Interrupted Carbonyl-Olefin Metathesis – Supplementary Material

Authors: Jacob R. Ludwig, Rebecca B. Watson,[†] Daniel J. Nasrallah,[†] Joseph B. Gianino, Paul M. Zimmerman, Ren A. Wiscons, and Corinna S. Schindler[†]*

University of Michigan, Willard Henry Dow Laboratory, Department of Chemistry, 930 North University Ave., Ann Arbor, MI 48109, US

Table of Contents

1. General Information

General Laboratory Procedures. All moisture-sensitive reactions were performed under an atmosphere of nitrogen in flame-dried round bottom flasks or glass vials fitted with rubber septa and/or septa equipped screw caps. Stainless steel syringes were used to transfer air or moisture-sensitive liquids. Gas chromatography (GC) was conducted on a Shimadzu GC-2010 Plus system using a Shimadzu SHRXI-5MS column. Column chromatography was performed using silica gel Silia Flash® 40-63 micron (230-400 mesh) from Silicycle.

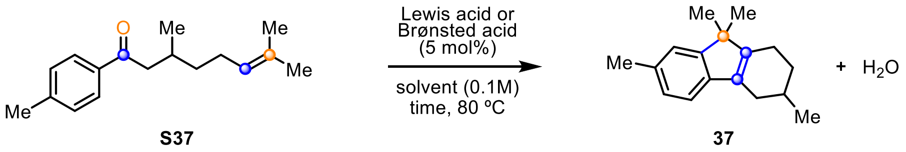
Materials and Instrumentation. All chemicals were purchased from Sigma-Aldrich, VWR, Oakwood or Acros and were used as received unless otherwise stated. Tetrahydrofuran was dried by being passed through columns of activated alumina. (*E*)-(4-bromobut-2-en-2-yl)benzene,(*31*) (2-bromoethylidene)cyclohexane,(*32*) 1-bromo-3-ethylpent-2-ene,(*33*) (2-bromoethylidene)cyclopentane,(*34*) 1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-one,(*35*) (2-oxo-2-(*p*-tolyl)ethyl)phosphonate,(*36*) 3-(1,3-dioxoisoindolin-2-yl)propanal,(*37*) diethyl 2-(3-methylbut-2-en-1-yl)malonate,(*38*) 1-(4-(*tert*-butyl)phenyl)prop-2-en-1-one,(*39*) ethyl 2-(((trifluoromethyl)sulfonyl)oxy)cyclohex-1-ene-1-carboxylate(*40*) and (3*R*,6*S*)-3-methyl-6-(prop-1-en-2-yl)cyclohex-1-en-1-yl trifluoromethanesulfonate(*41*) were prepared according to literature procedures. Proton Nuclear Magnetic Resonance NMR (^{1}H NMR) spectra and Carbon Nuclear Magnetic Resonance (^{13}C NMR) spectra were recorded on a Varian Unity Plus 400, Varian MR400, Varian vnmrs 500, Varian Inova 500, Varian Mercury 500, and Varian vnmrs 700 spectrometers. Chemical shifts for protons are reported in parts per million and are references to the NMR solvent peak ($CDCl_3$: δ 7.26). Chemical shifts for carbons are reported in parts per million and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$: δ77.16). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants in Hertz (Hz). Mass spectroscopic (MS) data was recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Michigan in Ann Arbor, MI on an Agilent Q-TOF HPLC-MS with ESI high resolution mass spectrometer. Infrared (IR) spectra were obtained using either an Avatar 360 FT-IR or Perkin Elmer Spectrum BX FT-IR spectrometer. IR data are represented as frequency of absorption (cm^{-1}).

Abbreviations used: GC = gas chromatography, TfOH = triflic acid, PhH = benzene, PhCl = chlorobenzene, PhMe = toluene, $PhCF_3$ = trifluoromethylbenzene, IBX = 2-iodoxybenzoic acid, n-BuLi = n-butyllithium, TBAF = tetrabutylammonium fluoride, NaH = sodium hydride, Et_2O = diethyl ether, PBr_3 = phosphorus tribromide, PPh_3 = triphenylphosphine tBuOK = potassium tert-butoxide, TPPO = triphenylphosphine oxide, $HSiCl_3$ = trichlorosilane, DIPA = diisopropylamine, LDA = lithium diisopropylamide, MsCl = methanesulfonyl chloride, MnO_2 = manganese dioxide, NaOH = sodium hydroxide, TEBAC = benzyltriethylammonium chloride, KOH = potassium hydroxide, KI = potassium iodide, K_2CO_3 = potassium carbonate, Na_2CO_3 = sodium carbonate, $Pd(PPh_3)_4$ = tetrakis(triphenylphosphine)palladium(0), EtOH = ethanol, $TiCl_4$ = titanium tetrachloride, $AlCl_3$ = aluminium chloride, AcOH = acetic acid, PTSA = p-Toluenesulfonic acid monohydrate, $AlCl_3$ = aluminium chloride, DCC = N,N'-dicyclohexylcarbodiimide, NMM = N-methylmorpholine, N_2 = nitrogen, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, TEA = triethylamine, TEBAC = triethylbenzylammonium chloride, MeMgBr = methylmagnesium bromide, EtOAc = ethyl acetate, DMF = dimethylformamide, DCM = dichloromethane, DCE = 1,2-dichloroethane, HCl = hydrogen chloride, NaHCO3 = sodium bicarbonate, DIPEA = *N,N*-diisopropylethylamine, S = starting material or substrate for a given product (following the numbering scheme used in the main text), P = product for a given substrate (following the numbering scheme used in the main text), F = fluorene product from oxidation of a given tetrahydrofluorene (following the numbering scheme used in the main text), C = computationally generated structure, THF = tetrahydrofuran, Na_2SO_4 = sodium sulfate, $MgSO_4$ = magnesium sulfate, DMSO = dimethyl sulfoxide, TLC = thin layer chromatography.

2. Optimization of Reaction Conditions

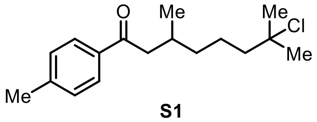
To a 20 mL scintillation vial containing a magnetic stir bar was added the appropriate solid Lewis acid, solvent, and substrate (0.205 mmol). For liquid Lewis acids, the order of addition was substrate, solvent and Lewis acid. The reactions were allowed to stir for the indicated time and the indicated temperature. After reaching completion as judged by TLC or 24 h, the reaction was filtered through a silica plug eluting with DCM. The filtrate was concentrated under reduced pressure, and the crude mixture was diluted in a volumetric flask with toluene (5 mL). An aliquot (350 mL) of this solution was added to another volumetric flask, dodecane (3-15 mL) was added as an internal standard, and the mixture was diluted to 1 mL with toluene before being subjected to quantitative GC analysis. GC yield was based on a linear calibration curve (minimum of 5 points) with dodecane.

Table S1. Lewis acid evaluation.



entry	Lewis/Brønsted acid	solvent	time (h)	yield (%)[*]	conversion (%)[*]
1	$ZnCl_2$	DCE	24	0[†]	6[†]
2	$TiCl_4$	DCE	24	0[†]	74[†,‡]
3	$AlCl_3$	DCE	24	0[†]	6[†]
4	$FeCl_3$	DCE	24	15	51
5	$Fe(OTf)_3$	DCE	2	81	99
6	$Bi(OTf)_3$	DCE	4	78	98
7	$Mg(OTf)_2$	DCE	24	80	99
8	$In(OTf)_3$	DCE	24	84	99
9	AgOTf & *t*BuCl	DCE	4	75	98
10	TfOH	DCE	24	77	99
11	TfOH	PhCl	3	87	99
12	TfOH	PhMe	2	67	98
13	TfOH	$PhCF_3$	2	80	99
14	TfOH	PhH	2	80	98
15	TfOH	PhH (rt)	24	0	42
16	TfOH	PhH (0.02 M)	2	82	99
17	TfOH	PhH (0.02 M)[§]	2	94	99

Conditions: All reactions were performed using 50 mg of aryl ketone at 80 ºC or room temperature for 2-24 hours. [*]Percent yield and percent conversion determined by GC using dodecane as an internal standard. [†]Percent yield and percent conversion determined by ^{1}H-NMR using dimethyl terephthalate as an internal standard. [‡]The formation of tertiary chloride **S1** was observed in 64% yield. [§]Benzene was degassed prior to use.

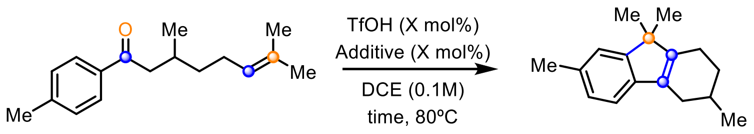


S1

Table S1 Details: Our initial studies focused on elucidating the inherent difference in reactivity between $FeCl_3$ and $Fe(OTf)_3$. When Lewis acids varying in strength (e.g. $ZnCl_2$, $TiCl_4$, $AlCl_3$) were used at elevated temperatures of 80 ˚C, no formation of the desired product was observed. When catalytic amounts of $FeCl_3$ were used, the product was detected in 15% yield. However, the use of triflate-based Lewis acids $Fe(OTf)_3$, $Bi(OTf)_3$, $Mg(OTf)_2$ and $In(OTf)_3$ resulted in the formation of the tetrahydrofluorene product in up to 84% yield. Based on these results we hypothesized that this transformation was in fact Brønsted acid-catalyzed relying on triflic acid (TfOH) as the active catalyst, and the optimal reaction conditions were ultimately established as 5 mol% TfOH at 80 ˚C in degassed benzene. The increased yields observed with aromatic solvents could be a result of their weak basicity, ultimately leading to decreased side reactions (*22*).

3. Brønsted Acid Evaluation

Table S2. Effect of acid strength on interrupted carbonyl-olefin metathesis reaction.



S37 **37**

entry	TfOH (X mol%)	Additive (X mol%)*	pK_a: (H$_2$O)†	(DMSO)‡	(DCE)§	time (h)	yield (%)‖	conv. (%)‖
1	5	-	-14	0.3	-11.4	2	71	99
2	-	MsOH (5 mol%)	-2.6	1.6	-	24	8	26
3	-	TFA (5 mol%)	-0.25	3.45	-	24	0	14
4	-	Tf$_2$NH (5 mol%)	-	-	-12.3	1	44	98
5	5	benzoic acid (10 mol%)	-7.8	-	-	21	51	99
6	5	THF (10 mol%)	-2.05	-	-	24	32	86
7	5	anisole (10 mol%)	-6.5	-	-	24	27	80
8	5	nitrobenzene (10 mol%)	-12.4	-	-	24	26	77
9	5	DMSO (10 mol%)	-1.8	-	-	24	10	41

Conditions: All reactions were performed using 50 mg of aryl ketone at 80°C for 2-24 hours. *2 mmol additive were mixed with 1 mmol TfOH in 5 mL DCE and 50 μL of this solution was added to the reaction. †See (*42*). ‡See (*43*). §See (*44*). ‖Percent yield and percent conversion determined by NMR using dimethyl terephthalate as an internal standard.

4. Initial Mechanistic Hypothesis

Figure S1. Initial mechanistic hypothesis and experimental studies for the formation of tetrahydrofluorenes from aryl ketones. *Percent yield determined by ^{1}H-NMR using dimethyl terephthalate as an internal standard.

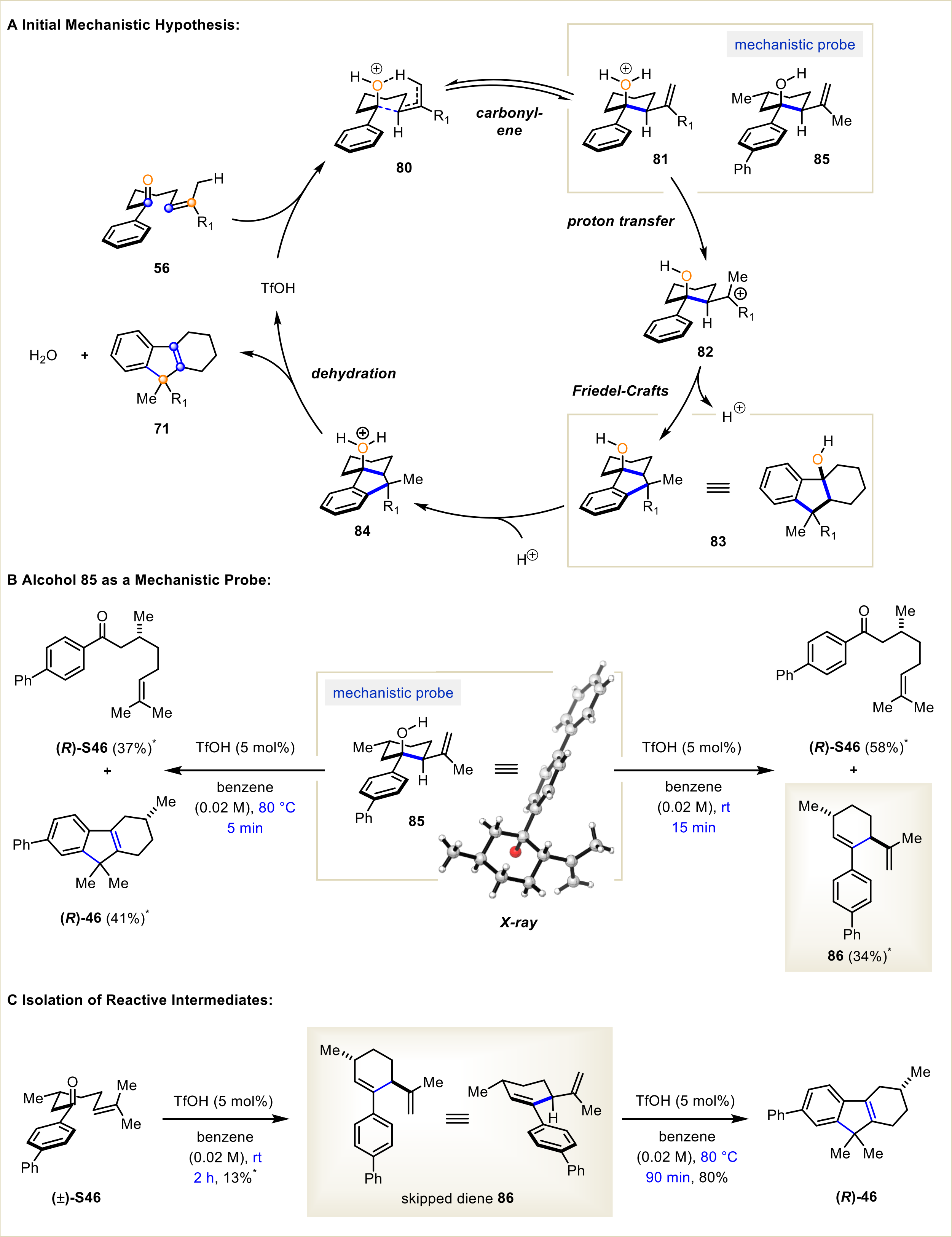
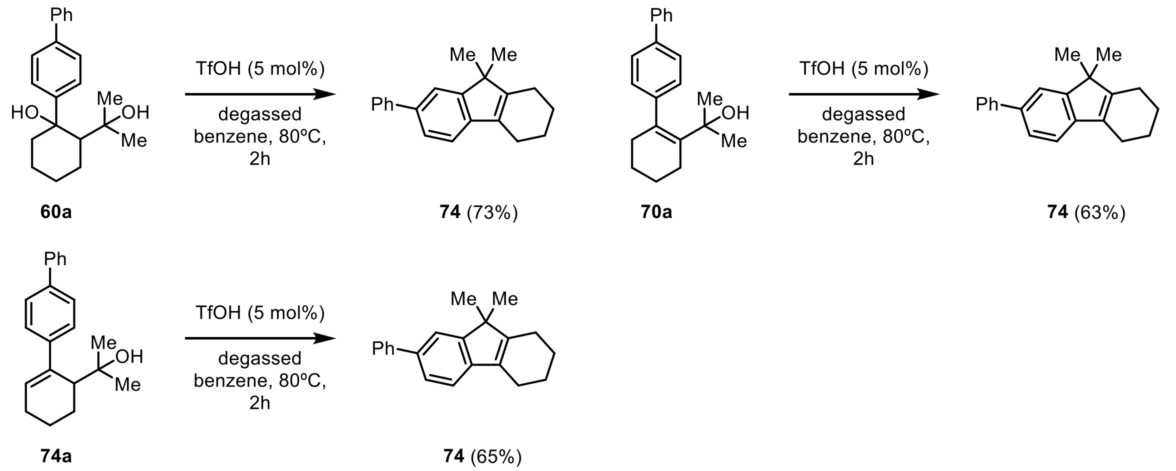

