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HETEROGENEOUS IRON CATALYZED CYCLOPROPANATION REACTION

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Dedicated to Lord Shiva

Thesis Certificate

This is to certify that the thesis entitled **“Heterogeneous Iron Catalyzed Cyclopropanation Reaction”** submitted by Abhijnan Sarkar to the Università degli Studi di Milano (University of Milan) for the award of the degree of Doctor of Philosophy (PhD) in Chemistry is a bona fide record of research work carried out by him under my supervision. Any kind of information taken from previous reports published elsewhere which has adopted for the documentation in the content of thesis are cited and acknowledged with references. The contents of this thesis, in full or in parts, have not been submitted to any other Institute or University for the award of any degree or diploma.

Date : September 30, 2019
Place : Milano, Italy

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Without mentioning the name, I finally greet everyone who supported me in various stages and situations of my life - no matter whenever, whatever and however!!

Difficult roads often lead to beautiful destinations. At this stage I would like to recycle myself to be useful for something else in chemistry and beyond. Let see.

ABHIJNAN SARKAR

Abstract

Until now, NGR (nitrogen-enriched graphene) catalysts have mostly been employed for hydrogenation/oxidation reactions. In this piece of work, we expand the field of applicability of an iron NGR catalyst to cyclopropanation reactions.

In this work, a heterogeneous Fe-based nitrogen-doped carbon supported catalyst has been successfully employed for the cyclopropanation reaction of alkenes. According to best of our knowledge, this is the first example of a heterogeneous Fe-catalyzed cyclopropanation reaction in today's date. These kinds of materials, generally employed for reduction or oxidation reaction, are now indeed effective catalyst also for carbene transfer reactions.

The activity of Fe/Phen@C-800in the reaction was initially explored by using ethyl diazoacetate and α-methylstyrene as substrates as the model transformation. Various parameters such as solvent, temperature, time and catalyst support etc. were changed. The nature of the solvent has a minimal influence both on the reaction yield and diasteroselectivity making this reaction versatile from the media profile. The variation of the reaction temperature furnished the product in slightly lower yield. When a 5-fold amount of the olefin with respect to the diazo compound was used, homocoupling products (diethyl fumarate and diethyl maleate) deriving from EDA were detected in very low amount (<5 %). Even when the amount of olefin was decreased (1.5 eq) homocoupling sideproducts increased, although a very good yield of the cyclopropane was maintained, demonstrating the applicability of the procedure even to more expensive olefins. Interestingly, the catalyst is water tolerant and only a slight decreased yield was obtainedusing a "wet" solvent. A change in the catalyst support from carbon to inorganic oxides (MgO or SiO_2) does not significantly affect the yield and the diastero selectivity. Furthermore control experiments effected by employing catalysts prepared by the same procedure employed for Fe/Phen@C-800, but omitting either $Fe(OAc)_2$ or Phen, resulted in no detectable formation of cyclopropane.

Fe/Phen@C-800-catalysts showed good results in dimethoxyethane at 60 °C for 4 h, affording high yields of the desired cyclopropanes (mixture of *cis* and *trans* isomers) and only <5 % ethyl maleate and fumarate. The model reaction has been successfully scaled-upto 15-fold without significant variations of yield and diasteroisomeric ratio.

The developed protocol allows obtaining several cyclopropanes from aromatic and aliphatic olefins and different diazocompounds. High to excellent yields were obtained for terminal

olefins, including geminally substituted ones. Aliphatic olefins require longer reaction times. A moderate trans diastereoselectivity was observed in all cases. The catalysts do not show any activity towards internal olefins and can be used to selectively cyclopropanate a terminal olefin in a substrate containing both internal and terminal olefinic groups. The selectivity for the terminal double bond can be explained by the lack of activity of the catalyst in the case of internal olefins, most likely due to a hindered approach of the substrate to the carbene formed on the surface of the catalyst.

Mono substituted diazo compounds (ester or ketone) afforded the corresponding cyclopropanesin excellent yields. More sterically demanding diazocompounds such as t-BDA has a dramatic effect on the diasteroselection, furnishing the *cis*- isomer only in traces. Disubstituted diazomethanes proved to be more challenging. Mono substituted diazo compounds such as diphenyldiazomethane failed to afford corresponding cyclopropanes under standard conditions, although it yielded the product in moderate yield at a higher temperature and longer reaction time (100°C for 8h in toluene), while the more stable diazomalonate did not react even under these conditions.

The catalysts was recycled several times, but a gradual deactivation is immediately observed since the first recycle. In principle, the loss of activity can be attributed either to metal leaching or to deactivation of the catalyst. After the 1st recycle, ICP analysis of the solutionshowed that only 0.1% of the initial iron had been lost in solution. This result indicates that the loss of recycling ability is not due to metal leaching. In order to make the whole process both efficient and effective, two routes of reactivation were explored.

Attempted reactivation of the catalyst at 300 °C seems to have a slightly positive effect but that at 400 °C is not effective.The initial catalyst activity was effectively restored using an oxidative reactivation protocol under mild conditions (H_2O_2, 3 v/v% aqueous solution), which may be of more general use even for other reactions if olefins or other polymerizable compounds are employed as substrates.

Oxidative regeneration is typical for catalyst that suffer of physicochemical deactivation (e.g. fouling or poisoning). Indeed, we verified that complete deactivation of the catalyst occurs even by treating the material only with styrene under the reaction conditions and the activity is restored by oxidative treatment. This result indicates the polymerization of the olefin on the catalytic surface as a possible cause for the deactivation rather than a mechanical or thermal modification of the catalyst.

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Abbreviations

atm	Atmosphere
MW	Molecular weight
g	gram
mg	milligram
mL	milliliter
Equiv.	Equivalent
mmol	Millimole
mol	Mole
h	Hour/hours
°C	Degrees Celsius
Temp.	Temperature
RT	Room temperature
Cat.	Catalyst
NGR	Nitrogen-doped-graphene
Conv.	Conversion
Sel.	Selectivity
DCM	Dichloromethane
DME	Dimethoxy ethane
EDA	Ethyl diazoacetate
t-BDA	Tertiary butyl diazoacetate
EDG	Electron-donating group
EWG	Electron-withdrawing group
Phen	1,10-phenanthroline
UNIMI	Università degli Studi di Milano
Ac	Acetyl
Ar	Aryl
Benz.	Benzene
Bn	Benzyl
^{t}Bu	Tert-butyl
e.g.	For example

Me	Methyl
Et	Ethyl
ABF	Annular bright field
ADF	Annular dark field
HAADF	High angle annular dark field
ICP	Inductively coupled plasma
XPS	X-ray photoelectron spectroscopy
STEM	Scanning transmission electron microscopy
EDXS	Energy dispersive-X-ray spectrometer
EELS	Electron energy loss spectrometer
IR	Infrared spectroscopy
FT-IR	Fourier transform infrared spectroscopy
TEM	Transmission electron microscopy
NMR	Nuclear magnetic resonance
^{1}H NMR	Proton nuclear magnetic resonance
^{13}C NMR	Carbon-13 nuclear magnetic resonance
^{19}F NMR	Fluorine-19 nuclear magnetic resonance
nd	Not detected
s	Singlet
d	Doublet
t	Triplet
q	Quartet
m	Multiplet
J	Coupling constant
ppm	Parts per million
dr	Diastreomeric ratio

Chapter 1

Introduction

1.1 The Cyclopropane Ring

The smallest cycloalkane unit is "the cyclopropanes" has a unique combination of reactivity and structural properties. Cyclopropanes and their derivatives have been found in various natural products such as terpenes, pheromones, fatty acid metabolites and in some amino acids.[1,2] Cyclopropanes are extremely important synthetic intermediates while preparing various cyclic and acyclic compounds. Unique electronic, conformational and steric properties of the cyclopropyl group continue to fascinate researchers of various disciplines.[3] The construction of the cyclopropane ring requires three -CH_2- groups to be accommodated into acyclic 3-membered ring arrangement where all C-C-C bond angles are equal to 60°(Figure 1.1).[4] These bond angles are significantly much lower than the ideal 109.5° for sp^3-hybridized carbons, which results into an angular strain [Bayer Strain]. The reduced overlap is considered to be the source of the angular strain.[5]

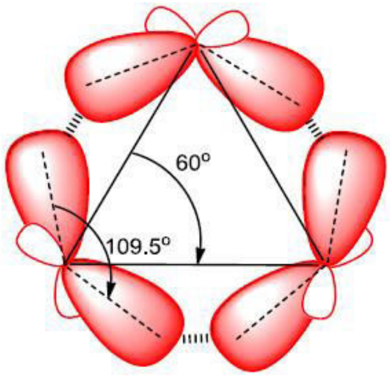


Figure 1.1: The Coulson-Moffitt model.[2,4]

In addition, cyclopropanes suffers high torsional strain because of the coplanar arrangement of the carbon atoms which mandates that C-H bonds be eclipsed within the structure. The relief of strain is associated with ring opening,[4] rationalizing the high reactivity of the cyclopropyl group.

σ bonds are considered as localized entities which is in accordance to classic approaches in organic chemistry.[4] By aiding σ-conjugation concept, some of the chemical and physical properties of cyclopropanes can be explained. Three carbon-carbon σ-bonds form a cyclic array of 6 electrons, which follows Huckel's 4n+2 rule of aromaticity; therefore cyclopropane is aromatic. σ-aromaticity explains chemical properties of cyclopropanes such as their reactivity towards electrophiles.

The reactivity of cyclopropanes are significantly higher than those of typical alkanes. Higher reactivity of cyclopropanes originates from unusual chemical skeleton structure, relatively shorter C-C bonds, enhanced both the π-character of the C-C bonds than normal, shorter and stronger C-H bonds than those in alkanes. Kinetic stability of cyclopropanes under ring strain (27.5 kcal mol^{-1}) is also noteworthy.[6] Relief of strain lead to significant challenges for their construction and manipulation, defending in certain tactical limitations. Cyclopropanes can also be extended in their uses to 'lock' a molecule in its bioactive conformation; therefore creating a potential increase in its application.[3]

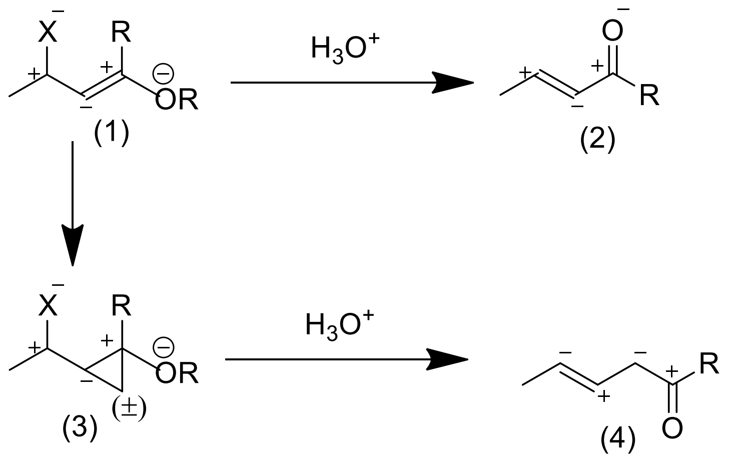
From previous discussion, it is clear that high ring strain, torsional strain, limited degrees of freedom, excellent reactivity and many other remarkable properties make cyclopropanes attractive for various chemical transformations!

1.2 Uses of Cyclopropanes and Their Derivatives

The importance of cyclopropanes in organic synthesis originates from the distinctive characteristics of the three member ring and the similarity of its chemistry to that of a carbon-carbon double bond.[7]

Chemists usually adopt the incorporation of a cyclopropyl group as a good synthetic strategy for changes in either the consonant or the dissonant relationships within the carbon framework of the products. This can be demonstrated by the following example -

Hydrolysis of 1 results into enone 2 in which the consonant relationship of charges has been retained. Another good strategy is the incorporation of the odd carbon in the form of a cyclopropane. Incorporating cyclopropane in 3 allows for the cleavage to 4, where the consonance (or dissonance) will be dictated solely on the basis of further use or will depend on other functionalities surrounding the olefin.[8]

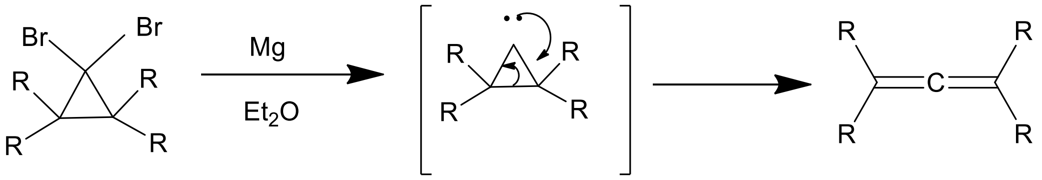


This remarkable features of cyclopropanes becomes a useful “synthetic wedge tool” to design carbon frameworks in the desired product because it aids the addition of only one carbon. Applications of cyclopropanes and their derivatives in the preparation of organic compounds are extensive[9] and have been explored in virtually every synthetic sense that befits the utility of alkenes in synthesis.

1.2.1 Thermal Ring Fission

1.2.1.1 Cyclopropyl Carbene Rearrangement

By treating 1,1-dibromocyclopropane(5) with magnesium, an allene(7) is obtained,[10-11] which arises from the rearrangement of a cyclopropylcarbenoid(6).



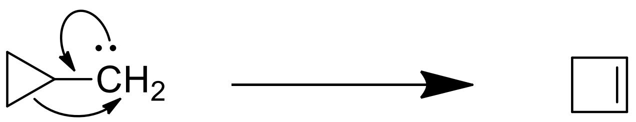
1,1 dibromocyclopropane
(5)

Cyclopropyl carbenoid
(6)

Allene
(7)

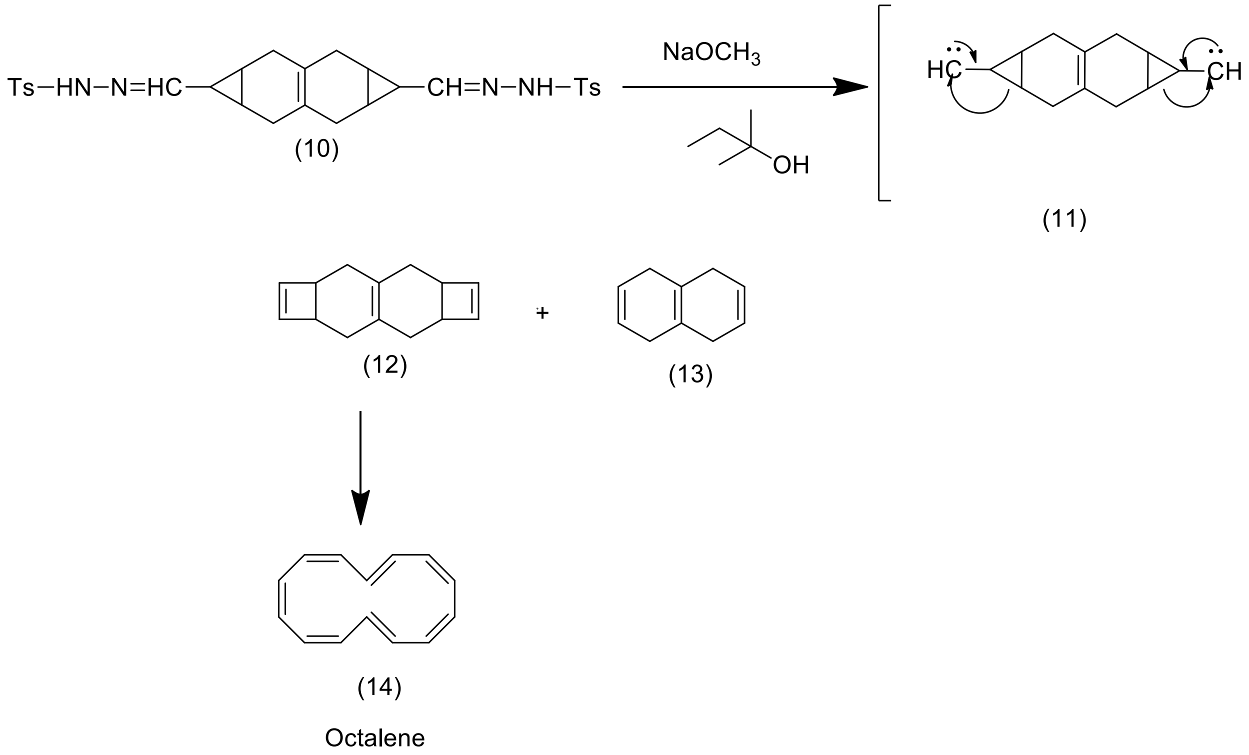
1.2.1.2 Cyclopropylmethyl Carbene Rearrangement

Formation of carbene(8) causes a ring expansion through a 1,2-migration of the cyclopropyl C-C bond, resulting in formation of a cyclobutene(9).[12]



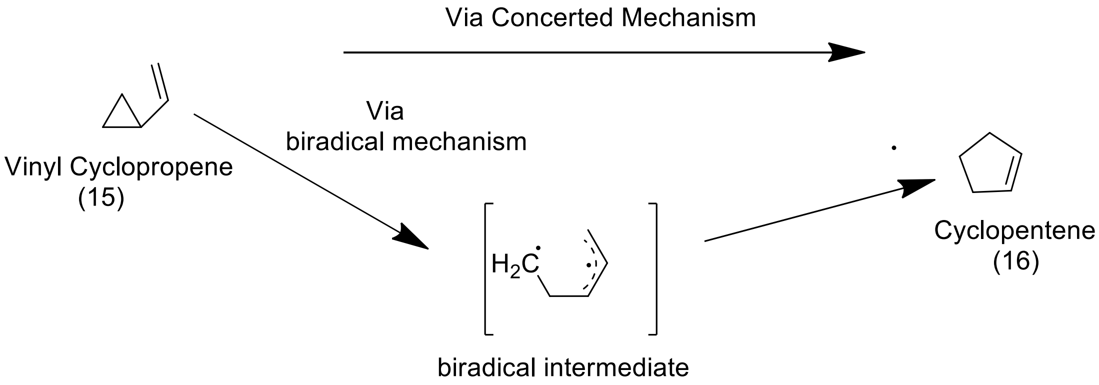
(8) (9)

This strategy has been successful in the synthesis of octalene(14).[11]



1.2.1.3 Vinylcyclopropane Rearrangement

Chemical properties of cyclopropanes are greatly influenced by conjugation with adjacent π-systems. Vinylcyclopropane(15) undergoes unimolecular rearrangement and cyclopentene(16) forms upon heating.[13,14] Mostly these rearrangements have biradical intermediates.[15] Although concerted processes have been reported in several articles.[16-17] The following examples show the utility of the vinylcyclopropane-cyclopentene rearrangement in substituted or annulated cyclopentenes synthesis.

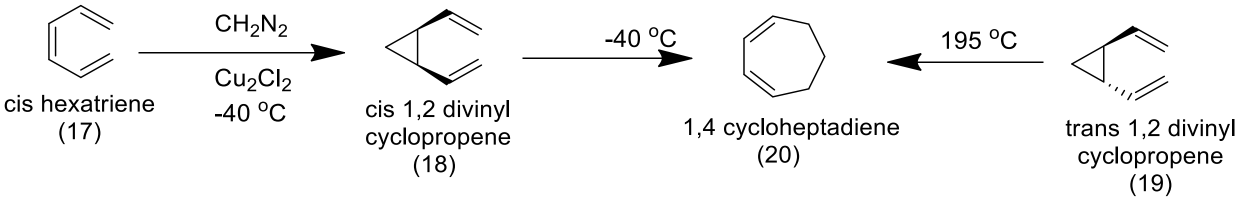


Researchers explored the usefulness of this rearrangement in order to develop numerous methodologies concerned with the preparation of functionalized cyclopentenes.[18]

1.2.1.4 Divinylcyclopropane Rearrangement

The preparation of seven-membered rings can be done via thermal rearrangement of divinylcyclopropanes. Cyclopropanation of cis-hexatriene(17) with diazomethane in the presence of cuprous chloride at -40 °C resulted in the isolation of 1,4-cycloheptadiene(20).[15a,19]

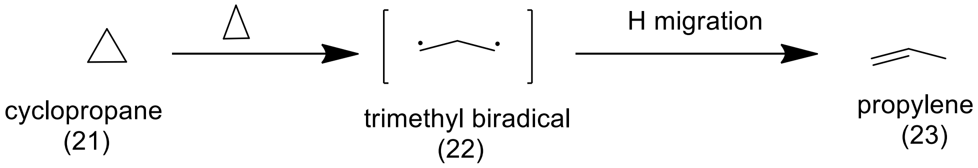
Earlier investigations[13b, 20] in which the attempted preparation of cis-1,2-divinylcyclopropane unexpectedly yielded 1,4-cyclopentadiene(19) also support this result. The results infer that the low activation energy for the Cope rearrangement of cis-l,2-divinylcyclopropane to 1,4-cycloheptadiene (18 → 20) allows this process to take place at lower temperatures. A biradical mechanism has been proposed for this isomerization.[15a,19]



Trans-1,2-divinylcyclopropane(19) is more stable than its cis isomer(18) and requires a higher temperature of 195 °C to isomerize to 1,4-cycloheptadiene.[15a,19]

1.2.1.5 Miscellaneous Thermal Fission

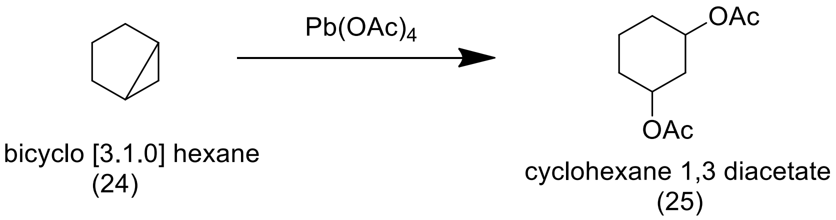
The mechanism of the thermal isomerization of cyclopropane(21) to propylene(23) is thought to involve cleavage of the three-membered ring to the trimethylene biradical(22) which undergoes a subsequent hydrogen migration process to yield propylene.[21]



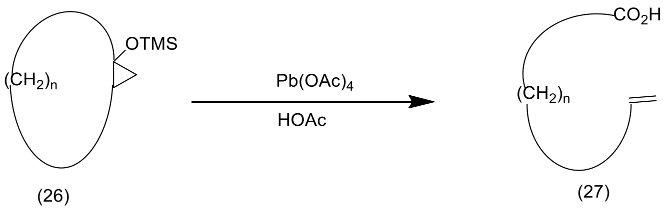
1.2.2 Oxidative and Reductive Ring Fission

1.2.2.1 Oxidative Fission

Oxidative cleavage of cyclopropanes involves the breakage of a carbon-carbon bond of the cyclopropyl group, followed by the formation of two bonds involving carbon atoms in a higher oxidation state. The steric and electronic effects of the substituents on the ring, as well as the properties of the oxidizing agents can facilitate regio- and stereospecific opening of the cyclopropane ring. For example, bicyclo[3.1.0] hexane(24) is cleaved by lead tetraacetateto provide cyclohexane 1,3 diacetate(25).[22]



This procedure has been found to be useful for the preparation of a homologous series of unsaturated acids.[23,24]

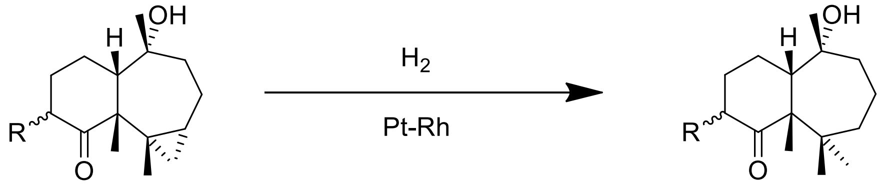


1.2.2.2 Reductive Fission

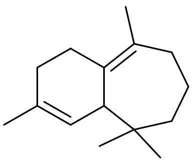
Cleavage of cyclopropane at the least substituted bond can be achieved by catalytic hydrogenation in a general synthesis of products containing gem-dimethyl groups.[25,26,27]

(28) (29)

Hydrogenation of cyclopropane(30) over platinum-rhodium catalyst results into ring opening and formation of gem-dimethyl compound(31), which is a starting material for β-himachalene(32) synthesis.[28]



(30) (31)



ß-himachalene
(32)

1.2.3 Electrophilic and Nucleophilic Ring Fission

1.2.3.1 Additions to Cyclopropanes

Simple fragmentation[29] of cyclopropane systems becomes possible when the ring is substituted with functionalities that offer a suitable reinforcement of unidirectional electron flow. Like alkenes, cyclopropanes are subject to addition reactions.

Any of its three bonds are prone to cleavage (Figure 1.2) based on the electron donors or acceptors substituent.

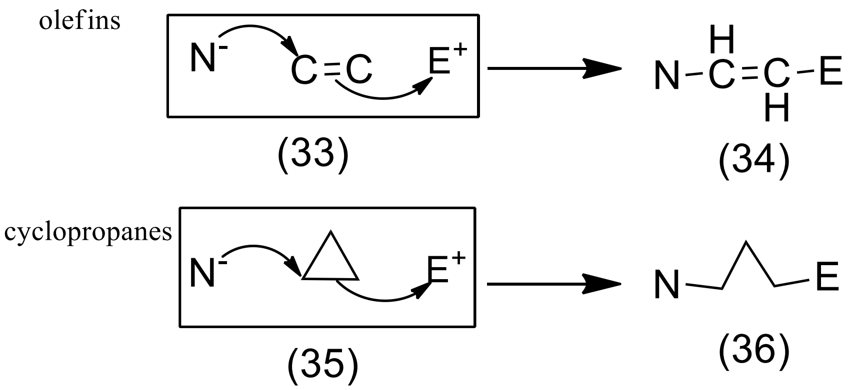


Figure 1.2: Simple bond fragmentation mechanism of C=C bonds in olefins and C-C bond in cyclopropane.

It is important to note that neither the nucleophile nor the electrophile may (or may not) be connected to the cyclopropane (Figure 1.2). Such connection distinguishes the reactive options of cyclopropanes from those of olefins which are equipped with similar donors or acceptors (Figure 1.3). The reactions can generally be carried on in either acidic or basic media.

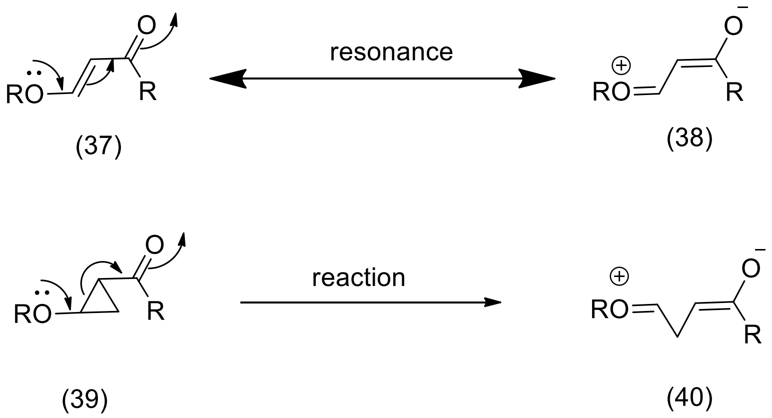
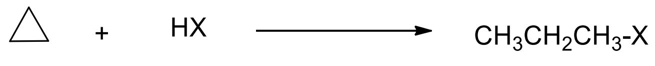


Figure 1.3: Mechanistic analogy of olefins and cyclopropanes equipped with similar donors and acceptors.

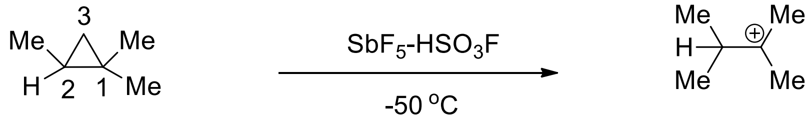
1.2.3.2 Electrophilic Additions

In direct analogy to the chemistry of alkenes, the cyclopropane ring behaves much like a carbon-carbon double bond. Treatment of a three-membered ring with various electrophiles results in addition of the electrophile followed by ring fission.[16,30]



(41) (42)

The electrophilic addition follows Markovnikov's rule for substituted cyclopropanes, although exceptions have been reported. Addition of SbF_5-HSO_3F to 1,1,2-trimethylcyclopropane(43) at -50 °C gave cleanly 2,3-dimethyl-2-butyl cation(44).[31] It appears that the protonation occurred at C-3, to generate the tertiarycarbocation(44).[31]

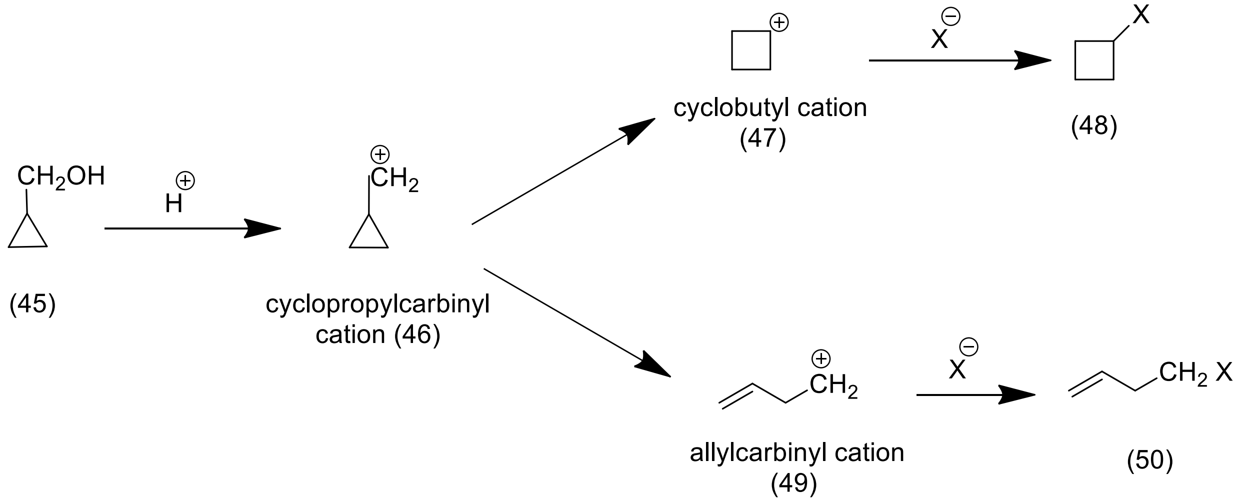


1,1,2-trimethylcyclopropane (43)

2,3-dimethyl-2-butyl cation (44)

1.2.3.3 Cyclopropylcarbinyl Cation and Related Rearrangements

For small-ring compounds, the cyclopropylcarbinyl cation system allows different possible rearrangements.[16] The intermediates of this rearrangement are either the cyclobutylcation(47) or the allylcarbinyl cation(49).

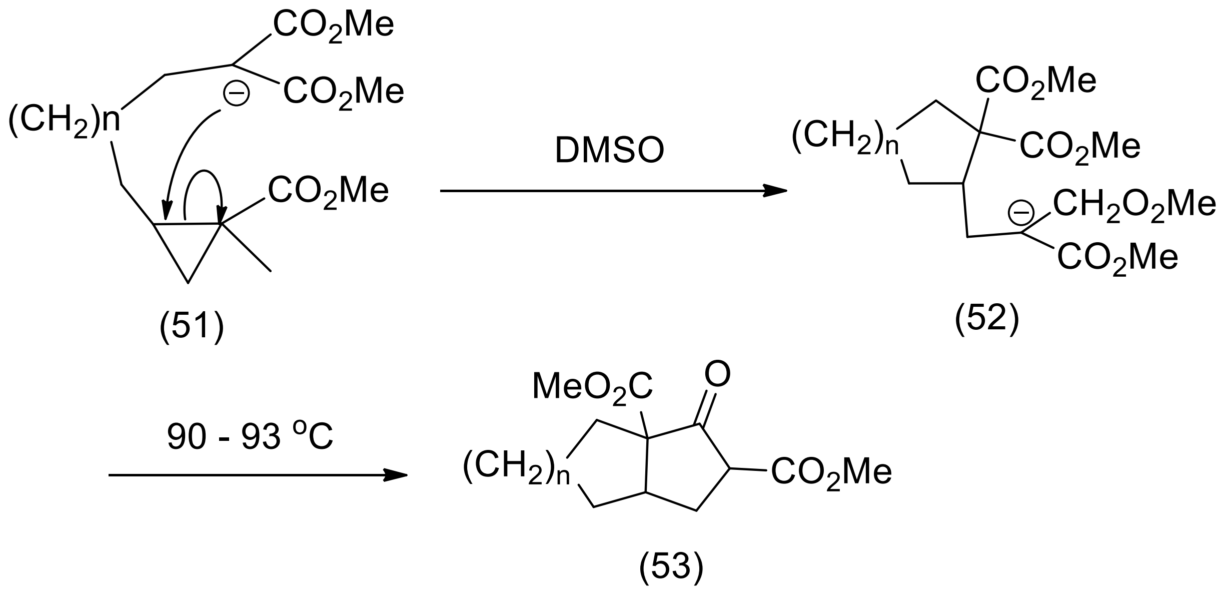


Conversion of cyclopropylcarbinyl cation(46) to cyclobutyl cation(47) is promoted by the relief of ring strain and the formation of a more stable carbocation. On the other hand, cyclopropylcarbinyl cation(46) will also endure ring fission to furnish allylcarbinyl cation(49). The application of these isomerizations is of great value to organic synthesis.

1.2.3.4 Nucleophilic Addition

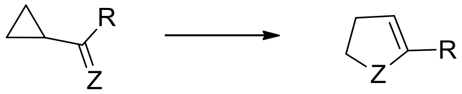
Cleavage of cyclopropanes by nucleophiles is achievable only when an electron-withdrawing group (W) is present on the ring.[32] This methodology is known as the homologous (or 1,5) version of the classical Michael addition[33] and widely applied in organic synthesis. Central to the approaches to cyclic compounds is the initial nucleophilic attack of an enolate, alkoxide, or amine on an activated cyclopropane, with subsequent intramolecular ring closure. The following example illustrates how this type of reaction can be applied intramolecularly in the preparation of some fused-ring compounds.

Anions(51) reacted rapidly at room temperature in DMSO via an intramolecular nucleophilic addition to the cyclopropyl group and52 formed. When 52 was heated, a 70% yield of the bicyclic ketones(53) was obtained.[34]



1.2.3.5 Imine-Cyclopropane and Carbonyl-Cyclopropane Rearrangement

Under appropriate conditions, cyclopropanes in conjugation with an unsaturated functional group can undergo the rearrangement (i.e., 54 - 55), as shown below.

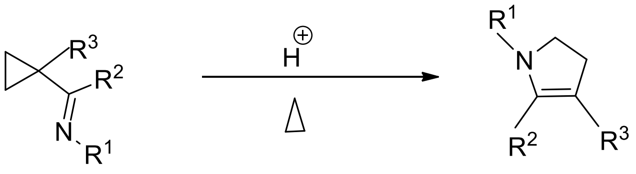


(54) (55)

Z = CH_2, NR, O

This rearrangement is a representative example of a heterocyclic variant of the vinylcyclopropane-cyclopentene rearrangement. Mechanistic details can involve thermolysis as well as protonation of the cyclopropyl ketone followed by either external or internal trapping of the cation; therefore, they need to be treated separately.

The following example illustrates the application of imine-cyclopropane and carbonyl-cyclopropane rearrangement in organic synthesis. Δ^2-pyrrolines(57) (which are useful intermediates in alkaloid synthesis) can be prepared by the acid-catalyzed thermal rearrangement of cyclopropylimines(56).[35]



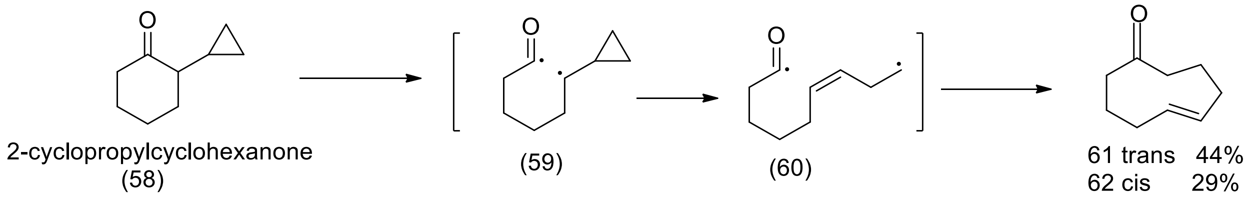
(56) (57)

$R^1 = R^2 = H$, R^3 = 3-pyridyl	68%
$R^1 = R^2 = H$, R^3 = 2-pyridyl	75%
$R^1 = CH_2Ph$, $R^2 = H$, $R^3 = Ph$	80%
$R^1 = H$, $R^2 = CH_3$, $R^3 = Ph$	54%

1.2.4 Miscellaneous Ring Fission

1.2.4.1 Fission Caused by Irradiation

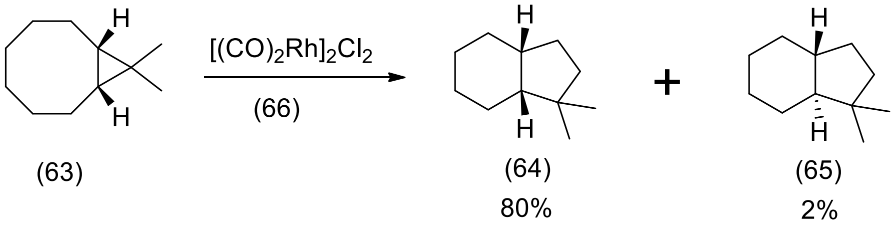
Upon irradiation, 2-cyclopropylcyclohexanone(58) gave a mixture of trans-(61) and cis-cyclonon-4-enones(62)as major products.[36] The proposed mechanism involves photochemically induced α-cleavage, followed by rearrangement of the resulting cyclopropylcarbinyl radical(59) and collapse of diradical(60).



More examples of cyclopropane ring isomerization to olefins have been published.[37,38,39]

1.2.4.2 Transition Metal Mediated Ring Fission

Transition metals promote the cleavage of cyclopropane derivatives. However, a reasonable and acceptable mechanism for such reactions is not clear because of uncertainty of the structures in the resulting products. Cyclopropane derivatives exhibit unusually low oxidation potentials which suggests the electron transfer may be involved in many of these reactions.[40] For example - heating(63) at 190 °C for 30 min in the presence of a catalytic amount of(66) gave a mixture consisting of 80% cis-dihydroindene(64) and 2% trans-dihydroindene(65).[41]



1.2.4.3 Free Radical Reactions of Cyclopropanes

Two competing pathways are possible for a radical ($X^{\bullet}$) reaction with a cyclopropane: (1) hydrogen abstraction or ring opening(Figure 1.4).[42] Generally, in case of extremely reactive radicals ($Cl^{\bullet}$, t-$BuO^{\bullet}$ and imidyl) hydrogen abstraction is observed[43,44] whereas ring opening is observed for less reactive radicals ($I^{\bullet}$, $Br^{\bullet}$).[45,46]

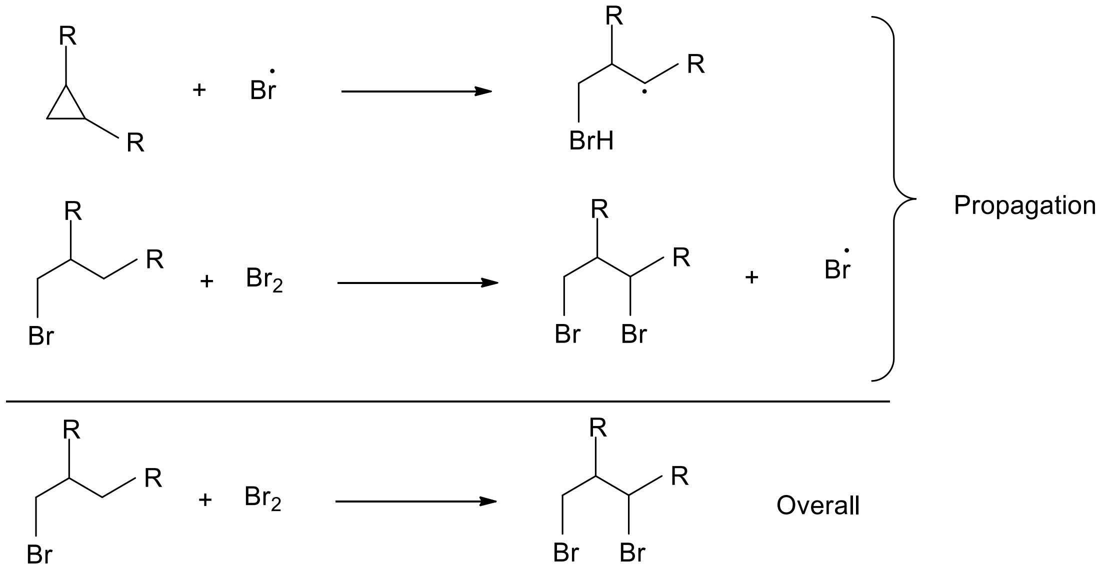
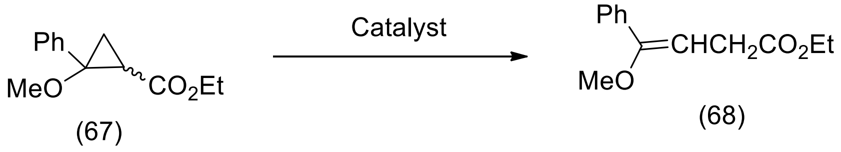


Figure 1.4: Pathways for a radical reaction with a cyclopropane.

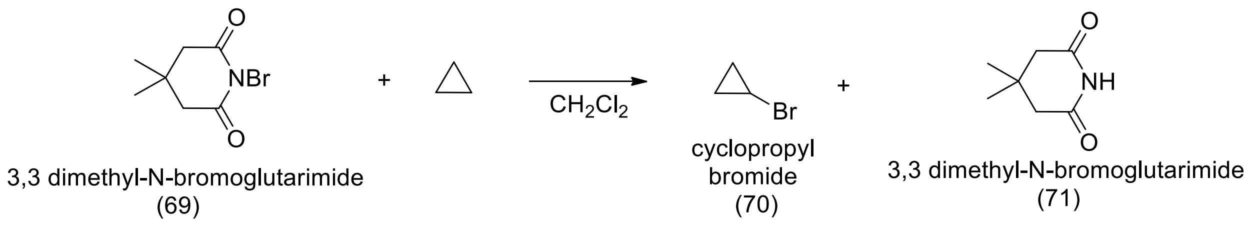
The products of the free radical bromination of alkylcyclopropanes arise from the formal 1,3-addition of Br_2. In a $S_H2$process, wherein $Br^{\bullet}$ attacks the least hindered carbon, to yield the most stable radical (Figure 1.5).[45]



catalyst	yield
$PtCl_2$.2PhCN	98
$[Rh(CO_2)Cl]_2$	98
Cu bronze	97

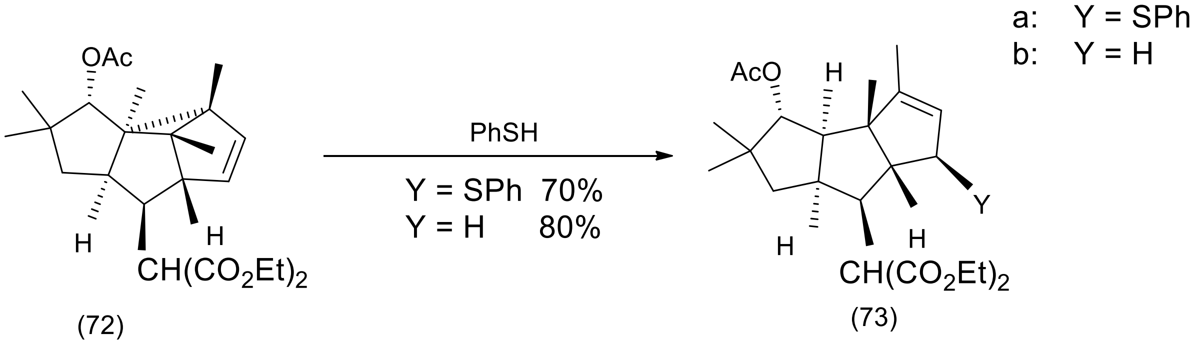
Figure 1.5: Free radical bromination of cyclopropane derivatives.

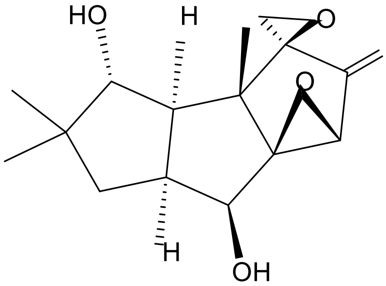
Cyclopropyl bromides can be prepared from cyclopropanes by the aid of imidyl radical chemistry. For example, the photoinitiated reaction of cyclopropane with 3,3-dimethyl-N-bromoglutarimide(69) produces cyclopropyl bromide(70) in an excellent yield. Imidyl radical rather than bromine atom is the chain-propagating species in this reaction.[44]



1.2.4.4 Rearrangement of the Cyclopropylcarbinyl Radical

By treating with 1 equiv of thiophenol at 100 °C, ring opening of tetracyclic acetate(72) was achieved. Addition of PhS$^{\bullet}$ to the double bond, followed by ring opening and trapping by PhSH produced 73a in 70% yield.[47] Reductive desulfurization produced 73b in 80% yield. 73b proved to be an important precursor to (±)-coriolin(74) and other oxygen-rich natural products.[47]





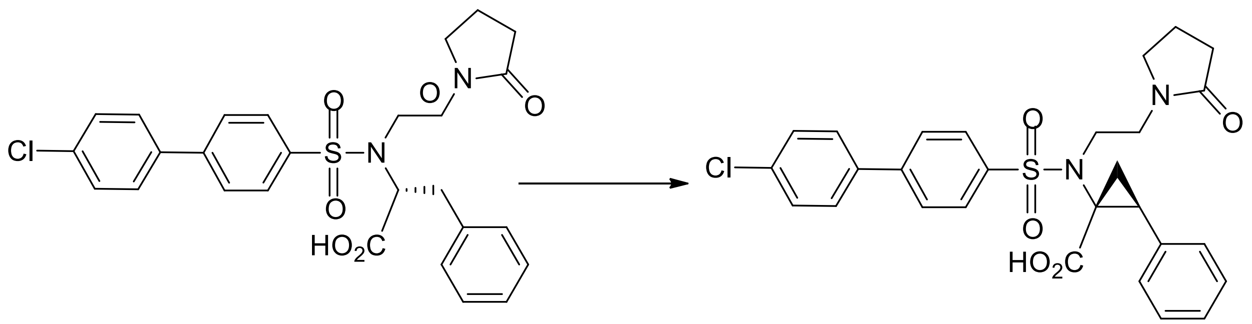
(±)-coriolin
(74)

1.2.5 Incorporation of Cyclopropane to Lock a Molecule in a Bioactive Conformation

Cyclopropane has the ability to lock a molecule in a bioactive conformation and thereby enhancing the potency. This utility of small cyclopropane group is often explored in medicinal chemistry for structure-activity relationship (SAR) studies.

Shiozaki reported the formation of compound 75 as a potent ADAMTS-5 (A disintegrin and metalloprotease with thrombospondin motifs) inhibitor, which saw an important increase in potency once acyclopropyl linker was introduced into the structure 76 (Scheme 1.1).[48]

The increase in activity was attributed with higher rigidity caused by the cyclopropane, which positions the pharmacophores in the optimal binding conformation.



(75) (76)

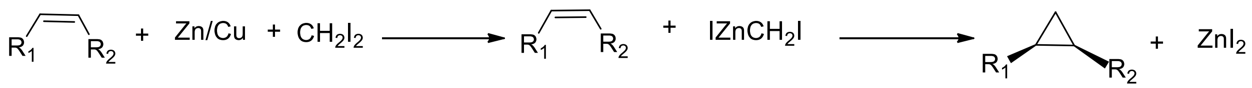
IC$_{50}$ (Agg-2) = 1.6 μM IC$_{50}$ (Agg-2) = 0.2 μM

Scheme 1.1: Insertion of a cyclopropane into a medicinally active molecule.[2,48]

1.3 Current Methods of Cyclopropane Preparation

1.3.1 Simmons-Smith Reaction

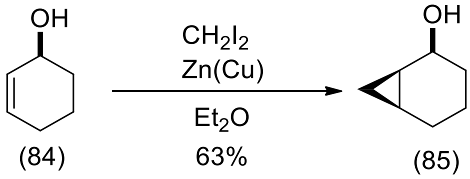
Over a long period of time, numerous methods for synthesizing cyclopropanes and their derivatives have been described.[49,50] In 1958, H. E. Simmons and R. D. Smith reported the formal cycloaddition of methylene and various olefins by treatment of diiodomethane with the zinc-copper couple Zn(Cu)[51,52] (Scheme 1.2). From the synthetic point of view, the Simmons-Smith cyclopropanation reaction is still one of the most often chosen strategies for the stereospecific formation of cyclopropanes because of two factors- (1) broad scope of olefins which can be employed as substrates and (2) the stereospecificity of the transformation.[52] Thereby, stereochemical information on the olefin can be transferred to the product.



(77) (78) (79) (80) (81) (82) (83)

Scheme 1.2: Simmons-Smith cyclopropanation.[53]

Diastereocontrol is an essential strategic feature which one has to consider in the planning of a synthesis. Diastereoselectivity is largely controlled by steric factors in olefin cyclopropanation. Additionally, when the substrate bears Lewis basic heteroatoms in proximity to the olefin a strong directing effect may be observed.[53,54,55,56,57] As a representative example, Scheme 1.3 is shown below, in which 2-cyclohexen-1-ol (84) is exposed to CH_2I_2 and Zn(Cu), providing 85 as a single diastereomer in 63% yield.



Scheme 1.3: Simmons-Smith cyclopropanation of 2-cyclohexen-1-ol.

Complicated preparation procedures of the zinc-copper couple and the reproducibility problems caused by variations in surface features of the alloy have led to the search of other protocols for generation of the zinc carbenoid.

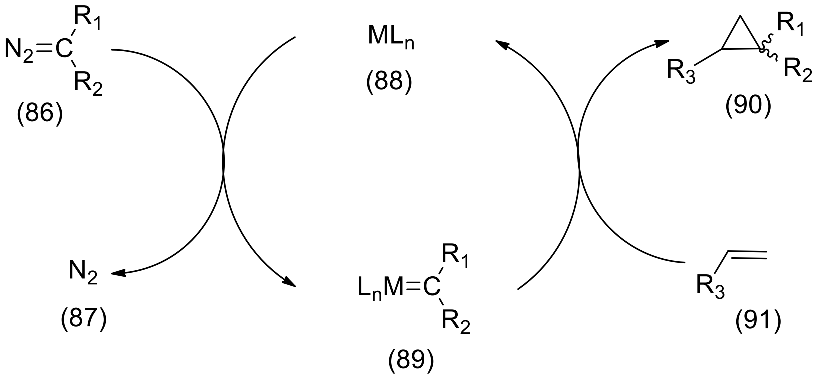
Furukawa et al.[57,58] developed a method for generation of the zinc carbenoid, in which diiodomethane is treated with $ZnEt_2$. This protocol has been widely adopted because it works over a wider range of temperatures and in a larger variety of solvents. The carbenoid species generated under Furukawa conditions shows higher activity with electron-rich olefins such as styrenes, enol ethers and enamines as well as for substrates containing Lewis basic directing groups.

The modifications by Furukawa et al.[58,59] have proven to be more effective due to the use of readily reactive organometallic reagents such as diethyl zinc, instead of metallic zinc and therefore allowing the zinc carbene generation step with diiodomethane to occur more efficiently.[53]

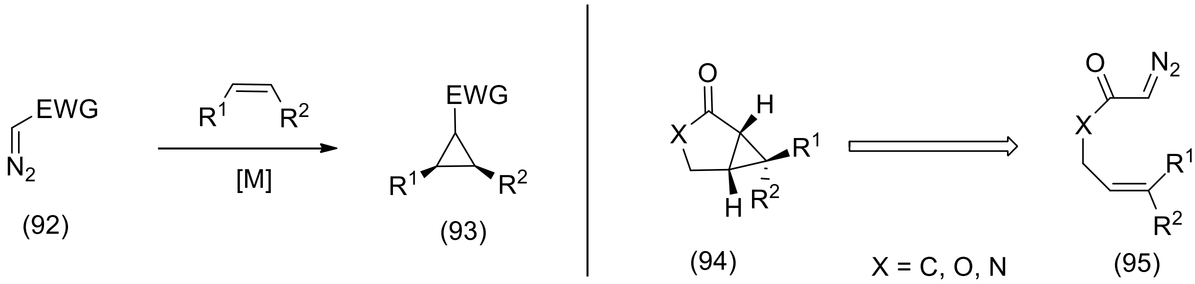
1.3.2 Diazo-Derived Carbenoids

Another method involves carbene transfer from aliphatic diazo compounds by using transition metals as catalysts such as ruthenium(Scheme 1.4).[55] By using copper and rhodium based catalysts, stereocontrolled and highly selective syntheses of functionalized cyclopropanes are achieved.[56]

Ruthenium complexes are also fascinating in this area and they became more attractive to researchers due to their ability to form a greater diversity of complexes created by a large number of oxidation states.[55]



Scheme 1.4: Catalytic cycle for carbenoid cyclopropane synthesis.[54]



Scheme 1.5: Diazo-derived carbenoids for cyclopropanation of olefins.

Before choosing a diazo-derived carbenoid pathway for a cyclopropanation reaction in the synthesis of complex molecules (Scheme 1.5), the following aspects are very important which must be taken into account:

(1) Alkyldiazo compounds are lacking of stabilizing groups and therefore are considered capricious.

Alkyldiazo compounds are typically generated in situ.[60,61,62,63,64,65]

(2) For an intermolecular cyclopropanation (such as 3 → 4) of the diazo compound to a mixture of the olefin,[66] a metal catalyst may be necessary to prevent carbene dimerization.

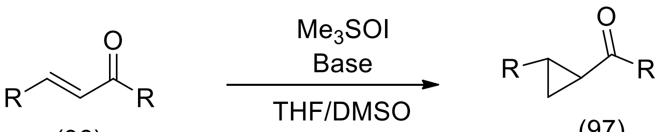
(3) Chemoselective discrimination between cyclopropanation and C–H insertion pathways can be an important issue. An elegant Study by Padwa, Doyle and co-workers[67] showed that chemoselectivity can be significantly influenced by the nature of the catalyst employed.

Intramolecular variant of this transformation (for example – Scheme 1.5, 95→94) has become a popular protocol in natural product synthesis, as two rings can be stereoselectively generated in a single step and highly substituted cyclopropanes can be accessed based on the olefin employed.[68,69,70,71,72,73]

1.3.3 Corey-Chaykovsky Cyclopropanation

Corey-Chaykovsky cyclopropanation(Scheme 1.6)[74] is a class of Michael-initiated ring closure reactions in which the reaction of a dimethylsulfoxoniummethylide (Corey‟s reagent) with α,β-unsaturated ketones gives cyclopropyl ketones[75] or with α,β-unsaturatednitriles gives the corresponding cyclopropylnitriles[76] in excellent yields.

Since the discovery of dimethylsulfoxoniummethylide, or “the Corey ylide” in1962, the latter has been found very useful in the synthesis of a wide variety of functional groups.[77] These include cyclopropanes, epoxides, and aziridines, and is one of the most straightforward and often cited cyclopropanation reactions.[75]

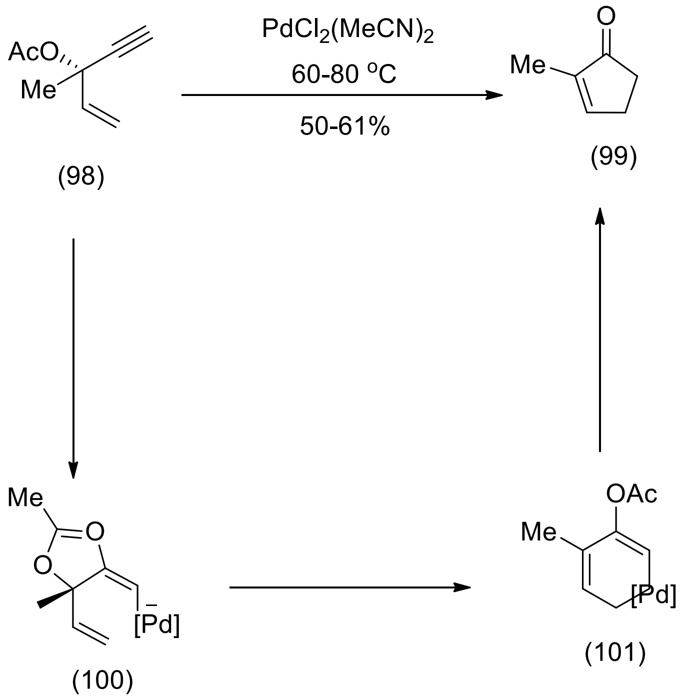


(96) (97)

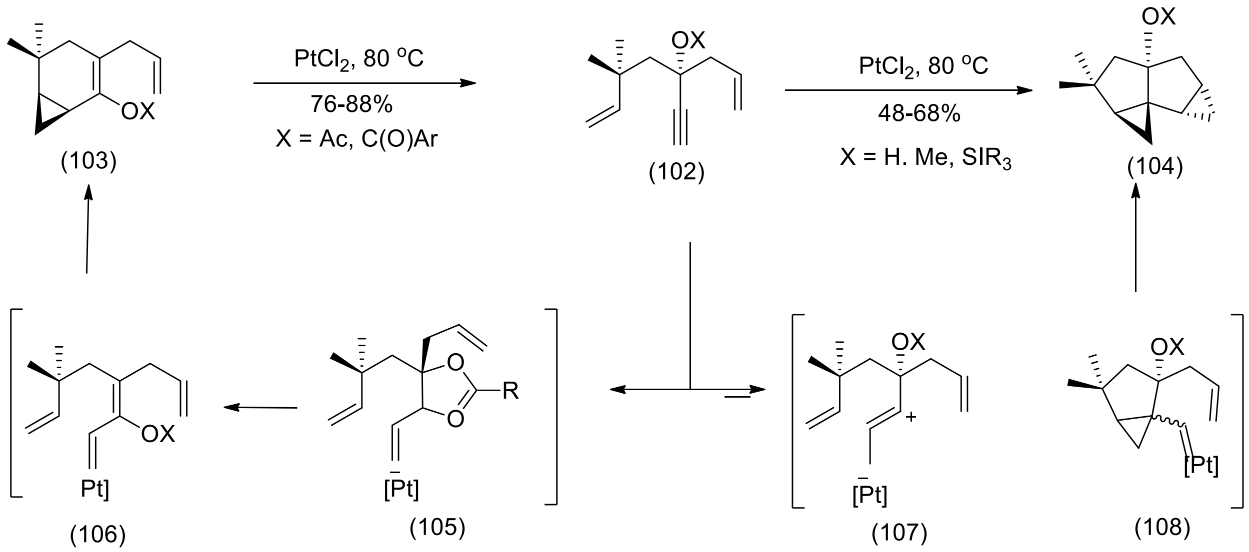
Scheme 1.6: General conditions for the Corey-Chaykovsky cyclopropanation.[74]

1.3.4 Cycloisomerization

Rautenstrauch developed a novel approach for the synthesis of cyclopentenones which is known as the Rautenstrauch rearrangement.[78] When enyne(98) was treated in presence of Pd(II) catalyst, cyclopentenone(99) was isolated in 50−61% yield. According to the mechanism proposed by Rautenstrauch, alkyne undergoes acetoxypalladation to give intermediate(100). On Subsequent displacement of the acetoxonium by the vinylpalladium species a palladacycle(101) has been formed which undergo reductive elimination and hydrolyze to form(99).

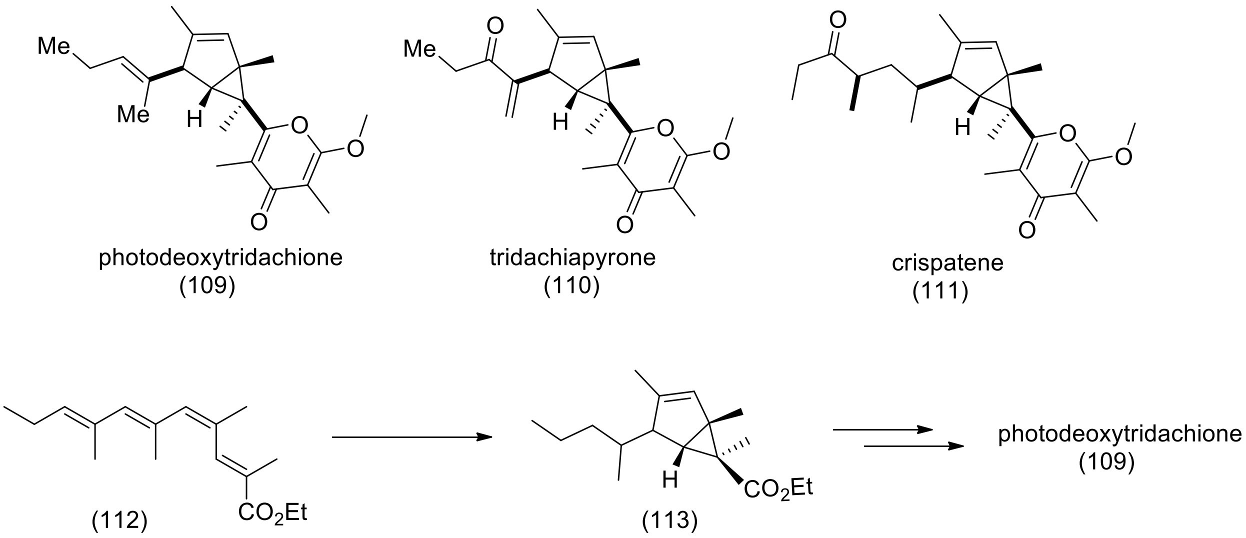


A pivotal invention was made by Fensterbank, Malacria and co-workers[79,80] when dienyne(102) was exposed to $PtCl_2$ at elevated temperatures (Scheme 1.7).



Scheme 1.7: Pt-catalyzed cycloisomerization of enynes and effect of oxygen substitution.

Inspired by these discoveries, Toste and coworkers[81,82] reported a notable gold(I) catalyzed Rautenstrauch rearrangement in which cyclopentenones generated in high yields from propargylic pivalates. In addition, Fürstner and co-workers[83] also contributed a versatile gold- and platinum catalyzed method for the synthesis of cyclopropane-substituted cyclopentanones from propargylic acetates. Inspired by biosynthetic considerations, Trauner and Miller and co-workers in 2003, reported a different cycloisomerization reaction which is conceptually distinct from previous work (Scheme 1.8).[84,85,86]

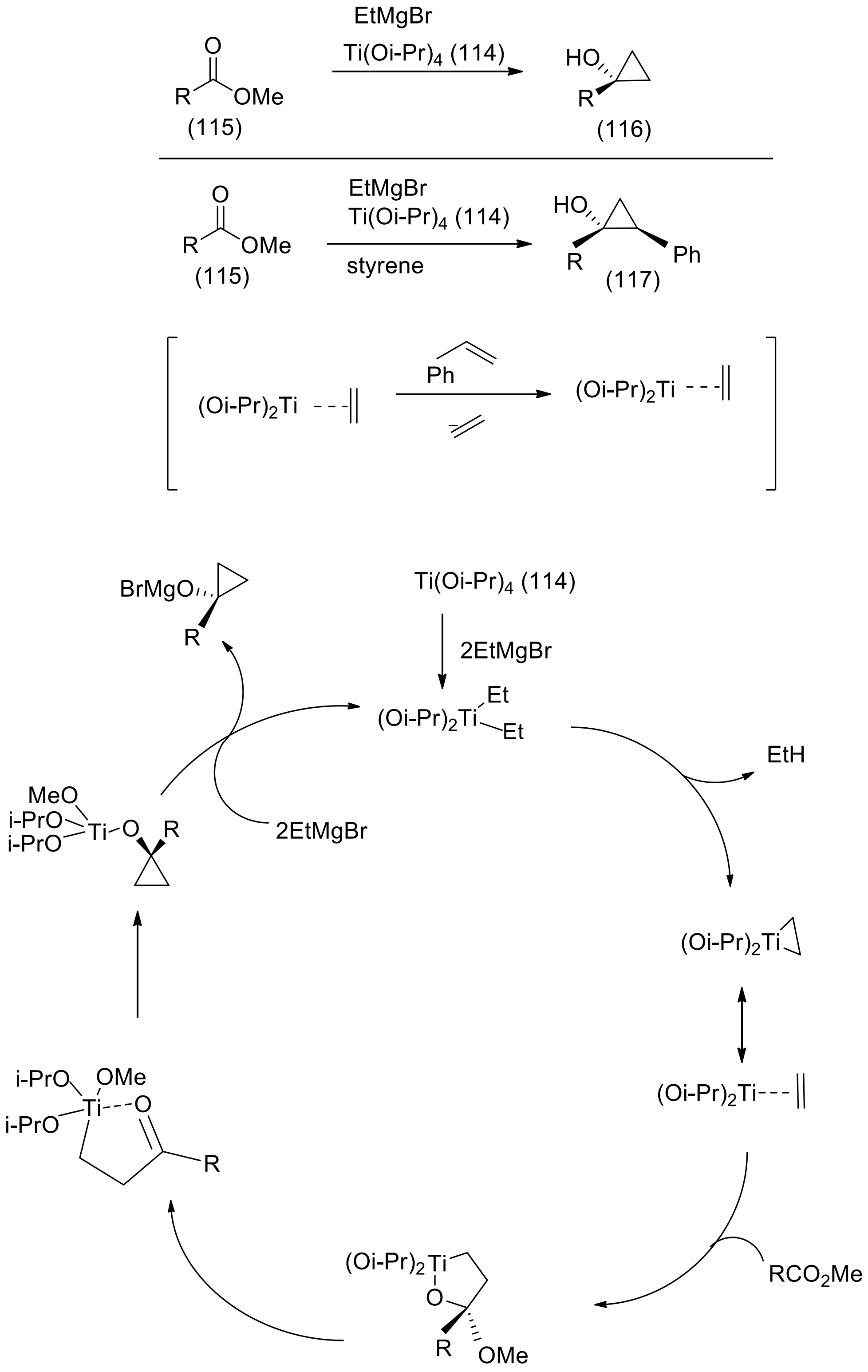


Scheme 1.8: Polypropionate natural products and Lewis acid-catalyzed cycloisomerization.

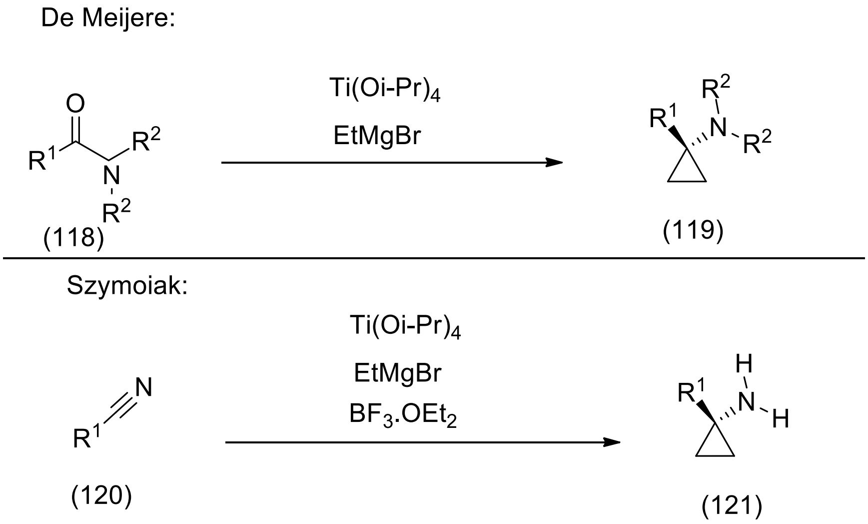
1.3.5 Kulinkovich Reaction

Kulinkovich et al.[87,88] published one of the most exciting reaction in modern organotitanium chemistry. In this reaction, treatment of aliphatic esters with ethylmagnesium bromide in the presence of Ti(OiPr)$_4$(114) generated 1-alkylcyclopropanolssuch as 116 (Scheme 1.9).[87,88,89] Kulinkovich and co-workers[90] also investigated the mechanism of this unusual cyclopropanation by taking the aid of deuterium labeling. Computational study by Wu and Yu,[91] concluded that the reaction proceeds through a titanacyclopropane, or Ti(II) olefin, intermediate.[92] This is important to note that exchange of ethylene with substituted olefins was possible which enables the generation of more substituted cyclopropanols (cf. 115→ 117).[93]

Chaplinski andde Meijere[94] and Bertus and Szymoniak,[95] contributed in two later modifications in which amides and nitriles serve as starting materials, culminating in the generation of aminocyclopropanes (Scheme 1.10).



Scheme 1.9: Kulinkovich reaction.



Scheme 1.10: Modification of Kulinkovich reaction.

1.3.6 Nucleophilic Displacement Reactions

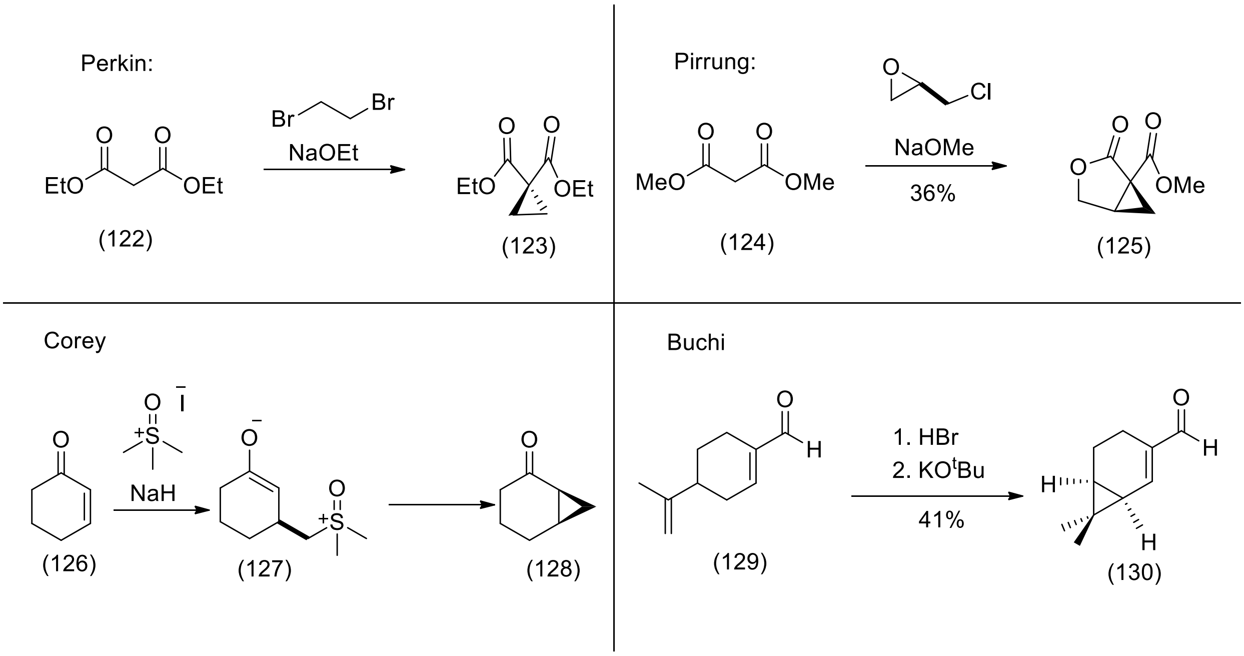
Cyclopropanation of diethyl malonate with 1,2-dibromoethylene in the presence of NaOEt (Scheme 1.11) was reported by W. H. Perkin[96] in 1884. Numerous studies established that stabilized carbanions undergo analogous double alkylation to furnish cyclopropanes.[97,98.99]

Pirrung et al.[100] prepared cyclopropanated γ-lactones from the reaction of malonates with epichlorohydrin and a base.

Corey and Chaykovsky[101,102] discovered that from the reaction of enones and dimethylsulfoxoniummethylide, cyclopropanes are formed. The process is known as the Corey−Chaykovsky reaction.

Buchi et al. in 1966[103] synthesized cyclopropane containing natural products which became a remarkable landmark in organic synthesis. During the total synthesis of aromadendrene, aldehyde 129 undergo addition of HBr followed by subsequent exposure of the crude bromide to KO^{t}Bu which formed cyclopropane 130 in 41% overall yield.

Notable advantages of this method are the high stereospecificity and broad substrate scope.



Scheme 1.11: Nucleophilic cyclopropanations.

1.4 Different Types of Transition Metal Catalysts for Cyclopropanation Reaction

Transition metal-catalyzed cyclopropanation of olefins via carbene transfer with diazo reagents represents one of the most impactful approaches to the stereoselective preparation of chiral cyclopropane derivatives.[104] Copper, rhodium and more recently, ruthenium and cobalt based catalysts showed high stereocontrol and efficacy in constructing the cyclopropane ring structure.[104] Fewer reports have been published on catalysts based on gold,[105] iron,[106] iridium[107] and osmium[108].

