128.82, 125.99, 125.61, 123.19, 123.13, 75.01, 20.59.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3060 (w), 2928 (w), 1739 (s, C=O), 1592, 1562, 1474, 1426, 1370, 1229 (s), 1192, 1071, 1020, 996, 962, 779, 683.

4.6.73 (*E*)-1,3-Di(naphthalen-2-yl)allyl acetate (**125**)[150]



$C_{25}H_{20}O_2$

[352.43]

(*E*)-1,3-Di(naphthalen-2-yl)prop-2-en-1-one (551 mg, 1.79 mmol, 1.0 equiv) was dispersed in dry MeOH (5.5 mL) and dry THF (5.5 mL). $NaBH_4$ (133 mg, 3.52 mmol, 1.0 equiv) was added in small portions. The reaction was monitored by TLC and after 1 hour MeOH was removed in vacuo (bath temp. 40 °C) and the residue dissolved in EtOAc. The resulting solution was washed with brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) to afford a yellow solid.

This solid was dissolved in dry CH_2Cl_2 (8 mL), the solution cooled with an ice bath and Et_3N (0.95 mL, 6.9 mmol, 3.9 equiv) and acetic anhydride (0.65 mL, 6.9 mmol, 3.9 equiv) were added. The reaction was monitored by TLC and after 24 hours additional Et_3N (0.95 mL, 6.9 mmol, 3.9 equiv) and acetic anhydride (0.65 mL, 6.9 mmol, 3.9 equiv) were added. After another 5 days saturated $NaHCO_3$ solution was added. The organic layer was washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo (bath temp. 40 °C) affording a white solid (424 mg, 1.20 mmol, 67%).

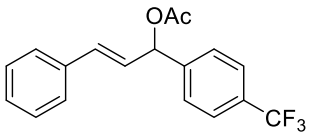
^{1}H NMR (300 MHz, DMSO-d_6) δ 8.04 – 7.81 (m, 8H), 7.74 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.62 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.57 – 7.46 (m, 4H), 6.91 (d, *J* = 15.8 Hz, 1H), 6.75 (dd, *J* = 15.8, 6.7 Hz, 1H), 6.60 (d, *J* = 6.7 Hz, 1H), 2.17 (s, 3H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 169.57, 136.91, 133.41, 133.10, 132.79, 132.70, 132.60, 131.83, 128.34, 128.31, 128.18, 127.95, 127.92, 127.58, 127.55, 126.76, 126.44, 126.33, 126.20, 125.54, 124.88, 123.62, 75.95, 21.06.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3056, 1738 (s, C=O), 1651 (w), 1599, 1508, 1479, 1435 (w), 1368, 1231 (s), 1172 (w), 1125, 1018, 963, 894, 858, 814, 746, 673 (s), 660.

mp 109-111 °C

4.6.74 (*E*)-3-Phenyl-1-(4-(trifluoromethyl)phenyl)allyl acetate (**126**)



$C_{18}H_{15}F_3O_2$

[320.31]

(*E*)-3-Phenyl-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (1.00 g, 3.62 mmol, 1.0 equiv) was dispersed in dry MeOH (30 mL). $NaBH_4$ (139 mg, 3.67 mmol, 1.0 equiv) was added and the reaction monitored by TLC. After 2 hours the solvent was removed in vacuo (bath temp. 40 °C) and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) to afford a yellow oil.

This oil was dissolved in dry CH_2Cl_2 (10 mL) and Et_3N (1.0 mL, 7.2 mmol, 2.0 equiv) and acetic anhydride (0.70 mL, 7.4 mmol, 2.1 equiv) were added. The reaction was monitored by TLC and after 12 days saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, the combined organic layers washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo affording a yellowish oil (1.04 g, 3.24 mmol, 90%).

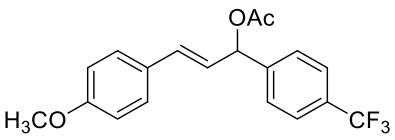
^{1}H NMR (300 MHz, C_6D_6) δ 7.35 (d, *J* = 8.2 Hz, 2H), 7.14 – 6.97 (m, 6H), 6.55 (dd, *J* = 15.9, 1.1 Hz, 1H), 6.45 (d, *J* = 7.0 Hz, 1H), 6.14 (dd, *J* = 15.9, 7.0 Hz, 1H), 1.69 (s, 3H).

^{19}F NMR (282 MHz, C_6D_6) δ -62.27.

^{13}C NMR (75 MHz, C_6D_6) δ 169.08 (C=O), 143.91, 136.33, 133.67, 130.30 (q, *J* = 32.3 Hz, *o*-CF_3), 128.90, 128.55, 127.61, 127.15, 127.09, 125.80 (q, *J* = 3.9 Hz, *m*-CF_3), 124.86 (q, *J* = 272.3 Hz, CF_3), 75.48 (C-OAc), 20.64 (CH_3).

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3029 (w), 1741 (s, C=O), 1621, 1496 (w), 1449 (w), 1419, 1372, 1327 (s), 1231 (s), 1166, 1125, 1067, 1017, 965, 880 (w), 838, 765, 745, 693, 605, 533.

4.6.75 (*E*)-3-(4-Methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)allyl acetate (**127**)



$C_{19}H_{17}F_3O_3$

[350.34]

(*E*)-3-(4-Methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (1.00 g, 3.26 mmol, 1.0 equiv) was dispersed in dry MeOH (25 mL). $NaBH_4$ (125 mg, 3.30 mmol, 1.0 equiv) was added and the reaction monitored by TLC. After 1 hour the solvent was removed in vacuo (bath temp. 40 °C) and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) to afford a colorless oil.

This oil was dissolved in dry CH_2Cl_2 (10 mL) and Et_3N (1.0 mL, 7.2 mmol, 2.2 equiv) and acetic anhydride (0.70 mL, 7.4 mmol, 2.3 equiv) were added. The reaction was monitored by TLC and after 12 days saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, the combined organic layers washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) affording a yellowish oil (1.00 g, 2.85 mmol, 87%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.40 – 7.33 (m, 2H), 7.23 – 7.17 (m, 2H), 7.15 – 7.09 (m, 2H), 6.74 – 6.66 (m, 2H), 6.57 (dd, *J* = 15.9, 1.0 Hz, 1H), 6.50 (d, *J* = 7.2 Hz, 1H), 6.09 (dd, *J* = 15.9, 7.2 Hz, 1H), 3.26 (s, 3H), 1.72 (s, 3H).

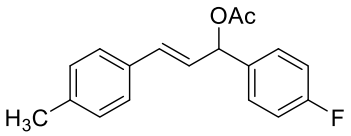
^{19}F NMR (282 MHz, C_6D_6) δ -62.24.

^{13}C NMR (75 MHz, C_6D_6) δ 169.14 (C=O), 160.41 (*ipso*-OCH_3), 144.21 (*p*-OCH_3), 133.60 (*m*-OCH_3), 130.20 (q, *J* = 32.3 Hz, *o*-CF_3), 128.99, 127.58, 127.17, 125.78 (q, *J* = 3.8 Hz,

m-CF_3), 124.89 (q, *J* = 272.0 Hz, CF_3), 124.87, 114.43 (*o*-OCH_3), 75.80 (C-OAc), 54.81 (OCH_3), 20.70 (CH_3).

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 2938 (w), 2839 (w), 1739 (s, C=O), 1607, 1513, 1466 (w), 1420, 1371, 1326, 1232, 1174, 1124, 1067, 1017, 965, 839, 605 (w), 529.

4.6.76 (*E*)-1-(4-Fluorophenyl)-3-(*p*-tolyl)allyl acetate (**128**)



$C_{16}H_{13}FO$

[284.33]

(*E*)-1-(4-Fluorophenyl)-3-(*p*-tolyl)prop-2-en-1-one (721 mg, 3.00 mmol, 1.0 equiv) was dispersed in dry MeOH (20 mL). $NaBH_4$ (119 mg, 3.15 mmol, 1.0 equiv) was added and the reaction monitored by TLC. After 1 hour additional $NaBH_4$ (17.0 mg, 0.449 mmol, 0.15 equiv) was added. After another 45 minutes the solvent was removed in vacuo (bath temp. 40 °C) and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) to afford a colorless oil.

This oil was dissolved in dry CH_2Cl_2 (10 mL) and Et_3N (1.0 mL, 7.2 mmol, 2.4 equiv) and acetic anhydride (0.70 mL, 7.4 mmol, 2.5 equiv) were added. The reaction was monitored by TLC and after 3 days saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, the combined organic layers washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) affording a slightly yellowish oil (749 mg, 2.63 mmol, 88%).

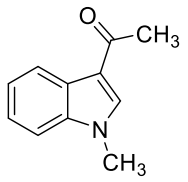
^{1}H NMR (300 MHz, C_6D_6) δ 7.19 – 7.10 (m, 4H), 6.94 – 6.88 (m, 2H), 6.85 – 6.76 (m, 2H), 6.60 (dd, *J* = 15.9, 1.2 Hz, 1H), 6.52 (dd, *J* = 6.8, 1.1 Hz, 1H), 6.23 (dd, *J* = 15.9, 6.8 Hz, 1H), 2.07 (s, 3H), 1.69 (s, 3H).

^{19}F NMR (282 MHz, C_6D_6) δ -113.98

^{13}C NMR (75 MHz, C_6D_6) δ 169.19, 162.90 (d, *J* = 245.9 Hz), 138.10, 136.01 (d, *J* = 3.2 Hz), 133.89, 133.08, 129.61, 129.38 (d, *J* = 8.1 Hz), 127.07, 126.86, 115.66 (d, *J* = 21.3 Hz), 75.56, 21.18, 20.77.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3025 (w), 2923 (w), 2863 (w), 1739 (s, C=O), 1605, 1510 (s), 1432, 1370, 1297, 1229 (s), 1158, 1120, 1095, 1065, 1016, 966, 880, 836, 806, 781, 608, 563, 543, 516.

4.6.77 3-Acetyl-1-methylindole (**130**)[151]



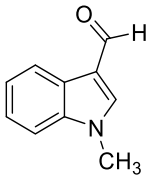
$C_{11}H_{11}NO$

[173.22]

3-Acetylindole (2.00 g, 12.6 mmol, 1.0 equiv) was dissolved in dry DMF (25 mL) and cooled with an ice bath. A dispersion of 60% NaH in mineral oil (607 mg, 15.2 mmol, 1.2 equiv) was added and the ice bath removed after 10 minutes. After another 10 minutes iodomethane (0.94 mL, 15 mmol, 1.2 equiv) was added and the reaction monitored by TLC. After 1 hour the reaction was quenched with H_2O. The resulting solution was extracted with EtOAc four times. The combined organic layers were washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo to afford a brown oil. Purification by column chromatography (*n*-hexane/EtOAc 60:40, R_f = 0.24) yielded a slightly orange solid (2.01 g, 11.6 mmol, 92%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 – 8.31 (m, 1H), 7.69 (s, 1H), 7.37 – 7.27 (m, 3H), 3.83 (s, 3H), 2.52 (s, 3H).

4.6.78 1-Methylindole-3-carboxaldehyde (**132**)[151]



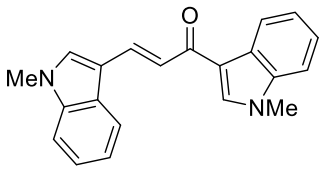
$C_{10}H_9NO$

[159.19]

Indole-3-carboxaldehyde (2.00 g, 13.8 mmol, 1.0 equiv) was dissolved in dry DMF (25 mL) and cooled with an ice bath. A dispersion of 60% NaH in mineral oil (667 mg, 16.7 mmol, 1.2 equiv) was added and the ice bath removed after 10 minutes. After another 5 minutes iodomethane (1.0 mL, 16 mmol, 1.2 equiv) was added and the reaction monitored by TLC. After 1 hour the reaction was quenched with H_2O. The resulting solution was extracted with EtOAc four times. The combined organic layers were washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo to afford a brown oil. Purification by column chromatography (*n*-hexane/EtOAc 1:1, R_f = 0.26) yielded a slightly yellow solid (2.14 g, 13.4 mmol, 97%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.37 – 8.22 (m, 1H), 7.66 (s, 1H), 7.43 – 7.28 (m, 3H), 3.86 (s, 3H).

4.6.79 (*E*)-1,3-Bis(1-methyl-1*H*-indol-3-yl)prop-2-en-1-one (**133**)



$C_{21}H_{18}N_2O$

[314.39]

Version 1:[148]

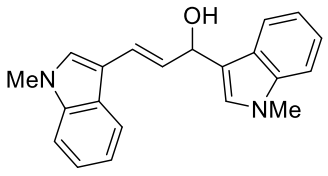
3-Acetyl-1-methylindole (1.30 g, 7.50 mmol, 1.0 equiv) was dispersed in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.4 equiv) and 1-methyl-1*H*-indole-3-carbaldehyde (1.19 g, 7.50 mmol, 1.0 equiv) were added. The reaction was monitored by TLC which did not show any transformation. After 8 days H_2O and CH_2Cl_2 were added. The aqueous phase was extracted with CH_2Cl_2 three times and the combined organic layers washed with H_2O, saturated NH_4Cl solution and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. The ^{1}H NMR spectrum of this raw material showed the combined spectra of the starting materials.

Version 2:[152]

3-Acetyl-1-methylindole (175 mg, 1.01 mmol, 1.0 equiv) and 1-methyl-1*H*-indole-3-carbaldehyde (161 mg, 1.01 mmol, 1.0 equiv) were dissolved in MeOH (10 mL) and a 50 wt% KOH solution (1.0 mL, 18 mmol, 18 equiv) was added. The reaction was monitored by TLC which again did not show any transformation. After 1 day the solution was refluxed. After another 7 days MeOH was removed in vacuo and the resulting residue dissolved in EtOAc/H_2O. The aqueous phase was extracted with EtOAc and the combined organic layers washed with 1M HCl, H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid (285 mg, 0.907 mmol, 91%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 – 8.53 (m, 1H), 8.13 – 7.98 (m, 2H), 7.83 (s, 1H), 7.45 – 7.28 (m, 8H), 3.84 (s, 3H), 3.78 (s, 3H).

4.6.80 (*E*)-1,3-Bis(1-methyl-1*H*-indol-3-yl)prop-2-en-1-ol (**134**)



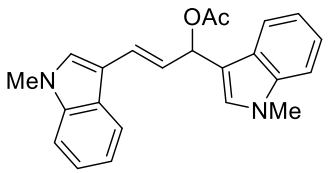
$C_{21}H_{20}N_2O$

[316.40]

(*E*)-1,3-Bis(1-methyl-1*H*-indol-3-yl)prop-2-en-1-one (285 mg, 0.907 mmol, 1.0 equiv) was dispersed in dry MeOH (20 mL) and $NaBH_4$ (60.3 mg, 1.59 mmol, 1.8 equiv) was added. TLC did not show any transformation. After 22 hours MeOH was removed in vacuo and the residue dissolved in EtOAc/H_2O. The aqueous phase was extracted twice with EtOAc and the combined organic layers washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a slightly green solid (280 mg, 0.885 mmol, 98%).

^{1}H NMR (300 MHz, C_6D_6) δ 9.28 (dt, *J* = 8.0, 1.0 Hz, 1H), 8.56 (d, *J* = 15.6 Hz, 1H), 8.26 – 8.15 (m, 1H), 7.69 (d, *J* = 15.5 Hz, 1H), 7.47 – 7.13 (m, 7H), 6.93 (dt, *J* = 8.1, 0.9 Hz, 2H), 6.56 (s, 1H), 2.78 (s, 3H), 2.74 (s, 3H).

4.6.81 (*E*)-1,3-Bis(1-methyl-1*H*-indol-3-yl)allyl acetate (**135**)

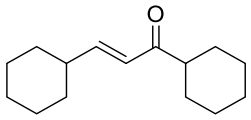


$C_{23}H_{22}N_2O_2$

[358.44]

(*E*)-1,3-Bis(1-methyl-1*H*-indol-3-yl)prop-2-en-1-ol (280 mg, 0.885 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (5 mL) and Et_3N (0.50 mL, 3.6 mmol, 4.1 equiv) and acetic anhydride (0.34 mL, 3.6 mmol, 4.1 equiv) were added. TLC did not show any transformation. After 7 days saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, the combined organic layers washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo affording a yellow solid (251 mg). The ^{1}H NMR of this raw material showed only substrate signals.

4.6.82 (*E*)-1,3-Dicyclohexylprop-2-en-1-one (**138**)

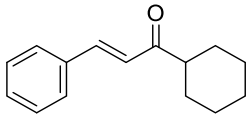


$C_{15}H_{24}O$

[220.36]

Cyclohexyl methyl ketone (1.00 mL, 7.27 mmol, 1.0 equiv) was dissolved in EtOH (2.0 mL) and a 11 wt% NaOH solution (4.0 mL, 11 mmol, 1.5 equiv) and cyclohexanecarboxaldehyde (0.88 mL, 7.3 mmol, 1.0 equiv) were added. The reaction was monitored by TLC and after 8 days H_2O and CH_2Cl_2 were added. The aqueous phase was extracted with CH_2Cl_2 three times and the combined organic layers washed with H_2O and saturated NH_4Cl solution, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. Attempted purification of this oil did not afford the desired compound in sufficient purity.

4.6.83 (*E*)-1-Cyclohexyl-3-phenylprop-2-en-1-one (**140**)[153]



$C_{15}H_{18}O$

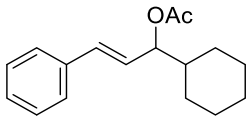
[214.31]

Cyclohexyl methyl ketone (1.89 g, 15.0 mmol, 1.0 equiv) was dissolved in H_2O/EtOH (1:1, 20 mL) and benzaldehyde (1.5 mL, 15 mmol, 1.0 equiv) and a 5M KOH solution (5 mL) were added and the resulting solution stirred vigorously. The reaction was monitored by TLC and after 1 day quenched with 1M HCl (approx. 6 mL). Since the pH turned out acidic the solution was neutralized by addition of saturated $NaHCO_3$ solution. The resulting solution was extracted with CH_2Cl_2 three times. The combined organic layers were washed with H_2O and brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellowish oil. This oil was dissolved in EtOAc and washed five times with $NaHSO_3$ solution (~50 mL), twice with H_2O and once with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification

by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.40) yielded a slightly yellowish oil (1.89 g, 8.82 mmol, 59%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, *J* = 16.0 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.43 – 7.35 (m, 3H), 6.81 (d, *J* = 16.0 Hz, 1H), 2.66 (tt, *J* = 11.2, 3.4 Hz, 1H), 1.94 – 1.62 (m, 5H), 1.56 – 1.16 (m, 5H).

4.6.84 (*E*)-1-Cyclohexyl-3-phenylallyl acetate (**142**)



$C_{17}H_{22}O_2$

[258.36]

(*E*)-1-Cyclohexyl-3-phenylprop-2-en-1-one (643 mg, 3.00 mmol, 1.0 equiv) was dispersed in dry MeOH (20 mL). $NaBH_4$ (119 mg, 3.15 mmol, 1.0 equiv) was added and the reaction monitored by TLC. After 1 hour the solvent was removed in vacuo (bath temp. 40 °C) and the residue dissolved in EtOAc. The resulting solution was washed with saturated $NaHCO_3$ solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) to afford a colorless oil.

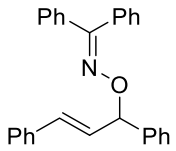
This oil was dissolved in dry CH_2Cl_2 (10 mL) and Et_3N (1.0 mL, 7.2 mmol, 2.4 equiv) and acetic anhydride (0.70 mL, 7.4 mmol, 2.5 equiv) were added. The reaction was monitored by TLC and after 4 days additional Et_3N (1.0 mL, 7.2 mmol, 2.4 equiv) and acetic anhydride (0.70 mL, 7.4 mmol, 2.5 equiv) were added. After another 2 days saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, the combined organic layers washed with H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C) affording a yellowish oil (613 mg, 2.37 mmol, 79%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.26 – 7.19 (m, 2H), 7.13 – 6.99 (m, 3H), 6.64 (d, *J* = 15.9 Hz, 1H), 6.11 (dd, *J* = 15.9, 7.8 Hz, 1H), 5.42 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 1.85 – 1.77 (m, 1H), 1.75 (s, 3H), 1.72 – 1.48 (m, 5H), 1.25 – 0.85 (m, 5H).

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3027 (w), 2928 (s), 2853, 1737 (s, C=O), 1495 (w), 1449, 1370, 1331, 1238 (s), 1185 (w), 1088 (w), 1064 (w), 1043, 1017, 968, 950, 749, 694.

iii. Allyl Oximes

4.6.85 (*E*)-Diphenylmethanone *O*-(1,3-diphenylallyl) oxime (**143**)



$C_{28}H_{23}NO$

[389.50]

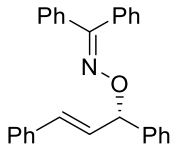
(*E*)-1,3-Diphenylallyl ethyl carbonate (346 mg, 1.23 mmol, 1.0 equiv) and diphenylmethanone oxime (242 mg, 1.23 mmol, 1.0 equiv) were dissolved in dry, degassed MeCN (7 mL). $Pd(PPh)_4$ (60.0 mg, 0.0519 mmol, 4.2 mol%) was added and the reaction monitored by TLC. After 26 hours the solvent was removed in vacuo to afford a brown oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.27) yielded a colorless oil (435 mg, 1.12 mmol, 91%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 – 7.16 (m, 20H), 6.59 (dd, *J* = 15.9, 0.9 Hz, 1H), 6.42 (dd, *J* = 15.9, 6.5 Hz, 1H), 5.94 (dd, *J* = 6.5, 1.0 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.32, 140.91, 136.85, 136.72, 133.60, 132.01, 129.56, 129.35, 128.88, 128.62, 128.46, 128.27, 128.18, 128.10, 127.83, 127.70, 127.26, 126.78, 86.33.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3060, 3028, 2925 (w), 1600, 1494, 1445, 1327, 1301, 1219, 1167, 1069, 1027, 964 (s), 922, 770, 746, 695 (s), 667.

4.6.86 (*S*,*E*)-Diphenylmethanone *O*-(1,3-diphenylallyl) oxime ((*S*)-**143**)[84]



$C_{28}H_{23}NO$

[389.50]

From Carbonate:

$[PdCl(C_3H_5)]_2$ (4.4 mg, 0.012 mmol, 6.2 mol% Pd) and (*R*)-diphenyl(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (11.8 mg, 0.025 mmol, 6.5 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 20 minutes the yellow solution was cooled with an ice bath and a solution of (*E*)-1,3-diphenylallyl ethyl carbonate (108 mg, 0.383 mmol, 1.0 equiv) and diphenylmethanone oxime (79.0 mg, 0.401 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) was added. The reaction was monitored by TLC and after 4 hours the reaction solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo to afford a brown oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.29) yielded a colorless oil (139 mg, 0.357 mmol, 93%, 81% ee - IC, *n*-hexane/*i*PrOH 99:1, 0.3 ml/min).

From Acetate:

$[PdCl(C_3H_5)]_2$ (3.0 mg, 0.0082 mmol, 4.1 mol% Pd) and (*R*)-diphenyl(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (7.8 mg, 0.017 mmol, 4.2 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 25 minutes the yellow solution was cooled with an ice bath and a solution of (*E*)-1,3-diphenylallyl acetate (121 mg, 0.480 mmol, 1.2 equiv) and diphenylmethanone oxime (79.1 mg, 0.401 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) as well as DIPEA (0.14 mL, 0.804 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 21 hours additional diphenylmethanone oxime (16.1 mg, 0.0816 mmol, 0.2 equiv) was added. After another 30 hours the reaction solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.29) yielded a colorless oil (150 mg, 0.385 mmol, 80%, 88% ee - IC, *n*-hexane/*i*PrOH 99:1, 0.3 ml/min).

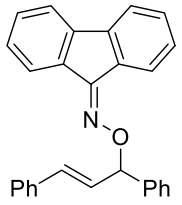
$[PdCl(C_3H_5)]_2$ (3.0 mg, 0.0082 mmol, 3.4 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (9.0 mg, 0.017 mmol, 3.5 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 25 minutes the yellow solution was cooled with an ice bath and a solution of (*E*)-1,3-diphenylallyl acetate (122 mg, 0.484 mmol, 1.0 equiv) and diphenylmethanone oxime (99.0 mg, 0.502 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) as well as dry, degassed DIPEA (0.15 mL, 0.861 mmol, 1.8 equiv) were added. The reaction was monitored by TLC and after 24 hours additional diphenylmethanone oxime (53.4 mg, 0.271 mmol, 0.56 equiv) was added. After another 24 hours the reaction solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.29) yielded a colorless oil (147 mg, 0.378 mmol, 78%, 90% ee - IC, *n*-hexane/*i*PrOH 99:1, 0.3 ml/min).

$[PdCl(C_3H_5)]_2$ (3.0 mg, 0.0082 mmol, 3.9 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (10.8 mg, 0.021 mmol, 5.0 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled with an ice bath and a solution of (*E*)-1,3-diphenylallyl acetate (105 mg, 0.416 mmol, 1.0 equiv) and diphenylmethanone oxime (320 mg, 1.62 mmol, 3.9 equiv) in dry, degassed MeCN (4.4 mL) as well as dry, degassed DIPEA (0.28 mL, 1.61 mmol, 3.9 equiv) were added. The reaction was monitored by TLC and after 3 days the reaction solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo to afford an orange solid. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.29) yielded a colorless oil (123 mg, 0.316 mmol, 76%, 92% ee - IC, *n*-hexane/*i*PrOH 99:1, 0.3 ml/min).

$[PdCl(C_3H_5)]_2$ (3.7 mg, 0.010 mmol, 5.0 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (10.4 mg, 0.020 mmol, 5.0 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-diphenylallyl acetate (101 mg, 0.400 mmol, 1.0 equiv) and diphenylmethanone oxime (80.0 mg, 0.406 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) as well as dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 2 days the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (Al_2O_3 – neutral, III; *n*-hexane/EtOAc 99:1) yielded a colorless oil (122 mg, 0.313 mmol, 78%, 91% ee - IC, *n*-hexane/*i*PrOH 99:1, 0.3 ml/min).

$[PdCl(C_3H_5)]_2$ (3.4 mg, 0.0093 mmol, 4.6 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (10.0 mg, 0.0192 mmol, 4.9 mol%) were dissolved in dry CH_2Cl_2 (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-diphenylallyl acetate (102 mg, 0.404 mmol, 1.0 equiv) and diphenylmethanone oxime (79.2 mg, 0.402 mmol, 1.0 equiv) in dry CH_2Cl_2 (1.4 mL) as well as 2,4,6-collidine (0.10 mL, 0.75 mmol, 1.9 equiv) were added. The reaction was monitored by TLC but showed no conversion after 2 days.

4.6.87 (*E*)-9*H*-Fluoren-9-one *O*-(1,3-diphenylallyl) oxime (**144**)



$C_{28}H_{21}NO$

[387.48]

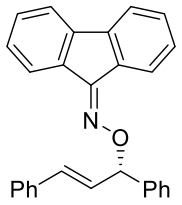
(*E*)-1,3-Diphenylallyl ethyl carbonate (108 mg, 0.383 mmol, 1.0 equiv) and 9*H*-fluoren-9-one oxime (74.7 mg, 0.383 mmol, 1.0 equiv) were dissolved in dry, degassed MeCN (5 mL). $Pd(PPh)_4$ (17.9 mg, 0.0155 mmol, 4.0 mol%) was added and the reaction monitored by TLC. After 16 hours the solvent was removed in vacuo to afford a brown oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.33) yielded a highly viscous yellow oil (143 mg, 0.369 mmol, 96%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.72 (ddt, *J* = 30.9, 7.5, 1.0 Hz, 2H), 7.62 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.60 – 7.54 (m, 2H), 7.51 – 7.20 (m, 12H), 6.77 (d, *J* = 16.0 Hz, 1H), 6.65 (dd, *J* = 16.0, 6.2 Hz, 1H), 6.13 (d, *J* = 6.2 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 152.76, 141.57, 140.49, 140.30, 136.68, 135.74, 132.92, 131.05, 130.77, 129.93, 129.49, 129.06, 128.70, 128.68, 128.39, 128.09, 128.03, 127.92, 127.39, 126.88, 121.98, 119.95, 119.92, 87.78.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3059 (w), 3027 (w), 1607, 1494, 1449, 1322, 1155, 1018, 959 (s), 923, 783, 745, 732, 697, 638.

4.6.88 (*S*,*E*)-9*H*-Fluoren-9-one *O*-(1,3-diphenylallyl) oxime ((*S*)-**144**)

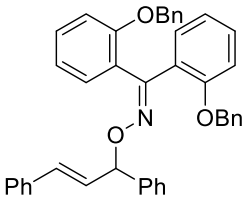


$C_{28}H_{21}NO$

[387.48]

$[PdCl(C_3H_5)]_2$ (4.4 mg, 0.012 mmol, 6.2 mol% Pd) and (*R*)-diphenyl(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (11.2 mg, 0.024 mmol, 6.2 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 20 minutes the yellow solution was cooled with an ice bath and a solution of (*E*)-1,3-diphenylallyl ethyl carbonate (110 mg, 0.390 mmol, 1.0 equiv) and 9*H*-fluoren-9-one oxime (78.1 mg, 0.400 mmol, 1.0 equiv) in dry, degassed MeCN (4.4 mL) was added. The reaction was monitored by TLC and after 6 hours the reaction solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.33) yielded a highly viscous yellow oil (147 mg, 0.379 mmol, 97%, 81% ee - IC, *n*-hexane/*i*PrOH 99:1, 0.3 ml/min).

4.6.89 (*E*)-Bis(2-(benzyloxy)phenyl)methanone *O*-(1,3-diphenylallyl) oxime (**145**)



$C_{42}H_{35}NO_3$

[601.75]

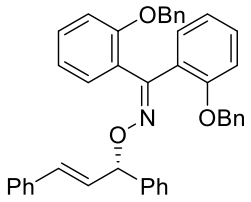
(*E*)-1,3-Diphenylallyl ethyl carbonate (156 mg, 0.553 mmol, 1.0 equiv) and bis(2-(benzyloxy)phenyl)methanone oxime (230 mg, 0.562 mmol, 1.0 equiv) were dissolved in dry, degassed MeCN (3 mL). $Pd(PPh)_4$ (29.7 mg, 0.0227 mmol, 4.6 mol%) was added and the reaction monitored by TLC. After 22 hours the solvent was removed in vacuo to afford a brown oil. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.29) yielded a highly viscous yellow oil (266 mg, 0.442 mmol, 80%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.31 – 7.14 (m, 19H), 7.10 (dd, *J* = 7.1, 2.8 Hz, 2H), 6.96 (dd, *J* = 7.6, 1.9 Hz, 2H), 6.86 (ddt, *J* = 18.0, 8.2, 3.5 Hz, 4H), 6.48 (d, *J* = 16.0 Hz, 1H), 6.33 (dd, *J* = 16.0, 6.4 Hz, 1H), 5.86 (d, *J* = 6.4 Hz, 1H), 4.78 (d, *J* = 1.9 Hz, 4H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.06, 155.73, 154.84, 141.11, 137.39, 136.98, 136.84, 131.59, 131.44, 130.23, 129.93, 129.75, 129.41, 128.51, 128.31, 128.25, 127.68, 127.65, 127.60, 127.41, 127.38, 127.20, 127.01, 126.86, 126.74, 125.31, 120.81, 120.17, 112.79, 112.44, 85.70, 70.31, 69.94.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3060 (w), 3030, 2869, 1599, 1493, 1448, 1274, 1238, 1109, 1023, 962, 914, 748 (s), 696.

4.6.90 (*S*,*E*)-Bis(2-(benzyloxy)phenyl)methanone *O*-(1,3-diphenylallyl) oxime ((*S*)-**145**)



$C_{42}H_{35}NO_3$

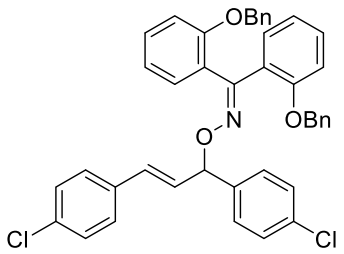
[601.75]

$[PdCl(C_3H_5)]_2$ (4.4 mg, 0.012 mmol, 6.2 mol% Pd) and (*R*)-diphenyl(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (11.8 mg, 0.025 mmol, 6.5 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 20 minutes the yellow solution was cooled with an ice bath

and a solution of (*E*)-1,3-diphenylallyl ethyl carbonate (109 mg, 0.386 mmol, 1.0 equiv) and diphenylmethanone oxime (164 mg, 0.400 mmol, 1.0 equiv) in dry, degassed MeCN (2.4 mL) was added. The reaction was monitored by TLC and after 4 hours the reaction solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.29) yielded a colorless oil (166 mg, 0.276 mmol, 72%).

The enantiomeric excess was not determined due to insufficient separation by chiral HPLC.

4.6.91 (*E*)-Bis(2-(benzyloxy)phenyl)methanone *O*-(1,3-bis(4-chlorophenyl)allyl) oxime (**146**)



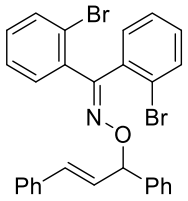
$C_{42}H_{33}Cl_2NO_3$

[670.63]

(*E*)-1,3-Bis(4-chlorophenyl)allyl ethyl carbonate (254 mg, 0.723 mmol, 1.0 equiv) and bis(2-(benzyloxy)phenyl)methanone oxime (296 mg, 0.723 mmol, 1.0 equiv) were dissolved in dry, degassed MeCN (5 mL). $Pd(PPh)_4$ (34.1 mg, 0.0295 mmol, 4.1 mol%) was added and the reaction monitored by TLC. After 16 hours the solvent was removed in vacuo to afford a brown oil. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.29) yielded an off-white solid (350 mg, 0.522 mmol, 72%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.34 – 7.07 (m, 19H), 7.00 – 6.81 (m, 6H), 6.38 (d, *J* = 16.0 Hz, 1H), 6.24 (dd, *J* = 16.0, 6.3 Hz, 1H), 5.79 (dd, *J* = 6.3, 1.0 Hz, 1H), 4.80 (s, 2H), 4.77 (s, 2H).

4.6.92 (*E*)-Bis(2-bromophenyl)methanone *O*-(1,3-diphenylallyl) oxime (**147**)



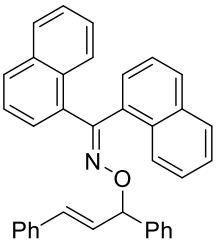
$C_{28}H_{21}Br_2NO$

[547.29]

(*E*)-1,3-Diphenylallyl ethyl carbonate (53.1 mg, 0.188 mmol, 1.0 equiv) and bis(2-bromophenyl)methanone oxime (68.0 mg, 0.191 mmol, 1.0 equiv) were dissolved in dry, degassed MeCN (1 mL). $Pd(PPh)_4$ (14.0 mg, 0.0121 mmol, 6.4 mol%) was added and the reaction monitored by TLC. After 18 hours the solvent was removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.29) yielded a highly viscous yellow oil. The yield could not be determined due to insufficient purity of the obtained compound.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.00 (m, 18H), 6.59 (d, *J* = 16.0 Hz, 1H), 6.45 (dd, *J* = 15.9, 6.4 Hz, 1H), 5.95 (d, *J* = 6.4 Hz, 1H).

4.6.93 (*E*)-Di(naphthalen-1-yl)methanone *O*-(1,3-diphenylallyl) oxime



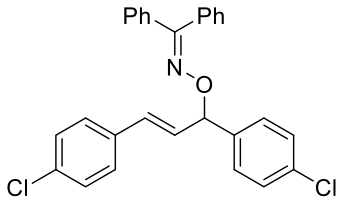
$C_{28}H_{21}Br_2NO$

[547.29]

(*E*)-1,3-Diphenylallyl ethyl carbonate (60.0 mg, 0.213 mmol, 1.0 equiv) and the solid obtained by oxime formation reaction of di(naphthalen-1-yl)methanone (64.0 mg) were dissolved in

dry, degassed MeCN (1 mL). $Pd(PPh)_4$ (10.0 mg, 0.00865 mmol, 4.1 mol%) was added and the reaction monitored by TLC. Since TLC showed no transformation the reaction solution was discarded.

4.6.94 (*E*)-Diphenylmethanone *O*-(1,3-bis(4-chlorophenyl)allyl) oxime (**149**)



$C_{28}H_{21}Cl_2NO$

[458.38]

(*E*)-1,3-Bis(4-chlorophenyl)allyl ethyl carbonate (270 mg, 0.769 mmol, 1.0 equiv) and diphenylmethanone oxime (165 mg, 0.837 mmol, 1.1 equiv) were dissolved in dry, degassed MeCN (5 mL). $Pd(PPh)_4$ (37.0 mg, 0.0320 mmol, 4.2 mol%) was added and the reaction monitored by TLC. After 23 hours the solvent was removed in vacuo to afford a brown oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.34) yielded a highly viscous yellow oil (287 mg, 0.626 mmol, 81%).

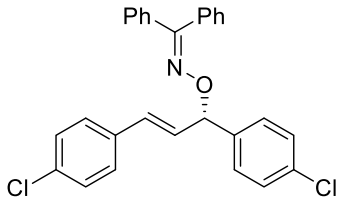
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 – 7.23 (m, 18H), 6.51 (dd, *J* = 16.0, 1.1 Hz, 1H), 6.36 (dd, *J* = 15.9, 6.3 Hz, 1H), 5.89 (dd, *J* = 6.3, 1.0 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.77, 139.24, 136.45, 135.10, 133.62, 133.58, 133.44, 131.09, 129.60, 129.54, 129.43, 129.00, 128.81, 128.70, 128.67, 128.32, 128.17, 128.14, 127.99, 85.37.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3058 (w), 1593, 1490, 1444, 1405, 1326, 1301, 1091, 1013, 965, 907, 828, 772, 696, 658.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{28}H_{22}Cl_2NO$, 458.107; found, 458.107; $[M – Ph_2C{=}N{-}O]^+$ calcd for $C_{15}H_{11}Cl_2$, 261.023; found, 261.023.

4.6.95 (*S*,*E*)-Diphenylmethanone *O*-(1,3-bis(4-chlorophenyl)allyl) oxime ((*S*)-**149**)



$C_{28}H_{21}Cl_2NO$

[458.38]

$[PdCl(C_3H_5)]_2$ (3.0 mg, 0.0082 mmol, 4.0 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (8.7 mg, 0.017 mmol, 4.2 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled with an ice bath and a solution of (*E*)-1,3-bis(4-chlorophenyl)allyl acetate (130 mg, 0.405 mmol, 1.0 equiv) and diphenylmethanone oxime (130 mg, 0.659 mmol, 1.6 equiv) in dry, degassed MeCN (2.4 mL) as well as dry, degassed DIPEA (0.29 mL, 1.7 mmol, 4.1 equiv) were added. The reaction was monitored by TLC and after 2 days the reaction solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.34) yielded a colorless oil (167 mg, 0.364 mmol, 90%, 86% ee - IC, *n*-hexane/*i*PrOH 99.5:0.5, 1.0 ml/min).

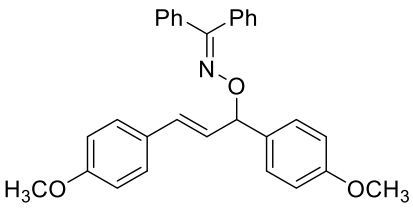
$[\alpha]_D^{20}$ – 8.34 (*c* 1.00, $CHCl_3$)

$[PdCl(C_3H_5)]_2$ (3.7 mg, 0.010 mmol, 5.1 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (10.7 mg, 0.0205 mmol, 5.2 mol%) were dissolved in dry, degassed MeCN (0.5 mL). After 30 minutes the yellow solution was cooled with an ice bath and a solution of (*E*)-1,3-bis(4-chlorophenyl)allyl acetate (127 mg, 0.395 mmol, 1.0 equiv) and diphenylmethanone oxime (315 mg, 1.60 mmol, 4.0 equiv) in dry, degassed MeCN (5.5 mL) as well as dry, degassed DIPEA (0.28 mL, 1.6 mmol, 4.1 equiv) were added. The reaction was monitored by TLC and after 24 hours the reaction solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo to afford a yellow solid. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.34) yielded a colorless oil (167 mg, 0.364 mmol, 92%, 84% ee - IC, *n*-hexane/*i*PrOH 99.5:0.5, 1.0 ml/min). After 4 days the ee had reduced to 81%.

$[PdCl(C_3H_5)]_2$ (3.7 mg, 0.010 mmol, 4.6 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (10.4 mg, 0.0200 mmol, 4.6 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-bis(4-chlorophenyl)allyl acetate (140 mg, 0.436 mmol, 1.0 equiv) and diphenylmethanone oxime (86.0 mg, 0.436 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) as well as dry, degassed DIPEA (0.14 mL, 0.80 mmol, 1.8 equiv) were added. The reaction was monitored by TLC and after 24 hours the solvent removed in vacuo. Purification by column chromatography (Al_2O_3 – neutral, III; *n*-hexane/EtOAc 99:1) yielded a colorless oil (166 mg, 0.362 mmol, 83%, 84% ee - IC, *n*-hexane/*i*PrOH 99.5:0.5, 1.0 ml/min).

$[PdCl(C_3H_5)]_2$ (3.7 mg, 0.010 mmol, 5.0 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (10.6 mg, 0.0204 mmol, 5.1 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to -20 °C and a solution of (*E*)-1,3-bis(4-chlorophenyl)allyl acetate (129 mg, 0.402 mmol, 1.0 equiv) and diphenylmethanone oxime (79.4 mg, 0.403 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) as well as dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 24 hours the solvent removed in vacuo. Purification by column chromatography (Al_2O_3 – neutral, III; *n*-hexane/EtOAc 99:1) yielded a colorless oil (152 mg, 0.332 mmol, 83%, 66% ee - IC, *n*-hexane/*i*PrOH 99.5:0.5, 1.0 ml/min).

4.6.96 (*E*)-Diphenylmethanone *O*-(1,3-bis(4-methoxyphenyl)allyl) oxime (**150**)



$C_{30}H_{27}NO_3$

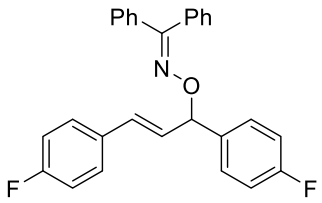
[449.55]

(*E*)-1,3-Bis(4-methoxyphenyl)allyl acetate (248 mg, 0.794 mmol, 1.0 equiv) and diphenylmethanone oxime (180 mg, 0.913 mmol, 1.0 equiv) were dissolved in dry, degassed CH_2Cl_2 (5 mL). $Pd(PPh)_4$ (55.3 mg, 0.0479 mmol, 6.0 mol%) and DIPEA (0.13 mL, 0.75 mmol, 0.94 equiv) were added and the reaction monitored by TLC. After 4 days the

solvent was removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.29) yielded a yellow solid (298 mg, 0.663 mmol, 84%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.71 – 7.62 (m, 2H), 7.47 – 7.36 (m, 4H), 7.22 – 6.98 (m, 8H), 6.86 – 6.76 (m, 2H), 6.72 – 6.59 (m, 3H), 6.48 (dd, *J* = 15.9, 6.4 Hz, 1H), 6.18 – 6.09 (m, 1H), 3.28 (s, 3H), 3.25 (s, 3H).

4.6.97 (*E*)-Diphenylmethanone *O*-(1,3-bis(4-fluorophenyl)allyl) oxime (**151**)



$C_{28}H_{21}F_2NO$

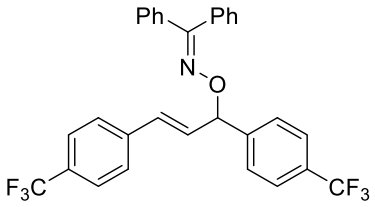
[425.48]

(*E*)-1,3-Bis(4-fluorophenyl)allyl acetate (280 mg, 0.971 mmol, 1.0 equiv) and diphenylmethanone oxime (193 mg, 0.979 mmol, 1.0 equiv) were dissolved in dry, degassed MeCN (5 mL). $Pd(PPh)_4$ (59.0 mg, 0.0511 mmol, 5.3 mol%) and DIPEA (0.68 mL, 3.9 mmol, 4.0 equiv) were added and the reaction monitored by TLC. Since the reaction was incomplete after 24 hours additional $Pd(PPh)_4$ (25.0 mg, 0.0216 mmol, 2.2 mol%) was added. After another 24 hours the solvent was removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.31) yielded a highly viscous colorless oil (205 mg, 0.481 mmol, 50%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 – 7.27 (m, 14H), 7.09 – 6.92 (m, 4H), 6.51 (d, *J* = 16.0 Hz, 1H), 6.31 (dd, *J* = 16.0, 6.4 Hz, 1H), 5.88 (d, *J* = 6.4 Hz, 1H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -114.10, -114.85.

4.6.98 (*E*)-Diphenylmethanone *O*-(1,3-bis(4-(trifluoromethyl)phenyl)allyl) oxime (**152**)



$C_{30}H_{21}F_6NO$

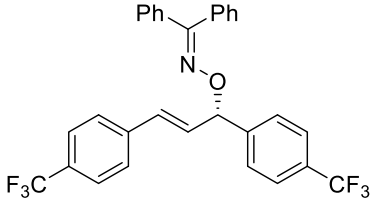
[525.49]

(*E*)-1,3-Bis(4-(trifluoro)phenyl)allyl acetate (300 mg, 0.773 mmol, 1.0 equiv) and diphenylmethanone oxime (155 mg, 0.786 mmol, 1.0 equiv) were dissolved in dry, degassed MeCN (5 mL). $Pd(PPh)_4$ (51.0 mg, 0.0441 mmol, 5.7 mol%) and DIPEA (0.28 mL, 1.6 mmol, 2.1 equiv) were added and the reaction monitored by TLC. After 3 days the solvent was removed in vacuo to afford a yellow solid. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.43) yielded a highly viscous yellow oil (204 mg, 0.388 mmol, 50%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.75 – 7.56 (m, 2H), 7.40 – 7.33 (m, 4H), 7.28 – 7.10 (m, 7H), 7.08 – 7.01 (m, 3H), 6.84 (d, *J* = 8.1 Hz, 2H), 6.37 (d, *J* = 16.0 Hz, 1H), 6.23 (dd, *J* = 16.0, 6.4 Hz, 1H), 5.90 (d, *J* = 6.3 Hz, 1H).

^{19}F NMR (282 MHz, C_6D_6) δ -62.20, -62.24.

4.6.99 (*S*,*E*)-Diphenylmethanone *O*-(1,3-bis(4-(trifluoromethyl)phenyl)allyl) oxime ((*S*)-**152**)

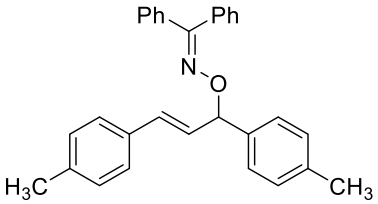


$C_{30}H_{21}F_6NO$

[525.49]

$[PdCl(C_3H_5)]_2$ (4.0 mg, 0.011 mmol, 5.0 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (11.7 mg, 0.0225 mmol, 5.1 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled with an ice bath and a solution of (*E*)-1,3-bis(4-chlorophenyl)allyl acetate (170 mg, 0.438 mmol, 1.0 equiv) and diphenylmethanone oxime (90.2 mg, 0.457 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) as well as dry, degassed DIPEA (0.16 mL, 0.92 mmol, 2.1 equiv) were added. The reaction was monitored by TLC and after 3 days the reaction solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.43) yielded a colorless oil (174 mg, 0.331 mmol, 76%).

4.6.100 (*E*)-Diphenylmethanone *O*-(1,3-di-*p*-tolylallyl) oxime (**153**)



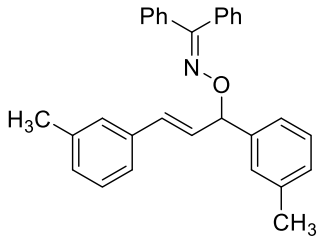
$C_{30}H_{27}NO$

[417.55]

(*E*)-1,3-Di-*p*-tolylallyl acetate (235 mg, 0.838 mmol, 1.0 equiv) and diphenylmethanone oxime (169 mg, 0.857 mmol, 1.0 equiv) were dissolved in dry, degassed MeCN (5 mL). $Pd(PPh)_4$ (58.0 mg, 0.0502 mmol, 6.0 mol%) and DIPEA (0.28 mL, 1.6 mmol, 1.9 equiv) were added and the reaction monitored by TLC. After 7 days the solvent was removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 99:1, R_f = 0.19) yielded a highly viscous colorless oil (141 mg, 0.338 mmol, 40%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.68 – 7.61 (m, 2H), 7.44 – 7.36 (m, 4H), 7.19 – 7.07 (m, 5H), 7.06 – 6.98 (m, 5H), 6.88 (d, *J* = 7.9 Hz, 2H), 6.67 (d, *J* = 16.0 Hz, 1H), 6.54 (dd, *J* = 16.0, 6.3 Hz, 1H), 6.13 (d, *J* = 6.3 Hz, 1H), 2.10 (s, 3H), 2.05 (s, 3H).

4.6.101 (*E*)-Diphenylmethanone *O*-(1,3-di-*m*-tolylallyl) oxime (**154**)



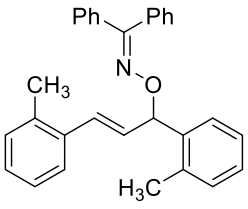
$C_{30}H_{27}NO$

[417.55]

(*E*)-1,3-Di-*m*-tolylallyl acetate (192 mg, 0.685 mmol, 1.0 equiv) and diphenylmethanone oxime (139 mg, 0.705 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (5 mL). $Pd(PPh)_4$ (59.9 mg, 0.0518 mmol, 7.6 mol%) and DIPEA (0.24 mL, 1.4 mmol, 2.0 equiv) were added and the reaction monitored by TLC. After 22 hours the solvent was removed in vacuo (bath temp. 40 °C). Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.43) yielded a highly viscous colorless oil (191 mg, 0.457 mmol, 67%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.70 – 7.57 (m, 2H), 7.46 – 7.27 (m, 4H), 7.22 – 6.80 (m, 12H), 6.69 (dd, *J* = 15.9, 0.9 Hz, 1H), 6.56 (dd, *J* = 15.9, 6.4 Hz, 1H), 6.14 (d, *J* = 6.4 Hz, 1H), 2.11 (s, 3H), 2.02 (s, 3H).

4.6.102 (*E*)-Diphenylmethanone *O*-(1,3-di-*o*-tolylallyl) oxime (**155**)



$C_{30}H_{27}NO$

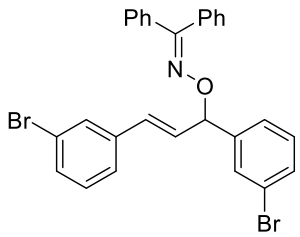
[417.55]

(*E*)-1,3-Di-*o*-tolylallyl acetate (250 mg, 0.892 mmol, 1.0 equiv) and diphenylmethanone oxime (177 mg, 0.897 mmol, 1.0 equiv) were dissolved in dry, degassed MeCN (5 mL). $Pd(PPh)_4$

(49.1 mg, 0.0425 mmol, 4.8 mol%) and DIPEA (0.61 mL, 3.50 mmol, 3.9 equiv) were added and the reaction monitored by TLC. Since the reaction was incomplete after 24 hours additional $Pd(PPh)_4$ (20.0 mg, 0.0173 mmol, 1.9 mol%) was added. After another 24 hours the solvent was removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.46) yielded a highly viscous colorless oil (185 mg, 0.443 mmol, 50%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 – 7.40 (m, 8H), 7.38 – 7.28 (m, 4H), 7.24 – 7.12 (m, 6H), 6.80 (dd, *J* = 15.7, 1.2 Hz, 1H), 6.28 (dd, *J* = 15.7, 6.1 Hz, 1H), 6.17 (dd, *J* = 6.1, 1.2 Hz, 1H), 2.43 (s, 3H), 2.30 (s, 3H).

4.6.103 (*E*)-Diphenylmethanone *O*-(1,3-bis(3-bromophenyl)allyl) oxime (**156**)



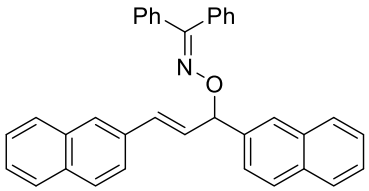
$C_{28}H_{21}Br_2NO$

[547.29]

(*E*)-1,3-Bis(3-bromophenyl)allyl acetate (313 mg, 0.763 mmol, 1.0 equiv) and diphenylmethanone oxime (154 mg, 0.781 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (5 mL). $Pd(PPh)_4$ (60.0 mg, 0.0519 mmol, 6.8 mol%) and DIPEA (0.27 mL, 1.6 mmol, 2.0 equiv) were added and the reaction monitored by TLC. After 22 hours the solvent was removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.34) yielded a highly viscous yellow oil (358 mg, 0.654 mmol, 86%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.63 (t, *J* = 1.9 Hz, 1H), 7.62 – 7.56 (m, 2H), 7.38 – 6.94 (m, 12H), 6.82 – 6.72 (m, 2H), 6.61 (t, *J* = 7.8 Hz, 1H), 6.29 (dd, *J* = 15.9, 1.0 Hz, 1H), 6.10 (dd, *J* = 15.9, 6.6 Hz, 1H), 5.82 (d, *J* = 6.6 Hz, 1H).

4.6.104 (*E*)-Diphenylmethanone *O*-(1,3-di(naphthalen-2-yl)allyl) oxime (**157**)[150]



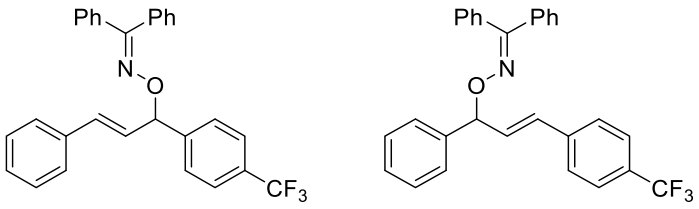
$C_{36}H_{27}NO$

[489.62]

(*E*)-1,3-Di(naphthalen-2-yl)allyl acetate (141 mg, 0.400 mmol, 1.0 equiv) and diphenylmethanone oxime (80.0 mg, 0.406 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (10 mL). $Pd(PPh)_4$ (27.0 mg, 0.0234 mmol, 5.8 mol%) and DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added and the reaction monitored by TLC. After 3 days the solvent was removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.22) yielded a highly viscous yellow solid (93.8 mg, 0.192 mmol, 48%).

^{1}H NMR (300 MHz, C_6D_6) δ 7.94 (d, *J* = 1.5 Hz, 1H), 7.71 – 7.50 (m, 8H), 7.49 – 7.44 (m, 4H), 7.35 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.30 – 7.08 (m, 7H), 7.05 – 6.98 (m, 3H), 6.82 (d, *J* = 16.0 Hz, 1H), 6.71 (dd, *J* = 16.0, 6.0 Hz, 1H), 6.34 (d, *J* = 6.0 Hz, 1H).

4.6.105 (*E*)-Diphenylmethanone *O*-(3-phenyl-1-(4-(trifluoromethyl)phenyl)allyl) oxime (**158**)
(*E*)-Diphenylmethanone *O*-(1-phenyl-3-(4-(trifluoromethyl)phenyl)allyl) oxime (**159**)



$C_{29}H_{22}F_3NO$

[457.50]

(*E*)-3-Phenyl-1-(4-(trifluoromethyl)phenyl)allyl acetate (255 mg, 0.796 mmol, 1.0 equiv) and diphenylmethanone oxime (158 mg, 0.801 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2

(5 mL). $Pd(PPh)_4$ (48.0 mg, 0.0415 mmol, 5.2 mol%) and DIPEA (0.28 mL, 1.6 mmol, 2.0 equiv) were added and the reaction monitored by TLC. After 19 hours the solvent was removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.40) yielded a highly viscous yellowish oil (265 mg, 0.579 mmol, 73%, **158**:**159** 0.94:1.00).

Minor product **158**:

^{1}H NMR (300 MHz, C_6D_6) δ 7.67 – 7.57 (m, 2H), 7.44 – 7.31 (m, 4H), 7.28 – 6.97 (m, 14H), 6.55 (dd, *J* = 15.9, 1.1 Hz, 1H), 6.31 (dd, *J* = 15.9, 6.8 Hz, 1H), 5.95 (d, *J* = 6.8 Hz, 1H).

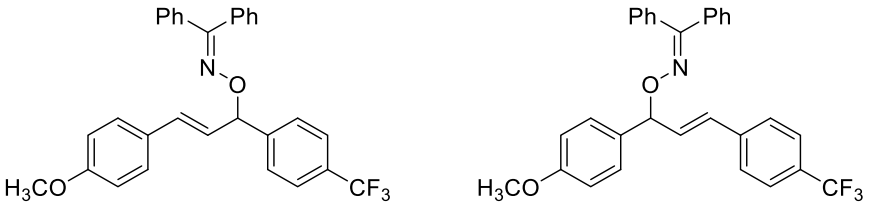
^{19}F NMR (282 MHz, C_6D_6) δ -62.14.

Major product **159**:

^{1}H NMR (300 MHz, C_6D_6) δ 7.67 – 7.57 (m, 2H), 7.44 – 7.31 (m, 4H), 7.28 – 6.97 (m, 12H), 6.83 (d, *J* = 8.1 Hz, 2H), 6.42 (s, 1H), 6.40 (d, *J* = 5.0 Hz, 1H), 6.04 (d, *J* = 5.0 Hz, 1H).

^{19}F NMR (282 MHz, C_6D_6) δ -62.17.

4.6.106 (*E*)-Diphenylmethanone *O*-(3-(4-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)allyl) oxime (**160**) (*E*)-Diphenylmethanone *O*-(1-(4-methoxyphenyl) -3-(4-(trifluoromethyl)phenyl)allyl) oxime (**161**)



$C_{30}H_{24}F_3NO_2$

[487.52]

(*E*)-3-(4-Methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)allyl acetate (270 mg, 0.771 mmol, 1.0 equiv) and diphenylmethanone oxime (153 mg, 0.776 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (5 mL). $Pd(PPh)_4$ (45.6 mg, 0.0395 mmol, 5.1 mol%) and DIPEA (0.28 mL,

1.6 mmol, 2.0 equiv) were added and the reaction monitored by TLC. After 2 days the solvent was removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.49) yielded a highly viscous yellow oil (225 mg, 0.462 mmol, 60%, **160**:**161** 0.14:1.00).

Minor product **160**:

^{1}H NMR (300 MHz, C_6D_6) δ 7.70 – 7.59 (m, 2H), 7.43 – 7.31 (m, 4H), 7.30 – 6.99 (m, 8H), 6.91 – 6.85 (m, 2H), 6.71 – 6.65 (m, 2H), 6.56 (d, *J* = 15.9 Hz, 1H), 6.25 (dd, *J* = 15.9, 7.0 Hz, 1H), 5.99 (d, *J* = 7.0 Hz, 1H), 3.25 (s, 3H).

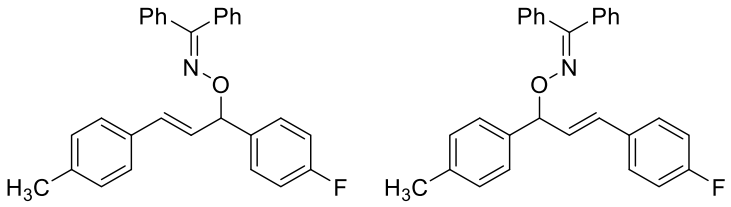
^{19}F NMR (282 MHz, C_6D_6) δ -62.11.

Major product **161**:

^{1}H NMR (300 MHz, C_6D_6) δ 7.70 – 7.59 (m, 2H), 7.43 – 7.31 (m, 4H), 7.30 – 6.99 (m, 8H), 6.91 – 6.85 (m, 2H), 6.85 – 6.78 (m, 2H), 6.46 (s, 1H), 6.46 (s, 1H), 6.04 (t, *J* = 2.5 Hz, 1H), 3.28 (s, 3H).

^{19}F NMR (282 MHz, C_6D_6) δ -62.16.

4.6.107 (*E*)-Diphenylmethanone *O*-(1-(4-fluorophenyl)-3-(*p*-tolyl)allyl) oxime (**162**)
(*E*)-Diphenylmethanone *O*-(3-(4-fluorophenyl)-1-(*p*-tolyl)allyl) oxime (**163**)



$C_{29}H_{24}FNO$

[421.52]

(*E*)-1-(4-Fluorophenyl)-3-(*p*-tolyl)allyl acetate (212 mg, 0.740 mmol, 1.0 equiv) and diphenylmethanone oxime (149 mg, 0.755 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (5 mL). $Pd(PPh)_4$ (45.2 mg, 0.0391 mmol, 5.3 mol%) and DIPEA (0.26 mL, 1.5 mmol,

2.0 equiv) were added and the reaction monitored by TLC. After 24 hours the reaction was heated to 30 °C bath temp. After another 2 days the solvent was removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.43) yielded a highly viscous colorless oil (218 mg, 0.517 mmol, 70%, **162**:**163** 0.94:1.00).

Minor product **162**:

^{1}H NMR (300 MHz, C_6D_6) δ 7.67 – 7.59 (m, 2H), 7.43 – 7.33 (m, 3H), 7.25 – 7.07 (m, 5H), 7.03 (ddd, *J* = 5.8, 2.4, 1.2 Hz, 4H), 6.87 – 6.76 (m, 2H), 6.71 – 6.63 (m, 2H), 6.48 (d, *J* = 15.9 Hz, 1H), 6.34 (ddd, *J* = 15.9, 6.3, 0.3 Hz, 1H), 6.07 (d, *J* = 6.3 Hz, 1H), 2.10 (s, 3H).

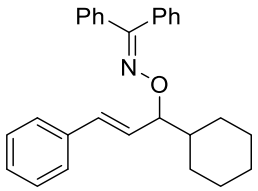
^{19}F NMR (282 MHz, C_6D_6) δ -114.36.

Major product **163**:

^{1}H NMR (300 MHz, C_6D_6) δ 7.67 – 7.59 (m, 2H), 7.43 – 7.33 (m, 3H), 7.25 – 7.07 (m, 5H), 7.03 (ddd, *J* = 5.8, 2.4, 1.2 Hz, 4H), 6.90 (d, *J* = 7.9 Hz, 2H), 6.87 – 6.76 (m, 2H), 6.60 (d, *J* = 16.0 Hz, 1H), 6.41 (dd, *J* = 16.0, 6.6 Hz, 1H), 5.99 (d, *J* = 6.6 Hz, 1H), 2.06 (s, 3H).

^{19}F NMR (282 MHz, C_6D_6) δ -114.78.

4.6.108 (*E*)-Diphenylmethanone *O*-(1-cyclohexyl-3-phenylallyl) oxime (**164**)



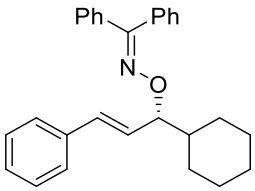
$C_{29}H_{24}FNO$

[421.52]

(*E*)-1-Cyclohexyl-3-phenylallyl acetate (194 mg, 0.745 mmol, 1.0 equiv) and diphenylmethanone oxime (149 mg, 0.755 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (5 mL). $Pd(PPh)_4$ (50.1 mg, 0.0434 mmol, 5.8 mol%) and DIPEA (0.26 mL, 1.5 mmol,

2.0 equiv) were added and the reaction monitored by TLC. After 2 days additional $Pd(PPh)_4$ (10.0 mg, 0.00865 mmol, 1.2 mol%) was added and after another 2 days the reaction was heated to 30 °C bath temp. After another 2 days TLC still did not show sufficient transformation. The solvent was removed in vacuo. Purification by column chromatography did not yield the desired compound.

4.6.109 (*E*)-Diphenylmethanone *O*-(1-cyclohexyl-3-phenylallyl) oxime ((*S*)-**164**)

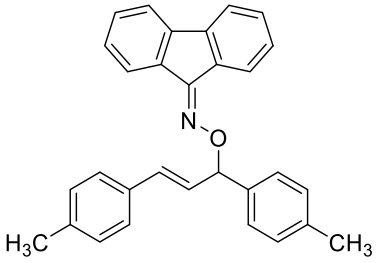


$C_{29}H_{24}FNO$

[421.52]

$[PdCl(C_3H_5)]_2$ (2.0 mg, 0.0055 mmol, 2.5 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (7.2 mg, 0.0138 mmol, 3.2 mol%) were dissolved in dry, degassed MeCN (0.7 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1-cyclohexyl-3-phenylallyl acetate (113 mg, 0.434 mmol, 1.0 equiv) and diphenylmethanone oxime (89.7 mg, 0.455 mmol, 1.0 equiv) in dry, degassed MeCN (2.0 mL) as well as dry, degassed DIPEA (0.15 mL, 0.86 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 2 days the reaction was heated to 30 °C bath temp. After another 2 days TLC still did not show sufficient transformation. The solvent was removed in vacuo (bath temp. 30 °C). Purification by column chromatography did not yield the desired compound.

4.6.110 (*E*)-9H-Fluoren-9-one *O*-(1,3-di-p-tolylallyl) oxime (**186**)



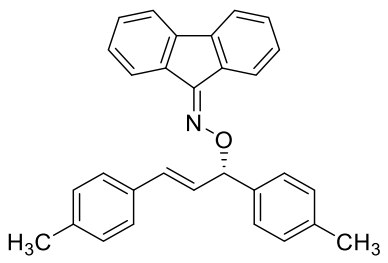
$C_{30}H_{25}NO$

[415.54]

(*E*)-1,3-Di(*p*-tolyl)allyl acetate (116 mg, 0.414 mmol, 1.0 equiv) and 9*H*-fluoren-9-one oxime (82.3 mg, 0.422 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (11 mL). $Pd(PPh)_4$ (25.0 mg, 0.0216 mmol, 5.2 mol%) was added and the reaction monitored by TLC. After 22 hours the solvent was removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.49) yielded a highly viscous yellowish oil (156 mg, 0.375 mmol, 91%).

^{1}H NMR (300 MHz, C_6D_6) δ 8.76 – 8.70 (m, 1H), 7.89 (dt, *J* = 7.4, 1.0 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.30 (ddt, *J* = 9.3, 7.5, 0.9 Hz, 2H), 7.21 – 7.16 (m, 2H), 7.13 – 7.01 (m, 5H), 6.95 (dd, *J* = 7.5, 1.1 Hz, 1H), 6.90 (dd, *J* = 8.0, 0.9 Hz, 2H), 6.76 (s, 1H), 6.74 (d, *J* = 5.1 Hz, 1H), 6.24 (d, *J* = 5.1 Hz, 1H), 2.11 (s, 3H), 2.07 (s, 3H).

4.6.111 (*R*,*E*)-9H-Fluoren-9-one *O*-(1,3-di-p-tolylallyl) oxime ((*S*)-**186**)



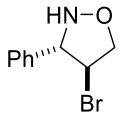
$C_{30}H_{25}NO$

[415.54]

$[PdCl(C_3H_5)]_2$ (1.8 mg, 0.0049 mmol, 2.7 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.5 mg, 0.0125 mmol, 3.4 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes a solution of (*S*,*E*)-diphenylmethanone *O*-(1,3-di-*p*-tolylallyl) oxime (151 mg, 0.362 mmol, 1.0 equiv) and 9*H*-fluoren-9-one oxime (82.3 mg, 0.422 mmol, 1.0 equiv) in dry, degassed MeCN (9.4 mL) was cooled to 0 °C and the catalyst solution as well as dry, degassed DIPEA (0.13 mL, 0.75 mmol, 2.1 equiv) were added. The reaction was monitored by TLC and after 24 hours the solvent was removed in vacuo (bath temp. 30 °C). Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.49) yielded a highly viscous yellowish oil (150 mg). The ^{1}H NMR spectrum showed a mixture of the desired compound and the substrate.

iv. Isoxazolidines

4.6.112 *trans*-4-Bromo-3-phenylisoxazolidine (**166**)[88]



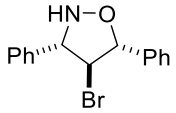
$C_9H_{10}BrNO$

[228.09]

(*E*)-Diphenylmethanone *O*-cinnamyl oxime (135 mg, 0.431 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (10 mL). $Br^+(coll)_2PF_6^-$ (221 mg, 0.474 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (20 mL) was added and the resulting mixture stirred for 2 hours. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (CH_2Cl_2, R_f = 0.43) yielded a yellow oil (68.4 mg, 0.300 mmol, 70%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 – 7.28 (m, 5H), 5.39 (s, 1H), 4.72 (d, *J* = 2.9 Hz, 1H), 4.63 (dt, *J* = 5.8, 3.2 Hz, 1H), 4.36 (ddd, *J* = 9.8, 5.8, 0.6 Hz, 1H), 4.22 (dd, *J* = 9.8, 3.3 Hz, 1H).

4.6.113 *trans*,*trans*-4-Bromo-3,5-diphenylisoxazolidine (**167**)



$C_{15}H_{14}BrNO$

[304.19]

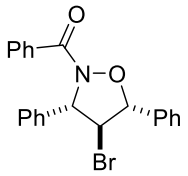
(*E*)-Diphenylmethanone *O*-(1,3-diphenylallyl) oxime (129 mg, 0.331 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (10 mL). $Br^+(coll)_2PF_6^-$ (172 mg, 0.368 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2.5 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (10 mL) was added and the resulting mixture stirred for 2 hours. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography did not afford the desired product in pure form. The ^{1}H NMR data of the title compound was derived from the spectrum of the raw material.

^{1}H NMR (300 MHz, $CDCl_3$) δ 14.53 (br s, 1H), 7.46 – 7.26 (m, 10H), 5.25 (d, *J* = 6.9 Hz, 1H), 4.88 (d, *J* = 5.1 Hz, 1H), 4.33 (dd, *J* = 6.9, 5.1 Hz, 1H).

Contains benzophenone and 2,4,6-collidine as impurities.

In a second attempt the silica gel for column chromatography was deactivated by addition of 1 vol% Et_3N to the mobile phase prior to submission of the raw material. This procedure did not afford the desired product in pure form either.

4.6.114 *trans*,*trans*-(4-Bromo-3,5-diphenylisoxazolidine-2-yl(phenyl)methanone (**168**)



$C_{22}H_{18}BrNO_2$

[408.30]

From (*E*)-Diphenylmethanone *O*-(1,3-diphenylallyl) oxime:

(*E*)-Diphenylmethanone *O*-(1,3-diphenylallyl) oxime (100 mg, 0.257 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (6 mL). $Br^+(coll)_2PF_6^-$ (134 mg, 0.287 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 3 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (12 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (6 mL). Et_3N (0.10 mL, 0.72 mmol, 2.8 equiv) and benzoyl chloride (0.10 mL, 0.86 mmol, 3.3 equiv) were added and the resulting solution stirred overnight. After 2 days H_2O was added, the aqueous phase extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown solid. To remove unreacted benzoyl chloride, this raw product was dissolved in CH_2Cl_2 and H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.33) yielded a slightly yellowish solid (60.9 mg, 0.149 mmol, 58%).

(*E*)-Diphenylmethanone *O*-(1,3-diphenylallyl) oxime (325 mg, 0.834 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (20 mL). $Br^+(coll)_2PF_6^-$ (430 mg, 0.920 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 3.5 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (40 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (20 mL). Et_3N (0.17 mL, 1.22 mmol, 1.5 equiv) and benzoyl chloride (0.15 mL, 1.29 mmol, 1.5 equiv) were added and the reaction monitored by TLC. After 17 hours H_2O and conc. NH_3 (4 mL) were added and the resulting solution stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a reddish solid. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (260 mg, 0.637 mmol, 76%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 – 7.84 (m, 2H), 7.62 – 7.56 (m, 2H), 7.53 – 7.35 (m, 11H), 5.88 (d, *J* = 5.6 Hz, 1H), 5.10 (d, *J* = 8.7 Hz, 1H), 4.30 (dd, *J* = 8.7, 5.6 Hz, 1H).

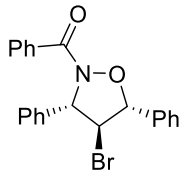
^{13}C NMR (75 MHz, $CDCl_3$) δ 171.75, 138.79, 132.96, 132.12, 132.07, 129.70, 129.63, 129.28, 128.91, 128.45, 128.18, 127.17, 126.18, 90.57, 70.82 (br s, C-N), 57.92.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3062 (w), 3033 (w), 1656 (s, C=O), 1601, 1578, 1495, 1448, 1337, 1219, 1182, 1028, 980, 913, 870, 809, 772, 737, 696 (s), 665.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{22}H_{19}BrNO_2$, 408.049; found, 408.060.

mp 85-87 °C

4.6.115 ((3*S*,4*S*,5*R*)-4-Bromo-3,5-diphenylisoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**168**)



$C_{22}H_{18}BrNO_2$

[408.30]

From (*S*,*E*)-Diphenylmethanone *O*-(1,3-diphenylallyl) oxime:

(*S*,*E*)-Diphenylmethanone *O*-(1,3-diphenylallyl) oxime (125 mg, 0.321 mmol, 1.0 equiv, 90% ee) was dissolved in dry CH_2Cl_2 (7 mL). $Br^+(coll)_2PF_6^-$ (170 mg, 0.364 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 3 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (14 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (7 mL). Et_3N (0.10 mL, 0.72 mmol, 2.2 equiv) and benzoyl chloride (0.06 mL, 0.52 mmol, 1.6 equiv) were added and the reaction monitored by TLC. After 18 hours H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a reddish solid. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (101 mg, 0.247 mmol, 77%, 79% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

(*S*,*E*)-Diphenylmethanone *O*-(1,3-diphenylallyl) oxime (120 mg, 0.308 mmol, 1.0 equiv, 92% ee) was dissolved in dry CH_2Cl_2 (7 mL). 2,4,6-Collidine (0.05 mL, 0.38 mmol, 1.2 equiv) was added and successively $Br^+(coll)_2PF_6^-$ (160 mg, 0.342 mmol, 1.1 equiv) was added under exclusion of light. The reaction was monitored by TLC and after 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (14 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was and extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid.

This raw product was dissolved in dry CH_2Cl_2 (7 mL). Et_3N (0.10 mL, 0.72 mmol, 2.3 equiv) and benzoyl chloride (0.06 mL, 0.52 mmol, 1.7 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (108 mg, 0.265 mmol, 86%, 91% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{20}$ – 1.40 (*c* 1.00, $CHCl_3$)

From (*S*,*E*)-9*H*-Fluoren-9-one *O*-(1,3-diphenylallyl) oxime:

(*S*,*E*)-9*H*-Fluoren-9-onemethanone *O*-(1,3-diphenylallyl) oxime (145 mg, 0.374 mmol, 1.0 equiv, 81% ee) was dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (192 mg, 0.411 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2.5 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (18 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford an orange oil.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.10 mL, 0.72 mmol, 1.9 equiv) and benzoyl chloride (0.10 mL, 0.86 mmol, 2.3 equiv) were added and the reaction monitored by TLC. After 2 days H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. The ^1H NMR spectrum of the obtained material did not show product formation.

From (*E*)-1,3-diphenylallyl acetate:

$[PdCl(C_3H_5)]_2$ (3.8 mg, 0.010 mmol, 5.0 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (10.8 mg, 0.021 mmol, 5.1 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-diphenylallyl acetate (103 mg, 0.408 mmol, 1.0 equiv) and diphenylmethanone oxime (118 mg, 0.598 mmol, 1.5 equiv) in dry, degassed MeCN (2.4 mL) and dry, degassed DIPEA (0.14 mL, 0.804 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 3 days the solvent was removed in vacuo to afford yellow oil.

2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (206 mg, 0.441 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 19 hours additional $Br^+(coll)_2PF_6^-$ (234 mg, 0.501 mmol, 1.2 equiv) was added and again after another 2 hours as well as after another 27 hours. Although TLC did not show sufficient transformation after another 18 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (20 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown oil.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.28 mL, 2.0 mmol, 4.9 equiv) and benzoyl chloride (0.23 mL, 2.0 mmol, 4.9 equiv) were added and the solution stirred

overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown oil. Purification by column chromatography did not afford the desired product.

$[PdCl(C_3H_5)]_2$ (3.8 mg, 0.010 mmol, 5.0 mol% Pd) and (*R*)-diphenyl(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (10.0 mg, 0.022 mmol, 5.3 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to -20 °C and a solution of (*E*)-1,3-diphenylallyl acetate (102 mg, 0.404 mmol, 1.0 equiv) and diphenylmethanone oxime (79.3 mg, 0.402 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.15 mL, 0.86 mmol, 2.1 equiv) were added. The reaction was monitored by TLC and after 40 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo to afford a yellow oil.

The obtained oil was dissolved in dry CH_2Cl_2 (8 mL) and 2,4,6-collidine (0.060 mL, 0.453 mmol, 1.1 equiv) was added. $Br^+(coll)_2PF_6^-$ (206 mg, 0.441 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 3 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.080 mL, 0.57 mmol, 1.4 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.5 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (3 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (103 mg, 0.252 mmol, 62%, 82% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[PdCl(C_3H_5)]_2$ (3.3 mg, 0.0090 mmol, 4.4 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (12.1 mg, 0.023 mmol, 5.7 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to -16 °C and a solution of (*E*)-1,3-diphenylallyl acetate (103 mg, 0.408 mmol, 1.0 equiv) and diphenylmethanone oxime (79.7 mg, 0.404 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.78 mmol, 1.9 equiv) were added. The

reaction was monitored by TLC and after 8 days the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O and brine, dried over Na_2SO_4 and the solvent removed in vacuo to afford a brown oil.

2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (209 mg, 0.447 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 3.5 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.080 mL, 0.57 mmol, 1.4 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.5 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (3 mL) were added and the mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (83.3 mg, 0.204 mmol, 50%, 88% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[PdCl(C_3H_5)]_2$ (3.6 mg, 0.0098 mmol, 4.9 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (11.4 mg, 0.022 mmol, 5.5 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-diphenylallyl acetate (101 mg, 0.400 mmol, 1.0 equiv) and diphenylmethanone oxime (79.0 mg, 0.401 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 20 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 25 °C) to afford a yellow oil.

2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (206 mg, 0.441 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 1 hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.080 mL, 0.57 mmol, 1.4 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.5 equiv) were added and the solution stirred

overnight. H_2O and conc. NH_3 (3 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (91.0 mg, 0.223 mmol, 56%, 88% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

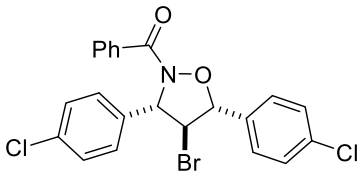
$[PdCl(C_3H_5)]_2$ (1.9 mg, 0.0052 mmol, 2.6 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.2 mg, 0.012 mmol, 2.9 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-diphenylallyl acetate (102 mg, 0.406 mmol, 1.0 equiv) and diphenylmethanone oxime (83.2 mg, 0.422 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 24 hours additional diphenylmethanone oxime (80.5 mg, 0.408 mmol, 1.0 equiv) was added. After another 2 days the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

2,4,6-Collidine (0.060 mL, 0.45 mmol, 1.1 equiv) was added to the obtained oil and the mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (210 mg, 0.449 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.090 mL, 0.65 mmol, 1.6 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.7 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (108 mg, 0.265 mmol, 65%, 92% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{20}$ – 3.51 (*c* 1.00, $CHCl_3$)

4.6.116 *trans*,*trans*-(4-Bromo-3,5-bis(4-chlorophenyl)isoxazolidin-2-yl)(phenyl)methanone (**170**)



$C_{22}H_{16}BrCl_2NO_2$

[477.18]

(*E*)-Diphenylmethanone *O*-(1,3-bis(4-chlorophenyl)allyl) oxime (175 mg, 0.382 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (195 mg, 0.417 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2.5 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.080 mL, 0.57 mmol, 1.5 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.8 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (3 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) afforded a colorless solid (64.3 mg, 0.135 mmol, 35%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 – 7.82 (m, 2H), 7.57 – 7.47 (m, 3H), 7.46 – 7.27 (m, 8H), 5.83 (d, *J* = 5.9 Hz, 1H), 5.05 (d, *J* = 8.8 Hz, 1H), 4.17 (dd, *J* = 8.8, 5.9 Hz, 1H).

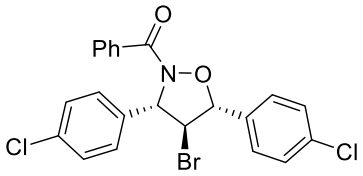
^{13}C NMR (75 MHz, $CDCl_3$) δ 171.99, 137.05, 135.84, 134.53, 132.36, 131.77, 131.26, 129.68, 129.55, 129.28, 128.44, 128.29, 127.59, 89.73, 70.25 (br s, C-N), 57.36.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3060 (w), 2924 (w), 1659 (s, C=O), 1600, 1578, 1491 (s), 1448, 1376, 1334, 1298, 1181, 1092 (s), 1014, 987, 918, 824, 732, 694, 664.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{22}H_{17}BrCl_2NO_2$, 475.981; found, 475.982.

mp 120-124 °C

4.6.117 ((3*S*,4*S*,5*R*)-4-Bromo-3,5-bis(4-chlorophenyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**170**)



$C_{22}H_{16}BrCl_2NO_2$

[477.18]

From (*S*,*E*)-Diphenylmethanone *O*-(1,3-bis(4-chlorophenyl)allyl) oxime:

(*S*,*E*)-Diphenylmethanone *O*-(1,3-bis(4-chlorophenyl)allyl) oxime (108 mg, 0.236 mmol, 1.0 equiv, 86% ee) was dissolved in dry CH_2Cl_2 (5 mL). 2,4,6-Collidine (0.050 mL, 0.38 mmol, 1.6 equiv) was added and successively $Br^+(coll)_2PF_6^-$ (121 mg, 0.259 mmol, 1.1 equiv) was added under exclusion of light. The reaction was monitored by TLC and after 2.5 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (10 mL) was added and the resulting mixture stirred for 2 hours. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid.

This raw product was dissolved in dry CH_2Cl_2 (5 mL). Et_3N (0.050 mL, 0.36 mmol, 1.5 equiv) and benzoyl chloride (0.050 mL, 0.43 mmol, 1.8 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) afforded a colorless solid (96.0 mg, 0.201 mmol, 85%, 79% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

(*S*,*E*)-Diphenylmethanone *O*-(1,3-bis(4-chlorophenyl)allyl) oxime (160 mg, 0.349 mmol, 1.0 equiv, 81% ee) was dissolved in dry CH_2Cl_2 (7 mL). 2,4,6-Collidine (0.10 mL, 0.75 mmol, 2.2 equiv) was added and successively $Br^+(coll)_2PF_6^-$ (181 mg, 0.387 mmol, 1.1 equiv) was added under exclusion of light. The reaction was monitored by TLC and after 2.5 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (14 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (7 mL). Et_3N (0.070 mL, 0.50 mmol, 1.4 equiv) and benzoyl chloride (0.060 mL, 0.52 mmol, 1.5 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown solid. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) afforded a colorless solid (110 mg, 0.231 mmol, 66%, 81% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

From (*E*)-1,3-bis(4-chlorophenyl)allyl acetate:

$[PdCl(C_3H_5)]_2$ (3.6 mg, 0.0098 mmol, 5.0 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (11.4 mg, 0.022 mmol, 5.6 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-bis(4-chlorophenyl)allyl acetate (127 mg, 0.395 mmol, 1.0 equiv) and diphenylmethanone oxime (79.0 mg, 0.401 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.78 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 20 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 25 °C) to afford a yellow oil.

2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (206 mg, 0.441 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 1 hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.080 mL, 0.57 mmol, 1.4 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.5 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (3 mL) were added and the resulting mixture stirred for

another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times. The combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (87.0 mg, 0.182 mmol, 47%, 79% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[PdCl(C_3H_5)]_2$ (3.8 mg, 0.010 mmol, 5.1 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (10.9 mg, 0.021 mmol, 5.3 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-bis(4-chlorophenyl)allyl acetate (126 mg, 0.392 mmol, 1.0 equiv) and diphenylmethanone oxime (79.2 mg, 0.402 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.78 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 18 hours the solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo (bath temp. 40 °C) to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.34) yielded a colorless oil, which was stored at 4 °C overnight.

2,4,6-Collidine (0.050 mL, 0.377 mmol, 1.0 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (7.5 mL). $Br^+(coll)_2PF_6^-$ (190 mg, 0.407 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (15 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (7.5 mL). Et_3N (0.080 mL, 0.57 mmol, 1.6 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.6 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (3 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (121 mg, 0.254 mmol, 69%, 65% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[PdCl(C_3H_5)]_2$ (3.8 mg, 0.010 mmol, 5.1 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (11.2 mg, 0.0215 mmol, 5.5 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-bis(4-chlorophenyl)allyl acetate (125 mg, 0.389 mmol, 1.0 equiv) and diphenylmethanone oxime (80.0 mg, 0.406 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.1 equiv) were added. The

reaction was monitored by TLC and after 25 hours the reaction solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo to afford a yellow oil. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.34) yielded a colorless oil (175 mg, 0.382 mmol, 98%, 75% ee - IC, *n*-hexane/*i*PrOH 99.5:0.5, 1.0 ml/min).

2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.2 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (7.5 mL). $Br^+(coll)_2PF_6^-$ (200 mg, 0.428 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 1 hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (15 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (7.5 mL). Et_3N (0.080 mL, 0.57 mmol, 1.6 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.6 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (3 mL) were added. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (84.3 mg, 0.177 mmol, 46%, 73% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[PdCl(C_3H_5)]_2$ (1.2 mg, 0.0033 mmol, 2.6 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (4.2 mg, 0.0081 mmol, 3.2 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-bis(4-chlorophenyl)allyl acetate (80.0 mg, 0.249 mmol, 1.0 equiv) and diphenylmethanone oxime (53.2 mg, 0.270 mmol, 1.1 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.090 mL, 0.52 mmol, 2.1 equiv) were added. The reaction was monitored by TLC and after 18 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

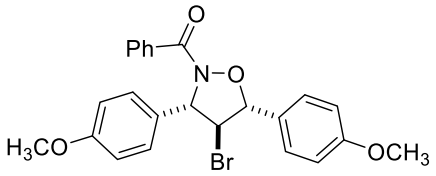
2,4,6-Collidine (0.040 mL, 0.30 mmol, 1.2 equiv) was added to the obtained oil and the resulting mixture was dissolved in dry CH_2Cl_2 (5 mL). $Br^+(coll)_2PF_6^-$ (133 mg, 0.285 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 1 hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (10 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (5 mL). Et_3N (0.060 mL, 0.43 mmol, 1.7 equiv) and benzoyl chloride (0.050 mL, 0.43 mmol, 1.7 equiv) were added and the solution stirred

overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a colorless solid (75.7 mg, 0.159 mmol, 64%, 91% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{20}$ – 21.34 (*c* 1.00, $CHCl_3$)

4.6.118 *trans*,*trans*-(4-Bromo-3,5-bis(4-methoxyphenyl)isoxazolidin-2-yl)(phenyl)methanone (**171**)



$C_{24}H_{22}BrNO_4$

[468.35]

(*E*)-Diphenylmethanone *O*-(1,3-bis(4-methoxyphenyl)allyl) oxime (128 mg, 0.285 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (6 mL). $Br^+(coll)_2PF_6^-$ (150 mg, 0.321 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 3 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (12 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

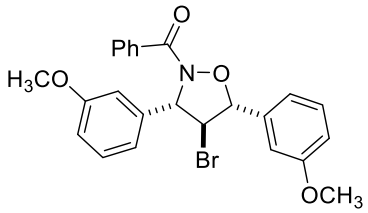
This raw product was dissolved in dry CH_2Cl_2 (6 mL). Et_3N (0.08 mL, 0.57 mmol, 2.0 equiv) and benzoyl chloride (0.07 mL, 0.60 mmol, 2.1 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 85:15, R_f = 0.29) afforded a yellow oil (49.4 mg, 0.105 mmol, 37%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 – 7.83 (m, 2H), 7.54 – 7.45 (m, 3H), 7.43 – 7.34 (m, 2H), 7.33 – 7.27 (m, 2H), 7.00 – 6.94 (m, 2H), 6.92 – 6.85 (m, 2H), 5.79 (d, *J* = 5.8 Hz, 1H), 5.05 (d, *J* = 8.8 Hz, 1H), 4.28 (dd, *J* = 8.8, 5.7 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.56, 160.72, 159.71, 132.26, 131.98, 130.90, 129.62, 128.81, 128.16, 127.52, 124.68, 114.66, 114.35, 90.43, 70.55 (br s, C-N), 58.08, 55.48, 55.44.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3003 (w), 2957 (w), 2933 (w), 2837 (w), 1656 (C=O), 1613, 1585, 1515 (s), 1448, 1386, 1339, 1305, 1253 (s), 1176, 1032, 975, 915, 830, 810, 732, 703, 664, 540.

4.6.119 *trans*,*trans*-(4-Bromo-3,5-bis(3-methoxyphenyl)isoxazolidin-2-yl)(phenyl)methanone (**172**)



$C_{24}H_{22}BrNO_4$

[468.35]

(*E*)-1,3-Bis(3-methoxyphenyl)allyl acetate (250 mg, 0.800 mmol, 1.0 equiv) and diphenylmethanone oxime (159 mg, 0.806 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (5 mL). $Pd(PPh)_4$ (48.0 mg, 0.0415 mmol, 5.2 mol%) and DIPEA (0.28 mL, 1.6 mmol, 2.0 equiv) were added and the reaction monitored by TLC. After 22 hours the reaction solution was filtered through a celite plug and the filtrate washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C).

The obtained oil was dissolved in dry CH_2Cl_2 (12 mL) and 2,4,6-collidine (0.12 mL, 0.91, 1.1 equiv) was added. $Br^+(coll)_2PF_6^-$ (411 mg, 0.880, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 1 hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O

(32 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown oil.

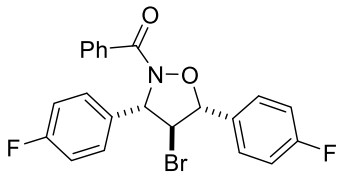
This raw product was dissolved in dry CH_2Cl_2 (12 mL). Et_3N (0.17 mL, 1.2 mmol, 1.5 equiv) and benzoyl chloride (0.14 mL, 1.2 mmol, 1.5 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.19) afforded a yellow oil (54.1 mg, 0.112 mmol, 14%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 – 7.85 (m, 2H), 7.53 – 7.47 (m, 1H), 7.45 – 7.23 (m, 4H), 7.20 – 7.12 (m, 2H), 6.97 (dt, *J* = 7.7, 1.3 Hz, 1H), 6.93 – 6.87 (m, 3H), 5.85 (d, *J* = 5.3 Hz, 1H), 5.09 (d, *J* = 8.5 Hz, 1H), 4.31 (dd, *J* = 8.5, 5.4 Hz, 1H), 3.85 (s, 3H), 3.76 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.86, 160.32, 159.91, 140.33, 134.60, 132.10, 130.42, 130.00, 129.62, 128.22, 119.36, 118.34, 115.05, 113.74, 112.70, 111.91, 90.52, 70.87 (br s, C-N), 57.91, 55.45, 55.36.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3060 (w), 3003 (w), 2958, 2938, 2836 (w), 1659 (C=O), 1602 (s), 1587, 1491, 1456, 1437, 1371, 1325, 1290 (s), 1263 (s), 1159, 1046, 994, 910, 875, 783, 763, 734, 695 (s), 666.

4.6.120 *trans*,*trans*-(4-Bromo-3,5-bis(4-fluorophenyl)isoxazolidin-2-yl)(phenyl)methanone (**173**)



$C_{22}H_{16}BrF_2NO_2$

[444.28]

(*E*)-Diphenylmethanone *O*-(1,3-bis(4-fluorophenyl)allyl) oxime (205 mg, 0.482 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (10 mL). $Br^+(coll)_2PF_6^-$ (249 mg, 0.533 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (20 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (10 mL). Et_3N (0.10 mL, 0.72 mmol, 1.5 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.4 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow solid. Purification by column chromatography (*n*-hexane/EtOAc 9:1, R_f = 0.29) afforded a yellowish oil (132 mg, 0.297 mmol, 62%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 – 7.82 (m, 2H), 7.60 – 7.47 (m, 3H), 7.46 – 7.30 (m, 4H), 7.19 – 7.01 (m, 4H), 5.83 (d, *J* = 5.9 Hz, 1H), 5.06 (d, *J* = 8.8 Hz, 1H), 4.19 (dd, *J* = 8.8, 5.9 Hz, 1H).

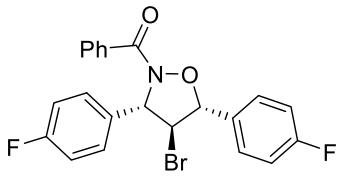
^{19}F NMR (282 MHz, $CDCl_3$) δ -111.06, -113.46.

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.93, 163.50 (d, *J* = 249.6 Hz), 162.80 (d, *J* = 247.2 Hz), 134.42 (d, *J* = 3.2 Hz), 132.28, 131.90, 129.67, 129.08 (d, *J* = 8.5 Hz), 128.61 (d, *J* = 3.3 Hz), 128.27, 127.99 (d, *J* = 8.3 Hz), 116.31 (d, *J* = 21.8 Hz), 116.10 (d, *J* = 21.9 Hz), 89.82, 70.23 (br s, C-N), 57.67.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3070 (w), 1654 (C=O), 1606, 1510 (s), 1336, 1299, 1228 (s), 1158, 984, 919, 834, 756, 702, 664, 553, 532.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{22}H_{17}BrF_2NO_2$, 444.041; found, 444.040.

4.6.121 ((3*S*,4*S*,5*R*)-4-Bromo-3,5-bis(4-fluorophenyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**173**)



$C_{22}H_{16}BrF_2NO_2$

[444.28]

$[PdCl(C_3H_5)]_2$ (3.7 mg, 0.010 mmol, 5.0 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (10.9 mg, 0.021 mmol, 5.2 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-bis(4-fluorophenyl)allyl acetate (116 mg, 0.402 mmol, 1.0 equiv) and diphenylmethanone oxime (79.0 mg, 0.400 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.78 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 28 hours the solution was filtered through a silica plug, washed with EtOAc and the solvent removed in vacuo (bath temp. 40 °C) to afford a yellow oil, which was stored at 4 °C overnight. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.34) yielded a colorless oil (161 mg, 0.378 mmol, 94%).

2,4,6-Collidine (0.055 mL, 0.415 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (195 mg, 0.417 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.080 mL, 0.57 mmol, 1.6 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.6 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (3 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a yellowish oil (108 mg, 0.243 mmol, 64%, 87% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{27}$ – 4.85 (*c* 1.00, $CHCl_3$)

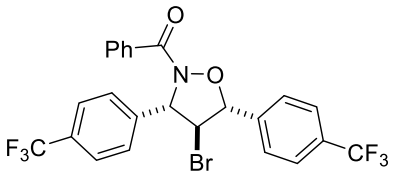
$[PdCl(C_3H_5)]_2$ (1.9 mg, 0.0052 mmol, 2.6 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.2 mg, 0.012 mmol, 2.9 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-bis(4-fluorophenyl)allyl acetate (117 mg, 0.406 mmol, 1.0 equiv) and diphenylmethanone oxime (84.1 mg, 0.426 mmol, 1.1 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 17 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

2,4,6-Collidine (0.060 mL, 0.45 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture was dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (213 mg, 0.456 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (6 mL). Et_3N (0.090 mL, 0.65 mmol, 1.6 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.7 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a yellowish oil (110 mg, 0.248 mmol, 61%, 92% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{20}$ – 5.88 (*c* 1.00, $CHCl_3$)

4.6.122 *trans*,*trans*-(4-Bromo-3,5-bis(4-(trifluoro)phenyl)isoxazolidin-2-yl)(phenyl)methanone (**174**)



$C_{24}H_{16}BrF_6NO_2$

[544.29]

(*E*)-Diphenylmethanone *O*-(1,3-bis(4-(trifluoro)phenyl)allyl) oxime (179 mg, 0.341 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (7 mL). $Br^+(coll)_2PF_6^-$ (179 mg, 0.383 mmol, 1.1 equiv) was added under exclusion of light. After 2 hours additional $Br^+(coll)_2PF_6^-$ (350 mg, 0.749 mmol, 2.2 equiv) was added. After another 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (28 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (7 mL). Et_3N (0.080 mL, 0.57 mmol, 1.7 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.8 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.16) afforded a yellowish oil (29.5 mg, 0.0542 mmol, 16%). The low yield might be due to a leakage of the chromatography column.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 – 7.83 (m, 2H), 7.72 (s, 4H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.56 – 7.49 (m, 3H), 7.43 (ddt, *J* = 8.4, 6.8, 1.2 Hz, 2H), 5.95 (d, *J* = 6.0 Hz, 1H), 5.15 (d, *J* = 8.8 Hz, 1H), 4.20 (dd, *J* = 8.8, 6.0 Hz, 1H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -62.67, -62.91.

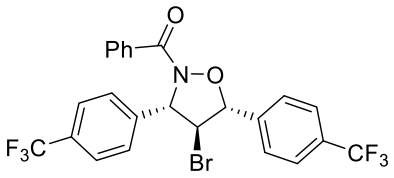
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.23, 142.32, 136.71, 132.57, 132.04 (q, *J* = 32.8 Hz), 131.54, 131.00 (q, *J* = 32.6 Hz), 129.74, 128.38, 127.33, 126.60, 126.44 (q, *J* = 3.7 Hz),

126.05 (q, *J* = 3.7 Hz), 125.72 (q, *J* = 16.6 Hz), 122.10 (q, *J* = 16.8 Hz), 89.50, 70.32 (br s, C-N), 56.86.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3071 (w), 2360 (w), 2336 (w), 1660 (m, C=O), 1606, 1511 (s), 1448, 1379, 1334, 1299, 1229 (s), 1183 (w), 1159, 984, 919, 835, 813, 702, 664.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{24}H_{17}BrF_6NO_2$, 544.034; found, 544.035.

4.6.123 ((3*S*,4*S*,5*R*)-4-Bromo-3,5-bis(4-(trifluoro)phenyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**174**)



$C_{24}H_{16}BrF_6NO_2$

[544.29]

(*E*)-Diphenylmethanone *O*-(1,3-bis(4-(trifluoro)phenyl)allyl) oxime (143 mg, 0.272 mmol, 1.0 equiv) and 2,4,6-collidine (0.040 mL, 0.30 mmol, 1.1 equiv) were dissolved in dry CH_2Cl_2 (6 mL). $Br^+(coll)_2PF_6^-$ (141 mg, 0.302 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours additional $Br^+(coll)_2PF_6^-$ (280 mg, 0.600 mmol, 2.2 equiv) was added. After another 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (24 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.080 mL, 0.57 mmol, 1.6 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.6 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (3 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.16) yielded a yellowish oil (45.3 mg, 0.0832 mmol, 31%, 81% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{21}$ – 9.74 (*c* 1.00, $CHCl_3$)

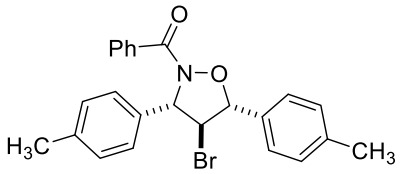
$[PdCl(C_3H_5)]_2$ (2.0 mg, 0.0055 mmol, 2.5 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.4 mg, 0.012 mmol, 2.8 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-bis(4-(trifluoromethyl)phenyl)allyl acetate (169 mg, 0.435 mmol, 1.0 equiv) and diphenylmethanone oxime (88.6 mg, 0.449 mmol, 1.1 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.15 mL, 0.86 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 19 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

2,4,6-Collidine (0.070 mL, 0.53 mmol, 1.2 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (9 mL). $Br^+(coll)_2PF_6^-$ (227 mg, 0.486 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours additional $Br^+(coll)_2PF_6^-$ (230 mg, 0.492 mmol, 1.1 equiv) was added and again after another hour $Br^+(coll)_2PF_6^-$ (225 mg, 0.482 mmol, 1.1 equiv) was added once more. After another 30 minutes a 10 wt% solution of $Na_2S_2O_5$ in H_2O (18 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (9 mL). Et_3N (0.090 mL, 0.65 mmol, 1.5 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.6 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.16) yielded a yellowish oil (89.7 mg, 0.165 mmol, 38%, 91% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{20}$ – 10.50 (*c* 1.00, $CHCl_3$)

4.6.124 *trans*,*trans*-(4-Bromo-3,5-di-*p*-tolylisoxazolidin-2-yl)(phenyl)methanone (**175**)



$C_{24}H_{22}BrNO_2$

[436.35]

(*E*)-Diphenylmethanone *O*-(1,3-di-*p*-tolylallyl) oxime (139 mg, 0.333 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (7 mL). $Br^+(coll)_2PF_6^-$ (175 mg, 0.375 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (14 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (7 mL). NEt_3 (0.080 mL, 0.57 mmol, 1.7 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.8 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.20) afforded an off-white solid (113 mg, 0.259 mmol, 78%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (dt, *J* = 7.1, 1.4 Hz, 2H), 7.52 – 7.44 (m, 3H), 7.42 – 7.35 (m, 2H), 7.25 (td, *J* = 6.0, 1.3 Hz, 4H), 7.17 (d, *J* = 7.9 Hz, 2H), 5.81 (d, *J* = 5.7 Hz, 1H), 5.05 (d, *J* = 8.8 Hz, 1H), 4.27 (dd, *J* = 8.8, 5.7 Hz, 1H), 2.38 (s, 3H), 2.34 (s, 3H).

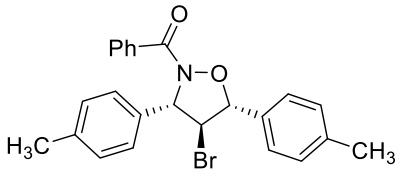
^{13}C NMR (75 MHz, $CDCl_3$) δ 171.54, 139.75, 138.21, 135.89, 132.24, 131.96, 129.92, 129.88, 129.63, 129.60, 128.14, 127.25, 126.15, 90.55, 70.68 (br s, C-N), 58.04, 21.39, 21.31.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3029, 2922, 1660 (s, C=O), 1602 (w), 1578, 1515, 1492 (w), 1448, 1379, 1335, 1308, 1181, 1112 (w), 1021, 976, 914 (s), 813 (s), 768, 746 (s), 700, 665, 528.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{24}H_{23}BrNO_2$, 436.091; found, 436.091.

mp 117-120 °C

4.6.125 ((3*S*,4*S*,5*R*)-4-Bromo-3,5-di-*p*-tolylisoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**175**)



$C_{24}H_{22}BrNO_2$

[436.35]

$[PdCl(C_3H_5)]_2$ (3.6 mg, 0.0098 mmol, 5.4 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (11.1 mg, 0.021 mmol, 5.4 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-di-*p*-tolylallyl acetate (102 mg, 0.364 mmol, 1.0 equiv) and diphenylmethanone oxime (80.0 mg, 0.406 mmol, 1.1 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.78 mmol, 2.1 equiv) were added. The reaction was monitored by TLC and after 23 hours the solvent removed in vacuo (bath temp. 40 °C). Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.54) yielded a colorless oil (149 mg, 0.357 mmol, 98%) which turned into a solid while being stored at 4 °C overnight.

2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.3 equiv) was added to the obtained solid and the resulting mixture dissolved in dry CH_2Cl_2 (7 mL). $Br^+(coll)_2PF_6^-$ (190 mg, 0.407 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (14 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (7 mL). Et_3N (0.080 mL, 0.57 mmol, 1.6 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.7 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (3 mL) were added and the resulting mixture stirred for

another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.20) yielded an off-white solid (74.4 mg, 0.171 mmol, 48%, 55% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{21}$ – 6.17 (*c* 1.00, $CHCl_3$)

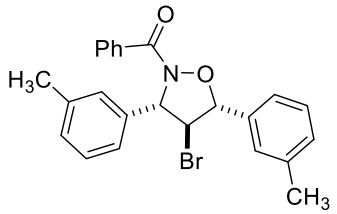
$[PdCl(C_3H_5)]_2$ (2.2 mg, 0.0060 mmol, 2.8 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.8 mg, 0.013 mmol, 3.0 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-di-*p*-tolylallyl acetate (120 mg, 0.428 mmol, 1.0 equiv) and diphenylmethanone oxime (85.2 mg, 0.432 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 23 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (208 mg, 0.445 mmol, 1.0 equiv) was added under exclusion of light and the reaction monitored by TLC. After 1 hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.080 mL, 0.57 mmol, 1.4 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.5 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.20) yielded an off-white solid (128 mg, 0.293 mmol, 69%, 87% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{20}$ – 11.72 (*c* 1.00, $CHCl_3$)

4.6.126 *trans*,*trans*-(4-Bromo-3,5-di-*m*-tolylisoxazolidin-2-yl)(phenyl)methanone (**176**)



$C_{24}H_{22}BrNO_2$

[436.35]

(*E*)-Diphenylmethanone *O*-(1,3-di-*m*-tolylallyl) oxime (181 mg, 0.433 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (9 mL) and 2,4,6-collidine (0.070 mL, 0.53 mmol, 1.2 equiv) was added. $Br^+(coll)_2PF_6^-$ (229 mg, 0.490 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours additional $Br^+(coll)_2PF_6^-$ (209 mg, 0.447 mmol, 1.0 equiv) was added. After another hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (18 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (9 mL). Et_3N (1.0 mL, 7.2 mmol, 17 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.6 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) afforded a slightly yellowish oil (65.6 mg, 0.150 mmol, 35%).

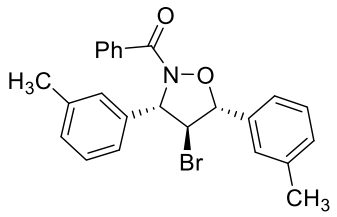
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (dt, *J* = 7.0, 1.5 Hz, 2H), 7.54 – 7.46 (m, 1H), 7.45 – 7.28 (m, 5H), 7.25 – 7.15 (m, 5H), 5.85 (d, *J* = 5.7 Hz, 1H), 5.06 (d, *J* = 8.8 Hz, 1H), 4.31 (dd, *J* = 8.8, 5.7 Hz, 1H), 2.42 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.66, 139.02, 138.75, 138.71, 132.85, 132.21, 132.00, 130.49, 129.68, 129.21, 129.18, 128.81, 128.17, 127.90, 126.91, 124.37, 123.22, 90.67, 70.79 (br s, C-N), 57.88, 21.67, 21.52.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3029, 2920, 1660 (s, C=O), 1608, 1578, 1491, 1448, 1378, 1334, 1184, 1029, 979, 945, 910, 882, 787, 761, 735, 697 (s), 666.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{24}H_{23}BrNO_2$, 436.091; found, 436.091.

4.6.127 ((3*S*,4*S*,5*R*)-4-Bromo-3,5-di-*m*-tolylisoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**176**)



$C_{24}H_{22}BrNO_2$

[436.35]

$[PdCl(C_3H_5)]_2$ (1.8 mg, 0.0049 mmol, 2.5 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (7.2 mg, 0.014 mmol, 3.5 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-di-*m*-tolylallyl acetate (111 mg, 0.396 mmol, 1.0 equiv) and diphenylmethanone oxime (82.3 mg, 0.417 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 12 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

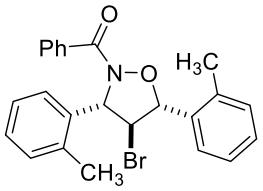
2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (215 mg, 0.460 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.090 mL, 0.65 mmol, 1.6 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.7 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for

another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a slightly yellowish oil (118 mg, 0.270 mmol, 68%, 92% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{20}$ – 9.50 (*c* 1.00, $CHCl_3$)

4.6.128 *trans*,*trans*-(4-Bromo-3,5-di-*o*-tolylisoxazolidin-2-yl)(phenyl)methanone (**177**)



$C_{24}H_{22}BrNO_2$

[436.35]

(*E*)-Diphenylmethanone *O*-(1,3-di-*o*-tolylallyl) oxime (161 mg, 0.386 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (199 mg, 0.426 mmol, 1.1 equiv) was added to under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.080 mL, 0.57 mmol, 1.5 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.6 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a slightly yellowish solid (133 mg, 0.305 mmol, 79%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.6 Hz, 2H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.44 – 7.13 (m, 9H), 6.07 (s, 1H), 5.42 (d, *J* = 8.3 Hz, 1H), 4.43 (dd, *J* = 8.4, 4.9 Hz, 1H), 2.54 (s, 3H), 2.26 (s, 3H).

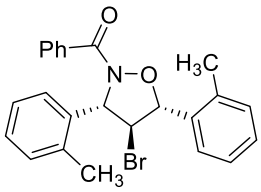
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.08, 138.18, 137.57, 135.99, 132.35, 131.98, 131.01, 130.99, 130.82, 129.57, 129.47, 128.33, 128.24, 126.95, 126.55, 126.53, 126.28, 87.57, 68.29 (br s, C-N), 56.83, 20.18, 19.54.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3027 (w), 1662 (s, C=O), 1602 (w), 1578 (w), 1493, 1448, 1376, 1328, 1179, 1029 (w), 972, 918, 813 (w), 746 (s), 696, 665.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{24}H_{23}BrNO_2$, 436.091; found, 436.091.

mp 90-92 °C

4.6.129 ((3*S*,4*S*,5*R*)-4-Bromo-3,5-di-*o*-tolylisoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**177**)



$C_{24}H_{22}BrNO_2$

[436.35]

$[PdCl(C_3H_5)]_2$ (3.7 mg, 0.010 mmol, 5.1 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (11.0 mg, 0.021 mmol, 5.4 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-di-*o*-tolylallyl acetate (109 mg, 0.389 mmol, 1.0 equiv) and diphenylmethanone oxime (78.8 mg, 0.400 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.78 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 23 hours the solution was filtered through a silica

plug, washed with EtOAc and the solvent removed in vacuo (bath temp. 40 °C). Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.46) yielded a colorless oil (152 mg, 0.364 mmol, 94%).

2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.2 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (7 mL). $Br^+(coll)_2PF_6^-$ (187 mg, 0.400 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 1 hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (14 mL) was added and the resulting mixture stirred for 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (7 mL). Et_3N (0.080 mL, 0.57 mmol, 1.6 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.6 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (3 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a slightly yellowish solid (109 mg, 0.250 mmol, 69%, 30% ee - IB, *n*-hexane/*i*PrOH 99.5:0.5, 0.8 ml/min).

$[\alpha]_D^{27}$ – 5.23 (*c* 1.00, $CHCl_3$)

$[PdCl(C_3H_5)]_2$ (1.9 mg, 0.0052 mmol, 2.6 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.0 mg, 0.012 mmol, 2.8 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-di-*o*-tolylallyl acetate (114 mg, 0.407 mmol, 1.0 equiv) and diphenylmethanone oxime (84.3 mg, 0.427 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 17 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

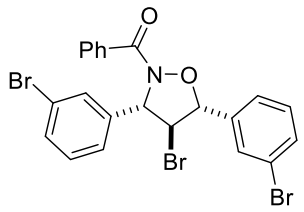
2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (211 mg, 0.452 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture

stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.090 mL, 0.65 mmol, 1.6 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.7 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) yielded a slightly yellowish solid (116 mg, 0.266 mmol, 65%, 30% ee - IB, *n*-hexane/*i*PrOH 99.5:0.5, 0.8 ml/min).

$[\alpha]_D^{20}$ – 4.65 (*c* 1.00, $CHCl_3$)

4.6.130 *trans*,*trans*-(4-Bromo-3,5-bis(3-bromophenyl)isoxazolidin-2-yl)(phenyl)methanone (**178**)



$C_{22}H_{16}Br_3NO_2$

[566.09]

(*E*)-1,3-Bis(3-bromophenyl)allyl acetate (313 mg, 0.763 mmol, 1.0 equiv) and diphenylmethanone oxime (161 mg, 0.816 mmol, 1.1 equiv) were dissolved in dry CH_2Cl_2 (5 mL). $Pd(PPh)_4$ (55.2 mg, 0.0478 mmol, 6.3 mol%) and DIPEA (0.27 mL, 1.6 mmol, 2.0 equiv) were added and the reaction monitored by TLC. After 12 hours the reaction solution was washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 40 °C).

The obtained oil was dissolved in dry CH_2Cl_2 (15 mL) and 2,4,6-collidine (0.11 mL, 0.83, 1.1 equiv) was added. $Br^+(coll)_2PF_6^-$ (402 mg, 0.860, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours additional $Br^+(coll)_2PF_6^-$ (202 mg, 0.432, 0.57 equiv) was added. After another 30 minutes a 10 wt% solution of $Na_2S_2O_5$ in H_2O

(30 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a brown oil.

This raw product was dissolved in dry CH_2Cl_2 (15 mL). Et_3N (0.16 mL, 1.1 mmol, 1.5 equiv) and benzoyl chloride (0.13 mL, 1.0 mmol, 1.4 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.16) afforded a yellow oil (178 mg, 0.314 mmol, 41%).

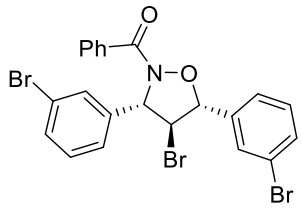
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 – 7.85 (m, 2H), 7.72 (t, *J* = 1.9 Hz, 1H), 7.51 (dt, *J* = 8.1, 1.6 Hz, 5H), 7.47 – 7.38 (m, 2H), 7.37 – 7.20 (m, 3H), 5.85 (d, *J* = 6.0 Hz, 1H), 5.02 (d, *J* = 8.8 Hz, 1H), 4.20 (dd, *J* = 8.8, 6.0 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.13, 140.61, 134.95, 132.94, 132.41, 131.80, 131.63, 130.92, 130.54, 129.94, 129.75, 129.16, 128.30, 125.78, 124.93, 123.42, 123.04, 89.49, 70.00 (br s, C-N), 57.01.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3061 (w), 2925 (w), 1660 (s, C=O), 1597, 1573, 1476, 1448, 1431, 1370, 1333 (s), 1201, 1184, 1095, 1073, 997, 909, 881, 785 (s), 755, 733 (s), 693 (s), 663.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{22}H_{17}Br_3NO_2$, 563.880; found, 563.881.

4.6.131 ((3*S*,4*S*,5*R*)-4-Bromo-3,5-bis(3-bromophenyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**178**)



$C_{22}H_{16}Br_3NO_2$

[566.09]

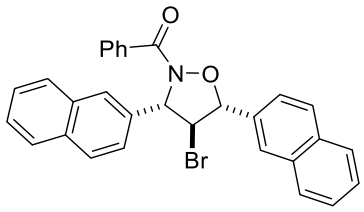
$[PdCl(C_3H_5)]_2$ (1.7 mg, 0.0046 mmol, 2.5 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.1 mg, 0.012 mmol, 3.1 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1,3-bis(3-bromophenyl)allyl acetate (153 mg, 0.373 mmol, 1.0 equiv) and diphenylmethanone oxime (77.3 mg, 0.392 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.13 mL, 0.75 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 12 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.2 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (7.5 mL). $Br^+(coll)_2PF_6^-$ (198 mg, 0.424 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (15 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (7.5 mL). Et_3N (0.080 mL, 0.57 mmol, 1.5 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.6 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.11) yielded a yellow oil (145 mg, 0.256 mmol, 69%, 93% ee - IB, *n*-hexane/*i*PrOH 99:1, 0.8 ml/min).

$[\alpha]_D^{20}$ – 24.40 (*c* 1.00, $CHCl_3$)

4.6.132 *trans*,*trans*-(4-bromo-3,5-di(naphthalen-2-yl)isoxazolidin-2-yl)(phenyl)methanone (**179**)[150]



$C_{30}H_{22}BrNO_2$

[508.42]

(*E*)-Diphenylmethanone *O*-(1,3-di(naphthalen-2-yl)allyl) oxime (70.0 mg, 0.143 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (3.5 mL). $Br^+(coll)_2PF_6^-$ (73.4 mg, 0.157 mmol, 1.1 equiv) was added to under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo to afford a yellow oil.

This raw product was dissolved in dry CH_2Cl_2 (4 mL). Et_3N (0.030 mL, 0.22 mmol, 1.5 equiv) and benzoyl chloride (0.030 mL, 0.26 mmol, 1.8 equiv) were added and the solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.16) yielded a white solid (30.5 mg, 0.0599 mmol, 42%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 – 8.06 (m, 1H), 8.00 – 7.79 (m, 9H), 7.75 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.59 – 7.36 (m, 8H), 6.09 (d, *J* = 5.6 Hz, 1H), 5.33 (d, *J* = 8.7 Hz, 1H), 4.50 (dd, *J* = 8.7, 5.6 Hz, 1H).

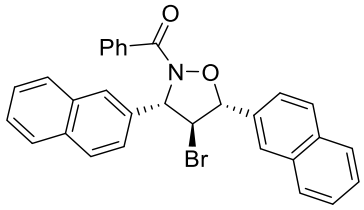
^{13}C NMR (75 MHz, $CDCl_3$) δ 171.97, 136.00, 133.87, 133.50, 133.30, 133.02, 132.17, 132.12, 130.10, 129.70, 129.53, 128.99, 128.25, 128.23, 127.90, 127.87, 127.54, 127.01, 126.76, 126.74, 126.55, 125.46, 123.75, 123.67, 90.97, 71.29 (br s, C-N), 57.79.

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3057, 1657 (s, C=O), 1602, 1508, 1448, 1325 (s), 1271, 1182, 893, 858, 815 (s), 750 (s), 700, 666.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{30}H_{23}BrNO_2$, 508.091; found, 508.091.

mp 106-108 °C

4.6.133 ((3*S*,4*S*,5*R*)-4-bromo-3,5-di(naphthalen-2-yl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**179**)



$C_{30}H_{22}BrNO_2$

[508.42]

$[PdCl(C_3H_5)]_2$ (1.9 mg, 0.0052 mmol, 2.6 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.2 mg, 0.012 mmol, 2.9 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes a solution of (*E*)-1,3-Di(naphthalen-2-yl)allyl acetate (143 mg, 0.406 mmol, 1.0 equiv) and diphenylmethanone oxime (82.3 mg, 0.417 mmol, 1.0 equiv) in dry, degassed MeCN (9.4 mL) was cooled to 0 °C and the yellow catalyst solution and dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 17 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

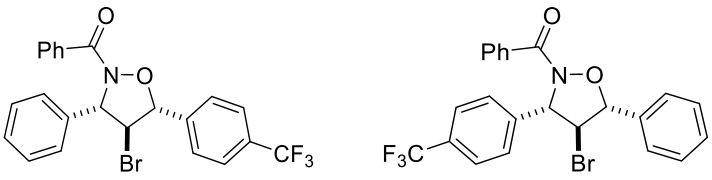
2,4,6-Collidine (0.060 mL, 0.453 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (214 mg, 0.458 mmol,

1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.090 mL, 0.65 mmol, 1.6 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.7 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.16) yielded a white solid (136 mg, 0.267 mmol, 66%, 93% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{20}$ – 68.50 (*c* 1.00, $CHCl_3$)

4.6.134 *trans*,*trans*-(4-Bromo-3-phenyl-5-(4-(trifluoromethyl)phenyl)isoxazolidin-2-yl)(phenyl)methanone (**180**) *trans*,*trans*-(4-Bromo-5-phenyl-3-(4-(trifluoromethyl)phenyl)isoxazolidin-2-yl)(phenyl)methanone (**181**)



$C_{23}H_{17}BrF_3NO_2$

[476.29]

(*E*)-Diphenylmethanone *O*-(3-phenyl-1-(4-(trifluoromethyl)phenyl)allyl) oxime/ (*E*)-Diphenylmethanone *O*-(1-phenyl-3-(4-(trifluoromethyl)phenyl)allyl) oxime (242 mg, 0.529 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (10 mL) and 2,4,6-collidine (0.080 mL, 0.60 mmol, 1.1 equiv) was added. $Br^+(coll)_2PF_6^-$ (282 mg, 0.604 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours additional $Br^+(coll)_2PF_6^-$ (272 mg, 0.582 mmol, 1.1 equiv) was added. After another hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (20 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (10 mL). NEt_3 (0.11 mL, 0.79 mmol, 1.5 equiv) and benzoyl chloride (0.090 mL, 0.77 mmol, 1.5 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) afforded a colorless oil (115 mg, 0.241 mmol, 46%, **180**:**181** 0.75:1.00).