A Initial Mechanistic Hypothesis:
mechanistic probe
carbonyl-ene
80
81
85
56
proton transfer
82
TfOH
H2O +
71
dehydration
Friedel-Crafts
H⊕
84
83
H⊕
Me
R1
B Alcohol 85 as a Mechanistic Probe:
(R)-S46 (37%)*
+
(R)-46 (41%)*
TfOH (5 mol%)
benzene
(0.02 M), 80 °C
5 min
mechanistic probe
85
X-ray
TfOH (5 mol%)
benzene
(0.02 M), rt
15 min
(R)-S46 (58%)*
+
86 (34%)*
Ph
Me
C Isolation of Reactive Intermediates:
(±)-S46
TfOH (5 mol%)
benzene
(0.02 M), rt
2 h, 13%*
skipped diene 86
TfOH (5 mol%)
benzene
(0.02 M), 80 °C
90 min, 80%
(R)-46

Figure S1 Details: Based on the literature precedent of transformations between carbonyls and olefins, we initially considered a mechanistic hypothesis relying on a carbonyl-ene reaction to form alcohol **81** upon nucleophilic addition between the carbonyl and olefin functionalities (Fig. S1-A). Subsequent proton transfer would lead to carbocation **82** which could undergo Friedel-Crafts alkylation to form alcohol **83**. Protonation of **83** followed by dehydration would provide tetrahydrofluorene **71** upon final deprotonation. To gain experimental support for this mechanistic hypothesis, we independently synthesized alcohol **85** as a mechanistic probe molecule for the carbonyl-ene reaction step. Alcohol **85**, prepared from (-)-isopulegol, was selected for its crystalline nature, allowing for its relative configuration to be established by X-ray crystallography. Significantly, the *syn*-orientation of the alcohol and alkene groups in **85** is what would be expected for the product of a concerted carbonyl-ene reaction. When this alcohol was converted under the optimized reaction conditions, the formation of the desired tetrahydrofluorene product **(*R*)-46** was observed in 41% yield together with aryl ketone **(*R*)-S46** in 37% yield (Fig. S1-B). This result suggested reversible formation of alcohol **85** under the optimized reaction conditions. Moreover, when alcohol **85** was subjected to identical reaction conditions albeit at ambient temperatures, an unexpected product, diene **86** was observed in 34% yield along with aryl ketone **(*R*)-S46** in 58% yield. Converting the aryl ketone substrate **S46** under the same conditions also led to the observation of diene **(±)-86** although in low yields of 13% (Fig. S1-C). To further elucidate the role of diene **86** in the reaction, this compound was independently synthesized from (-)-isopulegol and subjected to the optimized conditions using catalytic TfOH at elevated temperatures, resulting in the formation of tetrahydrofluorene **(*R*)-46** in 80% yield. In order to determine the likelihood of the formation of **86** as an intermediate during the carbocyclization, the reaction was monitored by ^{1}H-NMR analysis. As expected, consumption of aryl ketone **S46** and concomitant formation of tetrahydrofluorene **46** was observed; however only trace amounts of diene **(±)-86** was detected and alcohol **(±)-85** was not observed (see p. S10 below for details). Taken together, the NMR experiments, the observation of diene **86**, and the reversibility of alcohol formation (**85**) under the optimal reaction conditions provide key mechanistic insights but do not unequivocally establish alcohol **85** and diene **86** as essential reactive intermediates. Furthermore, these results do not unambiguously support our initial mechanistic hypothesis relying on a carbonyl-ene pathway and led us to consider other possible modes of reactivity between carbonyls and olefins. The fact that carbonyl-ene product **85** was found to result in tetrahydrofluorene **(*R*)-46** upon treatment with TfOH can be attributed to its reversible formation from aryl ketone **(*R*)-S46** under the optimized reaction conditions.

5. Cyclization of Mechanistic Probes

Figure S2. Formation of tetrahydrofluorene product from intermediates that could form during the interrupted carbonyl-olefin metathesis reaction.

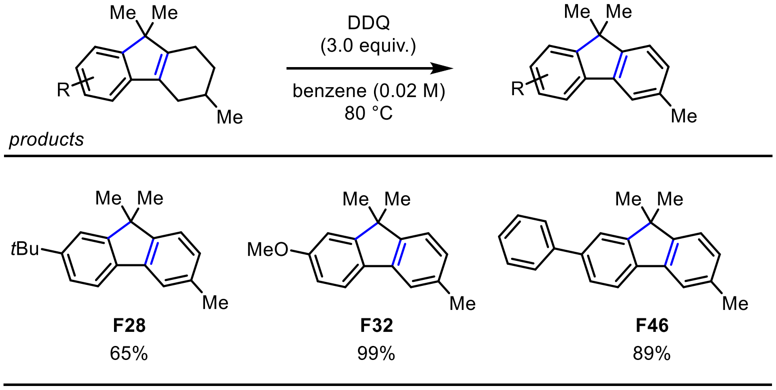
Conversion of **60a**, **70a**, and **74a** under the optimized reaction conditions form tetrahydrofluorene **74**:



6. Applications

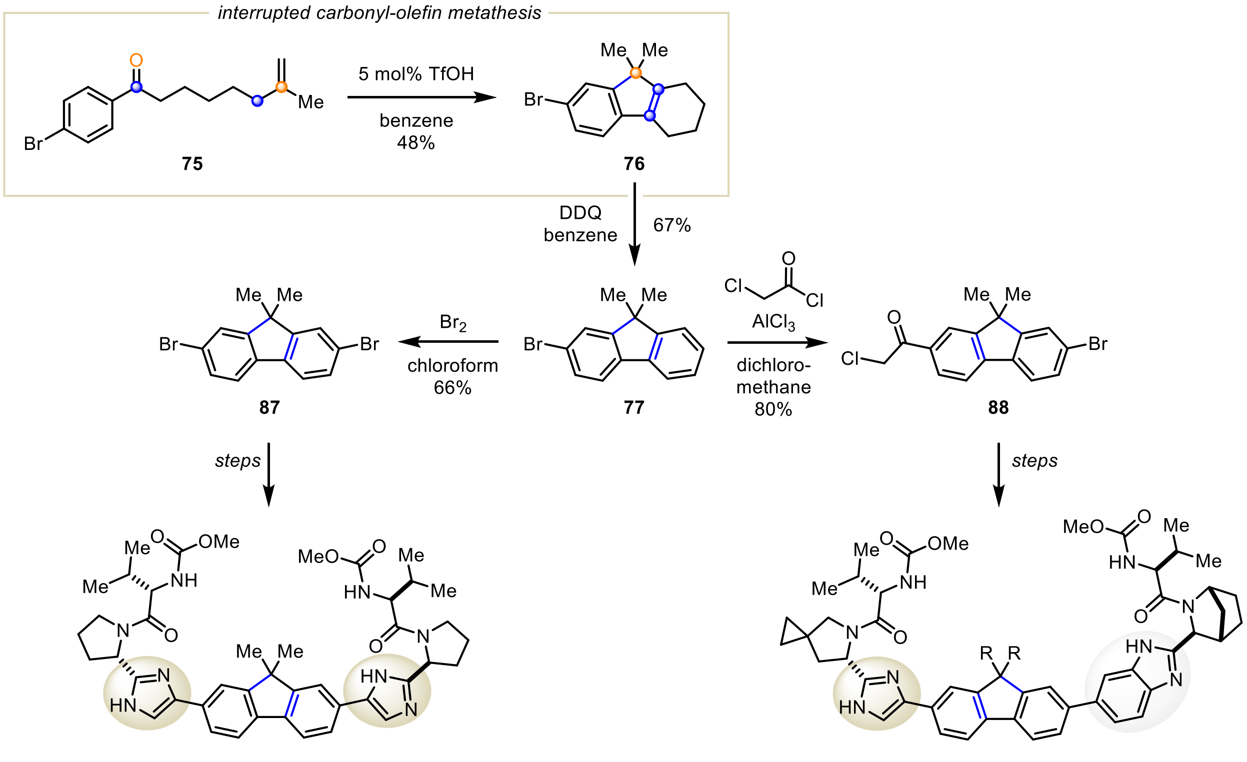
Table S3. Oxidation of tetrahydrofluorenes to the fluorenes.

Oxidation to Fluorenes:



Conditions: Tetrahydrofluorene (1.0 equiv.), DDQ (3.0 equiv.) in benzene (0.02 M) at 80 °C.

Figure S3. Synthesis of fluorene intermediates that could be used to prepare known and new Ledipasvir analougs.



Known Ledipasvir analog (**78**)
HCV GT1b replicon EC_{50} = 14 pM

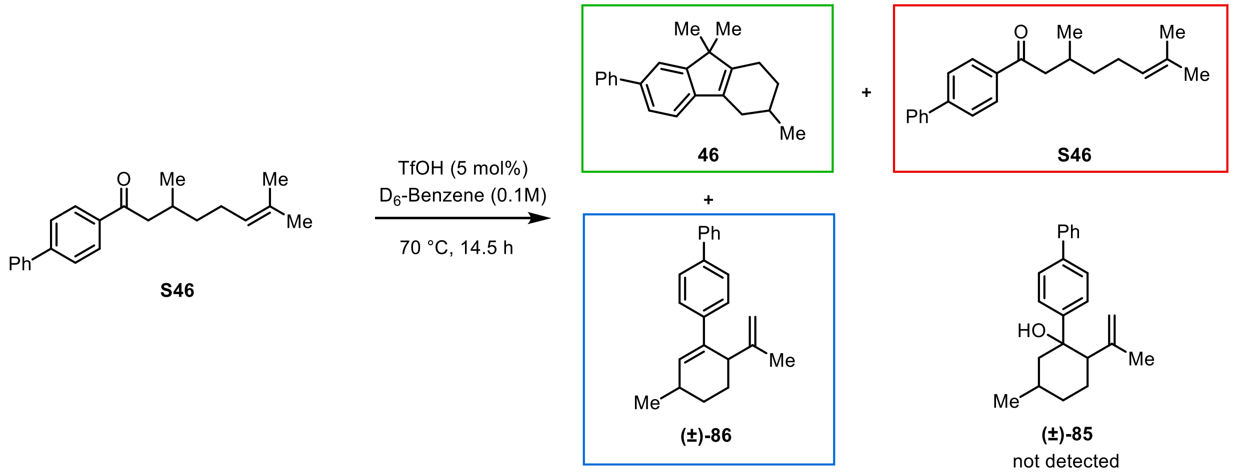
New Ledipasvir analog (R = Me; **79**)
Ledipasvir (R = F; **13**) HCV GT1b replicon EC_{50} = 4 pM

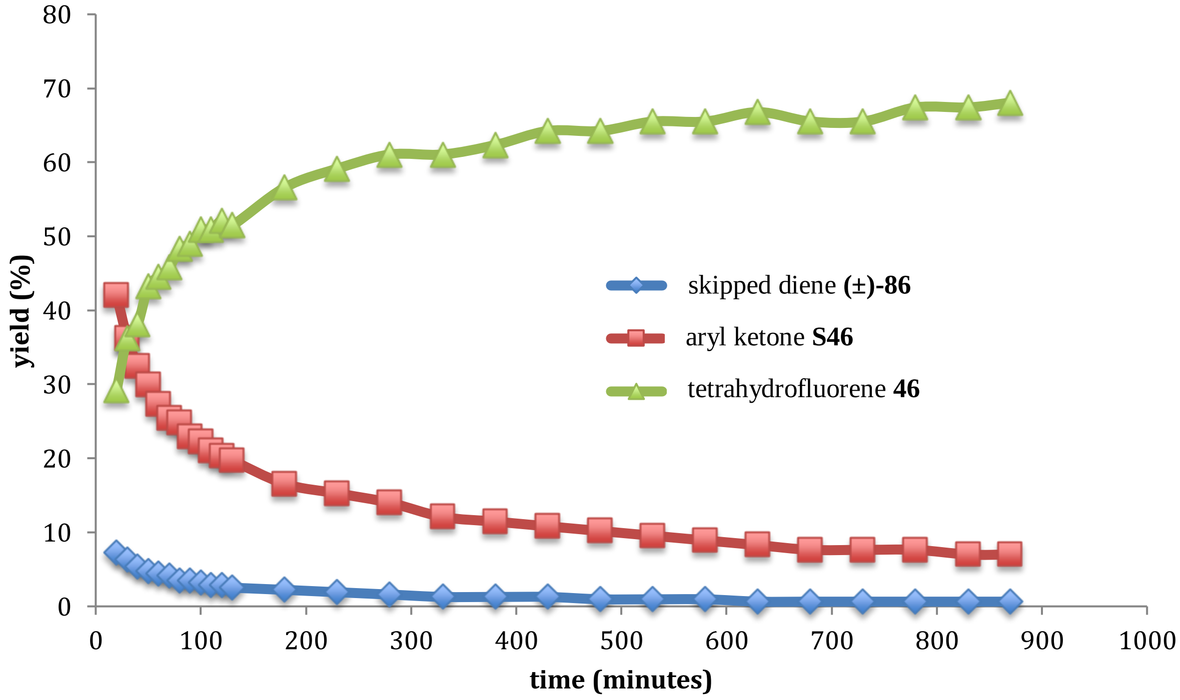
__**Figure S3 Details:**__ Under the optimized reaction conditions, aryl ketone **75** yields tetrahydrofluorene **76**, which upon subsequent oxidation results in fluorene **77**. A single transformation of **77** gives rise to either bisfunctionalized fluorenes **87** or **88** that could be further advanced to Ledipasvir derivatives **78** or **79**, respectively, using previously described synthetic procedures (*28*).