The properties of the transition metals made the differences in the catalytic effects and the scope of applications. For example, because of the air and moisture stability of Au catalysts, a range of precursors can effectively carry on the cyclopropanation reaction using Au catalysts. On the other hand, some of the Rh-catalyzed cyclopropanation reactions involve a C–H activation process.[109]

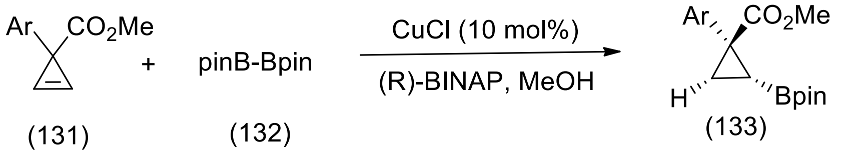
Both Cu[110] and Zn[111] salts are inexpensive compared to the noble metals and zinc is even less toxic. In recent times, some new organozinc reagents were reported that efficiently cyclopropanate some traditionally unreactive alkenes and thereby expand the substrate scope of alkene substrates for olefin cyclopropanation.

1.4.1 Copper-Based Catalysts

Copper is inexpensive with respect to noble metals. In most cases Cu-mediated cyclopropanation can be done under mild reaction conditions with good functional group tolerance and excellent chemical selectivity.

Noyori and coworkers in 1966 first introduced asymmetric cyclopropanation with the use of a copper complex of a chiral salen ligand as the catalyst.[112] This is also the first example of enantioselective reaction in a homogenous phase that was catalyzed by a transition metal.

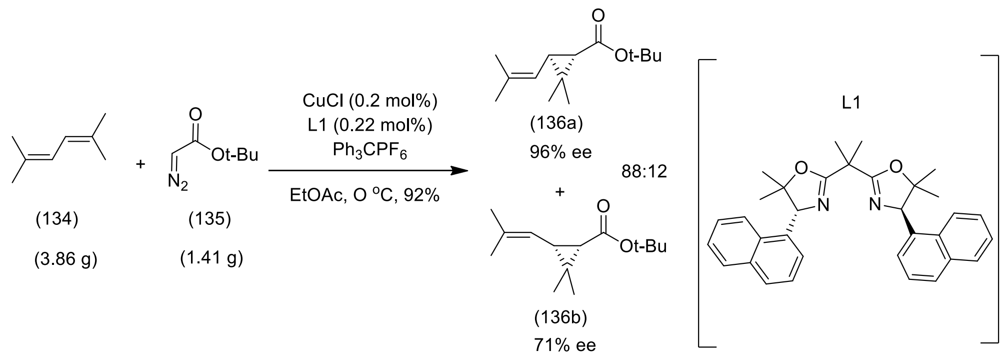
In 2014, Lin et al.[113] developed a Cu(I)-catalyzed enantio-selective hydroboration of 3,3-substituted cyclopropenes(131) which gave optically active trans-cyclopropylboronates(133) with excellent enantio-selectivities, superior to the previous reports. Here it is worth mentioning that when the Rh-based catalystwas used, cis-borylated cyclopropanes were obtained (Scheme 1.12).



12 examples
upto 88%, 95% ee

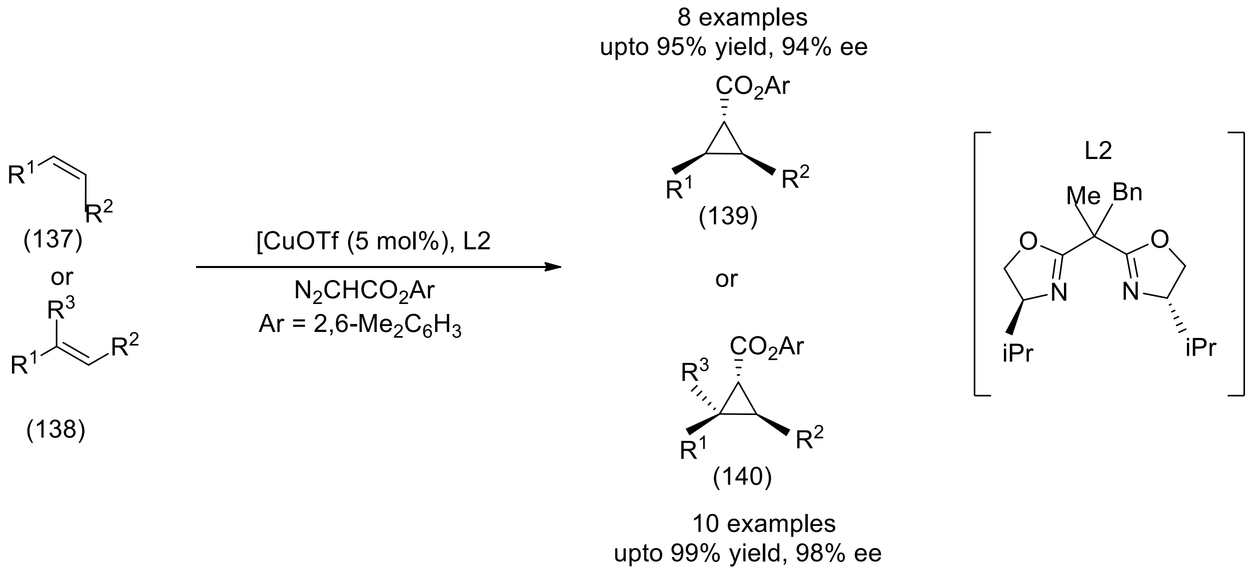
Scheme 1.12: Cu-Catalyzed enantio-selective synthesis of cyclopropylboronates.

Copper-catalyzed diazo decomposition led to the asymmetric cyclopropanation of 2,5-dimethyl-2,4-hexadiene and produces chrysanthemic acid t-butyl ester (136a and 136b) in good yield and high enantioselectivities.[114] Chrysanthemic acid t-butyl ester is a key intermediate to pyrethroid insecticides.



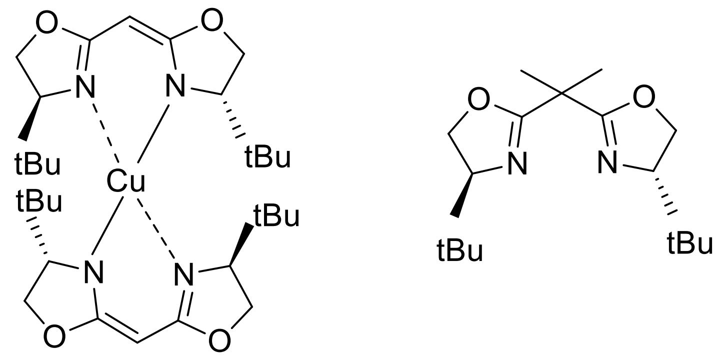
Scheme 1.13: Copper catalyzed Cyclopropanation of 2,5-dimethyl-2,4-hexadiene.

By using BOX/Cu(I) as the catalyst, Tang and coworkers achieved the cyclopropanation of both cis- and trans-1,2-disubstitutedalkenes 137 and 138, respectively, with high diastereo- and enantio-selectivity. The pendant group of bidentate bisoxazoline (BOX ligands) was assumed to have a positive effect on the yield (Scheme 1.14).



Scheme 1.14: Asymmetric cyclopropanation of Z- or E-alkenes.

For copper-catalyzed cyclopropanation, bidentate bisoxazoline (Box) ligands have most extensively been studied among all other chiral ligands developed so far. Progress in ligand modification has been carry forwarded to chiral semicorrin C1[115] and bisoxazoline ligands L3[116] (Figure 1.6). Different classes of chiral bisoxazolines bearing different geometries and electronic properties of the bridging atoms have been reported (Figure 1.7).[117,118,119,120,121,122,123,104]



C1

L3

Figure 1.6: Chiral copper semicorrin complex and chiral bisoxazoline ligand.

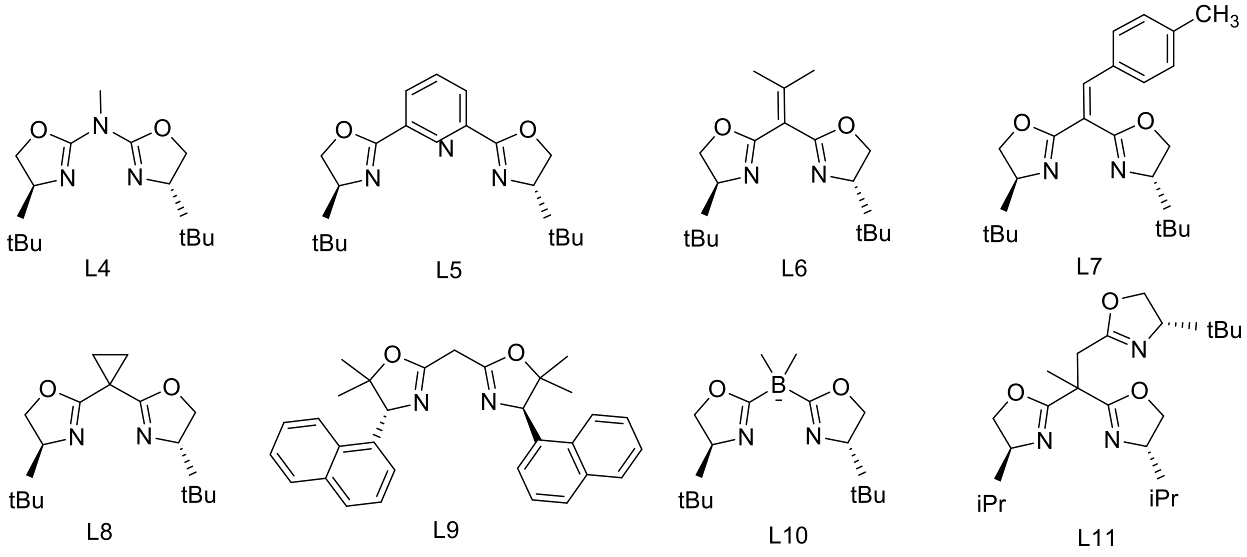


Figure 1.7: Different chiral bisoxazoline ligands.[104]

Apart from bisoxazolines (BOX), other ligands such as C_2-symmetric bipyridine-derived ligand L12,[124]**,** C_1-symmetric bispidine ligand L13,[125] chiral binaphthyldiimine L14,[126] amino alcohol L15,[127] and L16[128] were also investigated and employed in the asymmetric cyclopropanation reactions of a series of alkenes with diazoesters (Figure 1.8).

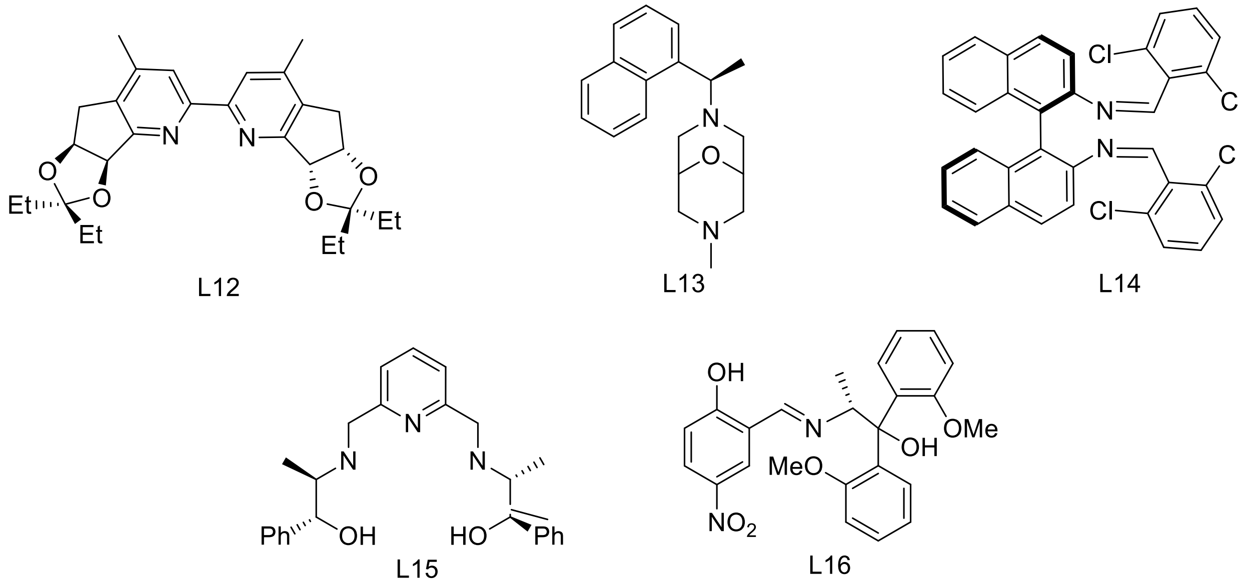
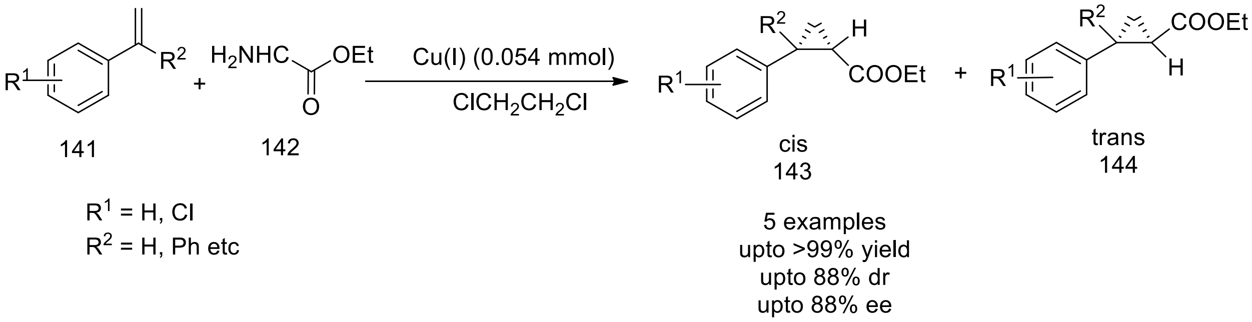


Figure 1.8: Other chiral chelating ligands of copper catalyst.[104]

Homogeneous catalysis has some inbuilt problems if compared to its heterogeneous counterpart, such as recyclability and difficulty of separation. Caselli and coworkers[129] have introduced acyclopropanation reaction using a new heterogenized catalytic system based on a chiral Cu(I) complex, and carbon dioxide (CO_2) as a vector(Scheme 1.15). In this newly developed heterogenized system, the catalysts were found to be stable, robust, and easily recyclable. So it should find its accountability in terms of synthetic value in cyclopropane construction.[130]



Scheme 1.15: Continuous flow asymmetric cyclopropanation reactions using Cu(I) catalyst and CO_2 as a vector.

1.4.2 Rhodium-Based Catalysts

Rhodium complexes are popular for their ability to activate C–H bonds. However, they also show efficient catalytic ability towards cyclopropanation reactions. Due to the particular atomic structure of rhodium, Rh-carbenoids are more vulnerable to steric interference compared to the corresponding Au-carbenoids, which makes the chiral Rh catalysts to show high regio-, diastereo-, and enantio-control in the cyclopropanation process. Noticeably, some Rh-catalyzed cyclopropanations are initiated by C–H activation. Under the action of Rh-based catalytic systems for cyclopropanation reactions, diazo compounds have been widely used to generate carbene intermediates.

Rhodium complexes are also a well-known family of catalysts for enantioselective cyclopropanation. The dirhodium(II) complexes have already established to be effective catalytic systems for enantioselective cyclopropanation. Because of the electrophilic nature of Rh-bound carbenes, Rh-catalyzed cyclopropanation reactions generally take place in electron rich and electron neutral alkenes rather than electron deficient alkenes.

It is important to mention that after the development of dirhodium(II) carboxamidate and carboxylate catalysts, highly stereoselective reactions with α-diazocarbonyl compounds have been achieved via a variety of reaction modes. Doyle et al. in 1991 first reported Rh_2(5S-MEPY)$_4$ (C2, Figure 1.9), which showed unique advantages for enantioselective intramolecular cyclopropanation with allylic diazoacetates (up to 98% ee)[131] and homo allylicdiazoacetates 145(up to 90% ee) (eq. 1, Figure 1.9).[131b]

During intermolecular cyclopropanation, the dirhodium complexes of the azetidinone-based ligand Rh_2[(S,R)-MenthAZ]$_4$ (C5, Figure 1.9) was effective in catalyzing cyclopropanation of terminal olefins using vinyldiazolactone147(eq. 2, Figure 1.9).[104,132]

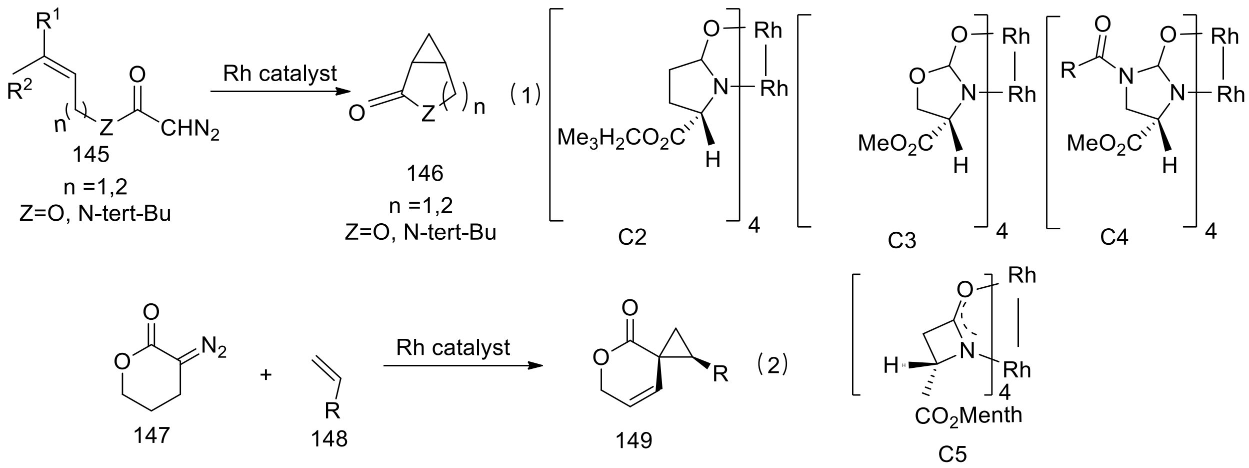


Figure 1.9: Different chiral dirhodium(II) carboxamidates.

McKervey and coworkers first reported ligand derived from *N*-arylsulfonylproline for cyclopropanation of α-diazoketones.[133] Later, Davies et al. reported one of its derivatives, Rh_2(SDOSP) (C6, Figure 1.10) for cyclopropanation of olefins with vinyldiazomethanes.[134] They further demonstrated that the catalyst C6 was particularly suitable for the cyclopropanation reactions with donor/acceptor substituted diazoesters. High enantioselectivity was consistently noticed with a range of diazo reagents with aryl or vinyl functionality as the electron-donating group.[135]

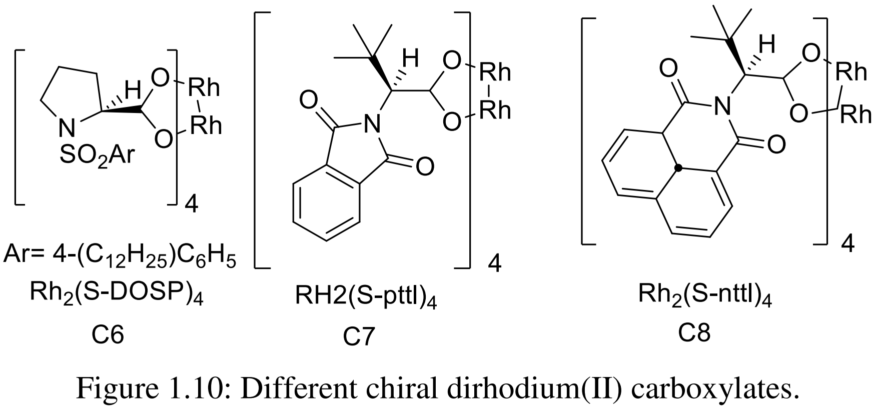
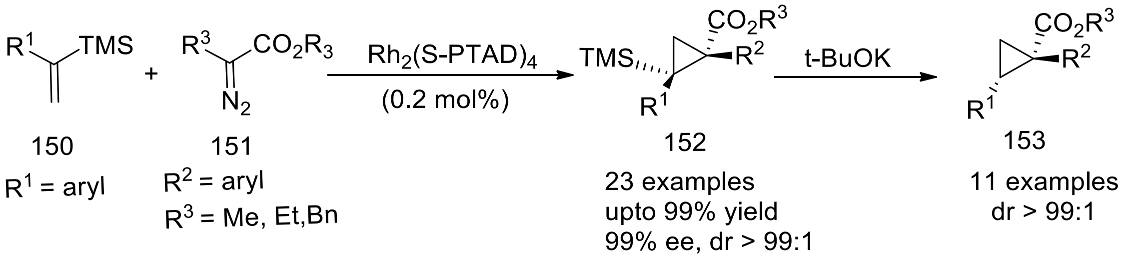


Figure 1.10: Different chiral dirhodium(II) carboxylates.

Shortly, Rovis and coworkers[109b] developed the first Rh(III)-catalyzed cyclopropanation via C–H activation (Scheme 1.16). Most importantly, the newly designed monosubstituted isopropylcyclopentadienyl ligand considerably improved the yield and diastereoselectivity. This is also a rare example of carbocycle synthesis via Rh(III) catalysis.

Rh-catalyzed asymmetric cyclopropanations between styrenes and aryl diazoacetates are mostly trans-selective. In 2016, Gu et al.[136] prepared an unique optically active cis-cyclopropane carboxylates 153 using Rh-catalyzed cyclopropanation followed by desilylation (Scheme 1.16), in which the inversion in configuration was found. This synthetic strategy is useful for the synthesis of chiral (Z)-1,2-diarylcyclopropane carboxylates, which are typically hard to obtain using traditional methods.



Scheme 1.16: Preparation of optically active cis-cyclopropane carboxylates.

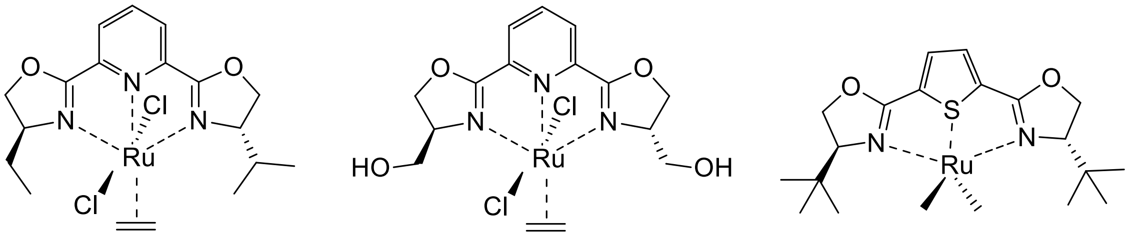
Monomeric rhodium complexes are rare for catalytic asymmetric cyclopropanation. Bergman et al. employed monomeric rhodium(II)-catalyzed asymmetric cyclopropanation with EDA using bisoxazoline as ligand[137] which falls under a rare example of monomeric rhodium complexes.

In recent times, a new chiral diene ligand for rhodium(I)-catalyzed asymmetric cyclopropanation was reported which is the first successful catalytic system to solve the reactivity and selectivity issue of metal malonate carbene.[138]

1.4.3 Ruthenium-Based Catalysts

Compared to rhodium, the attention given to ruthenium arose from two major driving forces - (1) the price of ruthenium is approximately one tenth of the price of rhodium, and (2) ruthenium complexes have the potential for greater diversity because of larger number of oxidation states and the superior coordination chemistry which ruthenium can offer than those available to rhodium.

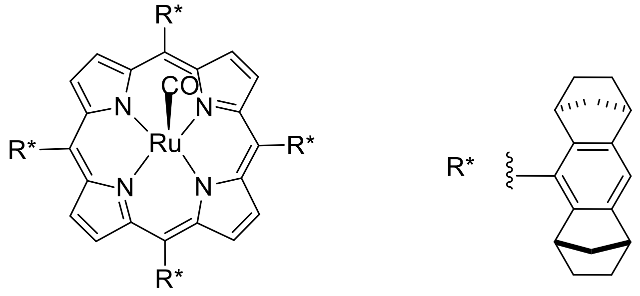
Nishiyama et al.[139] first developed the chiral Ru(pybox) catalyst C9(Figure 1.11) which become one of the most promising catalysts for the cyclopropanation of alkenes with diazoacetates, affording corresponding cyclopropanes in high diastereoselectivities and excellent enantioselectivities (up to 99% ee). Water soluble catalyst C10(Figure 1.11)[140] and ruthenium-thiobox catalysts such as C11(Figure 1.11)[141] can also be highlighted as a representative examples of further derivatization of the pybox ligand.[104]



C9 C10 C11

Figure 1.11: Chiral ruthenium bis(oxazoline)pyridines complex.

Both Berkessel's group and Che's group reported ruthenium porphyrin complex 154(Figure 1.12) which was successfully employed to catalyze cyclopropanation.[142] Ruthenium porphyrin complexes brought the attention of researchers due to the high catalyst turnovers (~ 1.1*10^4) and high stereoselectivities for cyclopropanation of styrene derivatives with EDA. Simonneaux and coworkers employed the same ruthenium porphyrin complexes for group and atom-transfer reactions toward the synthesis of trifluoromethylphenyl cyclopropanes[143] and cyclopropylphosphonates.[144]



154

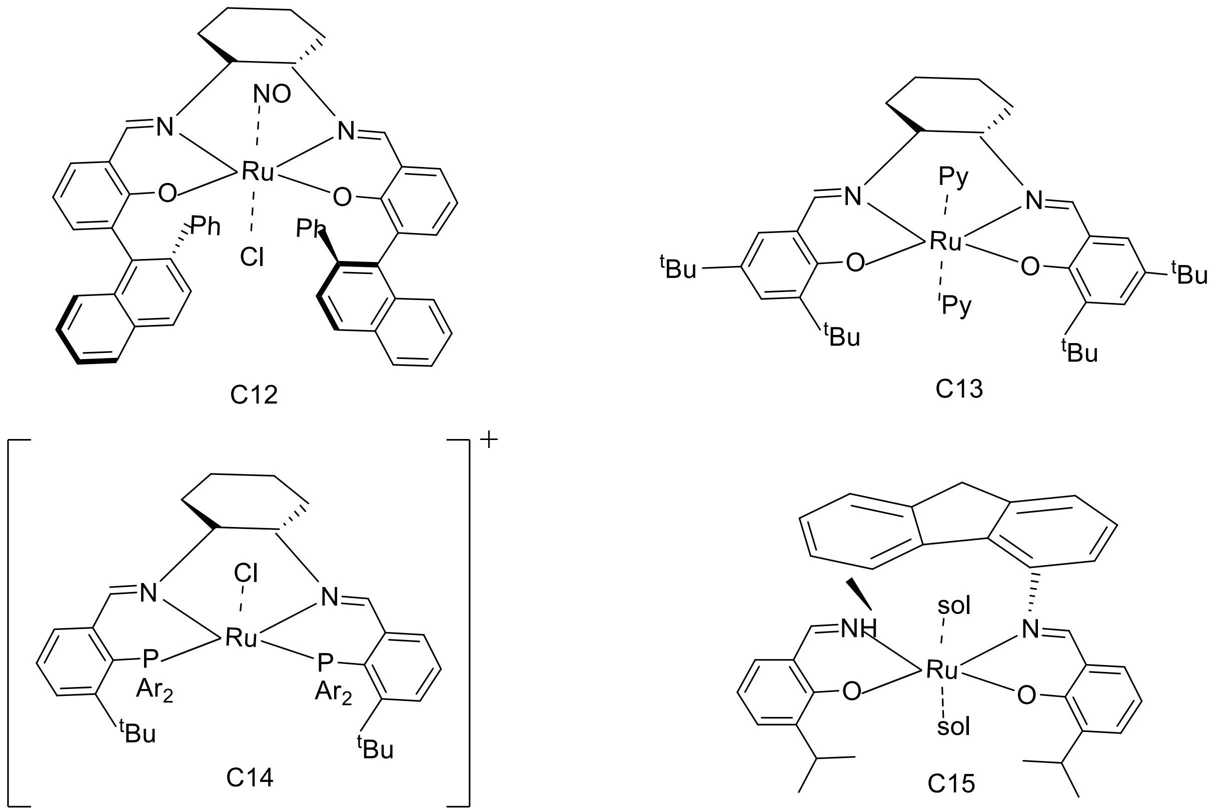
Figure 1.12: Chiral ruthenium porphyrin.[104]

Following the success of ruthenium salen for catalytic epoxidation, it's use was extended to cyclopropanation. According to the study of Katsuki et al., a high enantio-and cis-selective cyclopropanation can be achieved by the salen complex based catalytic system C12(Figure 1.13).[145]

However, even under irradiation conditions, the reaction gives low product yields. Afterward, Nguyen and coworkers developed the ruthenium salen complexes containing trans-coordinatedpyridine ligands such as C13 (Figure 1.13). These complexes are very efficient catalysts for the asymmetric cyclopropanation of both electron-rich and electron-deficient terminal olefins with EDA. Additionally, they afford high reaction yield and predominantly trans-products with outstandingly high enantioselectivities.[146]

In 2001, Mezzetti et al. introduced the first Ru-based catalytic systems, [RuCl(P-NNP)]+ (C14a) [a five-coordinate ruthenium complexes] having diphosphinodiimino ligand which gave high cis-selectivity (Figure 1.13).[147]

Scott and coworkers reported another ruthenium complex with a biaryldiimine ligand (C15) (Figure 1.13) to afford excellent diastereoselectivity and enantioselectivity in cyclopropanation.[148]



C14a: Ar = C_6H_5
C14b: Ar = p-CF_3-C_6H_4

Figure 1.13: Chiral ruthenium salen and other Schiff-base complexes.[104]

1.4.4 Cobalt-Based Catalysts

Cobalt complexes are one of the most fascinating solutions in catalysis due to their large abundance and the unique reactivity. In 1978, chiral (dioxamato)Co(II) catalysts derived from camphor have been applied for the cyclopropanation of different olefins.[149] The catalysts showed moderate to high reactivity and selectivity. Since then, researchers systematically studied more and more cobalt complexes in the following years. The Co(II) salen catalytic system is attractive due to its high enantioselectivity. However, another property which makes them more interesting is their high cis-selectivity and great chemical yield, which cannot be obtained by the use of ruthenium (NO) salen.

Katsuki et al. studied both Co(III) salenC17 and Co(II) salenC18(Figure 1.14) for intermolecular cyclopropanation.[150] Both systems afforded excellent enantioselectivities. Co(III) salenC16 favored a trans selectivity whereas Co(II) salenC17 favored a cis-selectivity.[104]

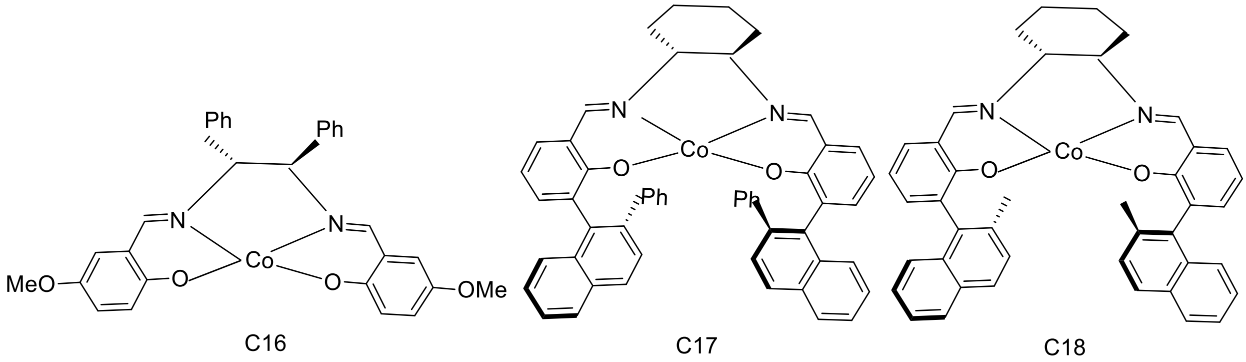


Figure 1.14: Chiral cobalt salen complexes.[104]

Zhang and coworkers prepared a number of Co(II) porphyrin complexes which were very efficient catalysts for diastereo- and enantioselective cyclopropanation reactions. The application of these catalysts are not only limited to simple styrene derivatives, the latter also successfully cyclopropanate various challenging substrates such as electron deficient olefins with EDA or *t*BDA.[151] Moreover, activating the relative stable acceptor/acceptor diazo reagents (for example- α-nitro-diazoacetates[152] and α-cyanodiazoacetates[153]) could be accomplished by Co(II) porphyrin system for carbene transfer cyclopropanation.

1.5 Catalytic Mechanisms

The mechanism of the cyclopropanation of olefin via diazo reagent decomposition is considered to involve carbene formation followed by the interaction of the olefin to produce the cyclopropanes and its derivatives. Common accepted mechanisms for cyclopropanation from transition metal catalyzed carbene transfer reactions are mainly of three types: 1. concerted asynchronous mechanism; 2. coordination mechanism and 3. stepwise radical addition mechanism.[104] Based on the characteristic features of different transition metals, their mechanisms are dissimilar because their demands for diazo and olefins in terms of steric and electronic nature are dissimilar, too.

1.5.1 Concerted Asynchronous Mechanism

According to this mechanism, extremely reactive metal carbene intermediate I1 has formed from interaction of the diazo compound and the catalyst with parallel extrusion of nitrogen, followed by the attack from alkene (I2, Figure 1.15)in a side-on approach. Cyclopropane product formed via a concerted mechanism from the interaction between carbene with one of the carbon atoms from the C=C bond followed by the final ring closure. Copper[154], rhodium[134,155] and ruthenium[156] based metal complexes those carbene complexes are very electrophilic and falls under Fisher-type carbene usually follow this mechanism.

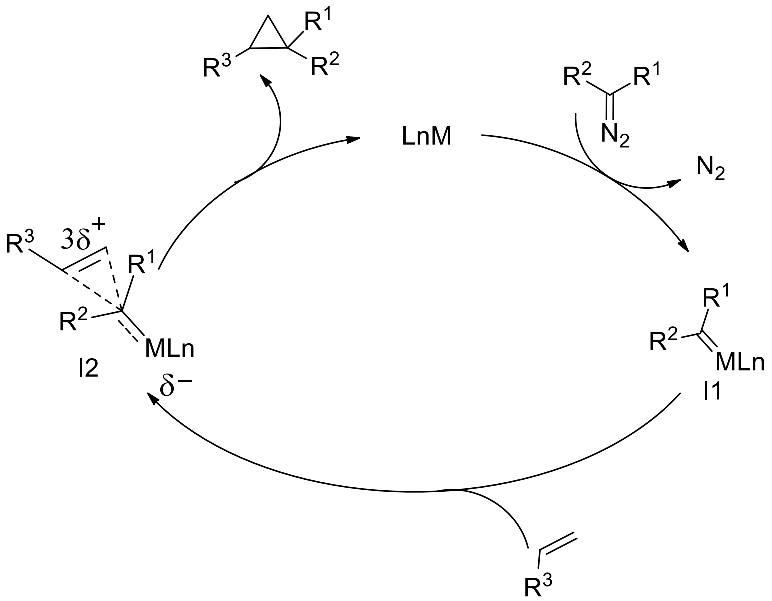


Figure 1.15: Concerted asynchronous mechanism.

1.5.2 The Coordination Mechanism

The coordination mechanism (Figure 1.16) and the concerted mechanism are complementary to each other. But the real scenario of coordination mechanism is still not clear.[157] It is believed that complexes may rearrange to metallacyclobutane (I4, Figure 1.16) via the simultaneous coordination of carbene and alkene at the metal center (I3, Figure 1.16). Thus, reductive elimination of the metal fragment generated the desired cyclopropanes.

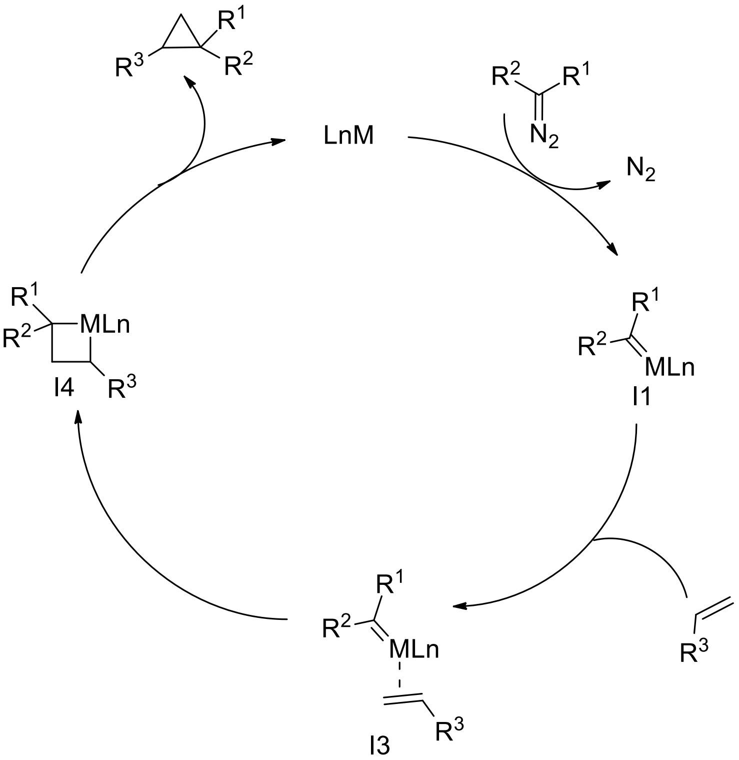


Figure 1.16: The coordination mechanism.

1.5.3 Stepwise Radical Addition Mechanism

This mechanism (Figure 1.17) was only postulated for cobalt carbene complexes which involve metalloradical carbene I5 formation.[158] Metalloradical carbene specie is best described as a one-electron-reduced Fischer-type carbene,[159] followed by the radical addition to alkenes, form a new carbene based free carbon radical I6, the final step of ring closure generate the desired cyclopropane product.

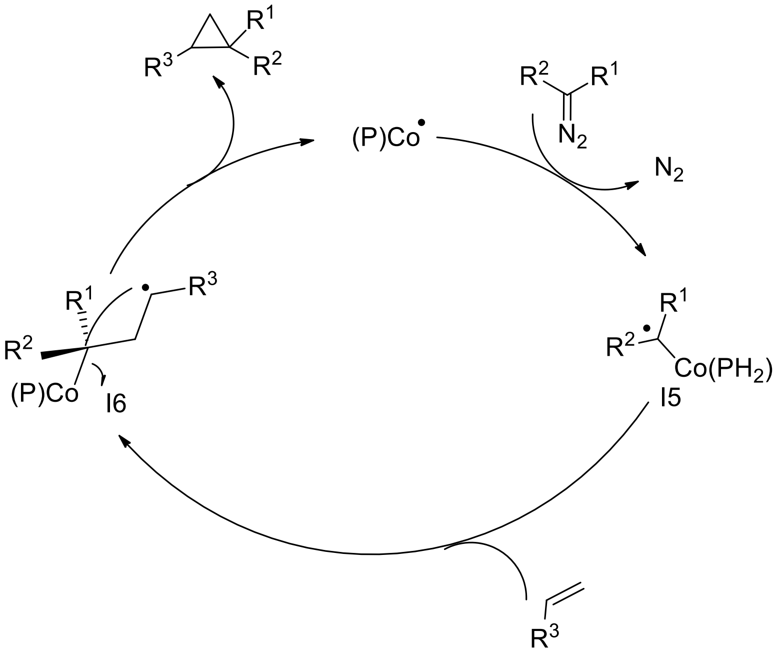


Figure 1.17: Stepwise radical addition mechanism.

Chapter 2

Project Description

Catalysis is central to modern chemical industry and about 90% of the currently applied industrial processes employ some form of catalyst. Most of the reported catalysts, both homogeneous and heterogeneous, are based on noble metals. However, apart from the economic reasons to replace them, concern is raising about the limited amount of these metals that is available on the Earth crust and the serious risk that mankind may run out of them in a few decades. An increasing attention has thus been devoted in recent years to the development of catalysts based on much more abundant first row elements. Among these, cobalt and especially iron have attracted the largest interest. However, it should be remembered that these two metals were deeply investigated in the first part of the 20th century and they were replaced by their second and third transition series congeners because the latter displayed such a better activity/selectivity performance to make their much higher price a less important point. Examples of large-scale processes that followed this process are methanol carbonylation to acetic acid, initially run with cobalt (BASF process), then with rhodium (Monsanto process) and now with iridium (BP Cativa process), and propylene hydroformylation (initially cobalt and now almost exclusively rhodium). It is clear that simply going back to a surpassed chemistry cannot be the solution and new ways have to be found to make first-row transition metals as active and as selective as their heavier counterparts or at least to approach the performance of the latter.

Whereas the use of non-innocent ligands is gaining interest in the field of homogeneous catalysis as a way of "nobilitating" first-row transition metals, an approach that is gaining an increasing attention in the field of heterogeneous catalysts is the thermolysis of preformed metal complexes.[160] Such an approach was originally developed to increase the activity of graphite electrodes in electrochemical processes, especially oxygen reduction, (by pyrolysing in an inert atmosphere metal complexes with nitrogen ligands adsorbed on graphite electrodes).[161] The aim was to make them more competitive with platinum electrodes reducing the overpotentials typical of graphite. The pyrolysis approach has been recently revamped by the group of Beller at the Likat in Rostock (Germany).[162,163,164,165,166,167,168,169,170,171,172,173,174,175] Beller and coworkers prepared several previously known complexes, mostly based on cobalt or iron, , but nickel was also investigated,[176] with heterocyclic nitrogen ligands, most often phenanthroline. The so obtained complexes were adsorbed on activated carbon powder or other inorganic supports (alumina, ceria, silica) and the resulting solids were pyrolyzed in an argon atmosphere at temperatures ranging from 400 to 1000 °C. Under these conditions, the complexes decompose and generate core shell metal or metal oxide nanoparticles, covered by nitrogen-enriched graphitic layers. The latter still enclose part of the metal, which remains coordinated to some nitrogen atoms, though the original ligand is no longer present as a clearly identifiable molecule, but is fused in the graphitic layer. If the thermolysis temperature is too low to fully decompose the ligand (e.g. below 350 °C) the obtained material has no catalytic activity, but if graphitization has occurred, the obtained materials display catalytic activities that are not observable either with the starting complex or with heterogeneous catalyst based on the reduced metal or any metal oxide. (Figures 2.1 and 2.2)

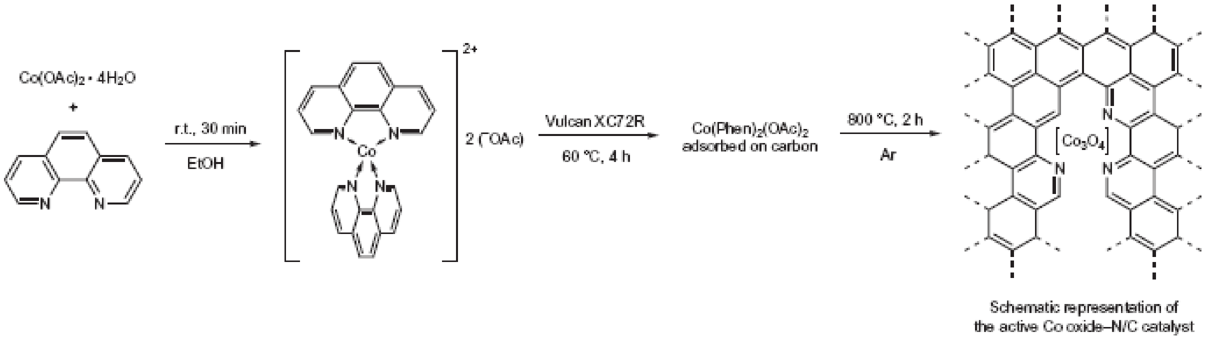


Figure 2.1: Synthesis of an active cobalt oxide–nitrogen/carbon catalyst by pyrolysis of a cobalt(II) acetate–phenanthroline complex on carbon.[173]

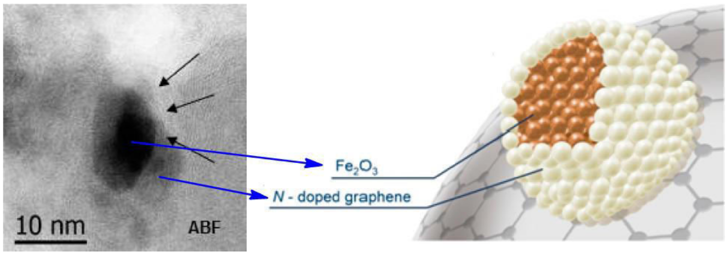


Figure 2.2: Nanoscaled Fe/Fe_2O_3 particles surrounded by nitrogen-doped graphene layers.[165]

Moreover, no catalytic activity is observed if the ligand itself is thermolyzed under the same conditions, but in the absence of the metal. This is a relevant point because nitrogen-enriched graphite is known to have catalytic properties itself,[177] even though it should be noted that such properties are usually displayed only by materials that have a much higher nitrogen content (such as C_3N_4) than the one featured by the materials obtained in the works by Beller and others. Moreover, even materials obtained by absorbing a simple metal salt (without any nitrogen ligand) on carbon and thermolyzing the so obtained solid have no catalytic activity, indicating that all components of the system are necessary to get the final result. As a strong point, the presented catalytic materials display complete air and moisture stability for months, thus avoiding the use of distilled solvents and an inert atmosphere.

The pyrolyzed material are usually named indicating first the metal or metal oxide that constitute the core of the nanoparticle, than "NGr", meaning nitrogen-doped-graphene, and finally the support employed in the preparation, preceded by the symbol @. For example, Co_3O_4/NGr@C is catalyst where the core is mainly Co_3O_4(the composition of the core is rarely uniform, some metallic cobalt is always present in cobalt catalysts) and has been generated by adsorbing a cobalt complex (the identity of the ligand is not indicated in the name) on activated carbon. Such materials have been characterized by a range of techniques. In all cases, nanoparticles of different sizes were detected with a metal/metal oxide core, surrounded by a few nitrogen-enriched graphene layers. These layers completely cover some of the nanoparticles, but leave some metal/metal oxide areas exposed in others. Moreover, some metal atoms are retained in the graphitic layer, bound to some of the nitrogen atoms originally coordinated to the metal in the starting complex.

Nitrogen-doped porous carbon (NPC) materials have drawn intensive attention for heterogeneous catalytic reactions or catalyst supports.[160,178,179,180,174,164,181,182,183,184] Conventional porous carbon materials such as activated carbon (AC) was traditionally synthesized through pyrolysis and the physical or chemical activation of raw materials such as coal, wood or fruit shells at elevated temperatures.[185] AC has long been used as an excellent sorbent and support for NPs in catalytic reactions[186] due to its various valuable properties: high specific area, large pore volume, different available surface properties such as heteroatom doping and hydrophilicity, and low cost. Although it has a wide range of newly developed applications, AC still suffers from limitations arising from the methods used in the production. The main drawbacks are as follows: 1) the pores are restricted mainly to micropores with a very narrow size distribution, which limits the mass transfer of molecules in reactions; 2) the micropores (<2 nm) largely restrict the full utilization of deposited NPs (usually >2 nm), causing the NPs to disperse only on the carbon surface and further aggregate and leach easily; 3) the architecture and nano-dimensions of AC cannot be easily tuned for specific catalytic uses; and 4) the surface functional groups need to be further tailored for specific needs by secondary functionalization to create, for example, N-containing groups. To overcome all these limitations, nitrogen-doped porous carbon materials have recently become a hot topic in research.

Usually, nitrogen functionalities can enhance the interaction between carbon surfaces and reaction molecules.[187] Hydrophilicity of NPC can be enhanced through nitrogen doping and therefore greatly improve catalyst dispersion in aqueous media and in turn contribute to a better catalytic performance.[188] Spin density and charge distribution of carbon atoms will be influenced by the neighboring nitrogen dopants,[183,189] which may generate increased defects and more active sites. On the other hand, the electronegativity ingenerated in the carbon structure because of the doped nitrogen may stabilize deposited metal with small size and narrow distribution and increase the metal–carbon binding energy. All in all in turn improves the catalytic activity and reaction stability of the consequential NPC supported catalyst in heterogeneous catalytic reactions.[178,182,104] Therefore, in addition to N-CNTs[190] and N-graphene[191] in the NPC family, new generations of NPC materials are also promising catalysts or catalyst supports because of their excellent properties, ease of handling and large-scale production. In the following paragraphs, the general structure of N-enriched graphitic catalysts has been illustrated by two representative examples.

Beller and coworkers described the use of a nanostructured iron-based catalyst for the tandem reductive amination between nitroarenes and aldehydes using hydrogen as reductant.[192,202] These iron-based nanoparticles and agglomerates with varying sizes from 5 to 200 nm were prepared from $Fe(OAc)_2$ and 1,10-phenanthroline, which were adsorbed and subsequently pyrolyzed at 800°C for 2 hours onto Vulcan XC72R as carbon support under an argon atmosphere (metal/ligand (M/L) ratio 1:3).[193,194] The metal-based particles are surrounded by individually nitrogen-enriched graphene-type layers (NGr), which are formed through the carbonization of the nitrogen ligand (Figure 2.3 C).[194,195,196] The as obtained core–shell structured nanoiron-based catalyst is illustrated in Figure 2.2.

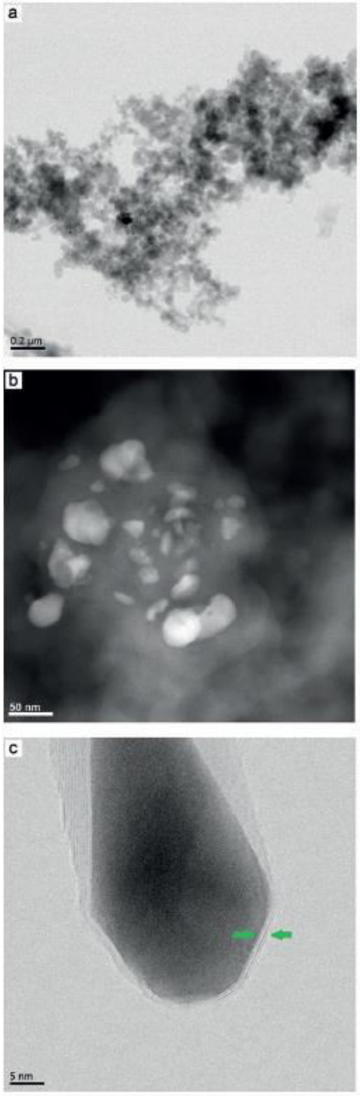


Figure 2.3: Selected a) BF- and b) HAADF-TEM images of the carbon supported iron-based catalyst. c) Visualization of graphene-layers of Fe_2O_3/NGr@C by BF-TEM.[202]

The presence of such a composite is established by the X-ray diffraction (XRD) study (Figure 2.4) as well as Energy dispersive X-ray (EDX) spectroscopy with the observed elements (Figure 2.5). X-ray photoelectron spectroscopy (XPS) revealed two distinct nitrogen species (pyridinic, pyrrolic) incorporated in the graphene lattice as well as nitrogen atoms bound to the iron (Figure 2.6).

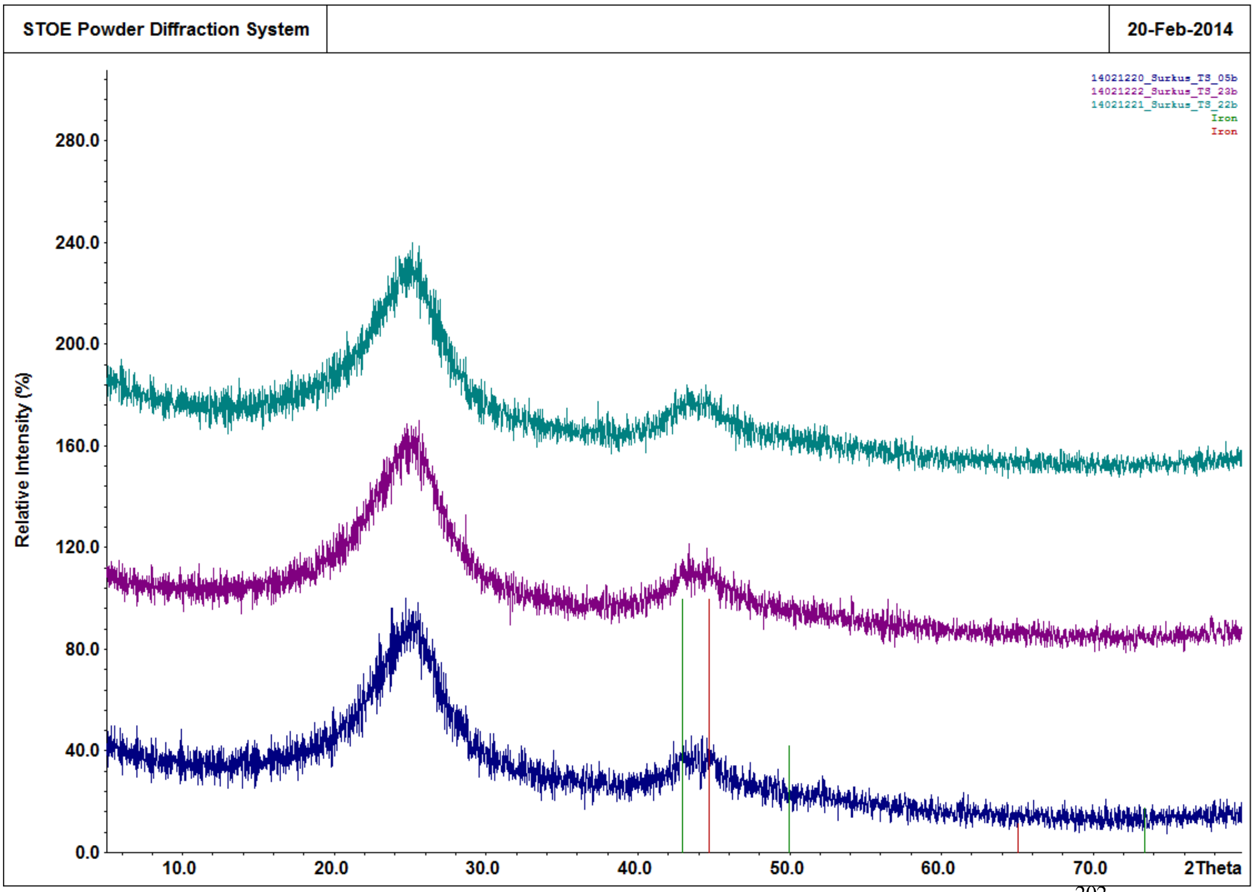


Figure 2.4: Diffraction pattern of Fe_2O_3/NGr@C for 1g-, 5g- and 10g-scale.[202]

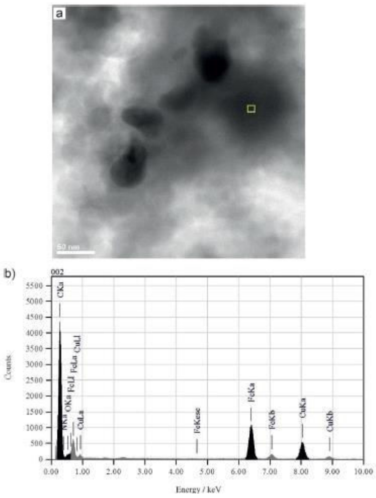


Figure 2.5: Selected EDX spectrum of Fe_2O_3/NGr@C catalyst.[202]

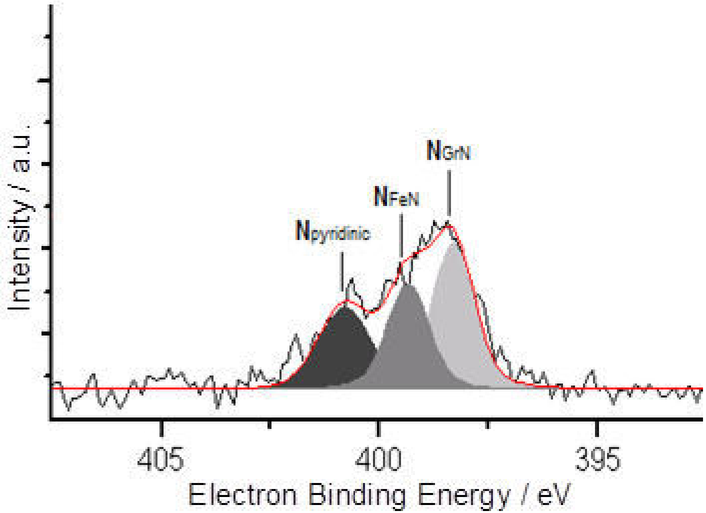


Figure 2.6: N1s spectrum of the Fe_2O_3/NGr@C catalyst.[202]

Catalysts based on silica and MgO have never been reported before. No characterization was made apart from the elemental analysis for these catalysts because it was considered that it would have been worth to spent time on that only if they had provided better results, which was not our case.

Another representative example of N-enriched graphitic catalyst can be illustrated by core-shell structured Co_3O_4/NGr@C catalyst for general and selective reductive amination, reported by Beller et al.[170] A defined complex prepared from $Co(OAc)_2$ and 1,10-phenanthroline was adsorbed and subsequently pyrolysed onto Vulcan XC72R as carbon support under Ar atmosphere (M/L ratio 1 : 2). Prof. Beller's research group noticed that pyrolysis at 800 °C for 2 h led to the most active hydrogenation and oxidation catalyst system. The material consists of well-defined cobalt-based nanoparticles with varying sizes of 2–20 nm as well as particles and agglomerates in the range of 20–200 nm. SEM images depict the chemical constitution of the catalyst surface which is a high contrast image of unequally distributed particles against the background(HAADF). (Figure 2.7)

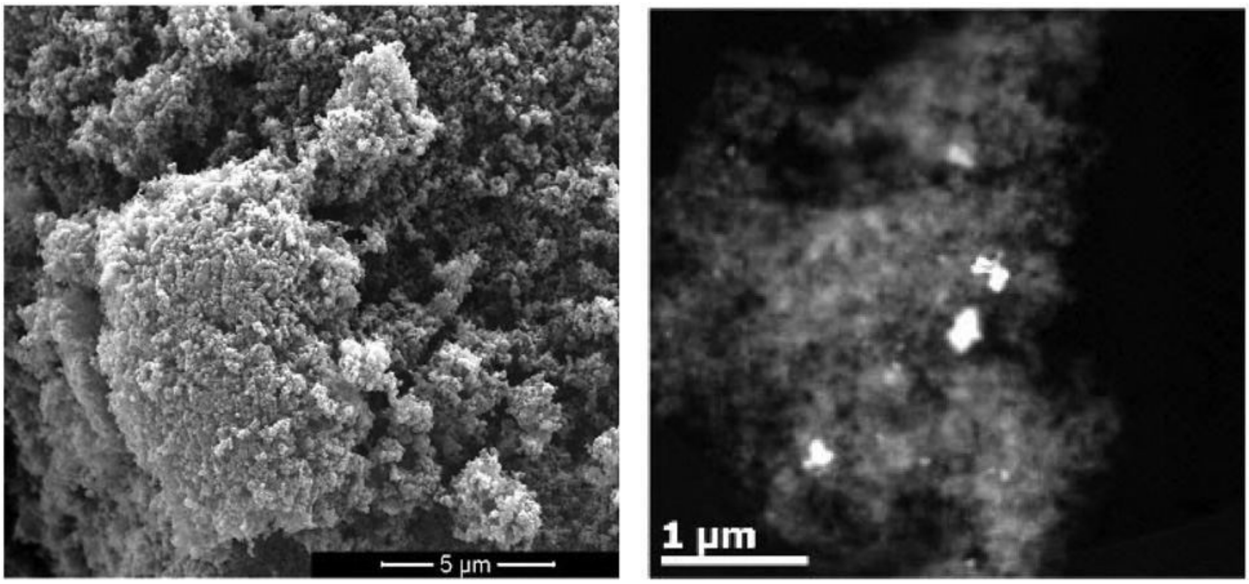


Figure 2.7: SEM (left) and HAADF-TEM (right) images of the carbon supported cobalt catalyst.[170]

They scaled up the catalyst preparation to 10 g-scale and they obtained defined crystallites, which contain active single nanoparticles as core–shell structured Co/Co_3O_4 nanocomposites. The presence of such composites is confirmed by XRD powder diffraction and EPR measurements and corresponding elements were also confirmed by EDX-mapping (Figure 2.8a). In addition, the Co-based particles are encapsulated by individually nitrogen riched graphene-type layers (NGr), which were formed through the carbonization of the nitrogen ligand (Figure 2.8b).[195] Three distinct nitrogen species were detected by XPS analysis: pyridinic and pyrrolic nitrogen as well as quaternary amine species. Deconvolution indicated that around 64% of all N atoms are bound to the metal ions. Based on spectroscopic studies, Beller and coworkers designed a simple 3D-model to get a general idea about the core–shell structured catalyst (Figure 2.8c). This simple 3D-model is analogous to the Fe_2O_3/NGR@C as discussed earlier (Figure 2.2).

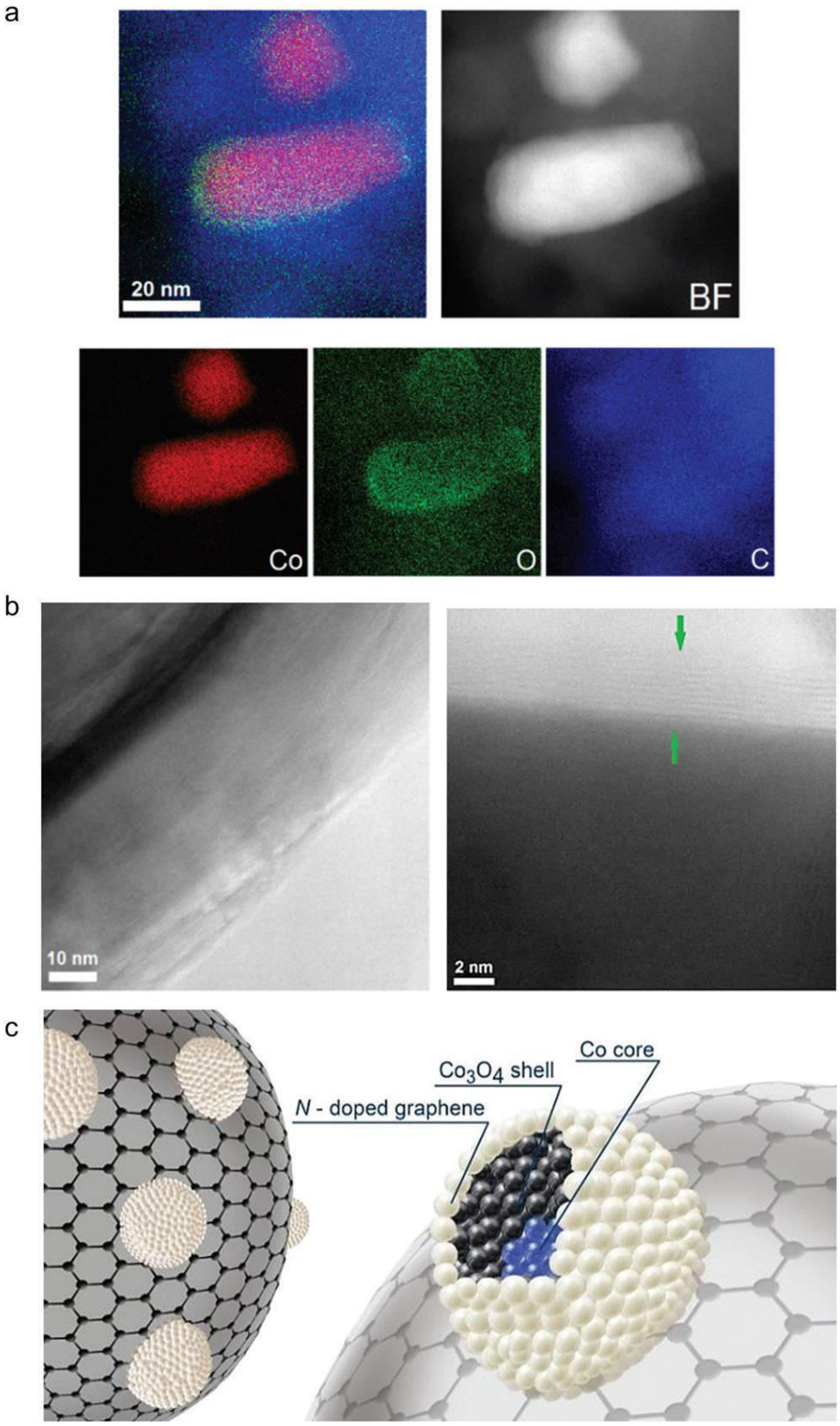


Figure 2.8: (a) EDXS-mapping of Co/Co_3O_4 crystallites; cobalt (red), oxygen(green) and carbon (blue) of Co_3O_4/NGr@C. (b) Bright field TEM images to illustrate formed graphene layers. (c) Illustration of multi core–shell structured Co-Co_3O_4/NGr@C nanoparticles.[170]

The identity of the catalytically active species has not been definitely identified in general. It may be the metal atom retained in the surface graphitic layer or a part of the metal/metal oxide core close to the edge of the graphene layer, so that a close proximity exists between some metal and nitrogen atoms. However, a growing evidence in favor of the former hypothesis is being accumulated recently[173,174,197,198] and this possibility has been considered as a working hypothesis in the following.

At the University of Milan, our research group has recently started a collaboration with Prof. Beller and two joint papers have already been published.[199] Thus, the conditions to take the project to a successful end are present. Catalysts were prepared and characterized in Rostock, where the necessary apparatus is present, while other activities described below have been conducted in Milano.

2.1 Objective of the Project

The aim of this project is to expand the field of applicability of a the class of catalysts described above and in particular, of that based on iron.

Up to now NGr catalysts have been most often used for the hydrogenation of nitrobenzene[164,167,169,173,174,199a,200] and fewer reports have been published on the hydrogenation of other polar substrates,[162,169] several oxidation or oxidative coupling reactions,[166,168,171-172,175,197,201] and a few reactions involving hydrogen transfer.[163,165,167,170,202] In the work in collaboration with the group of Ragaini,[199a] it was shown that the addition of triethylamine promotes the activity of both Fe_2O_3/NGr@C and Co-Co_3O_4/NGr@C catalysts in the hydrogenation of nitroarenes. This observation is consistent with a heterolytic activation of dihydrogen and points to a catalyst in which the oxidation state of the metal is not low (0/-1). Indeed the coordination environment in the NGr layer should not be suitable for stabilizing such low oxidation states. Thus, if one wants to identify a new reaction for which these catalysts may be active, he should look for a reaction that is catalyzed by metal in the +1/+3 oxidation state, rather than in the 0/-1 range. A reaction that is promising on this respect is olefin cyclopropanation. Such a reaction is known to be catalyzed by both Co(II) and Fe(II) complexes with nitrogen ligands,[203] a configuration that should be analogous to the one adopted by the metal in the NGr layer.

Along with soluble metal catalysts, extensively discussed in Chapter 1, immobilized complexes (mainly based on Cu and, to a less extent, on Ru and Rh) were also described.

However, very few works described the use of nanostructured or truly heterogeneous catalysts. After an isolated pioneering work by Mayoral in 1997,[204] Cu NPs onto TiO_2-Al_2O_3,[205] Al_2O_3[206] and core-shell Fe-Fe_xO_y[207] were reported. More recently, the groups of Coleman and Mack described the use of an Ag foil as recyclable catalyst under mechanochemical conditions.[208]

Diazo compounds are typically employed as carbene precursors in cyclopropanation reactions. In this work, the use of ethyldiazoacetate has to be initially tested as the carbene source. Since ethyldiazoacetate is relatively stable, with respect to other diazo derivatives, and commercially available at a convenient price. Other in-house prepared diazo derivatives have also tested to verify and prove the general applicability of the reaction. These diazo derivatives (except for other diazoacetates) need to be synthesized and used within a limited amount of time because they tend to decompose even when stored under dinitrogen and in a refrigerator. In any case, it should be noted that the ethyl ester group that remains attached to the cyclopropyl moiety adopting this procedure is a versatile group. It can be hydrolyzed to the corresponding carboxylic group that, in turn, can be transformed into other functional groups by classical organic reactions such as amidation, reduction and even Curtius rearrangement.

Different olefins were also employed. Styrene and substituted styrenes were initially tested because they are quite reactive in this kind of transformation and commercially available with numerous substituent both on the aryl ring and on the double bond, allowing for an analysis of the effect of electronic and steric effects on the outcome of the reaction. Other olefins have than been tested to verify if the reaction can also be run on aliphatic olefins (terminal, internal, cyclic).

Chapter 3

Results and Discussions

Many homogeneous complexes have been reported to successfully catalyze olefin cyclopropanation by diazo compounds (Fe, Ru, Co, Cu).[209] Along with soluble metal catalysts, immobilized complexes (mainly based on Cu and to a less extent on Ru and Rh) were also described. However, very few works described the use of nanostructured or truly heterogeneous catalysts. After an isolated pioneering work by Mayoral in 1997,[204] Cu NPs onto TiO_2-Al_2O_3,[205]Al_2O_3[206] and core-shell Fe-Fe_xO_y[207] were reported. More recently, the groups of Coleman and Mack described the use of an Ag foil as recyclable catalyst under mechanochemical conditions.[208]

Yet now research has not extensively progressed on heterogeneous catalysts for cyclopropanation reaction. Anyway, with regard to the use of heterogeneous catalysts, copper bronze is a traditional catalyst in cyclopropanation reactions. Fraile et al. reported several copper-exchanged and $CuCl_2$-supported solids, together with copper oxide, which promote cyclopropanation reaction of styrene with ethyl diazoacetate.[204] The most interesting result revealed from their study is the fine tuning of trans/cis stereoselectivity by altering the nature of the catalyst. The authors concluded from their experimental study that the less sterically hindered cyclopropane (trans or exo) is obtained as a major product when the reaction occurs on homogeneous copper catalysts. However, in some cases by using Cu(II)-exchanged K10-montmorillonite most hindered (cis or endo) cyclopropane product is predominantly obtained, so that the selectivity is reversed with regard to that observed with copper homogeneous catalysts.

Few other copper based heterogeneous catalysts have been reported for cyclopropanation reactions using supports, such as a polymer,[210] aluminum oxide,[205] silica gel,[211] zeolite,[212] or clay.[213] In 2003, Liu et al. reported that CuO over monolayer TiO_2-Al_2O_3 catalyzed the cyclopropanation of ethyl diazoacetate with styrene in yields up to 94%.[205] Copper bronze is a traditional catalyst in cyclopropanation reactions.[204]

In 2008, Lim et al. achieved asymmetric cyclopropanation using chiral aza(bisoxazoline)-copper (I) catalyst on siliceous mesocellular form (MCF) to provide the desired products in about 80% yield and 92% ee up to eight cycles without significant loss of catalytic activity.[211b] In 2011, Shi et al. reported metal-organic frameworks (MOFs) based on copper

(I) sulfate and 4,4'-bipyridine catalyzing the cyclopropanation of styrene.[214] The catalysts showed high trans diastereoselectivity and were reusable up to three times, despite a low styrene conversion of 30%.

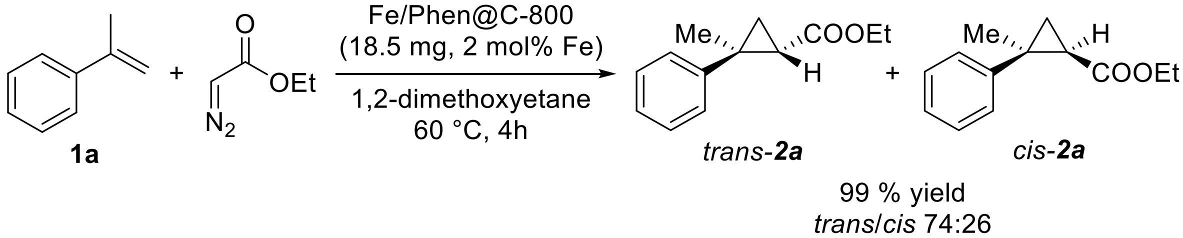
Li et al. demonstrated simple bare copper-plated iron nanoparticles (Cu@FeNPs) as a good catalyst for the cyclopropanation of ethyl diazoacetate with styrene derivatives.[215] The catalysts are magnetically recoverable. The catalyst provided the desired cyclopropanes in moderate to very good yields with trans selectivity. Li and coworkers scaled up the reaction to 1 g. The catalysts were recycled up to five times and showed no significant loss of catalytic activity. The same authors also explored the reaction mechanism. The majority of Cu after reaction features an oxidation state of +1.