Minor product **180**:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.84 (m, 2H), 7.67 – 7.35 (m, 12H), 5.88 (d, *J* = 5.5 Hz, 1H), 5.18 (d, *J* = 8.6 Hz, 1H), 4.25 (dd, *J* = 8.6, 5.5, 1H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -62.96.

Major product **181**:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 – 7.89 (m, 2H), 7.72 (s, 4H), 7.67 – 7.35 (m, 8H), 5.96 (d, *J* = 6.1 Hz, 1H), 5.09 (d, *J* = 8.9 Hz, 1H), 4.25 (dd, *J* = 8.9, 6.1, 1H).

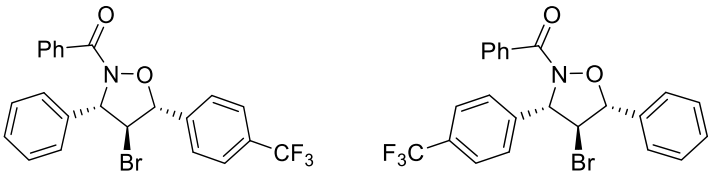
^{19}F NMR (282 MHz, $CDCl_3$) δ -62.72.

Combined ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.15 (C=O, minor), 171.86 (C=O, major), 142.67, 138.47, 137.26, 132.50, 132.34, 132.30, 131.96, 131.78 (q, *J* = 32.8 Hz, minor), 131.72, 130.80 (q, *J* = 32.5 Hz, major), 129.92, 129.77, 129.61, 129.39, 129.03, 128.64, 128.31, 128.27, 127.36, 127.14, 126.65, 126.34 (q, *J* = 3.9 Hz, major), 126.13, 125.94 (q, *J* = 3.8 Hz, minor), 124.08 (q, *J* = 272.0 Hz, major), 123.85 (q, *J* = 272.8 Hz, minor), 90.49 (C-O, major), 89.63 (C-O, minor), 71.06 (br s. C-N, minor), 70.17 (br s, C-N, major), 57.76 (C-Br, minor), 57.07 (C-Br, major).

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 3064 (w), 3034 (w), 2928 (w), 1660 (s, C=O), 1621, 1602, 1579, 1496, 1449, 1421, 1379, 1326 (s), 1168, 1127 (s), 1068, 1028, 1018, 988, 913, 840, 811, 760, 733, 697, 667, 600.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{23}H_{18}BrF_3NO_2$, 476.047; found, 476.047.

4.6.135 ((3*S*,4*S*,5*R*)-4-bromo-3-phenyl-5-(4-(trifluoromethyl)phenyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**180**) ((3*S*,4*S*,5*R*)-4-bromo-5-phenyl-3-(4-(trifluoromethyl)phenyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**181**)



$C_{23}H_{17}BrF_3NO_2$

[476.29]

$[PdCl(C_3H_5)]_2$ (1.8 mg, 0.0049 mmol, 2.5 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.2 mg, 0.012 mmol, 3.0 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-3-phenyl-1-(4-(trifluoromethyl)phenyl)allyl acetate (128 mg, 0.400 mmol, 1.0 equiv) and diphenylmethanone oxime (85.1 mg, 0.431 mmol, 1.1 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 14 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

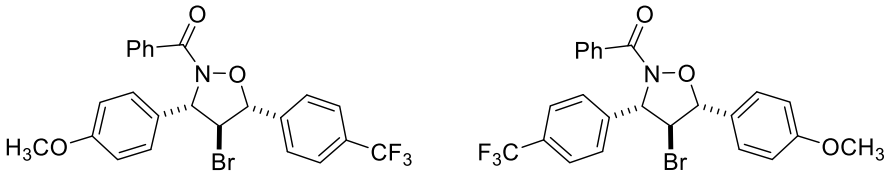
2,4,6-Collidine (0.060 mL, 0.45 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (210 mg, 0.449 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 1.5 hours additional $Br^+(coll)_2PF_6^-$ (207 mg, 0.443 mmol, 1.1 equiv) was added. After another hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.090 mL, 0.65 mmol, 1.6 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.5 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in

vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.17) afforded a colorless oil (86.8 mg, 0.182 mmol, 46%, **180**:**181** 0.97:1.00, **180** 95% ee, **181** 75% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min)

$[\alpha]_D^{20}$ – 5.78 (*c* 1.00, $CHCl_3$)

4.6.136 *trans*,*trans*-(4-Bromo-3-(4-methoxyphenyl)-5-(4-(trifluoromethyl)phenyl)isoxazolidin-2-yl)(phenyl)methanone (**182**) *trans*,*trans*-(4-Bromo-5-(4-methoxyphenyl)-3-(4-(trifluoromethyl)phenyl)isoxazolidin-2-yl)(phenyl)methanone (**183**)



$C_{24}H_{19}BrF_3NO_3$

[506.32]

(*E*)-Diphenylmethanone *O*-(3-(4-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)allyl) oxime/ (*E*)-Diphenylmethanone *O*-(1-(4-methoxyphenyl)-3-(4-(trifluoromethyl)phenyl)allyl) oxime (202 mg, 0.414 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (8 mL) and 2,4,6-collidine (0.060 mL, 0.45 mmol, 1.1 equiv) was added. $Br^+(coll)_2PF_6^-$ (214 mg, 0.458 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours additional $Br^+(coll)_2PF_6^-$ (211 mg, 0.452 mmol, 1.1 equiv) was added. After another hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.090 mL, 0.65 mmol, 1.6 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.7 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5 to 90:10, R_f = 0.26) afforded a colorless oil (139 mg, 0.275 mmol, 66%, **182**:**183** 0.09:1.00).

Minor product **182**:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 – 7.82 (m, 2H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.55 – 7.45 (m, 5H), 7.45 – 7.36 (m, 2H), 7.00 – 6.93 (m, 2H), 5.79 (d, *J* = 5.5 Hz, 1H), 5.17 (d, *J* = 8.5 Hz, 1H), 4.23 (dd, *J* = 8.5, 5.5, 1H), 3.84 (s, 3H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -62.86.

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.94 (C=O), 160.67 (C-OCH_3), 138.22 (*p*-CF_3), 133.09, 132.88, 132.56 (q, *J* = 33.0 Hz, *ipso*-CF_3), 131.25, 130.41, 129.13, 128.30, 128.19, 126.76 (q, *J* = 3.7 Hz, *o*-CF_3), 124.70 (q, *J* = 272.5 Hz, CF_3), 115.58, 90.39 (CH-O), 71.70 (br s, C-N), 58.85 (C-Br), 56.26 (OCH_3).

Major product **183**:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (dt, *J* = 7.1, 1.4 Hz, 2H), 7.73 (d, *J* = 1.2 Hz, 4H), 7.58 – 7.47 (m, 1H), 7.42 (ddt, *J* = 8.3, 6.5, 1.2 Hz, 2H), 7.33 – 7.27 (m, 2H), 6.94 – 6.86 (m, 2H), 5.96 (d, *J* = 6.2 Hz, 1H), 5.05 (d, *J* = 9.0 Hz, 1H), 4.25 (dd, *J* = 9.0, 6.2 Hz, 1H), 3.79 (s, 3H).

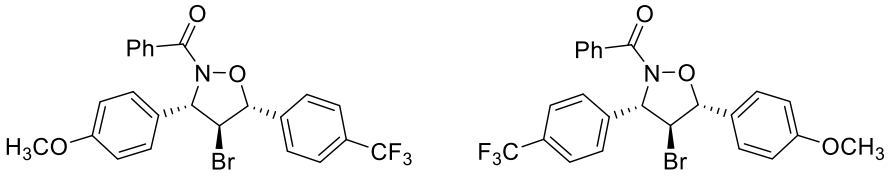
^{19}F NMR (282 MHz, $CDCl_3$) δ -62.63.

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.70 (C=O), 160.87 (C-OCH_3), 142.76 (*p*-CF_3), 132.26 (*p*-Ph), 131.75 (C-C=O), 130.73 (q, *J* = 32.9 Hz, *ipso*-CF_3), 129.75 (*o*-Ph), 128.77 (*m*-OCH_3), 128.22 (*m*-Ph), 126.63 (*m*-CF_3), 126.30 (q, *J* = 3.7 Hz, *o*-CF_3), 124.09 (q, *J* = 272.2 Hz, CF_3), 124.00 (*p*-OCH_3), 114.42 (*o*-OCH_3), 90.41 (CH-O), 70.08 (br s, C-N), 56.94 (C-Br), 55.42 (OCH_3).

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 2936 (w), 2839 (w), 1656, 1615, 1579, 1517, 1448, 1419, 1325 (s), 1254, 1175, 1125, 1067, 1031, 1018, 975, 920, 830, 810, 756, 704, 665, 605 (w), 539 (w).

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{24}H_{20}BrF_3NO_3$, 506.057; found, 506.058.

4.6.137 ((3*S*,4*S*,5*R*)-4-bromo-3-(4-methoxyphenyl)-5-(4-(trifluoromethyl)phenyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**182**) ((3*S*,4*S*,5*R*)-4-bromo-5-(4-methoxyphenyl)-3-(4-(trifluoromethyl)phenyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**183**)



$C_{24}H_{19}BrF_3NO_3$

[506.32]

$[PdCl(C_3H_5)]_2$ (2.0 mg, 0.0055 mmol, 2.6 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.3 mg, 0.012 mmol, 2.8 mol%) were dissolved in dry, degassed MeCN (0.6 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-3-(4-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)allyl acetate (150 mg, 0.428 mmol, 1.0 equiv) and diphenylmethanone oxime (87.7 mg, 0.445 mmol, 1.0 equiv) in dry, degassed MeCN (1.4 mL) and dry, degassed DIPEA (0.15 mL, 0.86 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 20 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

2,4,6-Collidine (0.070 mL, 0.53 mmol, 1.2 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8.5 mL). $Br^+(coll)_2PF_6^-$ (220 mg, 0.471 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours additional $Br^+(coll)_2PF_6^-$ (218 mg, 0.467 mmol, 1.1 equiv) was added. After another hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (17 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (8.5 mL). Et_3N (0.090 mL, 0.65 mmol, 1.5 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.6 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5 to 90:10, R_f = 0.26) afforded a colorless oil (94.3 mg, 0.186 mmol, 44%, **182**:**183** 0.30:1.00, **182** 94% ee, **183** 45% ee).

$[\alpha]_D^{20}$ – 7.92 (*c* 1.00, $CHCl_3$)

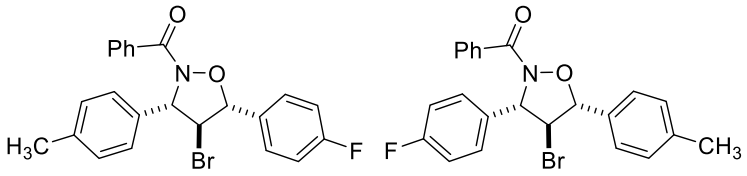
$[PdCl(C_3H_5)]_2$ (2.0 mg, 0.0055 mmol, 2.6 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (6.3 mg, 0.012 mmol, 2.8 mol%) were dissolved in dry, degassed toluene (0.6 mL). After 30 minutes a solution of (*E*)-3-(4-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)allyl acetate (136 mg, 0.388 mmol, 1.0 equiv) and diphenylmethanone oxime (80.2 mg, 0.407 mmol, 1.0 equiv) in dry, degassed toluene (4.4 mL) was cooled to 0 °C and the yellow catalyst solution and dry, degassed DIPEA (0.14 mL, 0.80 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 14 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

2,4,6-Collidine (0.060 mL, 0.45 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (8 mL). $Br^+(coll)_2PF_6^-$ (201 mg, 0.430 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours additional $Br^+(coll)_2PF_6^-$ (202 mg, 0.432 mmol, 1.1 equiv) was added. After another hour a 10 wt% solution of $Na_2S_2O_5$ in H_2O (16 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (8 mL). Et_3N (0.090 mL, 0.65 mmol, 1.9 equiv) and benzoyl chloride (0.070 mL, 0.60 mmol, 1.6 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5 to 90:10, R_f = 0.26) afforded a colorless oil (97.6 mg, 0.193 mmol, 50%, **182**:**183** 0.16:1.00, **182** 94% ee, **183** 23% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min).

$[\alpha]_D^{20}$ – 4.86 (*c* 1.00, $CHCl_3$)

4.6.138 *trans*,*trans*-(4-Bromo-5-(4-fluorophenyl)-3-(*p*-tolyl)isoxazolidin-2-yl)(phenyl)methanone (**184**) *trans*,*trans*-(4-Bromo-3-(4-fluorophenyl)-5-(*p*-tolyl)isoxazolidin-2-yl)(phenyl)methanone (**185**)



$C_{23}H_{19}BrFNO_2$

[440.31]

(*E*)-Diphenylmethanone *O*-(1-(4-fluorophenyl)-3-(*p*-tolyl)allyl) oxime/ (*E*)-Diphenylmethanone *O*-(3-(4-fluorophenyl)-1-(*p*-tolyl)allyl) oxime (207 mg, 0.491 mmol, 1.0 equiv) were dissolved in dry CH_2Cl_2 (10 mL) and 2,4,6-collidine (0.080 mL, 0.60 mmol, 1.2 equiv) was added. $Br^+(coll)_2PF_6^-$ (261 mg, 0.559 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (20 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (10 mL). Et_3N (0.090 mL, 0.65 mmol, 1.3 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.4 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.14) afforded a colorless oil (142 mg, 0.323 mmol, 66%, **184**:**185** 0.99:1.00).

Minor product **184**:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 – 7.81 (m, 2H), 7.60 – 7.51 (m, 3H), 7.42 – 7.16 (m, 6H), 7.09 – 7.01 (m, 2H), 5.80 (d, *J* = 5.6 Hz, 1H), 5.08 (d, *J* = 8.7 Hz, 1H), 4.23 (dd, *J* = 8.7, 5.6, 1H), 2.38 (s, 3H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -111.34.

Major product **185**:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 – 7.86 (m, 2H), 7.51 – 7.43 (m, 3H), 7.42 – 7.16 (m, 6H), 7.16 – 7.09 (m, 2H), 5.85 (d, *J* = 6.0 Hz, 1H), 5.03 (d, *J* = 8.9 Hz, 1H), 4.23 (dd, *J* = 8.9, 6.0, 1H), 2.35 (s, 3H).

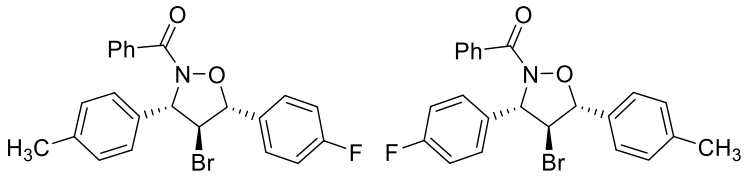
^{19}F NMR (282 MHz, $CDCl_3$) δ -113.69.

Combined ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.82 (C=O, minor), 171.68 (C=O, major), 163.48 (d, *J* = 249.1 Hz, minor), 162.77 (d, *J* = 247.0 Hz, major), 139.93, 138.35, 135.71, 134.60 (d, *J* = 3.1 Hz, major), 132.16, 132.13, 132.11, 131.98, 129.99, 129.71, 129.66, 129.59, 129.58, 129.11 (d, *J* = 8.8 Hz, minor), 128.92 (d, *J* = 3.1 Hz, minor), 128.23, 128.19, 128.03 (d, *J* = 8.6 Hz, major), 127.20, 126.08, 116.22 (d, *J* = 21.5 Hz, major), 116.01 (d, *J* = 22.0 Hz, minor), 90.49 (C-O, major), 89.90 (C-O, minor), 70.89 (br s, C-N, minor), 70.10 (br s, C-N, major), 58.13 (C-Br, minor), 57.63 (C-Br, major), 21.40 (CH_3, major), 21.32 (CH_3, minor).

IR (thin film) $\tilde{\nu}_{max}$ (cm^{-1}) 2923 (w), 1657 (s, C=O), 1605, 1578, 1511 (s), 1448, 1379, 1335, 1228 (s), 1159, 978, 914 (s), 837, 814, 745 (s), 702, 664, 557.

HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{23}H_{20}BrFNO_2$, 440.066; found, 440.066.

4.6.139 ((3*S*,4*S*,5*R*)- 4-Bromo-5-(4-fluorophenyl)-3-(*p*-tolyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**184**) ((3*S*,4*S*,5*R*)- 4-Bromo-3-(4-fluorophenyl)-5-(*p*-tolyl)isoxazolidin-2-yl)(phenyl)methanone ((*S*,*S*,*R*)-**185**)



$C_{23}H_{19}BrFNO_2$

[440.31]

$[PdCl(C_3H_5)]_2$ (2.1 mg, 0.0057 mmol, 2.5 mol% Pd) and (*R*)-bis(3,5-dimethylphenyl)(2'-vinyl-[1,1'-binaphthalen]-2-yl)phosphane (7.4 mg, 0.014 mmol, 3.1 mol%) were dissolved in dry, degassed MeCN (0.7 mL). After 30 minutes the yellow solution was cooled to 0 °C and a solution of (*E*)-1-(4-fluorophenyl)-3-(*p*-tolyl)allyl acetate (132 mg, 0.461 mmol, 1.0 equiv) and diphenylmethanone oxime (95.7 mg, 0.485 mmol, 1.0 equiv) in dry, degassed MeCN (2.3 mL) and dry, degassed DIPEA (0.16 mL, 0.92 mmol, 2.0 equiv) were added. The reaction was monitored by TLC and after 12 hours the solution was diluted with EtOAc, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the solvent removed in vacuo (bath temp. 30 °C).

2,4,6-Collidine (0.070 mL, 0.53 mmol, 1.1 equiv) was added to the obtained oil and the resulting mixture dissolved in dry CH_2Cl_2 (9 mL). $Br^+(coll)_2PF_6^-$ (241 mg, 0.516 mmol, 1.1 equiv) was added under exclusion of light and the reaction monitored by TLC. After 2 hours a 10 wt% solution of $Na_2S_2O_5$ in H_2O (18 mL) was added and the resulting mixture stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 three times, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo.

The raw product was dissolved in dry CH_2Cl_2 (9 mL). Et_3N (0.10 mL, 0.72 mmol, 1.6 equiv) and benzoyl chloride (0.080 mL, 0.69 mmol, 1.5 equiv) were added and the resulting solution stirred overnight. H_2O and conc. NH_3 (2 mL) were added and the resulting mixture stirred for another 30 minutes. The aqueous phase was extracted with CH_2Cl_2 three time, the combined organic layers washed with brine, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (*n*-hexane/EtOAc 95:5, R_f = 0.14) afforded a colorless oil (128 mg, 0.291 mmol, 63%, **184**:**185** 0.71:1.00, **184** 93% ee, **185** 86% ee - IB, *n*-hexane/*i*PrOH 98:2, 0.4 ml/min).

$[\alpha]_D^{20}$ – 8.10 (*c* 1.00, $CHCl_3$)

5 Literature

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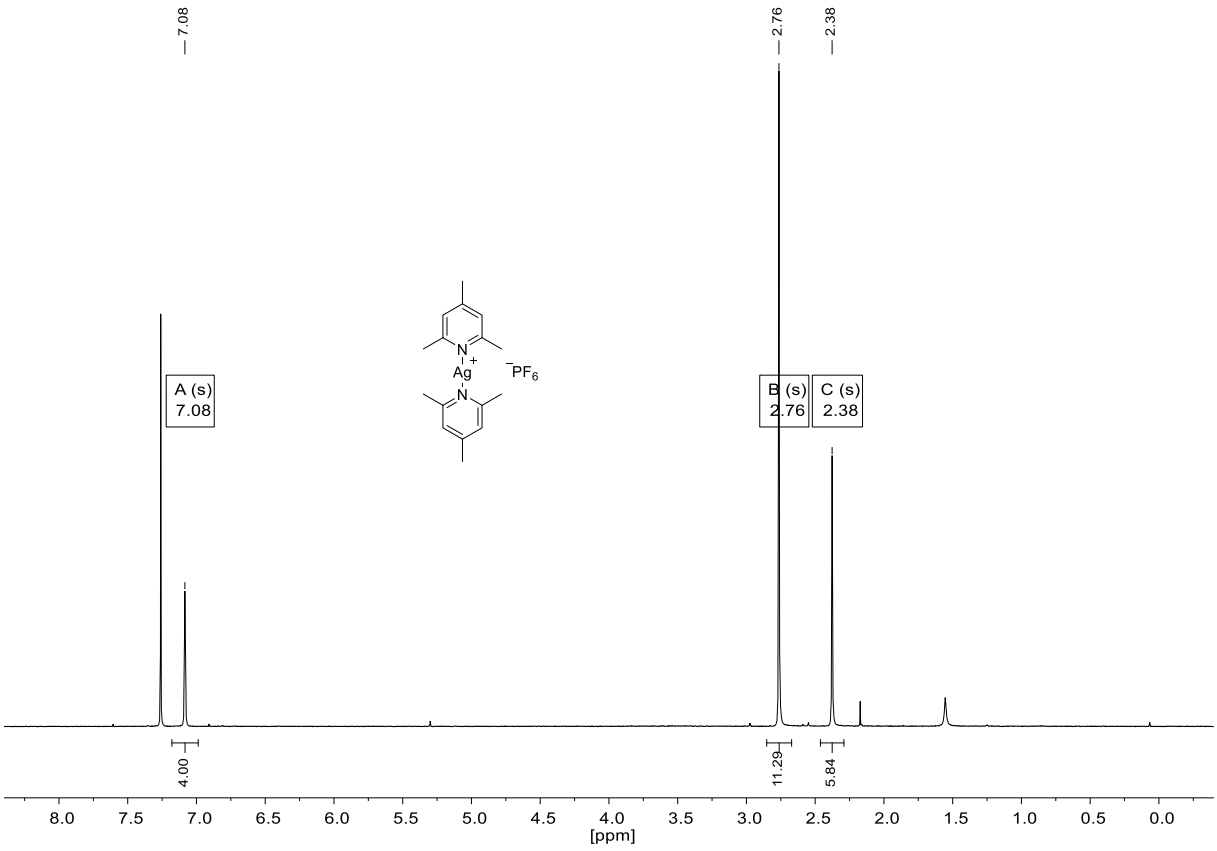
6 Spectra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11.29
5.84
8.0
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7.0
6.5
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5.5
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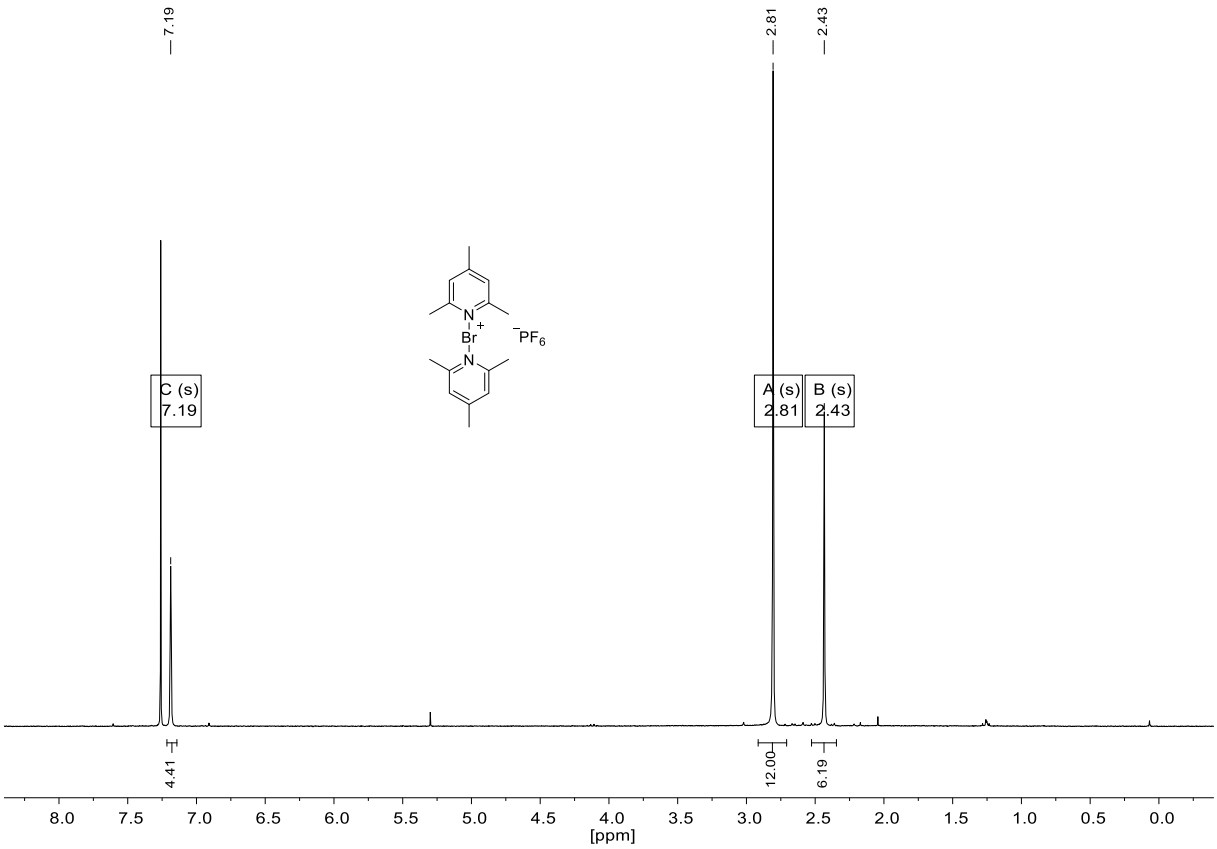
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6.19
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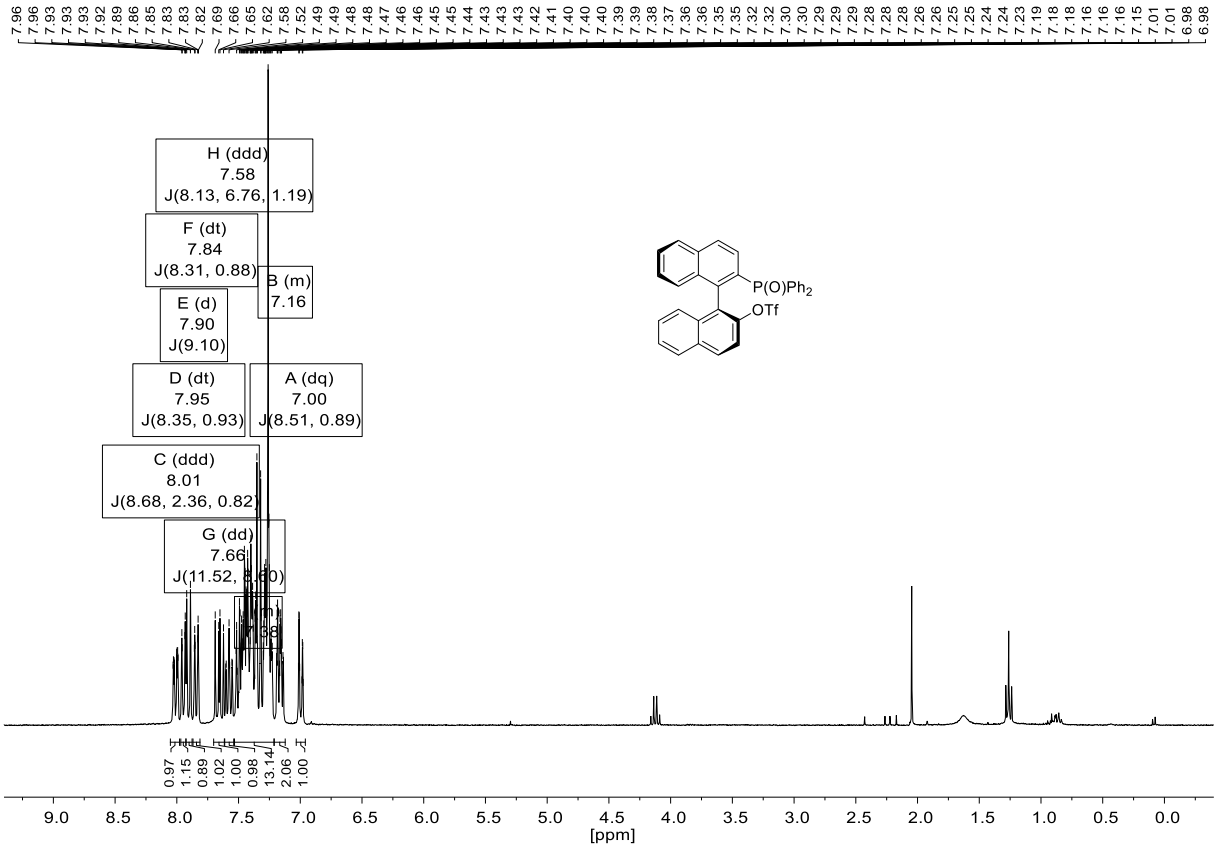
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J(8.13, 6.76, 1.19)
F (dt)
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J(8.31, 0.88)
B (m)
7.16
E (d)
7.90
J(9.10)
D (dt)
7.95
J(8.35, 0.93)
A (dq)
7.00
J(8.51, 0.89)
C (ddd)
8.01
J(8.68, 2.36, 0.82)
G (dd)
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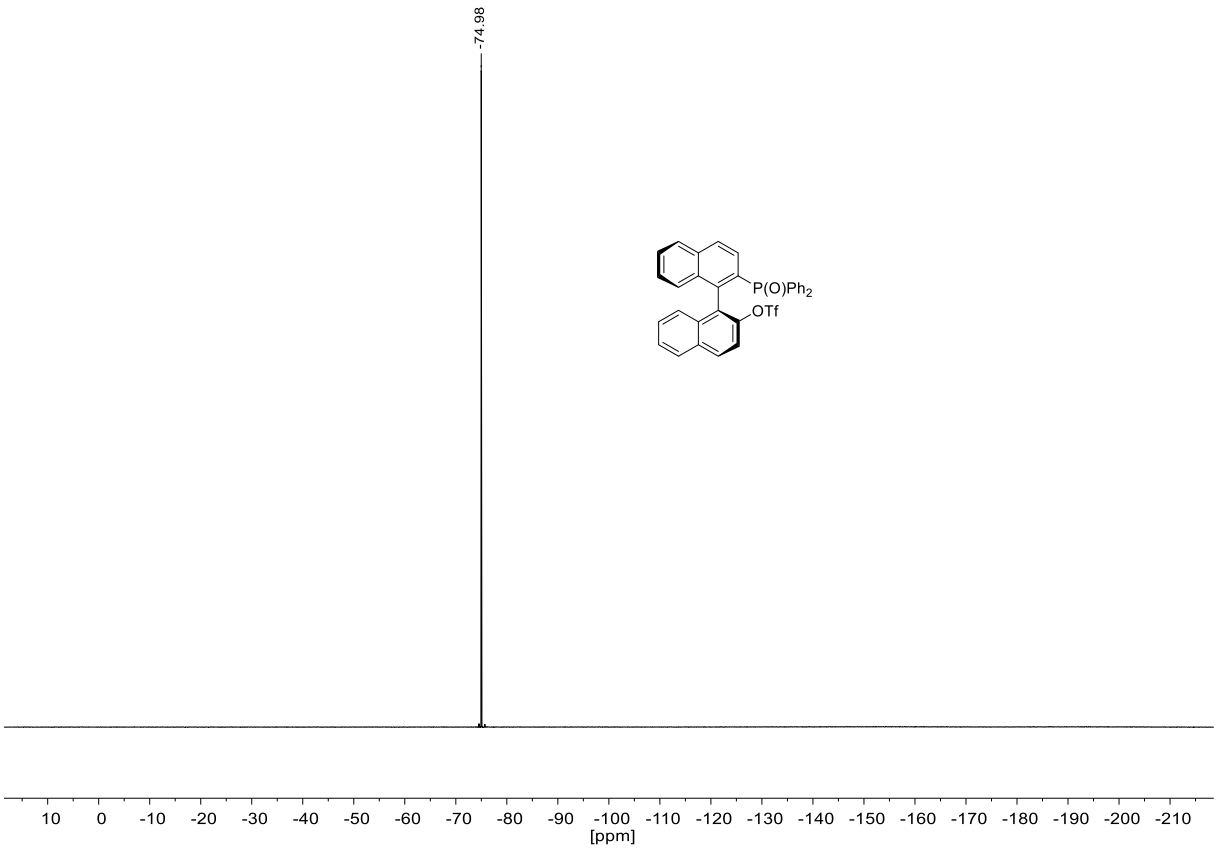
P(O)Ph2
OTf
[ppm]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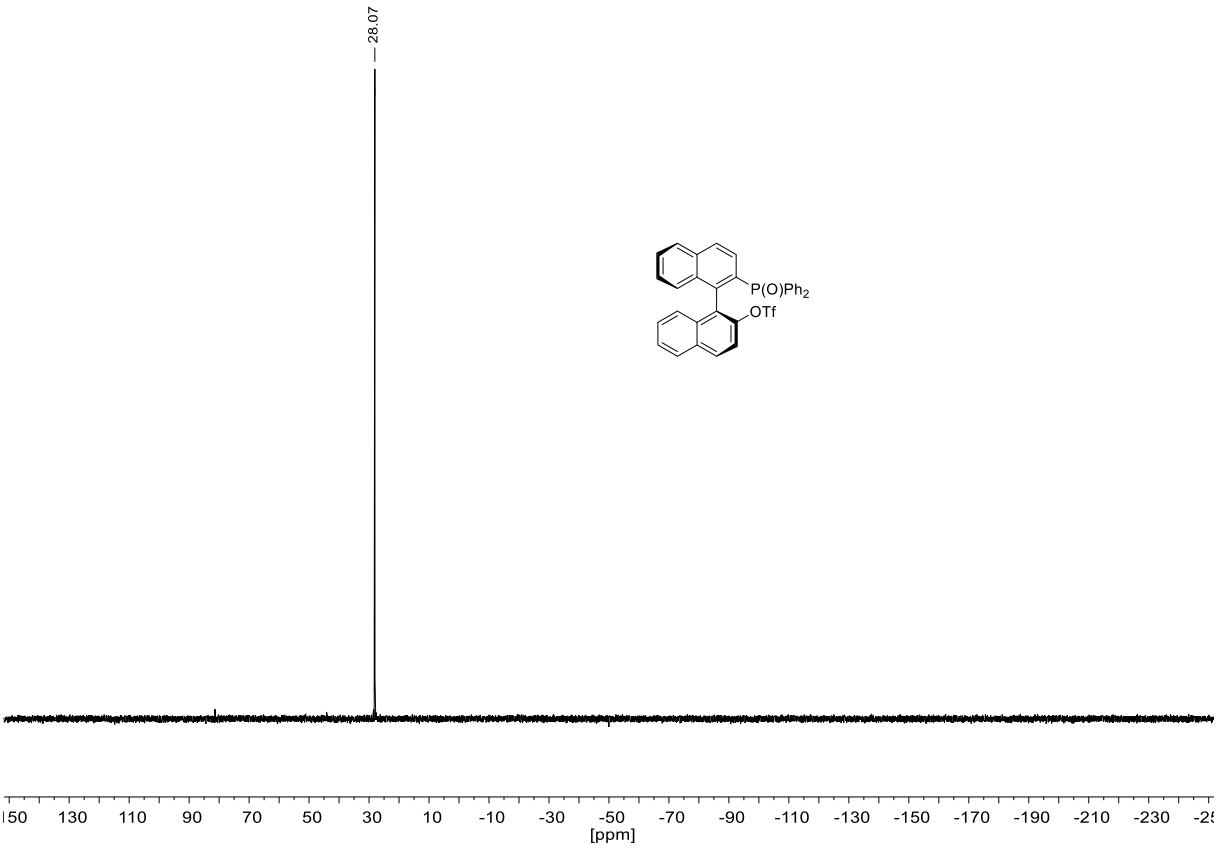
[ppm]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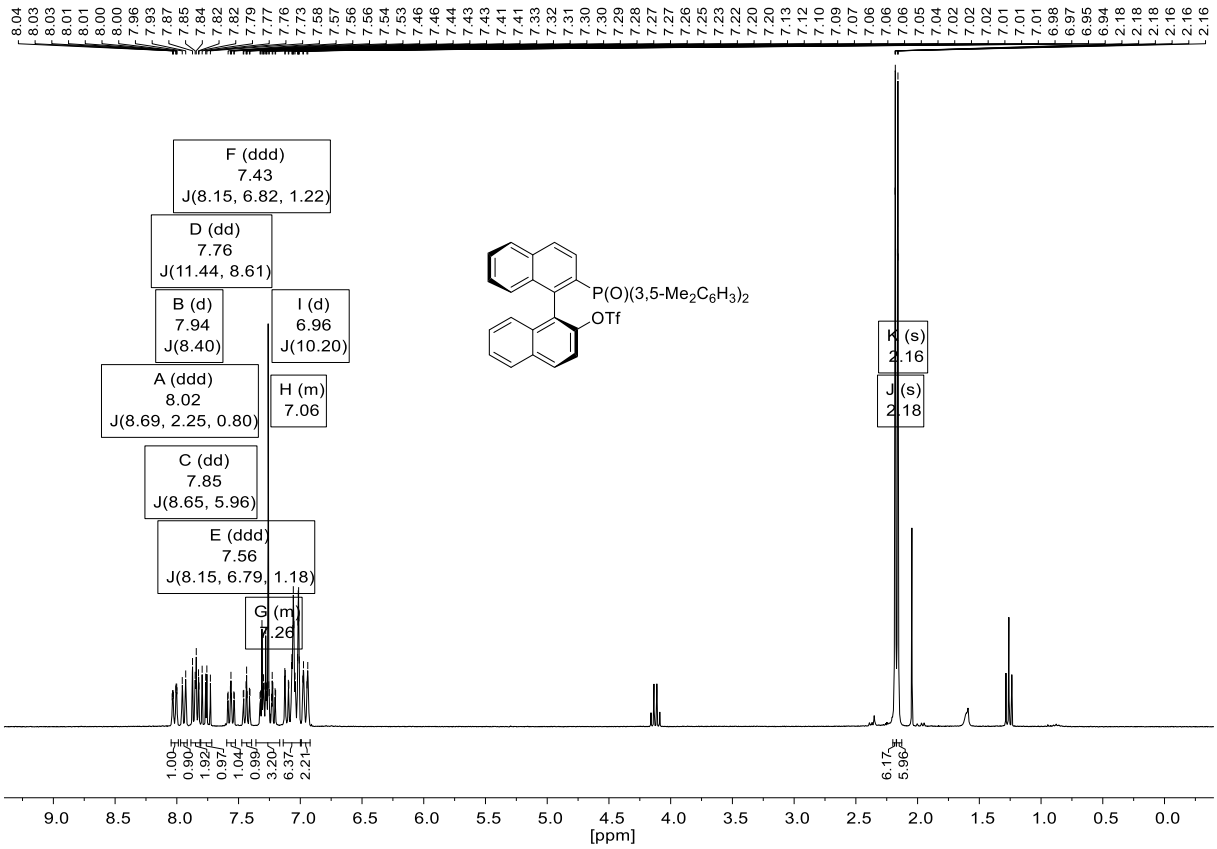
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B (d)
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J(8.40)
I (d)
6.96
J(10.20)
A (ddd)
8.02
J(8.69, 2.25, 0.80)
H (m)
7.06
C (dd)
7.85
J(8.65, 5.96)
E (ddd)
7.56
J(8.15, 6.79, 1.18)
G (m)
7.26
P(O)(3,5-Me2C6H3)2
OTf
K (s)
2.16
J (s)
2.18
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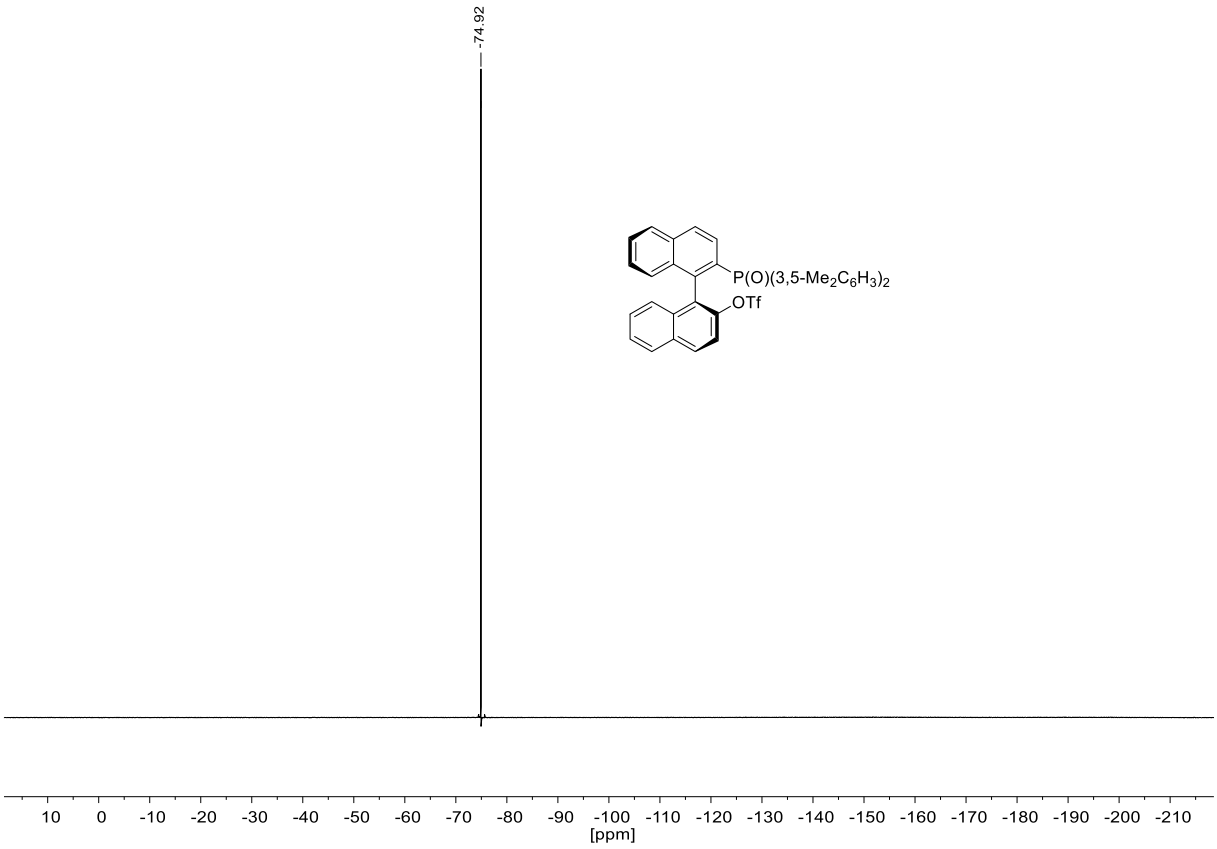
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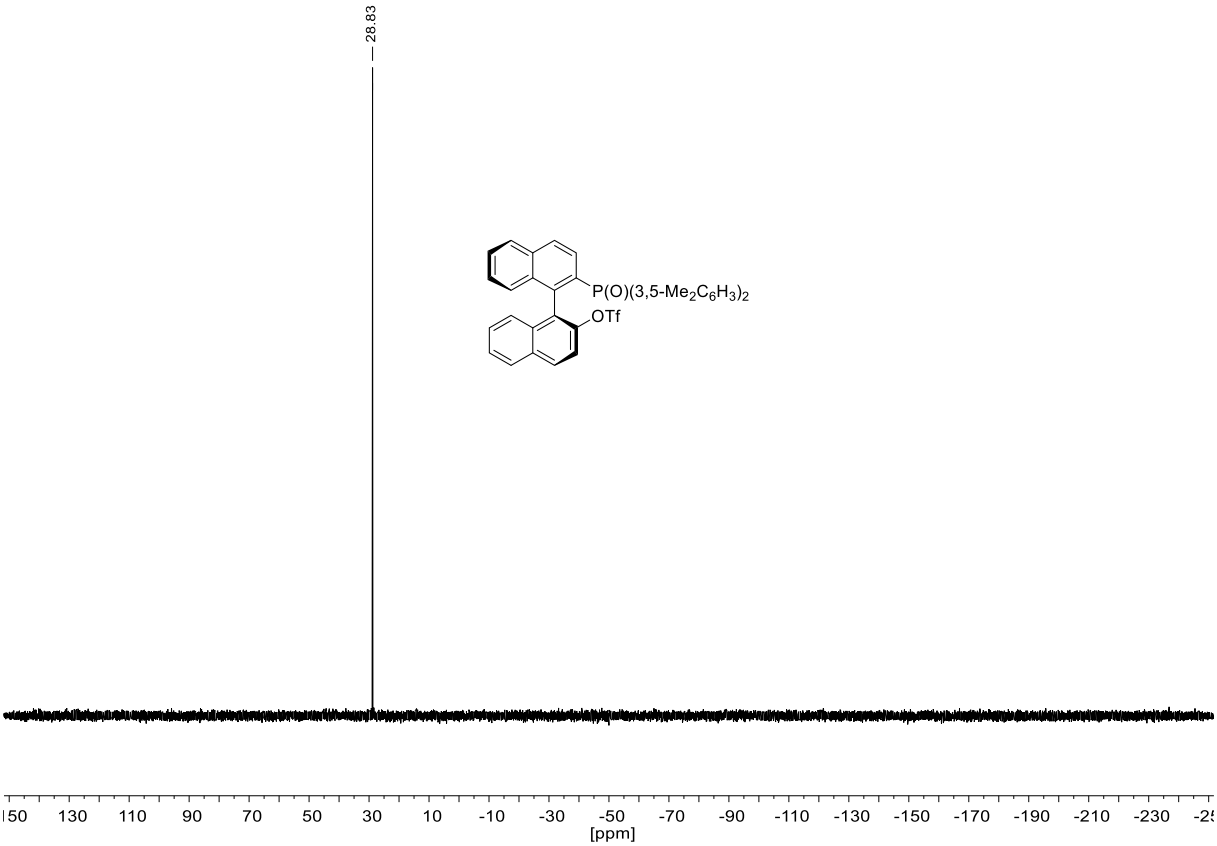
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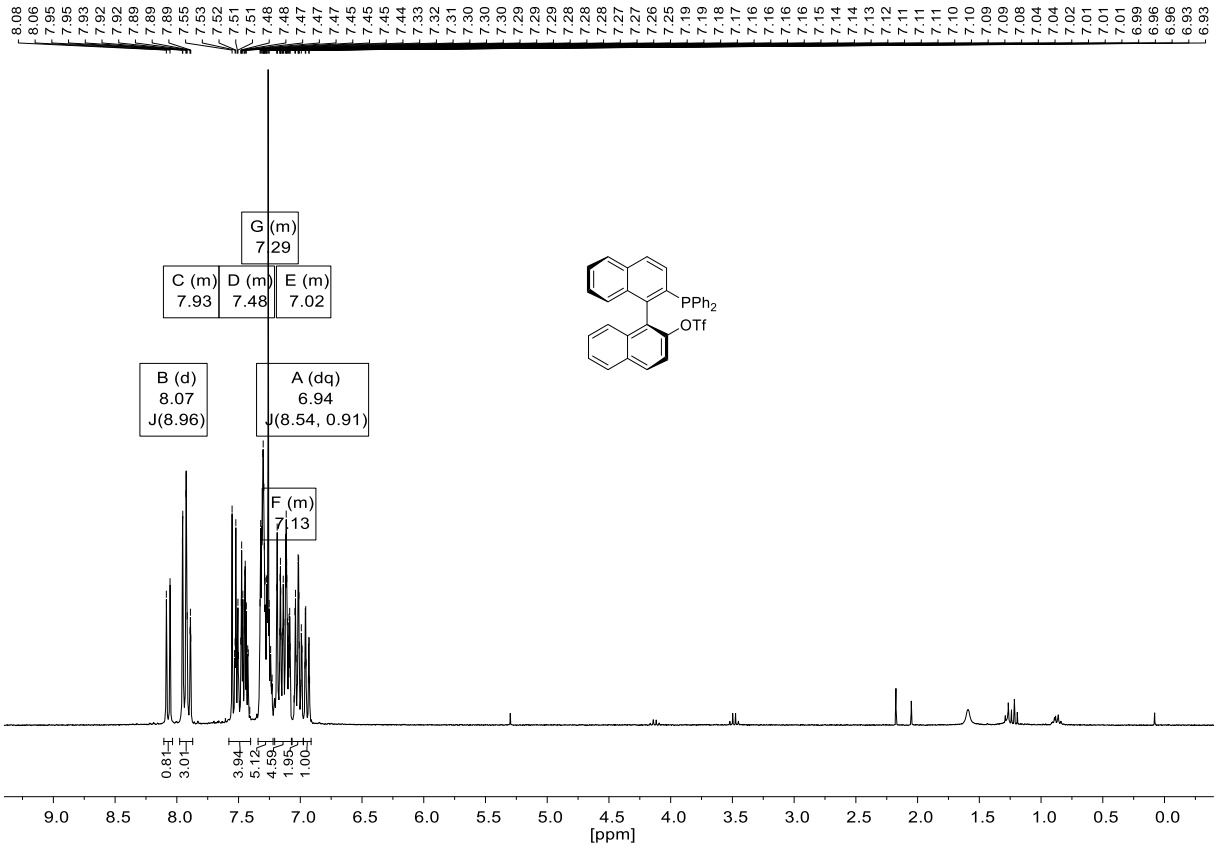
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D (m)
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B (d)
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A (dq)
6.94
J(8.54, 0.91)
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PPh2
OTf
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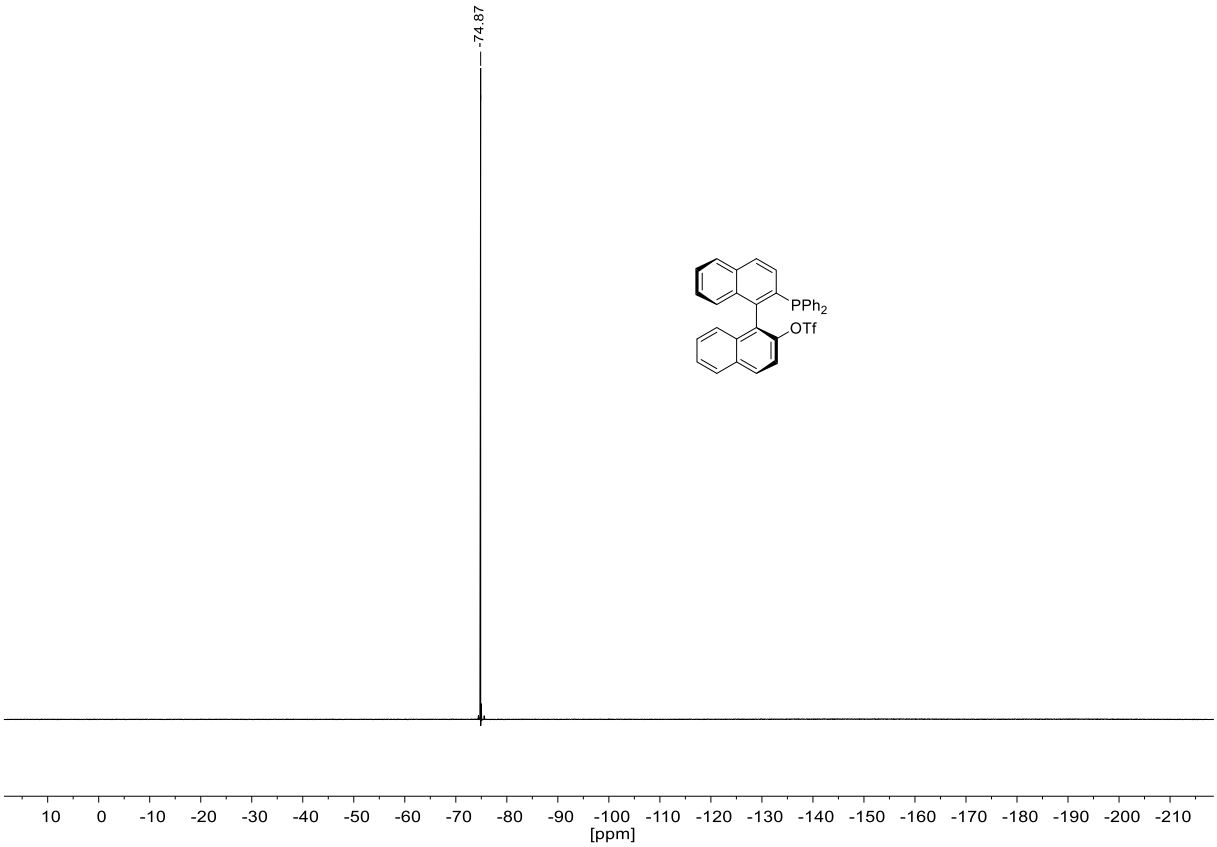
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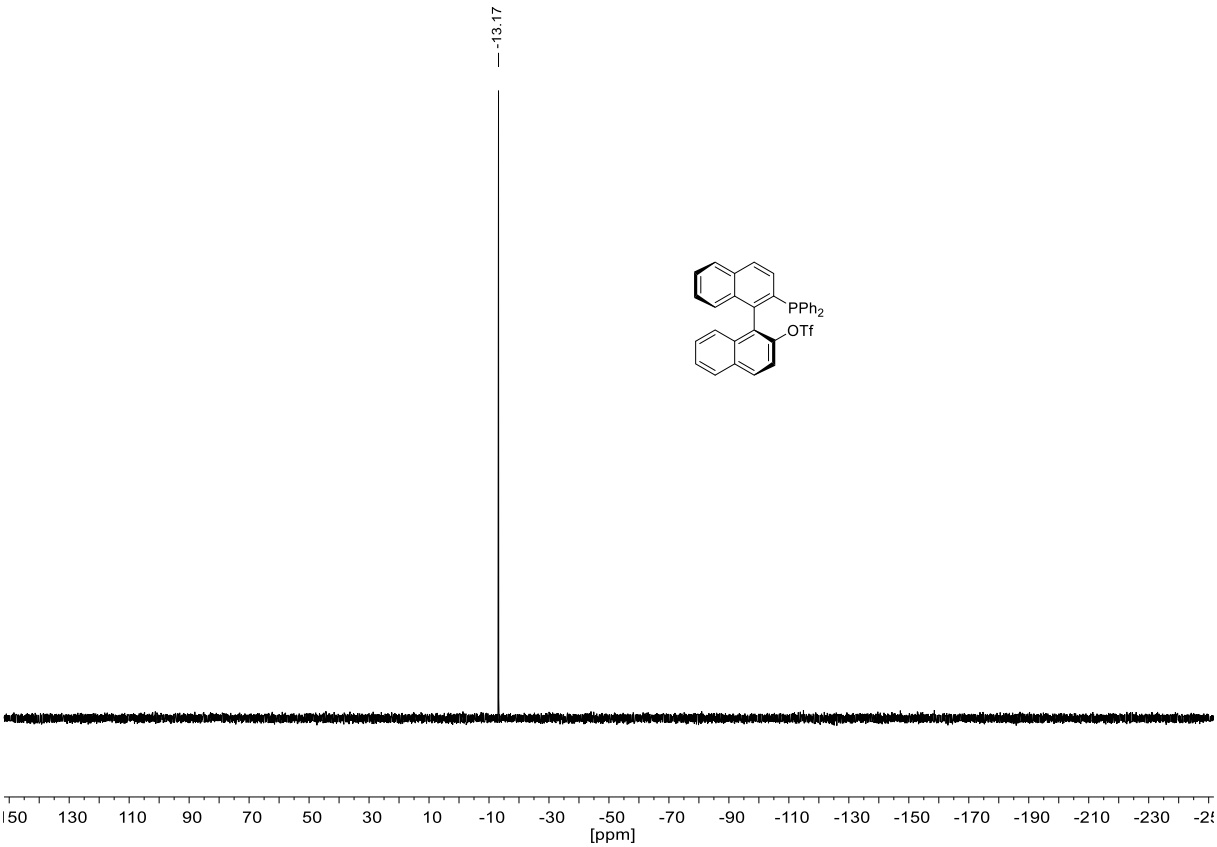
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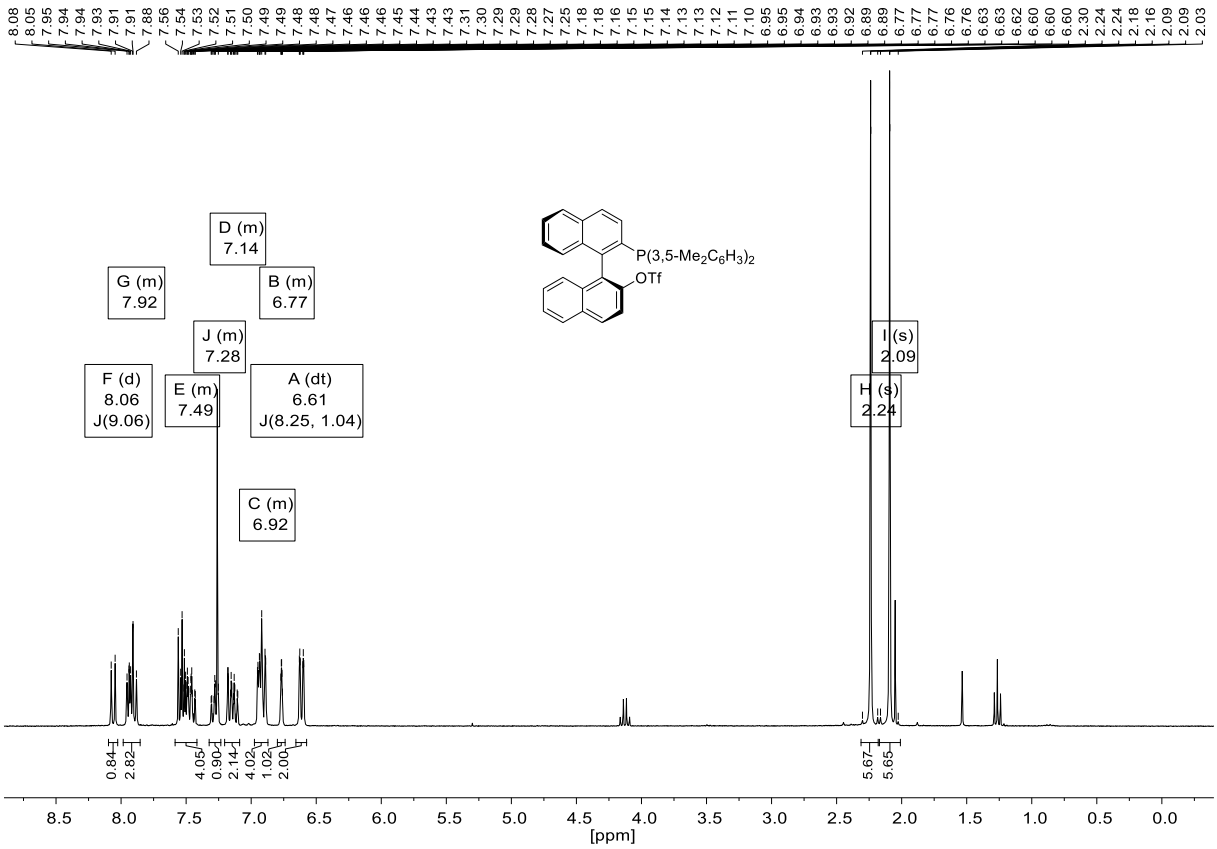
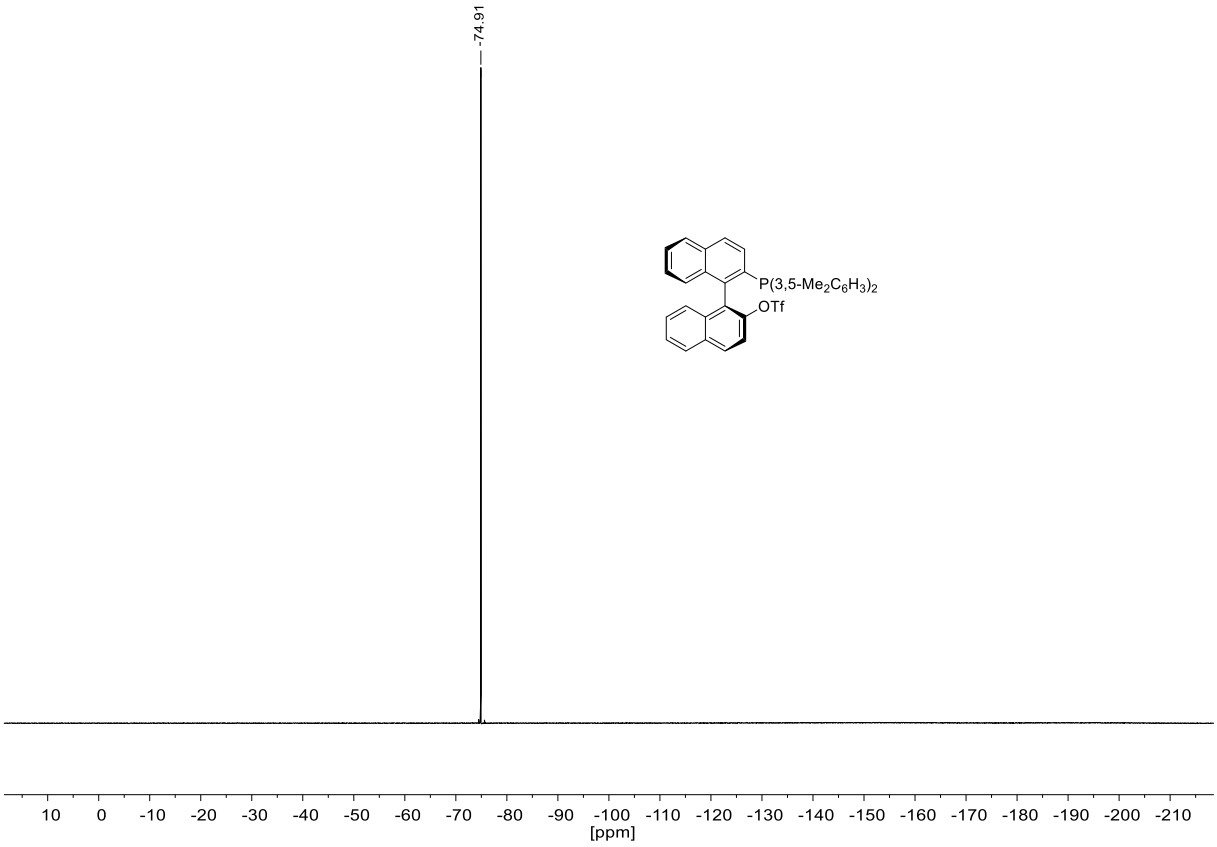
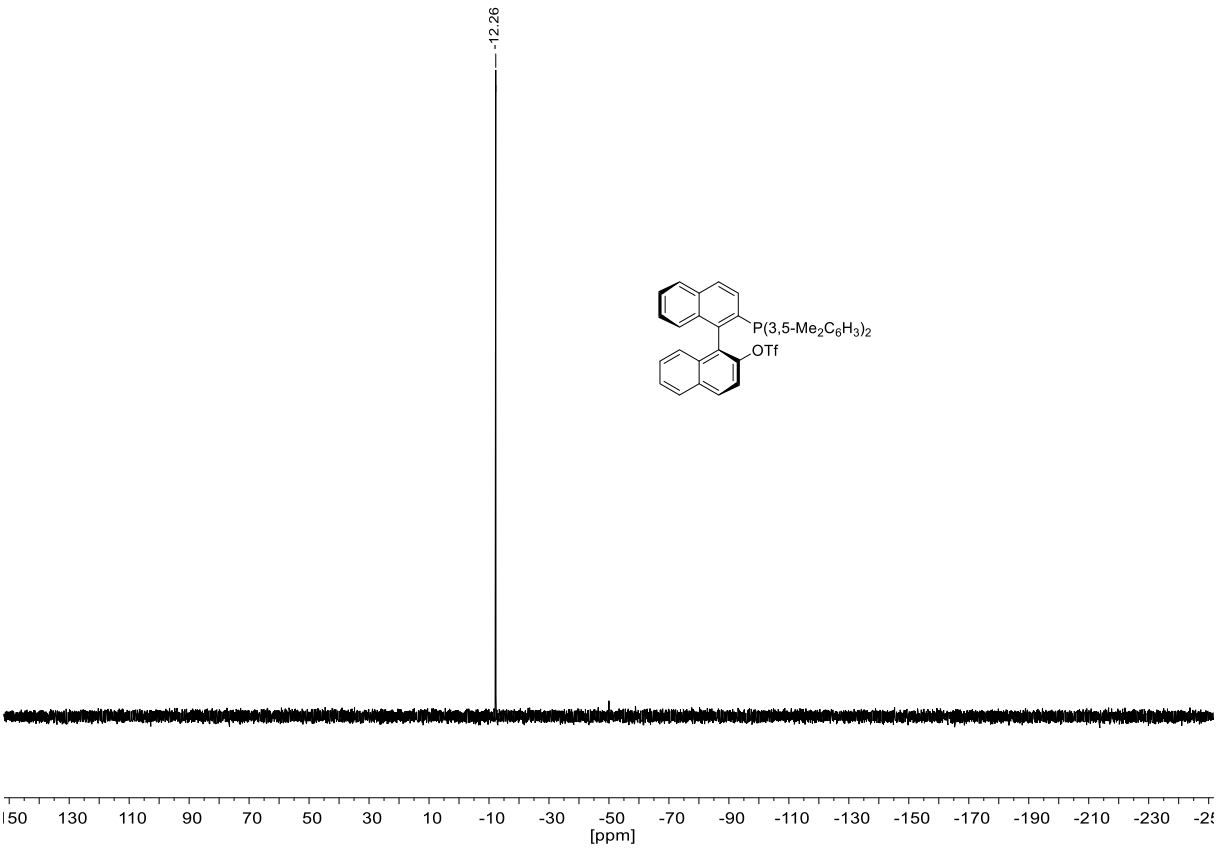
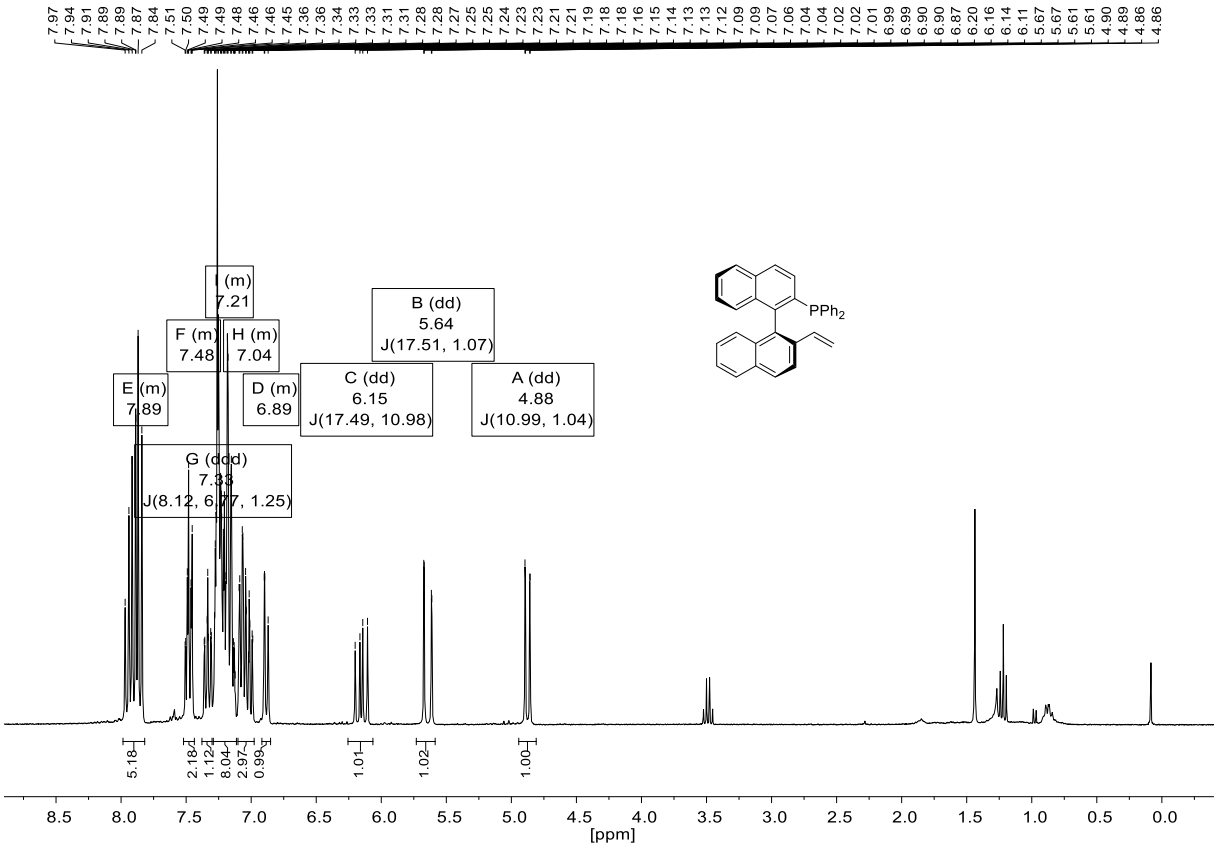
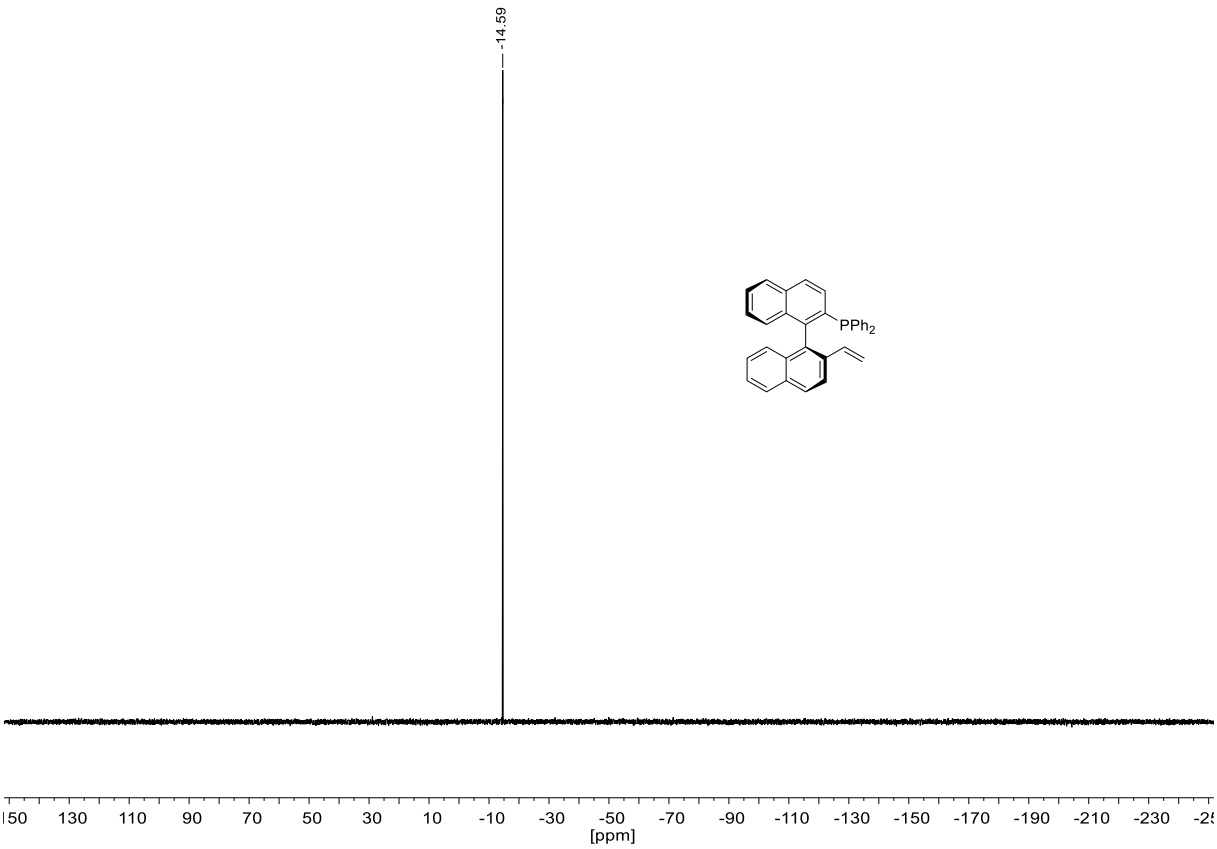
[ppm]

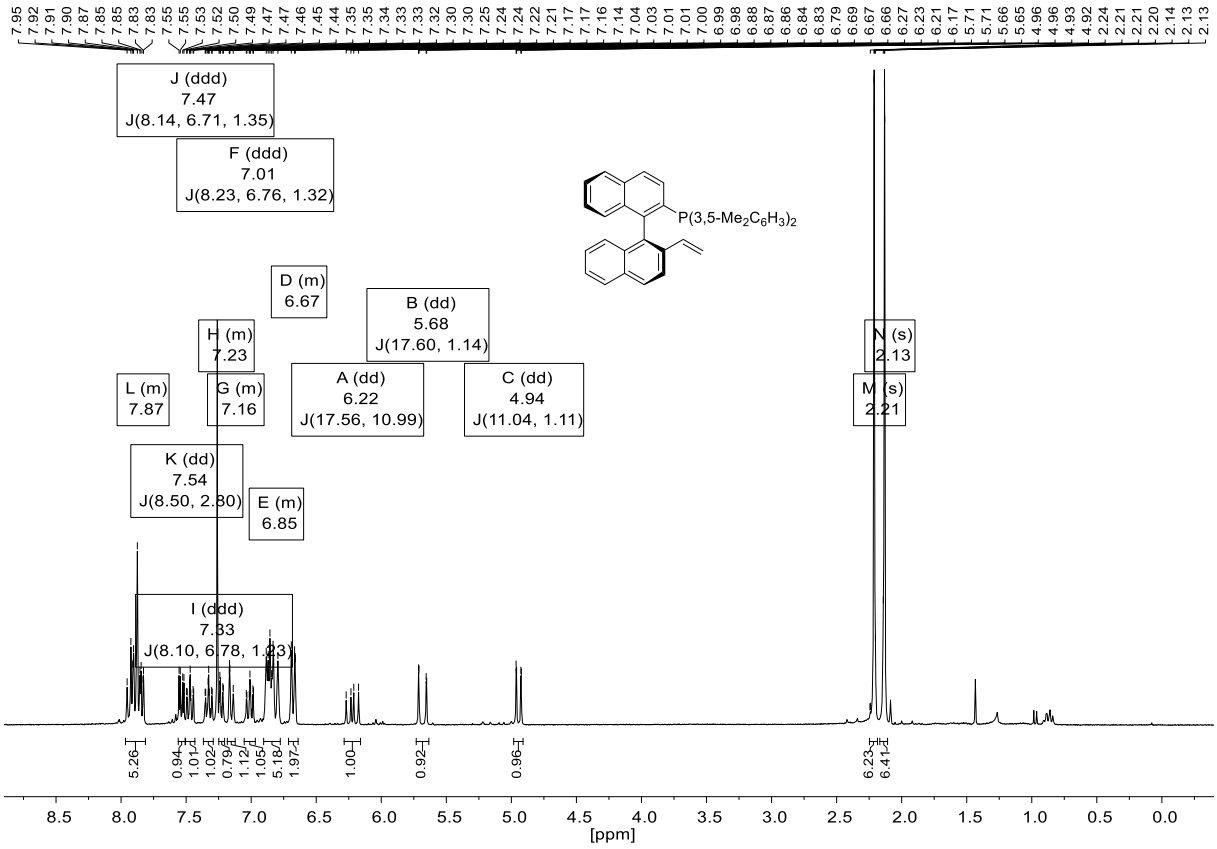

8.08 8.05 7.95 7.94 7.94 7.93 7.91 7.91 7.88 7.56 7.54 7.53 7.52 7.51 7.50 7.49 7.49 7.48 7.48 7.47 7.46 7.46 7.46 7.45 7.44 7.43 7.43 7.31 7.30 7.29 7.29 7.28 7.27 7.25 7.18 7.18 7.16 7.15 7.15 7.14 7.13 7.13 7.12 7.11 7.10 6.95 6.95 6.94 6.93 6.93 6.92 6.89 6.89 6.77 6.77 6.77 6.76 6.63 6.63 6.62 6.60 6.60 6.60 2.30 2.24 2.24 2.18 2.16 2.09 2.09 2.03
D (m) 7.14
G (m) 7.92
B (m) 6.77
J (m) 7.28
F (d) 8.06 J(9.06)
E (m) 7.49
A (dt) 6.61 J(8.25, 1.04)
C (m) 6.92
I (s) 2.09
H (s) 2.24
P(3,5-Me2C6H3)2
OTf
0.84 2.82 4.05 0.90 2.14 4.02 1.02 2.00 5.67 5.65
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

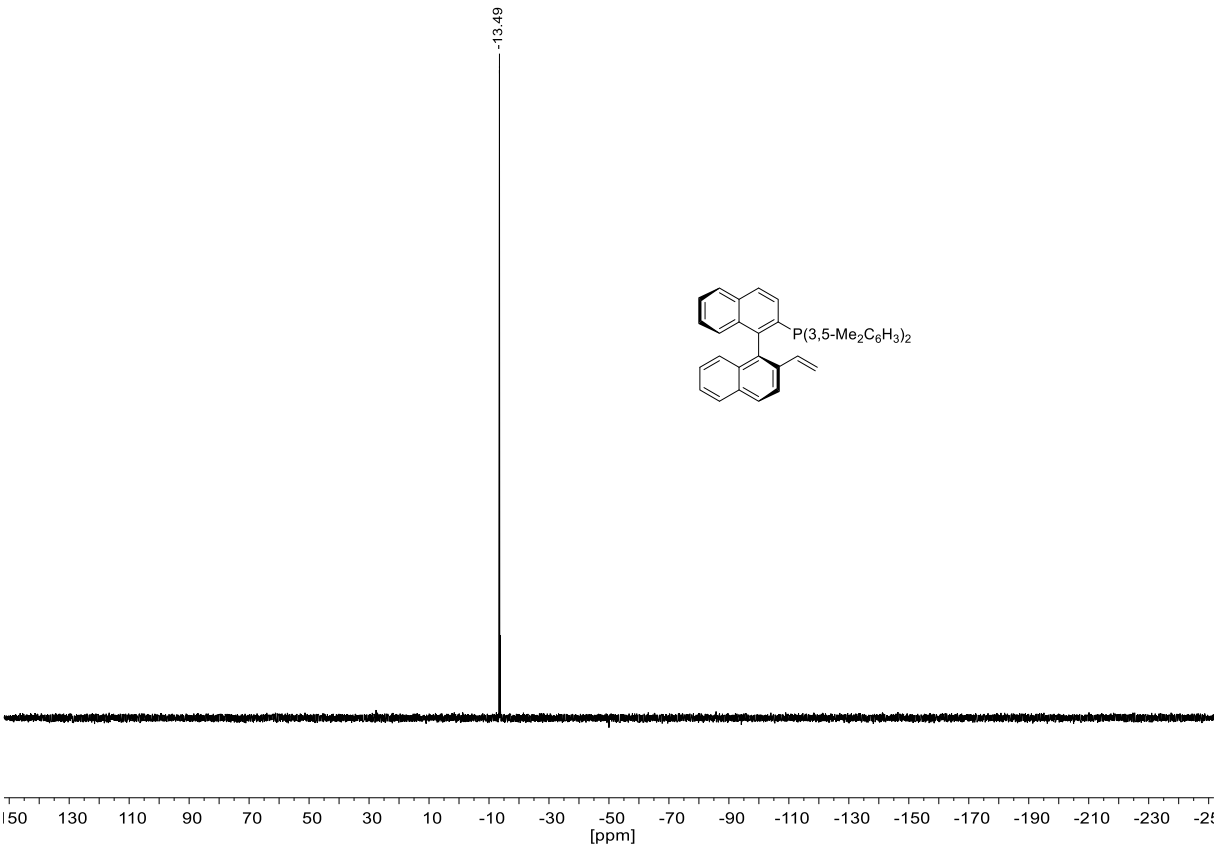

-74.91
P(3,5-Me2C6H3)2
OTf
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

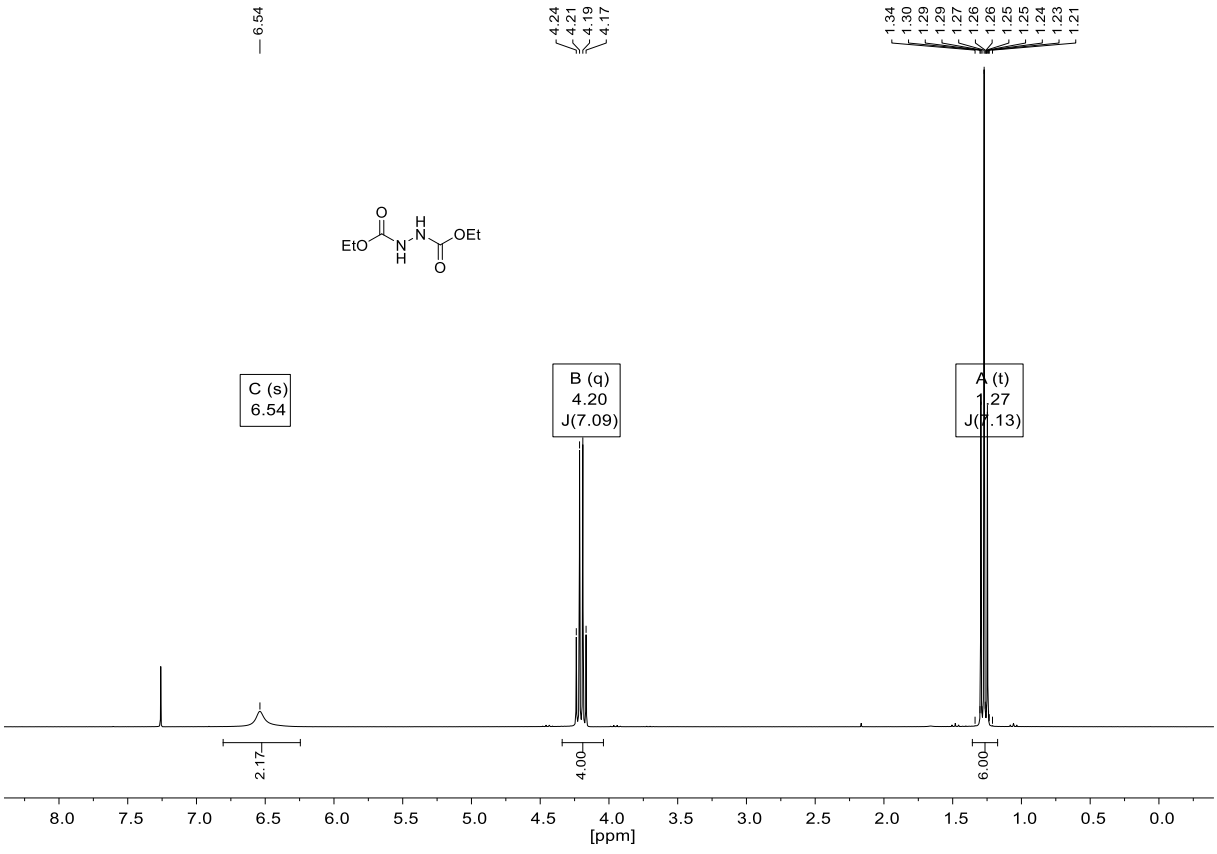

-12.26
P(3,5-Me2C6H3)2
OTf
[ppm]

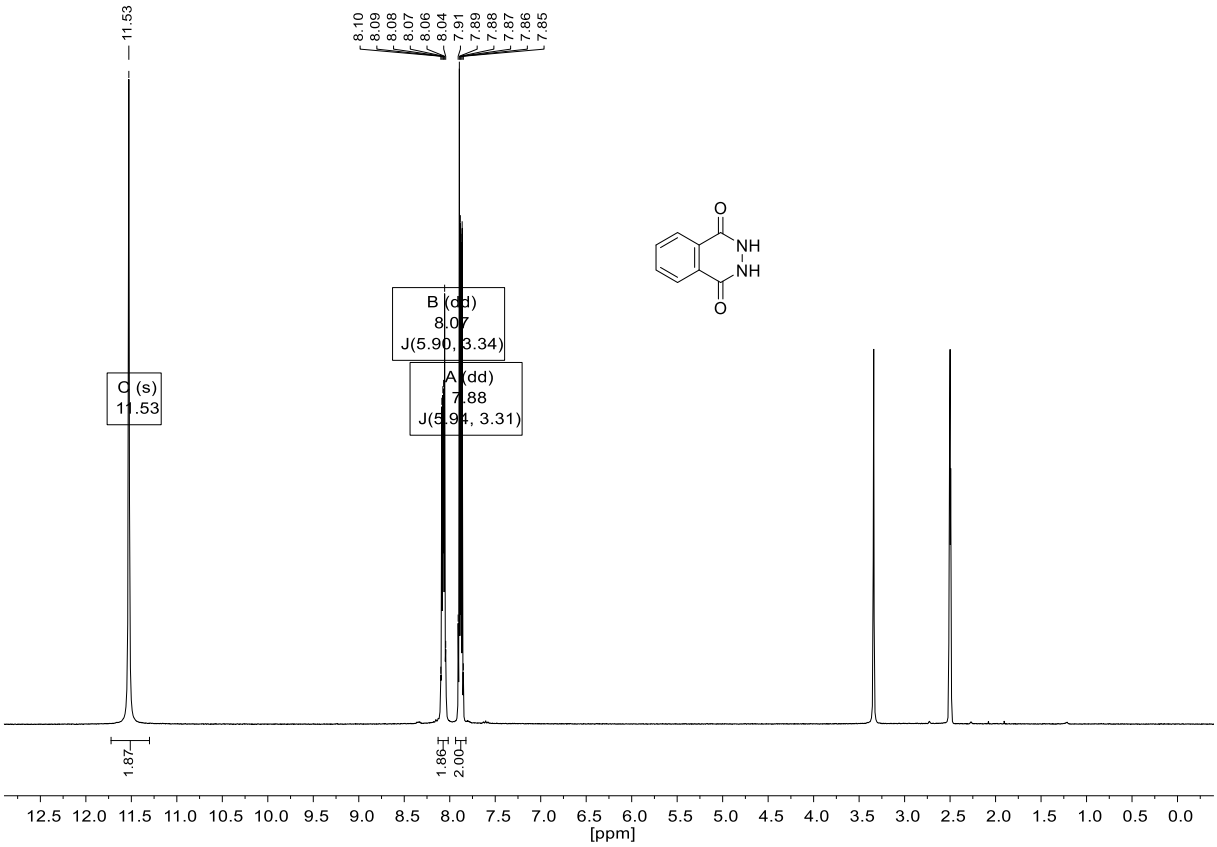

I (m)
7.21
F (m)
7.48
H (m)
7.04
E (m)
7.89
D (m)
6.89
B (dd)
5.64
J(17.51, 1.07)
C (dd)
6.15
J(17.49, 10.98)
A (dd)
4.88
J(10.99, 1.04)
G (ddd)
7.33
J(8.12, 6.77, 1.25)
PPh2
[ppm]

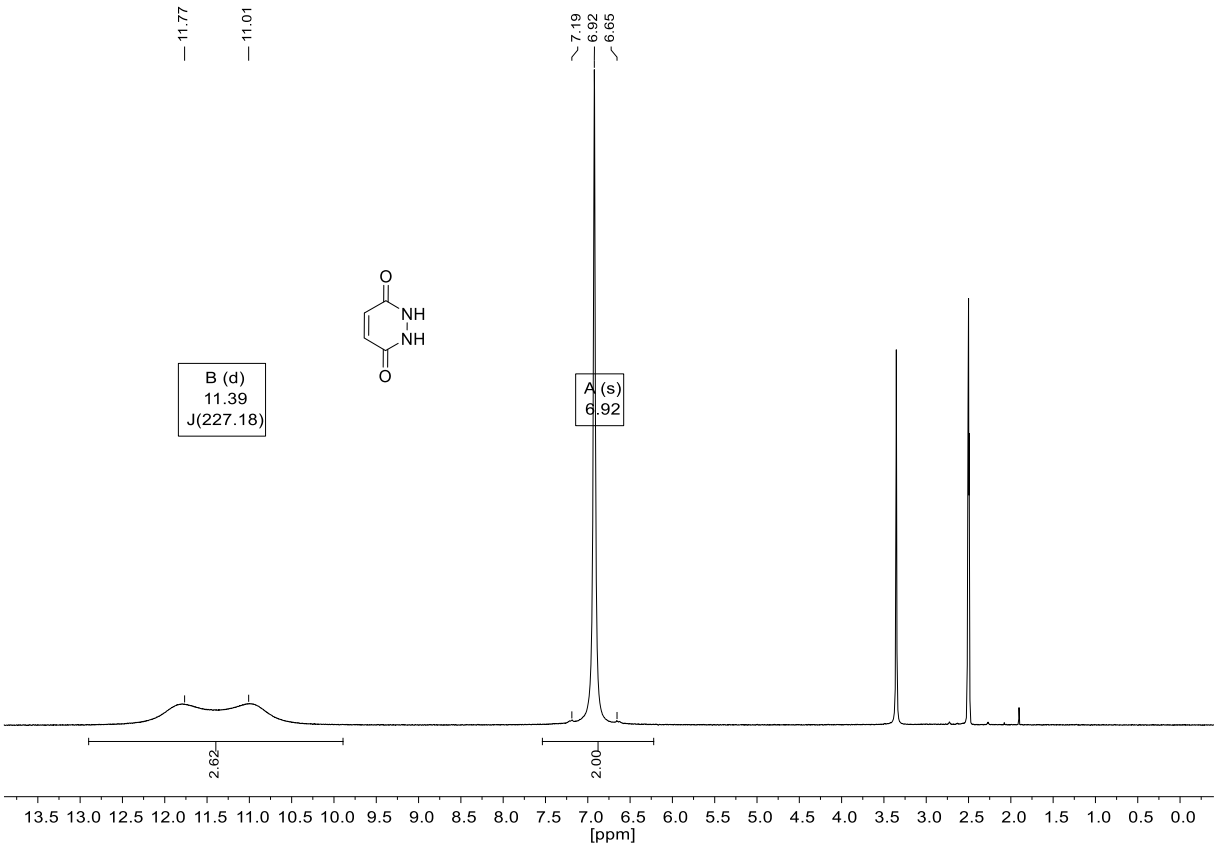

-14.59
PPh2
150 130 110 90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230
[ppm]

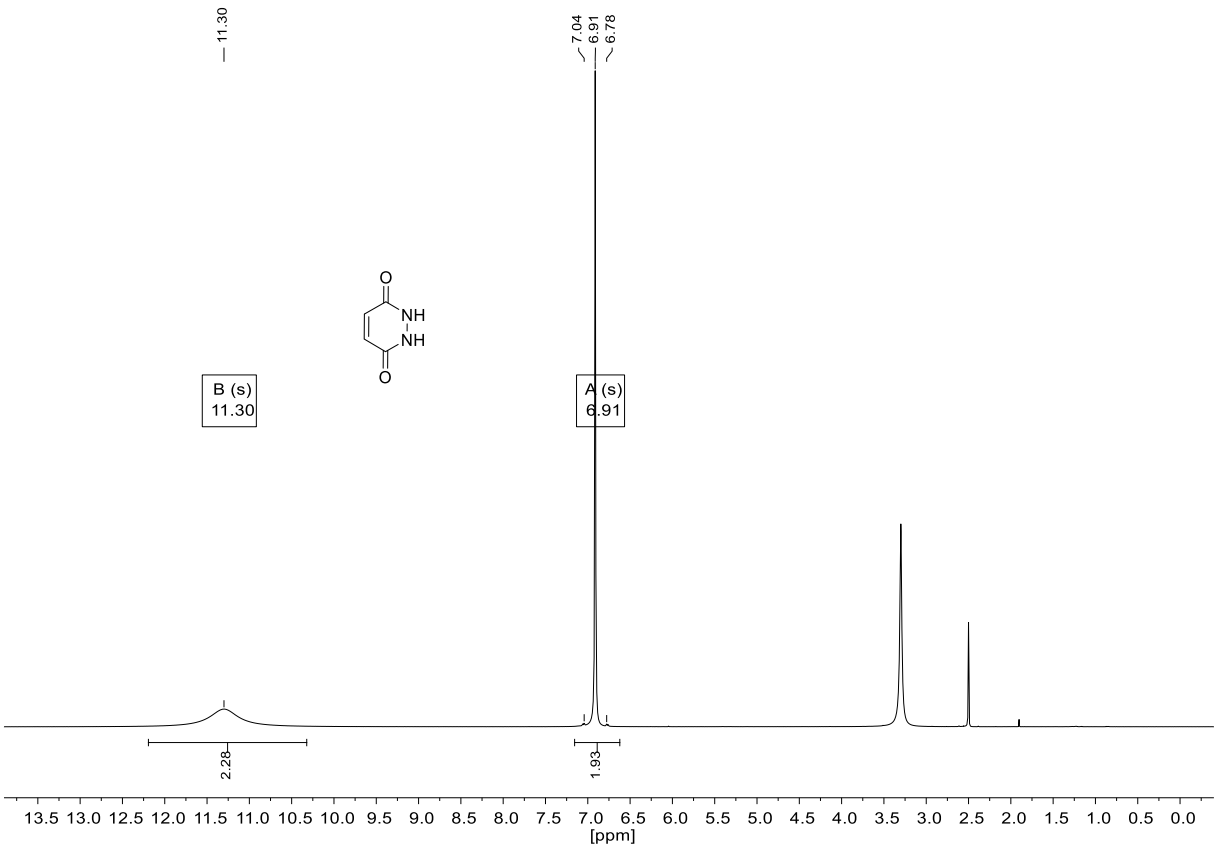

J (ddd)
7.47
J(8.14, 6.71, 1.35)
F (ddd)
7.01
J(8.23, 6.76, 1.32)
P(3,5-Me2C6H3)2
D (m)
6.67
B (dd)
5.68
J(17.60, 1.14)
H (m)
7.23
N (s)
2.13
L (m)
7.87
G (m)
7.16
A (dd)
6.22
J(17.56, 10.99)
C (dd)
4.94
J(11.04, 1.11)
M (s)
2.21
K (dd)
7.54
J(8.50, 2.80)
E (m)
6.85
I (ddd)
7.33
J(8.10, 6.78, 1.33)
5.26
0.94
1.01
1.02
0.79
1.12
1.05
5.18
1.97
1.00
0.92
0.96
6.23
6.41
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

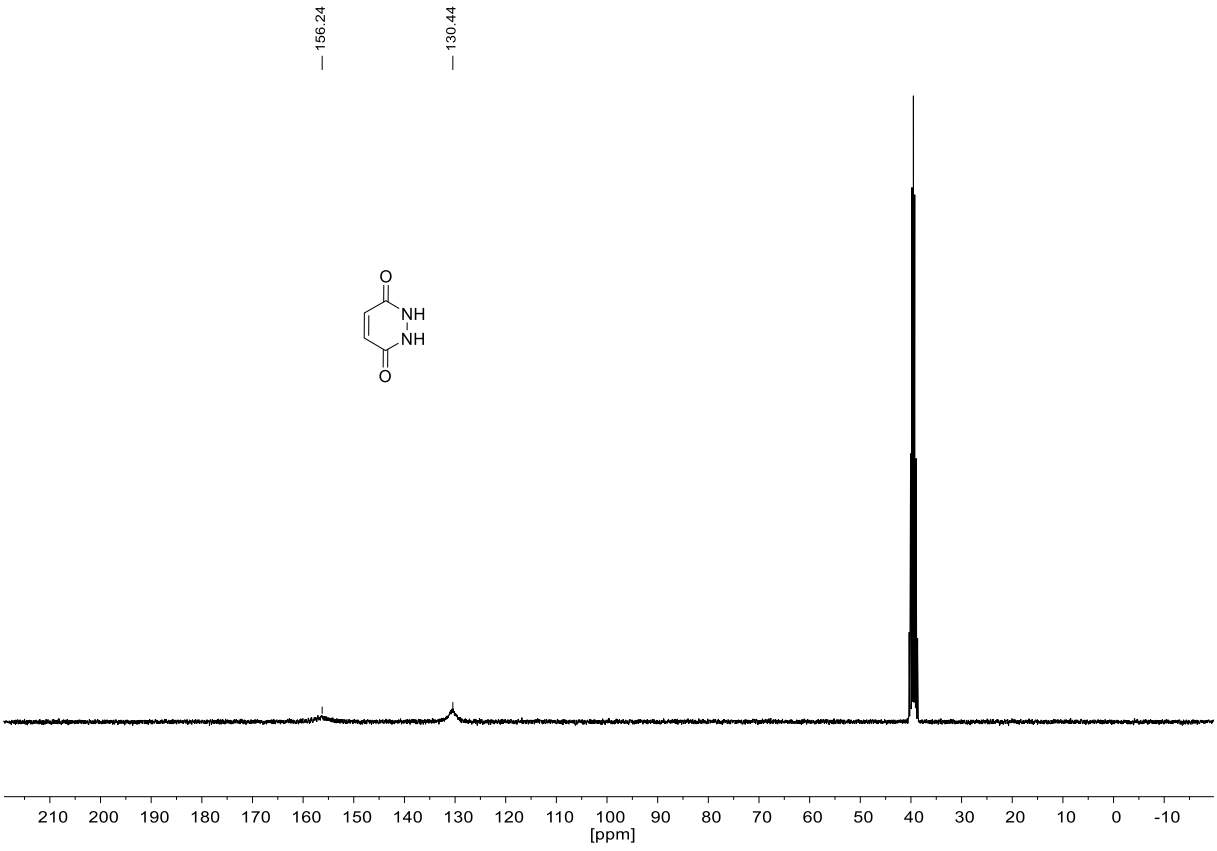

-13.49
P(3,5-Me2C6H3)2
[ppm]

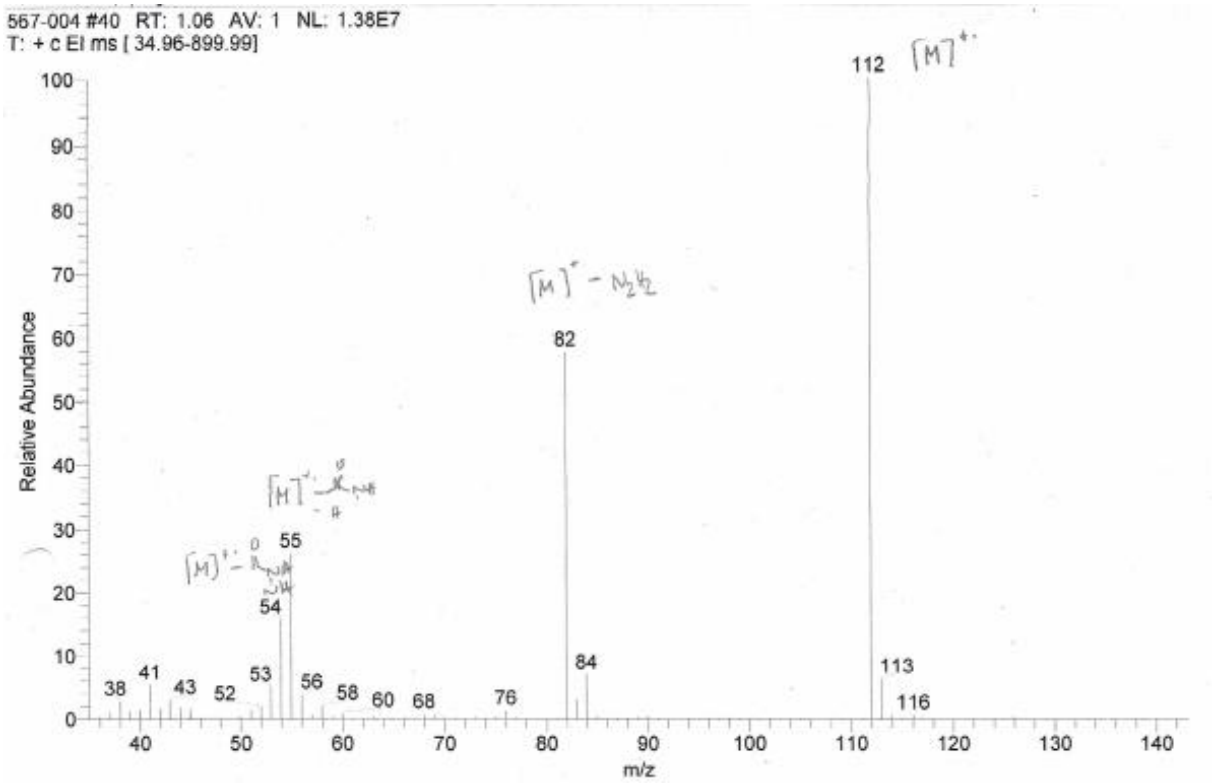

6.54
4.24
4.21
4.19
4.17
1.34
1.30
1.29
1.29
1.27
1.26
1.26
1.25
1.25
1.24
1.23
1.21
EtO
OEt
C (s)
6.54
B (q)
4.20
J(7.09)
A (t)
1.27
J(7.13)
2.17
4.00
6.00
[ppm]

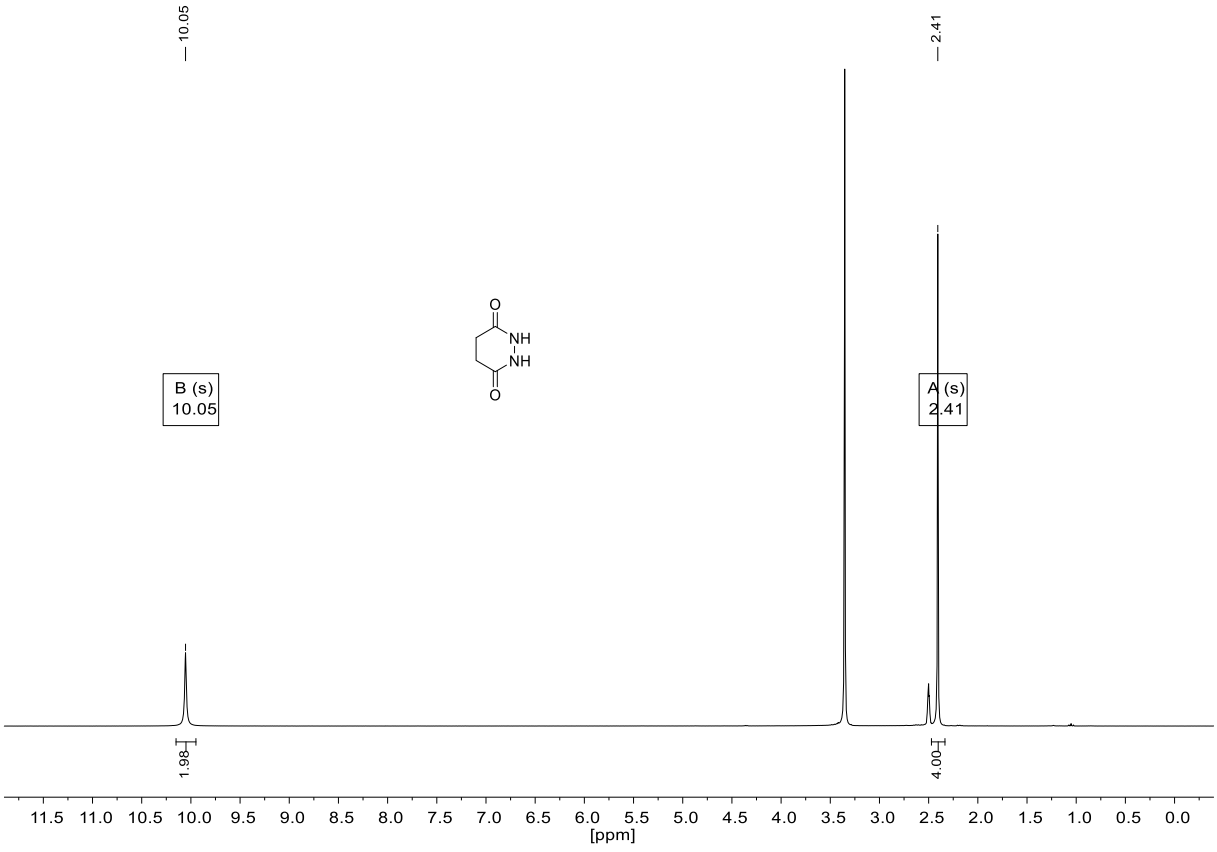

11.53
8.10
8.09
8.08
8.07
8.06
8.04
7.91
7.89
7.88
7.87
7.86
7.85
O
NH
NH
O
B (dd)
8.07
J(5.90, 3.34)
A (dd)
7.88
J(5.94, 3.31)
C (s)
11.53
1.87
1.86
2.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

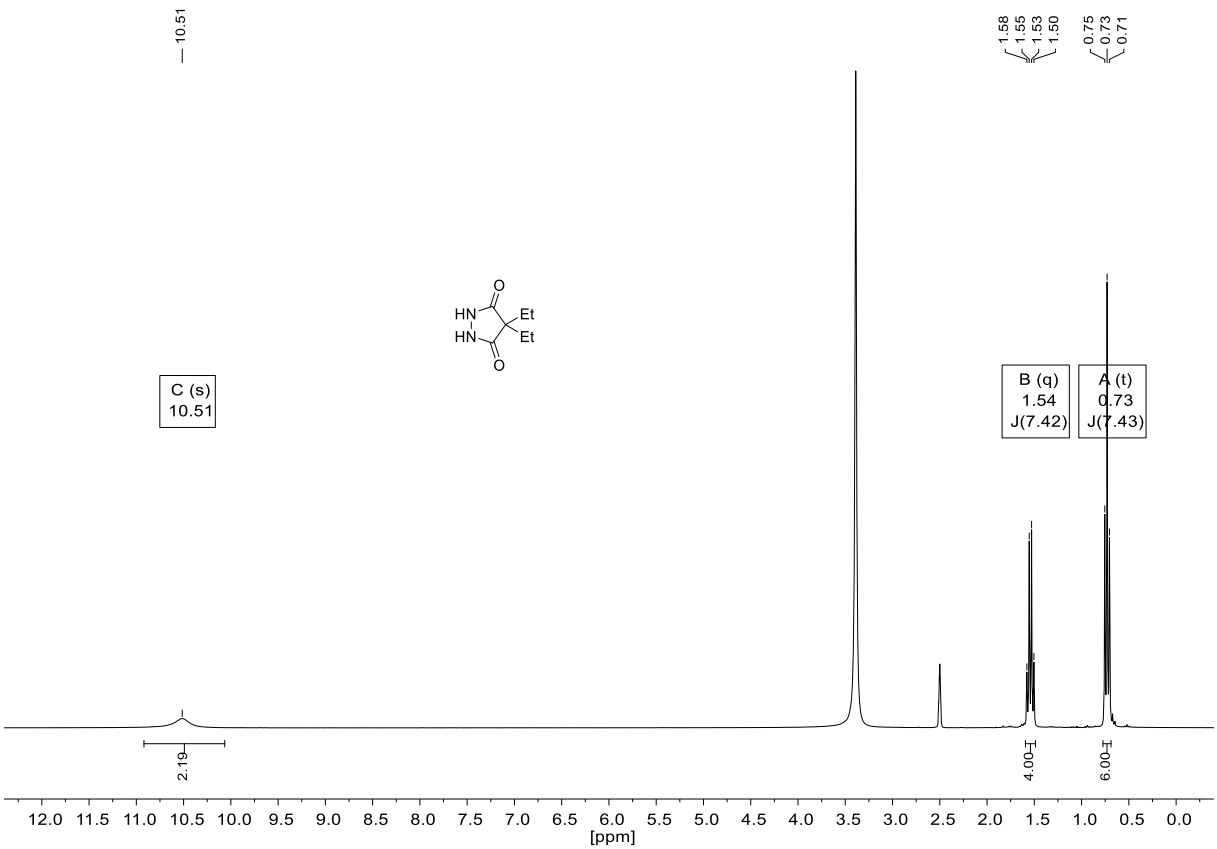

11.77
11.01
7.19
6.92
6.65
O
NH
NH
O
B (d)
11.39
J(227.18)
A (s)
6.92
2.62
2.00
13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

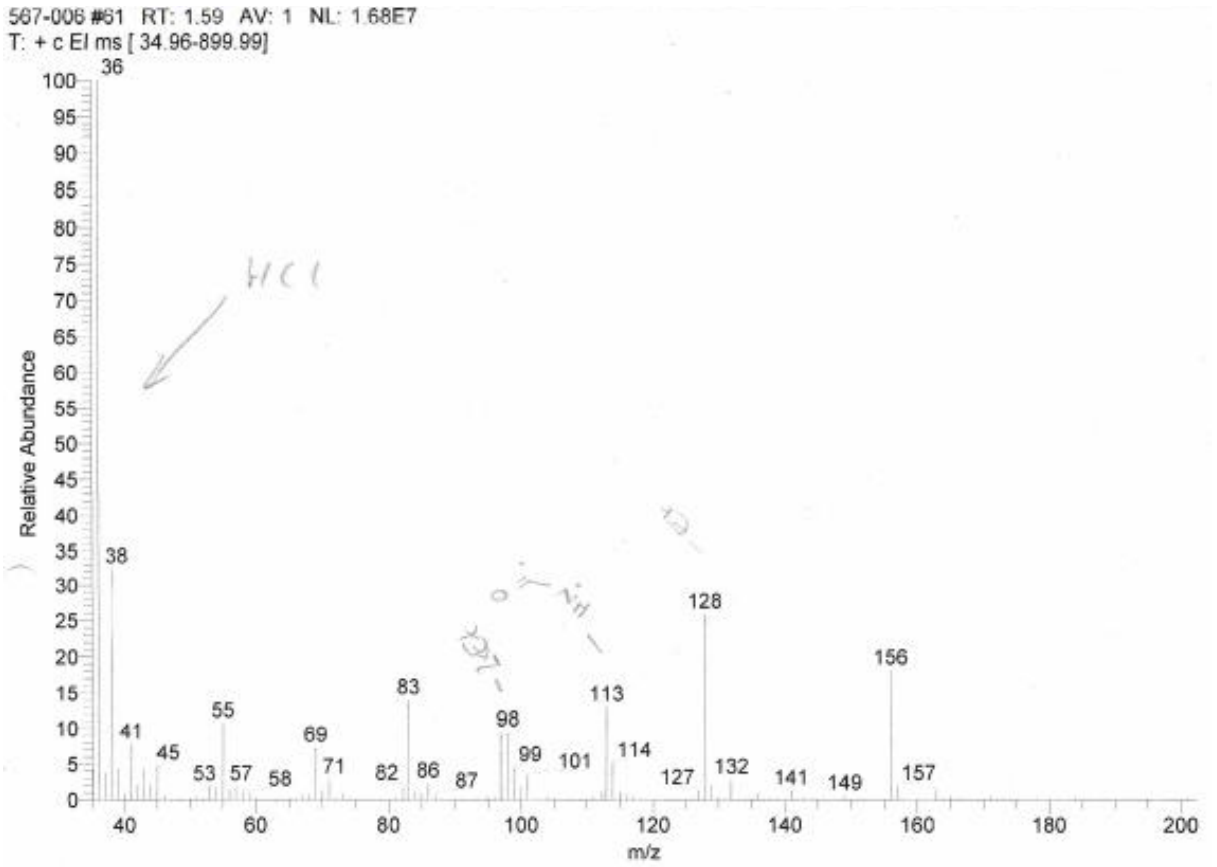

11.30
7.04
6.91
6.78
O
NH
NH
O
B (s)
11.30
A (s)
6.91
2.28
1.93
13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

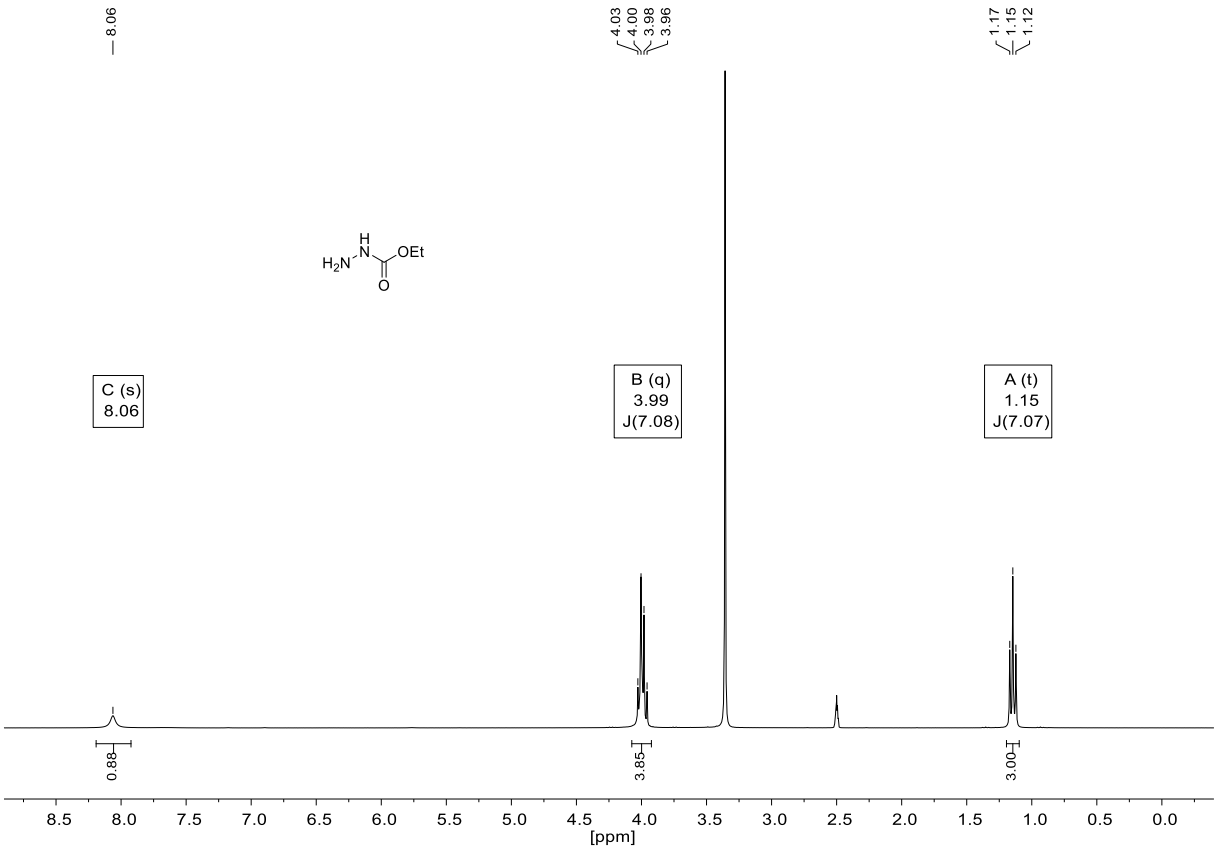

156.24
130.44
O
NH
NH
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

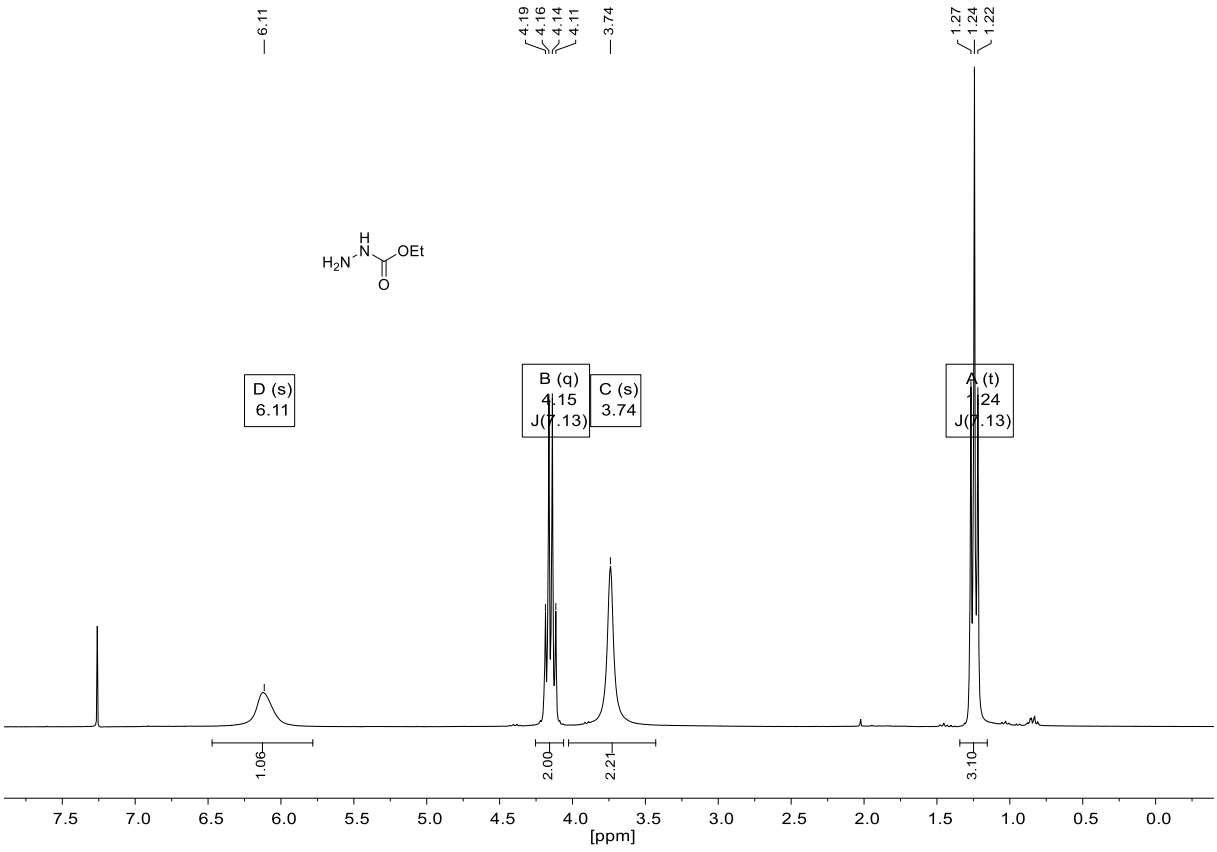

567-004 #40 RT: 1.06 AV: 1 NL: 1.38E7
T: + c EI ms [34.96-899.99]
Relative Abundance
m/z
112
82
55
54
84
113
116
41
43
52
53
56
58
60
68
76
38

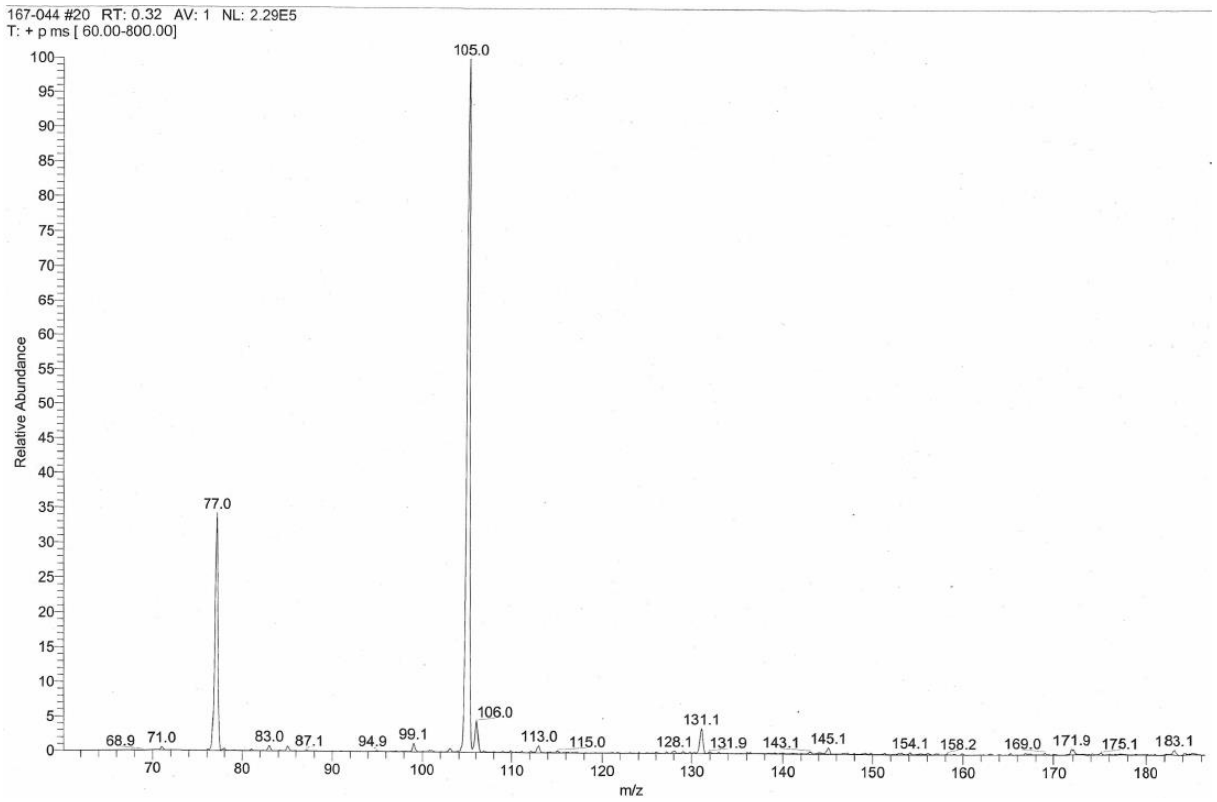

10.05
2.41
B (s)
10.05
A (s)
2.41
1.98
4.00
[ppm]

