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Exploring N-nucleophiles for diversification of a complex cyclohexenone scaffold

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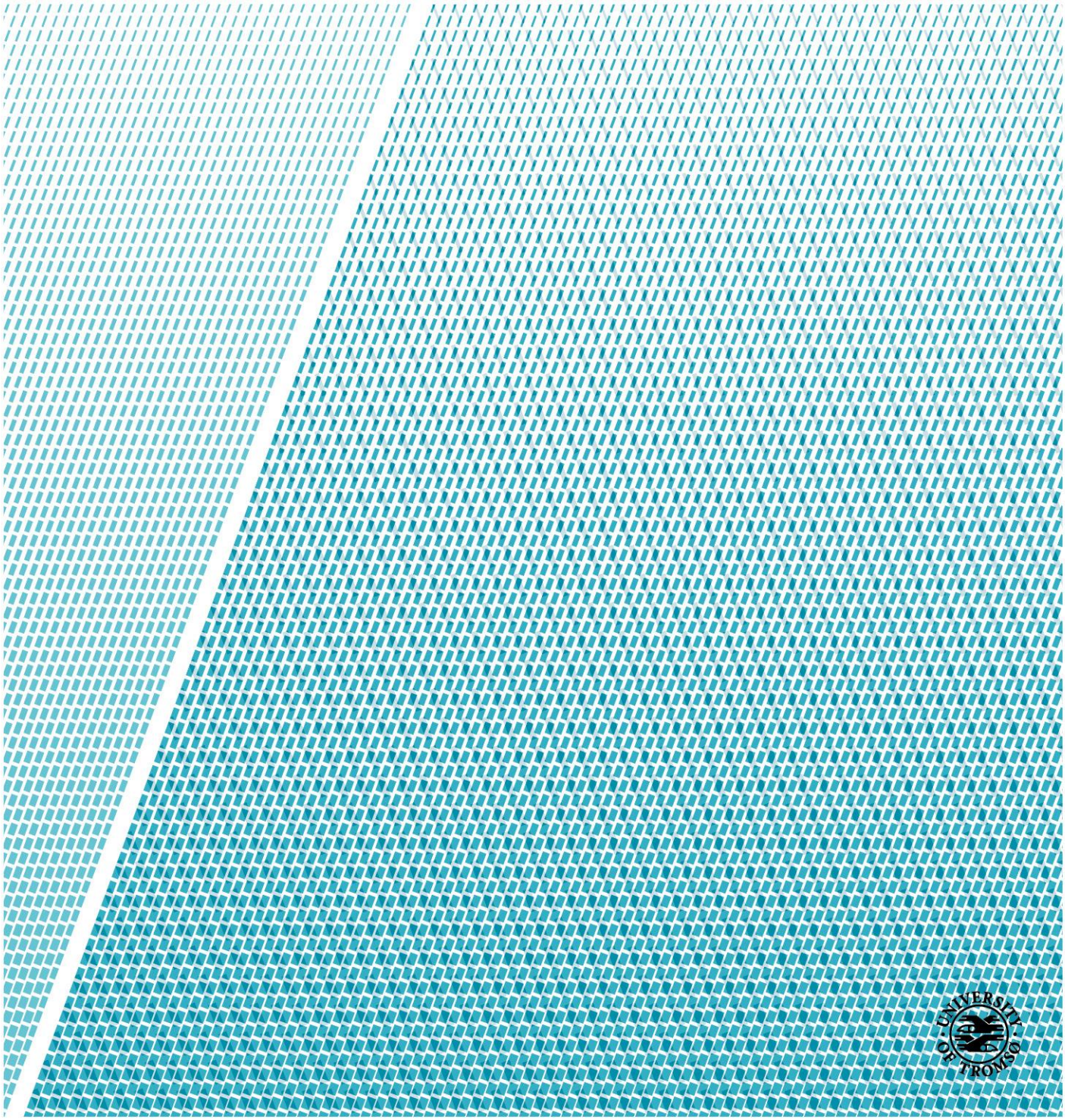
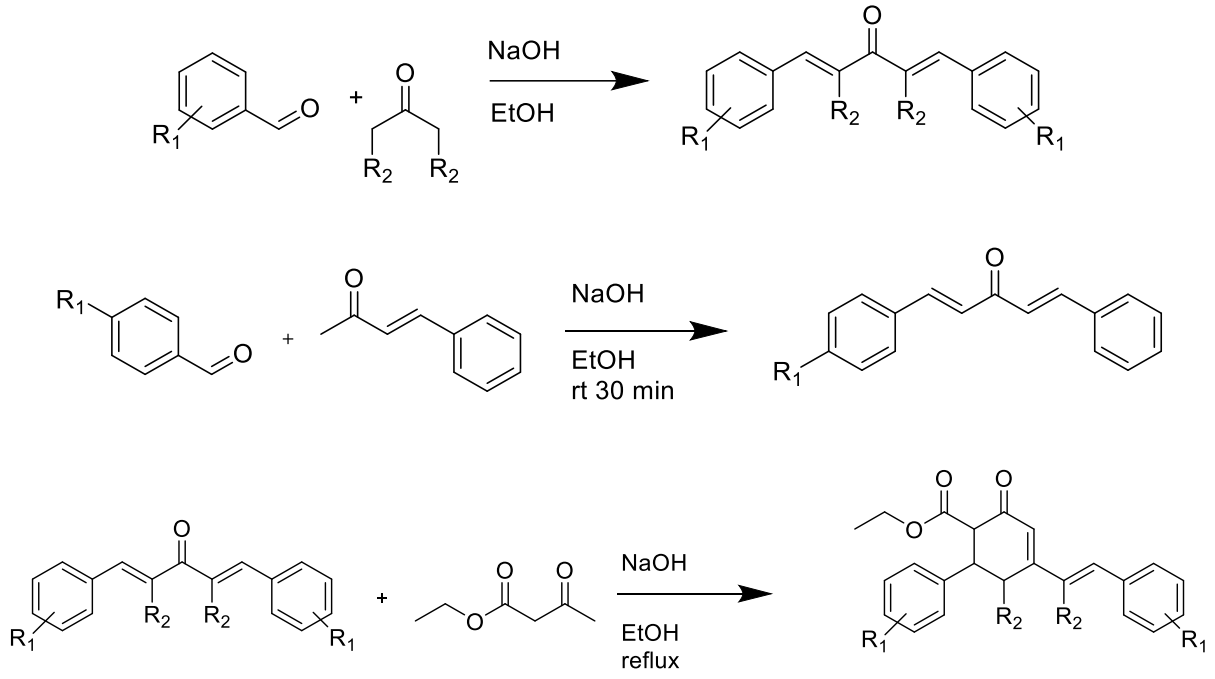
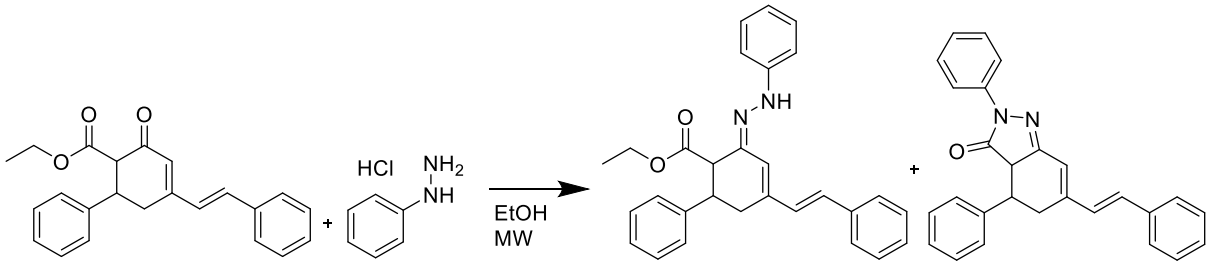


Abstract

In this thesis, synthesis of 3 different dibenzylideneacetone (DBA)-analogues and 4 different ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate-analogues (structure shown below) that have not been reported before were synthesized, as well as a range of analogues that have been reported before. Both symmetrical and unsymmetrical DBA-analogues were made. The yields of many of these reactions were low, but with high potential within optimization, especially in work-up.



Further on, the reactivity of the cyclohexenone scaffold molecule with phenylhydrazine was explored, and although products were not isolated, they were identified using NMR, and the reaction attempted optimized with the help of internal standard and NMR.



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I would also like to give a huge thanks to all my coworkers within and around the Hansen group, both in lab, office and corridors, socially and work-related. All the engineers at the institute who have helped me, also need a huge thanks. My co-supervisor associate professor Annette Bayer and her group also deserves a thanks for all the good feedback and help on group meetings. I would also like to thank my colleagues Tone and Vijay specifically for a lot of help.

Lastly, I need to thank my amazing girlfriend for all the support, and for having put through with taking care of my son so much in my absence. She has been amazing, and both her and my son's patience and support has been outstanding.

Abbreviations

COSY	=	Correlation spectroscopy
d	=	Doublet
DBA	=	Dibenzylideneacetone ((1*E*, 4*E*)-1,5-Diphenylpenta-1,4-dien-3-one)
DCM	=	Dichloromethane
DDQ	=	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DFT	=	Density functional theory
DOS	=	Diversity-oriented synthesis
Eqv	=	Equivalents
EtOH	=	Ethanol
HMBC	=	Heteronuclear multiple-bond correlation
HSQC	=	Heteronuclear single-quantum correlation
IR	=	Infrared Spectroscopy
m	=	Multiplet (NMR) or medium (IR)
m/z	=	Mass to charge ratio.
MS	=	Mass Spectrometry
MW	=	Microwave reaction
NMR	=	Nuclear magnetic resonance
q	=	quartet
ROESY	=	Rotating-frame nuclear Overhauser effect correlation
rt	=	Room temperature
s	=	Singlet (NMR) or strong (IR)
sat.	=	Saturated
t	=	Triplet
THF	=	Tetrahydrofuran
TLC	=	Thin layer chromatography
TOCSY	=	Total correlated spectroscopy
UV	=	Ultraviolet
v|v	=	Volume per volume
w	=	weak

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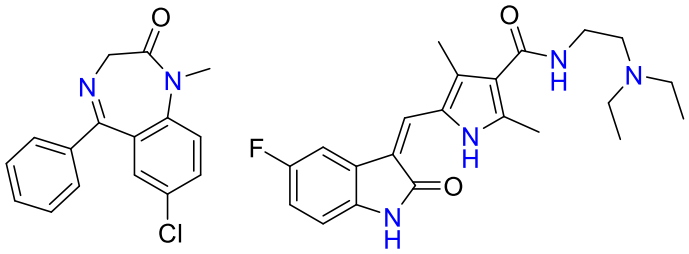
1 Introduction

1.1 Relevance

The development of modern pharmaceuticals often relies the production of large amounts of relatively small organic molecules with a large span in chemical structures, or so-called chemical libraries. [1-2] These chemical libraries contain a large span of chemical diversity which can be used to chart which features of the chemical structures that are the most important for medicinal activity. We can further use this information to discover what an optimal medicinal agent should look like. [1-2] Chemical libraries can also be utilized to discover unique and new structural elements or even combination of known structural elements to give the molecule specific medicinal properties. This new molecule or new combination of structural elements can then be the starting point for developing new medicinal agents. To make these libraries practical, simple, predictable and versatile chemical methods play a major role and because of this, chemical libraries are valuable tools for medicinal design. [1-2]

Nitrogen-containing heterocyclic compounds play a major role in modern chemistry, but is also abundant in natural products, medicinal agents and overall modern organic materials (examples in figure 1.1). Nitrogen's ability to take part in a molecule's covalent bonding with various metals, Lewis acids and to act as a strong hydrogen-bond acceptor or donor, stem from the presence of a lone electron pair or in some cases highly polarized bonds between N and H capable of strong, directed interactions. This is often why nitrogen's position in a molecule plays a key role in the molecule's specific biological activity. [3] As such, this thesis will focus on producing parts of a chemical library with initial emphasis on introducing nitrogen-containing molecules into a scaffold molecule being diversified through Diversity-Oriented Synthesis (DOS).



Valium
CNS depressant

Sunitinib
Anti cancer agent

Figure 1.1: Examples of nitrogen being abundant in pharmaceuticals

There are two kinds of extreme synthetic strategies in organic chemistry; diversity-oriented synthesis (DOS) and target-oriented synthesis (TOS) (see figure 1.2). [4] While target-oriented synthesis focuses on finding the best suited pathway to one specific target molecule, diversity-oriented synthesis focuses on generating chemical libraries with as much diversity as possible from a specific starting material using a set of reactants. Because of this, TOS has been considered a weaker strategy to make chemical libraries than DOS. [5-6]

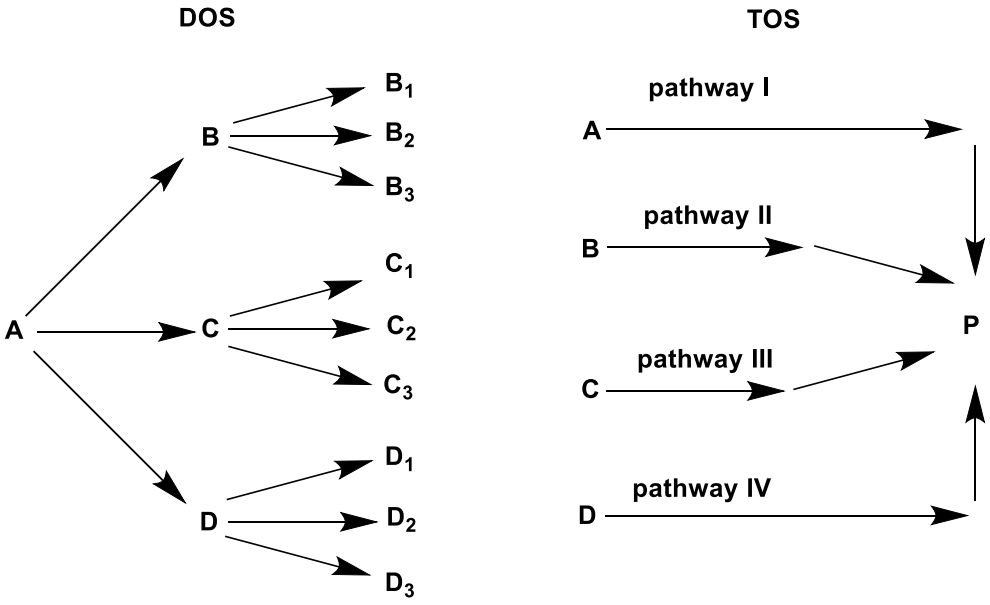


Figure 1.2: Difference between DOS and TOS

DOS can further be divided into four methods; skeletal diversification, functional group diversification, scaffold diversification and stereochemical diversification. In this thesis the main focus will be scaffold diversification where a variety of R groups are put on a scaffold molecule through varying the R groups on the reactants, as well as some skeletal diversification. [4-6]

In modern drug discovery, screening small synthetic molecules, natural products or natural extracts for bioactivity plays a central role. [7] Hits on bioactivity opens for structural optimization to increase metabolic properties such as the affinity, selectivity, efficacy, potency, stability and bioavailability. This kind of approach towards drug discovery is regarded as bioprospecting. In addition to bioprospecting, chemoprospecting from well-defined libraries serve as a promising and complementary approach for small-molecule discovery. [8] The relationship between the chemical 3D-structure of a molecule and its biological activity is known as its structure-activity relationship (SAR). SAR is dependent on the action mechanism of the drug to the specific biological molecules which are usually highly complex supramolecular structures consisting of proteins. SAR-screening is usually done by altering substituents or inserting new chemical groups. [8]

Cyclohexenone derivatives have shown to have good potential for drug discovery and has been found to play an important role within medicinal chemistry in the form of bioactive natural products such as phorbasins, carvotacetones, antheminones and gabosines. [9] These groups of natural products are known for biological activity such as anti-tumor, anti-plasmodial, anti-leishmanial and more. [9] DBA-analogues explored in this project also resemble curcumin shown in figure 1.3. Monocarbonyl-analogues of curcumin are being explored for both anti-tumor activity and anti-inflammatory activity as well as anti-bacterial and anti-fungal activity. [10-12] Many of the molecules in this thesis also resemble molecules tested as α-amylase inhibitors by Bale et al. [13] There is also the possibility of discovering other uses for the library of molecules made in this thesis, but it is also important to note that the methods used in this thesis also might be used on other molecules to quickly add diversity on another scaffold for same or other reasons as those mentioned here.

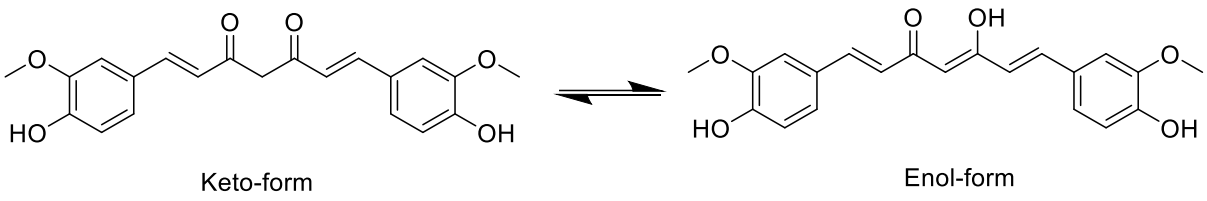
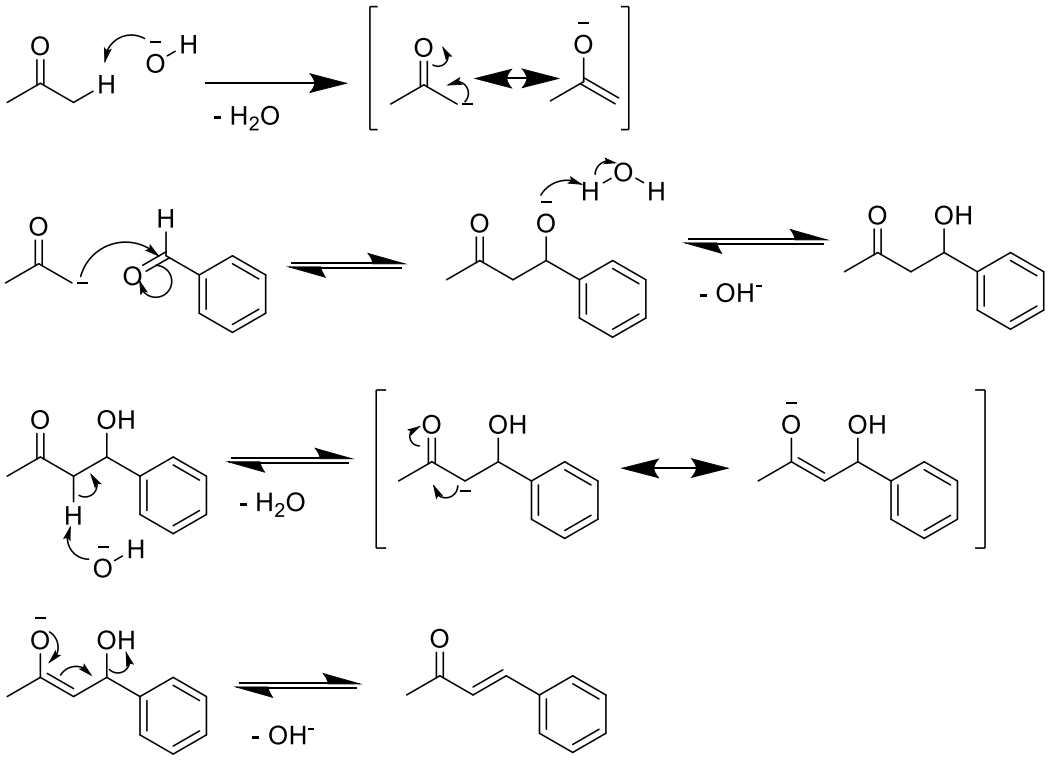


Figure 1.3: Curcumin

1.2 Claisen-Schmidt condensation

The Claisen-Schmidt condensation is a base-catalyzed reaction between an aldehyde and a ketone. A Claisen-Schmidt condensation that is often used in organic synthesis courses is the reaction between benzaldehyde and acetone in the presence of NaOH to form DBA. [14] The mechanism of this reaction is well known and half of it is shown in scheme 1.1. First an enolate is formed from the ketone, before it reacts with an aldehyde. Lastly, the proton between the ketone and hydroxy groups is stripped, and the enolate π-electrons shift towards the neighbouring carbon making the hydroxy-group leave.



Scheme 1.1: Claisen-Schmidt condensation mechanism

As to why this reaction is trans-selective this can be explained by 3D structure. For the double bond to be formed, the leaving OH-group must be perpendicular to the enolate plane. The most stable perpendicular position would be the one where the Ph group is the furthest away from the O^-, which is the one shown in figure 1.4 giving the trans-isomer.

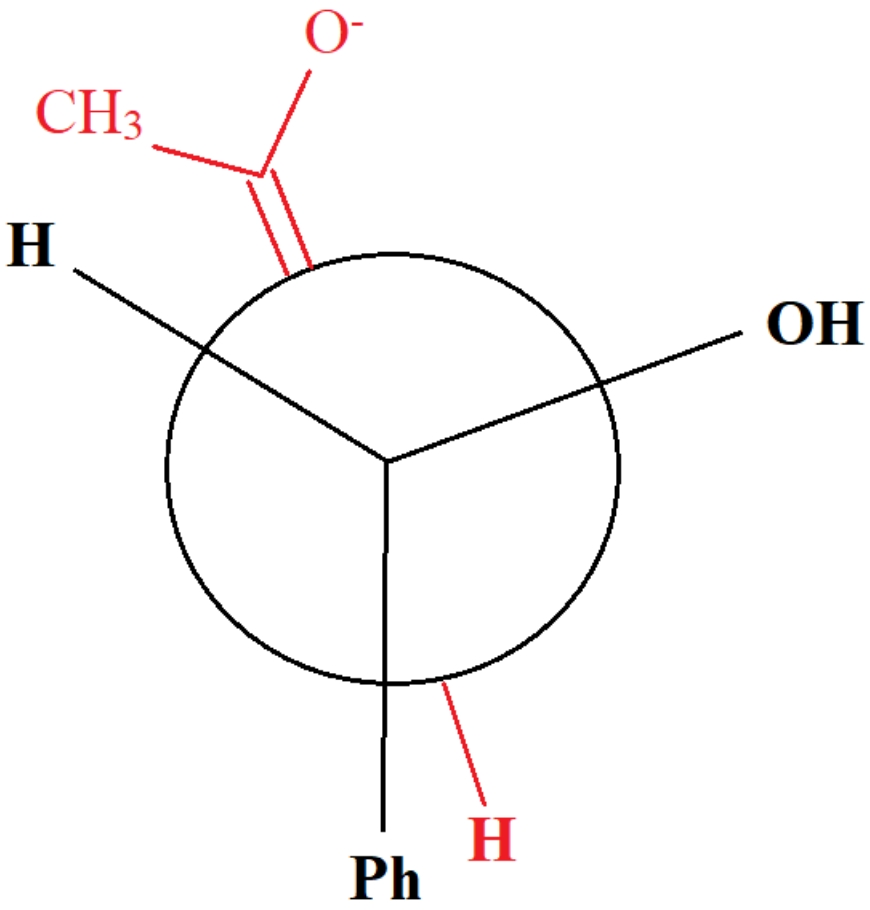
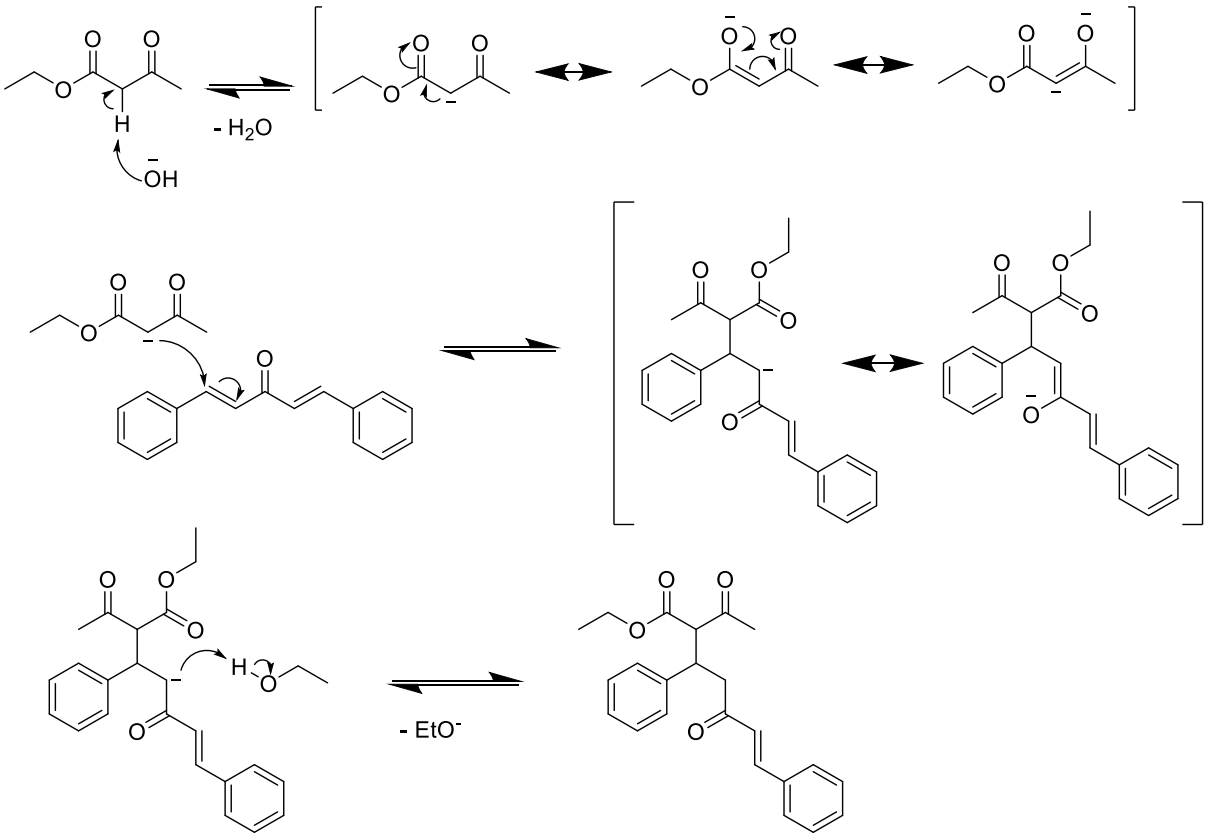


Figure 1.4: Newman projection of Claisen-Schmidt intermediate

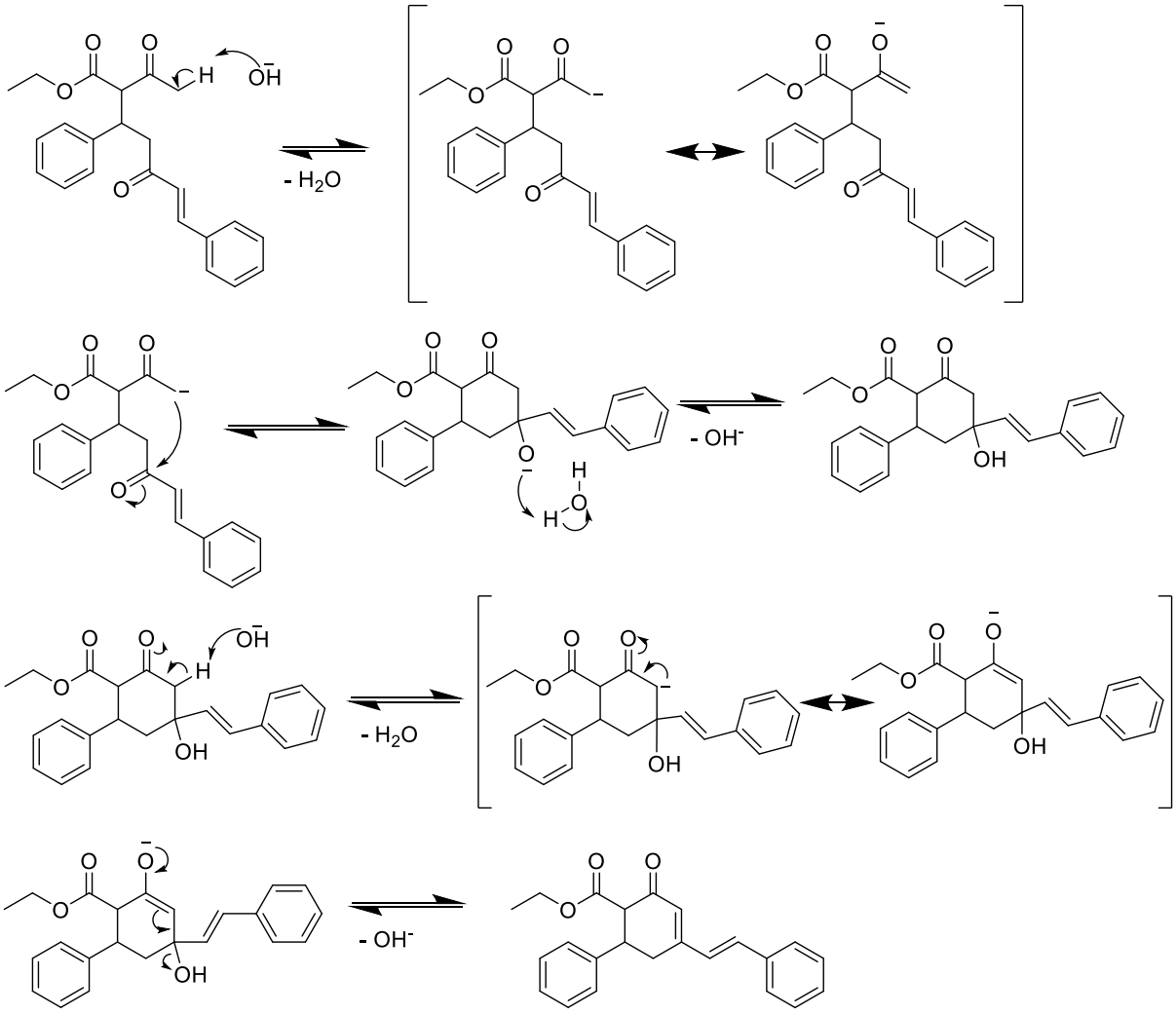
1.3 Michael addition and Robinson annulation

A Michael addition is a reaction between a nucleophilic enolate ion and an α,β-unsaturated carbonyl compound (mechanism shown in scheme 1.2). In scheme 1.2 the enolate ion is formed from ethyl acetoacetate, and it undergoes a nucleophilic attack on the double bond forming an enolate, which after protonation on the carbon yields the product.



Scheme 1.2: Michael addition mechanism

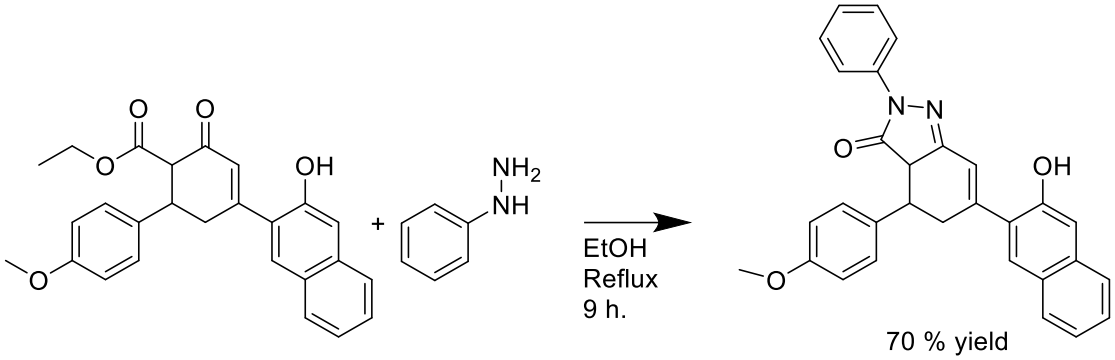
The Robinson annulation starts with a Michael addition and is an intramolecular reaction forming a cyclohexenone (mechanism shown in scheme 1.3). First the terminal α-proton is stripped, forming an enol. The enol then attacks the carbonyl on the molecule forming a cyclic compound. After protonation of the O^-, another α-proton is stripped, and the π-electrons in the enol formed shift towards the neighbouring carbon, making the hydroxy group leave. The Hansen research group has previously concluded that the 3D structure of the product in scheme 1.3 has a trans double bond and to most likely be the anti-diastereomer. [15-16] For simplification the diastereomeric structure will not be used throughout most of this thesis.



Scheme 1.3: Robinson annullation mechanism

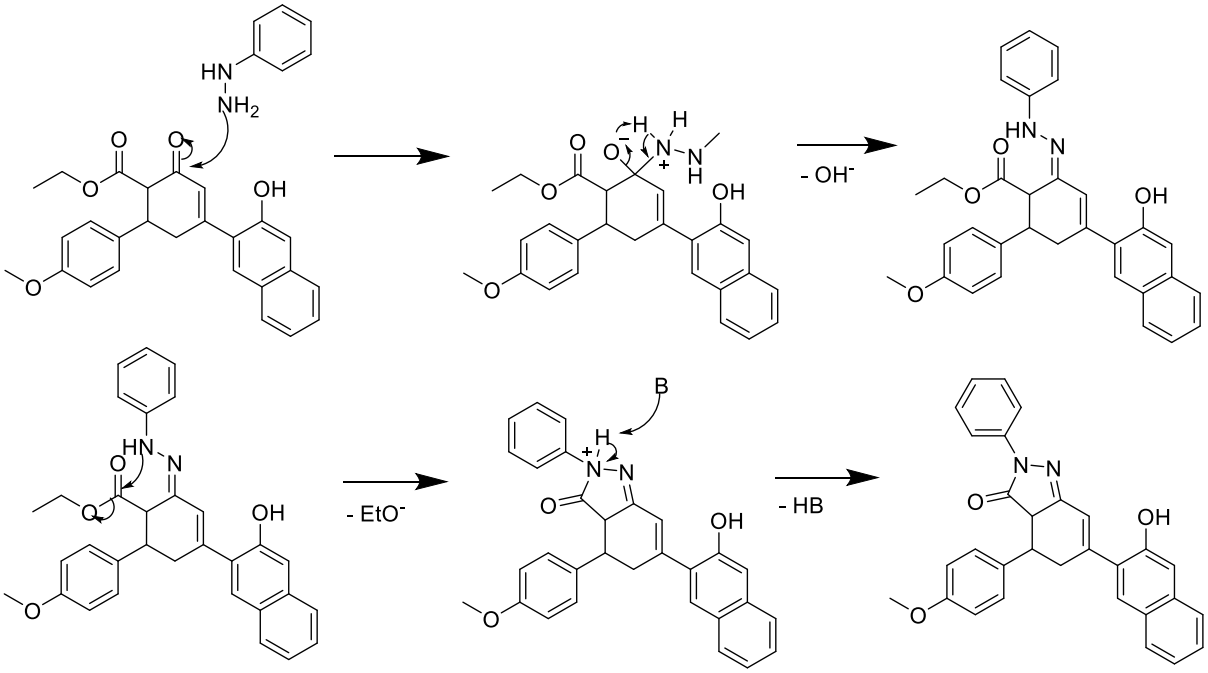
1.4 Nucleophilic addition of hydrazine

Hydrazines are nucleophiles that can take part in a nucleophilic attack. Scheme 1.4 shows an example of such a reaction from the literature. [17] By varying the substituents or structural elements on the reactants, a highly substituted trihydroindazole can be made accessible.



Scheme 1.4: Example of hydrazine reaction in literature [17]

The proposed mechanism for this reaction is shown in scheme 1.5. First a hydrazone is formed, then cyclization occurs. An analogue of the substrate in scheme 1.4 has been determined by previous work in the Hansen group to most likely be the anti-diastereomer. [15-16] It is unlikely that the diastereomer is changed from anti to syn in this reaction, but as the 3D structure has not been confirmed, it has been decided to draw structure without this specification.



Scheme 1.5: The proposed mechanism of the hydrazine reaction

1.5 Previous work in research group

Previous work on molecules included in this thesis by the Hansen research consists of the MSc thesis of Phenias Buhire and Khurelbaatar Sengee. Both Buhire and Sengee have synthesized DBA and the cyclohexenone scaffold molecule of this thesis (**7a**) in their work. According to DFT calculations done by Dr. Taye Demissie and complex 2D NMR techniques mentioned in these works, the anti-diastereomer shown in figure 1.5 is 4.21 kJ/mol more stable than the syn-diastereomer and the double bond was found to be trans (see figure 1.5). [15-16]

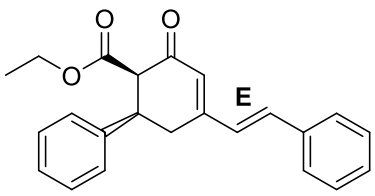


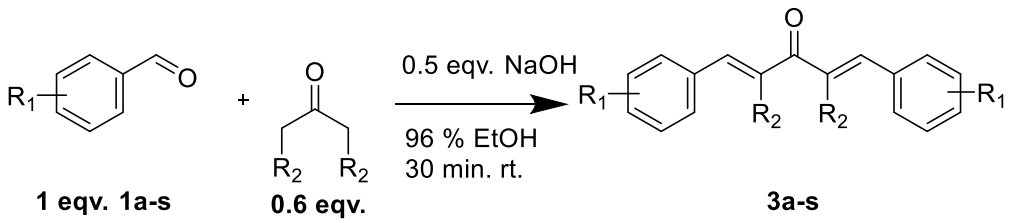
Figure 1.5: 3D structure of cyclohexenone scaffold molecule (7a)

As to distinguish my thesis from the work of Buhire and Sengee, my thesis is focused on diversifying the complex cyclohexenone scaffold molecule (**7a**) with emphasis on reaction with

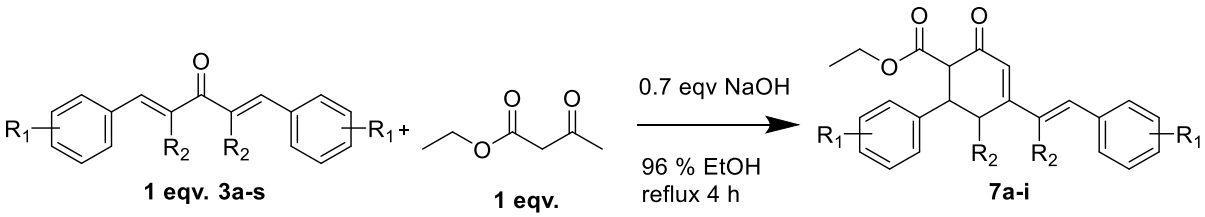
phenylhydrazines. It was also interesting in my thesis to diversity the scaffold molecule (**7a**) with emphasis on R-groups on the phenyl rings. Buhire's main focus was optimization of the synthesis of **7a** as well as hydrogenation, Krapcho decarboxylation, inverse electron demand Diels-Alder, Luche reduction and alkylation of **7a**. Sengee's main focus was isomeric determination and isomeric optimization of **7a** as well as alkylation and acylation of **7a**.

1.6 Aims of the thesis

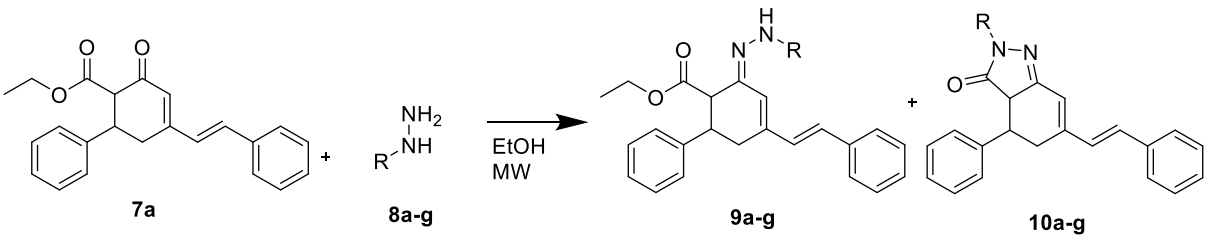
As mentioned, the main focus in this thesis is the production of a chemical library using DOS with focus on the complex cyclohexenone scaffold molecule (**7a**) and emphasis on attempting to react analogues of this molecule with phenylhydrazines. The main goal of DOS is availability of new structures, which means this thesis aims can be split into two main parts; the synthesis of scaffold molecule analogues (see scheme 1.6 and 1.7) and reacting the scaffold molecule with different hydrazines (see scheme 1.8).



Scheme 1.6: Synthesis of symmetrical DBA-analogues



Scheme 1.7: Synthesis of scaffold molecule analogues



Scheme 1.8: Hydrazine reaction with scaffold molecule

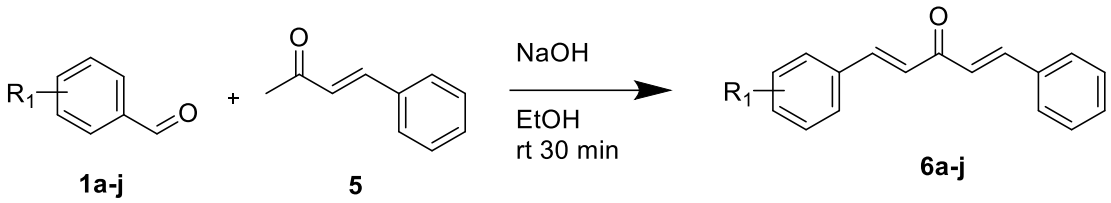
The aims of this thesis were because of this split into the following partial aims:

- Synthesize the scaffold molecule **7a** and explore its reactivity with phenylhydrazines according to scheme 1.8.

- Synthesize analogues of DBA and scaffold molecules according to scheme 1.6 and 1.7.

- Synthesize unsymmetrical DBA-analogues according to scheme 1.9.

- Explore other reactions that can diversify the scaffold molecule.

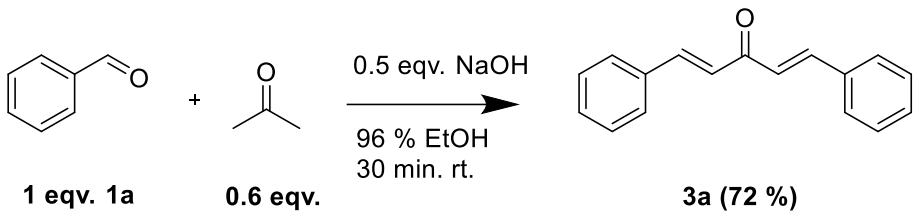


Scheme 1.9: Synthesis of unsymmetrical DBA-analogues

2 Results and discussion

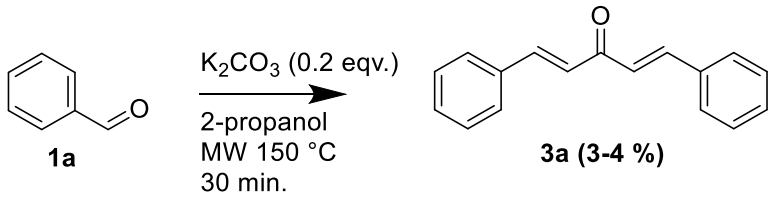
2.1 Synthesis of DBA

DBA is the first intermediate in synthesis of the scaffold molecule, and because of this, DBA and its analogues play a central role in this thesis. Unsubstituted DBA is as mentioned earlier readily used in organic synthesis courses and is well explored in the literature, but its analogues are not as well explored. However, in order to make the unsubstituted scaffold molecule and explore its reactivity with phenylhydrazines, DBA (**3a**) was synthesized according to literature (see scheme 2.1). The isolated yield of 72 % achieved was also according to literature. [18-20] Spectra can be found in appendix page 18 – 21.



Scheme 2.1: Synthesis of DBA (3a)

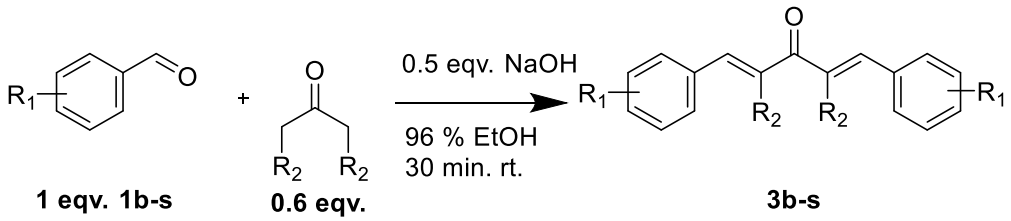
The alternative synthesis of DBA done by Setrawala et. al. was also interesting, and it was attempted to shorten the reaction time by converting it to a MW reaction (see scheme 2.2). [21] However, this conversion gave bad yields (3 – 4 %) and was therefore not explored any further.



Scheme 2.2: Alternative synthesis of DBA (3a)

2.2 Synthesis of symmetrical DBA-analogues

After establishment of the synthesis of unsubstituted DBA, Diversity-Oriented Synthesis of DBA-analogues could begin, starting with the symmetrical DBA-analogues as described in scheme 2.3. As mentioned earlier, substituted DBA-analogues are less explored in the literature, and this combined with the possibility to react the analogues with ethyl acetoacetate to form analogues of the scaffold molecule makes it interesting in a DOS-perspective. Varying the R_2-groups to contain cyclic compounds would also introduce skeletal-DOS to this project.

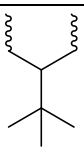
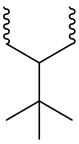


Scheme 2.3: Synthesis of symmetrical DBA-analogues (3b-s)

As can be seen in table 2.2, 1 symmetrical DBA-analogue that has not been reported before was synthesized (**3o**) and identified (spectra in appendix page 42 - 47). The yield for the new compound was 42 % for **3o**. In addition to this, 4 symmetrical DBA-analogues that have only been reported using harsher conditions* were synthesized (**3p**, **3q**, **3r**, **3s** spectra in appendix page 48 – 75). The yields of these compounds were 43 % for **3p**, 60 % for **3q** and 12 % for **3r** and **3s**. 3 symmetrical DBA-analogues that have been reported before using same method were also synthesized in the yields of 17 % for **3b** (66 % in lit. [13]), 30 % for **3c** (96 % in lit. [22]) and 17 % for **3d** (96 % in lit. [22]) (spectra in appendix page 22 – 41). The lower yields compared to literature is likely caused by unoptimized recrystallization, as there were not many side products according to TLC, and TLC of the liquid left after recrystallization showed that product was still dissolved. However, obtaining optimal yields is not a goal within DOS or this thesis, only the availability of new structures is. Further on 10 more DBA-analogues were attempted synthesized without success. Of these compounds, 5 have not been reported before (**3f**, **3g**, **3k**, **3l**, **3m**), 4 have only been reported using harsher conditions* (**3e**, **3h**, **3j**, **3n**) and 1 has previously been reported using similar conditions without information about reaction time (**3i**). [23]

* For **3p** and **3q** a [(Mt/PEG)-SO_3H] nanocatalyst was used in the literature. [24] For **3r** and **3s** a nano-TiO2/HOAc catalyst was used in the literature. [25] For **3e** longer reaction time was used. [26] For **3h** and **3n** 1:1 acetic acid and HCl as solvent and 18 h reaction time was used. [27] For **3j** the reaction was refluxed. [28]

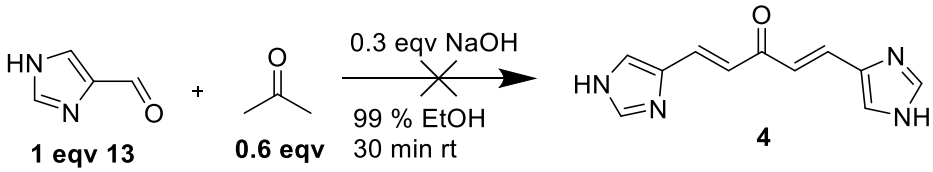
Table 2.1: Results from DOS of symmetrical DBA-analogues

3	**R_1**	**R_2**	**Isolated yield**	**Reported yield**
b	4-bromo	H	17 %	66 % [13]
c	2,6-dichloro	H	30 %	96 % [22]
d	4-chloro	H	17 %	96 % [22]
e	4-trifluoromethyl	H	None	36 %* [26]
f	4-phenyl	H	No reaction	Not reported before
g	4-butyl	H	None	Not reported before
h	4-hydroxy	H	No reaction	"good"* [27]
i	4-cyano	H	None	80 % [23]
j	4-nitro	H	None	84 %* [28]
k	4-acetamido	H	None	Not reported before
l	4-benzyloxy-3-methoxy	H	None	Not reported before
m	4-bromo-3,5-dimethoxy	H	No reaction	Not reported before
n	4-hydroxy-3-methoxy	H	No reaction	"good"* [27]
o	4-*tert*-butoxy	H	42 %	Not reported before
p	4-bromo		43 %	95 %* [24]
q	4-chloro		60 %	98 %* [24]
r	4-bromo		12 %	87 %* [25]
s	4-chloro		12 %	98 %* [25]

* Harsher conditions used, see last page for details.

To sum up results from table 2.2, the reaction seemed to work well for halides, and a strong electron-donating group (4-*tert*-butoxy). The strong electron-withdrawing cyano-group should have worked according to literature, so it is likely that it would work if tried again. As for the strong electron-withdrawing nitro- and trifluoromethyl-groups, these have been reported using reflux for nitro and longer reaction time for trifluoromethyl. The same goes for the strong electron-donating hydroxy-group and methoxy-groups in **7h** and **7n** which have been reported using 1:1 acetic acid and HCl as solvent and 18 h reaction time.

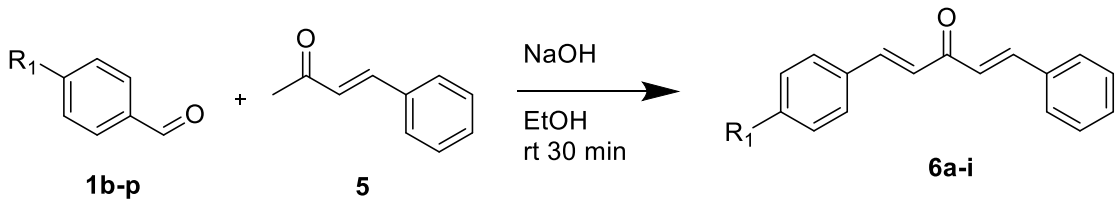
In this thesis the reaction shown in scheme 2.4 was also attempted, but NMR of the crude showed that no reaction had occurred. This is likely because of the different abilities of **13** compared to benzaldehyde.



Scheme 2.4: Attempted synthesis of compound 4

2.3 Synthesis of unsymmetrical DBA-analogues

The synthesis of unsymmetrical DBA-analogues varies slightly from the synthesis of symmetrical DBA-analogues. The difference is that instead of acetone, **5** is used as shown in scheme 2.5. By using the commercially available **5**, half of the DBA-molecule is already installed, so that it is possible to diversify the other half of the molecule with substituted aldehydes **1b-p** to afford the unsymmetrical DBA-analogues **6a-i**.



Scheme 2.5: Synthesis of unsymmetrical DBA-analogues (6a-i)

As can be seen in table 2.3, 2 unsymmetrical DBA-analogues that have not been reported before were synthesized (**6d**, **6h**) and identified (spectra in appendix page 100 – 107 and 114 – 119). The yield for the new compounds were 8 % for **6d** and 5 % for **6h**. In addition to this, 3 unsymmetrical DBA-analogues that have only been reported using harsher conditions* were synthesized (**6b**, **6c**, **6g**, spectra in appendix page 84 – 99 and 108 – 113). The yields of these compounds were 34 % for **6b**, 20 % for **6c** and 10 % for **6g**. 1 unsymmetrical DBA-analogue that has been reported before using the same method was also synthesized (**6a**) in 51 % yield (60 % in lit. [29], spectra in appendix page 76 – 83). Furthermore, 3 more DBA-analogues were attempted synthesized without success, of which 2 have not been reported before (**6f**, **6i**), and the last (**6e**) has only been reported before using 4-(4-hydroxyphenyl)but-3-enon and benzaldehyde. [30]

* For **6b** and **6g** LiOH was used and for **6c**, $Ca(OH)_2$ was used. [31-32]

Table 2.2: Results from DOS of unsymmetrical DBA-analogues

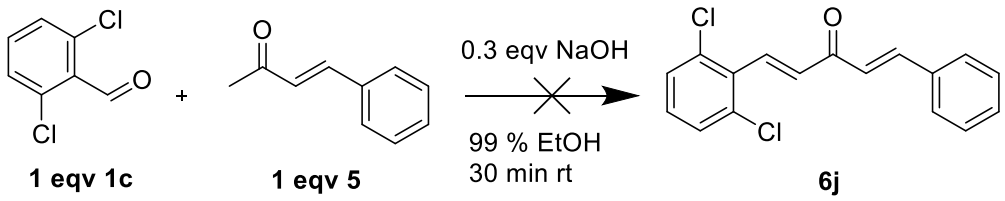
6	**R_1**	**Isolated yield**	**Reported yield**
a	Bromo	51 %	60 % [29]
b	Chloro	34 %	87 %* [31]
c	Trifluoromethyl	20 %	99 %* [32]
d	Phenyl	8 %	Not reported before
e	Hydroxy	No reaction	Reported using 4-(4-hydroxyphenyl)but-3-enon and benzaldehyde [30].
f	Cyano	No sign of anticipated product with the use of NMR	Not reported before
g	Nitro	10 %	90 %* [31]
h	*Tert*-butoxy	5 %	Not reported before
i	Iso-propyl	No sign of anticipated product with the use of NMR	Not reported before

* For **6b** and **6g** LiOH was used and for **6c**, $Ca(OH)_2$ was used. [31-32]

To sum up the results from table 2.3, the reaction seemed to work well for halides (**6a**, **6b**) as well as for electron-donating groups such as *tert*-butoxy (**6h**) and phenyl (**6d**), and strong electron-withdrawing groups such as nitro (**6g**) and trifluoromethyl (**6c**). Comparing these results to the results in table 2.2, the main differences is the strong electron-withdrawing groups nitro and trifluoromethyl, and weak electron-donating phenyl-group which worked for the synthesis of unsymmetrical DBA-analogues, but not the symmetrical DBA-analogues. As the reaction worked for the synthesis of the unsymmetrical DBA-analogues, and as the symmetrical DBA-analogues with 4-trifluoromethyl (**3e**), and 4-nitro (**3j**) have been reported before using

different reaction conditions, it is likely the reaction should work if tried again (possibly with longer reaction times and followed by TLC). [26] [28] Some possible explanation as to why reactions that should work did not work, are reaction time and solubility issues as well as stirring problems caused by precipitation in most reactions.

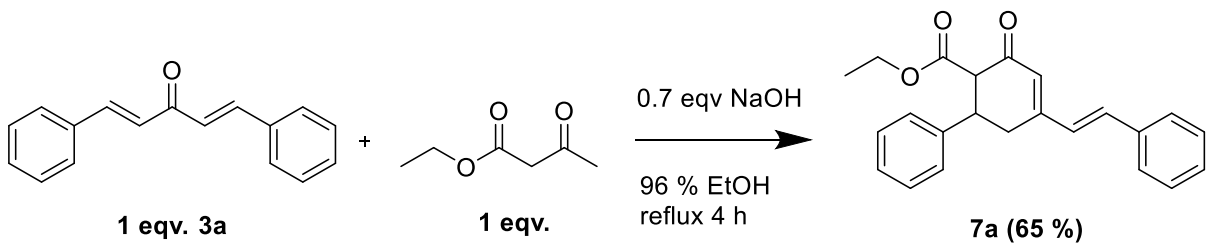
The reaction shown in scheme 2.6 was also attempted, but NMR of the crude showed no sign of the anticipated product. As **1c** worked for synthesis of the symmetrical DBA-analogue (**3c**), this reaction should likely work if tried again.



Scheme 2.6: Attempted synthesis of compound 6j

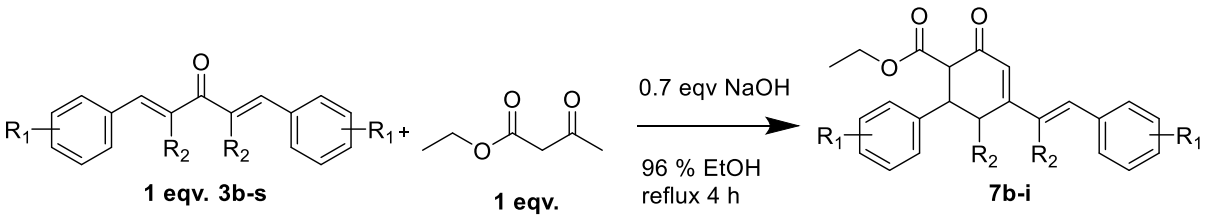
2.4 Synthesis of cyclohexenone scaffold molecule and analogues

A central intermediate scaffold in this project is the cyclohexenone (**7a**) formed via base-catalyzed Robinson annulation between DBAs and ethyl acetoacetate (shown in scheme 2.7). The intermediate is particularly versatile as it has several reactive sites amendable to diversity synthesis. The cyclohexenone scaffold (**7a**) was synthesized and isolated in 65 % yield according to previous work in the Hansen research group. [15-16] Spectra can be found in appendix page 120 – 125.



Scheme 2.7: Synthesis of cyclohexenone scaffold molecule (7a)

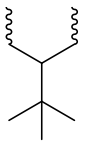
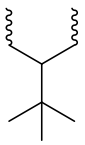
After the synthesis of **7a** was established, Diversity-Oriented Synthesis from the already isolated symmetrical DBA-analogues to make **7b-i** according to the reaction shown in scheme 2.8 could begin.



Scheme 2.8: Synthesis of cyclohexenone scaffold molecule analogues (7b-i)

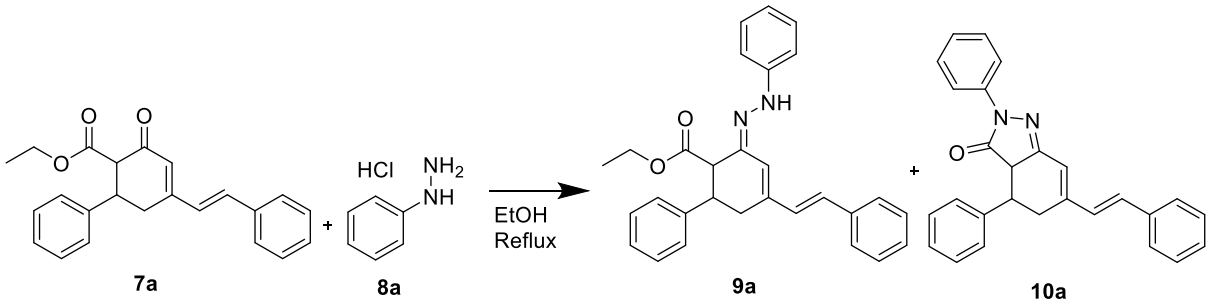
As can be seen in table 2.4, 4 analogues of the cyclohexenone scaffold molecule that have not been reported before were synthesized (**7b-e**) and identified (spectra in appendix page 126 – 151). The isolated yields of the new compounds were 38 % for **7b**, 22 % for **7c**, 9 % for **7d** and 11 % for **7e**. What also can be seen in table 2.4 is that synthesis of **7f-i** was unsuccessful. This could possibly be explained by the synthesis of **7f-i** introducing fused bicycles with higher strain in the structure which typically have higher energy states.

Table 2.3: Results from synthesis of scaffold molecule analogues 7b-i

7	R_1	R_2	Isolated yield
b	4-bromo	H	38 %
c	2,6-dichloro	H	22 %
d	4-chloro	H	9 %
e	4-*tert*-butoxy	H	11 %
f	4-bromo		No reaction
g	4-chloro		No reaction
h	4-bromo		No reaction
i	4-chloro		No reaction

2.5 The hydrazine reaction

The cyclohexenone scaffold (**7a**) is virtually unexplored in the literature. As **7a** contains both double bonds, a ketone and an ester group, several DOS routes are possible. In this thesis the reactivity of **7a** with phenylhydrazine hydrochloride (**8a**) was explored, and as mentioned in introduction the expected intermediate and product from this reaction can be seen in scheme 2.9.



Scheme 2.9: Expected products from the hydrazine reaction, where 9a is an intermediate in the formation of 10a

Two possible conclusions that could be drawn from the initial reactions shown in table 2.5, is that DCM and water likely were not suitable solvents for this reaction, and that the phenylhydrazine (**8b**) was likely too old to be used. As there was a lot of phenylhydrazine hydrochloride (**8a**) available, this was used in future reactions. More possible conclusion to draw from table 2.5 is that MW reactions had, as expected, less by-products and gave easier work-up and was also the only reaction condition where I was able to identify any products. As suspected, **9a** and **10a** also turns out to be two of the products from the reaction depending on reaction conditions, though they have only been likely confirmed using impure NMR samples.

All the reactions in table 2.5 were closely followed by TLC, and all entries where a reaction occurred had many spots from early on. To test what would happen after prolonged reaction condition, the reaction was run for 48 hours followed by TLC (entry 5, table 2.5). No conclusions could be drawn from this test.

Table 2.4: Initial hydrazine reaction entries

Entry	Solvent	Heating condition	7:8 ratio	Results and observations
1	96 % EtOH	Conventional, reflux 24 h	1:1	Many spots on the TLC, and no pure NMR spectra after several purification attempts (column chromatography)
2	DCM	Conventional, reflux 24 h	1:2	No reaction according to TLC and crude NMR.
3	96 % EtOH*	Conventional, reflux 24 h	1:1	Many spots on the TLC, and no pure NMR spectra after several purification attempts (column chromatography)
4	96 % EtOH	Conventional, reflux 24 h	1:2	Many spots on the TLC, and no pure NMR spectra after several purification attempts (column chromatography)
5	96 % EtOH	Conventional, reflux 48 h	1:2	Many spots on the TLC, and no pure NMR spectra after several purification attempts (column chromatography)
6	96 % EtOH	Conventional, reflux 48 h	1:2**	No reaction
7	Water	MW 160°C 1 h	1:2	No reaction
8	96 % etanol	MW 160 °C 1 h	1:1	NMR shows that **9a** was likely a product. Issues with isolating **9a**
9	96 % ethanol	MW 160 °C 1 h	1:2	NMR shows that **10a** was likely a product. Issues with isolating **10a**

* A few drops of H_2SO_4 as catalyst.

** An old and opened bottle of phenylhydrazine (**8b**) was used.

One of the possible reasons why it was hard to isolate **9a** and **10a** could be because they have the same R_f value (even the same spot on the TLC). In addition to this, other by-products likely have the same R_f as well, further complicating work-up. However, as explained in table 2.5, I was able to identify **9a** (entry 8) and **10a** (entry 9) with the help of 1D and 2D NMR spectra of the impure fractions from column chromatography containing these compounds (spectra in appendix page 152 – 169). As for the column chromatography, several solvent systems were attempted both with and without grading. Ethyl acetate and heptane varying from 1 % to 15 % ethyl acetate seemed to be the most successful, but even when fractions were collected, solvent evaporated and the fractions sent through column again they were not pure. Recrystallization was also attempted in various other solvents such as ethanol and water without success.

2.5.1 Rough optimization of the hydrazine reaction using internal standard NMR yields

As the NMR spectra of two of the products from the hydrazine reaction (**9a**, **10a**) have been identified, but neither of these were successfully isolated after many attempts, it was decided to use internal standard and NMR as a way of obtaining approximate yields. The internal standard used was butylbenzene. As **9a** had more overlapping ^{1}H NMR spectra (with other products and internal standard) and because **9a** was an intermediate in the formation of **10a**, it was decided to focus on using **10a** in this study. Using NMR for quantification is not without problems as the integral in NMR used for quantification depends on many factors and optimally the peaks should be singlets with no overlapping. It should however be noted that internal standard and NMR was successfully used for quantification in the thesis of Kristoffersen. [33] It should also be noted that the intention was to isolate and verify the yields, so isolation of **10a** was attempted alongside the NMR yield experiments. The protons used for identification are shown in figure 2.1.

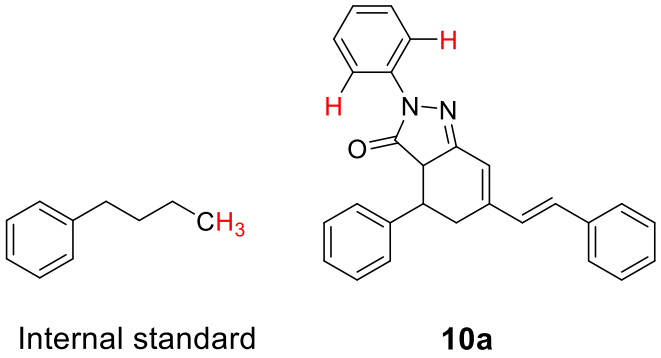


Figure 2.1: Marked protons used for internal standard NMR-yield

As can be seen in table 2.6, chloroform and 99 % ethanol seem to be promising solvents for this reaction. In table 2.9 different reaction times were tested, but unfortunately yield of **10a** seems to go down over time. The spectral data from these experiments can be found in Appendix page 170 – 176.

Table 2.5: Finding optimal solvent conditions using internal standard of butylbenzene and NMR

Conditions*	**Amount of cyclohexenone scaffold (7a) [mmol]**	**Amount of ex. St. [mmol]**	**Integral****	**NMR yield 10a**
96 % ethanol	0.0372	0.0395	0.3623	19 %
Toluene	0.0364	0.0410	0.2356	13 %
99 % ethanol	0.0381	0.0402	0.4009	21 %
Chloroform***	0.0352	0.0253	0.6472	23 %
Acetonitrile	0.0320	0.1833	0.0694	20 %

* Ratio between the cyclohexenone scaffold (**7a**) and the phenylhydrazine hydrochloride (**8a**) reactants was set to 1:2.

** Integral of the benzene ortho protons on C26 and C30 when integral of the methyl tops from butylbenzene internal standard are set as 3 (see figure 2.1)

*** The septum of the MW vials lasted very short with this solvent.

Example of calculation:

$$\frac{\text{Areal stoff } (A_s)}{\text{Areal intern standard } (A_{is})} = \frac{\text{Antall mol stoff}(n_s)}{\text{Antall mol internstandard } (n_{is})}$$

$$\frac{3 * A_s}{2 * A_{is}} = \frac{n_s}{n_{is}}$$

$$n_s = \frac{3 * A_s * n_{is}}{2 * A_{is}} = \frac{3 * 0.3623 * 0.0395}{2 * 3.000} = 0.0072\ mmol$$

$$\%_s = \frac{100 * n_s}{n_{reactant}} = \frac{100 * 0.0072}{0.0372} = 19\ \%$$

Table 2.6: Finding optimal time condition with internal standard of butylbenzene

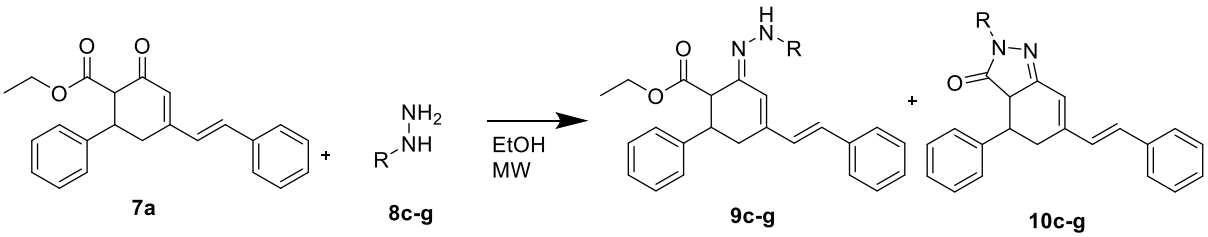
Time*	**Amount of reactant [mmol]**	**Amount of ex. St. [mmol]**	**Relative integral****	**NMR yield 10a**
0.5 h	0.0364	0.0305	0.1505	6 %
1 h	0.0381	0.0402	0.4009	21 %
2 h	0.0294	0.0320	0.3183	17 %

* Ratio between the cyclohexenone scaffold (**7a**) and the phenylhydrazine hydrochloride (**8a**) reactants was set to 1:2.

** Integral of the benzene ortho protons on C26 and C30 when integral of the methyl tops from butylbenzene internal standard are set as 3 (see figure 2.1)

2.6 Continued attempts of forming pyrazolones.

With few results from continued attempts of isolating **9a** and **10a**, it was decided that a possible solution was to test different kinds of hydrazines (see scheme 2.10), but as seen in table 2.8 this was not successful. The only possible conclusion to draw from table 2.8 was that **7c** did not react, which could be explained by its structural difference from the other hydrazines.



Scheme 2.10: Attempted synthesis of compounds 9c-g and 10c-g

Table 2.7: Reaction between scaffold cyclohexenone molecule (7a) and different hydrazines

Entry	R	Observations
1	*Tert*-butyl (**8c**)	No reaction
2	4-cyanophenyl (**8d**)	Many spots on the TLC, and no pure NMR spectra after several purification attempts (column chromatography)
3	2,4,6-trichlorophenyl (**8e**)	Many spots on the TLC, and no pure NMR spectra after several purification attempts (column chromatography)
4	3-nitrophenyl (**8f**)	Many spots on the TLC, and no pure NMR spectra after several purification attempts (column chromatography)
5	2-nitrophenyl (**8g**)	Many spots on the TLC, and no pure NMR spectra after several purification attempts (column chromatography)

After few results from the reactions in table 2.5-2.7, it was discovered that the concentration of the reagents in the reaction had been a bit low compared to similar reactions in literature. This could in turn reduce the possibility of bimolecular reactions to occur. As a consequence of this, the reaction was attempted with higher molar concentration (see table 2.8) as well as at room temperature in different solvents. The two solvents tested at room temperature was 99 % ethanol and concentrated acetic acid, both followed by TLC over 24 hours. Unfortunately, none of these changes seemed to work. One possible explanation for why increasing the concentration did not work, could be that the solvent was saturated before all the reactants were dissolved. This means that the actual concentration may not have been higher because of solubility issues.

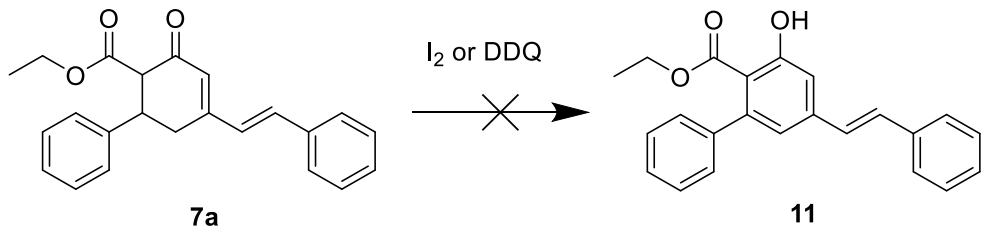
Table 2.8: Overview of concentration in the hydrazine reactions

Entry	Concentration of cyclohexenone substrate	Concentration of 8a/8b	Comment
Kanagarajan [12]	25 mM	25 mM	From literature
Regaila [18]	167 mM	333 mM	From literature
Soliman [17]	667 mM	1333 mM	From literature
Table 2.5 entry 5	11 mM	23 mM	Attempt with conventional heating
Table 2.5 entry 9	32 mM	66 mM	Attempt with MW
1*	114 mM	254 mM	Same issues as before

* This was the highest load possible, and as the reaction occurred inside the MW reactor, it was impossible to tell if it all dissolved during reaction.

2.7 Other reactions

As mentioned earlier, the cyclohexenone scaffold (**7a**) is virtually unexplored in the literature, and as **7a** contains both double bonds, a ketone and an ester group, several DOS routes are possible. One of the possible reactions would be the oxidation of the ketone to form a highly substituted phenol (see scheme 2.11), a reaction which has been done on similar molecules by Liang et al. and Kristoffersen. [33-34] The reactions were followed by TLC and both methods were unsuccessful (see table 2.11). Auto-flash chromatography was used to attempt purification of the products from the I_2 reaction, and a chromatogram can be seen in appendix page 177.



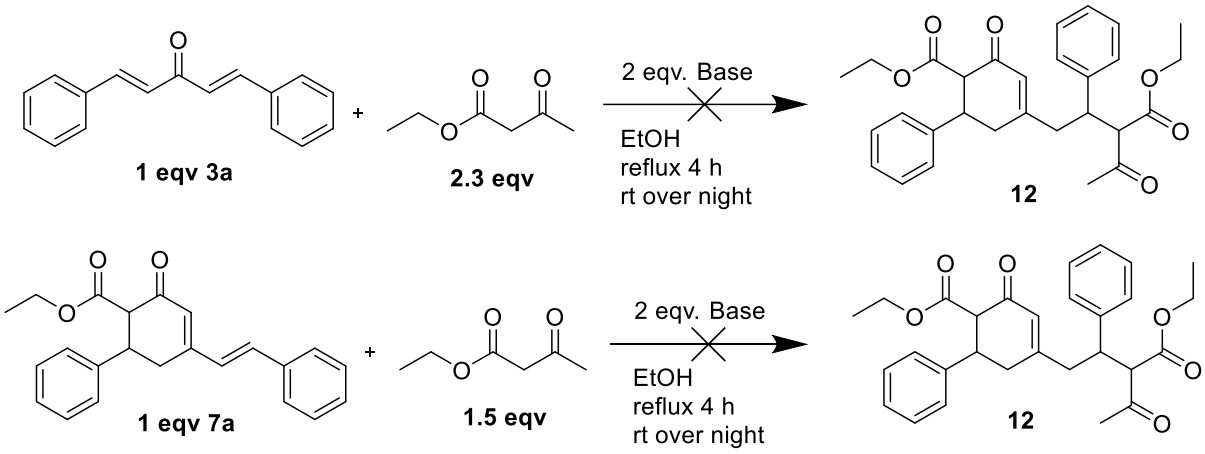
Scheme 2.11: Attempted synthesis of compound 11

Table 2.9: Results from attempted oxidation of compound 7a

Reaction conditions	Results/observations
I_2 reflux 24 h	Several spots on TLC, no sign of anticipated product using NMR on fractions from column chromatography
I_2 MW 200 °C 30 min	Several spots on TLC, no sign of anticipated product using NMR on fractions from column chromatography
DDQ rt 1 h	No reaction
DDQ reflux 2 h	No reaction

According to Afsah et al. it should be possible for **3a** to react twice with ethyl acetoacetate in the same reaction instead of just once. [19] To do this, the ratio between the substrate and reactant should according to Afsah et al. be increased to 1:2 and the base be switched to sodium

ethoxide. [19] The reaction was attempted both from **3a** and from **7a** of which both were closely followed by TLC, but without success. Increasing the ratio between **3a** and ethyl acetoacetate up to 1:4 with 2.5 eqv. of base and increasing the ratio between **7a** and ethyl acetoacetate up to 1.5 with 3 eqv. of base, both combined with reflux over night was also unsuccessful (see scheme 2.12). Both NaOH and $NaOCH_3$ were tested as base. The base used was later found to have been opened long ago, which could be the reason why it was not successful.



Scheme 2.12: Attempted synthesis of compound 12

2.8 Characterization of molecules

2.8.1 Characterization of compound 3a

The structure of DBA (**3a**) is well documented in the literature. [14-16] As can be seen in table 2.12, the protons on the double bonds (C2 and C6 as well as C3 and C5, see figure 2.2) had the same chemical shift suggesting symmetry in the molecule. In addition to this, the coupling constant of 16 Hz for these protons, strongly suggest that the molecule is the trans-trans isomer. The NMR-peaks have been identified in table 2.10 and 2.11. The full spectra of compound **3a** can be found in appendix page 18 – 21.

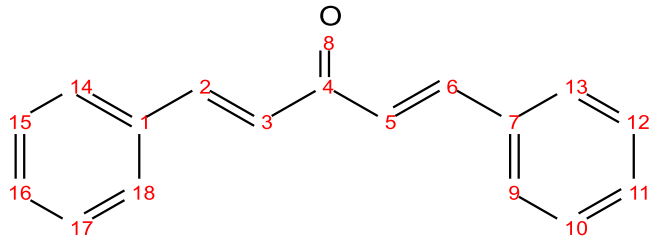


Figure 2.2: Numbered compound 3a

Table 2.10: ^1H NMR of compound 3a

δ_H	**Belongs to protons on (see figure 2.2)**
7.75 (d, *J* = 16 Hz, 2H)	C2 and C6
7.65-7.60 (m, 4H)	C9, C13, C14 and C18
7.45-7.40 (m, 6H)	C10, C11, C12, C15, C16 and C17
7.09 (d, *J* = 16 Hz, 2H)	C3 and C5

Table 2.11: ^{13}C NMR of compound 3a

δ_C*	**Belongs to (see figure 2.2)**
143.5	C2 and C6
135.0	C1 and C7
130.7	C11 and C16
129.2	C9, C13, C14 and C18
128.6	C10, C12, C15 and C17
125.6	C3 and C5

* Note that the carbonyl carbon was not seen in the ^{13}C NMR. This is likely due to tertiary carbons having a higher relaxation time, and thus longer experiment time on the NMR instrument, or other types of NMR experiments, would be needed. Because **3a** already is well documented in the literature and everything else was according to literature, this was not considered necessary.

2.8.2 Characterization of DBA-analogues (3b-s and 6a-h)

The NMR-spectra of **3b-s** and **5a-h** varies only slightly from the NMR-spectra of **3a**, and thus only one example from each will be explained. The full spectra of compound **3b-s** can be found in appendix page 22 - 75 and full spectra of compound **6a-h** can be found in appendix page 76 – 119.

For compound **3b**, the main difference in proton spectra from **3a** would be the integral and multiplicity of the peak for the protons on C1, C3, C9 and C11 (see figure 2.3) as C2 and C10 no longer have protons attached to them. In addition, the peaks will have a slightly different chemical shift because of the Br. In the carbon spectra **3b** has got different chemical shifts compared to **3a**. All of this can be seen in table 2.12 and 2.13 where NMR peaks have been identified, and the differences will be similar for compound **3c-s**.

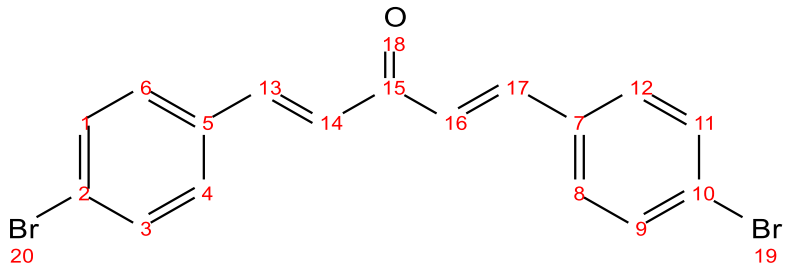


Figure 2.3: Numbered compound 3b

Table 2.12: ^{1}H NMR of compound 3b

δ_H	**Belongs to protons on (see figure 2.3)**
7.66 (d, *J* = 16 Hz, 2H)	C13 and C17
7.55 (d, *J* = 8 Hz, 4H)	C4, C6, C8 and C12
7.50 (d, *J* = 8 Hz, 4H)	C1, C3, C9 and C11
7.04 (d, *J* = 16 Hz, 2H)	C14 and C16

Table 2.13: ^{13}C NMR of compound 3b

δ_C	**Belongs to (see figure 2.3)**
188.5	C15
142.3	C13 and C17
133.8	C5 and C7
132.4	C1, C3, C9 and C11
129.9	C4, C6, C8 and C12
125.9	C14 and C16
125.0	C2 and C10

As for compound **6a**, the NMR spectra will vary more from **3a** than **3b** does. The main difference in proton NMR would be that the molecule no longer is symmetrical. This means that the protons on C1, C3 and C9, C10, C11 as well as C4, C6 and C8, C12 (see figure 2.4) now give a total of four peaks instead of two (see table 2.16). In addition to this, the chemical shifts of **6a** and **3a** will also be slightly different because of the Br group. In the carbon NMR, C13 and C17 as well as C14 and C16 also gives 4 peaks instead of 2 because of the unsymmetrical form of the molecule. All of this can be seen in table 2.14 and 2.15 where the NMR peaks have been identified, and the differences will be similar for compound **6b-h**.

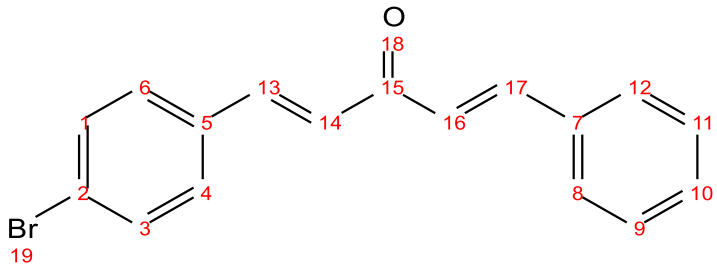


Figure 2.4: Numbered compound 6a

Table 2.14: ^1H NMR of compound 6a

δ_H	**Belongs to protons on (see figure 2.4)**
7.72 (d, *J* = 16 Hz, 1H)	C17
7.64 (d, *J* = 16 Hz, 1H)	C13
7.61 – 7.57 (m, 2H)	C8 and C12
7.51 (d, *J* = 8 Hz, 2H)	C4 and C6
7.43 (d, *J* = 8 Hz, 2H)	C1 and C3
7.39 (t, *J* = 4 Hz, 3H)	C9, C10 and C11
7.04 (dd, *J* = 16 Hz, *J* = 2 Hz, 2H)	C14 and C16

Table 2.15: ^{13}C NMR of compound 6a

δ_C	**Belongs to (see figure 2.4)**
188.6	C15
143.6	C17
141.8	C13
134.7	C5
133.7	C7
132.2	C1 and C3
130.7	C10
129.8	C4 and C6
129.0	C8 and C12
128.5	C9 and C11
125.8	C14
125.4	C16
124.8	C2

2.8.3 Characterization of compound 7a

As mentioned earlier in this thesis, previous master students in the Hansen group have identified the 3D structure of **7a**. [15-16] Buhire and Sengee mentioned that the two protons on the chiral centres (C1 and C2, see figure 2.5) had overlapping peaks and the diastereomer could not be verified with 2D NMR. However, using DFT, Dr. Taye Demissie confirmed that the anti-diastereomer was likely the most stable diastereomer. [15-16] HSQC was also used by Buhire and Sengee to verify the overlapping of the ^{1}H-NMR peaks (C1, C2) mentioned above. [15-16] As for the double bond, the coupling constant of 16 Hz for the protons on the double bond (C10 and C14) strongly suggests that the double bond is trans. This is further on confirmed by TOCSY showing that the two protons on C3 and C10 as well as the two protons on C5 and C14 are adjacent, which Buhire and Sengee also pointed out. [15-16] The full spectra of compound **7a** can be found in appendix page 120 – 125 and the NMR-peaks have been identified in table 2.16.

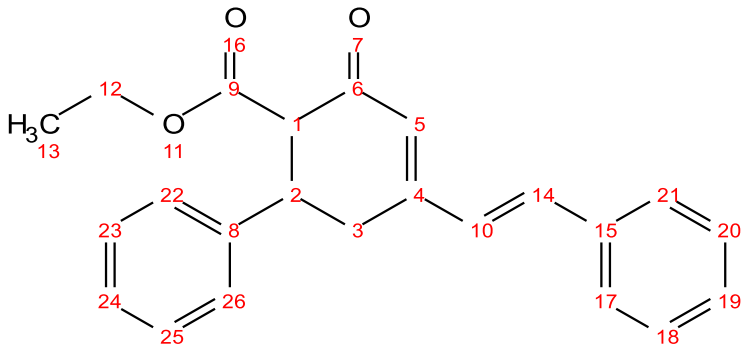


Figure 2.5: Numbered compound 7a

Table 2.16: ^1H NMR of compound 7a

δ_H	**Belongs to protons on (see figure 2.5)**
7.47 (dd, *J* = 8 Hz, *J* = 2 Hz, 2H)	C17 and C21
7.40 – 7.30 (m, 8H)	C18, C19, C20, C22, C23, C24, C25 and C26
7.00 (d, *J* = 16 Hz, 1H)	C10
6.93 (d, *J* = 16 Hz, 1H)	C14
6.21 (d, *J* = 2 Hz, 1H)	C5
4.04 (q, *J* = 7 Hz, 2H)	C12
3.80 – 3.72 (m*, 2H)	C1 and C2
3.06 (dd, *J* = 18 Hz, J = 4 Hz, 1H)	C3
2.73 (ddt, *J* = 18, J = 10 Hz, J = 2 Hz, 1H)	C3
1.04 (t, *J* = 7 Hz, 3H)	C13

* Singlet overlapped with what looks like a quartet.

2.8.4 Characterization of scaffold molecule analogues (7b-e)

The NMR-spectra of **7b-e** varies only slightly from the NMR-spectra of **7a**, and thus only one example will be explained. The full spectra of compounds **7b-e** can be found in appendix page 126 – 151.

For compound **7b**, the main difference from **7a** is related to the peaks of the phenyl-protons which now are split into three doublets with integrals of 4, 2 and 2. Otherwise chemical shifts are different from **7a** too, and the peaks of the protons on the double bond (C10 and C14, see figure 2.6) overlap making it almost look like a singlet. The same changes are valid for compounds **7c-e**. The NMR-peaks have been identified in table 2.17.

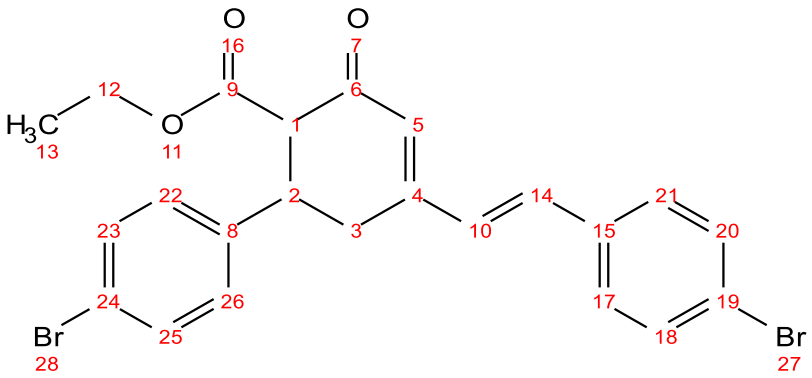


Figure 2.6: Numbered compound 7b

Table 2.17: ^1H NMR of compound 7b

δ_H	**Belongs to protons on (see figure 2.6)**
7.46 (dd, *J* = 9 Hz, *J* = 2 Hz, 4H)	C17, C18, C20 and C21
7.31 (d, *J* = 9 Hz, 2H)	C23 and C25
7.18 (d, *J* = 9 Hz, 2H)	C22 and C26
6.91* (d, *J* = 17 Hz, 1H)	C10
6.86* (d, *J* = 17 Hz, 1H)	C14
6.17 (s, *J* = 2 Hz, 1H)	C5
4.03 (q, *J* = 7 Hz, 2H)	C12
3.70 – 3.66 (m**, 2H)	C2 and C1
2.97 (d, *J* = 18 Hz, 1H)	C3
2.65 (d, *J* = 17 Hz, 1H)	C3
1.05 (t, *J* = 7 Hz, 3H)	C13

* Overlapped with each other.

** Singlet overlapped with what looks like a quartet.

2.8.5 Characterization of compound 9a

As with compound **7a**, 2D NMR was used to identify ^{1}H-NMR signals of **9a** and starting with COSY where as expected the protons on C14 and C15, on C1 and C3, C5 and C10, on C20/C22 and C19/C23 as well as on C21 and C20/22 give signals to each other (see figure 2.7). In addition to this the protons on C29/C33 and C30/C31/32 give signal to each other, as well as the barely visible signal between the protons on C24/C28 and C25/C26/C27. Using TOCSY the protons on C1 and C5 as well as the protons on C5 and C11 give signal to each other, the latter confirming the trans-isomer. Lastly TOCSY gives signal between the protons on C20/C22 and C19/C23. HSQC was also used to confirm ^{13}C signals, and together with the previous information, this gives a likely verification of **9a**. However, to be 100 % sure this is indeed **9a** both MS data and NMR data on isolated **9a** would be needed. The NMR-peaks have been identified in table 2.18 and the full spectra of compound **9a** can be found in appendix page 152 – 161.

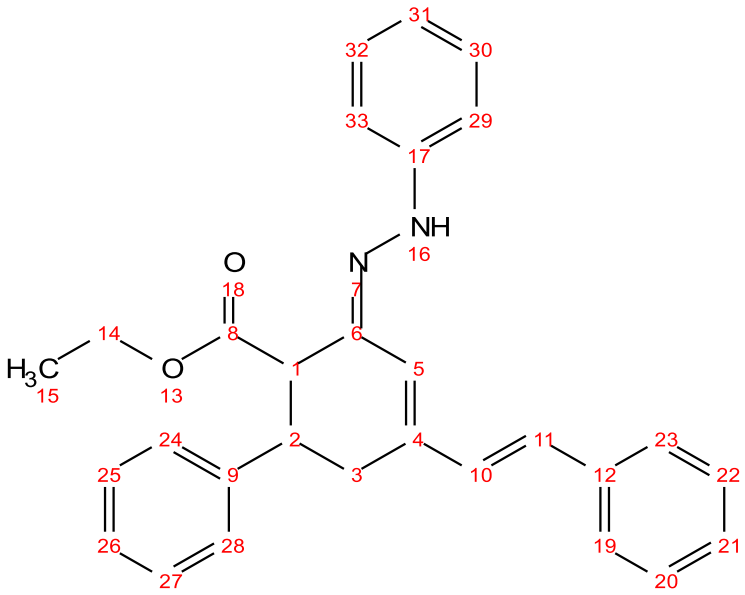


Figure 2.7: Numbered compound 9a

Table 2.18: ^1H NMR of compound 9a

δ_H	**Belongs to protons on (see figure 2.7)**
7.67 (d, *J* = 8 Hz, 2H)	C20 and C22
7.52 (d, *J* = 8 Hz, 2H)	C29 and C33
7.48 (s*, 1H)	C21
7.45 (d, *J* = 9 Hz, 2H)	C19 and C23
7.33 (d, *J* = 7 Hz, 3H)	C30, C31, C32
7.27 (d, *J* = 6 Hz, 3H)	C25, C26, C27
7.21 (d, *J* = 9 Hz, 2H)	C24 and C28
7.16 (s, 1H)	C10
7.12 (s, 1H)	C11
6.75 (s, 1H)	C5
4.46 (dd, *J* = 8 Hz, *J* = 5 Hz, 1H)	C1
3.99 (q, *J* = 7 Hz, 1H)	C14
3.87 (q, *J* = 7 Hz, 1H)	C14
2.99 (dd, *J* = 17 Hz, *J* = 8 Hz, 1H)	C3
2.83 (dd, *J* = 17 Hz, *J* = 5 Hz, 1H)	C3
1.25 (overlapped, 1H)	C2
1.01 (t, *J* = 7 Hz, 3H)	C15

* This is likely a triplet overlapping the two duplets next to it making it look like a singlet.

2.8.6 Characterization of 10a

As with compound **9a**, 2D NMR was also used to identify NMR signals of **10a** starting with COSY where as expected the proton on C2 gives signal to the protons on C1 and C3 (see figure 2.8). There is also a COSY signal between the protons on C10 and C11 as well as between the protons on C3 and C5. Lastly in the COSY there is a signal between the protons on C21/C22/C23/C27/C28/C29 and the protons on C20/C24 as well as on C26/C30. Using TOCSY all the protons on the cyclohexenone ring (C1, C2, C3 and C5) give signal to each other. HSQC was also used to confirm ^{13}C signals, and together with the previous information, this gives a likely verification of **10a**. However, to be 100 % sure this is indeed **10a** both MS data and NMR data on isolated **10a** would be needed. The NMR-peaks have been identified in table 2.19 and the spectra of compound **10a** can be found in appendix page 162 – 169.