Can, Li and coworkers developed a few heterogeneous catalysts based on cupric oxide supported on different inorganic supports and employed them to catalyze the cyclopropanation of styrene and 2,5-dimethyl-2,4-hexadiene with ethyl diazoacetate (EDA).[205] The catalytic performance for cyclopropanation was found to strongly depend on the nature of the support. Cupric oxide showed much higher catalytic activity for cyclopropanation after being dispersed on most of the supports. A novel catalyst, CuO/TiO_2-Al_2O_3, in which Al_2O_3 is modified with a monolayer of TiO_2, was found to be most active and selective for the cyclopropanation reaction. The highest activity and selectivity to cyclopropanes (over 93% yield) were achieved on the CuO/TiO_2-Al_2O_3 catalyst. The catalysts with the monolayer loading of cupric oxide on the corresponding support provide the highest yield, selectivity and trans:cis ratio to cyclopropanes. Under the reaction conditions, copper(II) might be reduced to the lower valence state, which shows higher activity for the cyclopropanation reactions.

Kantam et al. prepared Alumina supported copper (Cu–Al_2O_3) nanoparticles which constitute an effective catalyst for the aziridination and cyclopropanation of olefins using PhI = NTs and EDA as nitrene and carbene sources respectively.[206] The catalyst was recycled for several cycles and showed consistent activity.

Hence, we became interested in developing a novel and sustainable catalytic protocol for this reaction. We initially explored the activity of Fe/Phen@C-800in the reaction of α-methylstyrene**1a** with ethyl diazoacetate (EDA) as the model transformation (Scheme 3.1). The Fe/Phen@C-800 catalyst is able to efficiently catalyze this reaction affording the cyclopropane**2a** from very high to excellent yields and with a moderate diasteroselectivity in favor of the trans- isomer.

Control experiments effected by employing catalysts prepared by the same procedure employed for Fe/Phen@C-800, but omitting either Fe(OAc)$_2$ or Phen, or by using Fe(OAc)$_2$ and Phen as such resulted in no detectable formation of cyclopropane (Table 3.1, entries 6 - 8).

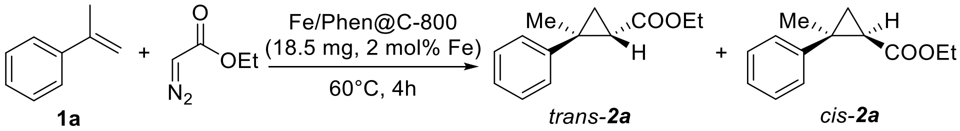


Scheme 3.1: Cyclopropanation of **2a** using Fe/Phen@C-800 as catalyst.

The nature of the solvent has a minimal influence both on the reaction yield and diasteroselectivity making this reaction versatile from the media profile. 1,2-Dimethoxyethane (DME) was then chosen as the solvent for further optimization (Table 3.1, entry 5). The variation of the reaction temperature (Table 3.2, entries 1, 2 and 4) furnished the product in slightly lower yield. It should be underlined that in all the cases in which a 5-fold amount of the olefin with respect to the diazo compound has been used, homocoupling products (diethyl fumarate and diethyl maleate) deriving from EDA were detected in very low amount (<5 %). Only when the amount of **1a** was decreased (1.5 eq) homocoupling side products increased, although a very good yield of the cyclopropane was maintained (Table 3.3, entry 3), demonstrating the applicability of the procedure even to more expensive olefins. Interestingly, the catalyst is water tolerant and only a slightly decreased yield was obtained using a “wet” solvent (Table 3.3, entry 4).

In addition, we verified that a change in the catalyst support from carbon to inorganic oxides (MgO or SiO$_2$) does not affect the yield and the diasteroselectivity (Scheme 3.2).

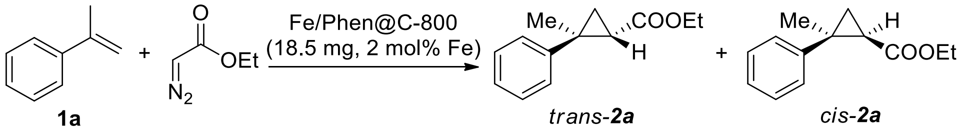
Given the good results obtained and the apparent robustness of the catalyst, the reaction scope was investigated (Scheme 3.3).



Entry	Solvent	Diethylfumarateyield [%][b]	Diethylmaleate yield [%][b]	2a yield [%][b]	*trans*:*cis* ratio[b]
1	Benzene	traces	3	96	72:28
2	1,2-Dichloroethane	-	1	96	79:21
3	*n*-Hexane	1	5	84	74:26
4	CH_3CN	-	1	89	75:25
5	**1,2-Dimethoxyethane**	**-**	**>1**	**99**	**74:26**
6[c]	1,2-Dimethoxyethane	<1	<1	<1	-
7[d]	1,2-Dimethoxyethane	<1	<1	<1	-
8[e]	1,2-Dimethoxyethane	<1	<1	<1	-

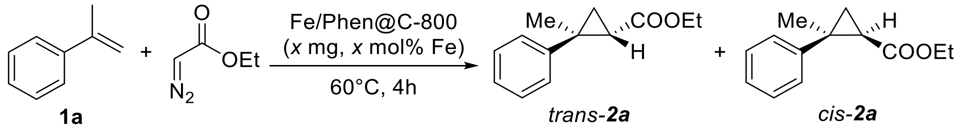
Table 3.1: Cyclopropanation of **1a** with Fe/Phen@C-800 as catalyst: effect of solvent and control experiments.[a]

[a] Reaction conditions: 0.50 mmol EDA, 2.50 mmol**1a**, 18.5 mg Fe/Phen@C-800 (corresponding to 2 mol% Fe), 3 mL solvent, at 60 °C for 4h. [b] Determined by ^1H NMR spectroscopy (2,4-dinitrotoluene as an internal standard). [c] The reaction was conducted using Fe@C-800 as catalyst. [d] The reaction was conducted using Phen@C-800 as catalyst. [e] The reaction was conducted using $Fe(OAc)_2$ (1.7 mg, 1,0 10^{-2}mmol) + Phen (3.8 mg, 2.1 10^{-2}mmol) as catalyst.



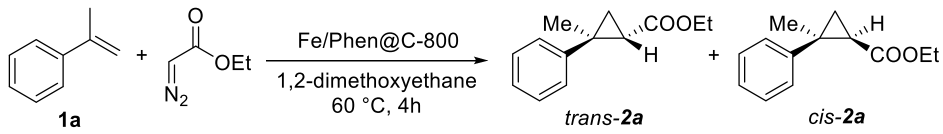
Entry	Temperature [° C]	Time [h]	Diethylmaleate yield [%][b]	Diethylmaleate yield [%][b]	2a yield [%]	***trans*:*cis*** ratio
1	50	4	-	1	98	73:27
2	40	4	-	2	92	75:25
3	40	6	-	3	97	74:26
4	70	4	-	2	97	71:29

Table 3.2: Cyclopropanation of **1a** with Fe/Phen@C-800as catalyst: effect of temperature.[a]
[a] Reaction conditions: 0.50 mmol EDA, 2.50 mmol**1a**, 18.5 mg Fe/Phen@C-800 (corresponding to 2 mol% Fe), 3 mL DME. [b] Determined by ^{1}H NMR spectroscopy (2,4-dinitrotoluene as an internal standard).



Entry	Cat. loading [mg]	Olefin loading (eq)	Diethylfumarate yield [%][b]	Diethylmaleate yield [%][b]	2a yield [%]	***trans*:*cis*** ratio
1	14.9	5	-	>1	85	73:27
2	9.8	5	-	1	71	74:26
3	18.5	1.5	2	10	86	70:30
4[c]	18.5	5	-	-	71	73:27

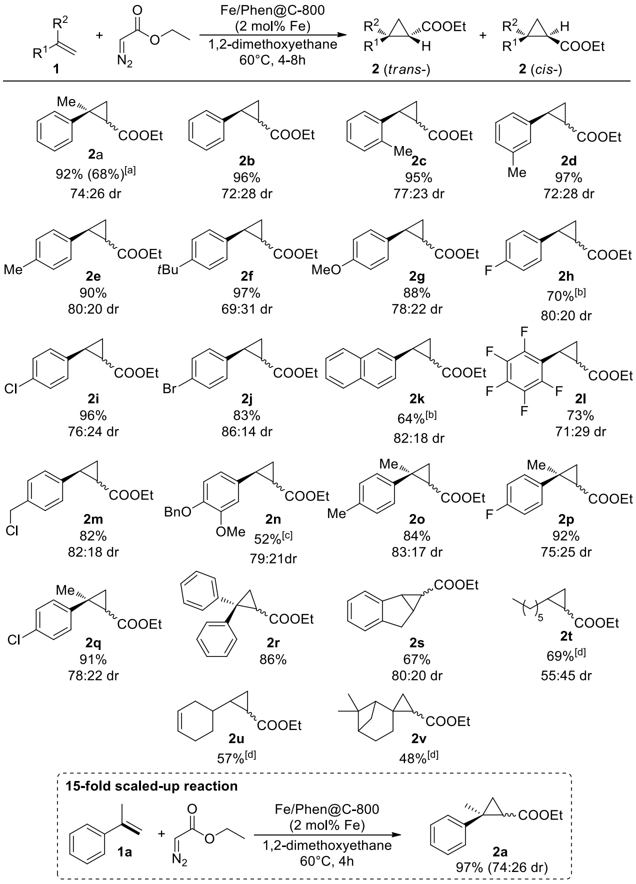
Table 3.3: Cyclopropanation of **1a** with Fe/Phen@C-800 as catalyst: effect of catalyst and olefin loading.[a]
[a] Reaction conditions: 0.50 mmol EDA, 2.50 mmol**1a**, x mg Fe/Phen@C-800 (corresponding to x(2/18.5) mol% Fe), 3 mL DME. [b] Determined by ^{1}H NMR spectroscopy (2,4-dinitrotoluene as internal standard). [c] Water was added (10 v/v%)



	yield	-	trans/cis
Fe/Phen@C-800	99%	-	74:26
Fe/Phen@MgO-800	98%	-	76:24
Fe/Phen@SiO_2-800	97%	-	76:24

Scheme 3.2: Cyclopropanation of **1a** with different Fe-catalysts under optimized conditions: effect of the support.[a]

[a] Reaction conditions: 0.50 mmol EDA, 2.50 mmol**1a**, 18.5 mg Fe/Phen@support-800, 3 mL solvent, at 60°C for 4h. Yields and d.r. determined by ^{1}H NMR spectroscopy (2,4-dinitrotoluene as an internal standard).



Scheme 3.3: Substrate scope with respect to olefins.

Reaction conditions: 0.50 mmol EDA, 2.50 mmol alkene, 18.5 mg Fe/Phen@C-800 (corresponding to 2 mol% Fe), 3 mL DME at 60°C for 4h. Yields refer to the isolated compounds (sum of the *trans*- and *cis*- diasteroisomers). Diastereomeric ratios (dr) are based on separated diasteromers. [a] Isolated yield of the major isomer in parentheses, dr measured by ^{1}H NMR. [b] Only major isomer isolated, drmeasured by ^{1}H NMR.[c] 1.5 mmol alkene was employed. [d] Reaction time: 8h. Isolated as isomeric mixture. Where possible, dr measured by ^{1}HNMR.

Styrene and its simple methyl derivatives (**1b-1e**) gave the corresponding cyclopropanes in high yield regardless of the position of the methyl moiety on the arene ring. Either substrates with mildly (1f) or strongly (**1g**) electron-donating groups afforded the corresponding cyclopropanes in very high yields. Halogen containing substrates (**1h-1j, 1m, 1p, 1q**) were well tolerated, maintaining intact the C-X bond, which could serve for further functionalization, and also a very electron poor substrate such as pentafluoro styrene (**1p**) afforded the cyclopropane in good yield. In addition a styrene substituted with a benzyloxy group **(1 n)** afforded the corresponding cyclopropane in good yield. The benzyloxy group is widely used in organic chemistry as protecting group for hydroxyl moieties. Indeed cleavage of the benzyl ether could allow further functionalization and thus to synthesize more complex molecules. Notably, more challenging aliphatic substrates such as 1-octene (**1t**) and β-pinene gave the product in satisfactory yields. Using vinyl cyclohexene (**1u)** the cyclopropanation reaction occurs regioselectively on the terminal olefinic bond maintaining intact the internal one. The selectivity for the terminal double bond in **1u**is explained by the lack of activity of the catalyst in the case of internal olefin (Figure 3.1), most likely due to a hindered approach of the substrate to the carbene formed on the surface of the catalyst.

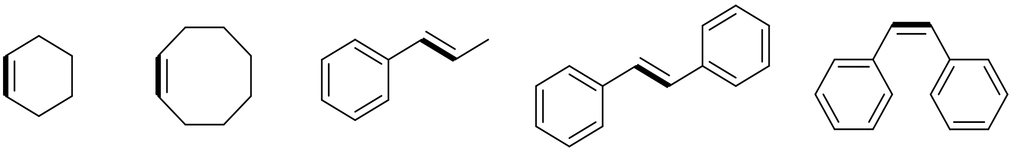
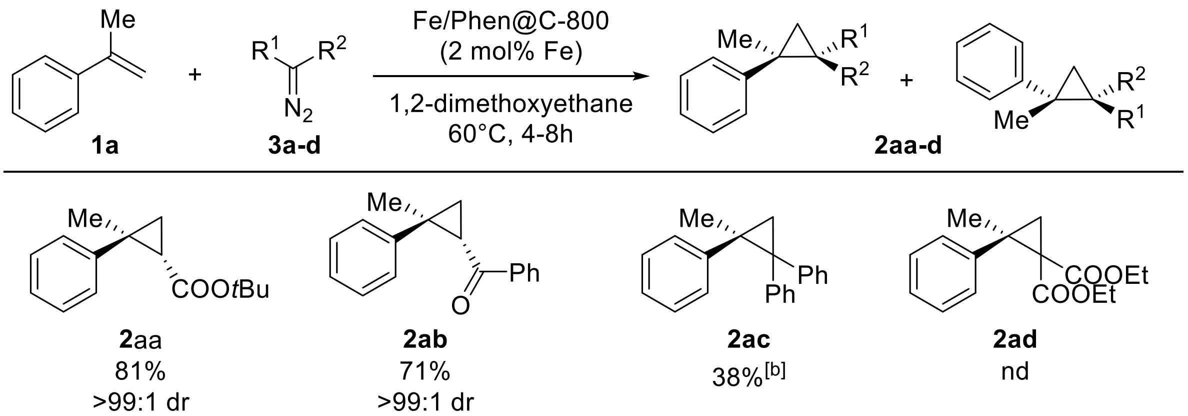


Figure 3.1: Examples of internal olefins unreactive under optimized reaction conditions.[a]
[a] Reaction conditions: 0.50 mmol EDA, 2.50 mmol**1a**, 18.5 mg Fe/Phen@C-800 (corresponding to 2 mol% Fe), 3 mL 1,2-dimethoxyethane, at 60°C for 8h.

Under the optimized conditions, the scope of some diazo compound was also examined (Scheme 3.4). Mono substituted diazo compounds (ester or ketone) afforded the corresponding cyclopropanes**2aa** – **2ab** in excellent yields. Interestingly the use of more sterically demanding diazo compounds has a dramatic effect on the diastero selection, furnishing the *cis-* isomer only in traces. Disubstituted diazomethanes proved to be more challenging. Diphenyl diazomethane failed to afford **2ac** under standard conditions, although it yielded the product in moderate yield at a higher temperature and longer reaction time (100°C for 8h in toluene), while the more stable diazomalonate did not react even under these conditions.



Scheme 3.4: Substrate scope with respect to diazo compounds.
Reaction conditions: 0.50 mmol3a-d, 2.50 mmol alkene, 18.5 mg Fe/Phen@C-800 (2 mol% Fe), 3 mL DME, at 60°C for 4h. Isolated yields are reported, dr measured by ^{1}H NMR. [b] Reaction conditions: 100°C in toluene for 8h.

In order to better demonstrate the practical utility of this protocol, the scalability and recyclability of the system were studied. The model reaction has been successfully scaled-up to 15-fold without significant variations of yield and diasteroisomeric ratio compared to the small-scale run. Regarding the recyclability, a progressive decrease of the activity was observed along the runs (D.1 in Figure 3.2, cycles 1-5). ICP analysis of the solution after the first run showed a negligible (*ca.* 0.1%) loss of iron from the catalyst, so that this cannot be the reason for deactivation. In order to make the whole process both efficient and effective, two routes of reactivation were explored. The spent catalyst obtained after 5 runs (Fe/Phen@C-800_S) was thermally treated under inert atmosphere (R.1 in Figure 3.2). However, despite a partial reactivation was gained, still complete conversion of EDA was not achieved. On the contrary, by subjecting Fe/Phen@C-800_S to mild oxidizing conditions (H_2O_2 3 v/v% aqueous solution), the initial catalyst activity was restored (R.2 in Figure 3.2). The reactivated, Fe/Phen@C-800_R, could be further recycled as the fresh one (Figure 3.2, cycle 7). Oxidative regeneration is typical for catalyst that suffers of physicochemical deactivation (e.g. fouling or poisoning). The phenomenon is derived from the adsorption or chemisorption of species on the active sites thus decreasing the overall activity.[216] Olefins (and in particular styrenes) may undergo polymerization or oligomerization processes. Indeed, we verified that complete deactivation of the catalyst occurs even by treating the material only with styrene under the reaction conditions and the activity is restored by oxidative treatment (refer to Chapter 4 for experimental details). This result indicates the polymerization of the olefin on the catalytic surface as a possible cause for the deactivation rather than a mechanical or thermal modification of the catalyst.

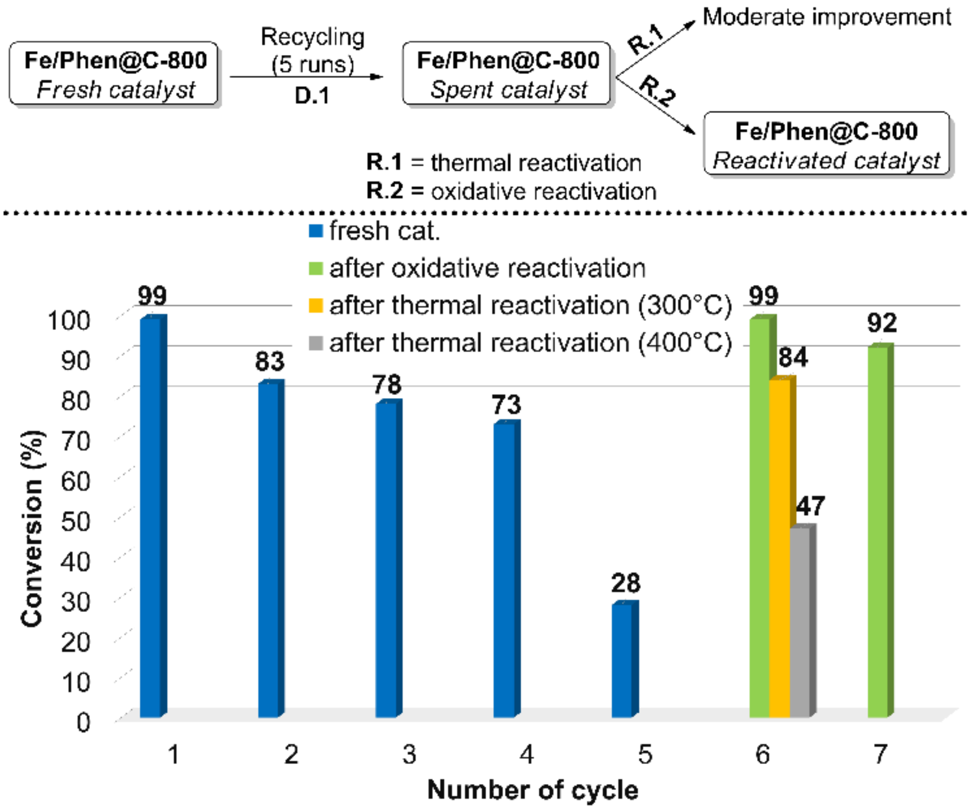


Figure 3.2: Recycling and reactivation steps.

To further elucidate the reason for the declined activity, the fresh, spent and regenerated catalysts were characterized by X-ray photoelectron spectroscopy (XPS) and scanning transmission electron microscopy (STEM). XPS N1s analysis showed common peaks at around 399 eV, 400 eV and 401 eV for all the materials (Figure 3.3-7). These results are in agreement with three different nitrogen bonding situations, namely N bonded in residual organic matrices and/or Fe-N_x centers, pyrrolic-N and graphitic-N, respectively.[194, 217] A minor peak at 398.1 eV ascribed to pyridinic-N has been detected in Fe/Phen@C-800_S. C1s XPS displayed an analogous pattern for all the materials (Figure 3.3). Indeed, signals corresponding to C=C (284.8 eV), C=N or C-O (approximately at 285 eV), C-N or C=O (285-291 eV) functionalities can be detected.[218] Deconvolution of the Fe2$p_{3/2}$ region shows four pairs of peaks that can be attributed to various Fe states. Peaks at around 708 eV, 711 eV and 714 eV in the region correspond to Fe(0), Fe(II) and Fe(III), respectively.[219] Additionally, the peak at 710 eV suggests the presence of Fe-N_x bonds which is in agreement with the previous results from N1s spectra.[220] Finally, the interpretation of the O1s region is not trivial because of the large amount of oxygen functionalities both derived from oxygen groups present in the carbonaceous matrix[221] and iron oxides.[222]

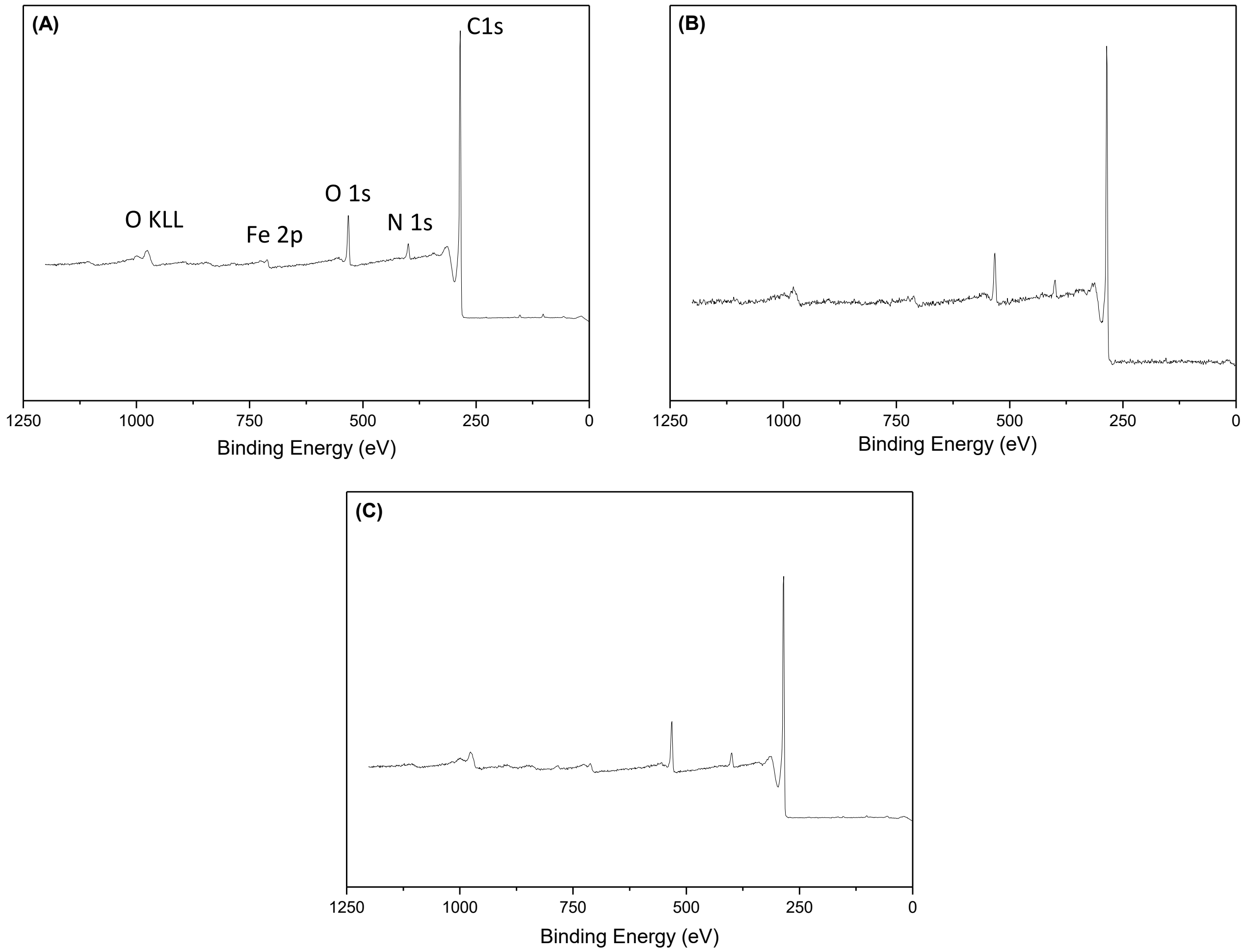


Figure 3.3: XPS analyses (survey) of Fe/Phen@C-800 (A), Fe/Phen@C-800_S (B) and Fe/Phen@C-800_R (C).

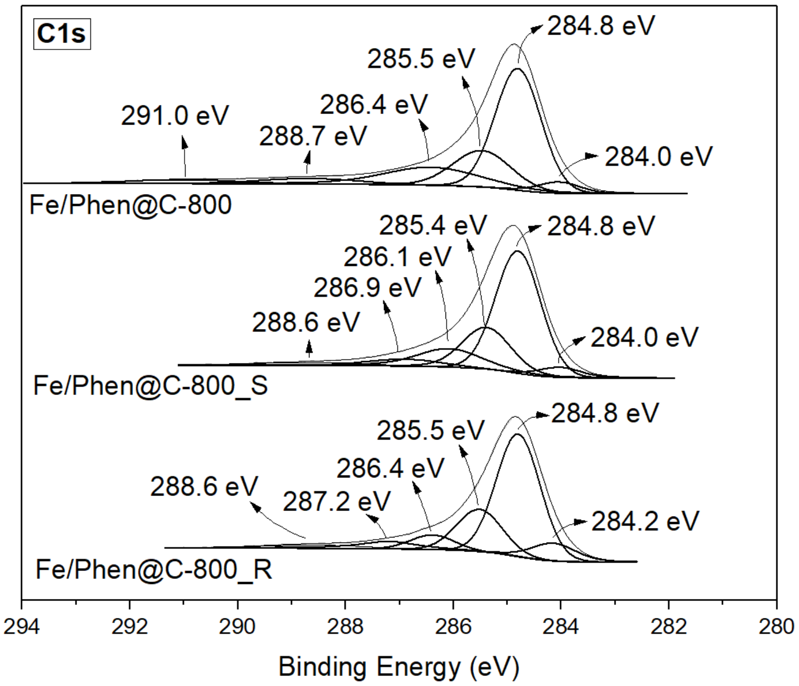


Figure 3.4: XPS analyses (C1s) of Fe/Phen@C-800, Fe/Phen@C-800_S and Fe/Phen@C-800_R.

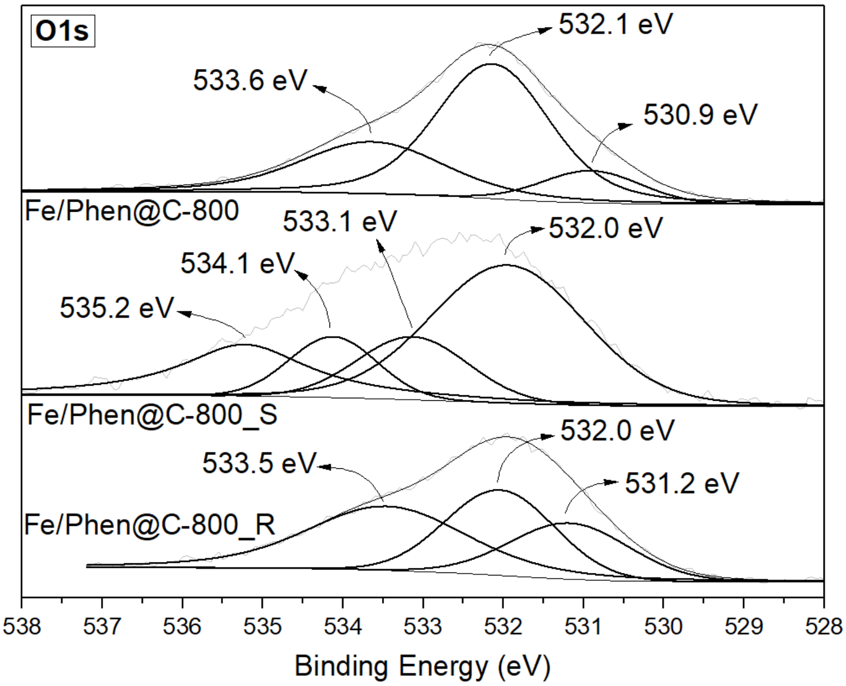


Figure 3.5: XPS analyses (O1s) of Fe/Phen@C-800, Fe/Phen@C-800_S and Fe/Phen@C-800_R.

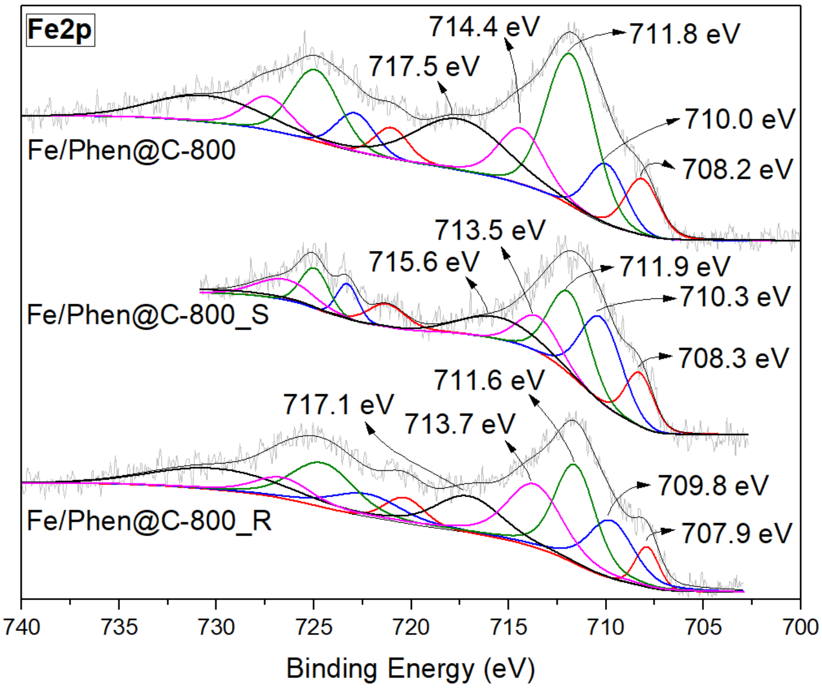


Figure 3.6: XPS analyses (Fe2p) of Fe/Phen@C-800, Fe/Phen@C-800_S and Fe/Phen@C-800_R.

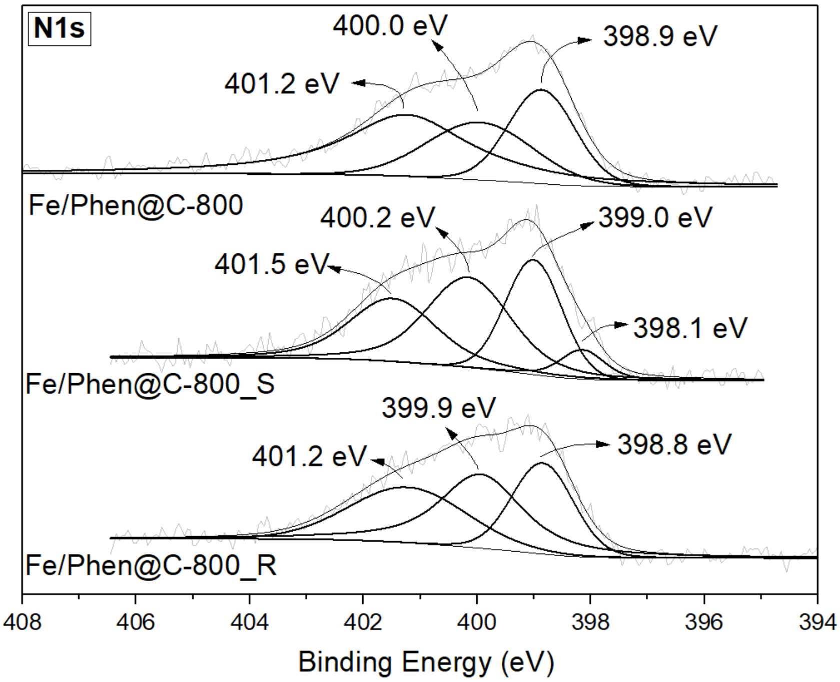


Figure 3.7: XPS analyses (N1s) of Fe/Phen@C-800, Fe/Phen@C-800_S and Fe/Phen@C-800_R.

For this reason, unambiguous assignments are not possible. STEM images and analytical data of the three materials were then acquired. As depicted in Figure 3.8, the annular dark field (ADF) STEM images and related elemental maps showed the presence of Fe, N, O on carbon support. Nitrogen is mainly distributed in a phase also containing C, O and Fe on the surface of the support alongside Fe-based particles.

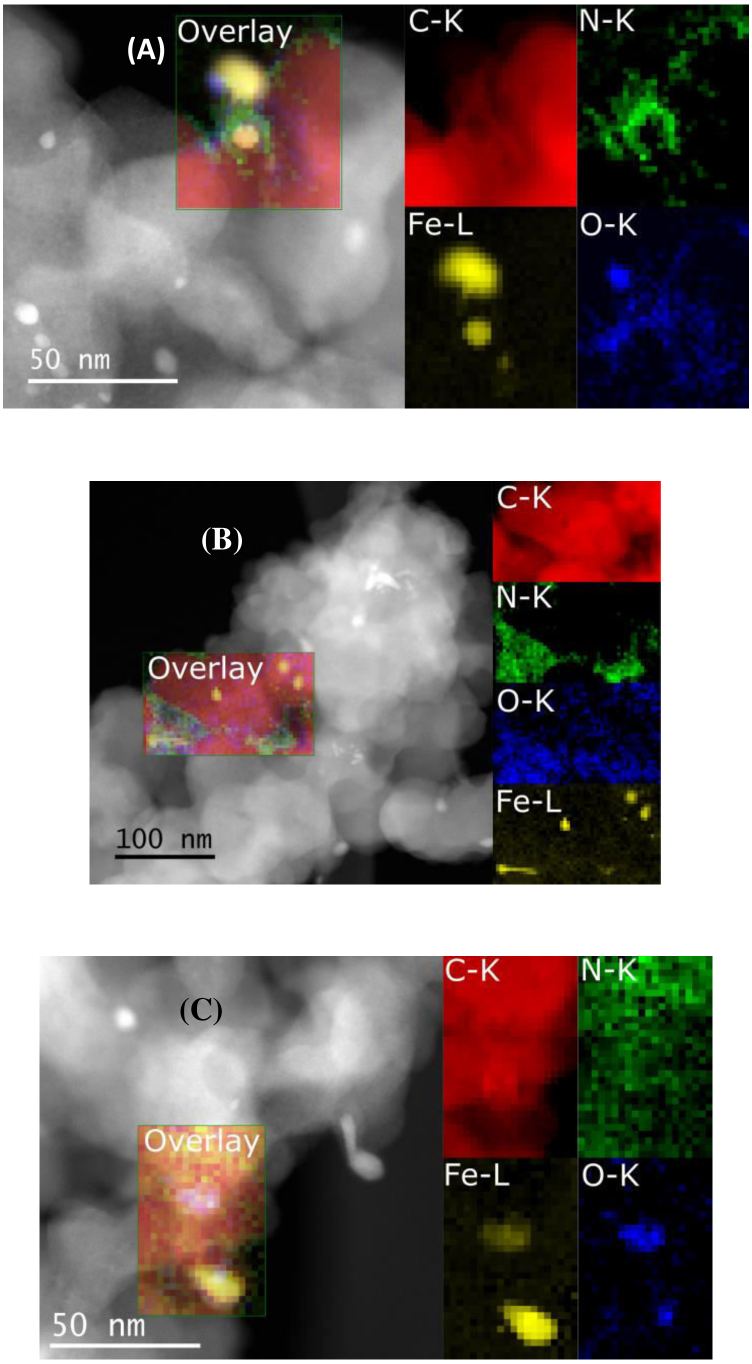


Figure 3.8: ADF-STEM images and EELS elemental maps of Fe/Phen@C-800 (A), Fe/Phen@C-800_S (B) and Fe/Phen@C-800_R (C).

In addition to the elemental maps, the different contrast visible in both the annular bright field (ABF) and high angle annular dark field (HAADF) images (Figure 3.9) confirmed the predominant presence of probably metallic Fe NPs in addition to Fe oxide NPs. Whereas layers of graphene cover the former, the latter is uncovered thus indicating a possible protecting role of graphene towards oxidation. The nitrogen-doped amorphous carbonaceous matrix attached to the support showed the presence of dispersed Fe clusters. Their identity is also confirmed by electron energy loss spectra (Figure 3.12 B). The complex pattern revealed by Fe2p XPS spectra reflects the variety of iron functionalities (metallic Fe, FeO_x, FeN_x centers) in the material. Spent catalyst (Fe/Phen@C-800_S) showed similar structures: still defined Fe-based NPs (mainly metallic and in less extent oxidic) enveloped in carbon shells and dispersed iron clusters can be clearly observed (Figure 3.8B, Figure 3.10 and Figure 3.12C). Finally, the reactivated catalyst Fe/Phen@C-800_R generally showed more extended oxidic particles, however maintaining intact the small iron clusters (Figure 3.8C, 3.11, S12D). The general morphology and distribution of Fe, N, O and C remains similar between the three different states of the catalyst as shown by the STEM data. Combined with the small changes in electronic structure revealed by XPS, the data are consistent with the deactivation of the catalyst being due to fouling, which is removed by the H_2O_2 treatment, rather than by a structural change of the catalyst itself.

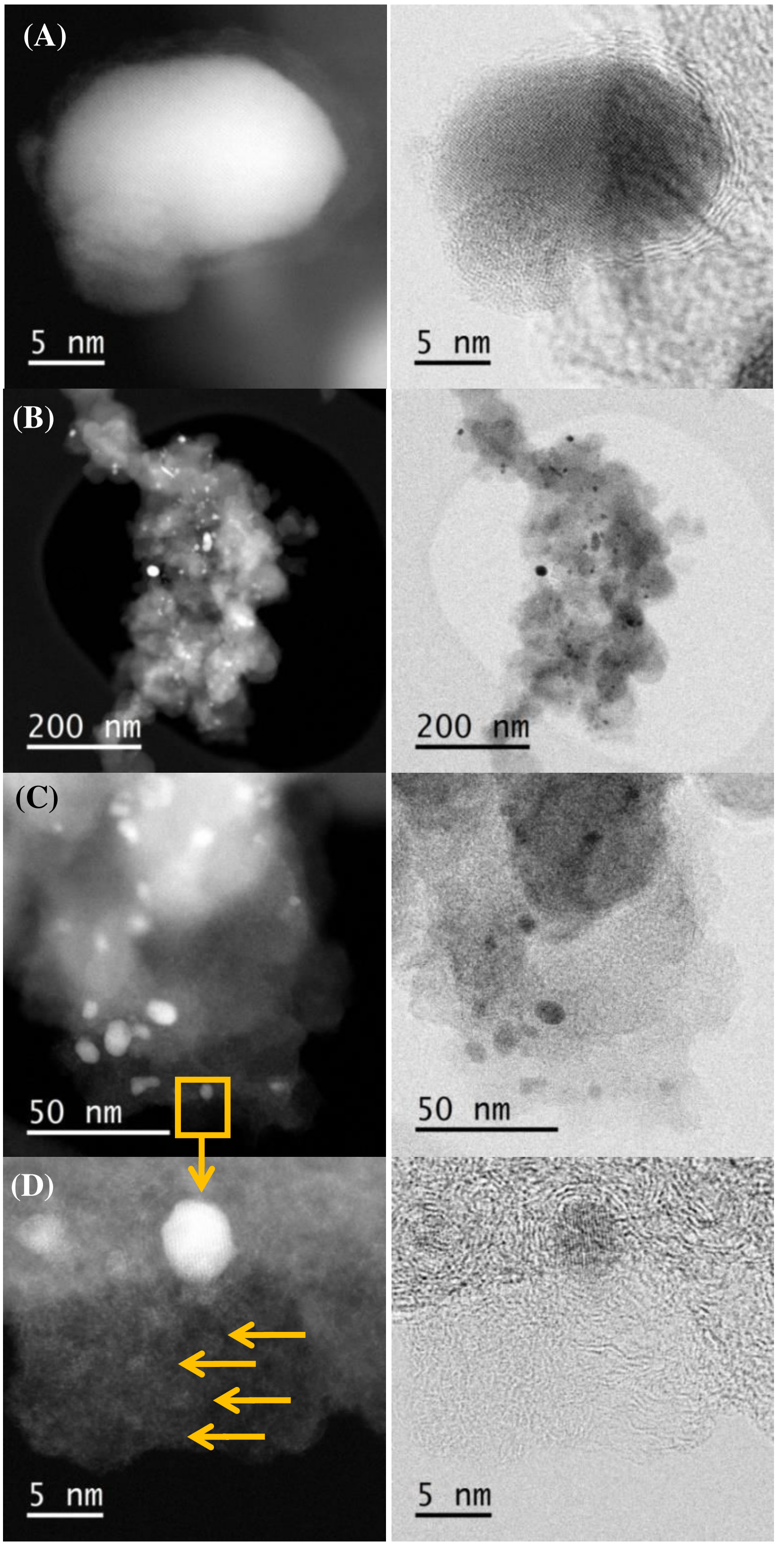


Figure 3.9: HAADF- (left column) and ABF- (right column) STEM images of Fe/Phen@C-800 (A) showing high resolution images of a metallic Fe particle accompanied by a small Fe oxide particle (refer to Figure 3.8A), the ABF image on the right highlights the enclosure of the metallic particle by some graphene layers. Line (B) shows a representative overview of an agglomeration of some support particles with their Fe particles, line (C) a more detailed view of the edge regions of some support particles and (D) high resolution images of the mixed C, N, O phase containing Fe clusters (some marked by arrows, refer to Figure 3.12 B).

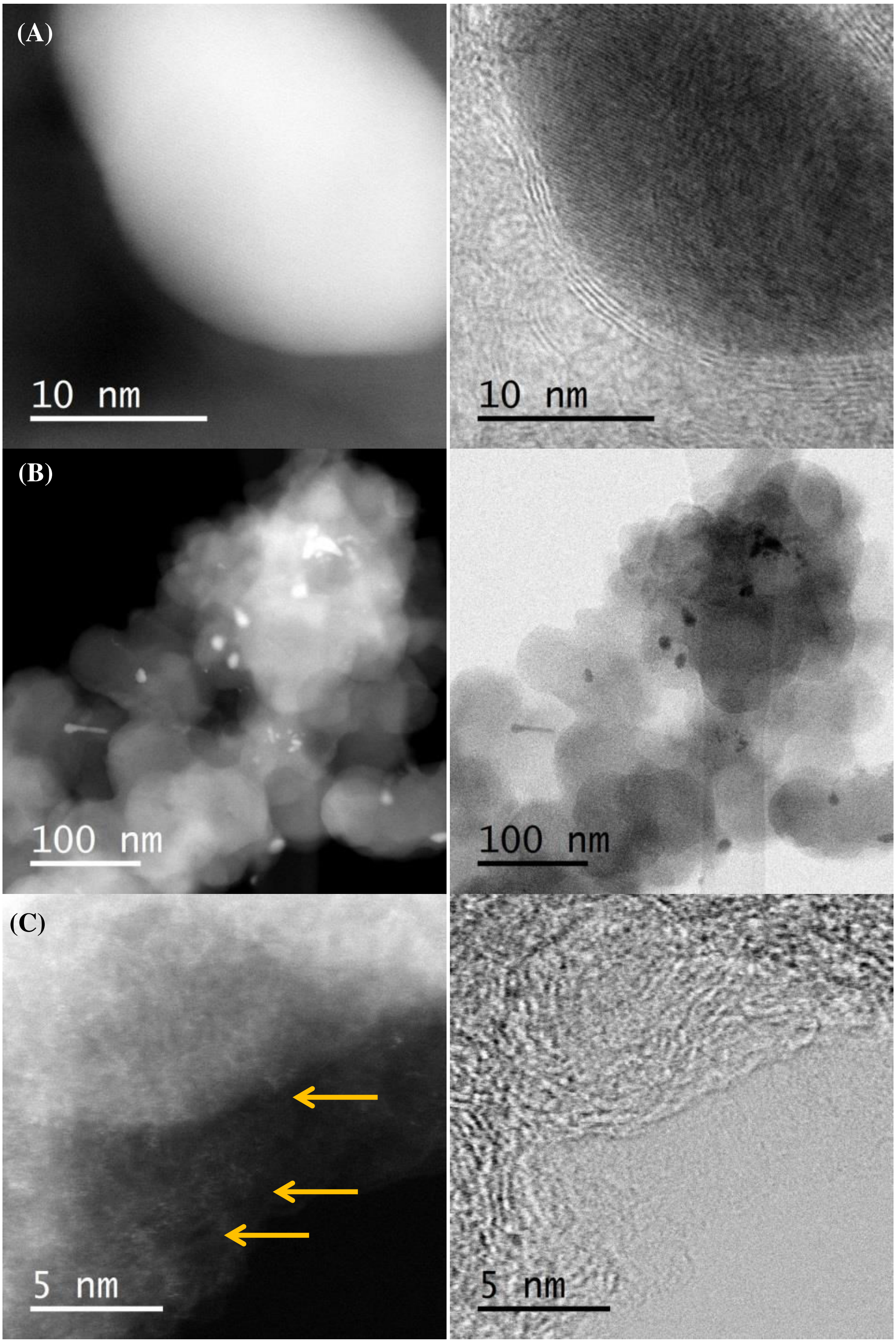


Figure 3.10: HAADF- (left column) and ABF- (right column) STEM images of Fe/Phen@C-800_S. Line (A) showing a carbon enclosed metallic Fe particle, line (B) a general overview (corresponding to the area of Figure 3.8B) and line (C) a high resolution image of the C, N, O phase with its Fe clusters.

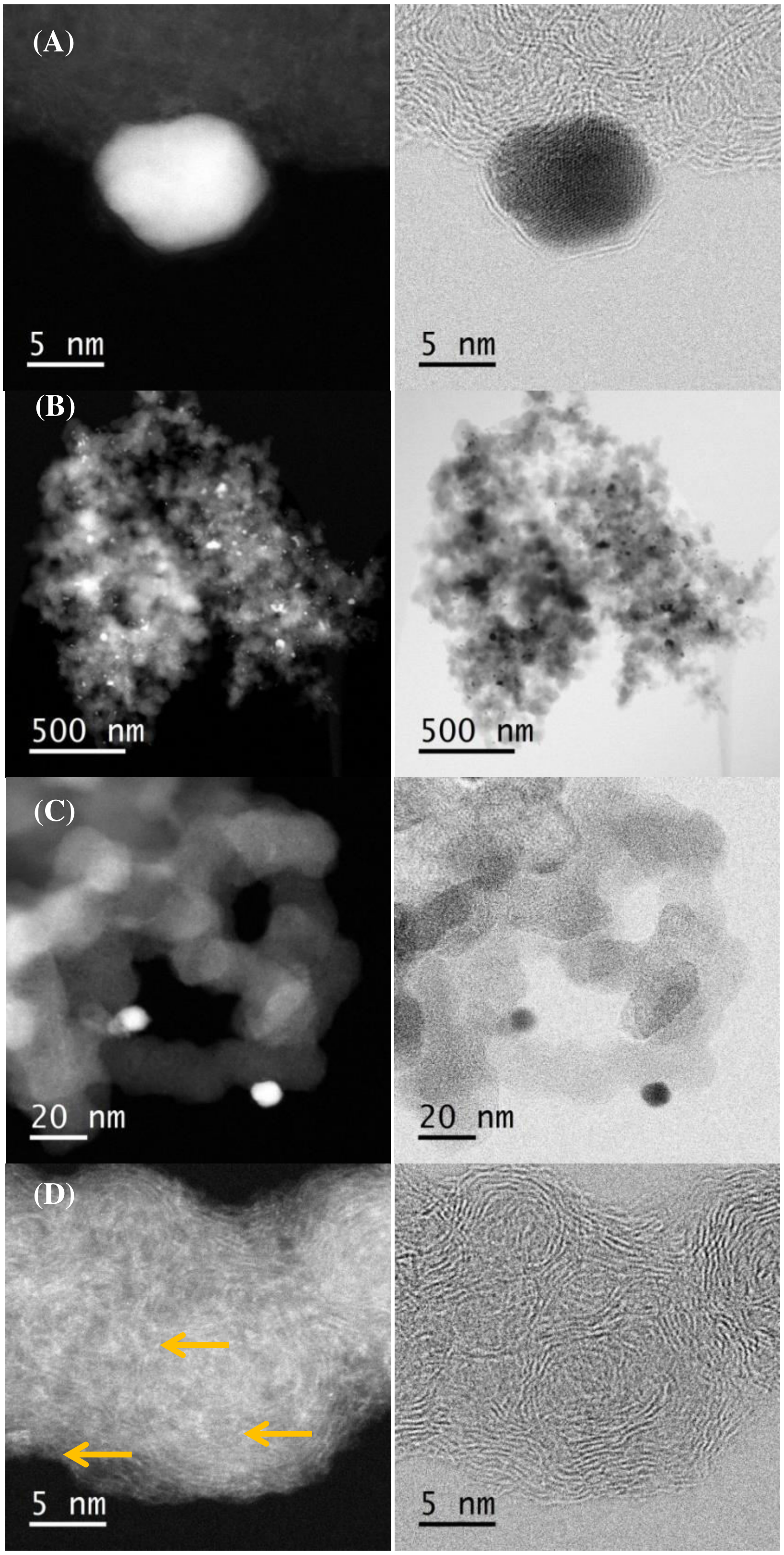


Figure 3.11: HAADF- (left column) and ABF- (right column) STEM images of Fe/Phen@C-800_R.Line (A) showing a carbon enclosed metallic Fe particle, line (B) a representative general overview of agglomerated support particles with their Fe particles. Line (C) a close up of the edge of such an agglomeration and line (D) a high resolution image of the C, N, O phase with its Fe clusters.

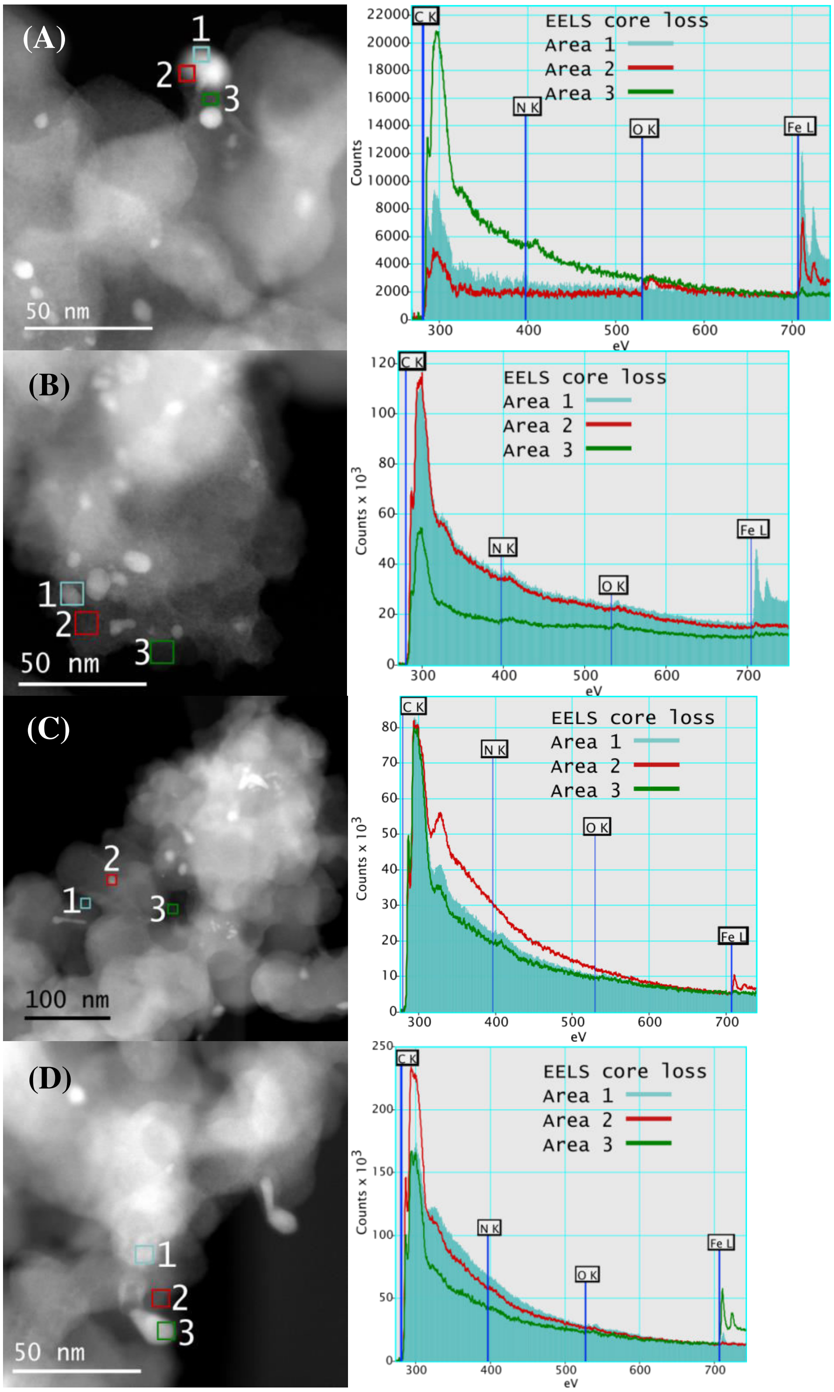


Figure 3.12 ADF-STEM images and EELS spectra from indicated areas of Fe/Phen@C-800 (A and B), Fe/Phen@C-800_S (C) and Fe/Phen@C-800_R (D). Lines (A), (C) and (D) show exemplary spectra of the spectrum imaging data sets used to calculate the corresponding elemental maps in Figure 3.8. They also show a certain N and Fe content besides the carbon in areas close to the surface of the support particles. Area 3 in line (B) shows the spectrum of the region also shown in high resolution in Figure 3.9D, verifying the presence of Fe at this position and supporting the interpretation of the clusters with brighter contrast there to be of Fe.

	C [at.%]	**O [at.%]**	**N [at.%]**	**Fe [at.%]**
Fe/Phen@C-800	87.42	3.53	7.69	0.56
Fe/Phen@C-800_S	85.69	3.43	9.99	0.54
Fe/Phen@C-800_R	85.63	3.85	9.22	0.79

Table 3.4: Elemental compositions (near-surface region)for the fresh (Fe/Phen@C-800), spent(Fe/Phen@C-800_S) and reactivated (Fe/Phen@C-800_R) Fe-based catalysts based on XPS quantitative analysis.

In conclusion, we demonstrated that the non-noble metal catalyst prepared by pyrolysis of a molecularly defined complex impregnated either on carbonaceous or inorganic support, can effectively catalyze cyclopropanation reactions. These kinds of materials, generally employed for reduction or oxidation reaction, are indeed effective catalyst also for carbene transfer reactions. The developed protocol allows obtaining several cyclopropanes from aromatic and aliphatic olefins and different diazocompounds. The deactivation of the catalyst upon recycling has been also studied and an oxidative regeneration protocol was effectively developed, which may be of more general use even for other reactions if olefins or other polymerizable compounds are employed as substrates.

Chapter 4

Experimental Details

4.1 General Aspects

Unless otherwise stated, all the catalytic reactions were performed under N_2 atmosphere using distilled solvents. Ethyl diazoacetate (EDA, Sigma Aldrich) was stored at 4-8°C (purity 97%, as indicated by the certificate of analysis for the specific lot). α-Methyl styrene was purchased from Acros Organics and purified by distillation over calcium hydride prior of its use in catalysis. All other substrates were purchased from various suppliers and used without any purification. Employed solvents were purified using standard techniques.

For the preparation of the catalytic materials, absolute ethanol was purchased from Alfa Aesar, $Fe(OAc)_2$ was purchased from Sigma Aldrich (trace metal basis >99.999%) and 1,10-phenanthroline (Phen) was purchased as monohydrate from Alfa Aesar. However, before use, it was dissolved in distilled CH_2Cl_2, dried over Na_2SO_4 followed by filtration under a dinitrogen atmosphere and evaporation of the solvent in vacuo. Both $Fe(OAc)_2$ and Phen were weighed in the air but stored under Ar to avoid oxidation and water uptake. Vulcan XC 72R, Aerosil OX 50 and MgO (nanopowder, > 99% trace metals basis) were purchased from Cabot Corporation, Evonik Industries and Alfa Aesar, respectively.

Diazo compounds **3b**,[223] **3c**,[224] **3d**[225] were prepared according to literature procedures.

4.2 Analytical Details

^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature (at frequencies of 300MHz for the proton and 75MHz for the carbon) on a Bruker AC 300 FT or on a Bruker Avance DRX 400 (at frequencies of 400 MHz for the proton and 100 MHz for the carbon). Chemical shifts are reported in ppm relative to TMS; the data are reported as follows: proton multiplicities (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet and br=broad), coupling constants and finally integration.

IR spectra were registered on a Varian Scimitar FTS-1000.

The scanning transmission electron microscopy (STEM) measurements were performed at 200kV with a probe aberration-corrected JEM-ARM200F (JEOL, Corrector: CEOS). The microscope is equipped with a JED-2300 (JEOL) energy-dispersive x-ray-spectrometer (EDXS) and an Enfinium ER (GATAN) electron energy loss spectrometer (EELS) with Dual EELS for chemical analysis. The solid samples were deposed without any pretreatment on holey carbon supported by a Cu-grid (mesh 300) and transferred to the microscope.

The XPS (X-ray Photoelectron Spectroscopy) measurements were performed on an ESCALAB 220iXL (Thermo Fisher Scientific) with monochromated Al Kα radiation (E = 1486.6 eV). Samples are prepared on a stainless steel holder with conductive double sided adhesive carbon tape. The electron binding energies were obtained with charge compensation using a flood electron source and referenced to the C1s core level of adventitious carbon at 284.8 eV (C-C and C-H bonds). For quantitative analysis, the peaks were deconvoluted with Gaussian-Lorentzian curves using the software Unifit 2017. The peak areas were normalized by the transmission function of the spectrometer and the element specific sensitivity factor of Scofield.[226]

4.3 Procedure for Catalyst Preparation

For the catalyst preparation we followed a procedure published by some of us.[164] In order to obtain 1 g of the final catalytically active material, 94 mg of $Fe(OAc)_2$ (0.5 mmol) were dissolved in 20 mL of absolute ethanol. Then, 291 mg of Phen (1.5 mmol) were added and the as obtained brown solution was stirred at 60 °C for 2 hours. Subsequently, the support (Vulcan® XC-72R, Aerosil OX 50 or MgO, 615 mg) was added portion wise. The heterogeneous mixture was maintained under stirring for 18 h at room temperature (23 °C). Then, ethanol was carefully removed by rotary evaporation and the solid material was dried for at least 4 hours under vacuum. The as obtained solid was transferred into a crucible equipped with lid and placed in the pyrolysis chamber of an AUSTROMAT 264 pyrolytic oven. The oven was heated to 800 °C for 2 h (temperature ramp of 25 K/min) flushing 10 $mL\cdot min^{-1}$ of Ar. Once the heating was stopped, the chamber was allowed to cool down to room temperature (Ar was flushed until the temperature reached 50 °C). The as obtained catalysts are referred as Fe/Phen@C-800, Fe/Phen@SiO_2-800, and Fe/Phen@MgO-800 respectively in the whole text.

By using the same procedure, catalyst without the addition of either Phen or $Fe(OAc)_2$ were prepared (they are referred to as Fe@C-800 and Phen@C-800, respectively).

4.4 Procedure for Catalytic Reactions and Product Isolation

In a typical catalytic reaction, the catalyst (18.5 mg) was placed in an oven dried Schlenk tube which was evacuated and backfilled with nitrogen. Solvent (2mL) was added followed by α-methyl styrene (2.50 mmol) and a stock solution of EDA (0.5 mmol, 1 mL, [EDA] = 0.5 M,). The mixture was then heated at 60 ^{o}C and stirred for 4 hours under a N_2 atmosphere. Once the reaction was completed, the internal standard (2,4-dinitrotoluene) was added the catalyst was removed by filtration over Celite. The solvent was evaporated, the crude mixture dissolved in $CDCl_3$ and analyzed by means of NMR and IR spectroscopy to determine conversion, yield and diastereomeric ratio. Isolated compounds were obtained by purification by column chromatography on silica gel. In the following, all compounds have been drawn as a single enantiomer for simplicity, but they are obviously racemic mixtures.

4.5 Procedure for Catalyst Recycling and Regeneration

After completion of the reaction, the reaction mixture was completely transferred to a centrifuge tube and the spent catalyst was separated by centrifugation at 6000 rpm for 5-10 minutes. Isolated solid material was washed with dichloromethane (3x10 mL), separated by centrifugation again, dried under vacuum (8 h) and used for another cycle under the reaction conditions described in section 4.4.

The thermal reactivation of the spent catalyst was performed under dinitrogen for 3 h at 300 or 400 °C.

Oxidative reactivation was performed using H_2O_2. Specifically, the spent catalyst was stirred with an aqueous solution of H_2O_2 (3 %) at room temperature for 16 h. Afterwards, the mixture was centrifuged (6000 rpm for 5-10 minutes) and the isolated solid was washed with distilled water (3x10 mL), dried for 8 h under vacuum and reused in a catalytic run.

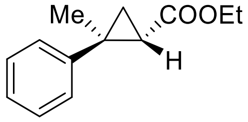
The spent and regenerated catalysts are referred as Fe/Phen@C-800_S and Fe/Phen@C-800_R, respectively.

	C [wt.%]	H [wt.%]	N [wt.%]	Fe [wt.%]
Fe/Phen@C-800	64.77	0.45	3.85	2.95
Fe/Phen@C-800_S	61.31	3.23	1.35	2.07
Fe/Phen@C-800_R	50.65	3.02	0.76	2.27
Fe/Phen@MgO-800	19.03	0.13	0.84	3.31
Fe/Phen@SiO_2-800	20.97	0.08	1.09	3.77

Table 4.1: Elemental compositions of the fresh, deactivated and reactivated Fe-based catalysts based on CHN and AAS Fe analysis.

4.6 Characterization of the Reaction Products

trans-Ethyl 2-methyl-2-phenylcyclopropane-1-carboxylate (2a)



trans-

Only the trans isomer was isolated in a pure form.

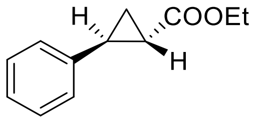
Obtained as colorless oil after column chromatography (eluent hexane + 0.2 % AcOEt). Yield 68%.

^{1}H NMR (400 MHz $CDCl_3$) δ 7.30 (d, J = 4.3 Hz, 4H), 7.24 – 7.18 (m, 1H), 4.20 (qd, J = 7.1, 2.6 Hz, 2H), 2.04 – 1.92 (m, 1H), 1.53 (s, 3H), 1.43 (dq, J = 8.3, 4.7 Hz, 2H), 1.30 ppm (t, J = 7.1 Hz, 3H).

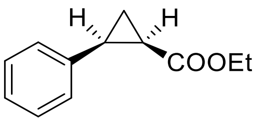
^{13}C NMR (101 MHz, $CDCl_3$) δ 172.17, 145.93, 128.43, 127.29, 126.43, 60.49, 30.55, 27.88, 20.78, 19.88, 14.41 ppm.

Data are in accordance with the one reported in the literature.[227]

Ethyl 2-phenylcyclopropane-1-carboxylate (2b)



trans-



cis-

Obtained as yellow oil (trans) and colorless oil (cis) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield trans69%, cis 27% (trans:cis = 72:28).

For trans isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 7.1 Hz, 2H), 7.24 – 7.17 (m, 1H), 7.15 – 7.05 (m, 2H), 4.17 (q, J = 7.1 Hz, 2H), 2.52 (ddd, J = 9.4, 6.5, 4.2 Hz, 1H), 1.90 (ddd, J = 8.4, 5.3, 4.2 Hz, 1H), 1.67 – 1.51 (m, 1H), 1.34 – 1.30 (m, 1H), 1.28 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.40, 140.13, 128.45, 126.45, 126.17, 60.69, 26.16, 24.17, 17.04, 14.26 ppm.

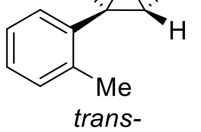
For cis isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (s, 4H), 7.22 – 7.15 (m, 1H), 3.87 (q, J = 7.1 Hz, 2H), 2.58 (q, J = 8.7 Hz, 1H), 2.08 (ddd, J = 9.1, 7.9, 5.7 Hz, 1H), 1.72 (dt, J = 7.4, 5.4 Hz, 1H), 1.33 (td, J = 8.2, 5.1 Hz, 1H), 0.97 ppm(t, J = 7.1 Hz, 3H).

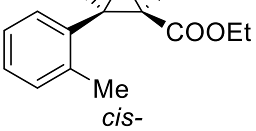
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.96, 136.57, 129.29, 127.86, 126.62, 60.15, 25.45, 21.81, 14.02, 11.10 ppm.

Data are in accordance with[228] and[229] for trans and cis isomers, respectively.

Ethyl 2-(o-tolyl)cyclopropane-1-carboxylate (2c)



trans-



cis-

Obtained as colorless oil (trans) and colorless oil (cis) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield trans 73%, cis 21% (trans:cis = 77:23).

For trans isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (tt, J = 6.4, 3.3 Hz, 3H), 7.03 – 6.96 (m, 1H), 4.20 (qd, J = 7.1, 2.4 Hz, 2H), 2.52 (ddd, J = 9.1, 6.9, 4.6 Hz, 1H), 2.39 (s, 3H), 1.84 – 1.73 (m, 1H), 1.67 – 1.52 (m, 2H), 1.30 ppm (t, J = 7.1 Hz, 4H, overlap of -CH_3 signal with that of one proton of the cyclopropane scaffold).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.90, 138.02, 137.85, 129.85, 126.71, 125.89, 125.85, 60.66, 24.64, 22.35, 19.57, 15.37, 14.34 ppm.

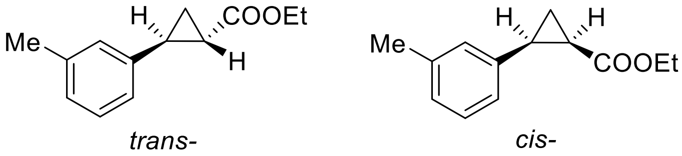
For cis isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.18 (m, 1H), 7.13 (dd, J = 5.8, 3.5 Hz, 3H), 3.85 (q, J = 7.1 Hz, 2H), 2.45 (q, J = 8.4 Hz, 1H), 2.34 (s, 3H), 2.20 – 2.10 (m, 1H), 1.75 (dt, J = 7.5, 5.2 Hz, 1H), 1.35 (td, J = 8.2, 5.0 Hz, 1H), 0.93 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.15, 129.39, 129.11, 126.76, 125.34, 60.05, 24.44, 21.16, 19.33, 13.93, 11.22 ppm.

Data are in accordance with the one reported in the literature.[227]

Ethyl 2-(m-tolyl)cyclopropane-1-carboxylate (2d)



Obtained as yellow oil (trans) and colorless oil (cis) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield trans 70%, cis 27% (trans:cis = 72:28).

For trans isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (t, J = 7.6 Hz, 1H), 7.02 (d, J = 7.5 Hz, 1H), 6.95 – 6.86 (m, 2H), 4.17 (q, J = 7.1 Hz, 2H), 2.55 – 2.43 (m, 1H), 2.33 (s, 3H), 1.96 – 1.84 (m, 1H), 1.58 (dt, J = 9.5, 4.9 Hz, 1H), 1.28 ppm (t, J = 7.1 Hz, 4H, overlap of -CH_3 signal with that of one proton of the cyclopropane scaffold).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.45, 140.07, 138.09, 128.36, 127.22, 126.99, 123.16, 60.62, 26.14, 24.10, 21.36, 16.99, 14.27 ppm.

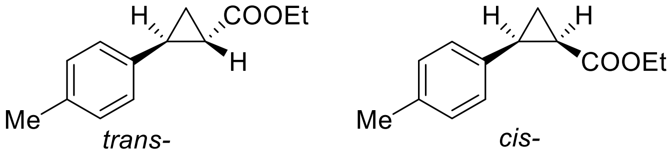
For cis isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (t, J = 7.5 Hz, 1H), 7.11 – 7.04 (m, 2H), 7.00 (d, J = 7.4 Hz, 1H), 3.89 (q, J = 7.1 Hz, 2H), 2.54 (q, J = 8.6 Hz, 1H), 2.31 (s, 3H), 2.06 (ddd, J = 9.2, 7.9, 5.7 Hz, 1H), 1.69 (dt, J = 7.4, 5.5 Hz, 1H), 1.38 – 1.22 (m, 1H), 0.98 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.02, 137.32, 136.48, 130.12, 127.75, 127.39, 126.29, 60.12, 25.40, 21.70, 21.34, 14.03, 11.10 ppm.

Data are in accordance with the one reported in the literature.[227]

Ethyl 2-(p-tolyl)cyclopropane-1-carboxylate (2e)



Obtained as colorless oil (trans) and colorless oil (cis) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield trans- 72%, cis 18% (trans:cis = 80:20).

For trans isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, J = 7.9 Hz, 2H), 7.00 (d, J = 8.0 Hz, 2H), 4.17 (q, J = 7.1 Hz, 1H), 2.50 (ddd, J = 9.7, 6.4, 4.3 Hz, 1H), 2.32 (s, 3H), 1.87 (dt, J = 9.1, 4.7 Hz, 1H), 1.58 (dt, J = 9.4, 4.7 Hz, 1H), 1.28 ppm (t, J = 7.3 Hz, 4H, overlap of -CH_3 signal with that of one proton of the cyclopropane scaffold).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.49, 137.06, 136.06, 129.13, 126.12, 60.63, 25.93, 24.05, 20.99, 16.92, 14.28 ppm.

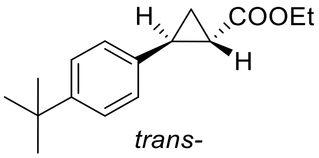
For cis isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 7.9 Hz, 2H), 7.06 (d, J = 7.9 Hz, 2H), 3.89 (q, J = 7.1 Hz, 2H), 2.54 (q, J = 8.2 Hz, 1H), 2.30 (s, 3H), 2.14 – 1.96 (m, 1H), 1.80 – 1.62 (m, 1H), 1.39 – 1.20 (m, 1H), 1.01 ppm (t, J = 7.1 Hz, 3H).

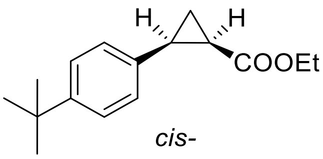
^{13}C NMR (101 MHz, $CDCl_3$) δ 129.13, 128.59, 60.14, 25.20, 21.68, 14.07, 11.19, 1.01 ppm. Three quaternary C were not detected.

Data are in accordance with the one reported in the literature.[227]

Ethyl 2-(4-(tert-butyl)phenyl)cyclopropane-1-carboxylate (2f)



trans-



cis-

Obtained as yellow oil (trans) and pale-yellow oil (cis) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield trans- 67%, cis 30% (trans:cis = 69:31).

For trans isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 8.3 Hz, 2H), 4.16 (q, J = 7.1 Hz, 2H), 2.49 (ddd, J = 9.4, 6.5, 4.2 Hz, 1H), 1.88 (ddd, J = 8.4, 5.2, 4.2 Hz, 1H), 1.58 (dt, J = 9.3, 4.9 Hz, 1H), 1.30 (s, 9H), 1.27 ppm (t, J = 7.2 Hz, 4H, overlap of $-CH_3$ signal with that of one proton of the cyclopropane scaffold).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.50, 149.46, 137.10, 125.84, 125.37, 60.62, 31.33, 25.85, 24.12, 16.95, 14.27 ppm.

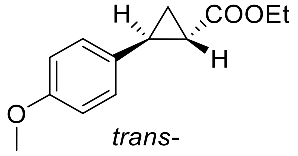
For cis isomer:

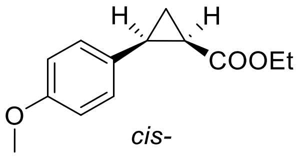
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 8.3 Hz, 2H), 7.19 (d, J = 8.2 Hz, 2H), 3.87 (qd, J = 7.1, 5.1 Hz, 2H), 2.54 (q, J = 8.6 Hz, 1H), 2.05 (ddd, J = 9.2, 7.9, 5.7 Hz, 1H), 1.69 (dt, J = 7.4, 5.4 Hz, 1H), 1.29 (s, 10H, overlap of $-C(CH_3)_3$ signal with that of one proton of the cyclopropane scaffold), 0.92 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.07, 149.39, 133.50, 128.90, 124.76, 60.09, 34.39, 31.34, 25.05, 21.84, 13.91, 11.13 ppm.

