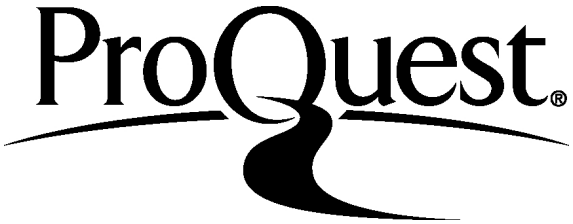
TRANSITION METAL CATALYZED REACTIONS OF ELECTROPHILIC INTERMEDIATES TO FORM C-C BONDS AND SET STEREOGENIC CENTERS

by

Srimoyee Dasgupta

A dissertation submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry and Biochemistry

Fall 2015



TRANSITION METAL CATALYZED REACTIONS OF ELECTROPHILIC INTERMEDIATES TO FORM C-C BONDS AND SET STEREOGENIC CENTERS

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Srimoyee Dasgupta

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Member of dissertation committee

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The journey of the last five and a half years has been one of the most rewarding yet challenging experiences in my life. My foremost gratitude goes to my advisor, Mary P. Watson, for her amazing training. I am very grateful to her for having given me the opportunity to work with her inspite of not having a background in organic chemistry. Under her efficient guidance, I thoroughly enjoyed organic chemistry and am very satisfied to have accomplished such beautiful work picking up new skills and utilizing my former ones. Under her supervision and mentorship, I not only grew as an independent scientist but also as an individual. I thank her from the bottom of my heart for being such a wonderful mentor.

I am also very grateful to my dissertation committee members for their consideration at all times. My heartfelt thanks go to the departmental staff and help for their constant support and help, without which our scientific research would undoubtedly see a dead end.

I also take this opportunity to thank all my lab mates for being such a wonderful team. My colleagues, Danielle, Qi, Jixin, Hari have taught me a lot and without their help, I couldnot have successfully finished my projects. I am also grateful to Tom and Clarissa, my undergraduates for their amazing contribution. Danielle, Qi and Jixin…thanks for being such great friends too. Kelsey, Corey, Jennie, Songnan, Tatsiana, Drew and all…it was a pleasure working with all of you. We really make a beautiful team, lead by Mary. I really am going to miss this second home!

I also thank my friends, especially my room mates, Aditi and Sudha, who have seen me through most of graduate school. Finally, I express my love and gratitude to my parents and my brother for having constant faith in me. I could not have accomplished this without your unconditional love and support. I may have been absent from your lives for the past seven years, but I am a reflection of your values and morals and I only wish to make you all proud every day!

Lastly, I express my deepest gratitude and love to my husband, Saikat for being with me like a pillar of support every second of this journey. I may have solved problems in chemistry, but you solve every problem in my life with a smile. Thank you for being there always!

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ABSTRACT

(1) The first project I have worked on is titled Nickel Catalyzed Cyclization of *N*-Benzoylaminals for Isoindolinone Synthesis. My studies demonstrated the functional group tolerance and contributed strongly to our mechanistic understanding of this cyclization reaction. These results were published in *Organic Letters* in 2011. [1]

(2) The second project I have worked on is titled Enantioselective, Copper(I)-Catalyzed Alkynylation of Oxocarbenium Ions to Set $\boldsymbol{\alpha,\alpha}$-diaryl Tetrasubstituted Stereocenters. In summary, I have developed the first example of an enantioselective addition of alkynes to a cyclic oxocarbenium ion to set tetrasubstituted stereocenters. The success of this reaction relied on identification of a Cu/PyBox catalyst, along with $CHCl_3$ as solvent, $BF_3{\cdot}OEt_2$ as Lewis acid, and MTBD as base. Under the optimized conditions, a variety of ketals and alkynes underwent the reaction in good to excellent yields and enantioselectivites. These results have been published in *Angewandte Chemie International Edition*, ASAPs.[2]

(3) The third project I have worked on is titled Enantioselective, Copper(I)-Catalyzed Alkynylation of Iminium Ions to Set $\boldsymbol{\alpha,\alpha}$-diaryl, Tetrasubstituted Stereocenters. Here I have demonstrated the first example of enantioselective addition of alkynes to cyclic iminium ions to set diaryl tetrasubstituted stereocenters. These results are ready to be published in the fall of 2015.

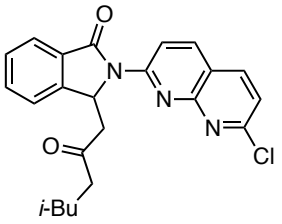
Chapter 1

NICKEL CATALYZED CYCLIZATION OF *N*-BENZOYLAMINALS FOR ISOINDOLINONE SYNTHESIS

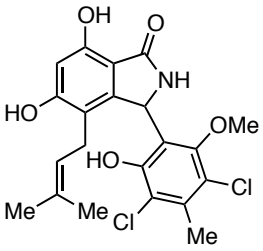
1.1 Introduction

Isoindolinones are important nitrogen heterocycle scaffolds that include a number of biologically active compounds and natural products. [3-7]

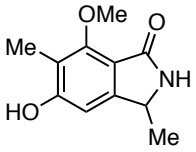
Figure 1.1: Biologically Active Isoindolinones



1-1
Pagoclone



1-2
Pestalachloride A
(natural product)



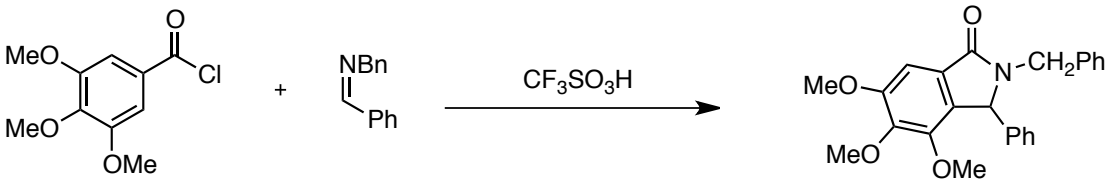
1-3
Marilince C
(natural product)

Despite this biological relevance, known methods for synthesis of isoindolinones have shortcomings. For example, Klumpp's method of cyclization of iminium ions under stoichiometric Bronsted acid or Campbell's chemistry of trapping iminium ions with aryl lithium nucleophiles, as shown below (Scheme 1.1), require harsh conditions like corrosive acids, high temperatures or strongly basic reagents.

Also specific substitution patterns in substrates has often restricted the synthetic route and scope of the products that can be prepared via these methods. [8,9]

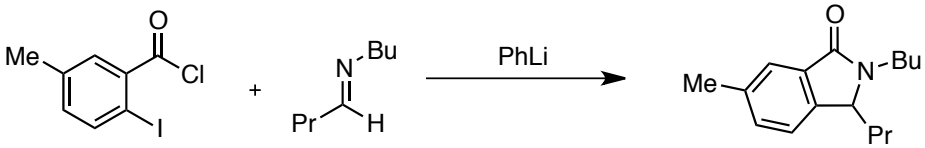
Scheme 1.1: Pror Art in Isoindolinone Synthesis

A. *Klumpp*



1-4 **1-5** **1-6** 70%

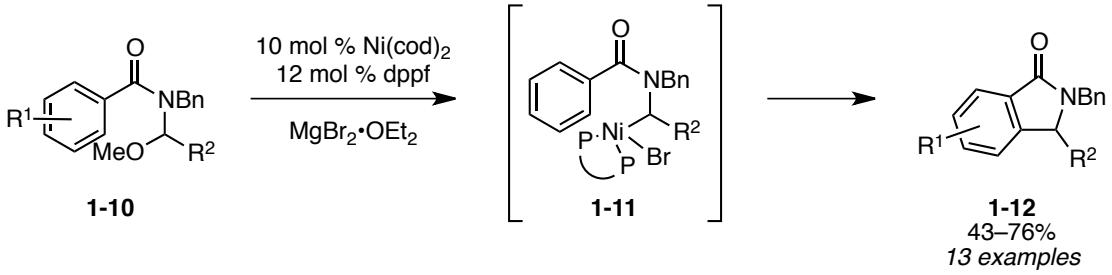
B. *Campbell*



1-7 **1-8** **1-9** 90%

My colleague , Danielle Shacklady McAtee discovered a nickel-catalyzed cyclization of *N*-benzoyl aminals, **1-10** to enable access to 3-aryl substituted isoindolinones, **1-12** in our laboratory. This Ni-catalyzed process involves aromatic C–H functionalization of the benzoyl group and offers a convergent 3-step approach for preparing isoindolinones from benzoyl chlorides, primary amines and aldehydes. These conditions are mild and suggested broad functional group tolerance may be possible, allowing broader scope than previous methods. As described below, my investigation of the scope of benzoyl groups revealed reasonable functional group tolerance and is consistent with a metal-mediated electrophilic aromatic substitution reaction.

Scheme 1.2: Our Route for Isoindolinone Synthesis



1-10 **1-11** **1-12**
43–76%
13 examples

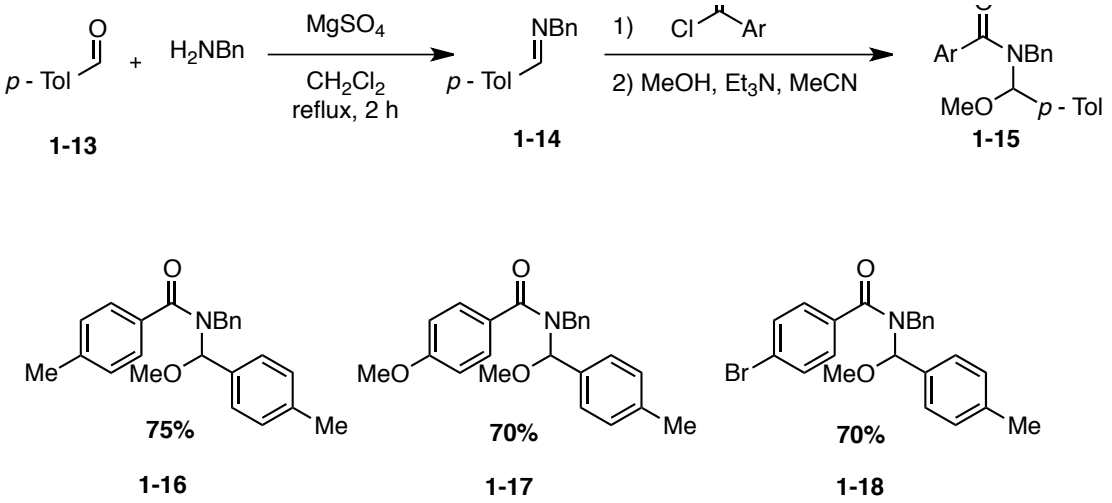
1.2 Results and Discussion

Synthesis of Aminal Substrates

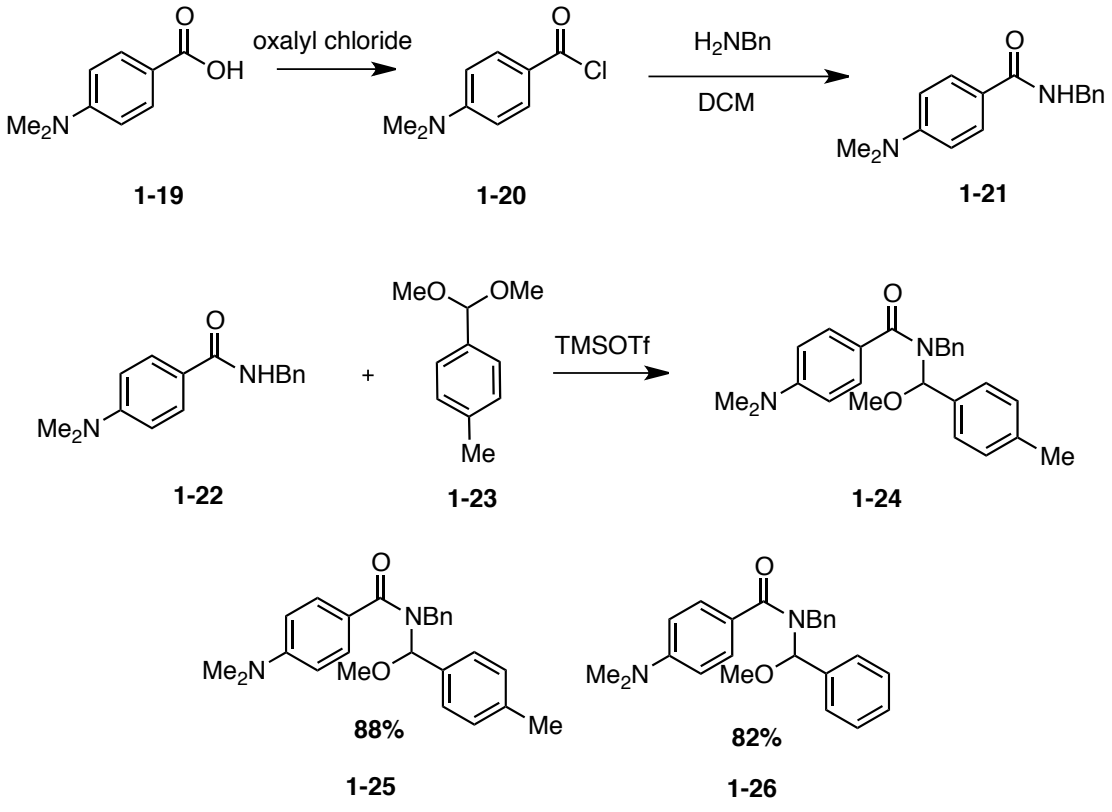
The aminal starting materials were made via two different routes. The first route involved a condensation reaction between an aldehyde and an amine to form an imine, which was used in the next step without further purification. To a solution of the imine, MeOH and Et_3N, acid chloride was then added to access the resulting aminals which had to be purified via silica gel chromatography. The substrates made via this route are **1-16**, **1-17** and **1-18** as shown in scheme 1.3.

Alternatively, secondary amide **1-21** can be formed first and then condensed with an oxocarbenium ion, generated in situ by addition of TMSOTf to acetal **1-23**. The substrates made via this route are **1-25** and **1-26** (Scheme 1.4).[10]

Scheme 1.3: Route A for Synthesis of Aminal Starting Material



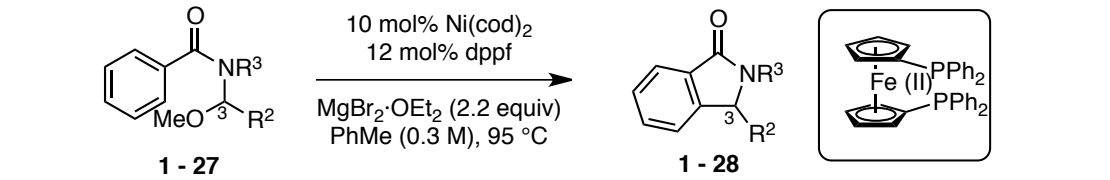
Scheme 1.4: Route B for Synthesis of Aminal Starting Material



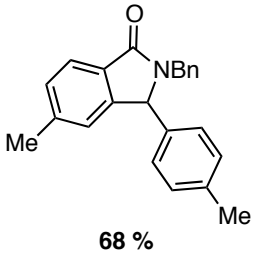
Scope of Cyclization : Benzoyl Substitution

Under the optimized reaction conditions, substrates containing both electron-rich and electron-neutral benzoyl groups underwent the reaction in good yields (**1-29 - 33**, Scheme 1.5). A number of functional groups are tolerated, including aryl bromides, ethers and amines. Highly electron-poor substituents on the benzoyl fragment (**1-34 – 36)** prevent cyclization. This observation along with other mechanistic work by my colleague, Danielle, later on helps us hypothesize that the mechanism for this reaction proceeds via an electrophilic aromatic substitution to generate the benzoyl carbocation that undergoes rearomatization followed by reductive elimination to give product. Danielle also demonstrated great scope in the C_3 substitution of the aminal moiety. A select scope of hers is shown in Scheme 1.6.

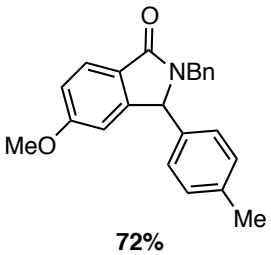
Scheme 1.5: Scope of Cyclization: Benzoyl Substitution



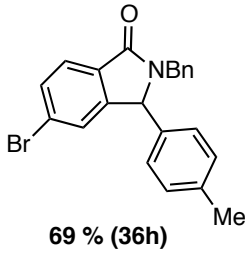
1 - 27 **1 - 28**



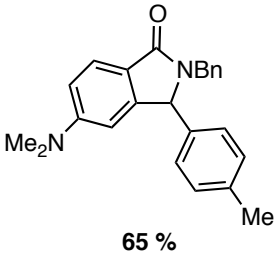
68 %
1 - 29



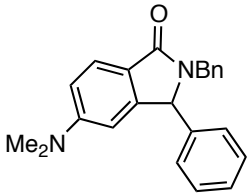
72%
1 - 30



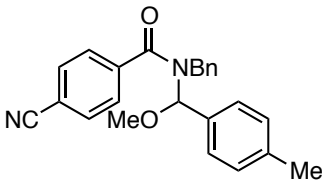
69 % (36h)
1 - 31



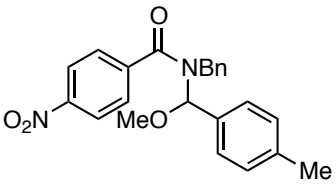
65 %
1 - 32



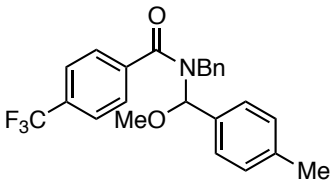
62 % (36h)
1 - 33



0%
1-34

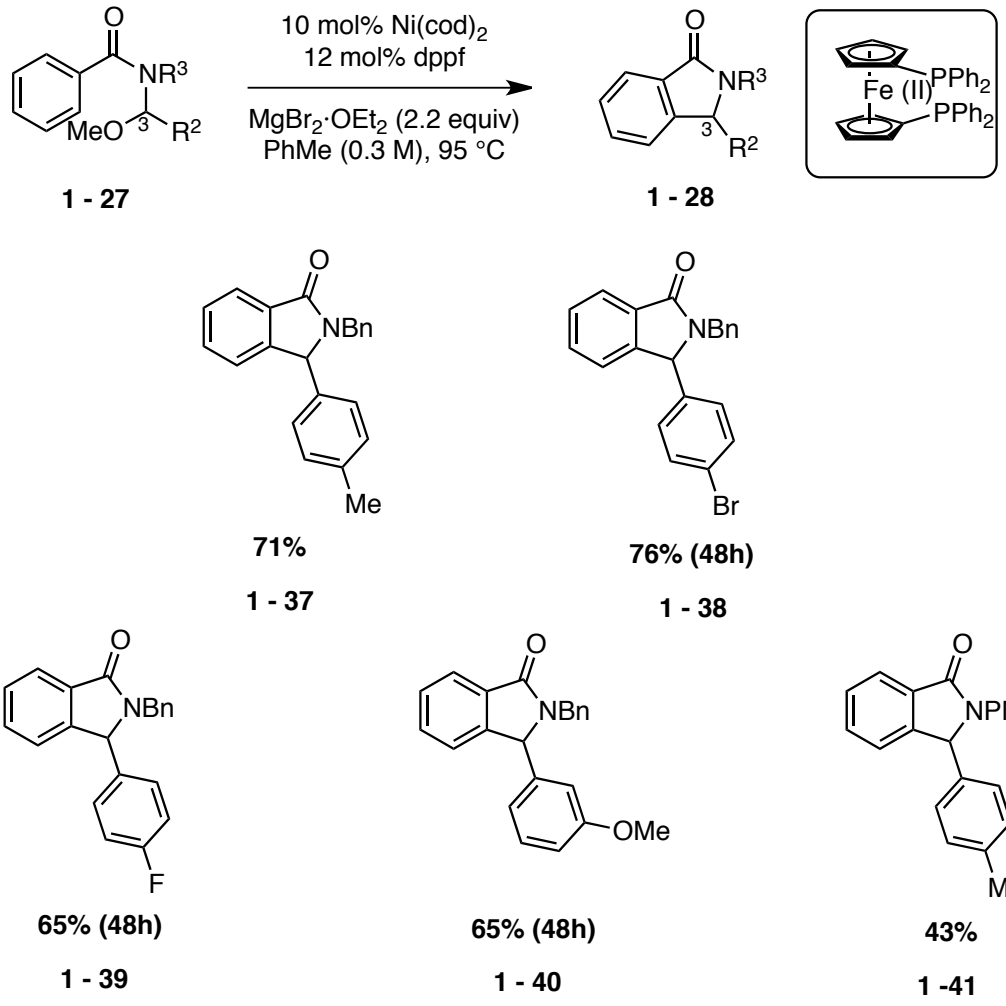


0%
1-35



0%
1-36

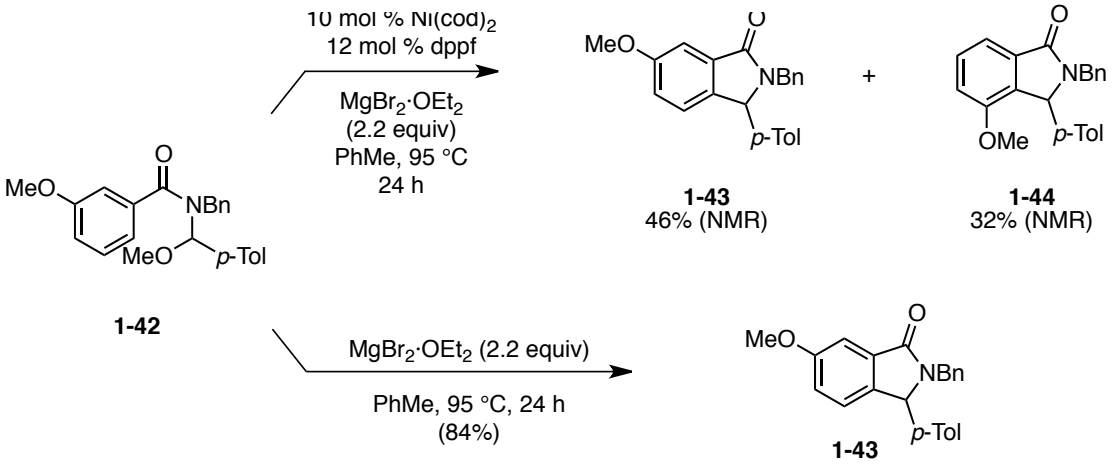
Scheme 1.6: Scope of Cyclization: C_3 Substitution



For substrates with meta-substituted benzoyl groups, regioisomeric products were observed. For example, cyclization of aminal **1-42** resulted in a 46:32 ratio of isoindolinones **1-43** and **1-44** (Scheme 1.7). This observation proved critical in our mechanistic understanding of this reaction. Although both regioisomers are observed when a nickel catalyst is used, substrate **1-42** also underwent cyclization in the presence of Lewis acid alone. This result is in sharp contrast to the cyclizations of the

other aminals discussed above, which produced only trace isoindolinone in the absence of a nickel catalyst. Although regioisomer **1-43** may form via a Lewis acid-mediated pathway even in the presence of a Ni catalyst, product **1-44** clearly requires the nickel catalyst. This difference in regioselectivity clearly indicates that the nickel catalyst affects the C–C bond-forming step.

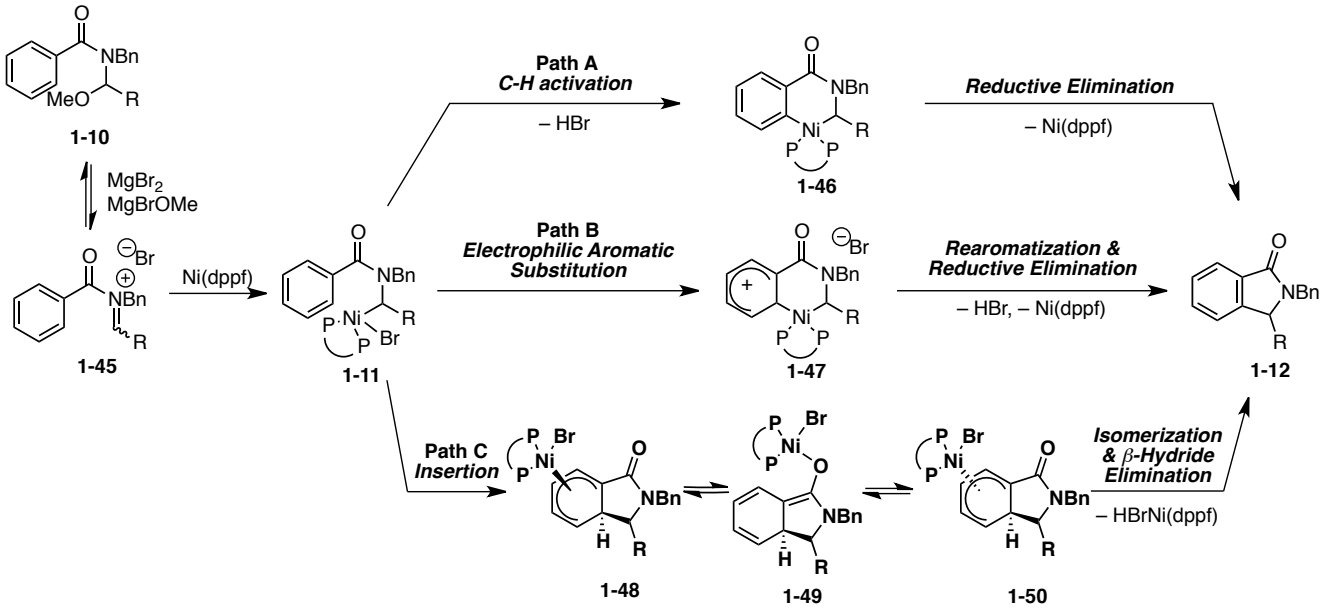
Scheme 1.7: Meta Substitution on the Benzoyl Fragment



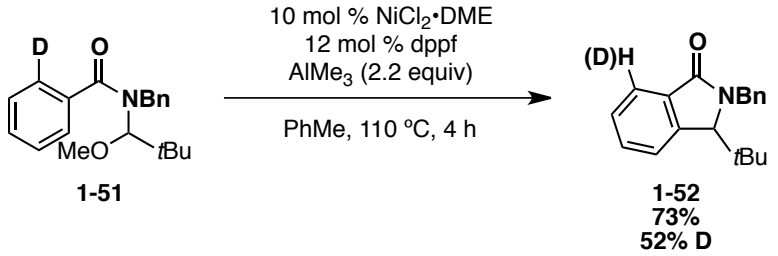
My colleague, Danielle Schacklady McAtee had conducted a few mechanistic experiments to further understand the nickel catalyzed cyclization pathway. The first pathway is via a C-H activation leading to metallacycle **1-46**, followed by reductive elimination to yield product. Path B is an electrophilic aromatic substitution reaction furnishing the benzoyl carbocation **1-47** followed by rearomatization and reductive elimination to give product. The last possible mechanism, Path C is a nickel insertion pathway to provide a nickel allyl intermediate , followed by isomerization and β −hydride elimination to access product. Lack of an intramolecular kinetic isotope

effect (Scheme 1.9) lead us to hypothesize that path A, C – H activation is not the operable mechanism.

Scheme 1.8: Potential Mechanisms for Isoindolinone Formation



Scheme 1.9: Intra-molecular Kinetic Isotope Effect



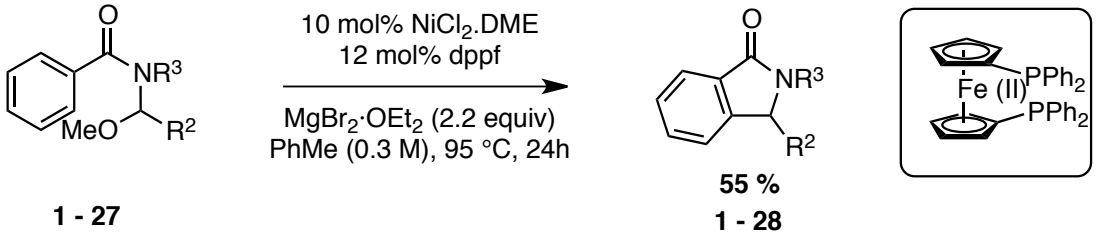
It was difficult to differentiate between pathway B and C. The electronic character of the benzoyl fragment affects both iminium formation and subsequent cyclization. Although we could not exclude either possibility we favor path B, due to

the fact that I had observed, electron-withdrawing groups on the benzoyl ring inhibit cyclization. Further, in path B, cyclization of the benzoyl ring may be favored over cyclization of the benzyl ring due to the conformational constraints imposed by the amide.

1.3 Role of DPPF Ligand in Ni (II) Catalyst Reduction to Ni (0)

During the course of these studies, we discovered that a Ni (II) pre-catalyst can be used in place of $Ni(COD)_2$ (Scheme 1.10). As discussed above, we hypothesize that the cyclization reaction proceeds via a Ni(0) catalyst. This then begs the question of how $NiCl_2$.DPPF, presumably formed in situ from dppf and $NiCl_2$.DME, is reduced to a (DPPF)Ni(0) catalyst under our reaction conditions.

Scheme 1.10: Ni(II) as an Efficient Catalyst with Ligand DPPF



1 - 27 **55 %** **1 - 28**

One possibility would be ligand acting as a reductant as shown by Buchwald and group whose palladium catalyzed C-O bond forming reaction proposed $Pd(OAc)_2$ being reduced to Pd(0) by phosphine ligand which in turn got oxidized to phosphine oxide.[11] To investigate that, we conducted a few variable tempaerature ^{31}PNMR and ^{1}H NMR studies on our system. On heating $NiCl_2$.DME and DPPF at

100 °C in solvent, *d*-toluene, although the ^{31}P signal for DPPF disappears, no new ^{31}P signal appears. This suggests that either no phosphine oxide was formed or the phosphine oxide formed precipitated from the reaction and hence was not observed. Given these results, we hypothesize that possibly it was the iron centre from the ferrocenyl moiety in the DPPF ligand donating electrons to nickel(II). Further supporting that hyposthesis was the fact that ligands like BINAP and tri-ortho tolylphosphine, which do not have an iron centre, failed to cyclize with Ni(II) catalyst but worked with Ni(0) complexes only (Table 1.1, entries 3-7).

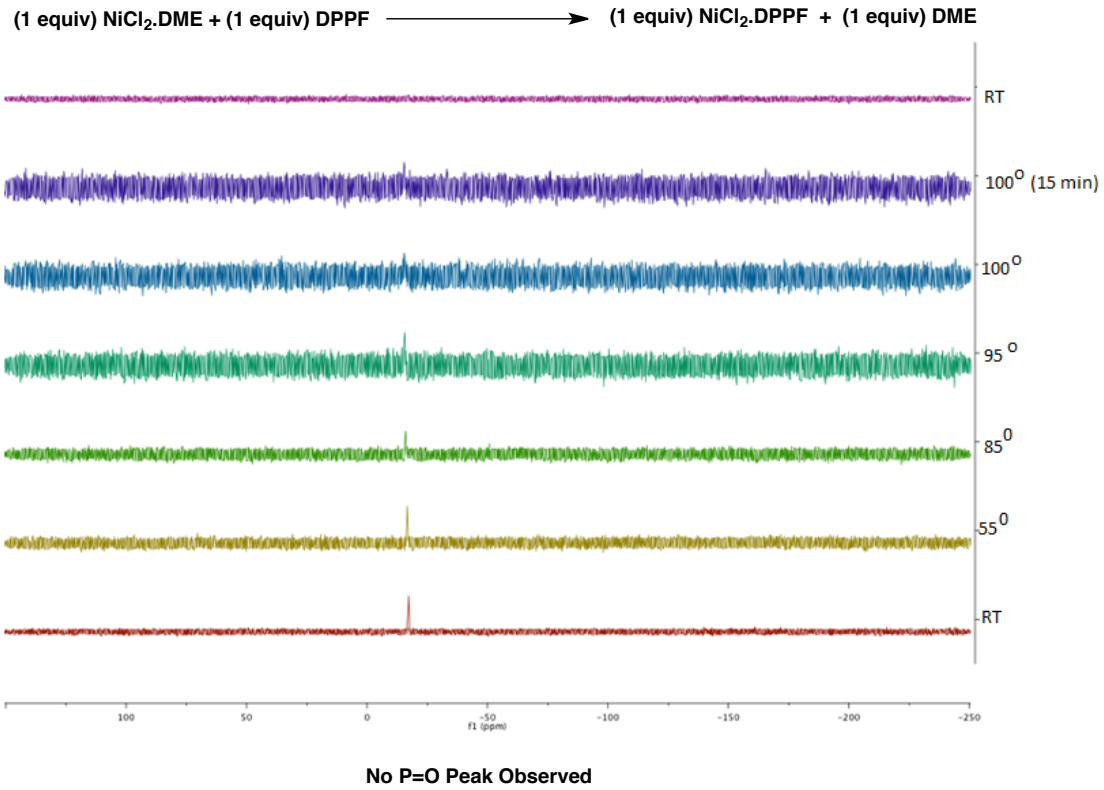
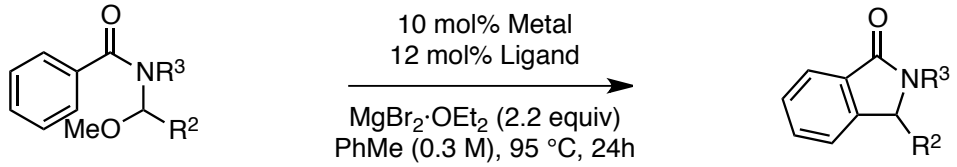


Figure 1.2: Variable Temperature ^{31}P NMR

Few precedents in literature also exist showing that this redox-active ligand DDPF can confer its electro-activity to its complexes.[12,13] To test this theory further in our system we planned to make corresponding Ni(I)DPPF and Ni(0)DPPF complexes and study their electrochemistry which will prove if a Ni(II)→Ni(I)→Ni(0) reduction is possible via the iron centre in DPPF or not. In progress to this plan, I had isolated a Ni(I) crystal structure of Ni(I)DPPF (Figure 1.3). Further investigation of this system is required to further validate our hypothesis.

Table 1-1: Preliminary Experiments



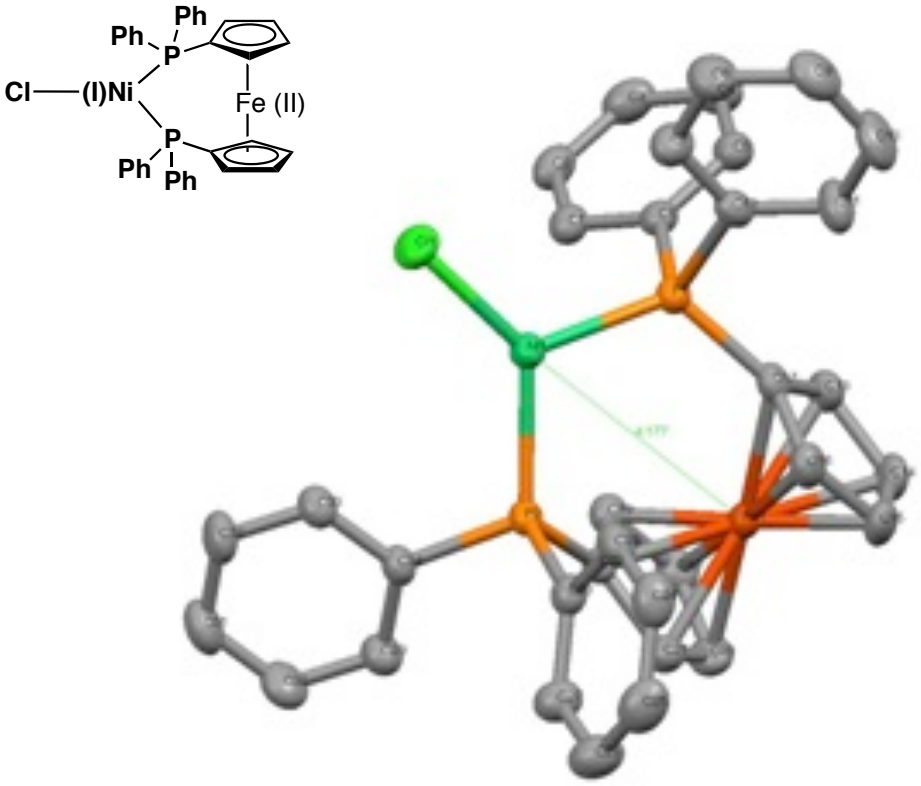
1 - 27 **1 - 28**

Entry	**[Ni]**	**Ligand (mol%)**	**Additives (mol%)**	**Product yield (%)[a]**	**Amide yield(%)[a]**
1	$Ni(COD)_2$	DPPF (12)		67	17
2	$NiCl_2$·DME	DPPF (12)		64	22
3[b]	$Ni(COD)_2$	BINAP (12)		56	36
4[b]	$NiCl_2$·DME	BINAP (12)		3	Significant
5[b]	$NiCl_2$·DME	BINAP (12)	Ferrocene (20)	15	80
6	$NiCl_2$·DME	P(*o*-Tol)$_3$ (22)		9	38
7	$NiCl_2$·DME	P(*o*-Tol)$_3$ (22)	Ferrocene (20)	17	28

8	$NiCl_2$·DPPF		28	21
9	$NiCl_2$·DPPF	DPPF (10)	62	31
10	$NiCl_2$·DPPF	BINAP (10)	38	21

[a] Conditions: Yield determined by NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. [b] Performed by Danielle McAtee.

Figure 1.3: Crystal Structure of Ni(I) (DPPF) Cl



1.4 Summary

In summary, I examined the scope of benzoyl fragments that can be used in this novel, nickel-catalyzed cyclization. My studies demonstrated the functional group tolerance and contributed strongly to our mechanistic understanding of this cyclization reaction. These results were published in *Organic Letters* in 2011. [1]

1.5 Experimental Procedures

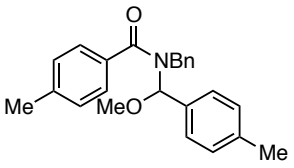
General Information

Aminal cyclizations were set up in a N_2-atmosphere glovebox in oven-dried 1-dram vials sealed with Teflon-lined caps; all other reactions were performed in oven-dried round-bottomed flasks unless otherwise noted. Flasks were fitted with rubber septa, and reactions were conducted under a positive pressure of N_2. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed on silica gel 60 (40-63μm, 60Å). Thin layer chromatography (TLC) was performed on glass plates coated with silica gel 60 with F254 indicator. Commercial reagents were purchased from Sigma Aldrich, Acros, Fisher, Strem, or Cambridge Isotopes Laboratories and used as received with the following exceptions: toluene, CH_2Cl_2, and Et_2O were dried by passing through drying columns.[1] Toluene was then degassed by sparging with N_2 and stored over activated

4Å MS in a N_2-atmosphere glovebox. MeCN, Et_3N, and $(i\text{-Pr})_2NEt$ were distilled from CaH_2. MeOH was distilled from CaH_2 and magnesium. BaO_2 was dried at 100 °C under high vacuum overnight and stored in a N_2-atmosphere glovebox. TMSOTf was distilled before use. *t*-Butyllithium was titrated following the procedure of Suffert.[2] $CDCl_3$ was stored over oven-dried potassium carbonate. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on 400 or 600 MHz spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.28; $(CD_3)_2CO$ = δ 2.08). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$ = δ 77.07) Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), integration. For ^{13}C NMR, multiplicities were distinguished using an ATP pulse sequence; typical methylene and quaternary carbons appear 'up' (u); methine and methyl carbons appear 'down' (dn). Infrared (IR) spectra were obtained using FTIR spectrophotometers with material loaded onto a NaCl plate. The mass spectral data were obtained at the University of Delaware spectrometry facility.

Preparation of Aminal Substrates:

Synthesis of *N*-benzyl-*N*-(methoxy(p-tolyl)methyl)-4-methylbenzamide (1-16)

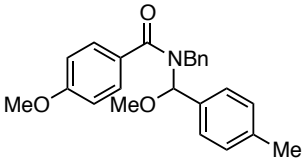


In a round-bottomed flask equipped with a nitrogen inlet and an oil bubbler to monitor gas flow, a solution of 4-methylbenzoic acid (500 mg, 3.67 mmol, 1.0 equiv), CH_2Cl_2 (3.0 mL), and DMF (50 μL, 0.65 mmol, 0.12 equiv) was cooled to 0 °C. Oxalyl chloride (631 μL, 7.34 mol, 2.0 equiv) was then added dropwise via syringe, and the immediate evolution of gas was observed by increased flow through the bubbler. The reaction mixture was stirred at 0 °C until gas flow slowed and was then stirred at room temperature for 1 hour. The reaction mixture was concentrated using a rotary evaporator. Residual oxalyl chloride was removed by repeatedly diluting the resulting residue with dry CH_2Cl_2 and subsequently concentrating the mixture (3.0 mL x 5). The crude acid chloride generated was used in the subsequent step without further purification.

The crude acid chloride (567 mg, 3.67 mmol, 1.2 equiv) was dissolved in CH_3CN (2.0 mL) and added to a solution of *N*-(4-methylbenzylidene)-1-phenylmethanamine[Error! Bookmark not defined.] (639 mg, 3.05 mmol, 1.0 equiv) in CH_3CN 2.0 mL). The reaction mixture was stirred for 20 minutes, before a solution of methanol (193 μL, 4.77 mmol, 1.3 equiv), triethylamine (716 μL, 5.14 mmol, 1.4 equiv) and CH_3CN (1.0 mL) was added. A precipitate immediately formed. Upon completion of the addition, the mixture was filtered through a Celite plug, which was then rinsed with Et_2O (5.0 mL x 4). The filtrate was concentrated, and the resulting oil

was purified by silica gel chromatography (10–20% EtOAc/hexanes) to give aminal **1-16** (988 mg, 75%) as an amorphous yellow solid (mp: 80–88 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 6.94 (m, 13H), 5.94 (s, 1H), 4.69 (br s, 1H), 4.28 (d, J = 13.5 Hz, 1H), 3.18 (s, 3H), 2.39 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 139.9, 138.7, 138.2, 134.6, 133.6, 129.3, 129.1, 128.9, 127.9, 127.0, 126.6, 126.5, 90.5, 55.5, 45.1, 21.4, 21.2; FTIR (thin film) 3031.0, 2927.3, 2826.3, 1643.9, 1612.3, 1512.4, 1495.4, 1434.6, 1403.6, 1338.7, 1318.1, 1207.6, 1179.3, 1129.2, 1087.2, 1073.5, 1021.4, 957.8, 885.8, 826.2, 781.8, 754.5, 725.2, 699.1, 604.8, 567.2, 528.2 cm^{-1}; HRMS (ESI+) $[M + Na]^+$ calculated for $C_{24}H_{25}NO_2Na$: 382.1778, found: 382.1777.

Synthesis of *N*-benzyl-4-methoxy-*N*-(methoxy(p-tolyl)methyl)benzamide (1-17)

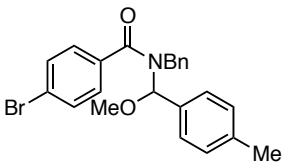


In a round-bottomed flask equipped with a nitrogen inlet and an oil bubbler to monitor gas flow, a solution of 4-methoxybenzoic acid (500 mg, 3.28 mmol, 1.0 equiv), CH_2Cl_2 (3.0 mL), and DMF (50 μL, 0.645 mmol, 0.19 equiv) was cooled to 0 °C. Oxalyl chloride (310 μL, 3.61 mmol, 1.1 equiv) was then added dropwise via syringe, and the immediate evolution of gas was observed by increased flow through the bubbler. The reaction mixture was stirred at 0 °C until gas flow slowed and was then stirred at room temperature for 1 hour. The reaction mixture was concentrated using a rotary evaporator. Residual oxalyl chloride was removed by repeatedly diluting the resulting residue with dry CH_2Cl_2 and subsequently concentrating the mixture (3.0 mL

x 5). The crude acid chloride generated was used in the subsequent step without further purification.

The acid chloride (560 mg, 3.28 mmol, 1.2 equiv) was dissolved in CH_3CN (2.0 mL) and added to a solution of *N*-(4-methylbenzylidene)-1-phenylmethanamine (572 mg, 2.73 mmol, 1.0 equiv) in CH_3CN (2.0 mL). The reaction mixture was stirred for 20 minutes, before a solution of methanol (144 μL, 3.56 mmol, 1.3 equiv), triethylamine (534 μL, 3.83 mmol, 1.4 equiv) and CH_3CN (1.0 mL) was added. A precipitate immediately formed. Upon completion of the addition, the mixture was filtered through a Celite plug, which was then rinsed with Et_2O (5.0 mL x 4). The filtrate was concentrated, and the resulting oil was purified by silica gel chromatography (10–20% EtOAc/hexanes) to give aminal **1-17** (718 mg, 70%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 6.73 (m, 13H), 6.04 (s, 1H), 4.63 (d, *J* = 12.0 Hz, 1H), 4.32 (d, *J* = 13.5 Hz, 1H), 3.84 (s, 3H), 3.23 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.8, 138.7, 138.2, 134.7, 129.2, 128.9, 128.7, 127.9, 126.6, 126.5, 124.4, 113.9, 90.8, 55.6, 55.4, 45.1, 21.2; FTIR (thin film) 3031.0, 2927.3, 2826.3, 1643.9, 1612.26, 1512.4, 1495.4, 1434.6, 1403.6, 1338.7, 1318.1, 1207.6, 1179.3, 1129.2, 1087.2, 1073.5, 1021.4, 957.8, 885.8, 826.2, 781.8, 754.5, 725.2, 699.1, 604.8, 567.2, 528.2 cm^{-1}; HRMS (ESI+) $[M + Na]^+$ calculated for $C_{24}H_{25}NO_2Na$: 398.1727, found: 398.1725.

Synthesis of *N*-benzyl-4-bromo-*N*-(methoxy(p-tolyl)methyl)benzamide (1-18)

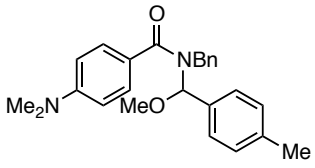


In a round-bottomed flask equipped with a nitrogen inlet and an oil bubbler to monitor gas flow, a solution of 4-bromobenzoic acid (500 mg, 2.47 mmol, 1.0 equiv), CH_2Cl_2 (3.0 mL), and DMF (50 μL, 0.65 mmol, 0.2 equiv) was cooled to 0 °C. Oxalyl chloride (238 μL, 2.73 mol, 1.1 equiv) was then added dropwise via syringe, and the immediate evolution of gas was observed by increased flow through the bubbler. The reaction mixture was stirred at 0 °C until gas flow slowed and was then stirred at room temperature for 1 hour. The reaction mixture was concentrated using a rotary evaporator. Residual oxalyl chloride was removed by repeatedly diluting the resulting residue with dry CH_2Cl_2 and subsequently concentrating the mixture (3.0 mL x 5). The crude acid chloride generated was used in the subsequent step without further purification.

Crude acid chloride (655 mg, 2.96 mmol, 1.2 equiv) was dissolved in CH_3CN (2.0 mL) and added to a solution of *N*-(4-methylbenzylidene)-1-phenylmethanamine (431 mg, 2.06 mmol, 1.0 equiv) in CH_3CN (2.0 mL). The reaction mixture was stirred for 20 minutes, before a solution of methanol (110 μL, 2.68 mmol, 1.3 equiv), triethylamine (402 μL, 2.88 mmol, 1.4 equiv) and CH_3CN (1.0 mL) was added. A precipitate immediately formed. Upon completion of the addition, the mixture was filtered through a Celite plug, which was then rinsed with Et_2O (5.0 mL x 4). The filtrate was concentrated, and the resulting oil was purified by silica gel chromatography (10–20% EtOAc/hexanes) to give aminal **1-18** (612 mg, 70%) as an

amorphous white solid (mp: 80–85 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.03 (m, 12H), 6.66 (s, 1H), 5.84 (s, 1H), 4.69 (br s, 1H), 4.26 (d, J = 13.0 Hz, 1H), 3.17 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 138.4, 138.3, 135.4, 134.2, 131.9, 129.3, 129.0, 128.6, 128.0, 126.8, 126.4, 124.0, 90.6, 55.6, 45.2, 21.2; FTIR (thin film) 3031.4, 2930.5, 2826.6, 1643.9, 1590.3, 1513.3, 1493.1, 1435.9, 1405.3, 1339.4, 1318.5, 1206.8, 1179.1, 1127.6, 1087.7, 1072.1, 1012.8, 957.7, 886.5, 832.2, 780.3, 739.6, 698.3, 613.4, 565.3, 508.0; HRMS (ESI+) $[M + Na]^+$ calculated for $C_{23}H_{22}N_1O_2\ Br_1Na$: 446.0726, found: 446.0725.

Synthesis of *N*-benzyl-4-(dimethylamino)-*N*-(methoxy(p-tolyl)methyl)benzamide (1-25)[10]



In a round-bottomed flask equipped with a nitrogen inlet and an oil bubbler to monitor gas flow, a solution of 4-(dimethylamino)benzoic acid (500 mg, 3.02 mmol, 1.0 equiv) and CH_2Cl_2 (3.0 mL) was cooled to 0 °C. Oxalyl chloride (285 μL, 3.33 mmol, 1.2 equiv) was then added dropwise via syringe, and the immediate evolution of gas was observed by increased flow through the bubbler. The reaction mixture was stirred at 0 °C until gas flow slowed and was then stirred at room temperature for 1 hour. The resulting solution of acid chloride was used in the subsequent step without purification.

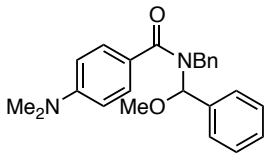
After the oil bubbler was removed, the solution of acid chloride generated was cooled to 0 °C. A solution of benzyl amine (827 μL, 7.56 mmol, 2.5 equiv) and CH_2Cl_2 (2.0 mL) was added dropwise via syringe. A precipitate immediately formed.

The reaction mixture was then stirred at 0 °C for 30 minutes and was then stirred at room temperature for 1 hour. H_2O (20 mL) was added. The mixture was extracted with EtOAc (30 mL). The organic layer was washed with saturated NaCl (10 mL), dried ($MgSO_4$), filtered and concentrated to give *N*-benzyl-4-(dimethylamino)benzamide (676 mg, 88%) as a pale yellow solid.

A colorless solution of *p*-Tolualdehyde acetal (523 mg, 3.15 mmol, 1.6 equiv) and CH_2Cl_2 (4 mL) was cooled to 0 °C. TMSOTf (570 µ(, 3.15 mmol, 1.6 equiv) was then added dropwise via syringe. The solution turned pink. After stirring at 0 °C for 10 min, a solution of *N*-benzyl-4-(dimethylamino)benzamide (500 mg, 1.97 mmol, 1.0 equiv), (*i*-Pr)$_2$NEt (520 µE , 3.15 mmol, 1.6 equiv) and CH_2Cl_2 (2 mL) was added dropwise via syringe. The solution immediately turned yellow. The mixture was then stirred for 2 hours at room temperature. The mixture was filtered through a silica gel plug, which was then rinsed with Et_2O (5 mL x 4). The filtrate was concentrated, and the resulting oil was purified by silica gel chromatography (10–20% EtOAc/hexanes) to give aminal **1-25** (703 mg, 92%) as a white solid (mp: 115–125 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.14 (m, 11H), 6.68 (d, J = 8.7 Hz, 2H), 6.23 (s, 1H), 4.58 (d, J = 15.0 Hz, 1H), 4.37 (d, J = 14.9 Hz, 1H), 3.26 (s, 3H), 3.01 (s, 6H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 151.5, 139.0, 138.0, 135.1, 129.1, 128.8, 128.6, 127.9, 126.6, 126.5, 123.1, 111.3, 90.6, 55.6, 45.4, 40.4, 21.2; FTIR (thin film) 3031.6, 2926.7, 2823.8, 2353.2, 2318.4, 1636.3, 1608.4, 1524.3, 1495.2, 1434.5, 1395.2, 1361.4, 1317.4, 1226.8, 1195.0, 1178.3, 1127.6, 1072.4, 945.3, 886.3, 822.8,

785.9, 764.9, 735.4, 700.1, 620.1, 598.9, 568.5, 538.2, 508.4 cm^{-1}; HRMS (ESI+) [M + Na]$^+$ calculated for $C_{25}H_{28}N_2O_2Na$: 411.2048, found: 411.2046.

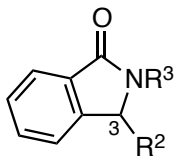
Synthesis of *N*-benzyl-4-(dimethylamino)-*N*-(methoxy(phenyl)methyl)benzamide (1-26)[10]



A colorless solution of 1-(dimethoxymethyl)-benzene (479 μL, 3.15 mmol, 1.6 equiv) and CH_2Cl_2 (4 mL) was cooled to 0 °C. TMSOTf (570 μL, 3.15 mmol, 1.6 equiv) was then added dropwise via syringe. The solution turned pink. After stirring at 0 °C for 10 min, a solution of *N*-benzyl-4-(dimethylamino)benzamide (500 mg, 1.97 mmol, 1.0 equiv), (*i*-Pr)$_2$NEt (520 μL , 3.15 mmol, 1.6 equiv) and CH_2Cl_2 (2 mL) was added dropwise via syringe. The solution immediately turned yellow. The mixture was then stirred for 2 hours at room temperature. The mixture was filtered through a silica gel plug, which was then rinsed with Et_2O (5 mL x 4). The filtrate was concentrated, and the resulting oil was purified by silica gel chromatography (10–20% EtOAc/hexanes) to give aminal **1-26** (604 mg, 82%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.11 (m, 12H), 6.69 (d, J = 8.6 Hz, 2H), 6.32 (s, 1H), 4.57 (d, J = 15.0 Hz, 1H), 4.43 (d, J = 15.0 Hz, 1H), 3.30 (s, 3H), 3.01 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 151.6, 138.9, 138.1, 129.1, 128.5, 128.4, 128.2, 127.9, 126.7, 126.5, 123.0, 111.3, 55.6, 45.4, 40.2, 31.0; FTIR (thin film) 2929.6, 1633.4, 1607.7, 1524.7, 1494.2, 1453.1, 1433.7, 1393.2, 1361.8, 1314.7, 1194.0, 1173.3, 1127.3, 1087.9, 1069.9, 1029.8, 945.2, 824.5, 755.9, 712.6, 698.8, 666.3, 591.2, 518.1 cm^{-1}; HRMS (ESI+) [M + Na]$^+$ calculated for $C_{24}H_{26}N_2O_2Na$: 397.1892, found: 397.1883.

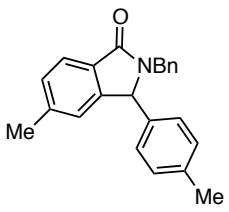
Preparation of Isoindolinones

General Procedure A ($MgBr_2 \cdot OEt_2$). In a N_2-atmosphere glovebox, $Ni(cod)_2$ (3.8 mg, 0.0138 mmol, 10 mol %) was weighed into a 1-dram vial equipped with a magnetic stir bar. Dppf (8.9 mg, 0.0166 mmol, 12 mol %), aminal **1-27** (0.138 mmol, 1.0 equiv), $MgBr_2 \cdot OEt_2$ (78.6 mg, 0.304 mmol, 2.2 equiv), and then PhMe (500 μL, 0.28 M) were added. The vial was capped with a Teflon-lined cap and heated in an aluminum heating block at 95 °C. After cooling to room temperature, the crude material was directly purified by silica gel chromatography (10–20% EtOAc/hexanes) to furnish isoindolinone **1-28**.

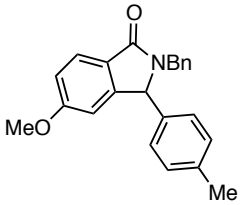


2-benzyl-3-*p*-tolylisoindolin-1-one (1-28). Prepared via General Procedure A ($MgBr_2 \cdot OEt_2$) with a reaction time of 24 hours. Crude material was purified by silica gel chromatography to give **1-28** (run 1: 30 mg, 67%; run 2: 33 mg, 73%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.93 (m, 1H), 7.53 – 7.43 (m, 2H), 7.36 – 7.26 (m, 3H), 7.26 – 7.10 (m, 5H), 6.98 (d, J = 8.0 Hz, 2H), 5.42 (d, J = 14.8 Hz, 1H), 5.23 (s, 1H), 3.74 (d, J = 14.9 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 146.6, 138.6, 137.2, 133.7, 131.9, 131.4, 129.8, 128.7, 128.5, 128.3, 127.8, 127.6, 123.7, 123.1, 63.3, 43.7, 21.2; FTIR (thin film) 3031.1, 2921.2, 1694.6, 1637.8, 1400.1 cm^{-1}; HRMS (ESI+) $[M + H]^+$ calculated for $C_{22}H_{20}NO$: 314.1545, found: 314.1551.

2-benzyl-5-methyl-3-p-tolylisoindolin-1-one (1-29): Prepared via General Procedure A ($MgBr_2 \cdot OEt_2$) with a reaction time of 24 hours. Crude material was purified by silica gel chromatography to give **1-29** as a white crystalline solid (run 1: 32.2 mg, 68%; run 2: 33.1 mg, 70%, mp: 156–162 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.8 Hz, 1H), 7.40 – 7.12 (m, 8H), 7.04 – 6.82 (m, 3H), 5.40 (d, J = 14.9 Hz, 1H), 5.18 (s, 1H), 3.72 (d, J = 14.9 Hz, 1H), 2.39 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 146.9, 142.5, 138.5, 137.3, 133.9, 129.8, 129.3, 128.9, 128.7, 128.5, 127.8, 127.5, 123.6, 123.5, 63.1, 43.7, 21.9, 21.3; FTIR (thin film) 3028.5, 2920.9, 1693.5, 1620.3, 1512.9, 1494.2, 1453.9, 1434.9, 1397.9, 1356.9, 1284.1, 1209.8, 1181.0, 1144.1, 1123.6, 1074.8, 1028.9, 829.9, 756.7, 736.4, 703.7, 677.5, 609.6, 518.8 cm^{-1}; HRMS (ESI+) $[M + H]^+$ calculated for $C_{23}H_{22}NO$: 328.1696, found: 328.1695.

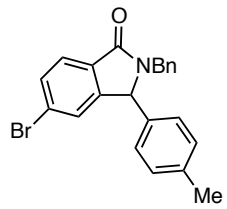


2-benzyl-5-methoxy-3-p-tolylisoindolin-1-one (1-30): Prepared via General Procedure A ($MgBr_2 \cdot OEt_2$) with a reaction time of 24 hours. Crude material was purified by silica gel chromatography to give **1-30** as a white crystalline solid (run 1: 36.2 mg, 73%; run 2: 36.7 mg, 74%, mp: 165–170 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.4 Hz, 1H), 7.34 – 7.25 (m, 3H), 7.22 – 7.16 (m, 4H), 7.01 – 6.96 (m, 3H), 6.59 (d, J = 2.2 Hz, 1H), 5.38 (d, J = 14.9 Hz, 1H), 5.16 (s, 1H), 3.76 (s, 3H), 3.70 (d, J = 14.9 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 163.0, 148.8, 138.5, 137.4, 133.8, 129.8, 128.7, 128.4, 127.8, 127.5, 125.0, 124.0, 115.0,



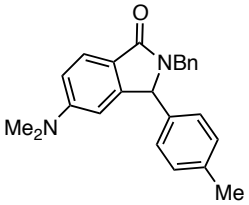
107.8, 63.1, 55.6, 43.7, 21.3; FTIR (thin film) 2358.5, 1690.5, 1610.7, 1512.1, 1489.4, 1455.3, 1436.8, 1395.8, 1358.9, 1338.4, 1285.0, 1248.9, 1218.8, 1180.5, 1146.3, 1103.7, 1027.9, 971.8, 846.7, 762.9 cm^{-1}; HRMS (ESI+) $[M + H]^+$ calculated for $C_{23}H_{22}NO_2$: 344.1645, found: 344.1642.

2-benzyl-5-(bromo)-3-phenylisoindolin-1-one (1-31): Prepared via General



Procedure A ($MgBr_2 \cdot OEt_2$) with a reaction time of 24 hours. Crude material was purified by silica gel chromatography to give **1-31** as a white crystalline solid (run 1: 37.5 mg, 66%; run 2: 39.2 mg, 69%, mp: 172–178 °C): ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.1 Hz, 1H), 7.68 – 7.56 (m, 1H), 7.42 – 7.12 (m, 8H), 6.97 (d, J = 8.0 Hz, 2H), 5.39 (d, J = 14.8 Hz, 1H), 5.19 (s, 1H), 3.71 (d, J = 14.8 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 148.2, 139.0, 136.8, 132.8, 131.9, 130.4, 130.0, 128.8, 128.42, 128.36, 127.7, 126.6, 126.5, 125.2, 62.9, 43.8, 21.3; FTIR (thin film) 2948.7, 2923.5, 2855.9, 1695.9, 1607.3, 1512.8, 1494.3, 1454.4, 1417.5, 1395.1, 1314.6, 1162.7, 1112.8, 1076.2, 1054.0, 972.4, 902.4, 816.4, 754.9, 702.7, 678.9, 508.0 cm^{-1}; HRMS (ESI+) $[M + H]^+$ calculated for $C_{22}H_{19}N_1O_1Br_1$: 392.0645, found: 392.0639.

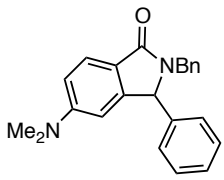
2-benzyl-5-(dimethylamino)-3-p-tolylisoindolin-1-one (1-32): Prepared via General



Procedure A ($MgBr_2 \cdot OEt_2$) with a reaction time of 36 hours. Crude material was purified by silica gel chromatography to give **1-32** as a yellow crystalline solid (run 1: 31.3 mg, 61%; run 2: 32.3 mg, 63%, mp: 173–183 °C): ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.6 Hz,

1H), 7.34 – 7.23 (m, 3H), 7.19 (dd, J = 10.4, 4.5 Hz, 4H), 7.00 (d, J = 8.0 Hz, 2H), 6.76 (dd, J = 8.6, 2.3 Hz, 1H), 6.30 (d, J = 2.0 Hz, 1H), 5.37 (d, J = 15.0 Hz, 1H), 5.13 (s, 1H), 3.67 (d, J = 15.0 Hz, 1H), 2.95 (s, 6H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 153.2, 148.9, 138.3, 137.7, 134.7, 129.7, 128.6, 128.4, 127.9, 127.3, 124.6, 119.1, 112.0, 105.1, 63.2, 43.7, 40.5, 21.3; FTIR (thin film) 3026.7, 2918.4, 1683.5, 1613.7, 1512.3, 1433.5, 1393.5, 1361.4, 1289.7, 1226.7, 1181.5, 1097.1, 820.0, 760.5, 703.1 cm^{-1}; HRMS (ESI+) $[M + H]^+$ calculated for $C_{24}H_{25}N_2O$: 357.1961, found: 357.1694.

2-benzyl-5-(dimethylamino)-3-phenylisoindolin-1-one (1-33): Prepared via General Procedure A ($MgBr_2 \cdot OEt_2$) with a reaction time of 36 hours. Crude material was purified by silica gel chromatography to give **1-33** as a yellow crystalline solid (run 1: 31.7 mg, 64%; run 2: 32.7 mg, 66%, mp: 170–180 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.6 Hz, 1H), 7.43 – 7.06 (m, 9H), 6.76 (dd, J = 8.6, 2.3 Hz, 2H), 6.30 (d, J = 1.9 Hz, 1H), 5.38 (d, J = 15.0 Hz, 1H), 5.15 (s,1H), 3.68 (d, J = 15.0 Hz, 1H), 2.95 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 153.1, 148.8, 137.9, 137.7, 133.8, 129.0, 128.6, 128.4, 127.9, 127.3, 124.8, 119.1, 112.0, 105.3, 63.5, 43.5, 40.6; FTIR (thin film) 2920.3, 2854.9, 1681.9, 1613.3, 1513.7, 1494.9, 1453.9, 1393.2, 1362.1, 1290.2, 1226.9, 1182.5, 1133.7, 1097.7, 1072.7, 1028.4, 828.6, 761.2, 732.9, 704.6, 605.0, 523.0 cm^{-1}; HRMS (ESI+) $[M + H]^+$ calculated for $C_{23}H_{23}N_2O$: 343.1805, found: 343.1801.



Chapter 2

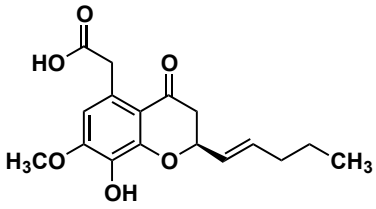
ENANTIOSELECTIVE, COPPER(I)-CATALYZED ALKYNYLATION OF OXOCARBENIUM IONS TO SET α,α-DIARYL TETRASUBSTITUTED STEREOCENTERS

2.1 Introduction

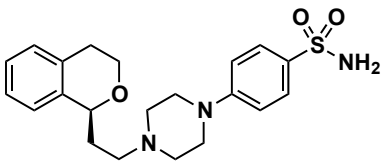
Substituted benzopyrans comprise of a number of important molecular targets like the antibacterial natural product aposphaerin A, dopamine D4 receptor agonist U-101387, HIV-1 reverse transcriptase inhibitor Efavirenz and vitamin E (Figure 2.1).[14-17]

We envisioned that enantioselective addition to a cyclic oxocarbenium ion might prove to be an efficient alternative strategy to set α-diaryl, tetrasubstituted stereocenters on oxygen heterocycles. By tethering one aryl group to the oxygen, the otherwise similar aryl substituents are differentiated by freedom of rotation and by their relationship to the oxygen substituents (alkyl vs. lone pair). These factors make the geometry of the oxocarbenium ion similar to that of a trisubstituted olefin, which has been used in other enantioselective transformations.[18,19] Here, however, the oxocarbenium ion reacts as an electrophile in contrast to its alkene analogue.

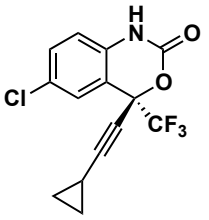
Figure 2.1: Biological Activity of Cyclic Ethers with Tetrasubstituted Stereocenters



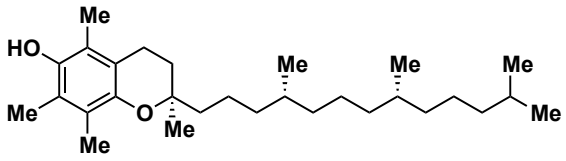
2-1
aposphaerin A
(antibacterial)



2-2
U-101387
(dopamine D4 receptor agonist)



2-3
efavirenz (HIV-1 reverse transcriptase inhibitor)

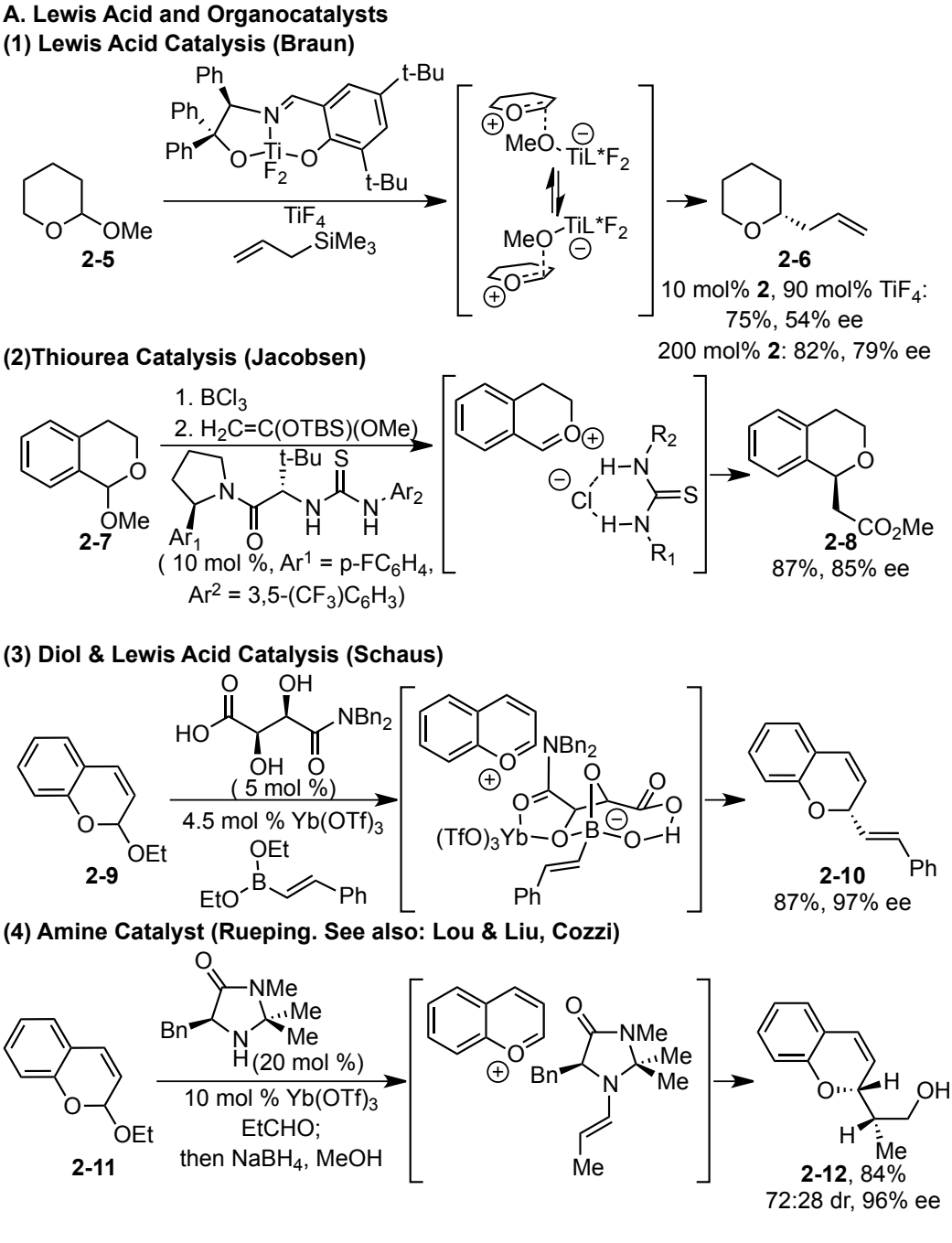


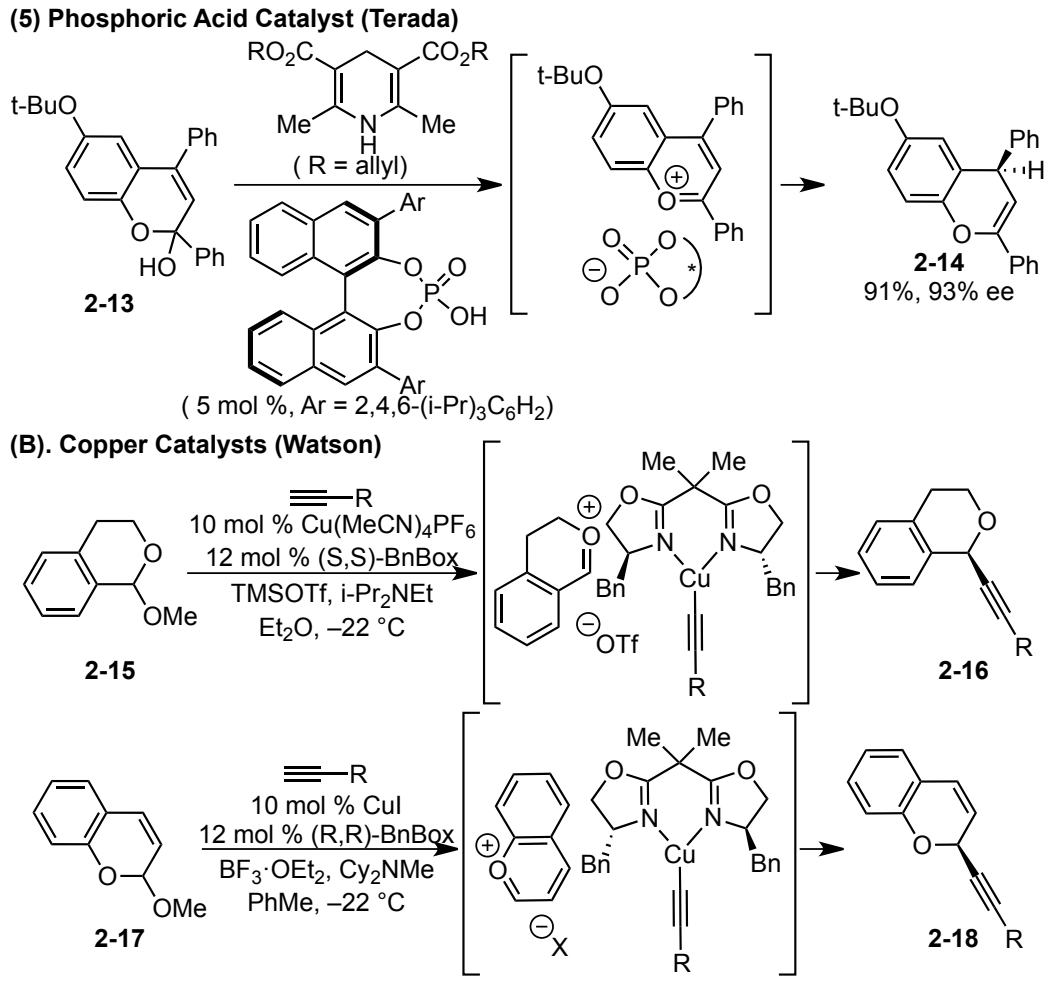
2-4
vitamin E (a-tocopherol)

However, controlling enantioselectivity in such additions represents a long-standing challenge in asymmetric catalysis. Few enantioselective methods are known and the majority rely on organo- or Lewis acid catalysts.[20-31] Braun reported a single example of allylation of dihydropyranyl acetal catalyzed by a chiral titanium (IV) (Scheme 2.1,1).[20] The Jacobsen group has developed enantioselective additions of silyl ketene acetals to 1-chloroisochromans using a chiral thiourea catalyst (Scheme 2.1,2**)**.[21] The Schaus group has shown the use of tartaramide catalyst for the enantioselective addition of vinyl and electron-rich aryl boronic esters to chromene acetals (Scheme 2.1,3).[22] More recently, Rueping and Lou and Liu has demonstrated

the enantioselective addition of enamines to oxocarbenium ions using organocatalyst (Scheme 2.1, 4).[24] Terada has also shown Bronsted acid catalyzed enantioselective

Scheme 2.1:Prior Art in Enantioselective Addition to Oxocarbenium Ions





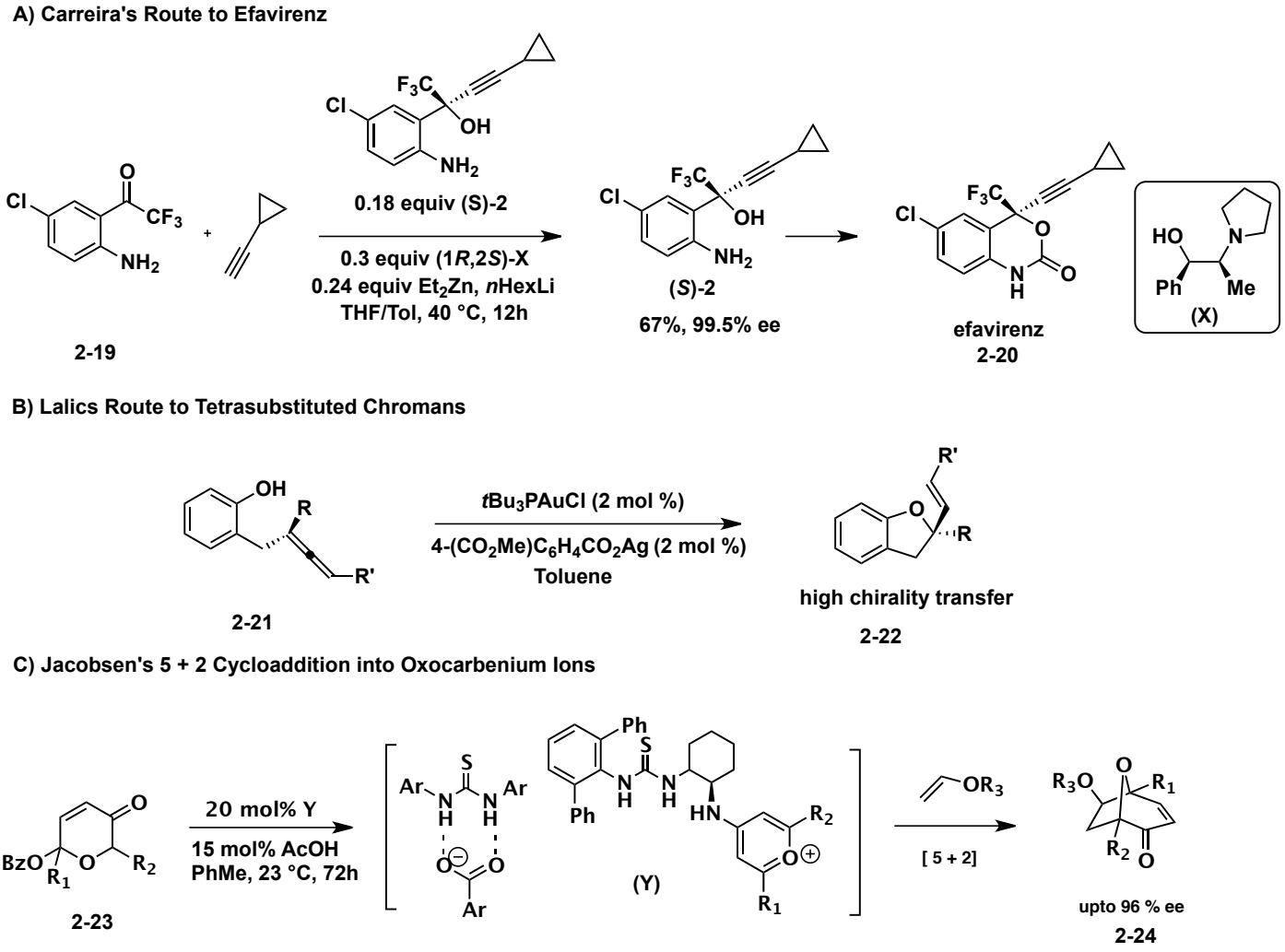
addition of hydrides to chromene acetals (Scheme 2.1, 5).[28] Our group has also shown alkynylation of isochroman and chromene acetals using a chiral Cu/bis(oxazoline) catalyst to set *tertiary* stereogenic centers. These reports represent the first examples of an enantioselective addition of an organometallic nucleophile to a prochiral cyclic oxocarbenium ion (Scheme 2.1, B). [32,33]

Notably, this method and all other reported intermolecular, enantioselective additions to cyclic oxocarbenium ions result in tertiary stereocenters; none of these methods enables formation of a tetrasubstituted stereogenic center. Instead the common strategy for asymmetric synthesis of these molecules is to first set the stereocenter, and then do a cyclization.[17,34,35] An example of such an approach is enantioselective additions to ketone substrates, which generally require significant differences in the electronic or steric character of their substituents to achieve high ee's.[17,36-43] In particular, enantioselective additions to diaryl ketones are rare, and none allow addition of an acetylide to our knowledge.[44-46] However, Carreira's route of asymmetric autocatalytic zinc acetylide addition to ketones enables an effecient synthesis of a key precursor to efavirenz (Scheme 2.2,A).[17] Lalic and group also demonstrated that exo-selective cyclizations of allenols provide an efficient approach to the synthesis of THFs, THPs and chromans containing a tetra-substituted stereocenter (Scheme 2.2,B)[34]. Only a single method exists for the formation of tetrasubstituted stereocenters via enantioselective addition to oxocarbenium ions; Jacobsen's thiourea-catalyzed [5+2] cycloaddition of pyrilium ions enables formation of α-dialkyl tetrasubstituted stereocenters on 8-oxabicylcooctanes (Scheme 2.2, C).[31,47]

We envisioned that transition metal catalysis may also enable the formation of diaryl-substituted quaternary stereocenters via enantioselective alkynylation of the cyclic ketals. However, in contrast to setting a tertiary stereocenter, wherein the electrophilic carbon is substituted by two very different groups (H vs Ar),

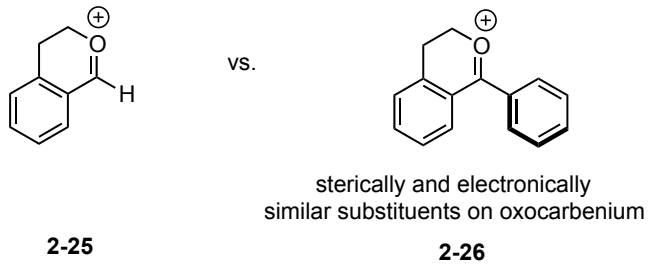
enantioselective formation of a diaryl, tetrasubstituted stereocenter requires that the catalyst differentiates between two sterically and electronically similar aryl substituents (Scheme 2.3, **2-26**).

Scheme 2.2: Representative Routes to α -Tetrasubstituted Cyclic Ethers



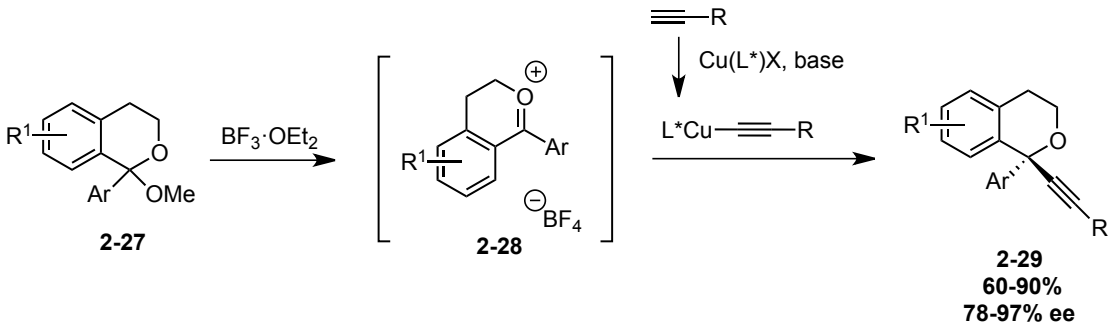
The only difference the two similar aryl groups enjoy is the freedom of rotation exhibited by the α –substituted phenyl group and by their relationship to the oxygen substituents (alkyl vs. lone pair) (Scheme 2.3). In addition, the steric hindrance of an additional substituent at the α –carbon to the oxocarbenium may create additional challenge by sterically hindering nucleophilic addition at that electrophilic carbon center. Tackling these challenges, we have identified a Cu/Py-Box catalyst capable of enantioselective alkynylation of isochroman ketals to give cyclic ethers with fully substituted α –stereocenters (Scheme 2.3)

Scheme 2.3: Enantioselective Alkynylation of Ketals to Set Diaryl-Substituted Quaternary Stereocenters



2-25 **2-26**

Current Work:

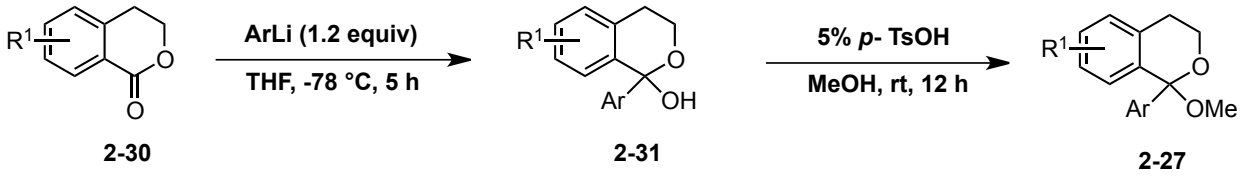


2-27 **2-28** **2-29**
60-90%
78-97% ee

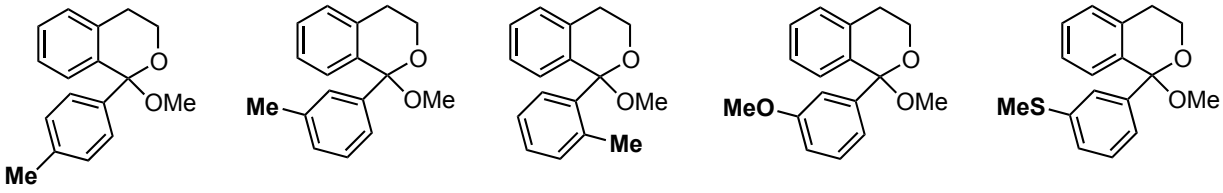
2.2 Results and Discussion

Synthesis of Ketal Substrates

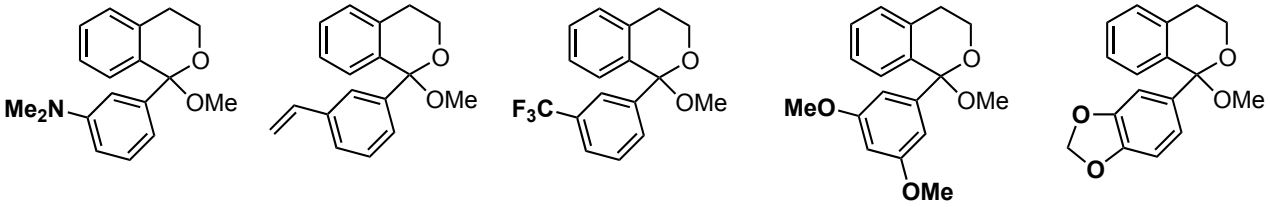
Scheme 2.4: Synthesis of Ketal Substrates



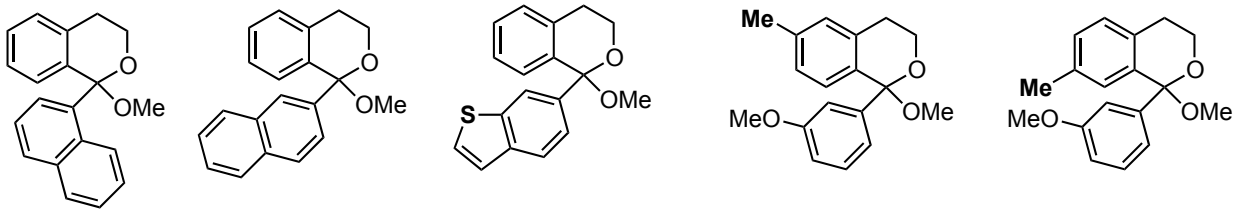
2-30 **2-31** **2-27**



2-32, 47% **2-33, 66%** **2-34, 57%** **2-35, 61%** **2-36, 68%**



2-37, 71% **2-38, 42%** **2-39, 55%** **2-40, 42%** **2-41, 35%**



2-42, 63% **2-43, 62%** **2-44, 63%** **2-45, 39%** **2-46, 62%**

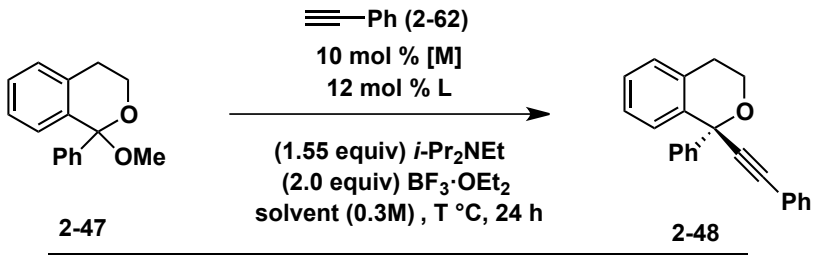
The ketal substrates were synthesized by addition of aryl lithium reagents to isochromanones to generate hemiketals (Scheme 2.4, **2-31**). These hemiketals are observed as a mixture of both ring open and cyclic forms. Subsequent treatment with catalytic TsOH in MeOH delivers ketals (**2-27**). As these compounds decompose under acidic conditions, they require the use of deactivated silica gel for purification. I have deactivated silica gel by treating it with 1% Et_3N in hexanes on the columns. These ketals are stable and can be stored at room temperature Substrates synthesized via this route are shown in Scheme 2.4.

Optimization of Alkynylation of Ketals

The reaction of isochroman ketal **2-47** and phenylacetylene **2-62** were selected as the model reaction for optimization of the alkynylation. Under conditions very similar to those used in the formation of tertiary stereocenters, no reactivity was observed (Table 2.1, entry 1). However, changing the Lewis acid to $BF_3 \cdot Et_2O$ effectively gave a yield of 60% in the absence of chiral ligands (Table 2.1,entry 2). When bis-(oxazoline) (Box) ligands were screened, ligand **2-58**, BnBox, gave racemic product but ligand **2-59**, IndBox, gave 13% yield of product **2-48** in 20% ee at -20 °C in solvent Ether, using Copper Iodide and Huning's base (Table 2.1, entries 3-4). Changing the solvent to chloroform increased the yield to 88% but in 15% ee only (Table 2.1, entry 5). Having identified chloroform as a promising solvent, other copper sources and bases were screened. We soon found copper (tetrakis acetonitrile) hexa-florophosphate with Huning's base gave an yield of 83% and ee of 37% with ligand **2-**

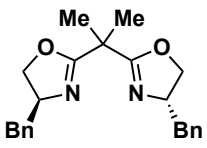
59 and an yield of 24% and an ee of 27% with ligand **2-60**, Ph-Pybox. (Table 2.2, entries 1-2). The base MTBD gave even greater enantioselectivity of 84% (Table 2.2, entry 3). A slightly higher ee of 87% was observed when copper(I) thiophenolate was used in place of copper (tetrakis acetonitrile) hexa-florophosphate (Table 2.2, entry 4).

Table 2-1: Optimization of Alkynylation of Ketal 2-47[a]

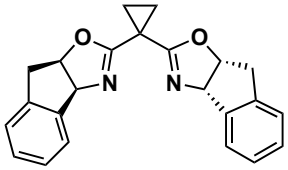


entry	[M]	L*	solvent	T	yield (%)[b]	ee (%)[c]
1[d]	CuI	-	Et_2O	r.t.	0	-
2	CuI	-	Et_2O	r.t.	60	-
3	CuI	2-58	Et_2O	-20	68	0
4	CuI	2-59	Et_2O	-20	13	20
5	CuI	2-59	$CHCl_3$	-20	88	15

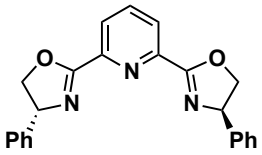
[a]Conditions: Ketal **2-47** (0.08 mmol, 1.0 equiv), [M] (0.008 mmol, 10 mol%), L*(0.01 mmol, 12 mol%), alkyne **2-62** (0.096 mmol, 1.2 equiv), $BF_3.Et_2O$ (0.16 mmol, 2.0 equiv), *i*-Pr_2NEt (0.12 mmol, 1.5 equiv), solvent (0.3M), T °C. [b]Determined by 1H NMR analysis using 1,3,5-trimethoxybenzene as internal standard. [c]Determined by chiral HPLC analysis. [d]1.2 equiv of TMSOTf replaced $BF_3 \cdot Et_2O$.



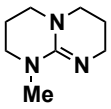
2-54, BnBox



2-59, IndBox

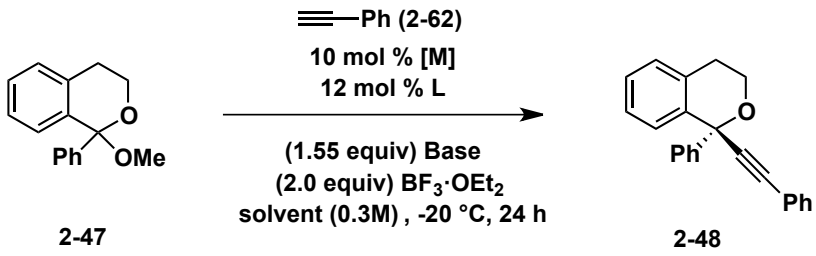


2-60, Ph-PyBox



2-61, MTBD

Table 2-2: Optimization of Alkynylation of Ketal 2-47[a]



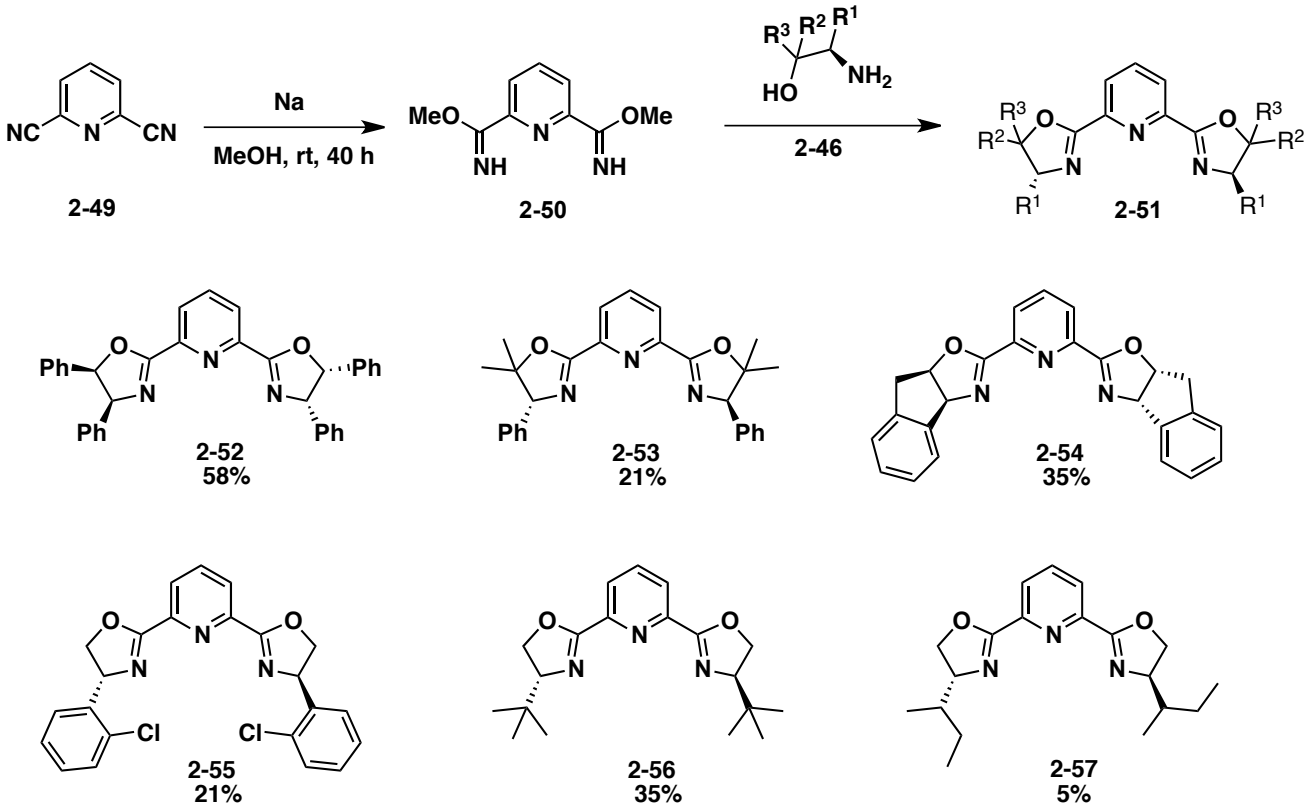
2-47 2-48

entry	[M]	L*	base	yield (%)[b]	ee (%)[c]
1	$Cu(MeCN)_4PF_6$	2-59	*i*Pr_2NEt	83	37
2	$Cu(MeCN)_4PF_6$	2-60	*i*Pr_2NEt	24	27
3	$Cu(MeCN)_4PF_6$	2-60	MTBD	22	84
4[d]	CuSPh	2-60	MTBD	12	87
5[d,e]	CuSPh	2-60	MTBD	87	78
6[d]	CuSPh	2-52	MTBD	n.d	77
7[d]	CuSPh	2-53	MTBD	n.d	81
8[d]	CuSPh	2-54	MTBD	n.d	39
9[d]	CuSPh	2-55	MTBD	n.d	48
10[d]	CuSPh	2-56	MTBD	n.d	73
11[d]	CuSPh	2-57	MTBD	n.d	38

[a]Conditions: Ketal **2-47**(0.08 mmol, 1.0 equiv), [M] (0.008 mmol, 10 mol%), L*(0.01 mmol, 12 mol%), alkyne **2-62** (0.096 mmol, 1.2 equiv), $BF_3 \cdot Et_2O$ (0.16 mmol, 2.0

equiv), base (0.12 mmol, 1.5 equiv), $CHCl_3$ (0.3M), -20 °C, 24 h, unless otherwise noted. MTBD = 7-Methyl-1,5,7-triazabicyclo(4.4.0)dec-5-ene, [b]Determined by 1H NMR analysis using 1,3,5-trimethoxybenzene as internal standard. [c]Determined by chiral HPLC analysis. [d]1.55 equiv of base in place of 1.5 equiv. 0.15M $CHCl_3$ in place of 0.3M. [e] 4 °C temperature in place of -20 °C.

Scheme 2.5: Synthesis of PyBox Ligands



In an effort to further increase the enantioselectivity and obtain synthetically useful yields, a variety of other substituted pyridine bis-(oxazoline) ligands were synthesized (Scheme 2.5) and examined in the alkynylation conditions, but none showed better enantioselctivity than **2-60** (Table 2.2, entries 6 – 11). Notably *t*BuBox (**2-56**) provides the same sense of enantioinduction as PhPyBox (**2-60**), suggesting

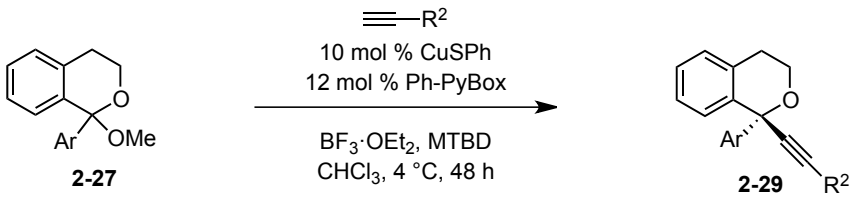
that the effect of the ligand substituents is likely largely due to steric repulsion, instead of an attractive interaction with the phenyl groups. Having identified PhPyBox as the optimal ligand, we achieved a synthetically useful yield of 87% with 78% ee of the alkynylated product by increasing the reaction temperature to 4 °C (Table 2.2, entry 5).

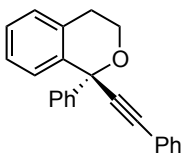
Substrate Scope

Scope of the Ketal

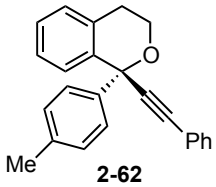
Under these optimized conditions (Table 2.2, entry 5), a wide variety of isochroman ketals reacted with aryl alkynes in high yields and enantioselectivities (Scheme 2.6). With respect to the 1-aryl substituent (Ar), substrates with electron donating groups on all para, meta and ortho positions show reactivity (**2-62 - 64**). However poor enantioselectivity is observed in the case of the ortho tolyl substituent probably due to steric crowding (**2-64**). A range of other functional groups also demonstrated great yields and enantioselectivities including electron withdrawing meta methoxy (**2-65**), thiol (**2-66**), amino (**2-67**), vinyl (**2-68**), trifluoromethyl (**2-69**), acetal (**2-71**) and heterocycle (**2-74**). Both 1 and 2 subtituted napthyl isochroman acetals worked well too (**2-72, 2-73**). Methyl substitutions on the 6 and 7 position of the benzo-pyran ring also showed great reactivity and selectivity (**2-75, 2-76**).

Scheme 2.6: Scope of the Ketal Substrates

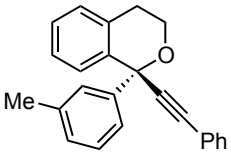




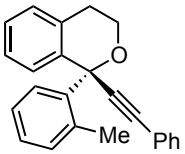
2-48
92%, 78% ee



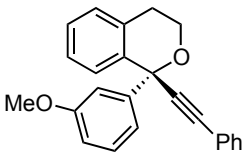
2-62
66%, 70% ee



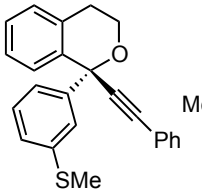
2-63
94%, 87% ee



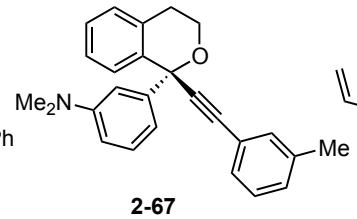
2-64
67%, 36% ee



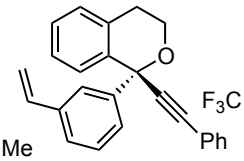
2-65
86%, 94% ee



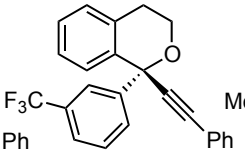
2-66
86%, 94% ee



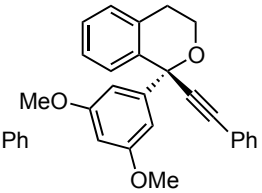
2-67
82%, 93% ee



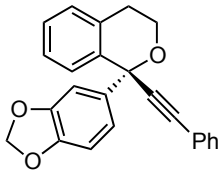
2-68
76%, 87% ee



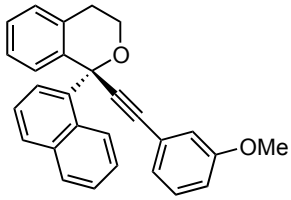
2-69
58%, 79% ee



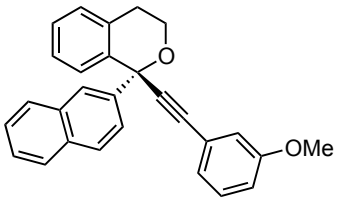
2-70
89%, 95% ee



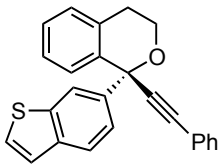
2-71
78%, 85% ee



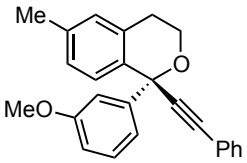
2-72
70%, 95% ee



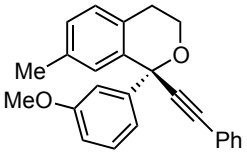
2-73
77%, 82% ee



2-74
71%, 87% ee



2-75
80%, 93% ee

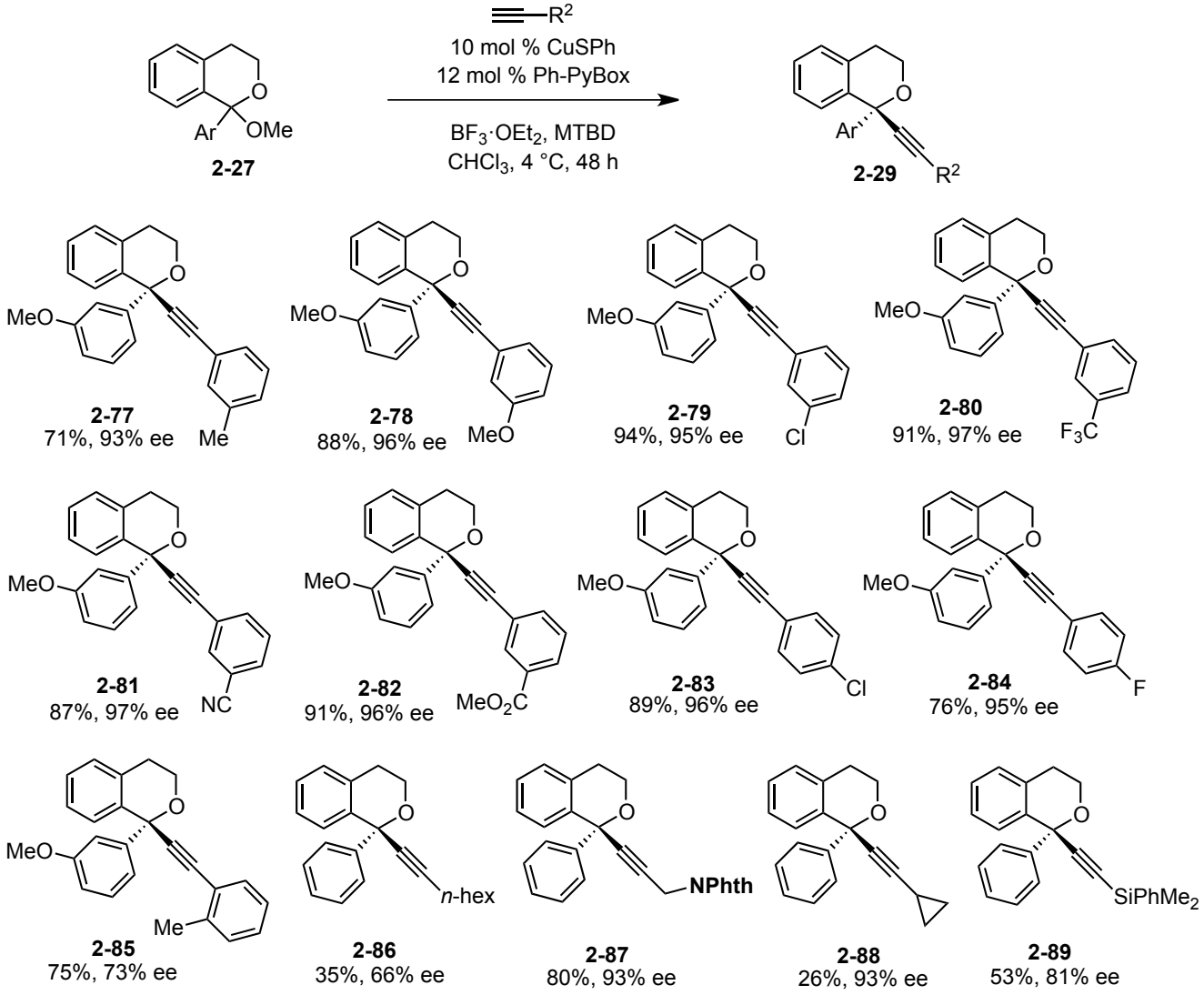


2-76
65%, 89% ee

Substrate Scope of the Alkynes

Good yields and high enantioselectivities were observed using a wide range of aryl acetylenes (Scheme 2.7). Electron-donating groups at both meta and ortho positions worked well (**2-77, 2-85**). Electron-withdrawing groups at both meta and para positions were very well tolerated including methoxy (**2-78**), trifloromethyl (**2-80**), cyano (**2-81**), ester (**2-82**) and halides (**2-79, 2-83, 2-84**). With respect to alkyl-substituted alkynes, 1-octyne gave low yield and modest enantioselectivity (**2-86**). However, addition of propargyl phthalimide resulted in 80% yield of product **2-87** in 93% ee. High enantioselectivity was also observed in the addition of cyclopropylacetylene (**2-88**). Silyl acetylenes also underwent addition. The addition of (trimethylsilyl)acetylene resulted in modest yield (40% by ^{1}H NMR), but relatively high enantioselectivity (82% ee, not shown). (Dimethylphenylsilyl)acetylene showed greater reactivity, giving 53% yield and 80% ee of silyl-protected acetylene **2-89**. Electron donating groups like para position amino and methyl substituents on phenyl acetylene also reacted with very low enantioselectivities for our system.

Scheme 2.7: Scope of the Alkyne Substituents

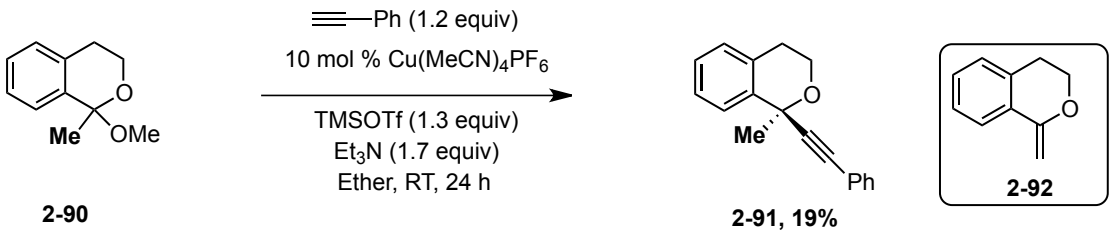


Reactivity of Alkyl Substituted Isochroman Ketals

1-Alkylisochroman ketals are poor substrates under these conditions; 1-Methyl ketal (**2-90**) was used as a model substrate. However, under the optimized conditions for the enantioselective transformation, no desired product was observed. I was

successfully able to make ketal **2-90** by careful addition of methyl lithium to isochromanone and subsequent ketal formation. Initial screening of the ketal **2-90** have shown alkynylation in a very low 19% yield (**2-91**) under the conditions shown below in the absence of any chiral ligands (Scheme 2.8). I hypothesize that the non-planar alkyl substituent may impose more steric hindrance in the approach of a nucleophile than the phenyl substituent which may lie planar in conjugation with the oxocarbenium ion. Alkyl substituted oxocarbeniums are also prone to elimination leading to less formation of desired product. Although I did not observe the elimination product (**2-92**), this type of enol ether may polymerize in the presence of $BF_3 \cdot Et_2O$.[48]

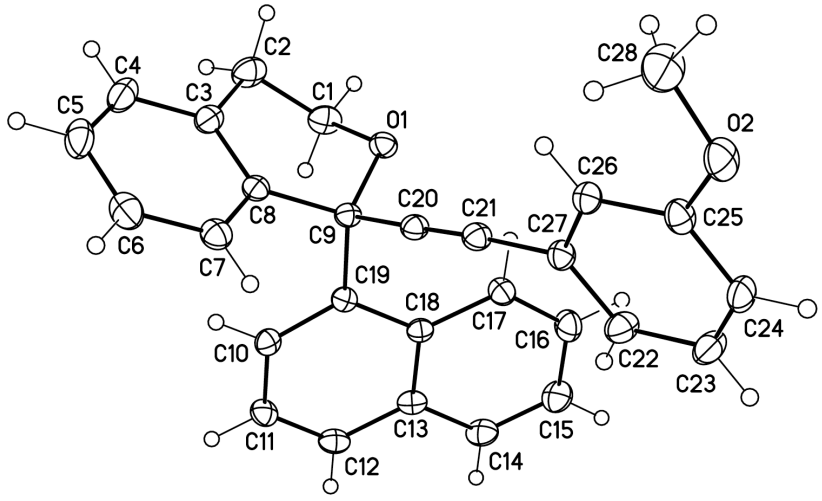
Scheme 2.8: Scope of Alkyl Substituted Isochroman Ketals



Determination of Stereochemistry

The absolute configuration of **2-72** was determined by X-ray crystallography.[49] The configurations of other products were assigned by analogy. X-ray quality crystals were obtained from slow evaporation of **2-72** in diethyl ether. The crystal structure demonstrated that the absolute configuration is ***S*** (Figure 2.2).

Figure 2.2 **:** Molecular diagram of 2-67 with ellipsoids at 30% probability. H-atoms omitted for clarity. (CCDC 973167)

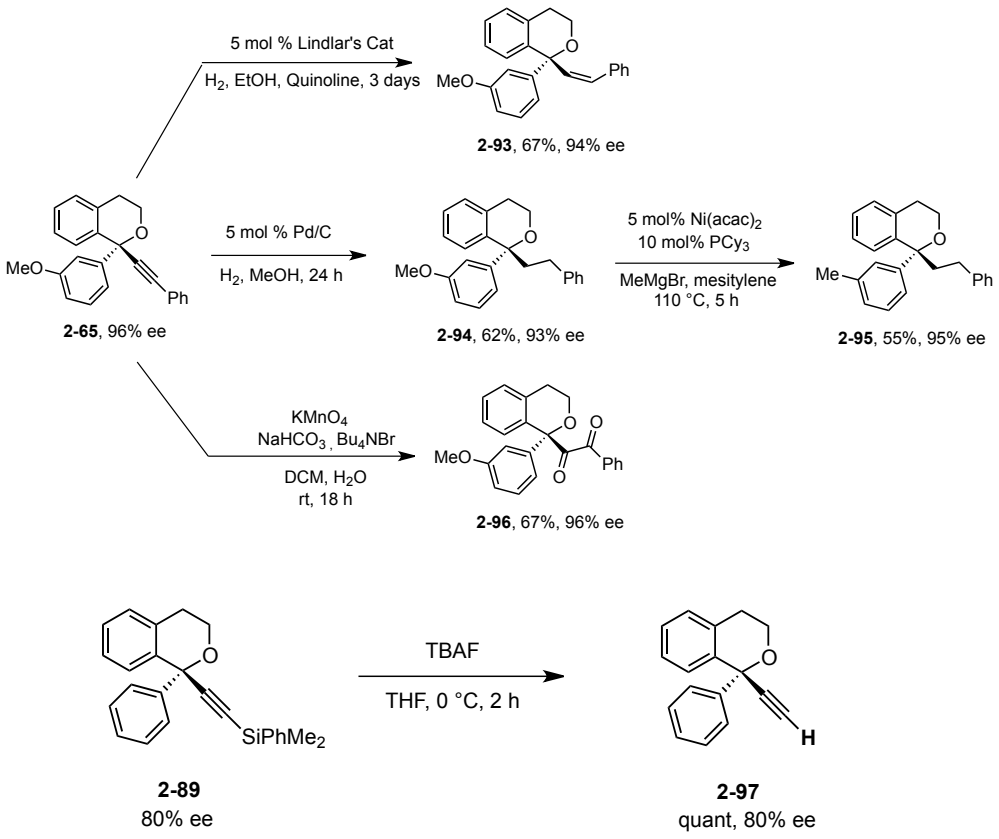


Elaboration of Products

The alkyne products can be easily elaborated. I was successfully able to reduce alkyne **2-65** to give both vinyl- and alkyl-substituted isochromans **2-93** and **2-94**, respectively, in good yields and high enantiopurities (Scheme 2.9). Oxidation to diketone **2-90** was also accomplished in 67% yield and perfect stereochemical fidelity.[50] However, I was unable to further oxidize the diketone to the carboxylic acid. As noted above, *m*-methoxyphenyl-substituted isochroman products are formed in the highest enantioselectivities. I was able to functionalize the *m*-methoxyphenyl-substituted isochroman via cross coupling. For example, it can be converted to a *m*-

methyl group without loss in ee (**2-95**).[51] Finally, deprotection of silyl acetylene **2-89** was accomplished in quantitative yield and perfect stereochemical fidelity to deliver terminal alkyne **2-97**.

Scheme 2.9: Elaboration of Products



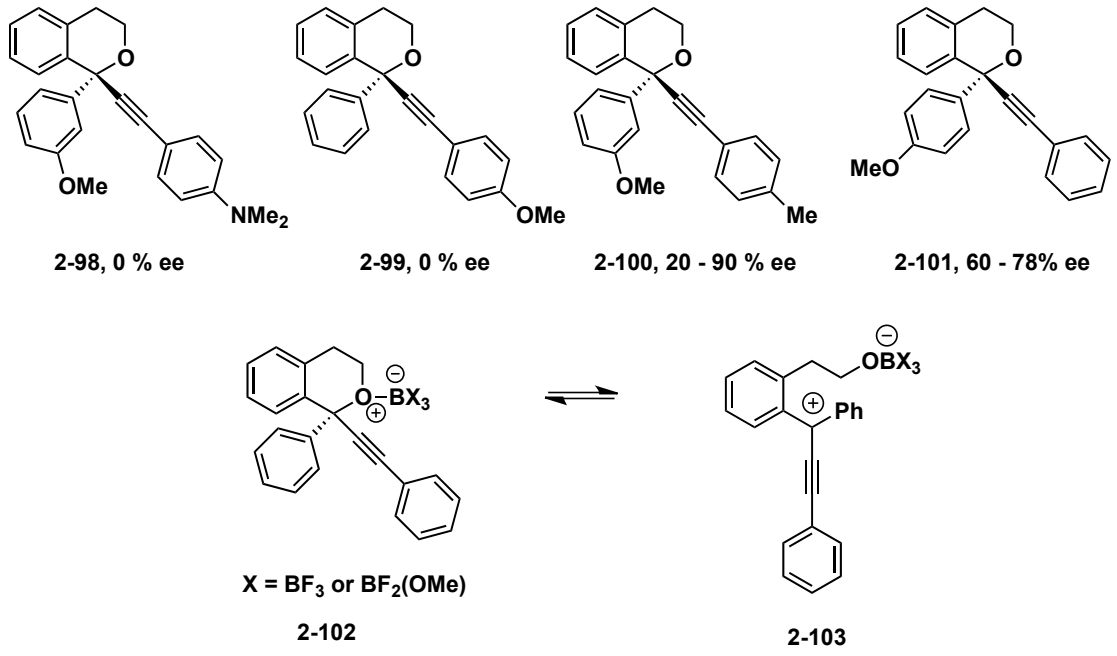
2.3 Mechanistic Studies

Challenging Substrates

Aryl acetylenes with electron-rich *p*-substituents, such as *p*-(dimethylamino) (**2-98**), *p*-methoxy (**2-99)** and *p*-methyl (**2-100**) and 4-methoxy substituent on the

isochroman ketal (**2- 101**) led to low or irreproducible enantioselectivities (Scheme 2.10). I hypothesize that these electron-rich isochroman products may undergo epimerization via a Lewis acid-induced ionization of the benzylic C–O bond, leading to a trityl-like cation (**2-103**) (Scheme 2.10).

Scheme 2.10: Challenging Substrates

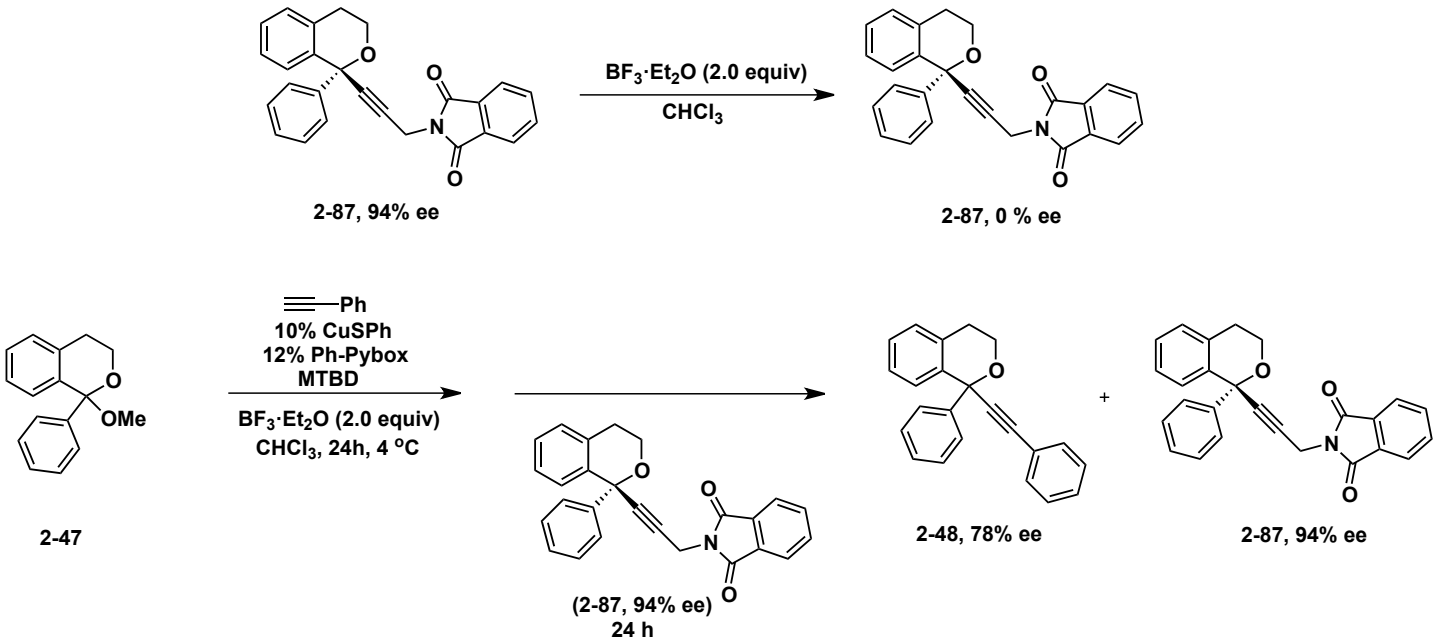


Role of $BF_3 \cdot Et_2O$

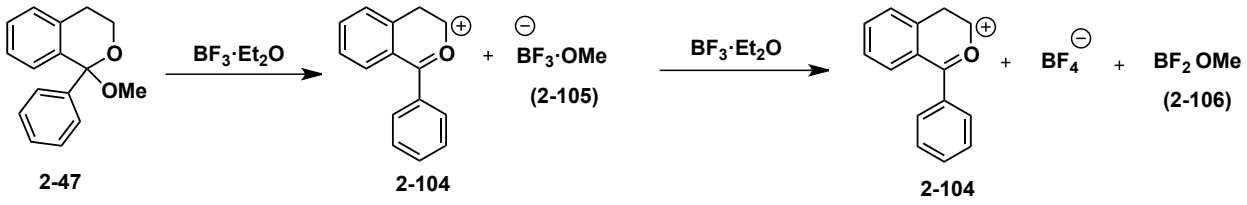
We were intrigued by the requirement for two equivalents of Lewis acid, which were essential both for yield and enantioselectivity. We noticed that phthalimide-substituted alkyne (**2-87**) epimerizes under 2.0 equivalents of $BF_3 \cdot Et_2O$ in $CHCl_3$ (Scheme 2.11). However it retains its enantiopurity if it is added into another reaction after 24 hours. This result suggests that $BF_3 \cdot Et_2O$ is probably consumed

during the course of the reaction and hence it failed to epimerize **2-87**. After these systematic epimerization experiments and NMR study, I hypothesize that BF_3 undergoes disproportionation with BF_3OMe^- to form BF_4^- and BF_2OMe in the process of generating the oxocarbenium ion (Scheme 2.12). The formation of BF_4^- was observed by ^{19}F NMR and by Electrospray Negative Mode Mass Spectrometry in the reaction of ketal **2-47** with BF_3 (2.0 equiv). Similar disproportionation of anionic BF_3OR^- species with neutral BF_3 has been reported in the literature.[52] The oxocarbenium ion (**2-104**) was quantitatively formed in reaction of ketal **2-47** with 2.0 equivalents of $BF_3{\cdot}Et_2O$ and was observed by ^1H, ^{13}C and mass spectrometry. Howeevr only 55% of oxocarbenium (**2-104**) was observed with 1.0 equivalent of $BF_3{\cdot}Et_2O$ and ketal **2-47,** suggesting that two equivalents of Lewis acid are required for complete ionization of the ketal.

Scheme 2.11: Epimerization Studies



Scheme 2.12: Proposed Disproportionation

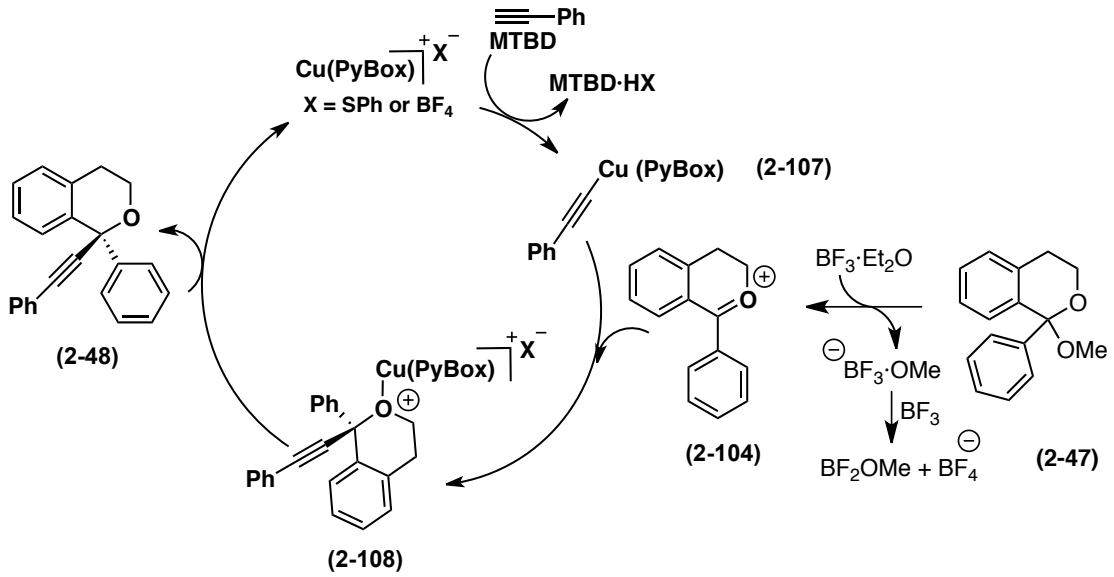


These experiments explain why electron-rich products are formed in low or variable enantioselectivities. Although BF_2OMe is not Lewis acidic enough to epimerize the majority of our products, it is likely acidic enough to ionize the most electron-rich compounds. The consumption of two equivalents of BF_3 for complete ionization of the ketal also explains why our reaction requires two equivalents of Lewis acid for high reactivity.

Proposed Mechanism

My working mechanistic hypothesis is shown in Scheme 2.13. The reaction likely proceeds via initial formation of copper acetylide (**2-107**), which then attacks the oxocarbenium ion intermediate (**2-104**) generated from ketal **(2-47)** in the presence of two equivalents of Lewis acid, $BF_3{\cdot}Et_2O$**.** We are also intrigued by several observations made during our optimization studies: (1) why are two equivalents of BF_3 required? (2) why does base affect the enantioselectivity? (3) what is the origin for enantioselectivity? Further investigation is needed to fully answer these questions, but our preliminary experiments are described below.

Scheme 2.13: Proposed Mechanism



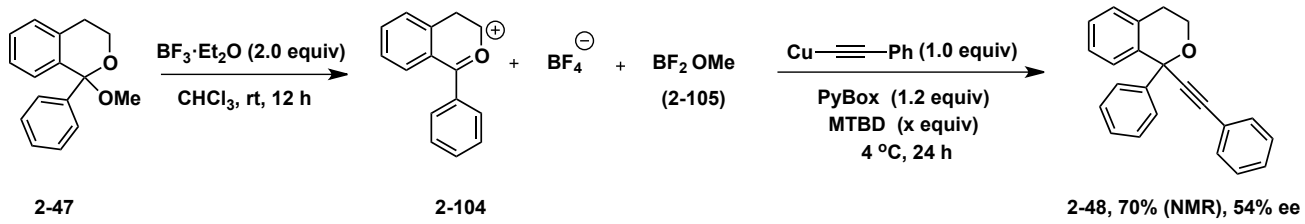
Role of Base in Imparting Enantioselectivity

As shown in Table 2.3, base has a significant influence on the enantioselectivity, despite its absence from our proposed C-C bond-forming step. We envision three possibilities to explain this: (1) base prevents epimerization of the products, (2) base coordinates oxocarbenium ion (**2-104**) and (3) base ligates Cu. To begin to answer these questions, I studied the reaction of oxocarbenium ion **2-104** with various species likely present under the catalytic reaction conditions. As discussed above, addition of two equivalents of $BF_3 \cdot Et_2O$ to ketal **2-47** results in quantitative formation of oxocarbenium (**2-104**), as observed by ^1H and ^{13}C NMR spectroscopy. I observed that on adding stoichiometric Copper acetylide and Ph-PyBox ligand to a solution of oxocarbenium (**2-104**) in $CHCl_3$, the desired product is formed in 70% yield (NMR) and 54% ee (Table 2.3, entry 1). However, on adding one quivalent of

base along with the copper acetylide and Ph-PyBox ligand, the enantioselctivity of the product increases to 69% (Table 2.3, entry 2). I then conducted another experiment wherein I added excess base, MTBD to see if the enantioselectivity increases further. However, five equivalents of MTBD completely shuts down the reaction leading to unidentified by-products (Table 2.3, entry 3). Notably the ee's of the stoichiometric reactions do not match that of the catalytic reaction (78% ee). I also observed that when MTBD (1.0 equiv) is added to the reaction of ketal (**2-47)** and $BF_3 \cdot Et_2O$ (2.0 equiv), oxocarbenium ion (**2-104**) is not observed (Scheme 2.14). By ^{13}C NMR, the product formed here has no signal at 201.29 ppm, corresponding to the oxocarbenium ion (**2-104**), but a peak at 66 ppm, corresponding to an aminal is seen suggesting MTBD coordinates to the oxocarbenium (**2-104**). By ^{1}H NMR, the protons of the ketal, MTBD are also shifted and do not correspond to free ketal, oxocarbenium species or free MTBD respectively. The proton NMR peaks observed here do not match that of MTBD coordinated to free $BF_3 \cdot Et_2O$ either. (In a separate experiment, between MTBD and $BF_3 \cdot Et_2O$, I have observed that MTBD coordinates to my Lewis acid by ^{1}H and ^{19}F NMR.) I also observe the BF_4^- counter anion here (Scheme 2.14) at a chemical shift different than that of the oxocarbenium species (**2-104**). These experiments indicate that MTBD can coordinate to the oxocarbenium ion during the course of the reaction. Given that excess base shuts down the alkynylation, it seems likely that the alkynylation proceeds through the oxocarbenium ion. An aminal species may form reversibly in a reservoir off the catalytic cycle. From these experiments, we cannot assertively conclude the role of base in imparting enantioselectivity. However,

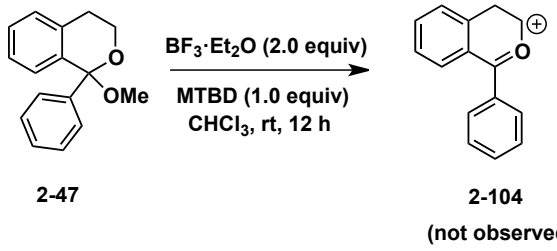
I have determined a potentially important equilibrium occurring under the reaction conditions. Further experiments need to be conducted to conclusively figure out its role in affecting enantioselectivity.

Table 2-3: Role of Base in Imparting Enantioselectivity



Entry	Equiv of MTBD	Yield (%)	ee (%)
1.	0	70	54
2.	1.0	60	69
3.	5.0	0	n.d.

Scheme 2.14: Role of Base in Imparting Enantioselectivity



Active Catalyst Elucidation of Copper Ph-PyBox Complex

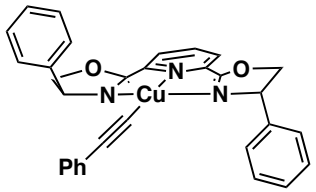
We are currently investigating how the copper/Ph-PyBox catalyst imparts enantioselectivity in this reaction. The enantiodetermining step is likely the C–C bond formation (Scheme 2.13). To understand this step, we must determine the structure of

copper acetylide (**2-107**). Although Ph-PyBox ligands often enforce a square planar geometry on a M–X fragment, four-coordinated square planar copper(I) complexes are improbable due to steric crowding, and a structure like **2-109** is likely not the active complex in this case (Figure 2.3). We considered that Ph-PyBox may act instead as a bidentate ligand, with either the pyridine or one oxazoline arm dissociating, but models for these types of coordination geometries resulted in much lower enantioselectivities (Figure 2.3, **2-110**: 4% ee; **2-111**: 28% ee).[53,54]

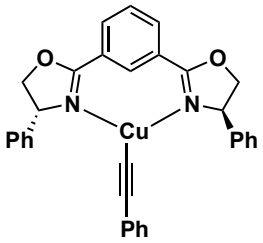
Another possibility is a dimeric (or other higher order) copper/Ph-PyBox catalyst. Dinuclear copper catalysts have been proposed to proceed via dicopper acetylide intermediates in related reactions.[55-59] Cu_2(Ph-PyBox)$_2$(X)$_2$ complexes have been previously reported,[55,60,61] and I synthesized Cu_2(Ph-PyBox)$_2$(PF_6)$_2$ (**2-112**) and Cu(Ph-PyBox)$_2$$PF_6$ (**2-113**) complexes in 48% and 22% yields respectively (Scheme 2.15). On testing these complexes under our reaction conditions, I observed Cu_2(Ph-Ph-PyBox)$_2$(PF_6)$_2$ (**2-112**) gave our usual enantioselectivity, but only when 20 mol % more Ph-PyBox ligand was added (Table 2.4, entry 2). Complex Cu(Ph-PyBox)$_2$$PF_6$ (**2-113**) however gave the yield and enantioselectivity we usually observe insitu under our normal reaction conditions (Table 2.4. entry 3). Attempts to crystallize complex Cu(Ph-PyBox)$_2$$PF_6$ (**2-113**) repeatedly gave the higher order complex of Cu_2(Ph-PyBox)$_3$(PF_6)$_2$·H_2O (Figure 2.4). There is no crystal structure reported in literature for complex Cu(Ph-PyBox)$_2$$PF_6$ (**2-113**) but it is mentioned that attempts to crystallize it always resulted in Cu_2(Ph-PyBox)$_2$(PF_6)$_2$ (**2-112**).[60,61] This suggests that in solution there could be an aggregate of various higher order copper Ph-PyBox complex.

Consistent with the presence of higher order copper/Ph-PyBox species, a positive nonlinear correlation is observed between the ee of Ph-PyBox and ee of product (Fig. 2.5).[62] Although this data does not exclude the possibility that these higher order copper species may exist in an off-cycle reservoir, we currently favor a dicopper acetylide intermediate, given their importance in other copper acetylide chemistry. Due to the multiple possible catalyst structures, we cannot yet propose a detailed rationale for the observed stereochemistry. However, we hypothesize that the role of the phenyl substituents on (*R*)-Ph-PyBox is largely steric in nature, because (*R*)-*t*-Bu-PyBox results in the same major enantiomer (Table 2.2).

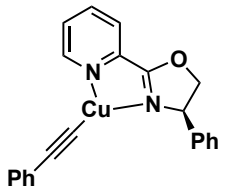
Figure 2.3 : Possible Active Catalyst Structures



(2-109)



(2-110)



(2-111)

Scheme 2.15: Synthesis of Copper Ph-PyBox Complexes

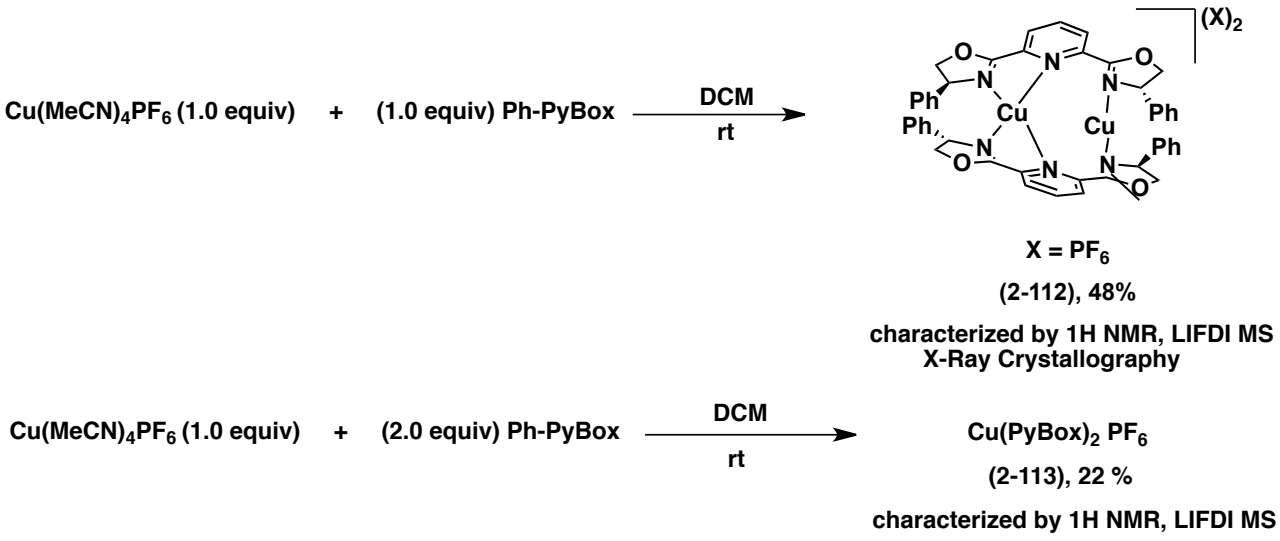
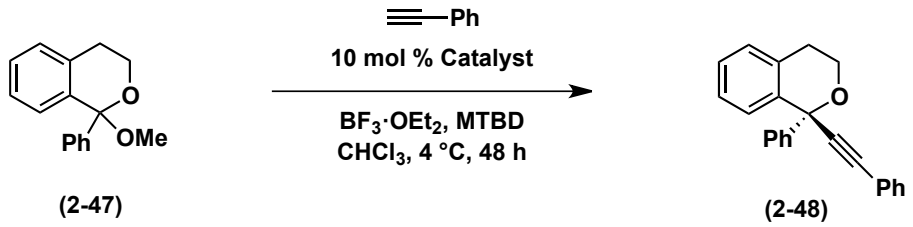


Table 2-4: Reactivity of Copper Ph-PyBox Complexes



Catalyst (10 mol%)	Ligand (20 mol%)	Yield %(NMR)	ee (%)
$Cu_2(Ph\text{-}PyBox)_2(PF_6)_2$		100	66
$Cu_2(Ph\text{-}PyBox)_2(PF_6)_2$	Ph-PyBox	77	78
$Cu(Ph\text{-}PyBox)_2PF_6$		100	80

Figure 2.4 : Crystal Structure of $Cu_2(Ph\text{-}PyBox)_3(PF_6)_2 \cdot H_2O$. Molecular diagram of Figure 2.5 with ellipsoids at 30% probability. H-atoms omitted for clarity.

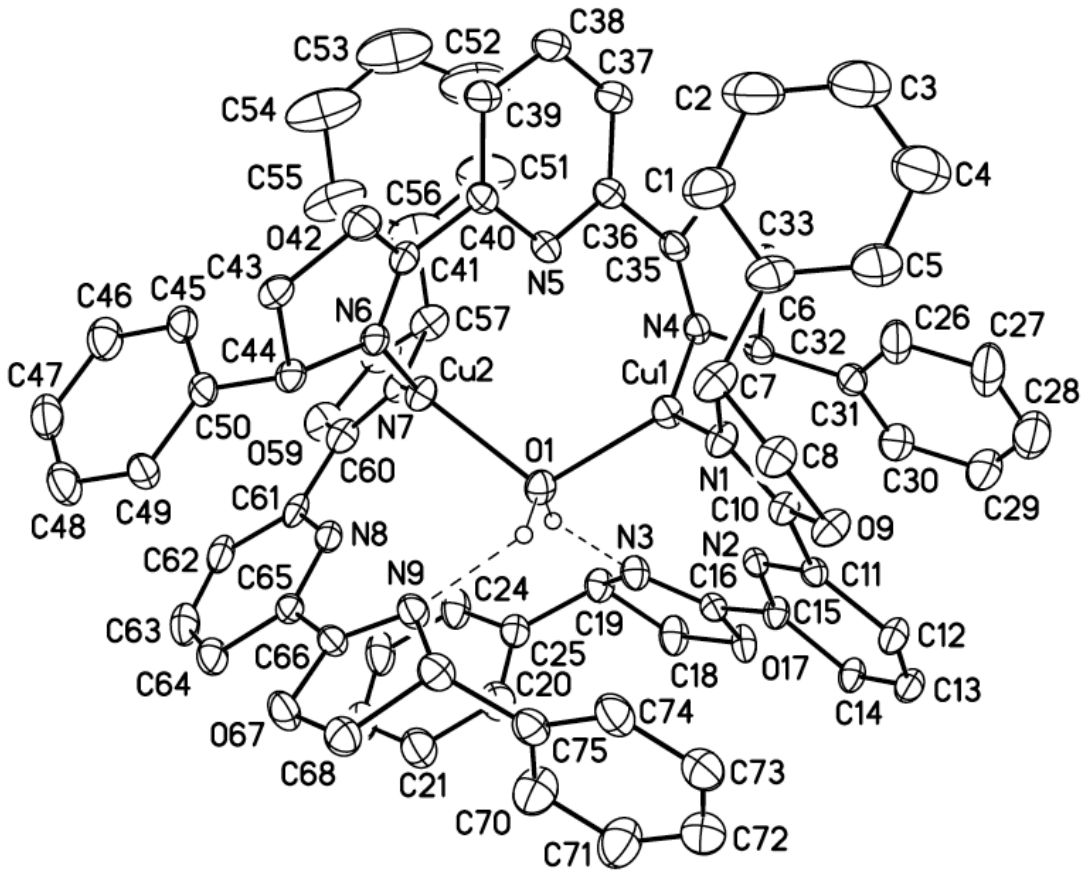
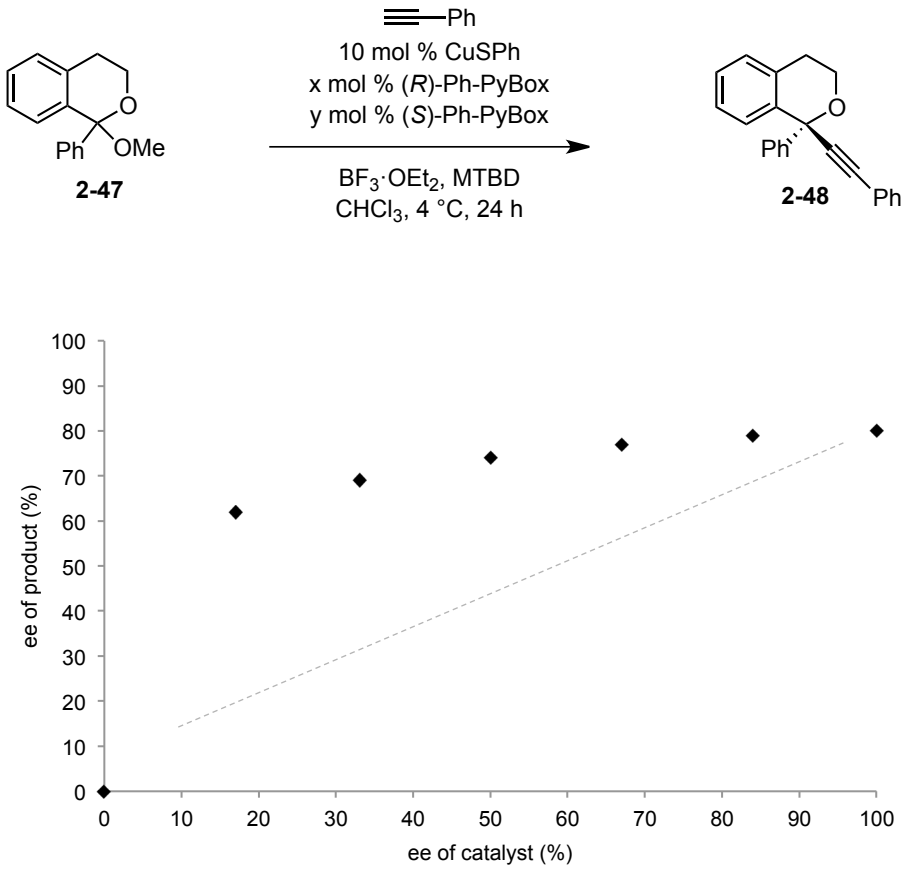


Figure 2.5 : Positive Nonlinear Effect

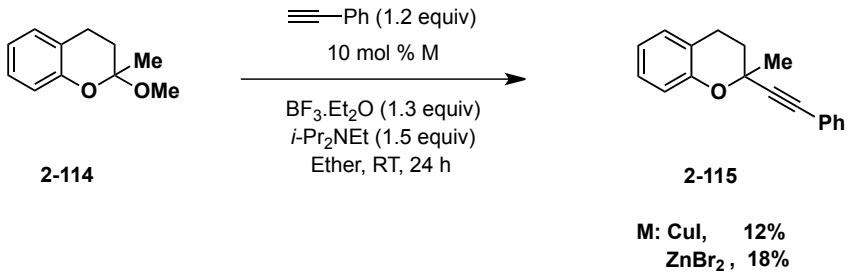


2.4 Tetrasubstituted Stereocenters on Chromene Ketals

Alkynylation of 2-methoxy-2-methylchroman

I have also investigated alkynylation of chroman ketals. The preparation of ketal **2-114** was achieved in quantitative yield by cyclization of 4-(2-hydroxyphenyl) butan-2-one under catalytic amount of acid in methanol. After subjecting ketal **2-114** to phenyl acetylene with various copper and zinc salts and Lewis acids like TMSOTf and $BF_3.Et_2O$, alkynylation was observed to give the desired product in low yields (Scheme 2.16). Investigation of other bases, solvents and varying parameters like temperature and equivalents of reagents, did not improve the yield. A variety of commercially available chiral ligands have also been tested under the current conditions, but no enantioselectivity was observed. We hypothesize three factors leading to less reactivity here: a). the oxocarbenium generated is not very stabilized here making it difficult to form b). there could be prominent steric hindrance at the oxocarbenium due to the methyl group and c). this oxocarbenium ion can undergo elimination reactions. To overcome these challenges, we modified the design of our substrate and continued working on more stable chromene ketals like **2-111** (Scheme 2.16).

Scheme 2.16: Alkynylation of 2-methoxy-2-methylchroman



2-114 **2-115**

M: CuI, 12%
$ZnBr_2$, 18%

2.5 Summary

In summary, I have developed the first example of an enantioselective addition of alkynes to a cyclic oxocarbenium ion to set $\alpha,\alpha-diaryl$ tetrasubstituted stereocenters. The success of this reaction relied on identification of a Cu/Ph-PyBox catalyst, along with $CHCl_3$ as solvent, $BF_3{\cdot}OEt_2$ as Lewis acid, and MTBD as base. Under the optimized conditions, a variety of ketals and alkynes underwent the reaction in good to excellent yields and enantioselectivites. We have recently published this work in *Angewandte Chemie Internationl Edition*, ASAP.

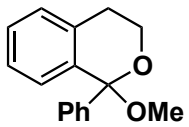
2.6 Experimental Procedures

General Information

Reactions were performed either in a N_2-atmosphere glovebox in oven-dried 1-dram vials with Teflon-lined caps or in oven-dried round-bottomed flasks unless otherwise noted. Flasks were fitted with rubber septa, and reactions were conducted under a positive pressure of N_2. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed on silica gel 60 (40-63μm, 60Å). Thin layer chromatography (TLC) was performed on glass plates coated with silica gel 60 with F254 indicator. Commercial reagents were purchased from Sigma Aldrich, Acros, Fisher, Strem, or Cambridge Isotopes Laboratories and used as received with the following exceptions: tetrahydrofuran, CH_2Cl_2, and Et_2O were dried by passing through drying columns.[63] MeOH was

distilled from CaH_2. $CHCl_3$, MTBD, and $BF_3 \cdot OEt_2$ were purchased in sure-seal bottles, immediately transferred to a N_2-atmosphere glovebox upon receipt, and used as such. $CDCl_3$ was stored over oven-dried potassium carbonate. Alkynes were degassed before use by either freeze-pump-thaw cycles or sparging with N_2. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on 400 MHz spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$ = δ 77.07). Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), integration. Infrared (IR) spectra were obtained using FTIR spectrophotometers with material loaded onto a NaCl plate. The mass spectral data were obtained at the University of Delaware spectrometry facility. Optical rotations were measured using a 2.5 mL cell with a 0.1 dm path length. Isochromanone,[64] 6-methylisochromanone,[65] and 7-methylisochromanone[66] were prepared as described in the literature. 3-(Cyano)phenylacetylene[66] and methyl 3-ethynylbenzoate[67] were prepared as described in the literature.