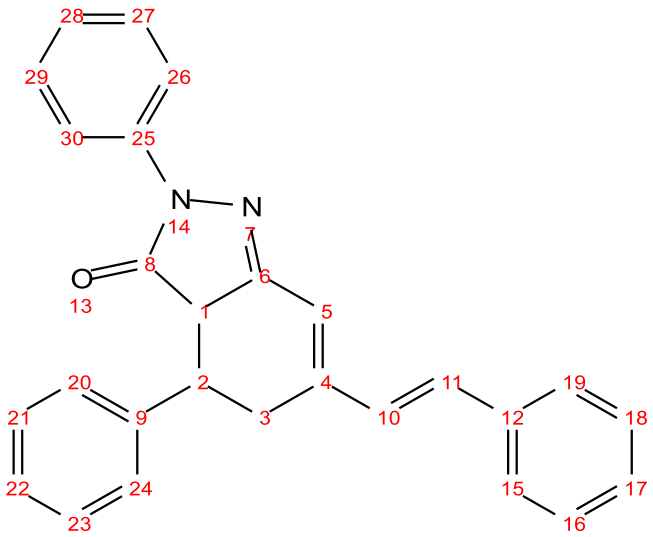


Figure 2.8: Numbered compound 10a

Table 2.19: ^1H NMR of compound 10a

δ_H	**Belongs to protons on (see figure 2.8)**
7.90 (d, *J* = 8 Hz, 2H)	C26 and C30
7.47 – 7.41 (m, 5H)	C15, C16, C17, C18 and C19
7.36 (t, *J* = 8 Hz, 6H)	C21, C22, C23, C27, C28 and C29
7.19 – 7.13 (m, 2H)	C20 and C24
6.99 (d, *J* = 16 Hz, 1H)	C10
6.79 (d, *J* = 16 Hz, 1H)	C11
6.61 (s, 1H)	C5
3.82 (d, *J* = 13 Hz, 1H)	C1
3.32 (td, *J* = 10 Hz, *J* = 5 Hz, 1H)	C2
3.06 (dd, *J* = 17 Hz, *J* = 5 Hz, 1H)	C3
2.69 (dd, *J* = 17 Hz, *J* = 12 Hz, 1H)	C3

3 Conclusions

Overall in this thesis 7 compounds that have not been reported synthesized before were synthesized, isolated and identified (see figure 3.1), of which 1 was a symmetrical DBA-analogue (**3o** with 42 % yield), 2 were unsymmetrical DBA-analogues (**6d** with 8 % yield and **6h** with 5 % yield) and 4 were analogues of the cyclohexenone scaffold (**7b-e** with 38 %, 22 %, 9 % and 11 % yield). In addition to this, 7 compounds that have only been reported using different reaction conditions were synthesized, isolated and identified (structures in appendix 1), of which 4 were symmetrical DBA-analogues (**3p** with 43 % yield, **3q** with 60 % yield, **3r** with 12 % yield and **3s** with 12 % yield) and 3 were unsymmetrical DBA-analogues (**6b** with 34 % yield, **6d** with 20 % yield and **6g** with 10 % yield). 4 compounds that have been synthesized before using similar method were also synthesized (structures in appendix 1), of which 3 were symmetrical DBA-analogues (**3b** with 17 % yield, **3c** with 30 % yield and **3d** with 17 % yield) and 1 was unsymmetrical DBA-analogue (**6a** with 51 % yield).

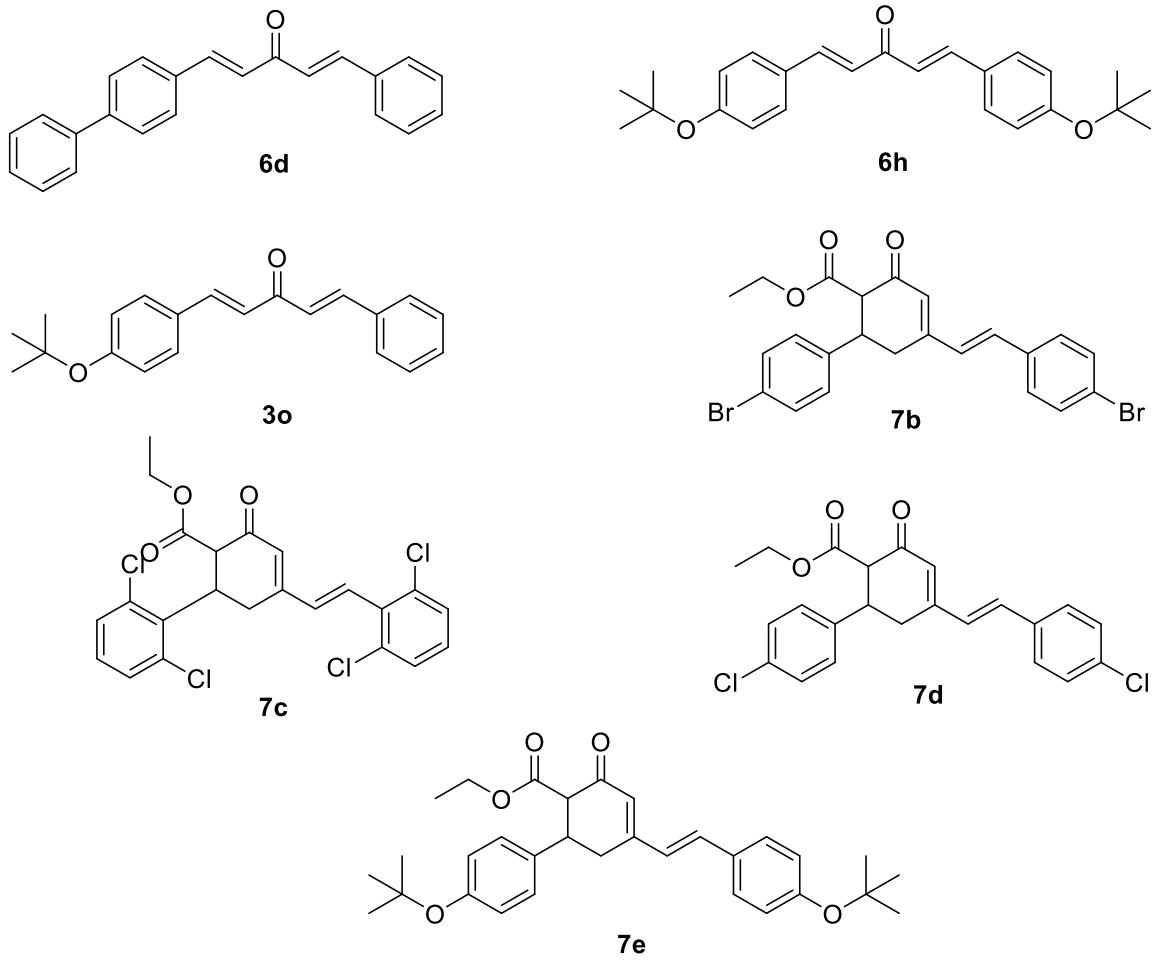


Figure 3.1: Overview of new compounds synthesized

In the synthesis of DBA-analogues, a total of 13 reactions were unsuccessful, of which 7 have not been reported before (**3f**, **3g**, **3k**, **3l**, **3m**, **6f** and **6i**). In addition to this, 4 of these reactions have been reported before using different reaction conditions (**3e**, **3h**, **3j**, **3n**), 1 has only been reported switching the functional groups on the substrates (**6e**) and 1 has been reported using similar conditions (**3i**). The synthesis of the 4 cyclohexenone scaffold molecule analogues with added cyclopentane and cyclohexane structural elements (**7f-i**) was also unsuccessful. The structures of all these compounds can be found in appendix 1.

Looking at the structures of the successful DBA-analogue synthesises, it is hard to draw any clear conclusions as the reactions worked for both strong electron-donating groups such as 4-*tert*-butoxy (**3o**, **6h**) as well as strong electron withdrawing groups such as 4-trifluoromethyl

and 4-nitro (for unsymmetrical DBA-analogues **6c** and **6g**). The weak electron-withdrawing chloro- and bromo-group also worked well, even when adding cyclopentane and cyclohexane elements on the ketone. The latter was however not successful when synthesizing the cyclohexenone scaffold analogues. The low yields for all these reactions could be explained by unoptimized work-up, as in most cases some product was still left dissolved after recrystallization according to TLC. However, obtaining optimal yields is not a goal within DOS or this thesis, only the availability of new structures is.

Lastly two products from the hydrazine reaction (see figure 3.2) have been likely identified with the help of NMR, and the yield of one of these (**10a**) has been attempted optimized with the help of internal standard and NMR. In addition to this, a few other reactions have also been explored in this thesis without much success. This means that in a conclusion two out of the four partial aims mentioned in section 1.6 were quite successful, while the two partial aims involving the hydrazine reaction and other reactions were not as successful.

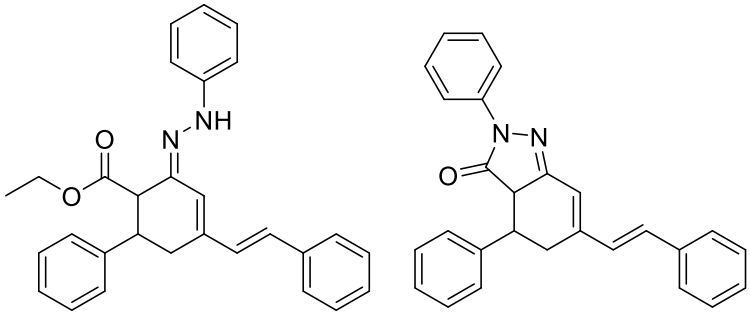


Figure 3.2: Compound 9a and 10a

4 Further work

Most of the successful synthesises of DBA-analogues and cyclohexenone scaffold-molecule analogues have a bit low yields, and for most of the work-ups there was still product dissolved in the solvent after recrystallization. This means that most reactions done in this thesis could use some optimization of work up, either by optimizing recrystallization conditions or possibly changing to column chromatography. In addition to this, 3 of the R-groups (4-nitro, 4-

trifluoromethyl and 4-phenyl) only worked for synthesis of the unsymmetrical DBA-analogues. As the reaction worked for unsymmetrical synthesis, it should likely also work for symmetrical synthesis. Two of these (4-trifluoromethyl and 4-nitro) have also been reported synthesized using longer reaction time and reflux for the latter. This means that all the reactions that did not work should be attempted over longer time, attempted refluxed or possibly attempted using a catalyst similar to those used in alternative reaction conditions mentioned in results section. These reactions should also be closely followed by TLC.

As for the hydrazine reaction, the two likely identified compounds should be isolated and confirmed and MS-data as well as NMR-data on pure compound should be collected. The yields from the internal standard NMR optimization should also be confirmed by isolation. For this to be achieved, work-up needs to be optimized. One possible solution could be to use HPLC or UPLC in an attempt to optimize the separation. It is also possible to run the sample through HPLC/UPLC twice, first separating peaks, then a second time to isolate compounds from peaks that are not pure. UPLC was successfully used by Sengee to separate the two diastereomers of **7a**, so it could work for **9a**/**10a**. [15]

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6 Experimental section

6.1 Materials

All chemicals used during synthesis are commercially available and were used without further purification. Nitrogen was used as an inert gas, and the desiccation of solvents were carried out according to standard procedures. The solvent mixtures used in recrystallization or for chromatographic separation were used in a volume ratio (v:v). All non-MW reactions were carried out with a magnetic stirrer and with silica oil heating bath. TLC was carried out on Merck TLC aluminium oxide 60 F_{254} neutral, and visualization under UV-light. Davasil 35 – 70 µm was used for column chromatography. For column chromatography auto-flash was also used when specified. Solvents were removed using a rotary evaporator with water heating bath, water cooling and vacuum down to 10 mbar. For drying, a vacuum pump going down to 10^{-3} mbar equipped with a liquid nitrogen cooling trap was used. pH paper was used for determination of pH. VWR micropipettes were used for precise volume measurement. If nothing else is specified on ethanol concentration, rectified ethanol (96 %) was used.

6.2 Analytical methods

IR-spectroscopy: Agilent Cary 630 FTIR.

Auto-flash column chromatography: Biotage SP01 using Biotage SNAP prepacked columns.

MS-spectrometry: Thermo Scientific ITQ 1100 detector. Experiments and predictions were performed by the responsible engineer.

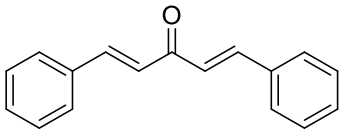
NMR-spectroscopy: Bruker Ascend 400. MestReNova software version 12.0.2-20910 and Bruker TopSpin version 3.5 pl 7 was used for analysis.

Microwave reactor: Anton Paar Monowave 300.

6.3 Synthesis

6.3.1 Synthesis of symmetrical DBA-analogues

(1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one (3a)



Method 1*:

Benzaldehyde **1a** (16.0 g, 0.151 mol) and NaOH (3.01 g, 75.3 mmol) was dissolved in a mixture of distilled water (220 mL) and ethanol (220 mL) in a round bottom flask. Acetone (6.53 mL, 88.2 mmol) was added to the mixture, the first half dropwise, before the reaction was stirred at room temperature for 30 minutes and sat. ammonium chloride was added until the reaction mixture was basic. The resulting solid was collected in a Büchner funnel, washed with distilled water and recrystallized in 70 % ethanol. The yellow solid was dried under vacuum to yield **3a** (12.6 g, 71 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.75 (d, *J* = 16 Hz, 2H), 7.65-7.60 (m, 4H), 7.45-7.40 (m, 6H), 7.09 (d, *J* = 16 Hz, 2H)

^{13}C NMR**: (100.64 MHz, chloroform-*d*) δ_C: 143.5, 135.0, 130.7, 129.2, 128.6, 125.6

R_f: 0.51 (heptane:Ethyl acetate, 2:1)

Spectra can be found in appendix page 18 – 21.

The data is consistent with literature data. [15-16]

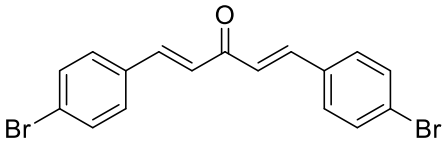
* Some of **3a** used was already made by previous students in the Hansen group, and just needed recrystallization before use.

** Note that the carbonyl carbon was not seen in the ^{13}C NMR. This is likely due to tertiary carbons having a higher relaxation time, and thus longer experiment time on the NMR instrument or other types of NMR experiments would be needed. Because **3a** already is well documented in the literature, this was not considered necessary.

Method 2:

Benzaldehyde **1a** (507 mg, 4.78 mmol) and potassium carbonate (133 mg, 0.96 mmol) was dissolved in 2-propanol (20 mL) in a microwave reaction vial before the reaction was heated to 150 °C for 20 minutes. The reaction mixture was then cooled to room temperature before saturated ammonium chloride was added until the reaction mixture was basic. The resulting solid was then collected in a Büchner funnel and washed with distilled water. Both TLC and crude-NMR showed that the reaction had not occurred.

(1*E*,4*E*)-1,5-bis(4-bromophenyl)penta-1,4-dien-3-one (3b)



4-bromobenzaldehyde **1b** (701 mg, 3.789 mmol) and NaOH (53 mg, 1.33 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (165 µL, 2.23 mmol) was added dropwise to the mixture and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The yellow solid was dried under vacuum to yield **3b** (127 mg, 17 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.66 (d, *J* = 16 Hz, 2H), 7.55 (d, *J* = 8 Hz, 4H), 7.50 (d, *J* = 8 Hz, 4H), 7.04 (d, *J* = 16 Hz, 2H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 188.5, 142.3, 133.8, 132.4, 129.9, 125.9, 125.0

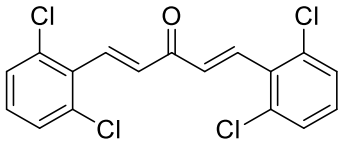
R_f: 0.43 (heptane:ethyl acetate, 2:1)

m/z: calculated for $C_{17}H_{12}OBr_2ONa$ $[M+Na]^+$: 414.9127, found: 414.9125

IR: υ [cm^{-1}] = 1652 (s), 1585 (s), 1562 (s), 1488 (m), 1406 (m), 1324 (m), 1186 (m), 1108 (w), 1074 (m), 985 (s), 870 (m), 821 (s), 721 (m), 698 (m)

Spectra can be found in appendix page 22 - 28 and the data is consistent with literature data. [13]

(1*E*,4*E*)-1,5-bis(2,6-dichlorophenyl)penta-1,4-dien-3-one (3c)



2,6-dichlorobenzaldehyde **1c** (702 mg, 4.01 mmol) and NaOH (51 mg, 1.28 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (170 µL, 2.30 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The yellow solid was dried under vacuum to yield **3c** (225 mg, 30 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.81 (d, *J* = 16 Hz, 2H), 7.38 (d, *J*= 8 Hz, 4H), 7.22 (d, *J* = 16 Hz, 2H*), 7.21 (t, *J* = 8 Hz, 2H*)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 188.0, 136.5, 134.3, 132.2, 131.4, 129.1, 128.0

m/z: Calculated for $C_{17}H_{11}OCl_4$ $[M+H]^+$: 370.9559, found: 370.9564

R_f: 0.42 (heptane:ethyl acetate, 2:1)

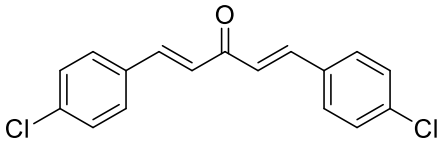
IR: υ [cm^{-1}] = 166 (s), 1603 (s), 1581 (s), 1559 (s), 1428 (s), 1313 (s), 1197 (s), 978 (s), 776 (s), 736 (s)

Spectra can be found in appendix page 29 – 35.

The data is consistent with literature data. [22]

* Overlapping integral.

(1*E*,4*E*)-1,5-bis(4-chlorophenyl)penta-1,4-dien-3-one (3d)



4-chlorobenzaldehyde **1d** (877 mg, 6.24 mmol) and NaOH (87 mg, 2.18 mmol) was dissolved in a mixture of distilled water (5mL) and ethanol (5 mL), before acetone (272 µL, 3.67 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The yellow solid was dried under vacuum to yield **3d** (160 mg, 17 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.68 (d, *J* = 16 Hz, 2H), 7.54 (d, *J* = 8 Hz, 4H), 7.38 (d, *J* = 8 Hz, 4H), 7.02 (d, *J* = 16 Hz, 2H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 187.5, 141.2, 135.6, 132.3, 128.7, 128.4, 124.8

m/z: Calculated for $C_{17}H_{12}OCl_2Na$ $[M+Na]^+$: 325.0157, found: 325.0160

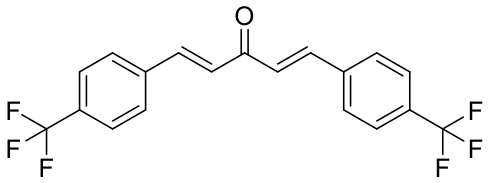
R_f: 0.41 (heptane:ethyl acetate, 2:1)

IR: υ [cm^{-1}] = 1652 (s), 1629 (s), 1588 (s), 1566 (s), 1491 (s), 1406 (s), 1324 (s), 1190 (s), 1089 (s), 1015 (s), 985, 821 (s), 754 (s), 713 (s)

Spectra can be found in appendix page 36 – 41.

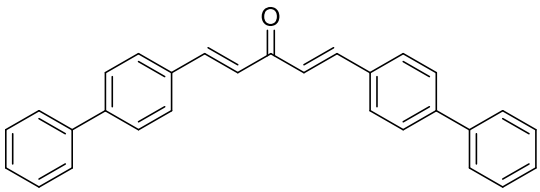
The data is consistent with literature data. [13] [36]

(1*E*,4*E*)-1,5-bis(4-trifluorimethylphenyl)penta-1,4-dien-3-one (3e)



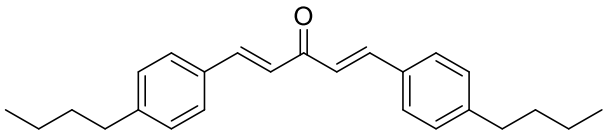
4-trifluoromethylbenzaldehyde **1e** (549 µL, 4.02 mmol) and NaOH (48 mg, 1.20 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (175 µL, 2.36 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride and extracted with 2X30 mL DCM. The DCM was evaporated, and crude dried under vacuum. The ^{1}H and ^{13}C NMR spectra of the crude was not identified as the expected product, so no further analysis was carried out.

(1*E*,4*E*)-1,5-bis(4-biphenyl)penta-1,4-dien-3-one (3f)



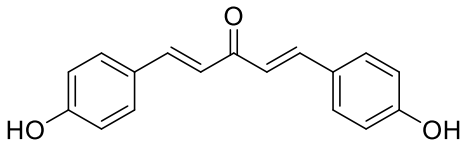
4-phenylbenzaldehyde **1f** (701 mg, 3.85 mmol) and NaOH (58 mg, 1.45 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (252 µL, 3.40 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid showed that no reaction had occurred.

(1*E*,4*E*)-1,5-bis(4-butylphenyl)penta-1,4-dien-3-one (3g)



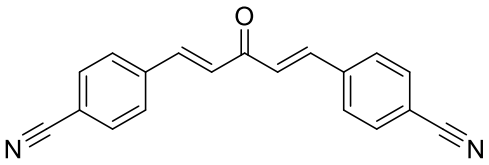
4-butylbenzaldehyde **1g** (517 µL, 3.08 mmol) and NaOH (24 mg, 0.60 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (134 µL, 1.81 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride and extracted with 2X30 mL DCM. The DCM was evaporated, and crude dried under vacuum. The ^{1}H and ^{13}C NMR spectra of the obtained solid was not identified as the expected product, so no further analysis was carried out.

(1*E*,4*E*)-1,5-bis(4-hydroxyphenyl)penta-1,4-dien-3-one (3h)



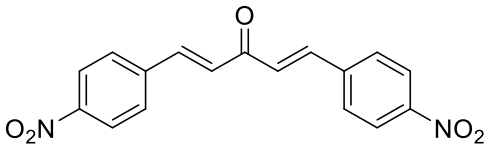
4-hydroxybenzaldehyde **1h** (706 mg, 5.78 mmol) and NaOH (40 mg, 1.00 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (167 µL, 2.26 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid showed that no reaction had occurred.

(1*E*,4*E*)-1,5-bis(4-cyanophenyl)penta-1,4-dien-3-one (3i)



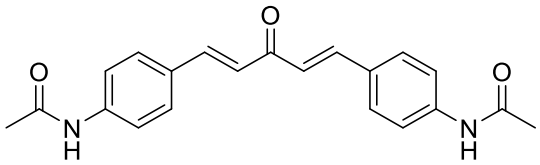
4-cyanobenzaldehyde **1i** (702 mg, 5.35 mmol) and NaOH (72 mg, 1.80 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (233 µL, 3.15 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid was not identified as the expected product, so no further analysis was carried out.

(1*E*,4*E*)-1,5-bis(4-nitrophenyl)penta-1,4-dien-3-one (3j)



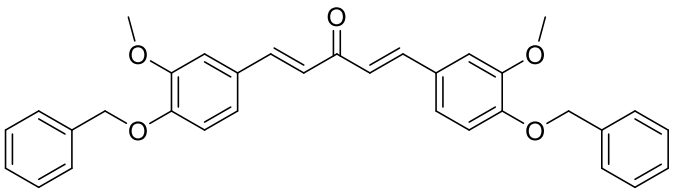
4-nitrobenzaldehyde **1j** (702 mg, 4.65 mmol) and NaOH (67 mg, 1.68 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (202 µL, 2.73 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid was not identified as the expected product, so no further analysis was carried out.

(1*E*,4*E*)-1,5-bis(4-acetamidophenyl)penta-1,4-dien-3-one (3k)



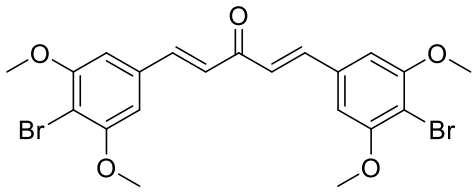
4-acetamidobenzaldehyde **1k** (702 mg, 4.30 mmol) and NaOH (53 mg, 1.33 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (187 µL, 2.53 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid was not identified as the expected product, so no further analysis was carried out.

(1*E*,4*E*)-1,5-bis(4-benzyloxy-3-methoxyphenyl)penta-1,4-dien-3-one (3l)



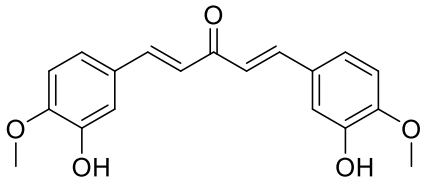
4-benzyloxy-3-methoxybenzaldehyde **1l** (702 mg, 3.08 mmol) and NaOH (38 mg, 0.95 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (170 µL, 2.30 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride and extracted with 2X30 mL DCM. The DCM was evaporated, and the crude dried under vacuum. The ^{1}H and ^{13}C NMR spectra of the crude was not identified as the expected product, so no further analysis was carried out.

(1*E*,4*E*)-1,5-bis(4-bromo-3,5-dimethoxyphenyl)penta-1,4-dien-3-one (3m)



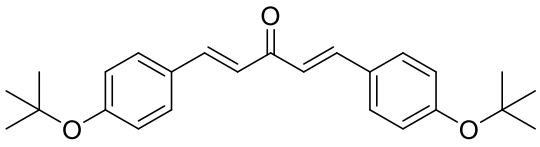
4-bromo-3,4-dimethoxybenzaldehyde **1m** (733 mg, 3.00 mmol) and NaOH (31 mg, 0.78 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (130 µL, 1.76 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid showed that no reaction had occurred.

(1*E*,4*E*)-1,5-bis(3-hydroxy-4-methoxyphenyl)penta-1,4-dien-3-one (3n)



3-hydroxy-4-methoxybenzaldehyde **1n** (702 mg, 4.61 mmol) and NaOH (46 mg, 1.15 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (201 µL, 2.72 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid showed that no reaction had occurred.

(1*E*,4*E*)-1,5-bis(4-*tert*-butoxyphenyl)penta-1,4-dien-3-one (3o)



4-*tert*-butoxybenzaldehyde **1o** (490 µL, 2.80 mmol) and NaOH (43 mg, 1.08 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (156 µL, 2.11 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The yellow solid was dried under vacuum to yield **3o** (225 mg, 42 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.70 (d, *J* = 16 Hz, 2H), 7.53 (d, *J* = 8 Hz, 4H), 7.02 (d, *J* = 8 Hz, 4H), 6.98 (d, *J* = 16 Hz, 2H), 1.40 (s, 18H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 188.0, 157.1, 141.9, 128.8, 128.5, 123.3, 122.9, 78.5, 28.1

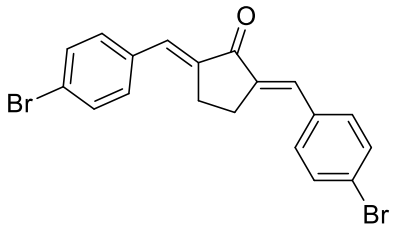
m/z: Calculated for $C_{25}H_{31}O_3$ $[M+H]^+$: 379.2268, found: 379.2267

R_f: 0.79 (heptane:ethyl acetate, 1:1)

IR: υ [cm^{-1}] = 2981 (m), 1670 (w), 1618 (s), 1588 (s), 1570 (s), 1506 (s), 1413 (s), 1369 (s), 1335 (s), 1246 (s), 1160 (s), 1093 (s), 992 (s), 888 (s), 855 (s), 691 (s)

Spectra can be found in appendix page 42 – 47.

(2*E*, 5*E*)-2,5-bis(4-bromophenylmethylene)cyclopentanone (3p)



4-bromobenzaldehyde **1b** (702 mg, 3.79 mmol) and NaOH (38 mg, 0.95 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before cyclopentanone **2b** (196 µL, 2.65 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, before extraction with 2X35 mL DCM. After removal of solvent, the crude was recrystallized in 70 % ethanol. The yellow solid was dried under vacuum to yield **3p** (339 mg, 43 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.57 (d, *J* = 8 Hz, 4H), 7.52 (s, 2H), 7.45 (d, *J* = 8 Hz, 4H), 3.08 (s, 4H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 196.1, 137.8, 134.7, 132.9, 132.2, 124.0, 26.6

m/z: Calculated for $C_{19}H_{15}OBr_2$ $[M+H]^+$: 416.9484, found: 416.9483

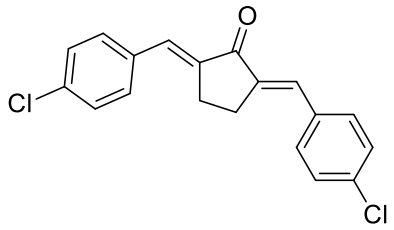
R_f: 0.78 (heptane:ethyl acetate, 1:1)

IR: υ [cm^{-1}] = 1696 (s), 1607 (s), 1581 (s), 1488 (m), 1402 (s), 1253 (m), 1175 (m), 1078 (s), 1007 (m), 689 (s), 821 (s), 687 (s)

Spectra can be found in appendix page 48 – 55.

The data is consistent with literature data. [35]

(2*E*, 5*E*)-2,5-bis(4-chlorophenylmethylene)cyclopentanone (3q)



4-chlorobenzaldehyde **1d** (707 mg, 3.82 mmol) and NaOH (39 mg, 0.98 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before cyclopentanone **2b** (262 µL, 3.54 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, before extraction with 2X35 mL DCM. After removal of solvent, the crude was recrystallized in 70 % ethanol. The yellow solid was dried under vacuum to yield **3q** (379 mg, 60 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.52 (d, *J* = 8 Hz, 6H), 7.41 (d, *J* = 8 Hz, 4H), 3.09 (s, 4H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 196.1, 137.6, 135.6, 134.2, 132.8, 132.0, 129.2, 26.6

m/z: Calculated for $C_{19}H_{15}OCl_2$ $[M+H]^+$: 329.0494, found: 329.0495

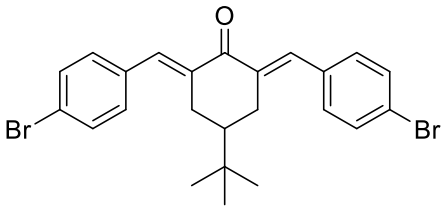
R_f: 0.79 (heptane:ethyl acetate, 1:1)

IR: υ [cm^{-1}] = 1698 (s), 1611 (s), 1585 (s), 1559 (m), 1488 (m), 1406 (s) 1253 (m) 1175 (s), 1093 (s), 933 (s), 821 (s), 691 (s)

Spectra can be found in appendix page 56 – 63.

The data is consistent with literature data. [36]

(2E, 6E)-2,6-bis(4-bromophenylmethylene)-4-*tert*-butylcyclohexanone (3r)



4-bromobenzaldehyde **1b** (711 mg, 3.84 mmol), NaOH (46 mg, 1.15 mmol) and 4-*tert*-butylcycloheksanon **2c** (346 mg, 2.24 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, before extraction with 2X35 mL DCM. After removal of solvent, the crude was recrystallized in 70 % ethanol. The yellow solid was dried under vacuum to yield **3r** (113 mg, 12 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.68 (d, *J* = 3 Hz, 2H), 7.55 (d, *J* = 8 Hz, 4H), 7.32 (d, *J* = 8 Hz, 4H), 3.09 (dd, *J* = 15 Hz, *J* =3 Hz, 2H), 2.40 (t, *J* = 14 Hz, 2H), 1.47 (tt, *J* = 13 Hz, *J* = 3 Hz, 1H), 0.94 (s, 9H)

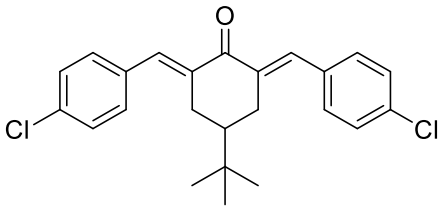
^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 189.4, 135.7, 134.9, 133.9, 130.9, 122.1, 43.4, 31.7, 28.6, 26.4

R$_f$: 0.79 (heptane:ethyl acetate, 1:1)

Spectra can be found in appendix page 64 – 69.

The data is consistent with literature data. [25]

(2E, 6E)-2,6-bis(4-chlorophenylmethylene)-4-tertbutylcyclohexanone (3s)



4-chlorobenzaldehyde **1d** (880 mg, 6.26 mmol), NaOH (64 mg, 1.60 mmol) and 4-*tert*-butylcycloheksanon **2c** (552 mg, 3.58 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, before extraction with 2X35 mL DCM. After removal of solvent, the crude was recrystallized in 70 % ethanol. The yellow solid was dried under vacuum to yield **3s** (151 mg, 12 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.70 (d, *J* = 2 Hz, 2H), 7.39 (s, 8H), 3.10 (dd, *J* = 16 Hz, *J* = 2 Hz, 2H), 2.41 (t, *J* = 13 Hz, 2H), 2.48 (tt, *J* = 13 Hz, *J* = 3 Hz, 1H), 0.95 (s, 9H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 190.2, 136.5, 135.8, 134.7, 134.5, 131.6, 128.9, 44.4, 32.7, 29.6, 27.4

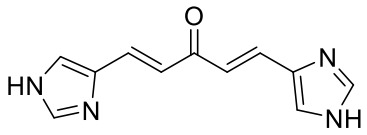
m/z: Calculated for $C_{24}H_{25}OCl_2$ $[M+H]^+$: 399.1277, found: 399.1274

R_f: 0.80 (heptane:ethyl acetate, 1:1)

Spectra can be found in appendix page 70 – 75.

The data is consistent with literature data. [37]

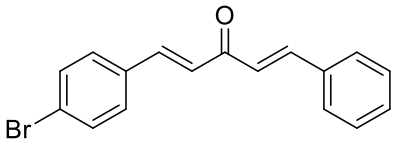
(1*E*,4*E*)-1,5-bis(1-H-imidazol-3-yl)penta-1,4-dien-3-one (4)



1H-imidazole-3-carbaldehyde **12** (159 mg, 1.65 mmol) and NaOH (17 mg, 0.43 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before acetone (72 µL, 0.97 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid showed that no reaction had occurred.

6.3.2 Synthesis of unsymmetrical DBA-analogues

(1*E*,4*E*)-1-(4-bromophenyl)penta-1,4-dien-3-one (6a)



4-bromobenzaldehyde **1b** (1430 mg, 7.73 mmol), NaOH (82 mg, 2.05 mmol) and (E)-4-phenylbut-3-enon **5** (1133 mg, 7.75 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The yellow solid was dried under vacuum to yield **6a** (1231 mg, 51 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.72 (d, *J* = 16 Hz, 1H), 7.64 (d, *J* = 16 Hz, 1H), 7.61 – 7.57 (m, 2H), 7.51 (d, *J* = 8 Hz, 2H), 7.43 (d, *J* = 8 Hz, 2H), 7.39 (t, *J* = 4 Hz, 3H), 7.04 (dd, *J* = 16 Hz, *J* = 2 Hz, 2H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 188.6, 143.6, 141.8, 134.7, 133.7, 132.2, 130.7, 129.8, 129.0, 128.5, 125.8, 125.4, 124.8

m/z: Calculated for $C_{17}H_{14}BrO$ $[M+H]^+$: 313.0223, found: 313.0228

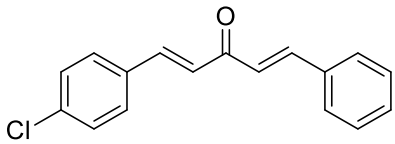
R_f: 0.79 (heptane:ethyl acetate, 1:1)

IR: υ [cm^{-1}] = 1652 (m), 1596 (m), 1488 (w), 1451 (w), 1402 (w), 1328 (w), 1190 (w), 1074 (m), 981 (s), 817 (s), 762 (s), 717 (s), 695 (s)

Spectra can be found in appendix page 76 – 83.

The data is consistent with literature data. [38]

(1*E*,4*E*)-1-(4-chlorophenyl)penta-1,4-dien-3-one (6b)



4-chlorobenzaldehyde **1d** (665 mg, 4.73 mmol), NaOH (47 mg, 1.18 mmol) and (E)-4-phenylbut-3-enon **5** (757 mg, 5.18 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The yellow solid was dried under vacuum to yield **6b** (430 mg, 34 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.69 (d, *J* = 16 Hz, 1H), 7.62 (d, *J* = 16 Hz, 1H), 7.57 – 7.53 (m, 2H), 7.45 (d, *J* = 8 Hz, 2H), 7.36 (t, *J* = 3 Hz, 3H), 7.31 (d, *J* = 8 Hz, 2H), 7.00 (dd, *J* = 16 Hz, *J* = 6 Hz, 2H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 188.4, 143.4, 141.6, 136.2, 134.6, 133.2, 130.5, 129.5, 129.1, 128.9, 128.4, 125.6, 125.3

m/z: Calculated for $C_{17}H_{13}ClONa$ $[M+Na]^+$: 291.0547, found: 291.0550

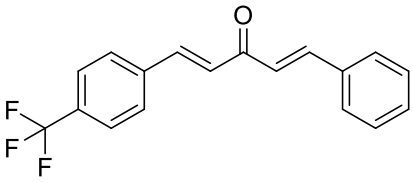
R_f: 0.79 (heptane:ethyl acetate, 1:1)

IR: υ [cm^{-1}] = 1652 (s), 1596 (s), 1491 (s), 1451 (m), 1410 (m), 1331 (s), 1194 (s), 1093 (s), 981 (s), 821 (s), 762 (s), 695 (s)

Spectra can be found in appendix page 84 – 91.

The data is consistent with literature data. [31]

(1*E*,4*E*)-1-(4-trifluorimethylphenyl)penta-1,4-dien-3-one (6c)



4-trifluoromethylbenzaldehyde **1e** (557 µL, 4.08 mmol), NaOH (42 mg, 1.05 mmol) and (E)-4-phenylbut-3-enon **5** (655 mg, 4.48 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The yellow solid was dried under vacuum to yield **6c** (241 mg, 20 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.75 (d, *J* = 16 Hz, 1H), 7.72 (d, *J* = 16 Hz, 1H), 7.68 (d, *J* = 8 Hz, 2H), 7.64 (d, *J* = 8 Hz, 2H), 7.62 – 7.58 (m, 2H), 7.41 (t, *J* = 3 Hz, 3H), 7.14 (d, *J* = 16 Hz, 1H), 7.07 (d, *J* = 16 Hz, 1H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 188.5, 144.0, 141.3, 138.3, 134.6, 130.8, 129.1, 128.5, 128.5, 127.4, 126.0, 125.9, 125.3

m/z: Calculated for $C_{18}H_{13}F_3ONa$ $[M+Na]^+$: 325.0811, found: 325.0813

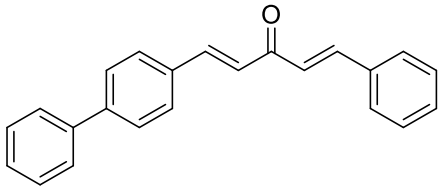
R_f: 0.81 (heptane:ethyl acetate, 1:1)

IR: υ [cm^{-1}] = 1655 (s), 1592 (s), 1324 (s), 1164 (s), 1112 (s), 1071 (s), 985 (s), 832 (s), 762 (s), 698 (s)

Spectra can be found in appendix page 92 - 99

The data is consistent with literature data. [39]

(1*E*,4*E*)-1-(4-biphenyl)penta-1,4-dien-3-one (6d)



4-phenylbenzaldehyde **1f** (789 mg, 4.33 mmol), NaOH (59 mg, 1.48 mmol) and (E)-4-phenylbut-3-enon **5** (697 mg, 4.77 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The yellow solid was dried under vacuum to yield **6d** (101 mg, 8 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.80 (d, *J* = 10 Hz, 2H), 7.76 (d, *J* = 10 Hz, 2H), 7.72 – 7.60 (m, 8H), 7.50 – 7.36 (m, 6H), 7.14 (d, *J* = 7 Hz, 1H), 7.10 (d, *J* = 7 Hz, 1H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 188.9, 143.4, 143.4, 140.2, 134.9, 133.9, 130.6, 129.1, 129.0, 128.5, 128.0, 127.7, 127.2, 125.6, 125.4

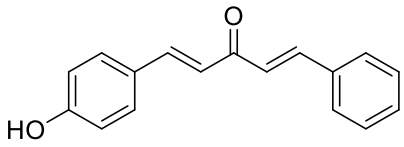
m/z: Calculated for $C_{23}H_{18}ONa$ $[M+Na]^+$: 333.1250, found: 333.1249

R_f: 0.81 (heptane:ethyl acetate, 1:1)

IR: υ [cm^{-1}] = 1648 (s), 1588 (s), 1488 (s), 1451 (s), 1413 (m), 1335 (s), 1190 (s), 985 (s), 851 (m), 832 (s), 769 (s), 728 (s), 698 (s), 695 (s)

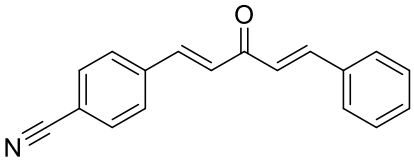
Spectra can be found in appendix page 100 – 107.

(1*E*,4*E*)-1-(4-hydroxyphenyl)penta-1,4-dien-3-one (6e)



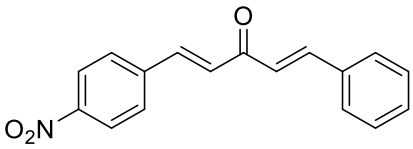
4-hydroxybenzaldehyde **1h** (779 mg, 6.38 mmol), NaOH (64 mg, 1.60 mmol) and (E)-4-phenylbut-3-enon **5** (1025 mg, 7.01 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid showed that no reaction had occurred.

(1*E*,4*E*)-1-(4-cyanophenyl)penta-1,4-dien-3-one (6f)



4-cyanobenzaldehyde **1i** (801 mg, 6.11 mmol), NaOH (77 mg, 1.93 mmol) and (E)-4-phenylbut-3-enon **5** (982 mg, 6.72 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid was not identified as the expected product, so no further analysis was carried out.

(1*E*,4*E*)-1-(4-nitrophenyl)penta-1,4-dien-3-one (6g)



4-nitrobenzaldehyde **1j** (1100 mg, 7.28 mmol), NaOH (91 mg, 2.27 mmol) and (E)-4-phenylbut-3-enon **5** (1172 mg, 8.02 mmol) was dissolved in distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The yellow solid was dried under vacuum to yield **6g** (208 mg, 10 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 8.26 (d, *J* = 9 Hz, 2H), 7.77 (d, *J* = 16 Hz, 1H*), 7.75 (d, *J* = 9 Hz, 2H*), 7.74 (d, *J* = 16 Hz, 1H*), 7.64 – 7.59 (m, 2H), 7.46 – 7.40 (m, 3H), 7.20 (d, *J* = 16 Hz, 1H), 7,07 (d, *J* = 16 Hz, 1H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 187.3, 147.6, 143.6, 140.1, 139.2, 133.6, 130.0, 128.2, 128.0, 127.8, 127.6, 124.3, 123.3

m/z: Calculated for $C_{17}H_{13}O_3NNa$ $[M+Na]^+$: 302.0788, found: 302.0787

R$_f$: 0.74 (heptane:ethyl acetate, 1:1)

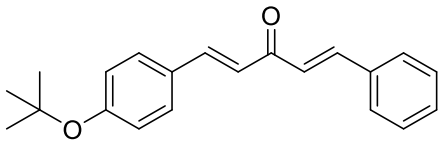
IR: υ [cm^{-1}] = 1652 (s), 1588 (s), 1518 (s), 1451 (m), 1339 (s), 1194 (s), 1108 (s), 985 (s), 866 (s), 832 (s), 765 (s), 695 (s)

* Overlapped, number of protons based on literature and peak identification.

Spectra can be found in appendix page 108 – 113.

The data is consistent with literature data. [31]

(1*E*,4*E*)-1-(4-*tert*-butoxyphenyl)penta-1,4-dien-3-one (6h)



4-*tert*-butoxybenzaldehyde **1o** (491 µL, 2.81 mmol), NaOH (29 mg, 0.73 mmol) and (E)-4-phenylbut-3-enon **5** (452 mg, 3.09 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The yellow solid was dried under vacuum to yield **6h** (46 mg, 5 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.74 (d, *J* = 4 Hz, 1H), 7.70 (d, *J* = 4 Hz, 1H), 7.63 – 7.59 (m, 2H), 7.54 (d, *J* = 9 Hz, 2H), 7.43 – 7.38 (m, 3H), 7.08 (d, *J* = 16 Hz, 1H), 7.04 – 6.96 (m, 3H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 188.0, 157.2, 142.2, 142.1, 134.0, 129.5, 128.6, 128.5, 129.1, 127.5, 124.7, 123.2, 122.8, 78.5, 28.0

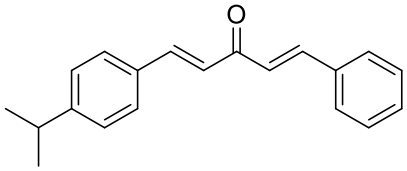
m/z: Calculated for $C_{21}H_{22}O_2Na$ $[M+Na]^+$: 329.1512, found: 329.1513

R_f: 0.74 (heptane:ethyl acetate, 1:1)

IR: υ [cm^{-1}] = 2977 (w), 1652 (s), 1588 (s), 1506 (s), 1464 (m), 1369 (s), 1328 (s), 1246 (s), 1167 (s), 1108 (s), 992 (s), 974 (s), 899 (s), 866 (s), 832 (s), 765 (s), 691 (s)

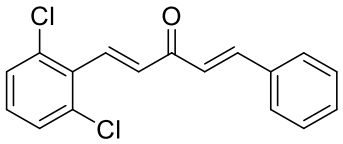
Spectra can be found in appendix page 114 – 119.

(1*E*,4*E*)-1-(4-isopropylphenyl)penta-1,4-dien-3-one (6i)



4-isopropylbenzaldehyde **1p** (734 µL, 4.84 mmol), NaOH (50 mg, 1.25 mmol) and (E)-4-phenylbut-3-enon **5** (778 mg, 5.32 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, before extraction with 2X35 mL DCM, removing the solvent and drying under vacuum. The ^{1}H and ^{13}C NMR spectra of the obtained solid was not identified as the expected product, so no further analysis was carried out.

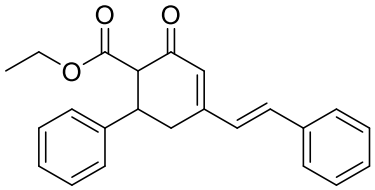
(1*E*,4*E*)-1-(2,6-dichlorophenyl)penta-1,4-dien-3-one (6j)



2,6-dichlorobenzaldehyde **1c** (842 mg, 4.81 mmol), NaOH (49 mg, 1.23 mmol) and (E)-4-phenylbut-3-enon **5** (706 mg, 4.83 mmol) was dissolved in a mixture of distilled water (5 mL) and ethanol (5 mL), before the reaction mixture was stirred at room temperature for 30 minutes. The reaction mixture was then made basic with sat. ammonium chloride, and the resulting solid was collected in a Büchner funnel and washed with distilled water before recrystallization in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid was not identified as the expected product.

6.3.3 Synthesis of scaffold molecule analogues

(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate (7a)



(1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one **3a** (862 mg, 3.71 mmol) and NaOH (110 mg, 2.75 mmol) was dissolved in ethanol (10 mL) before ethyl acetoacetate (475 µL, 3.72 mmol) was added and the reaction mixture refluxed for 4 hours. The reaction mixture was then cooled down to room temperature before sat. ammonium chloride (10 mL) was added, and the product was extracted with 2X35 mL DCM. After removal of the solvent, the crude was recrystallized in 70 % ethanol. The yellow solid was dried under vacuum to yield **7a** (837 mg, 65 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.47 (dd, *J* = 8 Hz, *J* = 2 Hz, 2H), 7.40 – 7.30 (m, 8H), 7.00 (d, *J* = 16 Hz, 1H), 6.93 (d, *J* = 16 Hz, 1H), 6.21 (d, *J* = 2 Hz, 1H), 4.04 (q, *J* = 7 Hz, 2H), 3.80 – 3.72 (m*, 2H), 3.06 (dd, *J* = 18 Hz, J = 4 Hz, 1H), 2.73 (ddt, *J* = 18 Hz, J = 10 Hz, J = 2 Hz, 1H), 1.04 (t, *J* = 7 Hz, 3H)

^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 194.3, 169.4, 155.9, 141.3, 136.4, 135.8, 129.6, 129.1, 129.0, 128.4, 127.7, 127.5, 127.5, 126.9, 61.1, 60.2, 43.9, 33.4, 14.1

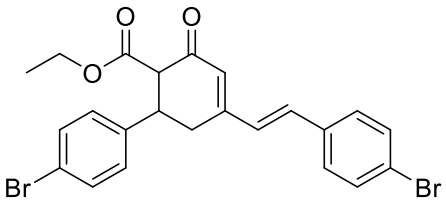
R_f: 0.36 (heptane:ethyl acetate, 1:1)

* Singlet overlapped with what looks like a quartet.

Spectra can be found in appendix page 120 – 125.

The data is consistent with literature data. [15-16]

(E)-Ethyl 6-(4-bromophenyl)-4-[2-(4-bromophenyl)ethenyl]-2-oxo-4-cyclohexene-1-carboxylate (7b)



(1*E*,4*E*)-1,5-bis(4-bromophenyl)penta-1,4-dien-3-one **3b** (151 mg, 0.39 mmol) and NaOH (2 mg, 0.05 mmol) was dissolved in ethanol (10 mL), before ethyl acetoacetate (50 µL, 0.39 mmol) was added and the reaction mixture refluxed for 4 hours. The reaction mixture was then cooled down to room temperature before sat. ammonium chloride (10 mL) was added, and the product was extracted with 2X35 mL DCM. After removal of the solvent, the crude was recrystallized in 70 % ethanol. The yellow solid was dried under vacuum to yield **7b** (78 mg, 38 %).

^{1}H NMR***: (400.18 MHz, chloroform-*d*) δ_H: 7.46 (dd, *J* = 9 Hz, *J* = 2 Hz, 4H), 7.31 (d, *J* = 9 Hz, 2H), 7.18 (d, *J* = 9 Hz, 2H), 6.91* (d, *J* = 17 Hz, 1H), 6.86* (d, *J* = 17 Hz, 1H), 6.17 (d, *J* = 2 Hz, 1H), 4.03 (qd, *J* = 7 Hz, J = 2 Hz, 2H), 3.70 – 3.66 (m**, 2H), 2.97 (d, *J* = 18 Hz, 1H), 2.65 (d, *J* = 17 Hz, 1H), 1.05 (t, *J* = 7 Hz, 3H)

^{13}C NMR***: (100.63 MHz, chloroform-*d*) δ_C: 193.6, 169.0, 155.2, 140.2, 135.0, 134.5, 132.2, 132.0, 129.1, 128.8, 128.7, 127.1, 123.6, 121.4, 61.1, 59.8, 43.1, 32.9, 14.1

R_f: 0.32 (heptane:ethyl acetate, 1:1)

m/z: Calculated for $C_{23}H_{21}Br_2O_3$ $[M+H]^+$: 502.9852, found: 502.9848

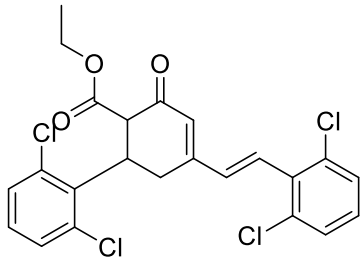
* Overlapped with each other

** Singlet overlapped with what looks like a quartet.

*** The spectra of this compound contained some impurities.

Spectra can be found in appendix page 126 – 133.

(E)-Ethyl 6-(2,6-dichlorophenyl)-4-(2-(2,6-dichlorophenyl)ethenyl)-2-oxo-4-cyclohexene-1-carboxylate (7c)



(1*E*,4*E*)-1,5-bis(2,6-dichlorophenyl)penta-1,4-dien-3-one **3c** (225 mg, 0.60 mmol) and NaOH (4 mg, 0.10 mmol) was dissolved in ethanol (10 mL), before ethyl acetoacetate (78 µL, 0.61 mmol) was added and the reaction mixture was refluxed for 4 hours. The reaction mixture was then cooled down to room temperature before sat. ammonium chloride (10 mL) was added, and the product was extracted with 2X35 mL DCM. After removal of the solvent, the crude was recrystallized in 70 % ethanol. The yellow solid was dried under vacuum to yield **7c** (64 mg, 22 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.37 (dd, *J* = 8 Hz, J = 1 Hz, 1H), 7.35 – 7.30 (m, 4H), 7.16 (t, *J* = 8 Hz, 1H), 7.15 (5, 8 Hz, 1H), 7.00 (s, 2H), 6.19 (s, 1H), 4.81 – 4.72 (m, 2H), 4.04 (q, *J* = 7 Hz, 2H), 3.42 (ddt, J = 18 Hz, *J* = 10 Hz, J = 2 Hz, 1H), 2.85 (dd, *J* = 18 Hz, J = 4 Hz, 1H), 1.05 (t, *J* = 7 Hz, 3H)

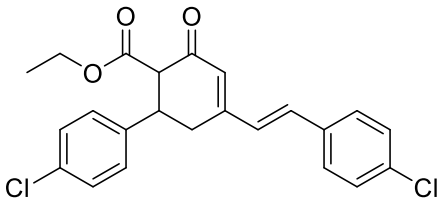
^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 193.8, 168.8, 155.2, 137.0, 136.7, 135.1, 134.7, 133.0, 130.5, 129.8, 129.4, 129.2, 129.1, 128.9, 127.9, 61.1, 56.0, 39.3, 27.2, 13.9

R_f: 0.30 (heptane:ethyl acetate, 1:1)

m/z: Calculated for $C_{23}H_{19}Cl_4O_3$ $[M+H]^+$: 483.0083, found: 483.0086

Spectra can be found in appendix page 134 – 139.

(E)-Ethyl 6-(4-chlorophenyl)-4-[2-(4-chlorophenyl)ethenyl]-2-oxo-4-cyclohexene-1-carboxylate (7d)



(1*E*,4*E*)-1,5-bis(4-chlorophenyl)penta-1,4-dien-3-one **3d** (97 mg, 0.23 mmol) and NaOH (2 mg, 0.05 mmol) was dissolved in ethanol (10 mL), before ethyl acetoacetate (46 µL, 0.36 mmol) was added and the reaction mixture was refluxed for 4 hours. The reaction mixture was then cooled down to room temperature before 10 mL sat. ammonium chloride was added, and the product was extracted with 2X35 mL DCM. After removal of the solvent, the crude was recrystallized in 70 % ethanol. The yellow solid was dried under vacuum to yield **7d** (9 mg, 9 %).

^{1}H NMR: (400.18 MHz, chloroform-*d*) δ_H: 7.37 (d, *J* = 8 Hz, 2H), 7.30 (dd, *J* = 8 Hz, J = 1 Hz, 4H), 7.25 – 7.20 (m, 3H), 6.90 (d, *J* = 16 Hz, 1H), 6.85 (d, J = 16 Hz, 1H), 6.17 (d, J = 2 Hz, 1H), 4.03 (qd, J = 7 Hz, J = 2 Hz, 2H), 3.70 – 3.66 (m, 2H), 2.97 (d, J = 18 Hz, 1H), 2.64 (d, J = 18 Hz, 1H), 1.04 (t, *J* = 7 Hz, 3H)

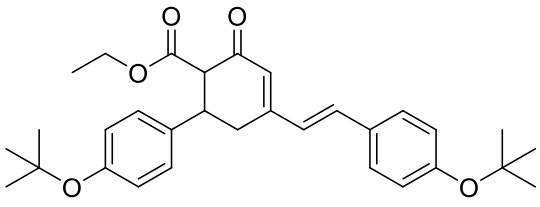
^{13}C NMR: (100.63 MHz, chloroform-*d*) δ_C: 193.8, 169.1, 155.3, 139.7, 135.5, 135.1, 134.2, 133.5, 129.3, 129.2, 128.8, 128.8, 128.7, 127.2, 61.3, 60.0, 43.2, 33.1, 14.1

R_f: 0.32 (heptane:ethyl acetate, 1:1)

m/z: Calculated for $C_{23}H_{21}Cl_2O_3$ $[M+H]^+$: 415.0862, found: 415.0863

Spectra can be found in appendix page 140 – 145.

(E)-Ethyl 2-oxo-6-(4-*tert*-butoxyphenyl)-4-[2-(4-*tert*-butoxyphenyl)ethenyl]-4-cyclohexene-1-carboxylate (7e)



(1*E*,4*E*)-1,5-bis(4-*tert*-butoxyphenyl)penta-1,4-dien-3-one **3o** (102 mg, 0.27 mmol) and NaOH (5 mg, 0.13 mmol) was dissolved in ethanol (10 mL), before ethyl acetoacetate (35 µL, 0.27 mmol) was added and the reaction mixture was refluxed for 4 hours. The reaction mixture was then cooled down to room temperature before sat. ammonium chloride (10 mL) was added, and the product was extracted with 2X35 mL DCM. After removal of the solvent, the crude was recrystallized in 70 % ethanol. The yellow solid was dried under vacuum to yield **7e** (16 mg, 11 %).

^{1}H NMR*: (400.18 MHz, chloroform-*d*) δ_H: 7.38 (d, *J* = 8 Hz, 2H), 7.20 (d, *J* = 8 Hz, 2H), 7.00 – 6.92 (m, 5H), 6.81 (d, *J* = 16 Hz, 1H), 6.15 (d, J = 2 Hz, 1H), 4.01 (q, *J* = 7 Hz, 2H), 3.70 – 3.64 (m, 2H), 3.01 (d, *J* = 18 Hz, 1H), 2.68 (q, J = 9 Hz, 1H), 1.36 (s, 9H), 1.33 (s, 9H), 0.98 (t, *J* = 7 Hz, 3H)

^{13}C NMR*: (100.63 MHz, chloroform-*d*) δ_C: 194.3, 169.5, 157.1, 156.4, 154.7, 136.0, 136.0, 130.7, 128.3, 127.9, 127.0, 126.2, 124.4, 124.1, 79.3, 78.6, 60.9, 60.5, 43.3, 33.2, 28.9, 14.1

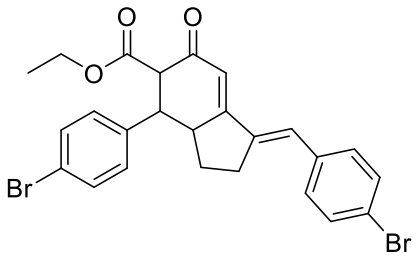
R_f: 0.29 (heptane:ethyl acetate, 1:1)

m/z: Calculated for $C_{31}H_{38}O_5Na$ $[M+Na]^+$: 513.2611, found: 513.2607

* The spectra of this compound contained some impurities.

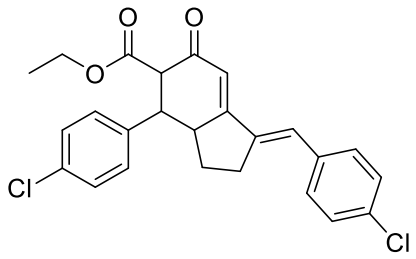
Spectra can be found in appendix page 146 – 151.

(E)-Ethyl 5-(4-bromophenyl)-1-[2-(4-bromophenyl)ethenyl]-7-oxo-2,3,4,5,6-pentahydroindene-6-carboxylate (7f)



(2*E*, 5*E*)-2,5-bis(4-bromophenylmethylene)cyclopentanone **3p** (329 mg, 0.79 mmol) and NaOH (6 mg, 0.15 mmol) was dissolved in ethanol (10 mL), before ethyl acetoacetate (101 µL, 0.79 mmol) was added and the reaction mixture was refluxed for 4 hours. The reaction mixture was then cooled down to room temperature before sat. ammonium chloride (10 mL) was added, and the product was extracted with 2X35 mL DCM. After removal of the solvent, the crude was recrystallized in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid showed that no reaction had occurred. The reaction was also attempted refluxed for 24 hours followed by TLC with the same result.

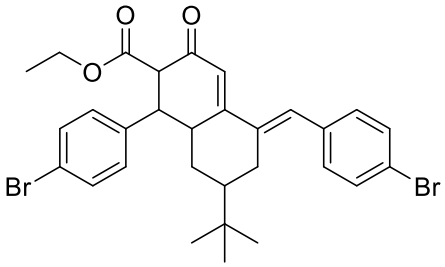
(E)-Ethyl 5-(4-chlorophenyl)-1-[2-(4-chlorophenyl)ethenyl]-7-oxo-2,3,4,5,6-pentahydroindene-6-carboxylate (7g)



(2*E*, 5*E*)-2,5-bis(4-chlorophenylmethylene)cyclopentanone **3q** (367 mg, 1.11 mmol) and NaOH (10 mg, 0.25 mmol) was dissolved in ethanol (10 mL), before ethyl acetoacetate (143 µL, 1.12 mmol) was added and the reaction mixture was refluxed for 4 hours. The reaction mixture was then cooled to room temperature before sat. ammonium chloride (10 mL) was added, and the product was extracted with 2X35 mL DCM. After removal of the solvent, the crude was recrystallized in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid

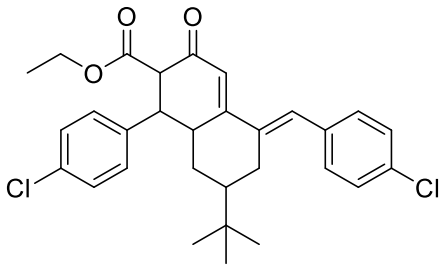
was not identified as the expected product, so no further analysis was carried out. The reaction was also attempted refluxed for 24 hours followed by TLC with the same result.

(E)-Ethyl 6-(4-bromophenyl)-1-[2-(4-bromophenyl)ethenyl]- 2,3,4,5,6,7-hexahydro-8-oxo-3-*tert*-butylindene-7-carboxylate (7h)



(2E, 6E)-2,6-bis(4-bromophenylmethylene)-4-*tert*-butylcyclohexanone **3r** (102 mg, 0.21 mmol) and NaOH (2 mg, 0.05 mmol) was dissolved in ethanol (10 mL), before ethyl acetoacetate (29 µL, 0.23 mmol) was added and the reaction mixture was refluxed for 4 hours. The reaction mixture was then cooled to room temperature before sat. ammonium chloride (10 mL) was added, and the product was extracted with 2X35 mL DCM. After removal of the solvent, the crude was recrystallized in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid showed that no reaction had occurred.

(E)-Ethyl 6-(4-chlorophenyl)-1-[2-(4-chlorophenyl)ethenyl]- 2,3,4,5,6,7-hexahydro-8-oxo-3-*tert*-butylindene-7-carboxylate (7i)

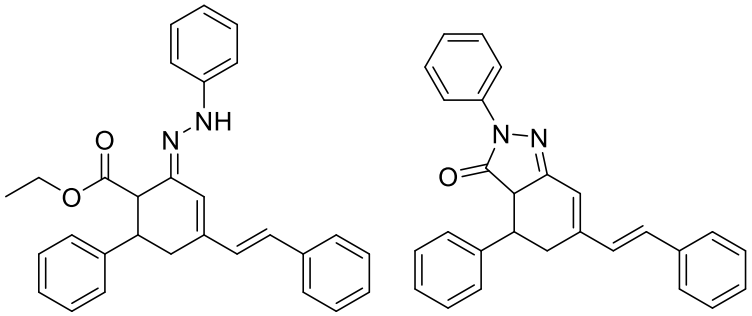


(2E, 6E)-2,6-bis(4-chlorophenylmethylene)-4-tertbutylcyclohexanone **3s** (127 mg, 0.32 mmol) and NaOH (3 mg, 0.08 mml) was dissolved in ethanol (10 mL), before ethyl acetoacetate (50 µL, 0.39 mmol) was added and the reaction mixture was refluxed for 4 hours. The reaction

mixture was then cooled to room temperature before sat. ammonium chloride (10 mL) was added, and the product was extracted with 2X35 mL DCM. After removal of the solvent, the crude was recrystallized in 70 % ethanol. The ^{1}H and ^{13}C NMR spectra of the obtained solid showed that no reaction had occurred.

6.3.4 Hydrazine reactions.

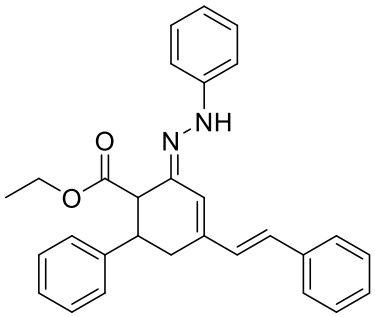
(E)-Ethyl 6-phenyl-4-(2-phenylethenyl)-2-phenylhydrazone-4-cyclohexene-1-carboxylate (9a) and (E)-2,5-diphenyl-3-oxo-7-(2-phenylethenyl)-4,5,6-trihydroindazole (10a)



(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (98.5 mg, 0.28 mmol) and phenylhydrazine hydrochloride **8a** (83.3 mg, 0.58 mmol) was dissolved in ethanol (25 mL), before the reaction mixture was refluxed for up to 48 hours followed by TLC. After cooling, distilled water acidified by a few drops of HCl (10 mL) was added, before extraction with 3X25 mL DCM. After removal of the solvent, the crude was purified with column chromatography, but after several attempts no pure fractions were obtained*.

* This is the less successful method using conventional heating, for MW reactions, see below.

(E)-Ethyl 6-phenyl-4-(2-phenylethenyl)-2-phenylhydrazone-4-cyclohexene-1-carboxylate (9a)



(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (49 mg, 0.14 mmol) and phenylhydrazine hydrochloride **8a** (83.3 mg, 0.58 mmol) was dissolved in ethanol (5 mL) in a MW vial, before it was heated to 160 °C for 1 hour. After cooling, distilled water acidified with a few drops HCl (10 mL) was added, before extraction with 3X25 mL DCM. After removal of the solvent, the crude was purified with column chromatography. After several attempts of purification, I managed to identify **9a** in an impure NMR sample*.

^{1}H NMR*: (400.18 MHz, DMSO-*d*) δ_H: 7.67 (d, *J* = 8 Hz, 2H), 7.52 (d, *J* = 8 Hz, 2H), 7.48 (s**, 1H), 7.45 (d, *J* = 9 Hz, 2H), 7.33 (d, *J* = 7 Hz, 3H), 7.27 (d, *J* = 6 Hz, 3H), 7.21 (d, *J* = 9 Hz, 2H), 7.16 (s, 1H), 7.12 (s, 1H), 6.75 (s, 1H), 4.46 (dd, *J* = 8 Hz, *J* = 5 Hz, 1H), 3.99 (q, *J* = 7 Hz, 1H), 3.87 (q, *J* = 7 Hz, 1H), 2.99 (dd, *J* = 17 Hz, *J* = 8 Hz, 1H), 2.83 (dd, *J* = 17 Hz, *J* = 5 Hz, 1H), 1.25 (overlapped, 1H), 1.01 (t, *J* = 7 Hz, 3H)

^{13}C NMR*: (100.63 MHz, DMSO-*d*) δ_C: 171.6, 157.9, 147.6, 137.5, 136.6, 136.5, 133.1, 129.3, 129.0, 128.9, 128.7, 128.3, 127.9, 127.2, 125.7, 119.6, 119.0, 45.8, 31.3, 22.1, 13.5, 1.2

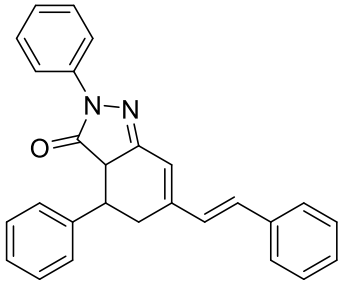
R_f: 0.56 (heptane:ethyl acetate, 1:1).

* This product was identified with ^{1}H and ^{13}C NMR, but it contained impurities. This is also the reason why no yield is given.

** This is likely a triplet overlapping the two duplets next to it making it look like a singlet.

Spectra can be found in appendix page 152 – 161.

(E)-2,5-diphenyl-3-oxo-7-(2-phenylethenyl)-4,5,6-trihydroindazole (10a)



(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (56 mg, 0.16 mmol) and phenylhydrazine hydrochloride **8a** (48 mg, 0.33 mmol) was dissolved in ethanol (5mL) in a MW vial, before the reaction mixture was heated to 160 °C for 1 hour. After cooling, distilled water acidified with a few drops HCl (10 mL) was added, before extraction with 3X25 mL DCM. After removal of the solvent, the crude was purified with column chromatography. After several attempts of purification, I managed to get an impure NMR sample to identify **10a**. NMR yield was later identified through internal standard (for procedure see next page).*

^{1}H NMR*: (400.18 MHz, chloroform-*d*) δ_H: 7.90 (d, *J* = 8 Hz, 2H), 7.47 – 7.41 (m, 5H), 7.36 (t, *J* = 8 Hz, 6H), 7.19 – 7.13 (m, 2H), 6.99 (d, *J* = 16 Hz, 1H), 6.79 (d, *J* = 16 Hz, 1H), 6.61 (s, 1H), 3.82 (d, *J* = 13 Hz, 1H), 3.32 (td, *J* = 10 Hz, *J* = 5 Hz, 1H), 3.06 (dd, *J* = 17 Hz, *J* = 5 Hz, 1H), 2.69 (dd, *J* = 17 Hz, *J* = 12 Hz, 1H)

^{13}C NMR*: (100.63 MHz, chloroform-*d*) δ_C: 170.5, 158.1, 146.5, 140.2, 138.4, 136.5, 132.3, 129.1, 129.0, 129.0, 128.9, 128.7, 127.9, 127.6, 127.1, 125.1, 119.4, 118.9, 50.6, 43.8, 35.9

R_f: 0.56 (heptane:ethyl acetate, 1:1).

* This product was identified with ^{1}H and ^{13}C NMR, but it contained impurities. This is also the reason why no yield is given.

Spectra can be found in appendix page 162 – 169.

Procedure for use of butylbenzene as internal standard for synthesis of 10a

(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (13 mg, 0.04 mmol) and phenylhydrazine hydrochloride **8a** (11 mg, 0.08 mmol) was dissolved in ethanol (5mL) in a MW vial, before the reaction mixture was heated to 160 °C for 1 hour. After cooling, distilled water acidified with a few drops HCl (10 mL) was added, before extraction with 3X25 mL DCM. After removal of the solvent, butylbenzene (5 mg, 0.04 mmol) was added before dissolving in 0.6 mL deuterated chloroform and transferal to an NMR tube and running ^{1}H NMR*.

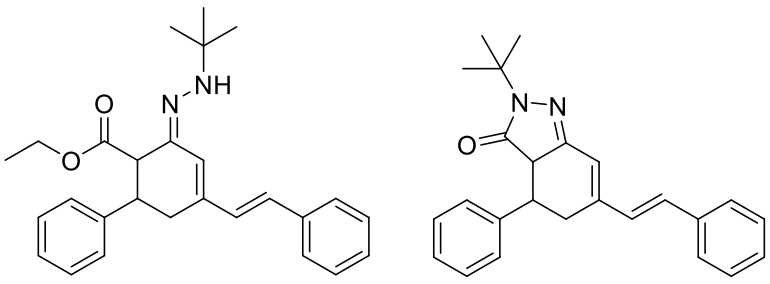
^{1}H NMR**: 7.90 (d, *J* = 8 Hz, 2H, belongs to **9a**), 0.93 (t, *J* = 7 Hz, 3H, belongs to internal standard).

* Due to likely lower yields of **9a**, **9a** being an intermediate in formation of **10a** and **9a** having less distinguishable peaks in ^{1}H NMR (from impurities, **10a** and internal standard), it proved hard to quantify **9a**.

** These are the peaks used to quantify **10a** from internal standard.

Spectra can be found in appendix page 170 – 176.

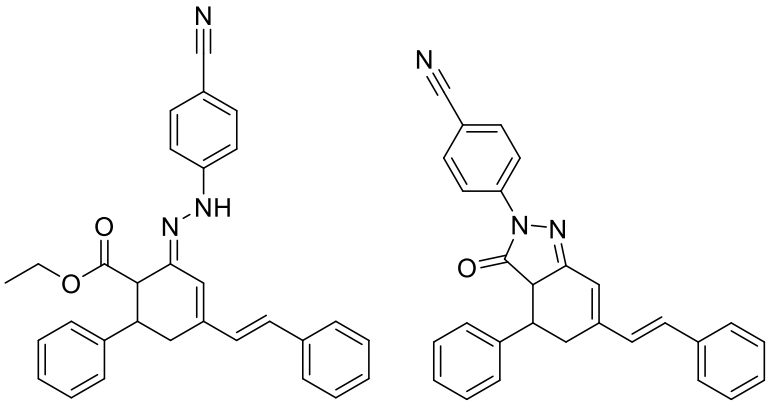
(E)-Ethyl 5-phenyl-3-(2-phenylethenyl)-2-(*tert*-butylhydrazone)-4-cyclohexane-1-carboxylate (9c) and (E)-3-oxo-7-phenylethenyl-2-*tert*-butyl-4,5,6-trihydroindazole (10c)



(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (208 mg, 0.60 mmol) and *tert*-butylhydrazine hydrochloride **8c** (131 mg, 1.05 mmol) was dissolved in ethanol (5mL) in a MW vial, before the reaction mixture was heated to 160 °C for 1 hour. After cooling,

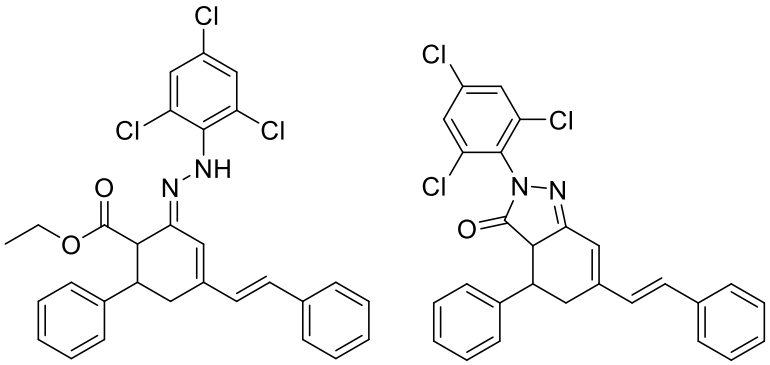
distilled water acidified with a few drops HCl (10 mL) was added, before extraction with 3X25 mL DCM. ^{1}H and ^{13}C NMR of the crude showed that no reaction had occurred.

(E)-Ethyl 6-phenyl-4-(2-phenylethenyl)-2-(4-cyanophenyl)hydrazone-4-cyclohexene-1-carboxylate (9d) and (E)-5-(4-cyanophenyl)-3-oxo-7-(2-phenylethenyl)-4,5,6-trihydroindazole (10d)



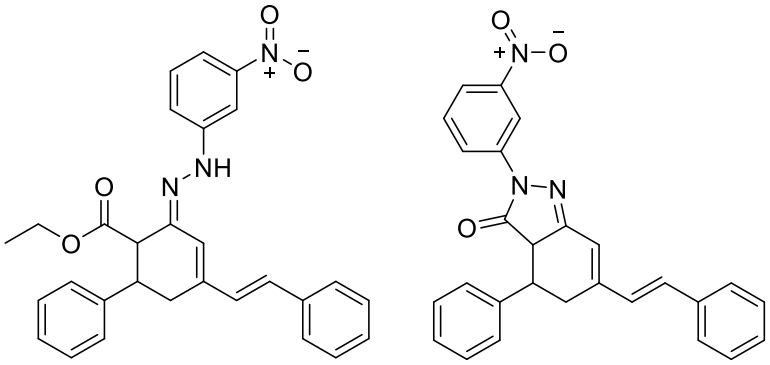
(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (214 mg, 0.87 mmol) and 4-cyanophenylhydrazine hydrochloride **8d** (209 mg, 1.23 mmol) was dissolved in ethanol (5mL) in a MW vial, before the reaction mixture was heated to 160 °C for 1 hour. After cooling, distilled water acidified with a few drops HCl (10 mL) was added, before extraction with 3X25 mL DCM. After removal of solvent, purification with column chromatography was attempted without success.

(E)-Ethyl 6-phenyl-4-(2-phenylethenyl)-2-(2,4,6-trichlorophenyl)hydrazone-4-cyclohexene-1-carboxylate (9e) and (E)-3-oxo-7-(2-phenylethenyl)-5-phenyl-2-(2,4,6-trichlorophenyl)-4,5,6-trihydroindazole (10e)



(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (205 mg, 0.59 mmol) and 2,4,6-trichlorophenylhydrazine hydrochloride **8e** (252 mg, 1.19 mmol) was dissolved in ethanol (5mL) in a MW vial, before the reaction mixture was heated to 160 °C for 1 hour. After cooling, distilled water acidified with a few drops HCl (10 mL) was added, before extraction with 3X25 mL DCM. After removal of solvent, purification with column chromatography was attempted without success.

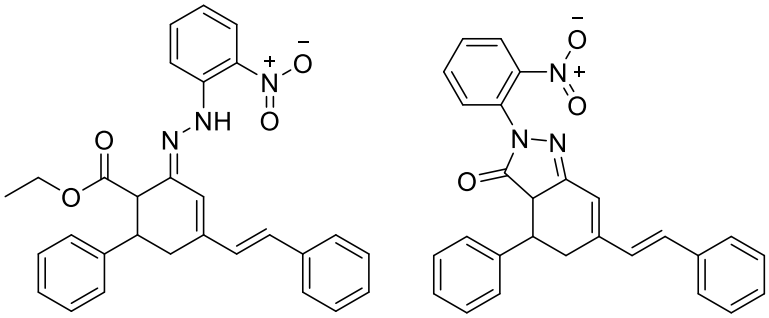
(E)-Ethyl 2-(3-nitrophenyl)hydrazone-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate (9f) and (E)-3-oxo-2-(3-nitrophenyl)-5-phenyl-7-(2-phenylethenyl)-4,5,6-trihydroindazole (10f)



(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (153 mg, 0.44 mmol) and 3-nitrophenylhydrazine hydrochloride **8f** (168 mg, 0.89 mmol) was dissolved in ethanol (5mL) in a MW vial, before the reaction mixture was heated to 160 °C for 1 hour. After

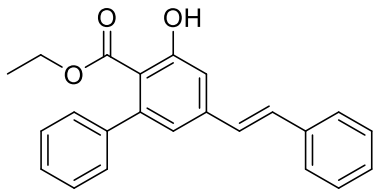
cooling, distilled water acidified with a few drops HCl (10 mL) was added, before extraction with 3X25 mL DCM. After removal of solvent, purification with column chromatography was attempted without success.

(E)-Ethyl 2-(2-nitrophenyl)hydrazone-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate (9g) and (E)-3-oxo-2-(2-nitrophenyl)-5-phenyl-7-(2-phenylethenyl)-4,5,6-trihydroindazole (10g)



(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (152 mg, 0.44 mmol) and 2-nitrophenylhydrazine **8g** (138 mg, 0.90 mmol) was dissolved in ethanol (5mL) in a MW vial, before the reaction mixture was heated to 160 °C for 1 hour. After cooling, distilled water acidified with a few drops HCl (10 mL) was added, before extraction with 3X25 mL DCM. After removal of solvent, purification with column chromatography was attempted without success.

(E)-Ethyl 2-hydroxy-6-phenyl-4-(2-phenylethenyl)-benzyl-1-carboxylate (11)



Method 1, conventional heating:

(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (172 mg, 0.50 mmol), DMSO (49 mg, 0.63 mmol) and I_2 (31 mg, 0.12 mmol) was added to a round bottom flask, before nitromethane (1 mL) was added. The reaction mixture was then refluxed for 24 hours, cooled, and ethyl acetate (20 mL) was added before the mixture was washed with $Na_2S_2O_3$ in distilled water (5 mL, 0.1 M). The water phase was then extracted with 3X5 mL ethyl acetate adding to the previous ethyl acetate phase. The solvent was then removed, and the crude worked up with column chromatography. The reaction was followed by TLC showing several spots, and NMR of the fractions from column chromatography showed no sign of the anticipated product. One of the chromatograms using Auto-flash for purification can be see in appendix page 177.

Method 1, MW heating:

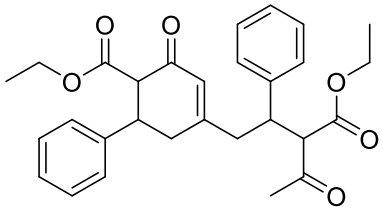
(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (169 mg, 0.490 mmol), DMSO (50 mg, 0.64 mmol) and I_2 (25 mg, 0.10 mmol) was added to a MW vial, before nitromethane (1 mL) was added. The reaction mixture was then heated to 200 °C for 30 minutes before cooling, and then continuing as with conventional heating written above. The reaction was followed by TLC showing several spots, and NMR of the fractions from column chromatography showed no sign of the anticipated product.

Method 2:

The glassware was dried prior to use, and the reaction was carried out under a $CaCl_2$ drying tube. (E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (75 mg, 0.22 mmol) and DDQ (55 mg, 0.24 mmol) was dissolved in dry THF (20 mL), before stirring at room temperature for 18 hours* succeeded by cooling and adding distilled water. The solid was then collected in a Büchner funnel and recrystallized in 70 % ethanol. The reaction was followed by TLC and the ^{1}H and ^{13}C NMR of the crystals formed showed that no reaction had occurred.

* The reaction was also attempted under reflux for 2 hours with the ratio of 1:1.2 between **7a** and DDQ with same result.

4-[(6-carboethoxy-5-phenyl-2cyclohexen-1-one-3-yl)methyl]-4-phenyl-3-carboethoxy-2-butanone (12)



Method 1*:

Ethyl acetoacetate (1.35 mL, 10.6 mmol) and $NaOCH_3$ (923 mg, 17.1 mmol) was dissolved in ethanol (10 mL) and left stirring for 1 hour. After an hour, (1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one **3a** (1001 mg, 3.10 mmol) was added and the reaction mixture was refluxed for 3 hours before letting the reaction mixture continue stirring at room temperature overnight. The reaction mixture was then acidified with dilute HCl and the solid collected in a Büchner funnel and recrystallized in 70 % ethanol. ^{1}H and ^{13}C NMR of the product formed showed that **7a** was formed instead of **11**.

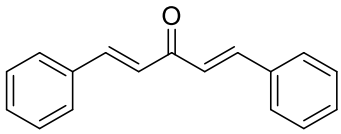
Method 2*.

Ethyl acetoacetate (548 µL, 4.30 mmol) and $NaOCH_3$ (468 mg, 8.66 mmol) was dissolved in ethanol (10 mL) and left stirring for 1 hour. After an hour, (E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate **7a** (1010 mg, 2.92 mol) was added and the reaction mixture was refluxed for 3 hours before letting the reaction mixture continue stirring at room temperature overnight. The reaction mixture was then acidified with dilute HCl and the solid collected in a Büchner funnel and recrystallized in 70 % ethanol. ^{1}H and ^{13}C NMR of the crystals showed that no reaction had occurred.

* The reactions were followed by TLC and were also attempted with higher ratio of ethyl acetoacetate and base and refluxed over night with same result.

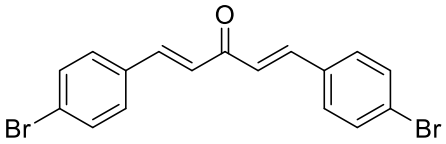
Appendix 1: List of molecules

(1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one (3a)



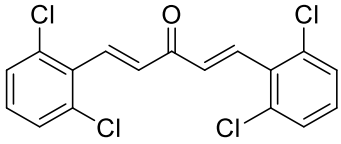
Spectra on page 18 – 21

(1*E*,4*E*)-1,5-bis(4-bromophenyl)penta-1,4-dien-3-one (3b)



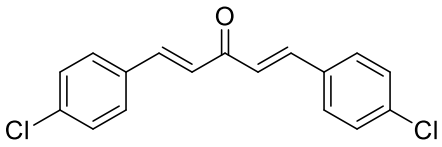
Spectra on page 22 – 28

(1*E*,4*E*)-1,5-bis(2,6-dichlorophenyl)penta-1,4-dien-3-one (3c)



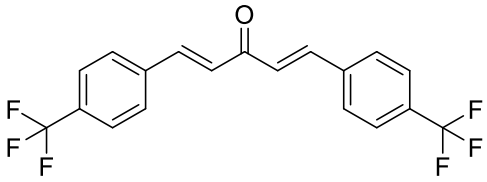
Spectra on page 29 – 35

(1*E*,4*E*)-1,5-bis(4-chlorophenyl)penta-1,4-dien-3-one (3d)

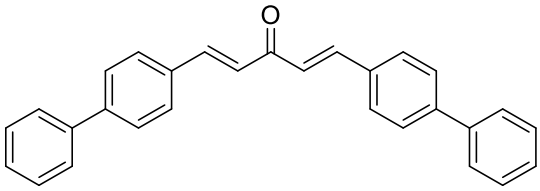


Spectra on page 36 – 41

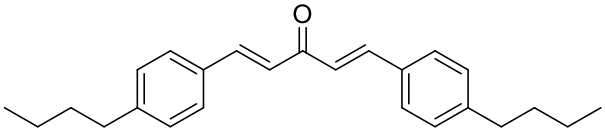
(1*E*,4*E*)-1,5-bis(4-trifluorimethylphenyl)penta-1,4-dien-3-one (3e)



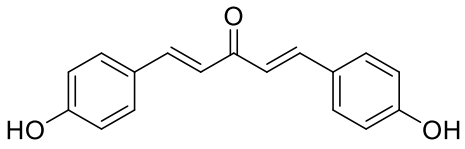
(1*E*,4*E*)-1,5-bis(4-biphenyl)penta-1,4-dien-3-one (3f)



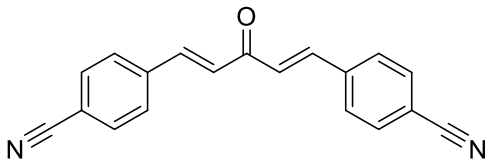
(1*E*,4*E*)-1,5-bis(4-butylphenyl)penta-1,4-dien-3-one (3g)



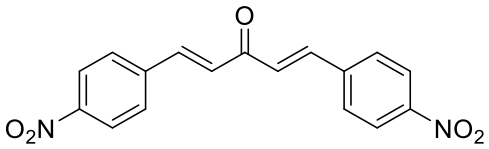
(1*E*,4*E*)-1,5-bis(4-hydroxyphenyl)penta-1,4-dien-3-one (3h)



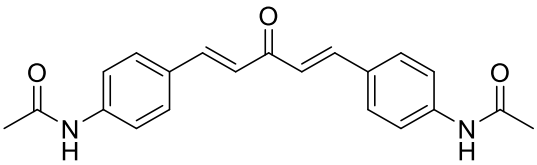
(1*E*,4*E*)-1,5-bis(4-cyanophenyl)penta-1,4-dien-3-one (3i)



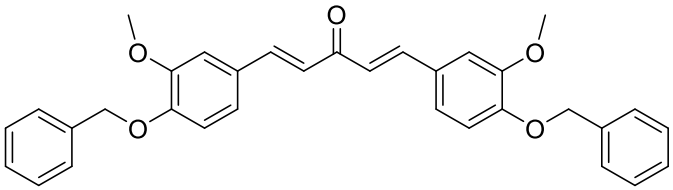
(1*E*,4*E*)-1,5-bis(4-nitrophenyl)penta-1,4-dien-3-one (3j)



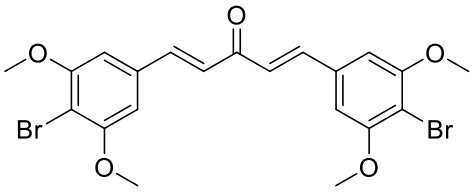
(1*E*,4*E*)-1,5-bis(4-acetamidophenyl)penta-1,4-dien-3-one (3k)



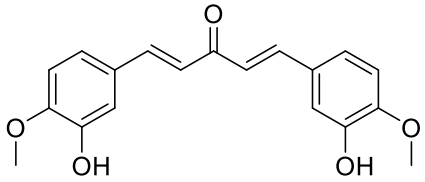
(1*E*,4*E*)-1,5-bis(4-benzyloxy-3-methoxyphenyl)penta-1,4-dien-3-one (3l)



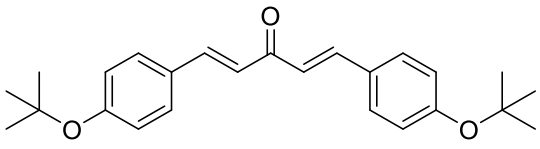
(1*E*,4*E*)-1,5-bis(4-bromo-3,5-dimethoxyphenyl)penta-1,4-dien-3-one (3m)



(1*E*,4*E*)-1,5-bis(3-hydroxy-4-methoxyphenyl)penta-1,4-dien-3-one (3n)

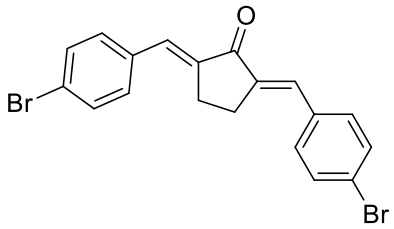


(1*E*,4*E*)-1,5-bis(4-*tert*-butoxyphenyl)penta-1,4-dien-3-one (3o)



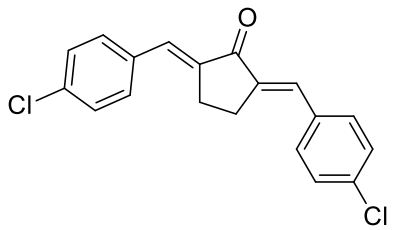
Spectra on page 42 – 47

(2*E*, 5*E*)-2,5-bis(4-bromophenylmethylene)cyclopentanone (3p)



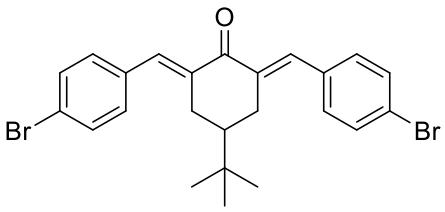
Spectra on page 48 – 55

(2*E*, 5*E*)-2,5-bis(4-chlorophenylmethylene)cyclopentanone (3q)



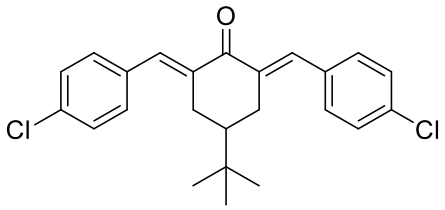
Spectra on page 56 – 63

(2E, 6E)-2,6-bis(4-bromophenylmethylene)-4-*tert*-butylcyclohexanone (3r)



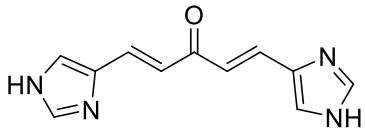
Spectra on page 64 – 69

(2E, 6E)-2,6-bis(4-chlorophenylmethylene)-4-tertbutylcyclohexanone (3s)

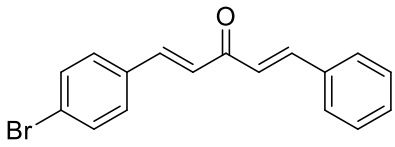


Spectra on page 70 – 75

(1*E*,4*E*)-1,5-bis(1-H-imidazol-3-yl)penta-1,4-dien-3-one (4)

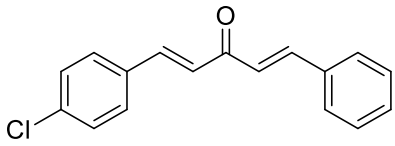


(1*E*,4*E*)-1-(4-bromophenyl)penta-1,4-dien-3-one (6a)



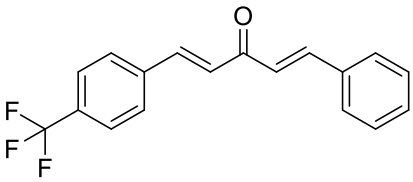
Spectra on page 76 – 83

(1*E*,4*E*)-1-(4-chlorophenyl)penta-1,4-dien-3-one (6b)



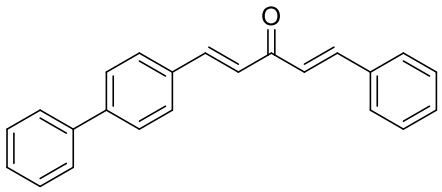
Spectra on page 84 – 91

(1*E*,4*E*)-1-(4-trifluorimethylphenyl)penta-1,4-dien-3-one (6c)



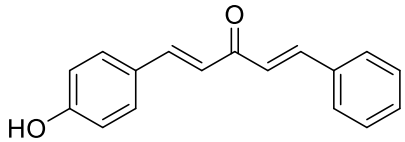
Spectra on page 92 – 99

(1*E*,4*E*)-1-(4-biphenyl)penta-1,4-dien-3-one (6d)

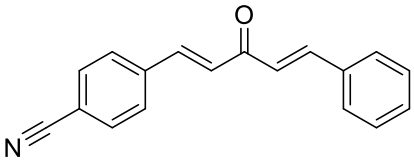


Spectra on page 100 – 107

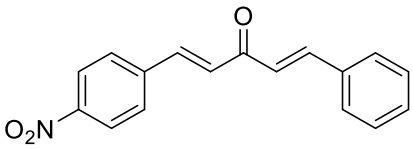
(1*E*,4*E*)-1-(4-hydroxyphenyl)penta-1,4-dien-3-one (6e)



(1*E*,4*E*)-1-(4-cyanophenyl)penta-1,4-dien-3-one (6f)

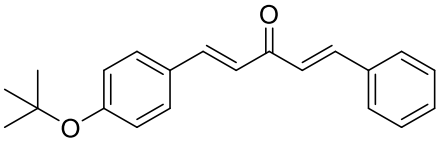


(1*E*,4*E*)-1-(4-nitrophenyl)penta-1,4-dien-3-one (6g)



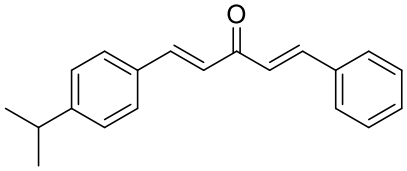
Spectra on page 108 – 113

(1*E*,4*E*)-1-(4-*tert*-butoxyphenyl)penta-1,4-dien-3-one (6h)

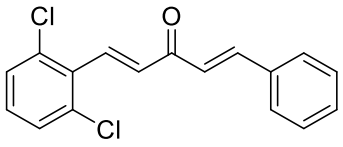


Spectra on page 114 – 119

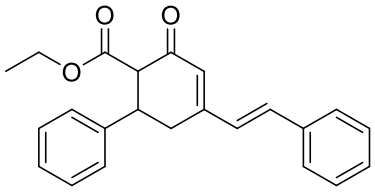
(1*E*,4*E*)-1-(4-isopropylphenyl)penta-1,4-dien-3-one (6i)



(1*E*,4*E*)-1-(2,6-dichlorophenyl)penta-1,4-dien-3-one (6j)

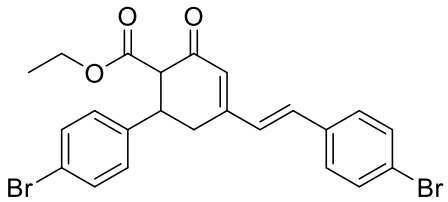


(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate (7a)



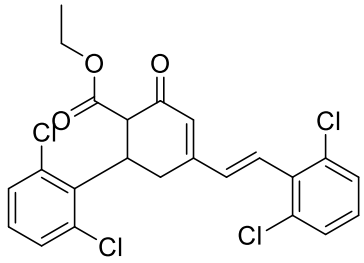
Spectra on page 120 – 125

(E)-Ethyl 6-(4-bromophenyl)-4-[2-(4-bromophenyl)ethenyl]-2-oxo-4-cyclohexene-1-carboxylate (7b)



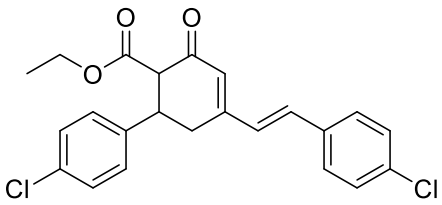
Spectra on page 126 - 133

(E)-Ethyl 6-(2,6-dichlorophenyl)-4-(2-(2,6-dichlorophenyl)ethenyl)-2-oxo-4-cyclohexene-1-carboxylate (7c)



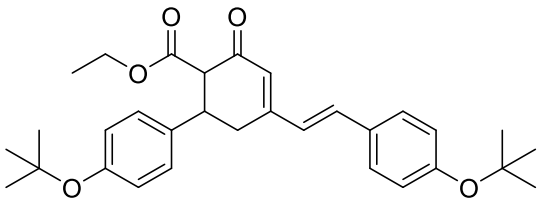
Spectra on page 134 - 139

(E)-Ethyl 6-(4-chlorophenyl)-4-[2-(4-chlorophenyl)ethenyl]-2-oxo-4-cyclohexene-1-carboxylate (7d)



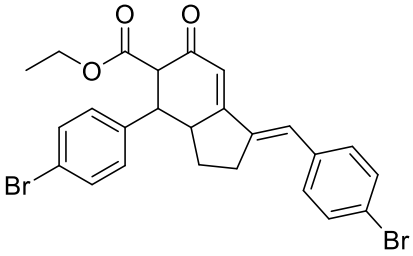
Spectra on page 140 – 145

(E)-Ethyl 2-oxo-6-(4-*tert*-butoxyphenyl)-4-[2-(4-*tert*-butoxyphenyl)ethenyl]-4-cyclohexene-1-carboxylate (7e)

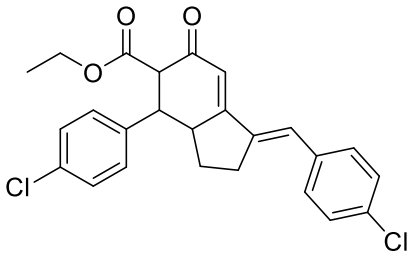


Spectra on page 146 – 151

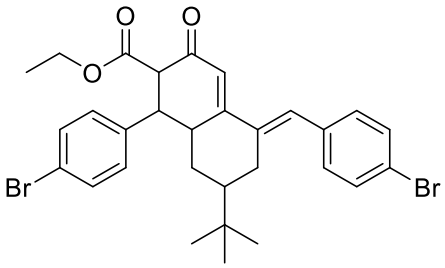
(E)-Ethyl 5-(4-bromophenyl)-1-[2-(4-bromophenyl)ethenyl]-7-oxo-2,3,4,5,6-pentahydroindene-6-carboxylate (7f)



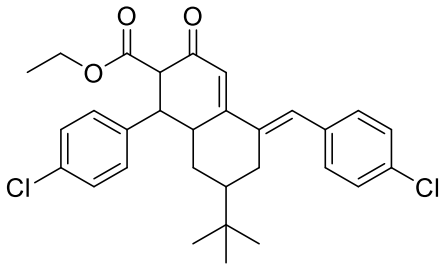
(E)-Ethyl 5-(4-chlorophenyl)-1-[2-(4-chlorophenyl)ethenyl]-7-oxo-2,3,4,5,6-pentahydroindene-6-carboxylate (7g)



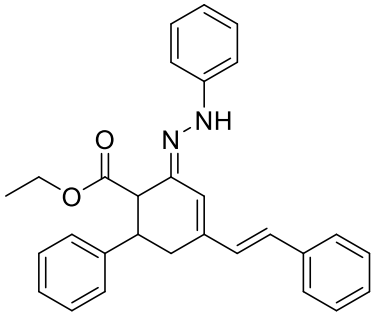
(E)-Ethyl 6-(4-bromophenyl)-1-[2-(4-bromophenyl)ethenyl]-2,3,4,5,6,7-hexahydro-8-oxo-3-*tert*-butylindene-7-carboxylate (7h)



(E)-Ethyl 6-(4-chlorophenyl)-1-[2-(4-chlorophenyl)ethenyl]-2,3,4,5,6,7-hexahydro-8-oxo-3-*tert*-butylindene-7-carboxylate (7i)

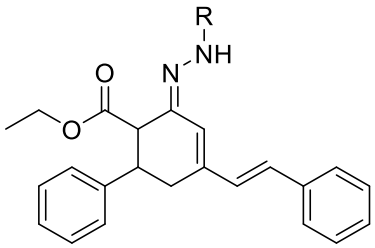


(E)-Ethyl 6-phenyl-4-(2-phenylethenyl)-2-phenylhydrazone-4-cyclohexene-1-carboxylate (9a)



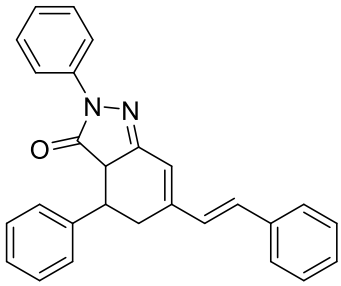
Spectra on page 152 – 161

(E)-Ethyl 6-phenyl-4-(2-phenylethenyl)-2-R-hydrazone-4-cyclohexene-1-carboxylate (9c-g)



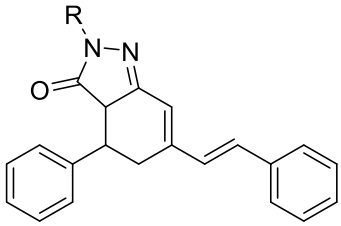
R = *tert*-butyl (**9c**), 4-cyanophenyl (**9d**), 2,4,6-trichlorophenyl (**9e**), 3-nitrophenyl (**9f**), 2-nitrophenyl (**9g**).