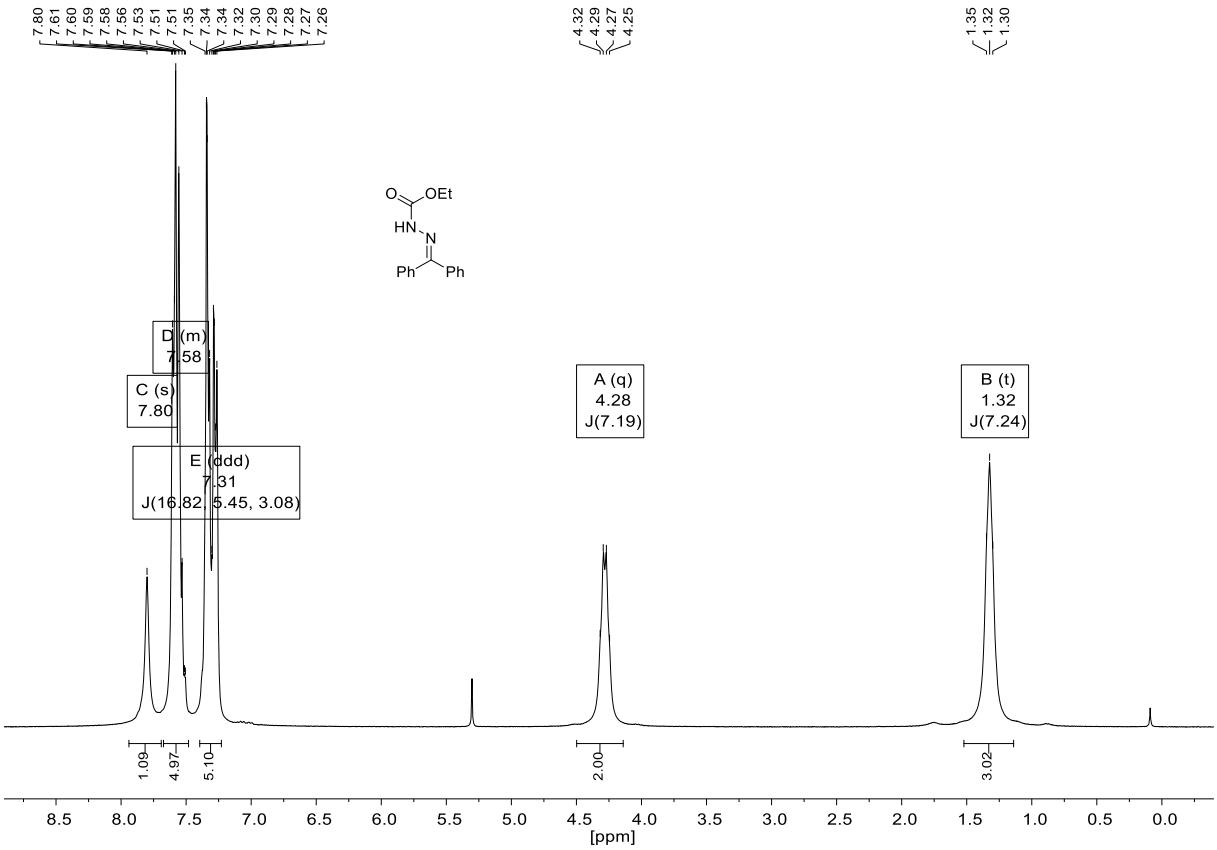

10.51
1.58
1.55
1.53
1.50
0.75
0.73
0.71
HN
HN
Et
Et
O
O
C (s)
10.51
B (q)
1.54
J(7.42)
A (t)
0.73
J(7.43)
2.19
4.00
6.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

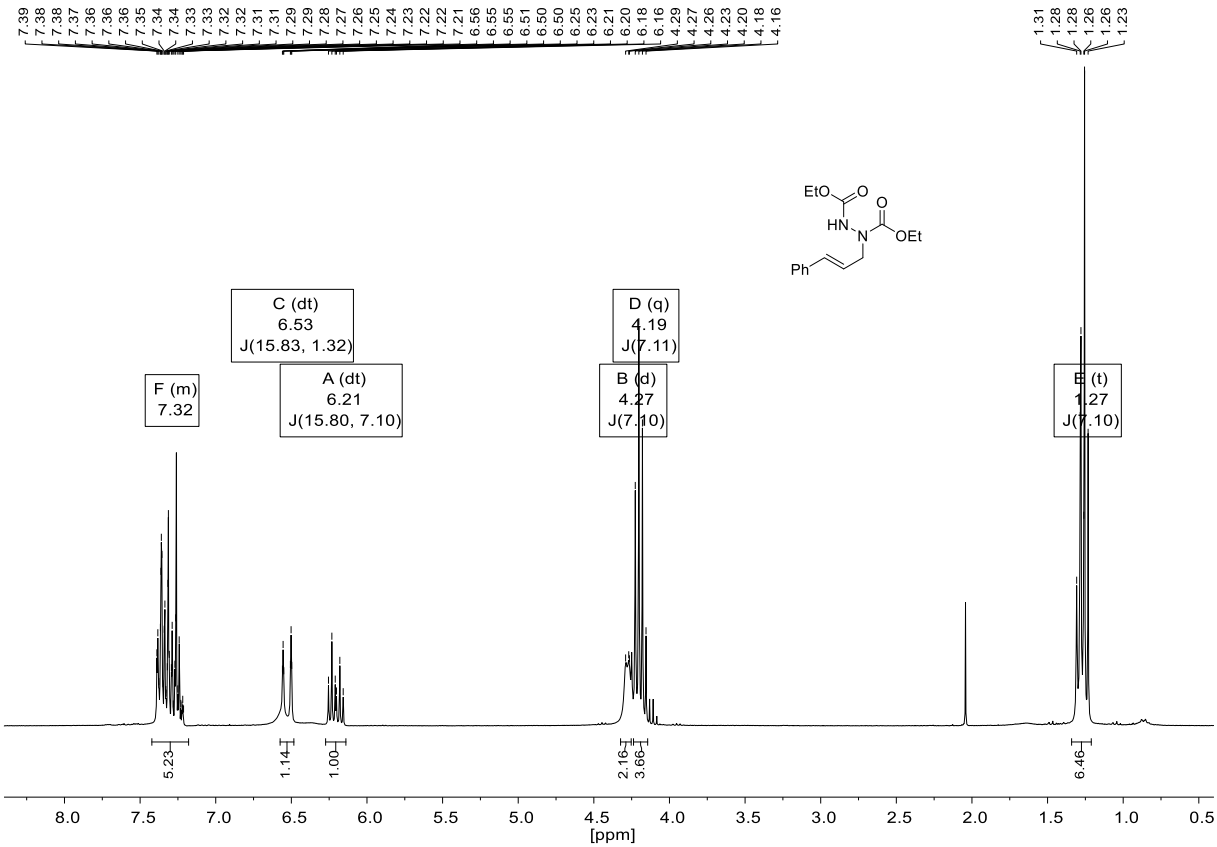

567-006 #61 RT: 1.59 AV: 1 NL: 1.68E7
T: + c EI ms [34.96-899.99]
HCl
Relative Abundance
m/z
36
38
41
45
53
55
57
58
69
71
82
83
86
87
98
99
101
113
114
127
128
132
141
149
156
157

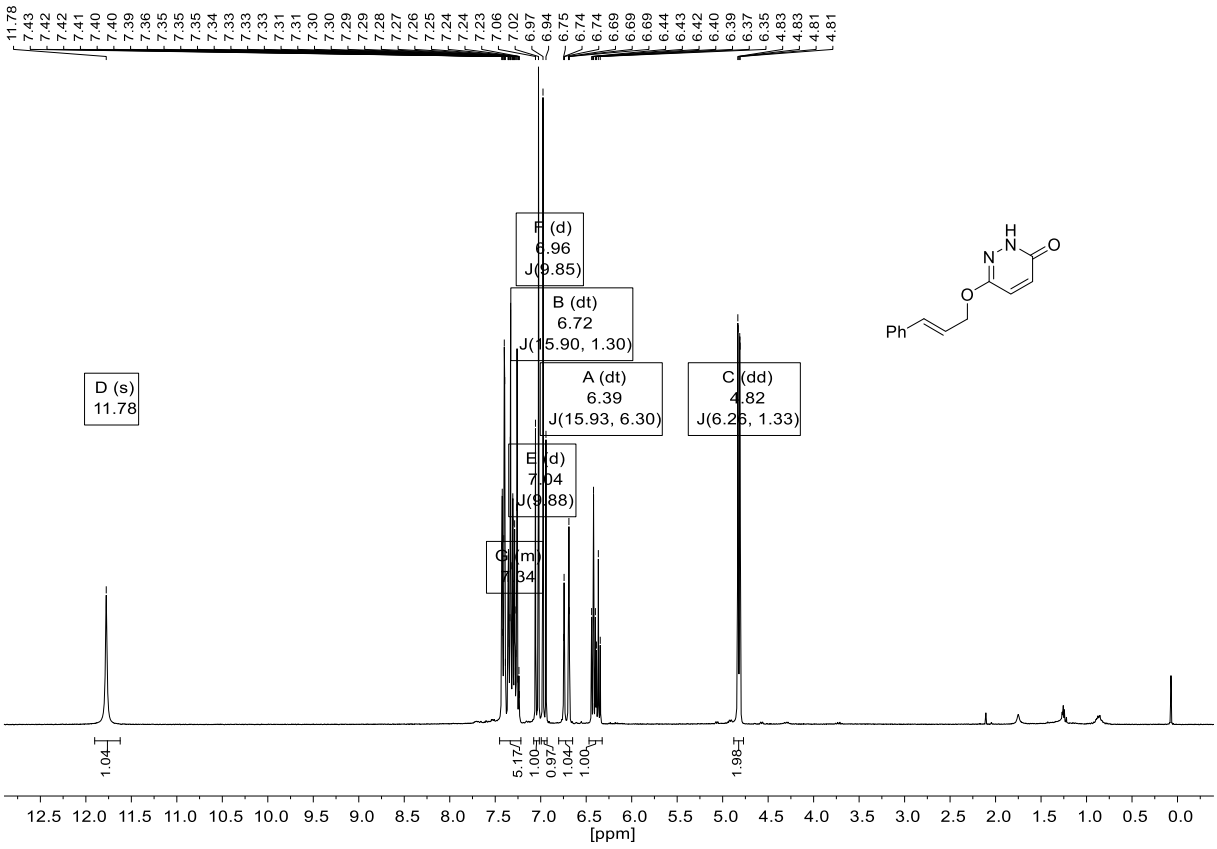

8.06
4.03
4.00
3.98
3.96
1.17
1.15
1.12
C (s)
8.06
B (q)
3.99
J(7.08)
A (t)
1.15
J(7.07)
0.88
3.85
3.00
[ppm]

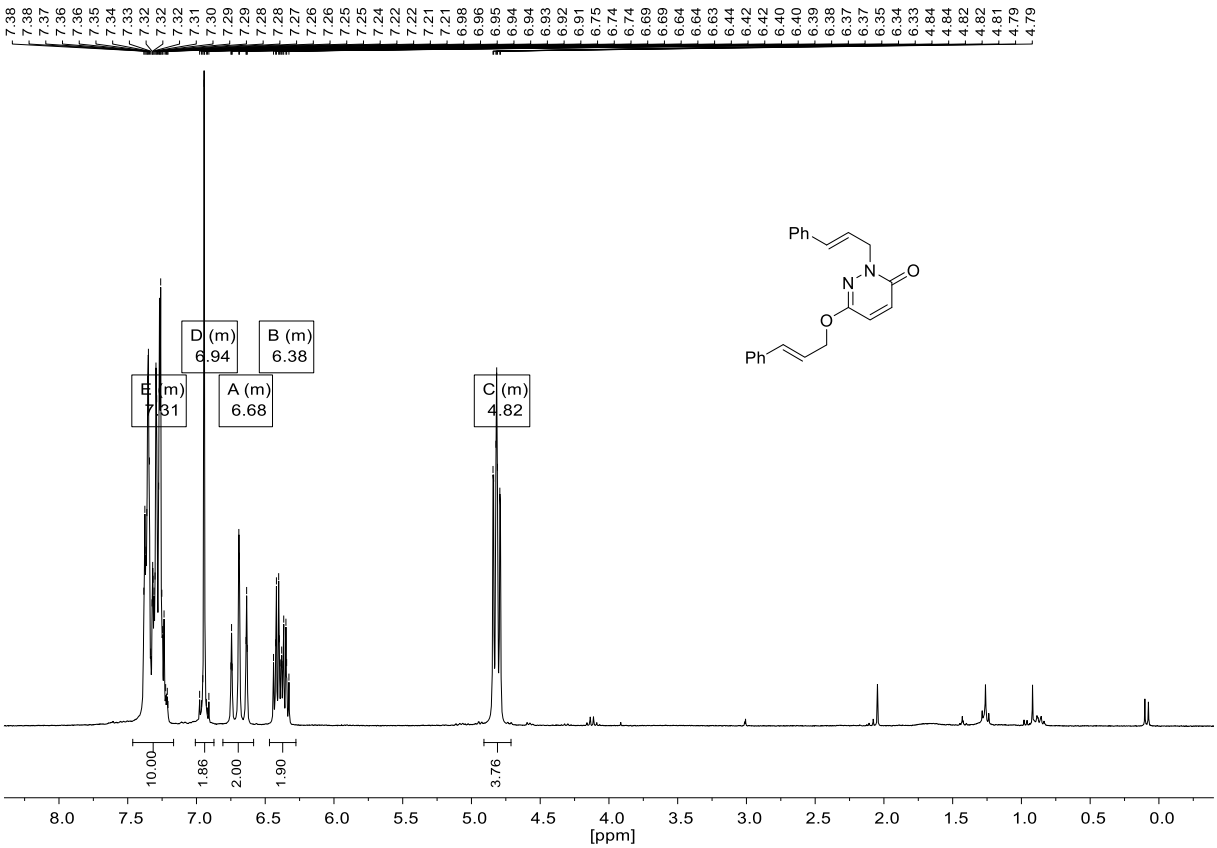

6.11
4.19
4.16
4.14
4.11
3.74
1.27
1.24
1.22
D (s)
6.11
B (q)
4.15
J(7.13)
C (s)
3.74
A (t)
1.24
J(7.13)
1.06
2.00
2.21
3.10
[ppm]

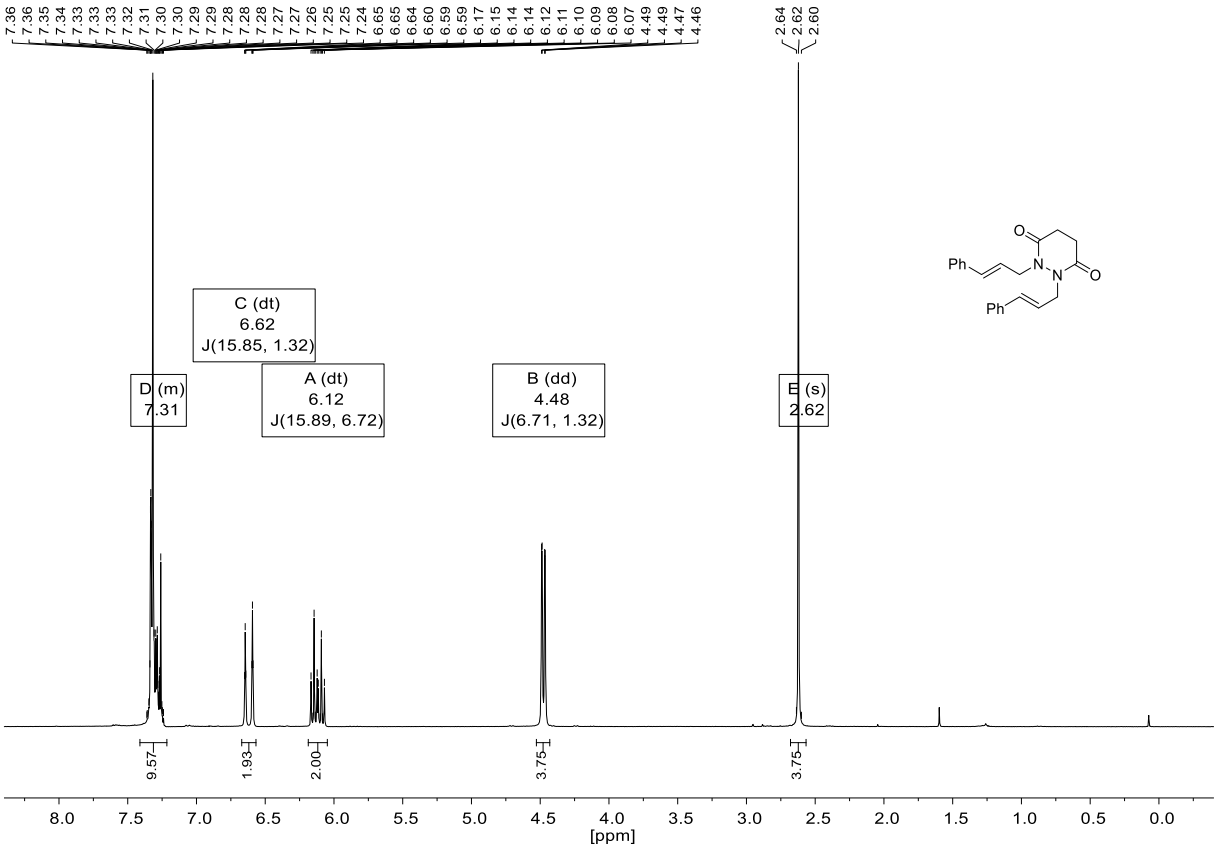

167-044 #20 RT: 0.32 AV: 1 NL: 2.29E5
T: + p ms [60.00-800.00]
Relative Abundance
m/z
105.0
77.0
106.0
131.1

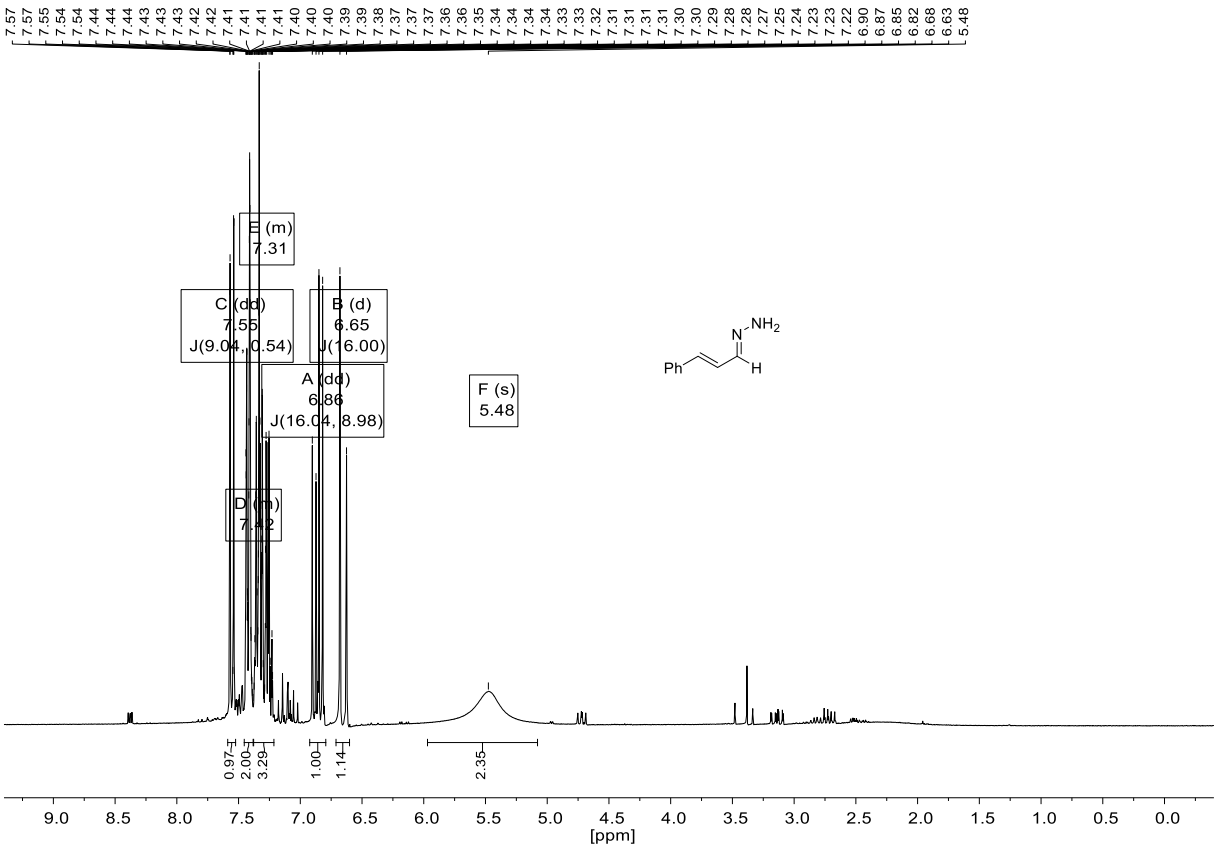

7.80
7.61
7.60
7.59
7.58
7.56
7.53
7.51
7.51
7.35
7.34
7.34
7.32
7.30
7.29
7.28
7.27
7.26
4.32
4.29
4.27
4.25
1.35
1.32
1.30
O
OEt
HN
N
Ph
Ph
D (m)
7.58
C (s)
7.80
E (ddd)
7.31
J(16.82, 5.45, 3.08)
A (q)
4.28
J(7.19)
B (t)
1.32
J(7.24)
1.09
4.97
5.10
2.00
3.02
[ppm]

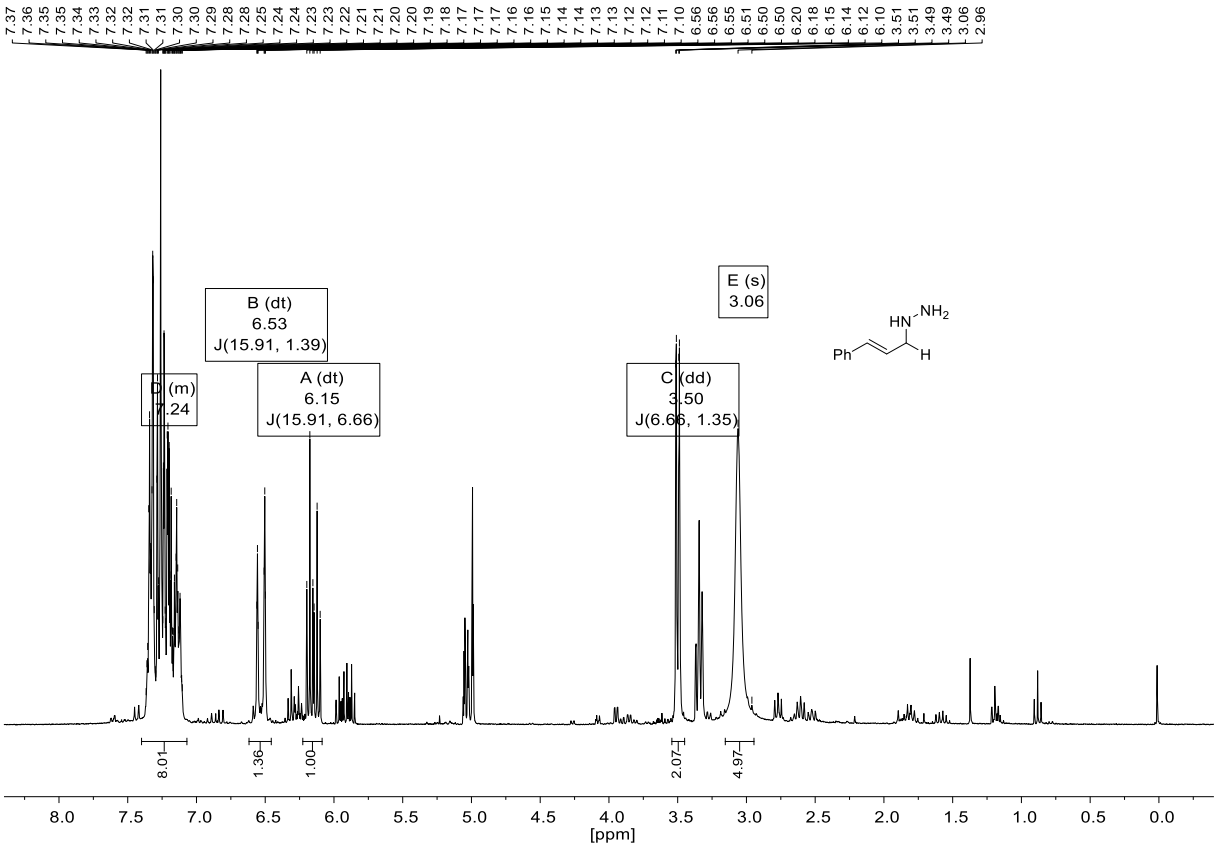

7.39 7.38 7.38 7.37 7.36 7.36 7.36 7.35 7.34 7.34 7.33 7.33 7.32 7.32 7.31 7.31 7.29 7.29 7.28 7.27 7.26 7.25 7.24 7.23 7.22 7.22 7.21 6.56 6.55 6.55 6.51 6.50 6.50 6.25 6.23 6.21 6.20 6.18 6.16 4.29 4.27 4.26 4.23 4.20 4.18 4.16
1.31 1.28 1.28 1.26 1.26 1.23
EtO
O
HN
N
O
OEt
Ph
C (dt)
6.53
J(15.83, 1.32)
D (q)
4.19
J(7.11)
F (m)
7.32
A (dt)
6.21
J(15.80, 7.10)
B (d)
4.27
J(7.10)
E (t)
1.27
J(7.10)
5.23
1.14
1.00
2.16
3.66
6.46
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
[ppm]

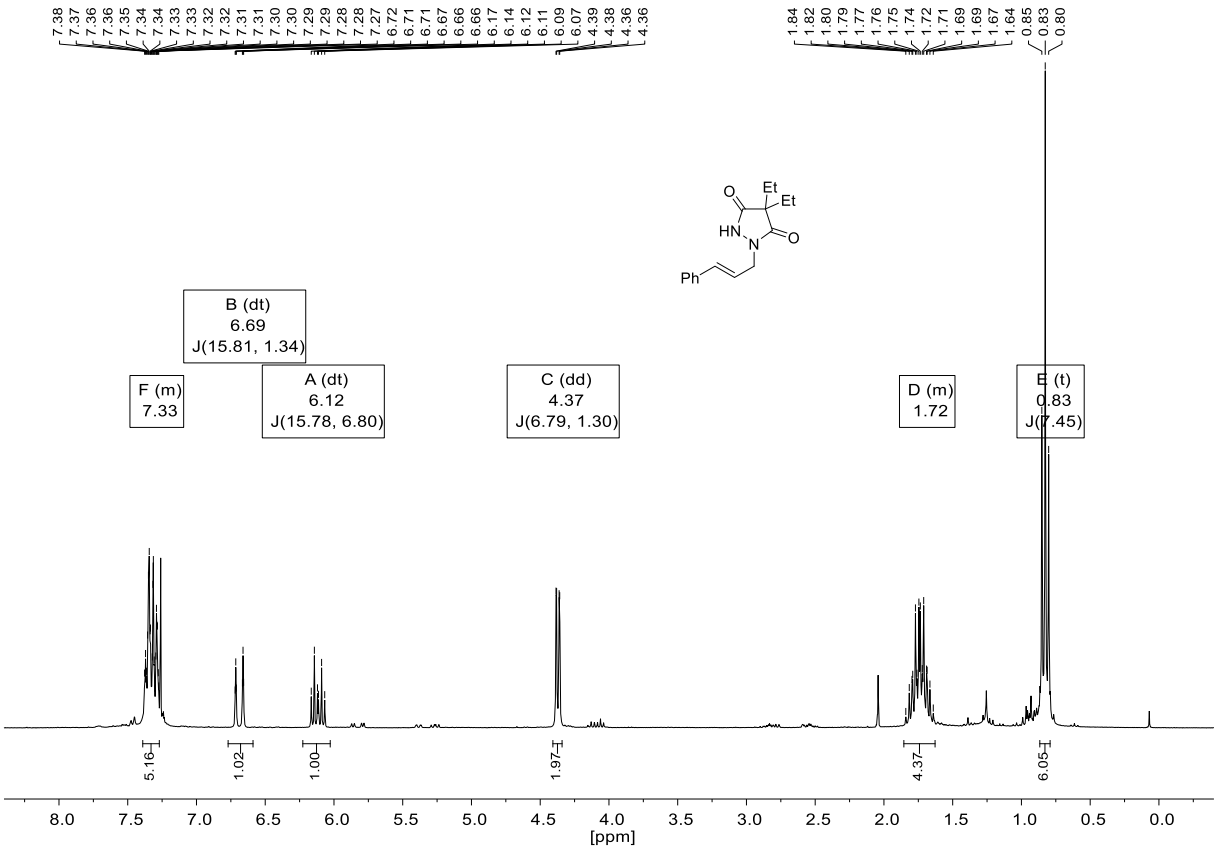

11.78 7.43 7.42 7.42 7.41 7.40 7.40 7.39 7.36 7.35 7.35 7.34 7.33 7.33 7.31 7.31 7.30 7.30 7.29 7.29 7.28 7.27 7.26 7.25 7.24 7.24 7.23 7.06 7.02 6.97 6.94 6.75 6.74 6.74 6.69 6.69 6.69 6.44 6.43 6.42 6.40 6.39 6.37 6.35 4.83 4.81 4.81
H
N
N
O
O
Ph
F (d)
6.96
J(9.85)
B (dt)
6.72
J(15.90, 1.30)
D (s)
11.78
A (dt)
6.39
J(15.93, 6.30)
C (dd)
4.82
J(6.26, 1.33)
E (d)
7.04
J(9.88)
G (m)
7.34
1.04
5.17
1.00
0.97
1.04
1.00
1.98
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

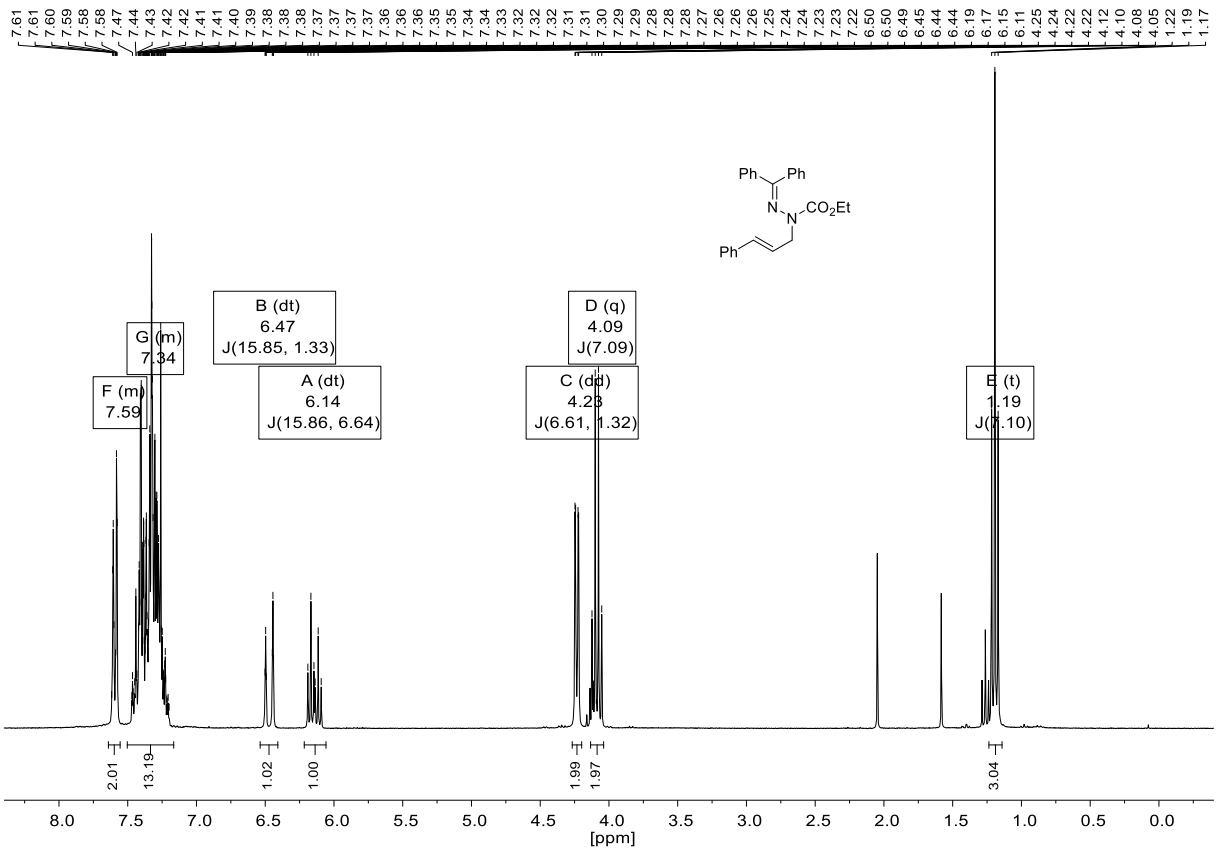

D (m)
6.94
B (m)
6.38
E (m)
7.31
A (m)
6.68
C (m)
4.82
10.00
1.86
2.00
1.90
3.76
[ppm]

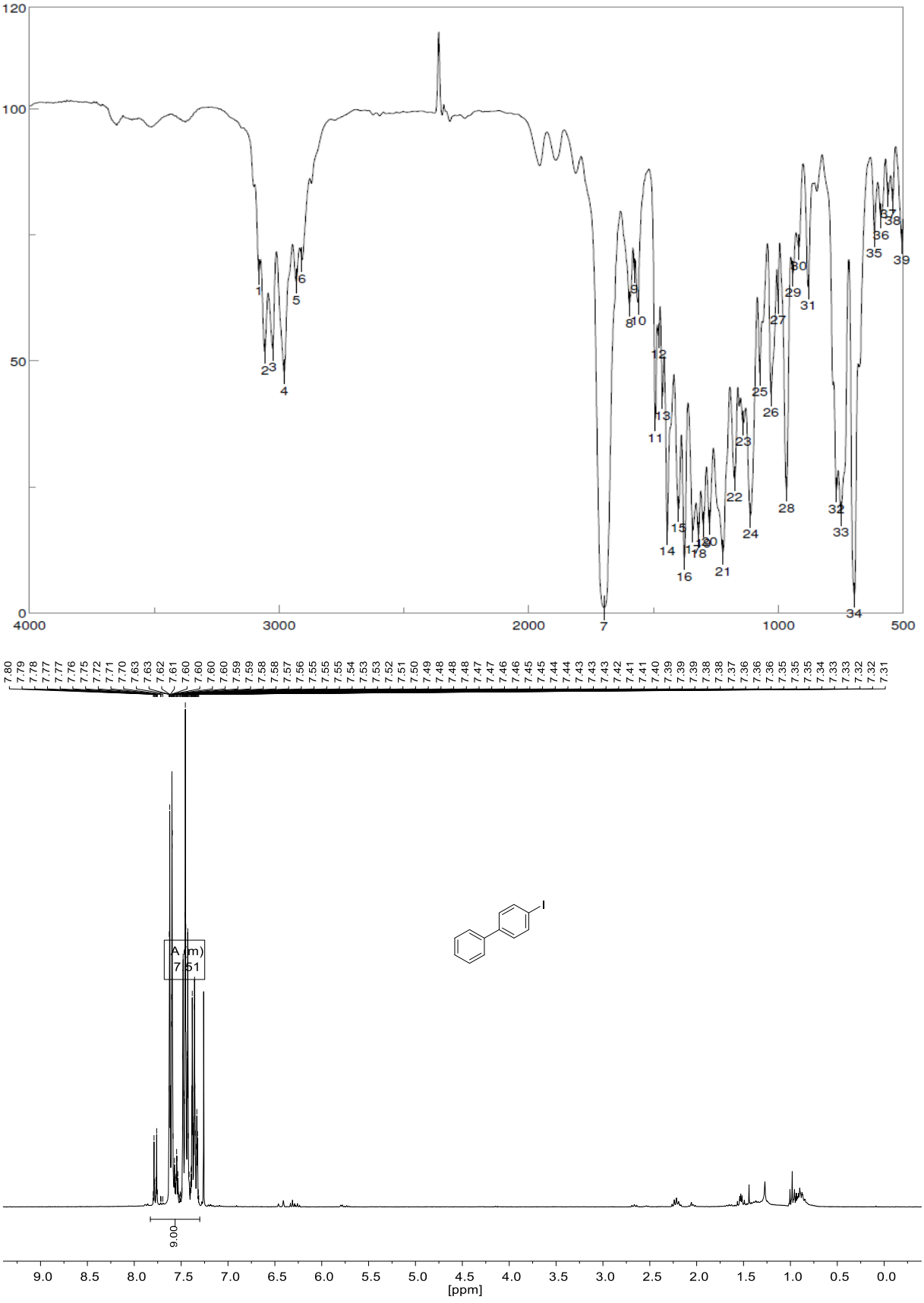

C (dt)
6.62
J(15.85, 1.32)
D (m)
7.31
A (dt)
6.12
J(15.89, 6.72)
B (dd)
4.48
J(6.71, 1.32)
E (s)
2.62
9.57
1.93
2.00
3.75
3.75
[ppm]

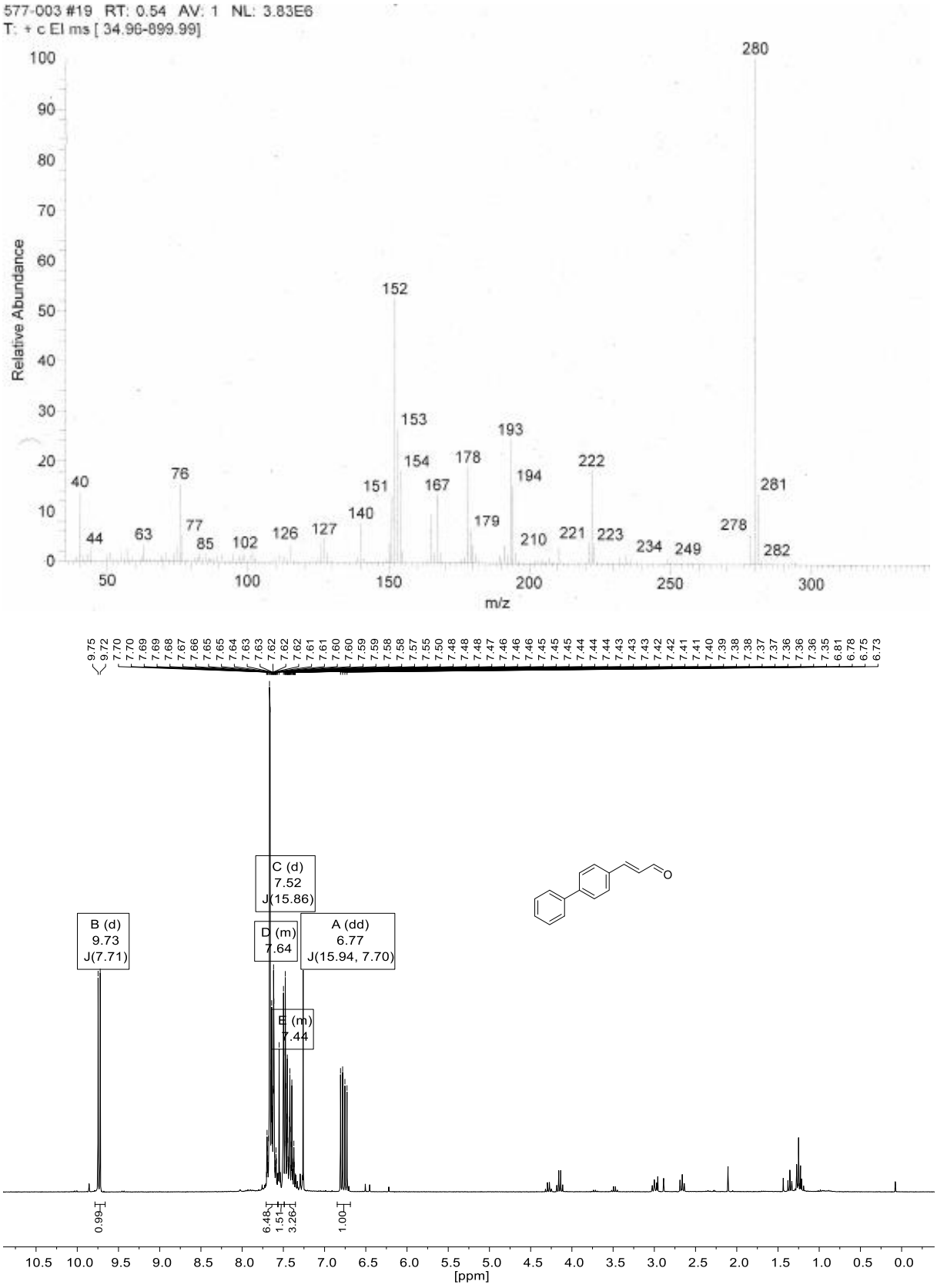

E (m)
7.31
C (dd)
7.55
J(9.04, 0.54)
B (d)
6.65
J(16.00)
A (dd)
6.86
J(16.04, 8.98)
F (s)
5.48
D (m)
7.42
NH2
N
Ph
H
0.97
2.00
3.29
1.00
1.14
2.35
[ppm]

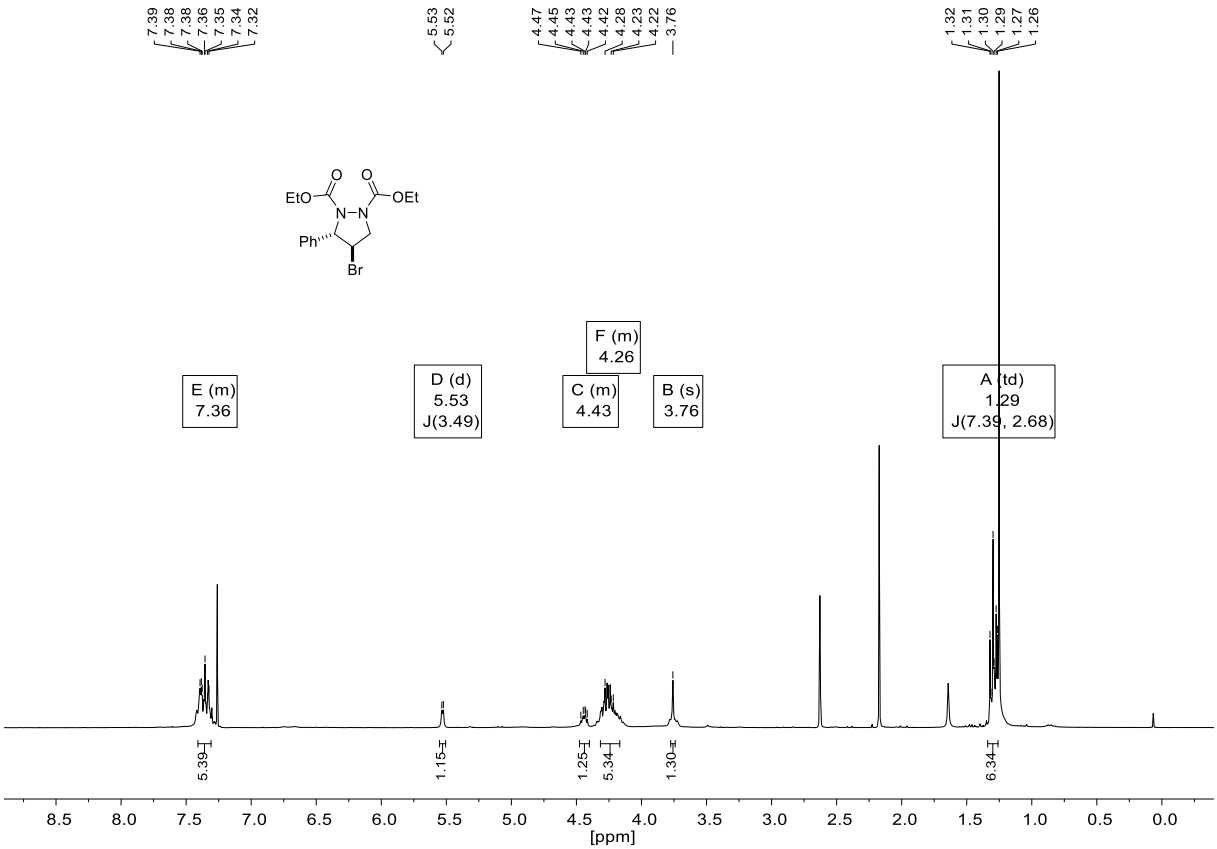

B (dt)
6.53
J(15.91, 1.39)
E (s)
3.06
D (m)
7.24
A (dt)
6.15
J(15.91, 6.66)
C (dd)
3.50
J(6.66, 1.35)
NH2
HN
Ph
H
8.01
1.36
1.00
2.07
4.97
[ppm]

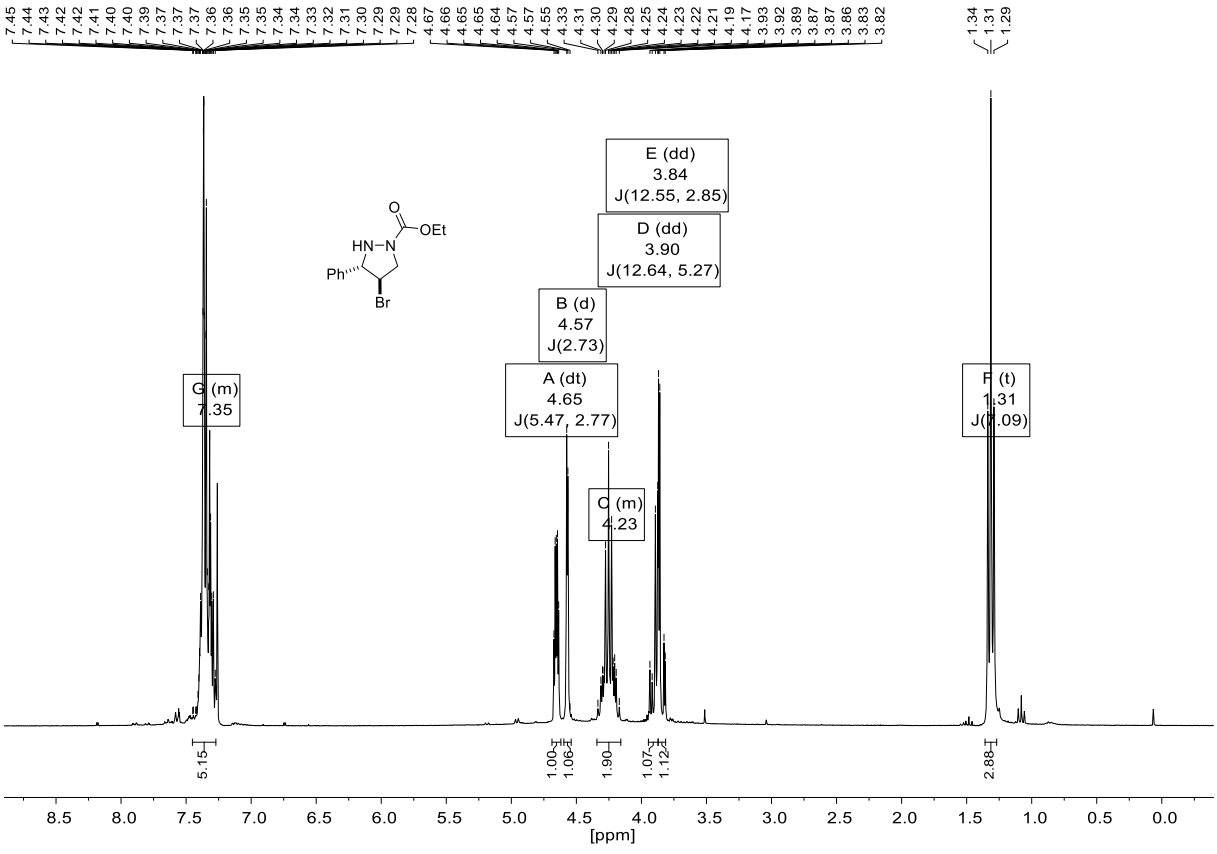

7.38 7.37 7.36 7.36 7.35 7.34 7.34 7.33 7.33 7.32 7.32 7.31 7.31 7.30 7.30 7.29 7.29 7.28 7.28 7.27 6.72 6.71 6.71 6.67 6.66 6.66 6.17 6.14 6.12 6.11 6.09 6.07 4.39 4.38 4.36 4.36
1.84 1.82 1.80 1.79 1.77 1.76 1.75 1.74 1.72 1.71 1.69 1.69 1.67 1.64 0.85 0.83 0.80
O
Et
Et
HN
N
O
Ph
B (dt)
6.69
J(15.81, 1.34)
F (m)
7.33
A (dt)
6.12
J(15.78, 6.80)
C (dd)
4.37
J(6.79, 1.30)
D (m)
1.72
E (t)
0.83
J(7.45)
5.16
1.02
1.00
1.97
4.37
6.05
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

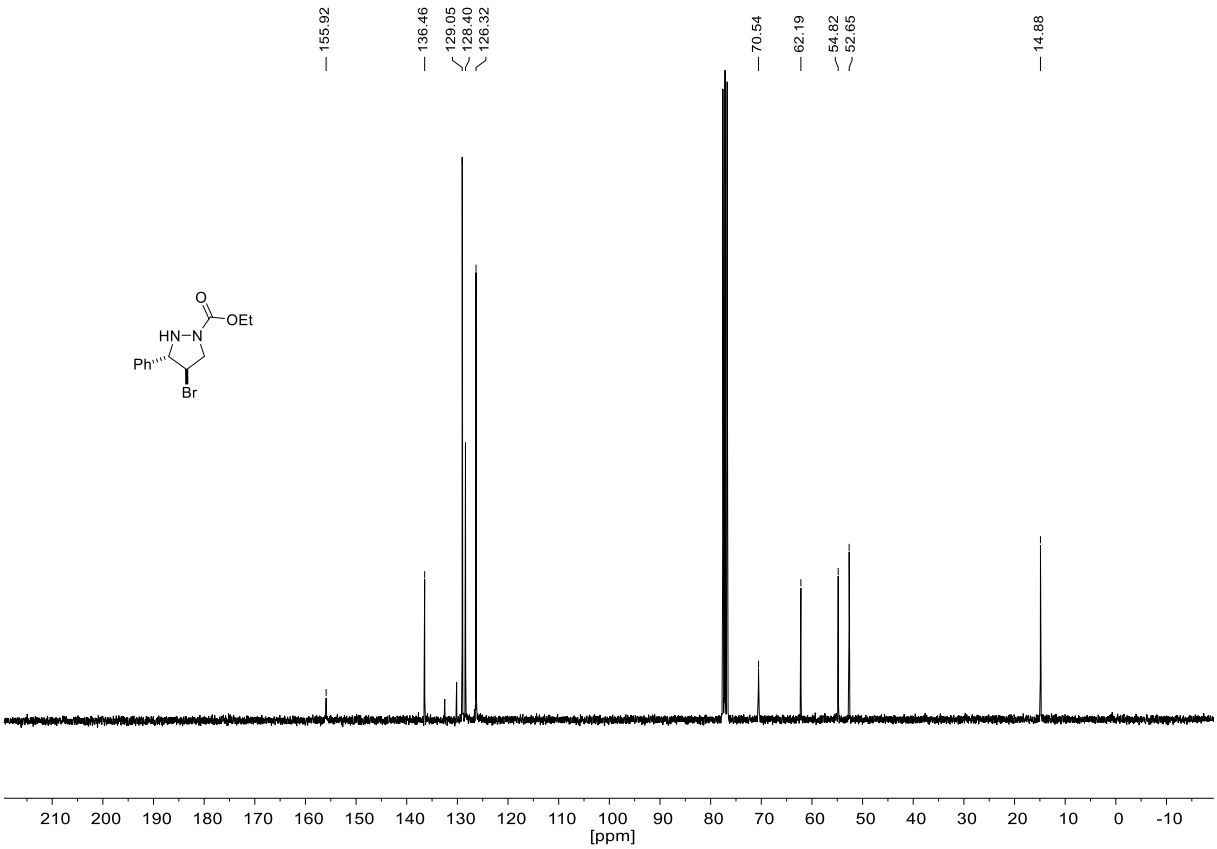

7.61 7.61 7.60 7.59 7.58 7.58 7.47 7.44 7.43 7.42 7.42 7.41 7.41 7.40 7.39 7.38 7.38 7.37 7.37 7.37 7.37 7.36 7.36 7.35 7.35 7.34 7.34 7.33 7.32 7.32 7.31 7.31 7.30 7.29 7.29 7.28 7.28 7.27 7.26 7.26 7.26 7.25 7.24 7.24 7.23 7.22 6.50 6.50 6.49 6.45 6.44 6.44 6.19 6.17 6.15 6.11 4.25 4.24 4.22 4.12 4.10 4.08 4.05 1.22 1.19 1.17
Ph
Ph
N
N
CO2Et
Ph
B (dt)
6.47
J(15.85, 1.33)
G (m)
7.34
F (m)
7.59
A (dt)
6.14
J(15.86, 6.64)
D (q)
4.09
J(7.09)
C (dd)
4.23
J(6.61, 1.32)
E (t)
1.19
J(7.10)
2.01
13.19
1.02
1.00
1.99
1.97
3.04
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

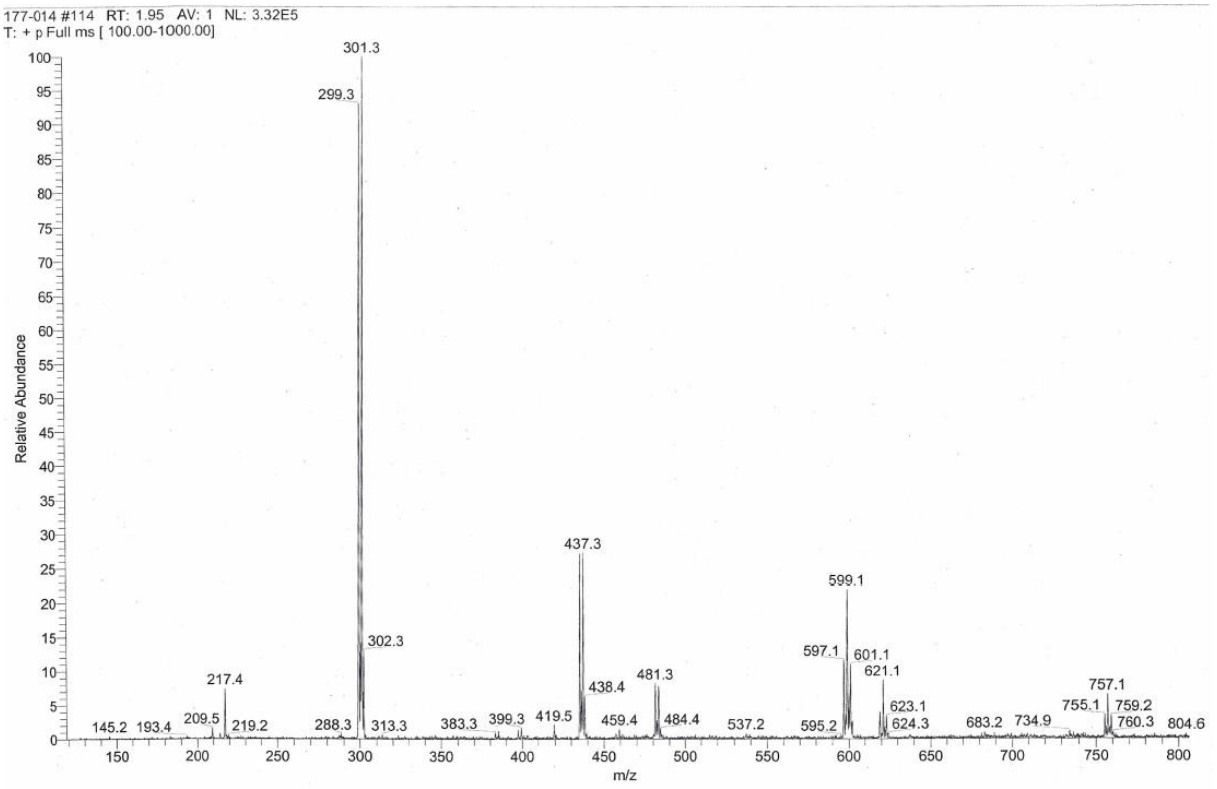

120
100
50
0
4000
3000
2000
1000
500
A (m)
7.51
9.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]
I

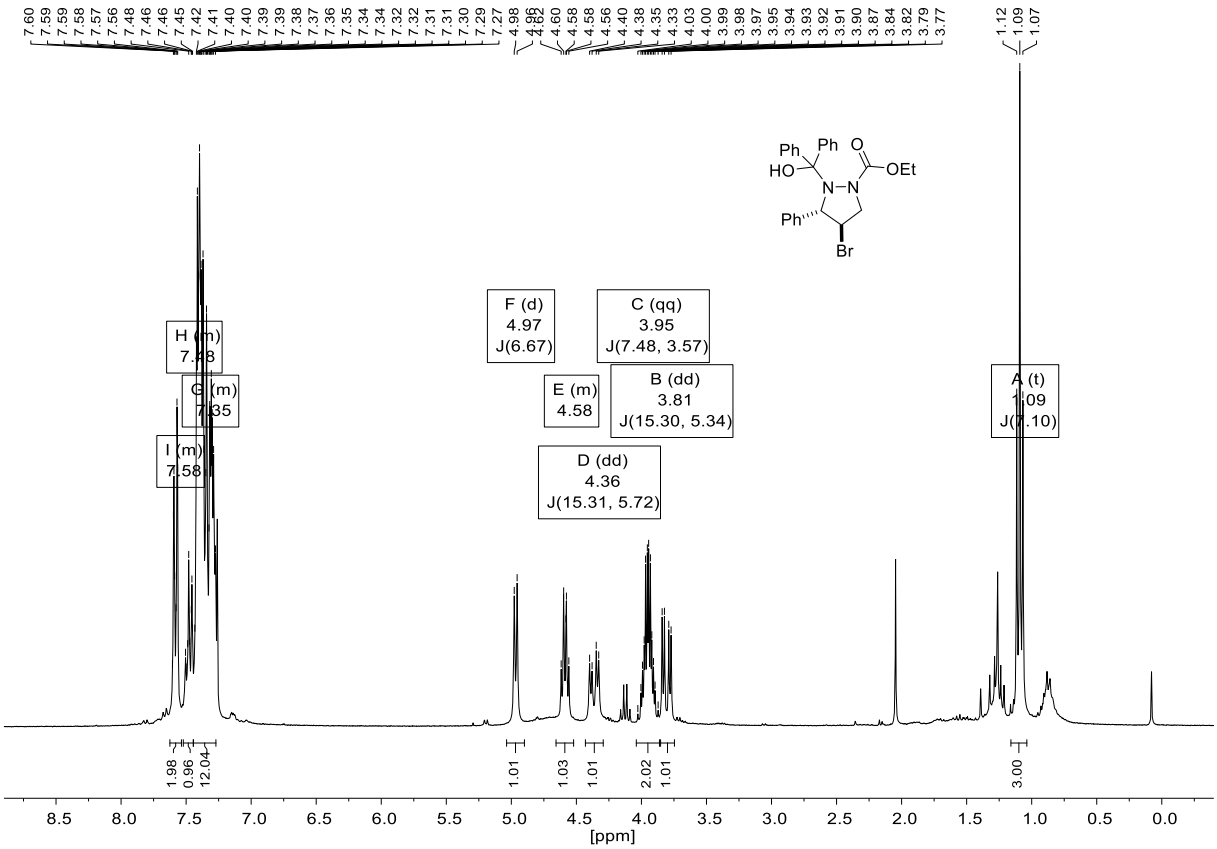

577-003 #19 RT: 0.54 AV: 1 NL: 3.83E6
T: + c EI ms [34.96-899.99]
Relative Abundance
m/z
B (d)
9.73
J(7.71)
C (d)
7.52
J(15.86)
D (m)
7.64
A (dd)
6.77
J(15.94, 7.70)
E (m)
7.44
O
[ppm]

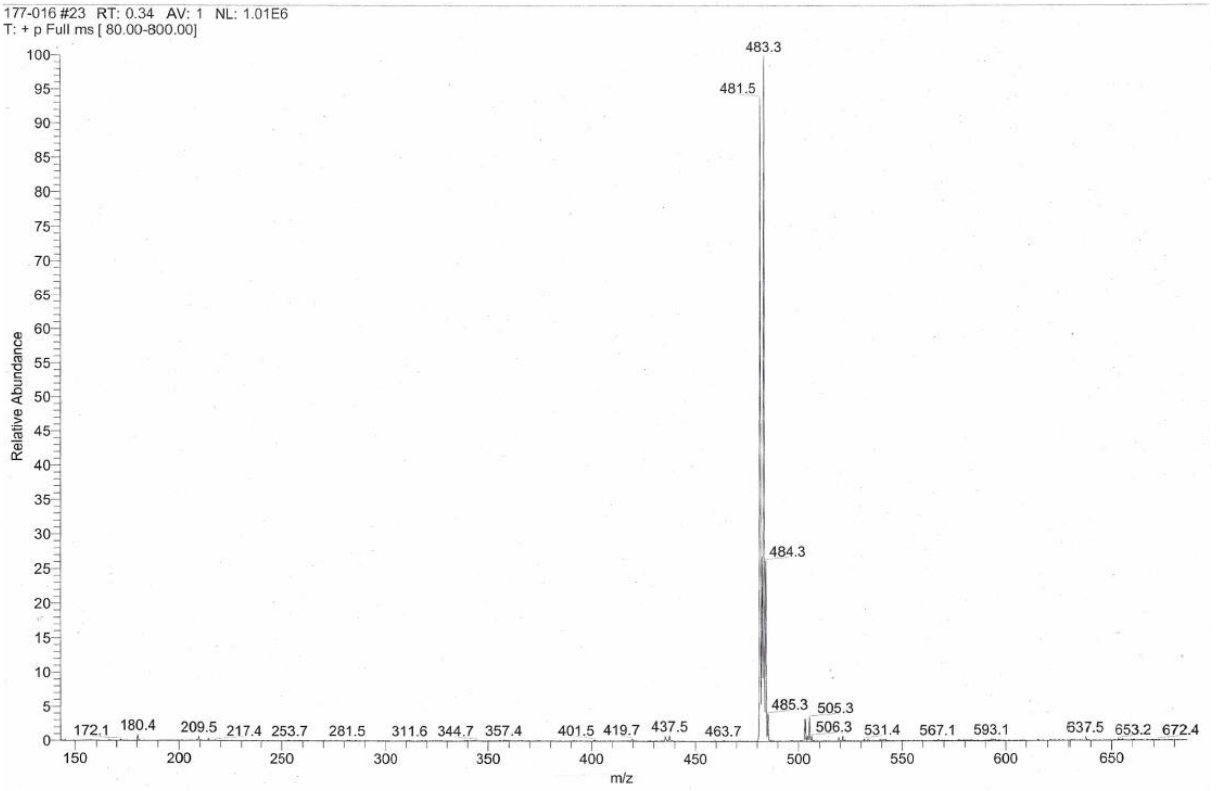

7.39
7.38
7.36
7.35
7.34
7.32
5.53
5.52
4.47
4.45
4.43
4.43
4.42
4.28
4.23
4.22
3.76
1.32
1.31
1.30
1.29
1.27
1.26
EtO
OEt
N–N
Ph
Br
E (m)
7.36
D (d)
5.53
J(3.49)
F (m)
4.26
C (m)
4.43
B (s)
3.76
A (td)
1.29
J(7.39, 2.68)
5.39
1.15
1.25
5.34
1.30
6.34
[ppm]

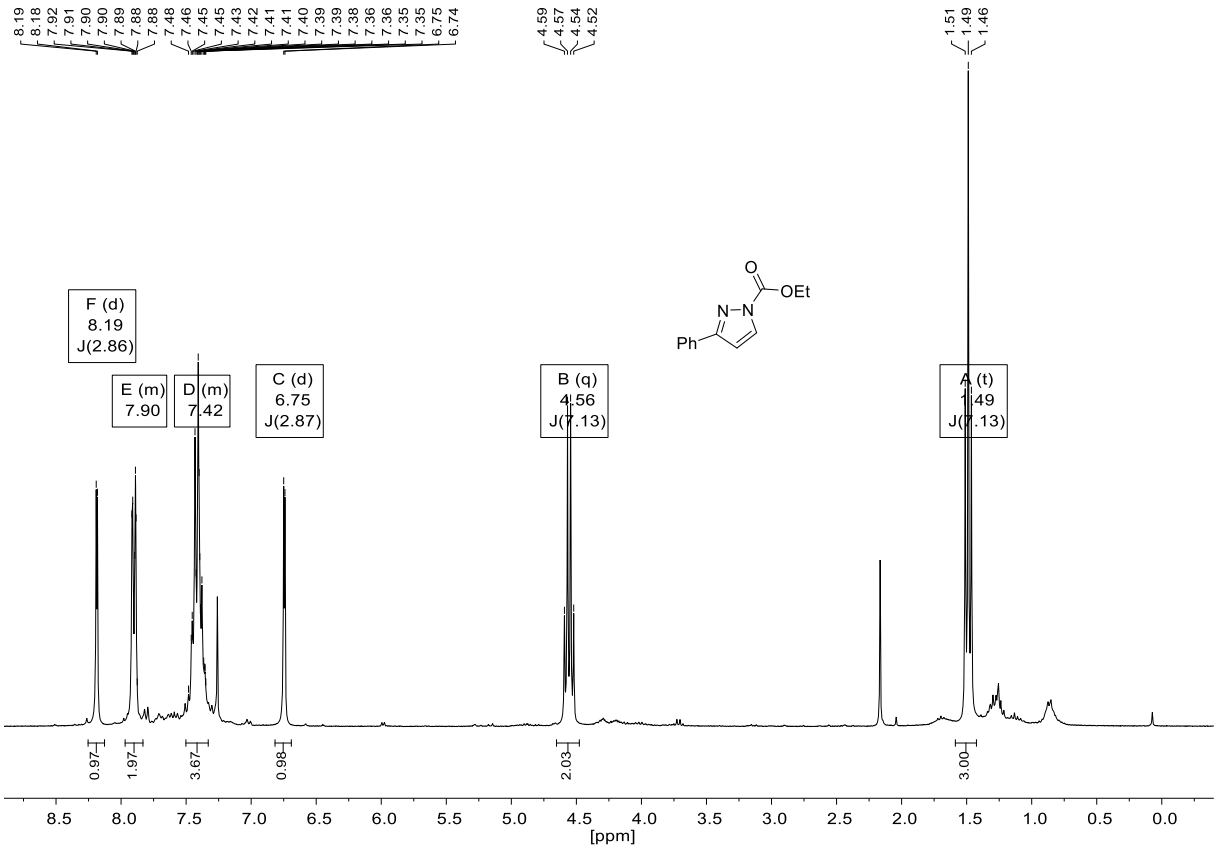

7.45
7.44
7.43
7.42
7.42
7.41
7.40
7.40
7.39
7.37
7.37
7.37
7.36
7.36
7.35
7.35
7.34
7.34
7.33
7.32
7.31
7.30
7.29
7.29
7.28
4.67
4.66
4.65
4.65
4.64
4.57
4.57
4.55
4.33
4.31
4.30
4.29
4.28
4.25
4.24
4.23
4.22
4.21
4.19
4.17
3.93
3.92
3.89
3.87
3.87
3.86
3.83
3.82
1.34
1.31
1.29
HN–N
OEt
Ph
Br
E (dd)
3.84
J(12.55, 2.85)
D (dd)
3.90
J(12.64, 5.27)
B (d)
4.57
J(2.73)
A (dt)
4.65
J(5.47, 2.77)
G (m)
7.35
C (m)
4.23
F (t)
1.31
5.15
1.00
1.06
1.90
1.07
1.12
2.88
[ppm]

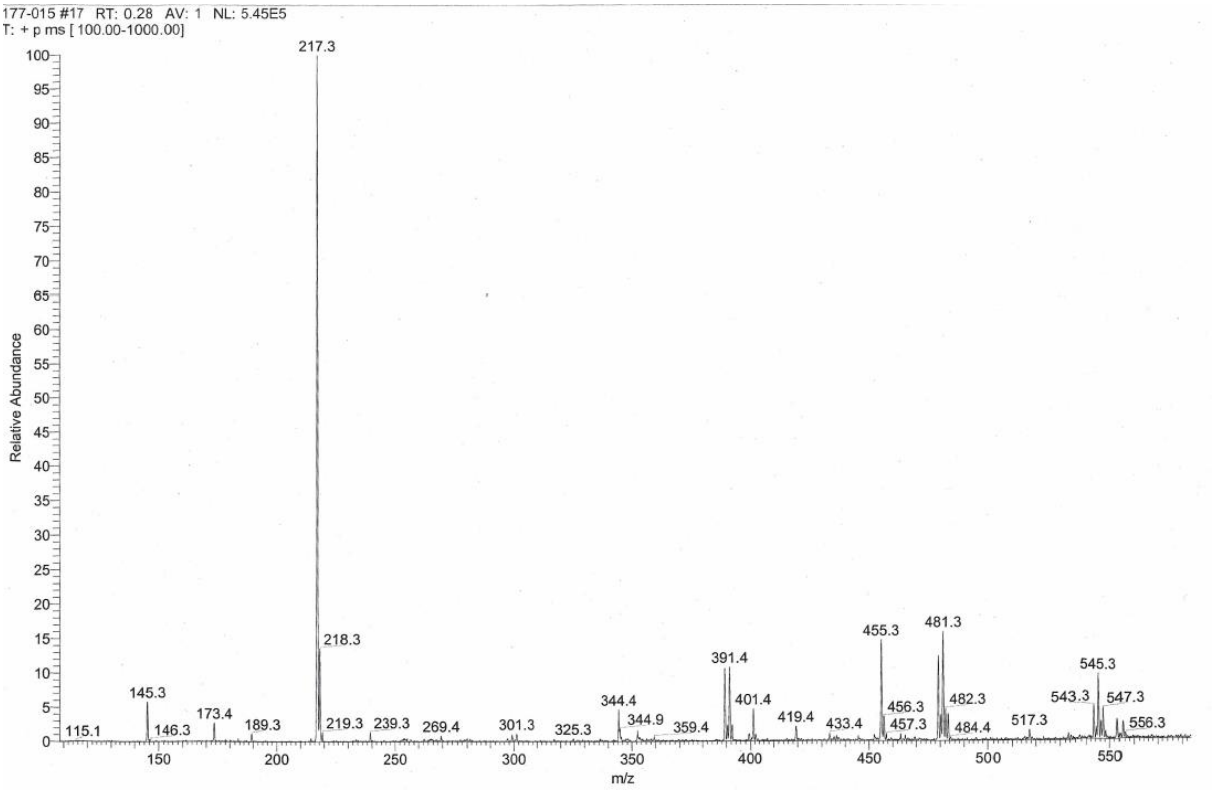

155.92
136.46
129.05
128.40
126.32
70.54
62.19
54.82
52.65
14.88
O
OEt
HN–N
Ph
Br
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

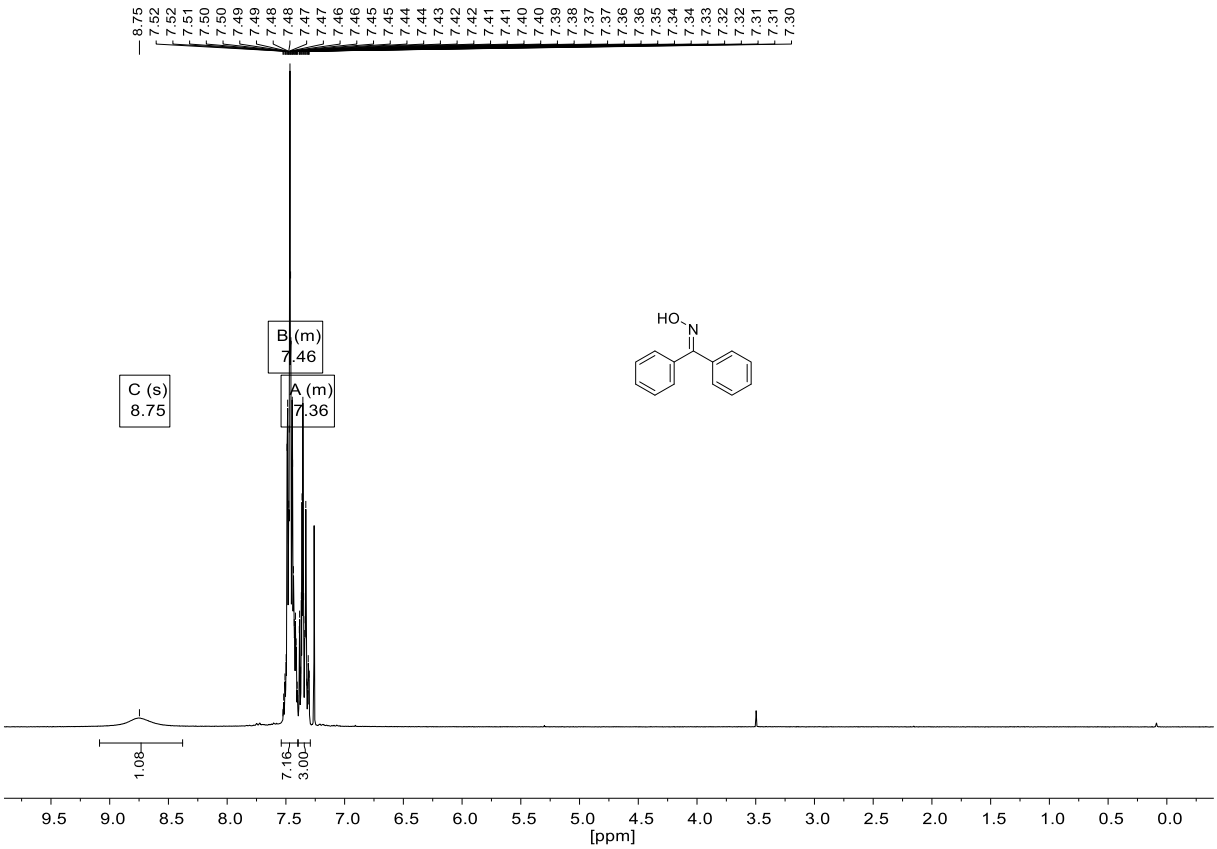

177-014 #114 RT: 1.95 AV: 1 NL: 3.32E5
T: + p Full ms [100.00-1000.00]
Relative Abundance
m/z
301.3
299.3
437.3
599.1
302.3
597.1
601.1
621.1
481.3
438.4
217.4
757.1
755.1
759.2
623.1
624.3
760.3
804.6
145.2
193.4
209.5
219.2
288.3
313.3
383.3
399.3
419.5
459.4
484.4
537.2
595.2
683.2
734.9

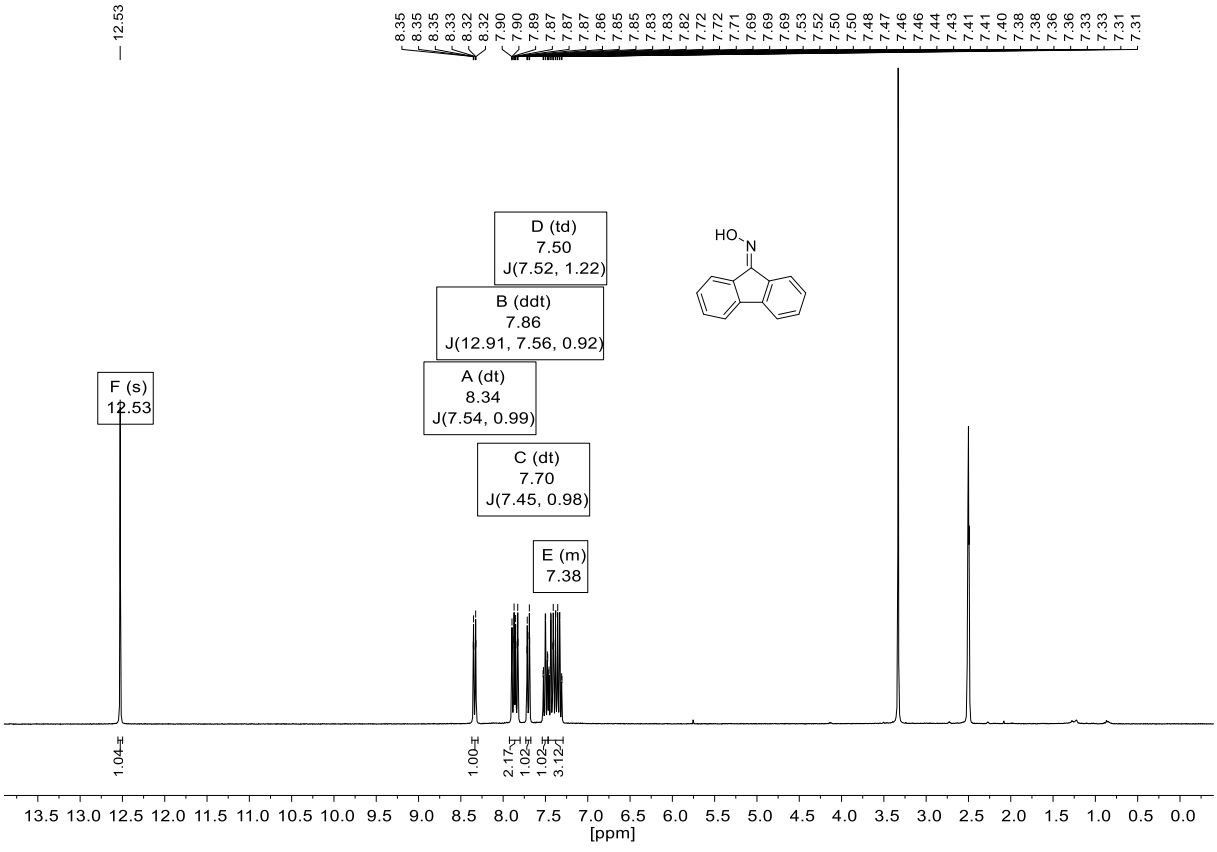

F (d)
4.97
J(6.67)
C (qq)
3.95
J(7.48, 3.57)
E (m)
4.58
B (dd)
3.81
J(15.30, 5.34)
D (dd)
4.36
J(15.31, 5.72)
A (t)
1.09
J(7.10)
[ppm]

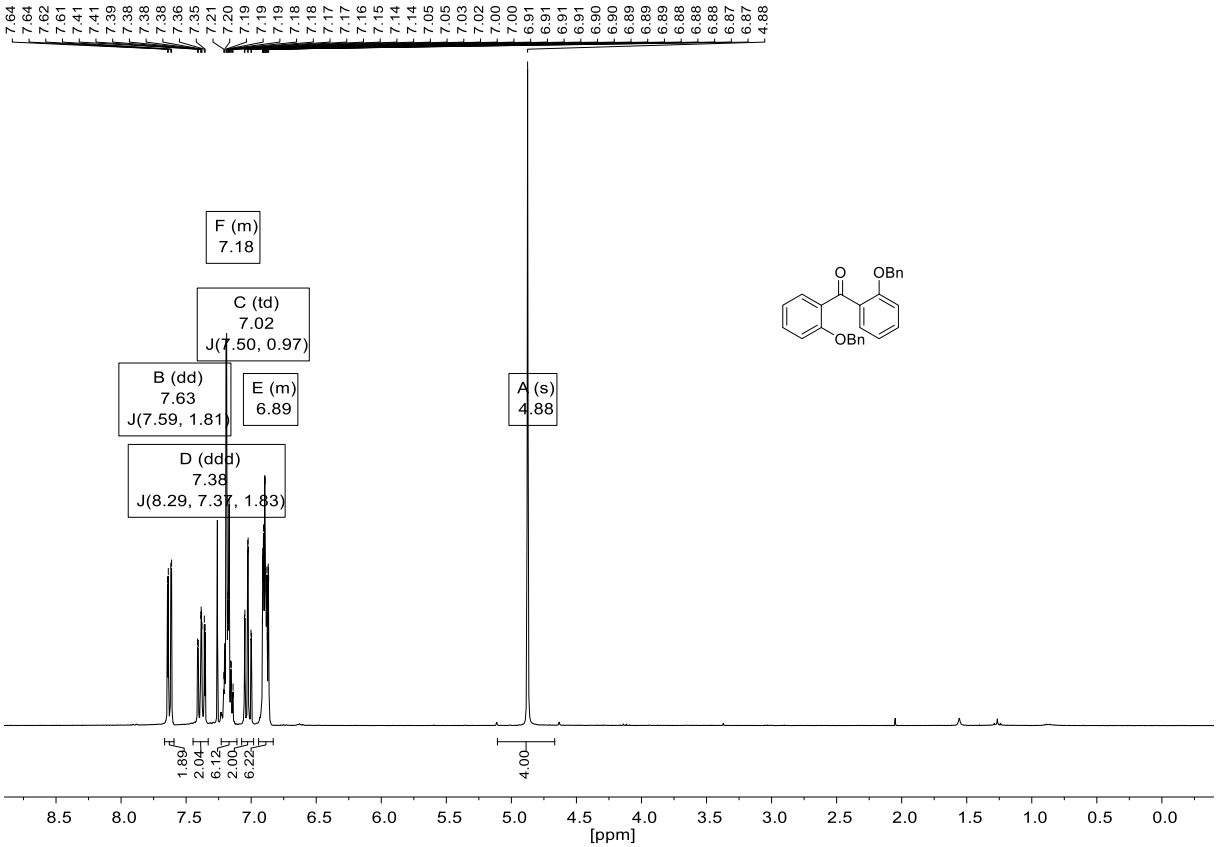

177-016 #23 RT: 0.34 AV: 1 NL: 1.01E6
T: + p Full ms [80.00-800.00]
Relative Abundance
m/z
483.3
481.5
484.3
485.3
505.3
506.3

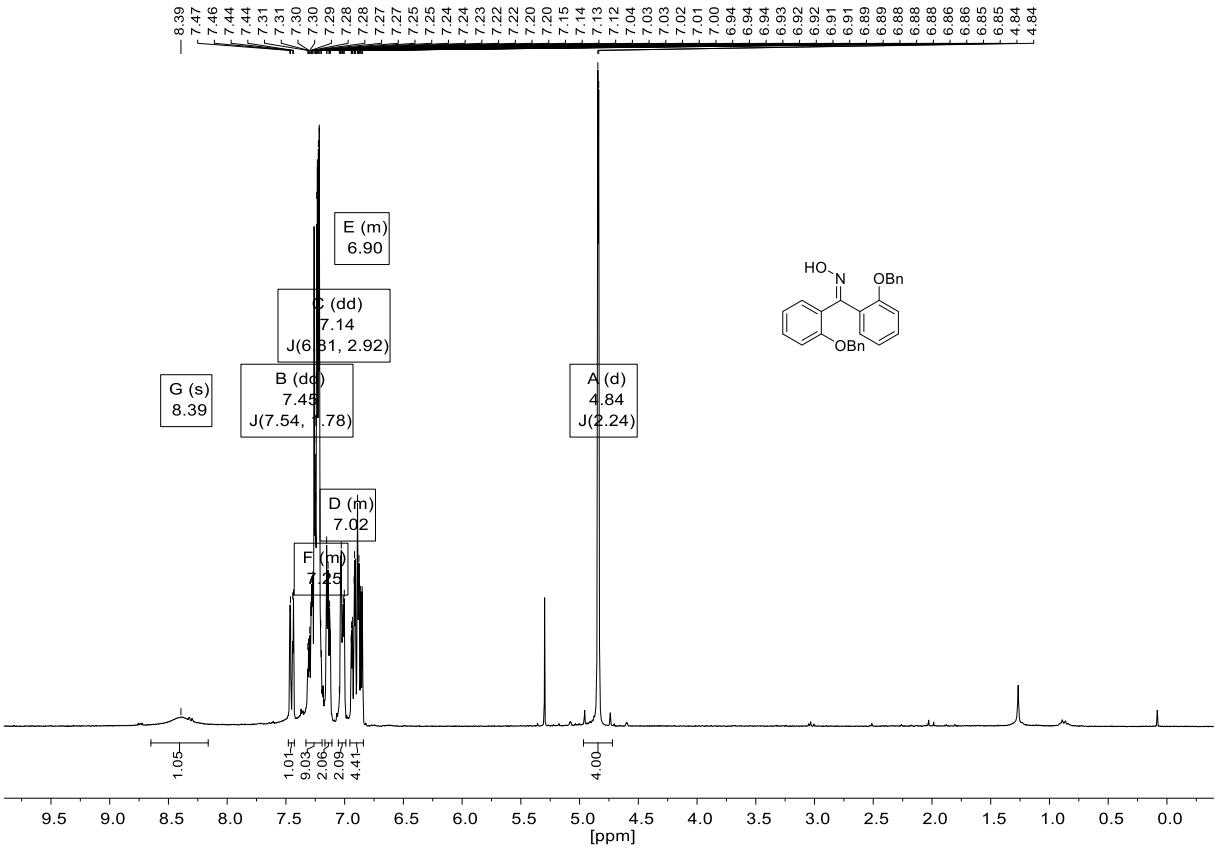

8.19
8.18
7.92
7.91
7.90
7.90
7.89
7.88
7.88
7.48
7.46
7.45
7.45
7.43
7.42
7.41
7.41
7.40
7.39
7.39
7.38
7.36
7.36
7.35
7.35
6.75
6.74
4.59
4.57
4.54
4.52
1.51
1.49
1.46
F (d)
8.19
J(2.86)
E (m)
7.90
D (m)
7.42
C (d)
6.75
J(2.87)
B (q)
4.56
J(7.13)
A (t)
1.49
J(7.13)
O
OEt
N–N
Ph
0.97
1.97
3.67
0.98
2.03
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

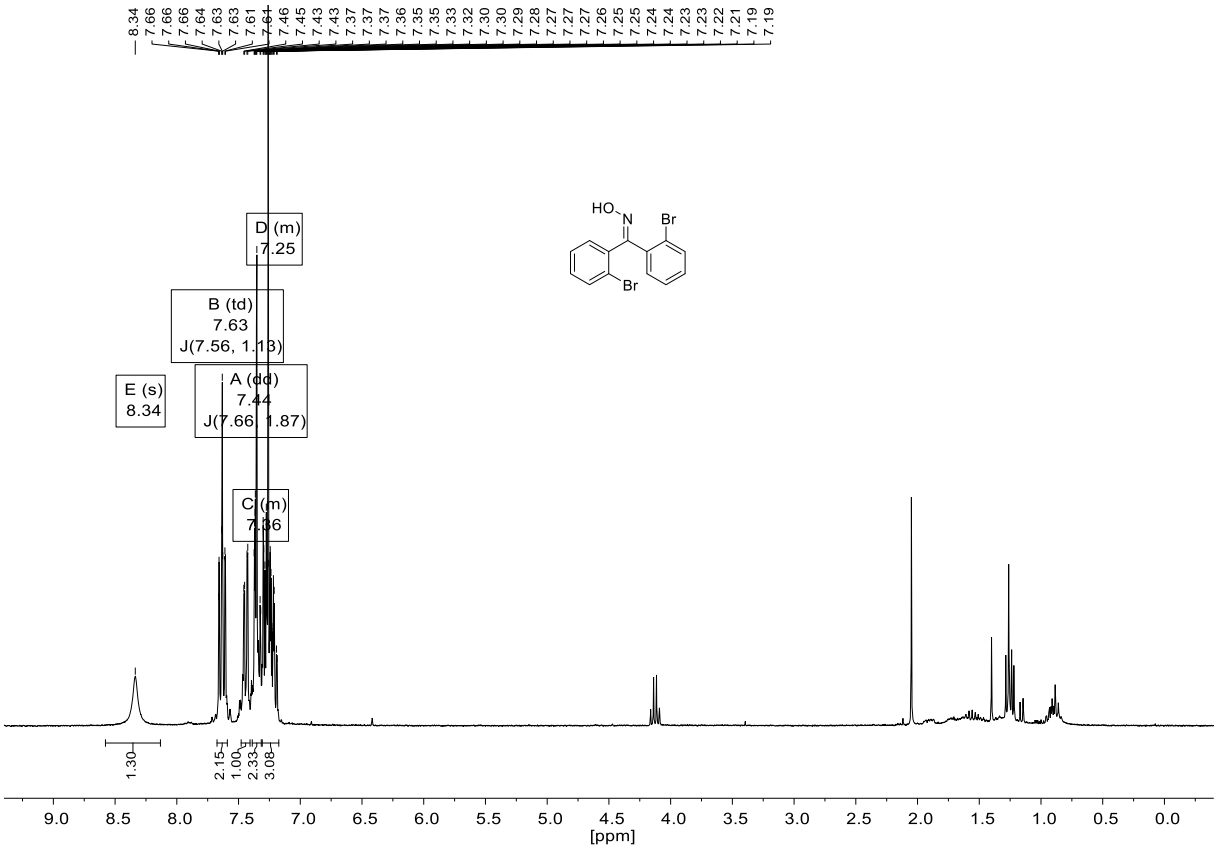

177-015 #17 RT: 0.28 AV: 1 NL: 5.45E5
T: + p ms [100.00-1000.00]
Relative Abundance
m/z
217.3
218.3
145.3
115.1
146.3
173.4
189.3
219.3
239.3
269.4
301.3
325.3
344.4
344.9
359.4
391.4
401.4
419.4
433.4
455.3
456.3
457.3
481.3
482.3
484.4
517.3
543.3
545.3
547.3
556.3

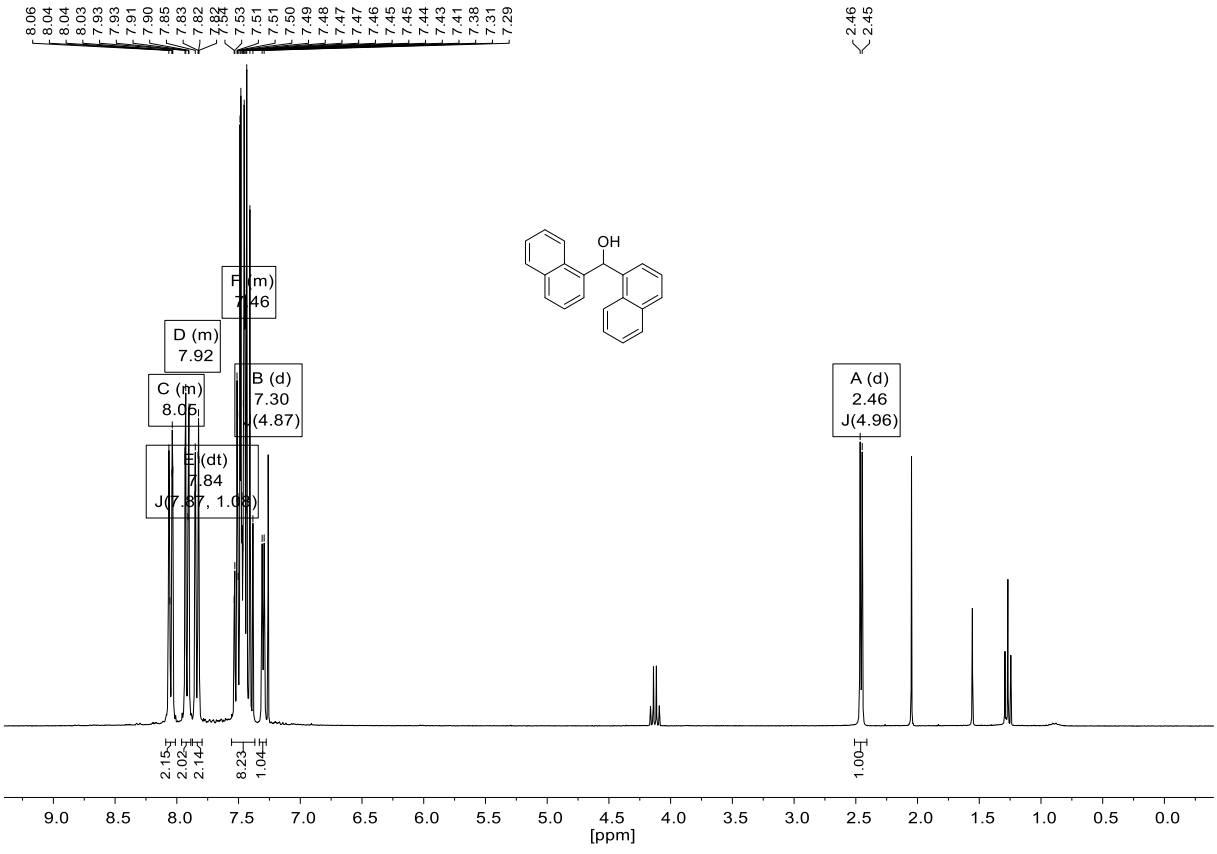

8.75
7.52
7.51
7.50
7.49
7.48
7.47
7.46
7.45
7.44
7.43
7.42
7.41
7.40
7.39
7.38
7.37
7.36
7.35
7.34
7.33
7.32
7.31
7.30
B (m)
7.46
C (s)
8.75
A (m)
7.36
HO
N
1.08
7.16
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

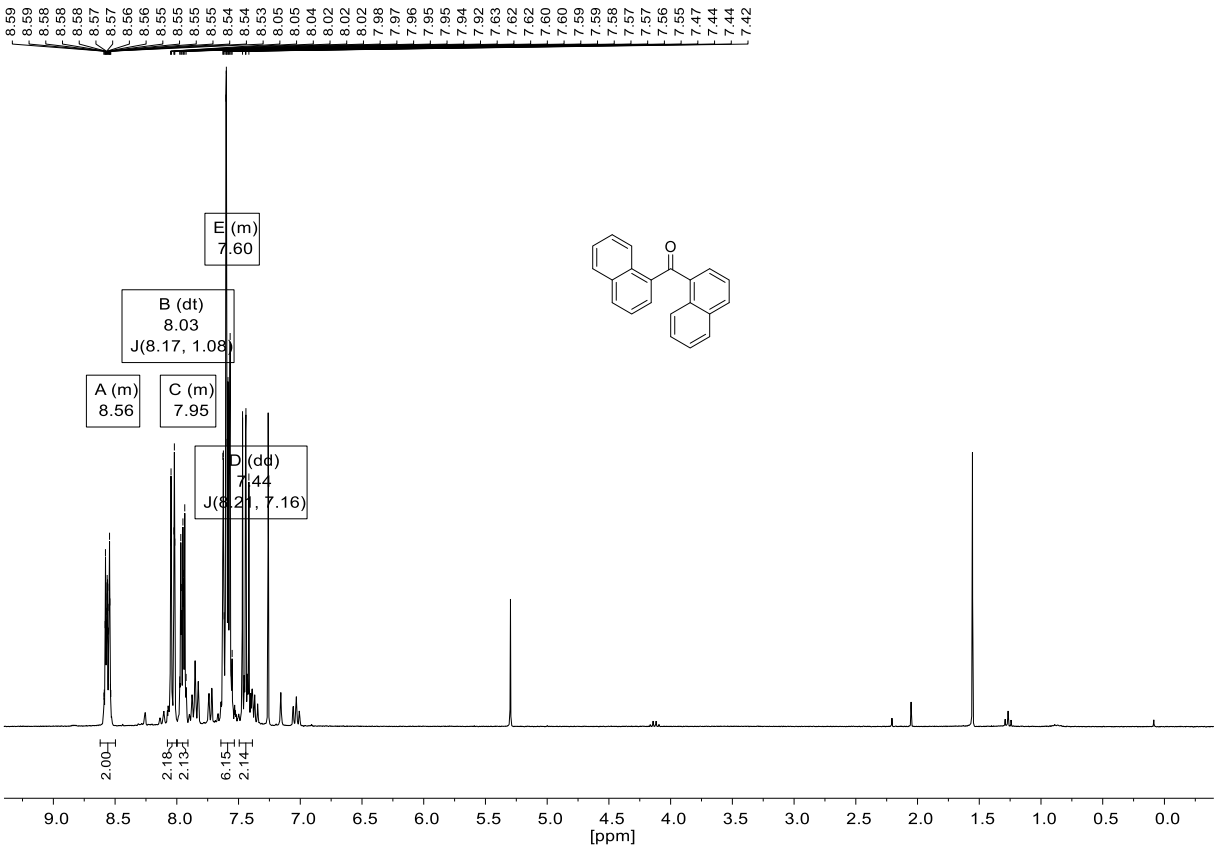

12.53
8.35
8.35
8.33
8.32
8.32
7.90
7.89
7.87
7.87
7.87
7.86
7.85
7.83
7.83
7.82
7.72
7.71
7.69
7.69
7.69
7.53
7.52
7.50
7.50
7.48
7.47
7.46
7.46
7.44
7.43
7.41
7.41
7.40
7.38
7.38
7.36
7.33
7.33
7.31
7.31
D (td)
7.50
J(7.52, 1.22)
B (ddt)
7.86
J(12.91, 7.56, 0.92)
A (dt)
8.34
J(7.54, 0.99)
C (dt)
7.70
J(7.45, 0.98)
E (m)
7.38
F (s)
12.53
HO
N
1.04
1.00
2.17
1.02
1.02
3.12
13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

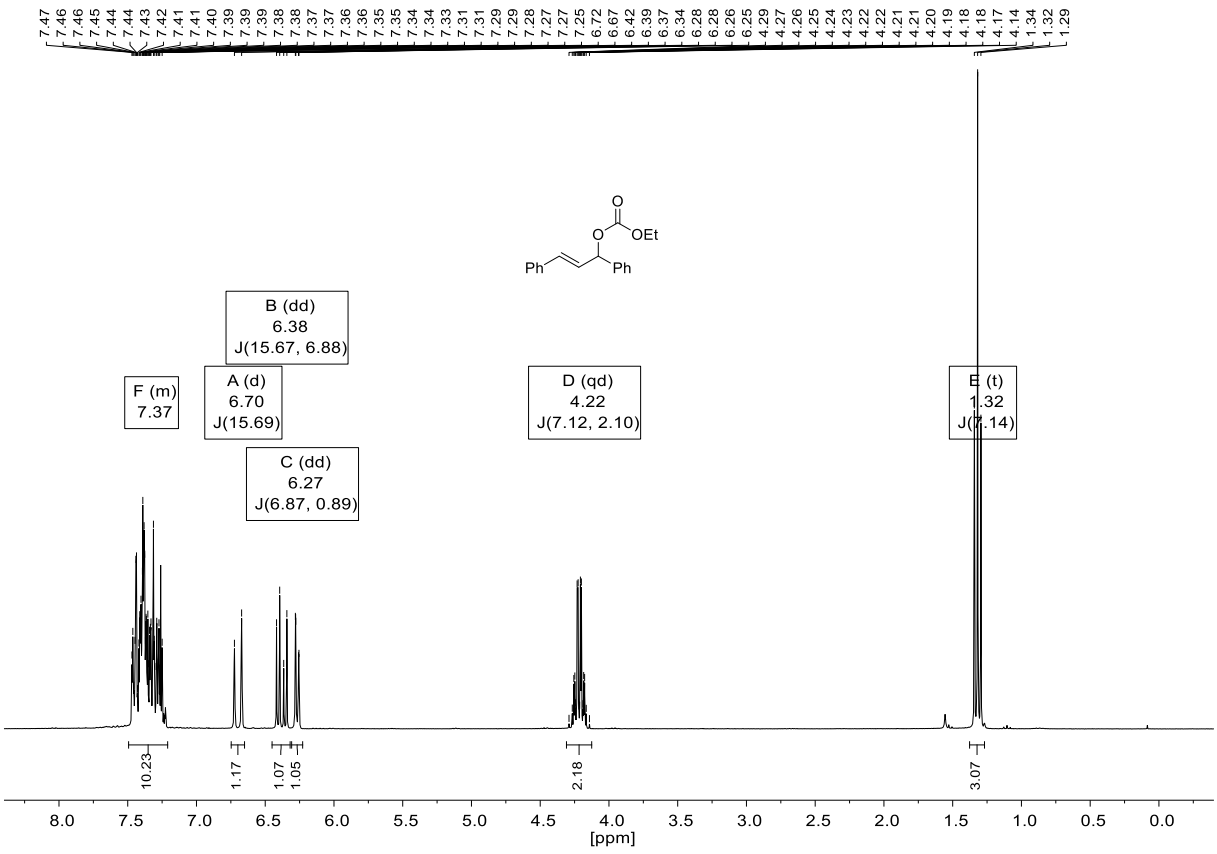

F (m)
7.18
C (td)
7.02
J(7.50, 0.97)
B (dd)
7.63
J(7.59, 1.81)
E (m)
6.89
D (ddd)
7.38
J(8.29, 7.37, 1.83)
A (s)
4.88
O
OBn
OBn
1.89
2.04
6.12
2.00
6.22
4.00
[ppm]

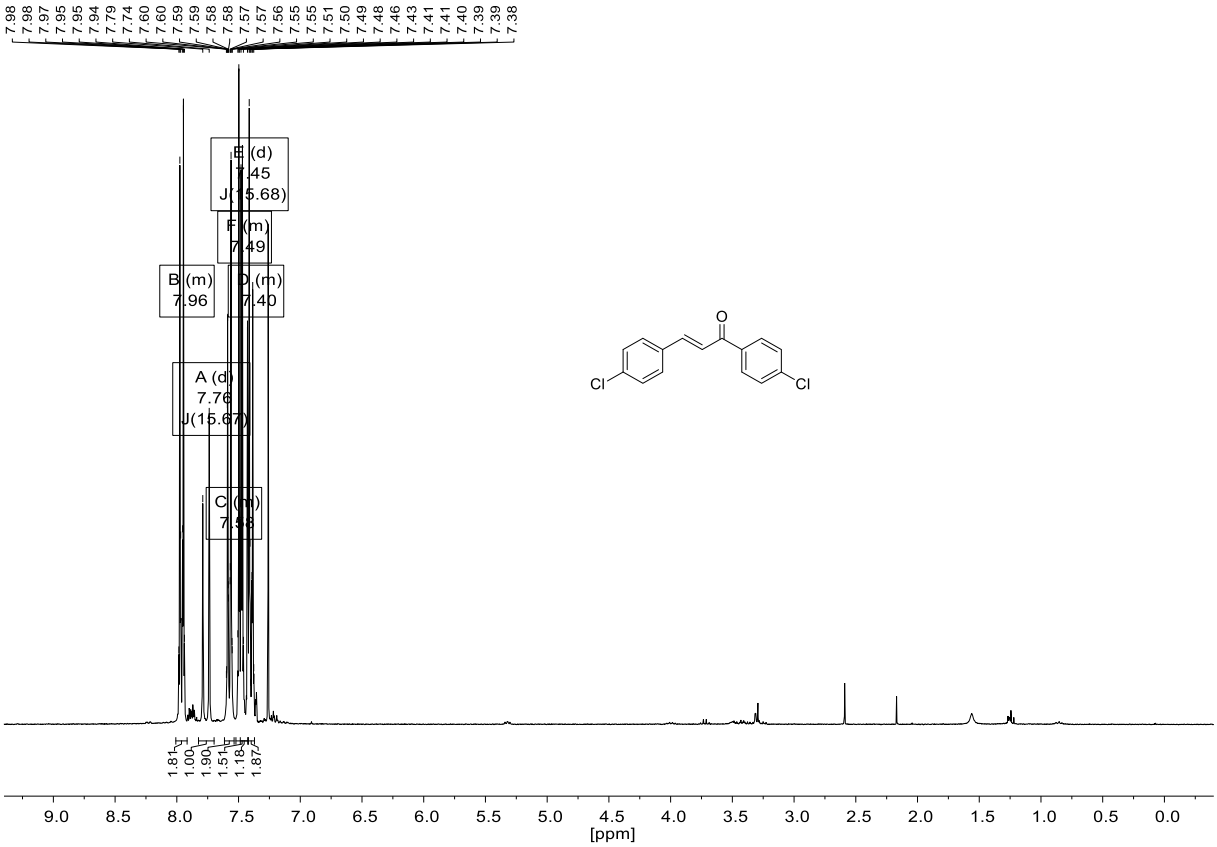

E (m)
6.90
C (dd)
7.14
J(6.81, 2.92)
G (s)
8.39
B (dd)
7.45
J(7.54, 1.78)
A (d)
4.84
J(2.24)
D (m)
7.02
F (m)
7.25
HO
N
OBn
OBn
1.05
1.01
9.03
2.06
2.09
4.41
4.00
[ppm]

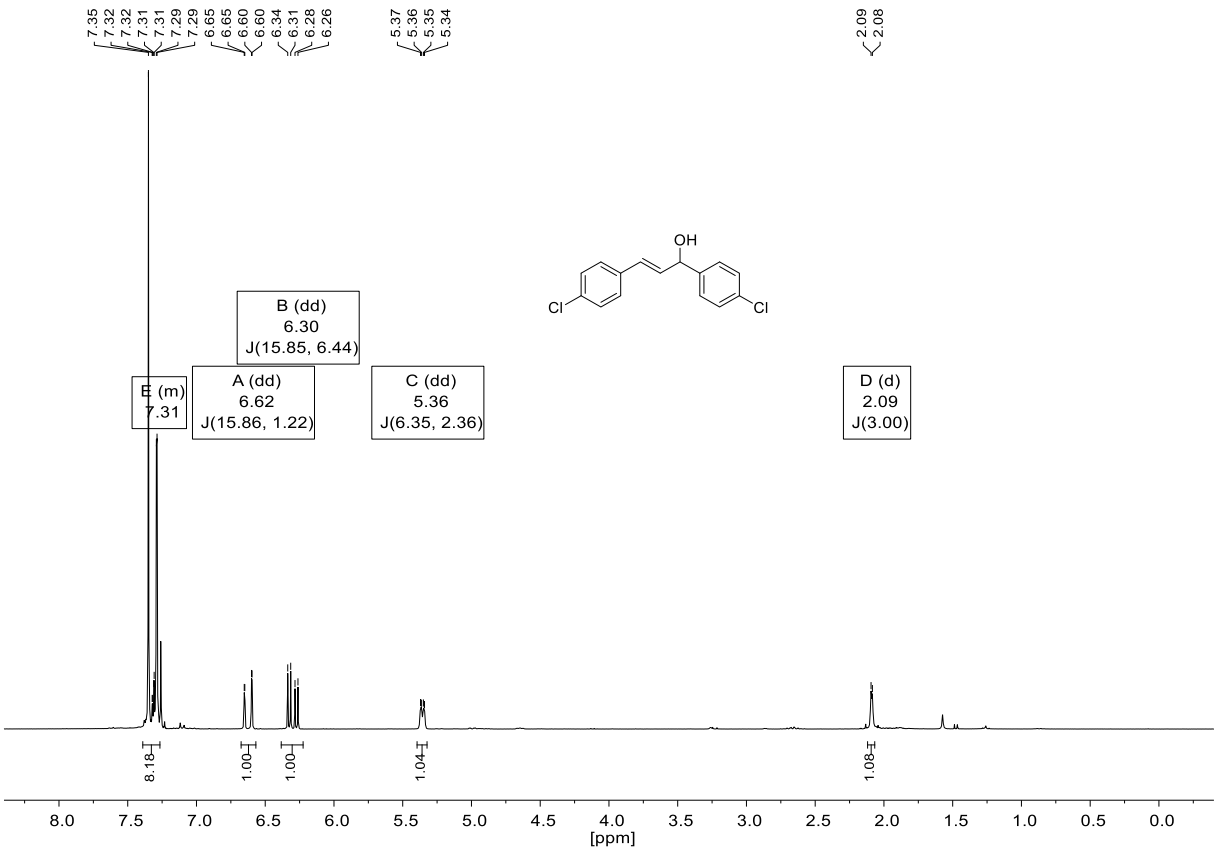

8.34
7.66
7.66
7.66
7.64
7.63
7.63
7.61
7.61
7.46
7.45
7.43
7.43
7.37
7.37
7.37
7.36
7.35
7.33
7.32
7.30
7.30
7.29
7.28
7.27
7.27
7.27
7.26
7.25
7.25
7.24
7.24
7.23
7.23
7.22
7.21
7.19
7.19
D (m)
7.25
B (td)
7.63
J(7.56, 1.13)
E (s)
8.34
A (dd)
7.44
J(7.66, 1.87)
C (m)
7.36
HO
N
Br
Br
1.30
2.15
1.00
2.33
3.08
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

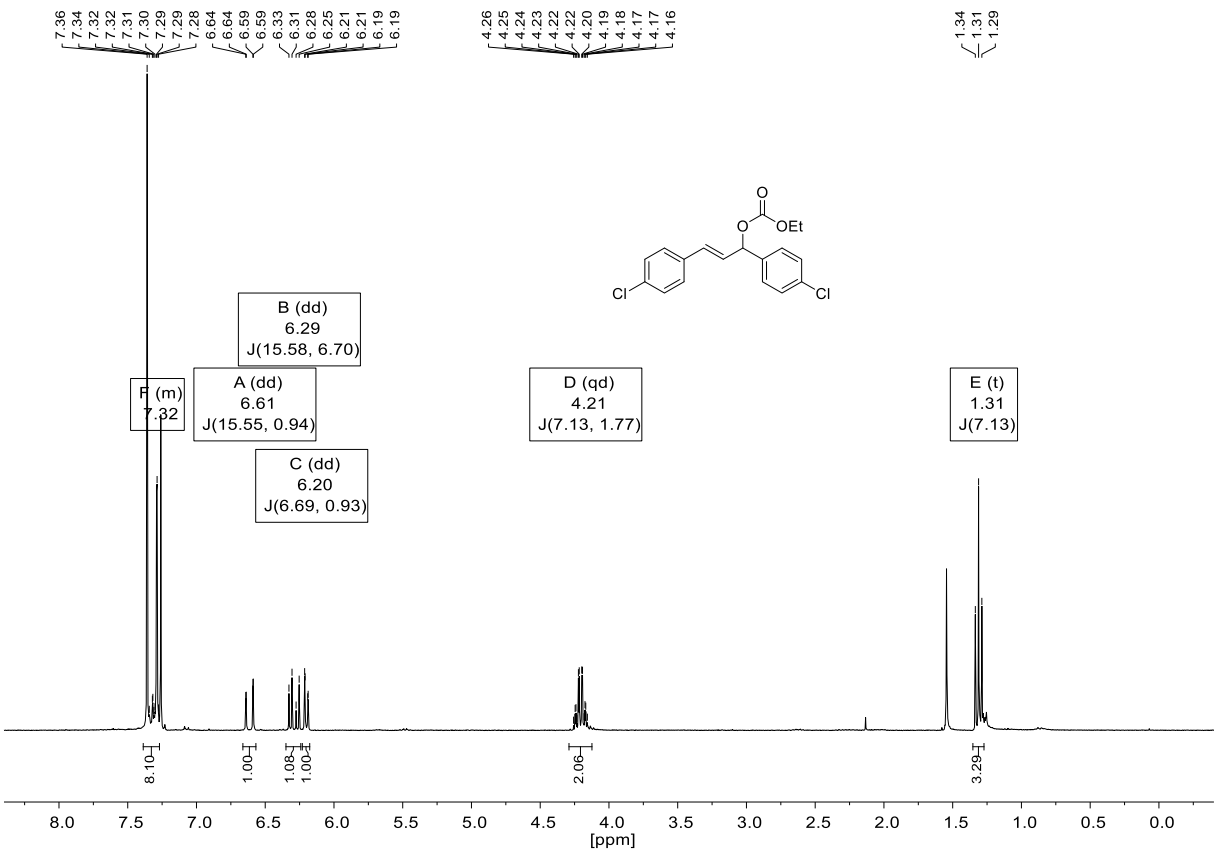

8.06
8.04
8.04
8.03
7.93
7.93
7.91
7.90
7.85
7.83
7.82
7.82
7.54
7.53
7.51
7.51
7.50
7.49
7.48
7.47
7.47
7.46
7.45
7.45
7.44
7.43
7.41
7.38
7.31
7.29
2.46
2.45
F (m)
7.46
D (m)
7.92
C (m)
8.05
B (d)
7.30
J(4.87)
E (dt)
7.84
J(7.87, 1.03)
A (d)
2.46
J(4.96)
OH
2.15
2.02
2.14
8.23
1.04
1.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

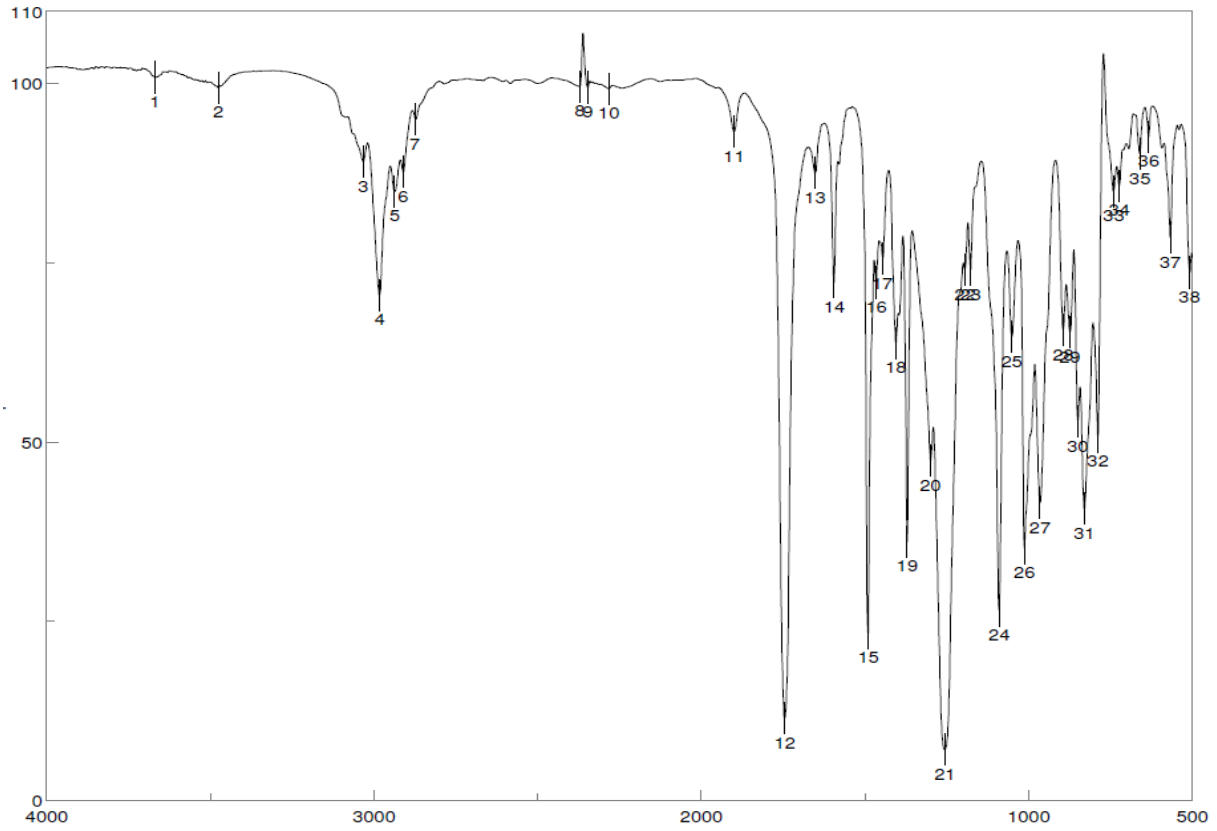

E (m)
7.60
B (dt)
8.03
J(8.17, 1.08)
A (m)
8.56
C (m)
7.95
D (dd)
7.44
J(8.21, 7.16)
O
2.00
2.18
2.13
6.15
2.14
[ppm]

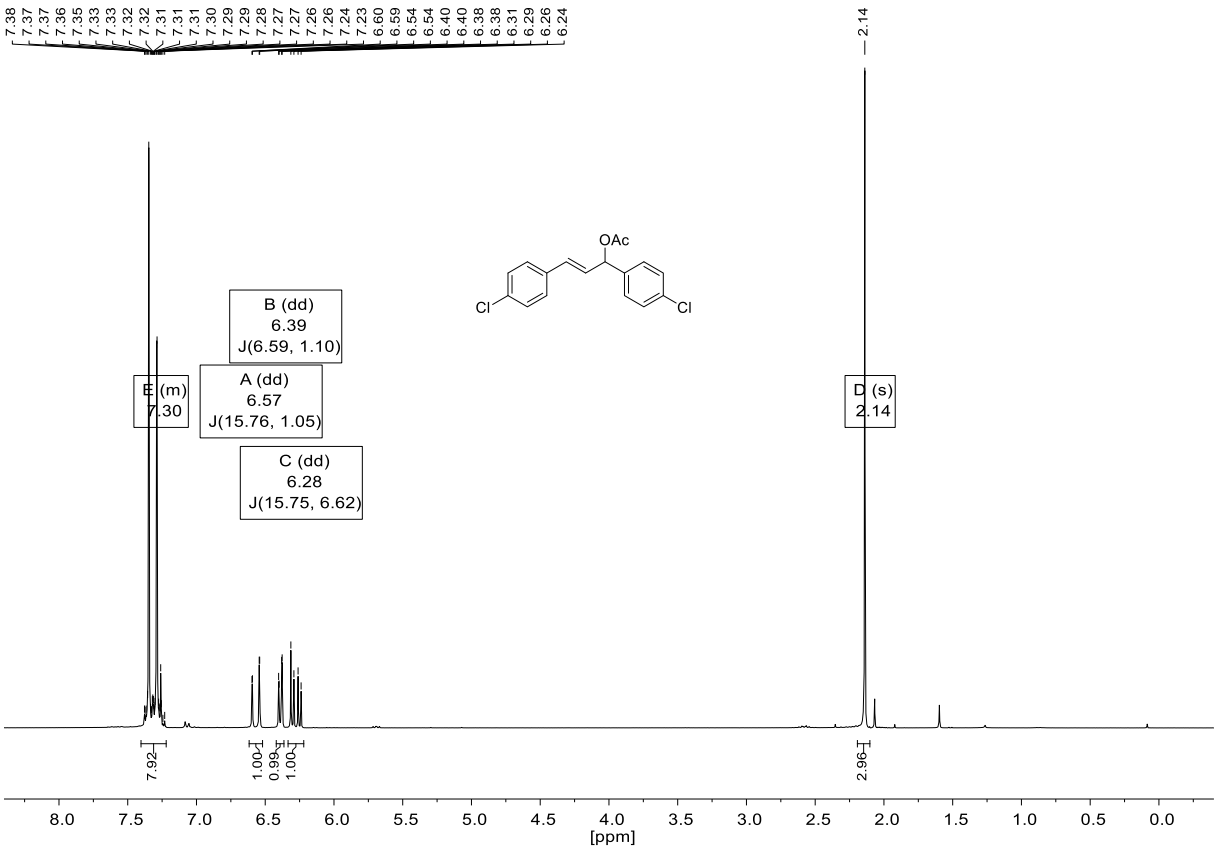

O
O
OEt
Ph
Ph
B (dd)
6.38
J(15.67, 6.88)
F (m)
7.37
A (d)
6.70
J(15.69)
C (dd)
6.27
J(6.87, 0.89)
D (qd)
4.22
J(7.12, 2.10)
E (t)
1.32
J(7.14)
10.23
1.17
1.07
1.05
2.18
3.07
[ppm]