7. NMR Experiments

To a J-young NMR tube was added aryl ketone **S46** (31 mg, 0.101 mmol), deuterated benzene (1 mL, 0.1 M), and mesitylene (3 µL) as an internal standard. The tube was subsequently heated to 70 °C (10 °C less than the optimized reaction conditions and boiling point of benzene to avoid an explosion in the instrument) in a 700 MHz NMR. The sample was shimmed and locked at this temperature. Following this, the NMR tube was removed, and TfOH (0.5 µL, 0.05 eq) was added to the sample. The NMR tube was subsequently returned to the instrument, and a ^{1}H NMR spectrum was collected immediately. A ^{1}H NMR spectrum was collected every ten minutes, for 14.5 hours. From these spectra, percent yield of **46**, **S46**, and **(±)-86** were calculated using the internal standard as reference. A graph of this data is shown below.

Figure S4. NMR Experiments.





8. Computational Investigations

All quantum chemical calculations utilized density functional theory (DFT) as implemented in the Q-Chem 4.3 quantum chemistry package.(*45*) The unrestricted B97-D density functional(*46*) with singlet spin was used in combination with the 6-31+G* basis set(*47*) to acquire gas phase geometries for the intermediates discussed. The reaction discovery tools developed by the Zimmerman group, specifically the Growing String Method (GSM),(*29*, *48*–*50*) were used to probe potential reaction paths and determine the exact transition state and minimum energy reaction path for each proposed elementary step. By optimizing the reaction path, GSM provides verification that the saddle point connects the reactant to product geometries through a single transition state. Frequency calculations were performed on all structures at the same level of theory to confirm that optimizations led to stable minima (intermediates) or transition states. Stable intermediates were characterized by all real frequencies, and transition states were identified by a single imaginary frequency. The ωB97X-D(*51*) density functional and the triple-zeta, polarized 6-311G* basis set(*47*) were used to calculate energies with the SMD solvent model(*52*) using benzene as the implicit solvent, in the ORCA software package.(*53*) After the initial protonation of the aryl ketone by triflic acid, water and hydronium were used as the respective base and acid for subsequent protonations and deprotonations. When calculating the solvation energies for the hydronium ion in benzene, an additional water molecule was included to partially stabilize the positive charge through hydrogen bonding (See Fig. S5). Thermodynamic corrections were applied to the solvated energies at a temperature of 353.15 K. Energies reported are solvent-phase Gibbs free energies.

Figure S5: Stabilization of hydronium by a water molecule in benzene for ORCA calculations.

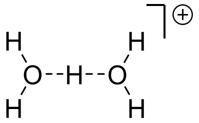


Figure S6: Complete reaction pathway for interrupted carbonyl olefin metathesis reaction.

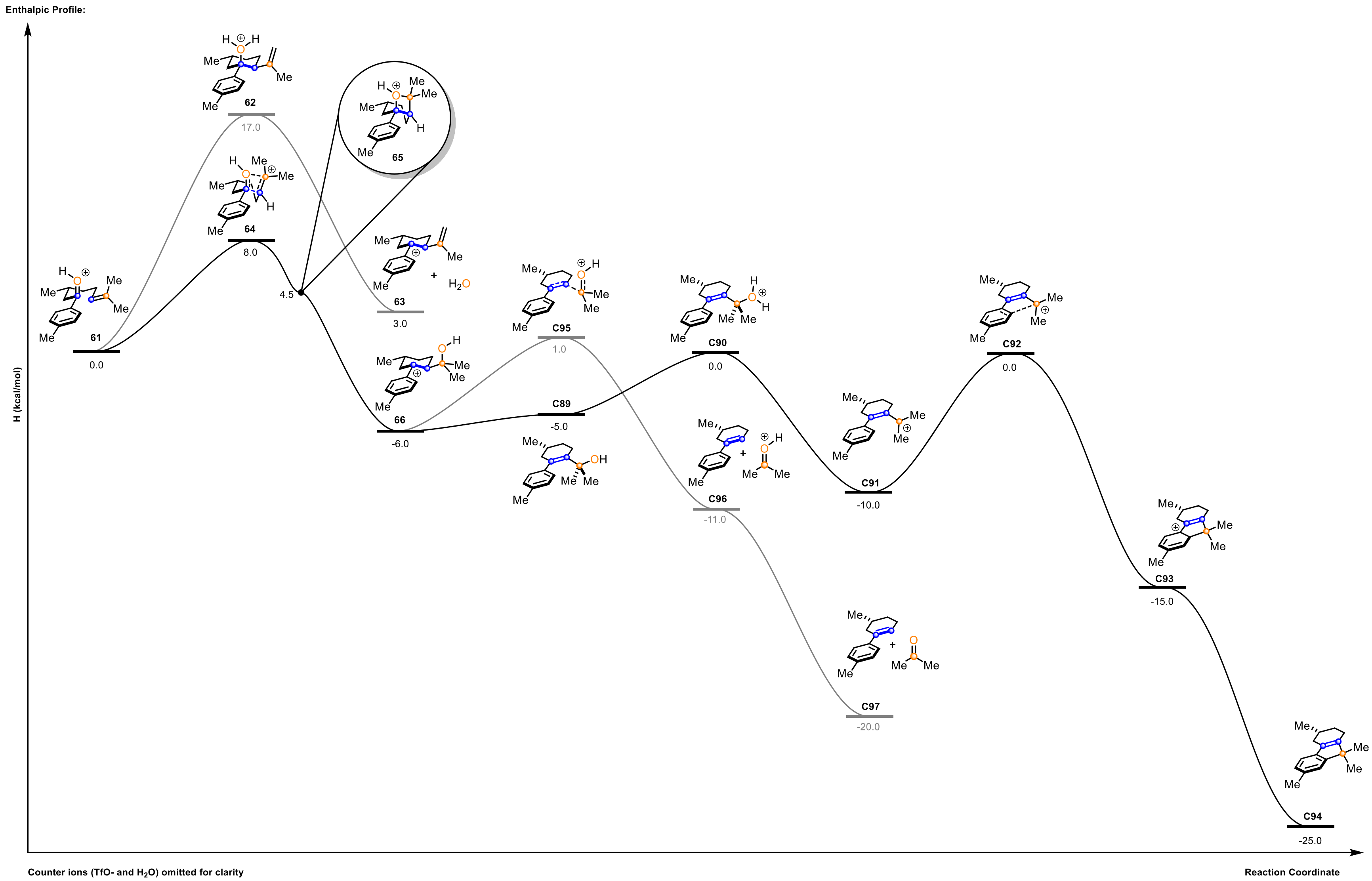
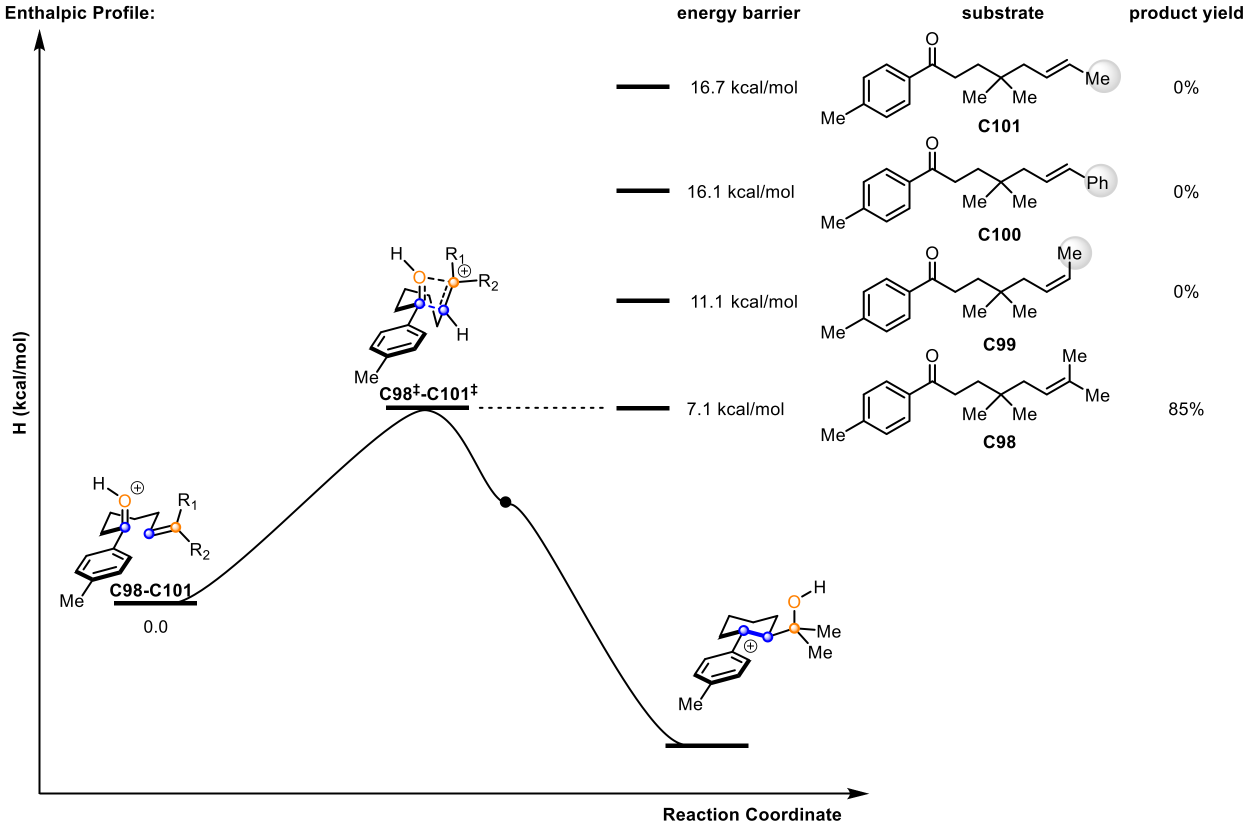

Enthalpic Profile:
H (kcal/mol)
61
0.0
62
17.0
64
8.0
4.5
65
63
3.0
H2O
66
-6.0
C95
1.0
C89
-5.0
C90
0.0
C96
-11.0
C91
-10.0
C97
-20.0
C92
0.0
C93
-15.0
C94
-25.0
Me
H
OH
+
Counter ions (TfO- and H2O) omitted for clarity
Reaction Coordinate

Figure S7: Correlation of energy barriers for the oxygen atom transfer step with the experimental yield of the tetrahydrofluorene product for substrates with varied alkene substitution.