(E)-2,5-diphenyl-3-oxo-7-(2-phenylethenyl)-4,5,6-trihydroindazole (10a)



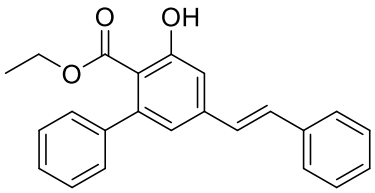
Spectra on page 162 – 169

(E)-3-oxo-2-(R)-5-phenyl-7-(2-phenylethenyl)-4,5,6-trihydroindazole (10c-g)

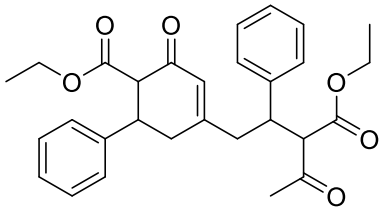


R = *tert*-butyl (**10c**), 4-cyanophenyl (**10d**), 2,4,6-trichlorophenyl (**10e**), 3-nitrophenyl (**10f**), 2-nitrophenyl (**10g**).

(E)-Ethyl 2-hydroxy-6-phenyl-4-(2-phenylethenyl)-benzyl-1-carboxylate (11)

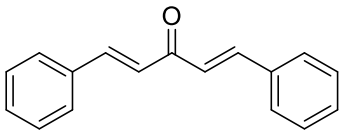


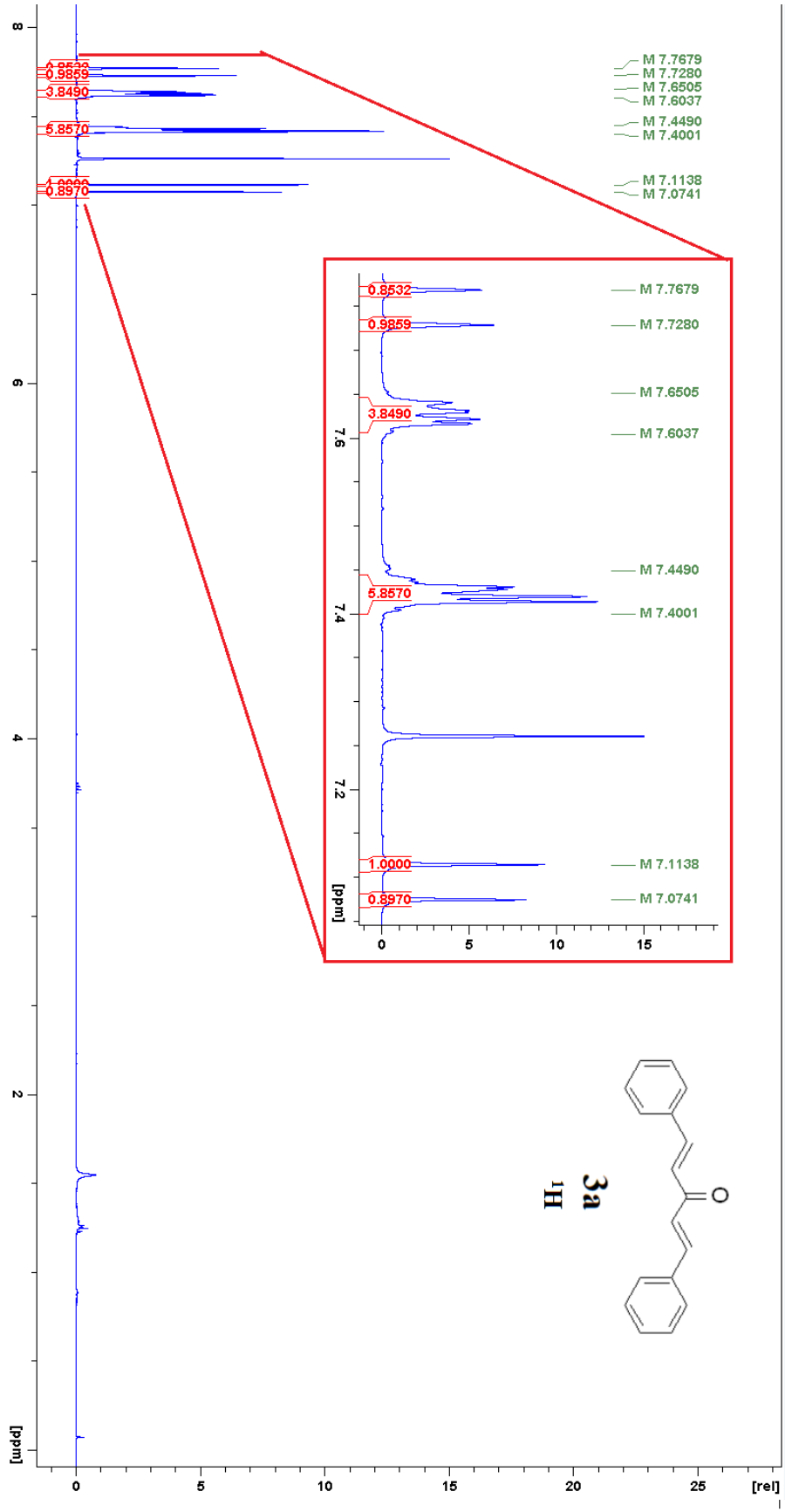
4-[(6-carboethoxy-5-phenyl-2cyclohexen-1-one-3-yl)methyl]-4-phenyl-3-carboethoxy-2-butanone (12)

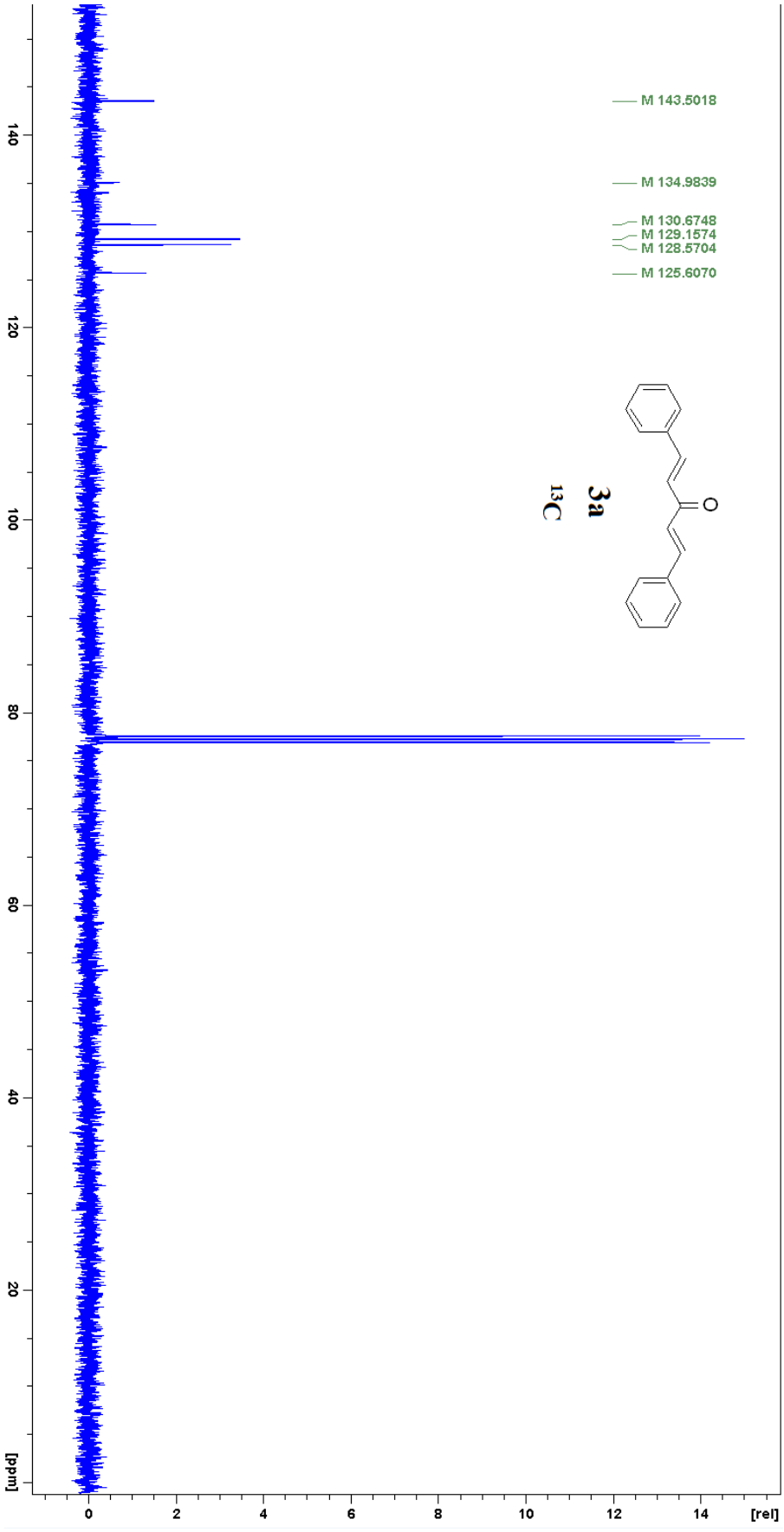


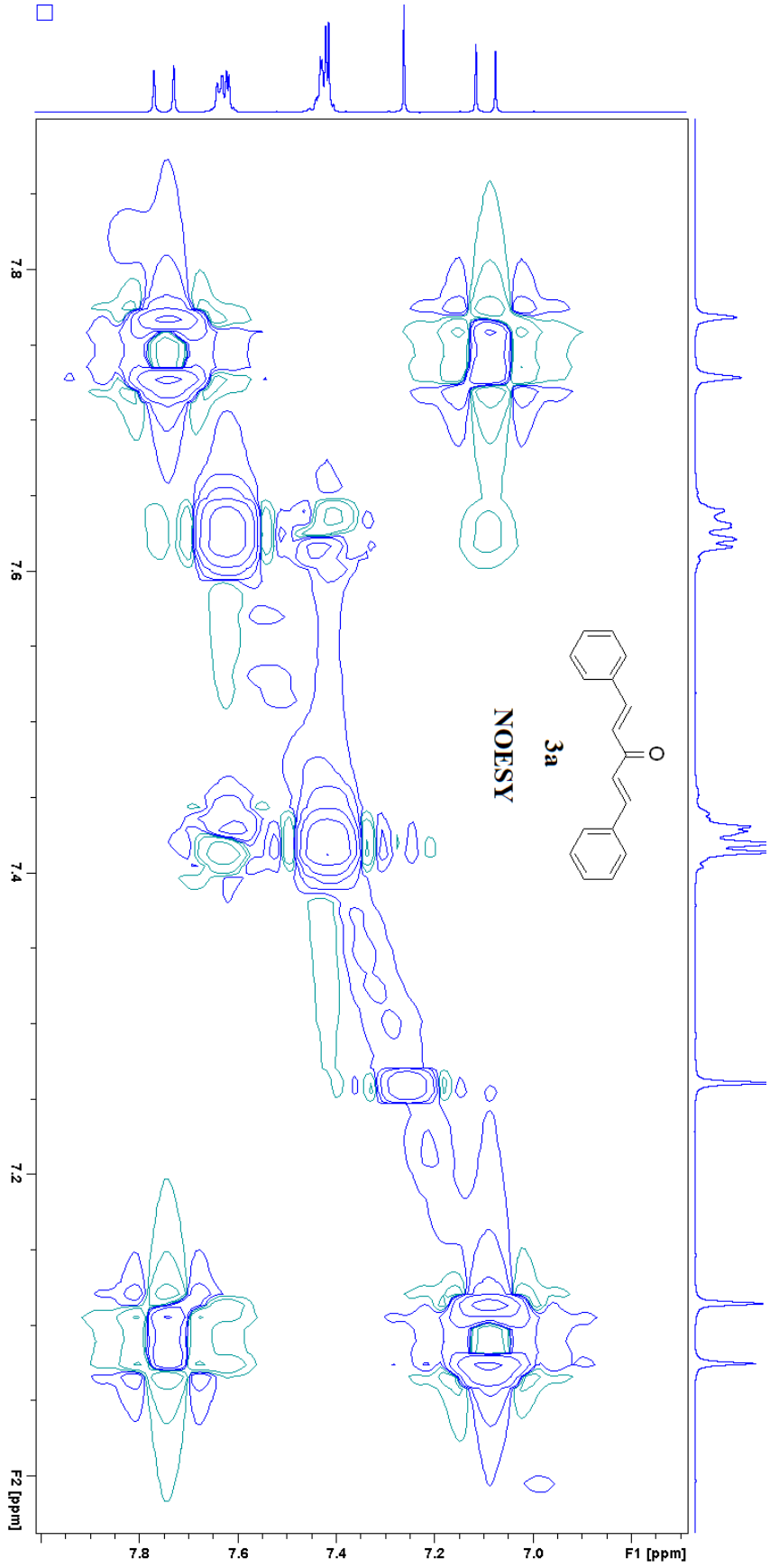
Appendix 2: Spectra of molecules.

(1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one (3a)

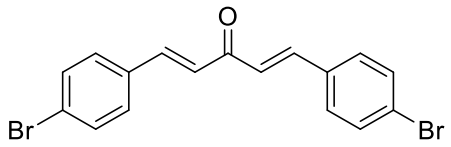


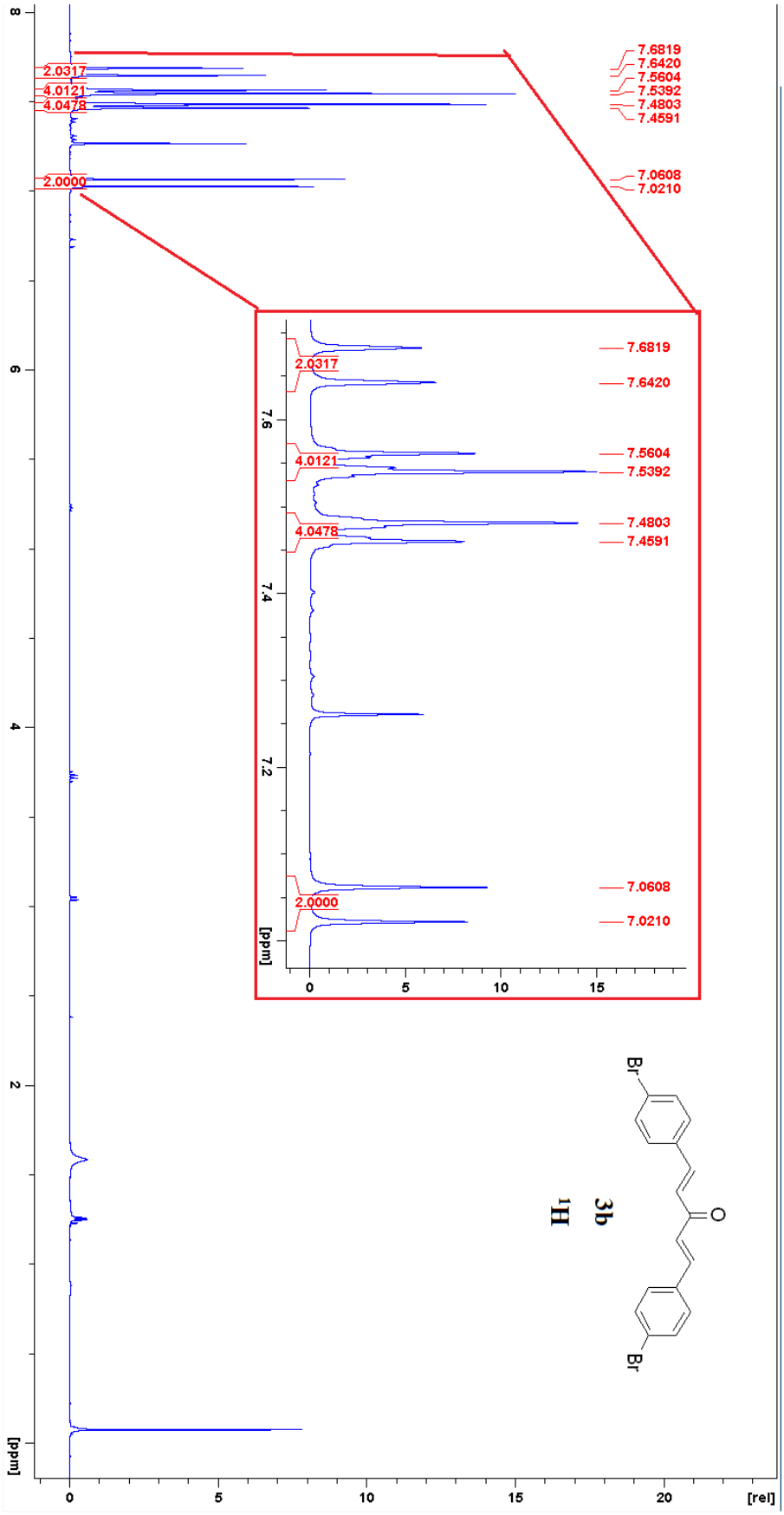

M 7.7679
M 7.7280
M 7.6505
M 7.6037
M 7.4490
M 7.4001
M 7.1138
M 7.0741
0.8532
0.9859
3.8490
5.8570
1.0000
0.8970
[ppm]
[rel]
3a
^{1}H
O

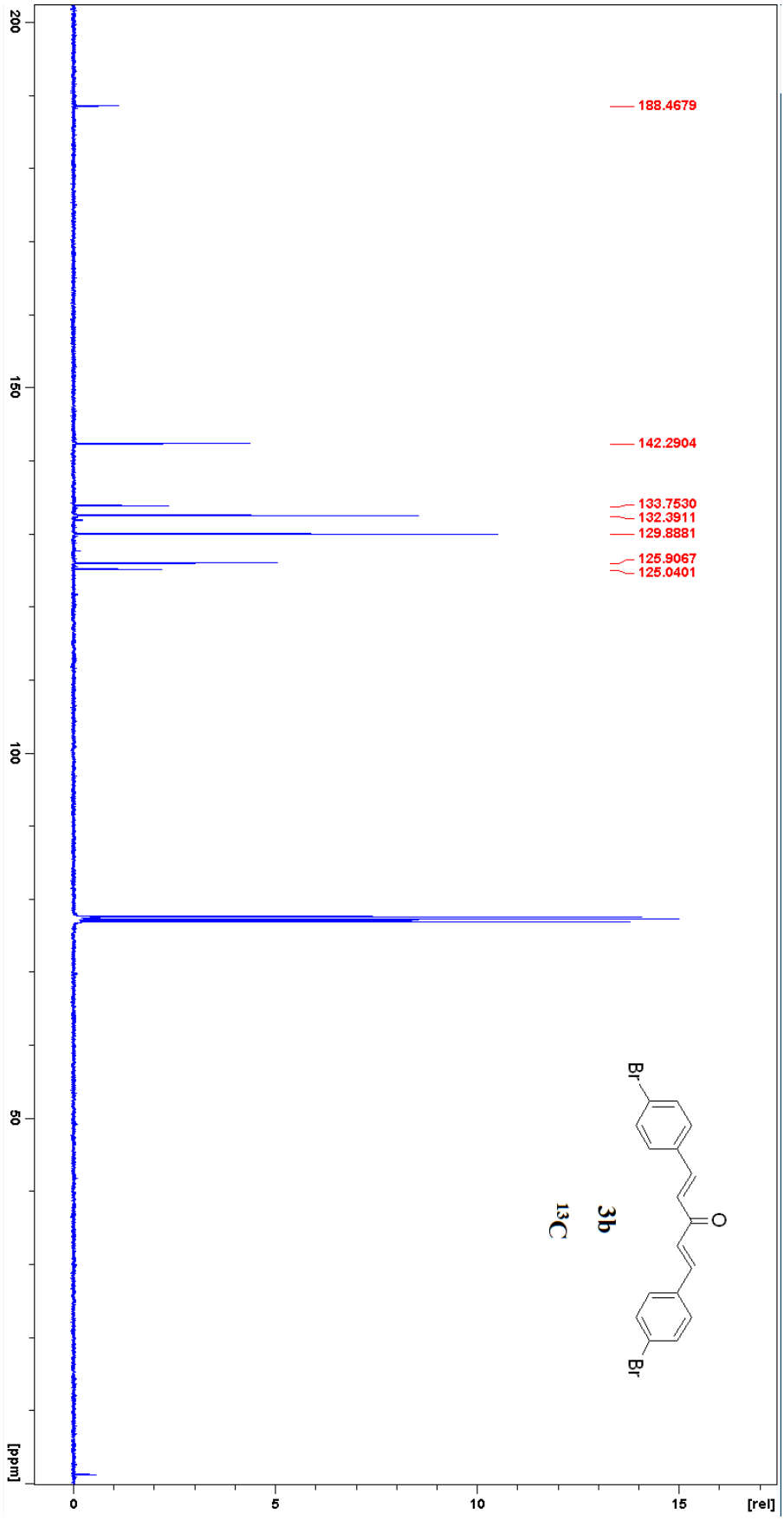

M 143.5018
M 134.9839
M 130.6748
M 129.1574
M 128.5704
M 125.6070
3a
^{13}C
O
[ppm]
[rel]

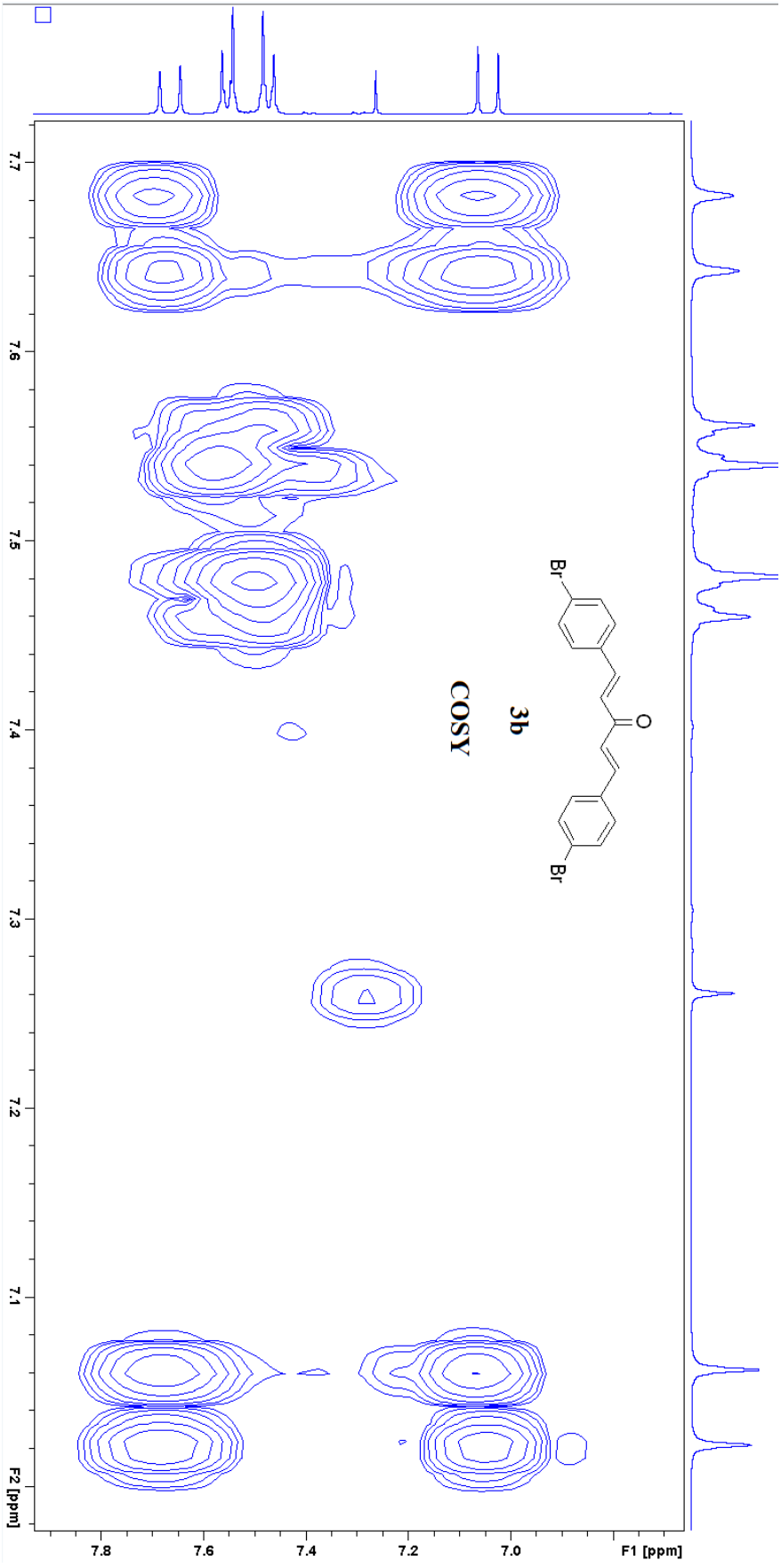

NOESY
3a
O
7.8
7.6
7.4
7.2
F2 [ppm]
7.8
7.6
7.4
7.2
7.0
F1 [ppm]

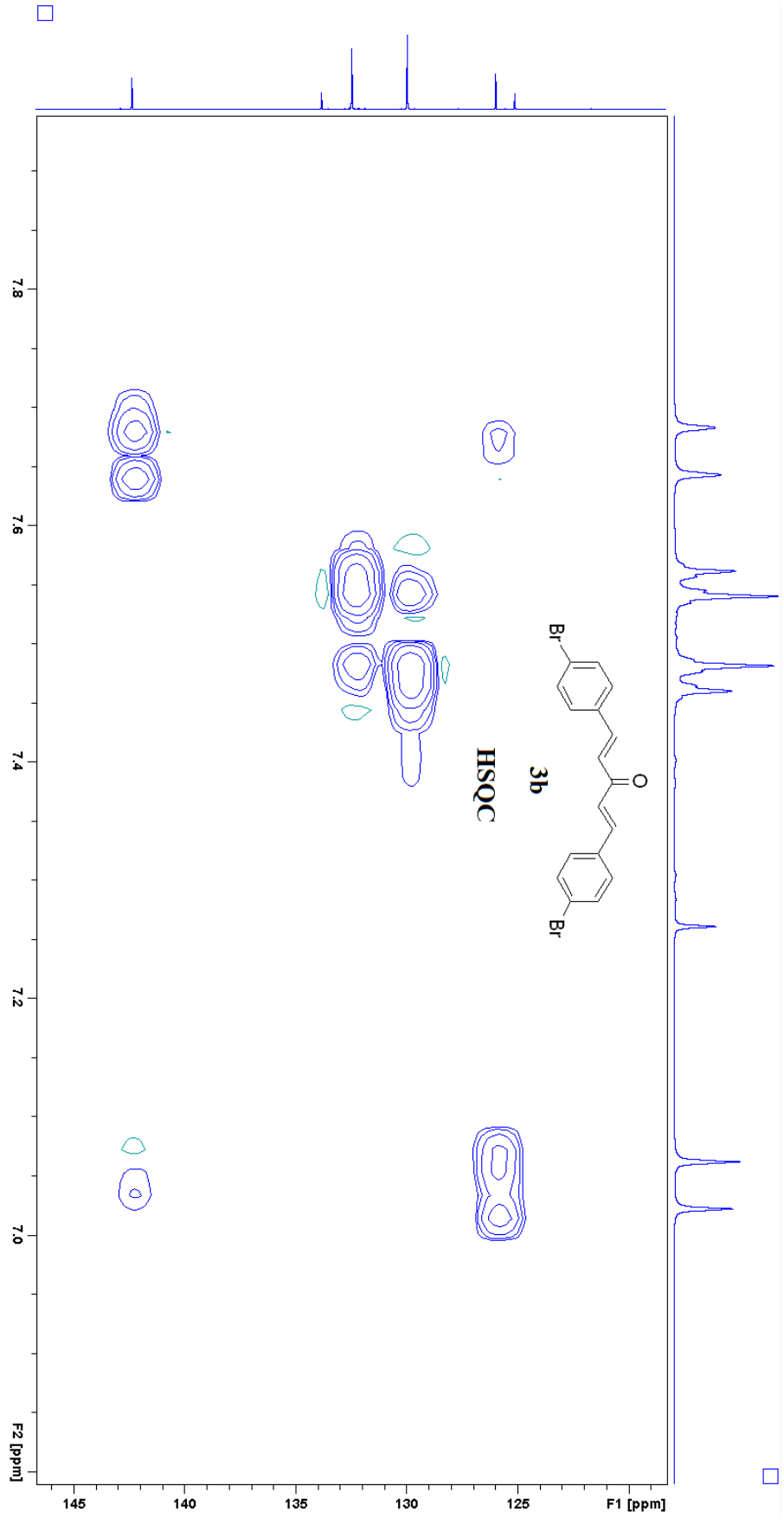
(1*E*,4*E*)-1,5-bis(4-bromophenyl)penta-1,4-dien-3-one (3b)

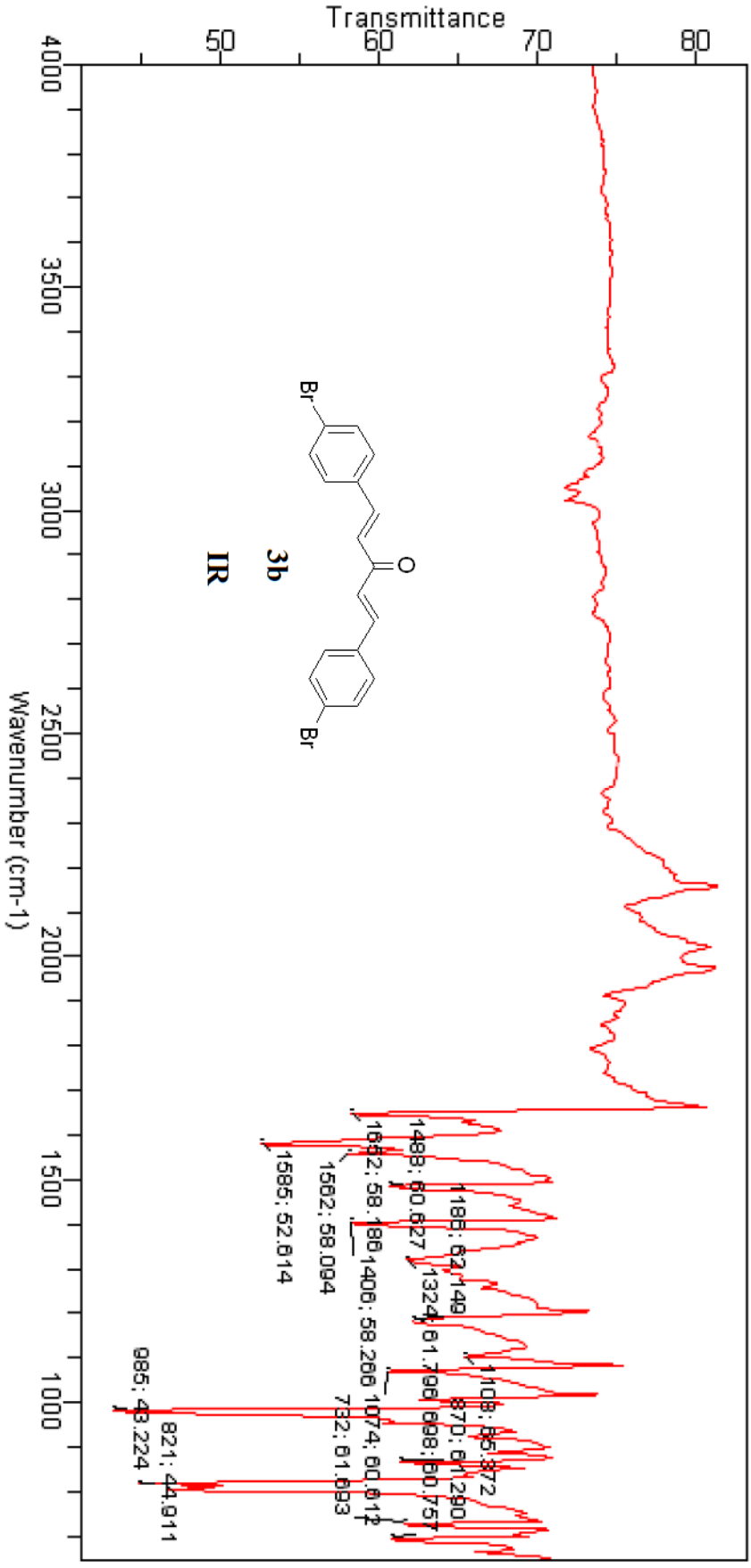


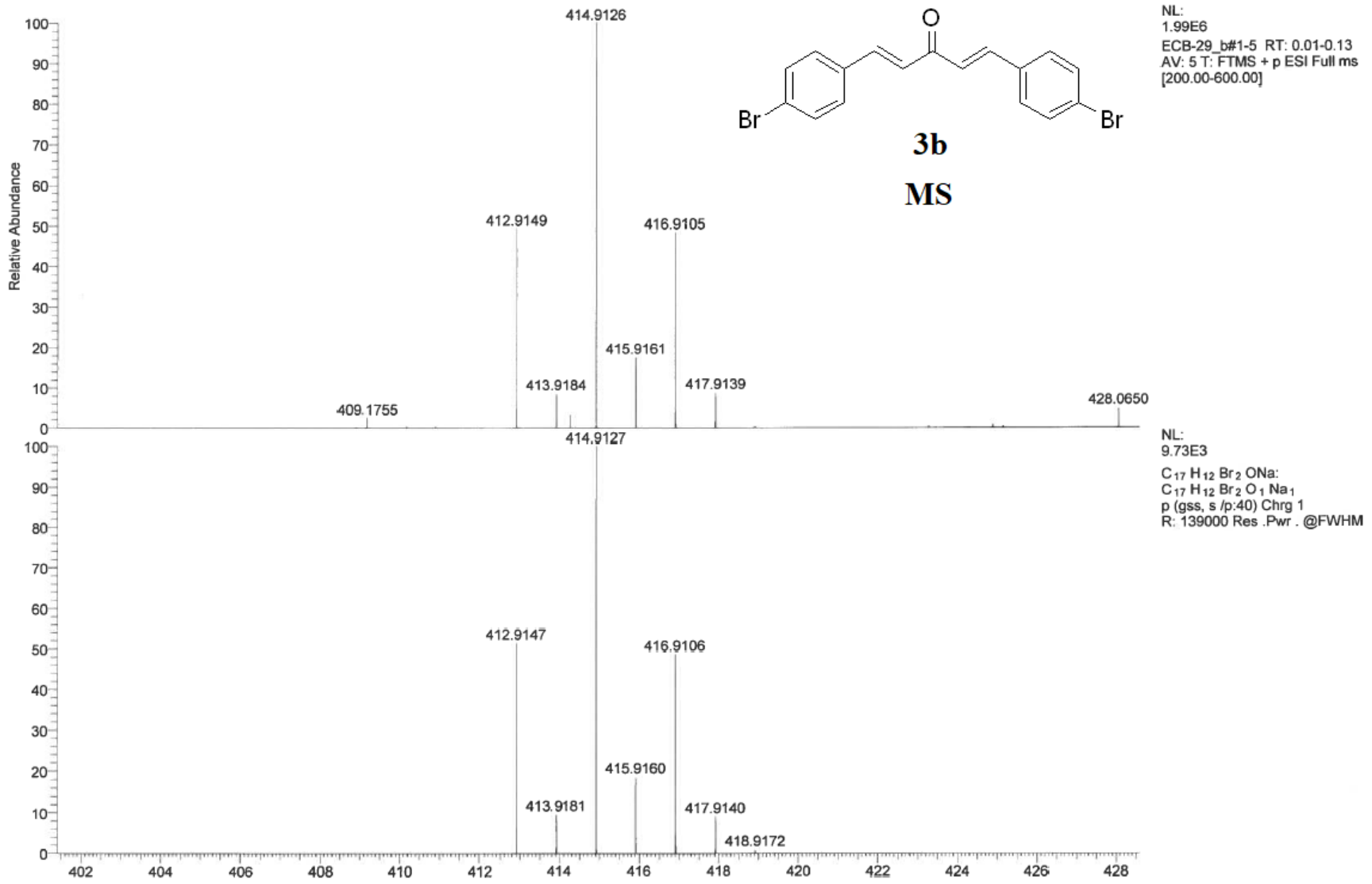

7.6819
7.6420
7.5604
7.5392
7.4803
7.4591
7.0608
7.0210
2.0317
4.0121
4.0478
2.0000
[ppm]
[rel]
Br
O
Br
3b
^{1}H


188.4679
142.2904
133.7530
132.3911
129.8881
125.9067
125.0401
200
150
100
50
[ppm]
0
5
10
15
[rel]
Br
O
Br
3b
^{13}C


COSY
3b
Br
Br
O
F2 [ppm]
F1 [ppm]
7.8
7.6
7.4
7.2
7.0
7.7
7.6
7.5
7.4
7.3
7.2
7.1


HSQC
3b
Br
Br
O
F2 [ppm]
F1 [ppm]
7.8
7.6
7.4
7.2
7.0
145
140
135
130
125

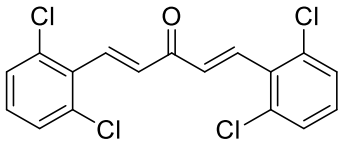

Transmittance
50
60
70
80
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
Br
O
Br
3b
IR
1585; 52.614
1562; 58.094
1652; 58.186
1488; 60.627
1406; 58.266
1324; 61.798
1185; 62.149
1108; 65.372
870; 61.290
808; 60.757
732; 61.693
1074; 60.612
985; 43.224
821; 44.911

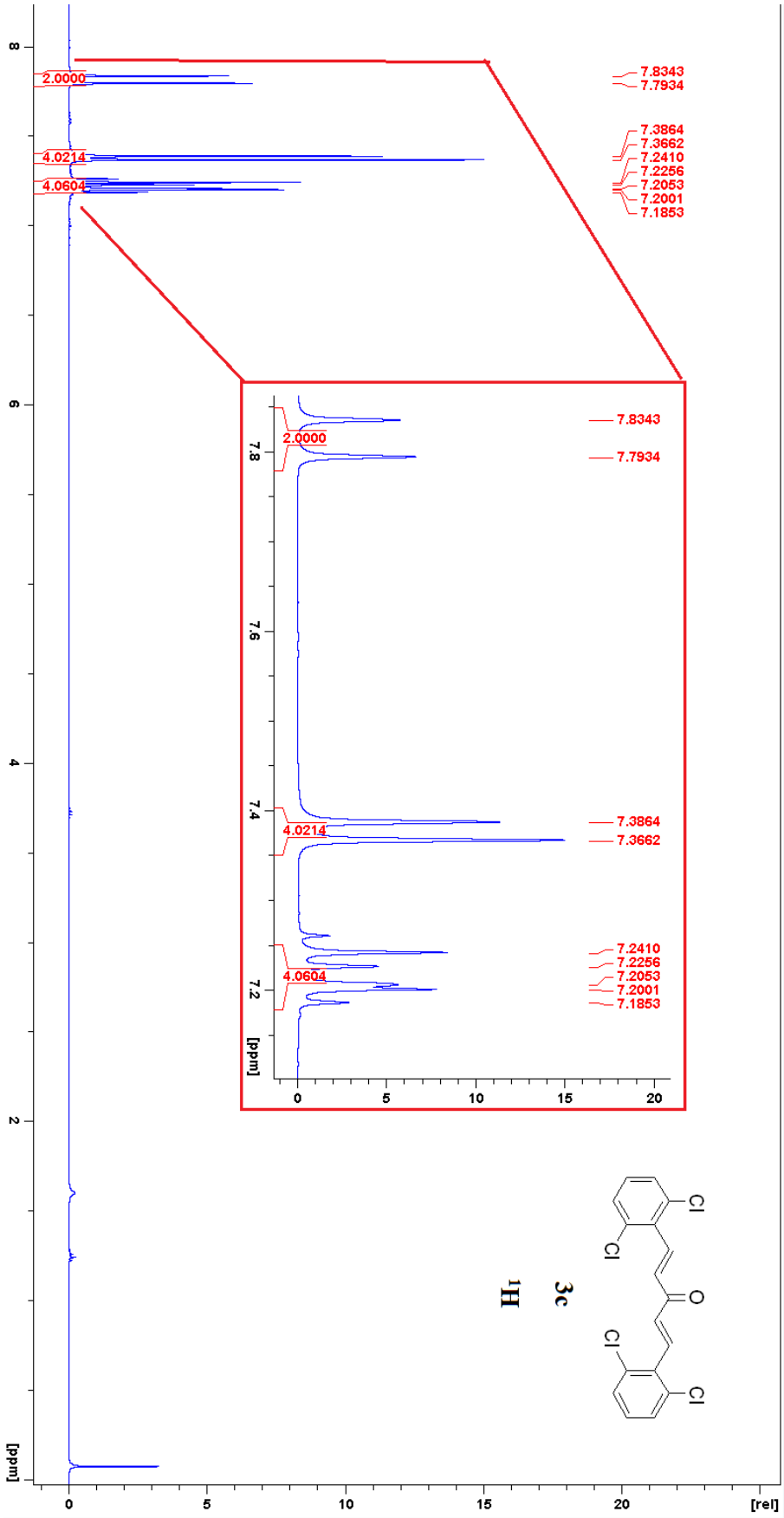

414.9126
412.9149
416.9105
415.9161
413.9184
417.9139
409.1755
428.0650
414.9127
412.9147
416.9106
415.9160
413.9181
417.9140
418.9172
Relative Abundance
NL:
1.99E6
ECB-29_b#1-5 RT: 0.01-0.13
AV: 5 T: FTMS + p ESI Full ms
[200.00-600.00]
NL:
9.73E3
C17 H12 Br2 ONa:
C17 H12 Br2 O1 Na1
p (gss, s /p:40) Chrg 1
R: 139000 Res .Pwr . @FWHM
Br
Br
O

3b

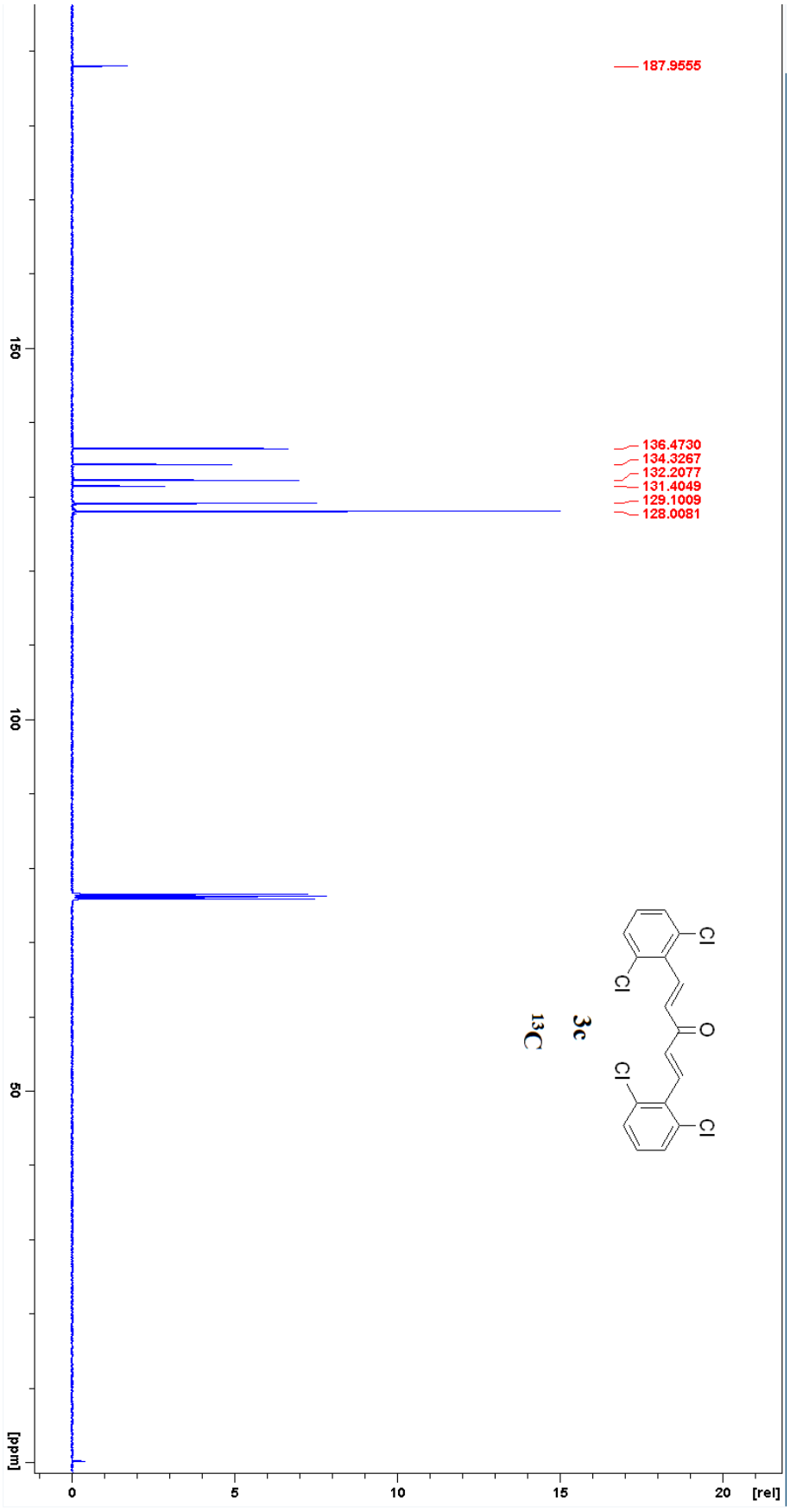
MS

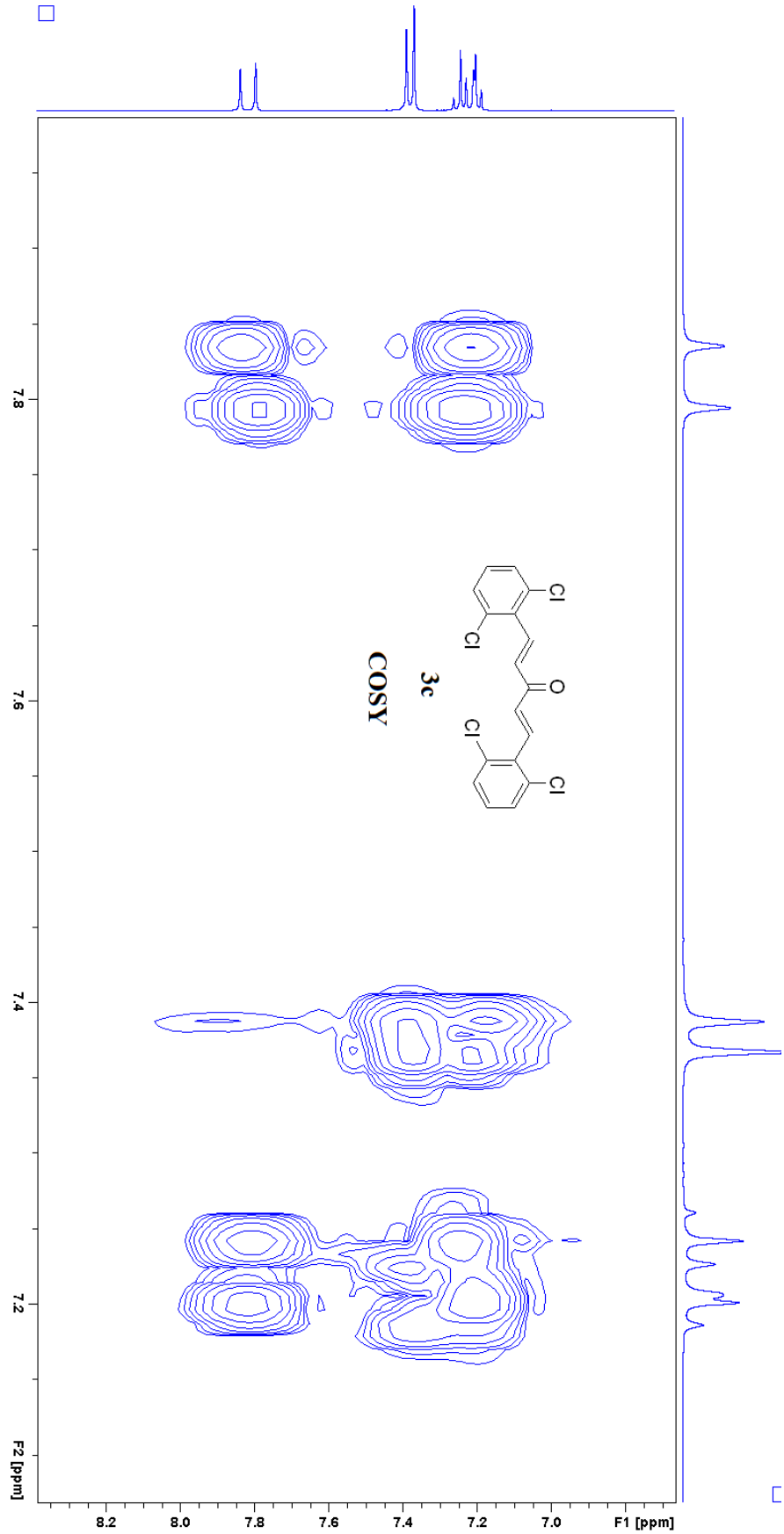
(1*E*,4*E*)-1,5-bis(2,6-dichlorophenyl)penta-1,4-dien-3-one (3c)

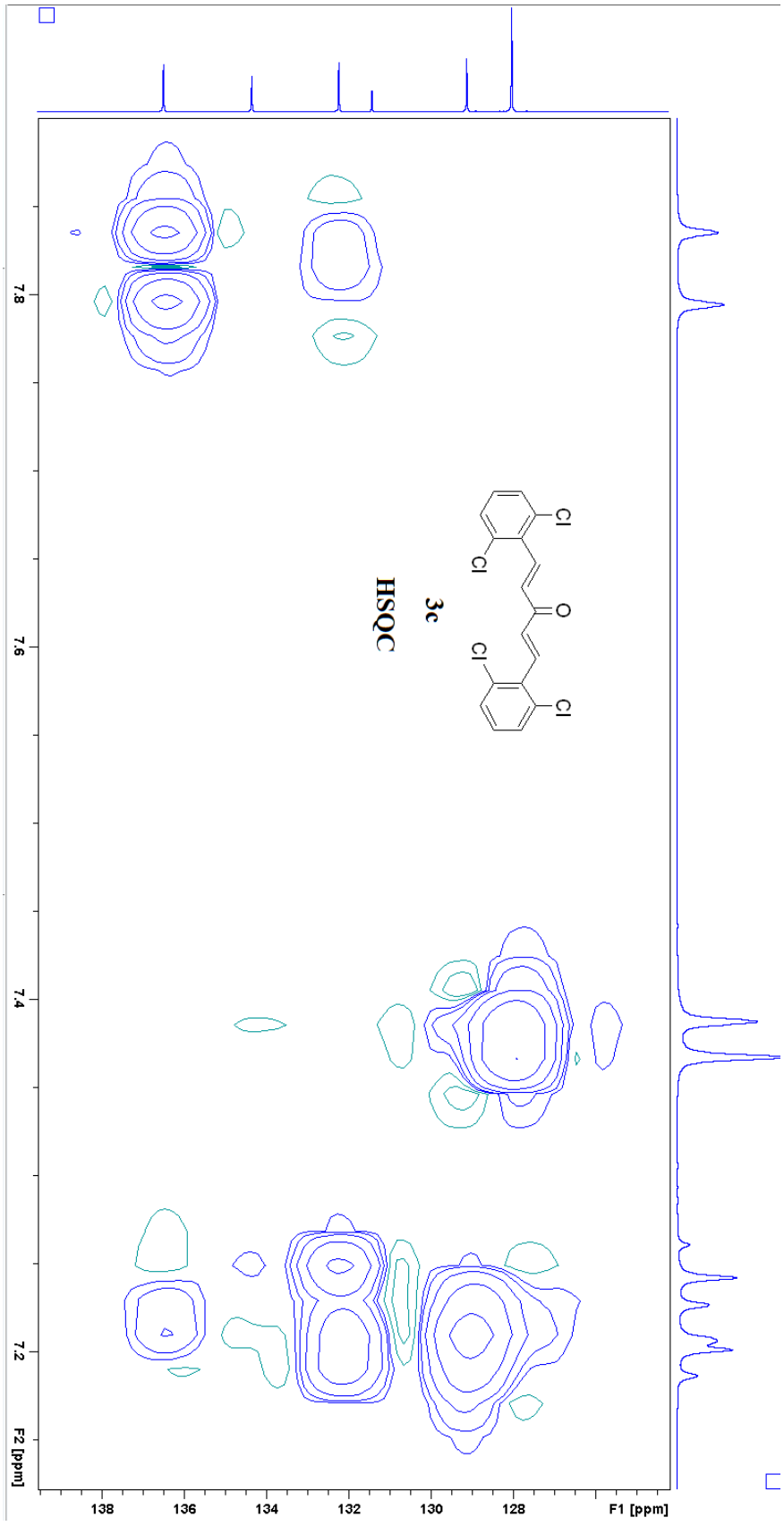


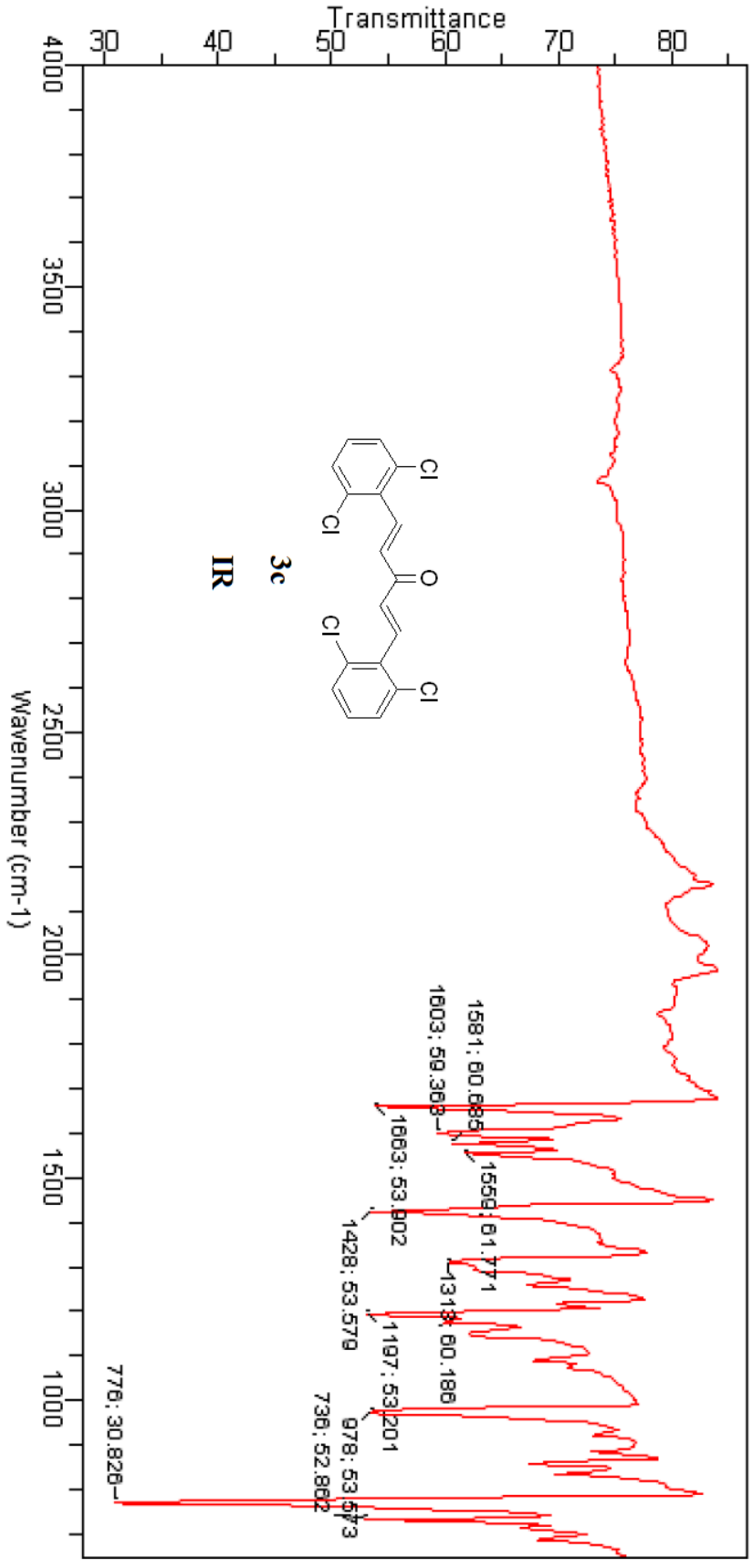

2.0000
4.0214
4.0604
7.8343
7.7934
7.3864
7.3662
7.2410
7.2256
7.2053
7.2001
7.1853
[ppm]
[rel]
Cl
Cl
O
Cl
Cl

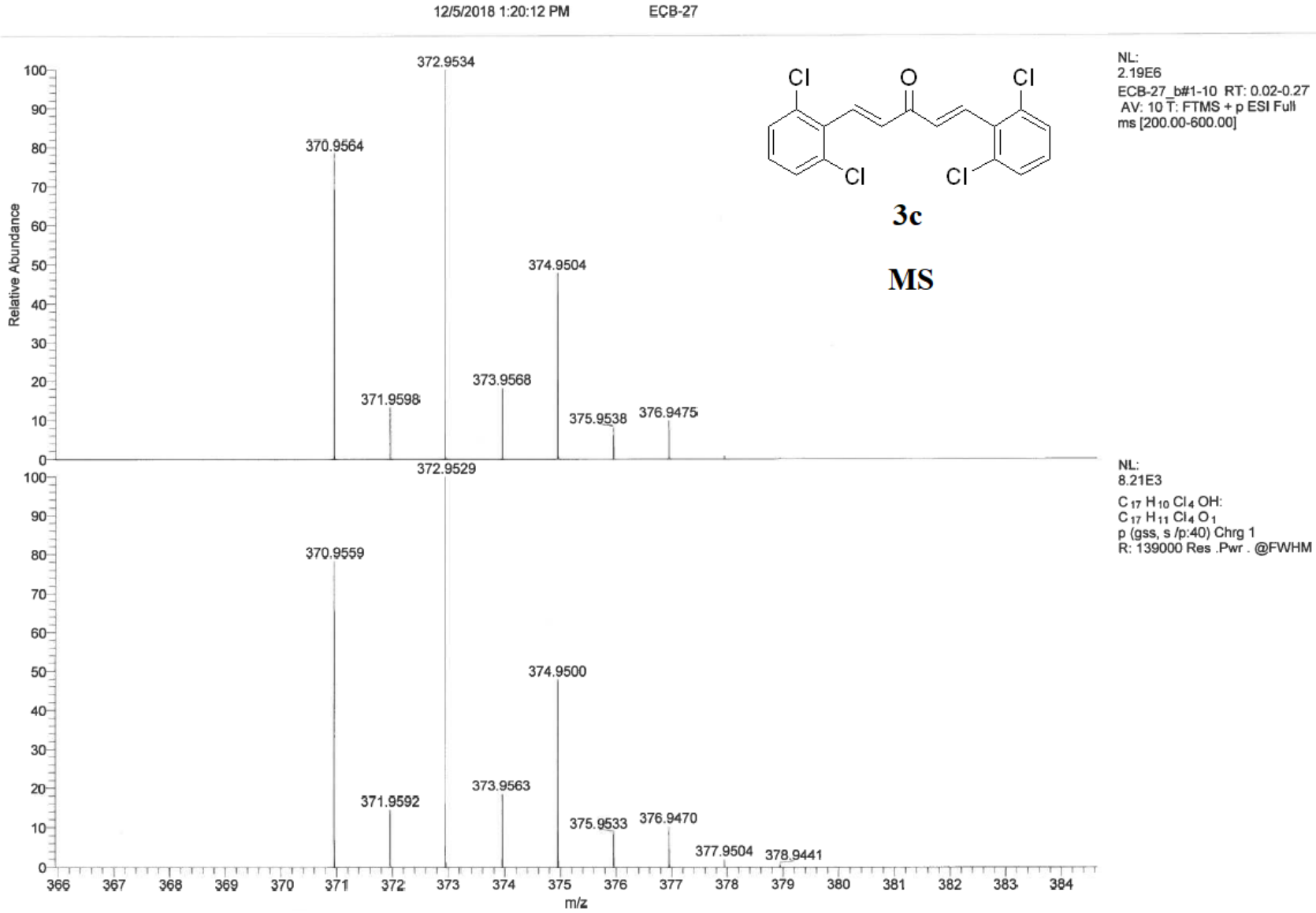
^{1}H **3c**


187.9555
136.4730
134.3267
132.2077
131.4049
129.1009
128.0081
150
100
50
[ppm]
0
5
10
15
20
[rel]
^{13}C
3c
Cl
Cl
O
Cl
Cl

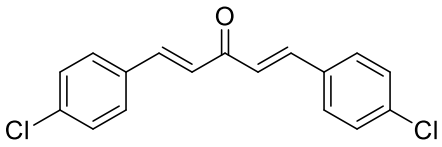

COSY
3c
Cl
Cl
O
Cl
Cl
7.8
7.6
7.4
7.2
F2 [ppm]
8.2
8.0
7.8
7.6
7.4
7.2
7.0
F1 [ppm]

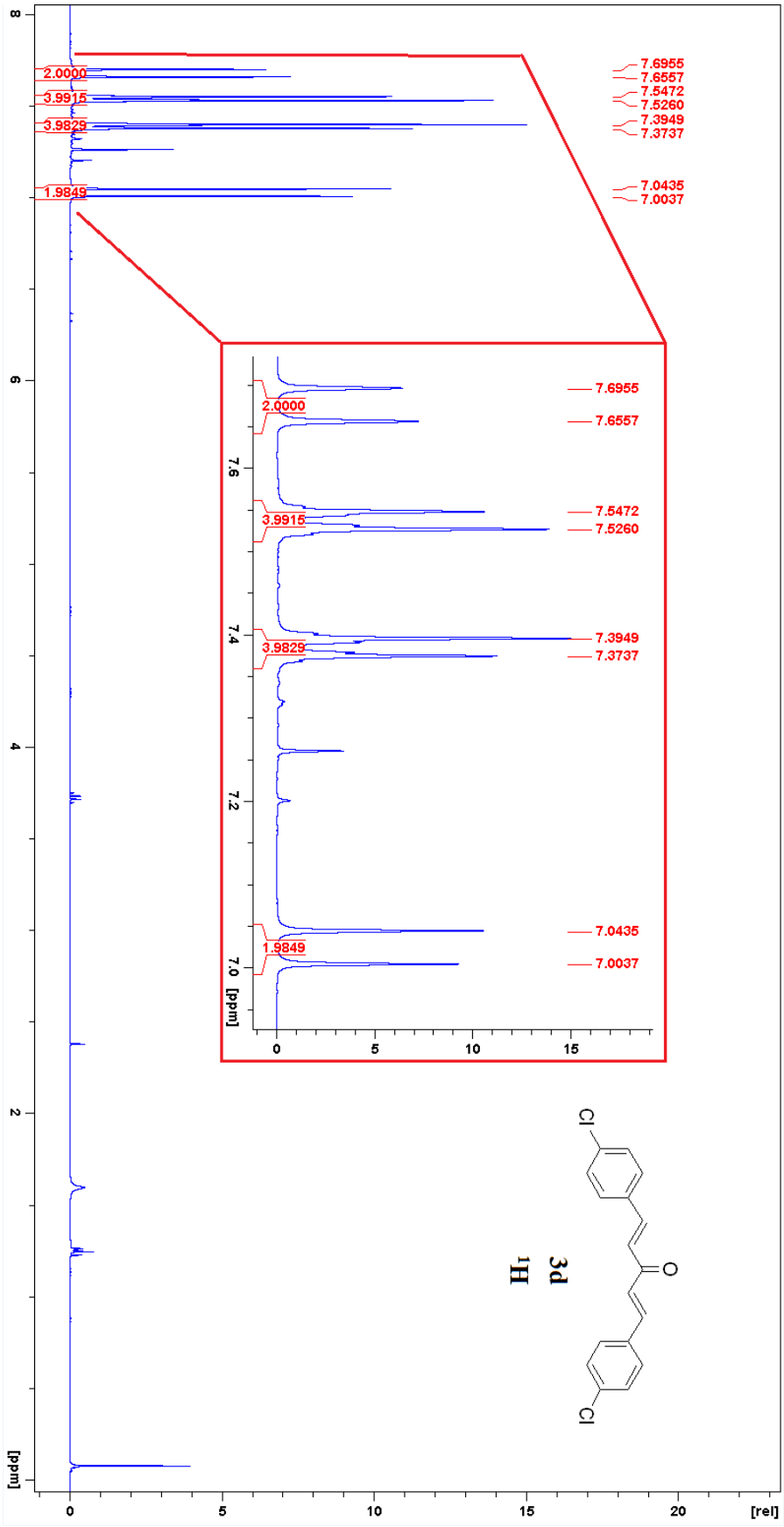

HSQC
3c
Cl
Cl
O
Cl
Cl
7.8
7.6
7.4
7.2
F2 [ppm]
138
136
134
132
130
128
F1 [ppm]

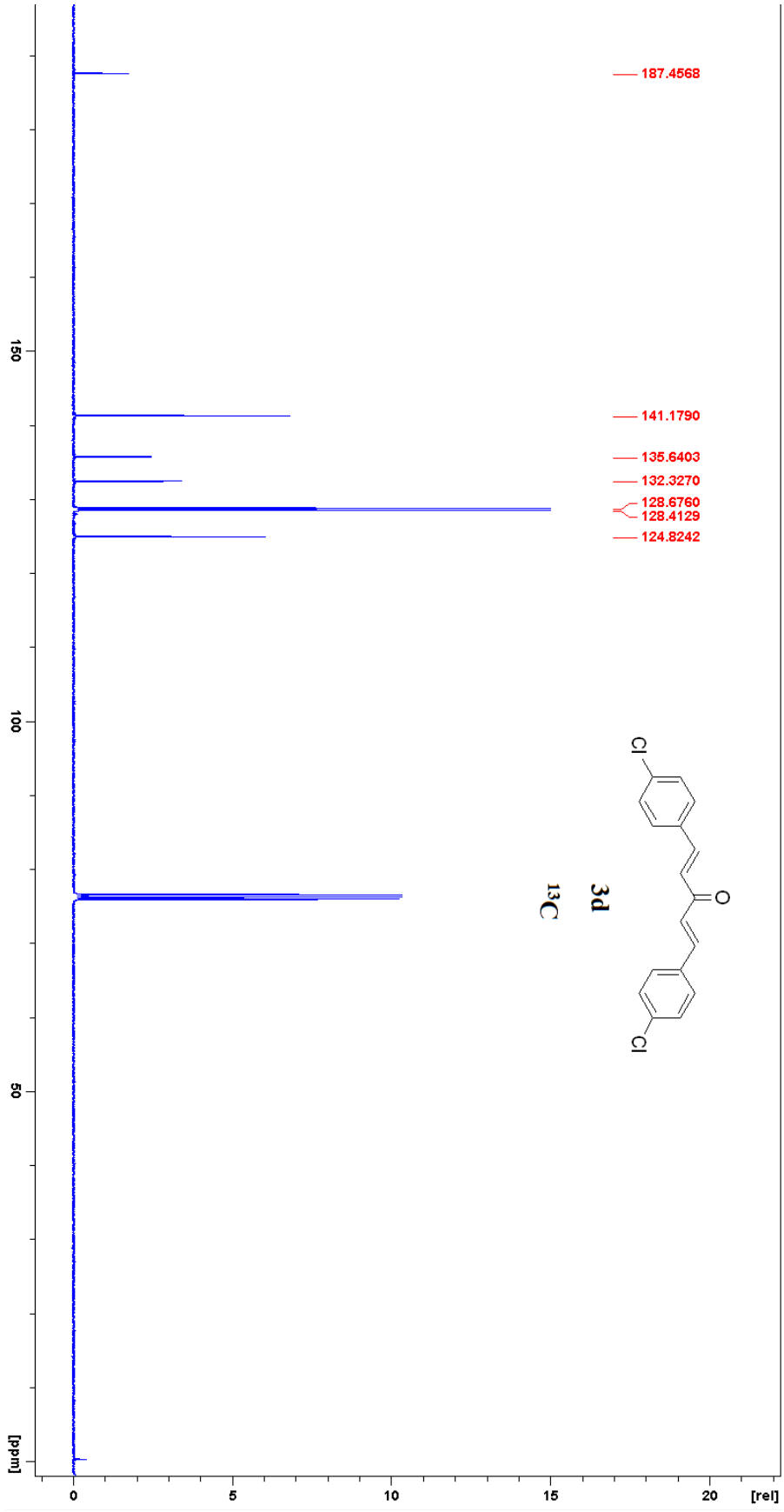

Transmittance
30
40
50
60
70
80
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
Cl
Cl
O
Cl
Cl
3c
IR
1603; 59.369
1581; 60.685
1559; 61.771
1663; 53.902
1428; 53.579
1313; 60.186
1197; 53.201
978; 53.573
736; 52.862
776; 30.826

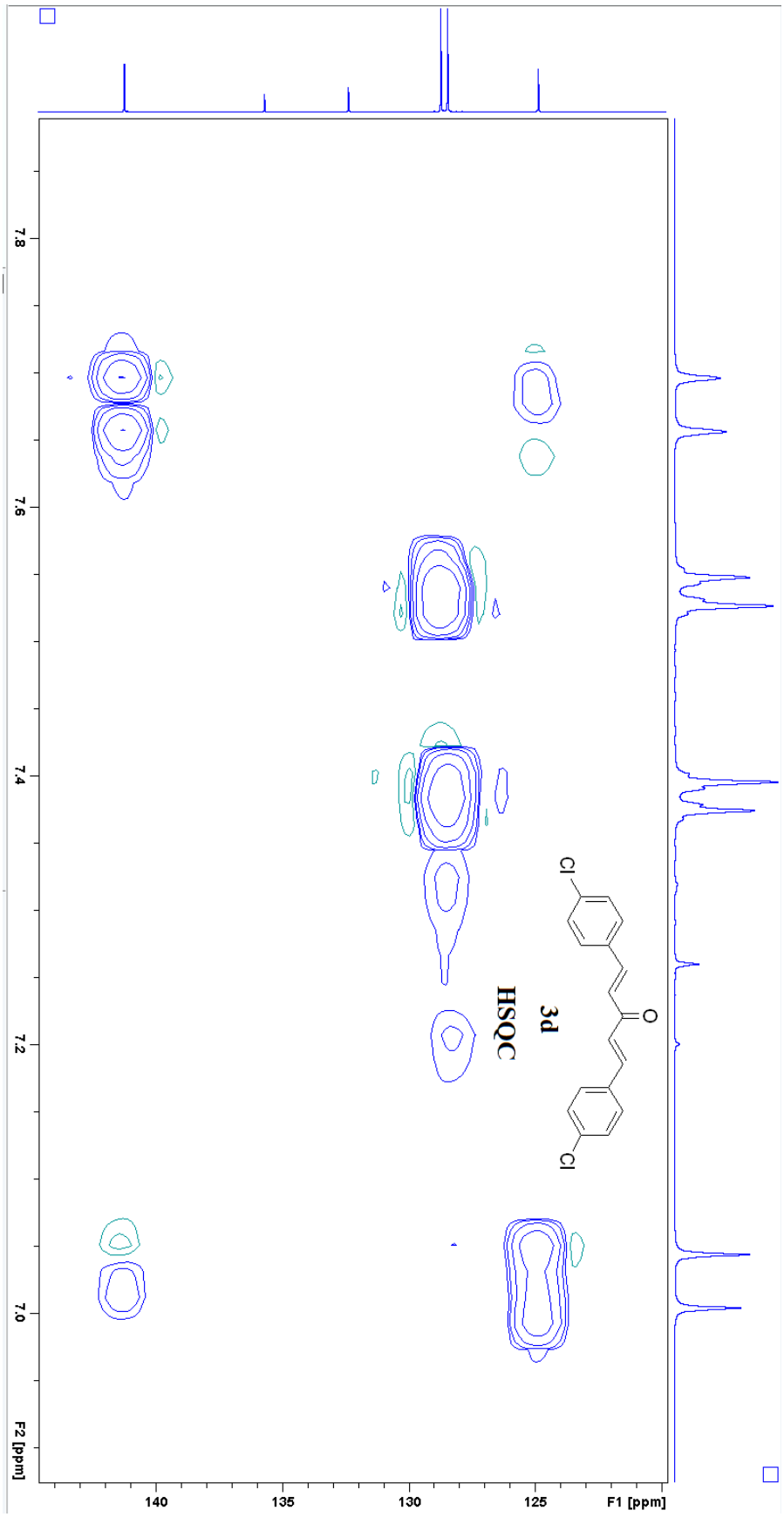

12/5/2018 1:20:12 PM
ECB-27
372.9534
370.9564
374.9504
373.9568
371.9598
375.9538
376.9475
372.9529
370.9559
374.9500
373.9563
371.9592
375.9533
376.9470
377.9504
378.9441
Relative Abundance
m/z
Cl
O
Cl
Cl
Cl
3c
MS
NL:
2.19E6
ECB-27_b#1-10 RT: 0.02-0.27
AV: 10 T: FTMS + p ESI Full
ms [200.00-600.00]
NL:
8.21E3
C17 H10 Cl4 OH:
C17 H11 Cl4 O1
p (gss, s /p:40) Chrg 1
R: 139000 Res .Pwr . @FWHM

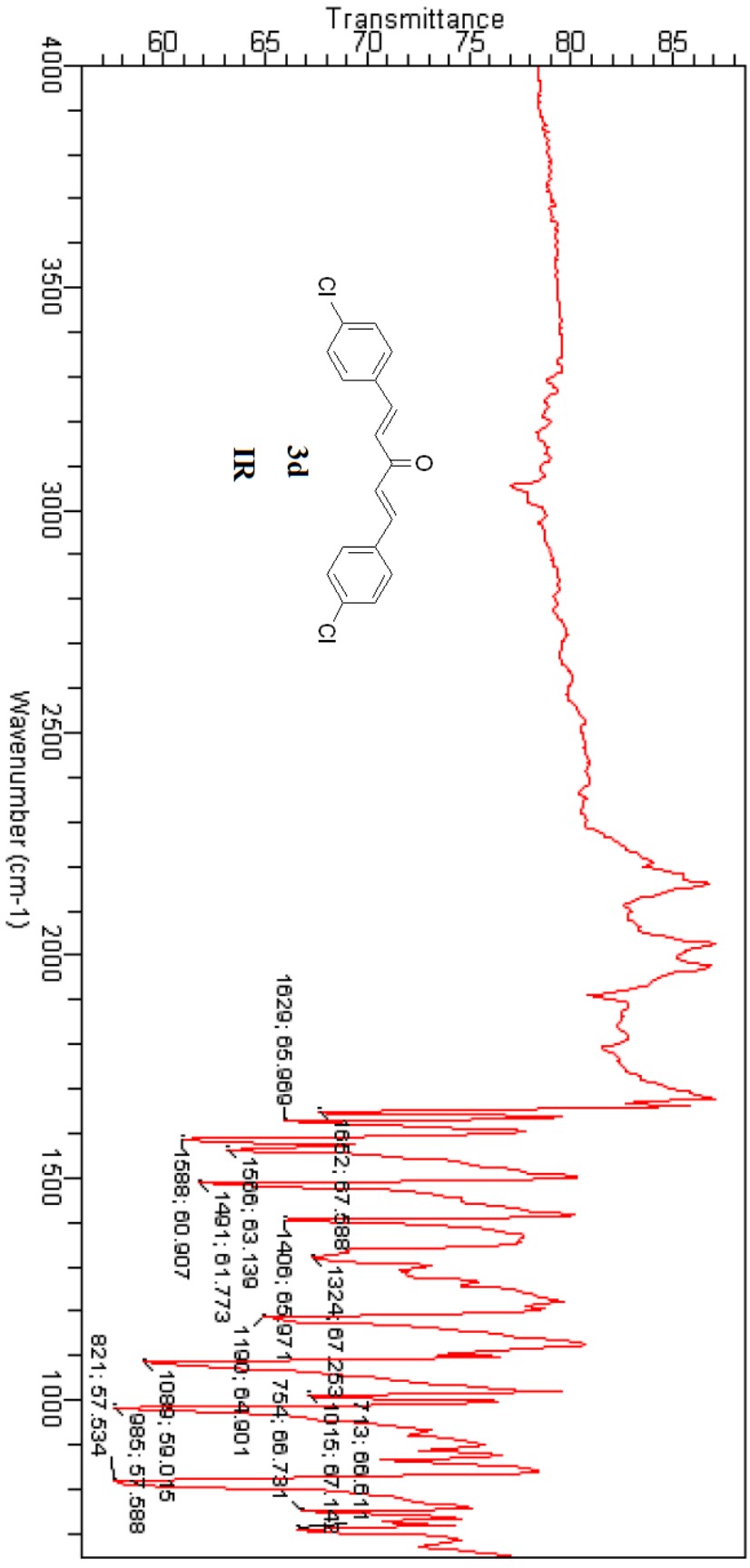
(1*E*,4*E*)-1,5-bis(4-chlorophenyl)penta-1,4-dien-3-one (3d)

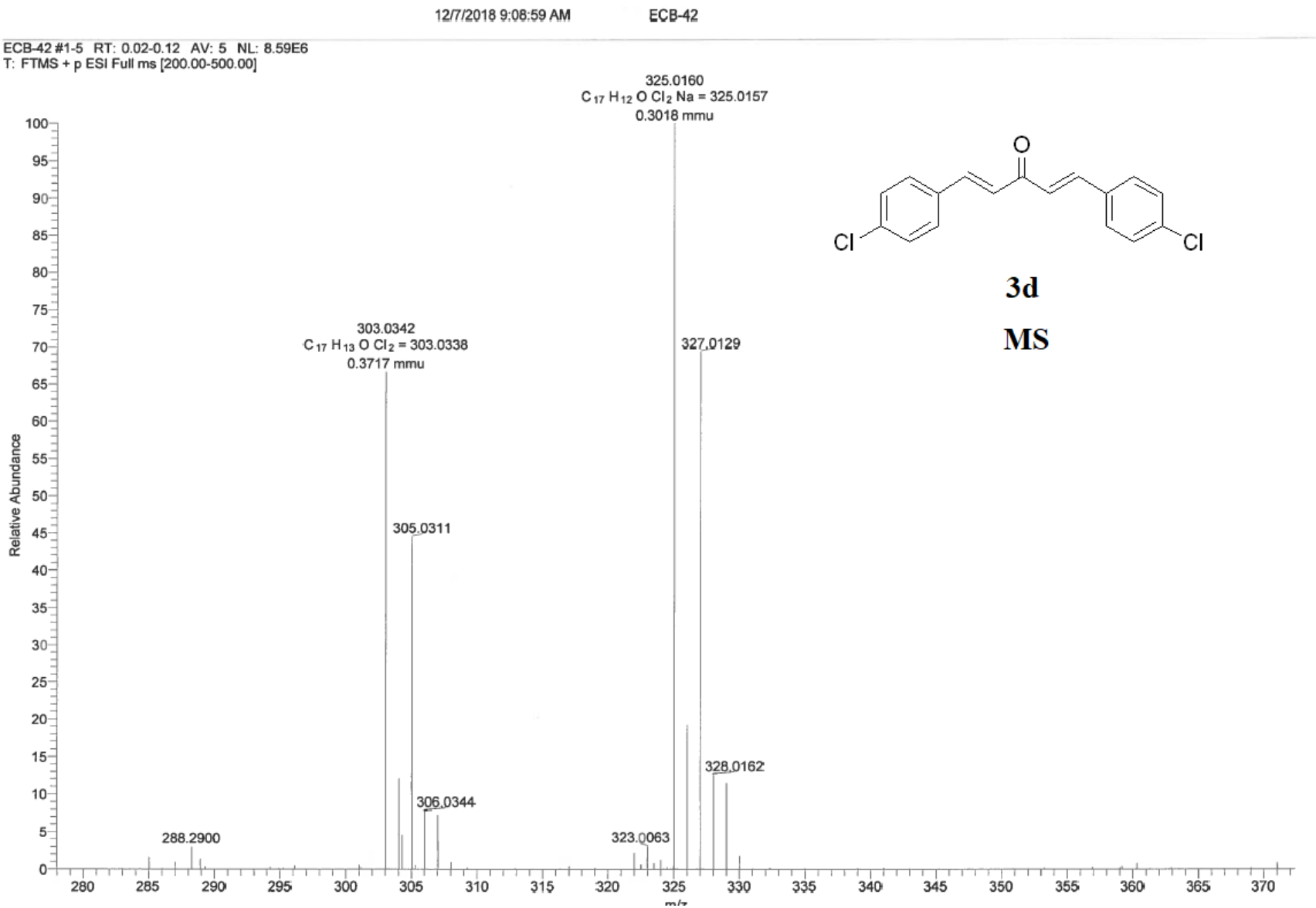



2.0000
3.9915
3.9829
1.9849
7.6955
7.6557
7.5472
7.5260
7.3949
7.3737
7.0435
7.0037
[ppm]
[rel]
3d
^{1}H
Cl
O
Cl


187.4568
141.1790
135.6403
132.3270
128.6760
128.4129
124.8242
150
100
50
[ppm]
0
5
10
15
20
[rel]
^{13}C
3d
Cl
O
Cl


7.8
7.6
7.4
7.2
7.0
F2 [ppm]
140
135
130
125
F1 [ppm]
HSQC
3d
Cl
O
Cl

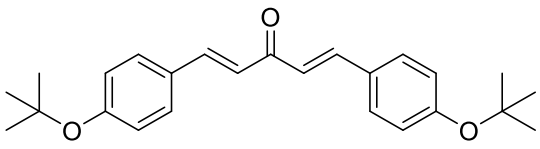

Transmittance
60
65
70
75
80
85
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
Cl
O
Cl
3d
IR
1629; 65.969
1588; 60.907
1491; 61.773
1406; 65.971
1324; 67.253
1190; 64.901
1088; 59.015
985; 57.588
821; 57.534
754; 66.731