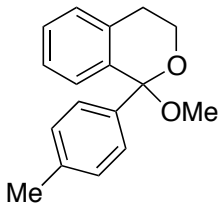
General Procedure 1: Preparation of 1-Methoxy-1-phenylisochroman (2-48).



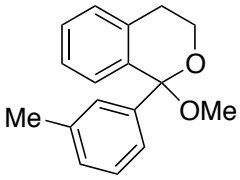
A solution of isochroman-1-one (2.29 g, 15.5 mmol, 1.0 equiv) and THF (30 mL) was cooled to –78 °C. PhLi (2.0 M in dibutyl ether, 9.3 mL, 18.6 mmol, 1.2 equiv) was added dropwise, and the reaction was stirred at –78 °C for 5 h. H_2O (40 mL) was then added, and the mixture was warmed to room temperature. CH_2Cl_2 (40 mL) was added. The aqueous layer was separated and extracted with CH_2Cl_2 (30 mL x 2). The combined organic layers were washed with sat. NaCl (30 mL), dried (Na_2SO_4), filtered and concentrated. The resulting pale yellow oil was purified by silica gel chromatography (20% EtOAc/hexanes) to give hemiketal **2-31** as an oil, which was directly used in the next step.

MeOH (20 mL) and *p*-TsOH (147.4 mg, 0.78 mmol, 0.05 equiv) were added to hemiketal **2-31**. The mixture was then stirred at room temperature for 12 h. K_2CO_3 (1.06 g, 7.7 mmol, 0.5 equiv) was added, and the mixture was concentrated. CH_2Cl_2 (40 mL) was added to the resulting solid, and the mixture was filtered through a short bed of Celite. The filtrate was then concentrated. The crude material was then purified by silica gel chromatography (5% Et_2O/hexanes with 2% Et_3N) to give compound **2-48** (3.01g, 81%) as a white solid (mp 55–59 °C): ^{1}H NMR (400 MHz, C_6D_6) δ 7.71 (d, J = 7.1 Hz, 2H), 7.37 – 7.35 (m, 1H), 7.20 – 7.18 (m, 2H), 7.09 – 7.06 (m, 1H), 6.96 – 6.88 (m, 2H), 6.84 – 6.82 (m, 1H), 3.96 (dt, J = 11.01, 3.48 Hz, 1H), 3.78 – 3.73 (m, 1H), 3.26 (s, 3H), 2.86 – 2.77 (m, 1H), 2.27 (dt, J = 16.11, 3.11 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.8, 137.5, 133.3, 128.5, 128.3, 128.1, 127.9, 127.5, 127.1,

126.6, 100.7, 59.6, 50.3, 28.6; FTIR (NaCl, thin film) 1489, 1448, 1205, 1120, 1052, 1007, 764, 703 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{16}H_{16}O_2$: 240.1, found: 240.1.

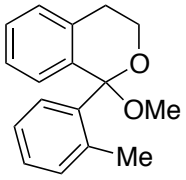


1-Methoxy-1-(*p*-tolyl)isochroman (2-32). Prepared via General Procedure 1 on a 1.4-mmol scale. The crude product was purified by silica gel chromatography (5% Et_2O/hexanes with 2% Et_3N) to give compound **2-32** (0.166 g, 47%) as a white solid (mp 81–84 °C): ^1H NMR (400 MHz, C_6D_6) δ 7.67 (d, J = 8.1 Hz, 2H), 7.46 – 7.37 (m, 1H), 7.03 (d, J = 7.9 Hz, 2H), 6.99 – 6.90 (m, 2H), 6.89 – 6.81 (m, 1H), 4.03 – 3.97 (m, 1H), 3.82 – 3.77 (m, 1H), 3.31 (s, 3H), 2.89 – 2.81 (m, 1H), 2.33 – 2.28 (m, Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (101 MHz, C_6D_6) δ 140.1, 138.7, 137.5, 133.9, 129.14, 129.05 128.6, 127.8, 127.5, 126.5, 101.2, 59.6, 50.0, 28.9, 21.1; FTIR (NaCl, thin film) 2937, 2361, 1518, 1480, 1452, 1179, 1052, 1009 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{17}H_{18}O_2$: 254.1, found: 254.1.

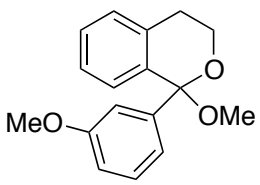


1-Methoxy-1-(*m*-tolyl)isochroman (2-33). Prepared via General Procedure 1 on a 2.0-mmol scale. The crude product was purified by silica gel chromatography (5% Et_2O/hexanes with 2% Et_3N) to give compound **2-33** (0.337 g, 66%) as colorless oil: ^1H NMR (400 MHz, C_6D_6) δ 7.65 (s, 1H), 7.58 (d, J = 7.8 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.15 (d, J = 4.1 Hz, 1H), 6.95 – 6.93 (m, 3H), 6.88 – 6.83 (m, 1H), 4.05 – 3.95 (m, 1H), 3.84 – 3.77 (m, 1H), 3.31 (s, 3H), 2.92 – 2.81 (m, 1H), 2.33 – 2.25 (m, 1H), 2.11 (s, 3H); ^{13}C NMR (101 MHz, C_6D_6) δ 142.5, 138.2, 137.6, 133.5, 128.7, 128.5, 128.3, 128.2, 127.6, 127.1, 126.2, 124.6, 100.9, 59.2, 49.7, 28.5, 21.2; FTIR (NaCl, thin film) 2937, 1268, 1229,

1169, 1120 1084, 1053 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{17}H_{18}O_2$: 254.1, found: 254.1.

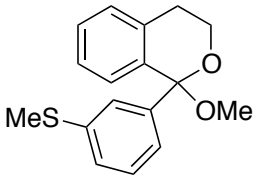


1-Methoxy-1-(*o*-tolyl)isochroman (2-34). Prepared via General Procedure 1 on a 2.0-mmol scale. The crude product was purified by silica gel chromatography (5% Et_2O/hexanes with 2% Et_3N) to give compound **2-34** (0.292 g, 57%) as colorless oil: ^1H NMR (400 MHz, C_6D_6) δ 7.73 (dd, J = 7.7, 1.5 Hz, 1H), 7.18 (s, 1H), 7.14 – 7.08 (m, 2H) 7.04 (d, J = 7.2 Hz, 1H), 7.02 – 6.92 (m, 1H), 6.90 – 6.83 (m, 2H), 3.99 – 3.90 (m, 1H), 3.74 – 3.67 (m, 1H), 3.30 (s, 3H), 2.90 – 2.79 (m, 1H), 2.33 (s, 3H), 2.31 – 2.24 (m, 1H); ^{13}C NMR (101 MHz, $C(O)(CD_3)_2$) δ 140.2, 138.4, 138.0, 134.7, 133.1, 128.93, 128.91, 128.7, 128.3, 128.2, 126.8, 125.8, 102.1, 60.1, 50.3, 28.4, 21.5; FTIR (NaCl, thin film) 2937, 1486, 1453, 1287, 1202 1119, 1068 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{17}H_{18}O_2$: 254.1, found: 254.1.

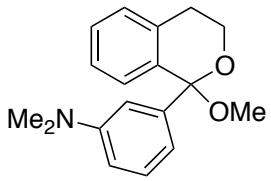


1-Methoxy-1-(3-methoxyphenyl)isochroman (2-35). Prepared via General Procedure 1 on a 11.5-mmol scale. The crude product was purified by silica gel chromatography (10% Et_2O/hexanes with 2% Et_3N) to give compound **2-35** (1.9 g, 61%) as a white solid (mp 70–73 °C): ^1H NMR (400 MHz, C_6D_6) δ 7.55 – 7.42 (m, 2H), 7.36 (d, 1H), 7.14 (d, J = 7.9 Hz, 1H), 7.02 – 6.88 (m, 2H), 6.89 – 6.82 (m, 1H), 6.74 – 6.72 (m, 1H), 4.01 – 3.94 (m, 1H), 3.80 – 3.76 (m, 1H), 3.30 (s, 3H), 3.29 (s, 3H), 2.93 – 2.71 (m, 1H), 2.30 – 2.25 (m, 1H); ^{13}C NMR (101 MHz, C_6D_6) δ 160.4, 144.6, 138.3, 133.9, 129.3, 128.9, 128.6, 127.5, 126.6, 120.2, 113.7, 113.6, 101.1, 59.6, 54.7, 50.1, 28.8; FTIR

(NaCl, thin film) 2937, 2830, 1599, 1486, 1452, 1268, 1072, 1051 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{17}H_{18}O_3$: 270.1, found: 270.1.

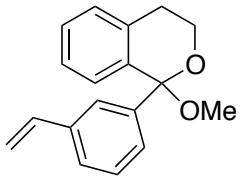


1-Methoxy-1-(3-(methylthio)phenyl)isochroman (2-36). Prepared via General Procedure 1 on a 1.7-mmol scale. The crude product was purified by silica gel chromatography (10% Et_2O/hexanes with 2% Et_3N) to give compound **2-30** (0.326 g, 68%) as a white solid (mp 73–76 °C): ^1H NMR (400 MHz, C_6D_6) δ 7.86 (s, 1H), 7.49 – 7.44 (m, 1H), 7.42 – 7.37 (m, 1H), 7.09 – 7.01 (m, 2H), 6.97 – 6.87 (m, 2H), 6.82 (d, J = 7.3 Hz, 1H), 3.94 – 3.91 (m, 1H), 3.76 – 3.72 (m, 1H), 3.25 (s, 3H), 2.85 – 2.71 (m, 1H), 2.28 – 2.22 (m, 1H), 1.97 (s, 3H); ^{13}C NMR (101 MHz, C_6D_6) δ 143.7, 139.4, 138.1, 133.9, 128.90, 128.87, 128.7, 127.6, 126.7, 126.2, 125.9, 124.5, 101.0, 59.7, 50.1, 28.8, 15.4; FTIR (NaCl, thin film) 2937, 2827, 1589, 1453, 1259, 1205, 1106 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{17}H_{18}O_2S$: 286.1, found: 286.1.

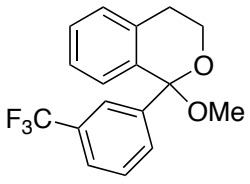


3-(1-Methoxyisochroman-1-yl)-*N*,*N*-dimethylaniline (2-37). Prepared via General Procedure 1 on a 2.7-mmol scale. The crude product was purified by silica gel chromatography (10% Et_2O/hexanes with 2% Et_3N) to give compound **2-37** (0.541 g, 71%) as a white solid (mp 89–93 °C): ^1H NMR (400 MHz, C_6D_6) δ 7.64 – 7.57 (m, 1H), 7.31 – 7.30 (m, 1H), 7.25 (d, J = 5.05 Hz, 2H), 6.99 – 6.92 (m, 2H), 6.90 – 6.84 (m, 1H), 6.57 (m, 1H), 4.08 – 4.02 (m, 1H), 3.88 – 3.83 (m, 1H), 3.38 (s, 3H), 2.95 – 2.87 (m, 1H), 2.52 (s, 6H), 2.35 – 2.29 (m, 1H); ^{13}C NMR (101 MHz, C_6D_6) δ 151.1, 143.5, 138.9, 133.9,

129.0, 128.7, 128.6, 127.5, 126.5, 116.5, 112.6, 112.2, 101.6, 59.6, 50.2, 40.3, 28.9; FTIR (NaCl, thin film) 3418, 2880, 2807, 1660, 1599, 1573, 1496, 1435 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{18}H_{21}NO_2$: 283.2, found: 283.2.

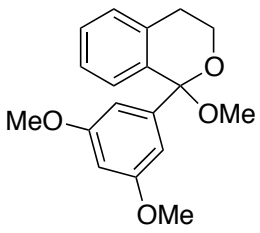


1-Methoxy-1-(3-vinylphenyl)isochroman (2-38). Prepared via General Procedure 1 on a 2.0-mmol scale. The crude product was purified by silica gel chromatography (5% Et_2O/hexanes with 2% Et_3N) to give compound **2-38** (0.224 g, 42%) as a white solid (mp 44–48 °C): ^1H NMR (400 MHz, C_6D_6) δ 7.92 (s, 1H), 7.61 (dt, *J* = 7.9, 1.3 Hz, 1H), 7.39 (dd, *J* = 7.36, 1.10 Hz, 1H), 7.20 - 7.11 (m, 2H), 6.96 – 6.89 (m, 2H), 6.84 – 6.82 (m, 1H), 6.60 (dd, *J* = 17.47, 6.68 Hz, 1H), 5.95 (dt, *J* = 10.89, 3.44 Hz, 1H), 5.63 (dd, *J* = 17.58, 0.68 Hz, 1H), 5.04 (dd, *J* = 10.86, 0.55 Hz, 1H), 3.79 – 3.74 (m, 1H), 3.26 (s, 3H), 2.86 – 2.78 (m, 1H), 2.27 (dt, *J* = 16.27, 3.13 Hz, 1H); ^{13}C NMR (101 MHz, C_6D_6) δ 142.9, 137.9, 137.7, 137.1, 133.6, 128.6, 128.32, 128.29 127.6, 127.2, 127.1, 126.3, 125.6, 113.6, 100.8, 59.25, 49.69, 28.5; FTIR (NaCl, thin film) 2938, 2884, 1665, 1489, 1453, 1286, 1167, 1093 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{18}H_{18}O_2$: 266.1, found: 266.1.

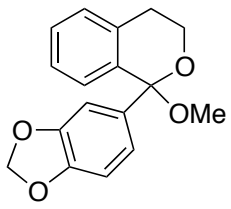


1-Methoxy-1-(3-(trifluoromethyl)phenyl)isochroman (2-39). Prepared General Procedure 1 on a 2.0-mmol scale. The crude product was purified by silica gel chromatography (5% Et_2O/hexanes with 2% Et_3N) to give compound **2-39** (0.341 g, 55%) as a white solid (mp 56–60 °C): ^1H NMR (400 MHz, C_6D_6) δ 8.20 (s, 1H), 7.66 (d, *J* = 7.9 Hz, 1H),

7.28 (d, J = 7.8 Hz, 1H), 7.23 – 7.21 (m, 1H), 7.00 – 6.82 (m, 3H), 6.78 (d, J = 7.1 Hz, 1H), 3.87 – 3.81 (m, 1H), 3.69 – 3.64 (m, 1H), 3.12 (s, 3H), 2.75 – 2.66 (m, 1H), 2.21 – 2.16 (m, 1H); ^{13}C NMR (101 MHz, C_6D_6) δ 143.9, 136.9, 133.6, 130.7, 130.5 (q, $J_{C\text{-}F}$ = 32.9 Hz), 128.6, 128.4, 128.3, 127.0, 126.4, 124.7 (q, $J_{C\text{-}F}$ = 272.5 Hz), 124.6 (q, $J_{C\text{-}F}$ = 3.7 Hz), 124.1 (q, $J_{C\text{-}F}$ = 3.9 Hz), 100.2, 59.4, 49.6, 28.3; FTIR (NaCl, thin film) 2940, 1489, 1439, 1332, 1200, 1197, 1165 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{17}H_{15}O_2F_3$: 308.1, found: 308.1.

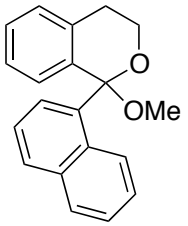


1-(3,5-Dimethoxyphenyl)-1-methoxyisochroman (2-40). Prepared via General Procedure 1 on a 2.9-mmol scale. The crude product was purified by silica gel chromatography (10% Et_2O/hexanes with 2% Et_3N) to give compound **2-40** (0.358 g, 42%) as a white solid (mp 115–118 °C): ^{1}H NMR (400 MHz, C_6D_6) δ 7.58 – 7.56 (m, 1H), 7.14 (d, J = 2.3 Hz, 2H), 6.98 – 6.92 (m, 2H), 6.86 – 6.84 (m, 1H), 6.53 (t, J = 2.3 Hz, 1H), 4.00 – 3.96 (m, 1H), 3.83 – 3.78 (m, 1H), 3.33 (s, 3H), 3.31 (s, 6H), 2.88 – 2.81 (m, 1H), 2.31 – 2.25 (m, 1H); ^{13}C NMR (101 MHz, C_6D_6) δ 161.5, 145.3, 138.3, 133.9, 128.8, 128.6, 127.6, 126.6, 106.2, 101.3, 100.3, 59.6, 54.8, 50.2, 28.8; FTIR (NaCl, thin film) 2938, 2834, 1596, 1457, 1425, 1321, 1293, 1204 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{18}H_{20}O_4$: 300.1, found: 300.1.

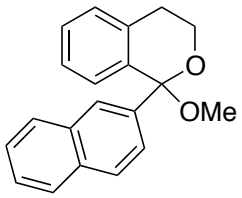


1-(Benzo[*d*][1,3]dioxol-5-yl)-1-methoxyisochroman (2-41). Prepared via General Procedure 1 on a 2.1-mmol scale. The crude product was purified by silica gel chromatography (5%

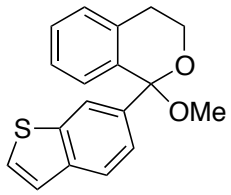
Et_2O/hexanes with 2% Et_3N) to give compound **2-41** (0.204 g, 35%) as a white solid (mp 82–86 °C): ^{1}H NMR (400 MHz, C_6D_6) δ 7.41 – 7.38 (m, 1H), 7.36 (d, *J* = 1.8 Hz, 1H), 7.15 – 7.10 (m, 1H), 7.00 – 6.94 (m, 2H), 6.84 – 6.82 (m, 1H), 6.66 (d, *J* = 8.1 Hz, 1H), 5.27 (d, *J* = 1.28 Hz, 1H), 5.25 (d, *J* = 1.28 Hz, 1H), 3.95 – 3.89 (m, 1H), 3.76 – 3.71 (m, 1H), 3.26 (s, 3H), 2.79 – 2.71 (m, 1H), 2.28 – 2.22 (m, 1H); ^{13}C NMR (101 MHz, C_6D_6) δ 148.4, 147.8, 138.5, 137.2, 133.9, 128.9, 128.6, 127.5, 126.6, 121.2, 108.6, 107.9, 101.1, 101.0, 59.7, 49.9, 28.8; FTIR (NaCl, thin film) 2938, 2834, 1596, 1457, 1425, 1204, 1153 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{17}H_{16}O_4$: 284.1, found: 284.1.



1-Methoxy-1-(naphthalen-1-yl)isochroman (2-42). Prepared via General Procedure 1 on a 2.0-mmol scale. The crude product was purified by silica gel chromatography (5% Et_2O/hexanes with 2% Et_3N) to give compound **2-42** (0.369 g, 63%) as a white solid (mp 91–94 °C): ^{1}H NMR (400 MHz, C_6D_6) δ 9.00 (d, *J* = 8.64, 1.3 Hz, 1H), 7.70 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.36 – 7.27 (m, 2H), 7.26 – 7.18 (m, 2H), 6.97 – 6.95 (m, 1H), 6.89 (d, *J* = 7.1, 1.4 Hz, 1H), 6.85 – 6.81 (m, 1H), 3.99 – 3.95 (m, 1H), 3.76 – 3.71 (m, 1H), 3.36 (s, 3H), 2.89 – 2.77 (m, 1H), 2.52 – 2.46 (m, 1H); ^{13}C NMR (101 MHz, $C(O)(CD_3)_2$) δ 138.5, 137.7, 135.8, 134.5, 132.2, 130.2, 129.4, 129.2, 128.5, 128.4, 128.0, 126.9, 126.8, 126.1, 126.0, 125.2, 103.0, 60.5, 50.6, 28.5; FTIR (NaCl, thin film) 3050, 2938, 2885, 2829, 1408, 1452, 1241, 1174 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{20}H_{18}O_2$: 290.1, found: 290.1.

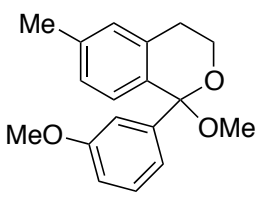


1-Methoxy-1-(naphthalen-2-yl)isochroman (2-43). Prepared via General Procedure 1 on a 2.0-mmol scale. The crude product was purified by silica gel chromatography (5% Et_2O/hexanes with 2% Et_3N) to give compound **2-43** (0.362 g, 62%) as a white solid (mp 113–116 °C): ^{1}H NMR (400 MHz, C_6D_6) δ 8.22 (s, 1H), 7.91 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 2H), 7.63 – 7.57 (m, 1H), 7.47 – 7.45 (m, 1H), 7.28 – 7.19 (m, 2H), 7.01 – 6.90 (m, 2H), 6.87 (d, *J* = 7.2 Hz, 1H), 4.05 – 3.99 (m, 1H), 3.85 – 3.80 (m, 1H), 3.34 (s, 3H), 2.93 – 2.82 (m, 1H), 2.37 – 2.31 (m, 1H); ^{13}C NMR (101 MHz, C_6D_6) δ 140.1, 137.9, 133.8, 133.31, 133.28, 128.8, 128.5, 128.3, 128.0, 127.6, 127.3, 126.6, 126.3, 126.0, 125.9, 125.6, 101.0, 59.4, 49.8, 28.5; FTIR (NaCl, thin film) 3058, 2937, 2884, 2828, 1489, 1452, 1177 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{20}H_{18}O_2$: 290.1, found: 290.1.

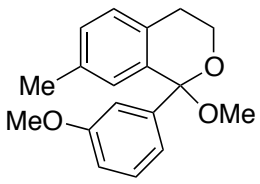


1-(Benzo[*b*]thiophen-6-yl)-1-methoxyisochroman (2-44). Prepared via General Procedure 1 on a 1.7-mmol scale. The crude product was purified by silica gel chromatography (10% Et_2O/hexanes with 2% Et_3N) to give compound **2-44** (0.314 g, 63%) as a white solid (mp 82–86 °C): ^{1}H NMR (400 MHz, C_6D_6) δ 8.37 (s, 1H), 7.89 – 7.87 (m, 1H), 7.69 (d, *J* = 8.26 Hz, 1H), 7.51 (d, *J* = 8.26 Hz, 1H), 7.08 – 7.01 (m, 4H), 6.97 (d, *J* = 7.34 Hz, 1H), 4.12 – 4.08 (m, 1H), 3.92 – 3.89 (m, 1H), 3.39 (s, 3H), 2.91 – 2.92 (m, 1H), 2.44 – 2.41 (m, 1H); ^{13}C NMR (101 MHz, C_6D_6) δ 140.8, 140.2, 140.0, 138.9, 134.4, 129.6, 129.2, 128.1, 127.6, 127.2, 124.9, 124.3, 124.1, 122.3, 101.9, 60.3, 50.6, 29.4;

FTIR (NaCl, thin film) 3629, 2186, 1198, 1071, 1052, 1009, 967, 825 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{18}H_{16}O_2S$: 296.1, found: 296.1.



1-Methoxy-1-(3-methoxyphenyl)-6-methylisochroman (2-45). Prepared via General Procedure 1 on a 1.7-mmol scale. The crude product was purified by silica gel chromatography (5% Et_2O/hexanes with 2% Et_3N) to give compound **2-45** (0.189 g, 39%) as colorless oil: ^1H NMR (400 MHz, C_6D_6) δ 7.65 – 7.64 (m, 1H), 7.51 (d, J = 8.25 Hz, 2H), 7.25 (s, 1H), 6.89 – 6.85 (m, 2H), 6.77 (s, 1H), 4.17 – 4.10 (m, 1H), 3.97 – 3.92 (m, 1H), 3.45 (s, 3H), 3.42 (s, 3H), 2.99 – 2.91 (m, 1H), 2.45 – 2.40 (m, 1H), 2.15 (s, 3H); ^{13}C NMR (101 MHz, C_6D_6) δ 160.4, 144.9, 136.9, 135.6, 133.8, 129.3, 129.1, 128.9, 127.5, 120.8, 113.7, 113.6, 101.3, 59.7, 54.7, 50.2, 28.9, 20.9; FTIR (NaCl, thin film) 2938, 1601, 1484, 1430, 1287, 1237, 1134 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{18}H_{20}O_3$: 284.1, found: 284.1.



1-Methoxy-1-(3-methoxyphenyl)-7-methylisochroman (2-46). Prepared via General Procedure 1 on a 2.2-mmol scale. The crude product was purified by silica gel chromatography (10% Et_2O/hexanes with 2% Et_3N) to give compound **2-46** (0.392 g, 62%) as colorless oil: ^1H NMR (400 MHz, C_6D_6) δ 7.53 – 7.52 (m, 1H), 7.39 (d, J = 7.9 Hz, 1H), 7.33 (s, 1H), 7.16 – 7.13 (m, 1H), 6.81 (d, J = 0.49 Hz, 2H), 6.72 – 6.69 (m, 1H), 3.98 (dt, J = 10.82, 3.61 Hz, 1H), 3.83 – 3.78 (m, 1H), 3.32 (s, 3H), 3.29 (s, 3H), 2.88 – 2.80 (m,

1H), 2.31 (dt, J = 16.08, 6.0, 2.95 Hz, 1H), 1.93 (s, 3H); ^{13}C NMR (101 MHz, C_6D_6) δ 160.0, 148.4, 144.4, 137.8, 135.6, 130.6, 128.9, 128.2, 128.19, 119.8, 113.5, 113.1, 100.9, 59.5, 54.4, 49.8, 28.2, 20.8; FTIR (NaCl, thin film) 2938, 1600, 1484, 1431, 1287, 1268, 1072, 1051 cm^{-1}; LRMS (EI+) [M+] calculated for $C_{18}H_{20}O_3$: 284.1, found: 284.1.

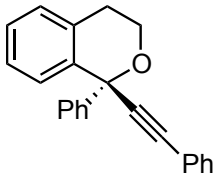
Enantioselective Alkynylation of Ketals

Racemic products were obtained using catalytic CuSPh, MTBD and $BF_3{\cdot}OEt_2$ in $CHCl_3$ at room temperature.

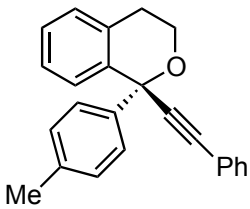
General Procedure 2: Enantioselective Alkynylation

In a N_2-atmosphere glovebox, CuSPh (3.45 mg, 0.02 mmol, 10 mol %) was weighed into a 2-dram vial. 2,6-Bis((*R*)-4-phenyl-4,5-dihydrooxazol-2-yl)pyridine (Ph-PyBox, **2-56**, 8.87 mg, 0.024 mmol, 12 mol %) and $CHCl_3$ (1.33 mL, 0.15 M) were added. The vial was capped with a septum-lined piercable cap. The mixture was stirred for 30 min at room temperature. Then alkyne (0.24 mmol, 1.2 equiv), MTBD (1-methyl-2,3,4,6,7,8-hexahydro-1*H*-pyrimido[1,2-*a*]pyrimidine, 45 μL, 0.31 mmol, 1.55 equiv), and ketal **2** (0.2 mmol, 1.0 equiv) were added. The vial was again sealed with a septum-lined piercable cap, removed from the glovebox, and cooled to 0 °C. After 10 min, $BF_3{\cdot}OEt_2$ (51 μL, 0.40 mmol, 2.0 equiv) was added via syringe, and the mixture was stirred for 48 h at 4 °C. The reaction mixture was then diluted with Et_2O (2 mL) and filtered through a plug of silica gel, which was then washed with more

Et_2O (10 mL). The filtrate was concentrated and purified by silica gel chromatography.

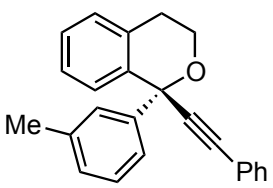


(*S*)-1-phenyl-1-(phenylethynyl)isochroman (2-48). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (0–1% CH_2Cl_2/PhMe) to give compound **2-48** (run 1: 56.5 mg, 91%; run 2: 57.6 mg, 93%) as colorless oil. The enantiomeric excess was determined to be 78% (run 1: 79% ee; run 2: 77% ee) by chiral HPLC analysis (CHIRALPAK IB 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 7.65 min, t_R(minor) = 6.11 min. $[\alpha]_D^{24}$ = 28.25° (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 – 7.68 (m, 2H), 7.54 – 7.52 (m, 2H), 7.40 – 7.32 (m, 6H), 7.24-7.18 (m, 2H), 7.14 (dt, *J* = 6.43, 1.87 Hz, 1H), 7.05 (d, *J* = 7.79 Hz, 1H), 4.46 (dt, *J* = 11.16, 3.56 Hz, 1H), 4.23 – 4.18 (m, 1H), 3.30 – 3.20 (m, 1H), 2.85 (dt, *J* = 16.38, 2.92 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 139.2, 133.0, 131.9, 128.9, 128.6, 128.40, 128.35, 128.32, 128.27, 127.9, 127.1, 126.4, 122.7, 90.4, 88.7, 77.8, 61.9, 28.7; FTIR (NaCl, thin film) 3060, 3024, 2929, 2869, 1598, 1489, 1448, 1280, 1088, 1061, 752, 693 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{23}H_{18}O_3$: 310.1358, found: 310.1361.



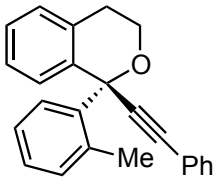
(*S*)-1-(phenylethynyl)-1-(*p*-tolyl)isochroman (2-62). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (0–1% CH_2Cl_2/PhMe) to give compound **2-62** (run 1: 47.9 mg, 67%; run 2: 45.3 mg, 64%) as colorless oil. The enantiomeric

excess was determined to be 70% (run 1: 71% ee; run 2: 69% ee) by chiral HPLC analysis (CHIRALPAK IB 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 7.31 min, t_R(minor) = 6.17 min. $[\alpha]_D^{24} = 26.25°$ (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.46 (m, 4H), 7.36 – 7.29 (m, 3H), 7.23 – 7.10 (m, 5H), 7.05 (d, *J* = 7.7 Hz, 1H), 4.47 – 4.37 (m, 1H), 4.21 – 4.13 (m, 1H), 3.29 – 3.17 (m, 1H), 2.88 – 2.79 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9, 139.3, 138.1, 133.1, 131.9, 128.95, 128.87, 128.6, 128.4, 128.3, 127.9, 127.1, 126.4, 122.8, 90.6, 88.4, 77.6, 61.9, 28.7, 21.3; FTIR (NaCl, thin film) 3024, 2927, 1598, 1510, 1489, 1280, 1180 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{20}O$; 324.1514, found: 324.1540.

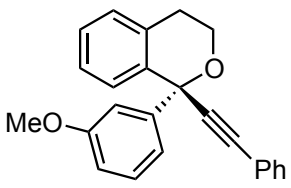


(*S*)-1-(phenylethynyl)-1-(*m*-tolyl)isochroman (2-63). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (3–5% Et_2O/hexanes) to give compound **2-63** (run 1: 61.2 mg, 94%; run 2: 60.8 mg, 94%) as colorless oil. The enantiomeric excess was determined to be 87% (run 1: 86% ee; run 2: 88% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 7.00 min, t_R(minor) = 6.11 min. $[\alpha]_D^{24} = –27.9°$ (c 2.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 6.7, 3.1 Hz, 2H), 7.42 – 7.37 (m, 1H), 7.25 (d, *J* = 4.0 Hz, 2H), 7.21 – 7.14 (m, 2H), 7.14 – 7.02 (m, 5H), 6.98 (dd, *J* = 7.7, 1.4 Hz, 1H), 4.37 (td, *J* = 11.2, 3.5 Hz, 1H), 4.12 – 4.09 (m, 1H), 3.24 – 3.09 (m, 1H), 2.76 (dd, *J* = 16.4, 3.0 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 139.3, 137.9, 132.9, 131.9, 129.1, 128.9, 128.6, 128.5, 128.4, 128.3, 128.1, 127.0, 126.4, 125.1,

122.8, 90.5, 88.6, 77.8, 62.0, 28.7, 21.7; FTIR (NaCl, thin film) 3022, 2923, 2867, 1605, 1489, 1462, 1427 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{20}O$; 324.1514, found: 324.1501.

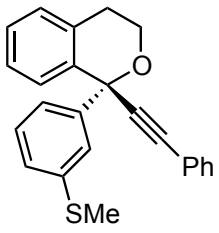


(*R*)-1-(phenylethynyl)-1-(*o*-tolyl)isochroman (2-64). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (0–4% CH_2Cl_2/PhMe) to give compound **2-64** (run 1: 50.8 mg, 71%; run 2: 45.0 mg, 63%) as colorless oil. The enantiomeric excess was determined to be 36% (run 1: 35% ee; run 2: 36% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 8.23 min, t_R(minor) = 5.77 min. $[\alpha]_D^{24}$ = –16.1° (c 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 – 8.14 (m, 1H), 7.55 – 7.48 (m, 2H), 7.37 – 7.30 (m, 3H), 7.28 (d, *J* = 4.8 Hz, 2H), 7.24 – 7.12 (m, 3H), 7.10 (dd, *J* = 7.2, 1.7 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 4.63 – 4.52 (m, 1H), 4.27 – 4.19 (m, 1H), 3.33 – 3.18 (m, 1H), 2.86 (d, *J* = 16.3 Hz, 1H), 2.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 139.0, 137.7, 132.9, 132.6, 131.8, 129.5, 128.64, 128.58, 128.56, 128.4, 127.2, 126.9, 126.6, 125.3, 122.9, 90.6, 90.5, 78.9, 61.9, 28.1, 20.6; FTIR (NaCl, thin film) 3061, 3020, 2964, 2930, 2870, 2360, 1599, 1489 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{20}O$; 324.1514, found: 324.1539.



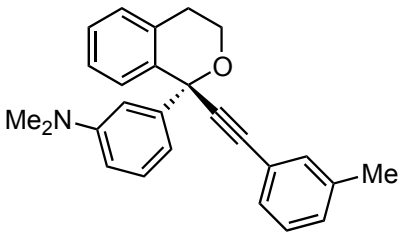
(*S*)-1-(3-methoxyphenyl)-1-(phenylethynyl)isochroman (2-65). Prepared via General Procedure 2. Crude material was

purified by silica gel chromatography (PhMe) to give compound **2-65** (run 1: 61.4 mg, 90%; run 2: 54.8 mg, 81%) as colorless oil. The enantiomeric excess was determined to be 96% (run 1: 96% ee; run 2: 95% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 9.37 min, t_R(minor) = 7.66 min. $[\alpha]_D^{24}$ = –44.1° (c 2.2, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 – 7.47 (m, 2H), 7.32 – 7.30 (m, 3H), 7.28 (d, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 1.7 Hz, 1H), 7.25 – 7.14 (m, 3H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 6.86 – 6.85 (m, 1H), 4.43 – 4.39 (m, 1H), 4.19 – 4.16 (m, 1H), 3.80 (s, 3H), 3.25 – 3.19 (m, 1H), 2.84 – 2.82 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 145.4, 138.9, 132.9, 131.9, 129.3, 128.9, 128.6, 128.4, 128.3, 127.1, 126.5, 122.7, 120.4, 114.0, 113.5, 90.37, 88.5, 77.7, 61.9, 55.4, 28.7; FTIR (NaCl, thin film) 2935, 2361, 2339, 1599, 1488, 1451, 1289, 1083 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{20}O_2$; 340.1463, found: 340.1451.



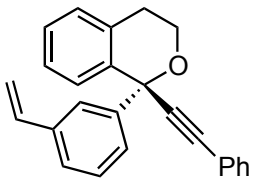
(*S*)-1-(3-(methylthio)phenyl)-1-(phenylethynyl)isochroman (2-66). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (PhMe) to give compound **2-66** (61.2 mg, 86%) as colorless oil. The enantiomeric excess was determined to be 95% by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 8.47 min, t_R(minor) = 6.91 min. $[\alpha]_D^{24}$ = –132.3° (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.62 (m, 1H), 7.53 – 7.48 (m, 2H), 7.42 – 7.38 (m, 1H), 7.33 (dd, *J* = 5.0, 2.0 Hz, 3H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.24 – 7.17 (m, 3H), 7.17 – 7.10

(m, 1H), 7.04 (d, J = 7.7 Hz, 1H), 4.49 – 4.39 (m, 1H), 4.23 – 4.15 (m, 1H), 3.30 – 3.18 (m, 1H), 2.89 – 2.78 (m, 1H), 2.48 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 138.8, 138.4, 132.9, 131.8, 128.9, 128.7, 128.6 128.3, 128.25, 127.1, 126.4, 126.3, 126.0, 124.8, 122.6, 90.1, 88.8, 77.7, 62.0, 28.6, 15.9; FTIR (NaCl, thin film) 2921, 2868, 2220, 1589, 1489, 1442, 1263 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{20}OS$; 356.1235, found: 356.1240.

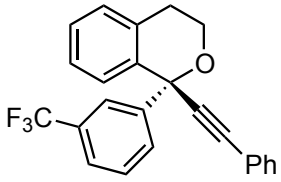


(*S*)-*N*,*N*-dimethyl-3-(1-(*m*-tolylethynyl)isochroman-1-yl)aniline (2-67). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (0–5% acetone/petroleum ether) to give compound **2-67** (run 1: 66.0 mg, 90%; run 2: 63.1 mg, 86%) as red oil. The enantiomeric excess was determined to be 93% (run 1: 93% ee; run 2: 93% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 9.59 min, t_R(minor) = 8.31 min. $[\alpha]_D^{24}$ = – 54.8° (c 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 9.8 Hz, 2H), 7.25 – 7.17 (m, 5H), 7.17 – 7.10 (m, 3H), 6.92 (d, J = 7.6 Hz, 1H), 6.72 (dd, J = 8.2, 2.6 Hz, 1H), 4.46 – 4.40 (m, 1H), 4.22 – 4.17 (m, 1H), 3.29 – 3.16 (m, 1H), 2.96 (s, 6H), 2.84 (d, J = 4.1 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.5, 144.6, 139.3, 137.9, 132.9, 132.4, 129.4, 129.0, 128.9, 128.8, 128.4, 128.2, 126.9, 126.3, 122.7, 116.5, 113.0, 112.5, 90.51, 88.45, 78.1, 61.9, 40.8, 28.7, 21.3; FTIR (NaCl, thin film)

3024, 2925, 2804, 1602, 1579, 1499, 1435, 1352 cm^{-1}; HRMS (;I+) [M+] calculated for $C_{26}H_{15}NO$; 367.1936, found: 367.1939.

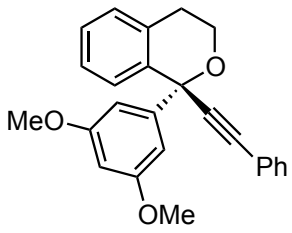


(*S*)-1-(phenylethynyl)-1-(3-vinylphenyl)isochroman (2-68). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (5–15% CH_2Cl_2/hexanes) to give compound **2-68** (51.1 mg, 76%) as colorless oil. The enantiomeric excess was determined to be 87% by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 7.14 min, t_R(minor) = 5.99 min. $[\alpha]_D^{24}$ = –71.6° (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.58 – 7.50 (m, 3H), 7.43 (d, *J* = 2.5 Hz, 1H), 7.37 – 7.30 (m, 4H), 7.25 – 7.17 (m, 2H), 7.13 (td, *J* = 7.2, 6.5, 2.1 Hz, 1H), 7.08 (d, *J* = 1.9 Hz, 1H), 6.74 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.76 (dd, *J* = 17.5, 1.0 Hz, 1H), 5.28 (d, *J* = 2.8, 1H), 4.46 (td, *J* = 11.2, 3.6 Hz, 1H), 4.26 – 4.20 (m, 1H), 3.33 – 3.18 (m, 1H), 2.85 (dt, *J* = 16.4, 3.0 Hz, 1H); ^{13}C NMR (101 MHz, $C(O)(CD_3)_2$) δ 144.7, 139.3, 137.4, 136.9, 133.1, 131.5, 128.9, 128.8, 128.6, 128.3, 127.9, 127.3, 126.9, 126.3, 125.7, 125.6, 122.5, 113.6, 90.5, 88.4, 77.5, 61.5, 28.2; FTIR (NaCl, thin film) 2361, 2340, 1653, 1489, 1083, 989, 911 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{20}O$; 336.1514, found: 336.1513.



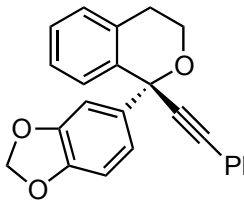
(*S*)-1-(phenylethynyl)-1-(3-(trifluoromethyl)phenyl)isochroman (2-69). Prepared via

General Procedure 2. Crude material was purified by silica gel chromatography (3% Et_2O/hexanes) to give compound **2-69** (run 1: 46.0 mg, 61%; run 2: 41.6 mg, 55%) as colorless oil. The enantiomeric excess was determined to be 79% (run 1: 78% ee; run 2: 79% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 7.88 min, t_R(minor) = 5.89 min. $[\alpha]_D^{24}$ = – 44.3° (c 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.56 – 7.45 (m, 3H), 7.39 – 7.30 (m, 3H), 7.24 – 7.17 (m, 2H), 7.17 – 7.09 (m, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 4.54 – 4.42 (m, 1H), 4.28 – 4.17 (m, 1H), 3.35 – 3.23 (m, 1H), 2.85 (d, *J* = 4.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.9, 138.4, 132.9, 131.9, 131.4, 130.6 (q, $J_{C\text{-}F}$ = 31.9 Hz), 129.2, 128.9, 128.8, 128.4, 128.2, 127.4, 126.7, 125.3 (q, $J_{C\text{-}F}$ = 3.7 Hz), 124.7 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.2 (q, $J_{C\text{-}F}$ = 271.9 Hz), 122.3, 89.5, 89.4, 77.5, 62.2, 28.5; FTIR (NaCl, thin film) 2931, 1599, 1490, 1443, 1330, 1261, 1166 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{17}OF_3$; 378.1232, found: 378.1206.



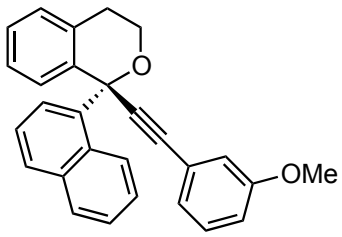
(*S*)-1-(3,5-dimethoxyphenyl)-1-(phenylethynyl)isochroman (2-70). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (5–10% Et_2O/hexanes) to give compound **2-70** (run 1: 66.7 mg, 90%; run 2: 64.1 mg, 87%) as colorless oil. The enantiomeric excess was determined to be 95% (run 1: 94% ee; run 2: 95% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% EtOAc/hexane, λ=254 nm); t_R(major) =

48.72 min, t_R(minor) = 42.67 min. $[\alpha]_D^{24}$ = 11.5° (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.38 (m, 2H), 7.22 – 7.20 (m, 3H), 7.09 – 7.08 (m, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 7.03 – 7.02 (m, 2H), 6.75 (d, *J* = 2.0 Hz, 2H), 6.33 (d, *J* = 1.9, 1H), 4.3 (dt, *J* = 11.5, 3.7 Hz, 1H), 4.09 – 4.06 (m, 1H), 3.67 (s, 6H), 3.13 – 3.08 (m, 1H), 2.73 (d, *J* = 16.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 146.2, 138.7, 132.8, 131.8, 129.1, 128.8, 128.5, 128.3, 128.2, 127.1, 126.4, 122.7, 106.4, 99.9, 90.4, 88.3, 61.9, 55.4, 28.5; FTIR (NaCl, thin film) 3327, 2962, 1991, 1653, 1597, 1490, 1457, 1426 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{22}O_3$; 370.1569, found: 370.1570.



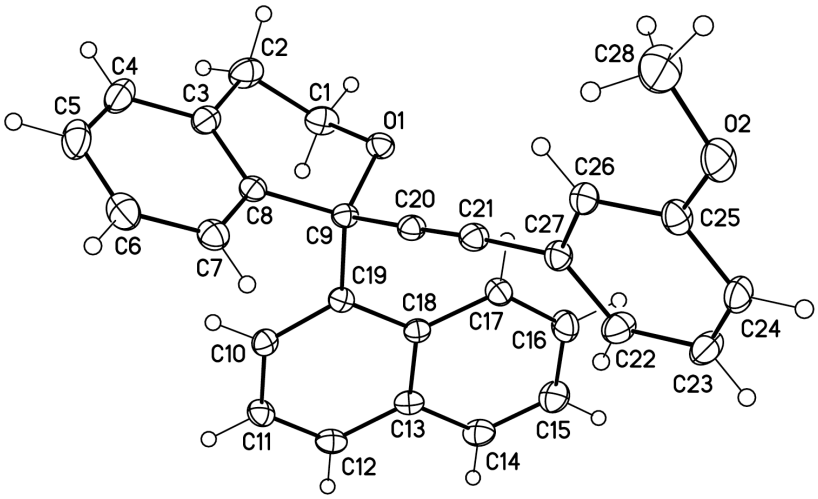
(*S*)-1-(benzo[*d*][1,3]dioxol-5-yl)-1-(phenylethynyl)isochroman (2-71). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (3–8% Et_2O/hexanes) to give compound **2-71** (run 1: 68.4 mg, 83%; run 2: 56.4 mg, 73%) as colorless oil. The enantiomeric excess was determined to be 85% (run 1: 86% ee; run 2: 84% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 20.00 min, t_R(minor) = 18.47 min. $[\alpha]_D^{24}$ = –27.1° (c 2.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.47 (m, 2H), 7.32 (dd, *J* = 5.1, 1.9 Hz, 3H), 7.25 – 7.21 (m, 1H), 7.21 – 7.10 (m, 3H), 7.08 – 7.03 (m, 2H), 6.79 (d, *J* = 8.1 Hz, 1H), 5.95 (s, 2H), 4.47 – 4.34 (m, 1H), 4.21 – 4.12 (m, 1H), 3.27 – 3.14 (m, 1H), 2.87 – 2.76 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.64, 147.60, 139.2, 137.9, 132.9, 131.9, 128.9, 128.6, 128.4 127.2, 126.5, 122.6, 121.7, 108.7, 107.6, 101.3, 90.4, 88.6, 77.6, 61.9, 29.8, 28.6; FTIR (NaCl, thin film)

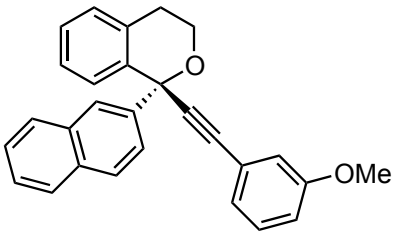
3061, 3021, 2896, 2360, 2339, 1504, 1486, cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{18}O_3$; 354.1256, found: 354.1238.



(*S*)-1-((3-methoxyphenyl)ethynyl)-1-(naphthalen-1-yl)isochroman (2-72). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (0–6% Et_2O/hexanes) to give compound **2-72** (run 1: 55.7 mg, 71%; run 2: 53.8 mg, 69%) as a white solid (mp 180–185 °C). The enantiomeric excess was determined to be 95% (run 1: 95% ee; run 2: 95% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 10.87 min, t_R(minor) = 8.57 min. $[\alpha]_D^{24}$ = –61.2° (c 1.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.7 Hz, 1H), 8.15 (d, *J* = 7.3 Hz, 1H), 7.96 – 7.80 (m, 2H), 7.56 – 7.33 (m, 3H), 7.33 – 7.18 (m, 3H), 7.18 – 7.00 (m, 4H), 6.91 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.65 – 4.58 (m, 1H), 4.24 – 4.19 (m, 1H), 3.82 (s, 3H), 3.46 – 3.32 (m, 1H), 3.07 – 3.01 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 139.3, 137.4, 134.9, 132.4, 130.6, 130.2, 129.4, 129.1, 128.7, 128.1, 127.5, 127.3, 126.8, 126.6, 125.7, 125.5, 124.5, 124.4, 123.8, 116.6, 115.2, 90.6, 90.5, 79.0, 61.9, 55.4, 28.2; FTIR (NaCl, thin film) 2930, 1599, 1489, 1289, 1207, 1159, 1085, 1046 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{28}H_{22}O_2$; 390.1620, found: 390.1608.

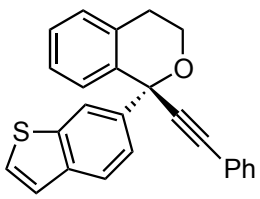
X-ray quality crystals were obtained from slow evaporation of **2-72** in diethyl ether. The crystal structure demonstrated that the absolute configuration is ***S*** (Figure 2.3).





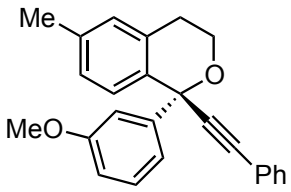
(*S*)-1-((3-methoxyphenyl)ethynyl)-1-(naphthalen-2-yl)isochroman (2-73). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (3–7% Et_2O/hexanes) to give compound **2-73** (run 1: 57.2 mg, 73%; run 2: 63.3 mg, 81%) as colorless oil. The enantiomeric excess was determined to be 83% (run 1: 82% ee; run 2: 84% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 11.01 min, t_R(minor) = 9.23 min. $[\alpha]_D^{24}$ = –67.5° (c 2.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.98 – 7.91 (m, 1H), 7.91 – 7.83 (m, 2H), 7.65 (dd,

J = 8.6, 1.9 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.35 – 7.26 (m, 3H), 7.21 (dt, J = 7.6, 1.2 Hz, 1H), 7.19 – 7.10 (m, 3H), 6.96 (dd, J = 8.3, 1.7 Hz, 1H), 4.54 (m, 1H), 4.30 – 4.25 (m, 1H), 3.86 (s, 3H), 3.41 – 3.27 (m, 1H), 2.95 (dd, J = 13.5, 2.67 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 140.9, 138.9, 133.2, 133.1, 132.8, 129.5, 128.9, 128.6, 128.5, 128.3, 127.6, 127.2, 126.9, 126.49, 126.45, 126.2, 125.8, 124.5, 123.7, 116.7, 115.3, 90.1, 88.8, 77.9, 62.0, 55.4, 28.7; FTIR (NaCl, thin film) 3059, 2963, 2933, 2870, 2833, 1597, 1575, 1489 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{28}H_{22}O_2$; 390.1620, found: 390.1622.

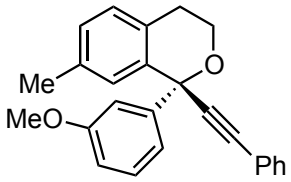


(*S*)-1-(benzo[*b*]thiophen-6-yl)-1-(phenylethynyl)isochroman (2-74). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (0–4% CH_2Cl_2/PhMe) to give compound **2-74** (run 1: 55.4 mg, 76%; run 2: 48.2 mg, 66%) as colorless oil. The enantiomeric excess was determined to be 87% (run 1: 87% ee; run 2: 86% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 8.86 min, t_R(minor) = 7.86 min. $[\alpha]_D^{24}$ = –47.5° (c 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.60 (dd, J = 8.4, 1.7 Hz, 1H), 7.58 – 7.52 (m, 2H), 7.47 (d, J = 5.4 Hz, 1H), 7.38 – 7.32 (m, 4H), 7.25 – 7.18 (m, 2H), 7.16 – 7.10 (m, 1H), 7.07 (d, J = 7.7 Hz, 1H), 4.54 – 4.42 (m, 1H), 4.27 – 4.17 (m, 1H), 3.35 – 3.22 (m, 1H), 2.93 – 2.81 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 139.6, 139.5, 139.2, 133.0, 131.9, 128.9, 128.7, 128.5, 128.4, 127.4, 127.2, 126.5, 124.5, 123.7, 123.5, 122.7, 121.9, 90.4, 88.9, 78.0, 62.1, 28.7; FTIR (NaCl, thin

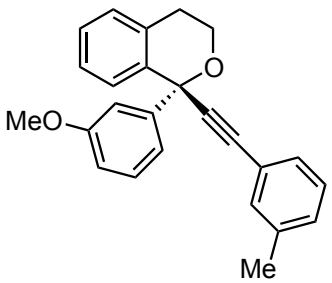
film) 2928, 1598, 1489, 1450, 1390, 1280, 1201 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{18}OS$; 366.1078, found: 366.1064.



(*S*)-1-(3-methoxyphenyl)-6-methyl-1-(phenylethynyl)isochroman (2-75). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (4–7% CH_2Cl_2/PhMe) to give compound **2-75** (56.7 mg, 80%) as colorless oil. The enantiomeric excess was determined to be 93% by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 9.55 min, t_R(minor) = 7.46 min. $[\alpha]_D^{24} = -41°$ (c 2.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.34 – 7.28 (m, 4H), 7.26 – 7.21 (m, 2H), 6.97 (s, 1H), 6.97 – 6.92 (m, 2H), 6.86 – 6.83 (m, 1H), 4.48 – 4.35 (m, 1H), 4.23 – 4.12 (m, 1H), 3.81 (s, 3H), 3.26 – 3.12 (m, 1H), 2.85 – 2.73 (m, 1H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 145.5, 136.8, 136.1, 132.8, 131.9, 129.4, 129.2, 128.6, 128.3, 128.2, 127.4, 122.8, 120.4, 113.9, 113.4, 90.5, 88.3, 77.7, 62.0, 55.4, 28.6, 21.2; FTIR (NaCl, thin film) 2932, 2360, 1599, 1489, 1290, 1082, 1052 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{22}O_2$; 354.1620, found: 354.1607.

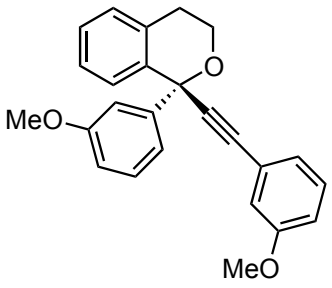


(*S*)-1-(3-methoxyphenyl)-7-methyl-1-(phenylethynyl)isochroman (2-76). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (4–7% CH_2Cl_2/PhMe) to give compound **2-76** (run 1: 46.9 mg, 66%; run 2: 45.1 mg, 64%) as colorless oil. The enantiomeric excess was determined to be 89% (run 1: 88% ee; run 2: 89% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 8.94 min, t_R(minor) = 7.24 min. $[\alpha]_D^{24}$ = –65.1° (c 1.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.33 (dd, *J* = 4.6, 2.1 Hz, 3H), 7.31 – 7.27 (m, 2H), 7.24 – 7.23 (m, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.91 – 6.86 (m, 2H), 4.48 – 4.34 (m, 1H), 4.22 – 4.12 (m, 1H), 3.82 (s, 3H), 3.26 – 3.12 (m, 1H), 2.85 – 2.74 (m, 1H), 2.24 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 145.5, 138.6, 135.9, 131.9, 129.9, 129.2, 128.7, 128.64, 128.61, 128.3, 128.2, 122.8, 120.4, 114.0, 113.4, 90.5, 88.3, 77.7, 62.1, 55.4, 28.3, 21.3; FTIR (NaCl, thin film) 2959, 2931, 2220, 1599, 1586, 1502, 1486, 1433 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{22}O_2$; 354.1620, found: 354.1617.



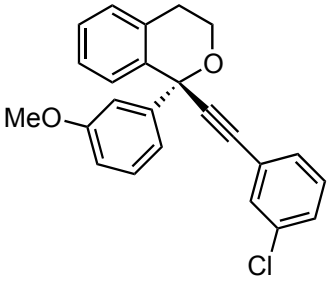
(*S*)-1-(3-methoxyphenyl)-1-(*m*-tolylethynyl)isochroman (2-77). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (1–4% CH_2Cl_2/PhMe) to give compound **2-77** (run 1: 47.4 mg, 67%; run 2: 52.5 mg, 74%) as colorless oil. The

enantiomeric excess was determined to be 93% (run 1: 93% ee; run 2: 92% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 8.84 min, t_R(minor) = 7.34 min. $[\alpha]_D^{24}$ = –56.0° (c 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 3H), 7.25 (d, *J* = 1.6 Hz, 1H), 7.24 – 7.19 (m, 2H), 7.19 – 7.16 (m, 2H), 7.16 – 7.09 (m, 2H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.89 – 6.84 (m, 1H), 4.48 – 4.37 (m, 1H), 4.24 – 4.13 (m, 1H), 3.80 (s, 3H), 3.31 – 3.15 (m, 1H), 2.88 – 2.77 (m, 1H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 145.4, 139.1, 138.0, 132.9, 132.5, 129.5, 129.2, 128.9, 128.88, 128.3, 128.2, 127.1, 126.4, 122.5, 120.4, 113.9, 113.5, 89.9, 88.7, 77.7, 61.9, 55.4, 28.6, 21.3; FTIR (NaCl, thin film) 2933, 2869, 2833, 1600, 1585, 1485, 1290, 1083 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{22}O_2$; 354.1620, found: 354.1592.



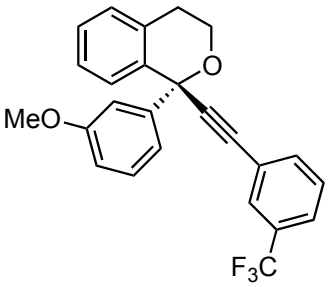
(*S*)-1-(3-methoxyphenyl)-1-((3-methoxyphenyl)ethynyl)isochroman (2-78). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (3–7% Et_2O/hexanes) to give compound **2-78** (run 1: 66.1 mg, 89%; run 2: 63.7 mg, 86%) as colorless oil. The enantiomeric excess was determined to be 96% (run 1: 96% ee; run 2: 96% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 12.4 min, t_R(minor) = 9.37 min. $[\alpha]_D^{24}$ = –40.7° (c 1.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.8 Hz, 1H), 7.31 – 7.27 (m, 3H), 7.26 – 7.23 (m, 1H), 7.23 – 7.17 (m, 2H), 7.17 – 7.13 (m, 1H), 7.13 –

7.09 (m, 1H), 7.06 (dd, J = 2.6, 1.4 Hz, 1H), 6.94 – 6.88 (m, 2H), 4.50 – 4.40 (m, 1H), 4.26 – 4.17 (m, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.31 – 3.21 (m, 1H), 2.92 – 2.82 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 159.3, 145.3, 138.9, 132.9, 129.4, 129.3, 128.9, 128.3, 127.2, 126.5, 124.5, 123.7, 120.4, 116.6, 115.3, 113.9, 113.5, 90.2, 88.4, 77.7, 61.9, 55.4, 55.37, 28.6; FTIR (NaCl, thin film) 2935, 1599, 1485, 1428, 1319, 1289, 1263, 1207 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{22}O_3$; 370.1569, found: 370.1565.

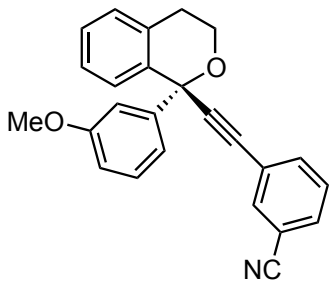


(*S*)-1-((3-chlorophenyl)ethynyl)-1-(3-methoxyphenyl)isochroman (2-79). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (3–6% Et_2O/hexanes) to give compound **2-79** (run 1: 66.4 mg, 93%; run 2: 68.4 mg, 95%) as colorless oil. The enantiomeric excess was determined to be 96% (run 1: 96% ee; run 2: 96% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 8.45 min, t_R(minor) = 7.39 min. $[\alpha]_D^{24}$ = – 45.0° (c 3.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 1.4 Hz, 1H), 7.41 (d, J = 6.7 Hz, 1H), 7.37 – 7.31 (m, 2H), 7.30 (t, 1H), 7.27 (d, J = 5.8 Hz, 1H), 7.25 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 7.10 (d, J = 7.6 Hz, 1H), 6.94 – 6.88 (m, 1H), 4.43 (dt, J = 11.1, 3.6 Hz, 1H), 4.24 – 4.19 (m, 1H), 3.84 (s, 3H), 3.32 – 3.20 (m, 1H), 2.87 (dt, J = 16.5, 3.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 145.1, 138.6, 134.2, 132.9, 131.7, 130.0, 129.6, 129.3, 128.94, 128.90, 128.2, 127.3, 126.5, 124.4, 120.3,

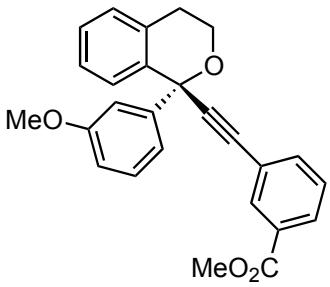
114.0, 113.5, 91.63, 87.02, 77.7, 62.0, 55.4, 28.6; FTIR (NaCl, thin film) 3064, 2935, 2871, 2834, 1593, 1562, 1485 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{19}O_2Cl$; 374.1074, found: 374.1070.



(*S*)-1-(3-methoxyphenyl)-1-((3-(trifluoromethyl)phenyl)ethynyl)isochroman (2-80). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (3–6% Et_2O/hexanes) to give compound **2-80** (run 1: 75.4 mg, 96%; run 2: 66.8 mg, 85%) as colorless oil. The enantiomeric excess was determined to be 97% (run 1: 97% ee; run 2: 97% ee) by chiral HPLC analysis (CHIRALPAK IB, 1.0 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 10.13 min, t_R(minor) = 9.06 min. $[\alpha]_D^{24}$ = –43.3° (c 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 7.12 (d, *J* = 7.7 Hz, 1H), 6.92 (dt, *J* = 8.2, 2.4, 1.1 Hz, 1H), 4.44 (td, *J* = 11.1, 3.6 Hz, 1H), 4.26 – 4.21 (m, 1H), 3.84 (s, 3H), 3.33 – 3.20 (m, 1H), 2.89 (dt, *J* = 16.5, 3.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 144.9, 138.4, 134.9, 132.9, 130.9 (q, $J_{C\text{-}F}$ = 32.7 Hz), 129.3, 128.9, 128.8, 128.6 (q, $J_{C\text{-}F}$ = 3.8 Hz), 128.2, 127.3, 126.5, 125.1 (q, $J_{C\text{-}F}$ = 3.7 Hz), 123.7 (q, $J_{C\text{-}F}$ = 272.0 Hz), 123.5, 120.2, 113.9, 113.4, 91.9, 86.7, 77.6, 61.9, 55.3, 28.5; FTIR (NaCl, thin film) 3072, 2936, 2872, 2835, 1601, 1586, 1486, 1451 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{19}O_2F_3$; 408.1337, found: 408.1318.

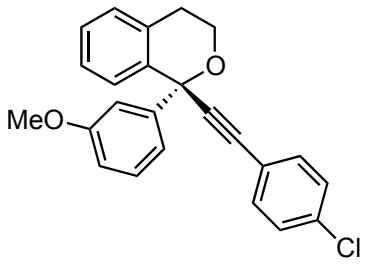


(*S*)-3-((1-(3-methoxyphenyl)isochroman-1-yl)ethynyl)benzonitrile (2-81). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (5–10% Et_2O/hexanes) to give compound **2-81** (run 1: 61.9 mg, 85%; run 2: 65.1 mg, 89%) as colorless oil. The enantiomeric excess was determined to be 97% (run 1: 97% ee; run 2: 97% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 23.14 min, t_R(minor) = 16.66 min. $[\alpha]_D^{24}$ = –28.2° (c 2.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.76 (d, *J* = 7.7 Hz, 1H), 7.66 (d, *J* = 7.98 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.38 – 7.34 (m, 1H), 7.33 – 7.27 (m, 3H), 7.24 – 7.19 (m, 2H), 7.13 (d, *J* = 7.9 Hz, 1H), 6.96 – 6.93 (m, 1H), 4.43 (dt, *J* = 10.6, 3.6 Hz, 1H), 4.28 – 4.23 (m, 1H), 3.85 (s, 3H), 3.35 – 3.20 (m, 1H), 2.90 (dt, *J* = 16.6, 3.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 144.8, 138.2, 135.9, 135.2, 132.9, 131.8, 129.4, 129.3, 129.0, 128.2, 127.4, 126.6, 124.2, 120.2, 118.1, 114.0, 113.4, 112.9, 92.9, 85.9, 77.6, 62.1, 55.4, 28.5; FTIR (NaCl, thin film) 2935, 2360, 2232, 1653, 1599, 1488, 1290, 1084 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{19}NO_2$; 365.1416, found: 365.1427.



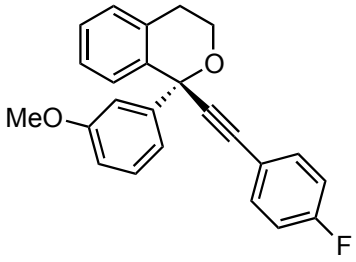
(*S*)-methyl 3-((1-(3-methoxyphenyl)isochroman-1-yl)ethynyl)benzoate (2-82). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (5–15% Et_2O/hexanes) to give compound

2-82 (run 1: 75.6 mg, 95%; run 2: 78.2 mg, 98%) as colorless oil. The enantiomeric excess was determined to be 96% (run 1: 95% ee; run 2: 96% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 14.31 min, t_R(minor) = 11.38 min. $[\alpha]_D^{24}$ = –46.0° (c 3.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 8.00 (d, *J* = 9.1 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.30 (t, *J* = 8.0 Hz, 1H), 7.25 – 7.23 (m, 2H), 7.21 – 7.18 (m, 2H), 7.16 – 7.12 (m, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.87 (dd, *J* = 7.8, 1.0 Hz, 1H), 4.42 (td, *J* = 11.1, 3.6 Hz, 1H), 4.22 – 4.17 (m, 1H), 3.92 (s, 3H), 3.80 (s, 3H), 3.27 – 3.19 (m, 1H), 2.84 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 159.5, 145.1, 138.6, 136.0, 133.0, 132.9, 130.4, 129.6, 129.3, 128.9, 128.5, 128.2, 127.2, 126.5, 123.1, 120.3, 113.9, 113.5, 91.3, 87.4, 77.7, 62.0, 55.3, 52.4, 28.6; FTIR (NaCl, thin film) 2951, 2835, 1725, 1600, 1485, 1437, 1296, 1105 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{26}H_{22}O_4$; 398.1518, found: 398.1525.



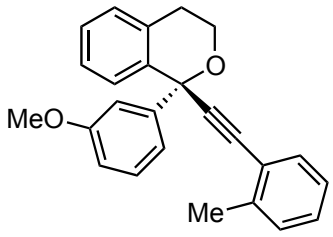
(*S*)-1-((4-chlorophenyl)ethynyl)-1-(3-methoxyphenyl)isochroman (2-83). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (3–5% Et_2O/hexanes) to give compound **2-83** (run 1: 65.3 mg, 87%; run 2: 68.4 mg, 91%) as colorless oil. The enantiomeric excess was determined to be 96% (run 1: 96% ee; run 2: 96% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 9.51 min, t_R(minor) = 8.13 min. $[\alpha]_D^{24}$ = –

39.5° (c 2.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.7 Hz, 3H), 7.23 – 7.19 (m, 2H), 7.19 – 7.13 (m, 2H), 7.11 (dd, *J* = 6.8, 1.9 Hz, 1H), 7.05 (d, *J* = 7.7 Hz, 1H), 6.87 – 6.85 (m, 1H), 4.38 (td, *J* = 11.0, 3.6 Hz, 1H), 4.19 – 4.14 (m, 1H), 3.79 (s, 3H), 3.27 – 3.15 (m, 1H), 2.83 (dt, *J* = 16.5, 3.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 145.2, 138.7, 134.7, 133.2, 132.9, 129.3, 128.9, 128.7, 128.3, 127.3, 126.5, 121.2, 120.3, 114.0, 113.5, 91.4, 87.3, 77.7, 62.0, 55.4, 28.6; FTIR (NaCl, thin film) 2934, 1601, 1586, 1489, 1451, 1290, 1269, 1084 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{19}O_2Cl$; 374.1074, found: 374.1071.

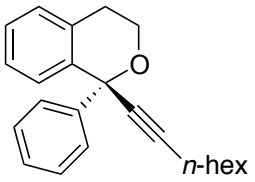


(*S*)-1-((4-fluorophenyl)ethynyl)-1-(3-methoxyphenyl)isochroman (2-84). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (1% CH_2Cl_2/PhMe) to give compound **2-84** (54.6 mg, 76%) as colorless oil. The enantiomeric excess was determined to be 95% by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 9.41 min, t_R(minor) = 8.14 min. $[\alpha]_D^{24}$ = –17.3° (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.46 (m, 2H), 7.31 – 7.27 (m, 1H), 7.25 – 7.21 (m, 3H), 7.19 – 7.18 (m, 1H), 7.16 – 7.11 (m, 1H), 7.07 (d, *J* = 7.2 Hz, 1H), 7.04 – 6.99 (m, 2H), 6.89 – 6.86 (m, 1H), 4.40 (dt, *J* = 11.3, 3.7 Hz, 1H), 4.21 – 4.16 (m, 1H), 3.80 (s, 3H), 3.27 – 3.18 (m, 1H), 2.84 (dt, *J* = 16.4, 3.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7 (d, $J_{C\text{-}F}$ = 254.0 Hz), 159.4, 145.2, 138.7, 133.8 (d, $J_{C\text{-}F}$ = 8.4 Hz), 132.9, 129.2, 128.9, 128.2,

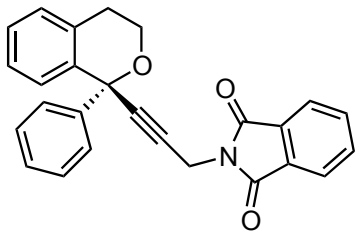
127.1, 126.4, 120.3, 118.7 (d, $J_{C\text{-}F}$ = 3.7 Hz), 115.6 (d, $J_{C\text{-}F}$ = 21.8 Hz), 113.9, 113.4, 90.0, 87.3, 77.6, 61.9, 52.3, 28.5; FTIR (NaCl, thin film) 1489, 1448, 1205, 1120, 1053, 1007, 764, 703 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{19}O_2F$; 358.1369, found: 358.1393.



(*S*)-1-(3-methoxyphenyl)-1-(*o*-tolylethynyl)isochroman (2-85). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (1% CH_2Cl_2/PhMe) to give compound **2-85** (run 1: 53.4 mg, 75%; run 2: 45.7 mg, 65%) as a white solid (mp 86–92 °C). The enantiomeric excess was determined to be 74% (run 1: 73% ee; run 2: 74% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 7.65 min, t_R(minor) = 6.85 min. $[\alpha]_D^{24}$ = 74.3° (c 0.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.5 Hz, 1H), 7.29 – 7.28 (m, 2H), 7.25 – 7.19 (m, 3H), 7.18 – 7.10 (m, 4H), 7.08 – 7.06 (m, 1H), 6.88 – 6.85 (m, 1H), 4.48 – 4.42 (m, 1H), 4.23 – 4.18 (m, 1H), 3.8 (s, 3H), 3.29 – 3.20 (m, 1H), 2.85 – 2.79 (m, 1H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 145.3, 140.4, 139.1, 132.8, 132.1, 129.4, 129.2, 128.8, 128.5, 128.2, 126.9, 126.3, 125.5, 122.5, 120.4, 113.8, 113.5, 94.2, 87.8, 77.9, 61.9, 55.3, 28.6, 20.9; FTIR (NaCl, thin film) 1600, 1485, 1289, 1083, 1051, 759, 741, 696 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{22}O_2$; 354.1620, found: 354.1611.

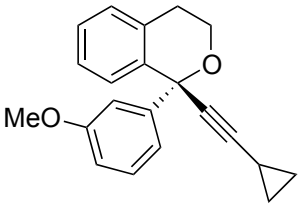


(*S*)-1-(oct-1-yn-1-yl)-1-phenylisochroman (2-86). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (0–5% Et_2O/hexanes) to give compound **2-86** (22 mg, 35%) as colorless oil. The enantiomeric excess was determined to be 66% by chiral HPLC analysis (CHIRALPAK IA 0.2 mL/min, 0.1% *i*-PrOH/hexane, λ=220 nm); t_R(major) = 27.64 min, t_R(minor) = 23.50 min. $[\alpha]_D^{24}$ = 31.9° (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 1.7, 8.3 Hz, 2H), 7.34 – 7.28 (m, 3H), 7.18 – 7.12 (m, 2H), 7.10 – 7.06 (m, 1H), 6.93 (d, J = 7.8 Hz, 1H), 4.34 (ddd, *J* = 3.7, 11.0, 11.3 Hz, 1H), 4.13 – 4.08 (m, 1H), 3.22 – 3.14 (m, 1H), 2.79 (dt, *J* = 3.1, 13.1 Hz, 1H), 2.32 (t, *J* = 7.2 Hz, 2H), 1.61 – 1.53 (m, 2H), 1.44 – 1.37 (m, 2H), 1.30 – 1.26 (m, 4H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 144.1, 139.8, 132.4, 128.4, 127.73, 127.68, 127.54, 127.51, 126.5, 125.7, 89.6, 81.1, 77.5, 61.2, 31.0, 28.2, 28.14, 28.11, 22.3, 18.0, 12.9; FTIR (NaCl, thin film) 3902, 3530, 2100, 2089, 1489, 1279, 1643, 1059, 568, 461, 440 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{23}H_{26}O$; 319.2062, found: 319.2069.



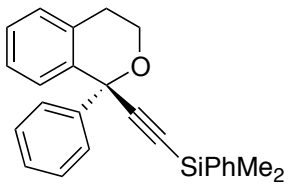
(*S*)-2-(3-(1-phenylisochroman-1-yl)prop-2-yn-1-yl)isoindoline-1,3-dione (2-87). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (5–15% Et_2O/hexanes) to give compound **2-87** (run 1: 59.1 mg, 75%; run 2: 66.9 mg, 85%) as a white solid (mp 126–129 °C). The enantiomeric excess was determined to be 93% (run 1: 93% ee; run

2: 92% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.8 mL/min, 3% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 26.38 min, t_R(minor) = 23.75 min. $[\alpha]_D^{24}$ = –46.3° (c 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.60 – 7.54 (m, 2H), 7.35 – 7.27 (m, 3H), 7.18 – 7.10 (m, 2H), 7.08 – 7.04 (m, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 4.60 (s, 2H), 4.40 – 4.29 (m, 1H), 4.17 – 4.05 (m, 1H), 3.25 – 3.11 (m, 1H), 2.82 – 2.72 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 143.3, 138.8, 134.3, 132.9, 132.1, 128.9, 128.3, 128.26, 128.23, 127.8, 127.1, 126.4, 123.6, 84.2, 82.3, 77.3, 61.9, 28.5, 27.7; FTIR (NaCl, thin film) 2926, 1772, 1719, 1449, 1421, 1392, 1117 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{26}H_{19}NO_3$; 393.1365, found: 393.1343.



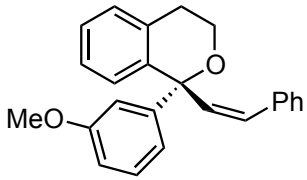
(*S*)-1-(cyclopropylethynyl)-1-(3-methoxyphenyl)isochroman (2-88). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (5–10% Et_2O/hexanes) to give compound **2-88** (16.0 mg, 26%) as colorless oil. The enantiomeric excess was determined to be 93% by chiral HPLC analysis (CHIRALPAK IA, 0.4 mL/min, 1% *i*-PrOH/hexane, λ=210 nm); t_R(major) = 20.72 min, t_R(minor) = 24.97 min. $[\alpha]_D^{24}$ = 70.0° (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (t, *J* = 7.9 Hz, 1H), 7.18 – 7.06 (m, 5H), 6.95 (d, J = 7.6 Hz, 1H), 6.83 – 6.81 (m, 1H), 4.29 (ddd, *J* = 3.6, 3.7, 11.2 Hz, 1H), 4.10 – 4.05 (m, 1H), 3.78 (s, 3H), 3.19 – 3.10 (m, 1H), 2.78 (dt, *J* = 3.2, 16.4 Hz, 1H), 1.38 – 1.32 (m, 1H), 0.82 – 0.74 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2,

145.7, 139.4, 132.7, 128.9, 128.7, 128.1, 126.8, 126.2, 120.3, 113.8, 113.2, 92.4, 77.2, 76.4, 61.5, 55.2, 28.5, 8.6, 8.5, –0.2; FTIR (NaCl, thin film) 3456, 2962, 2260, 1985, 1644, 1426, 568, 461, 423 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{21}H_{20}O_2$; 305.1542, found: 305.1549.

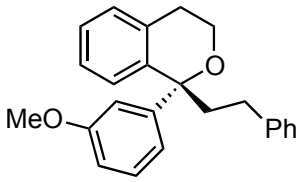


(*R*)-dimethyl(phenyl)((1-phenylisochroman-1-yl)ethynyl)silane (2-89). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (2–10% Et_2O/hexanes) to give compound **2-89** (run 1: 38.4 mg, 52%; run 2: 40.0 mg, 54%) as colorless oil. The enantiomeric excess was determined to be 81% (run 1: 80% ee; run 2: 81% ee) by chiral HPLC analysis (CHIRACEL ODH, 0.2 mL/min, 0.5% *i*-PrOH/hexane, λ=220 nm); t_R(major) = 27.29min, t_R(minor) = 25.67 min. $[\alpha]_D^{24}$ = 80.0° (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.63 (m, 4H), 7.40 – 7.33 (m, 6H), 7.24 – 7.17 (m, 2H), 7.15 – 7.11 (m, 1H), 7.01 (d, *J* = 7.7 Hz, 1H), 4.41 (ddd, *J* = 3.5, 10.9, 11.4 Hz, 1H), 4.21 – 4.16 (m, 1H), 3.28 – 3.20 (m, 1H), 2.83 (dt, *J* = 2.7, 16.5 Hz, 1H), 0.5 (s, 3H), 0.49 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 138.9, 136.9, 133.8, 132.9, 129.5, 128.8, 128.4, 128.24, 128.17, 127.9, 127.8, 127.0, 126.3, 108.1, 91.4, 77.7, 61.9, 28.5, –0.7, –0.8; FTIR (NaCl, thin film) 3491, 3021, 2896, 2360, 2339, 1642, 1486, 538, 429 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{24}OSi$; 368.1596, found: 368.1583.

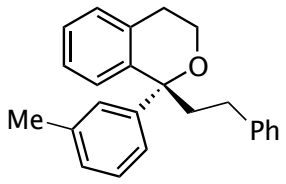
Elaboration of Alkyne Products



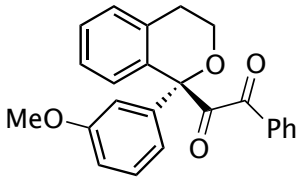
(*R*,*Z*)-1-(3-methoxyphenyl)-1-styrylisochroman (2-93). Alkyne **2-65** was prepared via General Procedure 2 on a 0.20-mmol scale. To a solution of alkyne **2-65** (68.1 mg, 0.20 mmol, 1.0 equiv) and EtOH (5 mL), Lindlar's catalyst (5%, 3.4 mg, 0.01 mmol Pd, 5 mol % Pd) and quinoline (5.25 μL, 0.04 mmol, 0.20 equiv) were added. The reaction mixture was evacuated and backfilled with H_2 thrice following which it was stirred under H_2 (1 atm) for 3 days. After consumption of alkyne **2-65** as determined by TLC analysis, the mixture was filtered through a short pad of Celite, which was then washed with Et_2O (15 mL). The filtrate was concentrated, and the crude material was purified by silica gel chromatography (PhMe) to give compound **2-93** (46.0 mg, 67%) as colorless oil. The enantiomeric excess was determined to be 94% by chiral HPLC analysis (CHIRALPAK IB, 1.0 mL/min, 0.5% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 10.70 min, t_R(minor) = 8.82 min. $[\alpha]_D^{24}$ = –11.6° (c 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.22 (d, *J* = 8.2 Hz, 1H), 7.19 – 7.12 (m, 4H), 7.12 – 7.08 (m, 2H), 7.08 – 7.04 (m, 2H), 7.01 – 6.94 (m, 1H), 6.83 – 6.78 (m, 1H), 6.71 (d, *J* = 12.8 Hz, 1H), 6.08 (d, *J* = 12.7 Hz, 1H), 3.84 – 3.78 (m, 1H), 3.76 (s, 3H), 3.56 – 3.49 (m, 1H), 3.07 – 2.97 (m, 1H), 2.75 – 2.65 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 147.9, 141.3, 136.7, 134.9, 133.5, 131.5, 129.9, 129.2, 128.8, 128.1, 127.3, 126.9, 126.5, 126.3, 120.8, 114.2, 112.8, 82.3, 60.6, 55.3, 28.7; FTIR (NaCl, thin film) 1599, 1483, 1289, 1247, 1042, 779, 756, 696 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{22}O_2$; 342.1620, found: 342.1619.



(*R*)-1-(3-methoxyphenyl)-1-phenethylisochroman (2-94). Alkyne **2-60** was prepared via General Procedure 2 on a 0.20-mmol scale. To a solution of alkyne **2-65** (25.0 mg, 0.07 mmol, 1.0 equiv) and MeOH (5 mL), 10% Pd/C (2.5 mg, 0.01 mmol Pd, 10.0 mol % Pd) was added. The reaction mixture was evacuated and backfilled with H_2 thrice following which it was stirred under H_2 (1 atm) for 12 h. After consumption of alkyne **2-60** as determined by TLC analysis, the mixture was filtered through a short pad of Celite, which was then washed with Et_2O (15 mL). The filtrate was concentrated, and the crude material was purified by silica gel chromatography (5% Et_2O/hexanes) to give compound **2-94** (15.7 mg, 62%) as colorless oil. The enantiomeric excess was determined to be 95% by chiral HPLC analysis (CHIRALPAK IB, 0.4 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 15.53 min, t_R(minor) = 14.26 min. $[\alpha]_D^{24}$ = 60.6° (c 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.25 – 7.17 (m, 5H), 7.17 – 7.12 (m, 3H), 6.99 – 6.93 (m, 2H), 6.80 – 6.75 (m, 1H), 3.99 – 3.91 (m, 1H), 3.77 (s, 3H), 3.74 – 3.66 (m, 1H), 3.19 – 3.08 (m, 1H), 2.87 – 2.76 (m, 1H), 2.69 – 2.61 (m, 1H), 2.60 – 2.49 (m, 1H), 2.43 – 2.31 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 147.9, 142.8, 137.7, 135.0, 129.5, 129.0, 128.5, 128.4, 127.5, 126.8, 125.8, 125.7, 119.9, 113.6, 112.3, 81.2, 60.2, 55.3, 45.1, 30.9, 29.2; FTIR (NaCl, thin film) 1489, 1448, 1205, 1120, 1053, 1007, 764, 703 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{24}O_2$; 344.1776, found: 344.1798.

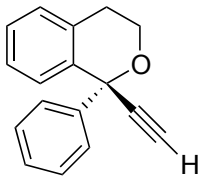


(*R*)-1-phenethyl-1-(*m*-tolyl)isochroman (2-95). This procedure was adapted from the literature.[51] In a N_2-atmosphere glovebox, alkane **2-94** (10.0 mg, 0.03 mmol, 1.0 equiv), $Ni(acac)_2$ (0.4 mg, 0.0015 mmol, 5 mol %), PCy_3 (0.78 mg, 0.003 mmol, 10 mol %) and mesitylene (0.2 mL, 0.13 M) were added combined in a 1-dram vial. The vial was sealed with a Teflon-lined cap equipped with a valve for addition of later reagents. The vial was removed from the glovebox. After 5 min, MeMgBr (0.10 mL, 0.30 mmol, 10 equiv) was added via syringe, and the mixture was stirred for 5 h at 110 °C. The reaction mixture was then cooled to room temperature, diluted with Et_2O (2 mL) and filtered through a plug of silica gel, which was then washed with Et_2O (10 mL). The filtrate was concentrated. The crude material was purified by silica gel chromatography (5% Et_2O/hexanes) to give compound **2-95** (5.0 mg, 55%) as colorless oil. The enantiomeric excess was determined to be 95% by chiral HPLC analysis (CHIRACEL ODH, 0.2 mL/min, 1% *i*-PrOH/hexane, λ=210 nm); t_R(major) = 27.68 min, t_R(minor) = 23.53 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.25 (m, 3H), 7.23 – 7.18 (m, 4H), 7.16 – 7.11 (m, 5H), 7.05 (d, *J* = 7.2 Hz, 1H), 3.96 – 3.91 (m, 1H), 3.69 (ddd, *J* = 3.8, 3.7, 11.2 Hz, 1H), 3.17 – 3.09 (m, 1H), 2.86 – 2.78 (m, 1H), 2.69 – 2.64 (m, 1H), 2.60 – 2.52 (m, 1H), 2.42 – 2.34 (m, 2H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.9, 142.8, 137.8, 137.6, 134.9, 129.3, 128.4, 128.3, 127.9, 127.84, 127.77, 127.5, 126.5, 125.7, 125.6, 124.6, 81.1, 60.0, 45.0, 30.8, 29.1, 21.7; FTIR (NaCl, thin film) 1644, 1489, 1448, 1205, 1120, 1053, 1007, 764, 703 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{24}O$; 328.1827, found: 328.1844.



(*R*)-1-(1-(3-methoxyphenyl)isochroman-1-yl)-2-phenylethane-1,2-dione (2-96). This procedure was adapted from the literature.[50] Alkyne **2-65** was prepared via General Procedure 2 on a 0.20-mmol scale. A solution of $KMnO_4$ (55.8 mg, 0.35 mmol, 3.0 equiv), $NaHCO_3$ (11.9 mg, 0.14 mmol, 1.2 equiv), tetrabutylammonium bromide (20 mg, 0.062 mmol, 0.52 equiv), and H_2O (1.0 mL) was added to a solution of alkyne **2-65** (40.0 mg, 0.12 mmol, 1.0 equiv) and CH_2Cl_2 (1.0 mL, 0.12 M). The reaction mixture was stirred at room temperature for 48 h. Excess $KMnO_4$ was destroyed by adding HCl (1 M, 1 mL) and Na_2SO_3 (20 mg) until the red color disappeared. The mixture was then washed with sat. $NaHCO_3$ and extracted with CH_2Cl_2 (5 mL). The organic layers were dried ($MgSO_4$) and filtered through a short pad of Celite, which was then washed with CH_2Cl_2 (10 mL). The filtrate was concentrated, and the crude material was purified by silica gel chromatography (3% CH_2Cl_2/toluene) to give compound **2-96** (29.1 mg, 67%) as yellow oil. The enantiomeric excess was determined to be 96% by chiral HPLC analysis (CHIRALPAK IA, 0.4 mL/min, 2% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 28.48 min, t_R(minor) = 26.17 min. $[\alpha]_D^{24}$ = 35.0° (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.4 Hz, 2H), 7.60 – 7.55 (m, 2H), 7.42 – 7.38 (m, 2H), 7.34 – 7.28 (m, 3H), 7.20 – 7.18 (m, 1H), 7.01 – 6.98 (m, 2H), 6.90 (dd, *J* = 2.0, 2.1 Hz, 1H), 3.89 – 3.84 (m, 1H), 3.79 (s, 3H), 3.7 – 3.6 (m, 1H), 2.92 – 2.83 (m, 1H), 2.58 (d, *J* = 16.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.4, 195.5, 159.5, 142.9, 134.9, 134.3, 132.8, 130.9, 129.5, 129.31, 129.30, 128.7, 128.2, 128.1, 126.2, 121.3, 115.1, 113.7, 87.1, 60.1, 55.3, 28.2; FTIR

(NaCl, thin film) 3445, 2900, 1720, 1680, 1662, 1429, 1205, 1132, 1053, 1022, 778, 720 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{24}H_{20}O_4$; 372.1393, found: 372.1385.



(*R*)-1-ethynyl-1-phenylisochroman (2-97). Alkyne **2-89** was prepared via General Procedure 2 on a 0.20-mmol scale. To a solution of alkyne **2-89** (37.0 mg, 0.10 mmol, 1.0 equiv) and THF (2 mL, 0.05 M), tetrabutyl-ammonium fluoride (0.1 mL, 1 M, 1.0 equiv) was added. The reaction mixture was stirred at 0 °C for 12 h. After consumption of alkyne **2-89** as determined by TLC analysis, the mixture was filtered through a short pad of silica gel, which was then washed with CH_2Cl_2 (15 mL). The filtrate was concentrated, and the crude material was purified by silica gel chromatography (0–10% Et_2O/hexanes) to give compound **2-97** (24.0 mg, quantitative) as colorless oil. The enantiomeric excess was determined to be 80% by chiral HPLC analysis (CHIRALPAK IA, 0.2 mL/min, 0.1% *i*-PrOH/hexane, λ=210 nm); t_R(major) = 35.74 min, t_R(minor) = 33.52 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.59 (m, 2H), 7.36 – 7.31 (m, 3H), 7.21 – 7.16 (m, 2H), 7.12 – 7.08 (m, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 4.36 (ddd, *J* = 3.4, 11.2, 11.3 Hz, 1H), 4.18 – 4.13 (m, 1H), 3.25 – 3.17 (m, 1H), 2.88 (s, 1H), 2.80 (dt, *J* = 2.8, 16.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 139.2, 132.9, 128.9, 128.0, 127.92, 127.89, 127.5, 126.9, 126.2, 84.7, 77.7, 77.0, 61.4, 28.1; FTIR (NaCl, thin film) 3270, 3100, 3061, 2930, 1599, 1489, 1205, 1120, 1053, 703 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{17}H_{14}O$; 235.1123, found: 235.1123.

Nonlinear Effect Experiment

In a N_2-atmosphere glovebox, CuSPh (1.4 mg, 0.0083 mmol, 10 mol %) was weighed into a 1-dram vial. A mixture of the enantiomers of 2,6-bis(4-phenyl-4,5-dihydrooxazol-2-yl)pyridine (Ph-PyBox, **2-56**, total = 3.7 mg, 0.010 mmol, 12 mol %) and $CHCl_3$ (0.56 mL, 0.15 M) were added. The vial was capped with a septum-lined piercable cap. The mixture was stirred for 30 min at room temperature. Then phenylacetylene (11 μL, 0.10 mmol, 1.2 equiv), MTBD (1-methyl-2,3,4,6,7,8-hexahydro-1*H*-pyrimido[1,2-*a*]pyrimidine, 18.5 μL, 0.13 mmol, 1.55 equiv), and ketal **2-47** (20.0 mg, 0.080 mmol, 1.0 equiv) were added. The vial was again sealed with a septum-lined piercable cap, removed from the glovebox, and cooled to 0 °C. After 10 min, $BF_3{\cdot}OEt_2$ (21 μL, 0.16 mmol, 2.0 equiv) was added via syringe, and the mixture was stirred for 24 h at 4 °C.

entry	mol % (*R*)-Ph-PyBox	mol % (*S*)-Ph-PyBox	ee of catalyst	ee of product
1	6	6	0	0
2	7	5	17	62
3	8	4	33	69
4	9	3	50	74
5	10	2	67	77
6	11	1	84	79
7	12	0	100	80

The reaction mixture was diluted with Et_2O (2 mL) and filtered through a plug of silica gel, which was then washed with more Et_2O (10 mL). Analytical samples of product were then prepared via preparatory TLC (50% CH_2Cl_2/PhMe) and analyzed by HPLC using a chiral stationary phase.

Chapter 3

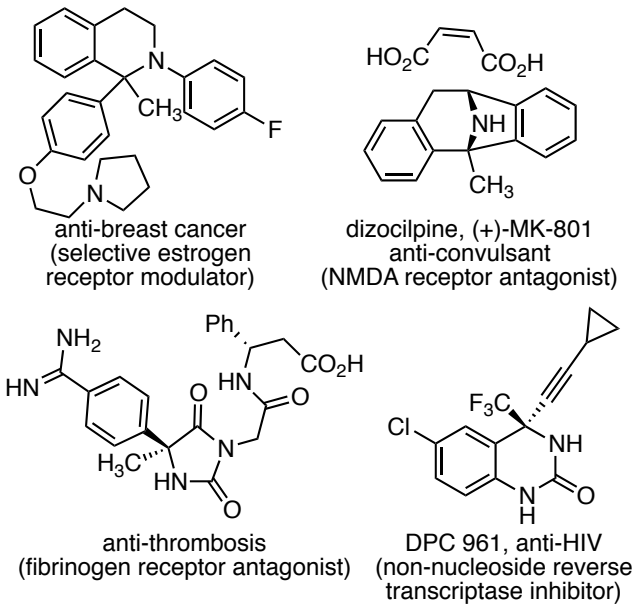
ENANTIOSELECTIVE, COPPER(I)-CATALYZED ALKYNYLATION OF IMINIUM IONS TO SET α,α-DIARYL, TETRASUBSTITUTED STEREOCENTERS

3.1 Introduction

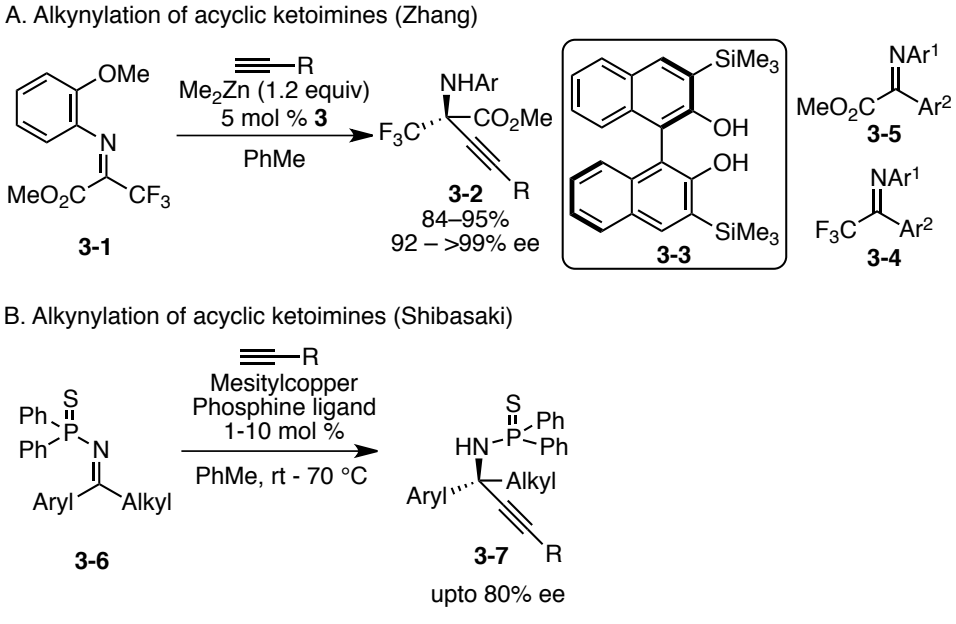
Alkyl amines represent prominent scaffolds in biologically active molecules. The importance of α-chiral cyclic amines in pharmaceuticals, natural products, and other bioactive molecules makes them relevant targets for synthesis. In particular, α-tetrasubstituted amines are known to show bio-activity against a range of diseases, including breast cancer, seizures, thrombosis and HIV (Fig.3.1).[68-70] A variety of synthetic routes are known to access α-trisubstituted amines. However there are extremely limited methods available to deliver highly enantioenriched amines with tetrasubstituted α-stereocenters.

A powerful approach for these compounds would be enantioselective addition to a ketoimine or iminium ion. Several carbon nucleophiles have been delivered via this strategy. The state-of-the-art in alkynylations of acyclic ketoimines utilizes ketoimines with trifluoromethyl and/or ester substituents (Scheme 3-1,A).[71-73] Enantioselective alkynylations of α-aryl-α-alkyl ketoimines have also been reported (Scheme 3-1,B).[74]

Figure 3.1: Bioactive ***α***- Tetrasubstituted Amines

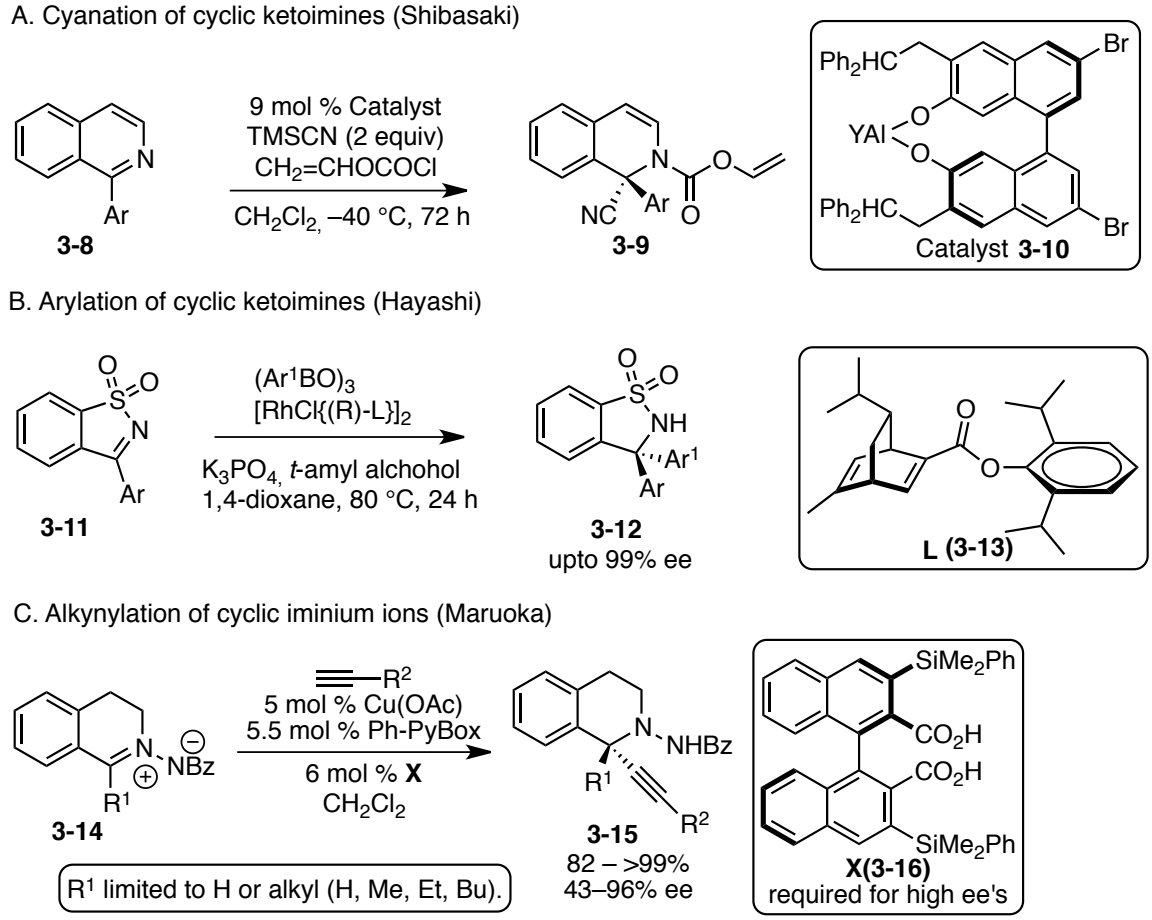


Scheme 3.1: Examples of Alkynylation of Acyclic Ketoimines to form Tetrasubstituted Stereocenters



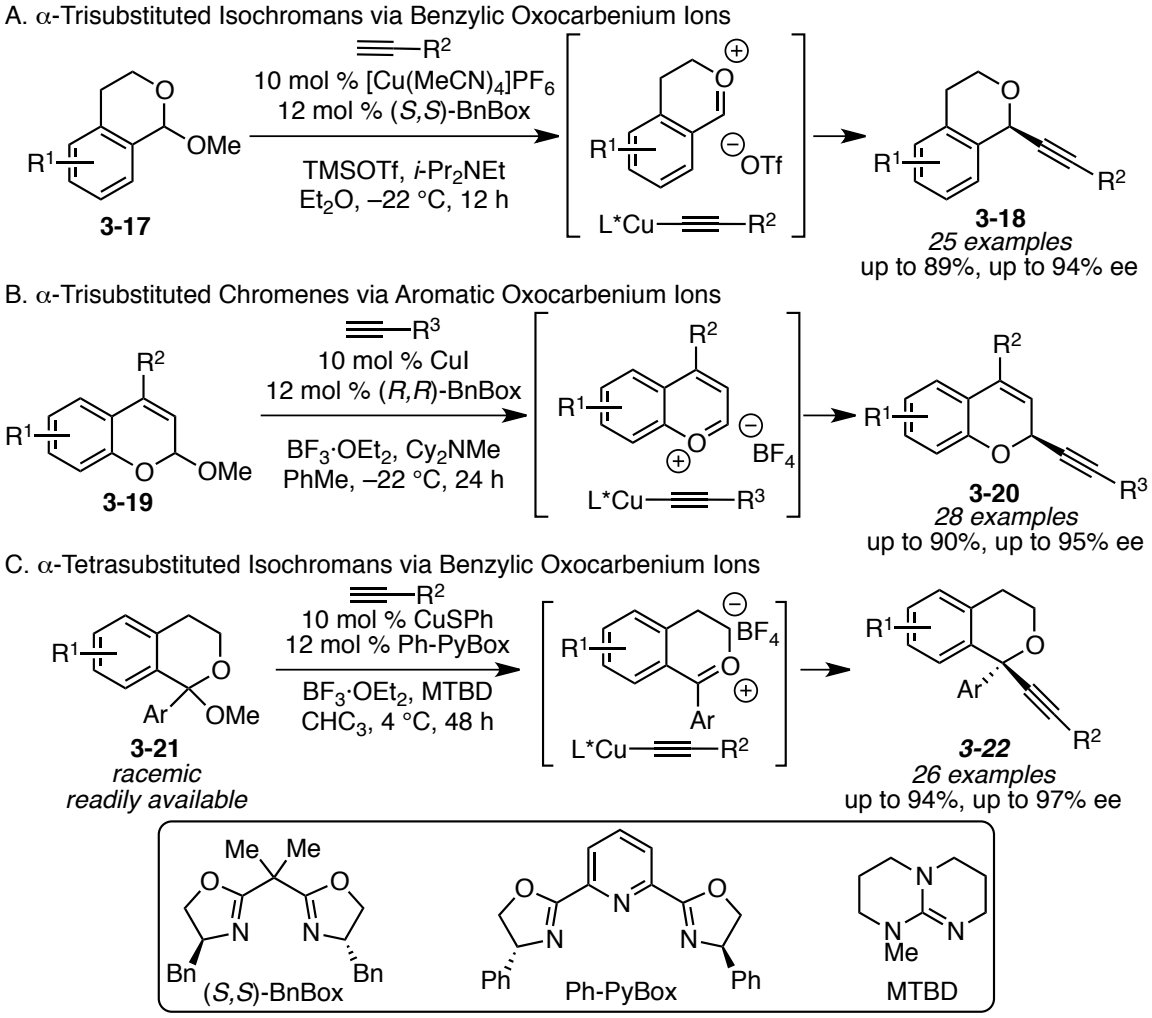
Although enantioselective reduction of α,α-diaryl ketimines have been accomplished,[75] currently enantioselective additions of cation nucleophiles to α,α-diaryl ketoimines require cyclic substrates, with one aryl group constrained in a ring. With this strategy, cyanation and arylation have been acco mplished in high ee's (Scheme 3.2, A and B).[76-78]

Scheme 3.2: Enantioselective Construction of Quaternary Stereocenters on Cyclic Ketimines



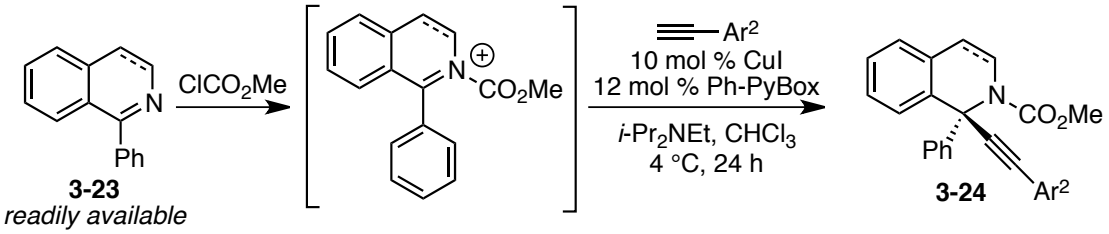
Also, Maruoka has shown that a Cu(Ph-PyBox)/Brønsted acid catalyst system enables alkynylation of alkyl-substituted isoquinolinium ions (Scheme 3.2 C).[79,80]. However this method is limited to alkyl-substituted isoquinolines and requires a chiral bronsted acid cocatalyst along with the chiral ligand, Ph-PyBox to form the tetrasubstituted alkynylated products in high enantiomeric excess

Scheme 3.3: Watson's Enantioselective Cu-Catalyzed Alkynylation of Oxocarbenium Ions



All methods mentioned above are limited to substrates with electronically and/or sterically different substituents on the electrophilic carbon as mentioned above.[81] Schreiber and group are the only ones who have shown one example of alkynylation of 1-phenyl substituted dihydroisoquinoliniums but without any stereoselection.[82] *Hence*, *no methods exist for enantioselective alkynylation of α,α-diaryl ketoimines or iminium ions with either cyclic or acyclic substrates to our knowledge*. Our group has demonstrated highly enantioselective, copper-catalyzed additions of alkynes to cyclic oxocarbenium ions, which are formed in situ from readily available, racemic acetals. In addition to α-trisubstituted products (Scheme 3.3 A–B)[32,33] in our group, I found a Cu/Ph-PyBox catalyst that enables high enantioselectivities in the formation of α-tetrasubstituted products (See Chapter 2).[83] Notably, the stereocenters formed are decorated with two aryl substituents, a highly challenging motif, and the catalyst must differentiate between these similar groups to provide high enantioselectivities. Excited by the potential generality of this catalyst, I have now developed analogous reactions of ketoiminium ions to form enantioenriched isoquinolines with diaryl, tetrasubstituted α-stereocenters (Scheme 3.4).

Scheme 3.4: Enantioselective Cu-Catalyzed Alkynylation to Form Isoquinolines with Tetrasubstituted Stereocenters

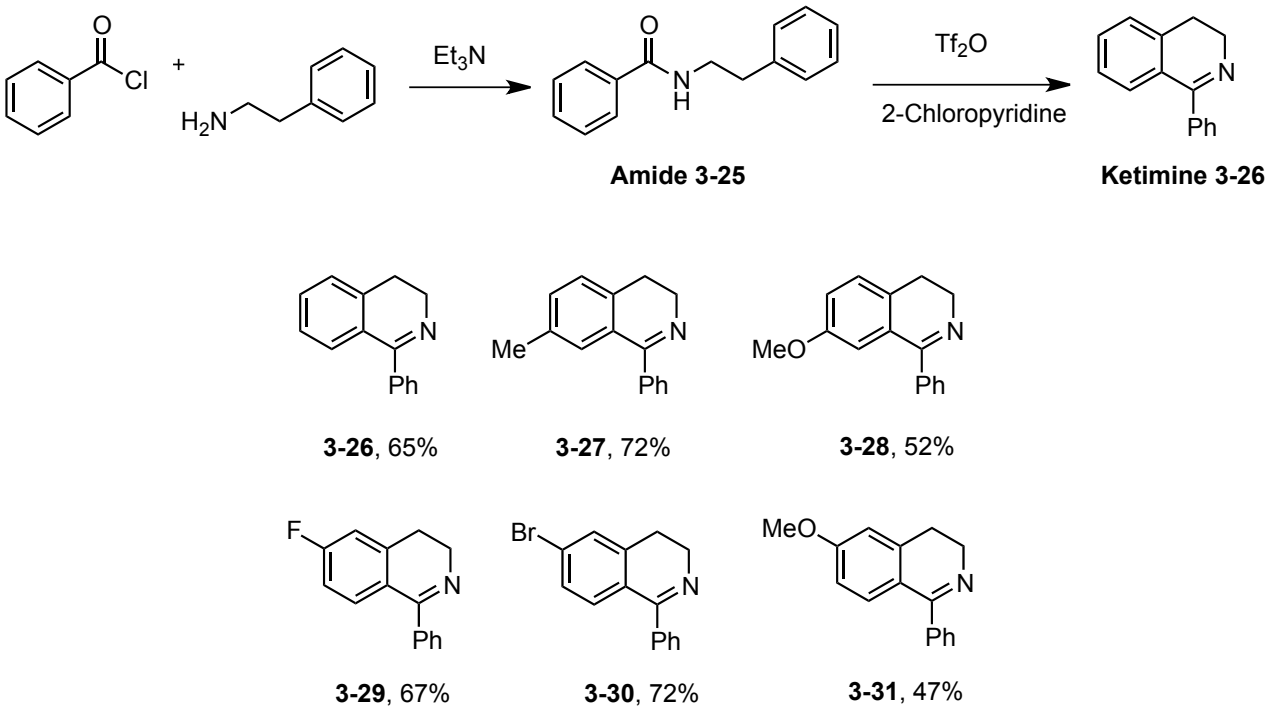


3.2 Results and Discussions

Synthesis of Isoquinoline Substrates

The isoquinoline substrates were synthesized in two steps from acid chlorides and amines. After amide formation, a Bischler-Napieralski reaction enables formation of isoquinoline **3-26** (Scheme 3.5). Because these cyclic imines are basic, it is safer to use deactivated silica gel for their purification. I have deactivated silica gel with 1% Et_3N on my columns. These ketimines are stable and can be stored at room temperature. Substrates synthesized via this route are shown in Scheme 3.5.

Scheme 3.5: Synthesis of Isoquinoline Substrates

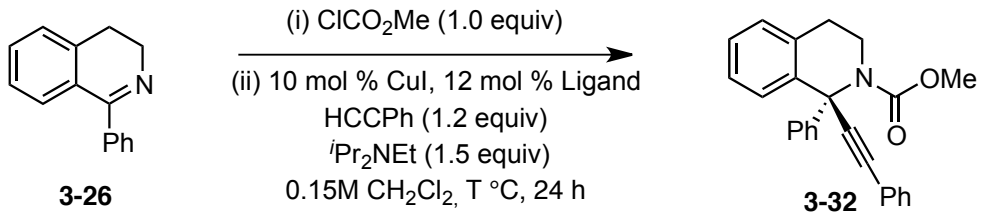


Optimization for Alkynylation of Ketimines

Isoquinoline **3-26** and phenylacetylene **2-62** were selected as model substrates for optimization of the alkynylation. Isoquinoline **3-26** was acylated in situ to generate an iminium ion (See Scheme 3.4, above). The solution of isoquinolinium ion was then transferred to a second vial containing the copper catalyst, alkyne, base and additional solvent. In the absence of ligands, CuI with Hunings base at room temperature gave an yield of 81% in solvent DCM (Table 3.1,entry 1). Use of other metal sources like Copper (tetrakis-acetonitrile) hexa-fluorophosphate and Copper thiophenolate showed lower reactivity (Table 3.1, entry 2,3). On investigating chiral ligands, Ph-PyBox (**L1**)

gave an initial enantioselectivity of 37% at room temperature (Table 3.1, entry 4). On decreasing the temperature to 4 °C, ligands

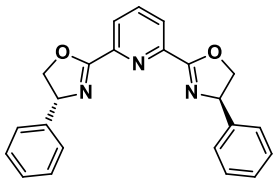
Table 3-1: Optimization of Alkynylation of Isoquinolines



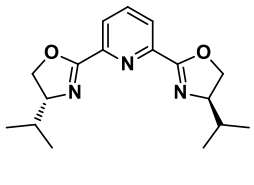
3-26 **3-32**

Entry	[Cu]	Ligand	T (°C)	Yield (%)	ee (%)
1	CuI	-	R.T.	81	-
2	$Cu(MeCN)_4PF_6$	-	R.T.	65	-
3	CuSPh	-	R.T.	50	-
4	CuI	L1	R.T.	85	37
5	CuI	L1	4	65	53
6	CuI	L2	4	89	20
7[b]	CuI	L1	4	72	19
8[c]	CuI	L1	4	60	0
9[d]	CuI	L1	4	80	89
10[d]	CuI	L1	-20	77	92
11[d,e]	CuI	L1	4	81	91
12[f]	CuI	L1	-20	64	83

[a]Conditions: Ketimine **3-26**(0.1 mmol, 1.0 equiv), [M] (0.01 mmol, 10 mol%), L*(0.012 mmol, 12 mol%), alkyne **2-62** (0.12 mmol, 1.2 equiv), Methylchloroformate (0.1 mmol, 1.0 equiv), base (0.15 mmol, 1.5 equiv), CH_2Cl_2 (0.15M), 24 h, unless otherwise noted, Yield determined by ^1H NMR analysis of crude mixture with internal standard 1,3,5-trimethoxybenzene, ee determined by standard HPLC analysis; [b] Et_3N used as base; [c] MTBD used as base, MTBD = 7-Methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene; [d] $CHCl_3$ as solvent; [e] 0.1M concentration; [f] Ethyl chloroformate used instead of methyl chloroformate in $CHCl_3$.



L1



L2

L1 and *i*-propyl-PyBox (**L2**) gave yields of 65% and 89% and ee's of 53% and 20% respectively (Table 3.1, entries 5 and 6). Because ligand **L1** showed better enantioselectivity, I pursued optimization of the other reaction parameters using the CuI/PhPyBox catalyst system. Other bases (Et_3N and MTBD) did not prove to be superior over Hunings base (Table 3.1, entries 7 and 8) and the formation of racemic . However changing solvent to $CHCl_3$ from DCM, increased both yield and enantioselectivity to 80 and 89% respectively (Table 3.1, entry 9). Having identified $CHCl_3$ as a promising solvent, I increased the enantioselectivity to 91% with a minute lowering in reactivity to 77% at a decreased temperature of -20 °C (Table 3.1, entry 10). Further we noticed that on diluting our solvent from 0.15M to 0.1M at 4 °C, we get favorable results of 81% yield and 91% enantioselctivity (Table 3.1, entry 11). I also tested other acylating agents and saw that ethylchloroformate showed poorer reactivity and selectivity compared to methyl chloroformate (Table 3.1, entry 12).

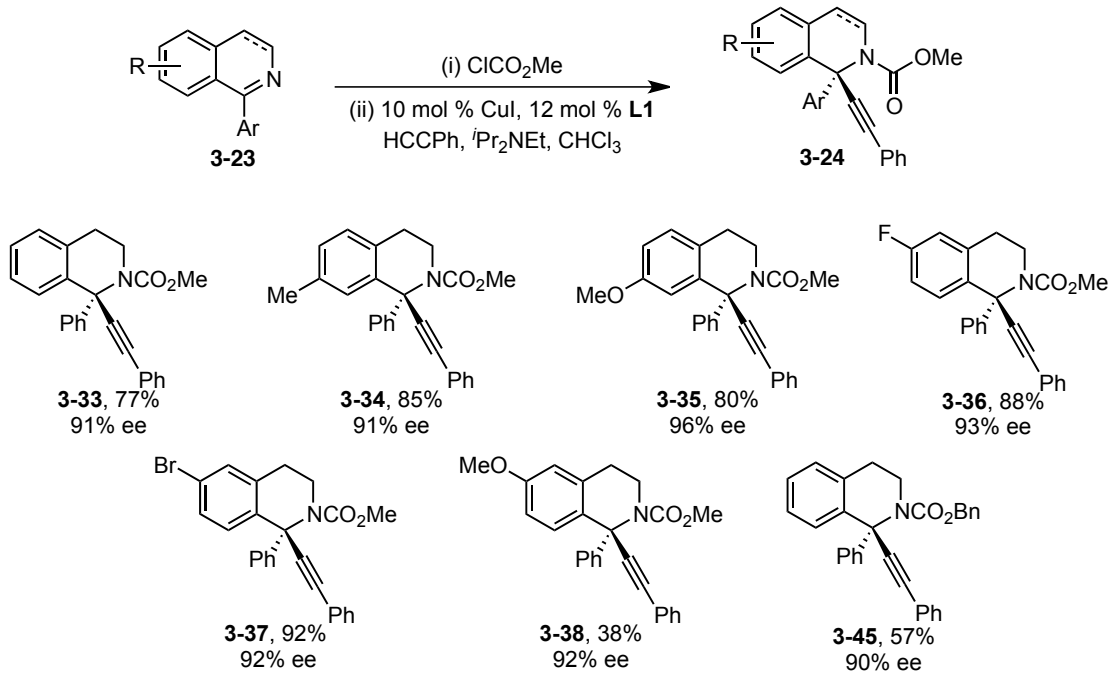
Substrate Scope

Scope on the Ketimine

Under these optimized conditions (Table 3.1, entry 11), a wide variety of isoquinolines reacted with phenyl acetylene in high yields and enantioselectivities (Scheme 3.6 and 3.7). With respect to substitution of the isoquinoline, substrates with electron-donating and electron-withdrawing groups on the 7 position of the isoquinoline show great reactivity and selectivity (Scheme 3.6, **3-34 - 35**). However poor reactivity is observed in the case of electron-donating substituents at the 6

position (**3-38**). This is probably due to the iminium ion being stabilized by the para position electron-donating methoxy group leading to lower reactivity. However high ee is obtained in this case with diluting the solvent to 0.05M. Halides are also well tolerated at the 6 position (**3-36 – 3-37**). I also observed that the acylating agent, benzylchloroformate works great in our system in place of methylchloroformate (**3-45**).

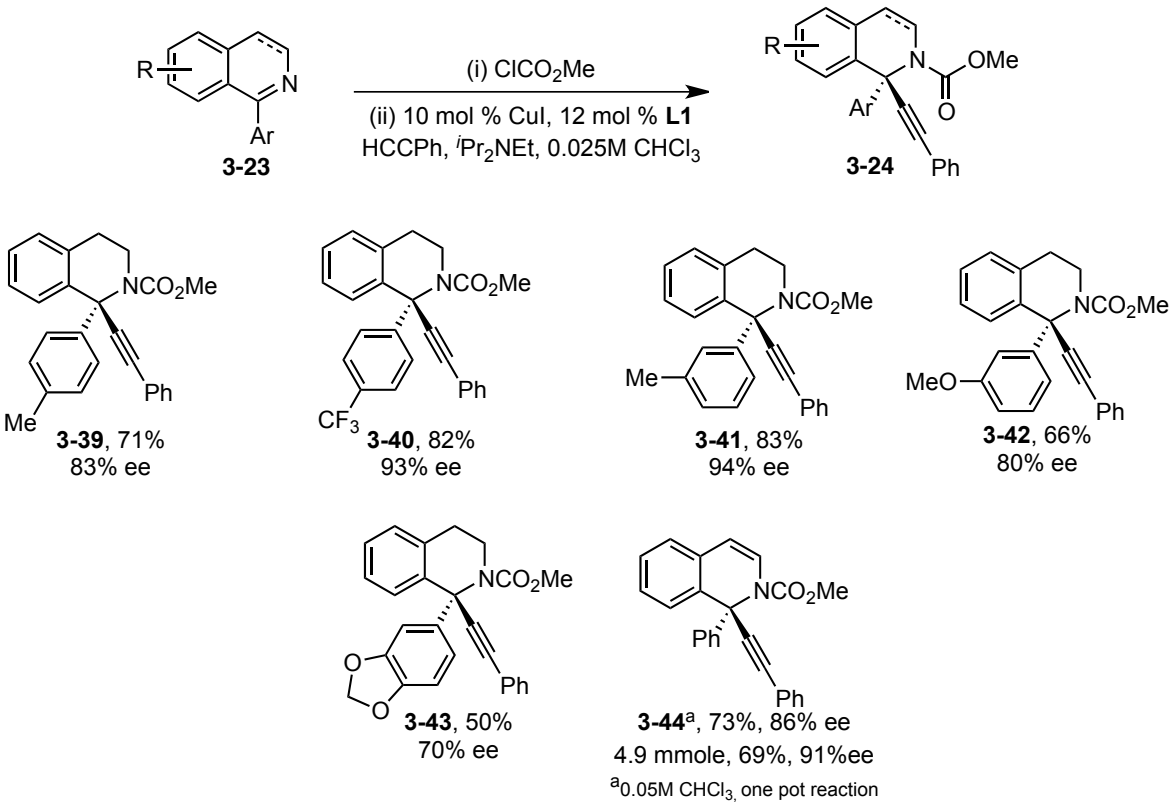
Scheme 3.6: Scope of the Isoquinoline



My colleague Jixin Liu and an undergraduate REU student Clarissa Schoffler also demonstrated broad scope in the 1-aryl substituent of the isoquinoline (Scheme 3.7). We observed high yields and ee's for electron-donating and electron-withdrawing groups at both meta and para positions (Scheme 3.7, **3-39** and **3-42**). An

acetal-substituted aryl group has shown modest reactivity and selectivity (**3-43**). Notably, alkynylation of aromatic isoquinolinium ions is also possible using our conditions (**3-44**).

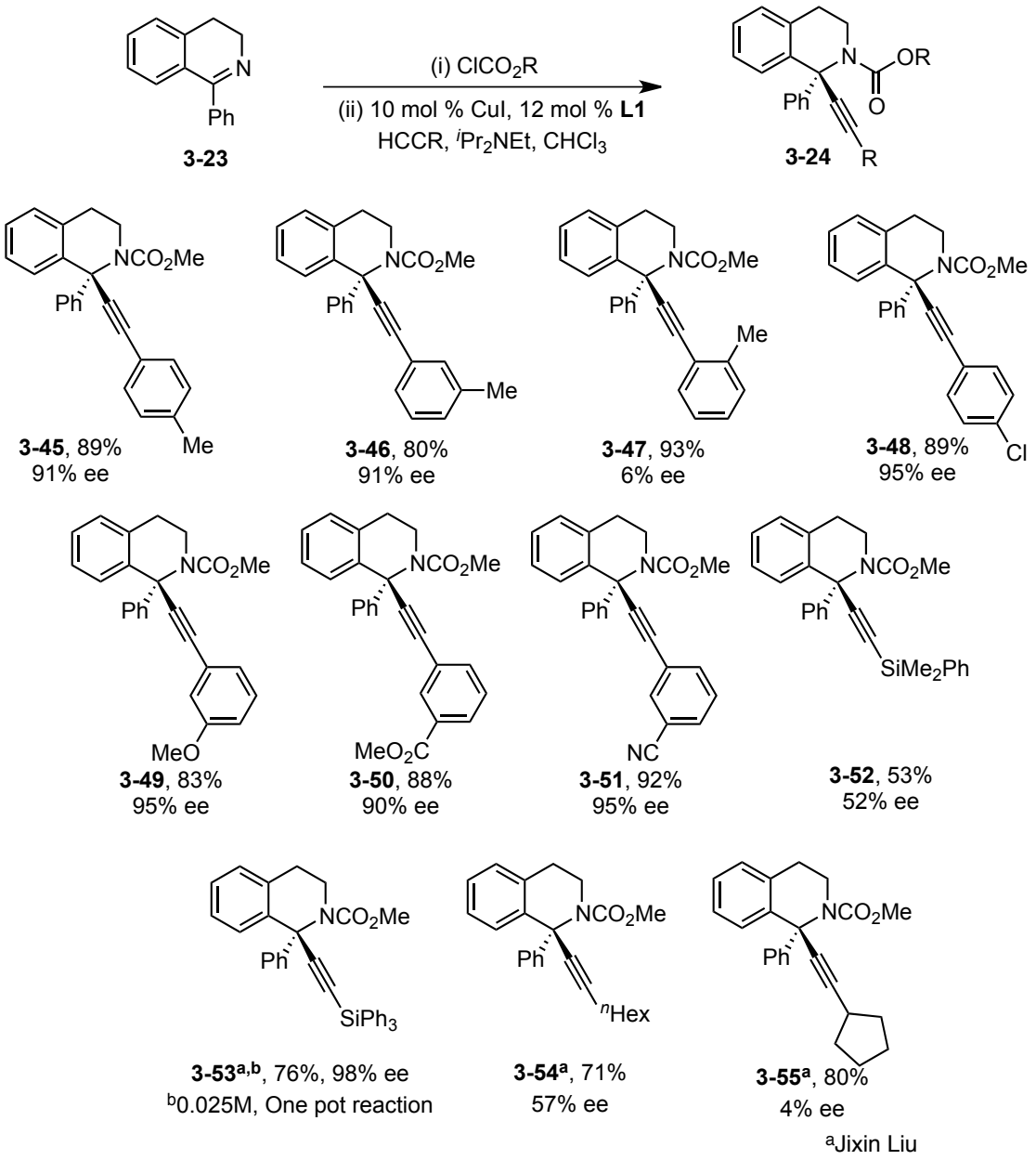
Scheme 3.7: Scope of the 1-Aryl Substituent



Scope of the Alkyne

Good yields and high enantioselectivities were observed using a wide range of aryl acetylenes with isoquinoline **3-23** (Scheme 3.8). Electron-donating groups at both meta and para positions of the arene worked great (**3-45**, **3-46**). The enantio-selectivity with an ortho tolyl group was however poor, likely indicating steric intolerance (**3-47**).

Scheme 3.8: Scope of the Alkyne



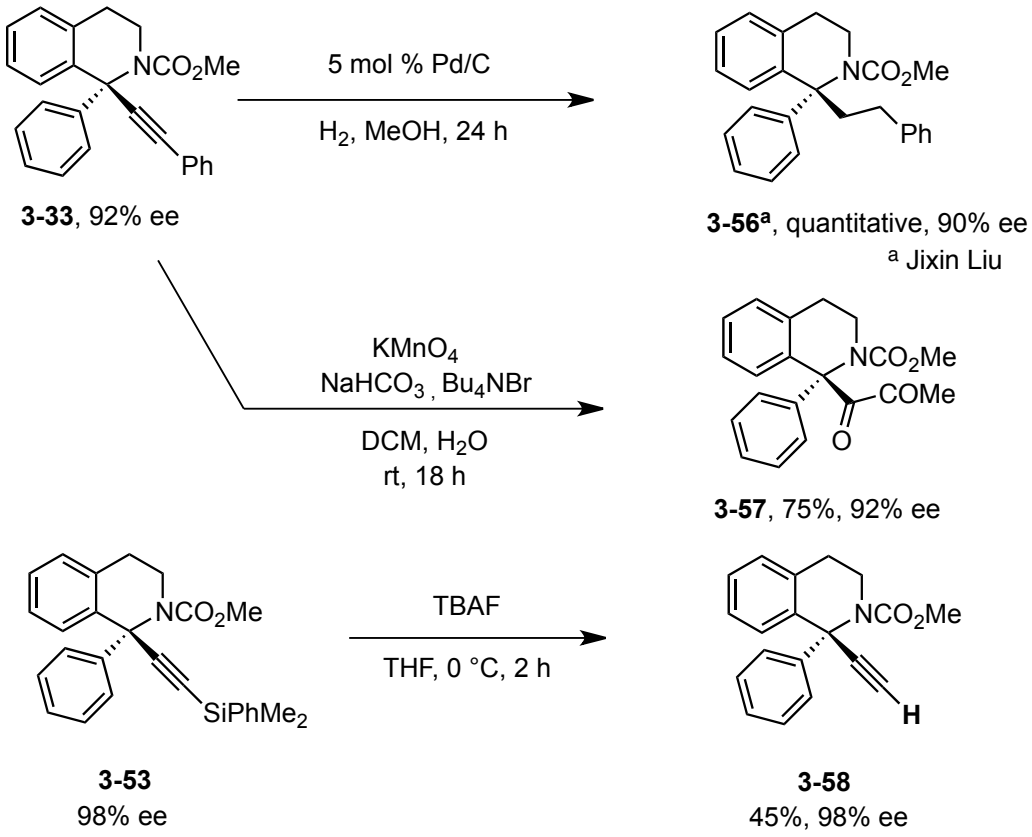
Electron-withdrawing groups at both meta and para positions were well tolerated like methoxy (**3-49**), ester (**3-50**),cyano (**3-51**), and halide (**3-48**). With

respect to alkyl-substituted alkynes, my colleague, Jixin Liu observed that addition of 1-octyne gave modest yield and enantioselectivity (**3-54**). Low enantioselectivity was also observed in the addition of cyclopentylacetylene (**3-55**). Silyl acetylenes also underwent addition. (Dimethylphenylsilyl)acetylene showed modest reactivity and selectivity giving 53% yield and 52% ee of silyl-protected acetylene **3-52**. Triphenylsilyl protected acetylenes however worked great in our system giving (**3-53**) in 76% yield and 98% ee.

Elaboration of Products

The alkyne products can be easily elaborated. Jixin Liu demonstrated that reduction of alkyne **3-33** gives alkyl-substituted isoquinoline **3-56** in quantitative yield and high enantiopurity (Scheme 3.9). I showed that oxidation of product **3-33** to diketone **3-57** was accomplished in 75% yield and perfect stereochemical fidelity.[50] I was unable to further oxidize the diketone to the carboxylic acid however, probably due to steric crowding at the α-sterocenter of the isoquinoline. Finally, I was also able to show that the deprotection of silyl acetylene **3-53** was accomplished in 45% yield and perfect stereochemical fidelity to deliver terminal alkyne **3-58**.

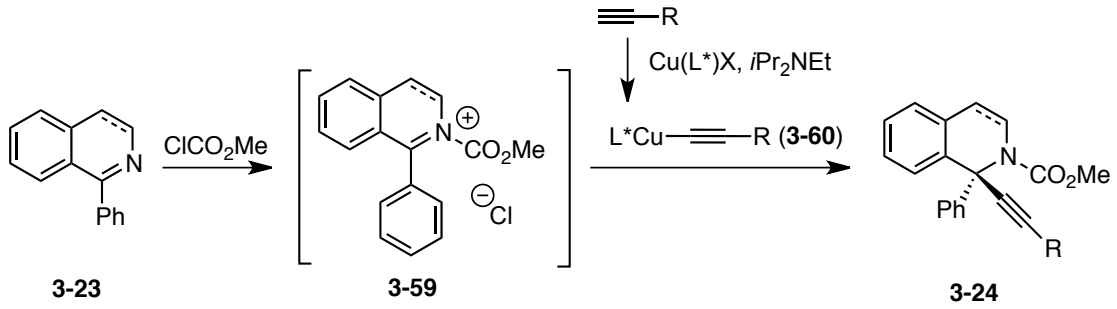
Scheme 3.9: Elaboration of Products



3.3 Proposed Mechanism and Investigation of Catalyst Aggregation

My working mechanistic hypothesis is shown in Scheme 3.10. The reaction likely proceeds via initial formation of copper acetylide (**3-60**), which then attacks the iminium ion intermediate (**3-59**) generated from ketimine **(3-23)** in the presence of methyl chloroformate.

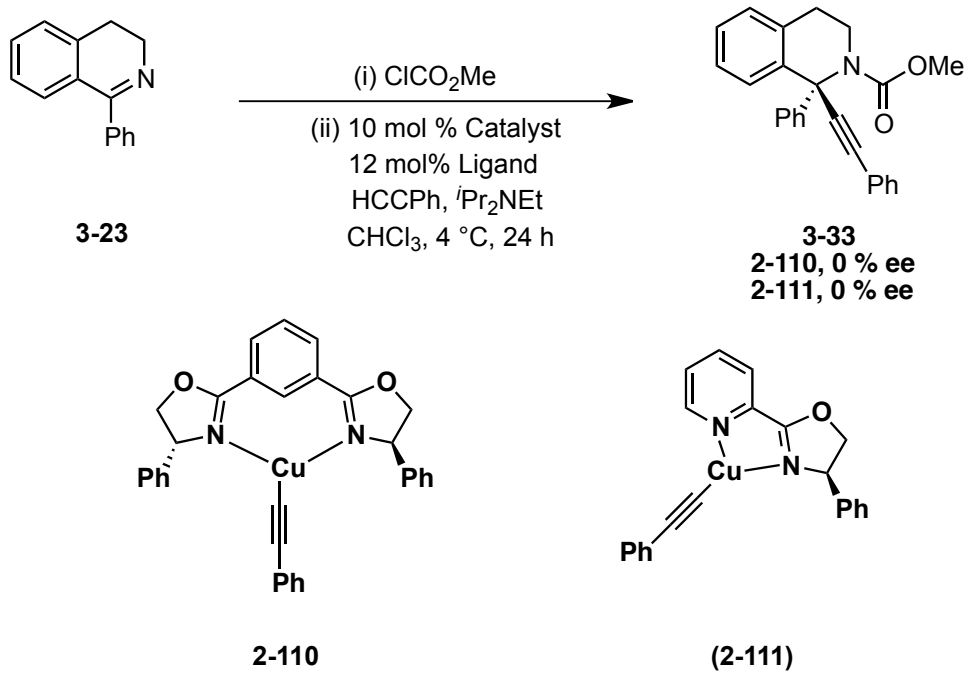
Scheme 3.10: Proposed Mechanism



We are currently investigating how the copper/Ph-PyBox catalyst imparts enantioselectivity in this reaction. The enantiodetermining step is likely the C–C bond formation (Scheme 3.10). To understand this step, we must determine the structure of copper acetylide **3-60**. In our tetrasubstituted oxocarbenium project (Chapter 2), we observed a positive nonlinear effect exhibited by our catalyst system suggesting dimeric (or other higher order) copper/Ph-PyBox catalyst species. Also, dinuclear copper catalysts have been proposed to proceed via dicopper acetylide intermediates in related reactions.[55-59] In this current system too, we hypothesize that we may have a dimeric copper/Ph-PyBox active catalyst. The possibility of a four-coordinate square planar copper(I) complex is improbable due to steric crowding, and likely not the active complex in this case too (Figure 2.4). As for the oxocarbenium ion case, we considered that Ph-PyBox may act instead as a bidentate ligand, with either the pyridine or one oxazoline arm dissociating, but our model ligands for these types of coordination geometries resulted in racemic products (Scheme 3.11).[53,54] Cu_2(Ph-PyBox)$_2$(X)$_2$ complexes have been previously reported,[55,60,61] and I synthesized Cu_2(Ph-PyBox)$_2$(I)$_2$ (**3-61**) in 49% yield (Scheme 3.12). I have also obtained a crystal

structure of this complex as a metal cluster (Figure 3.2). Ignoring any Cu-Cu interaction, each Cu atom in the complex is in a tetrahedral coordination environment except for the four Cu atoms in the anion which are trigonal planar. On testing this complex as a catalyst under our reaction conditions, isoquinoline **3-33** was formed in 83% yield (NMR) and 93% ee which is what we usually observe insitu under our normal reaction conditions (Scheme 3.11).

Scheme 3.11: Reactivity of Other Ligands



Scheme 3.12: Synthesis and Reactivity of $Cu_2(Ph\text{-}PyBox)_2(I)_2$

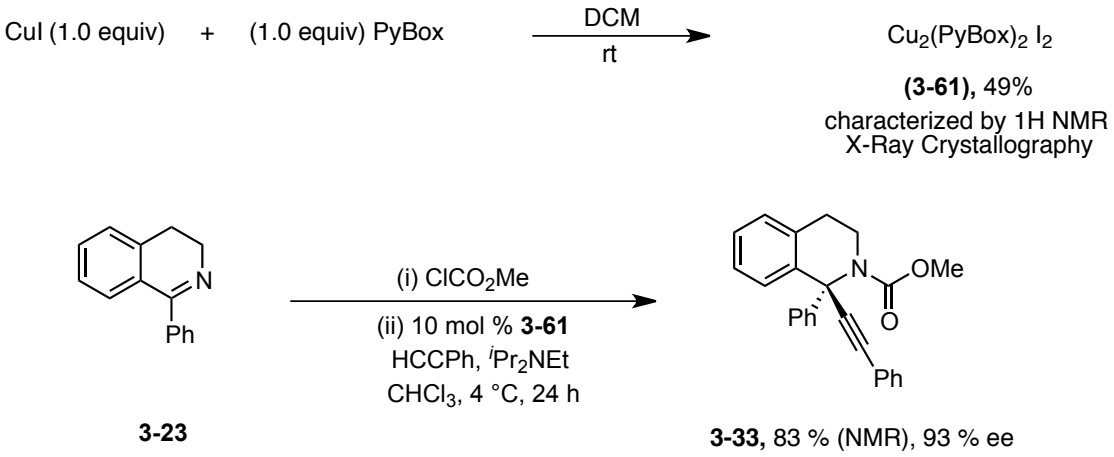
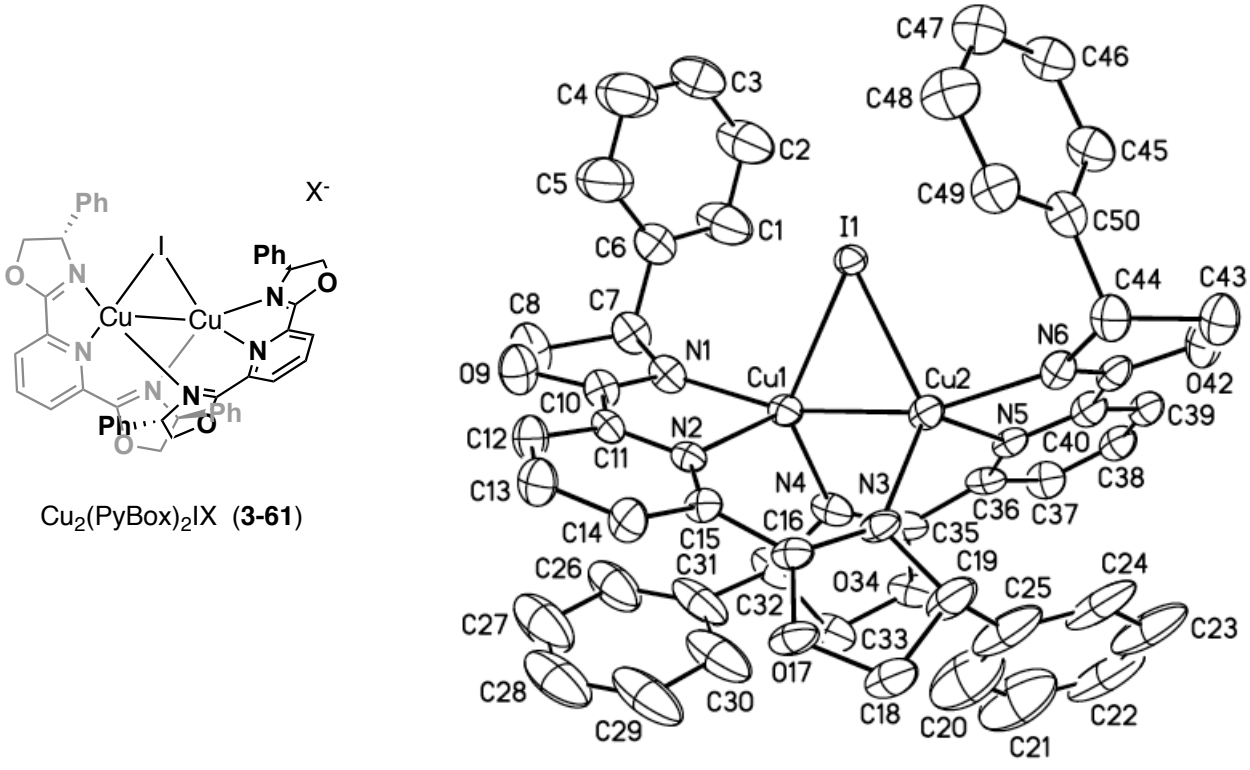


Figure 3.2 : X-ray crystal structure of $Cu_2(Ph\text{-}PyBox)_2I_2$



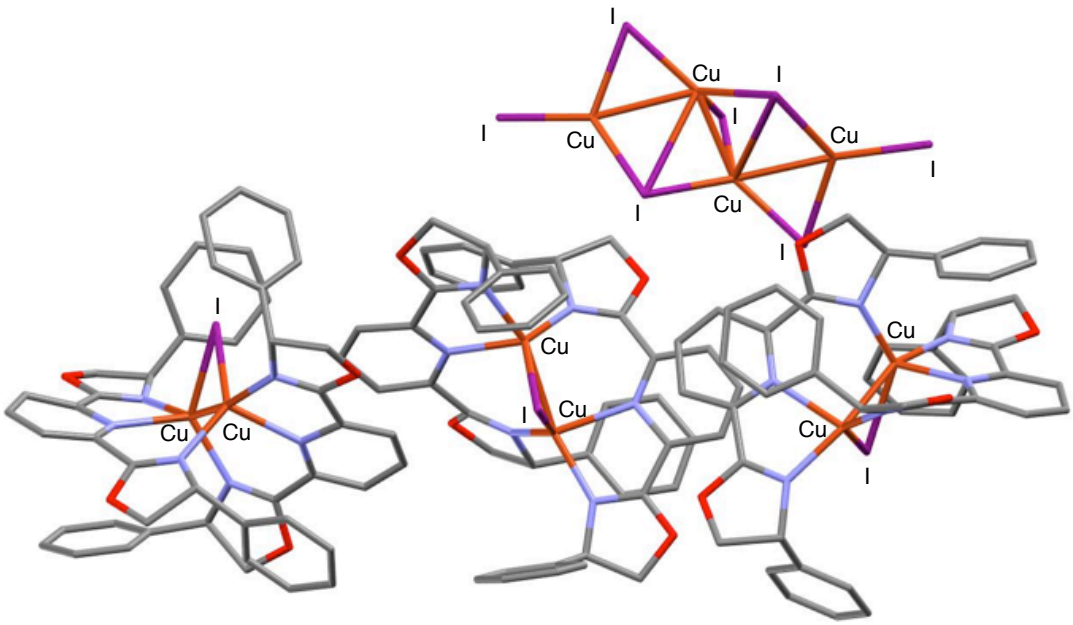
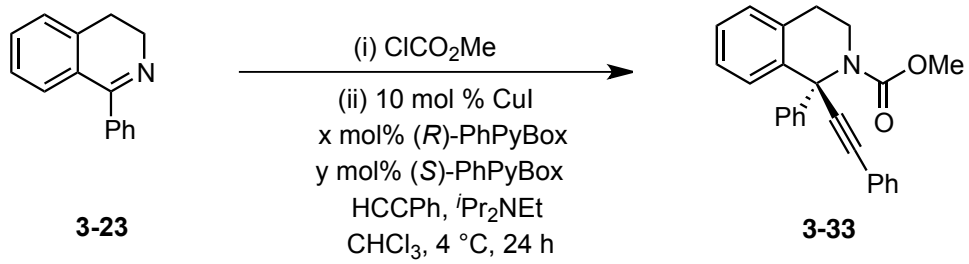
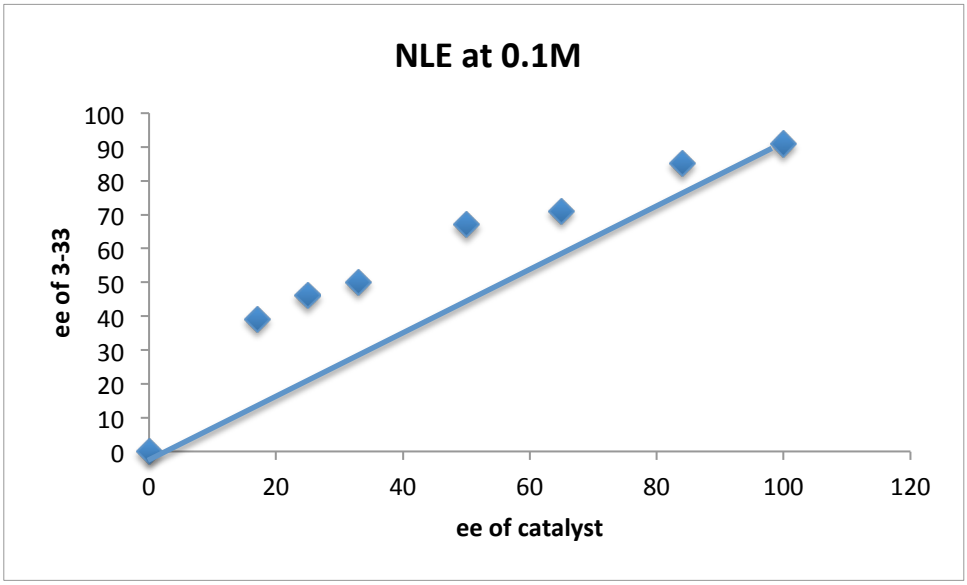


Figure 3.2 : Molecular diagram of **3-61** with ellipsoids at 30% probability. H-atoms omitted for clarity.

Figure 3.3: Non Linear Effects at 0.1 M



3-23 **3-33**

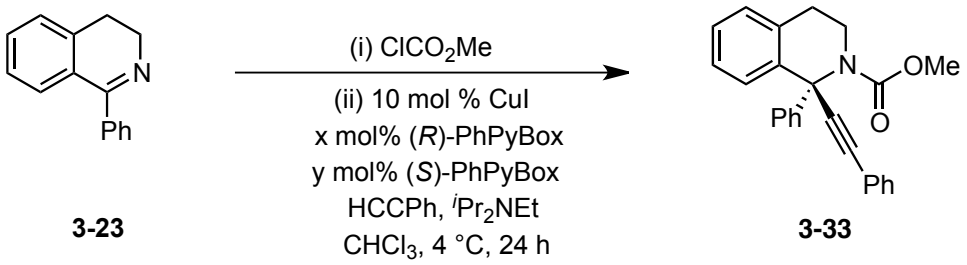


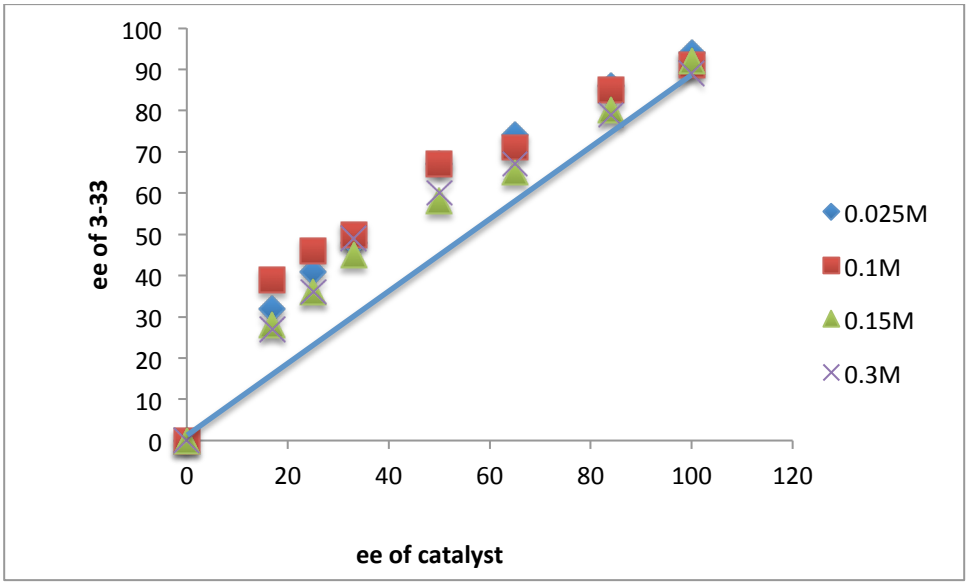
Consistent with the presence of higher order copper/Ph-PyBox species, a positive nonlinear correlation is observed between the ee of catalyst and ee of product (Fig. 3.3).[62] Although this data does not exclude the possibility that these higher order copper species may exist in an off-cycle reservoir, we currently favor a dicopper acetylide intermediate, given their importance in other copper acetylide chemistry.[55-59]

As discussed in our optimization, we observed that decreasing the reaction concentration increases enantioselctivity in our system. This result suggests a change in the active catalyst under different concentrations. Hence I conducted Non Linear Effect experiments under different concentrations and observed a positive deviation from linearity in all cases (Figure 3.4). The highest ee's are observed under the most dilute conditions (0.025 M). These experiments indicate that there is an aggregation of

catalyst in our system and each catalyst has same selectivity under various concentrations, but the concentrations of the catalysts change. Due to the complex nature of this system , we cannot propose a stereochemical model yet, but we favor a dimeric copper/PhPyBox acetylide like active catalyst in our system based on our experimental observations and previous precedents in the literature.