XYZ coordinates for all reported structures investigated computationally

Structure **61**

C	-1.85181336	2.63626569	0.49925813
C	-2.64692853	1.45722375	0.75126777
C	-1.87305432	3.45518019	-0.75242207
C	-0.46791825	3.83423832	-1.33380978
C	0.06607006	2.79261411	-2.34154987
C	-0.03289941	1.28733489	-1.95665580
H	1.11030049	3.06382218	-2.55736924
H	-0.47637843	2.92014498	-3.29410441
C	0.13912177	0.89342384	-0.50398495
H	0.67959735	0.72565700	-2.58617424
H	-1.02697531	0.92147564	-2.26174844
C	1.04534211	1.31094596	0.41914874
O	-1.19039141	3.24951836	1.47062075
C	-0.54418057	5.21396332	-2.01350999
H	0.22517420	3.90564141	-0.48603362

H	0.43466949	5.48010754	-2.44027695
H	-0.83321891	5.99693015	-1.29484223
H	-1.27939169	5.20564934	-2.83522962
C	-3.25636888	0.75051583	-0.32513132
C	-3.98900055	-0.40862626	-0.09141410
C	-4.16686245	-0.91130916	1.21816726
C	-3.58237506	-0.19917757	2.29397762
C	-2.84192277	0.95543333	2.07285348
H	-3.12076864	1.08862502	-1.35008184
H	-4.43302701	-0.94262811	-0.93269618
H	-3.72556592	-0.55947955	3.31375541
H	-2.45557357	1.48267065	2.94795885
C	2.16321983	2.29074773	0.17378522
H	2.23319768	2.60969986	-0.87091271
H	3.12374184	1.82632281	0.45698296
H	2.05430214	3.18438764	0.81441215
C	0.96657273	0.78834449	1.83446856
H	0.13159022	0.08509609	1.97566269
H	0.86047910	1.62989938	2.54974002
H	1.90080999	0.27855674	2.12609747
C	-4.97786947	-2.15322181	1.47611905
H	-5.11589870	-2.74516560	0.56052906
H	-5.97815699	-1.87813053	1.85530633
H	-4.50371670	-2.78155054	2.24588357
H	-0.54941947	0.11203419	-0.17326866
H	-2.50262362	2.99620067	-1.52167732
H	-2.37591217	4.39263899	-0.44839634
H	-1.08362884	2.68402906	2.26149355

Structure **62**

C	-1.29540825	1.92562210	0.17150785
C	-2.38996014	0.90710176	0.47570896
C	-1.66636126	2.97103319	-0.90012566
C	-0.45765255	3.77119481	-1.40721126
C	0.44418938	2.82447827	-2.23635268
C	0.41995161	1.36712624	-1.70047203
H	1.46967000	3.21963611	-2.27848301
H	0.07763595	2.81052205	-3.27498958
C	0.14090456	1.22947526	-0.18637666
H	1.35701116	0.84104644	-1.93654791
H	-0.37811511	0.80607884	-2.20859165
C	1.25036275	1.68152506	0.73883371
O	-1.10346444	2.75107466	1.44940837
C	-0.90181481	4.99067510	-2.22933599
H	0.09348720	4.13514715	-0.52318502
H	-0.02898657	5.52173958	-2.63963229

H	-1.48080011	5.69684003	-1.61403497
H	-1.53211409	4.66931931	-3.07483423
C	-3.71409772	1.11154107	0.02675238
C	-4.73489450	0.22070291	0.37532053
C	-4.48715846	-0.89680627	1.19704217
C	-3.16946992	-1.09629180	1.65205876
C	-2.14279364	-0.21320029	1.29969498
H	-3.95861494	1.96230159	-0.60731538
H	-5.74508683	0.39662168	0.00036389
H	-2.94393874	-1.95628008	2.28519911
H	-1.13700752	-0.42564407	1.66706949
C	2.40996878	2.48979678	0.24691274
H	2.89641833	1.94592114	-0.58107906
H	3.14368516	2.67082741	1.04219665
H	2.07900013	3.44970658	-0.17546402
C	1.08284225	1.46794896	2.10223400
H	0.44365177	0.65112722	2.45681166
H	0.02015407	2.33226480	1.95880723
H	1.85317055	1.80657218	2.79866713
C	-5.60606347	-1.83596710	1.58588303
H	-6.22475479	-2.09607504	0.71290613
H	-6.27073181	-1.35721207	2.32494148
H	-5.21784967	-2.76365548	2.03038408
H	0.00143419	0.16067431	0.02260594
H	-2.12319312	2.43924791	-1.74945254
H	-2.43468344	3.63492910	-0.47939826
H	-1.85270195	2.53498258	2.04567294

Structure **63**

C	-1.31440831	1.47216194	-0.62206939
C	-2.25299340	0.67199752	0.07911858
C	-1.65749427	2.79692368	-1.22582663
C	-0.47417964	3.80959694	-1.20166391
C	0.76125958	3.23633516	-1.95144269
C	0.70405078	1.69947981	-2.07917752
H	1.67291587	3.53673806	-1.41441074
H	0.82805770	3.67146874	-2.96079174
C	0.11420266	1.02449805	-0.80763691
H	1.70049859	1.28161906	-2.27148485
H	0.07037688	1.41084712	-2.93232087
C	0.98400233	1.31083922	0.44485659
C	-0.92807133	5.15759159	-1.78200869
H	-0.20737604	3.94996845	-0.14370949
H	-0.09709521	5.87899845	-1.75221007
H	-1.76919266	5.58238684	-1.21137204
H	-1.24079764	5.04257368	-2.83294593

C	-3.65003459	1.01252627	0.13963547
C	-4.54717417	0.21603576	0.82957104
C	-4.11115291	-0.94798178	1.51967260
C	-2.73605727	-1.29019574	1.47885464
C	-1.82996501	-0.51673189	0.76994649
H	-4.02095179	1.89202609	-0.38334188
H	-5.60504518	0.48193987	0.85188701
H	-2.39429585	-2.17821889	2.01192735
H	-0.77788267	-0.79152495	0.77556563
C	2.45706382	1.03208967	0.24423397
H	2.61744715	0.03149651	-0.19263403
H	2.99159468	1.08794349	1.20326676
H	2.91658522	1.76068868	-0.44315473
C	0.49856538	1.75236760	1.61993051
H	-0.55647615	1.96720509	1.79404170
H	1.17370864	1.91097077	2.46288315
C	-5.09831011	-1.79034484	2.27514663
H	-5.89049185	-2.15203476	1.59707517
H	-5.60259031	-1.18632550	3.04910719
H	-4.62074849	-2.65451080	2.75582892
H	0.13813630	-0.06703724	-0.96613954
H	-1.89587309	2.59906370	-2.29238876
H	-2.55380763	3.24791858	-0.78173902

Structure **64**

C	-1.21742888	2.03536732	0.26463124
C	-2.29361670	1.04892266	0.65213472
C	-1.72612354	3.08201104	-0.73902792
C	-0.61594758	3.96208406	-1.33506031
C	0.24693751	3.11461779	-2.30474182
C	0.30294366	1.60484078	-1.94360026
H	1.25866348	3.54298917	-2.37820291
H	-0.18260111	3.19129829	-3.31630501
C	0.08407491	1.20750718	-0.46431848
H	1.24702033	1.15752264	-2.29211228
H	-0.49575021	1.08331673	-2.49207871
C	1.12202318	1.47044282	0.52295825
O	-0.69256469	2.78708306	1.39183952
C	-1.20175755	5.19531299	-2.04104846
H	0.00869759	4.31476477	-0.49825715
H	-0.40257874	5.79352543	-2.50557182
H	-1.74287263	5.83674322	-1.32846677
H	-1.90295214	4.89019074	-2.83571447
C	-2.76171518	0.12299956	-0.30853985
C	-3.79044981	-0.76738395	-0.00367061
C	-4.40024949	-0.76850004	1.27153995

C	-3.94314728	0.16356318	2.22215849
C	-2.90879837	1.06074166	1.92302135
H	-2.30888605	0.09694080	-1.30205667
H	-4.13004657	-1.47837998	-0.75932082
H	-4.40721323	0.19464333	3.20979474
H	-2.63348580	1.80204290	2.67545585
C	2.13262565	2.53992297	0.40045729
H	1.89247151	3.28020455	-0.36503614
H	3.07966738	2.03628186	0.11088378
H	2.32626436	3.01626540	1.37328788
C	1.21349396	0.53746743	1.67612339
H	0.22287337	0.12946345	1.94131555
H	1.72593124	0.96691879	2.54786769
H	1.80502210	-0.33366564	1.32775545
C	-5.52855648	-1.72124056	1.58986944
H	-5.44937517	-2.64687344	1.00044621
H	-6.50126080	-1.25800847	1.34852985
H	-5.54374467	-1.98087034	2.65883007
H	-0.18891091	0.14602136	-0.41473571
H	-2.28603925	2.57488743	-1.54039917
H	-2.44767781	3.69158005	-0.17021079
H	-0.74977556	2.22770800	2.18753743

Structure **65**

C	-1.212822	1.850108	0.005107
C	-2.296917	0.940929	0.510441
C	-1.741765	3.065431	-0.743017
C	-0.633586	3.989903	-1.280496
C	0.279955	3.231349	-2.281803
C	0.418183	1.699517	-2.019106
H	1.268097	3.713977	-2.291825
H	-0.126004	3.358510	-3.297996
C	0.046253	1.194413	-0.610479
H	1.430858	1.350024	-2.271015
H	-0.259920	1.161974	-2.699954
C	0.929462	1.552148	0.609814
O	-0.339794	2.401224	1.242333
C	-1.234089	5.252870	-1.918943
H	-0.029322	4.304212	-0.413740
H	-0.438532	5.893478	-2.330213
H	-1.802106	5.840290	-1.180853
H	-1.912998	4.981376	-2.743781
C	-2.685773	-0.164557	-0.267251
C	-3.755718	-0.972064	0.140450
C	-4.453603	-0.711345	1.335574
C	-4.055000	0.398033	2.108637

C	-3.002425	1.224943	1.697838
H	-2.164872	-0.390448	-1.199781
H	-4.052262	-1.821598	-0.477293
H	-4.585140	0.626838	3.034540
H	-2.762835	2.110493	2.294906
C	2.062518	2.540636	0.490317
H	1.849227	3.337989	-0.226265
H	2.955077	1.991731	0.148957
H	2.290504	2.971013	1.475027
C	1.193275	0.408446	1.570555
H	0.287933	-0.194776	1.742685
H	1.602250	0.770837	2.525772
H	1.946226	-0.249562	1.108733
C	-5.612803	-1.579815	1.773698
H	-5.721091	-2.458608	1.122827
H	-6.557589	-1.011837	1.741361
H	-5.478582	-1.927229	2.810763
H	-0.076660	0.104319	-0.657553
H	-2.340989	2.657933	-1.576425
H	-2.441461	3.609122	-0.087461
H	-0.642176	1.945048	2.062130

Structure **66**

C	-1.40749826	1.61402222	-0.37926048
C	-2.43076435	0.78012838	0.16143609
C	-1.75757698	2.84160100	-1.17749867
C	-0.58015956	3.73666217	-1.60321583
C	0.50582966	2.90397896	-2.31408785
C	0.76455639	1.53295704	-1.63083674
H	1.43281468	3.49404674	-2.35917104
H	0.19254868	2.73056797	-3.35629718
C	0.05215491	1.30055391	-0.25931600
H	1.83829067	1.36141194	-1.47541172
H	0.41801641	0.72055031	-2.28757434
C	0.63952627	2.08756242	1.02068426
O	-0.36339160	3.07097498	1.37174948
C	-1.08473735	4.88453623	-2.49089800
H	-0.16047354	4.16181496	-0.68233363
H	-0.25005989	5.54037335	-2.78166508
H	-1.83367932	5.49633633	-1.96337820
H	-1.54505713	4.49029755	-3.41266463
C	-3.81505375	1.14357187	0.03440828
C	-4.81969401	0.34862909	0.56198752
C	-4.51472291	-0.85466453	1.24948064
C	-3.15494826	-1.23347564	1.37524061
C	-2.14093697	-0.44739858	0.84768294

H	-4.09054037	2.06061777	-0.48236126
H	-5.86285215	0.64837432	0.45137540
H	-2.90616778	-2.16432603	1.88684202
H	-1.11480832	-0.78864898	0.95736708
C	1.97954321	2.77261217	0.73037569
H	1.89638181	3.47961182	-0.10415823
H	2.76361542	2.03502953	0.50436619
H	2.29438855	3.32523044	1.63067585
C	0.78708821	1.09082656	2.18396704
H	-0.18380992	0.63983687	2.43558258
H	1.16013525	1.61991493	3.07637068
H	1.50771216	0.29754731	1.93252168
C	-5.60531762	-1.69664682	1.84833130
H	-6.55663113	-1.56939740	1.31189504
H	-5.77379097	-1.38871016	2.89683352
H	-5.32976741	-2.76139067	1.86280883
H	0.19876349	0.23837834	-0.03875585
H	-2.29356244	2.48218918	-2.08081703
H	-2.49337776	3.44182437	-0.61910325
H	-0.06306603	3.50961774	2.18885229

Structure **C89**

C	-1.25548560	1.95253064	-0.39130510
C	-2.34624119	1.13390919	0.22431876
C	-1.68067574	2.55299195	-1.72919760
C	-0.68474084	3.55944918	-2.33082679
C	0.73466863	2.99758610	-2.16603667
C	1.07053249	2.82650001	-0.67680897
H	1.47481016	3.65862579	-2.64779334
H	0.78992155	2.01719102	-2.67394163
C	-0.01126558	2.10579797	0.12246888
H	1.25599440	3.81895751	-0.22635886
H	2.02022158	2.27393612	-0.57084795
C	0.46072534	1.54025410	1.48319991
C	-1.02478830	3.86843714	-3.79597631
H	-0.74792124	4.49515104	-1.74511089
H	-0.33443436	4.62101035	-4.21148610
H	-2.05435566	4.25108012	-3.89471302
H	-0.94264839	2.95375431	-4.40794396
C	-3.44176615	1.73883830	0.87475481
C	-4.47906688	0.96176699	1.40382088
C	-4.46879468	-0.44313394	1.29226191
C	-3.38948703	-1.04574437	0.62033297
C	-2.34637380	-0.27119503	0.09035701
H	-3.45838780	2.82472343	0.98610830
H	-5.31060914	1.44901414	1.91985006

H	-3.36556934	-2.13309033	0.50911846
H	-1.51738408	-0.75171419	-0.43369263
C	1.42440981	2.51528555	2.19199385
H	0.93121265	3.48627955	2.35058848
H	2.34597009	2.67107753	1.61453898
H	1.68751842	2.09077170	3.17191982
C	1.17170660	0.18552087	1.23696055
H	0.45359569	-0.54445313	0.83151503
H	1.57240818	-0.19919488	2.18810936
H	2.00133237	0.29018714	0.51898960
C	-5.57151168	-1.28155328	1.90587618
H	-6.50267882	-0.70266403	2.00878441
H	-5.28693431	-1.63264559	2.91373560
H	-5.78385756	-2.17476841	1.29653571
O	-0.59168959	1.36483487	2.44283892
H	-1.22952856	0.73571826	2.06119482
H	-1.84492906	1.72417637	-2.44691581
H	-2.67107260	3.02873991	-1.60705761

Structure **C90**

C	-1.20319171	1.89943943	-0.46223690
C	-2.26824123	1.07080344	0.19264548
C	-1.63249607	2.47823179	-1.80221402
C	-0.69740726	3.56700138	-2.36109292
C	0.75453543	3.10264525	-2.17655633
C	1.08966890	2.92394670	-0.68655509
H	1.45535585	3.82577245	-2.62090339
H	0.89418001	2.14243485	-2.70390365
C	0.02255063	2.13390008	0.07282087
H	1.21881170	3.91039314	-0.20709231
H	2.06277541	2.41228840	-0.58985788
C	0.51843503	1.58140965	1.39685330
C	-1.02810769	3.87625749	-3.82812373
H	-0.84298159	4.48394010	-1.76082026
H	-0.37662851	4.67606741	-4.21274451
H	-2.07474099	4.20147422	-3.93847982
H	-0.88012245	2.98086386	-4.45466620
C	-3.29726330	1.68371684	0.95124595
C	-4.32088049	0.90984689	1.52734085
C	-4.36973863	-0.48395287	1.34343860
C	-3.35655069	-1.08648941	0.56403644
C	-2.32513854	-0.32978198	-0.00207307
H	-3.29145994	2.76865208	1.07982081
H	-5.10118580	1.40305734	2.11019113
H	-3.38462190	-2.16505333	0.39443109
H	-1.56581897	-0.81418843	-0.61910683