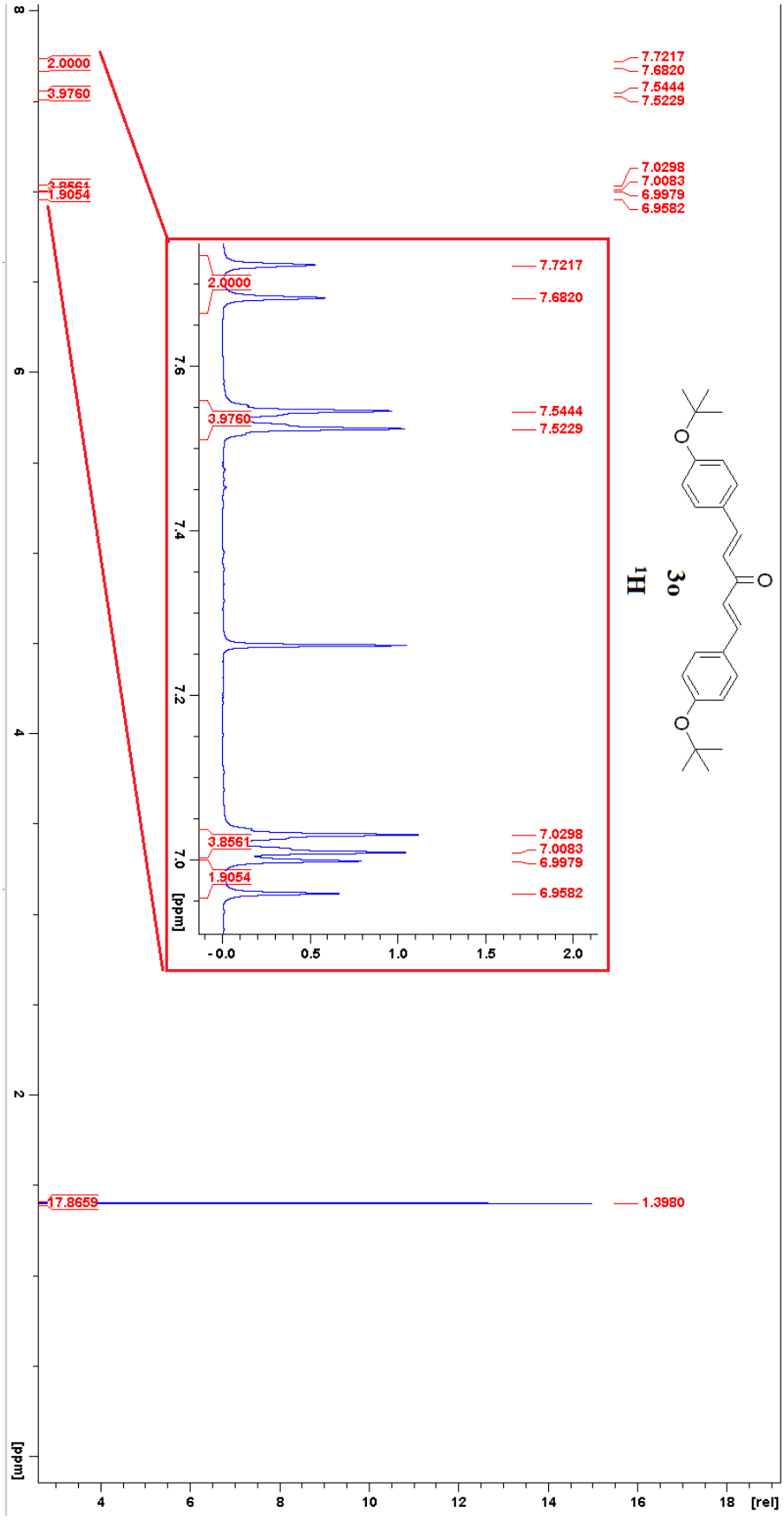

12/7/2018 9:08:59 AM
ECB-42
ECB-42 #1-5 RT: 0.02-0.12 AV: 5 NL: 8.59E6
T: FTMS + p ESI Full ms [200.00-500.00]
325.0160
C 17 H 12 O Cl 2 Na = 325.0157
0.3018 mmu
303.0342
C 17 H 13 O Cl 2 = 303.0338
0.3717 mmu
327.0129
305.0311
328.0162
306.0344
288.2900
323.0063
Relative Abundance
m/z
O
Cl
Cl

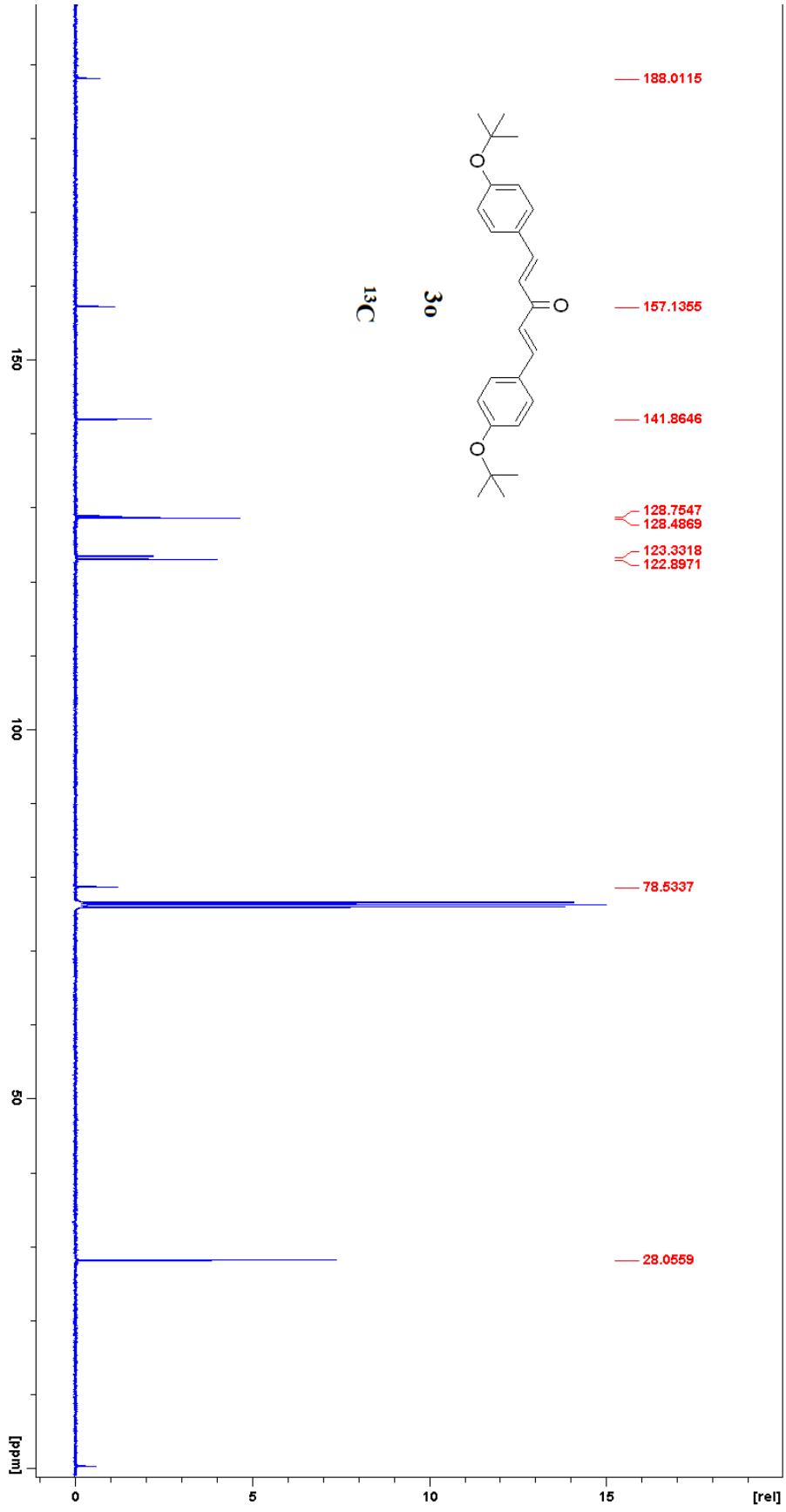
3d

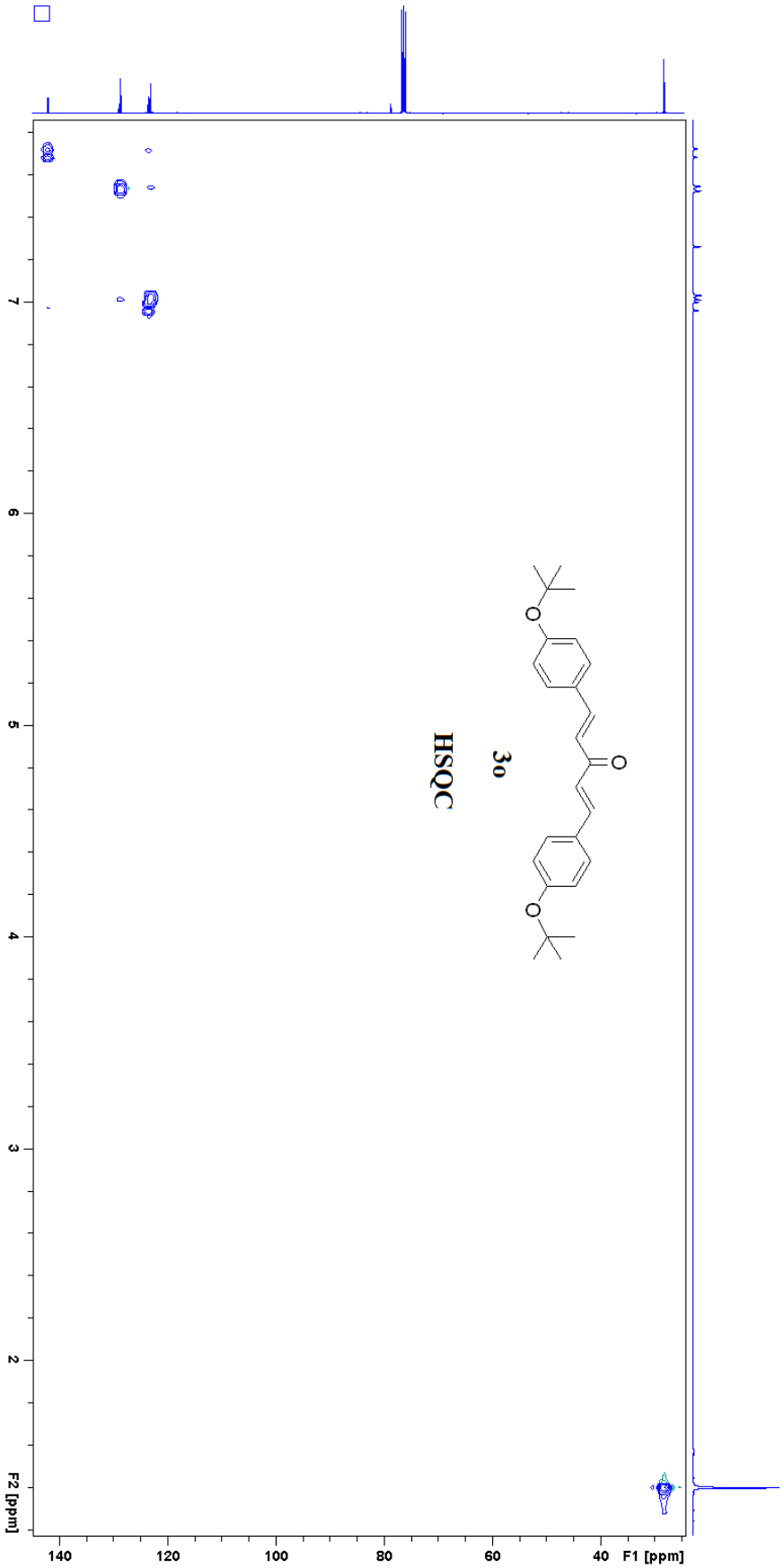
MS

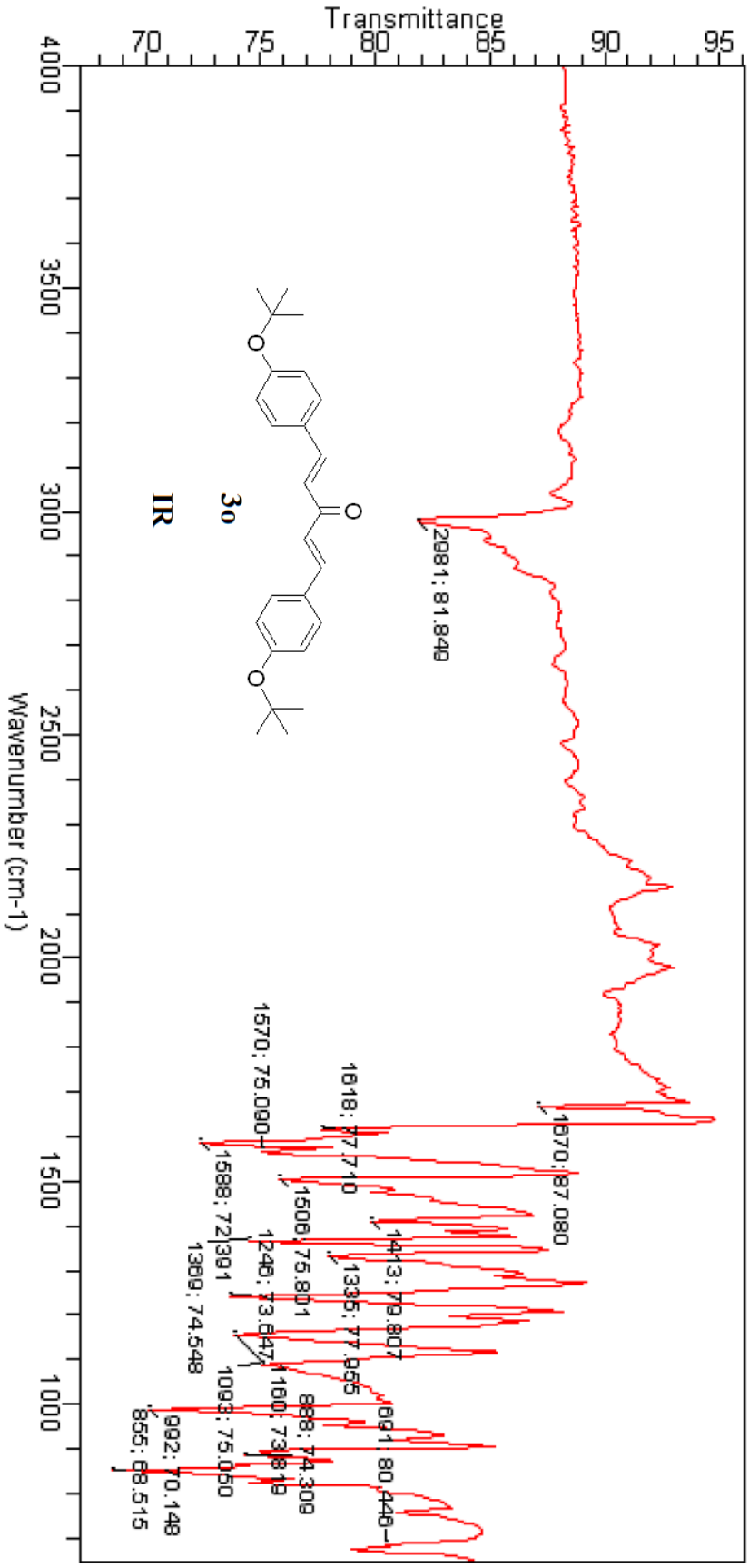
(1*E*,4*E*)-1,5-bis(4-*tert*-butoxyphenyl)penta-1,4-dien-3-one (3o)

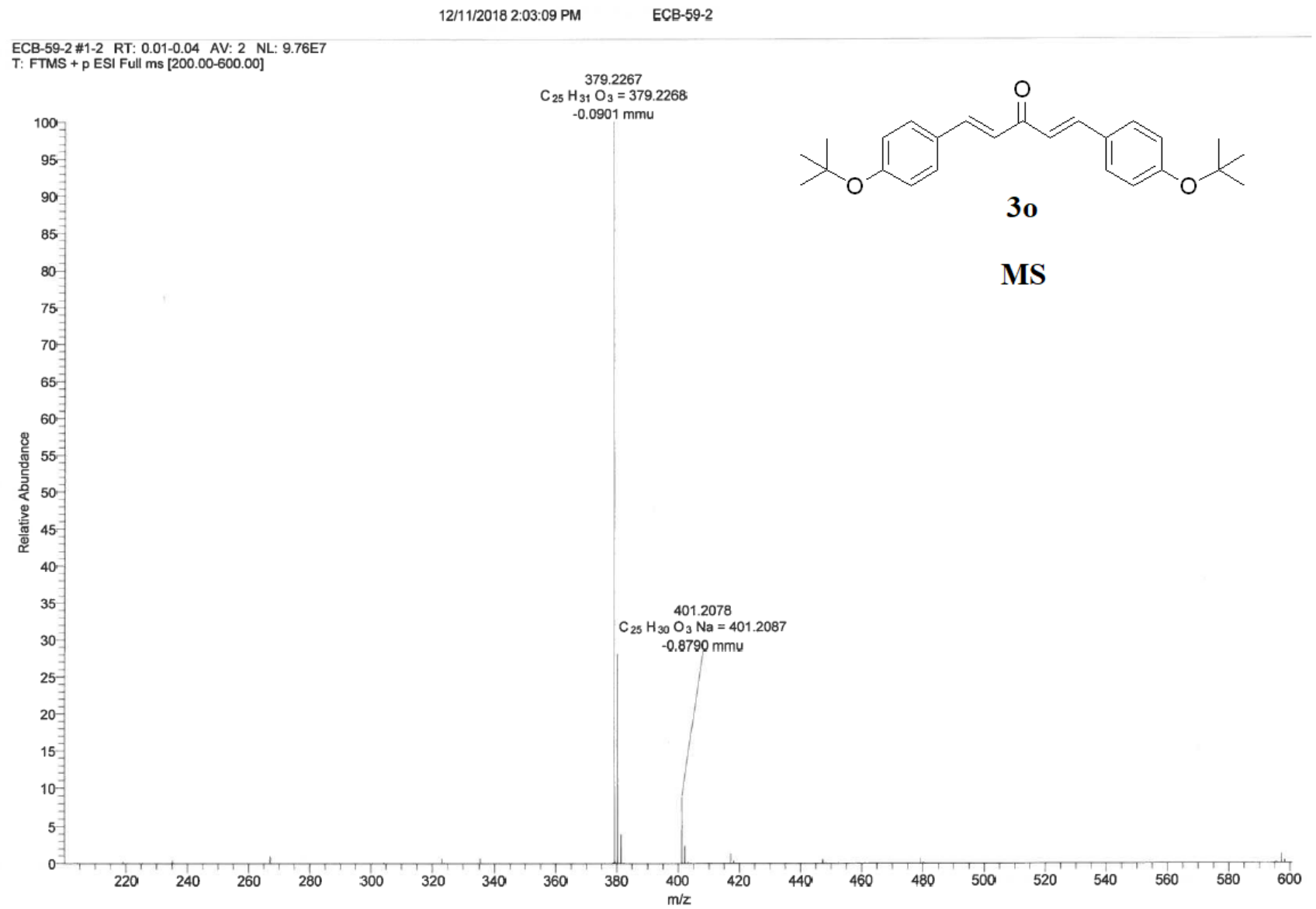



2.0000
3.9760
1.9054
17.8659
7.7217
7.6820
7.5444
7.5229
7.0298
7.0083
6.9979
6.9582
1.3980
[ppm]
[rel]
3.8561
^{1}H
3o


188.0115
157.1355
141.8646
128.7547
128.4869
123.3318
122.8971
78.5337
28.0559
^{13}C
3o
150
100
50
[ppm]
0
5
10
15
[rel]


HSQC
3o
F2 [ppm]
F1 [ppm]
140
120
100
80
60
40
2
3
4
5
6
7

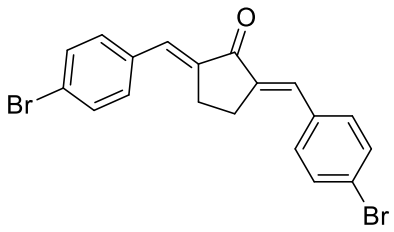

IR
3o
Transmittance
Wavenumber (cm-1)
4000
3500
3000
2500
2000
1500
1000
70
75
80
85
90
95
2981; 81.849
1670; 87.080
1618; 77.710
1570; 75.090
1588; 72.391
1506; 75.801
1443; 79.807
1369; 74.548
1335; 77.955
1246; 73.647
1093; 75.050
991; 80.446
888; 74.309
855; 68.515
992; 70.148

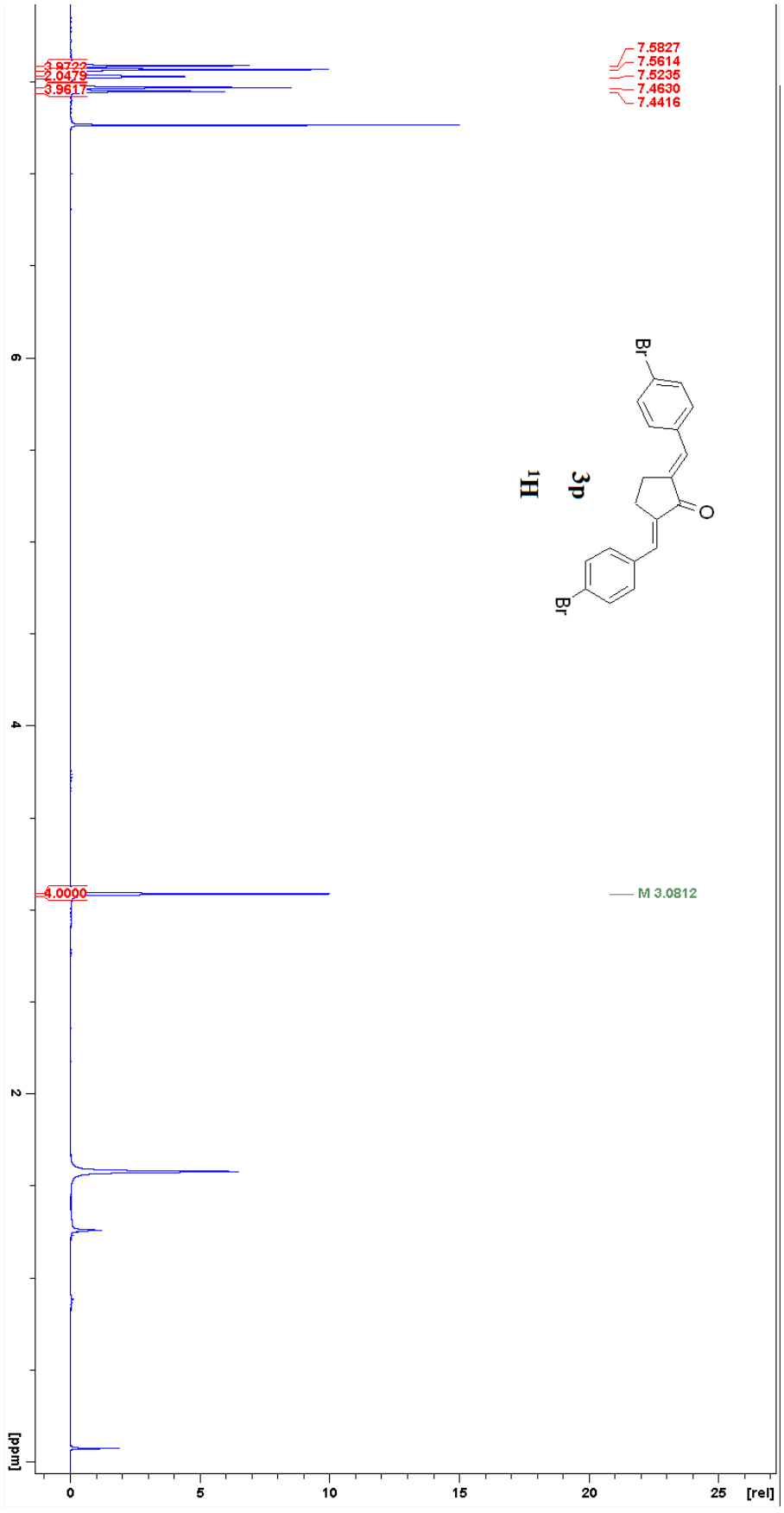

12/11/2018 2:03:09 PM ECB-59-2
ECB-59-2 #1-2 RT: 0.01-0.04 AV: 2 NL: 9.76E7
T: FTMS + p ESI Full ms [200.00-600.00]
379.2267
C25 H31 O3 = 379.2268
-0.0901 mmu
401.2078
C25 H30 O3 Na = 401.2087
-0.8790 mmu
Relative Abundance
m/z

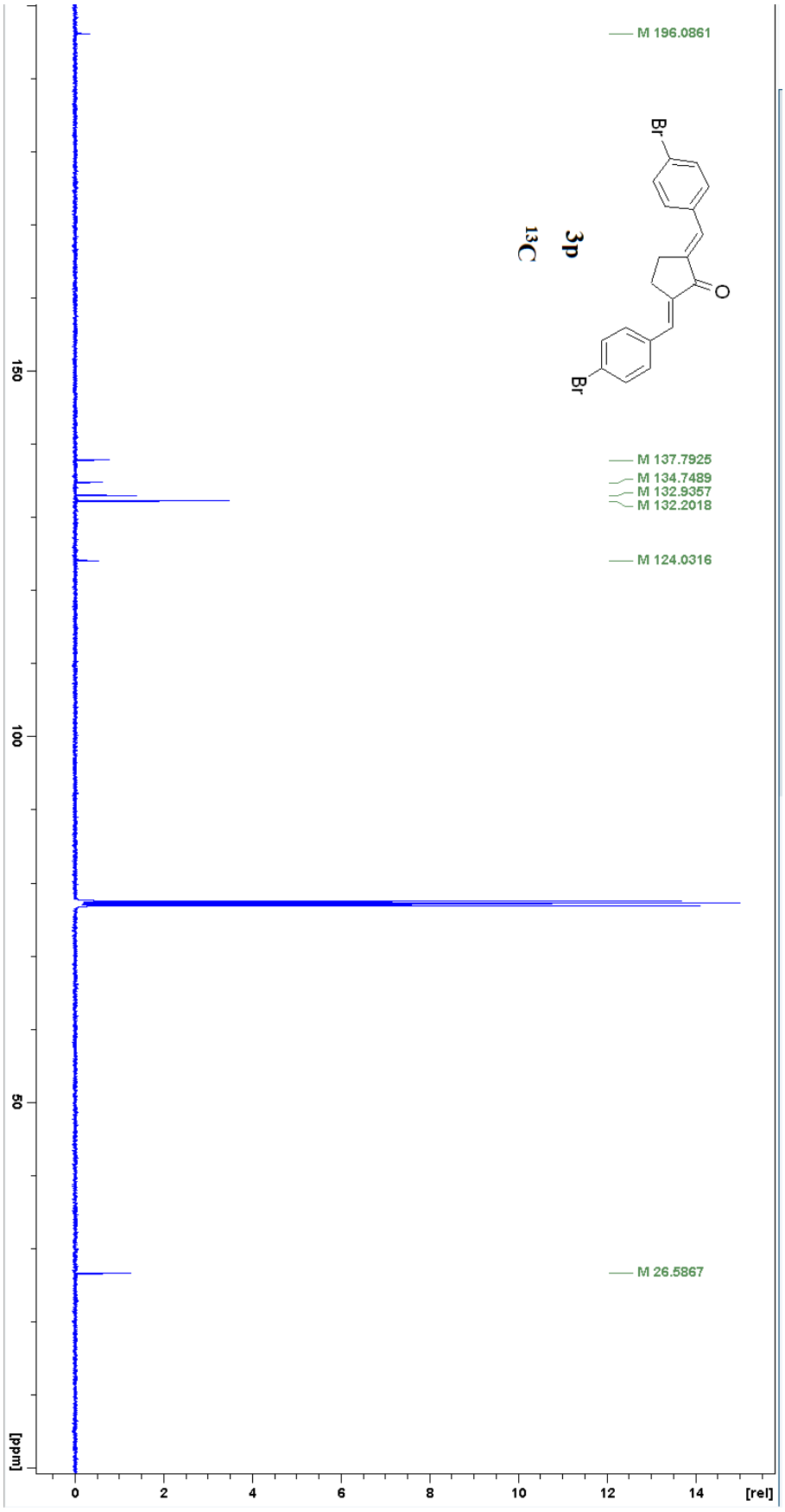
3o

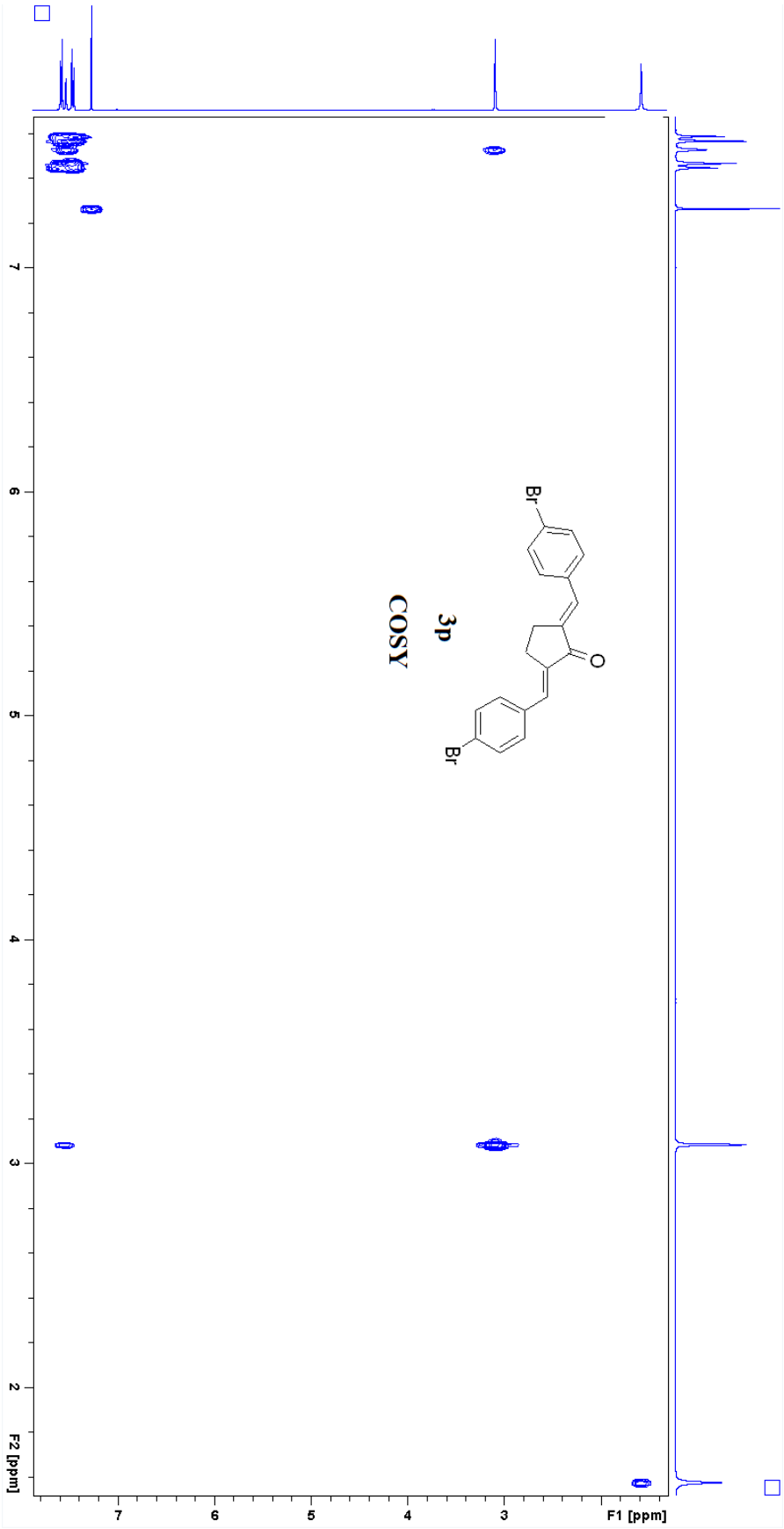
MS

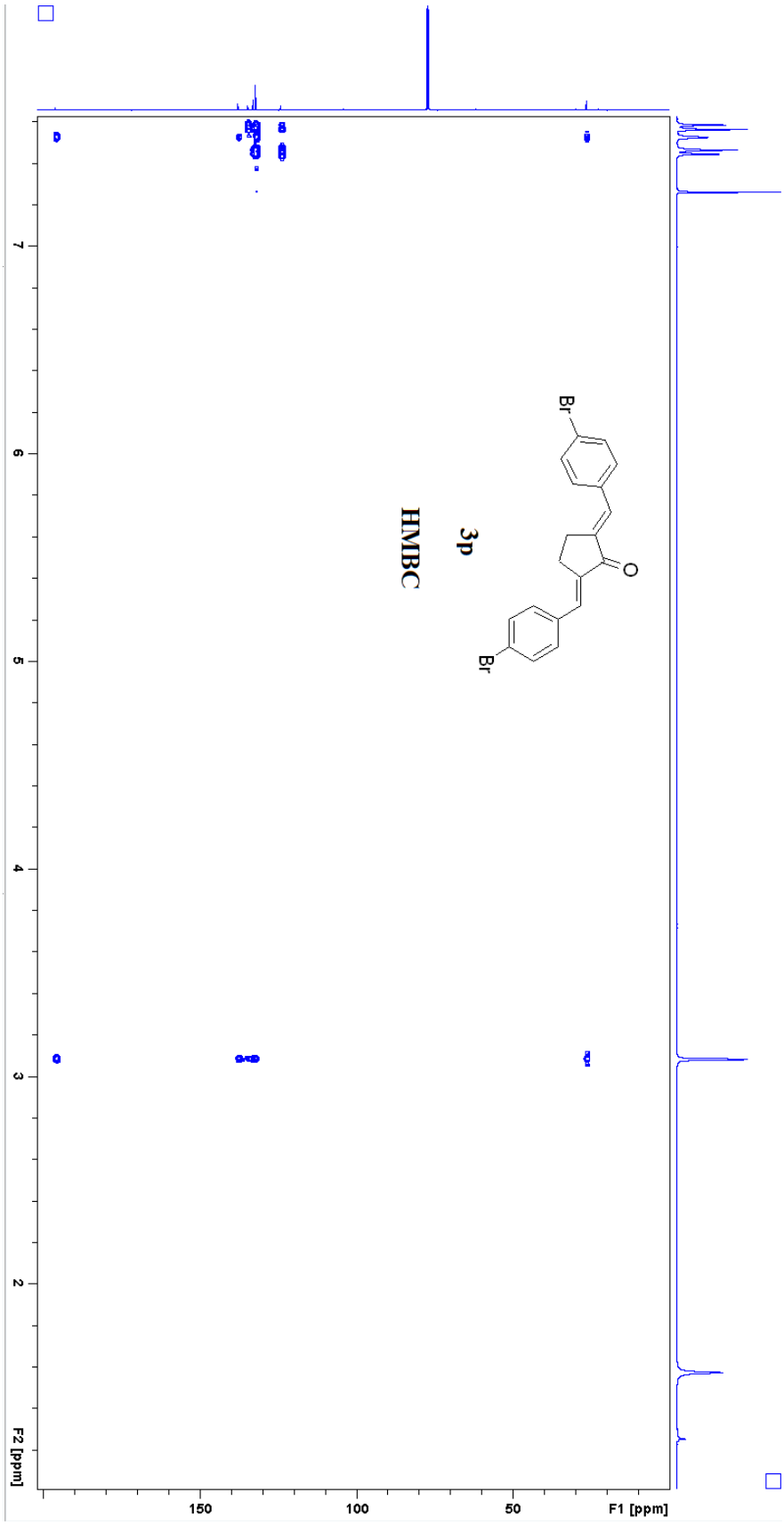
(2*E*, 5*E*)-2,5-bis(4-bromophenylmethylene)cyclopentanone (3p)

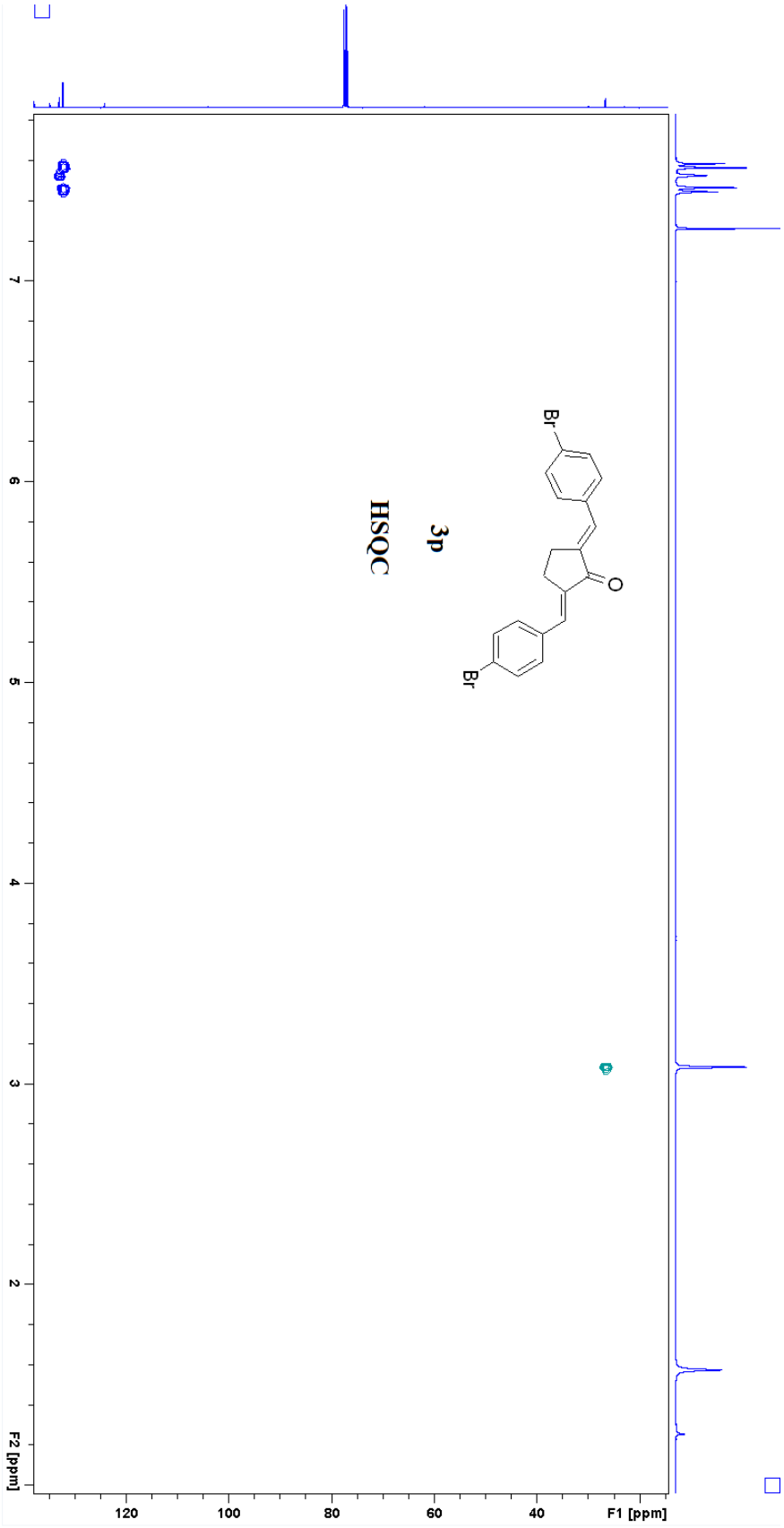


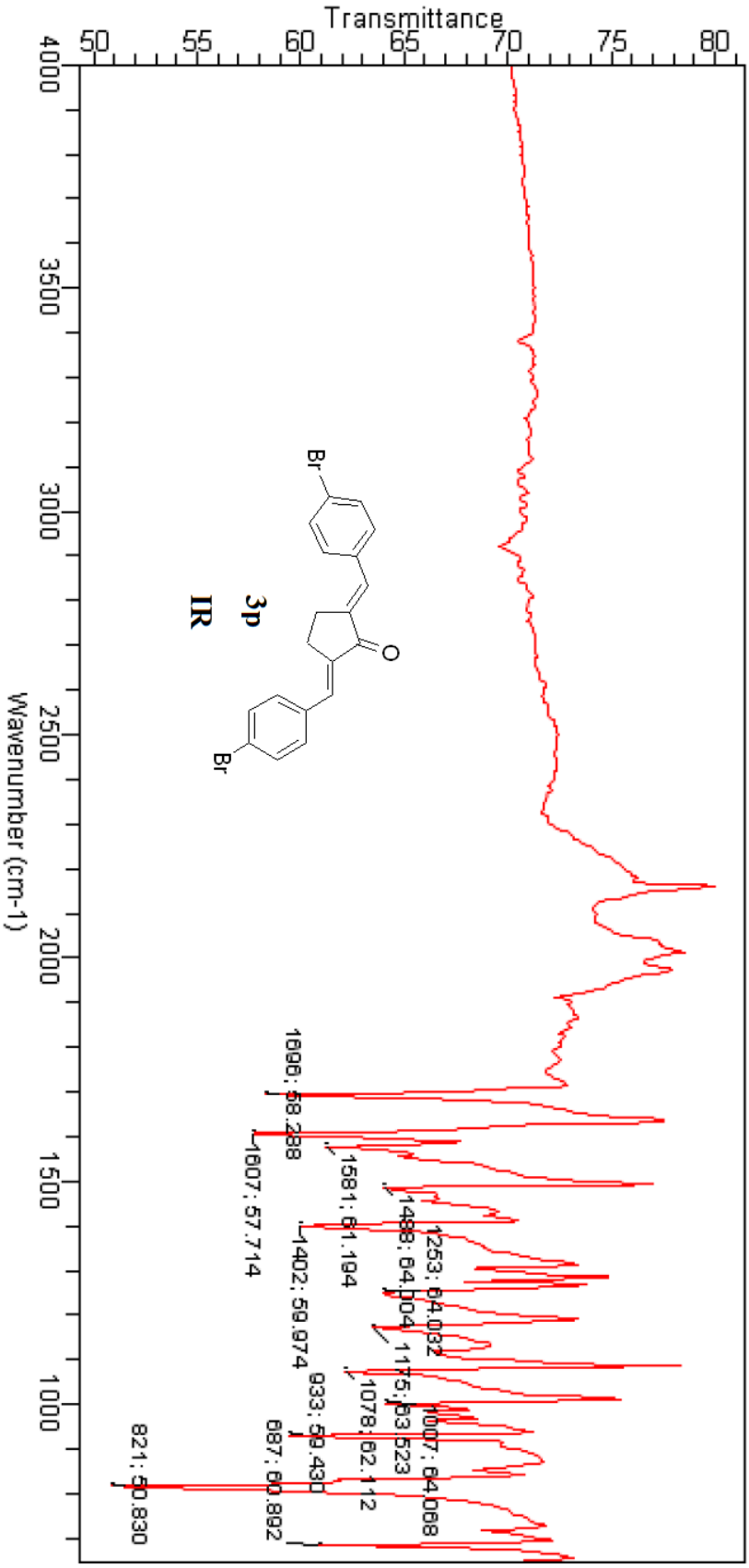

7.5827
7.5614
7.5235
7.4630
7.4416
3.9732
3.9617
4.0000
M 3.0812
Br
Br
O
3p
1H
[ppm]
[rel]

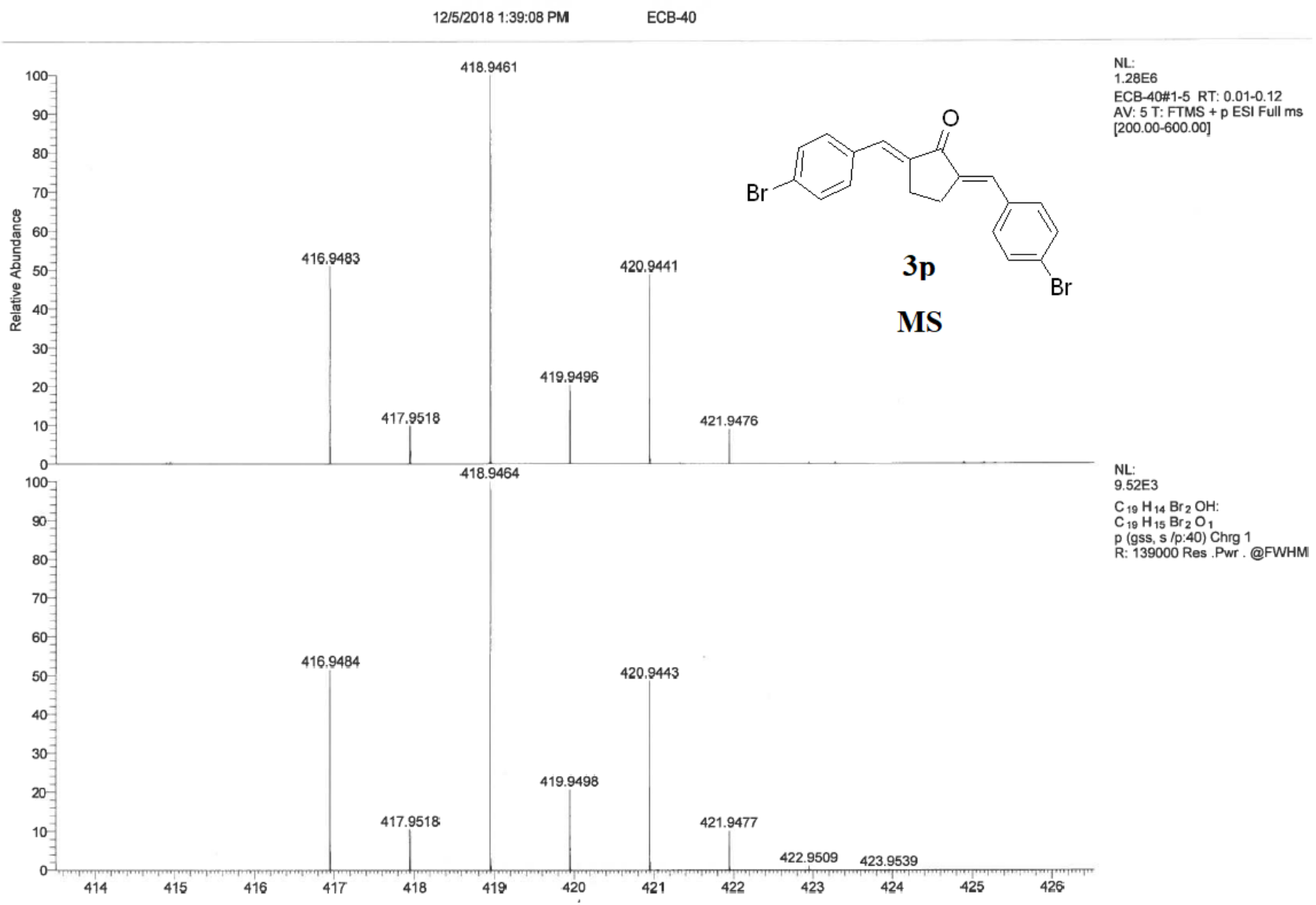

M 196.0861
Br
O
Br
3p
^{13}C
M 137.7925
M 134.7489
M 132.9357
M 132.2018
M 124.0316
M 26.5867
150
100
50
[ppm]
0
2
4
6
8
10
12
14
[rel]


3p
COSY
Br
O
Br
F2 [ppm]
F1 [ppm]
2
3
4
5
6
7

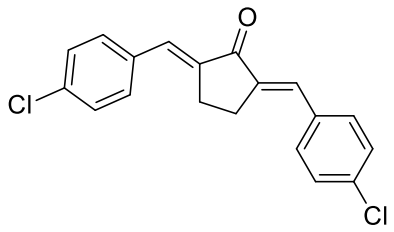

HMBC
3p
Br
O
Br
F2 [ppm]
F1 [ppm]
150
100
50
2
3
4
5
6
7

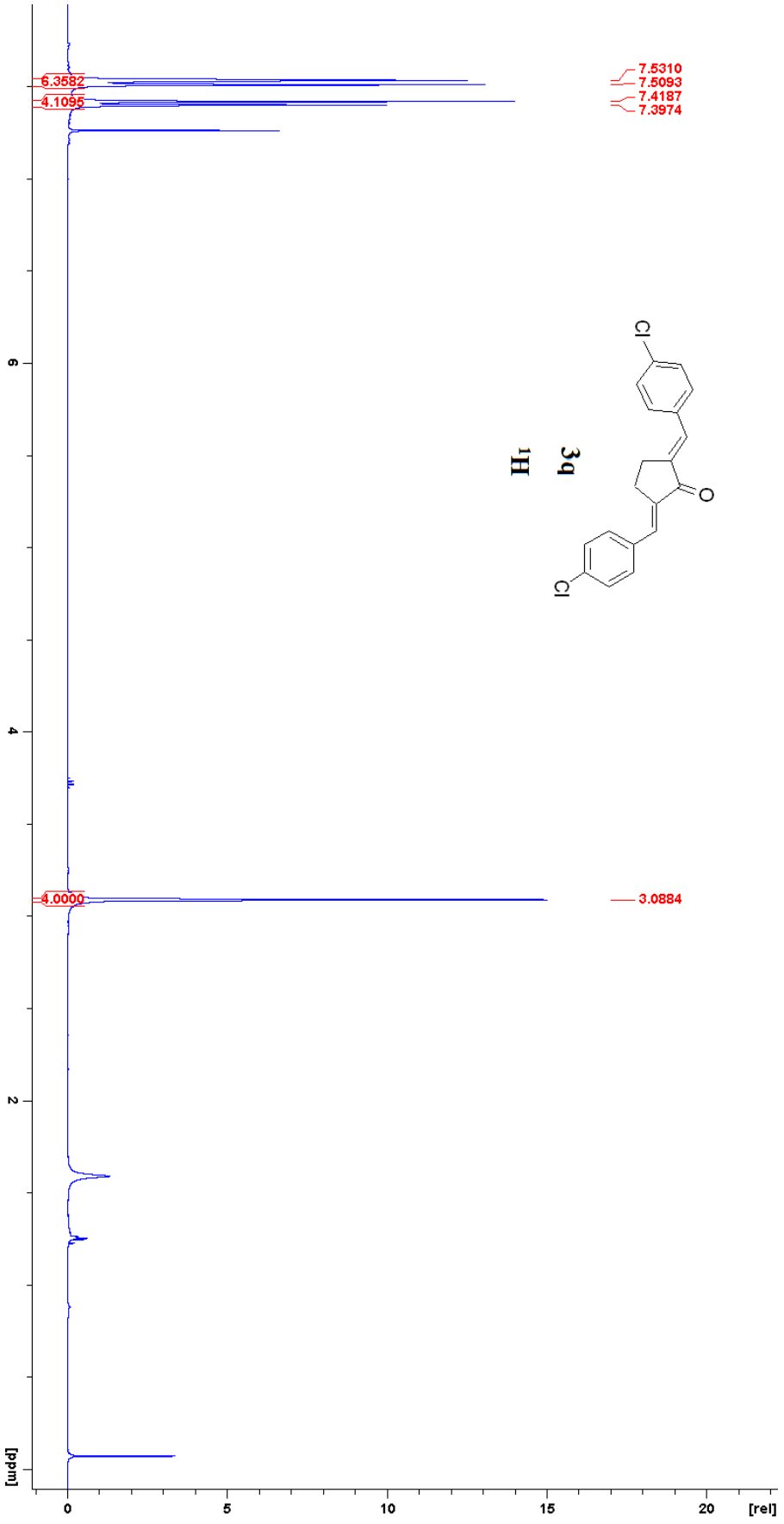

HSQC
3p
Br
O
Br
F2 [ppm]
F1 [ppm]
120
100
80
60
40
2
3
4
5
6
7

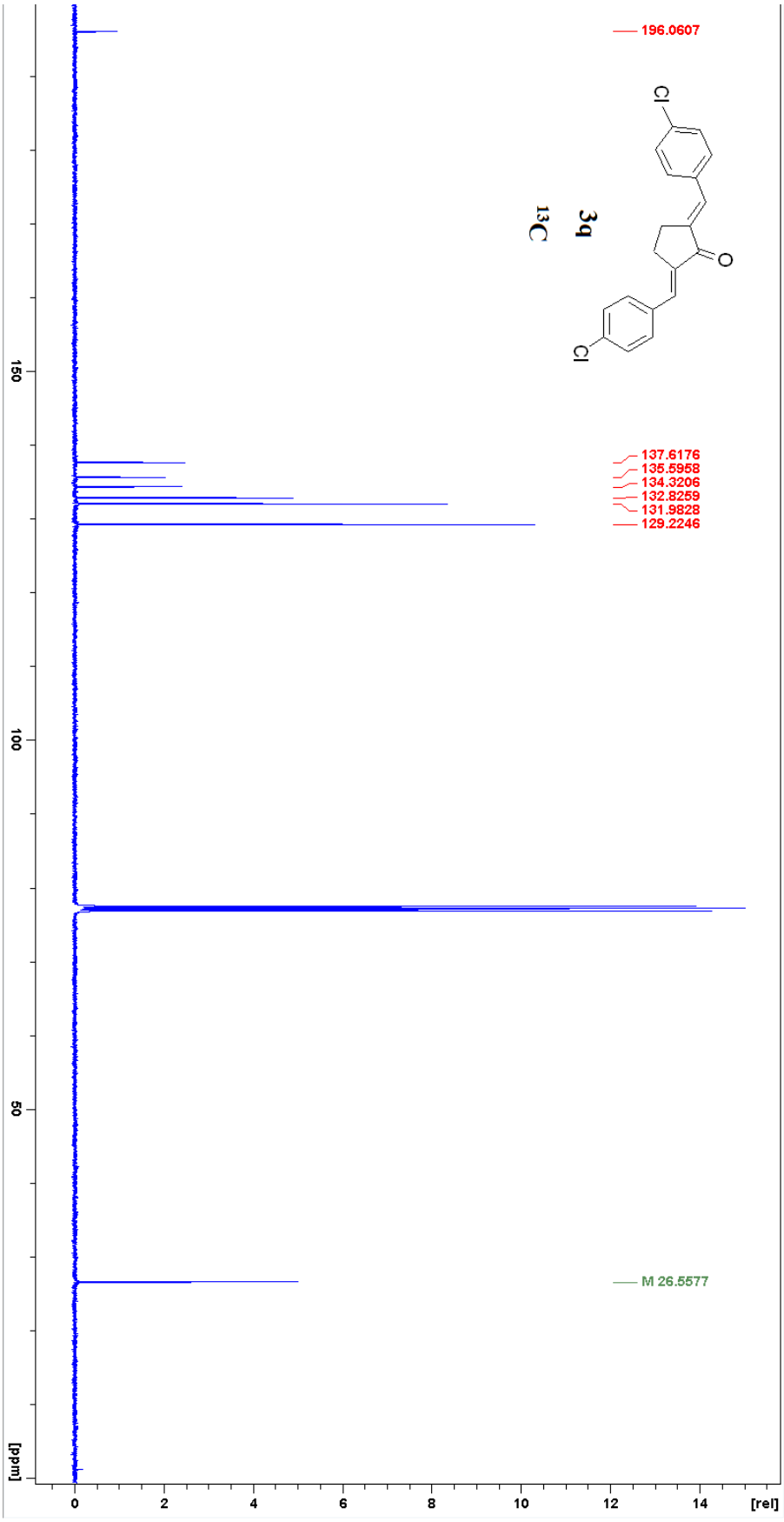

Transmittance
50
55
60
65
70
75
80
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
Br
O
Br
3p
IR
1696; 58.288
1607; 57.714
1581; 61.194
1488; 64.004
1402; 59.974
1253; 64.032
1175; 63.523
1078; 62.112
1007; 64.068
933; 59.430
821; 50.830
687; 60.892

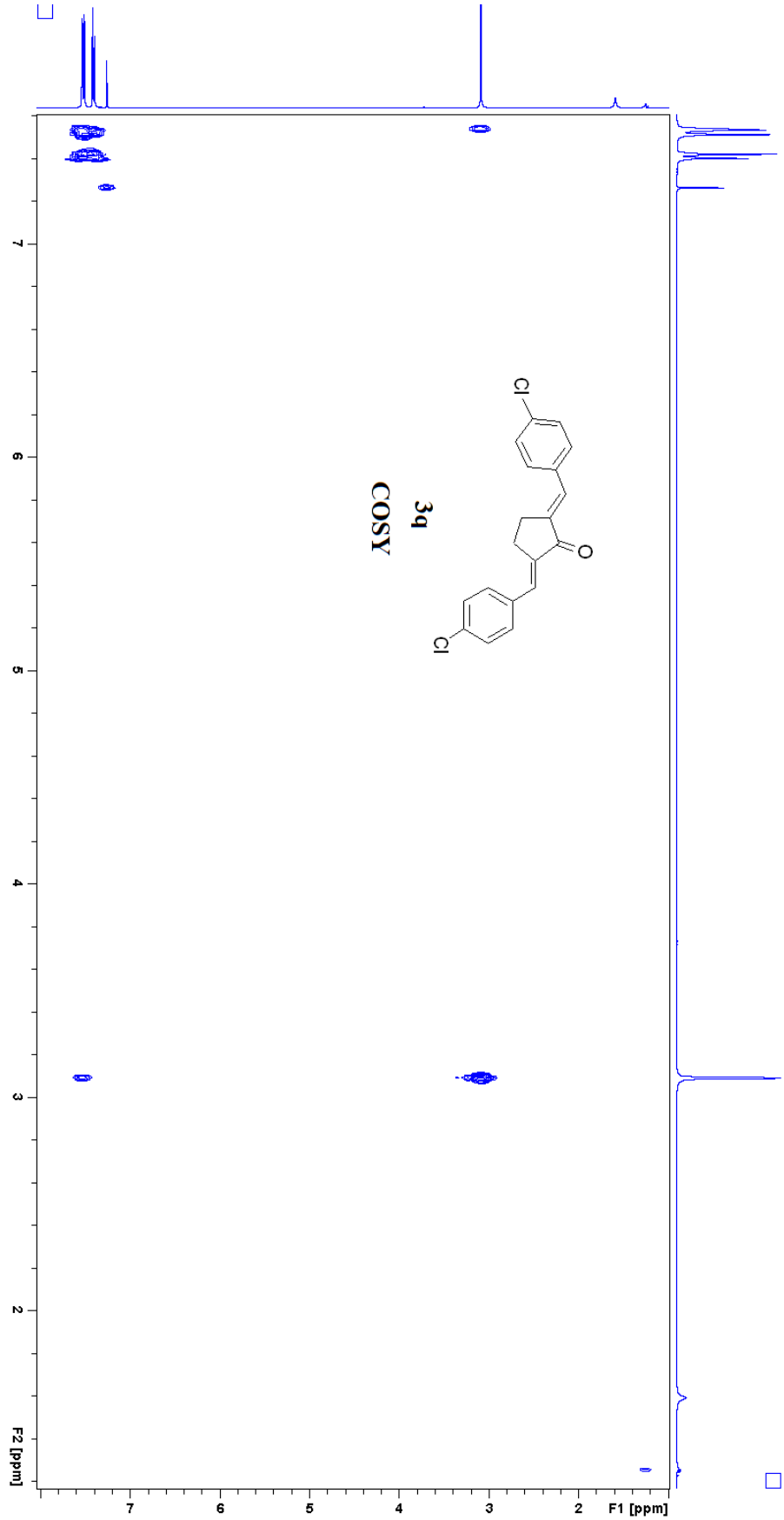

12/5/2018 1:39:08 PM
ECB-40
Relative Abundance
418.9461
416.9483
420.9441
419.9496
417.9518
421.9476
NL:
1.28E6
ECB-40#1-5 RT: 0.01-0.12
AV: 5 T: FTMS + p ESI Full ms
[200.00-600.00]
Br
O
Br
3p
MS
418.9464
416.9484
420.9443
419.9498
417.9518
421.9477
422.9509
423.9539
NL:
9.52E3
C19 H14 Br2 OH:
C19 H15 Br2 O1
p (gss, s /p:40) Chrg 1
R: 139000 Res .Pwr . @FWHM
414
415
416
417
418
419
420
421
422
423
424
425
426

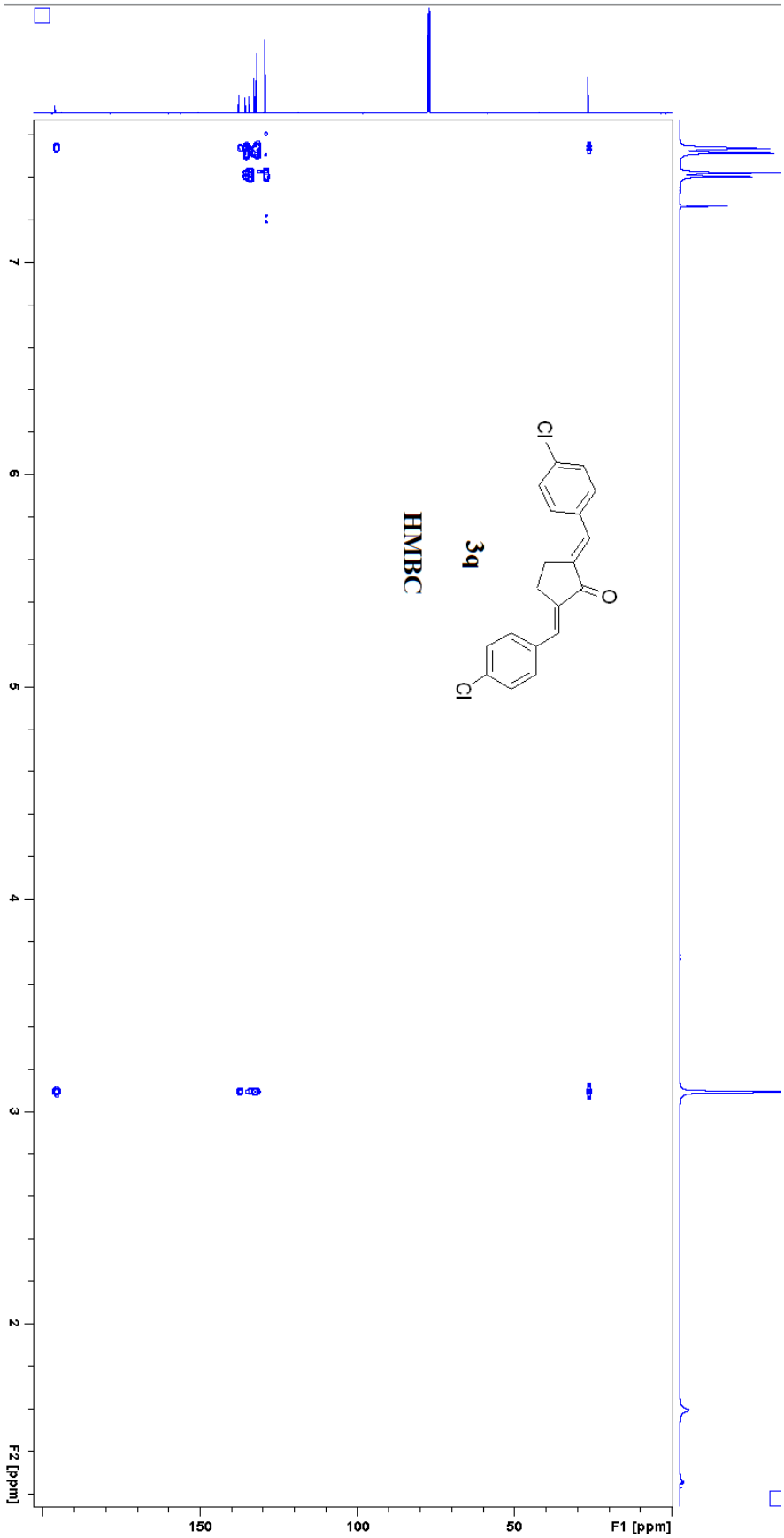
(2*E*, 5*E*)-2,5-bis(4-chlorophenylmethylene)cyclopentanone (3q)

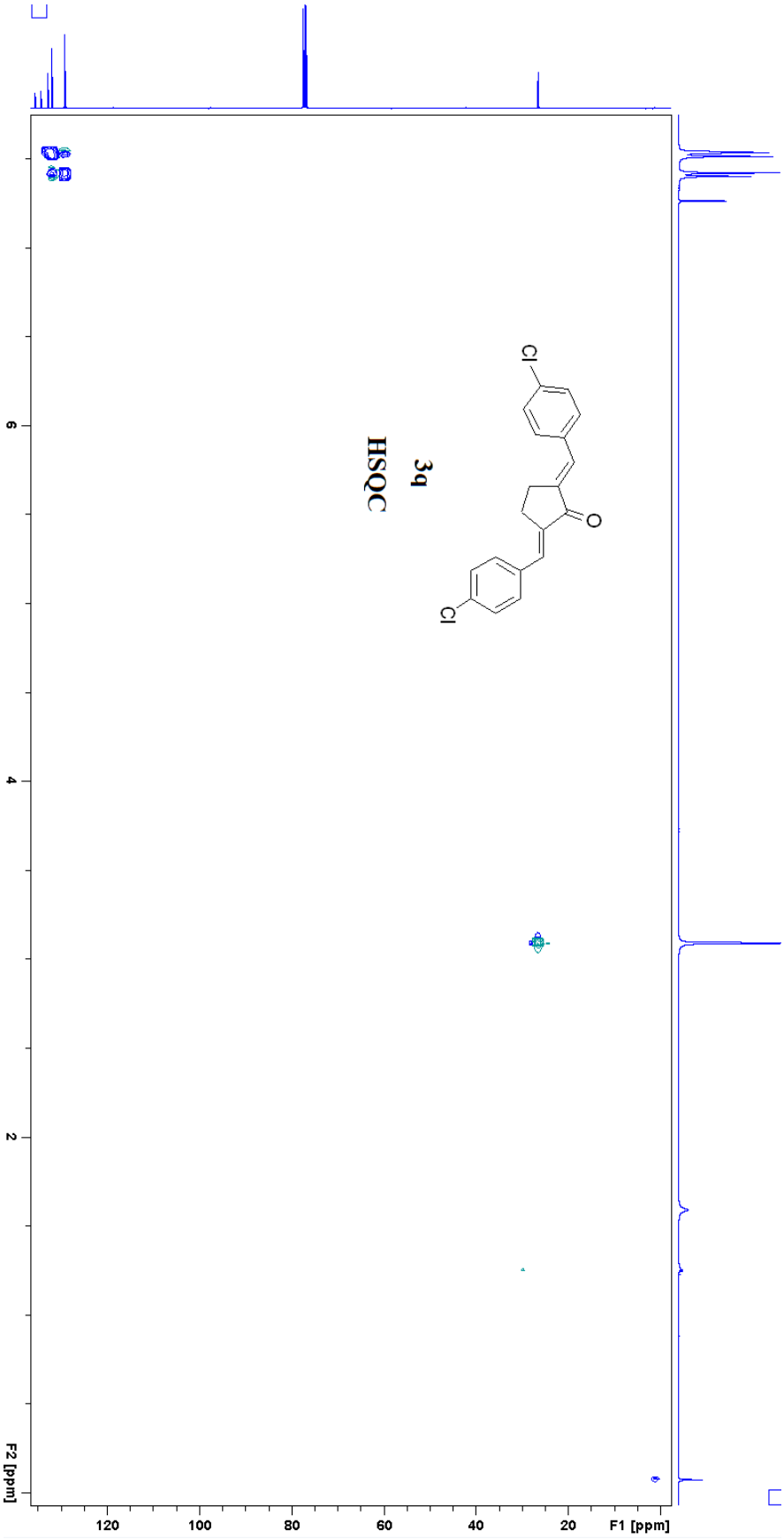


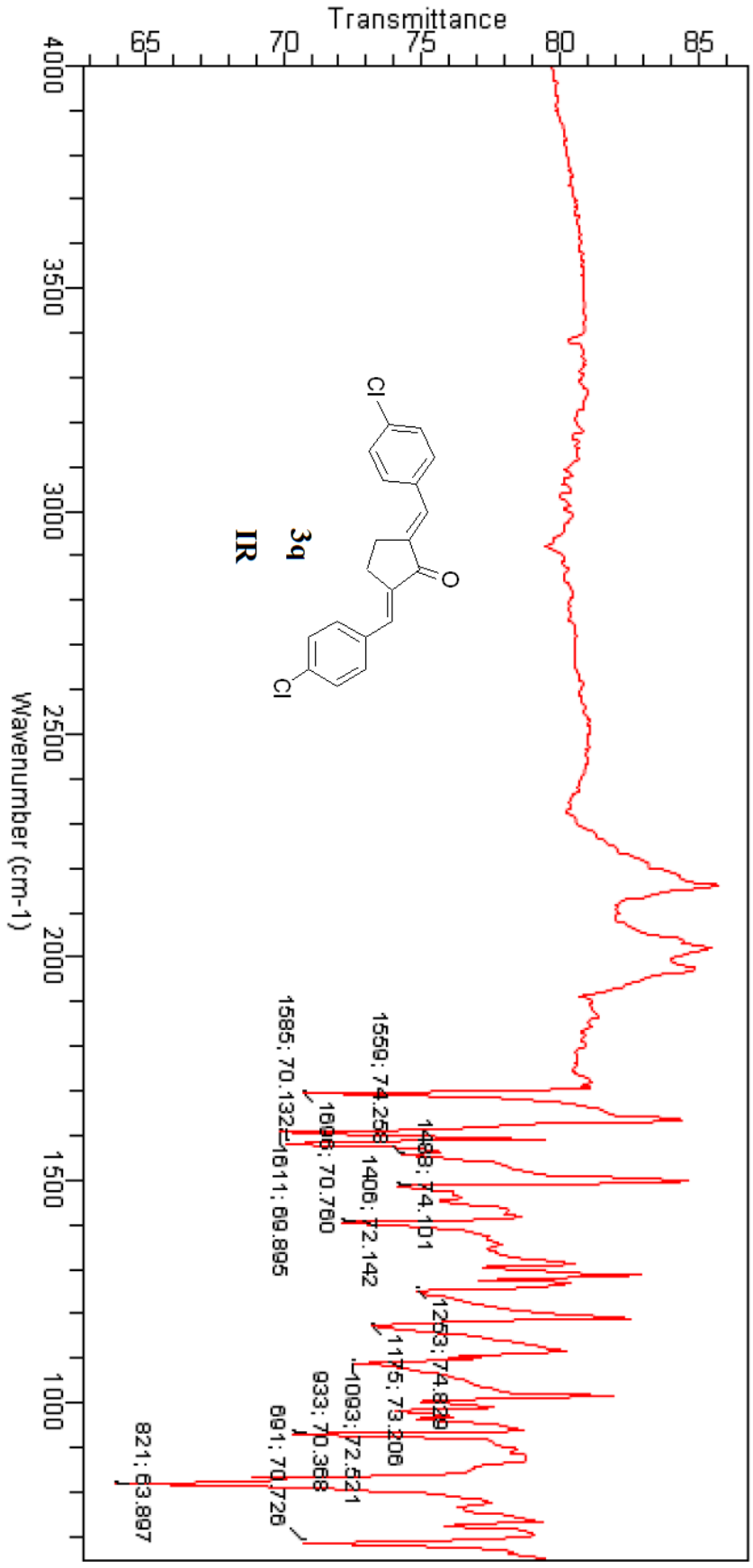

7.5310
7.5093
7.4187
7.3974
6.3582
4.1095
4.0000
3.0884
[ppm]
[rel]
0
5
10
15
20
2
4
6
^{1}H
3q
Cl
O
Cl


196.0607
137.6176
135.5958
134.3206
132.8259
131.9828
129.2246
M 26.5577
^{13}C 3q
Cl
O
Cl
150
100
50
[ppm]
0
2
4
6
8
10
12
14
[rel]

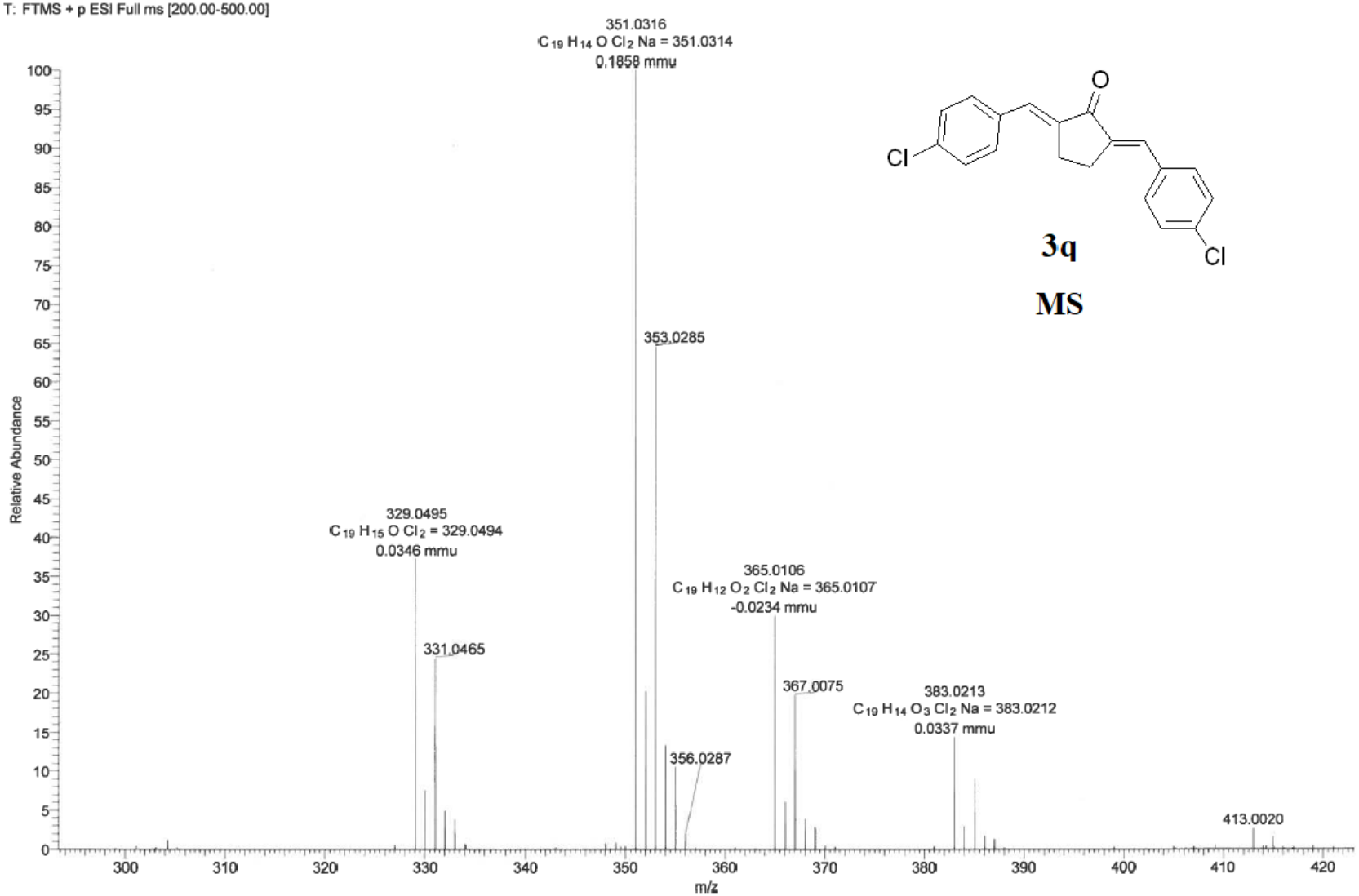

3q
COSY
Cl
O
Cl
F2 [ppm]
F1 [ppm]
7
6
5
4
3
2


HMBC
3q
Cl
O
Cl
F2 [ppm]
F1 [ppm]
150
100
50
2
3
4
5
6
7


HSQC
3q
Cl
O
Cl
F2 [ppm]
F1 [ppm]
120
100
80
60
40
20
2
4
6


Transmittance
65
70
75
80
85
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
3q
IR
Cl
O
Cl
1585; 70.132
1559; 74.258
1606; 70.760
1611; 69.895
1488; 74.101
1406; 72.142
1253; 74.829
1175; 73.206
1093; 72.521
933; 70.368
891; 70.726
821; 63.897

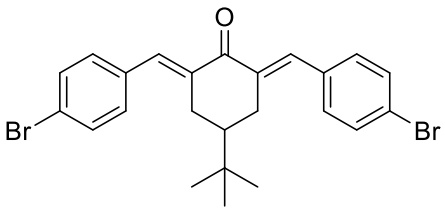
ECB-47 #1-5 RT: 0.00-0.11 AV: 5 NL: 2.87E7
T: FTMS + p ESI Full ms [200.00-500.00]

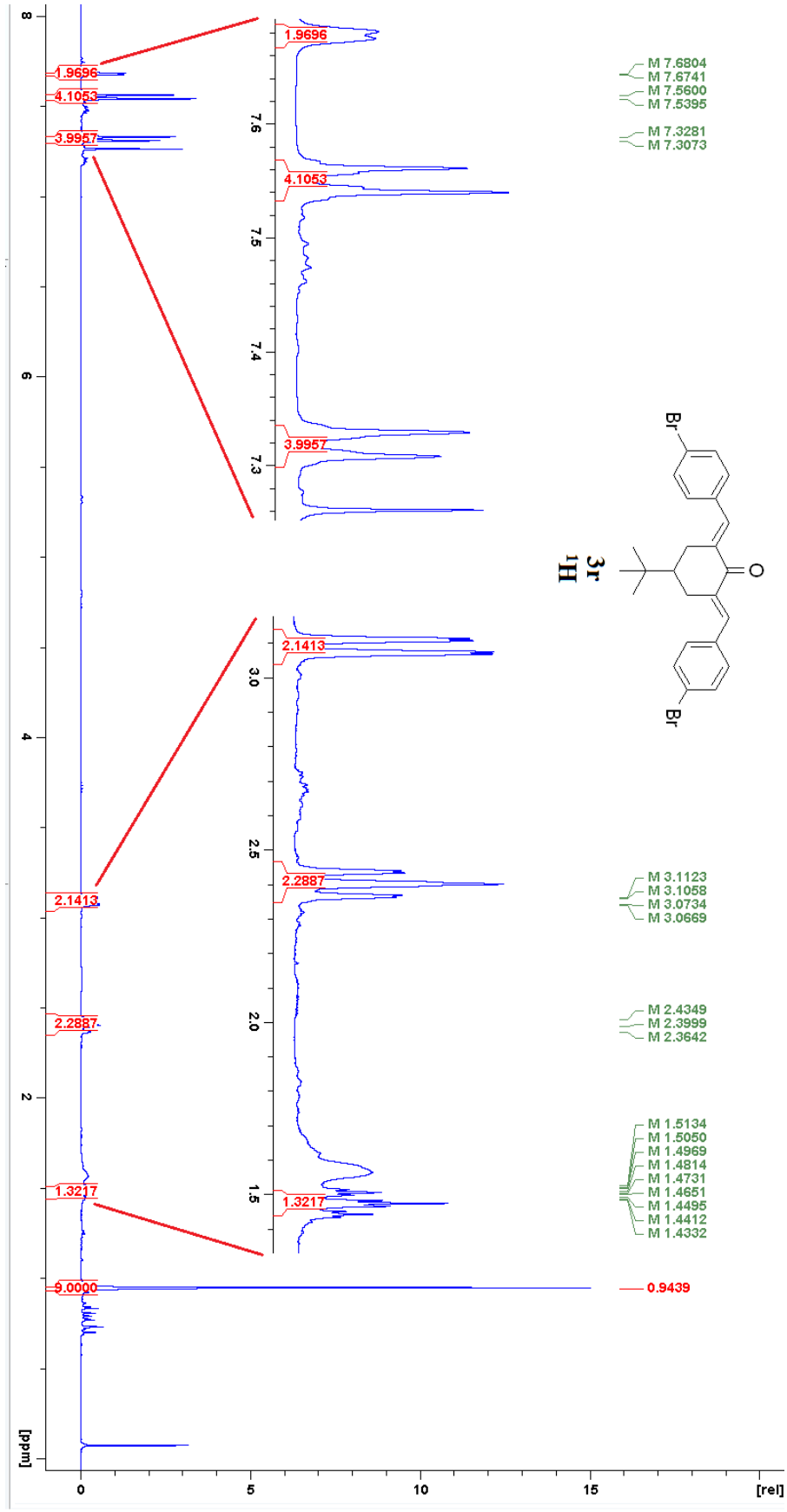


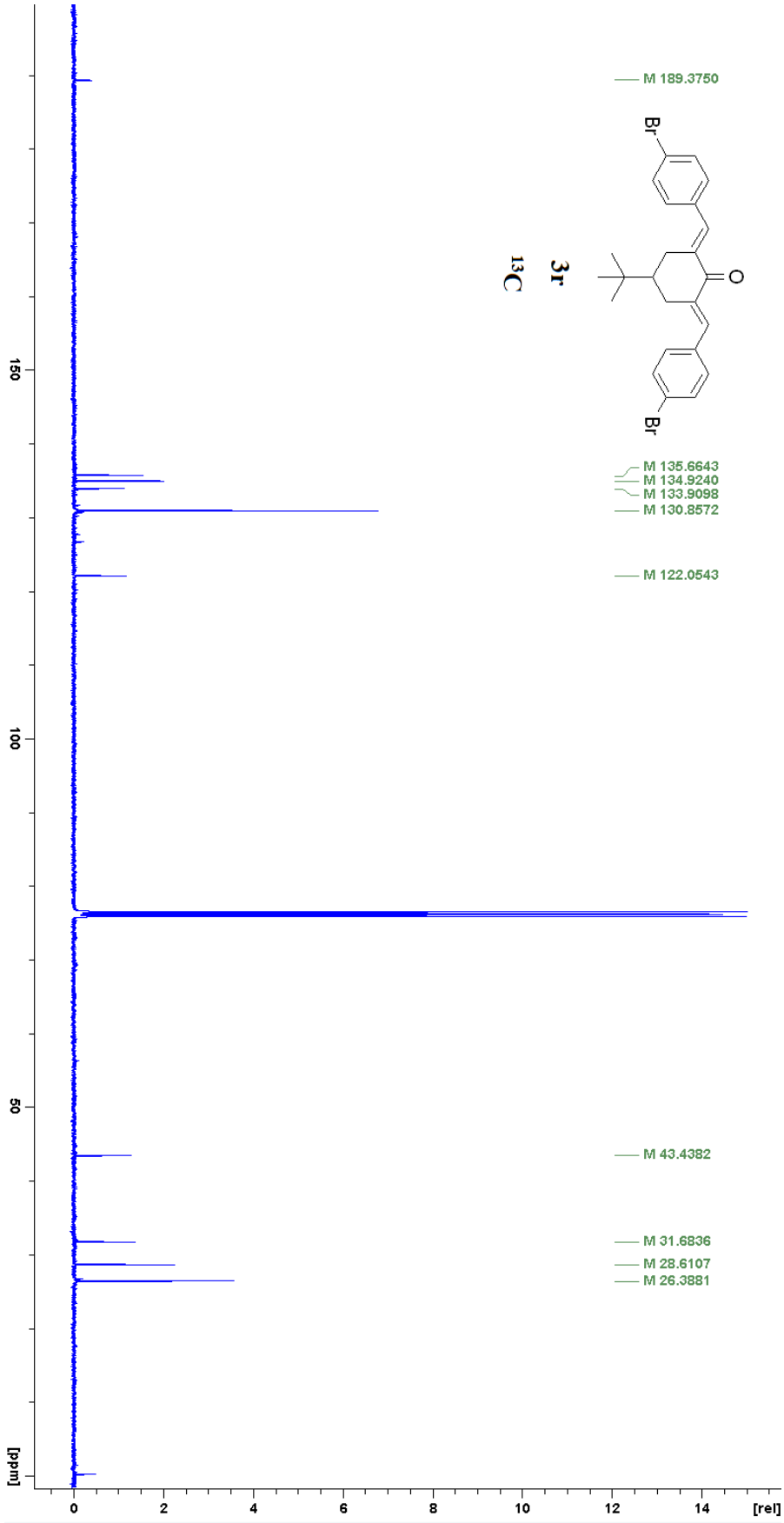
3q

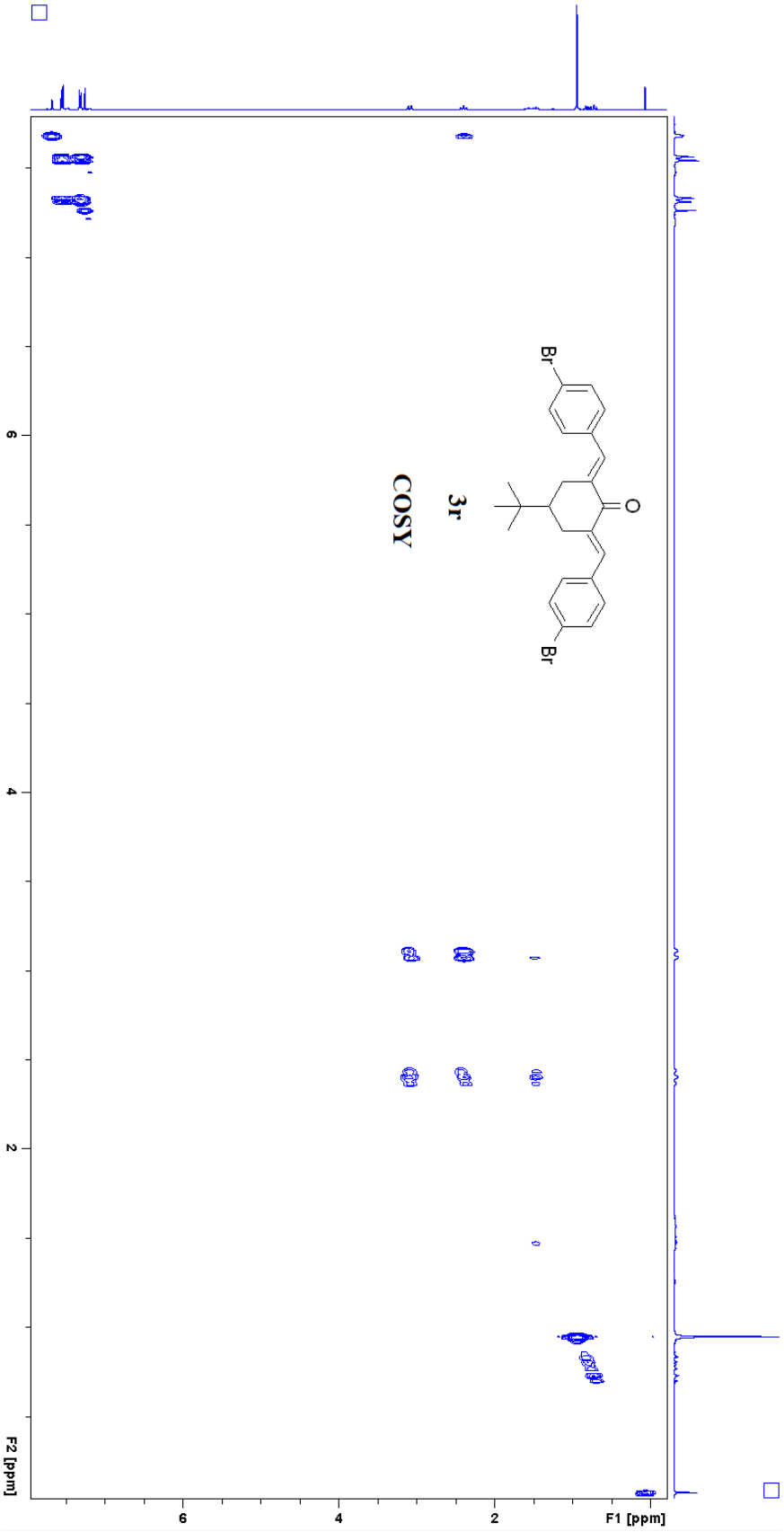
MS

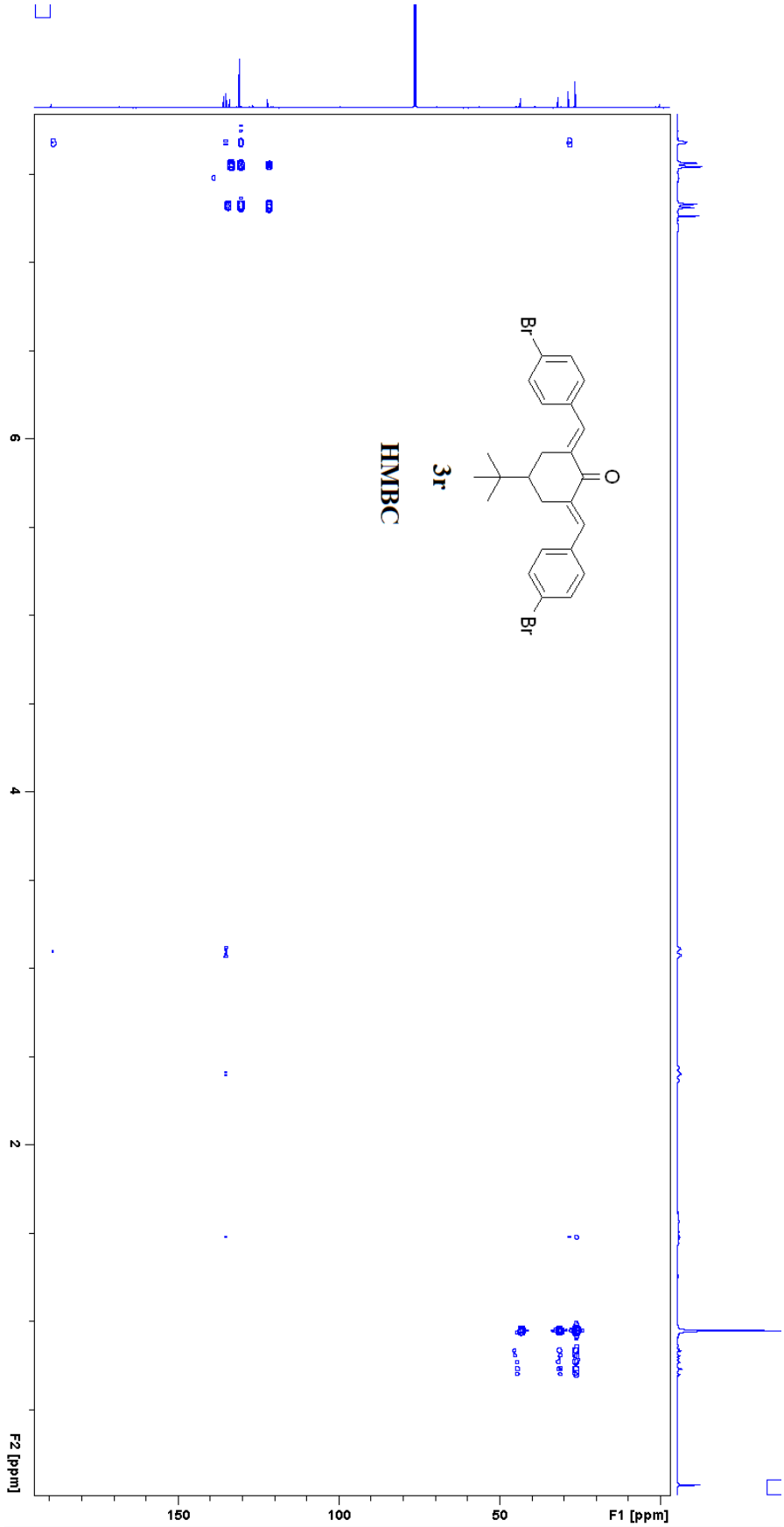
(2E, 6E)-2,6-bis(4-bromophenylmethylene)-4-*tert*-butylcyclohexanone (3r)