Data are in accordance with[228] and[230] for trans and cis isomer, respectively.

Ethyl 2-(4-methoxyphenyl)cyclopropane-1-carboxylate (2g)





Obtained as white crystalline solid (trans) and light yellow solid (cis) after column chromatography (eluent hexane + 3 % AcOEt). Yield trans 69%, cis- 19% (trans:cis = 78:22).

For trans isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, J = 8.7 Hz, 2H), 6.82 (d, J = 8.7 Hz, 2H), 4.16 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 2.48 (ddd, J = 10.3, 6.5, 4.2 Hz, 1H), 1.82 (dt, J = 9.2, 4.7 Hz, 1H), 1.55 (dt, J = 9.6, 4.9 Hz, 1H), 1.28 (t, J = 7.2 Hz, 3H), 1.24 ppm (dd, J = 5.2, 3.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.63, 158.34, 132.12, 127.40, 113.94, 60.69, 55.37, 25.68, 23.92, 16.80, 14.32 ppm.

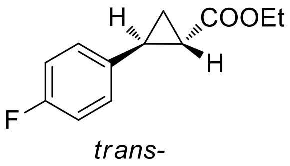
For cis isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, J = 8.4 Hz, 2H), 6.80 (d, J = 8.7 Hz, 2H), 3.89 (q, J = 7.1 Hz, 2H), 3.77 (s, 3H), 2.52 (q, J = 8.6 Hz, 1H), 2.03 (ddd, J = 9.1, 7.9, 5.6 Hz, 1H), 1.65 (dt, J = 7.4, 5.4 Hz, 1H), 1.39 – 1.18 (m, 1H), 1.01 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.11, 158.30, 130.26, 128.55, 113.31, 60.16, 55.19, 24.85, 21.70, 14.11, 11.27 ppm.

Data are in accordance with[228] and[229] for trans and cis isomer, respectively.

trans-Ethyl 2-(4-fluorophenyl)cyclopropane-1-carboxylate (2h)



Only trans isomer was isolated in the pure form.

Obtained as colorless oil (eluent hexane + 0.2 % AcOEt). Yield trans 70%.

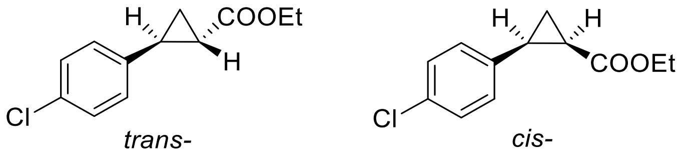
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (d, J = 8.7 Hz, 2H), 6.96 (d, J = 8.7 Hz, 2H), 4.17 (q, J = 7.1 Hz, 2H), 2.50 (ddd, J = 9.8, 6.4, 4.4 Hz, 1H), 1.98 – 1.79 (m, 1H), 1.58 (m, J = 5.1 Hz, 1H), 1.28 ppm (t, J = 7.2 Hz, 4H, overlap of -CH_3 signal with that of one proton of the cyclopropane scaffold).

^{13}C NMR (75 MHz, $CDCl_3$) δ 173.67, 163.59, 160.35, 136.12, 128.21, 128.10, 115.81, 115.53, 61.17, 25.83, 24.41, 17.30, 14.66 ppm.

^{19}F NMR (282 MHz, $CDCl_3$) δ -116.71 ppm.

Data are in accordance with the one reported in the literature.[228]

Ethyl 2-(4-chlorophenyl)cyclopropane-1-carboxylate (2i)



Obtained as colorless oils (transand cis) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield trans- 73%, cis- 23% (trans-:cis- = 76:24).

For trans isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, J = 8.5 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 4.17 (q, J = 7.1 Hz, 2H), 2.49 (ddd, J = 9.5, 6.4, 4.2 Hz, 1H), 1.86 (ddd, J = 8.5, 5.3, 4.3 Hz, 1H), 1.66 – 1.56 (m, 1H), 1.28 ppm (t, J = 7.1 Hz, 4H, overlap of -CH_3 signal with that of one proton of the cyclopropane scaffold).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.11, 138.64, 132.18, 128.55, 127.57, 60.80, 25.48, 24.15, 16.98, 14.11 ppm.

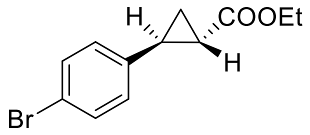
For cis isomer:

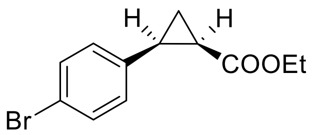
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (q, J = 8.5 Hz, 4H), 3.90 (q, J = 7.1 Hz, 2H), 2.52 (q, J = 8.6 Hz, 1H), 2.08 (ddd, J = 9.1, 8.0, 5.7 Hz, 1H), 1.67 (dt, J = 7.4, 5.4 Hz, 1H), 1.34 (td, J = 8.3, 5.1 Hz, 1H), 1.02 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.74, 135.10, 132.41, 130.62, 128.02, 60.32, 24.80, 21.83, 14.09, 11.32 ppm.

Data are in accordance with the one reported in the literature.[229]

Ethyl 2-(4-bromophenyl)cyclopropane-1-carboxylate (2j)


trans-


cis-

Obtained as white crystalline solid (trans) and colorless oil (cis) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield trans- 72%, cis- 11% (trans:cis = 86:14).

For trans isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.5 Hz, 2H), 6.97 (d, J = 8.5 Hz, 2H), 4.17 (q, J = 7.1 Hz, 2H), 2.47 (ddd, J = 10.2, 6.4, 4.2 Hz, 1H), 1.86 (ddd, J = 8.6, 5.3, 4.3 Hz, 1H), 1.69 – 1.41 (m, 1H, overlapping with proton derived from water traces), 1.28 ppm (t, J = 7.1 Hz, 4H, overlap with one proton of the cyclopropane scaffold).

^{13}C NMR (101 MHz, CDCl3) δ 173.11, 139.19, 131.50, 127.94, 120.14, 60.83, 25.56, 24.17, 17.00, 14.25 ppm.

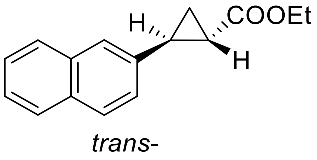
For cis isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.3 Hz, 2H), 3.90 (q, J = 7.1 Hz, 2H), 2.50 (q, J = 8.6 Hz, 1H), 2.08 (ddd, J = 9.1, 8.0, 5.7 Hz, 1H), 1.67 (dt, J = 7.4, 5.4 Hz, 1H), 1.34 (td, J = 8.2, 5.2 Hz, 1H), 1.02 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.16, 136.02, 131.40, 131.36, 120.92, 60.76, 25.29, 22.21, 14.49, 11.71 ppm.

Data are in accordance with the one reported in the literature.[228]

trans-Ethyl 2-(naphthalen-2-yl)cyclopropane-1-carboxylate (2k)



Only trans isomer was isolated in the pure form.

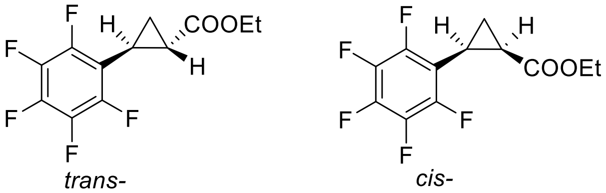
Obtained as colorless oil after column chromatography (eluent: hexane + 0.2 % AcOEt). Yield 64 %.

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.79 (t, J = 9.0 Hz, 3H), 7.58 (s, 1H), 7.52 – 7.39 (m, 1H), 7.22 (dd, J = 8.5, 1.5 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 2.71 (ddd, J = 9.5, 6.5, 4.3 Hz, 1H), 2.17 – 1.88 (m, 1H), 1.69 (dt, J = 9.6, 4.9 Hz, 1H), 1.44 (ddd, J = 8.4, 6.5, 4.6 Hz, 1H), 1.31 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) δ 173.77, 137.93, 133.78, 132.70, 128.57, 128.02, 127.80, 126.65, 125.88, 125.19, 124.98, 61.15, 26.81, 24.53, 17.42, 14.69 ppm.

Data are in accordance with the one reported in the literature.[231]

Ethyl 2-(perfluorophenyl)cyclopropane-1-carboxylate (2l)



Obtained as colorless oil (mixture of diasteroisomers) after column chromatography (eluent: hexane + 0.2 % AcOEt). Yield 73% (trans-:cis- = 71:29).

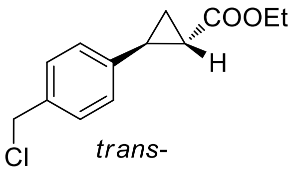
^{1}H NMR (300 MHz, CDCl$_3$) δ 4.20 (q, J = 7.1 Hz, 2H, trans), 4.06 (qd, J = 7.1, 1.9 Hz, 2H, cis), 2.45 (ddd, J = 9.6, 6.8, 5.2 Hz, 1H), 2.29 – 2.14 (m, 2H, trans+cis), 1.63 (dt, J = 9.9, 5.1 Hz, 2H, trans+cis), 1.58 – 1.47 (m, 2H, trans+cis), 1.30 (t, J = 7.1 Hz, 3H, trans), 1.19 ppm (t, J = 7.1 Hz, 3H, cis).

^{13}C NMR (75 MHz, CDCl$_3$) δ 173.11, 61.55, 61.24, 21.37, 19.33, 15.45, 15.08, 14.62, 14.48, 13.97, 13.56 ppm.

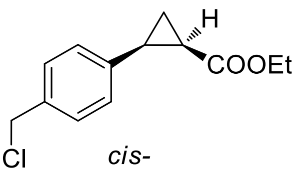
^{19}F NMR (282 MHz, $CDCl_3$) δ -141.56 (dd, J = 22.1, 7.7 Hz, cis), -143.85 (dd, J = 21.9, 7.7 Hz, trans), -156.54 (t, J = 21.0 Hz, cis), -156.78 (t, J = 21.0 Hz, trans), -162.91 (td, J = 21.8, 7.8 Hz, trans), -163.69 ppm (td, J = 22.0, 7.8 Hz, cis).

Data are in accordance with[228] and.[232]

Ethyl (2-(4-chloromethylphenyl)-2-methylcyclopropane-1-carboxylate (2m)



trans-



cis-

Obtained as colorless oil (both *trans* and *cis*) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield *trans-* 67%, *cis* 15% (*trans*:*cis* = 82:18).

For trans isomer:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, J = 8.1 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 4.56 (s, 2H), 4.17 (q, J = 7.1 Hz, 2H), 2.56 – 2.45 (m, 1H), 1.94 – 1.85 (m, 1H), 1.65 – 1.55 (m, 1H), 1.28 ppm(t, J = 7.1 Hz, 3H, overlap of -CH_3 signal with that of one proton of the cyclopropane scaffold).

^{13}C NMR (75 MHz, $CDCl_3$)δ173.39, 140.73, 135.87, 128.92, 126.69, 60.92, 46.12, 25.99, 24.42, 17.24, 14.39ppm.

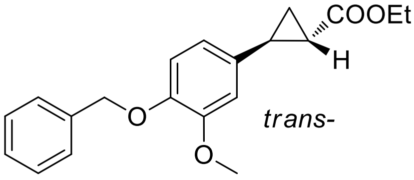
For cis isomer:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 8.5 Hz, 2H), 4.55 (s, 2H), 3.88 (qd, J = 7.1, 1.0 Hz, 2H), 2.56 (q, J = 8.5 Hz, 1H), 2.08 (ddd, J = 9.1, 7.8, 5.7 Hz, 1H), 1.74 – 1.65 (m, 1H), 1.34 (td, J = 8.2, 5.3 Hz, 1H), 0.99 ppm(t, J = 7.1 Hz, 3H).

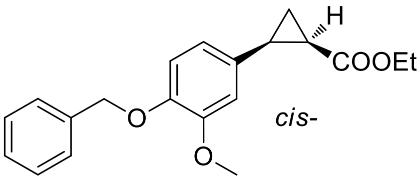
^{13}C NMR (75 MHz, $CDCl_3$) δ155.15, 137.15, 135.92, 129.81, 128.34, 60.42, 46.28, 25.31, 22.00, 14.19, 11.45ppm.

Data are in accordance with the one reported in the literature.[233]

Ethyl 2-(4-(benzyloxy)-3-methoxyphenyl)cyclopropanecarboxylate (2n)



trans-



cis-

Obtained as colorless oil (both trans and cis) after column chromatography (gradient elution hexne:AcOEt from 97:3 to 95:5). Yield trans-41%, cis 11% (trans:cis = 79:21).

For trans isomer:

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.34 (d, J = 7.2 Hz, 2H), 7.30 – 7.25 (m, 2H), 7.23 – 7.18 (m, 1H), 6.71 (d, J = 8.3 Hz, 1H), 6.59 (d, J = 2.0 Hz, 1H), 6.49 (dd, J = 8.3, 2.0 Hz, 1H), 5.04 (s, 2H),4.09 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 2.39 (ddd, J = 9.3, 6.5, 4.2 Hz, 1H), 1.76 (ddd, J = 8.5, 5.2, 4.2 Hz, 1H), 1.50 – 1.44 (m, 1H), 1.20 ppm(t, J = 7.2 Hz, 3H, overlap of -CH$_3$ signal with that of one proton of the cyclopropane scaffold).

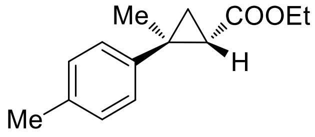
^{13}C NMR (100 MHz, CDCl$_3$) δ 173.59, 149.89, 147.10, 137.37, 133.47, 128.65, 127.93, 127.39, 118.23, 114.57, 110.83, 71.40, 60.80, 56.19, 26.10, 24.05, 16.89, 14.40 ppm.

For cis isomer:

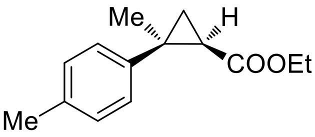
^{1}H NMR (300 MHz, CDCl$_3$) δ 7.42 (d, J = 7.1 Hz, 2H), 7.35 (t, J = 7.2 Hz, 2H), 7.29 (t, J = 6.9 Hz, 1H, overlapped with CDCl$_3$ signal), 6.82 (d, J = 1.2 Hz, 1H), 6.78 (d, J = 8.2 Hz, 1H), 6.74 (dd, J = 8.3 Hz, 1.2 Hz, 1H), 5.12 (s, 2H), 3.88 (q, J = 7.1 Hz, 2H, overlapped with -OCH$_3$signal),3.87 (s, 3H, -OCH$_3$), 2.52 (q, J = 8.6 Hz, 1H), 2.08 – 1.99 (m, 1H), 1.65 (dt, J = 7.1, 5.4 Hz, 1H), 1.29 (td, J = 8.1, 5.2 Hz, 1H), 0.98 ppm(t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 171.16, 149.32, 147.15, 137.49, 130.02, 128.63, 127.89, 127.44, 121.54, 113.83, 113.36, 71.24, 60.33, 56.13, 25.34, 22.00, 14.27, 11.46 ppm.

Ethyl (2-(4-methylphenyl)-2-methylcyclopropane-1-carboxylate (2o)



trans-



cis-

Obtained as colorless oil (both trans and cis) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield trans-67%, cis15% (trans:cis = 82:18).

For trans isomer:

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.11 (d, J = 8.1 Hz, 2H), 7.02 (d, J = 7.9 Hz, 2H), 4.11 (qd, J = 7.1, 2.7 Hz, 2H), 2.23 (s, 3H), 1.85 (dd, J = 8.3, 6.0 Hz, 1H), 1.43 (s, 3H), 1.36 – 1.27 (m, 2H), 1.21 ppm(t, J = 7.1 Hz, 3H).

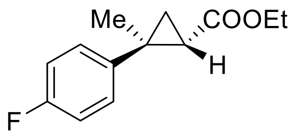
^{13}C NMR (100 MHz, CDCl$_3$) δ 172.38, 143.15, 136.15, 129.22, 127.30, 60.56, 30.41, 27.98, 21.07, 20.94, 20.07, 14.54 ppm.

For cis isomer:

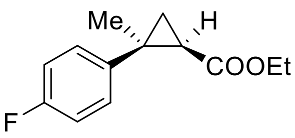
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.16 (d, J = 8.1 Hz, 2H), 7.07 (d, J = 7.9 Hz, 2H), 3.93 – 3.80 (m, 2H), 2.30 (s, 3H), 1.88 (dd, J = 7.8, 5.4 Hz, 1H), 1.75 (t, J = 5.0 Hz, 1H), 1.45 (s, 3H), 1.12 (dd, J = 7.8, 4.6 Hz, 1H), 0.99 ppm(t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 171.49, 138.99, 136.25, 129.03, 128.75, 60.22, 31.90, 28.79, 28.62, 21.24, 19.68, 14.19 ppm.

Ethyl (2-(4-fluorophenyl)-2-methylcyclopropane-1-carboxylate (2p)



trans-



cis-

Obtained as colorless oil (both trans and cis) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield trans- 70%, cis 23% (trans:cis = 76:24).

For trans isomer:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 4.19 (qd, J = 7.1, 2.5 Hz, 2H), 1.92 (dd, J = 8.4, 6.0 Hz, 1H), 1.50 (s, 3H), 1.43 (t, J = 5.3 Hz, 1H), 1.37 (dd, J = 8.4, 4.7 Hz, 1H), 1.30 ppm (t, J = 7.1 Hz, 3H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -116.67 ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.43, 163.42, 160.17, 142.15, 142.10, 129.44, 129.33, 115.73, 115.44, 60.97, 30.47, 28.16, 21.13, 20.55, 14.81 ppm.

For cis isomer:

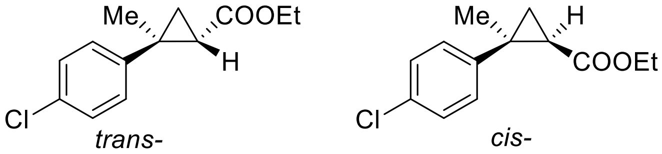
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (dd, J = 5.9, 2.7 Hz, 2H), 6.95 (t, J = 8.7 Hz, 2H), 3.86 (qq, J = 6.8, 3.7 Hz, 2H), 1.89 (dd, J = 7.8, 5.5 Hz, 1H), 1.74 (t, J = 5.0 Hz, 1H), 1.44 (s, 3H), 1.15 (dd, J = 7.8, 4.7 Hz, 1H), 0.99 ppm(t, J = 7.1 Hz, 3H).

^{19}F NMR (282 MHz, $CDCl_3$) δ -116.48 ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 130.68, 130.57, 115.53, 115.25, 60.59, 31.69, 30.10, 28.94, 20.05, 14.45 ppm. Quaternary C were not detected.

Data are in accordance with the one reported in the literature.[233]

Ethyl 2-(4-chlorophenyl)-2-methylcyclopropane-1-carboxylate (2q)



Obtained as light-yellow oil (trans) and colorless oil (cis) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield trans 71%, cis 20% (trans:cis = 78:22).

For trans isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (q, J = 8.6 Hz, 4H), 4.19 (ddq, J = 11.2, 7.1, 3.8 Hz, 2H), 1.92 (dd, J = 8.4, 6.0 Hz, 1H), 1.49 (s, 3H), 1.44 (t, J = 5.4 Hz, 1H), 1.37 (dd, J = 8.4, 4.8 Hz, 1H), 1.29 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.85, 144.43, 132.20, 128.74, 128.55, 60.59, 29.95, 27.83, 20.71, 19.80, 14.39 ppm.

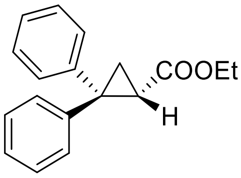
For cis isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (q, J = 8.5 Hz, 4H), 3.88 (ddq, J = 10.8, 7.1, 3.6 Hz, 2H), 1.91 (dd, J = 7.7, 5.6 Hz, 1H), 1.74 (t, J = 5.0 Hz, 1H), 1.44 (s, 3H), 1.15 (dd, J = 7.7, 4.7 Hz, 1H), 1.00 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.99, 140.44, 132.35, 130.12, 128.33, 60.22, 31.32, 28.53, 28.32, 19.55, 14.04 ppm.

Data are in accordance with the one reported in the literature.[234]

Ethyl 2,2-diphenylcyclopropane-1-carboxylate (2r)



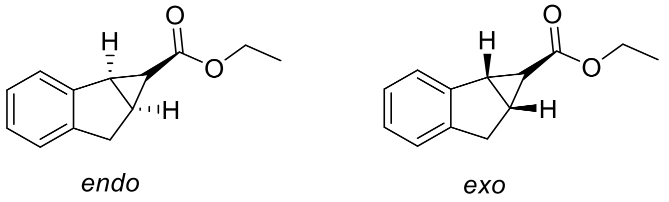
Obtained as colorless oil after column chromatography (eluent hexane + 0.2 % AcOEt). Yield 86%.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 – 7.02 (m, 10H), 4.11 – 3.75 (m, 2H), 2.57 (ddd, J = 8.1, 5.9, 0.7 Hz, 1H), 2.27 – 2.16 (m, 1H), 1.62 (dd, J = 8.2, 4.8 Hz, 1H), 1.04 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.01, 145.29, 140.67, 130.17, 128.84, 128.67, 127.99, 127.35, 126.90, 60.83, 40.21, 29.46, 20.51, 14.41 ppm.

Data are in accordance with the one reported in the literature.[233]

Ethyl 1,1a,6,6a-tetrahydrocyclopropa[a]indene-1-carboxylate (2s)



Obtained as pale yellow crystalline solid (exo) and colorless oil (endo) after column chromatography (eluent hexane + 0.2 % AcOEt). Yield exo 54%, endo 13% (endo:exo = 80:20).

For exo isomer:

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.37 – 7.31 (m, 1H), 7.19 – 7.08 (m, 3H), 4.15 (q, J = 7.1 Hz, 2H), 3.28 (dd, J = 17.5, 6.4 Hz, 1H), 3.04 (d, J = 17.7 Hz, 1H), 2.95 (d, J = 6.5 Hz, 1H), 2.44 (td, J = 6.4, 3.3 Hz, 1H), 1.27 (t, J = 7.1 Hz, 3H), 1.21 ppm (t, J = 2.8 Hz, 1H).

^{13}C NMR (75 MHz, CDCl$_3$) δ 172.75, 143.64, 141.77, 126.45, 126.33, 125.22, 123.94, 60.56, 35.36, 34.33, 30.75, 26.38, 14.29 ppm.

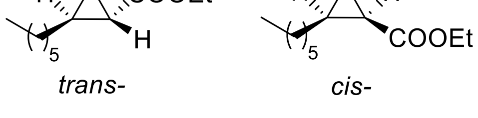
For endo isomer:

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32 – 7.28 (m, 1H), 7.12 (q, J = 3.6 Hz, 3H), 3.93 – 3.70 (m, 2H), 3.36 (d, J = 17.2 Hz, 1H), 3.23 (d, J = 6.8 Hz, 1H), 3.19 (d, J = 6.8 Hz, 1H), 3.08 – 2.82 (m, 1H), 2.27 (q, J = 6.8 Hz, 1H), 2.01 (t, J = 8.2 Hz, 1H), 0.95 ppm (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 169.57, 144.67, 139.88, 126.48, 125.98, 124.65, 123.90, 59.88, 32.43, 31.65, 24.65, 23.55, 13.95 ppm.

Data are in accordance with[235] and.[236]

Ethyl 2-hexylcyclopropane-1-carboxylate (2t)



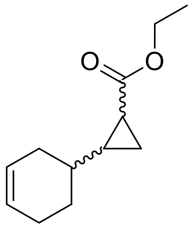
Obtained as colorless oil (mixture of trans and cis isomers) after column chromatography (eluent: hexane + 0.2 % AcOEt). Yield 69%. (trans:cis= 55:45)

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.31 – 3.97 (m, both isomers), 1.70 – 1.64 (m, 1H, cis), 1.54 – 1.19 (m, both isomers), 1.17 – 1.10 (m), 1.08 – 0.92 (m, 1H, cis), 0.90 – 0.80 (m, both isomers), 0.71 – 0.64ppm (m, 1H, trans).

^{13}C NMR (75 MHz, $CDCl_3$) δ 174.83, 60.43, 60.35, 33.21, 31.99, 31.94, 29.85, 29.77, 29.20, 29.11, 27.17, 23.11, 22.77, 22.13, 20.38, 18.39, 15.68, 14.52, 14.44, 14.23, 13.50 ppm.

Data are in accordance with the one reported in the literature.[237]

Ethyl 2-(cyclohex-3-en-1-yl)cyclopropane-1-carboxylate (2u)

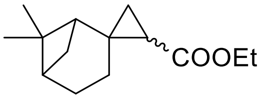


Obtained as colorless oil (mixture of 4 isomers) after column chromatography (eluent: hexane + 0.2 % AcOEt). Yield 57 %.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.64 (s, 2H), 4.12 (q, J = 7.0 Hz, 2H), 2.23 – 1.97 (m, 3H), 1.92 – 1.65 (m, 2H), 1.51 – 1.29 (m, 3H), 1.25 (t, J = 7.1, 3H), 1.19 – 1.10 (m, 1H), 1.09 – 0.95 (m, 1H), 0.81 – 0.70 ppm (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ174.71, 174.67, 127.16, 127.08, 126.36, 126.15, 60.46, 60.42, 37.75, 37.71, 31.92, 31.87, 31.69, 31.29, 31.09, 28.89, 28.80, 28.62, 28.58, 28.41, 28.17, 28.00, 27.56, 25.07, 24.96, 24.82, 19.23, 19.08, 18.19, 18.09, 14.51, 14.42, 14.40, 14.20, 12.70, 12.58 ppm.

Ethyl–6,6–dimethyl–spiro[bicycle[3.1.1]heptanes–2,1'–cyclopropane]–2'–carboxylate (2v)



Obtained as colorless oil after column chromatography (eluent: hexane + 0.2 % AcOEt). Yield 48 %.

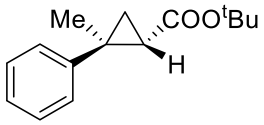
The product is a mixture of isomers. 1R,2R,2'R and 1R,2R,2'S isomers are detectable by ^{1}H and ^{13}C NMR as the major products in a ca. 58:42 ratio. ^{13}C NMR indicates the presence of two other diastereomer in minor amount. Assignment of 1R,2R,2'R and 1R,2R,2'S signals, isolated in the pure form were previously reported in the literature.[238]

Signals of the mixture are reported below indicating 1R,2R,2'R isomer as **2s-1** and 1R,2R,2'S as **2s-2**. When clearly distinguishable from the signals of the major isomers, minor isomers will be indicated as **2s-min**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.20 – 4.02 (m, 2H **2s-1** +2H **2s-2** + **2s-min**), 2.29 – 2.09 (m, 2H **2s-1** + 1H **2s-2**), 2.00 – 1.73 (m, 4H **2s-1** + 4H **2s-2**), 1.66 – 1.58 (m, 1H**2s-2**), 1.53 (d, J = 10.0 Hz, 1H**2s-2**), 1.44 (d, J = 10.0 Hz, 1H**2s-1**), 1.41 – 1.32 (m, 1H **2s-1** +1H **2s-2**), 1.30 – 1.24 (m, 4H **2s-1** +4H **2s-2**), 1.22 (s, 3H**2s-1**), 1.20 – 1.12 (m, 1H **2s-1** +4H **2s-2**), 1.04 (dd, J = 8.0, 4.5 Hz, 1H**2s-1**), 0.97 (s, 3H**2s-2**), 0.96 (s, 3H **2s-1**), 0.91 (dd, J = 8.1, 4.4 Hz, 1H**2s-2** overlapped with **2s-min**), 0.84 – 0.73 ppm (m, 1H**2s-min**).

^{13}C NMR (75 MHz, $CDCl_3$) δ 173.32 (**2s-min**), 172.91 (**2s-2**), 172.84 (**2s-1**), 60.43 (**2s-1**), 60.42 (**2s-2**), 60.35(**2s-min**), 52.97 (**2s-min**), 52.74 (**2s-2**), 45.07 (**2s-min**), 43.57 (**2s-1**), 41.22 (**2s-2**), 41.07 (**2s-1**), 40.89 (**2s-2**), 40.82 (**2s-min**), 40.69 (**2s-1**), 40.51 (**2s-min**), 40.13 (**2s-min**), 32.09 (**2s-1**), 32.02 (**2s-min**), 31.86 (**2s-min**), 31.39 (**2s-2**), 30.72 (**2s-min**), 28.69 (**2s-1**), 28.60 (**2s-min**), 28.56 (**2s-min**), 27.87 (**2s-min**), 27.11 (**2s-1**), 27.08 (**2s-2**), 26.97 (**2s-1**), 26.85 (**2s-2**), 26.68 (**2s-min**), 26.41 (**2s-2**), 26.00 (**2s-1**), 24.73 (**2s-1**), 24.61 (**2s-1**), 24.47 (**2s-min**), 24.23 (**2s-min**), 24.09 (**2s-2**), 23.73 (**2s-2**), 22.33 (**2s-2**), 22.07 (**2s-2**), 22.04 (**2s-min**),21.95 (**2s-2**),, 21.82 (**2s-min**), 21.34 (**2s-min**), 20.26 (**2s-min**), 19.65 (**2s-min**), 14.92 (**2s-min**), 14.84 (**2s-2**), 14.77 ppm (**2s-1**).

t-butyl–2–methyl–2–phenylcyclopropanecarboxylate (2aa)



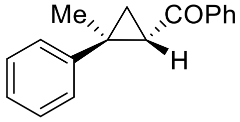
Obtained as trans isomer after column chromatography (eluent: hexane + 0.2 % AcOEt).Yield 81 %.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 4H), 7.23 – 7.16 (m, 1H), 1.90 (dd, J = 8.3, 6.1 Hz, 1H), 1.51 (s, 3H), 1.49 (s, 9H), 1.40 – 1.35 (m, 1H), 1.32 (t, J = 4.2 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.72, 146.61, 128.77, 127.54, 126.67, 80.77, 29.58, 28.69, 20.74, 20.00.

Data are in accordance with the one reported in the literature.[233]

(2-Methyl-2-phenylcyclopropyl)(phenyl)methanone (2ab)



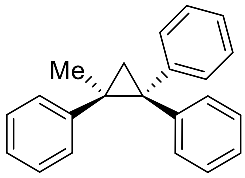
Obtained as colorless oil (onlytrans isomer)after column chromatography (eluent: hexane + 0.2 % AcOEt).Yield 71 %.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (dd, J = 8.3, 1.3 Hz, 2H), 7.61 – 7.54 (m, 1H), 7.52 – 7.45 (m, 2H), 7.42 – 7.38 (m, 4H), 7.34 – 7.25 (m, 1H), 2.93 (dd, J = 7.9, 6.2 Hz, 1H), 1.91 (dd, J = 6.1, 4.6 Hz, 1H), 1.64 (dd, J = 7.9, 4.5 Hz, 1H), 1.46 ppm (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 197.90, 146.19, 139.12, 133.16, 129.11, 129.01, 128.55, 127.07, 126.97, 34.49, 33.99, 21.35, 19.17 ppm.

Data are in accordance with the one reported in the literature.[239]

(2-Methylcyclopropane-1,1,2-triyl)tribenzene (2ac)



Obtained as white solid after column chromatography (eluent: hexane + 0.2 % AcOEt). Yield 38 %.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 – 7.57 (m, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.32 – 7.19 (m, 5H), 7.12 (ddd, J = 8.0, 6.1, 1.6 Hz, 3H), 7.07 – 6.92 (m, 3H), 2.29 (d, J = 5.2 Hz, 1H), 1.63 (d, J = 5.3 Hz, 1H), 1.44 ppm (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.12, 143.60, 143.56, 130.74, 129.95, 128.91, 128.76, 128.17, 127.90, 126.64, 126.01, 125.74, 43.35, 33.24, 26.62, 25.44 ppm.

Data are in accordance with the one reported in the literature.[240]

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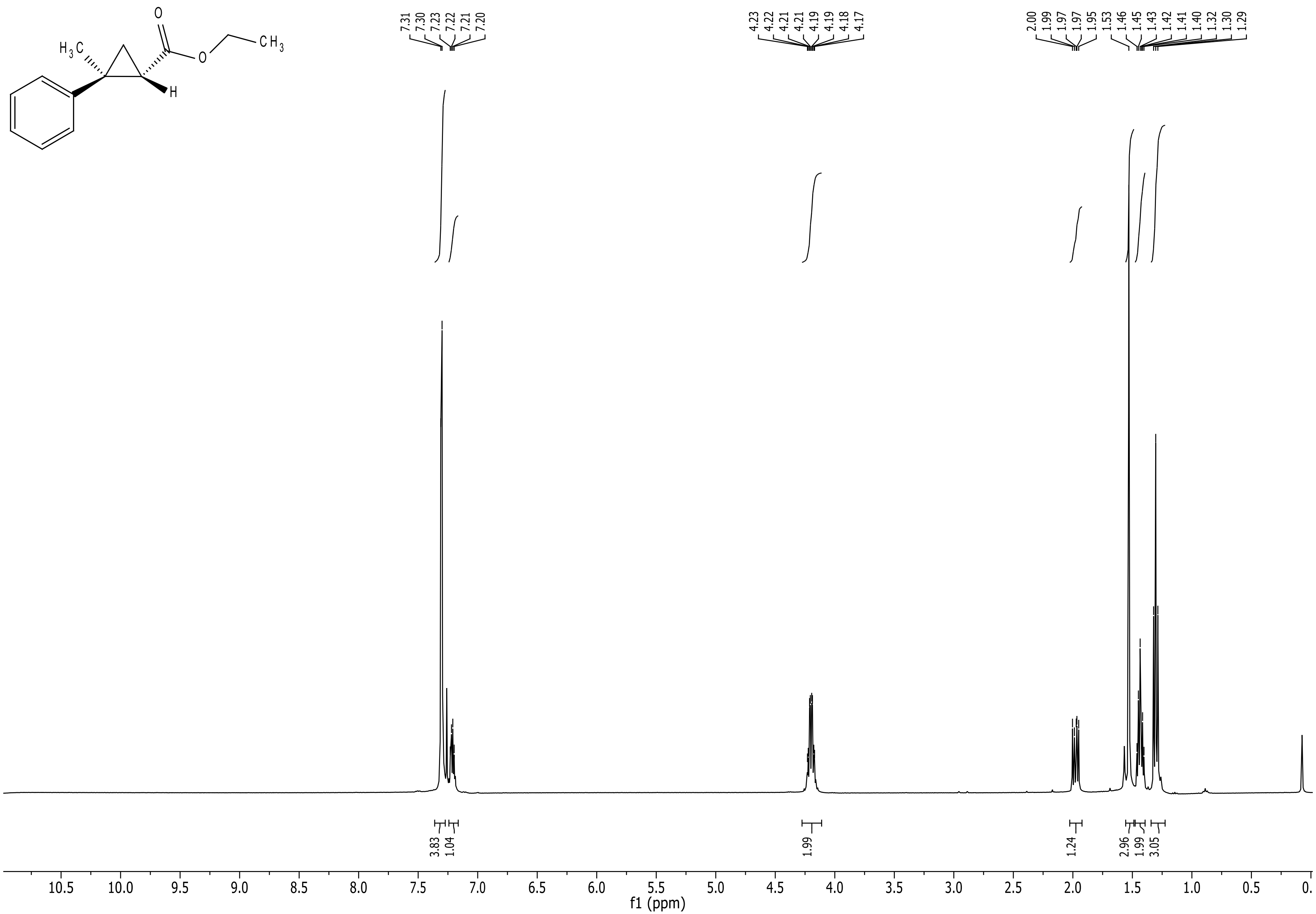
Appendices - NMR Spectra of Isolated Products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4.21
4.19
4.19
4.18
4.17
2.00
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1.97
1.97
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1.45
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1.29
3.83
1.04
1.99
1.24
2.96
1.99
3.05
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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2.0
1.5
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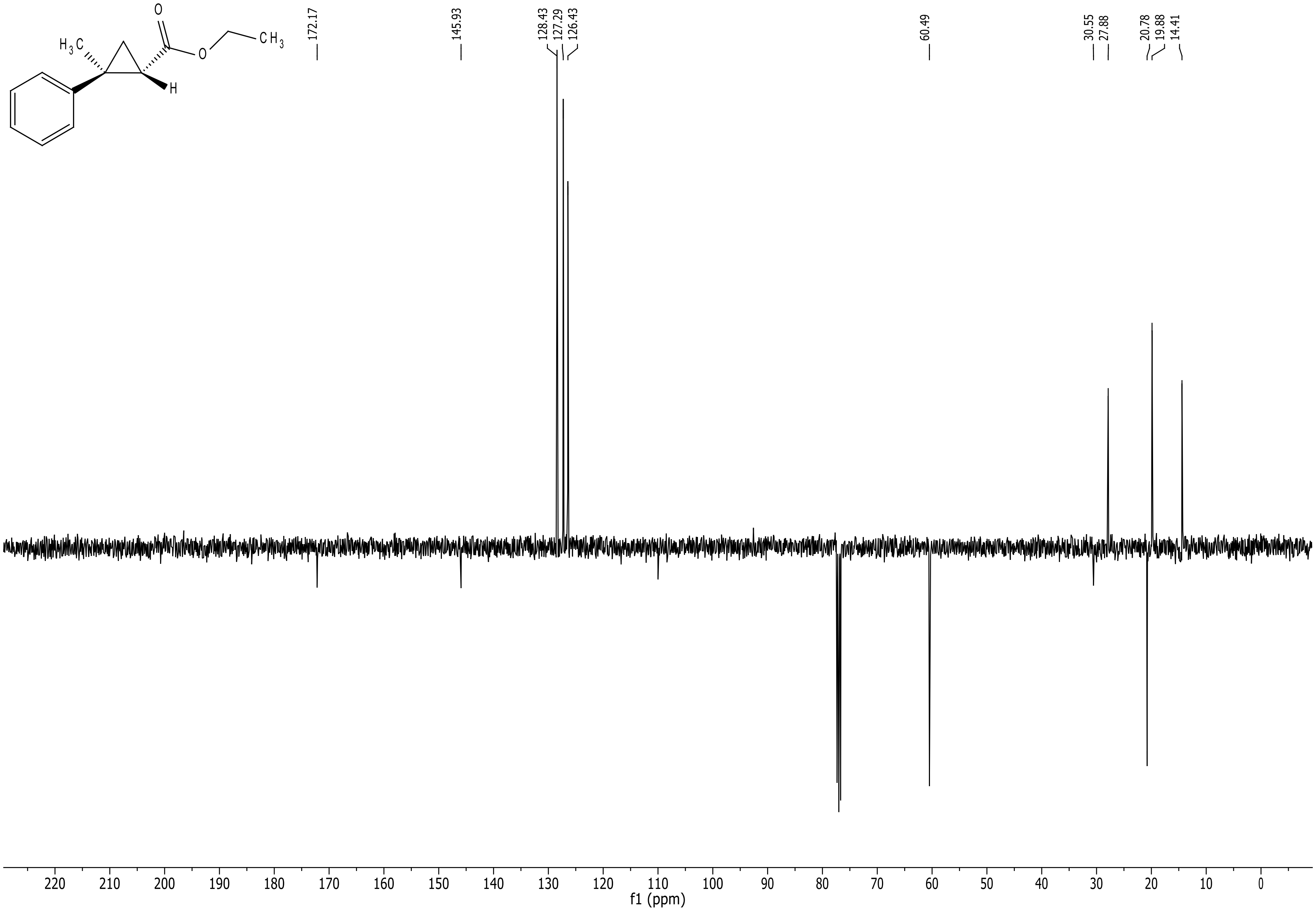
0.
f1 (ppm)



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60.49
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27.88
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19.88
14.41
H3C
O
O
CH3
H
220
210
200
190
180
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10
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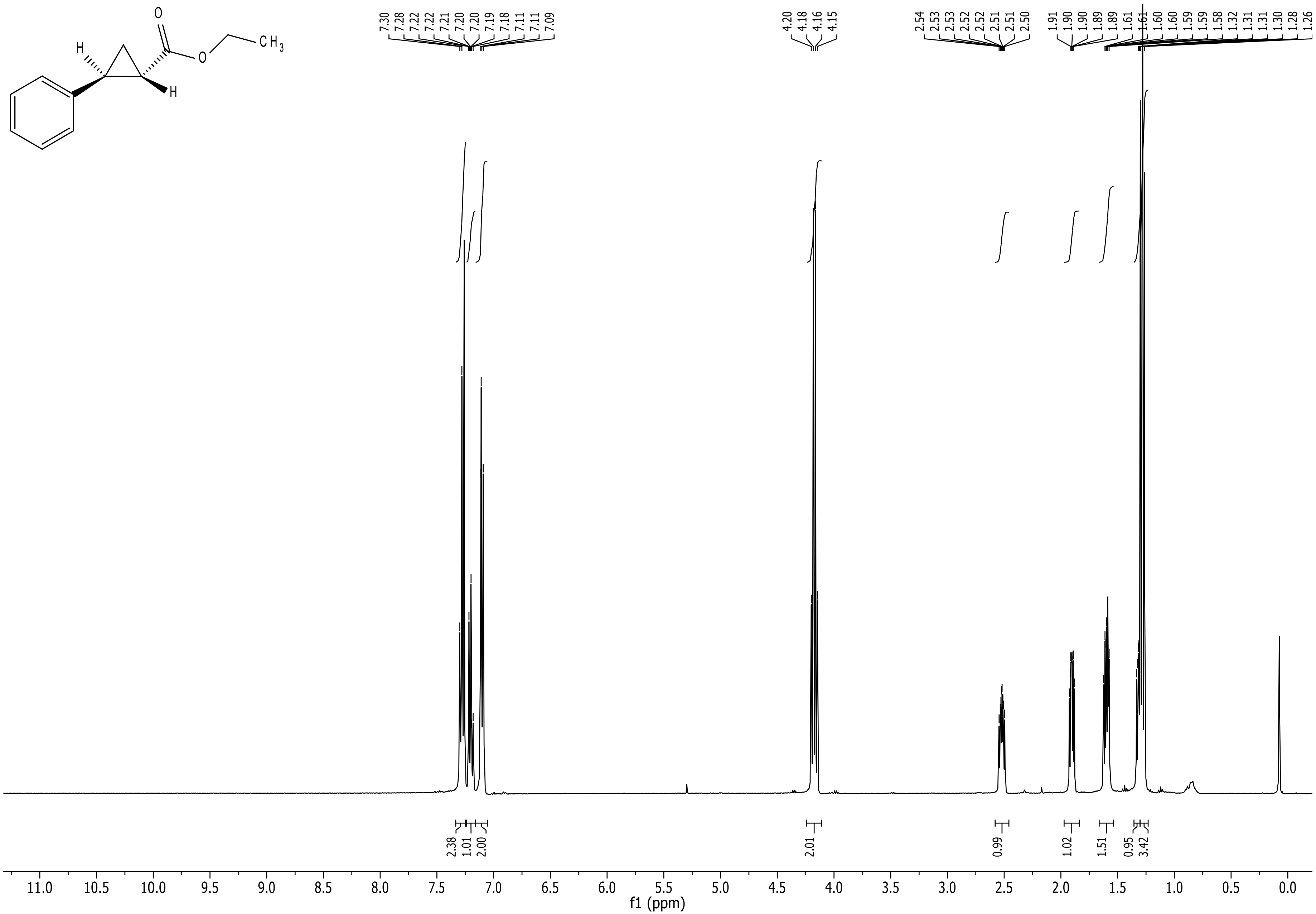
f1 (ppm)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H
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7.11
7.09
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4.16
4.15
2.54
2.53
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2.52
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1.90
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1.60
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1.59
1.58
1.32
1.31
1.31
1.30
1.28
1.26
2.38
1.01
2.00
2.01
0.99
1.02
1.51
0.95
3.42
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10.5
10.0
9.5
9.0
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8.0
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7.0
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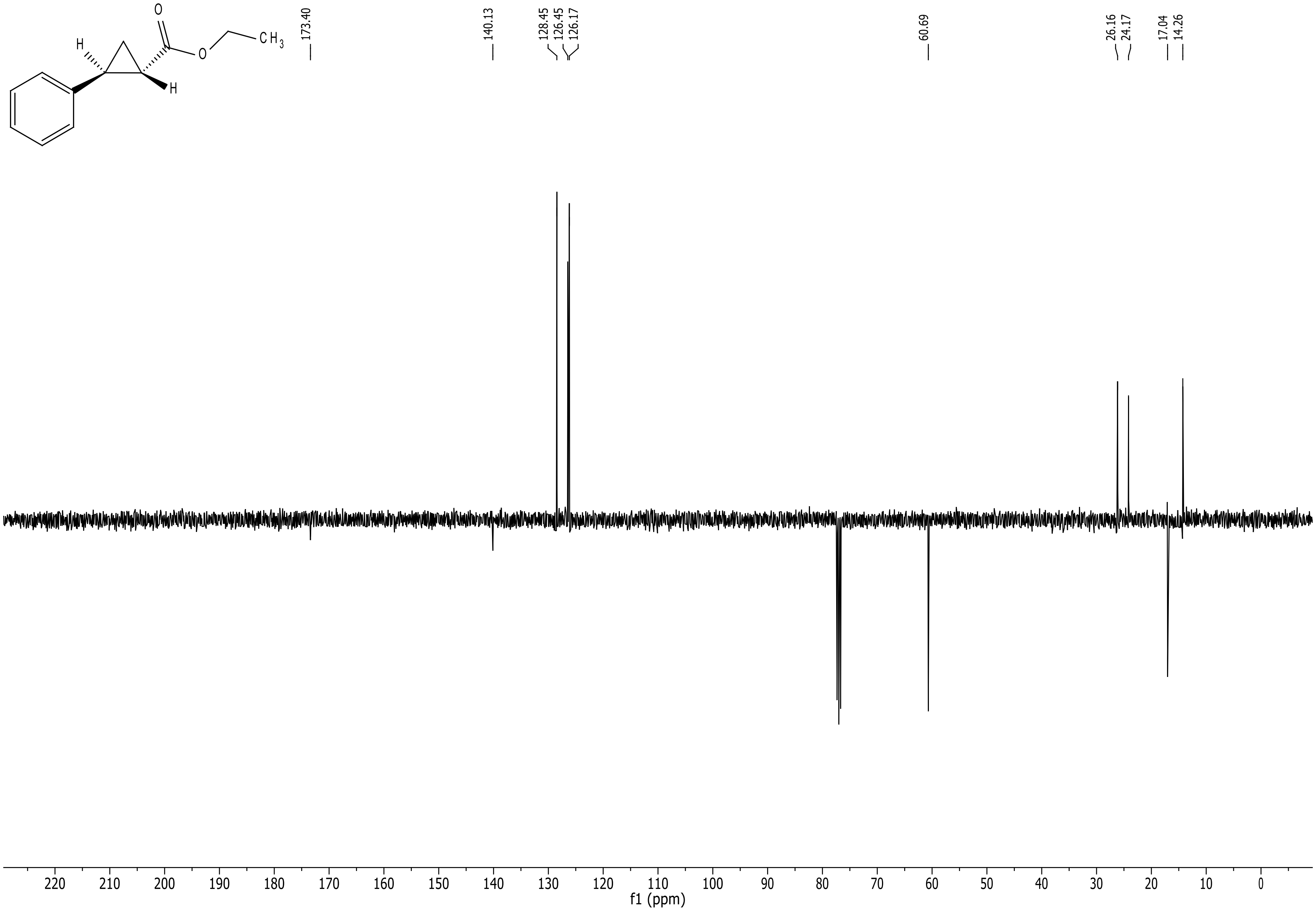
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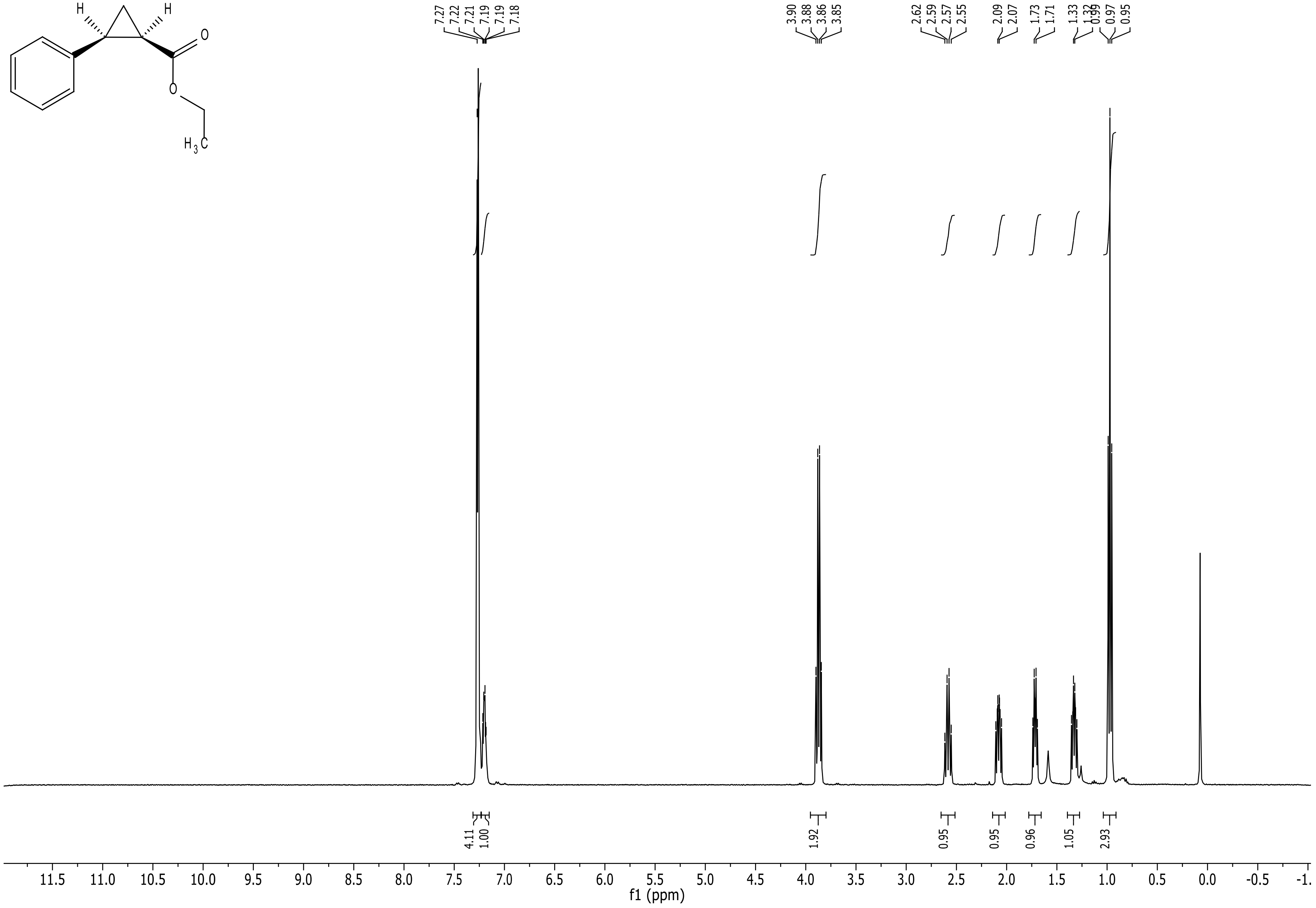
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2.59
2.57
2.55
2.09
2.07
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1.71
1.33
1.32
0.99
0.97
0.95
4.11
1.00
1.92
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0.95
0.96
1.05
2.93
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8.0
7.5
7.0
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6.0
5.5
5.0
4.5
4.0
3.5
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2.5
2.0
1.5
1.0
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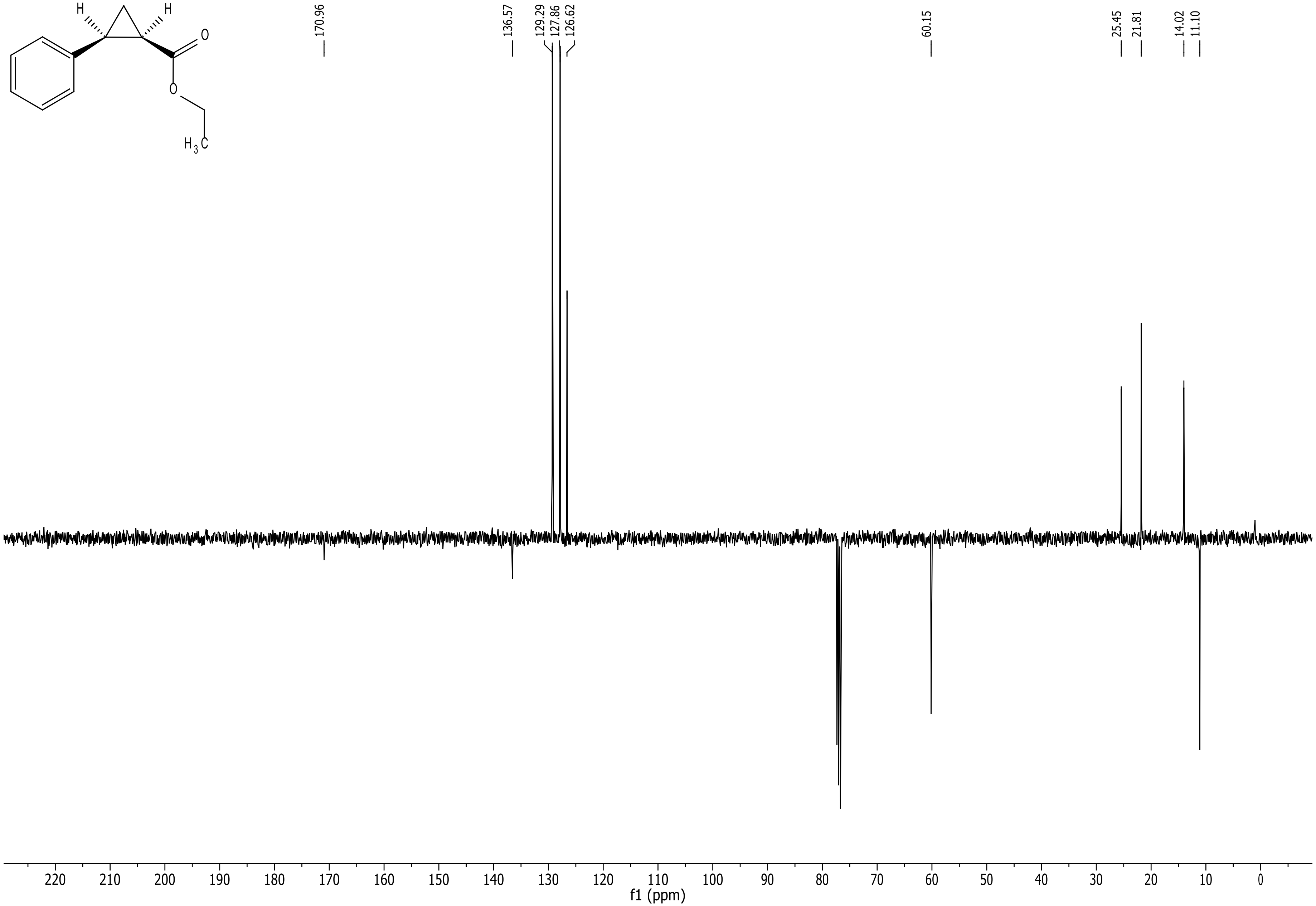
0.0
-0.5
-1.
f1 (ppm)


H
H
O
O
H3C
170.96
136.57
129.29
127.86
126.62
60.15
25.45
21.81
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11.10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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50
40
30
20
10
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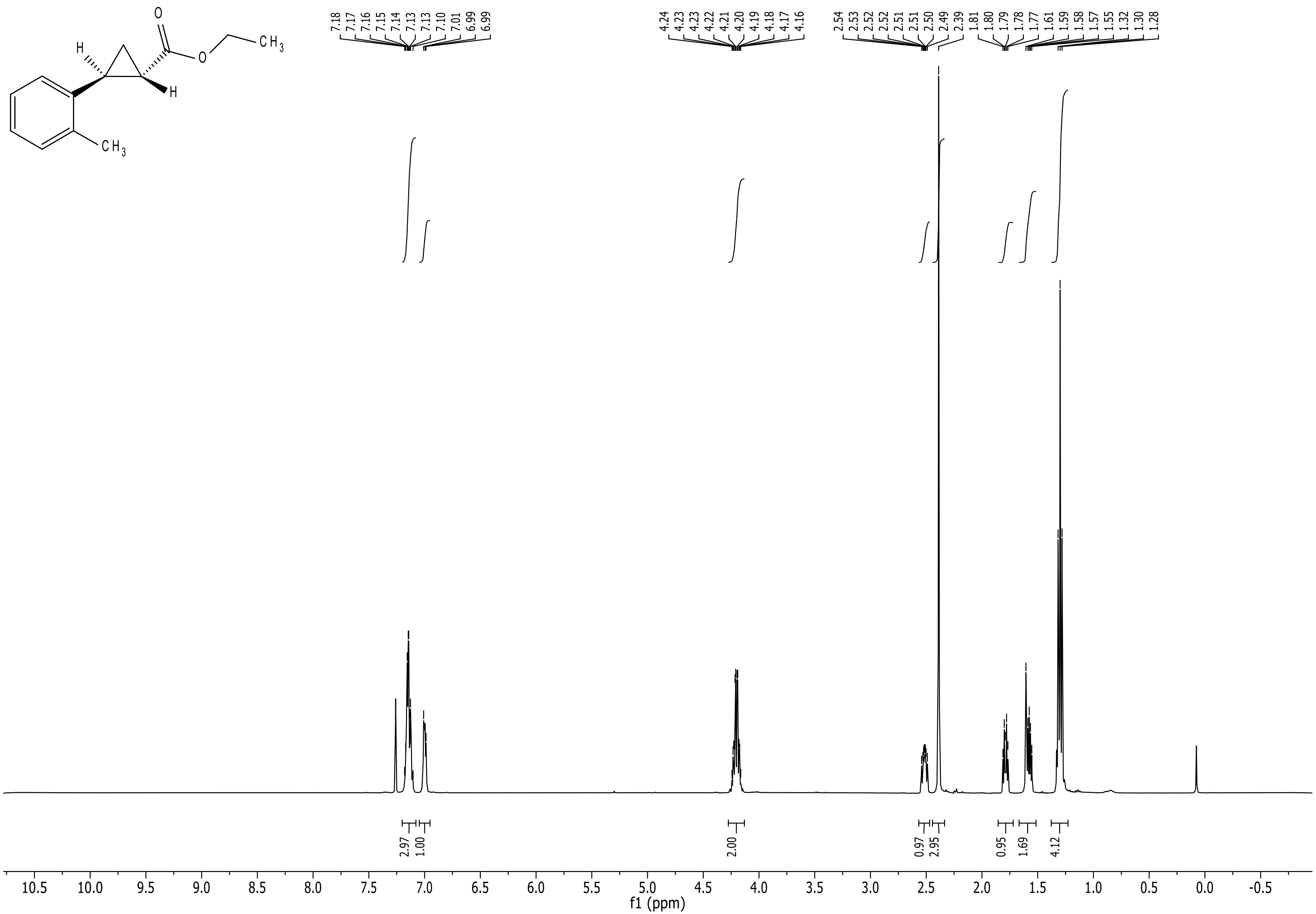
f1 (ppm)


O
O
CH3
H
H
CH3
7.18
7.17
7.16
7.15
7.14
7.13
7.13
7.10
7.01
6.99
6.99
4.24
4.23
4.23
4.22
4.21
4.20
4.19
4.18
4.17
4.16
2.54
2.53
2.52
2.52
2.51
2.51
2.50
2.49
2.39
1.81
1.80
1.79
1.78
1.77
1.61
1.59
1.58
1.57
1.55
1.32
1.30
1.28
2.97
1.00
2.00
0.97
2.95
0.95
1.69
4.12
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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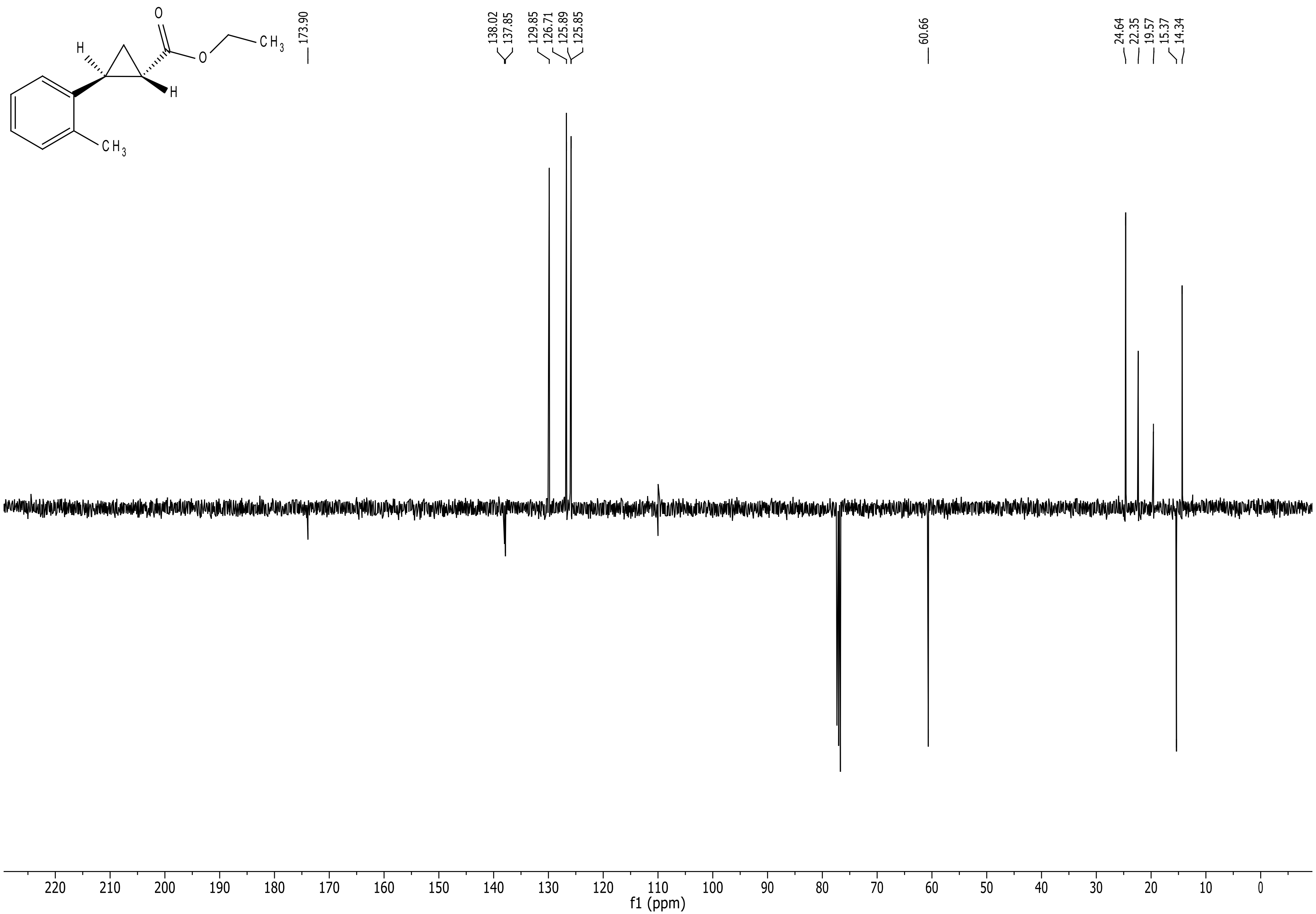
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



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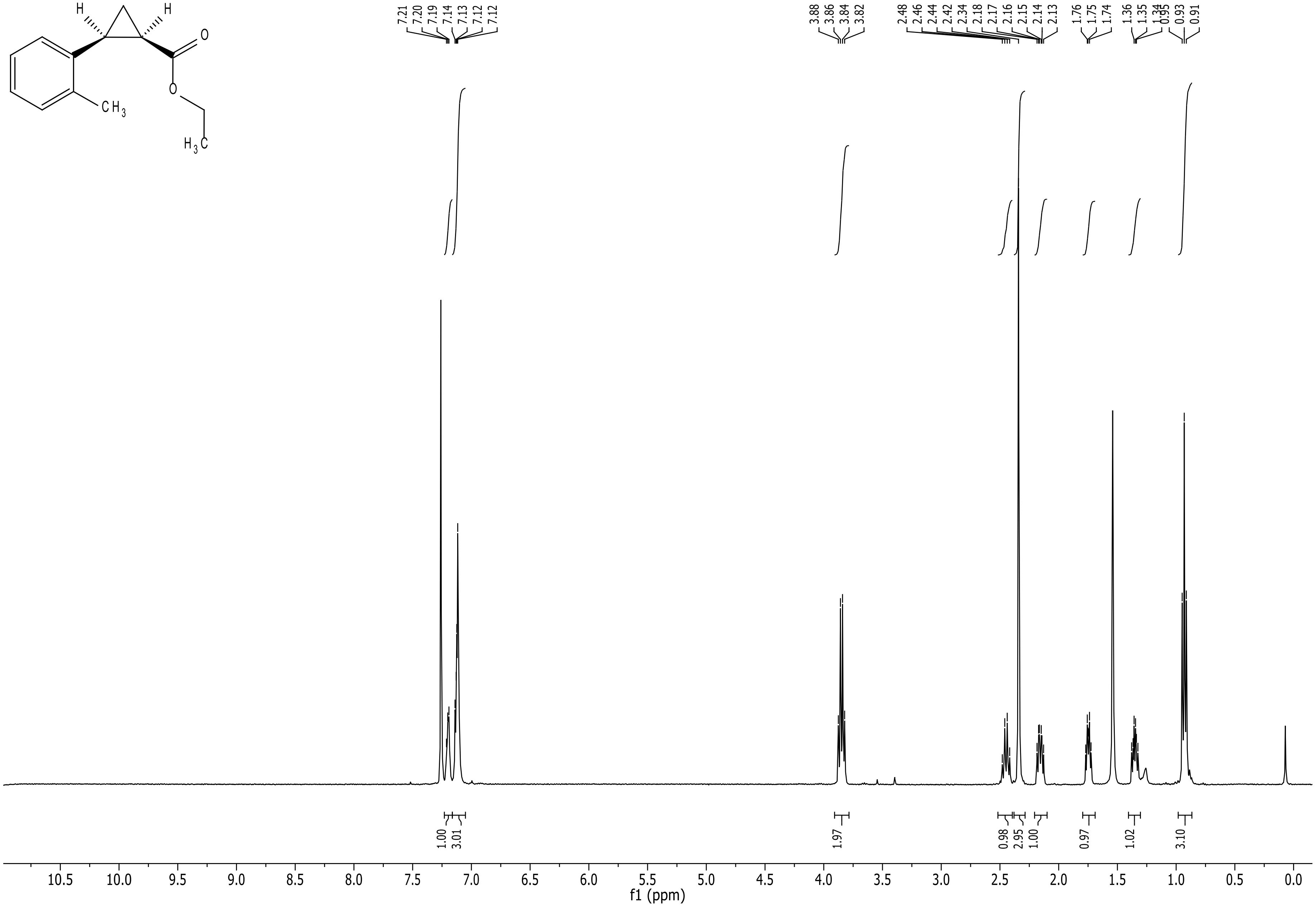
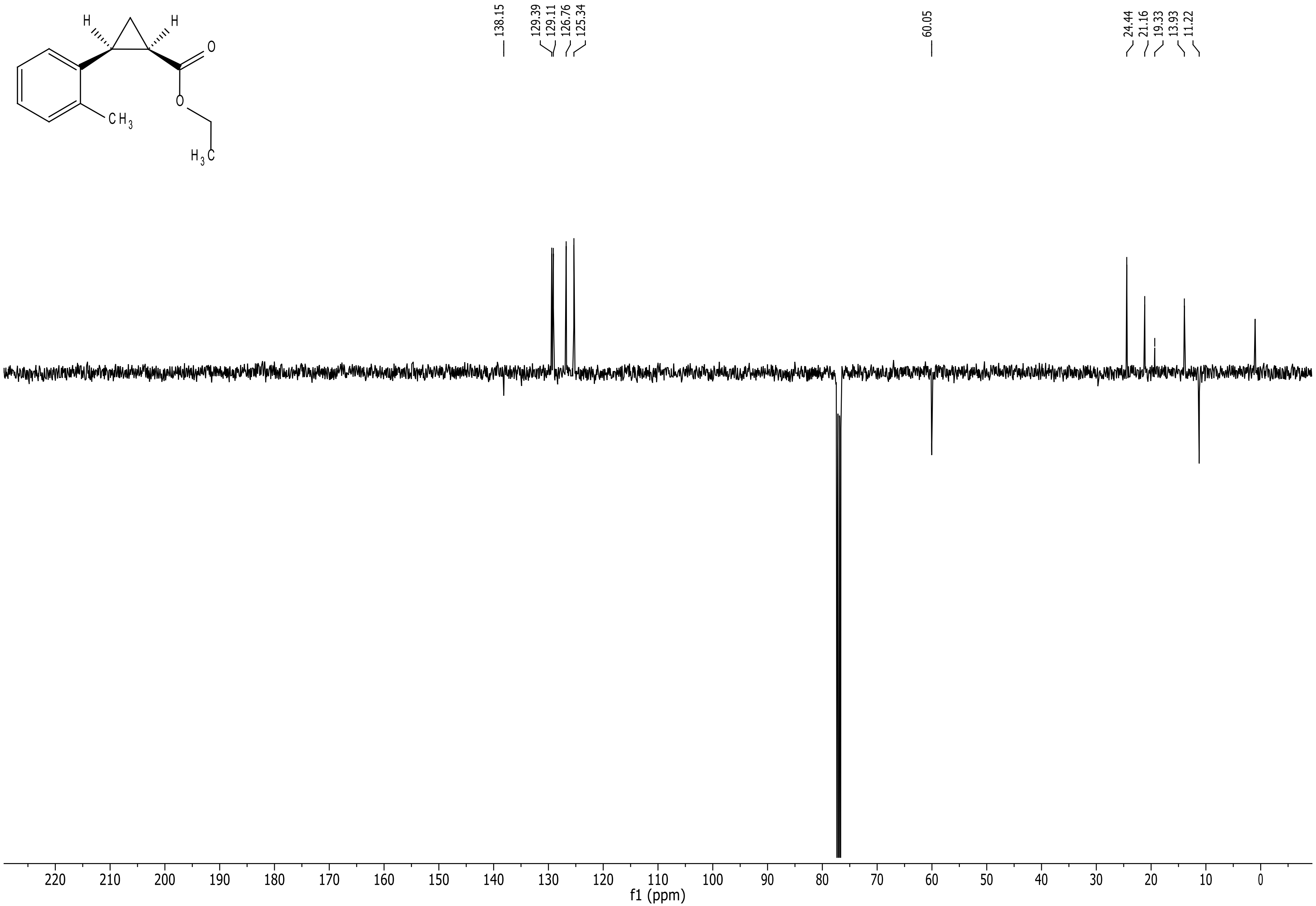
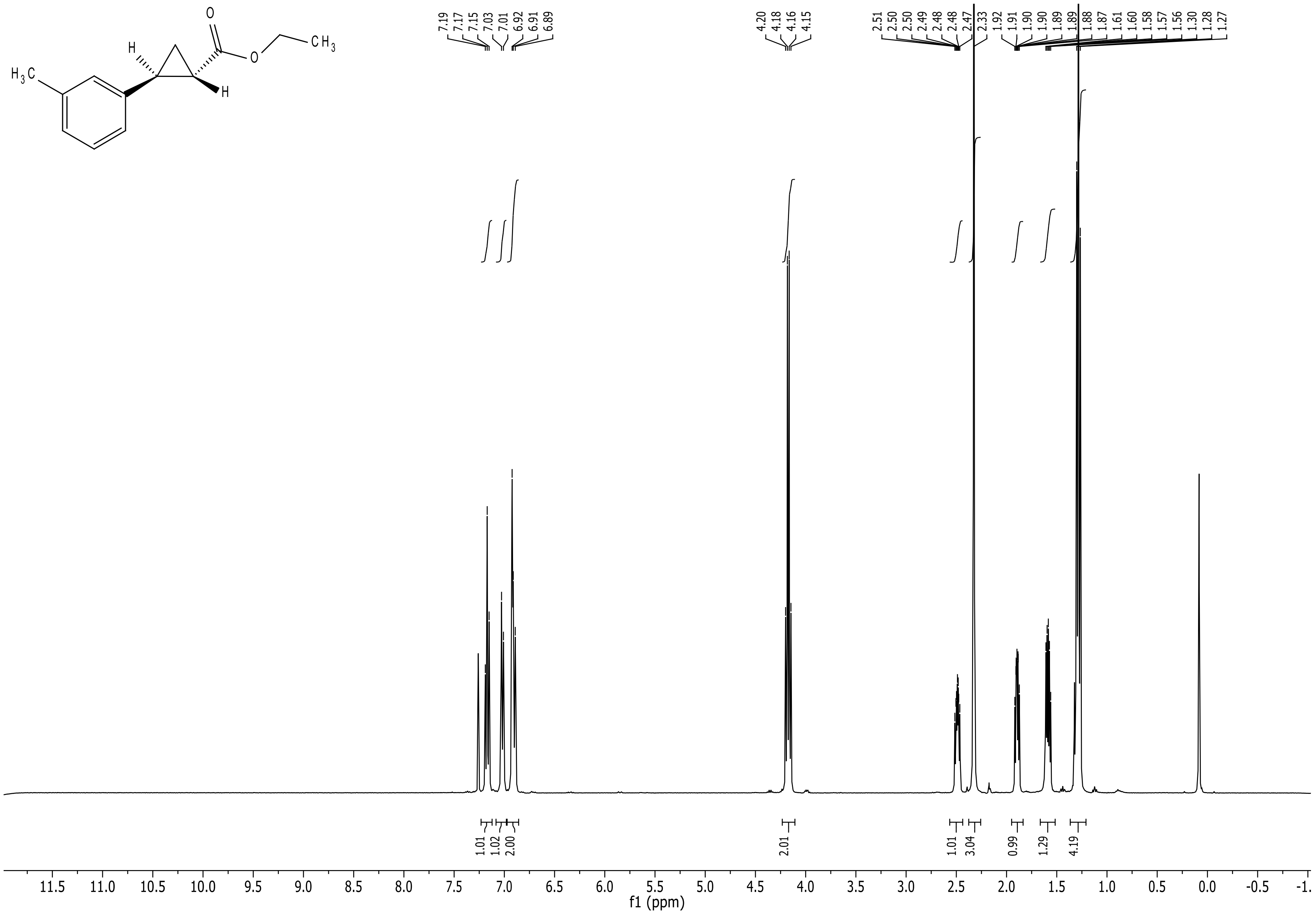
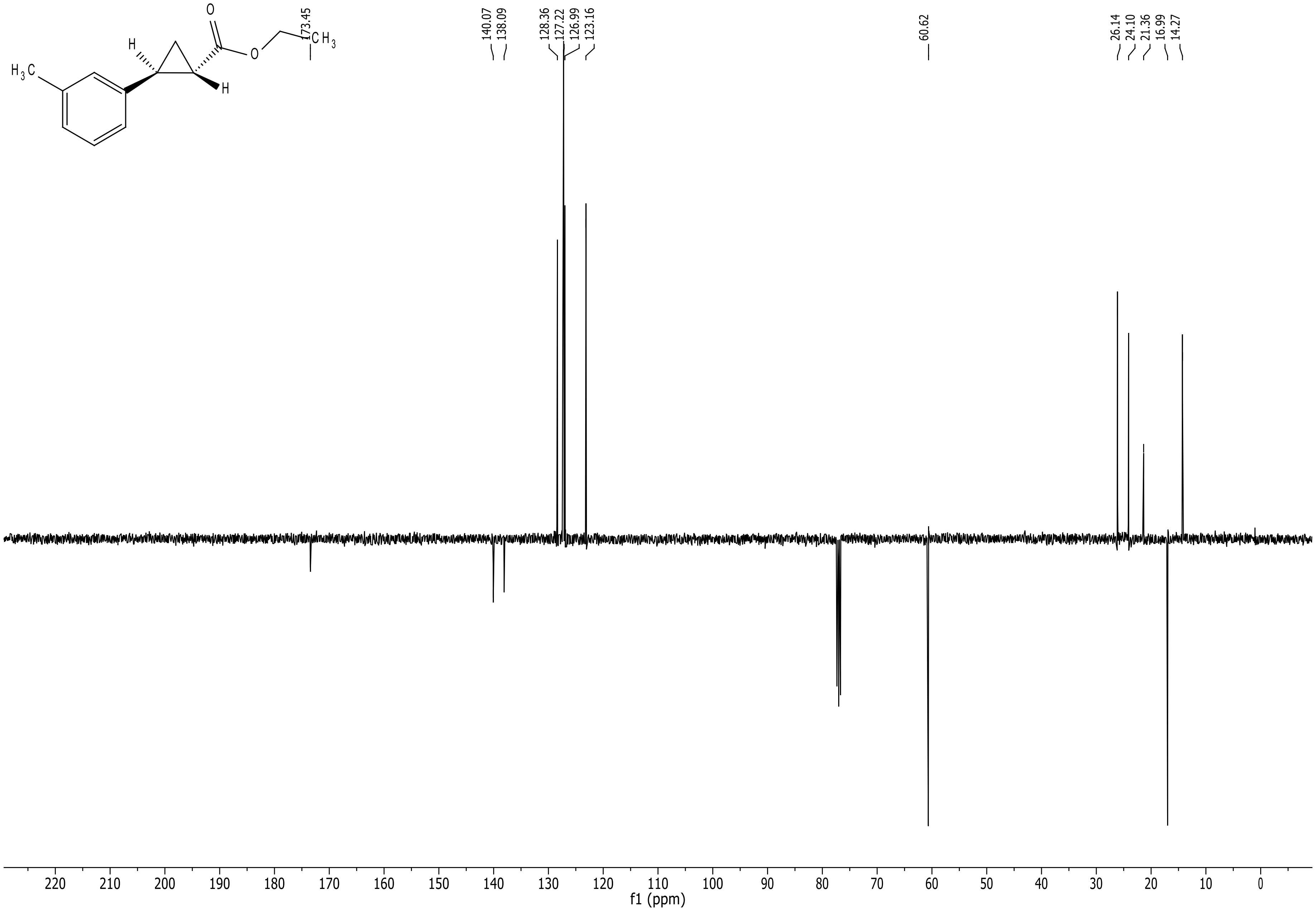
O
CH3
H
H
CH3
173.90
138.02
137.85
129.85
126.71
125.89
125.85
60.66
24.64
22.35
19.57
15.37
14.34
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