C	1.52057652	2.45127454	2.14489428
H	1.17082410	3.48841623	2.22315739
H	2.47640358	2.43817866	1.60333489
H	1.70236924	2.04457233	3.15060837
C	0.92213475	0.11252406	1.33722208
H	0.09523178	-0.51503697	0.98174247
H	1.29177640	-0.25057062	2.31074264
H	1.74796758	0.02650647	0.61392480
C	-5.46819392	-1.31949919	1.96231062
H	-6.29642463	-0.69063965	2.31914188
H	-5.08532181	-1.89569428	2.82185633
H	-5.86767493	-2.04481273	1.23657961
O	-0.75970454	1.63387391	2.46127037
H	-1.61104914	1.39957915	1.94217349
H	-1.70060584	1.64071137	-2.52360722
H	-2.66176033	2.86453551	-1.70472485
H	-0.62516600	0.93675443	3.13975522

Structure **C91**

C	-1.06484042	1.63918609	-0.65333970
C	-2.14576824	0.97259887	0.02249827
C	-1.12518596	1.83671719	-2.14546081
C	-0.82714775	3.31413123	-2.54439437
C	0.54745023	3.69331554	-1.98178768
C	0.60165162	3.55609962	-0.44973380
H	0.79580192	4.73138367	-2.25350568
H	1.31281901	3.04536963	-2.44216207
C	0.02747296	2.22513591	0.07444209
H	0.01234397	4.37261950	0.00608343
H	1.63730601	3.68555566	-0.11109086
C	0.58906982	1.62869346	1.20346641
C	-0.89879246	3.46901479	-4.06958927
H	-1.59660021	3.95264863	-2.07631688
H	-0.71882503	4.51654626	-4.35630105
H	-1.88674866	3.17484257	-4.45654099
H	-0.13458254	2.84156458	-4.55699090
C	-2.49261877	1.31926604	1.36563272
C	-3.53687012	0.67771443	2.02025615
C	-4.27502061	-0.34737962	1.38125052
C	-3.94037914	-0.69264119	0.04698467
C	-2.92223651	-0.03494570	-0.63108853
H	-1.96063270	2.13716871	1.85127396
H	-3.81140256	0.98044855	3.03195039
H	-4.50143558	-1.48346163	-0.45396237
H	-2.67562419	-0.33357235	-1.64977354
C	1.63243326	2.35564012	2.01236970

H	1.40060354	3.42385835	2.12785299
H	2.61535808	2.28918009	1.50844697
H	1.74828368	1.89373286	3.00323688
C	0.39505075	0.19297799	1.62071399
H	-0.23422930	-0.39449022	0.94459458
H	-0.02488091	0.14088345	2.63887552
H	1.39335646	-0.27685732	1.68180323
C	-5.39000418	-1.05838919	2.10068098
H	-5.83217937	-0.42598663	2.88390901
H	-4.99932543	-1.96888533	2.59060485
H	-6.17844894	-1.37789702	1.40309892
H	-0.34059552	1.21419051	-2.61555154
H	-2.09719621	1.52997195	-2.55129621

Structure **C92**

C	-1.33280487	1.88789975	-0.91910289
C	-2.36992376	1.23343082	-0.16471457
C	-1.39172171	2.19919861	-2.39300972
C	-0.52865492	3.44014944	-2.74109064
C	0.86670802	3.29144795	-2.10415443
C	0.80187949	3.21533738	-0.55968674
H	1.50766759	4.13881333	-2.39067280
H	1.34054940	2.37502940	-2.49523363
C	-0.26298306	2.23590823	-0.11090753
H	0.55820792	4.21216272	-0.14714023
H	1.78245041	2.93939978	-0.13960156
C	-0.24164163	1.64063629	1.22510410
C	-0.43865502	3.62316036	-4.26328392
H	-1.01767815	4.32614391	-2.29789959
H	0.12617041	4.53402097	-4.51352546
H	-1.44026834	3.70698160	-4.71338501
H	0.07487756	2.76252062	-4.72356465
C	-2.37677555	1.53946850	1.25352033
C	-3.05985731	0.67349104	2.15649381
C	-3.75251211	-0.43820434	1.68505163
C	-3.82116084	-0.65061400	0.26901603
C	-3.17643067	0.17721379	-0.64548032
H	-2.29103110	2.58532081	1.55327502
H	-3.08943638	0.91992790	3.21953367
H	-4.37890810	-1.51544065	-0.09710051
H	-3.19686976	-0.05314519	-1.71126187
C	0.28643388	2.46967099	2.37014860
H	-0.02455334	3.52165359	2.30800521
H	1.39114174	2.43821667	2.34860833
H	-0.02585905	2.04331013	3.33447737
C	0.05010101	0.15306312	1.34601219

H	-0.40835350	-0.42993959	0.53800388
H	-0.26946087	-0.23837506	2.32178945
H	1.14752026	0.03833089	1.27834778
C	-4.48378342	-1.37806351	2.61294476
H	-4.42149148	-1.04240227	3.65737596
H	-4.05616919	-2.39269058	2.54774315
H	-5.54649037	-1.45694691	2.33243026
H	-1.00279058	1.33220240	-2.95969089
H	-2.43402060	2.34773811	-2.71501257

Structure **C93**

C	-1.42621732	1.95458044	-0.94693069
C	-2.39824268	1.24383100	-0.18877664
C	-1.45056686	2.27028620	-2.42208666
C	-0.42537527	3.37729610	-2.77634204
C	0.93116275	3.07671144	-2.10586264
C	0.81646999	3.06022352	-0.56176221
H	1.67532924	3.82868715	-2.40685193
H	1.29893771	2.09594228	-2.45366370
C	-0.37170639	2.27978247	-0.10587379
H	0.70181358	4.09605783	-0.18585995
H	1.73303259	2.67524327	-0.08372503
C	-0.54341354	1.72450756	1.28840715
C	-0.28657539	3.52072767	-4.29887039
H	-0.80574146	4.32861490	-2.36144426
H	0.41103324	4.33336289	-4.55267687
H	-1.25938632	3.74472696	-4.76412533
H	0.09798656	2.58681832	-4.74137173
C	-2.08241599	1.35110869	1.26977563
C	-2.66809080	0.30031086	2.14532871
C	-3.64758960	-0.54237867	1.68048814
C	-4.05837087	-0.42535704	0.29698386
C	-3.47119604	0.44075645	-0.62123158
H	-2.59241952	2.28108407	1.61002597
H	-2.38109211	0.28377180	3.19897796
H	-4.85273857	-1.09181654	-0.04917420
H	-3.76885225	0.42022601	-1.67046313
C	-0.15012638	2.71508103	2.39925848
H	-0.70955584	3.65968477	2.31471200
H	0.92561894	2.93883686	2.34901953
H	-0.35394023	2.27519398	3.38776966
C	0.28626292	0.41505364	1.41279463
H	-0.01515430	-0.31580001	0.64801495
H	0.12352713	-0.01822247	2.41173978
H	1.35862541	0.63044597	1.29727080
C	-4.32665861	-1.56809818	2.55927657

H	-3.89663439	-1.57292142	3.57039882
H	-4.22289469	-2.57815635	2.13080169
H	-5.40560180	-1.35743252	2.64138936
H	-1.20683895	1.35346899	-2.99033184
H	-2.46288591	2.57363111	-2.73549408

Structure **C94**

C	-1.69549145	1.60920311	0.05875139
C	-2.90216203	0.67969535	0.10520604
C	-2.46364902	-0.66632937	0.03359487
C	-0.99977965	-0.66887146	-0.05689711
C	-0.54456136	0.61243078	-0.04730366
C	-4.25511987	0.98456836	0.19981996
C	-5.21032202	-0.06042360	0.22851430
C	-4.76326134	-1.39387577	0.15827690
C	-3.39582410	-1.71151844	0.06017088
C	-1.74885802	2.53598393	-1.17993591
H	-2.62275204	3.20406455	-1.11831452
H	-1.82431515	1.94323399	-2.10435720
H	-0.84007583	3.15815976	-1.23319963
C	-1.58430349	2.46086127	1.34724917
H	-1.55855669	1.81435812	2.23782629
H	-2.44721962	3.14098754	1.43316643
H	-0.66586408	3.07066049	1.32615121
H	-4.59132760	2.02494812	0.25187872
H	-5.50405782	-2.19765490	0.17984799
H	-3.07162501	-2.75355616	0.00531008
C	-0.10695482	-1.87927301	-0.14918745
C	0.90846487	0.98562336	-0.12955187
C	1.36788090	-1.51889523	0.15104671
H	-0.17697417	-2.32164229	-1.16264808
H	-0.44850372	-2.66667741	0.54687773
C	1.75836471	-0.22146064	-0.59103181
H	1.60106773	-0.38064153	-1.67313298
H	2.83083628	-0.01039576	-0.44432879
H	1.26510805	1.33836515	0.85850468
H	1.05078841	1.83739495	-0.81944972
C	-6.68758086	0.26263067	0.33566298
H	-7.01985612	0.90342794	-0.49943105
H	-6.91263427	0.80777174	1.26902619
H	-7.29827950	-0.65343682	0.32393407
C	2.30489733	-2.67919698	-0.21603605
H	1.44839249	-1.32289172	1.23618301
H	3.34553175	-2.45711317	0.07233395
H	2.28320765	-2.85656993	-1.30514612
H	1.99855951	-3.61218498	0.28573844

Structure **C95**

C	-1.22869532	1.62378395	-0.60819856
C	-2.23017711	0.77927385	0.04531922
C	-1.67669330	2.94456837	-1.20460903
C	-0.58937885	3.75874160	-1.94132805
C	0.33768724	2.79713913	-2.69968543
C	1.06101543	1.87438861	-1.70055105
H	1.07416180	3.36073977	-3.29163684
H	-0.25769903	2.19226733	-3.40574191
C	0.11385119	1.26839856	-0.68069764
H	1.87068120	2.44115376	-1.21305331
H	1.56023144	1.04154504	-2.22449941
C	0.55759697	2.30594780	1.47077903
O	0.17514832	3.57749897	1.35514412
C	-1.23919128	4.80236309	-2.86280961
H	0.01931051	4.28455939	-1.18599621
H	-0.47044514	5.40970290	-3.36447209
H	-1.89821974	5.47961890	-2.29554776
H	-1.84602799	4.30719564	-3.63924363
C	-3.45599755	1.32322243	0.52078956
C	-4.39615583	0.52269590	1.16905630
C	-4.17200626	-0.85821770	1.36381173
C	-2.96967277	-1.40989317	0.87086828
C	-2.02021044	-0.61494164	0.22863400
H	-3.67678480	2.38205191	0.38409905
H	-5.32689154	0.96822480	1.52605279
H	-2.79218964	-2.48169692	0.97681062
H	-1.12813842	-1.08751380	-0.18344019
C	2.04235260	2.13715922	1.37690022
H	2.49485537	2.84680288	0.67454725
H	2.31515142	1.10749110	1.11801646
H	2.44899825	2.35770356	2.38162385
C	-0.22764410	1.39158553	2.35982719
H	-1.31029126	1.56906041	2.30270395
H	0.10604709	1.58142964	3.39674857
H	-0.02897891	0.33862794	2.12571741
C	-5.19072620	-1.71102918	2.08027012
H	-6.21566992	-1.43471779	1.78823945
H	-5.11451373	-1.56551883	3.17227930
H	-5.03886977	-2.77996387	1.87288677
H	0.41834752	0.31665432	-0.24023015
H	-2.51380470	2.72804941	-1.89282948
H	-2.12267946	3.57248220	-0.41039261
H	-0.77049728	3.67738501	1.58769775

Structures **C96/C97** (see acetone+H and acetone)

C	-1.20281205	1.55109821	-0.81441068
C	-2.22117192	0.81451421	-0.01976026
C	-1.62732454	2.82953949	-1.52923769
C	-0.44260114	3.67286185	-2.04641365
C	0.57245092	2.75576764	-2.75176853
C	1.14510016	1.72477583	-1.76032376
H	1.38446954	3.35226022	-3.20053262
H	0.05654621	2.22734447	-3.57381409
C	0.06444985	1.08494929	-0.91966977
H	1.88433906	2.21882979	-1.09937902
H	1.70726409	0.94188880	-2.30077402
C	-0.93459638	4.80392673	-2.96058319
H	0.05999305	4.11981030	-1.16801314
H	-0.09545893	5.43597854	-3.29489804
H	-1.66595825	5.44438197	-2.43981234
H	-1.42686691	4.38702931	-3.85632869
C	-3.20906492	1.48295014	0.73886607
C	-4.14048886	0.77120122	1.50443444
C	-4.13438882	-0.63624365	1.53950064
C	-3.16485086	-1.30731755	0.77053989
C	-2.23232989	-0.59923998	0.00433142
H	-3.23728890	2.57363980	0.75245837
H	-4.88573441	1.31797863	2.08887013
H	-3.15302821	-2.40059144	0.76122097
H	-1.50970216	-1.14122699	-0.60870375
C	-5.12874590	-1.40093045	2.38909552
H	-6.12904129	-0.93974907	2.35062475
H	-4.81752140	-1.41591083	3.44891961
H	-5.21675537	-2.44659080	2.05499722
H	0.34415237	0.19072991	-0.35448735
H	-2.28563407	2.56319644	-2.37914189
H	-2.24758010	3.45450796	-0.86475656

Structure **C98**

C	-1.62183543	2.61747501	0.23708360
C	-2.38316478	1.53722417	0.82754429
C	-1.93687053	3.21711350	-1.10112253
C	-0.83743228	4.05587026	-1.79089550
C	0.27422385	3.27471904	-2.53685113
C	1.10543723	2.37226804	-1.57369103
C	1.24083208	4.33048009	-3.12243139
C	-0.31613959	2.46446157	-3.71055772
C	0.41674534	1.14028275	-1.04730113
H	1.49028937	3.00058847	-0.75603936
H	1.99009371	2.02972430	-2.14307345