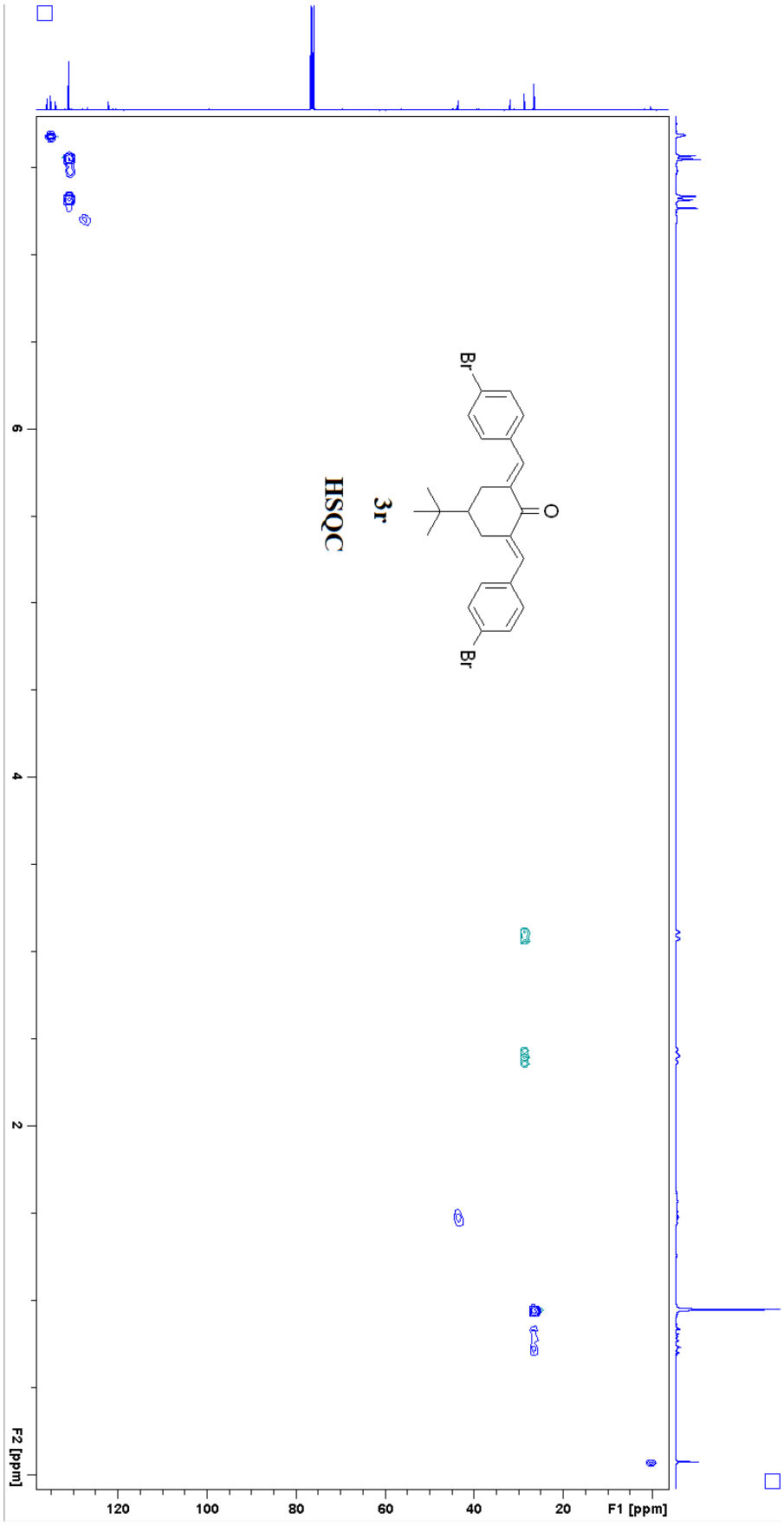



3r
1H
Br
Br
O
1.9696
4.1053
3.9957
2.1413
2.2887
1.3217
9.0000
M 7.6804
M 7.6741
M 7.5600
M 7.5395
M 7.3281
M 7.3073
M 3.1123
M 3.1058
M 3.0734
M 3.0669
M 2.4349
M 2.3999
M 2.3642
M 1.5134
M 1.5050
M 1.4969
M 1.4814
M 1.4731
M 1.4651
M 1.4495
M 1.4412
M 1.4332
0.9439
[ppm]
[rel]

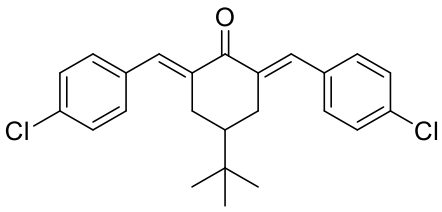

13C
3r
M 189.3750
M 135.6643
M 134.9240
M 133.9098
M 130.8572
M 122.0543
M 43.4382
M 31.6836
M 28.6107
M 26.3881
Br
Br
O
150
100
50
[ppm]
0
2
4
6
8
10
12
14
[rel]

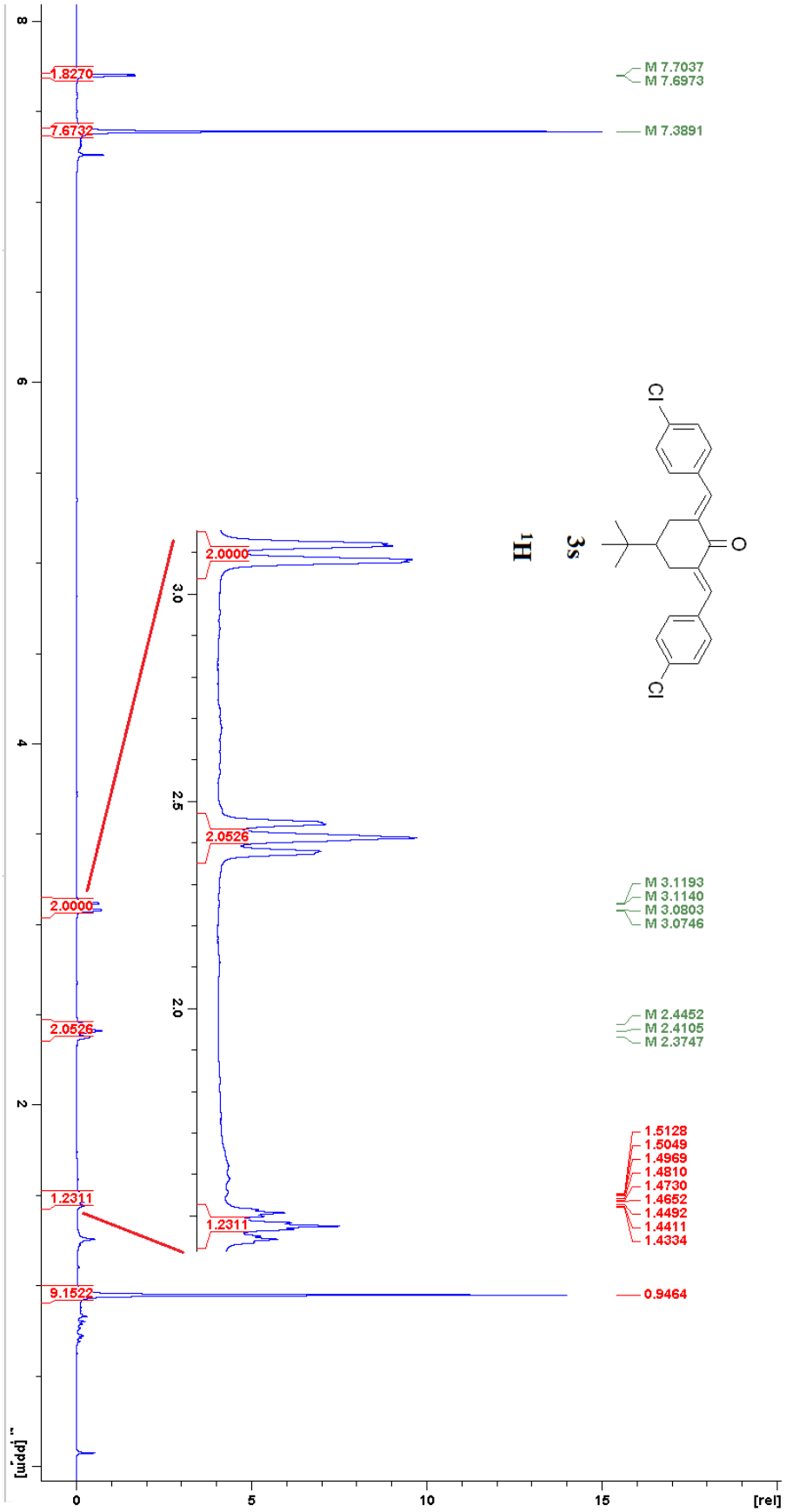

COSY
3r
Br
Br
O
F2 [ppm]
F1 [ppm]
6
4
2
6
4
2

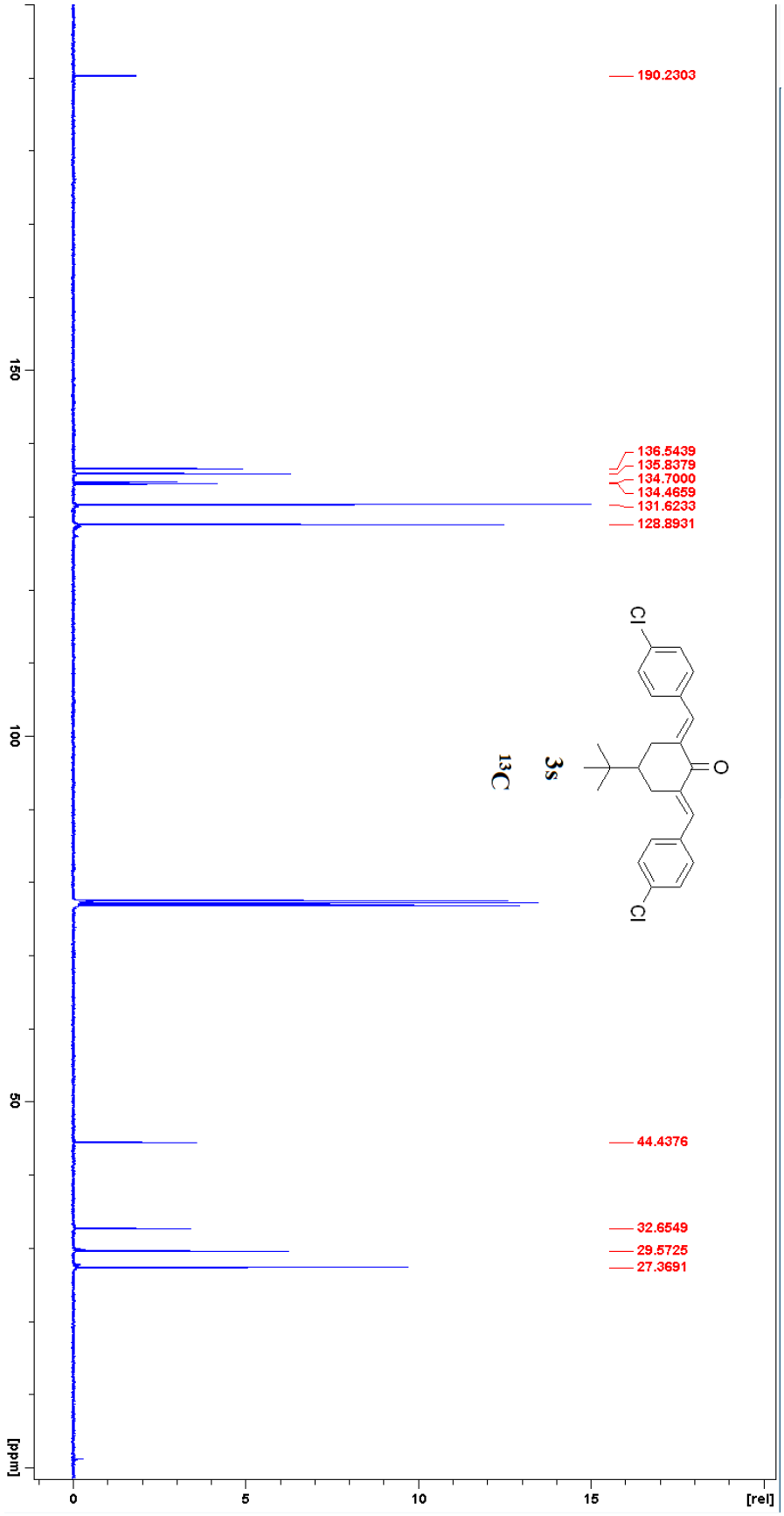

HMBC
3r
Br
Br
O
F2 [ppm]
F1 [ppm]
150
100
50
2
4
6

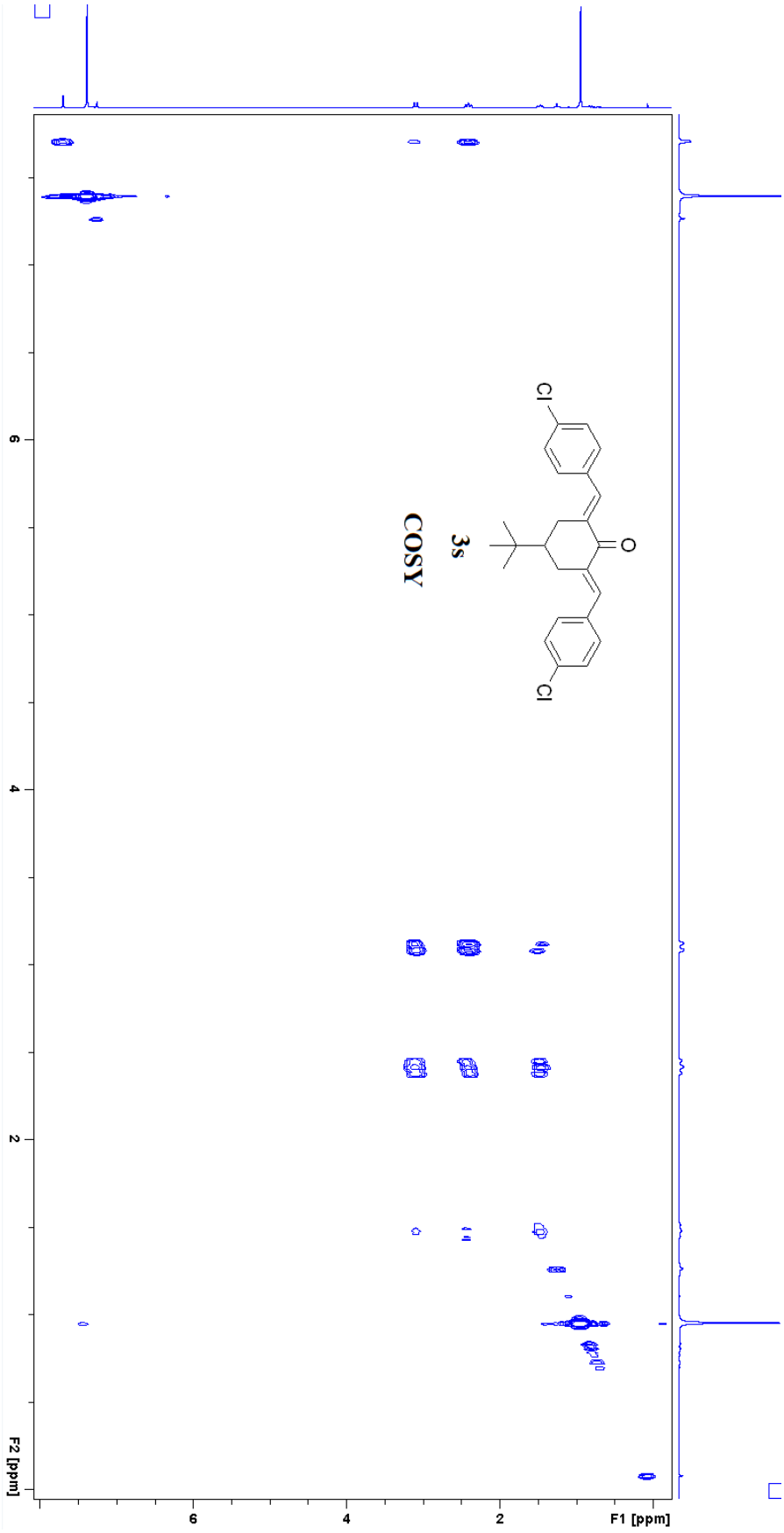

HSQC
3r
Br
Br
O
F2 [ppm]
F1 [ppm]
120
100
80
60
40
20
2
4
6

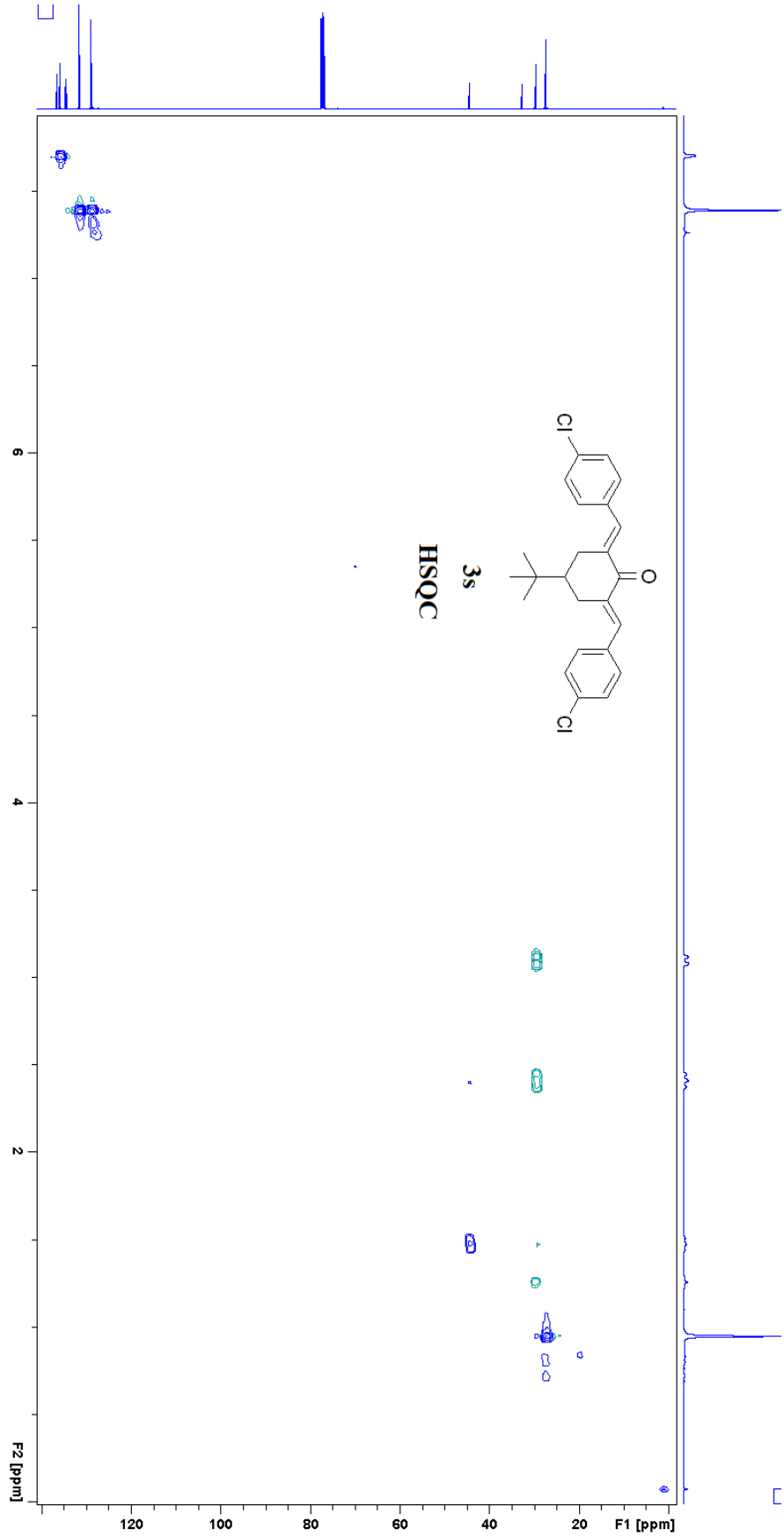
(2E, 6E)-2,6-bis(4-chlorophenylmethylene)-4-tertbutylcyclohexanone (3s)

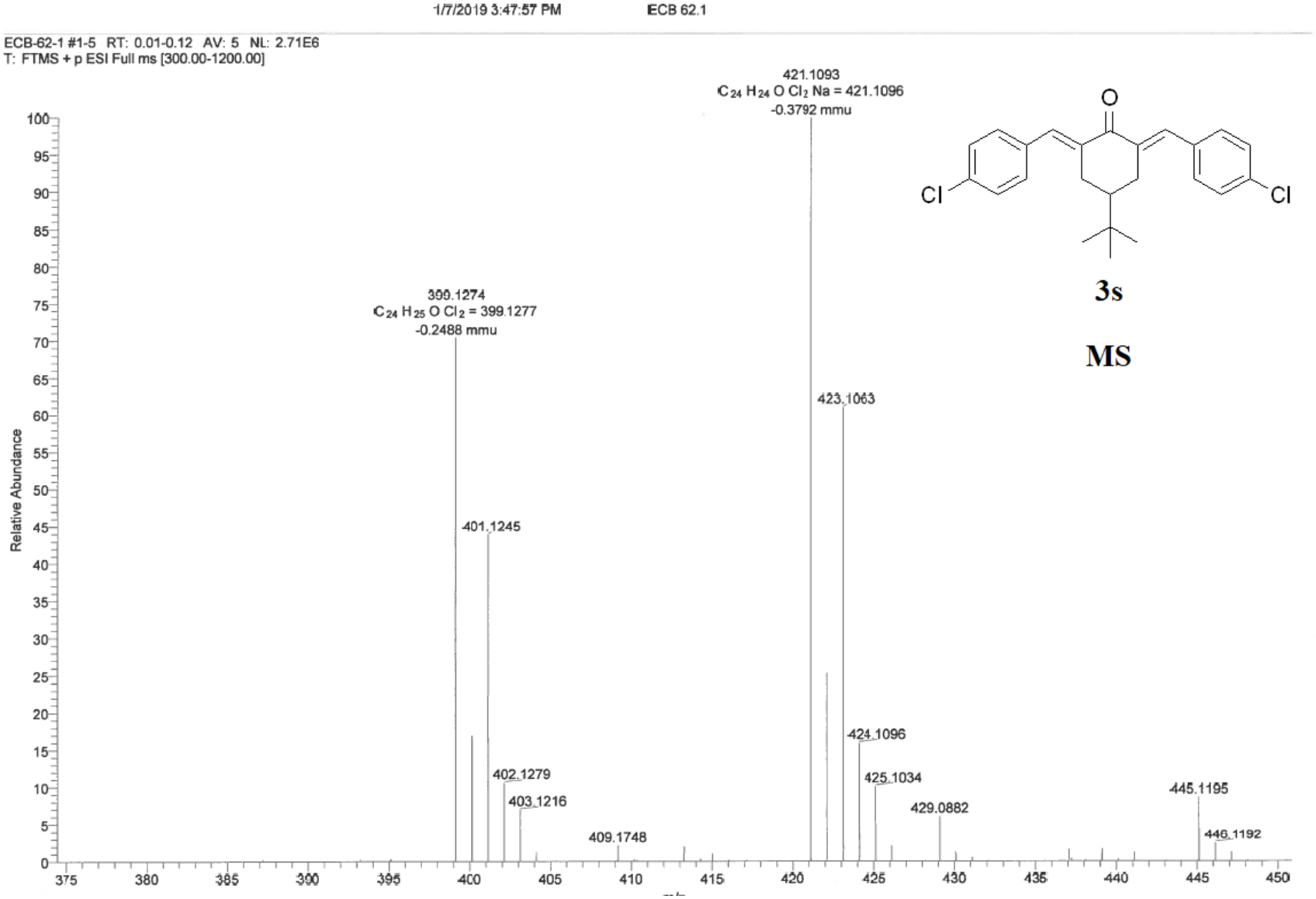



1H
3s
Cl
Cl
O
1.8270
7.6732
2.0000
2.0526
1.2311
9.1522
M 7.7037
M 7.6973
M 7.3891
M 3.1193
M 3.1140
M 3.0803
M 3.0746
M 2.4452
M 2.4105
M 2.3747
1.5128
1.5049
1.4969
1.4810
1.4730
1.4652
1.4492
1.4411
1.4334
0.9464
[ppm]
[rel]

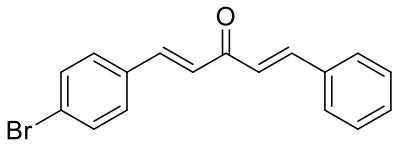

190.2303
136.5439
135.8379
134.7000
134.4659
131.6233
128.8931
44.4376
32.6549
29.5725
27.3691
150
100
50
[ppm]
0
5
10
15
[rel]
^{13}C
3s
Cl
O
Cl

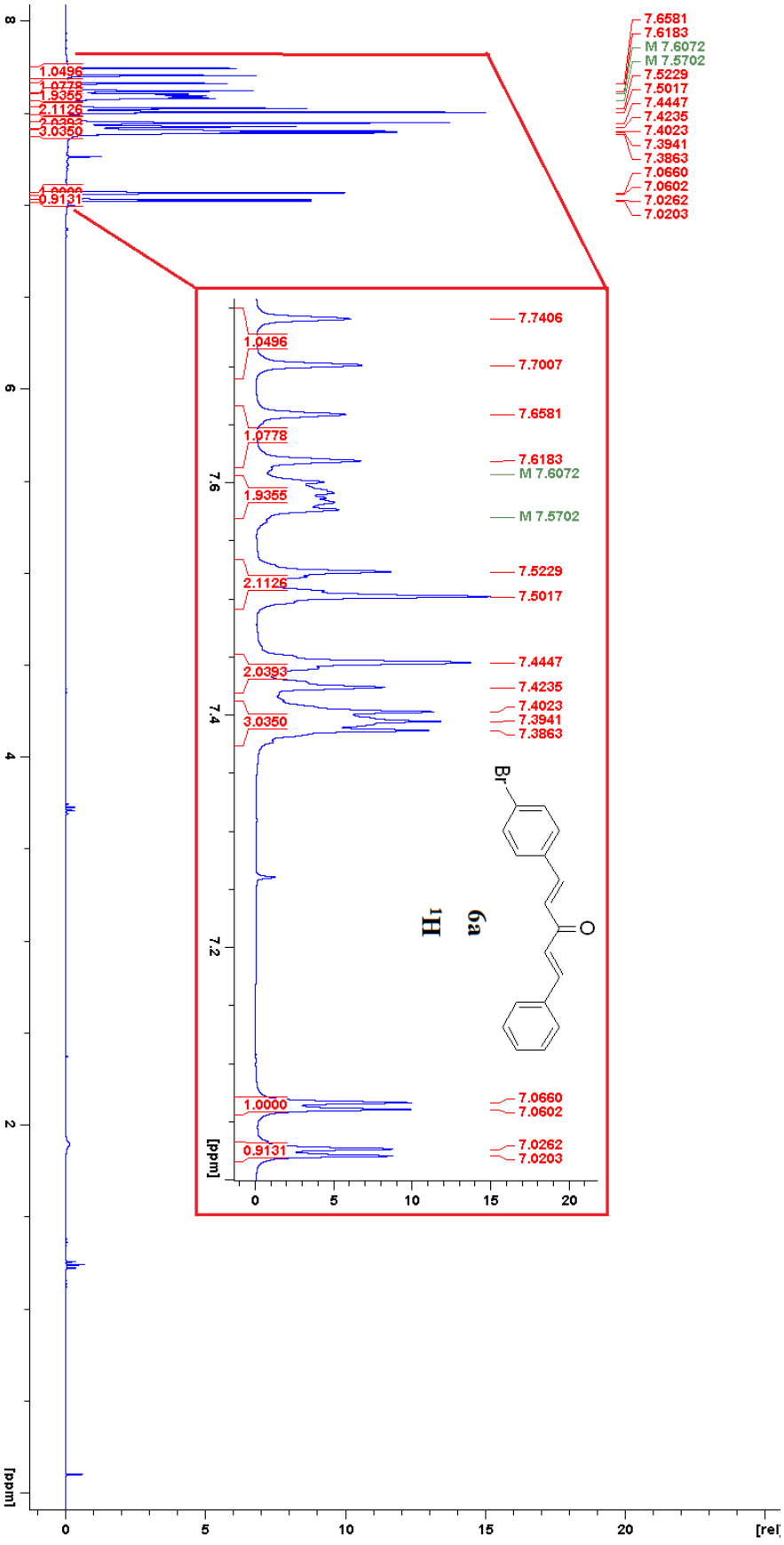

COSY
3s
Cl
O
Cl
F2 [ppm]
F1 [ppm]
6
4
2

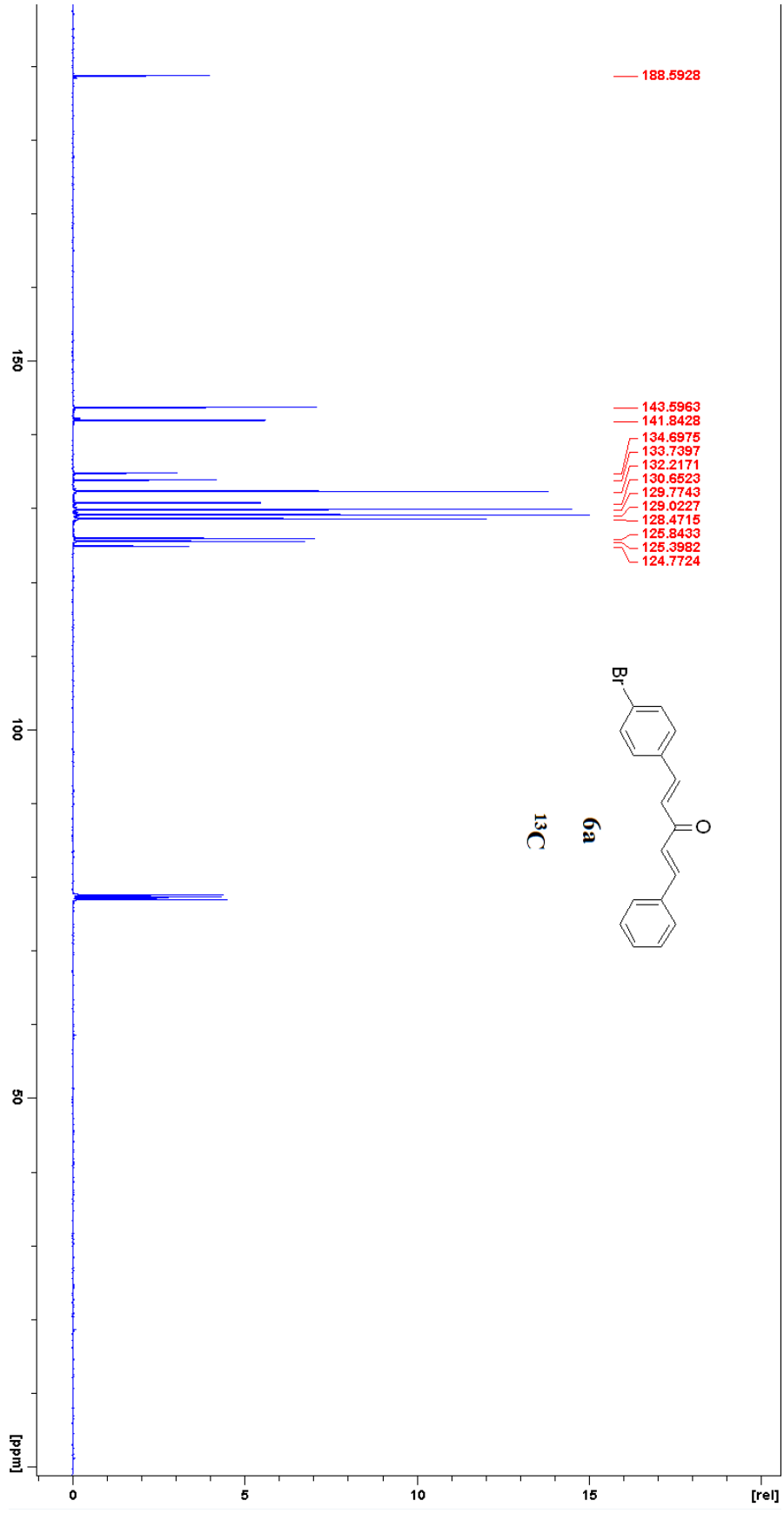

HSQC
3s
Cl
O
Cl
F2 [ppm]
F1 [ppm]
120
100
80
60
40
20
2
4
6

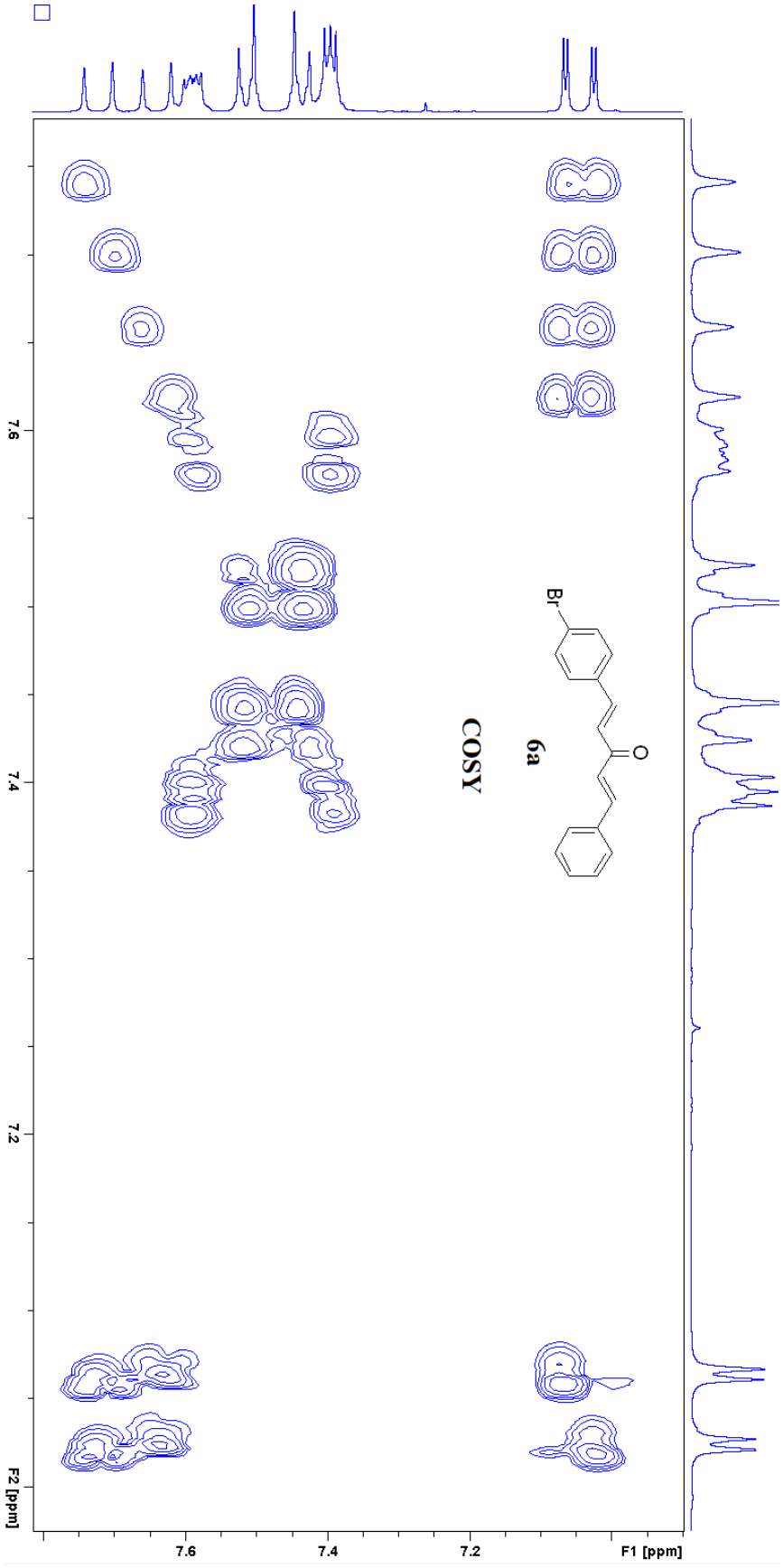

1/7/2019 3:47:57 PM
ECB 62.1
ECB-62-1 #1-5 RT: 0.01-0.12 AV: 5 NL: 2.71E6
T: FTMS + p ESI Full ms [300.00-1200.00]
421.1093
C24 H24 O Cl2 Na = 421.1096
-0.3792 mmu
399.1274
C24 H25 O Cl2 = 399.1277
-0.2488 mmu
401.1245
423.1063
424.1096
402.1279
425.1034
403.1216
429.0882
409.1748
445.1195
446.1192
Relative Abundance
O
Cl
Cl
3s
MS

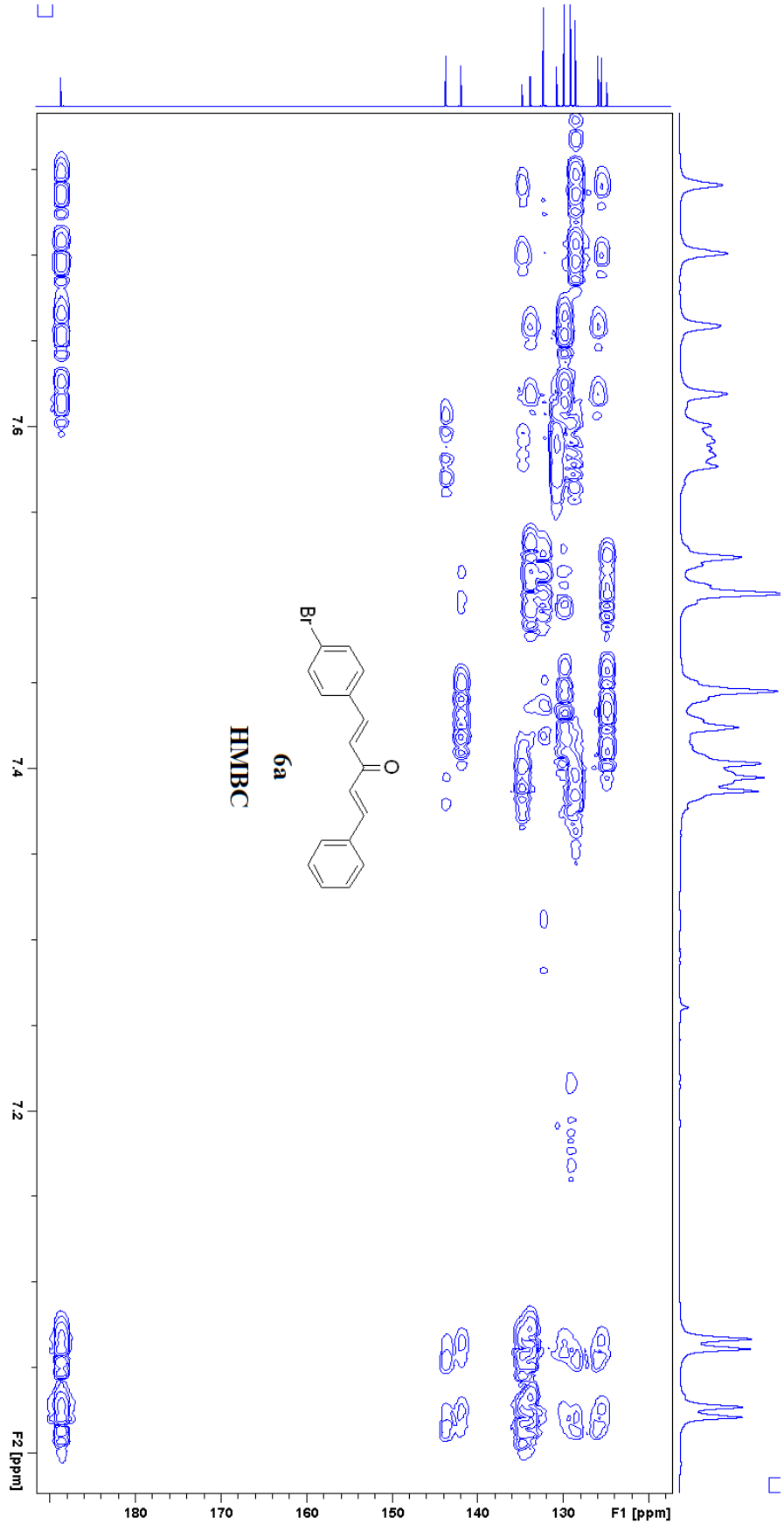
(1*E*,4*E*)-1-(4-bromophenyl)penta-1,4-dien-3-one (6a)

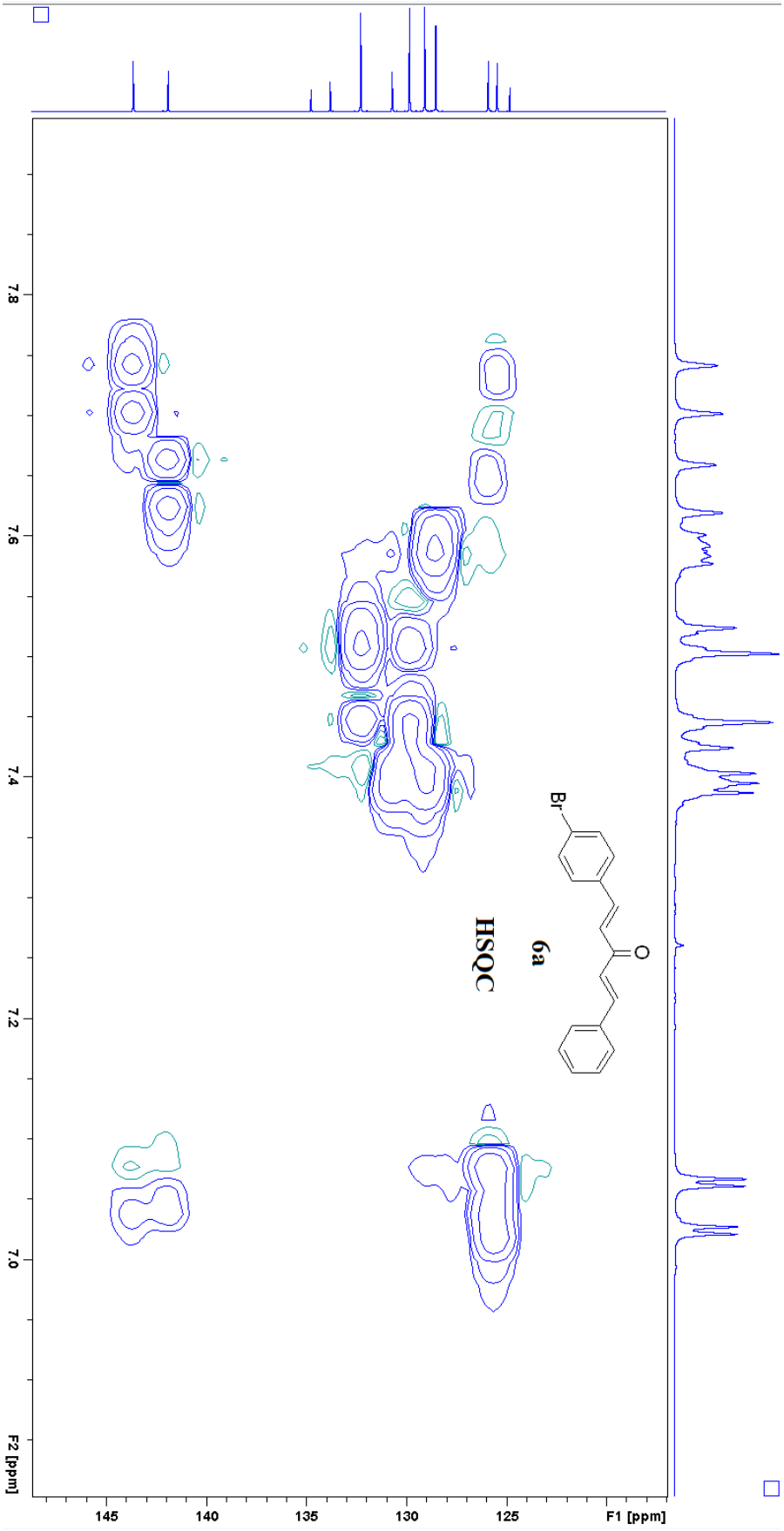


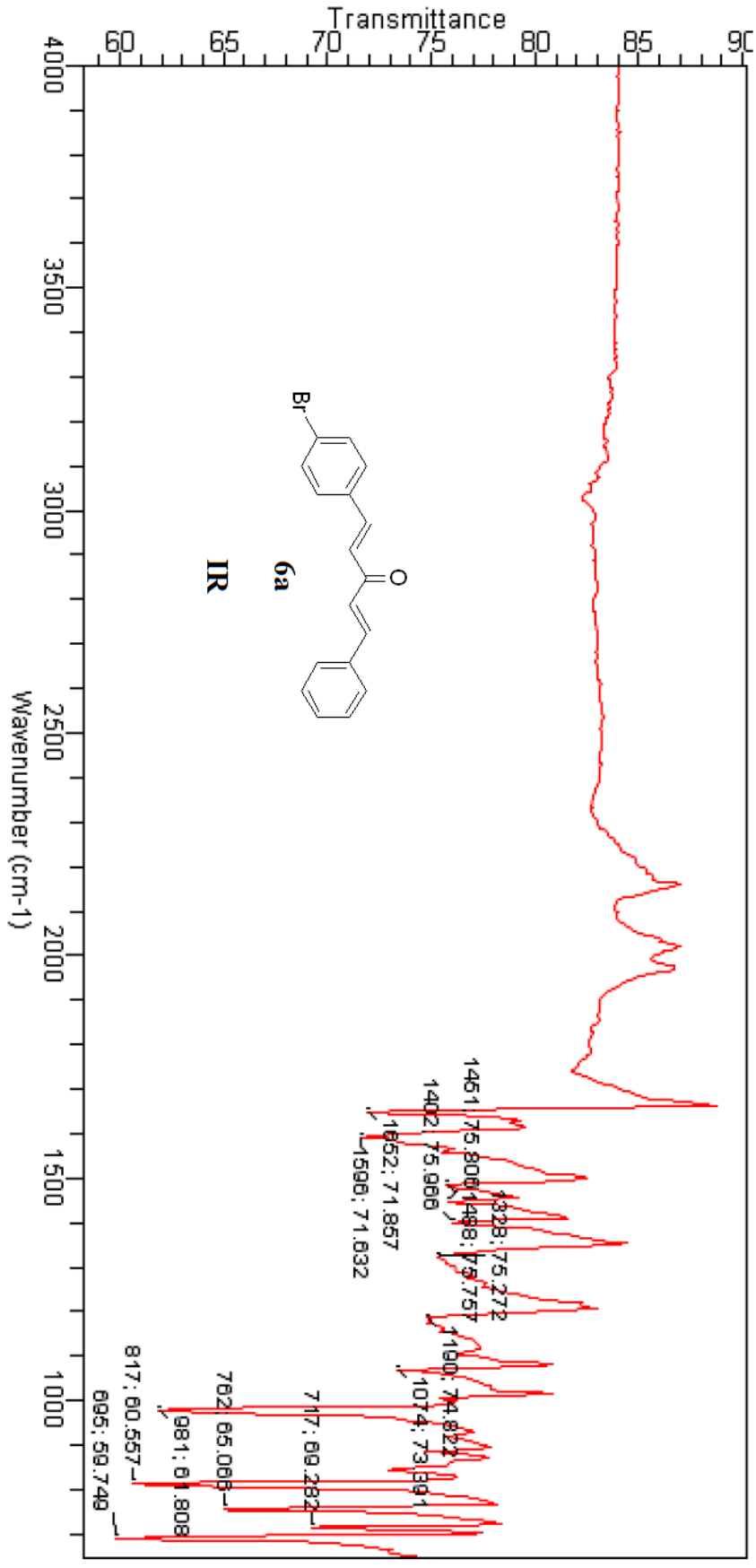

7.6581
7.6183
M 7.6072
M 7.5702
7.5229
7.5017
7.4447
7.4235
7.4023
7.3941
7.3863
7.0660
7.0602
7.0262
7.0203
1.0496
0.9131
7.7406
7.7007
7.6581
1.0778
7.6183
M 7.6072
1.9355
M 7.5702
7.5229
2.1126
7.5017
7.4447
2.0393
7.4235
7.4023
3.0350
7.3941
7.3863
Br
O
6a
1.0000
7.0660
7.0602
0.9131
7.0262
7.0203
7.6
7.4
7.2
[ppm]
0
5
10
15
20
[rel]


188.5928
143.5963
141.8428
134.6975
133.7397
132.2171
130.6523
129.7743
129.0227
128.4715
125.8433
125.3982
124.7724
150
100
50
[ppm]
0
5
10
15
[rel]
Br
O
6a
^{13}C

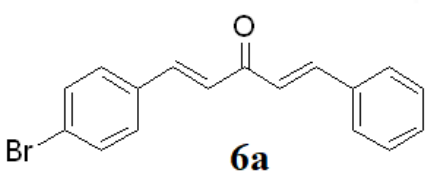

COSY
6a
Br
O
7.6
7.4
7.2
F2 [ppm]
7.6
7.4
7.2
F1 [ppm]


HMBC
6a
Br
O
F2 [ppm]
F1 [ppm]
7.6
7.4
7.2
180
170
160
150
140
130


HSQC
6a
Br
O
F2 [ppm]
F1 [ppm]
7.8
7.6
7.4
7.2
7.0
145
140
135
130
125


Transmittance
60
65
70
75
80
85
90
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
Br
O
6a
IR
1451; 75.806
1402; 75.966
1652; 71.857
1596; 71.632
1328; 75.272
1488; 75.757
1190; 74.822
1074; 73.891
981; 61.808
762; 65.066
717; 69.282
817; 60.557
695; 59.749

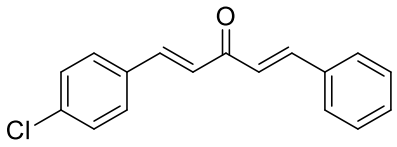
ECB-38 #1-5 RT: 0.01-0.12 AV: 5 NL: 1.06E7
T: FTMS + p ESI Full ms [200.00-600.00]

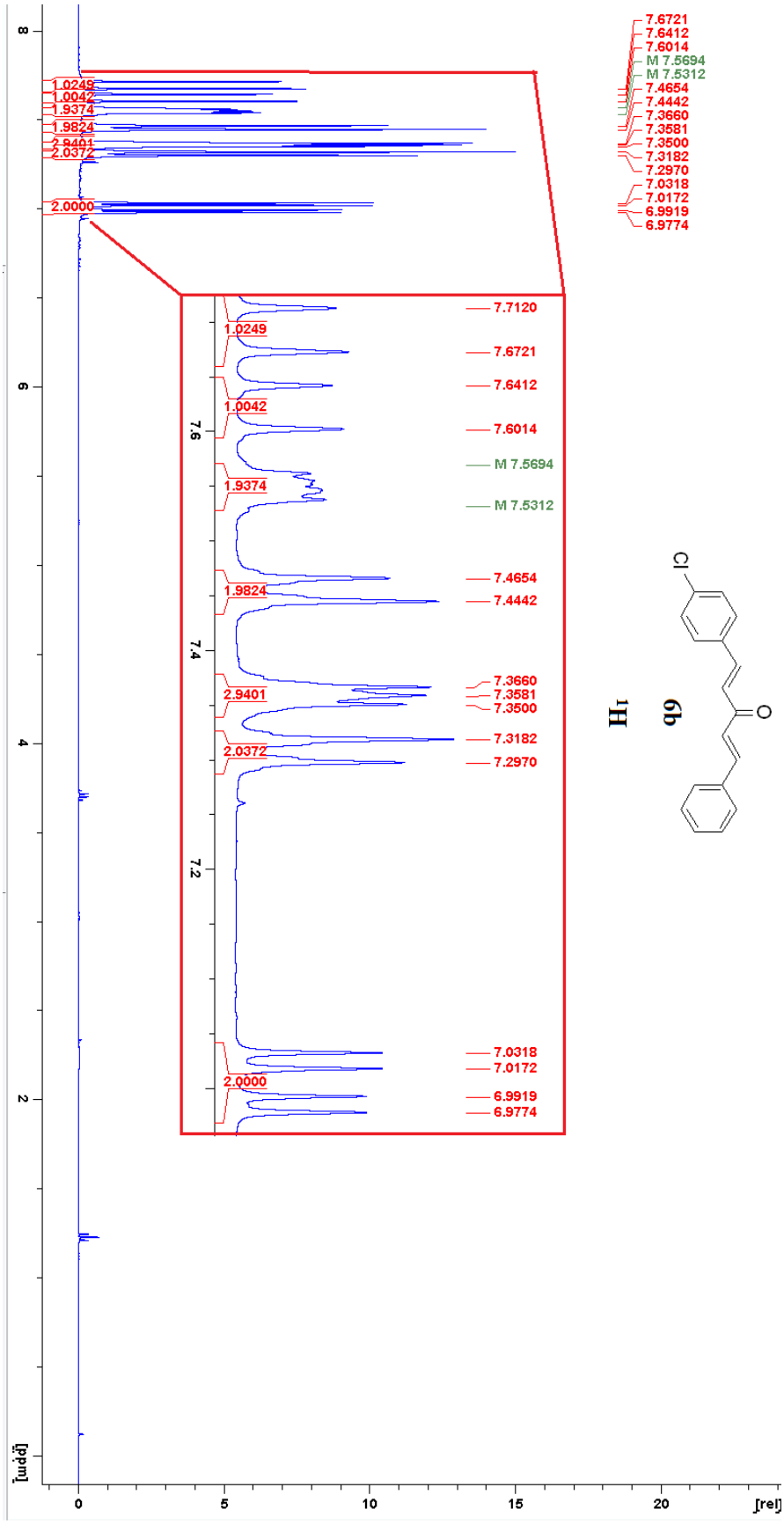


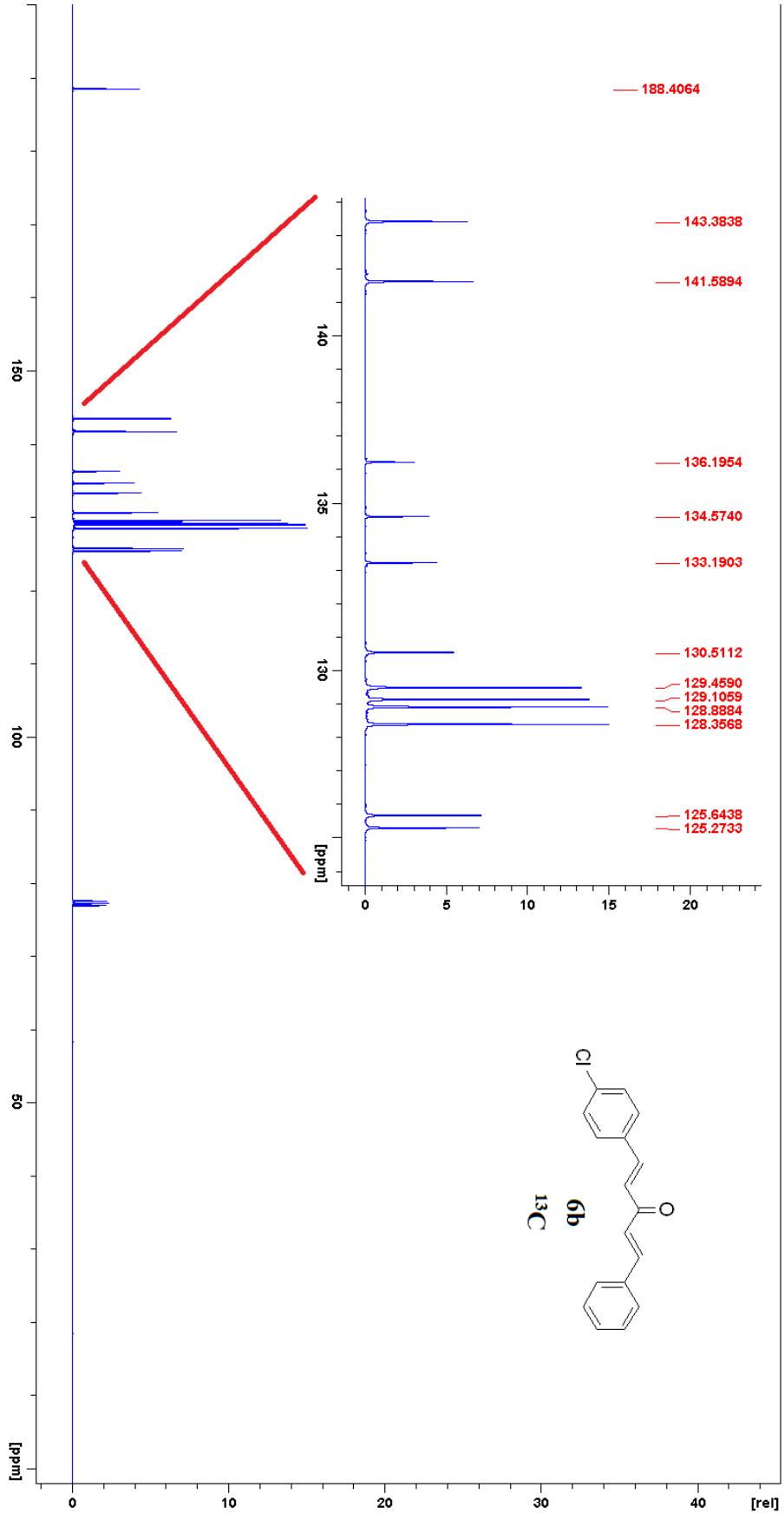
6a

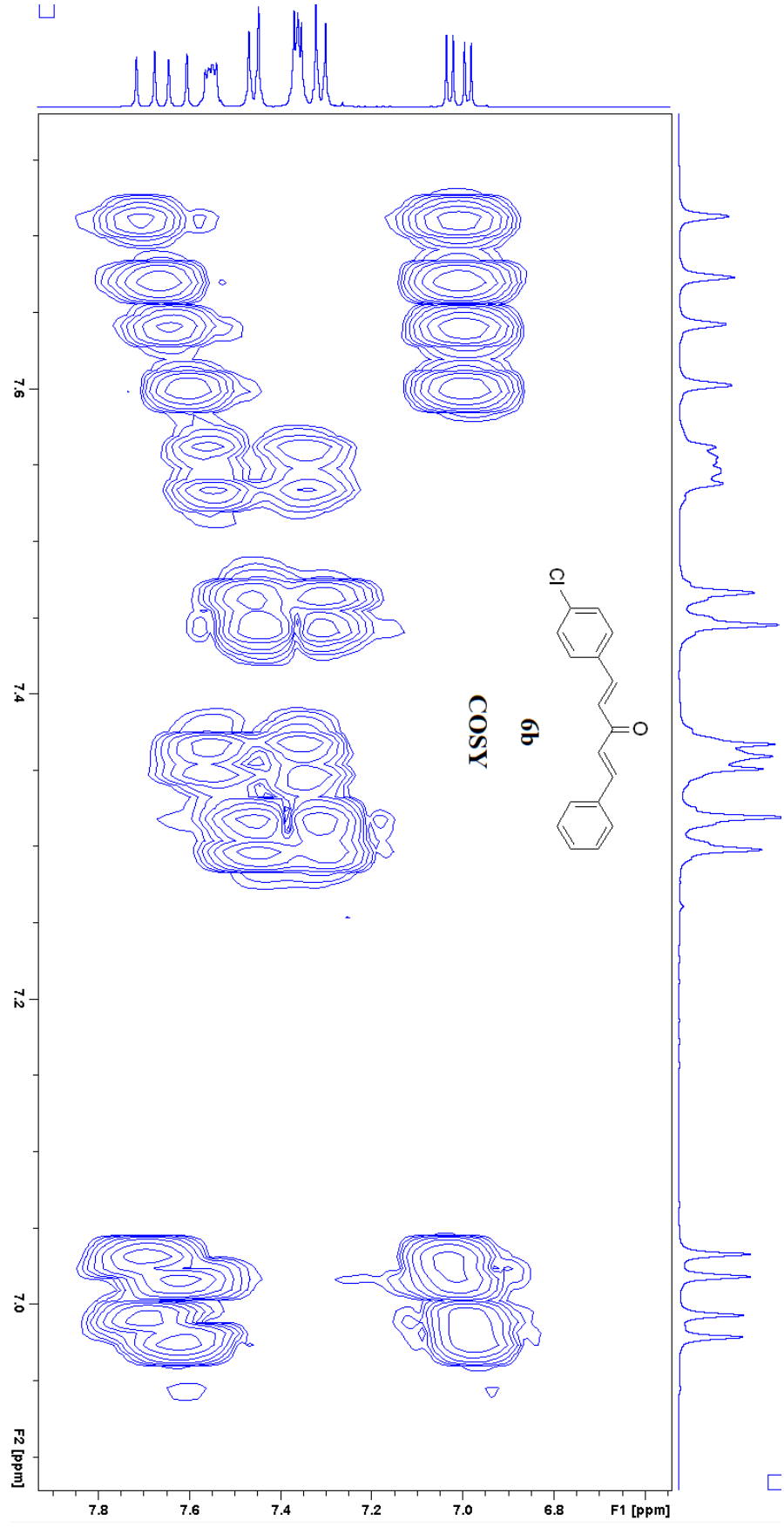
MS

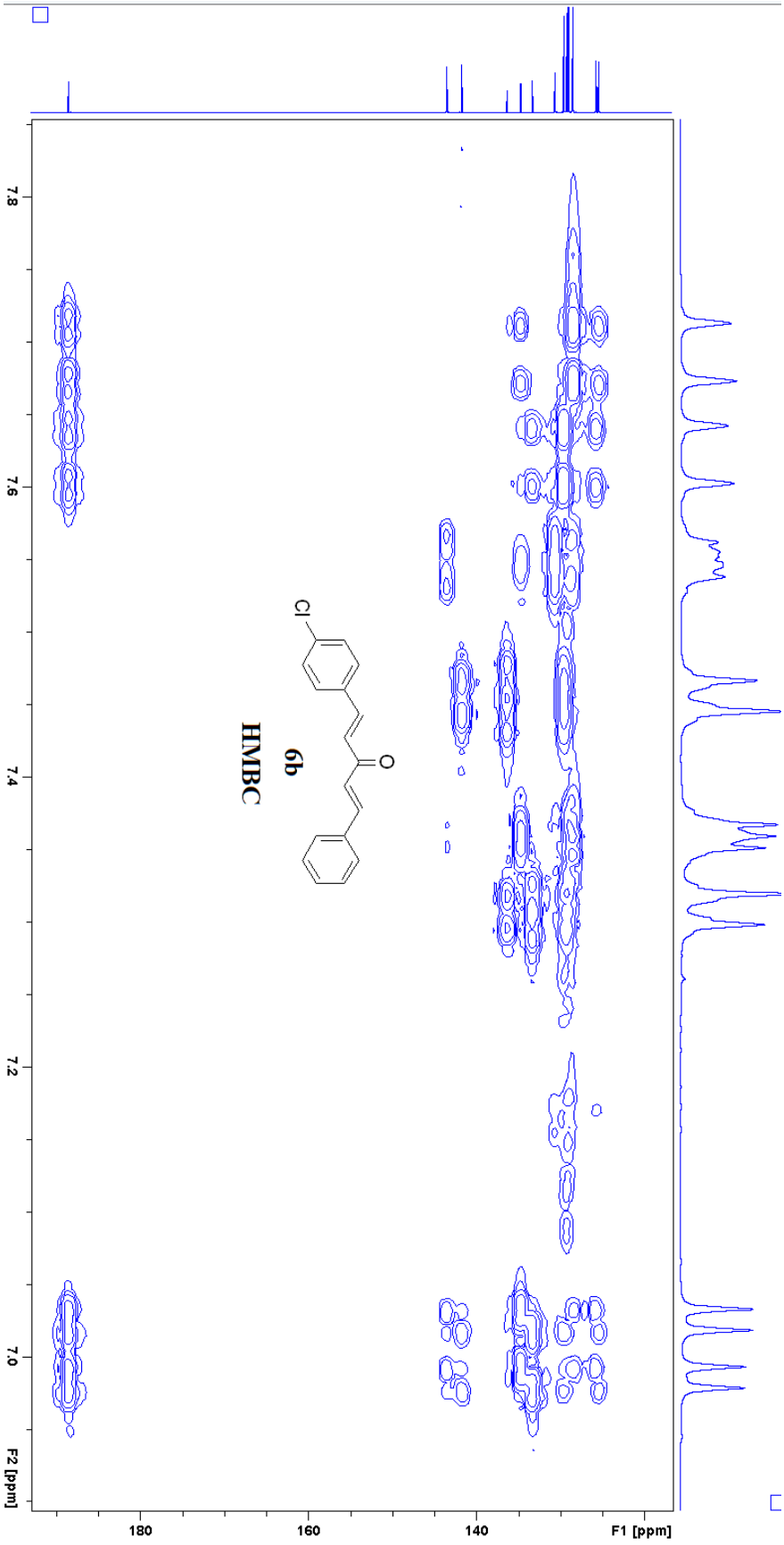
(1*E*,4*E*)-1-(4-chlorophenyl)penta-1,4-dien-3-one (6b)

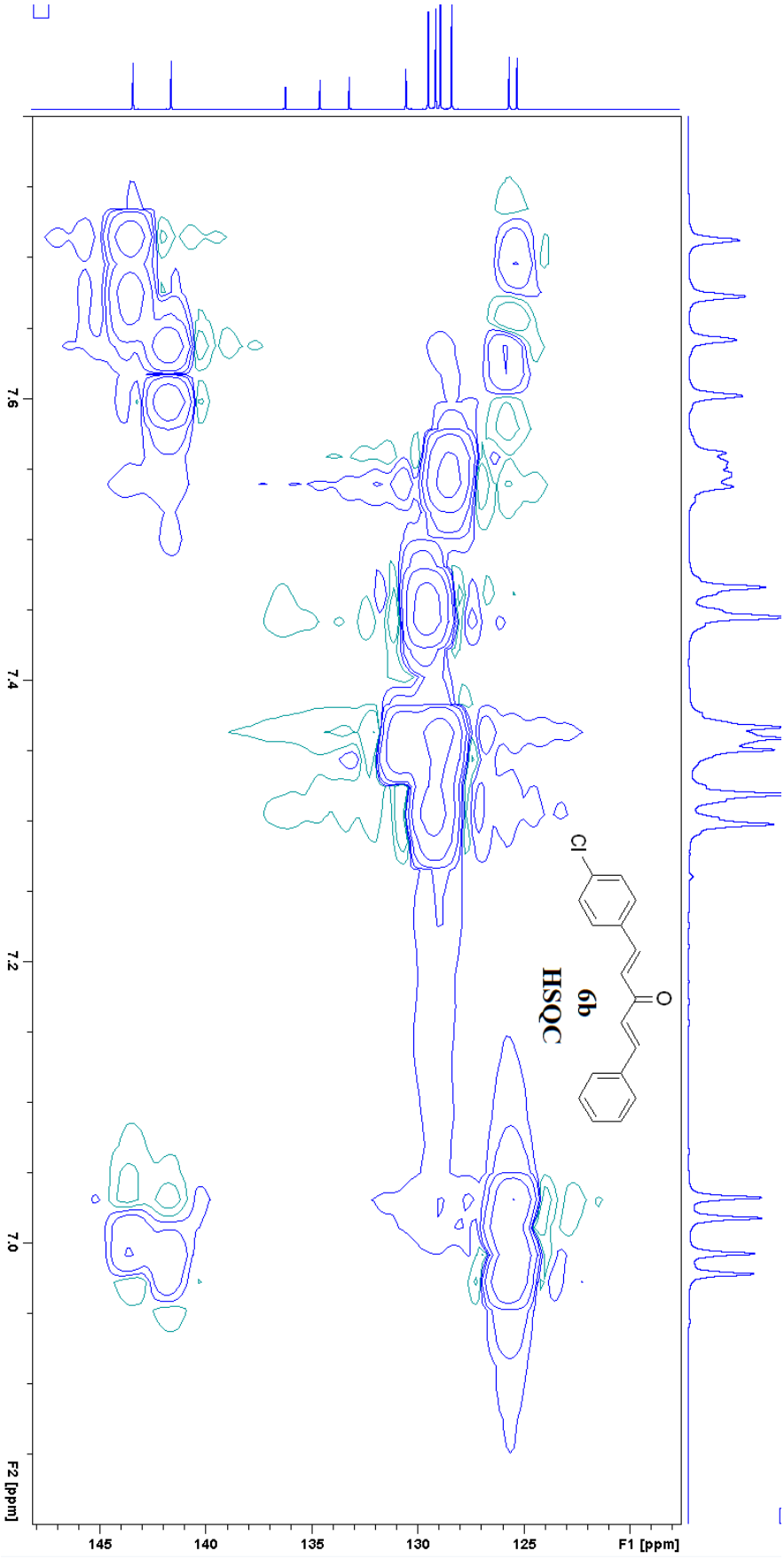


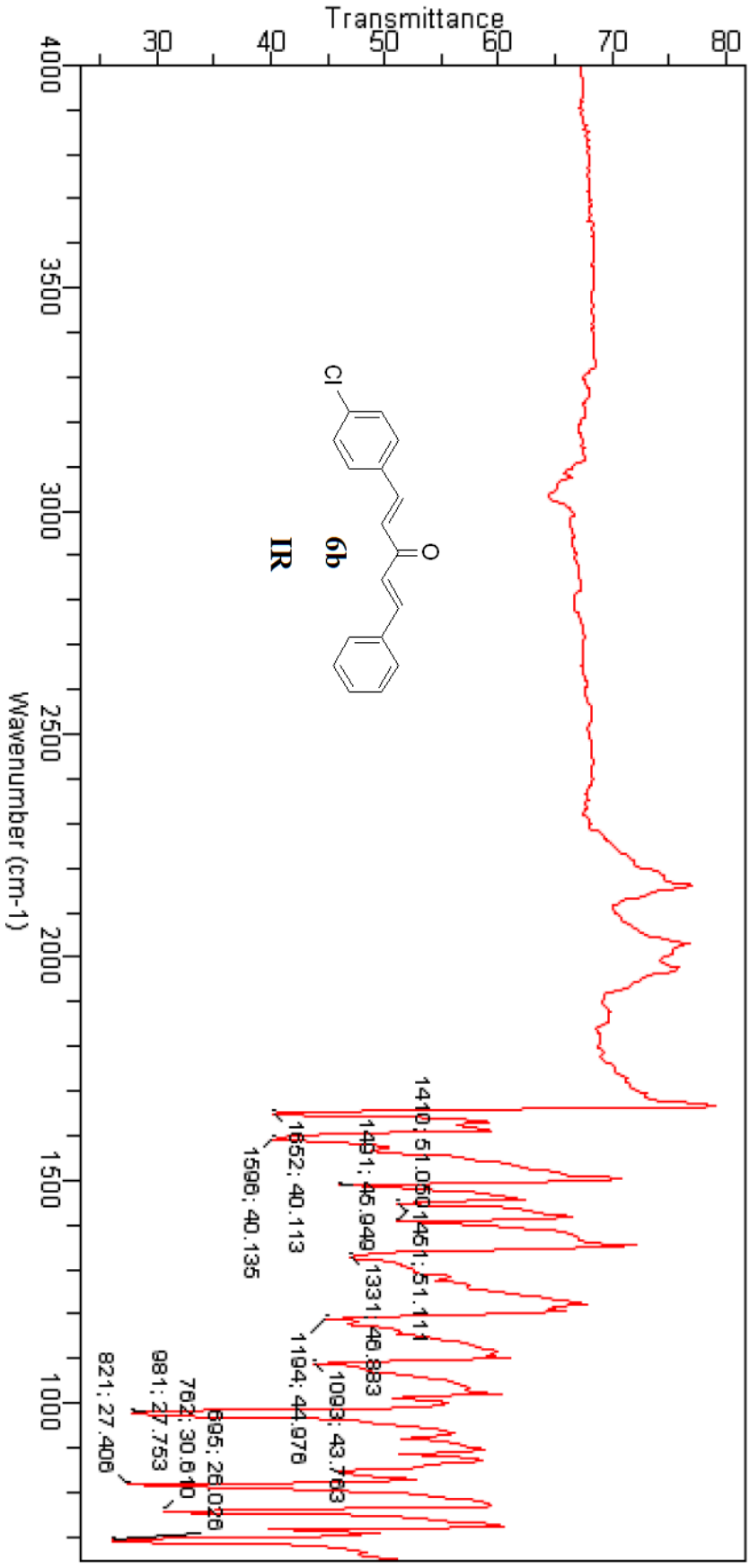

7.6721
7.6412
7.6014
M 7.5694
M 7.5312
7.4654
7.4442
7.3660
7.3581
7.3500
7.3182
7.2970
7.0318
7.0172
6.9919
6.9774
1.0249
1.0042
1.9374
1.9824
2.9401
2.0372
2.0000
7.7120
7.6
7.4
7.2
[ppm]
0
5
10
15
20
[rel]
Cl
O
6b
H_1


188.4064
143.3838
141.5894
136.1954
134.5740
133.1903
130.5112
129.4590
129.1059
128.8884
128.3568
125.6438
125.2733
[ppm]
[rel]
Cl
O
6b
^{13}C


COSY
6b
Cl
O
F2 [ppm]
F1 [ppm]
7.8
7.6
7.4
7.2
7.0
6.8

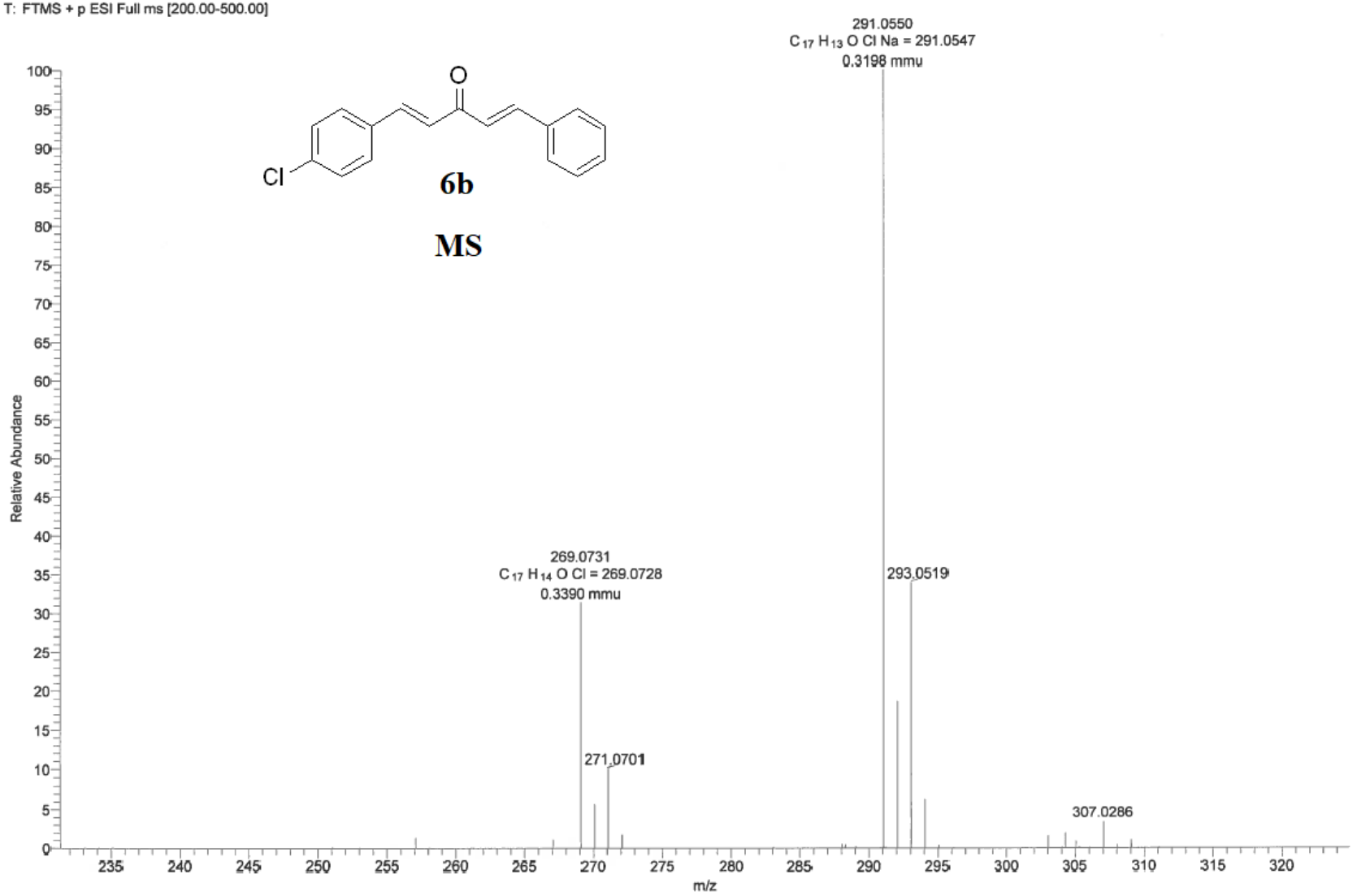

HMBC
6b
Cl
O
7.8
7.6
7.4
7.2
7.0
F2 [ppm]
180
160
140
F1 [ppm]


HSQC
6b
Cl
O
F2 [ppm]
F1 [ppm]
7.6
7.4
7.2
7.0
145
140
135
130
125

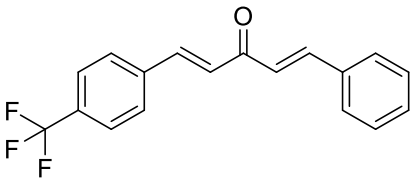

Transmittance
30
40
50
60
70
80
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
IR
6b
Cl
O
1410; 51.050
1652; 40.113
1491; 46.949
1596; 40.135
1451; 51.111
1331; 46.883
1194; 44.976
1093; 43.763
762; 30.610
695; 28.026
981; 27.753
821; 27.406

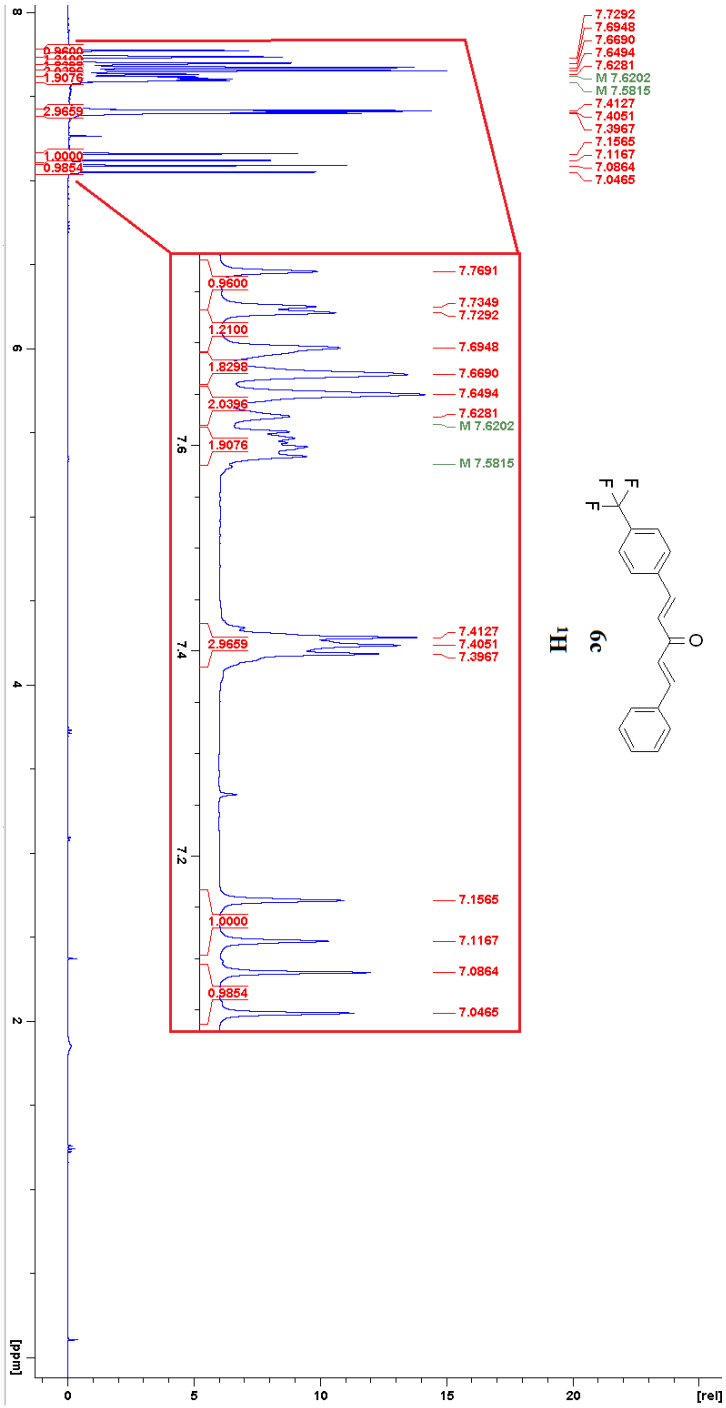
12/7/2018 9:12:22 AM ECB-43

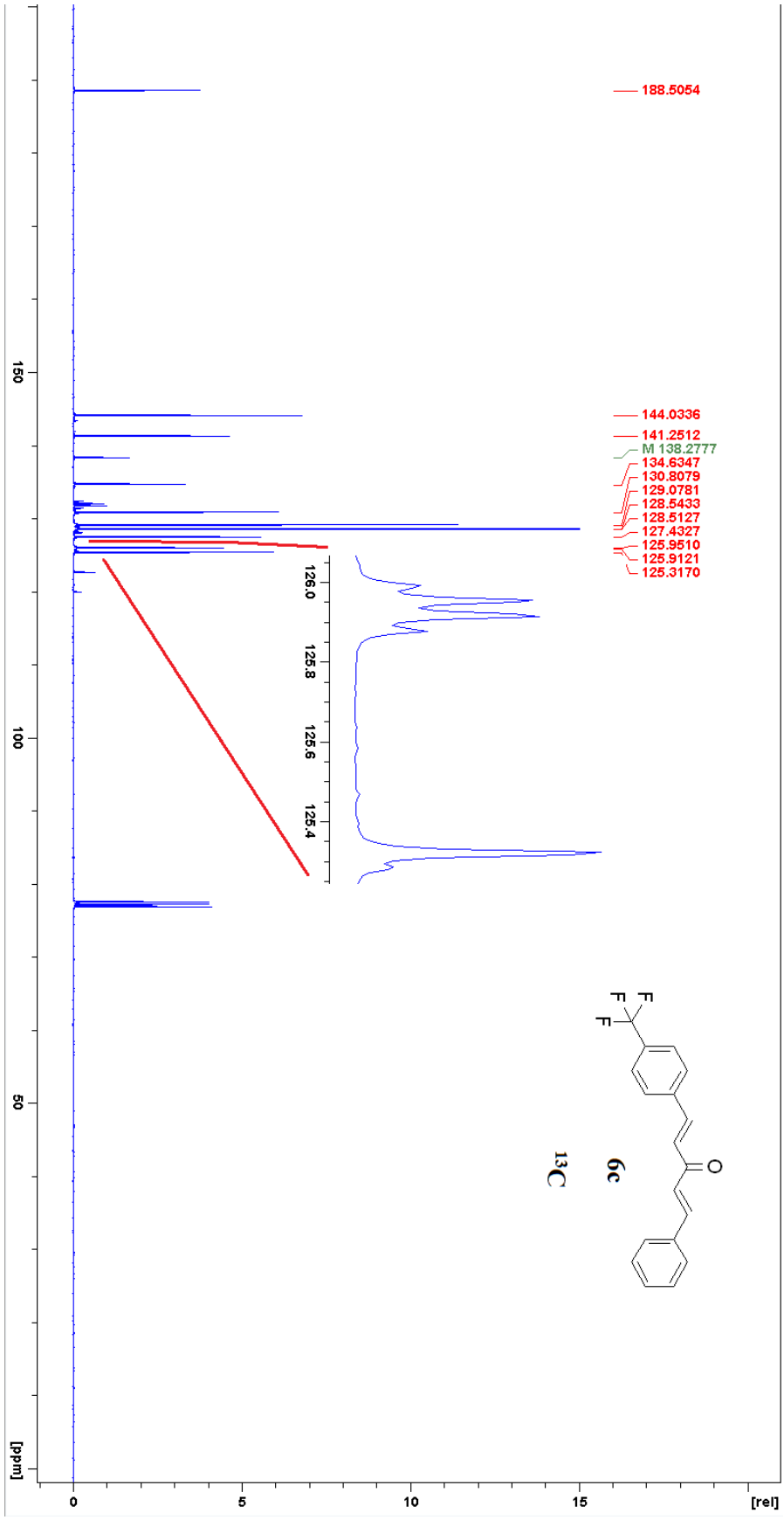
ECB-43 #1-4 RT: 0.00-0.08 AV: 4 NL: 2.87E7
T: FTMS + p ESI Full ms [200.00-500.00]

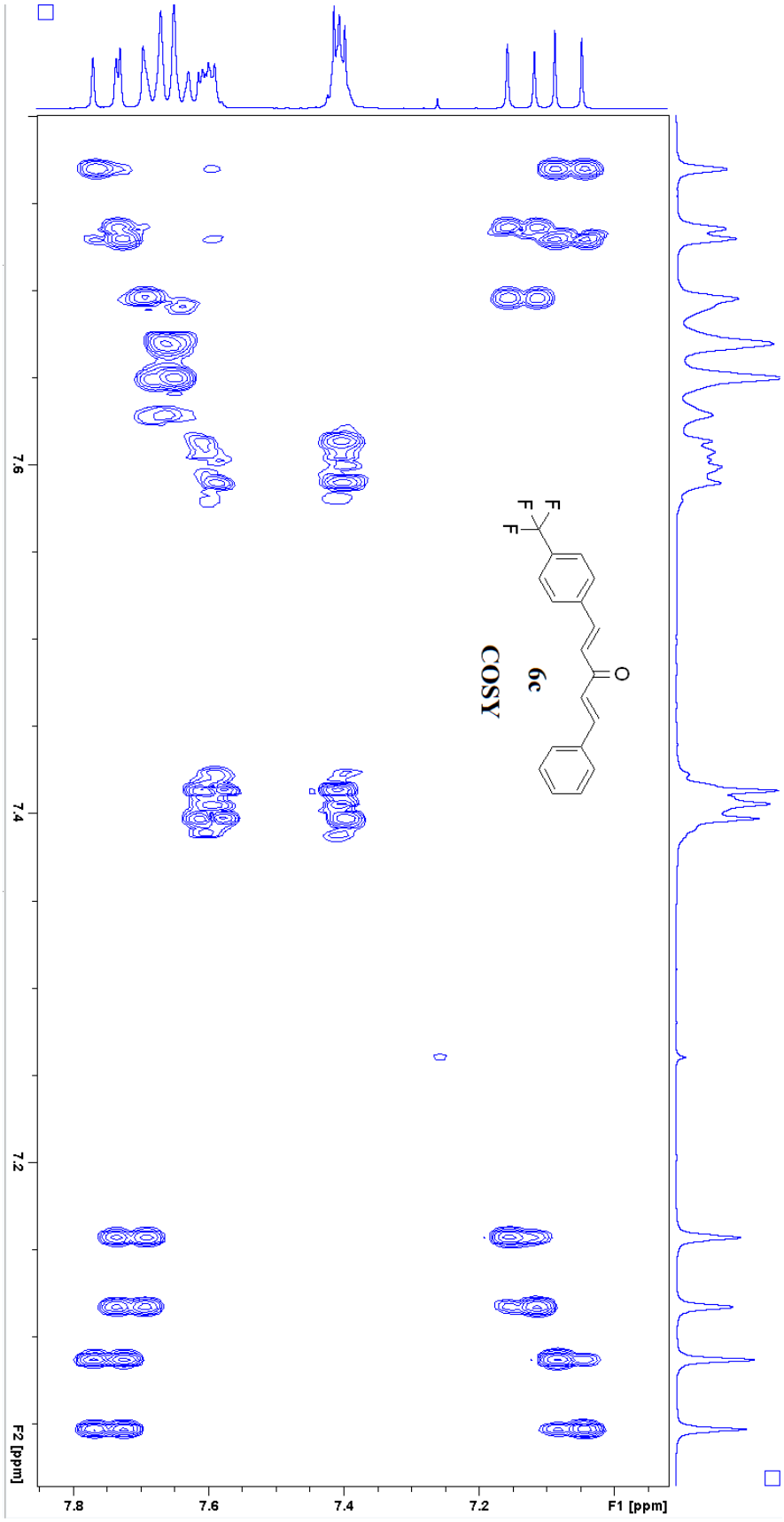


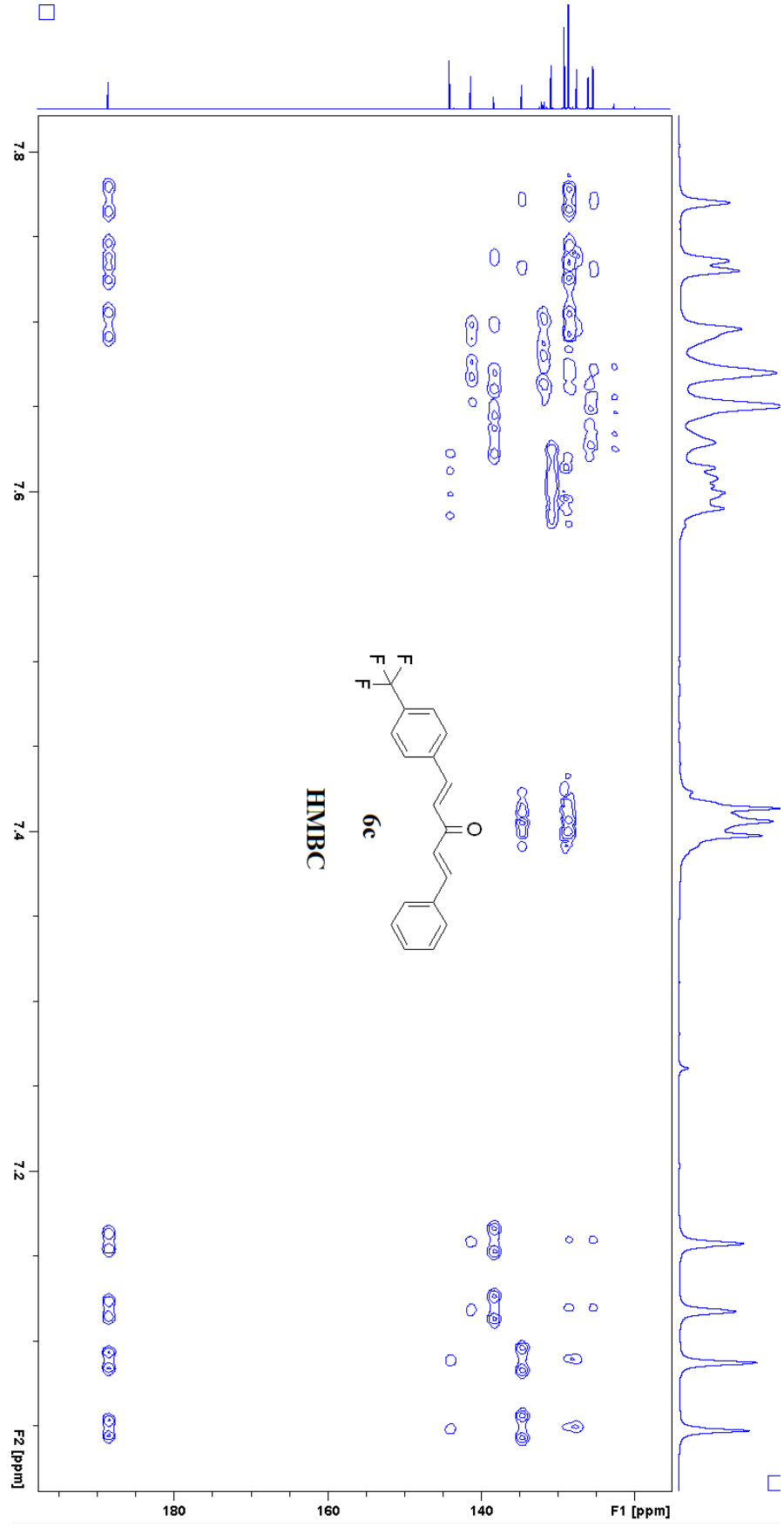
(1*E*,4*E*)-1-(4-trifluorimethylphenyl)penta-1,4-dien-3-one (6c)