Figure 3.4: Comparative NLE at Different Concentrations





3.4 Summary

In summary, I have developed the first example of an enantioselective addition of alkynes to iminium ions to form α,α–diaryl tetrasubstituted stereocenters. We have demonstrated a diverse substrate scope. Under the optimized conditions, a variety of isoquinolines and alkynes underwent the reaction in good to excellent yields and enantioselectivites. We also have preliminary results on copper/Ph-PyBox dimeric catalyst in our reaction system. I am now preparing a manuscript describing this work and plan to submit it in the fall of 2015.

3.5 Experimental Procedure

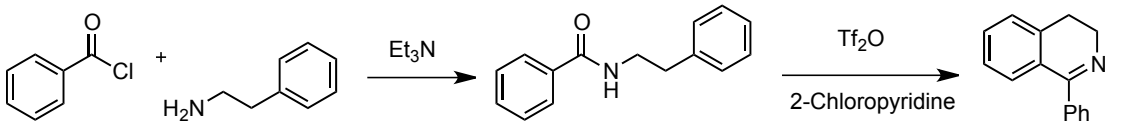
General Information

Reactions were performed either in a N_2-atmosphere glovebox in oven-dried 1-dram vials with Teflon-lined caps or in oven-dried round-bottomed flasks unless otherwise noted. Flasks were fitted with rubber septa, and reactions were conducted under a positive pressure of N_2. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed on silica gel 60 (40-63μm, 60Å). Thin layer chromatography (TLC) was performed on glass plates coated with silica gel 60 with F254 indicator. Commercial reagents were purchased from Sigma Aldrich, Acros, Fisher, Strem, or Cambridge Isotopes Laboratories and used as received with the following exceptions: tetrahydrofuran, CH_2Cl_2, and Et_2O were dried by passing through drying columns.[84] MeOH, *i*-Pr_2NEt was distilled from CaH_2. $CHCl_3$ and Methylchloroformate were purchased in sure-seal bottles. $CHCl_3$

and *i*-Pr_2NEt were stored in a N_2-atmosphere glovebox and used as such. $CDCl_3$ was stored over oven-dried potassium carbonate. Alkynes were degassed before use by either freeze-pump-thaw cycles or sparging with N_2. Proton nuclear magnetic resonance (^1H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on 400 MHz spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$ = δ 77.07). Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), integration. Infrared (IR) spectra were obtained using FTIR spectrophotometers with material loaded onto a NaCl plate. The mass spectral data were obtained at the University of Delaware spectrometry facility. Optical rotations were measured using a 2.5 mL cell with a 0.1 dm path length. 3-(Cyano)phenylacetylene[85] and methyl 3-ethynylbenzoate[86] were prepared as described in the literature[32].

Preparation of Ketimine Substrates

General Procedure 1: Preparation of 1-phenyl-3,4-dihydroisoquinoline (3-26).

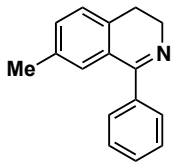


Amide 3-25 **Ketimine 3-26**

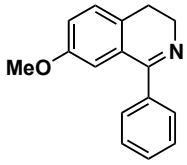
A solution of 2-phenylethanamine (4.2 g, 39.1 mmol, 1.1 equiv), triethylamine (5.4 mL, 46.2 mmol, 1.3 equiv), and CH_2Cl_2 (20 mL, 0.3 M) was cooled to 0 °C. Freshly distilled benzoyl chloride (3.46 mL, 35.6 mmol, 1.0 equiv) was slowly added. A precipitate immediately formed. The reaction mixture was warmed to room temperature and then further stirred for 1 h. H_20 (20 mL) was added. The mixture was extracted with EtOAc (30 mL). The organic layer was washed with sat. NaCl (10 mL), dried ($MgSO_4$), filtered and concentrated to give amide **3-25** (5.74 g, 86%). The spectral data for **3-25** matches that reported in the literature.[87]

A stirred mixture of amide **3-25** (1.778 g, 7.9 mmol, 1.0 equiv), 2-chloropyridine (0.90 mL, 9.5 mmol, 1.2 equiv), and CH_2Cl_2 (40 mL, 0.2 M) was cooled to –78 °C. Trifluoromethanesulfonic anhydride (1.46 mL, 8.7 mmol, 1.1 equiv) was added via syringe over 1 min. After 5 min, the reaction mixture was placed in an ice-water bath and warmed to 0 °C which was then allowed to warm up to room temperature. Upon consumption of amide **3-25** as determined by TLC, aq. NaOH (1 M, 10 mL) and then H_2O (20 mL) were added. The mixture was extracted with EtOAc (30 mL). The organic layer was washed with sat. NaCl (10 mL), dried ($MgSO_4$), filtered and concentrated. The crude material was purified by silica gel chromatography (10–15 % EtOAc/hexanes with 1% Et_3N) to give amine **3-26** (1.1 g, 65%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.56 (m, 2H), 7.48 – 7.33 (m, 4H), 7.31 – 7.20 (m, 3H), 3.92 – 3.79 (m, 2H), 2.89 – 2.75 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 139.0, 138.9, 130.7, 129.3, 128.8, 128.8, 128.2, 127.9, 127.4, 126.6, 47.7, 26.3; FTIR

(NaCl, thin film) 2938, 1608, 1565, 1445, 1351, 1304, 1286, 1189, 1020, 745, 501, cm^{-1}; HRMS (EI+) [M+] calculated for $C_{15}H_{13}N$; 208.1126, found: 208.1120.

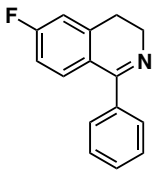


7-Methyl-1-phenyl-3,4-dihydroisoquinoline (3-27). Prepared via General Procedure 1 on a 4.2 mmol scale. The amide *N*-(4-methylphenethyl)benzamide was obtained as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.67 (m, 2H), 7.52 – 7.45 (m, 1H), 7.41 (ddt, *J* = 8.3, 6.7, 1.4 Hz, 2H), 7.14 (s, 4H), 6.11 (s, 1H), 3.71 (td, *J* = 6.9, 5.8 Hz, 2H), 2.90 (t, *J* = 6.8 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 136.2, 135.8, 134.7, 131.4, 129.4, 128.7, 128.6, 126.8, 41.2, 35.3, 21.1; Compound **3-27** was purified by silica gel chromatography (10–15% EtOAc/hexanes) and obtained as a yellow oil (0.678 g, 72%); ^{1}H NMR (400 MHz, $CDCl_3$) δ7.63 – 7.57 (m, 2H), 7.48 – 7.40 (m, 3H), 7.23 – 7.18 (m, 1H), 7.16 (d, *J* = 7.7 Hz, 1H), 7.10 – 7.05 (m, 1H), 3.86 – 3.80 (m, 2H), 2.76 (dd, *J* = 8.5, 6.1 Hz, 2H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 139.2, 136.2, 135.8, 131.3, 129.2, 128.8, 128.7, 128.4, 128.1, 127.2, 47.9, 25.9, 21.2; FTIR (NaCl, thin film) 1557, 1410, 1220, 1189, 1079, 541, 422 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{16}H_{15}N$; 222.1256, found: 222.1279.

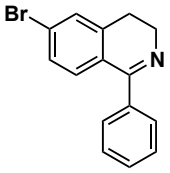


7-Methoxy-1-phenyl-3,4-dihydroisoquinoline (3-28). Prepared via General Procedure 1 on a 2.17 mmol scale. Crude material was purified by silica gel chromatography (10–15% EtOAc/hexanes) to give compound **3-28** (0.372 g, 52%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.58 (m, 2H), 7.46 – 7.40 (m, 3H), 7.19 (d, *J* = 8.3 Hz, 1H), 6.95 (dd, *J* = 8.2, 2.7 Hz, 1H), 6.82 (d, *J* = 2.6 Hz, 1H), 3.85 – 3.81 (m, 2H), 3.73 (s, 3H), 2.77 – 2.71

(m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 158.4, 138.2, 130.5, 129.5, 129.1, 128.5, 128.2, 127.9, 116.6, 113.8, 54.4, 47.0, 24.7; FTIR (NaCl, thin film) 1506, 1457, 1248, 1109, 551, 425 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{16}H_{15}NO$; 238.1232, found: 238.1231

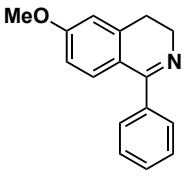


6-Fluoro-1-phenyl-3,4-dihydroisoquinoline (3-29). Prepared via General Procedure 1 on a 4.7 mmol scale. Crude material was purified by silica gel chromatography (10–15% EtOAc/hexanes) to give compound **3-29** (0.703 g, 67%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.56 (m, 2H), 7.49 – 7.39 (m, 3H), 7.32 – 7.27 (m, 1H), 7.00 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.94 (td, *J* = 8.6, 2.6 Hz, 1H), 3.89 – 3.82 (m, 2H), 2.88 – 2.78 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 163.7 (d, *J* = 250.0 Hz), 141.9 (d, *J* = 8.8 Hz), 138.8, 130.17 (d, *J* = 8.6 Hz), 129.4, 128.7, 128.2, 125.3 (d, *J* = 3.1 Hz), 114.5 (d, *J* = 21.7 Hz), 113.34 (d, *J* = 21.5 Hz), 47.3, 26.55; FTIR (NaCl, thin film) 1636, 1558, 1456, 1228, 1100, 545, 413 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{15}H_{12}FN$; 225.0965, found: 225.0965



6-bromo-1-phenyl-3,4-dihydroisoquinoline (3-30). Prepared via General Procedure 1 on a 3.29 mmol scale. The amide *N*-(3-bromophenethyl)benzamide was obtained as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.65 (m, 2H), 7.53 – 7.47 (m, 1H), 7.46 – 7.35 (m, 3H), 7.27 – 7.14 (m, 3H), 6.11 (s, 1H), 3.71 (td, *J* = 7.0, 6.0 Hz, 2H), 2.92 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 141.3, 134.5, 131.9, 131.6, 130.3, 129.8, 128.7, 127.5, 126.8, 122.7, 40.9, 35.4. Compound **3-30** was purified by silica gel

chromatography (10–15% EtOAc/hexanes) and obtained as a yellow oil (0.678 g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.53 (m, 2H), 7.47 – 7.36 (m, 4H), 7.25 (s, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 3.89 – 3.80 (m, 2H), 2.79 (dd, *J* = 8.5, 6.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 66.5, 140.9, 138.5, 130.5, 129.8, 129.6, 129.4, 128.7, 128.3, 127.6, 124.8, 47.4, 26.1; FTIR (NaCl, thin film) 3438, 2920, 2850, 1958, 1701, 1557, 1446, 1319 cm^{-1}.



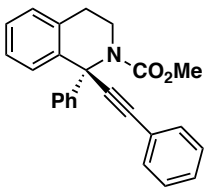
6-methoxy-1-phenyl-3,4-dihydroisoquinoline (3-38). Prepared via General Procedure 1 on a 1.96 mmol scale. The amide *N*-(3-bromophenethyl)benzamide was obtained as a white solid. The spectral data for **S7a** matches that reported in the literature.[88] Compound **3-38** was purified by silica gel chromatography (10–15% EtOAc/hexanes) and obtained as a yellow oil (0.219 g, 47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.63 (m, 2H), 7.48 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.31 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.25 – 7.19 (m, 4H), 7.19 – 7.07 (m, 4H), 4.40 (dt, *J* = 12.8, 4.5 Hz, 1H), 3.79 (ddd, *J* = 13.0, 10.3, 3.2 Hz, 1H), 3.55 (s, 3H), 3.26 (ddd, *J* = 15.0, 10.2, 4.2 Hz, 1H), 3.09 – 2.98 (m, 1H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 66.8, 161.2, 141.1, 139.2, 129.8, 129.2, 128.8, 128.1, 122.4, 112.9, 111.5, 55.4, 47.6, 26.9; FTIR (NaCl, thin film) 1558, 1436, 1220, 1189, 1020, 541, 422 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{16}H_{15}NO$; 237.1154, found: 237.1170

Enantioselective Alkynylation of Isoquinolines

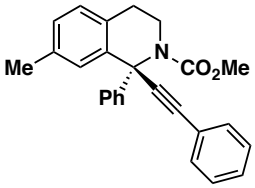
Racemic products were obtained using catalytic CuI, *i*-Pr_2NEt and CH_3COOCl in $CHCl_3$ at room temperature.

General Procedure 2: Enantioselective Alkynylation

In a N_2-atmosphere glovebox, isoquinoline **3-26** (0.30 mmol, 1.0 equiv) and $CHCl_3$ (1.5 mL) were combined in a 1-dram vial. This vial (vial A) was sealed with a septum-lined piercable cap and removed from the glovebox. Methyl chloroformate (23 μL, 0.30 mmol, 1.0 equiv) was then added dropwise. The reaction mixture was stirred for 1 h at room temperature and then cooled to 0 °C. In a N_2-atmosphere glovebox, CuI (5.7 mg, 0.03 mmol, 10 mol %), 2,6-bis((*R*)-4-phenyl-4,5-dihydrooxazol-2-yl)pyridine (Ph-PyBox, **L1**, 13.3 mg, 0.024 mmol, 12 mol %) and $CHCl_3$ (1.0 mL) were combined in a 2-dram vial (vial B). Vial B was capped with a septum-lined piercable cap, and the mixture was stirred for 30 min at room temperature inside the glove box. After 30 min, alkyne (0.36 mmol, 1.2 equiv) and *i*-Pr_2NEt (79 μL, 0.45 mmol, 1.5 equiv) were added to vial B. Vial B was again capped, removed from the glovebox, and cooled to 0 °C. After 10 min, the cooled mixture from vial A was transferred slowly via syringe to vial B. Vial A was rinsed with $CHCl_3$ (0.5 mL), which was then added to vial B. The mixture was then stirred for 48 h at 4 °C. The reaction mixture was diluted with Et_2O (2 mL) and filtered through a plug of silica gel, which was then washed with more Et_2O (10 mL). The filtrate was concentrated and purified by silica gel chromatography.

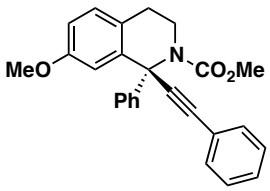


(*S*)-Methyl 1-phenyl-1-(phenylethynyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-33). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (10% CH_2Cl_2/PhMe) to give compound **3-33** (run 1: 86.9 mg, 79%; run 2: 45.0 mg, 74%) as colorless oil. The enantiomeric excess was determined to be 91% (run 1: 91% ee; run 2: 90% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.5 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 23.36 min, t_R(minor) = 21.83 min. $[\alpha]_D^{24}$ = 20.0° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.64 (m, 2H), 7.55 (ddd, *J* = 5.5, 3.0, 1.6 Hz, 2H), 7.40 – 7.30 (m, 5H), 7.27 – 7.21 (m, 2H), 7.16 (dddd, *J* = 12.6, 10.9, 7.2, 3.6 Hz, 3H), 4.43 (dt, *J* = 12.8, 4.4 Hz, 1H), 3.80 (ddd, *J* = 13.1, 10.4, 3.2 Hz, 1H), 3.58 (s, 3H), 3.28 (ddd, *J* = 15.0, 10.3, 4.3 Hz, 1H), 3.05 (ddd, *J* = 15.9, 4.7, 3.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.4, 146.8, 140.5, 132.9, 131.9, 129.7, 128.4, 128.3, 128.3, 128.1, 126.9, 126.7, 126.6, 125.9, 123.0, 90.5, 85.7, 62.5, 52.4, 42.1, 30.0; FTIR (NaCl, thin film) 3716, 2852, 1723, 1640, 1580, 1441, 1298, 425 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{21}NO_2$; 368.1651, found: 368.1627.



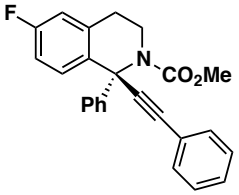
(*S*)-Methyl 7-methyl-1-phenyl-1-(phenylethynyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-34). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (15–30% CH_2Cl_2/PhMe) to give compound **3-34** (run 1: 92.6 mg, 81%; run 2: 101.7 mg, 89%) as colorless oil. The enantiomeric excess was determined to be 91% (run 1: 90% ee; run 2: 91% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.5 mL/min, 1% *i*-

PrOH/hexane, λ=254 nm); t_R(major) = 22.60 min, t_R(minor) = 19.15 min. $[\alpha]_D^{24}$ = 9.0° (c 10.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.68 (m, 2H), 7.61 – 7.53 (m, 2H), 7.42 – 7.32 (m, 5H), 7.29 – 7.22 (m, 1H), 7.10 (d, *J* = 7.8 Hz, 1H), 7.05 (d, *J* = 1.8 Hz, 1H), 6.99 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.44 (dt, *J* = 12.8, 4.4 Hz, 1H), 3.77 (ddd, *J* = 13.1, 10.5, 3.1 Hz, 1H), 3.59 (s, 3H), 3.25 (ddd, *J* = 15.1, 10.4, 4.2 Hz, 1H), 3.01 (dt, *J* = 15.8, 3.8 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4, 146.9, 140.1, 136.4, 131.9, 130.1, 129.9, 128.4, 128.3, 128.2, 128.1, 127.7, 126.7, 125.9, 123.1, 90.7, 85.6, 62.5, 52.4, 42.3, 29.7, 21.3; FTIR (NaCl, thin film) 3071, 2592, 1571, 1474, 1357, 1250, 1029, 830 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{26}H_{23}NO_2$; 382.1807, found: 382.1790.



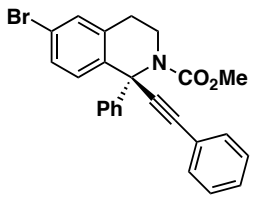
(*S*)-Methyl 7-methoxy-1-phenyl-1-(phenylethynyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-35). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (15–30% CH_2Cl_2/PhMe) to give compound **3-35** (run 1: 99.5 mg, 84%; run 2: 90.0 mg, 76%) as colorless oil. The enantiomeric excess was determined to be 96% (run 1: 95% ee; run 2: 96% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.4 mL/min, 0.5% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 66.88 min, t_R(minor) = 55.96 min. $[\alpha]_D^{24}$ = 15.0° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.58 (m, 2H), 7.49 (dq, *J* = 4.9, 1.7 Hz, 2H), 7.36 – 7.29 (m, 3H), 7.28 (d, *J* = 1.6 Hz, 1H), 7.26 (s, 1H), 7.21 – 7.16 (m, 1H), 7.06 (d, *J* = 8.2 Hz, 1H), 6.74 – 6.66 (m, 2H), 4.37 (dt, *J* = 12.8, 4.4 Hz, 1H), 3.69 (ddd, *J* = 13.0, 10.4, 3.1 Hz, 1H), 3.64 (s, 3H), 3.52 (s,

3H), 3.16 (ddd, J = 15.1, 10.5, 4.2 Hz, 1H), 2.93 (dt, J = 15.7, 4.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 156.4, 146.7, 141.4, 131.9, 129.2, 128.3, 128.2, 128.1, 126.7, 125.7, 125.3, 122.9, 114.7, 112.9, 90.4, 85.6, 62.5, 55.2, 52.4, 42.4, 29.2; FTIR (NaCl, thin film) 3142, 2947, 2592, 1540, 1385, 1327, 1105, 1079, 842 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{26}H_{23}NO_3$; 398.1756, found: 398.1736.

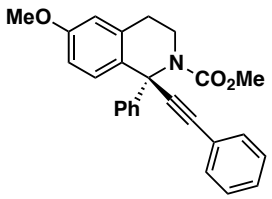


(*S*)-Methyl 6-fluoro-1-phenyl-1-(phenylethynyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-36). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (10–15% CH_2Cl_2/PhMe) to give compound **3-36** (run 1: 101.8 mg, 88%; run 2: 101.8 mg, 88%) as colorless oil. The enantiomeric excess was determined to be 93% (run 1: 93% ee; run 2: 93% ee) by chiral HPLC analysis (CHIRALPAK IA, 0.3 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 39.45 min, t_R(minor) = 36.18 min. $[\alpha]_D^{24}$ = 6.0° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.61 (m, 2H), 7.56 – 7.50 (m, 2H), 7.39 – 7.30 (m, 5H), 7.29 – 7.22 (m, 1H), 7.16 (dd, J = 8.9, 5.5 Hz, 1H), 6.88 (dd, J = 9.0, 2.7 Hz, 1H), 6.82 (td, J = 8.6, 2.8 Hz, 1H), 4.39 (dt, J = 12.9, 4.5 Hz, 1H), 3.79 (ddd, J = 13.1, 10.2, 3.2 Hz, 1H), 3.57 (s, 3H), 3.24 (ddd, J = 15.1, 10.2, 4.3 Hz, 1H), 3.01 (ddd, J = 15.9, 4.7, 3.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9 (d, J = 247.0 Hz), 156.3, 146.6, 136.3 (d, J = 3.1 Hz), 135.2 (d, J = 7.7 Hz), 131.7 (d, J = 8.4 Hz), 131.7, 128.5, 128.3, 128.2, 126.9, 125.9, 122.8, 114.5 (d, J = 3.8 Hz), 114.3 (d, J = 3.1 Hz), 90.2, 86.0, 62.2, 52.5, 41.9, 30.1; FTIR (NaCl, thin

film) 3142, 2592, 2020, 1570, 1489, 1383, 1327, 1160, 830 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{20}FNO_2$; 386.1556, found: 386.1536.

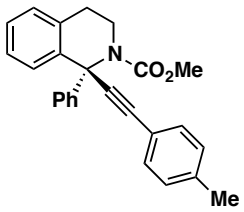


(*S*)-Methyl 6-bluoro-1-phenyl-1-(phenylethynyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-37). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (10–15% CH_2Cl_2/PhMe) to give compound **3-37** (run 1: 103 mg, 92%) as white solid. The enantiomeric excess was determined to be 92%ee by chiral HPLC analysis (CHIRALPAK AS-H, 3.0 mL/min, 10% MeOH(0.1%DEA)/CO2, λ=254 nm); t_R(major) = 4.94 min, t_R(minor) = 4.82 min.^{1}H NMR (400 MHz, $CDCl_3$) δ δ 7.60 – 7.55 (m, 2H), 7.49 – 7.45 (m, 2H), 7.35 – 7.26 (m, 6H), 7.23 – 7.17 (m, 2H), 7.01 (d, *J* = 8.7 Hz, 1H), 4.34 (dt, *J* = 12.9, 4.5 Hz, 1H), 3.73 – 3.67 (m, 1H), 3.52 (s, 3H), 3.24 – 3.16 (m, 1H), 3.00 – 2.93 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2, 146.2, 139.6, 135.1, 131.8, 131.5, 130.9, 130.1, 128.5, 128.3, 128.2, 126.9, 125.8, 122.7, 120.5, 89.8, 86.2, 62.2, 52.5, 41.8, 29.8; FTIR (NaCl, thin film) 3853, 3736, 1747, 1699, 1653, 1441, 1362, 1213 cm^{-1}.



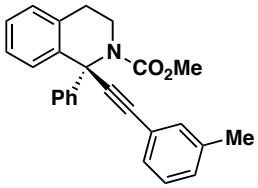
(*S*)-Methyl 6-methoxy-1-phenyl-1-(phenylethynyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-38). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (15–30% CH_2Cl_2/PhMe) to give compound **3-38** (45.0 mg, 38%) as colorless oil. The enantiomeric excess was determined to be 92% by chiral HPLC analysis (CHIRACEL ODH, 0.2 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R(major) =

75.03 min, t_R(minor) = 69.61 min. $[\alpha]_D^{24}$ = 7.0° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.60 (m, 2H), 7.55 – 7.48 (m, 2H), 7.38 – 7.26 (m, 5H), 7.25 – 7.18 (m, 1H), 7.11 – 7.04 (m, 1H), 6.71 – 6.64 (m, 2H), 4.35 (dt, *J* = 12.8, 4.6 Hz, 1H), 3.84 – 3.76 (m, 1H) 3.78 (s, 3H), 3.55 (s, 3H), 3.21 (ddd, *J* = 14.9, 10.1, 4.3 Hz, 1H), 2.99 (ddd, *J* = 15.9, 4.8, 3.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 156.4, 146.9, 134.4, 132.7, 131.8, 130.9, 128.3, 128.2, 128.0, 126.6, 125.8, 123.1, 113.5, 112.4, 90.6, 85.6, 62.0, 55.2, 52.4, 42.1, 30.3; FTIR (NaCl, thin film) 3072, 2290, 1570, 1474, 1383, 1186, 830, 724, 523 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{26}H_{23}NO_3$; 398.1756, found: 398.1732.

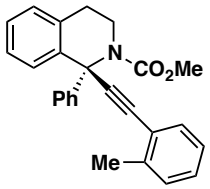


(*S*)-Methyl 1-phenyl-1-(*p*-tolylethynyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-45). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (15–30% CH_2Cl_2/PhMe) to give compound **3-45** (107 mg, 94%; run 2: 95.2 mg, 83%) as colorless oil. The enantiomeric excess was determined to be 91% (run 1: 91% ee; run 2: 90 % ee) by chiral HPLC analysis (CHIRALPAK IA, 0.7 mL/min, 2% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 13.34 min, t_R(minor) = 11.77 min. $[\alpha]_D^{24}$ = –6.9° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.50 (m, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 7.17 (t, *J* = 7.7 Hz, 2H), 7.10 – 7.05 (m, 2H), 7.04 – 7.00 (m, 3H), 7.00 – 6.95 (m, 2H), 4.27 (dt, *J* = 12.8, 4.4 Hz, 1H), 3.64 (ddd, *J* = 13.0, 10.4, 3.1 Hz, 1H), 3.42 (s, 3H), 3.12 (ddd, *J* = 15.2, 10.4, 4.3 Hz, 1H), 2.89 (dt, *J* = 15.8, 3.9 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5, 146.9, 140.6,

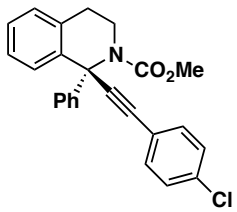
138.4, 132.9, 131.8, 129.7, 129.0, 128.3, 128.0, 126.9, 126.7, 126.5, 125.9, 119.9, 89.8, 85.9, 62.5, 52.3, 42.1, 30.0, 21.5; FTIR (NaCl, thin film) 3852, 2359, 1644, 1508, 1489, 1439, 1213, 1179, 517, 415 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{26}H_{23}NO_2$; 382.1807, found: 382.1791.



(*S*)-Methyl 1-phenyl-1-(*m*-tolylethynyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-46). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (15–30% CH_2Cl_2/PhMe) to give compound **3-46** (run 1: 89.3 mg, 78%; run 2: 93.7 mg, 82%) as colorless oil. The enantiomeric excess was determined to be 91% (run 1: 90% ee; run 2: 91% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.2 mL/min, 0.8% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 55.49 min, t_R(minor) = 51.05 min. $[\alpha]_D^{24}$ = 1.9° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.50 (m, 2H), 7.24 – 7.15 (m, 4H), 7.12 – 7.05 (m, 3H), 7.05 – 7.00 (m, 2H), 7.01 – 6.94 (m, 2H), 4.27 (dt, *J* = 12.8, 4.5 Hz, 1H), 3.64 (ddd, *J* = 13.2, 10.4, 3.1 Hz, 1H), 3.42 (s, 3H), 3.12 (ddd, *J* = 15.1, 10.4, 4.3 Hz, 1H), 2.89 (ddd, *J* = 15.8, 4.6, 3.0 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4, 146.9, 140.5, 137.9, 132.9, 132.4, 129.7, 129.2, 128.9, 128.3, 128.2, 128.1, 126.9, 126.7, 126.6, 125.9, 122.8, 90.1, 85.9, 62.5, 52.4, 42.1, 30.0, 21.3; FTIR (NaCl, thin film) 3442, 2870, 1646, 1488, 1280, 1178, 561, 404 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{26}H_{23}NO_2$; 382.1807, found: 382.1797.

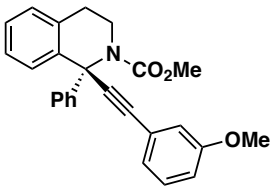


(*S*)-Methyl 1-phenyl-1-(*o*-tolylethynyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-47). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (10–15% CH_2Cl_2/PhMe) to give compound **3-47** (90.0 mg, 93%) as colorless oil. The enantiomeric excess was determined to be 5% by chiral HPLC analysis (CHIRALPAK IB, 0.2 mL/min, 0.8% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 46.57 min, t_R(minor) = 40.19 min. $[\alpha]_D^{24}$ = 40.0° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.63 (m, 2H), 7.48 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.31 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.25 – 7.19 (m, 4H), 7.19 – 7.07 (m, 4H), 4.40 (dt, *J* = 12.8, 4.5 Hz, 1H), 3.79 (ddd, *J* = 13.0, 10.3, 3.2 Hz, 1H), 3.55 (s, 3H), 3.26 (ddd, *J* = 15.0, 10.2, 4.2 Hz, 1H), 3.09 – 2.98 (m, 1H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4, 146.8, 140.5, 140.5, 132.9, 132.1, 129.7, 129.4, 128.3, 128.3, 128.0, 126.8, 126.7, 126.5, 125.9, 125.5, 122.8, 94.4, 84.6, 62.6, 52.4, 42.1, 30.0, 20.8; FTIR (NaCl, thin film) 3853, 2088, 1644, 1489, 1438, 1287, 1124, 532, 454 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{26}H_{23}NO_2$; 382.1807, found: 382.1809



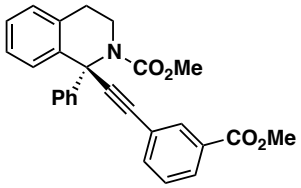
(*S*)-Methyl 1-((4-chlorophenyl)ethynyl)-1-phenyl-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-48). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (10–15% CH_2Cl_2/PhMe) to give compound **3-48** (run 1: 100.0 mg, 83%; run 2: 90.1 mg, 75%) as colorless oil. The enantiomeric excess was determined to be 95% (run 1: 94% ee; run 2: 96% ee) by chiral HPLC analysis (CHIRALPAK IA, 0.3 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 41.53 min, t_R(minor) = 36.08

min. $[\alpha]_D^{24}$ = 28.0° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.58 (m, 2H), 7.47 – 7.39 (m, 2H), 7.33 – 7.27 (m, 4H), 7.24 – 7.18 (m, 1H), 7.13 (dtd, *J* = 16.4, 7.4, 2.0 Hz, 4H), 4.37 (dt, *J* = 12.8, 4.5 Hz, 1H), 3.76 (ddd, *J* = 13.1, 10.3, 3.2 Hz, 1H), 3.54 (s, 3H), 3.23 (ddd, *J* = 14.9, 10.2, 4.3 Hz, 1H), 3.01 (ddd, *J* = 15.8, 4.7, 3.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 146.6, 140.2, 134.3, 133.1, 132.9, 129.6, 128.6, 128.4, 128.1, 126.9, 126.8, 126.7, 125.9, 121.5, 91.5, 84.6, 62.4, 52.4, 42.1, 29.9; FTIR (NaCl, thin film) 3581, 2282, 1678, 1565, 1485, 1358, 1213, 581, 425 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{25}H_{20}ClNO_2$; 402.1261, found: 402.1259

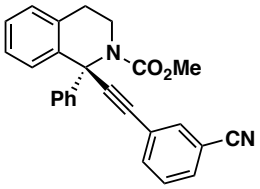


(*S*)-Methyl 1-((3-methoxyphenyl)ethynyl)-1-phenyl-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-49). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (15–30% CH_2Cl_2/PhMe) to give compound **3-49** (run 1: 97.4 mg, 82%; run 2: 98.6 mg, 83%) as colorless oil. The enantiomeric excess was determined to be 95% (run 1: 95% ee; run 2: 95% ee) by chiral HPLC analysis (CHIRACEL ODH, 0.4 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 63.87 min, t_R(minor) = 49.86 min. $[\alpha]_D^{24}$ = 8.0° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dt, *J* = 6.7, 1.1 Hz, 2H), 7.36 – 7.30 (m, 2H), 7.28 – 7.19 (m, 3H), 7.19 – 7.09 (m, 4H), 7.05 (dd, *J* = 2.6, 1.4 Hz, 1H), 6.92 (ddd, *J* = 8.5, 2.6, 1.0 Hz, 1H), 4.42 (dt, *J* = 12.8, 4.5 Hz, 1H), 3.84 (s, 3H), 3.79 (ddd, *J* = 13.1, 10.4, 3.3 Hz, 1H), 3.57 (s, 3H), 3.27 (ddd, *J* = 15.1, 10.4, 4.3 Hz, 1H), 3.04 (dt, *J* = 16.0, 3.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 156.4, 146.8, 140.4, 132.9, 129.7, 129.3, 128.3, 128.1, 126.9, 126.7,

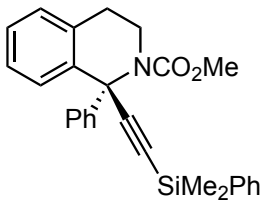
126.6, 125.89, 124.5, 124.0, 116.7, 114.9, 90.3, 85.6, 62.4, 55.4, 52.4, 42.1, 30.0; FTIR (NaCl, thin film) 3431, 2930, 2870, 1652, 1599, 1489, 1270, 1110, 464 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{26}H_{23}NO_3$; 398.1756, found: 398.1750



(*S*)-Methyl 1-((3-(methoxycarbonyl)phenyl)ethynyl)-1-phenyl-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-50). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (20–60% CH_2Cl_2/PhMe) to give compound **3-50** (run 1: 116.6 mg, 92%; run 2: 107.0 mg, 84%) as white solid. The enantiomeric excess was determined to be 90% (run 1: 90% ee; run 2: 90% ee) by chiral HPLC analysis (CHIRALPAK IB, 0.2 mL/min, 2% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 63.37 min, t_R(minor) = 58.29 min. $[\alpha]_D^{24}$ = 28.9° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (t, *J* = 1.6 Hz, 1H), 7.99 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.70 – 7.59 (m, 3H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.30 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.24 – 7.05 (m, 5H), 4.37 (dt, *J* = 12.8, 4.5 Hz, 1H), 3.93 (s, 3H), 3.77 (ddd, *J* = 12.9, 10.1, 3.2 Hz, 1H), 3.55 (s, 3H), 3.23 (ddd, *J* = 14.9, 10.2, 4.2 Hz, 1H), 3.01 (ddd, *J* = 15.9, 4.8, 3.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 156.3, 146.5, 140.2, 136.1, 133.0, 132.9, 130.3, 129.7, 129.3, 128.43, 128.4, 128.1, 126.9, 126.8, 126.6, 125.9, 123.5, 91.4, 84.7, 62.4, 52.5, 52.4, 42.1, 29.9; FTIR (NaCl, thin film) 3020, 2964, 2870, 1700, 1660, 1547, 1220, 1110, 528, 425 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{27}H_{23}NO_4$; 425.1627, found: 425.1641

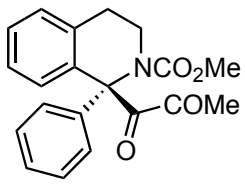


(*S*)-Methyl 1-((3-cyanophenyl)ethynyl)-1-phenyl-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-51). Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (20–60% CH_2Cl_2/PhMe) to give compound **3-51** (run 1: 110.5 mg, 94%; run 2: 106.1 mg, 90%) as white solid. The enantiomeric excess was determined to be 95% (run 1: 95% ee; run 2: 94% ee) by chiral HPLC analysis (CHIRACEL ODH, 0.4 mL/min, 1% *i*-PrOH/hexane, λ=254 nm); t_R(major) = 63.87 min, t_R(minor) = 49.86 min. $[\alpha]_D^{24}$ = 30.0° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 1.7 Hz, 1H), 7.72 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.33 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.27 – 7.21 (m, 1H), 7.21 – 7.09 (m, 4H), 4.35 (dt, *J* = 12.8, 4.6 Hz, 1H), 3.81 (ddd, *J* = 13.0, 9.9, 3.3 Hz, 1H), 3.58 (s, 3H), 3.25 (ddd, *J* = 14.6, 9.9, 4.2 Hz, 1H), 3.04 (ddd, *J* = 15.9, 5.2, 3.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 146.1, 139.8, 135.9, 135.2, 133.1, 131.6, 129.5, 129.2, 128.4, 128.2, 127.1, 126.9, 126.9, 125.8, 124.6, 118.1, 112.8, 93.2, 83.4, 62.3, 52.5, 42.2, 29.9; FTIR (NaCl, thin film) 3446, 2964, 1635, 1558, 1437, 1362, 1215, 526, 442 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{26}H_{20}N_2O_2$; 393.1603, found: 393.1586.



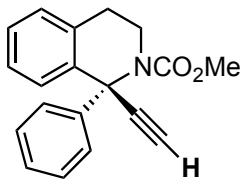
(*R*)-methyl 1-((dimethyl(phenyl)silyl)ethynyl)-1-phenyl-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-52) Prepared via General Procedure 2. Crude material was purified by silica gel chromatography (20–60% CH_2Cl_2/PhMe) to give compound **3-52** (run 1: 52.1 mg, 53%) as colorless oil. The enantiomeric excess was determined to be 52% ee by chiral HPLC analysis (CHIRALPAK IB, 0.2 mL/min,

0.8% *i*-PrOH/hexane, λ=210 nm); t_R(major) = 40.52 min, t_R(minor) = 32.85 min. $[\alpha]_D^{24}$ = 7.0° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.62 (m, 2H), 7.59 – 7.54 (m, 2H), 7.42 – 7.33 (m, 3H), 7.29 – 7.23 (m, 2H), 7.21 – 7.15 (m, 1H), 7.15 – 7.09 (m, 2H), 7.08 (dd, *J* = 7.3, 2.7 Hz, 1H), 4.34 (dt, *J* = 12.8, 4.5 Hz, 1H), 3.71 (ddd, *J* = 13.1, 10.3, 3.2 Hz, 1H), 3.49 (s, 3H), 3.20 (ddd, *J* = 15.0, 10.3, 4.2 Hz, 1H), 2.98 (ddd, *J* = 15.8, 4.7, 3.2 Hz, 1H), 0.45 (d, *J* = 3.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.46, 146.50, 140.03, 137.26, 133.79, 132.99, 129.69, 129.38, 128.27, 128.03, 127.85, 126.84, 126.67, 126.59, 125.78, 108.22, 88.08, 62.46, 52.25, 42.05, 29.95, -0.63, -0.67; FTIR (NaCl, thin film) 3641, 3048, 1700, 1558, 1437, 1362, 1215, 819, 526, 442, 80 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{27}H_{27}NO_2Si$; 426.1831, found: 426.1844.



(*R*)-methyl 1-(2-oxopropanoyl)-1-phenyl-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-57). This procedure was adapted from the literature.[50] Alkyne **3-33** was prepared via General Procedure 2 on a 0.07-mmol scale. A solution of $KMnO_4$ (30.8 mg, 0.21 mmol, 3.0 equiv), $NaHCO_3$ (6.54 mg, 0.84 mmol, 1.2 equiv), tetrabutylammonium bromide (12 mg, 0.035 mmol, 0.52 equiv), and H_2O (1.0 mL) was added to a solution of alkyne **3-33** (23.8 mg, 0.07 mmol, 1.0 equiv) and CH_2Cl_2 (1.0 mL, 0.12 M). The reaction mixture was stirred at room temperature for 48 h. Excess $KMnO_4$ was destroyed by adding HCl (1 M, 1 mL) and Na_2SO_3 (20 mg) until the red color disappeared. The mixture was then washed with sat. $NaHCO_3$ and extracted with CH_2Cl_2 (5 mL). The organic layers were dried ($MgSO_4$) and filtered through a short

pad of Celite, which was then washed with CH_2Cl_2 (10 mL). The filtrate was concentrated, and the crude material was purified by silica gel chromatography (3% CH_2Cl_2/toluene) to give compound **3-57** (19.4 mg, 75%) as yellow oil. The enantiomeric excess was determined to be 92% by chiral HPLC analysis (CHIRALPAK IC, 0.5 mL/min, 3% *i*-PrOH/hexane, λ=210 nm); t_R(major) = 17.40 min, t_R(minor) = 14.71 min. $[\alpha]_D^{24}$ = 7.0° (c 10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.08 (m, 1H), 7.59 – 7.52 (m, 1H), 7.45 (dd, *J* = 8.3, 6.9 Hz, 2H), 7.41 – 7.37 (m, 1H), 7.36 – 7.24 (m, 5H), 7.14 – 7.09 (m, 1H), 7.03 – 6.99 (m, 1H), 4.22 (ddd, *J* = 13.2, 5.2, 2.5 Hz, 1H), 3.53 (s, 2H), 3.46 (ddd, *J* = 16.3, 12.3, 5.2 Hz, 1H), 3.19 (td, *J* = 12.7, 3.1 Hz, 1H), 2.88 (dt, *J* = 15.7, 2.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.1, 186.2, 156.3, 142.4, 135.7, 133.2, 132.9, 132.8, 131.1, 129.4, 128.9, 128.4, 128.0, 127.8, 127.8, 127.6, 126.3, 71.7, 53.3, 38.9, 29.1; FTIR (NaCl, thin film) 3445, 2900, 1720, 1680, 1662, 1429, 1205, 1132, 1053, 1022, 778, 720, 523 cm^{-1}.



(*R*)-methyl 1-ethynyl-1-phenyl-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3-58). Alkyne **3-53** was prepared via General Procedure 2 on a 0.20-mmol scale. To a solution of alkyne **3-53** (30.0 mg, 0.08 mmol, 1.0 equiv) and THF (2 mL, 0.04 M), tetrabutyl-ammonium fluoride (0.1 mL, 1 M, 1.25 equiv) was added. The reaction mixture was stirred at 0 °C for 12 h. After consumption of alkyne **3-53** as determined by TLC analysis, the mixture was filtered through a short pad of silica gel, which was then washed with CH_2Cl_2 (15 mL). The filtrate was concentrated, and the crude material

was purified by silica gel chromatography (0–10% Et_2O/hexanes) to give compound **3-58** (10.0 mg, 45%) as colorless oil. The enantiomeric excess was determined to be 97% by chiral HPLC analysis (CHIRALPAK IB, 0.5 mL/min, 3.0% *i*-PrOH/hexane, λ=220 nm); t_R(major) = 23.67 min, t_R(minor) = 19.32 min. ^{1} H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 – 7.53 (m, 2H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.25 (s, 1H), 7.22 – 7.16 (m, 1H), 7.15 – 7.08 (m, 2H), 7.08 – 7.05 (m, 2H), 4.28 (dt, *J* = 12.8, 4.6 Hz, 1H), 3.72 (ddd, *J* = 13.0, 10.0, 3.3 Hz, 1H), 3.53 (s, 3H), 3.18 (ddd, *J* = 14.7, 10.0, 4.2 Hz, 1H), 2.97 (ddd, *J* = 15.8, 5.0, 3.3 Hz, 1H), 2.73 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 145.9, 139.9, 132.9, 129.5, 128.3, 128.1, 126.9, 126.8, 126.7, 125.8, 84.7, 73.9, 61.7, 52.5, 42.1, 29.9; FTIR (NaCl, thin film) 3270, 3100, 1716, 1685, 1442, 1363, 1216, 751 cm^{-1}; HRMS (EI+) [M+] calculated for $C_{19}H_{17}NO_2$; 292.1311, found: 292.1321.

Non-Linear Experimental Procedure

In a N_2-atmosphere glovebox, isoquinoline **3-26** (0.1 mmol, 1.0 equiv) and $CHCl_3$ (0.3 mL) were combined in a 1-dram vial. This vial (vial A) was sealed with a septum-lined piercable cap and removed from the glovebox. Methyl chloroformate (7.5 μL, 0.1 mmol, 1.0 equiv) was then added dropwise. The reaction mixture was stirred for 1 h at room temperature and then cooled to 0 °C. In a N_2-atmosphere glovebox, CuI (1.8 mg, 0.01 mmol, 10 mol %), 2,6-bis((*R*)-4-phenyl-4,5-dihydrooxazol-2-yl)pyridine (Ph-PyBox, **L1**, total = 4.3 mg, 0.012 mmol, 12 mol %) and $CHCl_3$ (0.57 mL) were combined in a 2-dram vial (vial B). Vial B was capped

with a septum-lined piercable cap, and the mixture was stirred for 30 min at room temperature inside the glove box. After 30 min, phenyl acetylene (0.12 mmol, 1.2 equiv) and *i*-Pr_2NEt (25 μL, 0.15 mmol, 1.5 equiv) were added to vial B. Vial B was again capped, removed from the glovebox, and cooled to 0 °C. After 10 min, the cooled mixture from vial A was transferred slowly via syringe to vial B. Vial A was rinsed with $CHCl_3$ (0.1 mL), which was then added to vial B. The mixture was then stirred for 24 h at 4 °C.

entry	mol % (*R*)-Ph-PyBox	mol % (*S*)-Ph-PyBox	ee of catalyst	ee of product
1	6	6	0	0
2	7	5	17	39
3	7.5	4.5	25	46
4	8	4	33	50
5	9	3	50	67
6	9.9	2.1	65	71
7	11	1	84	85
8	12	0	100	91

The reaction mixture was diluted with Et_2O (2 mL) and filtered through a plug of silica gel, which was then washed with more Et_2O (10 mL). Analytical samples of product were then prepared via preparatory TLC (50% CH_2Cl_2/PhMe) and analyzed by HPLC using a chiral stationary phase.

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If you want to number your bibliographic entries, change the style of the items to *Bib Entry - numbered*.

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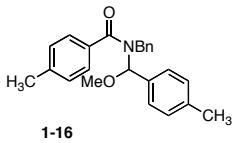
Appendix A

NMR AND HPLC SPECTRA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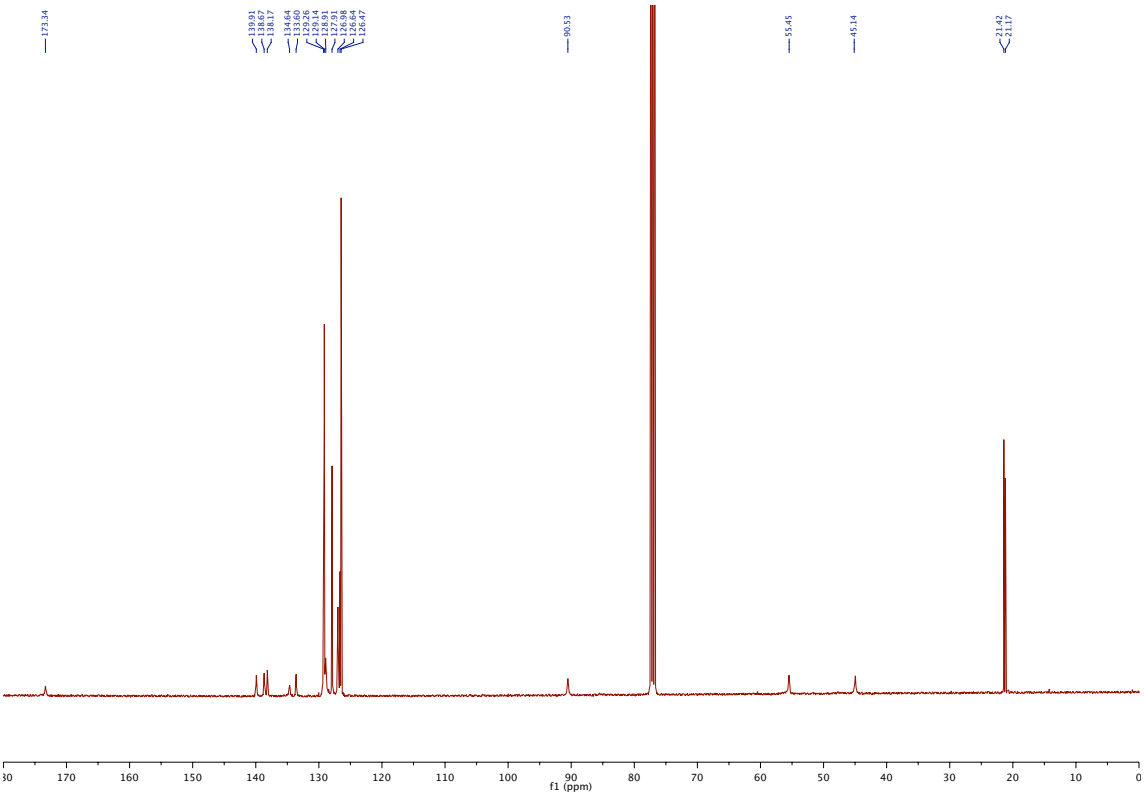
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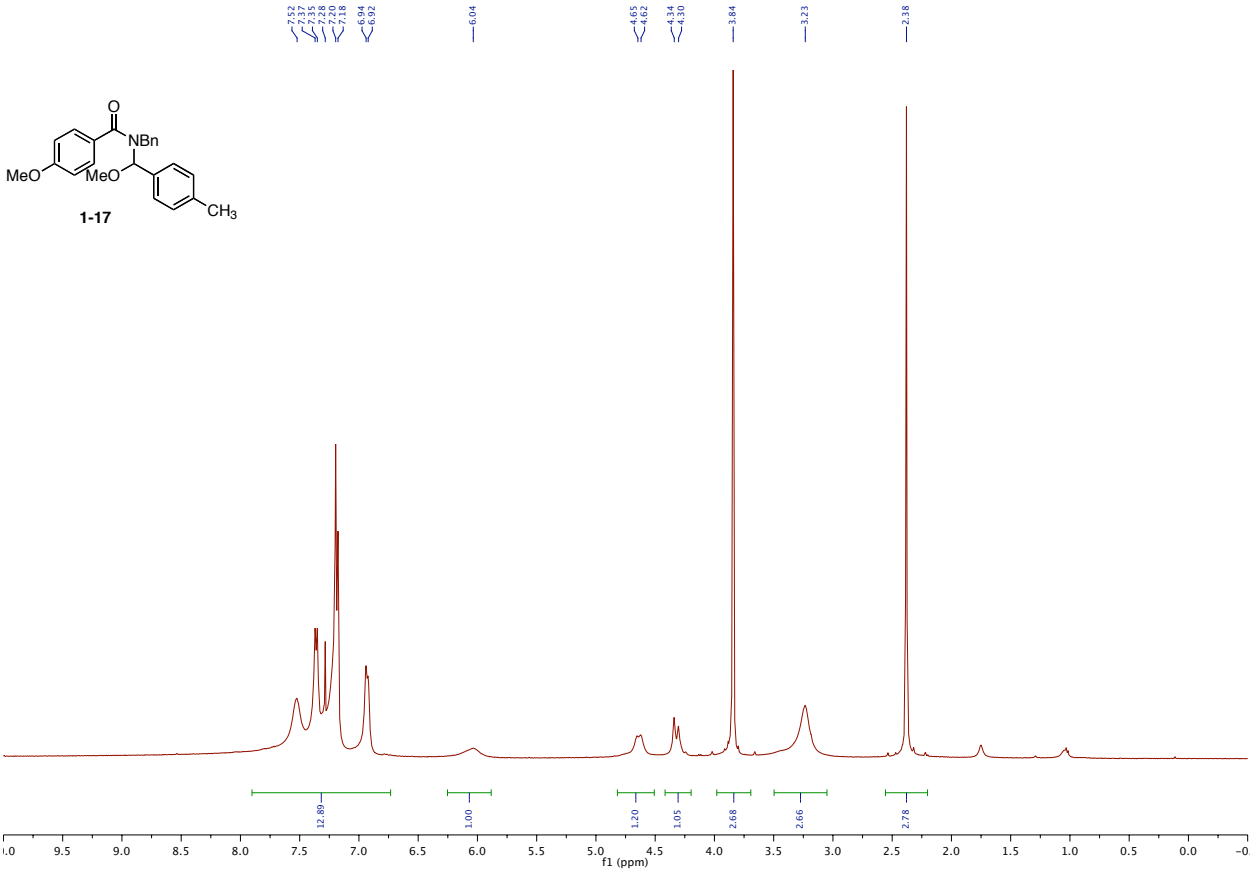
f1 (ppm)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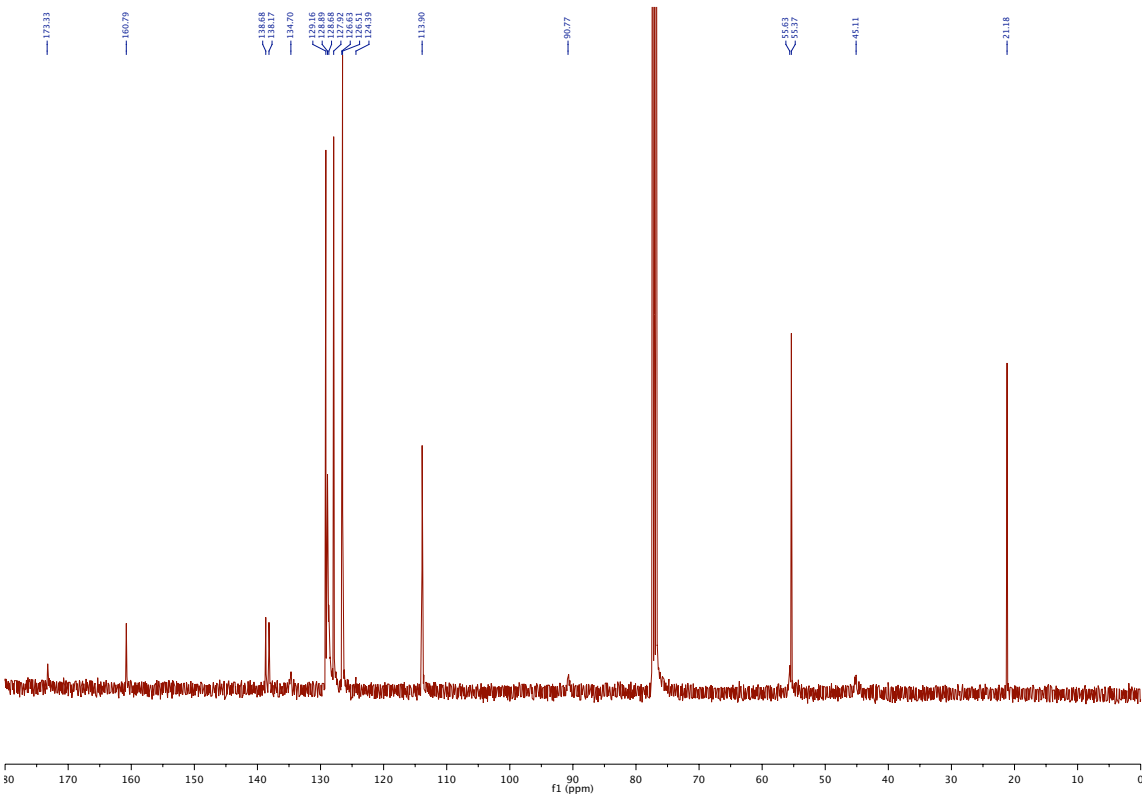
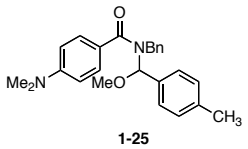
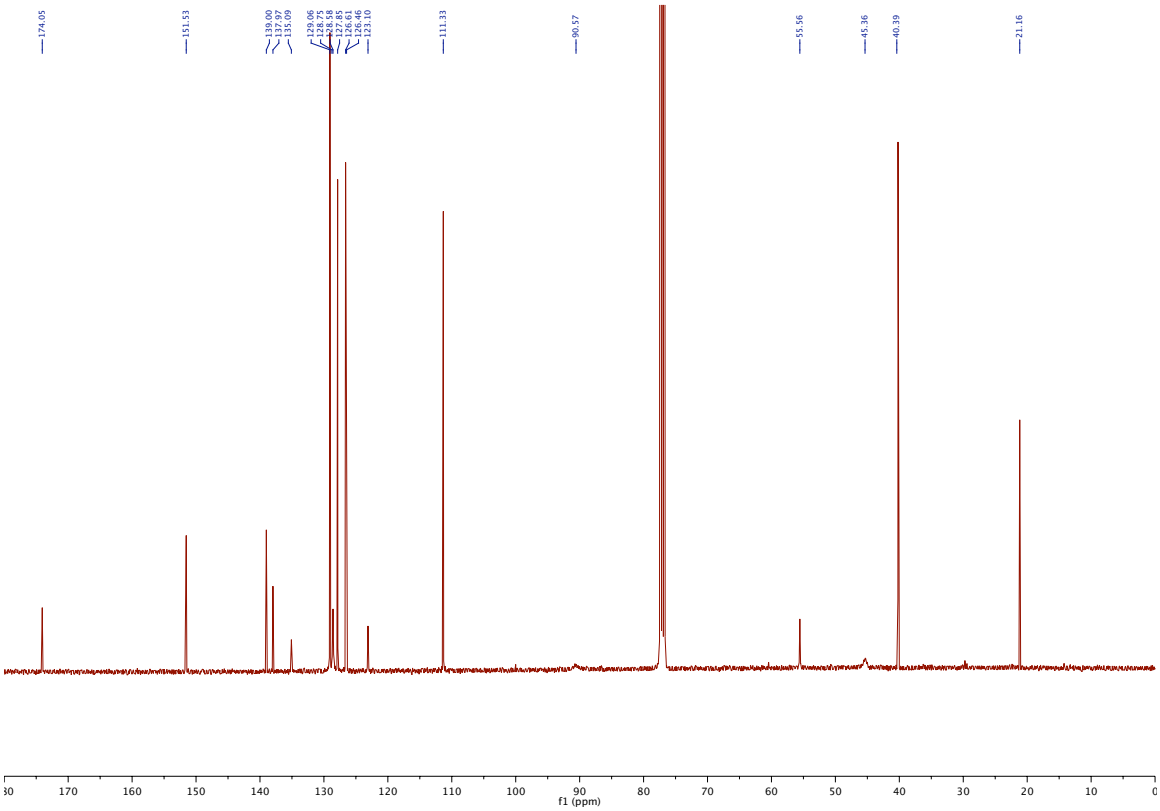
1.05
2.68
2.66
2.78
f1 (ppm)

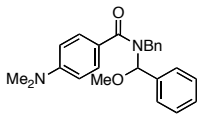

173.33
160.79
138.68
138.17
134.70
129.16
128.89
128.48
127.92
126.63
126.51
124.39
113.90
90.77
55.63
55.37
45.11
21.18
f1 (ppm)


O
NBn
Me2N
MeO
CH3

1-25

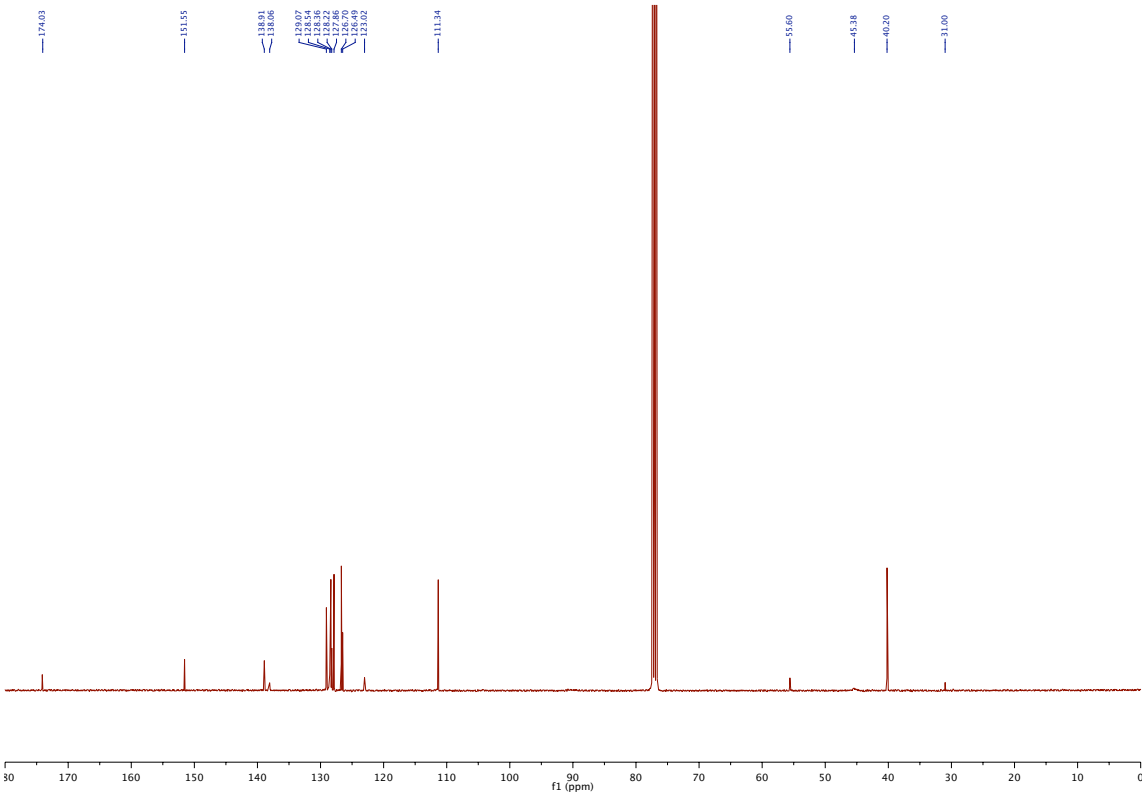
7.51
7.49
7.38
7.36
7.28
7.22
7.20
7.18
7.16
6.69
6.67
6.23
4.59
4.56
4.39
4.35
3.26
3.02
2.37
11.32
1.82
1.00
1.17
1.12
2.71
5.52
2.71
f1 (ppm)

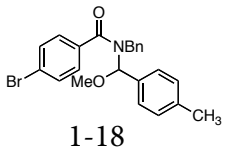

174.05
151.53
130.90
137.97
135.09
129.06
128.75
128.58
126.61
126.61
126.46
123.10
111.33
90.57
55.56
45.36
40.39
21.16
f1 (ppm)


O
NBn
Me2N
MeO

1-26

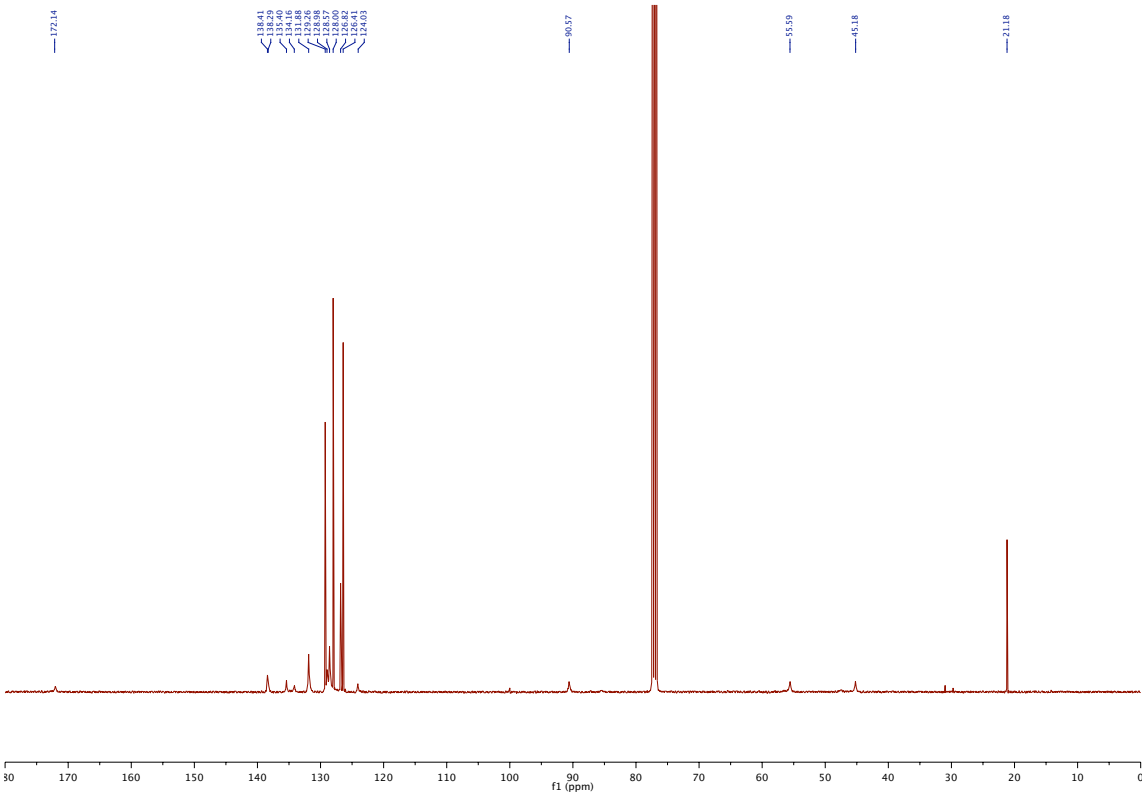
7.53
7.51
7.50
7.38
7.37
7.35
7.34
7.32
7.30
7.28
7.20
7.18
6.70
6.68
6.32
4.59
4.55
4.44
4.41
3.30
3.01
12.24
1.89
0.83
1.00
0.84
2.73
5.76
f1 (ppm)

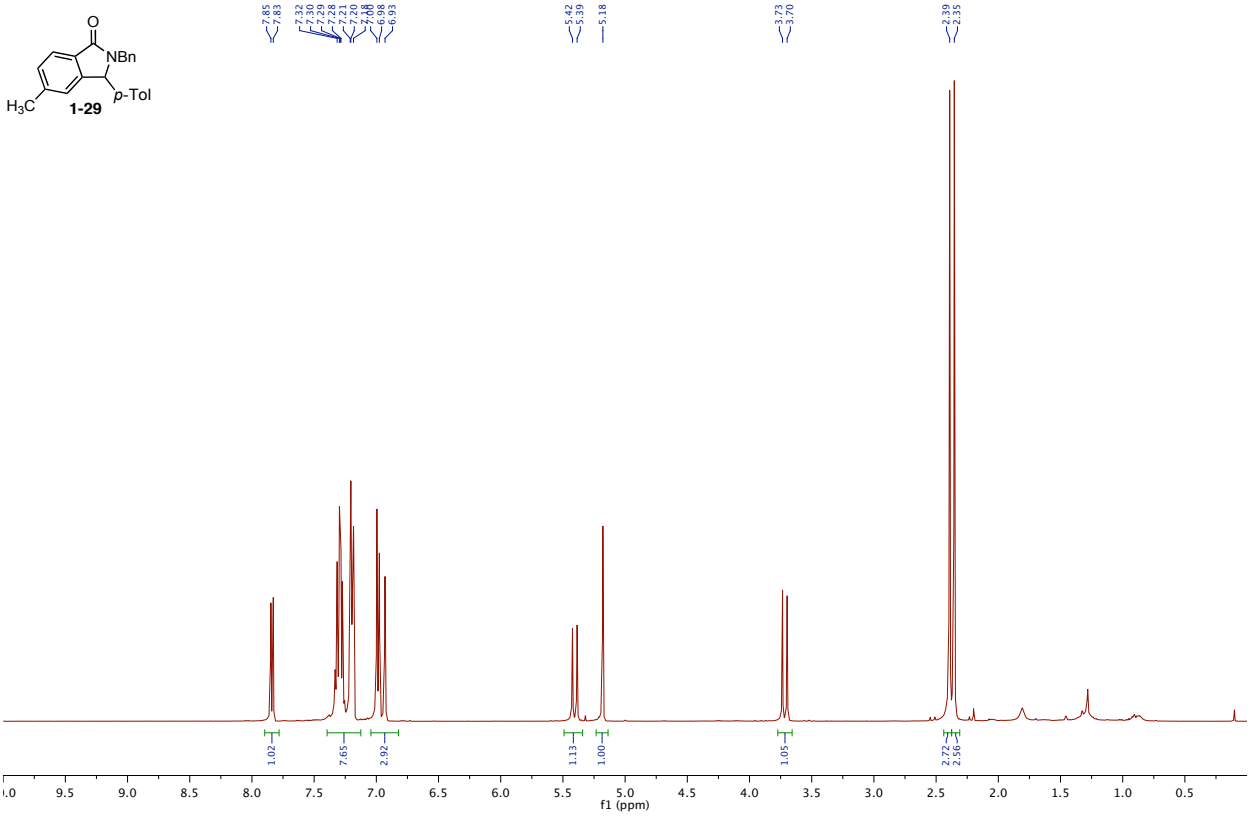

174.03
151.55
138.91
138.06
129.07
128.54
128.36
128.22
127.86
126.70
126.49
123.02
111.34
55.60
45.38
40.20
31.00
f1 (ppm)

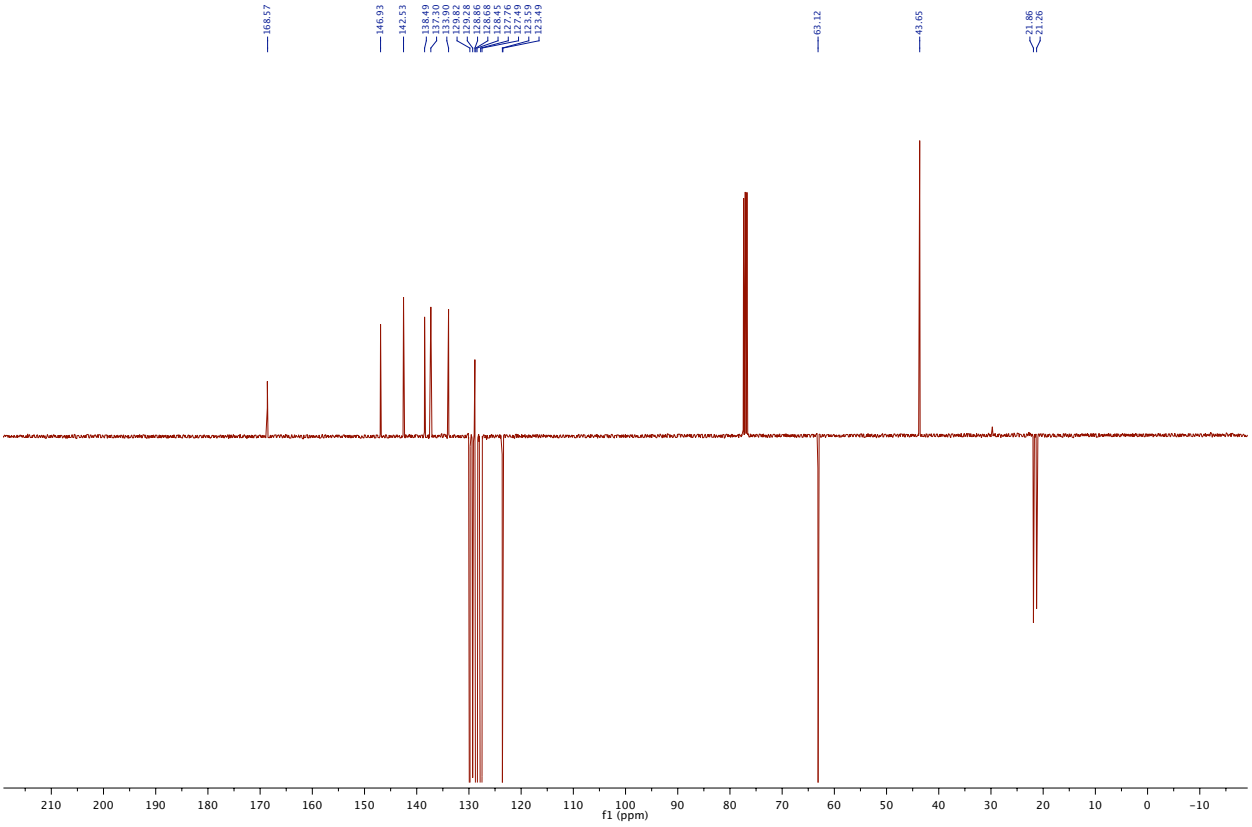

O
NBn
Br
MeO
CH3

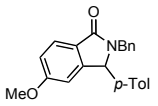
1-18

7.57
7.43
7.28
7.20
7.18
6.66
5.84
4.74
4.69
4.27
4.24
3.55
3.17
2.38
12.40
1.16
1.00
1.08
1.19
2.57
2.88
f1 (ppm)


172.14
138.41
138.29
135.40
134.16
131.88
129.26
128.98
128.57
128.00
127.63
126.41
124.03
90.57
55.59
45.18
21.18
f1 (ppm)

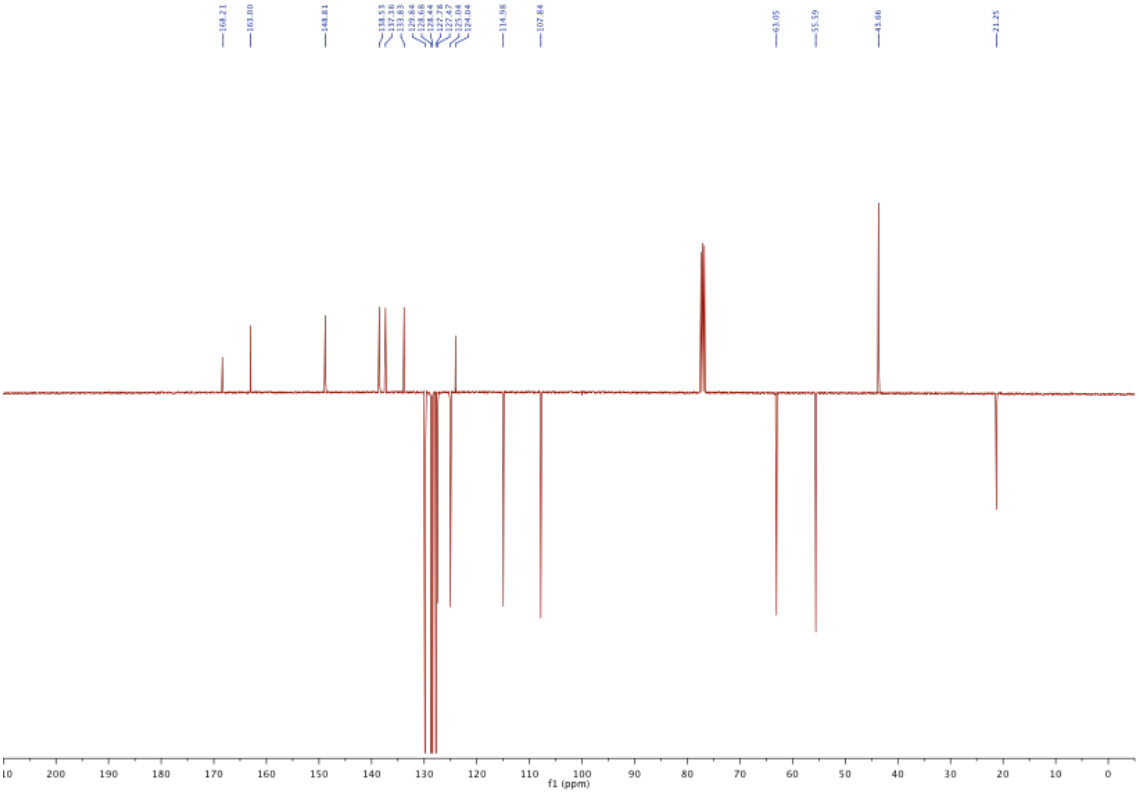

O
NBn
p-Tol
H3C
1-29
7.85
7.83
7.32
7.30
7.29
7.28
7.21
7.20
7.08
7.00
6.98
6.93
5.42
5.39
5.18
3.73
3.70
2.39
2.35
1.02
7.65
2.92
1.13
1.00
1.05
2.72
2.56
f1 (ppm)

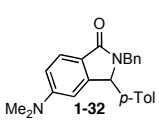

168.57
146.93
142.53
138.49
137.30
133.90
63.12
43.65
21.86
21.26
f1 (ppm)


O
NBn
p-Tol
MeO

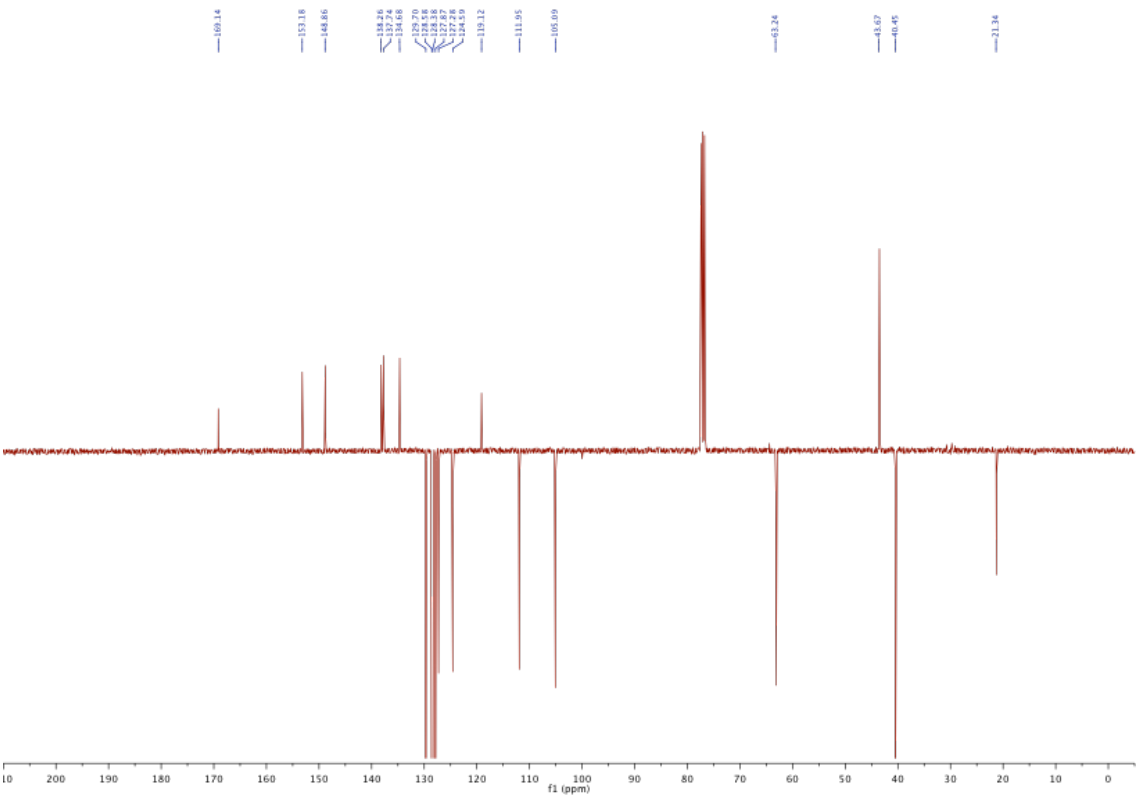
1-30

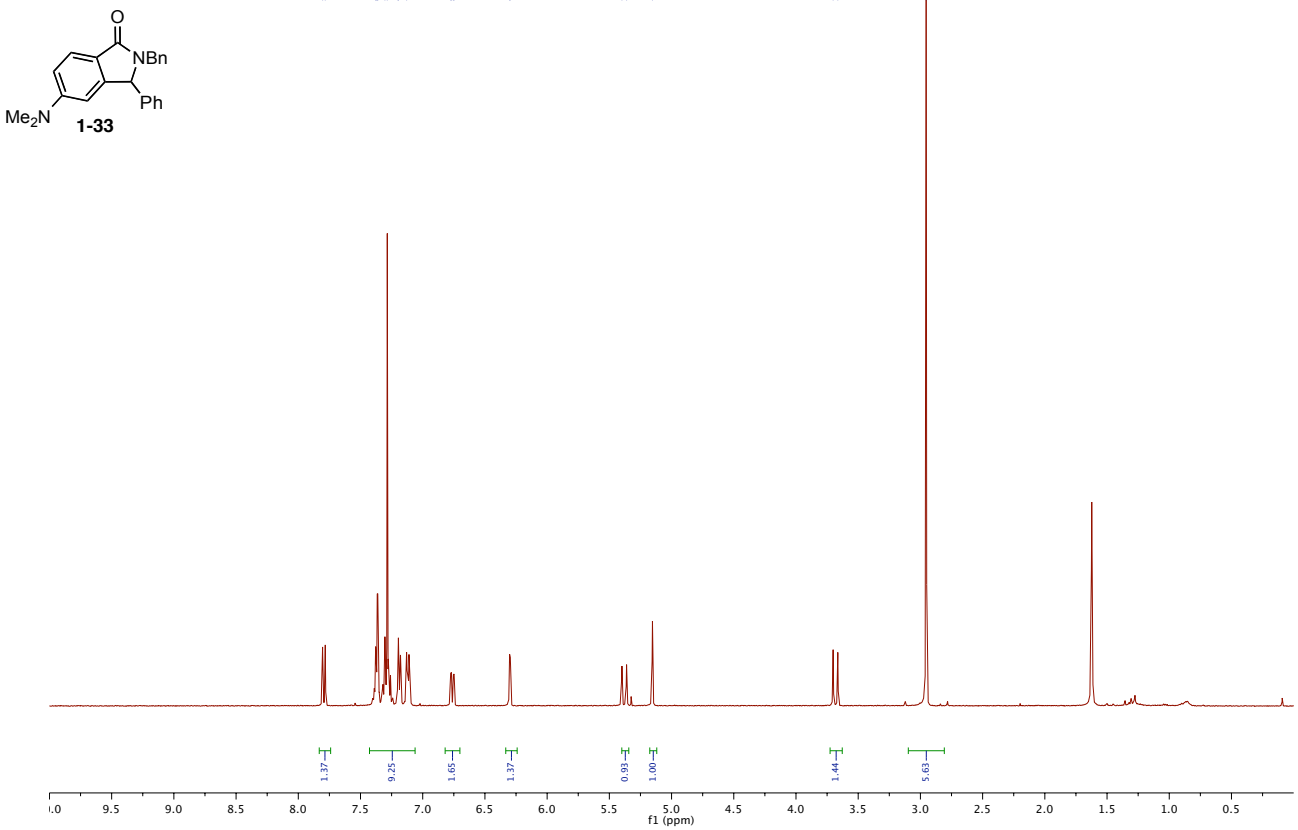
7.87
7.85
7.32
7.30
7.28
7.21
7.20
7.19
7.18
7.00
6.99
6.98
6.88
6.59
5.40
5.37
5.16
3.76
3.72
3.68
2.39
1.15
3.11
3.57
2.69
0.95
1.00
0.97
2.48
0.80
2.93
f1 (ppm)

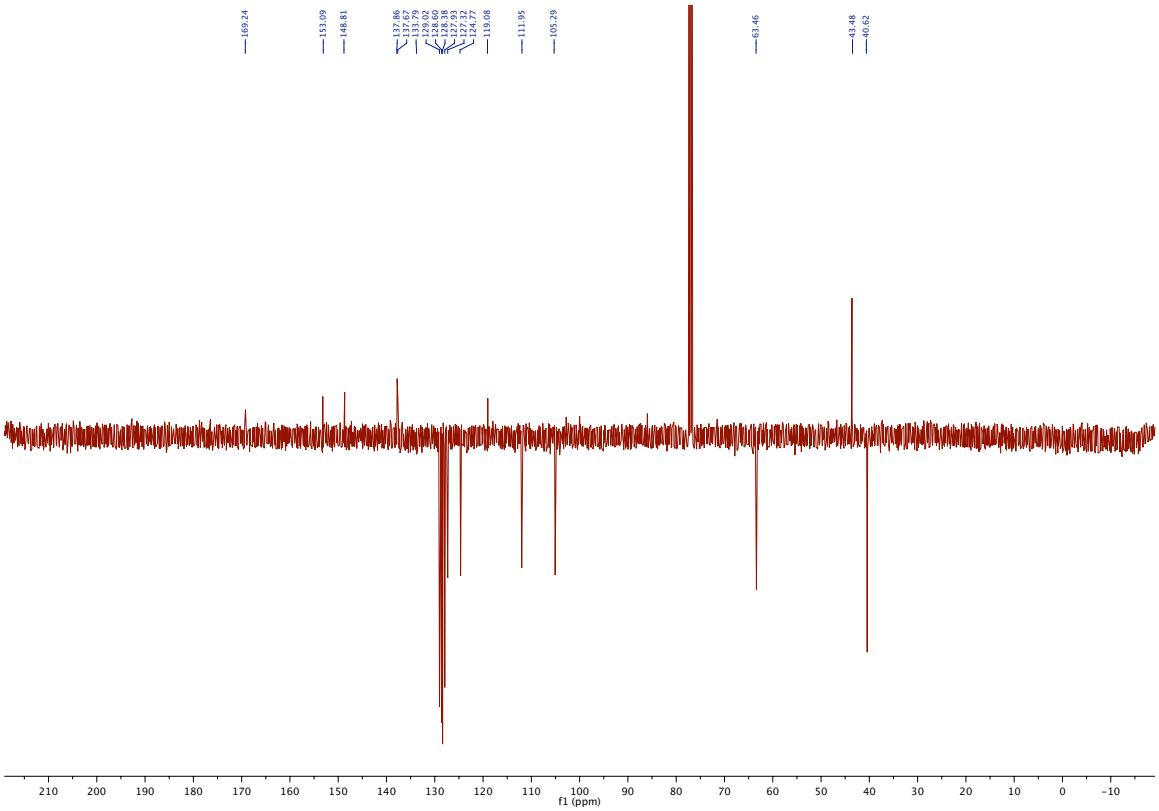

168.21
163.00
148.81
138.53
137.36
133.83
130.64
128.68
128.44
127.76
127.47
125.04
124.64
114.98
107.64
63.05
55.59
43.66
21.25
f1 (ppm)

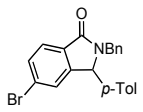

O
NBn
Me2N
1-32
p-Tol

7.80
7.78
7.30
7.28
7.27
7.21
7.20
7.19
7.17
7.01
6.99
6.97
6.76
6.75
6.74
6.31
6.30
5.39
5.35
5.13
3.69
3.65
2.95
2.39
1.26
3.59
3.75
2.12
1.03
1.03
1.02
0.89
1.14
6.87
2.81
f1 (ppm)


169.14
153.18
148.86
138.26
137.74
134.68
129.70
128.56
128.38
127.87
127.46
124.59
119.12
111.95
105.09
63.24
43.67
40.45
21.34
f1 (ppm)

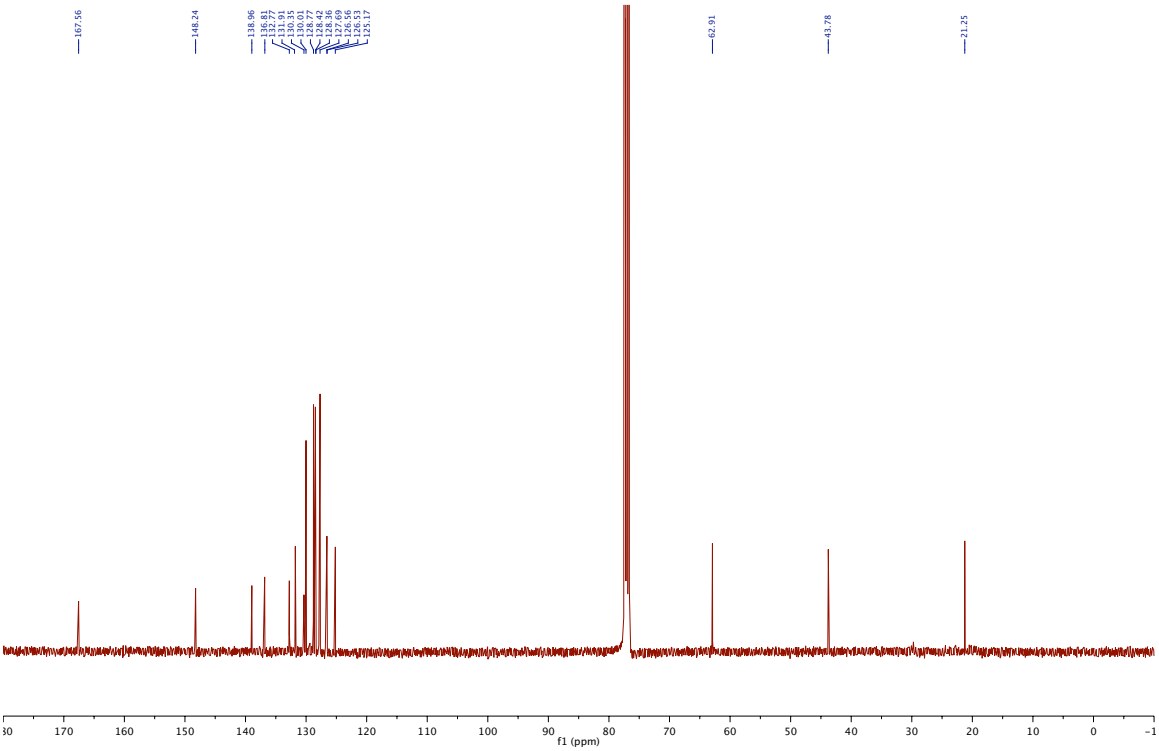

O
NBn
Ph
Me2N
1-33
7.80
7.78
7.38
7.37
7.36
7.30
7.28
7.20
6.78
6.77
6.75
6.30
6.30
5.40
5.36
5.15
3.70
3.66
2.95
1.37
9.25
1.65
1.37
0.93
1.00
1.44
5.63
f1 (ppm)


169.24
153.09
148.81
137.86
137.67
133.79
129.02
128.60
128.38
127.93
127.72
124.77
119.08
111.95
105.29
63.46
43.48
40.62
f1 (ppm)

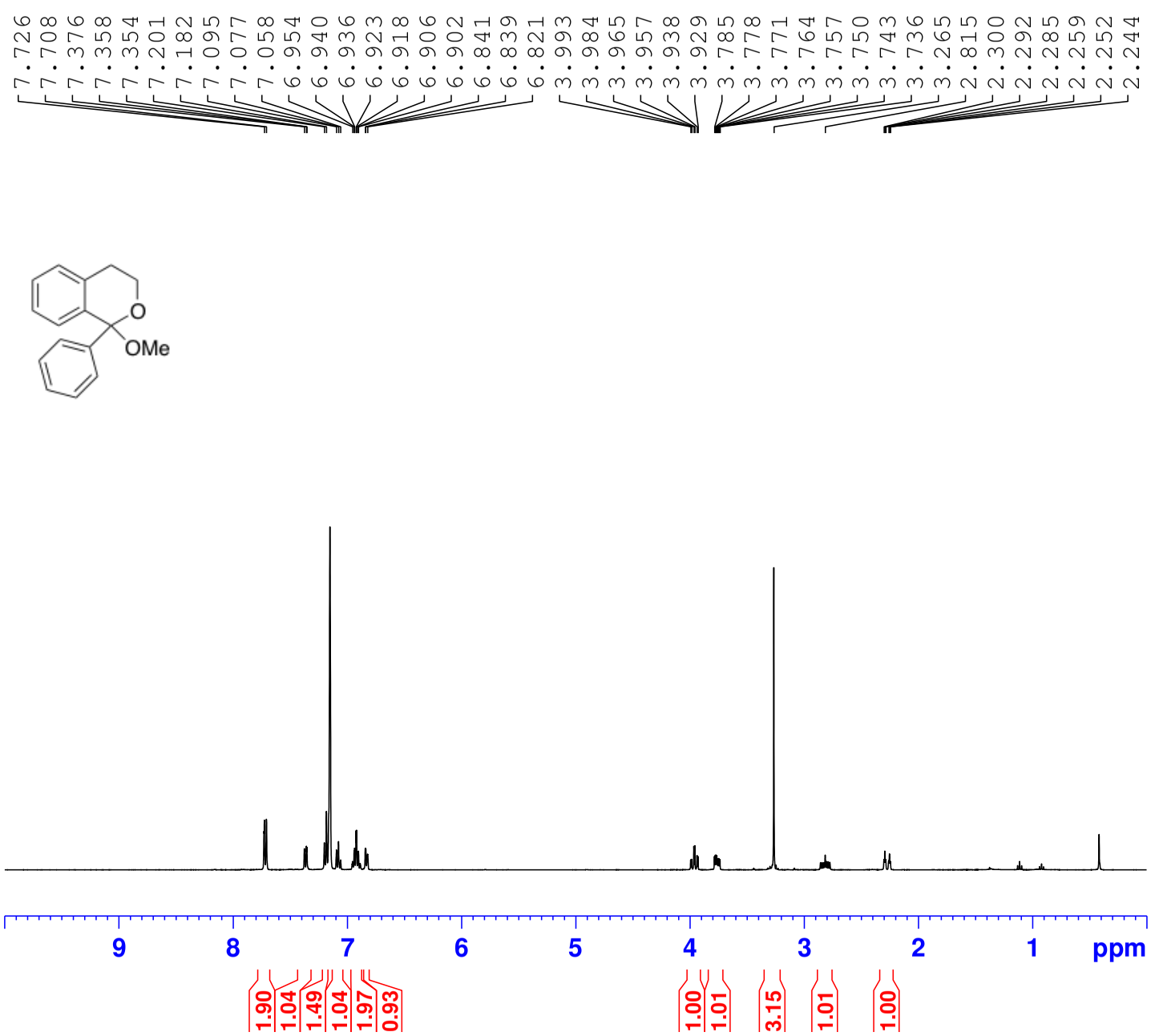

O
NBn
Br
p-Tol

1-31

7.82
7.80
7.63
7.62
7.62
7.31
7.28
7.27
7.20
6.98
6.96
5.40
5.37
5.19
3.73
3.70
2.40
1.16
1.17
6.86
1.95
0.98
1.07
1.13
2.68
f1 (ppm)


167.56
148.24
138.96
136.81
132.77
131.91
130.35
130.01
128.77
128.42
128.36
127.69
126.56
126.53
125.17
62.91
43.78
21.25
f1 (ppm)

2-48, 1H NMR



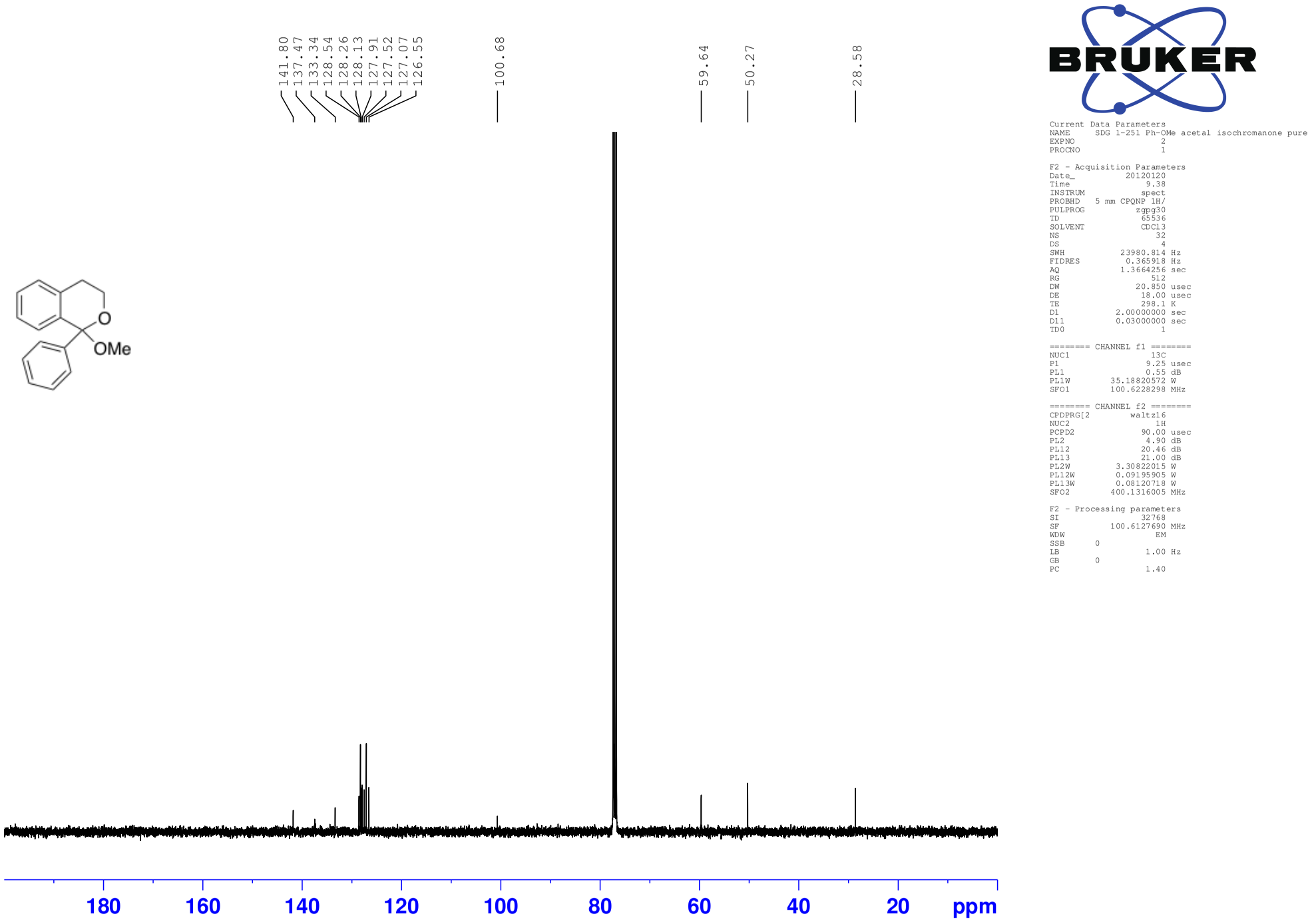
Current Data Parameters
NAME SDG 2-101 Ph OMe substrate
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120816
Time 19.20
INSTRUM spect
PROBHD 5 mm CPQNP 1H/
PULPROG zg30
TD 65536
SOLVENT C6D6
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9583745 sec
RG 12.7
DW 60.400 usec
DE 6.00 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 15.00 usec
PL1 4.90 dB
PL1W 3.30822015 W
SFO1 400.1324710 MHz

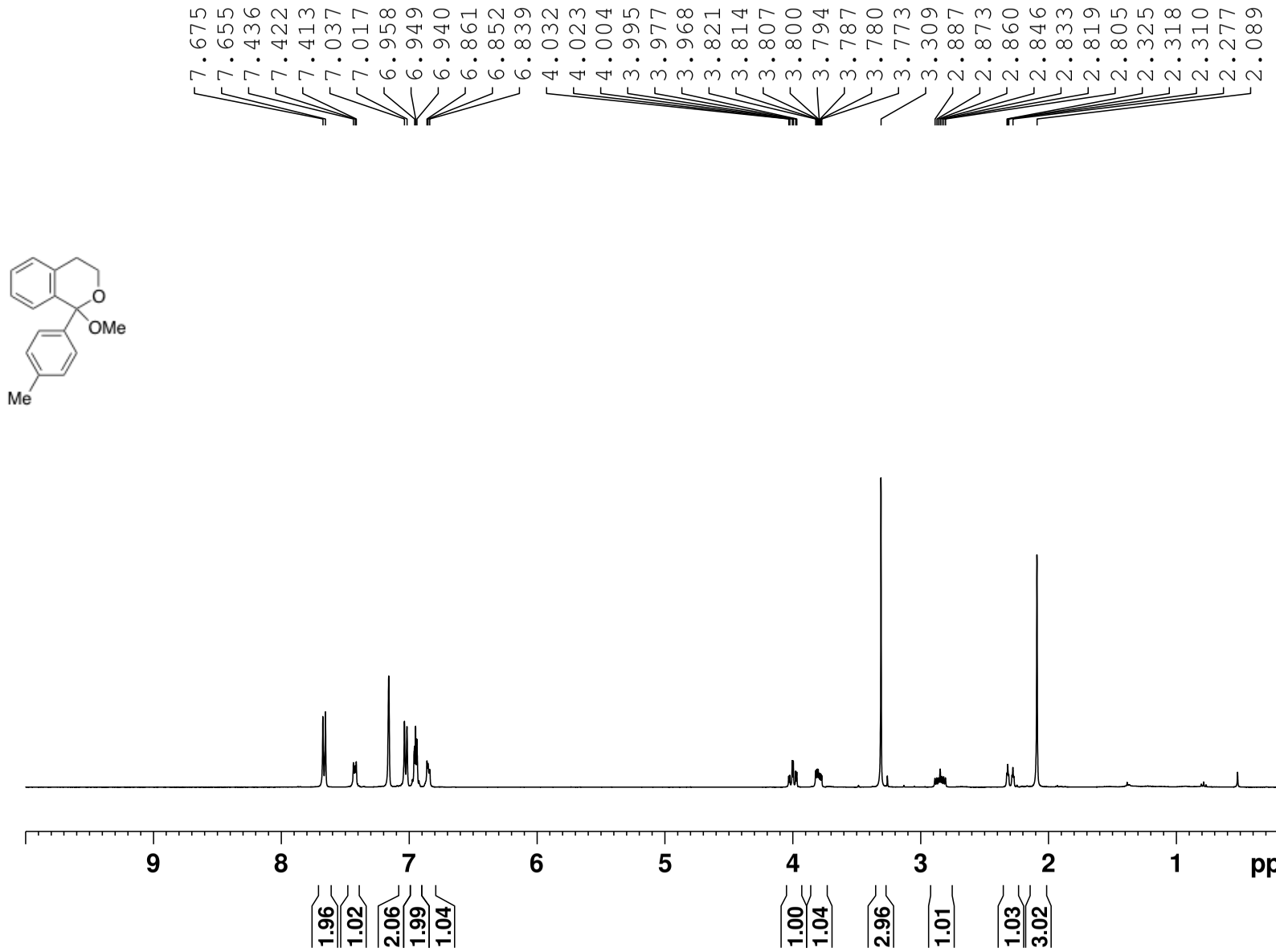
F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

2-48, 13C NMR

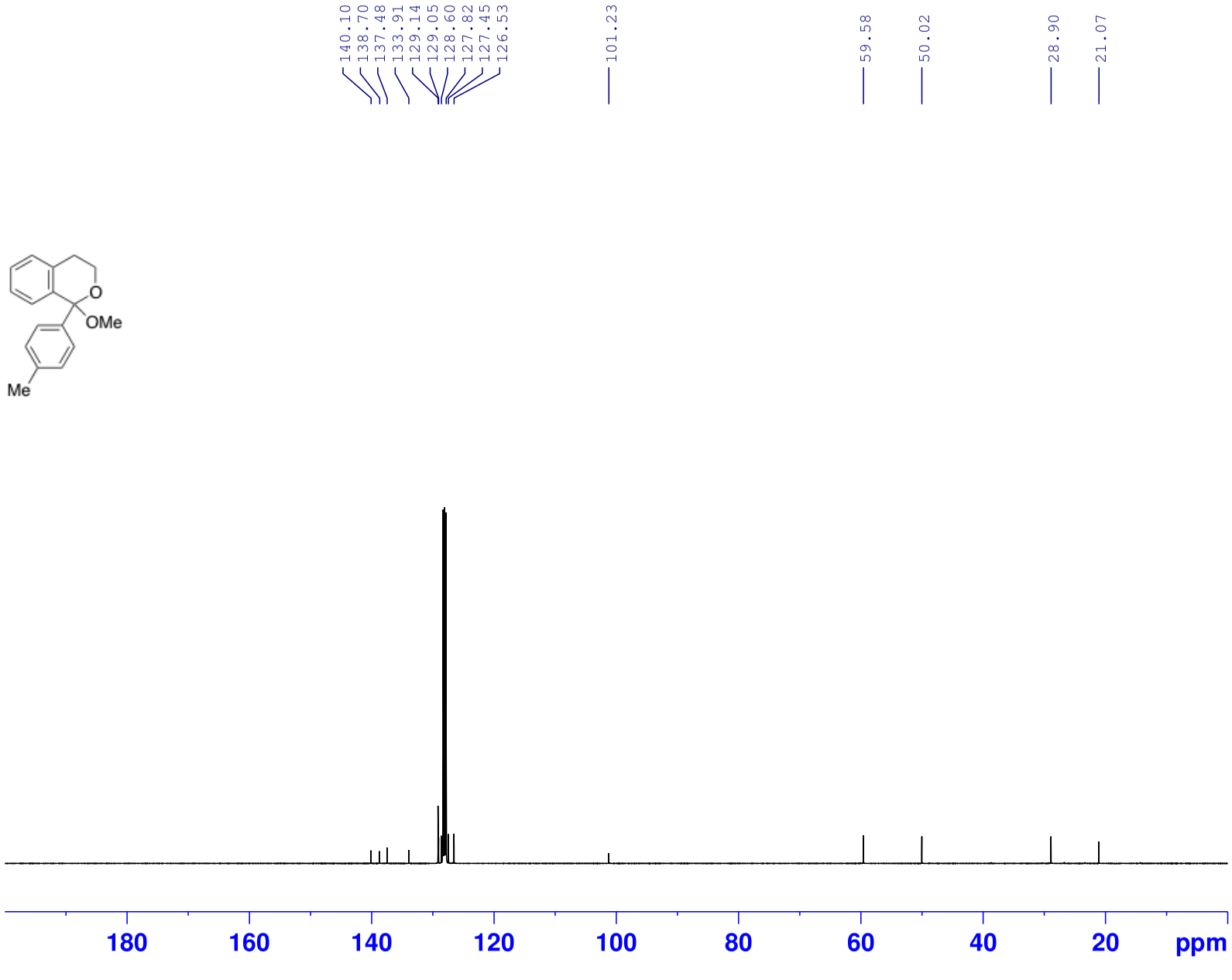


BRUKER

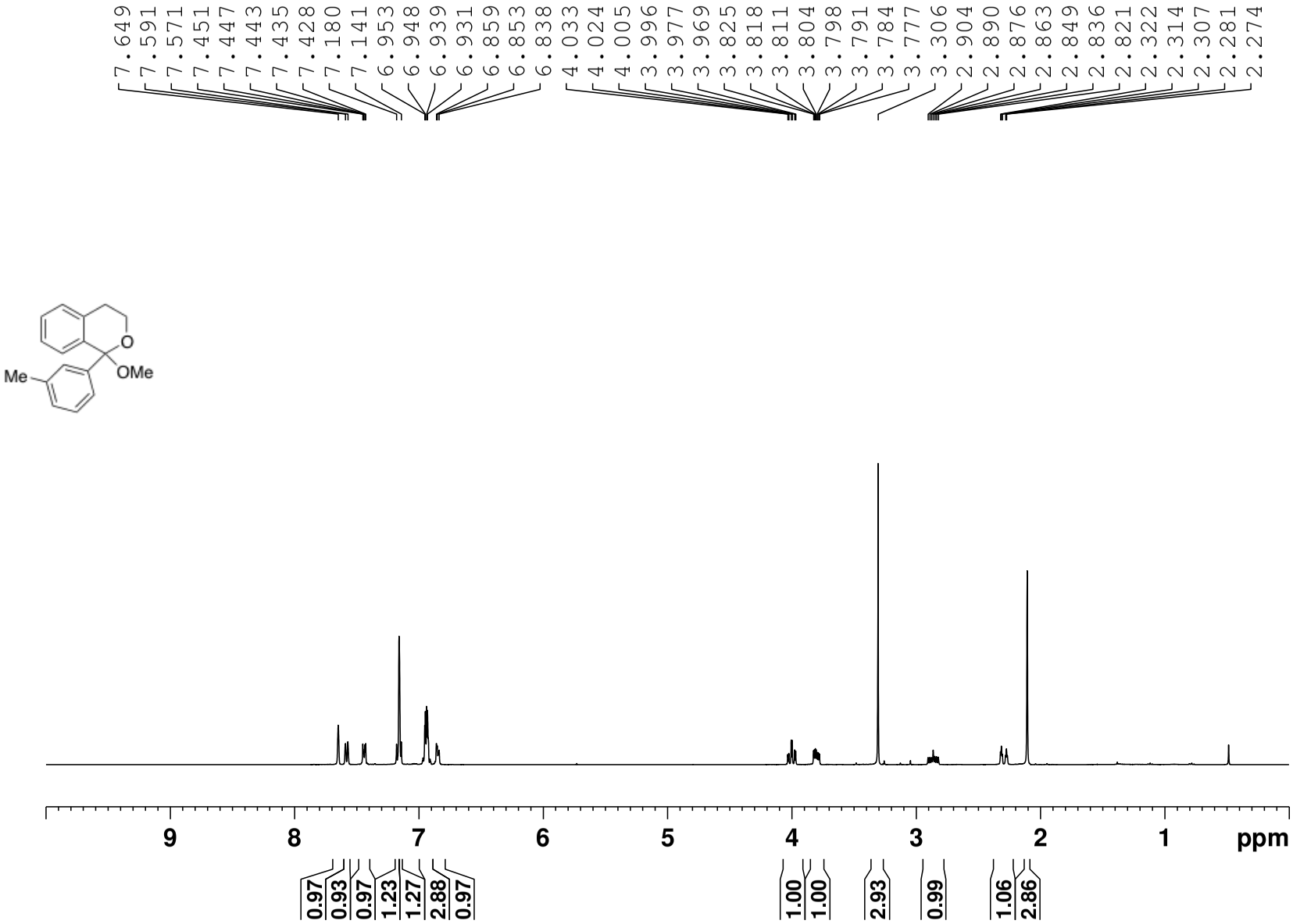
```
Current Data Parameters
NAME      SDG 1-251 Ph-OMe acetal isochromanone pure
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120120
Time                9.38
INSTRUM             spect
PROBHD   5 mm CPQNP 1H/
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     4
SWH            23980.814 Hz
FIDRES          0.365918 Hz
AQ              1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.1 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W         35.18820572 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2               90.00 usec
PL2                  4.90 dB
PL12                20.46 dB
PL13                21.00 dB
PL2W          3.30822015 W
PL12W         0.09195905 W
PL13W         0.08120718 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6127690 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```



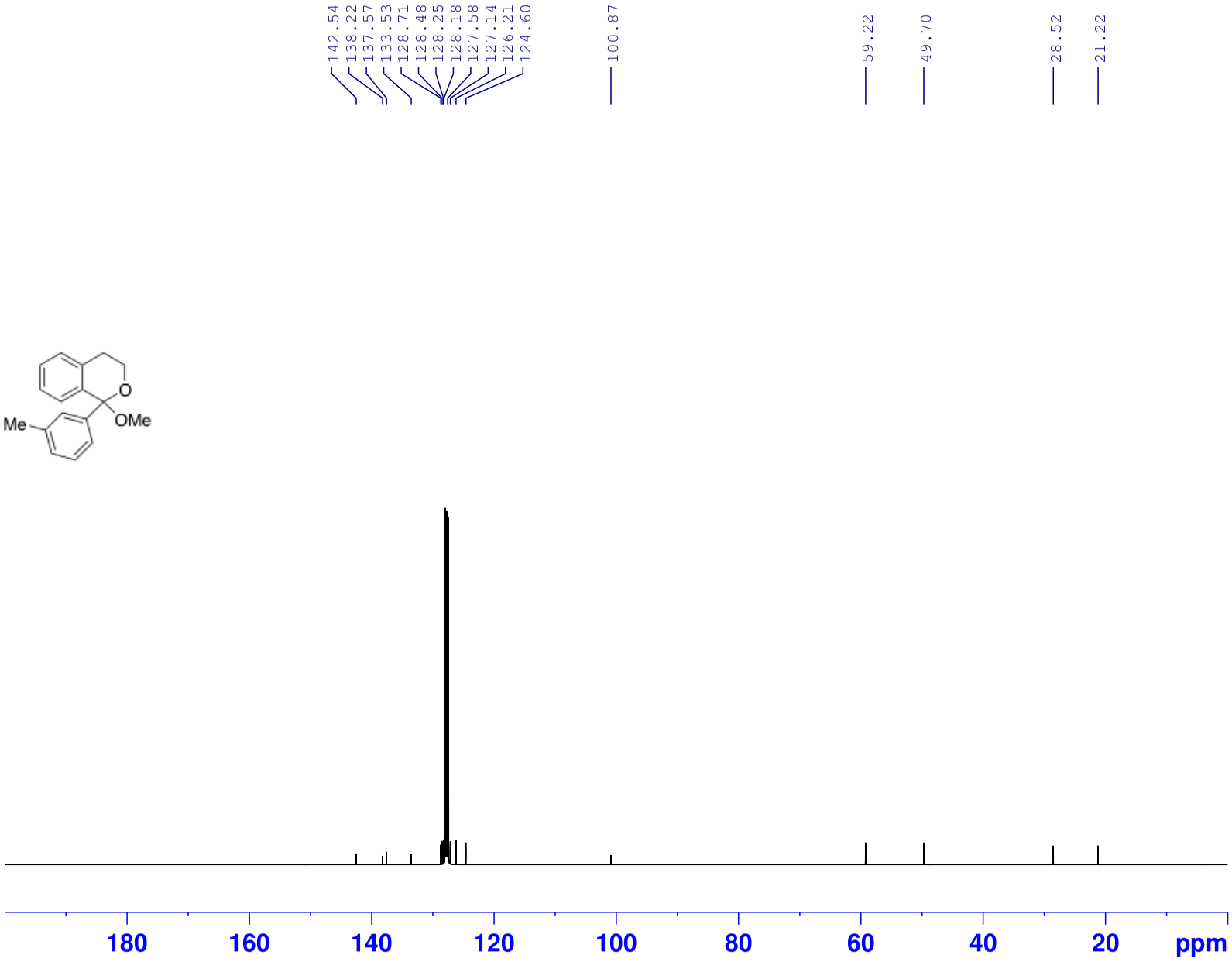

```
Current Data Parameters
NAME         TR_p-methyl
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130817
Time               14.29
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT              C6D6
NS                     16
DS                      2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                      4
DW                 60.400 usec
DE                  6.00 usec
TE                 298.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 15.00 usec
PL1                 4.90 dB
PL1W          3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1299964 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



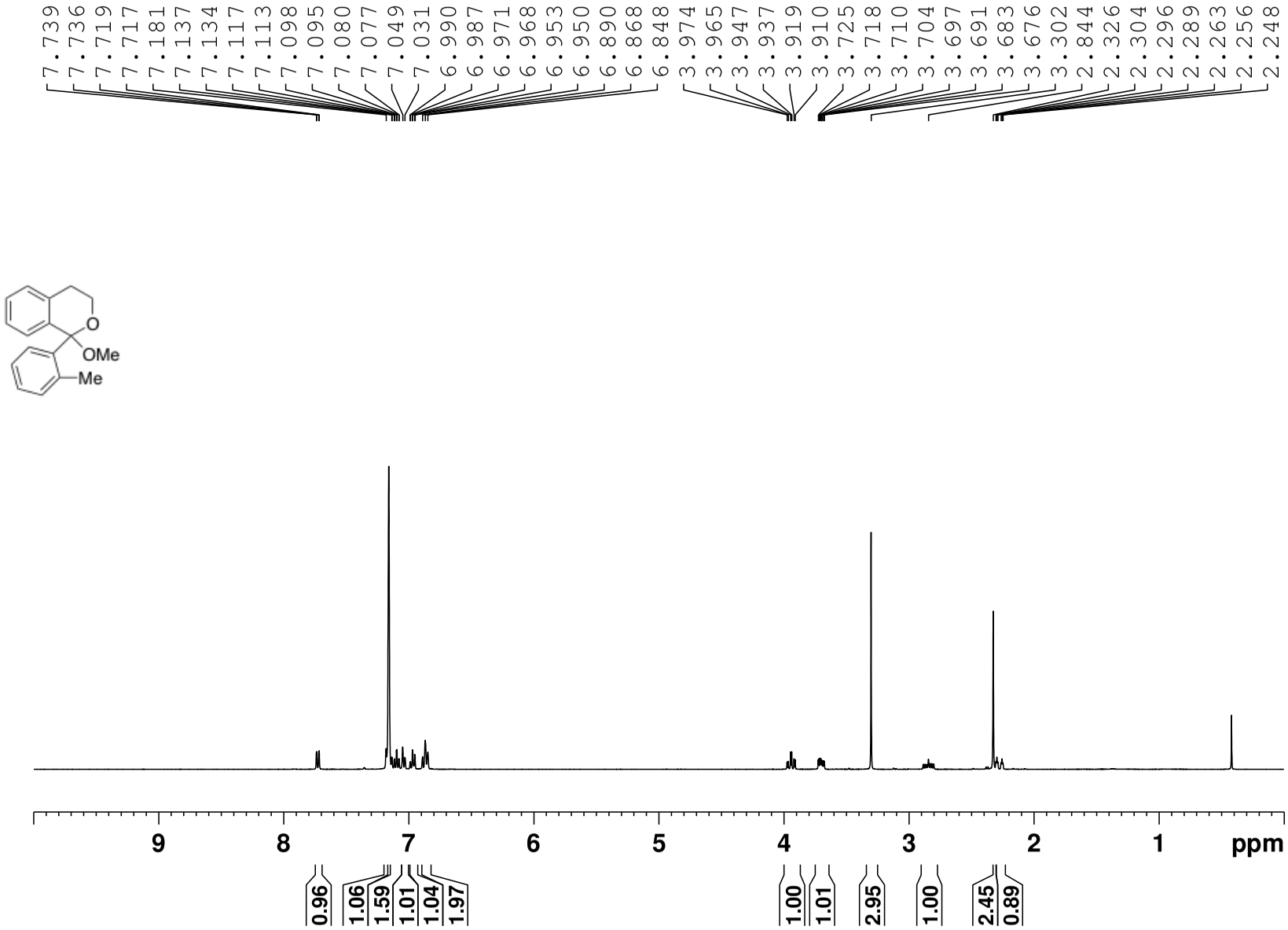

```
Current Data Parameters
NAME          TR_p-methyl
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20130817
Time                22.17
INSTRUM             spect
PROBHD    5 mm CPQNP 1H/
PULPROG           zgpg30
TD                 65536
SOLVENT              C6D6
NS                   1024
DS                      4
SWH             23980.814 Hz
FIDRES           0.365918 Hz
AQ               1.3664256 sec
RG                    512
DW                 20.850 usec
DE                 18.00 usec
TE                 298.2 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W          35.18820572 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W           3.30822015 W
PL12W          0.09195905 W
PL13W          0.08120718 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6127325 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```




```
Current Data Parameters
NAME         TR_m-methyl
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130809
Time               15.53
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT              C6D6
NS                     16
DS                      2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     8
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W          3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF           400.1299973 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

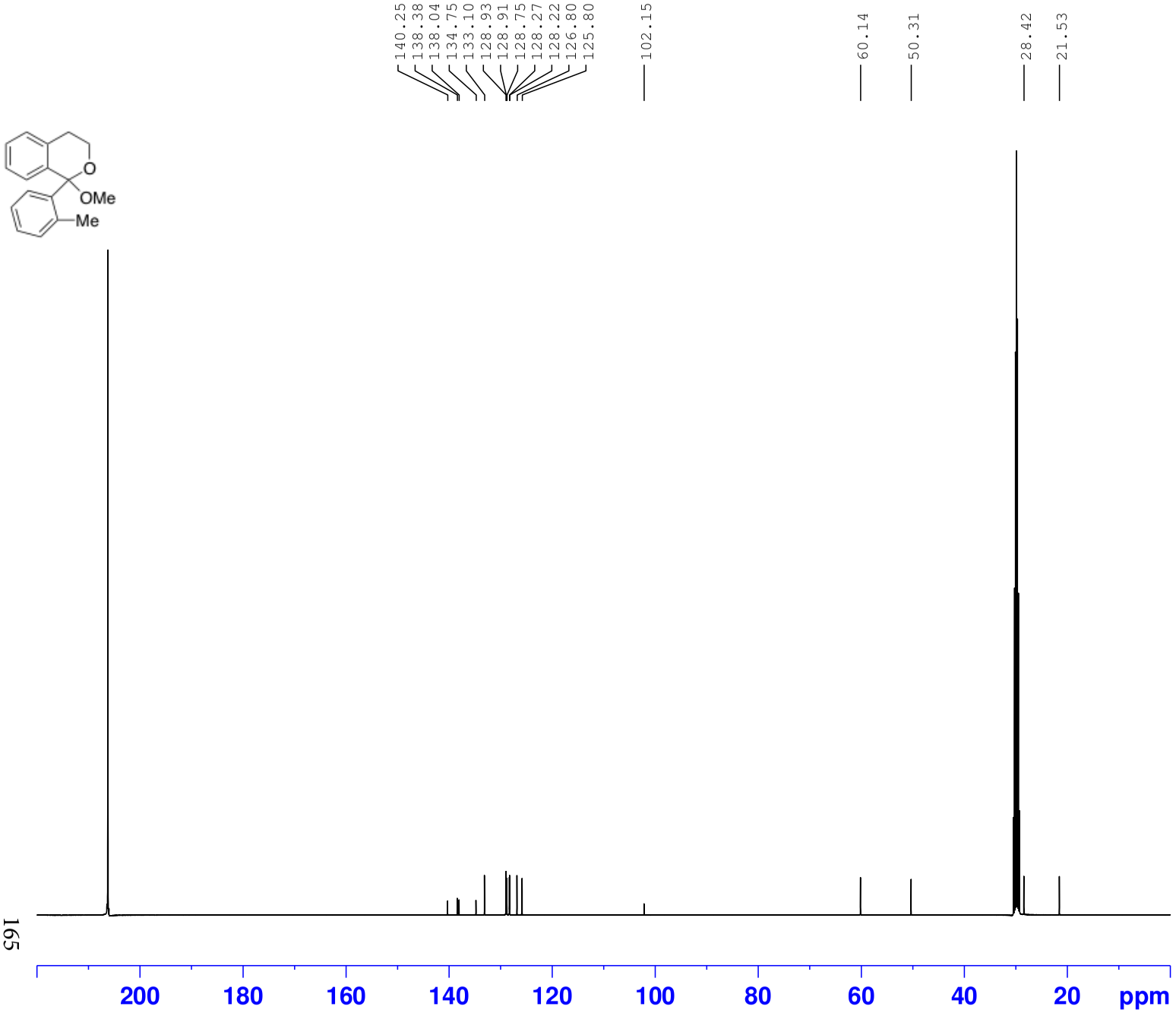



```
Current Data Parameters
NAME          TR_m-methyl
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20130810
Time                6.37
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG           zgpg30
TD                 65536
SOLVENT              C6D6
NS                   1024
DS                      4
SWH            23980.814 Hz
FIDRES          0.365918 Hz
AQ             1.3664256 sec
RG                    512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W         35.18820572 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W          3.30822015 W
PL12W         0.09195905 W
PL13W         0.08120718 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6127690 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```



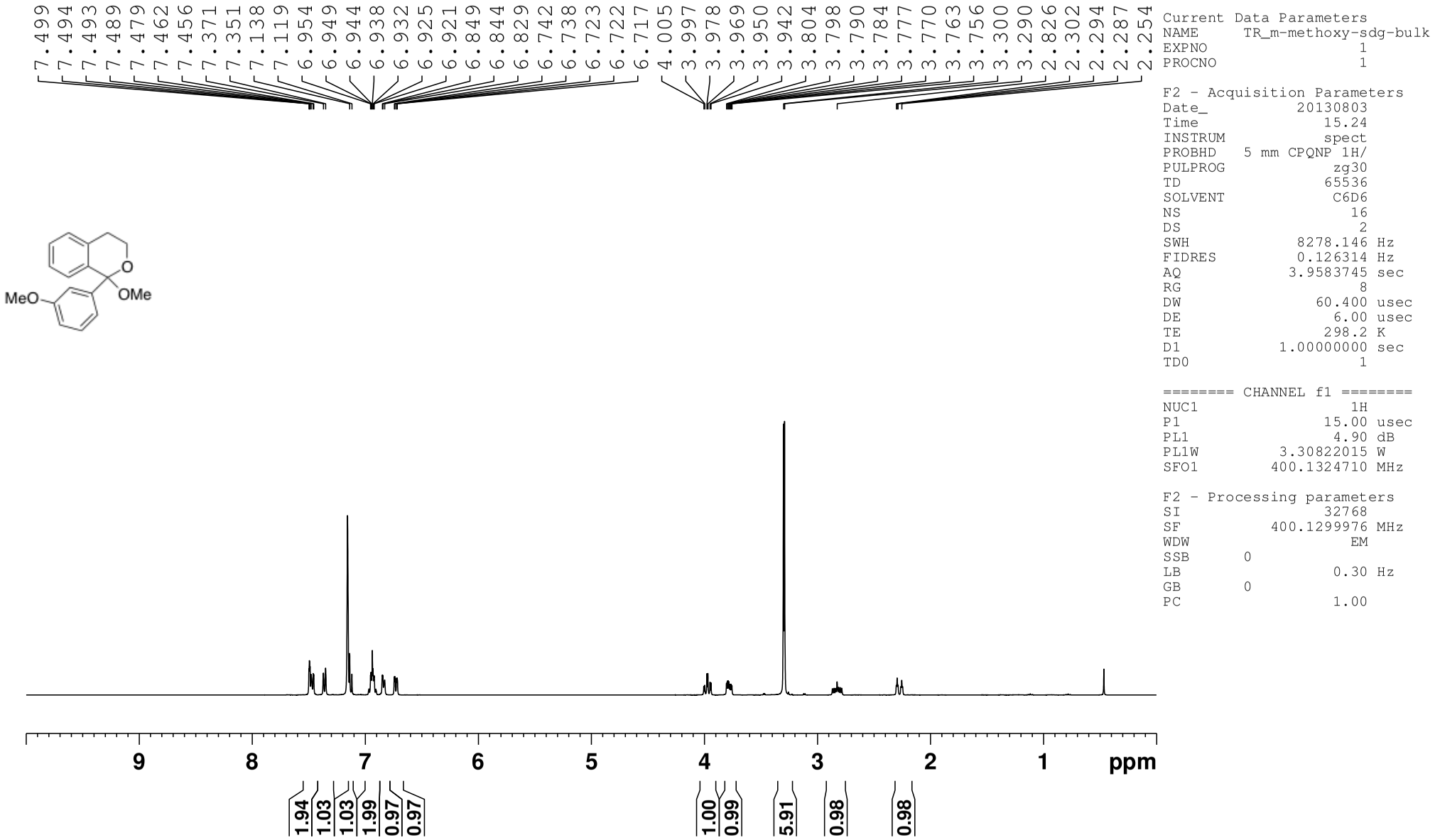

```
Current Data Parameters
NAME         TR_o-methyl
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130817
Time               14.36
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT             C6D6
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     9
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1299962 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-34, 13C NMR



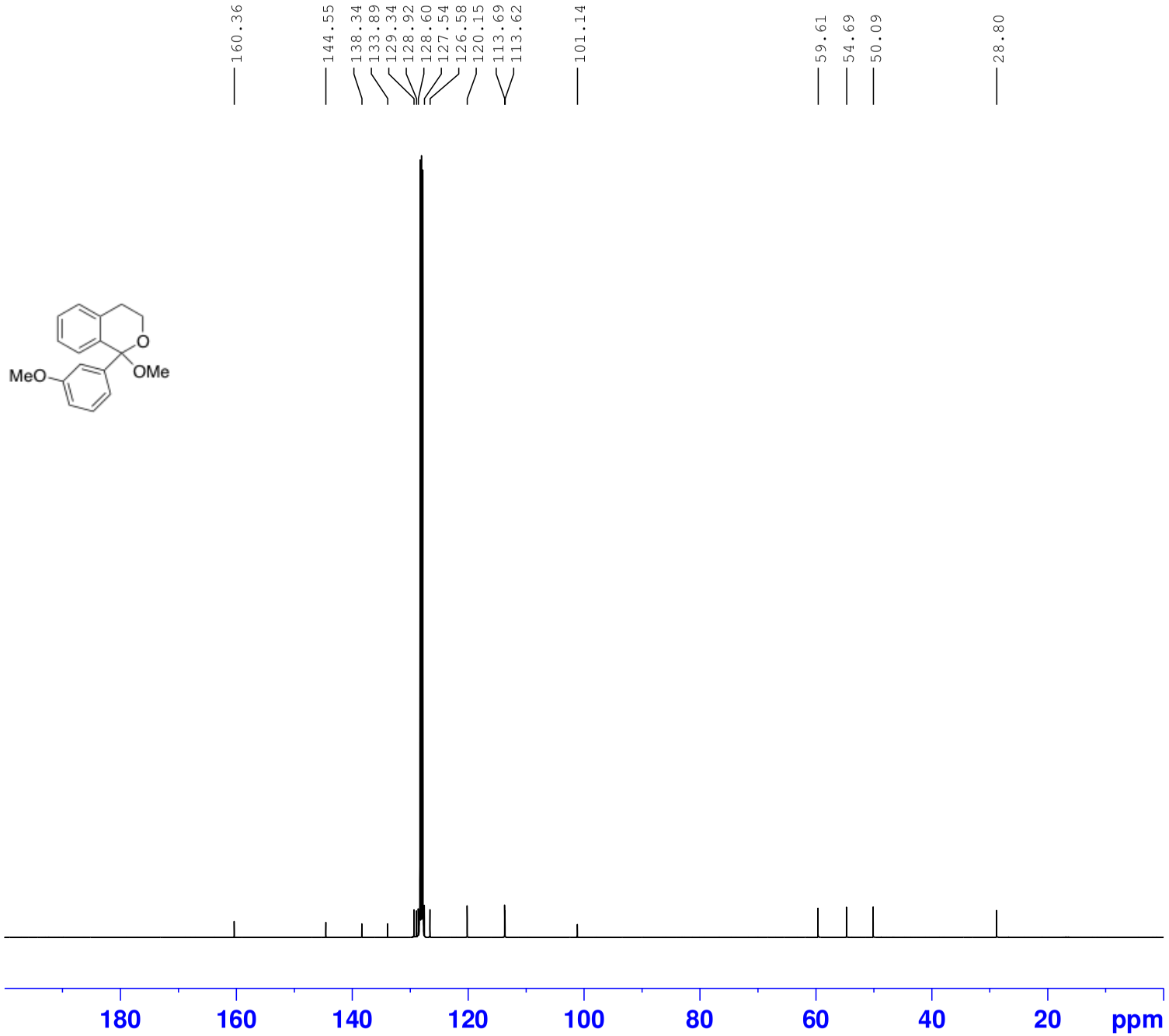

```
Current Data Parameters
NAME         TR_o-methyl
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131220
Time               23.15
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT         Acetone
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF         100.6126812 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

2-35, 1H NMR

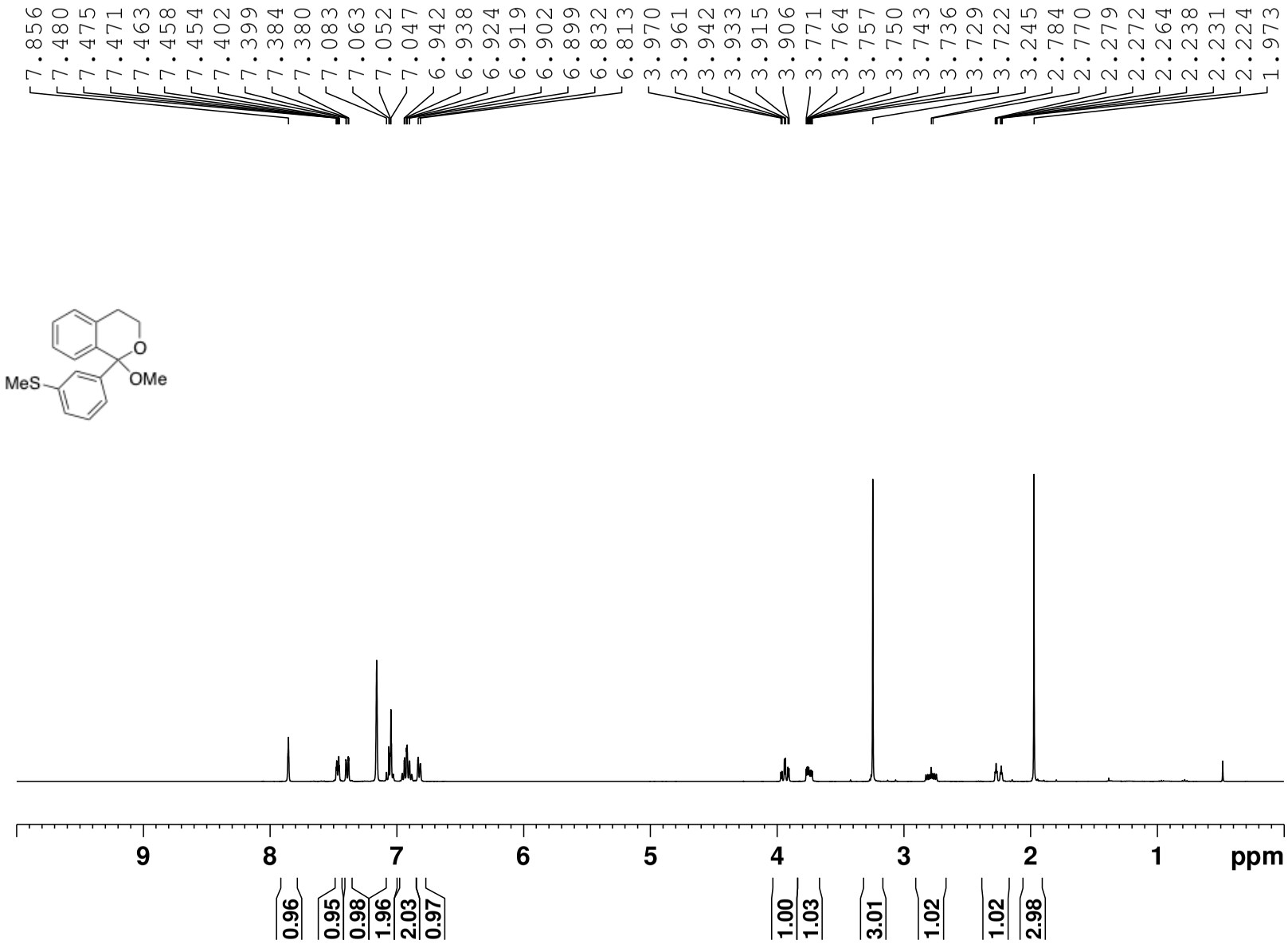



```
Current Data Parameters
NAME      TR_m-methoxy-sdg-bulk
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_              20130803
Time                  15.24
INSTRUM               spect
PROBHD   5 mm CPQNP 1H/
PULPROG                zg30
TD                    65536
SOLVENT                C6D6
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES             0.126314 Hz
AQ                3.9583745 sec
RG                       8
DW                  60.400 usec
DE                   6.00 usec
TE                  298.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   15.00 usec
PL1                   4.90 dB
PL1W            3.30822015 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF            400.1299976 MHz
WDW                      EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
```

2-35, 13C NMR

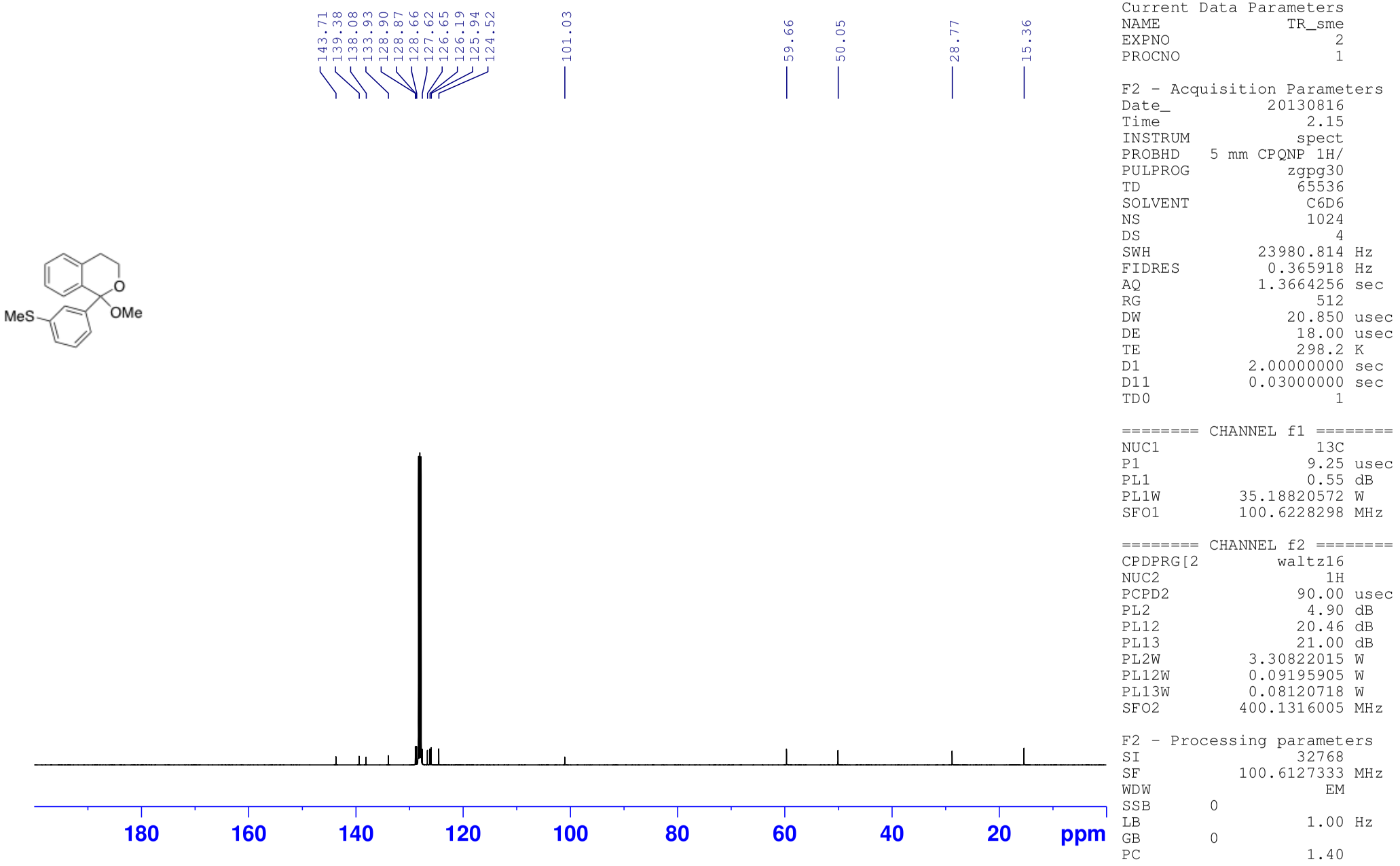



```
Current Data Parameters
NAME      TR_m-methoxy-sdg-bulk
EXPNO                         2
PROCNO                        1

F2 - Acquisition Parameters
Date_              20130803
Time                  23.10
INSTRUM               spect
PROBHD    5 mm CPQNP 1H/
PULPROG             zgpg30
TD                    65536
SOLVENT                C6D6
NS                     1024
DS                        4
SWH              23980.814 Hz
FIDRES            0.365918 Hz
AQ                1.3664256 sec
RG                      512
DW                   20.850 usec
DE                   18.00 usec
TE                   298.2 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    9.25 usec
PL1                   0.55 dB
PL1W          35.18820572 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2           waltz16
NUC2                    1H
PCPD2                90.00 usec
PL2                   4.90 dB
PL12                 20.46 dB
PL13                 21.00 dB
PL2W           3.30822015 W
PL12W          0.09195905 W
PL13W          0.08120718 W
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                    32768
SF            100.6127348 MHz
WDW                      EM
SSB       0
LB                    1.00 Hz
GB        0
PC                    1.40
```



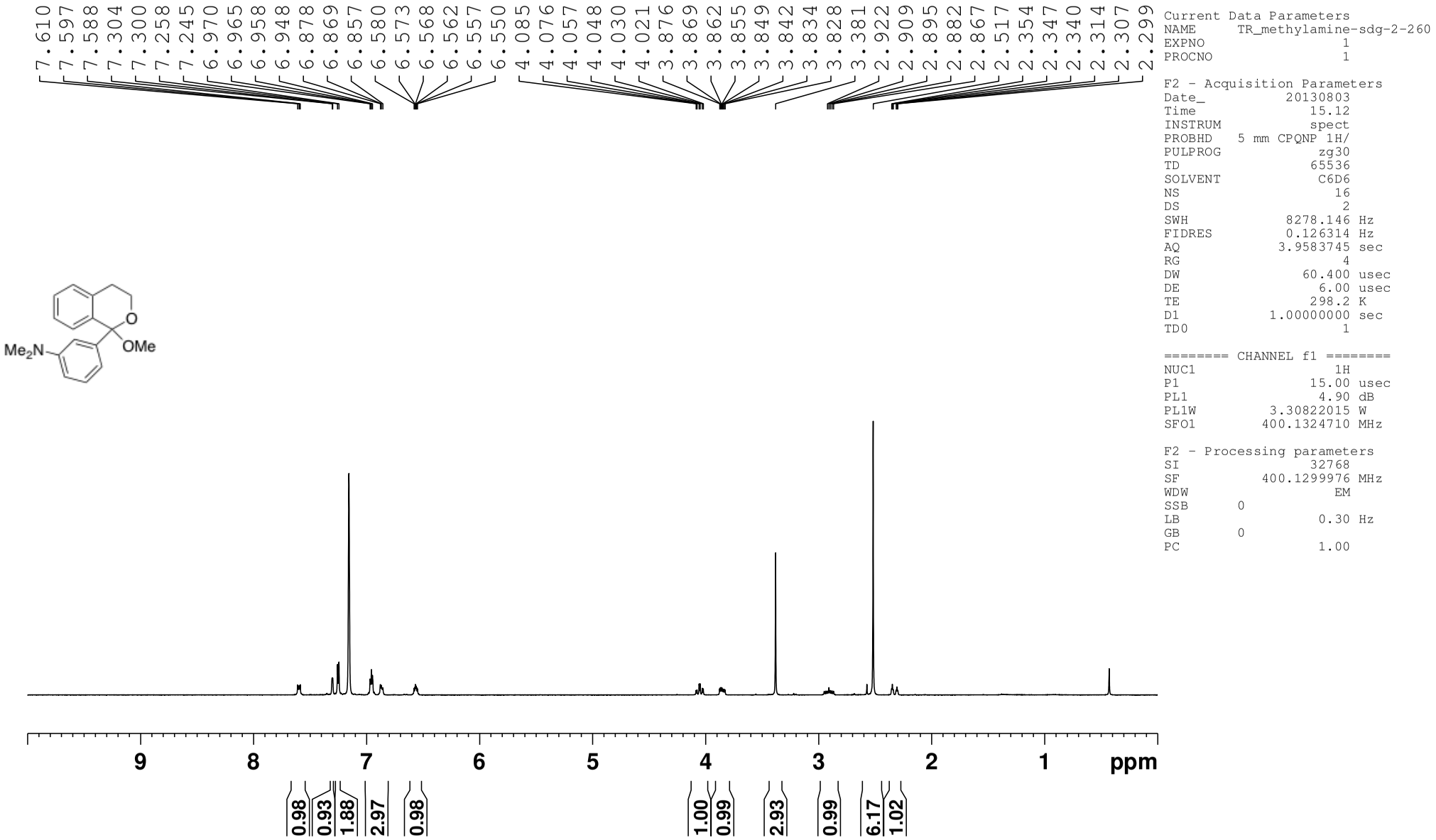

```
Current Data Parameters
NAME                  TR_sme
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20130816
Time                   1.15
INSTRUM               spect
PROBHD   5 mm CPQNP 1H/
PULPROG                zg30
TD                    65536
SOLVENT                C6D6
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9583745 sec
RG                       8
DW                  60.400 usec
DE                   6.00 usec
TE                   298.2 K
D1              1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                    15.00 usec
PL1                    4.90 dB
PL1W           3.30822015 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                     32768
SF           400.1299966 MHz
WDW                       EM
SSB       0
LB                     0.30 Hz
GB        0
PC                     1.00
```

2-36, 13C NMR



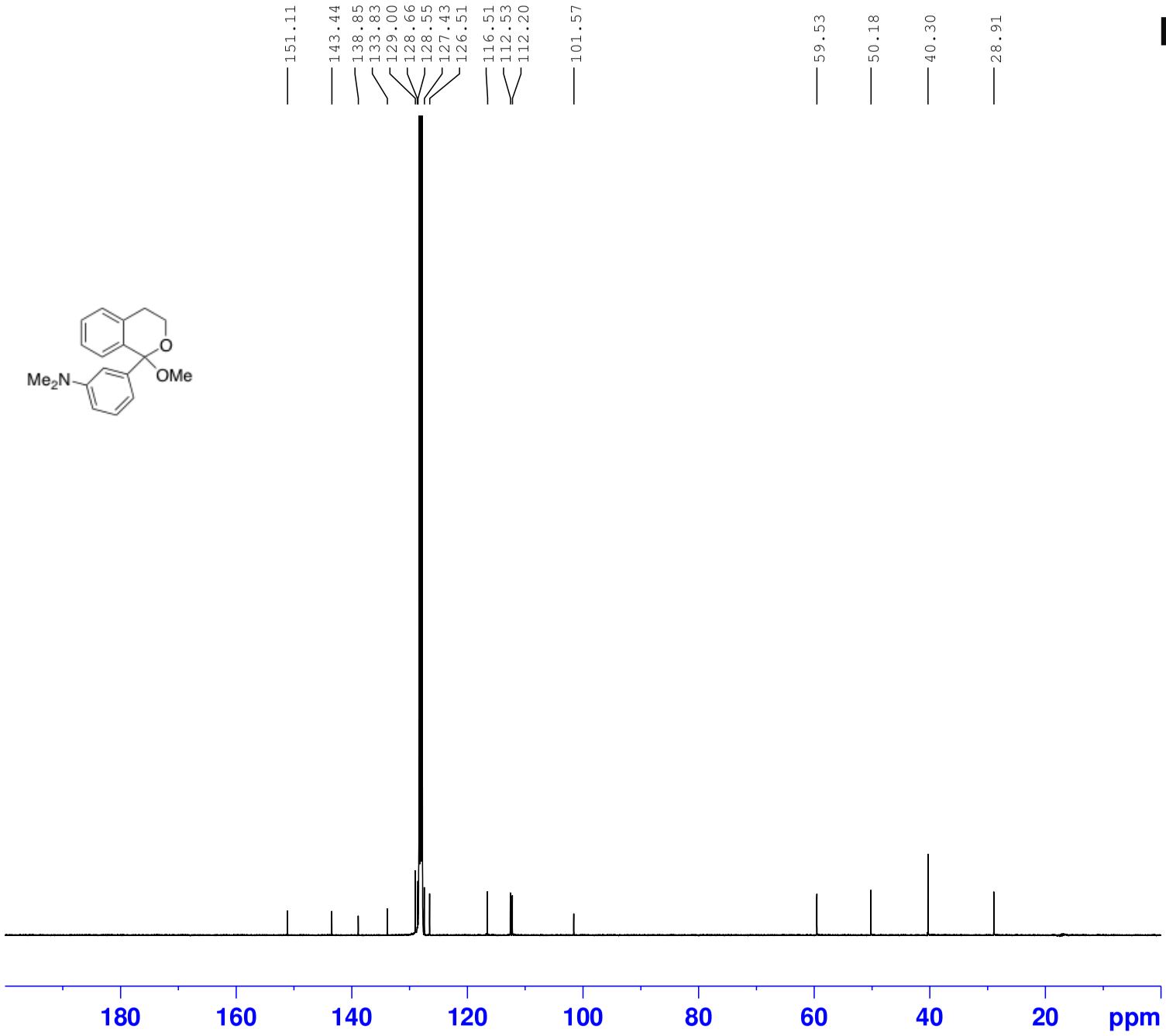