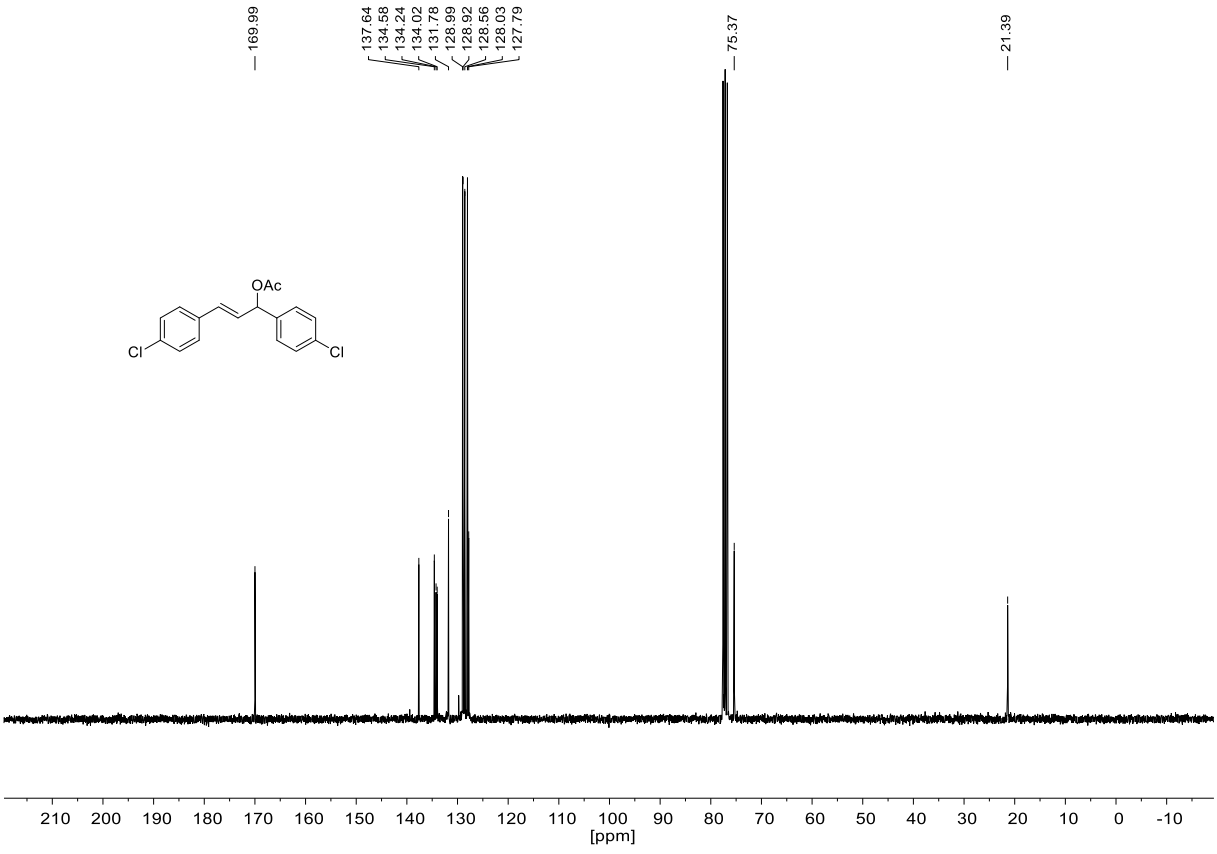

B (d)
7.45
J(15.68)
F (m)
7.49
B (m)
7.96
D (m)
7.40
A (d)
7.76
J(15.67)
C (m)
7.48
O
Cl
Cl
1.81
1.00
1.90
1.51
1.18
1.87
[ppm]

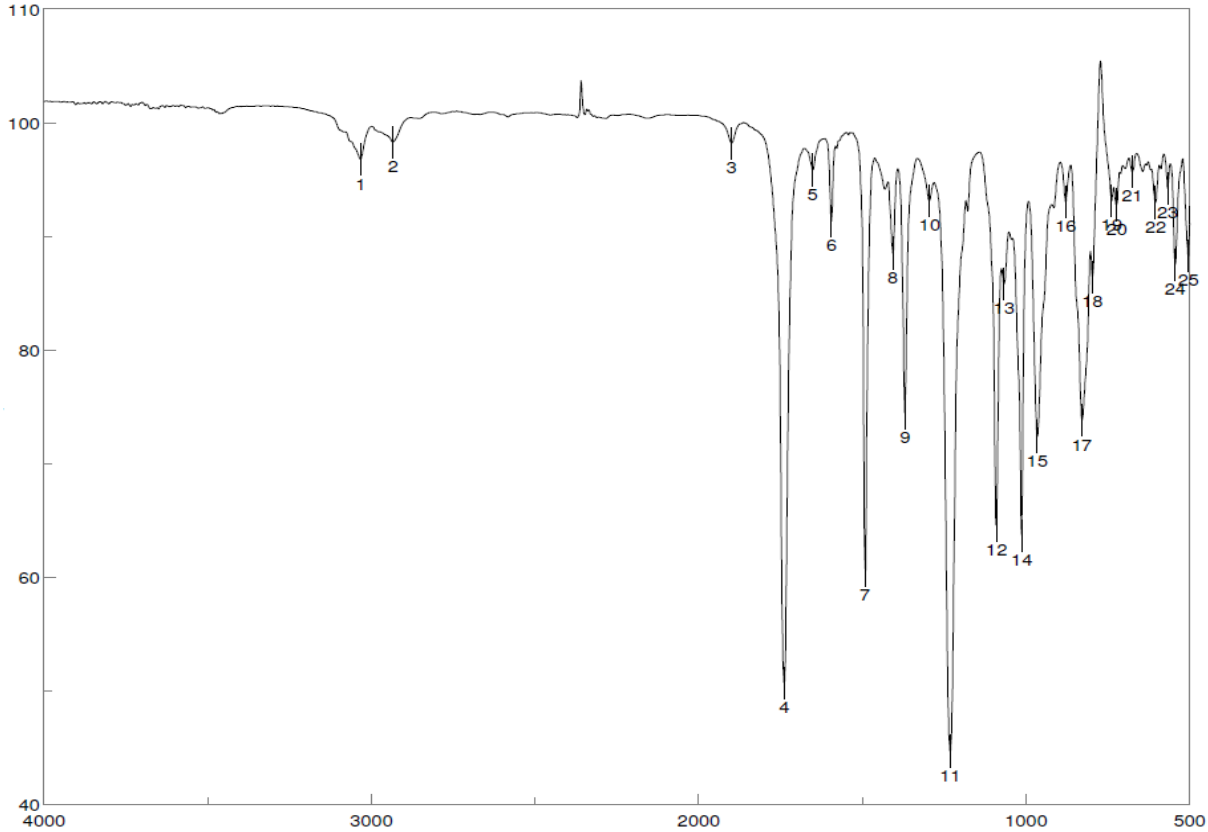

OH
Cl
Cl
B (dd)
6.30
J(15.85, 6.44)
E (m)
7.31
A (dd)
6.62
J(15.86, 1.22)
C (dd)
5.36
J(6.35, 2.36)
D (d)
2.09
J(3.00)
8.18
1.00
1.00
1.04
1.08
[ppm]

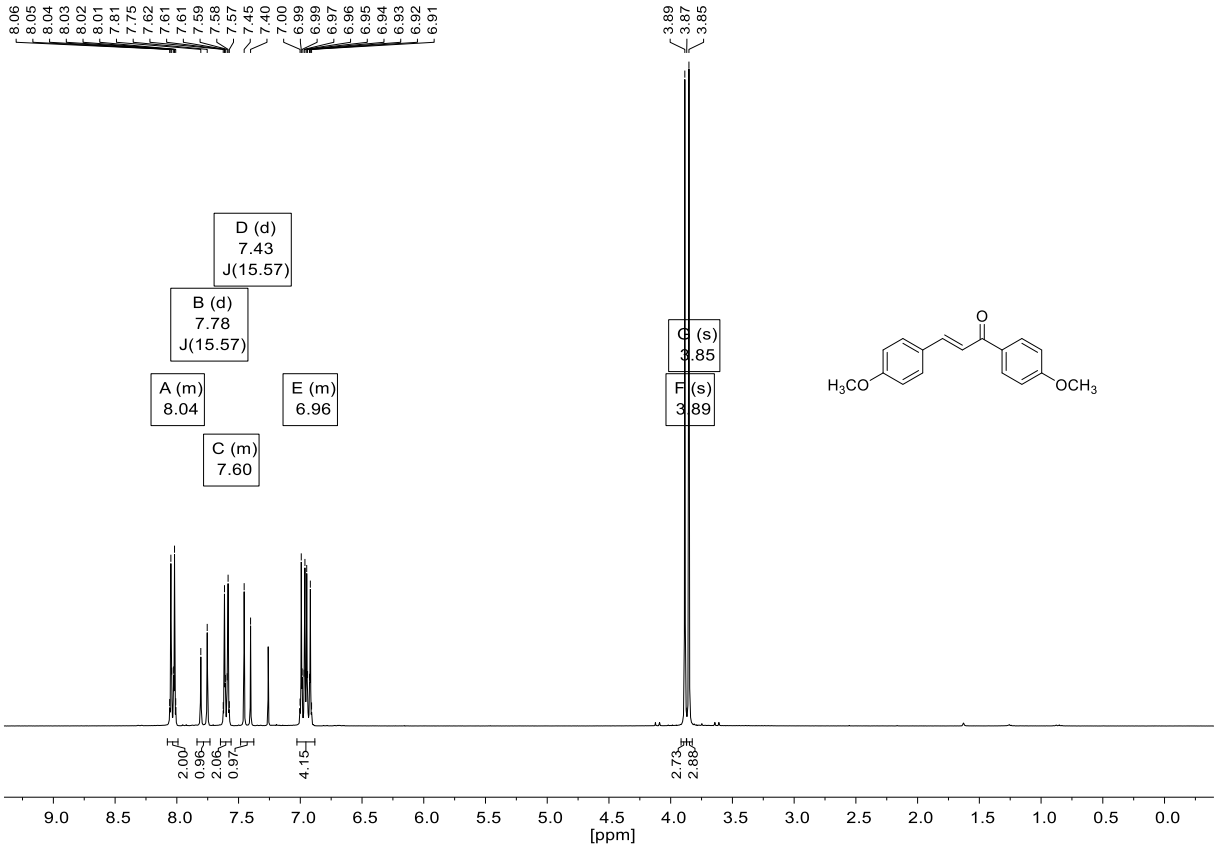

7.36
7.34
7.32
7.32
7.31
7.30
7.29
7.29
7.28
6.64
6.64
6.59
6.59
6.33
6.31
6.28
6.25
6.21
6.21
6.19
6.19
4.26
4.25
4.24
4.23
4.22
4.22
4.20
4.19
4.18
4.17
4.17
4.16
1.34
1.31
1.29
O
O
OEt
Cl
Cl
B (dd)
6.29
J(15.58, 6.70)
F (m)
7.32
A (dd)
6.61
J(15.55, 0.94)
C (dd)
6.20
J(6.69, 0.93)
D (qd)
4.21
J(7.13, 1.77)
E (t)
1.31
J(7.13)
8.10
1.00
1.08
1.00
2.06
3.29
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

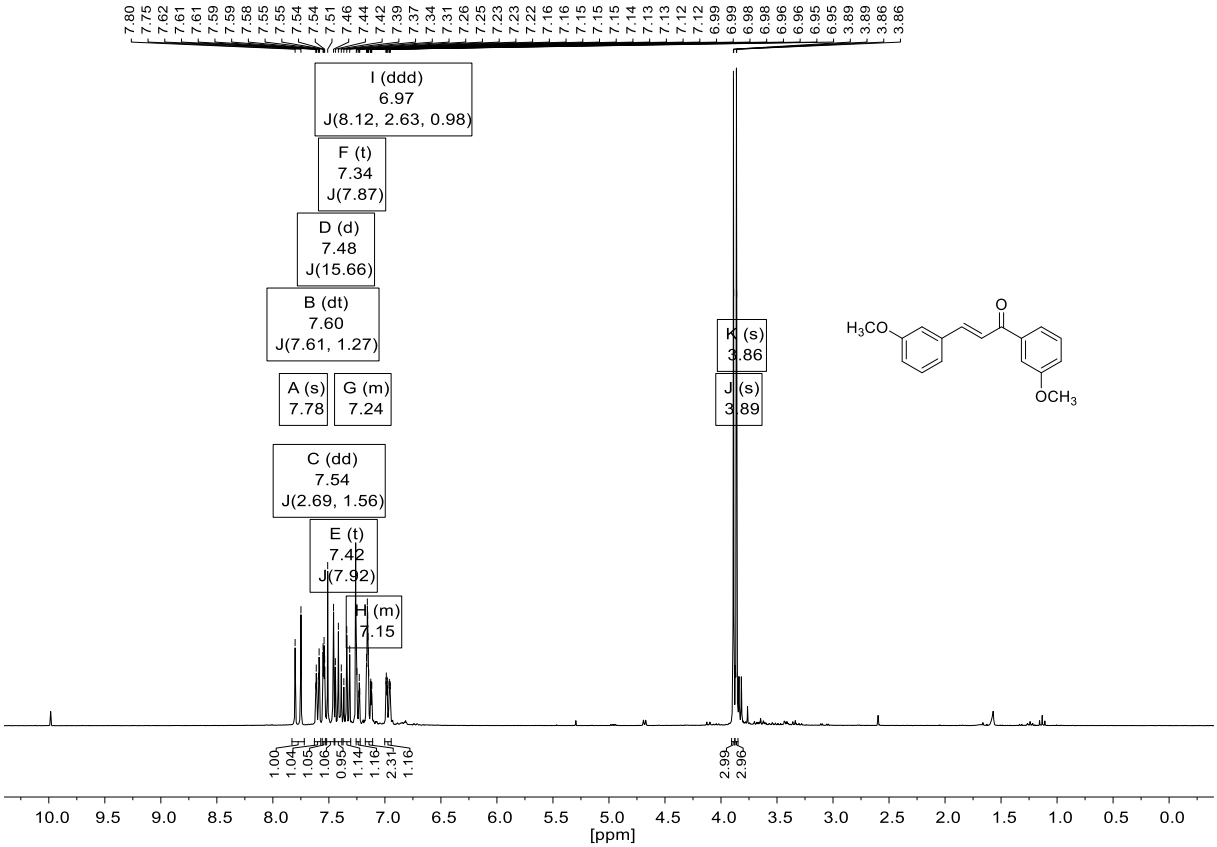

110
100
50
0
4000
3000
2000
1000
500

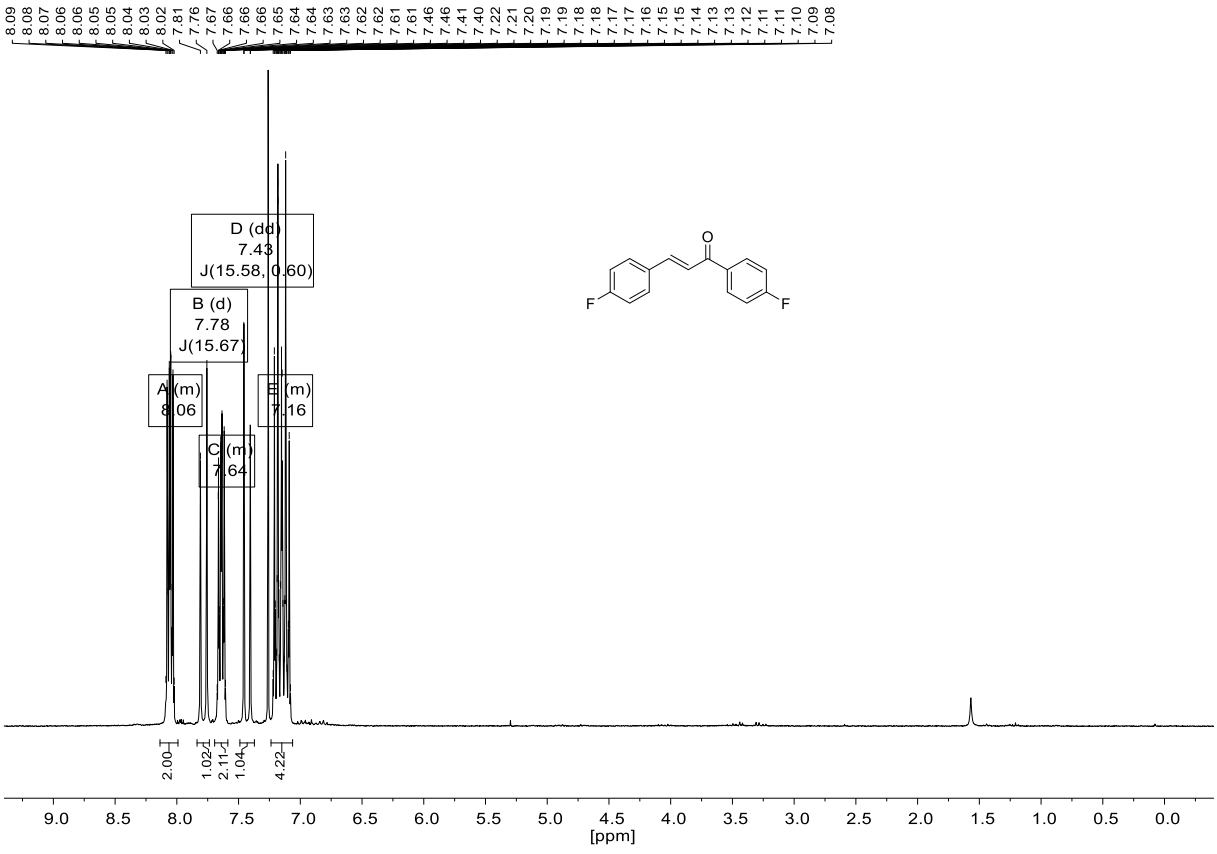

7.38
7.37
7.37
7.36
7.35
7.33
7.33
7.32
7.32
7.31
7.31
7.31
7.30
7.29
7.29
7.28
7.27
7.26
7.26
7.24
7.23
6.60
6.59
6.54
6.54
6.40
6.38
6.38
6.31
6.29
6.26
6.24
2.14
OAc
Cl
Cl
B (dd)
6.39
J(6.59, 1.10)
A (dd)
6.57
J(15.76, 1.05)
E (m)
7.30
C (dd)
6.28
J(15.75, 6.62)
D (s)
2.14
7.92
1.00
0.99
1.00
2.96
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

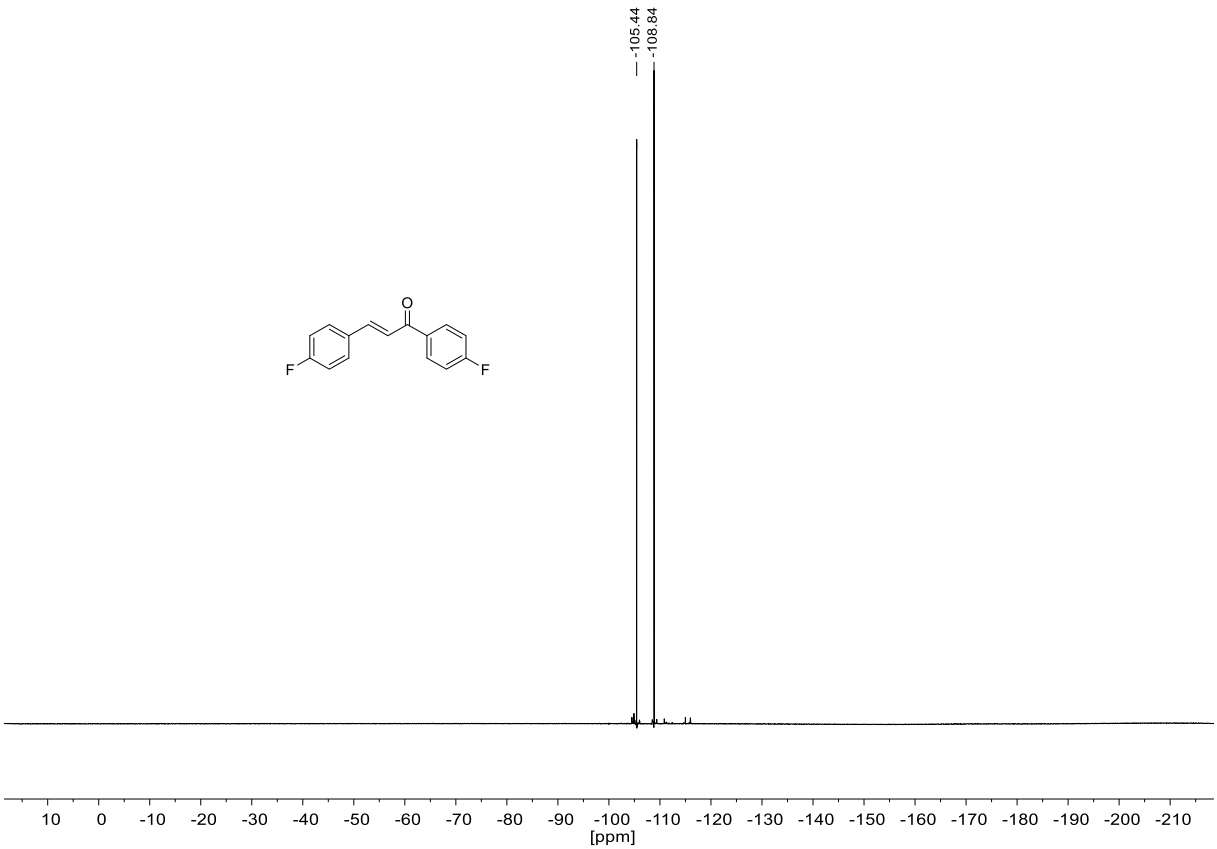

169.99
137.64
134.58
134.24
134.02
131.78
128.99
128.92
128.56
128.03
127.79
75.37
21.39
OAc
Cl
Cl
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
[ppm]

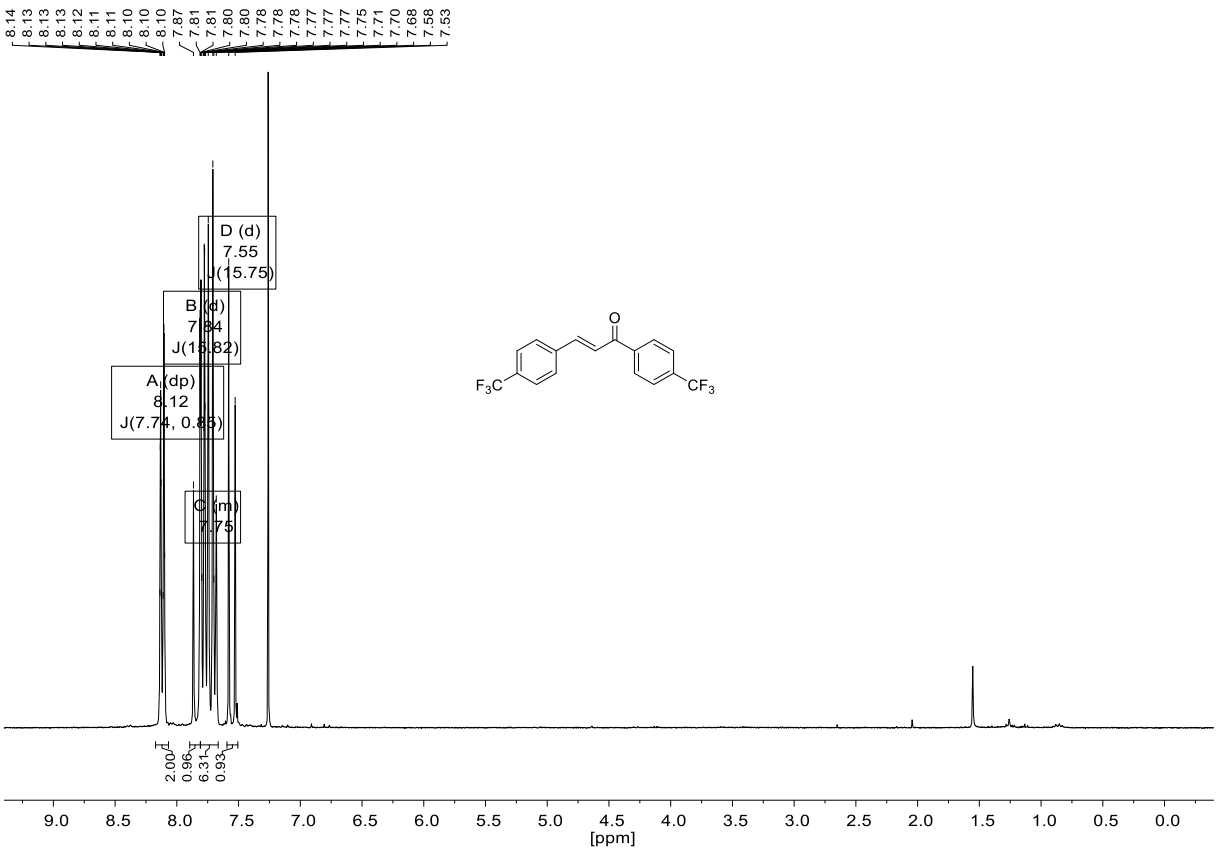

110
100
80
60
40
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

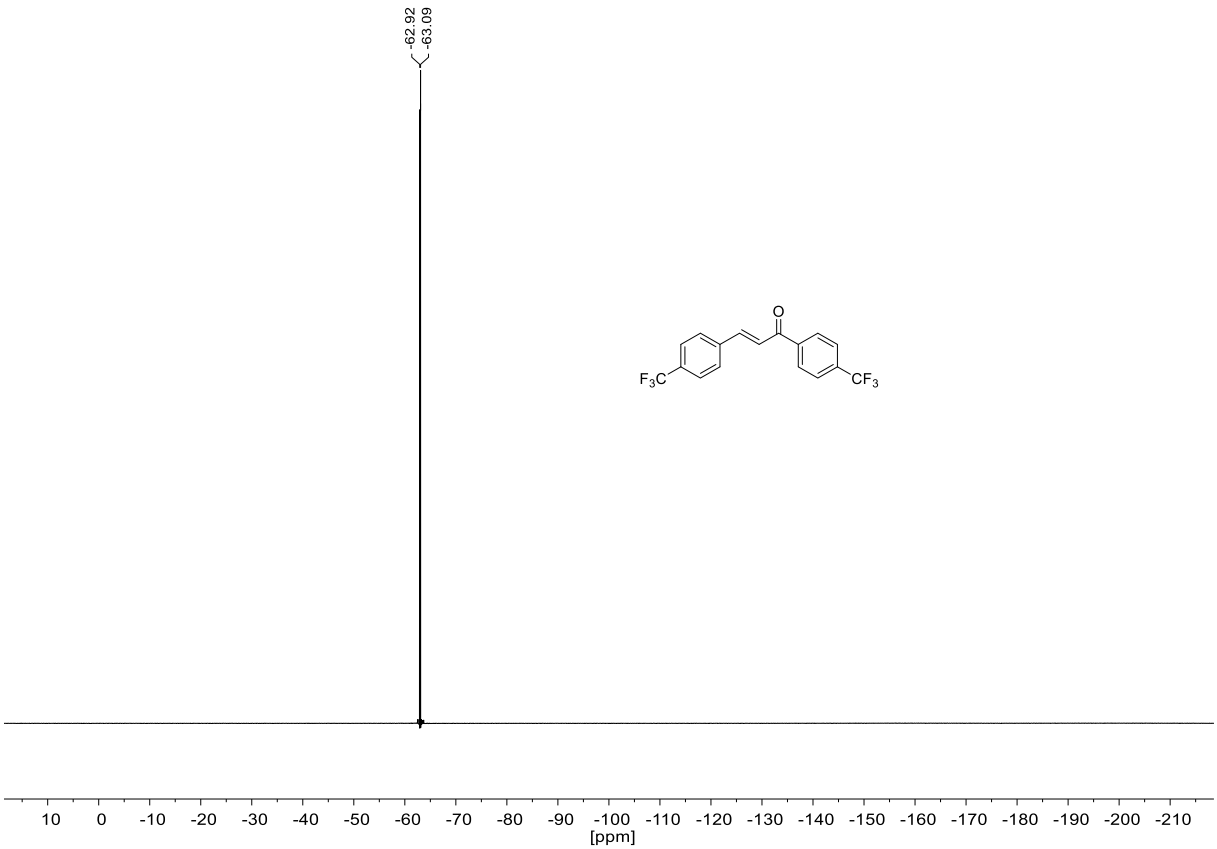

8.06
8.05
8.04
8.03
8.02
8.01
7.81
7.75
7.62
7.61
7.61
7.59
7.58
7.57
7.45
7.40
7.00
6.99
6.99
6.97
6.96
6.95
6.94
6.93
6.92
6.91
3.89
3.87
3.85
D (d)
7.43
J(15.57)
B (d)
7.78
J(15.57)
A (m)
8.04
E (m)
6.96
C (m)
7.60
G (s)
3.85
F (s)
3.89
H3CO
OCH3
2.00
0.96
2.06
0.97
4.15
2.73
2.88
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

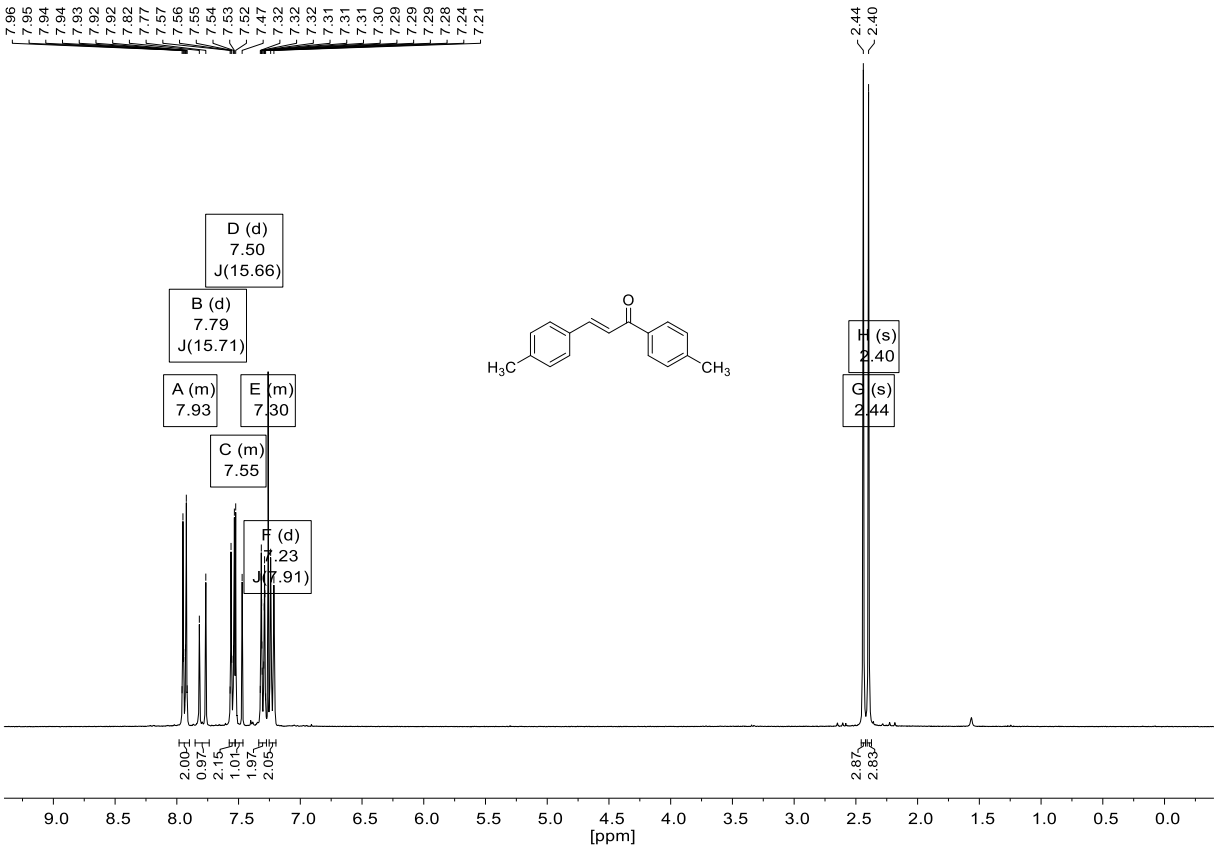

I (ddd)
6.97
J(8.12, 2.63, 0.98)
F (t)
7.34
J(7.87)
D (d)
7.48
J(15.66)
B (dt)
7.60
J(7.61, 1.27)
A (s)
7.78
G (m)
7.24
C (dd)
7.54
J(2.69, 1.56)
E (t)
7.42
J(7.92)
H (m)
7.15
K (s)
3.86
J (s)
3.89
H3CO
O
OCH3
[ppm]

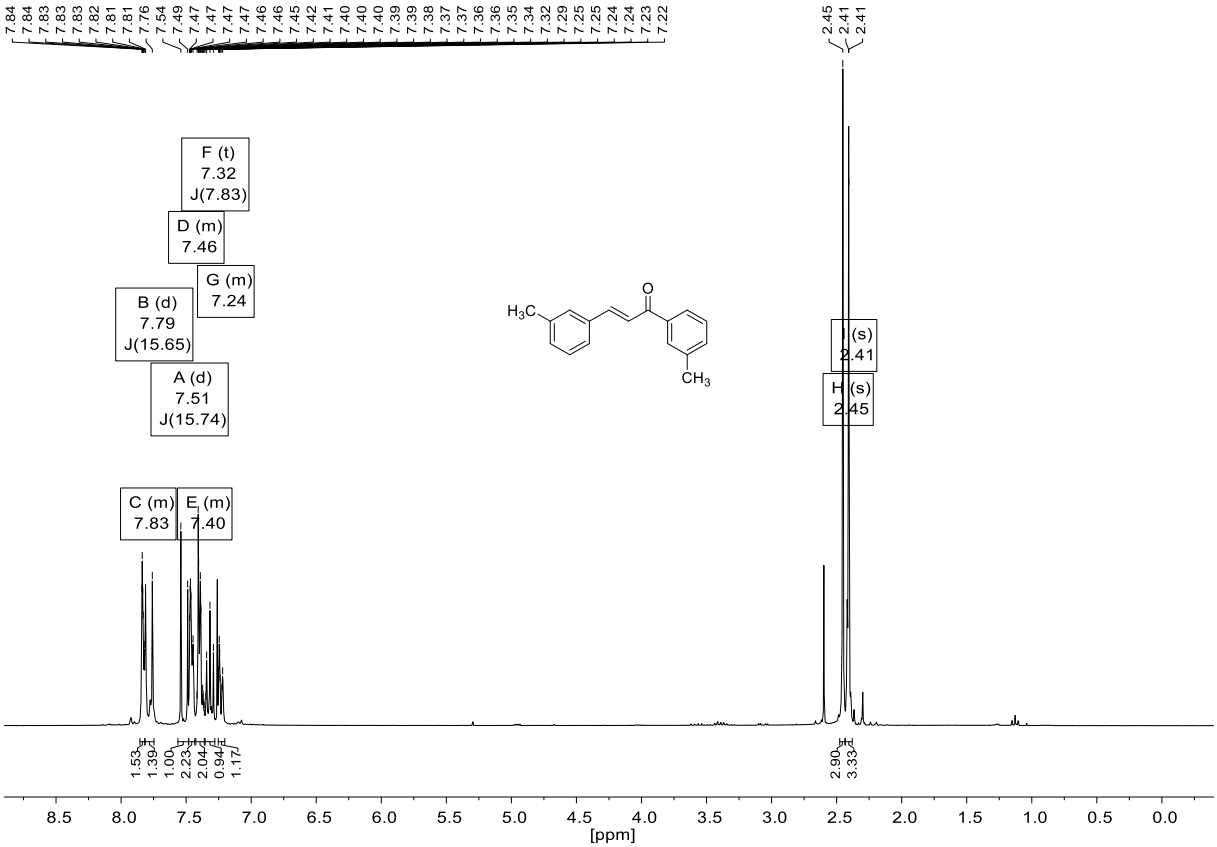

D (dd)
7.43
J(15.58, 0.60)
B (d)
7.78
J(15.67)
A (m)
8.06
E (m)
7.16
C (m)
7.64
F
O
F
[ppm]

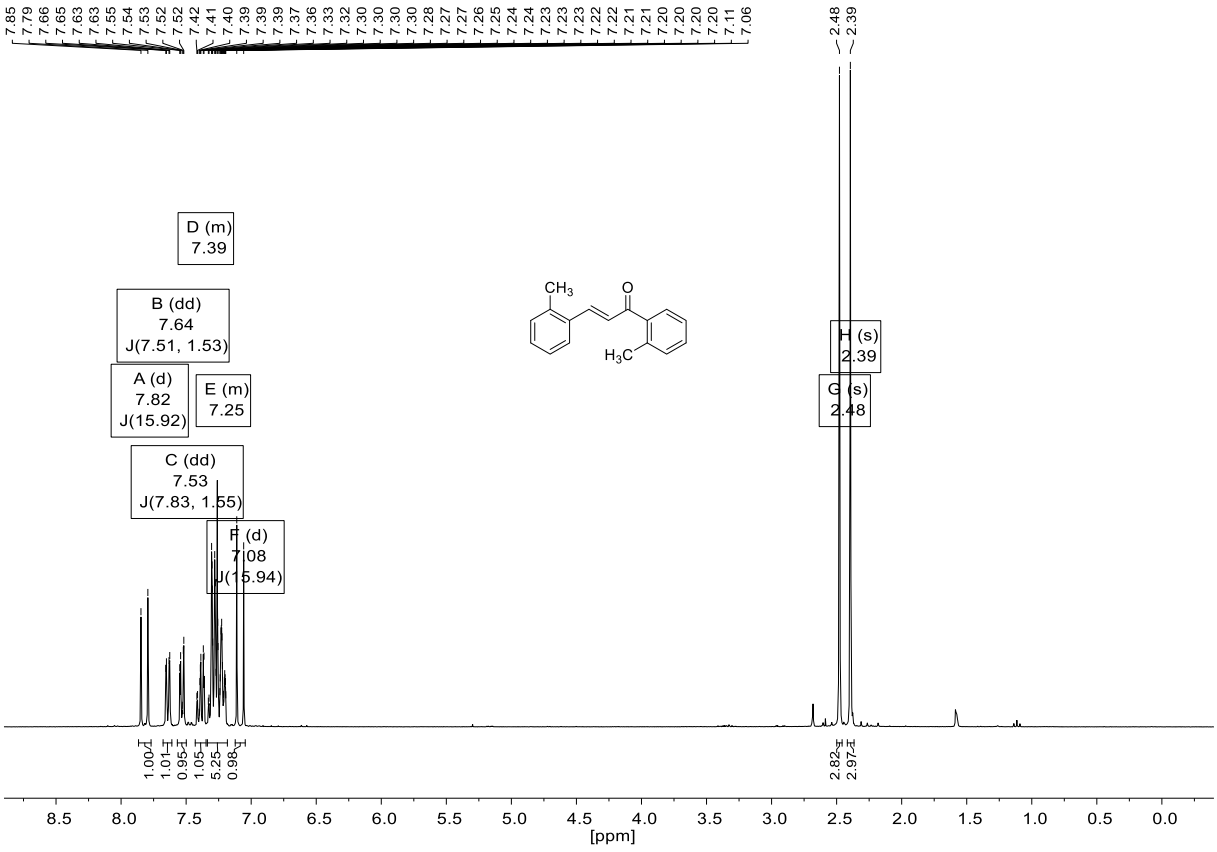

-105.44
-108.84
O
F
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

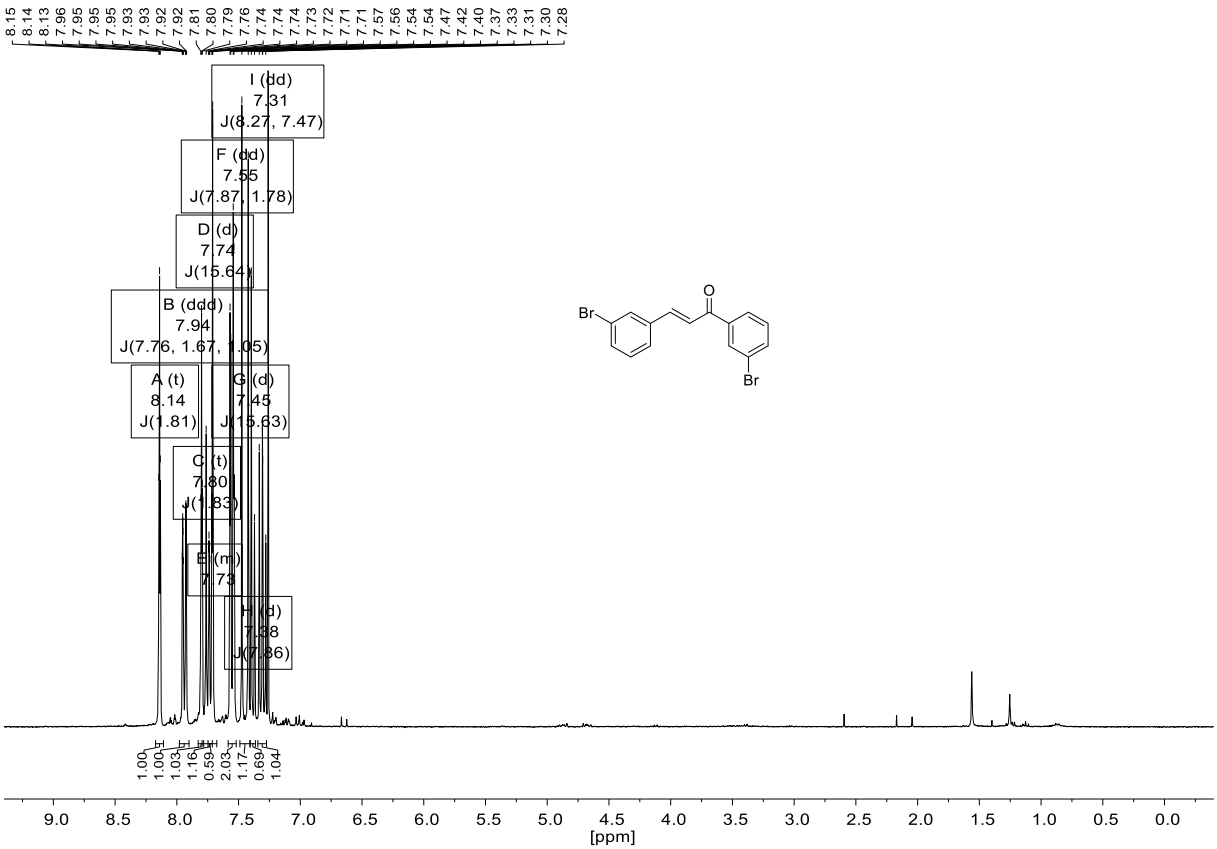

8.14 8.13 8.13 8.13 8.12 8.11 8.11 8.10 8.10 8.10 7.87 7.81 7.81 7.80 7.80 7.78 7.78 7.78 7.77 7.77 7.77 7.75 7.71 7.70 7.68 7.58 7.53
D (d)
7.55
J(15.75)
B (d)
7.54
J(15.82)
A (dp)
8.12
J(7.74, 0.85)
C (m)
7.75
O
F3C
CF3
2.00
0.96
6.31
0.93
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

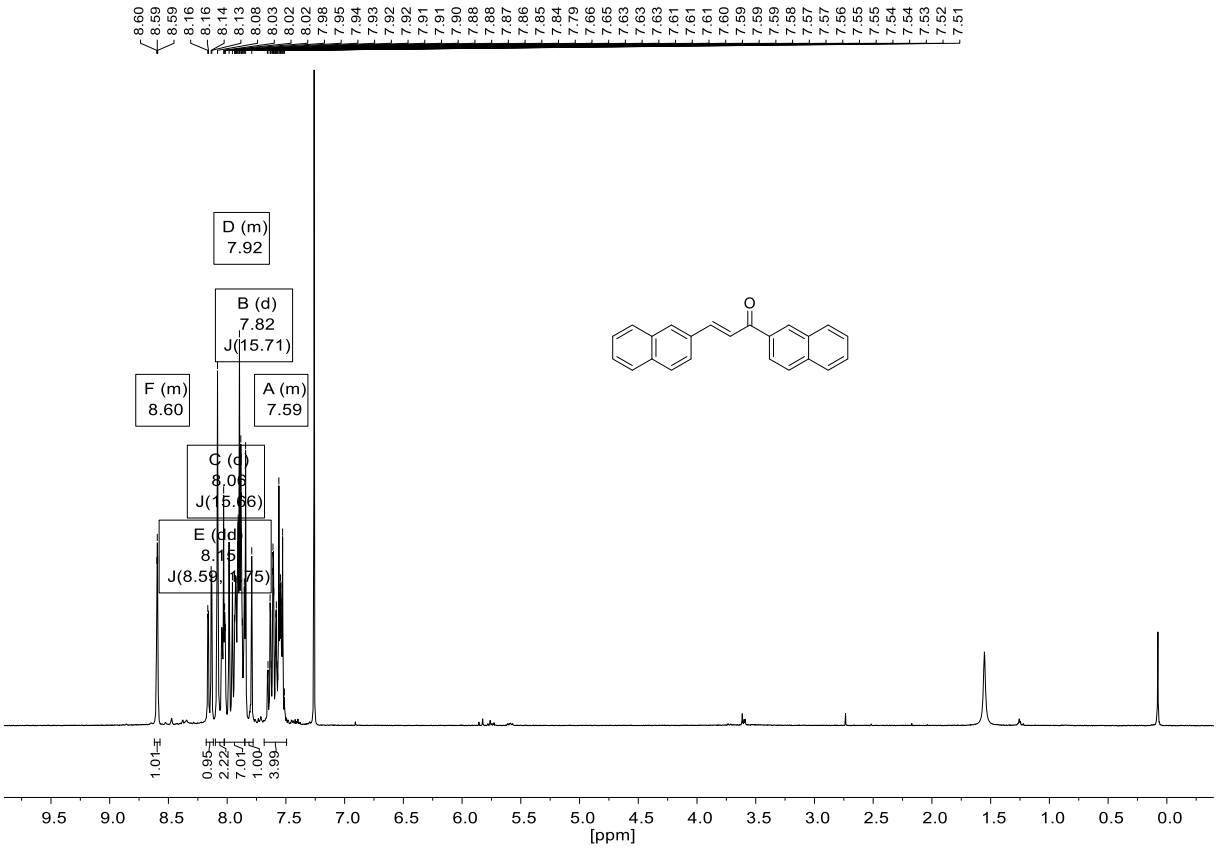

-62.92
-63.09
O
F3C
CF3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

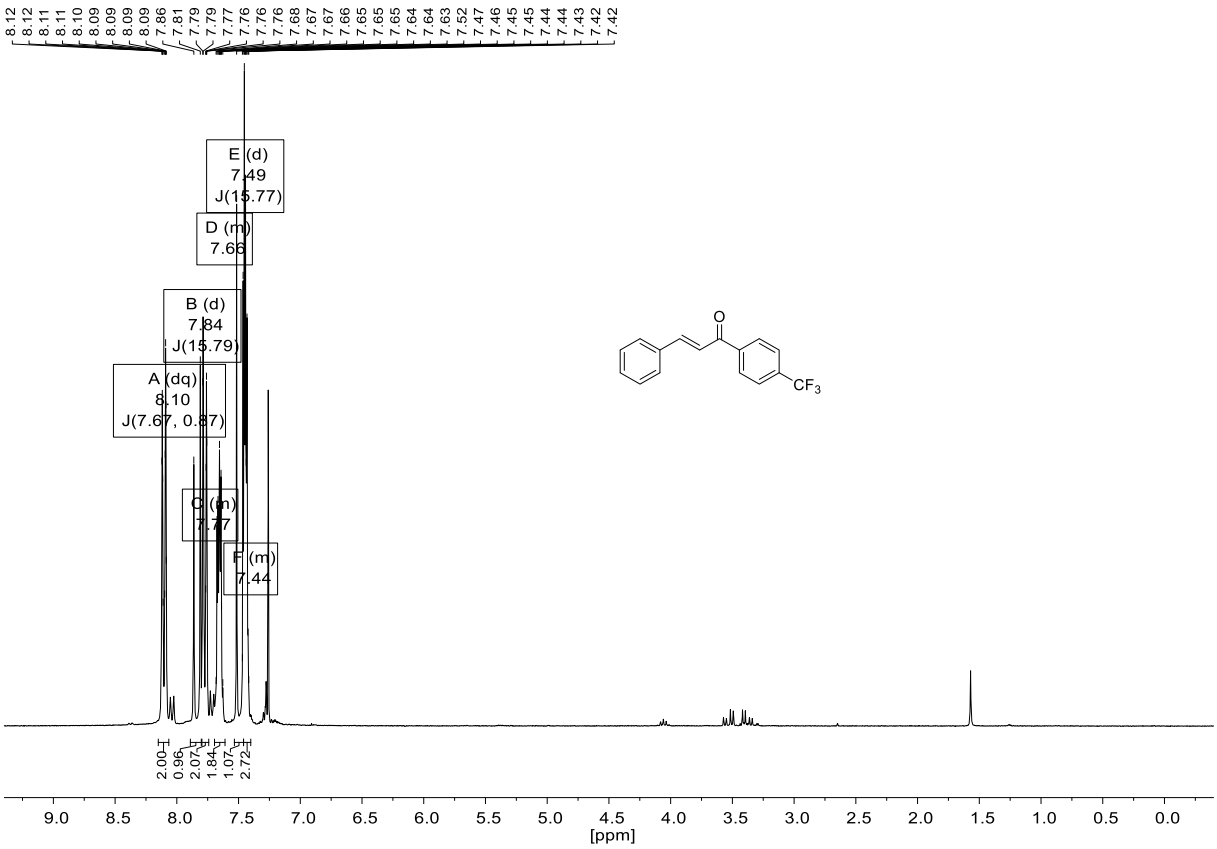

7.96 7.95 7.94 7.94 7.93 7.92 7.92 7.82 7.77 7.57 7.56 7.55 7.54 7.53 7.52 7.47 7.32 7.32 7.31 7.31 7.31 7.30 7.29 7.29 7.28 7.24 7.21
2.44 2.40
D (d) 7.50 J(15.66)
B (d) 7.79 J(15.71)
A (m) 7.93
E (m) 7.30
C (m) 7.55
F (d) 7.23 J(7.91)
O
H3C
CH3
H (s) 2.40
G (s) 2.44
2.00 0.97 2.15 1.01 1.97 2.05
2.87 2.83
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

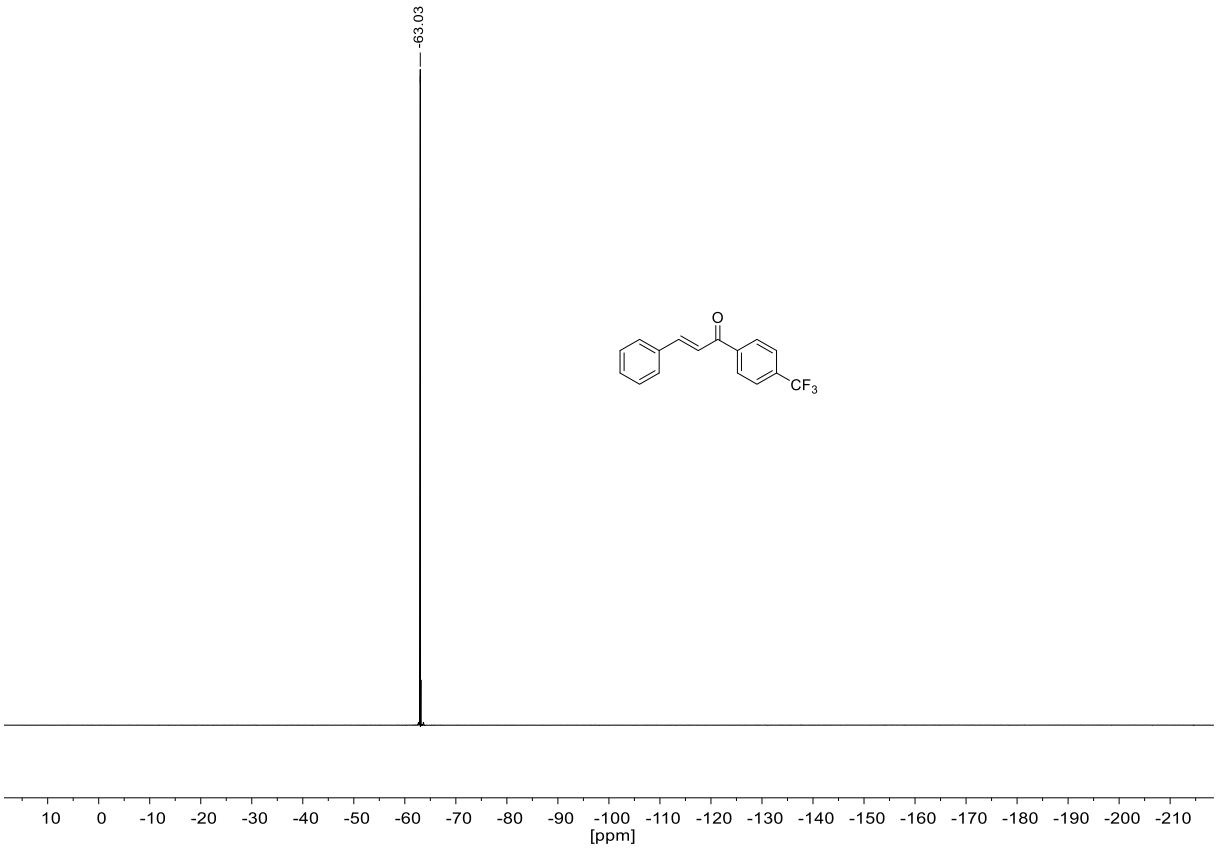

F (t)
7.32
J(7.83)
D (m)
7.46
G (m)
7.24
B (d)
7.79
J(15.65)
A (d)
7.51
J(15.74)
C (m)
7.83
E (m)
7.40
I (s)
2.41
H (s)
2.45
[ppm]

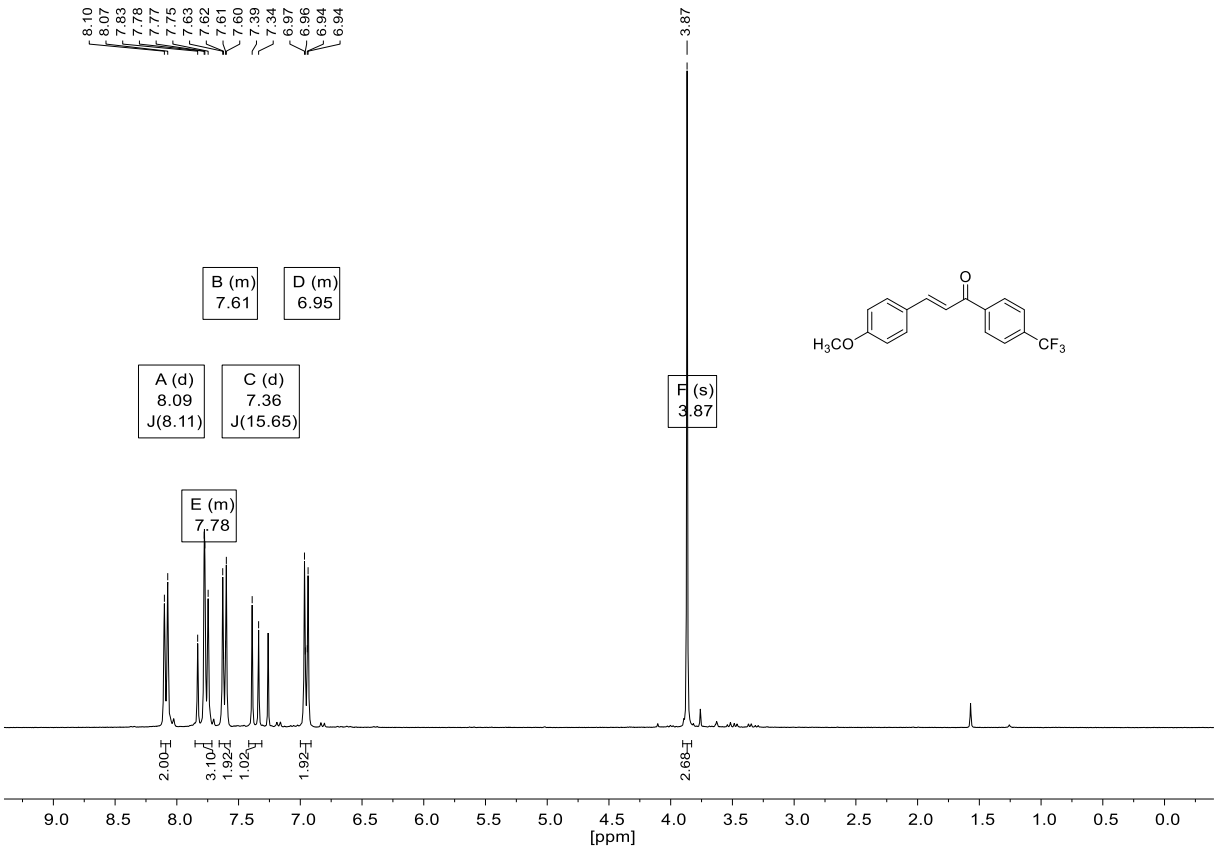

D (m)
7.39
B (dd)
7.64
J(7.51, 1.53)
A (d)
7.82
J(15.92)
E (m)
7.25
C (dd)
7.53
J(7.83, 1.55)
F (d)
7.08
J(15.94)
H (s)
2.39
G (s)
2.48
[ppm]

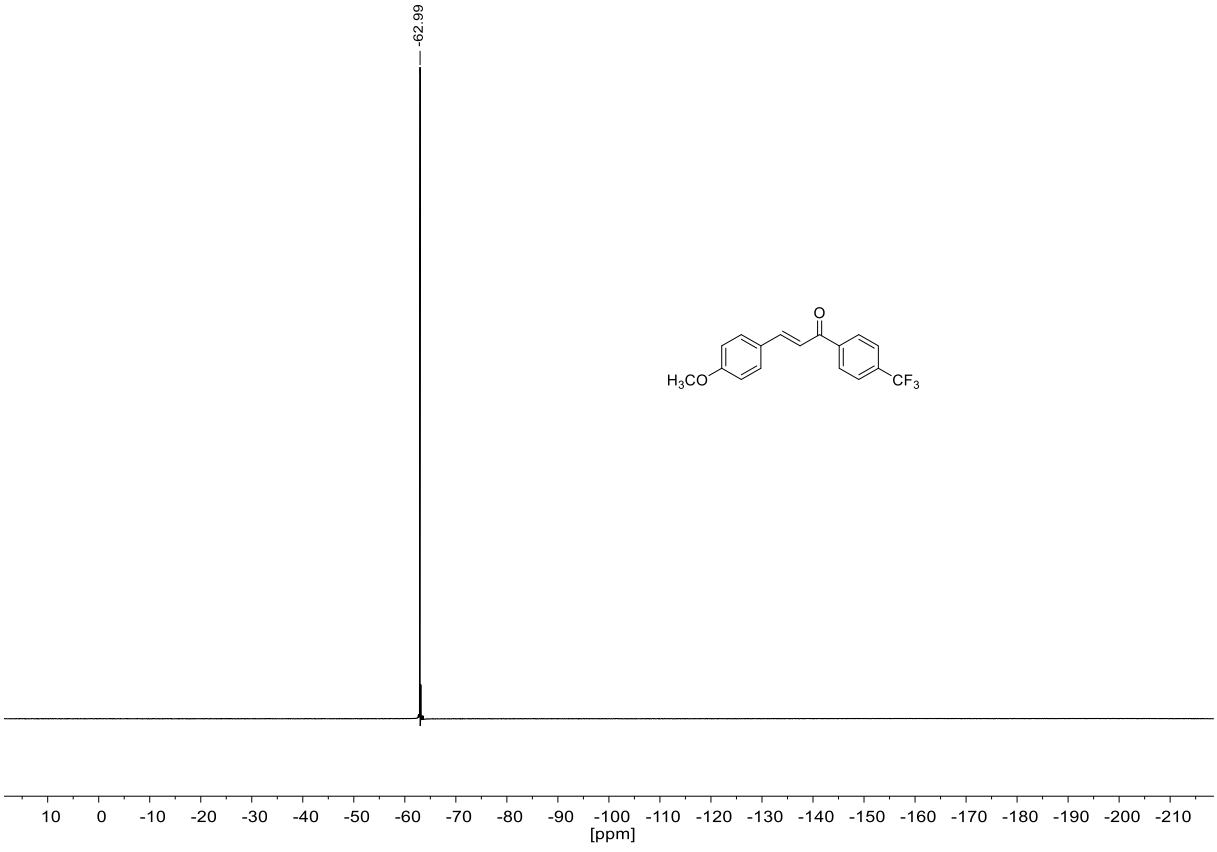

I (dd)
7.31
J(8.27, 7.47)
F (dd)
7.55
J(7.87, 1.78)
D (d)
7.74
J(15.64)
B (ddd)
7.94
J(7.76, 1.67, 1.05)
A (t)
8.14
J(1.81)
G (d)
7.45
J(15.63)
C (t)
7.80
J(1.83)
E (m)
7.73
H (d)
7.38
J(7.86)
Br
Br
O
[ppm]

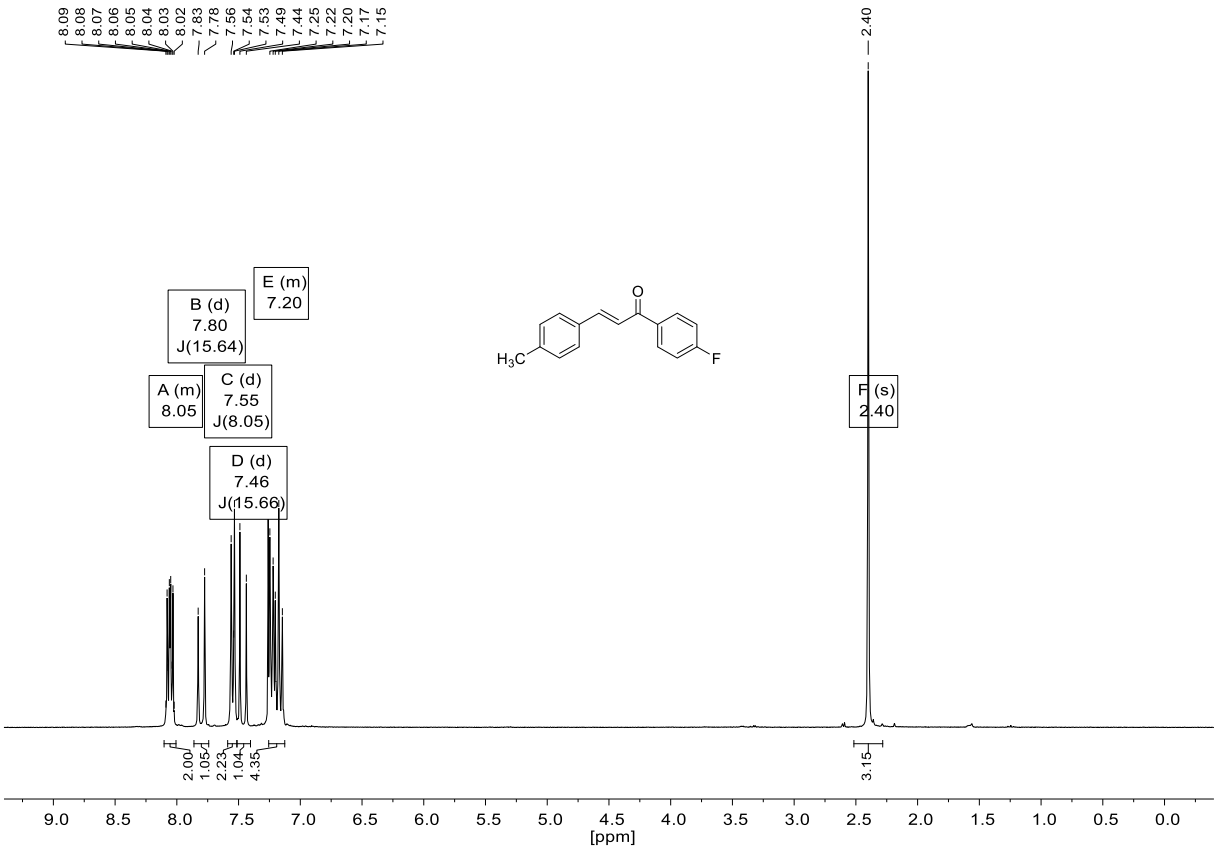

D (m)
7.92
B (d)
7.82
J(15.71)
F (m)
8.60
A (m)
7.59
C (d)
8.06
J(15.66)
E (dd)
8.15
J(8.59, 1.75)
O
[ppm]


E (d)
7.49
J(15.77)
D (m)
7.66
B (d)
7.84
J(15.79)
A (dq)
8.10
J(7.67, 0.87)
C (m)
7.77
F (m)
7.44
2.00
0.96
2.07
1.84
1.07
2.72
[ppm]

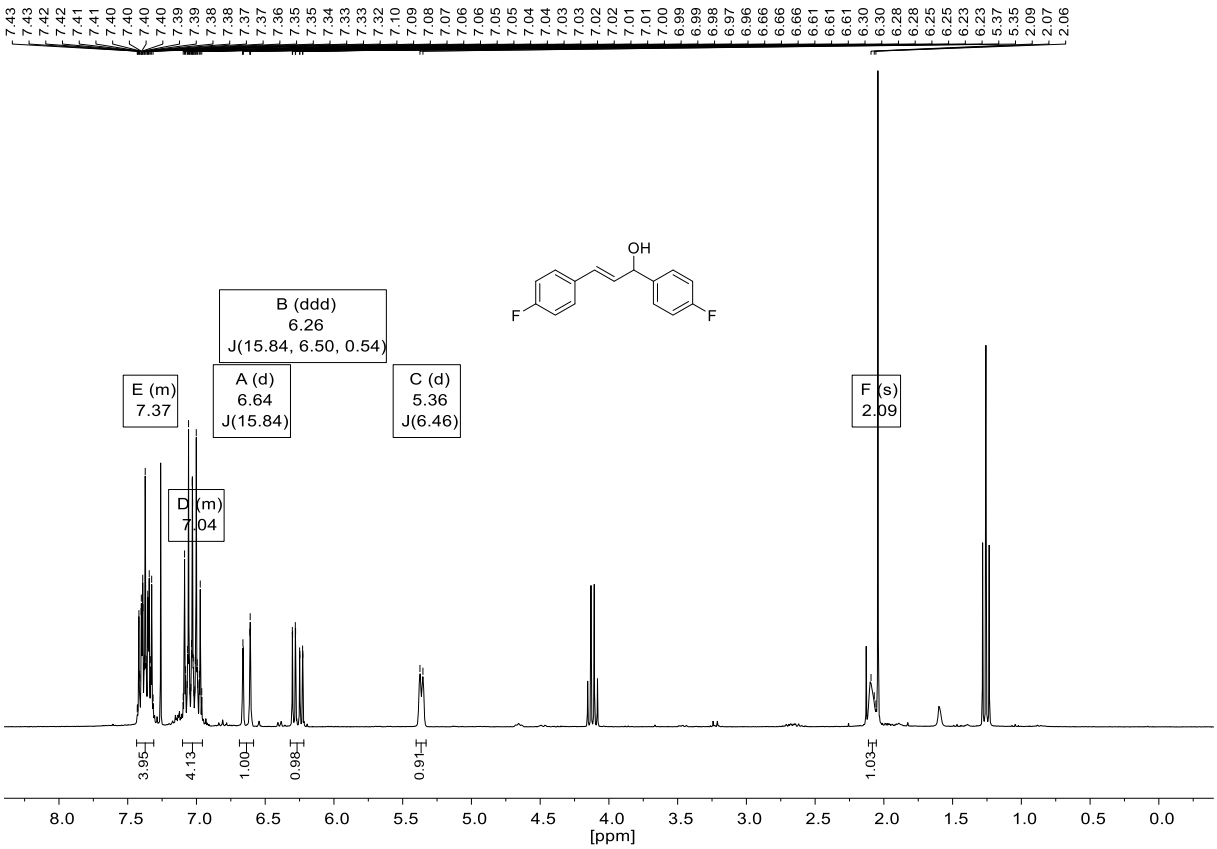

-63.03
[ppm]

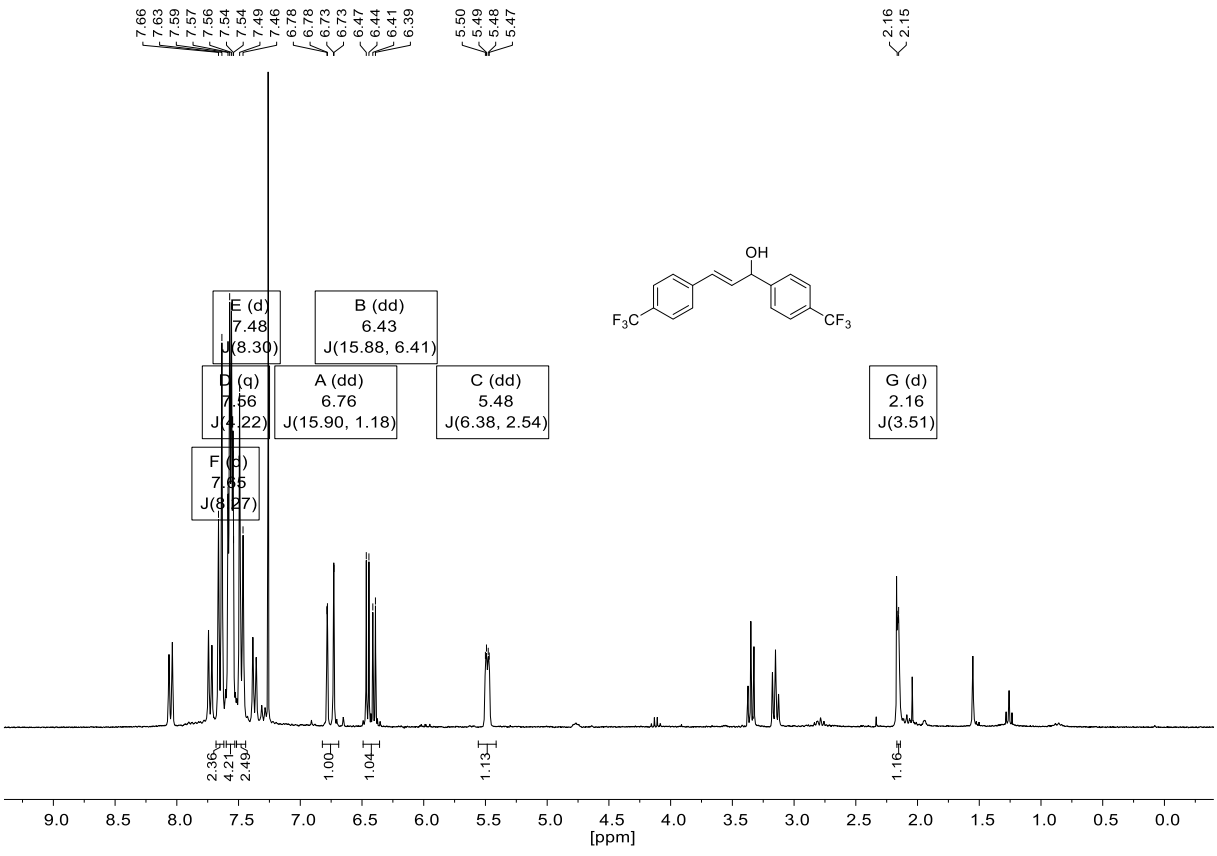

8.10
8.07
7.83
7.78
7.77
7.75
7.63
7.62
7.61
7.60
7.39
7.34
6.97
6.96
6.94
6.94
3.87
B (m)
7.61
D (m)
6.95
A (d)
8.09
J(8.11)
C (d)
7.36
J(15.65)
F (s)
3.87
E (m)
7.78
2.00
3.10
1.92
1.02
1.92
2.68
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]
O
H3CO
CF3

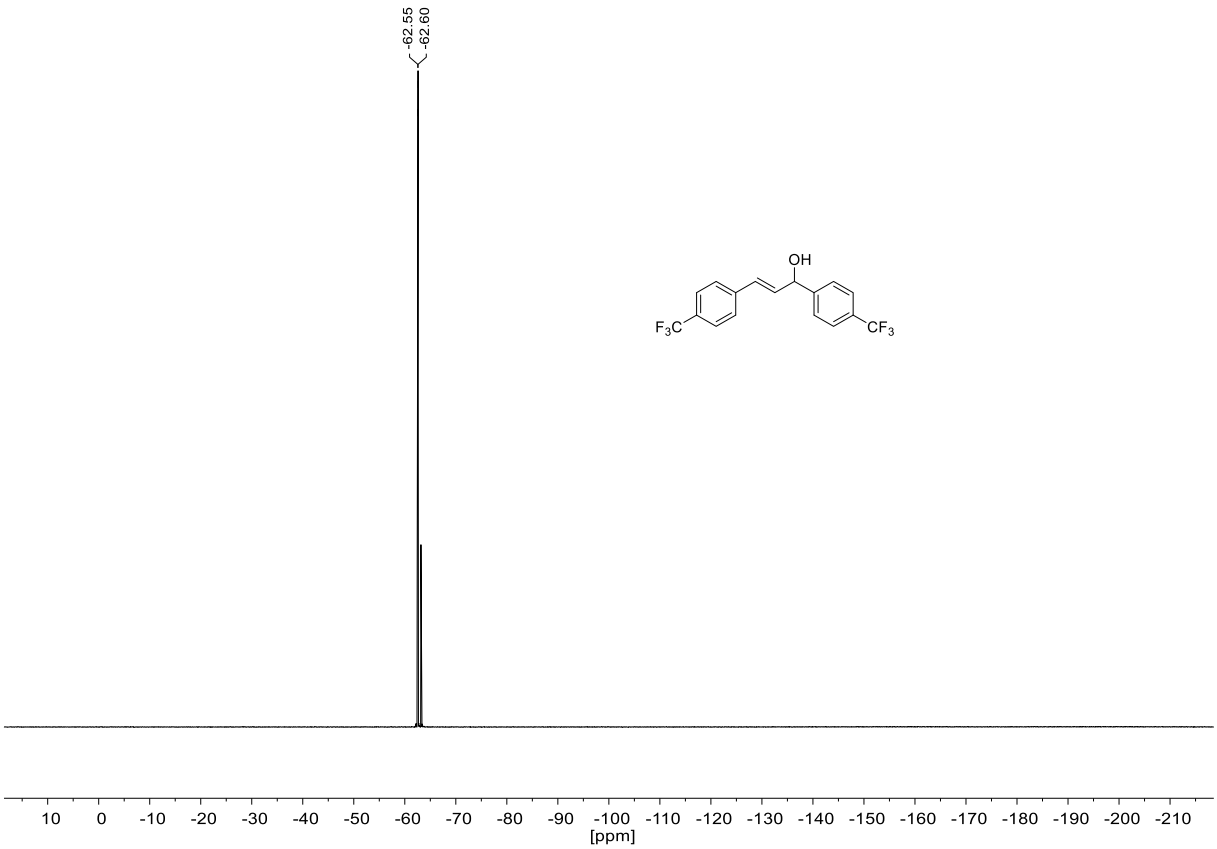

-62.99
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]
O
H3CO
CF3

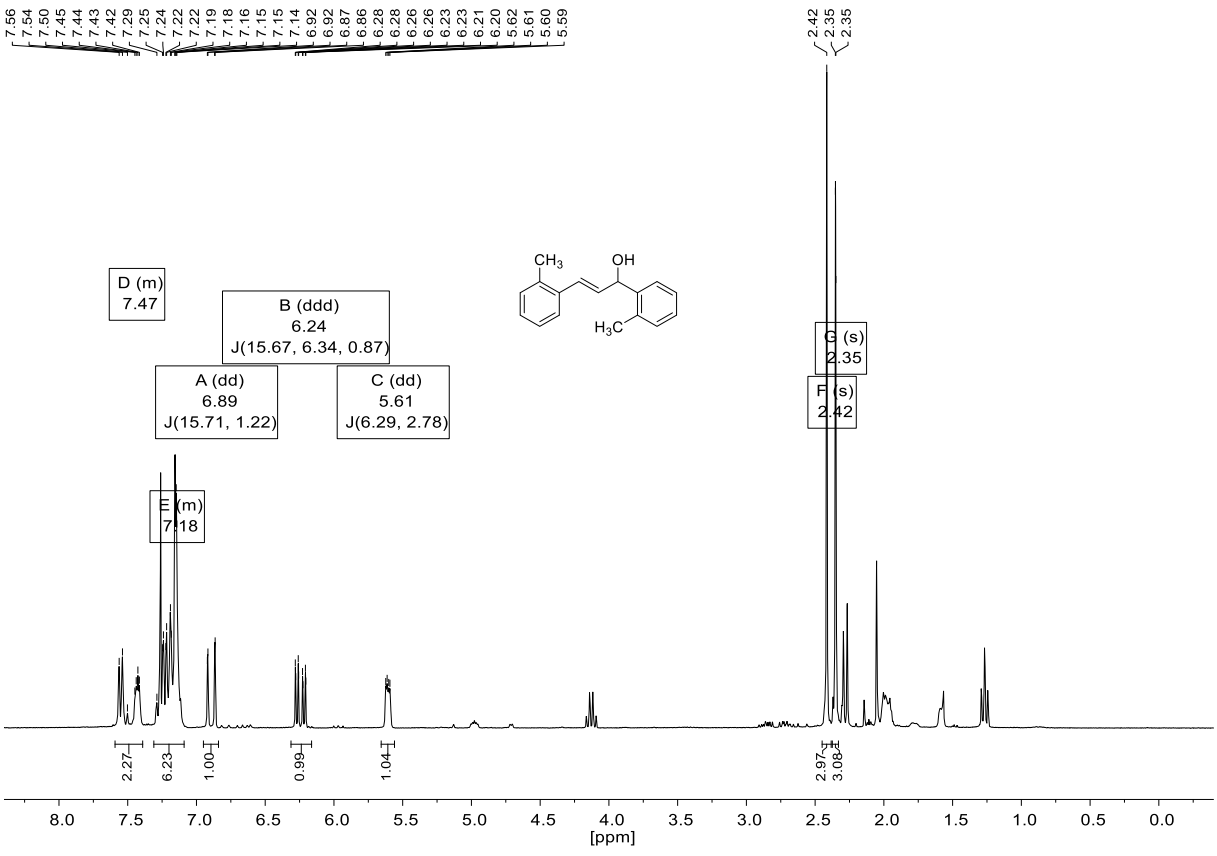

8.09
8.08
8.07
8.06
8.05
8.04
8.03
8.02
7.83
7.78
7.56
7.54
7.53
7.49
7.44
7.25
7.22
7.20
7.17
7.15
2.40
E (m)
7.20
B (d)
7.80
J(15.64)
A (m)
8.05
C (d)
7.55
J(8.05)
D (d)
7.46
J(15.66)
F (s)
2.40
O
H3C
F
2.00
1.05
2.23
1.04
4.35
3.15
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

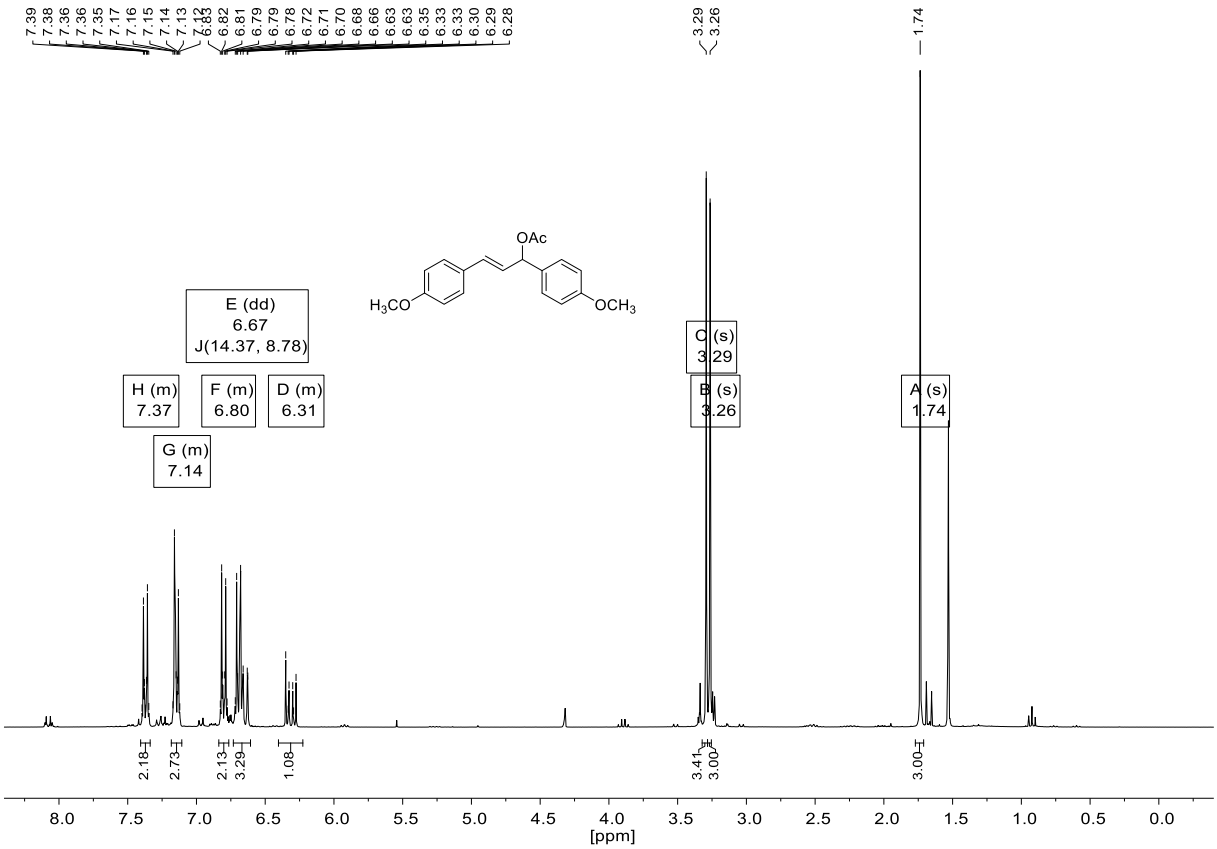

-105.85
O
H3C
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

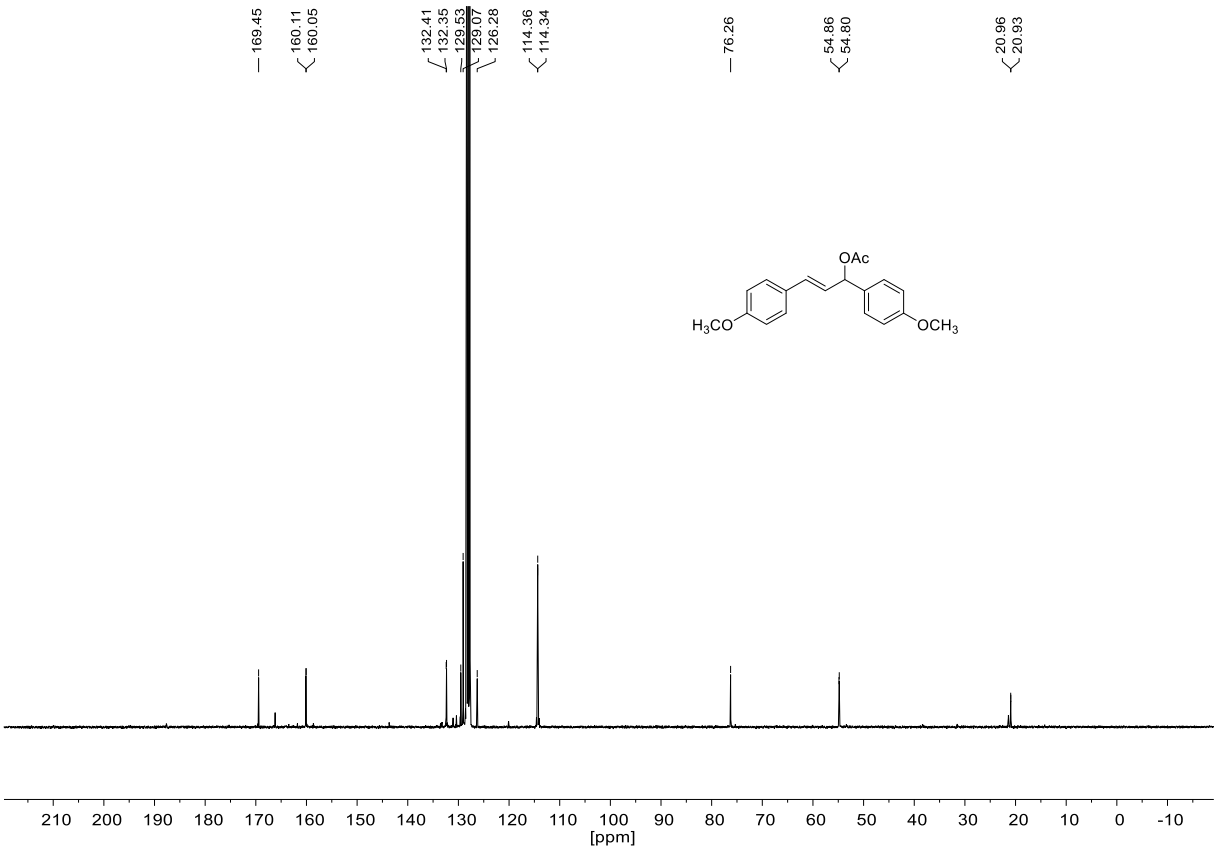

OH
F
F
B (ddd)
6.26
J(15.84, 6.50, 0.54)
A (d)
6.64
J(15.84)
C (d)
5.36
J(6.46)
E (m)
7.37
D (m)
7.04
F (s)
2.09
3.95
4.13
1.00
0.98
0.91
1.03
[ppm]

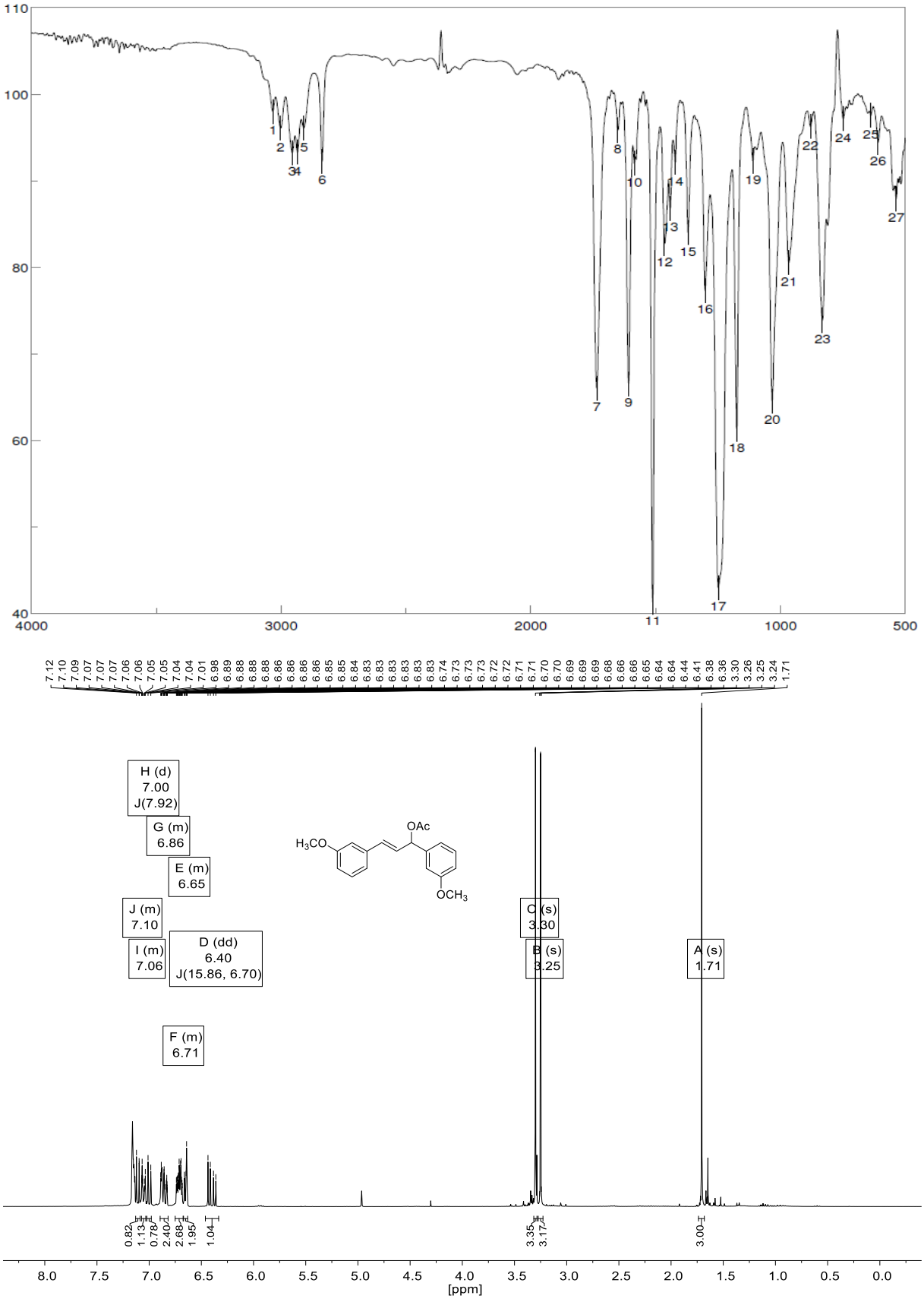

OH
F3C
CF3
E (d)
7.48
J(8.30)
B (dd)
6.43
J(15.88, 6.41)
D (q)
7.56
J(4.22)
A (dd)
6.76
J(15.90, 1.18)
C (dd)
5.48
J(6.38, 2.54)
G (d)
2.16
J(3.51)
F (d)
7.65
J(8.27)
2.36
4.21
2.49
1.00
1.04
1.13
1.16
[ppm]

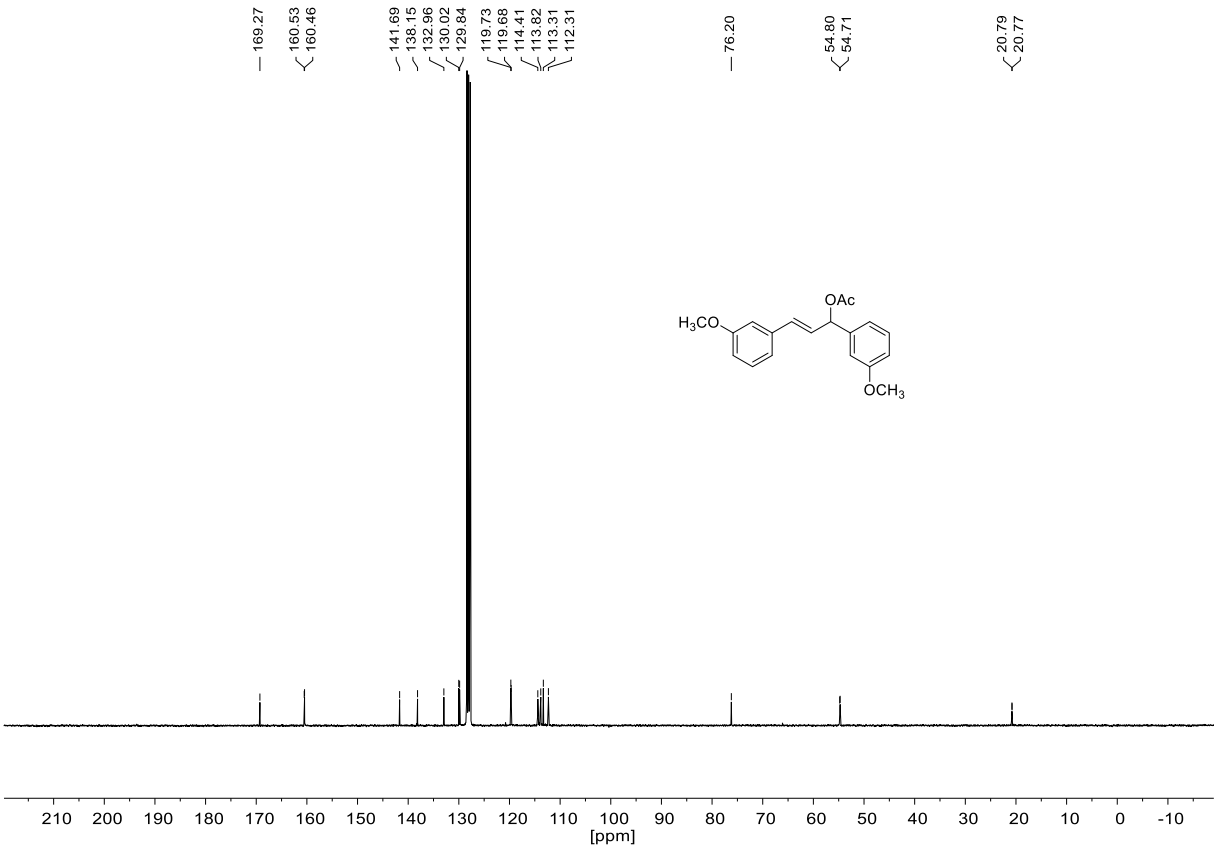

-62.55
-62.60
OH
F3C
CF3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

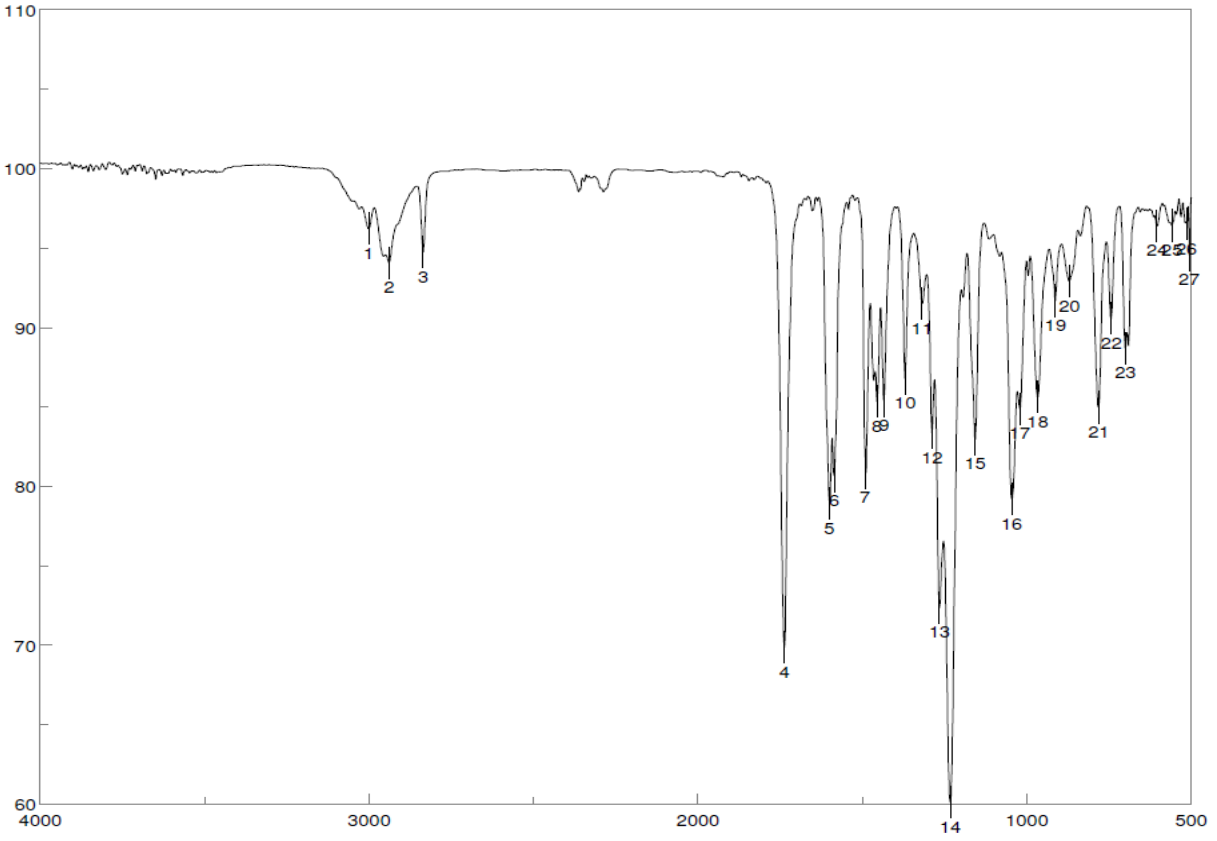

7.56 7.54 7.50 7.45 7.44 7.43 7.42 7.29 7.25 7.24 7.22 7.22 7.19 7.18 7.16 7.15 7.15 7.14 6.92 6.92 6.87 6.86 6.28 6.28 6.26 6.26 6.23 6.23 6.21 6.20 5.62 5.61 5.60 5.59
2.42 2.35 2.35
CH3 OH H3C
D (m) 7.47
B (ddd) 6.24 J(15.67, 6.34, 0.87)
A (dd) 6.89 J(15.71, 1.22)
C (dd) 5.61 J(6.29, 2.78)
E (m) 7.18
G (s) 2.35
F (s) 2.42
2.27 6.23 1.00 0.99 1.04 2.97 3.08
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

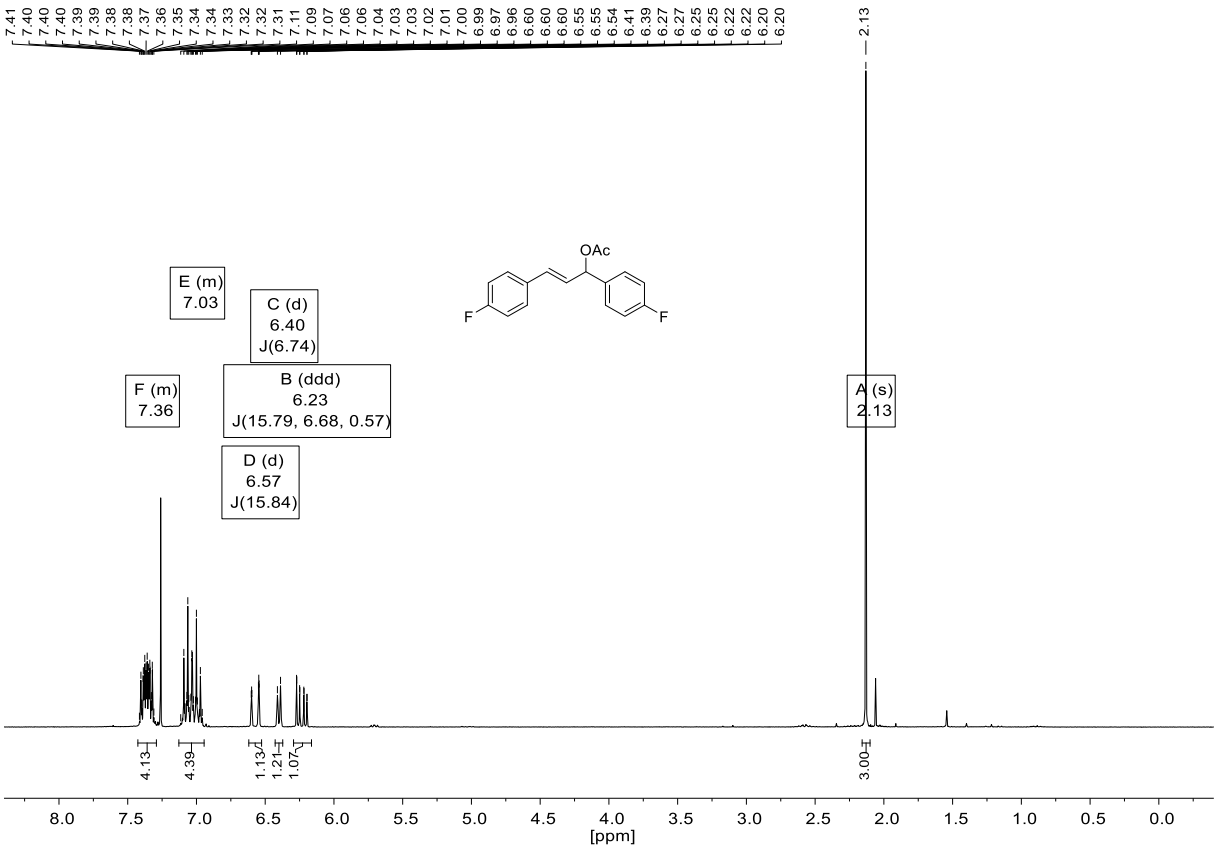

7.39
7.38
7.36
7.36
7.35
7.17
7.16
7.15
7.14
7.13
6.82
6.81
6.79
6.79
6.78
6.72
6.71
6.70
6.68
6.66
6.63
6.63
6.35
6.33
6.33
6.30
6.29
6.28
3.29
3.26
1.74
OAc
H3CO
OCH3
E (dd)
6.67
J(14.37, 8.78)
H (m)
7.37
F (m)
6.80
D (m)
6.31
G (m)
7.14
C (s)
3.29
B (s)
3.26
A (s)
1.74
2.18
2.73
2.13
3.29
1.08
3.41
3.00
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

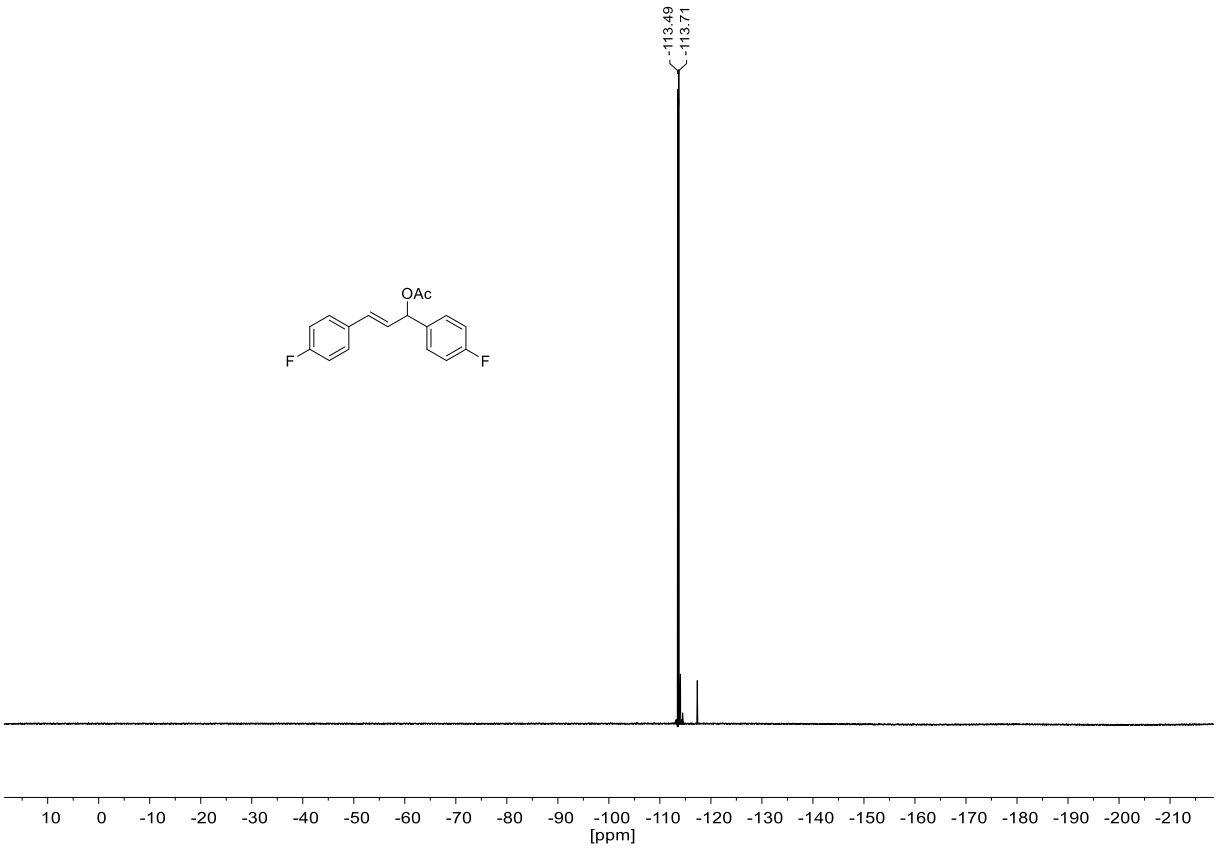

169.45
160.11
160.05
132.41
132.35
129.53
129.07
126.28
114.36
114.34
76.26
54.86
54.80
20.96
20.93
OAc
H3CO
OCH3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
[ppm]

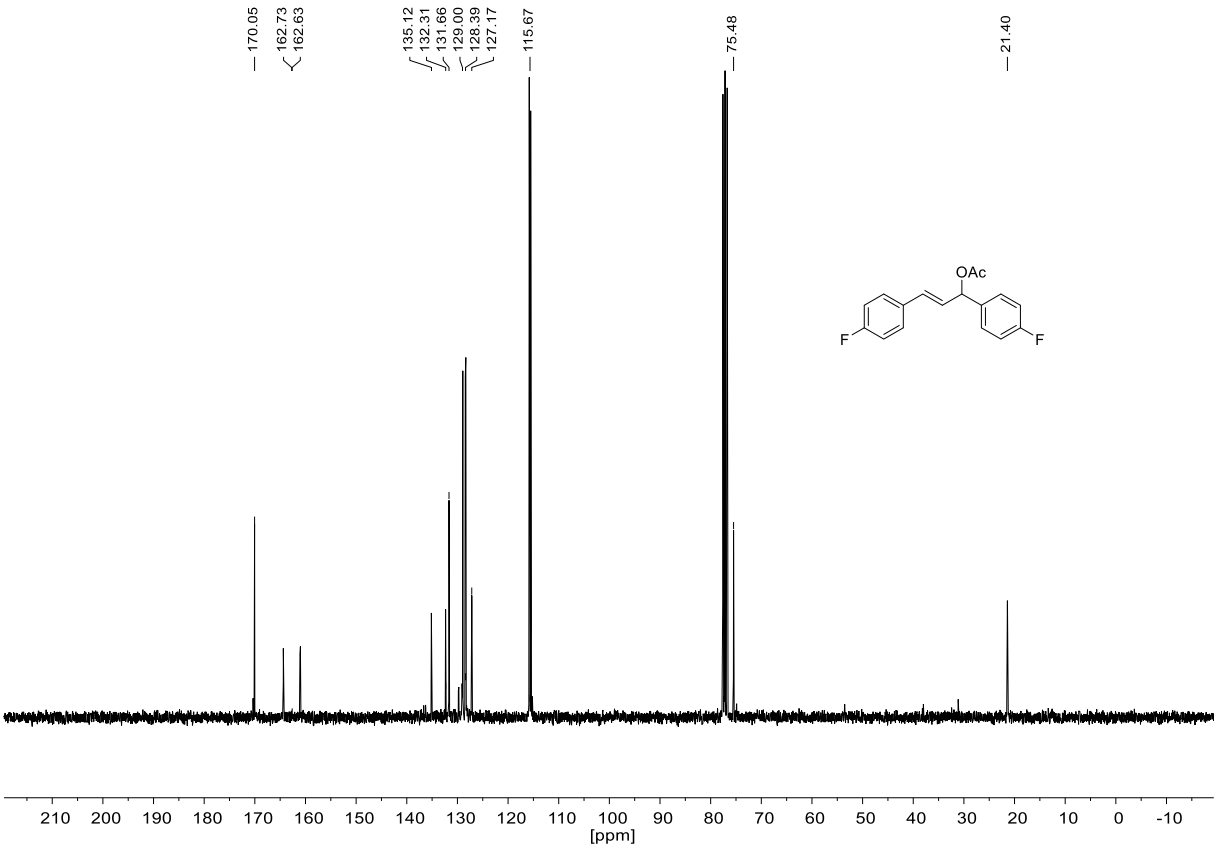

H (d)
7.00
J(7.92)
G (m)
6.86
E (m)
6.65
J (m)
7.10
I (m)
7.06
D (dd)
6.40
J(15.86, 6.70)
F (m)
6.71
C (s)
3.30
B (s)
3.25
A (s)
1.71
OAc
H3CO
OCH3
[ppm]

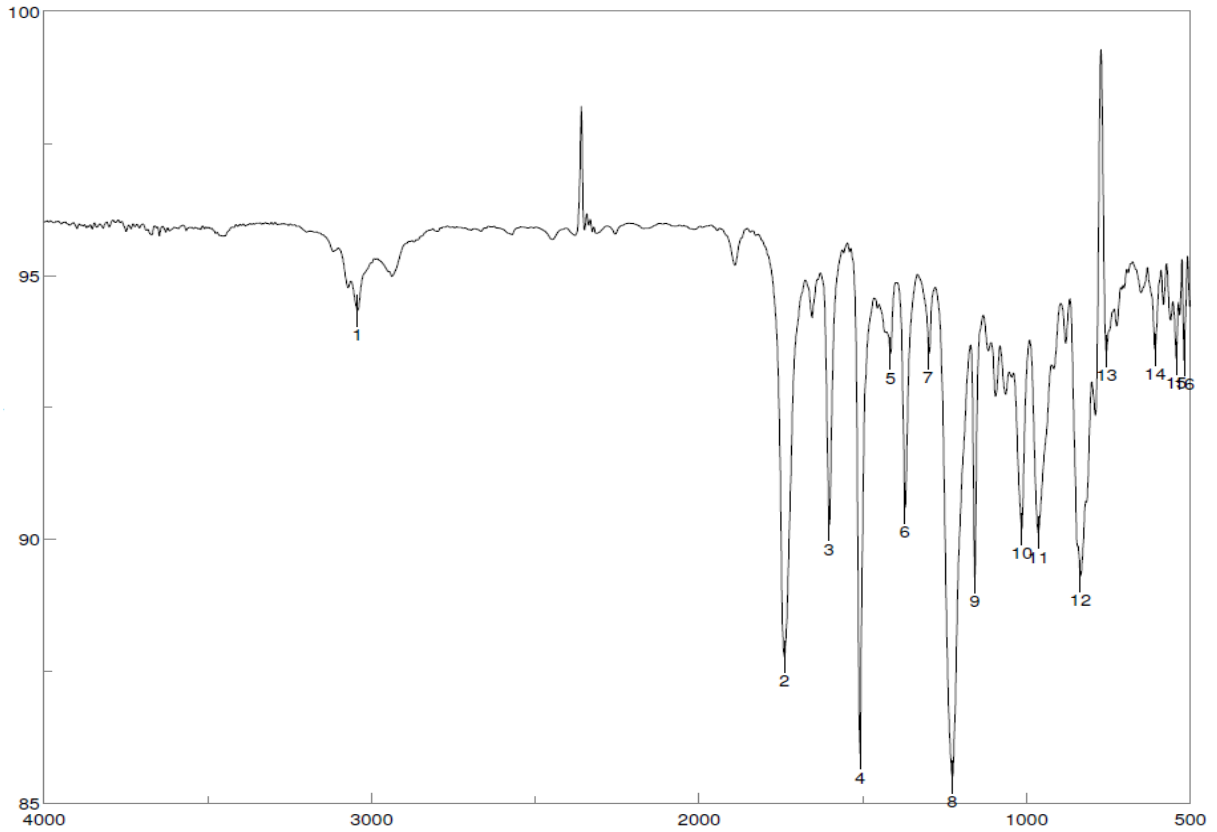

169.27
160.53
160.46
141.69
138.15
132.96
130.02
129.84
119.73
119.68
114.41
113.82
113.31
112.31
76.20
54.80
54.71
20.79
20.77
OAc
H3CO
OCH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

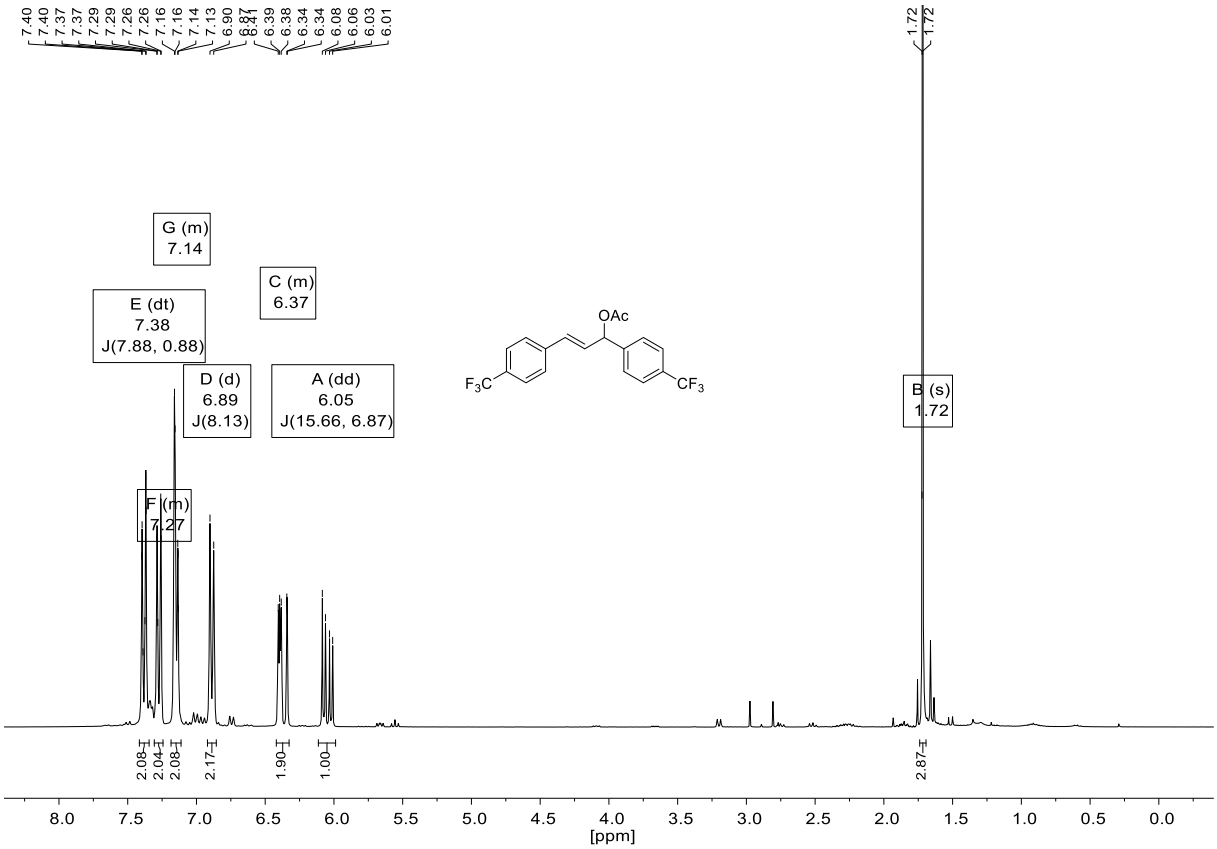

110
100
90
80
70
60
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27

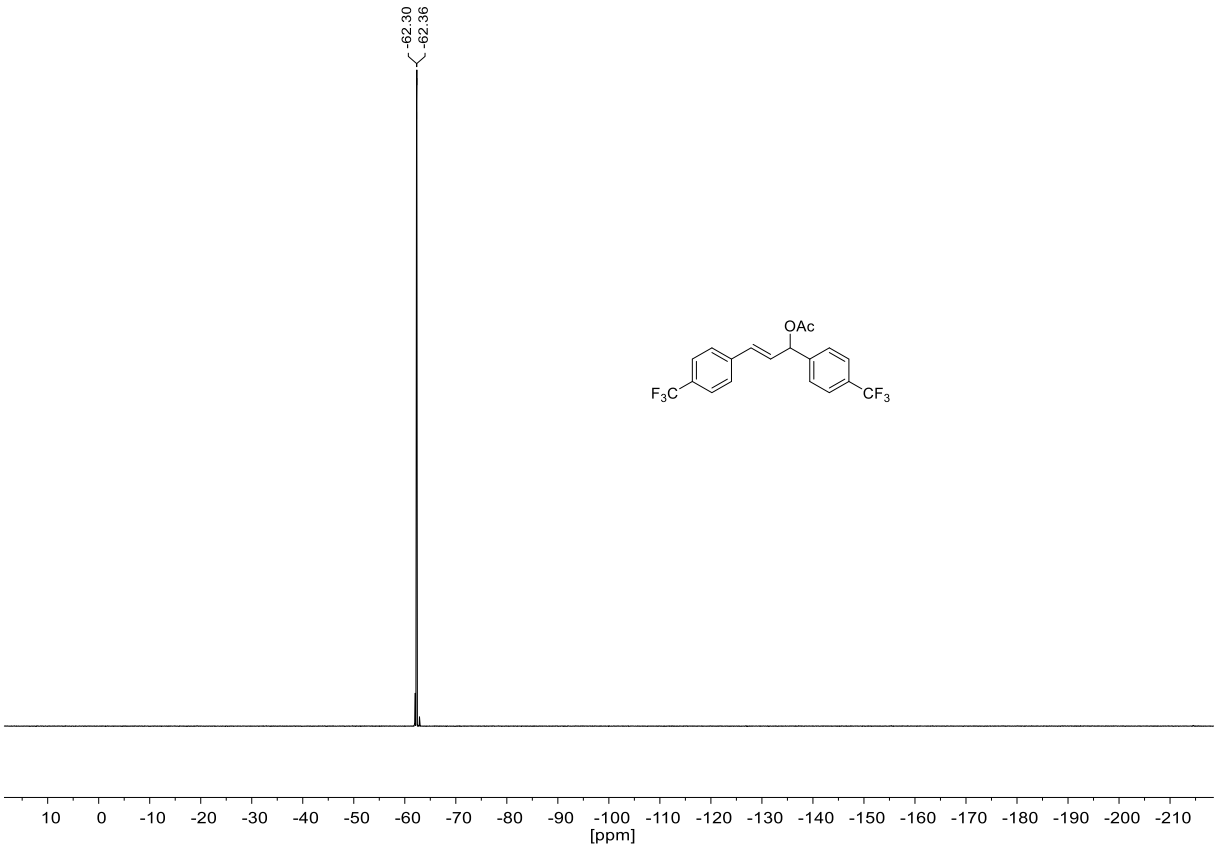

7.41 7.40 7.40 7.40 7.39 7.39 7.38 7.38 7.37 7.36 7.35 7.34 7.34 7.33 7.32 7.32 7.31 7.11 7.09 7.07 7.06 7.06 7.04 7.03 7.03 7.02 7.01 7.00 6.99 6.97 6.96 6.60 6.60 6.60 6.55 6.55 6.54 6.41 6.39 6.27 6.27 6.25 6.22 6.22 6.20 6.20
2.13
OAc
F
F
E (m)
7.03
C (d)
6.40
J(6.74)
F (m)
7.36
B (ddd)
6.23
J(15.79, 6.68, 0.57)
D (d)
6.57
J(15.84)
A (s)
2.13
4.13
4.39
1.13
1.21
1.07
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