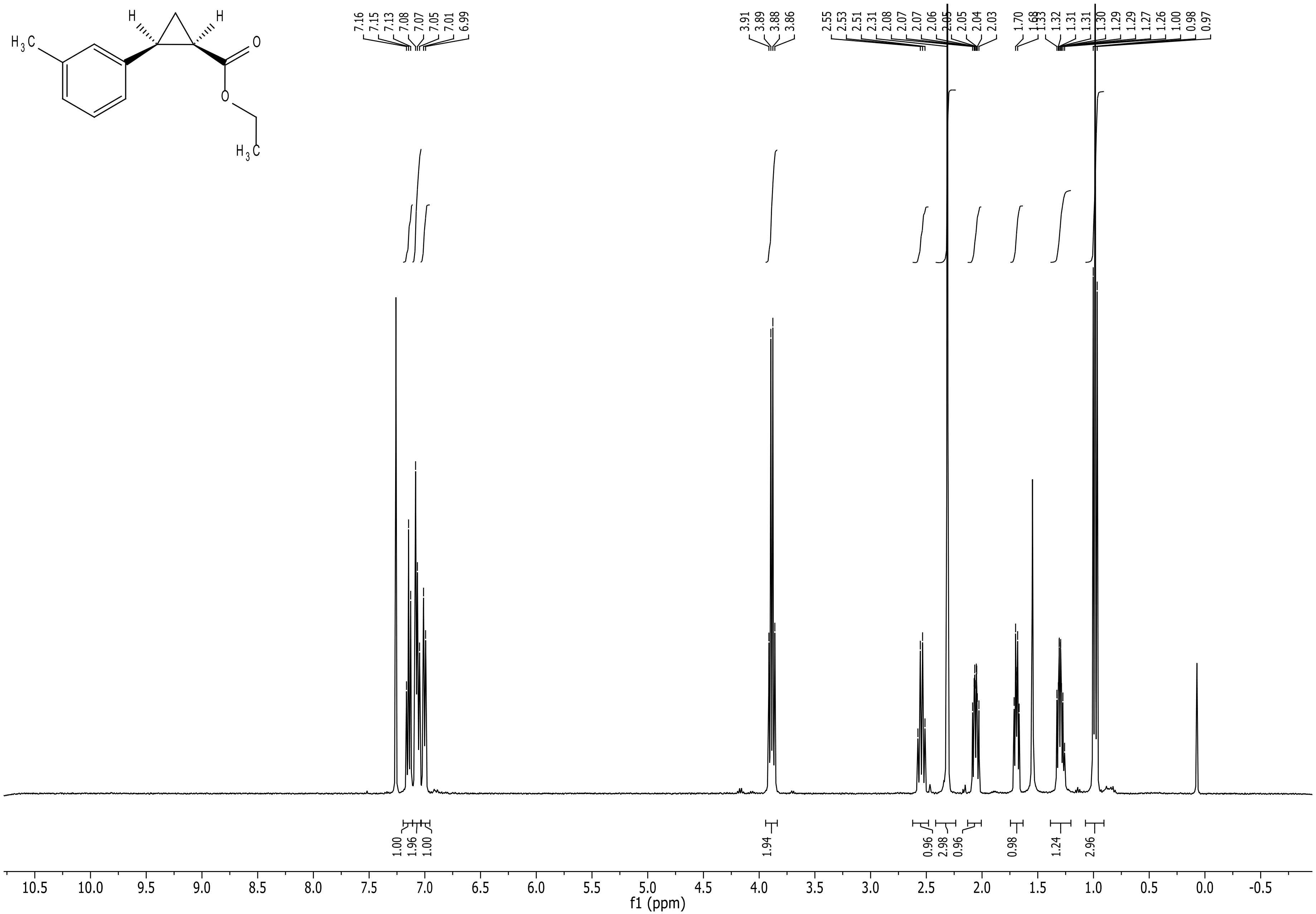

H
H
O
O
CH3
H3C
7.21
7.20
7.19
7.14
7.13
7.12
7.12
3.88
3.86
3.84
3.82
2.48
2.46
2.44
2.42
2.34
2.18
2.17
2.16
2.15
2.14
2.13
1.76
1.75
1.74
1.36
1.35
1.34
0.95
0.93
0.91
1.00
3.01
1.97
0.98
2.95
1.00
0.97
1.02
3.10
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

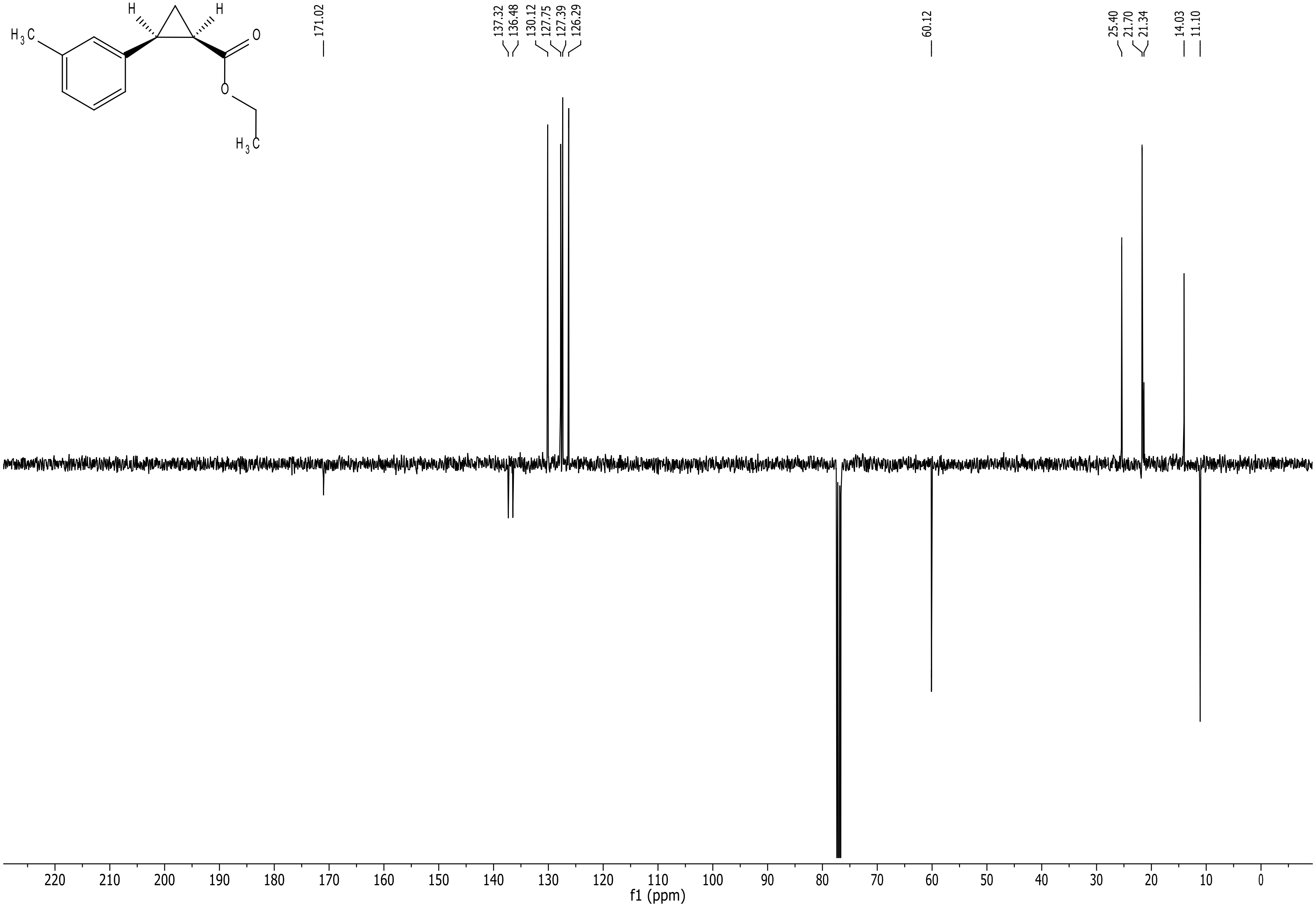

138.15
129.39
129.11
126.76
125.34
60.05
24.44
21.16
19.33
13.93
11.22
H
H
O
O
CH3
H3C
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


H
H
H3C
O
O
CH3
7.19
7.17
7.15
7.03
7.01
6.92
6.91
6.89
4.20
4.18
4.16
4.15
2.51
2.50
2.50
2.49
2.48
2.48
2.47
2.33
1.92
1.91
1.90
1.90
1.89
1.89
1.88
1.87
1.61
1.60
1.58
1.57
1.56
1.30
1.28
1.27
1.01
1.02
2.00
2.01
1.01
3.04
0.99
1.29
4.19
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)

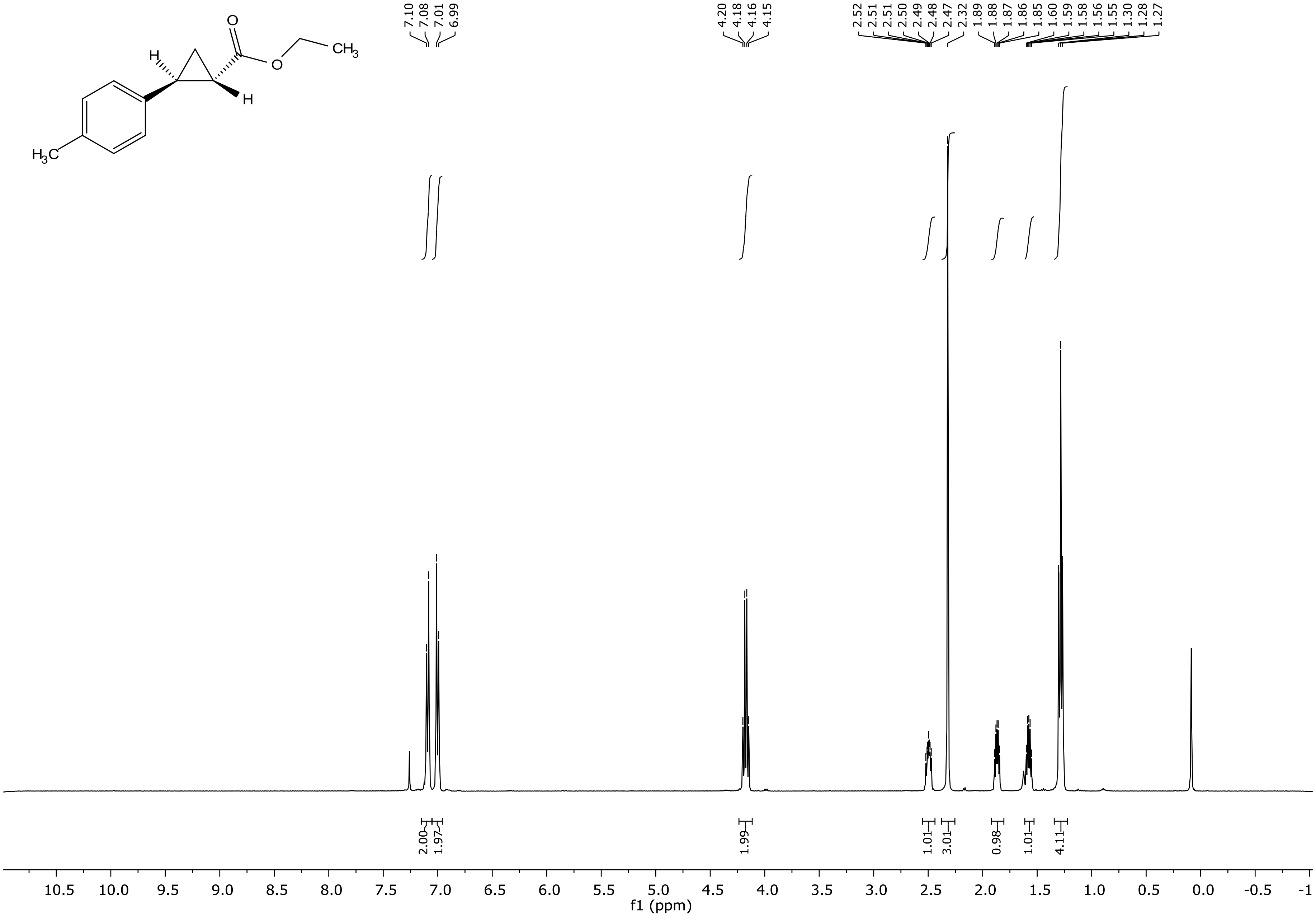


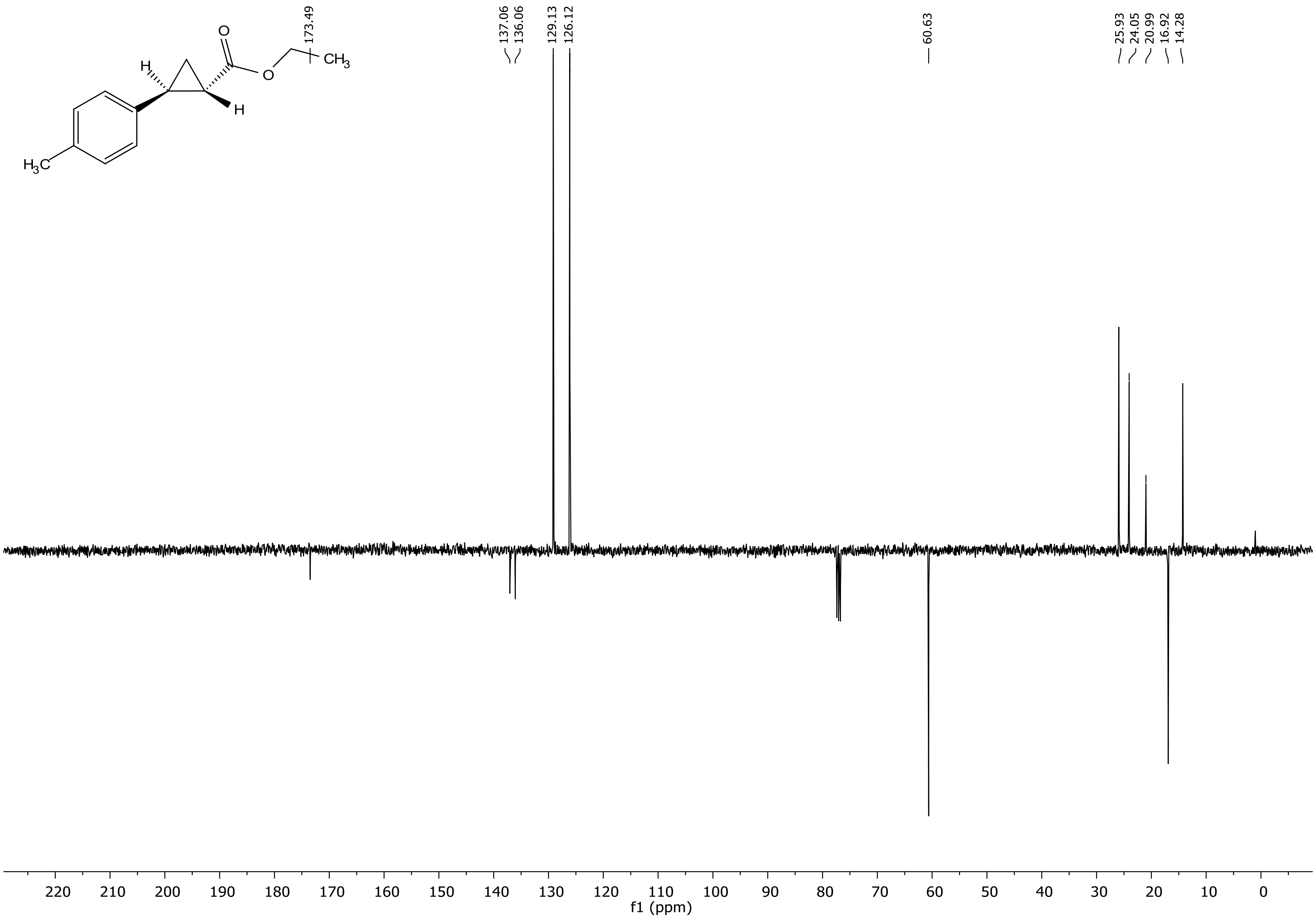
O
H
H
H_3C
O
CH3
173.45
140.07
138.09
128.36
127.22
126.99
123.16
60.62
26.14
24.10
21.36
16.99
14.27
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

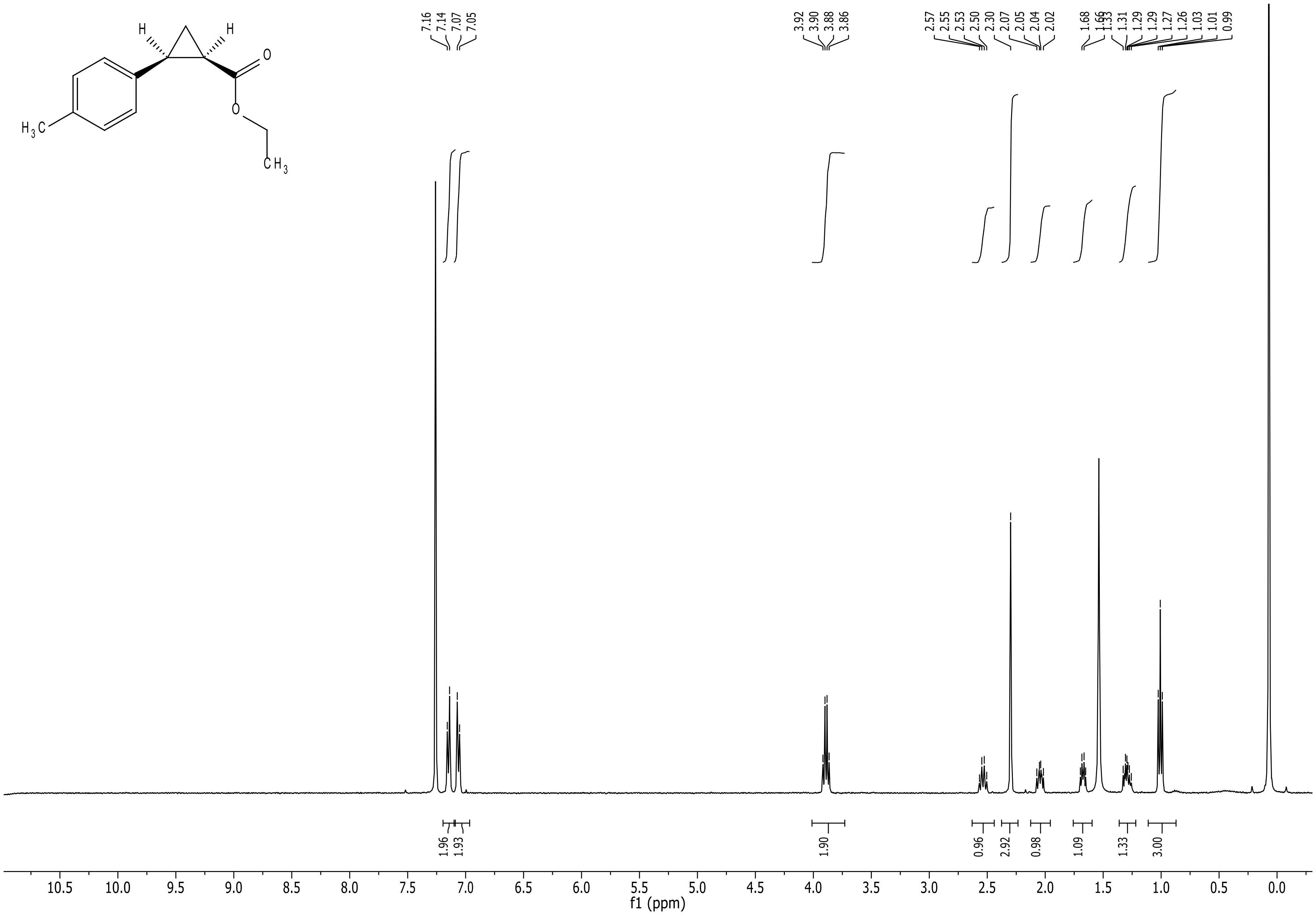

H3C
H
H
O
O
H3C
7.16
7.15
7.13
7.08
7.07
7.05
7.01
6.99
3.91
3.89
3.88
3.86
2.55
2.53
2.51
2.31
2.08
2.07
2.07
2.06
2.05
2.05
2.04
2.03
1.70
1.68
1.33
1.32
1.31
1.31
1.30
1.29
1.29
1.27
1.26
1.00
0.98
0.97
1.00
1.96
1.00
1.94
0.96
2.98
0.96
0.98
1.24
2.96
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

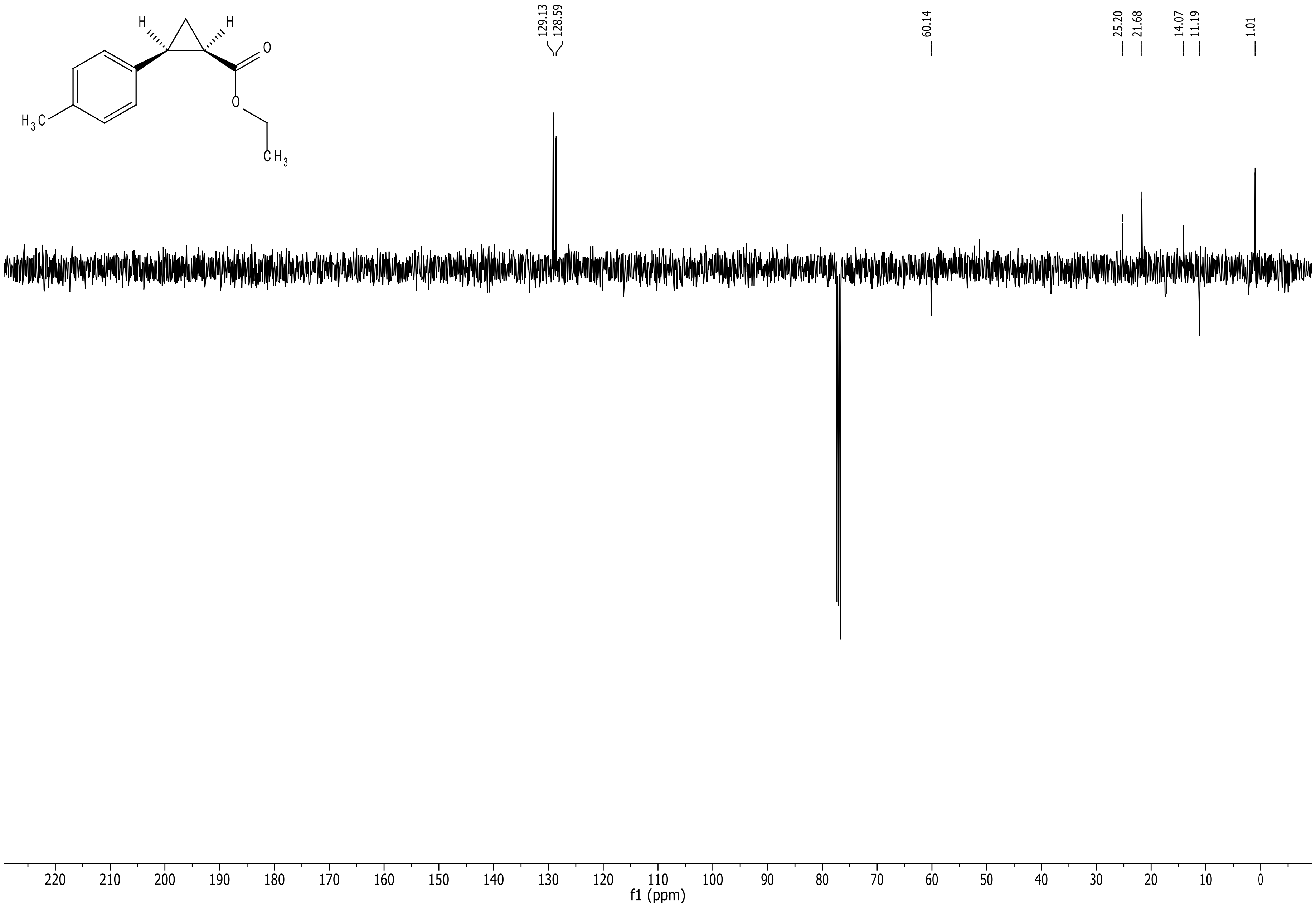


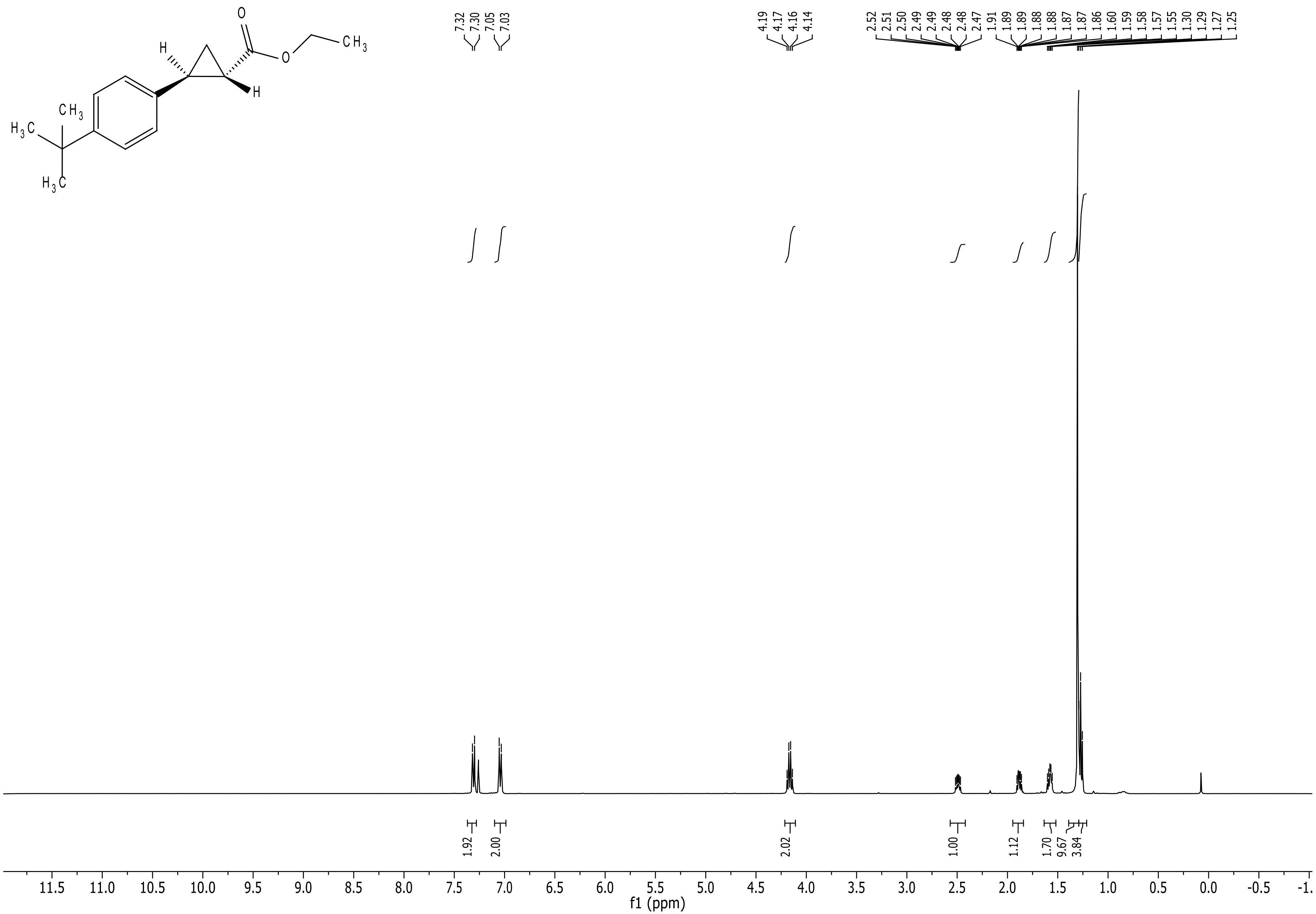
171.02
137.32
136.48
130.12
127.75
127.39
126.29
60.12
25.40
21.70
21.34
14.03
11.10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

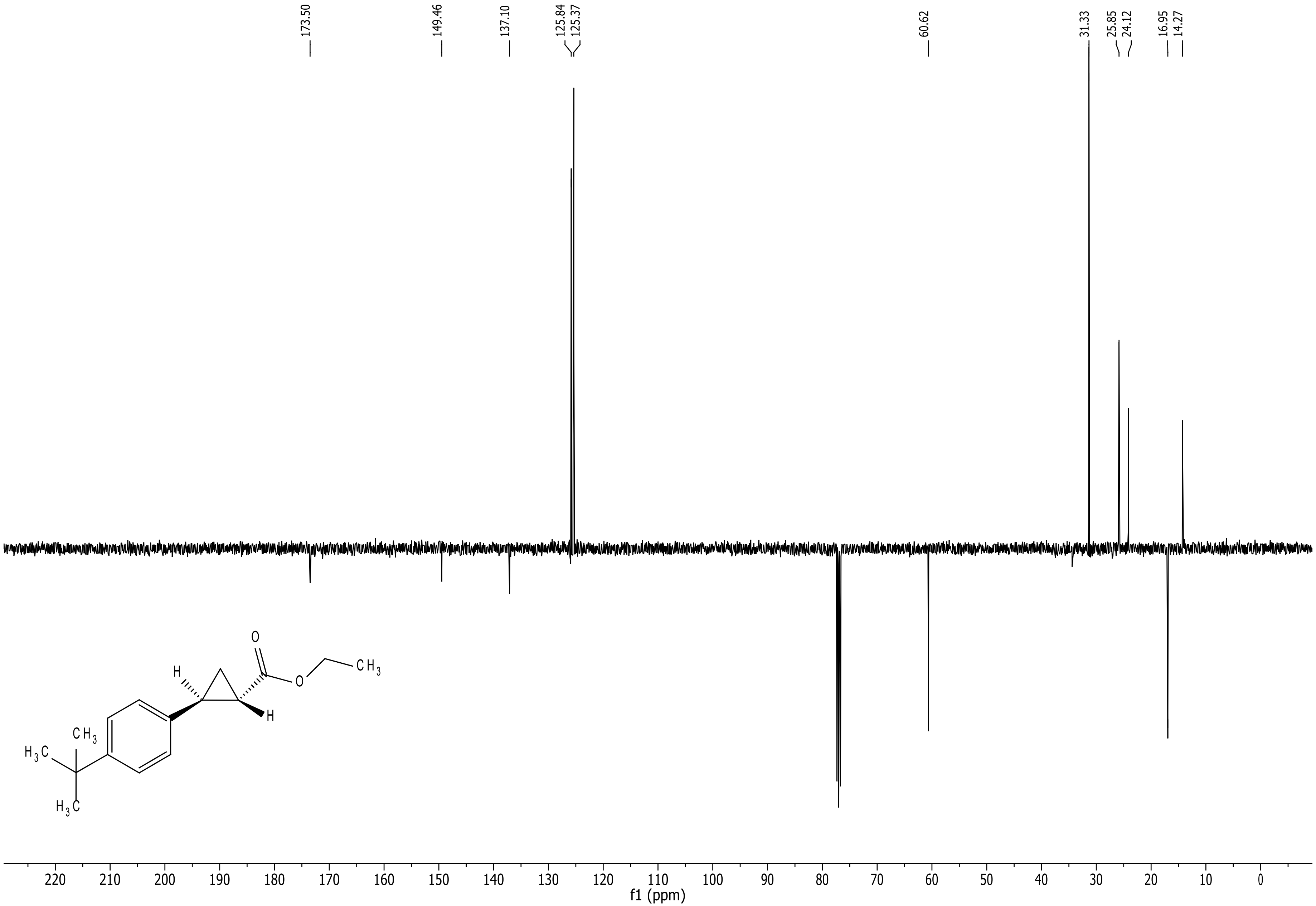

H
H
O
O
CH3
H3C
7.10
7.08
7.01
6.99
4.20
4.18
4.16
4.15
2.52
2.51
2.51
2.50
2.49
2.48
2.47
2.32
1.89
1.88
1.87
1.86
1.85
1.60
1.59
1.58
1.56
1.55
1.30
1.28
1.27
2.00
1.97
1.99
1.01
3.01
0.98
1.01
4.11
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

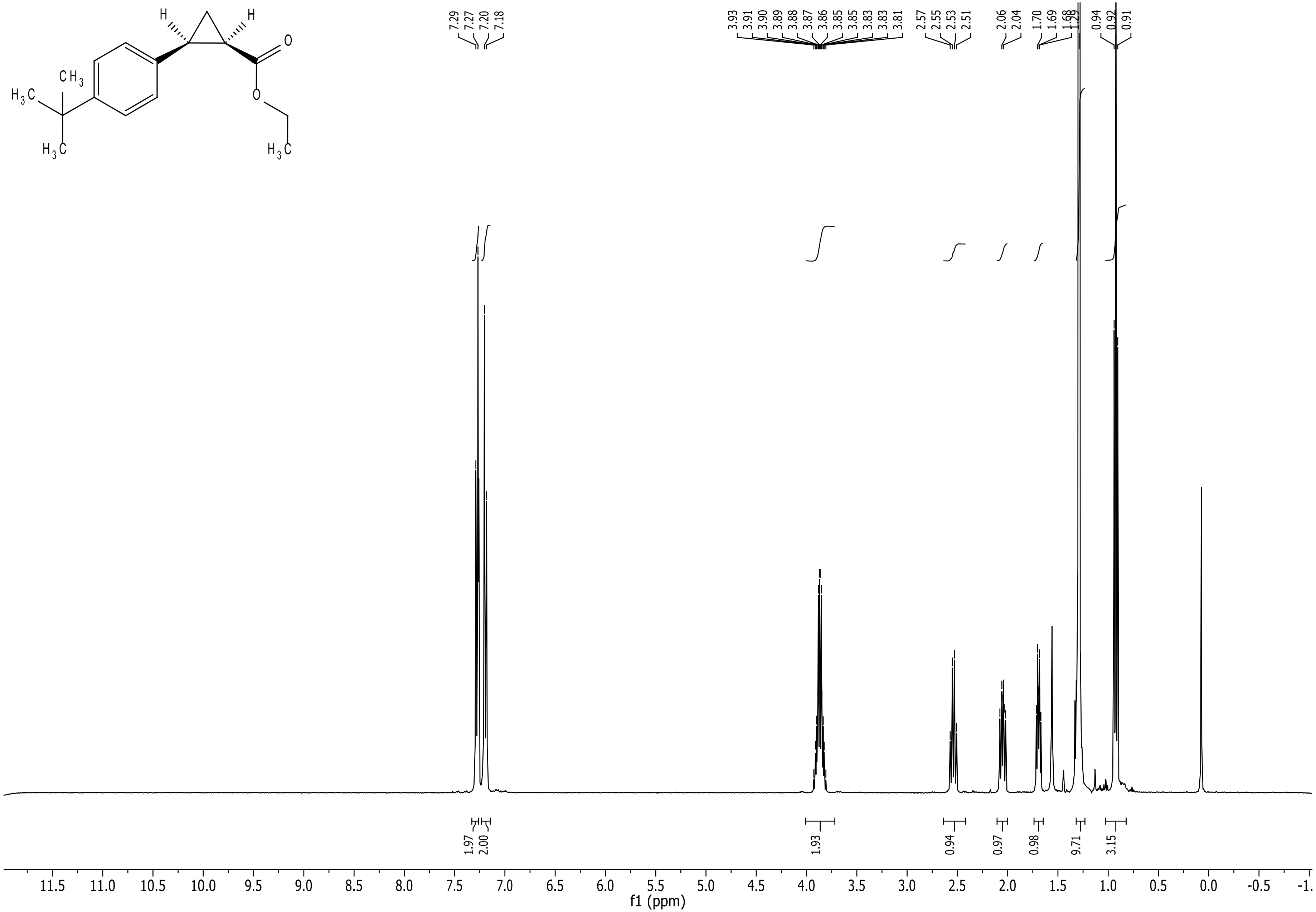

O
O
H
H
CH3
H3C
173.49
137.06
136.06
129.13
126.12
60.63
25.93
24.05
20.99
16.92
14.28
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

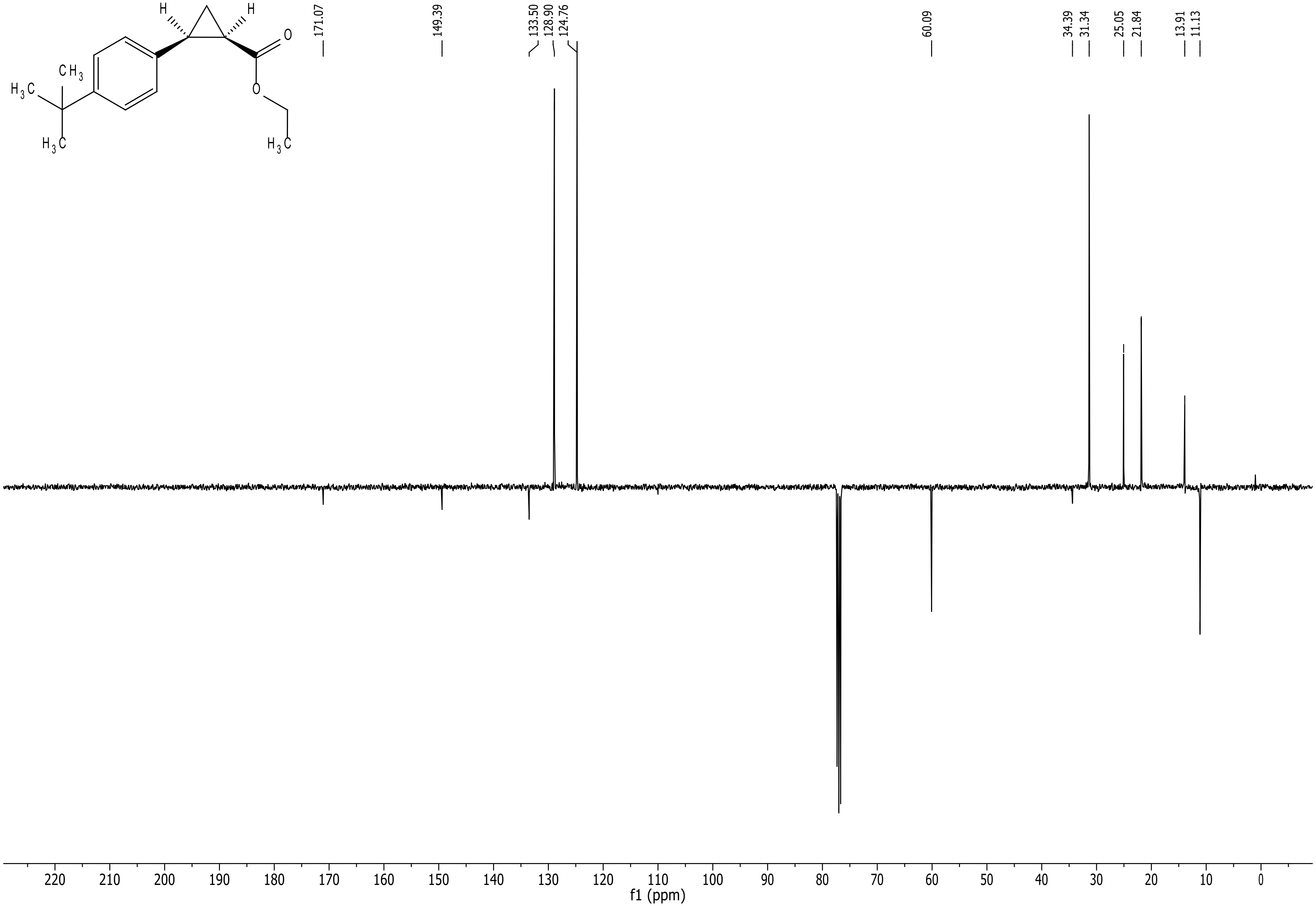

H
H
O
O
H_3C
CH_3
7.16
7.14
7.07
7.05
3.92
3.90
3.88
3.86
2.57
2.55
2.53
2.50
2.30
2.07
2.05
2.04
2.02
1.68
1.66
1.33
1.31
1.29
1.29
1.27
1.26
1.03
1.01
0.99
1.96
1.93
1.90
0.96
2.92
0.98
1.09
1.33
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

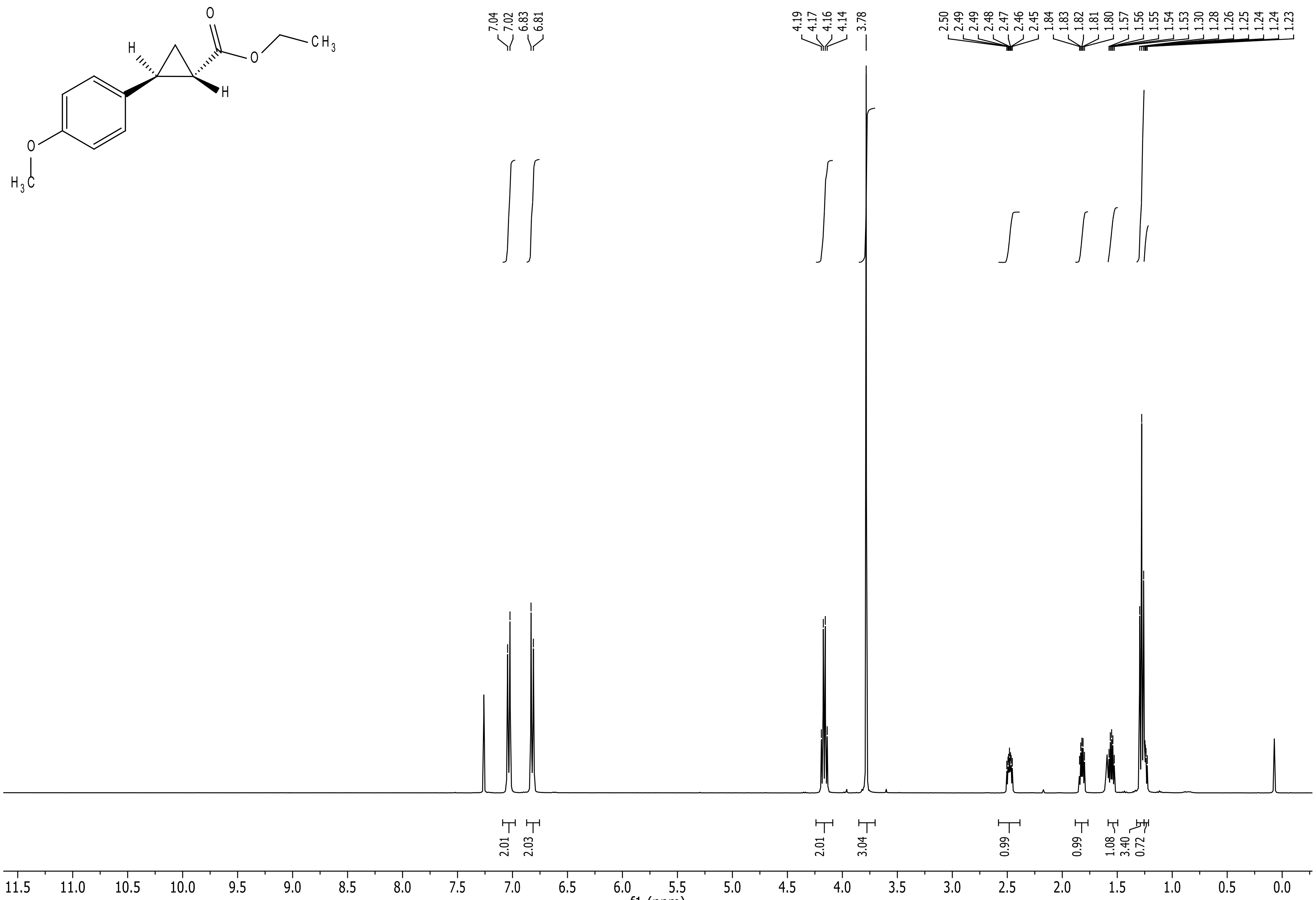

129.13
128.59
60.14
25.20
21.68
14.07
11.19
1.01
H
H
O
O
H3C
CH3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

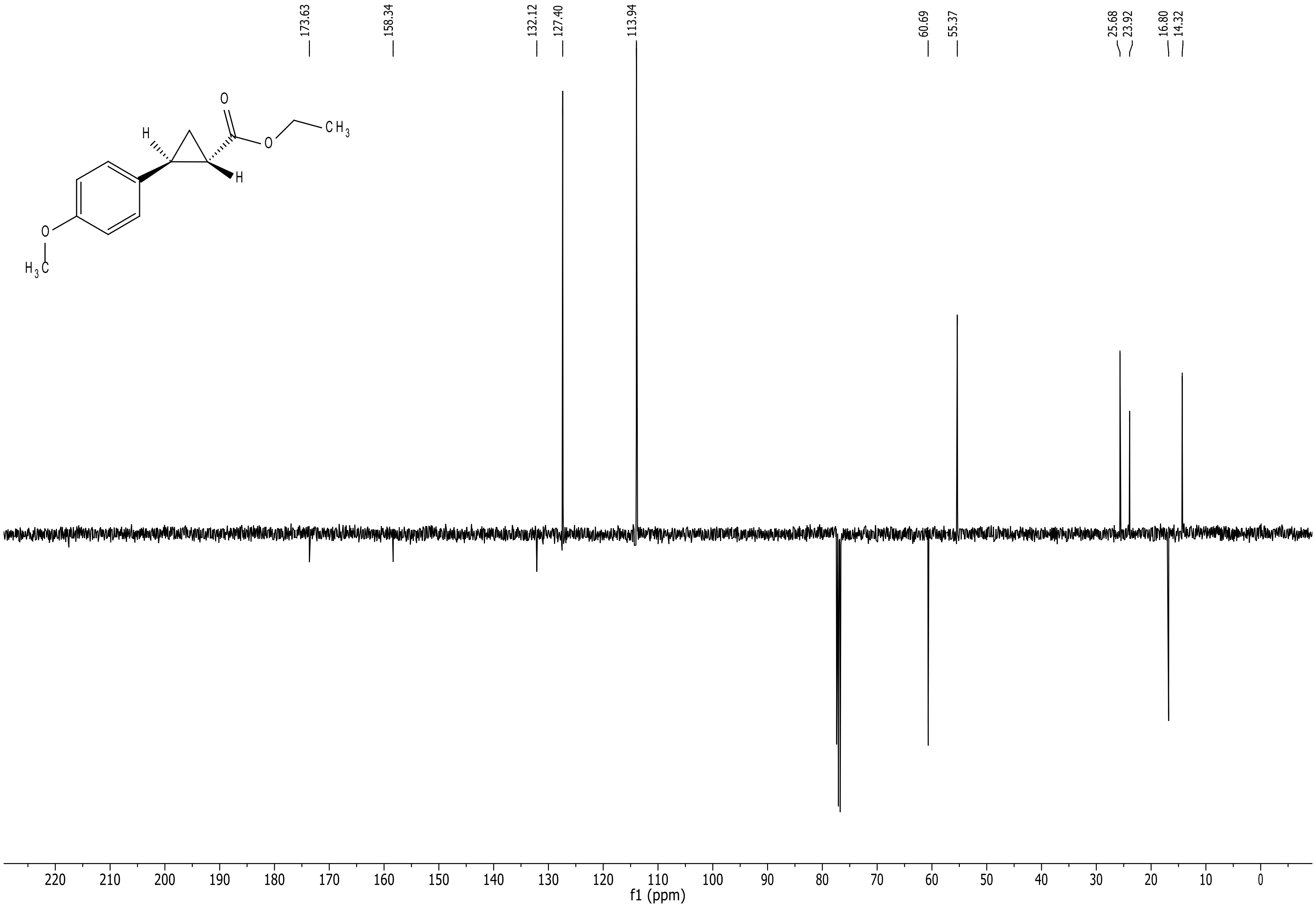

O
O
CH3
H
H
CH3
H3C
H3C
7.32
7.30
7.05
7.03
4.19
4.17
4.16
4.14
2.52
2.51
2.50
2.49
2.49
2.48
2.48
2.47
1.91
1.89
1.89
1.88
1.88
1.87
1.87
1.86
1.60
1.59
1.58
1.57
1.55
1.30
1.29
1.27
1.25
1.92
2.00
2.02
1.00
1.12
1.70
9.67
3.84
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)

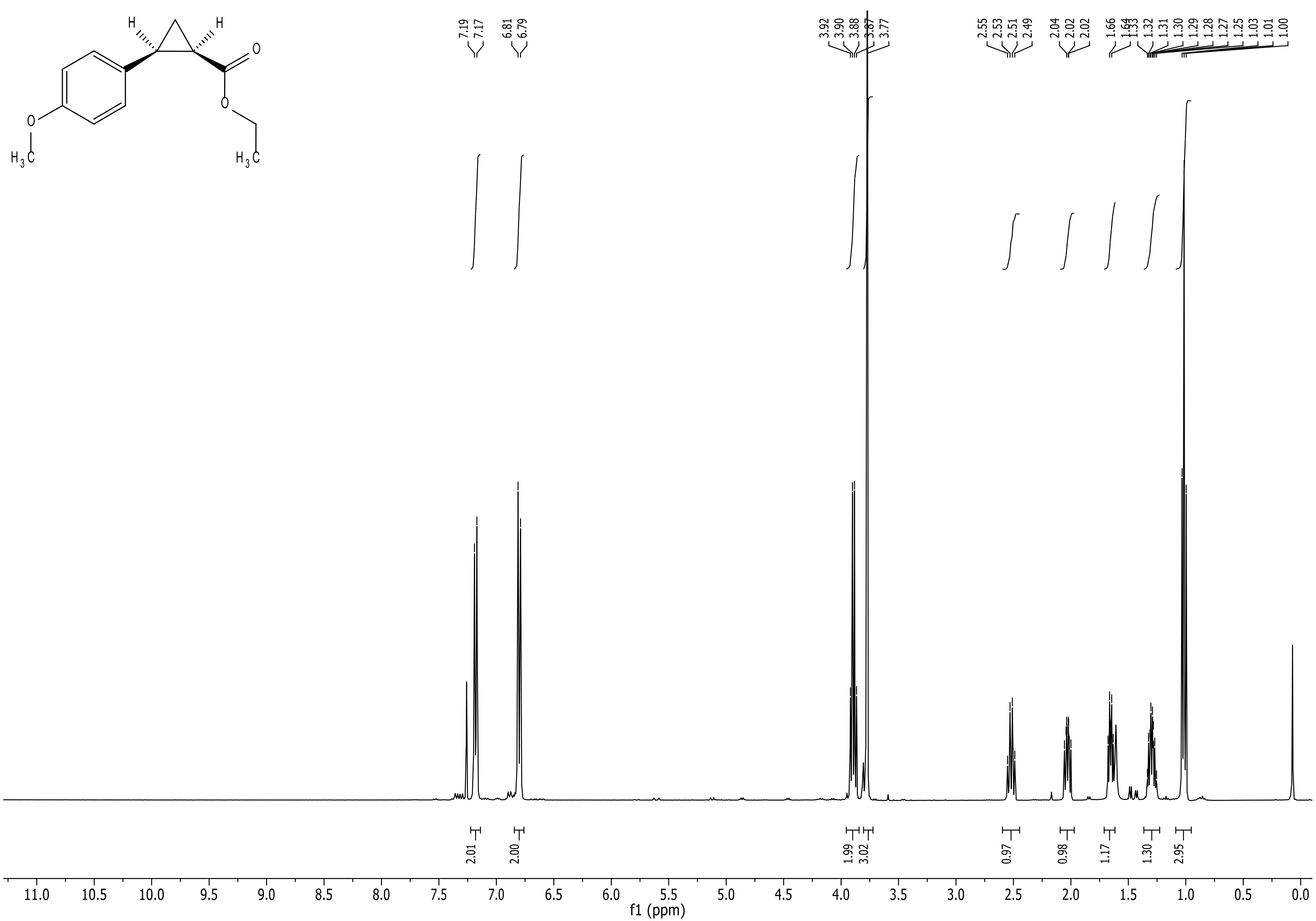

173.50
149.46
137.10
125.84
125.37
60.62
31.33
25.85
24.12
16.95
14.27
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
O
O
CH3
H
H
CH3
H3C
H3C

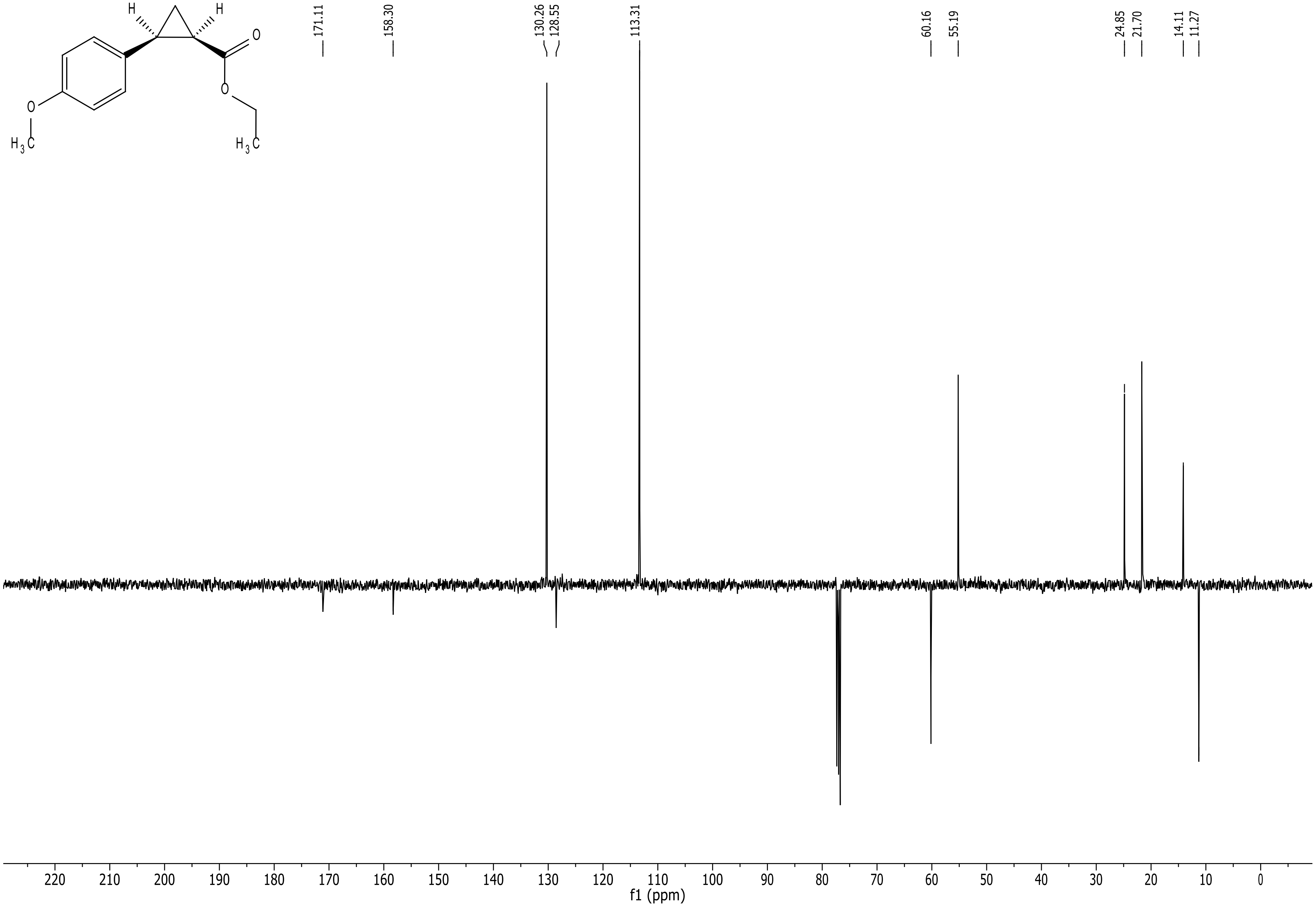

H
H
O
O
CH3
H3C
H3C
H3C
7.29
7.27
7.20
7.18
3.93
3.91
3.90
3.89
3.88
3.87
3.86
3.85
3.85
3.83
3.83
3.81
2.57
2.55
2.53
2.51
2.06
2.04
1.70
1.69
1.68
1.28
0.94
0.92
0.91
1.97
2.00
1.93
0.94
0.97
0.98
9.71
3.15
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)

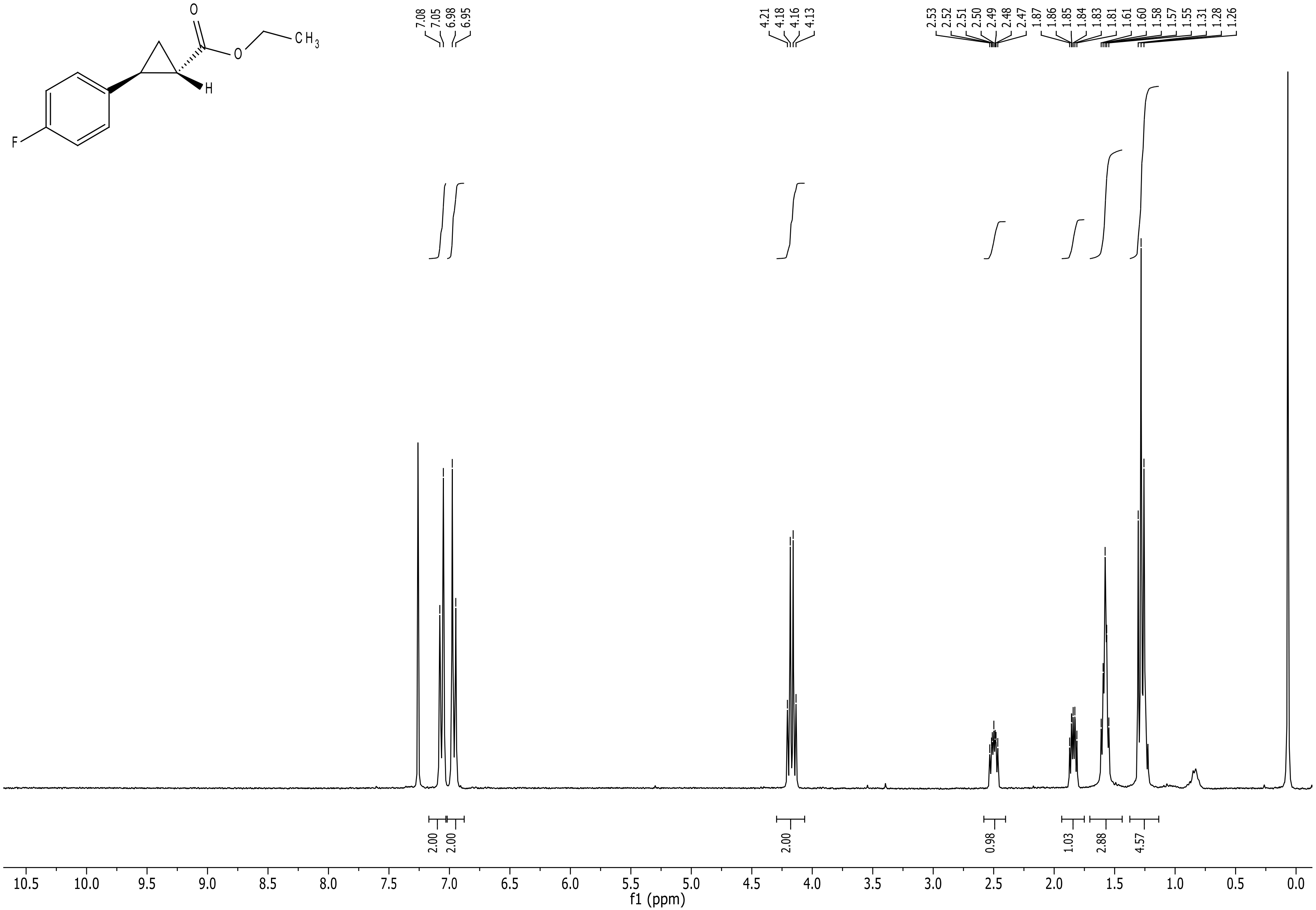

H
H
O
O
CH3
H3C
H3C
H3C
171.07
149.39
133.50
128.90
124.76
60.09
34.39
31.34
25.05
21.84
13.91
11.13
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

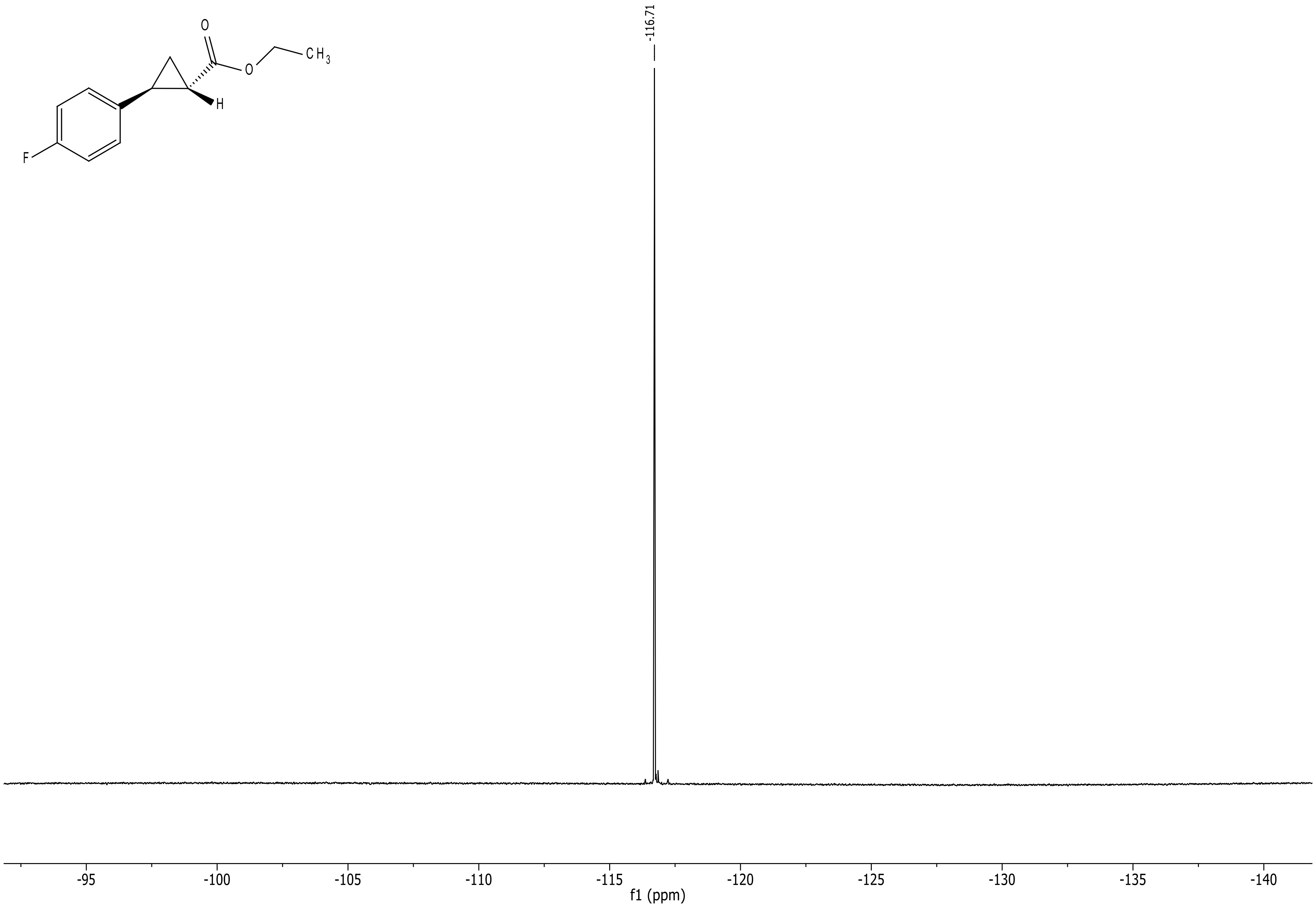

O
CH3
H
O
H
O
H3C
7.04
7.02
6.83
6.81
4.19
4.17
4.16
4.14
3.78
2.50
2.49
2.49
2.48
2.47
2.46
2.45
1.84
1.83
1.82
1.81
1.80
1.57
1.56
1.55
1.54
1.53
1.30
1.28
1.26
1.25
1.24
1.24
1.23
2.01
2.03
2.01
3.04
0.99
0.99
1.08
3.40
0.72
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

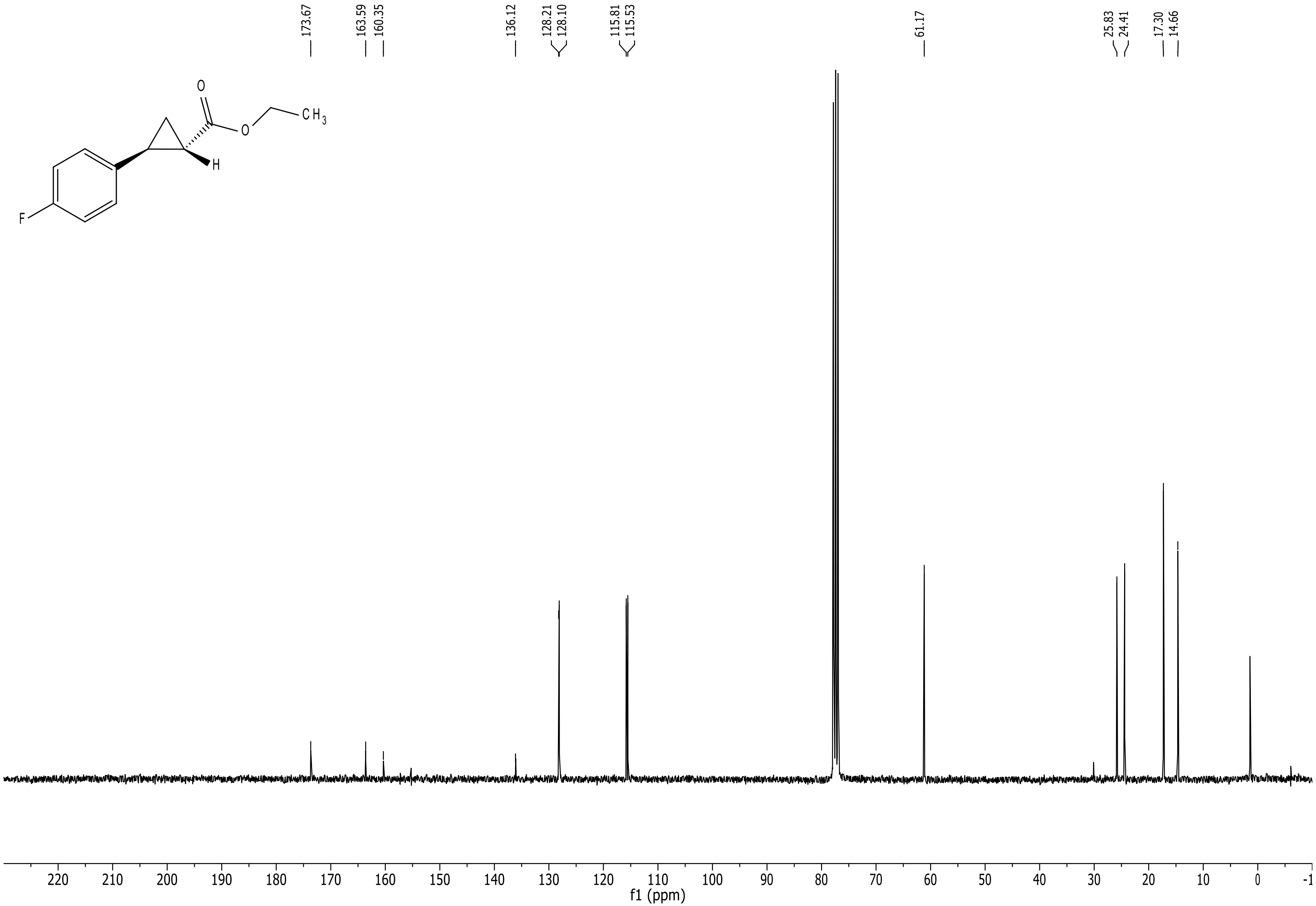

173.63
158.34
132.12
127.40
113.94
60.69
55.37
25.68
23.92
16.80
14.32
O
CH3
H
H
O
H3C
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