```
Current Data Parameters
NAME                 TR_sme
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_             20130816
Time                  2.15
INSTRUM              spect
PROBHD    5 mm CPQNP 1H/
PULPROG              zgpg30
TD                    65536
SOLVENT                C6D6
NS                     1024
DS                        4
SWH              23980.814 Hz
FIDRES            0.365918 Hz
AQ                1.3664256 sec
RG                      512
DW                   20.850 usec
DE                   18.00 usec
TE                   298.2 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    9.25 usec
PL1                   0.55 dB
PL1W          35.18820572 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2           waltz16
NUC2                    1H
PCPD2                90.00 usec
PL2                   4.90 dB
PL12                 20.46 dB
PL13                 21.00 dB
PL2W           3.30822015 W
PL12W          0.09195905 W
PL13W          0.08120718 W
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                    32768
SF           100.6127333 MHz
WDW                      EM
SSB       0
LB                    1.00 Hz
GB        0
PC                    1.40
```

2-37, 1H NMR



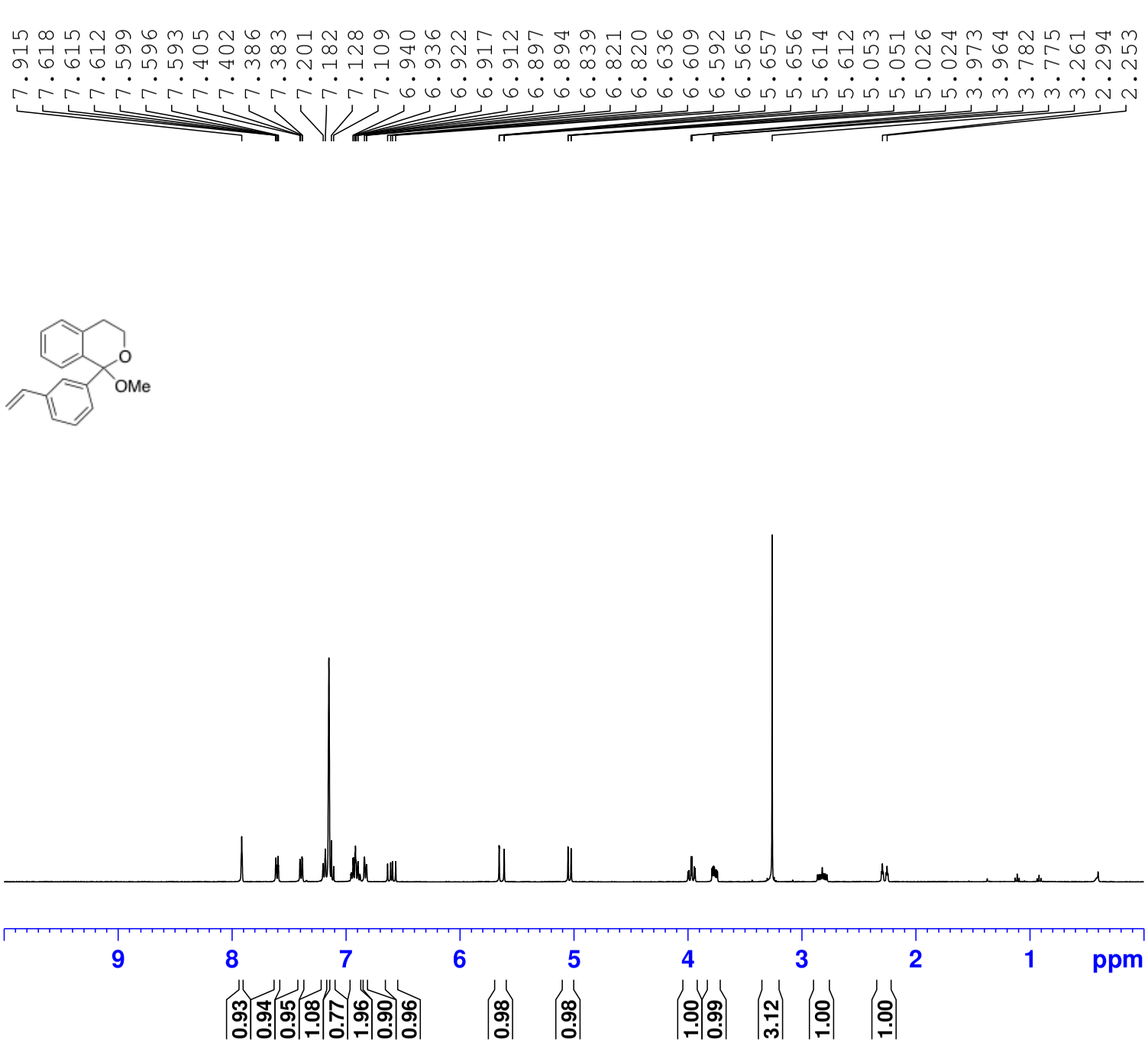

```
Current Data Parameters
NAME      TR_methylamine-sdg-2-260
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_          20130803
Time             15.12
INSTRUM          spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zg30
TD              65536
SOLVENT          C6D6
NS                 16
DS                  2
SWH          8278.146 Hz
FIDRES       0.126314 Hz
AQ           3.9583745 sec
RG                  4
DW             60.400 usec
DE              6.00 usec
TE             298.2 K
D1          1.00000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1                1H
P1             15.00 usec
PL1             4.90 dB
PL1W       3.30822015 W
SFO1     400.1324710 MHz

F2 - Processing parameters
SI                32768
SF        400.1299976 MHz
WDW                EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```

2-37, 13C NMR



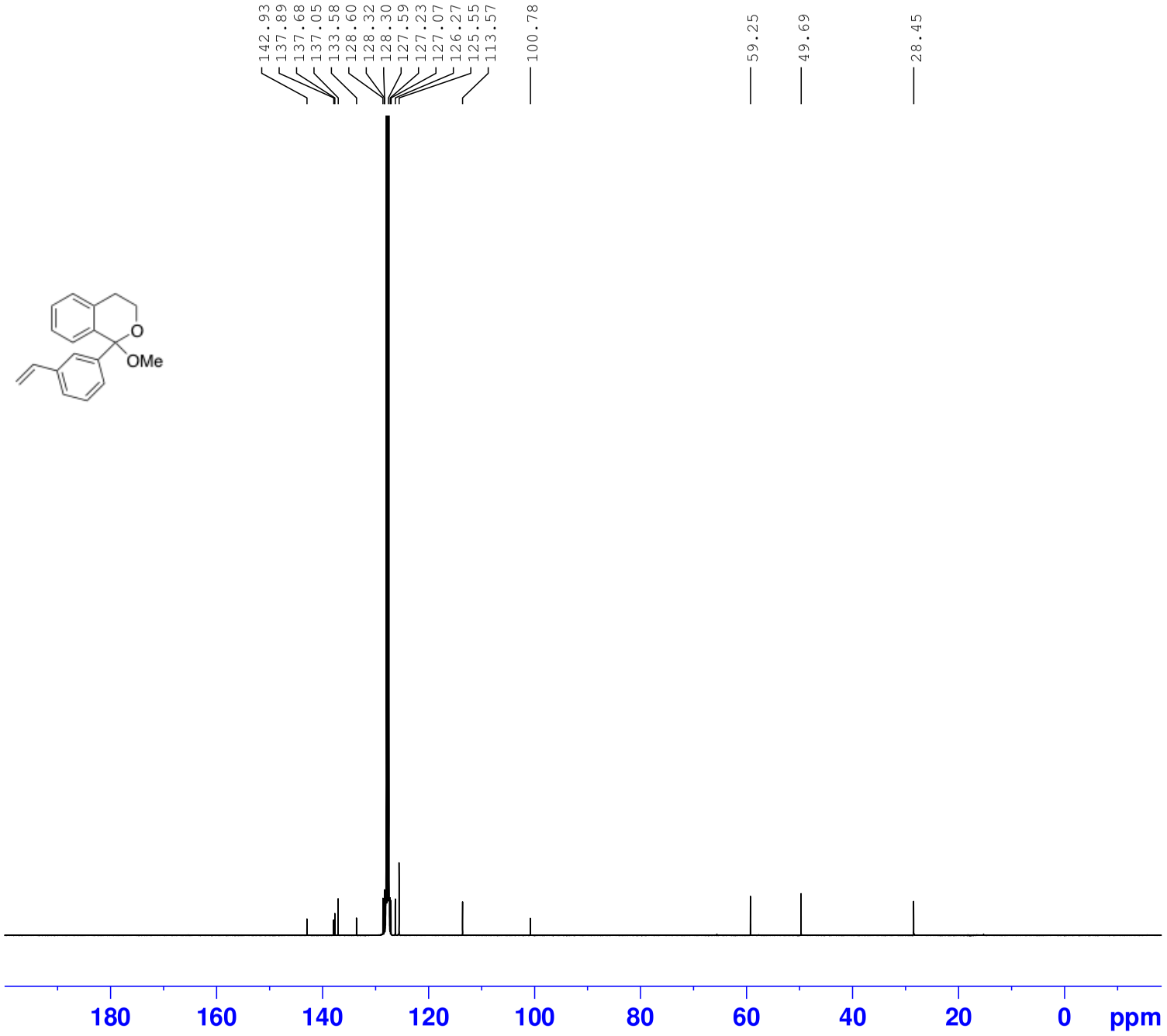

```
Current Data Parameters
NAME      TR_methylamine-sdg-2-260
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130803
Time              21.03
INSTRUM           spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT             C6D6
NS                  1024
DS                     4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.1 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   9.25 usec
PL1                  0.55 dB
PL1W         35.18820572 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2               90.00 usec
PL2                  4.90 dB
PL12                20.46 dB
PL13                21.00 dB
PL2W          3.30822015 W
PL12W         0.09195905 W
PL13W         0.08120718 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6127350 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

2-38, 1H NMR



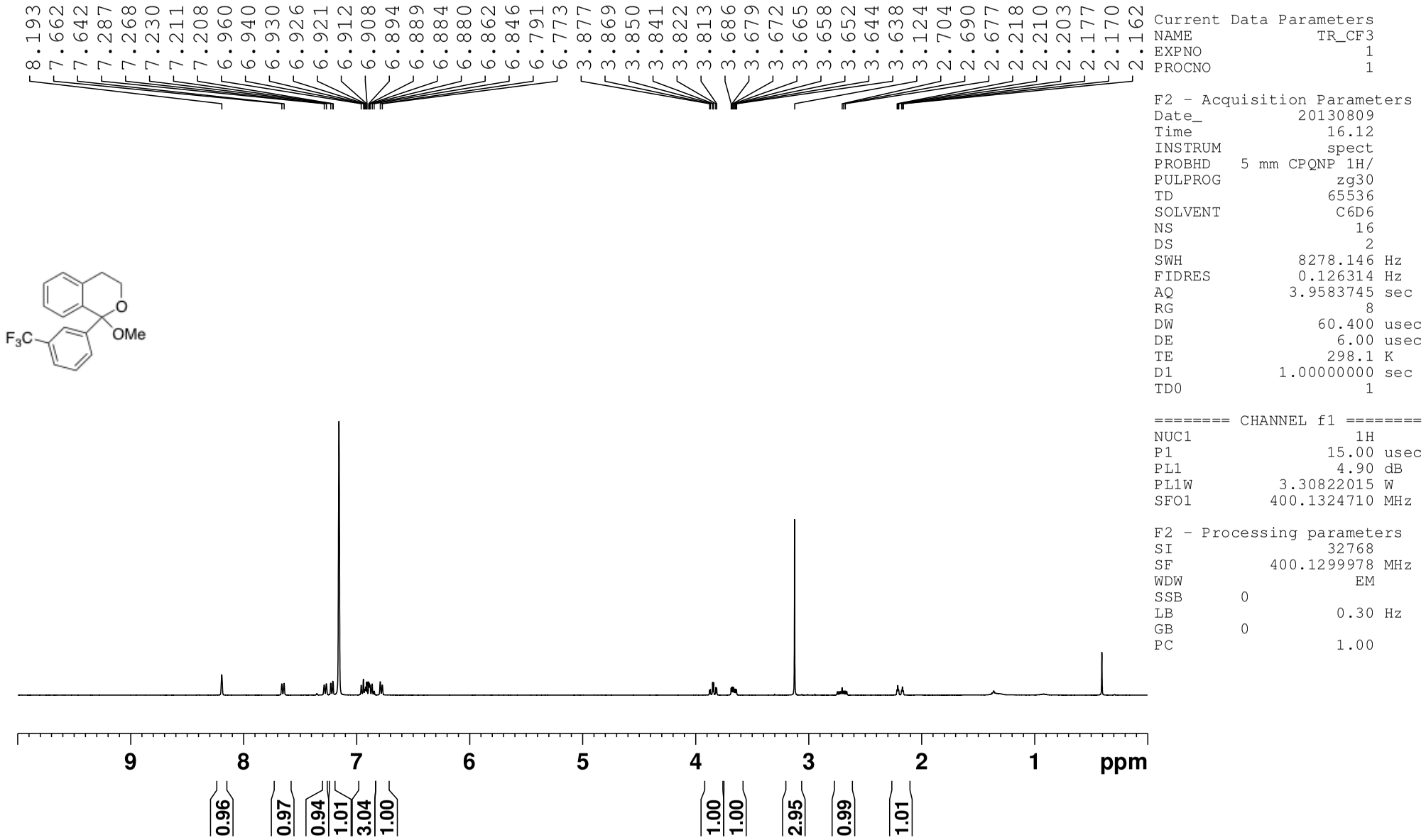
BRUKER

```
Current Data Parameters
NAME                  SDG-2-291
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20130525
Time                      19.21
INSTRUM                   spect
PROBHD    5 mm CPQNP 1H/
PULPROG                    zg30
TD                        65536
SOLVENT                    C6D6
NS                           16
DS                            2
SWH                    8278.146 Hz
FIDRES                 0.126314 Hz
AQ                     3.9583745 sec
RG                            8
DW                        60.400 usec
DE                         6.00 usec
TE                        298.2 K
D1                   1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                         1H
P1                        15.00 usec
PL1                        4.90 dB
PL1W                3.30822015 W
SFO1               400.1324710 MHz

F2 - Processing parameters
SI                        32768
SF                 400.1300000 MHz
WDW                          EM
SSB             0
LB                         0.30 Hz
GB              0
PC                         1.00
```



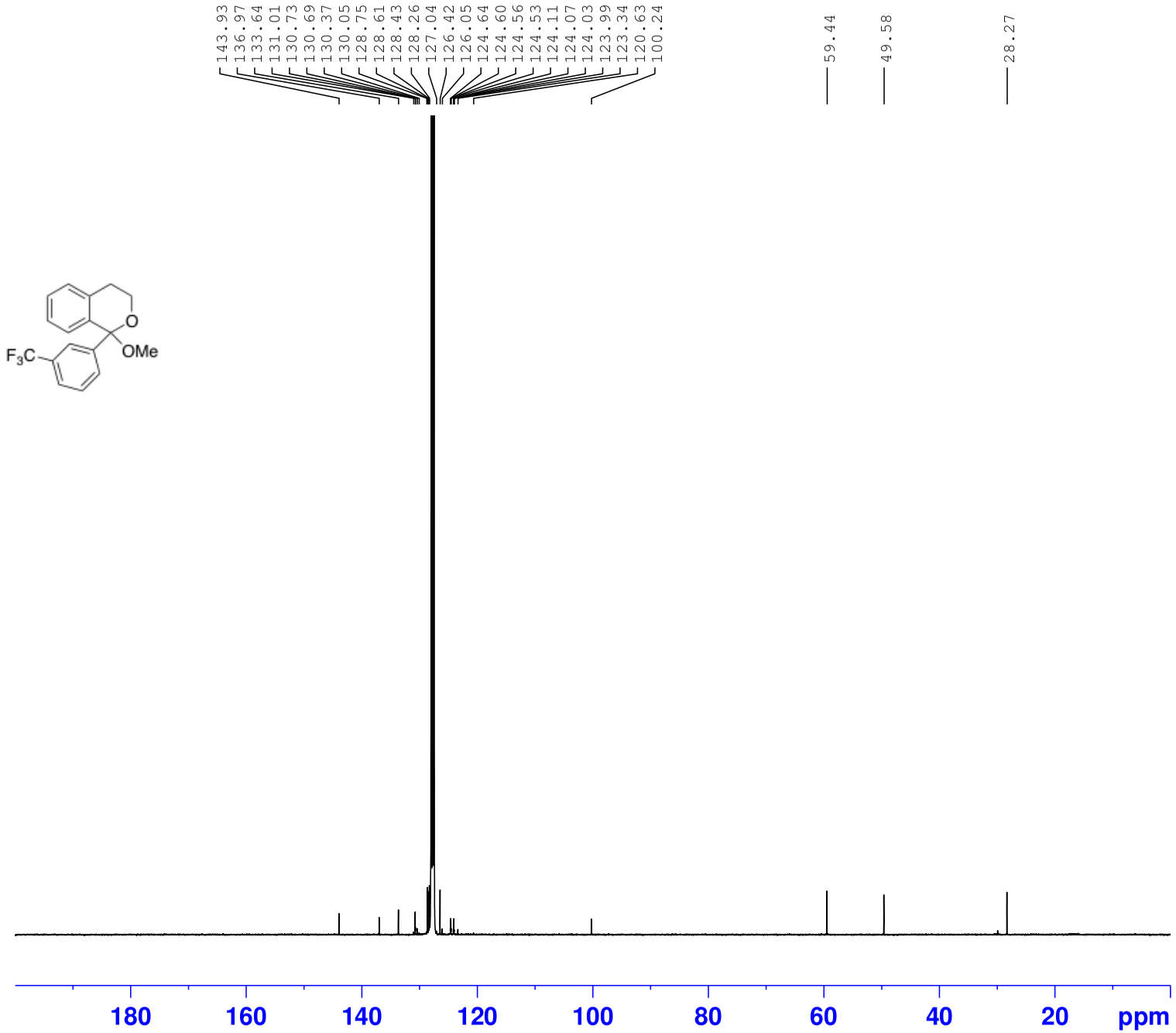

```
Current Data Parameters
NAME                 SDG-2-291
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20130526
Time                      2.02
INSTRUM                  spect
PROBHD    5 mm CPQNP 1H/
PULPROG                 zgpg30
TD                       65536
SOLVENT                   C6D6
NS                        1024
DS                           4
SWH                  23980.814 Hz
FIDRES                0.365918 Hz
AQ                    1.3664256 sec
RG                         512
DW                      20.850 usec
DE                      18.00 usec
TE                      298.2 K
D1                   2.00000000 sec
D11                  0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        13C
P1                        9.25 usec
PL1                       0.55 dB
PL1W                35.18820572 W
SFO1               100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2                waltz16
NUC2                        1H
PCPD2                    90.00 usec
PL2                       4.90 dB
PL12                     20.46 dB
PL13                     21.00 dB
PL2W                 3.30822015 W
PL12W                0.09195905 W
PL13W                0.08120718 W
SFO2               400.1316005 MHz

F2 - Processing parameters
SI                       32768
SF                 100.6127690 MHz
WDW                         EM
SSB              0
LB                        1.00 Hz
GB               0
PC                        1.40
```

2-39, 1H NMR




```
Current Data Parameters
NAME                  TR_CF3
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20130809
Time                  16.12
INSTRUM               spect
PROBHD   5 mm CPQNP 1H/
PULPROG                zg30
TD                    65536
SOLVENT                C6D6
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9583745 sec
RG                        8
DW                   60.400 usec
DE                    6.00 usec
TE                   298.1 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   15.00 usec
PL1                   4.90 dB
PL1W           3.30822015 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF             400.1299978 MHz
WDW                      EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
```

2-39, 13C NMR



Current Data Parameters

NAME	TR_CF3
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20130810
Time	22.07
INSTRUM	spect
PROBHD	5 mm CPQNP 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	C6D6
NS	1024
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664256 sec
RG	512
DW	20.850 usec
DE	18.00 usec
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

NUC1	13C
P1	9.25 usec
PL1	0.55 dB
PL1W	35.18820572 W
SFO1	100.6228298 MHz

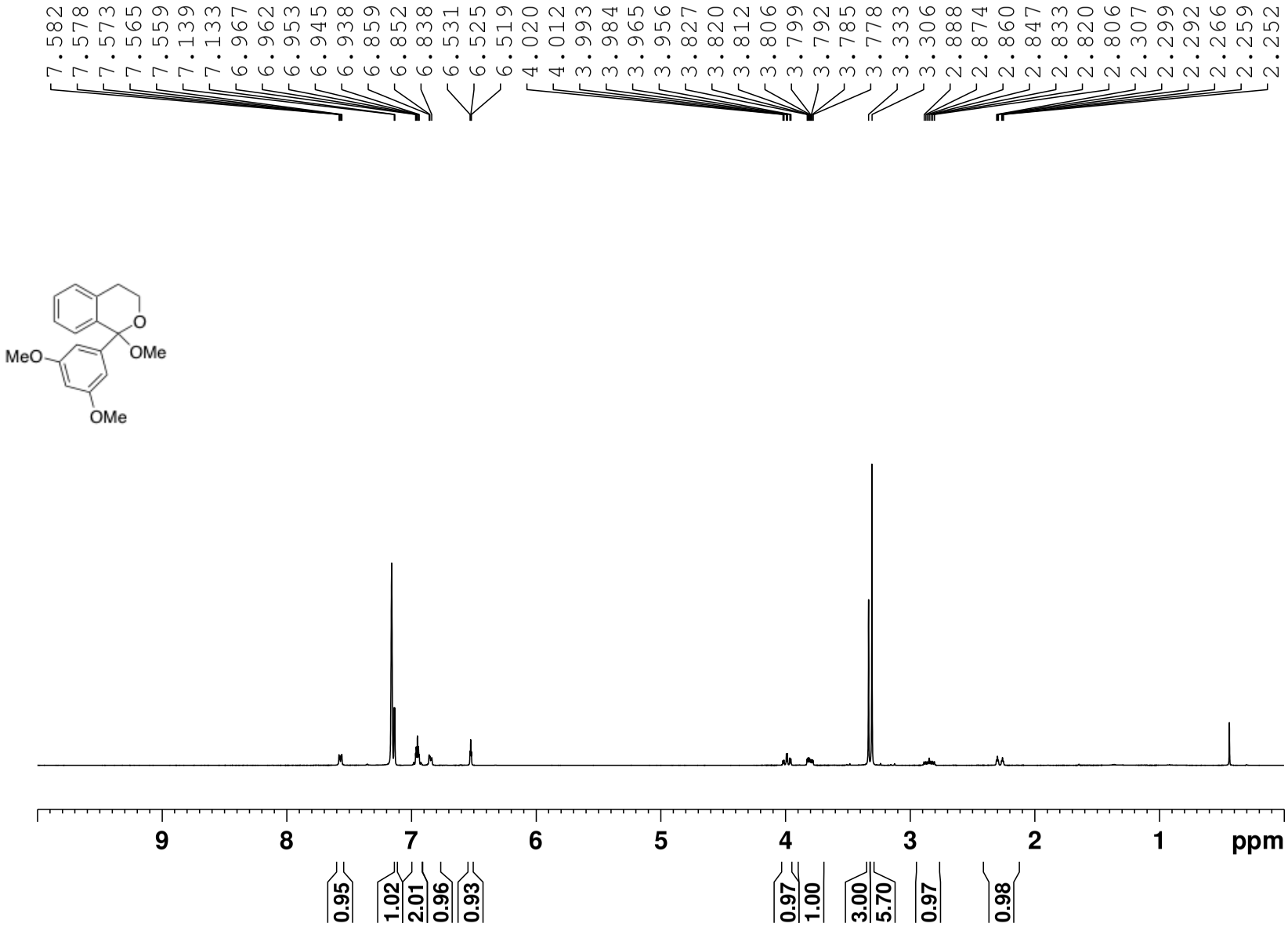
======== CHANNEL f2 ========

CPDPRG[2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	4.90 dB
PL12	20.46 dB
PL13	21.00 dB
PL2W	3.30822015 W
PL12W	0.09195905 W
PL13W	0.08120718 W
SFO2	400.1316005 MHz

F2 - Processing parameters

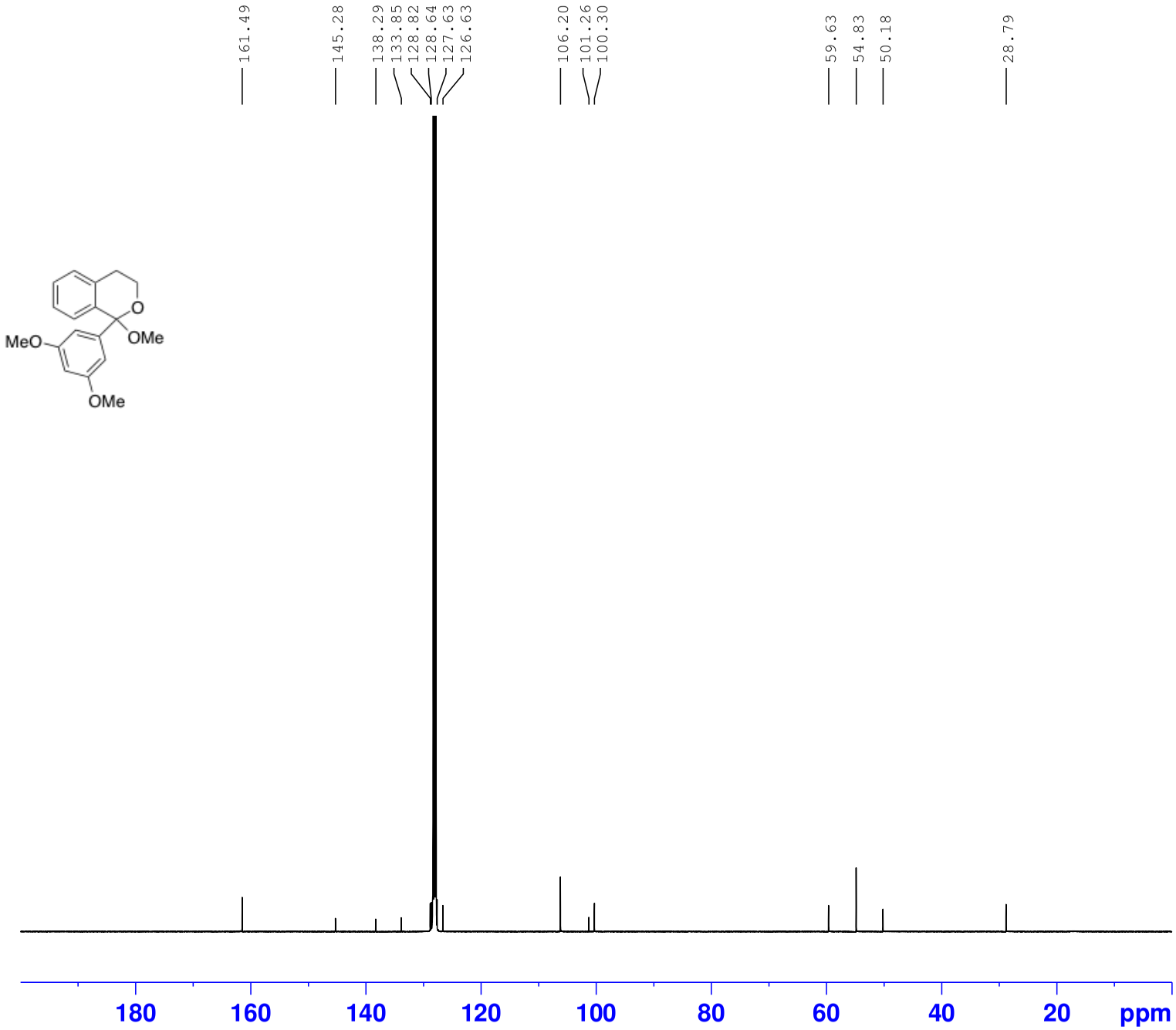
SI	32768
SF	100.6127690 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

2-40, 1H NMR

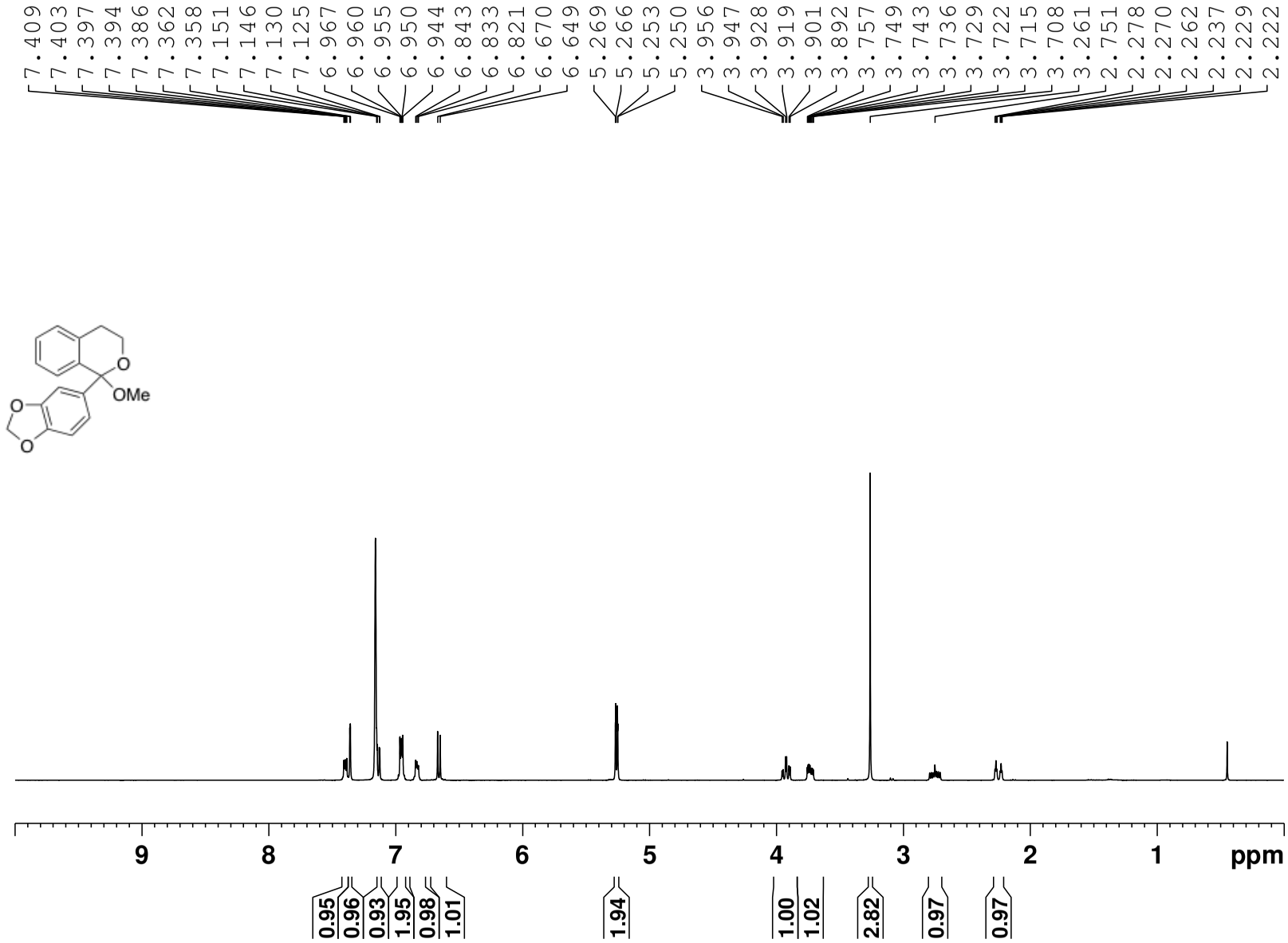



```
Current Data Parameters
NAME       TR_di-methoxy
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130809
Time               16.06
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT              C6D6
NS                     16
DS                      2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                   7.1
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1299966 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-40, 13C NMR

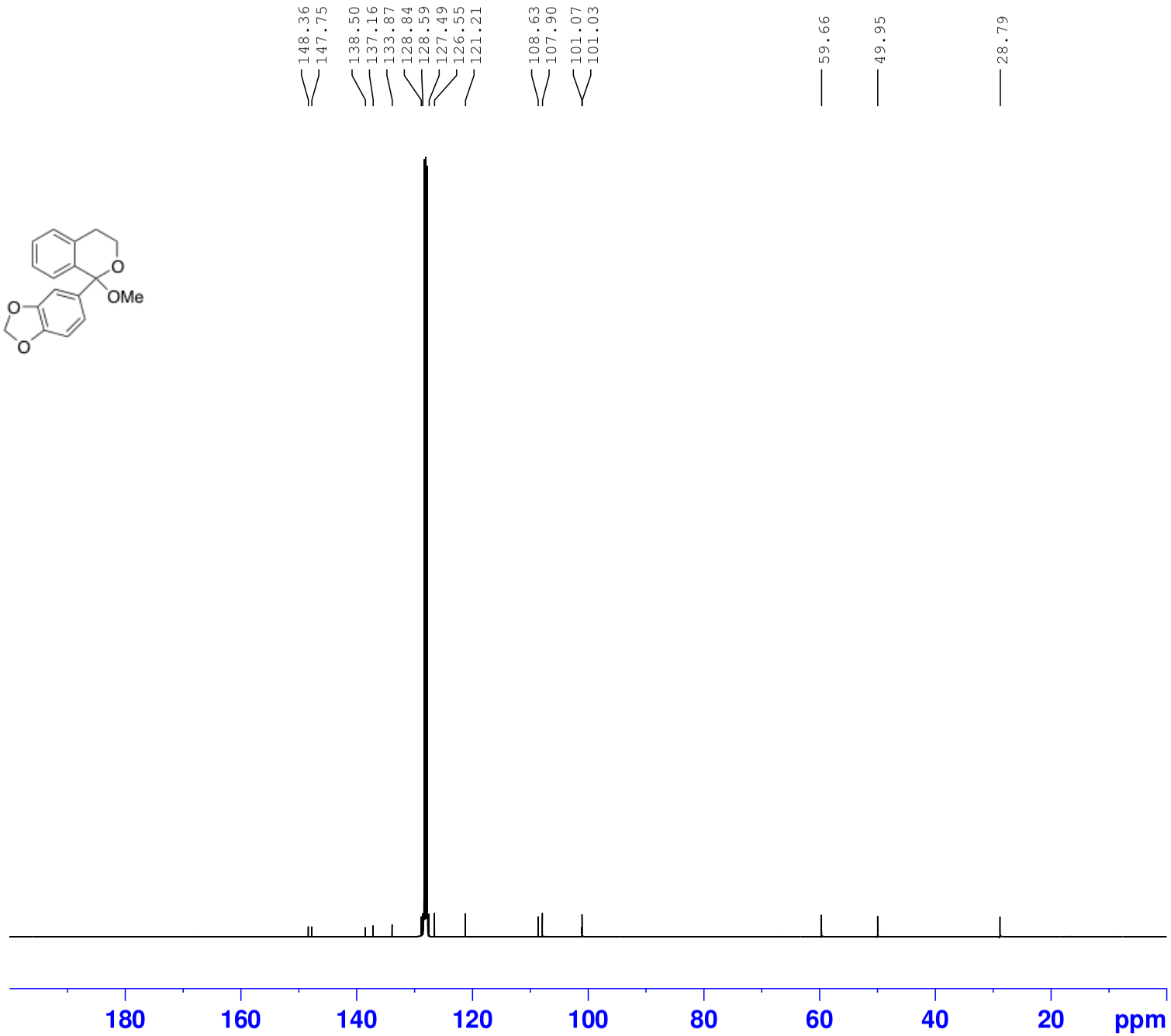



```
Current Data Parameters
NAME       TR_di-methoxy
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130810
Time               21.03
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT             C6D6
NS                  1024
DS                     4
SWH            23980.814 Hz
FIDRES          0.365918 Hz
AQ             1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W         35.18820572 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W          3.30822015 W
PL12W         0.09195905 W
PL13W         0.08120718 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF            100.6127332 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



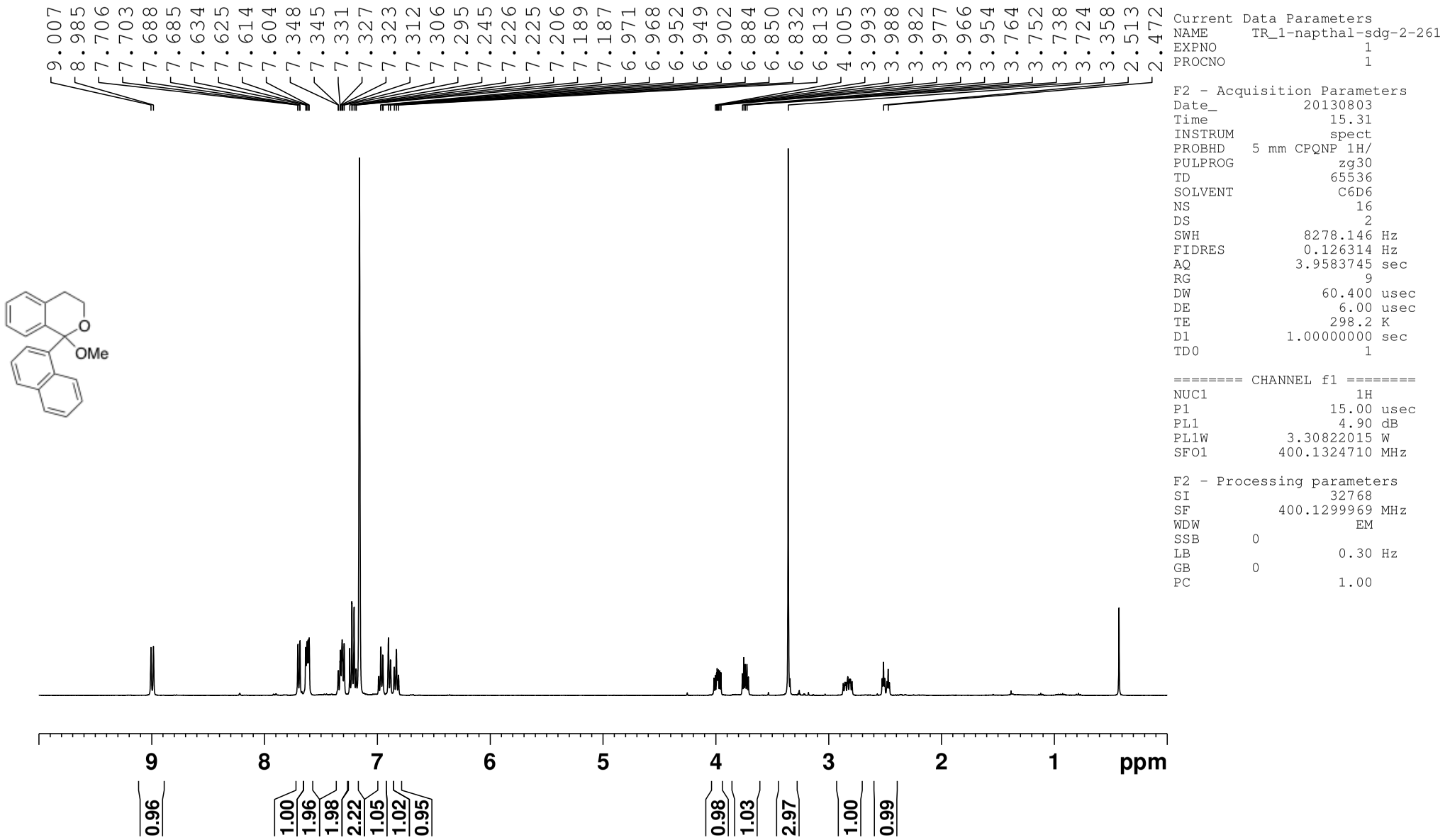

```
Current Data Parameters
NAME      TR_acetal-tr-1-121
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20130803
Time                  15.18
INSTRUM               spect
PROBHD   5 mm CPQNP 1H/
PULPROG                zg30
TD                    65536
SOLVENT                C6D6
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9583745 sec
RG                        9
DW                   60.400 usec
DE                    6.00 usec
TE                   298.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    15.00 usec
PL1                    4.90 dB
PL1W           3.30822015 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                     32768
SF           400.1299963 MHz
WDW                       EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
```

2-41, 13C NMR

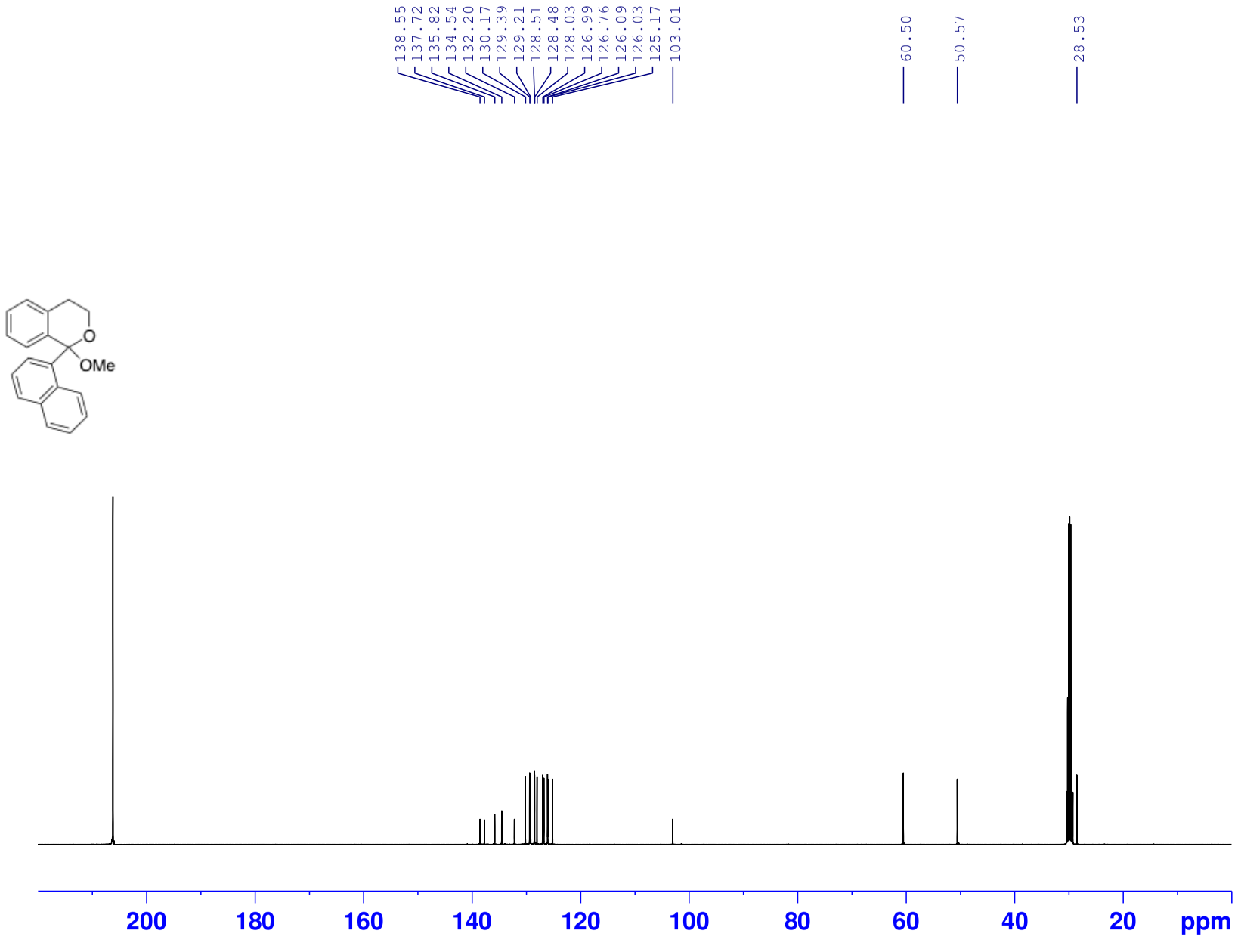



```
Current Data Parameters
NAME      TR_acetal-tr-1-121
EXPNO                      2
PROCNO                     1

F2 - Acquisition Parameters
Date_           20130803
Time              22.06
INSTRUM           spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT             C6D6
NS                  1024
DS                     4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                   512
DW               20.850 usec
DE               18.00 usec
TE               298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127338 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

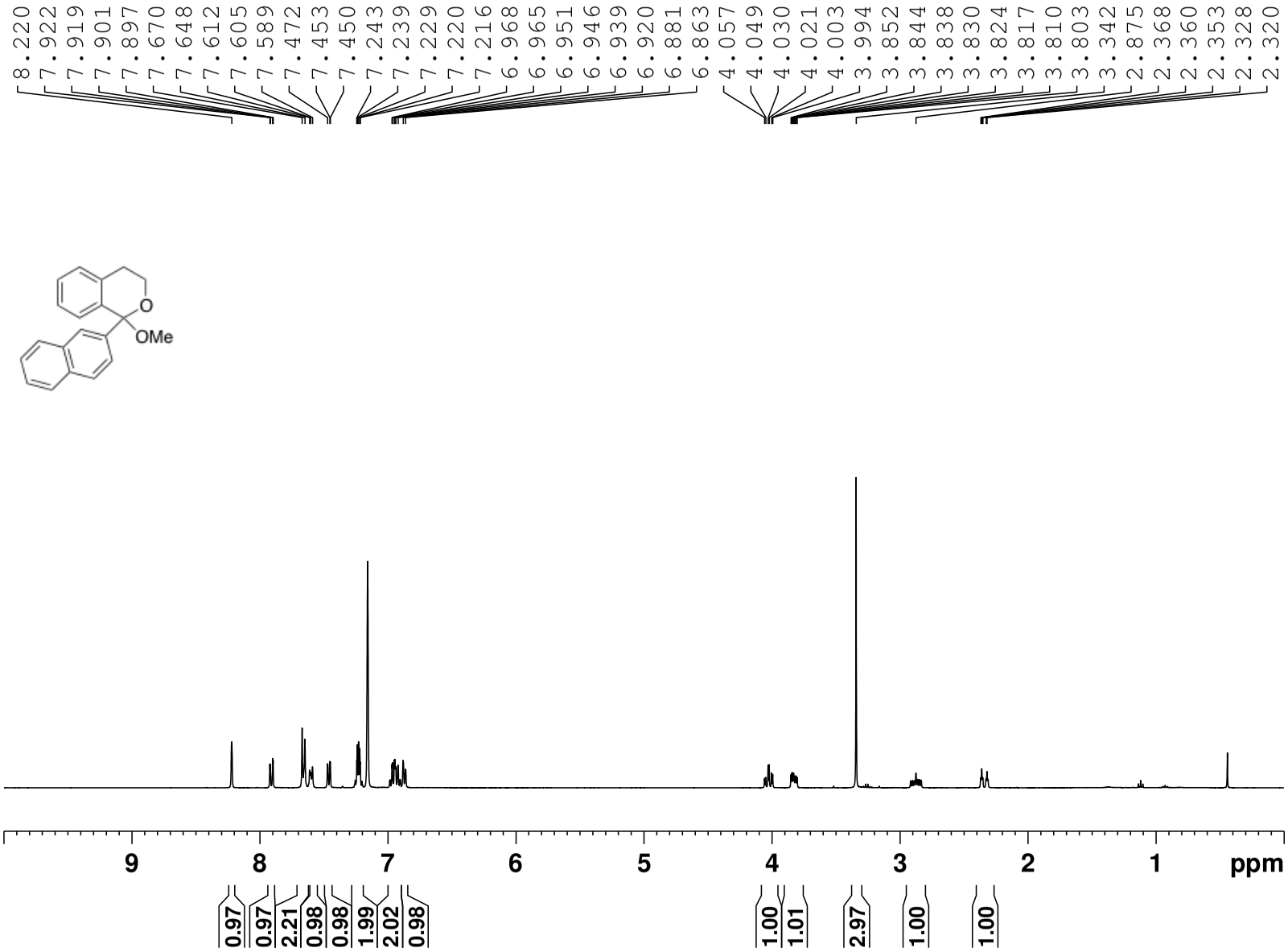
2-42, 1H NMR




```
Current Data Parameters
NAME      TR_1-napthal-sdg-2-261
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130803
Time              15.31
INSTRUM           spect
PROBHD   5 mm CPQNP 1H/
PULPROG           zg30
TD               65536
SOLVENT           C6D6
NS                  16
DS                   2
SWH            8278.146 Hz
FIDRES         0.126314 Hz
AQ            3.9583745 sec
RG                   9
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1299969 MHz
WDW                EM
SSB      0
LB                 0.30 Hz
GB       0
PC                 1.00
```

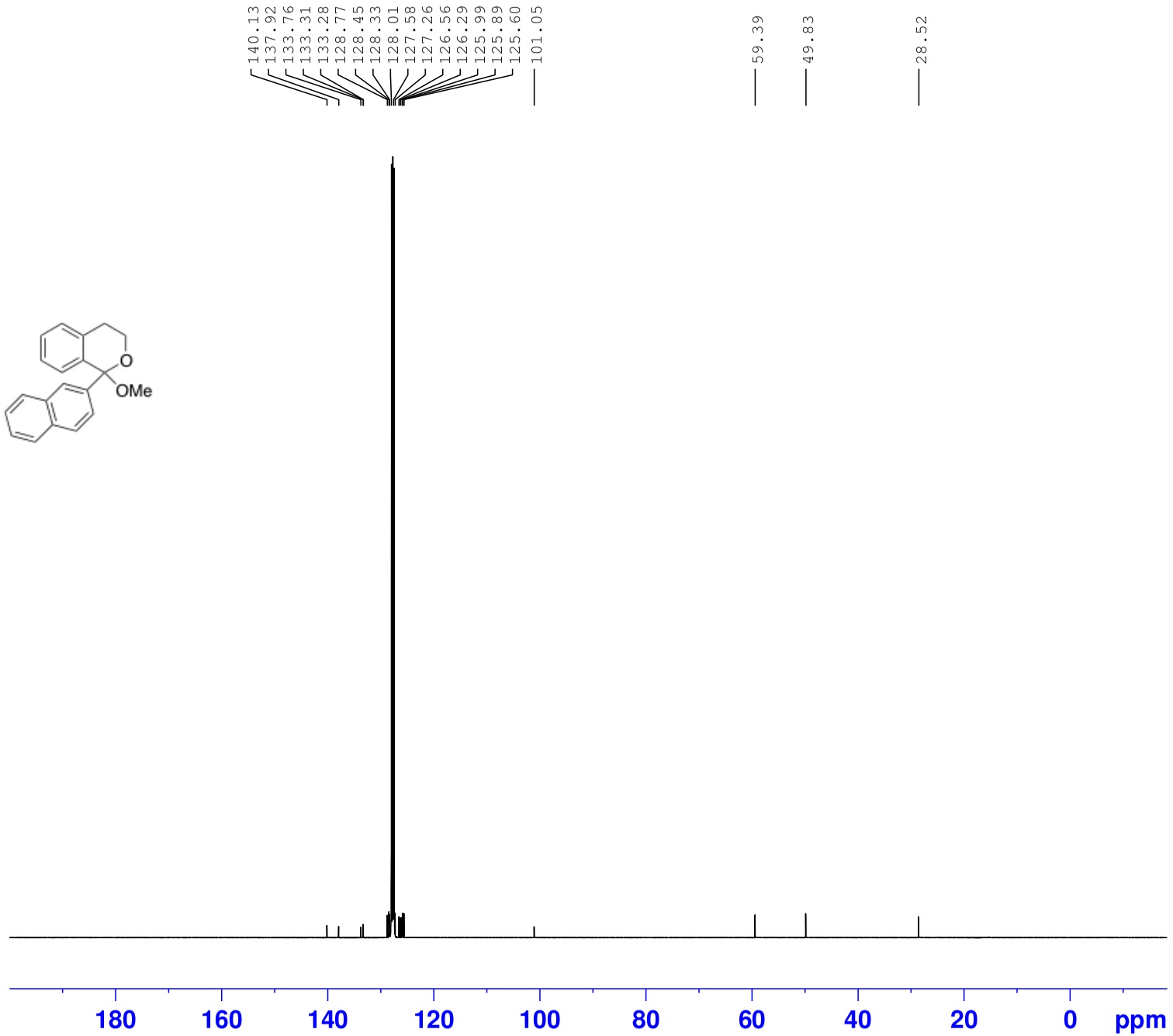



```
Current Data Parameters
NAME                  TR_1-nap
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20131220
Time                     21.09
INSTRUM                  spect
PROBHD    5 mm CPQNP 1H/
PULPROG                 zgpg30
TD                       65536
SOLVENT                Acetone
NS                          1024
DS                             4
SWH                 23980.814 Hz
FIDRES               0.365918 Hz
AQ                   1.3664256 sec
RG                           512
DW                      20.850 usec
DE                      18.00 usec
TE                       298.2 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                        13C
P1                         9.25 usec
PL1                        0.55 dB
PL1W               35.18820572 W
SFO1              100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2                waltz16
NUC2                        1H
PCPD2                    90.00 usec
PL2                       4.90 dB
PL12                     20.46 dB
PL13                     21.00 dB
PL2W                3.30822015 W
PL12W               0.09195905 W
PL13W               0.08120718 W
SFO2              400.1316005 MHz

F2 - Processing parameters
SI                        32768
SF                100.6126870 MHz
WDW                          EM
SSB          0
LB                        1.00 Hz
GB           0
PC                        1.40
```

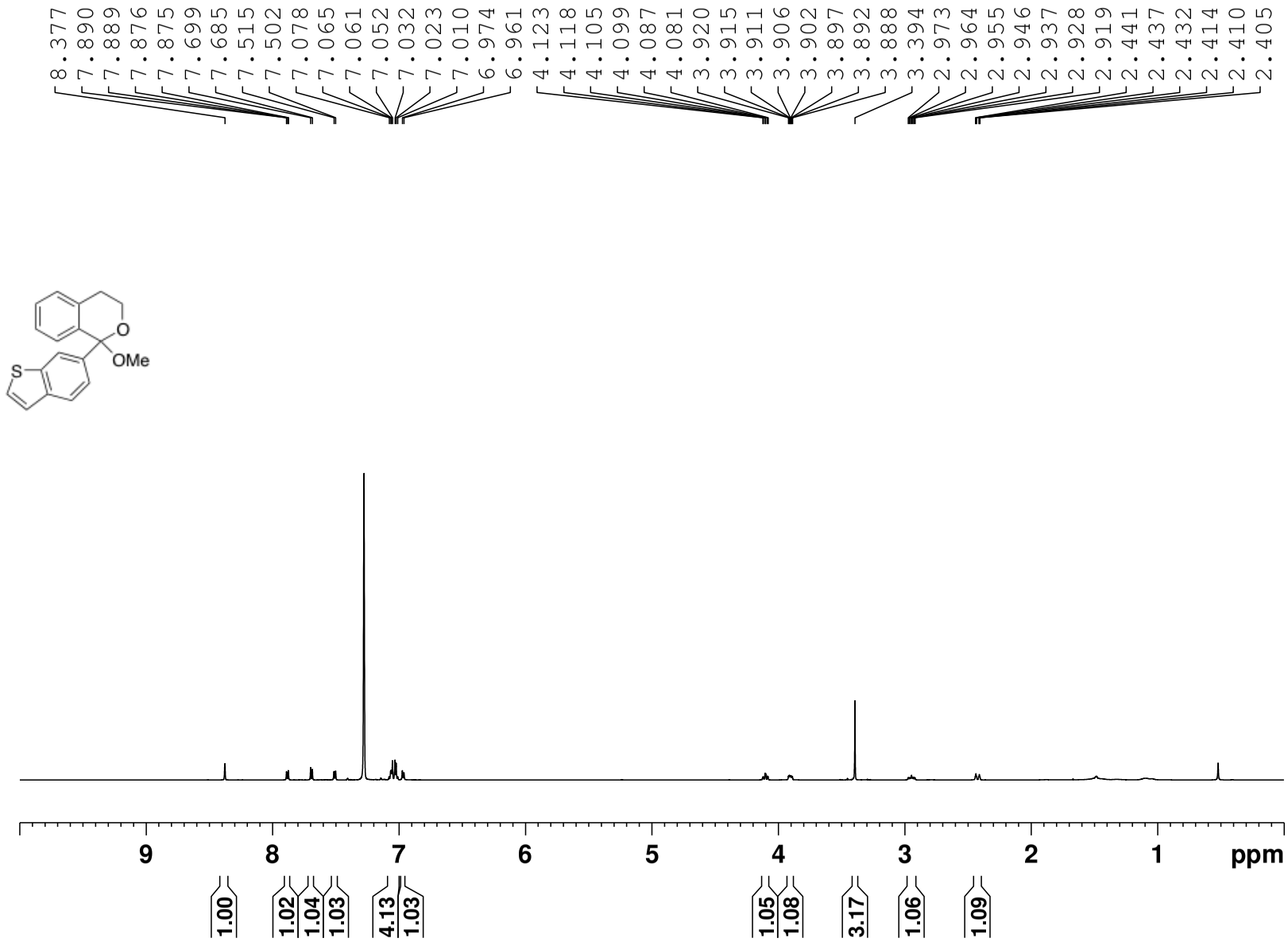



```
Current Data Parameters
NAME                  TR_2-nap
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20130816
Time                      3.28
INSTRUM                  spect
PROBHD    5 mm CPQNP 1H/
PULPROG                  zg30
TD                      65536
SOLVENT                  C6D6
NS                         16
DS                          2
SWH                  8278.146 Hz
FIDRES               0.126314 Hz
AQ                   3.9583745 sec
RG                        11.3
DW                      60.400 usec
DE                       6.00 usec
TE                       298.1 K
D1                1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       15.00 usec
PL1                       4.90 dB
PL1W               3.30822015 W
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                       32768
SF               400.1299969 MHz
WDW                         EM
SSB          0
LB                       0.30 Hz
GB           0
PC                       1.00
```

2-43, 13C NMR

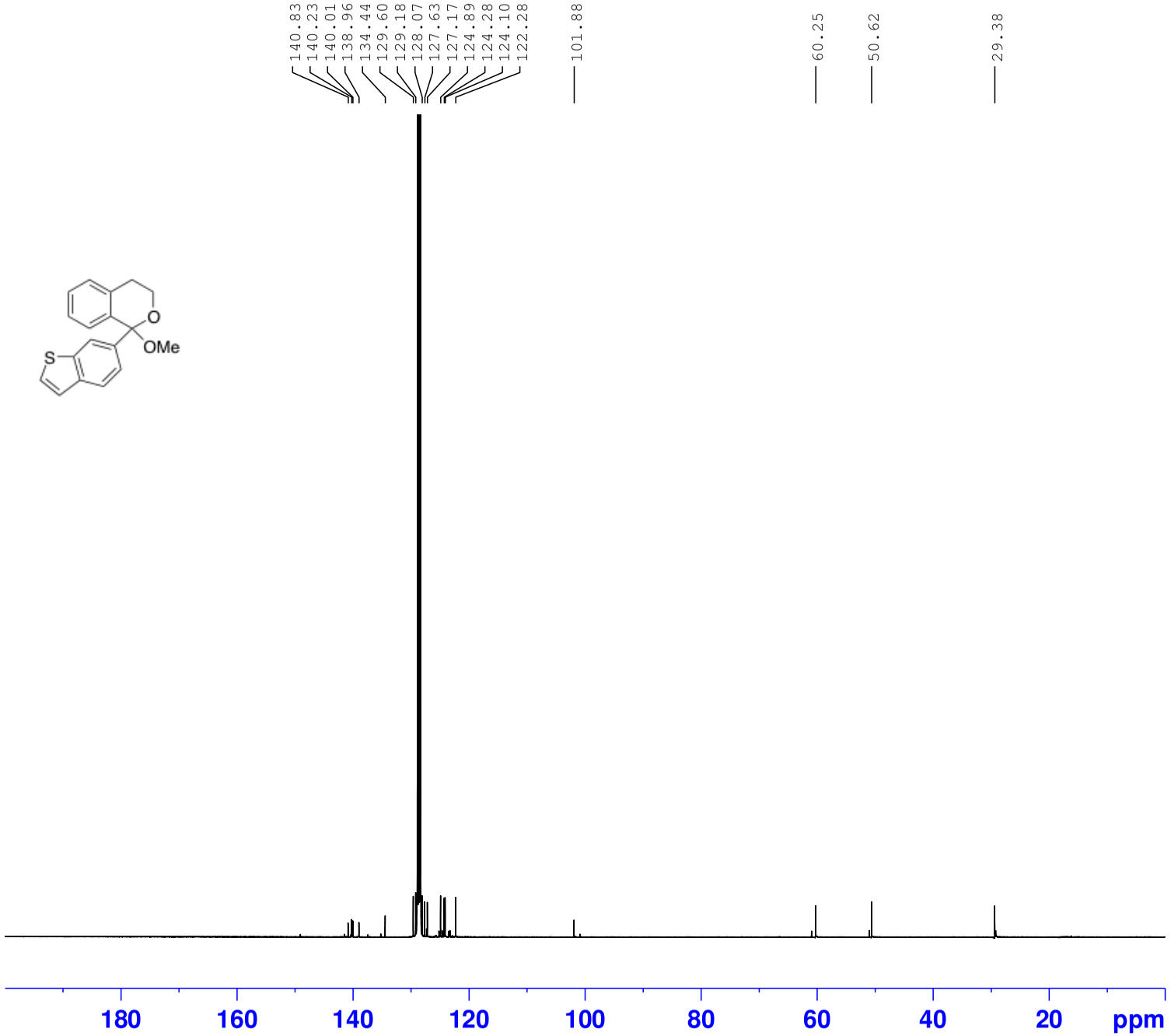



```
Current Data Parameters
NAME                 TR_2-nap
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_               20130816
Time                    4.28
INSTRUM                spect
PROBHD    5 mm CPQNP 1H/
PULPROG                zgpg30
TD                      65536
SOLVENT                 C6D6
NS                      1024
DS                         4
SWH                23980.814 Hz
FIDRES              0.365918 Hz
AQ                  1.3664256 sec
RG                        512
DW                     20.850 usec
DE                     18.00 usec
TE                     298.1 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                      9.25 usec
PL1                     0.55 dB
PL1W             35.18820572 W
SFO1            100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2              waltz16
NUC2                      1H
PCPD2                  90.00 usec
PL2                     4.90 dB
PL12                   20.46 dB
PL13                   21.00 dB
PL2W              3.30822015 W
PL12W             0.09195905 W
PL13W             0.08120718 W
SFO2            400.1316005 MHz

F2 - Processing parameters
SI                      32768
SF                100.6127690 MHz
WDW                        EM
SSB          0
LB                      1.00 Hz
GB           0
PC                      1.40
```



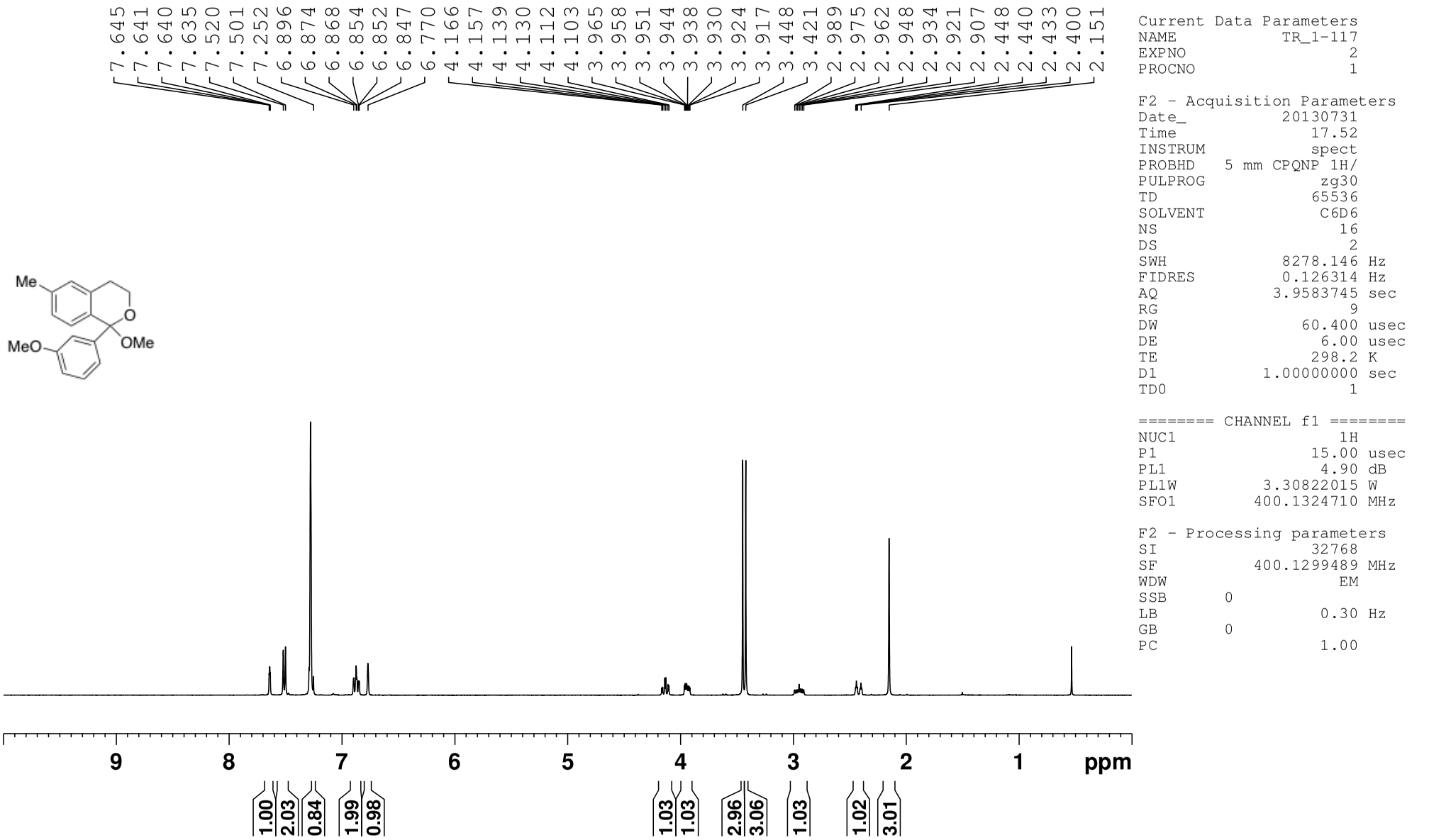

```
Current Data Parameters
NAME      SDG-2-273(3rd)
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140123
Time                4.35
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             C6D6
NS                   256
DS                     2
SWH             8403.361 Hz
FIDRES          0.128225 Hz
AQ             3.8993919 sec
RG                   161
DW                59.500 usec
DE                17.39 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         600.3233018 MHz
NUC1                   1H
P1                 10.77 usec
PLW1         26.00000000 W

F2 - Processing parameters
SI                 65536
SF           600.3199244 MHz
WDW                   EM
SSB      0
LB                 0.30 Hz
GB       0
PC                 1.00
```

2-44, 13C NMR



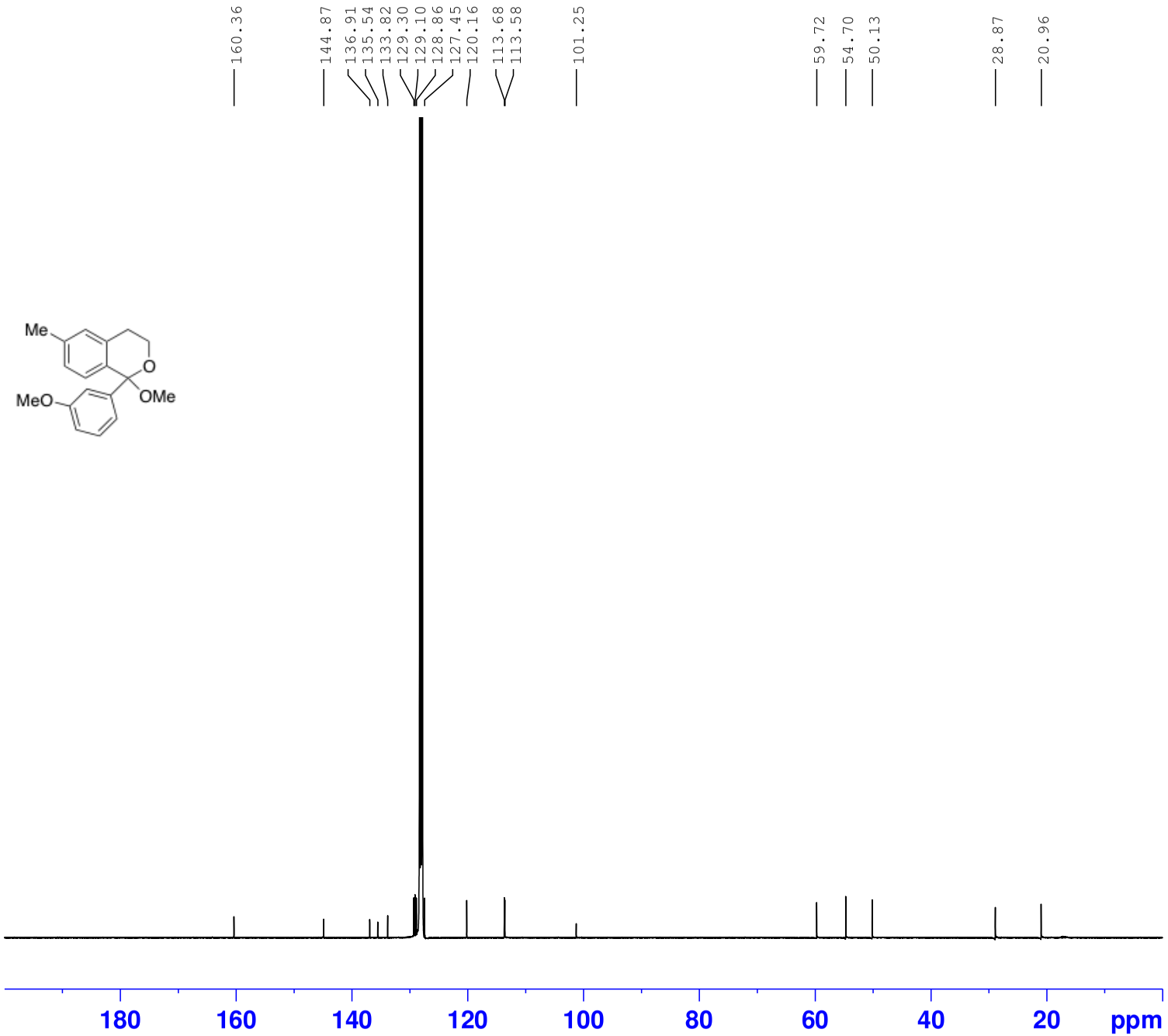

```
Current Data Parameters
NAME       TR_thiophene
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20130816
Time               3.21
INSTRUM           spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT            C6D6
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                9.25 usec
PL1               0.55 dB
PL1W       35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            90.00 usec
PL2               4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W        3.30822015 W
PL12W       0.09195905 W
PL13W       0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6126793 MHz
WDW                EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

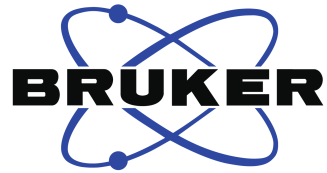
2-45, 1H NMR




```
Current Data Parameters
NAME                  TR_1-117
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20130731
Time                     17.52
INSTRUM                  spect
PROBHD   5 mm CPQNP 1H/
PULPROG                  zg30
TD                      65536
SOLVENT                  C6D6
NS                         16
DS                          2
SWH                  8278.146 Hz
FIDRES               0.126314 Hz
AQ                   3.9583745 sec
RG                          9
DW                      60.400 usec
DE                       6.00 usec
TE                      298.2 K
D1                 1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       15.00 usec
PL1                       4.90 dB
PL1W                3.30822015 W
SFO1              400.1324710 MHz

F2 - Processing parameters
SI                       32768
SF                400.1299489 MHz
WDW                         EM
SSB          0
LB                       0.30 Hz
GB           0
PC                       1.00
```

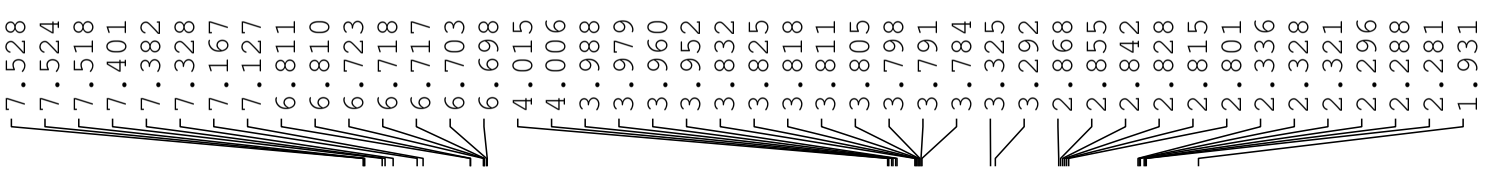
2-45, 13C NMR

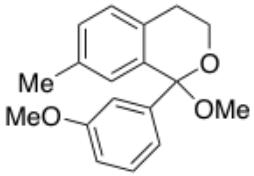


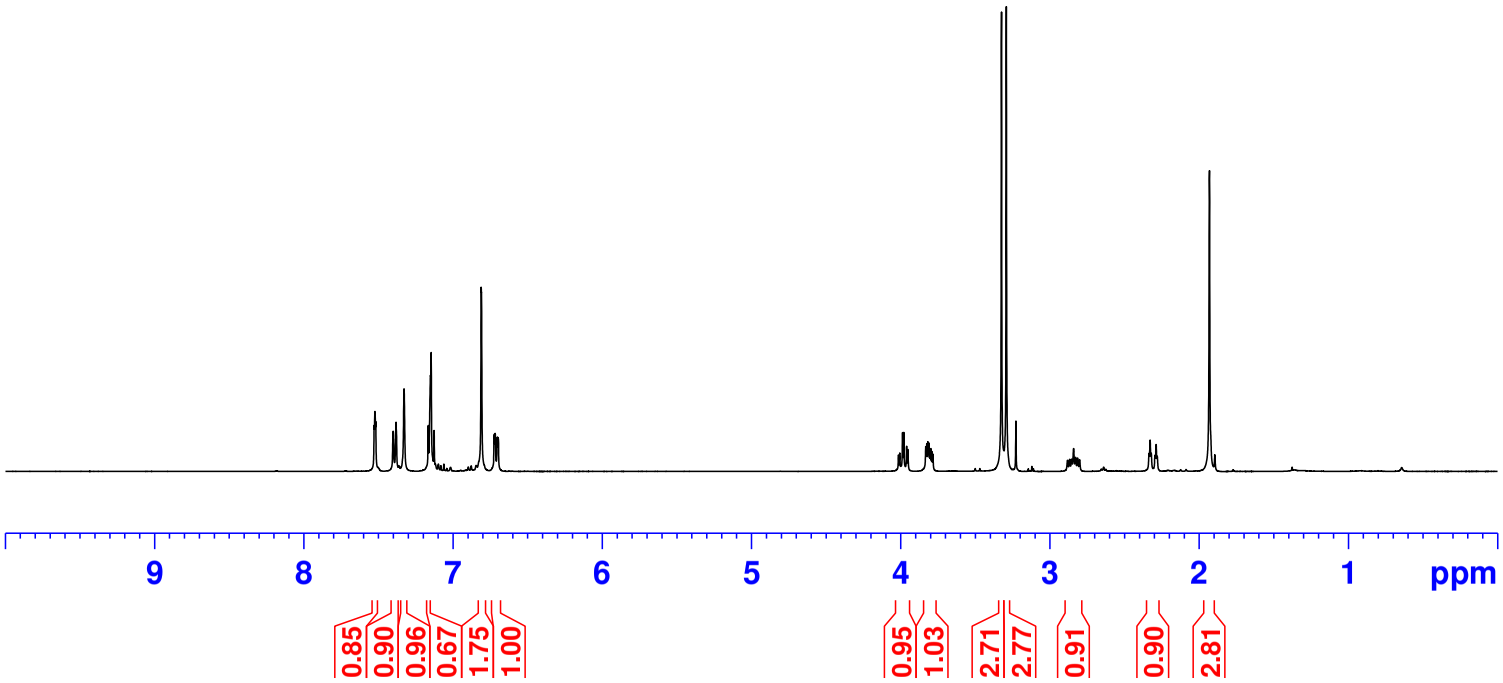



```
Current Data Parameters
NAME            TR_1-117
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130801
Time               23.20
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                 65536
SOLVENT              C6D6
NS                   1024
DS                      4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   9.25 usec
PL1                  0.55 dB
PL1W        35.18820572 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2               90.00 usec
PL2                  4.90 dB
PL12                20.46 dB
PL13                21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF          100.6127341 MHz
WDW                    EM
SSB       0
LB                   1.00 Hz
GB        0
PC                   1.40
```

2-46, 1H NMR







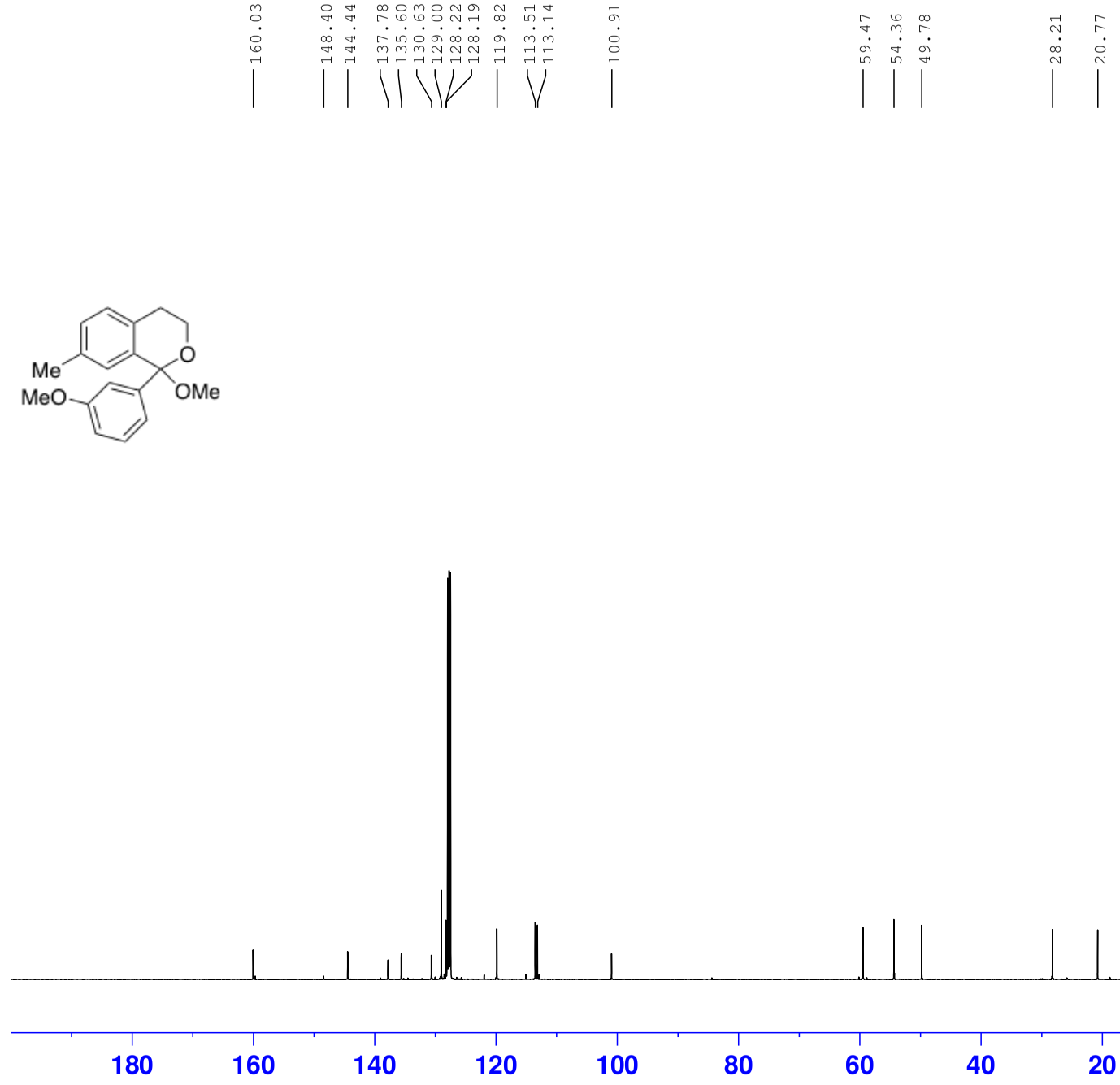
Current Data Parameters
NAME TR_1-143
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20131219
Time 10.50
INSTRUM spect
PROBHD 5 mm CPQNP 1H/
PULPROG zg30
TD 65536
SOLVENT C6D6
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9583745 sec
RG 4
DW 60.400 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 15.00 usec
PL1 4.90 dB
PL1W 3.30822015 W
SFO1 400.1324710 MHz

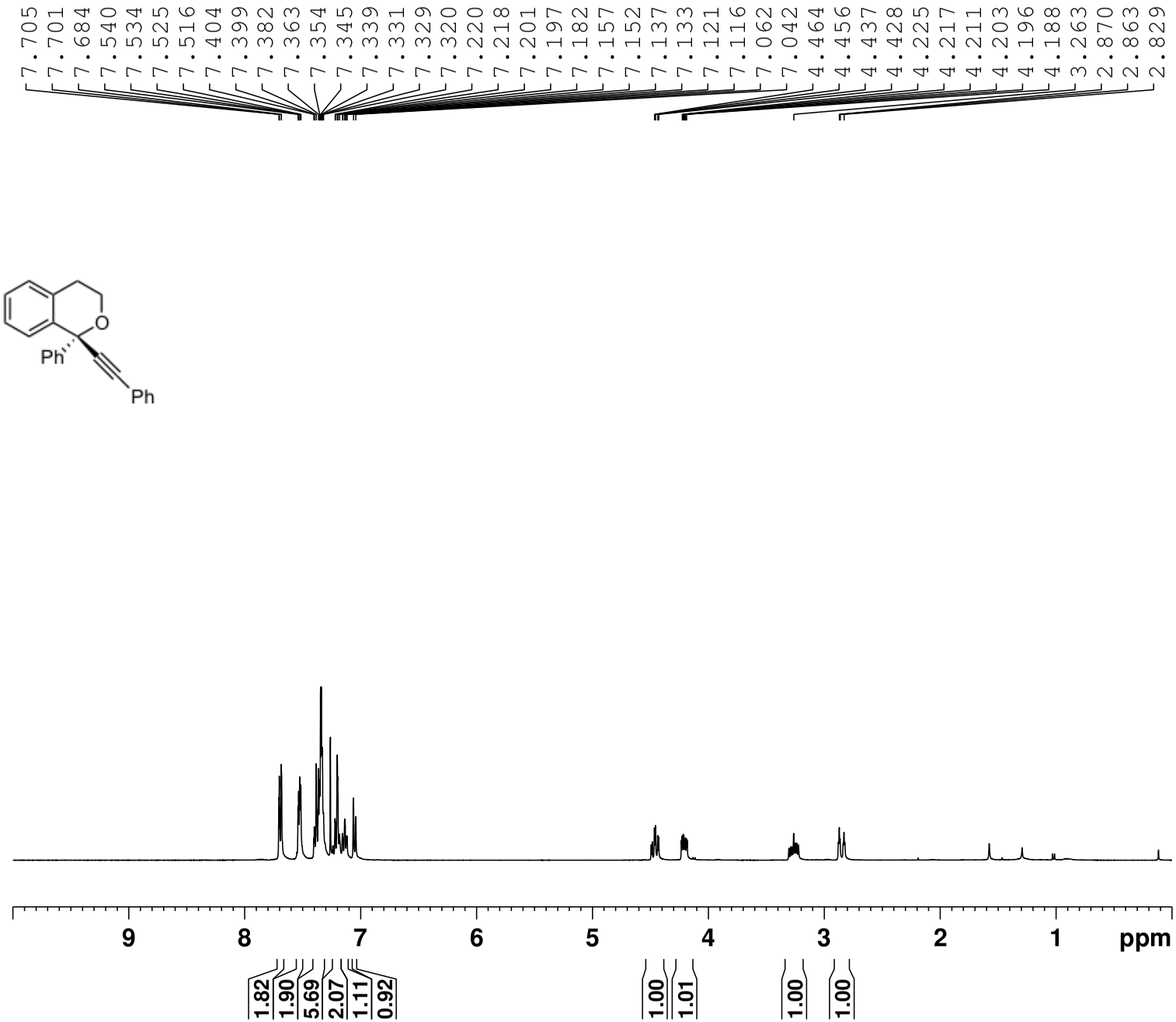
F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

2-46, 13C NMR




```
Current Data Parameters
NAME            TR_1-143
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131219
Time               21.08
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT             C6D6
NS                  1024
DS                     4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127690 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

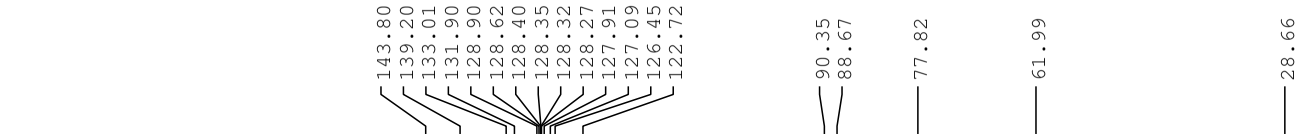
2-48, 1H NMR

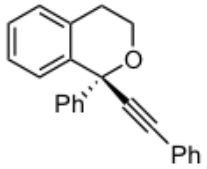


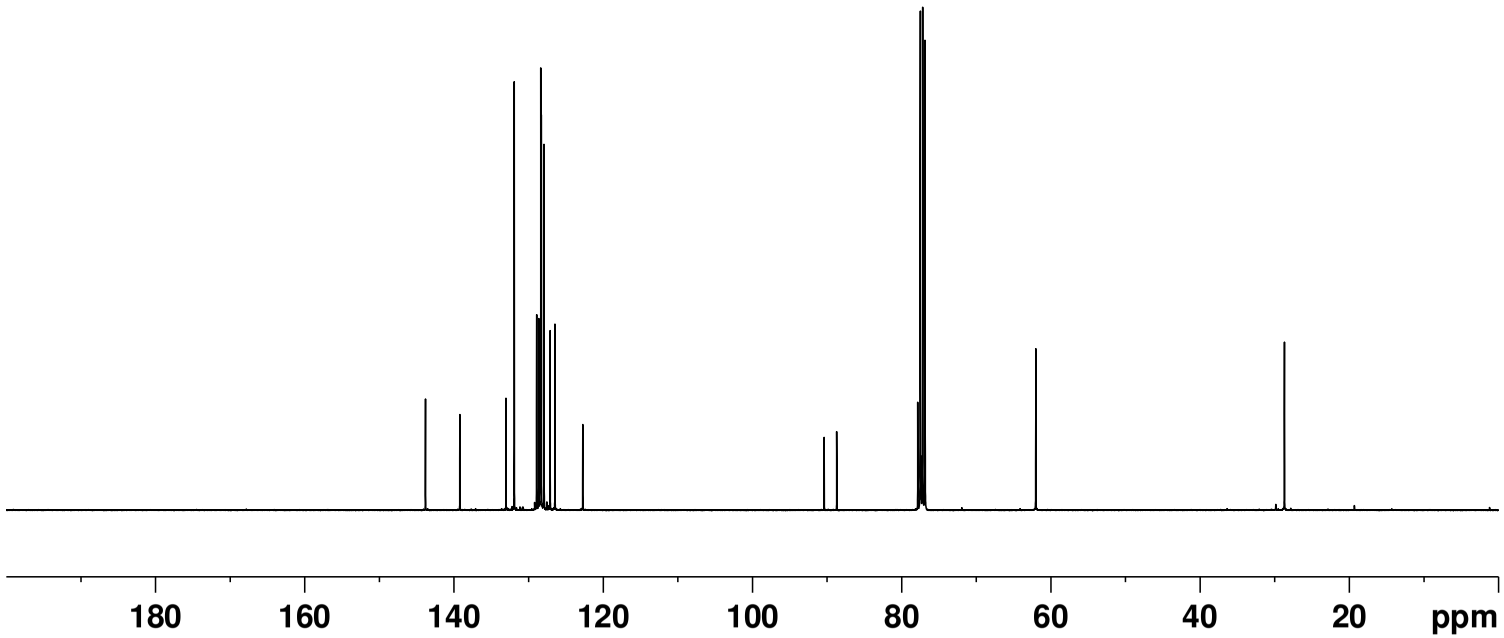
BRUKER

```
Current Data Parameters
NAME          SDG-3-93-2
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131220
Time               19.46
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     8
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W          3.30822015 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF           400.1300098 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-48, 13C NMR

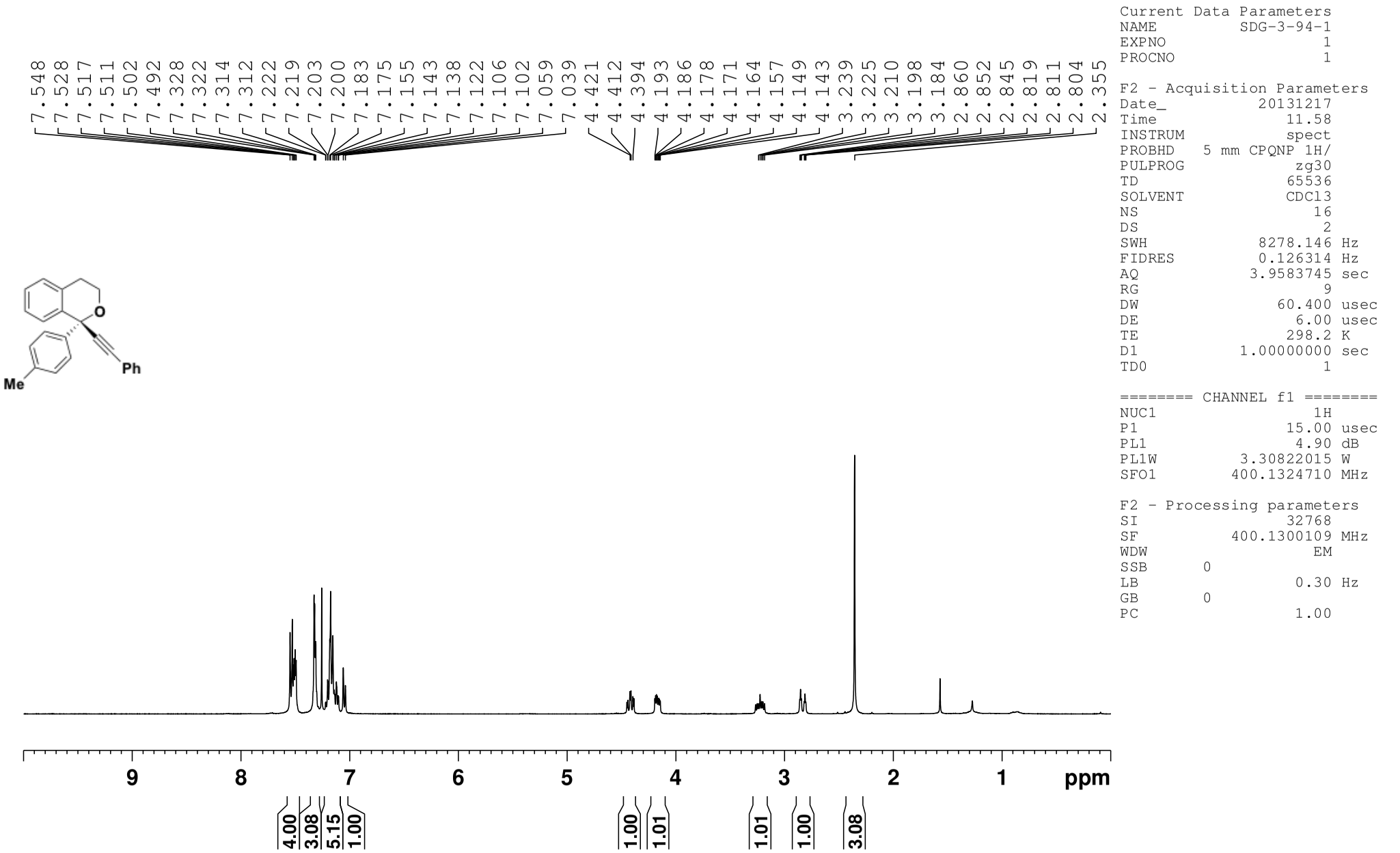




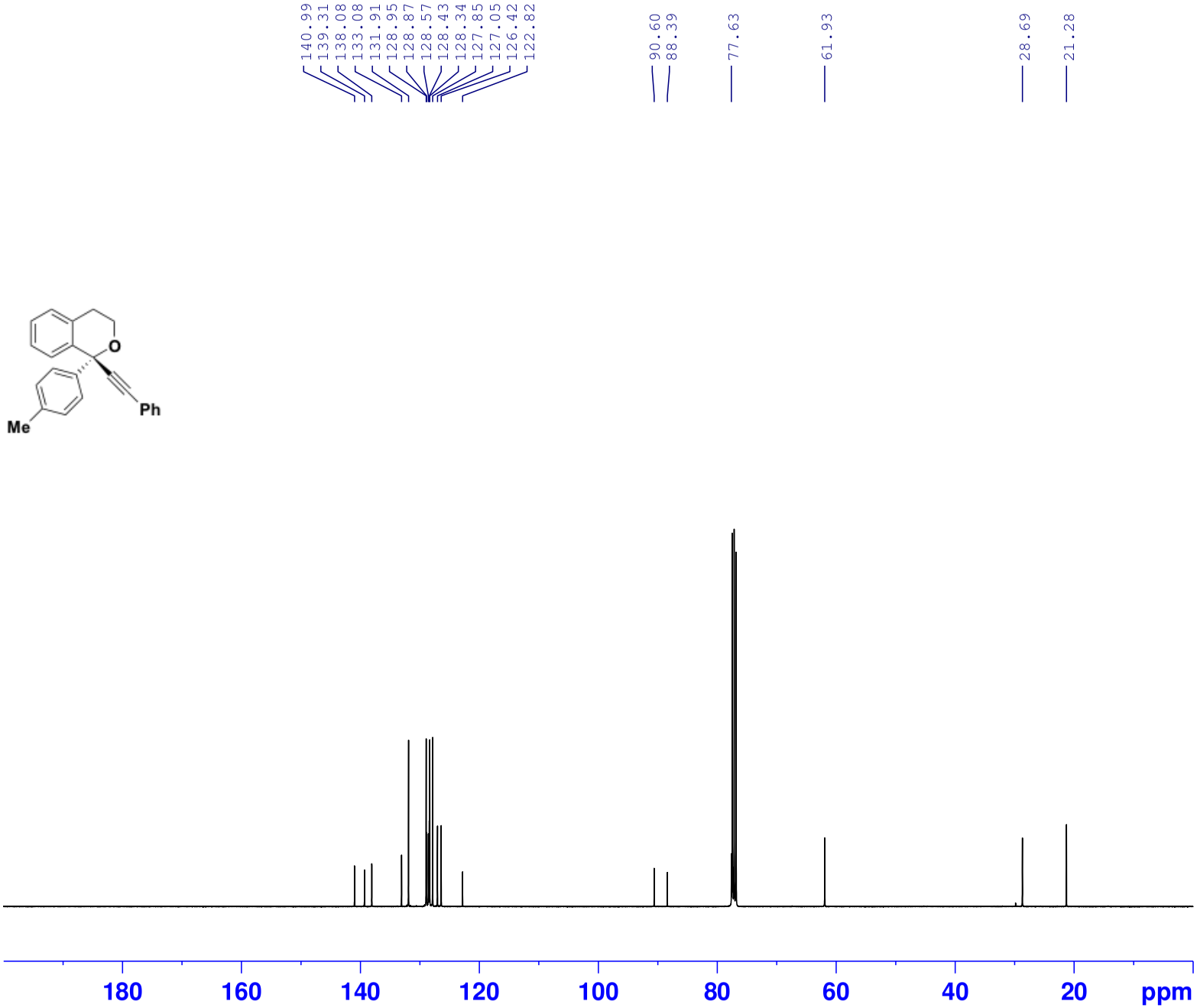



```
Current Data Parameters
NAME          SDG-3-93-2
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131221
Time                2.44
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG           zgpg30
TD                 65536
SOLVENT             CDCl3
NS                  1024
DS                     4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   9.25 usec
PL1                  0.55 dB
PL1W        35.18820572 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127640 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

2-62, 1H NMR

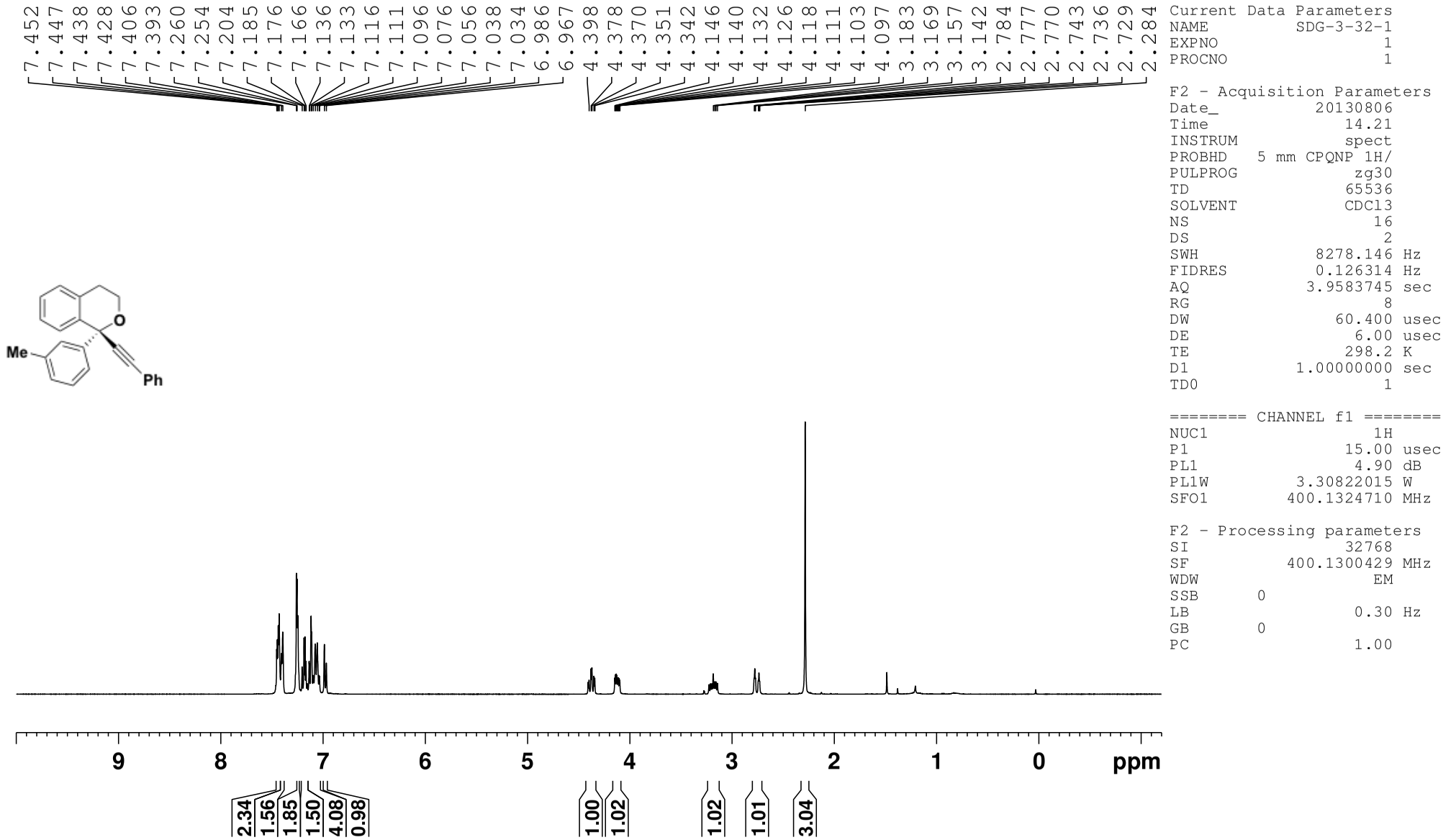



```
Current Data Parameters
NAME          SDG-3-94-1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131217
Time               11.58
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ             3.9583745 sec
RG                     9
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300109 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



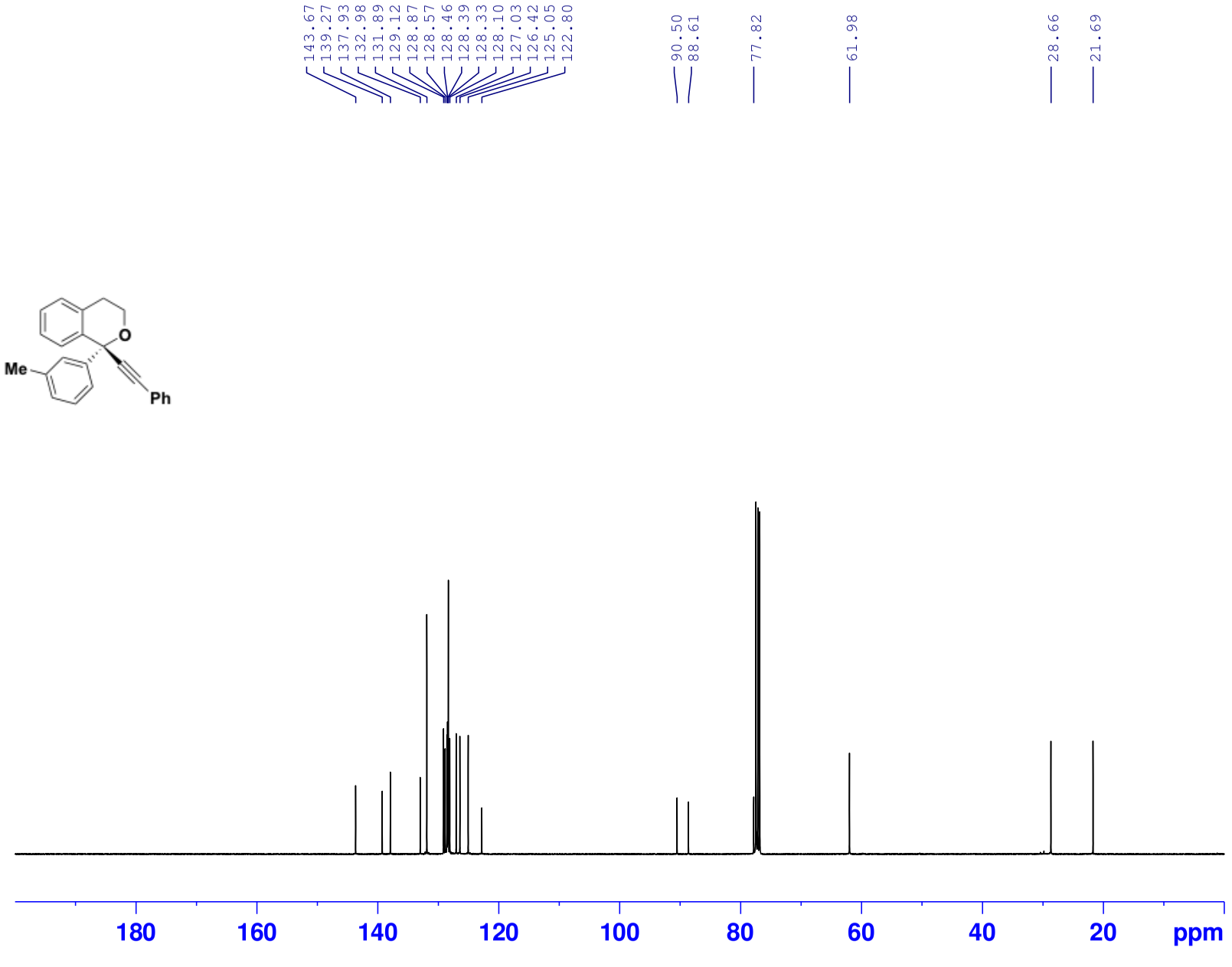

```
Current Data Parameters
NAME          SDG-3-94-1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131217
Time               21.03
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                9.25 usec
PL1               0.55 dB
PL1W       35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2            90.00 usec
PL2               4.90 dB
PL12             20.46 dB
PL13             21.00 dB
PL2W        3.30822015 W
PL12W       0.09195905 W
PL13W       0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF         100.6127608 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
```

2-63, 1H NMR



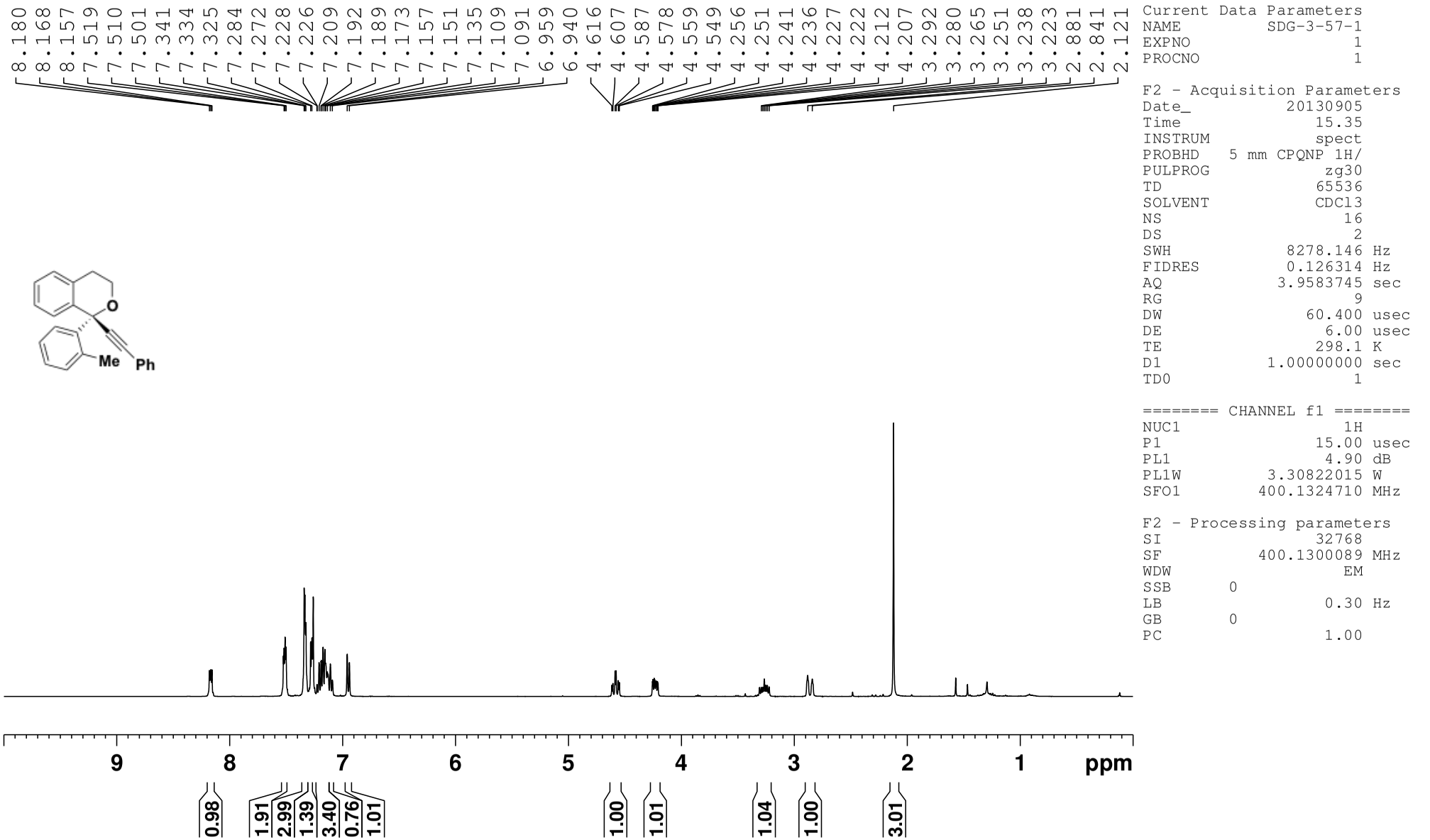

```
Current Data Parameters
NAME          SDG-3-32-1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130806
Time               14.21
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ             3.9583745 sec
RG                     8
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300429 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-63, 13C NMR



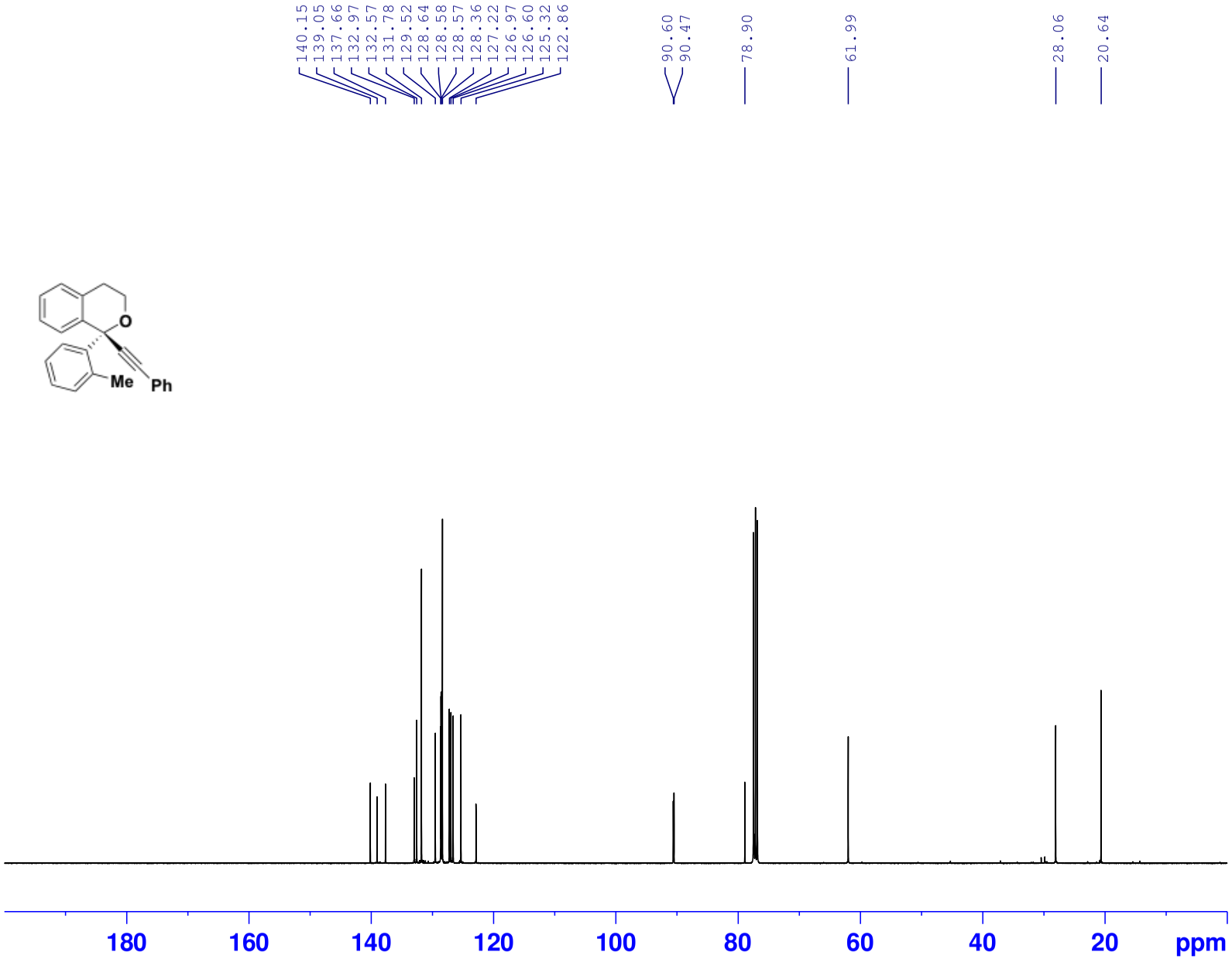

```
Current Data Parameters
NAME          SDG-3-32-1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130807
Time                2.37
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE               298.1 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                13C
P1                9.25 usec
PL1               0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                1H
PCPD2            90.00 usec
PL2               4.90 dB
PL12             20.46 dB
PL13             21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127642 MHz
WDW                   EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

2-64, 1H NMR

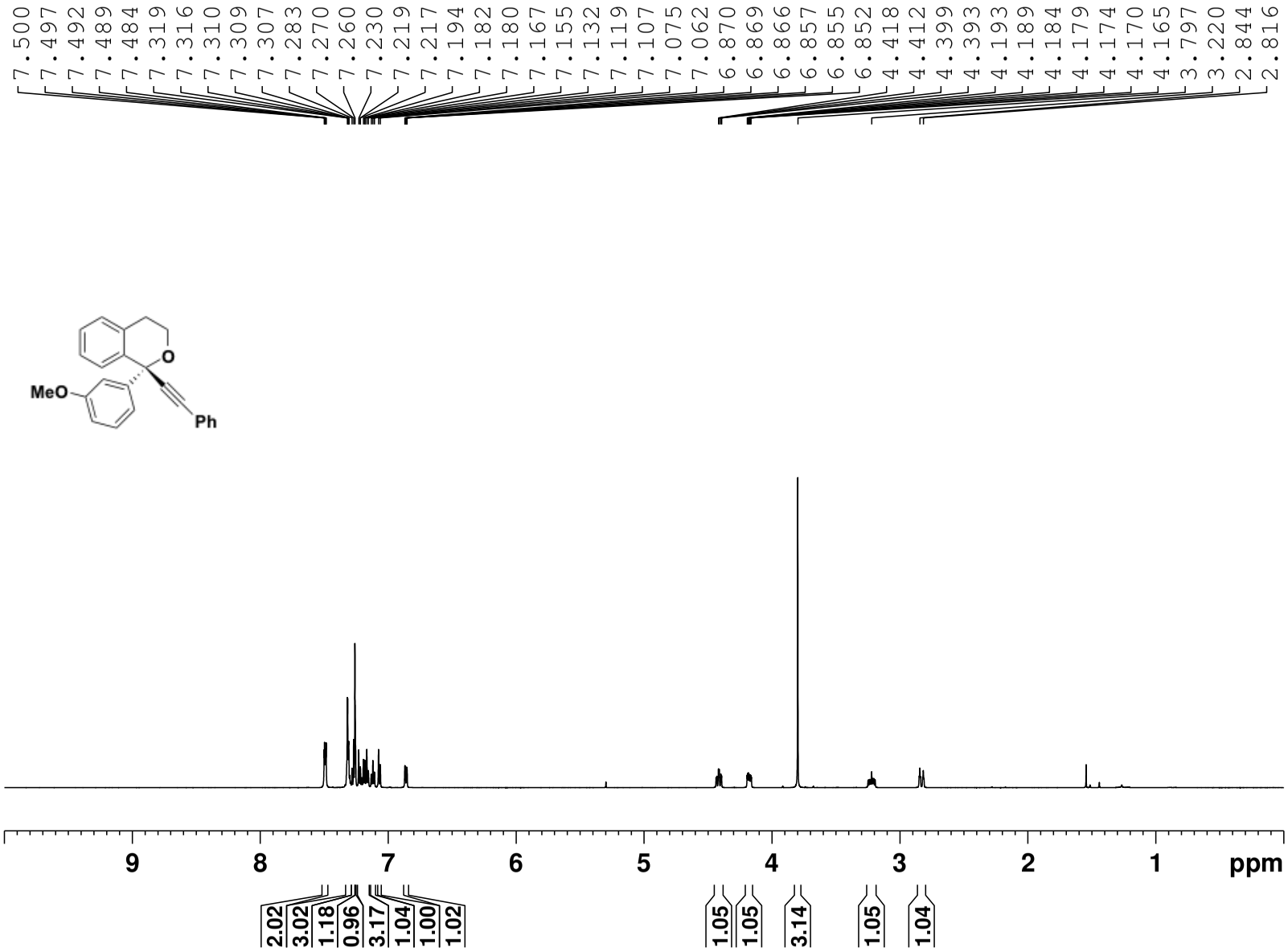



```
Current Data Parameters
NAME          SDG-3-57-1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130905
Time               15.35
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ             3.9583745 sec
RG                     9
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300089 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-64, 13C NMR

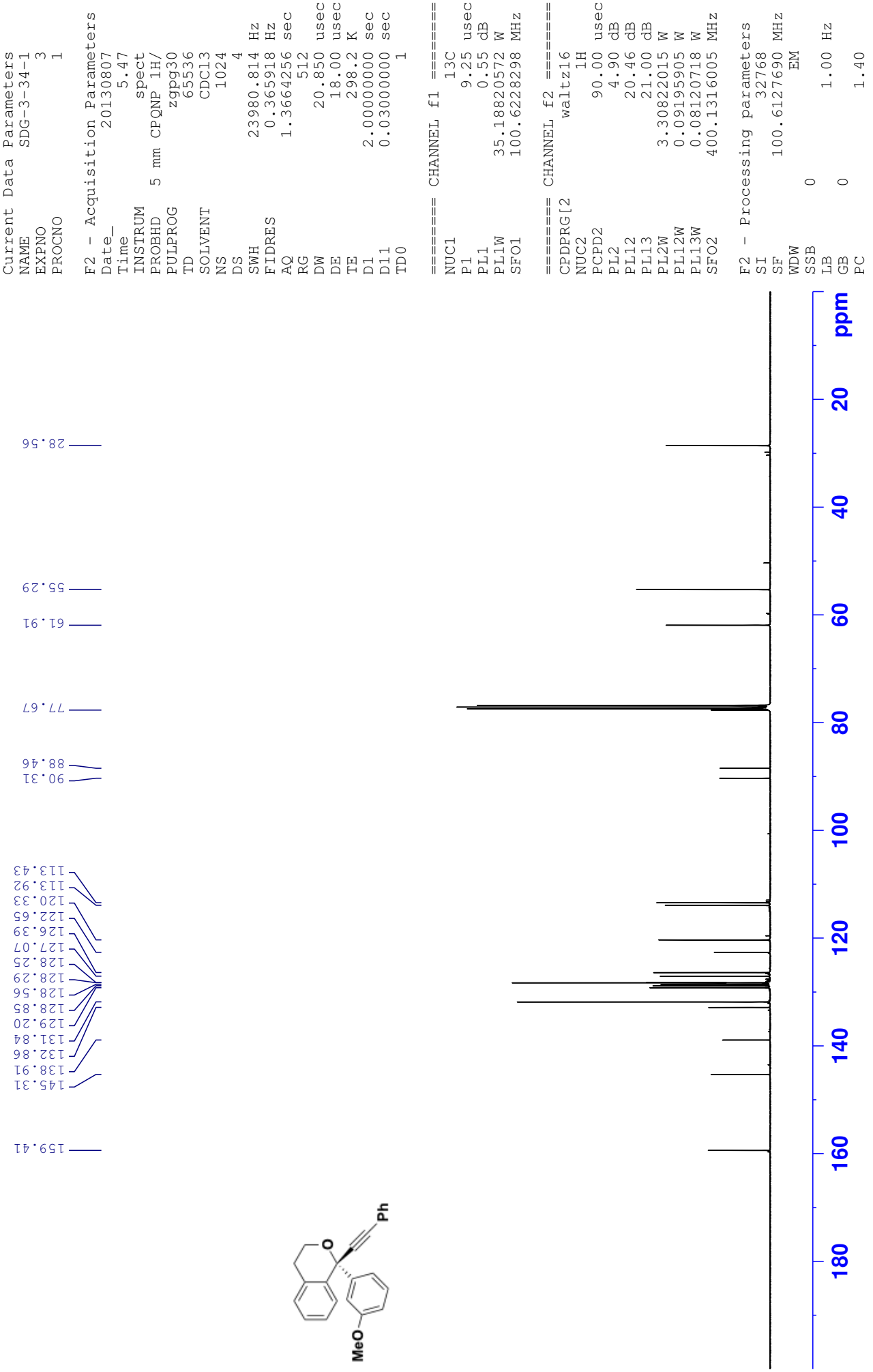



```
Current Data Parameters
NAME          SDG-3-57-1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130906
Time                0.31
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE                298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                 9.25 usec
PL1                0.55 dB
PL1W       35.18820572 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W        3.30822015 W
PL12W       0.09195905 W
PL13W       0.08120718 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6127627 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

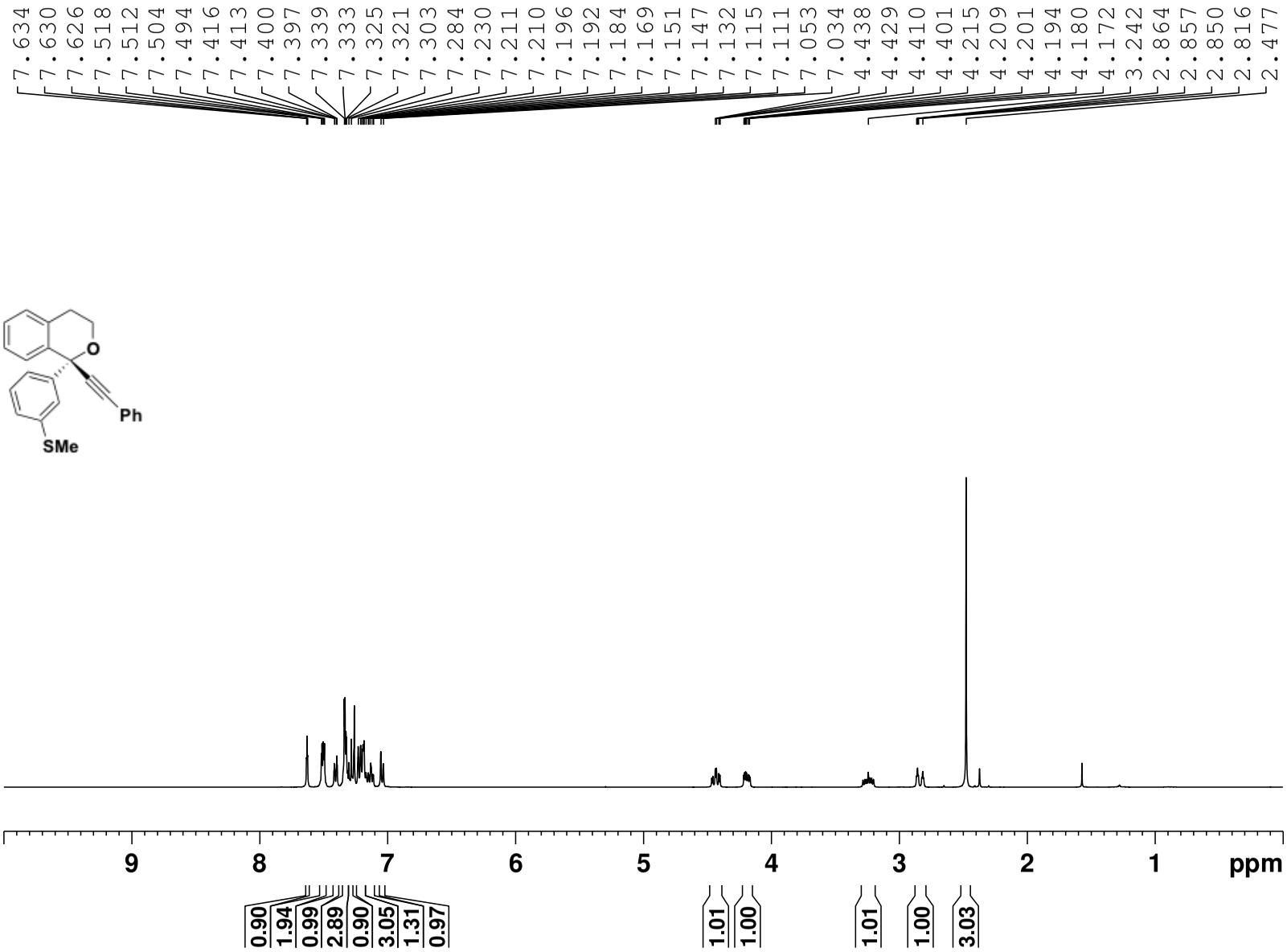



```
Current Data Parameters
NAME          SDG-3-61_2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130912
Time               15.19
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             8403.361 Hz
FIDRES          0.128225 Hz
AQ             3.8993919 sec
RG                   128
DW                59.500 usec
DE                17.39 usec
TE                298.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         600.3233018 MHz
NUC1                   1H
P1                 10.77 usec
PLW1        26.00000000 W

F2 - Processing parameters
SI                 65536
SF          600.3200160 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-65, 13C NMR

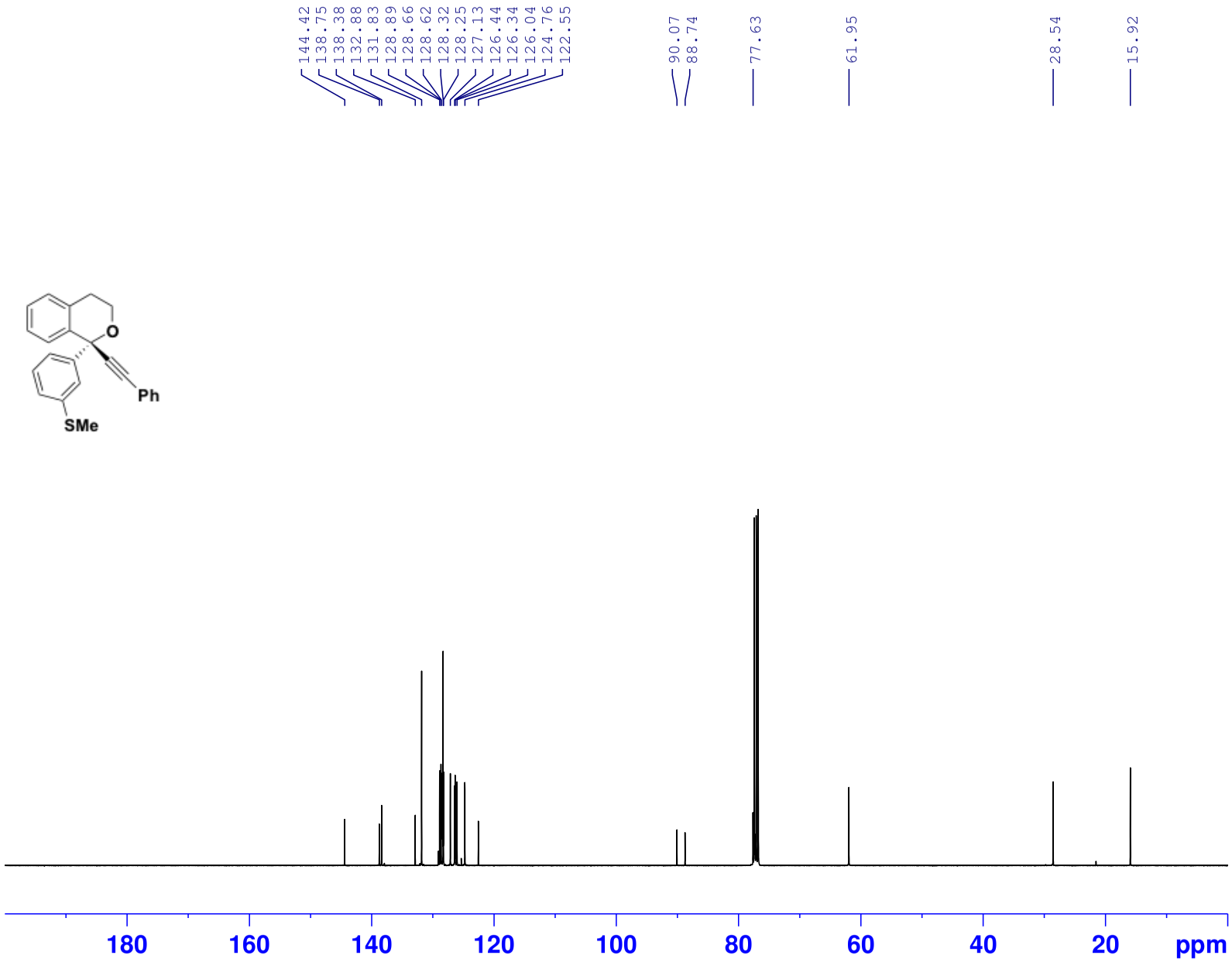

Current Data Parameters
NAME SDG-3-34-1
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130807
Time 5.47
INSTRUM spect
PROBHD 5 mm CPQNP 1H/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 512
DW 20.850 usec
DE 18.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.25 usec
PL1 0.55 dB
PL1W 35.18820572 W
SFO1 100.6228298 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 4.90 dB
PL12 20.46 dB
PL13 21.00 dB
PL2W 3.30822015 W
PL12W 0.09195905 W
PL13W 0.08120718 W
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
28.56
55.29
61.91
77.67
88.46
90.31
113.43
113.92
120.33
122.65
126.39
127.07
128.25
128.29
128.56
128.85
129.20
131.84
132.86
138.91
145.31
159.41
ppm
20
40
60
80
100
120
140
160
180
Ph
O
MeO

2-66, 1H NMR

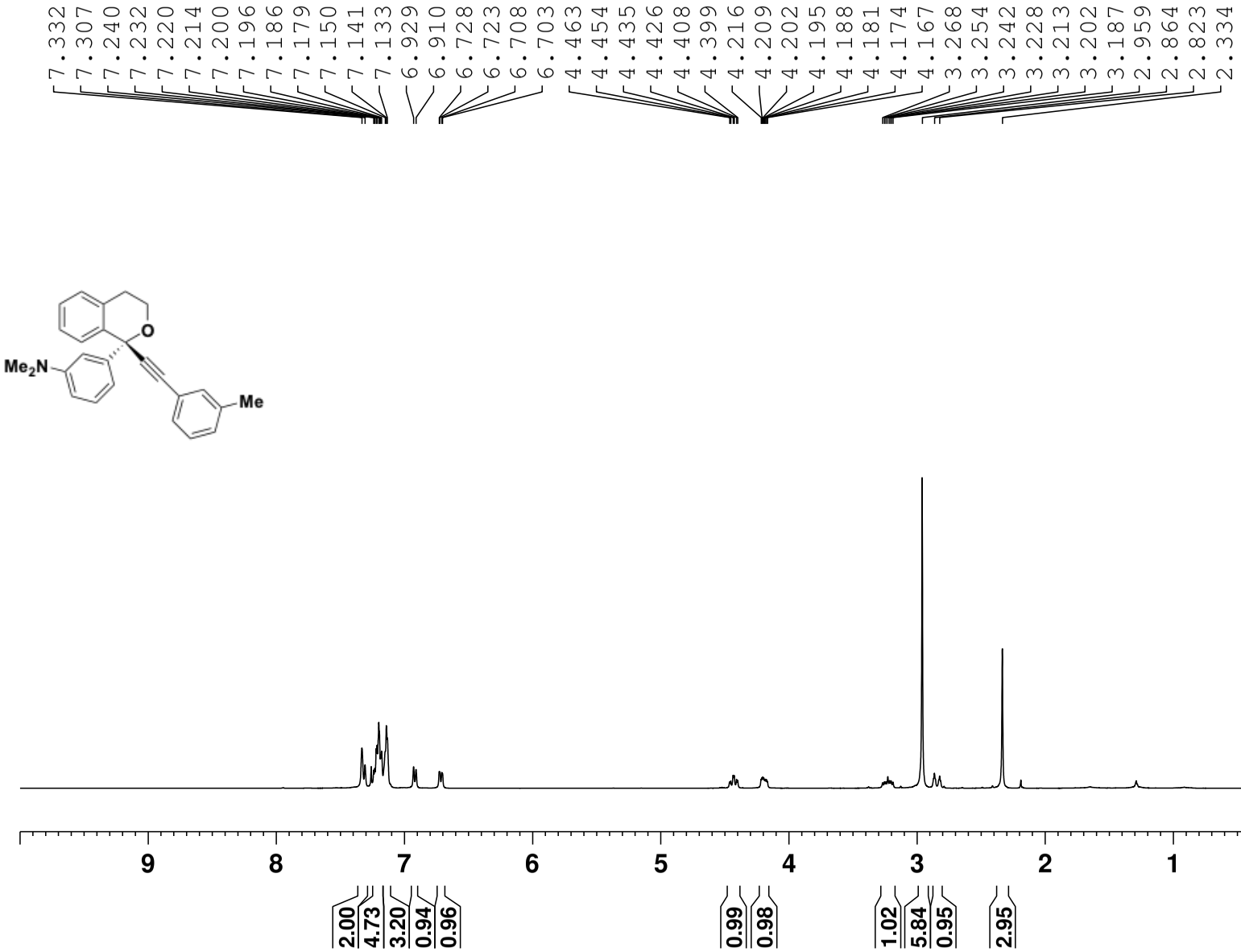



```
Current Data Parameters
NAME          SDG-3-80-2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131214
Time               15.18
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ             3.9583745 sec
RG                     8
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300096 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-66, 13C NMR

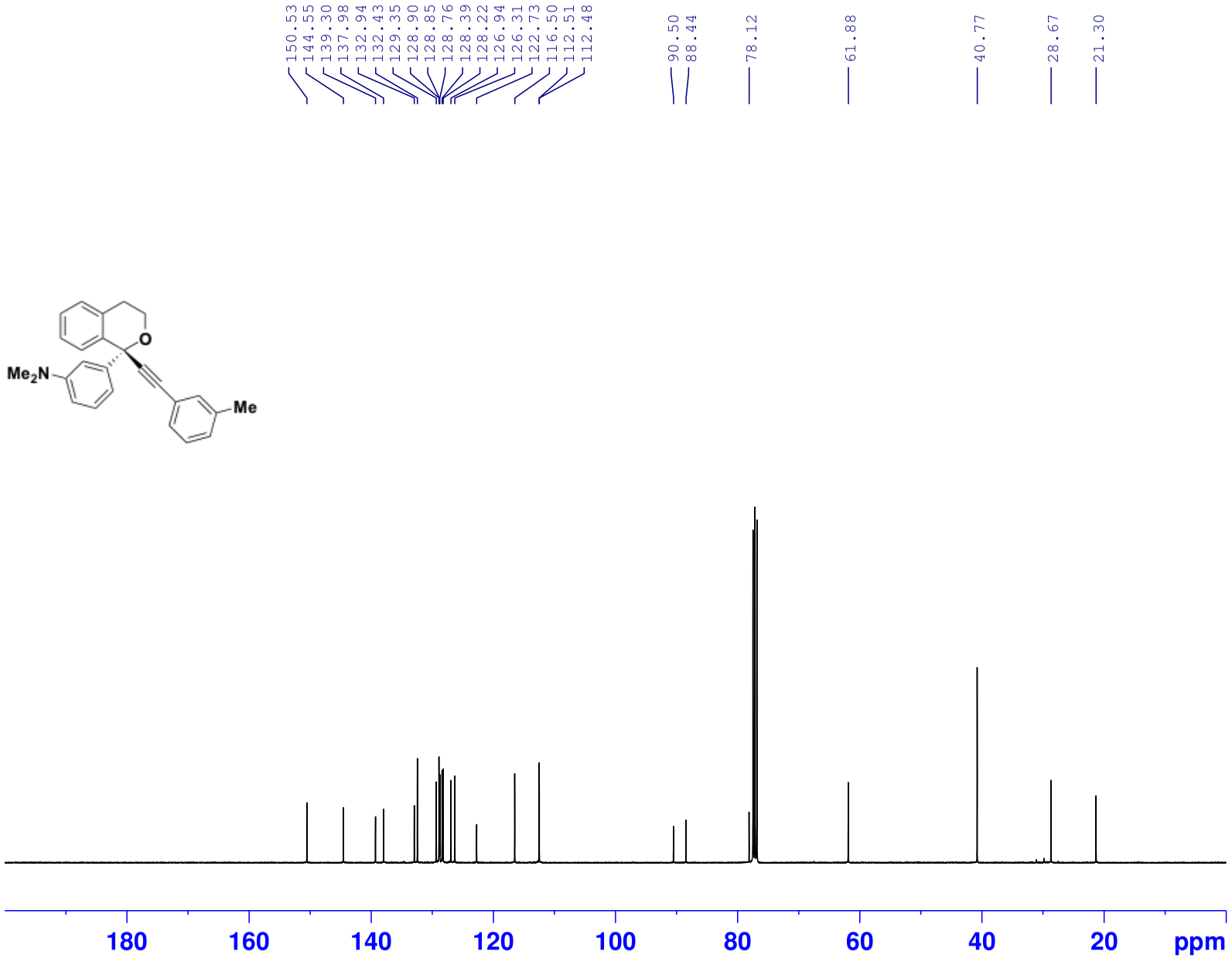



```
Current Data Parameters
NAME          SDG-3-80-2
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131215
Time                2.33
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                 9.25 usec
PL1                0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127690 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



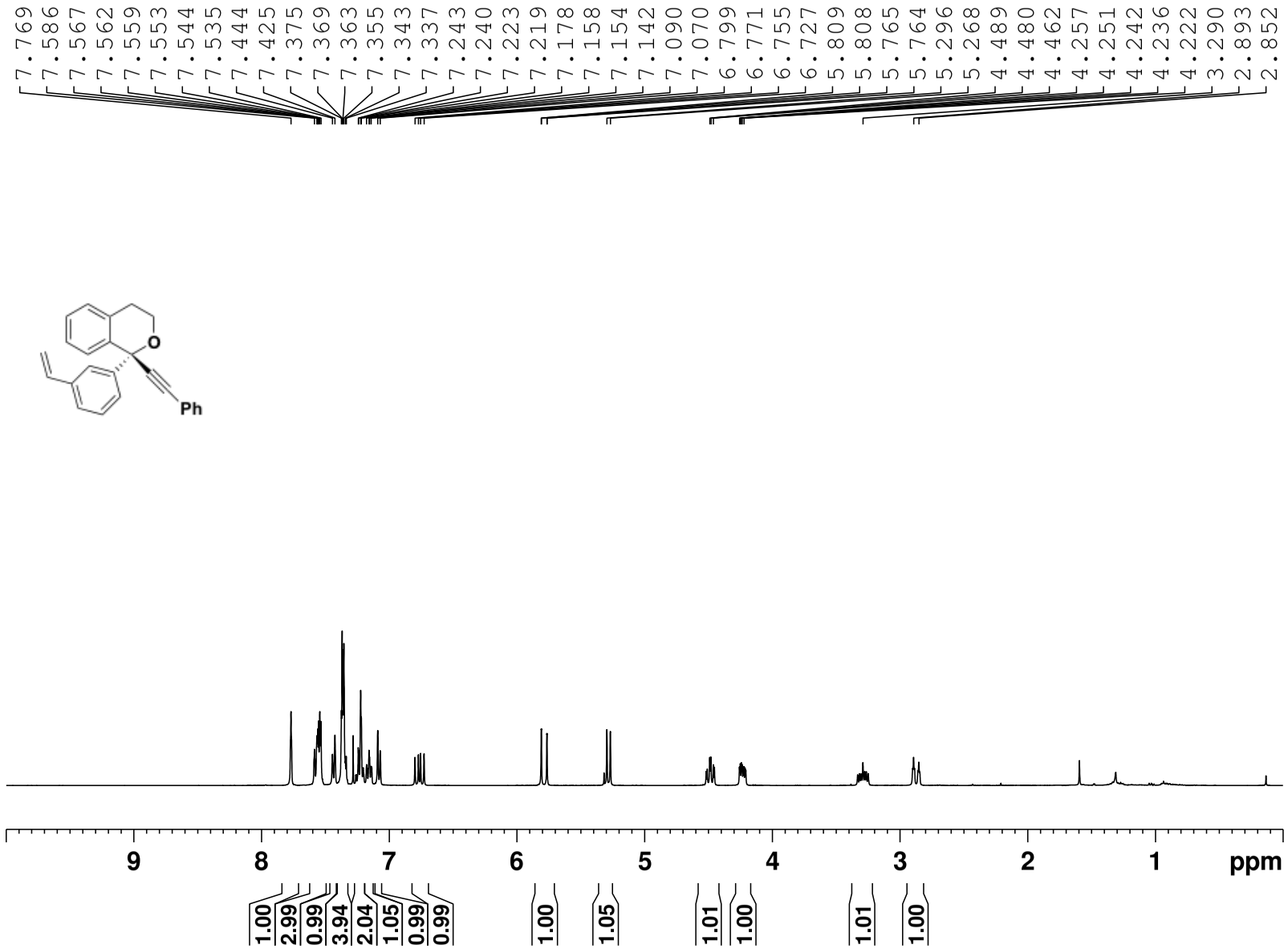

```
Current Data Parameters
NAME          SDG-3-12-1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130625
Time               10.56
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ             3.9583745 sec
RG                   6.3
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300097 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-67, 13C NMR




```
Current Data Parameters
NAME          SDG-3-12-1
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130625
Time               21.05
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   9.25 usec
PL1                  0.55 dB
PL1W         35.18820572 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W          3.30822015 W
PL12W         0.09195905 W
PL13W         0.08120718 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF           100.6127645 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

2-68, 1H NMR




```
Current Data Parameters
NAME          SDG-3-18-2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130703
Time                9.34
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ             3.9583745 sec
RG                     4
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300000 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-68, 13C NMR

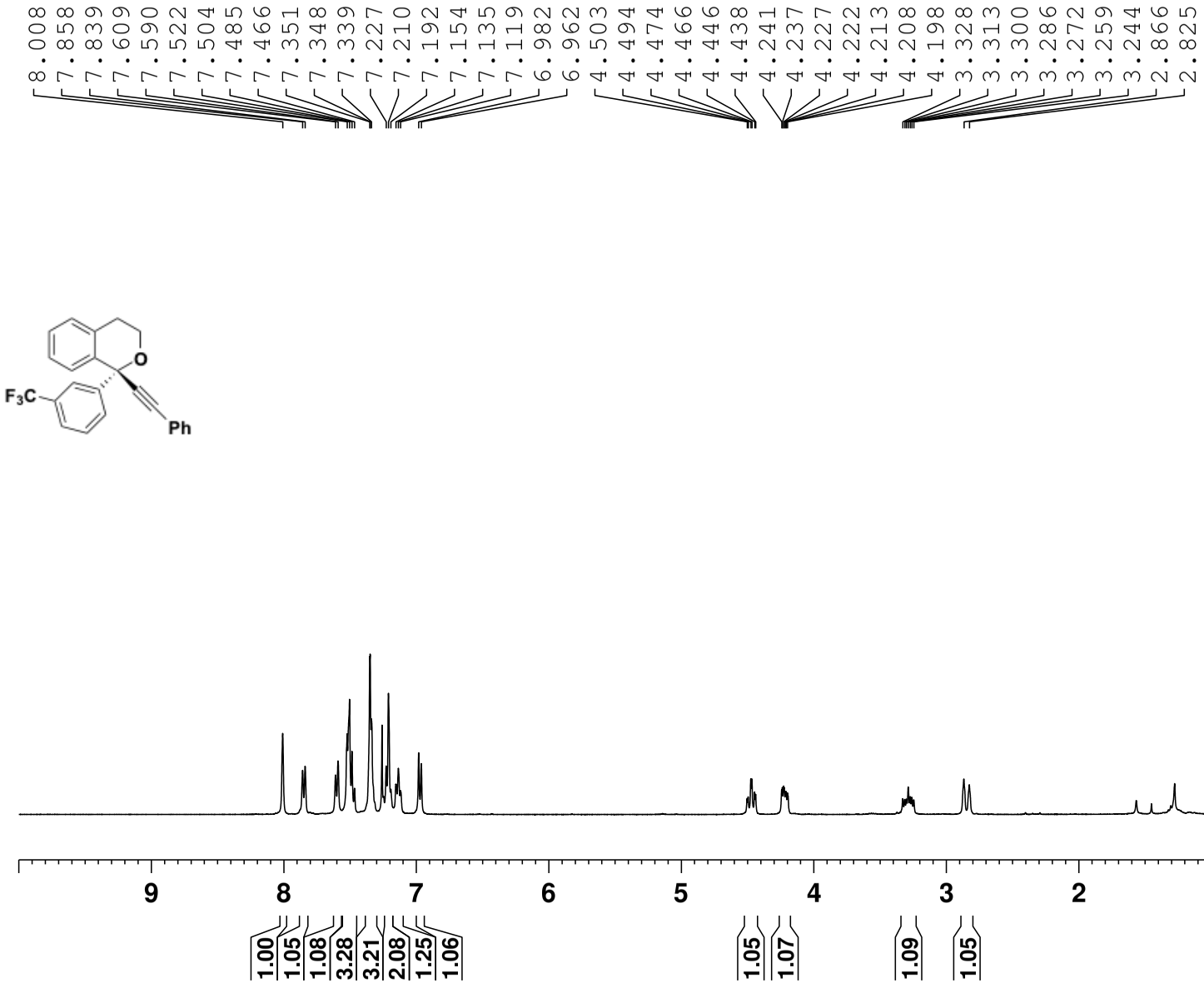
Current Data Parameters
NAME SDG-3-18-2-acetoneR
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150117
Time 20.14
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg55
TD 65536
SOLVENT Acetone
NS 2048
DS 4
SWH 34722.223 Hz
FIDRES 0.529819 Hz
AQ 0.9437184 sec
RG 2050
DW 14.400 usec
DE 19.34 usec
TE 298.0 K
D1 1.10000002 sec
D11 0.03000000 sec
TD0 1

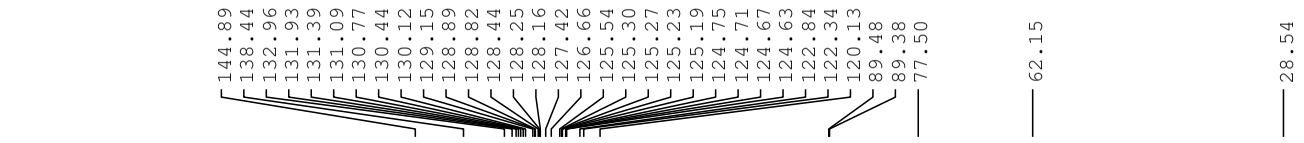
======== CHANNEL f1 ========
SFO1 150.9656784 MHz
NUC1 13C
P1 10.63 usec
PLW1 110.00000000 W

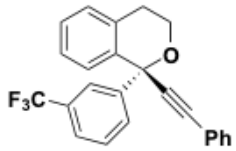
======== CHANNEL f2 ========
SFO2 600.3224013 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 22.00000000 W
PLW12 0.51885003 W
PLW13 0.25424001 W

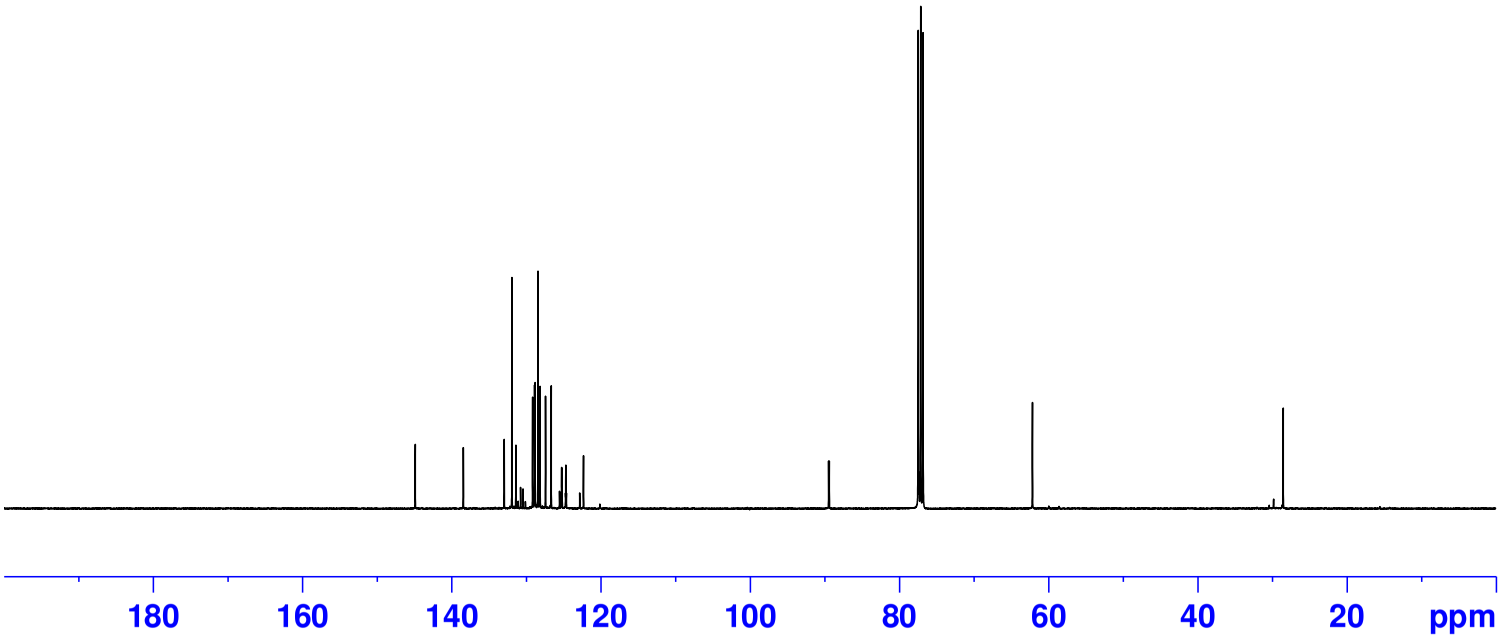
F2 - Processing parameters
SI 32768
SF 150.9505840 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40