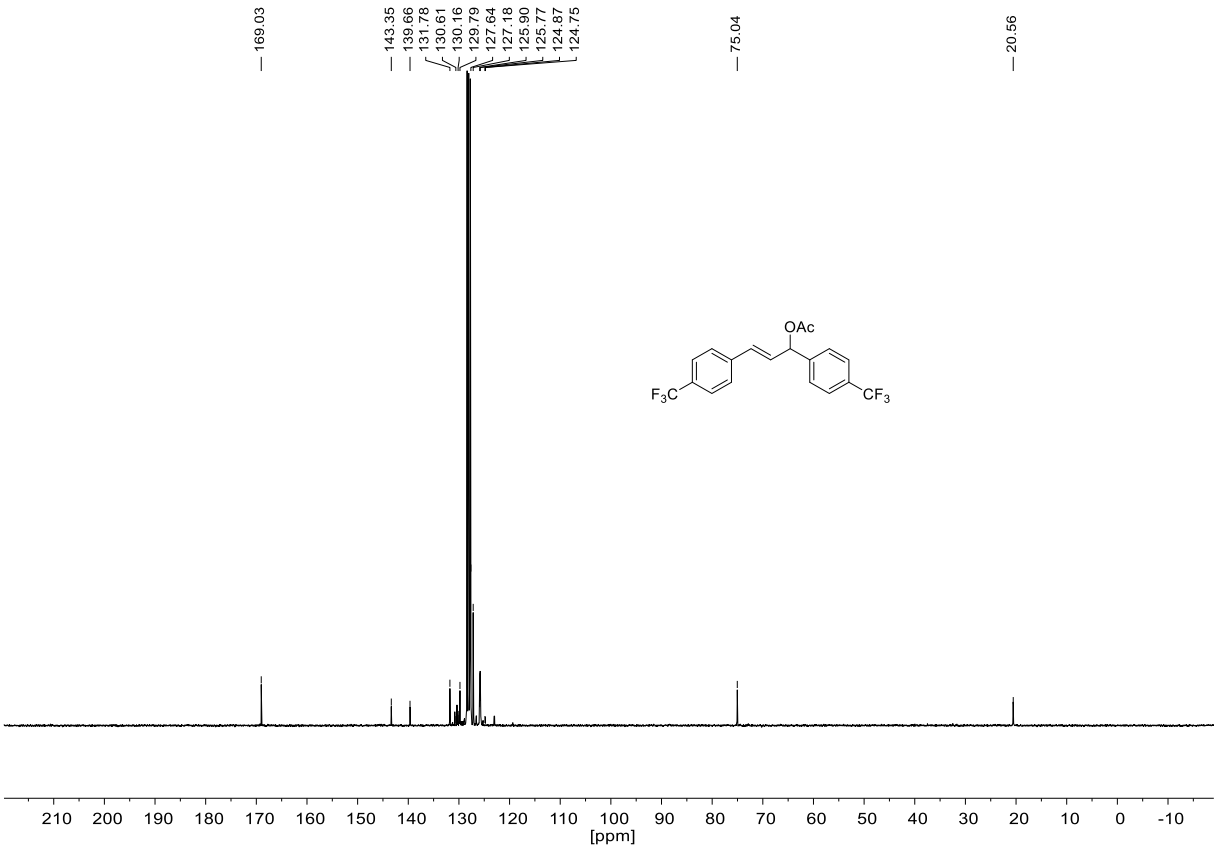

-113.49
-113.71
OAc
F
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

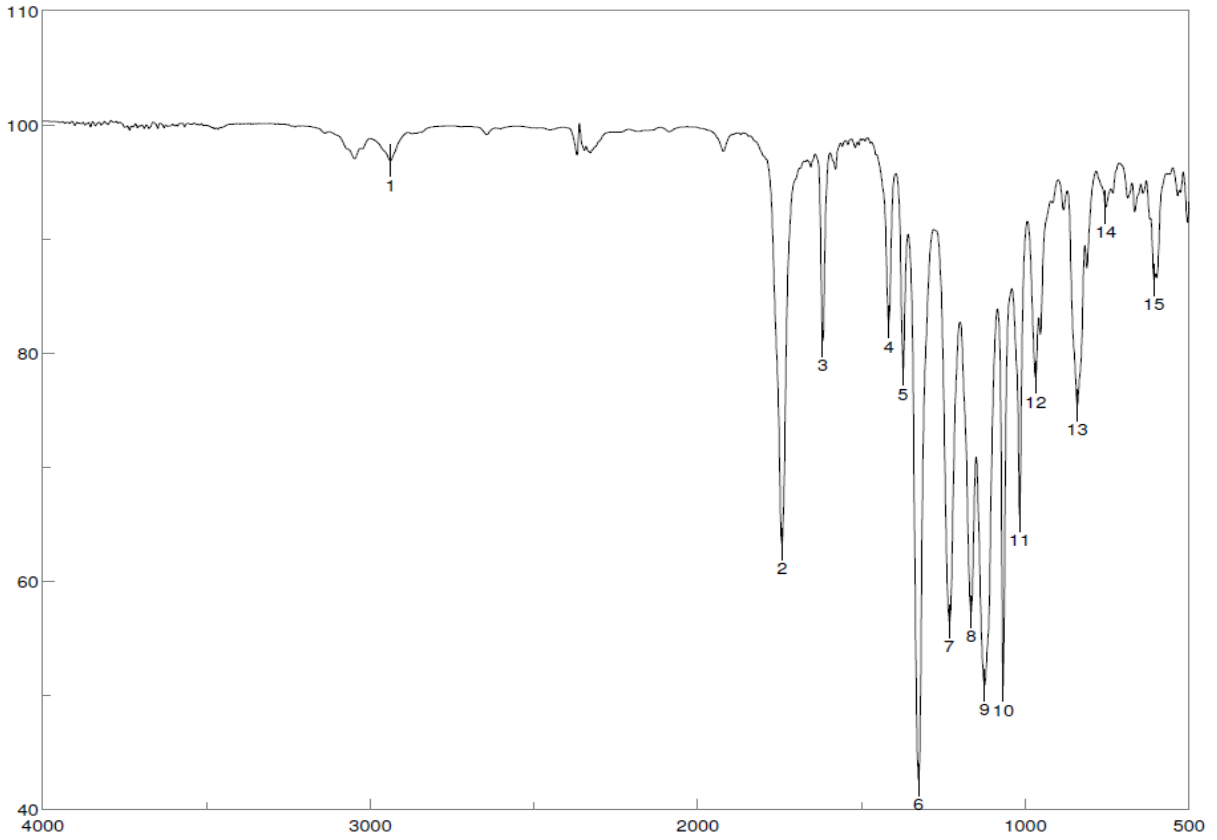

170.05
162.73
162.63
135.12
132.31
131.66
129.00
128.39
127.17
115.67
75.48
21.40
OAc
F
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

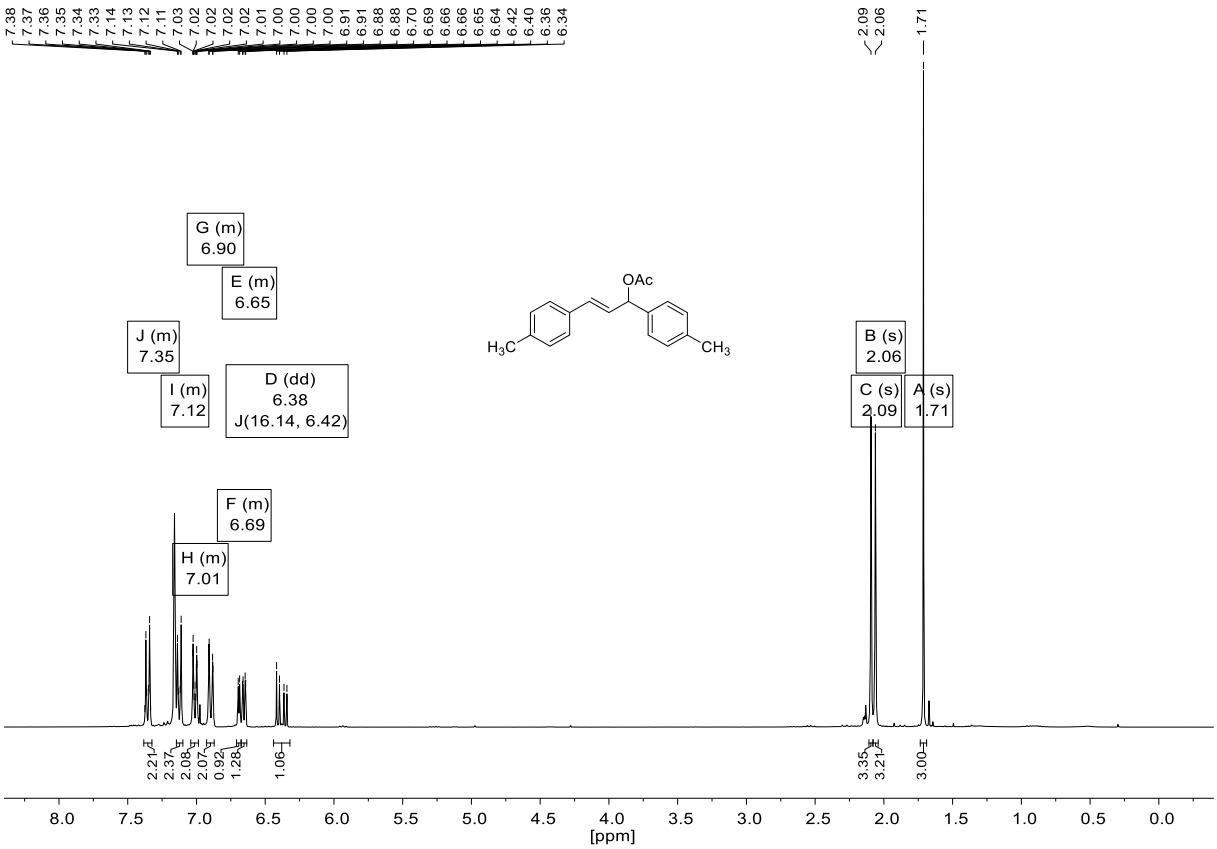

100
95
90
85
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

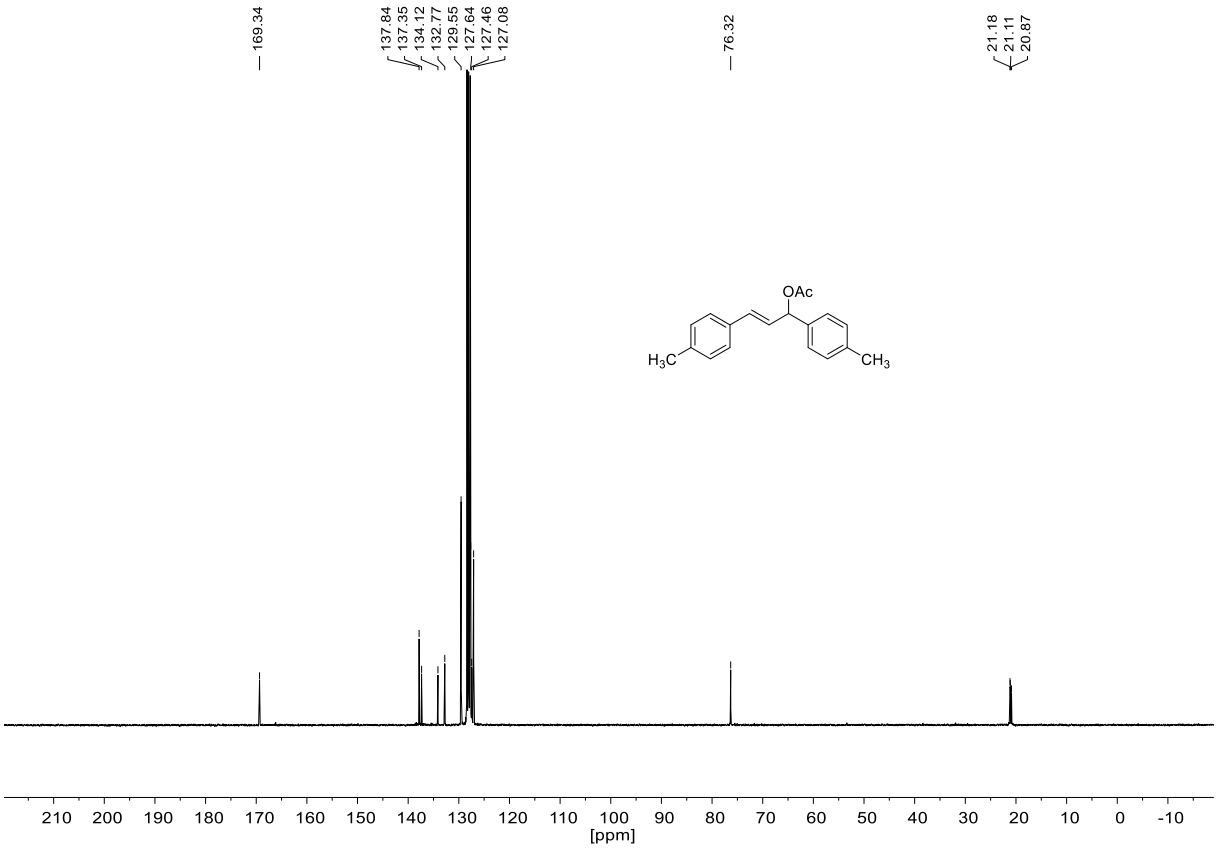

7.40
7.40
7.37
7.37
7.29
7.29
7.26
7.26
7.16
7.14
7.13
6.90
6.87
6.41
6.39
6.38
6.34
6.08
6.06
6.03
6.01
1.72
1.72
G (m)
7.14
C (m)
6.37
E (dt)
7.38
J(7.88, 0.88)
D (d)
6.89
J(8.13)
A (dd)
6.05
J(15.66, 6.87)
B (s)
1.72
F (m)
7.27
OAc
F3C
CF3
2.08
2.04
2.08
2.17
1.90
1.00
2.87
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

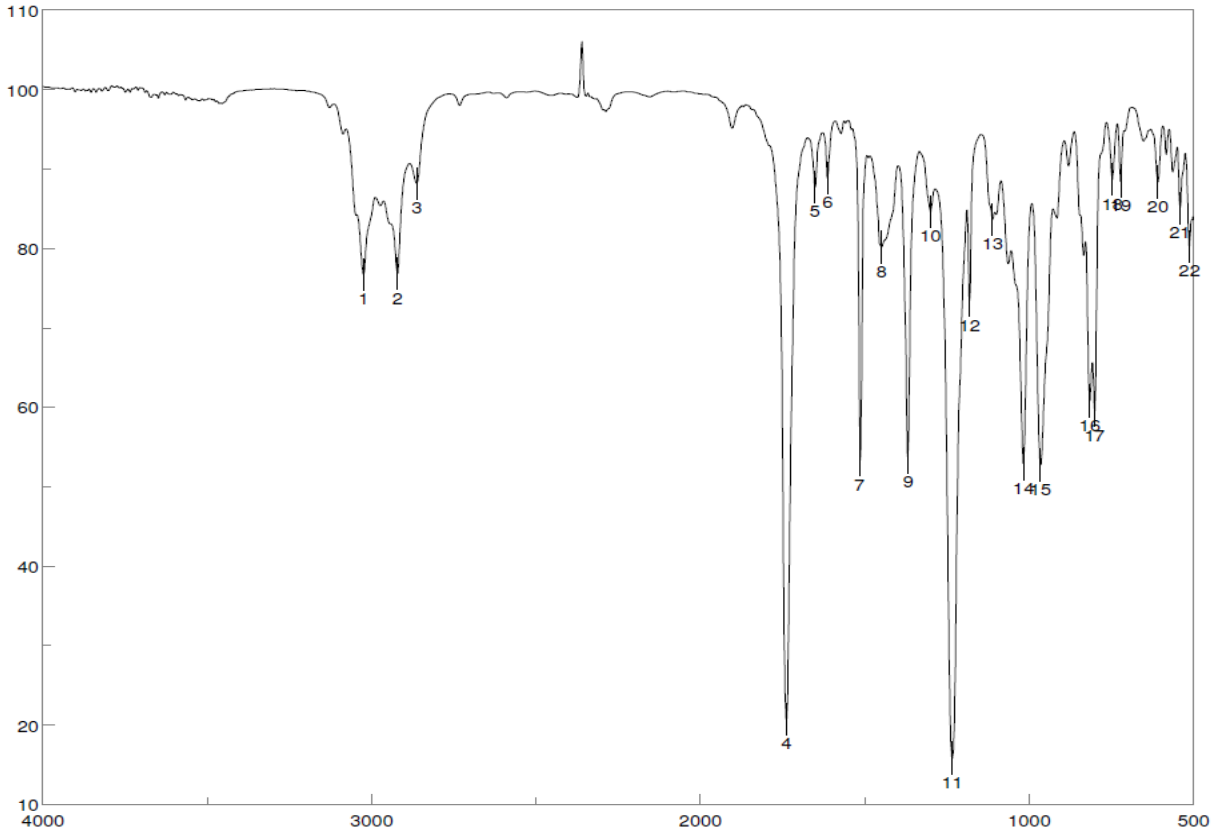

-62.30
-62.36
OAc
F3C
CF3
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
[ppm]

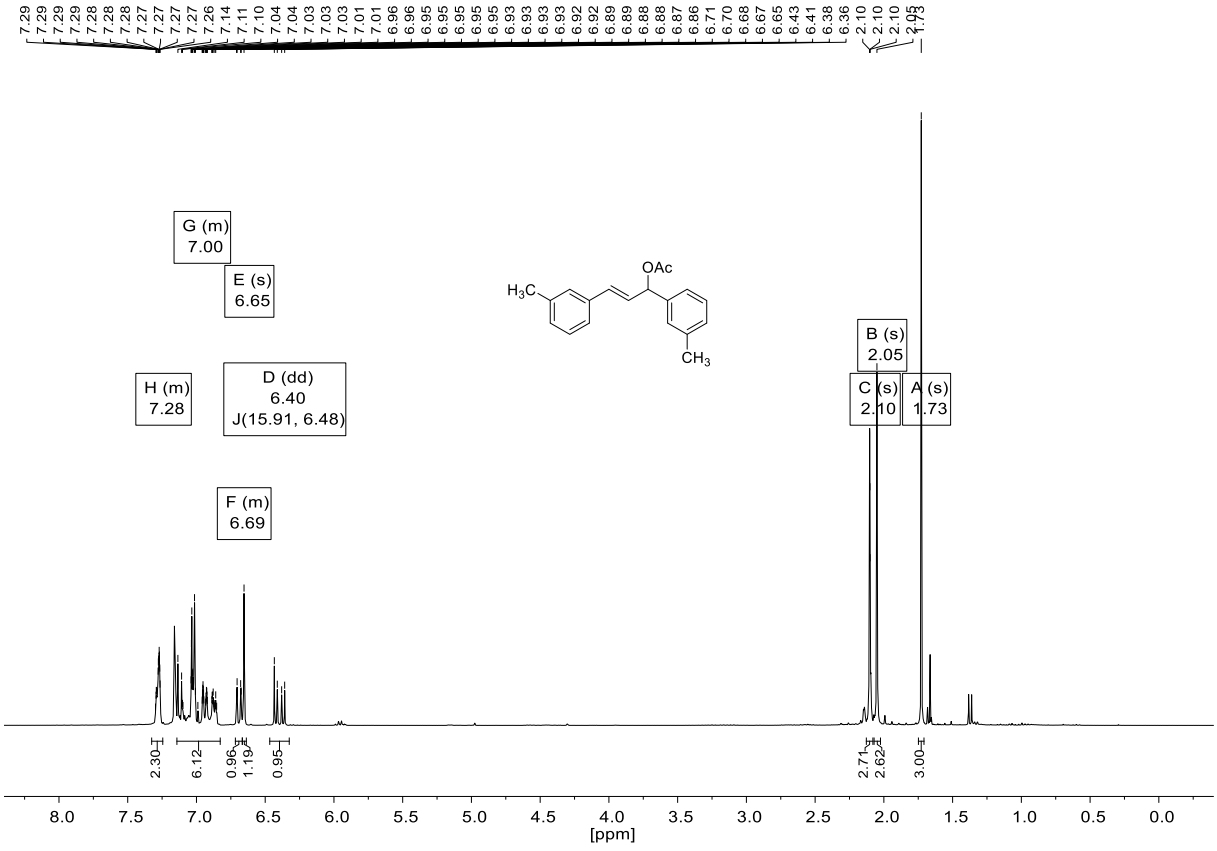

169.03
143.35
139.66
131.78
130.61
130.16
129.79
127.64
127.18
125.90
125.77
124.87
124.75
75.04
20.56
OAc
F3C
CF3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

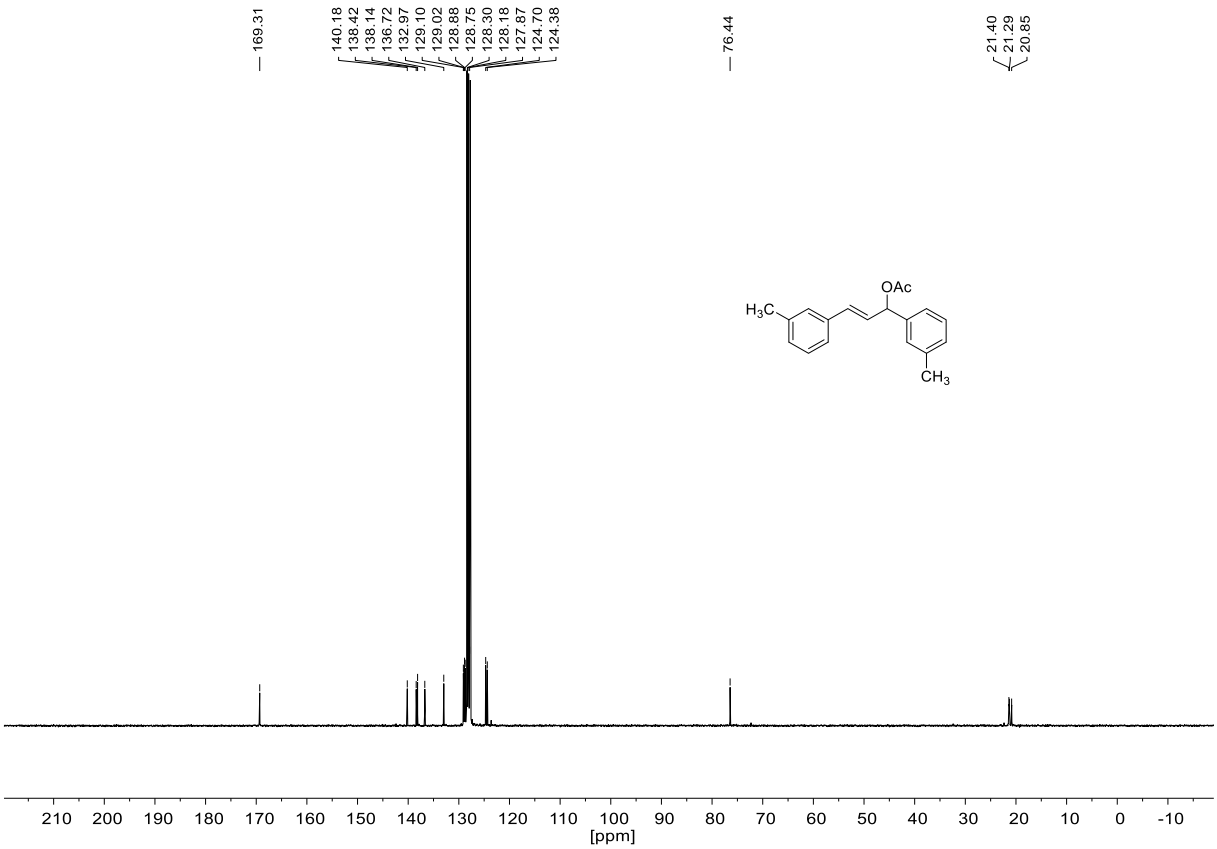

110
100
80
60
40
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15

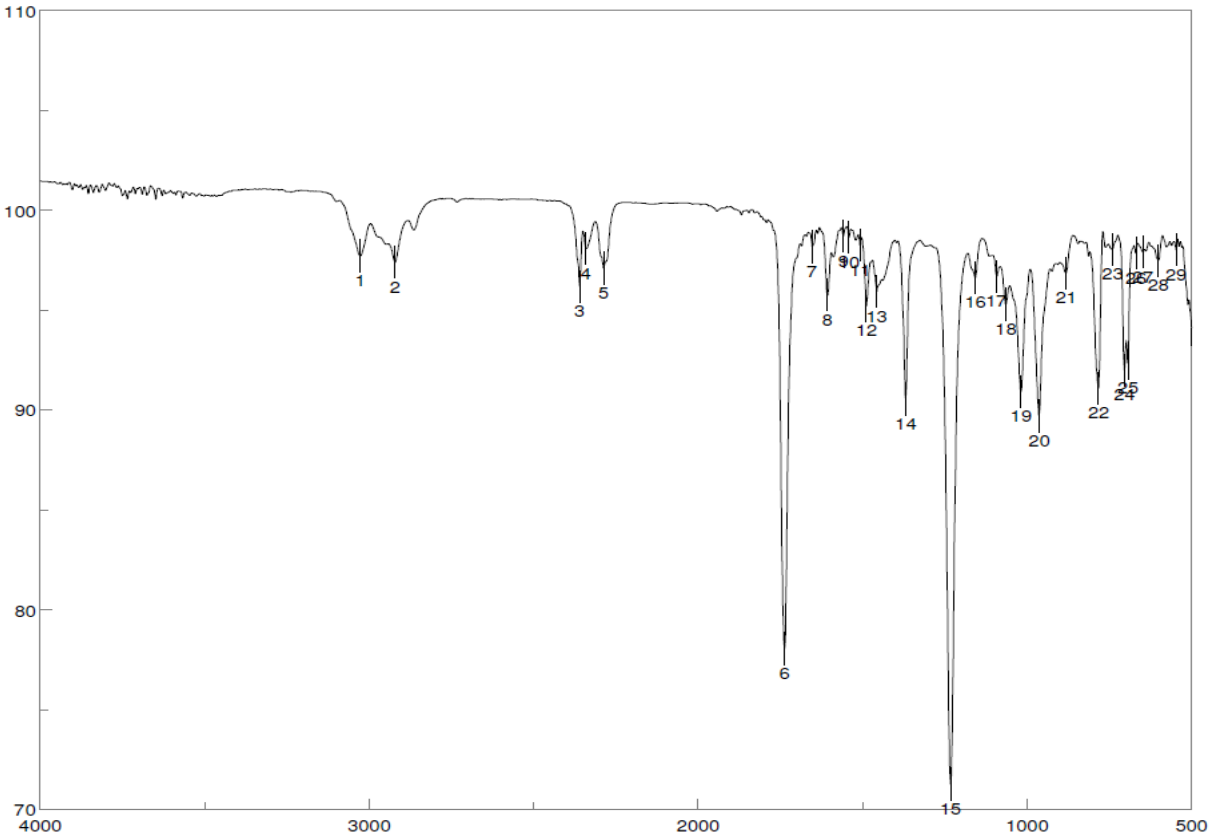

7.38
7.37
7.36
7.35
7.34
7.33
7.14
7.13
7.12
7.11
7.03
7.02
7.02
7.02
7.02
7.01
7.00
7.00
7.00
7.00
6.91
6.91
6.88
6.88
6.70
6.69
6.66
6.66
6.65
6.64
6.42
6.40
6.36
6.34
2.09
2.06
1.71
G (m)
6.90
E (m)
6.65
J (m)
7.35
I (m)
7.12
D (dd)
6.38
J(16.14, 6.42)
F (m)
6.69
H (m)
7.01
B (s)
2.06
C (s)
2.09
A (s)
1.71
OAc
H3C
CH3
2.21
2.37
2.08
2.07
0.92
1.28
1.06
3.35
3.21
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

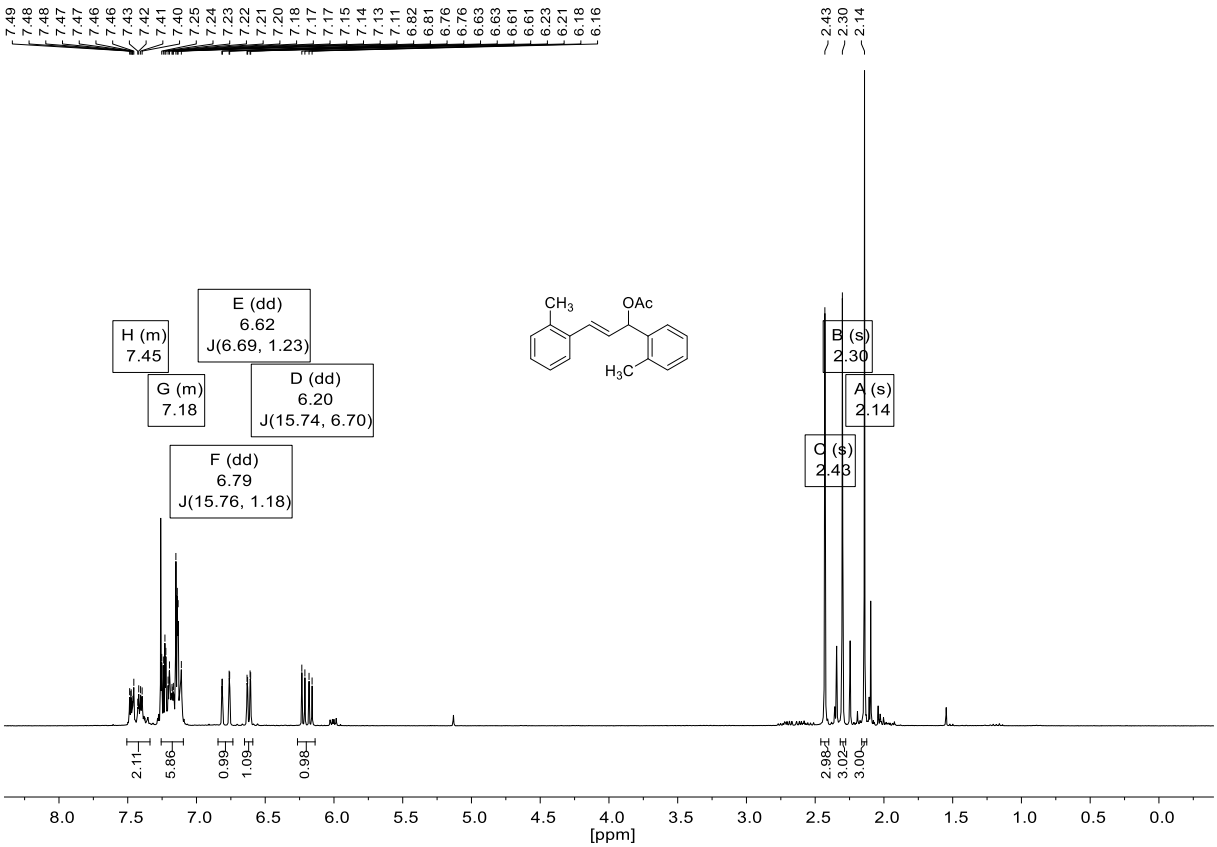

169.34
137.84
137.35
134.12
132.77
129.55
127.64
127.46
127.08
76.32
21.18
21.11
20.87
OAc
H3C
CH3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
[ppm]

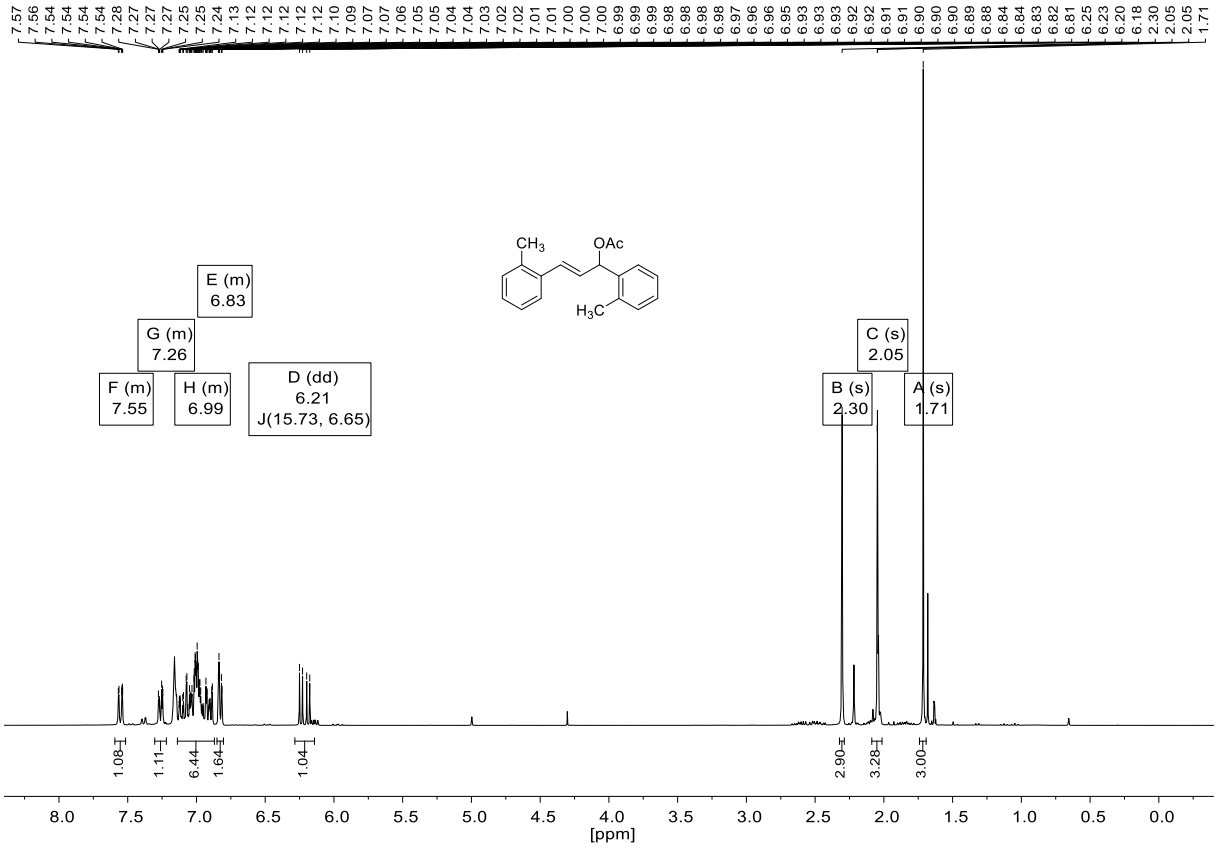

110
100
80
60
40
20
10
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

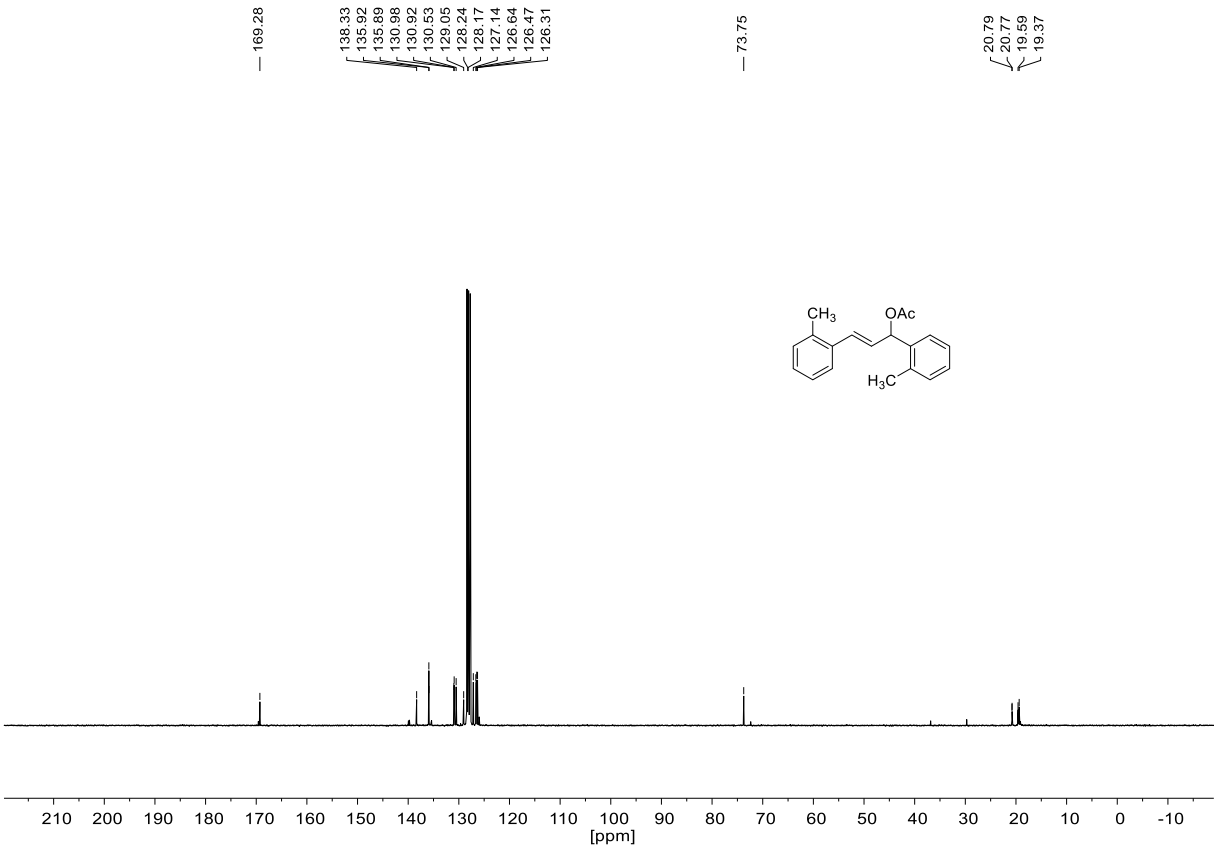

G (m)
7.00
E (s)
6.65
H (m)
7.28
D (dd)
6.40
J(15.91, 6.48)
F (m)
6.69
OAc
H3C
CH3
B (s)
2.05
C (s)
2.10
A (s)
1.73
2.30
6.12
0.96
1.19
0.95
2.71
2.62
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

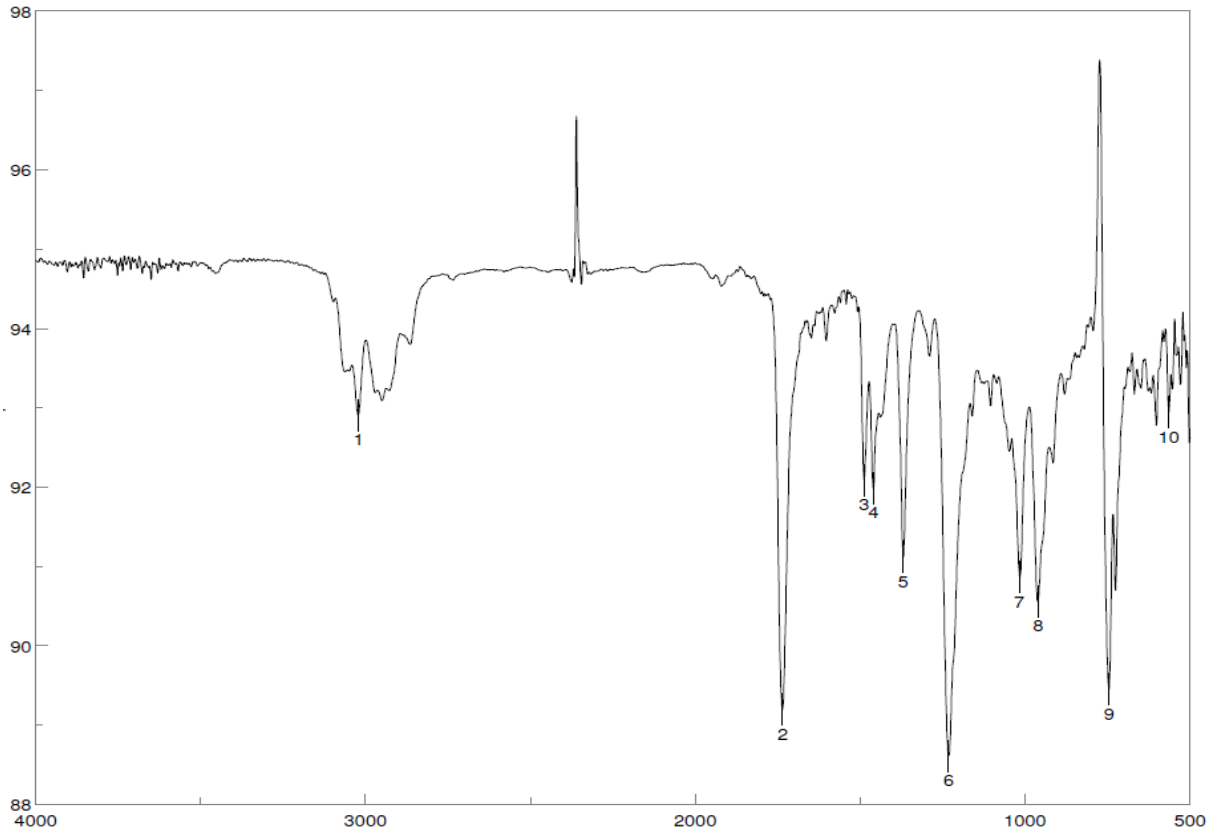

169.31
140.18
138.42
138.14
136.72
132.97
129.10
129.02
128.88
128.75
128.30
128.18
127.87
124.70
124.38
76.44
21.40
21.29
20.85
OAc
H3C
CH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

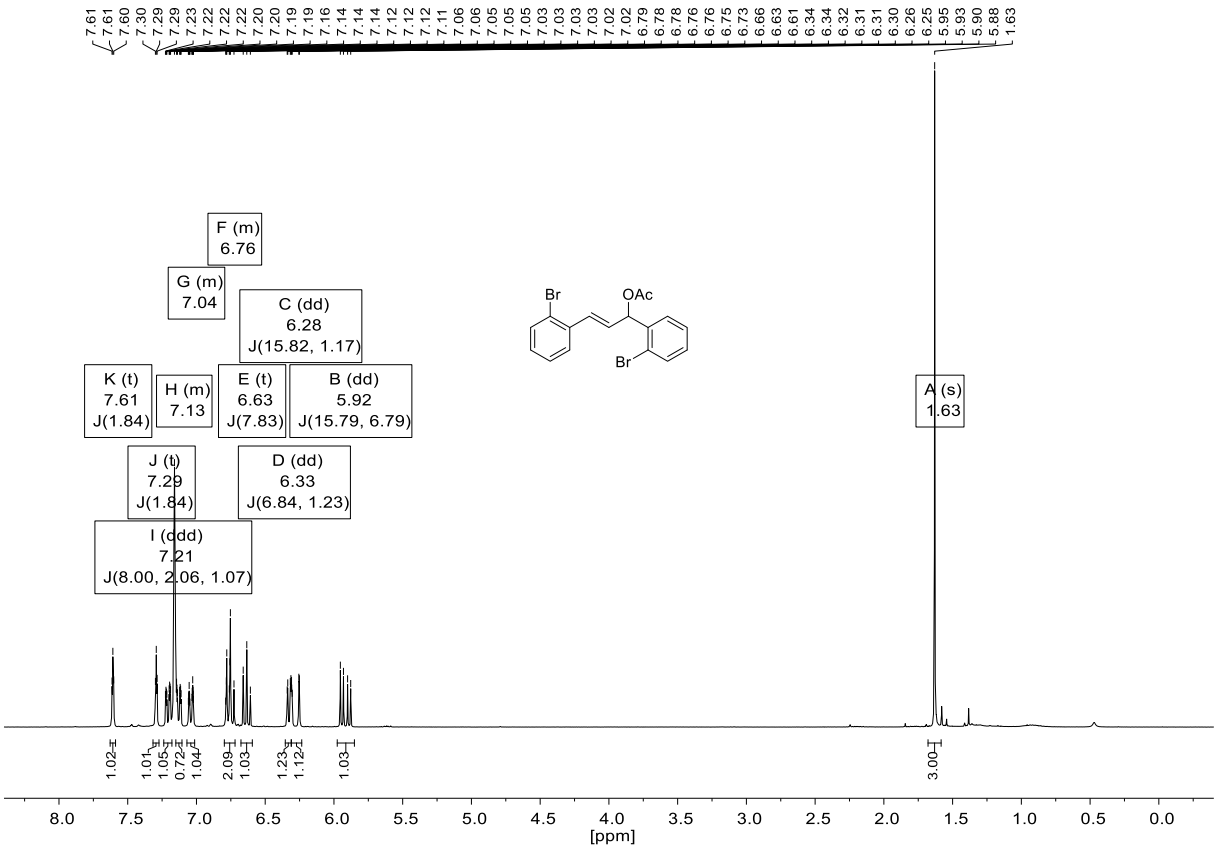

110
100
90
80
70
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29

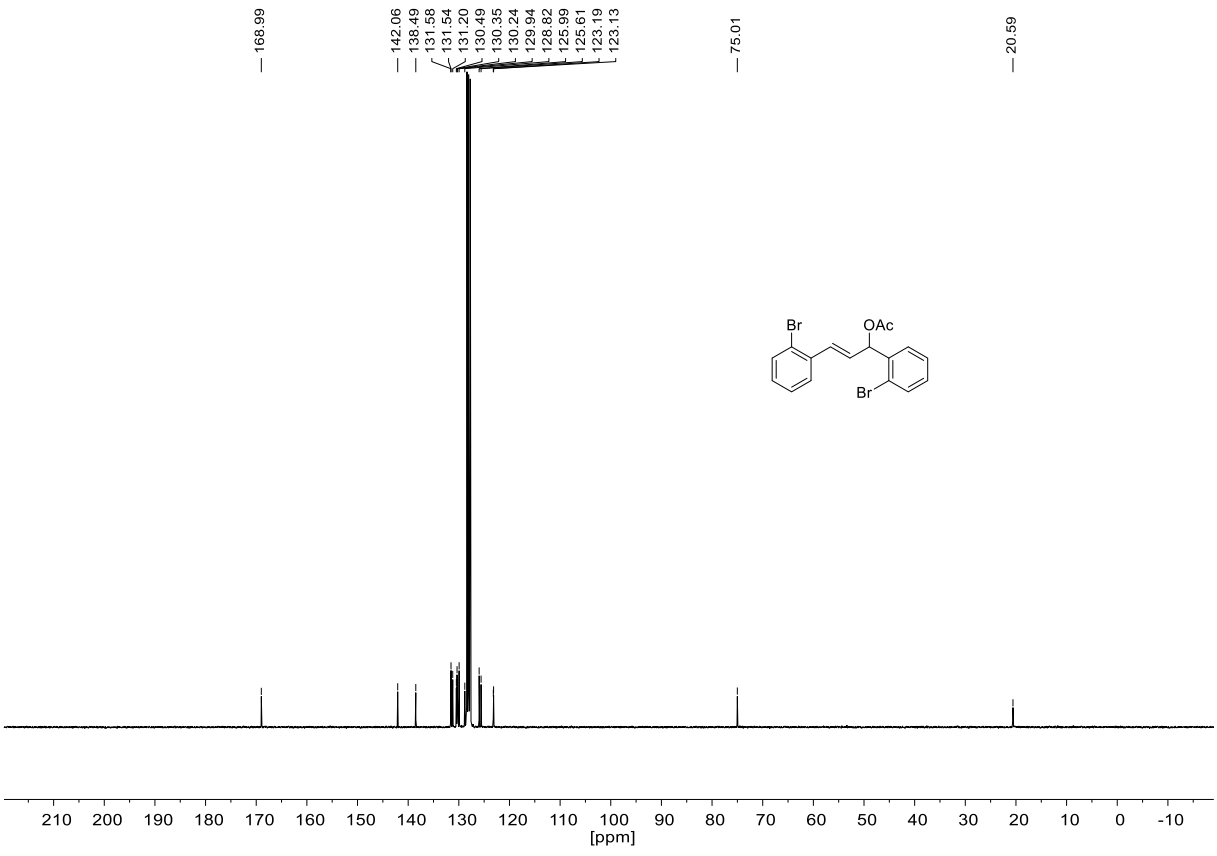

H (m)
7.45
G (m)
7.18
E (dd)
6.62
J(6.69, 1.23)
D (dd)
6.20
J(15.74, 6.70)
F (dd)
6.79
J(15.76, 1.18)
B (s)
2.30
A (s)
2.14
C (s)
2.43
CH3
OAc
H3C
2.11
5.86
0.99
1.09
0.98
2.98
3.02
3.00
[ppm]

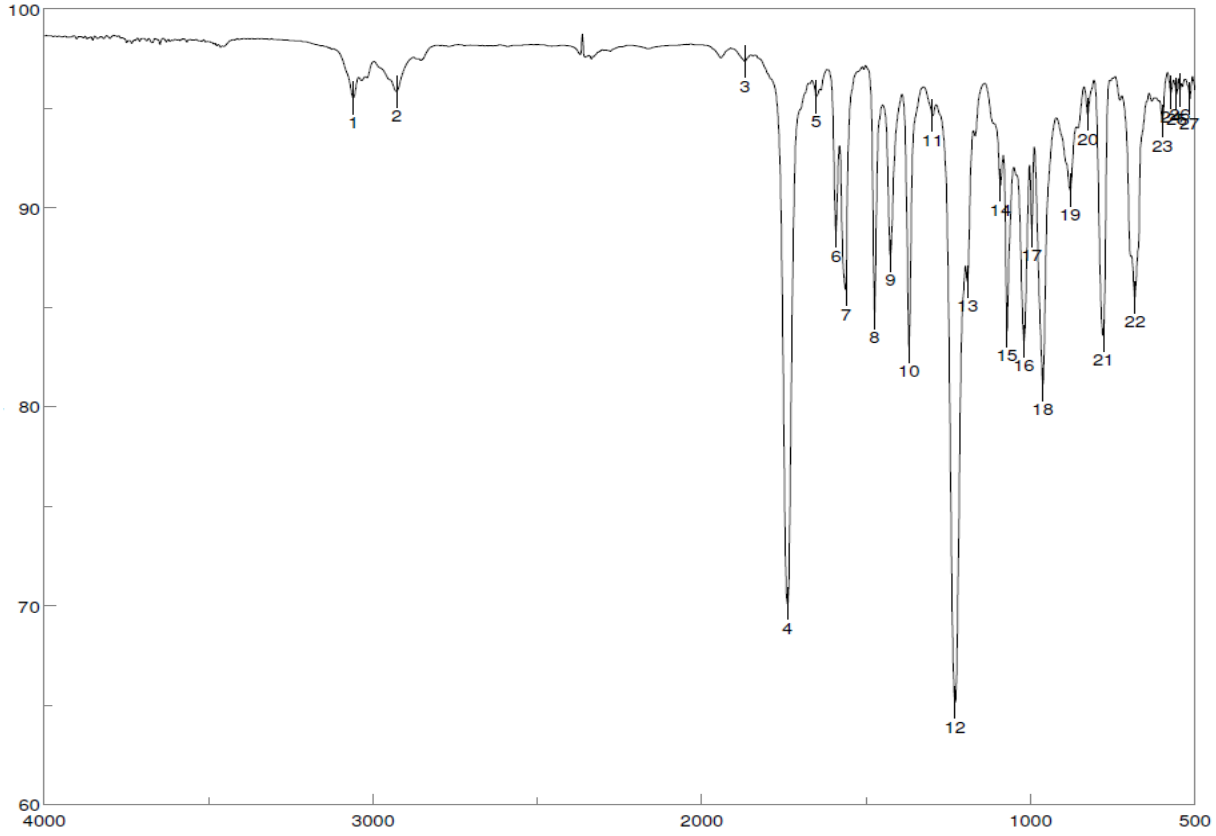

E (m)
6.83
G (m)
7.26
F (m)
7.55
H (m)
6.99
D (dd)
6.21
J(15.73, 6.65)
C (s)
2.05
B (s)
2.30
A (s)
1.71
CH3
OAc
H3C
1.08
1.11
6.44
1.64
1.04
2.90
3.28
3.00
[ppm]


169.28
138.33
135.92
135.89
130.98
130.92
130.53
129.05
128.24
128.17
127.14
126.64
126.47
126.31
73.75
20.79
20.77
19.59
19.37
CH3
OAc
H3C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]


98
96
94
92
90
88
1
2
3
4
5
6
7
8
9
10
4000
3000
2000
1000
500


F (m)
6.76
G (m)
7.04
C (dd)
6.28
J(15.82, 1.17)
K (t)
7.61
J(1.84)
H (m)
7.13
E (t)
6.63
J(7.83)
B (dd)
5.92
J(15.79, 6.79)
A (s)
1.63
J (t)
7.29
J(1.84)
D (dd)
6.33
J(6.84, 1.23)
I (ddd)
7.21
J(8.00, 2.06, 1.07)
Br
OAc
Br
[ppm]


168.99
142.06
138.49
131.58
131.54
131.20
130.49
130.35
130.24
129.94
128.82
125.99
125.61
123.19
123.13
75.01
20.59
Br
OAc
Br
[ppm]


100
90
80
70
60
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
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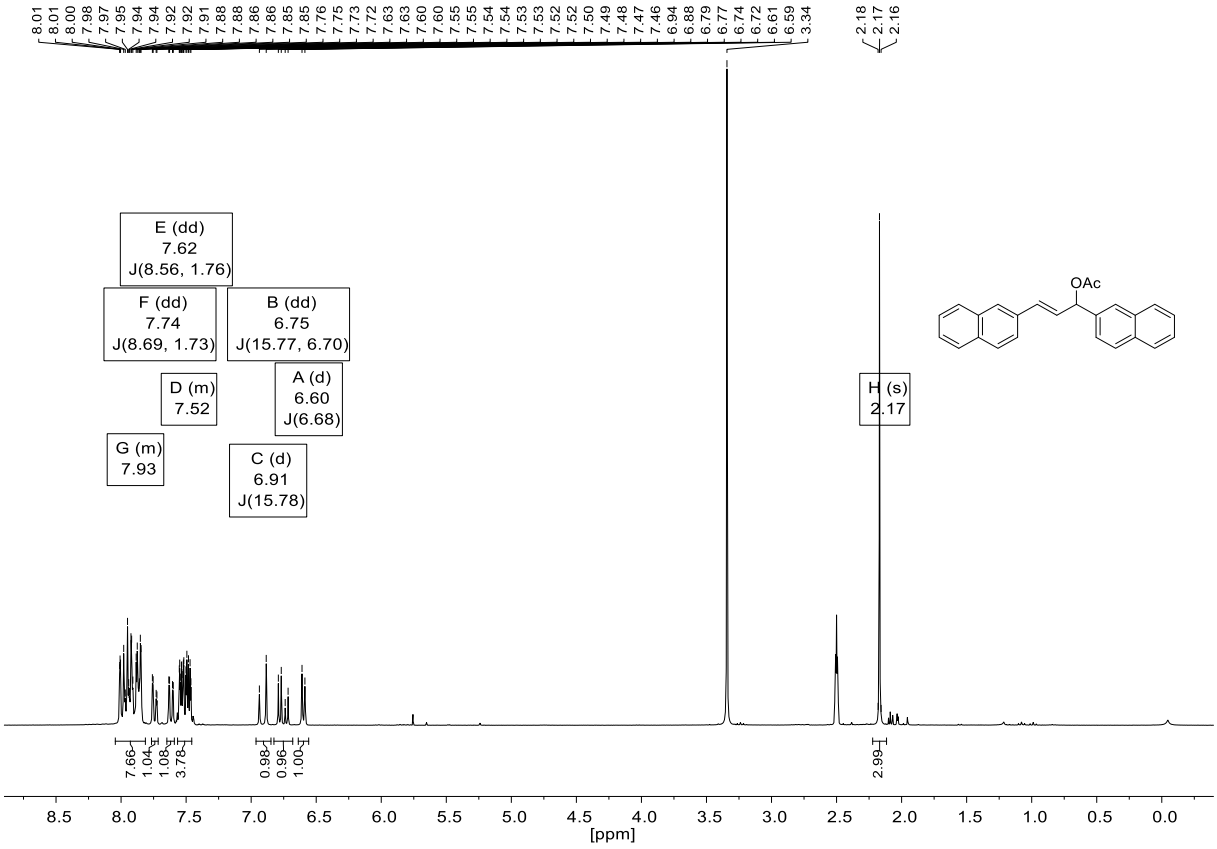
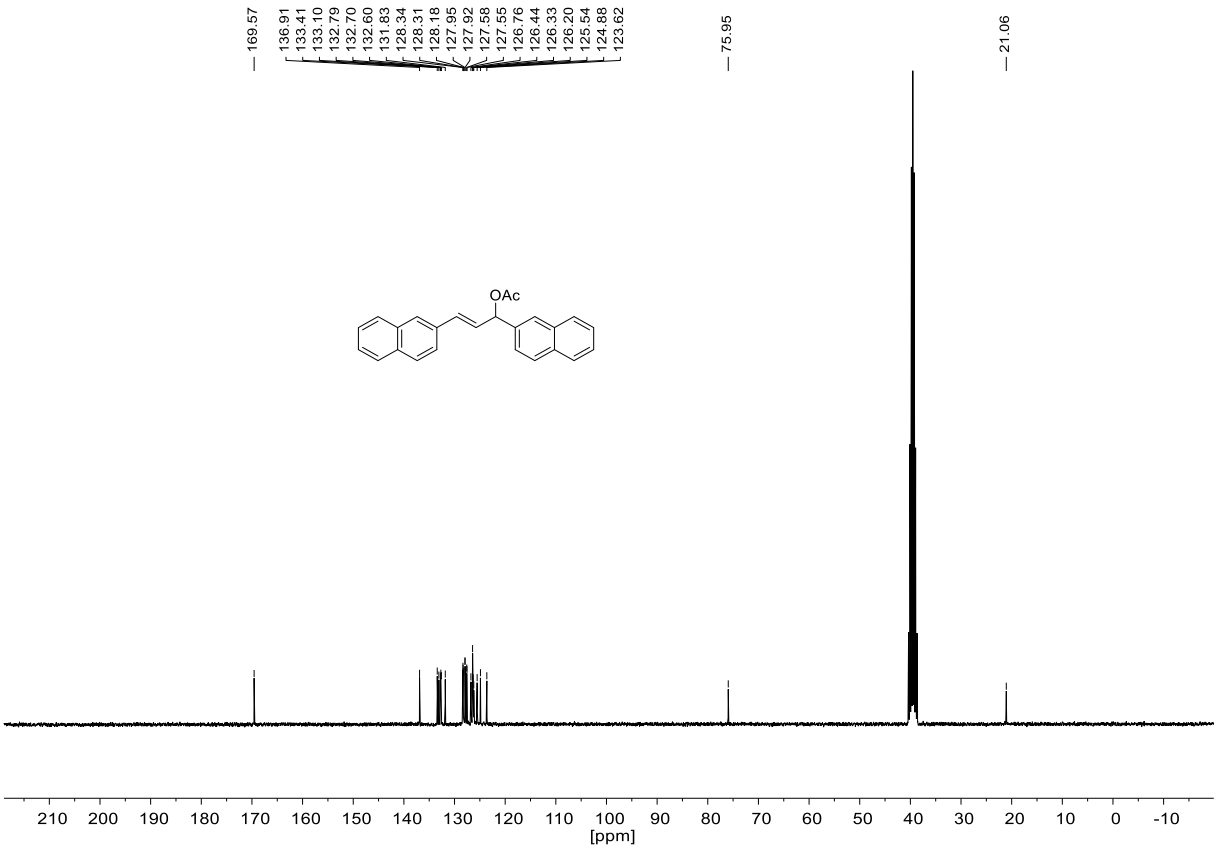
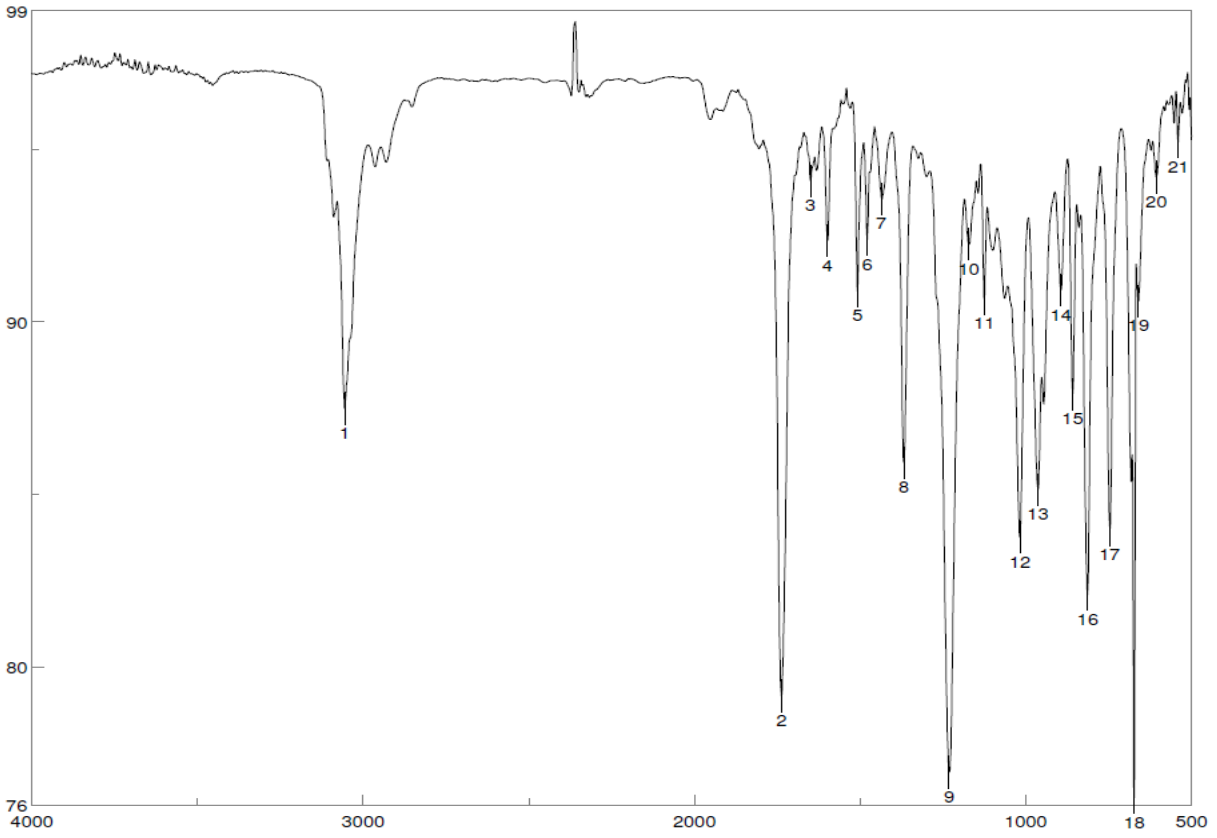
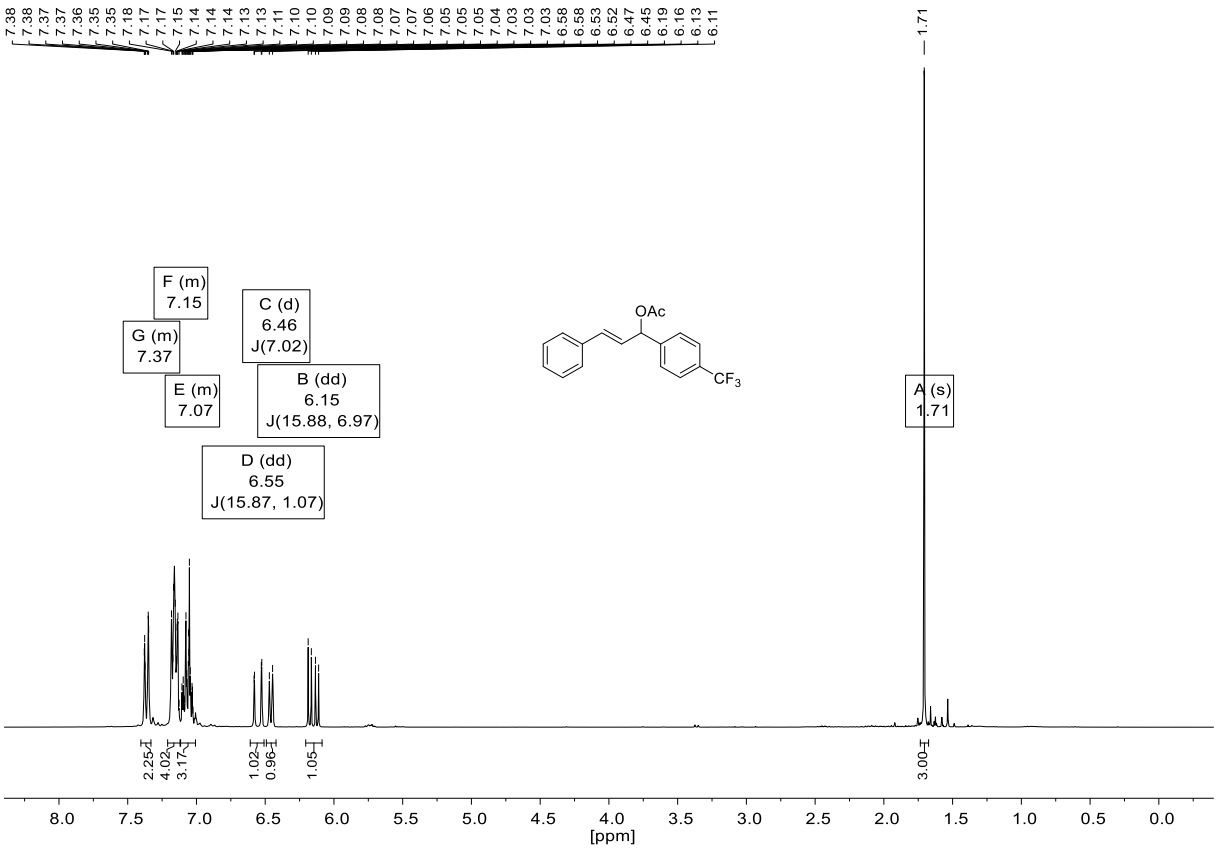
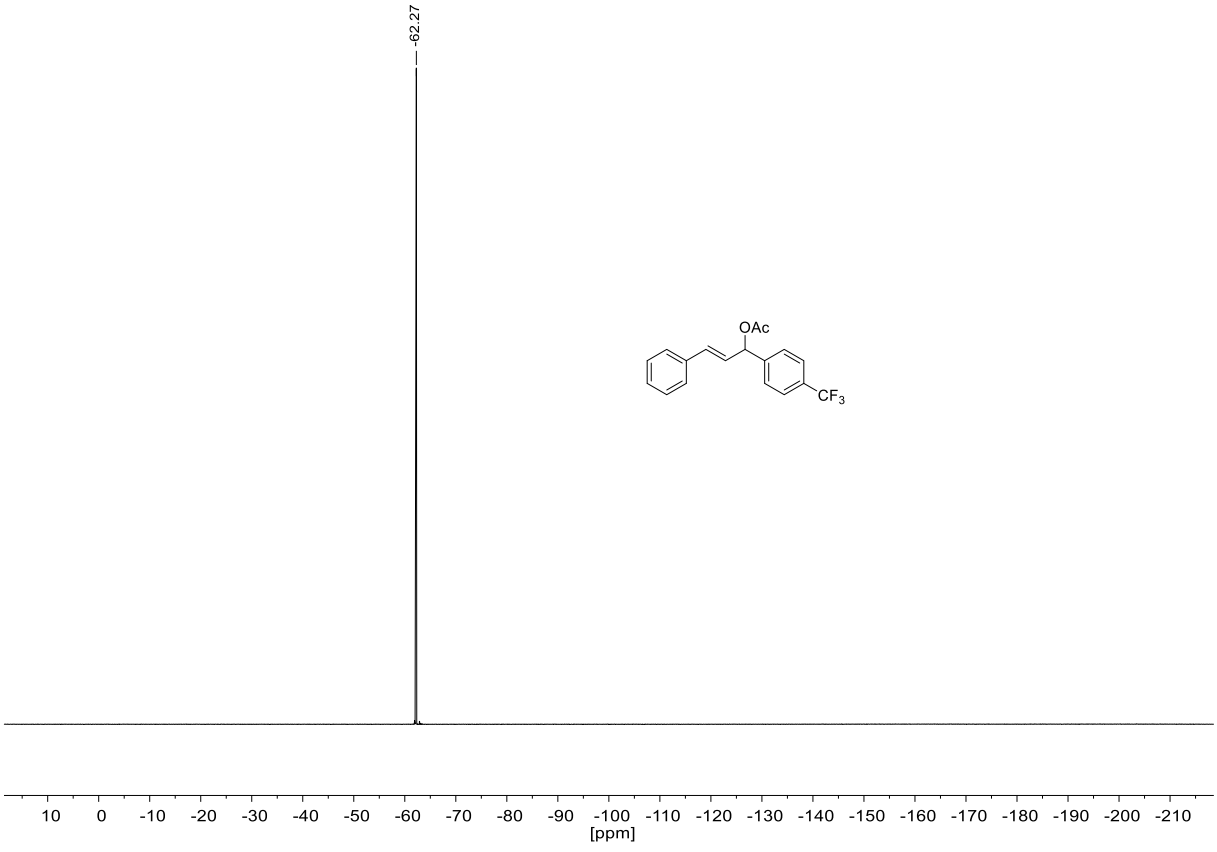
20
21
22
23
24
25
26
27

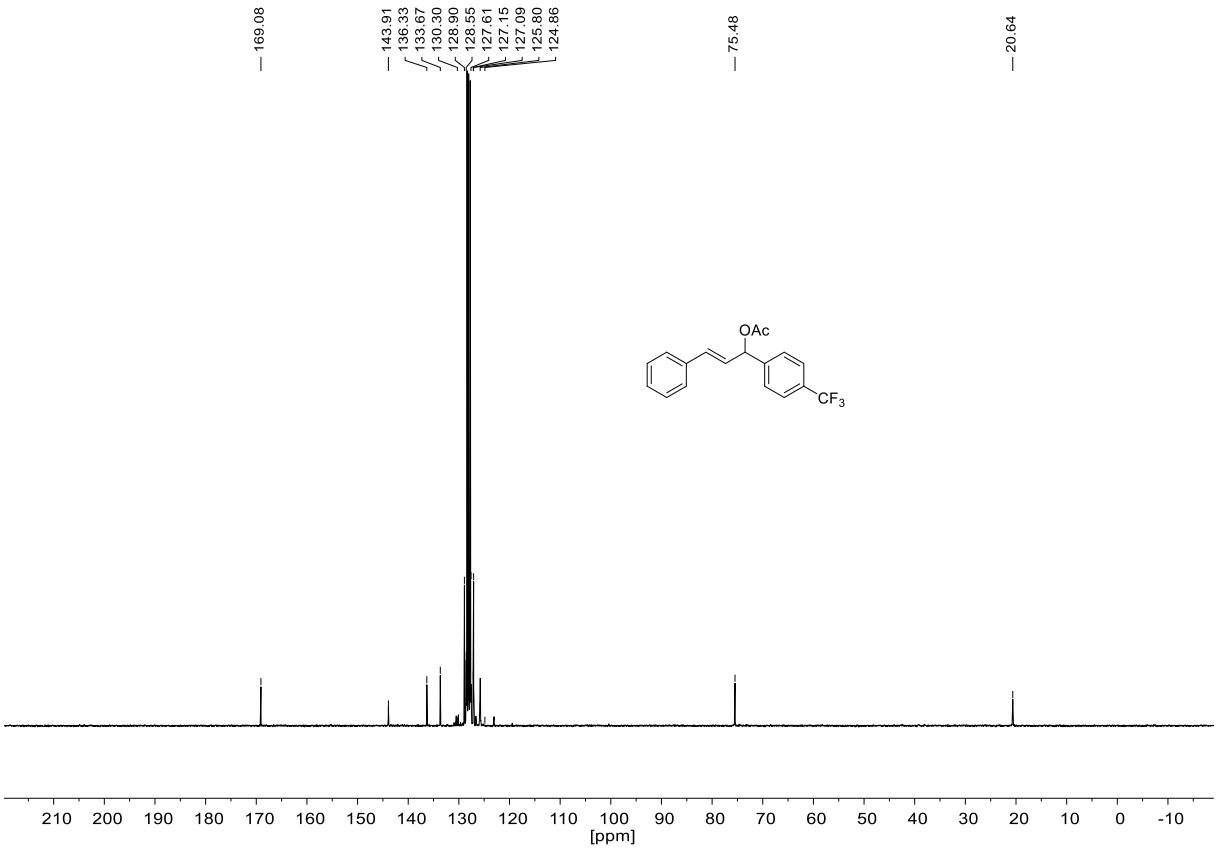

8.01 8.01 8.00 7.98 7.97 7.95 7.94 7.94 7.92 7.92 7.91 7.88 7.88 7.86 7.86 7.85 7.85 7.76 7.75 7.73 7.72 7.63 7.60 7.60 7.55 7.55 7.54 7.54 7.53 7.53 7.52 7.52 7.50 7.49 7.48 7.47 7.46 6.94 6.88 6.79 6.77 6.74 6.72 6.61 6.59 3.34
2.18 2.17 2.16
E (dd)
7.62
J(8.56, 1.76)
F (dd)
7.74
J(8.69, 1.73)
B (dd)
6.75
J(15.77, 6.70)
D (m)
7.52
A (d)
6.60
J(6.68)
G (m)
7.93
C (d)
6.91
J(15.78)
H (s)
2.17
OAc
7.66
1.04
1.05
3.78
0.98
0.96
1.00
2.99
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

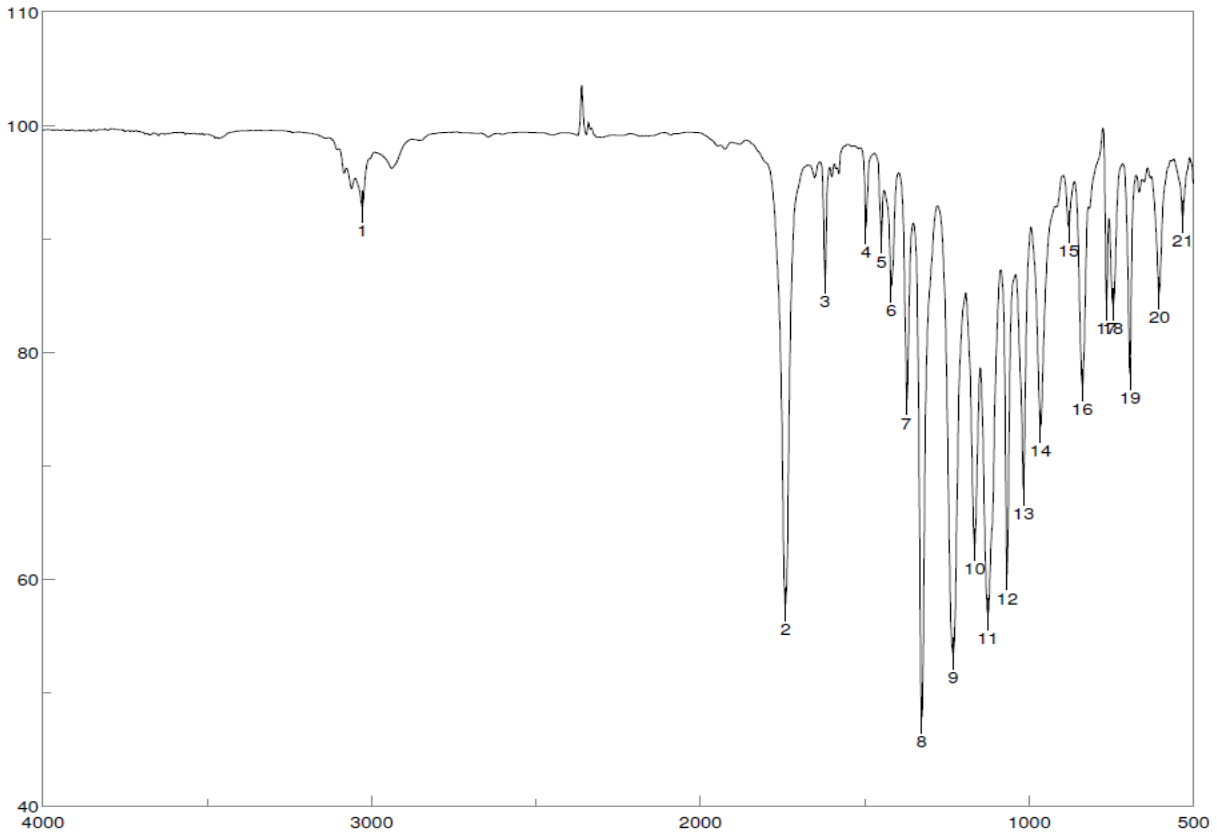

169.57
136.91
133.41
133.10
132.79
132.70
132.60
131.83
128.34
128.31
128.18
127.95
127.92
127.58
127.55
126.76
126.44
126.33
126.20
125.54
124.88
123.62
76.95
21.06
OAc
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

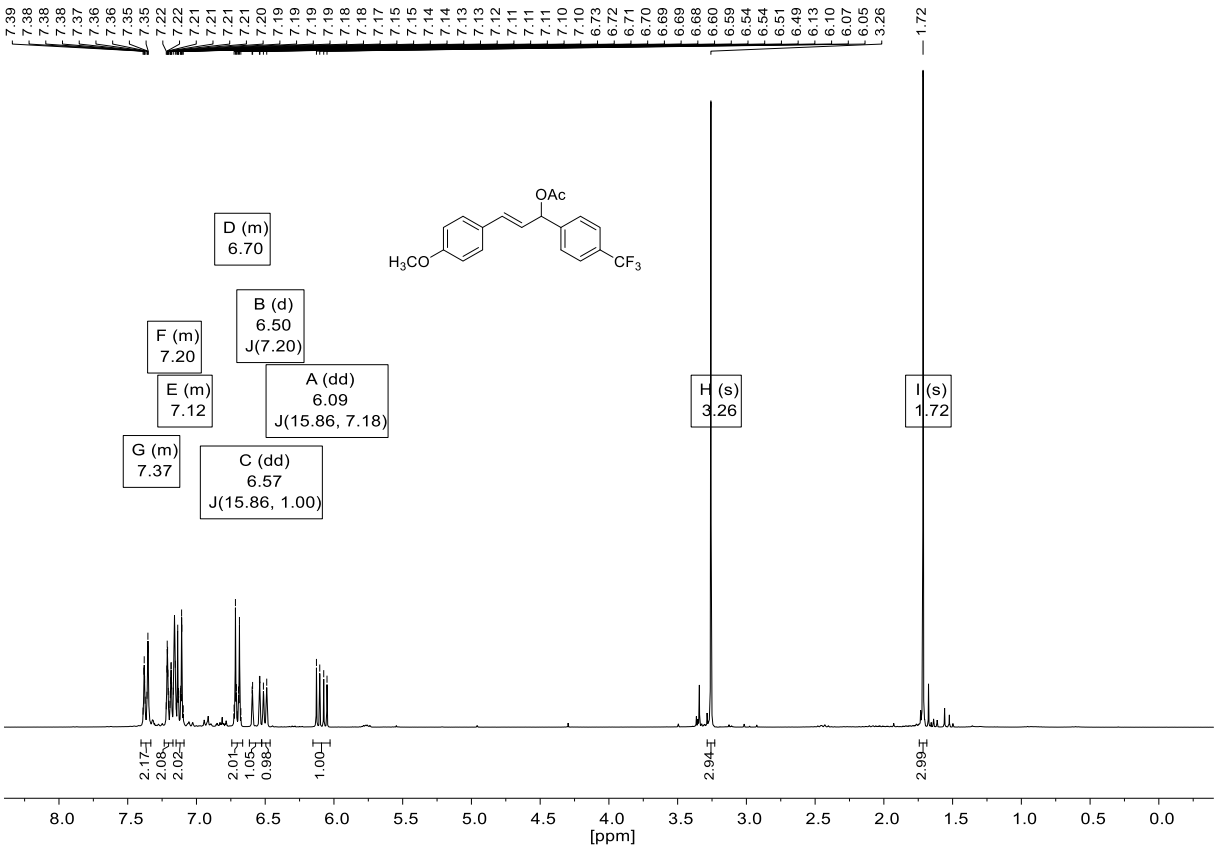

99
90
80
76
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21

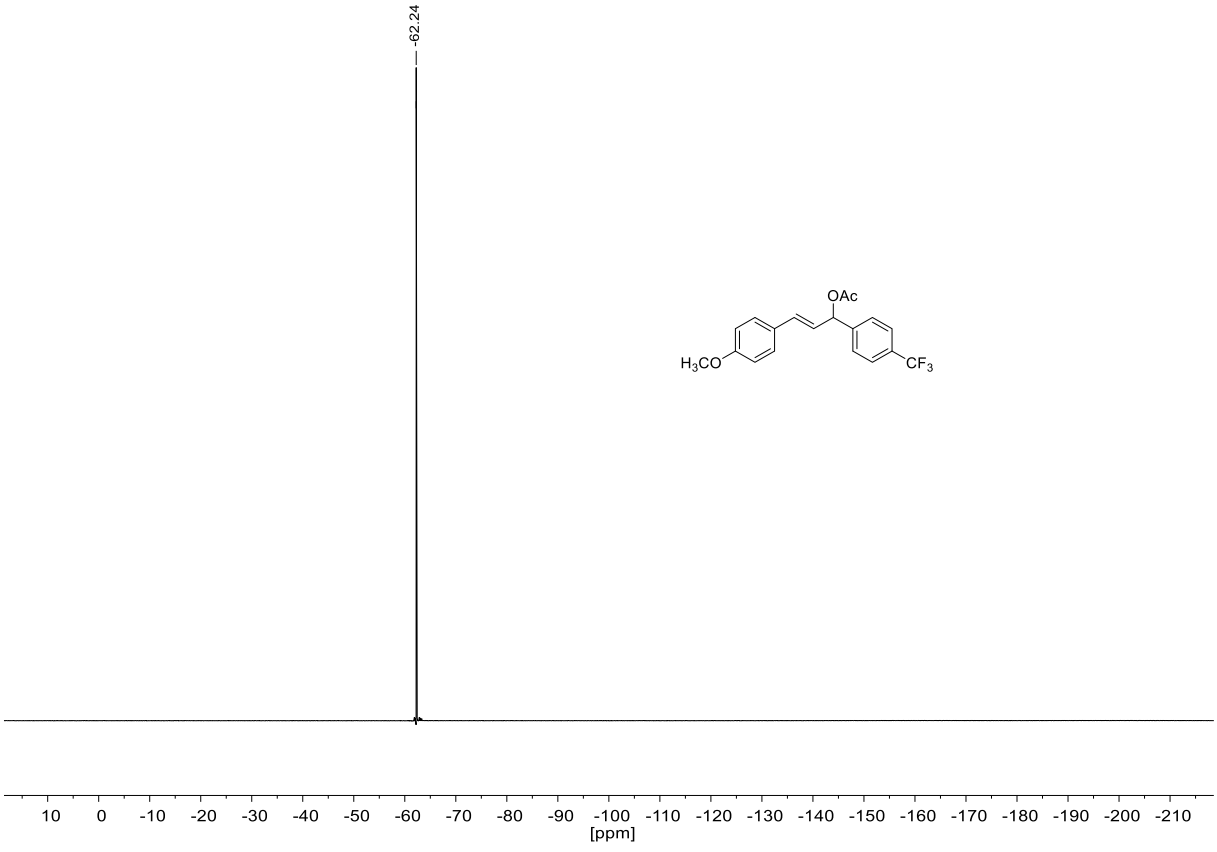

7.38 7.38 7.37 7.37 7.36 7.35 7.35 7.18 7.17 7.17 7.15 7.14 7.14 7.14 7.13 7.13 7.11 7.10 7.10 7.09 7.09 7.08 7.08 7.07 7.07 7.06 7.05 7.05 7.04 7.03 7.03 6.58 6.58 6.53 6.52 6.47 6.45 6.19 6.16 6.13 6.11
1.71
F (m) 7.15
G (m) 7.37
E (m) 7.07
C (d) 6.46 J(7.02)
B (dd) 6.15 J(15.88, 6.97)
D (dd) 6.55 J(15.87, 1.07)
A (s) 1.71
OAc
CF3
2.25
4.02
3.17
1.02
0.96
1.05
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

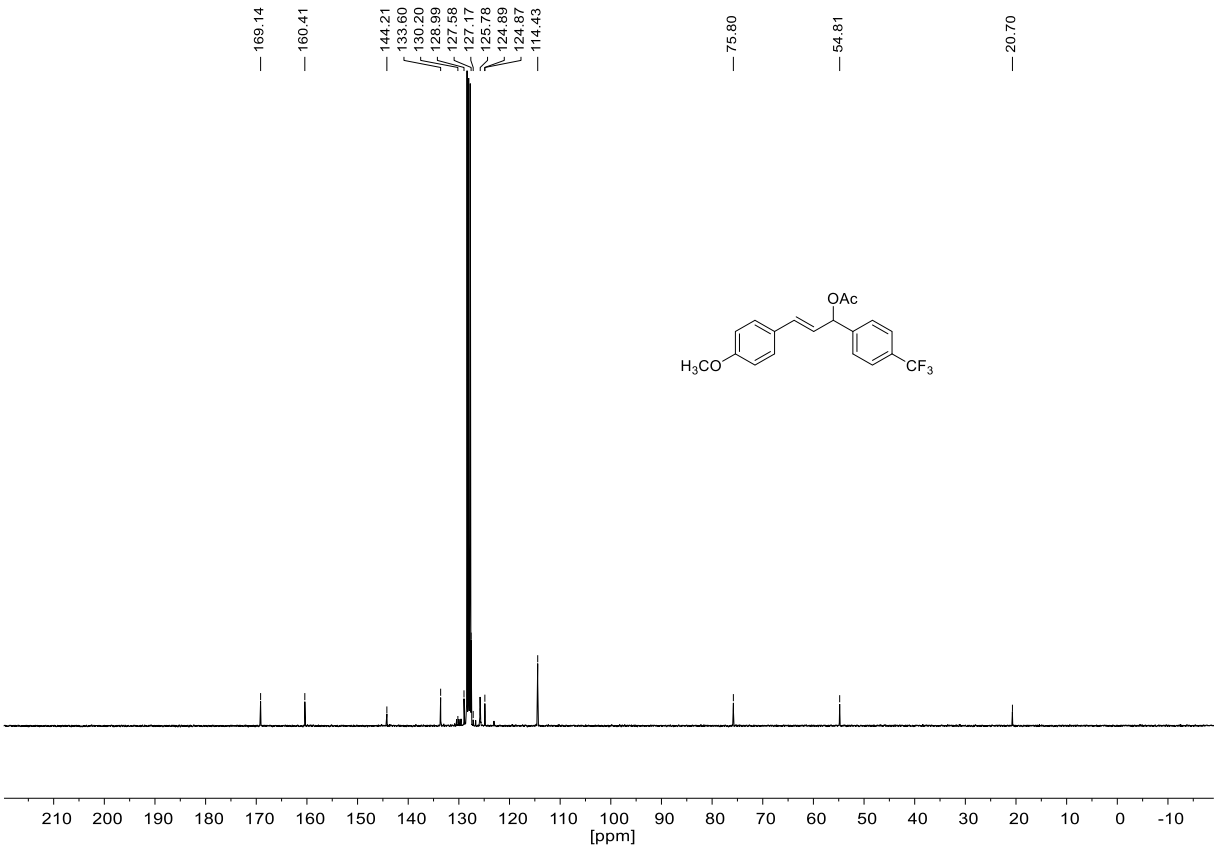

-62.27
OAc
CF3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

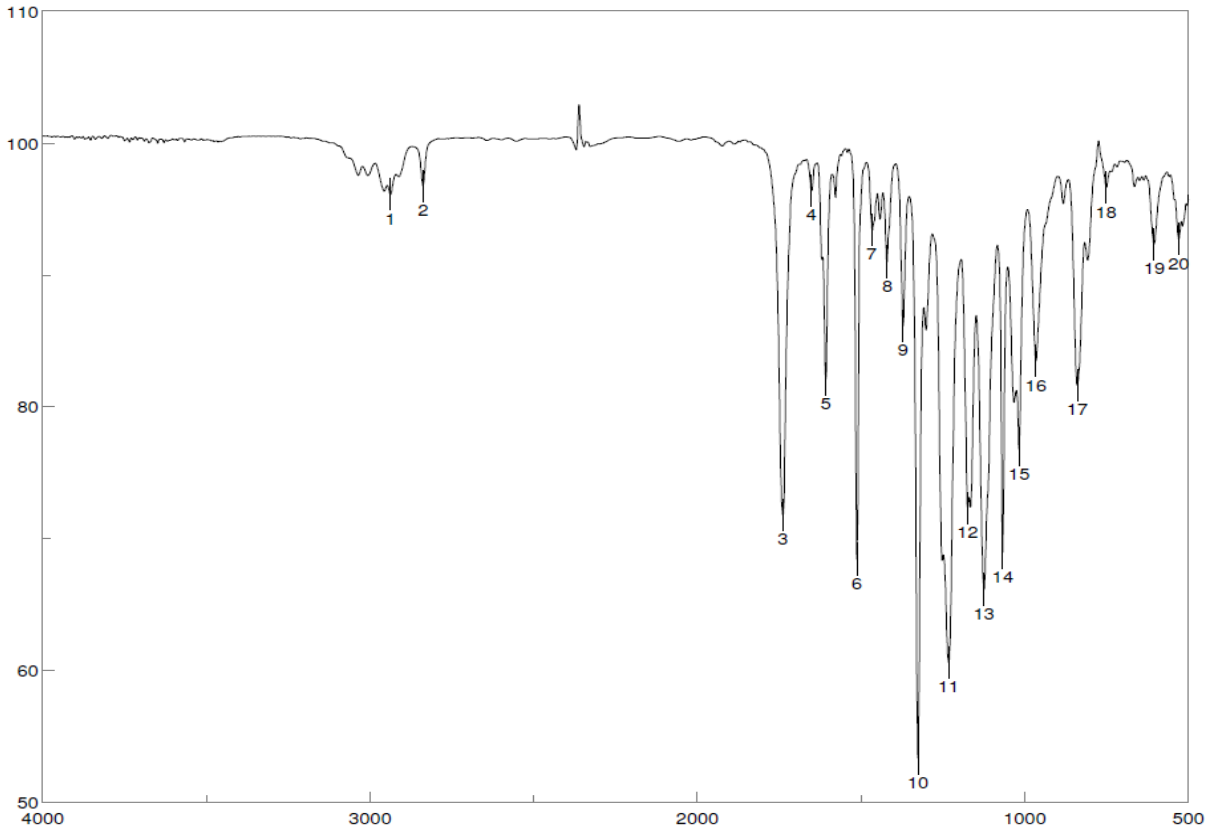

169.08
143.91
136.33
133.67
130.30
128.90
128.55
127.61
127.15
127.09
125.80
124.86
75.48
20.64
OAc
CF3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

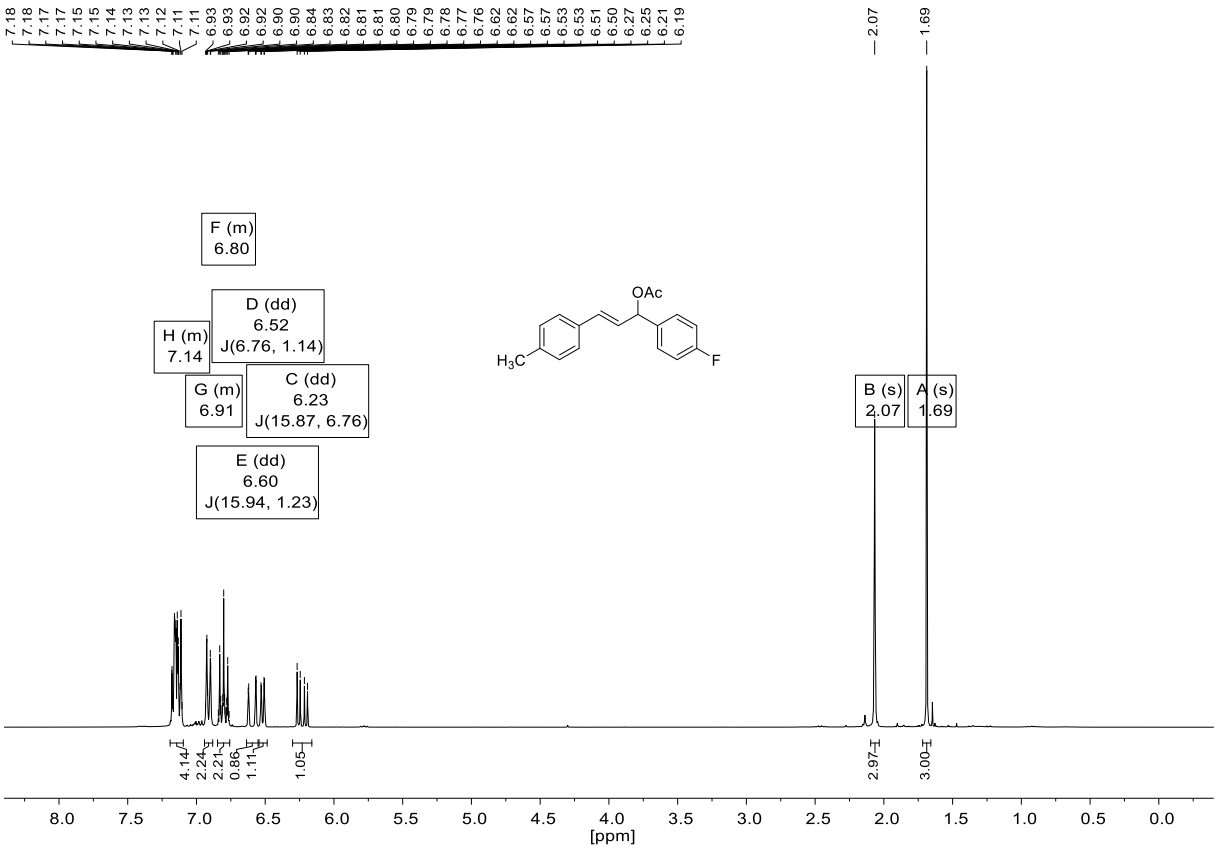

110
100
80
60
40
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21

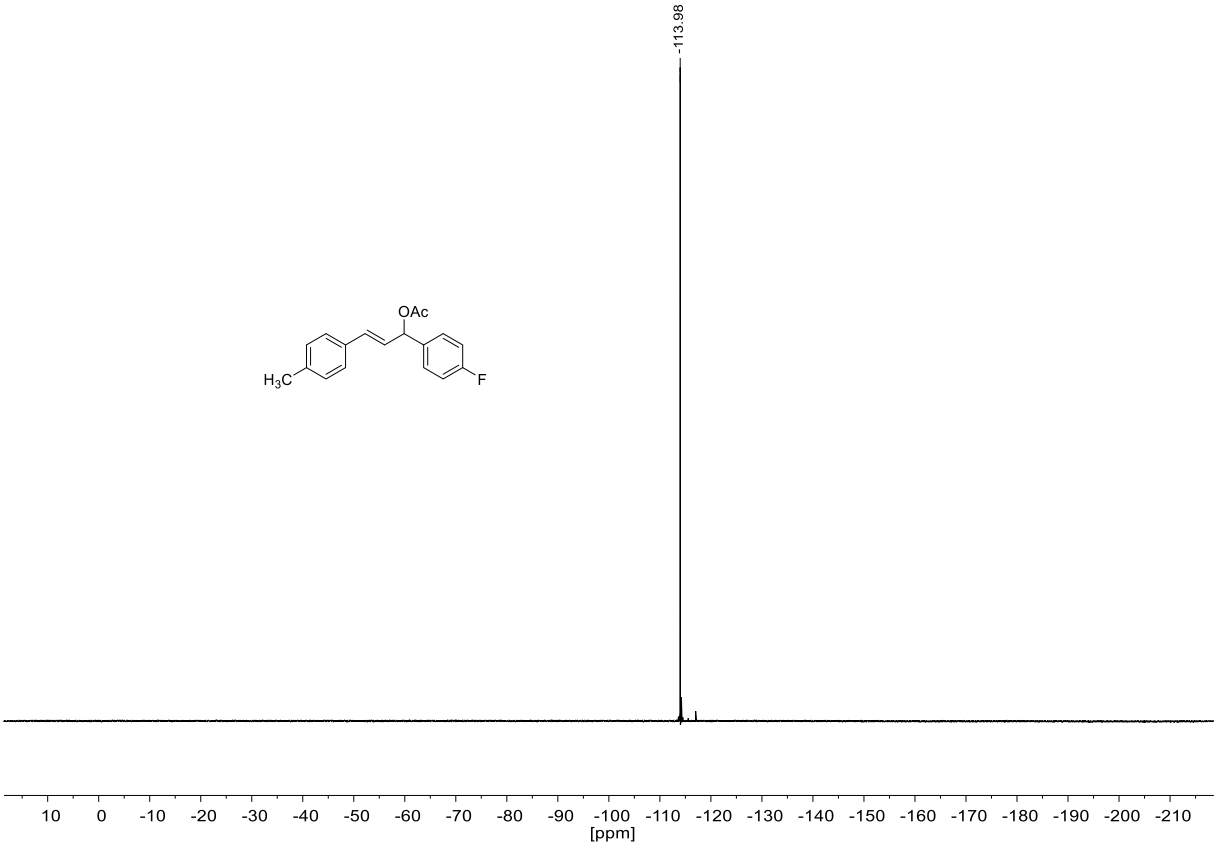

7.39 7.38 7.38 7.38 7.37 7.36 7.36 7.35 7.35 7.22 7.22 7.21 7.21 7.21 7.21 7.20 7.19 7.19 7.19 7.19 7.18 7.18 7.17 7.15 7.15 7.14 7.14 7.13 7.13 7.12 7.11 7.11 7.10 7.10 6.73 6.72 6.71 6.70 6.69 6.69 6.68 6.60 6.59 6.54 6.54 6.51 6.49 6.13 6.10 6.07 6.05 3.26 1.72
OAc
H3CO
CF3
D (m) 6.70
B (d) 6.50 J(7.20)
F (m) 7.20
E (m) 7.12
A (dd) 6.09 J(15.86, 7.18)
G (m) 7.37
C (dd) 6.57 J(15.86, 1.00)
H (s) 3.26
I (s) 1.72
2.17 2.08 2.02 2.01 1.05 0.98 1.00 2.94 2.99
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

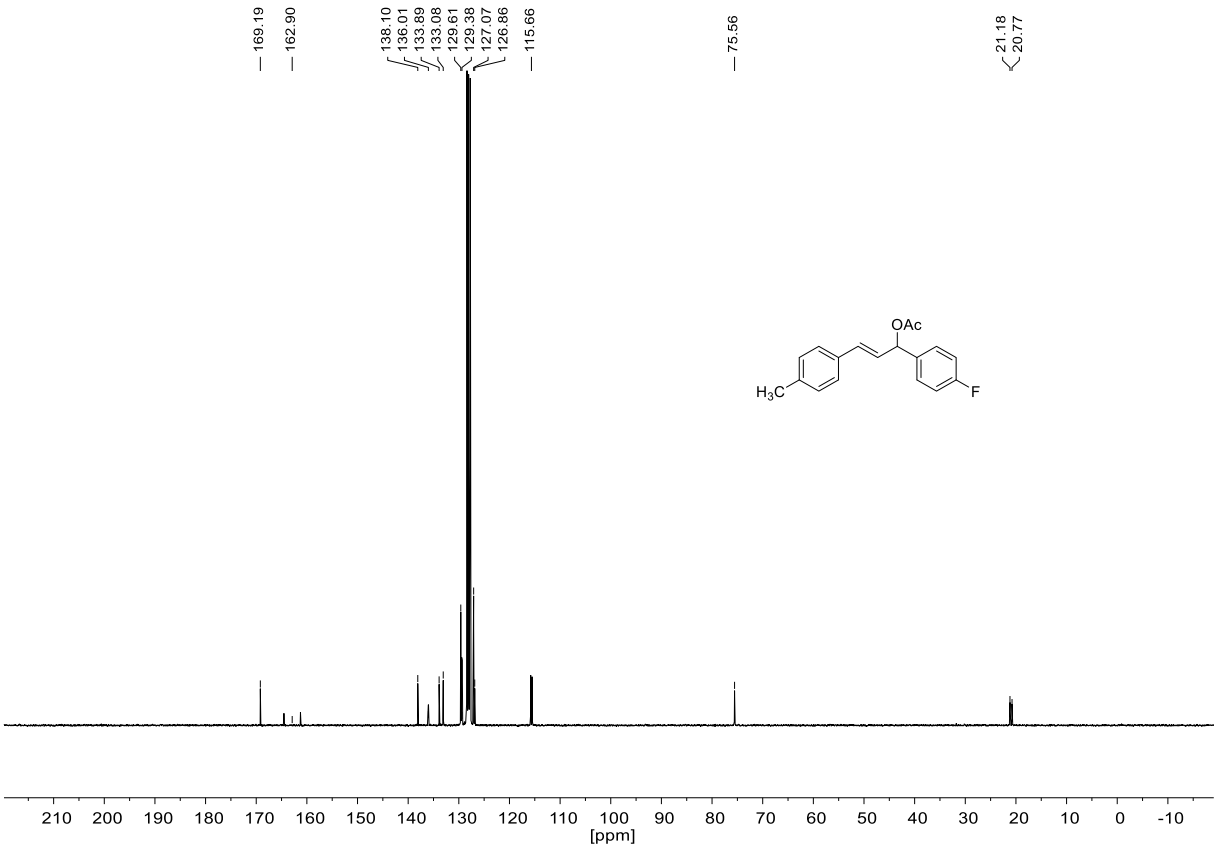

-62.24
OAc
H3CO
CF3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

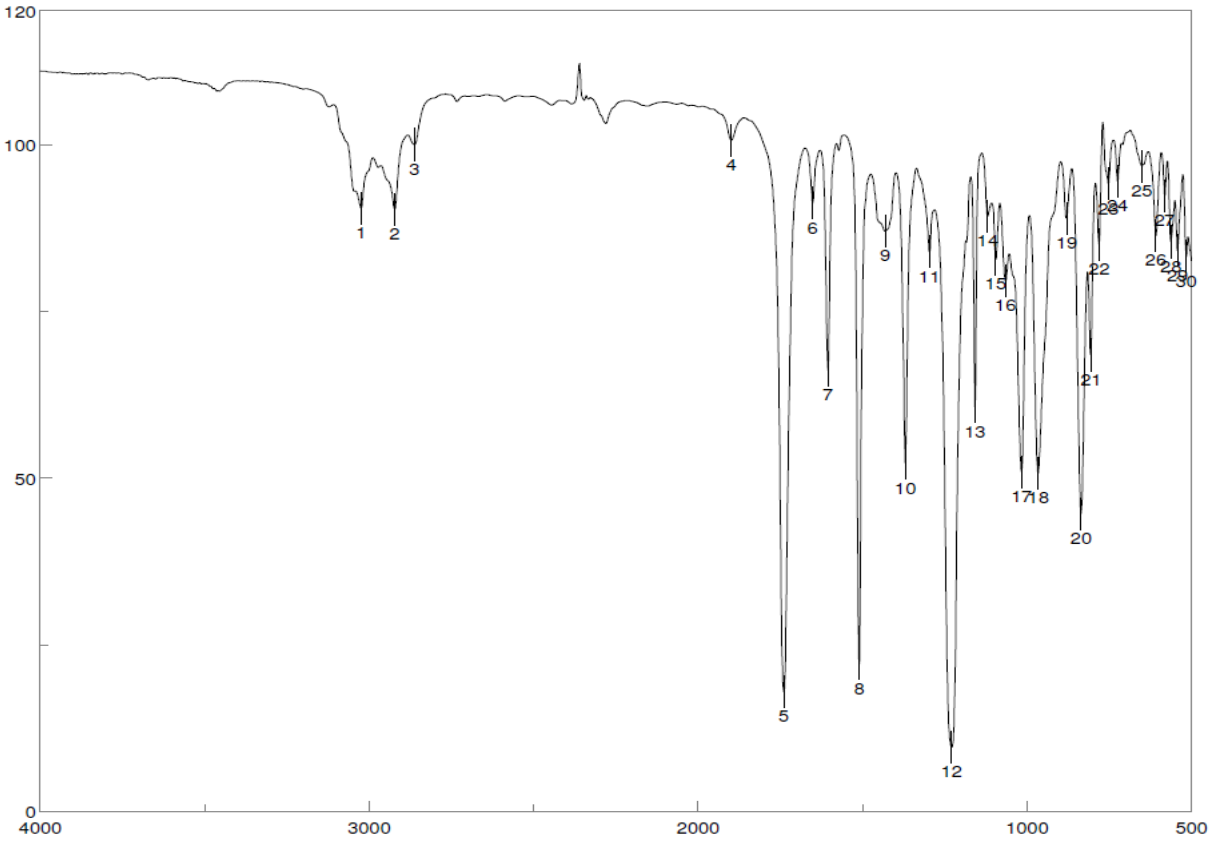

169.14
160.41
144.21
133.60
130.20
128.99
127.58
127.17
125.78
124.89
124.87
114.43
75.80
54.81
20.70
OAc
H3CO
CF3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

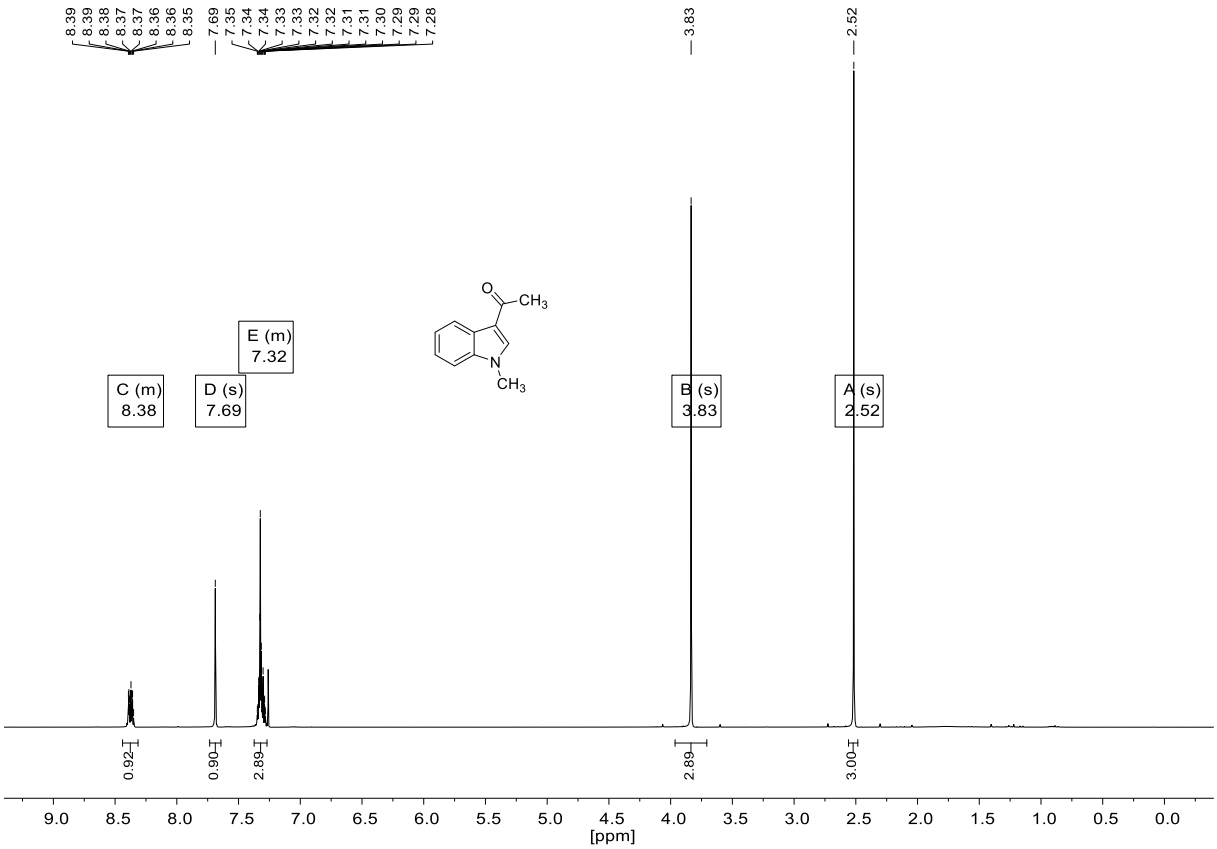

110
100
80
60
50
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20

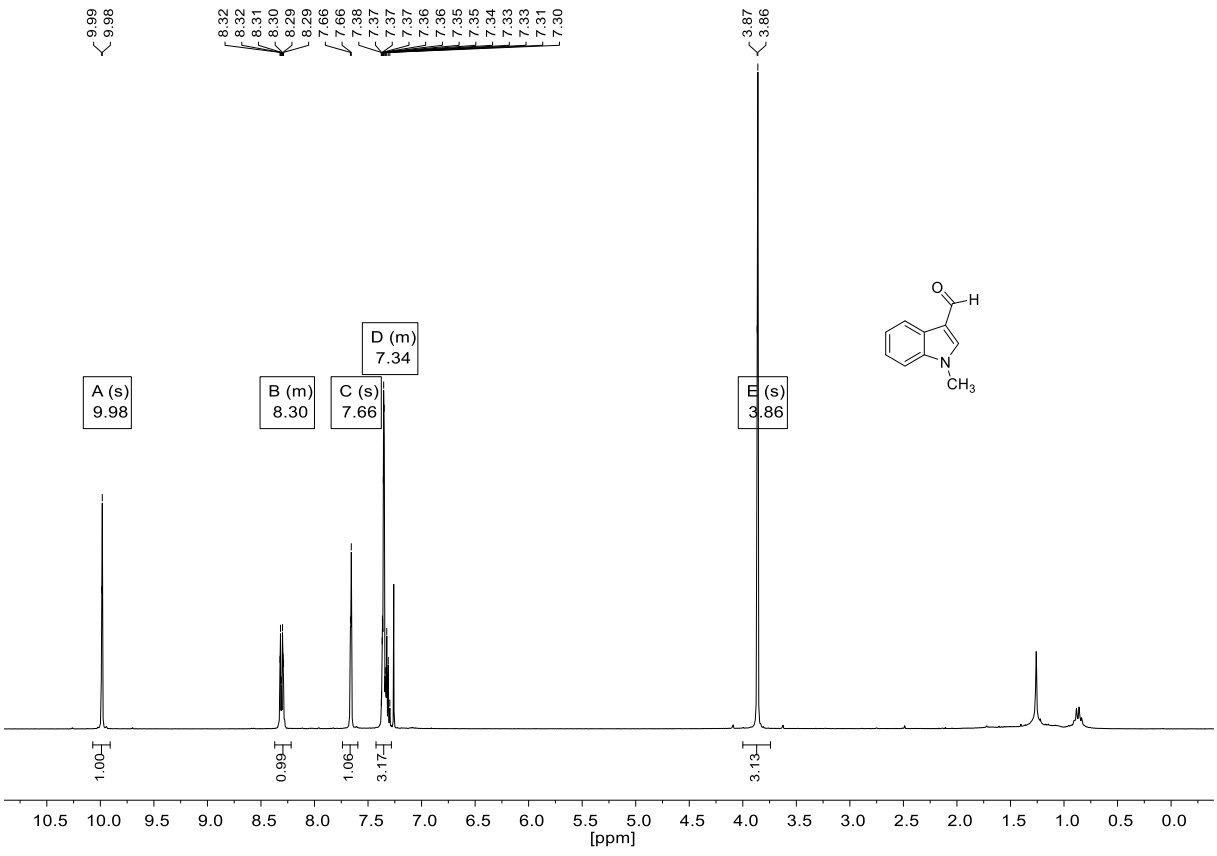

7.18 7.18 7.17 7.17 7.15 7.15 7.14 7.13 7.13 7.12 7.11 7.11 6.93 6.93 6.92 6.92 6.90 6.90 6.84 6.83 6.82 6.81 6.81 6.80 6.79 6.79 6.78 6.77 6.76 6.62 6.62 6.57 6.53 6.53 6.51 6.50 6.27 6.25 6.21 6.19
2.07
1.69
F (m) 6.80
D (dd) 6.52 J(6.76, 1.14)
H (m) 7.14
G (m) 6.91
C (dd) 6.23 J(15.87, 6.76)
E (dd) 6.60 J(15.94, 1.23)
OAc
H3C
F
B (s) 2.07
A (s) 1.69
4.14 2.24 2.21 0.66 1.11 1.05 2.97 3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

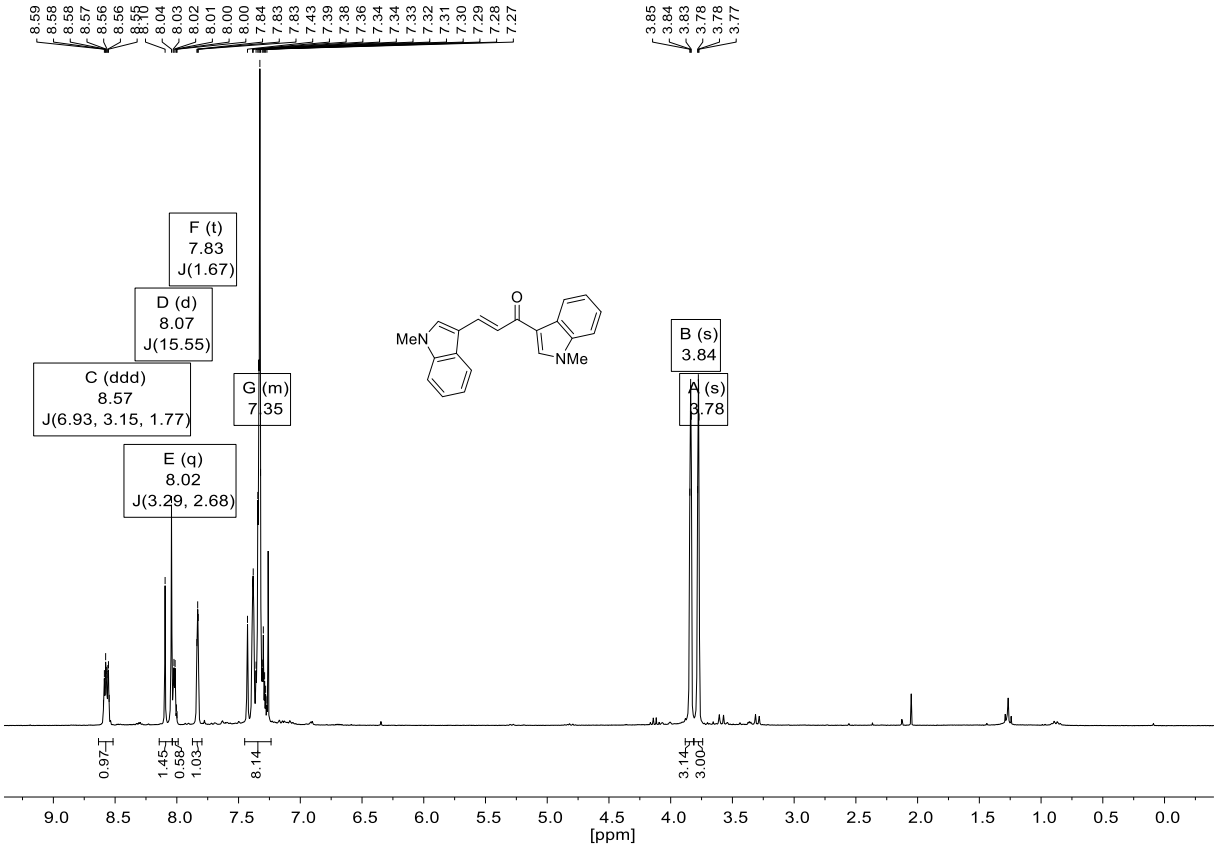

-113.98
OAc
H3C
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

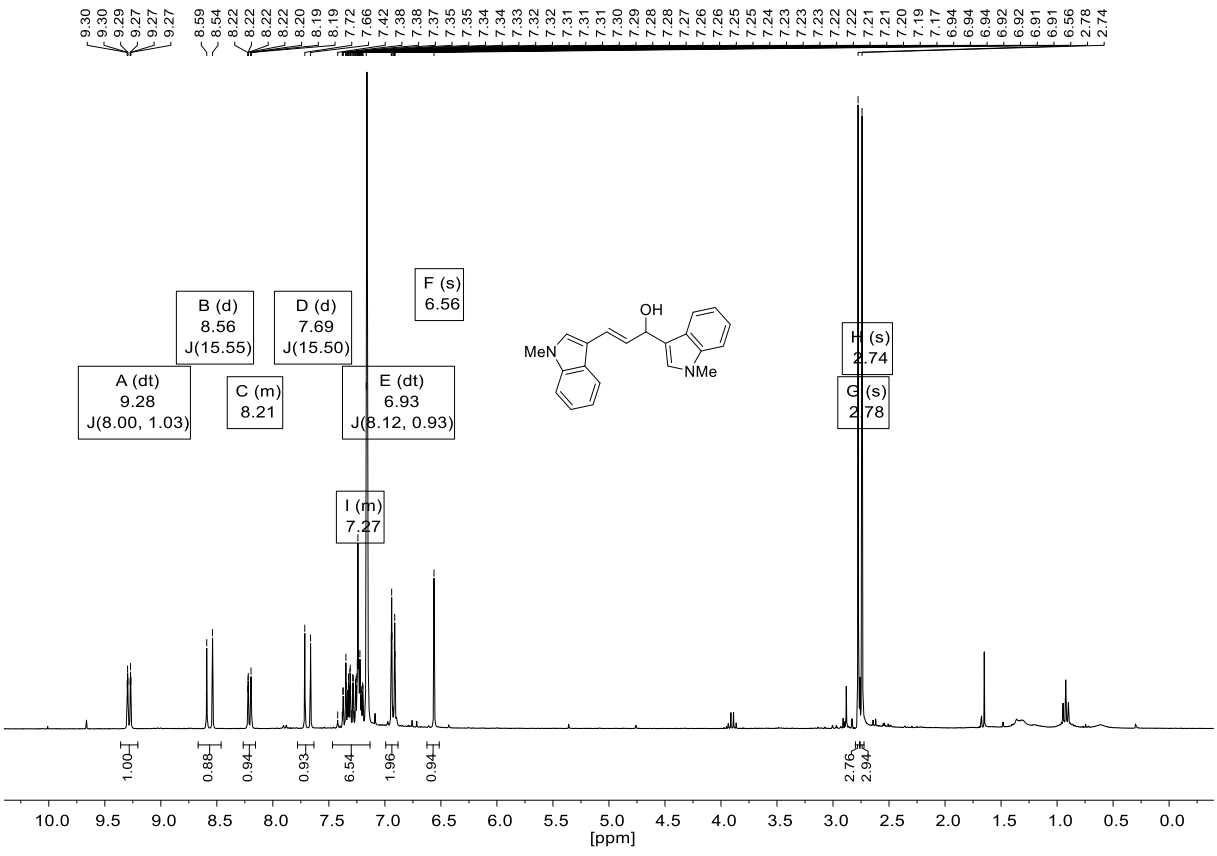

169.19
162.90
138.10
136.01
133.89
133.08
129.61
129.38
127.07
126.86
115.66
75.56
21.18
20.77
OAc
H3C
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

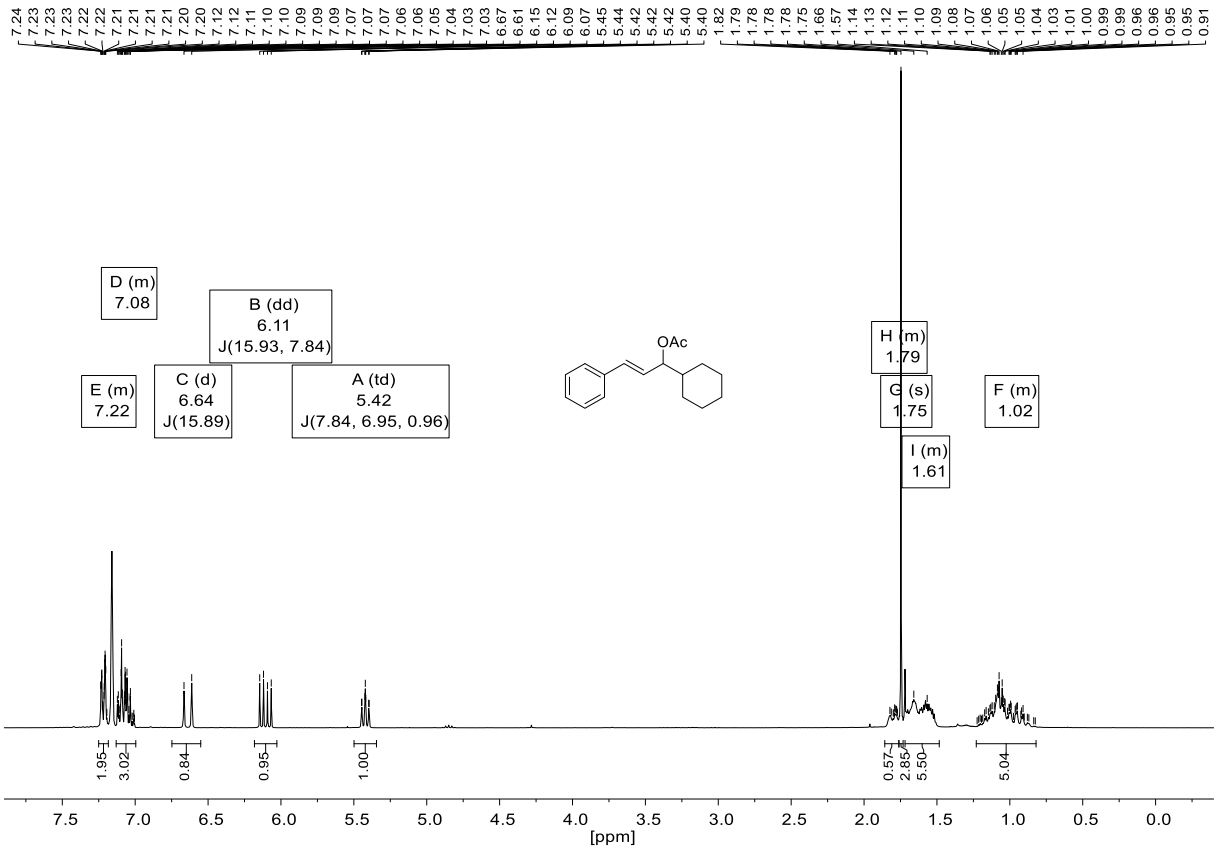

120
100
50
0
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
25
26
27
28
29
30