H
H
O
O
O
H3C
H3C
7.19
7.17
6.81
6.79
3.92
3.90
3.88
3.87
3.77
2.55
2.53
2.51
2.49
2.04
2.02
2.02
1.66
1.64
1.33
1.32
1.31
1.30
1.29
1.28
1.27
1.25
1.03
1.01
1.00
2.01
2.00
1.99
3.02
0.97
0.98
1.17
1.30
2.95
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


H
H
O
O
O
H3C
H3C
171.11
158.30
130.26
128.55
113.31
60.16
55.19
24.85
21.70
14.11
11.27
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
CH3
H
F
7.08
7.05
6.98
6.95
4.21
4.18
4.16
4.13
2.53
2.52
2.51
2.50
2.49
2.48
2.47
1.87
1.86
1.85
1.84
1.83
1.81
1.61
1.60
1.58
1.57
1.55
1.31
1.28
1.26
2.00
2.00
2.00
0.98
1.03
2.88
4.57
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


-116.71
O
O
CH3
H
F
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
f1 (ppm)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160.35
136.12
128.21
128.10
115.81
115.53
61.17
25.83
24.41
17.30
14.66
O
O
CH3
H
F
220
210
200
190
180
170
160
150
140
130
120
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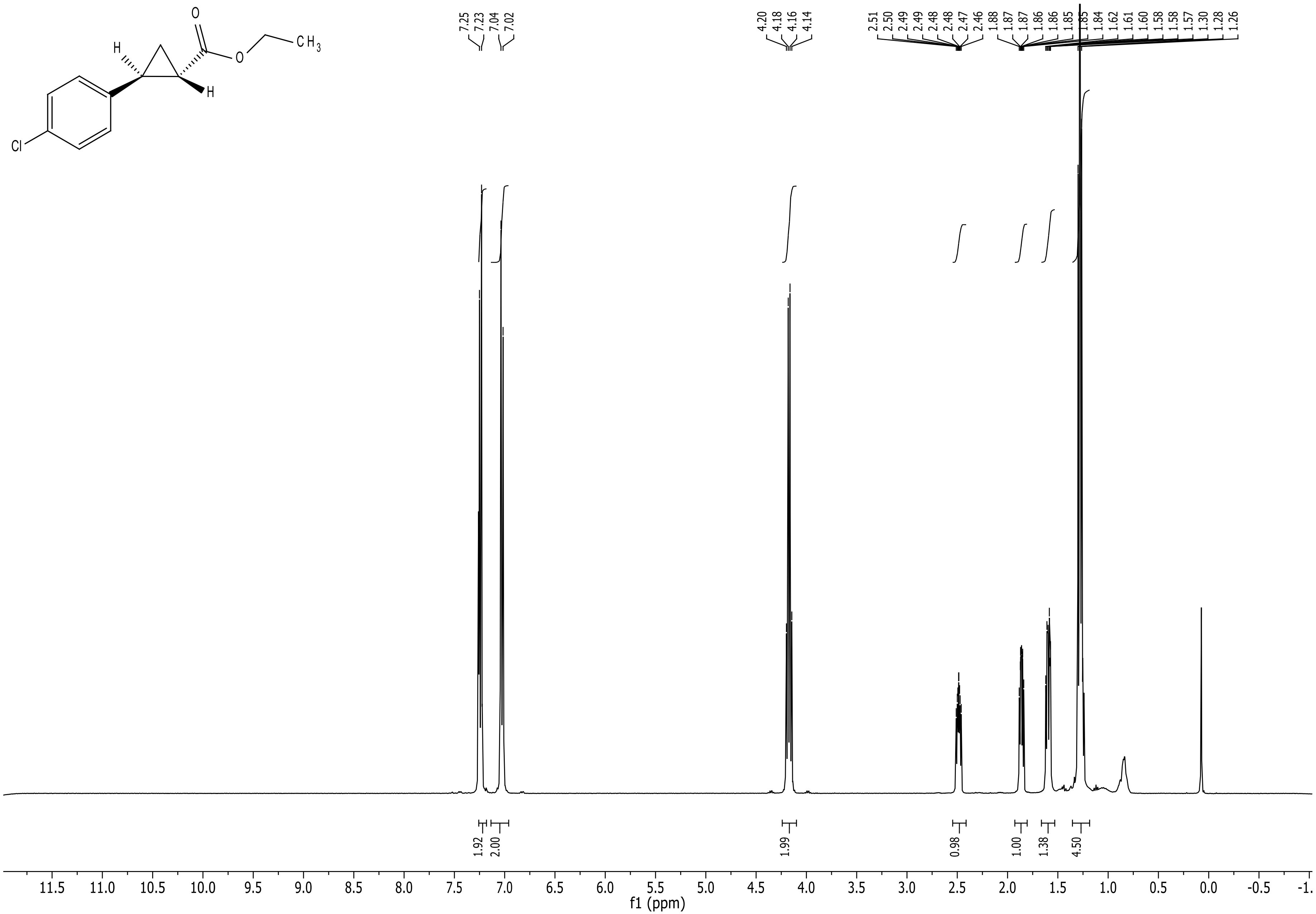
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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O
CH3
H
H
Cl
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7.23
7.04
7.02
4.20
4.18
4.16
4.14
2.51
2.50
2.49
2.49
2.48
2.48
2.47
2.46
1.88
1.87
1.87
1.86
1.86
1.85
1.85
1.84
1.62
1.61
1.60
1.58
1.58
1.57
1.30
1.28
1.26
1.92
2.00
1.99
0.98
1.00
1.38
4.50
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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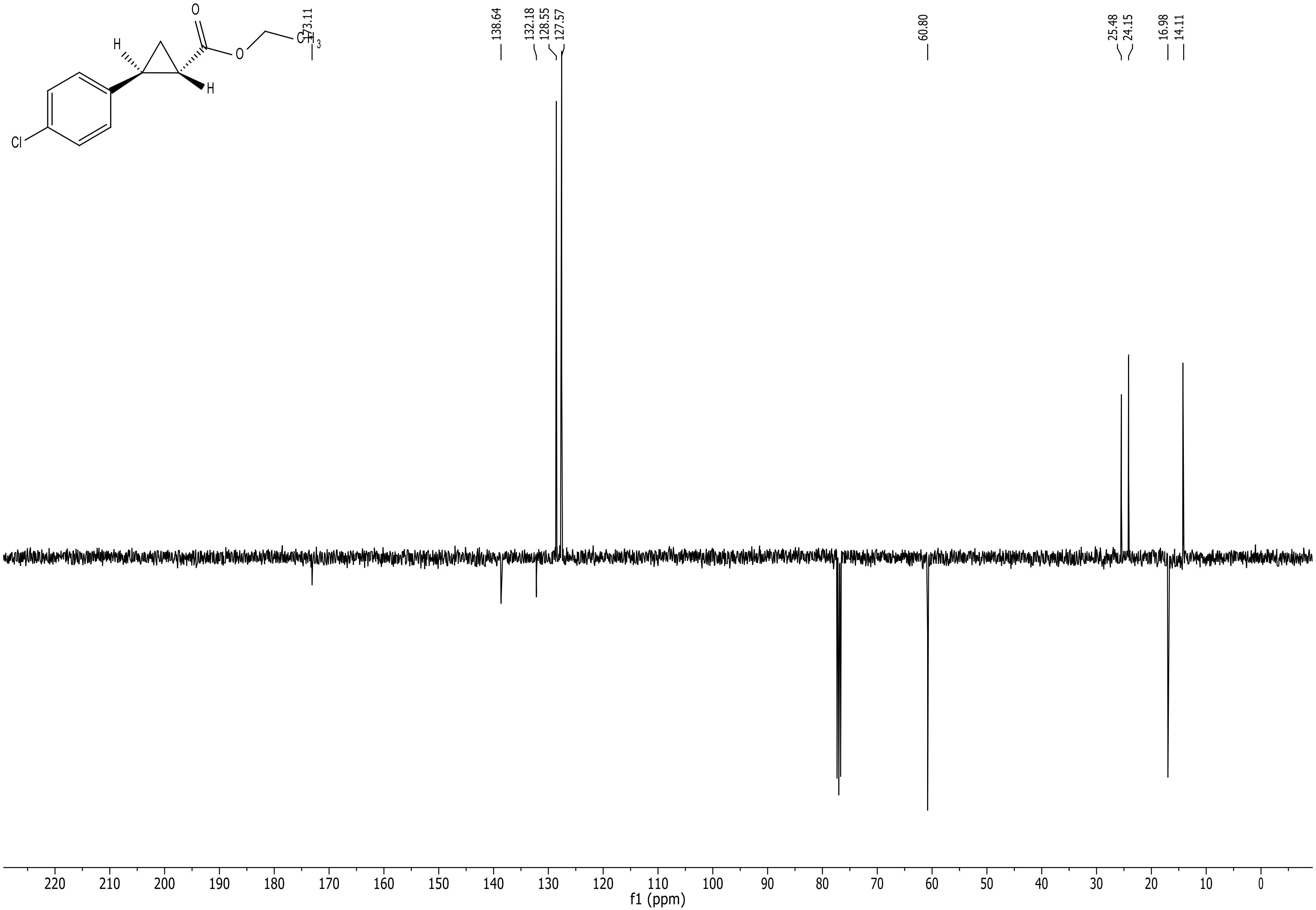
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)


O
H
O
CH3
H
Cl
173.11
138.64
132.18
128.55
127.57
60.80
25.48
24.15
16.98
14.11
220
210
200
190
180
170
160
150
140
130
120
110
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90
80
70
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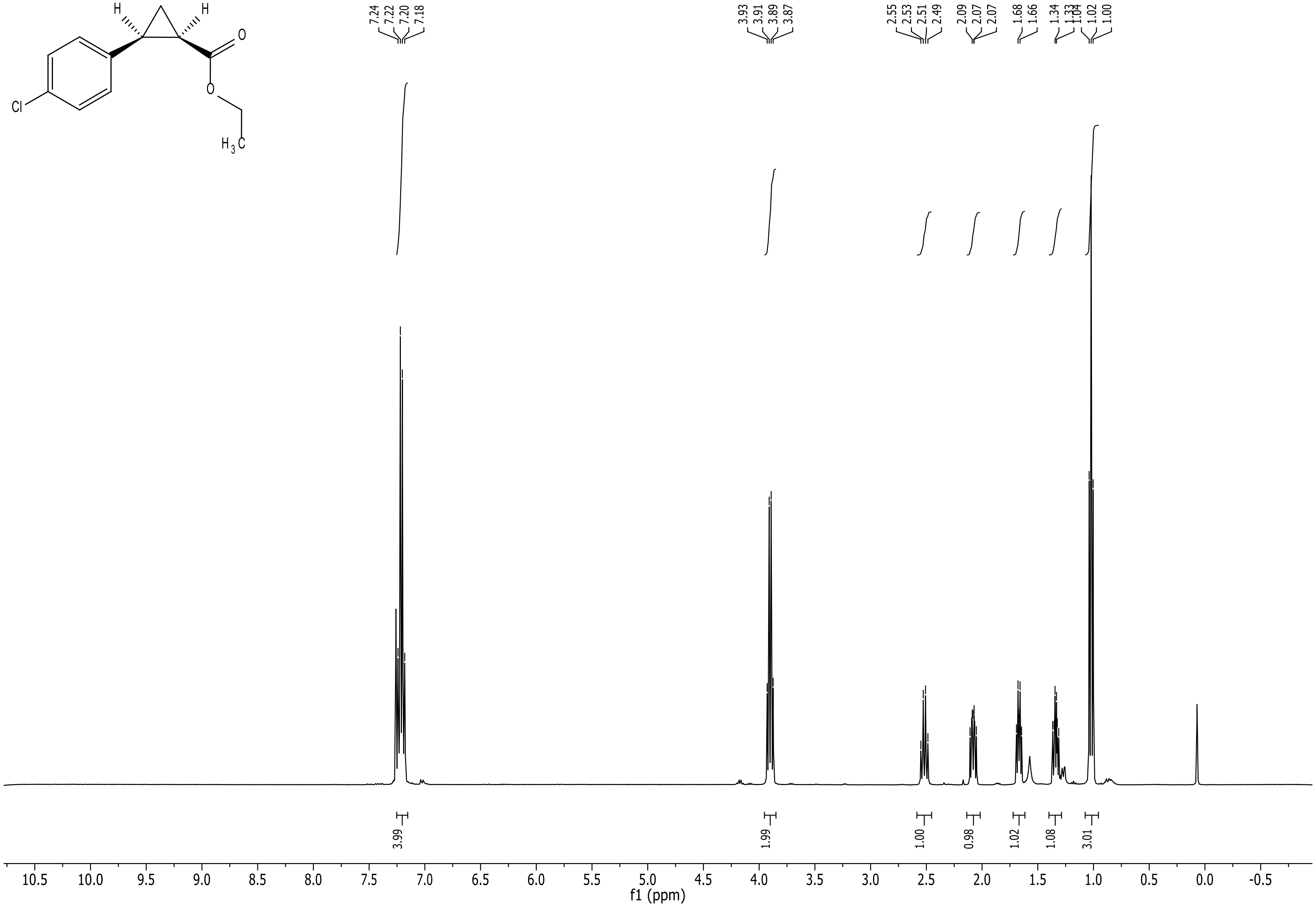
50
40
30
20
10
0
f1 (ppm)


H
H
O
O
Cl
H3C
7.24
7.22
7.20
7.18
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3.91
3.89
3.87
2.55
2.53
2.51
2.49
2.09
2.07
2.07
1.68
1.66
1.34
1.33
1.04
1.02
1.00
3.99
1.99
1.00
0.98
1.02
1.08
3.01
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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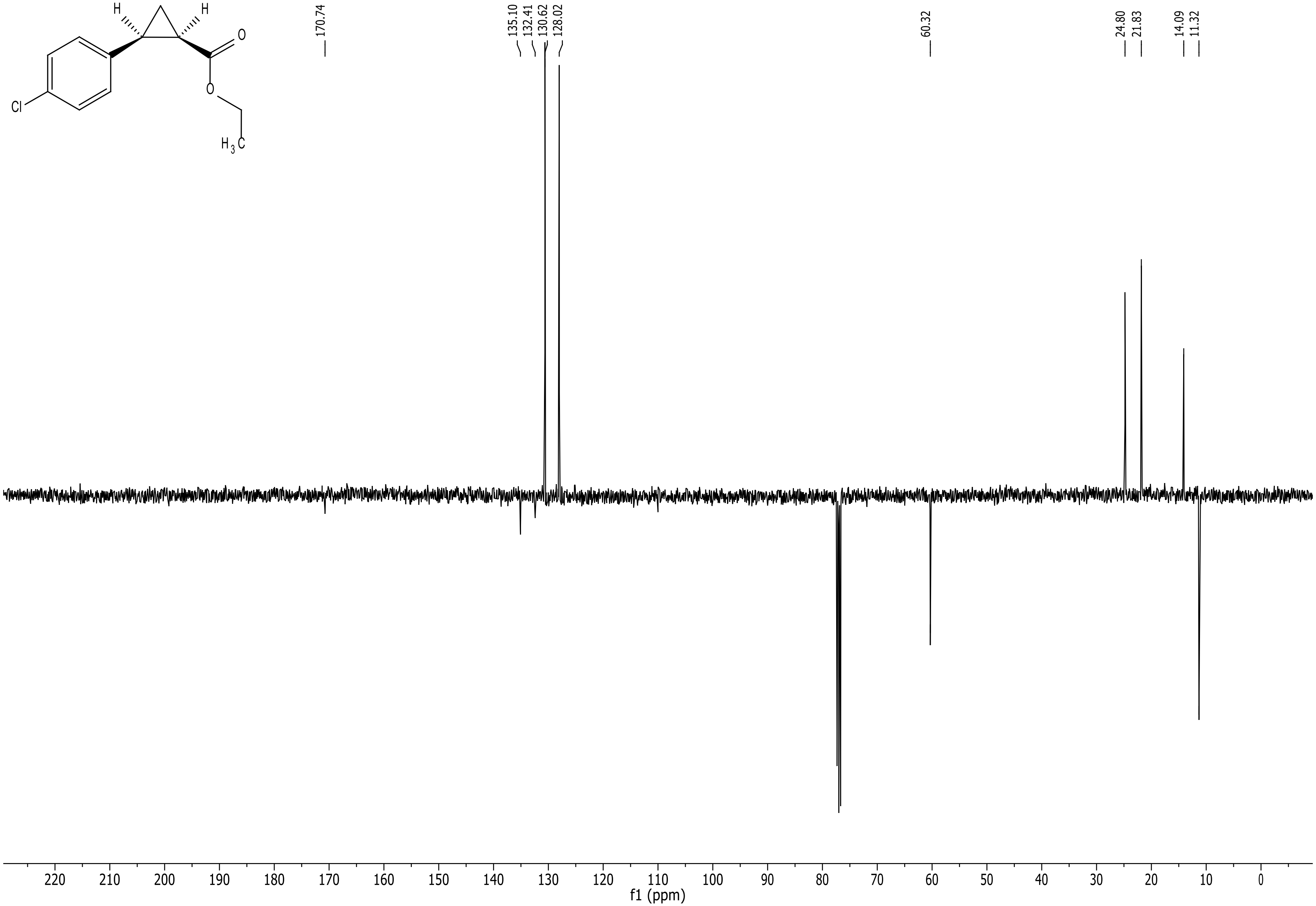
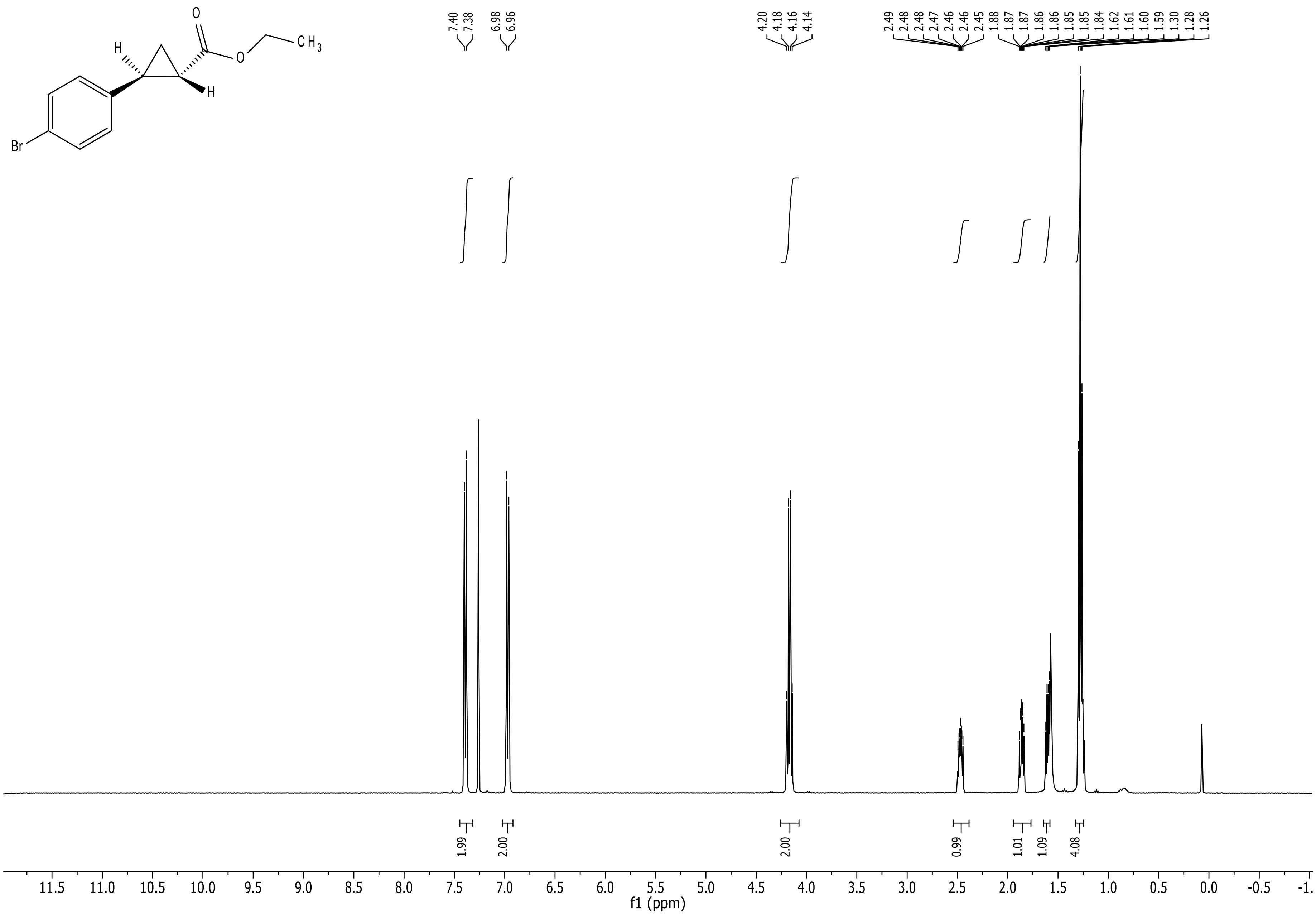
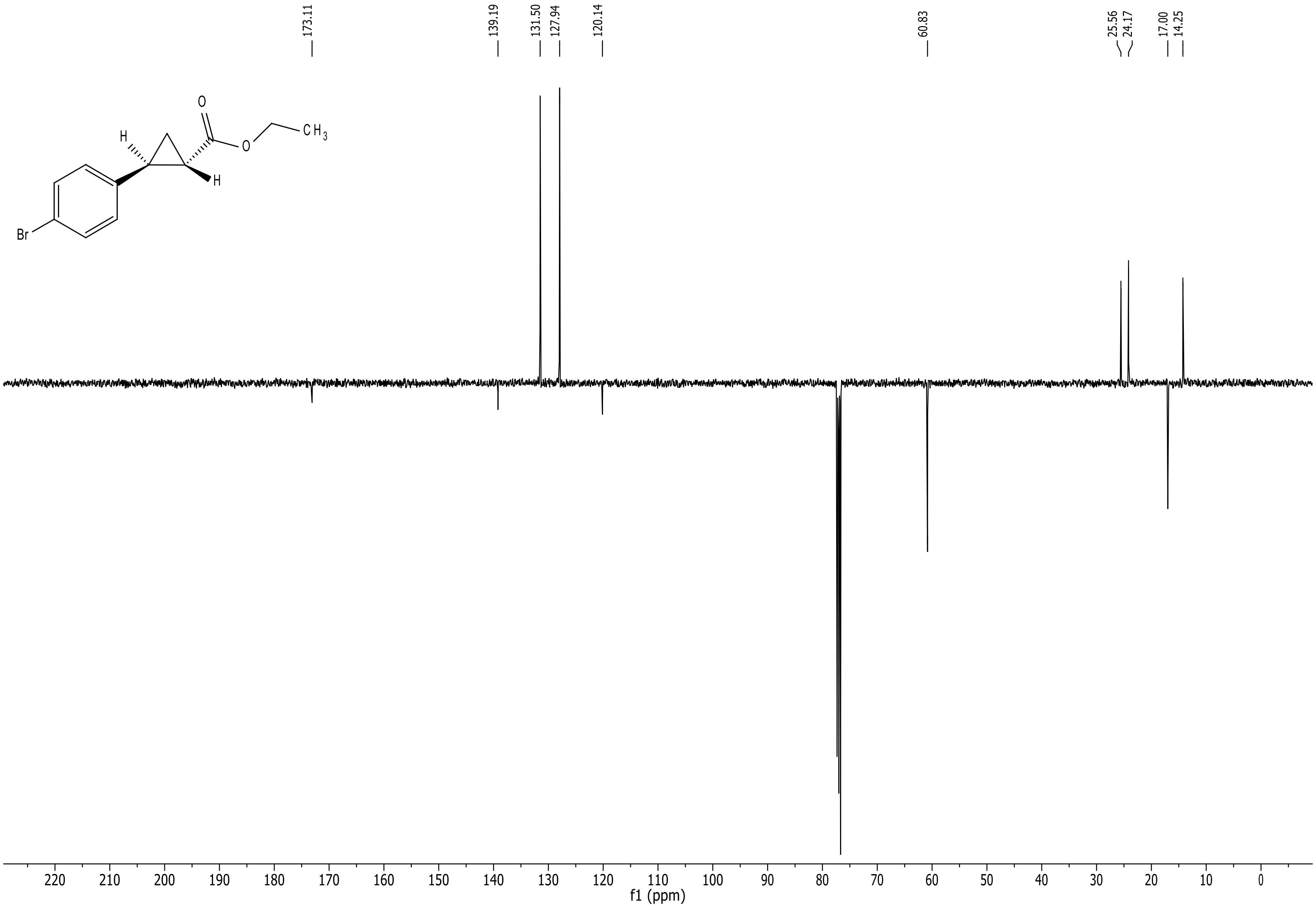
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


H
H
O
O
Cl
H3C
170.74
135.10
132.41
130.62
128.02
60.32
24.80
21.83
14.09
11.32
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
CH3
H
H
Br
7.40
7.38
6.98
6.96
4.20
4.18
4.16
4.14
2.49
2.48
2.48
2.47
2.46
2.46
2.45
1.88
1.87
1.87
1.86
1.86
1.85
1.85
1.84
1.62
1.61
1.60
1.59
1.30
1.28
1.26
1.99
2.00
2.00
0.99
1.01
1.09
4.08
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)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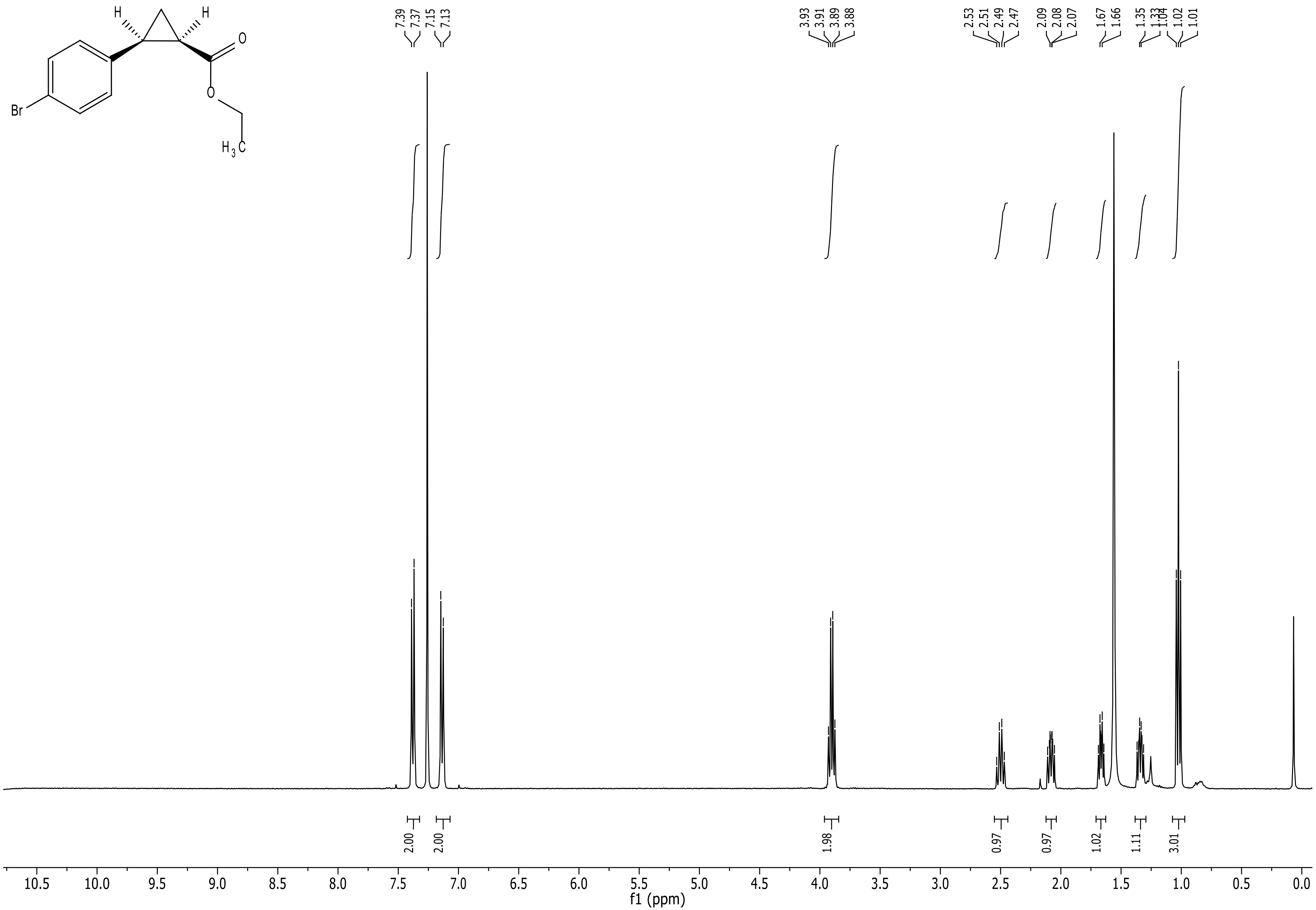
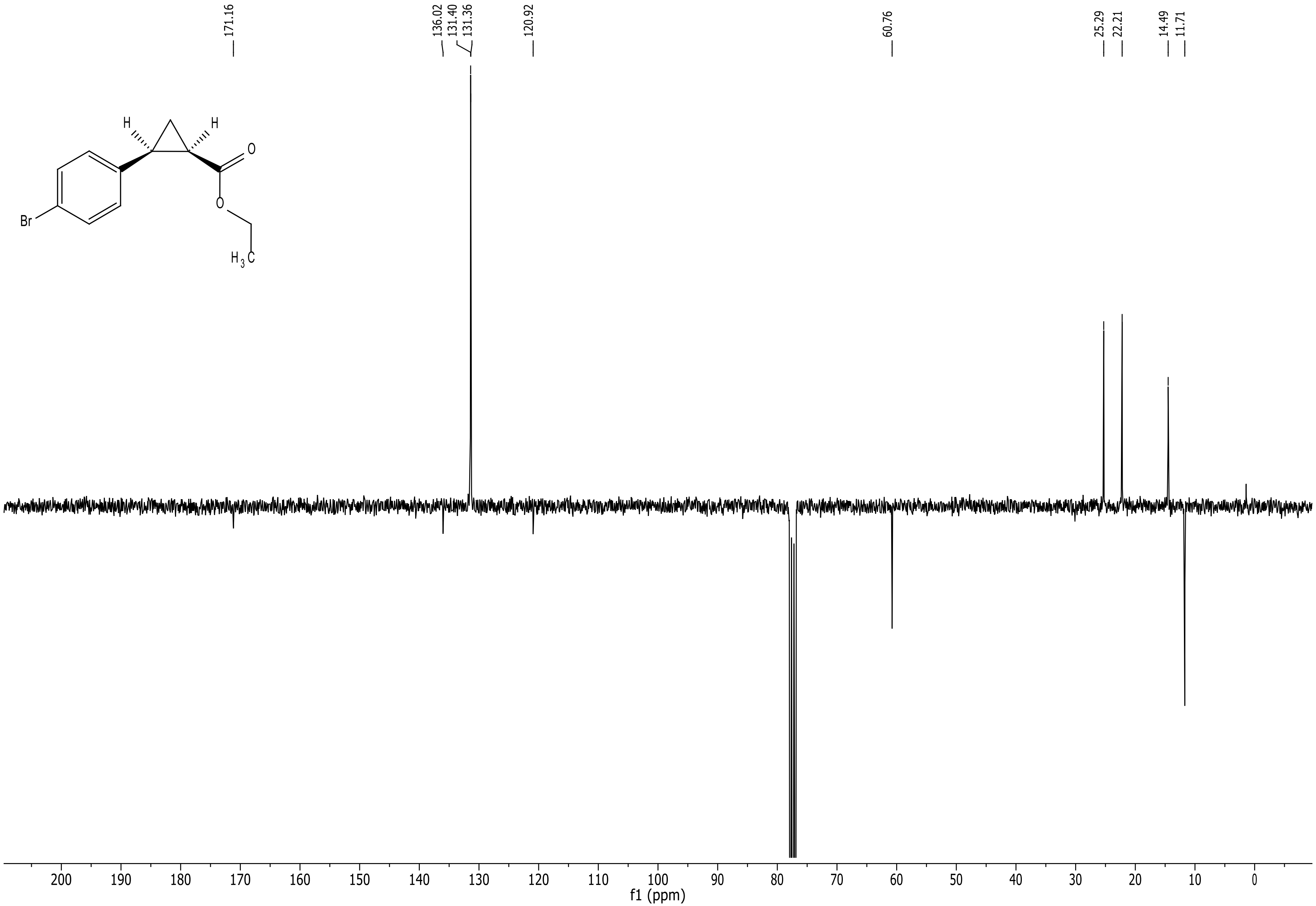
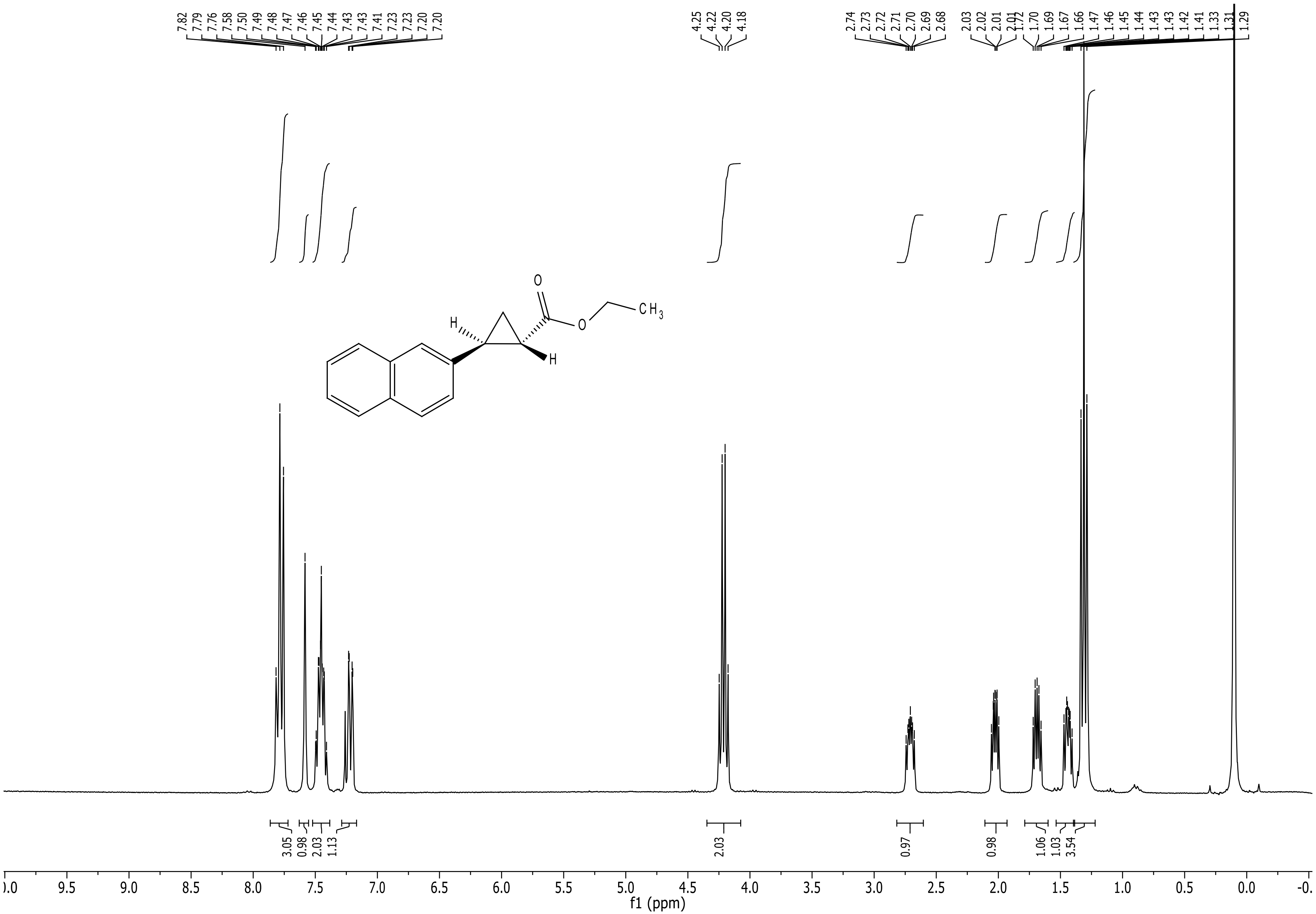
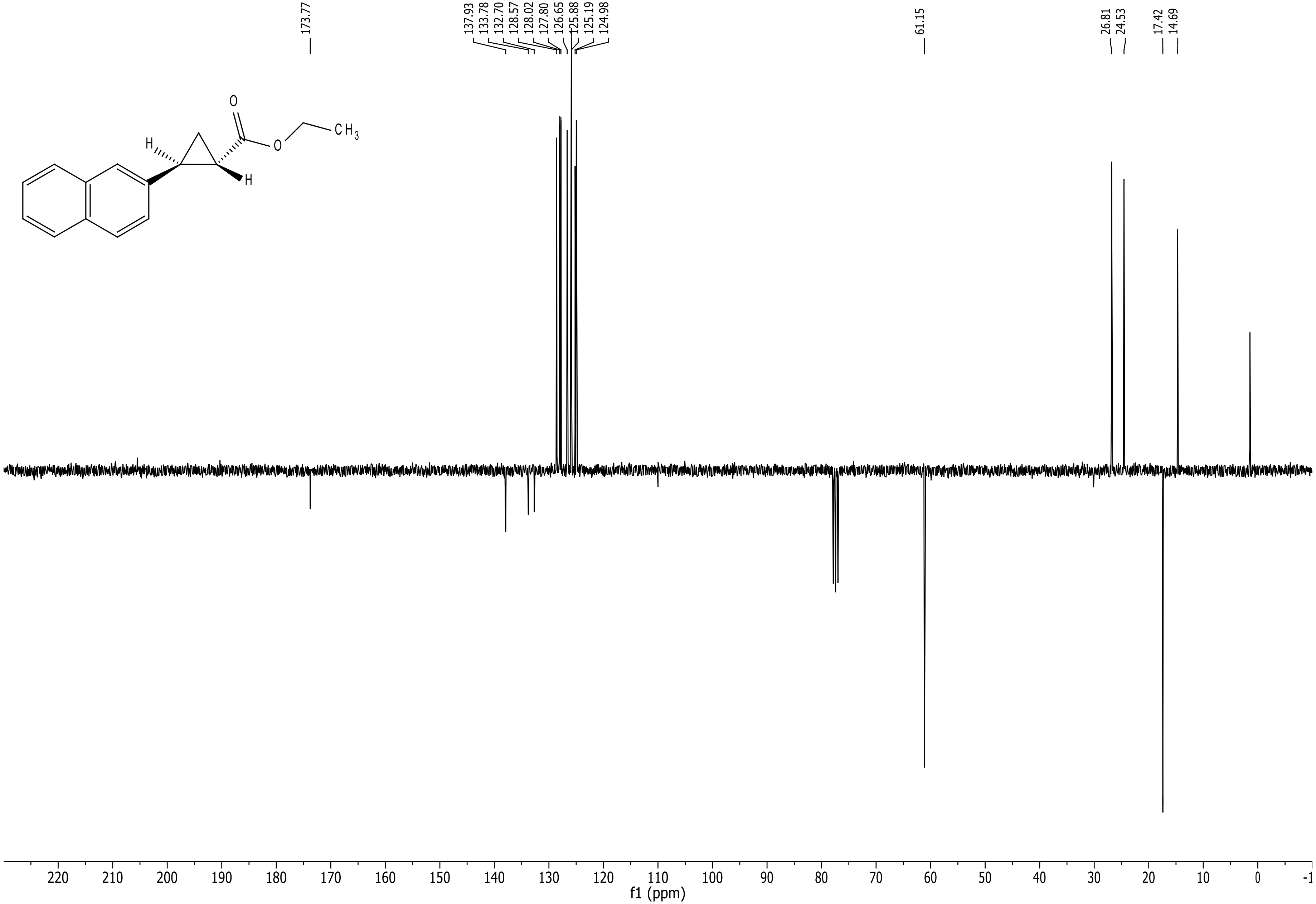
131.50
127.94
120.14
60.83
25.56
24.17
17.00
14.25
O
CH3
H
H
O
Br
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


H
H
O
O
Br
H3C
7.39
7.37
7.15
7.13
3.93
3.91
3.89
3.88
2.53
2.51
2.49
2.47
2.09
2.08
2.07
1.67
1.66
1.35
1.33
1.04
1.02
1.01
2.00
2.00
1.98
0.97
0.97
1.02
1.11
3.01
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


171.16
136.02
131.40
131.36
120.92
60.76
25.29
22.21
14.49
11.71
H
H
O
O
Br
H3C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.82
7.79
7.76
7.58
7.50
7.49
7.48
7.47
7.46
7.45
7.44
7.43
7.43
7.41
7.23
7.23
7.20
7.20
4.25
4.22
4.20
4.18
2.74
2.73
2.72
2.71
2.70
2.69
2.68
2.03
2.02
2.01
2.01
1.72
1.70
1.69
1.67
1.66
1.47
1.46
1.45
1.44
1.43
1.43
1.42
1.41
1.33
1.31
1.29
O
O
CH3
H
H
3.05
0.98
2.03
1.13
2.03
0.97
0.98
1.06
1.03
3.54
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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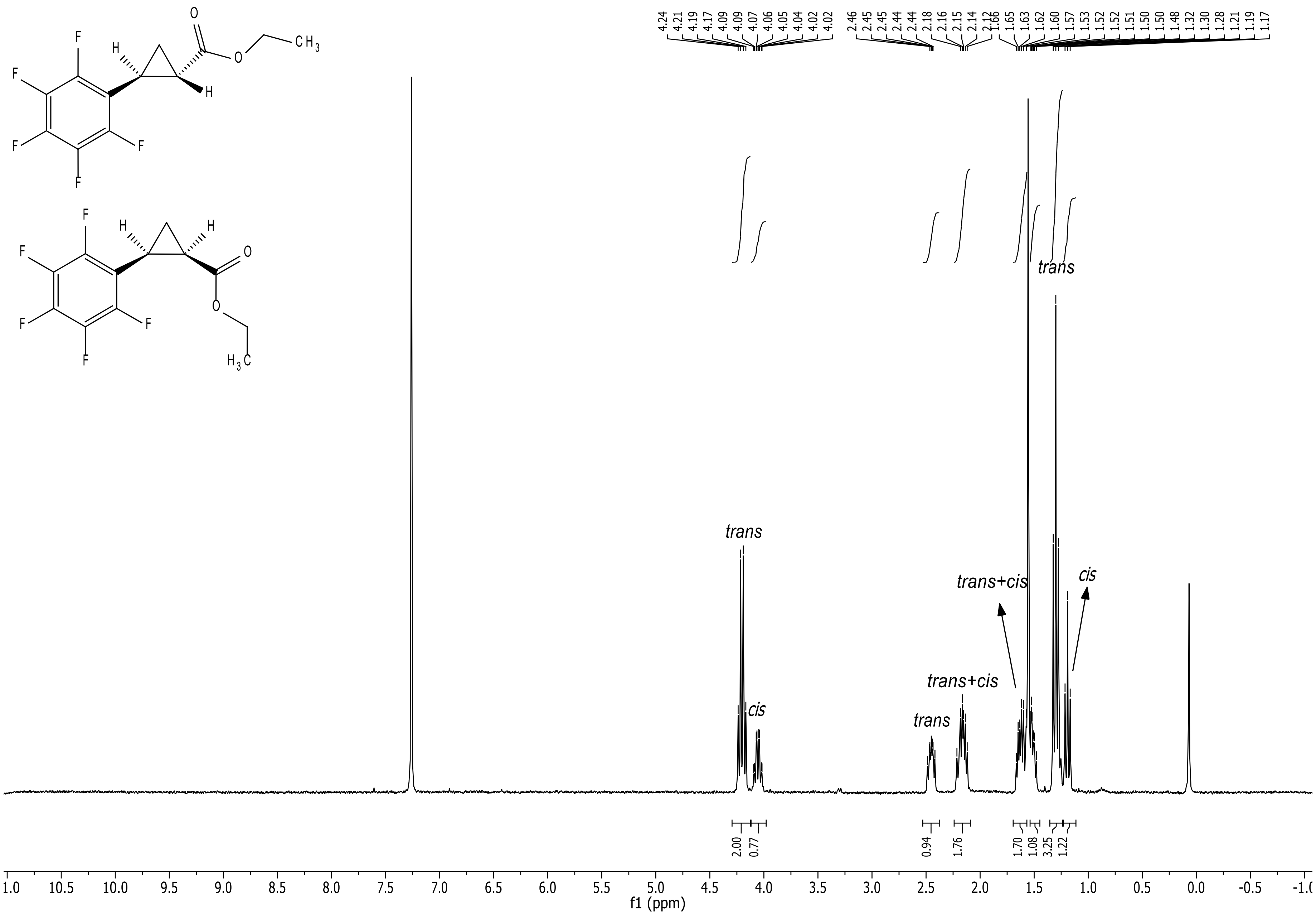
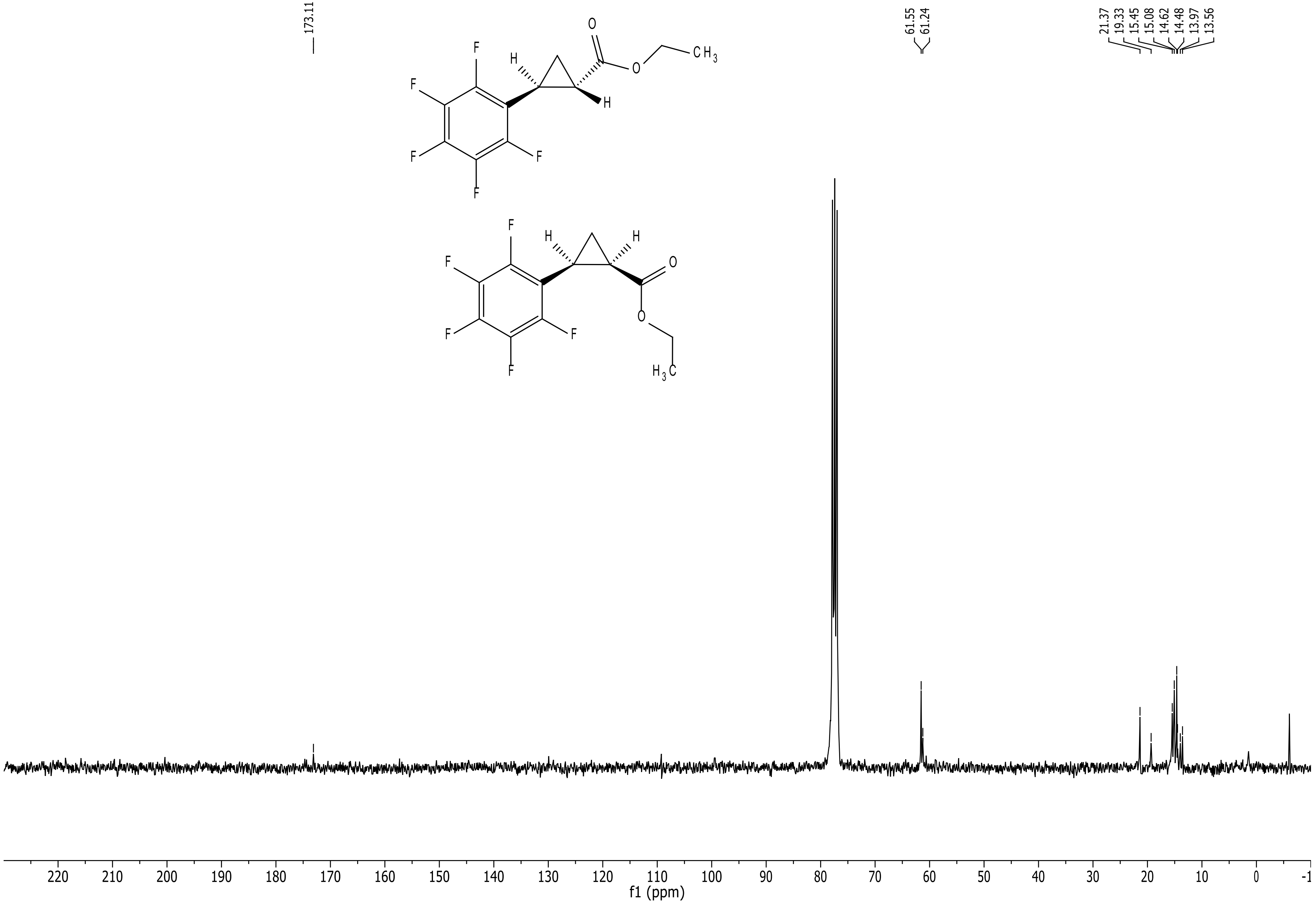
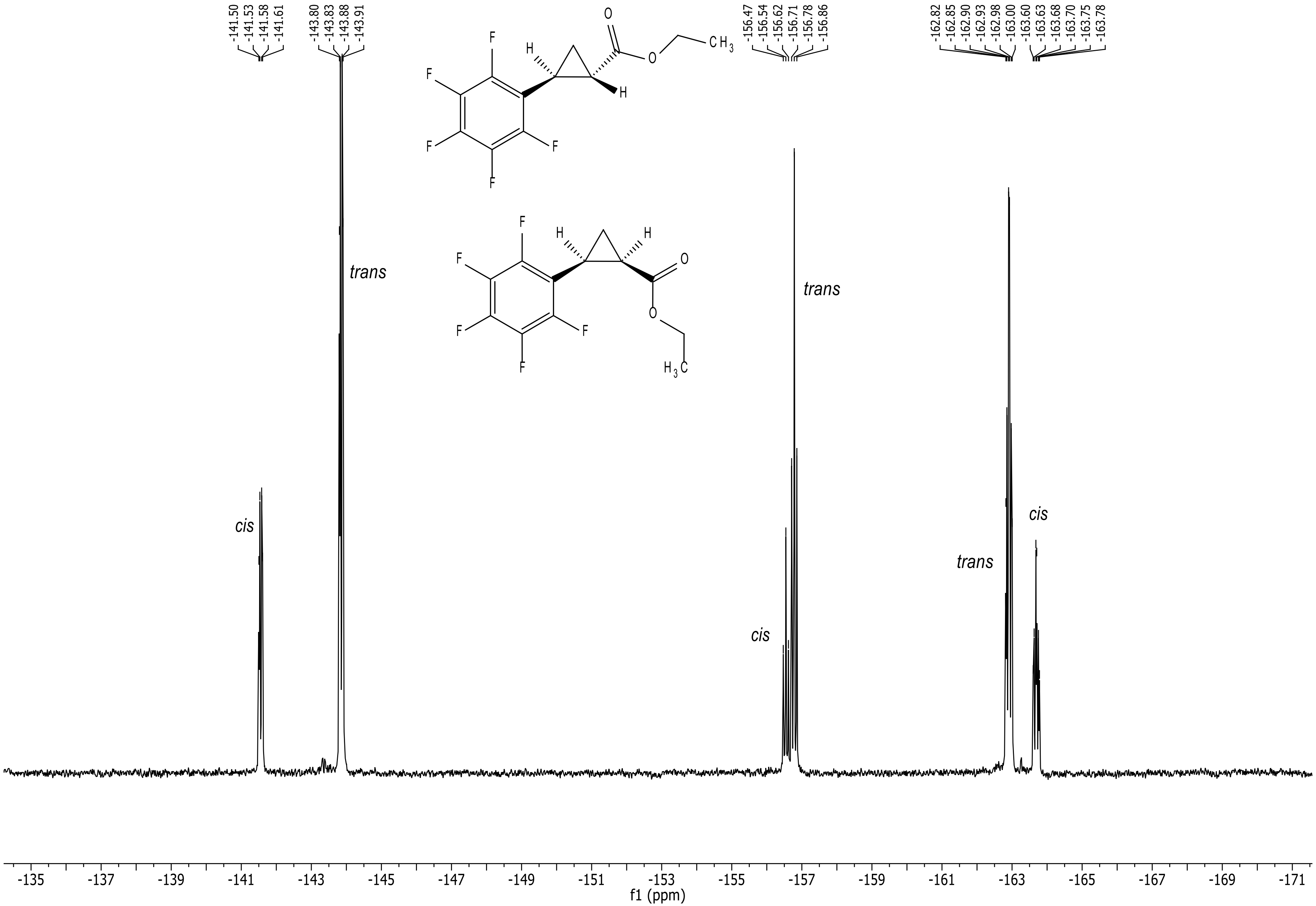
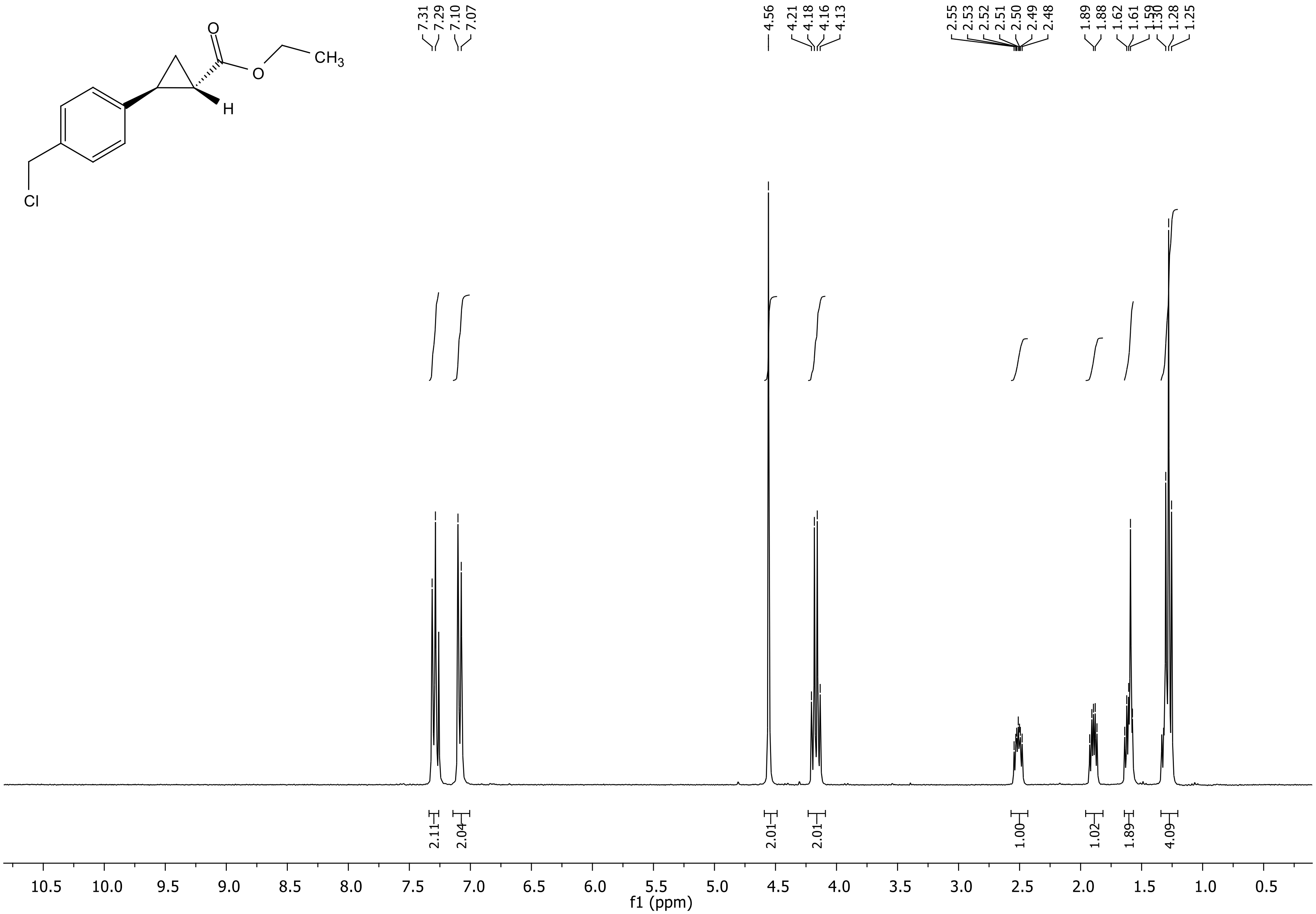
137.93
133.78
132.70
128.57
128.02
127.80
126.65
125.88
125.19
124.98
61.15
26.81
24.53
17.42
14.69
O
O
CH3
H
H
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

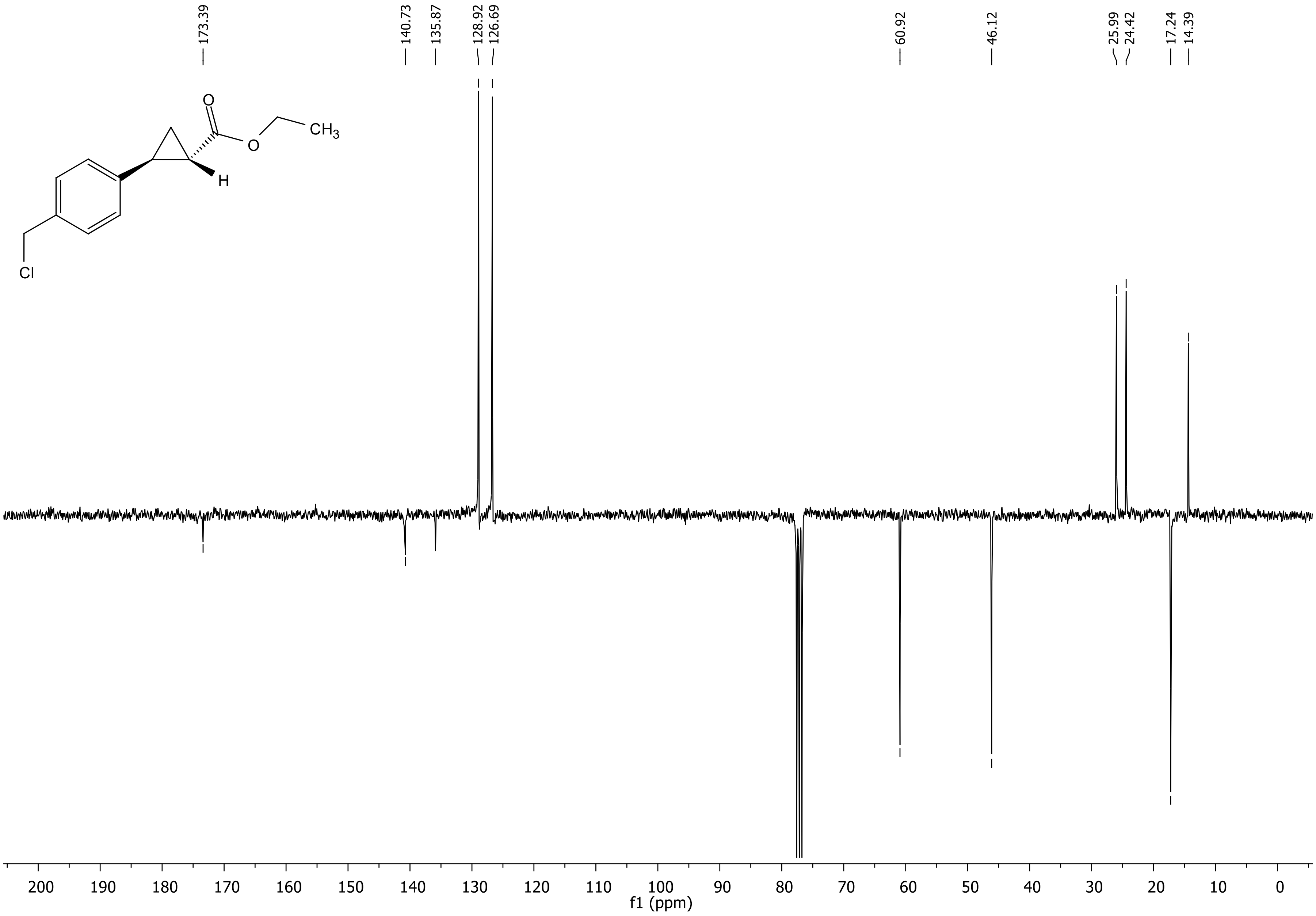


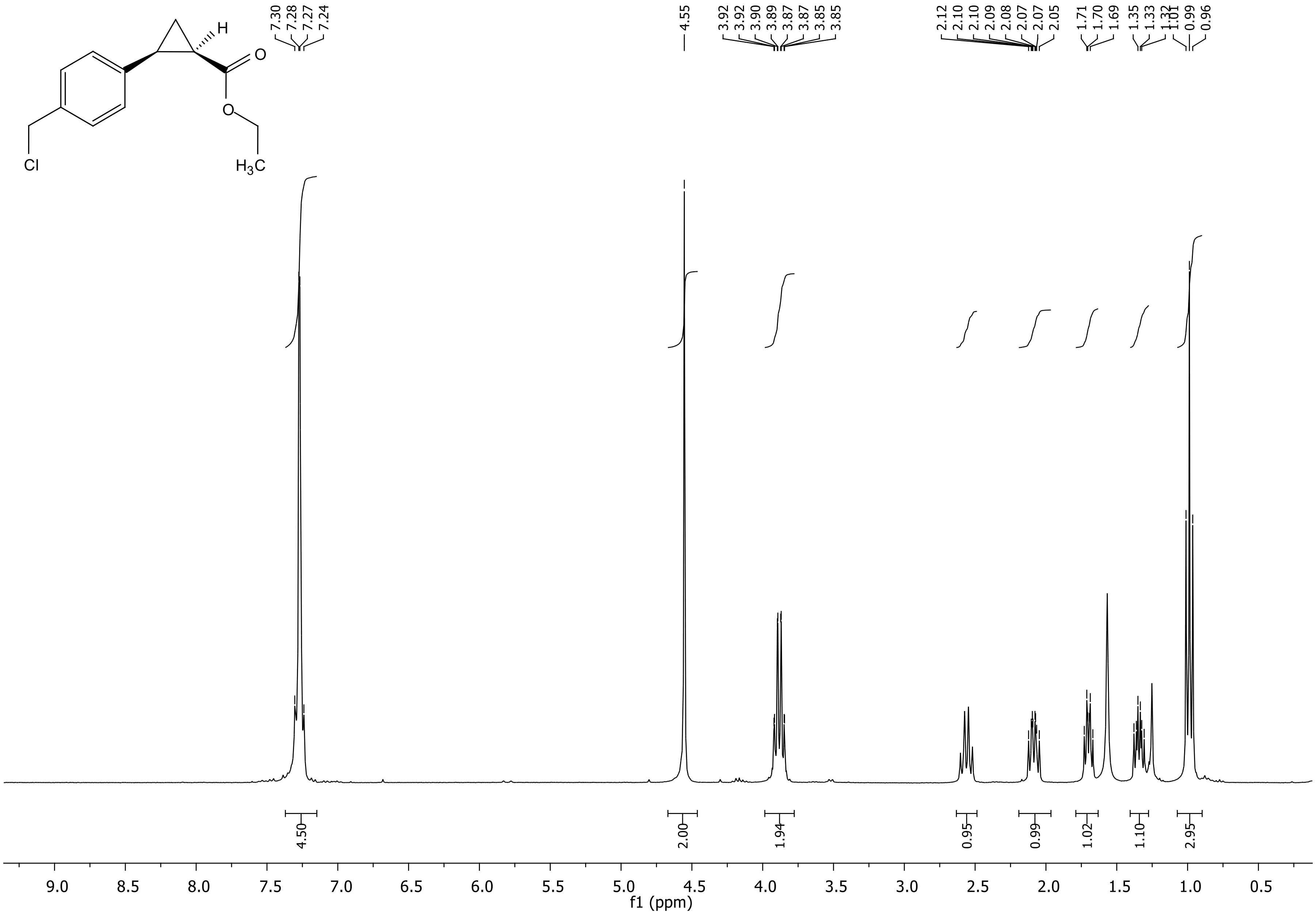
4.24 4.21 4.19 4.17 4.09 4.09 4.07 4.06 4.05 4.04 4.02 4.02
2.46 2.45 2.45 2.44 2.44 2.18 2.16 2.15 2.14 2.12 1.66 1.65 1.63 1.62 1.60 1.57 1.53 1.52 1.52 1.51 1.50 1.50 1.48 1.32 1.30 1.28 1.21 1.19 1.17
F
H
O
O
CH3
H
F
F
F
F
F
H
H
O
F
F
F
F
O
H3C
trans
cis
trans
trans+cis
trans+cis
trans
cis
2.00
0.77
0.94
1.76
1.70
1.08
3.25
1.22
1.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)

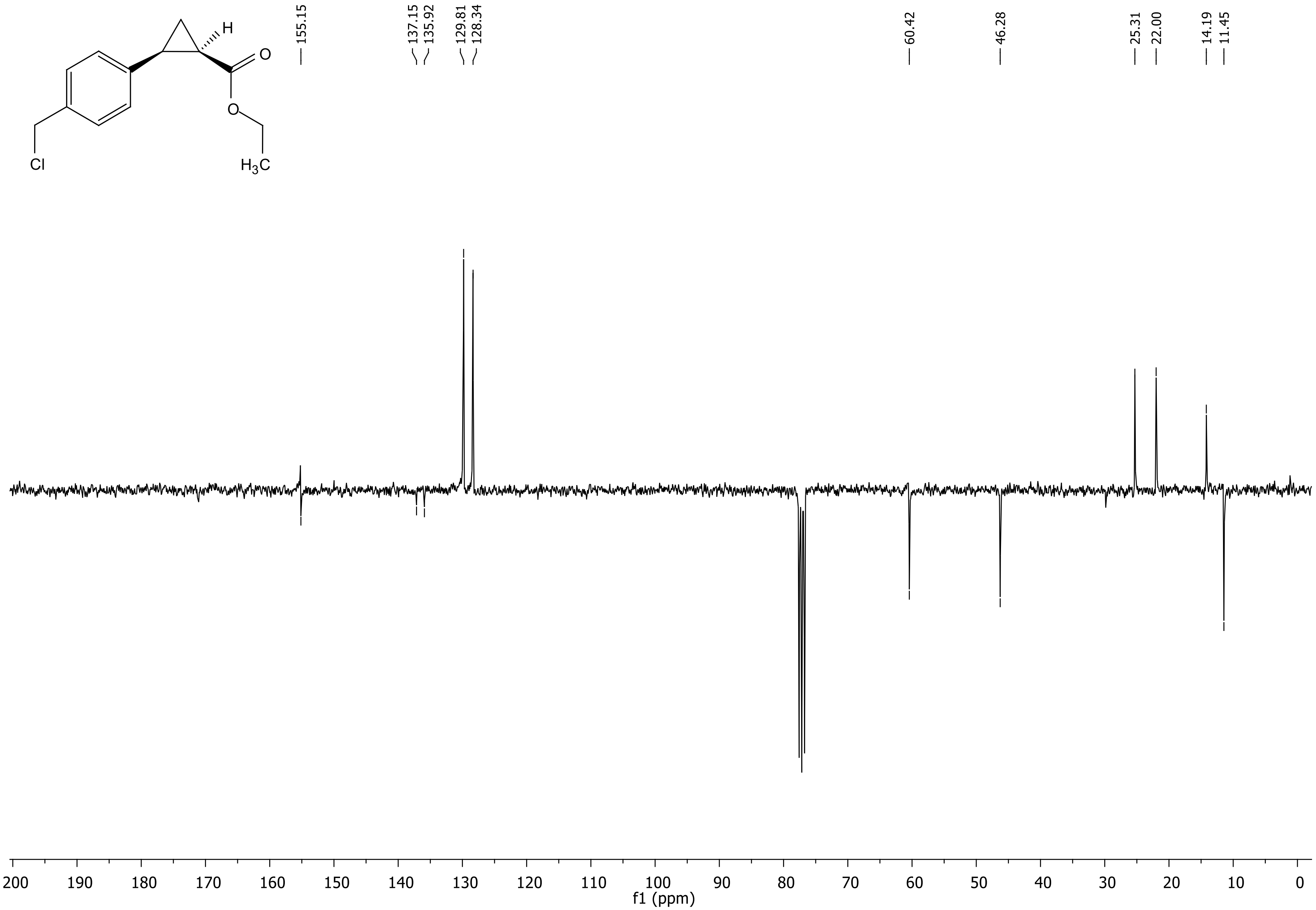

173.11
61.55
61.24
21.37
19.33
15.45
15.08
14.62
14.48
13.97
13.56
F
F
F
F
F
H
H
O
O
CH3
F
F
F
F
F
H
H
O
O
H3C
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


-141.50
-141.53
-141.58
-141.61
-143.80
-143.83
-143.88
-143.91
-156.47
-156.54
-156.62
-156.71
-156.78
-156.86
-162.82
-162.85
-162.90
-162.93
-162.98
-163.00
-163.60
-163.63
-163.68
-163.70
-163.75
-163.78
F
H
O
O
CH3
H
F
F
F
F
F
H
H
O
F
F
F
F
O
H3C
cis
trans
trans
cis
trans
cis
-135
-137
-139
-141
-143
-145
-147
-149
-151
-153
-155
-157
-159
-161
-163
-165
-167
-169
-171
f1 (ppm)

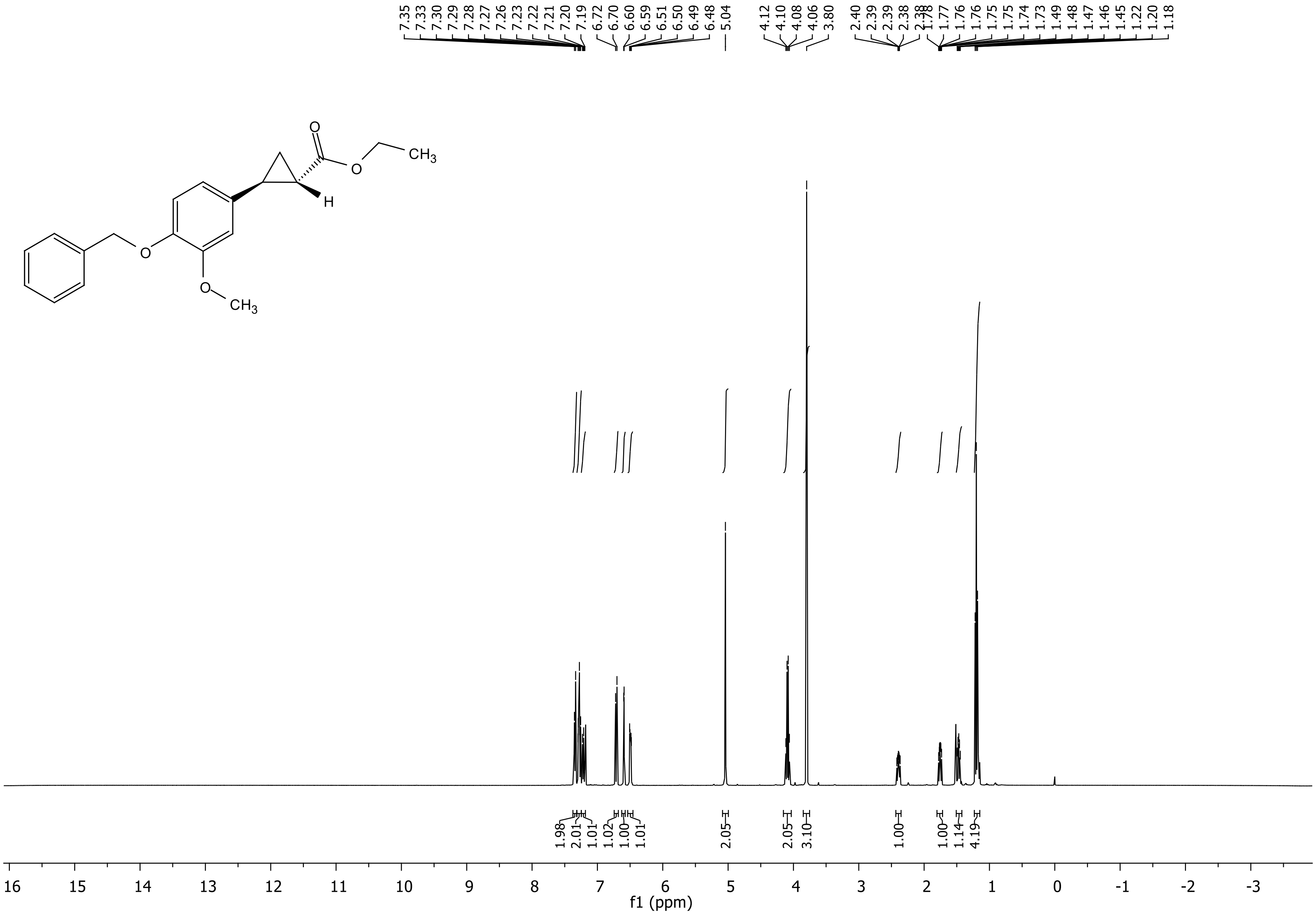

O
O
CH3
H
Cl
7.31
7.29
7.10
7.07
4.56
4.21
4.18
4.16
4.13
2.55
2.53
2.52
2.51
2.50
2.49
2.48
1.89
1.88
1.62
1.61
1.59
1.30
1.28
1.25
2.11
2.04
2.01
2.01
1.00
1.02
1.89
4.09
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