```
Current Data Parameters
NAME                  SDG-3-76
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20131105
Time                     19.31
INSTRUM                  spect
PROBHD   5 mm CPQNP 1H/
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                   8278.146 Hz
FIDRES                0.126314 Hz
AQ                   3.9583745 sec
RG                           4
DW                      60.400 usec
DE                       6.00 usec
TE                      298.2 K
D1                  1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       15.00 usec
PL1                       4.90 dB
PL1W                3.30822015 W
SFO1               400.1324710 MHz

F2 - Processing parameters
SI                       32768
SF                 400.1300105 MHz
WDW                         EM
SSB          0
LB                       0.30 Hz
GB           0
PC                       1.00
```







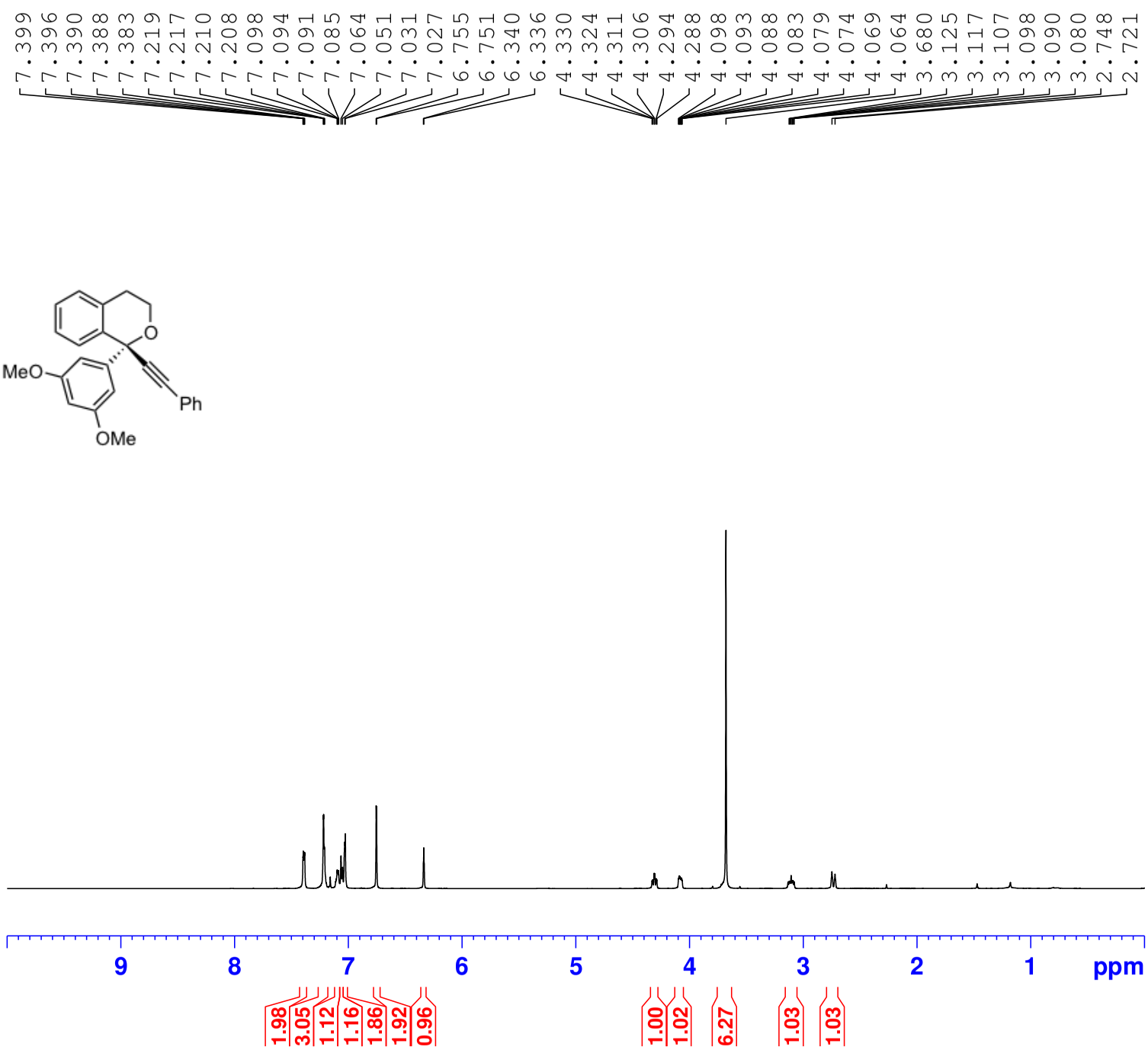
Current Data Parameters
NAME SDG-3-76-1
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20131105
Time 22.06
INSTRUM spect
PROBHD 5 mm CPQNP 1H/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 512
DW 20.850 usec
DE 18.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 9.25 usec
PL1 0.55 dB
PL1W 35.18820572 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 4.90 dB
PL12 20.46 dB
PL13 21.00 dB
PL2W 3.30822015 W
PL12W 0.09195905 W
PL13W 0.08120718 W
SFO2 400.1316005 MHz

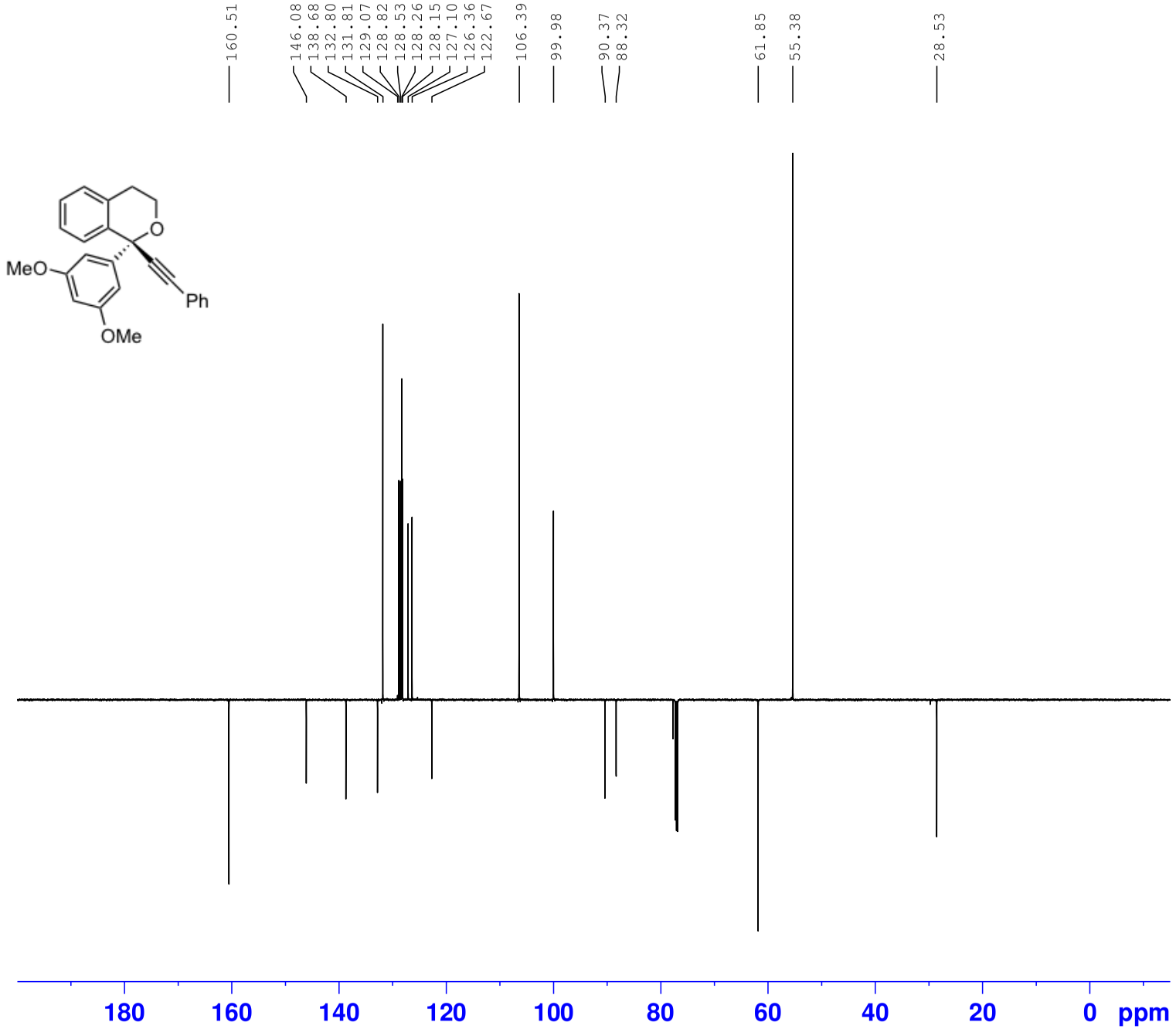
F2 - Processing parameters
SI 32768
SF 100.6127617 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



BRUKER

```
Current Data Parameters
NAME          SDG-3-102r
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140117
Time               10.46
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             8403.361 Hz
FIDRES          0.128225 Hz
AQ              3.8993919 sec
RG                    57
DW                59.500 usec
DE                17.39 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         600.3233018 MHz
NUC1                  1H
P1                10.77 usec
PLW1        26.00000000 W

F2 - Processing parameters
SI                 65536
SF           600.3200748 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-70, 13C/APT



Current Data Parameters
NAME SDG-3-102r
EXPNO 2
PROCNO 1

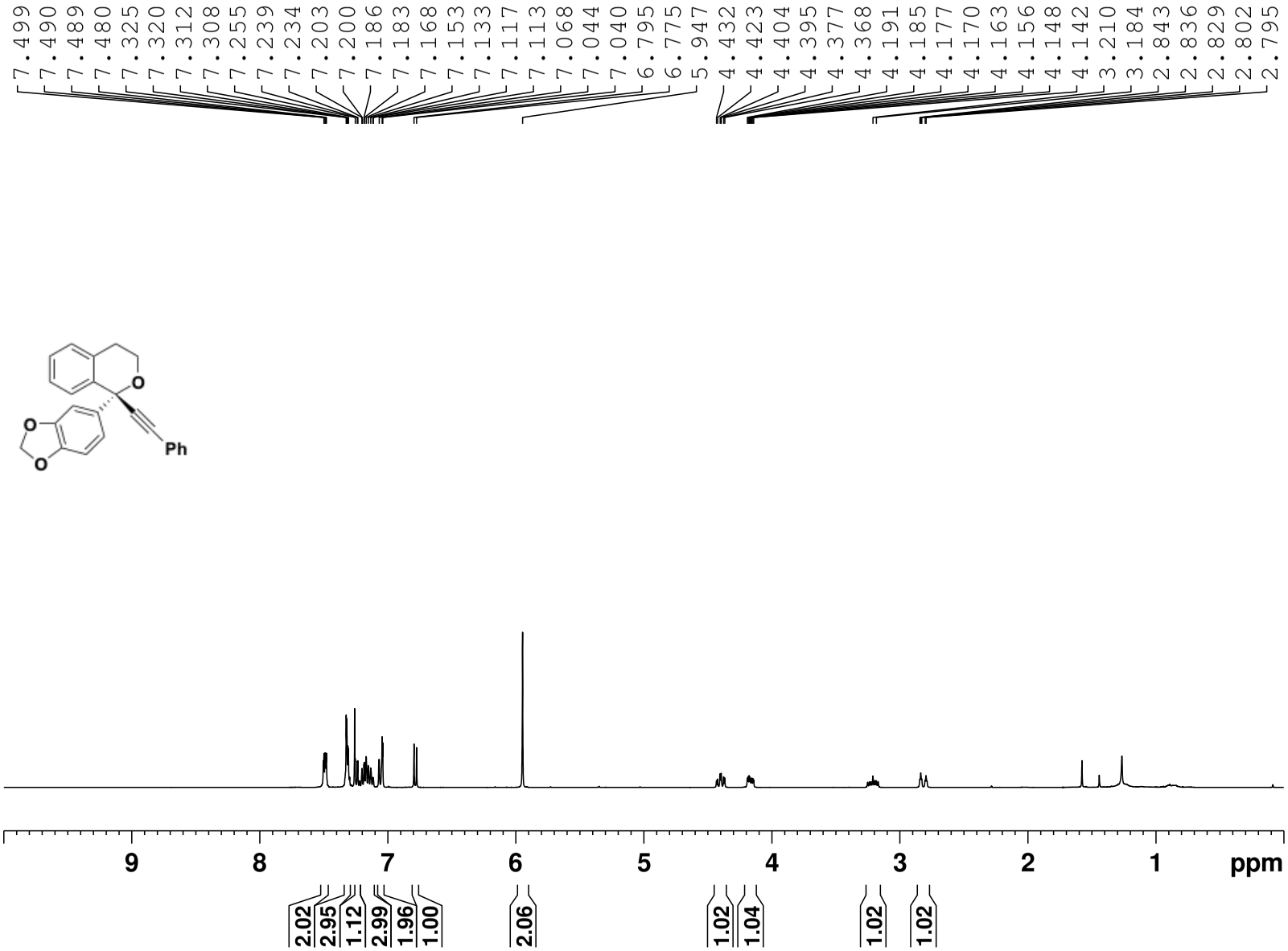
F2 - Acquisition Parameters
Date_ 20140118
Time 0.32
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG jmod.acqt0
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 34722.223 Hz
FIDRES 0.529819 Hz
AQ 0.9437184 sec
RG 2050
DW 14.400 usec
DE 18.88 usec
TE 298.0 K
CNST2 145.0000000
CNST11 1.0000000
D1 5.00000000 sec
D20 0.00689655 sec
TD0 1

======== CHANNEL f1 ========
SFO1 150.9656791 MHz
NUC1 13C
P1 10.63 usec
P2 21.26 usec
PLW1 110.00000000 W

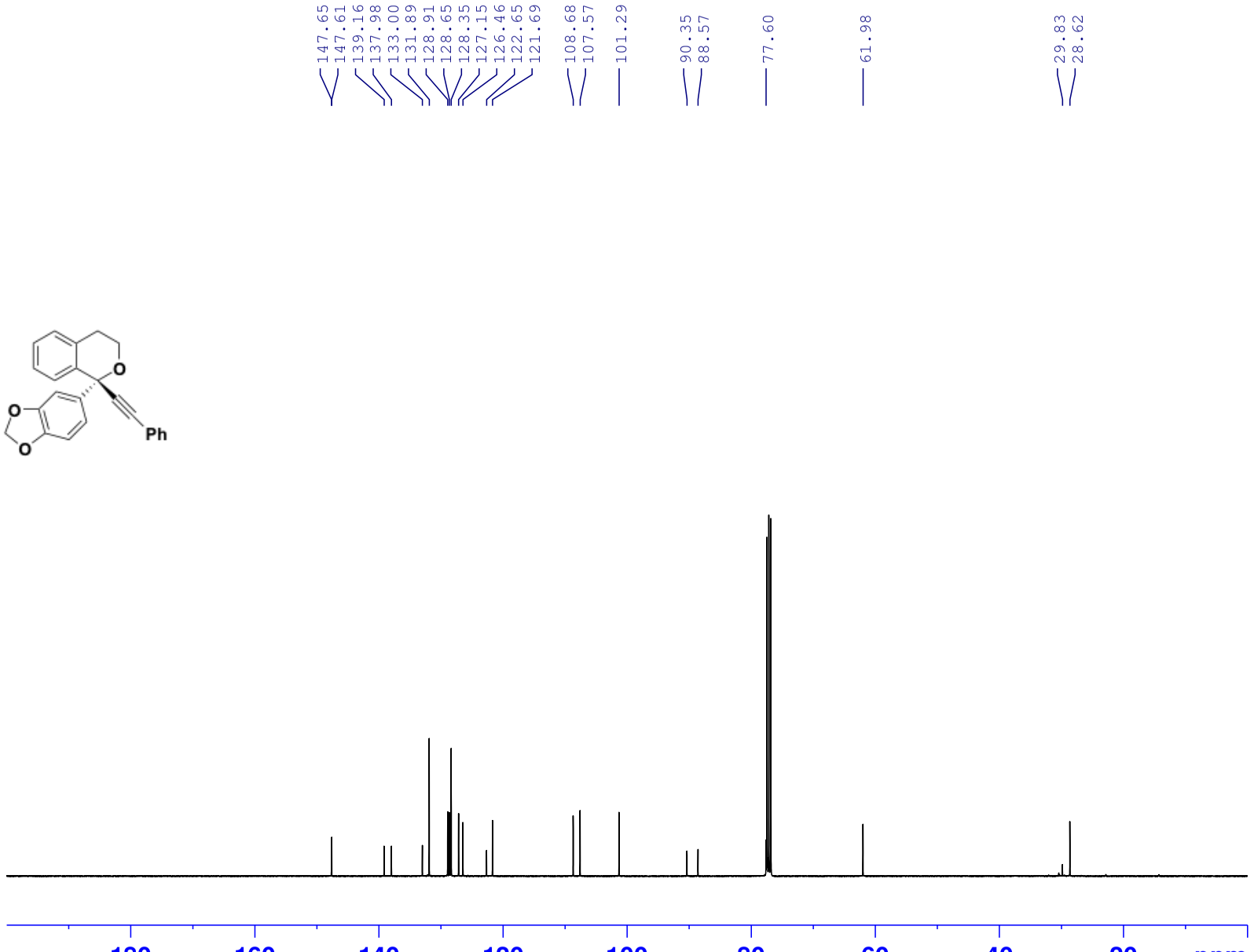
======== CHANNEL f2 ========
SFO2 600.3224013 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 22.00000000 W
PLW12 0.51885003 W

F2 - Processing parameters
SI 32768
SF 150.9505840 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

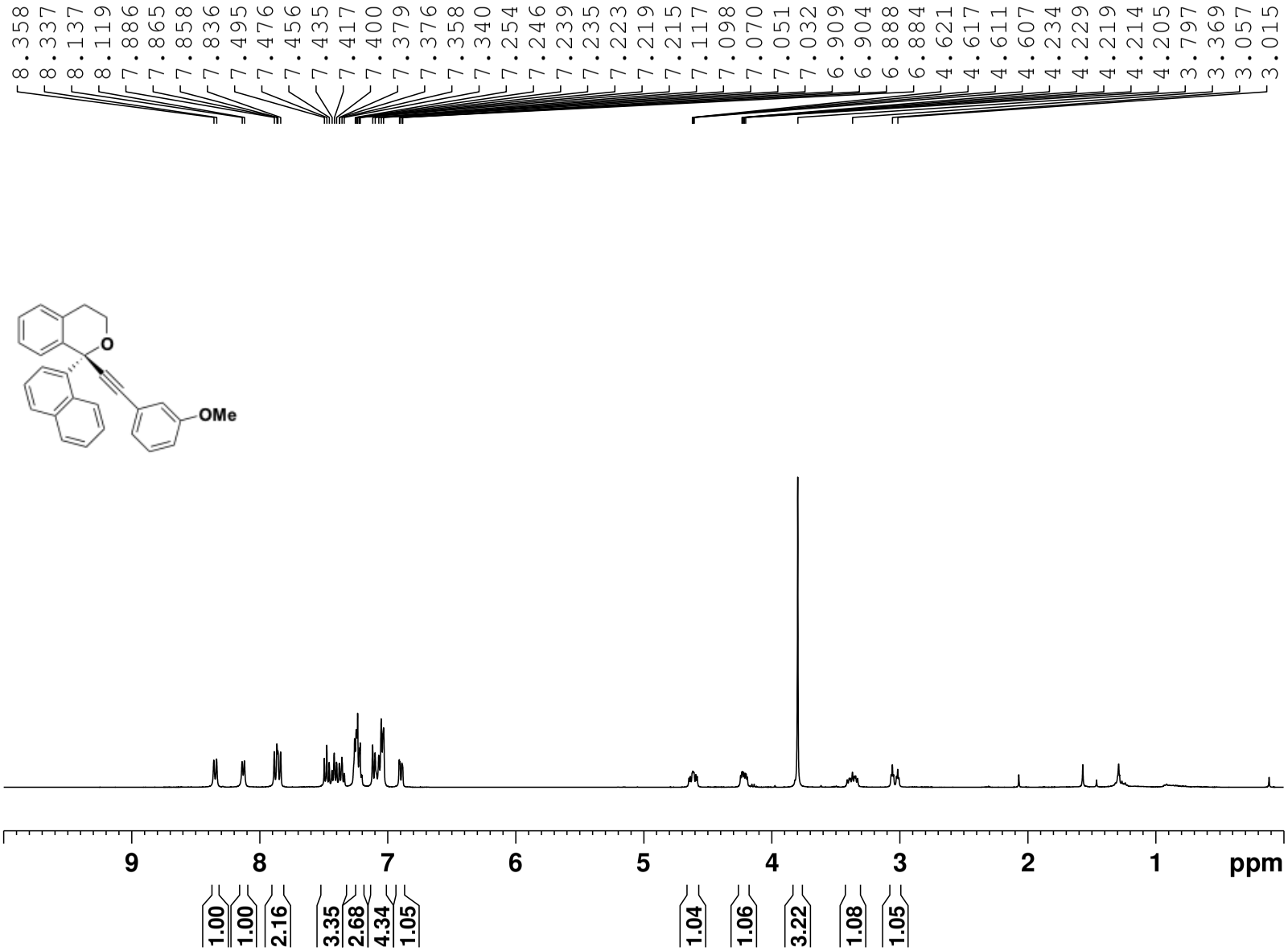
2-71, 1H NMR



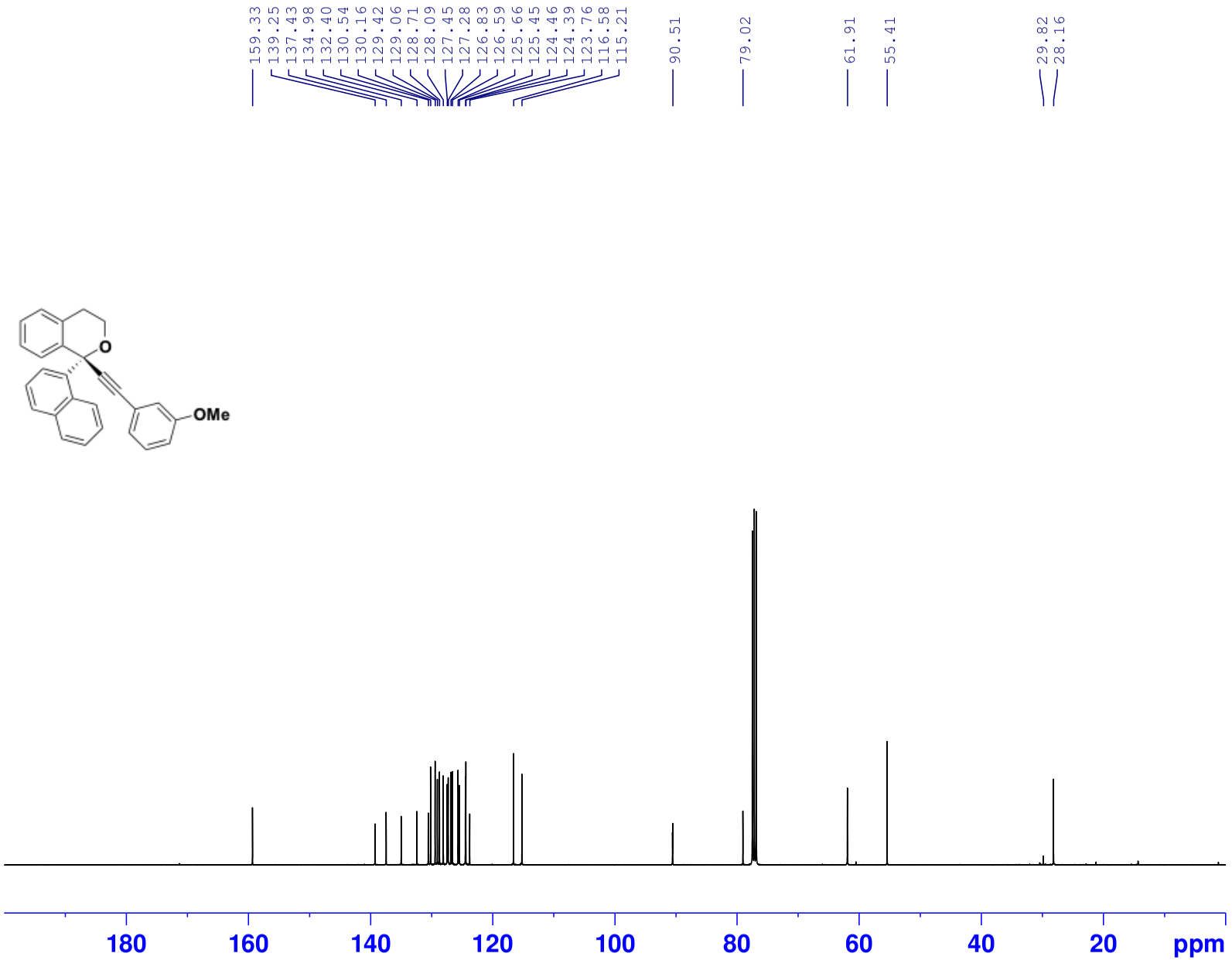

```
Current Data Parameters
NAME          SDG-3-38-2
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130910
Time               17.25
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ             3.9583745 sec
RG                  12.7
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300093 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```




```
Current Data Parameters
NAME          SDG-3-38-2
EXPNO                  6
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130910
Time               23.14
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   9.25 usec
PL1                  0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127608 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

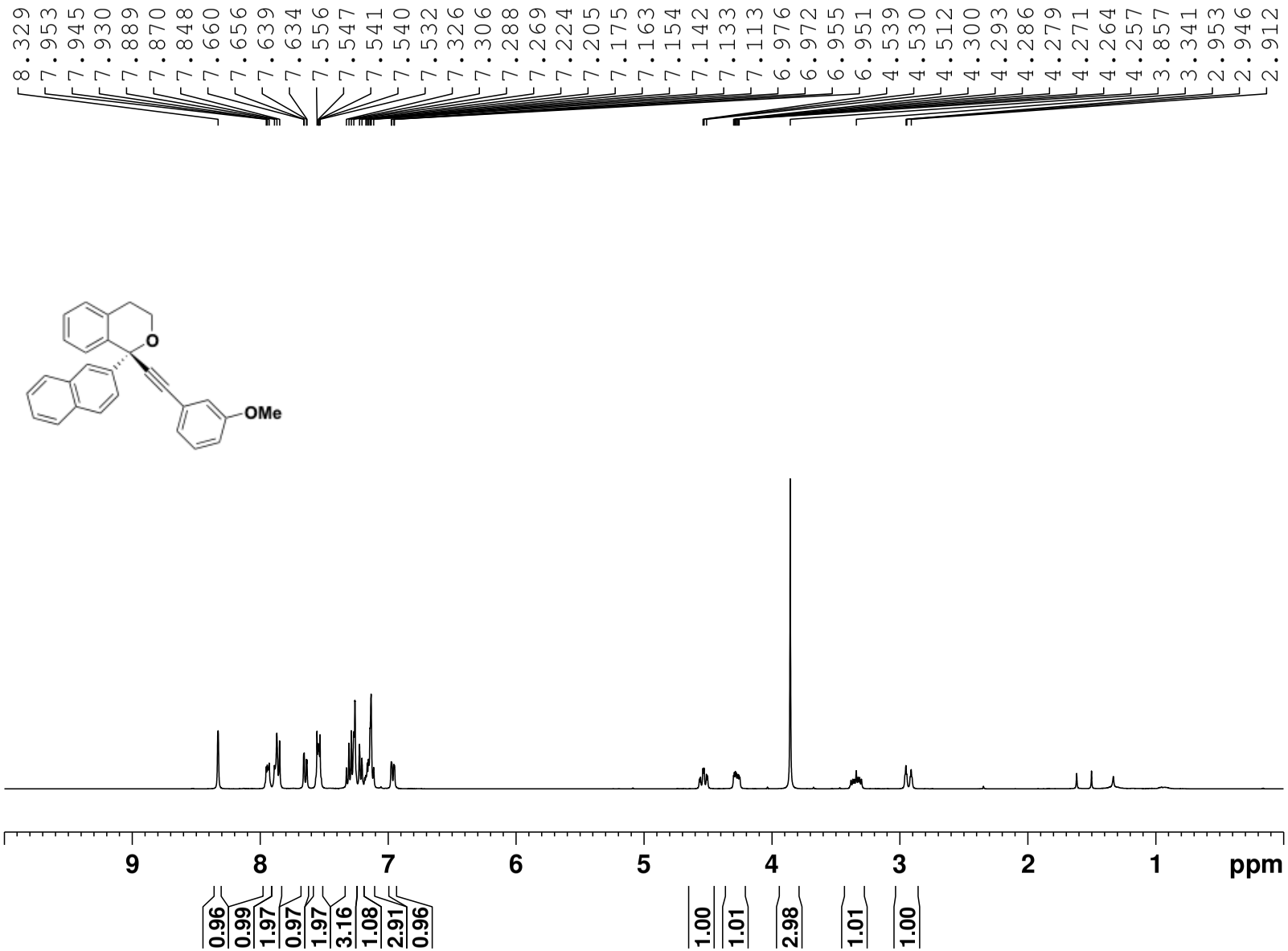



```
Current Data Parameters
NAME          SDG-3-20-2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130703
Time                9.52
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     4
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300094 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

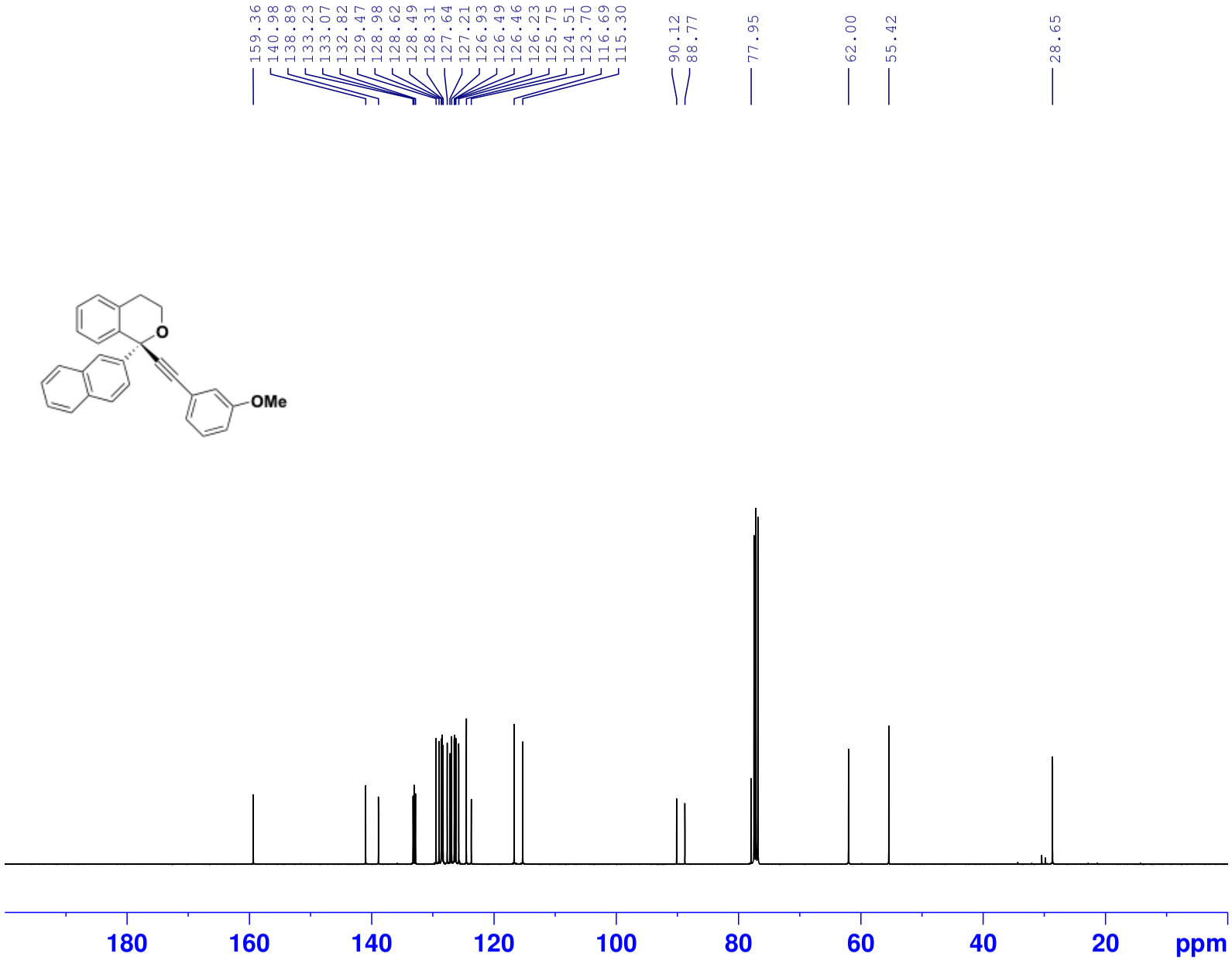



```
Current Data Parameters
NAME          SDG-3-20-2
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130704
Time                1.16
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE               298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                9.25 usec
PL1               0.55 dB
PL1W       35.18820572 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                1H
PCPD2            90.00 usec
PL2               4.90 dB
PL12             20.46 dB
PL13             21.00 dB
PL2W        3.30822015 W
PL12W       0.09195905 W
PL13W       0.08120718 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6127643 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

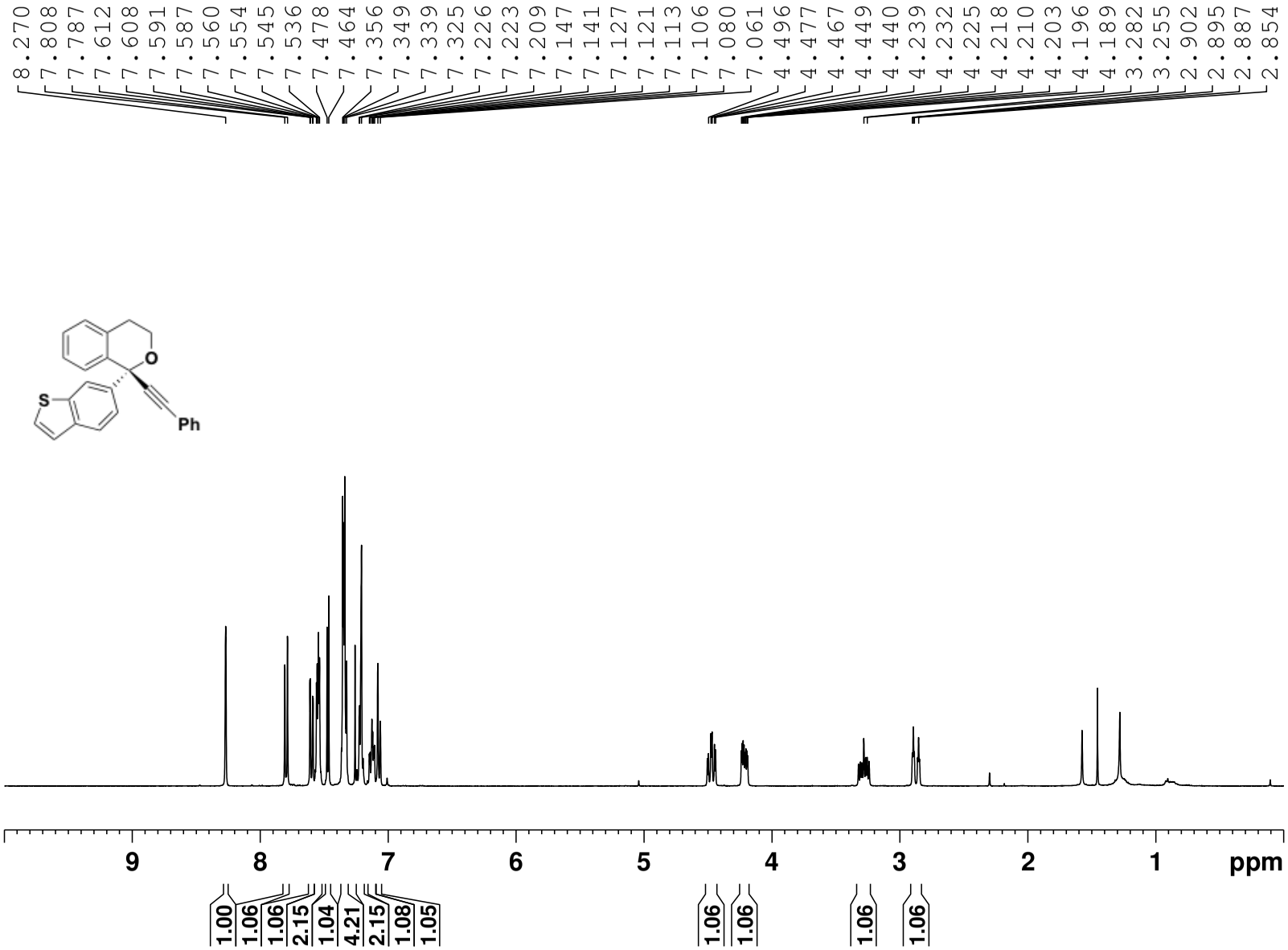
2-73, 1H NMR




```
Current Data Parameters
NAME          SDG-3-35-1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130806
Time               14.52
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     8
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1299978 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

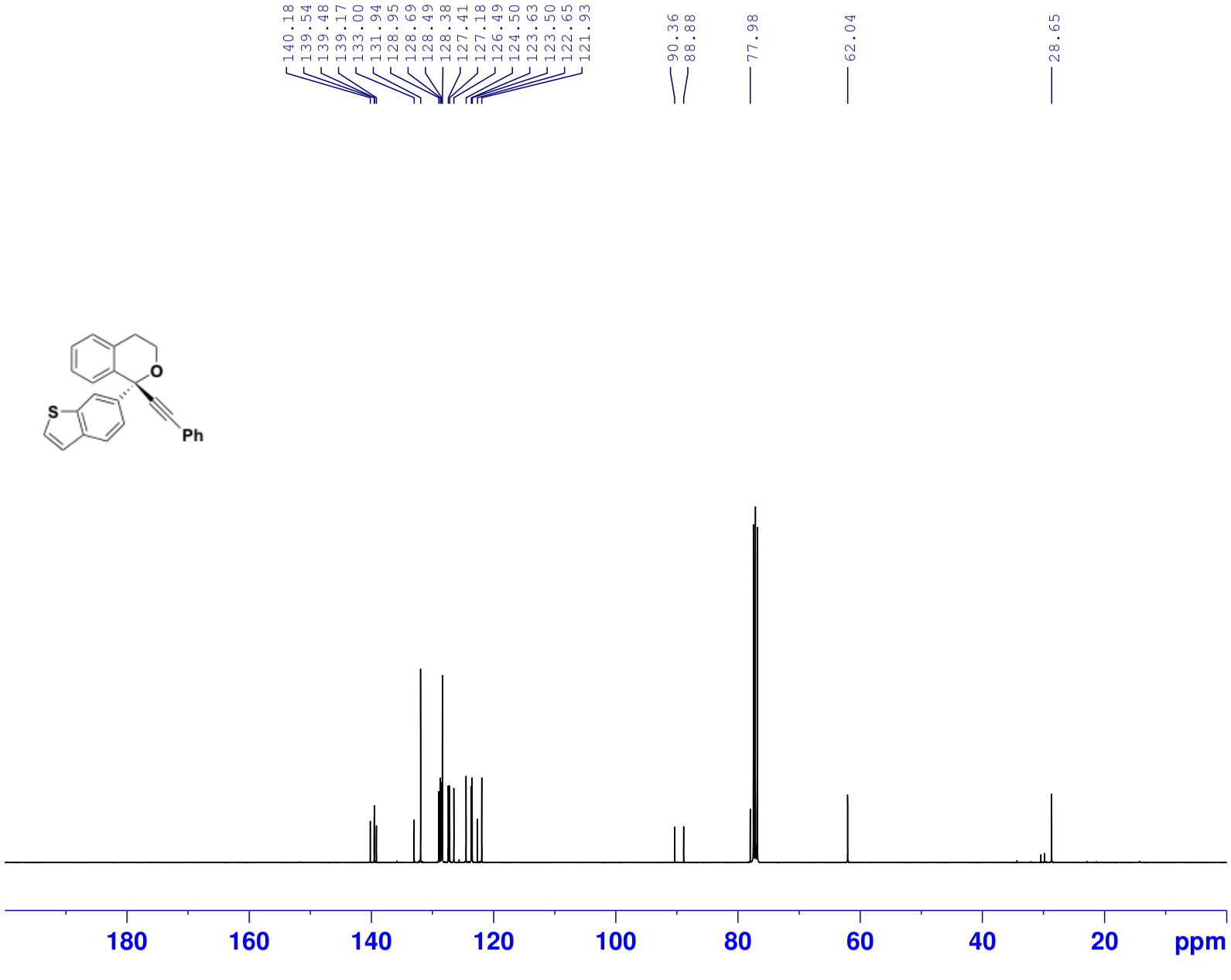



```
Current Data Parameters
NAME          SDG-3-35-1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130807
Time                7.53
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                  512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127660 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



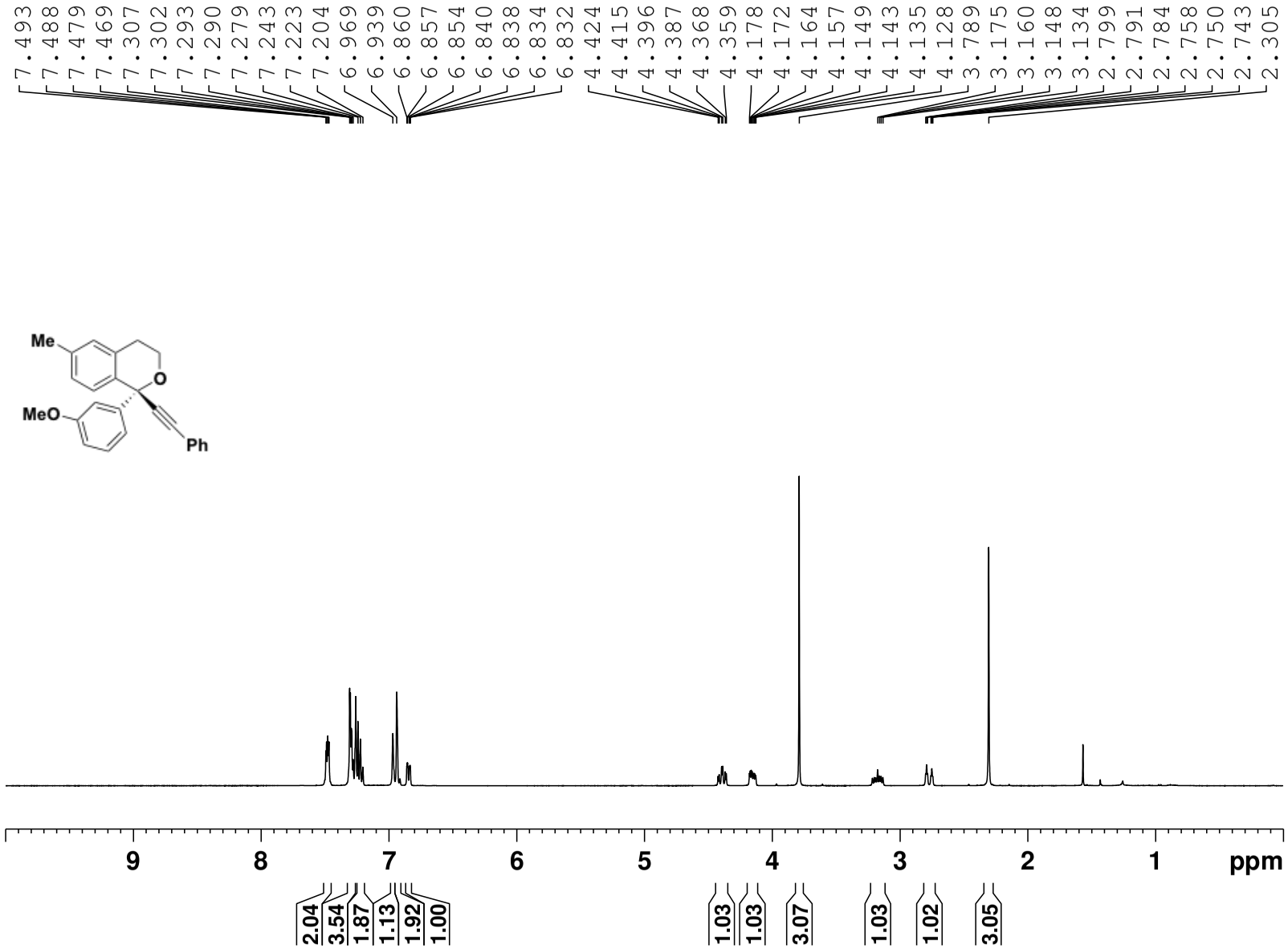

```
Current Data Parameters
NAME      SDG-3-37-2(2nd)
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130827
Time                1.52
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ             3.9583745 sec
RG                  10.1
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300094 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

2-74, 13C NMR



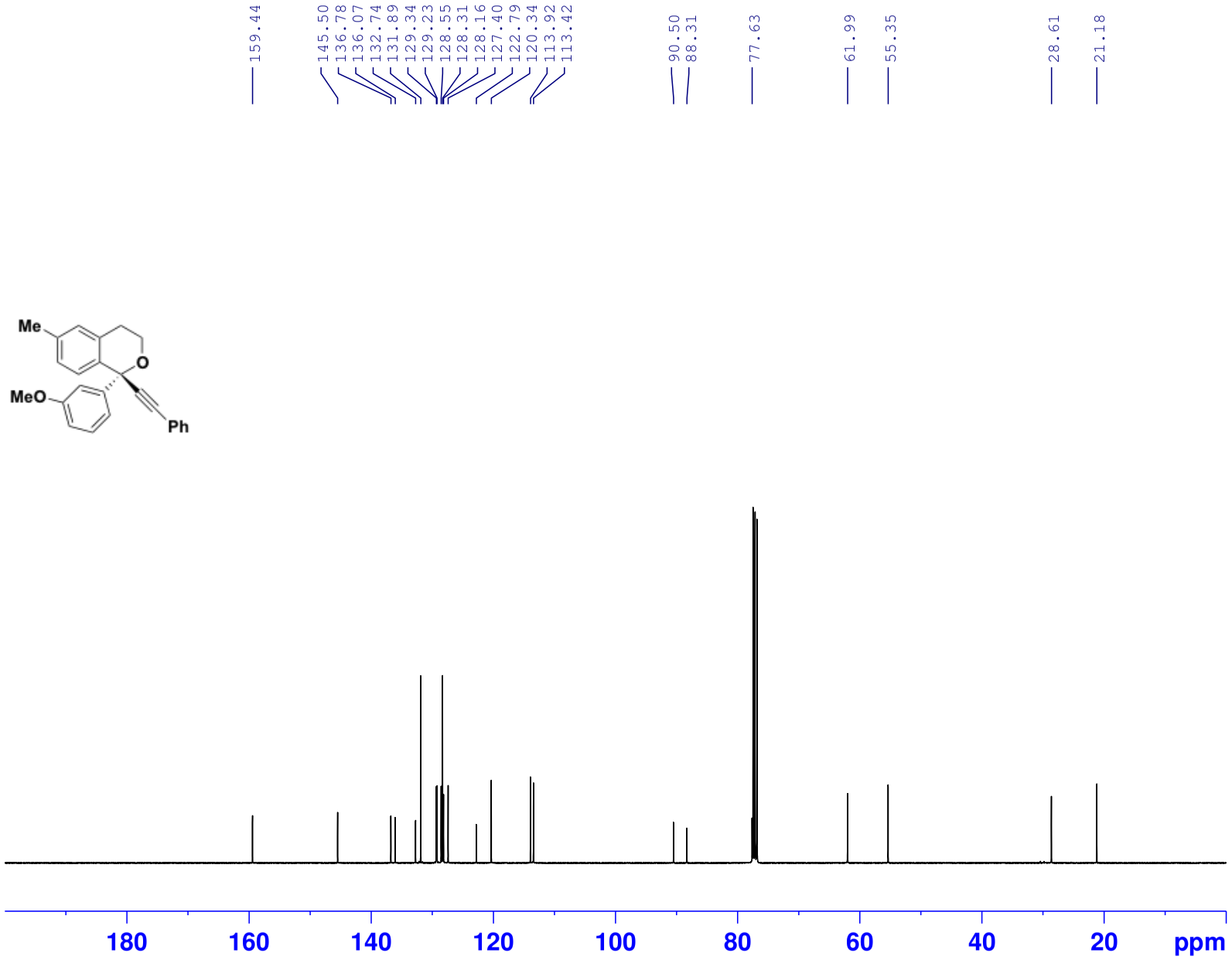

```
Current Data Parameters
NAME      SDG-3-37-2(2nd)
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130827
Time               22.07
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                  512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6127636 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

2-75, 1H NMR



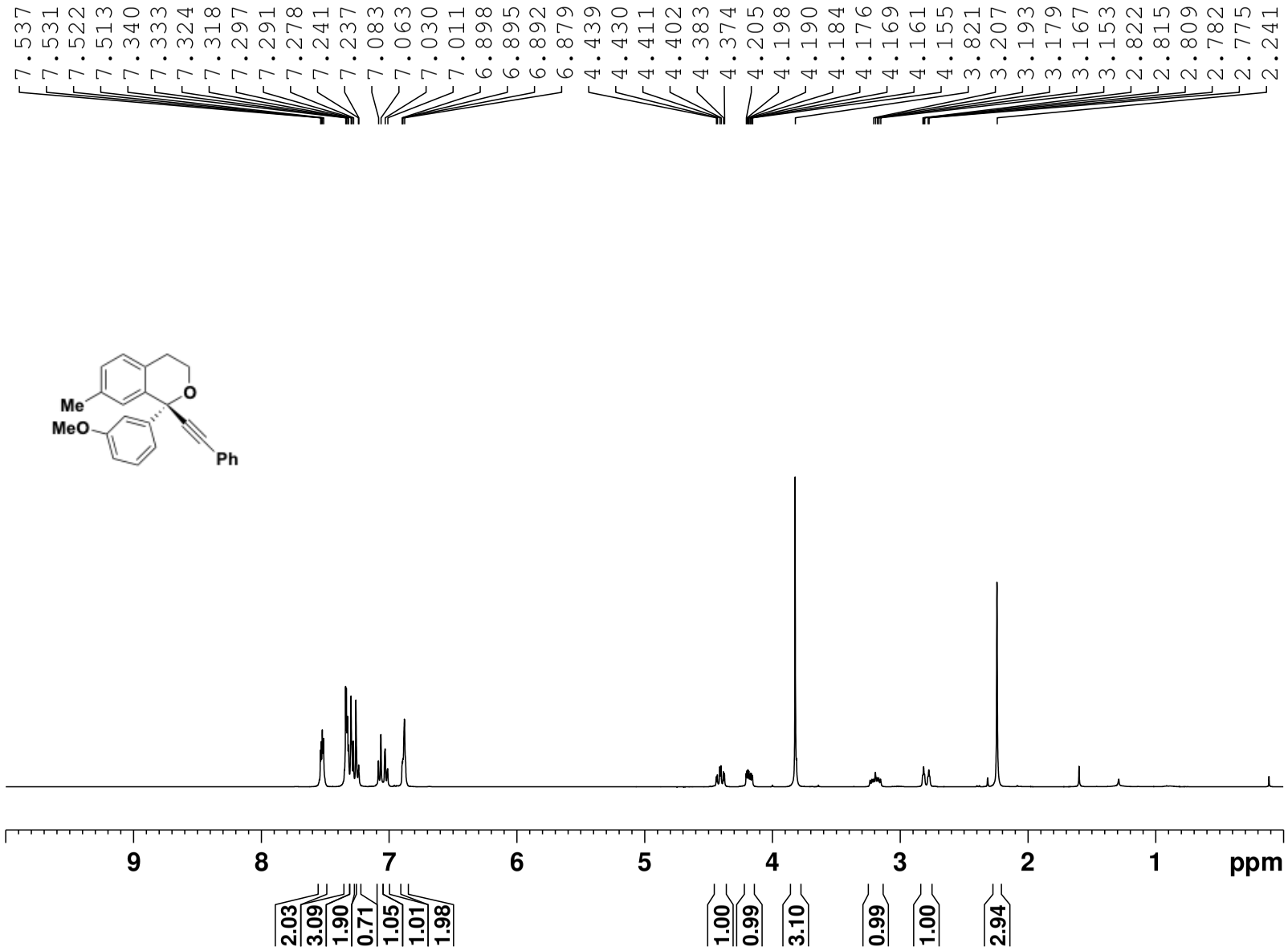

```
Current Data Parameters
NAME       SDG-3-59-1(1)
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130910
Time               16.05
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     9
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300157 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

2-75, 13C NMR



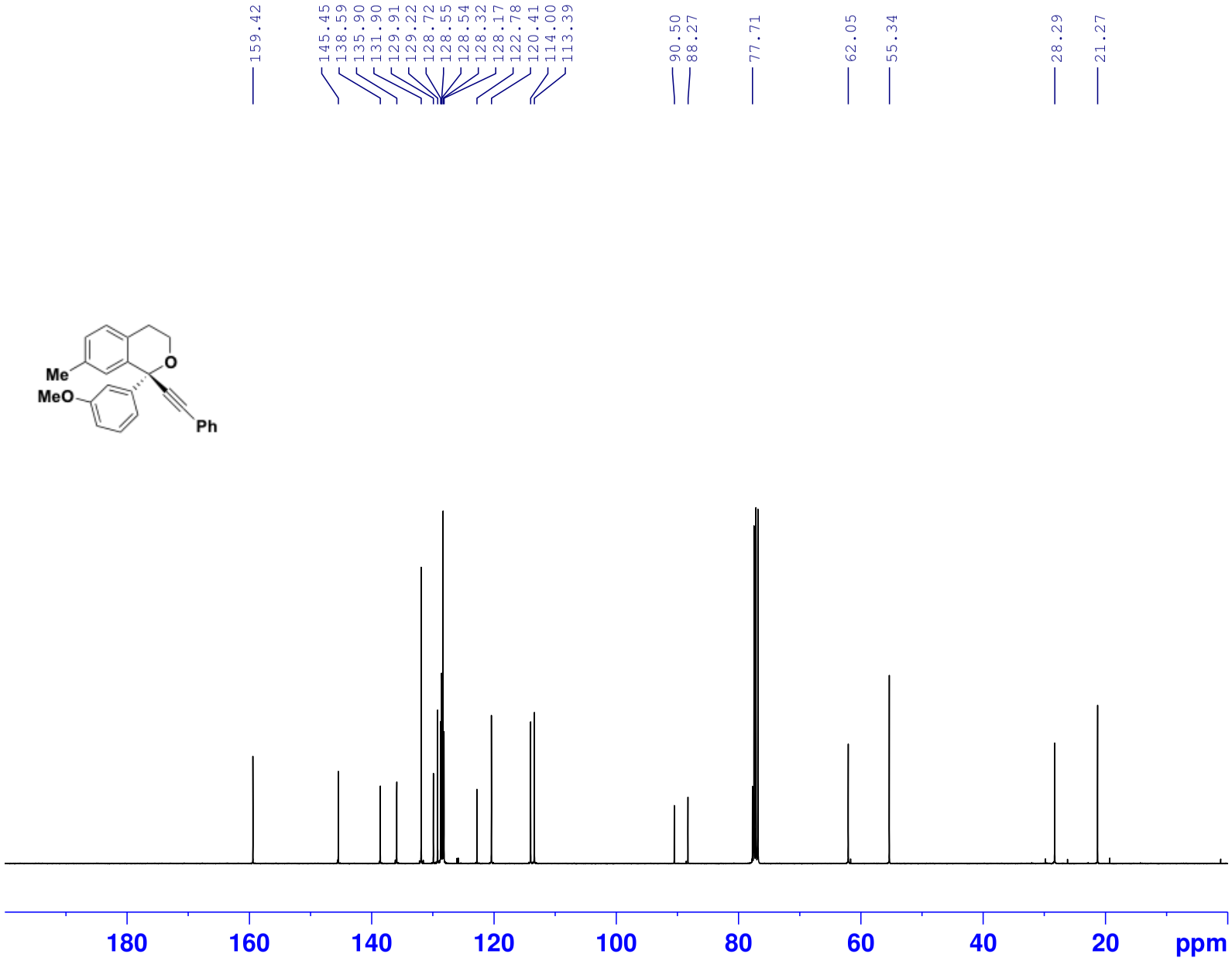

```
Current Data Parameters
NAME        SDG-3-59-1-1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130911
Time                0.17
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                 9.25 usec
PL1                0.55 dB
PL1W       35.18820572 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W        3.30822015 W
PL12W       0.09195905 W
PL13W       0.08120718 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6127621 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

2-76, 1H NMR



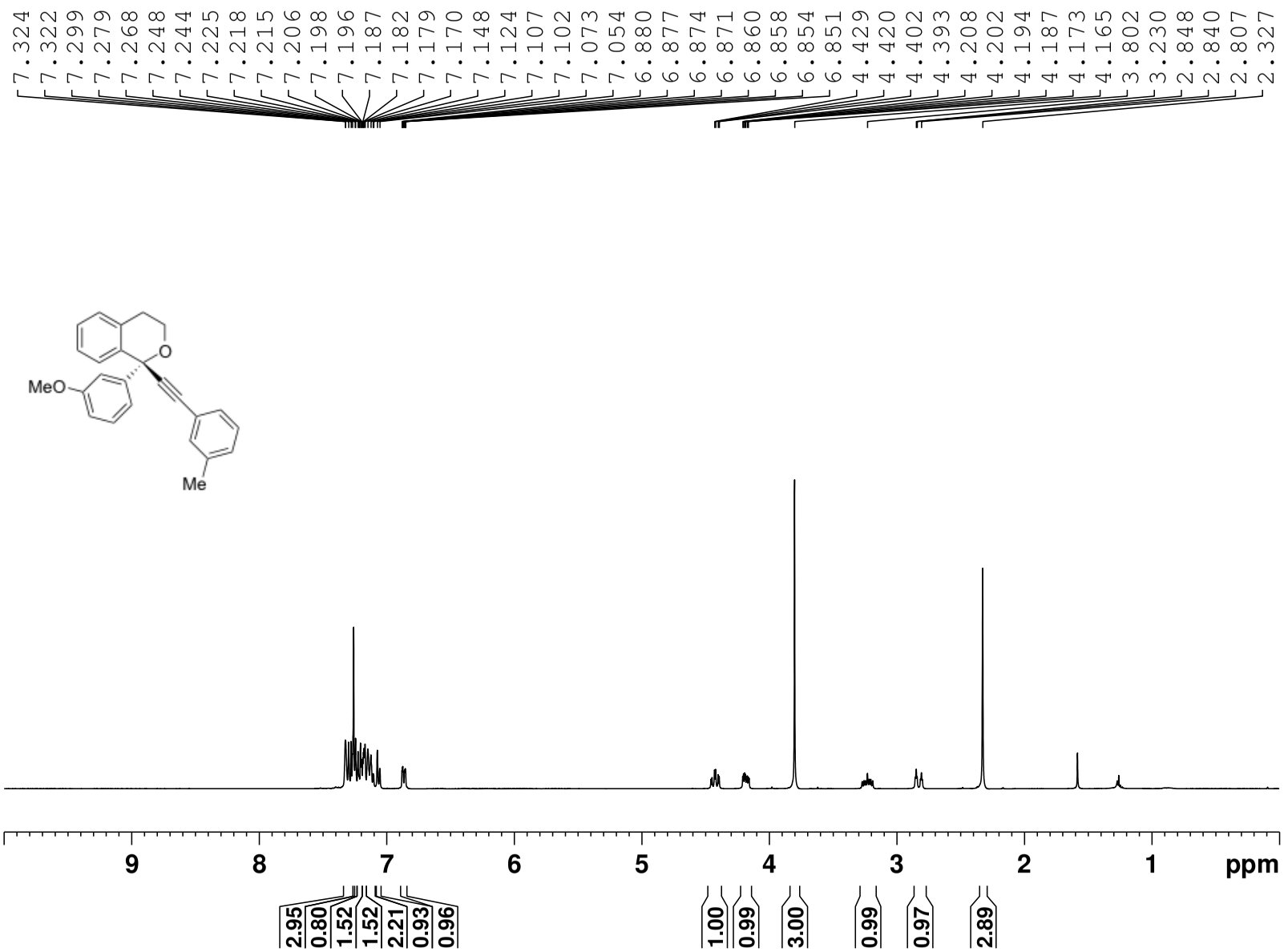

```
Current Data Parameters
NAME      SDG-3-84-2pure
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131126
Time               11.39
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     9
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300101 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-76, 13C NMR



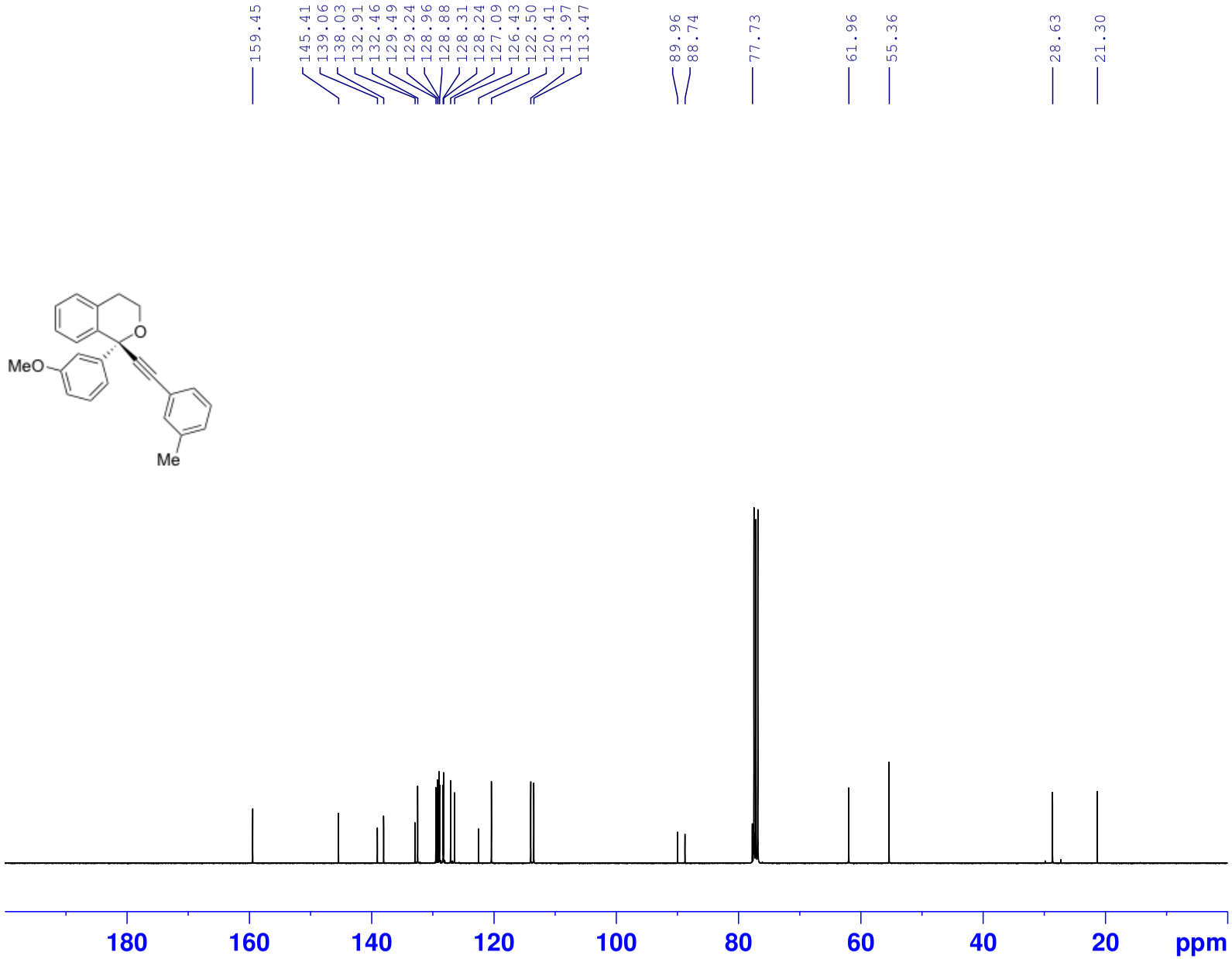

```
Current Data Parameters
NAME      SDG-3-84-2pure
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131127
Time                1.31
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE               298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                 9.25 usec
PL1                0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6127654 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

2-77, 1H NMR

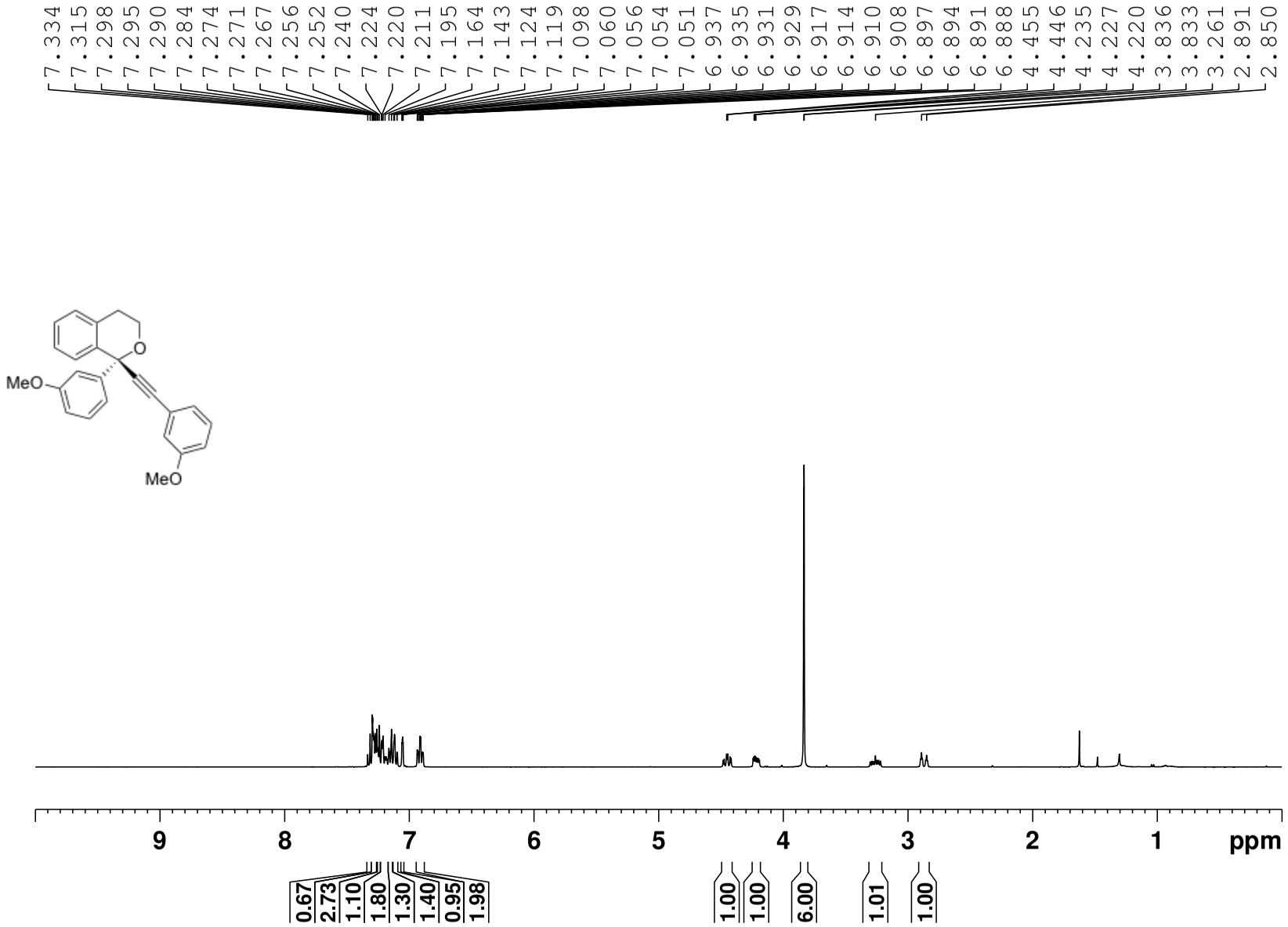



```
Current Data Parameters
NAME      SDG-3-77-1pure
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131126
Time               11.20
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                  10.1
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300102 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

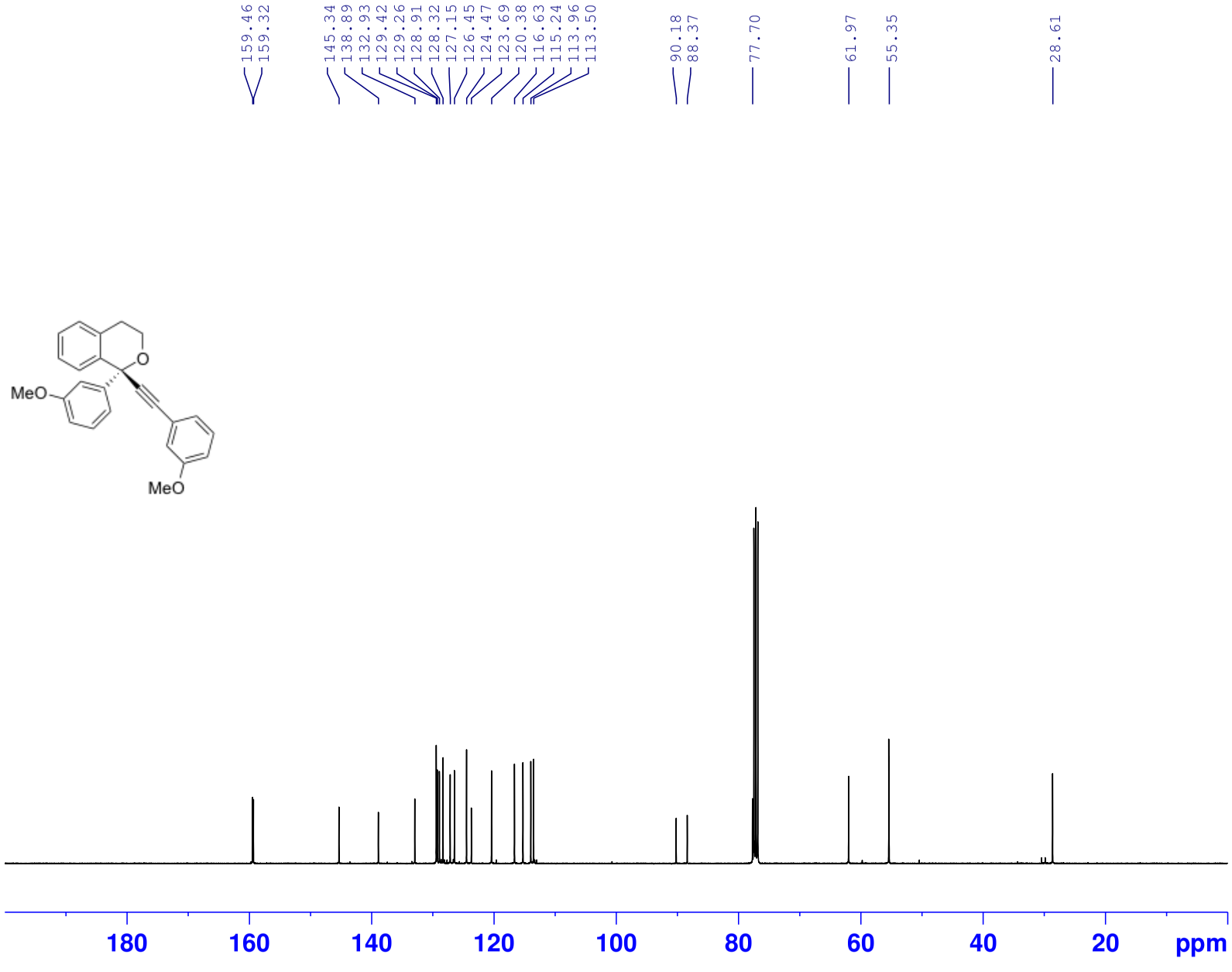
2-77, 13C NMR




```
Current Data Parameters
NAME      SDG-3-77-1pure
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131127
Time                5.08
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE                298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                 9.25 usec
PL1                0.55 dB
PL1W       35.18820572 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W        3.30822015 W
PL12W       0.09195905 W
PL13W       0.08120718 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6127619 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

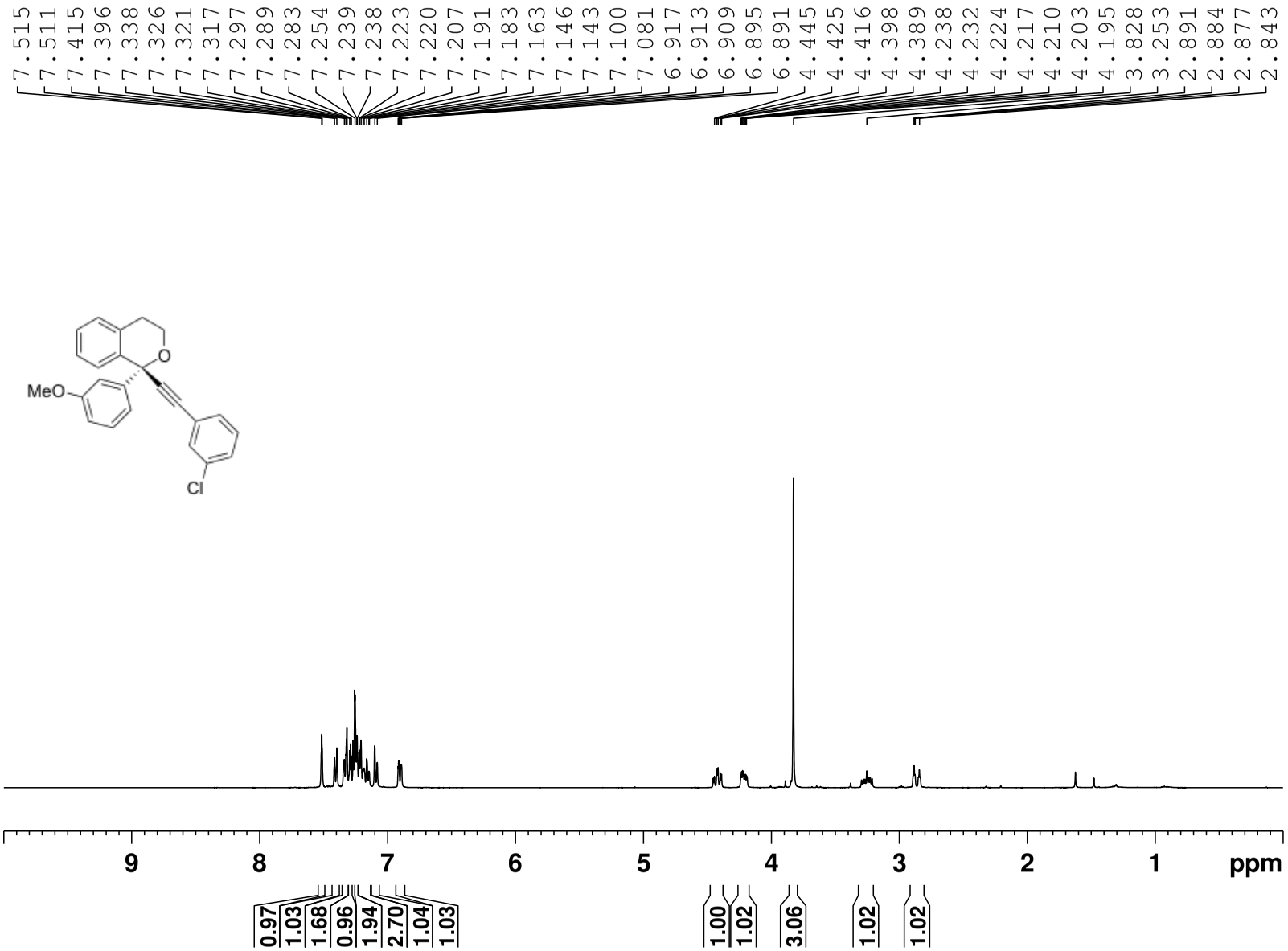



```
Current Data Parameters
NAME      SDG-3-23-3(2nd)
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130826
Time               19.52
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     8
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1299936 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```



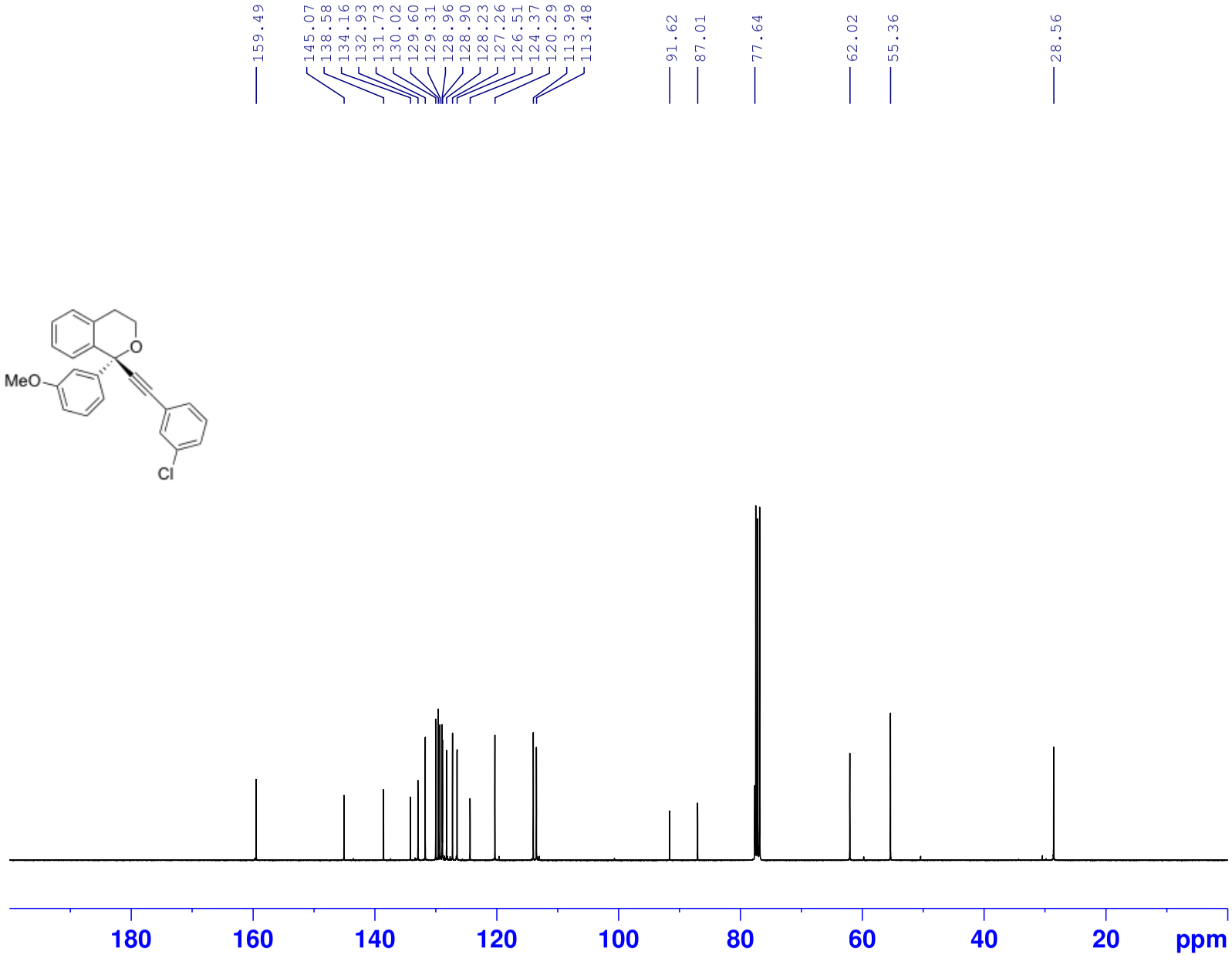

```
Current Data Parameters
NAME      SDG-3-23-3(1st)
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130827
Time                1.39
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE               298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                 9.25 usec
PL1                0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6127619 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

2-79, 1H NMR



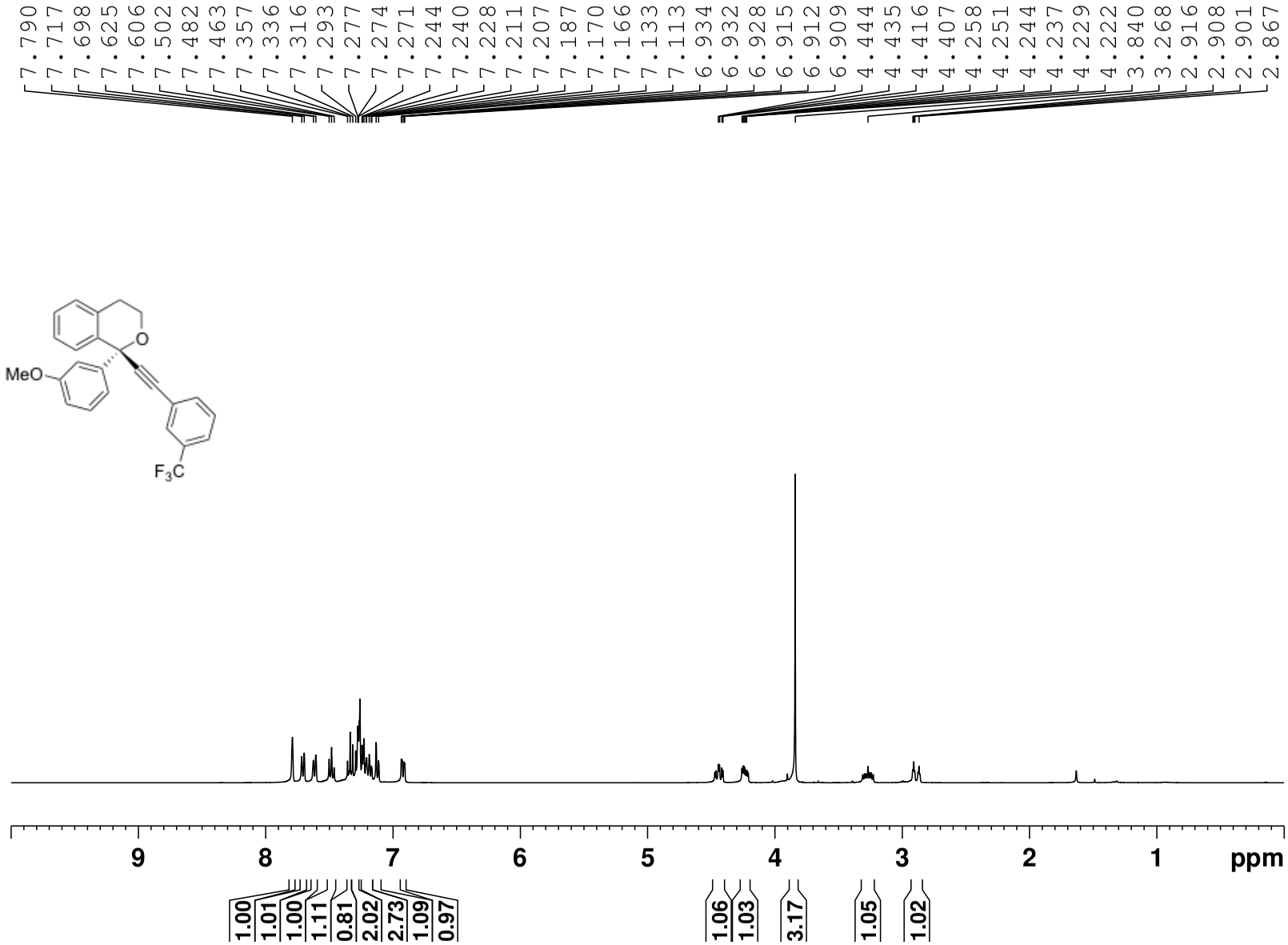

```
Current Data Parameters
NAME          SDG-3-30-1
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130806
Time               13.57
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     4
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300000 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-79, 13C NMR



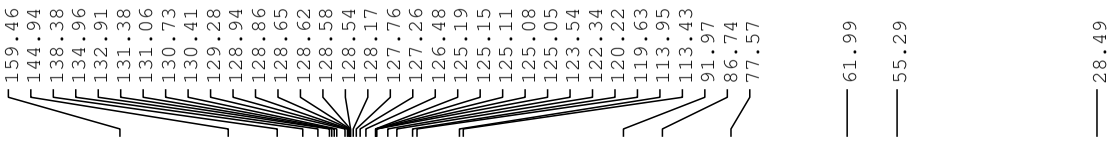

```
Current Data Parameters
NAME          SDG-3-30-2
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130806
Time               23.27
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   9.25 usec
PL1                  0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127633 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

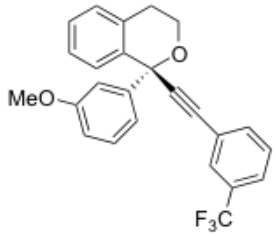
2-80, 1H NMR

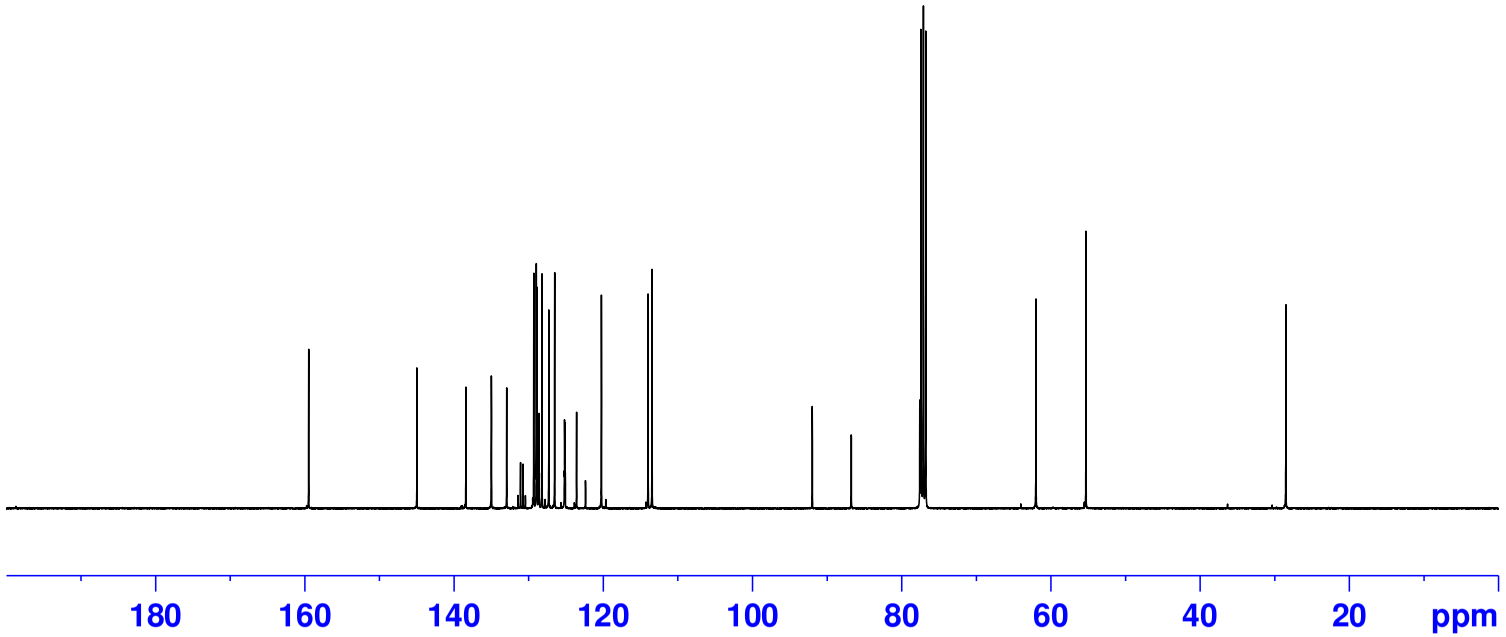



```
Current Data Parameters
NAME          SDG-3-31-2
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130806
Time               14.15
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     8
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1299958 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

2-80, 13C NMR



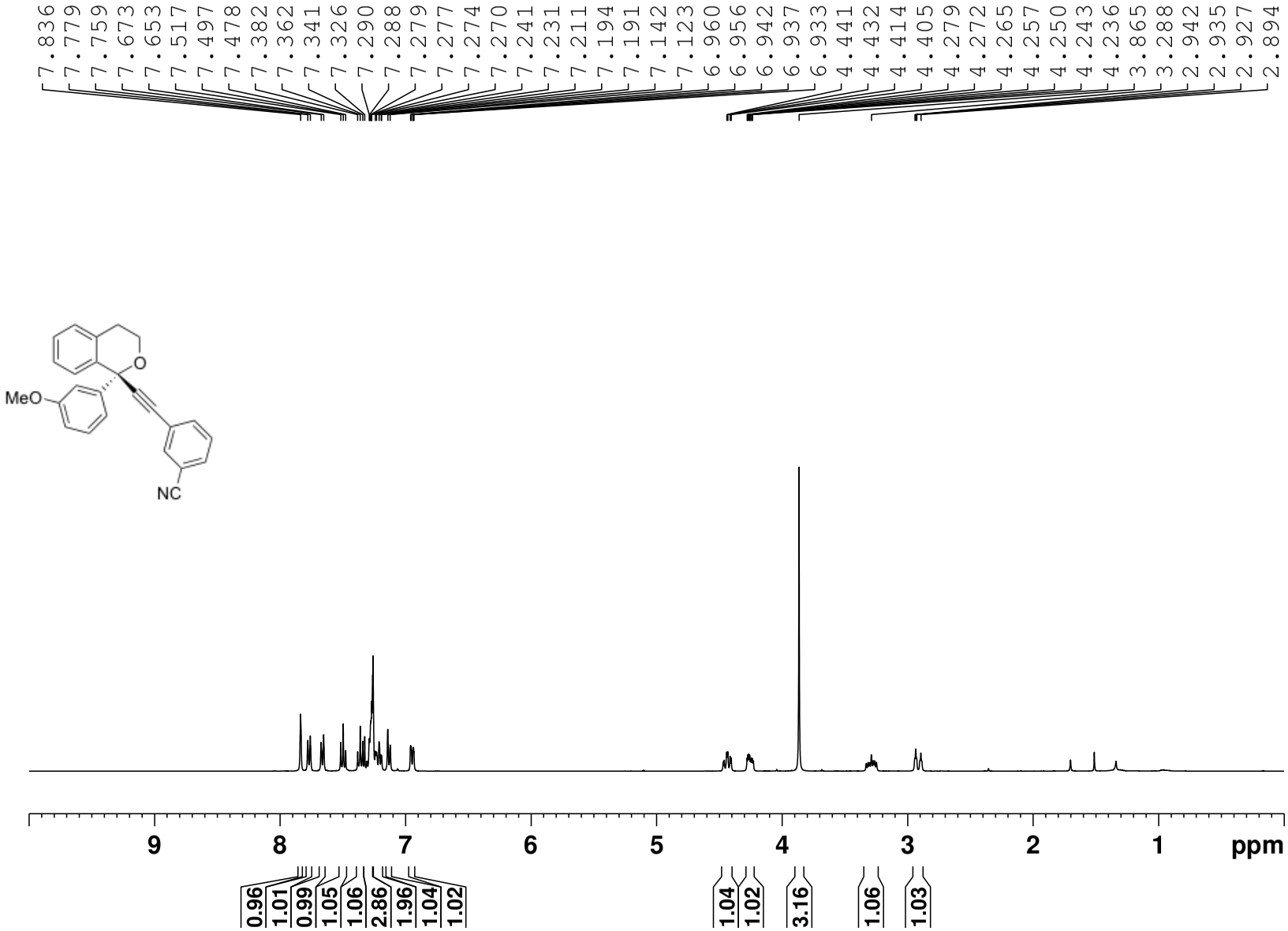




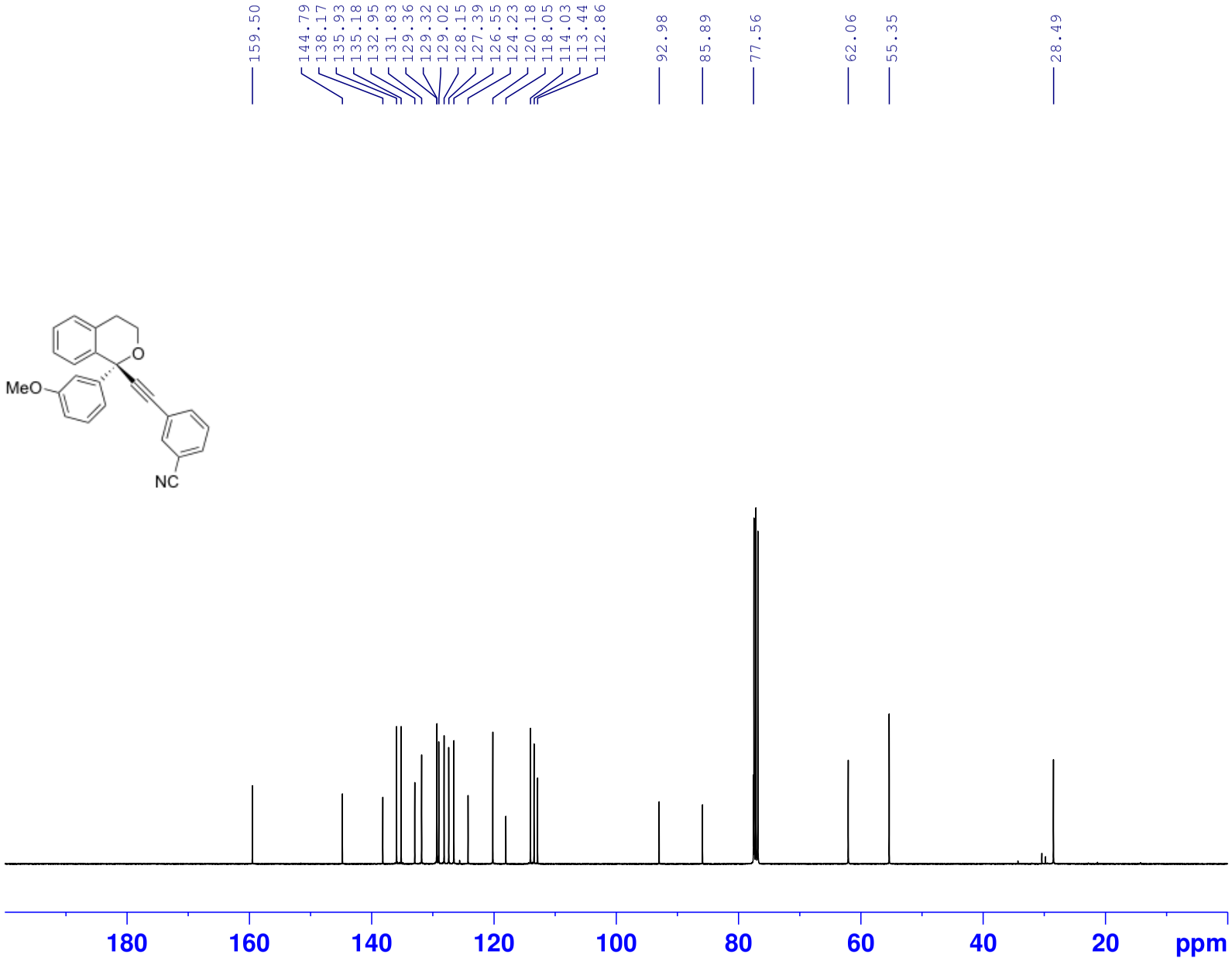
229

```
Current Data Parameters
NAME          SDG-3-31-2
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130807
Time                1.34
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                  512
DW                20.850 usec
DE                18.00 usec
TE                298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.25 usec
PL1                0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127690 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

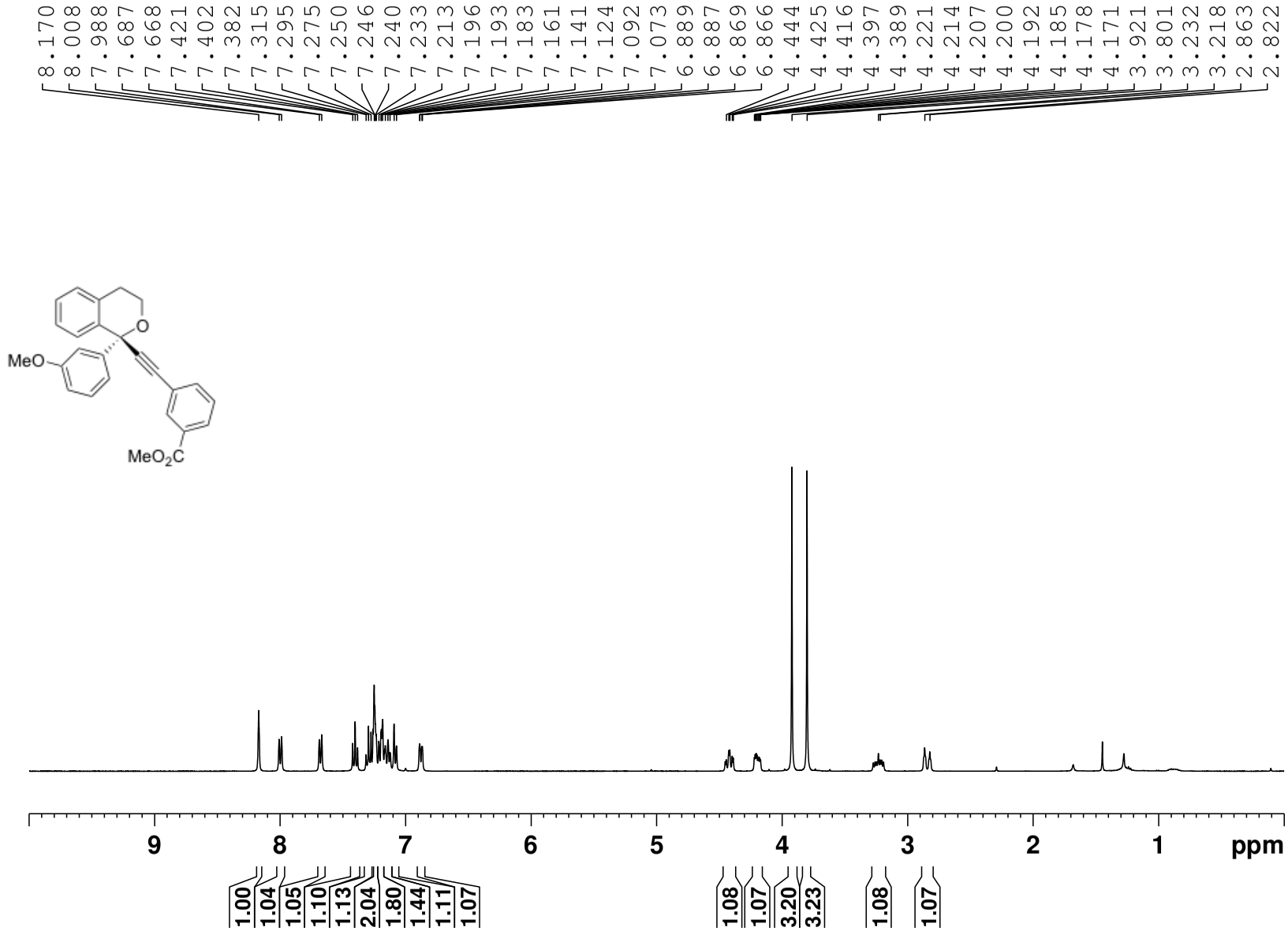
2-81, 1H NMR



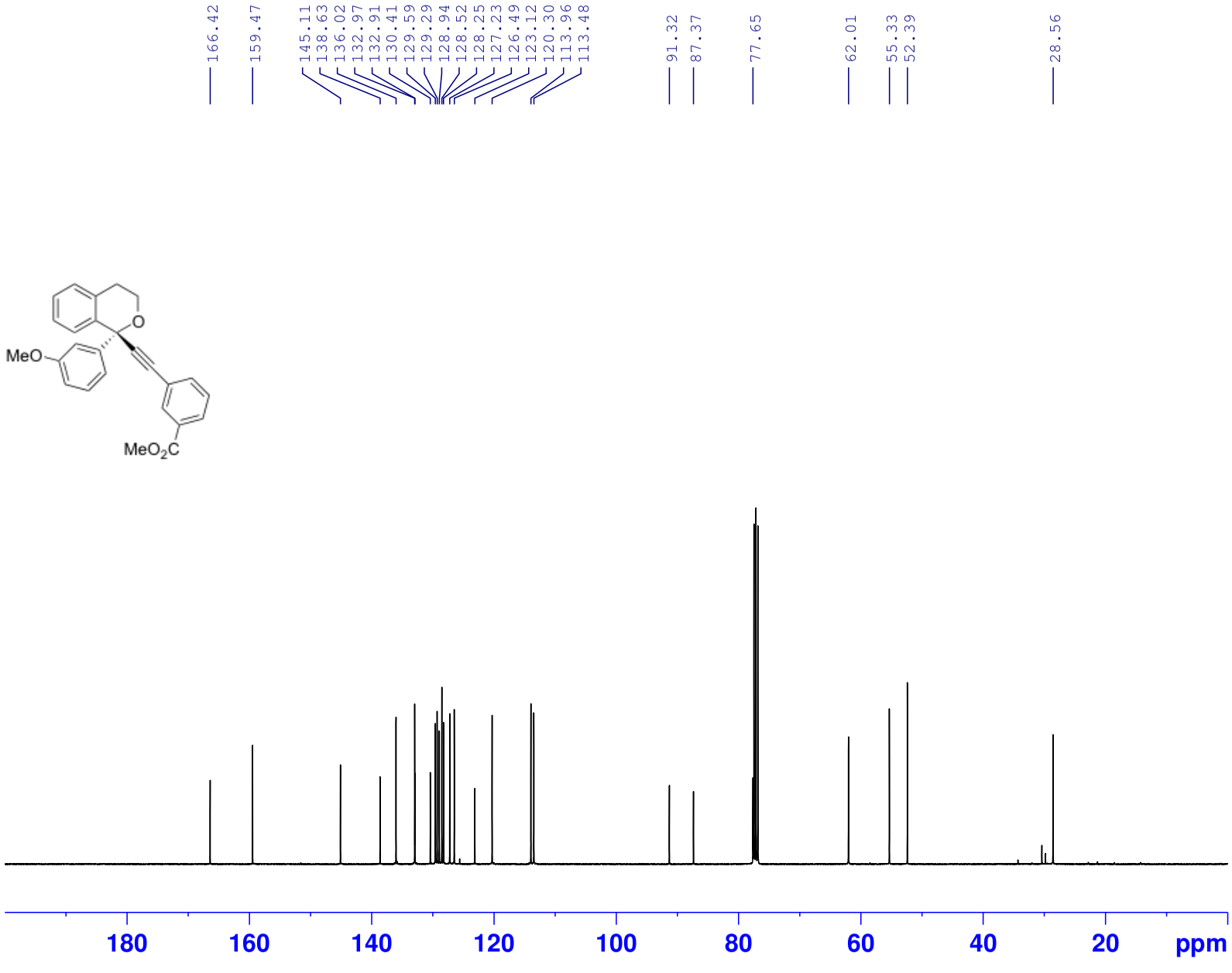

```
Current Data Parameters
NAME          SDG-3-40-1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130805
Time               12.24
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     8
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1299829 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```




```
Current Data Parameters
NAME          SDG-3-40-2
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130806
Time                0.17
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                  512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127654 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

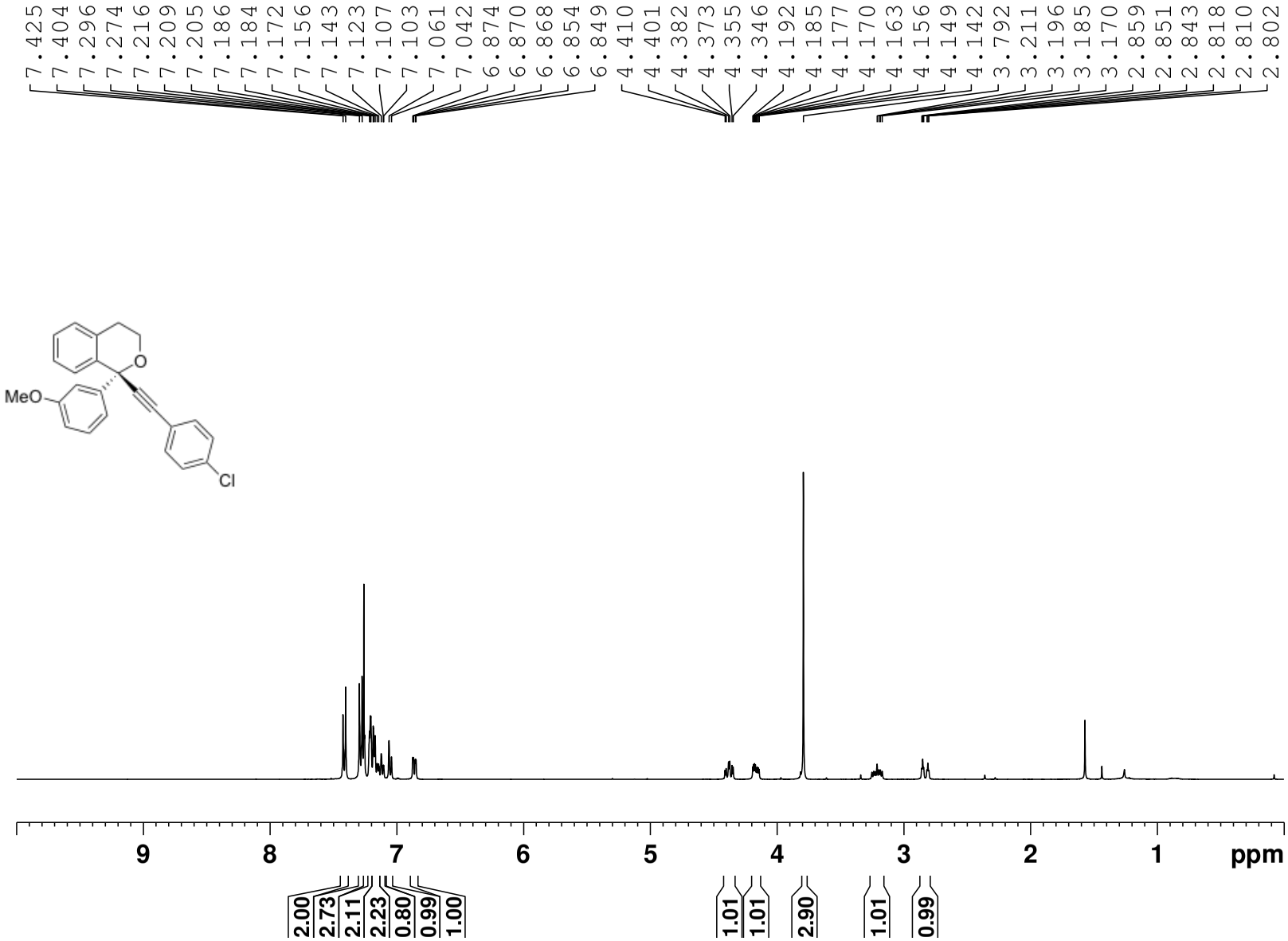



```
Current Data Parameters
NAME          SDG-3-39-1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130805
Time               12.12
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                   7.1
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300091 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



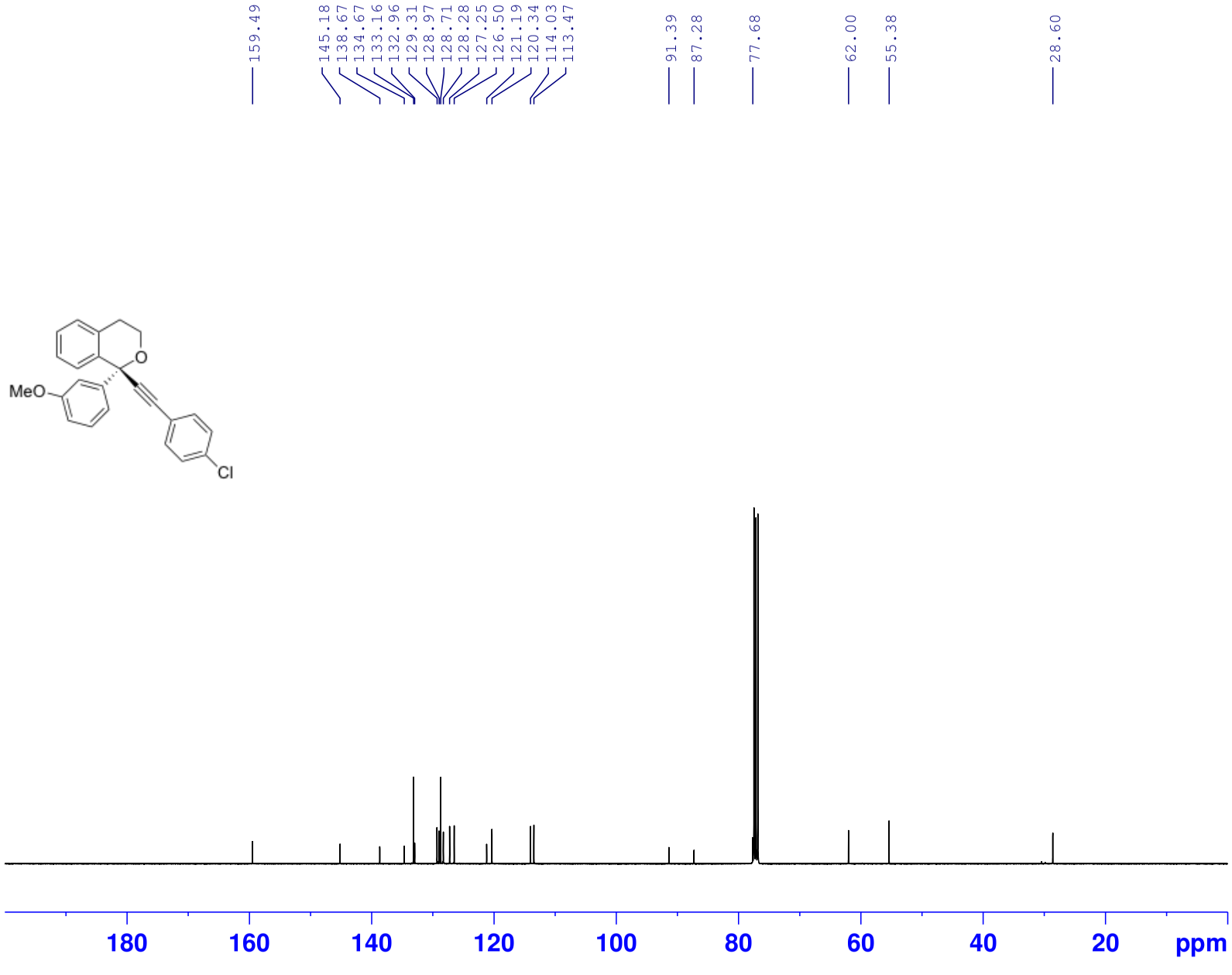

```
Current Data Parameters
NAME          SDG-3-39-1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130805
Time               21.07
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127649 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

2-83, 1H NMR

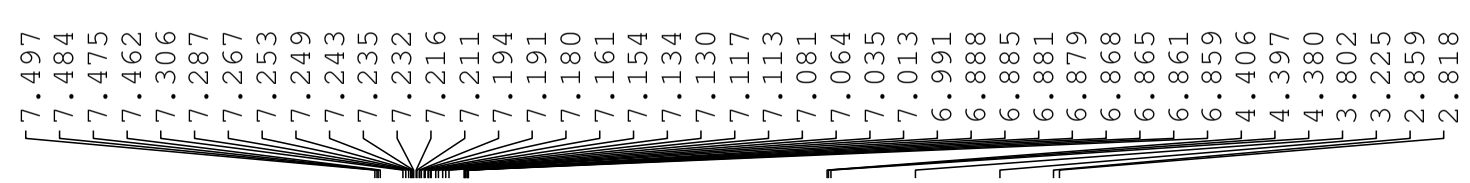


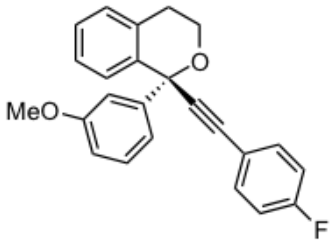

```
Current Data Parameters
NAME          SDG-3-90-1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131122
Time               11.20
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     9
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300099 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

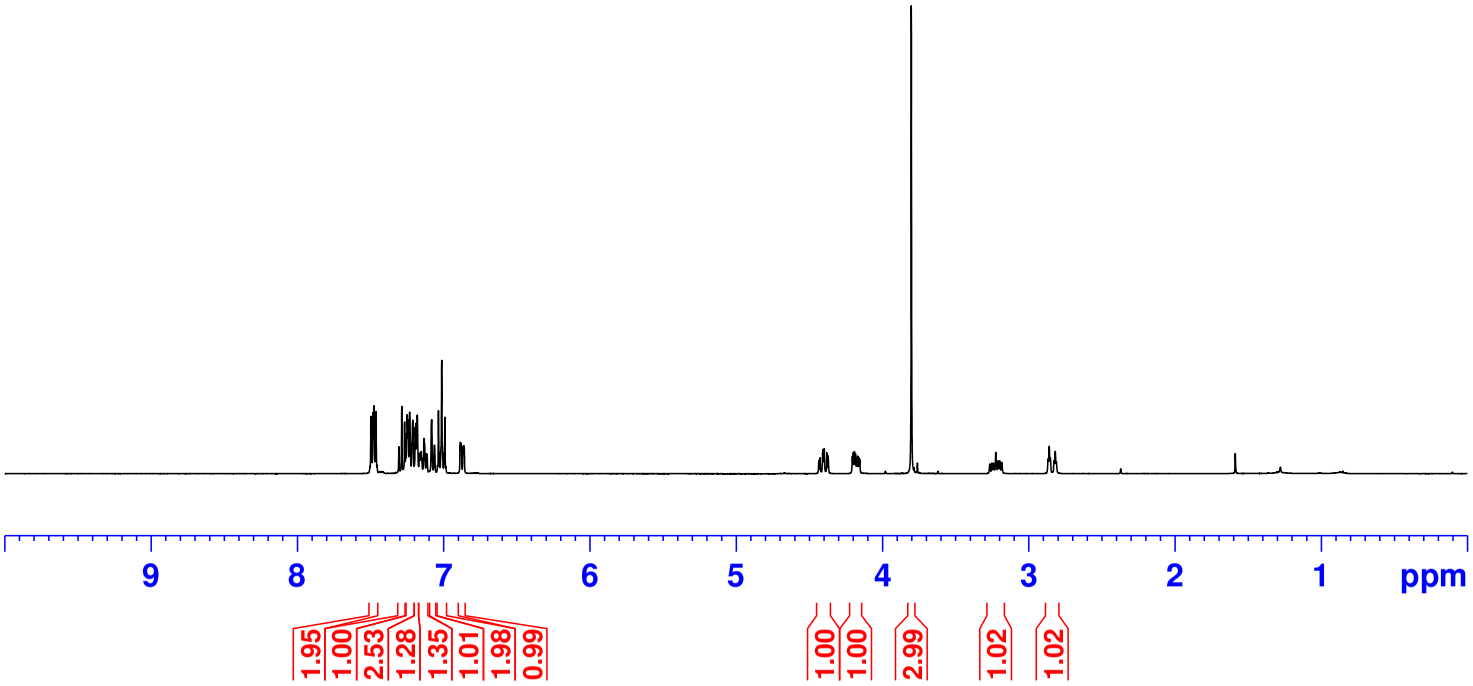
2-83, 13C NMR



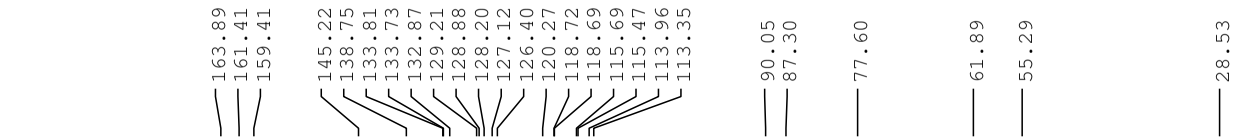

```
Current Data Parameters
NAME          SDG-3-90-1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131122
Time               23.06
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                  512
DW                20.850 usec
DE                18.00 usec
TE                298.1 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                13C
P1                9.25 usec
PL1               0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                1H
PCPD2            90.00 usec
PL2               4.90 dB
PL12             20.46 dB
PL13             21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127592 MHz
WDW                   EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

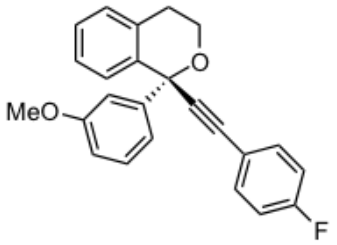


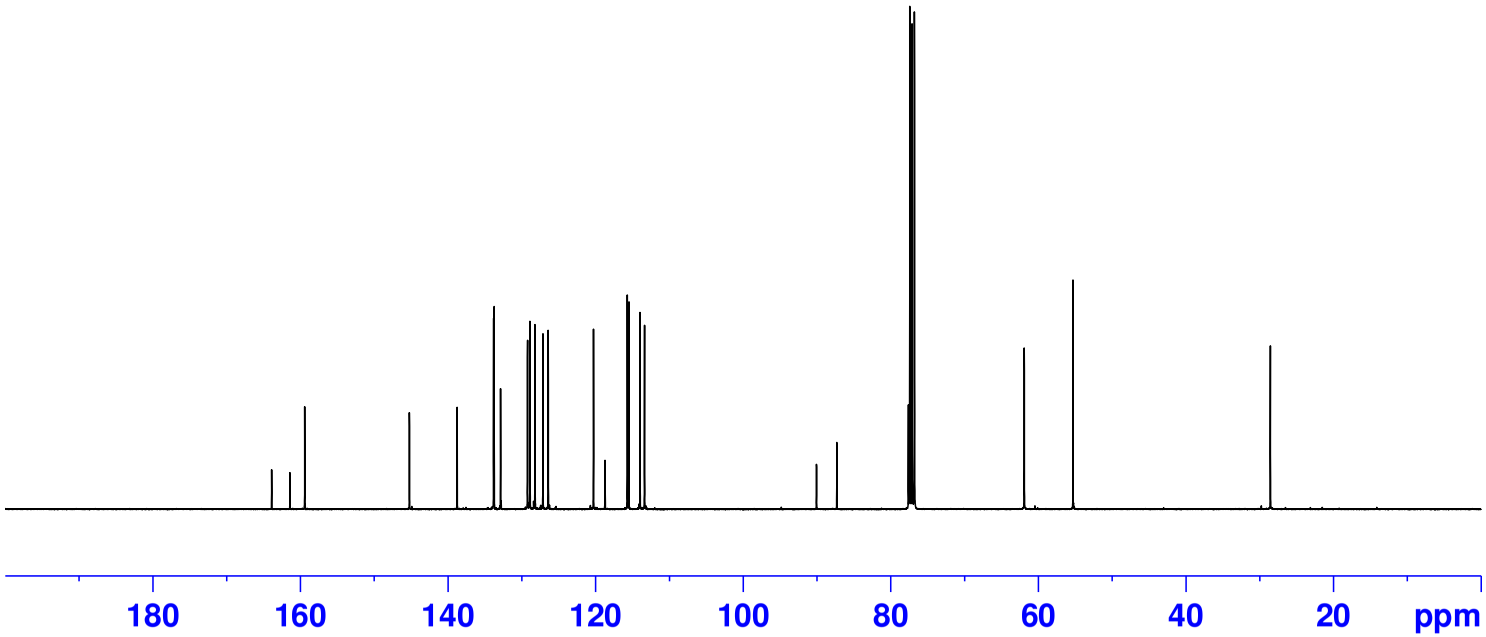




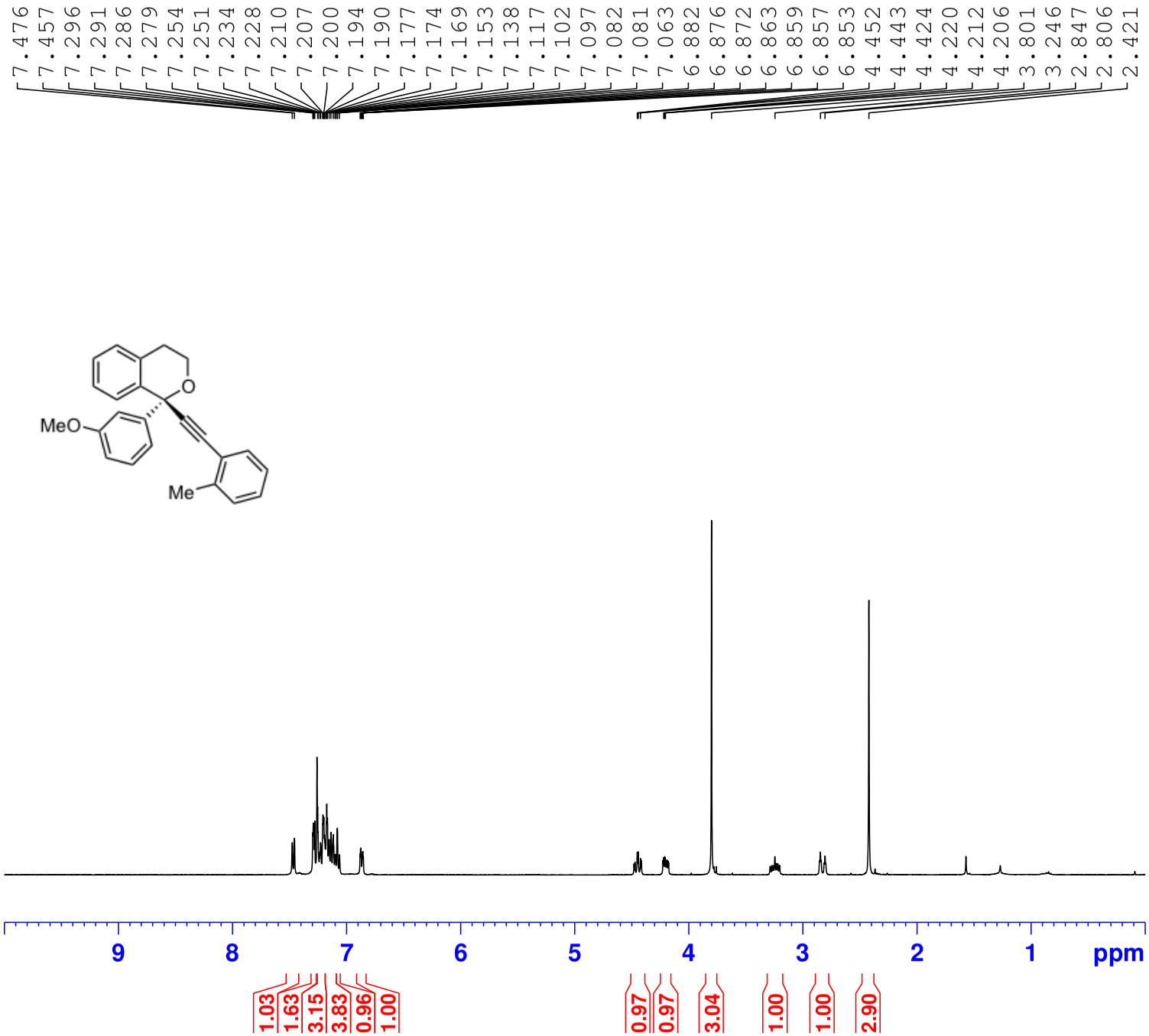

```
Current Data Parameters
NAME                  SDG-3-113
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20140205
Time                       0.56
INSTRUM                   spect
PROBHD    5 mm CPQNP 1H/
PULPROG                    zg30
TD                        65536
SOLVENT                   CDCl3
NS                           16
DS                            2
SWH                    8278.146 Hz
FIDRES                 0.126314 Hz
AQ                     3.9583745 sec
RG                         11.3
DW                       60.400 usec
DE                        6.00 usec
TE                       298.2 K
D1                  1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                         1H
P1                       15.00 usec
PL1                       4.90 dB
PL1W                 3.30822015 W
SFO1                400.1324710 MHz

F2 - Processing parameters
SI                        32768
SF                  400.1300100 MHz
WDW                          EM
SSB          0
LB                        0.30 Hz
GB           0
PC                        1.00
```







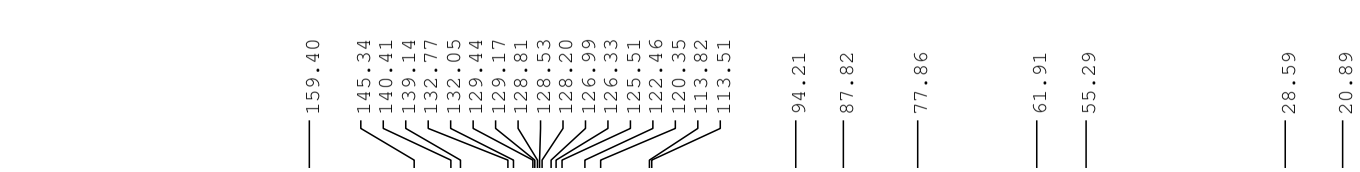

```
Current Data Parameters
NAME                  SDG-3-113
EXPNO                         2
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20140205
Time                       1.56
INSTRUM                   spect
PROBHD    5 mm CPQNP 1H/
PULPROG                 zgpg30
TD                         65536
SOLVENT                   CDCl3
NS                         1024
DS                            4
SWH                   23980.814 Hz
FIDRES                 0.365918 Hz
AQ                     1.3664256 sec
RG                          512
DW                       20.850 usec
DE                       18.00 usec
TE                       298.1 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                        13C
P1                        9.25 usec
PL1                       0.55 dB
PL1W                35.18820572 W
SFO1                100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2                waltz16
NUC2                        1H
PCPD2                    90.00 usec
PL2                       4.90 dB
PL12                     20.46 dB
PL13                     21.00 dB
PL2W                 3.30822015 W
PL12W                0.09195905 W
PL13W                0.08120718 W
SFO2                400.1316005 MHz

F2 - Processing parameters
SI                        32768
SF                  100.6127690 MHz
WDW                          EM
SSB             0
LB                        1.00 Hz
GB              0
PC                        1.40
```

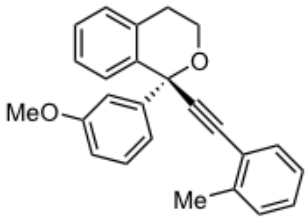


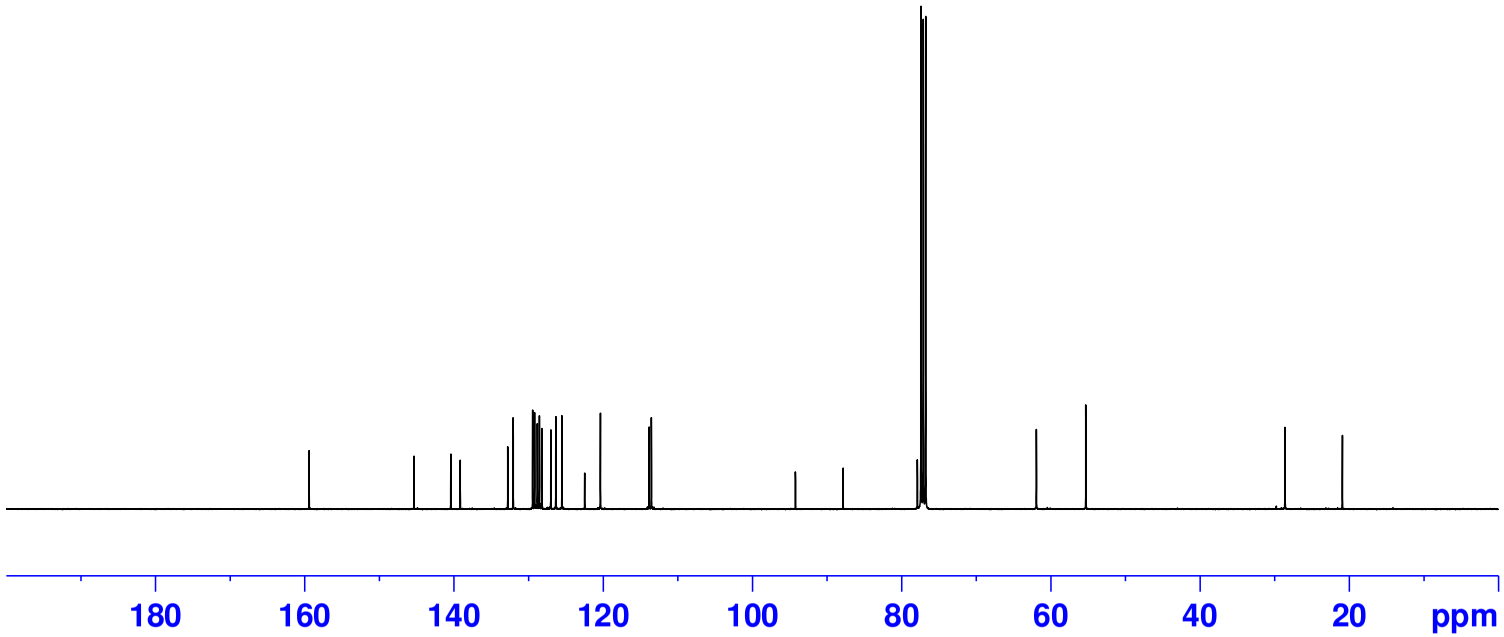
BRUKER

```
Current Data Parameters
NAME         SDG-3-116-2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140218
Time               15.17
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     4
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300101 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-85, 13C NMR

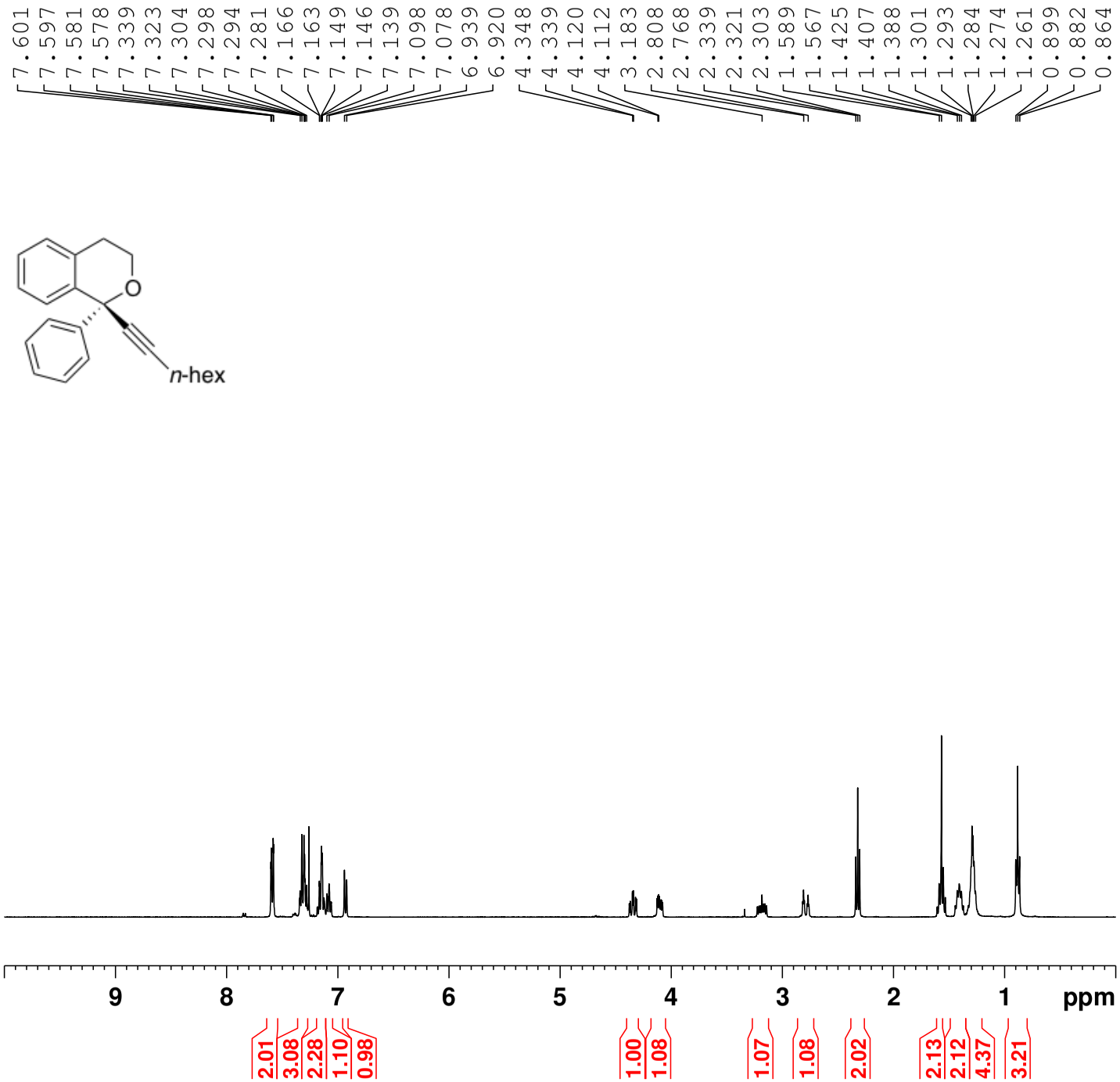






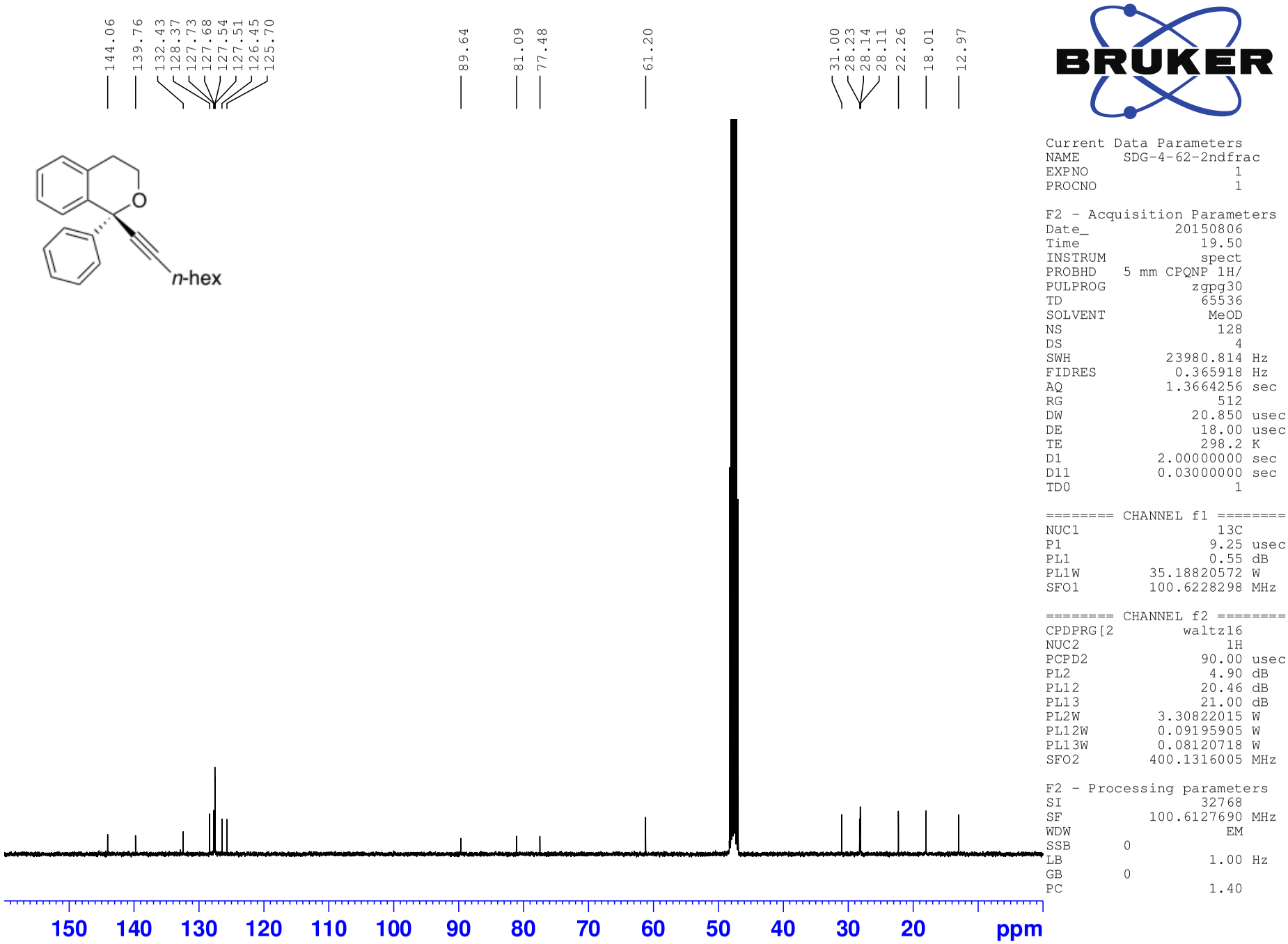

```
Current Data Parameters
NAME         SDG-3-116-2
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140218
Time               21.03
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                  512
DW                20.850 usec
DE                18.00 usec
TE                298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2               90.00 usec
PL2                  4.90 dB
PL12                20.46 dB
PL13                21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF         100.6127690 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

2-86, 1H NMR

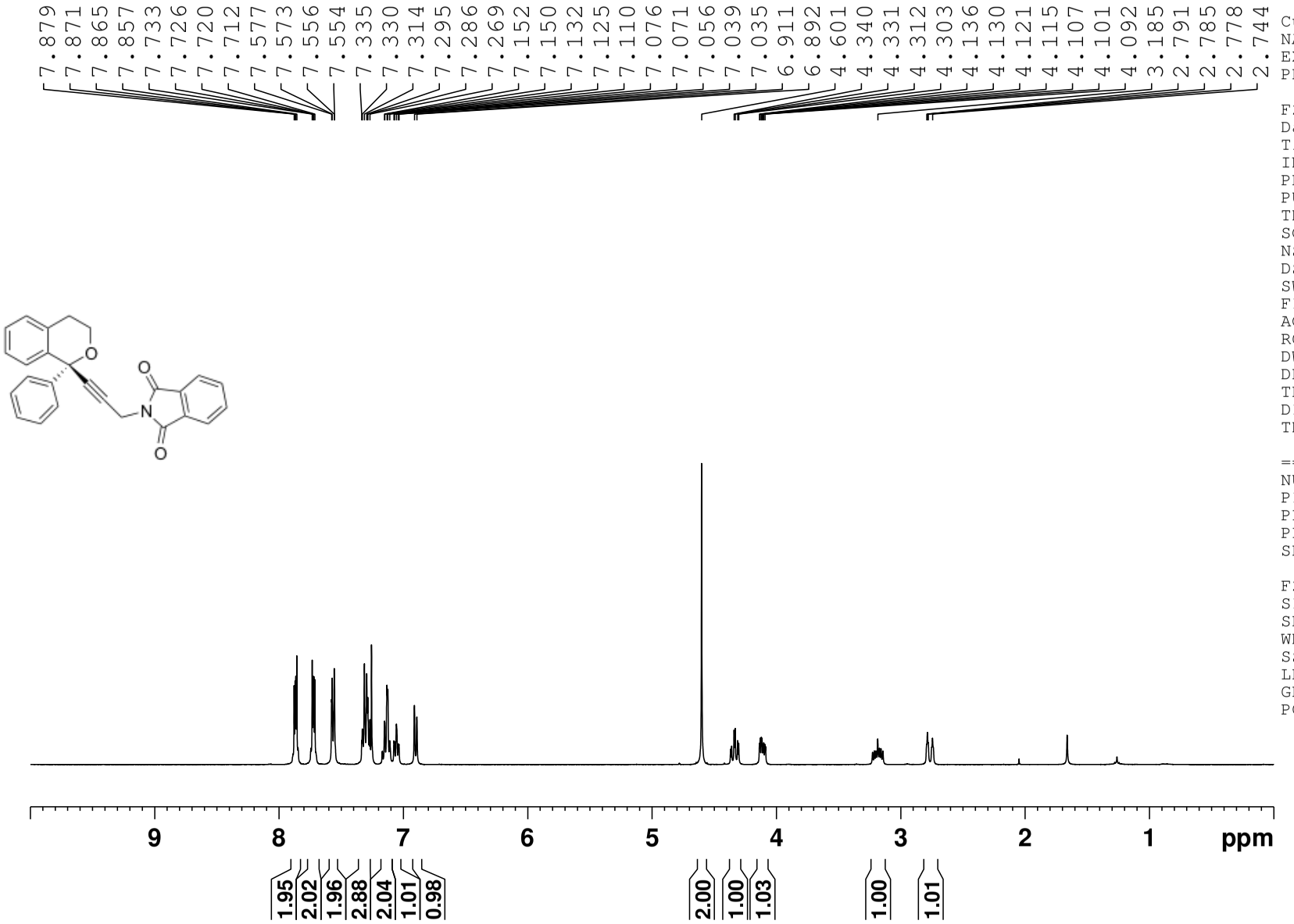



```
Current Data Paramet
NAME      SDG-4-34-1s
EXPNO
PROCNO

F2 - Acquisition Par
Date_            20150
Time               13
INSTRUM            sp
PROBHD   5 mm CPQNP
PULPROG             z
TD                 65
SOLVENT            CD
NS
DS
SWH             8278.
FIDRES          0.126
AQ              3.9583
RG                  1
DW                60.
DE                 6
TE                 29
D1           1.00000
TD0

======== CHANNEL f1
NUC1
P1                 15
PL1                 4
PL1W         3.30822
SFO1        400.1324

F2 - Processing para
SI                 32
SF          400.1300
WDW
SSB       0
LB                 0
GB        0
PC                 1
```

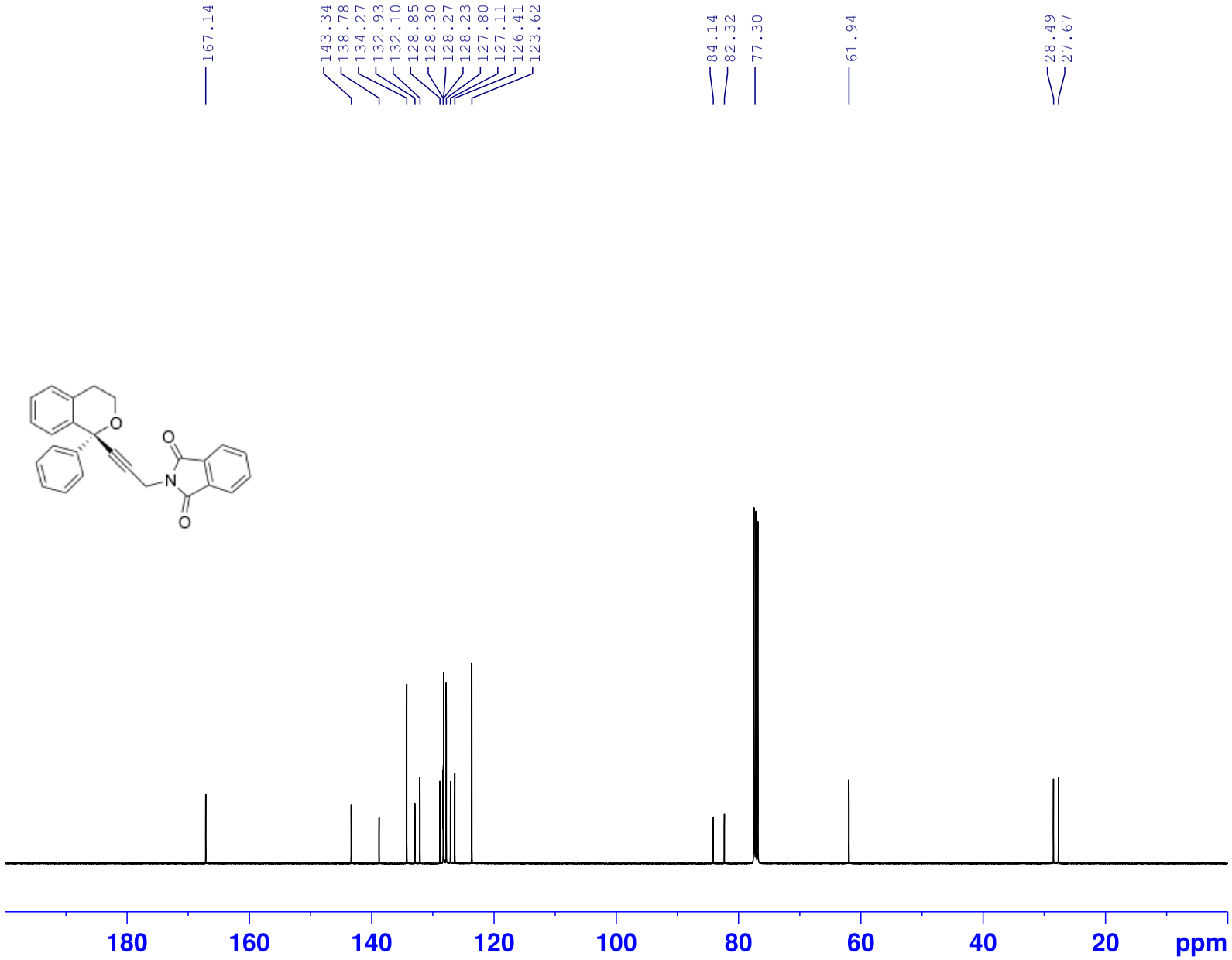
2-86, 13C NMR




```
Current Data Parameters
NAME      SDG-4-62-2ndfrac
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20150806
Time               19.50
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT             MeOD
NS                   128
DS                     4
SWH            23980.814 Hz
FIDRES          0.365918 Hz
AQ              1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   9.25 usec
PL1                  0.55 dB
PL1W        35.18820572 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2               90.00 usec
PL2                  4.90 dB
PL12                20.46 dB
PL13                21.00 dB
PL2W          3.30822015 W
PL12W         0.09195905 W
PL13W         0.08120718 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF          100.6127690 MHz
WDW                    EM
SSB       0
LB                   1.00 Hz
GB        0
PC                   1.40
```