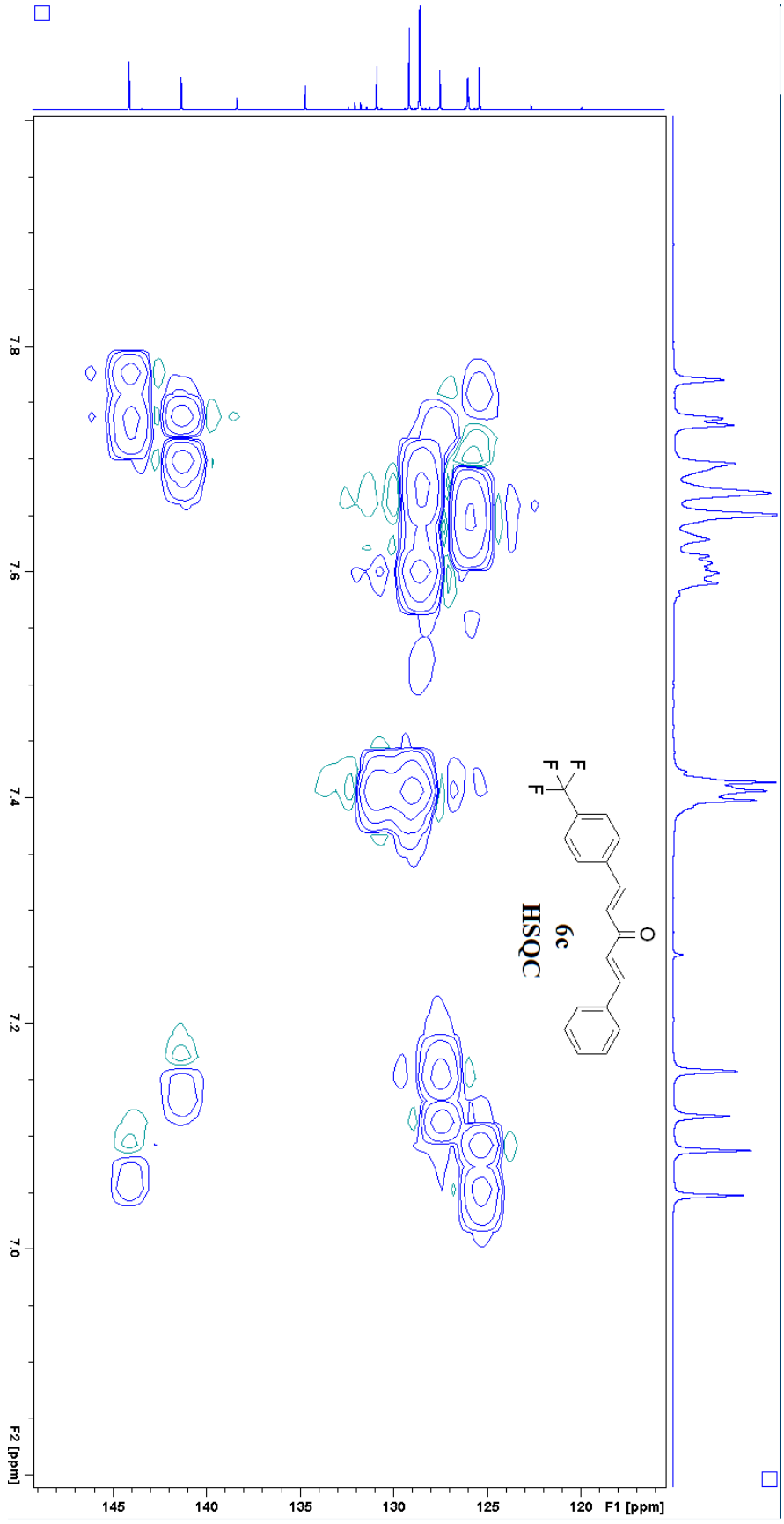


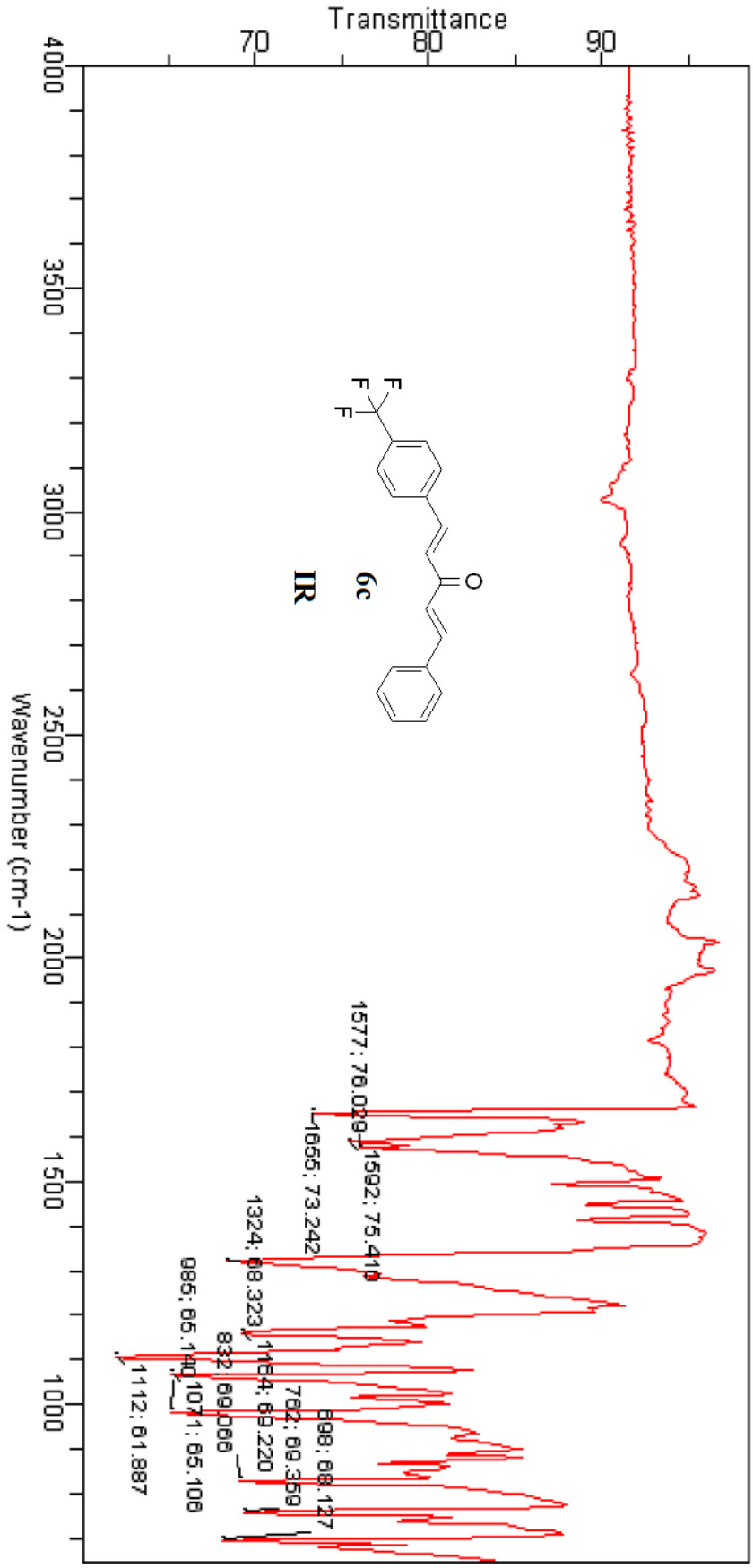

7.7292
7.6948
7.6690
7.6494
7.6281
M 7.6202
M 7.5815
7.4127
7.4051
7.3967
7.1565
7.1167
7.0864
7.0465
0.9600
2.9659
1.0000
0.9854
1.9076
7.7691
7.7349
1.2100
1.8298
2.0396
M 7.5815
7.4127
7.4051
7.3967
7.1565
7.1167
7.0864
7.0465
8
6
4
2
7.6
7.4
7.2
[ppm]
0
5
10
15
20
[rel]
F
F
F
O


188.5054
144.0336
141.2512
M 138.2777
134.6347
130.8079
129.0781
128.5433
128.5127
127.4327
125.9510
125.9121
125.3170
126.0
125.8
125.6
125.4
150
100
50
[ppm]
0
5
10
15
[rel]
F
F
F
O
^{13}C
6c

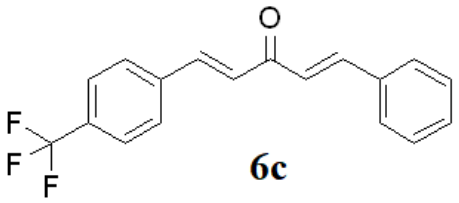

COSY
6c
F
F
F
O
7.6
7.4
7.2
F2 [ppm]
7.8
7.6
7.4
7.2
F1 [ppm]


HMBC
6c
F
F
F
O
7.8
7.6
7.4
7.2
F2 [ppm]
180
160
140
F1 [ppm]


HSQC
6c
F
F
F
O
7.8
7.6
7.4
7.2
7.0
F2 [ppm]
145
140
135
130
125
120
F1 [ppm]


Transmittance
70
80
90
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
IR
6c
F
F
F
O
1577; 76.029
1592; 75.419
1655; 73.242
1324; 68.323
1164; 69.220
832; 69.066
762; 69.359
698; 68.127
985; 65.140
1071; 65.106
1112; 61.887

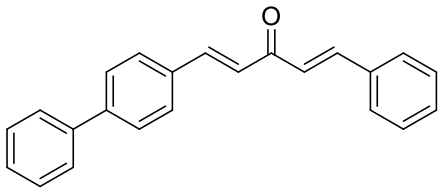
ECB-44 #4 RT: 0.09 AV: 1 NL: 2.95E7
T: FTMS + p ESI Full ms [200.00-500.00]

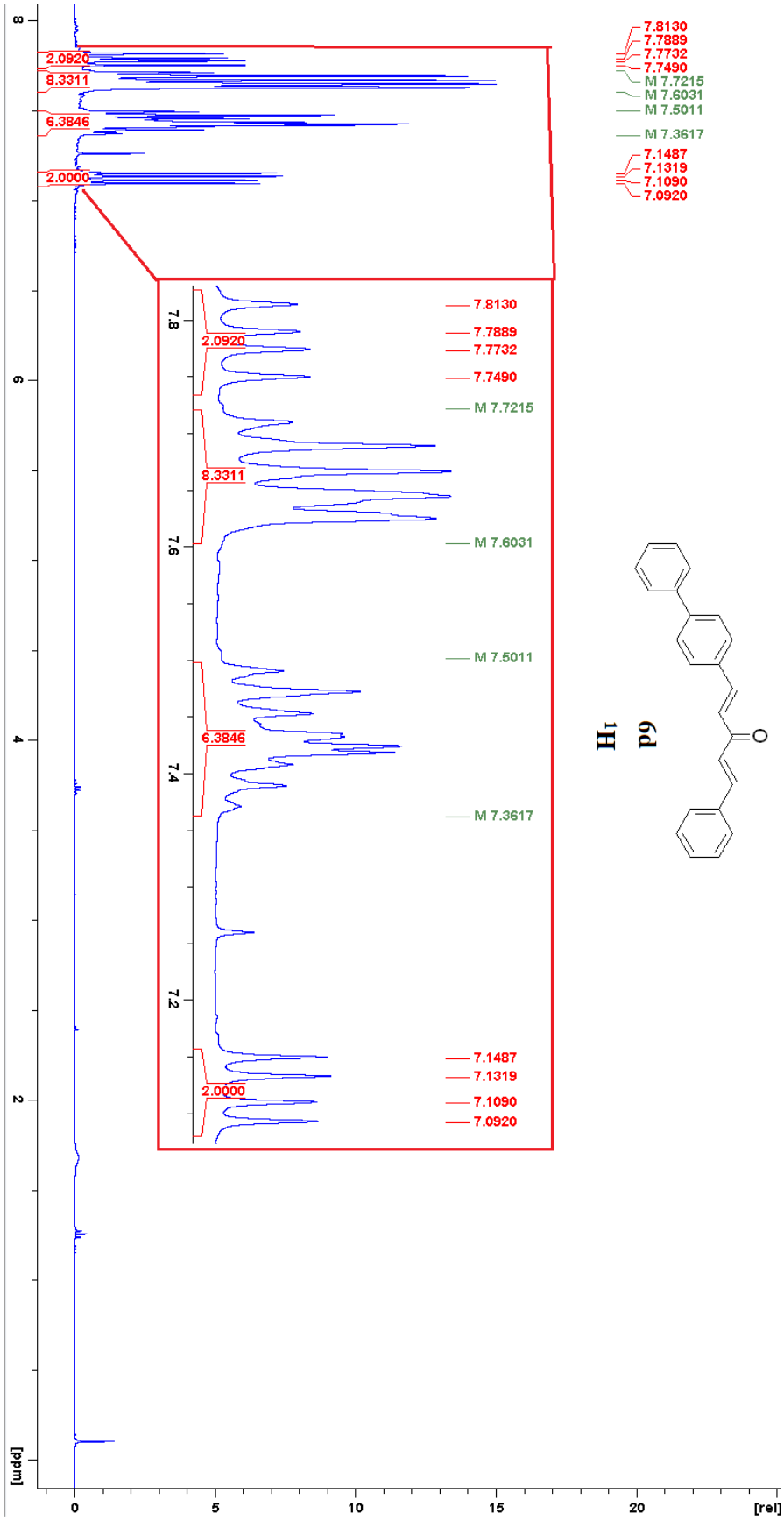


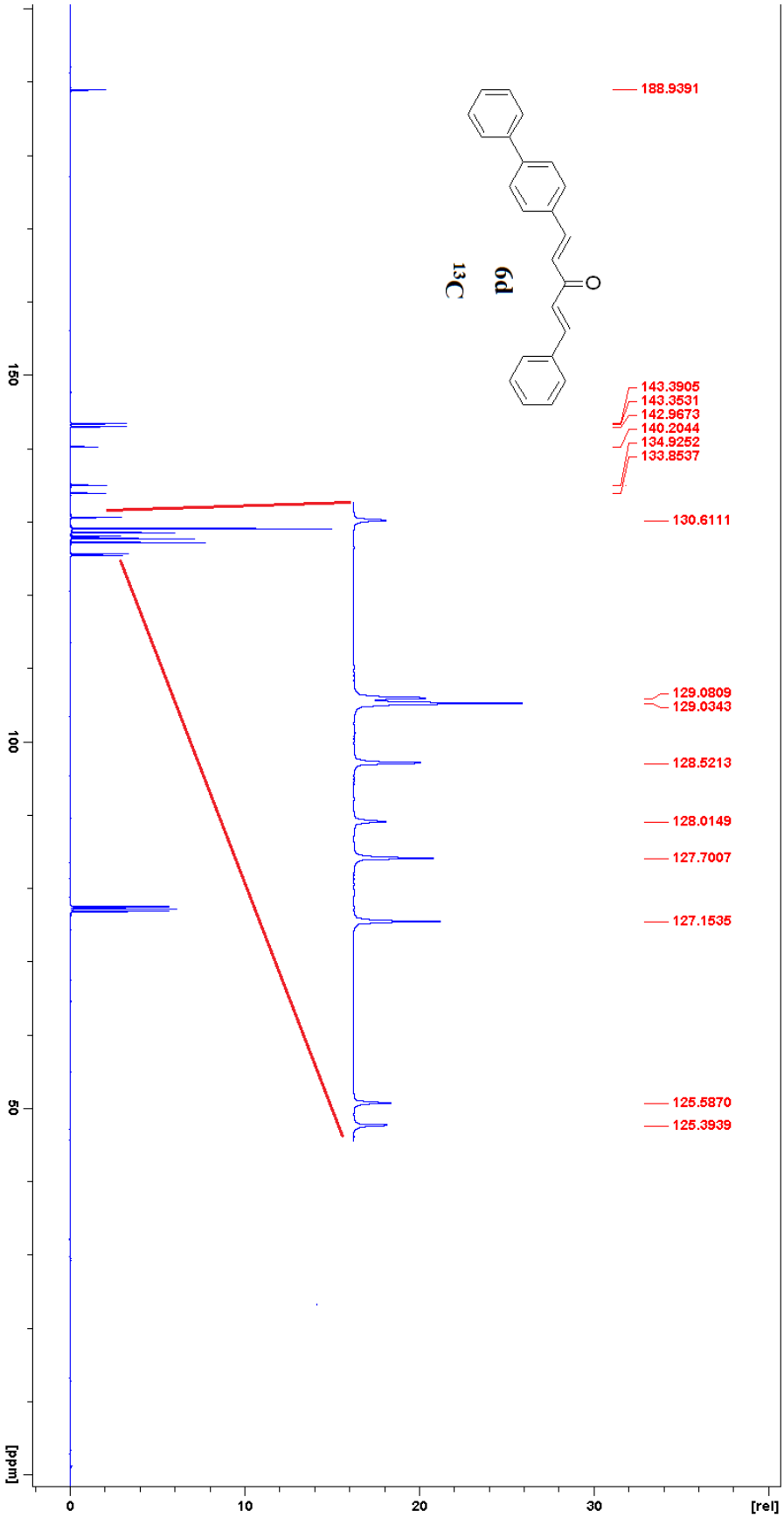
6c

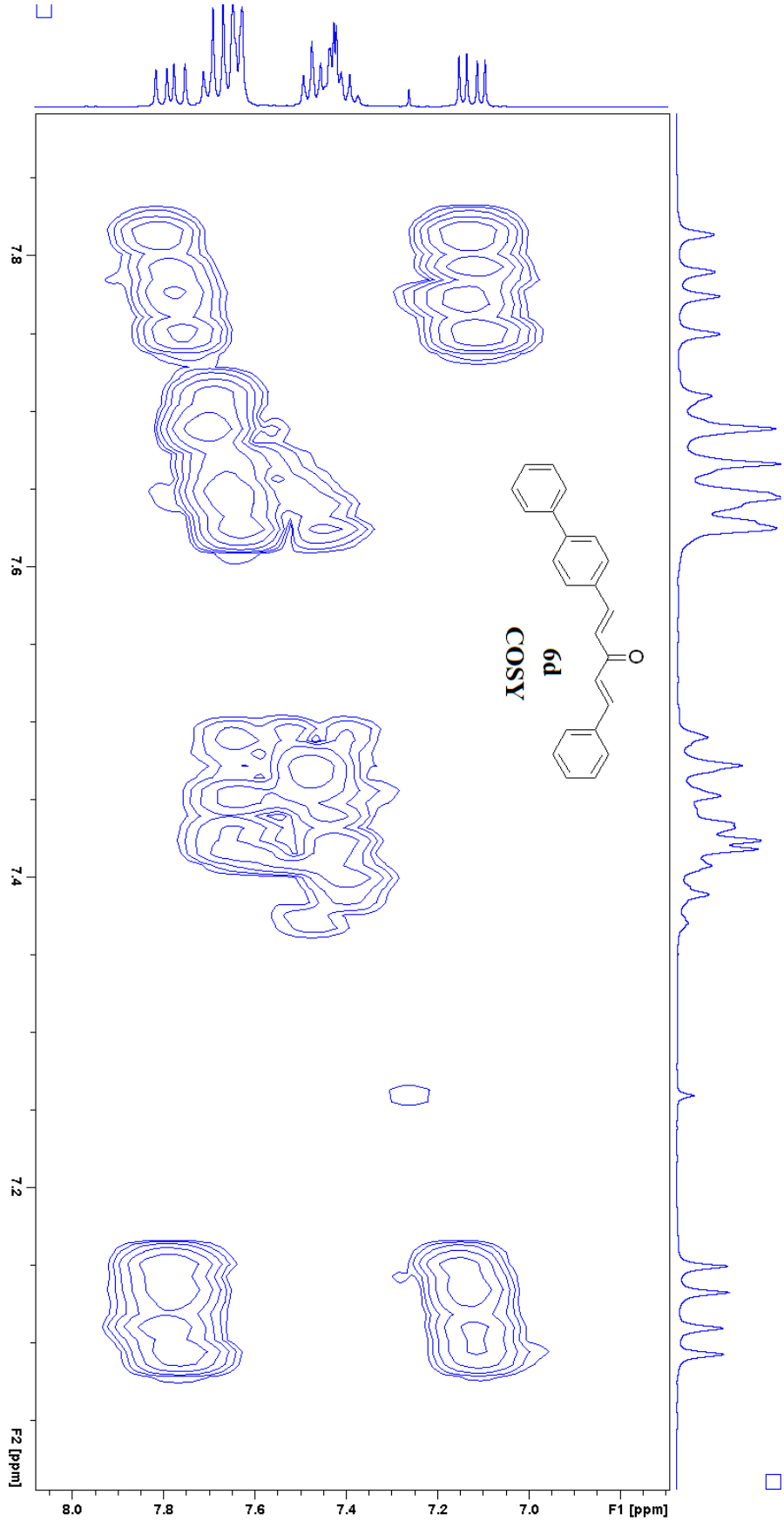
MS

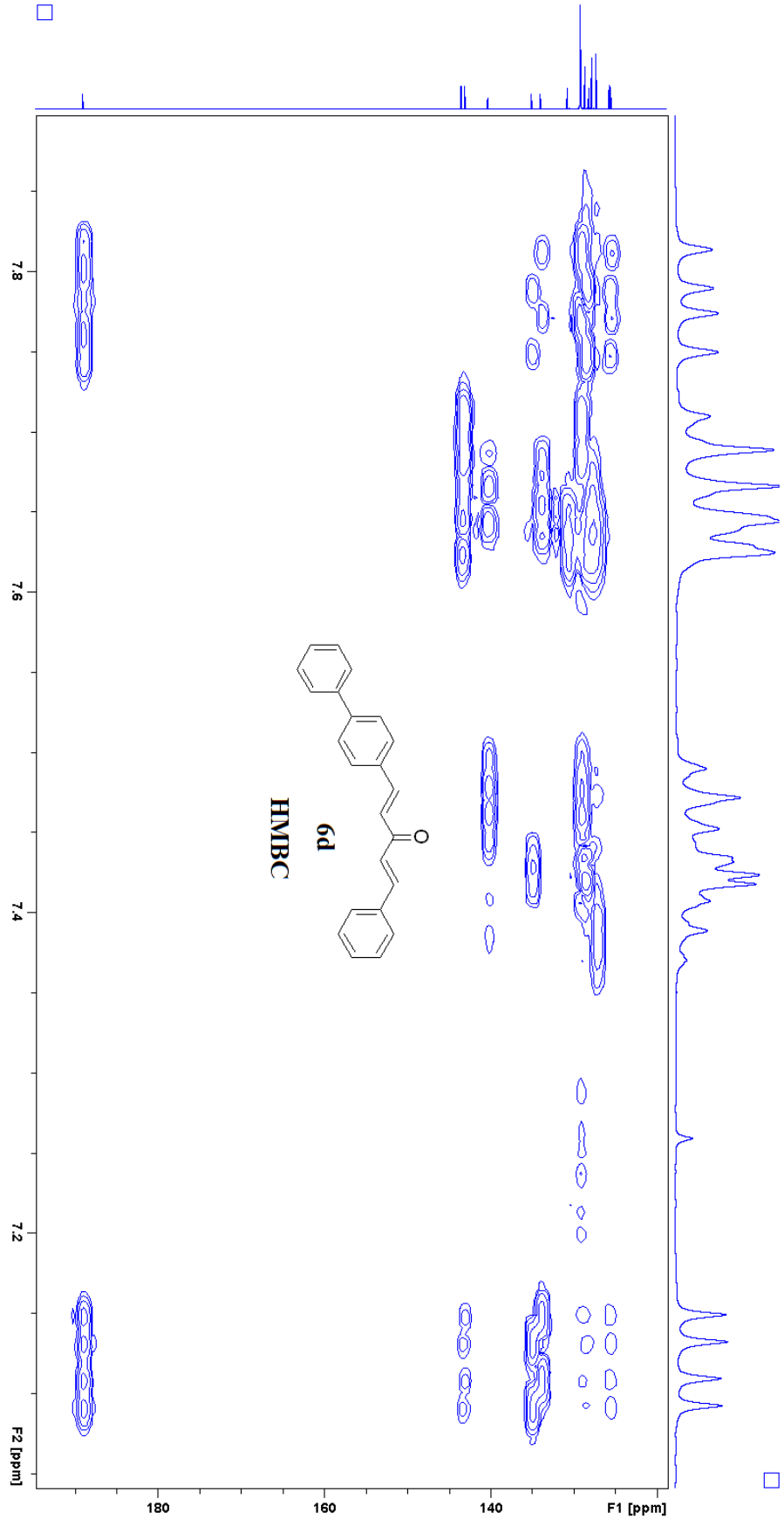
(1*E*,4*E*)-1-(4-biphenyl)penta-1,4-dien-3-one (6d)

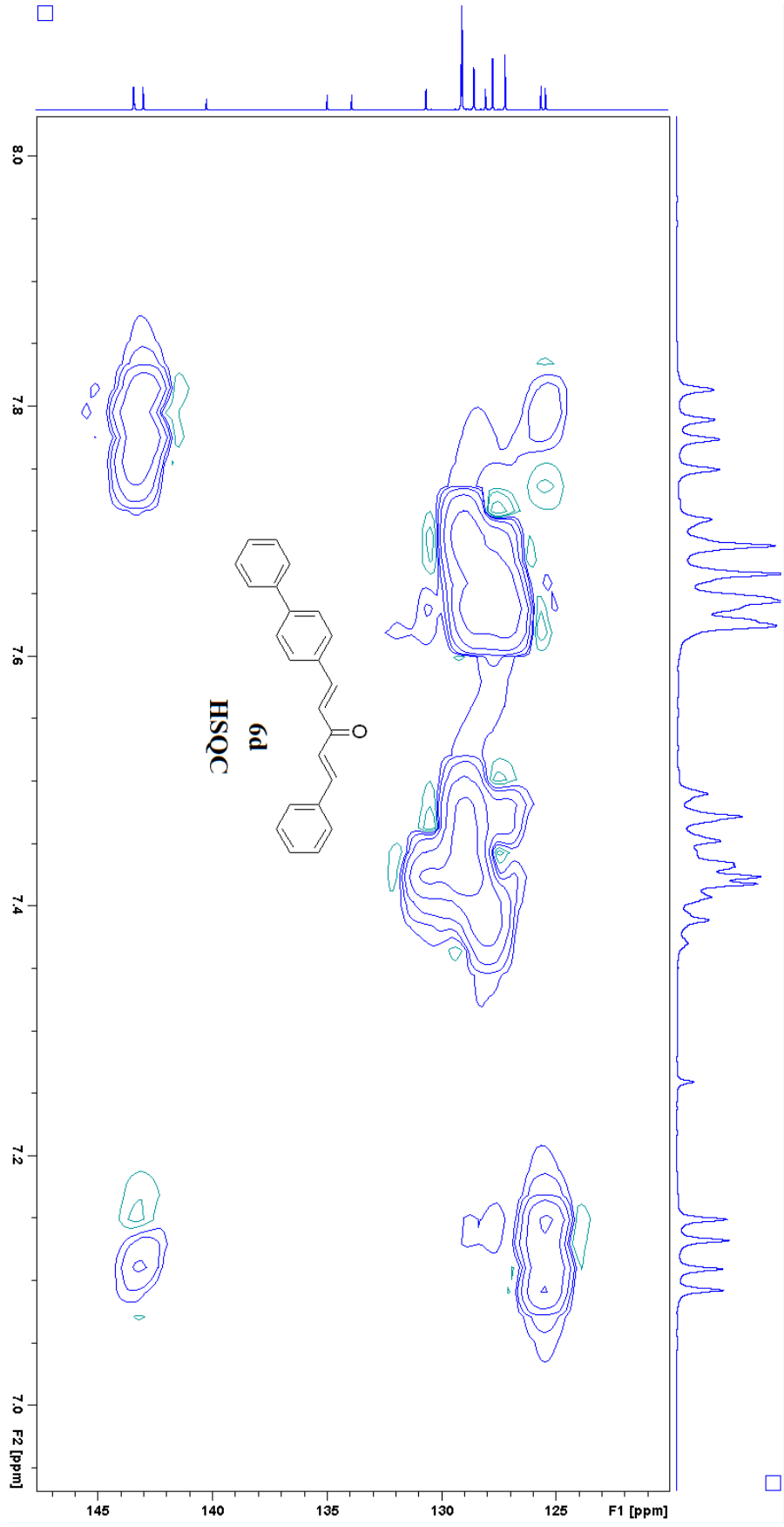


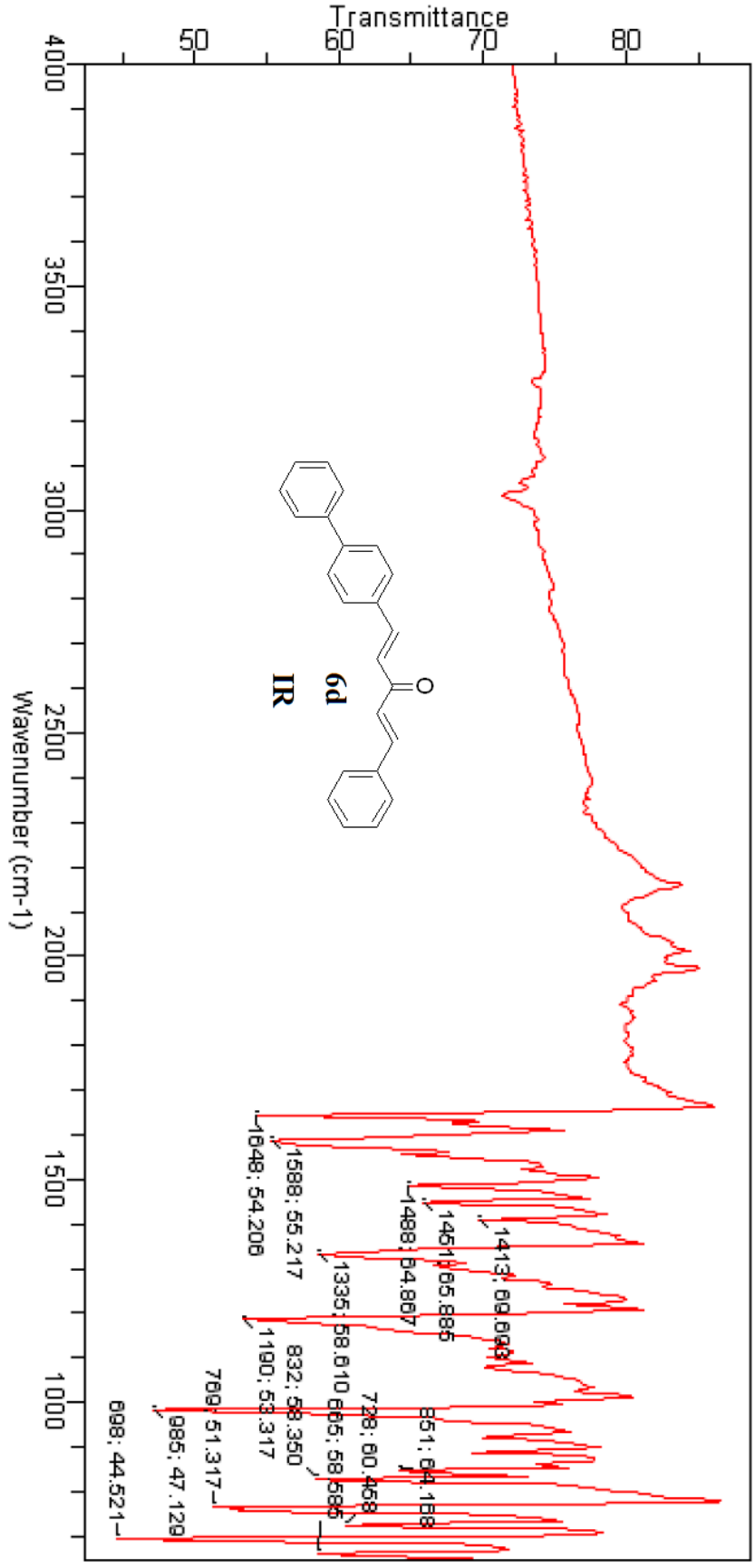

7.8130
7.7889
7.7732
7.7490
M 7.7215
M 7.6031
M 7.5011
M 7.3617
7.1487
7.1319
7.1090
7.0920
2.0920
8.3311
6.3846
2.0000
[ppm]
[rel]
^{1}H
6d

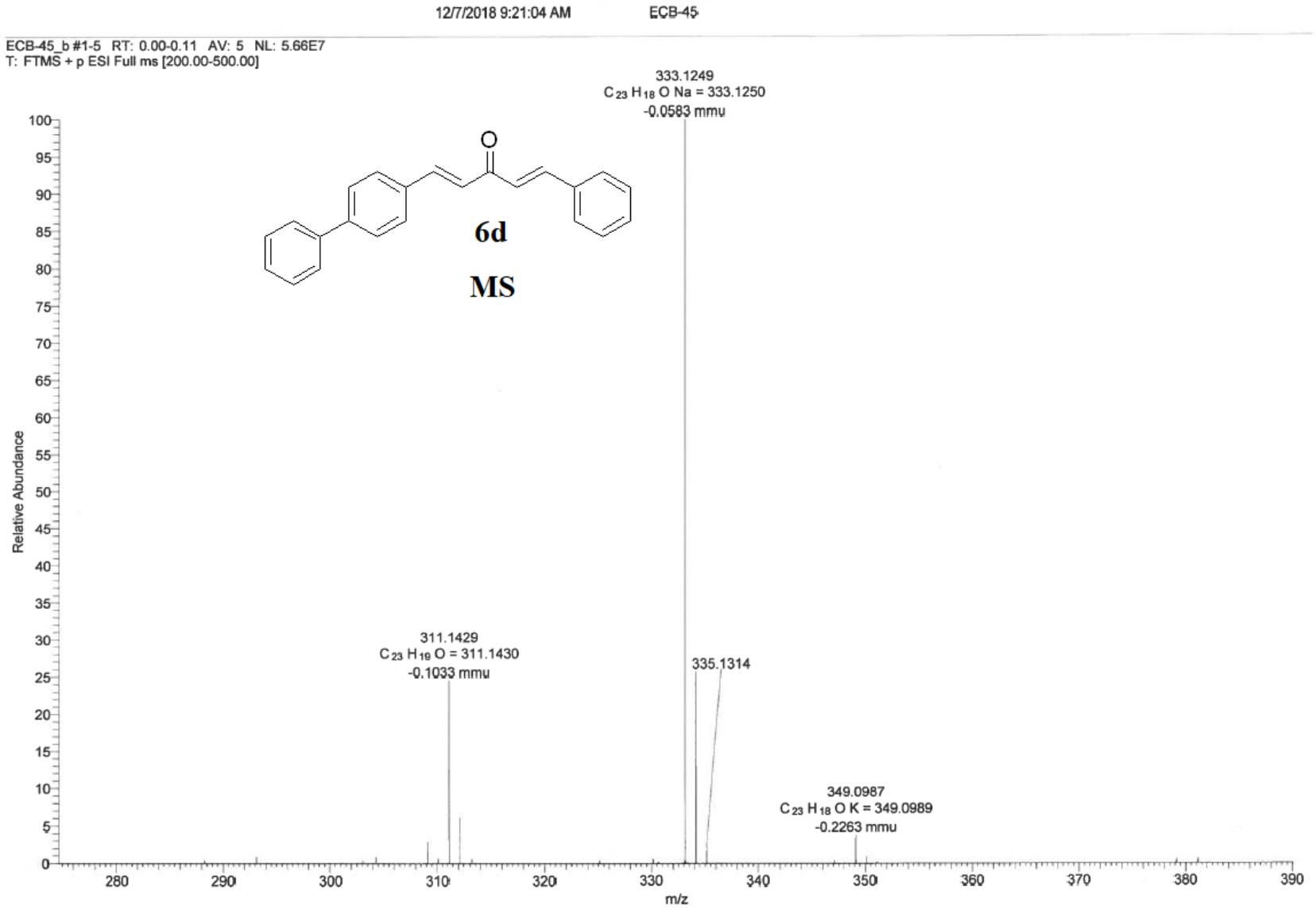

188.9391
143.3905
143.3531
142.9673
140.2044
134.9252
133.8537
130.6111
129.0809
129.0343
128.5213
128.0149
127.7007
127.1535
125.5870
125.3939
6d
^{13}C
150
100
50
[ppm]
0
10
20
30
[rel]


COSY
6d
O
7.8
7.6
7.4
7.2
F2 [ppm]
8.0
7.8
7.6
7.4
7.2
7.0
F1 [ppm]

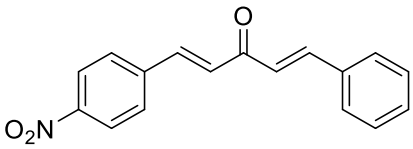

HMBC
6g
O
7.8
7.6
7.4
7.2
F2 [ppm]
180
160
140
F1 [ppm]

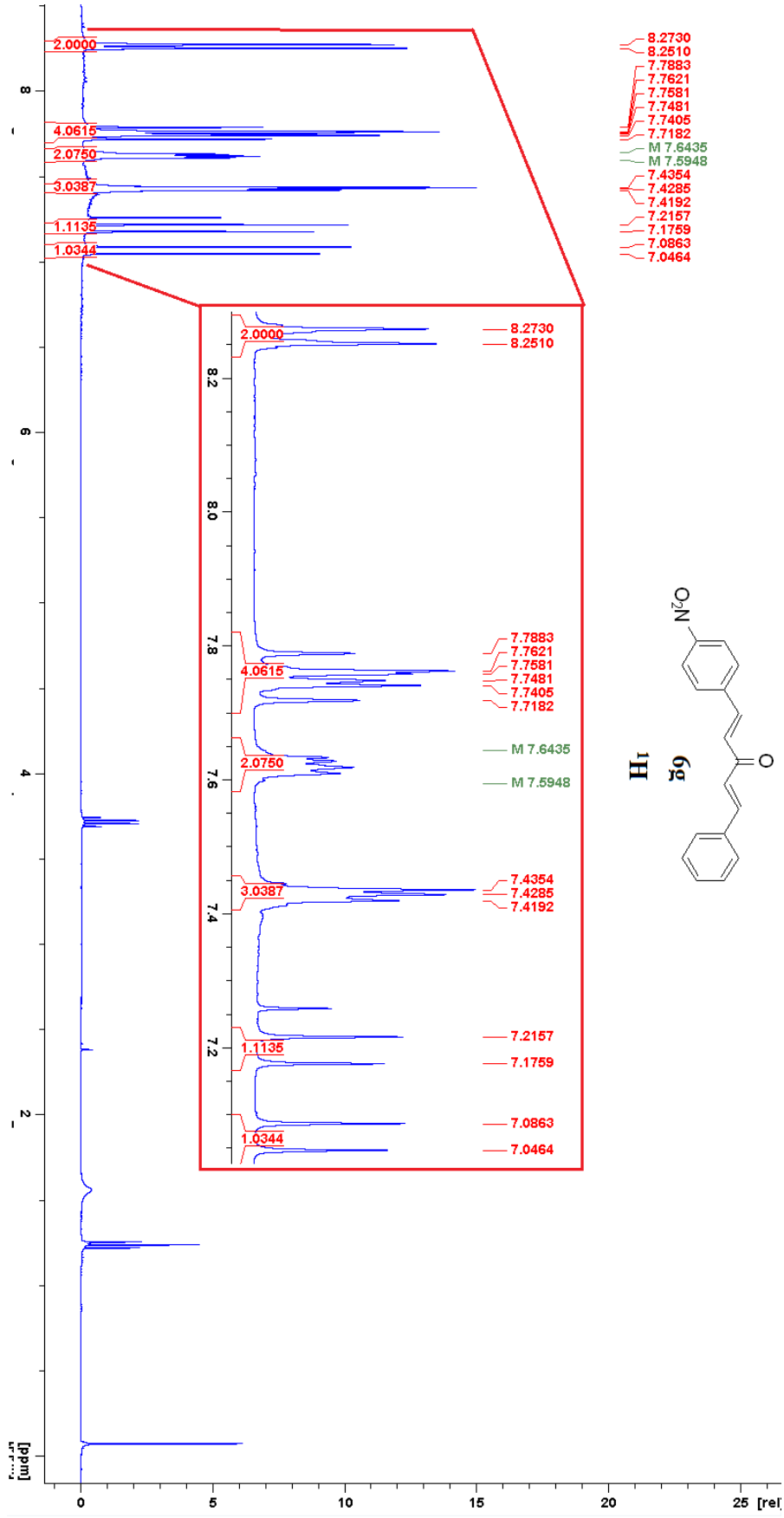

HSQC
6d
8.0
7.8
7.6
7.4
7.2
7.0
F2 [ppm]
145
140
135
130
125
F1 [ppm]

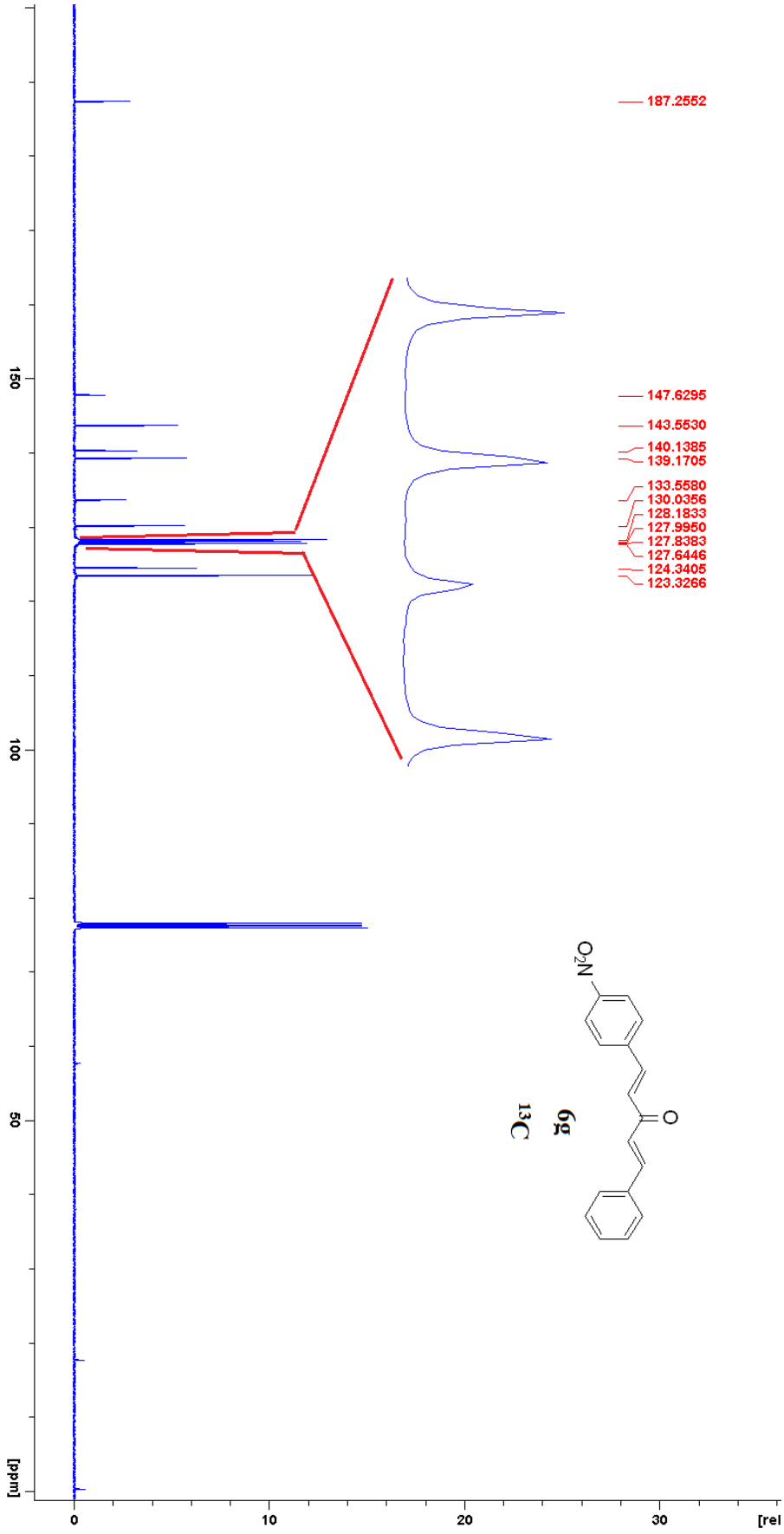

Transmittance
50
60
70
80
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
IR
6d
O
1648; 54.206
1588; 55.217
1488; 64.867
1451; 65.885
1413; 69.693
1335; 58.610
1190; 53.317
832; 58.350
769; 51.317
728; 60.458
695; 58.585
851; 64.158
985; 47.129
698; 44.521

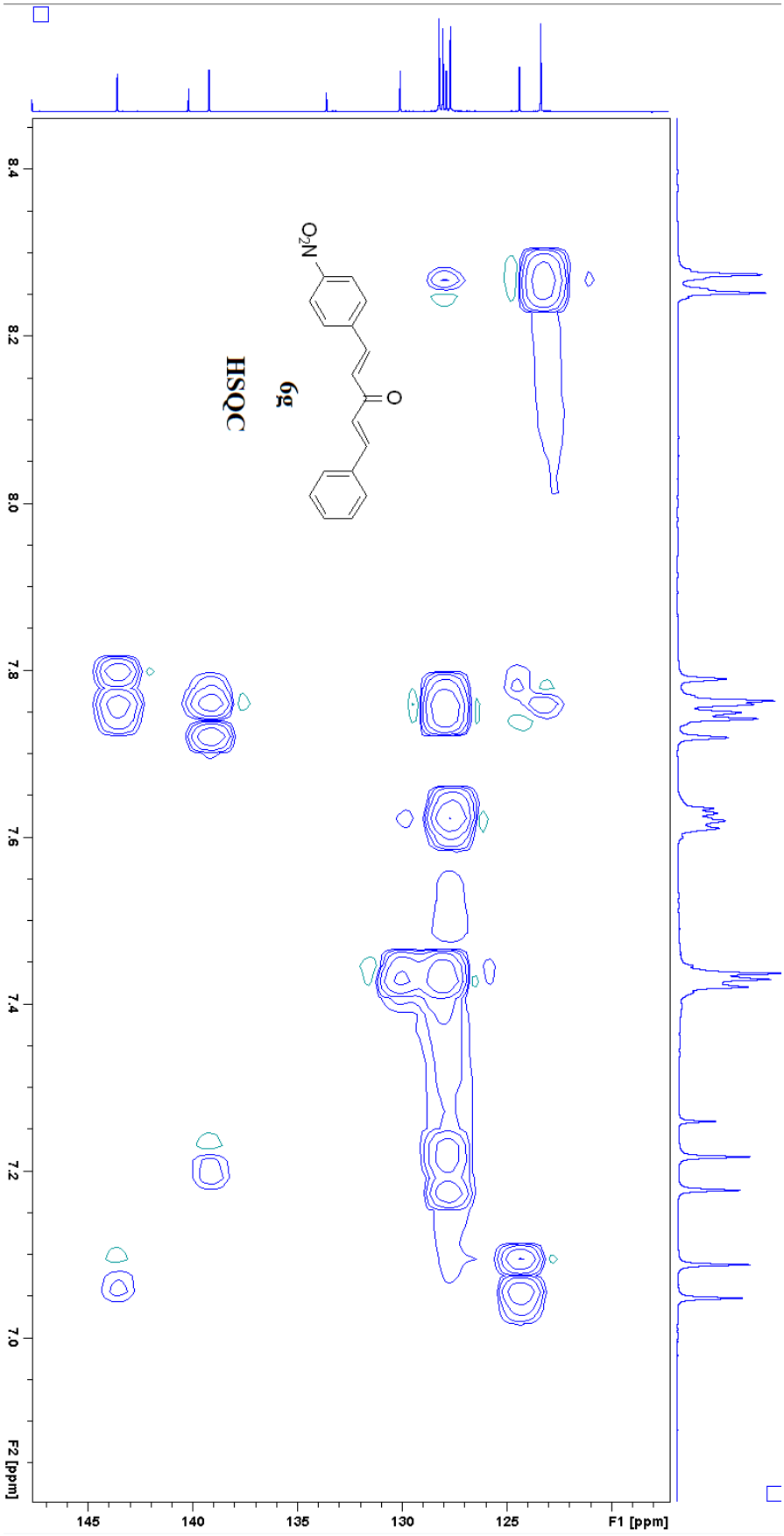

12/7/2018 9:21:04 AM ECB-45
ECB-45_b #1-5 RT: 0.00-0.11 AV: 5 NL: 5.66E7
T: FTMS + p ESI Full ms [200.00-500.00]
333.1249
C23 H18 O Na = 333.1250
-0.0583 mmu
O
6d
MS
311.1429
C23 H19 O = 311.1430
-0.1033 mmu
335.1314
349.0987
C23 H18 O K = 349.0989
-0.2263 mmu
Relative Abundance
m/z

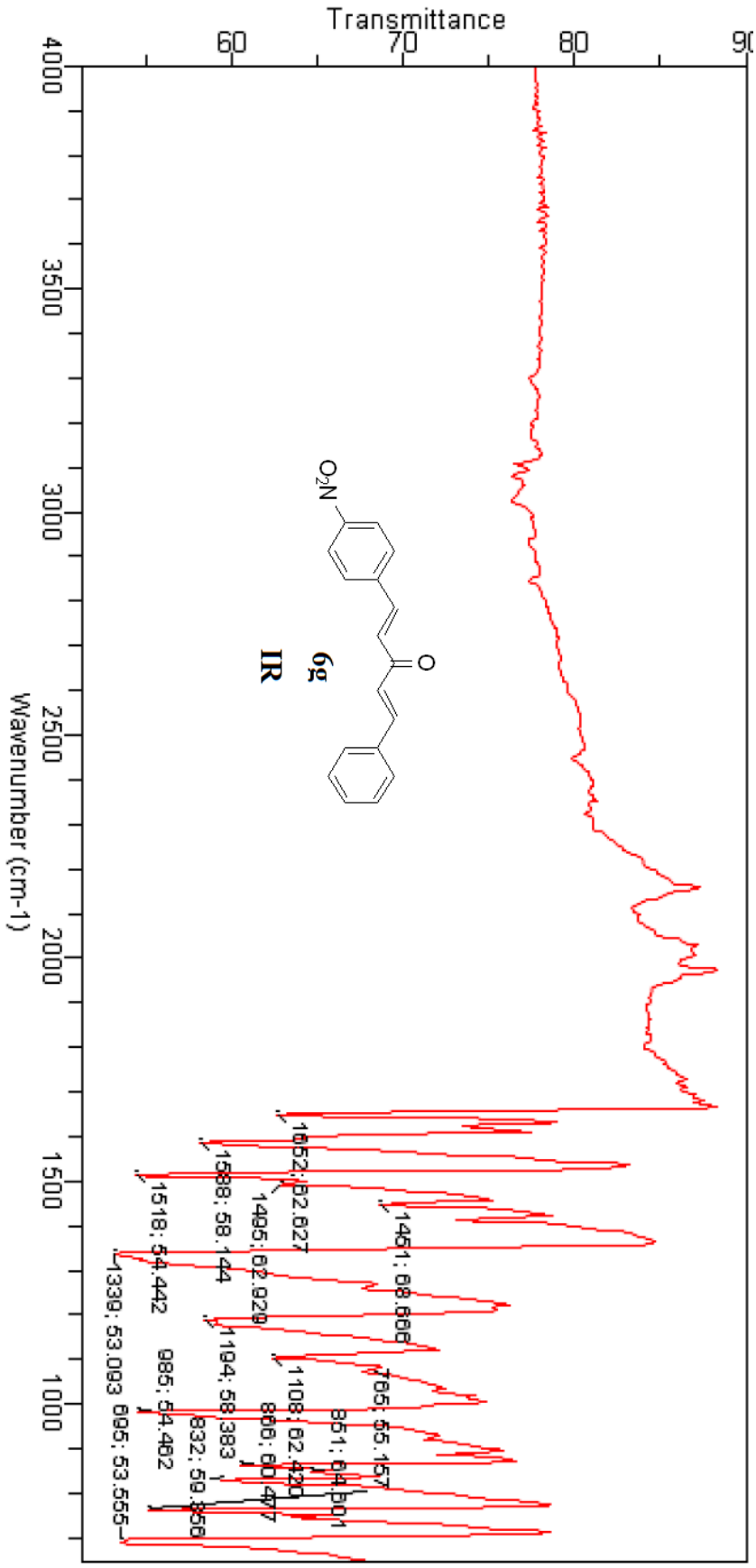
(1*E*,4*E*)-1-(4-nitrophenyl)penta-1,4-dien-3-one (6g)

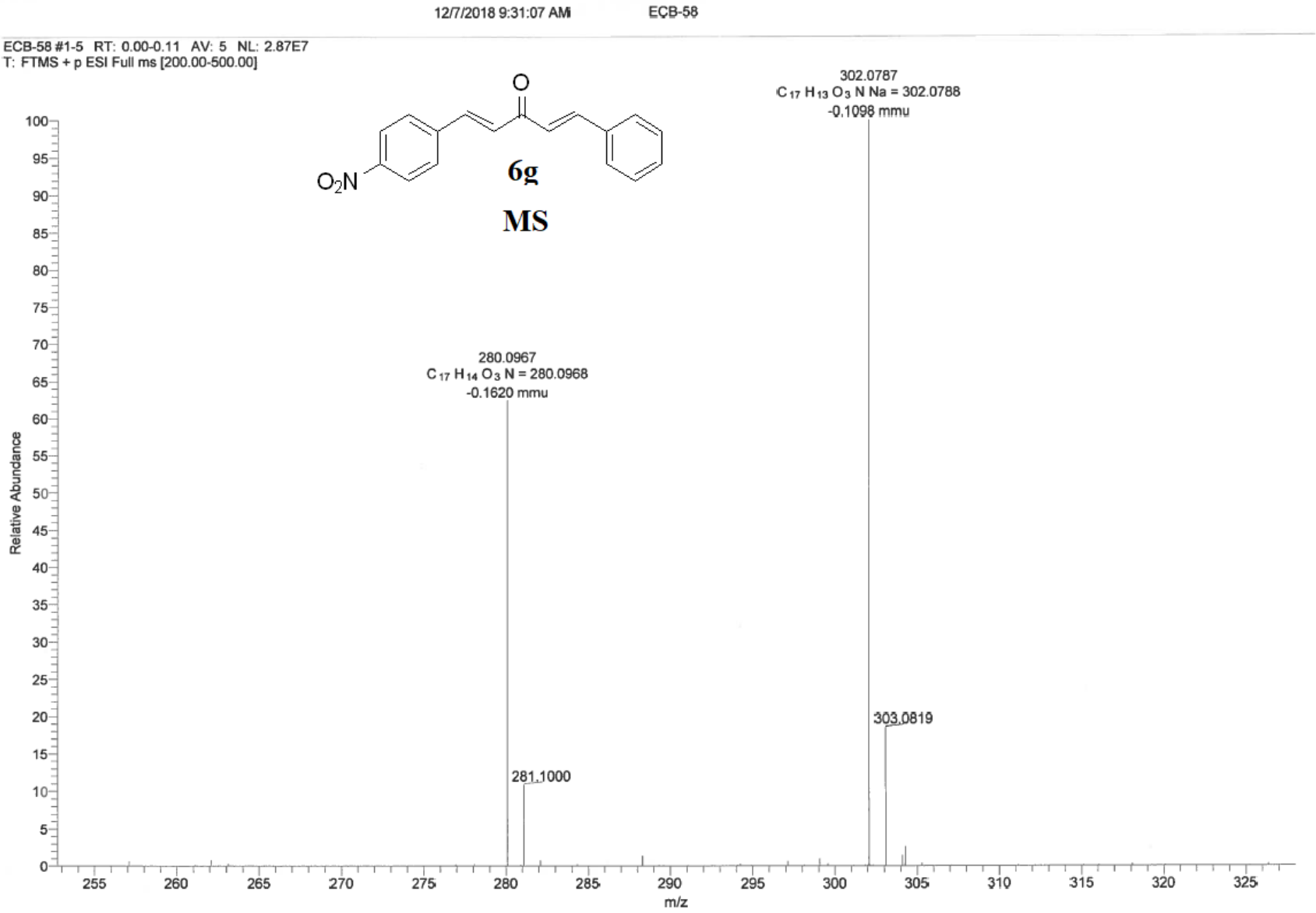



2.0000
4.0615
2.0750
3.0387
1.1135
1.0344
8.2730
8.2510
7.7883
7.7621
7.7581
7.7481
7.7405
7.7182
M 7.6435
M 7.5948
7.4354
7.4285
7.4192
7.2157
7.1759
7.0863
7.0464
[ppm]
0
5
10
15
20
25 [rel]
^{1}H 6g
O
O$_2$N

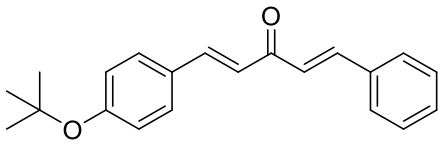

187.2552
147.6295
143.5530
140.1385
139.1705
133.5580
130.0356
128.1833
127.9950
127.8383
127.6446
124.3405
123.3266
150
100
50
[ppm]
0
10
20
30
[rel
^{13}C 6g
O_2N
O

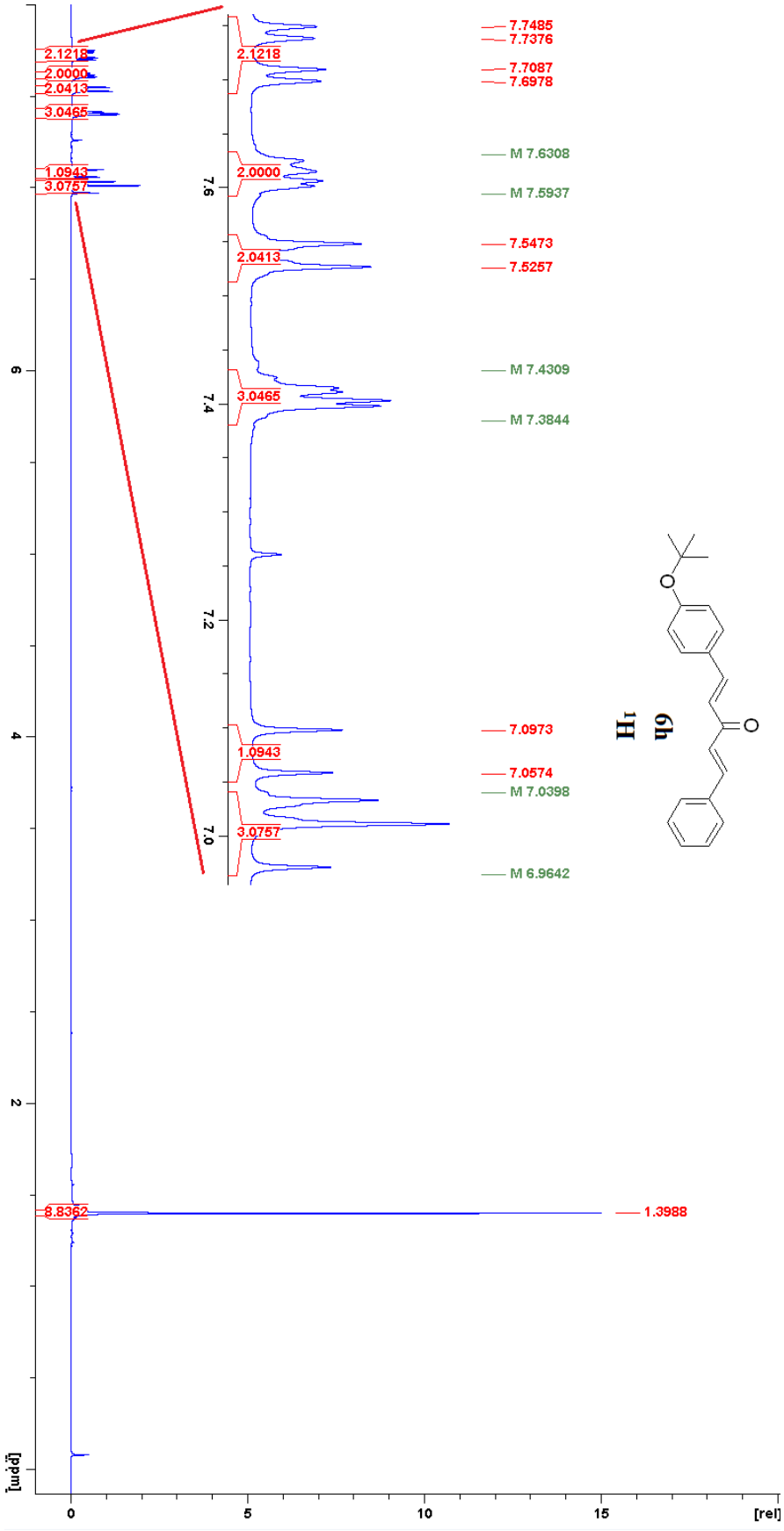

8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
F2 [ppm]
145
140
135
130
125
F1 [ppm]
O
O2N

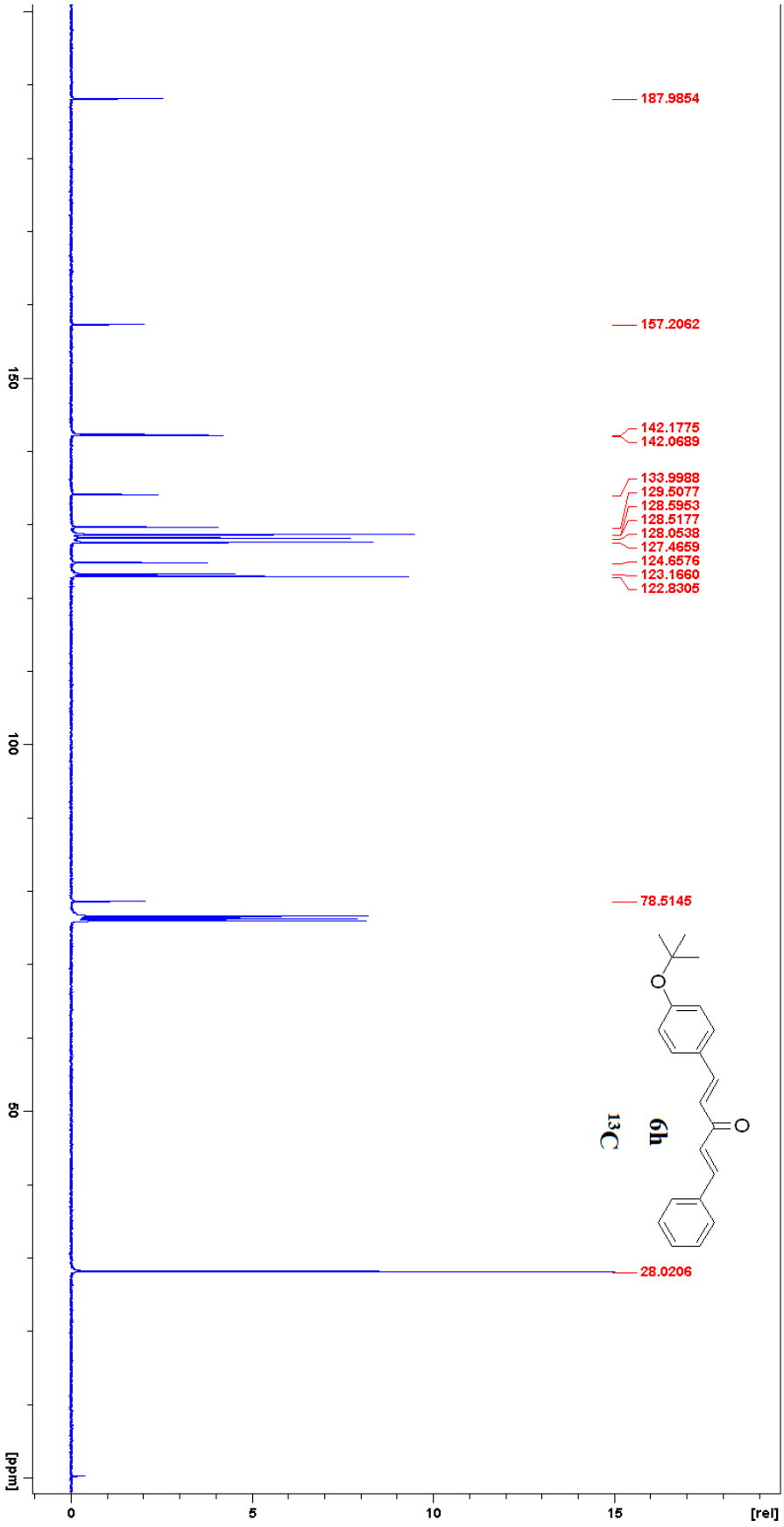

Transmittance
60
70
80
90
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
IR
6g
O2N
O
1652; 52.627
1588; 58.144
1518; 54.442
1495; 62.929
1451; 68.666
1339; 53.093
1194; 58.383
1108; 62.420
985; 54.462
851; 64.501
832; 59.856
765; 55.157
696; 53.555

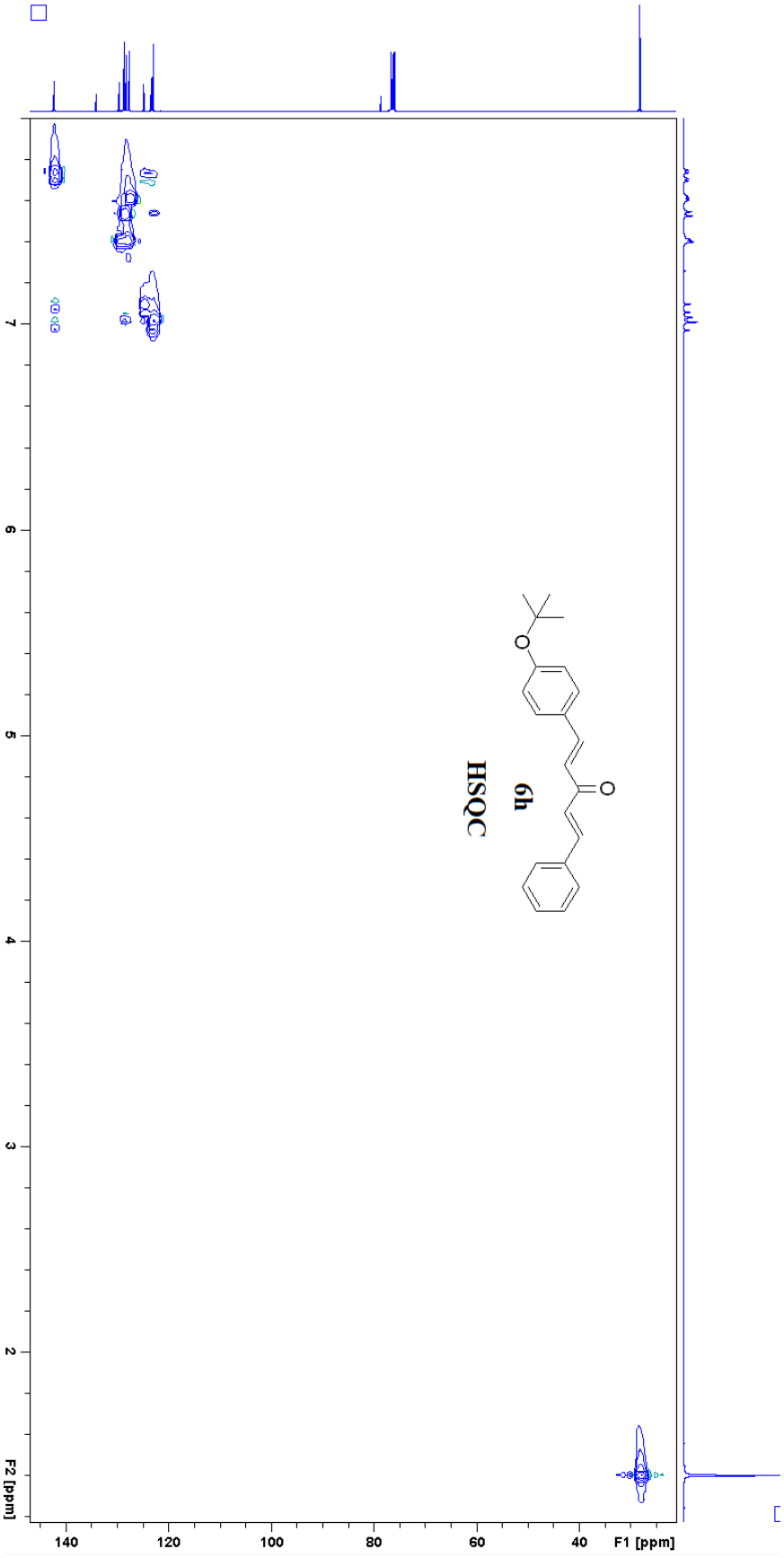

12/7/2018 9:31:07 AM
ECB-58
ECB-58 #1-5 RT: 0.00-0.11 AV: 5 NL: 2.87E7
T: FTMS + p ESI Full ms [200.00-500.00]
O
O2N
6g
MS
302.0787
C17 H13 O3 N Na = 302.0788
-0.1098 mmu
280.0967
C17 H14 O3 N = 280.0968
-0.1620 mmu
303.0819
281.1000
Relative Abundance
m/z

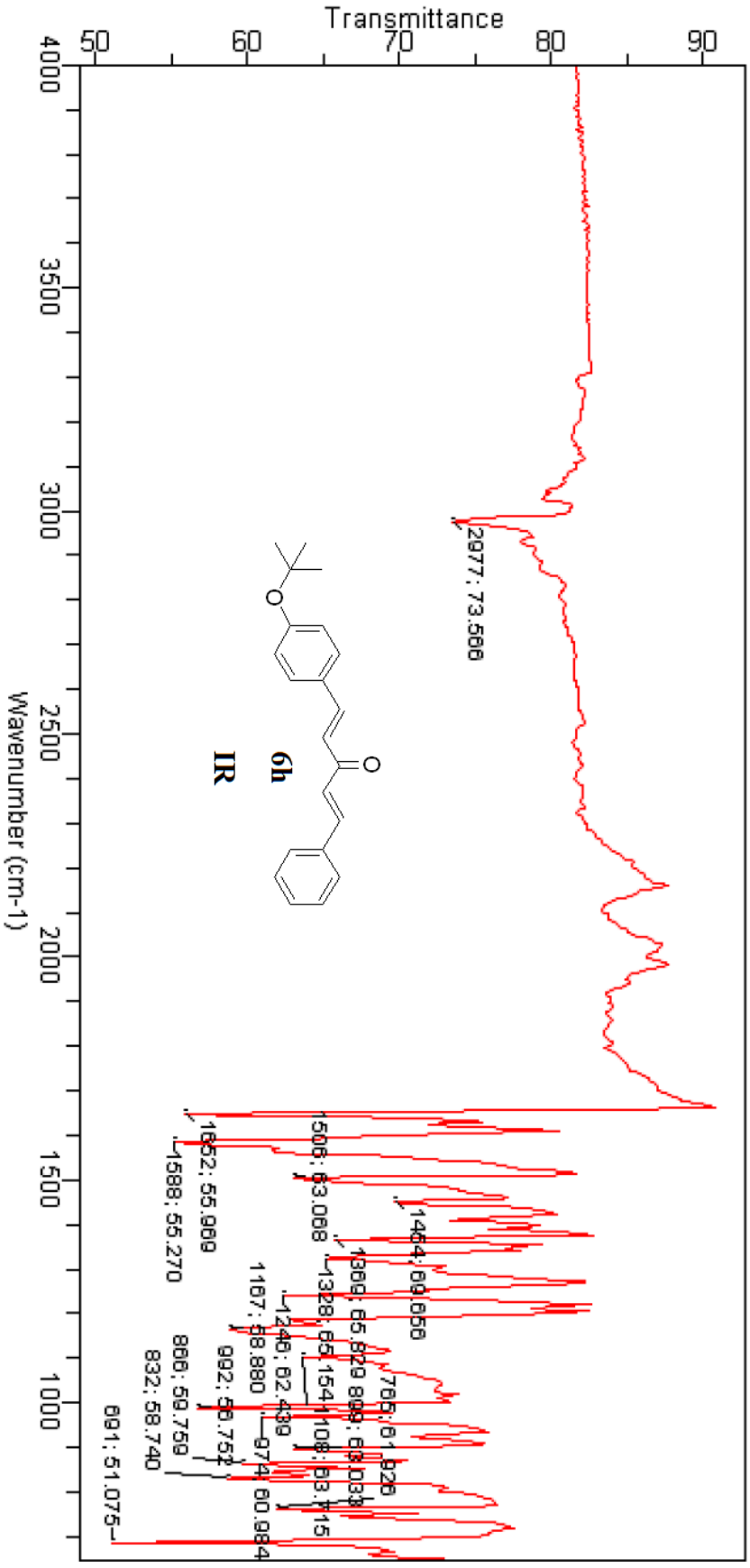
(1*E*,4*E*)-1-(4-*tert*-butoxyphenyl)penta-1,4-dien-3-one (6h)




2.1218
2.0000
2.0413
3.0465
1.0943
3.0757
8.8362
1.3988
7.7485
7.7376
7.7087
7.6978
M 7.6308
M 7.5937
7.5473
7.5257
M 7.4309
M 7.3844
7.0973
7.0574
M 7.0398
M 6.9642
[ppm]
[rel]
1H
6h

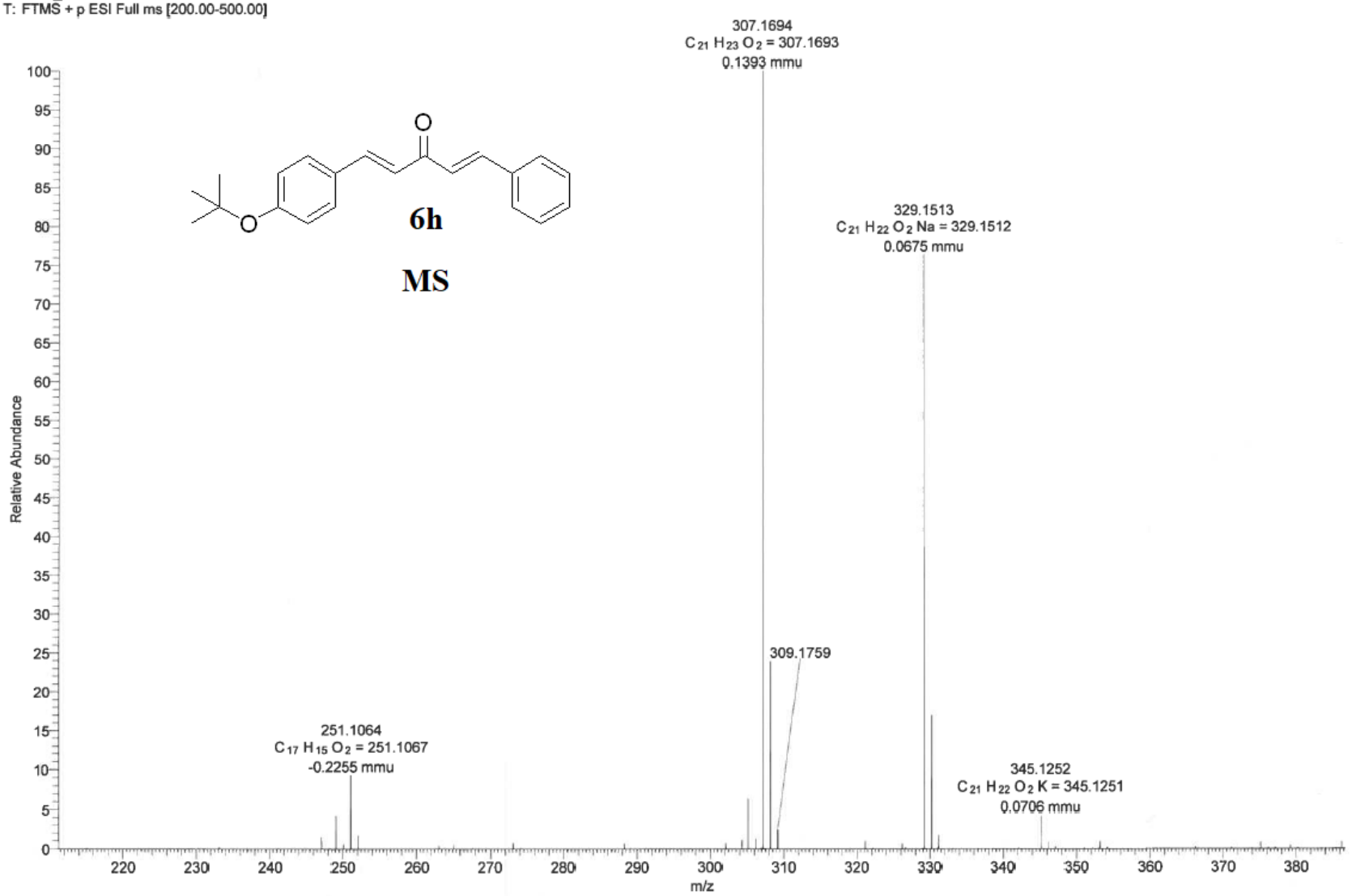

187.9854
157.2062
142.1775
142.0689
133.9988
129.5077
128.5953
128.5177
128.0538
127.4659
124.6576
123.1660
122.8305
78.5145
28.0206
O
O
^{13}C 6h
150
100
50
[ppm]
0
5
10
15
[rel]


HSQC
6h
F2 [ppm]
F1 [ppm]
140
120
100
80
60
40
2
3
4
5
6
7


Transmittance
50
60
70
80
90
4000
3500
3000
2500
2000
1500
1000
Wavenumber (cm-1)
IR
6h
O
O
2977; 73.566
1652; 55.969
1588; 55.270
1506; 63.068
1464; 69.656
1328; 65.154
1167; 58.880
992; 58.752
866; 59.759
832; 58.740
691; 51.075

12/7/2018 9:37:32 AM

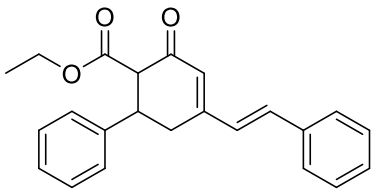
ECB-59_b #1-4 RT: 0.02-0.10 AV: 4 NL: 6.21E7
T: FTMS + p ESI Full ms [200.00-500.00]

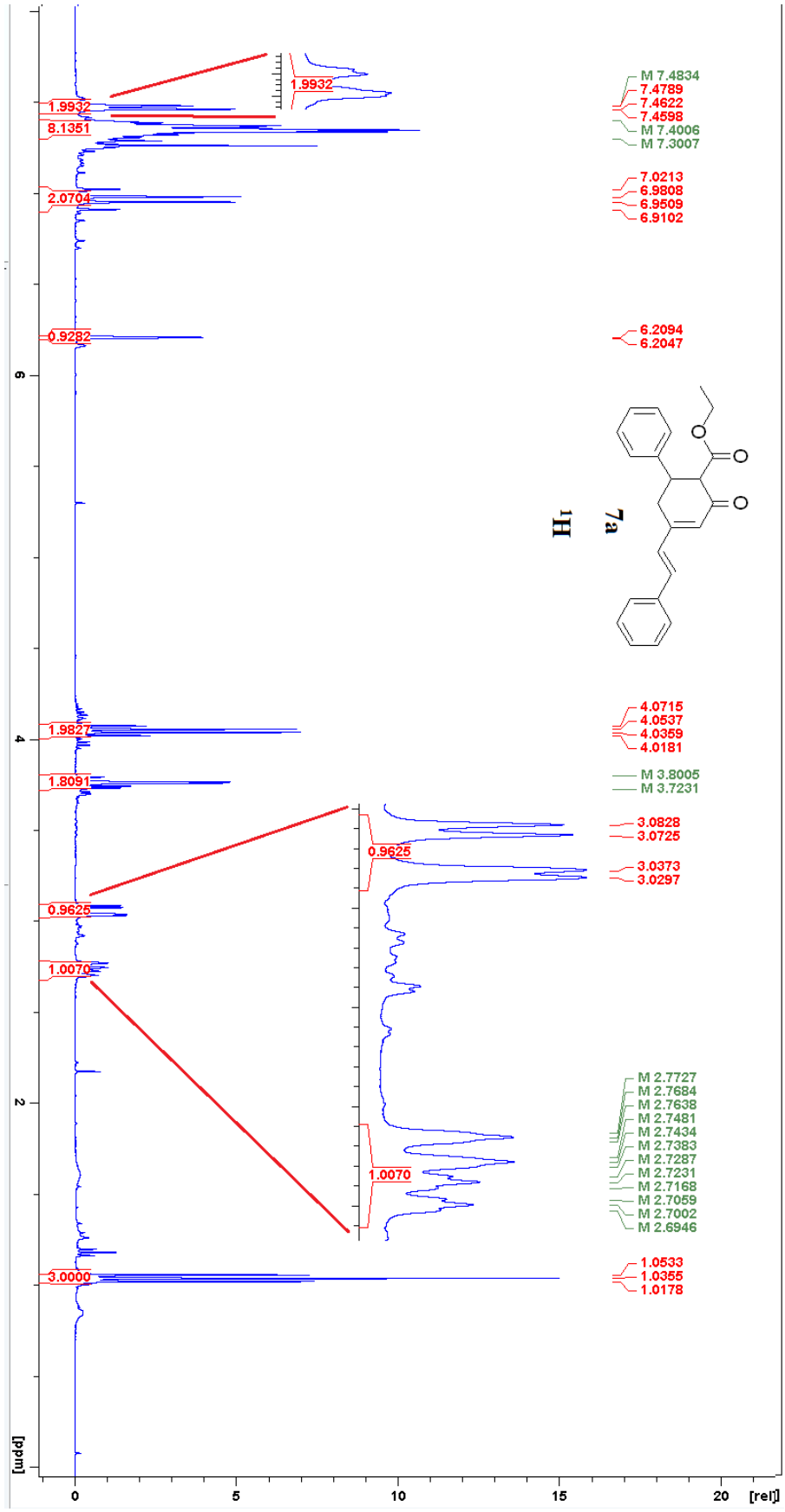


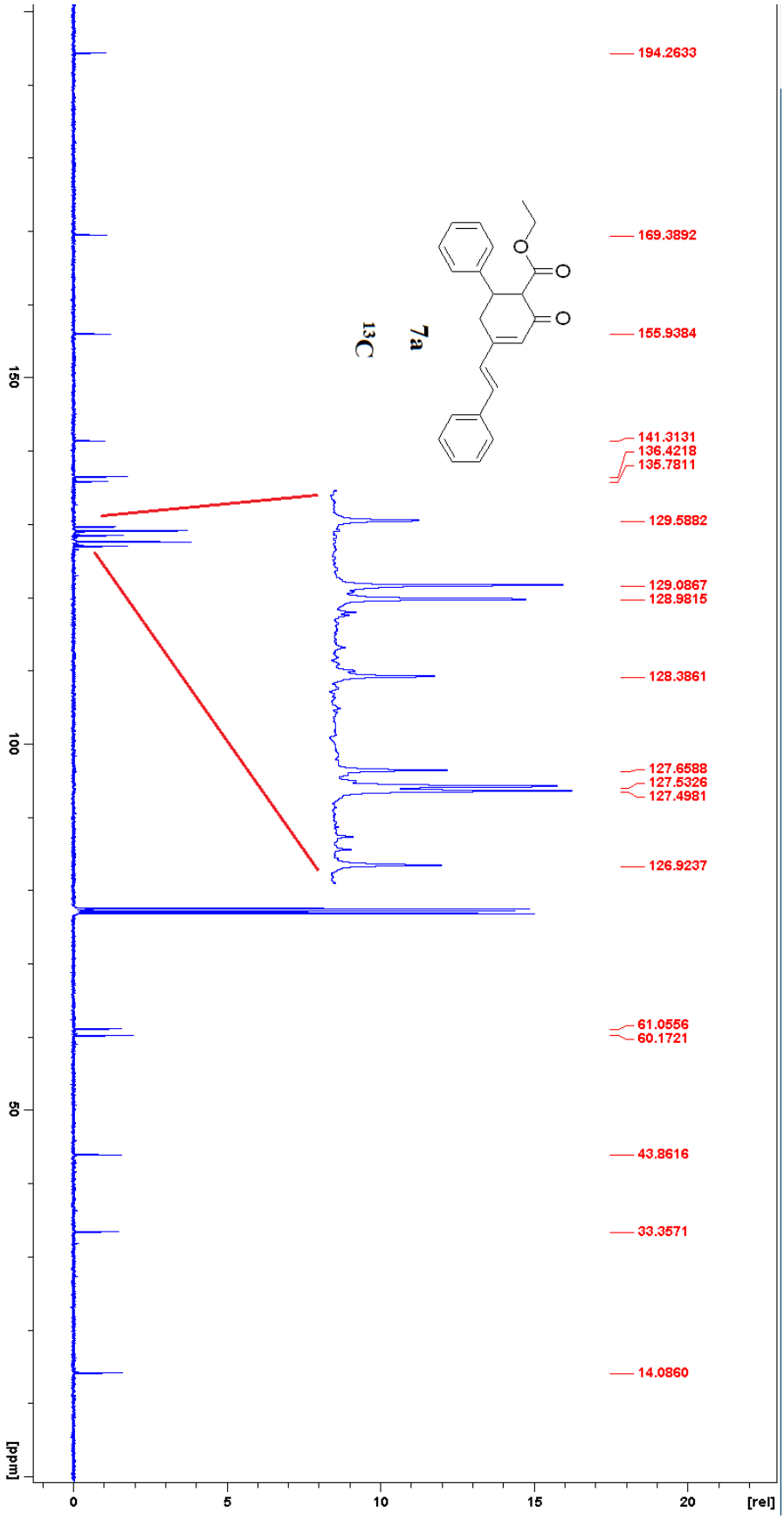
6h

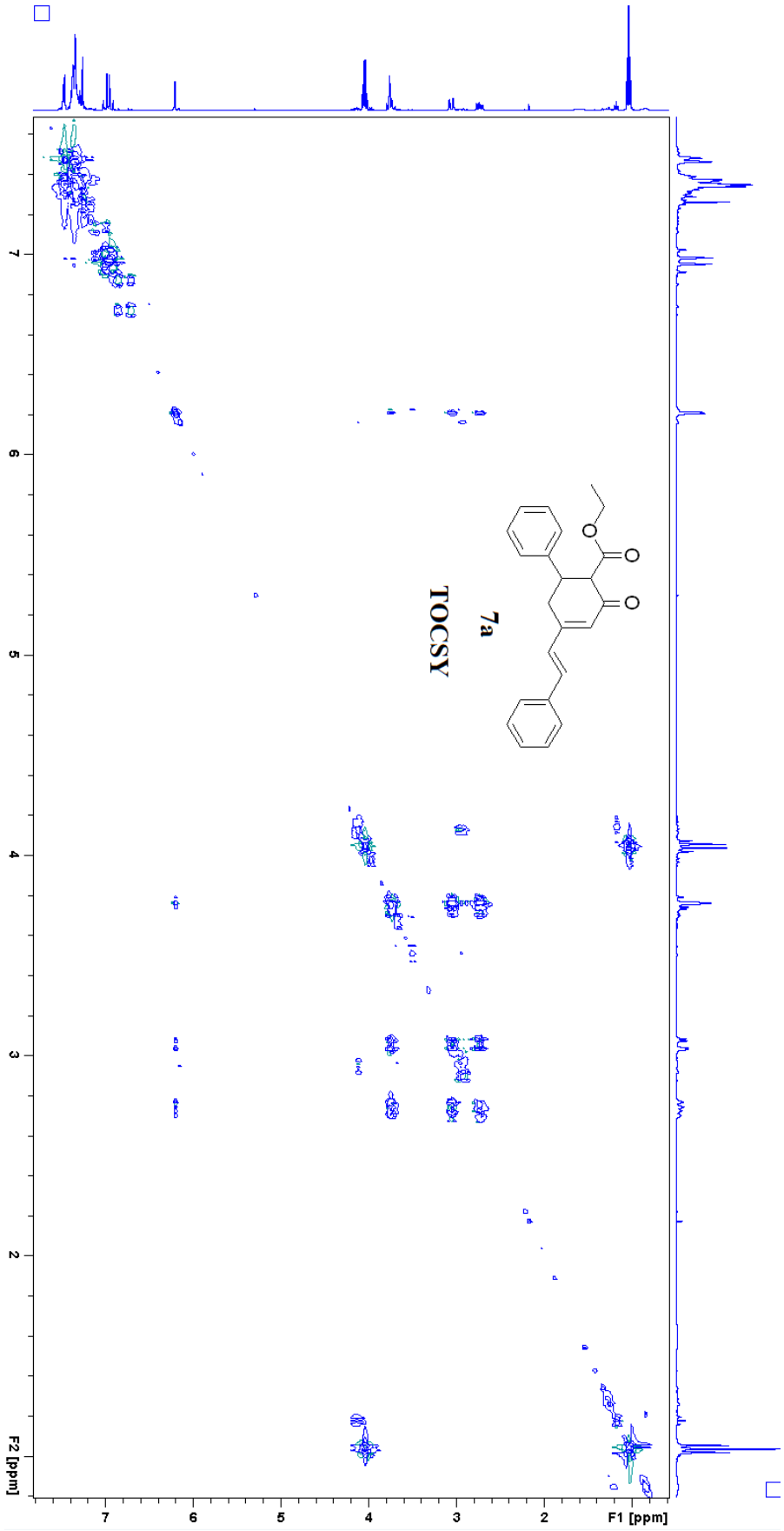
MS

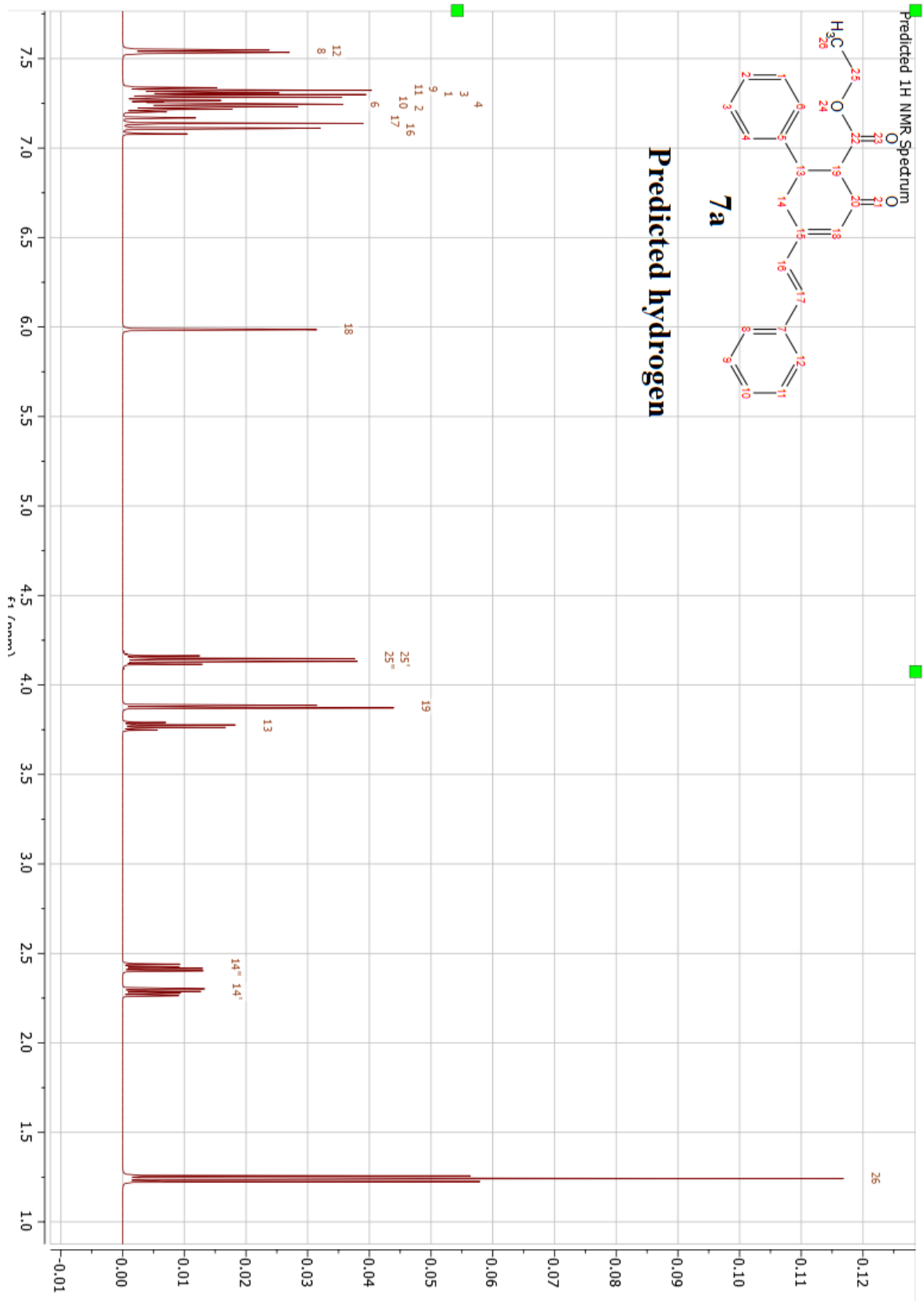
(E)-Ethyl 2-oxo-6-phenyl-4-(2-phenylethenyl)-4-cyclohexene-1-carboxylate (7a)