173.39
140.73
135.87
128.92
126.69
60.92
46.12
25.99
24.42
17.24
14.39
O
O
CH3
H
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


H
O
O
Cl
H3C
7.30
7.28
7.27
7.24
4.55
3.92
3.92
3.90
3.89
3.87
3.87
3.85
3.85
2.12
2.10
2.10
2.09
2.08
2.07
2.07
2.05
1.71
1.70
1.69
1.35
1.33
1.32
1.01
0.99
0.96
4.50
2.00
1.94
0.95
0.99
1.02
1.10
2.95
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



H
O
O
Cl
H_3C
155.15
137.15
135.92
129.81
128.34
60.42
46.28
25.31
22.00
14.19
11.45
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.35
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7.30
7.29
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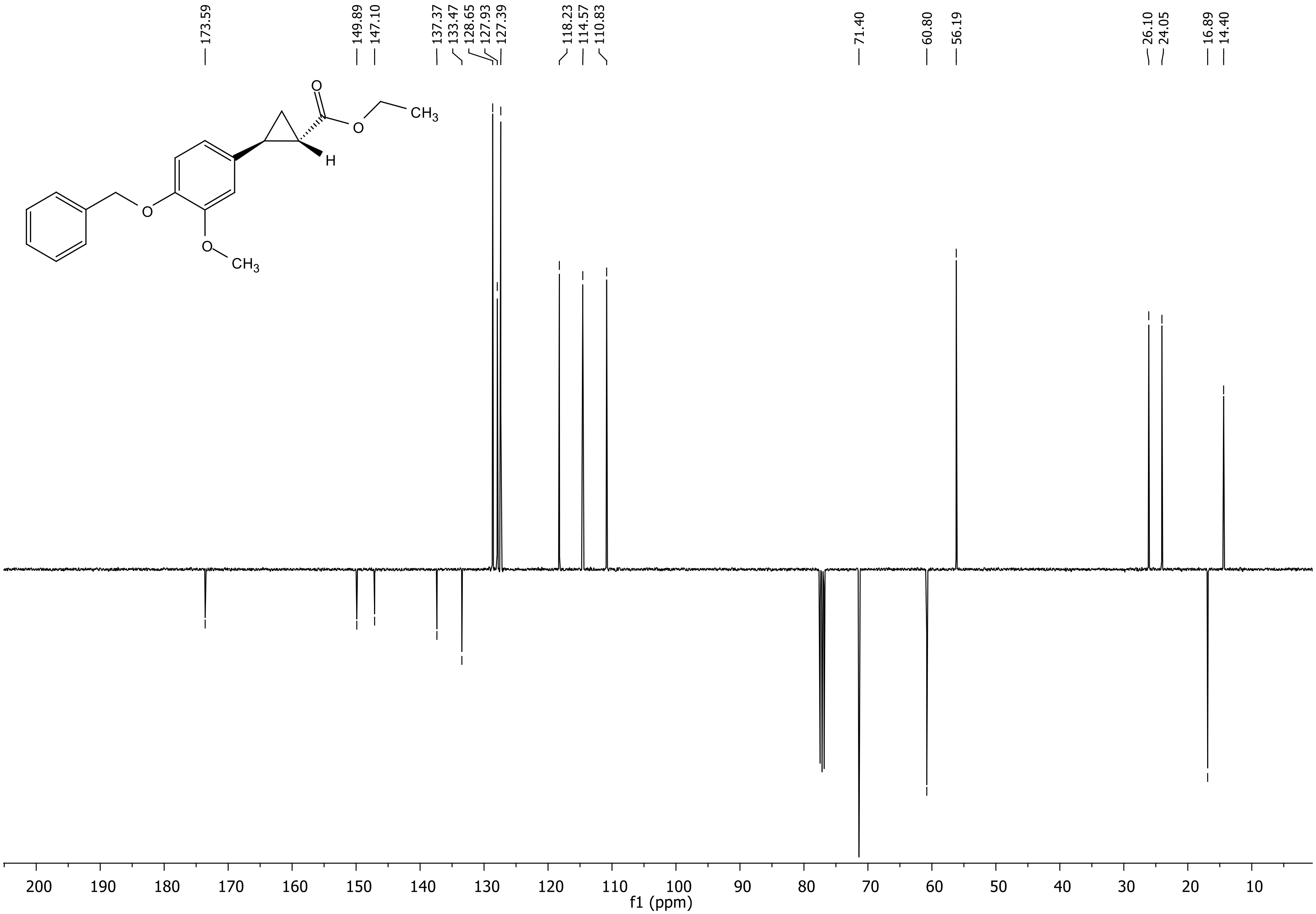
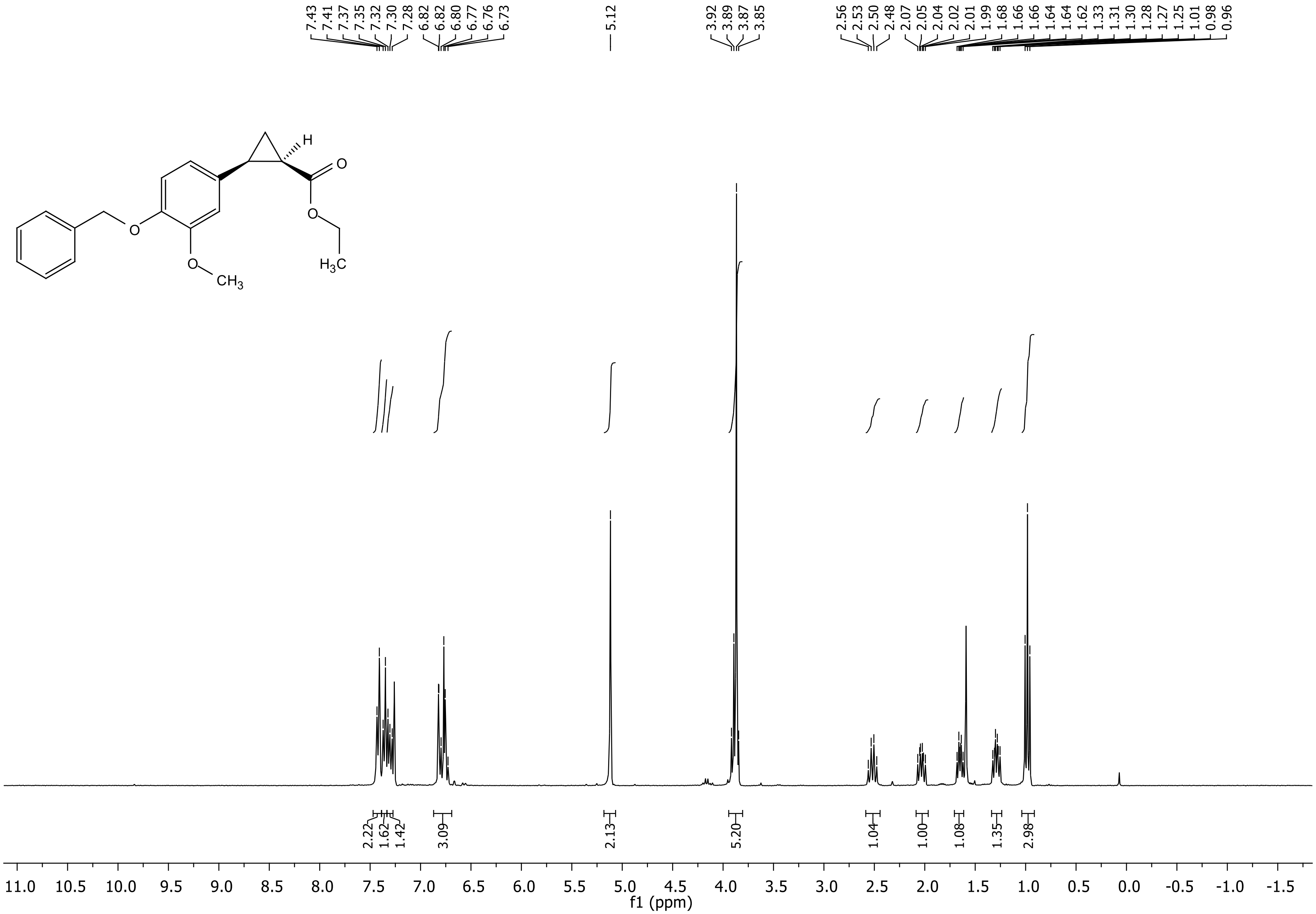
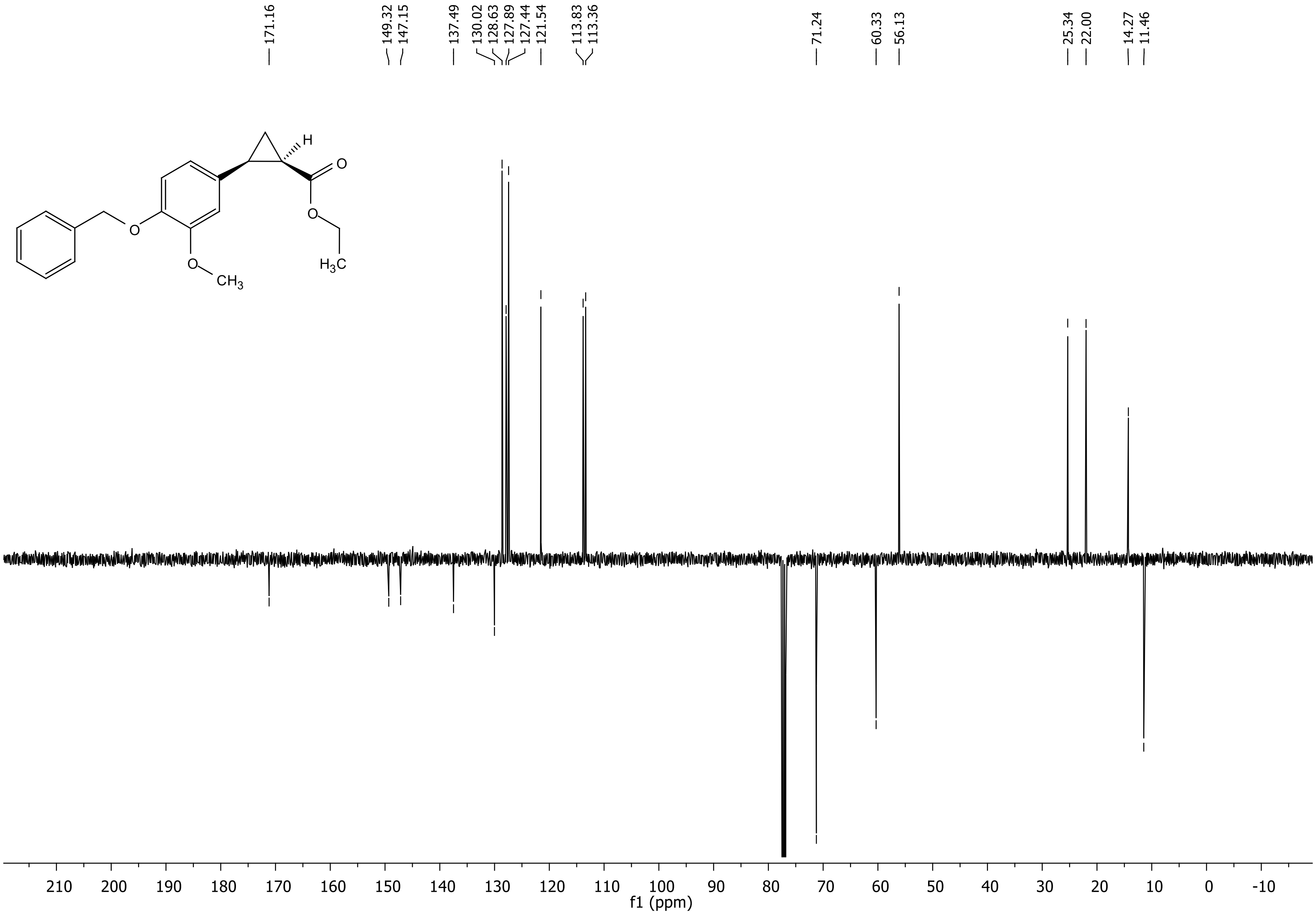
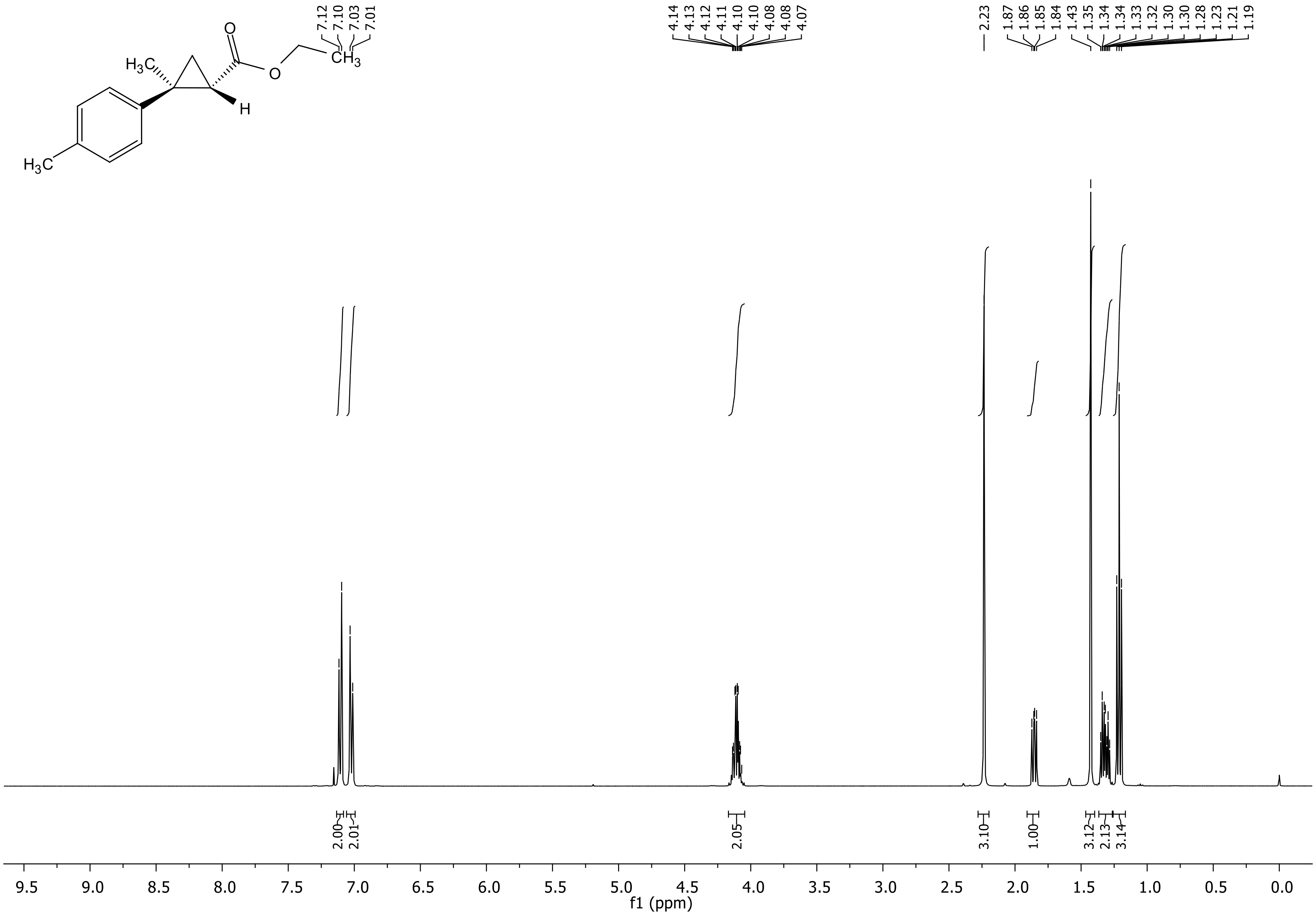
7.27
7.26
7.23
7.22
7.21
7.20
7.19
6.72
6.70
6.60
6.59
6.51
6.50
6.49
6.48
5.04
4.12
4.10
4.08
4.06
3.80
2.40
2.39
2.39
2.38
2.38
1.78
1.77
1.76
1.76
1.75
1.75
1.74
1.73
1.49
1.48
1.47
1.46
1.45
1.22
1.20
1.18
O
O
CH3
H
O
O
CH3
1.98
2.01
1.01
1.02
1.00
1.01
2.05
2.05
3.10
1.00
1.00
1.14
4.19
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
f1 (ppm)


173.59
149.89
147.10
137.37
133.47
128.65
127.93
127.39
118.23
114.57
110.83
71.40
60.80
56.19
26.10
24.05
16.89
14.40
O
O
CH3
H
O
O
CH3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.43
7.41
7.37
7.35
7.32
7.30
7.28
6.82
6.82
6.80
6.77
6.76
6.73
5.12
3.92
3.89
3.87
3.85
2.56
2.53
2.50
2.48
2.07
2.05
2.04
2.02
2.01
1.99
1.68
1.66
1.66
1.64
1.64
1.62
1.33
1.31
1.30
1.28
1.27
1.25
1.01
0.98
0.96
H
O
O
O
O
CH3
H3C
2.22
1.62
1.42
3.09
2.13
5.20
1.04
1.00
1.08
1.35
2.98
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
f1 (ppm)


171.16
149.32
147.15
137.49
130.02
128.63
127.89
127.44
121.54
113.83
113.36
71.24
60.33
56.13
25.34
22.00
14.27
11.46
H
O
O
O
O
CH3
H3C
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



7.12
7.10
7.03
7.01
4.14
4.13
4.12
4.11
4.10
4.10
4.08
4.08
4.07
2.23
1.87
1.86
1.85
1.84
1.43
1.35
1.34
1.34
1.33
1.32
1.30
1.30
1.28
1.23
1.21
1.19
O
O
H$_3$C
CH$_3$
H
H$_3$C
2.00
2.01
2.05
3.10
1.00
3.12
2.13
3.14
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
3.0
2.5
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1.0
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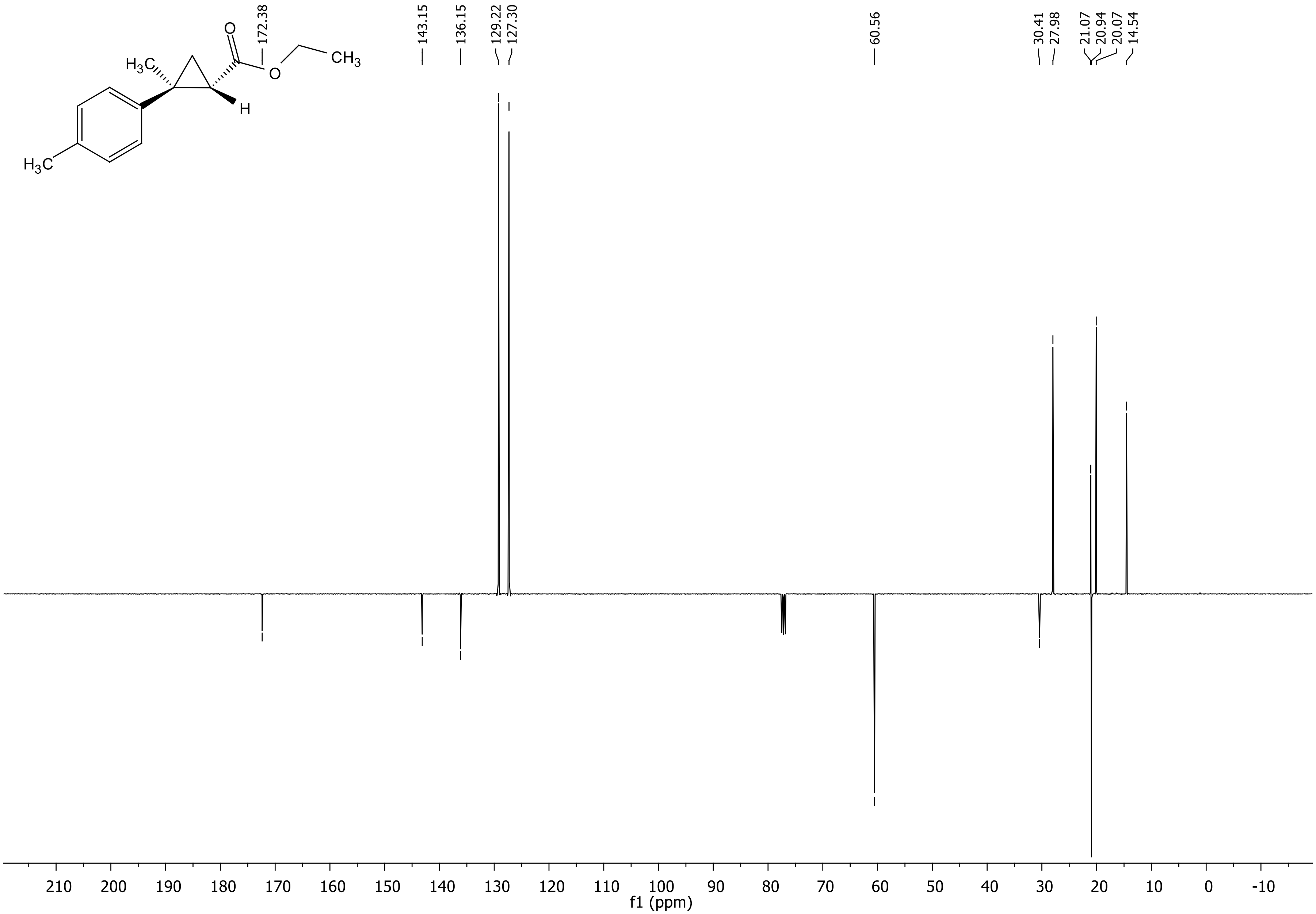
f1 (ppm)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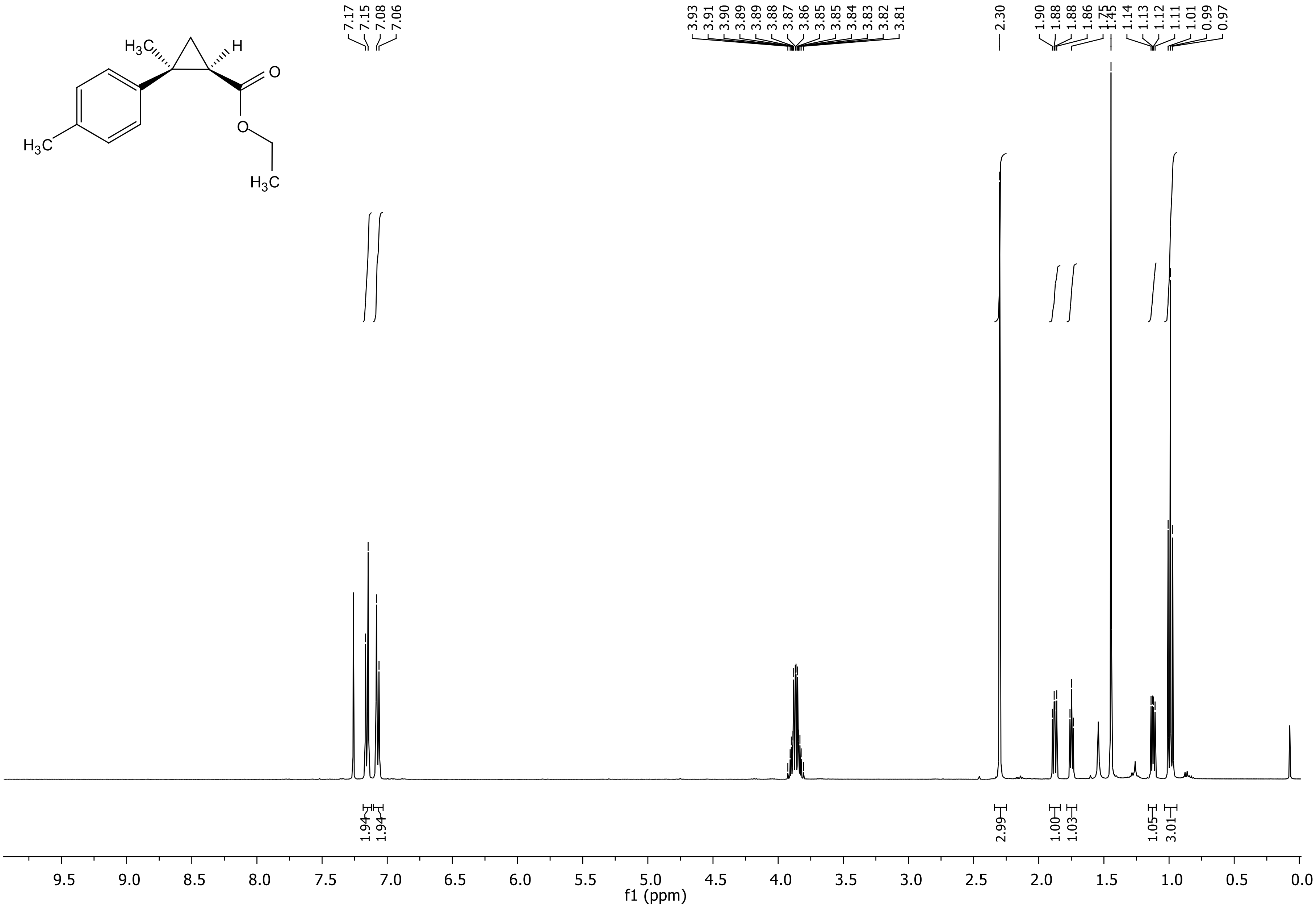
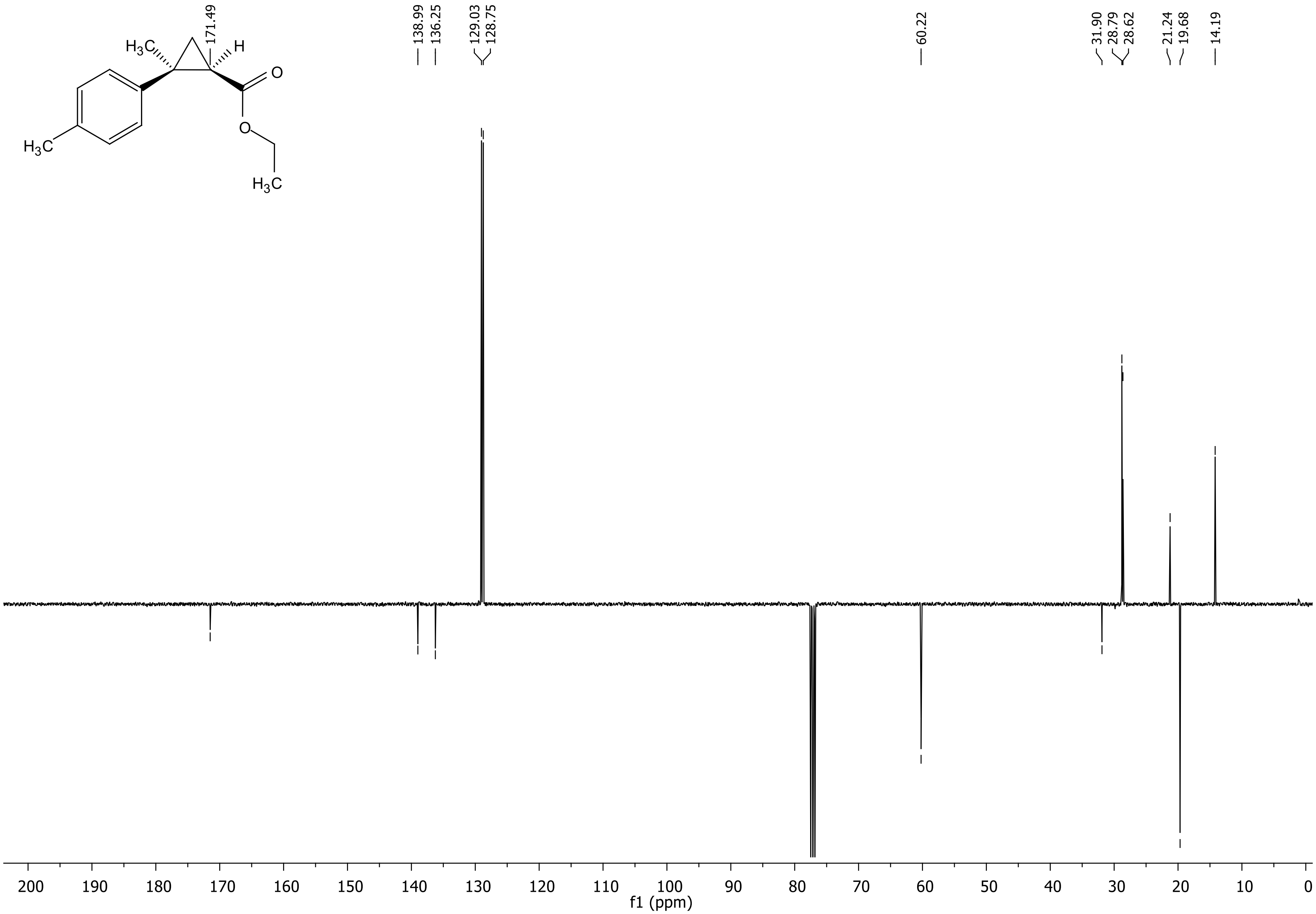
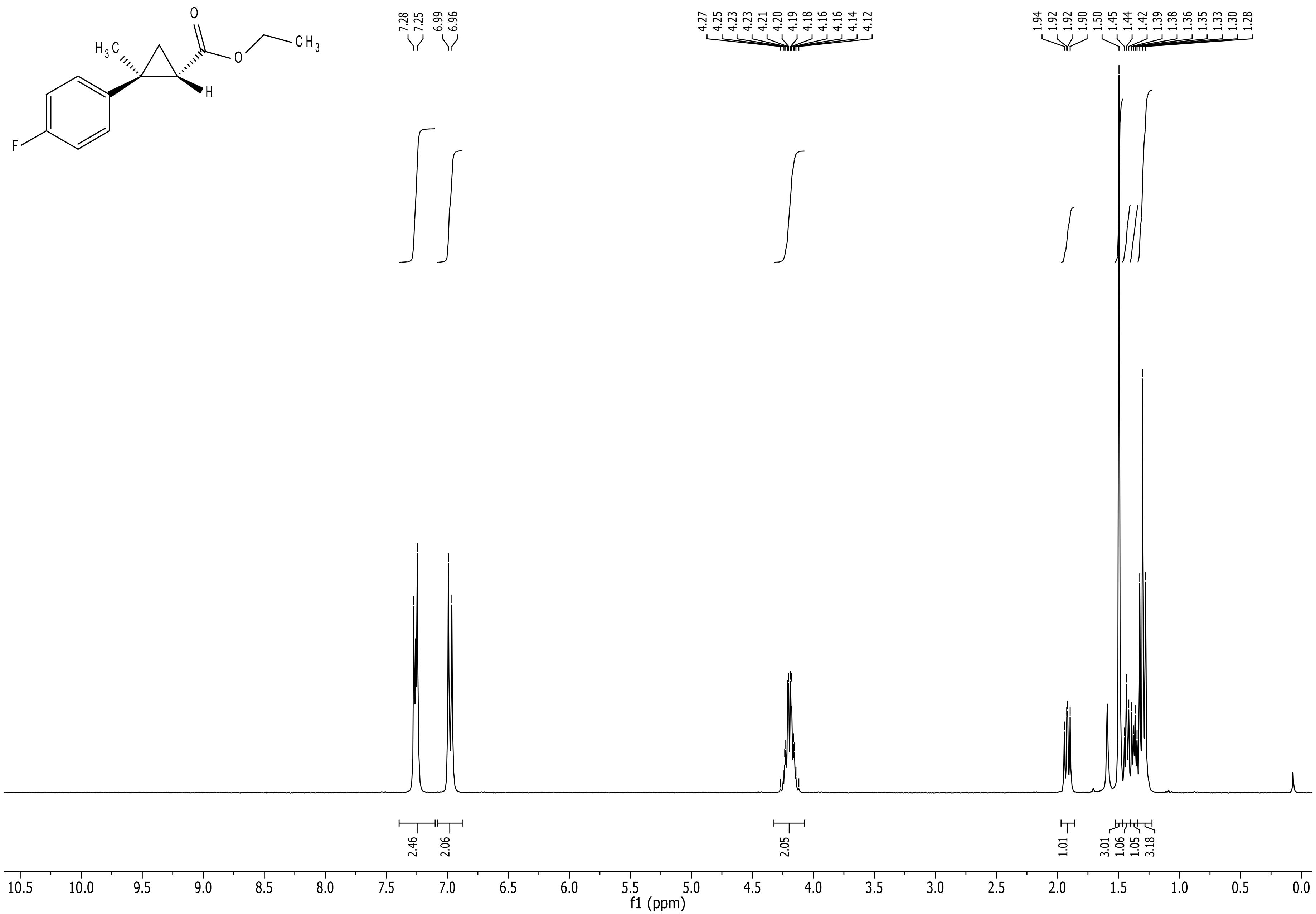
O
CH$_3$
H$_3$C
H
172.38
143.15
136.15
129.22
127.30
60.56
30.41
27.98
21.07
20.94
20.07
14.54
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


H$_3$C
H
O
O
H$_3$C
H$_3$C
7.17
7.15
7.08
7.06
3.93
3.91
3.90
3.89
3.89
3.88
3.87
3.86
3.85
3.85
3.84
3.83
3.82
3.81
2.30
1.90
1.88
1.88
1.86
1.75
1.45
1.14
1.13
1.12
1.11
1.01
0.99
0.97
1.94
1.94
2.99
1.00
1.03
1.05
3.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


171.49
138.99
136.25
129.03
128.75
60.22
31.90
28.79
28.62
21.24
19.68
14.19
H$_3$C
H
O
O
H$_3$C
H$_3$C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


H3C
O
O
CH3
H
F
7.28
7.25
6.99
6.96
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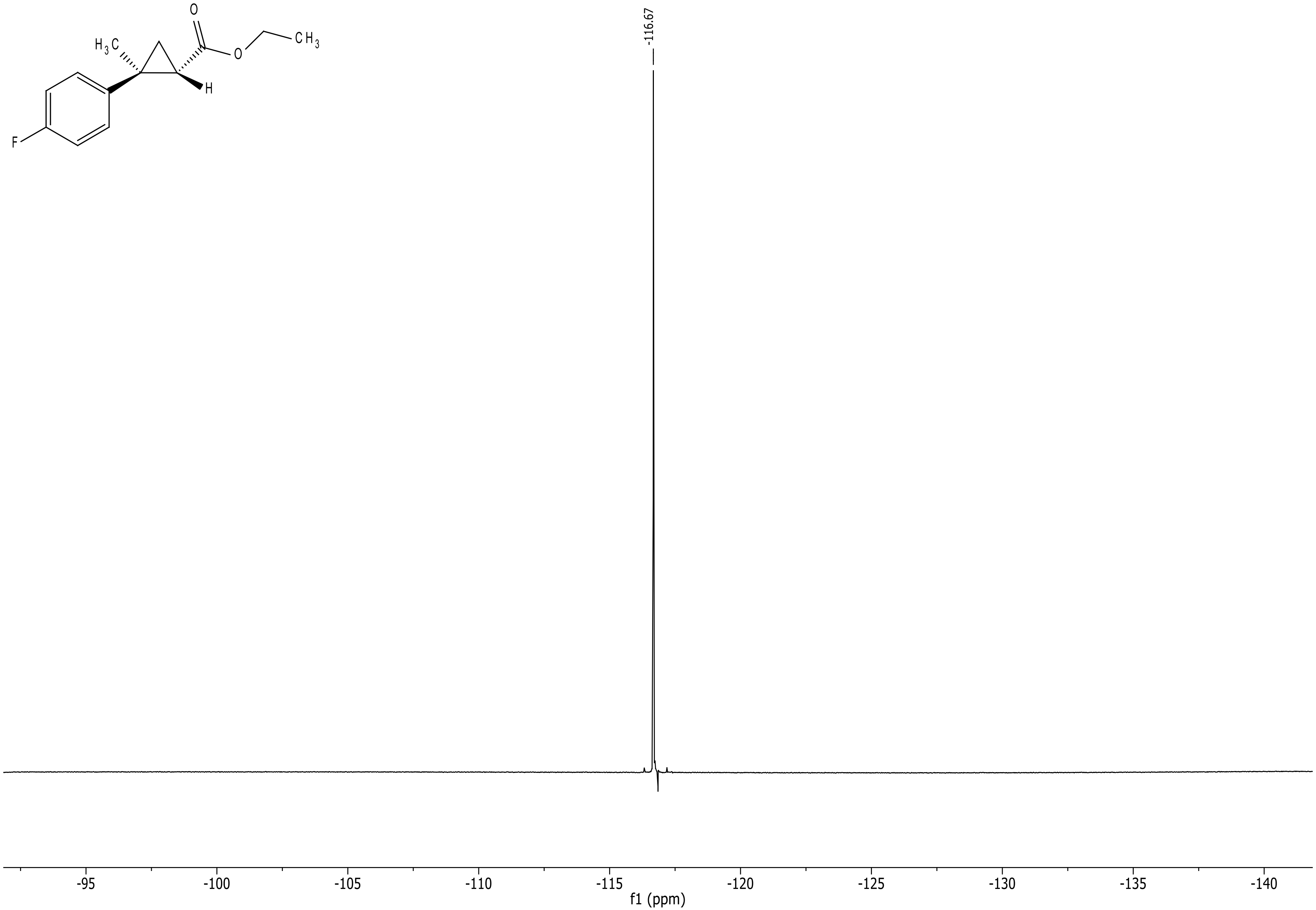
4.25
4.23
4.23
4.21
4.20
4.19
4.18
4.16
4.16
4.14
4.12
1.94
1.92
1.92
1.90
1.50
1.45
1.44
1.42
1.39
1.38
1.36
1.35
1.33
1.30
1.28
2.46
2.06
2.05
1.01
3.01
1.06
1.05
3.18
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


H3C
O
O
CH3
H
F
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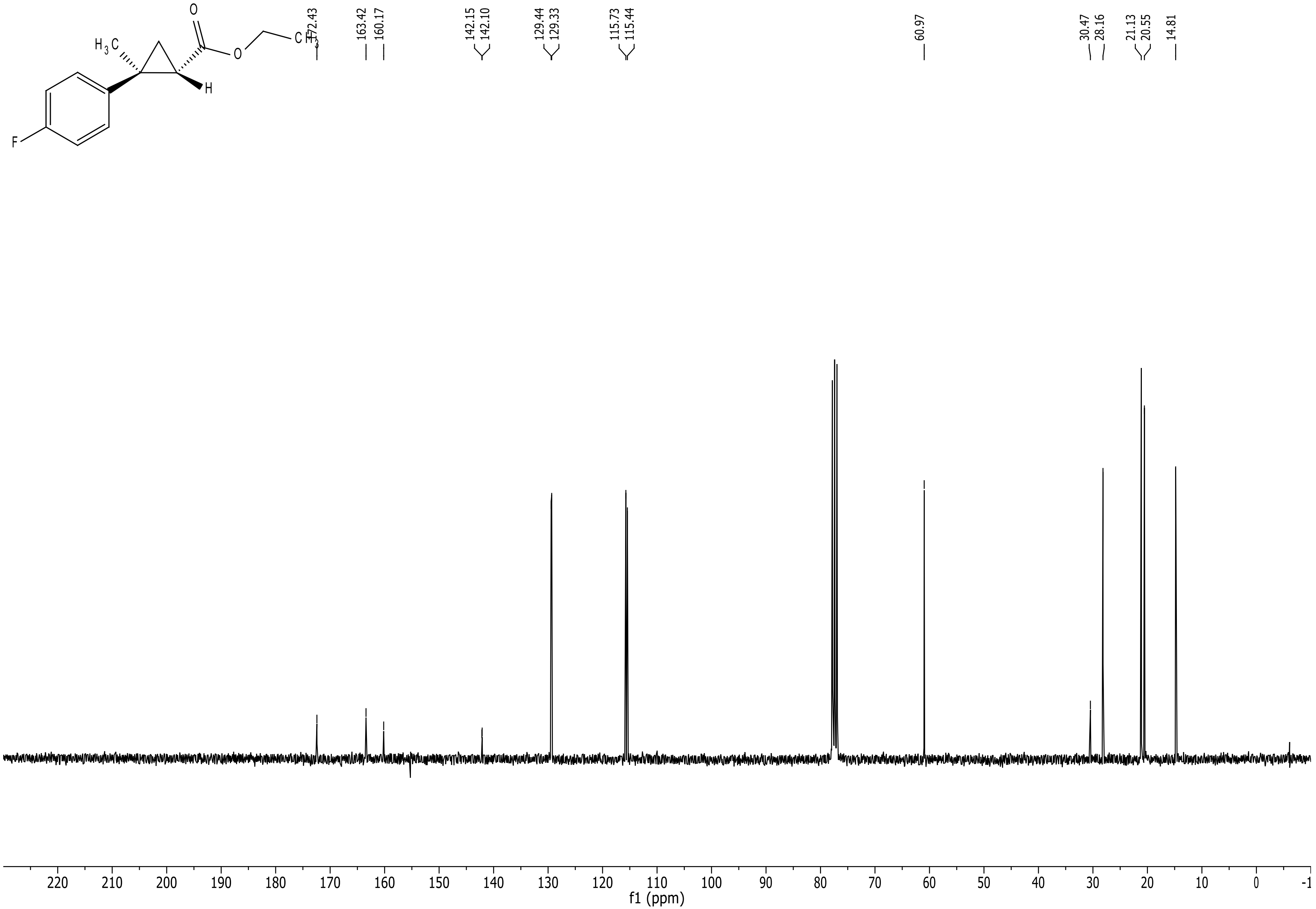
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
f1 (ppm)


O
H3C
O
CH3
H
F
172.43
163.42
160.17
142.15
142.10
129.44
129.33
115.73
115.44
60.97
30.47
28.16
21.13
20.55
14.81
220
210
200
190
180
170
160
150
140
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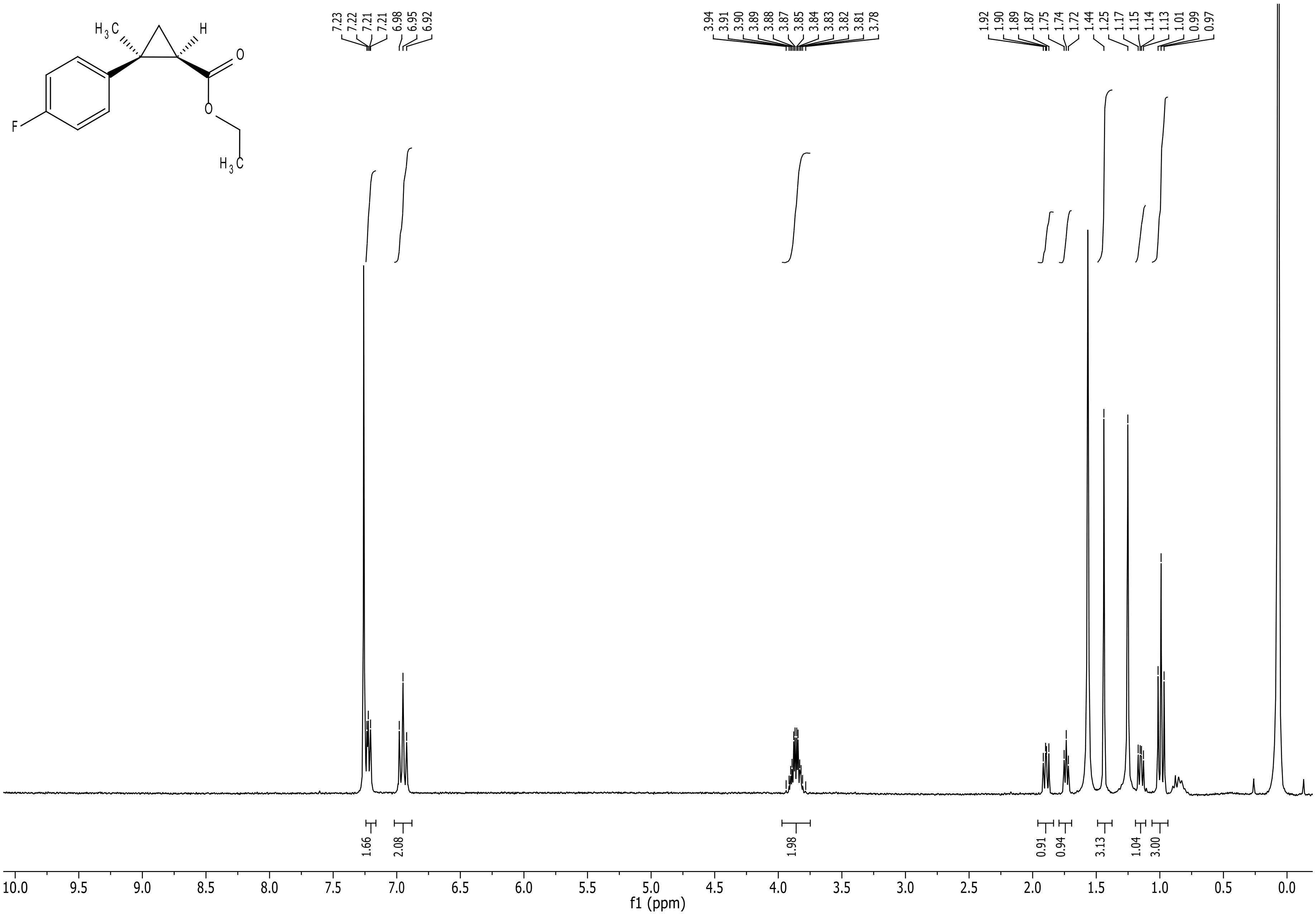
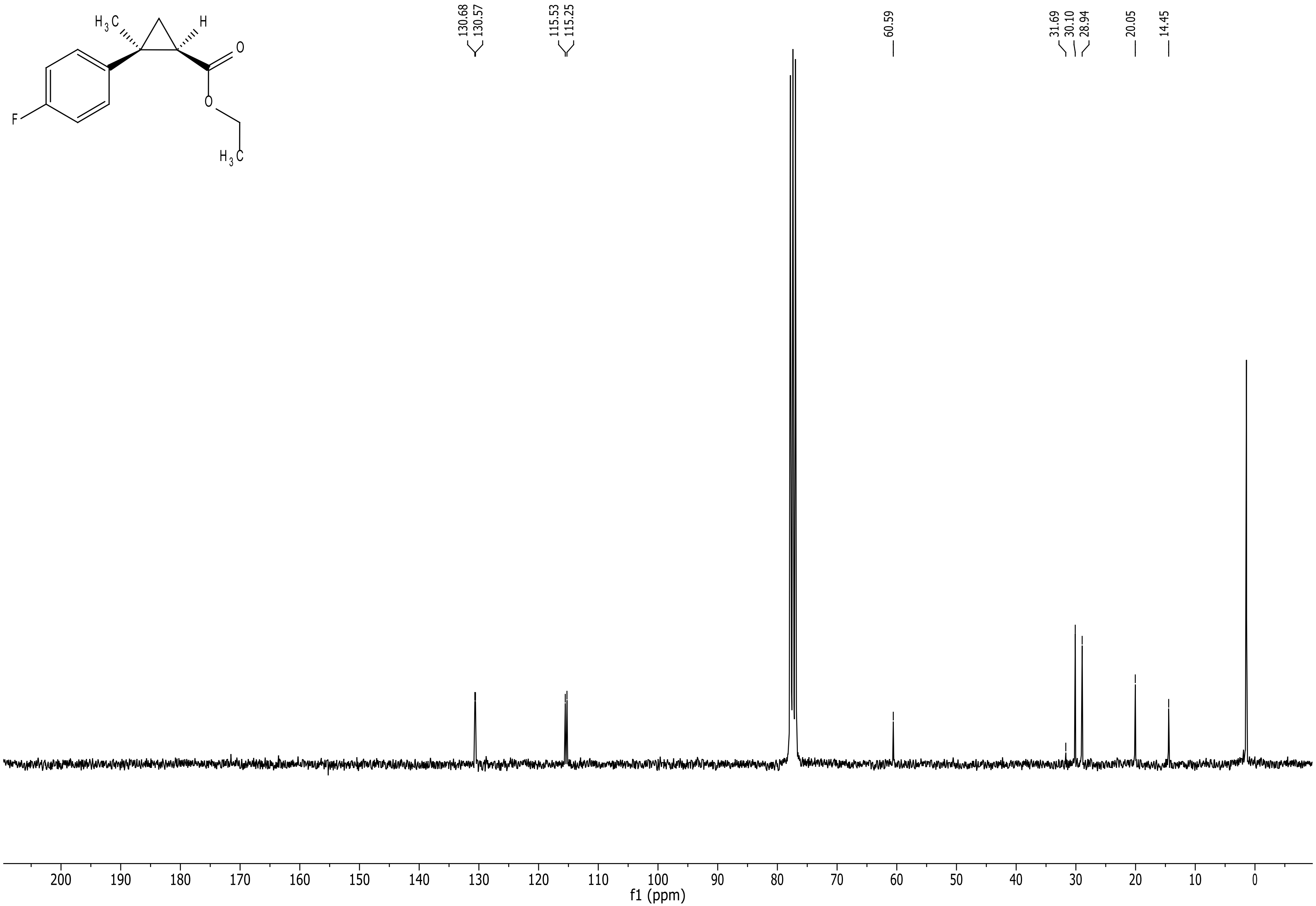
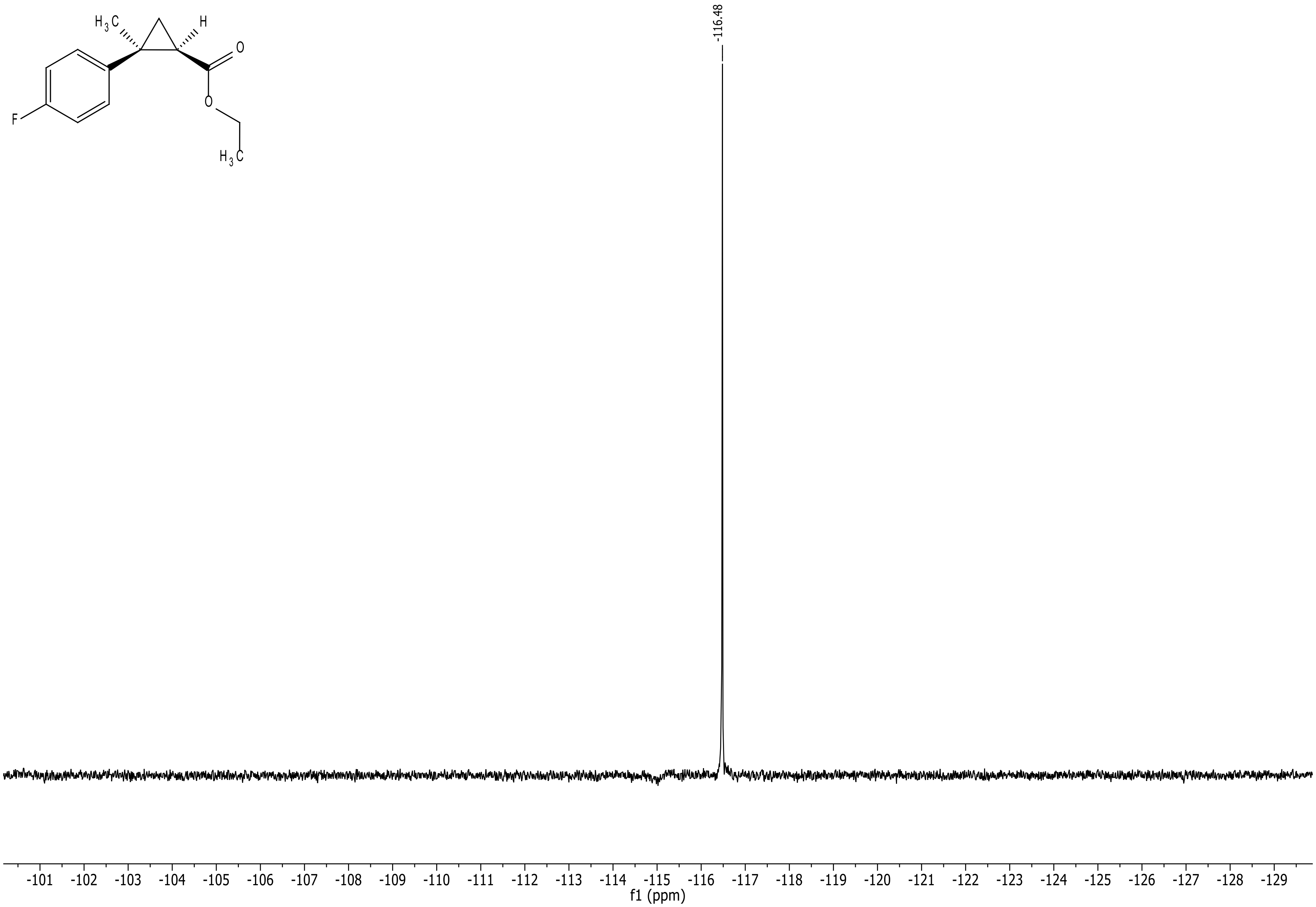
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


H3C
H
O
O
F
H3C
7.23
7.22
7.21
7.21
6.98
6.95
6.92
3.94
3.91
3.90
3.89
3.88
3.87
3.85
3.84
3.83
3.82
3.81
3.78
1.92
1.90
1.89
1.87
1.75
1.74
1.72
1.44
1.25
1.17
1.15
1.14
1.13
1.01
0.99
0.97
1.66
2.08
1.98
0.91
0.94
3.13
1.04
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


H3C
H
O
O
F
H3C
130.68
130.57
115.53
115.25
60.59
31.69
30.10
28.94
20.05
14.45
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-116.48
-101
-102
-103
-104
-105
-106
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-108
-109
-110
-111
-112
-113
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-115
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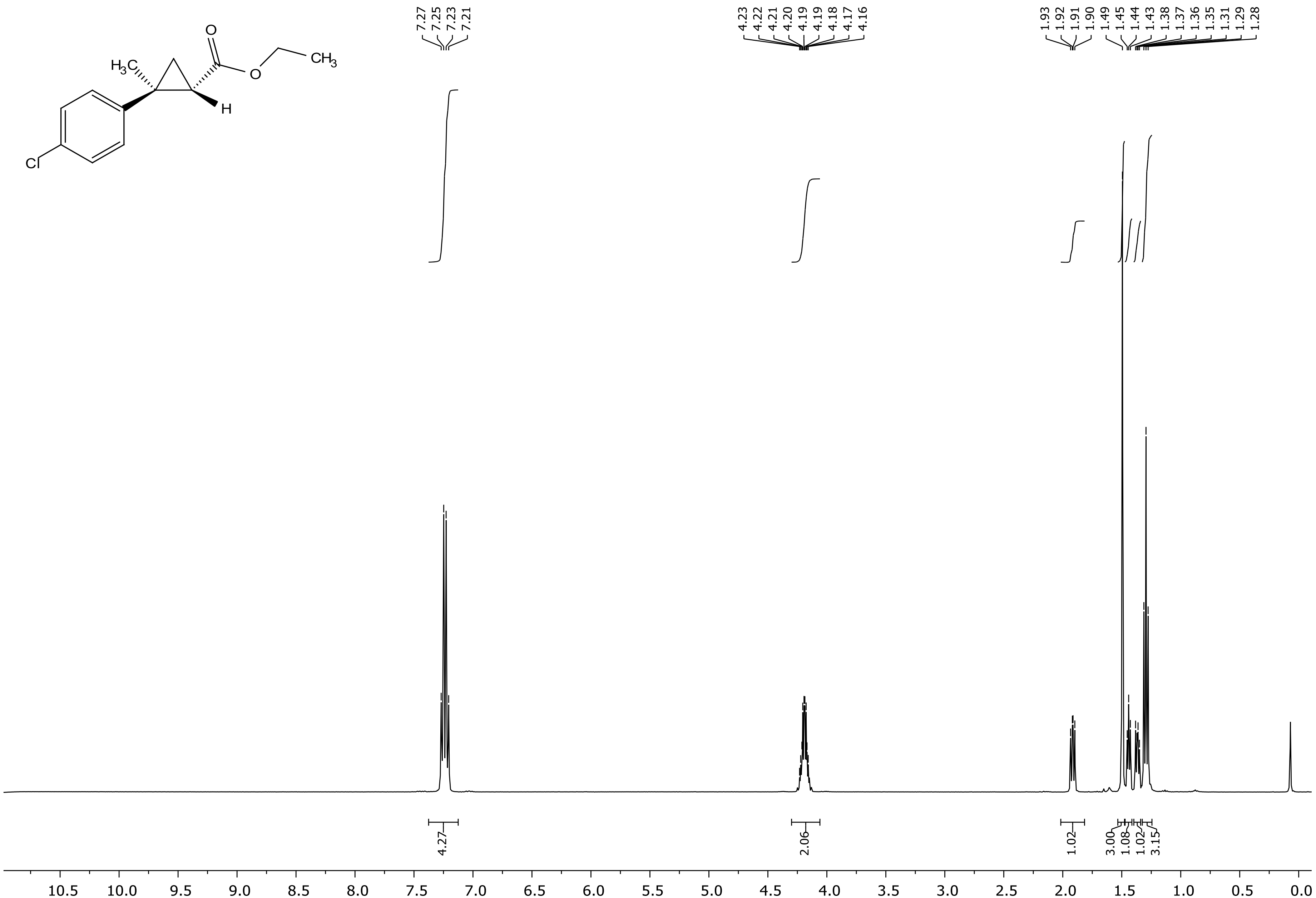
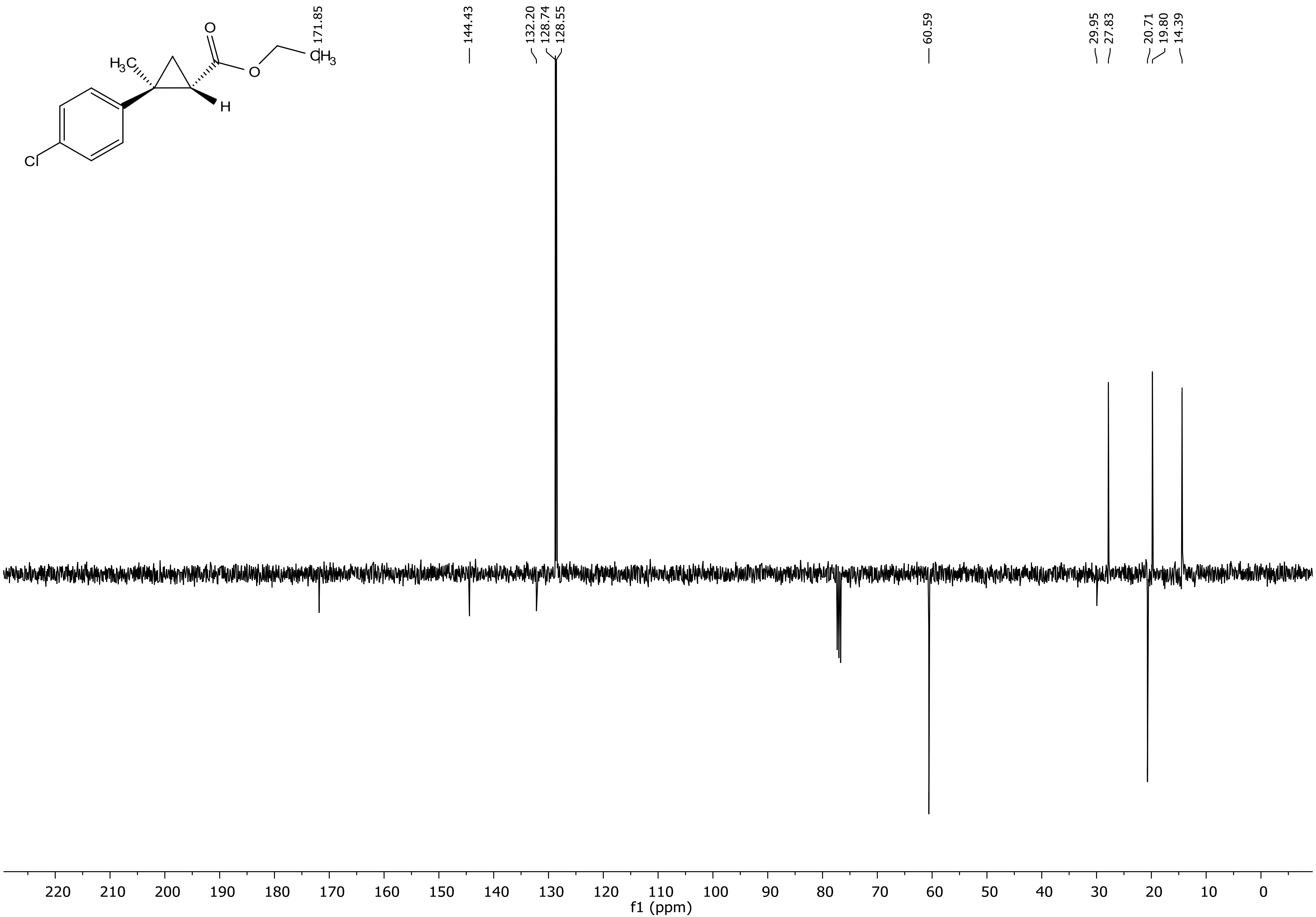
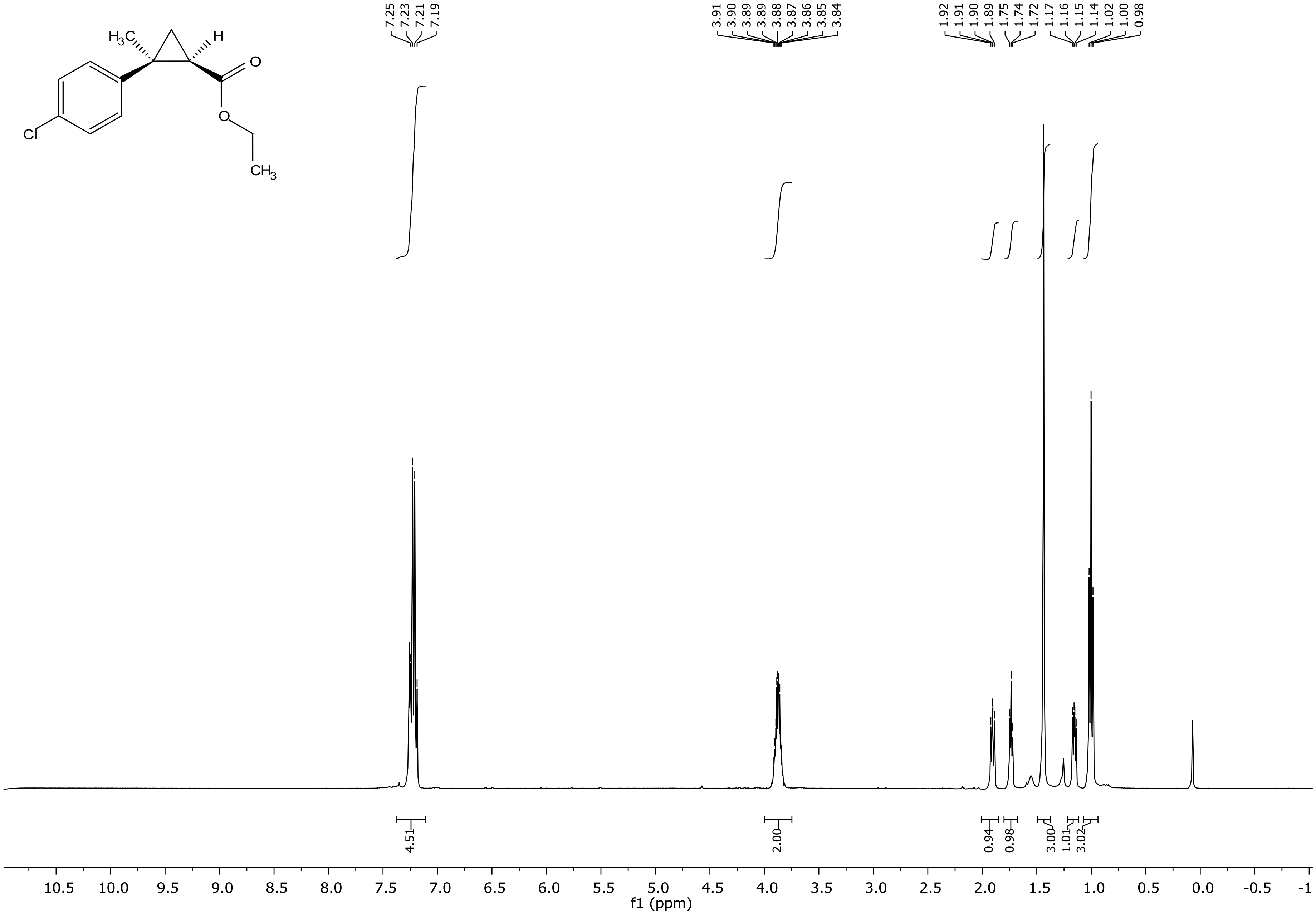
-126
-127
-128
-129
f1 (ppm)



O
O
CH3
H3C
H
Cl
7.27
7.25
7.23
7.21
4.23
4.22
4.21
4.20
4.19
4.19
4.18
4.17
4.16
1.93
1.92
1.91
1.90
1.49
1.45
1.44
1.43
1.38
1.37
1.36
1.35
1.31
1.29
1.28
4.27
2.06
1.02
3.00
1.08
1.02
3.15
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


171.85
144.43
132.20
128.74
128.55
60.59
29.95
27.83
20.71
19.80
14.39
O
O
H_3C
CH_3
H
Cl
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


H3C
H
O
O
Cl
CH3
7.25
7.23
7.21
7.19
3.91
3.90
3.89
3.89
3.88
3.87
3.86
3.85
3.84
1.92
1.91
1.90
1.89
1.75
1.74
1.72
1.17
1.16
1.15
1.14
1.02
1.00
0.98
4.51
2.00
0.94
0.98
3.00
1.01
3.02
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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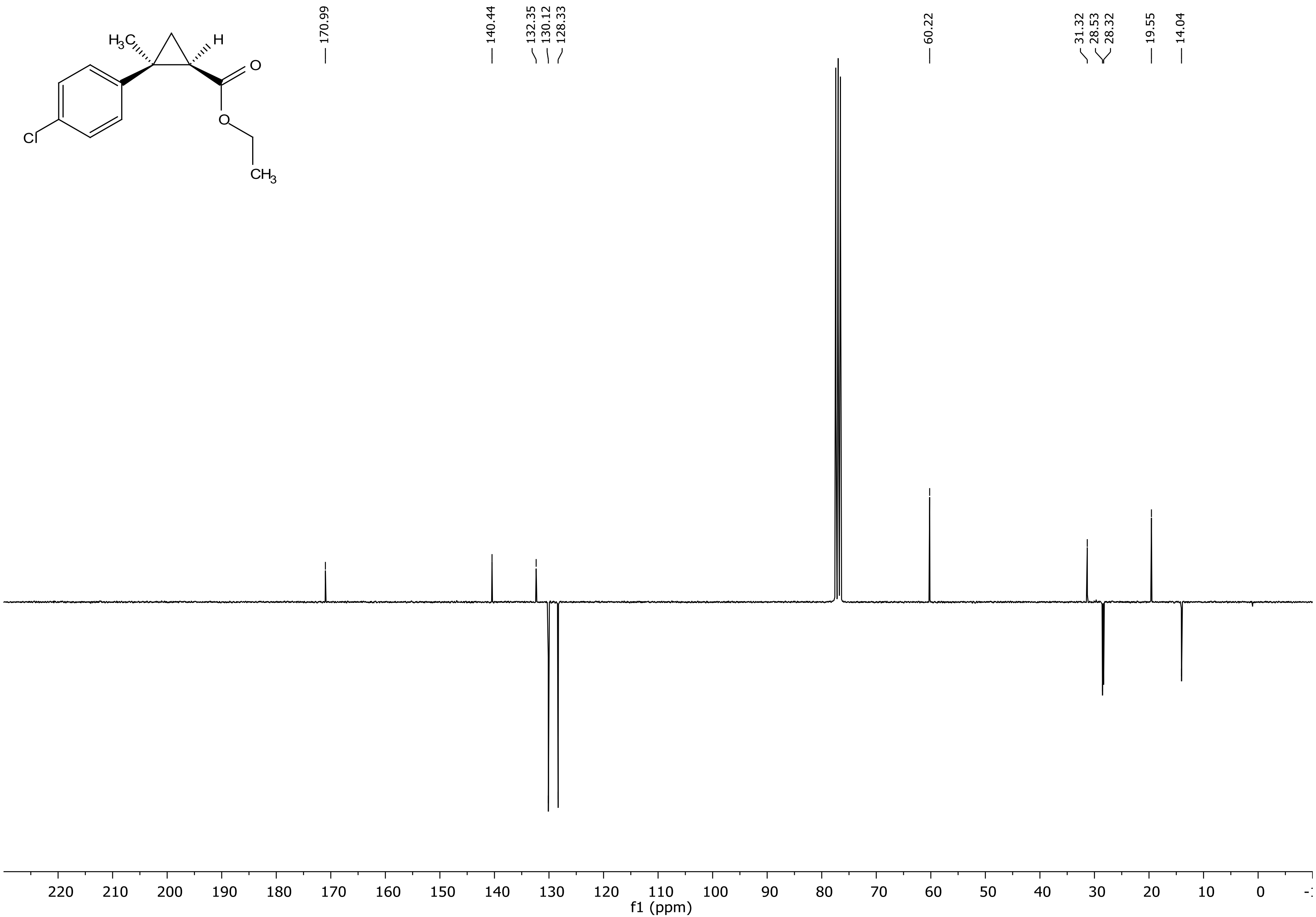
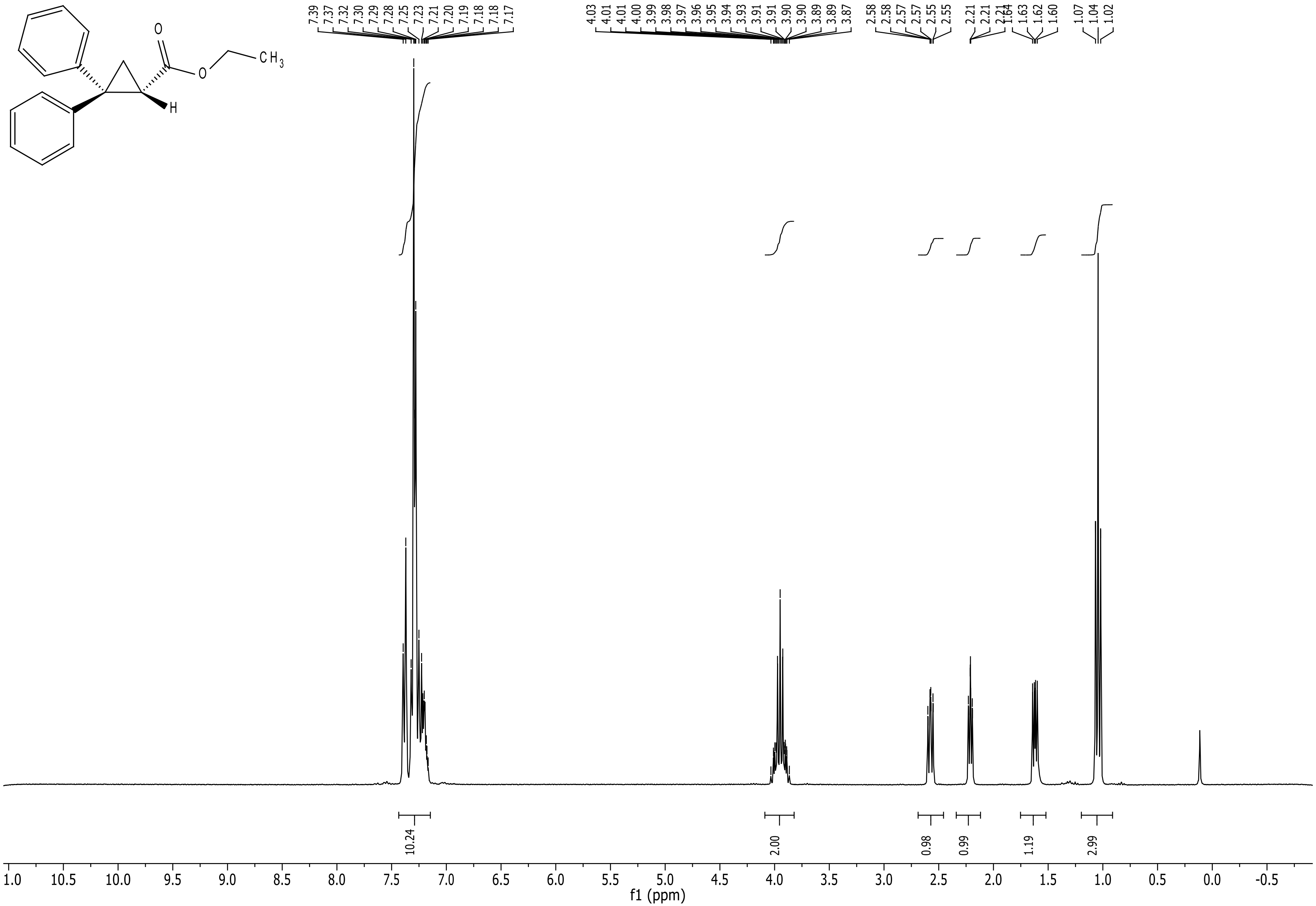
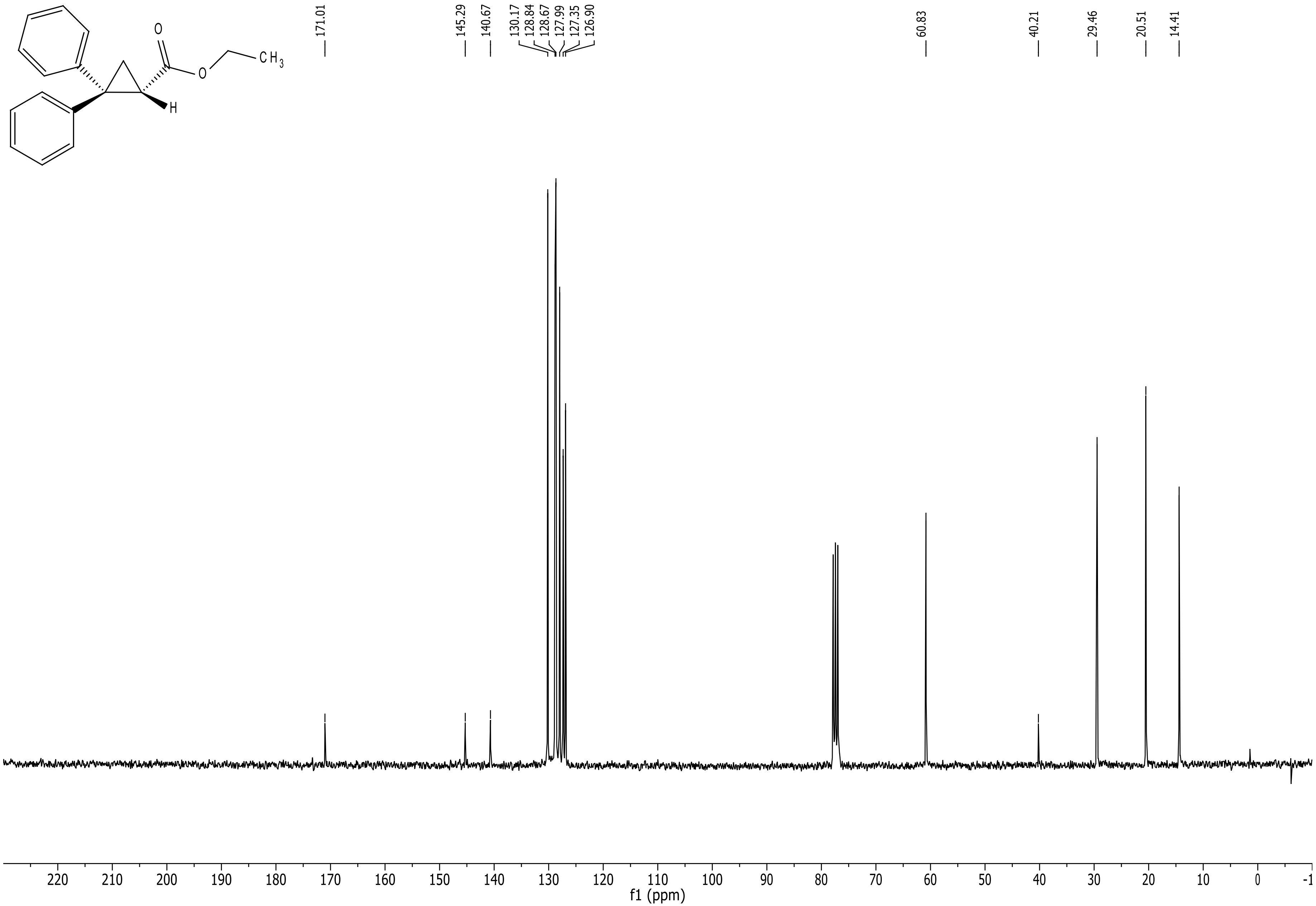
0.0
-0.5
-1
f1 (ppm)