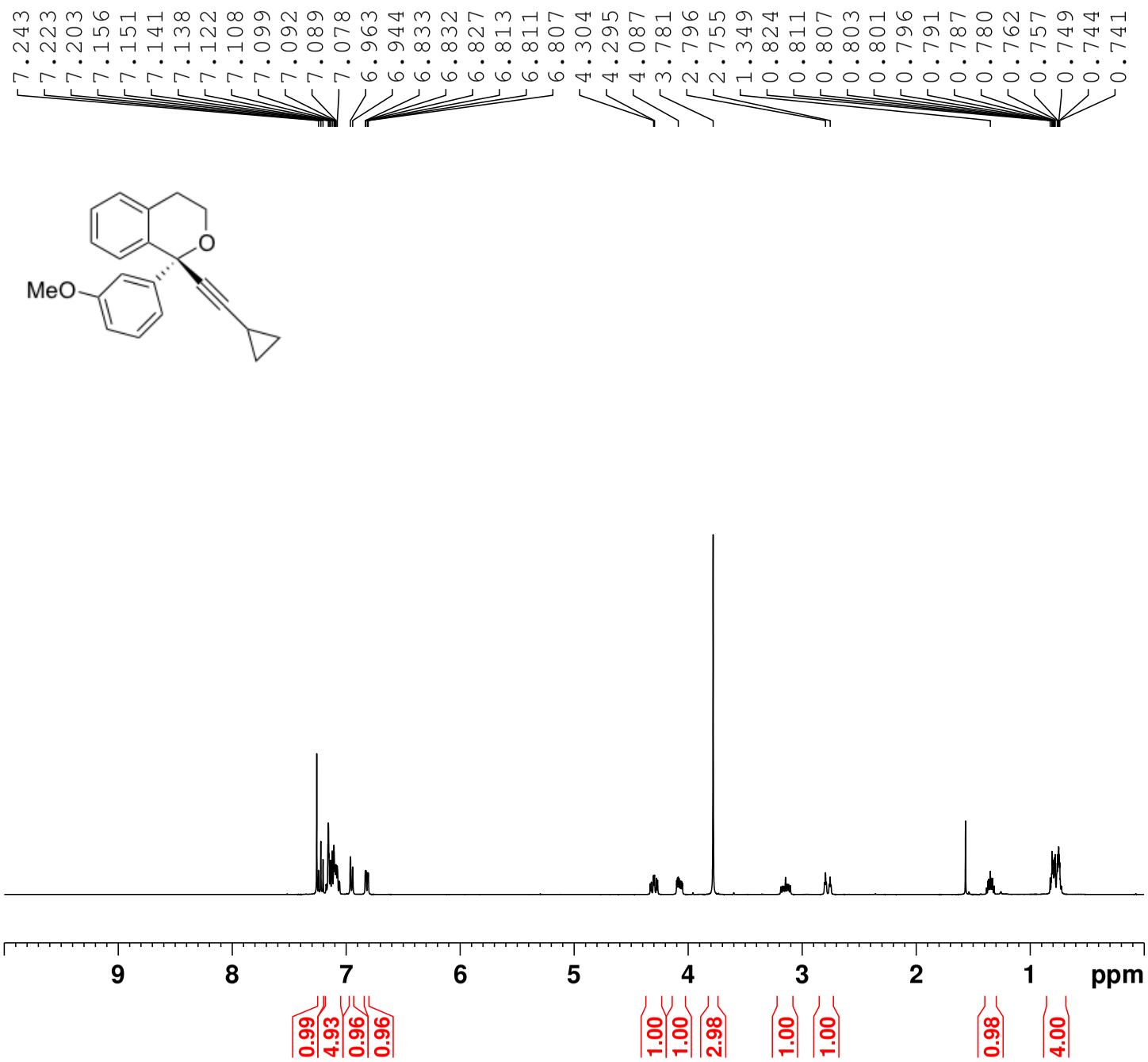



```
Current Data Parameters
NAME      SDG-3-82-1(1st)
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_           20131120
Time               13.36
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     8
DW                60.400 usec
DE                 6.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300113 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```



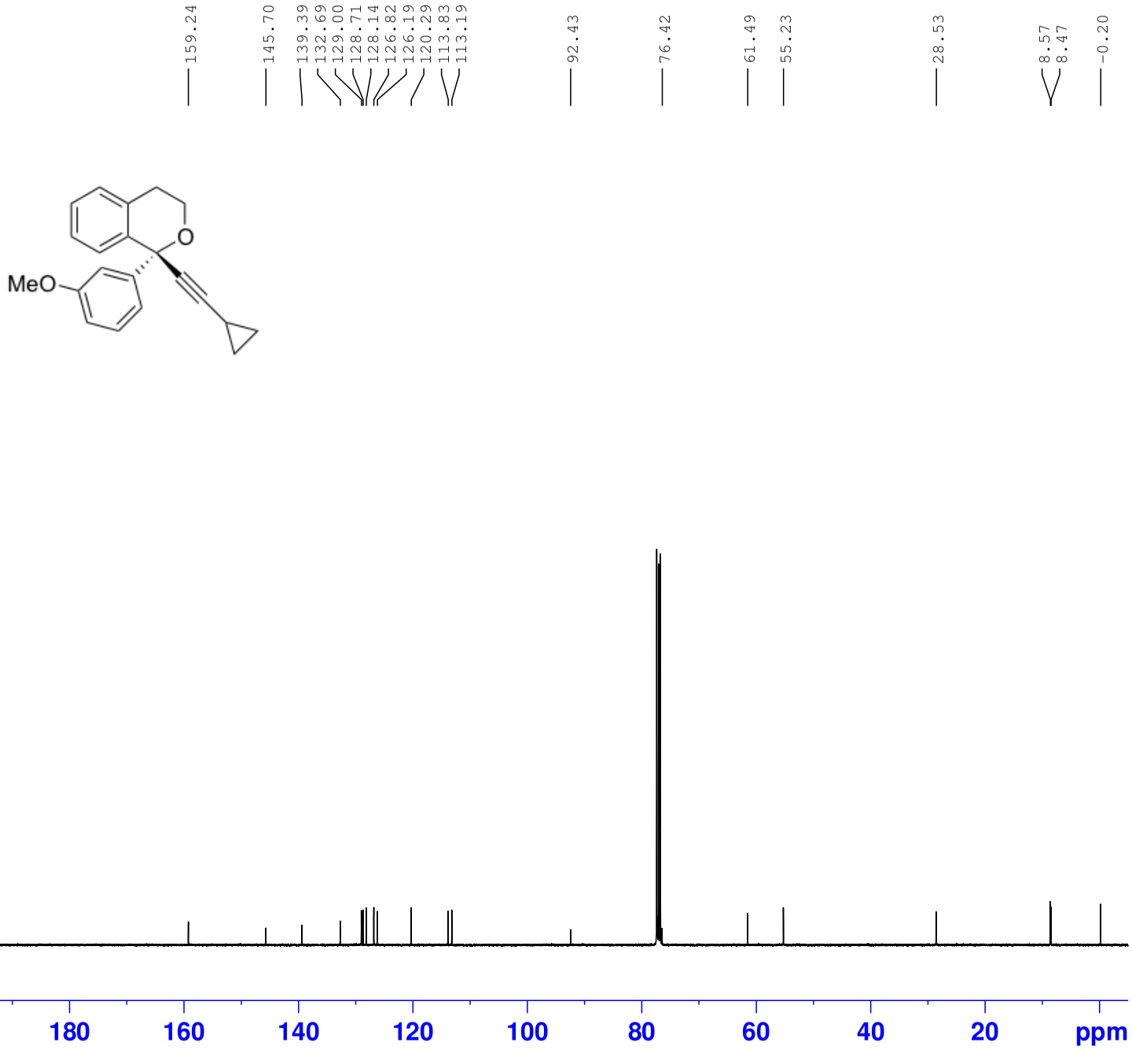

```
Current Data Parameters
NAME      SDG-3-82-1(1st)
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20131120
Time               22.10
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                  512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2              90.00 usec
PL2                 4.90 dB
PL12               20.46 dB
PL13               21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127624 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

2-88, 1H NMR



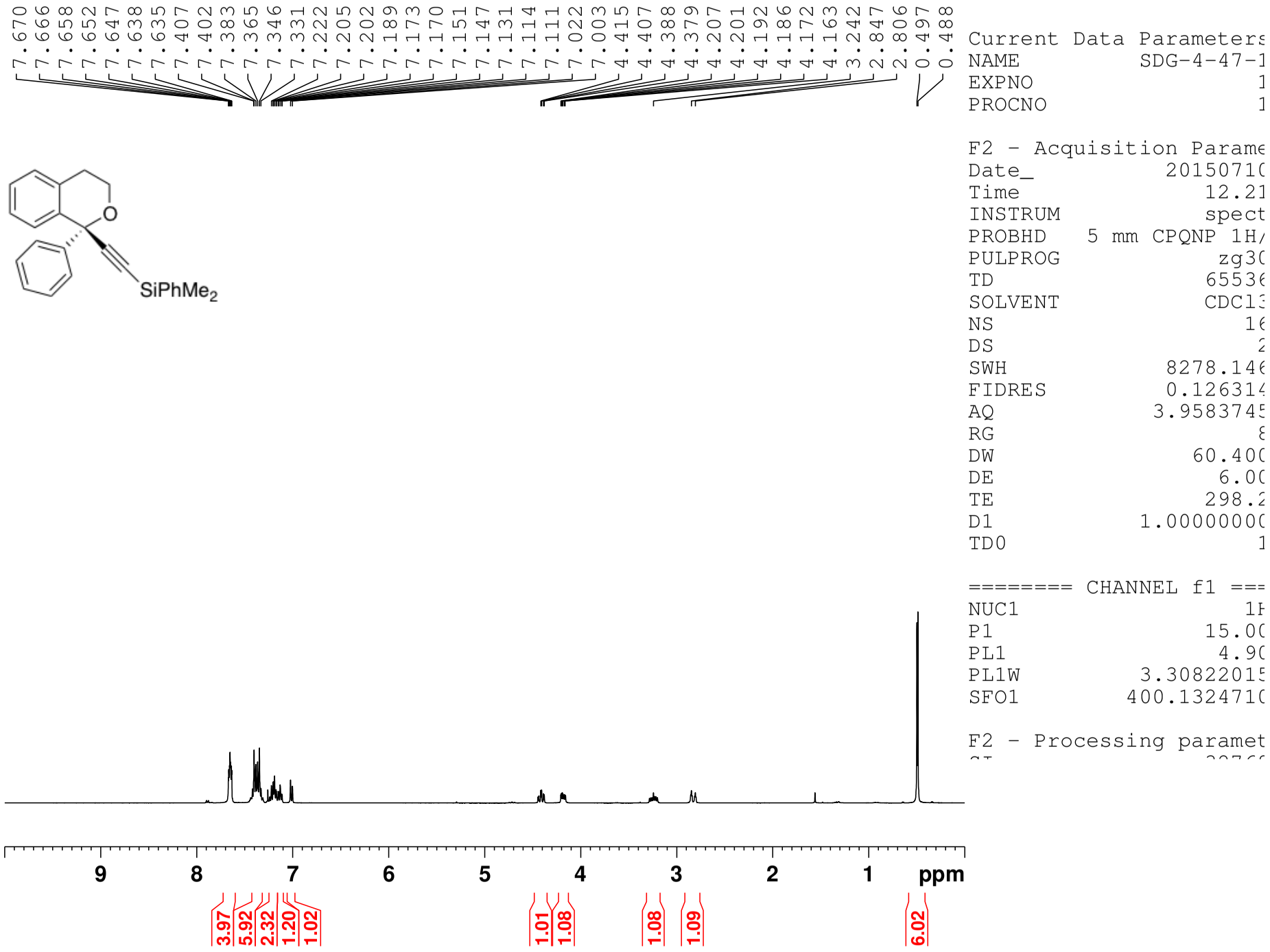

```
Current Data Parameter
NAME                 SDG-4-6
EXPNO
PROCNO

F2 - Acquisition Param
Date_              2015072
Time                  16.2
INSTRUM               spec
PROBHD   5 mm CPQNP 1H
PULPROG                zg3
TD                    6553
SOLVENT               CDCl
NS                       1
DS
SWH                8278.14
FIDRES             0.12631
AQ                3.958374
RG                      11.
DW                    60.40
DE                      6.0
TE                     298.
D1               1.0000000
TD0

======== CHANNEL f1 ==
NUC1                     1
P1                    15.0
PL1                    4.9
PL1W           3.3082201
SFO1          400.132471

F2 - Processing parame
SI                    3276
SF             400.130011
WDW                      E
SSB       0
LB                    0.3
GB        0
PC                    1.0
```

2-88, 13C NMR



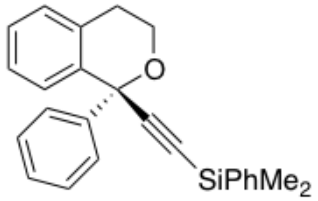

```
Current Data Parameters
NAME                 SDG-4-63
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_               20150728
Time                   16.25
INSTRUM                spect
PROBHD    5 mm CPQNP 1H/
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                         64
DS                          4
SWH                23980.814 Hz
FIDRES              0.365918 Hz
AQ                  1.3664256 sec
RG                        512
DW                     20.850 usec
DE                     18.00 usec
TE                     298.2 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     9.25 usec
PL1                    0.55 dB
PL1W             35.18820572 W
SFO1            100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2              waltz16
NUC2                      1H
PCPD2                 90.00 usec
PL2                    4.90 dB
PL12                  20.46 dB
PL13                  21.00 dB
PL2W              3.30822015 W
PL12W             0.09195905 W
PL13W             0.08120718 W
SFO2            400.1316005 MHz

F2 - Processing parameters
SI                      32768
SF              100.6127690 MHz
WDW                        EM
SSB       0
LB                     1.00 Hz
GB        0
PC                     1.40
```

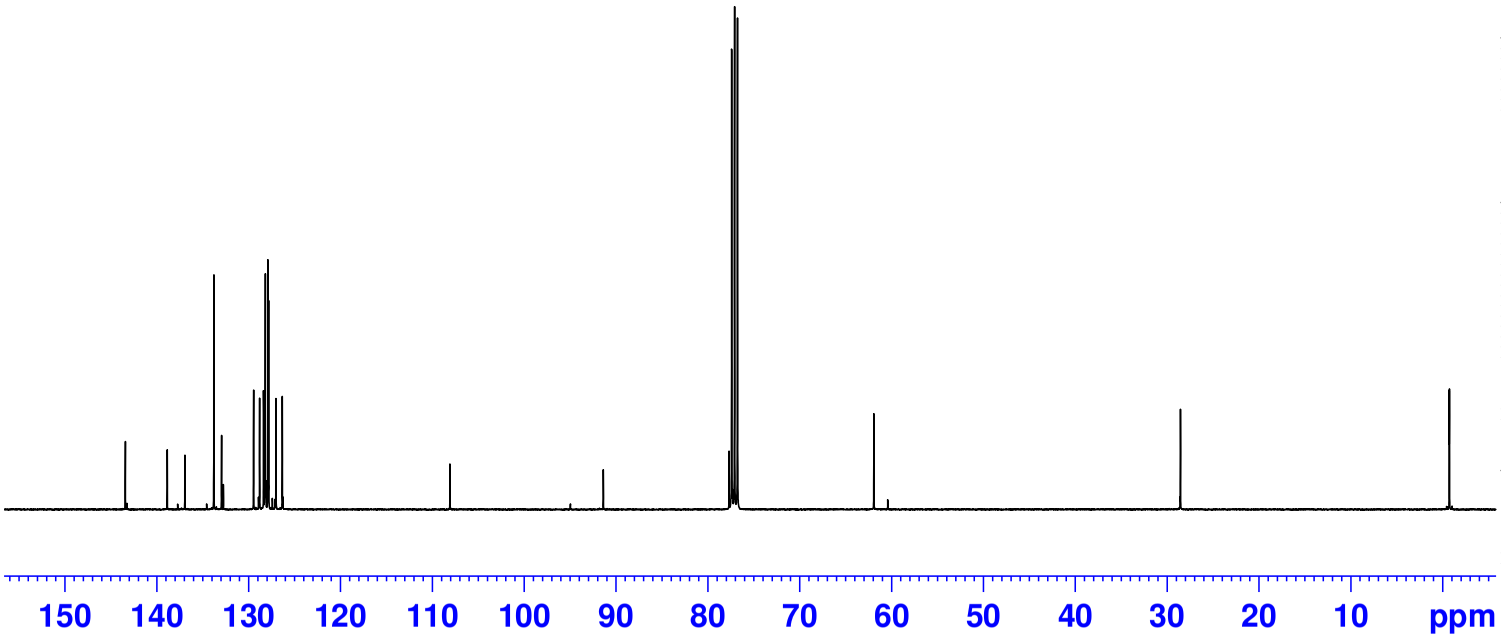
2-89, 1H NMR


7.670
7.666
7.658
7.652
7.647
7.638
7.635
7.407
7.402
7.383
7.365
7.346
7.331
7.222
7.205
7.202
7.189
7.173
7.170
7.151
7.147
7.131
7.114
7.111
7.022
7.003
4.415
4.407
4.388
4.379
4.207
4.201
4.192
4.186
4.172
4.163
3.242
2.847
2.806
0.497
0.488
O
SiPhMe2
Current Data Parameters
NAME SDG-4-47-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parame
Date_ 2015071
Time 12.21
INSTRUM spect
PROBHD 5 mm CPQNP 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146
FIDRES 0.126314
AQ 3.9583745
RG 8
DW 60.400
DE 6.00
TE 298.2
D1 1.0000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 15.00
PL1 4.90
PL1W 3.30822015
SFO1 400.1324710
F2 - Processing paramet
9
8
7
6
5
4
3
2
1
ppm
3.97
5.92
2.32
1.20
1.02
1.01
1.08
1.08
1.09
6.02

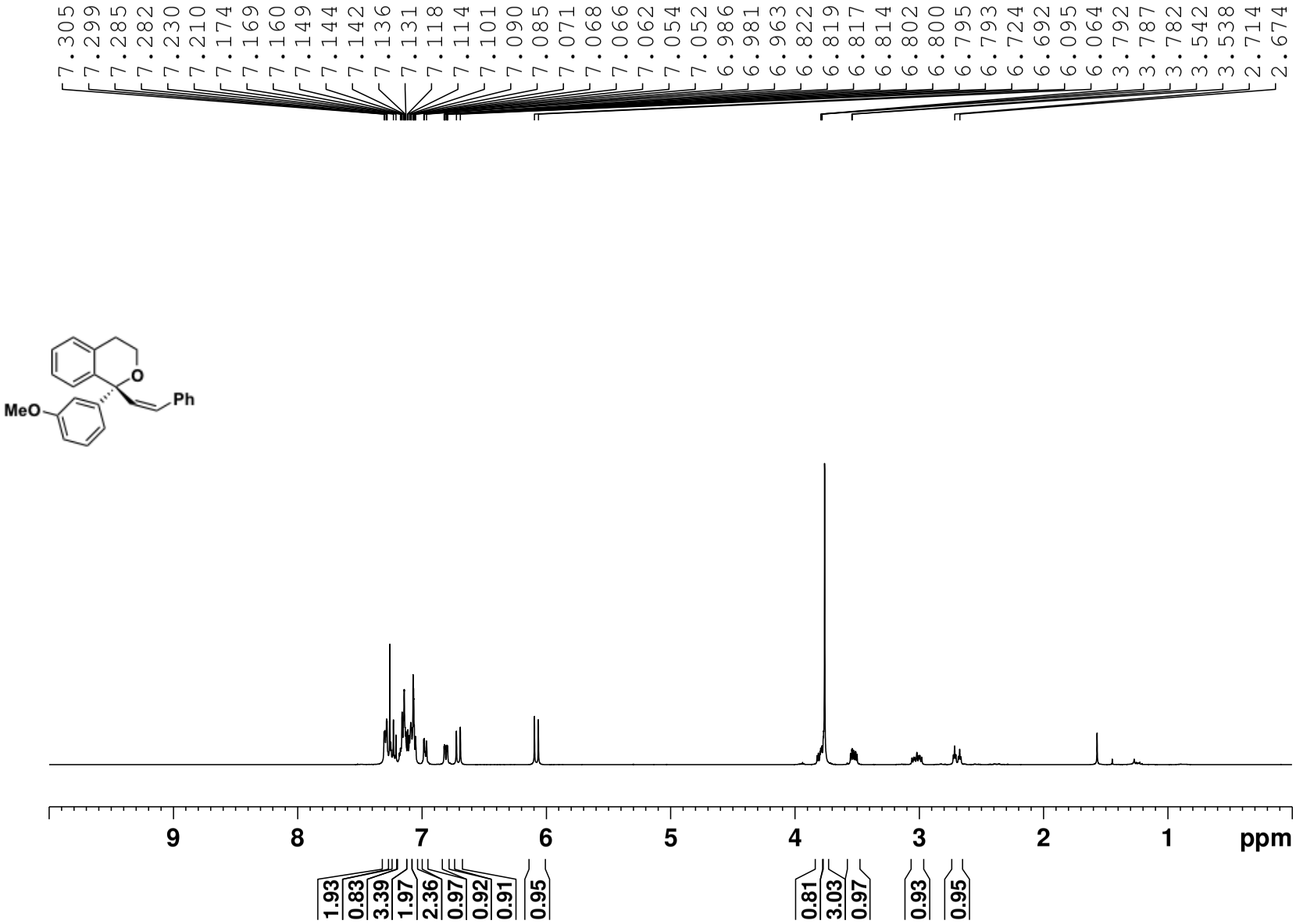
2-89, 13C NMR

143.42
138.86
136.94
133.79
132.95
129.46
128.80
128.37
128.24
128.17
127.89
127.82
127.02
126.33
108.07
91.37
77.68
61.92
28.53
-0.73
-0.76



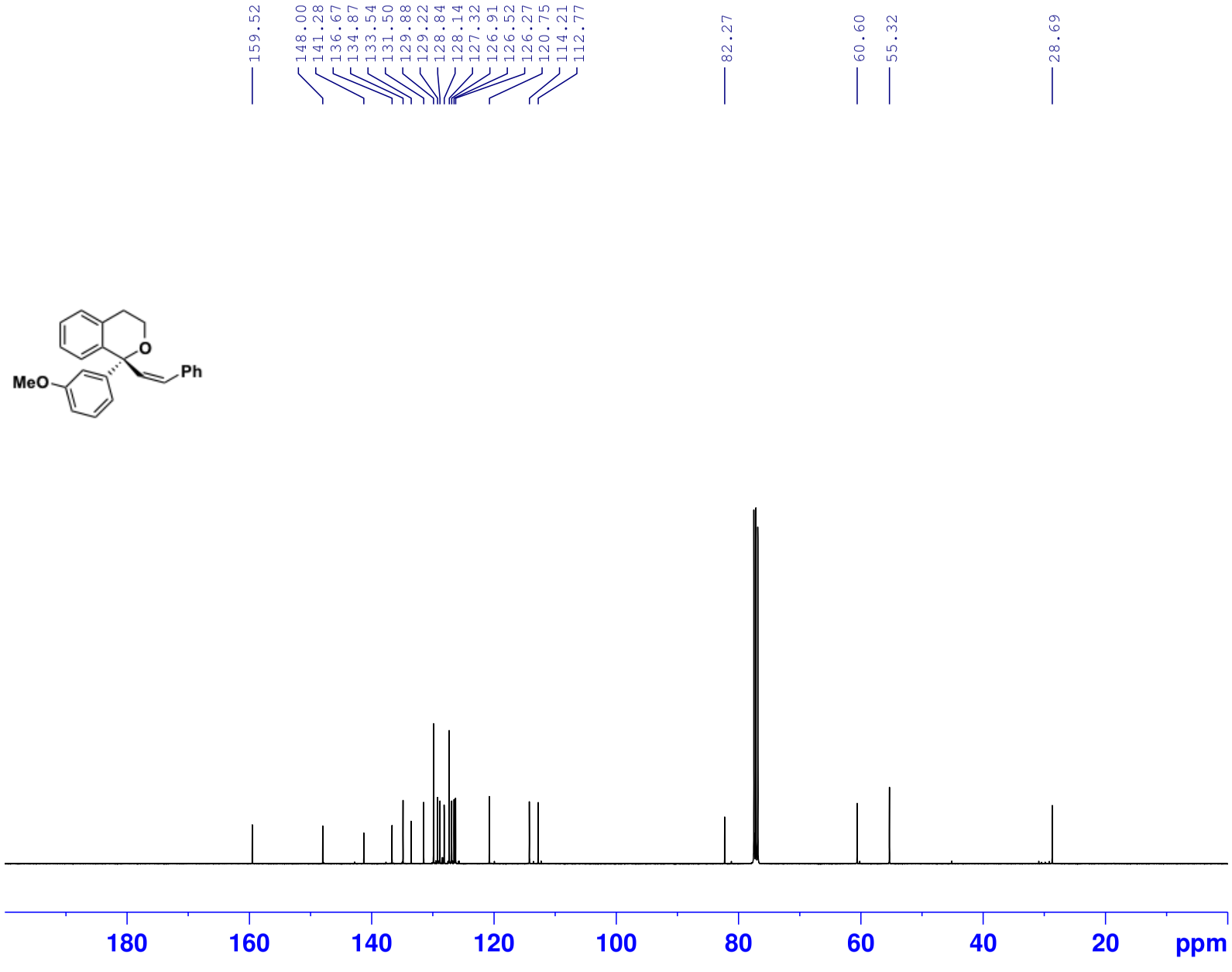



```
Current Data Parameters
NAME          SDG-4-47-2
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150710
Time              21.03
INSTRUM           spect
PROBHD   5 mm CPQNP 1H/
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE               298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                9.25 usec
PL1               0.55 dB
PL1W       35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            90.00 usec
PL2               4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W        3.30822015 W
PL12W       0.09195905 W
PL13W       0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF         100.6127690 MHz
WDW                EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

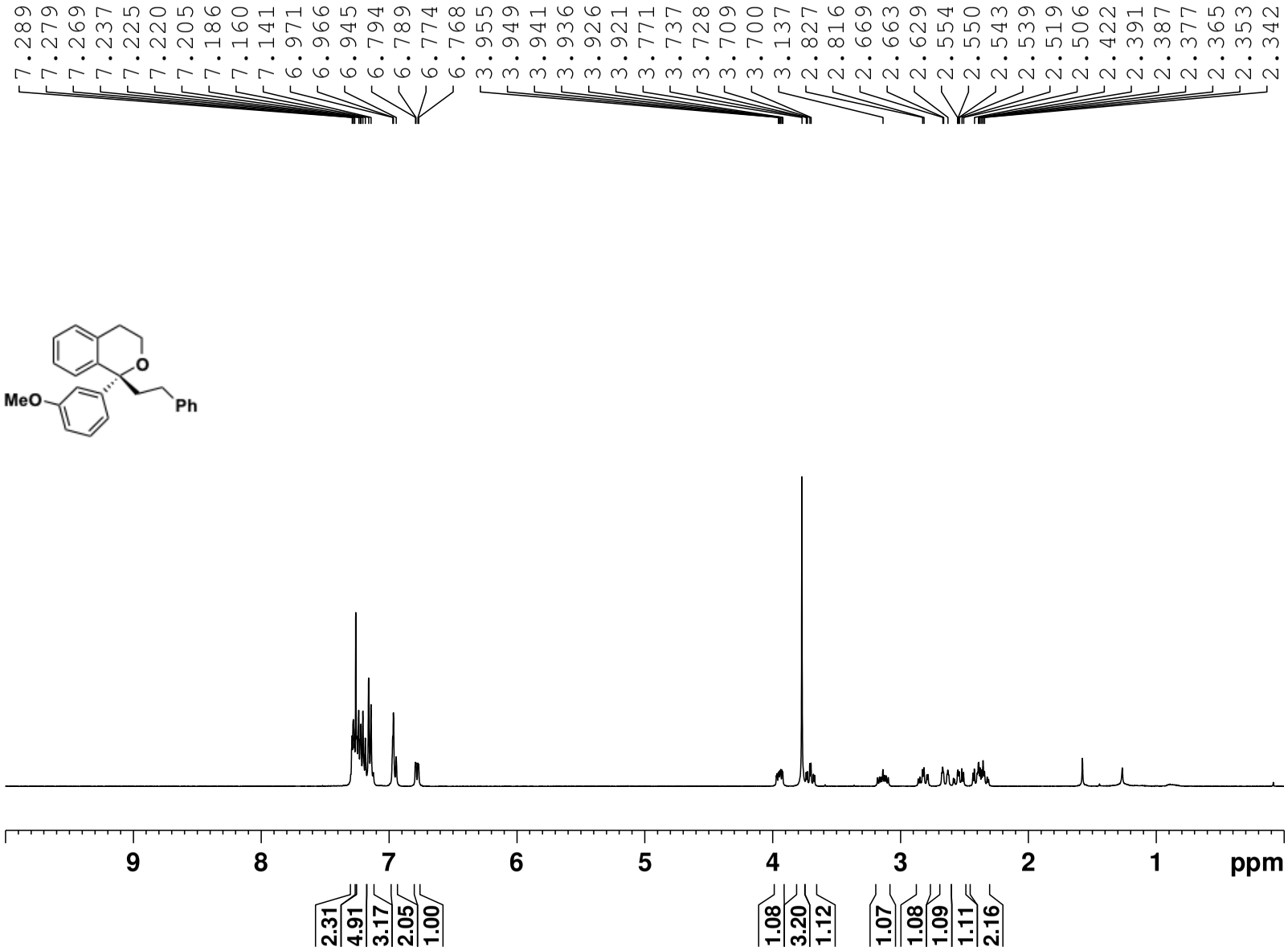



```
Current Data Parameters
NAME            SDG-3-81
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131115
Time               11.52
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                     8
DW                60.400 usec
DE                 6.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.00 usec
PL1                4.90 dB
PL1W         3.30822015 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300101 MHz
WDW                   EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```

2-93, 13C NMR

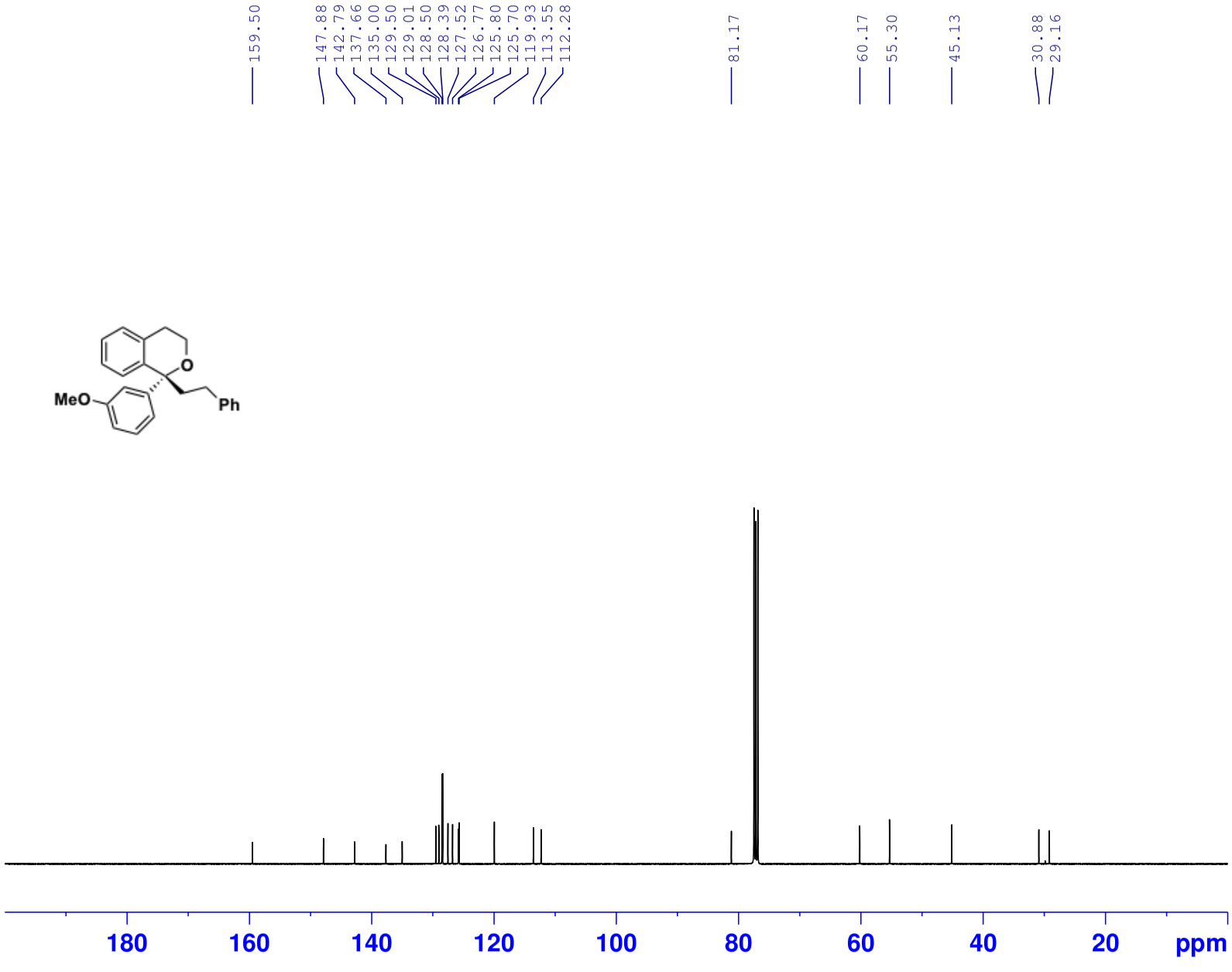



```
Current Data Parameters
NAME                 SDG-3-81
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_               20131115
Time                   21.03
INSTRUM                spect
PROBHD    5 mm CPQNP 1H/
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                       1024
DS                          4
SWH                23980.814 Hz
FIDRES              0.365918 Hz
AQ                  1.3664256 sec
RG                        512
DW                     20.850 usec
DE                     18.00 usec
TE                     298.2 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     9.25 usec
PL1                    0.55 dB
PL1W              35.18820572 W
SFO1             100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2              waltz16
NUC2                      1H
PCPD2                 90.00 usec
PL2                    4.90 dB
PL12                  20.46 dB
PL13                  21.00 dB
PL2W               3.30822015 W
PL12W              0.09195905 W
PL13W              0.08120718 W
SFO2             400.1316005 MHz

F2 - Processing parameters
SI                        32768
SF               100.6127593 MHz
WDW                          EM
SSB          0
LB                     1.00 Hz
GB           0
PC                     1.40
```



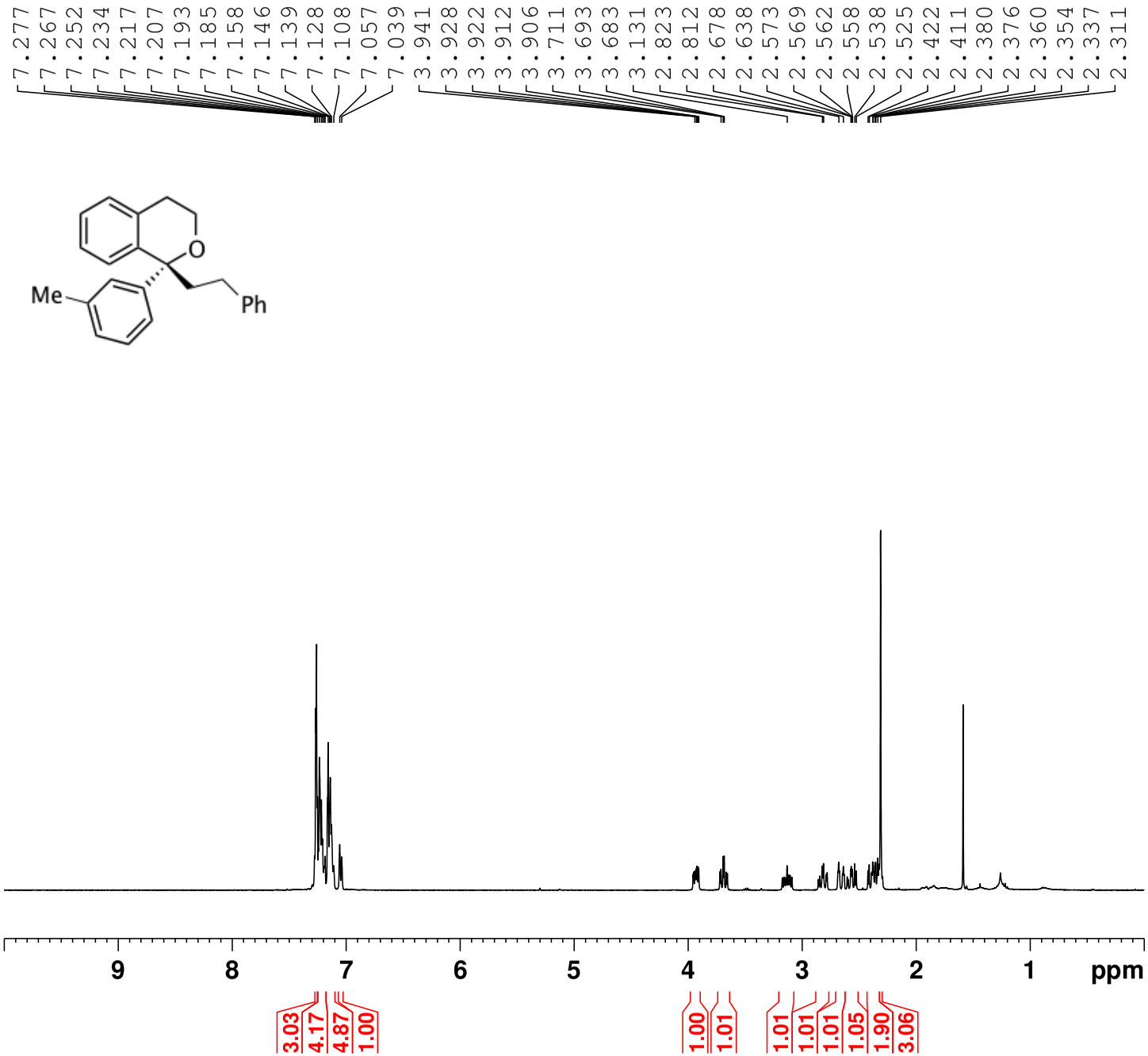

```
Current Data Parameters
NAME                  SDG-3-66
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20131116
Time                     13.19
INSTRUM                  spect
PROBHD    5 mm CPQNP 1H/
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8278.146 Hz
FIDRES               0.126314 Hz
AQ                   3.9583745 sec
RG                          4
DW                     60.400 usec
DE                      6.00 usec
TE                      298.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      15.00 usec
PL1                      4.90 dB
PL1W               3.30822015 W
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                      32768
SF               400.1300097 MHz
WDW                        EM
SSB          0
LB                      0.30 Hz
GB           0
PC                      1.00
```

2-94, 13C NMR



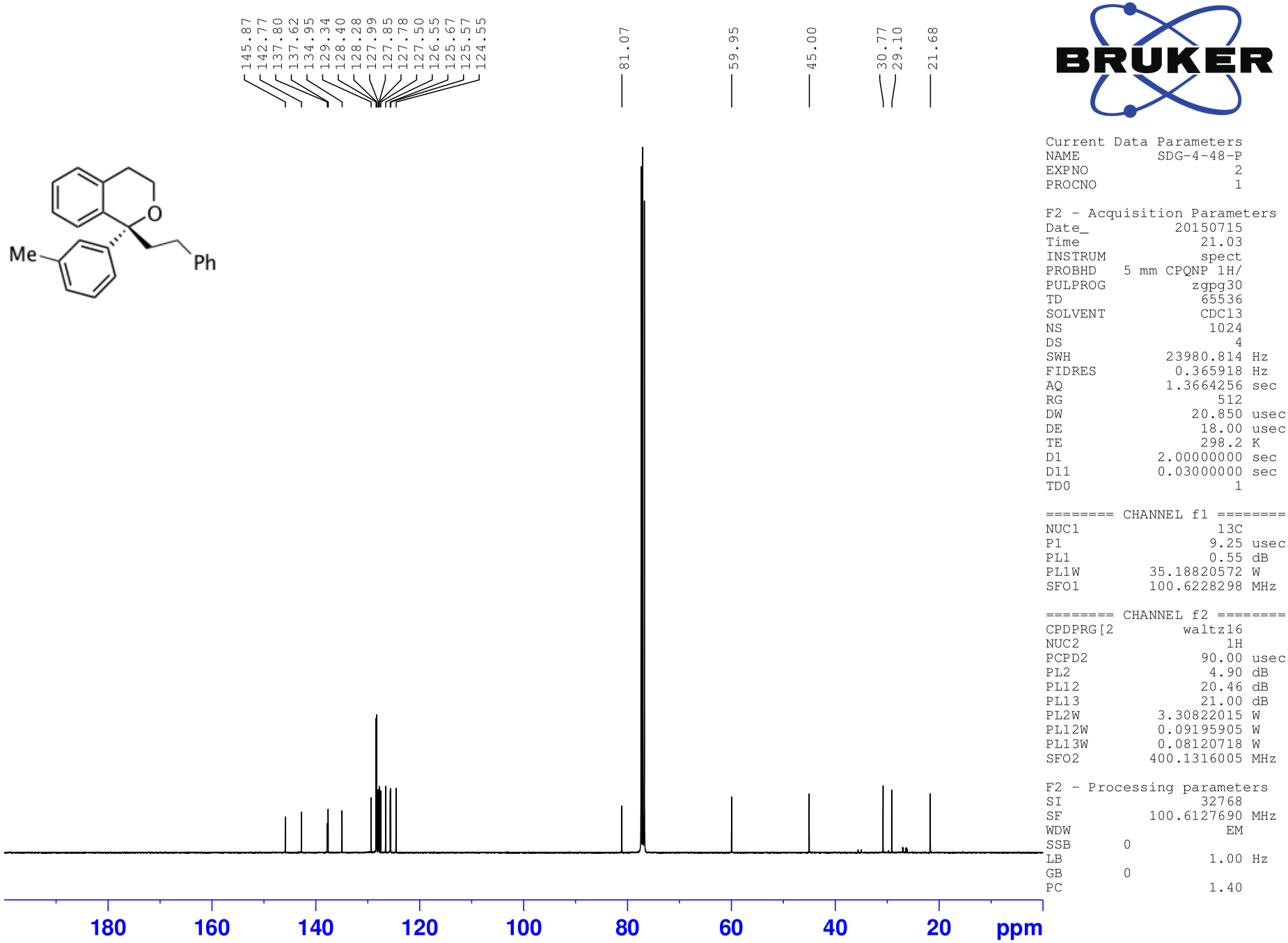

```
Current Data Parameters
NAME            SDG-3-66
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131116
Time               23.39
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2                4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127587 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

2-95, 1H NMR



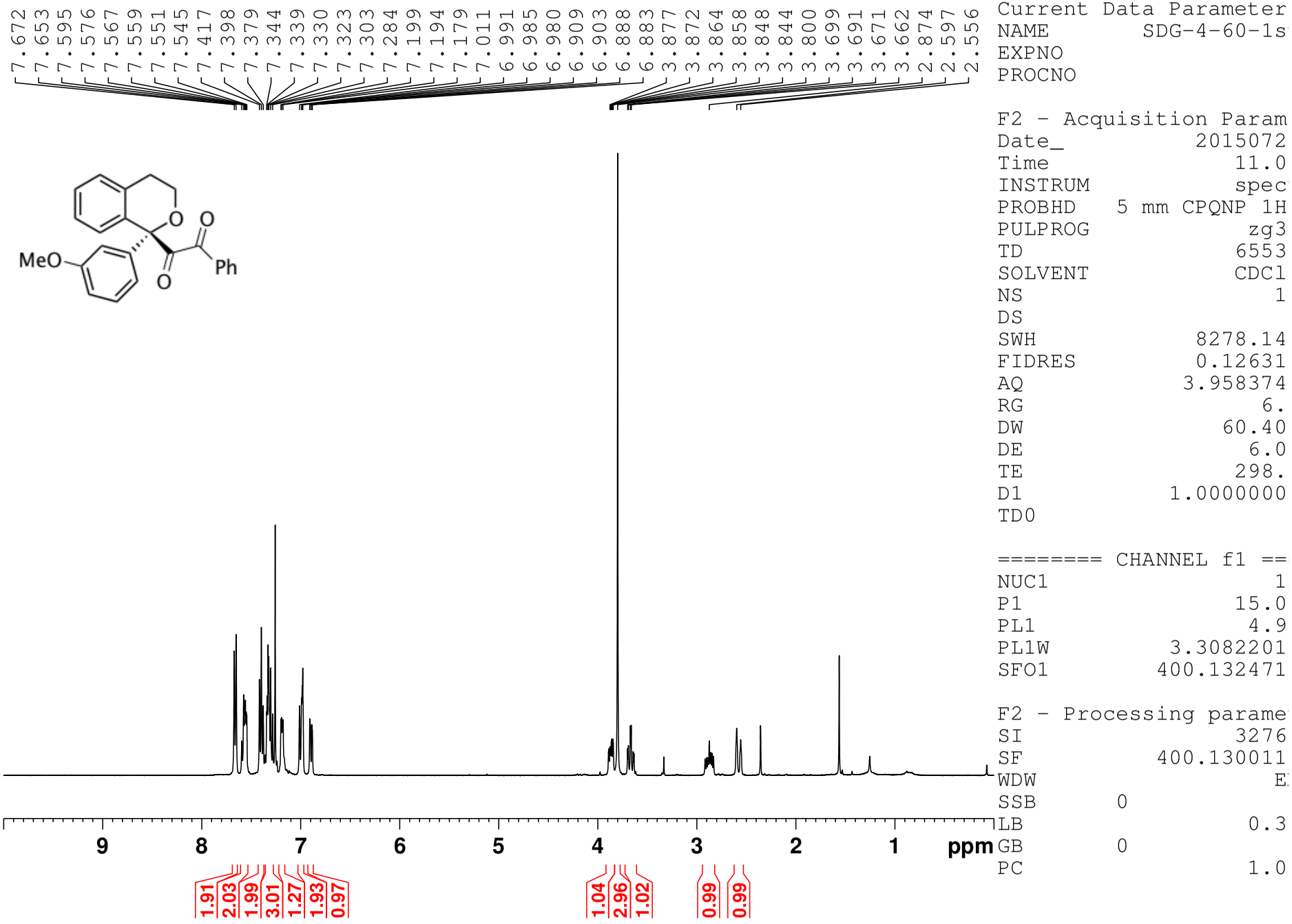

```
Current Data Parameter
NAME          SDG-4-48-
EXPNO
PROCNO

F2 - Acquisition Param
Date_           2015071
Time              14.3
INSTRUM           spec
PROBHD   5 mm CPQNP 1H
PULPROG            zg3
TD                6553
SOLVENT           CDCl
NS                   1
DS
SWH            8278.14
FIDRES         0.12631
AQ            3.958374
RG                  7.
DW                60.40
DE                 6.0
TE                298.
D1           1.0000000
TD0

======== CHANNEL f1 ==
NUC1                 1
P1                15.0
PL1                4.9
PL1W         3.3082201
SFO1        400.132471

F2 - Processing parame
SI                3276
SF          400.130010
WDW                  E
SSB       0
LB                0.3
GB        0
PC                1.0
```

2-95, 13C NMR



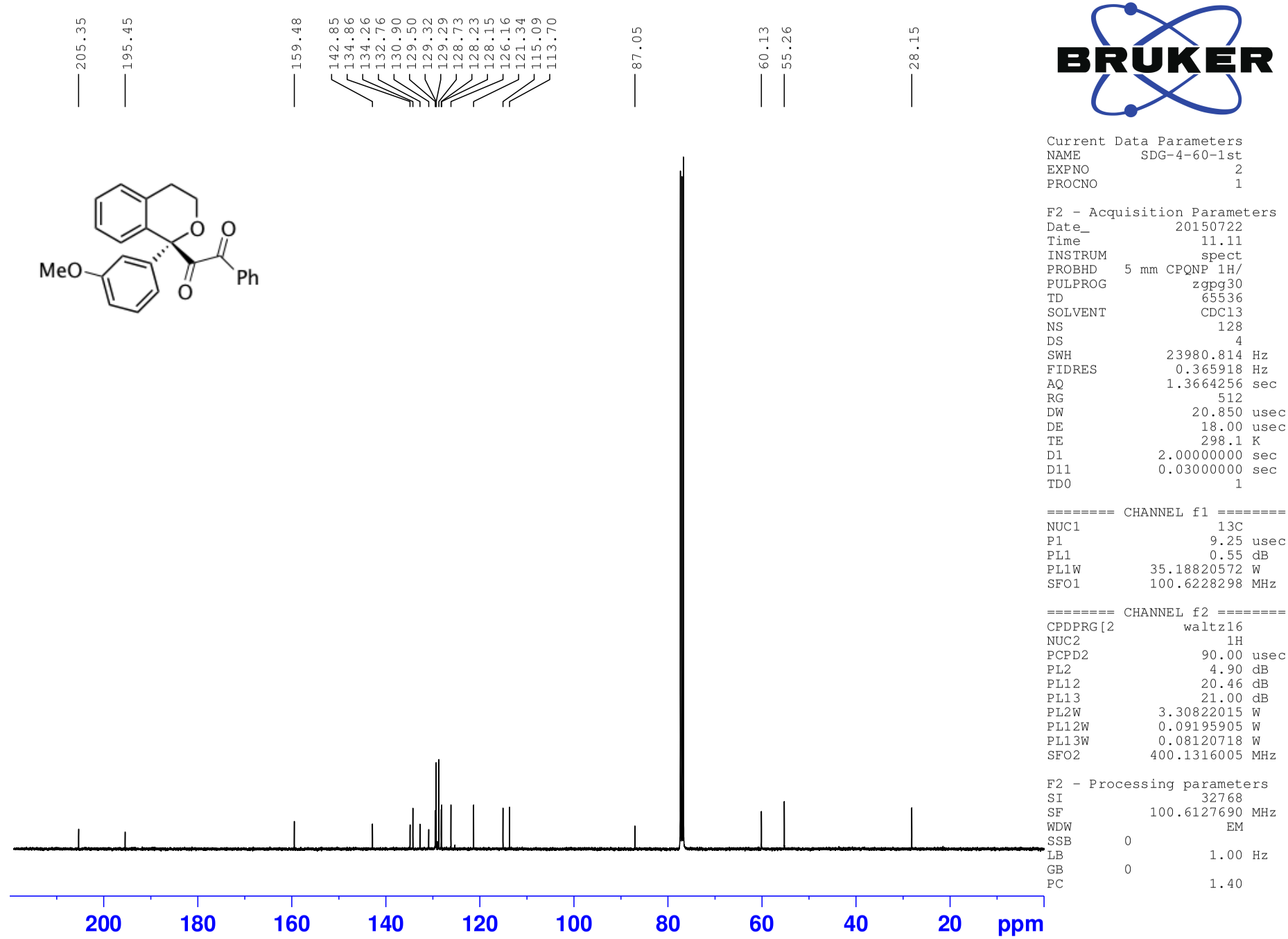

```
Current Data Parameters
NAME          SDG-4-48-P
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150715
Time              21.03
INSTRUM           spect
PROBHD   5 mm CPQNP 1H/
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE               298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                9.25 usec
PL1               0.55 dB
PL1W       35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            90.00 usec
PL2               4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W        3.30822015 W
PL12W       0.09195905 W
PL13W       0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF         100.6127690 MHz
WDW                EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

2-96, 1H NMR



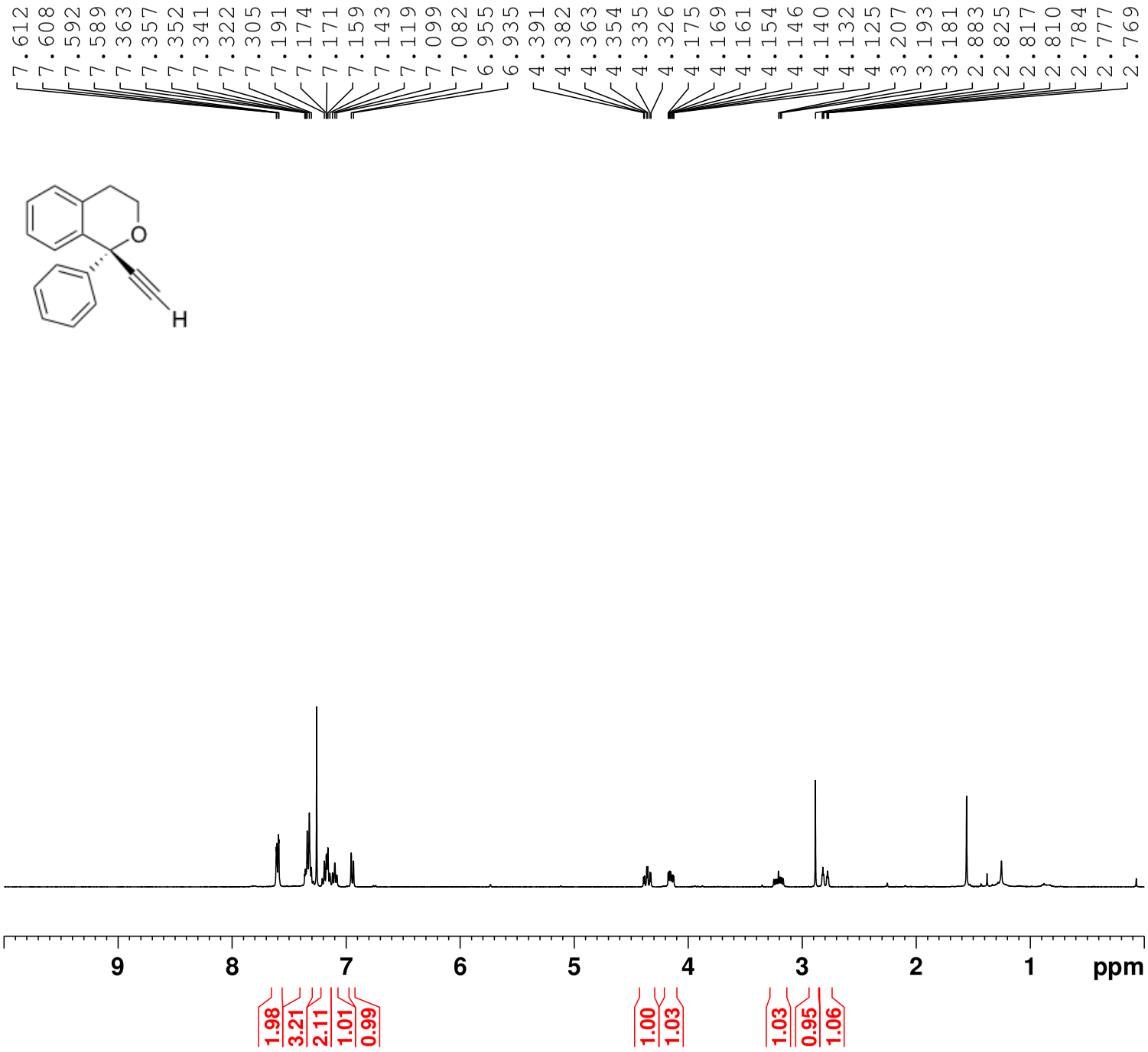

```
Current Data Parameter
NAME        SDG-4-60-1s
EXPNO
PROCNO

F2 - Acquisition Param
Date_            2015072
Time                11.0
INSTRUM             spec
PROBHD   5 mm CPQNP 1H
PULPROG              zg3
TD                  6553
SOLVENT             CDCl
NS                     1
DS
SWH              8278.14
FIDRES           0.12631
AQ              3.958374
RG                    6.
DW                60.40
DE                  6.0
TE                 298.
D1             1.0000000
TD0

======== CHANNEL f1 ==
NUC1                   1
P1                  15.0
PL1                  4.9
PL1W          3.3082201
SFO1         400.132471

F2 - Processing parame
SI                  3276
SF           400.130011
WDW                    E
SSB       0
LB                  0.3
GB        0
PC                  1.0
```

2-96, 13C NMR



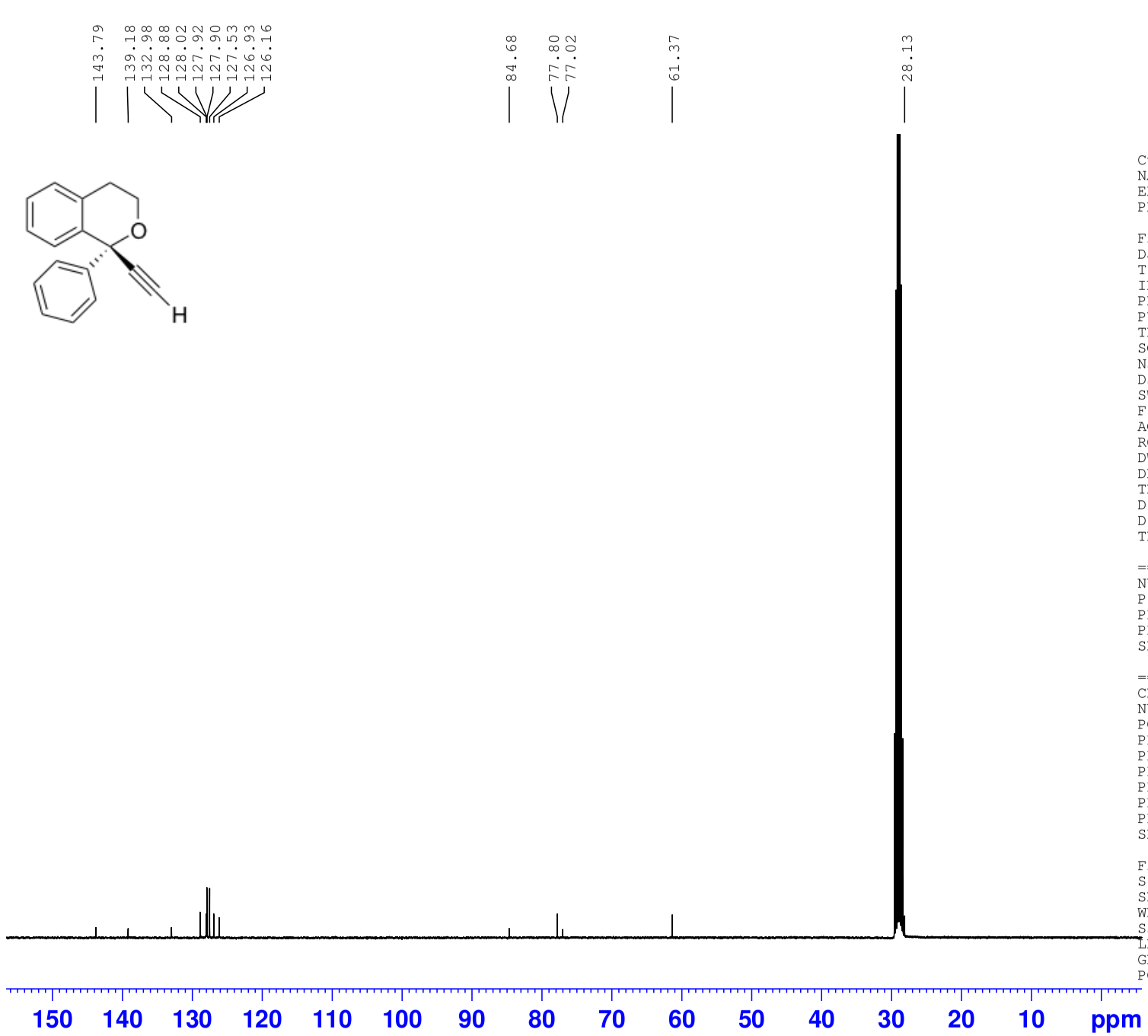

```
Current Data Parameters
NAME        SDG-4-60-1st
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150722
Time               11.11
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  128
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664256 sec
RG                  512
DW               20.850 usec
DE               18.00 usec
TE               298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                9.25 usec
PL1               0.55 dB
PL1W       35.18820572 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            90.00 usec
PL2               4.90 dB
PL12              20.46 dB
PL13              21.00 dB
PL2W        3.30822015 W
PL12W       0.09195905 W
PL13W       0.08120718 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF         100.6127690 MHz
WDW                EM
SSB       0
LB               1.00 Hz
GB        0
PC                1.40
```

2-97, 1H NMR



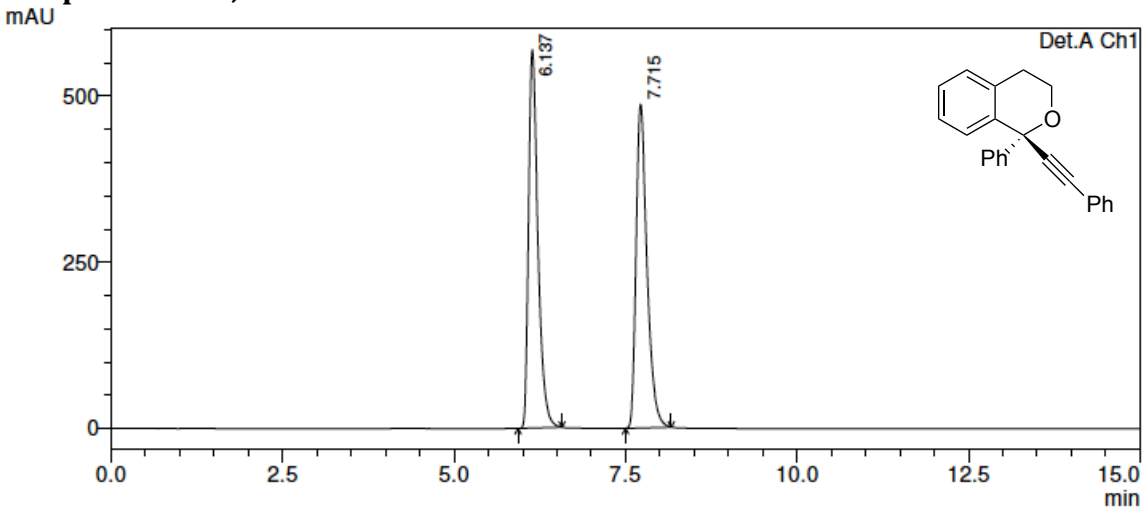

```
Current Data Parame
NAME        SDG-4-61
EXPNO
PROCNO

F2 - Acquisition Pa
Date_            2015
Time                1
INSTRUM             s
PROBHD    5 mm CPQNP
PULPROG
TD                  6
SOLVENT             C
NS
DS
SWH              8278
FIDRES           0.12
AQ              3.958
RG
DW                 60
DE
TE                  2
D1             1.0000
TD0

======== CHANNEL f1
NUC1
P1                  1
PL1
PL1W           3.3082
SFO1          400.132

F2 - Processing par
SI                  3
SF            400.130
WDW
SSB       0
LB
GB        0
PC
```