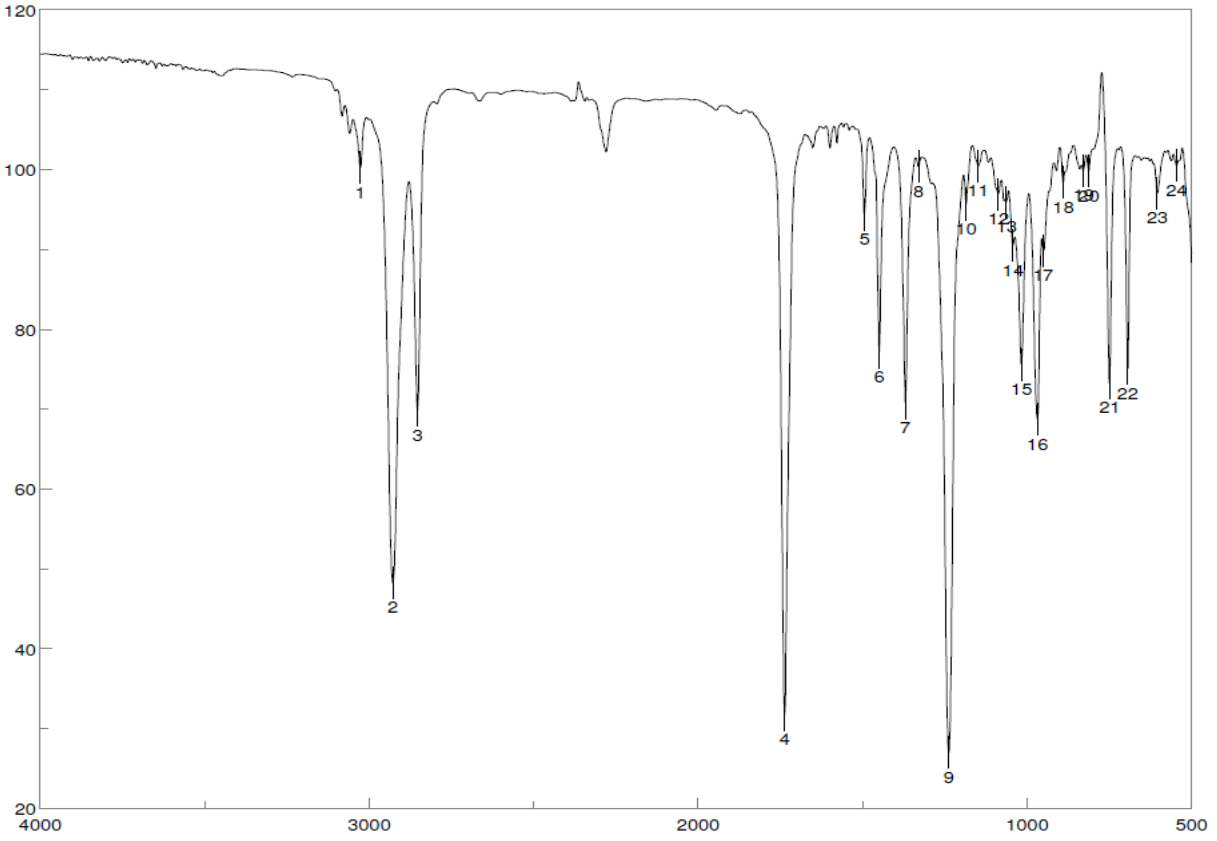

8.39
8.39
8.38
8.37
8.37
8.36
8.36
8.35
7.69
7.35
7.34
7.34
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.29
7.29
7.28
3.83
2.52
O
CH3
N
CH3
E (m)
7.32
C (m)
8.38
D (s)
7.69
B (s)
3.83
A (s)
2.52
0.92
0.90
2.89
2.89
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

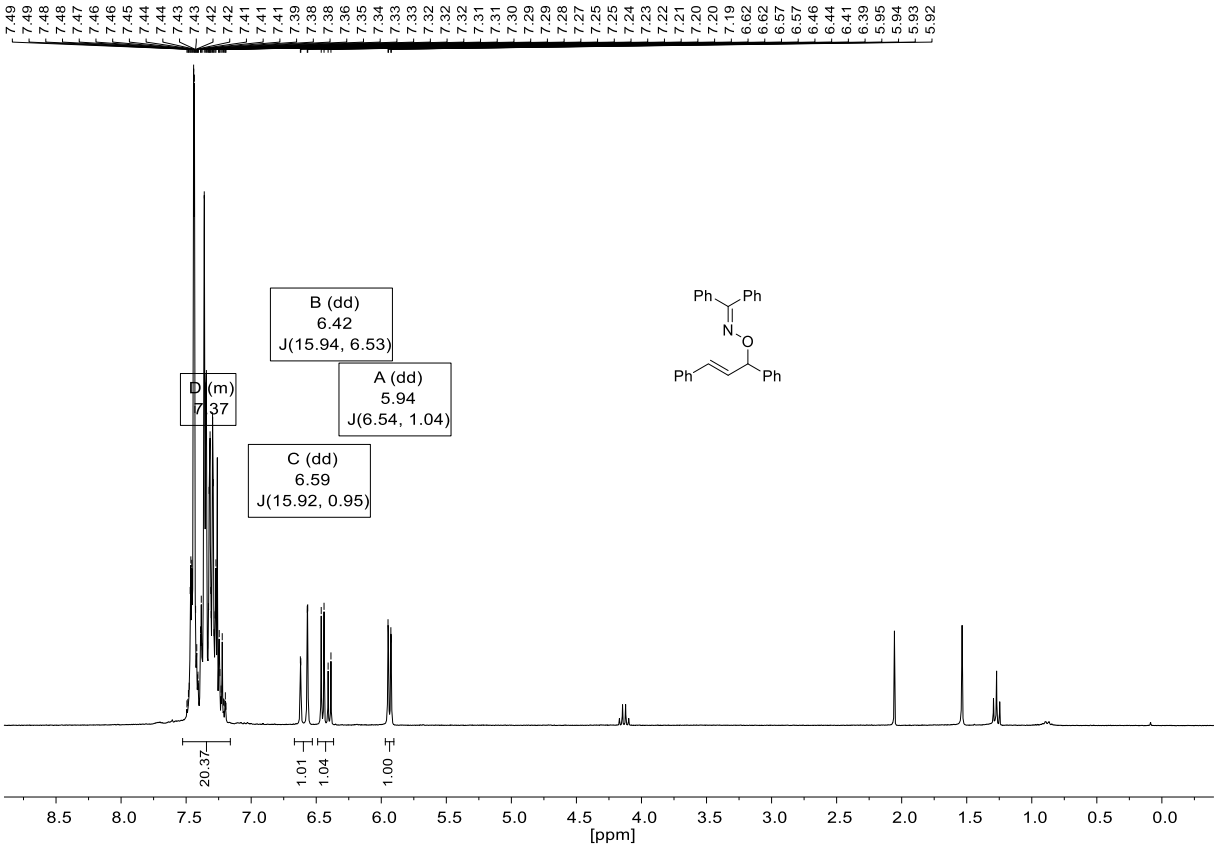

9.99
9.98
8.32
8.32
8.31
8.30
8.29
8.29
7.66
7.66
7.38
7.37
7.37
7.37
7.36
7.36
7.35
7.35
7.34
7.33
7.33
7.31
7.30
3.87
3.86
O
H
N
CH3
D (m)
7.34
A (s)
9.98
B (m)
8.30
C (s)
7.66
E (s)
3.86
1.00
0.99
1.06
3.17
3.13
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

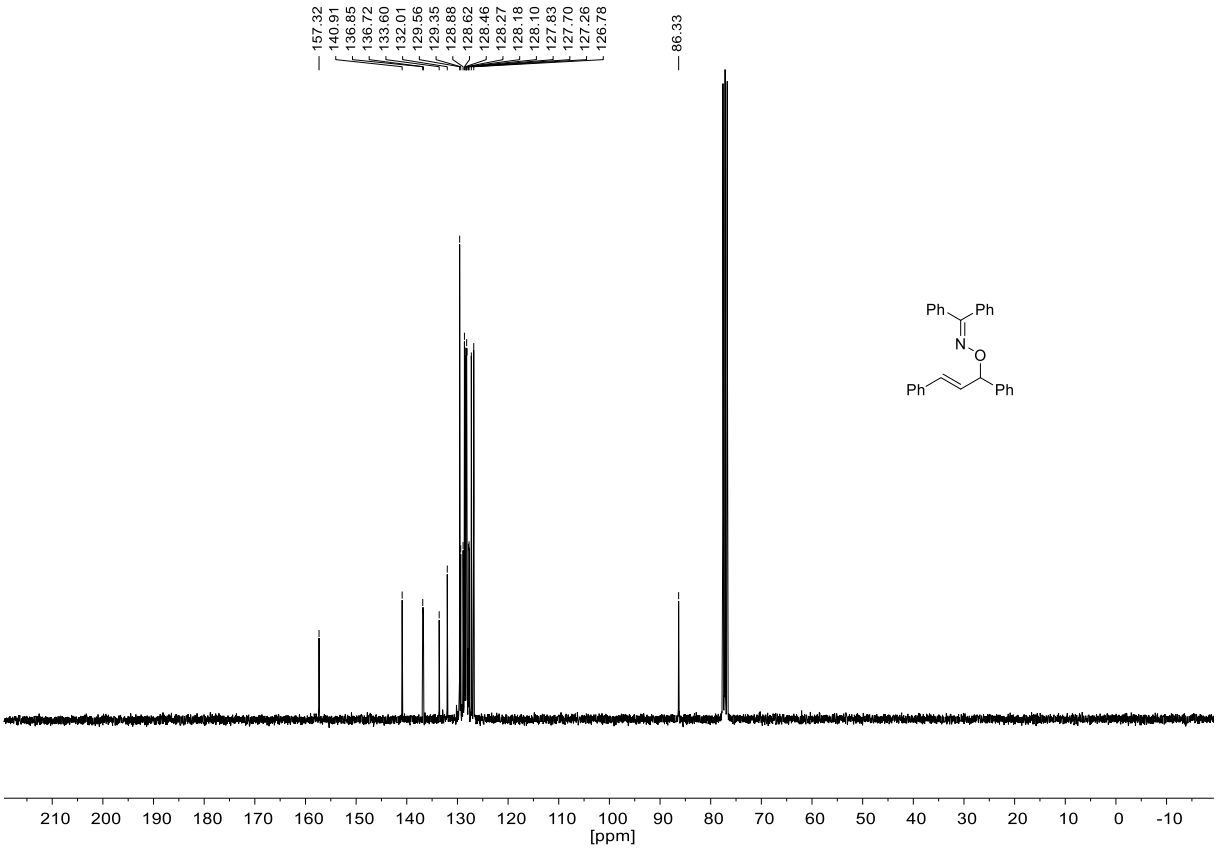

F (t)
7.83
J(1.67)
D (d)
8.07
J(15.55)
C (ddd)
8.57
J(6.93, 3.15, 1.77)
G (m)
7.35
E (q)
8.02
J(3.29, 2.68)
B (s)
3.84
A (s)
3.78
MeN
NMe
O
[ppm]

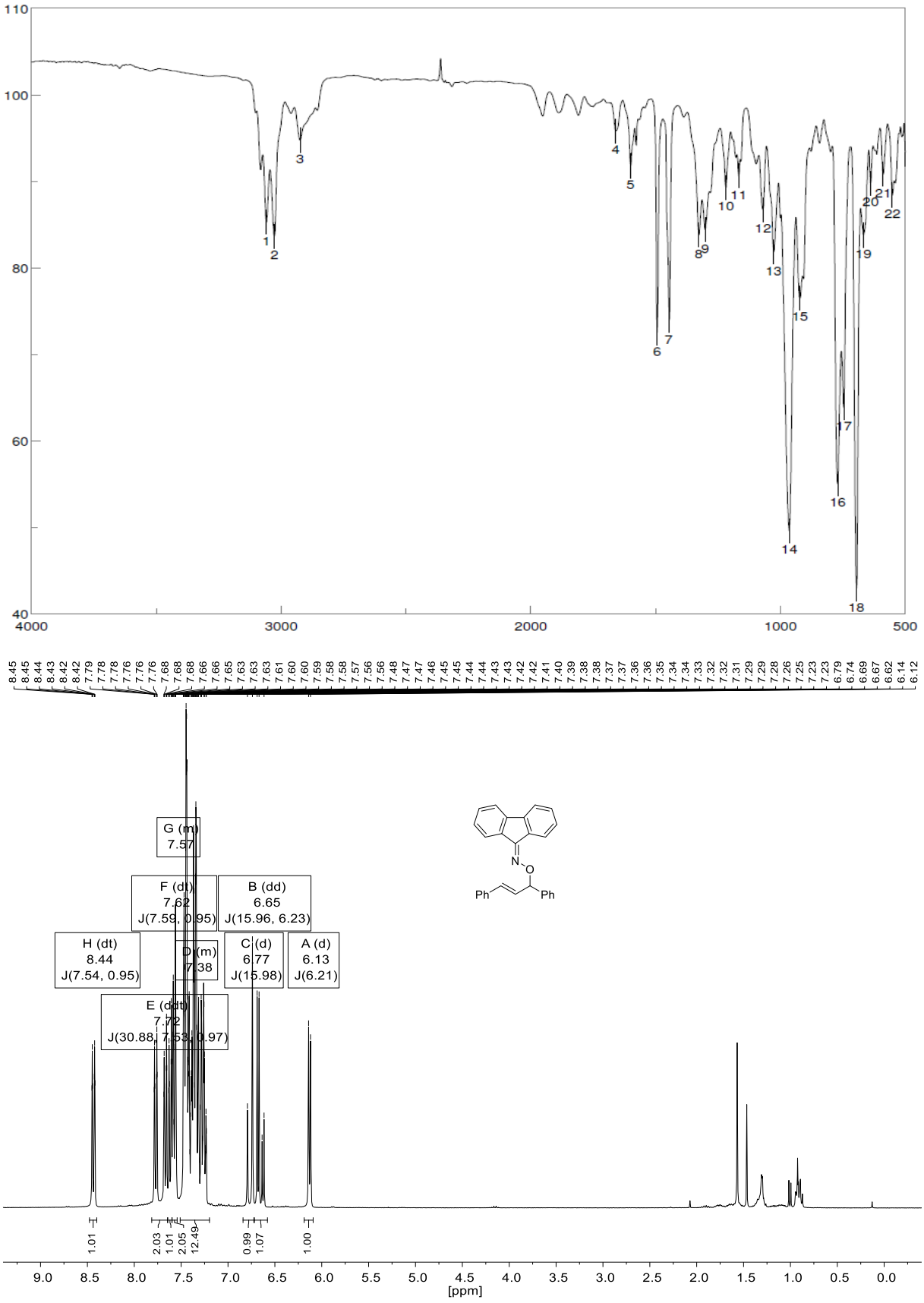

F (s)
6.56
B (d)
8.56
J(15.55)
D (d)
7.69
J(15.50)
A (dt)
9.28
J(8.00, 1.03)
C (m)
8.21
E (dt)
6.93
J(8.12, 0.93)
H (s)
2.74
G (s)
2.78
I (m)
7.27
OH
MeN
NMe
[ppm]

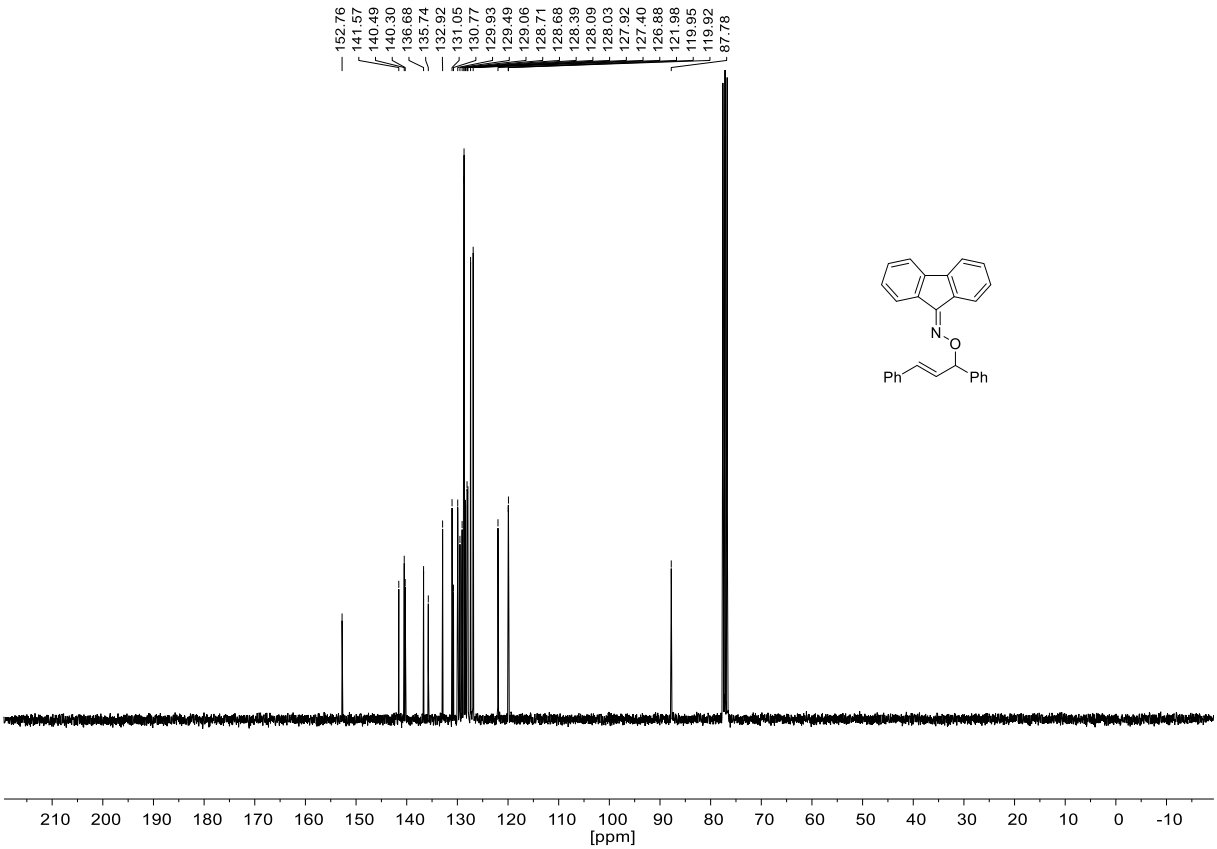

D (m)
7.08
B (dd)
6.11
J(15.93, 7.84)
E (m)
7.22
C (d)
6.64
J(15.89)
A (td)
5.42
J(7.84, 6.95, 0.96)
OAc
H (m)
1.79
G (s)
1.75
F (m)
1.02
I (m)
1.61
1.95
3.02
0.84
0.95
1.00
0.57
2.85
5.50
5.04
[ppm]

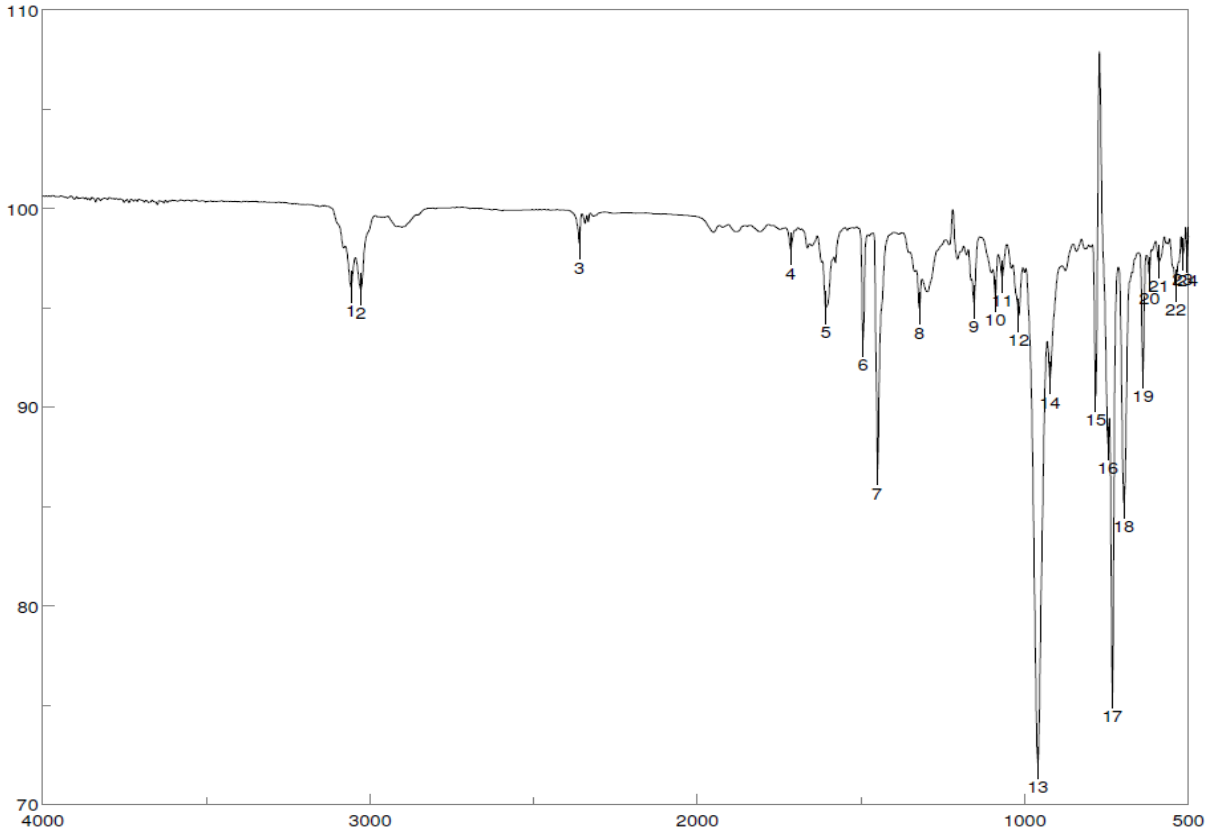

%T
cm-1

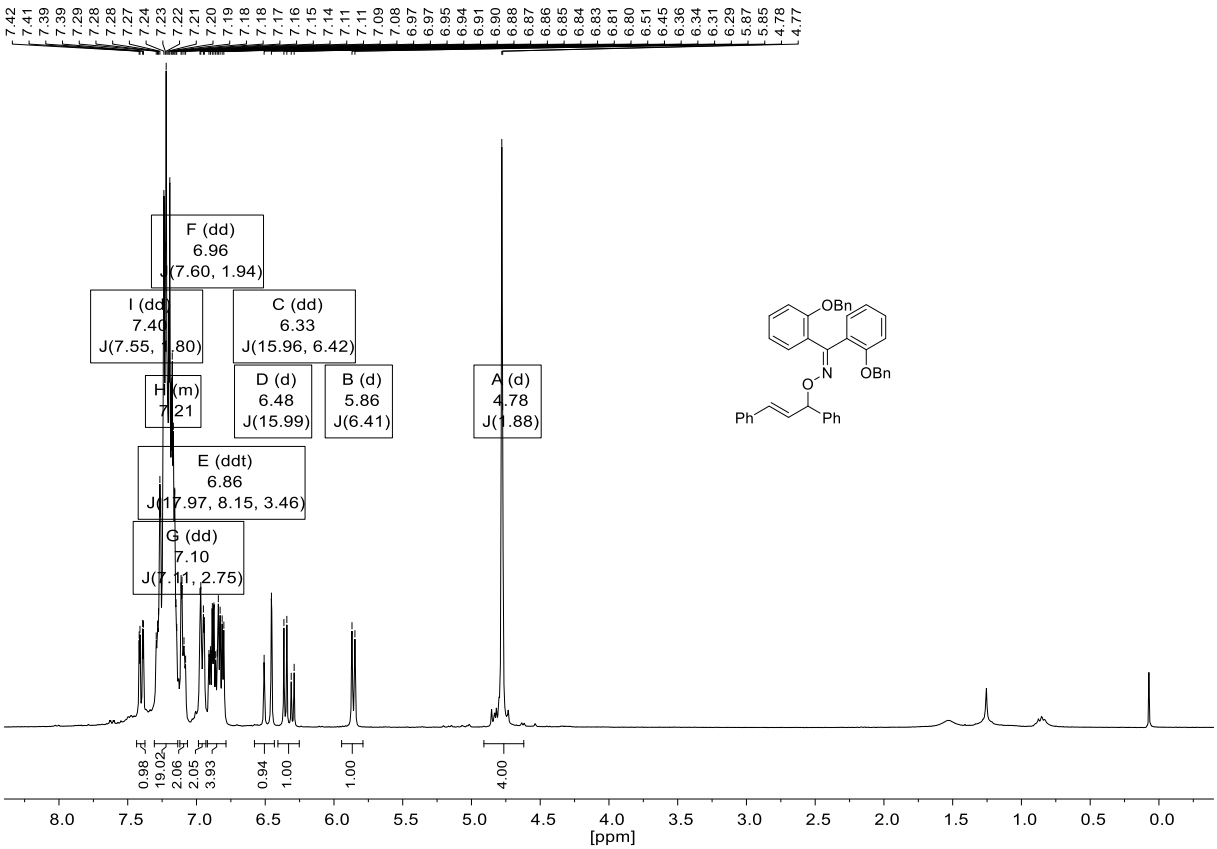

B (dd)
6.42
J(15.94, 6.53)
A (dd)
5.94
J(6.54, 1.04)
C (dd)
6.59
J(15.92, 0.95)
D (m)
7.37
20.37
1.01
1.04
1.00
[ppm]

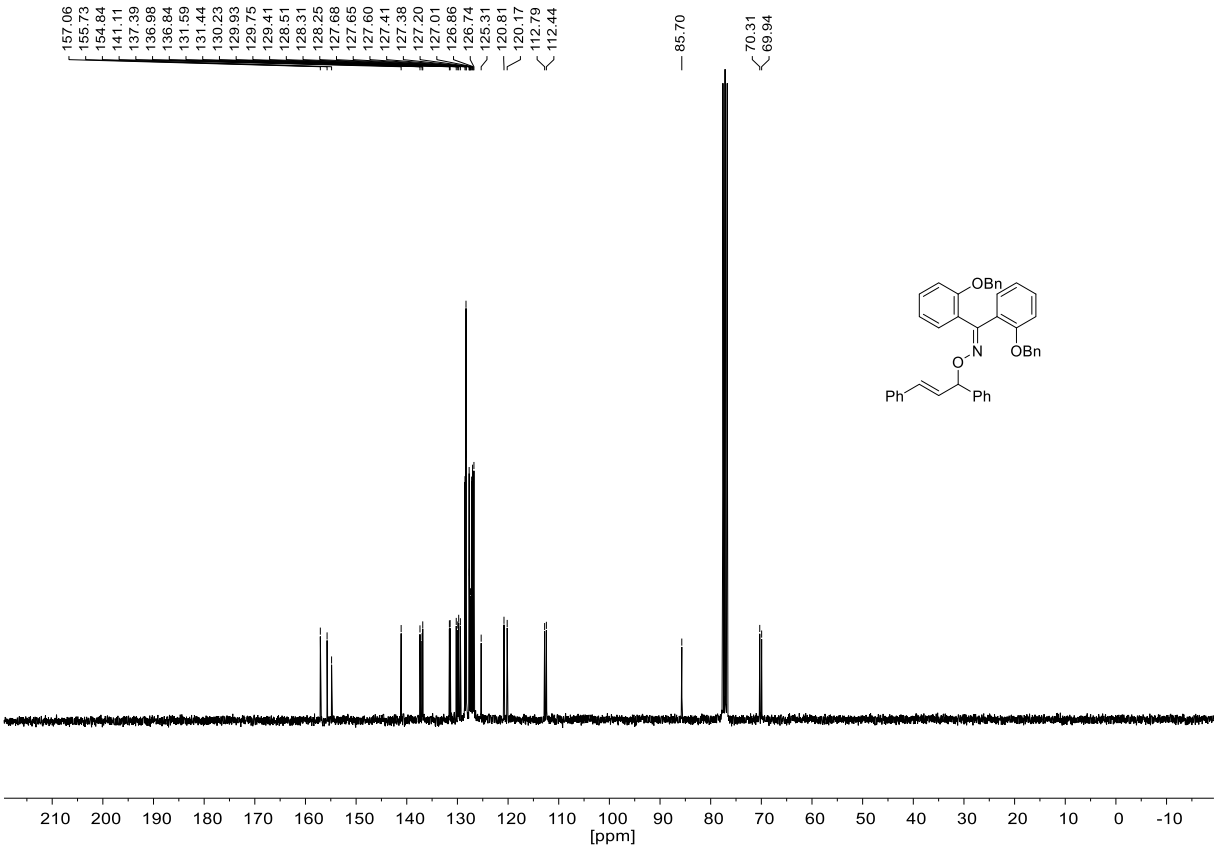

157.32
140.91
136.85
136.72
133.60
132.01
129.56
129.35
128.88
128.62
128.46
128.27
128.18
128.10
127.83
127.70
127.26
126.78
86.33
[ppm]

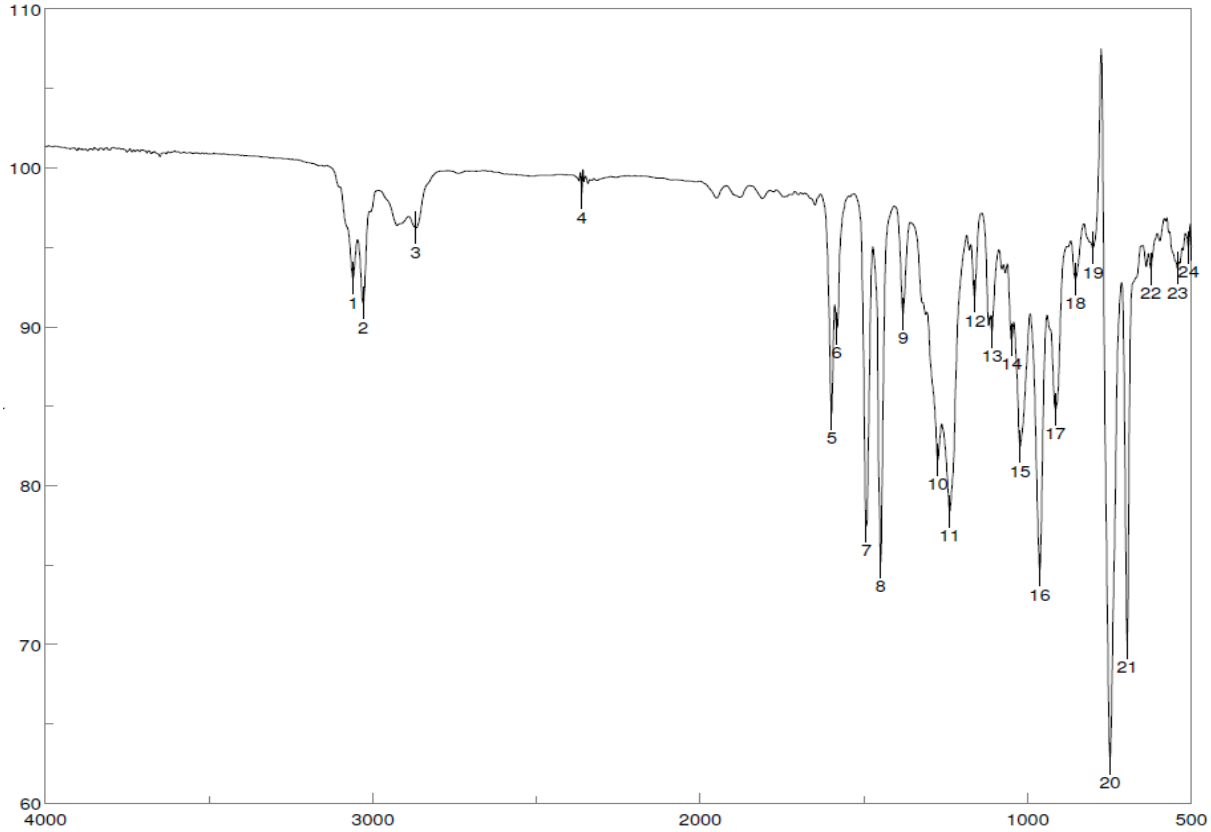

110
100
80
60
40
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
G (m)
7.57
F (dt)
7.62
J(7.59, 0.95)
B (dd)
6.65
J(15.96, 6.23)
H (dt)
8.44
J(7.54, 0.95)
D (m)
7.38
C (d)
6.77
J(15.98)
A (d)
6.13
J(6.21)
E (ddt)
7.72
J(30.88, 7.53, 0.97)
N
O
Ph
Ph
1.01
2.03
1.01
2.05
12.49
0.99
1.07
1.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

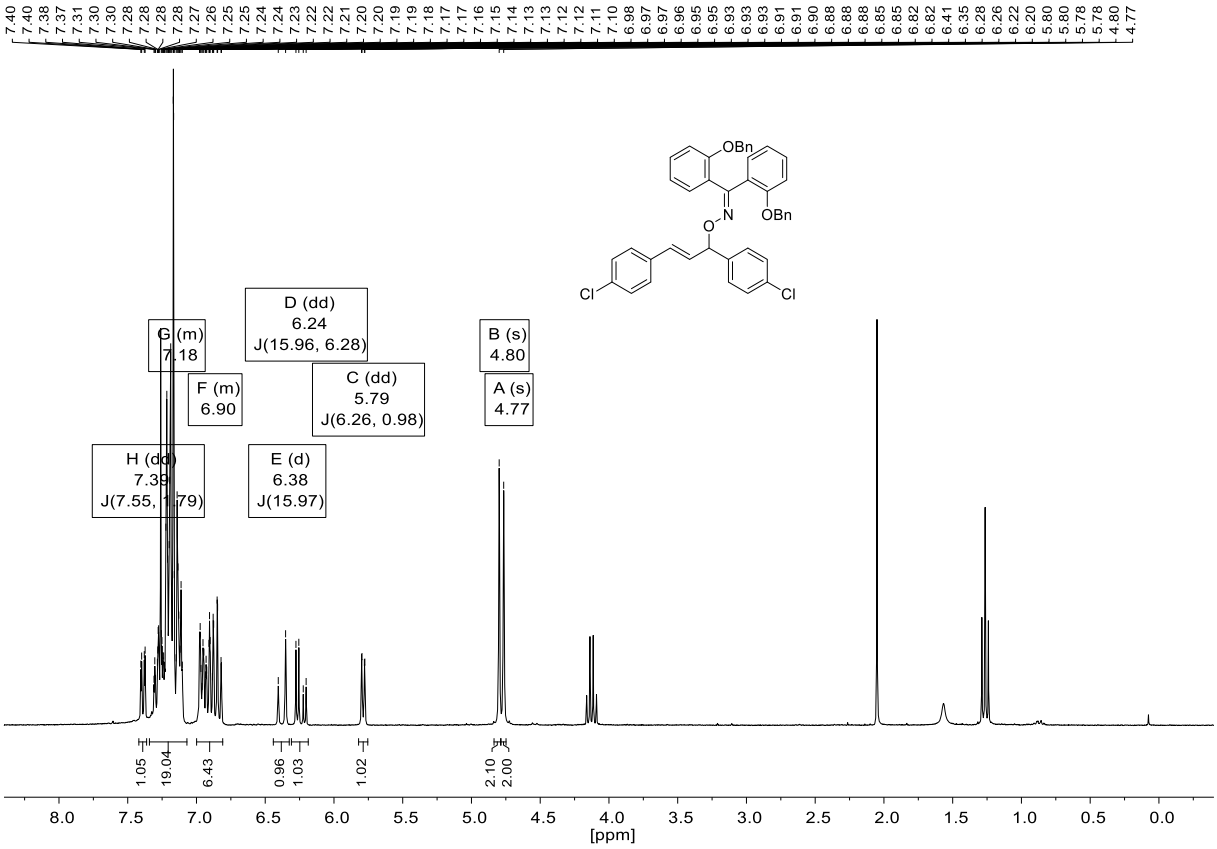

152.76
141.57
140.49
140.30
136.68
135.74
132.92
131.05
130.77
129.93
129.49
129.06
128.71
128.68
128.39
128.09
128.03
127.92
127.40
126.88
121.98
119.95
119.92
87.78
N
O
Ph
Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

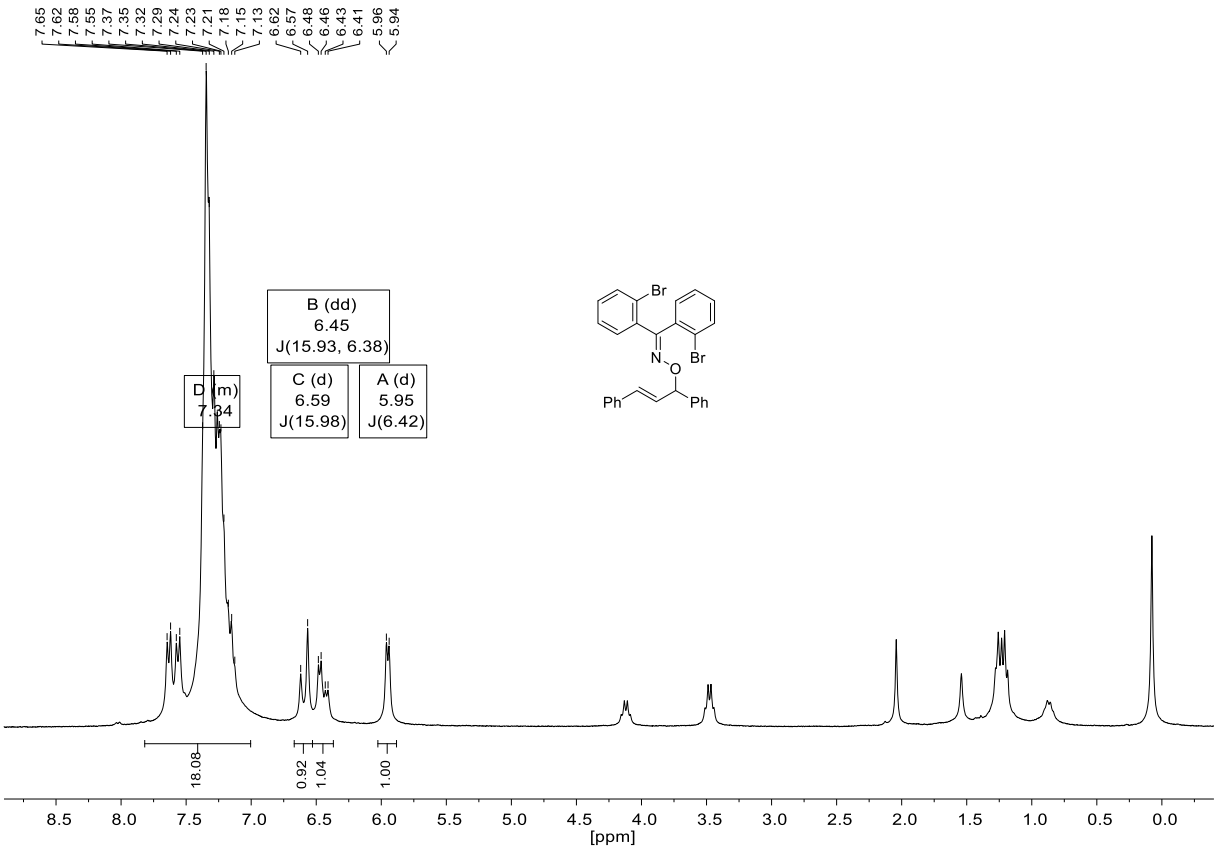

110
100
90
80
70
4000
3000
2000
1000
500
12
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

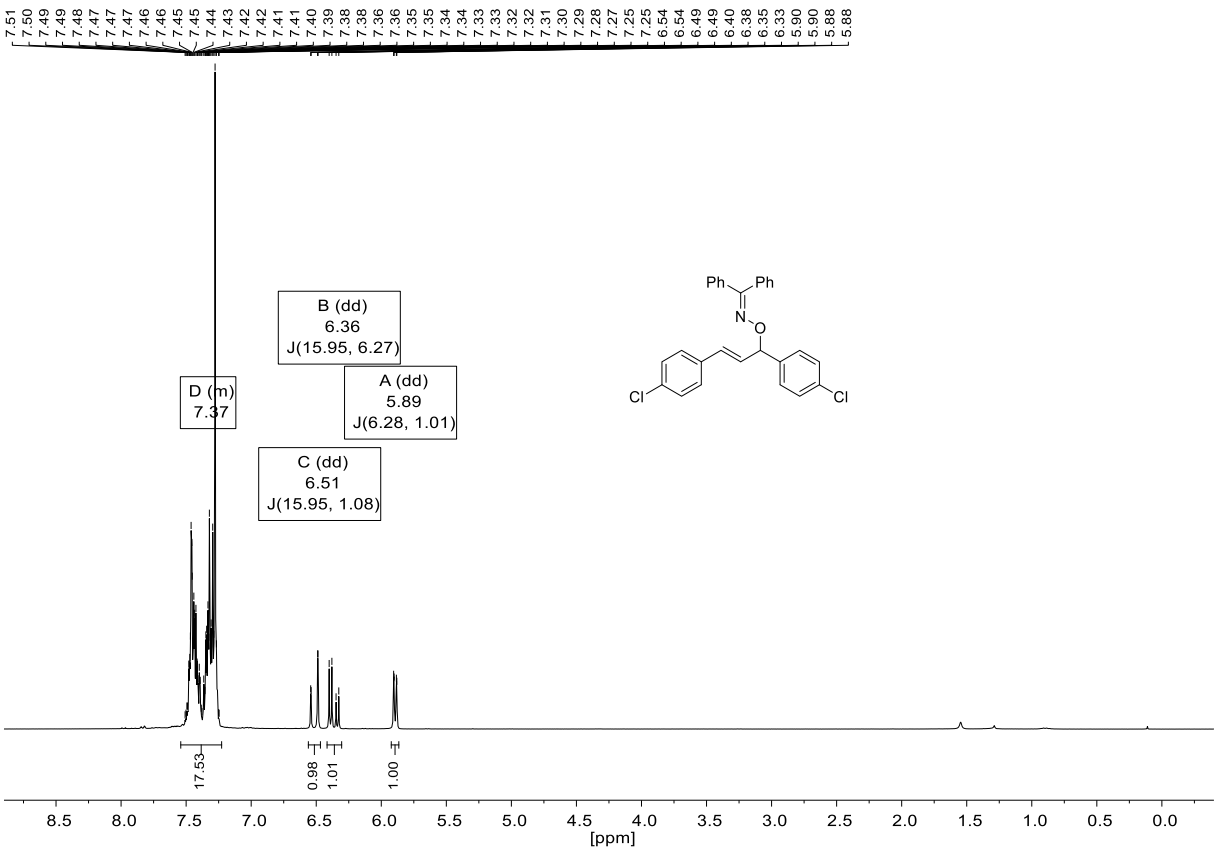

F (dd)
6.96
J(7.60, 1.94)
I (dd)
7.40
C (dd)
6.33
J(15.96, 6.42)
H (m)
7.21
D (d)
6.48
J(15.99)
B (d)
5.86
J(6.41)
A (d)
4.78
J(1.88)
E (ddt)
6.86
G (dd)
7.10
J(7.11, 2.75)
OBn
N
O
OBn
Ph
Ph
[ppm]

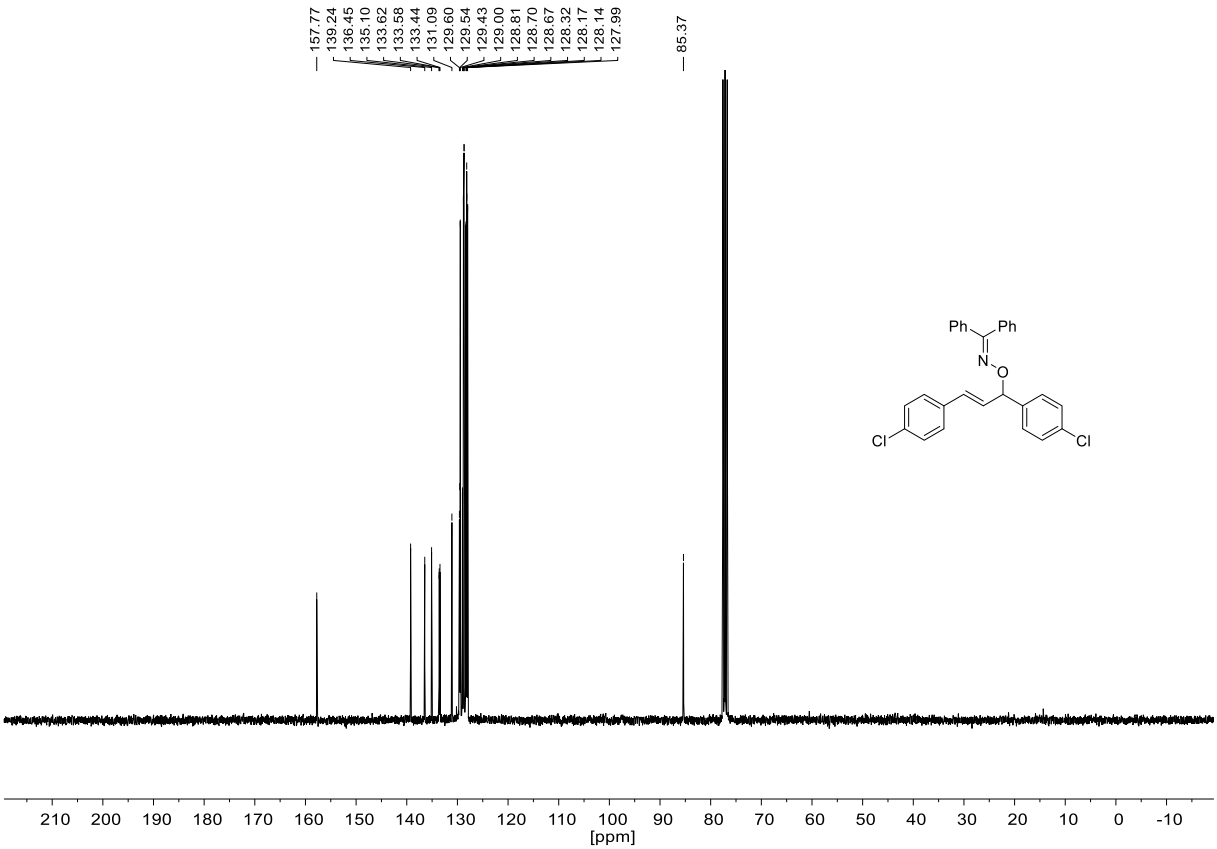

85.70
70.31
69.94
OBn
N
O
OBn
Ph
Ph
[ppm]

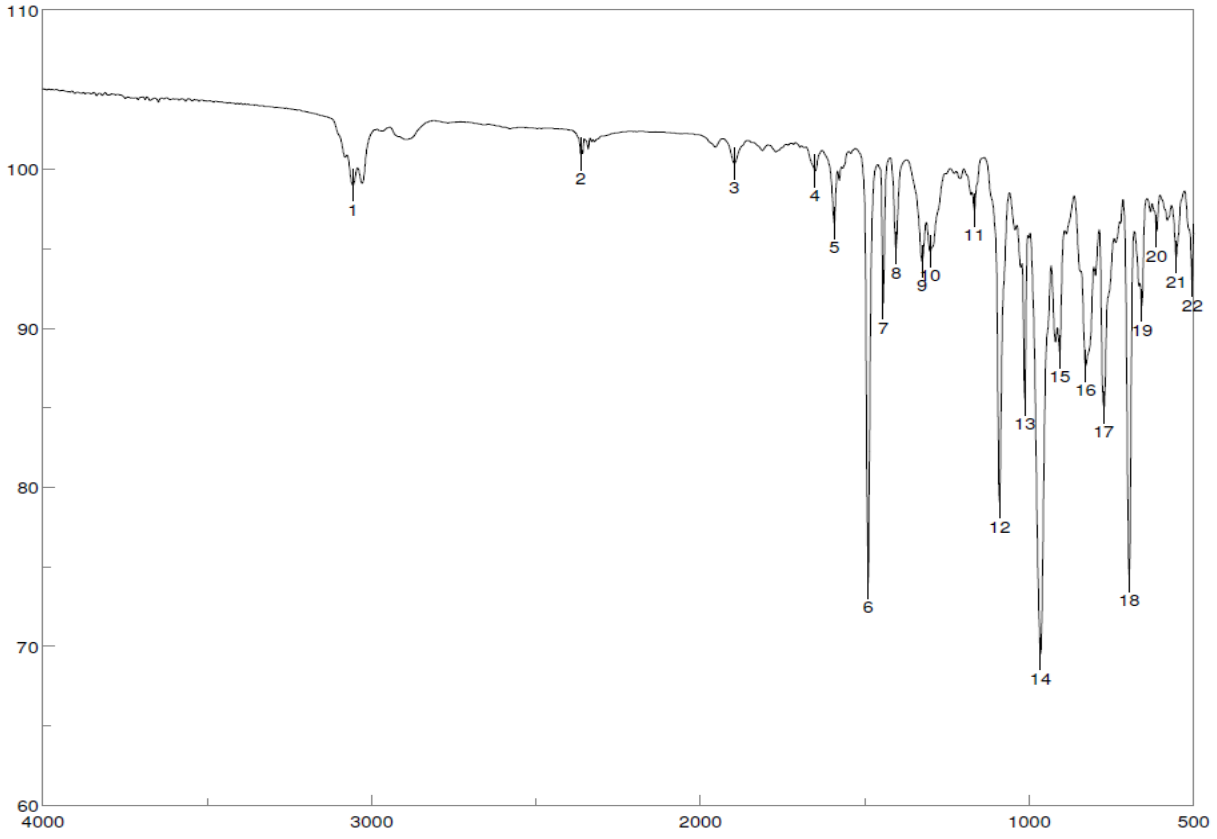

110
100
90
80
70
60
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24

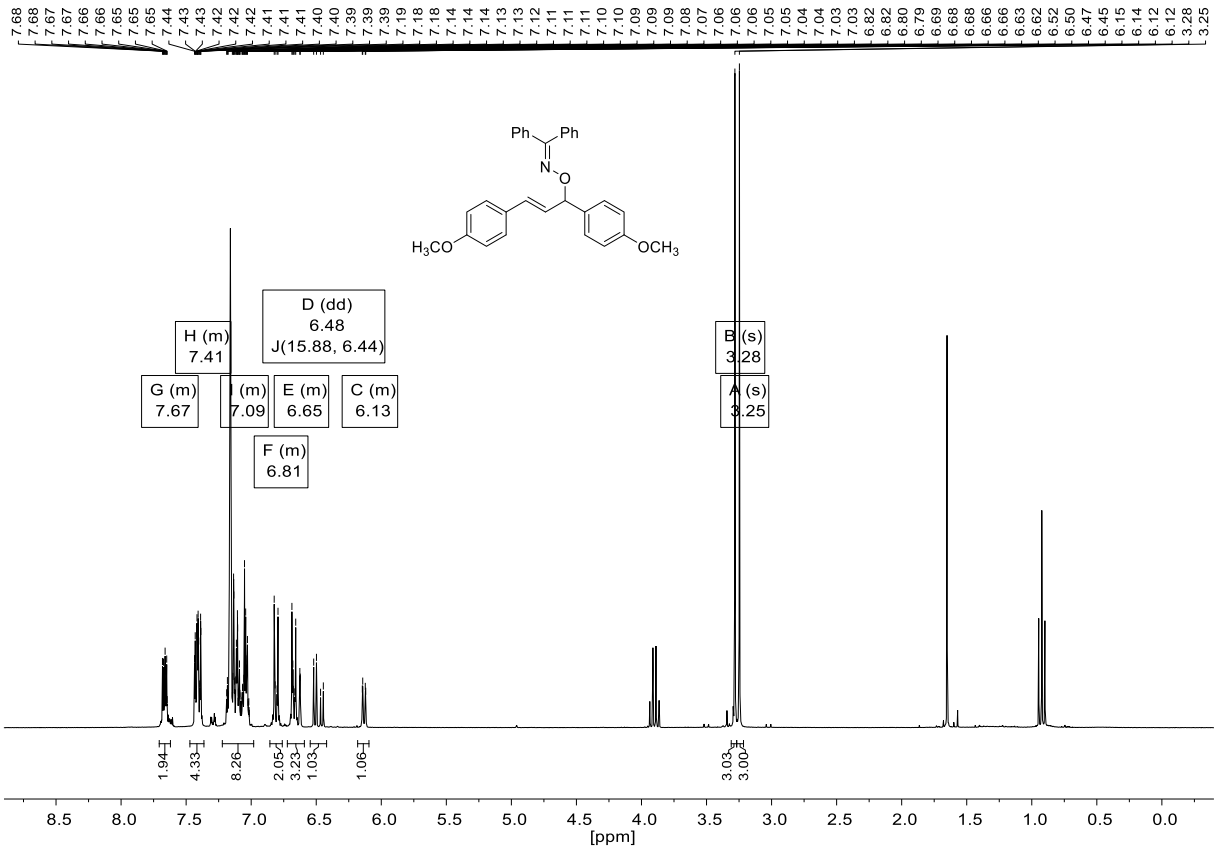

OBn
OBn
N
O
Cl
Cl
G (m)
7.18
F (m)
6.90
D (dd)
6.24
J(15.96, 6.28)
C (dd)
5.79
J(6.26, 0.98)
B (s)
4.80
A (s)
4.77
H (dd)
7.39
J(7.55, 1.79)
E (d)
6.38
J(15.97)
1.05
19.04
6.43
0.96
1.03
1.02
2.10
2.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

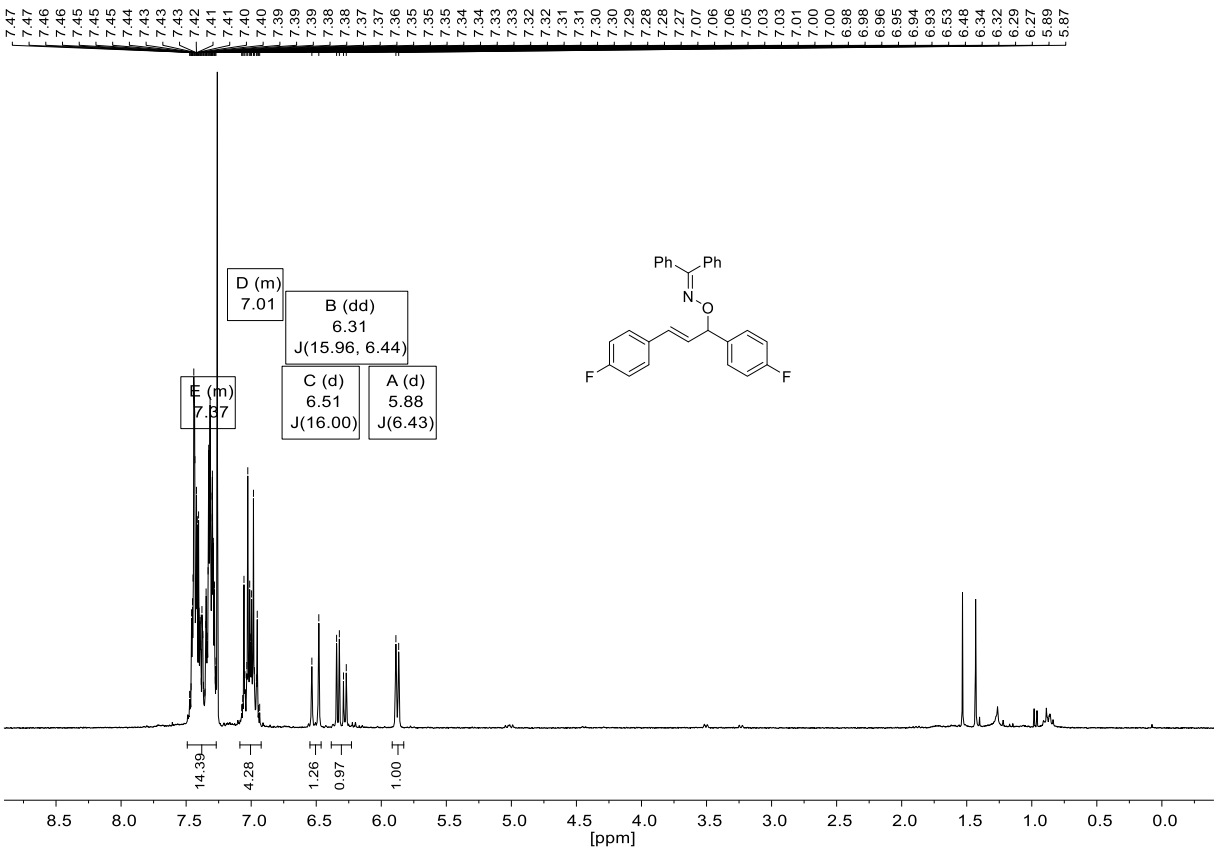

7.65
7.62
7.58
7.55
7.37
7.35
7.32
7.29
7.24
7.23
7.21
7.18
7.15
7.13
6.62
6.57
6.48
6.46
6.43
6.41
5.96
5.94
B (dd)
6.45
J(15.93, 6.38)
C (d)
6.59
J(15.98)
A (d)
5.95
J(6.42)
D (m)
7.34
Br
N
O
Br
Ph
Ph
18.08
0.92
1.04
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

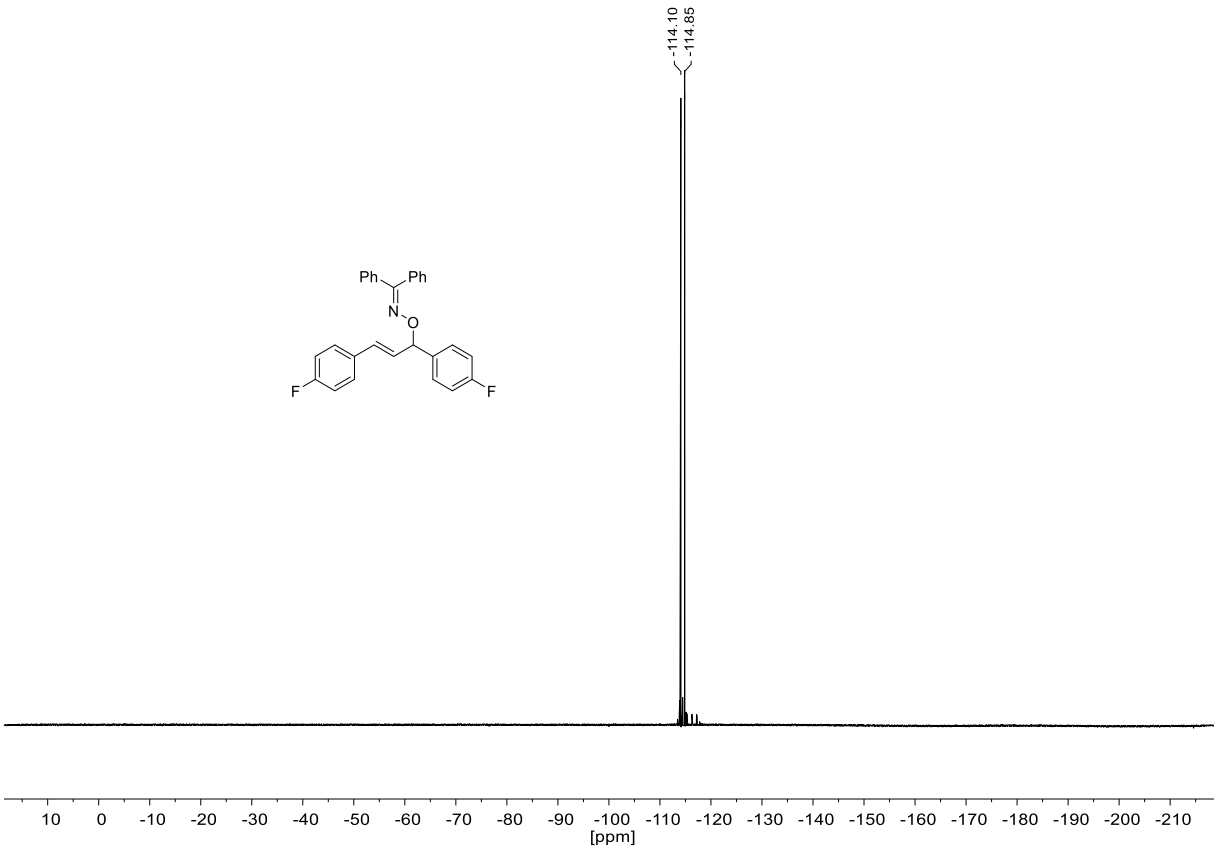

7.51
7.50
7.49
7.49
7.48
7.47
7.47
7.46
7.46
7.45
7.45
7.44
7.43
7.42
7.42
7.41
7.41
7.40
7.39
7.38
7.38
7.36
7.36
7.35
7.35
7.34
7.34
7.33
7.33
7.32
7.32
7.31
7.30
7.29
7.28
7.27
7.25
7.25
6.54
6.54
6.49
6.49
6.40
6.38
6.35
6.33
5.90
5.90
5.88
5.88
B (dd)
6.36
J(15.95, 6.27)
A (dd)
5.89
J(6.28, 1.01)
C (dd)
6.51
J(15.95, 1.08)
D (m)
7.37
Ph
Ph
N
O
Cl
Cl
17.53
0.98
1.01
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

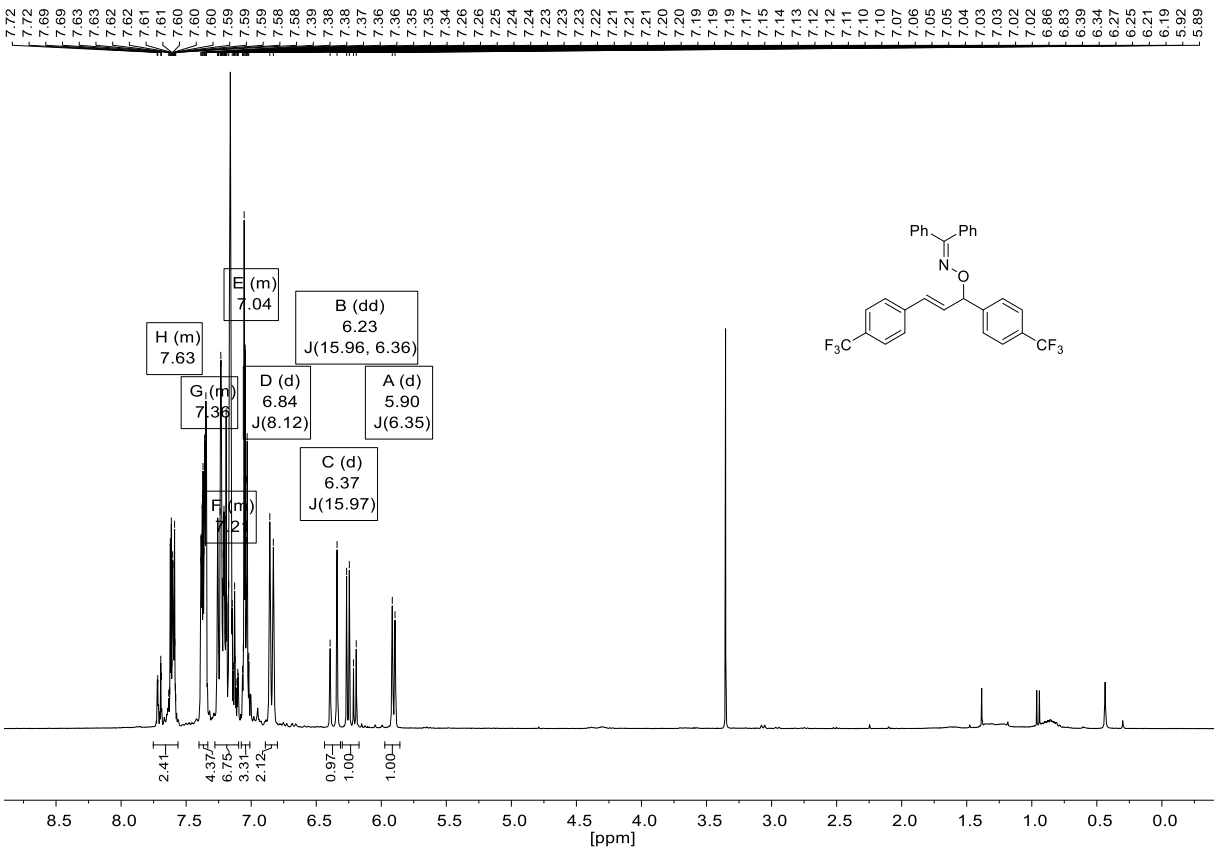

157.77
139.24
136.45
135.10
133.62
133.58
133.44
131.09
129.60
129.54
129.43
129.00
128.81
128.70
128.67
128.32
128.17
128.14
127.99
85.37
Ph
Ph
N
O
Cl
Cl
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]

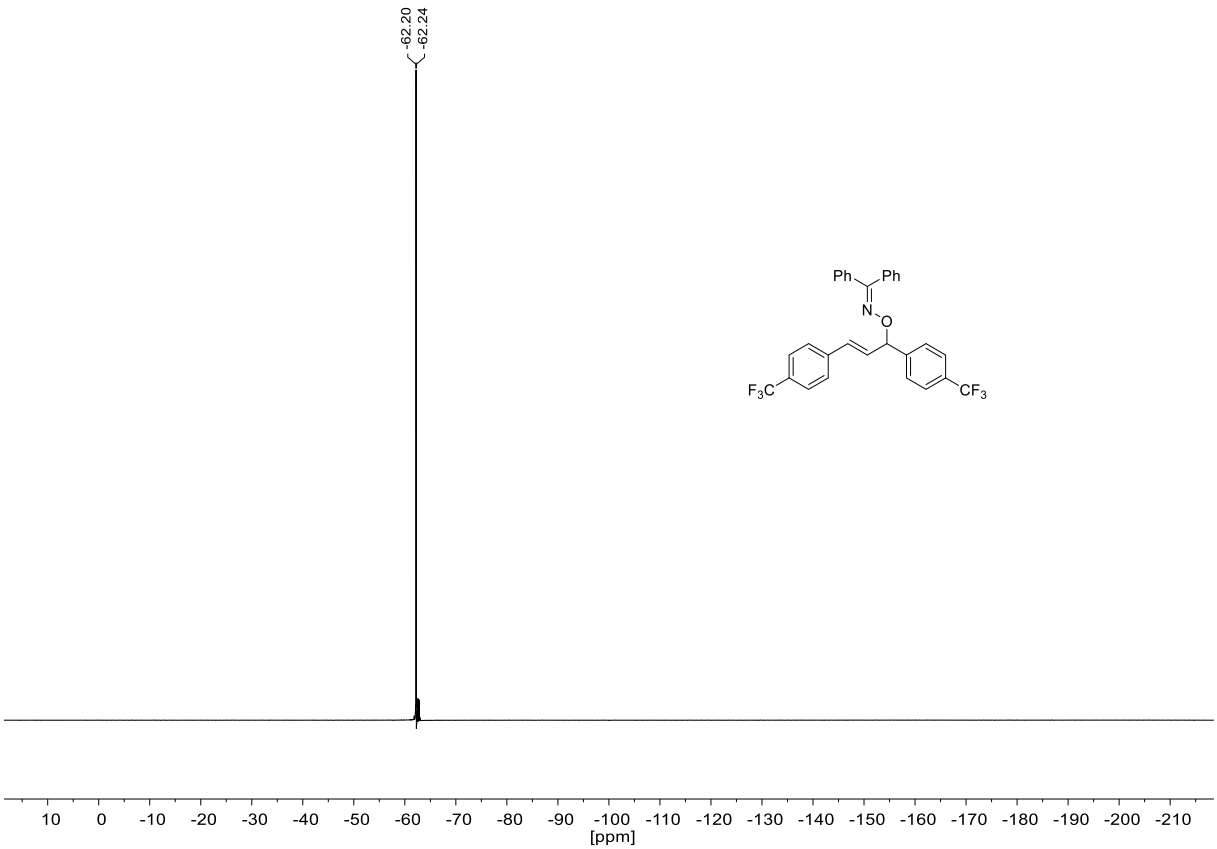

110
100
90
80
70
60
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

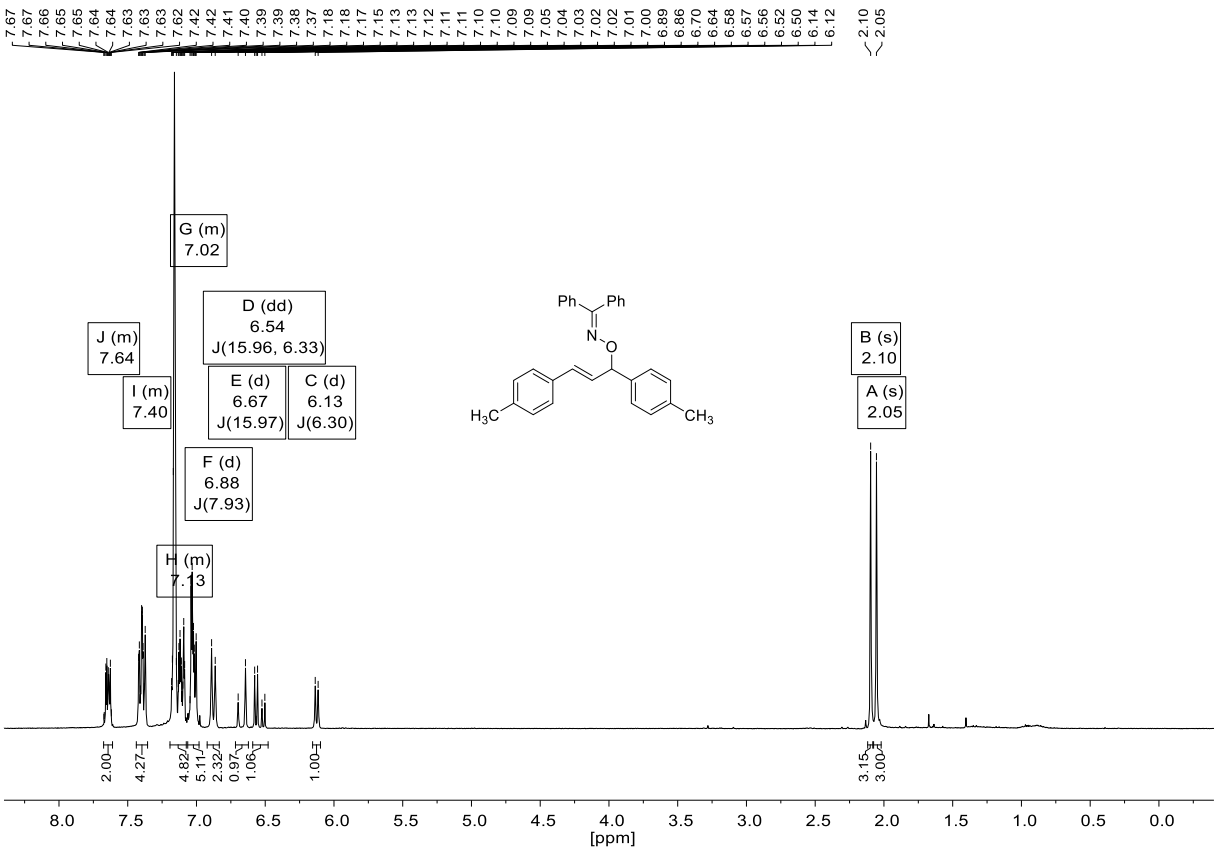

Ph
Ph
N
O
H3CO
OCH3
D (dd)
6.48
J(15.88, 6.44)
H (m)
7.41
G (m)
7.67
I (m)
7.09
E (m)
6.65
C (m)
6.13
F (m)
6.81
B (s)
3.28
A (s)
3.25
1.94
4.33
8.26
2.05
3.23
1.03
1.06
3.03
3.00
[ppm]

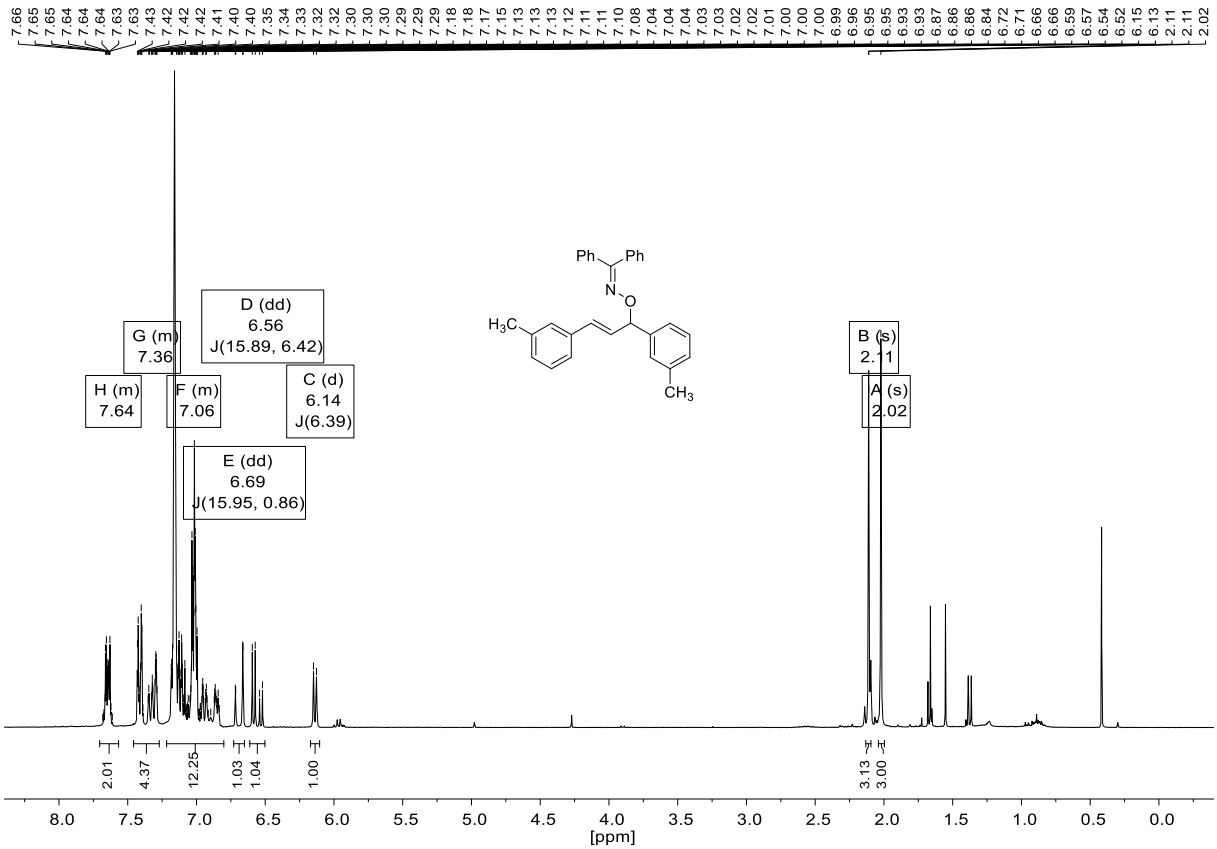

Ph
Ph
N
O
F
F
D (m)
7.01
B (dd)
6.31
J(15.96, 6.44)
E (m)
7.37
C (d)
6.51
J(16.00)
A (d)
5.88
J(6.43)
14.39
4.28
1.26
0.97
1.00
[ppm]

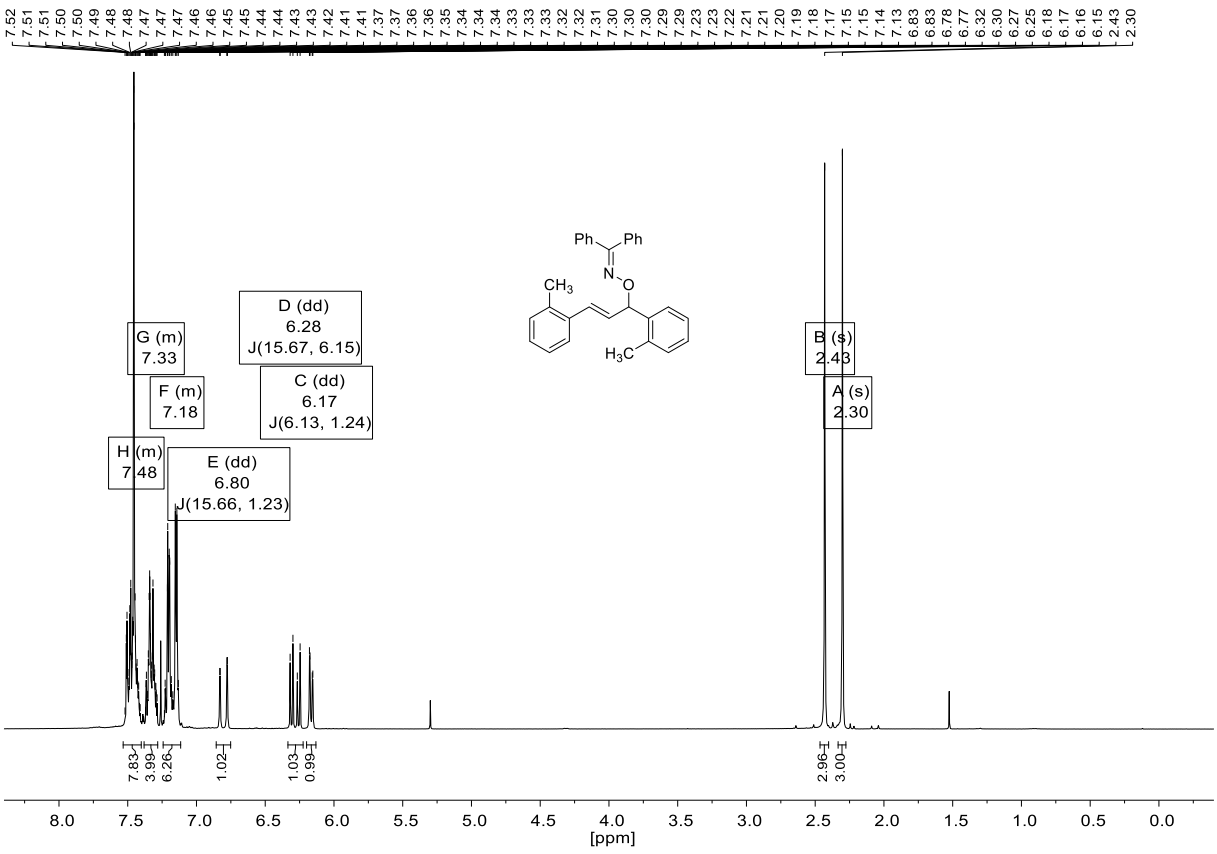

-114.10
-114.85
Ph
Ph
N
O
F
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

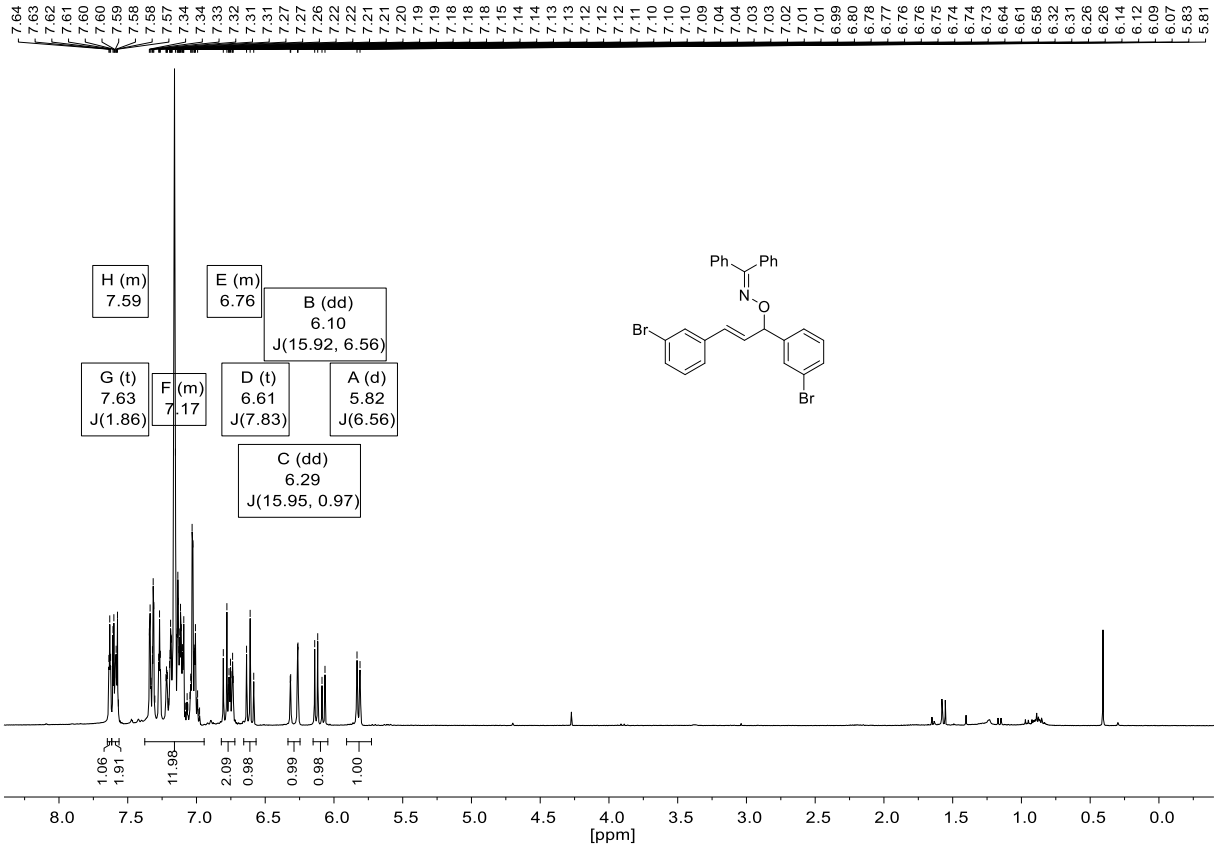

E (m)
7.04
B (dd)
6.23
J(15.96, 6.36)
H (m)
7.63
G1 (m)
7.36
D (d)
6.84
J(8.12)
A (d)
5.90
J(6.35)
C (d)
6.37
J(15.97)
F (m)
7.2
Ph
Ph
N
O
F3C
CF3
2.41
4.37
6.75
3.31
2.12
0.97
1.00
1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

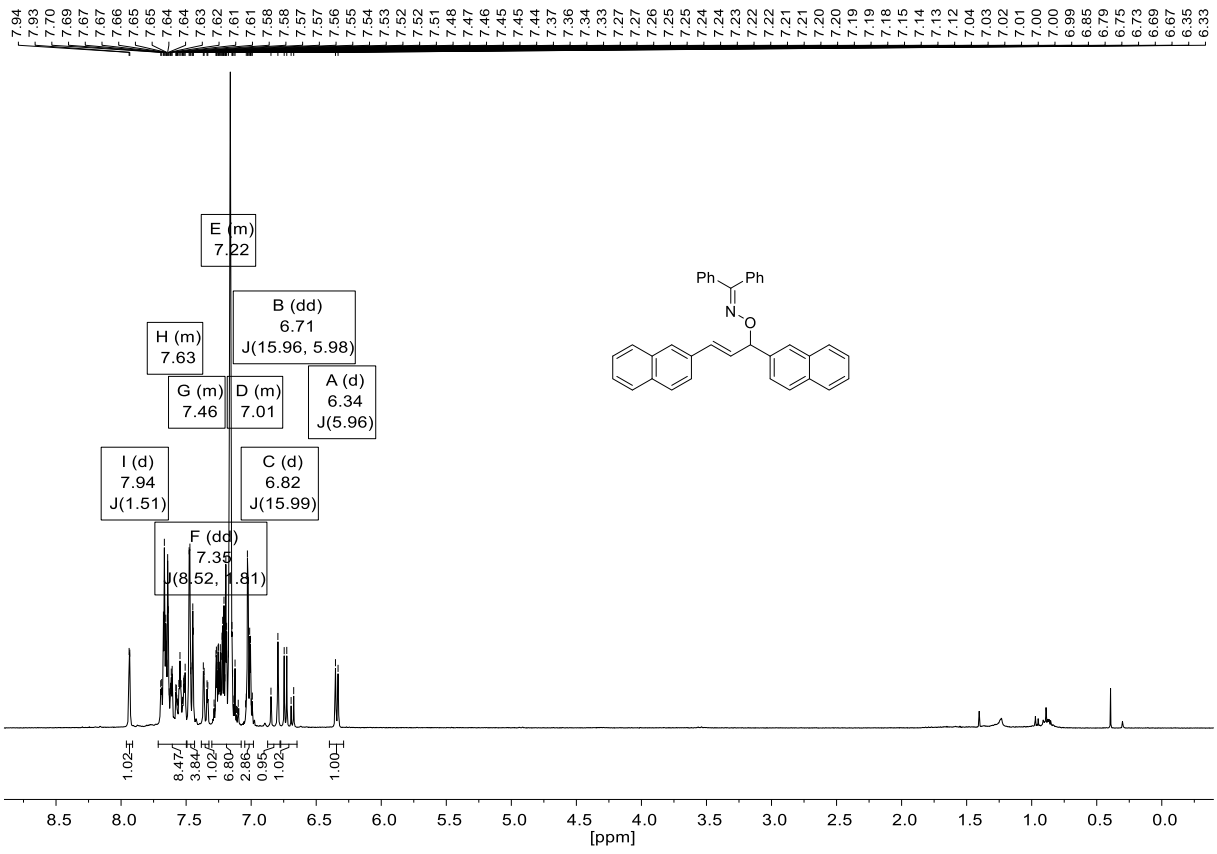

-62.20
-62.24
Ph
Ph
N
O
F3C
CF3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

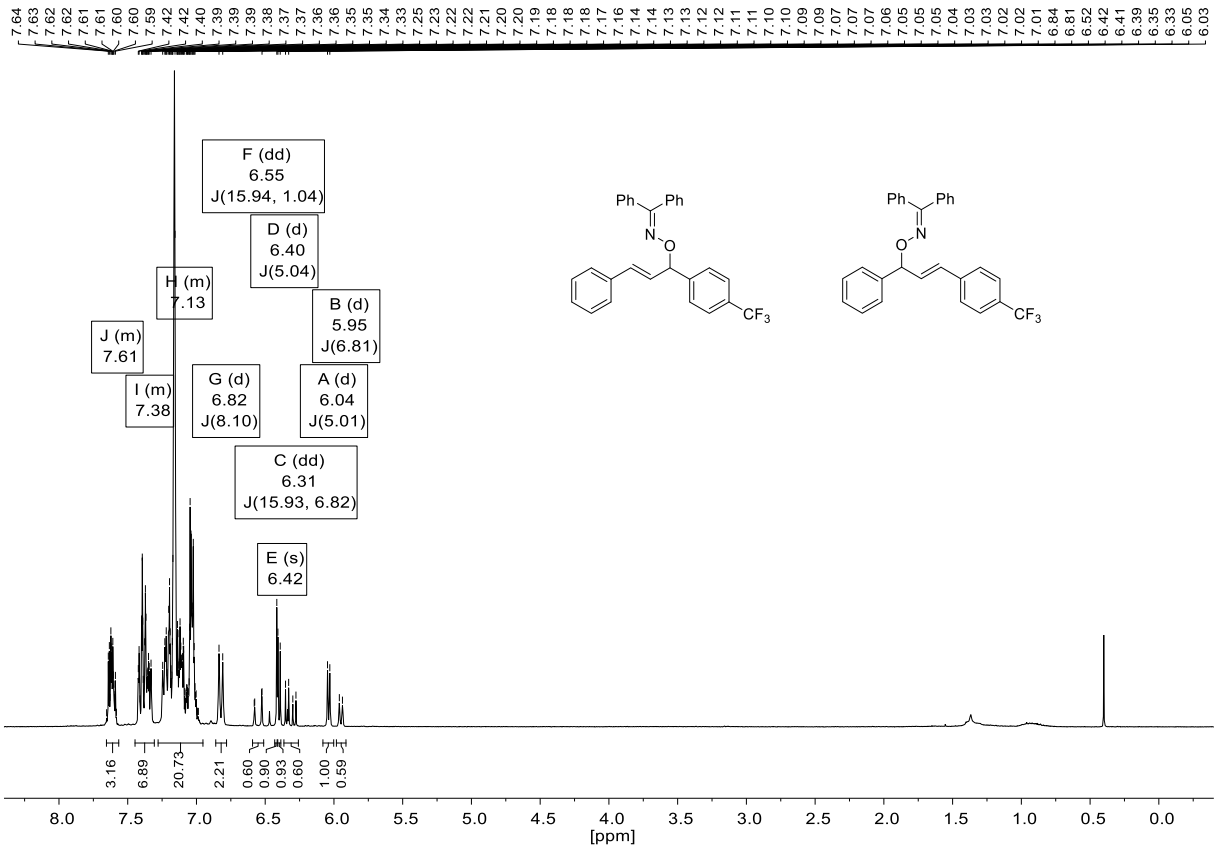

7.67 7.67 7.66 7.65 7.65 7.64 7.64 7.63 7.63 7.63 7.62 7.42 7.42 7.41 7.40 7.39 7.39 7.38 7.37 7.18 7.18 7.17 7.15 7.13 7.13 7.12 7.11 7.11 7.10 7.10 7.09 7.09 7.05 7.04 7.03 7.02 7.02 7.01 7.00 6.89 6.86 6.70 6.64 6.58 6.57 6.56 6.52 6.50 6.14 6.12 2.10 2.05
G (m) 7.02
D (dd) 6.54 J(15.96, 6.33)
J (m) 7.64
I (m) 7.40
E (d) 6.67 J(15.97)
C (d) 6.13 J(6.30)
F (d) 6.88 J(7.93)
H (m) 7.13
Ph
Ph
N
O
H3C
CH3
B (s) 2.10
A (s) 2.05
2.00 4.27 4.82 5.11 2.32 0.97 1.06 1.00 3.15 3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

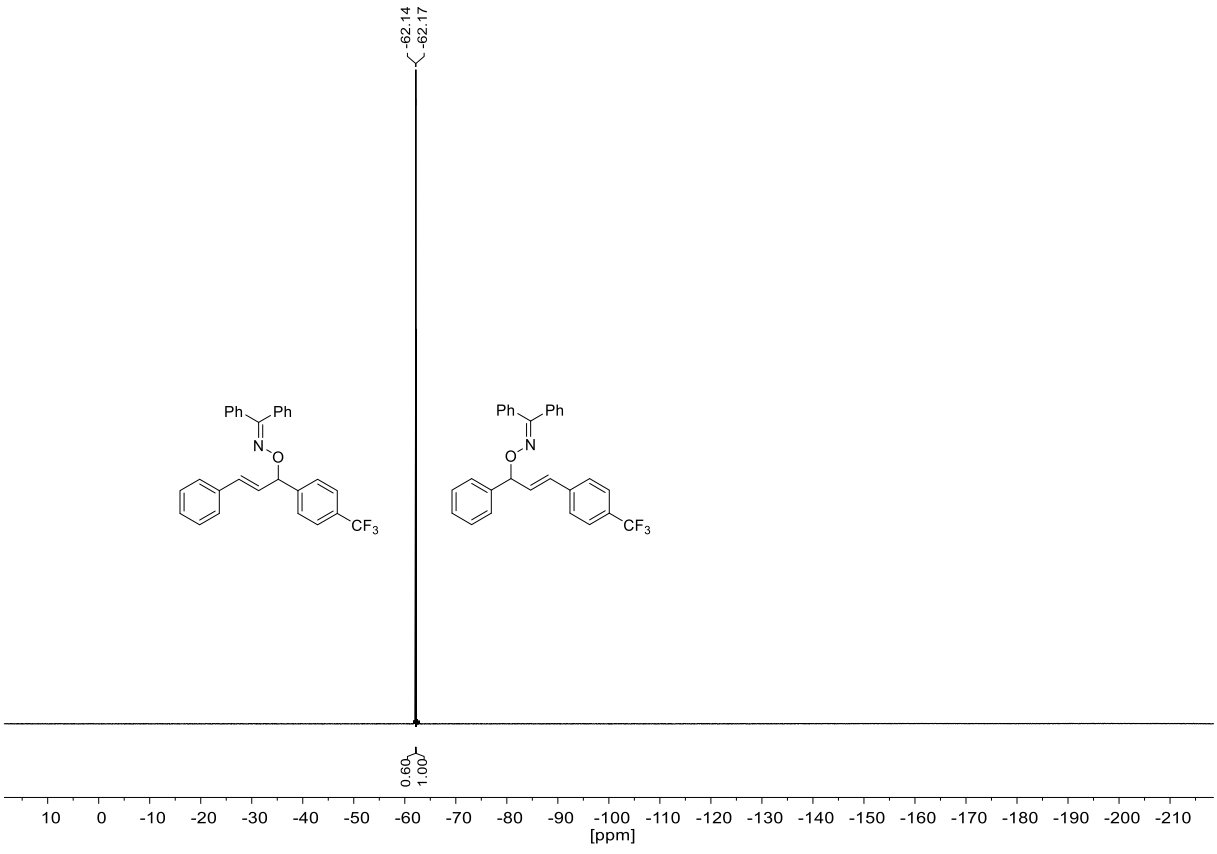

Ph
Ph
N
O
H3C
CH3
G (m)
7.36
D (dd)
6.56
J(15.89, 6.42)
H (m)
7.64
F (m)
7.06
C (d)
6.14
J(6.39)
E (dd)
6.69
J(15.95, 0.86)
B (s)
2.11
A (s)
2.02
2.01
4.37
12.25
1.03
1.04
1.00
3.13
3.00
[ppm]

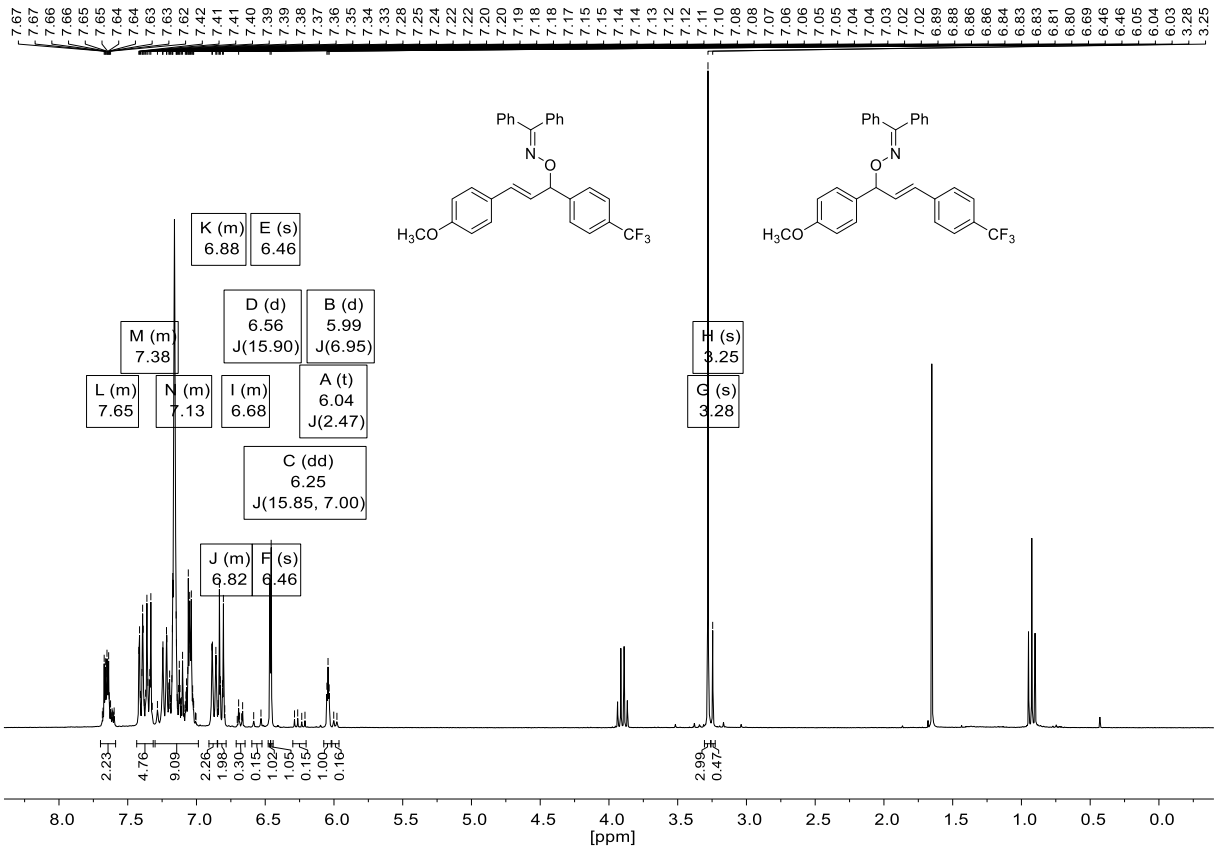

Ph
Ph
N
O
CH3
H3C
G (m)
7.33
D (dd)
6.28
J(15.67, 6.15)
F (m)
7.18
C (dd)
6.17
J(6.13, 1.24)
H (m)
7.48
E (dd)
6.80
J(15.66, 1.23)
B (s)
2.43
A (s)
2.30
7.83
3.99
6.26
1.02
1.03
0.99
2.96
3.00
[ppm]


H (m)
7.59
E (m)
6.76
B (dd)
6.10
J(15.92, 6.56)
G (t)
7.63
J(1.86)
F (m)
7.17
D (t)
6.61
J(7.83)
A (d)
5.82
J(6.56)
C (dd)
6.29
J(15.95, 0.97)
Ph
Ph
N
O
Br
Br
1.06
1.91
11.98
2.09
0.98
0.99
0.98
1.00
[ppm]

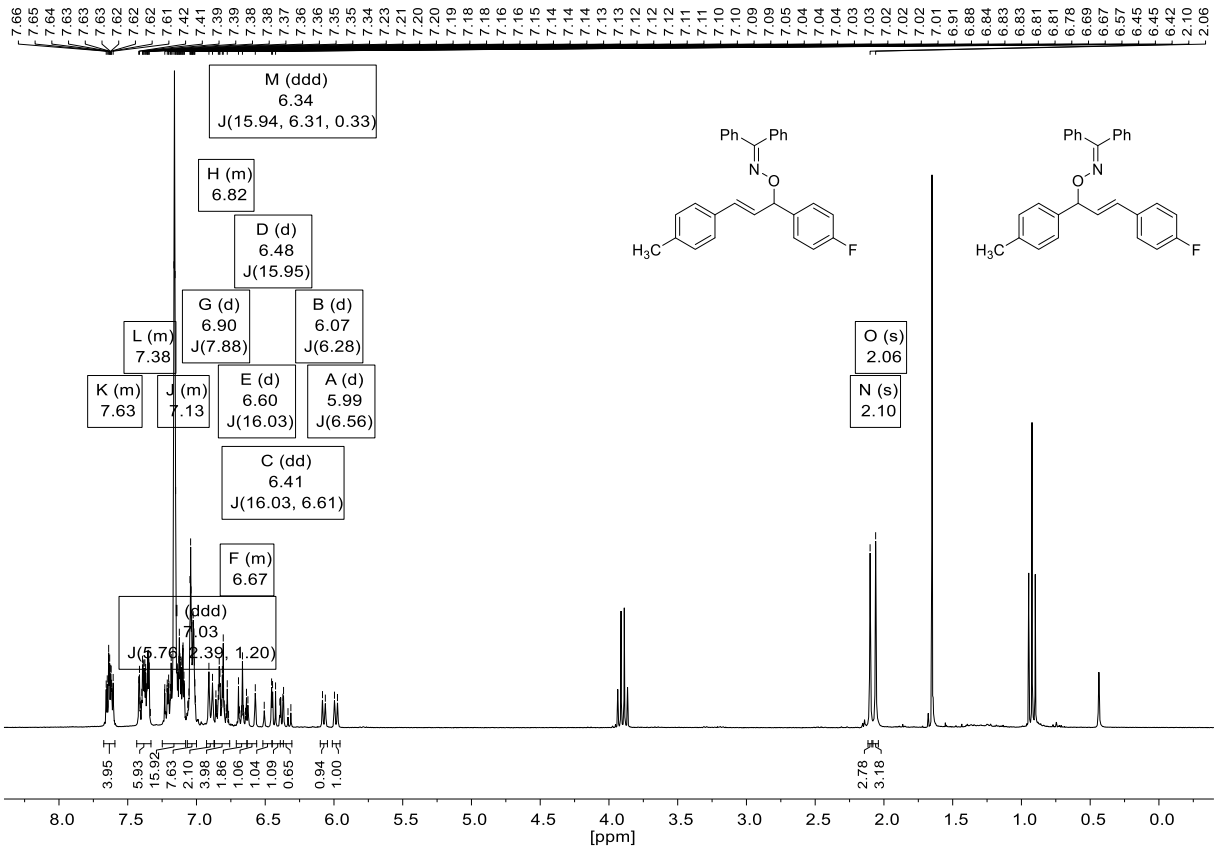

E (m)
7.22
B (dd)
6.71
J(15.96, 5.98)
H (m)
7.63
G (m)
7.46
D (m)
7.01
A (d)
6.34
J(5.96)
I (d)
7.94
J(1.51)
C (d)
6.82
J(15.99)
F (dd)
7.35
J(8.52, 1.81)
Ph
Ph
N
O
1.02
8.47
3.84
1.02
6.80
2.86
0.95
1.02
1.00
[ppm]


F (dd)
6.55
J(15.94, 1.04)
D (d)
6.40
J(5.04)
H (m)
7.13
B (d)
5.95
J(6.81)
J (m)
7.61
I (m)
7.38
G (d)
6.82
J(8.10)
A (d)
6.04
J(5.01)
C (dd)
6.31
J(15.93, 6.82)
E (s)
6.42
Ph
Ph
N
O
CF3
3.16
6.89
20.73
2.21
0.60
0.90
0.93
0.60
1.00
0.59
[ppm]

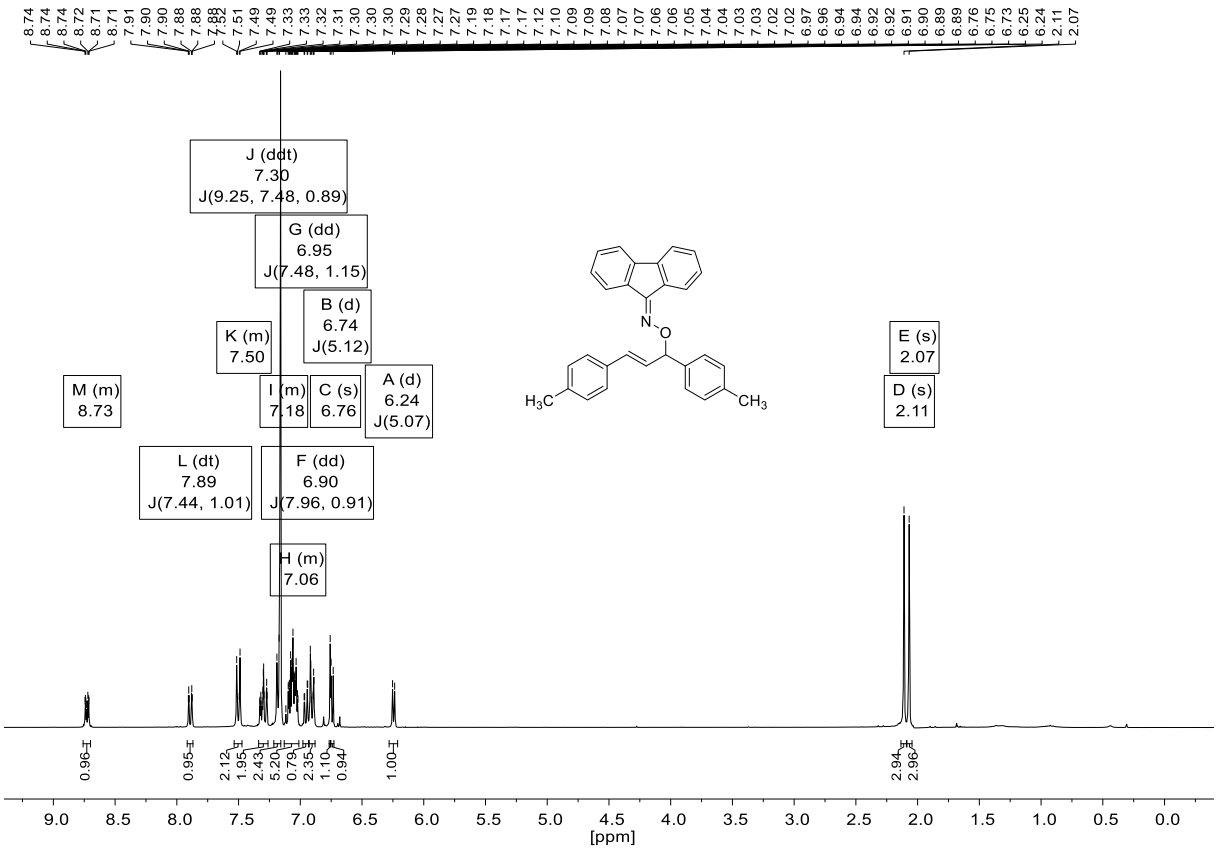

-62.14
-62.17
Ph
Ph
N
O
CF3
0.60
1.00
[ppm]

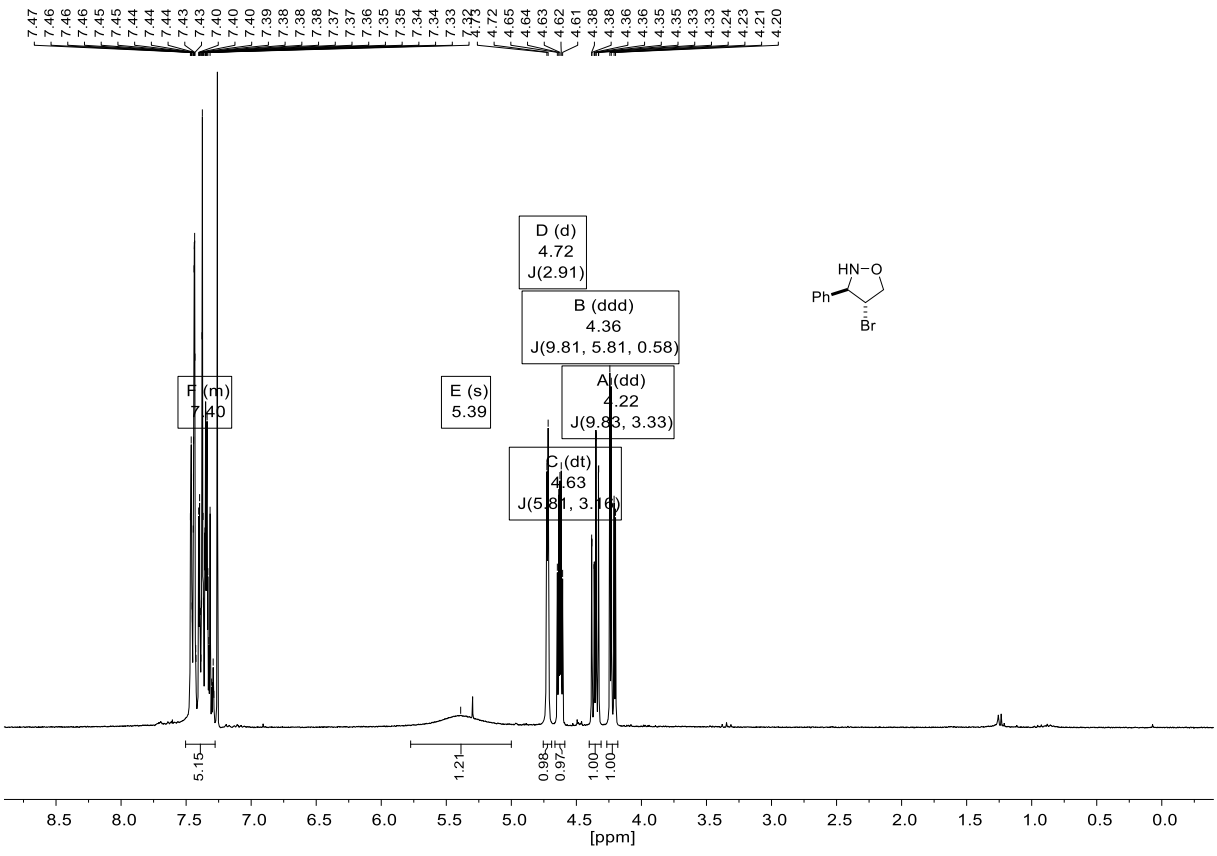

K (m) 6.88
E (s) 6.46
D (d) 6.56 J(15.90)
B (d) 5.99 J(6.95)
M (m) 7.38
L (m) 7.65
N (m) 7.13
I (m) 6.68
A (t) 6.04 J(2.47)
C (dd) 6.25 J(15.85, 7.00)
J (m) 6.82
F (s) 6.46
H (s) 3.25
G (s) 3.28
[ppm]

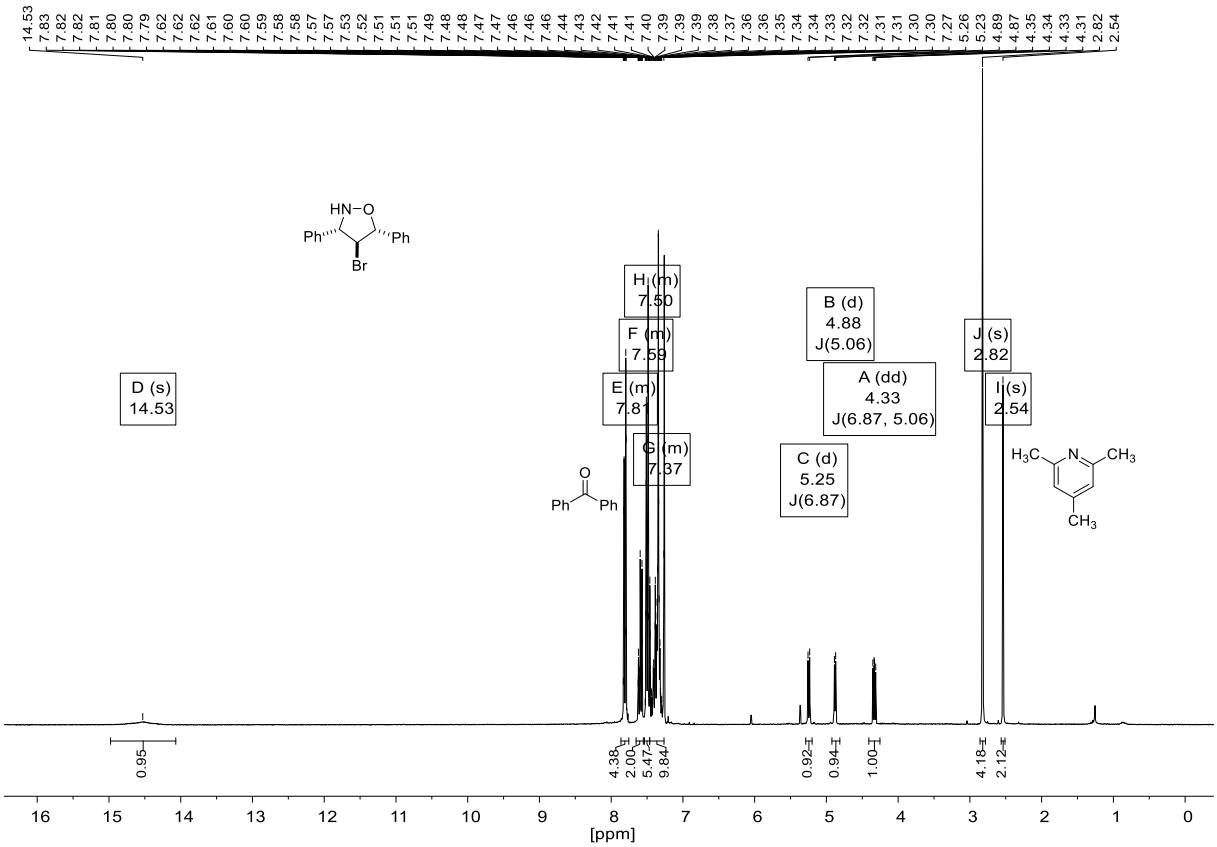

-62.11
-62.16
[ppm]

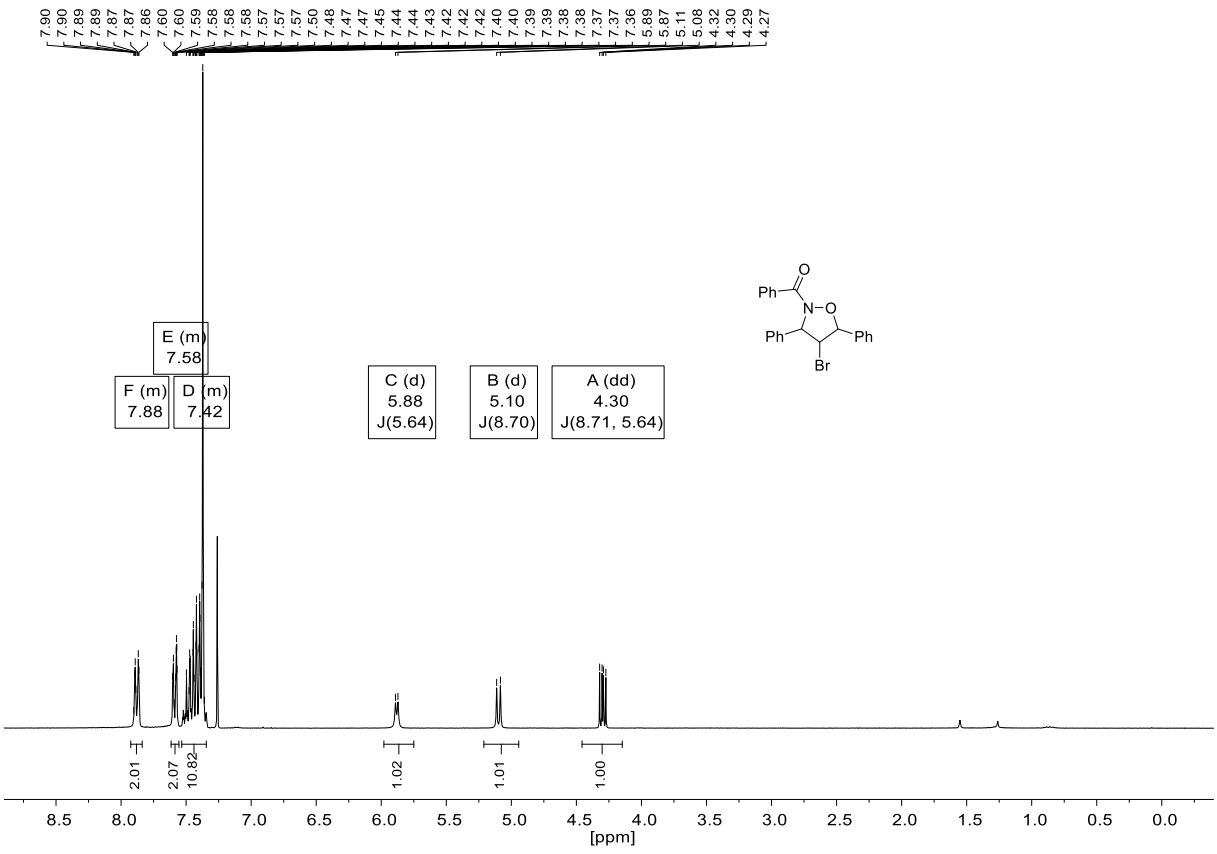

M (ddd)
6.34
J(15.94, 6.31, 0.33)
H (m)
6.82
D (d)
6.48
J(15.95)
G (d)
6.90
J(7.88)
B (d)
6.07
J(6.28)
L (m)
7.38
K (m)
7.63
J (m)
7.13
E (d)
6.60
J(16.03)
A (d)
5.99
J(6.56)
C (dd)
6.41
J(16.03, 6.61)
F (m)
6.67
I (ddd)
7.03
J(5.76, 2.39, 1.20)
O (s)
2.06
N (s)
2.10
[ppm]

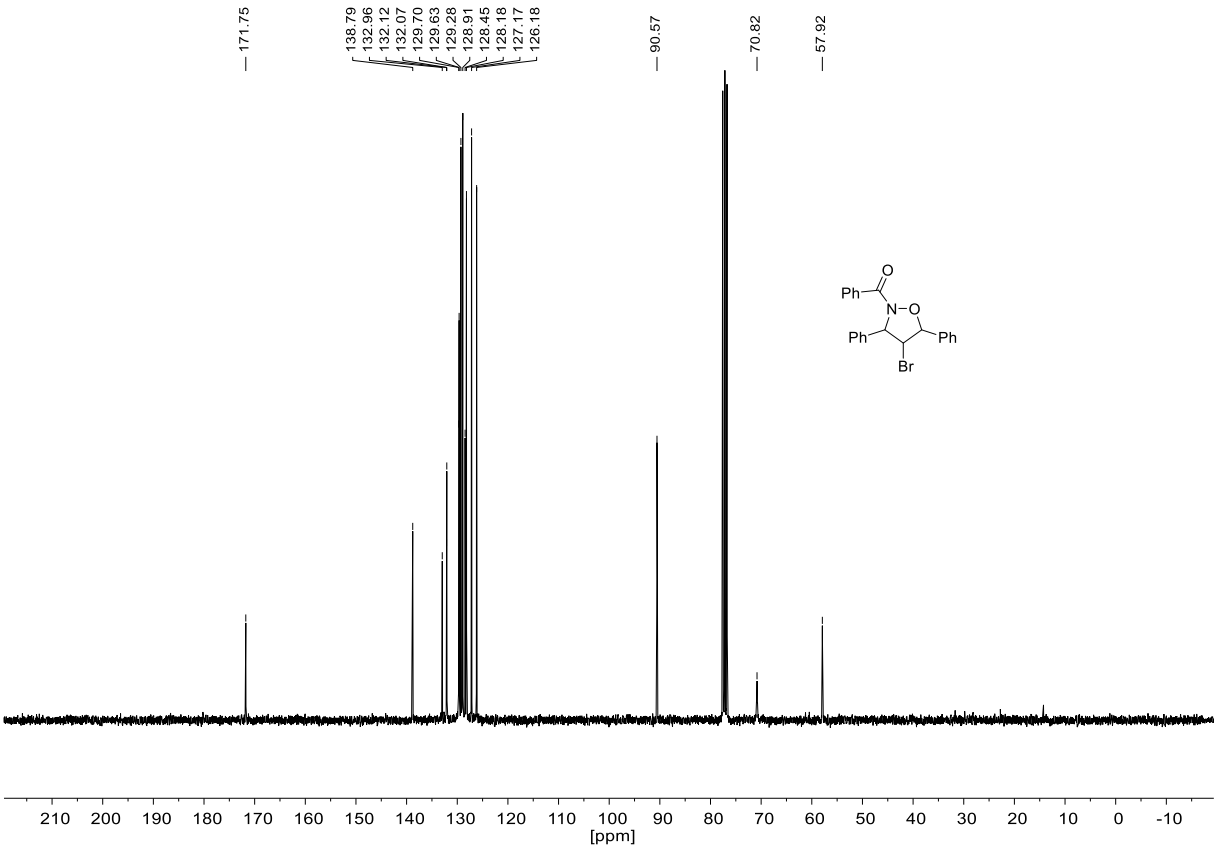

-114.36
-114.78
[ppm]