C	0.53547288	0.56649245	0.18267661
O	-0.80008428	3.35859484	0.96062663
H	-1.35354214	4.68824335	-2.52934857
H	-0.37741395	4.73446208	-1.05726204
C	-3.07737295	0.60329850	0.01068452
C	-3.82972258	-0.41736661	0.58209790
C	-3.93889067	-0.55186649	1.98554669
C	-3.25044643	0.37525380	2.80047646
C	-2.48566430	1.39639717	2.24148520
H	-2.98456839	0.64991846	-1.07250278
H	-4.34032638	-1.13354926	-0.06337261
H	-3.33335235	0.29950231	3.88569560
H	-2.03298395	2.12492778	2.91818999
C	1.30516818	1.16224028	1.33355708
H	1.69765059	2.16702337	1.13264442
H	2.16088398	0.51620768	1.59560058
H	0.67354231	1.18236236	2.24526563
C	-0.10881240	-0.76310997	0.48184953
H	-0.68793483	-1.14355830	-0.37117935
H	-0.77424400	-0.68681051	1.35987044
H	0.66319188	-1.51044270	0.73646091
C	-4.78822597	-1.63588901	2.59693622
H	-4.88136657	-2.50047473	1.92405081
H	-5.80634111	-1.25261463	2.78792670
H	-4.37898048	-1.97156819	3.56143672
H	-0.15350614	0.57105812	-1.78797523
H	-2.32183264	2.44240926	-1.77269795
H	-2.80180412	3.87740709	-0.88741854
H	-0.56231254	2.91943814	1.80302908
H	2.03362309	3.84073146	-3.70912345
H	1.71796830	4.91688662	-2.32042873
H	0.70203999	5.02439001	-3.78676015
H	0.48492572	1.93956629	-4.25435858
H	-0.81850113	3.14404114	-4.41673136
H	-1.05149558	1.70652064	-3.39520302

Structure **C98**‡

C	-1.11282429	2.12811404	0.16530259
C	-2.19225828	1.16257407	0.65077188
C	-1.76462868	3.27171218	-0.63171552
C	-0.81211821	4.07033481	-1.53232662
C	0.01049399	3.15466763	-2.47297000
C	0.88719604	2.24879471	-1.57554394
C	0.94420880	4.02493692	-3.33508365
C	-0.89378632	2.31547302	-3.39988989
C	0.10647004	1.40074687	-0.53978953

H	1.59463495	2.91508191	-1.06421592
H	1.48685562	1.56361197	-2.19690469
C	0.88847807	1.05966676	0.71527222
O	-0.30167707	2.67403655	1.29081064
H	-1.40725071	4.78024479	-2.12813847
H	-0.11519732	4.66402914	-0.91668670
C	-2.82993564	0.34060032	-0.30163493
C	-3.86401619	-0.52292398	0.06945711
C	-4.31142637	-0.59232989	1.40600218
C	-3.67388966	0.22732752	2.35313446
C	-2.62962041	1.08980351	1.98557439
H	-2.51140363	0.37727419	-1.34557205
H	-4.33553420	-1.15304930	-0.68735966
H	-3.99145098	0.18929376	3.39683635
H	-2.16502681	1.67862026	2.78069165
C	2.23143295	1.63099674	1.00769002
H	2.24736501	2.72187999	0.89481190
H	2.92290922	1.22598915	0.24245535
H	2.59656243	1.33992634	2.00110876
C	0.50859459	-0.15760087	1.47529387
H	-0.53198642	-0.46563146	1.33214421
H	0.77317657	-0.08307979	2.53967770
H	1.15465636	-0.95195399	1.04392223
C	-5.45047741	-1.50698207	1.79776368
H	-5.39707473	-2.46427254	1.25705855
H	-6.42062317	-1.04348782	1.54930864
H	-5.44576987	-1.71271701	2.87824521
H	-0.26337850	0.47207872	-0.99814653
H	-2.57069681	2.83759854	-1.23857751
H	-2.25953121	3.92527766	0.10764263
H	-0.86990825	2.89041830	2.05738764
H	1.58492458	3.40098834	-3.97885527
H	1.59444455	4.65012713	-2.70140721
H	0.35625415	4.69156003	-3.98502504
H	-0.28054835	1.69820560	-4.07555535
H	-1.52498219	2.97106059	-4.01976442
H	-1.56374025	1.63667764	-2.84788998

Structure **C99**

C	-1.94072966	2.69296110	-0.11184243
C	-2.84916864	1.73915847	0.48751728
C	-1.93626651	3.04567989	-1.56880746
C	-0.68940863	3.76627572	-2.13672753
C	0.52760113	2.88655717	-2.52710299
C	1.09916813	2.08392963	-1.31702847
C	1.63832742	3.85192556	-2.99923256

C	0.16522376	1.95184249	-3.70143026
C	0.25063114	0.94639487	-0.81696430
H	1.33717197	2.78641243	-0.50334310
H	2.06372057	1.65458360	-1.64783370
C	0.03332443	0.57908549	0.46902695
O	-1.22633585	3.51651737	0.63025571
H	-1.02624333	4.28544932	-3.04693224
H	-0.36880007	4.54915773	-1.43274379
C	-3.37468473	0.65593070	-0.27008589
C	-4.22754740	-0.26943297	0.31999387
C	-4.61051281	-0.15337164	1.67859909
C	-4.11473261	0.94095597	2.42294960
C	-3.24723764	1.86681376	1.84910532
H	-3.06817881	0.51318408	-1.30480786
H	-4.60595096	-1.10493278	-0.27085764
H	-4.43118668	1.07078029	3.45879771
C	-5.50845228	-1.18006245	2.31728827
H	-6.23120765	-1.58658183	1.59433422
H	-6.05231938	-0.76070149	3.17574644
H	-4.90368671	-2.02702928	2.68777972
H	-2.19675412	2.16232068	-2.16374713
H	-2.80799889	3.72495351	-1.66587990
C	0.55013908	1.24497559	1.71125316
H	1.07164438	2.19096394	1.50894923
H	1.25540489	0.58243066	2.24215906
H	-0.27815692	1.41895638	2.42823253
H	2.51798113	3.28324716	-3.33765696
H	1.95182999	4.51986373	-2.18068347
H	1.28724409	4.47292898	-3.83843014
H	1.03212823	1.33338826	-3.98180375
H	-0.12598085	2.54947265	-4.57918932
H	-0.66873467	1.26856143	-3.47274666
H	-2.94696643	2.73033028	2.44760530
H	-1.19885998	3.23258648	1.56792273
H	-0.58451839	-0.30785958	0.63921844
H	-0.18942975	0.30831663	-1.58864707

Structure **C99**‡

C	-1.49067882	2.35112716	-0.05678146
C	-2.60468758	1.43998460	0.43883503
C	-1.92649940	3.17436480	-1.27878152
C	-0.77909872	3.83430223	-2.05918442
C	0.30836464	2.81986568	-2.48420791
C	0.91323511	2.21873589	-1.19274388
C	1.42611429	3.56378432	-3.23934497
C	-0.26555920	1.71042151	-3.39158844

C	-0.12338693	1.51544604	-0.30047646
H	1.38128987	3.04327272	-0.63297217
H	1.70640570	1.49727835	-1.45035533
C	0.23769010	1.33204892	1.10894562
O	-0.96450981	3.23311868	0.99747583
H	-1.19755748	4.32810183	-2.94956162
H	-0.30996930	4.61713242	-1.44178361
C	-3.13283837	0.47173063	-0.44257677
C	-4.16984066	-0.37262762	-0.04193507
C	-4.71942329	-0.28507388	1.25636014
C	-4.18292716	0.67333093	2.13496180
C	-3.13345786	1.51750952	1.74074172
H	-2.72733323	0.37835853	-1.45276489
H	-4.56369698	-1.11122887	-0.74316981
H	-4.58971313	0.76084360	3.14402673
C	-5.83288111	-1.21302350	1.68661418
H	-6.60836961	-1.28668741	0.90807706
H	-6.30352808	-0.86944595	2.61887446
H	-5.44594031	-2.23231949	1.85701639
H	-2.51799463	2.53084644	-1.94434938
H	-2.62789111	3.93571245	-0.89007959
C	1.50637854	1.65223848	1.76013988
H	2.16416497	2.30802460	1.18107606
H	2.01195165	0.66601784	1.88721800
H	1.34618157	2.02055760	2.78627627
H	2.23011986	2.87057262	-3.53495882
H	1.86279215	4.35695369	-2.61077712
H	1.02581034	4.03033497	-4.15276061
H	0.53270685	1.01700167	-3.70090223
H	-0.70606101	2.14886696	-4.30046729
H	-1.05192261	1.11836108	-2.89582009
H	-2.73570964	2.23089741	2.46485865
H	-1.70673021	3.74154518	1.38537609
H	-0.50515601	0.81206632	1.72433454
H	-0.44995940	0.55212802	-0.72759698

Structure **C100**

C	-1.57791871	2.59903678	0.79314161
C	-2.34822267	1.41055720	1.05255524
C	-1.57210472	3.40909867	-0.47117376
C	-0.14105434	3.68457547	-1.04322660
C	0.36256748	2.67508721	-2.11636377
C	0.02884595	1.19105679	-1.79044791
C	1.88506126	2.87395595	-2.29342895
C	-0.32948737	2.99742572	-3.46222043
C	0.27351302	0.63460003	-0.41442026

H	0.54134509	0.55684431	-2.53806946
H	-1.04818152	1.02958768	-1.98638329
C	1.02498069	1.12987637	0.60017377
O	-0.86872508	3.19242881	1.73562724
H	-0.16395973	4.67983808	-1.51110927
H	0.56395629	3.75949381	-0.20575561
C	-3.15368874	0.82786928	0.02781883
C	-3.89154364	-0.32341836	0.27244484
C	-3.87331844	-0.94887362	1.54256598
C	-3.07496137	-0.37770143	2.55885984
C	-2.32832386	0.77281400	2.33018745
H	-3.19429293	1.27361477	-0.96328561
H	-4.49943045	-0.75327268	-0.52508150
H	-3.04097315	-0.84837749	3.54205043
H	-1.74069477	1.16325081	3.16182022
C	0.98308832	0.62970978	1.97755716
C	-4.70346868	-2.17590402	1.81416276
H	-4.91229120	-2.73475397	0.89036275
H	-5.67471731	-1.88230931	2.25097974
H	-4.20957466	-2.84170999	2.53748707
H	-0.30522804	-0.27175006	-0.21135092
H	-2.21207533	2.96872305	-1.24087916
H	-2.02084473	4.37953182	-0.19519411
H	1.58674165	2.05293657	0.45744074
C	0.53810539	-0.67009736	2.32371038
C	0.38904579	-1.04226867	3.66443836
C	0.65869053	-0.12441761	4.69512231
C	1.11934177	1.16375881	4.37441213
C	1.29658936	1.53074472	3.03104046
H	0.33013491	-1.39595707	1.53702868
H	0.06176371	-2.05447689	3.90817294
H	1.69538303	2.51849480	2.78409723
H	0.53684765	-0.41851405	5.73855709
H	1.36289051	1.87332294	5.16699306
H	-0.64909316	2.60585691	2.49900829
H	2.25462676	2.24545094	-3.11888705
H	2.44948514	2.60787786	-1.38772145
H	2.10543402	3.92438081	-2.54175837
H	-0.03008737	2.27254396	-4.23552240
H	-0.04993157	4.00448166	-3.80876487
H	-1.42871481	2.95613625	-3.37061184

Structure **C100**‡

C	-1.61781454	1.90543324	0.32301328
C	-2.75898908	0.94339221	0.59258729
C	-1.83154100	2.88751339	-0.83776293

C	-0.53136952	3.62127659	-1.20061382
C	0.50136654	2.65118390	-1.85171687
C	0.33233351	1.21137720	-1.27666650
C	1.93652616	3.17019287	-1.62561932
C	0.24324991	2.57751078	-3.37469436
C	-0.23890204	1.12505485	0.17045734
H	1.28491647	0.66165250	-1.33215145
H	-0.39173492	0.64529854	-1.88563833
C	0.62824980	1.74709131	1.20104976
O	-1.36326224	2.73027175	1.54281706
H	-0.75033961	4.44287383	-1.89899780
H	-0.11882497	4.09205434	-0.29361800
C	-3.88240778	0.81443116	-0.24707353
C	-4.89581546	-0.10223118	0.05865260
C	-4.82830889	-0.91809628	1.20600526
C	-3.70300100	-0.78762854	2.04719788
C	-2.68821698	0.12318243	1.74548336
H	-3.97854248	1.43363821	-1.13740483
H	-5.75876223	-0.18747581	-0.60457786
H	-3.62805326	-1.41102854	2.94077860
H	-1.82222305	0.20621095	2.40722107
C	1.24940652	1.10513402	2.30094793
C	-5.94109316	-1.88563110	1.53749446
H	-6.42163110	-2.26906985	0.62479529
H	-6.72273327	-1.38594673	2.13600250
H	-5.56853779	-2.73743775	2.12618979
H	-0.39934992	0.06450834	0.39254551
H	-2.17515592	2.32958310	-1.72185352
H	-2.62947920	3.58905031	-0.55225910
H	0.91560043	2.78408491	1.03573209
C	1.02769395	-0.26983663	2.63270488
C	1.69215134	-0.84144421	3.71298749
C	2.58540919	-0.06481157	4.48344249
C	2.81632682	1.29235703	4.17886529
C	2.15419085	1.87449553	3.10210903
H	0.33727434	-0.87158565	2.04345835
H	1.52692232	-1.88905899	3.96557554
H	2.31798897	2.92422150	2.85127500
H	3.10381702	-0.52250662	5.32774446
H	3.50781522	1.87913690	4.78373560
H	-2.00795815	2.46746967	2.22784875
H	2.66594463	2.53491639	-2.15331151
H	2.21460110	3.18437509	-0.55855625
H	2.03478648	4.19775745	-2.00938533
H	0.89528106	1.82554908	-3.84719632
H	0.44427259	3.55311821	-3.84394176