170.99
140.44
132.35
130.12
128.33
60.22
31.32
28.53
28.32
19.55
14.04
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
CH3
H
7.39
7.37
7.32
7.30
7.29
7.28
7.25
7.23
7.21
7.20
7.19
7.18
7.18
7.17
4.03
4.01
4.01
4.00
3.99
3.98
3.97
3.96
3.95
3.94
3.93
3.91
3.91
3.90
3.90
3.89
3.89
3.87
2.58
2.58
2.57
2.57
2.55
2.55
2.21
2.21
2.21
1.64
1.63
1.62
1.60
1.07
1.04
1.02
10.24
2.00
0.98
0.99
1.19
2.99
1.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


O
O
CH3
H
171.01
145.29
140.67
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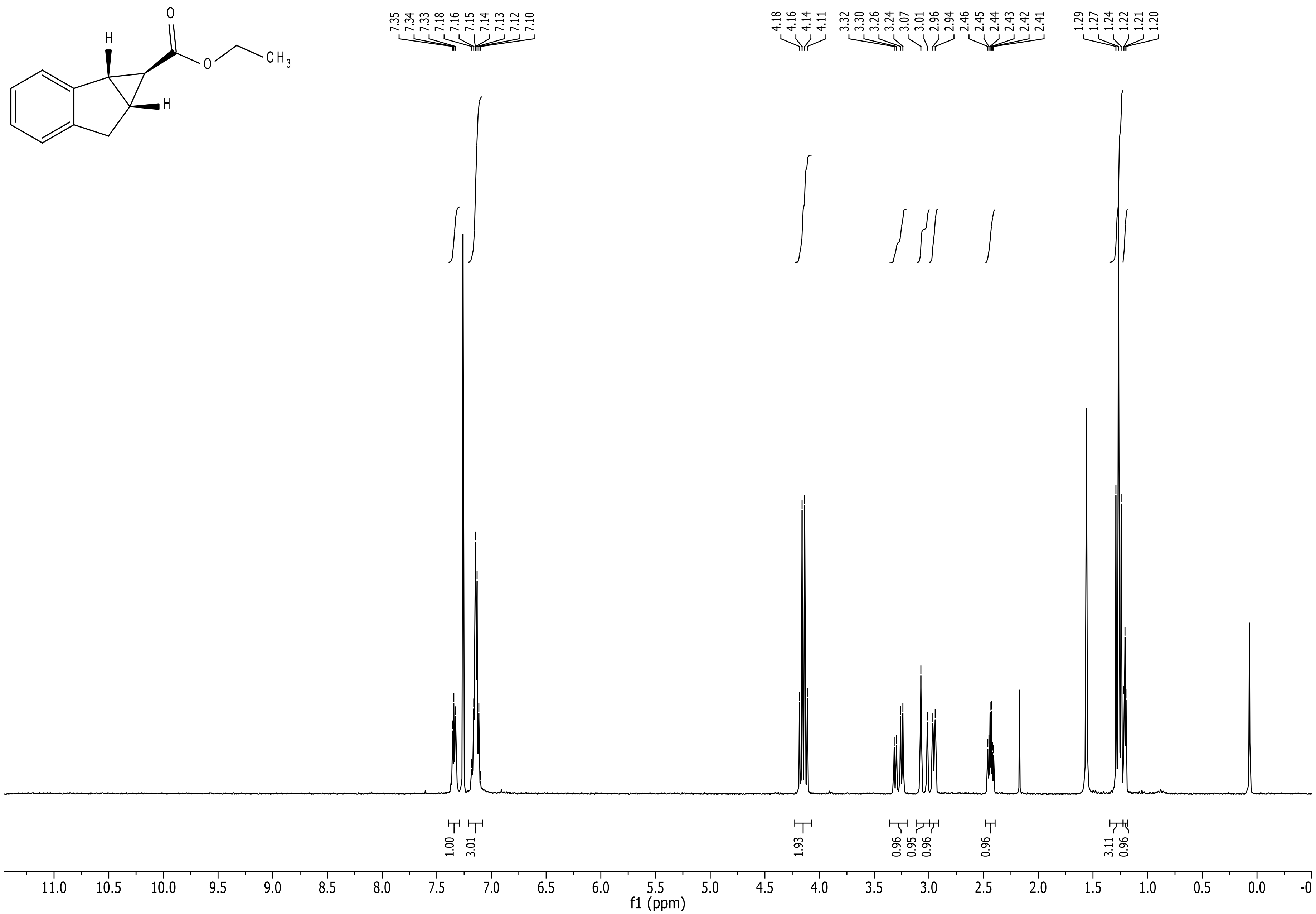
128.84
128.67
127.99
127.35
126.90
60.83
40.21
29.46
20.51
14.41
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


O
H
O
CH3
H
7.35
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7.33
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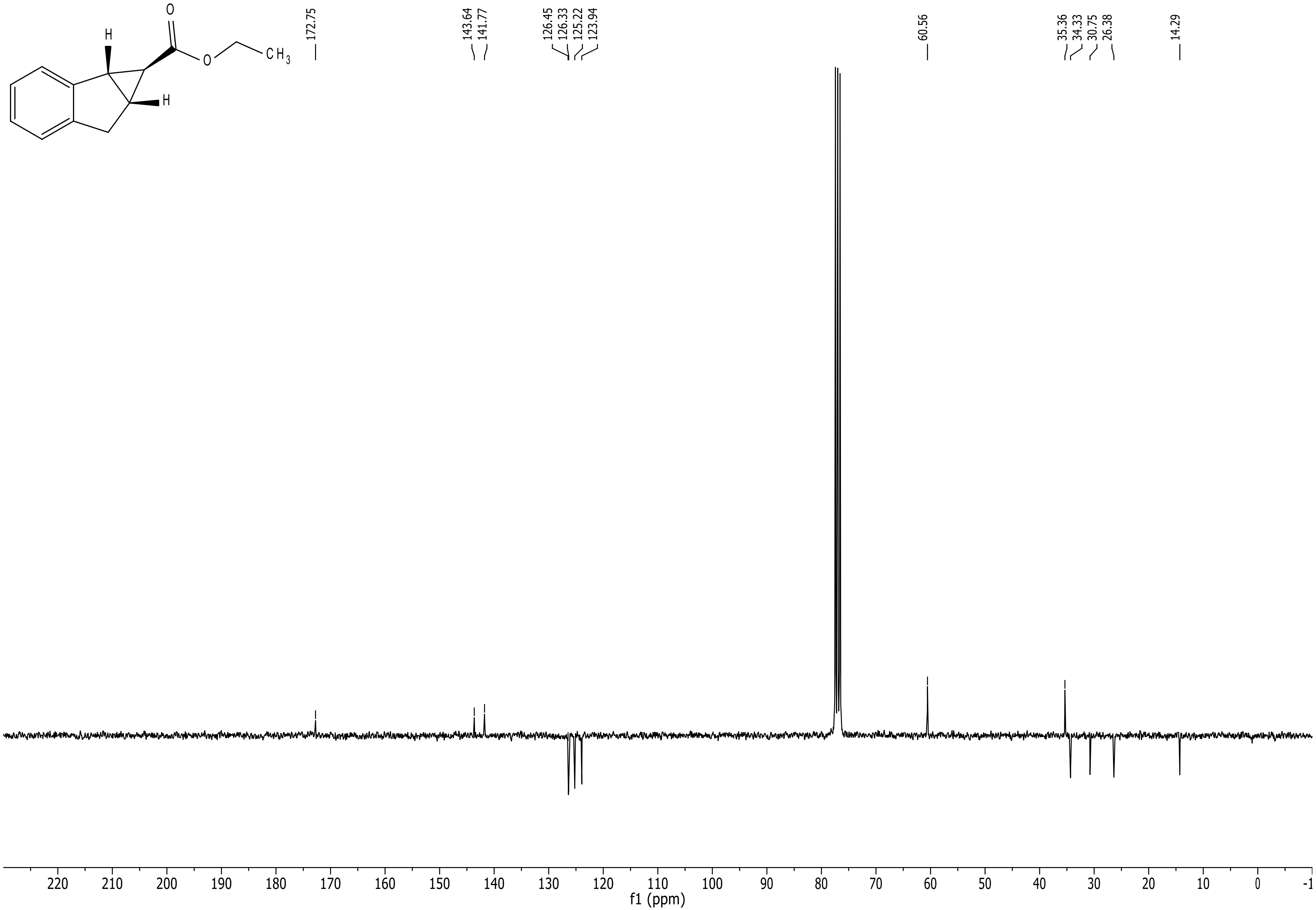
7.16
7.15
7.14
7.13
7.12
7.10
4.18
4.16
4.14
4.11
3.32
3.30
3.26
3.24
3.07
3.01
2.96
2.94
2.46
2.45
2.44
2.43
2.42
2.41
1.29
1.27
1.24
1.22
1.21
1.20
1.00
3.01
1.93
0.96
0.95
0.96
0.96
3.11
0.96
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)


O
H
H
O
CH3
172.75
143.64
141.77
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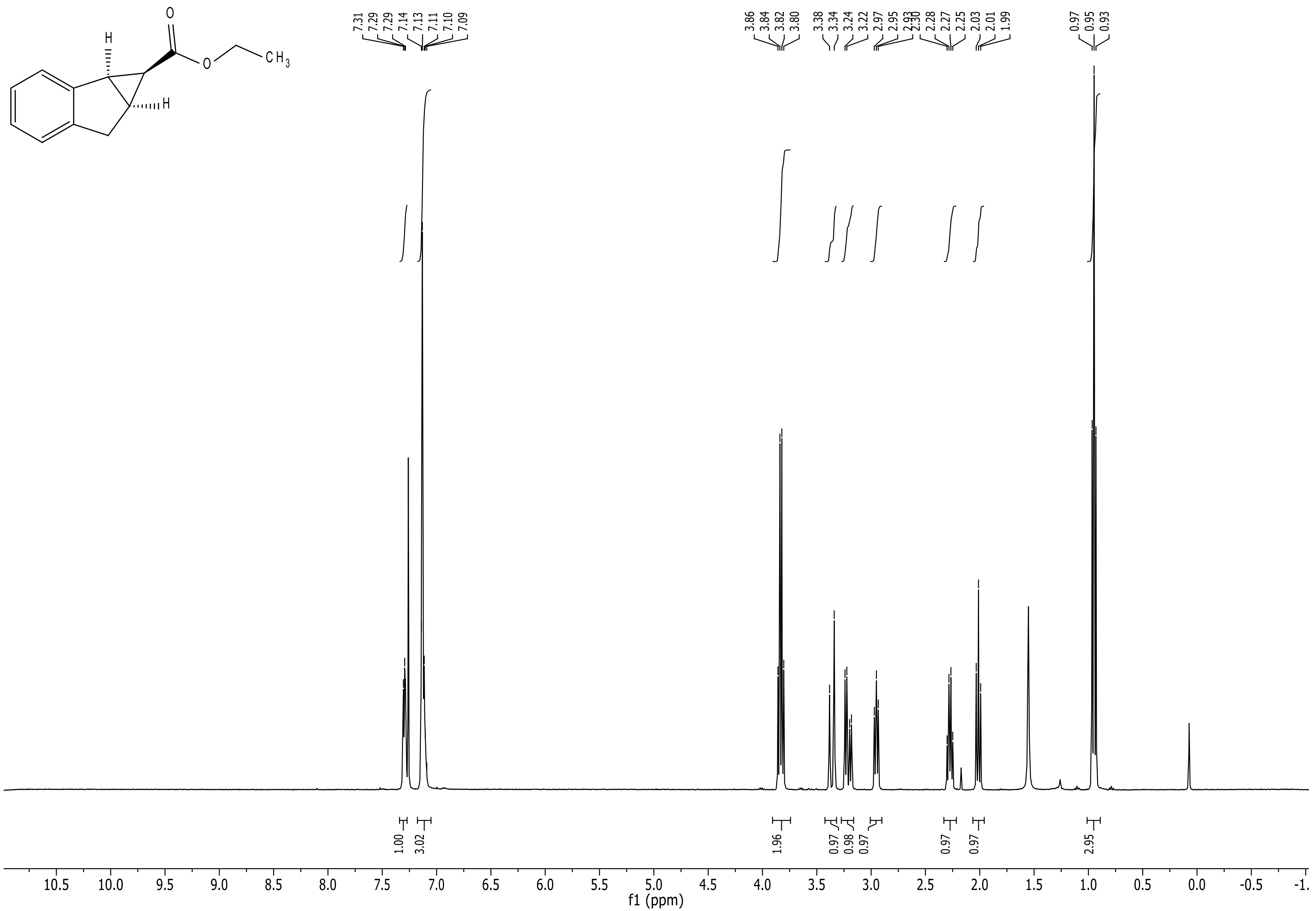
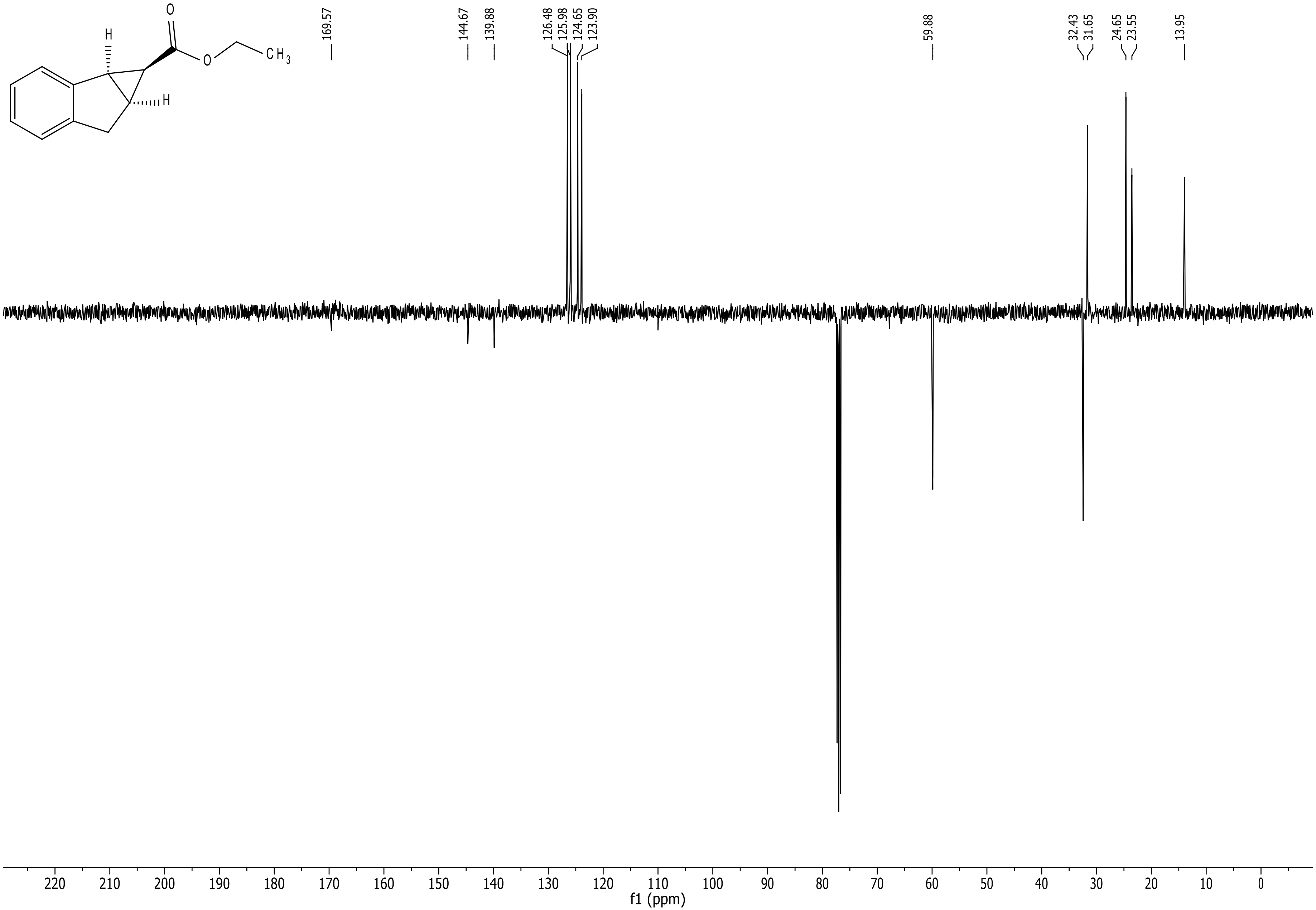
126.33
125.22
123.94
60.56
35.36
34.33
30.75
26.38
14.29
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


O
H
O
CH3
H
7.31
7.29
7.29
7.14
7.13
7.11
7.10
7.09
3.86
3.84
3.82
3.80
3.38
3.34
3.24
3.22
2.97
2.95
2.93
2.30
2.28
2.27
2.25
2.03
2.01
1.99
0.97
0.95
0.93
1.00
3.02
1.96
0.97
0.98
0.97
0.97
0.97
2.95
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)


O
H
O
CH3
H
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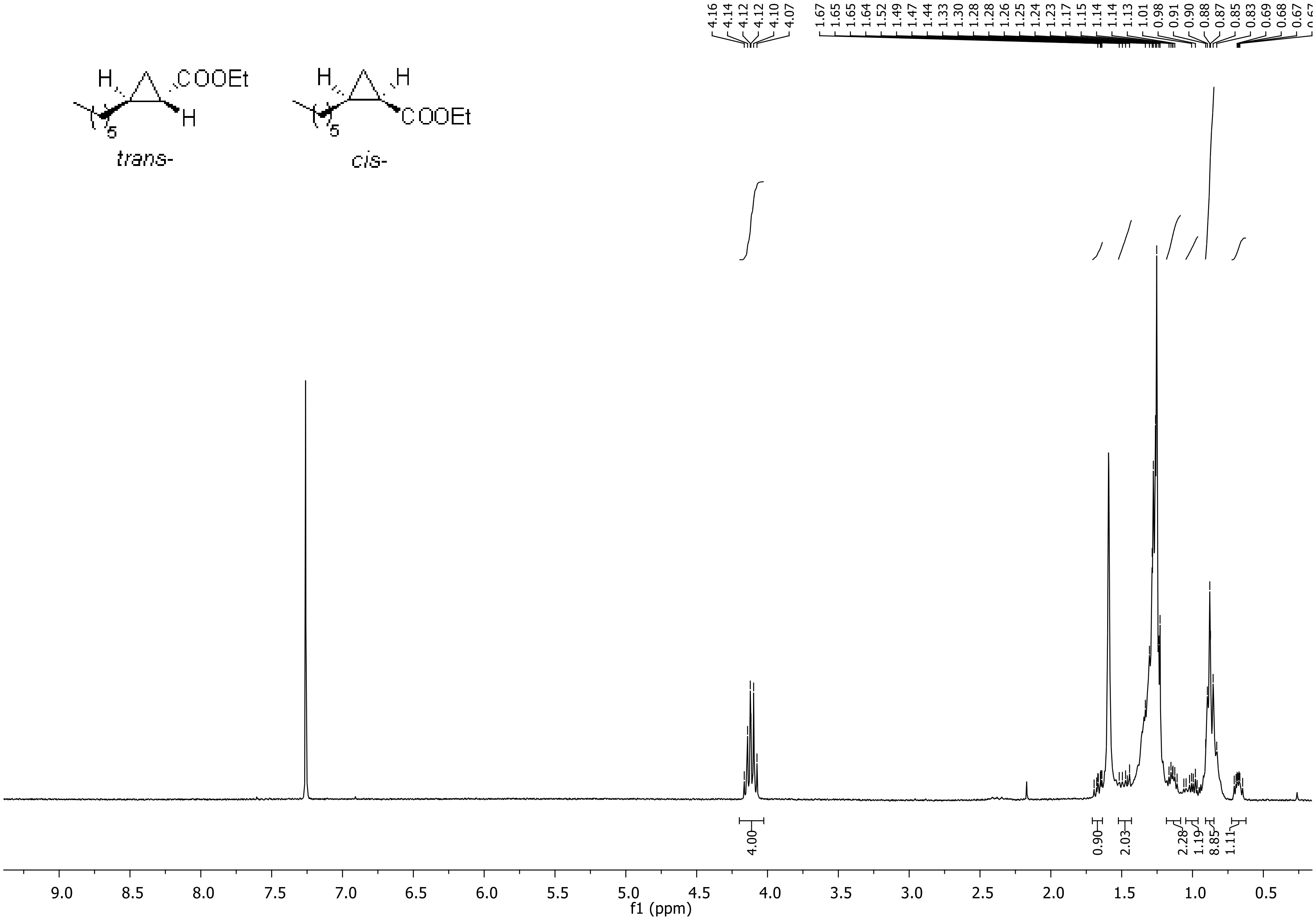
125.98
124.65
123.90
59.88
32.43
31.65
24.65
23.55
13.95
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


4.16
4.14
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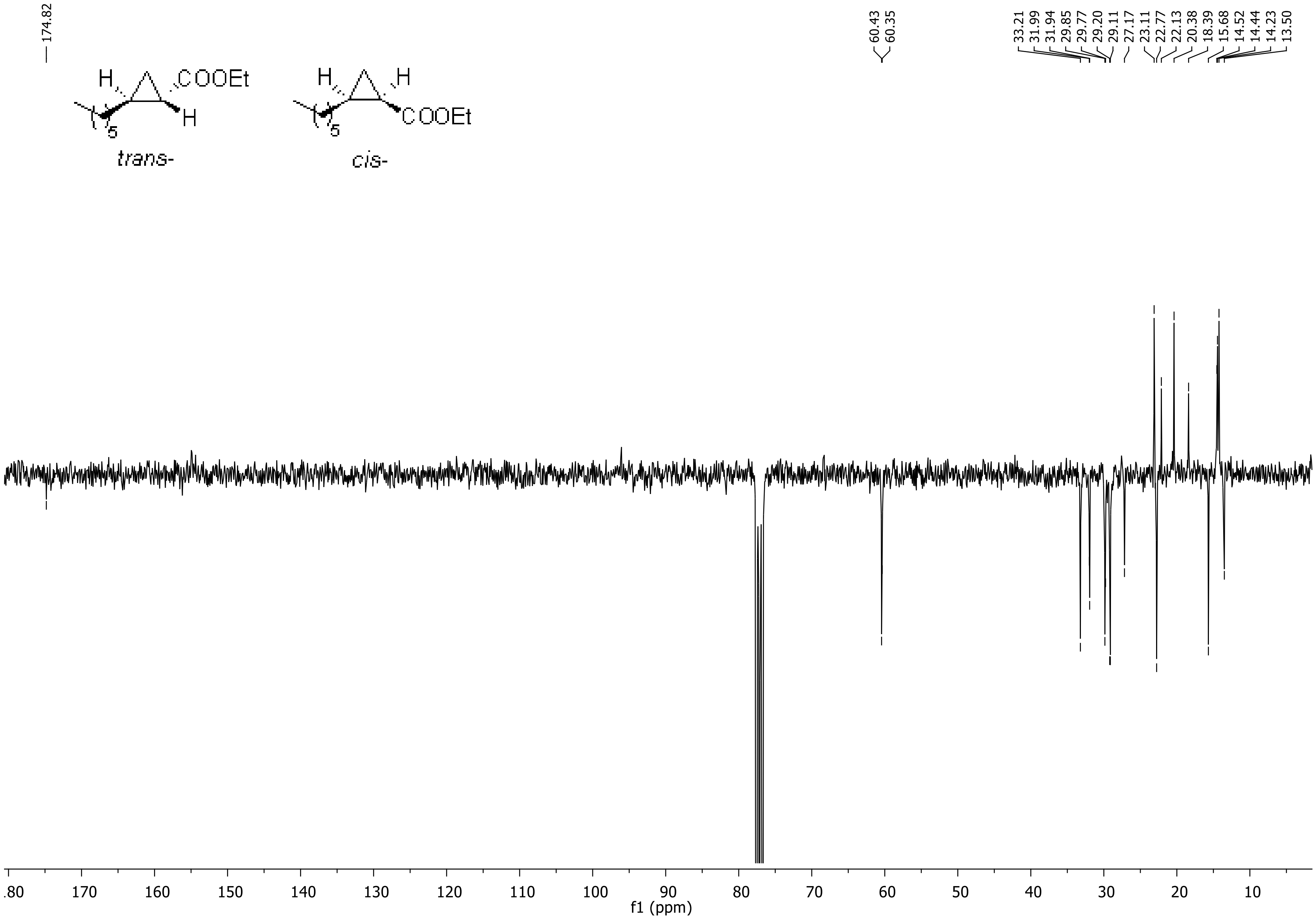
4.12
4.10
4.07
1.67
1.65
1.64
1.52
1.49
1.47
1.44
1.33
1.30
1.28
1.28
1.26
1.25
1.24
1.23
1.17
1.15
1.14
1.14
1.13
1.01
0.98
0.91
0.90
0.88
0.87
0.85
0.83
0.69
0.68
0.67
H
COOEt
H
5
trans-
H
H
COOEt
5
cis-
4.00
0.90
2.03
2.28
1.19
8.85
1.11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


174.82
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60.35
33.21
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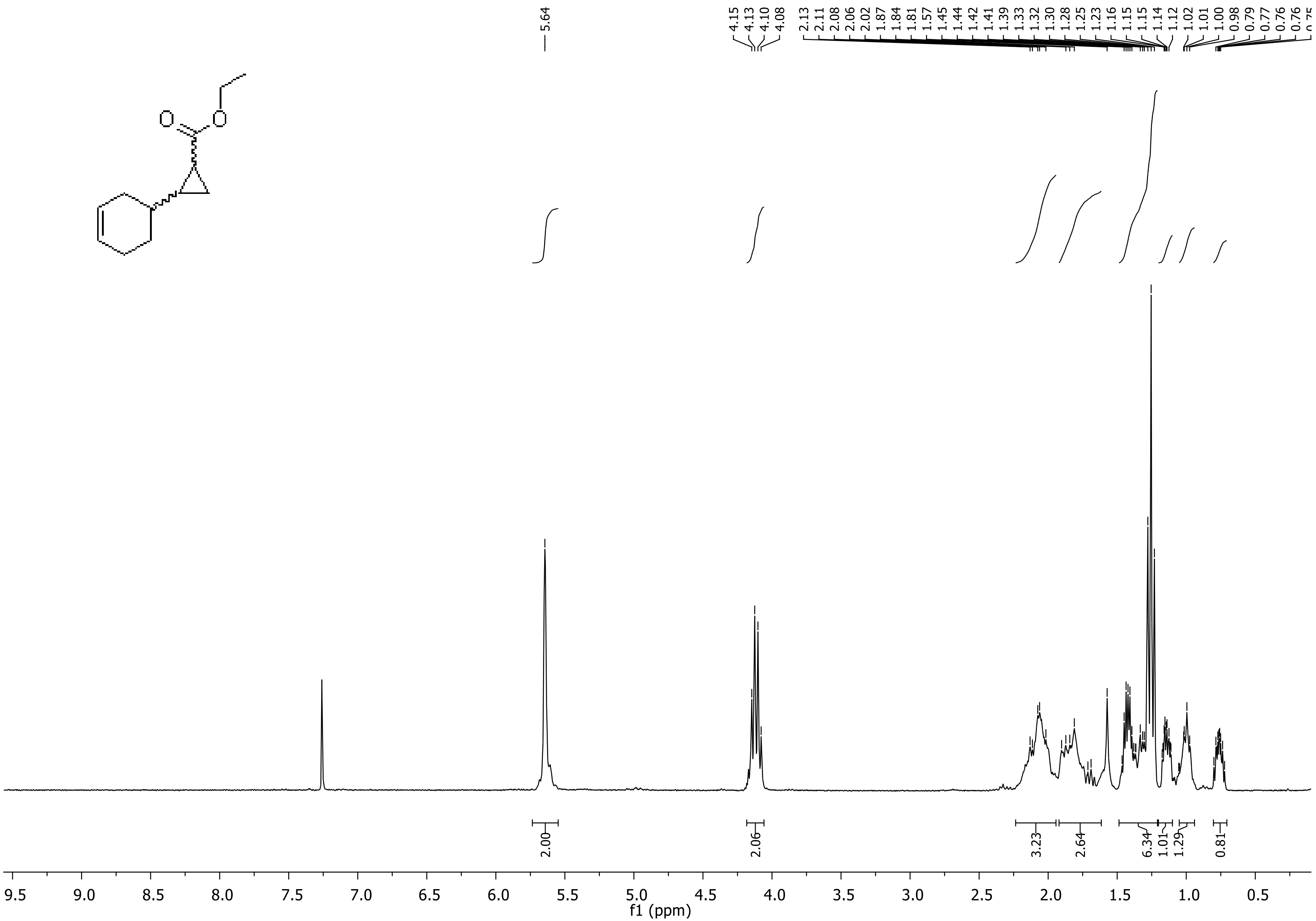
31.94
29.85
29.77
29.20
29.11
27.17
23.11
22.77
22.13
20.38
18.39
15.68
14.52
14.44
14.23
13.50
H
COOEt
H
( )5
trans-
H
H
COOEt
( )5
cis-
.80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


5.64
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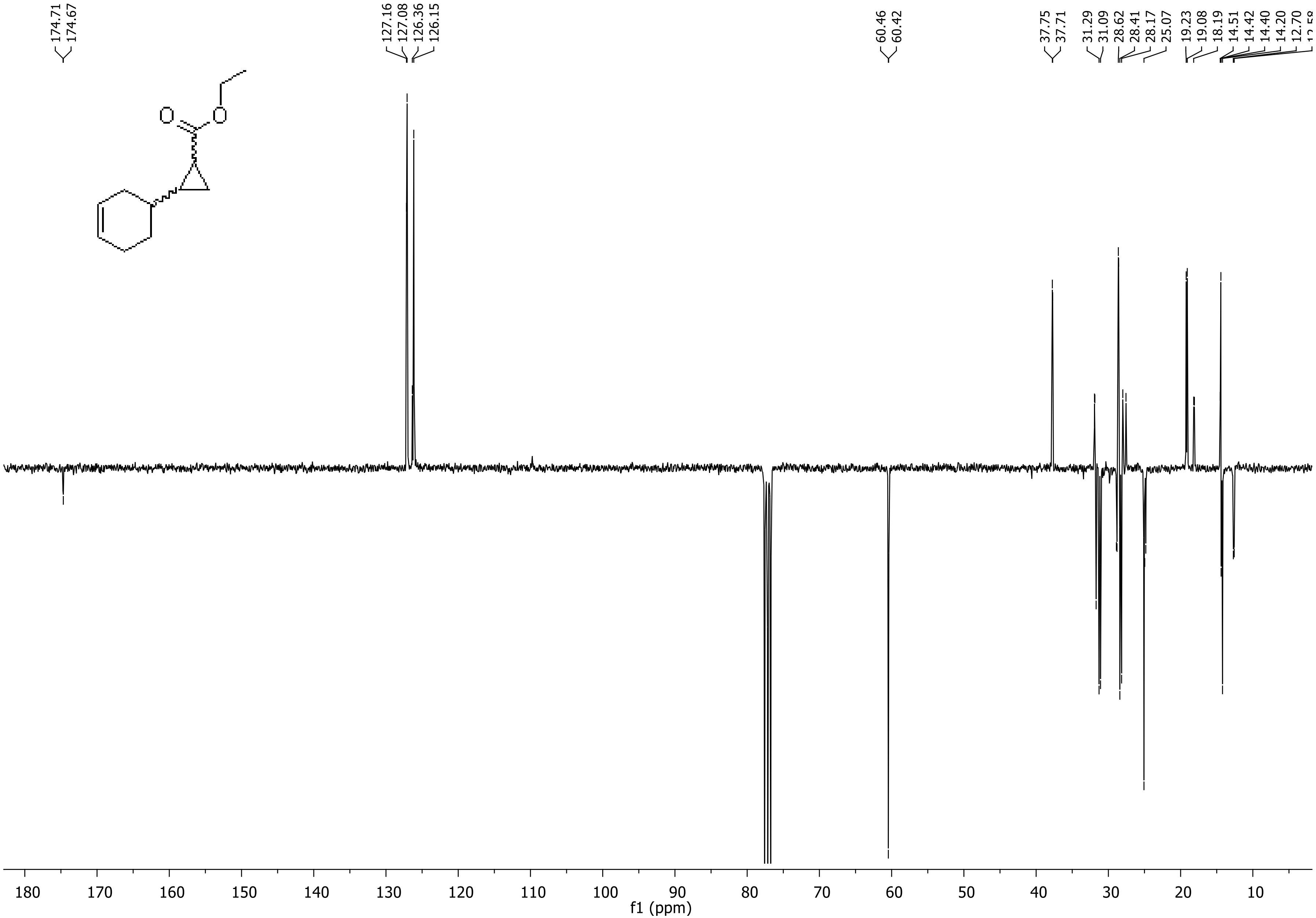
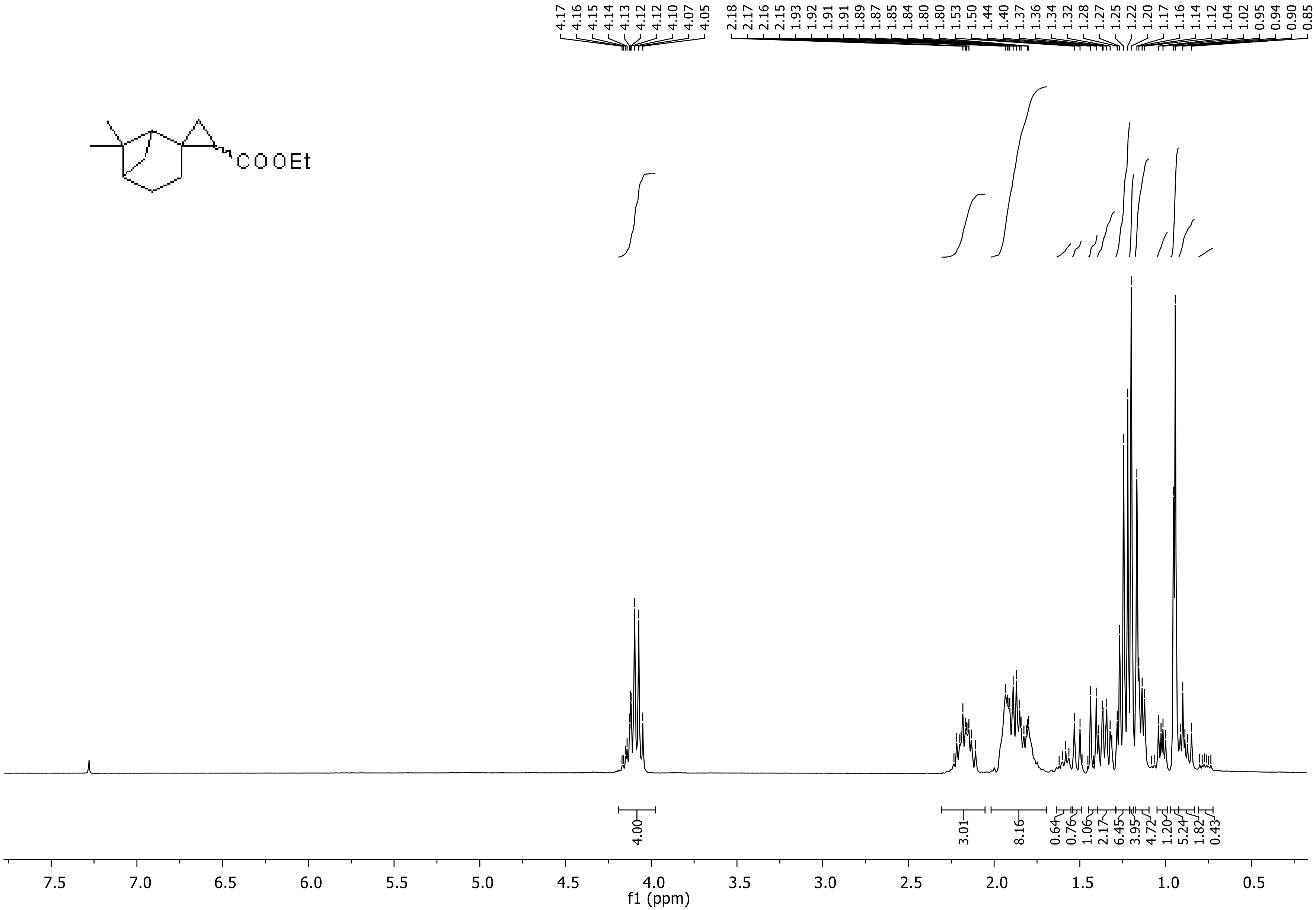
4.13
4.10
4.08
2.13
2.11
2.08
2.06
2.02
1.87
1.84
1.81
1.57
1.45
1.44
1.42
1.41
1.39
1.33
1.32
1.30
1.28
1.25
1.23
1.16
1.15
1.15
1.14
1.12
1.02
1.01
1.00
0.98
0.79
0.77
0.76
O
O
2.00
2.06
3.23
2.64
6.34
1.01
1.29
0.81
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


174.71
174.67
127.16
127.08
126.36
126.15
60.46
60.42
37.75
37.71
31.29
31.09
28.62
28.41
28.17
25.07
19.23
19.08
18.19
14.51
14.42
14.40
14.20
12.70
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


4.17
4.16
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4.14
4.13
4.12
4.12
4.10
4.07
4.05
2.18
2.17
2.16
2.15
1.93
1.92
1.91
1.91
1.89
1.87
1.85
1.84
1.80
1.53
1.50
1.44
1.40
1.37
1.36
1.34
1.32
1.28
1.27
1.25
1.22
1.20
1.17
1.16
1.14
1.12
1.04
1.02
0.95
0.94
0.90
0.85
COOEt
4.00
3.01
8.16
0.64
0.76
1.06
2.17
6.45
3.95
4.72
1.20
5.24
1.82
0.43
7.5
7.0
6.5
6.0
5.5
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3.5
3.0
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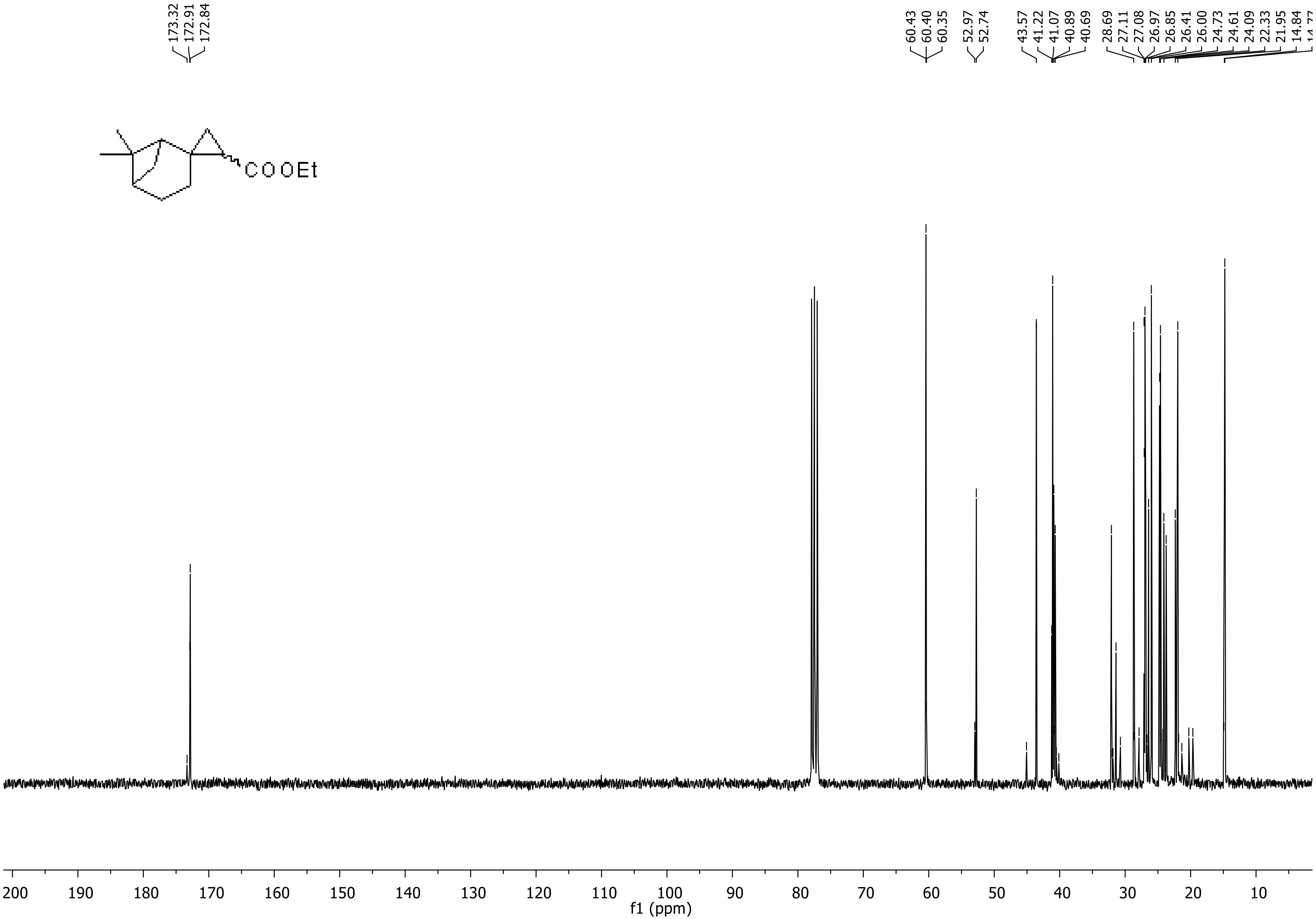
0.5
f1 (ppm)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28.69
27.11
27.08
26.97
26.85
26.41
26.00
24.73
24.61
24.09
22.33
21.95
14.84
COOEt
200
190
180
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140
130
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100
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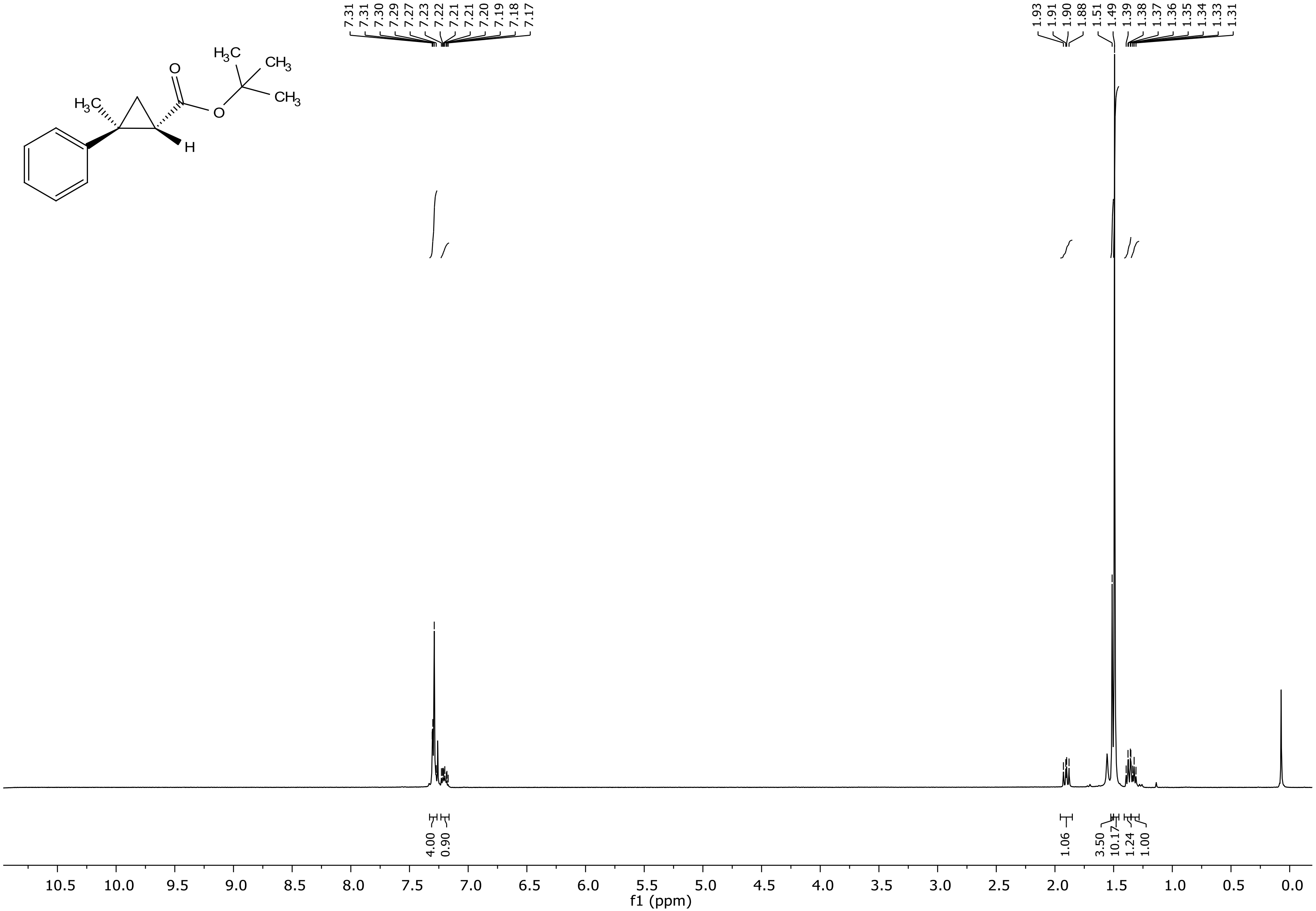
f1 (ppm)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7.19
7.18
7.17
1.93
1.91
1.90
1.88
1.51
1.49
1.39
1.38
1.37
1.36
1.35
1.34
1.33
1.31
H3C
CH3
CH3
O
O
H3C
H
4.00
0.90
1.06
3.50
10.17
1.24
1.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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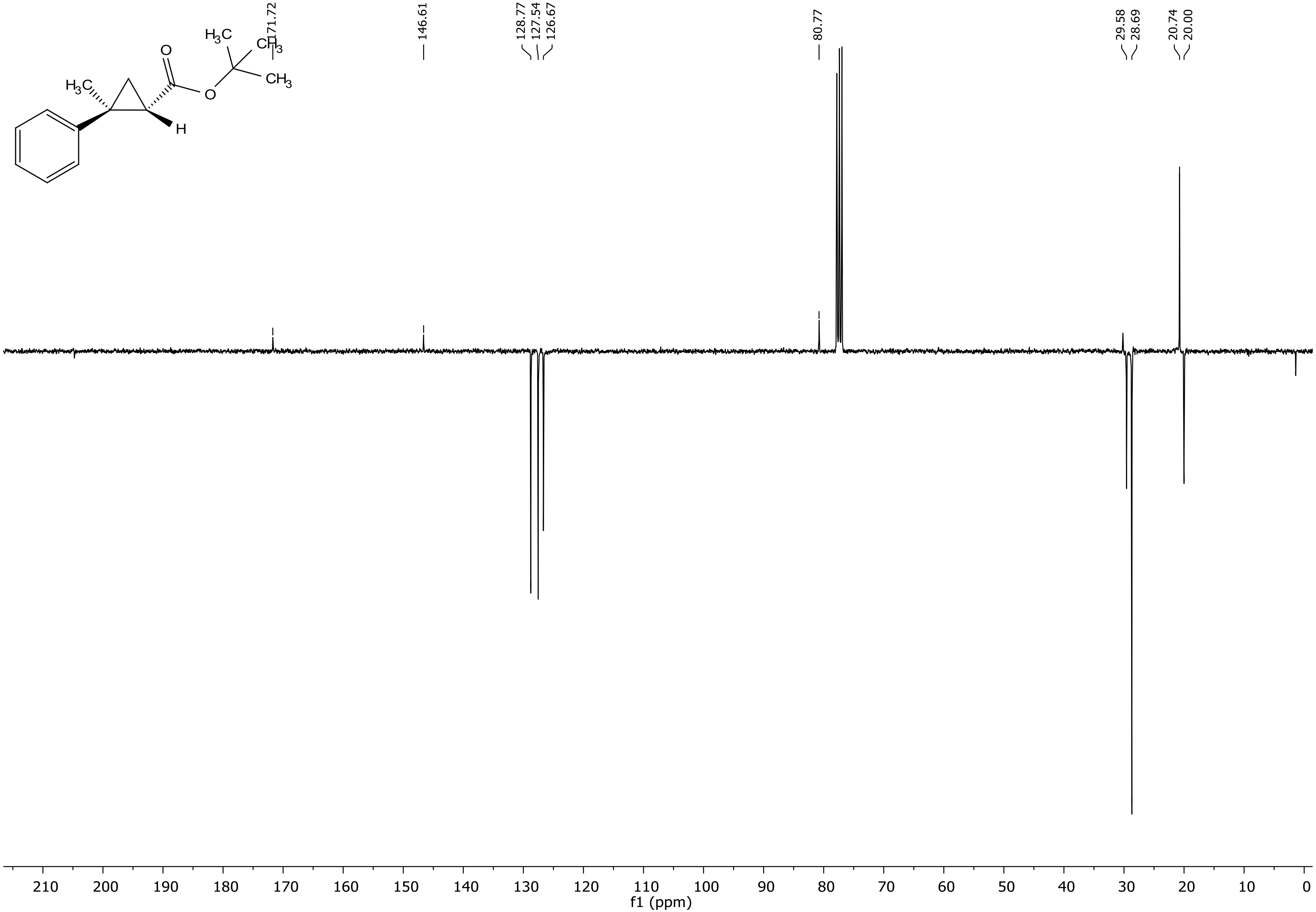
0.0
f1 (ppm)


H3C
CH3
CH3
O
O
H3C
H
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128.77
127.54
126.67
80.77
29.58
28.69
20.74
20.00
210
200
190
180
170
160
150
140
130
120
110
100
90
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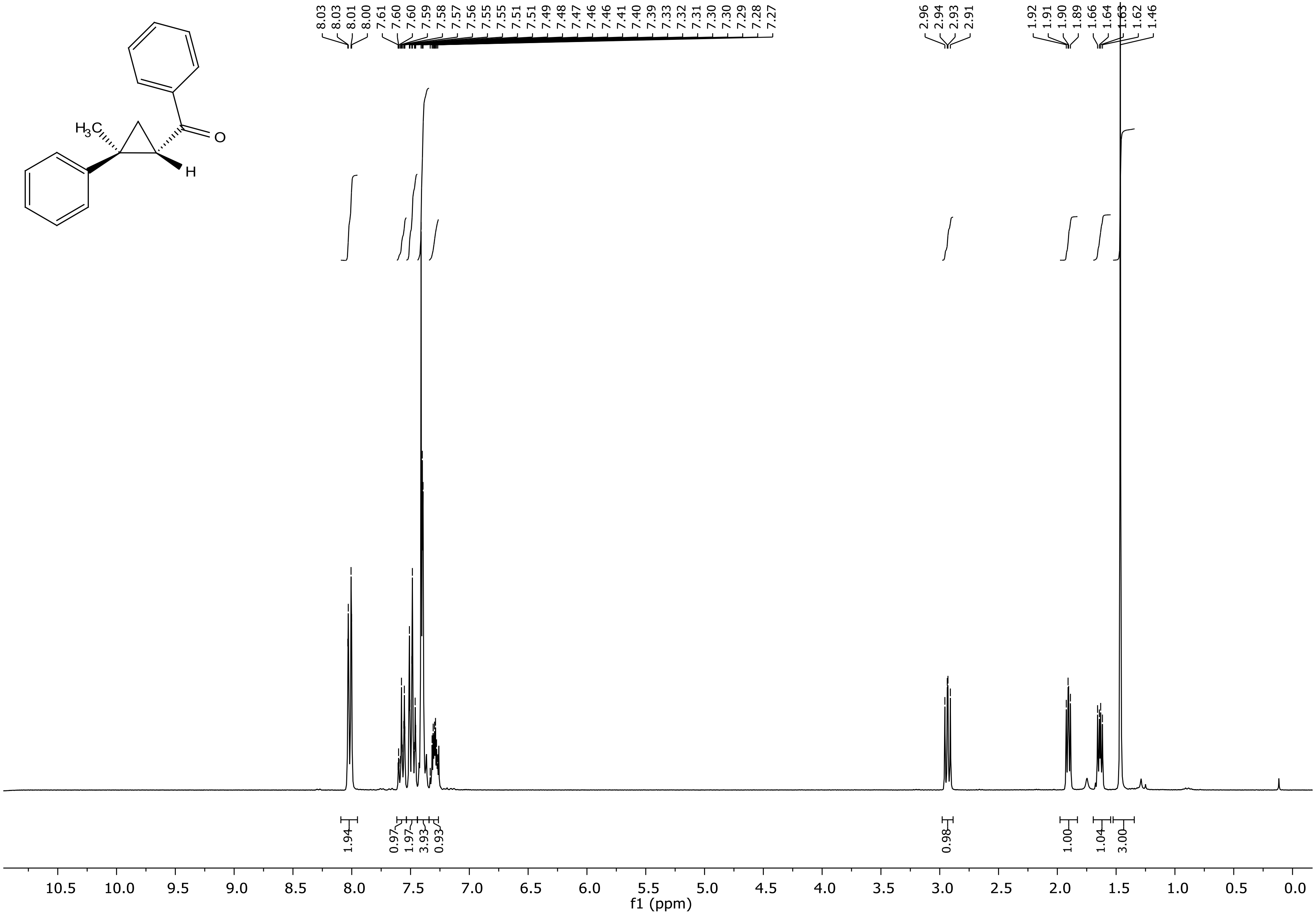
70
60
50
40
30
20
10
0
f1 (ppm)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8.03
8.01
8.00
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7.60
7.59
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7.57
7.56
7.55
7.55
7.51
7.51
7.49
7.48
7.47
7.46
7.46
7.41
7.40
7.39
7.33
7.32
7.31
7.30
7.30
7.29
7.28
7.27
2.96
2.94
2.93
2.91
1.92
1.91
1.90
1.89
1.66
1.64
1.63
1.62
1.46
H3C
O
H
1.94
0.97
1.97
3.93
0.93
0.98
1.00
1.04
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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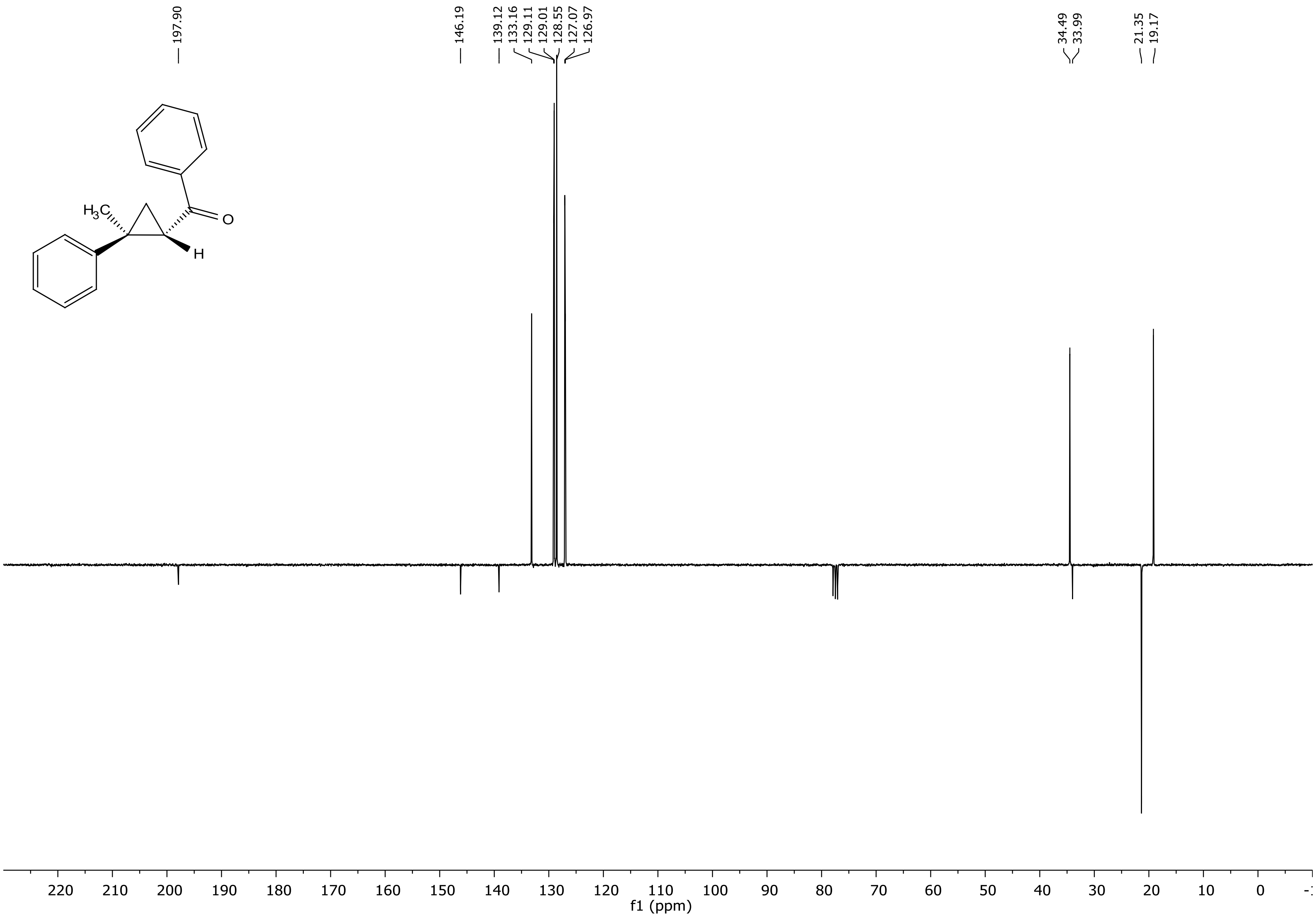
0.0
f1 (ppm)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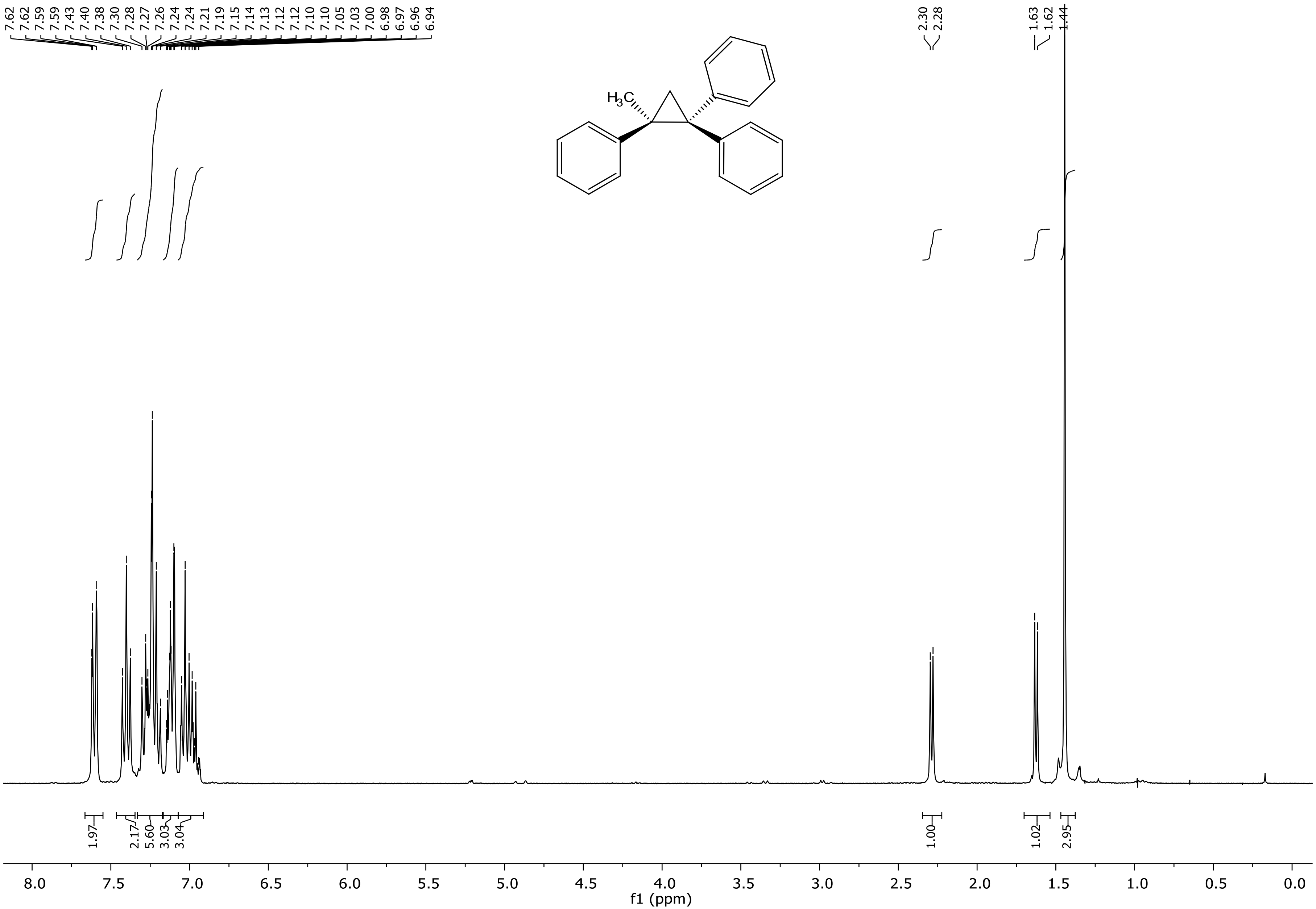
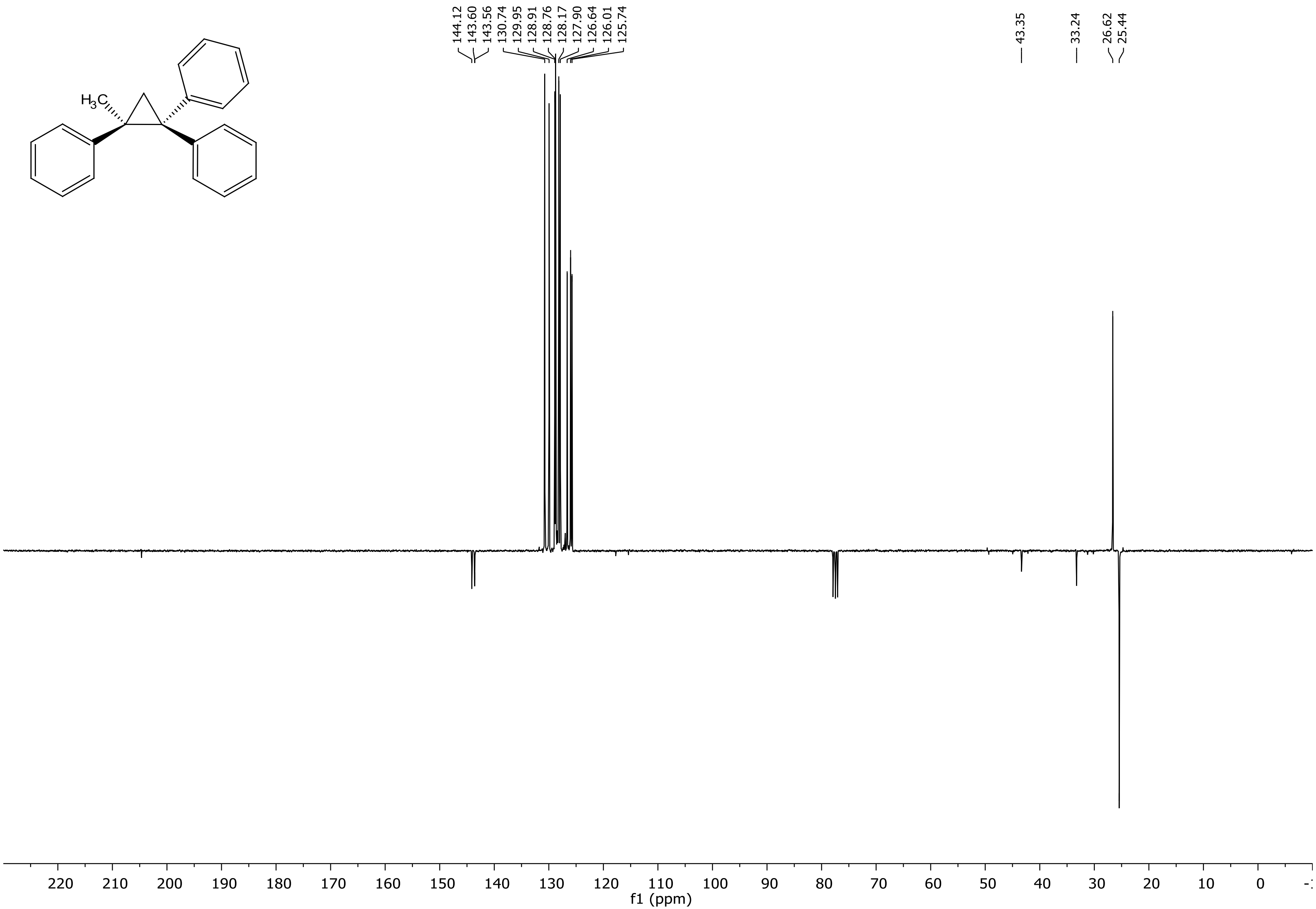
139.12
133.16
129.11
129.01
128.55
127.07
126.97
34.49
33.99
21.35
19.17
H3C
O
H
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.62
7.62
7.59
7.59
7.43
7.40
7.38
7.30
7.28
7.27
7.26
7.24
7.24
7.21
7.19
7.15
7.14
7.13
7.12
7.12
7.10
7.10
7.05
7.03
7.00
6.98
6.97
6.96
6.94
2.30
2.28
1.63
1.62
1.44
H_3C
1.97
2.17
5.60
3.03
3.04
1.00
1.02
2.95
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



144.12
143.60
143.56
130.74
129.95
128.91
128.76
128.17
127.90
126.64
126.01
125.74
43.35
33.24
26.62
25.44
H_3C
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Communications (Poster/Oral presentation)

1. Abhijnan Sarkar, Dario Formenti, Fabio Ragaini “Nitrogen-Enriched Graphene Modified Metal and Metal Oxide Nanoparticles as Innovative Catalysts: New Uses” at International School of Organometallic Chemistry ISOC 2017 at San Benedetto del Tronto, 2-6 September, 2017, organized by University of Camerino.
2. Abhijnan Sarkar, Dario Formenti, Francesco Ferretti, Kathrin Junge, Fabio Ragaini and Matthias Beller “Nitrogen-Enriched Graphene Modified Metal and Metal Oxide Nanoparticles as Innovative Catalysts: First Application to Cyclopropanation Reactions”: at Co.G.I.C.O XIII at Florence, 18 – 20 July, 2018.
3. Abhijnan Sarkar, Dario Formenti, Francesco Ferretti, Kathrin Junge, Fabio Ragaini and Matthias Beller "Nitrogen-Enriched Graphene Iron Oxide Nanoparticles as Innovative Catalysts: First Attempt to Cyclopropanation Reactions" at EUCOMOC XXIII, 16 - 20 June, 2019 at Helsinki, Finland.

Publication

1. Abhijnan Sarkar, Francesco Ferretti, Dario Formenti, Carsten Kreyenschulte, Stephan Bartling, Henrik Lund, Kathrin Junge, Matthias Beller and Fabio Ragaini "Iron/N-doped Graphene nano-structured Catalysts for General Cyclopropanation of Olefins" (manuscript submitted)