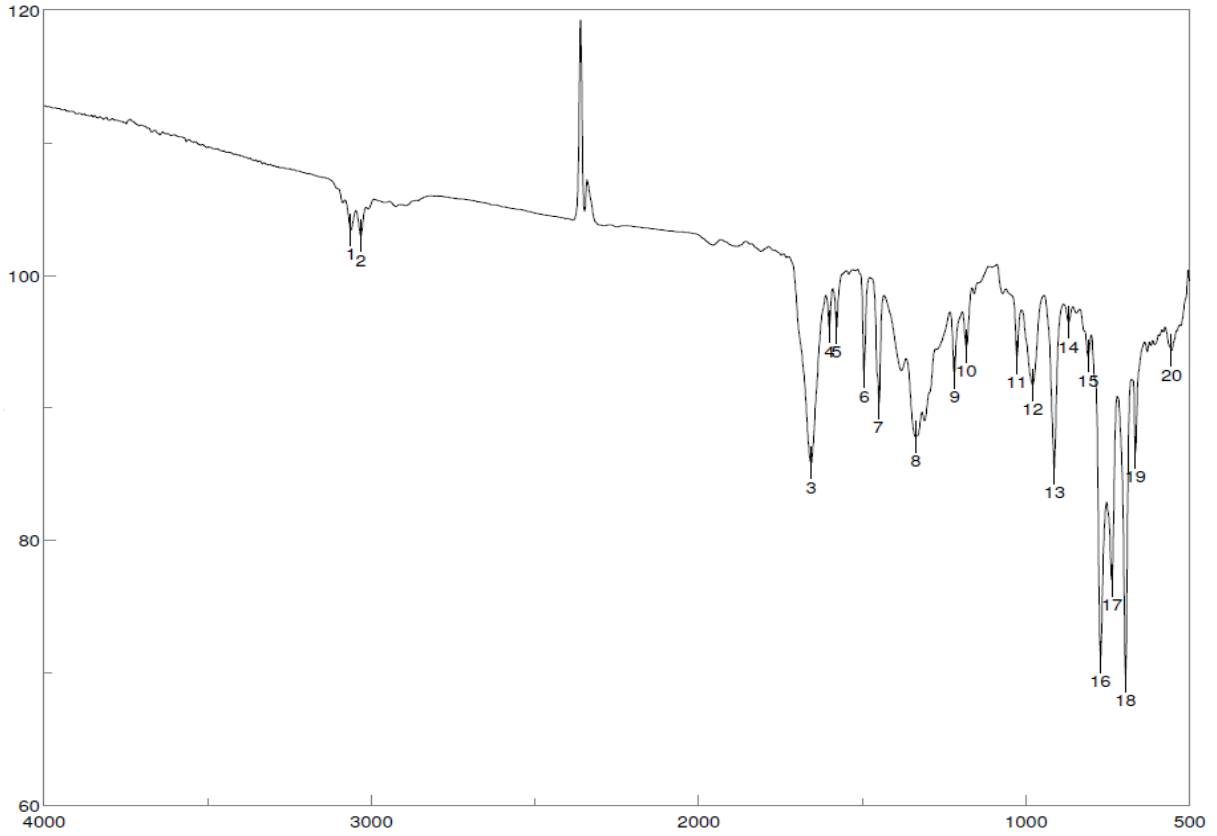

J (ddt)
7.30
J(9.25, 7.48, 0.89)
G (dd)
6.95
J(7.48, 1.15)
B (d)
6.74
J(5.12)
K (m)
7.50
M (m)
8.73
I (m)
7.18
C (s)
6.76
A (d)
6.24
J(5.07)
L (dt)
7.89
J(7.44, 1.01)
F (dd)
6.90
J(7.96, 0.91)
H (m)
7.06
E (s)
2.07
D (s)
2.11
[ppm]

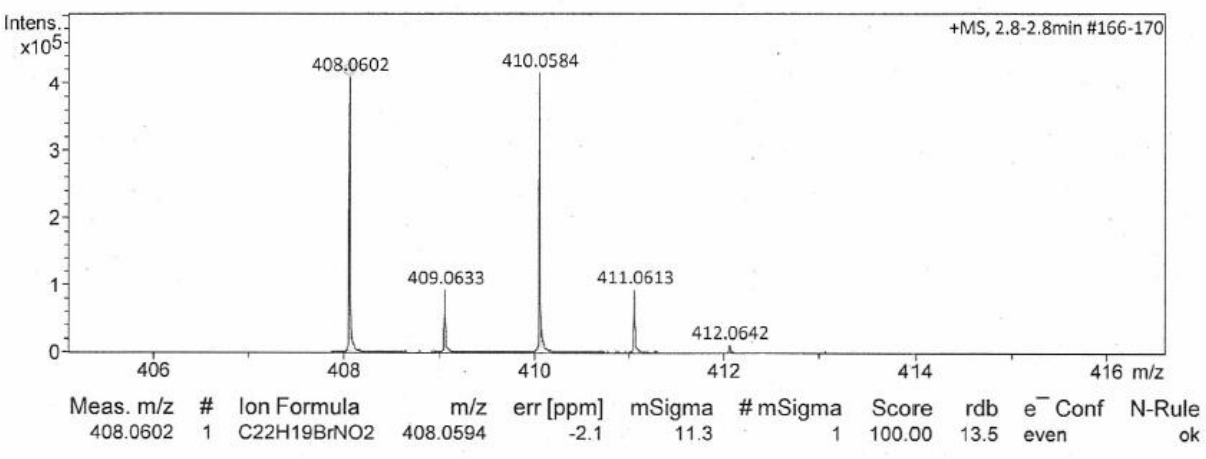

D (d)
4.72
J(2.91)
B (ddd)
4.36
J(9.81, 5.81, 0.58)
A (dd)
4.22
J(9.83, 3.33)
C (dt)
4.63
J(5.81, 3.16)
E (s)
5.39
F (m)
7.40
[ppm]


HN–O
Ph
Ph
Br
H (m)
7.50
F (m)
7.59
E (m)
7.81
G (m)
7.37
D (s)
14.53
B (d)
4.88
J(5.06)
A (dd)
4.33
J(6.87, 5.06)
C (d)
5.25
J(6.87)
J (s)
2.82
I (s)
2.54
O
Ph
Ph
H3C
N
CH3
CH3
0.95
4.38
2.00
5.47
9.84
0.92
0.94
1.00
4.18
2.12
[ppm]


O
Ph
N–O
Ph
Ph
Br
E (m)
7.58
F (m)
7.88
D (m)
7.42
C (d)
5.88
J(5.64)
B (d)
5.10
J(8.70)
A (dd)
4.30
J(8.71, 5.64)
2.01
2.07
10.82
1.02
1.01
1.00
[ppm]

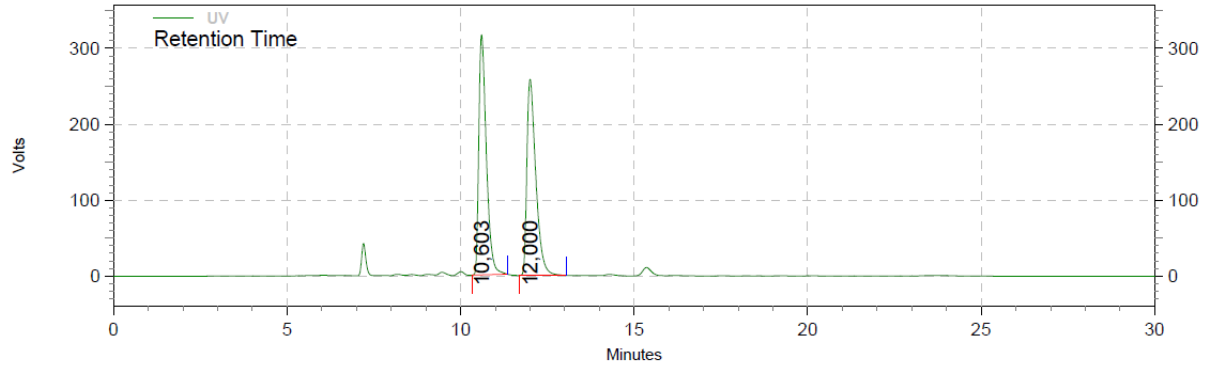

171.75
138.79
132.96
132.12
132.07
129.70
129.63
129.28
128.91
128.45
128.18
127.17
126.18
90.57
70.82
57.92
Ph
O
N
O
Ph
Ph
Br
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]


120
100
80
60
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20



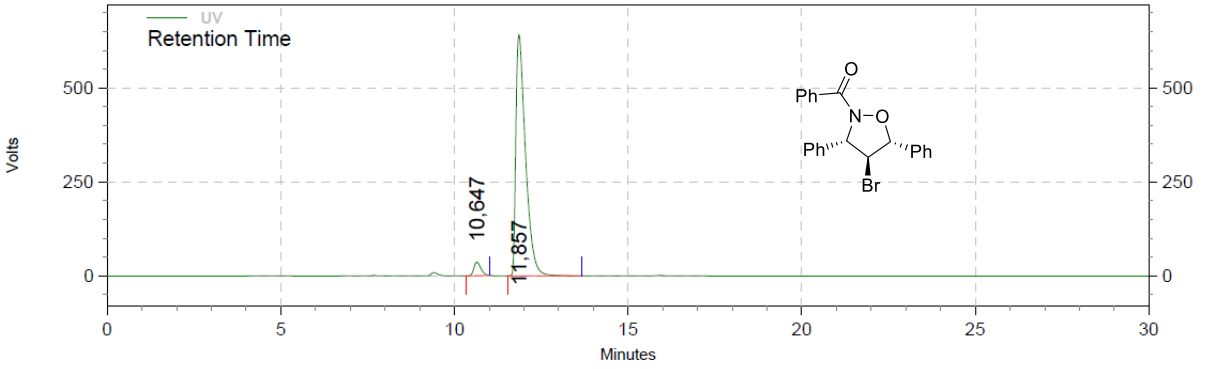
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
408.0602	1	C22H19BrNO2	408.0594	-2.1	11.3	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min



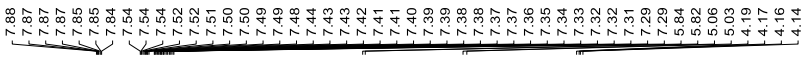
UV Results

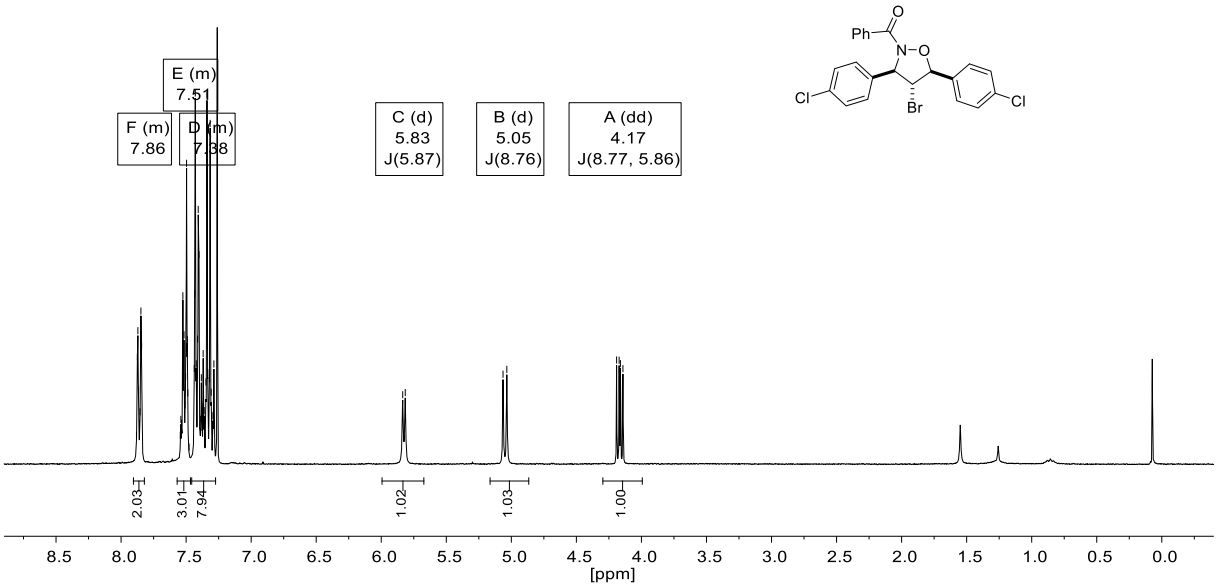
Retention Time	Area	Area %	Height	Height %
10,603	19086763	50,90	1264438	55,04
12,000	18410383	49,10	1032693	44,96

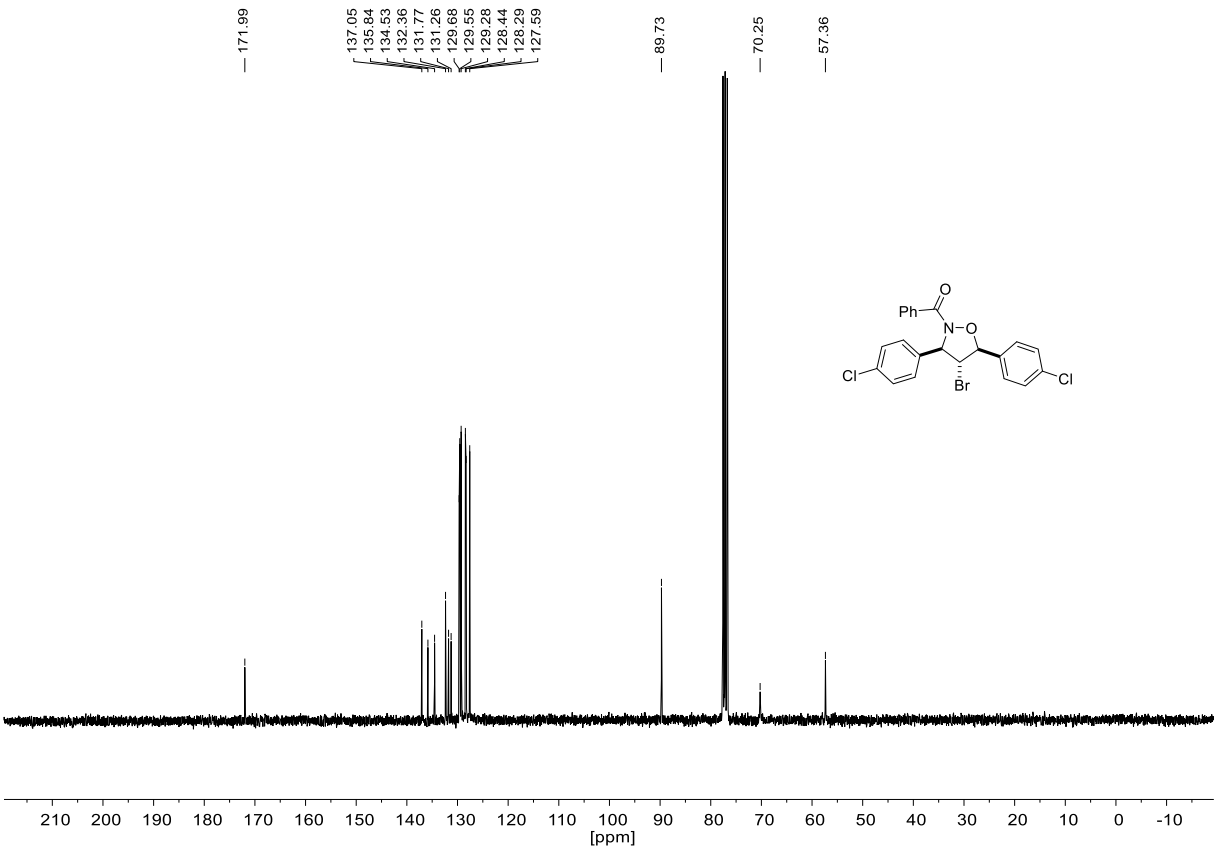


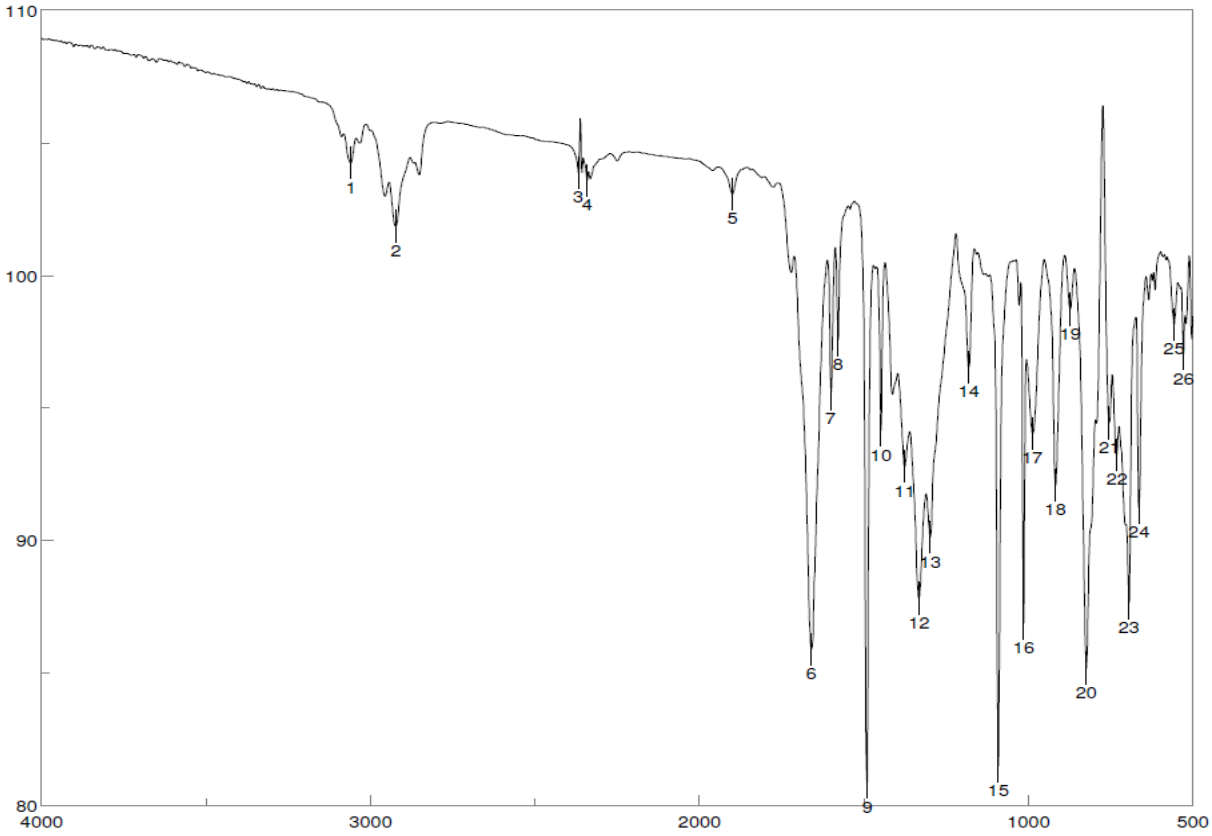
UV Results

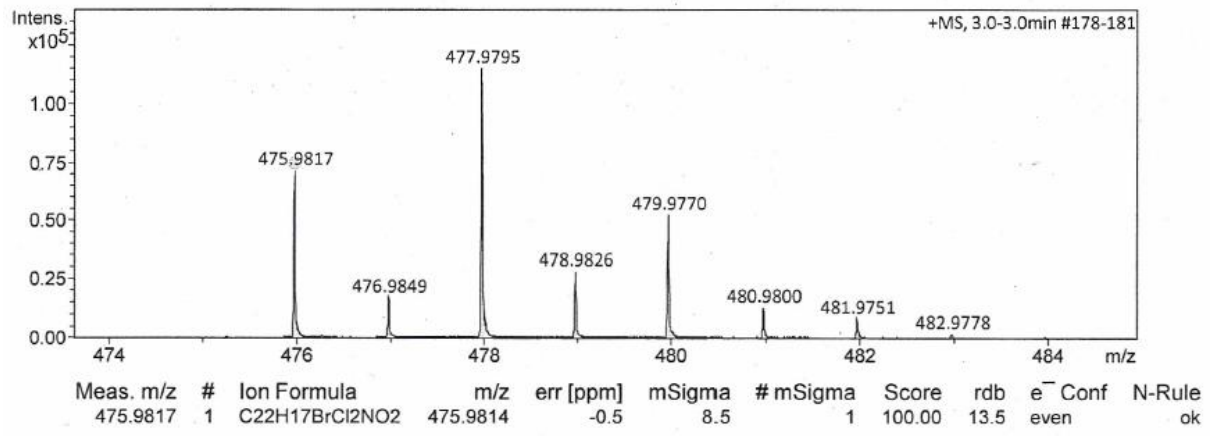
Retention Time	Area	Area %	Height	Height %
10,647	2025648	3,94	143150	5,28
11,857	49438639	96,06	2565609	94,72


7.88
7.87
7.87
7.85
7.85
7.84
7.54
7.54
7.54
7.52
7.52
7.51
7.50
7.50
7.49
7.49
7.48
7.44
7.43
7.43
7.42
7.41
7.41
7.40
7.39
7.39
7.38
7.37
7.37
7.36
7.35
7.34
7.33
7.32
7.32
7.31
7.29
7.29
5.84
5.82
5.06
5.03
4.19
4.17
4.16
4.14


E (m)
7.51
F (m)
7.86
D (m)
7.88
C (d)
5.83
J(5.87)
B (d)
5.05
J(8.76)
A (dd)
4.17
J(8.77, 5.86)
O
Ph
N
O
Cl
Br
Cl
2.03
3.01
7.94
1.02
1.03
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]

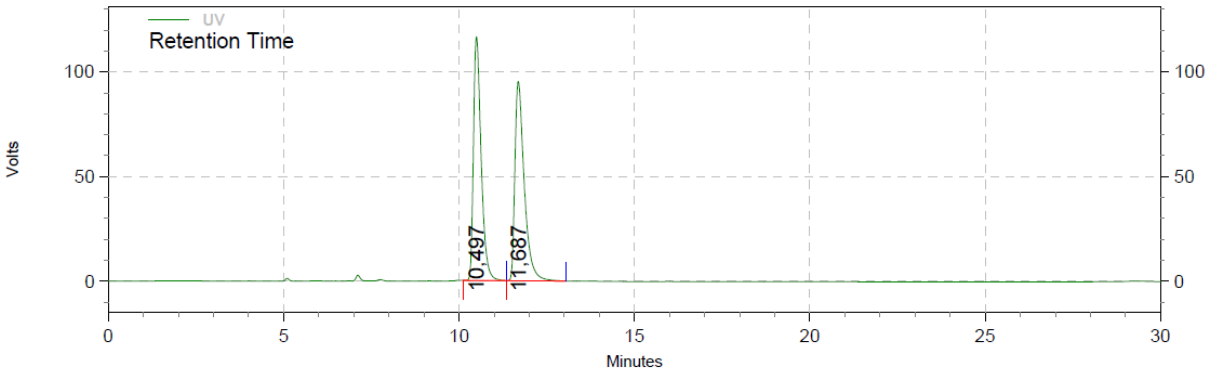

171.99
137.05
135.84
134.53
132.36
131.77
131.26
129.68
129.55
129.28
128.44
128.29
127.59
89.73
70.25
57.36
O
Ph
N
O
Cl
Br
Cl
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
[ppm]





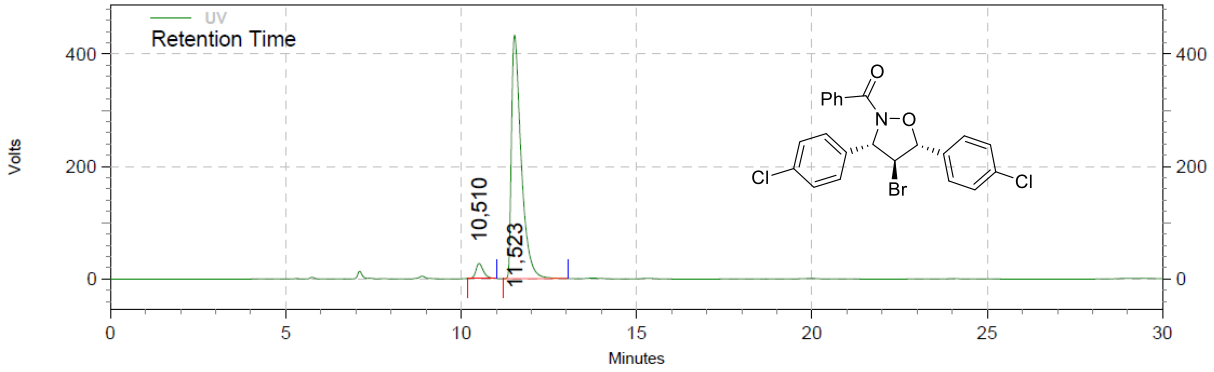
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
475.9817	1	C22H17BrCl2NO2	475.9814	-0.5	8.5	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min



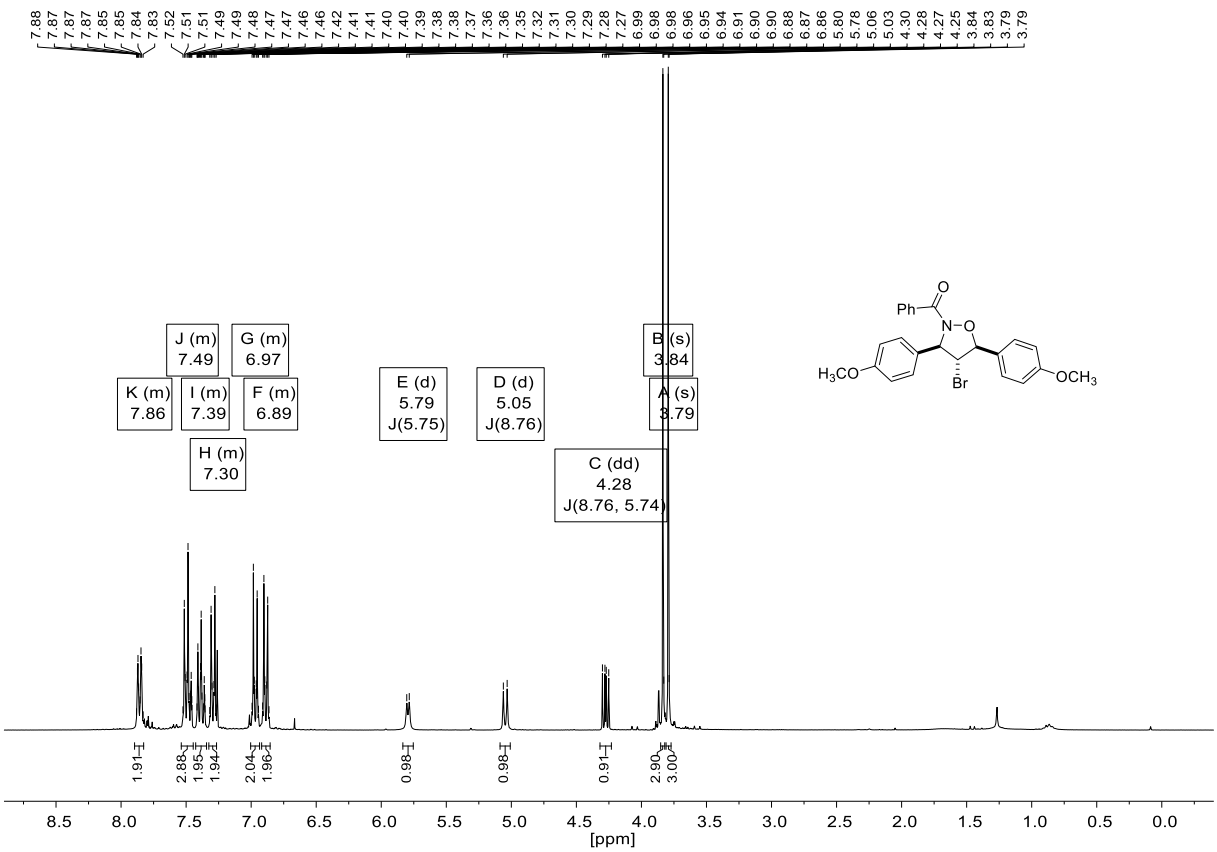
UV Results

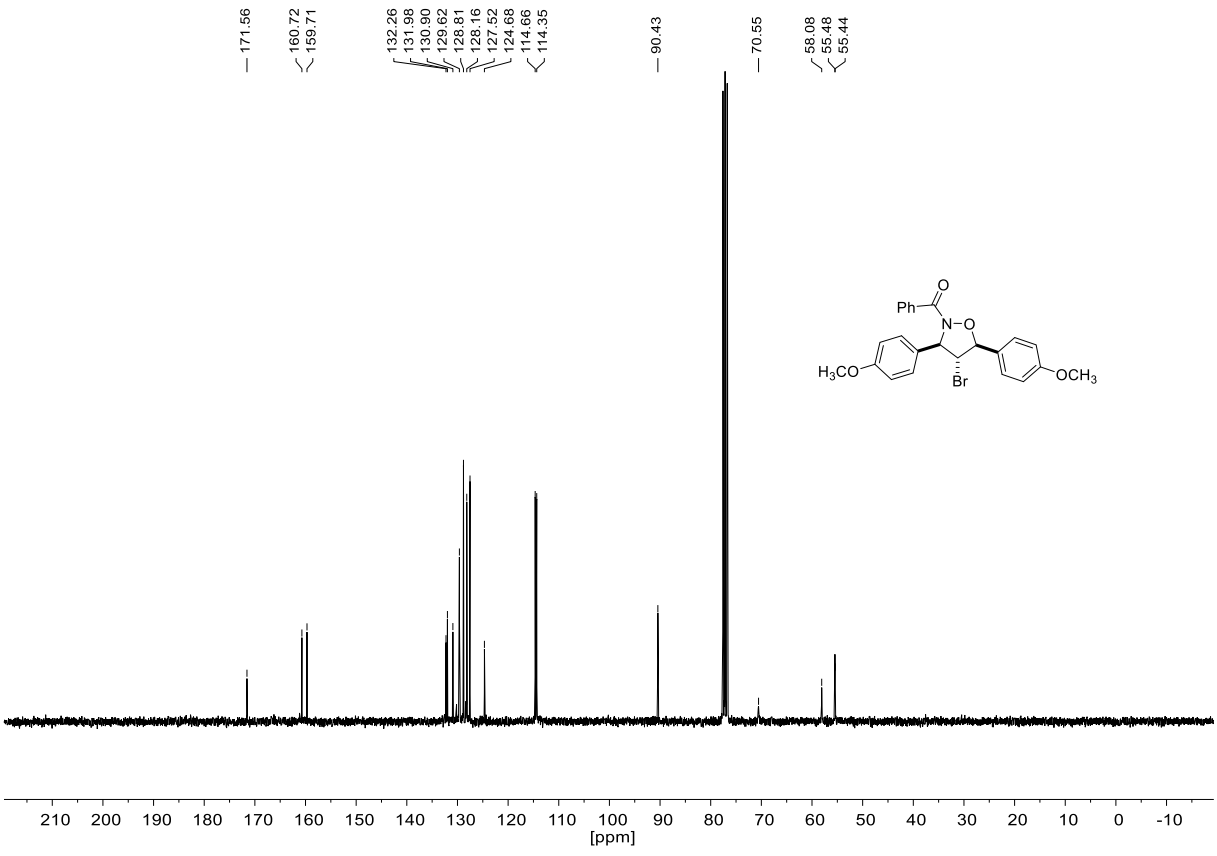
Retention Time	Area	Area %	Height	Height %
10,497	7093232	50,07	465836	55,00
11,687	7073049	49,93	381198	45,00

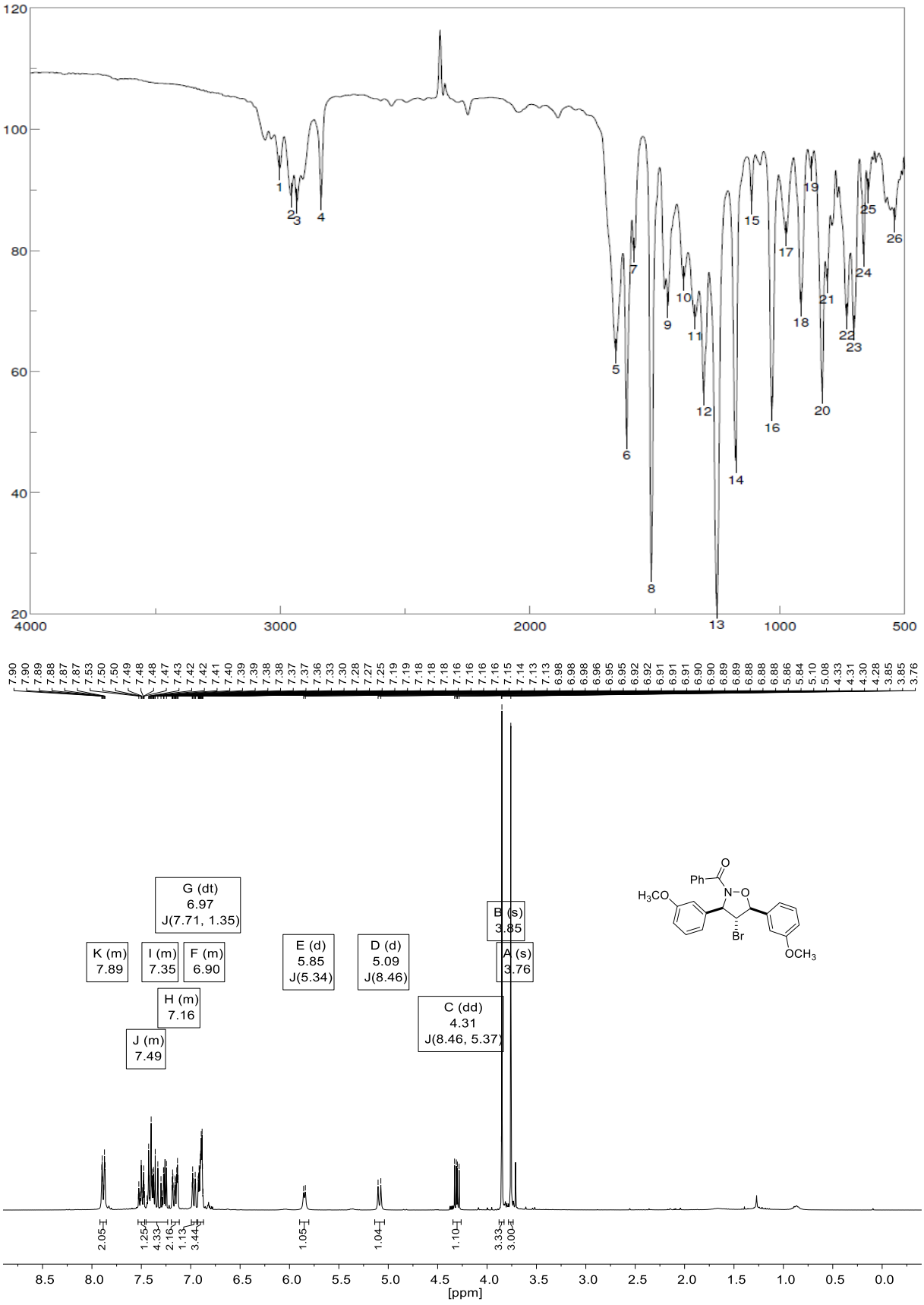


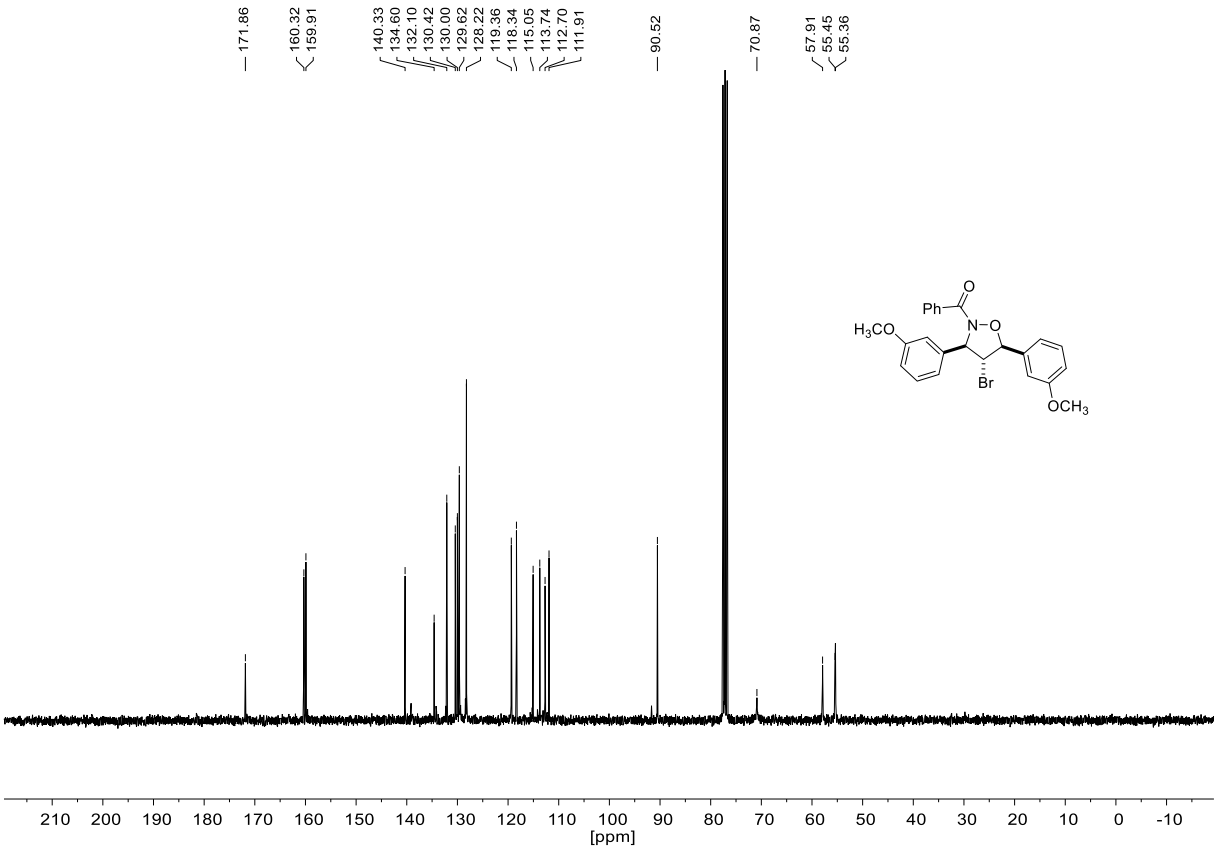
UV Results

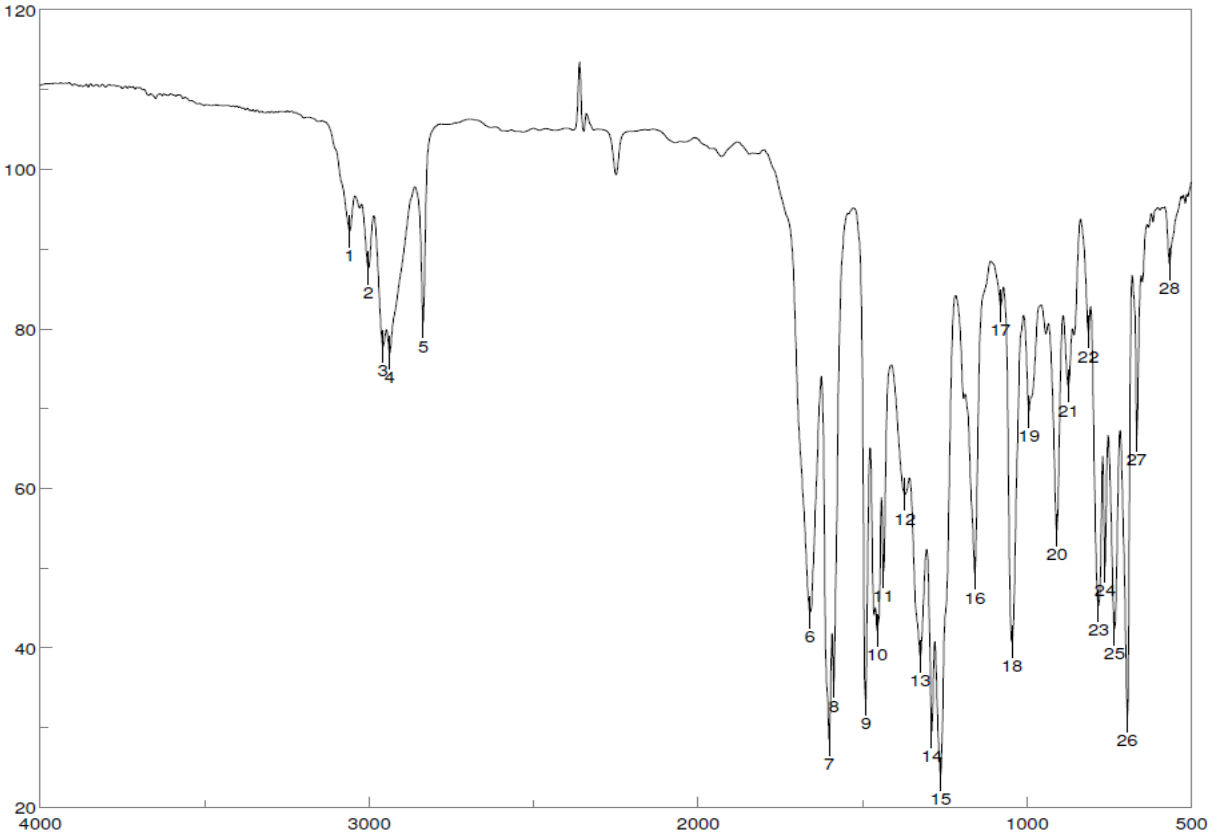
Retention Time	Area	Area %	Height	Height %
10,510	1603405	4,58	106974	5,81
11,523	33396149	95,42	1733447	94,19


J (m) 7.49
G (m) 6.97
K (m) 7.86
I (m) 7.39
F (m) 6.89
H (m) 7.30
E (d) 5.79 J(5.75)
D (d) 5.05 J(8.76)
C (dd) 4.28 J(8.76, 5.74)
B (s) 3.84
A (s) 3.79
Ph
O
N–O
H3CO
Br
OCH3
[ppm]


171.56
160.72
159.71
132.26
131.98
130.90
129.62
128.81
128.16
127.52
124.68
114.66
114.35
90.43
70.55
58.08
55.48
55.44
Ph
O
N–O
H3CO
Br
OCH3
[ppm]


G (dt)
6.97
J(7.71, 1.35)
K (m)
7.89
I (m)
7.35
F (m)
6.90
H (m)
7.16
J (m)
7.49
E (d)
5.85
J(5.34)
D (d)
5.09
J(8.46)
C (dd)
4.31
J(8.46, 5.37)
B (s)
3.85
A (s)
3.76
Ph
O
N
O
H3CO
Br
OCH3
[ppm]


171.86
160.32
159.91
140.33
134.60
132.10
130.42
130.00
129.62
128.22
119.36
118.34
115.05
113.74
112.70
111.91
90.52
70.87
57.91
55.45
55.36
Ph
O
N
O
H3CO
Br
OCH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]


120
100
80
60
40
20
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
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11
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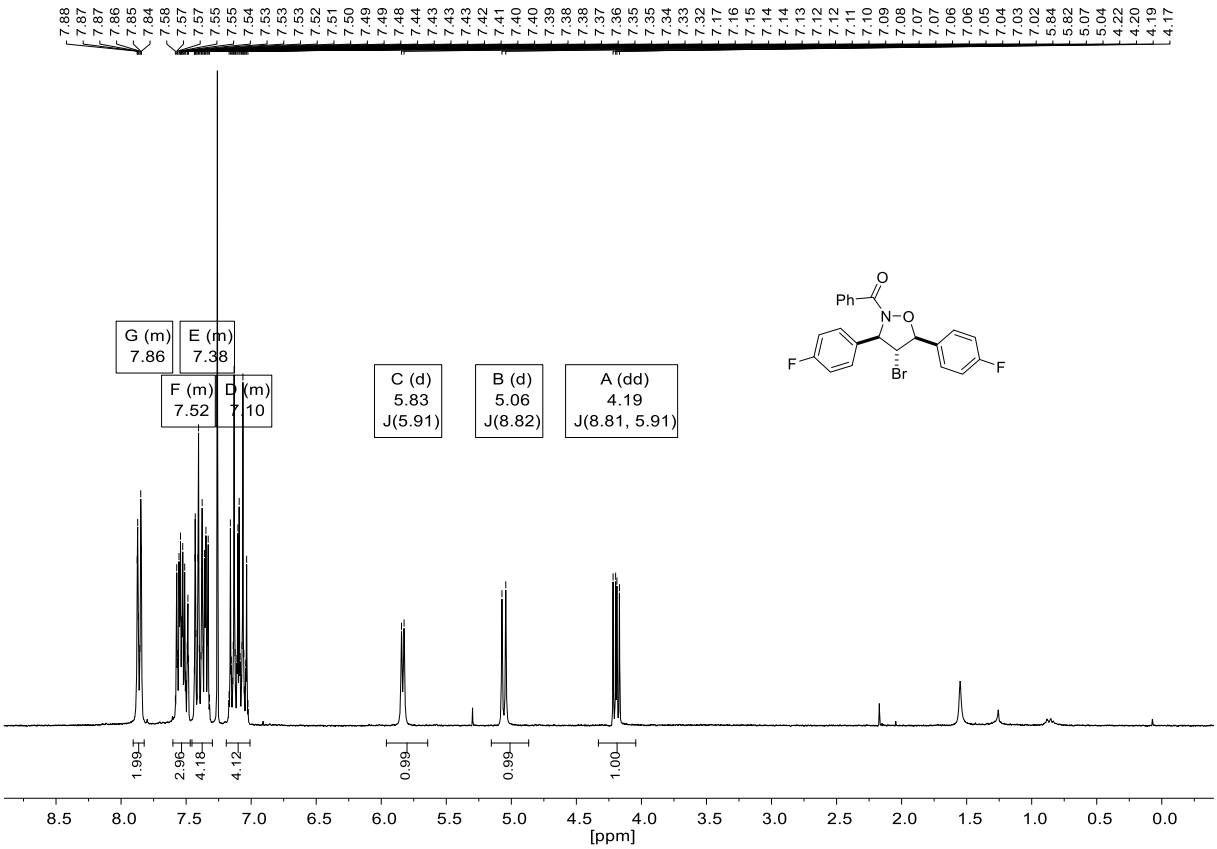
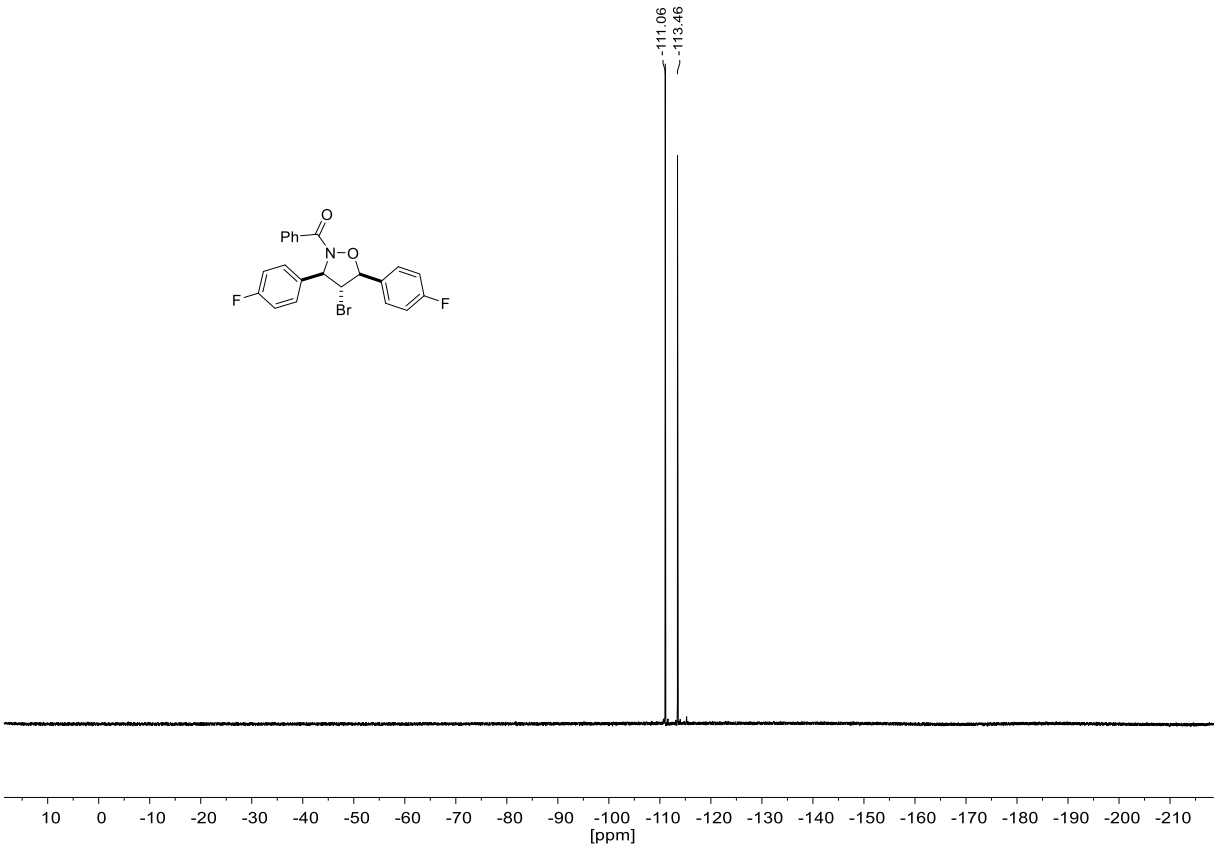
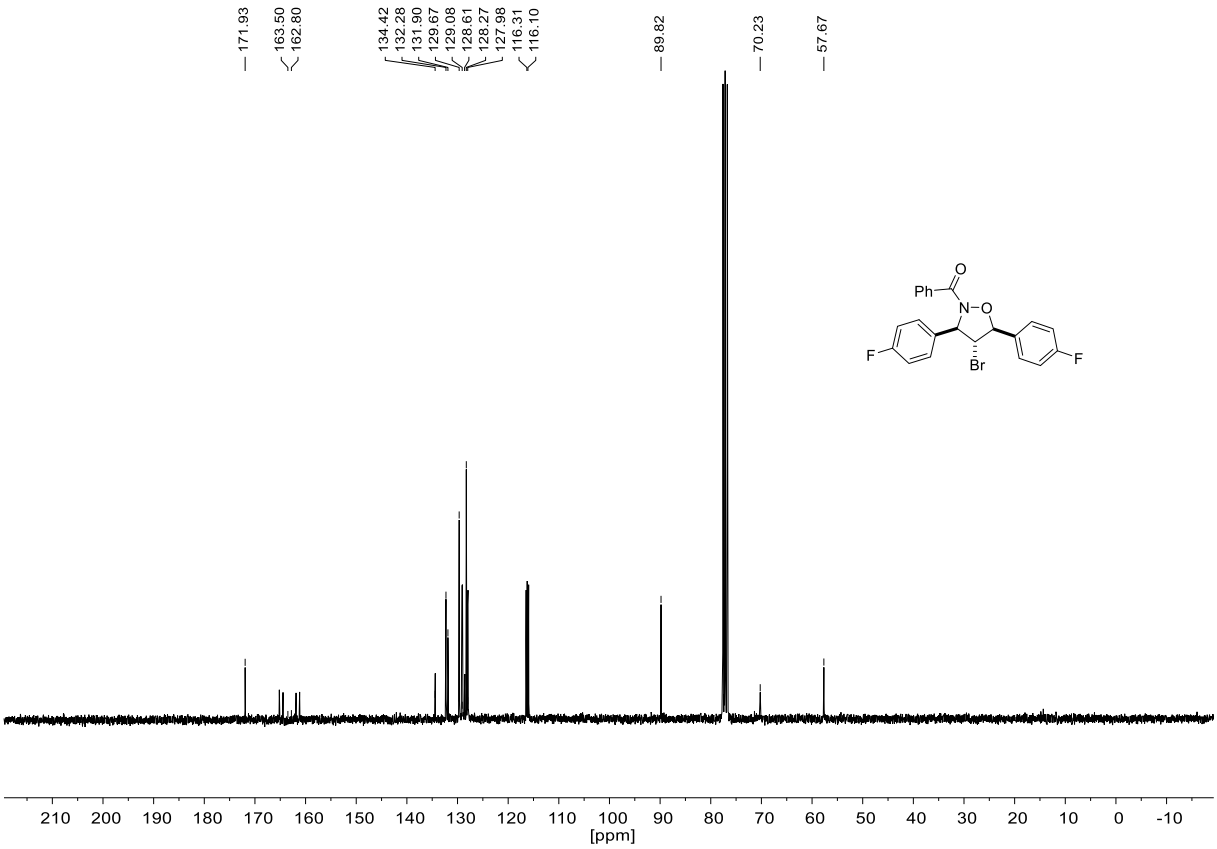
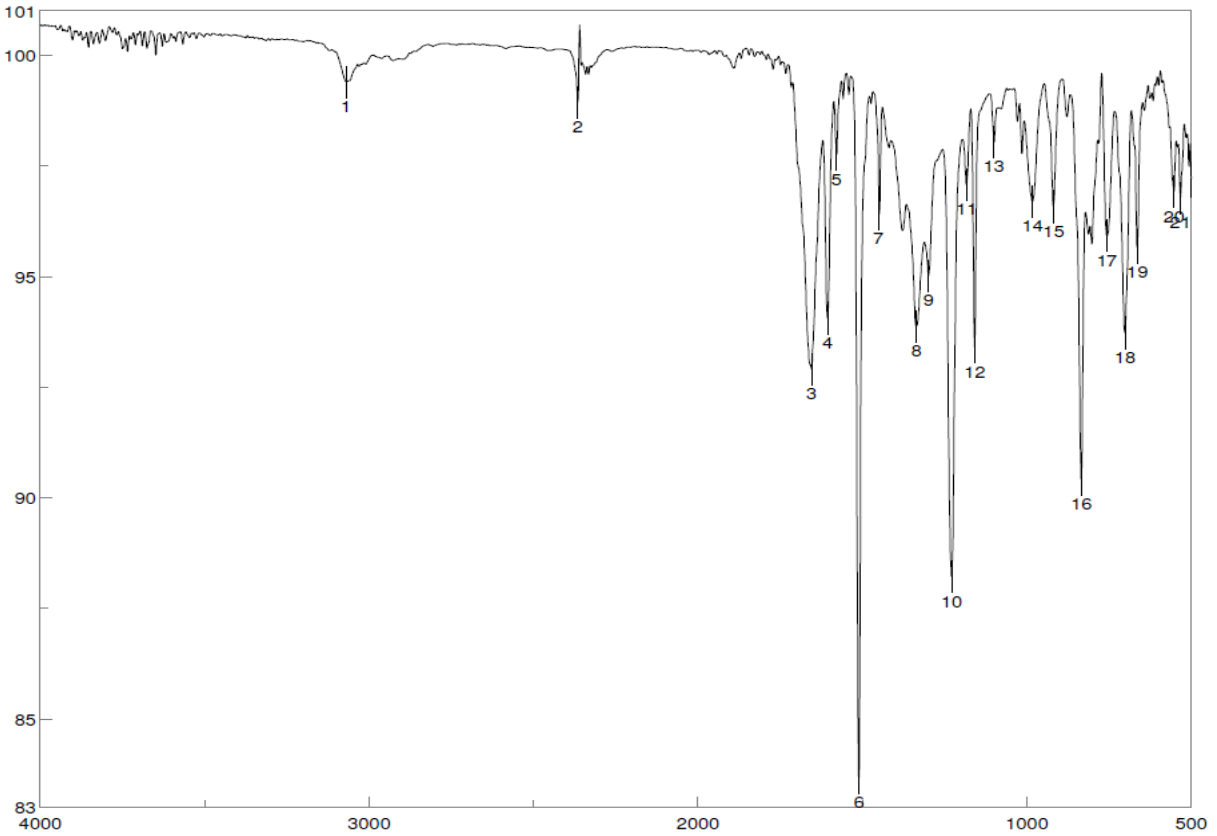
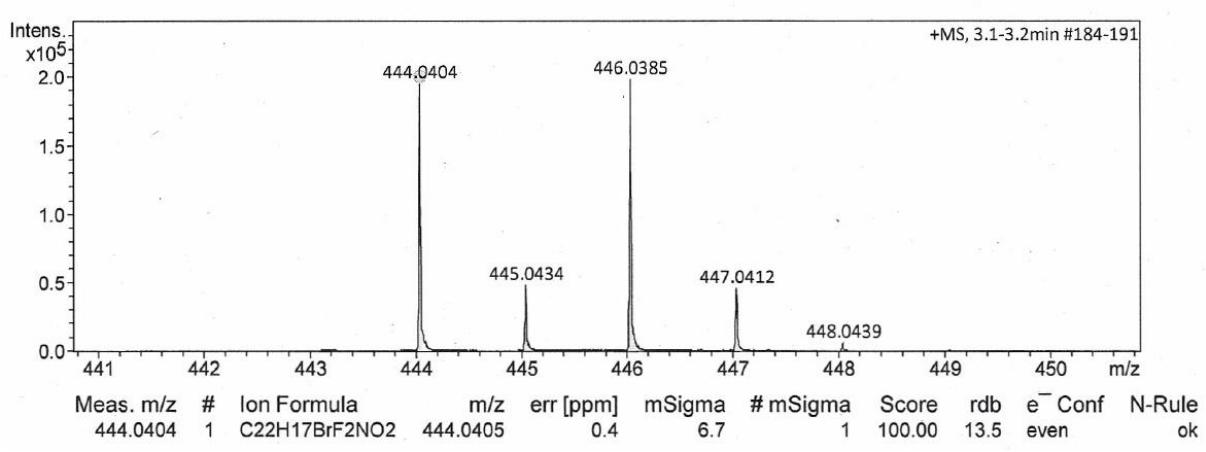
19
20
21
22
23
24
25
26
27
28


7.88 7.87 7.87 7.86 7.85 7.84 7.58 7.57 7.57 7.55 7.55 7.54 7.53 7.53 7.52 7.51 7.50 7.49 7.49 7.48 7.44 7.43 7.43 7.42 7.41 7.40 7.40 7.39 7.38 7.38 7.37 7.36 7.35 7.35 7.34 7.33 7.32 7.17 7.16 7.15 7.14 7.14 7.13 7.12 7.12 7.11 7.10 7.09 7.08 7.07 7.07 7.06 7.06 7.05 7.04 7.03 7.02 5.84 5.82 5.07 5.04 4.22 4.20 4.19 4.17
G (m) 7.86
E (m) 7.38
F (m) 7.52
D (m) 7.10
C (d) 5.83 J(5.91)
B (d) 5.06 J(8.82)
A (dd) 4.19 J(8.81, 5.91)
Ph
O
N
O
F
Br
F
1.99
2.96
4.18
4.12
0.99
0.99
1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]


-111.06
-113.46
Ph
O
N
O
F
Br
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

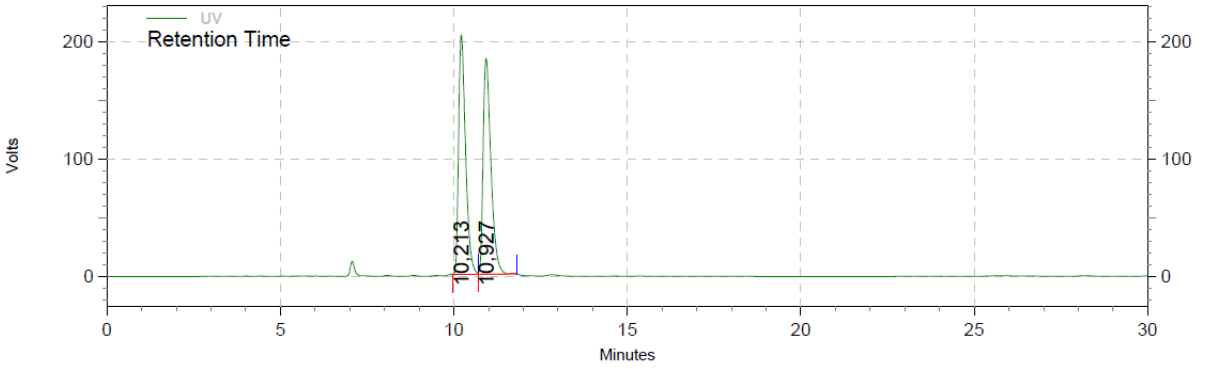

171.93
163.50
162.80
134.42
132.28
131.90
129.67
129.08
128.61
128.27
127.98
116.31
116.10
89.82
70.23
57.67
Ph
O
N
O
F
Br
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]


101
100
95
90
85
83
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21



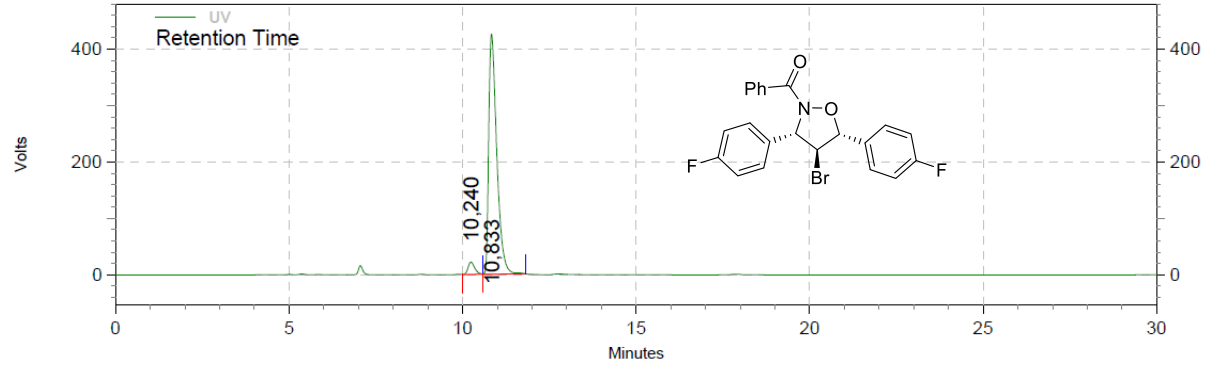
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
444.0404	1	C22H17BrF2NO2	444.0405	0.4	6.7	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min



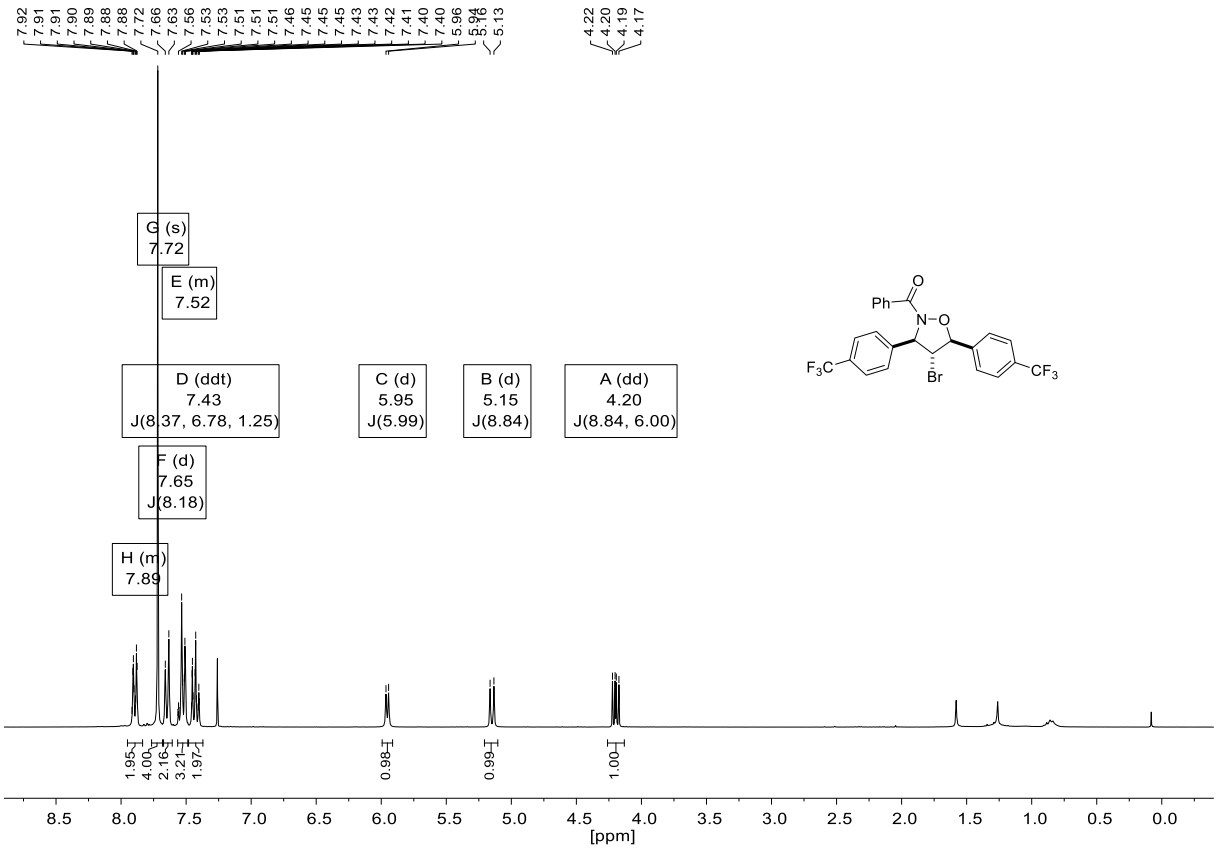
UV Results

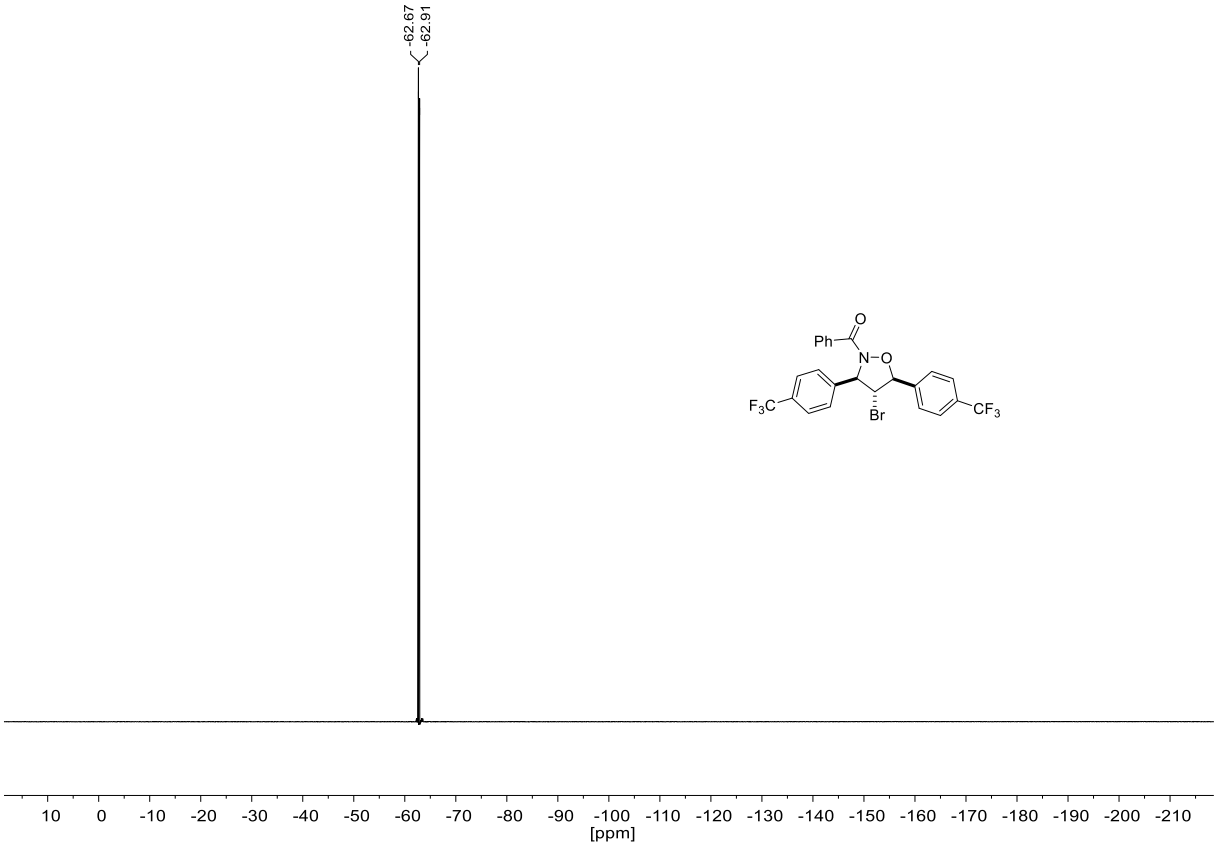
Retention Time	Area	Area %	Height	Height %
10,213	11423796	49,92	815512	52,56
10,927	11462555	50,08	736022	47,44

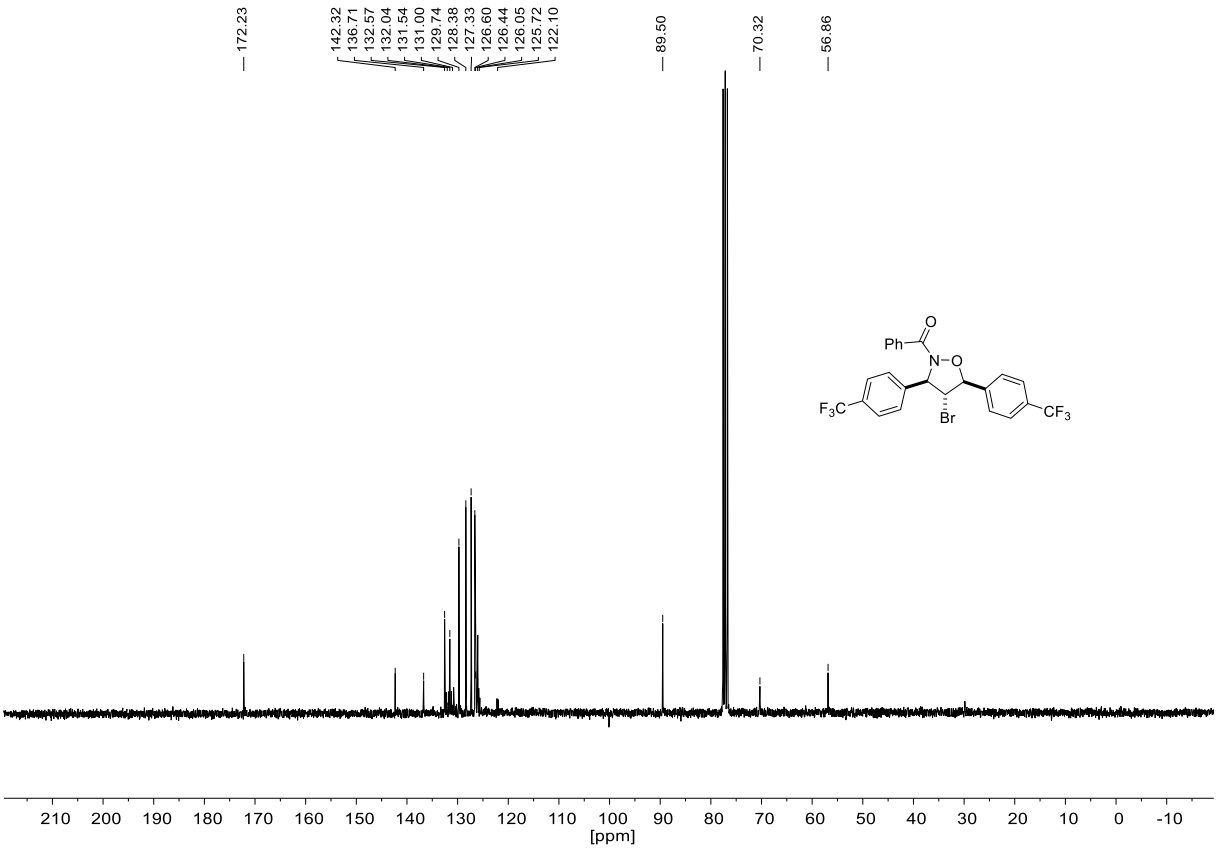


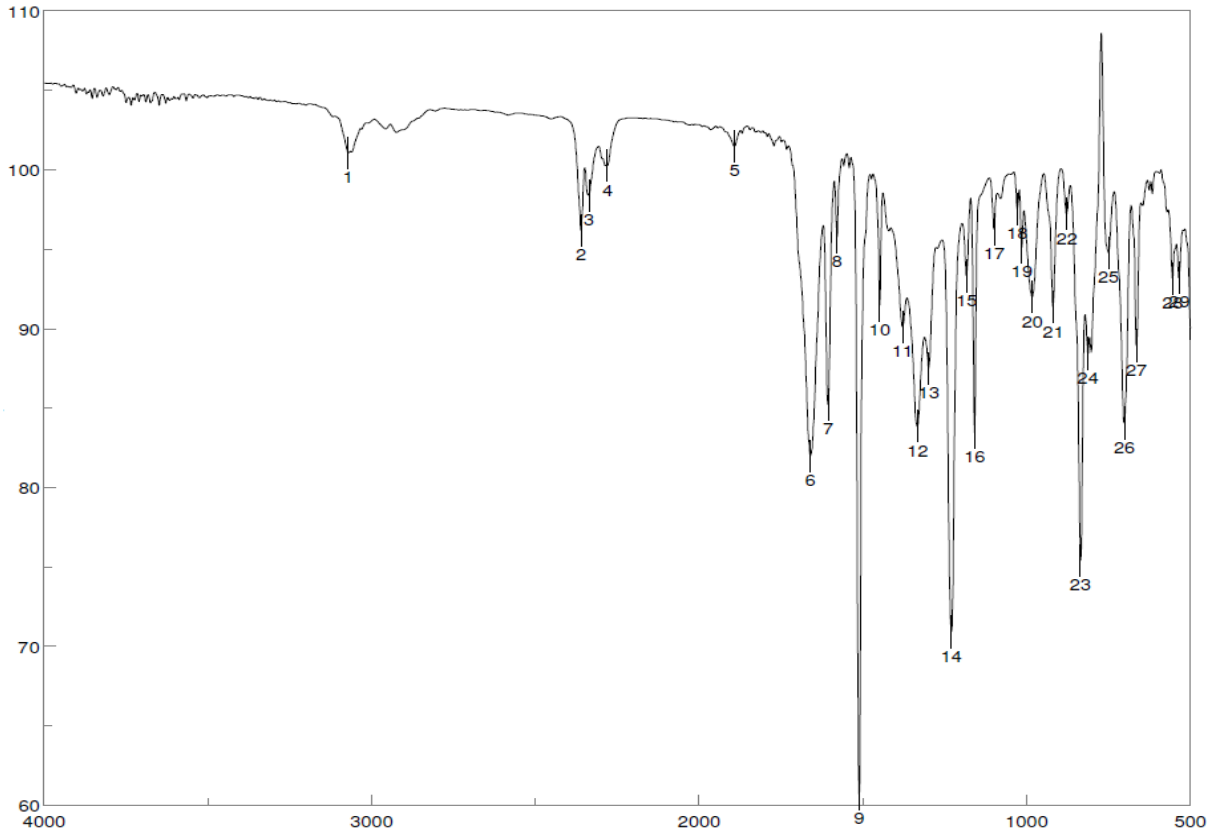
UV Results

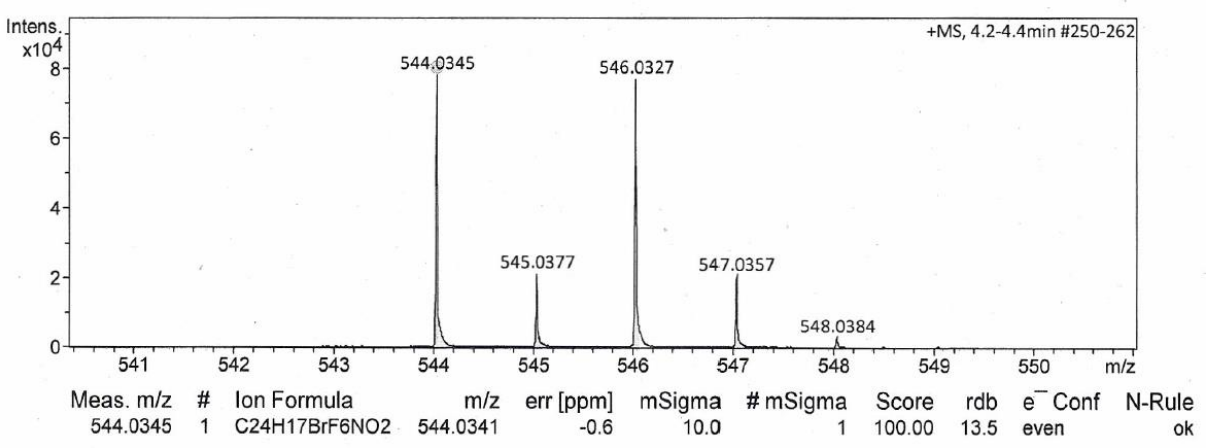
Retention Time	Area	Area %	Height	Height %
10,240	1169466	4,08	87518	4,89
10,833	27480468	95,92	1702697	95,11


7.92
7.91
7.91
7.90
7.89
7.88
7.88
7.72
7.66
7.63
7.56
7.53
7.53
7.51
7.51
7.51
7.46
7.45
7.45
7.45
7.43
7.43
7.42
7.41
7.40
7.40
5.96
5.94
5.93
5.13
4.22
4.20
4.19
4.17
G (s)
7.72
E (m)
7.52
D (ddt)
7.43
J(8.37, 6.78, 1.25)
C (d)
5.95
J(5.99)
B (d)
5.15
J(8.84)
A (dd)
4.20
J(8.84, 6.00)
F (d)
7.65
J(8.18)
H (m)
7.89
1.95
4.00
2.16
3.21
1.97
0.98
0.99
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
[ppm]
Ph
O
N
O
F3C
CF3
Br


-62.67
-62.91
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
[ppm]
Ph
O
N
O
F3C
CF3
Br

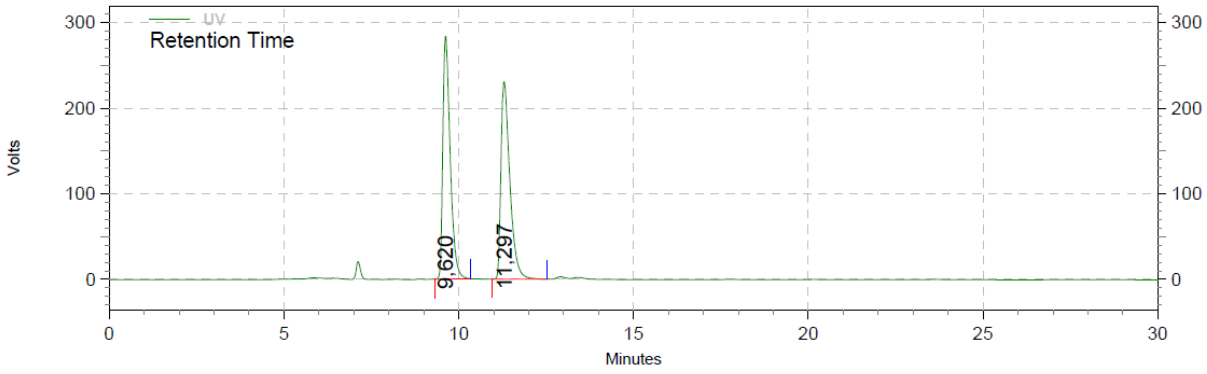

172.23
142.32
136.71
132.57
132.04
131.54
131.00
129.74
128.38
127.33
126.60
126.44
126.05
125.72
122.10
89.50
70.32
56.86
Ph
O
N
O
F3C
Br
CF3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]


110
100
90
80
70
60
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27



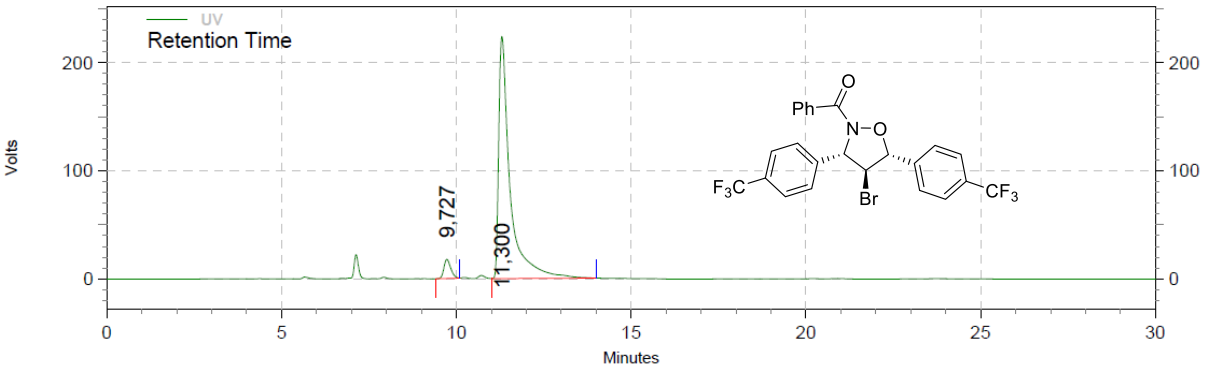
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
544.0345	1	C24H17BrF6NO2	544.0341	-0.6	10.0	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min



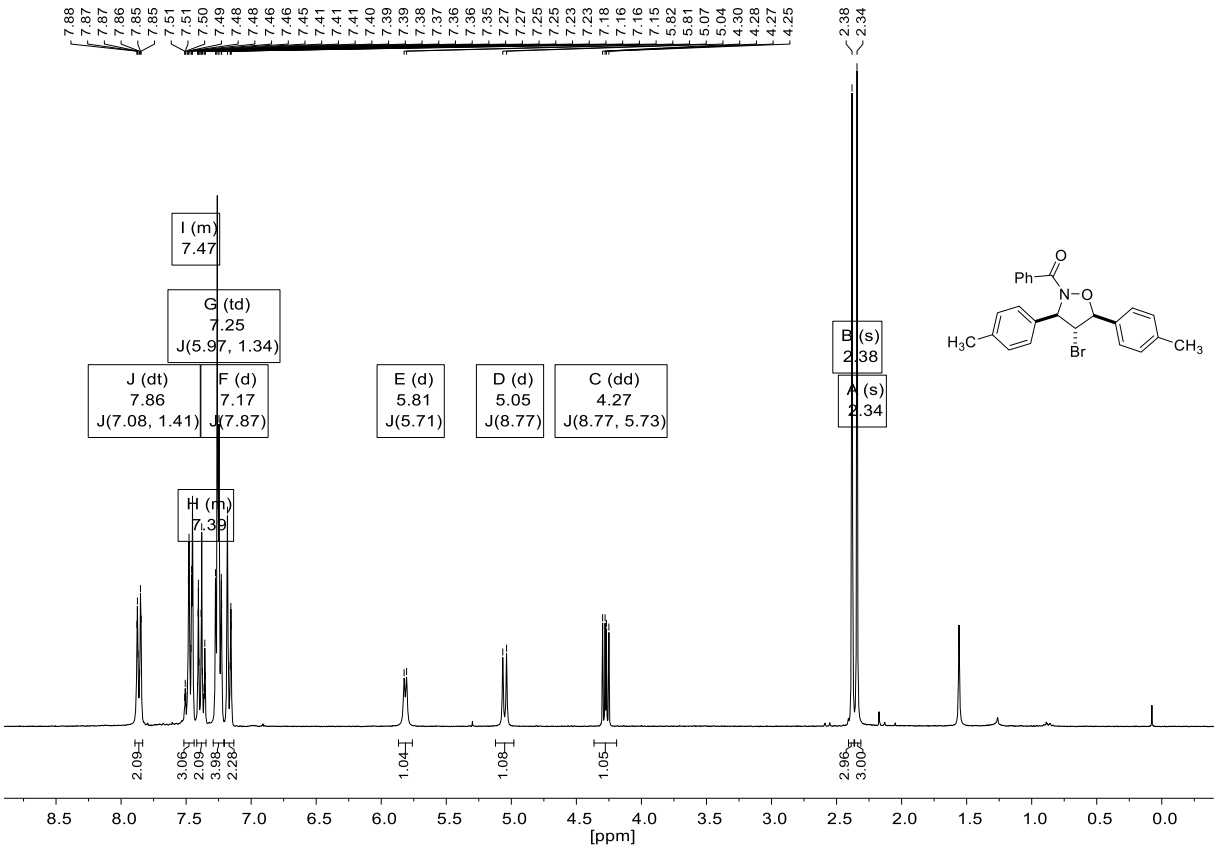
UV Results

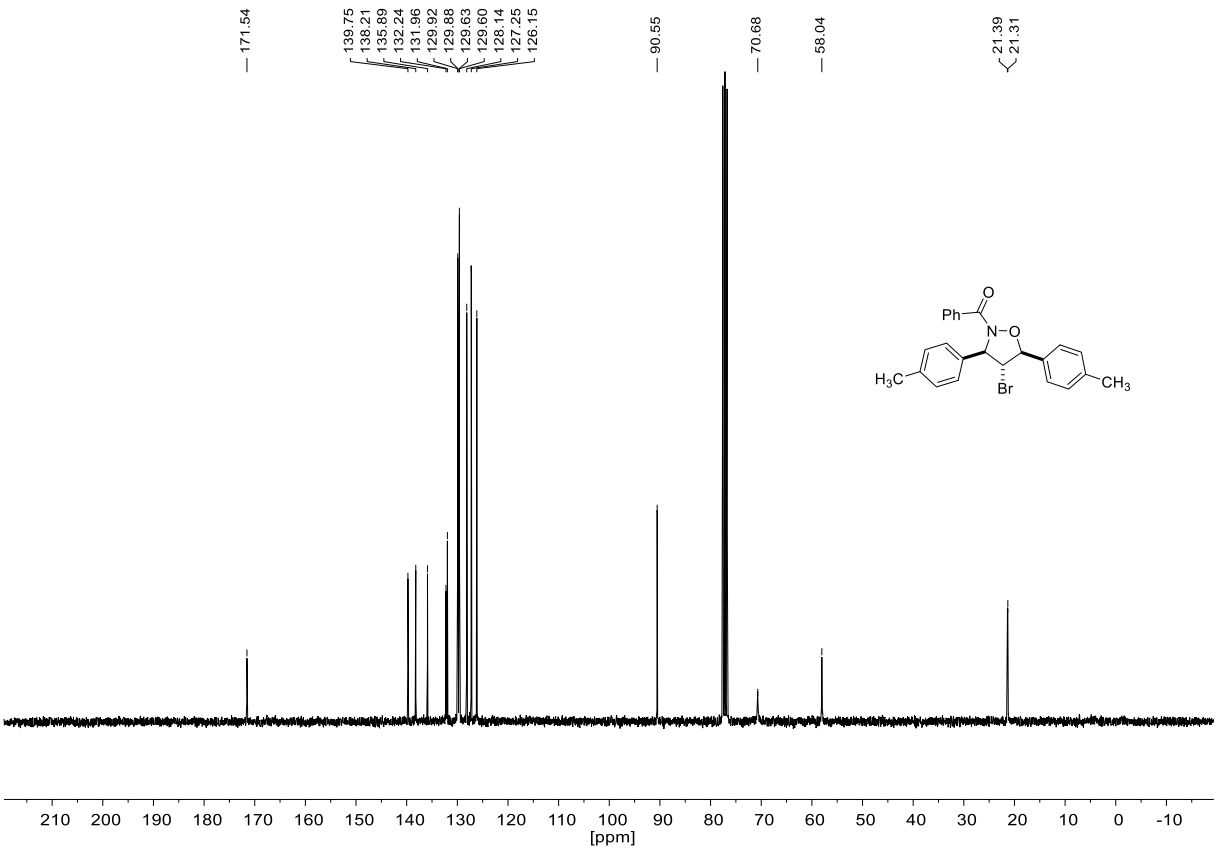
Retention Time	Area	Area %	Height	Height %
9,620	16554616	50,30	1134237	55,16
11,297	16359497	49,70	922144	44,84

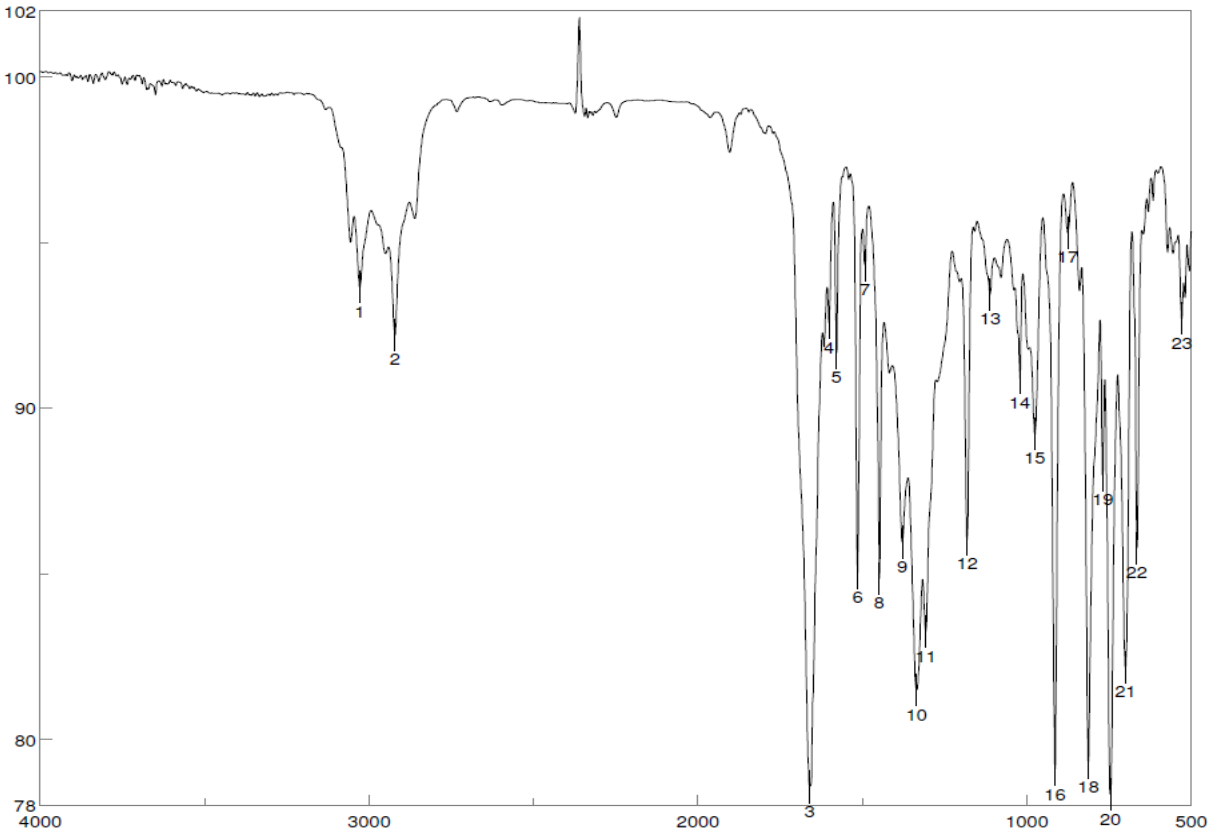


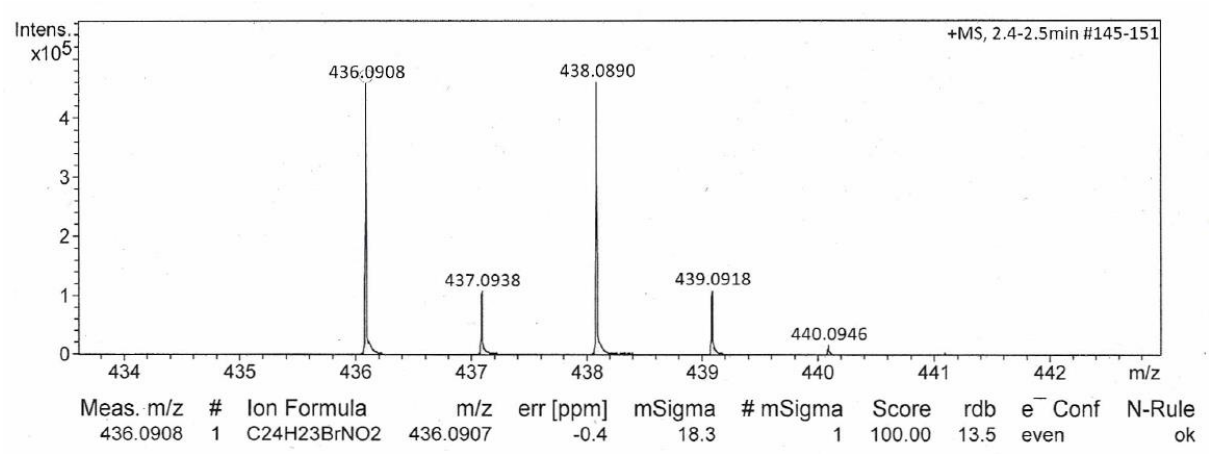
UV Results

Retention Time	Area	Area %	Height	Height %
9,727	958952	4,52	70601	7,31
11,300	20265671	95,48	895783	92,69


I (m)
7.47
G (td)
7.25
J(5.97, 1.34)
J (dt)
7.86
J(7.08, 1.41)
F (d)
7.17
J(7.87)
E (d)
5.81
J(5.71)
D (d)
5.05
J(8.77)
C (dd)
4.27
J(8.77, 5.73)
B (s)
2.38
A (s)
2.34
H (m)
7.39
Ph
O
N
O
Br
H3C
CH3
[ppm]

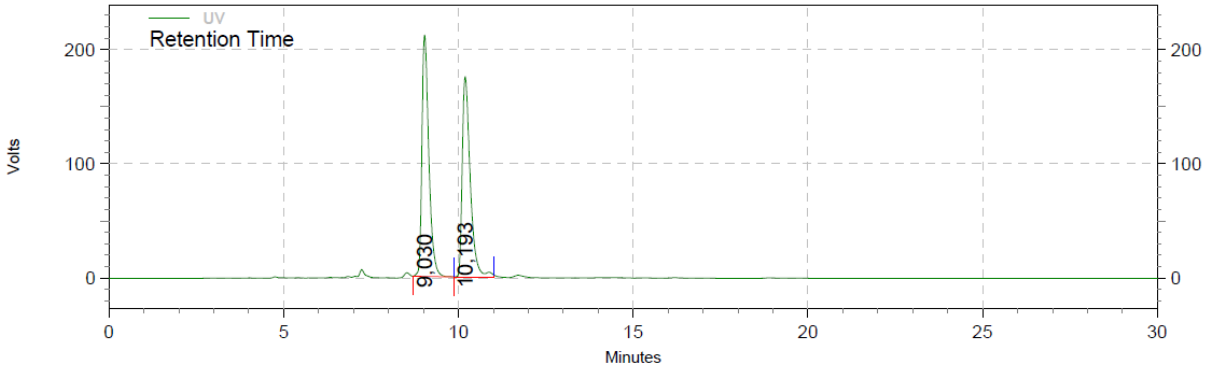

171.54
139.75
138.21
135.89
132.24
131.96
129.92
129.88
129.63
129.60
128.14
127.25
126.15
90.55
70.68
58.04
21.39
21.31
Ph
O
N
O
Br
H3C
CH3
[ppm]





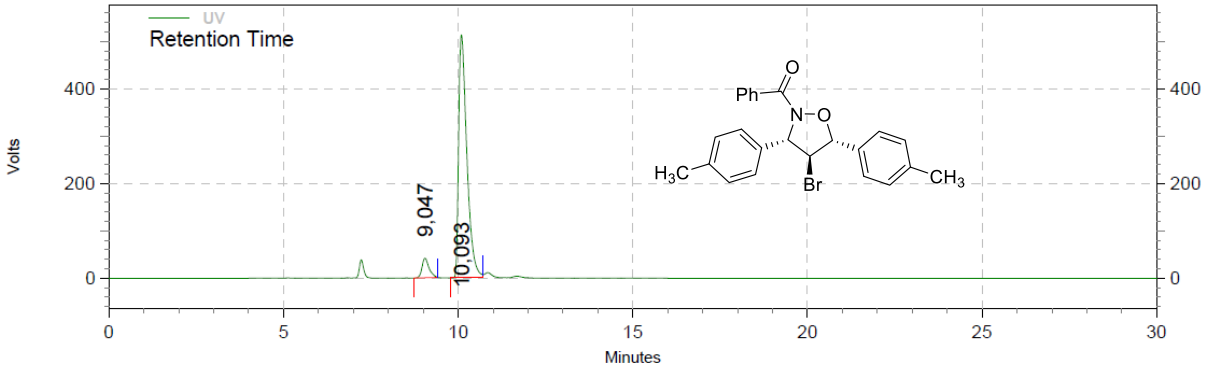
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
436.0908	1	C24H23BrNO2	436.0907	-0.4	18.3	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min



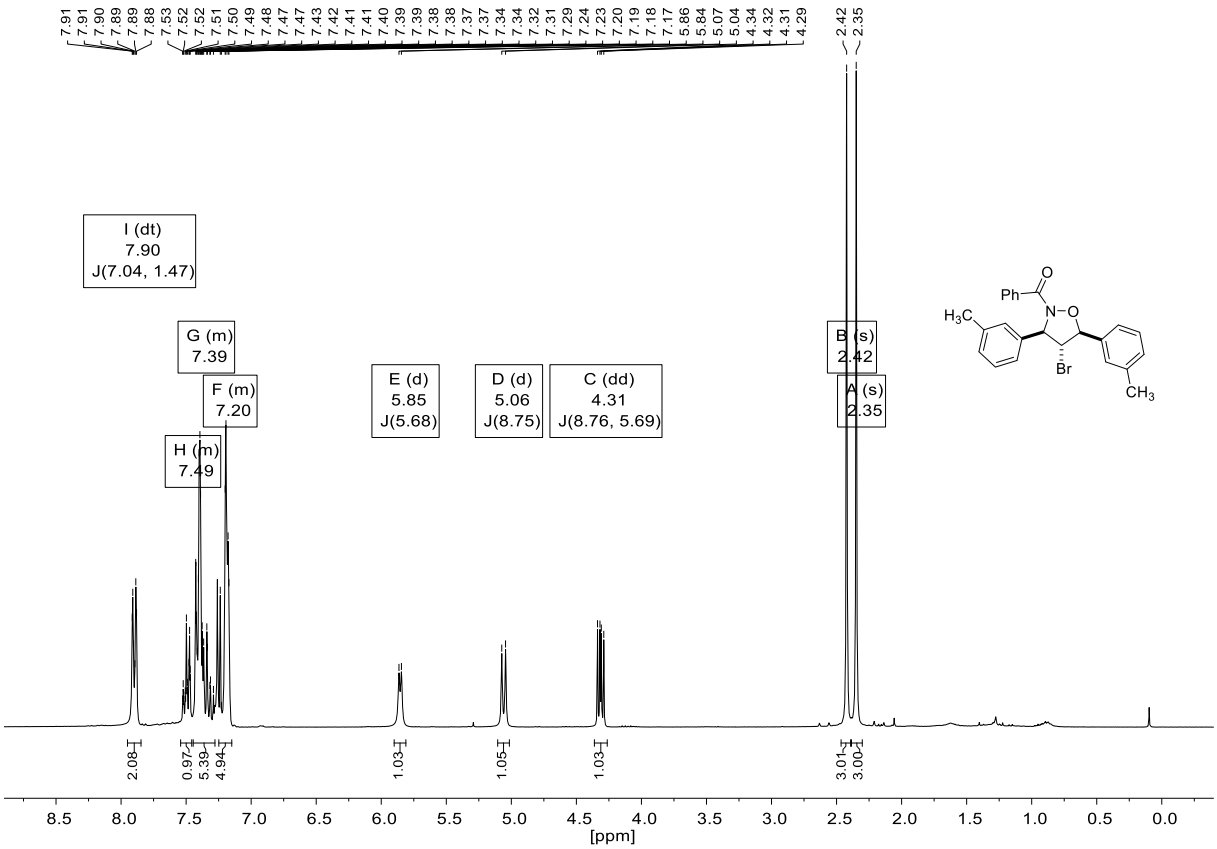
UV Results

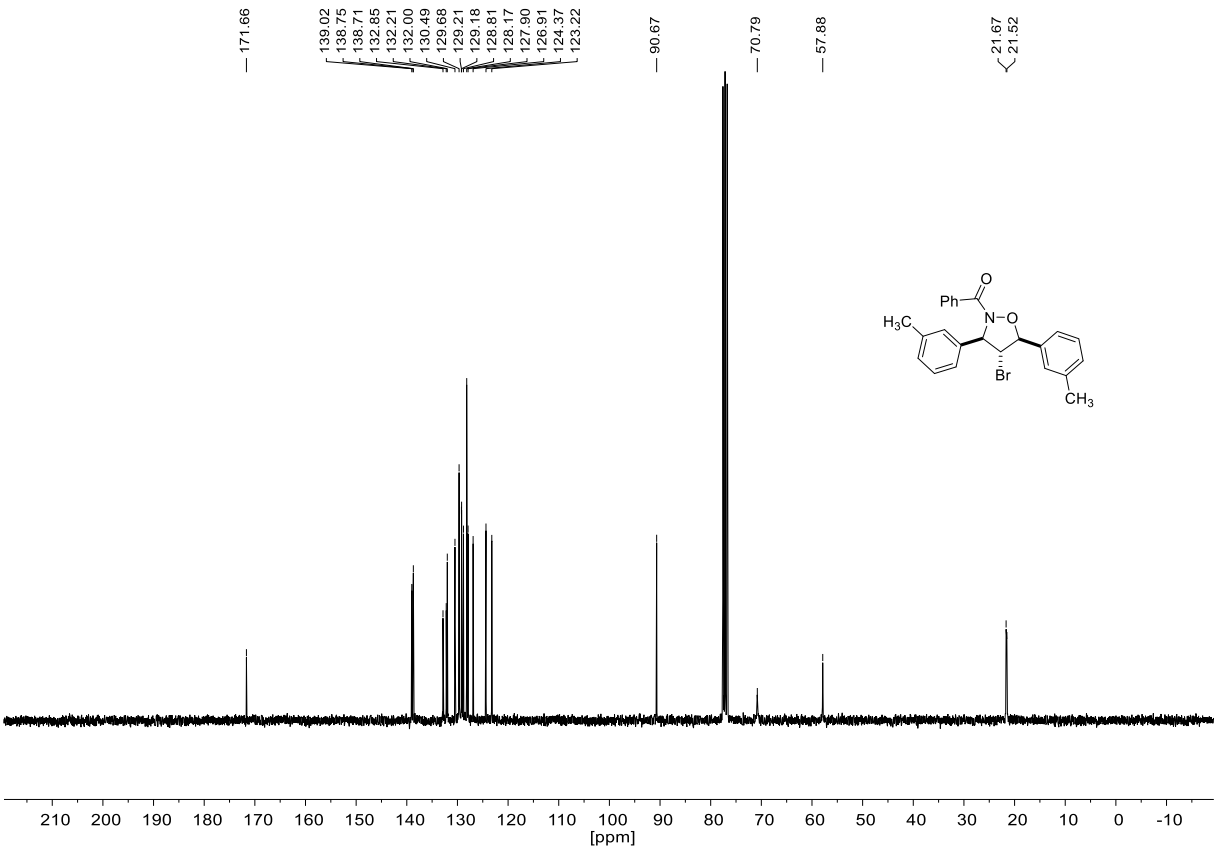
Retention Time	Area	Area %	Height	Height %
9,030	11564582	50,95	844730	54,66
10,193	11133561	49,05	700809	45,34

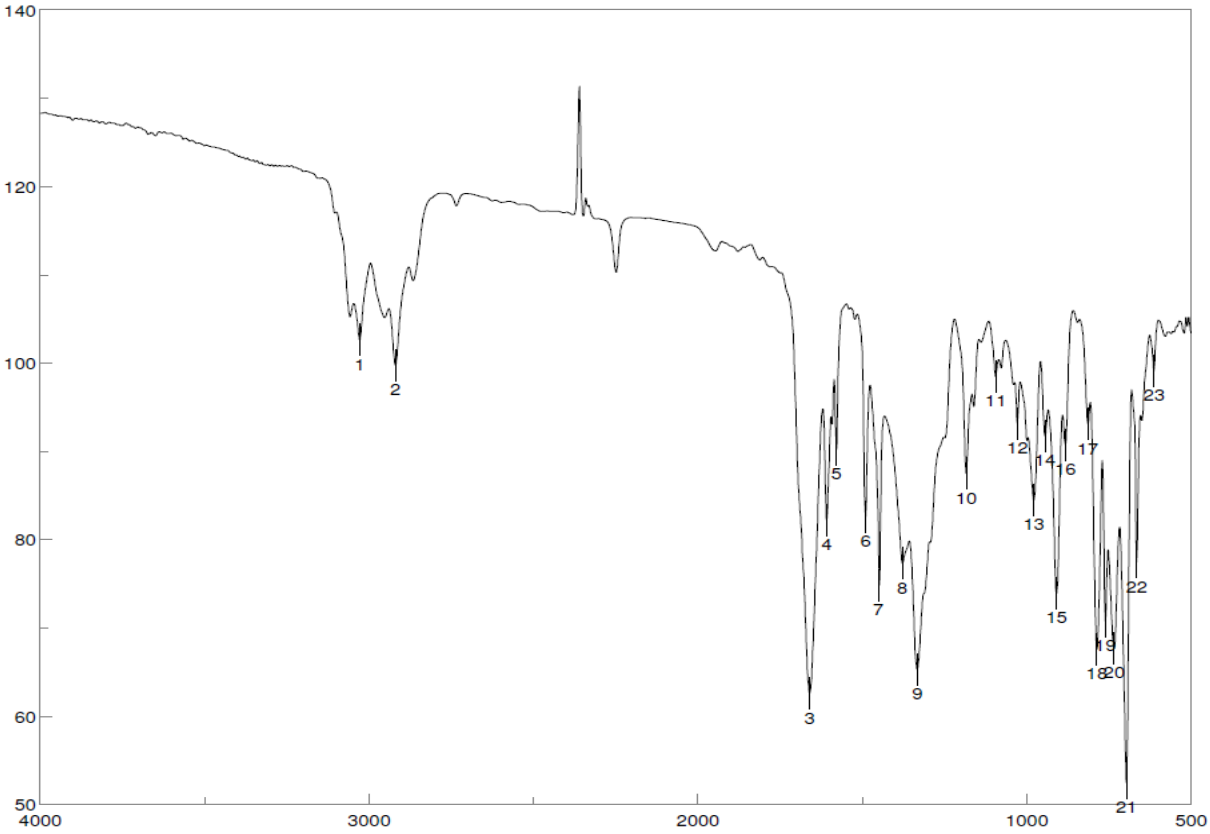


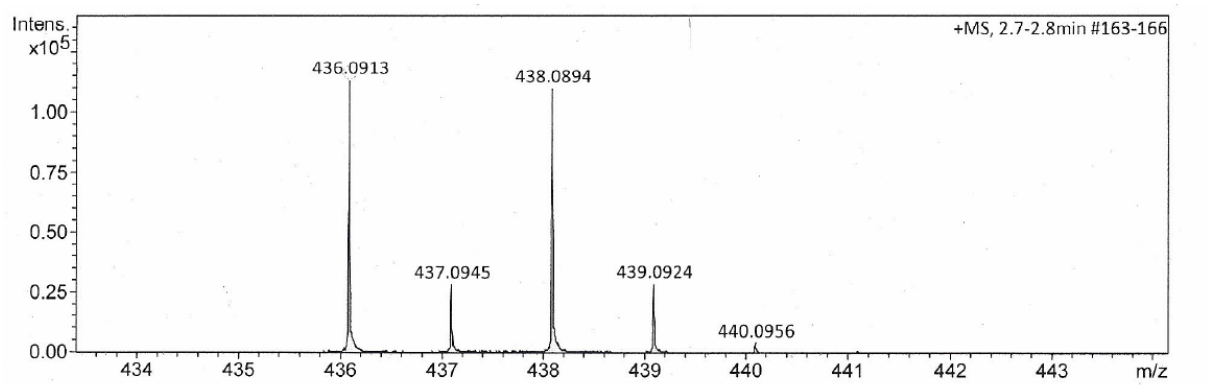
UV Results

Retention Time	Area	Area %	Height	Height %
9,047	2296347	6,38	164434	7,42
10,093	33686774	93,62	2051949	92,58


I (dt)
7.90
J(7.04, 1.47)
G (m)
7.39
F (m)
7.20
H (m)
7.49
E (d)
5.85
J(5.68)
D (d)
5.06
J(8.75)
C (dd)
4.31
J(8.76, 5.69)
B (s)
2.42
A (s)
2.35
2.08
0.97
5.39
4.94
1.03
1.05
1.03
3.01
3.00
[ppm]

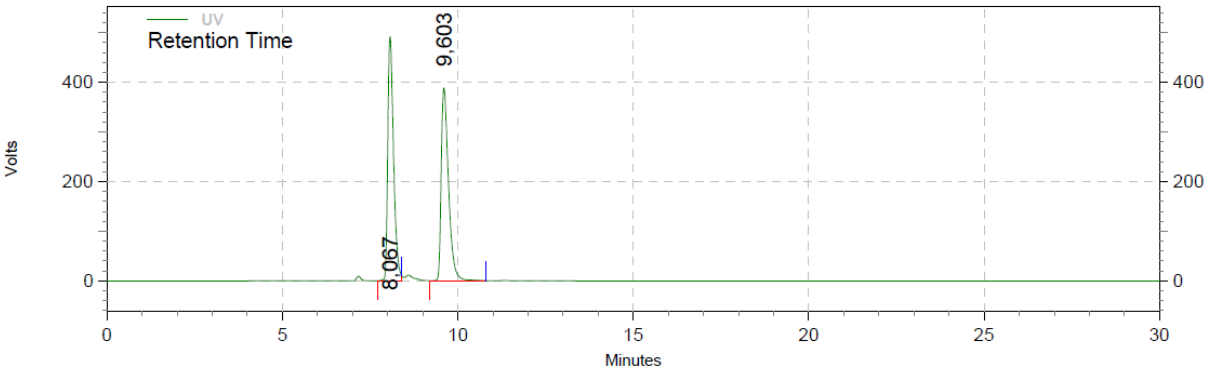

171.66
139.02
138.75
138.71
132.85
132.21
132.00
130.49
129.68
129.21
129.18
128.81
128.17
127.90
126.91
124.37
123.22
90.67
70.79
57.88
21.67
21.52
[ppm]





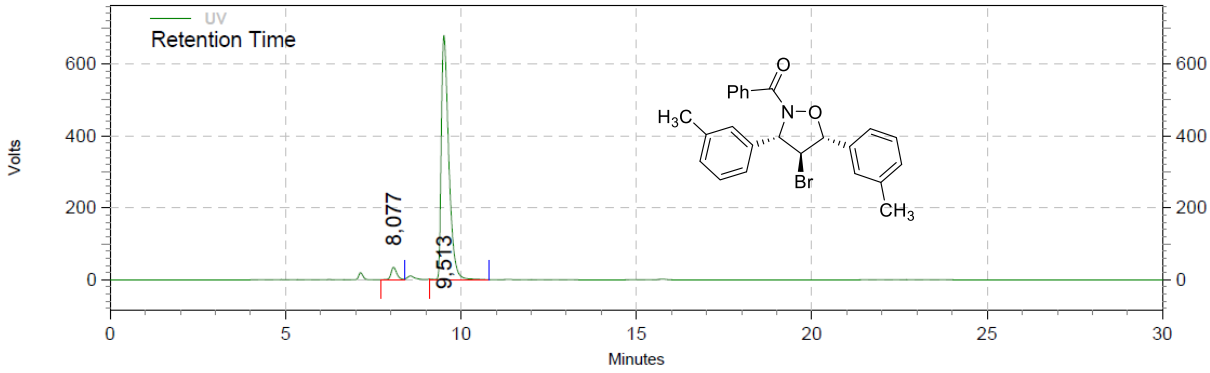
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e¯ Conf	N-Rule
436.0913	1	C24H23BrNO2	436.0907	-1.4	16.0	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min



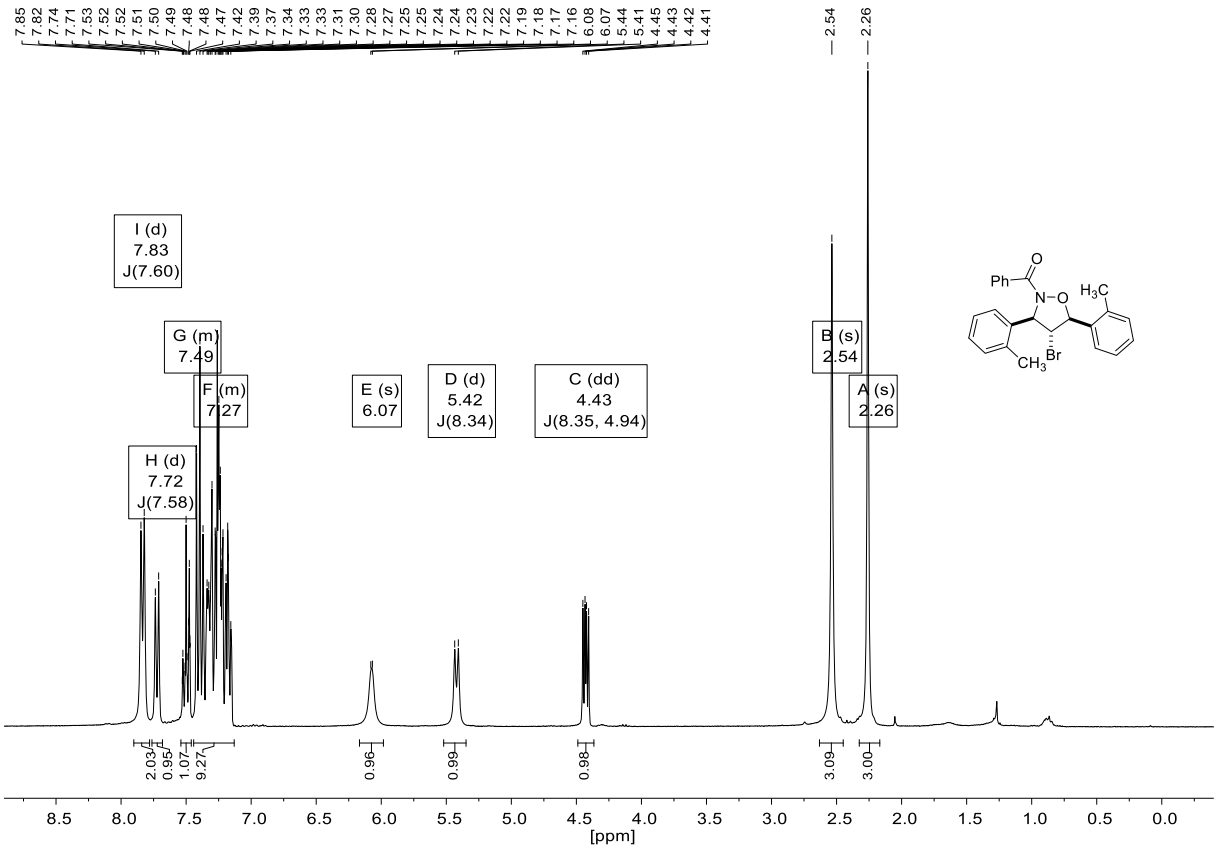
UV Results

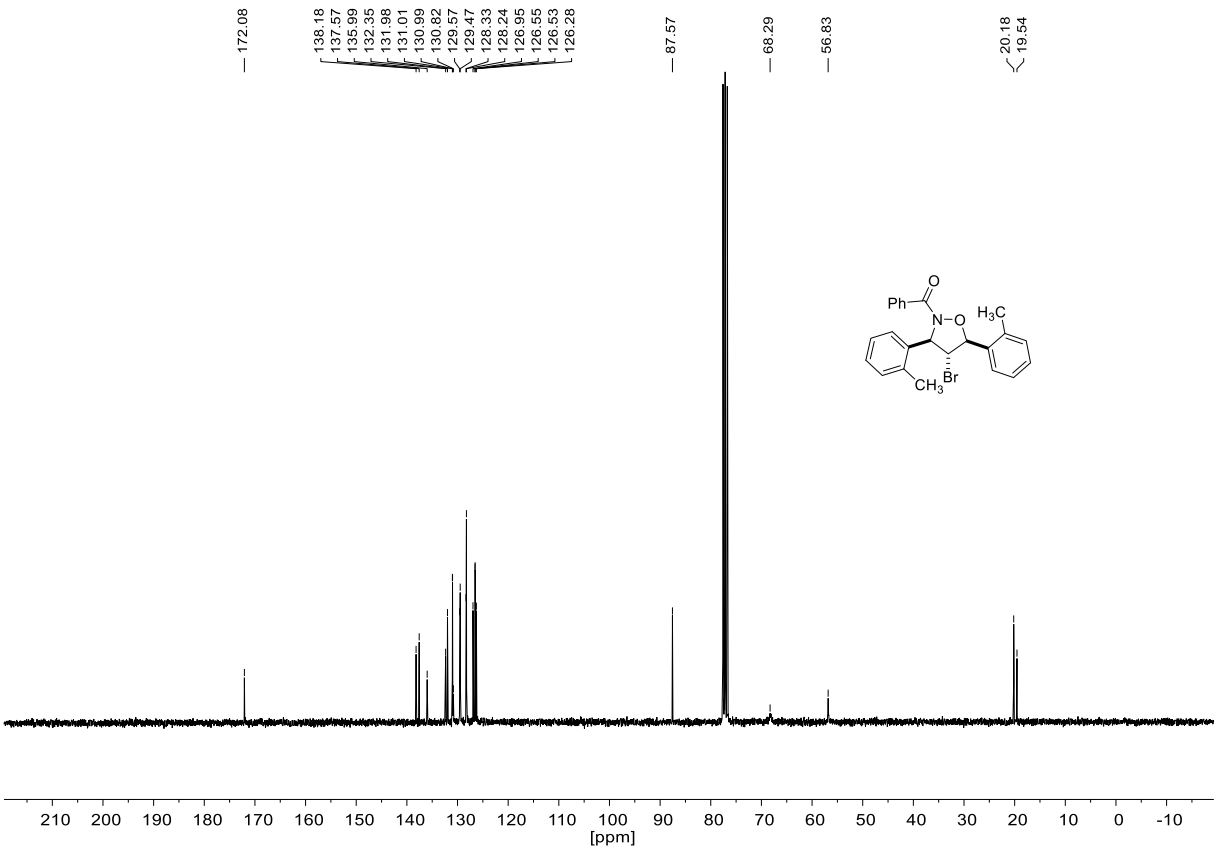
Retention Time	Area	Area %	Height	Height %
8,067	22508103	50,09	1967867	55,88
9,603	22430379	49,91	1553581	44,12