H	-0.80368766	2.30090184	-3.58098057

Structure **C101**

C	-1.98241265	2.68876618	0.51550658
C	-2.72169395	1.48559730	0.74460587
C	-1.86714286	3.44434101	-0.77769936
C	-0.40014933	3.74082090	-1.23363063
C	0.18953859	2.68870379	-2.21617281
C	-0.11265644	1.22679131	-1.78732973
C	1.70883384	2.93626204	-2.35365413
C	-0.44884138	2.90435320	-3.60985621
C	0.15289700	0.77946759	-0.36984041
H	0.43005926	0.55833972	-2.48042666
H	-1.18115834	1.02046770	-1.98653891
C	0.89424445	1.35015567	0.60206607
O	-1.46714263	3.26457685	1.59273437
H	-0.39919591	4.71868065	-1.73681900
H	0.25248080	3.84549629	-0.35280607
C	-3.43929513	0.84591296	-0.30829700
C	-4.13954894	-0.33154377	-0.06822676
C	-4.15938675	-0.92048367	1.21731610
C	-3.44805753	-0.28254756	2.26685834
C	-2.74835153	0.89375095	2.04694274
H	-3.45760410	1.26997013	-1.30972823
H	-4.68755189	-0.80915909	-0.88138835
H	-3.45525155	-0.72845749	3.26275401
H	-2.20258389	1.36384792	2.86276906
C	1.04373173	0.77774142	1.98408792
H	0.48540431	-0.16487785	2.09346849
H	0.68553892	1.49168190	2.74885702
H	2.10450750	0.58084256	2.21760798
C	-4.92723475	-2.18730046	1.48203185
H	-5.31392935	-2.63253158	0.55517106
H	-5.78122179	-1.97957155	2.15007941
H	-4.29381388	-2.92646575	1.99888995
H	-0.34340360	-0.16450270	-0.11346894
H	-2.40817798	2.94107026	-1.58239676
H	-2.38622984	4.40406854	-0.59802629
H	1.43007424	2.28351025	0.41502320
H	2.13066823	2.25161510	-3.10565528
H	2.25336665	2.77750658	-1.41243275
H	1.89652293	3.96755375	-2.69247561
H	-0.06207267	2.16147836	-4.32447093
H	-0.20656345	3.90802209	-3.99278082
H	-1.54732561	2.80002143	-3.58419915
H	-0.96158073	4.06751709	1.35074080

Structure **C101**‡

C	-1.41142022	2.02362584	0.36387738
C	-2.51353672	1.04528668	0.65216739
C	-1.76835221	3.13098074	-0.64930971
C	-0.54667874	3.79856859	-1.28964968
C	0.19849823	2.80053896	-2.23276091
C	0.06624200	1.34561594	-1.68703668
C	1.67810588	3.21303117	-2.37934342
C	-0.45990802	2.83273500	-3.63030711
C	-0.06384108	1.20131696	-0.14829704
H	0.90831330	0.72820091	-2.03371125
H	-0.84997085	0.87726973	-2.08294413
C	0.96606834	1.80231972	0.68021727
O	-0.89523869	2.62296981	1.59571806
H	-0.86804457	4.67386985	-1.87361106
H	0.12013341	4.18659410	-0.50268707
C	-3.31908119	0.51467361	-0.38739678
C	-4.28867440	-0.44942266	-0.11372339
C	-4.50057006	-0.92193074	1.20211216
C	-3.68644063	-0.40468586	2.23194886
C	-2.69923833	0.54637891	1.96437546
H	-3.18678374	0.84484185	-1.41771125
H	-4.89843675	-0.84556951	-0.92807664
H	-3.82645679	-0.76324948	3.25346386
H	-2.07147675	0.91807724	2.77313169
C	1.58590908	1.11264933	1.81968920
H	0.95234076	0.30375692	2.20962783
H	1.90012847	1.80857700	2.61157204
H	2.51738107	0.64497916	1.42692396
C	-5.57671125	-1.93920442	1.49097342
H	-5.60991439	-2.71704556	0.71196998
H	-6.56821766	-1.45348760	1.50561500
H	-5.42509077	-2.42005773	2.46809715
H	-0.20090445	0.14758168	0.12518369
H	-2.40462030	2.72028903	-1.44324977
H	-2.39294097	3.86100226	-0.10472367
H	1.34957956	2.78712797	0.41732173
H	2.19252234	2.56467657	-3.10615228
H	2.23476936	3.15529374	-1.42849551
H	1.74881651	4.25206913	-2.73650861
H	-0.02111869	2.06344818	-4.28496013
H	-0.31185629	3.81513593	-4.10408190
H	-1.54331722	2.64370252	-3.55887505
H	-1.49423859	3.34458153	1.87486191

H_3O-H_2O complex

O	-4.73564107	0.50823803	0.14516417
H	-4.42164184	-0.39154795	-0.08409871
H	-5.46284006	0.74336898	-0.46746310
O	-2.90075509	2.06326943	0.51584201
H	-2.75567388	2.80912262	-0.10242046
H	-2.89179248	2.41746806	1.42969772
H	-3.84321558	1.32824085	0.27704836

Acetone+H

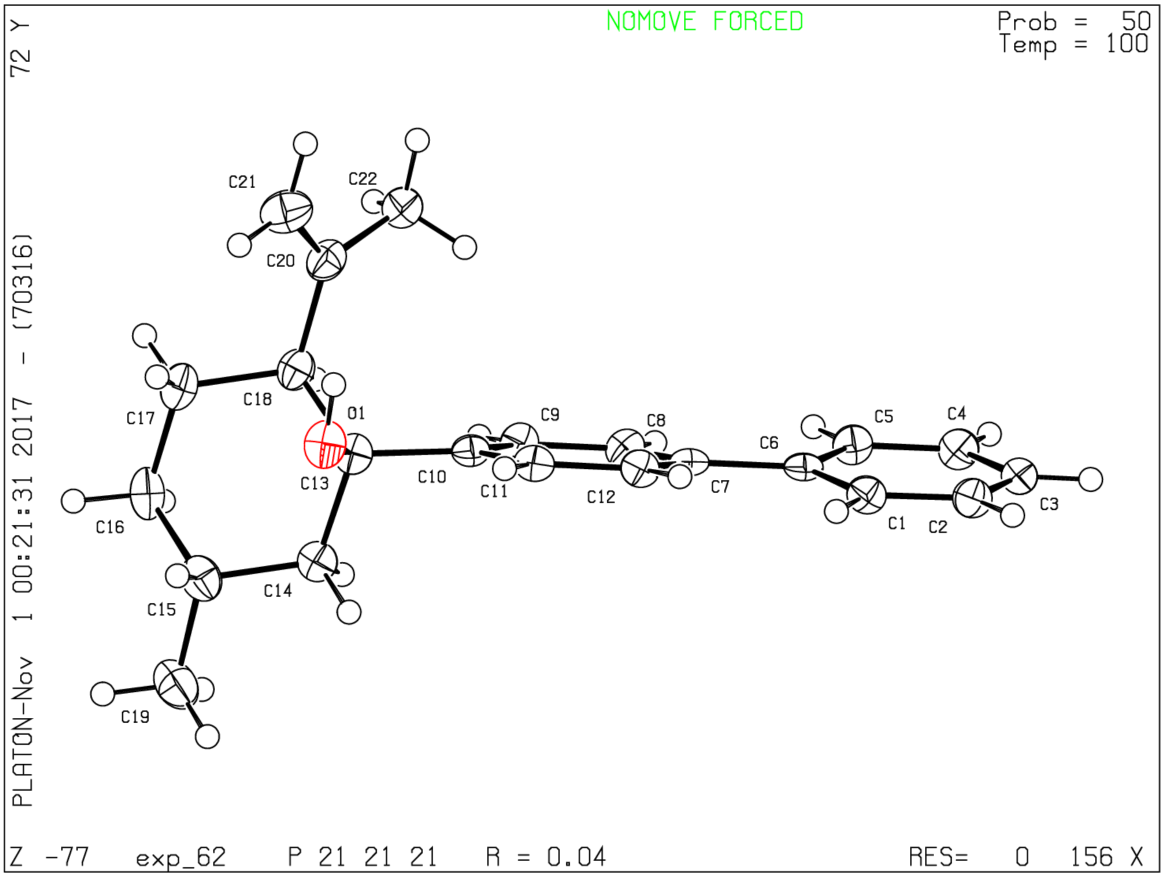
O	-1.18039508	1.53750850	0.06054508
C	-1.21684424	0.24735547	0.02106283
C	-2.49107893	-0.49521399	-0.12929484
H	-2.73089544	-0.94376544	0.85521958
H	-2.35616128	-1.34145744	-0.82216223
H	-3.33095468	0.13863376	-0.44853742
C	0.08955293	-0.43259691	0.13688337
H	-0.01043865	-1.36323535	0.71668054
H	0.86520941	0.22717976	0.54622449
H	0.38796805	-0.73771448	-0.88719887
H	-2.06498208	1.96010614	-0.04942254

Acetone

O	-1.23155445	1.56550638	0.10969315
C	-1.20740505	0.34574872	0.04536838
C	-2.47148296	-0.48504201	-0.18291767
H	-2.56567898	-1.26776802	0.58885569
H	-2.40490273	-1.00305801	-1.15567286
H	-3.35721754	0.16382503	-0.17295331
C	0.08920110	-0.45351301	0.18596834
H	0.04271467	-1.08166675	1.09281114
H	0.94778581	0.22736354	0.25383306
H	0.21523014	-1.13953586	-0.66914593

9. X-Ray Crystallographic Data

Structure Determination of 1-([1,1'-biphenyl]-4-yl)-5-methyl-2-(prop-1-en-2-yl)cyclohexan-1-ol (85)



(CCDC 1584828)

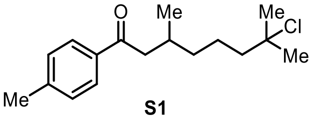
Single-crystal X-ray diffraction data was collected using a Rigaku XtaLAB Synergy-S X-ray diffractometer equipped with a low temperature device and a PhotonJet-S microfocus Cu source (λ = 1.54187 Å) operated at 50 kV and 1 mA. X-ray intensities were measured at 100(1) K with the HyPix-6000HE detector placed 32.01 mm from the sample. The data were processed with CrysAlisPro v38.46 (Rigaku Oxford Diffraction) and corrected for absorption. The structures were solved in OLEX2(*54*) using SHELXTL(*55*) and refined using SHELXL.(*56*) All non-hydrogen atoms were refined anisotropically with hydrogen atoms placed in a combination of refined and idealized positions. Additional details are presented in Table S4 and are given as Supporting Materials in a CIF file.

Table S4. Crystallographic Parameters.

Material	*Exp_62*
Space Group	$P2_12_12_1$
a Å	5.7198(2)
b Å	39.9212(14)
c Å	7.5730(3)
α (°)	90
β (°)	90
γ (°)	90
Volume (Å^3)	1729.23(11)
Temperature	100(1)
ρ_{calc} (g cm^{-3})	1.177
R_1/wR_2	3.86/11.86
GOF	1.153

10. Synthesis of Substrates, Intermediates and Products

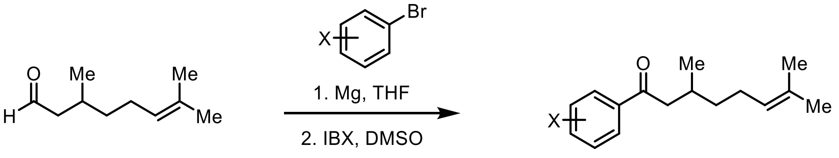
General procedure for Lewis acid evaluation (Table S1, Entries 1-3): To a 20 mL scintillation vial containing a magnetic stir bar was added the appropriate solid Lewis acid, solvent, and substrate (0.205 mmol). For liquid Lewis acids, the order of addition was substrate, solvent and Lewis acid. The reactions were allowed to stir for the indicated time at 80˚C, before being filtered through a silica plug using DCM as the eluent. The filtrate was concentrated under reduced pressure, dimethyl terephthalate was added, and the crude reaction was subjected to quantitative analysis by ^{1}HNMR.



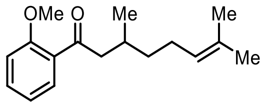
S1

7-chloro-3,7-dimethyl-1-(*p*-tolyl)octan-1-one (S1): The yield was determined to be 64% by ^{1}H NMR using dimethyl terephthalate as an internal standard. An analytically pure sample of **S1** was obtained as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 2H), 7.28 – 7.24 (m, 2H), 2.92 (dd, *J* = 15.7, 5.9 Hz, 1H), 2.75 (dd, *J* = 15.7, 7.8 Hz, 1H), 2.41 (s, 3H), 2.19 (tt, *J* = 13.5, 6.5 Hz, 1H), 1.76 – 1.67 (m, 2H), 1.60 – 1.45 (m, 8H), 1.40 (ddd, *J* = 10.3, 7.3, 5.2 Hz, 1H), 1.25 (dddd, *J* = 13.3, 10.0, 7.9, 5.4 Hz, 1H), 0.97 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (175 MHz; $CDCl_3$) δ 200.1, 143.8, 135.1, 129.4, 128.4, 71.4, 46.2, 46.0, 37.1, 32.7, 32.6, 29.9, 22.7, 21.8, 20.1; **IR** (Neat) 2943, 2871, 1680, 1607, 1461, 1452, 1369, 1285, 1181, 1007, 807, 764. **HRMS**: calcd for $C_{17}H_{26}ClO^+$: 281.1667 found: 281.1666.

General Procedure (A1): Grignard addition and IBX oxidation procedure for the synthesis of substrates

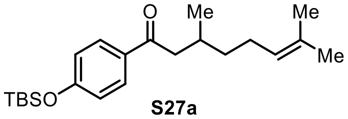


A flame-dried 100 mL round bottom flask equipped with a magnetic stir bar was charged with activated magnesium (2.0 eq). Dry THF (0.2 M) was then added, followed by aryl bromide (2.5 eq). The resulting mixture was stirred until the activated magnesium dissolved. The reaction flask was then cooled to 0 °C, and citronellal (1.0 eq) was added dropwise and stirred until judged complete by TLC analysis. The resulting reaction mixture was quenched with saturated ammonium chloride, and then partitioned between ethyl acetate and water. The aqueous layer was further extracted with ethyl acetate (x2) and the combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude alcohol was used without further purification. A magnetic stir bar and dry DMSO (0.3 M) were added to the flask containing the crude alcohol, followed by IBX (1.3 eq). The resulting mixture was stirred at room temperature until judged complete by TLC analysis, quenched with water, and filtered through celite eluting with ethyl acetate. The filtrate was then partitioned between ethyl acetate and water. The aqueous layer was further extracted with ethyl acetate (x2) and the combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude ketone was purified by column chromatography eluting with the indicated solvent to give the pure aryl ketone.