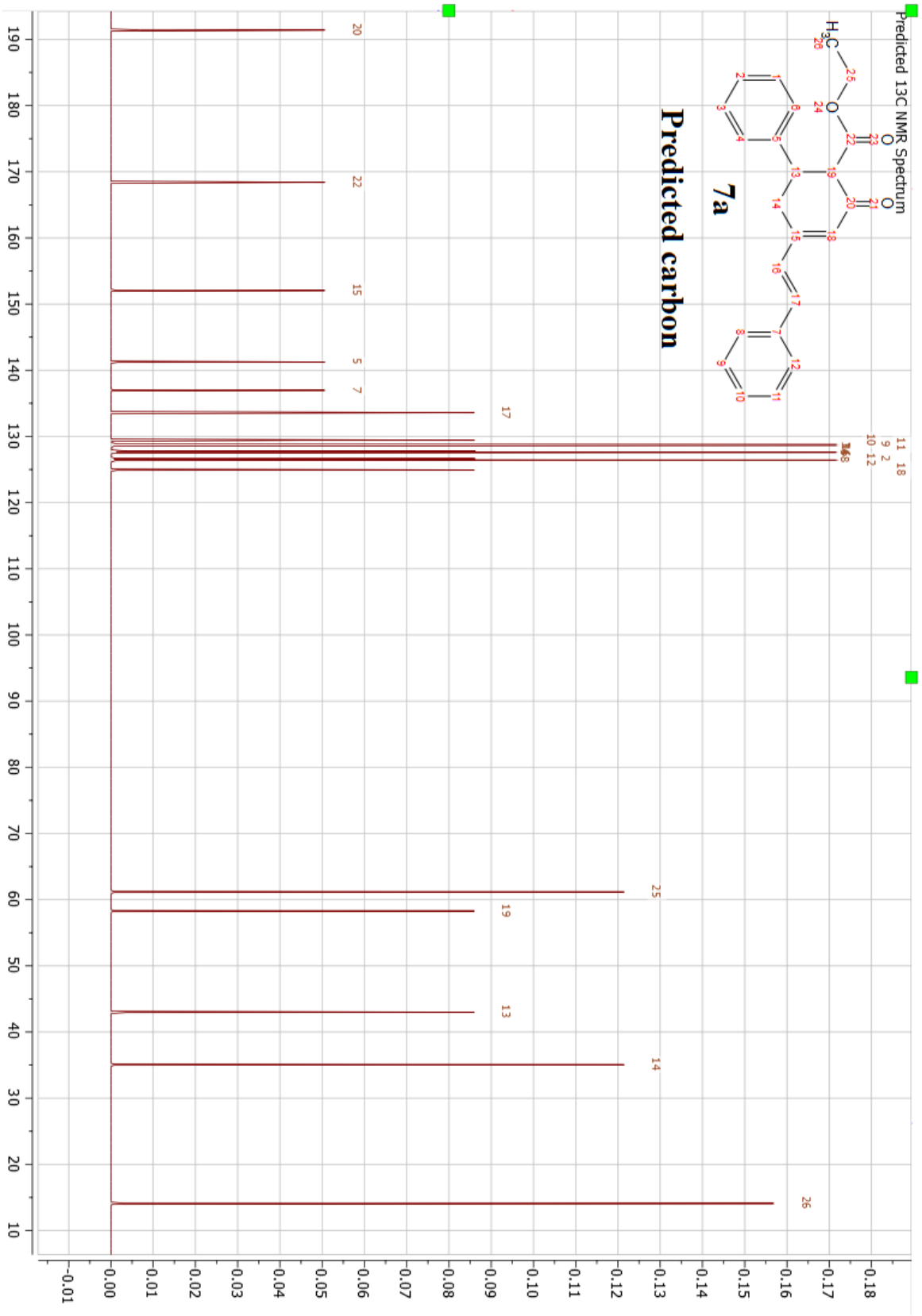



1.9932
1.9932
8.1351
2.0704
0.9282
1.9827
1.8091
0.9625
1.0070
3.0000
M 7.4834
7.4789
7.4622
7.4598
M 7.4006
M 7.3007
7.0213
6.9808
6.9509
6.9102
6.2094
6.2047
4.0715
4.0537
4.0359
4.0181
M 3.8005
M 3.7231
3.0828
3.0725
3.0373
3.0297
M 2.7727
M 2.7684
M 2.7638
M 2.7481
M 2.7434
M 2.7383
M 2.7287
M 2.7231
M 2.7168
M 2.7059
M 2.7002
M 2.6946
1.0533
1.0355
1.0178
1H
7a
[ppm]
[rel]

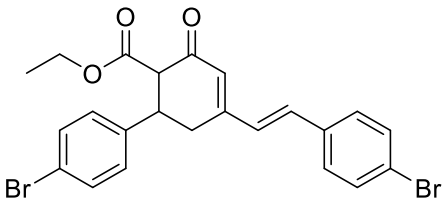

194.2633
169.3892
155.9384
141.3131
136.4218
135.7811
129.5882
129.0867
128.9815
128.3861
127.6588
127.5326
127.4981
126.9237
61.0556
60.1721
43.8616
33.3571
14.0860
^{13}C
7a
150
100
50
[ppm]
0
5
10
15
20
[rel]

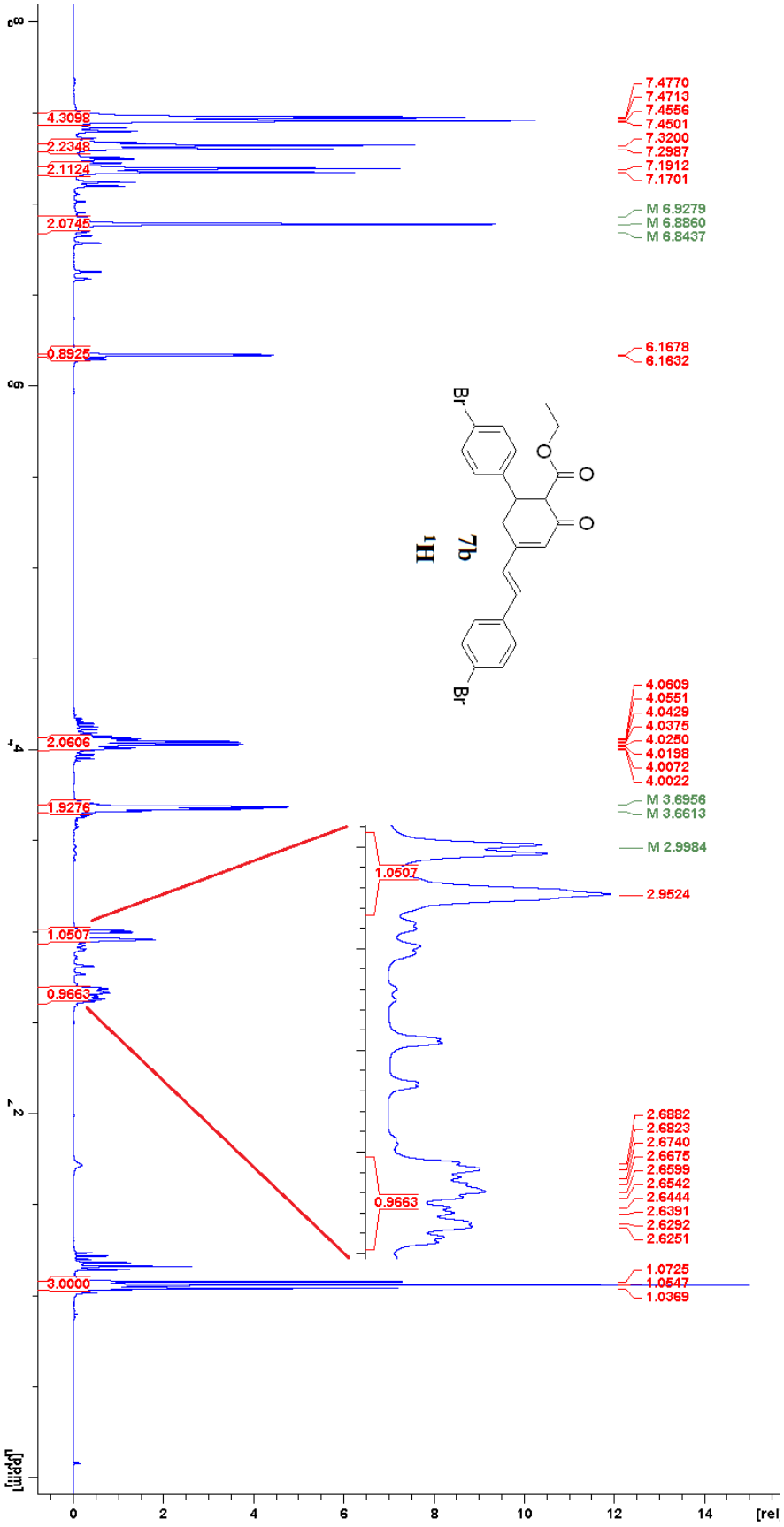

TOCSY
7a
F2 [ppm]
F1 [ppm]
7
6
5
4
3
2

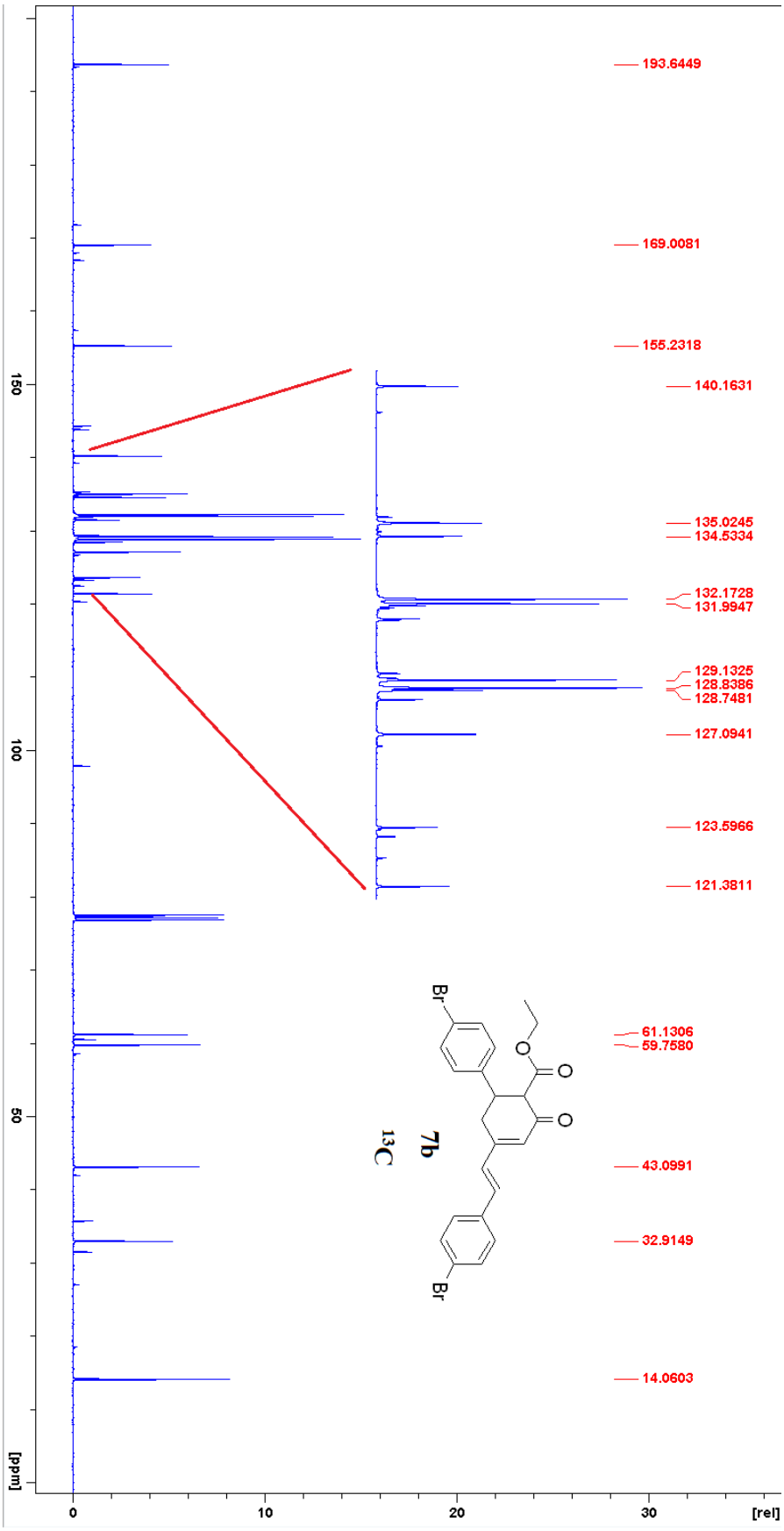

Predicted 1H NMR Spectrum
7a
Predicted hydrogen

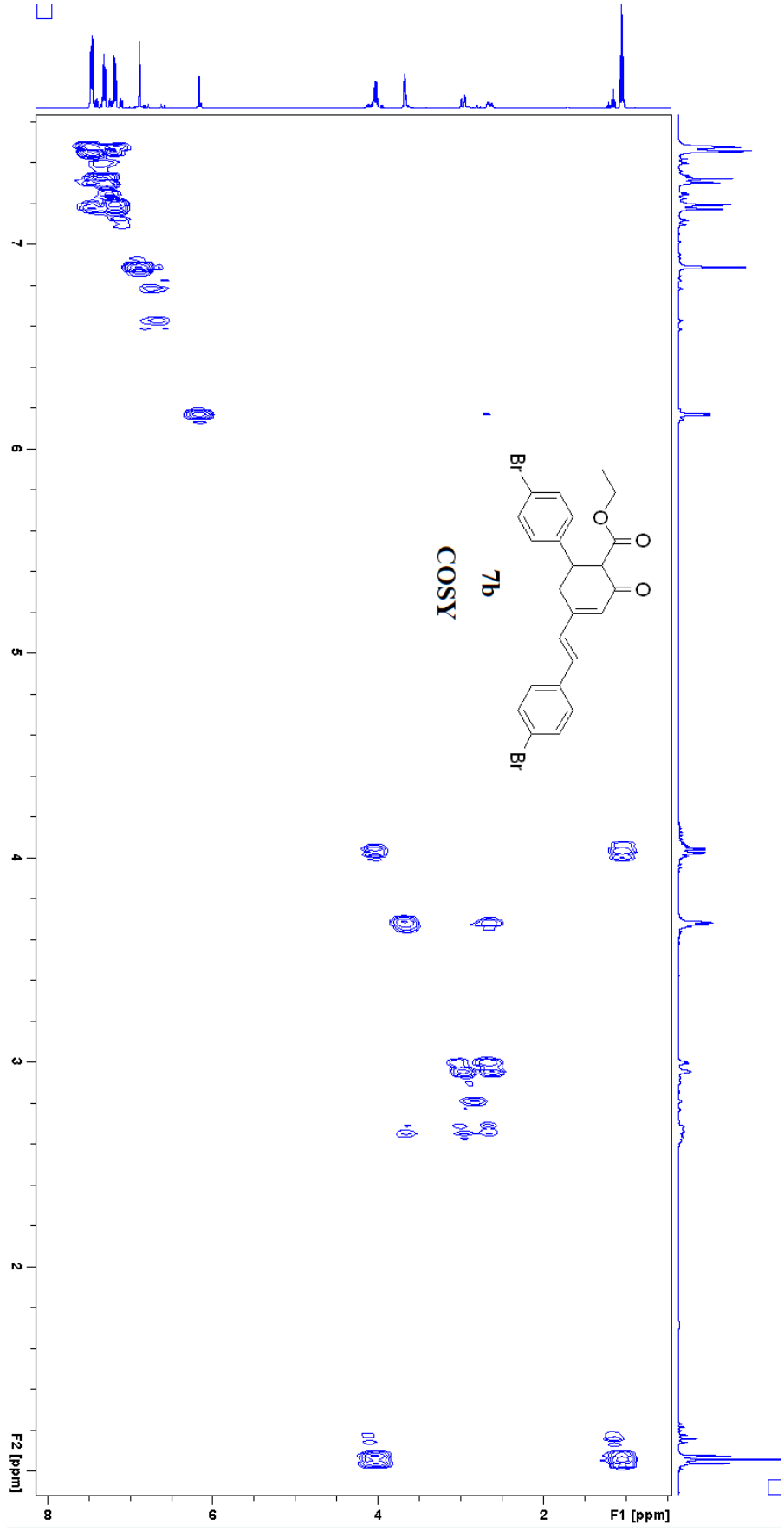

Predicted 13C NMR Spectrum
7a
Predicted carbon

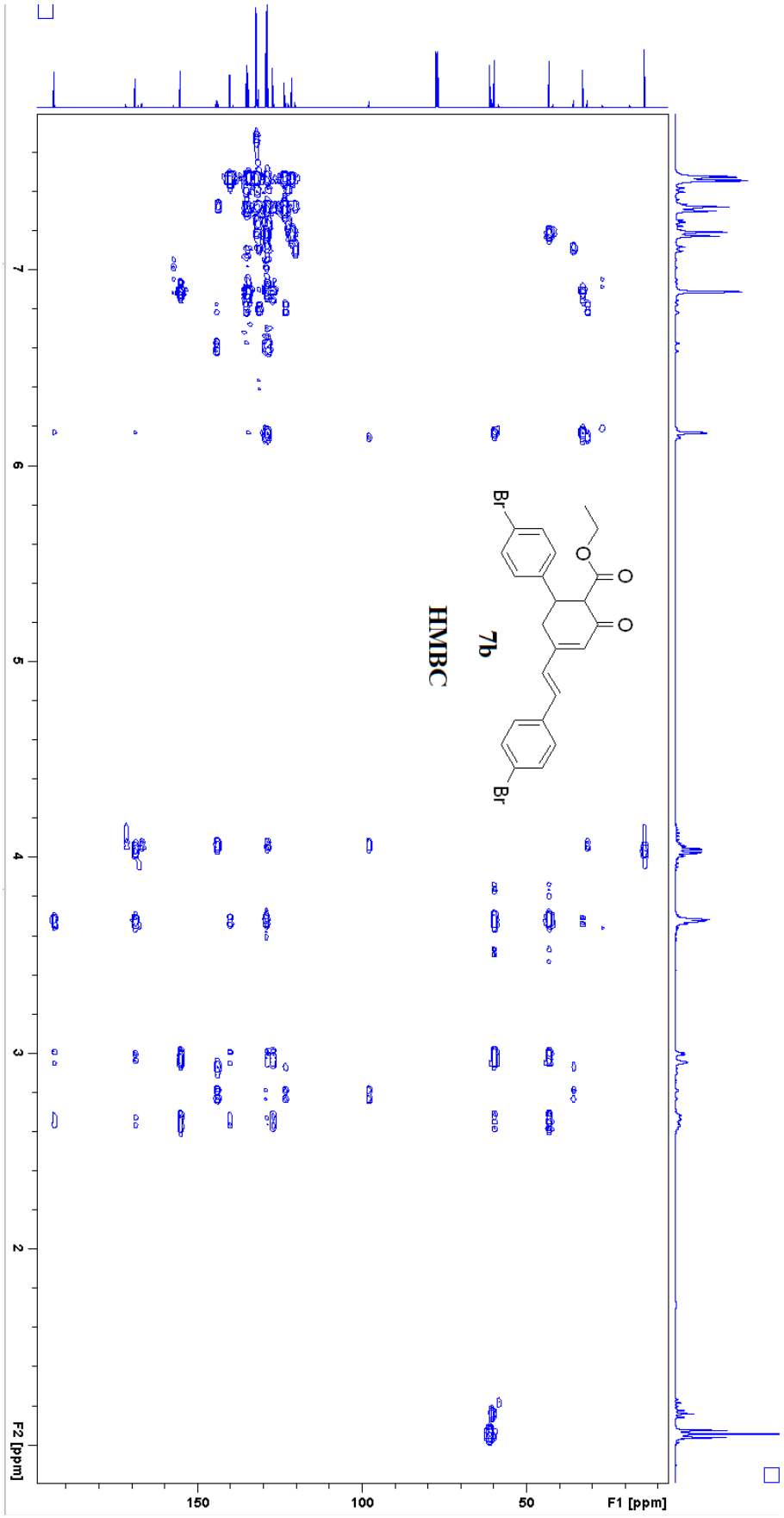
(E)-Ethyl 6-(4-bromophenyl)-4-[2-(4-bromophenyl)ethenyl]-2-oxo-4-cyclohexene-1-carboxylate (7b)

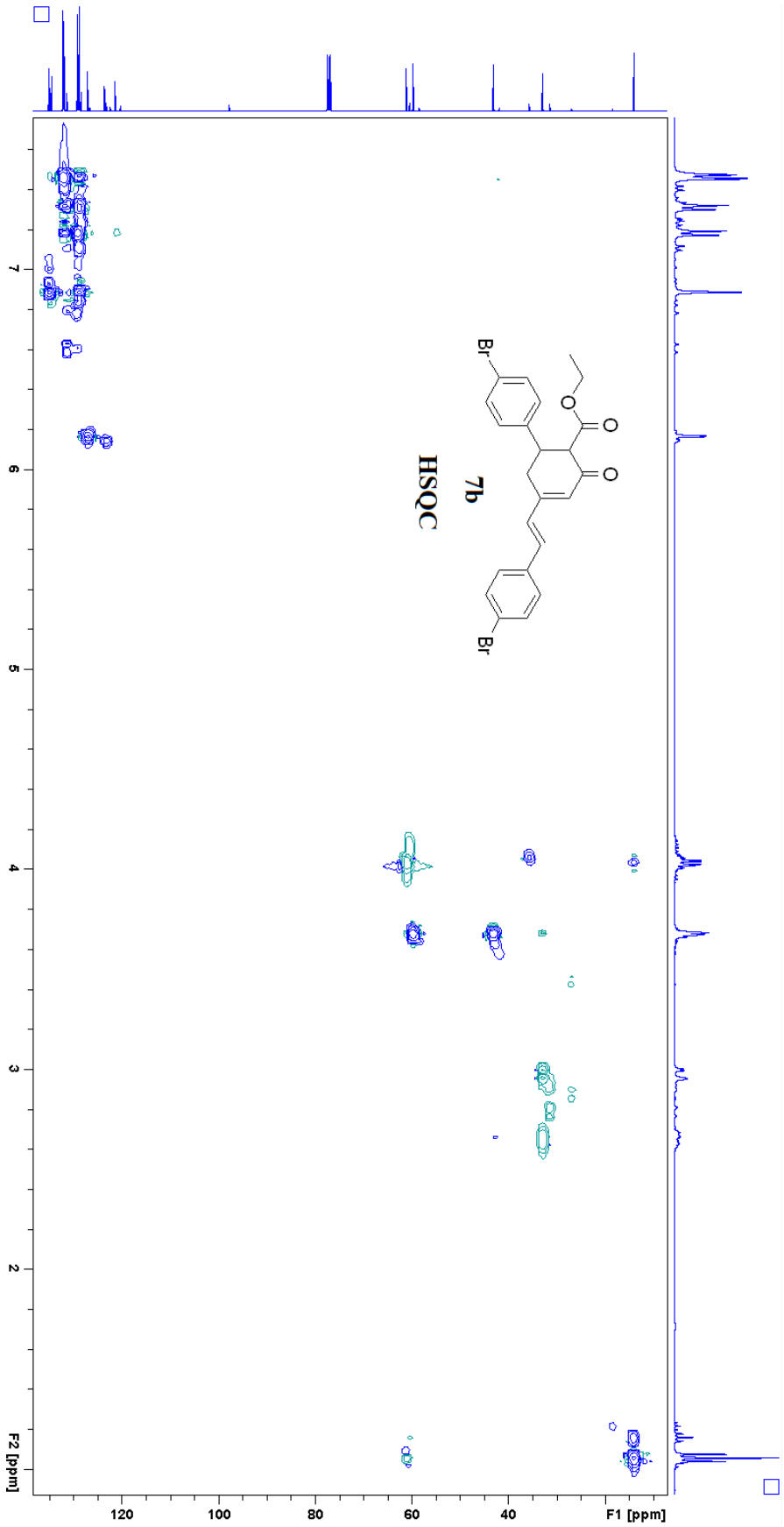



7b
^{1}H
Br
Br
O
O
O
8
6
4
2
[ppm]
0
2
4
6
8
10
12
14
[rel]
4.3098
2.2348
2.1124
2.0745
0.8925
2.0606
1.9276
1.0507
0.9663
3.0000
1.0507
0.9663
7.4770
7.4713
7.4556
7.4501
7.3200
7.2987
7.1912
7.1701
M 6.9279
M 6.8860
M 6.8437
6.1678
6.1632
4.0609
4.0551
4.0429
4.0375
4.0250
4.0198
4.0072
4.0022
M 3.6956
M 3.6613
M 2.9984
2.9524
2.6882
2.6823
2.6740
2.6675
2.6599
2.6542
2.6444
2.6391
2.6292
2.6251
1.0725
1.0547
1.0369

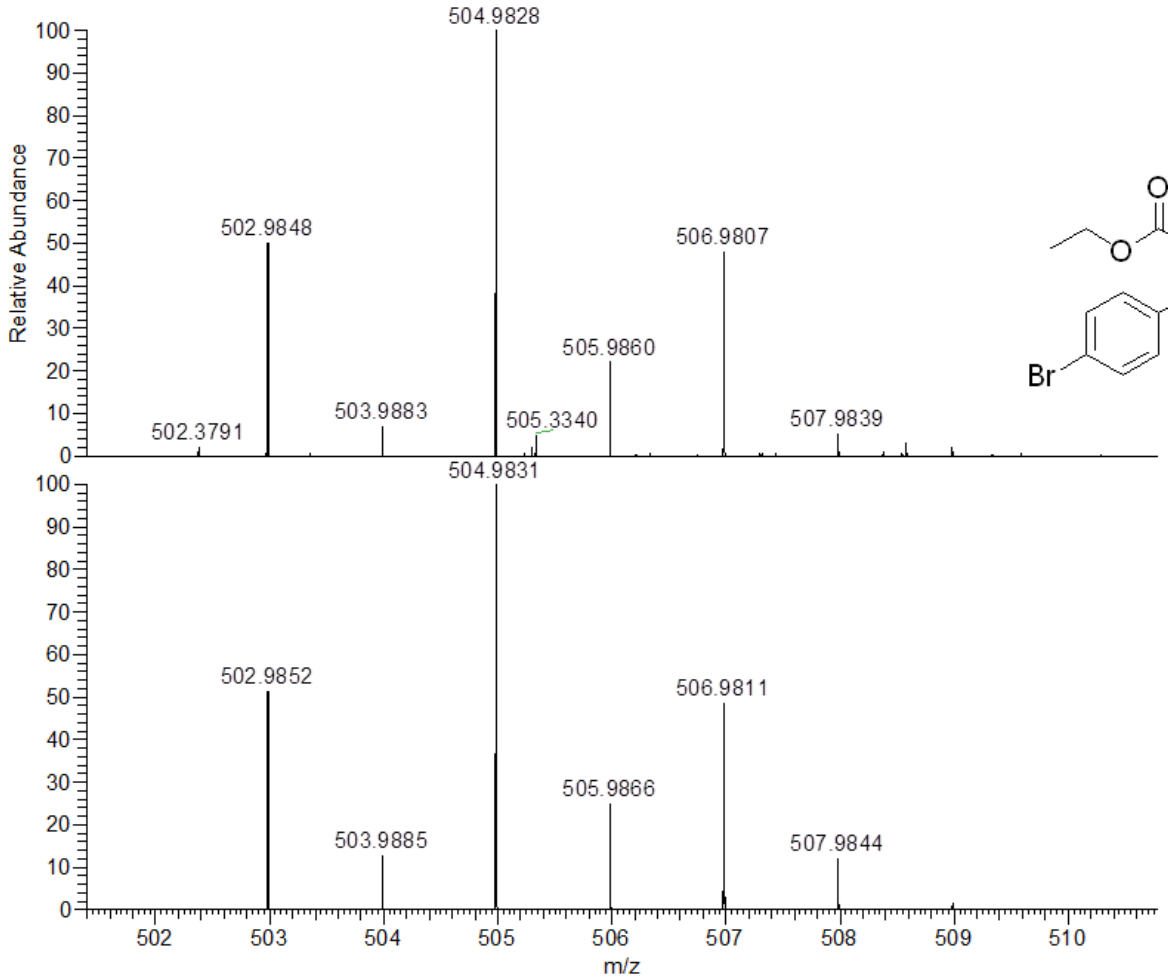

193.6449
169.0081
155.2318
140.1631
135.0245
134.5334
132.1728
131.9947
129.1325
128.8386
128.7481
127.0941
123.5966
121.3811
61.1306
59.7580
43.0991
32.9149
14.0603
150
100
50
[ppm]
0
10
20
30
[rel]
Br
O
O
O
Br
7b
^{13}C


COSY
7b
Br
Br
O
O
O
F2 [ppm]
F1 [ppm]
8
6
4
2
7
6
5
4
3
2

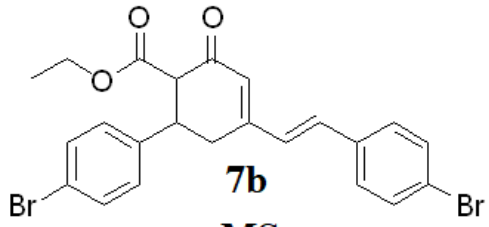

HMBC
7b
Br
Br
O
O
O
F2 [ppm]
F1 [ppm]
150
100
50
2
3
4
5
6
7


HSQC
7b
Br
Br
O
O
O
F2 [ppm]
F1 [ppm]
120
100
80
60
40
2
3
4
5
6
7

C:\Xcalibur\data\Erlend Brevik\ECB-35_b 1/25/2019 9:16:46 AM ECB-35
5 4.5 80



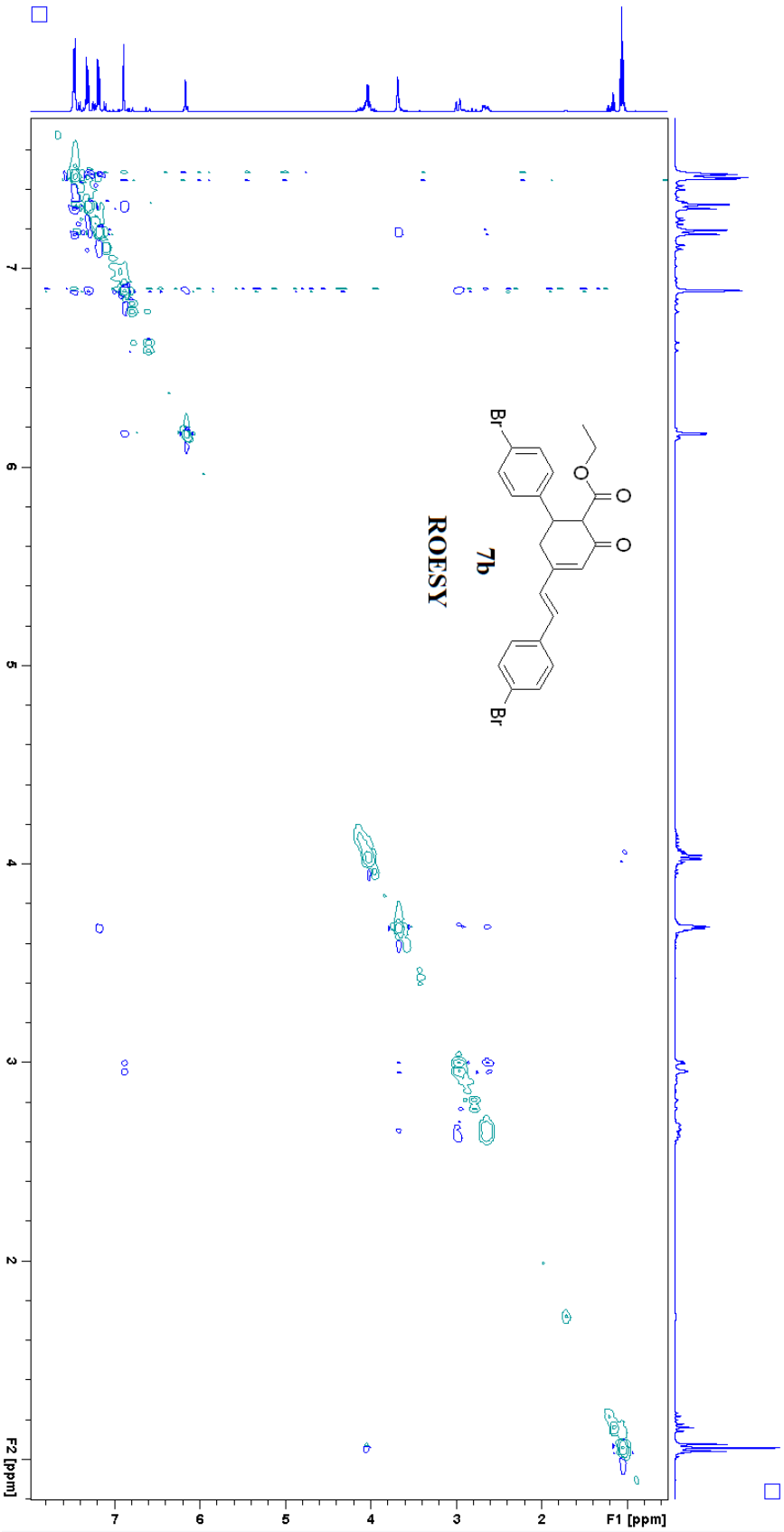
NL:
2.53E6
ECB-35_b#1-2 RT: 0.02-0.04
AV: 2 T: FTMS + p ESI Full ms
[200.00-800.00]



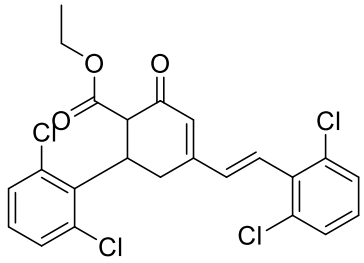
7b

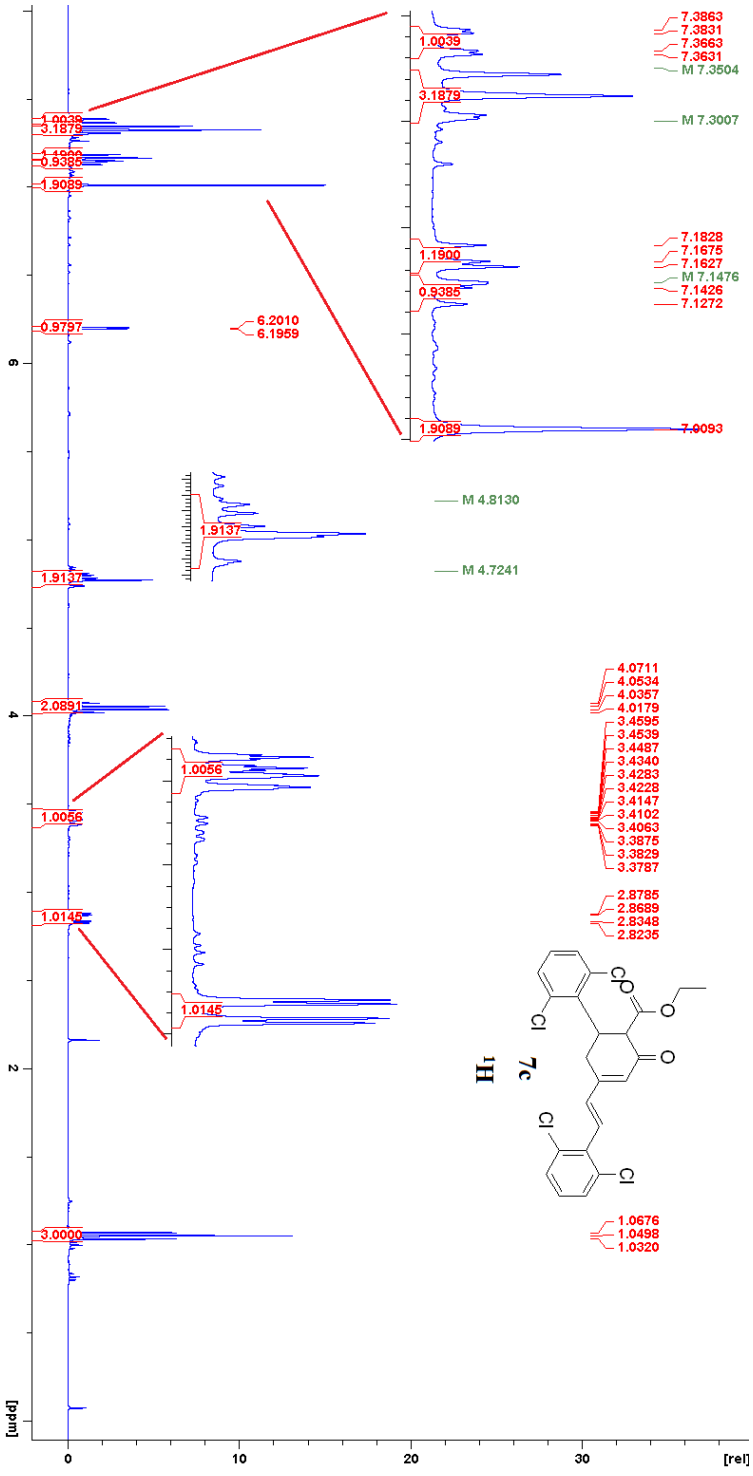
MS

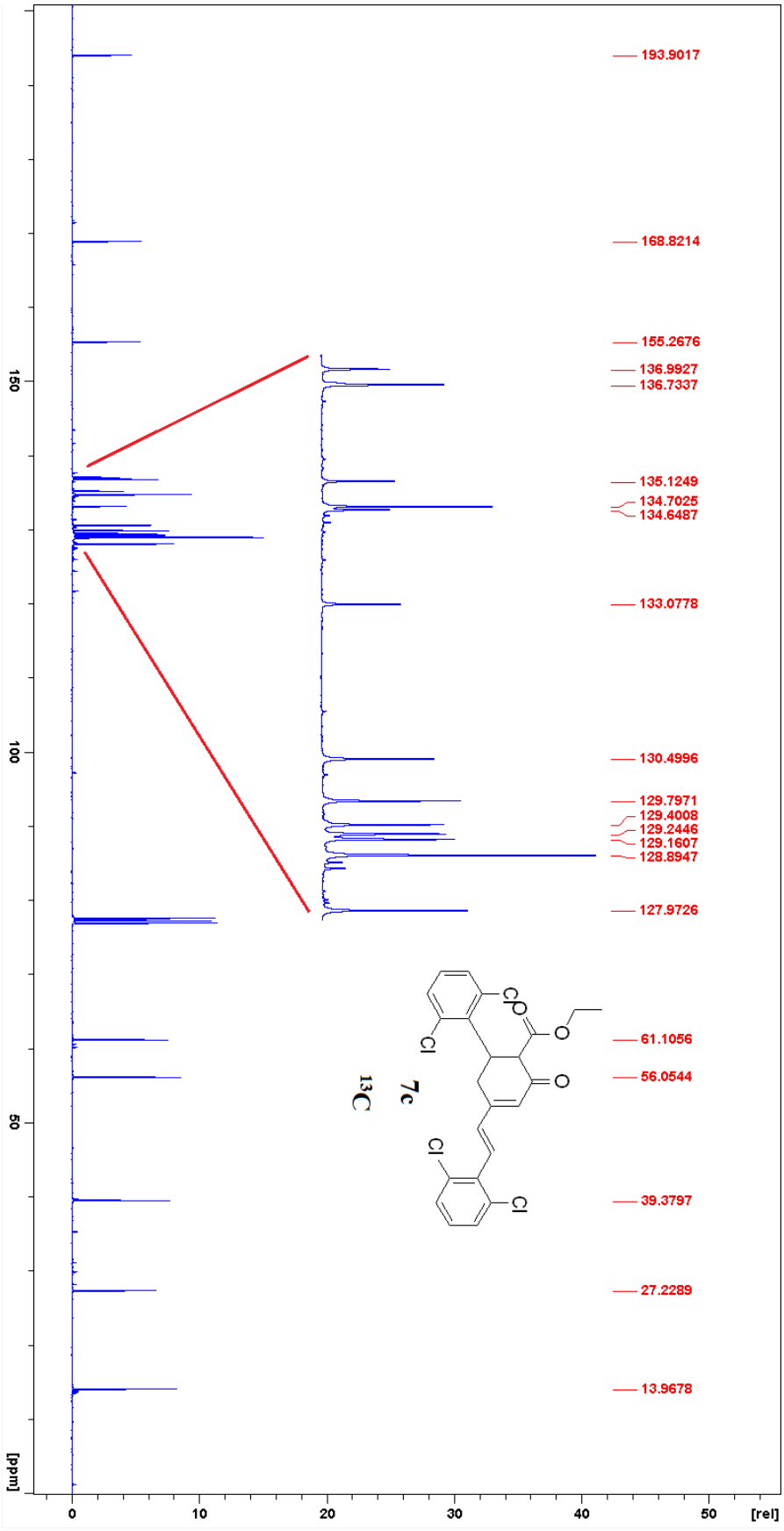
NL:
9.07E3
$C_{23}H_{20}Br_2O_3H$:
$C_{23}H_{21}Br_2O_3$
p (gss, s /p:40) Chrg 1
R: 121000 Res .Pwr . @FWHM

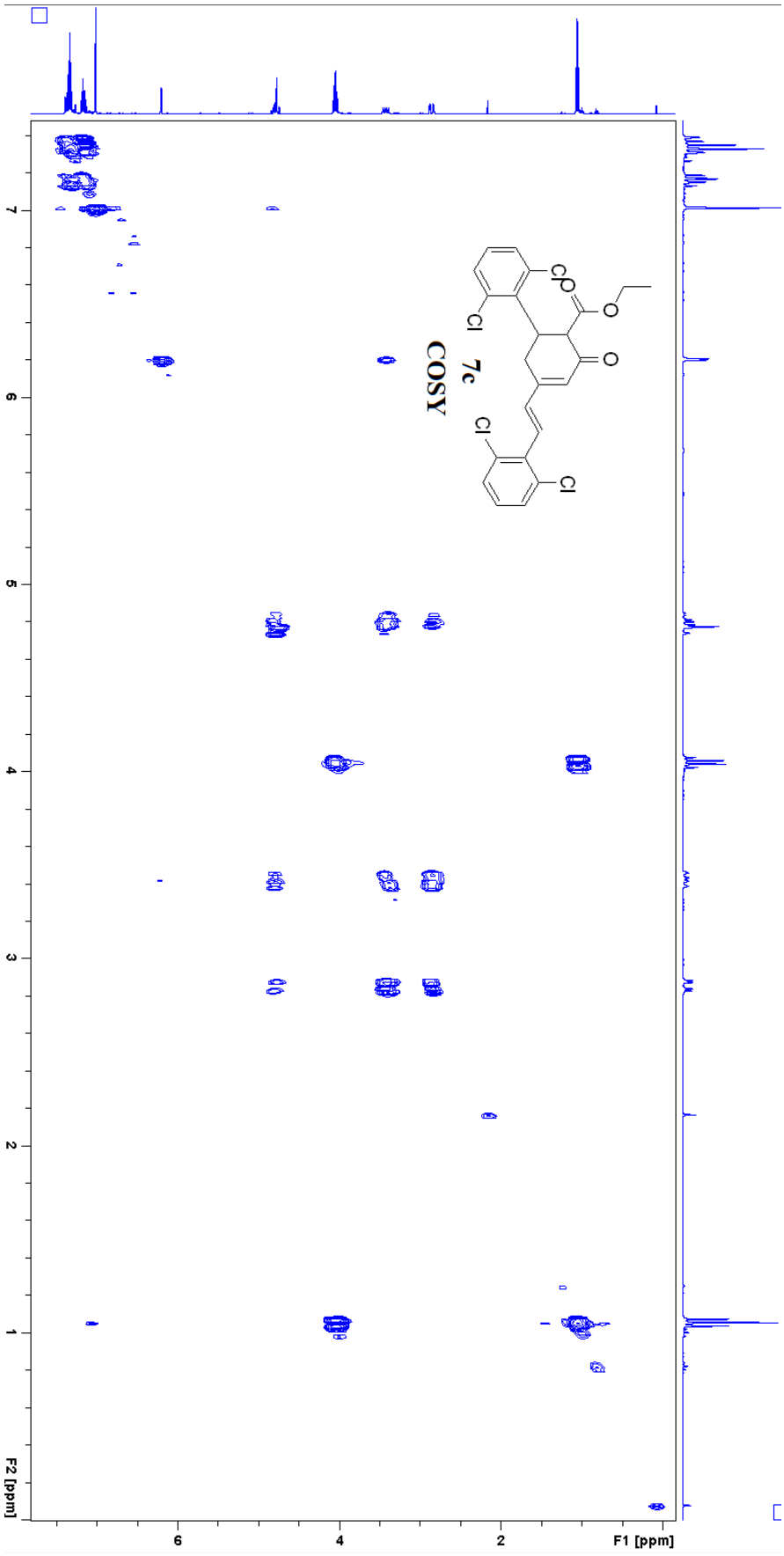

ROESY
7b
Br
Br
O
O
O
F2 [ppm]
F1 [ppm]
7
6
5
4
3
2

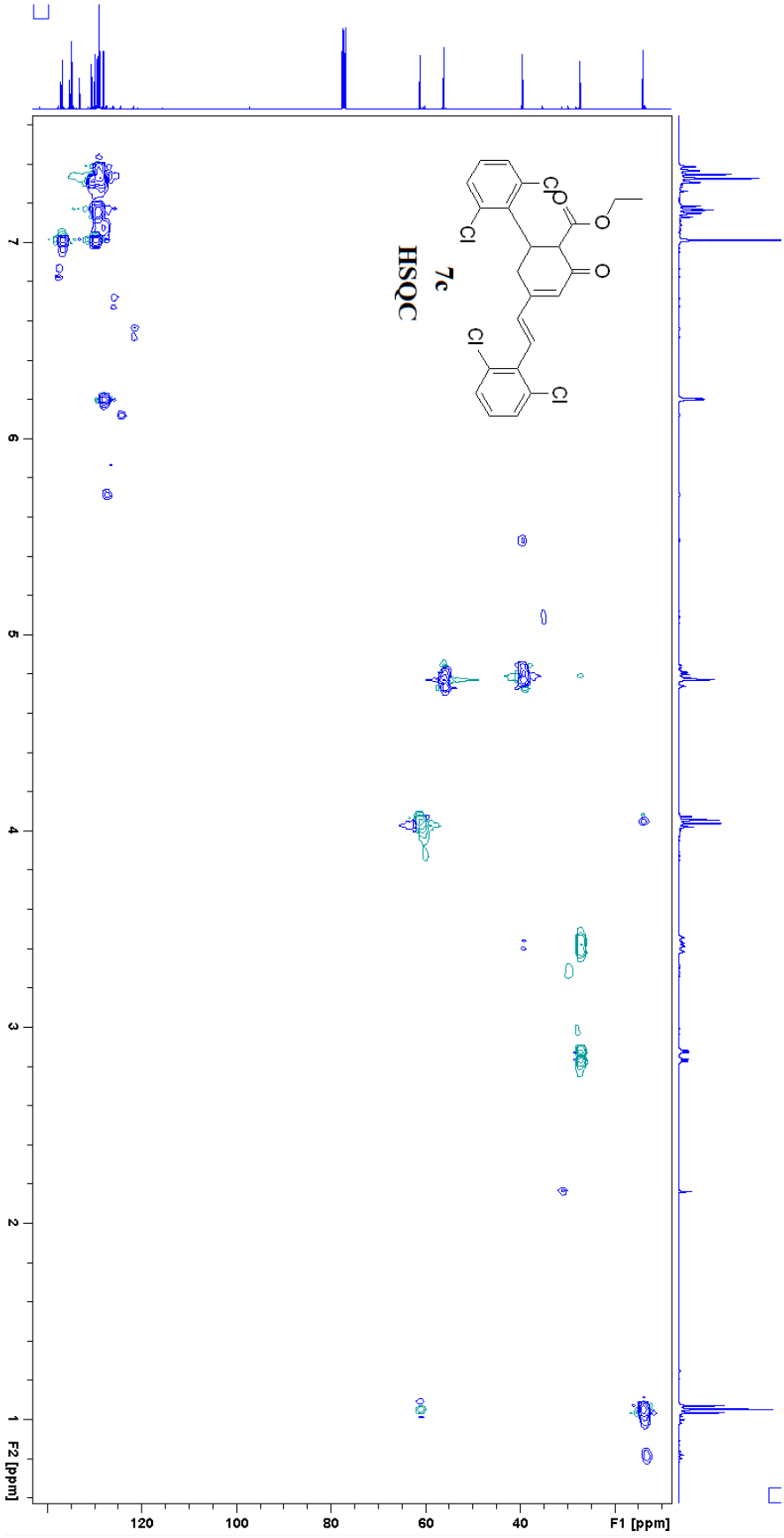
(E)-Ethyl 6-(2,6-dichlorophenyl)-4-(2-(2,6-dichlorophenyl)ethenyl)-2-oxo-4-cyclohexene-1-carboxylate (7c)



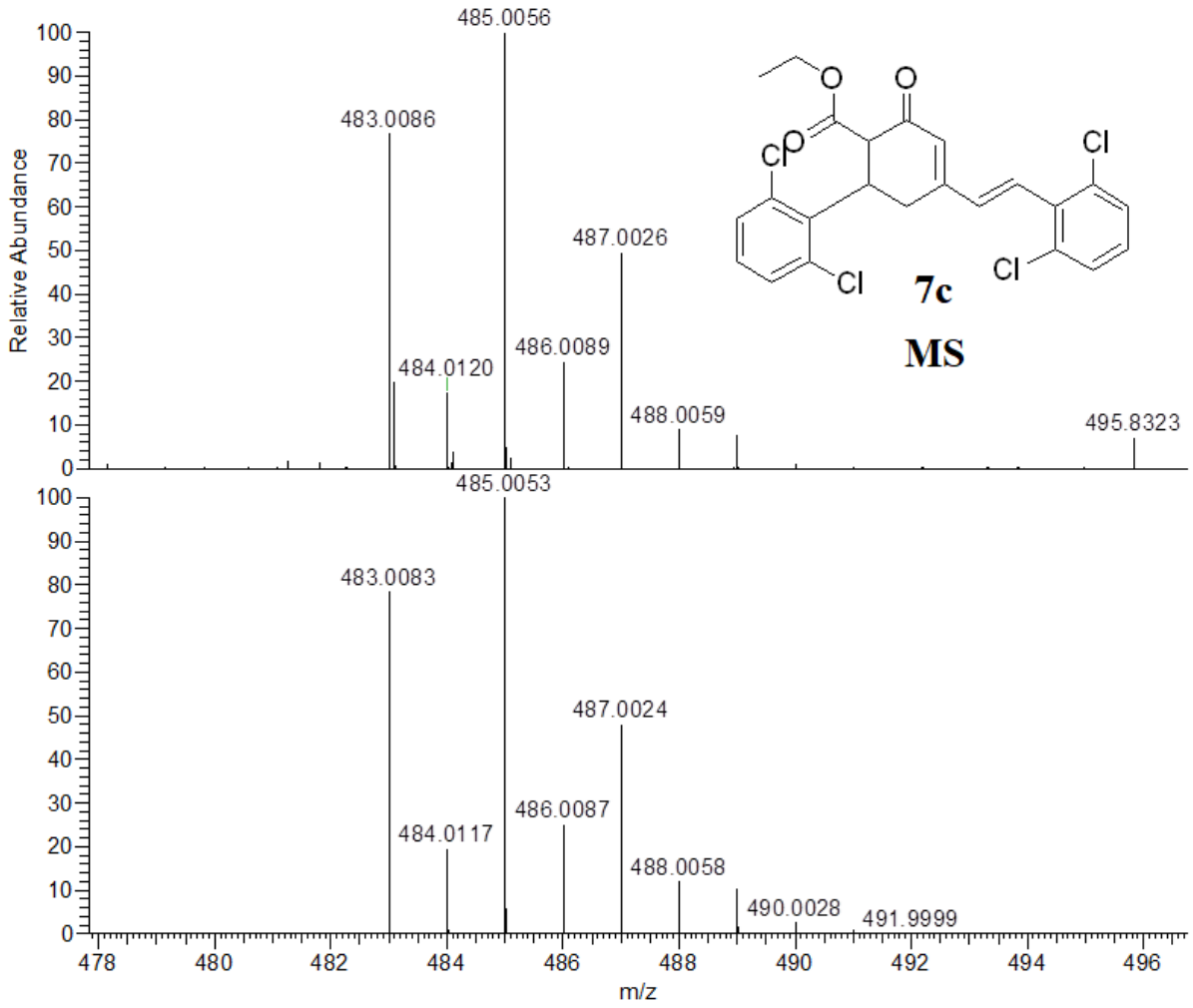

7.3863
7.3831
7.3663
7.3631
M 7.3504
M 7.3007
7.1828
7.1675
7.1627
M 7.1476
7.1426
7.1272
7.0093
1.0039
3.1879
1.1900
0.9385
1.9089
0.9797
6.2010
6.1959
M 4.8130
1.9137
M 4.7241
2.0891
1.0056
1.0145
4.0711
4.0534
4.0357
4.0179
3.4595
3.4539
3.4487
3.4340
3.4283
3.4228
3.4147
3.4102
3.4063
3.3875
3.3829
3.3787
2.8785
2.8689
2.8348
2.8236
3.0000
1.0676
1.0498
1.0320
^{1}H
7c
Cl
O
[ppm]
[rel]


193.9017
168.8214
155.2676
136.9927
136.7337
135.1249
134.7025
134.6487
133.0778
130.4996
129.7971
129.4008
129.2446
129.1607
128.8947
127.9726
61.1056
56.0544
39.3797
27.2289
13.9678
150
100
50
[ppm]
0
10
20
30
40
50
[rel]
^{13}C 7c
Cl
Cl
Cl
O
O
O


COSY
7c
Cl
O
O
Cl
Cl
F2 [ppm]
F1 [ppm]
1
2
3
4
5
6
7
2
4
6


HSQC
7c
Cl
O
O
O
Cl
Cl
F2 [ppm]
F1 [ppm]
120
100
80
60
40
1
2
3
4
5
6
7

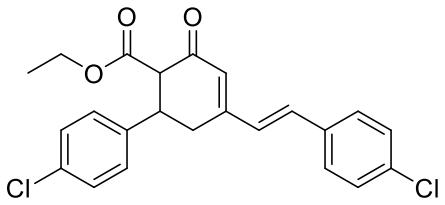
C:\Xcalibur\data\Erlend Brevik\ECB-33 1/25/2019 9:10:07 AM ECB-33
5 4.5 80

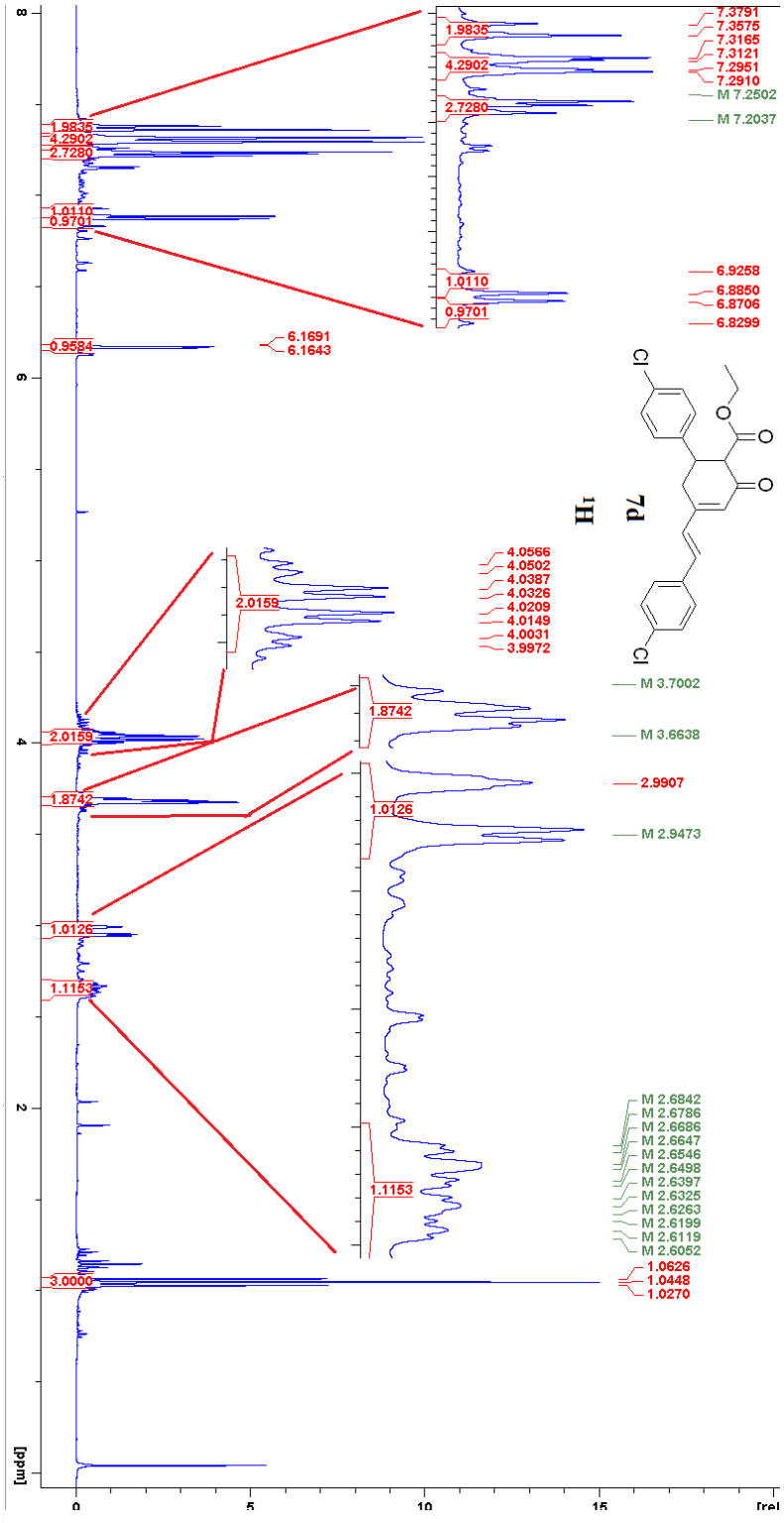


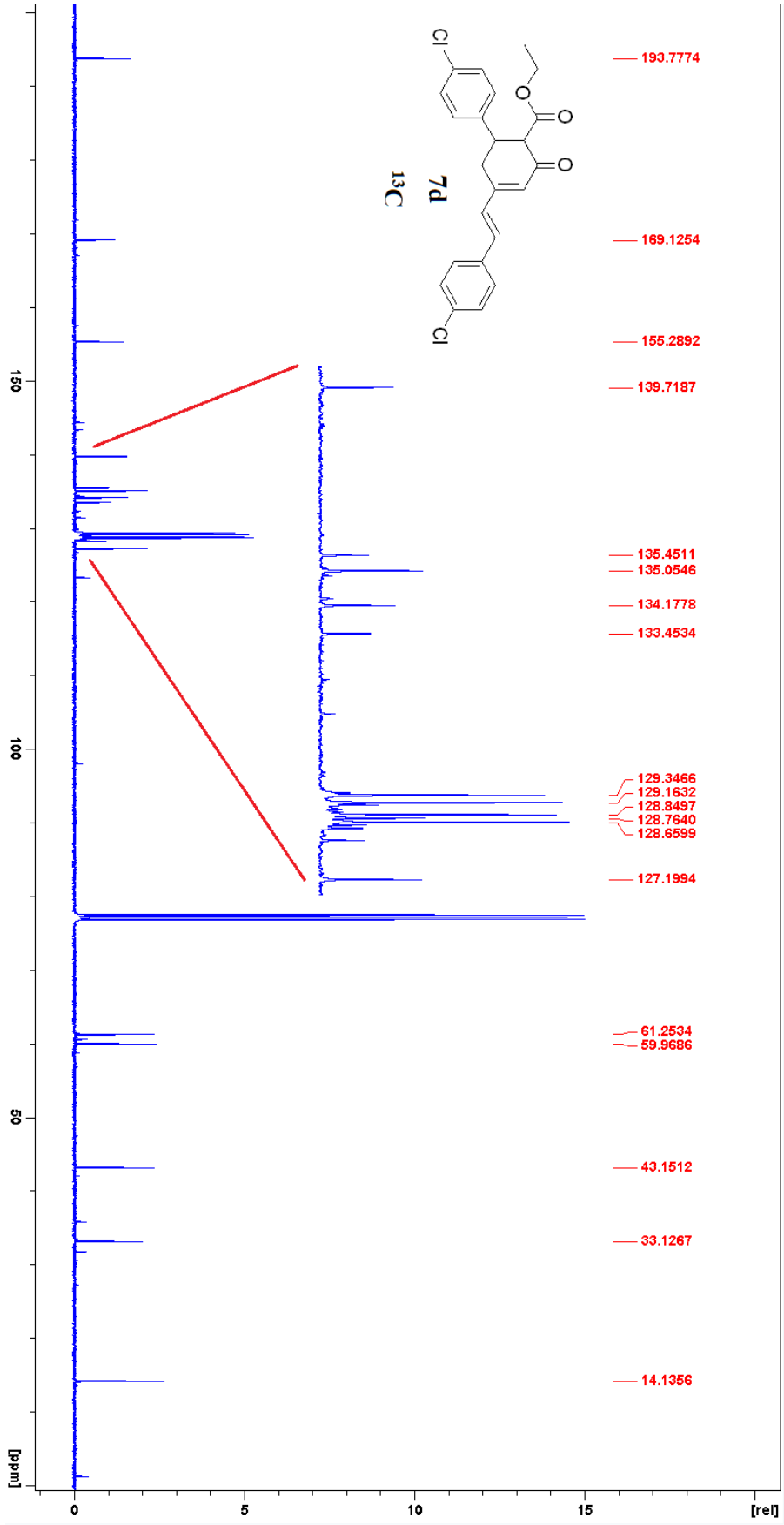
NL:
1.76E6
ECB-33#1-4 RT: 0.02-0.11
AV: 4 T: FTMS + p ESI Full ms
[200.00-800.00]

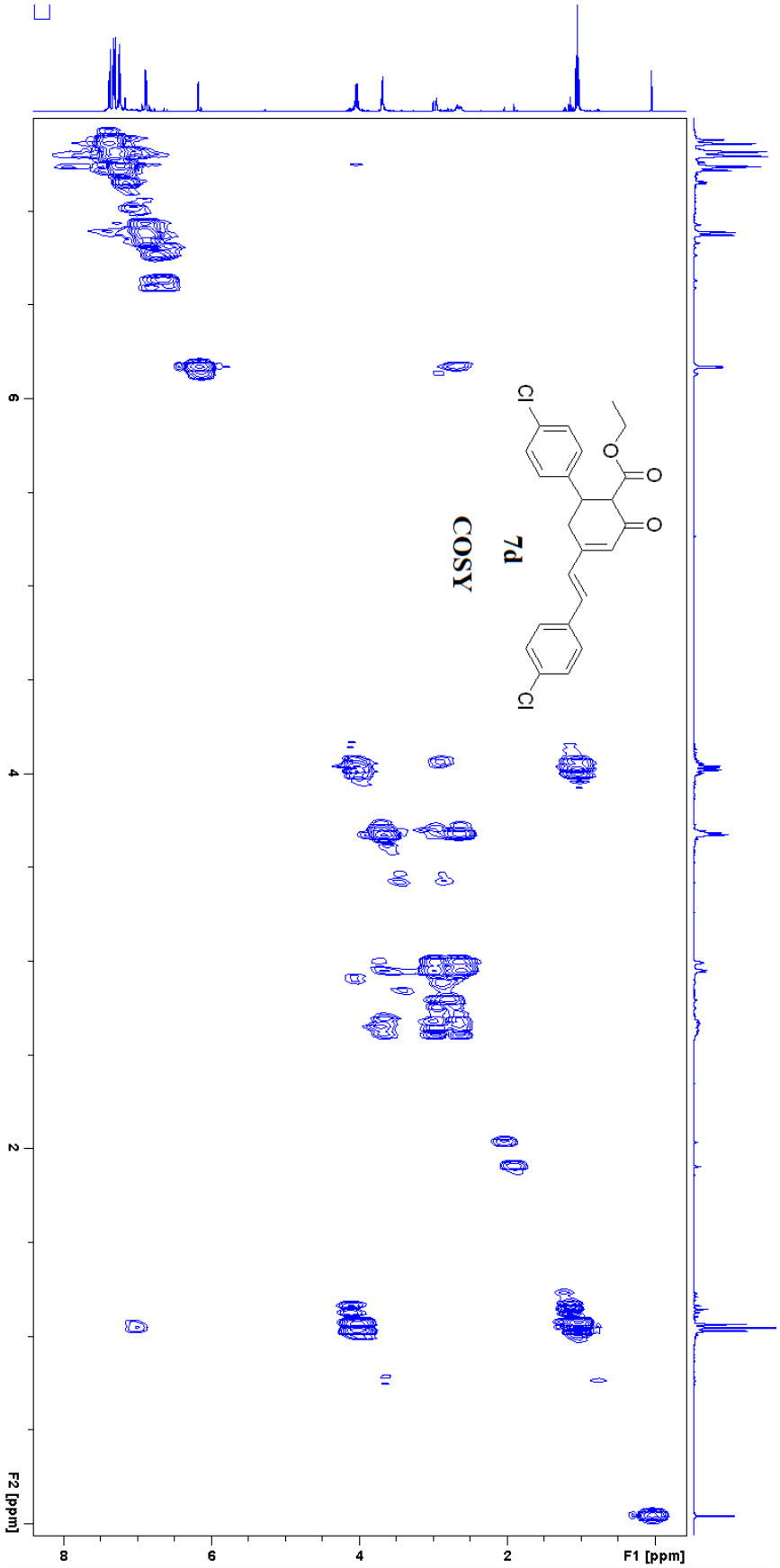
NL:
7.65E3
$C_{23}H_{18}Cl_4O_3H$:
$C_{23}H_{19}Cl_4O_3$
p (gss, s /p:40) Chrg 1
R: 121000 Res .Pwr . @FWHM

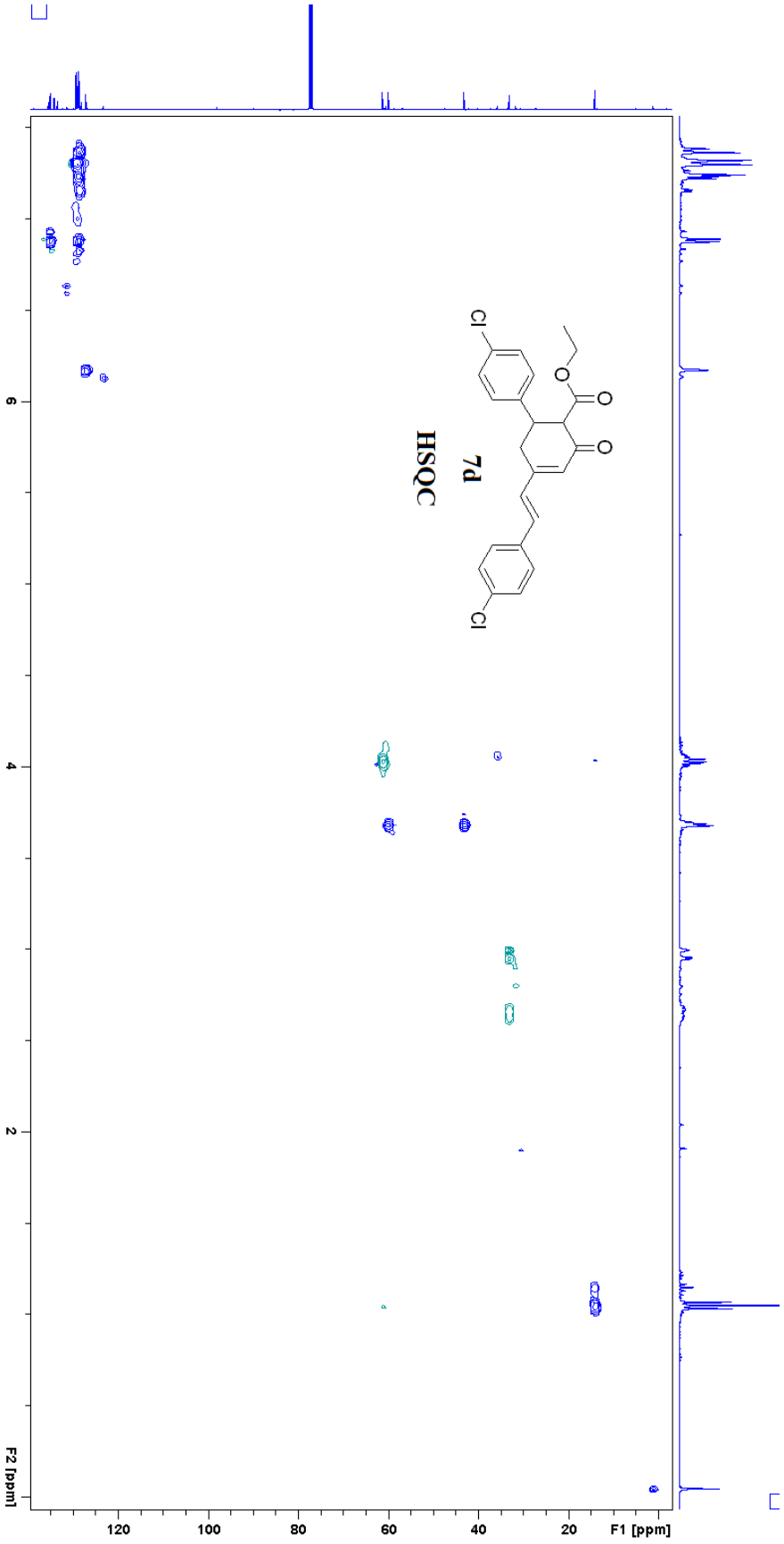
(E)-Ethyl 6-(4-chlorophenyl)-4-[2-(4-chlorophenyl)ethenyl]-2-oxo-4-cyclohexene-1-carboxylate (7d)



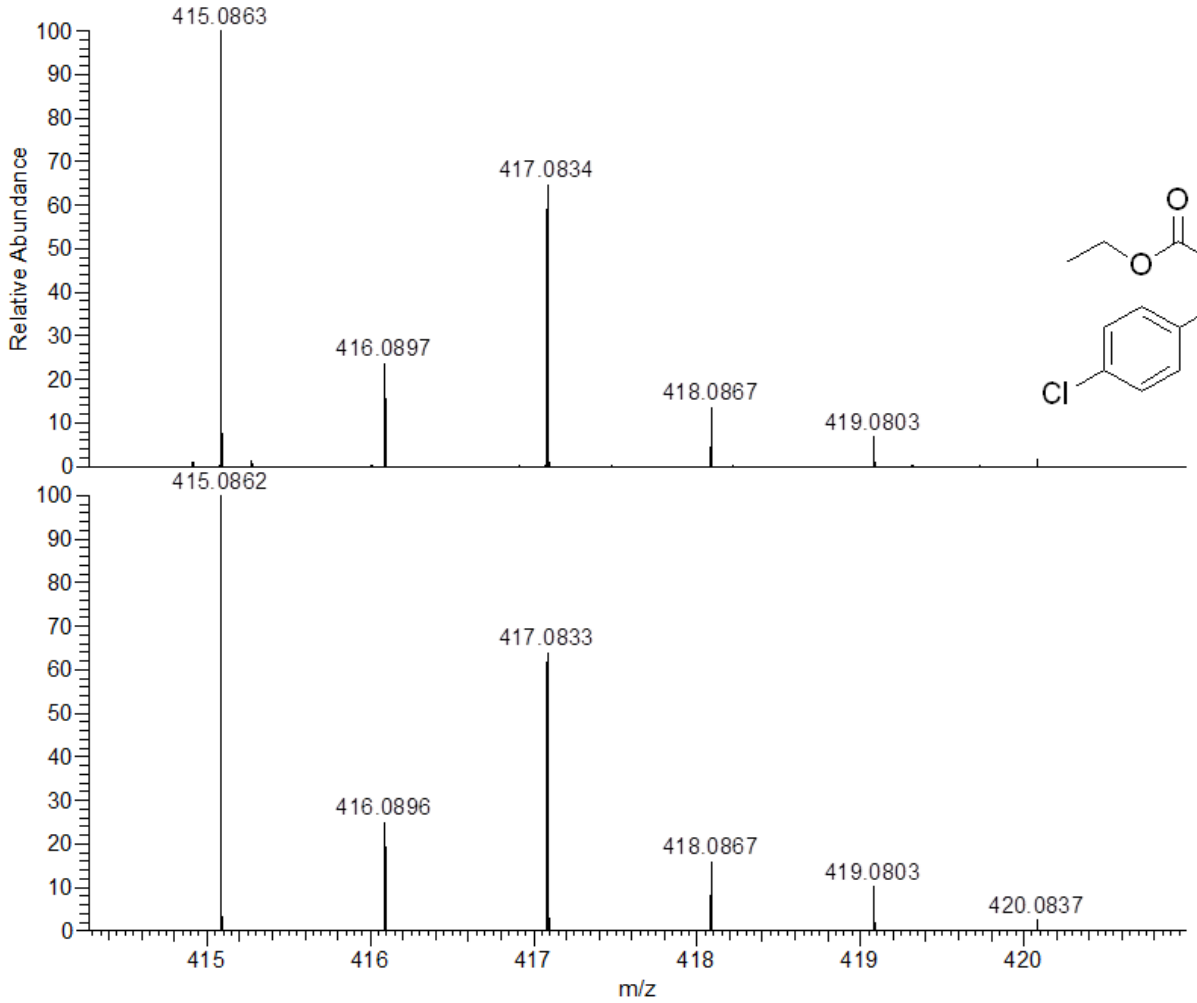

7.3791
7.3575
7.3165
7.3121
7.2951
7.2910
M 7.2502
M 7.2037
1.9835
4.2902
2.7280
1.0110
0.9701
6.9258
6.8850
6.8706
6.8299
0.9584
6.1691
6.1643
Cl
O
O
O
7d
Cl
4.0566
4.0502
4.0387
4.0326
4.0209
4.0149
4.0031
3.9972
2.0159
M 3.7002
1.8742
M 3.6638
2.9907
1.0126
M 2.9473
1.1153
M 2.6842
M 2.6786
M 2.6686
M 2.6647
M 2.6546
M 2.6498
M 2.6397
M 2.6325
M 2.6263
M 2.6199
M 2.6119
M 2.6052
3.0000
1.0626
1.0448
1.0270
[ppm]
0
5
10
15
[rel


193.7774
169.1254
155.2892
139.7187
135.4511
135.0546
134.1778
133.4534
129.3466
129.1632
128.8497
128.7640
128.6599
127.1994
61.2534
59.9686
43.1512
33.1267
14.1356
7d
13C
Cl
Cl
O
O
O
150
100
50
[ppm]
0
5
10
15
[rel]

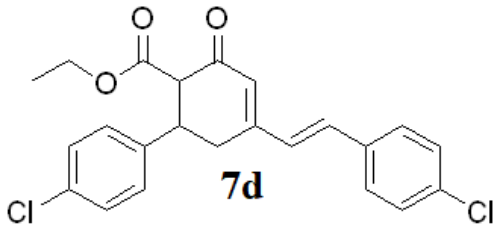

COSY
7d
Cl
Cl
O
O
O
F2 [ppm]
F1 [ppm]
8
6
4
2


HSQC
7d
Cl
O
O
O
Cl
F2 [ppm]
F1 [ppm]
120
100
80
60
40
20
2
4
6

C:\Xcalibur\data\Erlend Brevik\ECB-52 1/25/2019 9:26:39 AM ECB-52
5 4.5 80



NL:
8.14E5
ECB-52#1-4 RT: 0.01-0.09
AV: 4 T: FTMS + p ESI Full ms
[200.00-800.00]



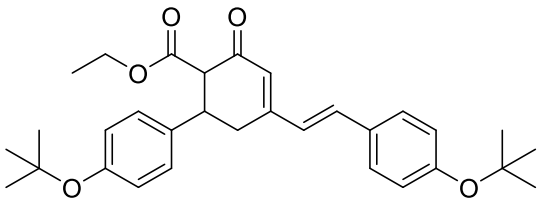
7d

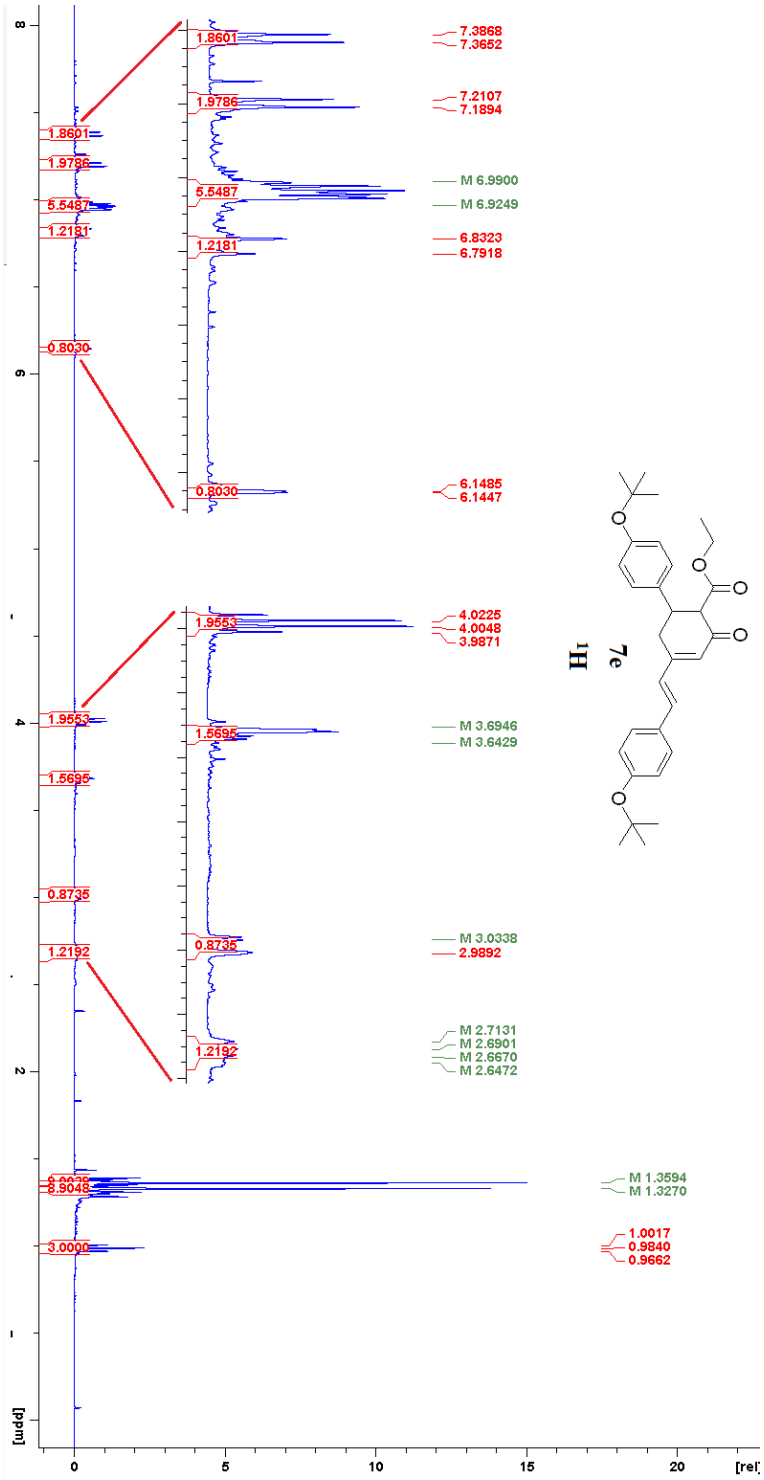
MS

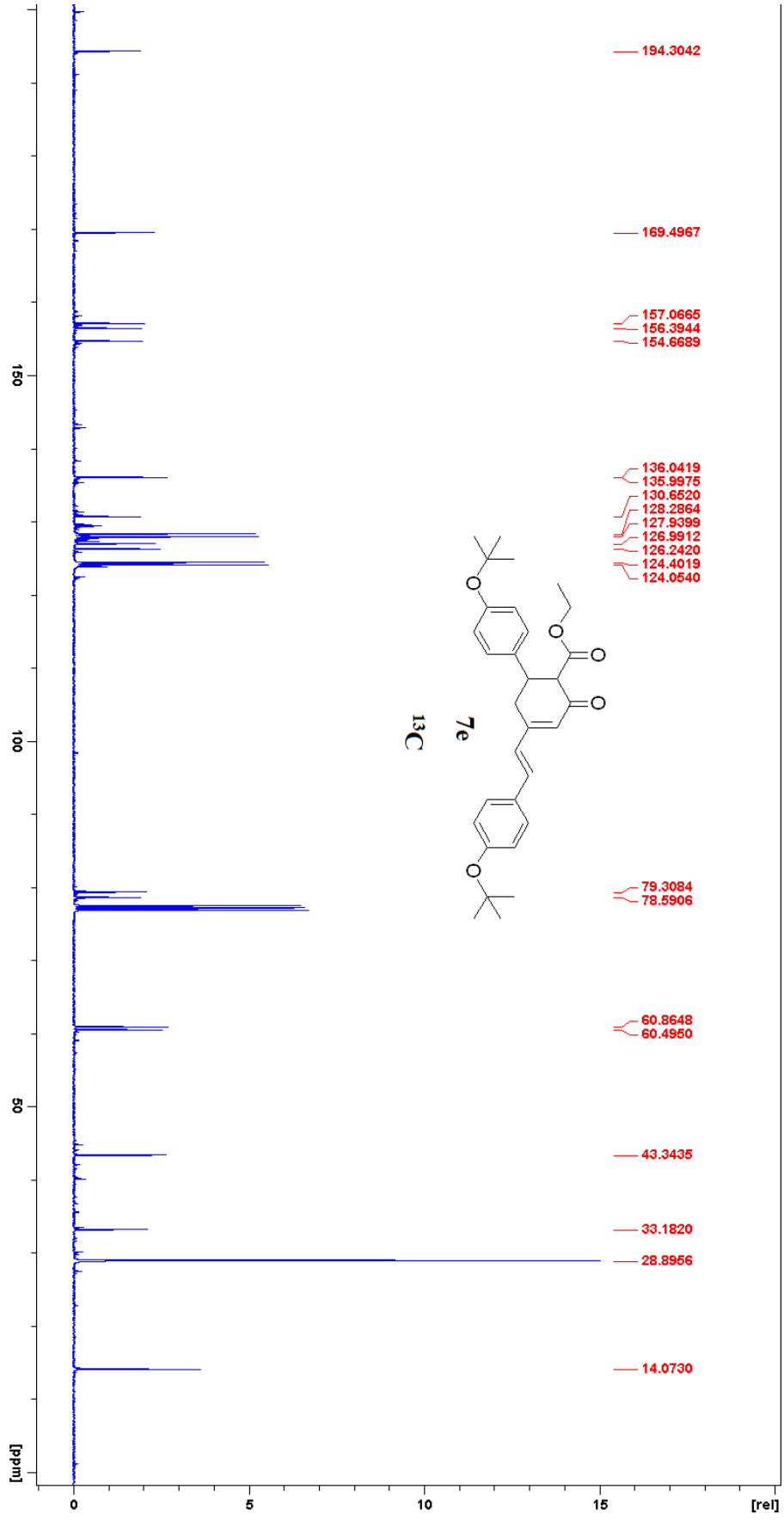
NL:
1.04E4

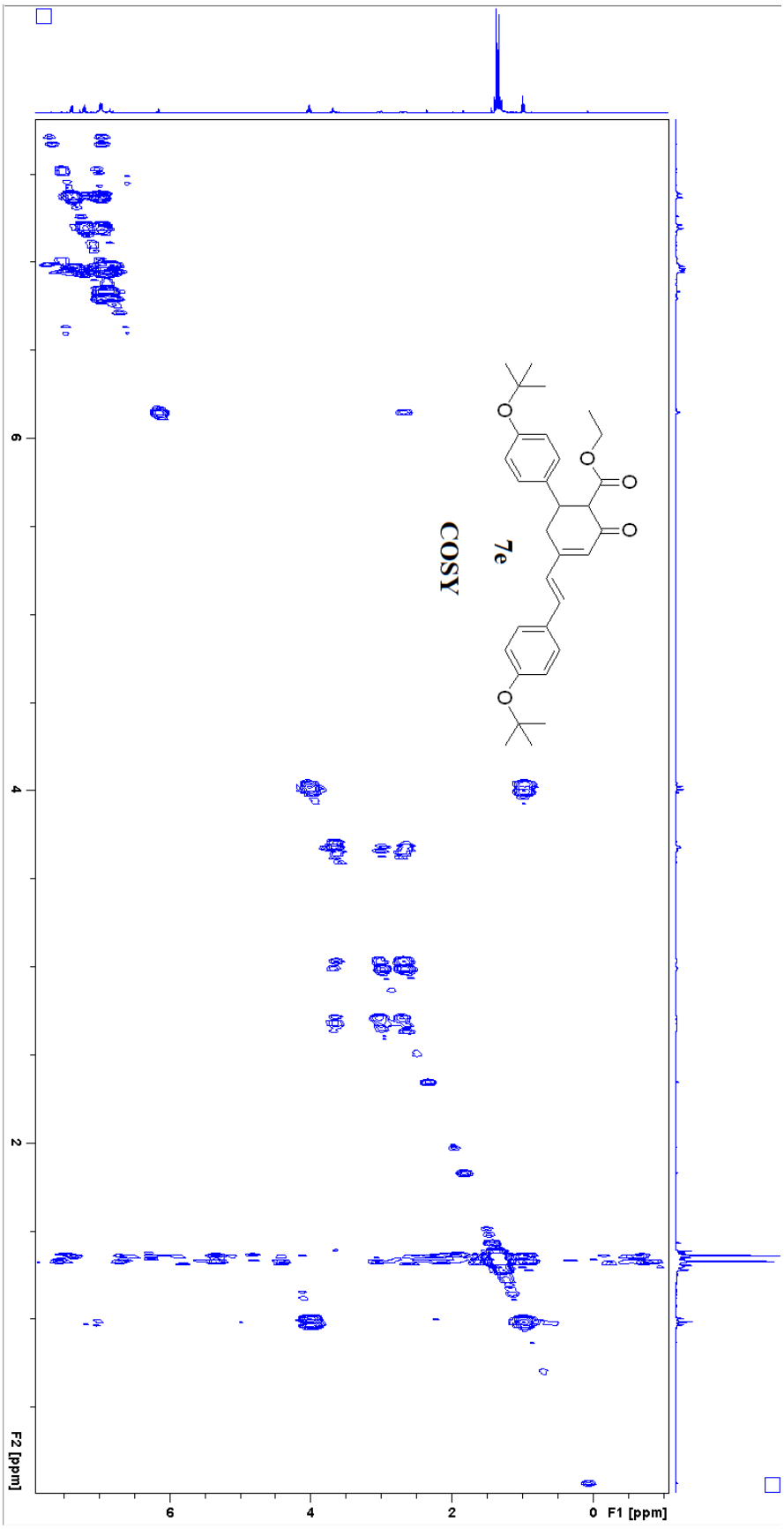
$C_{23}H_{20}Cl_2O_3H$:
$C_{23}H_{21}Cl_2O_3$
p (gss, s /p:40) Chrg 1
R: 130000 Res .Pwr . @FWHM

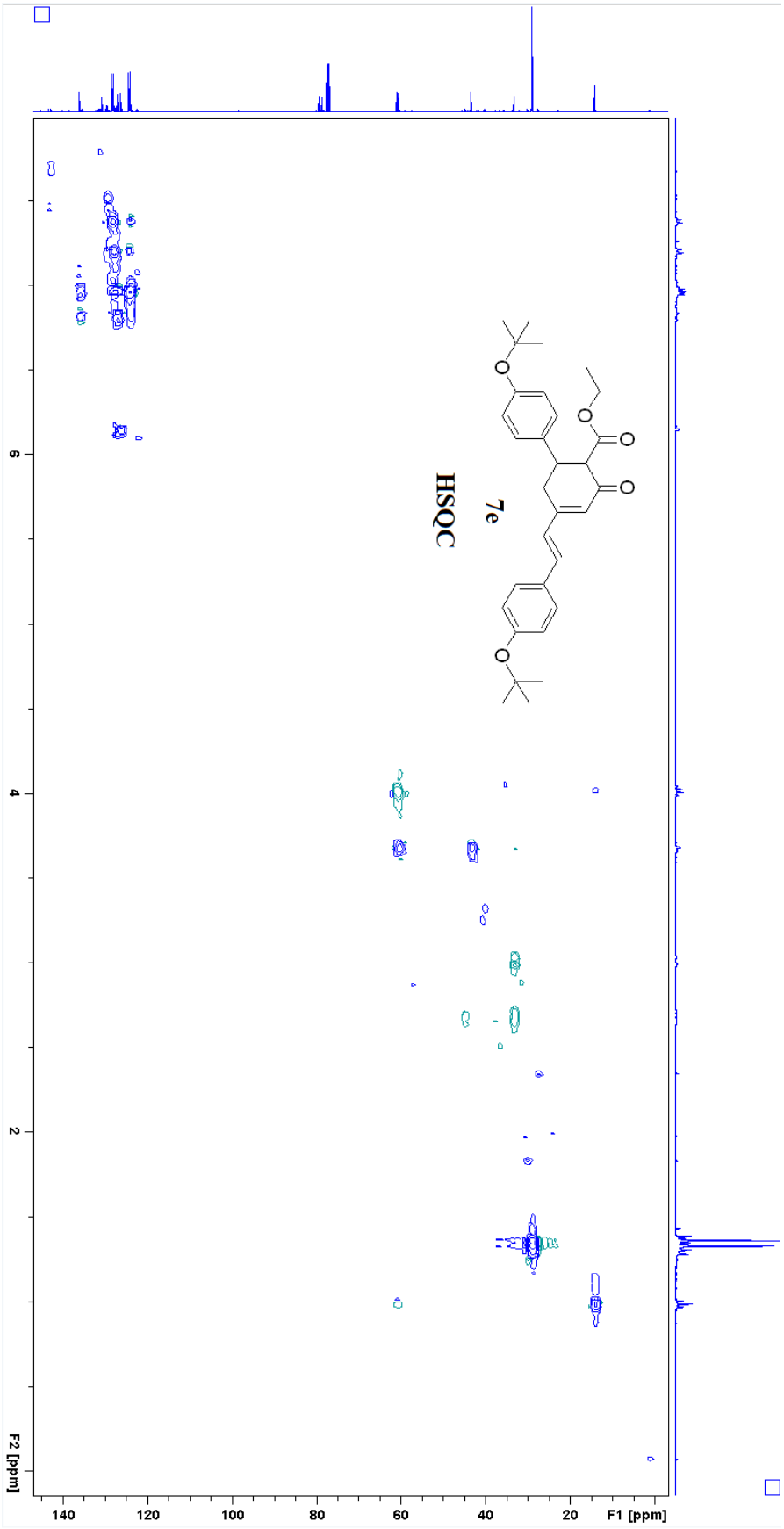
(E)-Ethyl 2-oxo-6-(4-*tert*-butoxyphenyl)-4-[2-(4-*tert*-butoxyphenyl)ethenyl]-4-cyclohexene-1-carboxylate (7e)