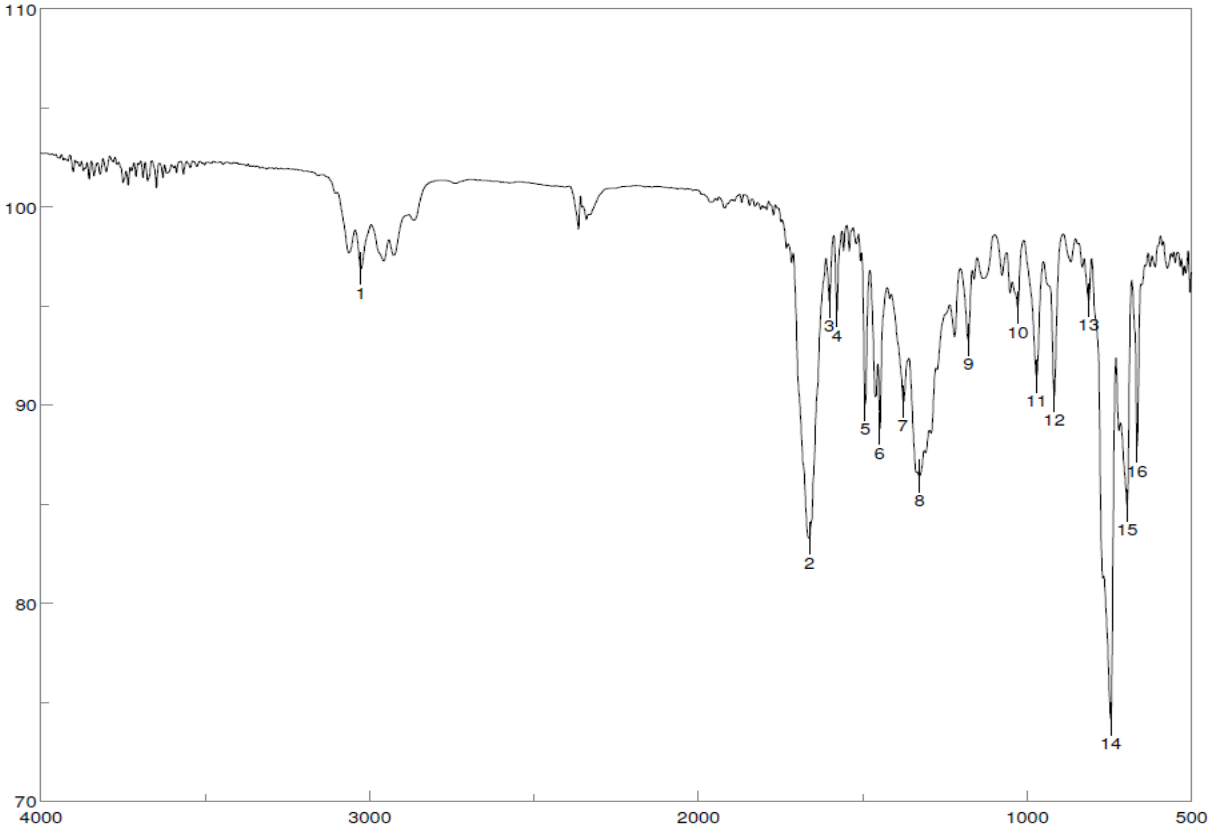


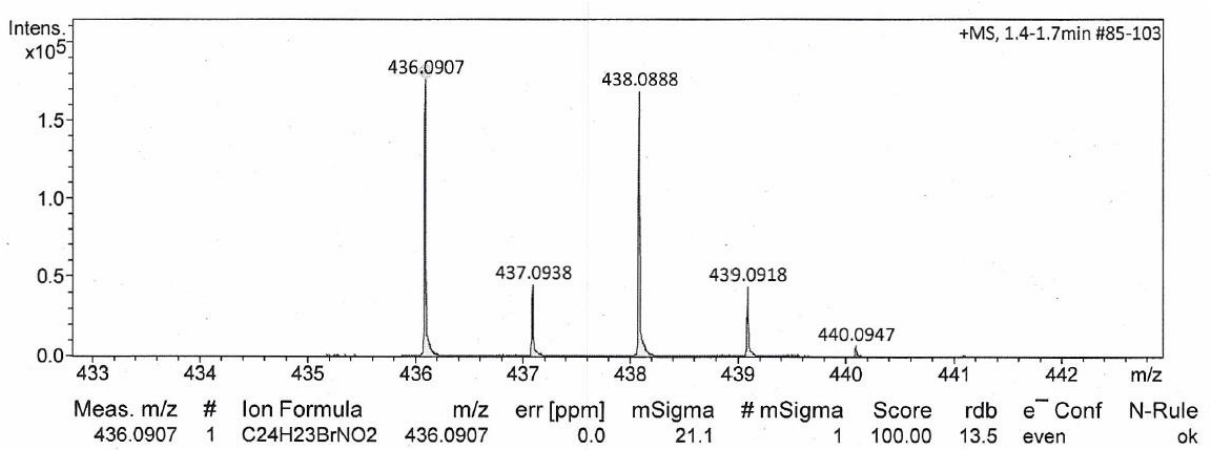
UV Results

Retention Time	Area	Area %	Height	Height %
8,077	1577302	3,79	136786	4,80
9,513	40040033	96,21	2715154	95,20


7.85 7.82 7.74 7.71 7.53 7.52 7.52 7.51 7.50 7.49 7.48 7.48 7.47 7.42 7.39 7.37 7.34 7.33 7.33 7.31 7.30 7.28 7.27 7.25 7.25 7.24 7.24 7.23 7.22 7.22 7.19 7.18 7.17 7.16 6.08 6.07 5.44 5.41 4.45 4.43 4.42 4.41
2.54 2.26
I (d) 7.83 J(7.60)
G (m) 7.49
F (m) 7.27
H (d) 7.72 J(7.58)
E (s) 6.07
D (d) 5.42 J(8.34)
C (dd) 4.43 J(8.35, 4.94)
B (s) 2.54
A (s) 2.26
2.03 0.95 1.07 9.27 0.96 0.99 0.98 3.09 3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

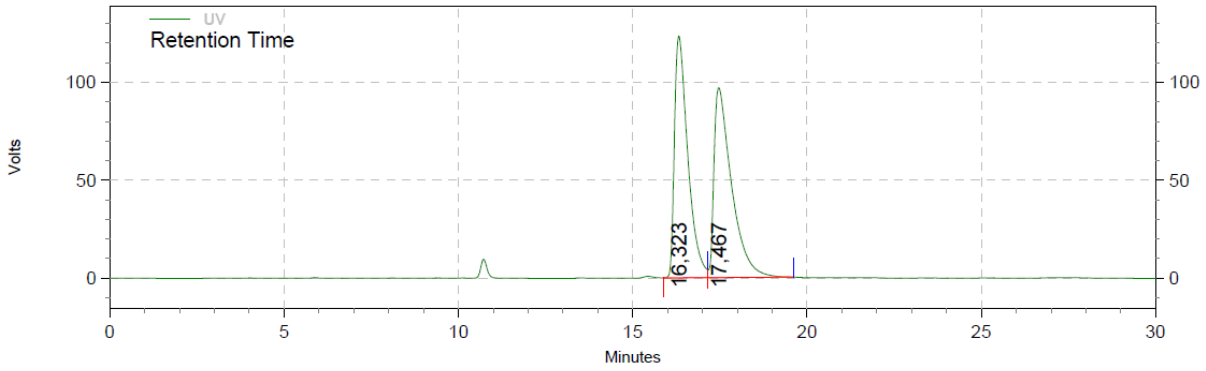

172.08
138.18 137.57 135.99 132.35 131.98 131.01 130.99 130.82 129.57 129.47 128.33 128.24 126.95 126.55 126.53 126.28
87.57
68.29
56.83
20.18 19.54
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]





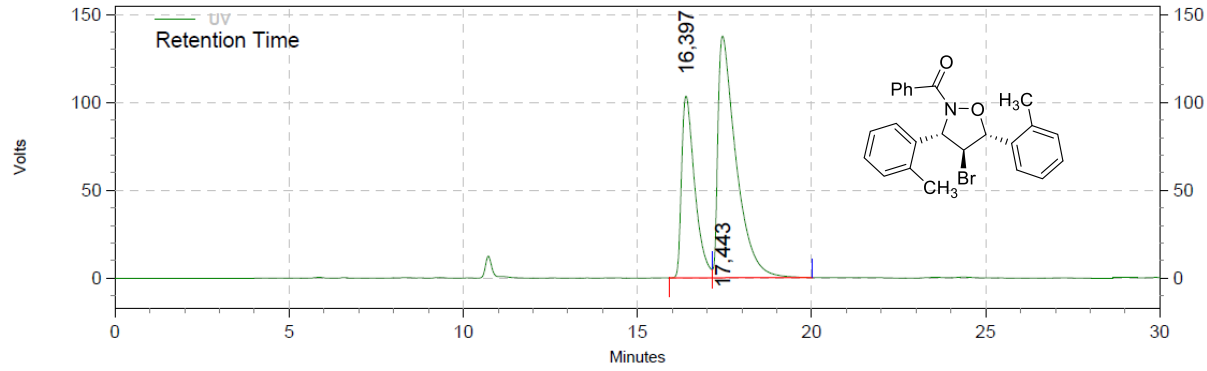
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e¯ Conf	N-Rule
436.0907	1	C24H23BrNO2	436.0907	0.0	21.1	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 99.5:0.5, 0.8 ml/min



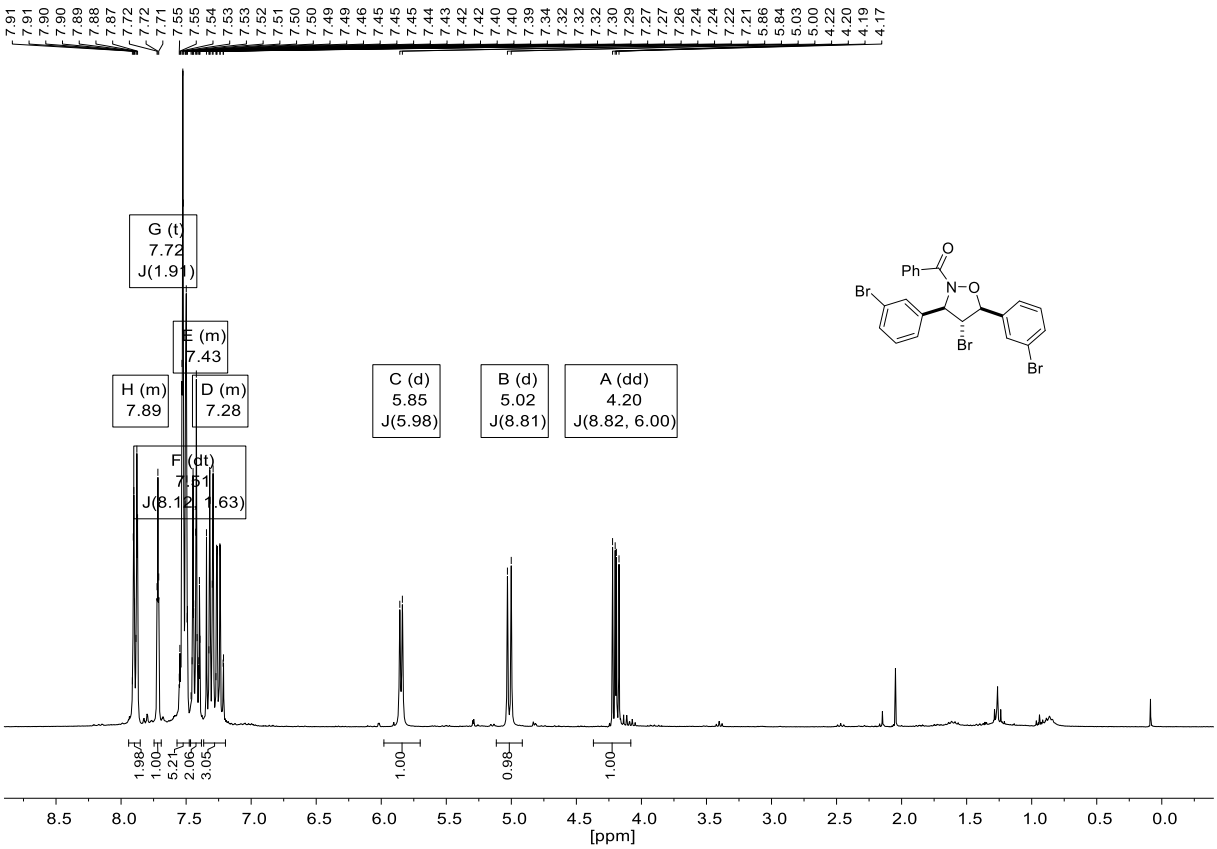
UV Results

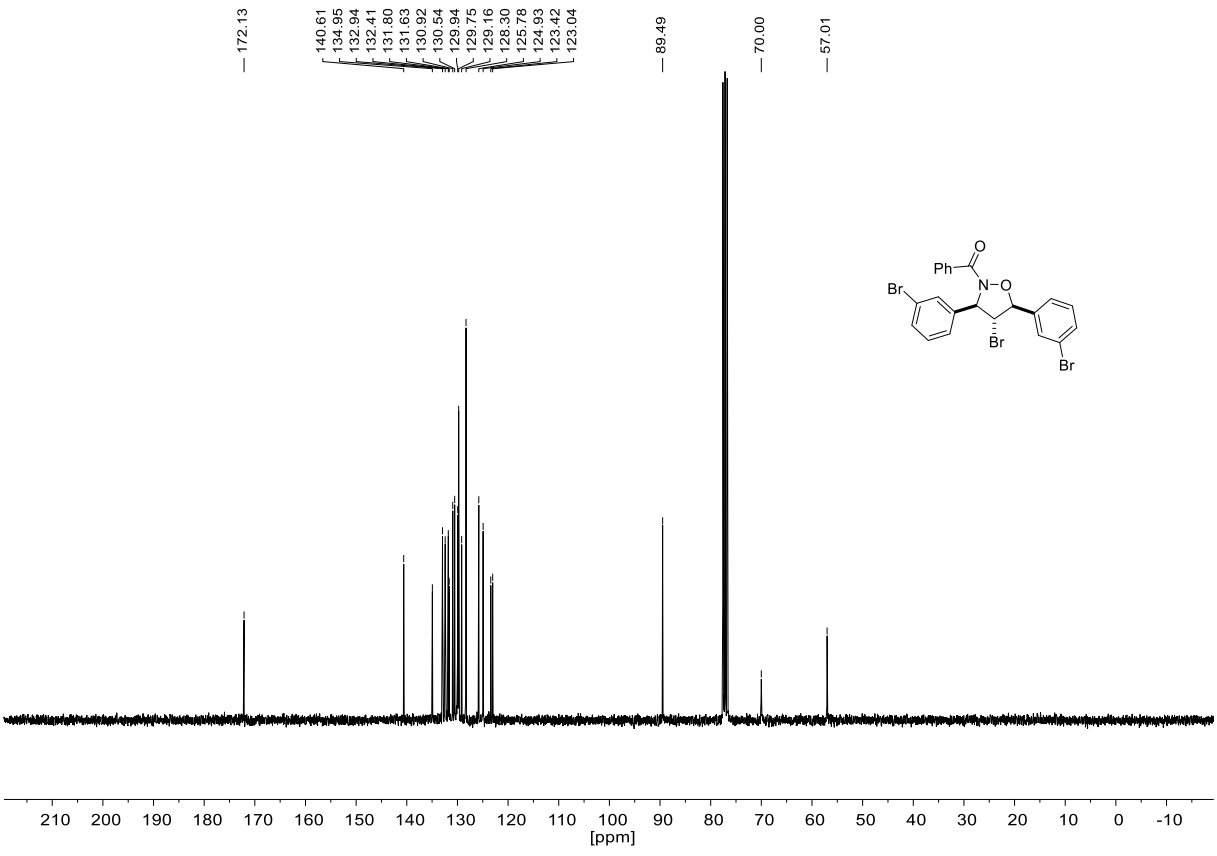
Retention Time	Area	Area %	Height	Height %
16,323	13148743	49,22	493705	56,02
17,467	13562933	50,78	387544	43,98

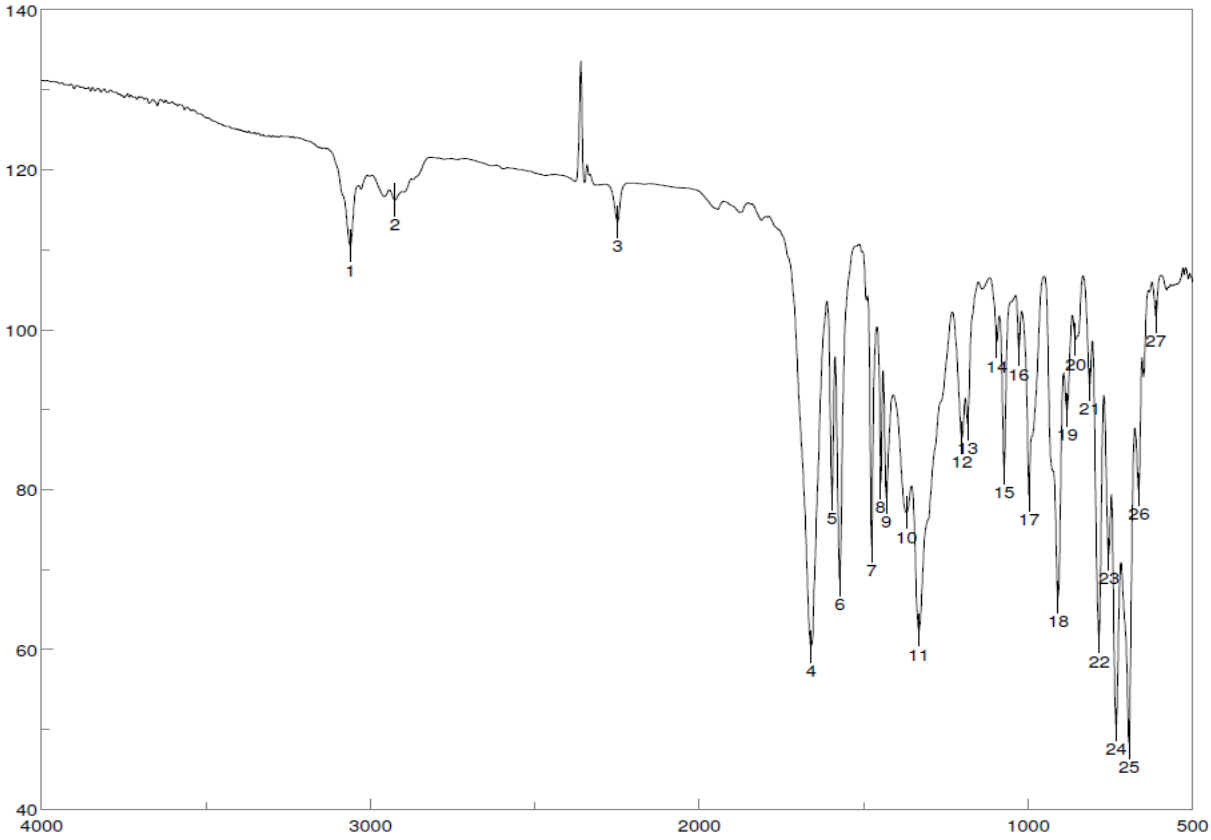


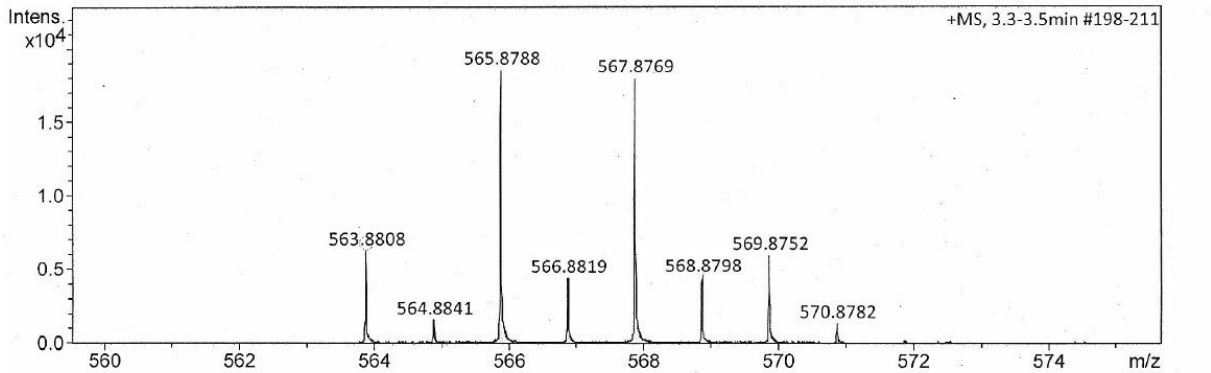
UV Results

Retention Time	Area	Area %	Height	Height %
16,397	10860330	35,20	413681	42,93
17,443	19988549	64,80	550032	57,07


7.91 7.91 7.90 7.90 7.89 7.88 7.87 7.72 7.72 7.71 7.55 7.55 7.54 7.53 7.53 7.52 7.51 7.50 7.50 7.49 7.49 7.46 7.45 7.45 7.45 7.44 7.43 7.42 7.42 7.40 7.40 7.39 7.34 7.32 7.32 7.30 7.29 7.27 7.27 7.26 7.24 7.22 7.21 5.86 5.84 5.03 5.00 4.22 4.20 4.19 4.17
G (t) 7.72 J(1.91)
E (m) 7.43
H (m) 7.89
D (m) 7.28
F (dt) 7.51 J(8.12, 1.63)
C (d) 5.85 J(5.98)
B (d) 5.02 J(8.81)
A (dd) 4.20 J(8.82, 6.00)
1.98 1.00 5.21 2.06 3.05 1.00 0.98 1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]
O
Ph
N
O
Br
Br
Br

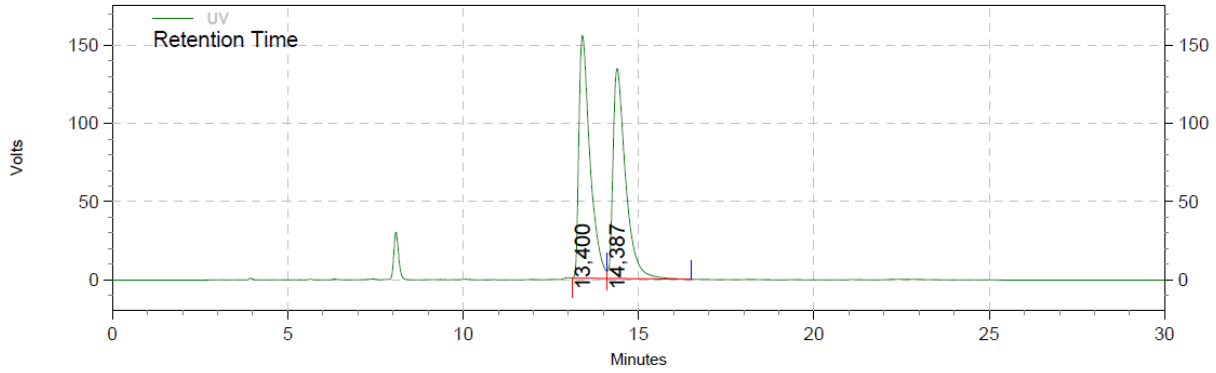

172.13
140.61 134.95 132.94 132.41 131.80 131.63 130.92 130.54 129.94 129.75 129.16 128.30 125.78 124.93 123.42 123.04
89.49
70.00
57.01
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]
O
Ph
N
O
Br
Br
Br





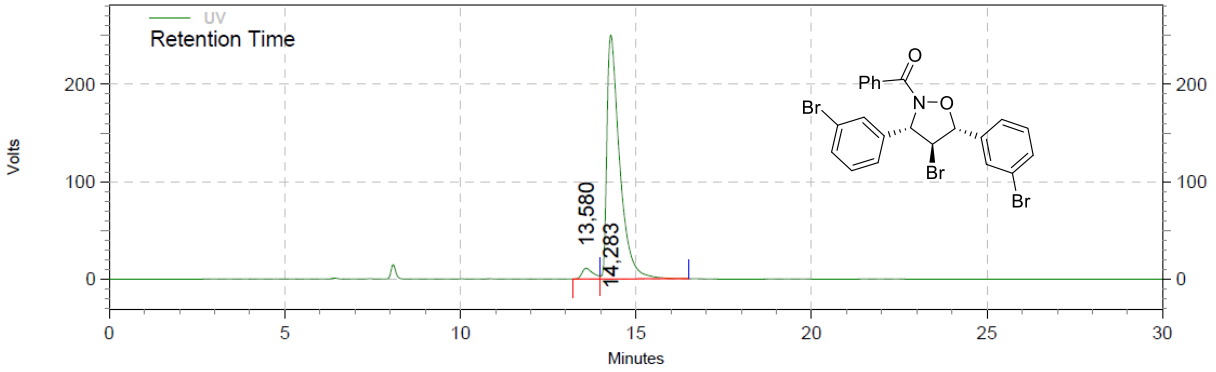
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
563.8808	1	C22H17Br3NO2	563.8804	-0.7	12.1	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 99:1, 0.8 ml/min



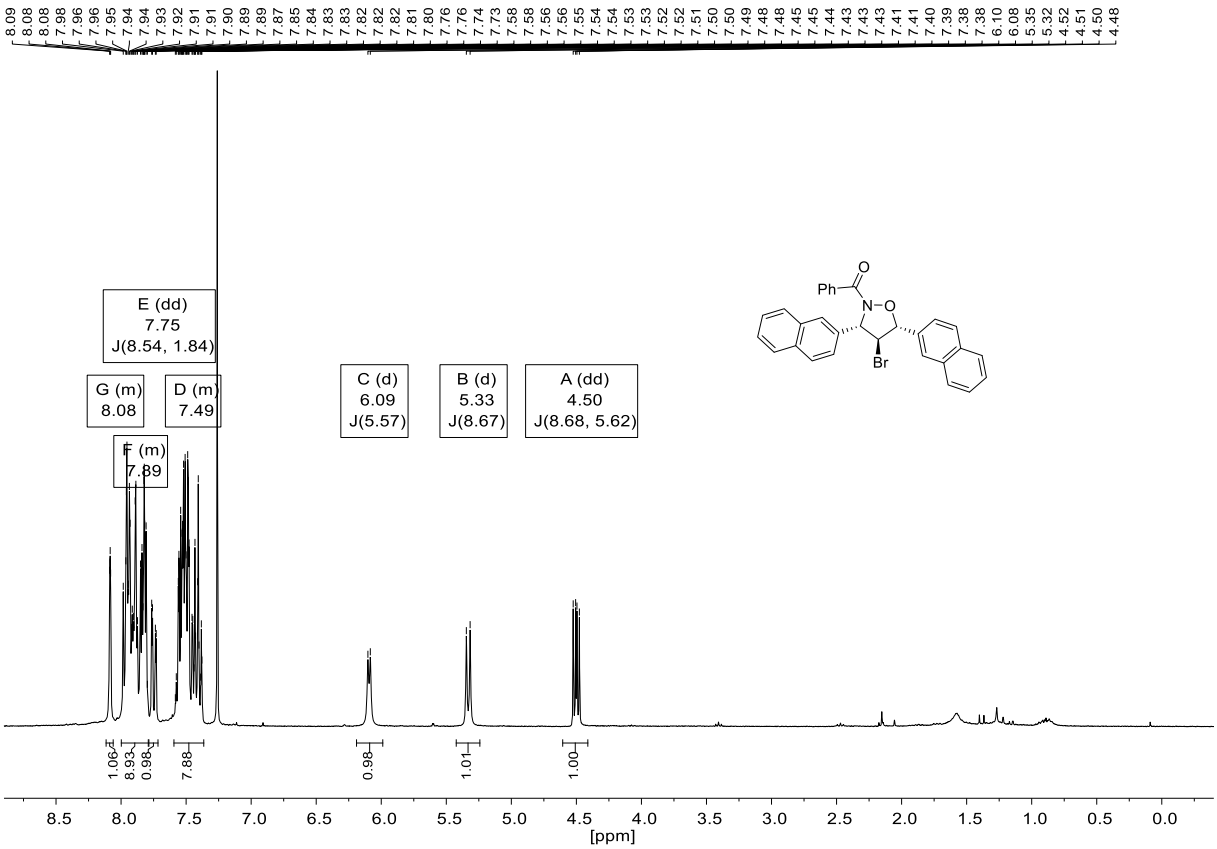
UV Results

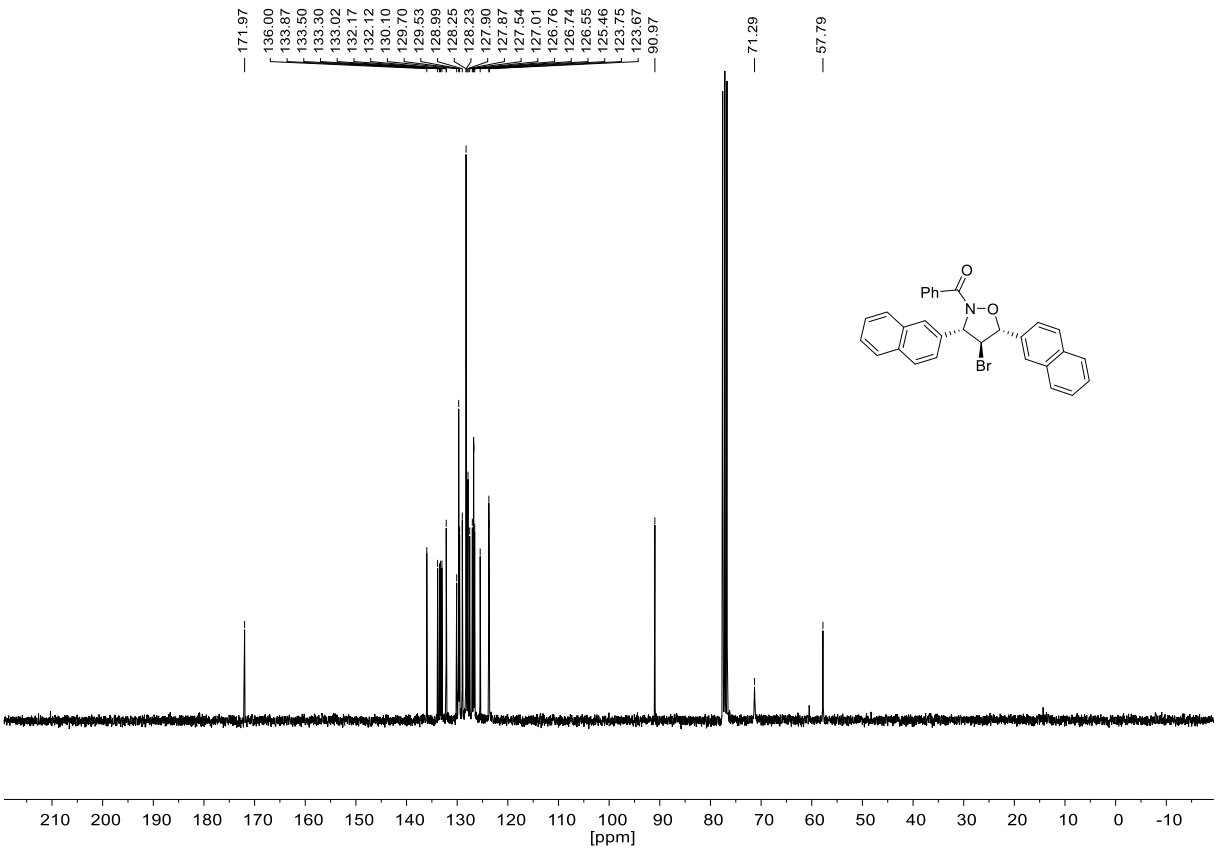
Retention Time	Area	Area %	Height	Height %
13,400	13658002	50,43	620671	53,62
14,387	13423920	49,57	536968	46,38

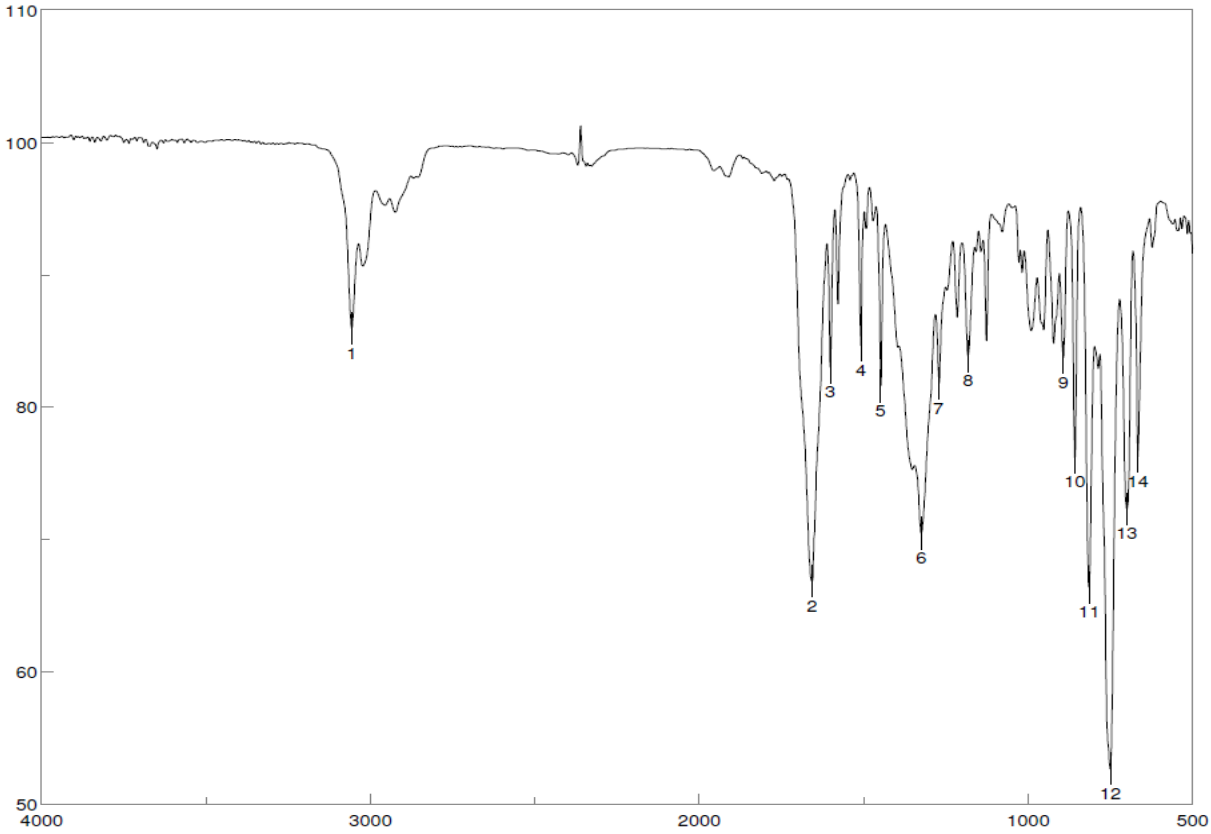


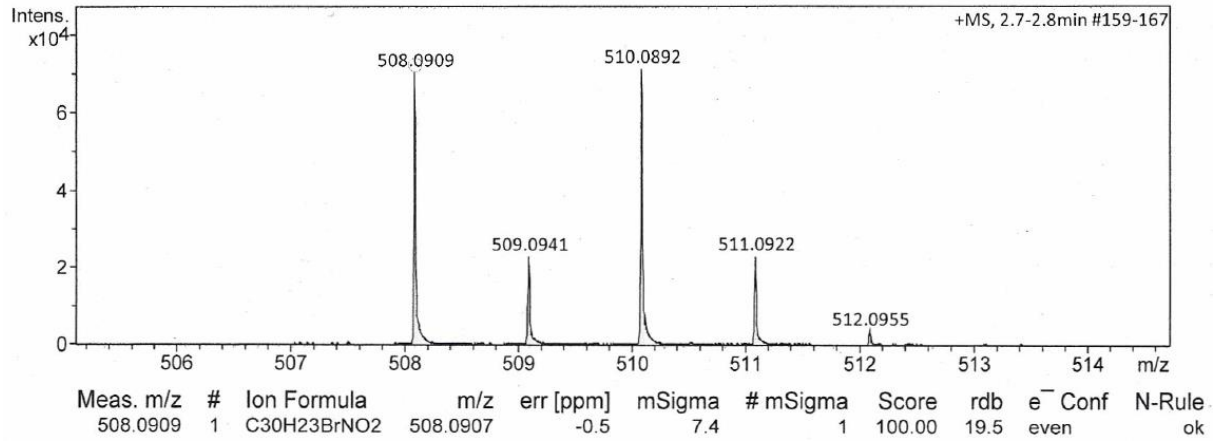
UV Results

Retention Time	Area	Area %	Height	Height %
13,580	976603	3,72	43926	4,20
14,283	25273490	96,28	1001695	95,80


E (dd)
7.75
J(8.54, 1.84)
G (m)
8.08
D (m)
7.49
F (m)
7.89
C (d)
6.09
J(5.57)
B (d)
5.33
J(8.67)
A (dd)
4.50
J(8.68, 5.62)
Ph
O
N
O
Br
[ppm]

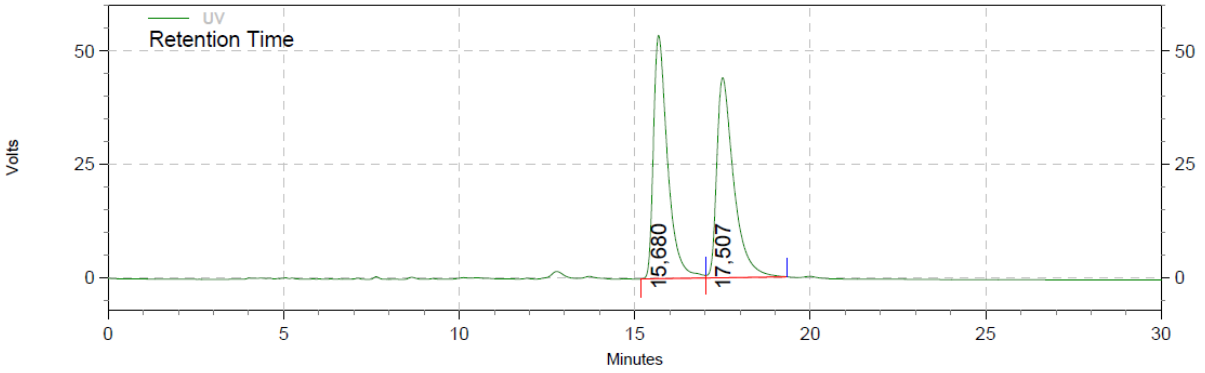

171.97
136.00
133.87
133.50
133.30
133.02
132.17
132.12
130.10
129.70
129.53
128.99
128.25
128.23
127.90
127.87
127.54
127.01
126.76
126.74
126.55
125.46
123.75
123.67
90.97
71.29
57.79
Ph
O
N
O
Br
[ppm]





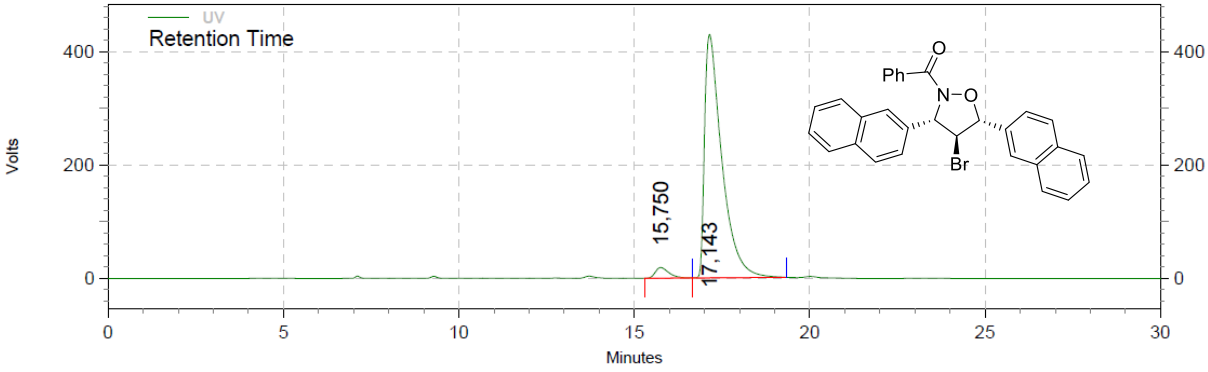
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
508.0909	1	C30H23BrNO2	508.0907	-0.5	7.4	1	100.00	19.5	even	ok

IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min



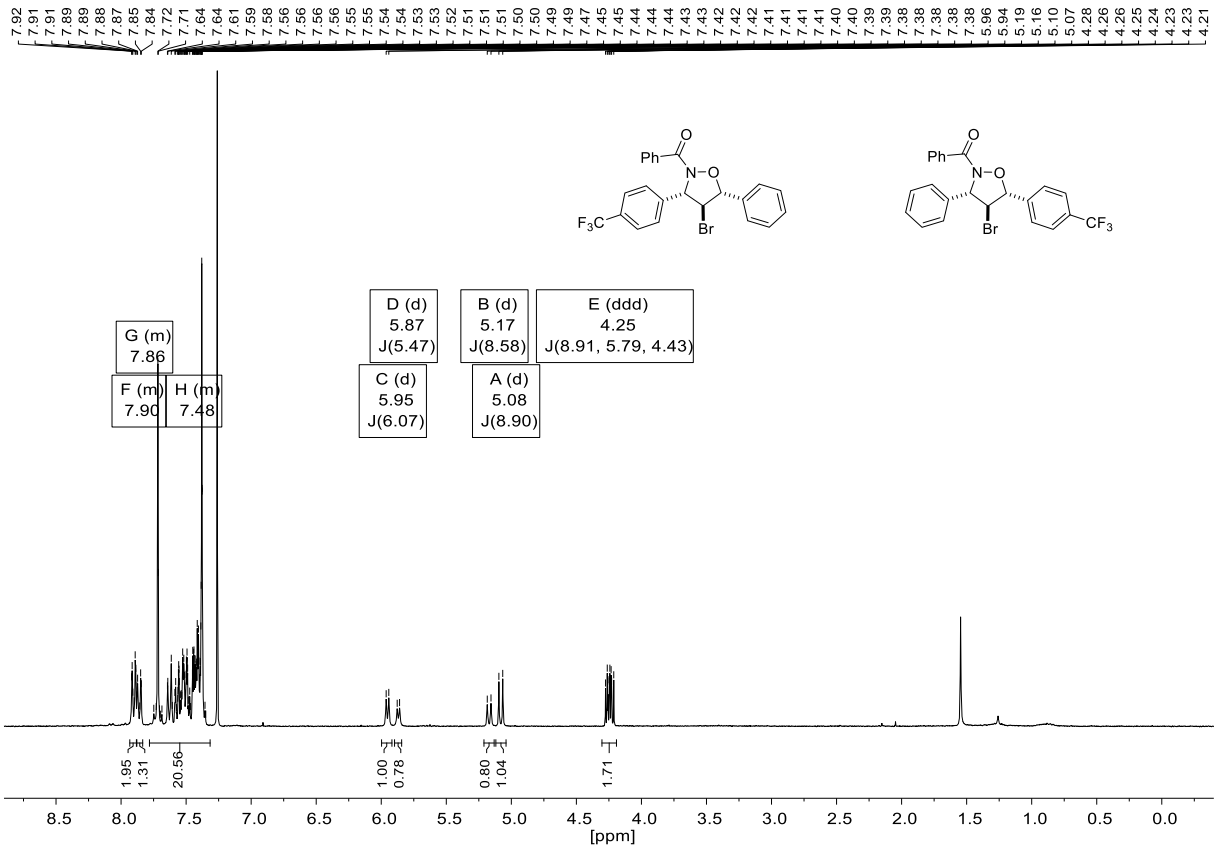
UV Results

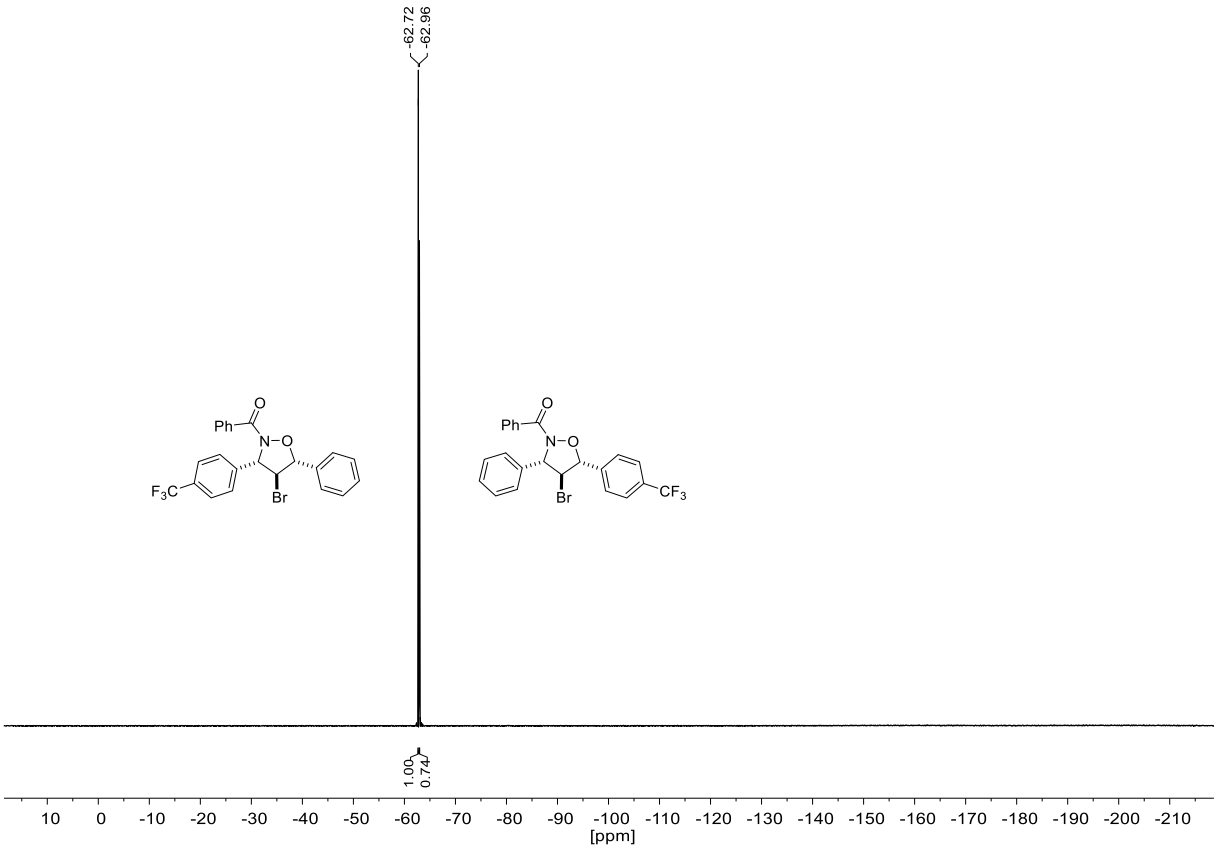
Retention Time	Area	Area %	Height	Height %
15,680	6036287	50,31	214951	54,88
17,507	5963050	49,69	176725	45,12

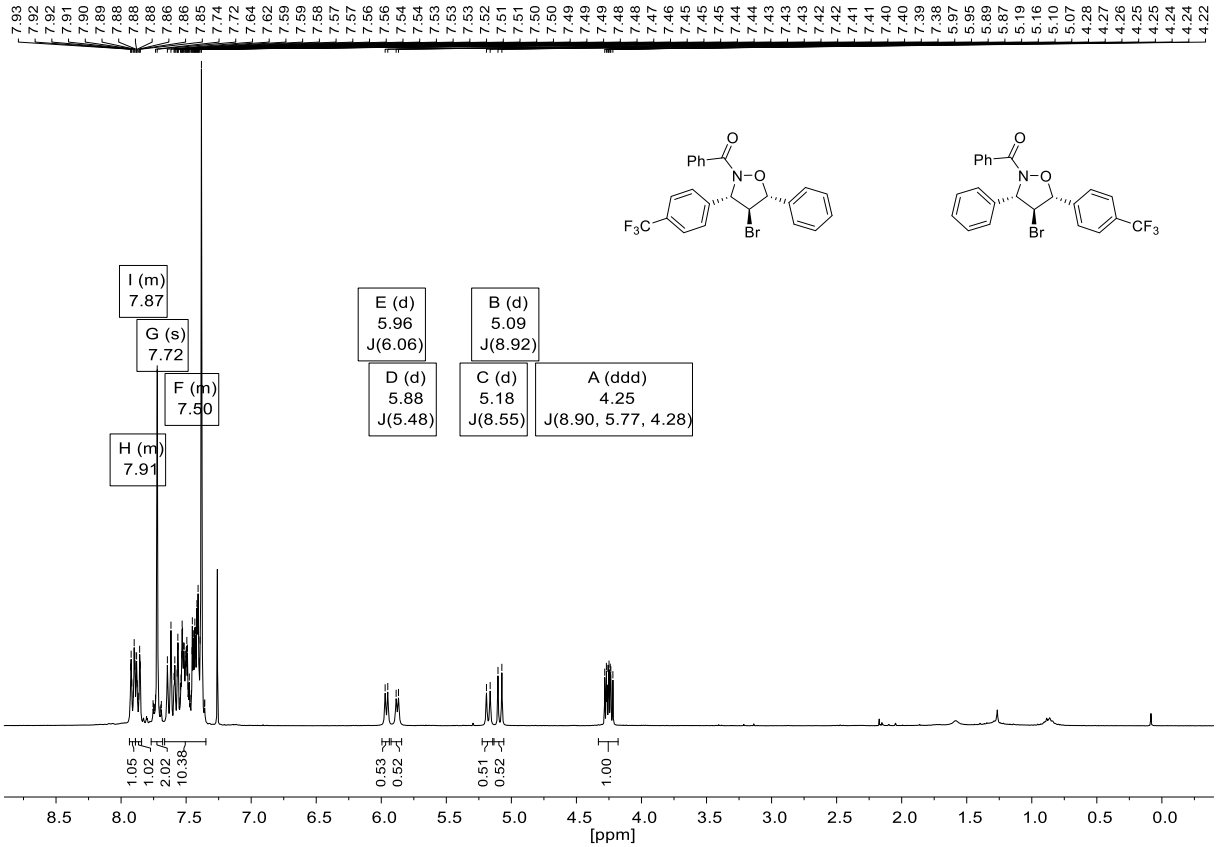


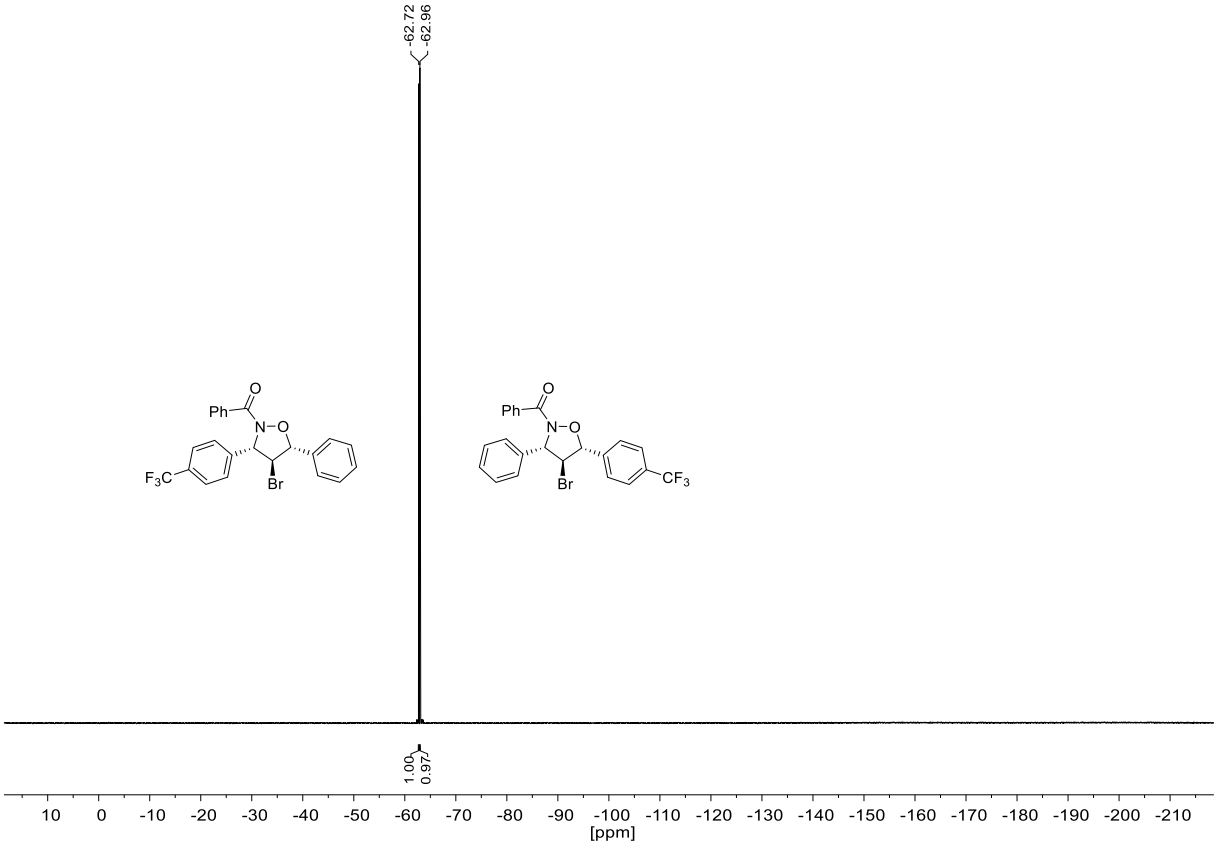
UV Results

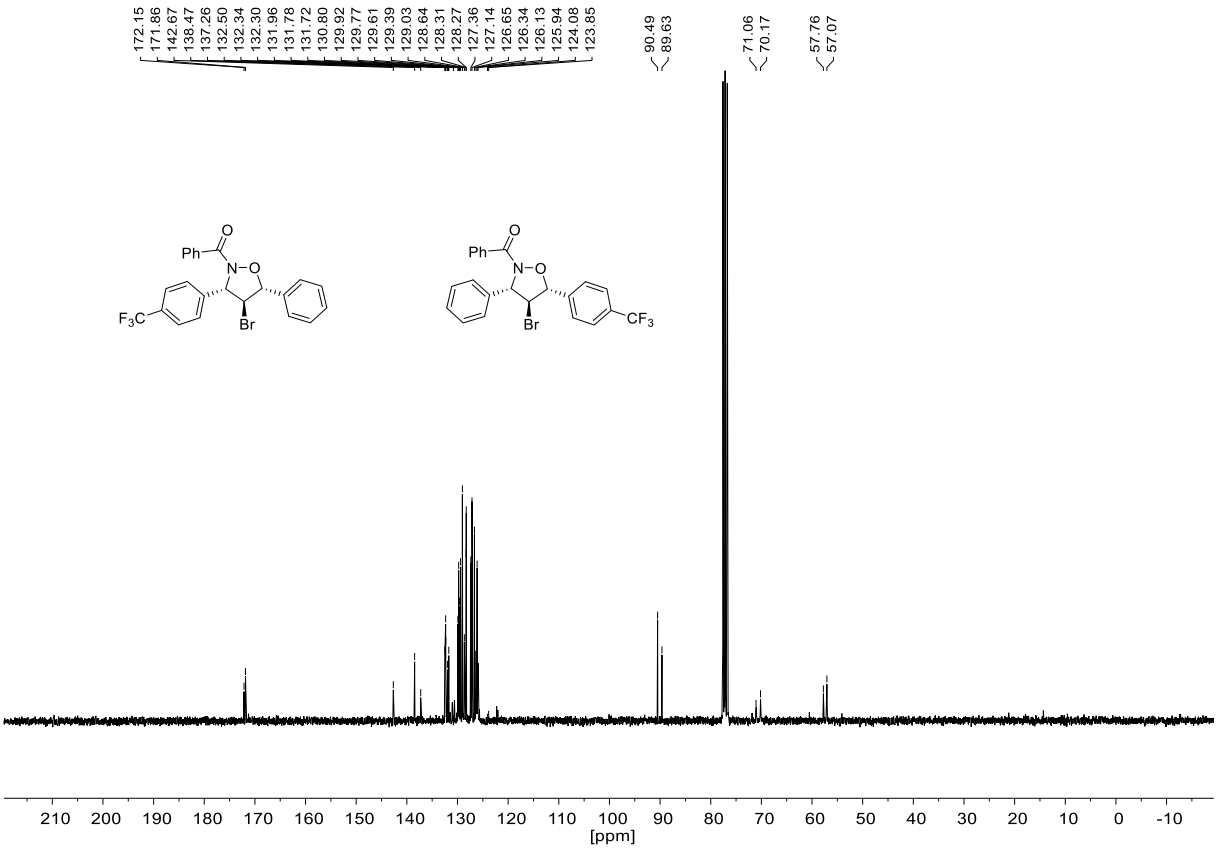
Retention Time	Area	Area %	Height	Height %
15,750	2025257	3,33	75296	4,20
17,143	58769348	96,67	1718643	95,80

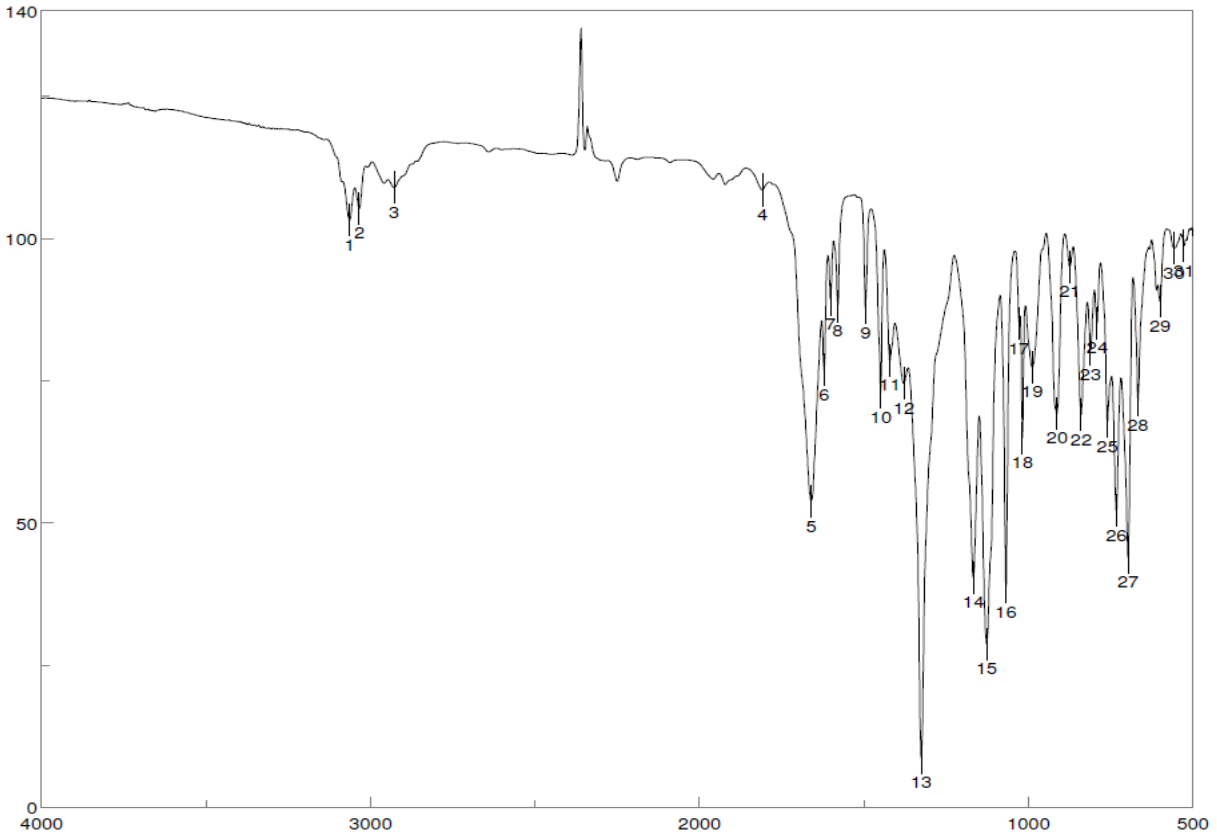

7.92 7.91 7.91 7.89 7.89 7.88 7.87 7.85 7.84 7.72 7.71 7.64 7.64 7.61 7.59 7.58 7.56 7.56 7.56 7.56 7.55 7.55 7.54 7.54 7.53 7.53 7.52 7.51 7.51 7.51 7.50 7.50 7.49 7.49 7.47 7.45 7.45 7.44 7.44 7.44 7.43 7.43 7.42 7.42 7.42 7.41 7.41 7.41 7.41 7.40 7.39 7.39 7.38 7.38 7.38 7.38 5.96 5.94 5.19 5.16 5.10 5.07 4.28 4.26 4.26 4.25 4.24 4.23 4.23 4.21
Ph
O
N–O
F3C
Br
CF3
G (m) 7.86
F (m) 7.90
H (m) 7.48
D (d) 5.87 J(5.47)
C (d) 5.95 J(6.07)
B (d) 5.17 J(8.58)
A (d) 5.08 J(8.90)
E (ddd) 4.25 J(8.91, 5.79, 4.43)
1.95
1.31
20.56
1.00
0.78
0.80
1.04
1.71
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

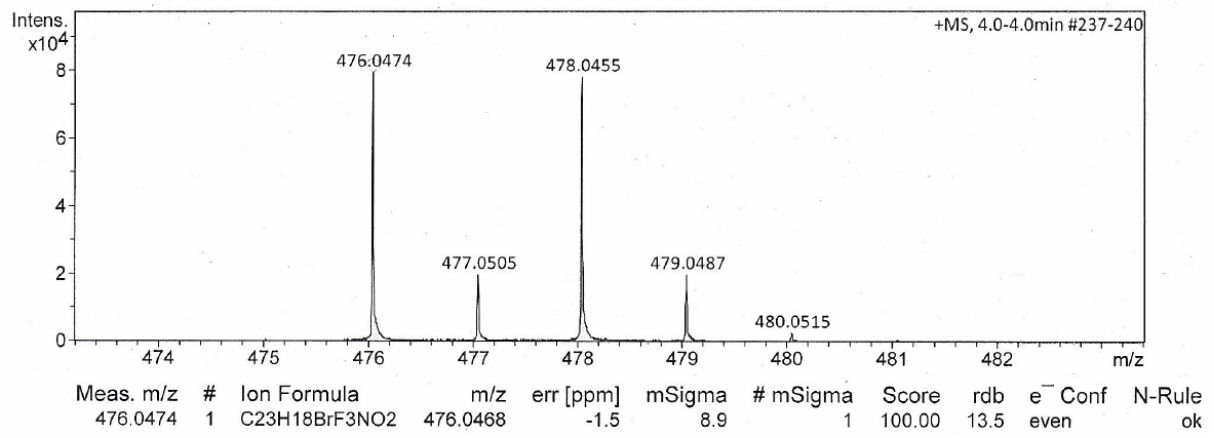

-62.72
-62.96
Ph
O
N–O
F3C
Br
CF3
1.00
0.74
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]


I (m)
7.87
G (s)
7.72
F (m)
7.50
H (m)
7.91
E (d)
5.96
J(6.06)
D (d)
5.88
J(5.48)
B (d)
5.09
J(8.92)
C (d)
5.18
J(8.55)
A (ddd)
4.25
J(8.90, 5.77, 4.28)
[ppm]


-62.72
-62.96
[ppm]

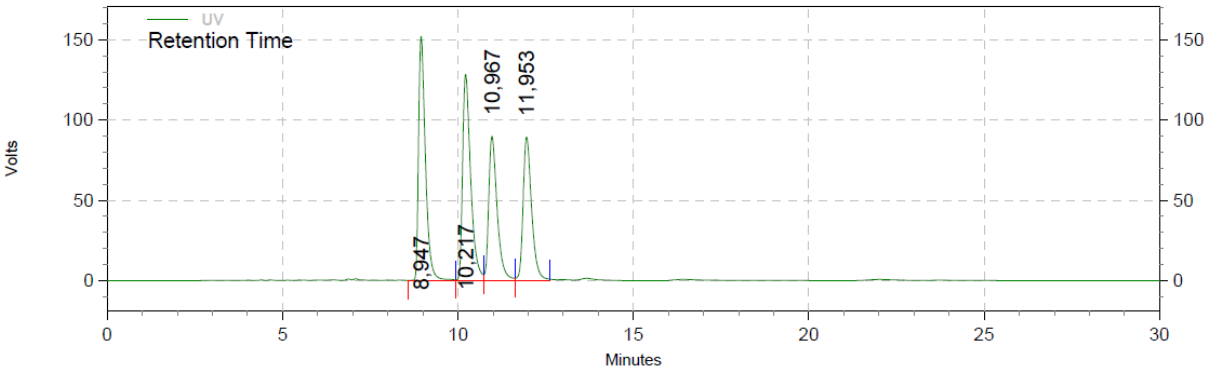

172.15
171.86
142.67
138.47
137.26
132.50
132.34
132.30
131.96
131.78
131.72
130.80
129.92
129.77
129.61
129.39
129.03
128.64
128.31
128.27
127.36
127.14
126.65
126.34
126.13
125.94
124.08
123.85
90.49
89.63
71.06
70.17
57.76
57.07
Ph
O
N–O
Br
F3C
CF3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]


140
100
50
0
4000
3000
2000
1000
500



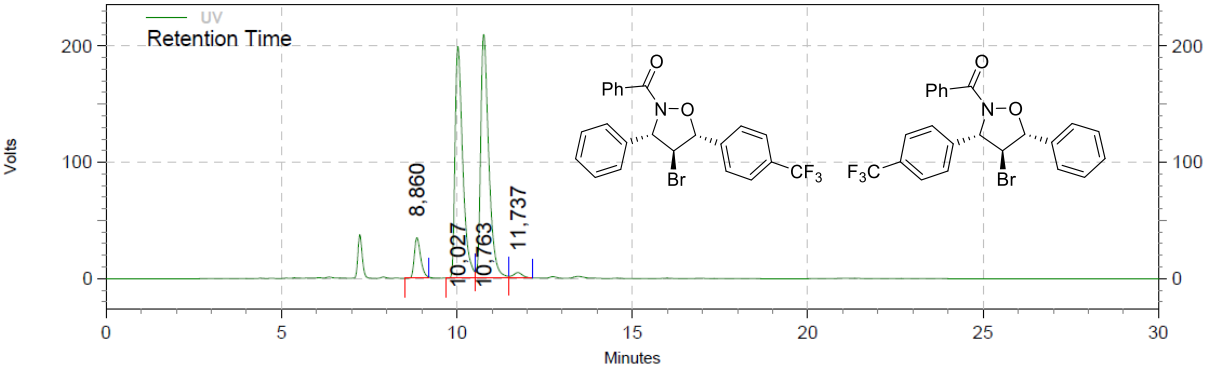
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
476.0474	1	C23H18BrF3NO2	476.0468	-1.5	8.9	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min



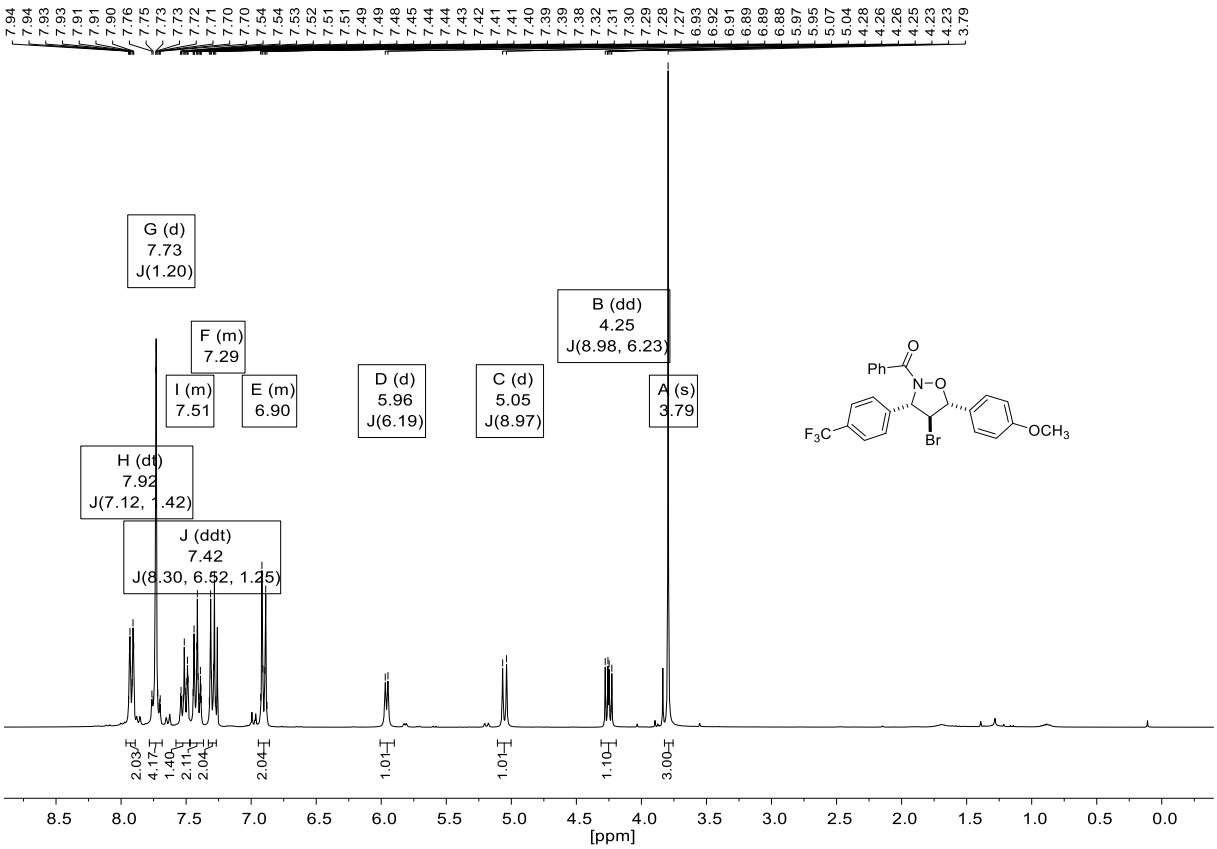
UV Results

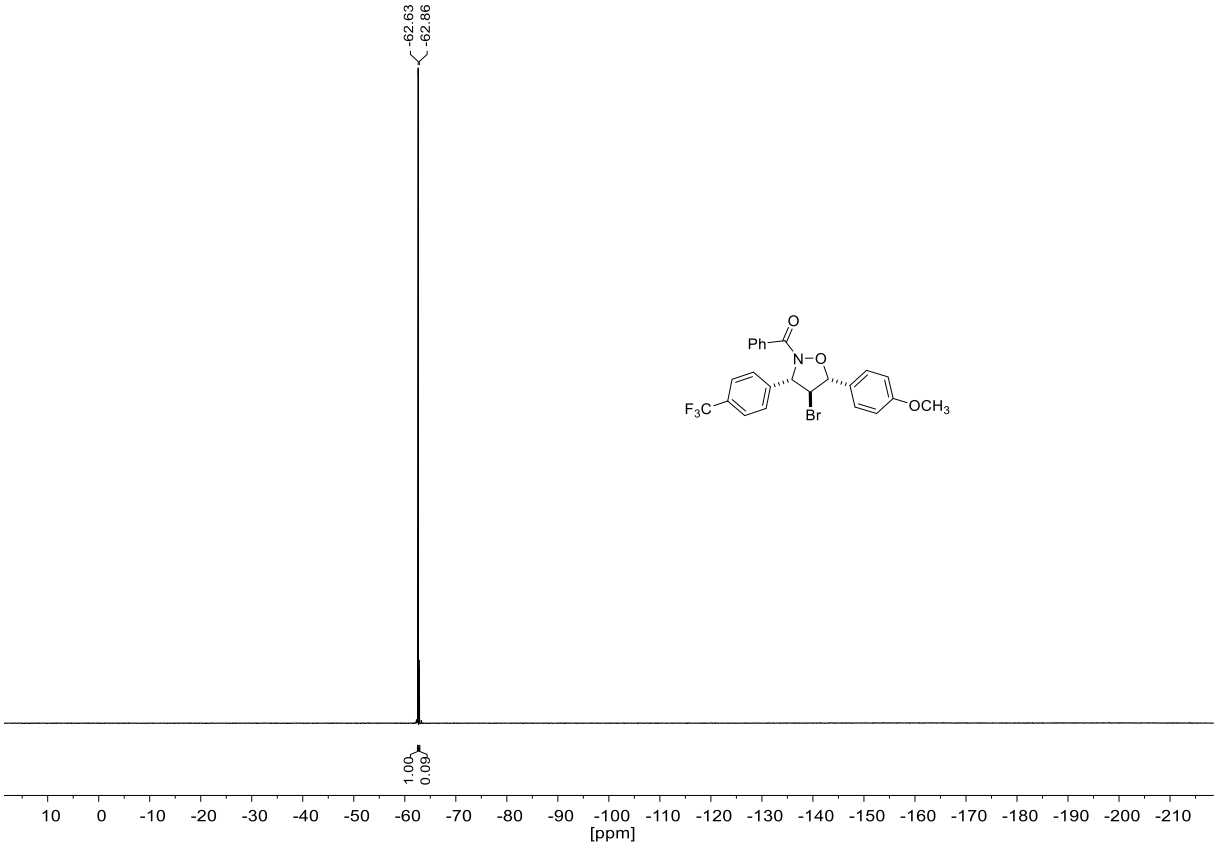
Retention Time	Area	Area %	Height	Height %
8,947	8298609	29,10	608200	33,08
10,217	8195291	28,73	513555	27,93
10,967	5998142	21,03	359304	19,54
11,953	6030067	21,14	357439	19,44

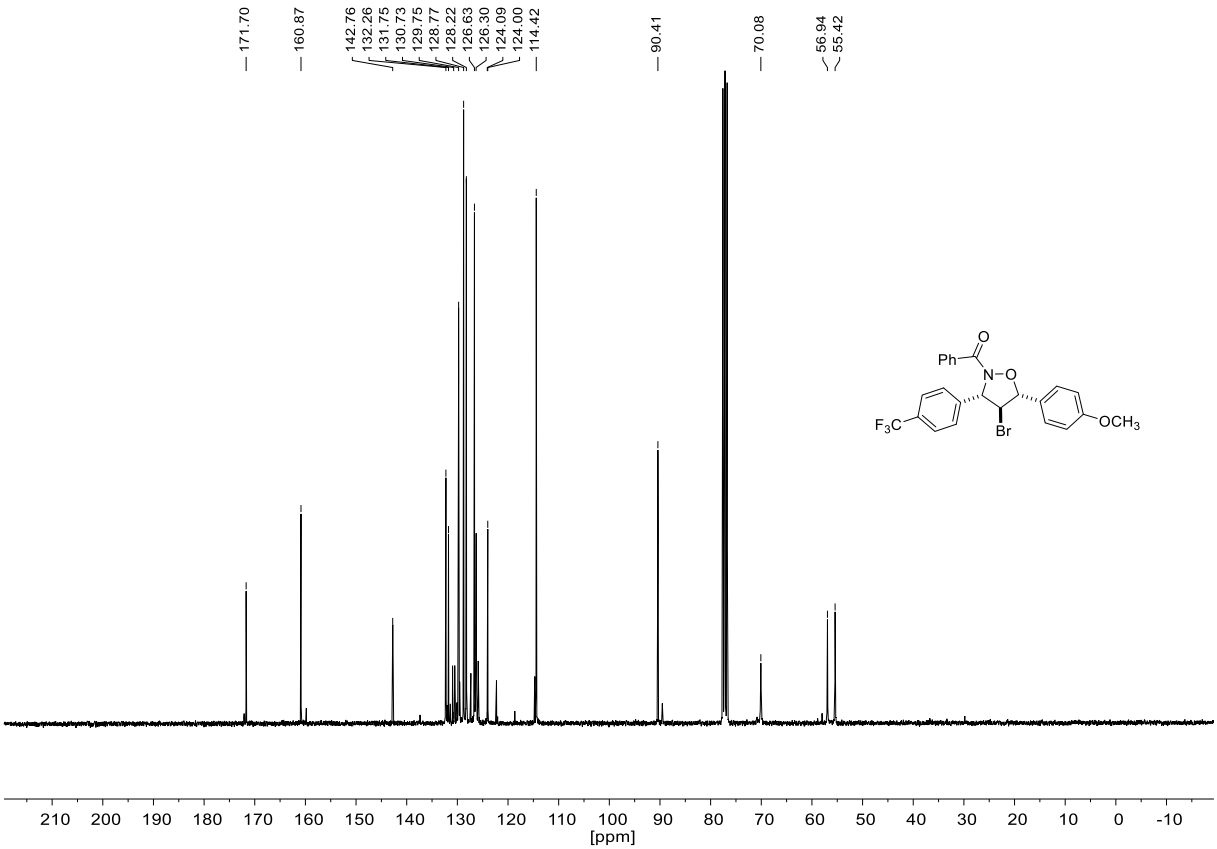


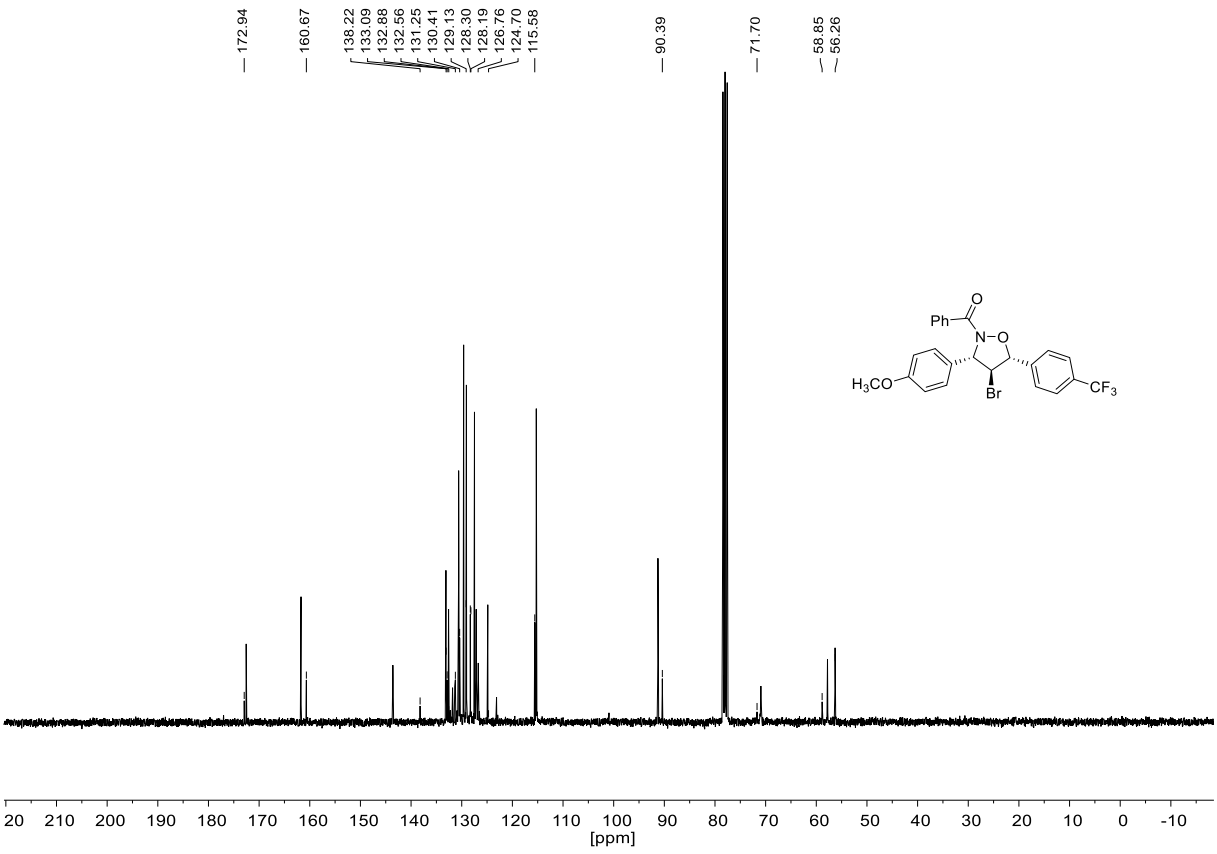
UV Results

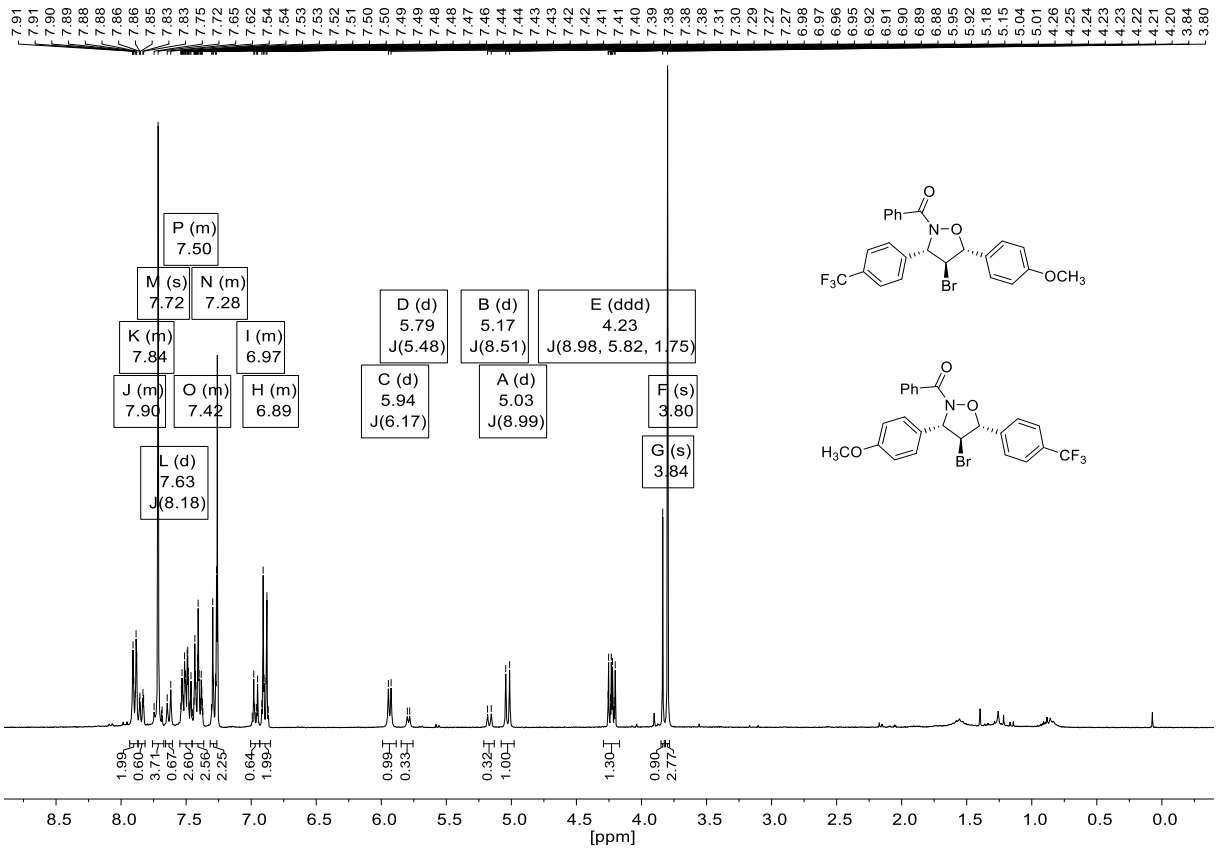
Retention Time	Area	Area %	Height	Height %
8,860	1777126	6,35	139486	7,78
10,027	12249827	43,80	796899	44,43
10,763	13557117	48,48	837923	46,71
11,737	382705	1,37	19463	1,09


G (d)
7.73
J(1.20)
F (m)
7.29
I (m)
7.51
E (m)
6.90
D (d)
5.96
J(6.19)
C (d)
5.05
J(8.97)
B (dd)
4.25
J(8.98, 6.23)
A (s)
3.79
H (dt)
7.92
J(7.12, 1.42)
J (ddt)
7.42
J(8.30, 6.52, 1.25)
Ph
O
N–O
F3C
Br
OCH3
[ppm]

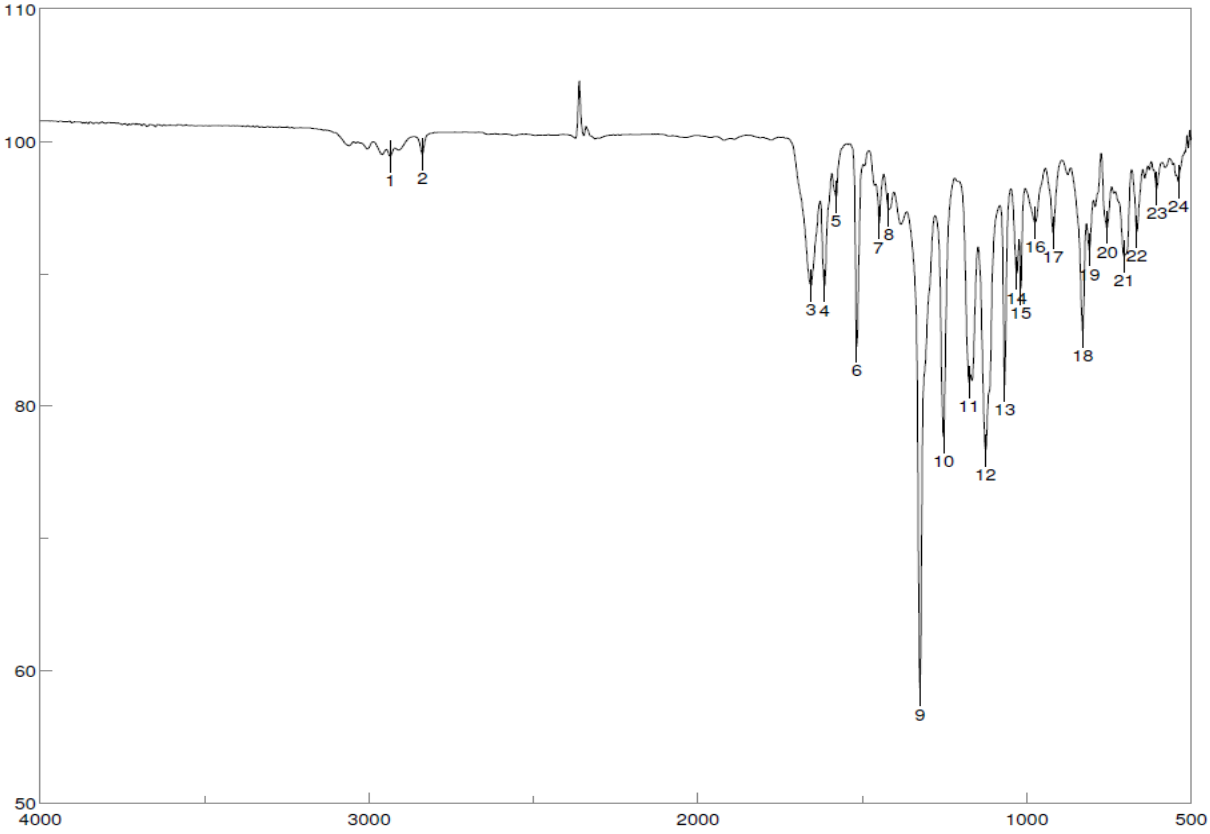

-62.63
-62.86
Ph
O
N–O
F3C
Br
OCH3
[ppm]

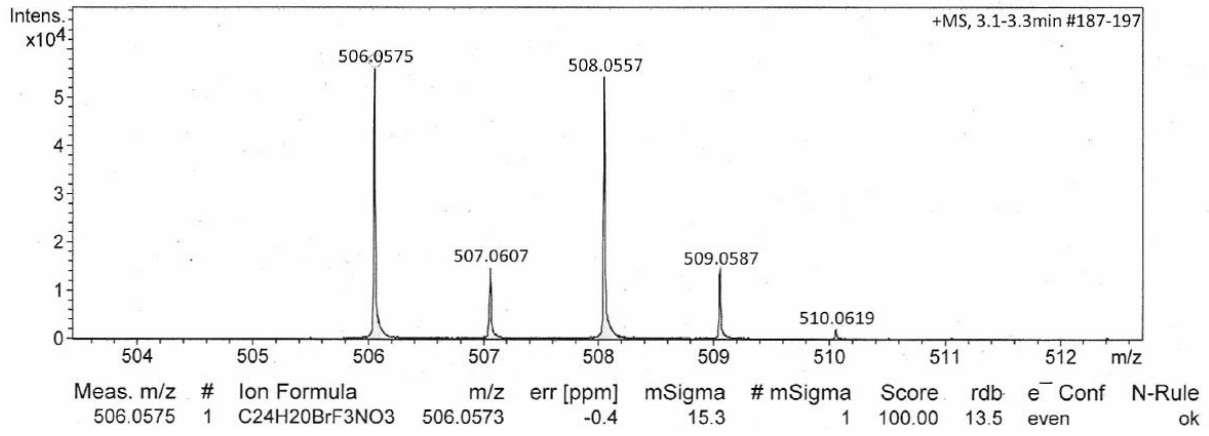

171.70
160.87
142.76
132.26
131.75
130.73
129.75
128.77
128.22
126.63
126.30
124.09
124.00
114.42
90.41
70.08
56.94
55.42
Ph
O
N–O
F3C
Br
OCH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]


172.94
160.67
138.22
133.09
132.88
132.56
131.25
130.41
129.13
128.30
128.19
126.76
124.70
115.58
90.39
71.70
58.85
56.26
Ph
O
N–O
H3CO
Br
CF3
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]


P (m) 7.50
M (s) 7.72
N (m) 7.28
K (m) 7.84
I (m) 6.97
J (m) 7.90
O (m) 7.42
H (m) 6.89
L (d) 7.63 J(8.18)
D (d) 5.79 J(5.48)
C (d) 5.94 J(6.17)
B (d) 5.17 J(8.51)
A (d) 5.03 J(8.99)
E (ddd) 4.23 J(8.98, 5.82, 1.75)
F (s) 3.80
G (s) 3.84
Ph
N–O
Br
F3C
OCH3
H3CO
CF3
[ppm]

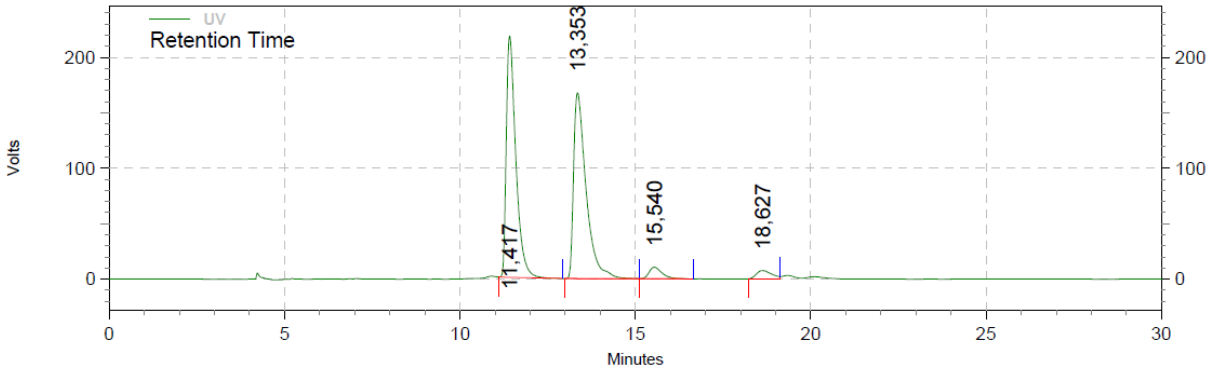

-62.63
-62.86
Ph
N–O
Br
F3C
OCH3
H3CO
CF3
[ppm]





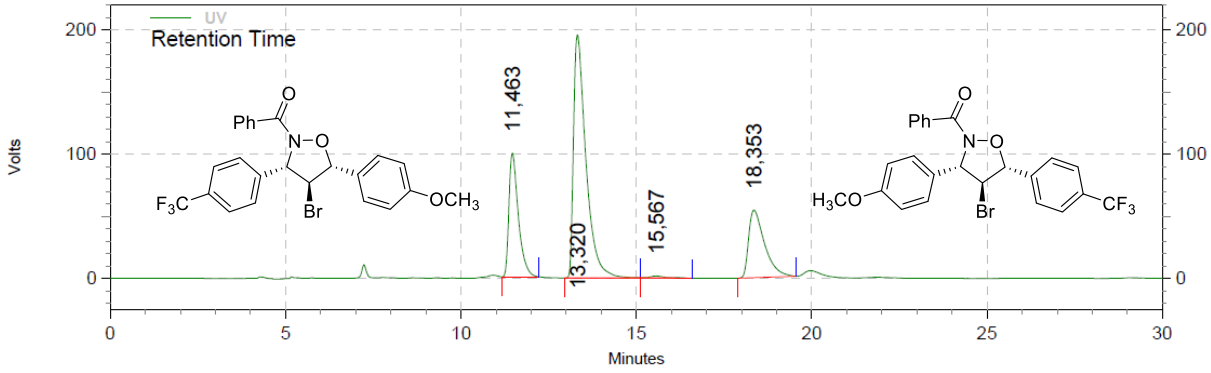
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
506.0575	1	C24H20BrF3NO3	506.0573	-0.4	15.3	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 98:2, 0.8 ml/min



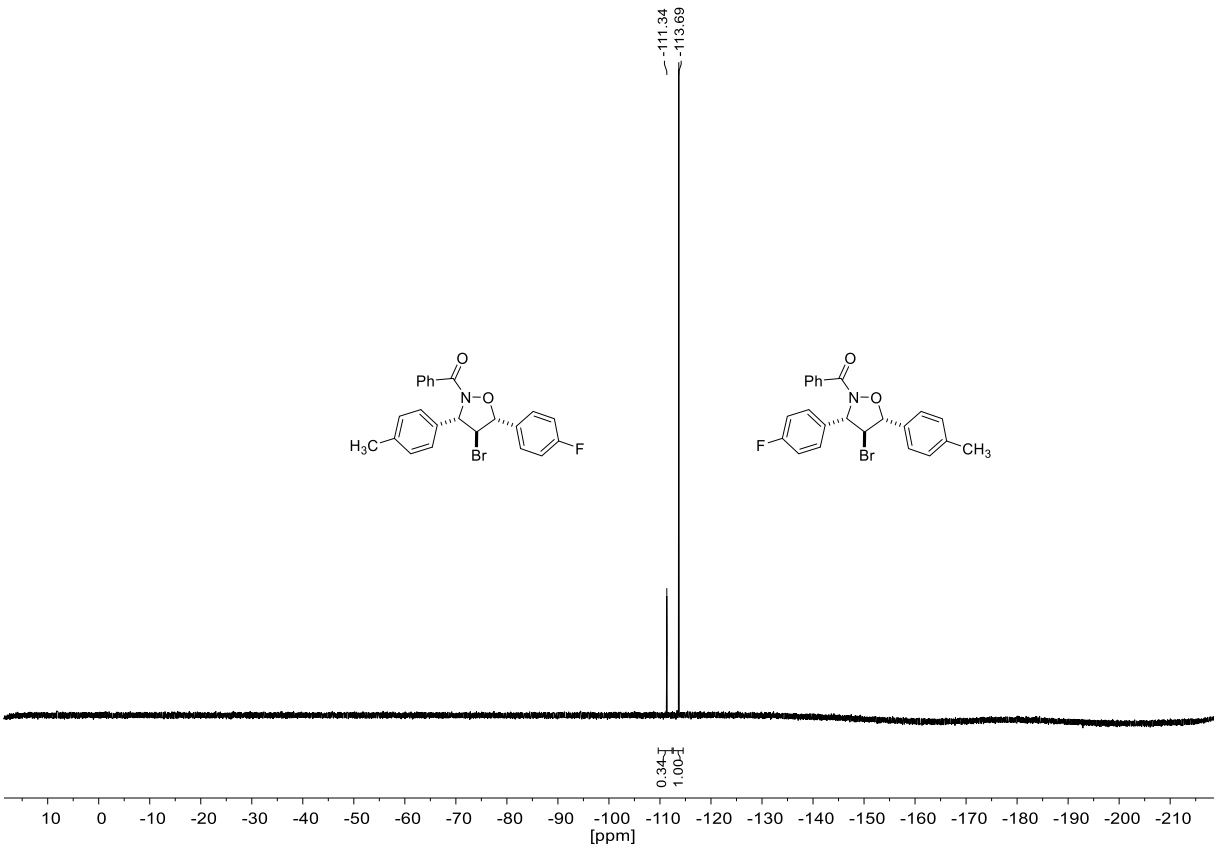
UV Results

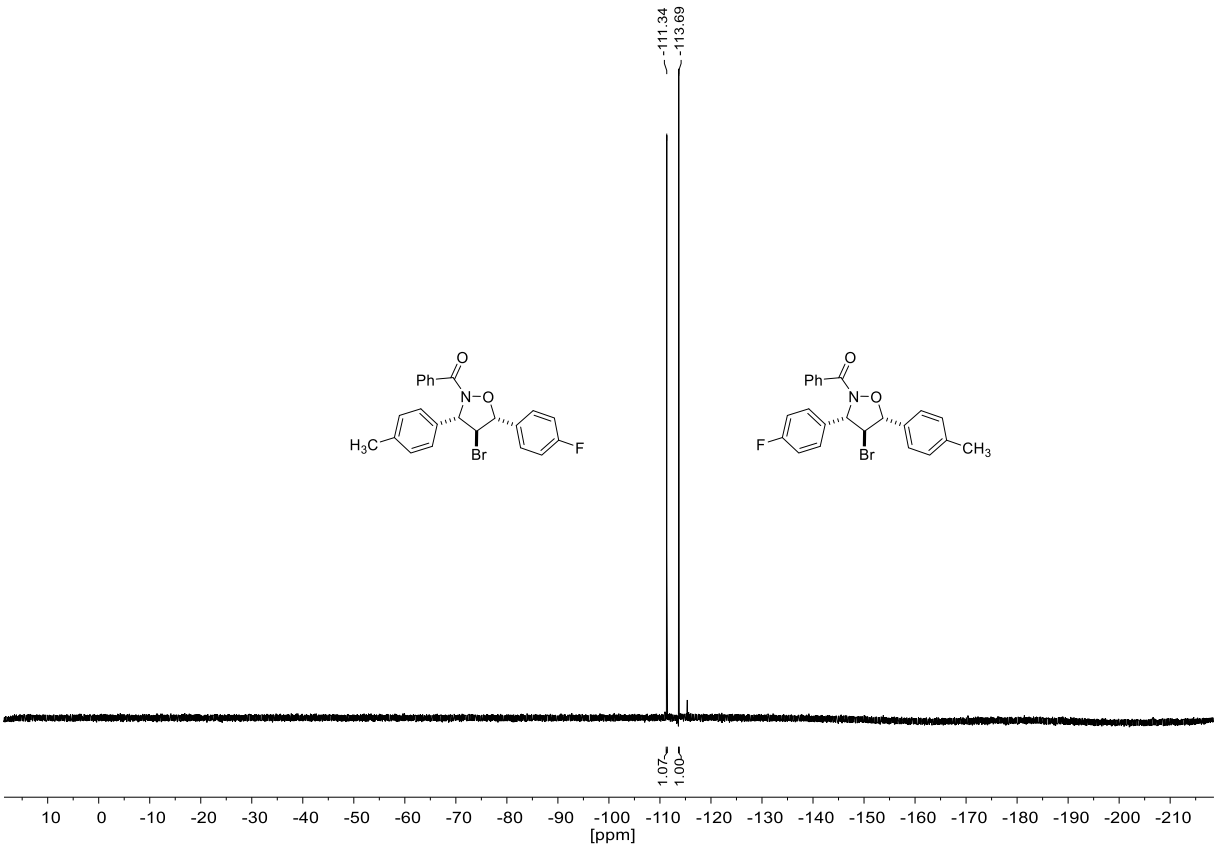
Retention Time	Area	Area %	Height	Height %
11,417	16424389	46,83	870411	53,98
13,353	16656979	47,50	670251	41,57
15,540	1078463	3,08	41792	2,59
18,627	909509	2,59	30082	1,87

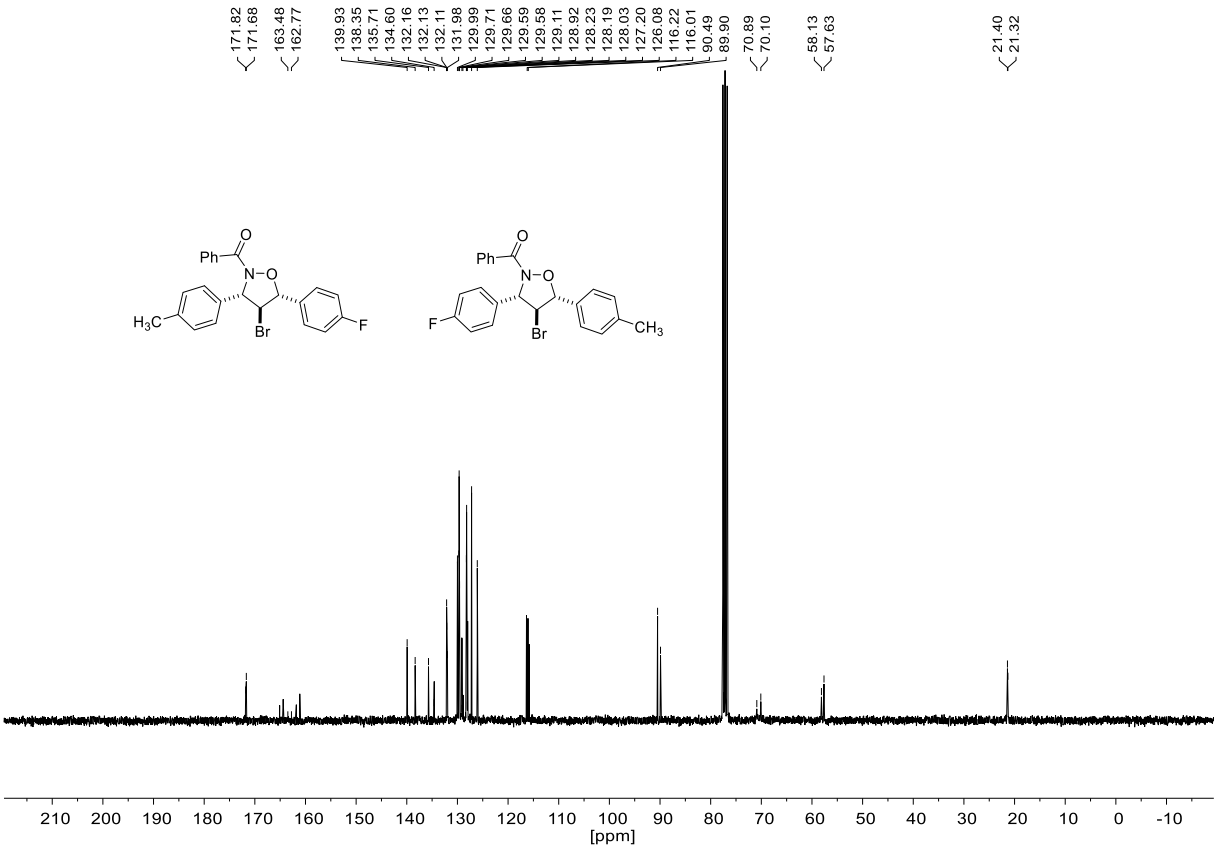


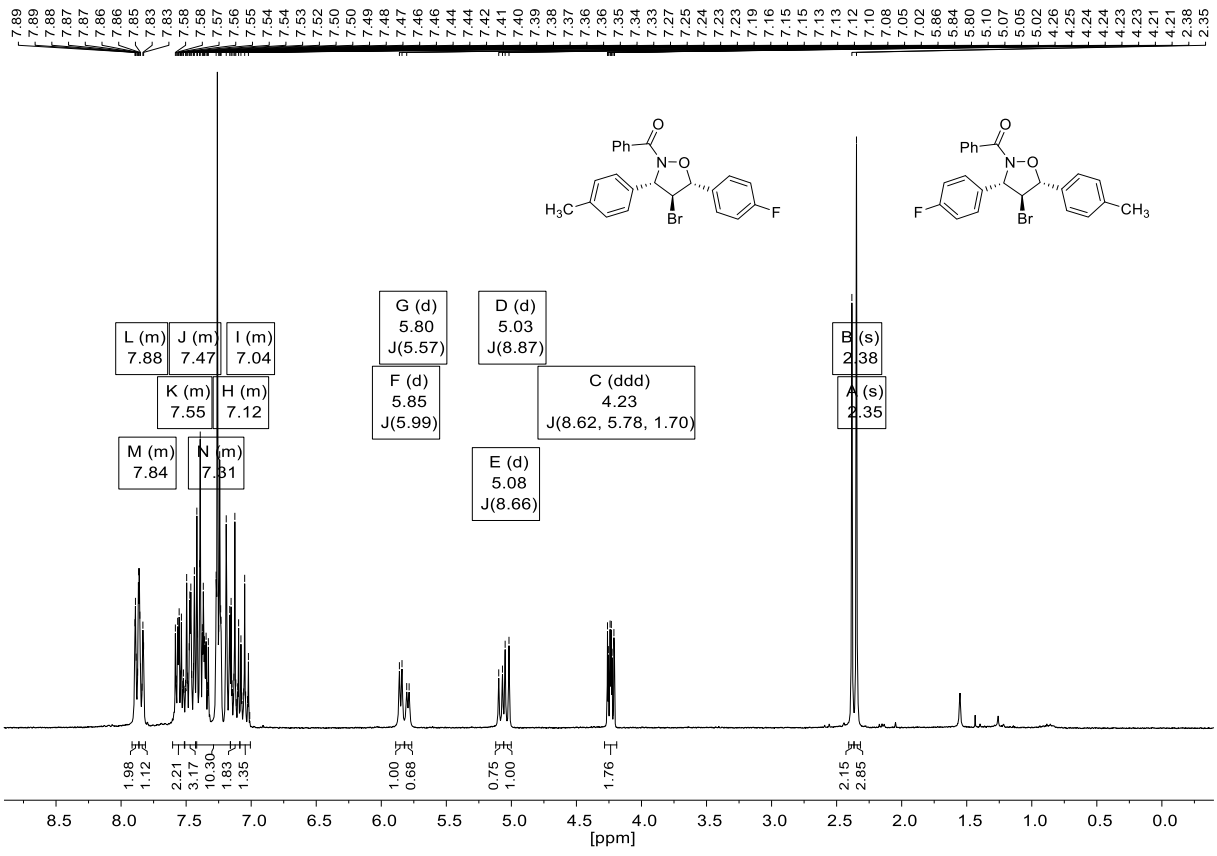
UV Results

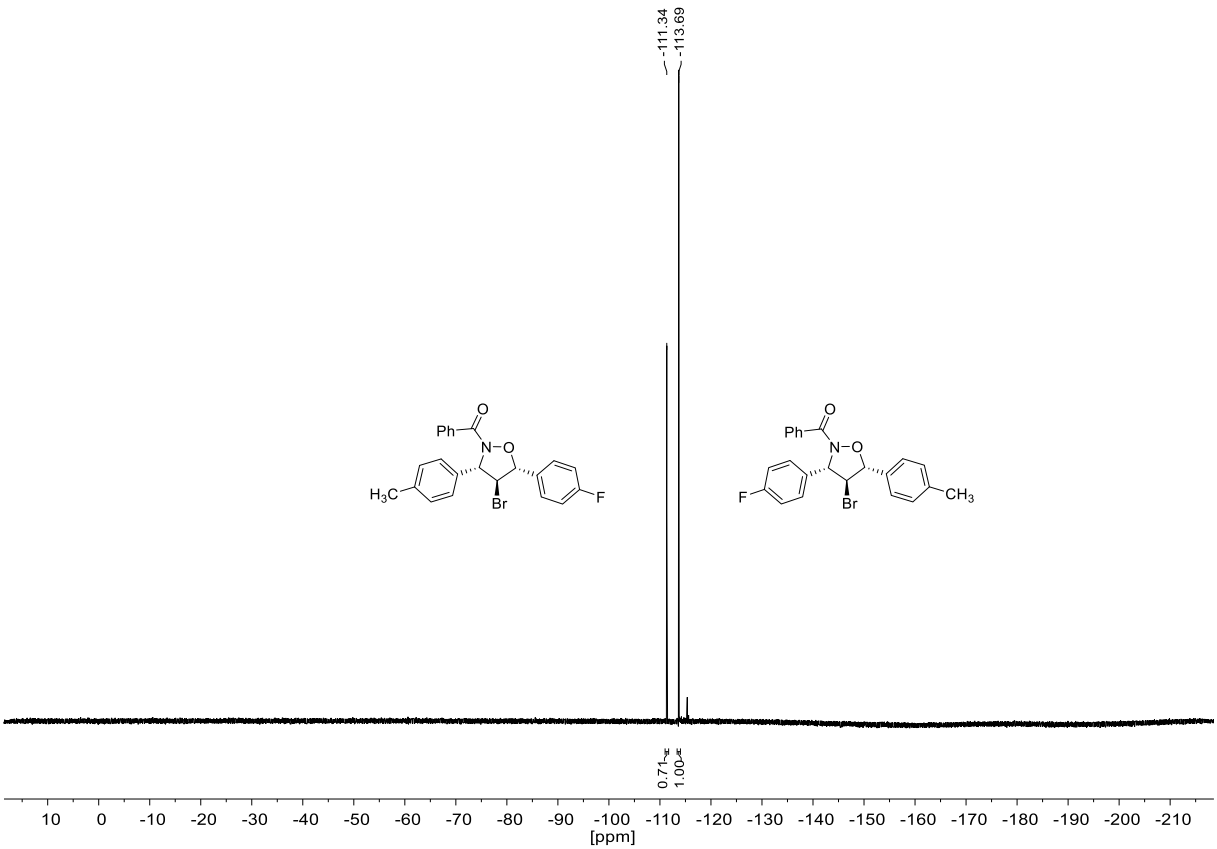
Retention Time	Area	Area %	Height	Height %
11,463	7413460	21,89	398070	28,34
13,320	19347816	57,14	782266	55,70
15,567	231493	0,68	6806	0,48
18,353	6867396	20,28	217353	15,48

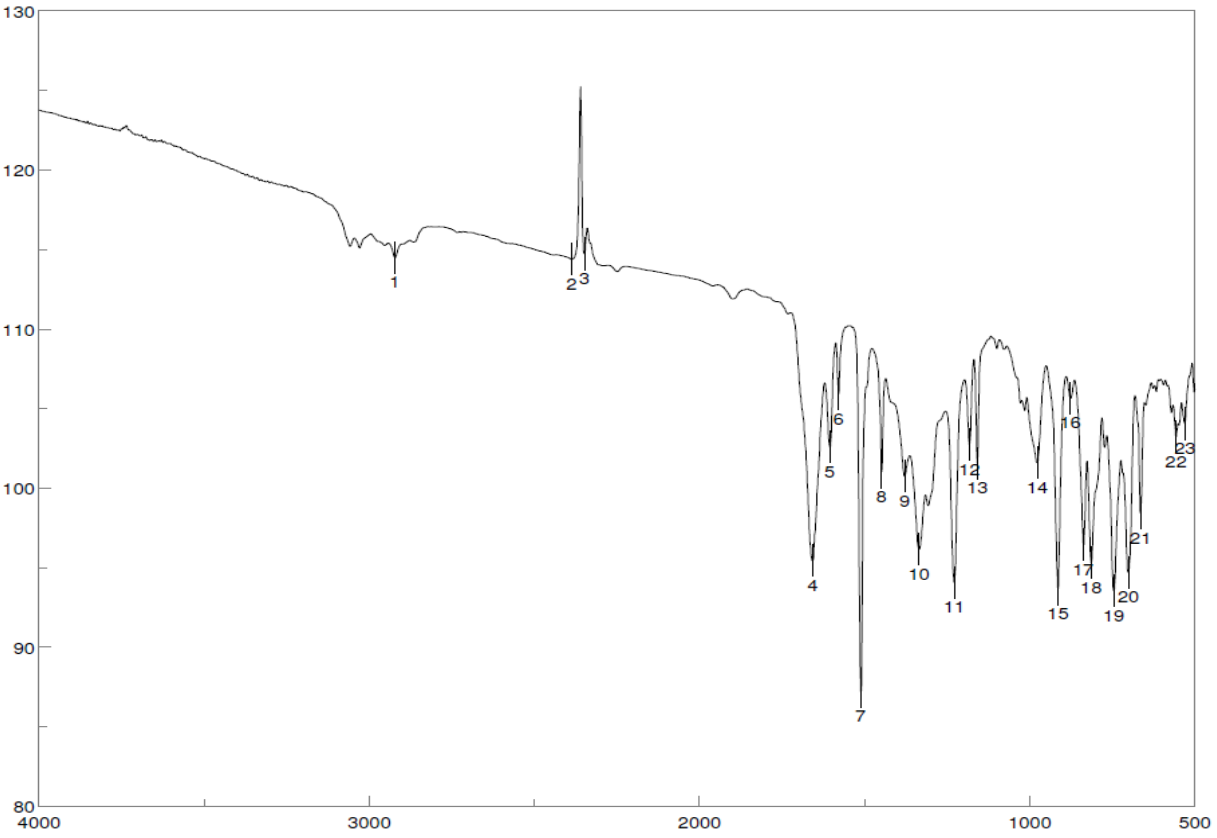

-111.34
-113.69
Ph
O
N
O
H3C
Br
F
F
CH3
0.34
1.00
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]

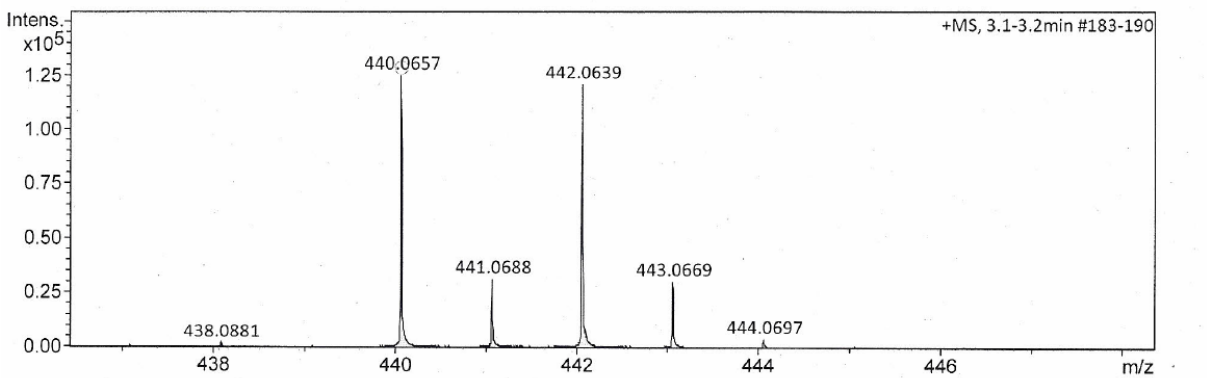

-111.34
-113.69
Ph
O
N
O
H3C
Br
F
F
CH3
1.07
1.00
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]


171.82
171.68
163.48
162.77
139.93
138.35
135.71
134.60
132.16
132.13
132.11
131.98
129.99
129.71
129.66
129.59
129.58
129.11
128.92
128.23
128.19
128.03
127.20
126.08
116.22
116.01
90.49
89.90
70.89
70.10
58.13
57.63
21.40
21.32
Ph
O
N–O
Br
H3C
F
CH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
[ppm]


7.89 7.89 7.88 7.87 7.87 7.86 7.86 7.85 7.83 7.83 7.58 7.58 7.57 7.56 7.55 7.54 7.54 7.53 7.52 7.50 7.50 7.49 7.48 7.47 7.46 7.46 7.44 7.44 7.42 7.41 7.40 7.39 7.38 7.37 7.36 7.35 7.34 7.33 7.27 7.25 7.24 7.23 7.23 7.19 7.16 7.15 7.15 7.13 7.13 7.12 7.10 7.08 7.05 7.02 5.86 5.84 5.80 5.10 5.07 5.05 5.02 4.26 4.25 4.24 4.24 4.23 4.23 4.21 4.21 2.38 2.35
L (m) 7.88
J (m) 7.47
I (m) 7.04
K (m) 7.55
H (m) 7.12
M (m) 7.84
N (m) 7.31
G (d) 5.80 J(5.57)
F (d) 5.85 J(5.99)
D (d) 5.03 J(8.87)
C (ddd) 4.23 J(8.62, 5.78, 1.70)
E (d) 5.08 J(8.66)
B (s) 2.38
A (s) 2.35
1.98 1.12 2.21 3.17 10.30 1.83 1.35 1.00 0.68 0.75 1.00 1.76 2.15 2.85
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
[ppm]

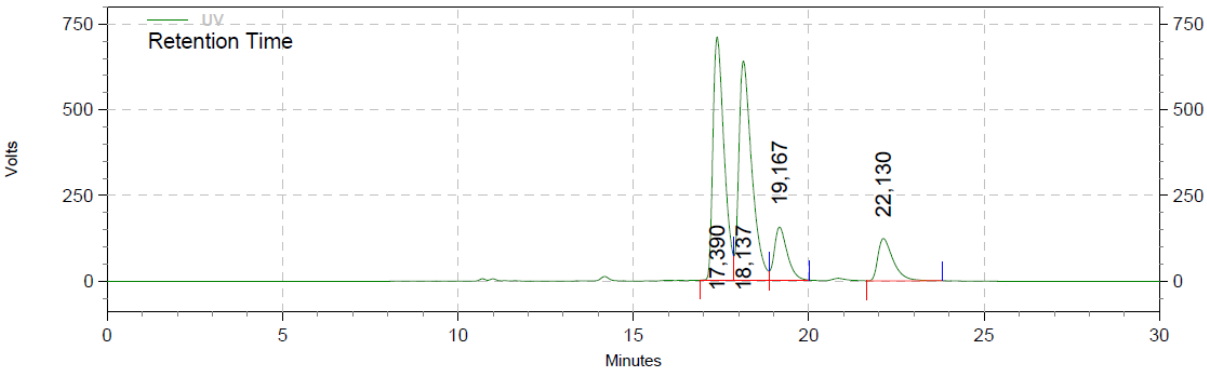

-111.34
-113.69
Ph
O
N
O
H3C
Br
F
Ph
O
N
O
F
Br
CH3
0.71
1.00
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
[ppm]


130
120
110
100
90
80
4000
3000
2000
1000
500
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23



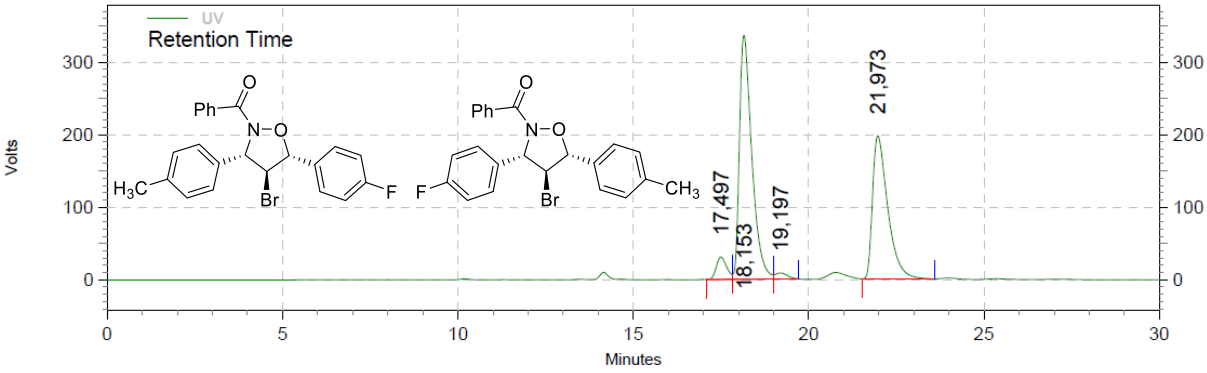
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
440.0657	1	C23H20BrFNO2	440.0656	-0.2	15.5	1	100.00	13.5	even	ok

IB, *n*-hexane/*i*PrOH 98:2, 0.4 ml/min



UV Results

Retention Time	Area	Area %	Height	Height %
17,390	62818543	39,39	2839351	43,60
18,137	65820128	41,27	2559204	39,30
19,167	15925916	9,99	619809	9,52
22,130	14912199	9,35	493733	7,58



UV Results

Retention Time	Area	Area %	Height	Height %
17,497	2514820	4,19	122839	5,37
18,153	32981224	54,90	1344281	58,72
19,197	820292	1,37	33744	1,47
21,973	23762955	39,55	788596	34,44