2-97, 13C NMR




```
Current Data Parameters
NAME        SDG-4-61-1st
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150728
Time               16.02
INSTRUM            spect
PROBHD   5 mm CPQNP 1H/
PULPROG          zgpg30
TD                 65536
SOLVENT          Acetone
NS                   128
DS                     4
SWH            23980.814 Hz
FIDRES          0.365918 Hz
AQ             1.3664256 sec
RG                   512
DW                20.850 usec
DE                18.00 usec
TE                298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.25 usec
PL1                 0.55 dB
PL1W        35.18820572 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2               90.00 usec
PL2                  4.90 dB
PL12                20.46 dB
PL13                21.00 dB
PL2W         3.30822015 W
PL12W        0.09195905 W
PL13W        0.08120718 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF          100.6127690 MHz
WDW                     EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

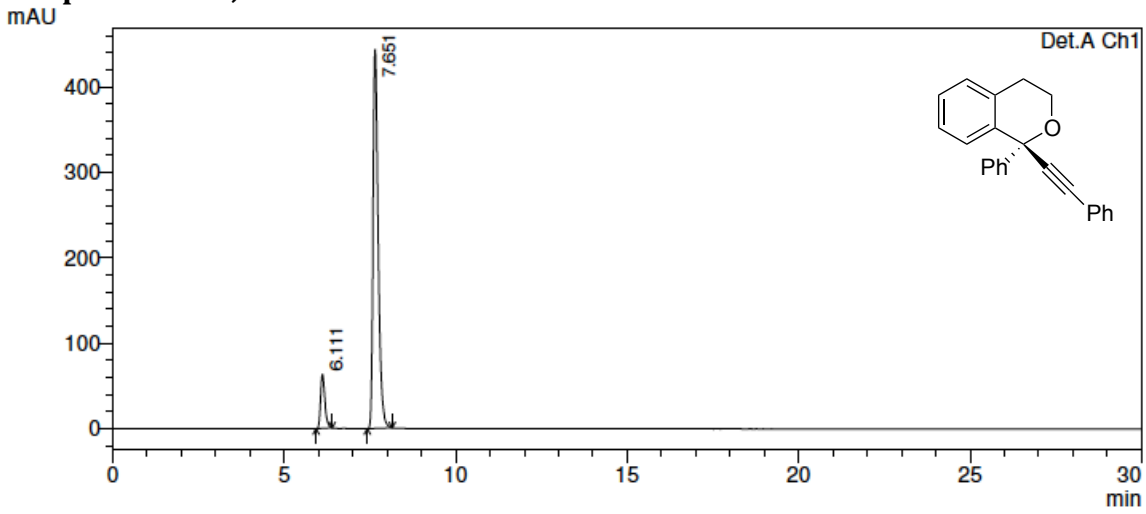
Compound 2-48, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.137	5378986	569674	50.046	53.901
2	7.715	5369181	487209	49.954	46.099
Total		10748167	1056884	100.000	100.000

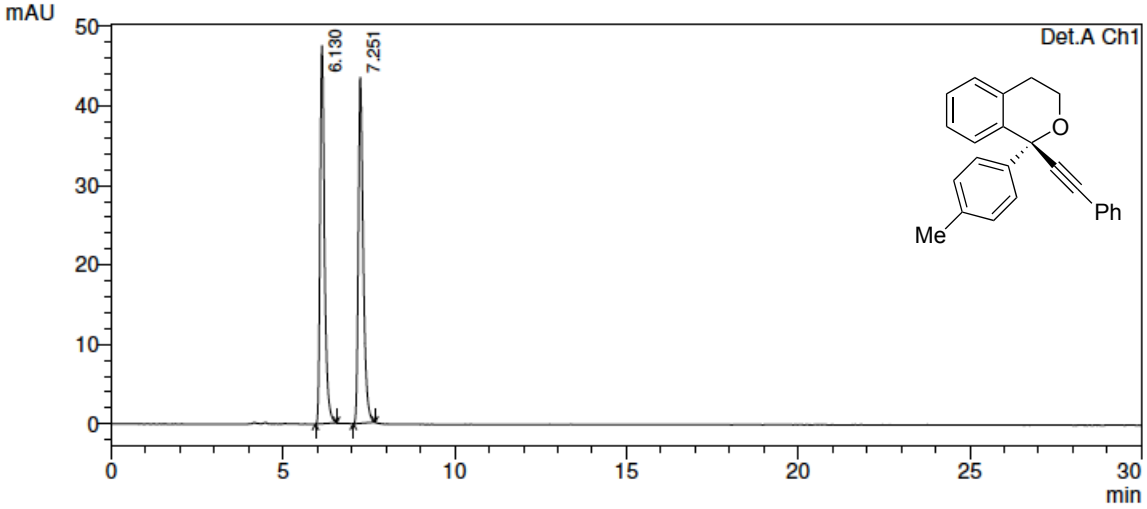
Compound 2-48, 79% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.111	553283	63266	10.679	12.489
2	7.651	4627976	443305	89.321	87.511
Total		5181260	506571	100.000	100.000

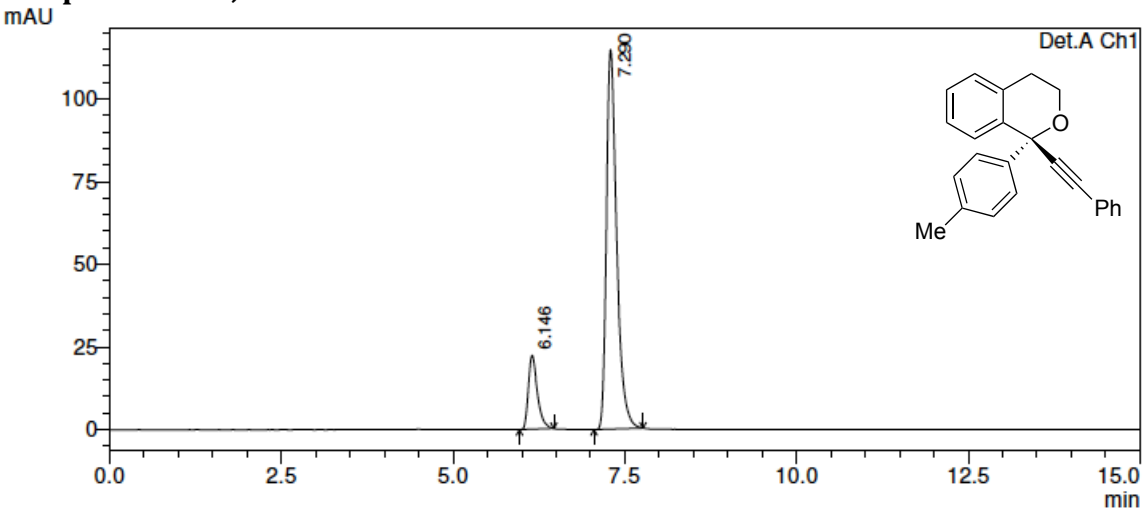
Compound 2-62, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.130	433114	47552	49.547	52.203
2	7.251	441041	43538	50.453	47.797
Total		874156	91089	100.000	100.000

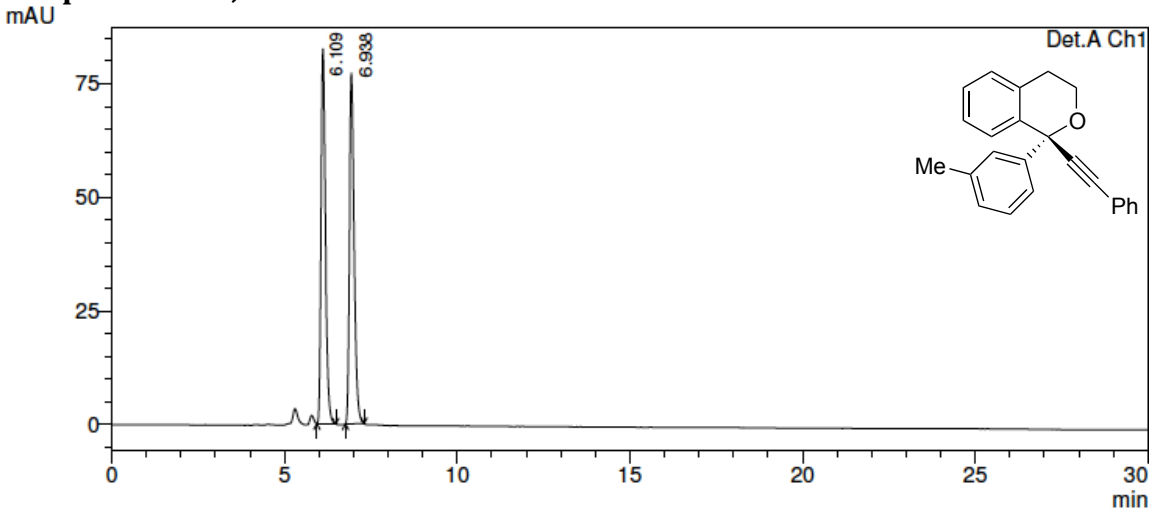
Compound 2-62, 70% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.146	203345	22333	14.605	16.301
2	7.290	1188932	114670	85.395	83.699
Total		1392277	137003	100.000	100.000

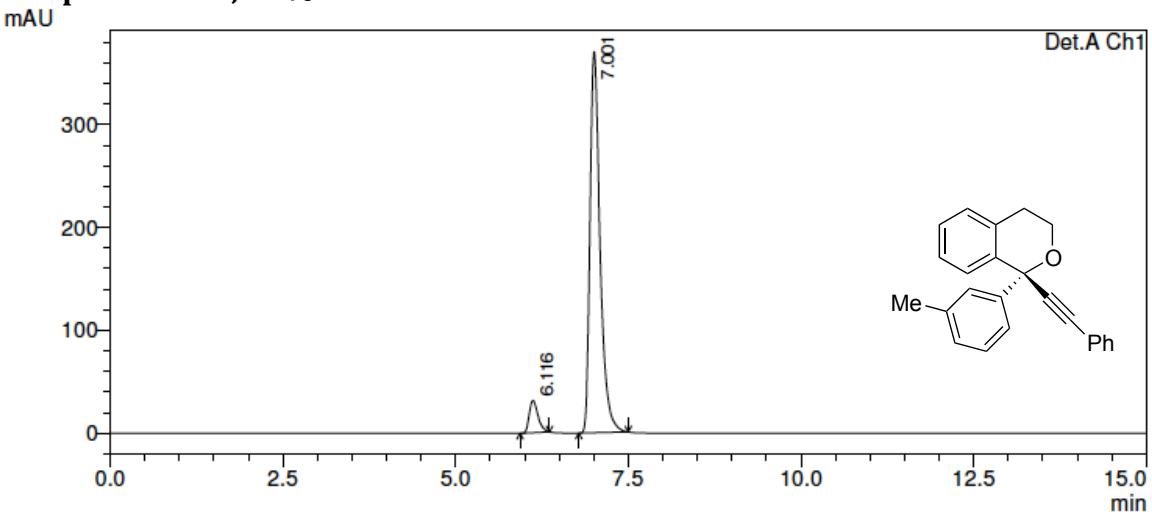
Compound 2-63, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.109	734549	82439	49.974	51.656
2	6.938	735324	77153	50.026	48.344
Total		1469872	159593	100.000	100.000

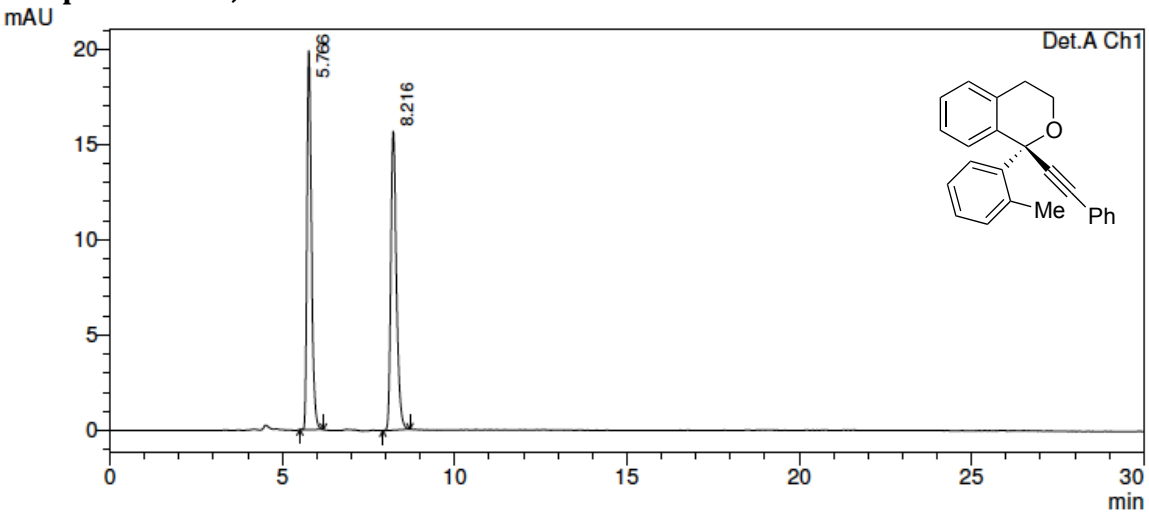
Compound 2-63, 86% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.116	273929	31288	6.820	7.788
2	7.001	3742863	370472	93.180	92.212
Total		4016792	401760	100.000	100.000

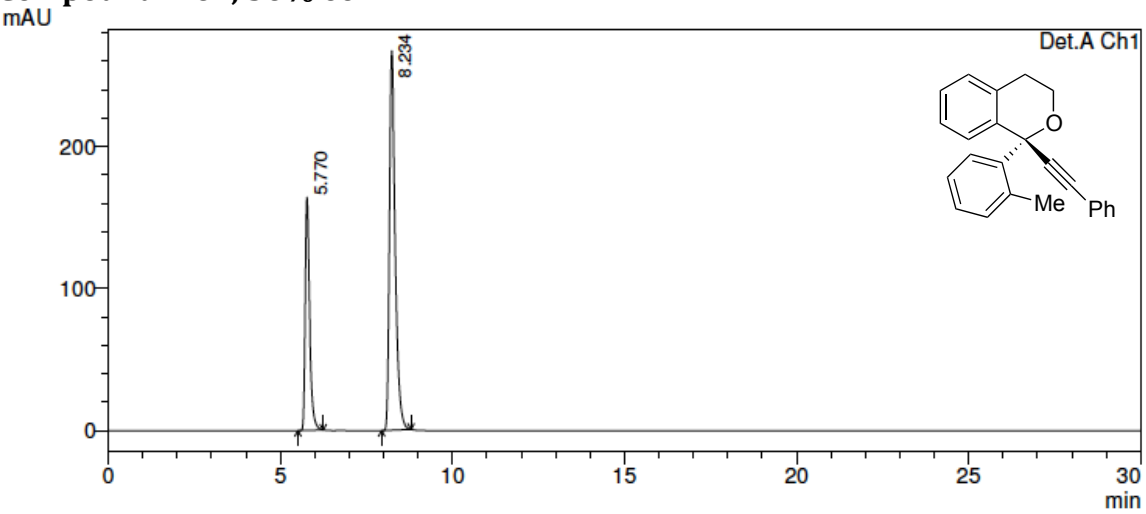
Compound 2-64, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.766	180022	19881	50.099	55.931
2	8.216	179309	15665	49.901	44.069
Total		359331	35546	100.000	100.000

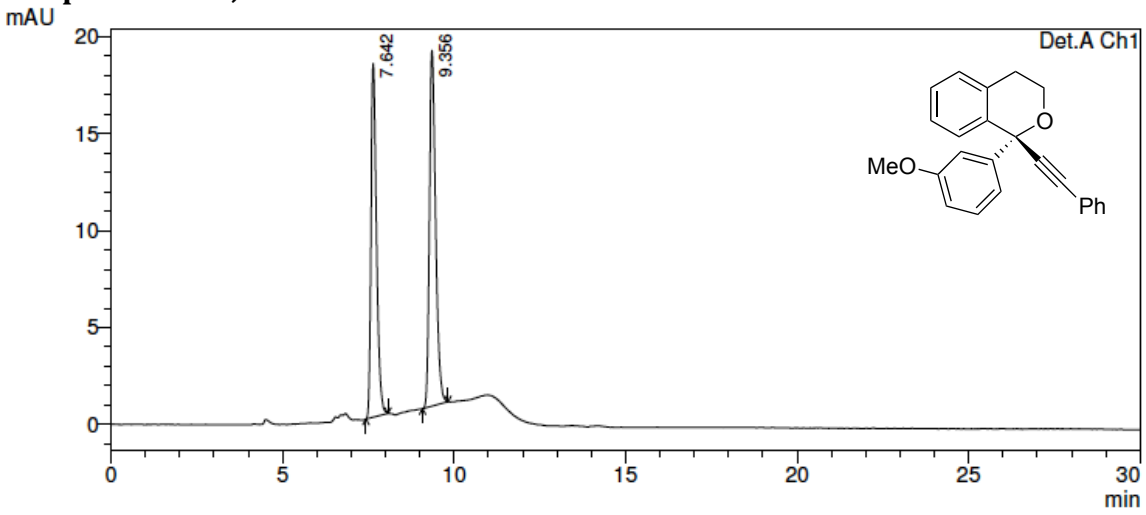
Compound 2-64, 36% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.770	1476938	163918	31.940	38.043
2	8.234	3147216	266952	68.060	61.957
Total		4624154	430870	100.000	100.000

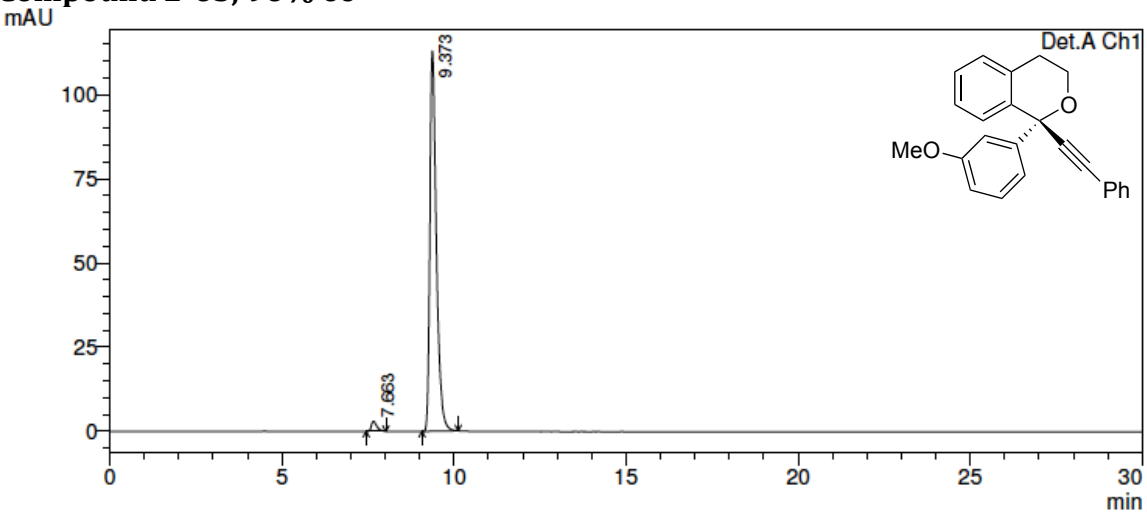
Compound 2-65, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.642	204098	18224	46.732	49.833
2	9.356	232640	18346	53.268	50.167
Total		436738	36570	100.000	100.000

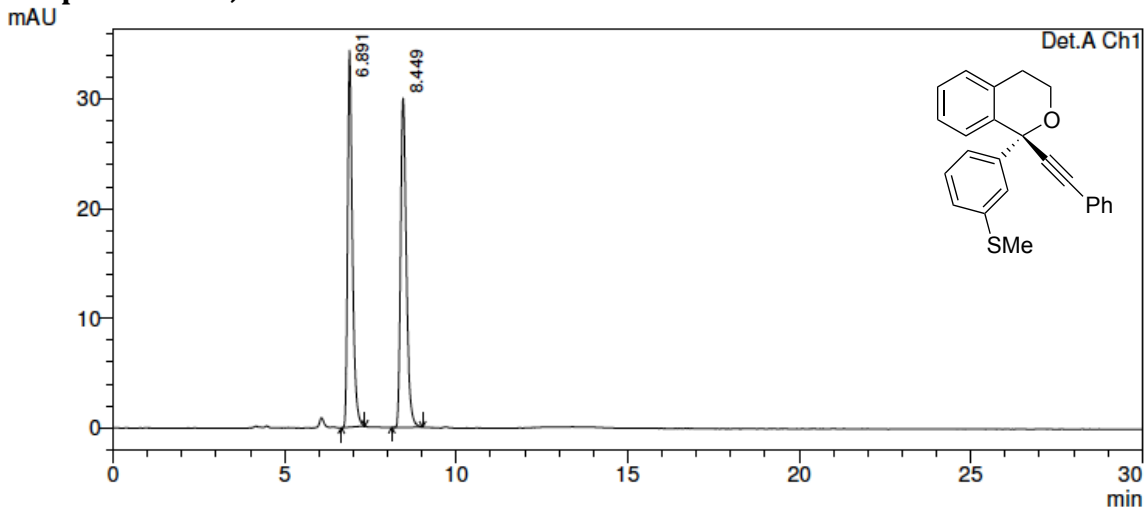
Compound 2-65, 96% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.663	33147	2962	2.177	2.555
2	9.373	1489278	112965	97.823	97.445
Total		1522425	115927	100.000	100.000

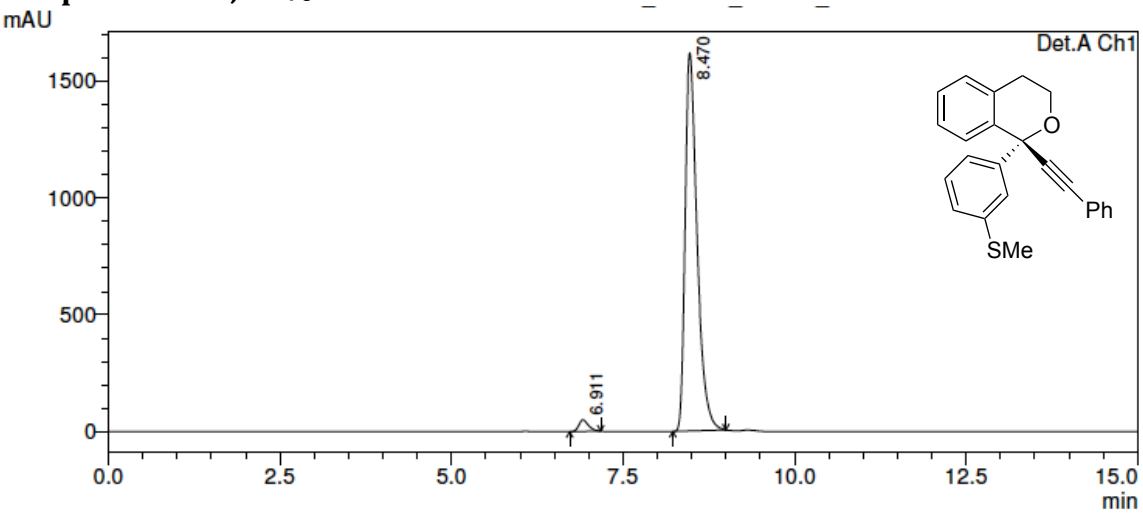
Compound 2-66, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.891	342545	34370	49.848	53.371
2	8.449	344632	30028	50.152	46.629
Total		687177	64398	100.000	100.000

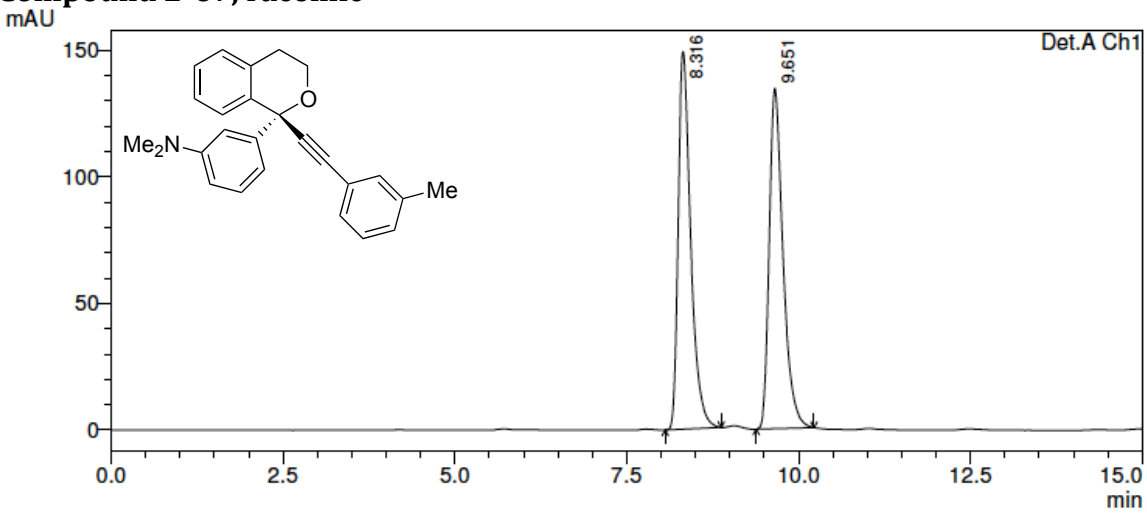
Compound 2-66, 95% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.911	480088	49197	2.386	2.951
2	8.470	19637880	1618163	97.614	97.049
Total		20117968	1667360	100.000	100.000

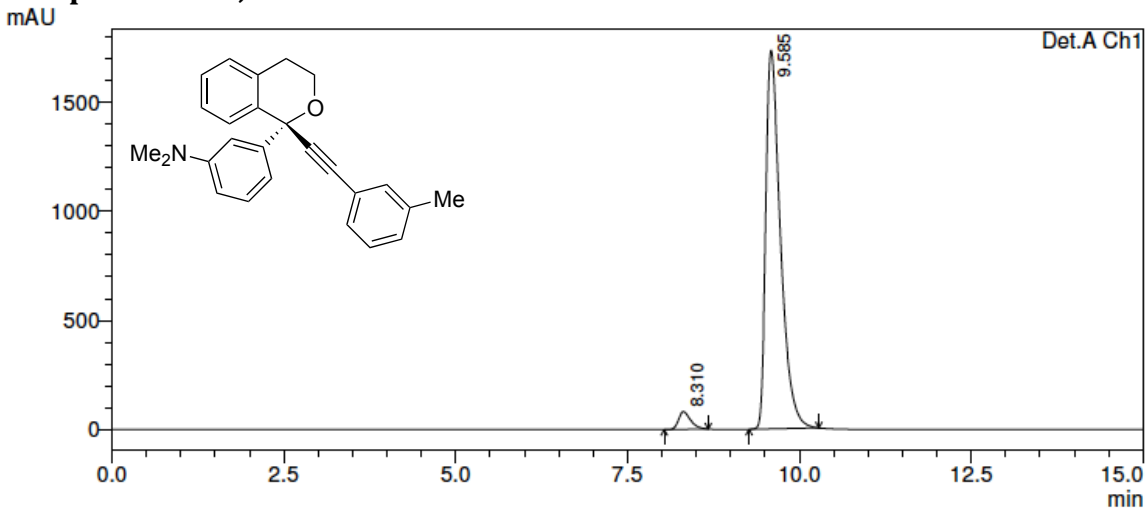
Compound 2-67, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.316	1883685	149057	50.115	52.583
2	9.651	1875060	134411	49.885	47.417
Total		3758745	283468	100.000	100.000

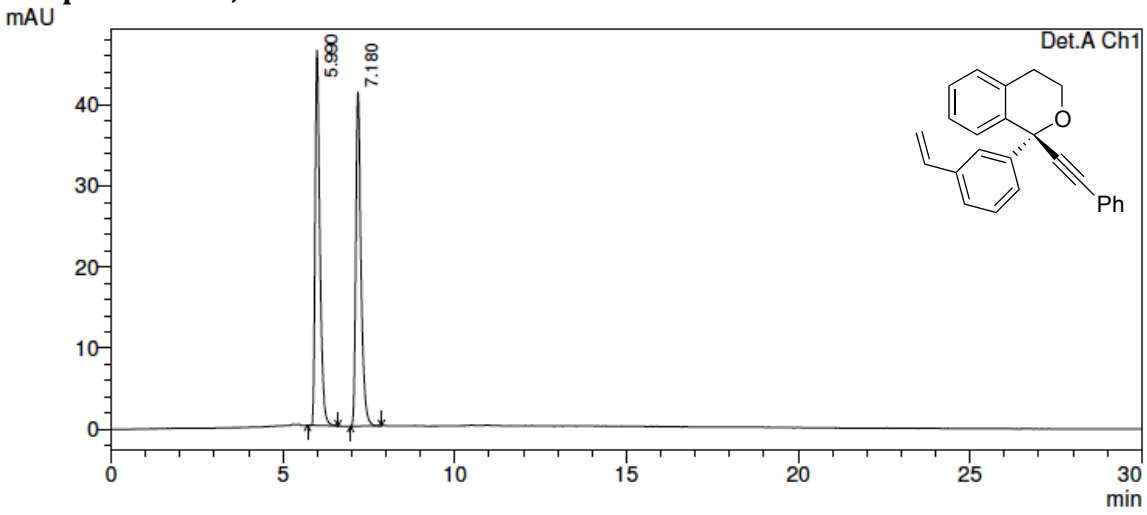
Compound 2-67, 93% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.310	982377	80440	3.670	4.432
2	9.585	25781805	1734464	96.330	95.568
Total		26764182	1814904	100.000	100.000

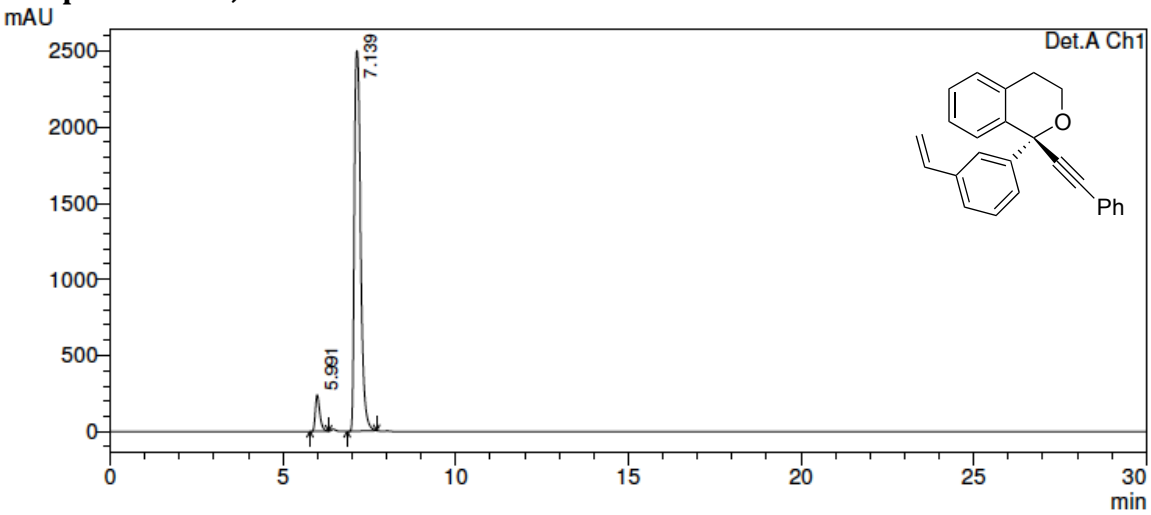
Compound 2-68, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.990	436076	46218	49.985	52.882
2	7.180	436330	41181	50.015	47.118
Total		872406	87399	100.000	100.000

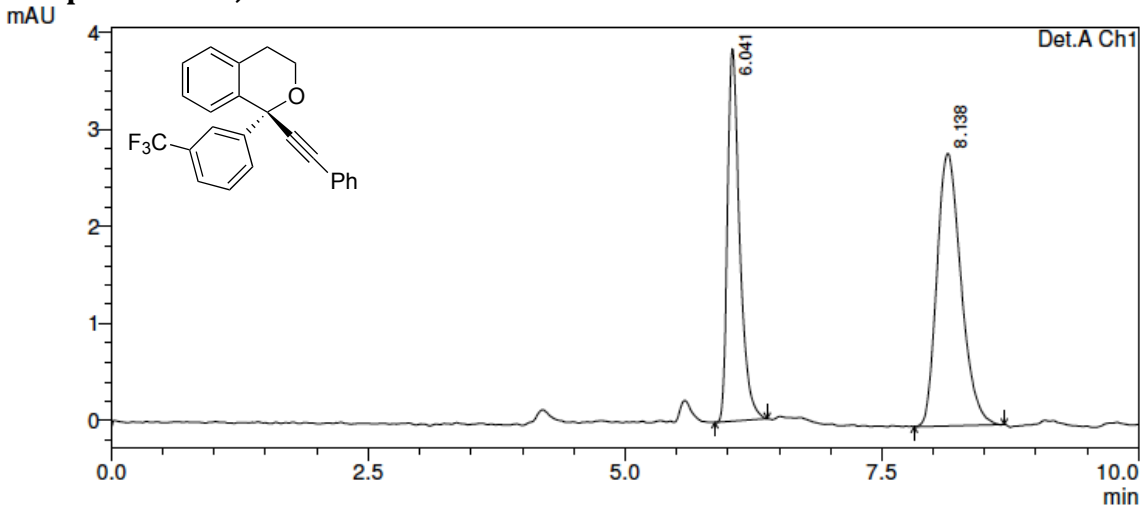
Compound 2-68, 87% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.991	2102213	239235	6.268	8.734
2	7.139	31434983	2499828	93.732	91.266
Total		33537196	2739063	100.000	100.000

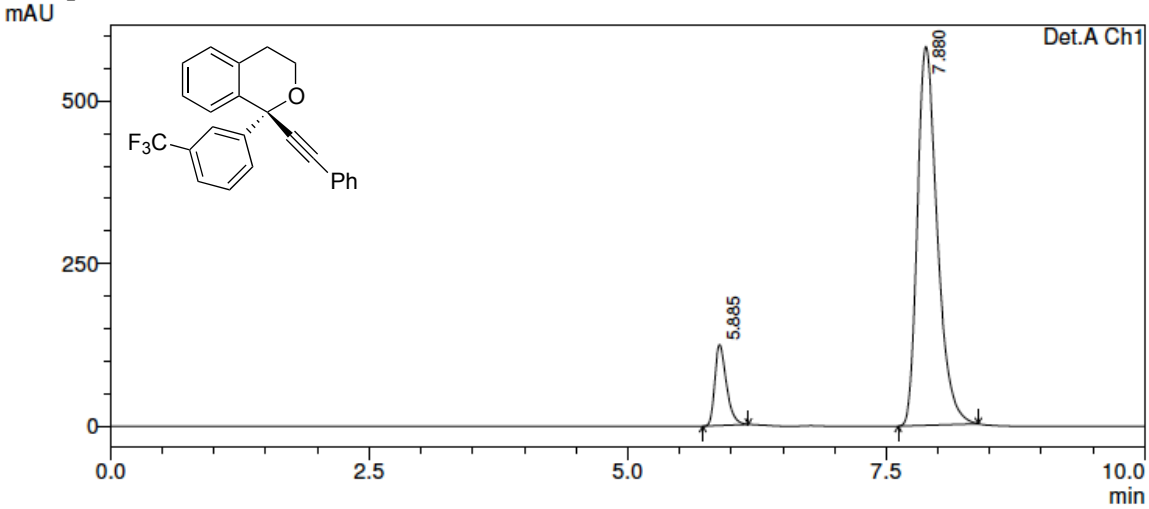
Compound 2-69, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.041	31663	3839	40.854	57.734
2	8.138	45840	2810	59.146	42.266
Total		77503	6649	100.000	100.000

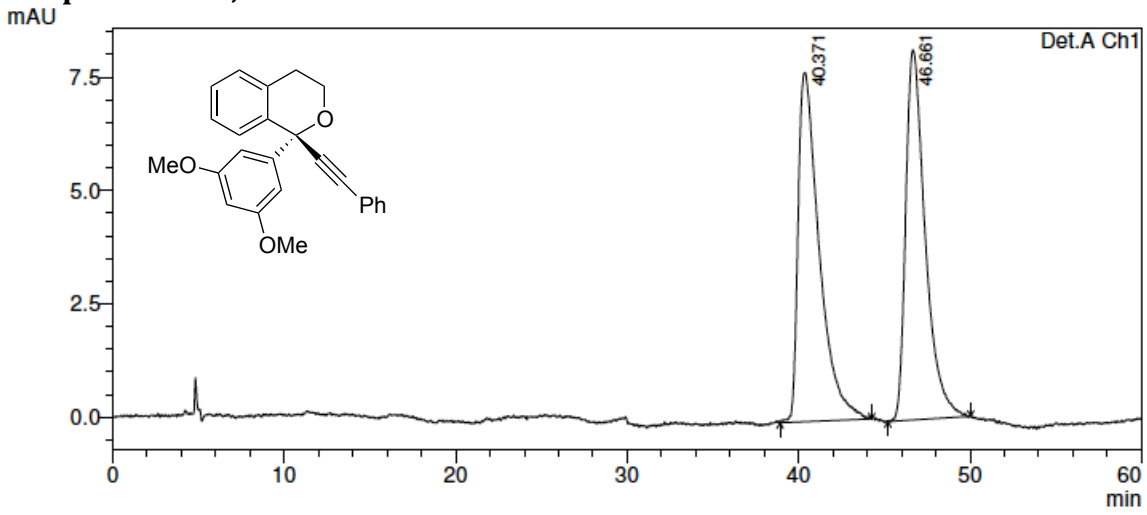
Compound 2-69, 78% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.885	972108	124497	11.071	17.606
2	7.880	7808197	582626	88.929	82.394
Total		8780305	707123	100.000	100.000

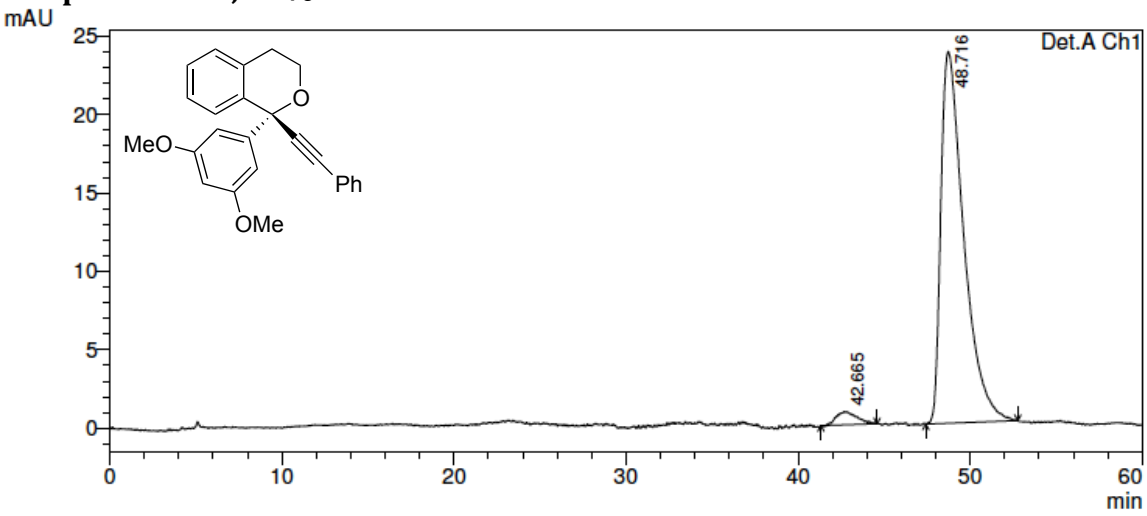
Compound 2-70, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	40.371	659200	7700	50.512	48.531
2	46.661	645835	8166	49.488	51.469
Total		1305035	15865	100.000	100.000

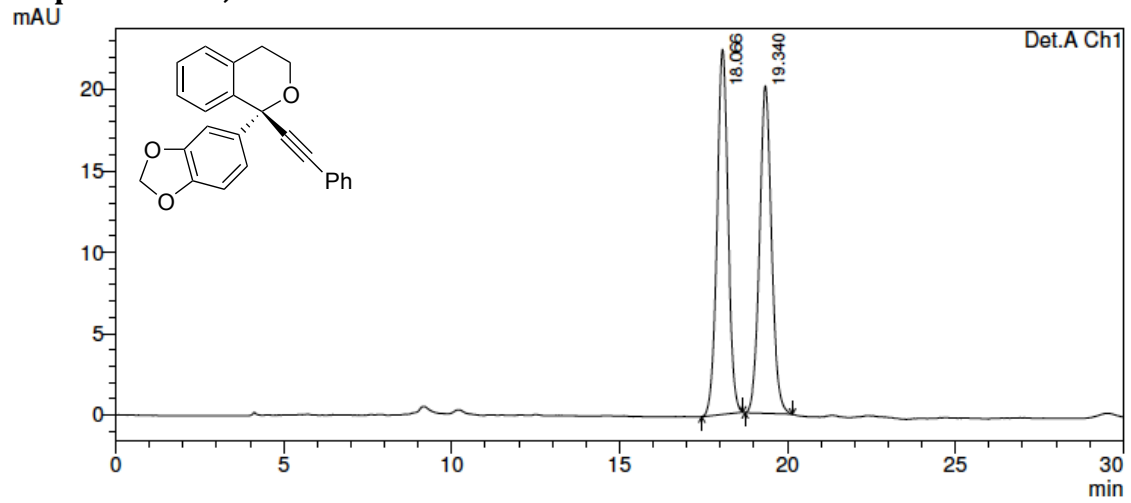
Compound 2-70, 94% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	42.665	70201	851	3.105	3.468
2	48.716	2191007	23684	96.895	96.532
Total		2261208	24534	100.000	100.000

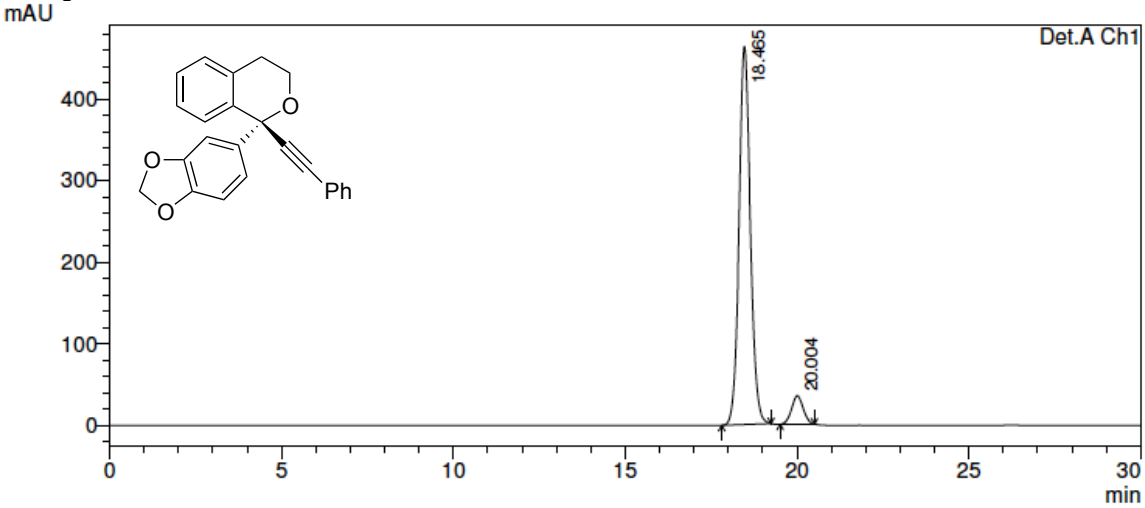
Compound 2-71, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.066	512349	22414	50.527	52.707
2	19.340	501656	20111	49.473	47.293
Total		1014004	42525	100.000	100.000

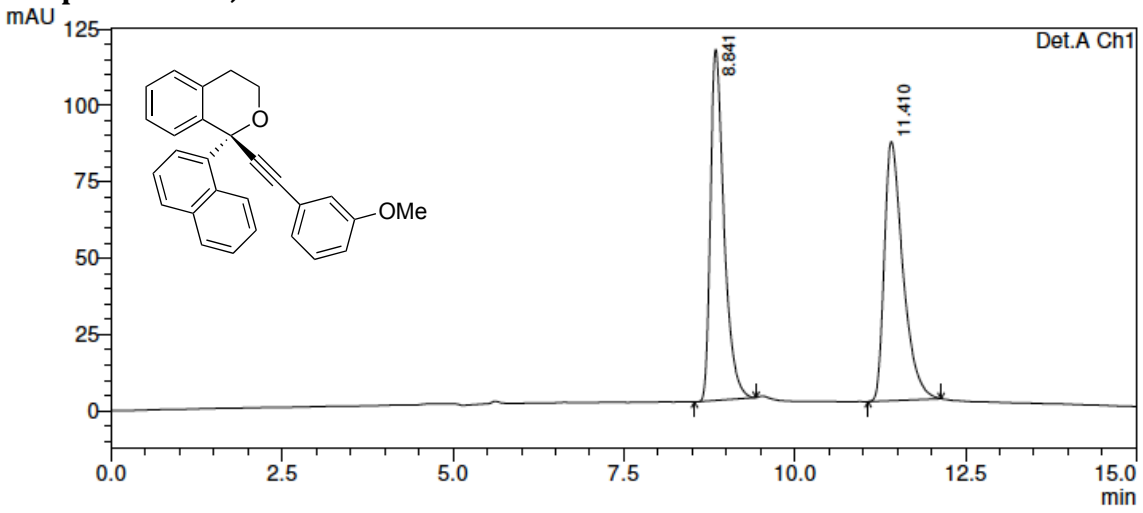
Compound 2-71, 86% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.465	10569569	463160	92.829	92.987
2	20.004	816500	34929	7.171	7.013
Total		11386070	498088	100.000	100.000

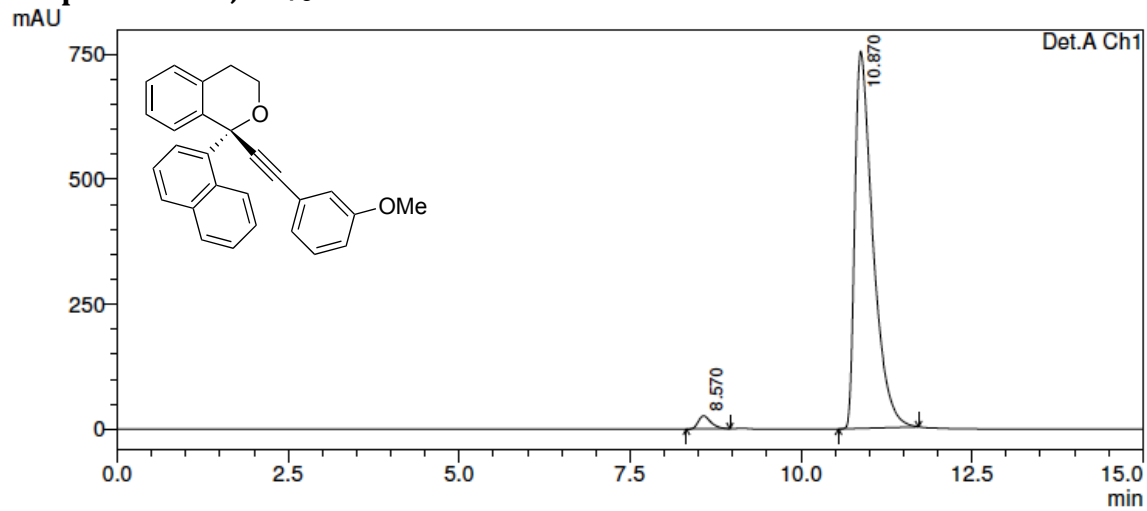
Compound 2-72, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.841	1590100	114877	49.670	57.522
2	11.410	1611207	84833	50.330	42.478
Total		3201307	199710	100.000	100.000

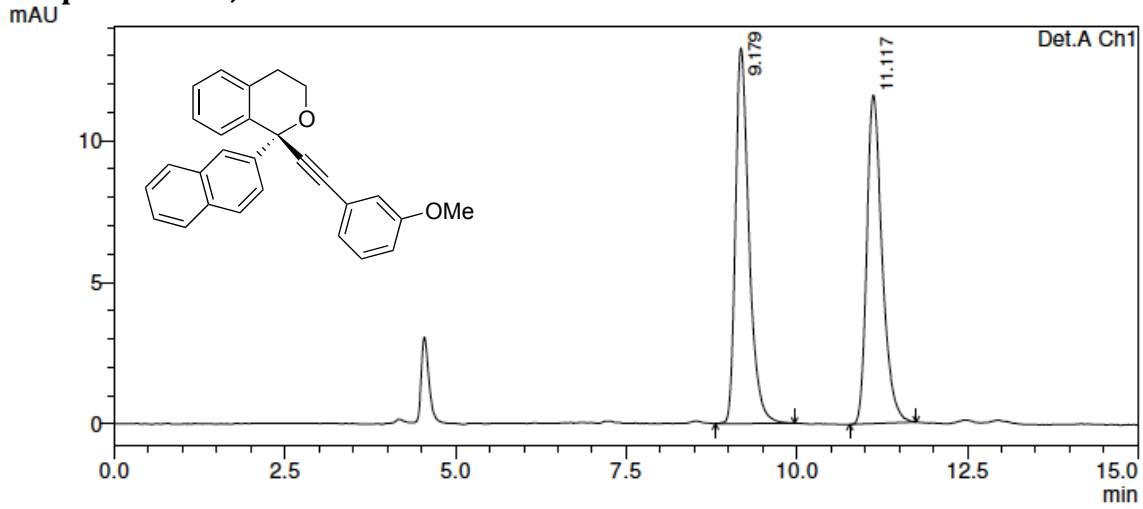
Compound 2-72, 95% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.570	335567	26116	2.358	3.343
2	10.870	13895866	755017	97.642	96.657
Total		14231433	781134	100.000	100.000

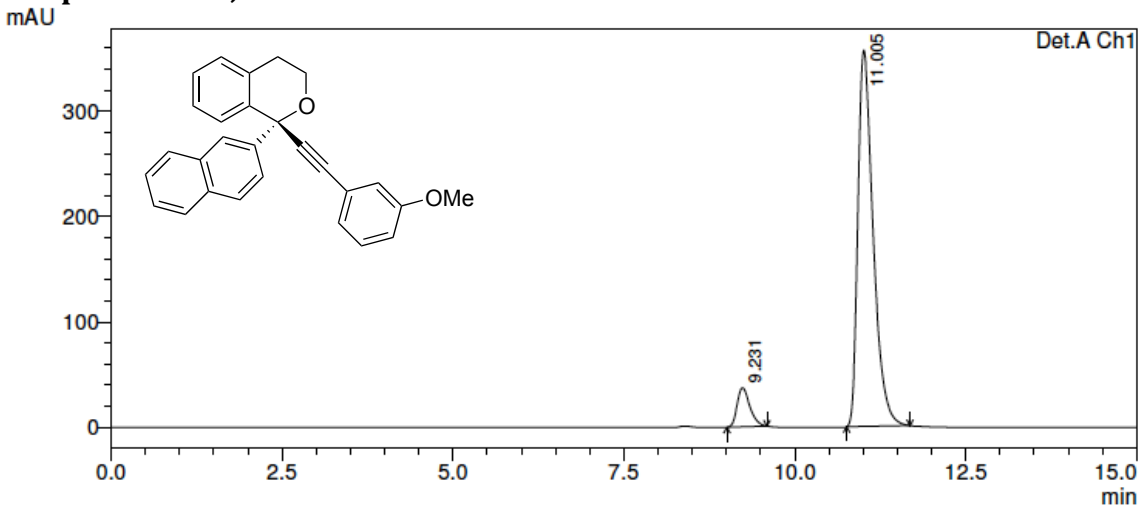
Compound 2-73, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.179	183064	13270	50.199	53.341
2	11.117	181613	11608	49.801	46.659
Total		364677	24878	100.000	100.000

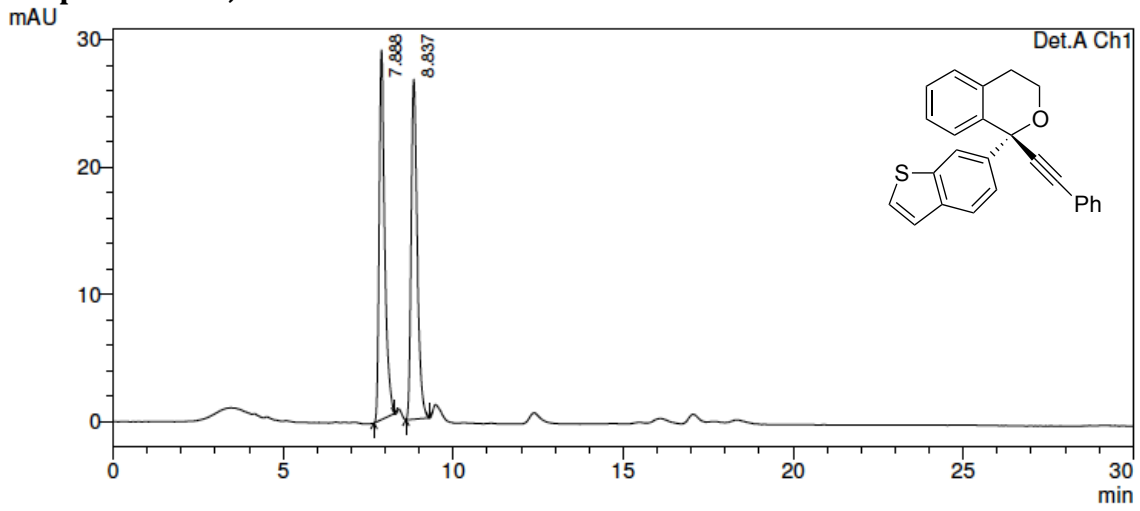
Compound 2-73, 84% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.231	479890	37101	7.979	9.414
2	11.005	5534742	357001	92.021	90.586
Total		6014632	394103	100.000	100.000

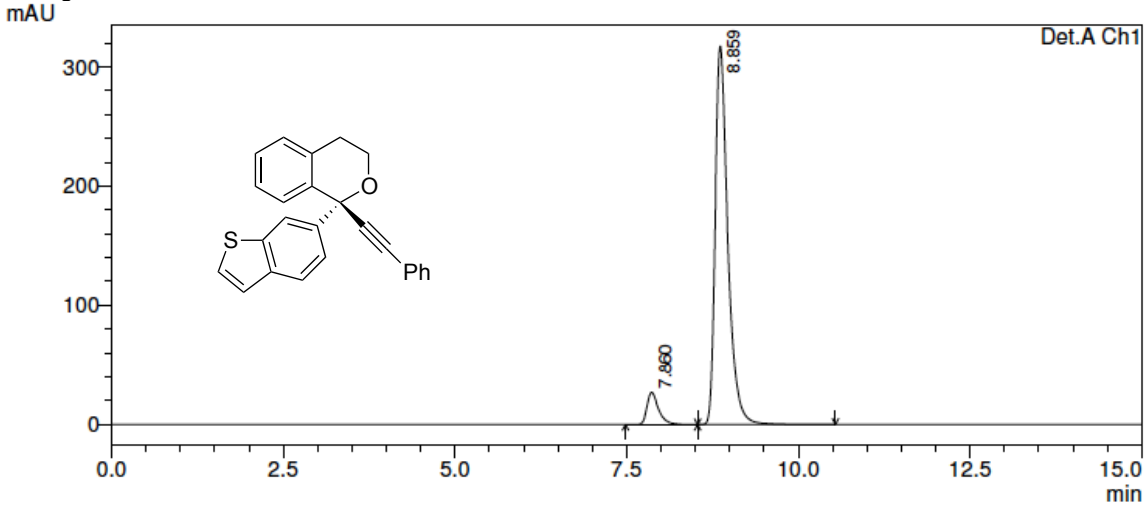
Compound 2-74, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.888	334891	29047	50.296	52.111
2	8.837	330952	26694	49.704	47.889
Total		665843	55741	100.000	100.000

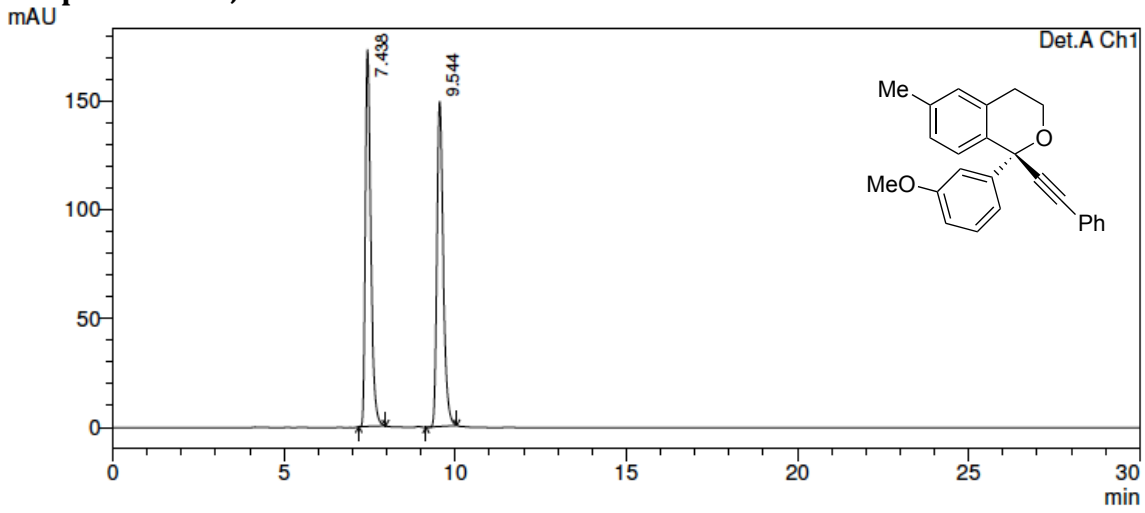
Compound 2-74, 86% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.860	292331	26558	6.801	7.732
2	8.859	4006302	316928	93.199	92.268
Total		4298632	343486	100.000	100.000

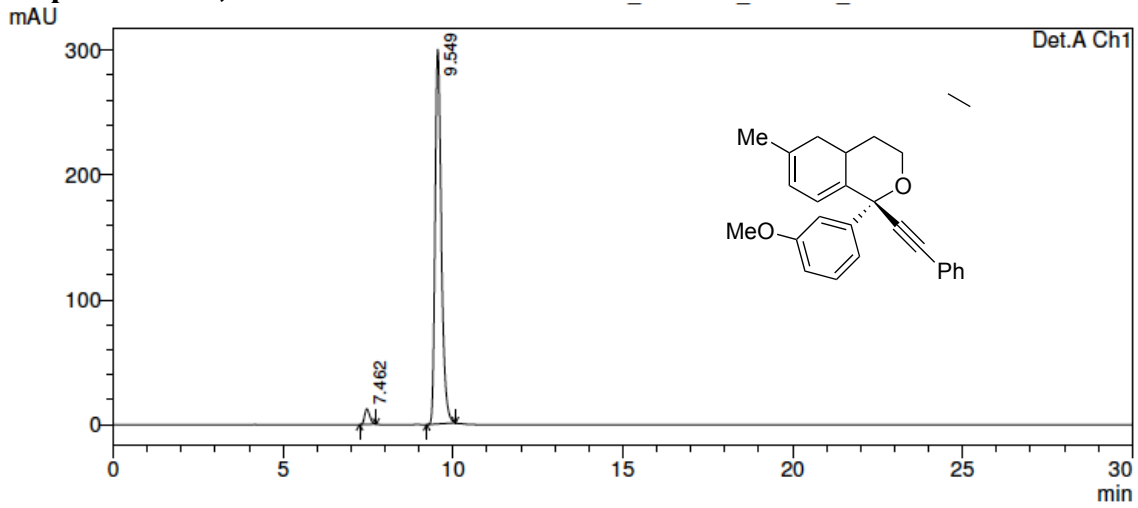
Compound 2-75, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.438	1906845	173117	50.029	53.676
2	9.544	1904620	149402	49.971	46.324
Total		3811465	322519	100.000	100.000

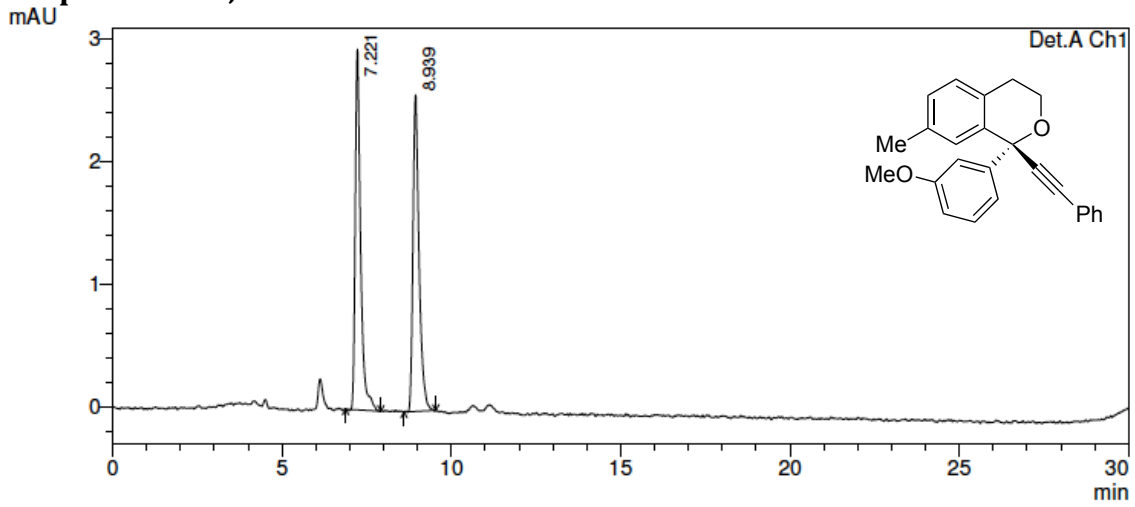
Compound 2-75, 93% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.462	129922	12454	3.270	3.986
2	9.549	3843725	300023	96.730	96.014
Total		3973647	312477	100.000	100.000

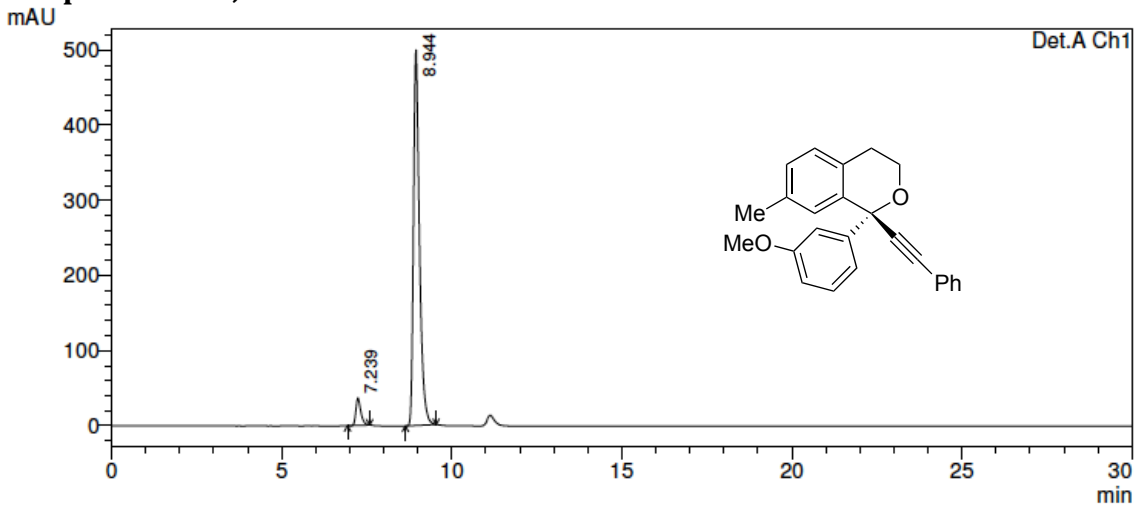
Compound 2-76, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.221	32994	2940	50.332	53.264
2	8.939	32559	2580	49.668	46.736
Total		65554	5519	100.000	100.000

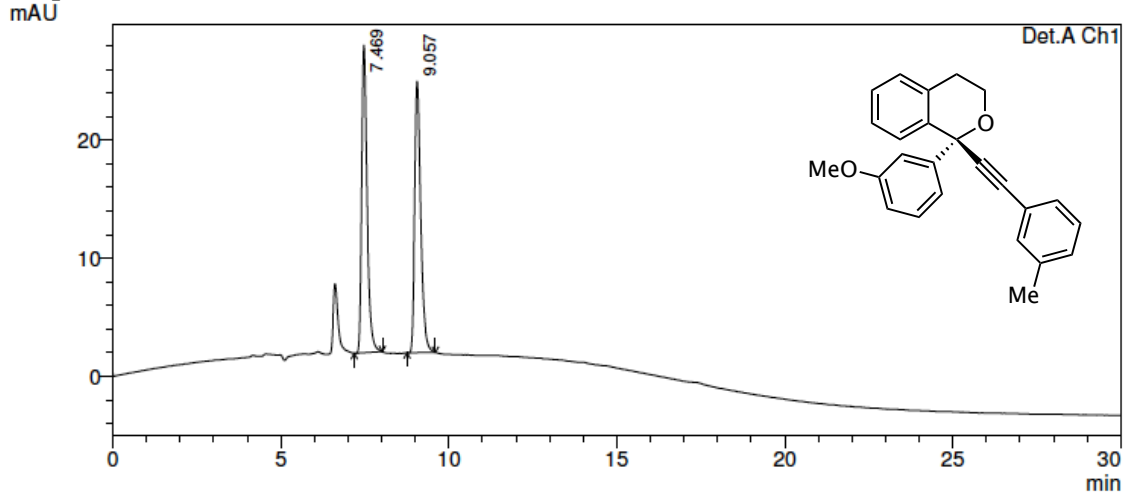
Compound 2-76, 89% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.239	375698	36677	5.731	6.839
2	8.944	6179751	499628	94.269	93.161
Total		6555449	536305	100.000	100.000

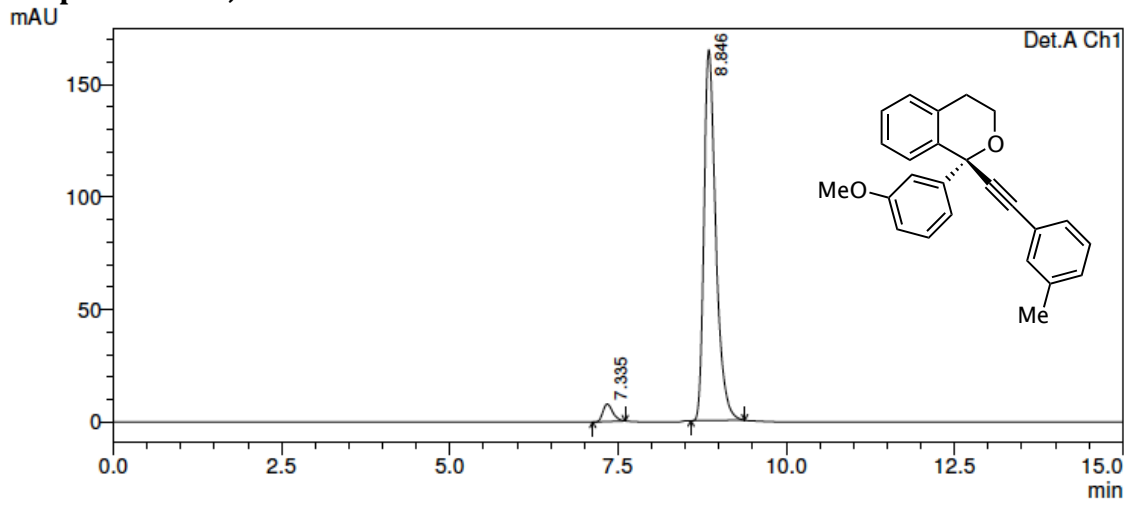
Compound 2-77, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.469	291296	26039	50.255	53.126
2	9.057	288340	22975	49.745	46.874
Total		579636	49014	100.000	100.000

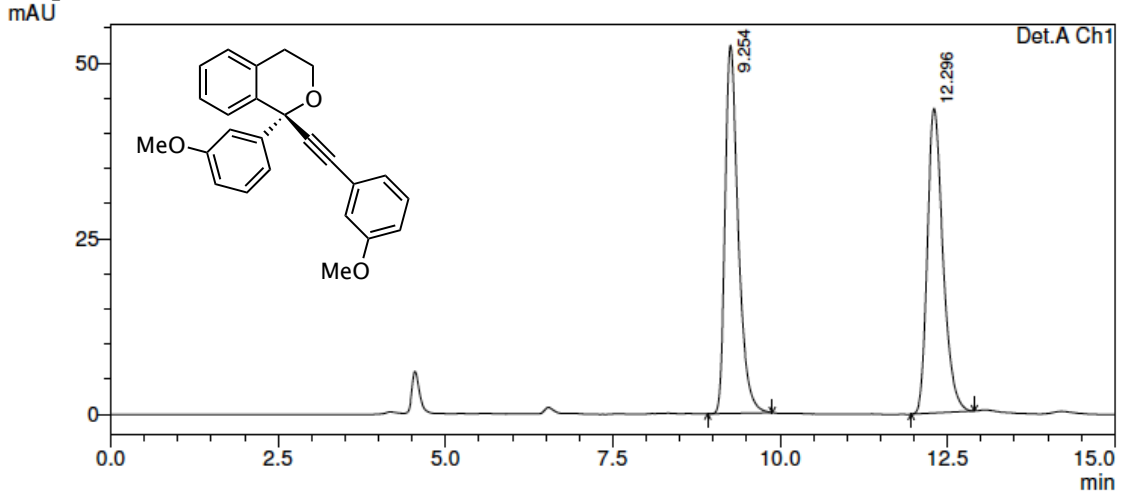
Compound 2-77, 92% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.335	79489	7760	3.789	4.494
2	8.846	2018315	164903	96.211	95.506
Total		2097804	172664	100.000	100.000

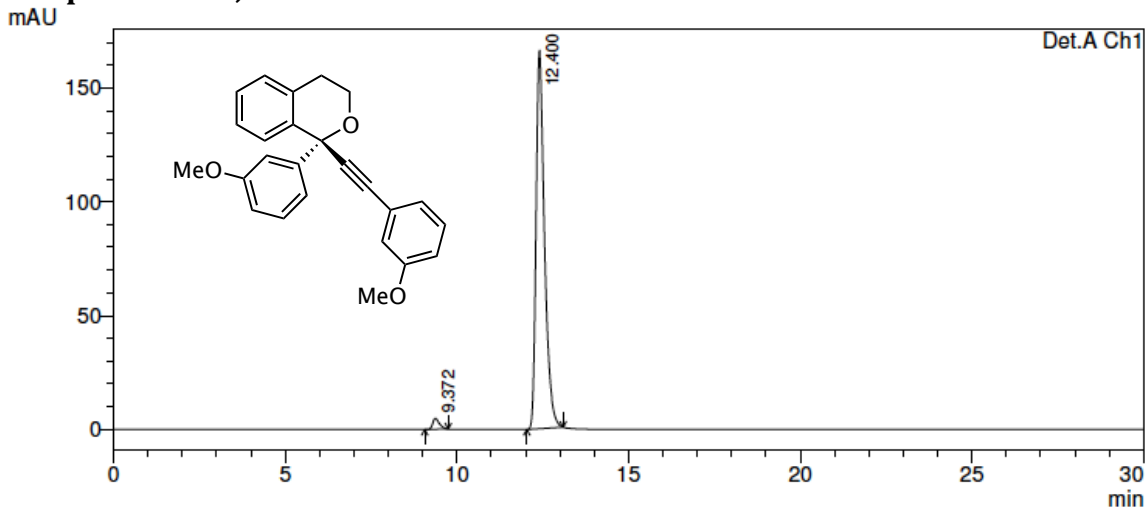
Compound 2-78, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.254	714401	52403	50.311	54.712
2	12.296	705567	43376	49.689	45.288
Total		1419968	95778	100.000	100.000

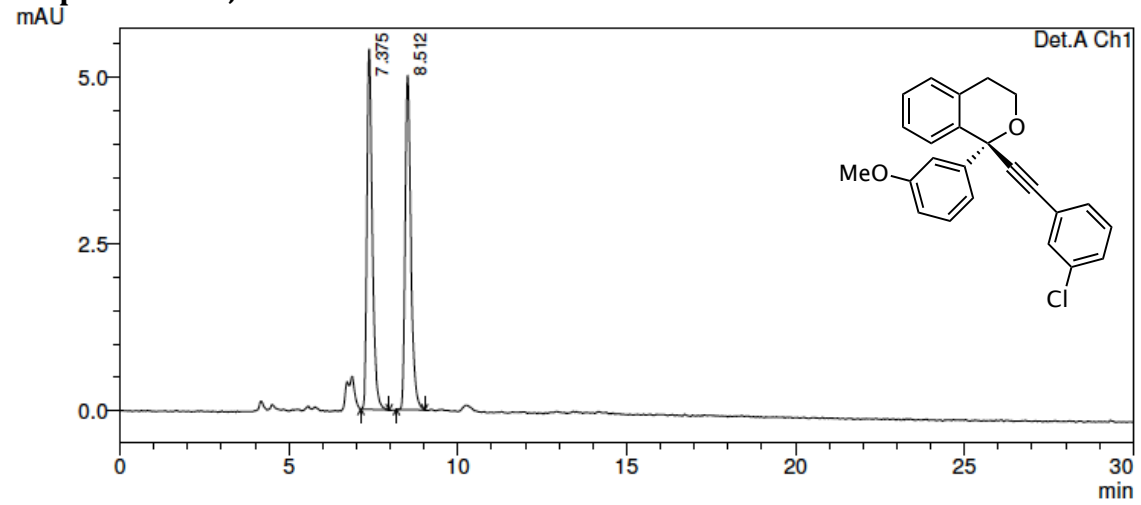
Compound 2-78, 96% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.372	64105	4768	2.195	2.790
2	12.400	2856992	166133	97.805	97.210
Total		2921098	170902	100.000	100.000

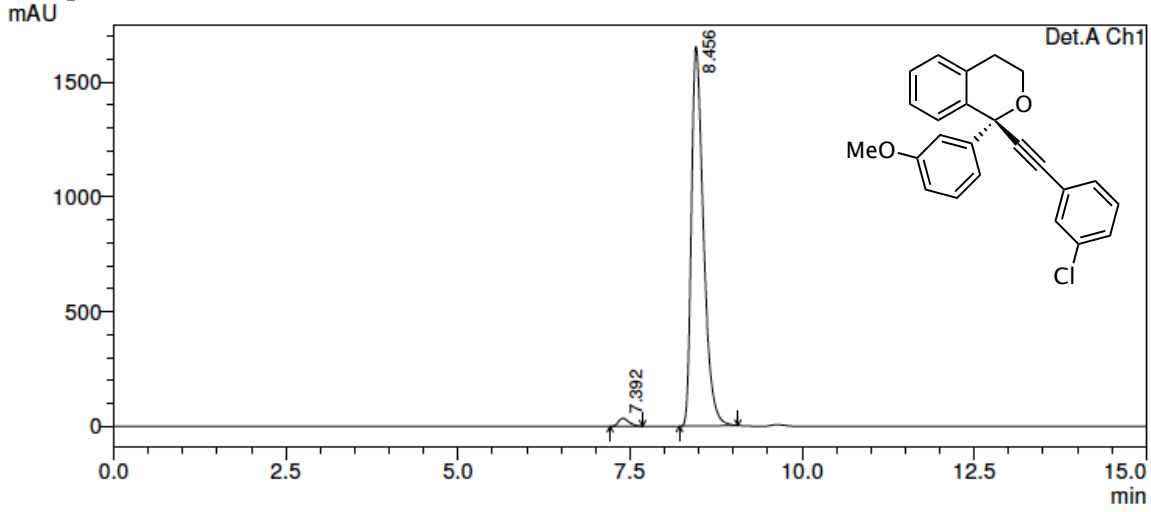
Compound 2-79, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.375	59300	5401	50.067	51.855
2	8.512	59140	5015	49.933	48.145
Total		118440	10416	100.000	100.000

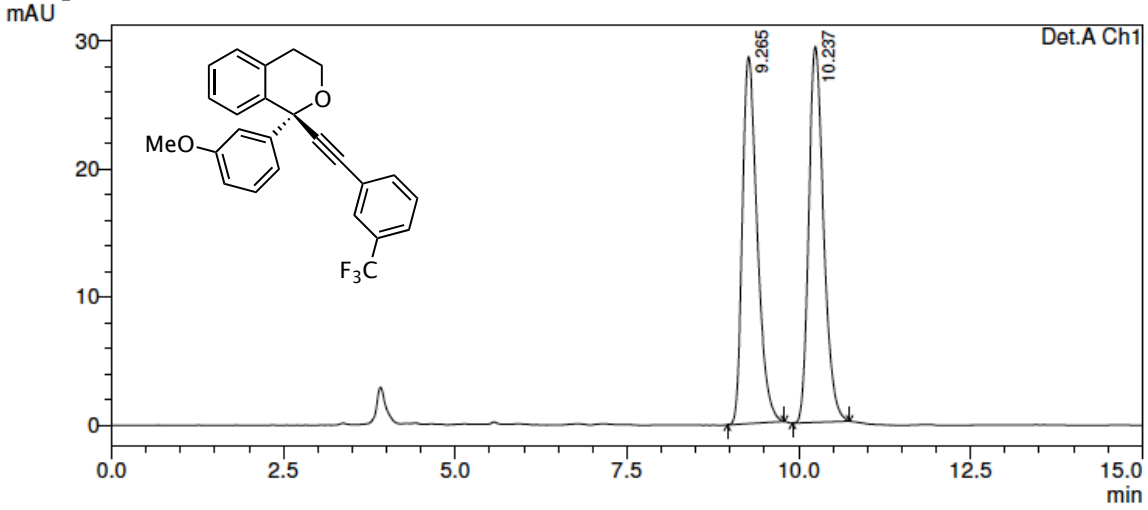
Compound 2-79, 96% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.392	364431	34802	1.772	2.060
2	8.456	20203612	1654547	98.228	97.940
Total		20568042	1689350	100.000	100.000

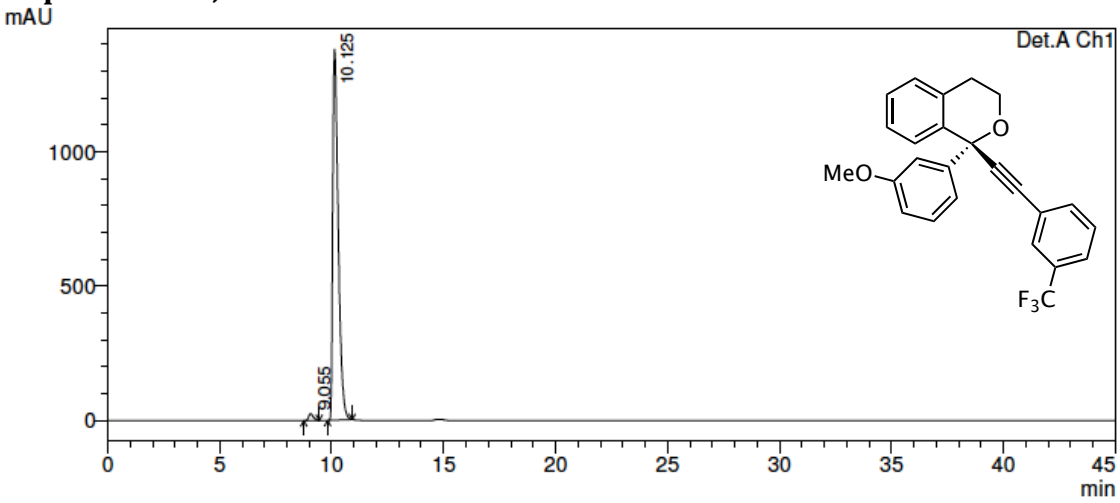
Compound 2-80, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.265	430794	28664	49.401	49.399
2	10.237	441249	29361	50.599	50.601
Total		872043	58025	100.000	100.000

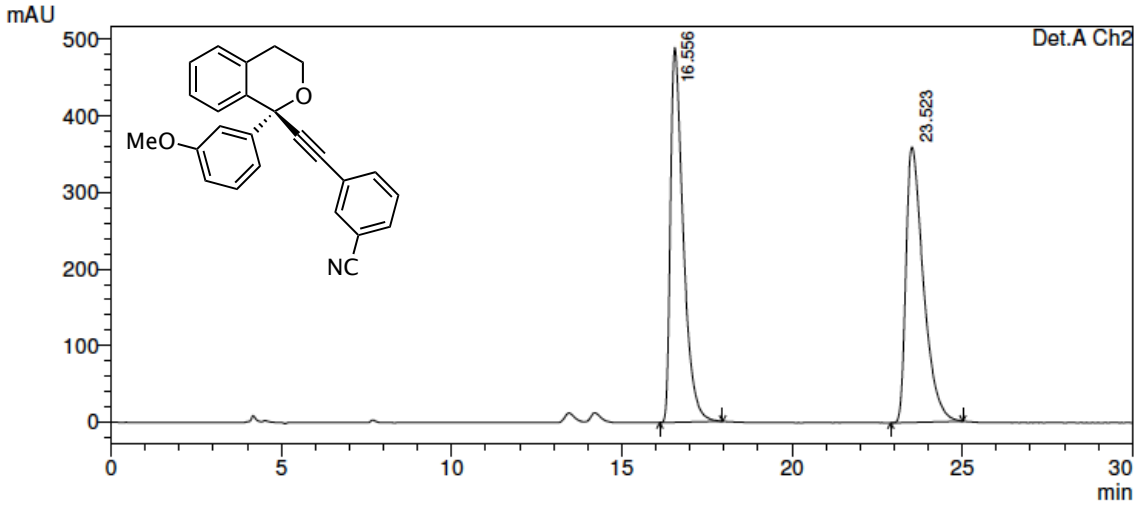
Compound 2-80, 97% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.055	361014	24922	1.509	1.774
2	10.125	23556221	1380041	98.491	98.226
Total		23917235	1404963	100.000	100.000

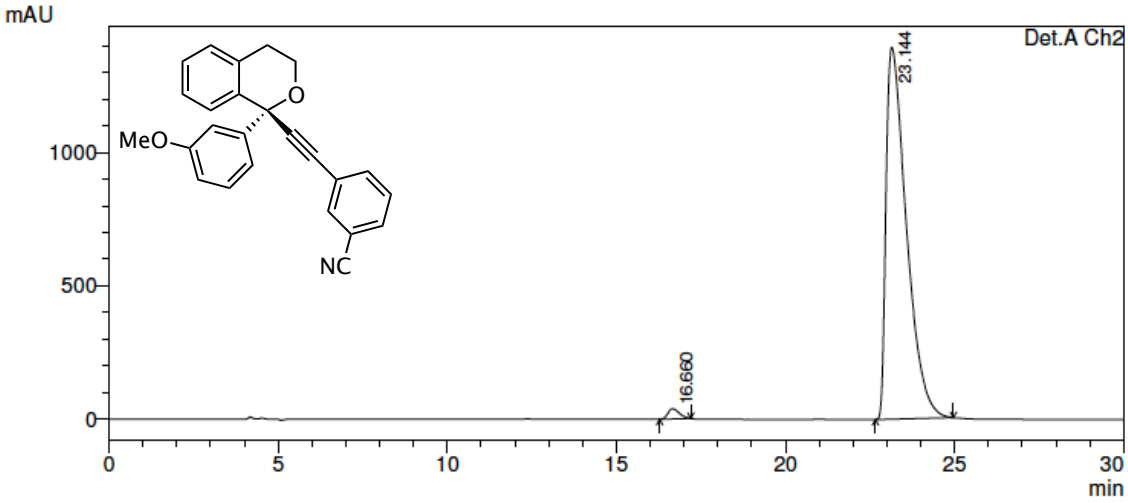
Compound 2-81, racemic



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.556	12828130	489213	50.034	57.649
2	23.523	12810664	359387	49.966	42.351
Total		25638793	848600	100.000	100.000

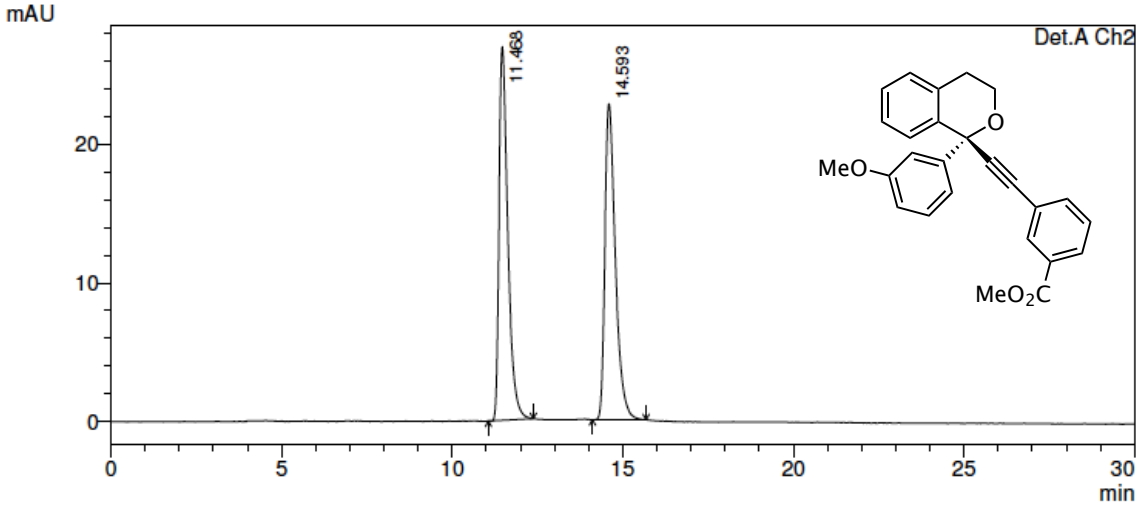
Compound 2-81, 97% ee



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.660	900275	38223	1.518	2.668
2	23.144	58388856	1394662	98.482	97.332
Total		59289131	1432885	100.000	100.000

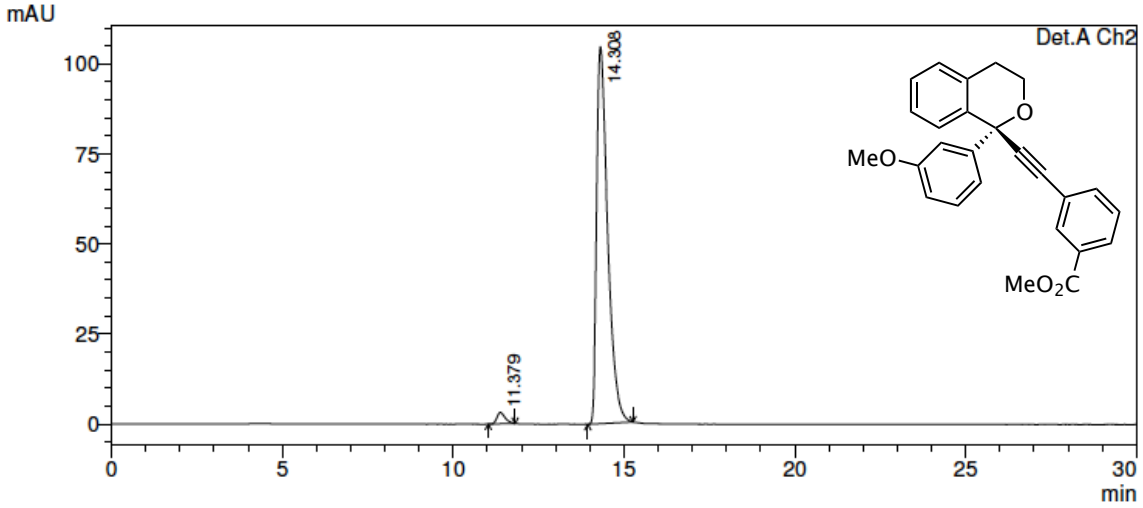
Compound 2-82, racemic



Detector A Ch2 280nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.468	482671	26962	49.804	54.175
2	14.593	486463	22807	50.196	45.825
Total		969135	49768	100.000	100.000

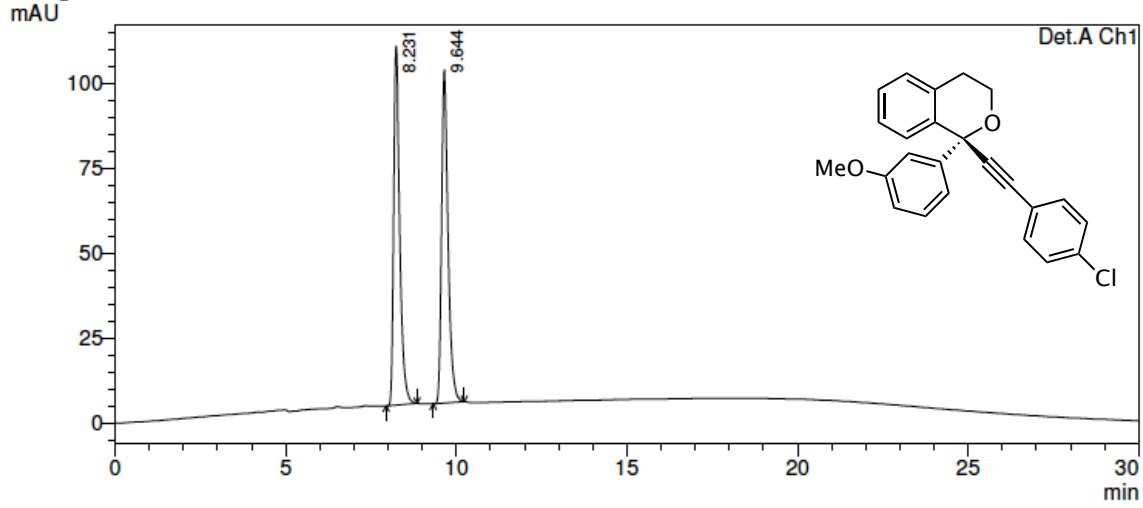
Compound 2-82, 96% ee



Detector A Ch2 280nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.379	53437	3197	2.227	2.964
2	14.308	2346529	104665	97.773	97.036
Total		2399966	107861	100.000	100.000

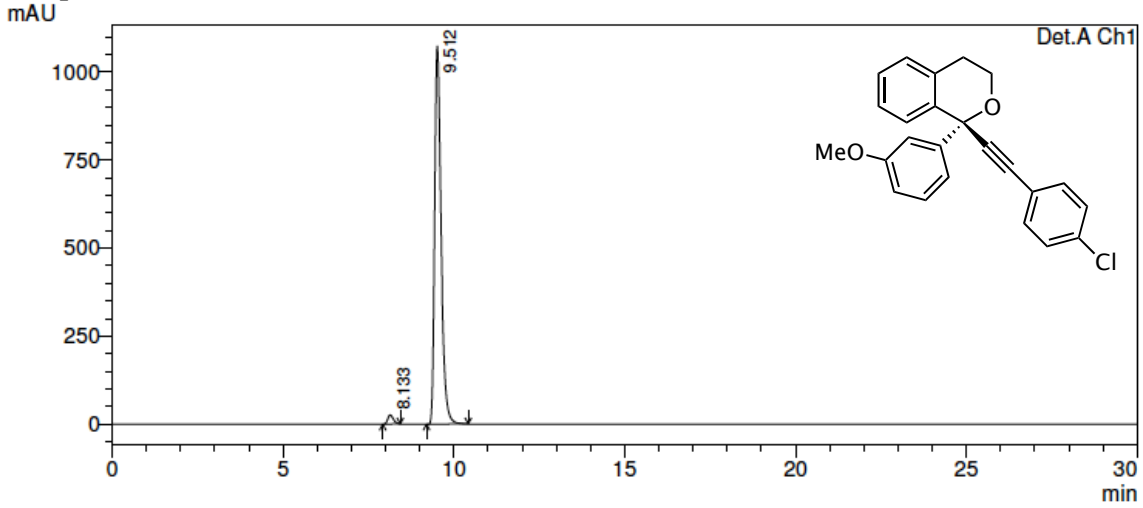
Compound 2-83, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.231	1306392	105599	49.953	51.859
2	9.644	1308855	98027	50.047	48.141
Total		2615247	203626	100.000	100.000

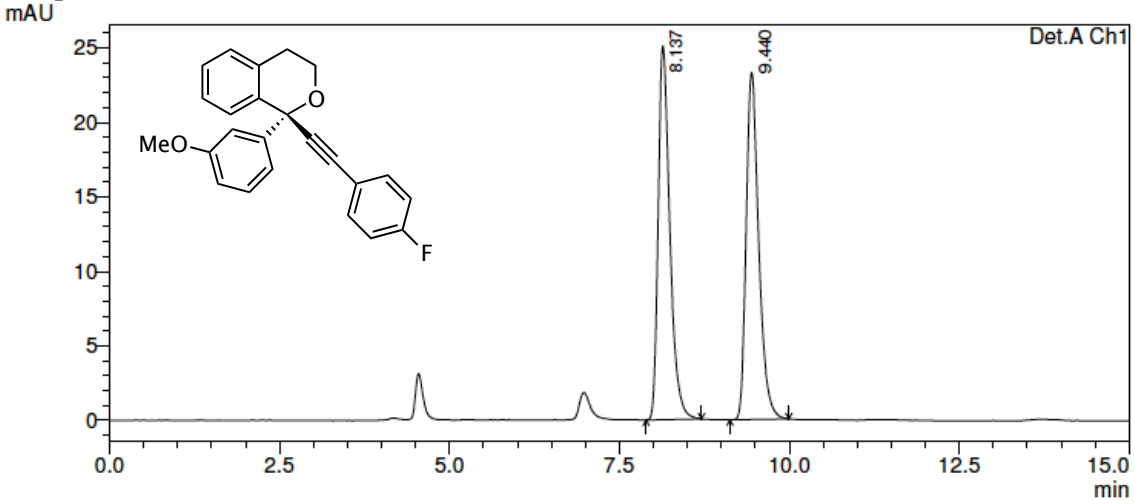
Compound 2-83, 96% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.133	289616	25743	2.034	2.343
2	9.512	13947399	1072809	97.966	97.657
Total		14237015	1098552	100.000	100.000

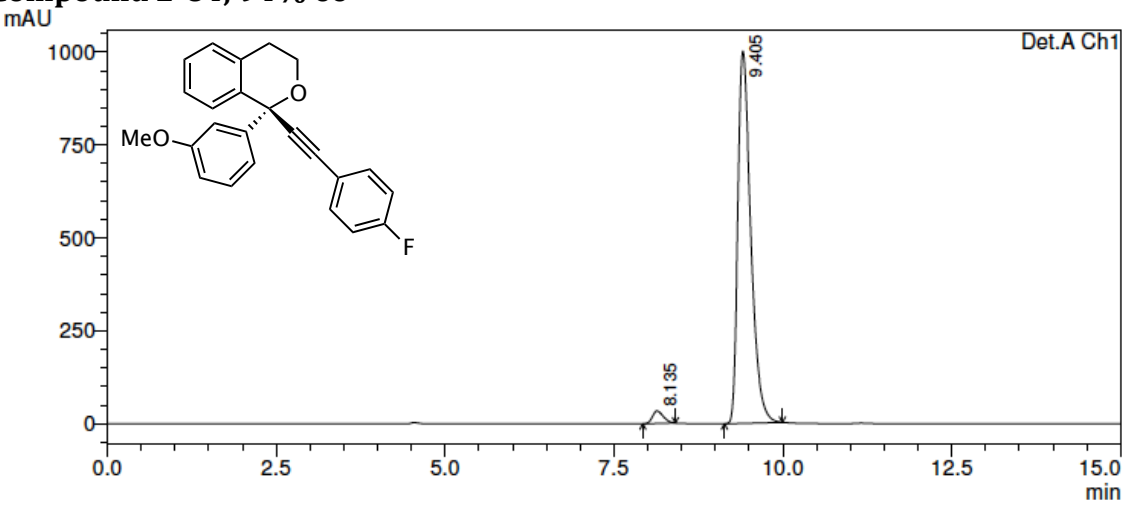
Compound 2-84, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.137	299054	25083	50.018	51.852
2	9.440	298840	23292	49.982	48.148
Total		597894	48375	100.000	100.000

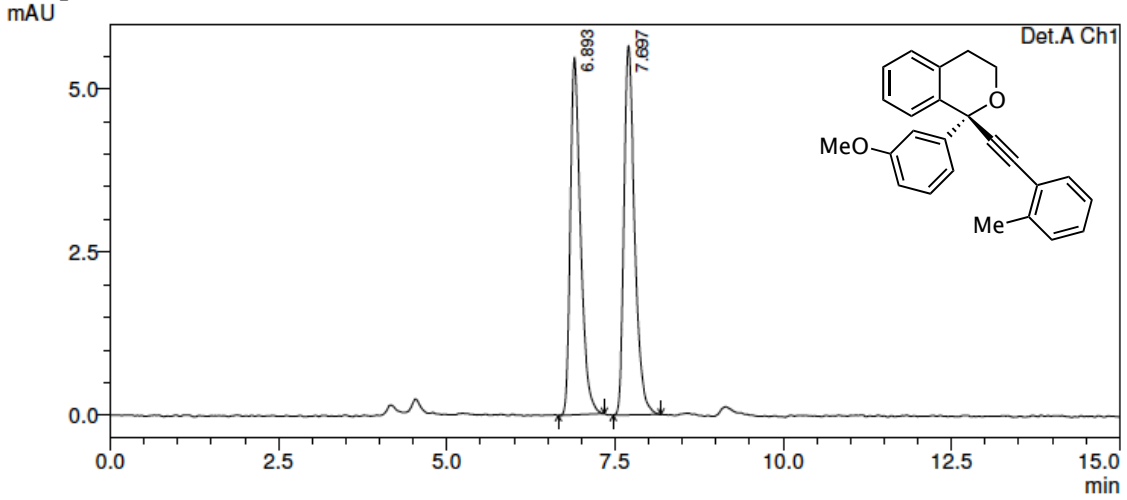
Compound 2-84, 94% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.135	377572	33785	2.752	3.264
2	9.405	13342353	1001273	97.248	96.736
Total		13719925	1035058	100.000	100.000

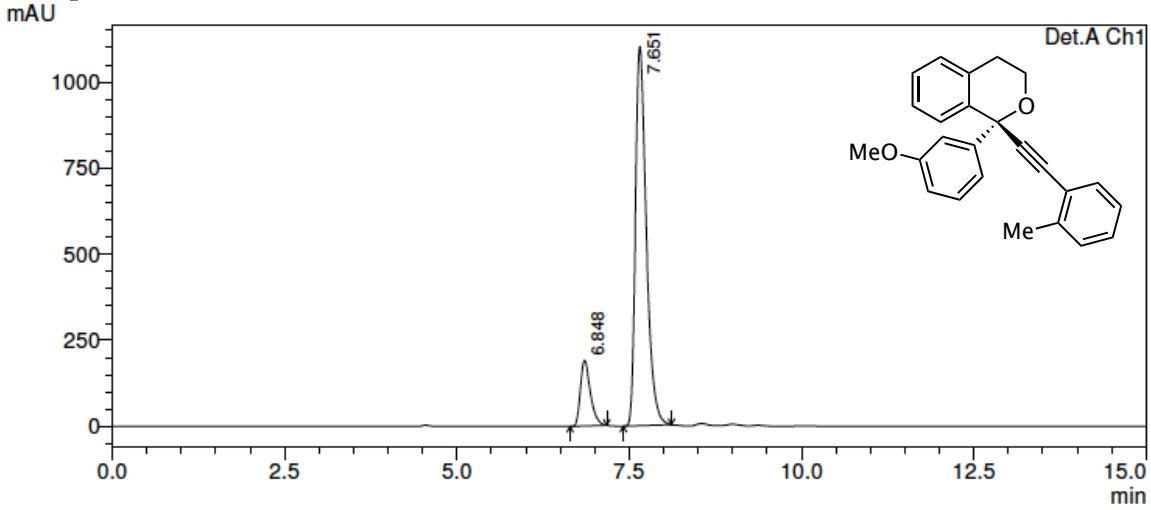
Compound 2-85, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.893	58319	5483	48.364	49.186
2	7.697	62266	5665	51.636	50.814
Total		120585	11148	100.000	100.000

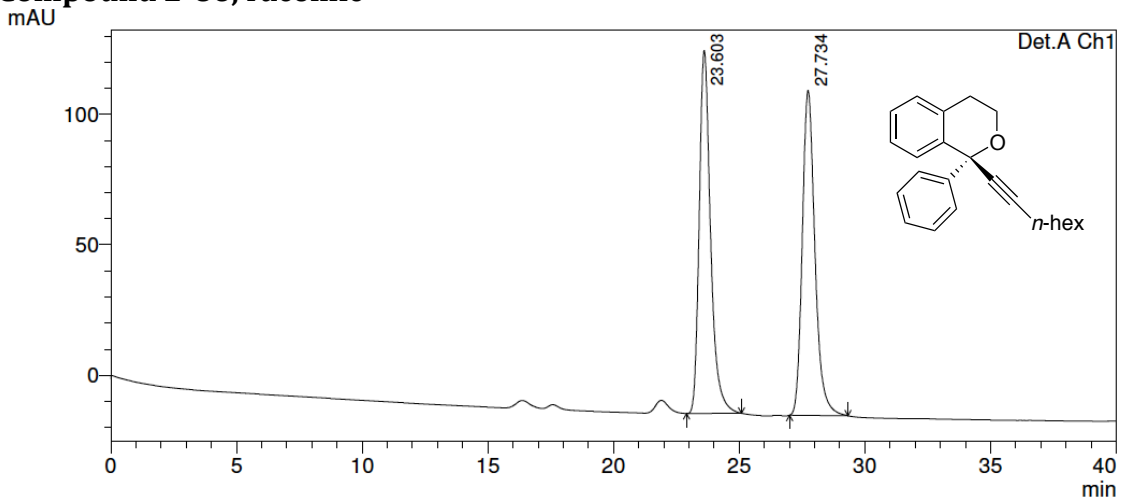
Compound 2-85, 73% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.848	1907067	190782	13.674	14.763
2	7.651	12039386	1101488	86.326	85.237
Total		13946453	1292269	100.000	100.000

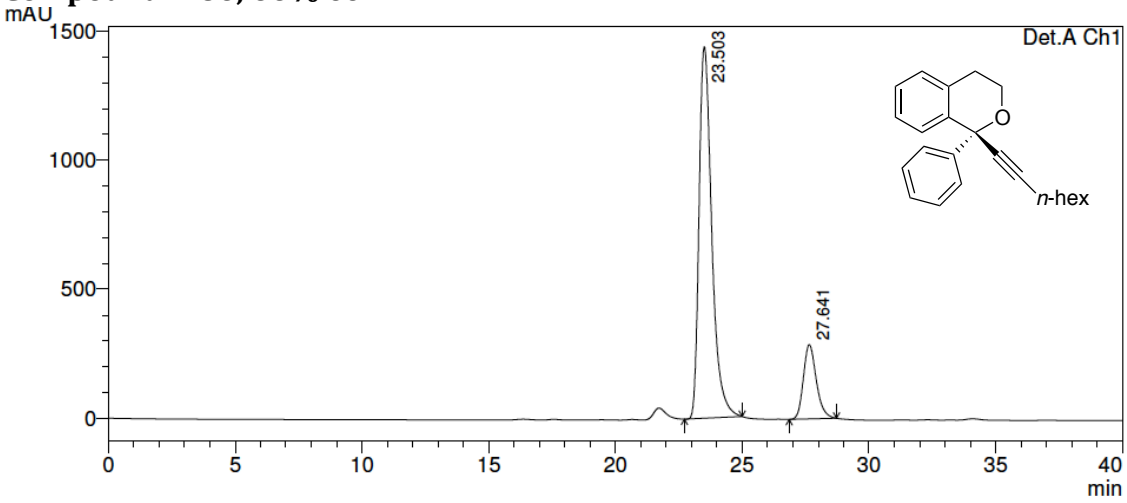
Compound 2-86, racemic



1 Det.A Ch1/220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.603	4372340	139162	49.990	52.748
2	27.734	4374054	124662	50.010	47.252
Total		8746394	263825	100.000	100.000

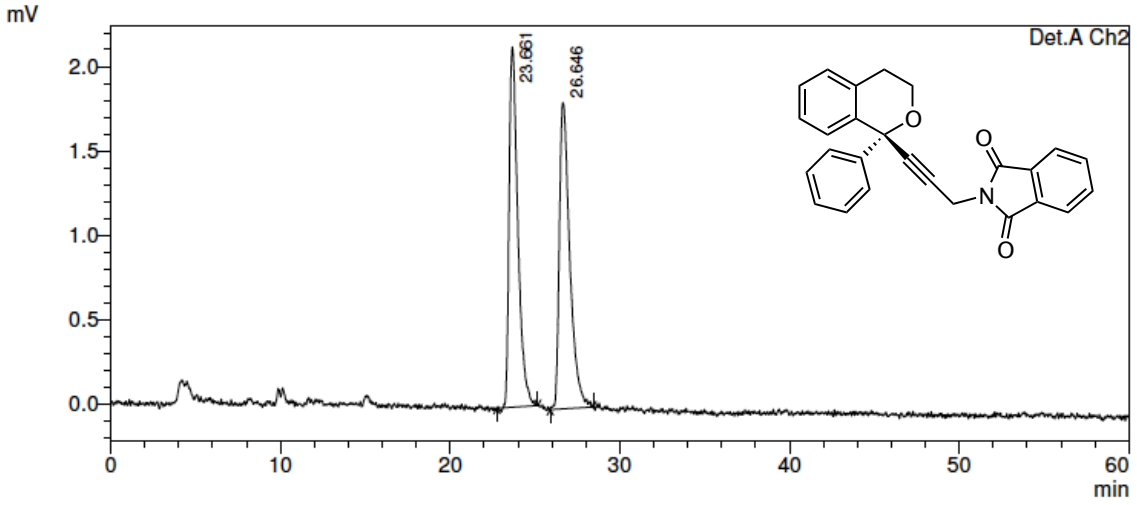
Compound 2-86, 66% ee



1 Det.A Ch1/220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.503	50218036	1440189	83.094	83.358
2	27.641	10216845	287519	16.906	16.642
Total		60434882	1727707	100.000	100.000

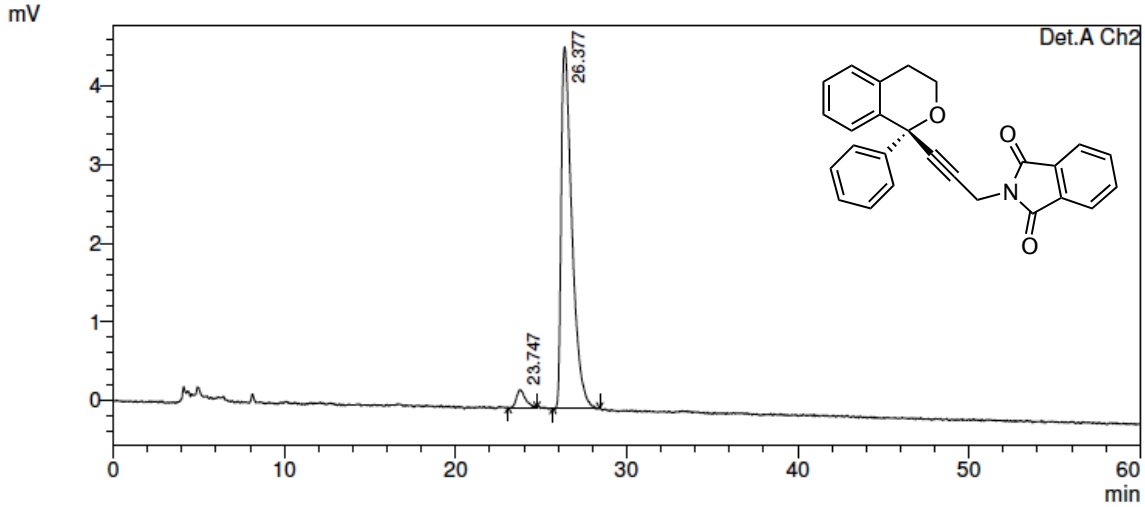
Compound 2-87, racemic



Detector A Ch2 280nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.661	76249	2136	49.571	54.065
2	26.646	77568	1815	50.429	45.935
Total		153818	3951	100.000	100.000

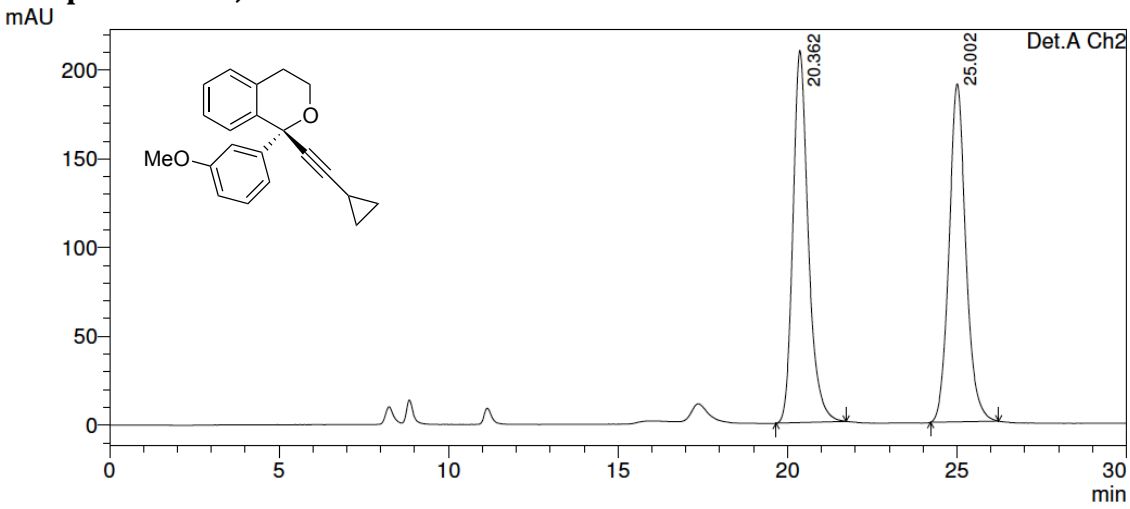
Compound 2-87, 92% ee



Detector A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.747	7880	224	3.803	4.649
2	26.377	199328	4601	96.197	95.351
Total		207208	4825	100.000	100.000

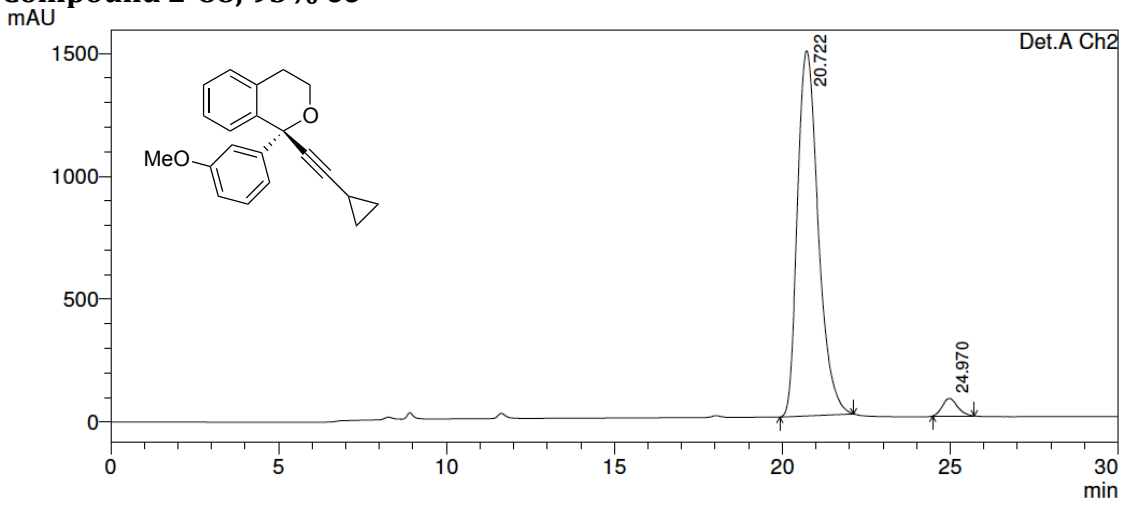
Compound 2-88, racemic



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.362	6611765	209722	50.167	52.421
2	25.002	6567862	190349	49.833	47.579
Total		13179627	400071	100.000	100.000

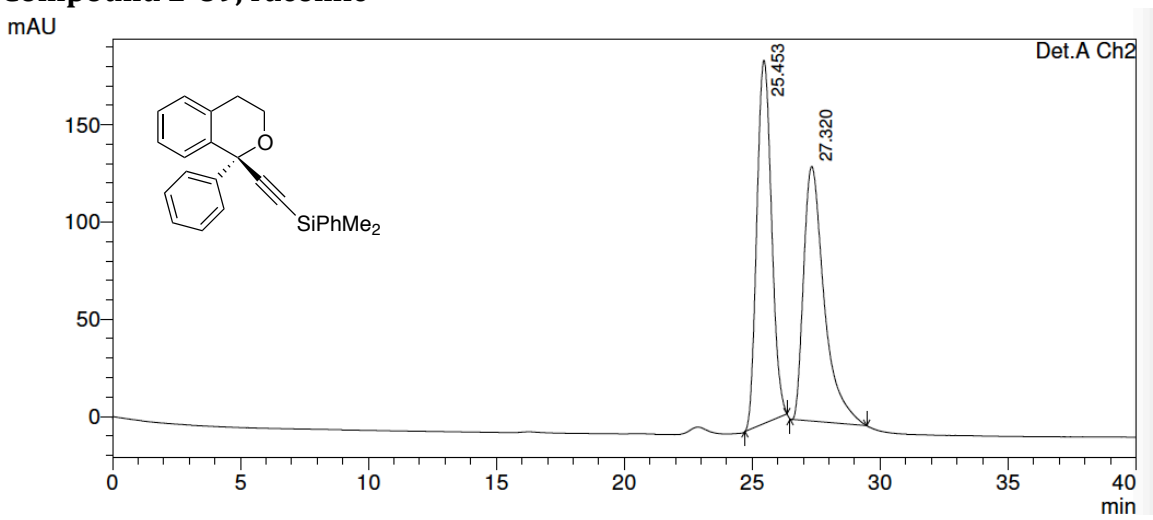
Compound 2-88, 93% ee



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.722	63985287	1486113	96.660	95.441
2	24.970	2210619	70982	3.340	4.559
Total		66195907	1557096	100.000	100.000

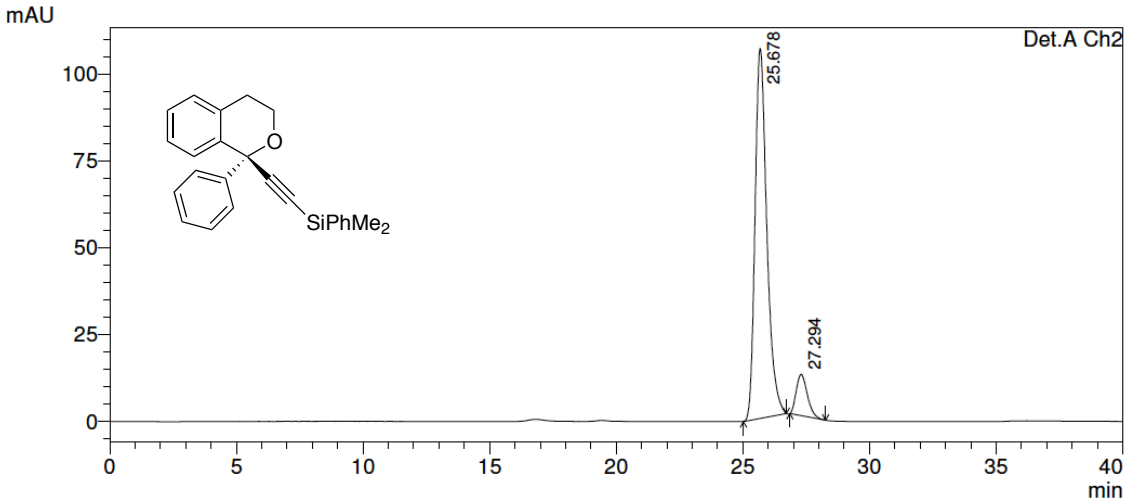
Compound 2-89, racemic



Detector A Ch2 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.453	7446429	186860	50.308	58.792
2	27.320	7355236	130973	49.692	41.208
Total		14801665	317833	100.000	100.000

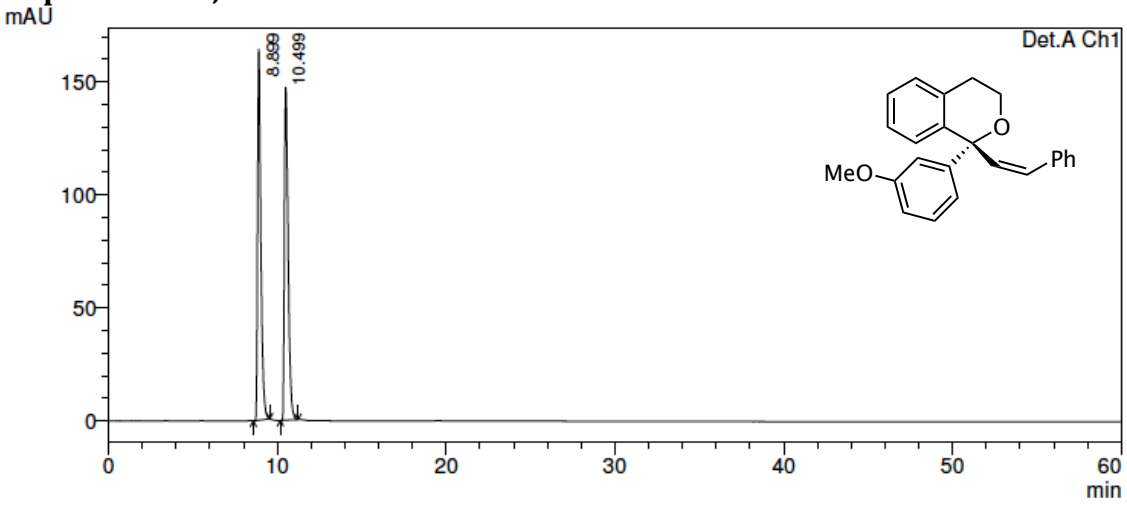
Compound 2-89, 81% ee



Detector A Ch2 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.678	3436456	106412	90.446	89.960
2	27.294	363014	11876	9.554	10.040
Total		3799470	118288	100.000	100.000

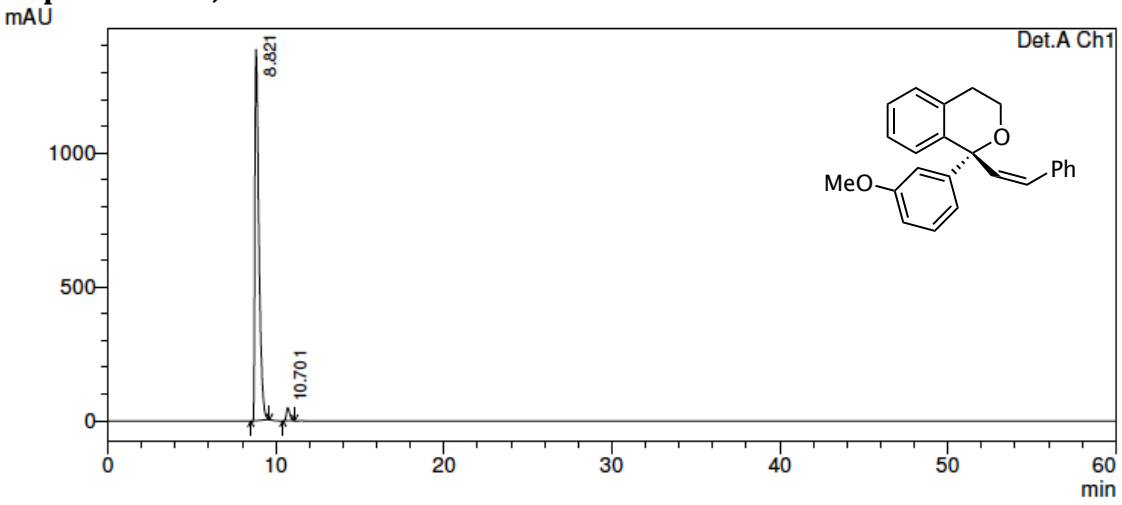
Compound 2-93, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.899	2237329	164162	50.086	52.717
2	10.499	2229648	147241	49.914	47.283
Total		4466977	311402	100.000	100.000

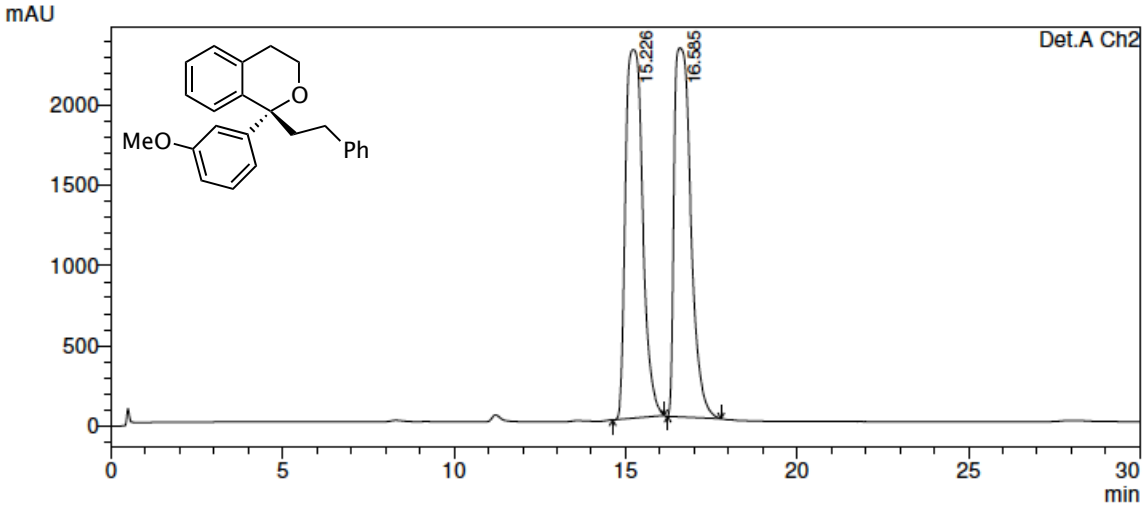
Compound 2-93, 94% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.821	22911107	1384670	97.088	96.620
2	10.701	687089	48442	2.912	3.380
Total		23598196	1433113	100.000	100.000

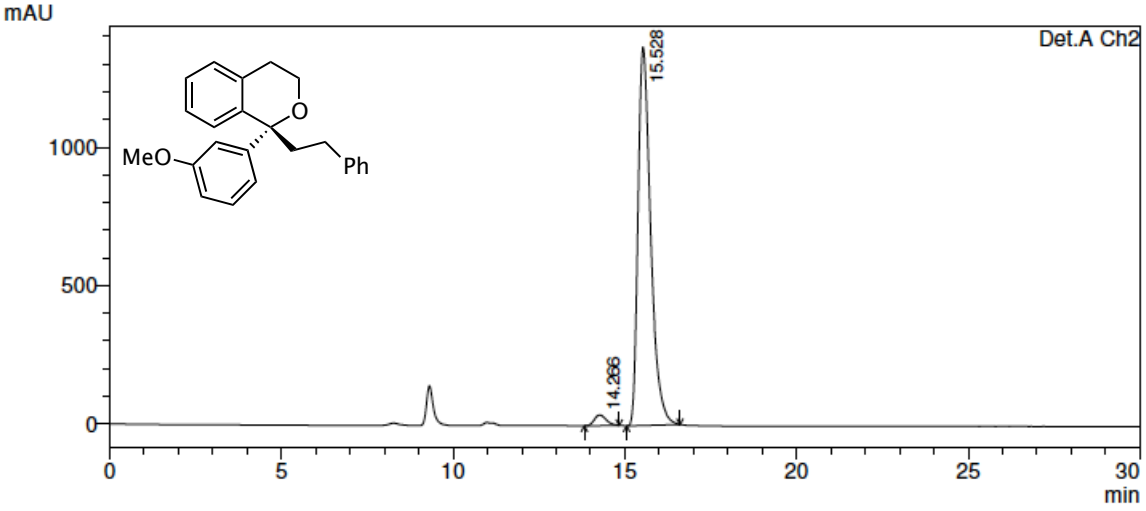
Compound 2-94, racemic



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.226	80122734	2297499	50.683	49.972
2	16.585	77964558	2300031	49.317	50.028
Total		158087292	4597529	100.000	100.000

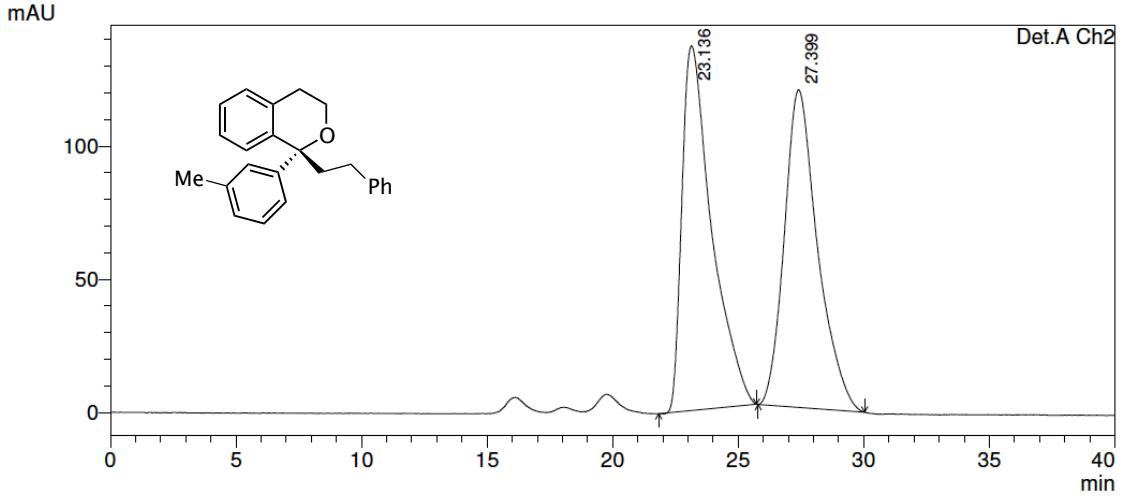
Compound 2-94, 95% ee



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.266	934747	38597	2.598	2.746
2	15.528	35040612	1366928	97.402	97.254
Total		35975359	1405526	100.000	100.000

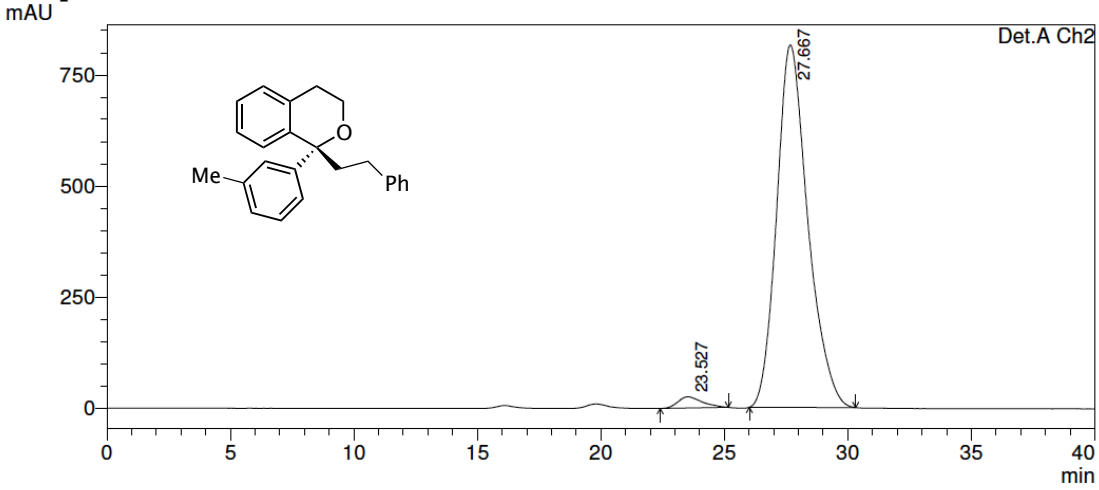
Compound 2-95, racemic



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.136	11283422	136984	50.630	53.437
2	27.399	11002501	119362	49.370	46.563
Total		22285923	256346	100.000	100.000

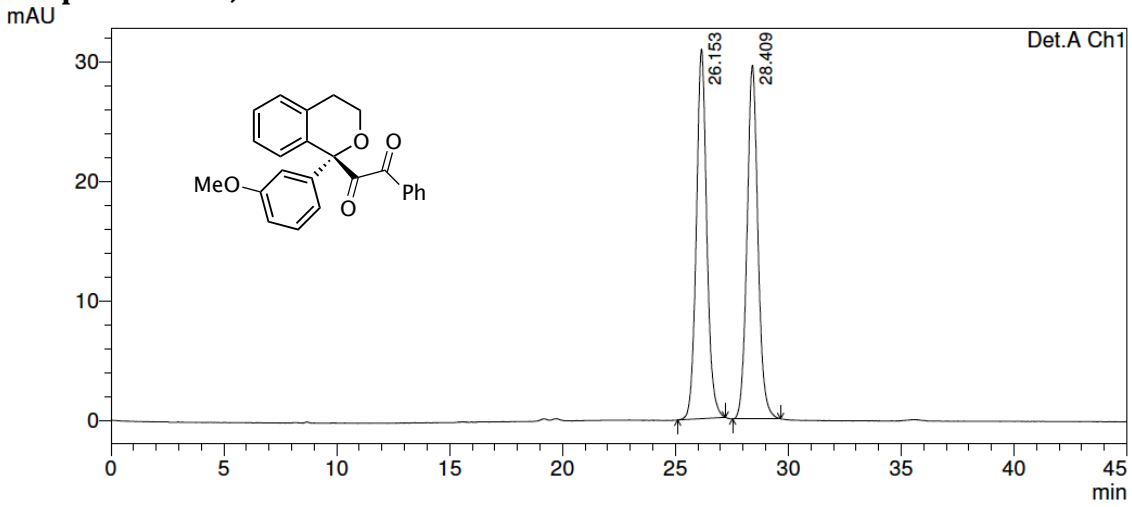
Compound 2-95, 95% ee



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.527	1738649	25224	2.364	2.999
2	27.667	71820543	815994	97.636	97.001
Total		73559192	841218	100.000	100.000

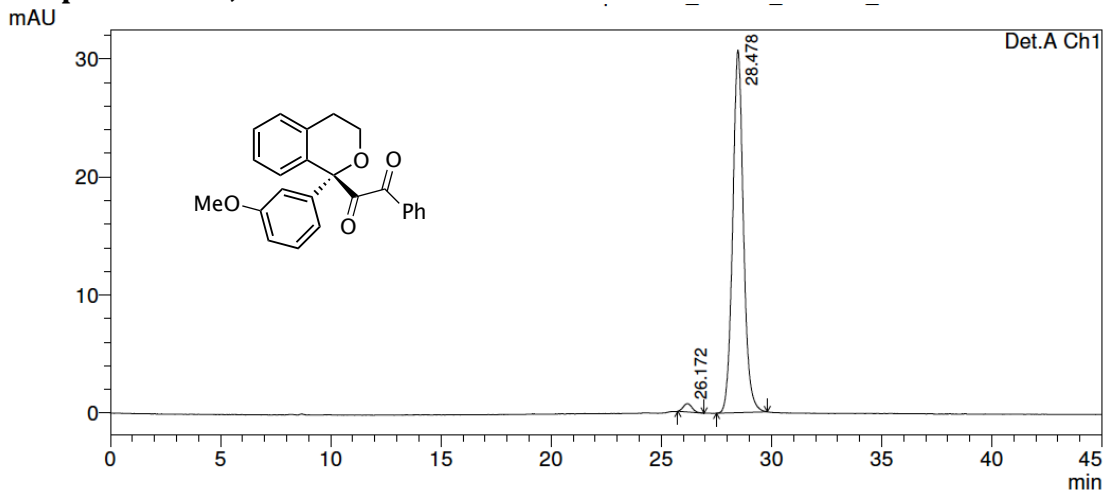
Compound 2-96, racemic



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.153	996623	30942	49.994	51.103
2	28.409	996843	29607	50.006	48.897
Total		1993466	60548	100.000	100.000

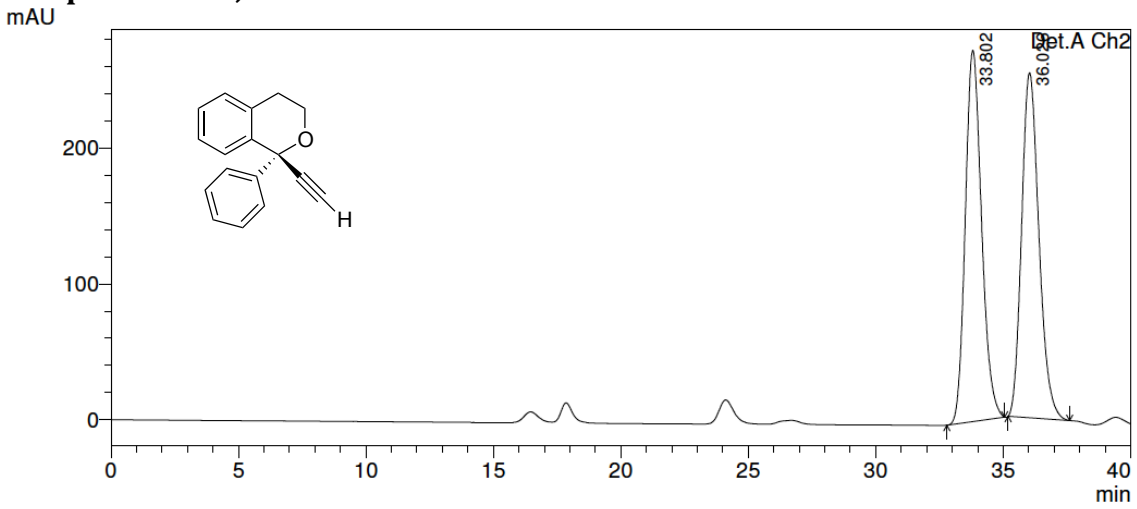
Compound 2-96, 96% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.172	19246	700	1.810	2.229
2	28.478	1044153	30710	98.190	97.771
Total		1063399	31410	100.000	100.000

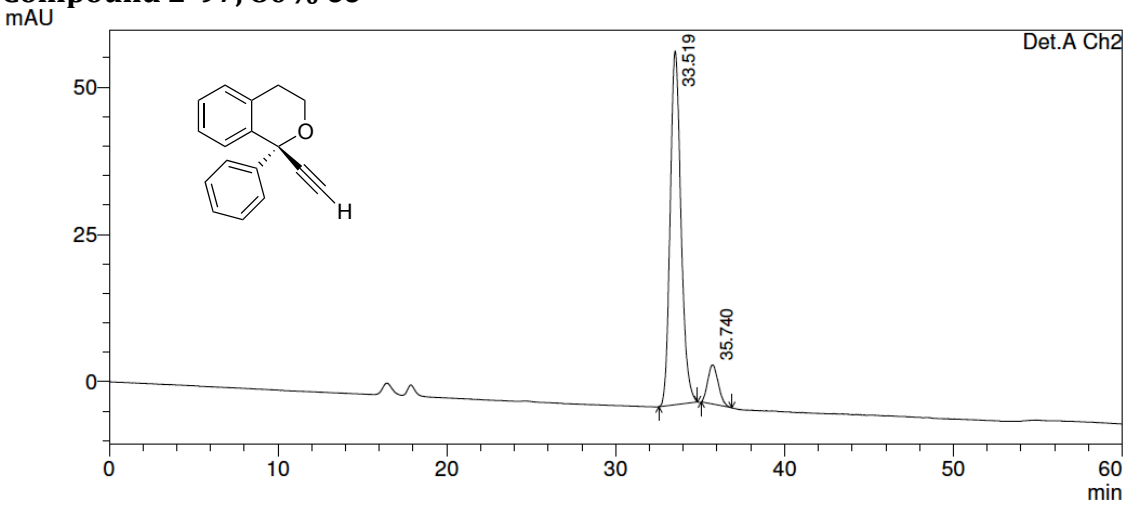
Compound 2-97, racemic



Detector A Ch2 210nm

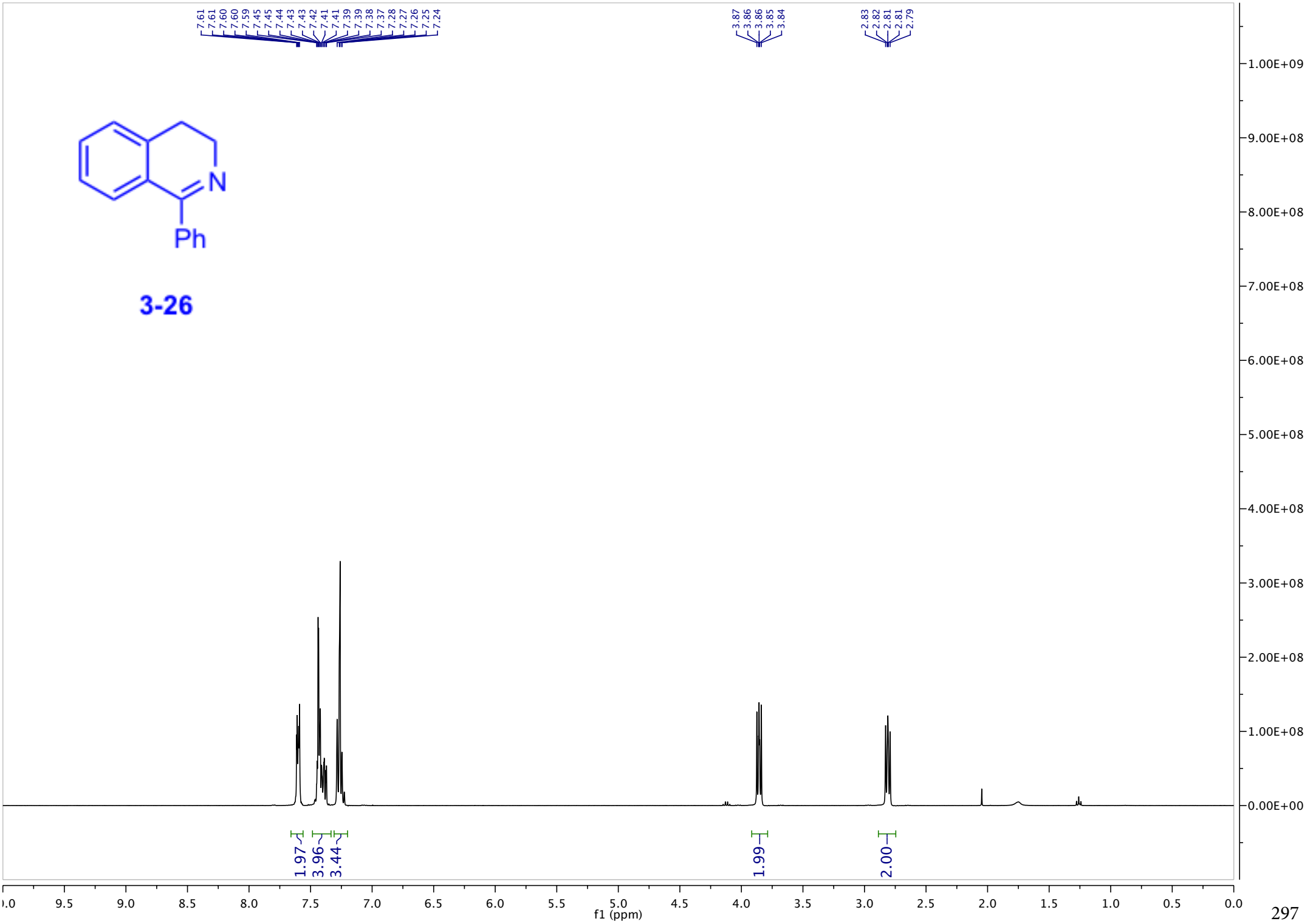
Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.802	12151686	273500	50.344	51.828
2	36.026	11985637	254204	49.656	48.172
Total		24137323	527704	100.000	100.000

Compound 2-97, 80% ee



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.519	2671897	60094	90.205	89.984
2	35.740	290133	6689	9.795	10.016
Total		2962029	66783	100.000	100.000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7.45
7.44
7.43
7.43
7.42
7.41
7.41
7.39
7.39
7.38
7.37
7.28
7.27
7.26
7.25
7.24
3.87
3.86
3.86
3.85
3.84
2.83
2.82
2.81
2.81
2.79
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Ph
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9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
1.97
3.96
3.44
1.99
2.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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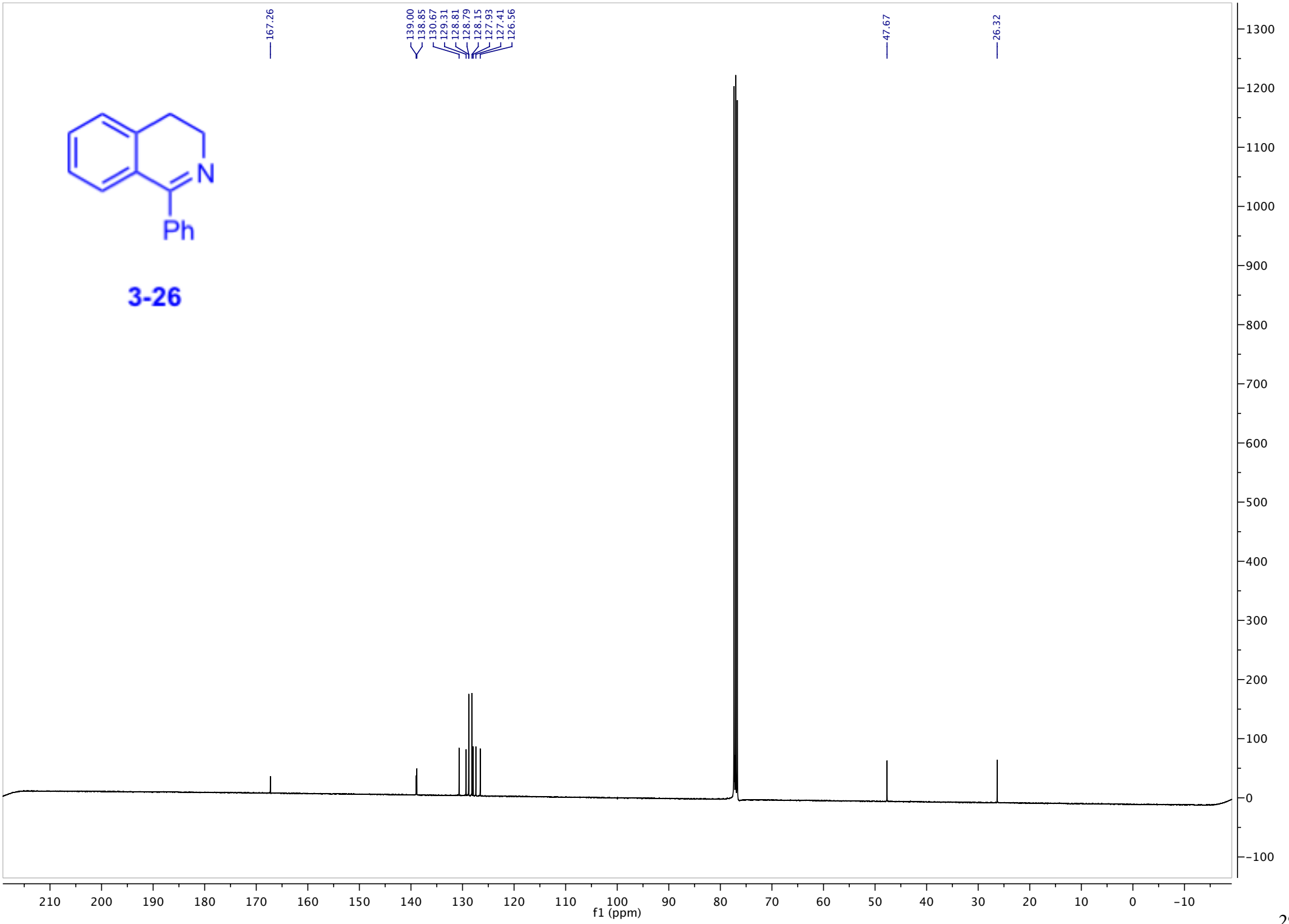
1.5
1.0
0.5
0.0
f1 (ppm)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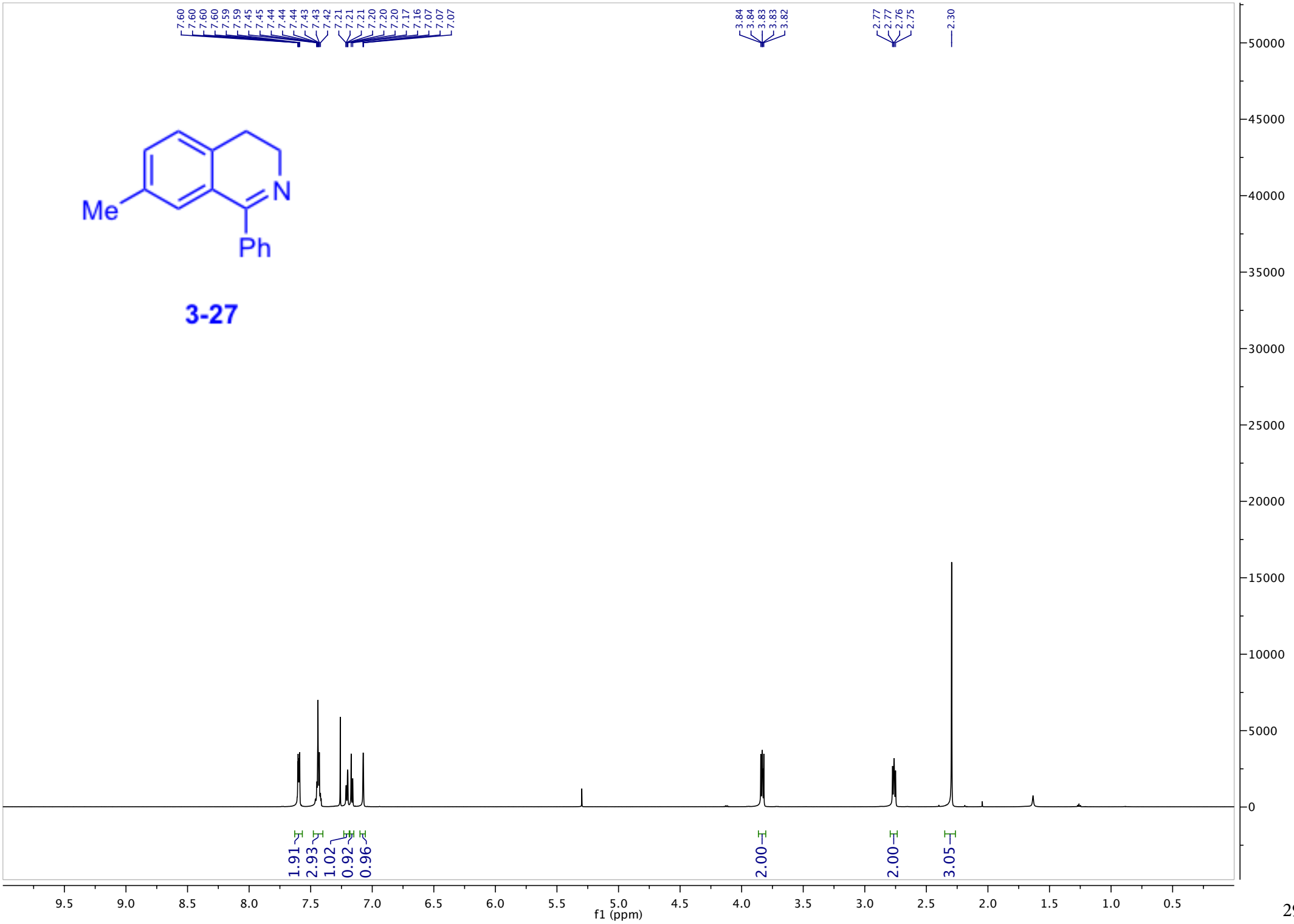
128.15
127.93
127.41
126.56
47.67
26.32
N
Ph
3-26
f1 (ppm)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7.43
7.43
7.42
7.21