1.8601
1.9786
5.5487
1.2181
0.8030
1.9553
1.5695
0.8735
1.2192
8.9048
3.0000
7.3868
7.3652
7.2107
7.1894
M 6.9900
M 6.9249
6.8323
6.7918
6.1485
6.1447
4.0225
4.0048
3.9871
M 3.6946
M 3.6429
M 3.0338
2.9892
M 2.7131
M 2.6901
M 2.6670
M 2.6472
M 1.3594
M 1.3270
1.0017
0.9840
0.9662
[ppm]
[rel]
0
5
10
15
20
7e
1H

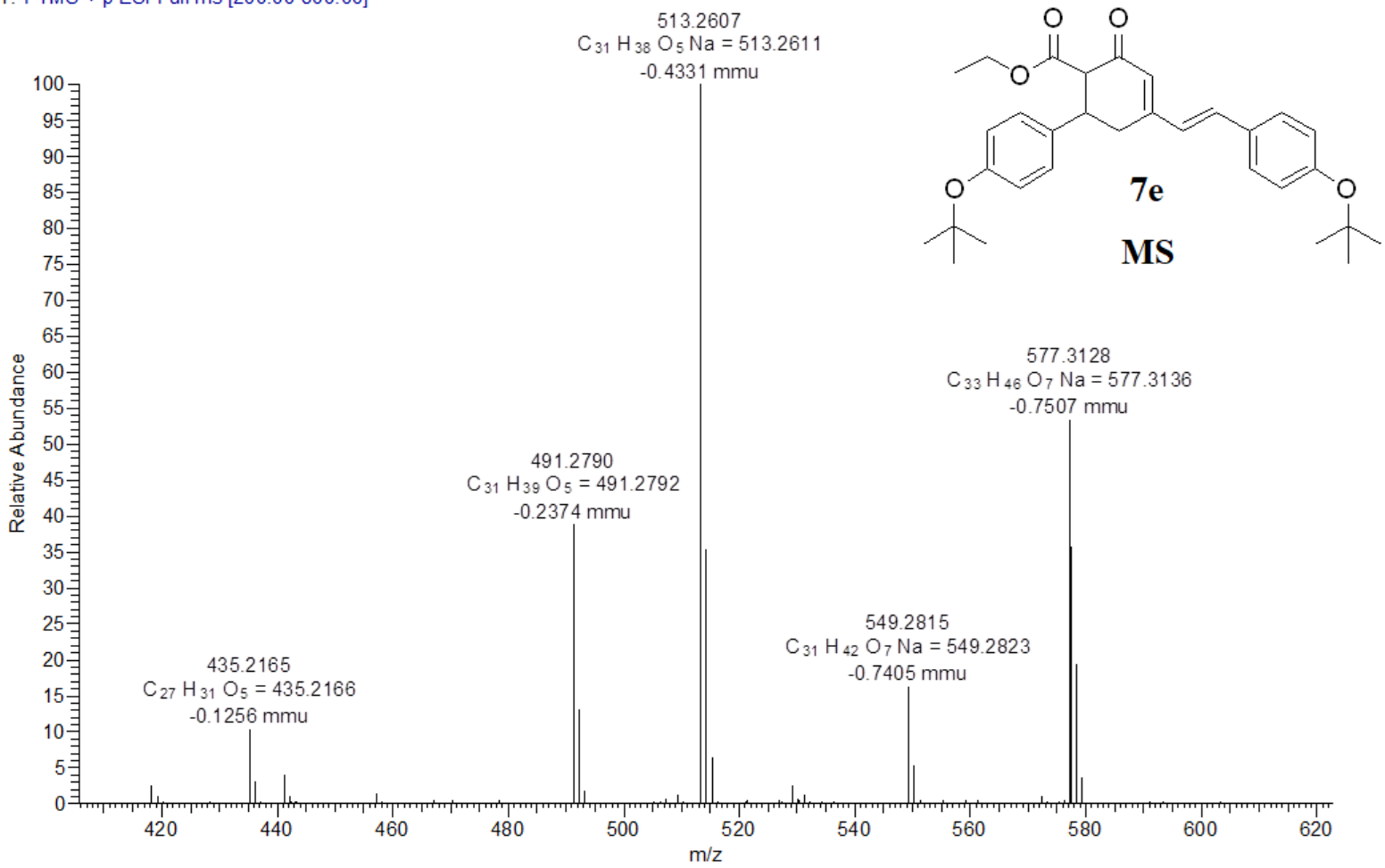

194.3042
169.4967
157.0665
156.3944
154.6689
136.0419
135.9975
130.6520
128.2864
127.9399
126.9912
126.2420
124.4019
124.0540
79.3084
78.5906
60.8648
60.4950
43.3435
33.1820
28.8956
14.0730
^{13}C
7e
[ppm]
150
100
50
0
5
10
15
[rel]


COSY
7e
F2 [ppm]
F1 [ppm]
6
4
2
0


HSQC
7e
F2 [ppm]
F1 [ppm]
140
120
100
80
60
40
20
2
4
6

C:\Xcalibur\data\Erlend Brevik\ECB-66 1/25/2019 9:32:58 AM ECB-52
5 4.5 100

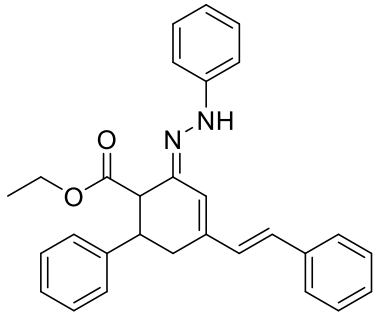
ECB-66 #1-4 RT: 0.01-0.10 AV: 4 NL: 4.33E7
T: FTMS + p ESI Full ms [200.00-800.00]

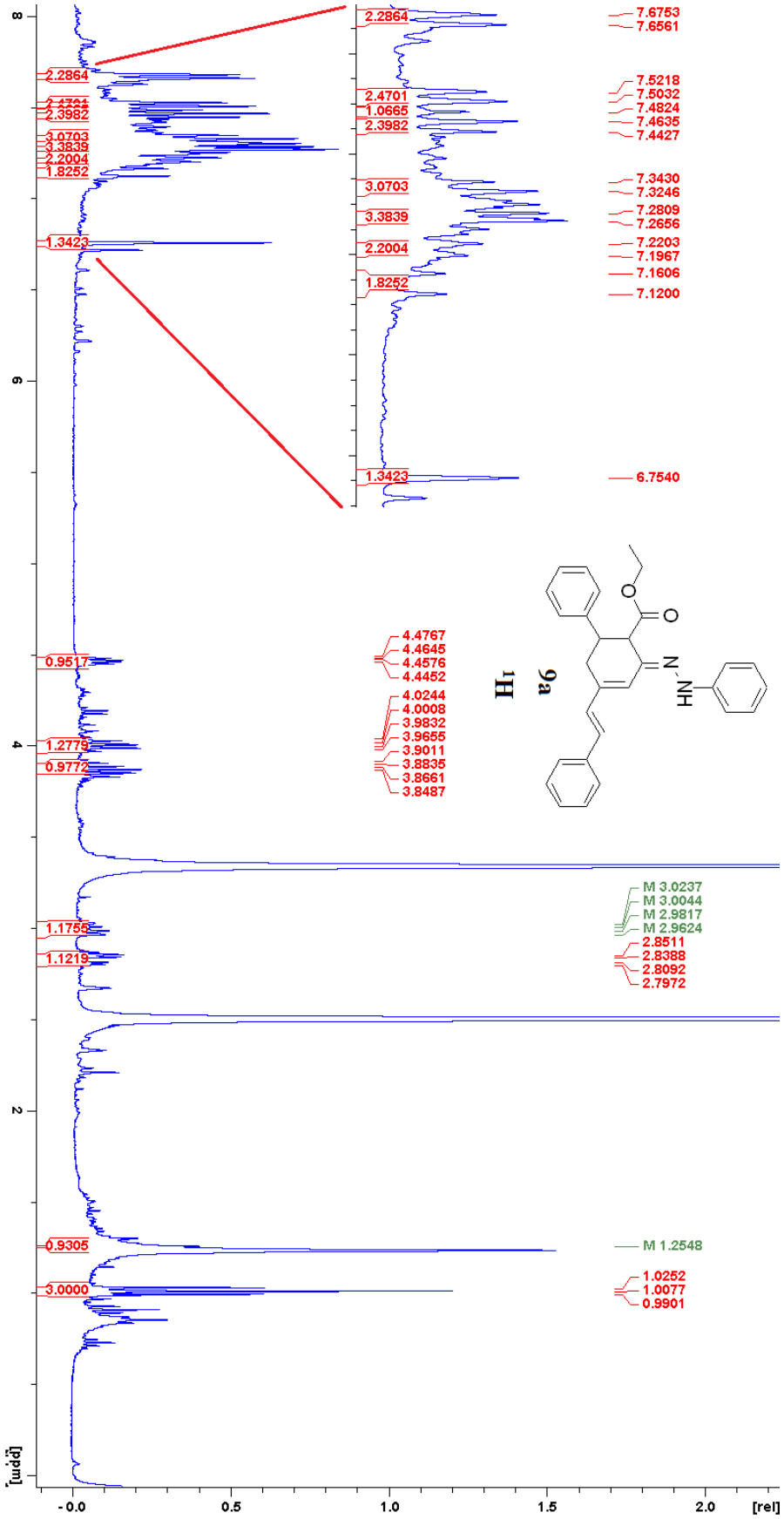


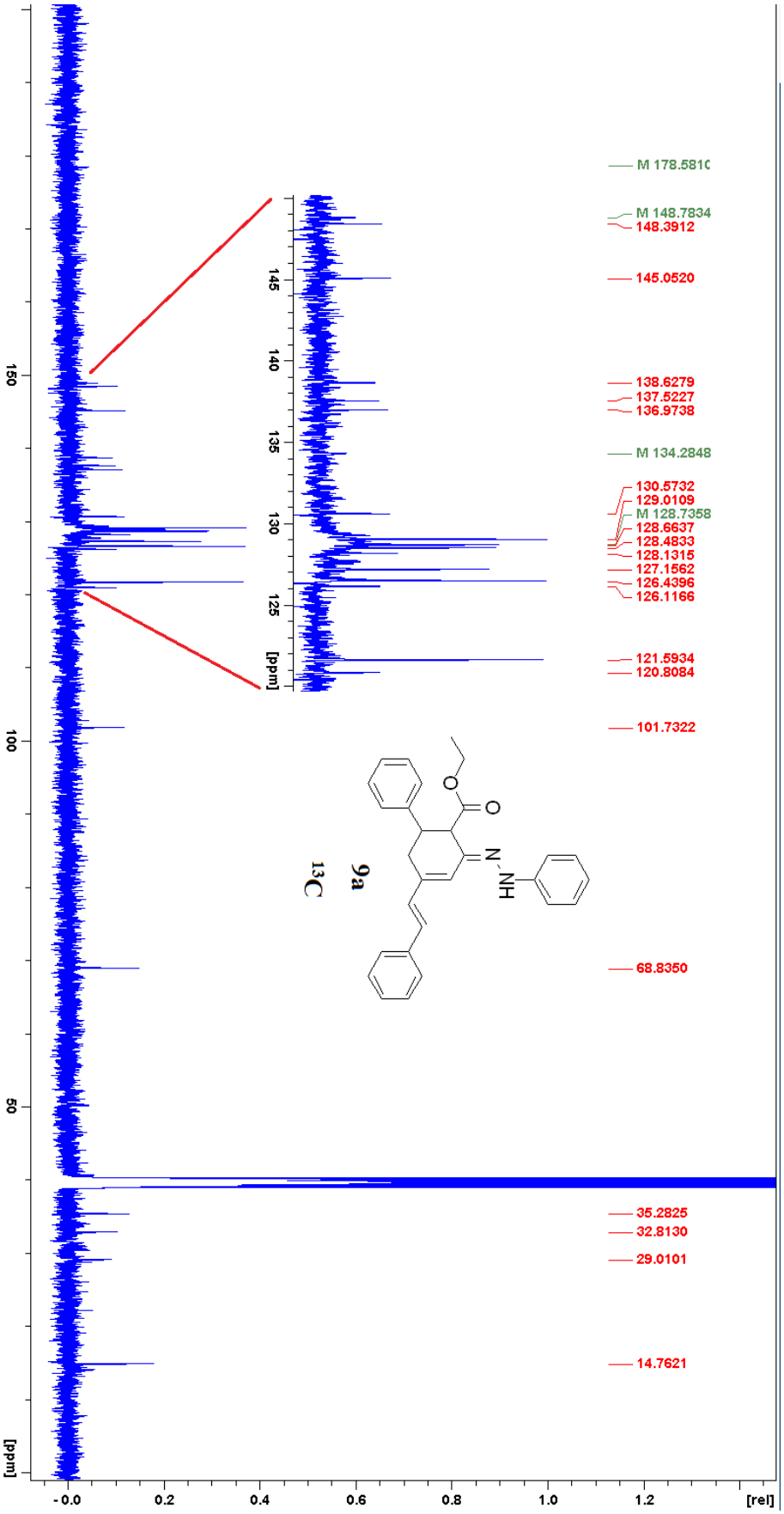
7e

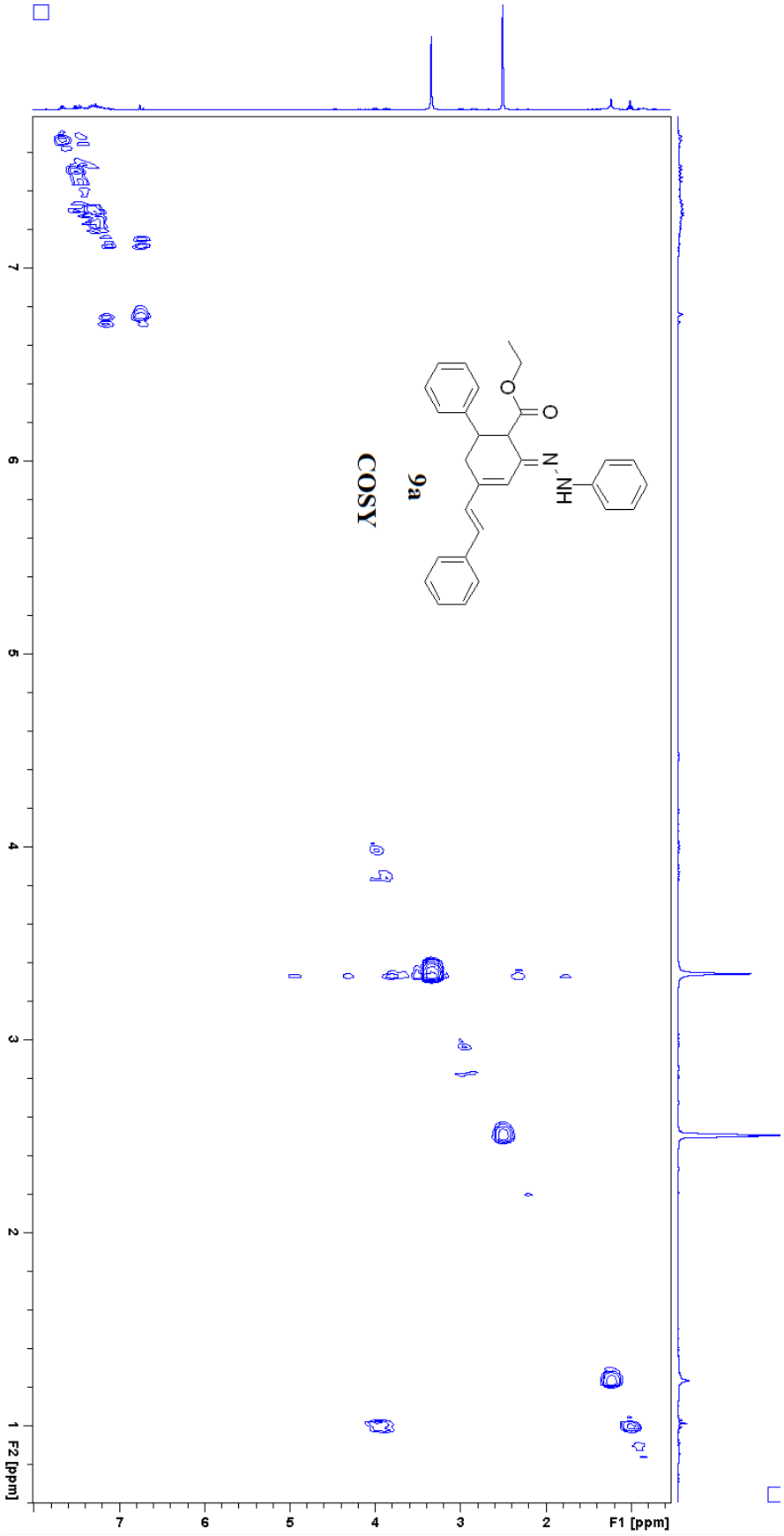
MS

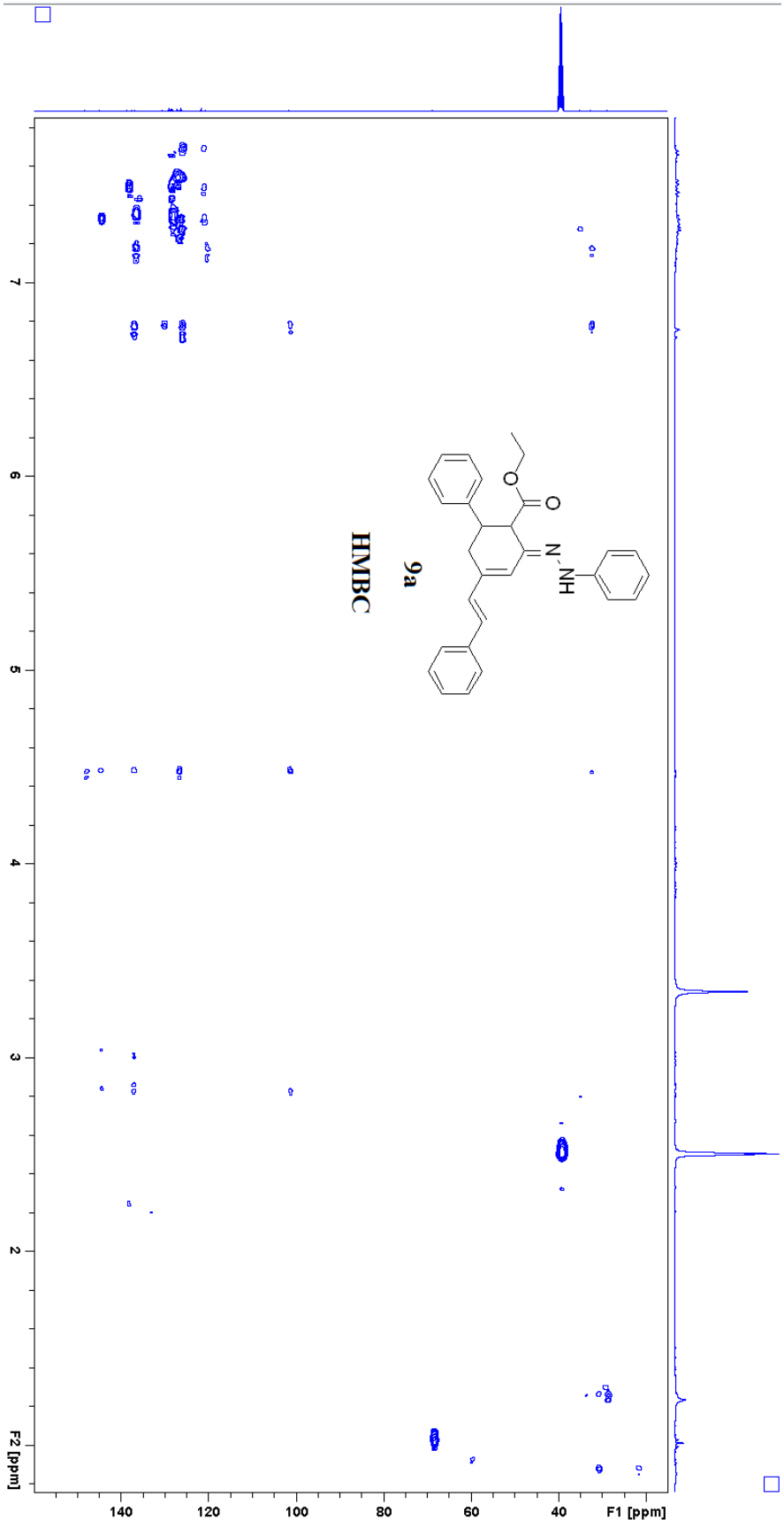
(E)-Ethyl 6-phenyl-4-(2-phenylethenyl)-2-phenylhydrazone-4-cyclohexene-1-carboxylate (9a)

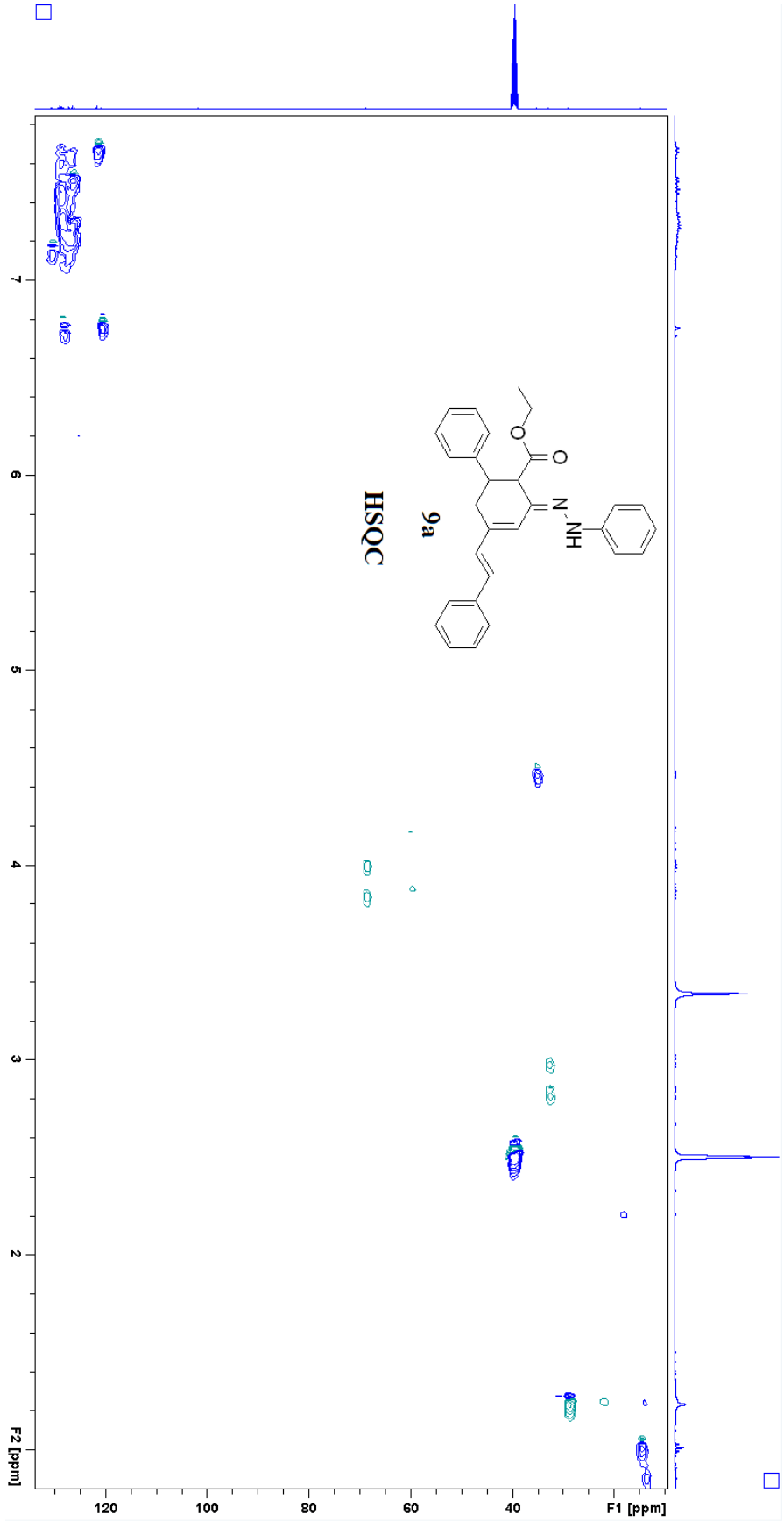


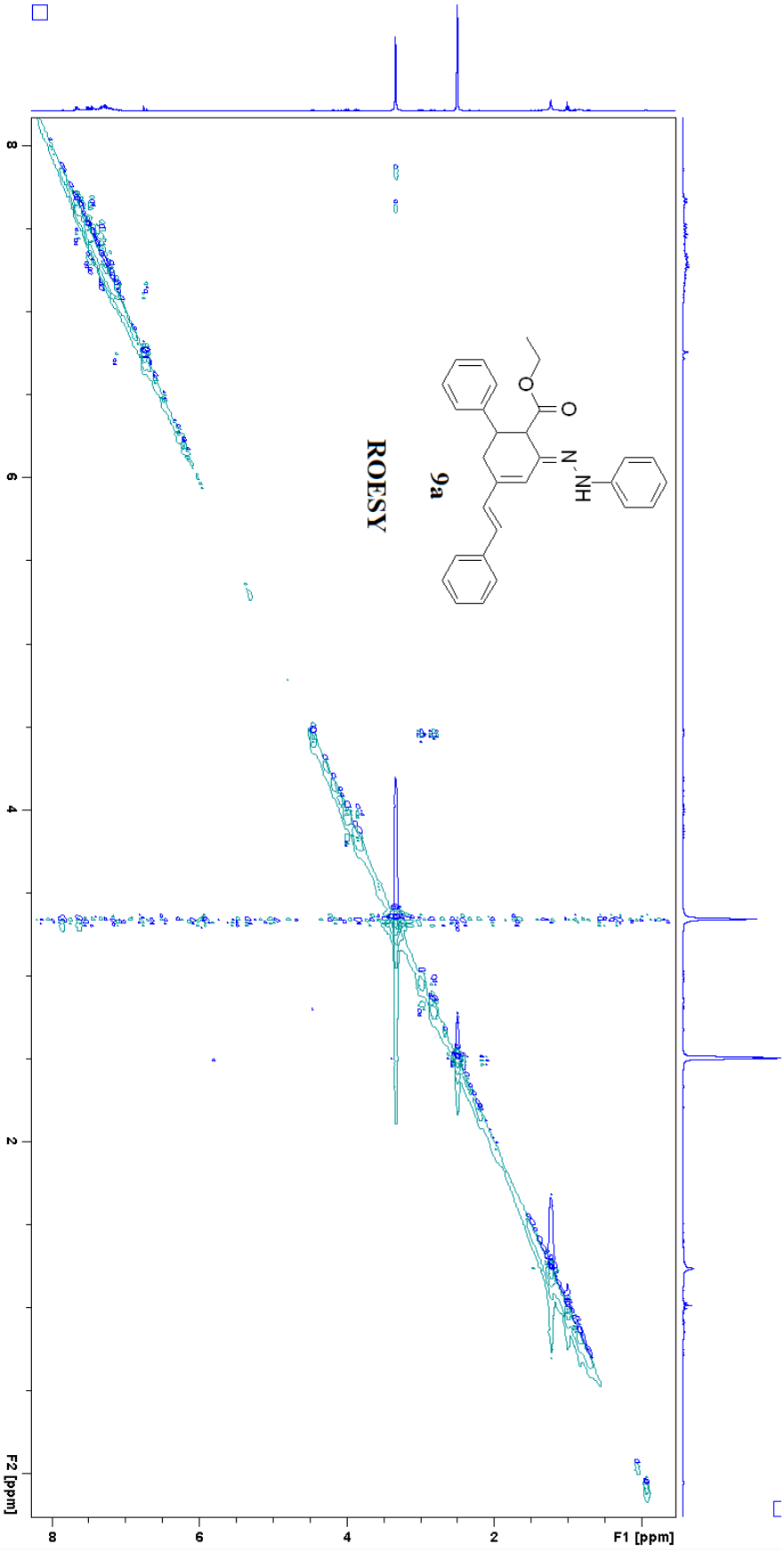

9a
1H
O
O
N
NH
2.2864
2.4701
1.0665
2.3982
3.0703
3.3839
2.2004
1.8252
1.3423
7.6753
7.6561
7.5218
7.5032
7.4824
7.4635
7.4427
7.3430
7.3246
7.2809
7.2656
7.2203
7.1967
7.1606
7.1200
6.7540
4.4767
4.4645
4.4576
4.4452
4.0244
4.0008
3.9832
3.9655
3.9011
3.8835
3.8661
3.8487
0.9517
1.2775
0.9772
1.1758
1.1219
0.9305
3.0000
M 3.0237
M 3.0044
M 2.9817
M 2.9624
2.8511
2.8388
2.8092
2.7972
M 1.2548
1.0252
1.0077
0.9901
8
6
4
2
[ppm]
-0.0
0.5
1.0
1.5
2.0
[rel]

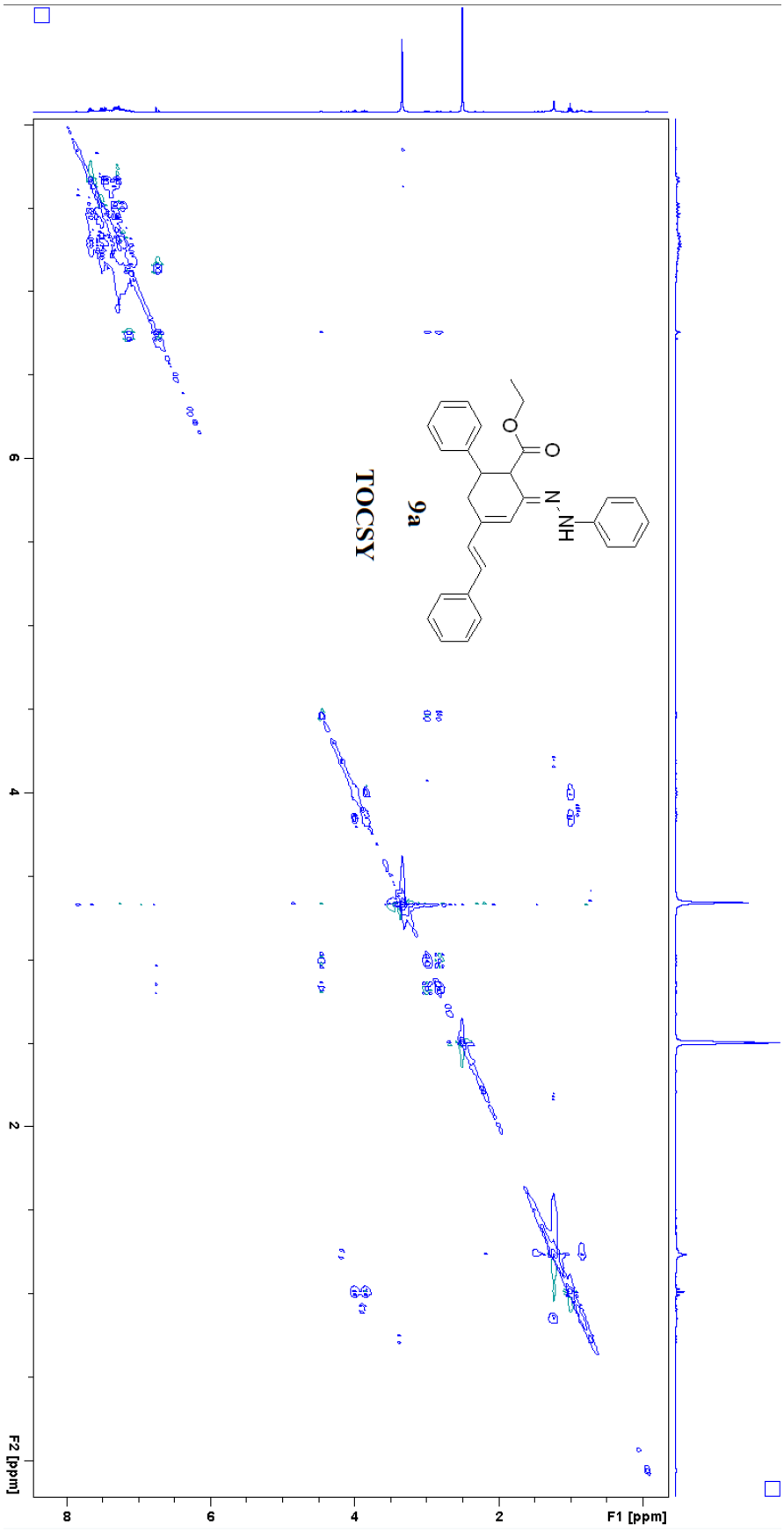

M 178.5810
M 148.7834
148.3912
145.0520
138.6279
137.5227
136.9738
M 134.2848
130.5732
129.0109
M 128.7358
128.6637
128.4833
128.1315
127.1562
126.4396
126.1166
121.5934
120.8084
101.7322
68.8350
35.2825
32.8130
29.0101
14.7621
[ppm]
[rel]
^{13}C 9a

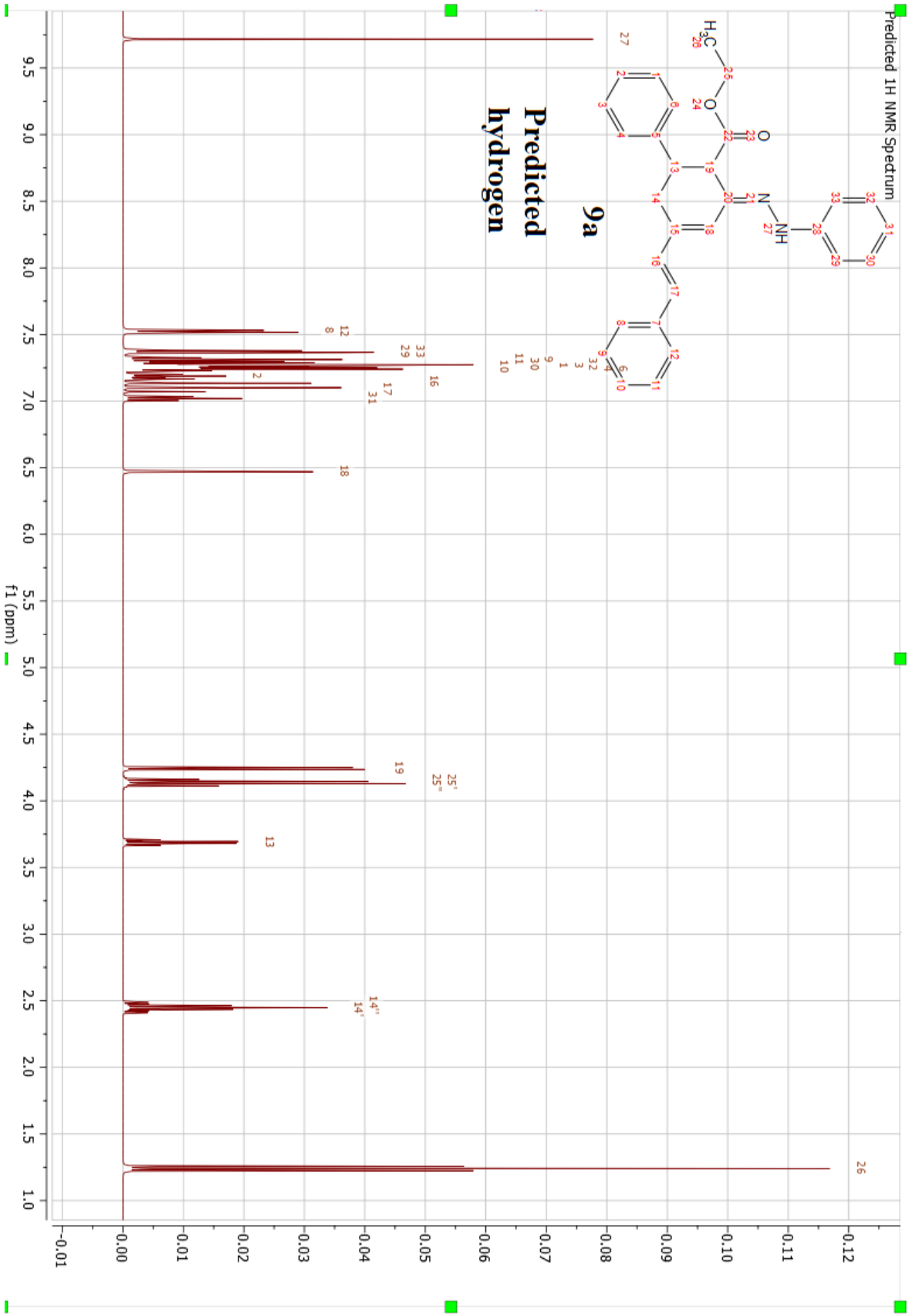

COSY
9a
F2 [ppm]
F1 [ppm]
1
2
3
4
5
6
7

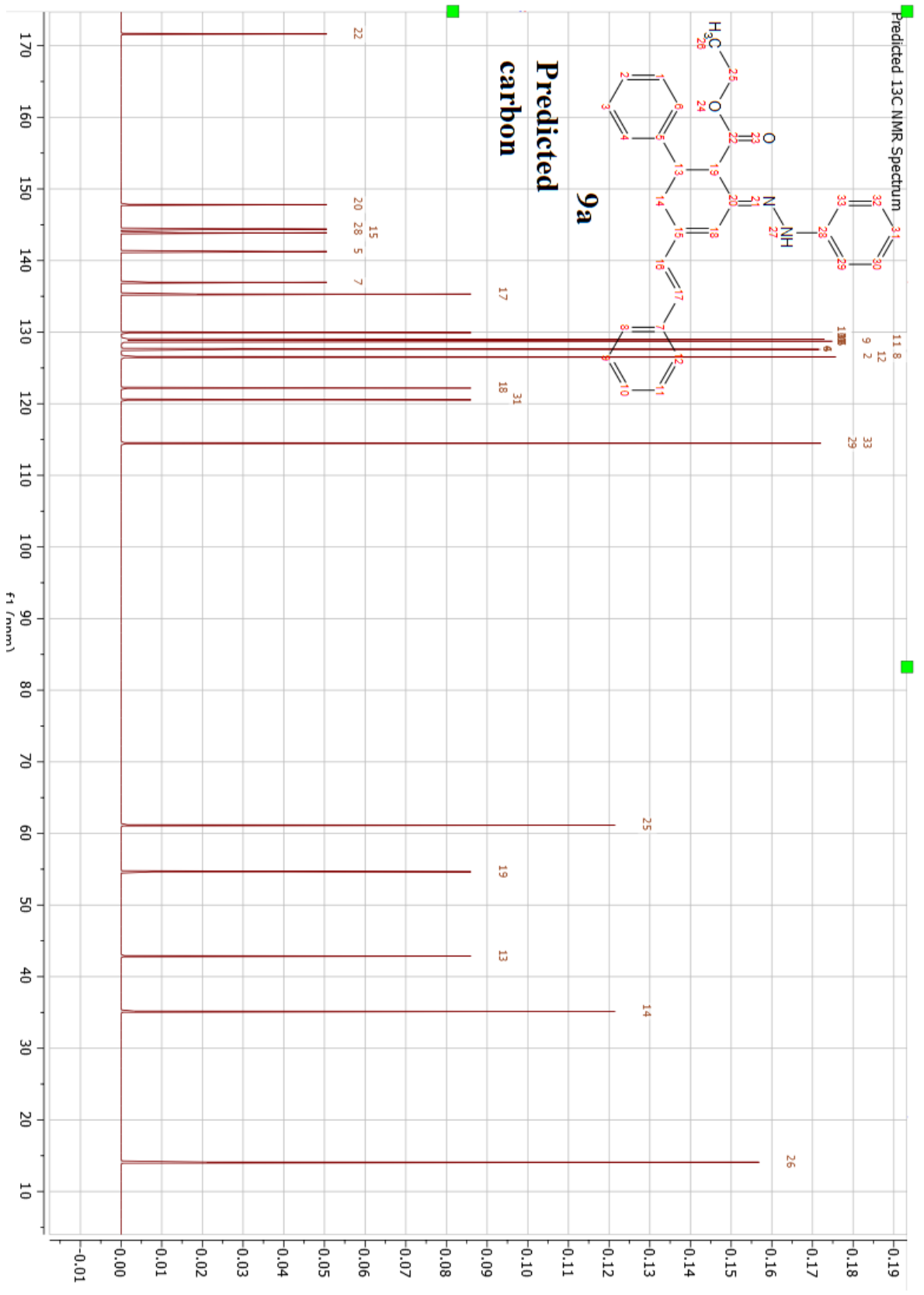

HMBC
9a
O
O
N
HN
F2 [ppm]
F1 [ppm]
140
120
100
80
60
40
2
3
4
5
6
7


HSQC
9a
F2 [ppm]
F1 [ppm]
120
100
80
60
40
2
3
4
5
6
7

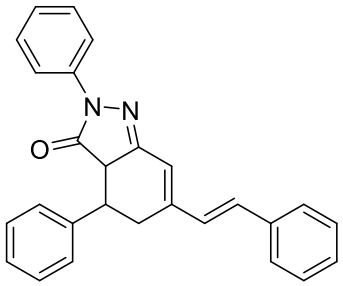

ROESY
9a
O
O
N
NH
F2 [ppm]
F1 [ppm]
8
6
4
2

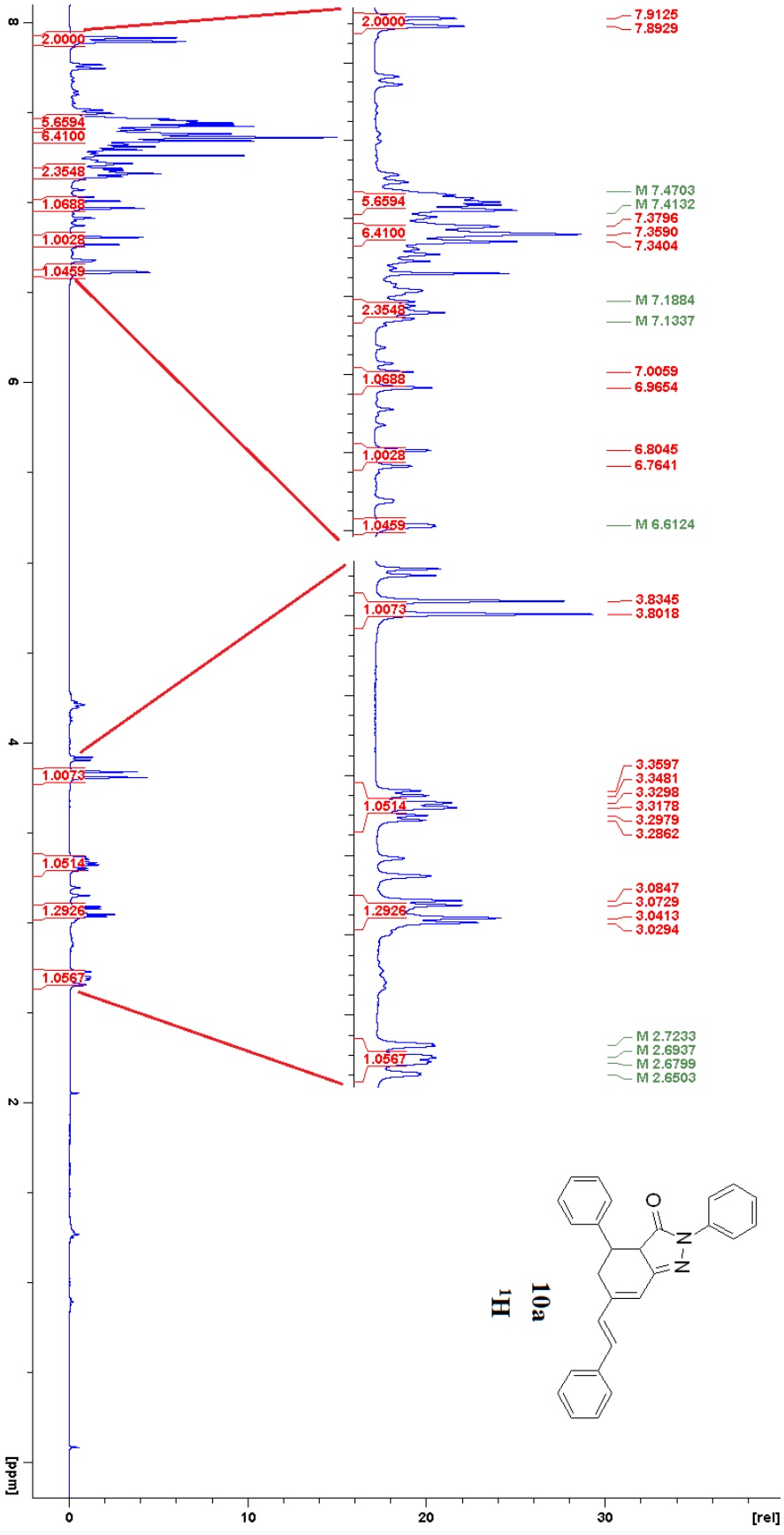

TOCSY
9a
O
O
N
NH
F2 [ppm]
F1 [ppm]
8
6
4
2

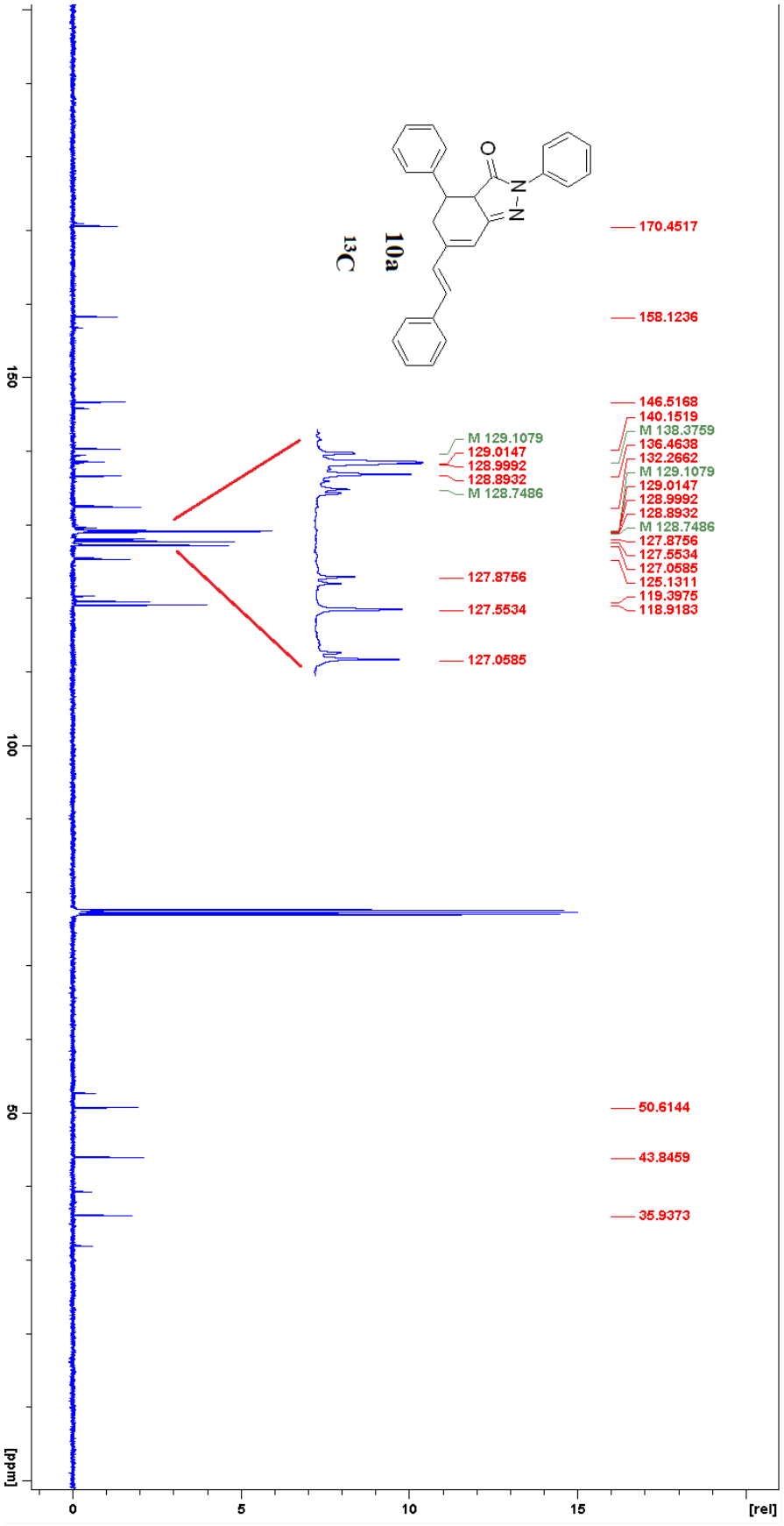

Predicted 1H NMR Spectrum
9a
Predicted hydrogen
f1 (ppm)

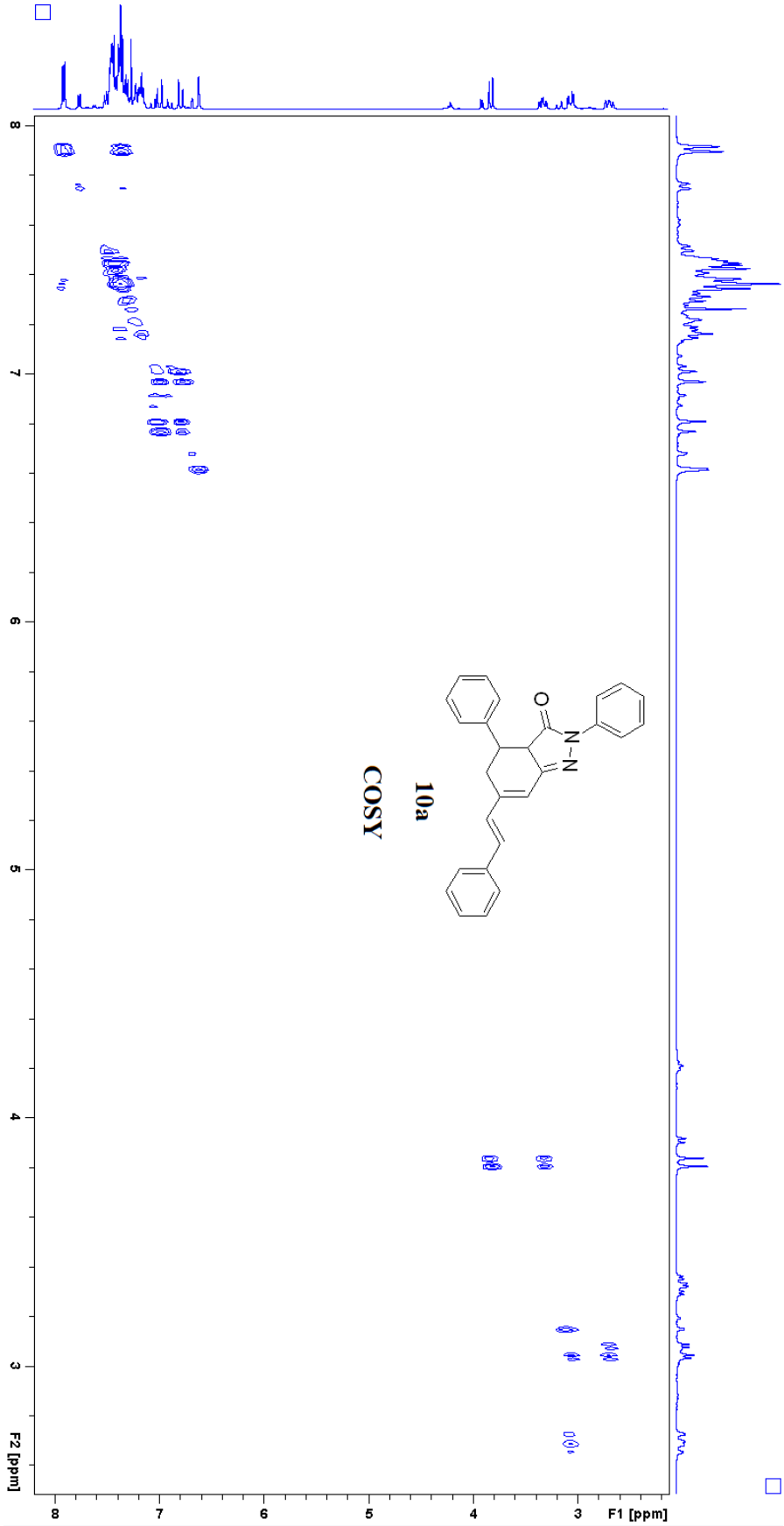

Predicted 13C NMR Spectrum
9a
Predicted carbon
f1 (ppm)

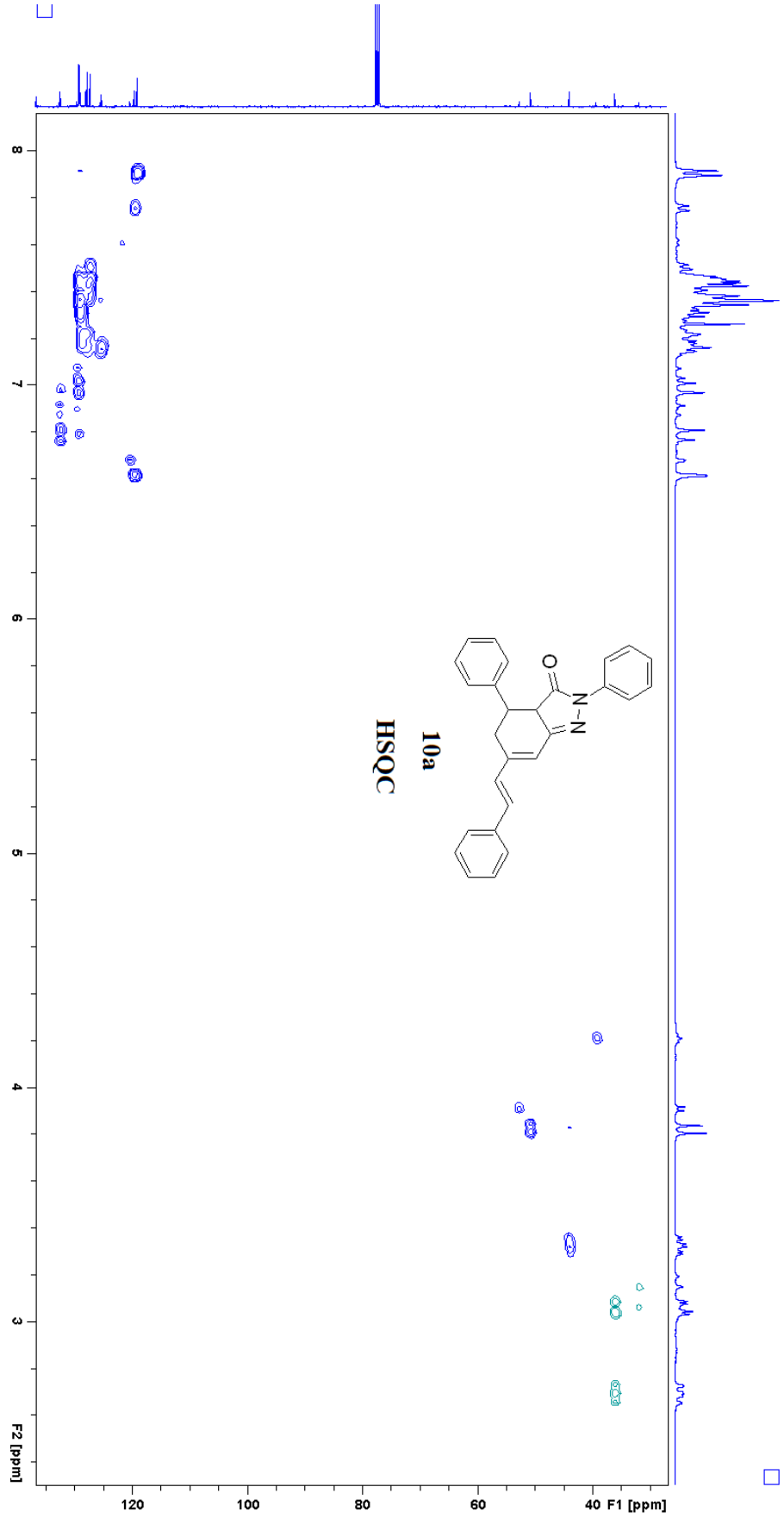
(E)-2,5-diphenyl-3-oxo-7-(2-phenylethenyl)-4,5,6-trihydroindazole (10a)

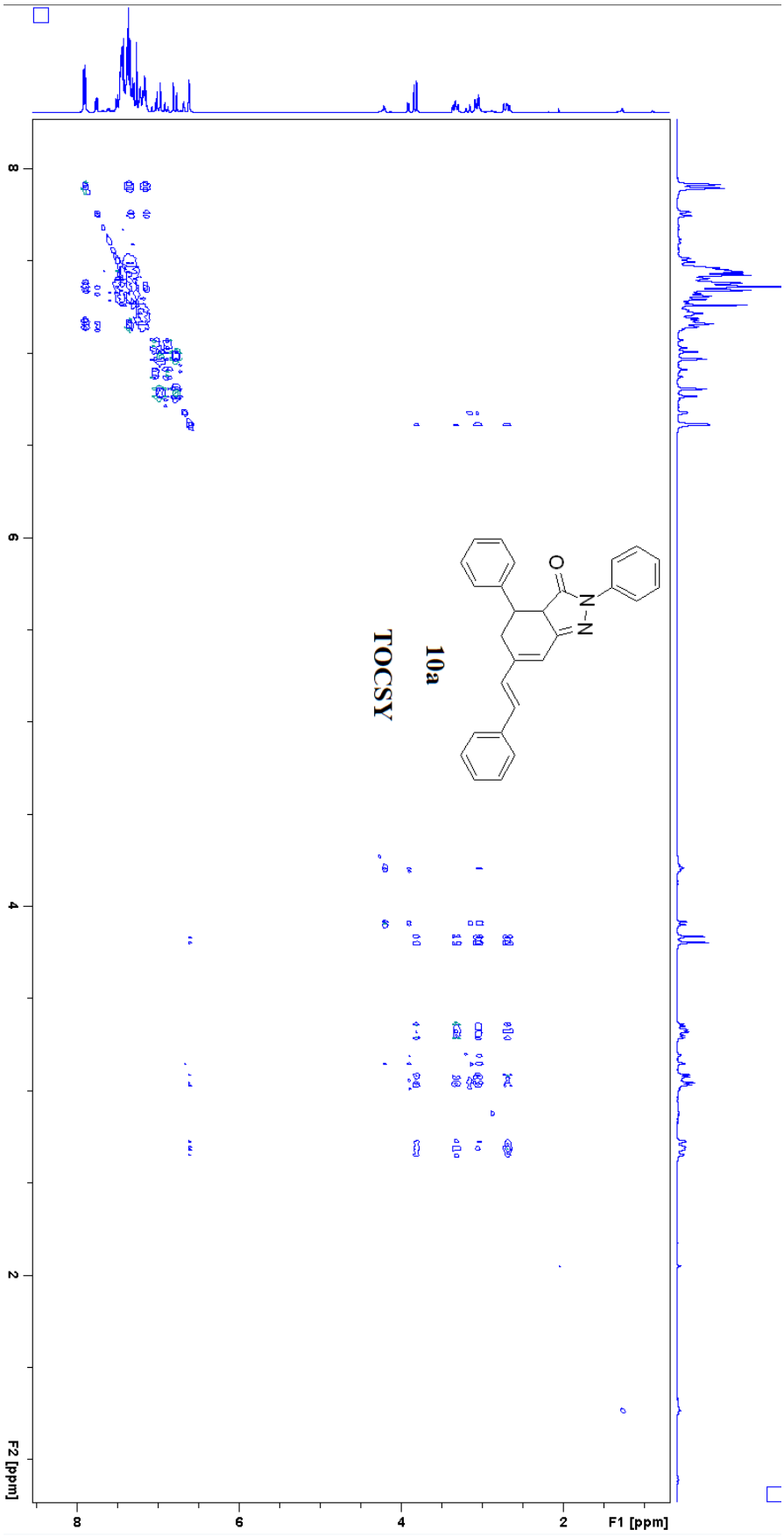


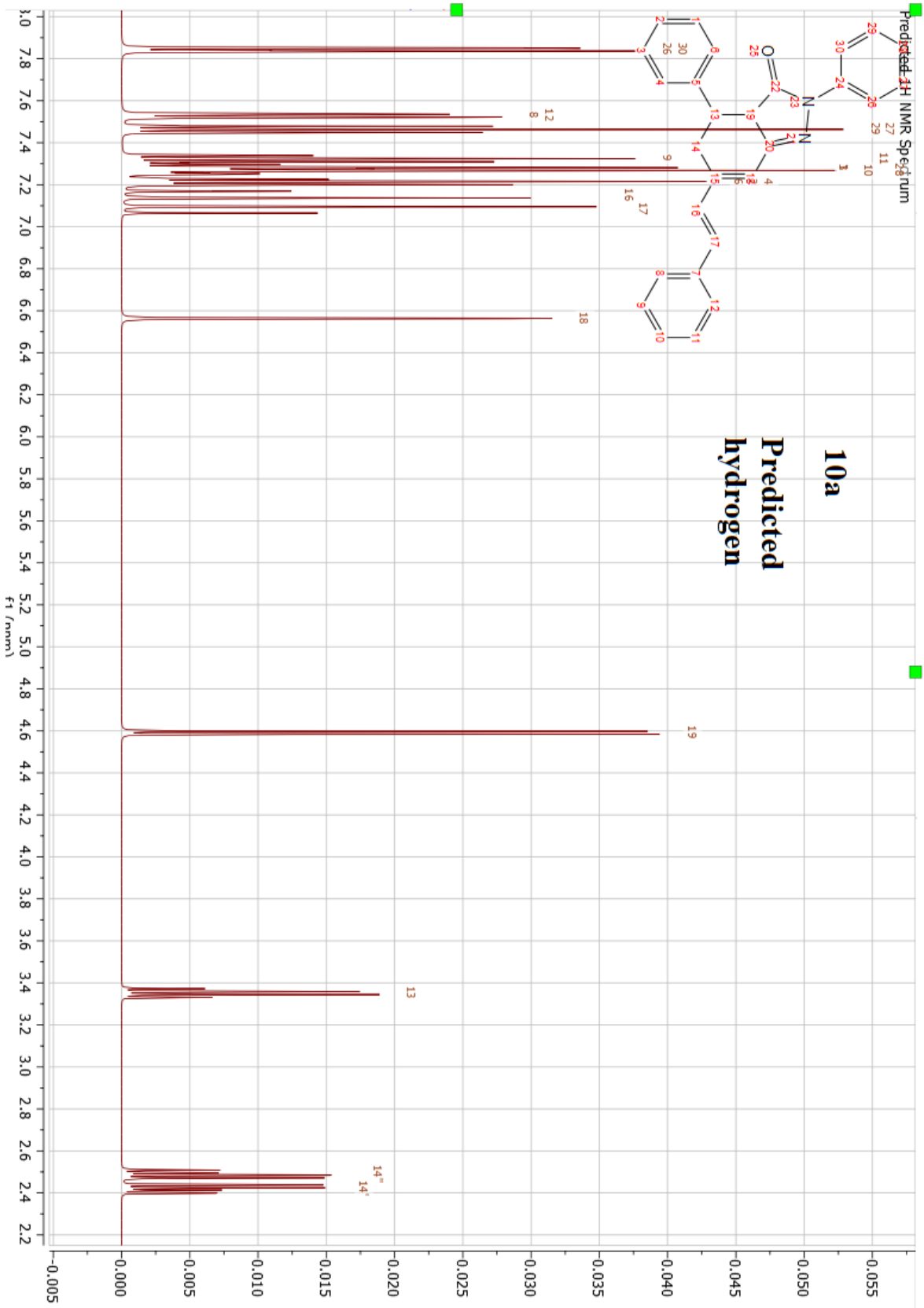

2.0000
5.6594
6.4100
2.3548
1.0688
1.0028
1.0459
1.0073
1.0514
1.2926
1.0567
7.9125
7.8929
M 7.4703
M 7.4132
7.3796
7.3590
7.3404
M 7.1884
M 7.1337
7.0059
6.9654
6.8045
6.7641
M 6.6124
3.8345
3.8018
3.3597
3.3481
3.3298
3.3178
3.2979
3.2862
3.0847
3.0729
3.0413
3.0294
M 2.7233
M 2.6937
M 2.6799
M 2.6503
1H
10a
[ppm]
[rel]

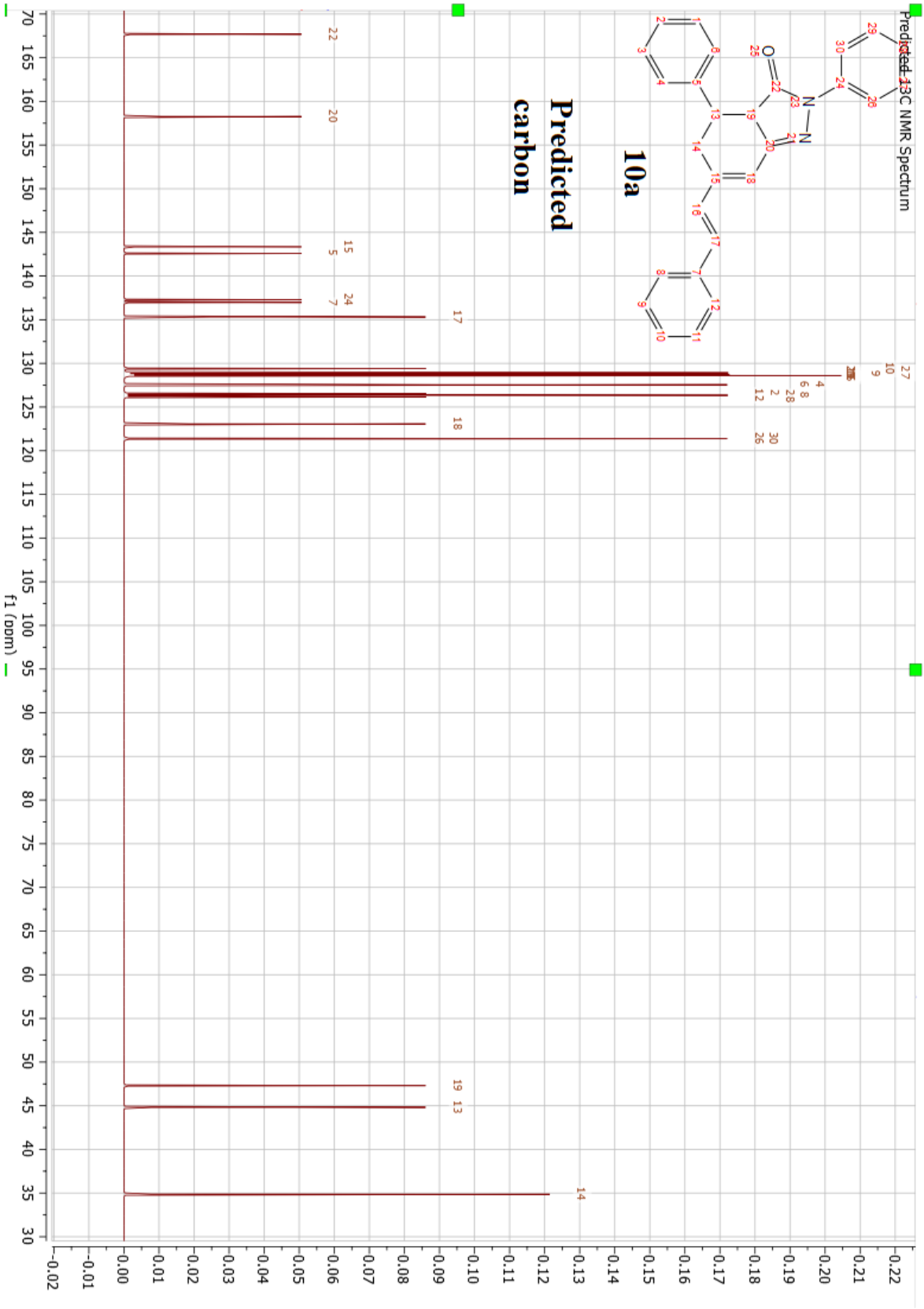

10a
^{13}C
O
N
N
170.4517
158.1236
146.5168
140.1519
M 138.3759
136.4638
132.2662
M 129.1079
129.0147
128.9992
128.8932
M 128.7486
127.8756
127.5534
127.0585
125.1311
119.3975
118.9183
M 129.1079
129.0147
128.9992
128.8932
M 128.7486
127.8756
127.5534
127.0585
50.6144
43.8459
35.9373
150
100
50
[ppm]
0
5
10
15
[rel]


COSY
10a
F2 [ppm]
F1 [ppm]
8
7
6
5
4
3
O
N
N

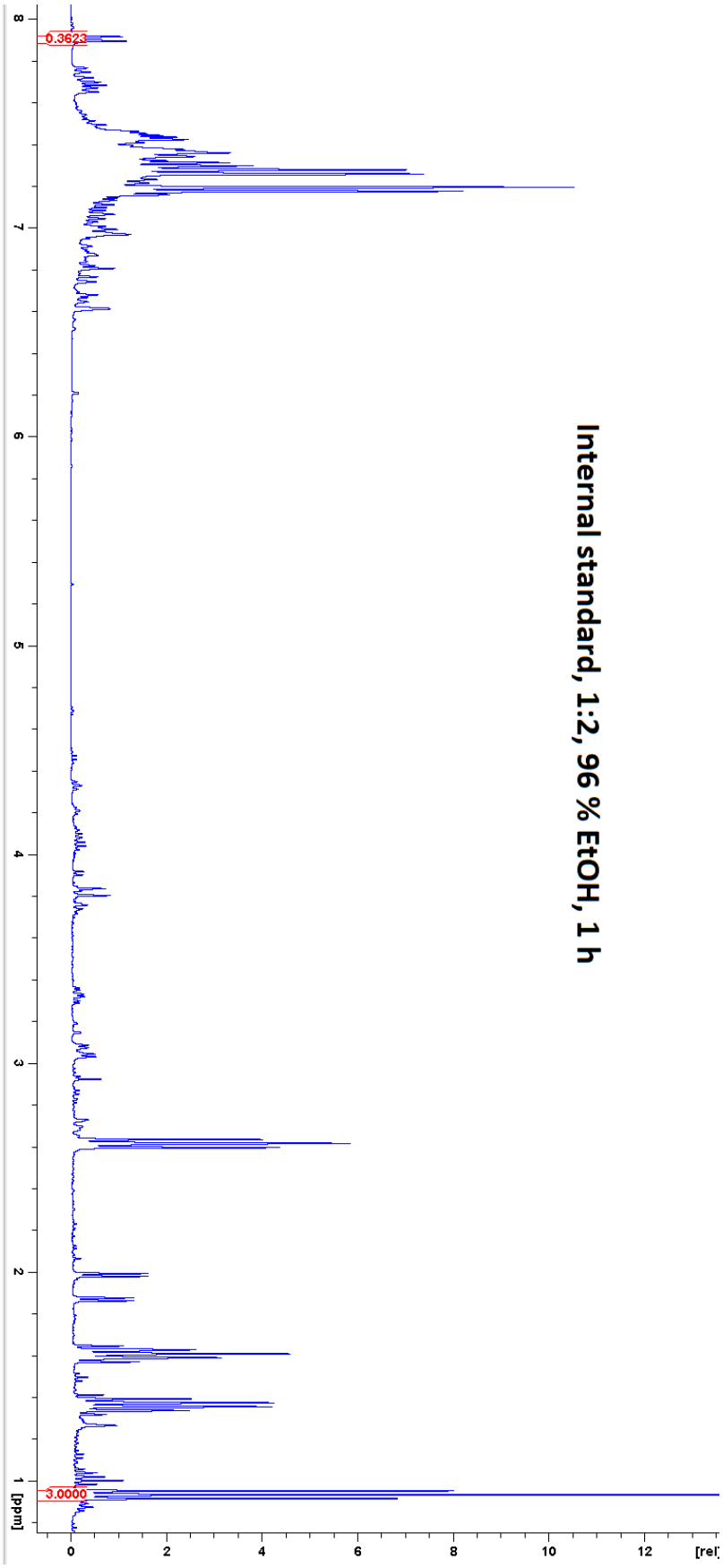

10a
HSQC
F2 [ppm]
F1 [ppm]
120
100
80
60
40
3
4
5
6
7
8
O
N
N

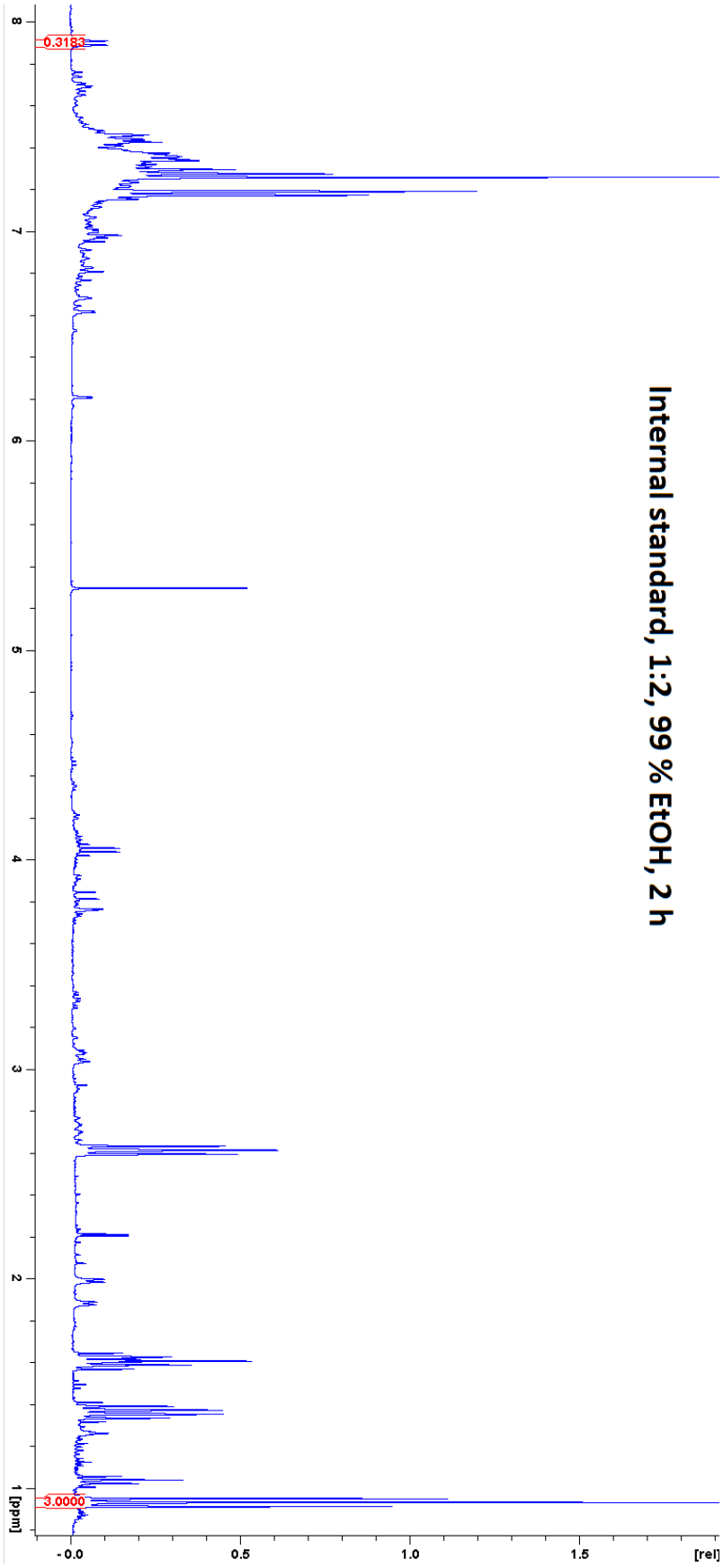

TOCSY
10a
F2 [ppm]
F1 [ppm]
8
6
4
2
O
N
N

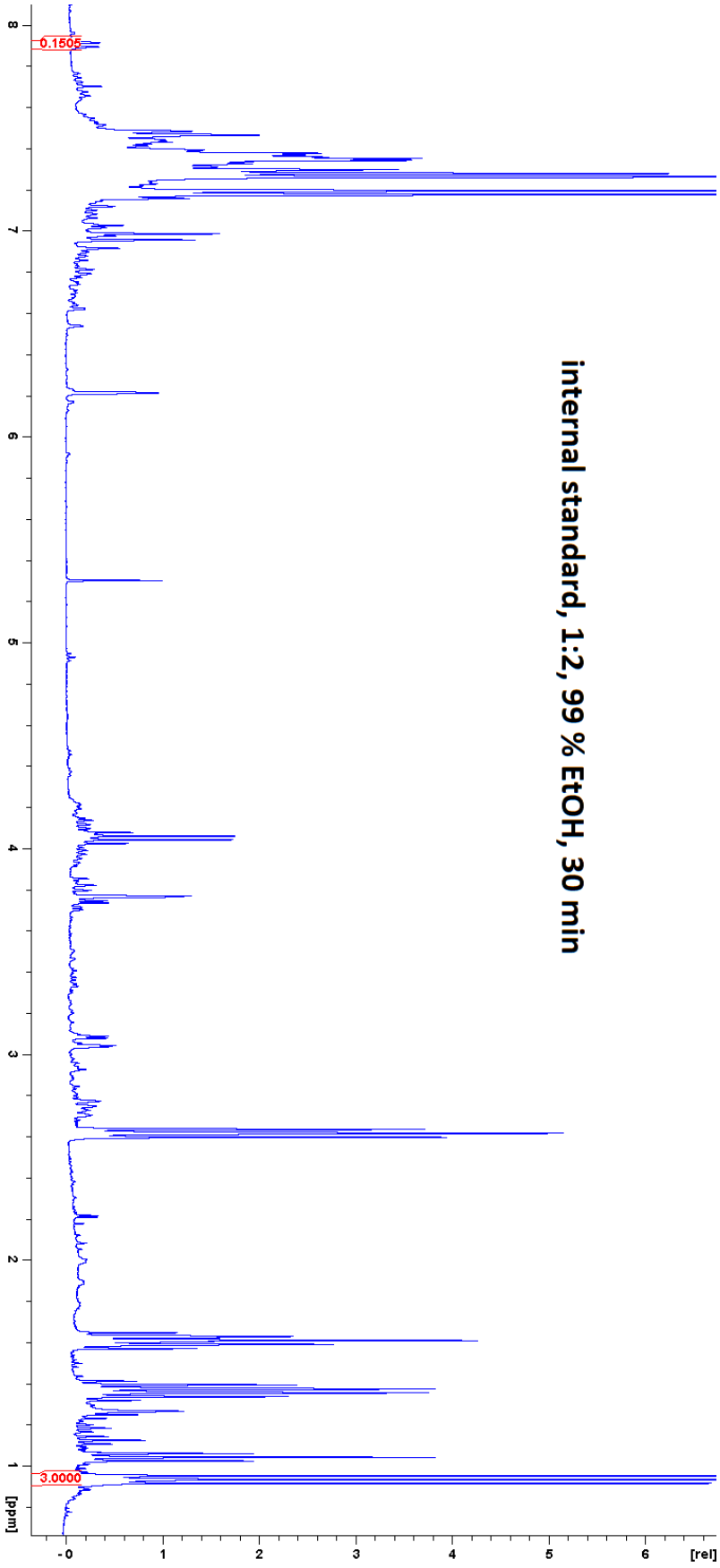

Predicted 1H NMR Spectrum
10a
Predicted hydrogen
f1 (ppm)

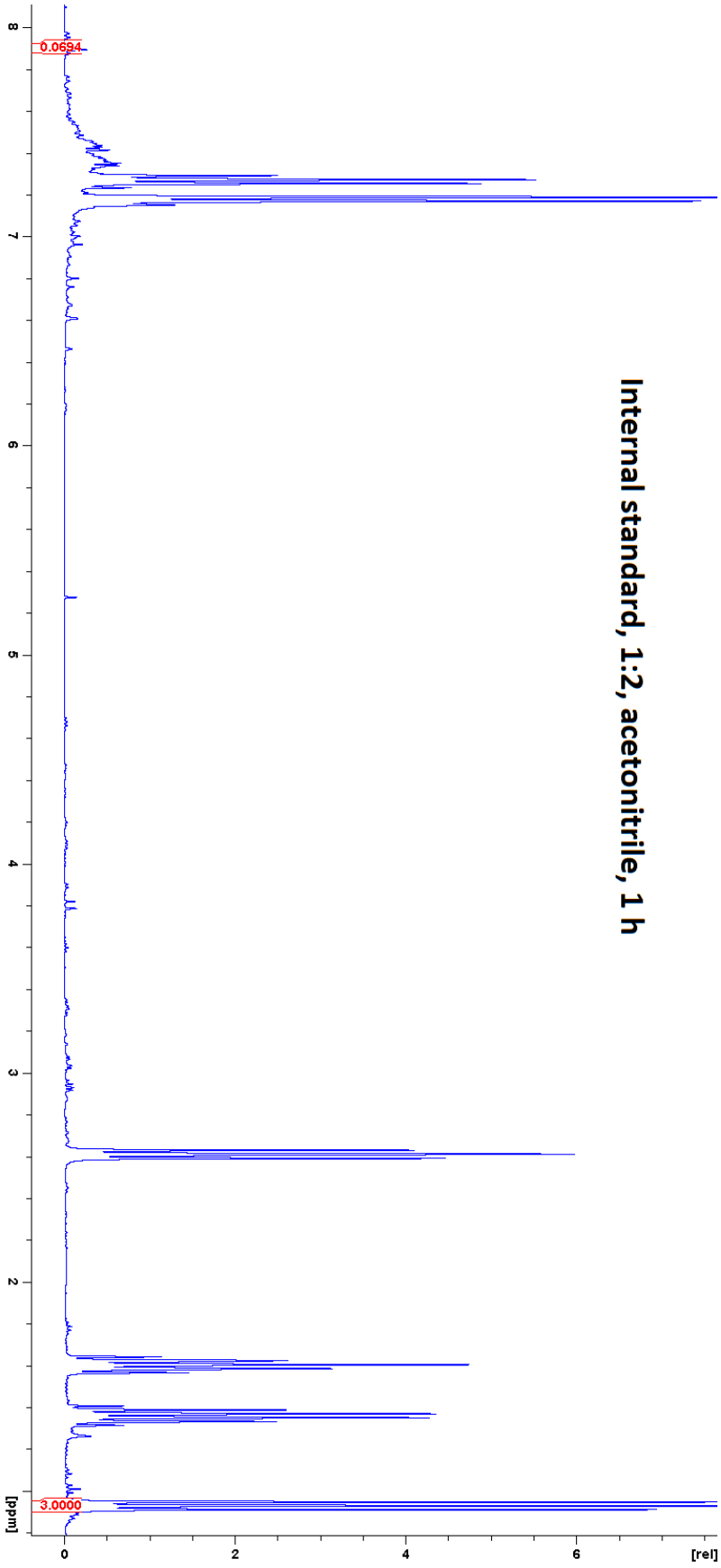

Predicted 13C NMR Spectrum
10a
Predicted carbon
f1 (ppm)

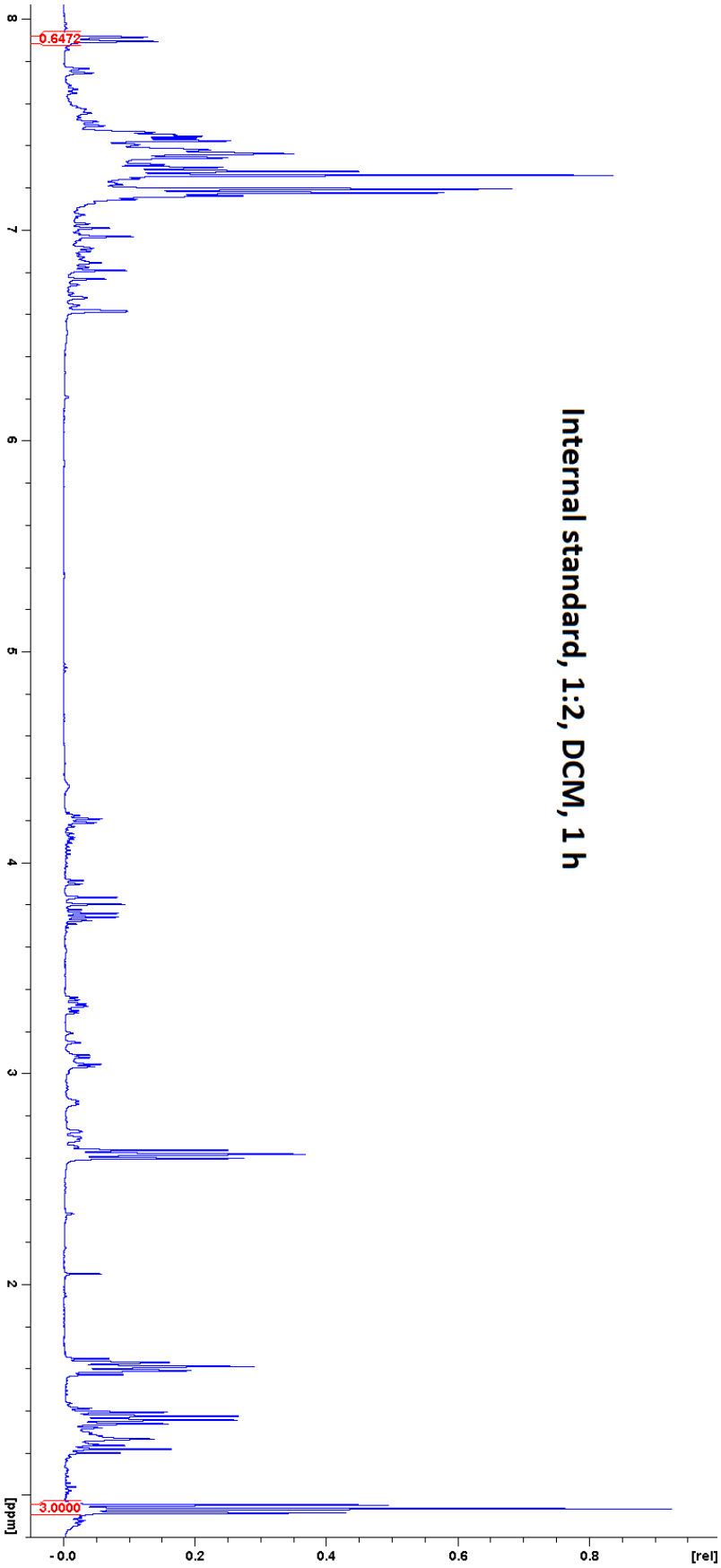
Spectra from internal standard NMR experiments.

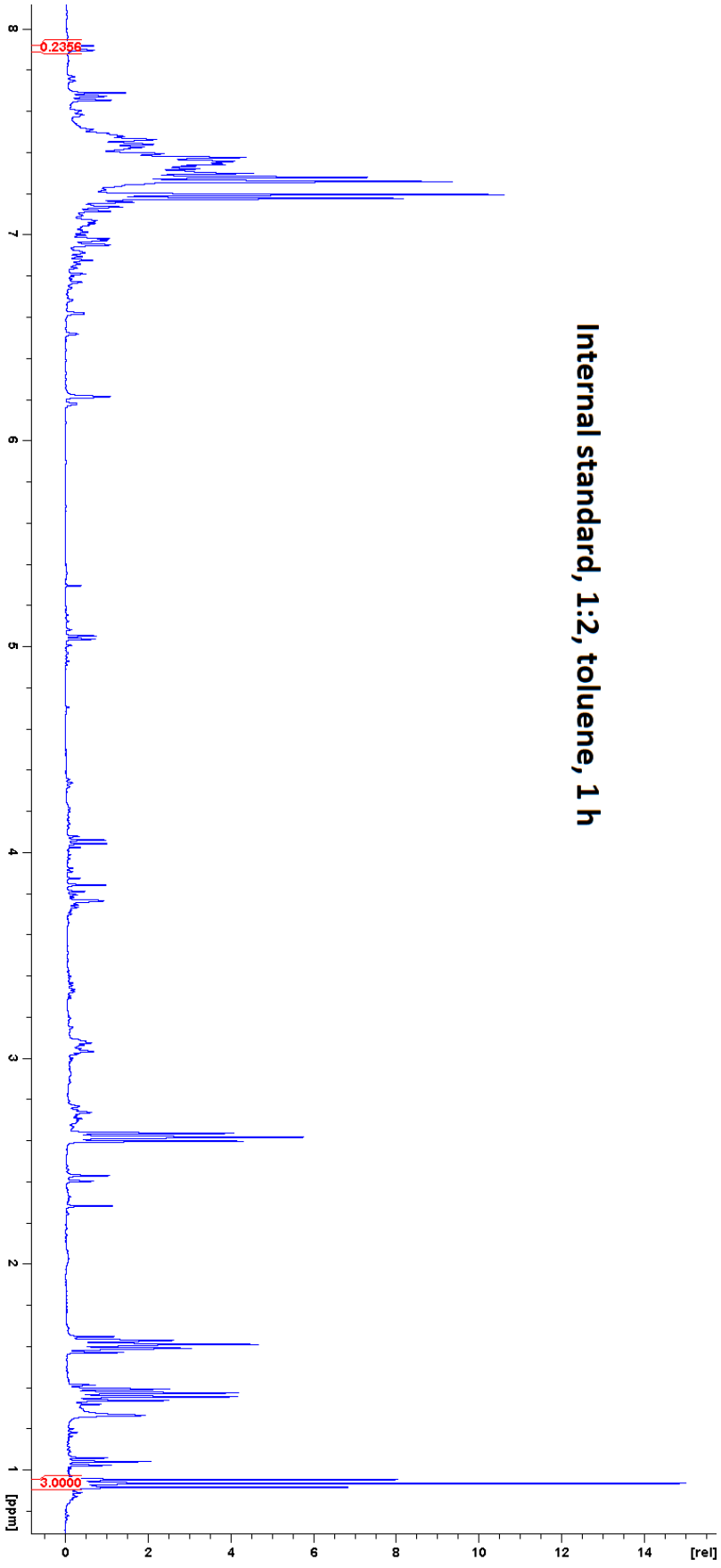

Internal standard, 1:2, 96 % EtOH, 1 h
0.3623
3.0000
[ppm]
[rel]


Internal standard, 1:2, 99 % EtOH, 2 h
0.3183
3.0000
8
7
6
5
4
3
2
1 [ppm]
-0.0
0.5
1.0
1.5
[rel]


0.1505
3.0000
internal standard, 1:2, 99 % EtOH, 30 min
[ppm]
[rel]


Internal standard, 1:2, acetonitrile, 1 h
0.0694
3.0000
[ppm]
[rel]
0
2
4
6
8


Internal standard, 1:2, DCM, 1 h
0.6472
3.0000
8
7
6
5
4
3
2
[ppm]
-0.0
0.2
0.4
0.6
0.8
[rel]


Internal standard, 1:2, toluene, 1 h
0.2356
3.0000
[ppm]
[rel]

Auto-flash chromatogram in work up of reaction between scaffold cyclohexenone molecule and I_2.