7.21
7.21
7.20
7.20
7.20
7.17
7.16
7.07
7.07
7.07
3.84
3.84
3.83
3.83
3.82
2.77
2.77
2.76
2.75
2.30
Me
N
Ph
3-27
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
1.91
2.93
1.02
0.92
0.96
2.00
2.00
3.05
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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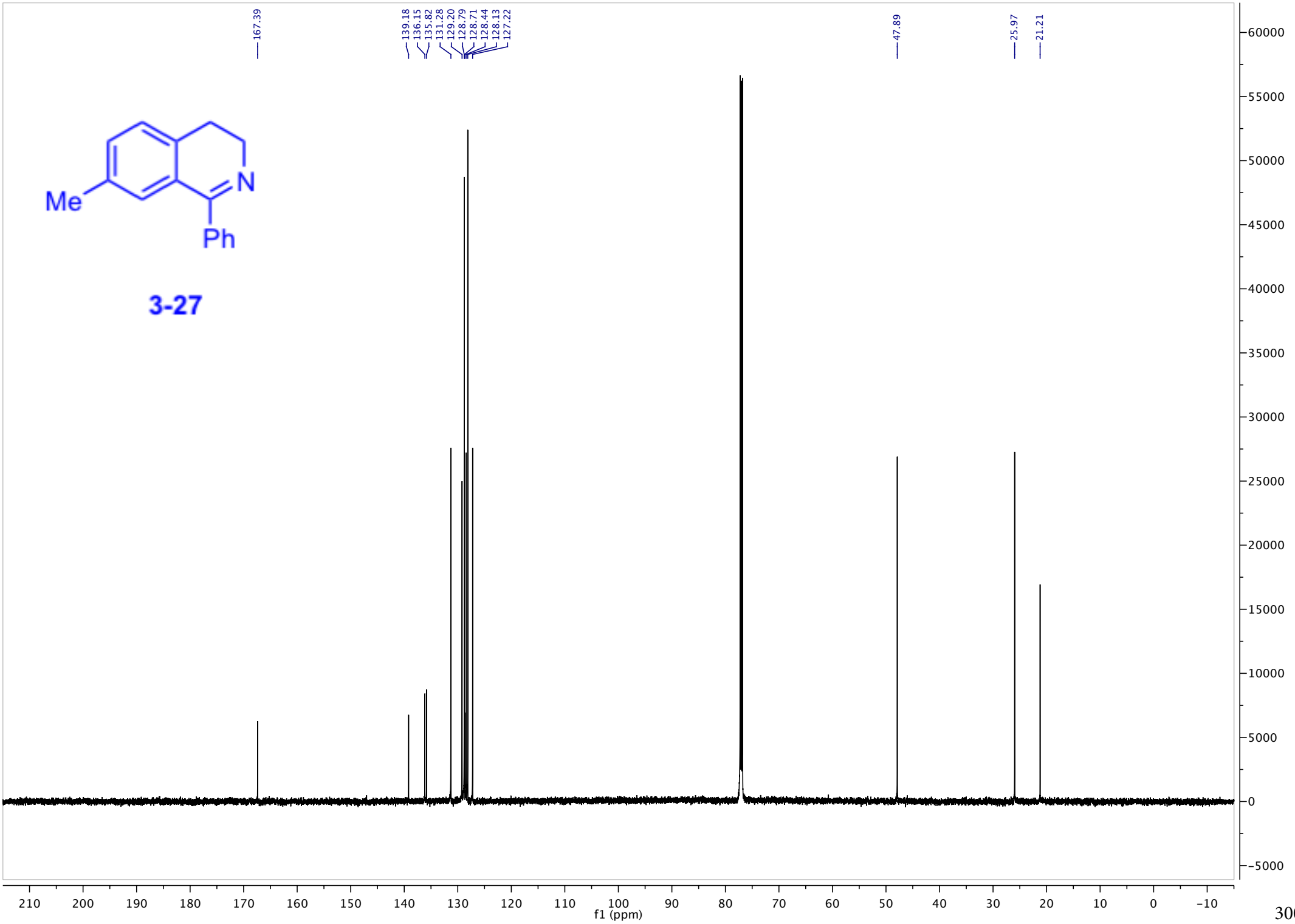
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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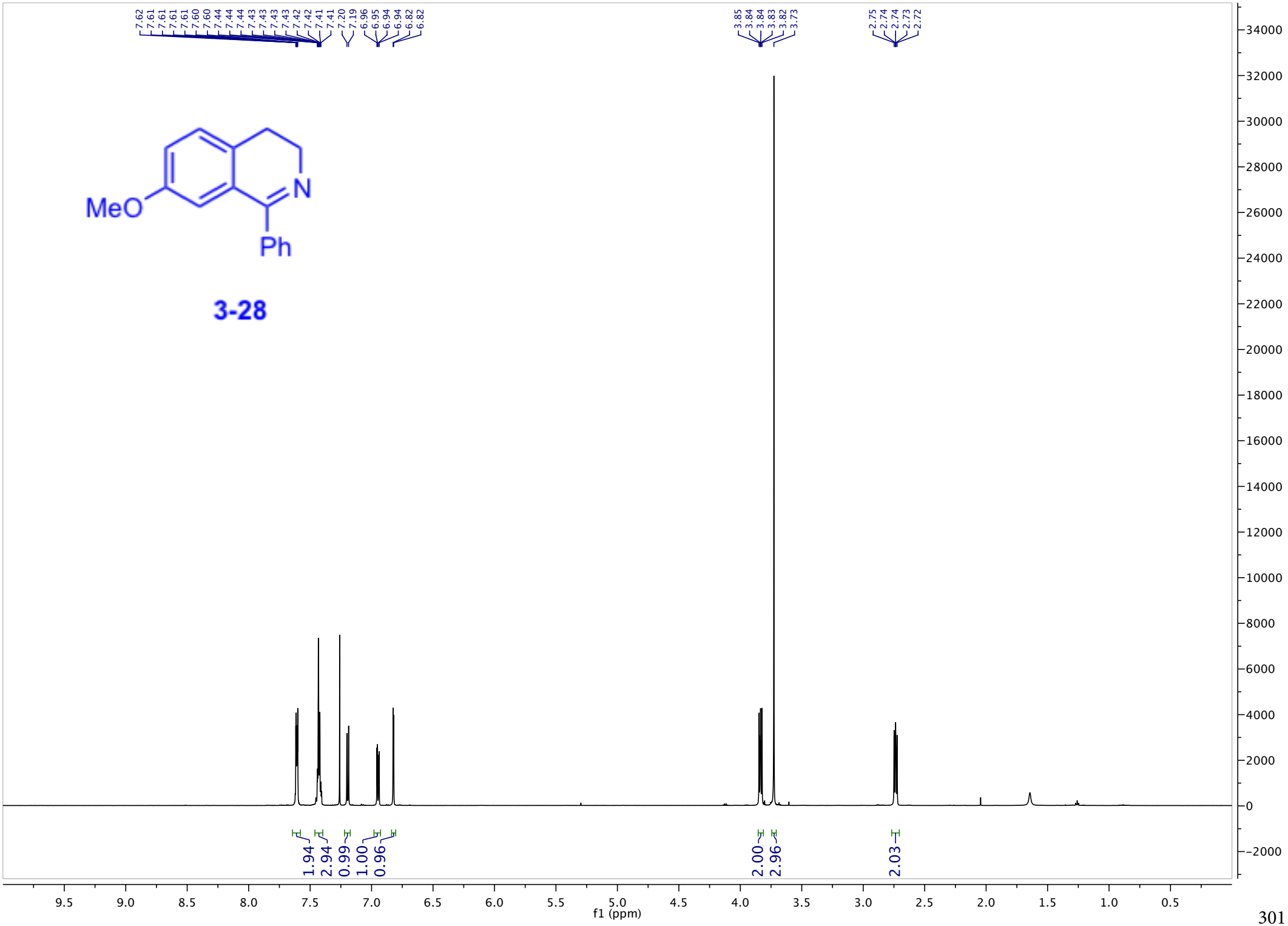
128.13
127.22
47.89
25.97
21.21
Me
N
Ph
3-27
f1 (ppm)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7.61
7.61
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7.60
7.60
7.44
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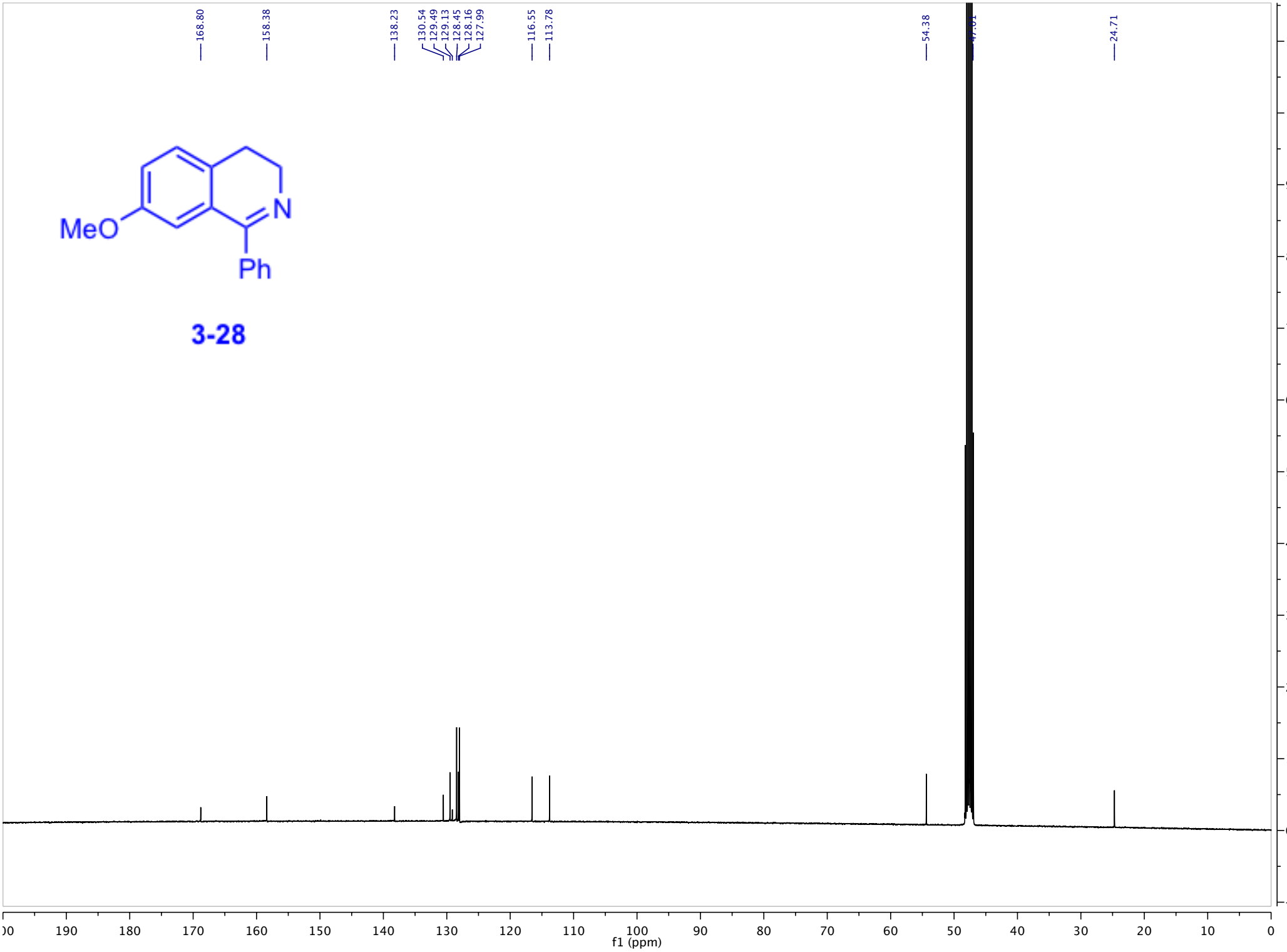
7.43
7.43
7.42
7.42
7.41
7.41
7.20
7.19
6.96
6.95
6.94
6.94
6.82
6.82
3.85
3.84
3.84
3.83
3.82
3.73
2.75
2.74
2.74
2.73
2.72
MeO
N
Ph
3-28
1.94
2.94
0.99
1.00
0.96
2.00
2.96
2.03
f1 (ppm)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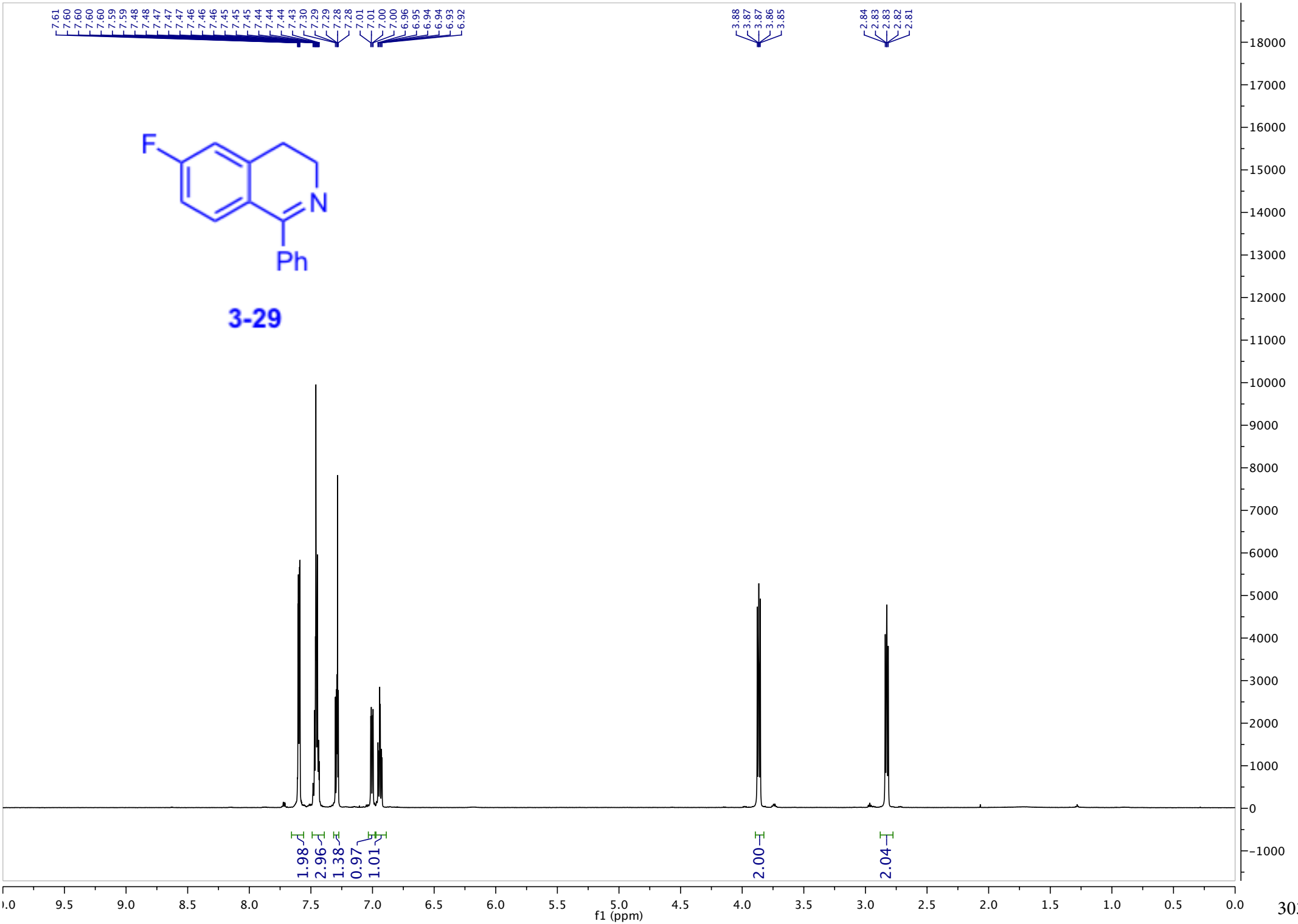
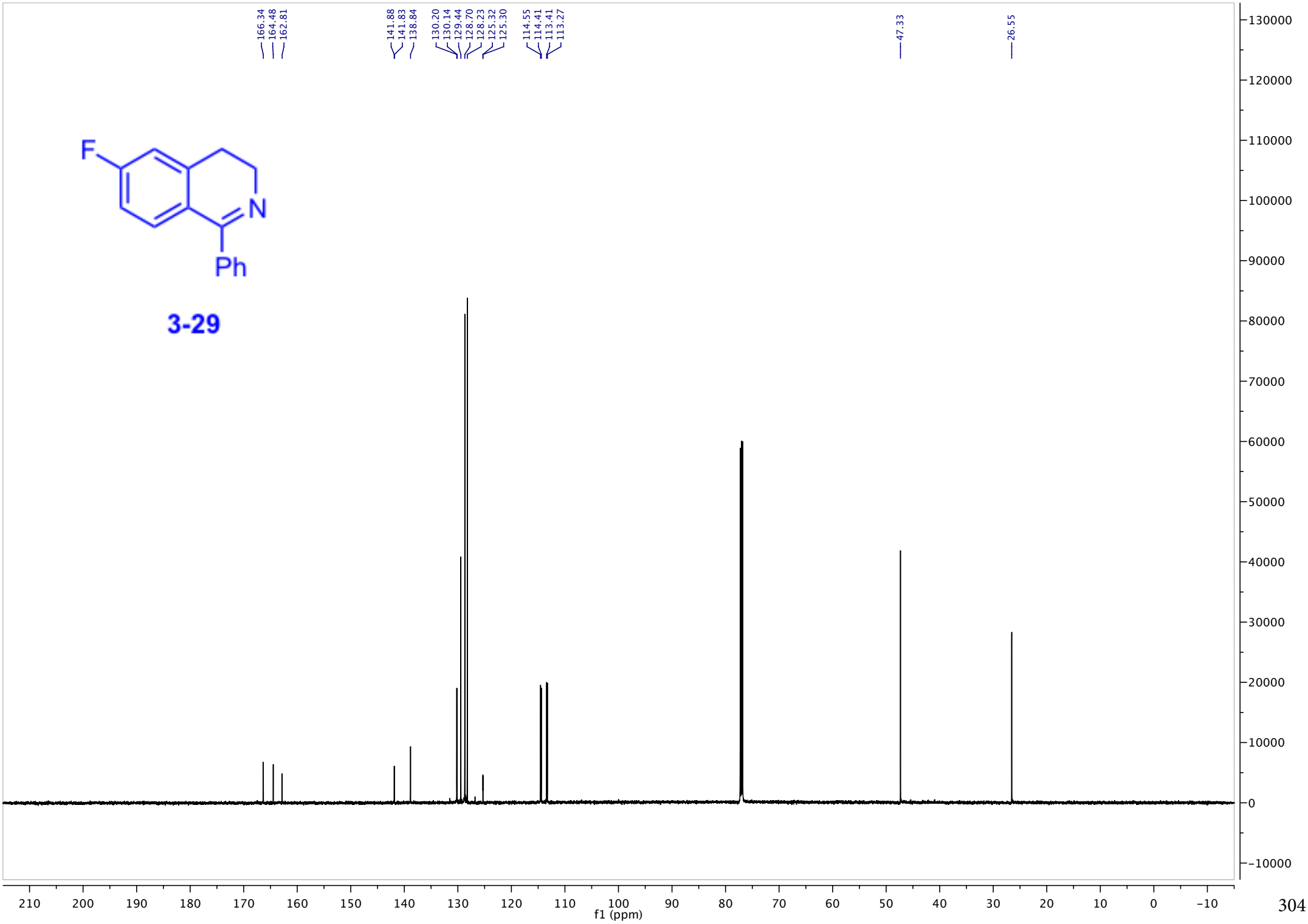
158.38
138.23
130.54
129.49
129.13
128.45
128.16
127.99
116.55
113.78
54.38
47.01
24.71
MeO
N
Ph
3-28
f1 (ppm)


7.61 7.60 7.60 7.60 7.59 7.59 7.48 7.48 7.47 7.47 7.47 7.46 7.46 7.45 7.45 7.45 7.44 7.44 7.44 7.43 7.30 7.29 7.29 7.28 7.28 7.01 7.01 7.00 7.00 6.96 6.95 6.94 6.94 6.93 6.92
3.88 3.87 3.87 3.86 3.85
2.84 2.83 2.83 2.82 2.81
F
N
Ph
3-29
1.98 2.96 1.38 0.97 1.01 2.00 2.04
f1 (ppm)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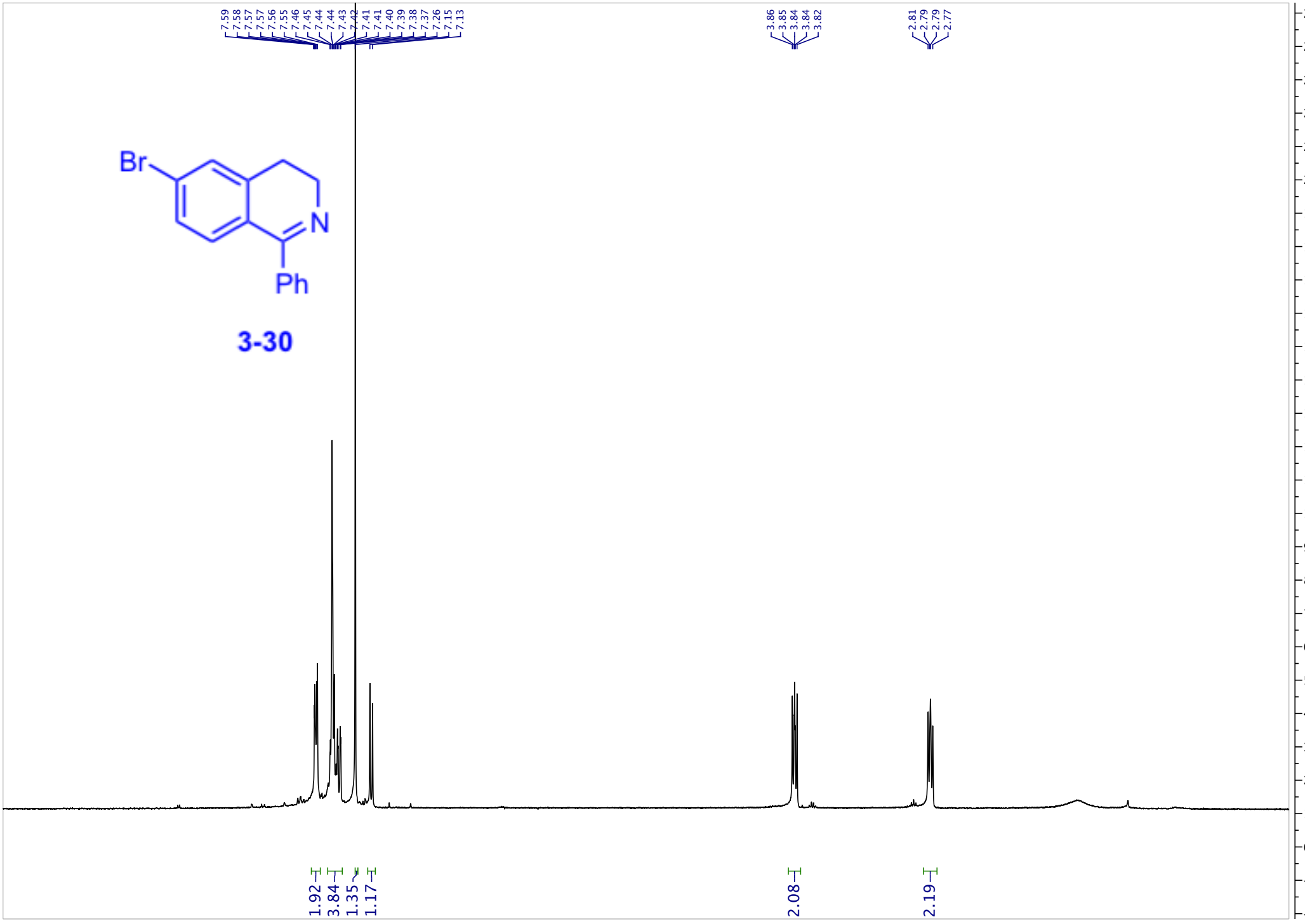
141.88
141.83
138.84
130.20
130.14
129.44
128.70
128.23
125.32
125.30
114.55
114.41
113.41
113.27
47.33
26.55
F
N
Ph
3-29
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
−10000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)


7.59
7.58
7.57
7.57
7.56
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7.44
7.43
7.42
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7.37
7.26
7.15
7.13
3.86
3.85
3.84
3.84
3.82
2.81
2.79
2.79
2.77
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Ph
3-30
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3.84
1.35
1.17
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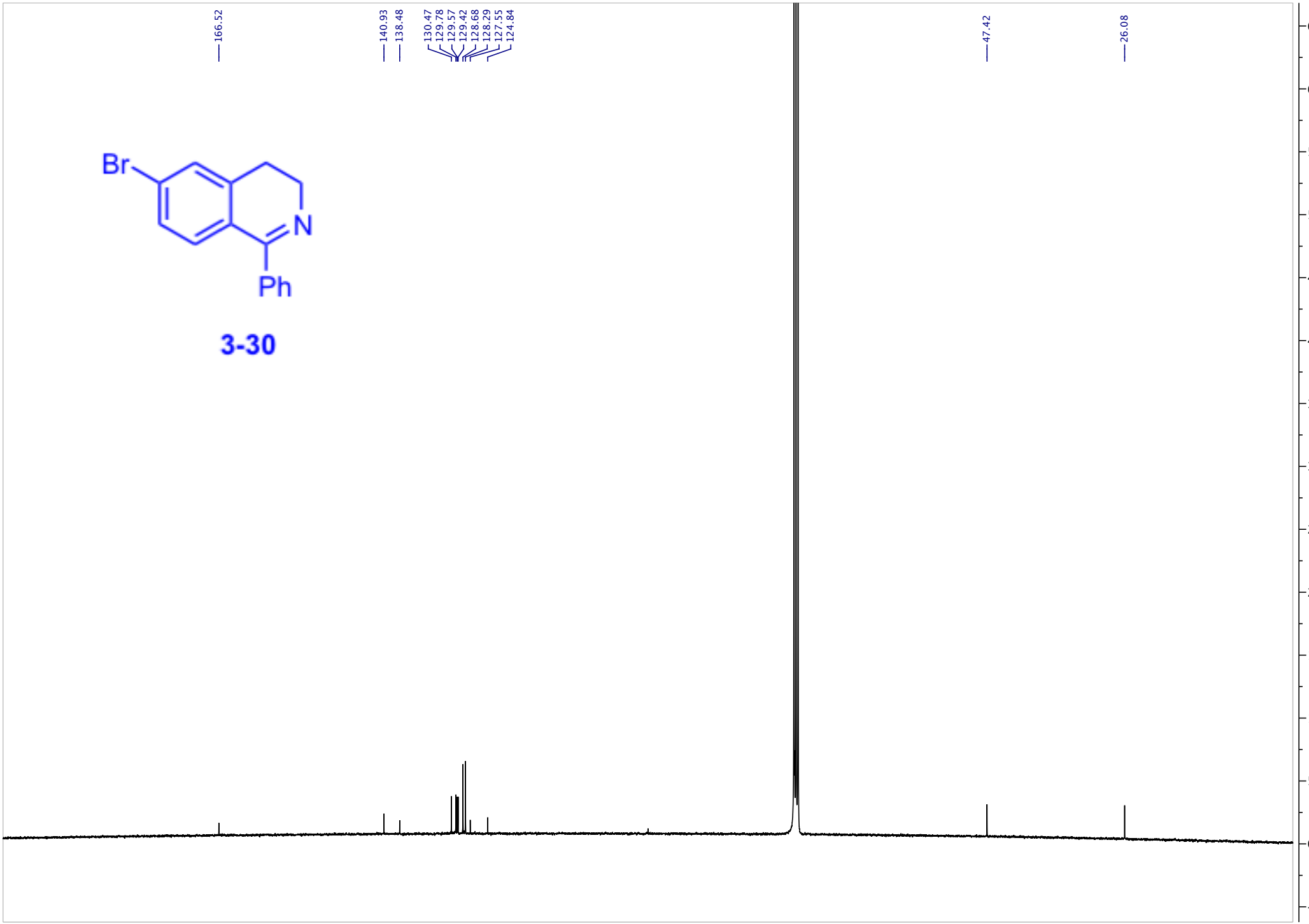
2.19
f1 (ppm)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130.47
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129.57
129.42
128.68
128.29
127.55
124.84
47.42
26.08
Br
N
Ph
3-30
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
190
180
170
160
150
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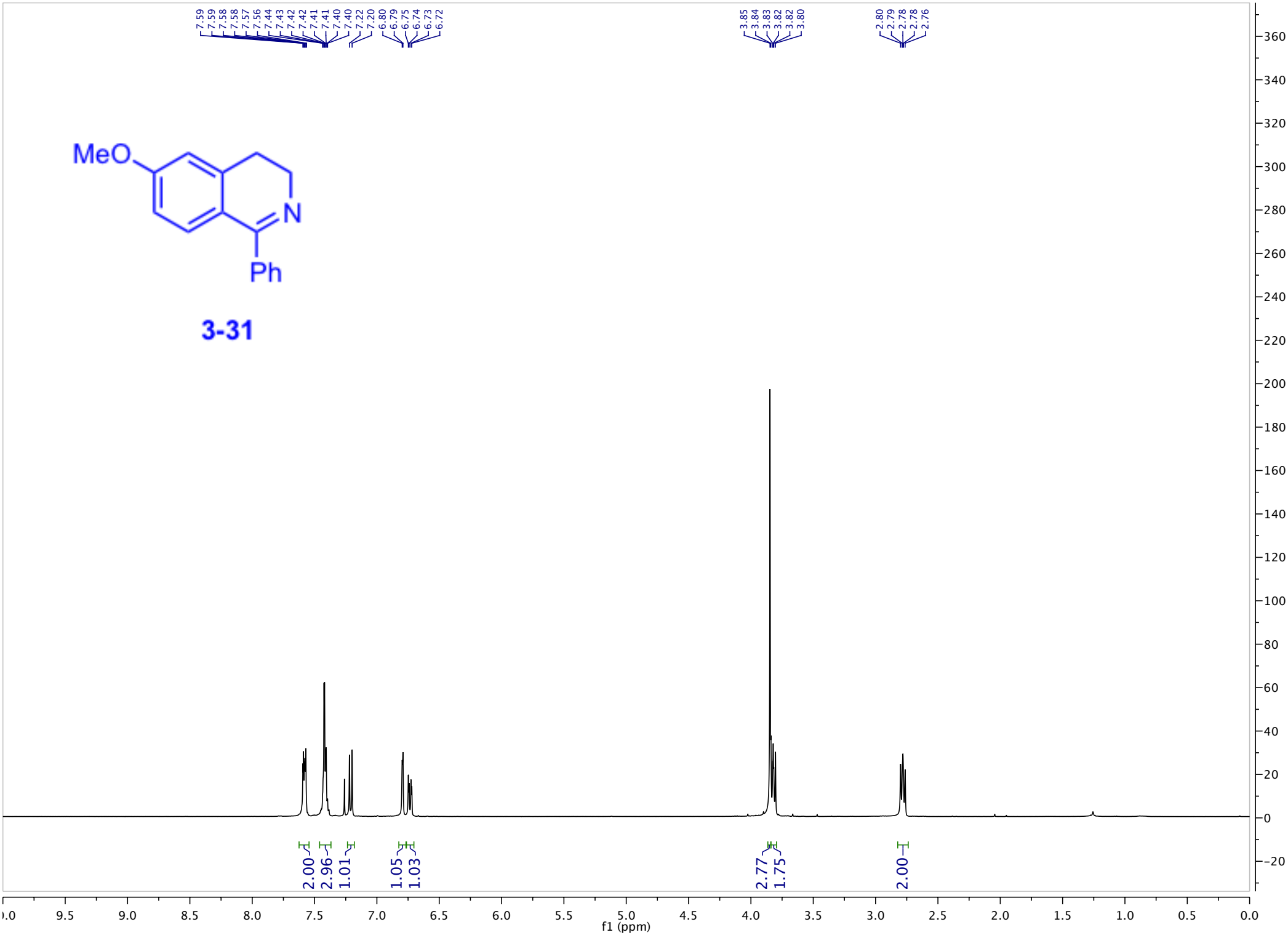
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.42
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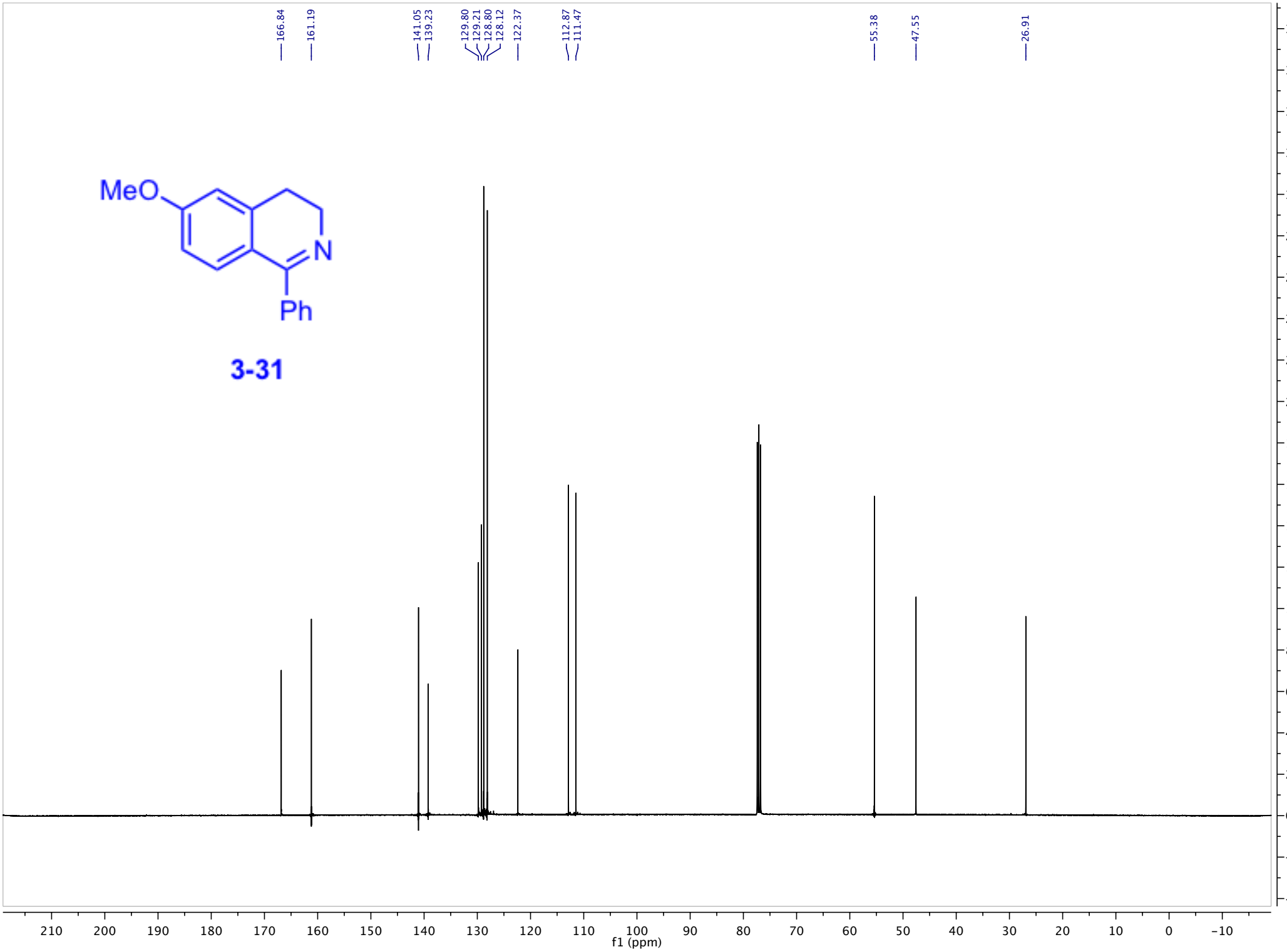
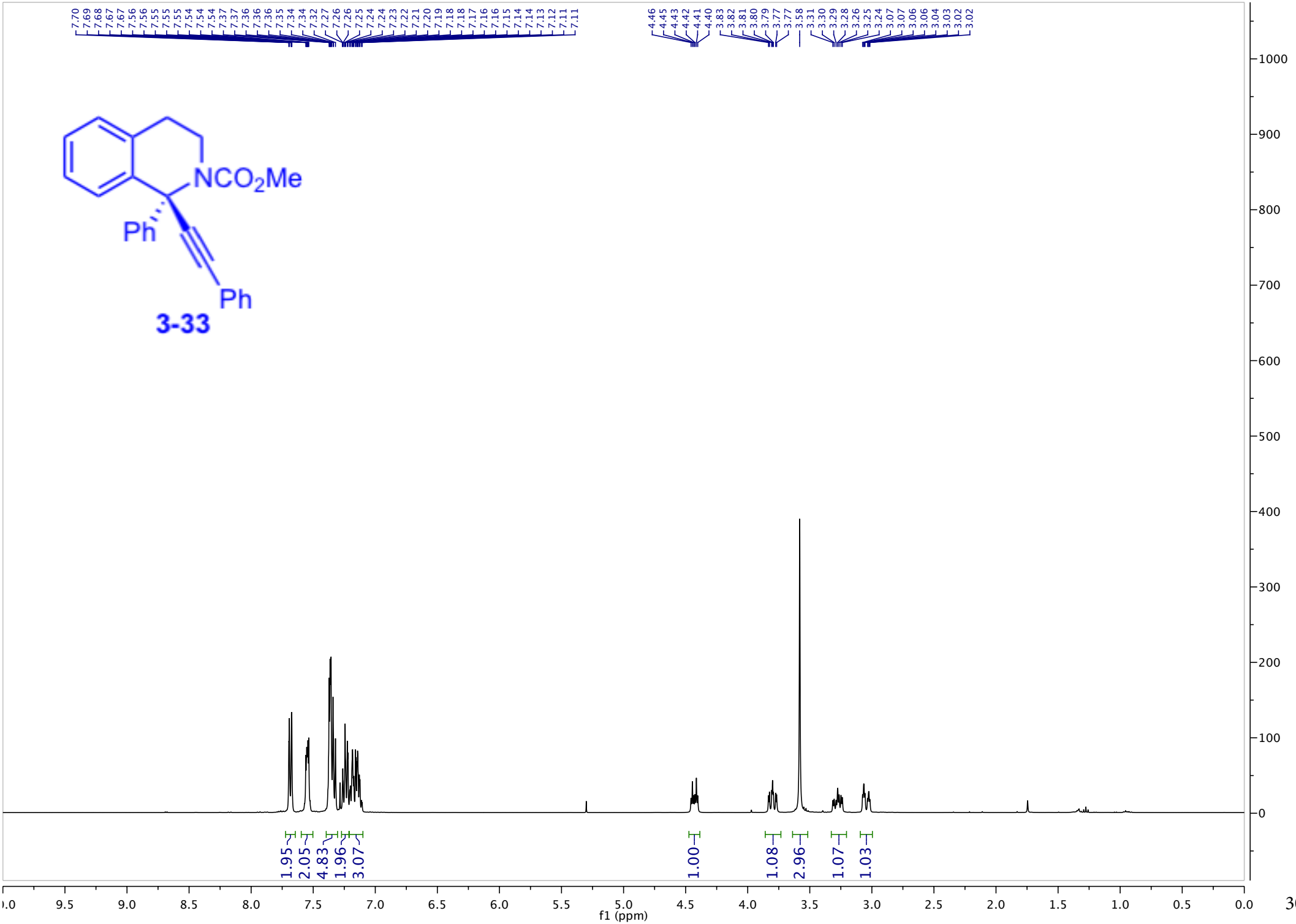
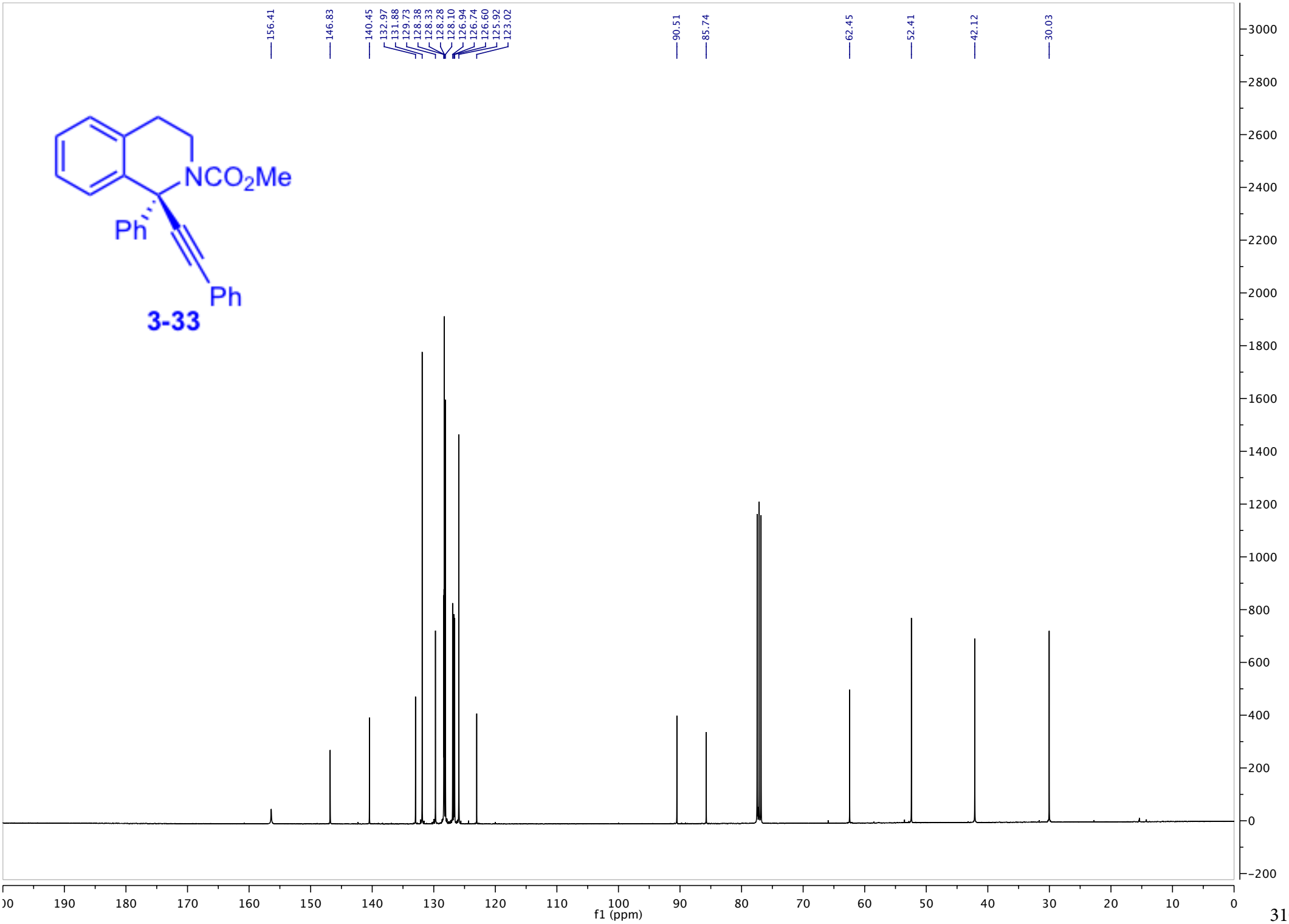
7.41
7.41
7.40
7.40
7.22
7.20
6.80
6.79
6.75
6.74
6.73
6.72
3.85
3.84
3.83
3.82
3.82
3.80
2.80
2.79
2.78
2.78
2.76
MeO
N
Ph
3-31
2.00
2.96
1.01
1.05
1.03
2.77
1.75
2.00
f1 (ppm)


166.84
161.19
141.05
139.23
129.80
129.21
128.80
128.12
122.37
112.87
111.47
55.38
47.55
26.91
MeO
N
Ph
3-31
f1 (ppm)


7.70 7.69 7.68 7.67 7.67 7.56 7.56 7.55 7.55 7.55 7.54 7.54 7.54 7.37 7.37 7.36 7.36 7.36 7.35 7.34 7.34 7.32 7.27 7.26 7.26 7.25 7.24 7.24 7.23 7.22 7.21 7.20 7.19 7.18 7.18 7.17 7.16 7.16 7.15 7.14 7.14 7.13 7.12 7.11 7.11
4.46 4.45 4.43 4.42 4.41 4.40 3.83 3.82 3.81 3.80 3.79 3.77 3.77 3.58 3.31 3.30 3.29 3.28 3.26 3.25 3.24 3.07 3.07 3.06 3.06 3.04 3.03 3.02 3.02
NCO2Me
Ph
Ph
3-33
1.95 2.05 4.83 1.96 3.07 1.00 1.08 2.96 1.07 1.03
f1 (ppm)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146.83
140.45
132.97
131.88
129.73
128.38
128.33
128.28
128.10
126.94
126.74
126.60
125.92
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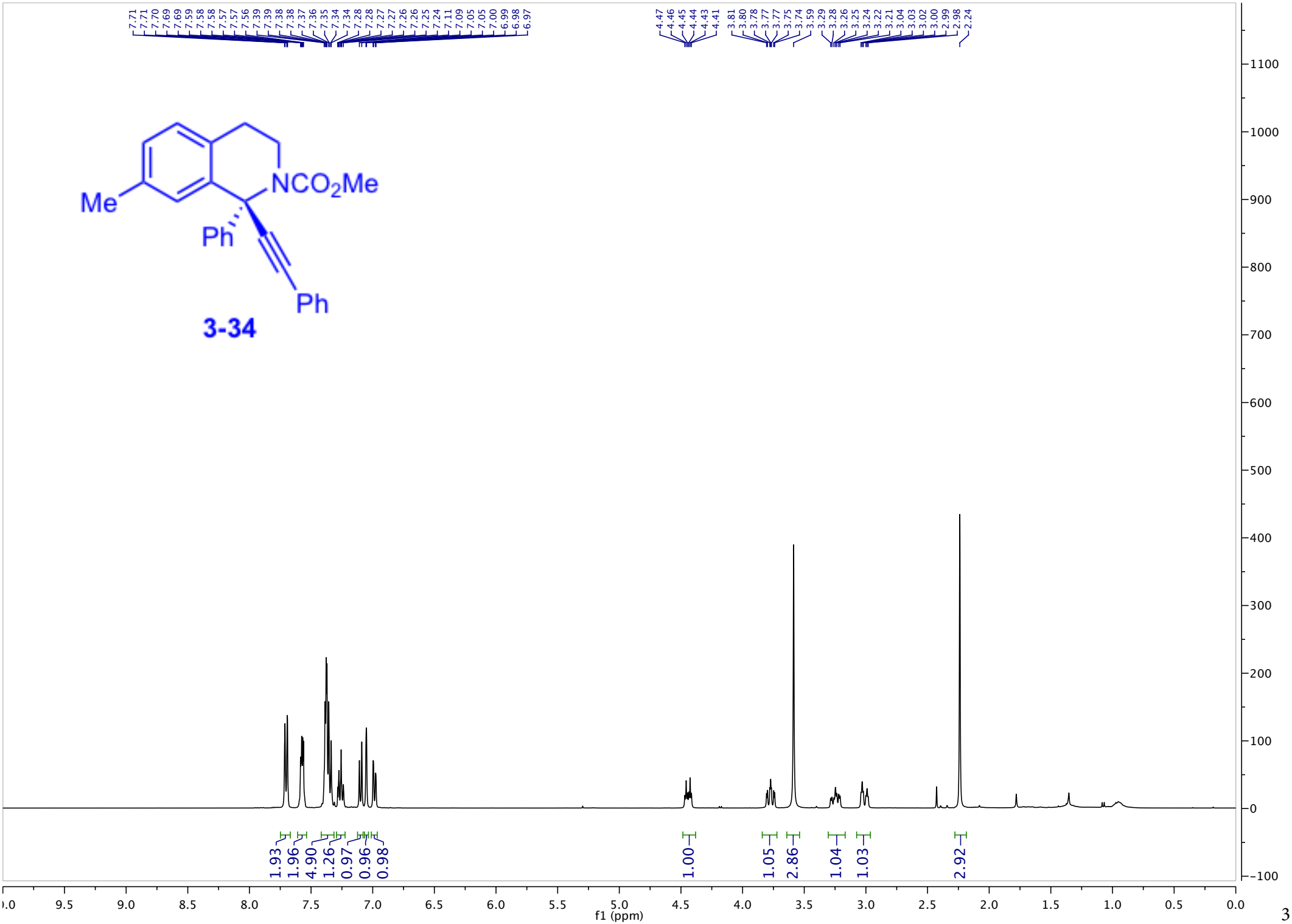
30.03
NCO2Me
Ph
Ph
3-33
f1 (ppm)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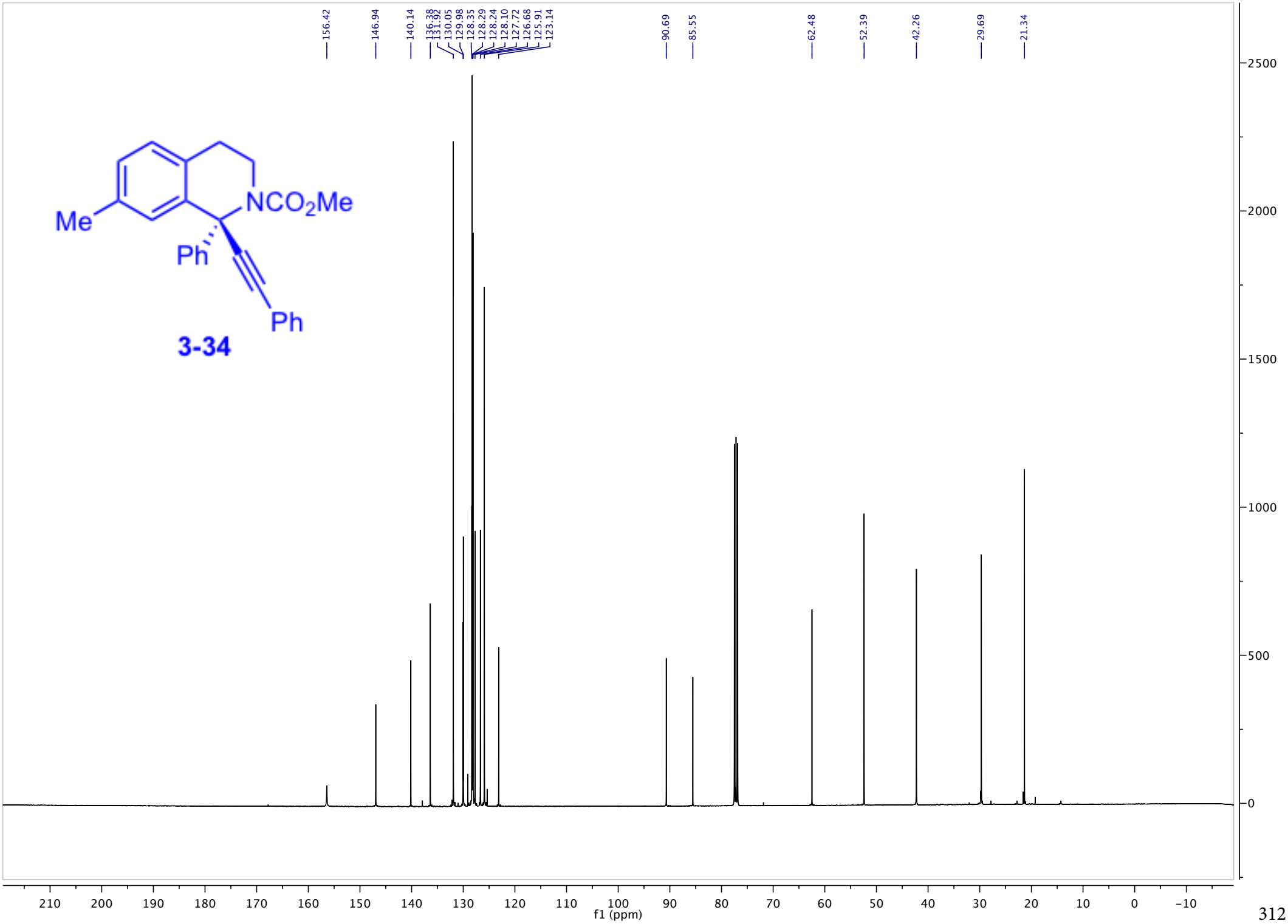
4.47 4.46 4.45 4.44 4.43 4.41 3.81 3.80 3.78 3.77 3.77 3.75 3.74 3.59 3.29 3.28 3.26 3.25 3.24 3.22 3.21 3.04 3.03 3.02 3.00 2.99 2.98 2.24
Me
NCO2Me
Ph
Ph
3-34
1.93 1.96 4.90 1.26 0.97 0.96 0.98
1.00 1.05 2.86 1.04 1.03 2.92
f1 (ppm)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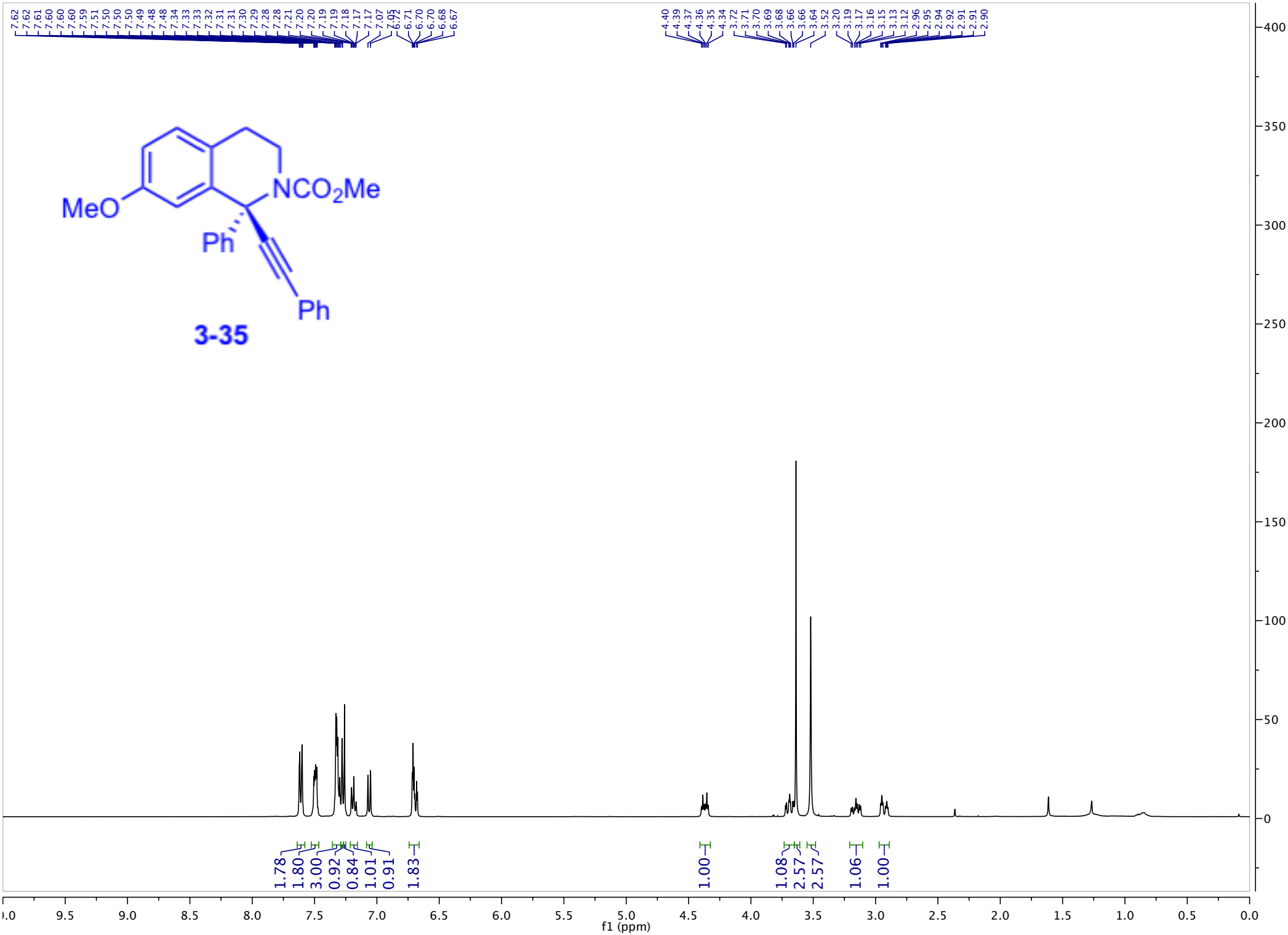
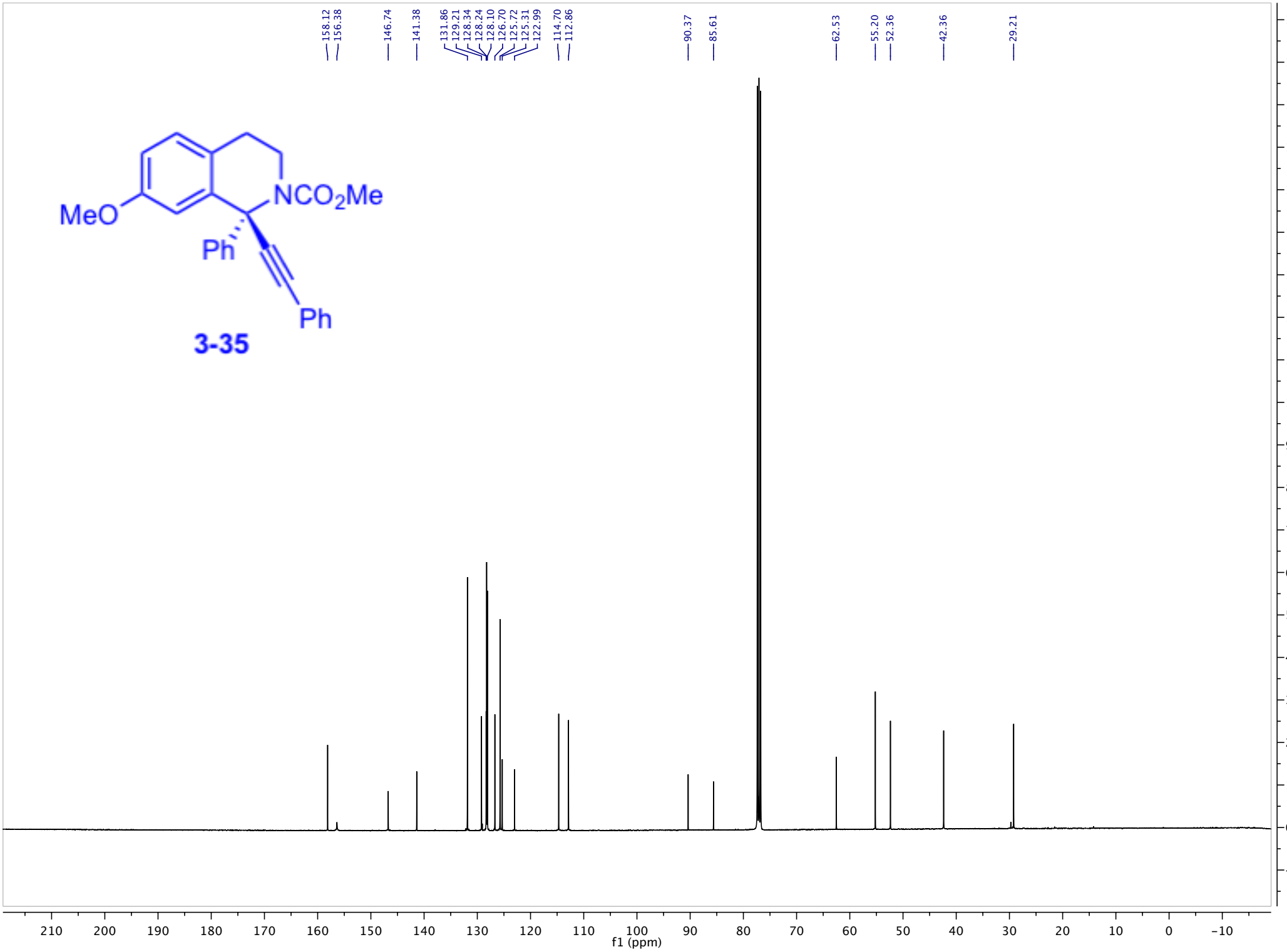
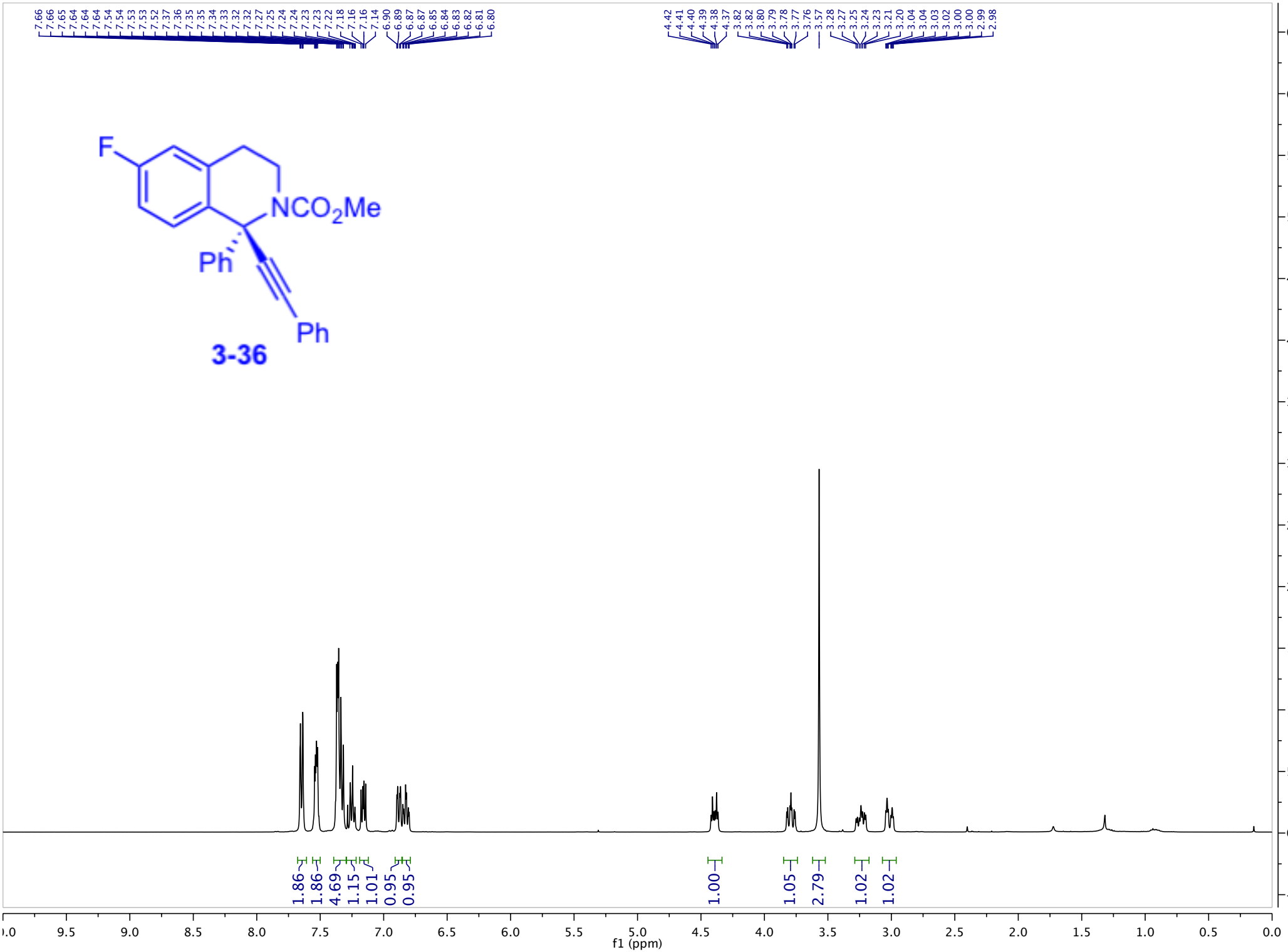
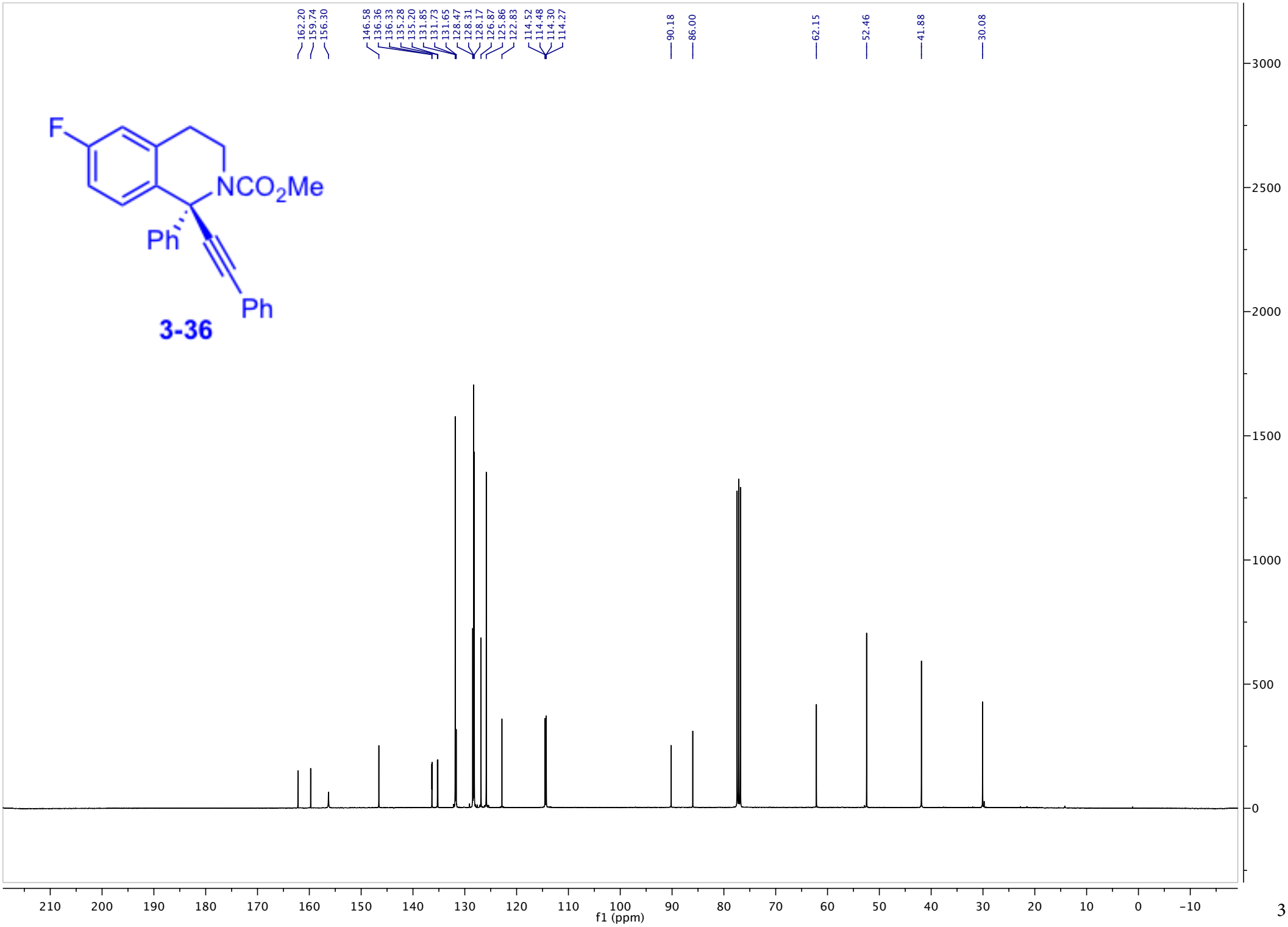
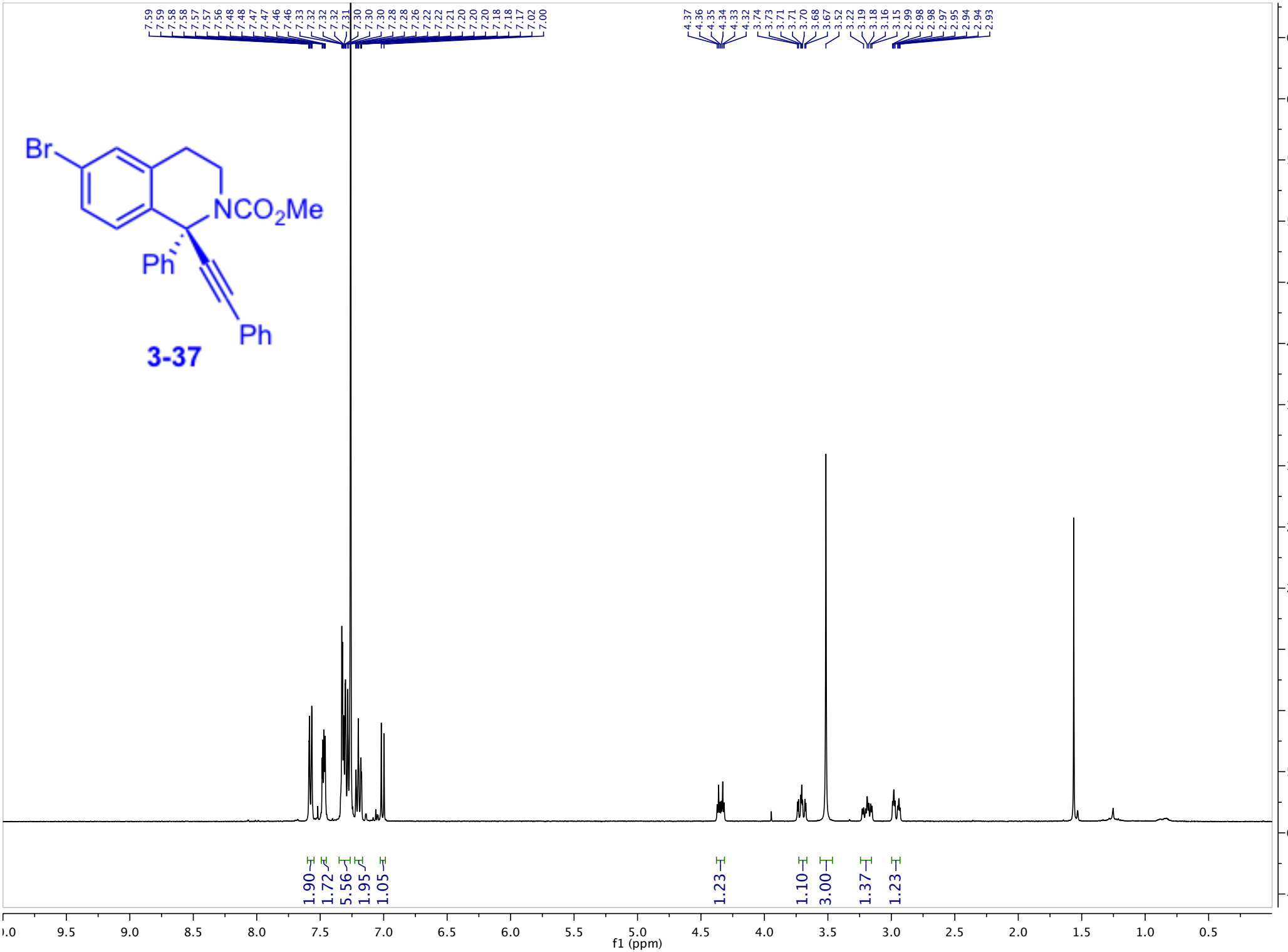
146.94
140.14
136.38
131.92
130.05
129.98
128.35
128.29
128.24
128.10
127.72
126.68
125.91
123.14
90.69
85.55
62.48
52.39
42.26
29.69
21.34
Me
NCO2Me
Ph
Ph
3-34
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

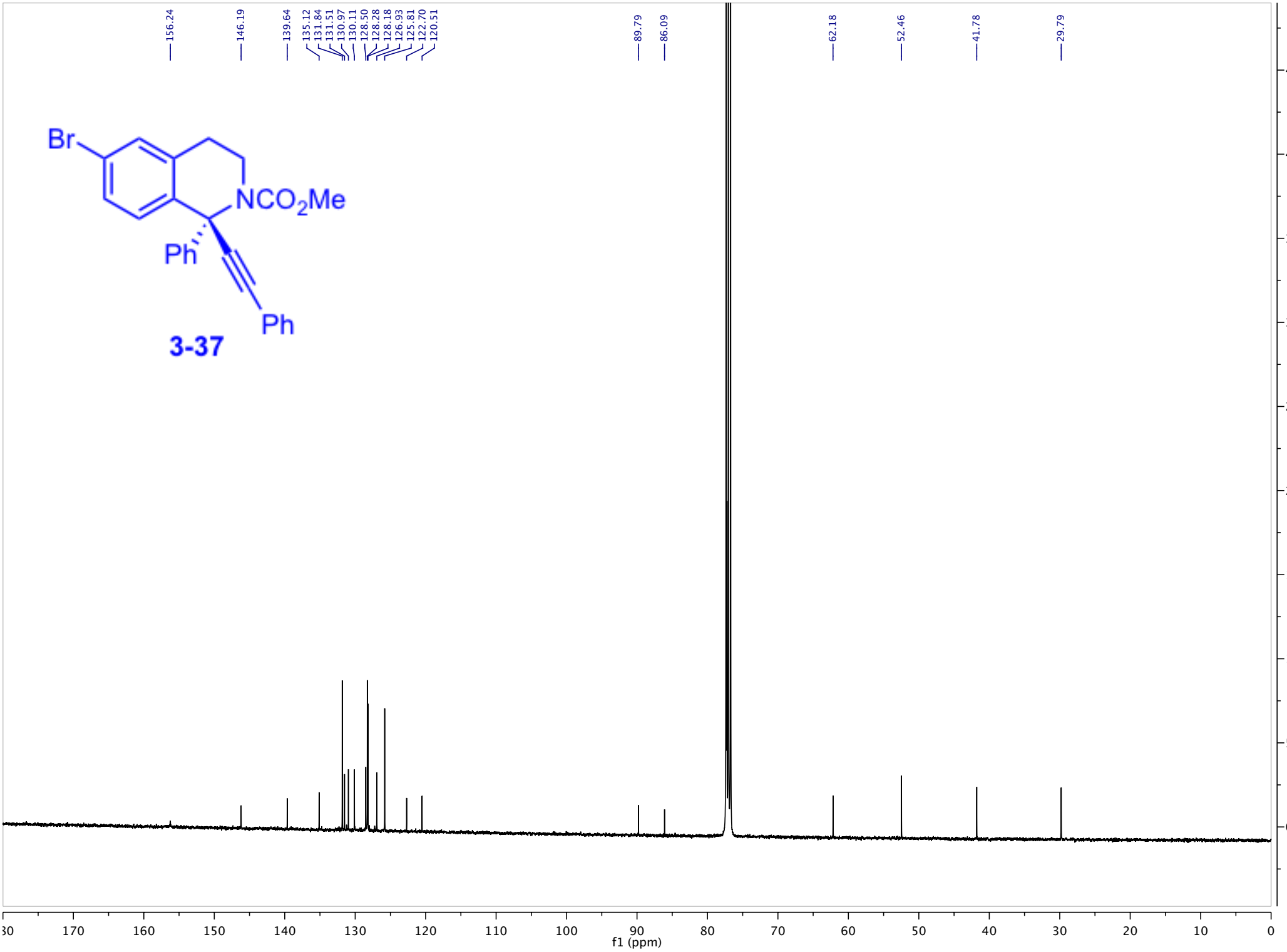

MeO
NCO2Me
Ph
Ph
3-35
f1 (ppm)

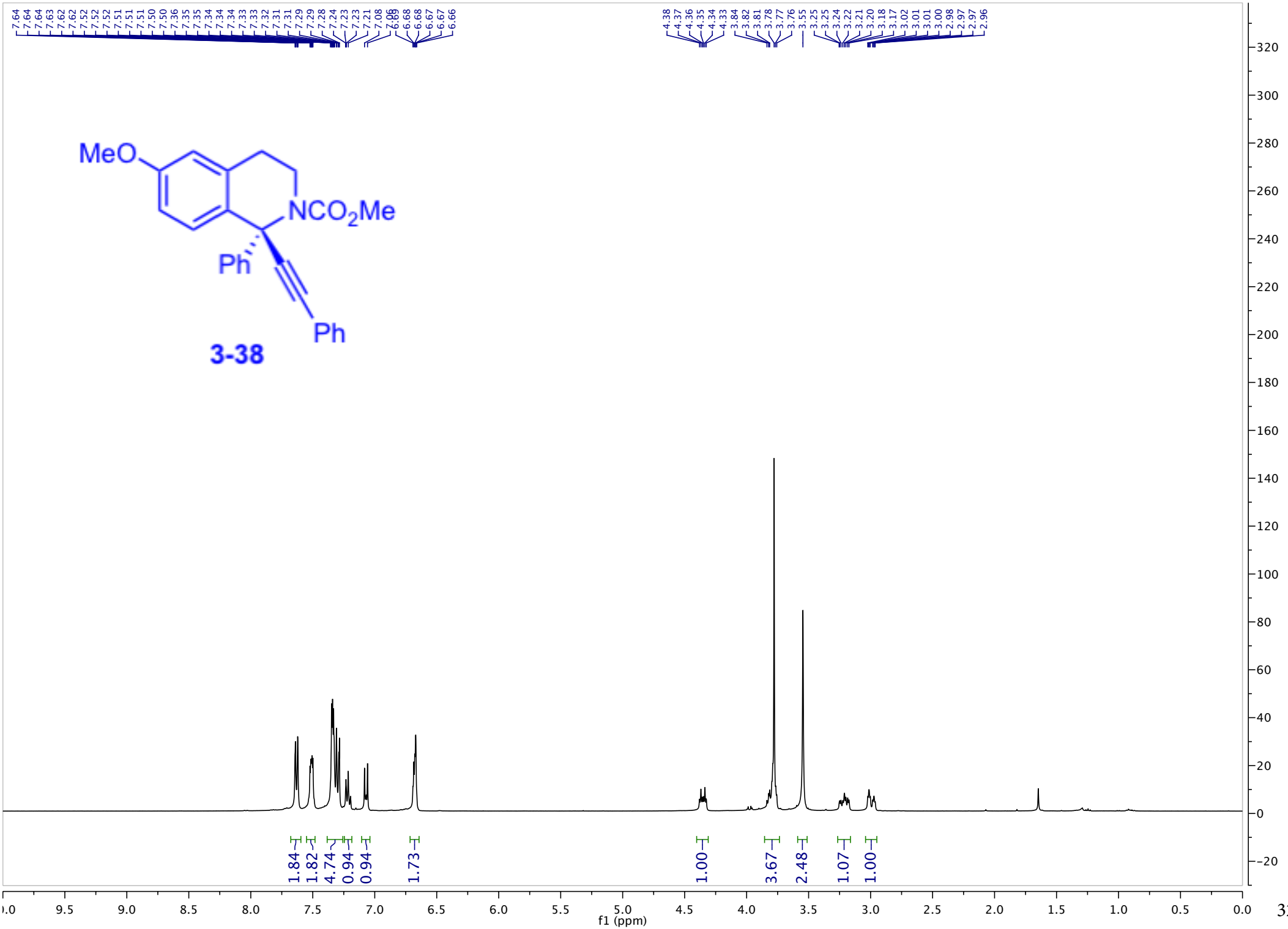

158.12
156.38
146.74
141.38
131.86
129.21
128.34
128.24
128.10
126.70
125.72
125.31
122.99
114.70
112.86
90.37
85.61
62.53
55.20
52.36
42.36
29.21
MeO
NCO2Me
Ph
Ph
3-35
f1 (ppm)

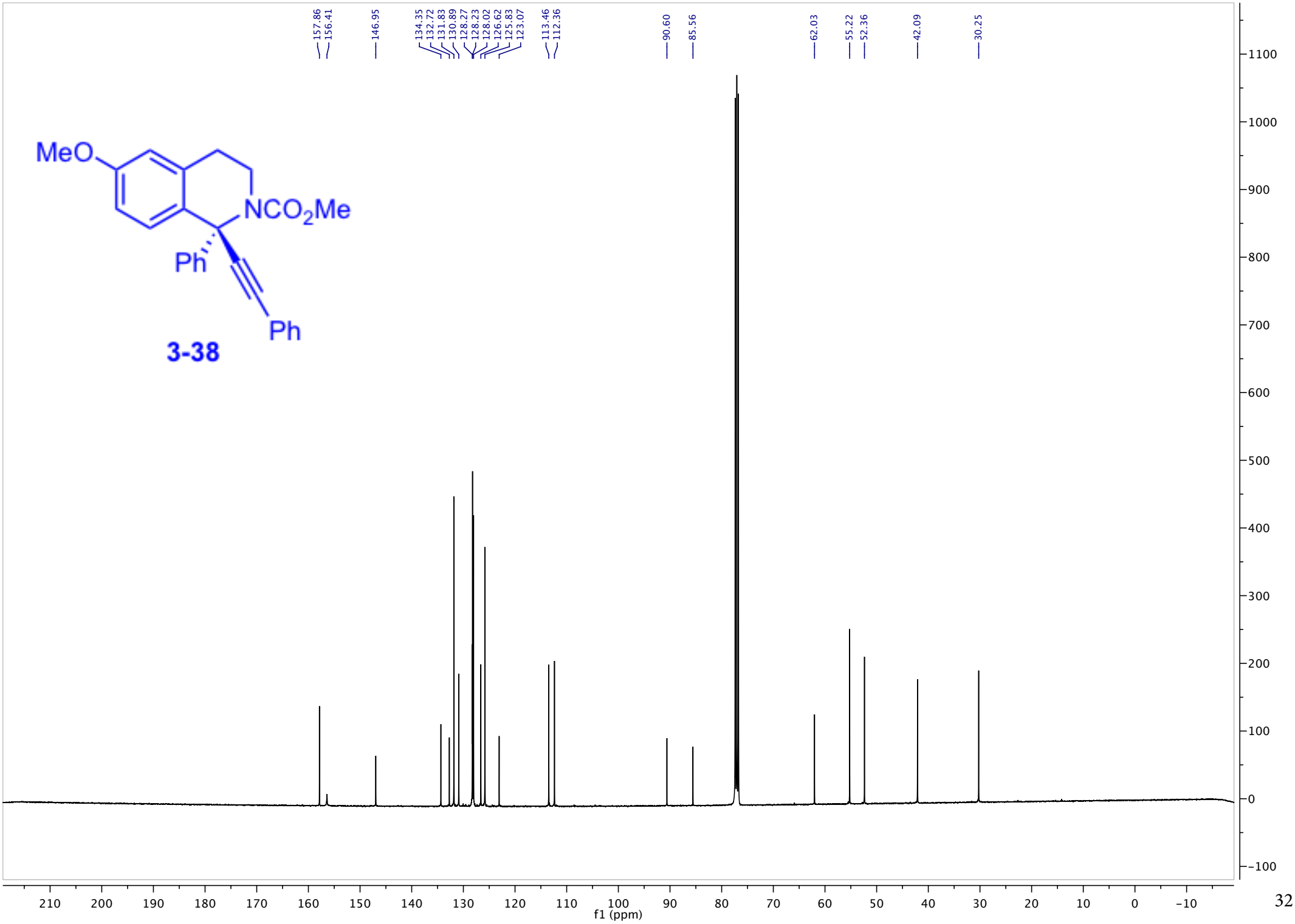

F
NCO2Me
Ph
Ph
3-36
f1 (ppm)

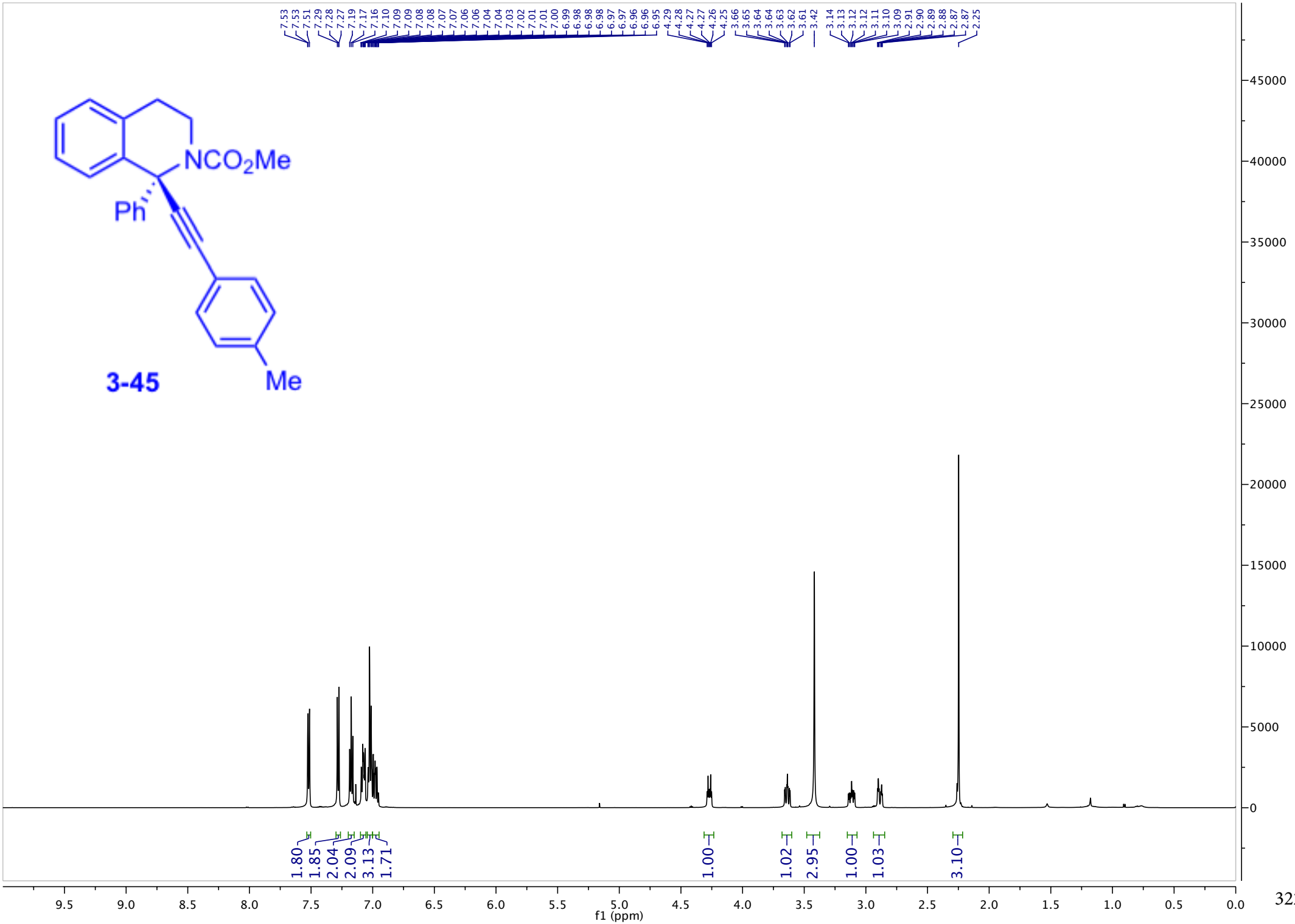

162.20
159.74
156.30
146.58
136.36
136.33
135.28
135.20
131.85
131.73
131.65
128.47
128.31
128.17
126.87
125.86
122.83
114.52
114.48
114.30
114.27
90.18
86.00
62.15
52.46
41.88
30.08
F
NCO2Me
Ph
Ph
3-36
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

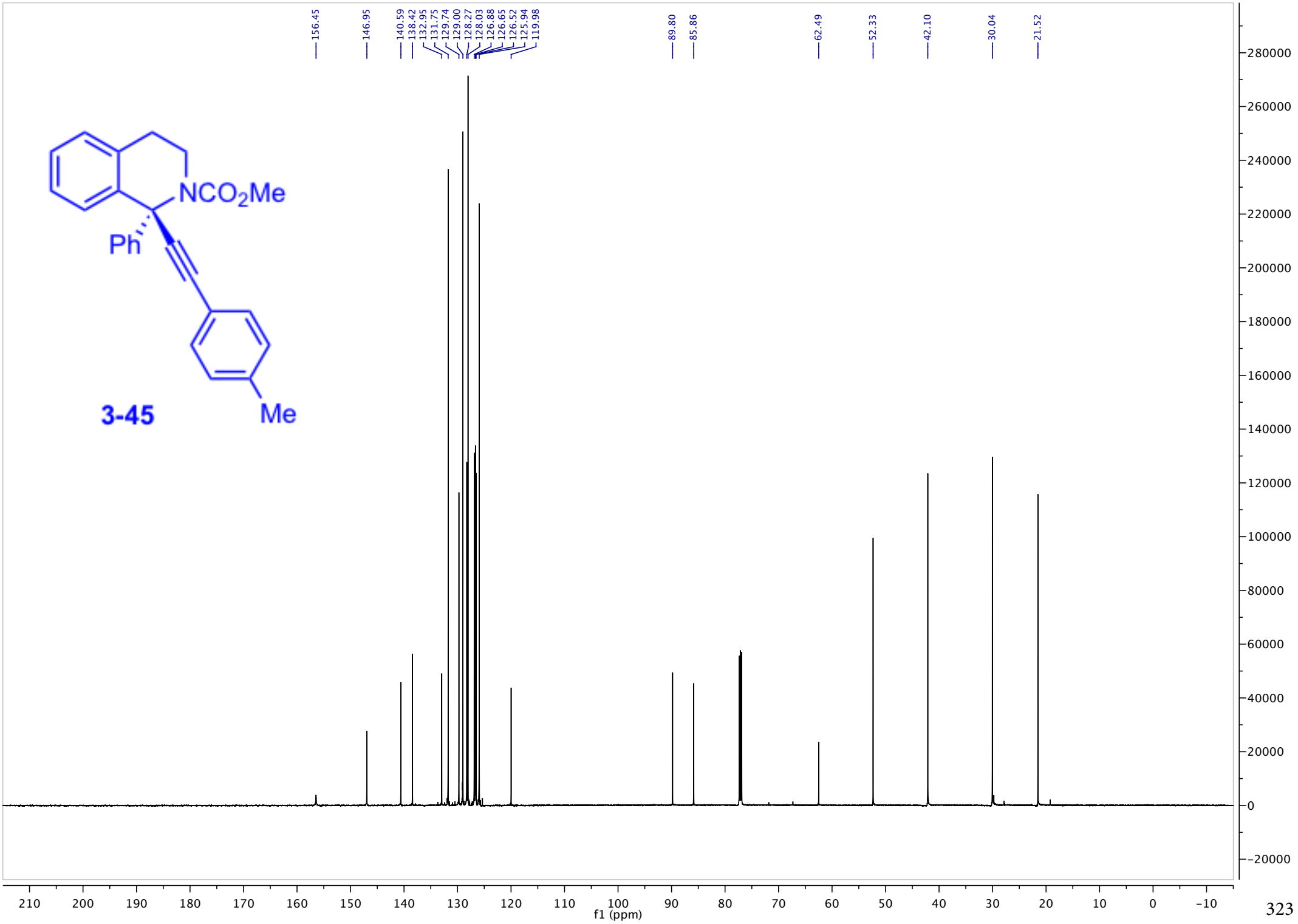

Br
NCO2Me
Ph
Ph
3-37
f1 (ppm)


156.24
146.19
139.64
135.12
131.84
131.51
130.97
130.11
128.50
128.28
128.18
126.93
125.81
122.70
120.51
89.79
86.09
62.18
52.46
41.78
29.79
Br
NCO2Me
Ph
Ph
3-37
450
400
350
300
250
200
150
100
50
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


MeO
NCO2Me
Ph
Ph
3-38
f1 (ppm)


157.86
156.41
146.95
134.35
132.72
131.83
130.89
128.27
128.23
128.02
126.62
125.83
123.07
113.46
112.36
90.60
85.56
62.03
55.22
52.36
42.09
30.25
MeO
NCO2Me
Ph
Ph
3-38
f1 (ppm)


NCO2Me
Ph
Me
3-45
f1 (ppm)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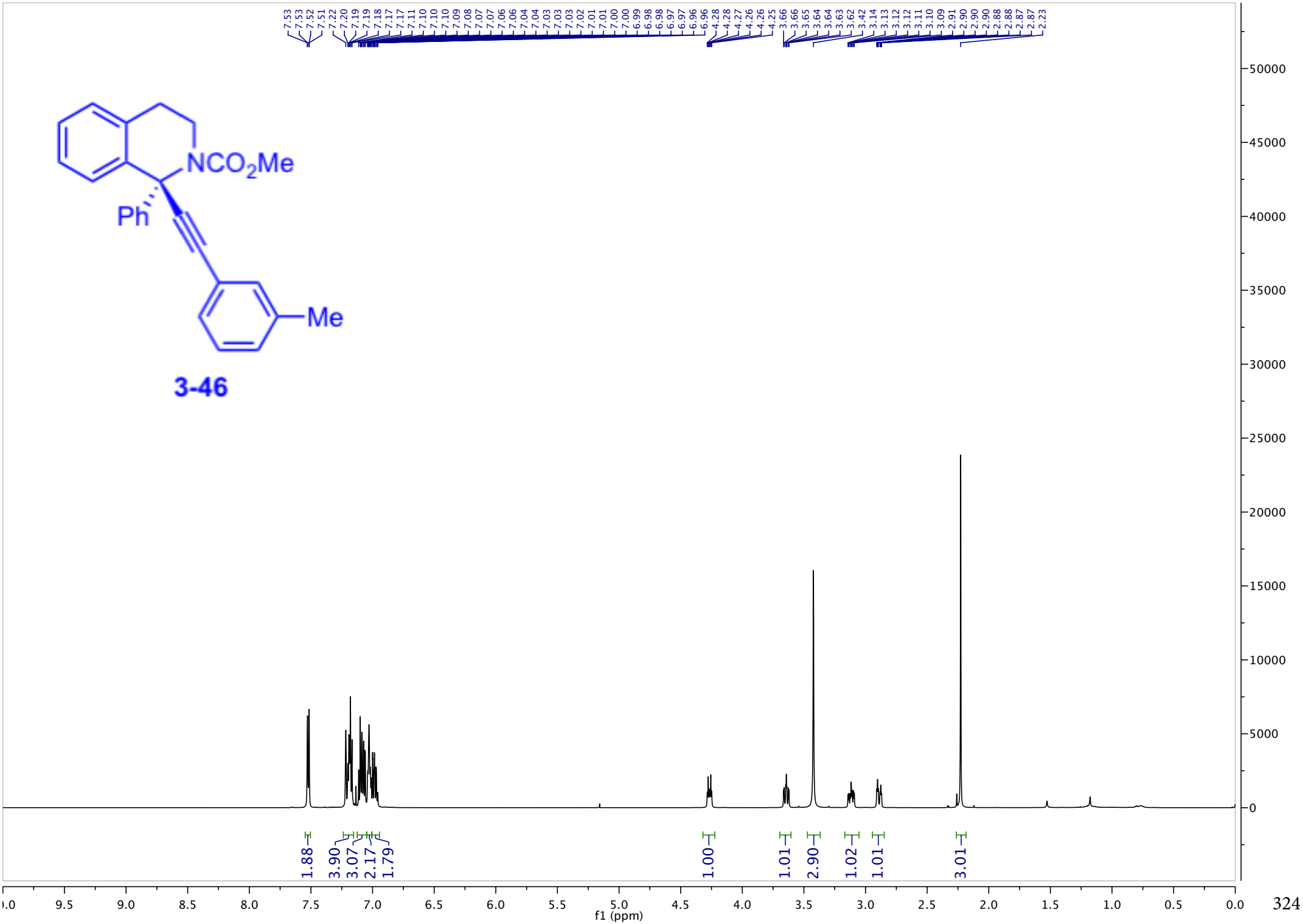
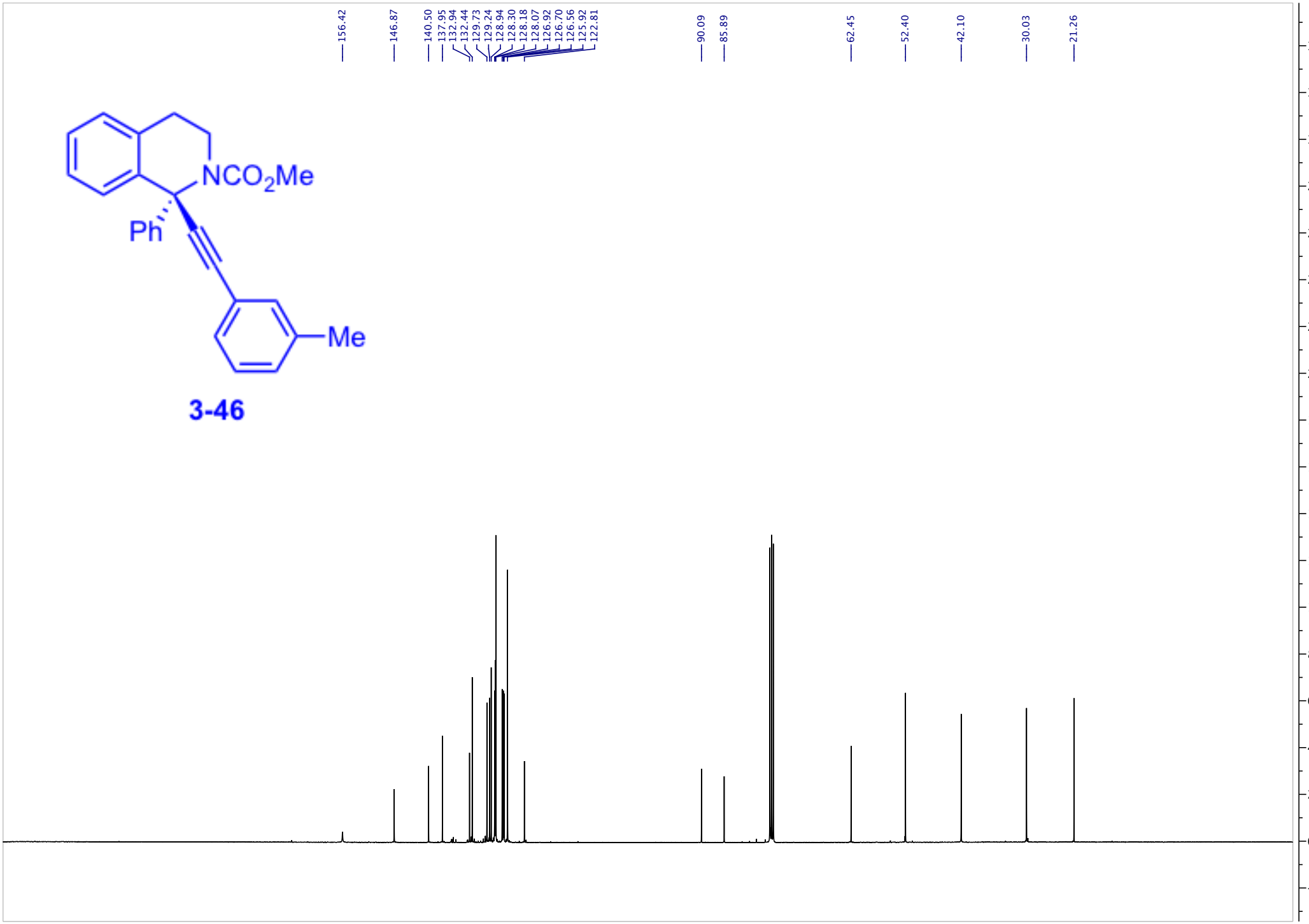
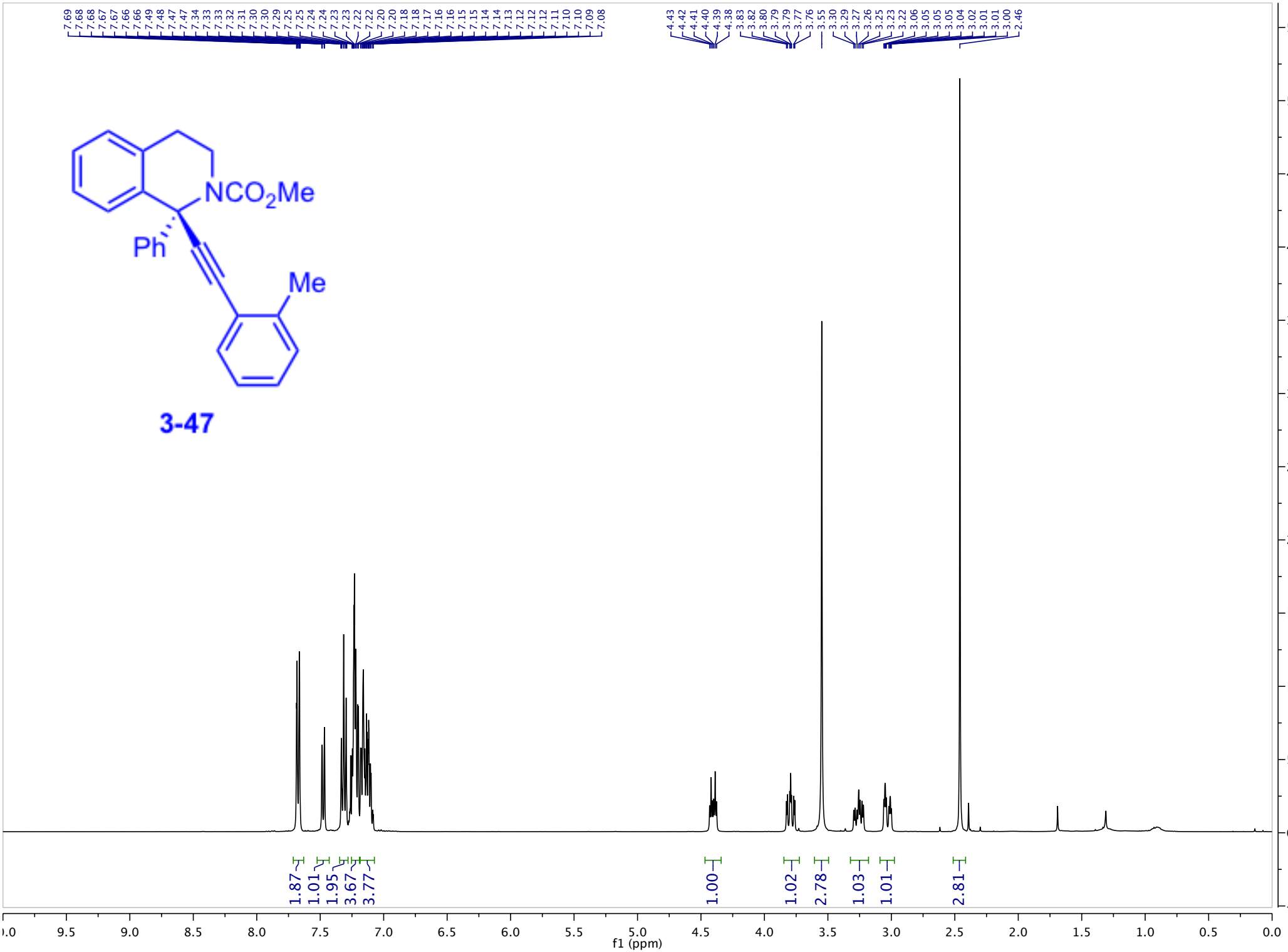
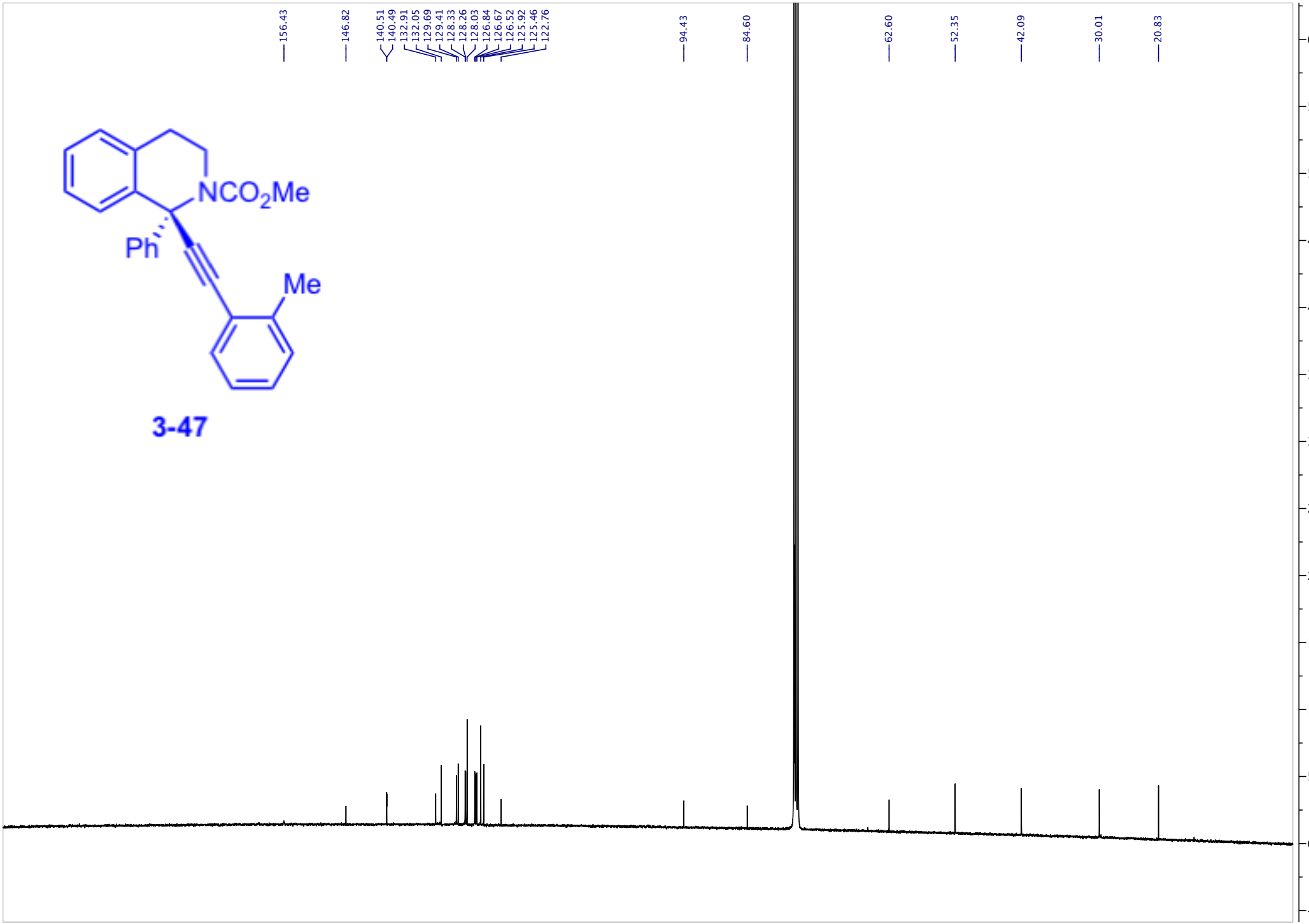
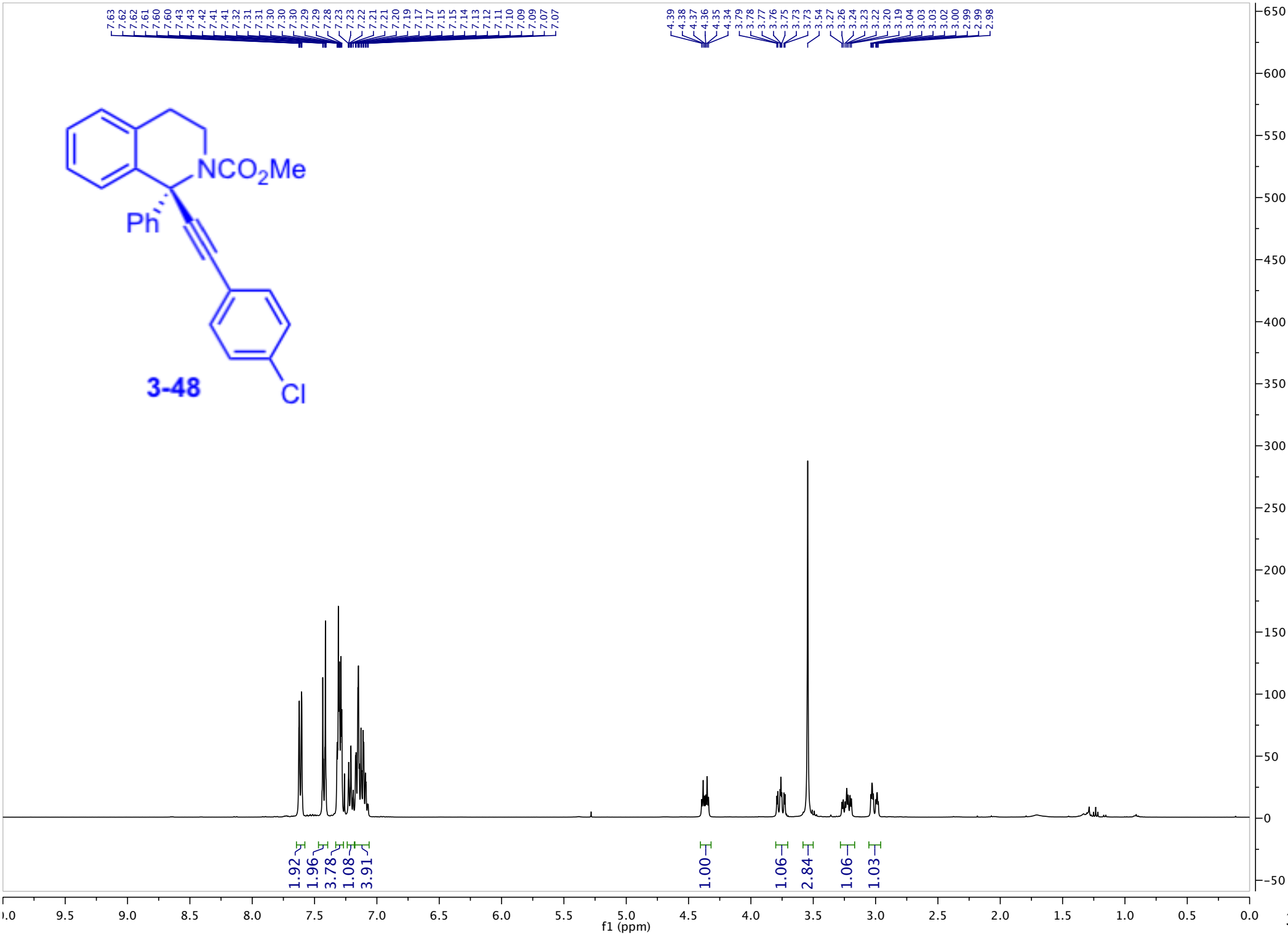
146.95
140.59
138.42
132.95
131.75
129.74
129.00
128.27
128.03
126.88
126.65
126.52
125.94
119.98
89.80
85.86
62.49
52.33
42.10
30.04
21.52
NCO2Me
Ph
3-45
Me
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

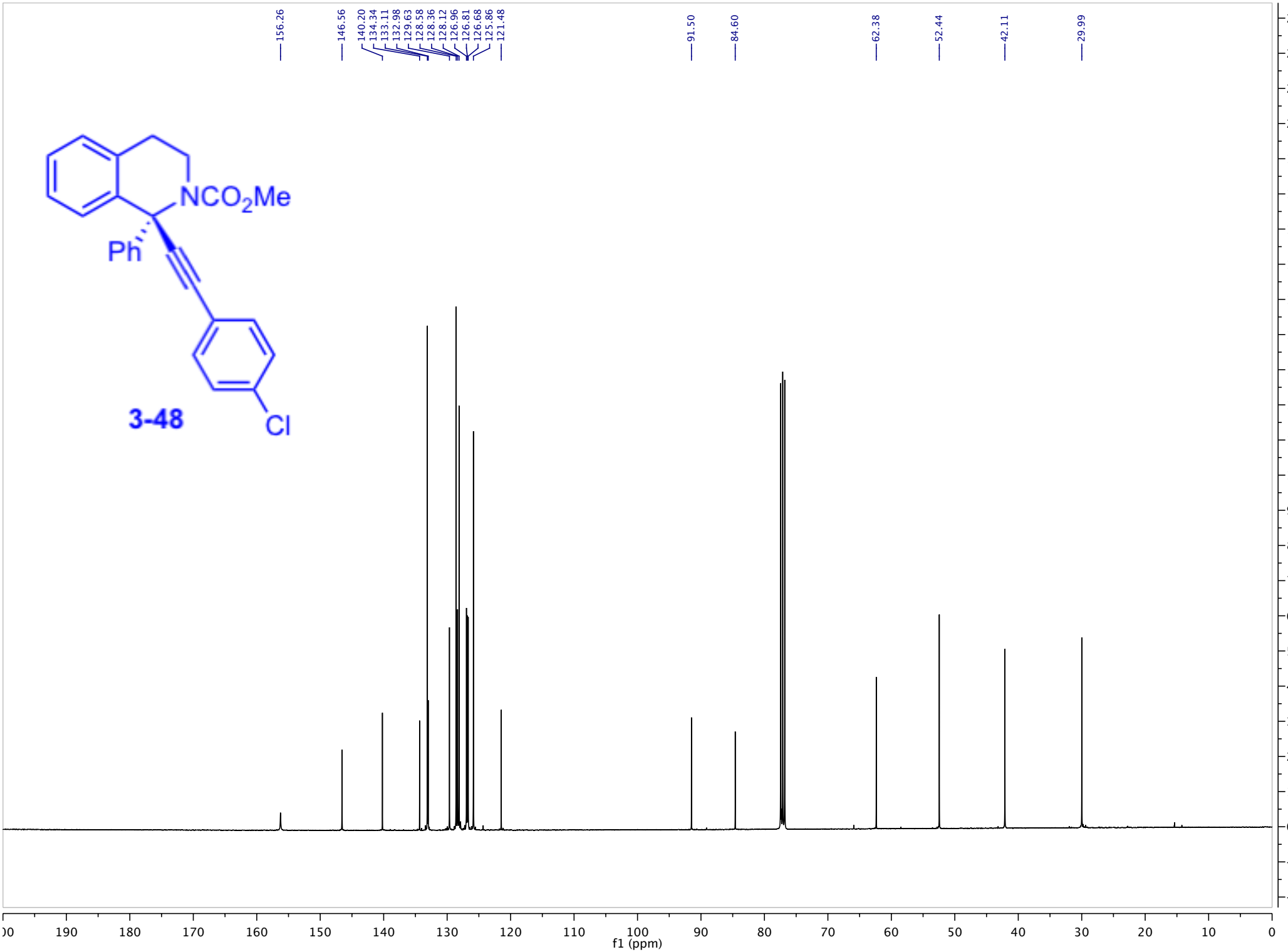

NCO2Me
Ph
Me
3-46
f1 (ppm)

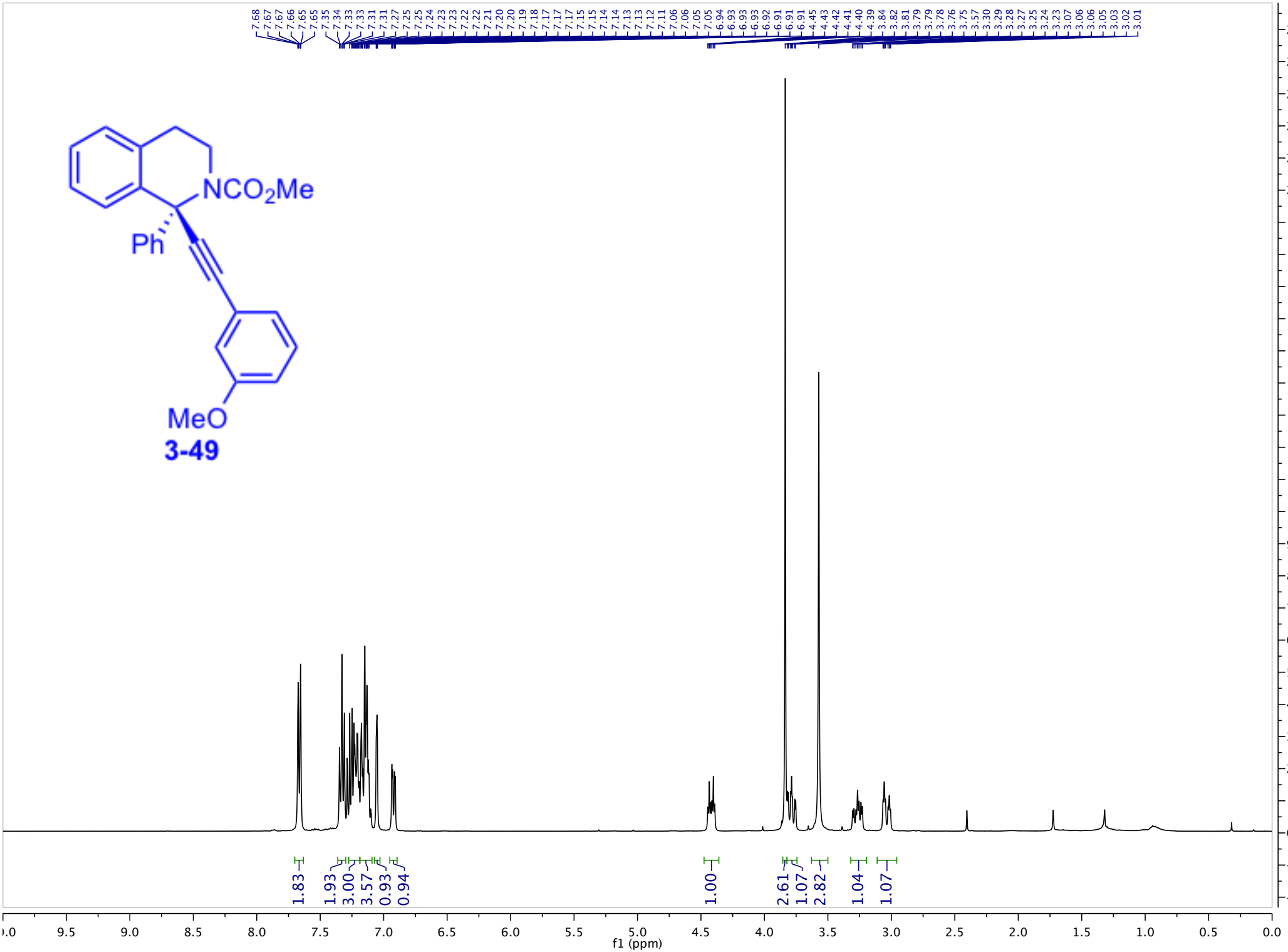

156.42
146.87
140.50
137.95
132.94
132.44
129.73
129.24
128.94
128.30
128.18
128.07
126.92
126.70
126.56
125.92
122.81
90.09
85.89
62.45
52.40
42.10
30.03
21.26
NCO2Me
Ph
Me
3-46
f1 (ppm)

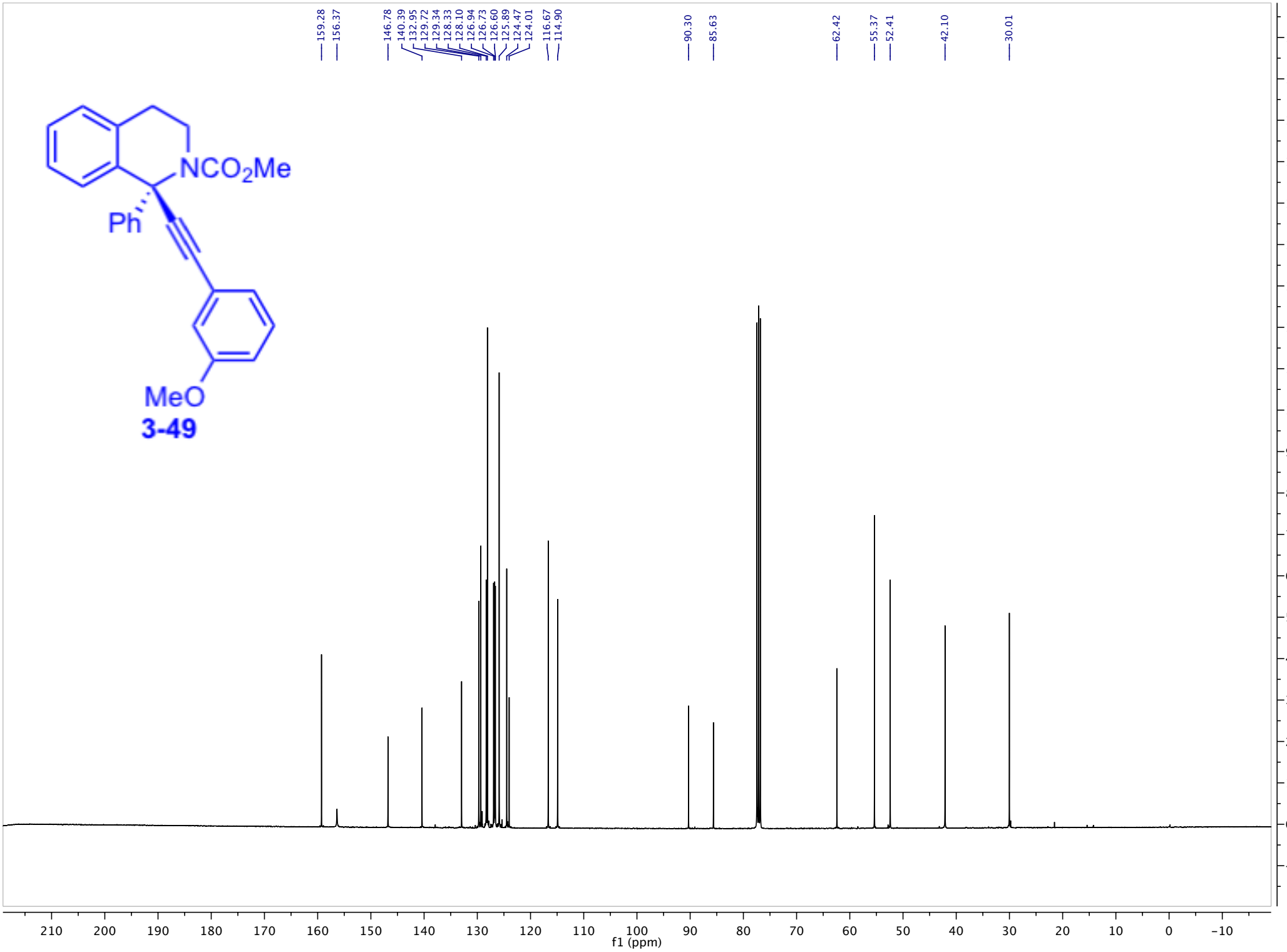

NCO2Me
Ph
Me
3-47
f1 (ppm)

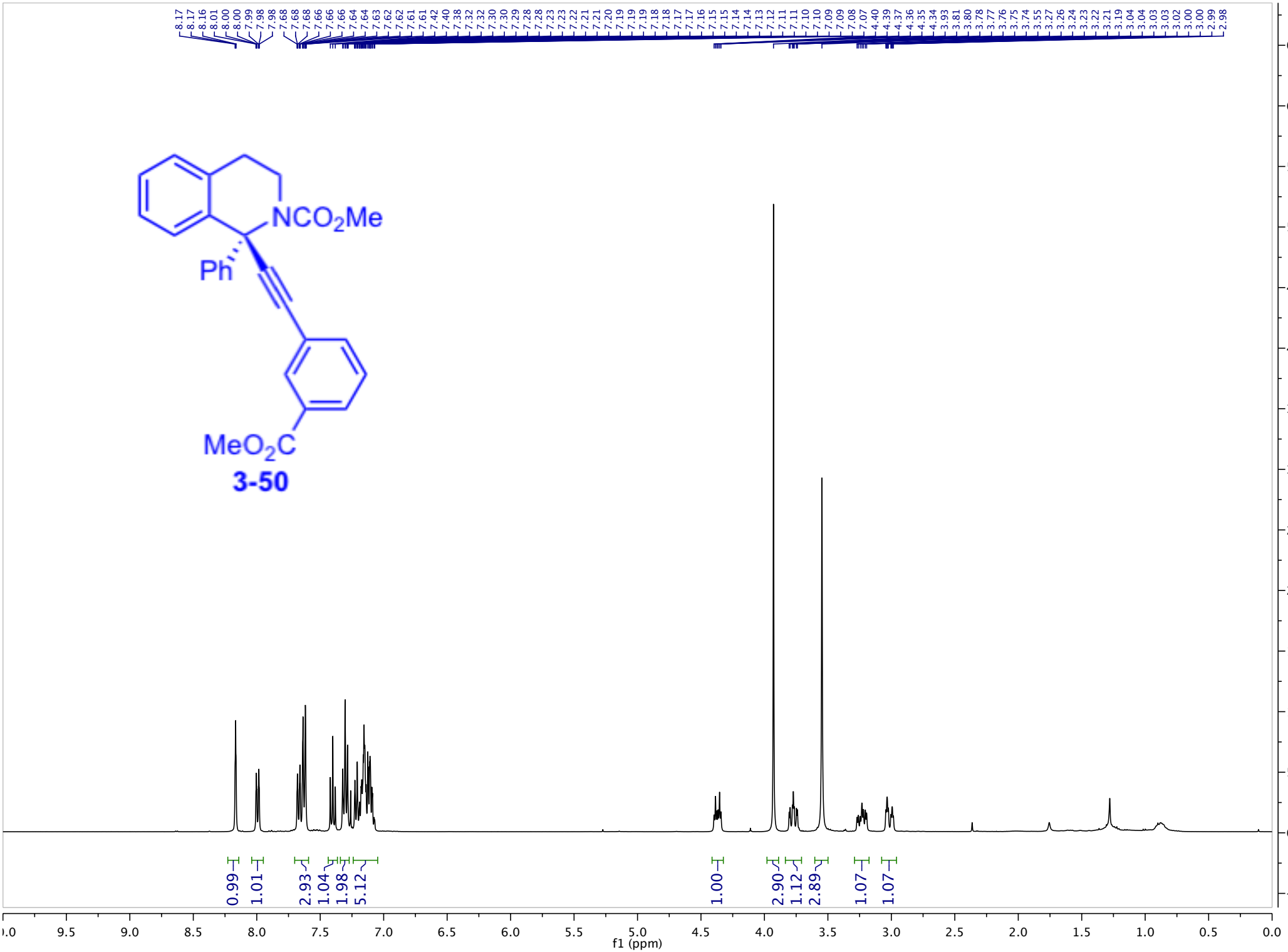

156.43
146.82
140.51
140.49
132.91
132.05
129.69
129.41
128.33
128.26
128.03
126.84
126.67
126.52
125.92
125.46
122.76
94.43
84.60
62.60
52.35
42.09
30.01
20.83
NCO2Me
Ph
Me
3-47
f1 (ppm)

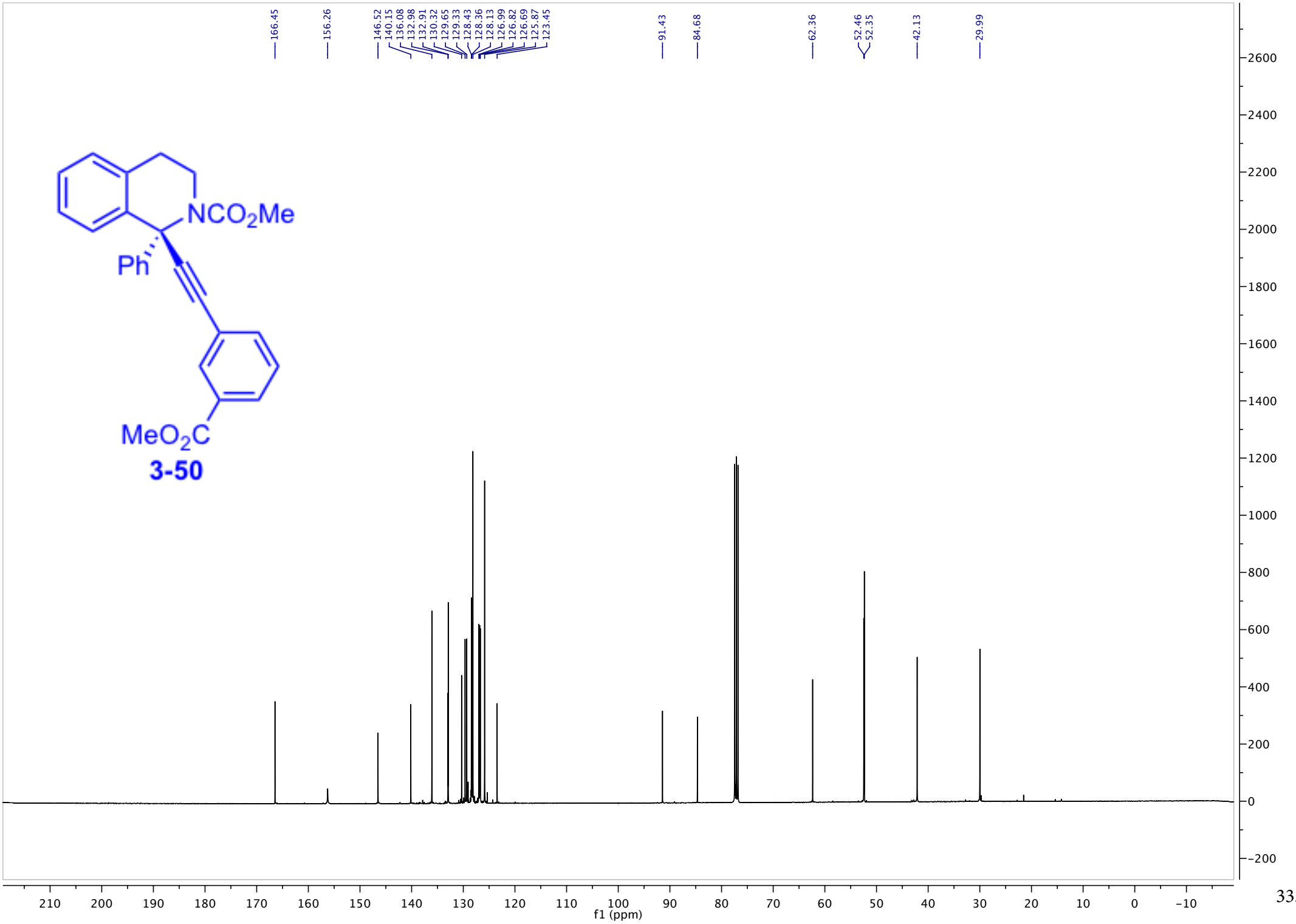

7.63 7.62 7.62 7.61 7.60 7.60 7.43 7.42 7.41 7.41 7.32 7.31 7.31 7.30 7.30 7.30 7.29 7.29 7.28 7.23 7.23 7.22 7.21 7.21 7.20 7.19 7.17 7.17 7.15 7.15 7.14 7.13 7.12 7.11 7.10 7.09 7.09 7.07 7.07
4.39 4.38 4.37 4.36 4.35 4.34 3.79 3.78 3.77 3.76 3.75 3.73 3.73 3.54 3.27 3.26 3.24 3.23 3.22 3.20 3.19 3.04 3.03 3.03 3.02 3.00 2.99 2.99 2.98
NCO2Me
Ph
Cl
3-48
1.92 1.96 3.78 1.08 3.91
1.00 1.06 2.84 1.06 1.03
650 600 550 500 450 400 350 300 250 200 150 100 50 0 -50
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)

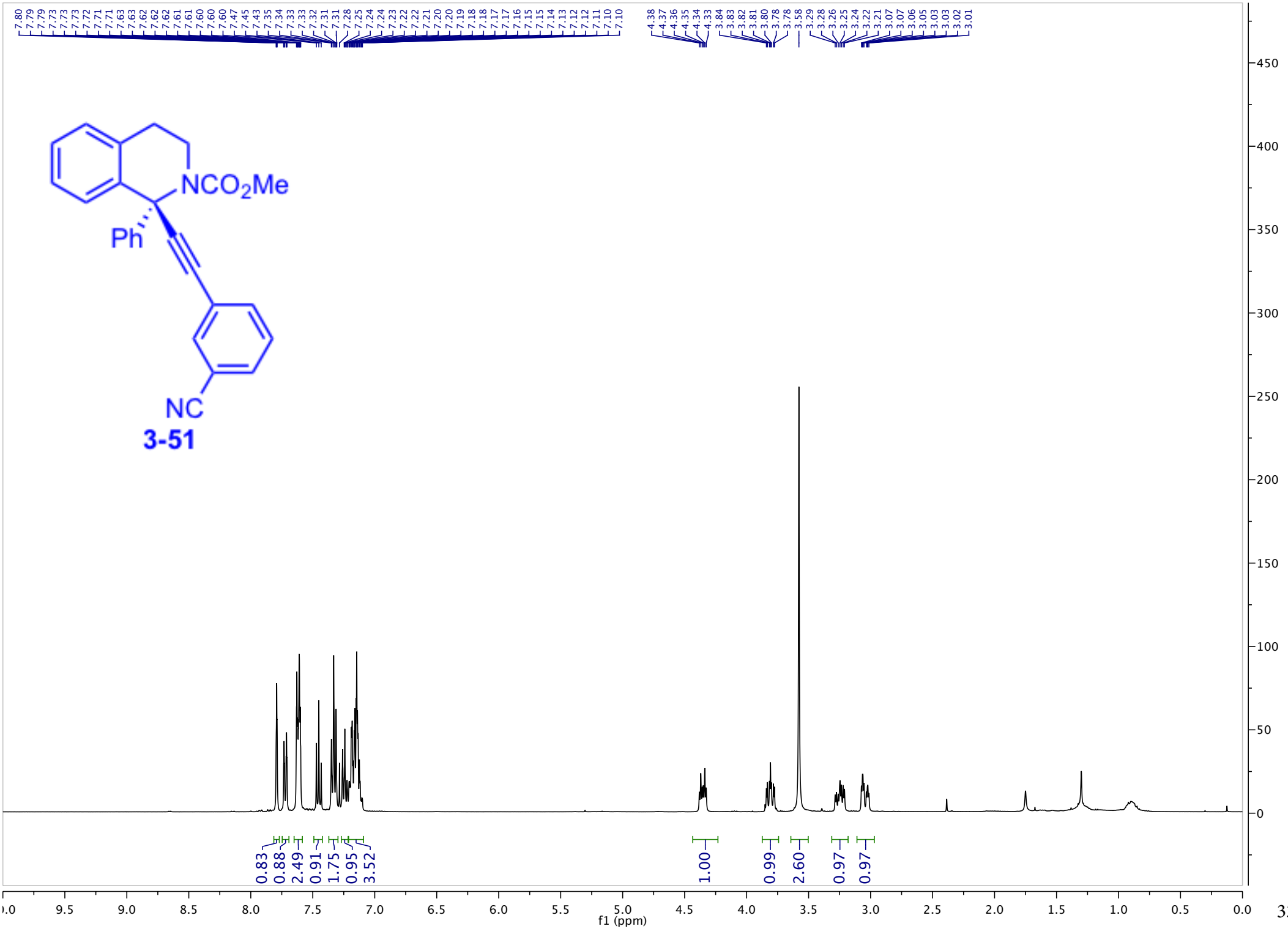

156.26
146.56
140.20
134.34
133.11
132.98
129.63
128.58
128.36
128.12
126.96
126.81
126.68
125.86
121.48
91.50
84.60
62.38
52.44
42.11
29.99
NCO2Me
Ph
Cl
3-48
f1 (ppm)

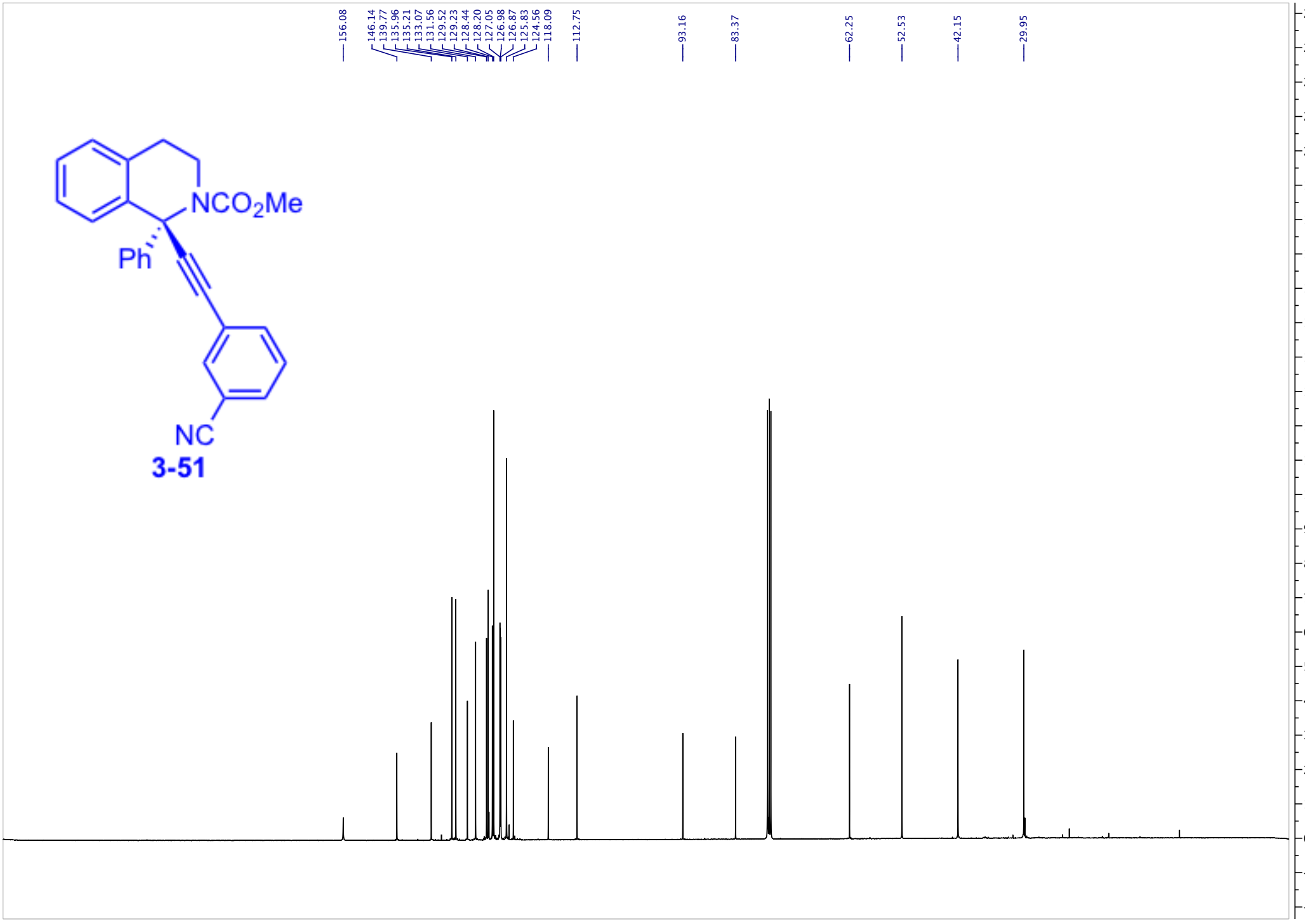

NCO2Me
Ph
MeO
3-49
f1 (ppm)

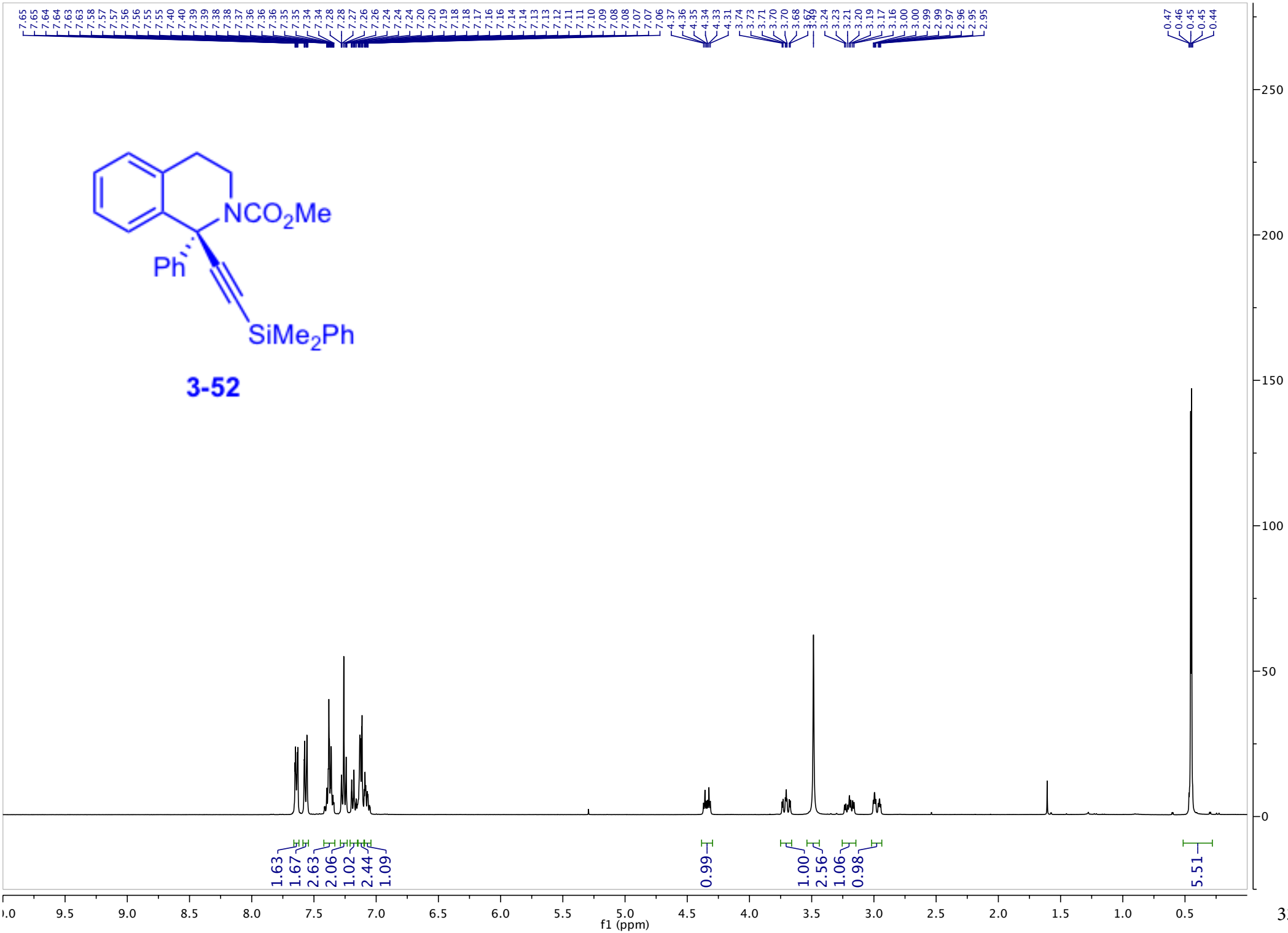

159.28
156.37
146.78
140.39
132.95
129.72
129.34
128.33
128.10
126.94
126.73
126.60
125.89
124.47
124.01
116.67
114.90
90.30
85.63
62.42
55.37
52.41
42.10
30.01
NCO2Me
Ph
MeO
3-49
f1 (ppm)

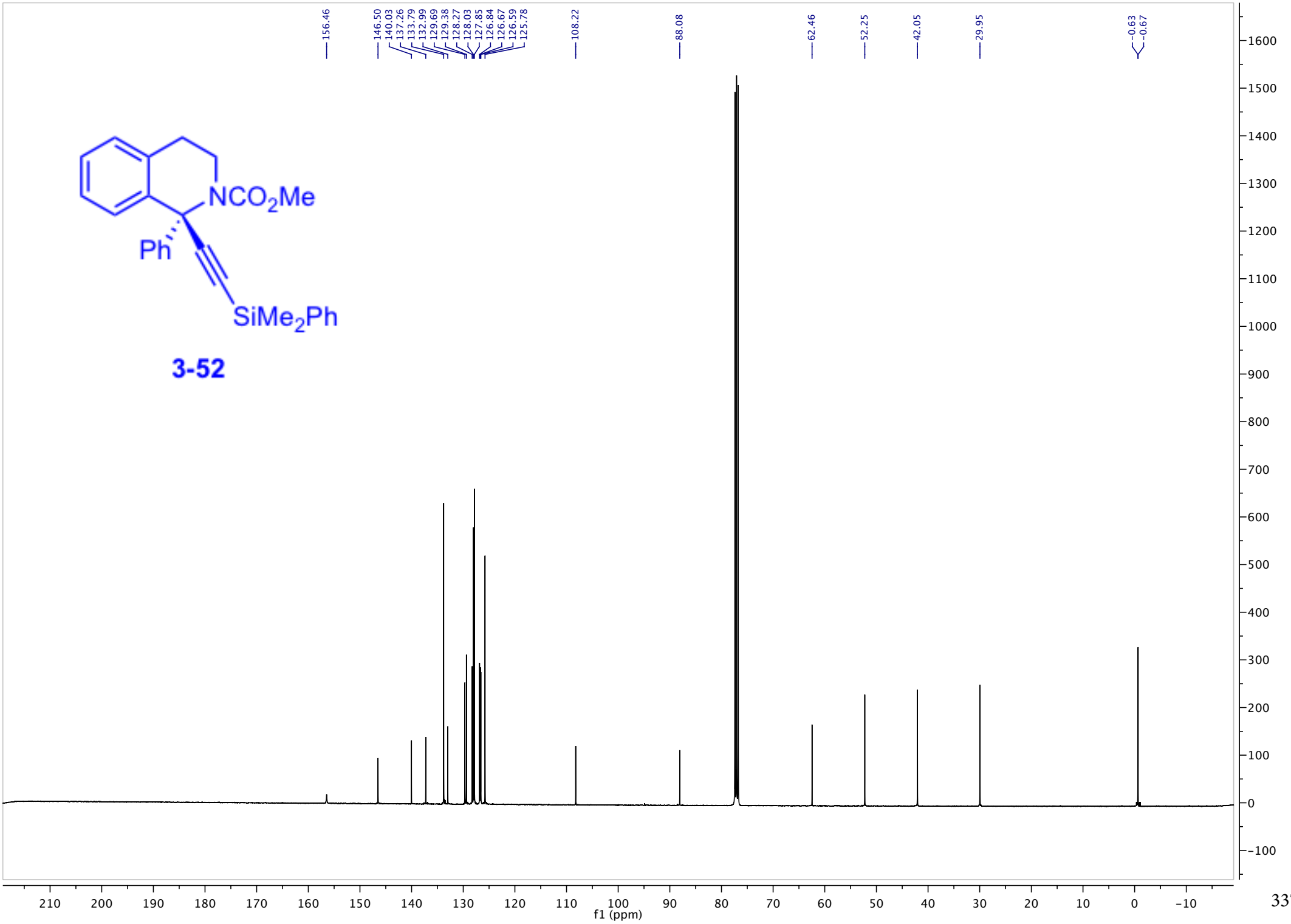

NCO2Me
Ph
MeO2C
3-50
f1 (ppm)

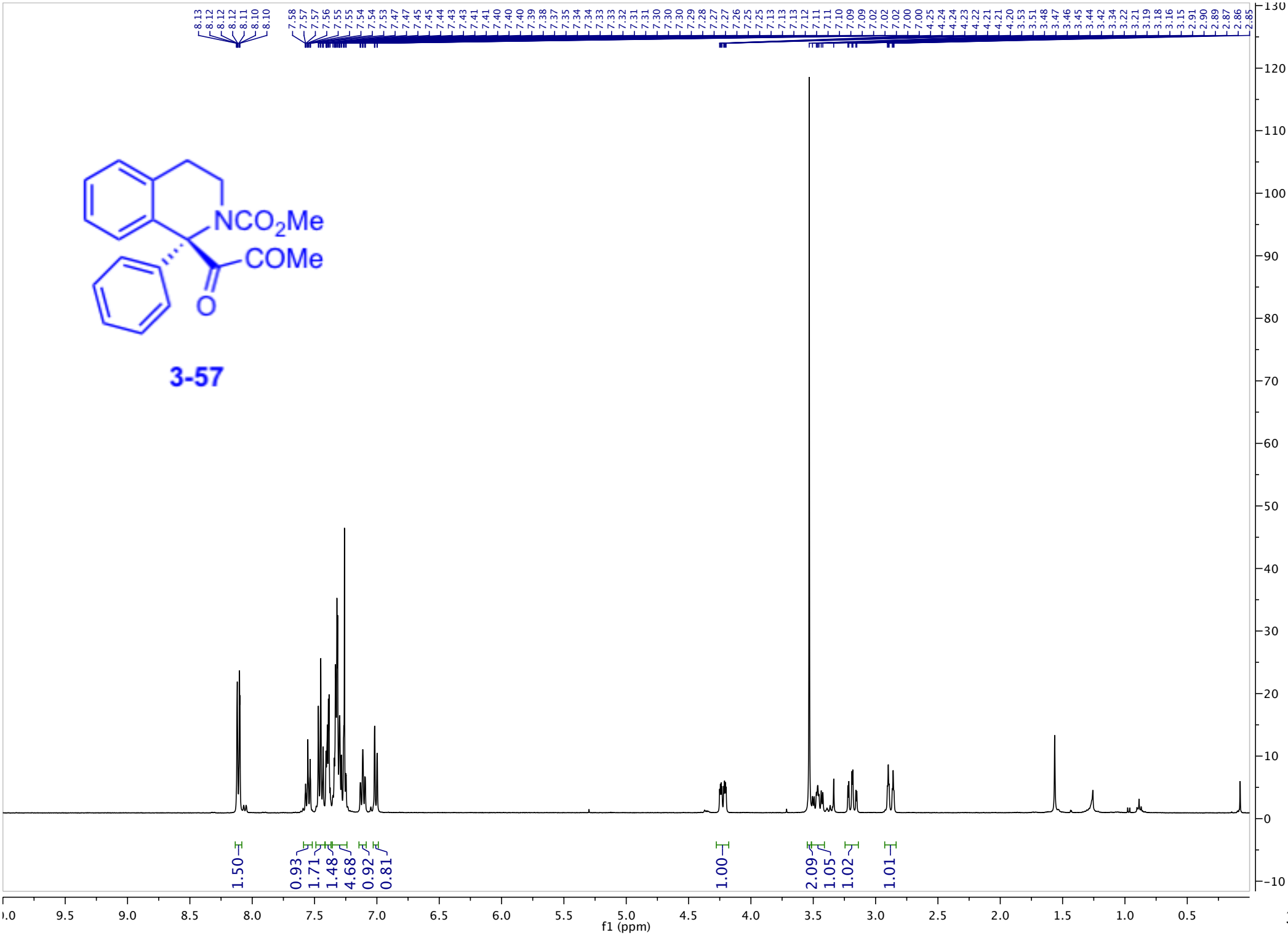

166.45
156.26
146.52
140.15
136.08
132.98
132.91
130.32
129.65
129.33
128.43
128.36
128.13
126.99
126.82
126.69
125.87
123.45
91.43
84.68
62.36
52.46
52.35
42.13
29.99
NCO2Me
Ph
MeO2C
3-50
f1 (ppm)

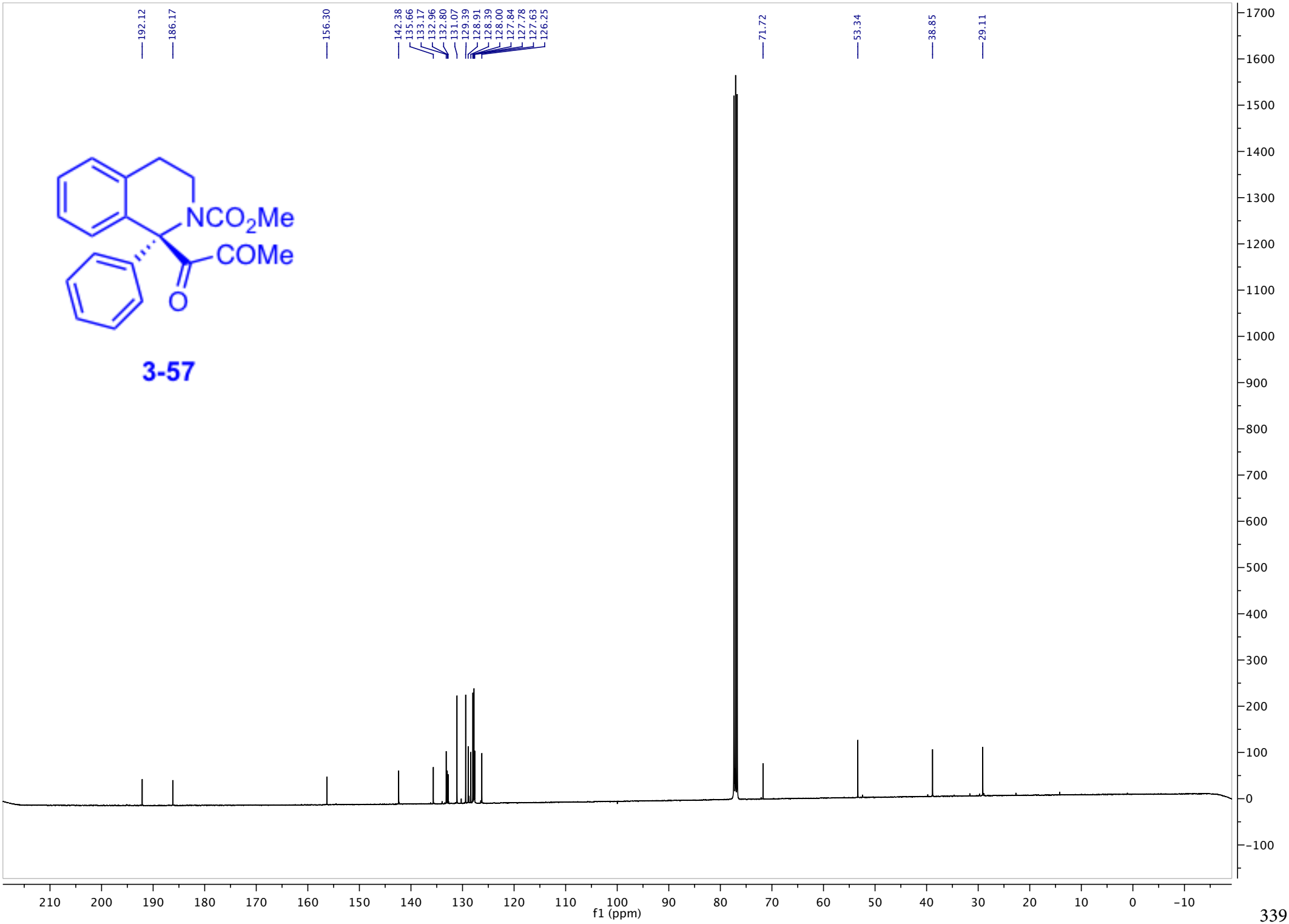

NCO2Me
Ph
NC
3-51
f1 (ppm)


156.08
146.14
139.77
135.96
135.21
133.07
131.56
129.52
129.23
128.44
128.20
127.05
126.98
126.87
125.83
124.56
118.09
112.75
93.16
83.37
62.25
52.53
42.15
29.95
NCO2Me
Ph
NC
3-51
f1 (ppm)


NCO2Me
Ph
SiMe2Ph
3-52
f1 (ppm)


156.46
146.50
140.03
137.26
133.79
132.99
129.69
129.38
128.27
128.03
127.85
126.84
126.67
126.59
125.78
108.22
88.08
62.46
52.25
42.05
29.95
-0.63
-0.67
NCO2Me
Ph
SiMe2Ph
3-52
f1 (ppm)


NCO2Me
COMe
O
3-57
f1 (ppm)


192.12
186.17
156.30
142.38
135.66
133.17
132.96
132.80
131.07
129.39
128.91
128.39
128.00
127.84
127.78
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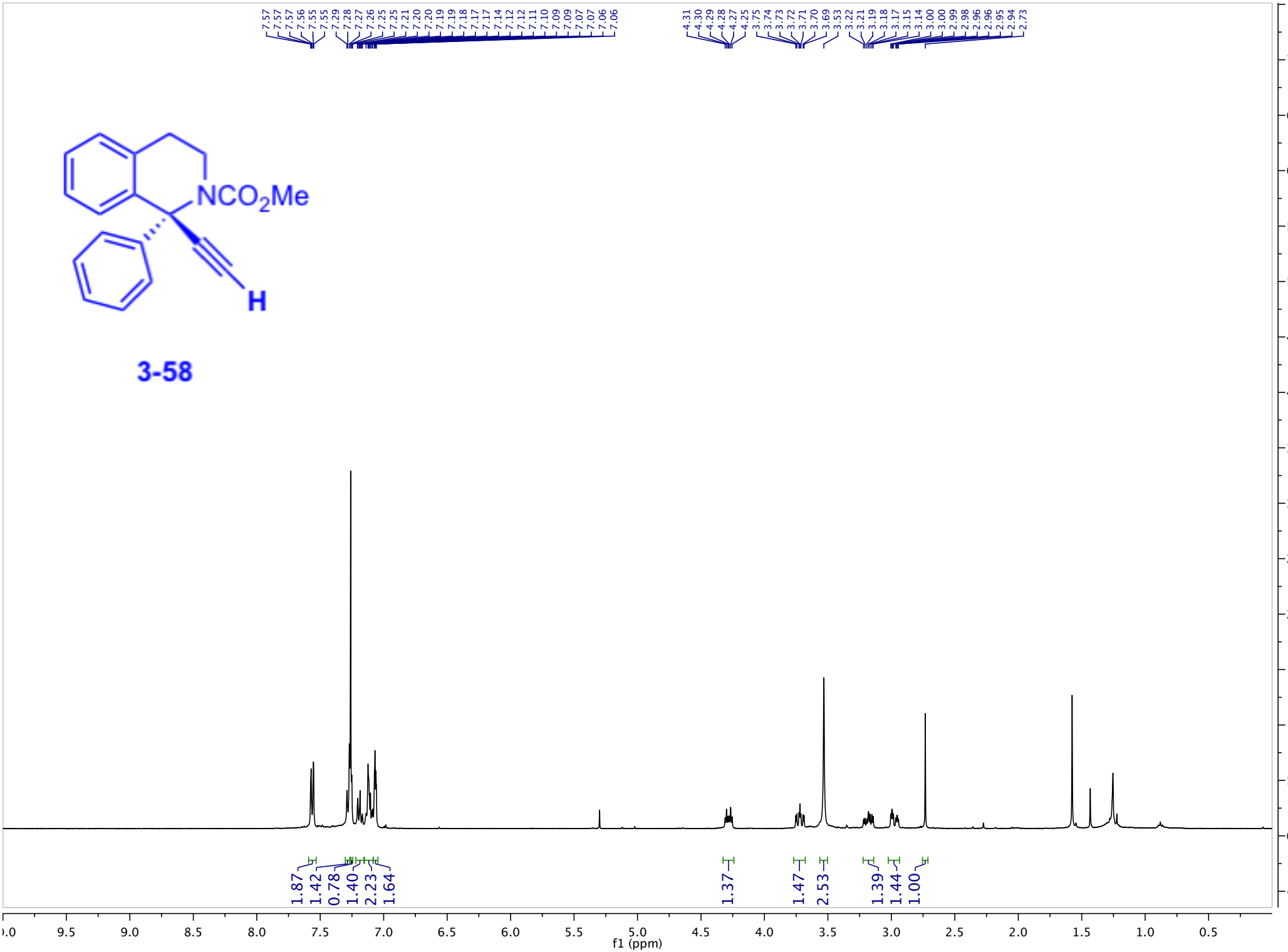
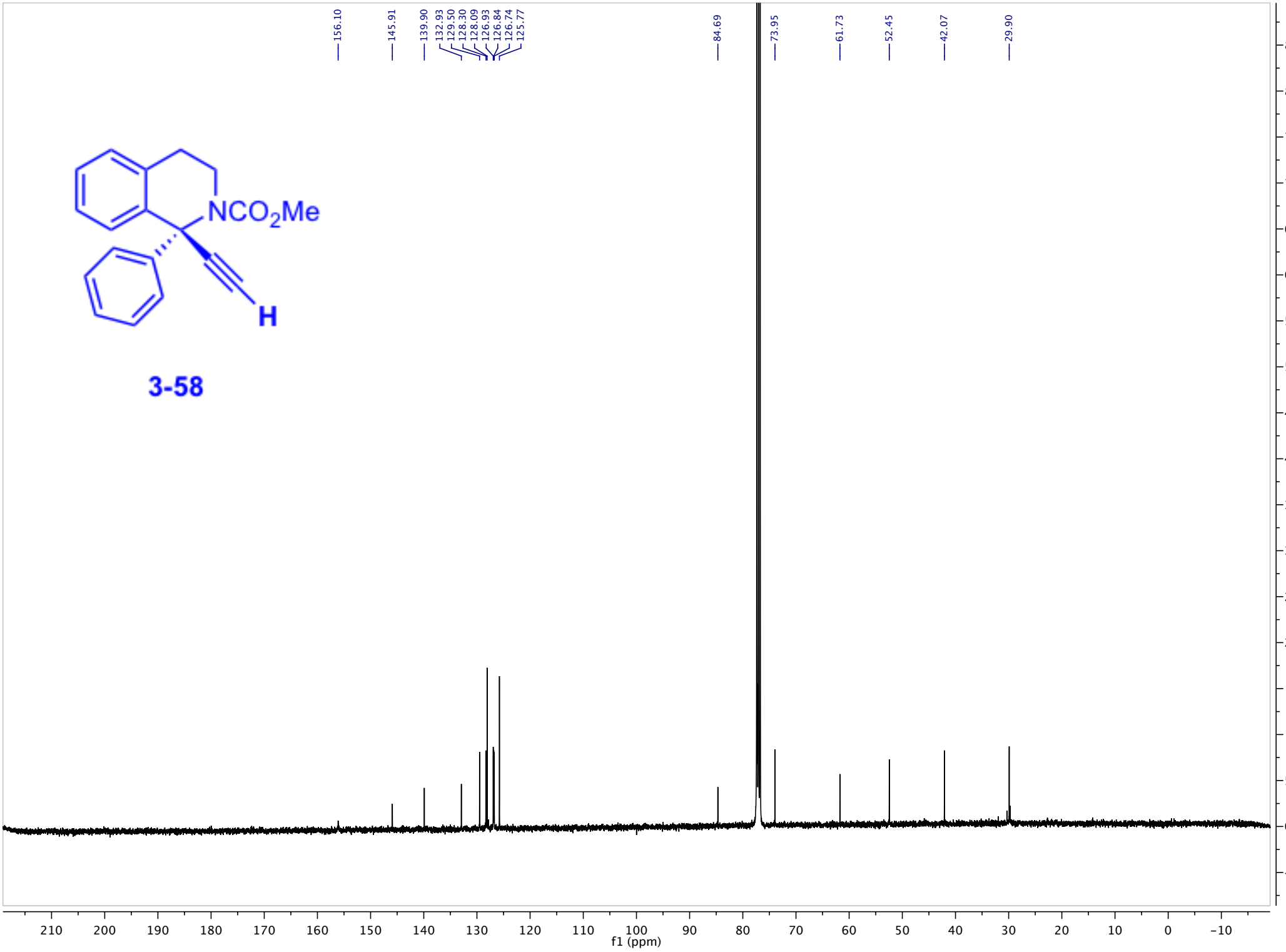
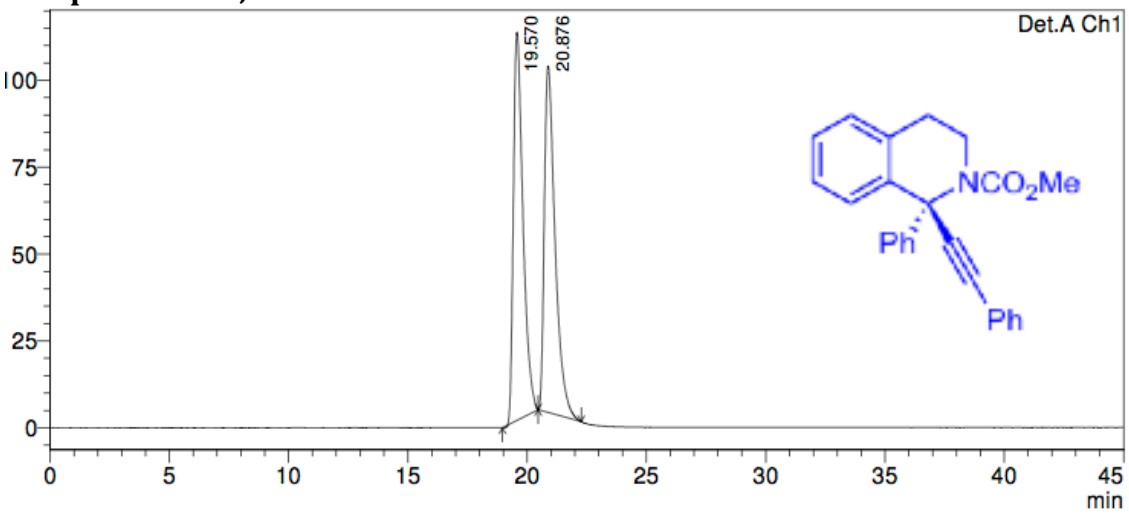
71.72
53.34
38.85
29.11
NCO2Me
COMe
O
3-57
f1 (ppm)


NCO2Me
H
3-58
f1 (ppm)


156.10
145.91
139.90
132.93
129.50
128.30
128.09
126.93
126.84
126.74
125.77
84.69
73.95
61.73
52.45
42.07
29.90
NCO2Me
H
3-58
f1 (ppm)

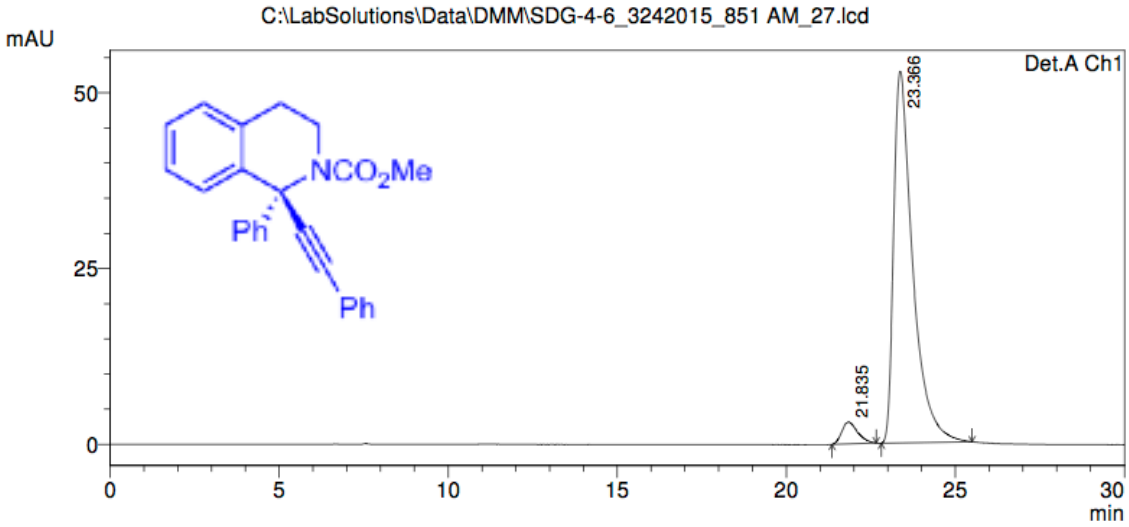
Compound 3-33, Racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.570	3124801	111675	49.924	52.836
2	20.876	3134307	99689	50.076	47.164
Total		6259108	211364	100.000	100.000

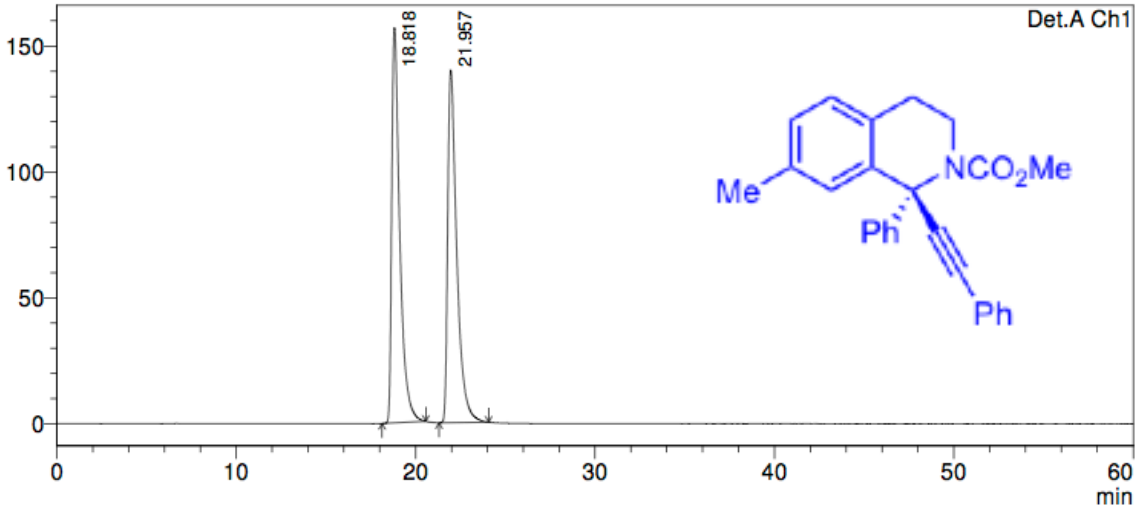
Compound 3-33, 91% ee



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.835	101631	3110	4.677	5.559
2	23.366	2071305	52844	95.323	94.441
Total		2172936	55955	100.000	100.000

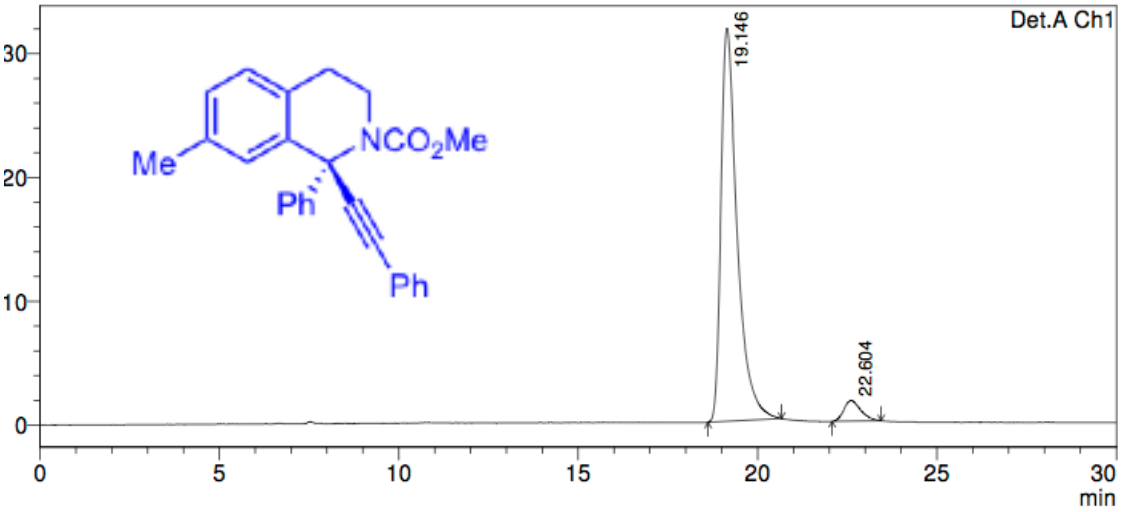
Compound 3-34, Racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.818	4893136	157005	49.889	52.851
2	21.957	4914970	140065	50.111	47.149
Total		9808106	297070	100.000	100.000

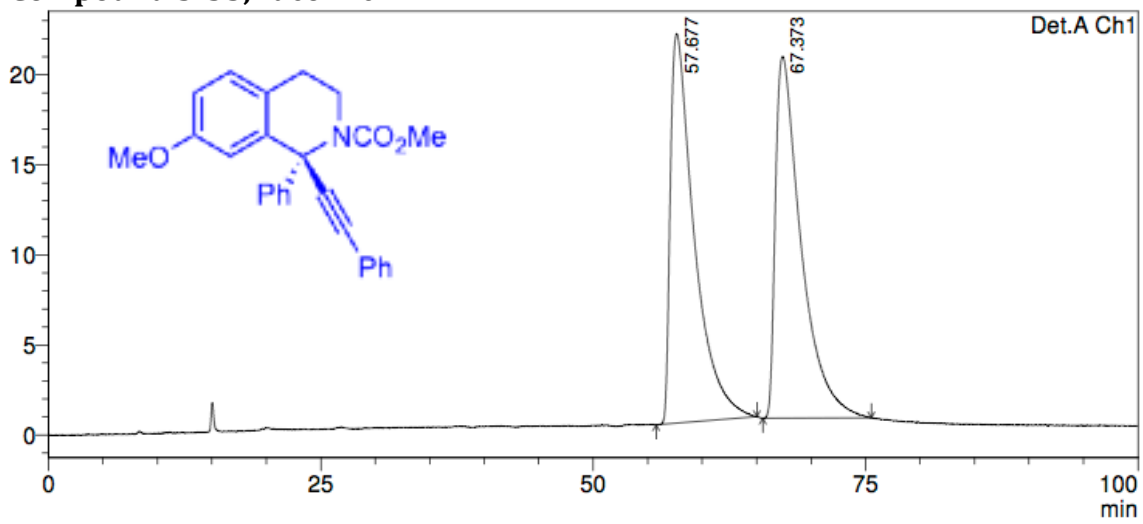
Compound 3-34, 90% ee



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.146	994312	31749	94.807	95.021
2	22.604	54466	1663	5.193	4.979
Total		1048778	33412	100.000	100.000

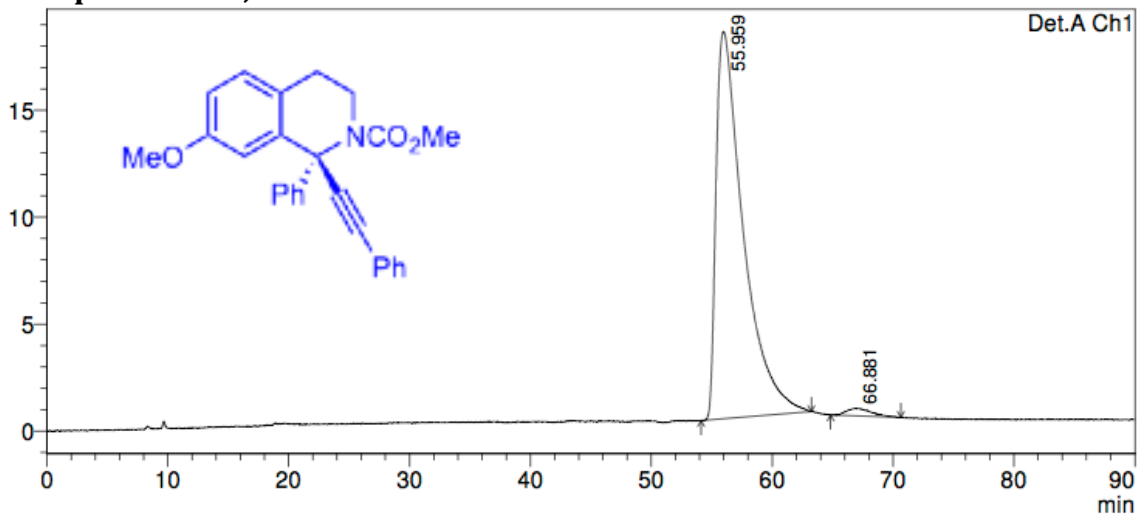
Compound 3-35, racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	57.677	3296021	21613	50.042	51.832
2	67.373	3290487	20085	49.958	48.168
Total		6586508	41698	100.000	100.000

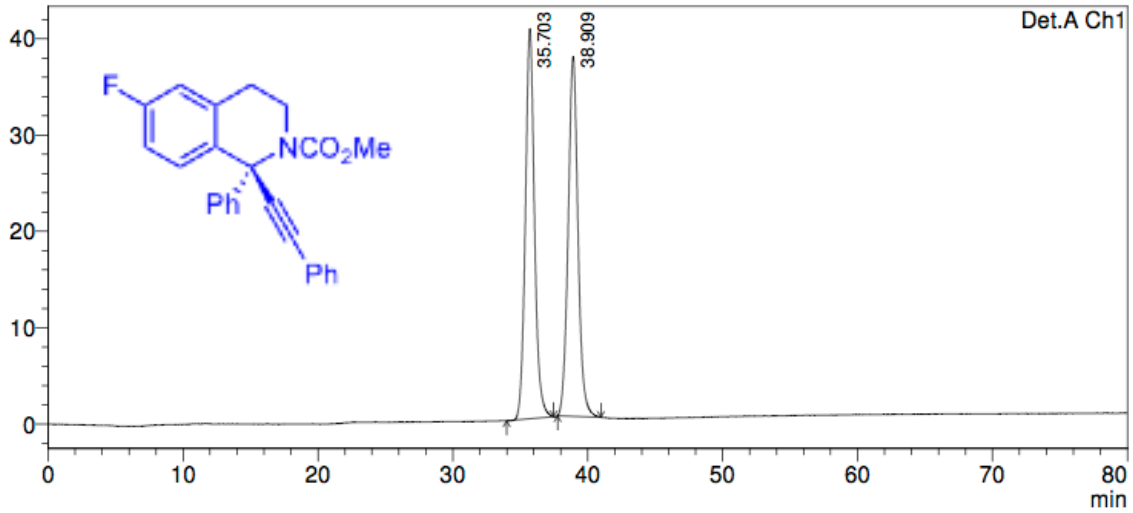
Compound 3-35, 97% ee



1 Det.A Ch1/254nm

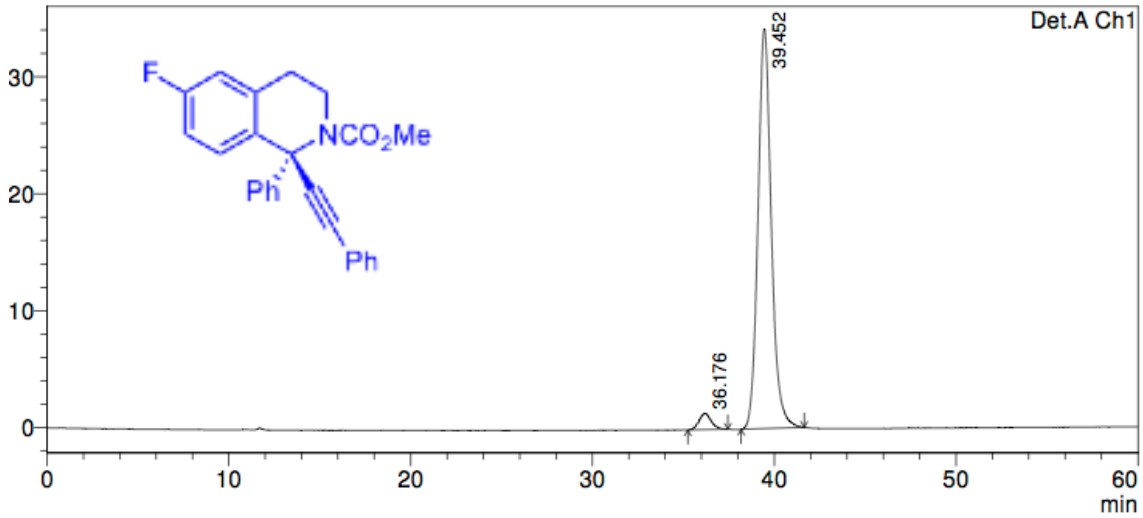
Peak#	Ret. Time	Area	Height	Area %	Height %
1	55.959	2836357	18097	98.260	98.071
2	66.881	50231	356	1.740	1.929
Total		2886588	18453	100.000	100.000

Compound 3-36, racemic



1 Det.A Ch1/254nm

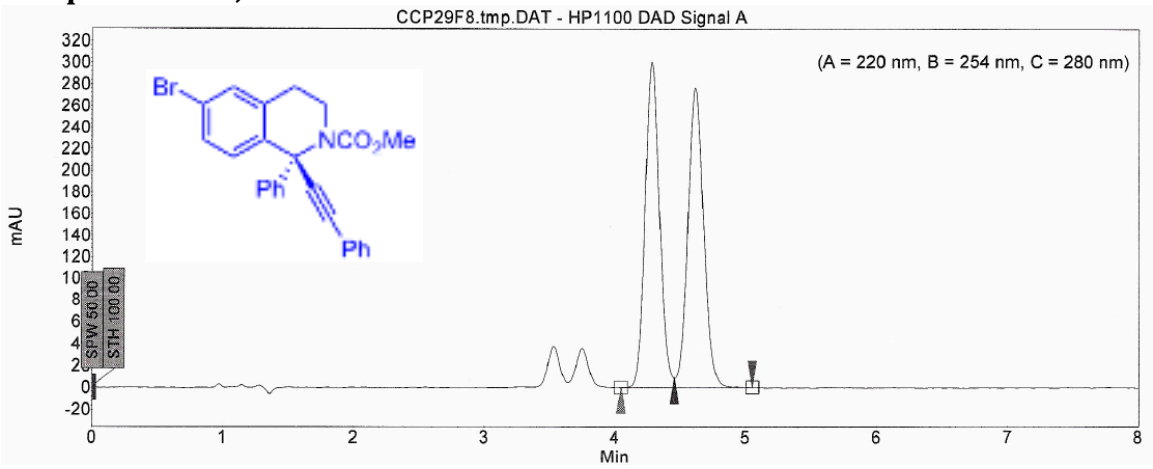
Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.703	1903348	40511	50.148	52.023
2	38.909	1892136	37360	49.852	47.977
Total		3795484	77871	100.000	100.000



1 Det.A Ch1/254nm

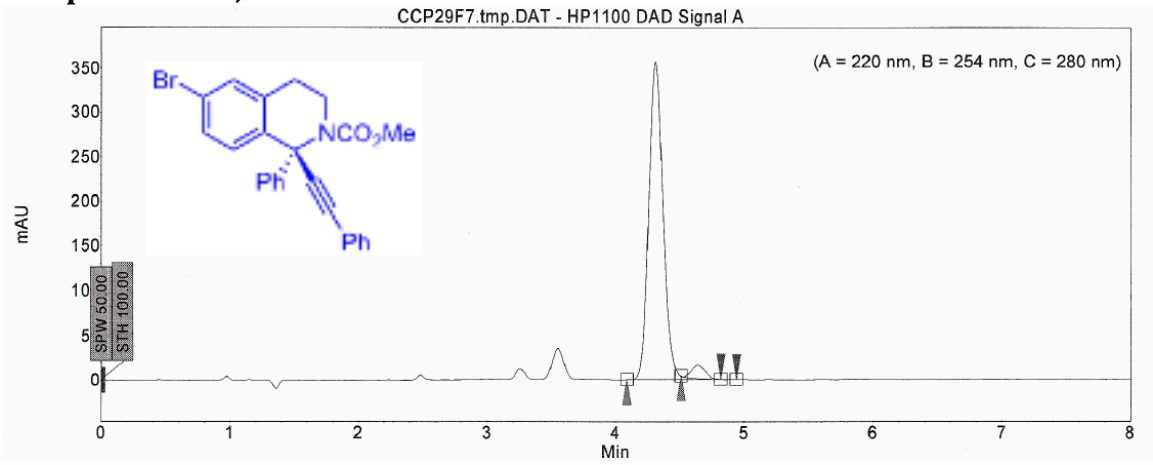
Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.176	63970	1380	3.537	3.883
2	39.452	1744506	34158	96.463	96.117
Total		1808476	35537	100.000	100.000

Compound 3-37, racemic



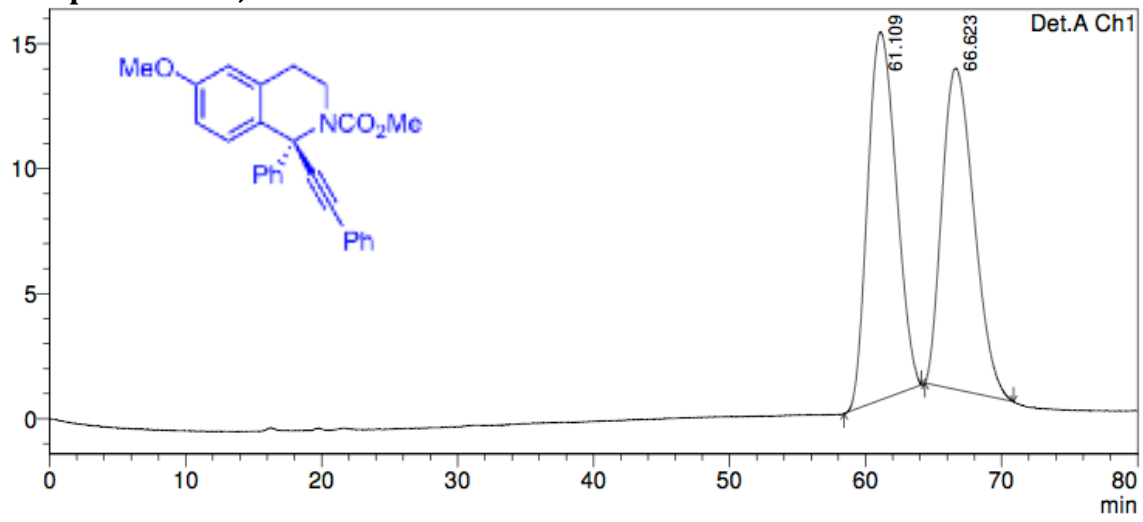
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.05	4.28	4.46	0.00	49.77	300.2	38.2	49.771
2	UNKNOWN	4.46	4.61	5.05	0.00	50.23	276.9	38.6	50.229
Total						100.00	577.1	76.8	100.000

Compound 3-37, 92% ee



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.08	4.31	4.94	0.00	96.20	356.5	46.1	96.196
2	UNKNOWN	4.51	4.64	4.82	0.00	3.80	14.5	1.8	3.804
Total						100.00	371.1	47.9	100.000

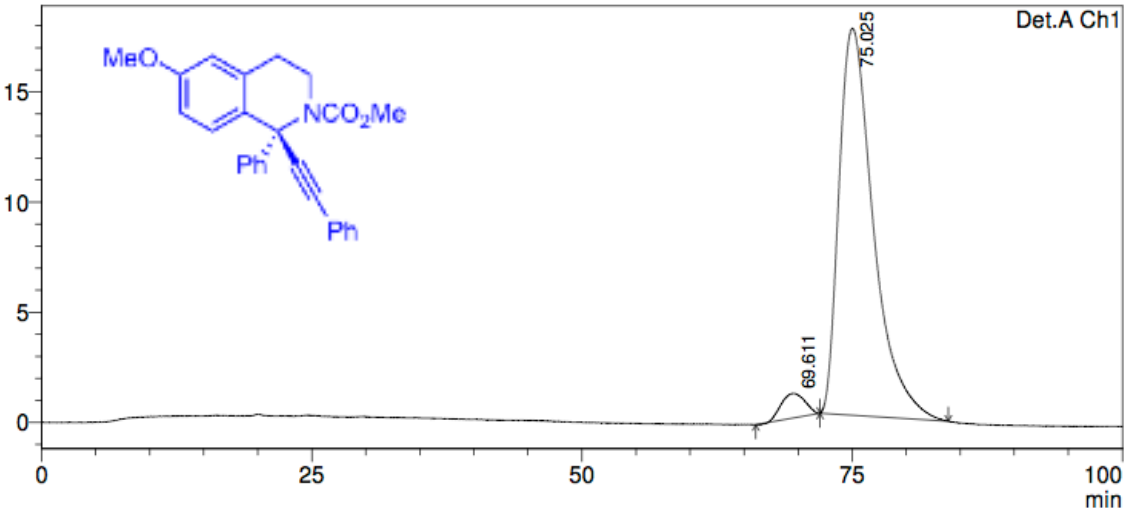
Compound 3-38, racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	61.109	2149339	14736	50.569	53.405
2	66.623	2100968	12857	49.431	46.595
Total		4250307	27594	100.000	100.000

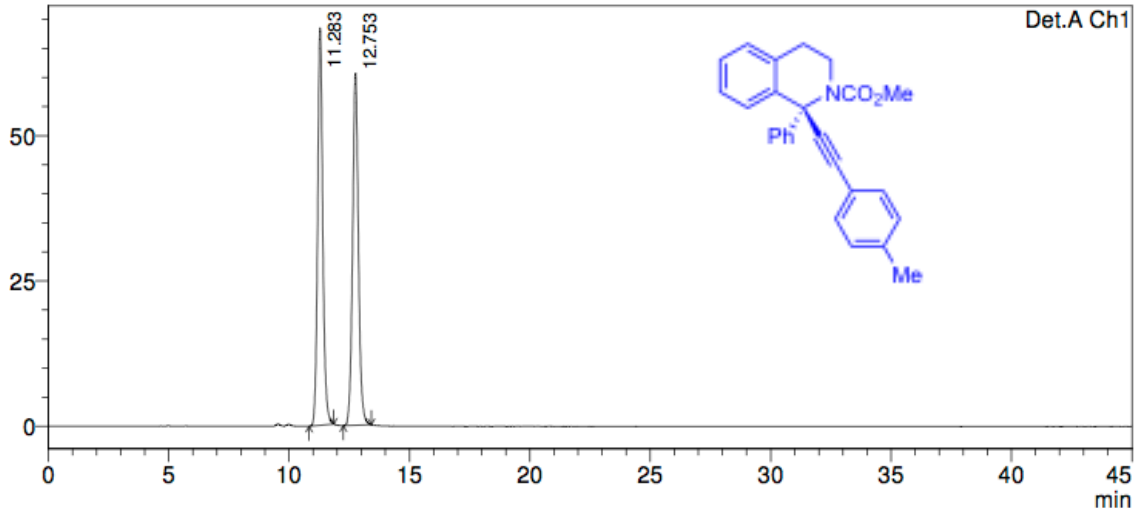
Compound 3-38, 92% ee



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	69.611	169465	1111	4.178	5.950
2	75.025	3886286	17563	95.822	94.050
Total		4055750	18674	100.000	100.000

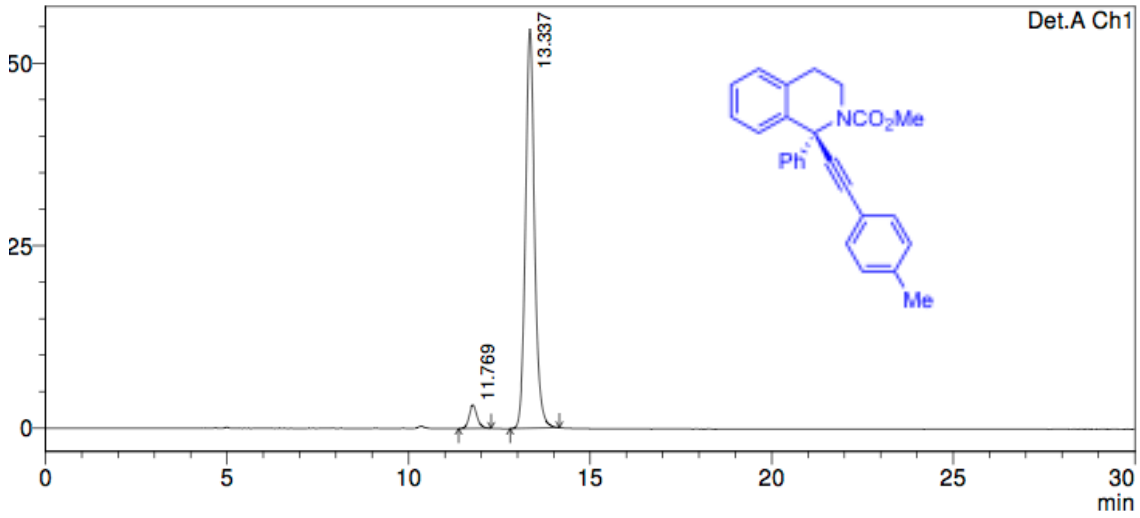
Compound 3-45, racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.283	1013323	68314	49.864	52.996
2	12.753	1018854	60590	50.136	47.004
Total		2032177	128905	100.000	100.000

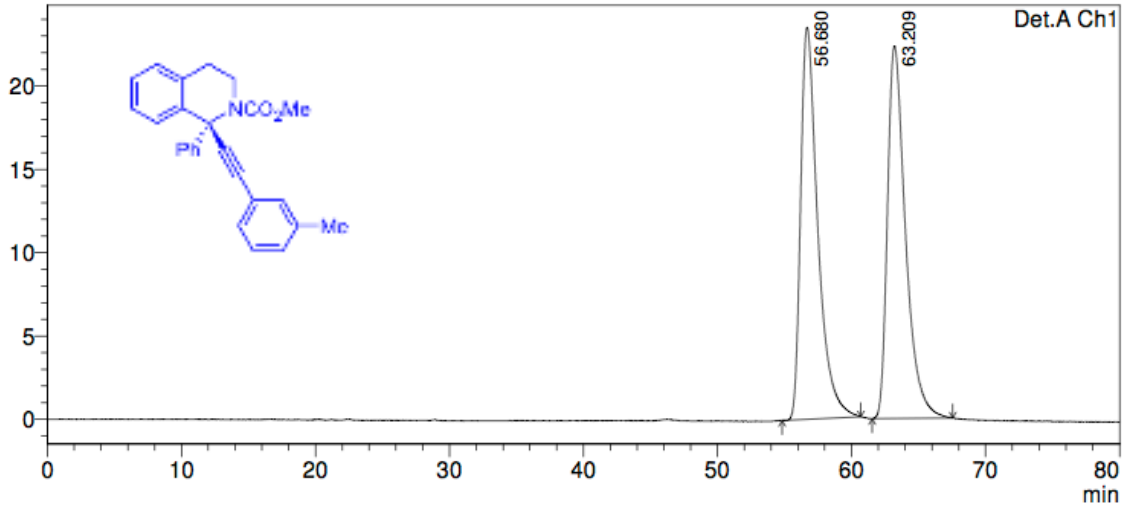
Compound 3-45, 90% ee



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.769	49513	3237	4.954	5.586
2	13.337	950003	54708	95.046	94.414
Total		999516	57945	100.000	100.000

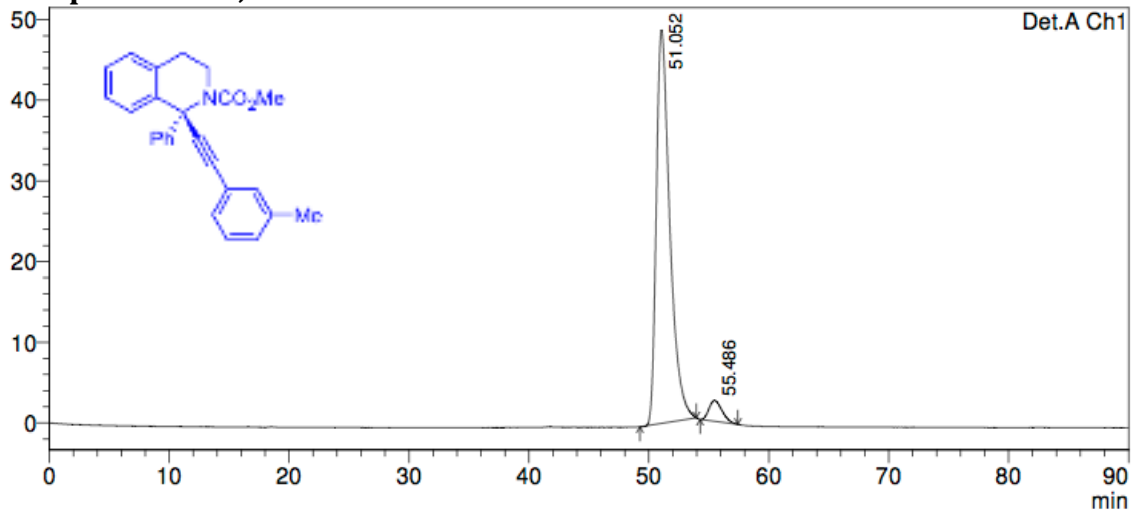
Compound 3-46, racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	56.680	2093844	23516	50.023	51.265
2	63.209	2091890	22355	49.977	48.735
Total		4185734	45872	100.000	100.000

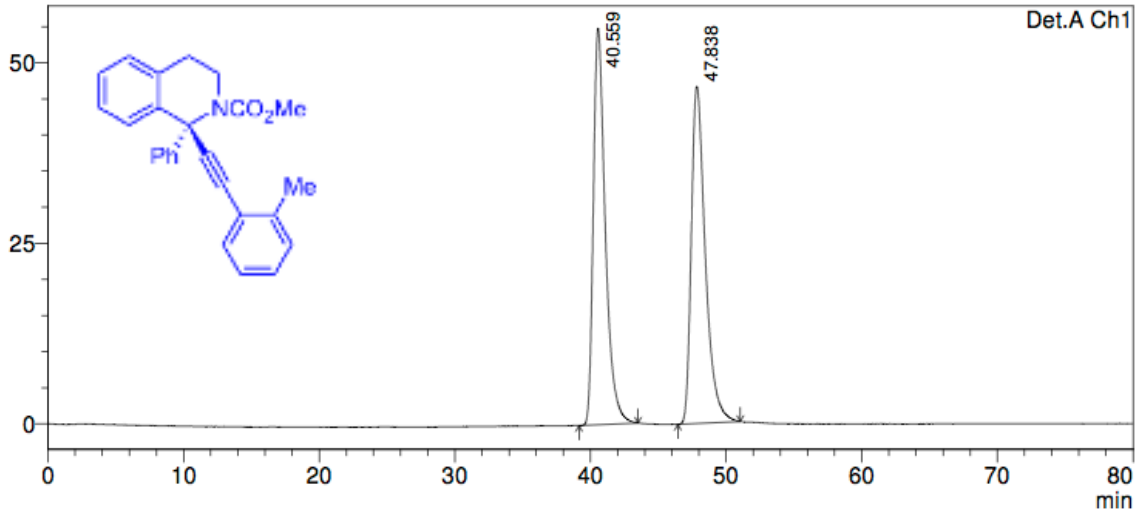
Compound 3-46, 90% ee



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	51.052	3825736	48785	95.045	94.942
2	55.486	199454	2599	4.955	5.058
Total		4025190	51384	100.000	100.000

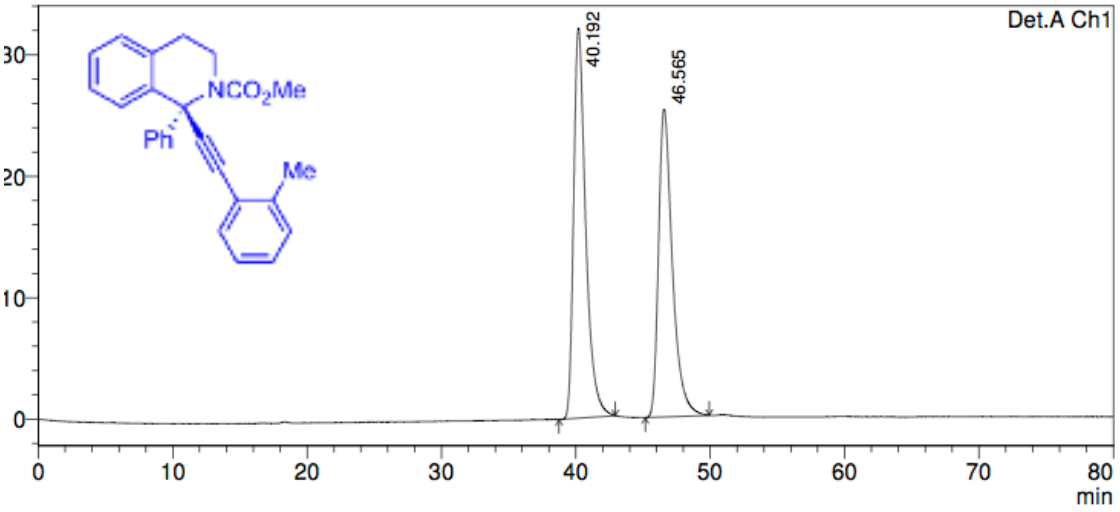
Compound 3-47, racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	40.559	3371815	54908	50.119	54.035
2	47.838	3355859	46707	49.881	45.965
Total		6727675	101615	100.000	100.000

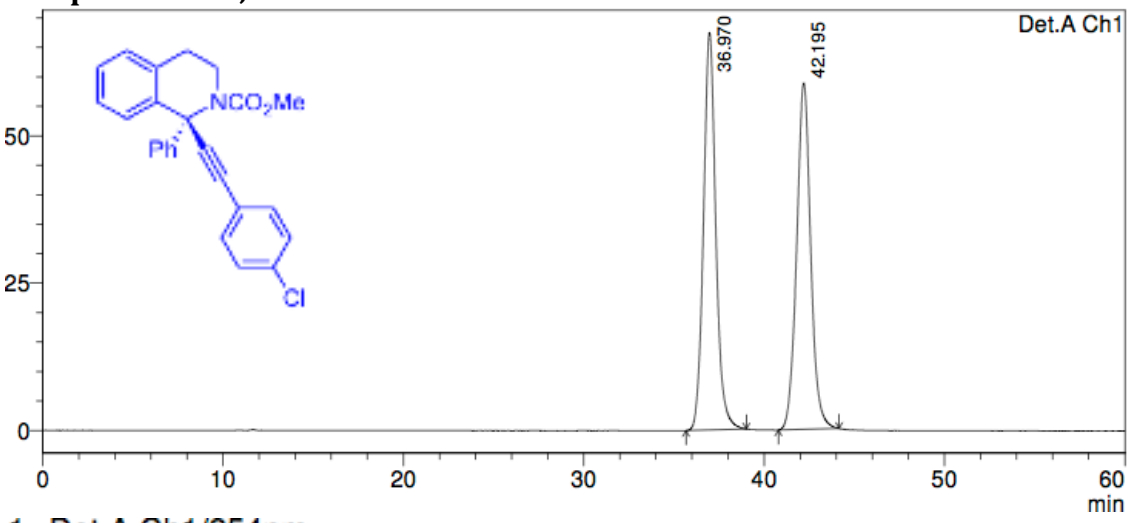
Compound 3-47, 5% ee



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	40.192	2000455	32120	52.413	55.900
2	46.565	1816295	25340	47.587	44.100
Total		3816750	57459	100.000	100.000

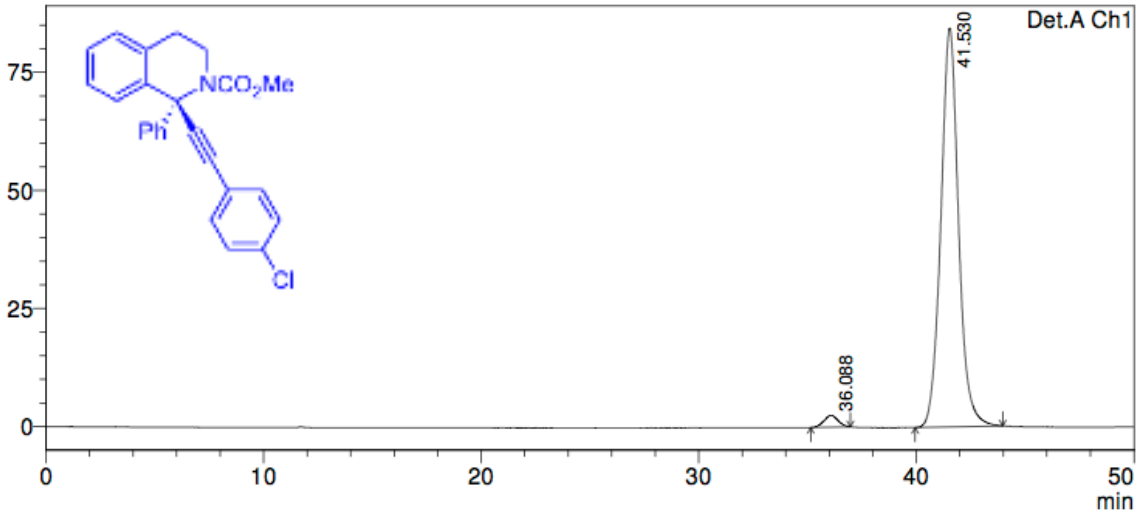
Compound 3-48, racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.970	3205955	67457	50.127	53.418
2	42.195	3189727	58823	49.873	46.582
Total		6395683	126280	100.000	100.000

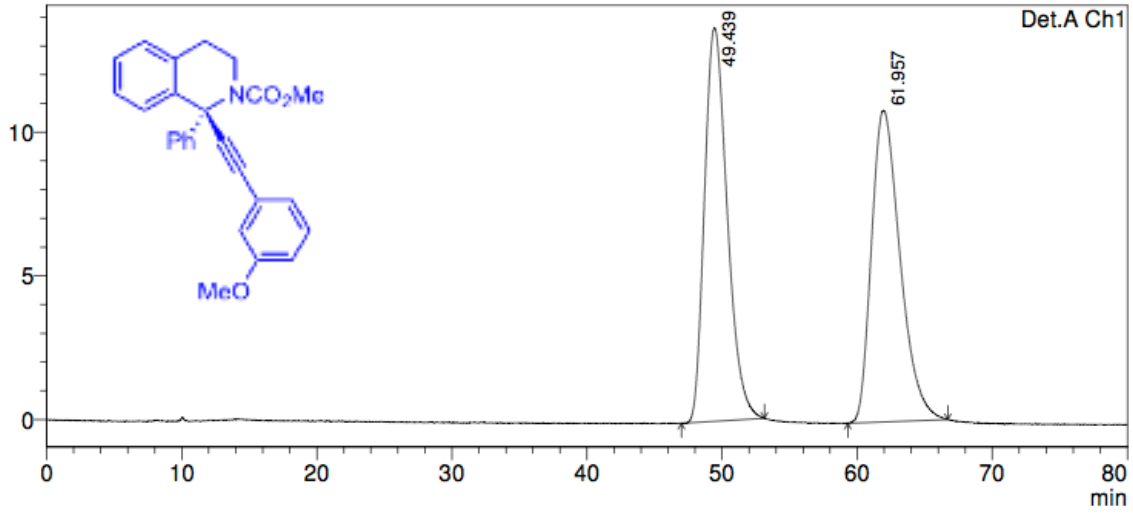
Compound 3-48, 95% ee



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.088	113139	2485	2.314	2.861
2	41.530	4775255	84373	97.686	97.139
Total		4888394	86858	100.000	100.000

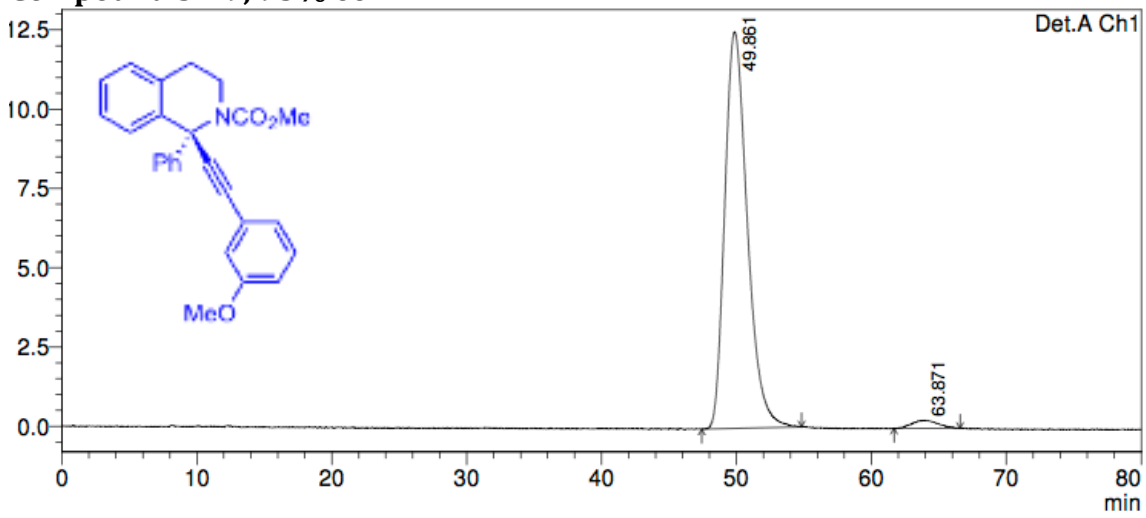
Compound 3-49, racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	49.439	1599586	13696	50.048	55.811
2	61.957	1596528	10844	49.952	44.189
Total		3196114	24540	100.000	100.000

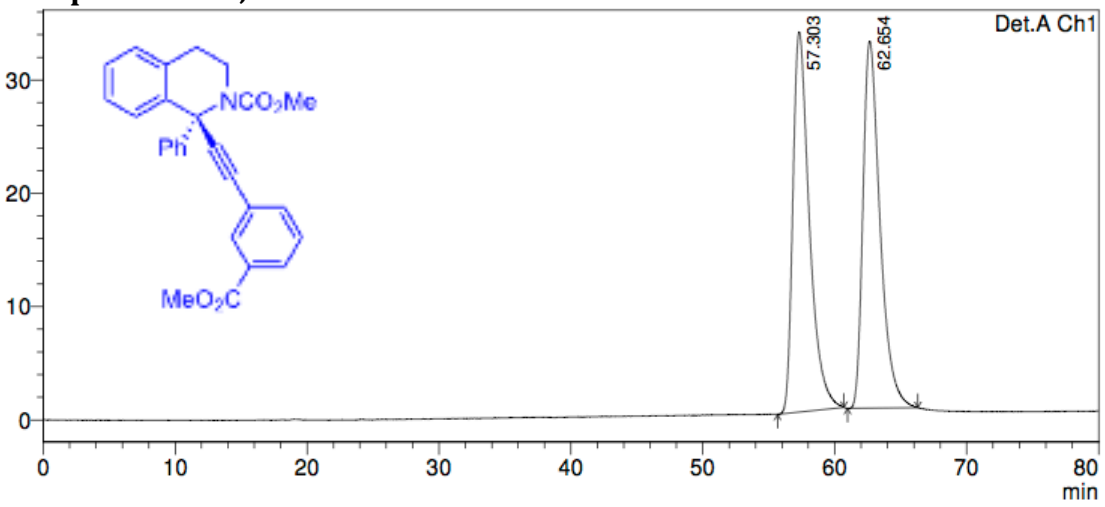
Compound 3-49, 95% ee



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	49.861	1450543	12498	97.721	98.015
2	63.871	33826	253	2.279	1.985
Total		1484369	12751	100.000	100.000

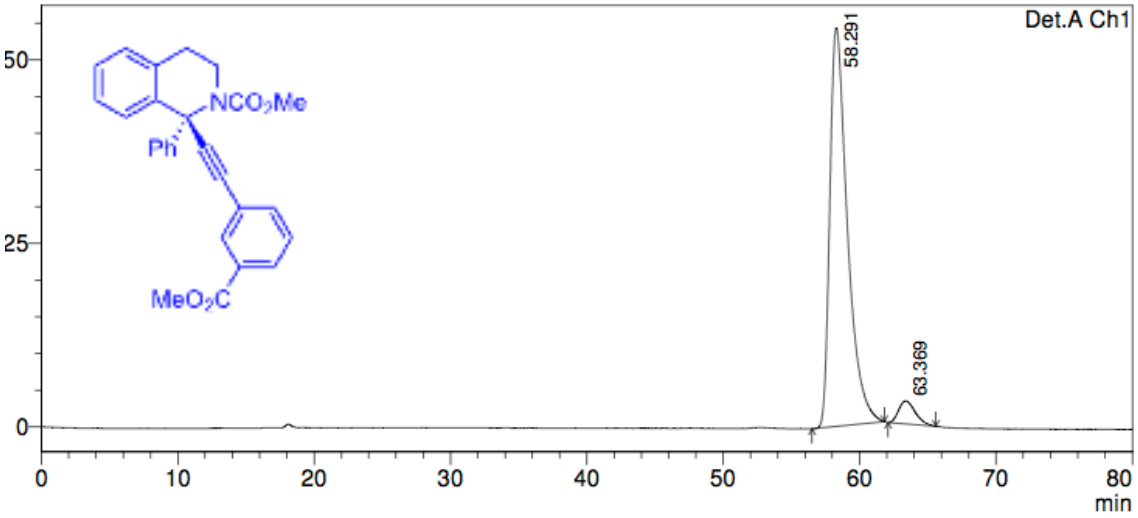
Compound 3-50, racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	57.303	2920351	33544	50.062	50.875
2	62.654	2913065	32390	49.938	49.125
Total		5833416	65934	100.000	100.000

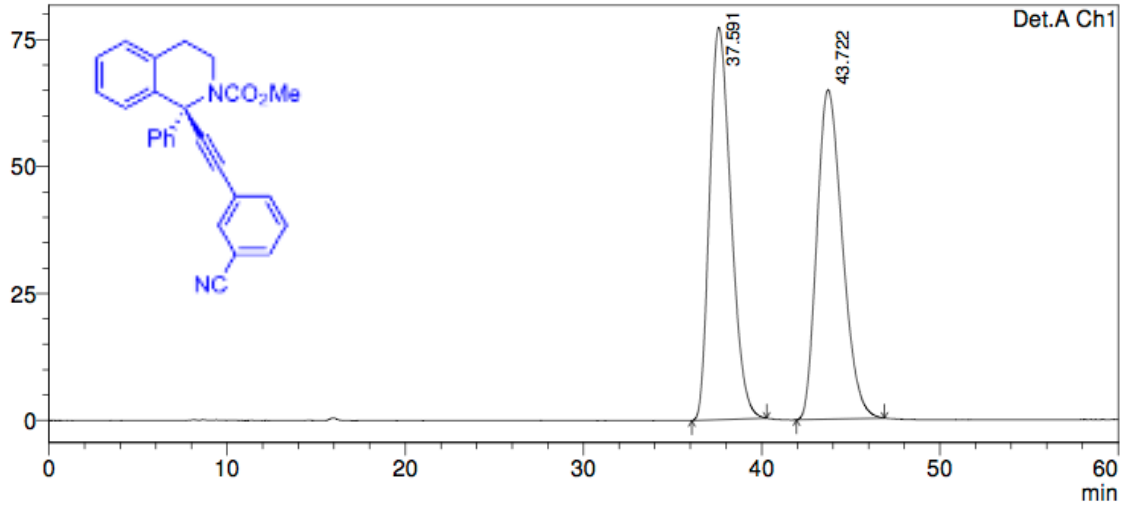
Compound 3-50, 90% ee



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	58.291	4858913	54265	94.812	94.528
2	63.369	265882	3141	5.188	5.472
Total		5124795	57407	100.000	100.000

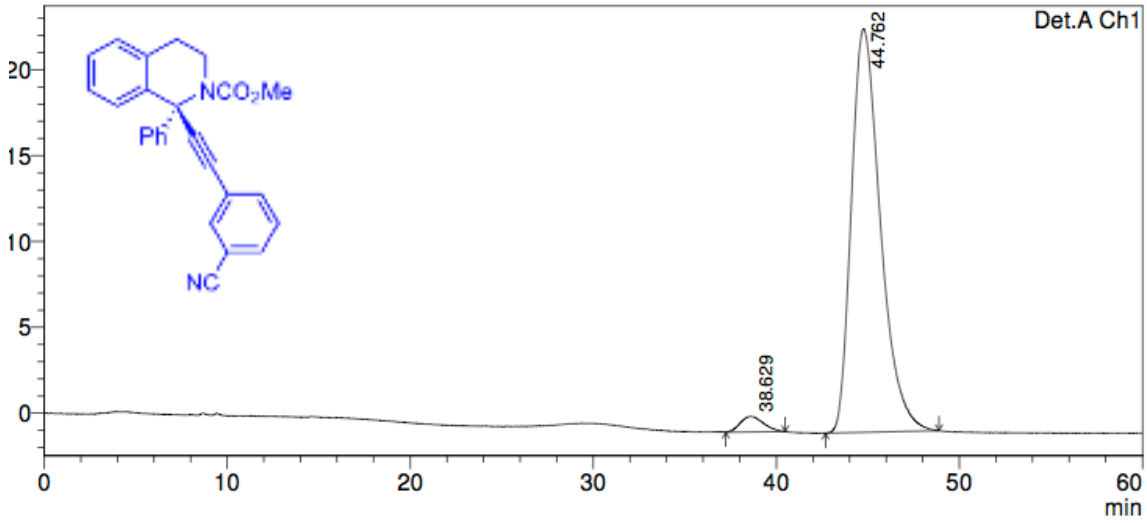
Compound 3-51, racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	37.591	6441558	77283	49.994	54.363
2	43.722	6443017	64878	50.006	45.637
Total		12884574	142161	100.000	100.000

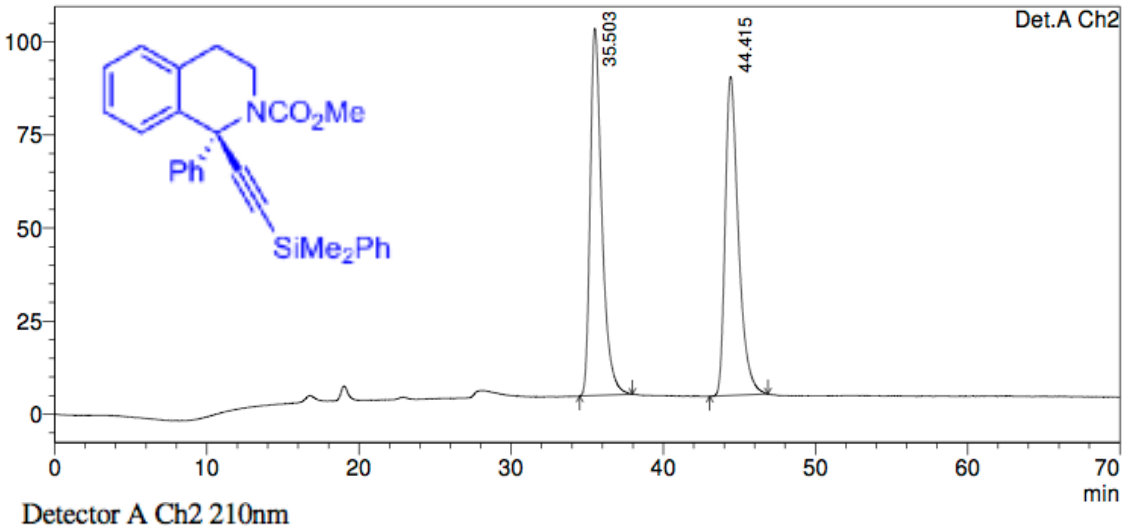
Compound 3-51, 94% ee



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	38.629	78910	900	2.952	3.689
2	44.762	2594290	23492	97.048	96.311
Total		2673200	24392	100.000	100.000

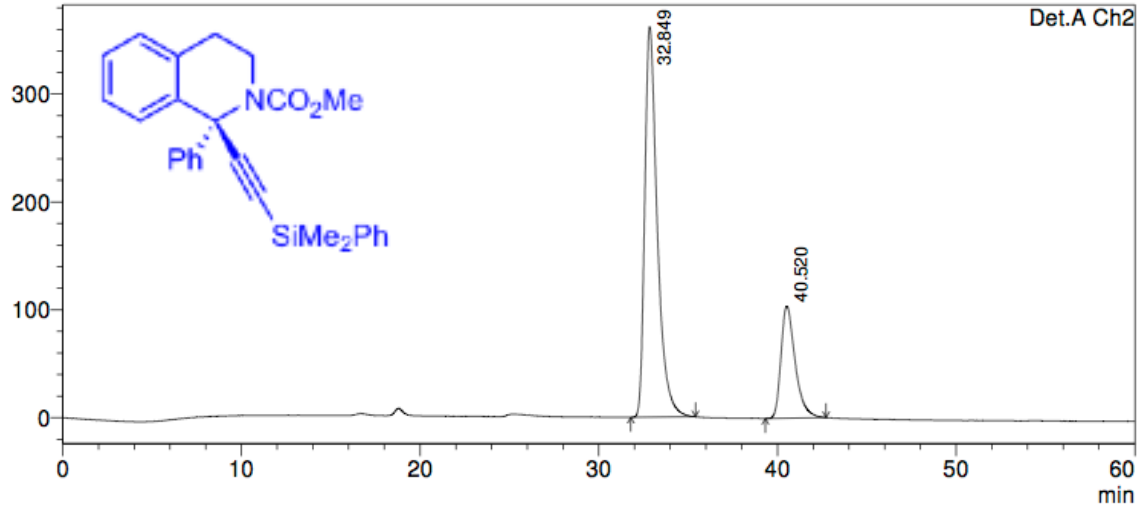
Compound 3-52, racemic



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.503	5253982	98595	50.316	53.526
2	44.415	5187921	85605	49.684	46.474
Total		10441904	184200	100.000	100.000

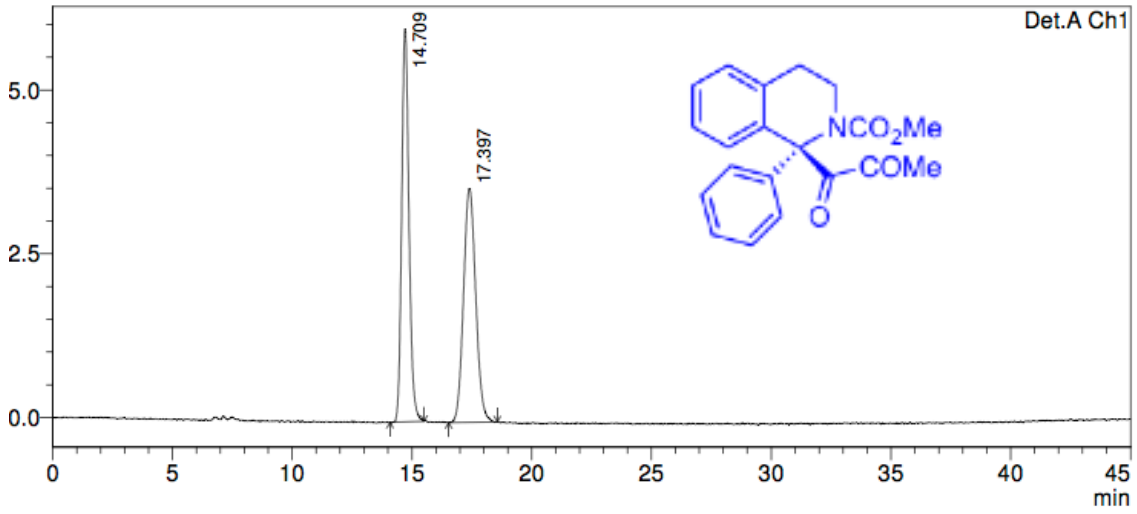
Compound 3-52, 51% ee



Detector A Ch2 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.849	17639462	361873	75.456	77.705
2	40.520	5737626	103825	24.544	22.295
Total		23377088	465698	100.000	100.000

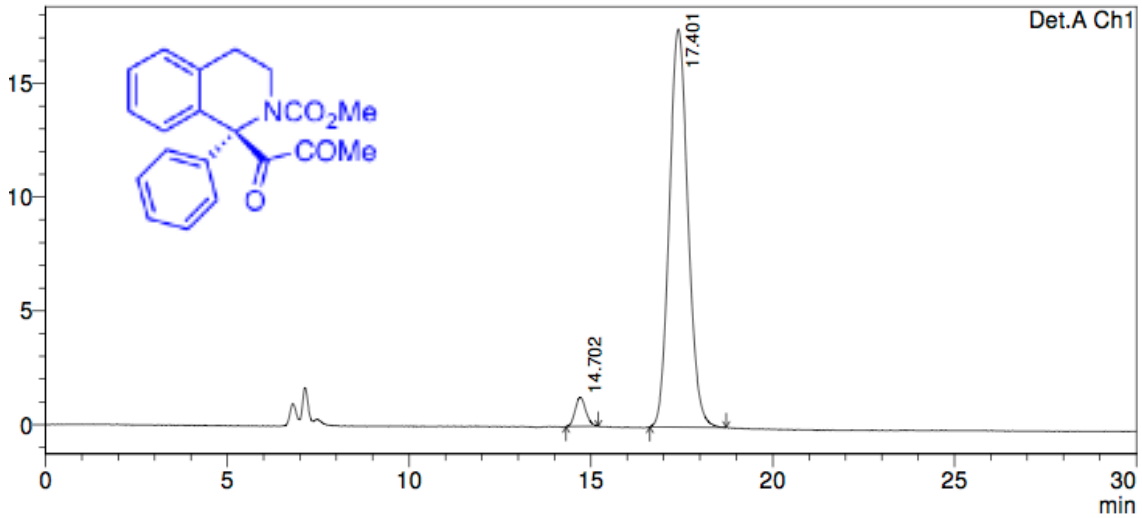
Compound 3-57, racemic



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.709	126657	6002	50.044	62.661
2	17.397	126436	3576	49.956	37.339
Total		253093	9578	100.000	100.000

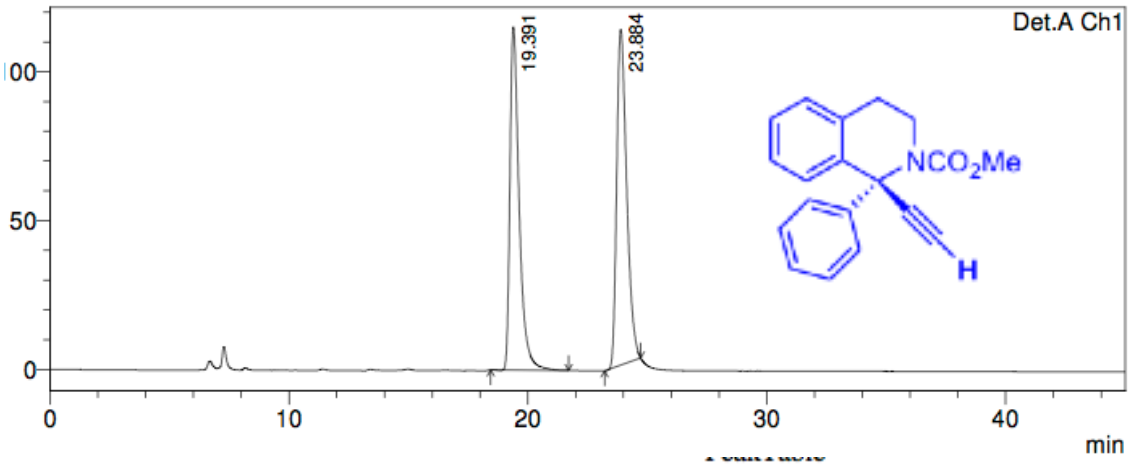
Compound 3-57, 92% ee



1 Det.A Ch1/254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.702	26240	1278	4.038	6.809
2	17.401	623612	17498	95.962	93.191
Total		649852	18776	100.000	100.000

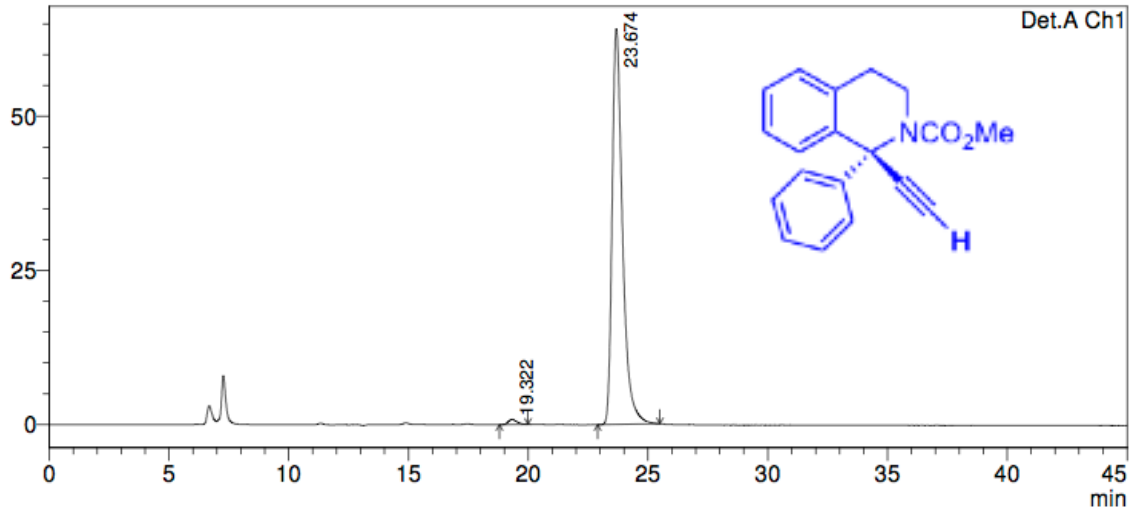
Compound 3-58, racemic



Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.391	3103713	115294	48.715	50.560
2	23.884	3267476	112740	51.285	49.440

Compound 3-58, 97% ee



Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.322	20585	816	1.052	1.255
2	23.674	1936717	64203	98.948	98.745
Total		1957302	65019	100.000	100.000

Appendix B

PERMISSION LETTERS

Title: Nickel(0)-Catalyzed Cyclization of N-Benzoylaminals for Isoindolinone Synthesis

Author: Danielle M. Shacklady-McAtee, Srimoyee Dasgupta, Mary P. Watson

Publication: Organic Letters

Publisher: American Chemical Society

Date: Jul 1, 2011

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