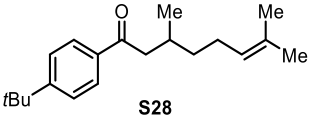
14

1-(2-methoxyphenyl)-3,7-dimethyloct-6-en-1-one (14): General procedure A1 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.91 g (72% over two steps) of **14** as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.60 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.08 (t, *J* = 6.6 Hz, 1H), 3.89 (s, 3H), 2.99 (dd, *J* = 15.9, 5.4 Hz, 1H), 2.74 (dd, *J* = 15.9, 8.2 Hz, 1H), 2.09 (dq, *J* = 13.3, 6.7 Hz, 1H), 2.04 – 1.94 (m, 2H), 1.66 (s, 3H), 1.59 (s, 3H), 1.40 – 1.32 (m, 1H), 1.23 (dt, *J* = 13.7, 7.9 Hz, 1H), 0.92 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 203.5, 158.2, 133.1, 131.4, 130.2, 129.4, 124.7, 120.8, 111.5, 55.6, 51.3, 37.4, 29.6, 25.9, 25.7, 20.0, 17.8; **IR** (Neat) 2957, 2925, 1672, 1596, 1484, 1463, 1436, 1376, 1294, 1243, 1179, 1162, 1116, 1054, 1024, 938, 816, 754. **HRMS**: calcd for $C_{17}H_{24}O_2^+$: 260.1776 found: 260.1778.



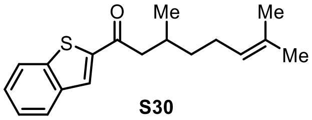
S27a

1-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-3,7-dimethyloct-6-en-1-one (S27a): General procedure A1 was employed on 6.48 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 1.44 g (62% over two steps) of **S27a** as a clear oil. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.87 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.10 (t, *J* = 6.9 Hz, 1H), 2.90 (dd, *J* = 15.5, 5.5 Hz, 1H), 2.68 (dd, *J* = 15.5, 8.2 Hz, 1H), 2.16 (td, *J* = 13.7, 7.0 Hz, 1H), 2.03 (qd, *J* = 14.8, 7.3 Hz, 2H), 1.67 (s, 3H), 1.60 (s, 3H), 1.46 – 1.36 (m, 1H), 1.34 – 1.20 (m, 1H), 0.99 (s, 9H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.23 (s, 6H); **^{13}C NMR** (100 MHz; $CDCl_3$) δ 199.3, 160.2, 131.6, 131.3, 130.4, 124.6, 120.0, 45.8, 37.4, 29.9, 25.9, 25.8, 25.7, 20.1, 18.4, 17.8, -4.2; **IR** (Neat) 2955, 2927, 2858, 1677, 1596, 1571, 1506, 1471, 1462, 1412, 1361, 1269, 1253, 1215, 1164, 1104, 1005, 907, 836, 807, 780, 734, 709, 690, 670. **HRMS**: calcd for $C_{22}H_{37}O_2Si^+$: 361.2557 found: 361.2558.



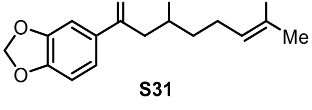
S28

1-(4-(*tert*-butyl)phenyl)-3,7-dimethyloct-6-en-1-one (S28): General procedure A1 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 1.07 g (77% over two steps) of **S28** as a yellow oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 5.10 (t, *J* = 7.0 Hz, 1H), 2.94 (dd, *J* = 15.5, 5.5 Hz, 1H), 2.72 (dd, *J* = 15.5, 8.2 Hz, 1H), 2.18 (td, *J* = 13.6, 6.9 Hz, 1H), 2.10 – 1.96 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.41 (ddt, *J* = 12.2, 9.6, 6.1 Hz, 1H), 1.34 (s, 9H), 1.31 – 1.24 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 200.3, 156.7, 135.0, 131.6, 128.2, 125.6, 124.6, 46.0, 37.4, 35.2, 31.3, 29.8, 25.9, 25.7, 20.1, 17.8; **IR** (Neat) 2963, 2913, 2870, 1680,1605, 1564, 1459, 1405, 1364, 1286, 1268, 1220, 1191, 1106, 1004, 936, 823, 738, 710, 668, 655, 638. **HRMS**: calcd for $C_{20}H_{31}O^+$: 287.2369 found: 287.2371.



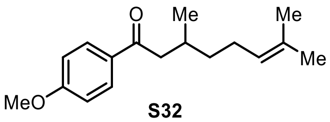
S30

1-(benzo[*b*]thiophen-2-yl)-3,7-dimethyloct-6-en-1-one (S30): General procedure A1 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.80 g (57% over two steps) of **S30** as a yellow solid. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.93 (s, 1H), 7.88 (t, *J* = 8.0 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 5.11 (t, *J* = 7.0 Hz, 1H), 2.99 (dd, *J* = 15.1, 5.7 Hz, 1H), 2.79 (dd, *J* = 15.1, 8.2 Hz, 1H), 2.31 – 2.15 (m, 1H), 2.05 (dtt, *J* = 21.5, 14.4, 7.0 Hz, 2H), 1.68 (s, 3H), 1.61 (s, 3H), 1.45 (ddt, *J* = 12.5, 9.5, 6.1 Hz, 1H), 1.37 – 1.27 (m, 1H), 1.00 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 195.0, 144.6, 142.7, 139.3, 131.8, 129.0, 127.5, 126.0, 125.1, 124.4, 123.2, 46.7, 37.3, 30.4, 25.9, 25.7, 20.1, 17.9; **IR** (Neat) 2955, 2908, 2851, 1658, 1594, 1557, 1514, 1457, 1428, 1376, 1331, 1287, 1251, 1218, 1173, 1156, 1081, 1014, 941, 920, 863, 833, 745, 725. **HRMS**: calcd for $C_{18}H_{22}OS^+$: 286.1391 found: 286.1389.



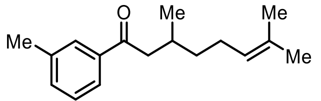
S31

1-(benzo[*d*][1,3]dioxol-5-yl)-3,7-dimethyloct-6-en-1-one (S31): General procedure A1 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.87 g (65% over two steps) of **S31** as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.55 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.43 (d, *J* = 1.7 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 6.04 (s, 2H), 5.15 – 5.04 (m, 1H), 2.88 (dd, *J* = 15.4, 5.5 Hz, 1H), 2.65 (dd, *J* = 15.4, 8.3 Hz, 1H), 2.18 – 2.10 (m, 1H), 2.08 – 1.95 (m, 2H), 1.68 (d, *J* = 0.7 Hz, 3H), 1.60 (s, 3H), 1.40 (ddt, *J* = 13.3, 9.6, 6.0 Hz, 1H), 1.27 (dddd, *J* = 13.5, 9.5, 7.7, 6.0 Hz, 1H), 0.95 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 198.6, 151.7, 148.3, 132.5, 131.7, 124.6, 124.5, 108.2, 107.9, 101.9, 45.8, 37.4, 30.0, 25.9, 25.7, 20.1, 17.8; **IR** (Neat) 2962, 2912, 1674, 1603, 1504, 1487, 1440, 1355, 1286, 1244, 1104, 1037, 934, 892, 807, 773, 737, 720. **HRMS**: calcd for $C_{17}H_{23}O_3^+$: 275.1642 found: 275.1642.



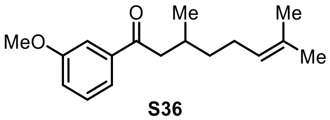
S32

1-(4-methoxyphenyl)-3,7-dimethyloct-6-en-1-one (S32): General procedure A1 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.52 g (41% over two steps) of **S32** as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.95 – 7.91 (m, 2H), 6.97 – 6.89 (m, 2H), 5.15 – 5.06 (m, 1H), 3.87 (s, 3H), 2.90 (dd, *J* = 15.4, 5.5 Hz, 1H), 2.69 (dd, *J* = 15.4, 8.2 Hz, 1H), 2.16 (td, *J* = 13.7, 6.9 Hz, 1H), 2.09 – 1.96 (m, 2H), 1.68 (d, *J* = 0.8 Hz, 3H), 1.60 (s, 3H), 1.41 (ddt, *J* = 13.3, 9.6, 6.0 Hz, 1H), 1.28 (dddd, *J* = 13.5, 9.5, 7.7, 5.9 Hz, 1H), 0.95 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 199.2, 163.4, 131.6, 130.8, 130.5, 124.6, 113.8, 55.6, 45.8, 37.4, 29.9, 25.9, 25.7, 20.1, 17.8; **IR** (Neat) 2962, 2912, 2848, 1673, 1599, 1576, 1509, 1456, 1418, 1364, 1306, 1288, 1256, 1220, 1169, 1111, 1031, 1000, 935, 894, 828, 809, 767, 741, 633. **HRMS**: calcd for $C_{17}H_{25}O_2^+$: 261.1849 found: 261.1850.



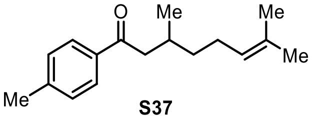
S34

3,7-dimethyl-1-(*m*-tolyl)oct-6-en-1-one (S34): General procedure A1 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.79 g (66% over two steps) of **S34** as a clear oil. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.74 (d, *J* = 11.1 Hz, 2H), 7.40 – 7.30 (m, 2H), 5.10 (t, *J* = 7.0 Hz, 1H), 2.95 (dd, *J* = 15.7, 5.5 Hz, 1H), 2.73 (dd, *J* = 15.7, 8.2 Hz, 1H), 2.41 (s, 3H), 2.17 (dq, *J* = 13.8, 6.9 Hz, 1H), 2.10 – 1.93 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.42 (ddt, *J* = 12.5, 9.4, 6.1 Hz, 1H), 1.35 – 1.22 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (100 MHz; $CDCl_3$) δ 200.8, 138.5, 137.7, 133.7, 131.6, 128.8, 128.5, 125.5, 124.6, 46.1, 37.4, 29.7, 25.9, 25.7, 21.5, 20.1, 17.8; **IR** (Neat) 2960, 2918, 1679, 1603, 1585, 1452, 1376, 1287, 1243, 1155, 1110, 1040, 1000, 983, 782, 756, 722, 690, 661. **HRMS**: calcd for $C_{17}H_{24}O^+$: 244.1827 found: 244.1830.



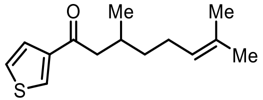
S36

1-(3-methoxyphenyl)-3,7-dimethyloct-6-en-1-one (S36): General procedure A1 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.95 g (75% over two steps) of **S36** as a yellow oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.52 (d, *J* = 7.7 Hz, 1H), 7.48 (dd, *J* = 2.5, 1.6 Hz, 1H), 7.36 (t,*J* = 7.9 Hz, 1H), 7.13 – 7.08 (m, 1H), 5.21 – 4.96 (m, 1H), 3.86 (s, 3H), 2.95 (dd, *J* = 15.7, 5.5 Hz, 1H), 2.73 (dd, *J* = 15.7, 8.2 Hz, 1H), 2.17 (td, *J* = 13.7, 6.9 Hz, 1H), 2.09 – 1.96 (m, 2H), 1.68 (d, *J* = 0.8 Hz, 3H), 1.60 (s, 3H), 1.41 (ddt, *J* = 13.3, 9.6, 6.0 Hz, 1H), 1.28 (dddd, *J* = 13.5, 9.5, 7.8, 6.0 Hz, 1H), 0.96 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 200.4, 159.9, 139.0, 131.7, 129.6, 124.5, 120.9, 119.4, 112.5, 55.6, 46.2, 37.3, 29.8, 25.9, 25.7, 20.1, 17.8; **IR** (Neat) 2962, 2913, 1681, 1596, 1583, 1485, 1451, 1429, 1376, 1363, 1324, 1286, 1256, 1196, 1175, 1110, 1082, 1047, 1027, 994, 864, 784, 755, 686. **HRMS**: calcd for $C_{17}H_{25}O_2^+$: 283.1669 found: 283.1670.



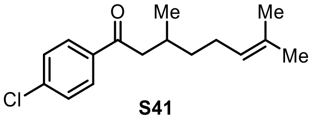
S37

3,7-dimethyl-1-(*p*-tolyl)oct-6-en-1-one (S37): General procedure A1 was employed on 3.24 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.85 g (73% over two steps) of **S37** as a clear oil. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 7.85 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.9 Hz, 2H), 5.10 (t, *J* = 7.0 Hz, 1H), 2.93 (dd, *J* = 15.5, 5.5 Hz, 1H), 2.71 (dd, *J* = 15.5, 8.2 Hz, 1H), 2.41 (s, 3H), 2.16 (td, *J* = 13.7, 6.9 Hz, 1H), 2.02 (pd, *J* = 14.5, 6.9 Hz, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.41 (ddt,*J* = 12.3, 9.5, 6.1 Hz, 1H), 1.33 – 1.23 (m, 1H), 0.95 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (125 MHz; CDCl$_3$) δ 200.2, 143.7, 135.2, 131.6, 129.4, 128.4, 124.6, 46.0, 37.4, 29.8, 25.9, 25.7, 21.8, 20.1, 17.8; **IR** (Neat) 2962, 2915, 1678, 1606, 1573, 1450, 1406, 1376, 1285, 1222, 1204, 1180, 1109, 1009, 936, 900, 805, 764, 741. **HRMS**: calcd for $C_{17}H_{25}O^+$: 245.1900 found: 245.1900.



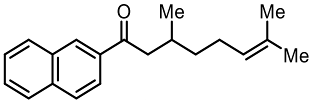
S38

3,7-dimethyl-1-(thiophen-3-yl)oct-6-en-1-one (S38): General procedure A1 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.46 g (40% over two steps) of **S38** as a yellow oil.**^{1}H NMR** (700 MHz; CDCl$_3$) δ 8.06 – 7.98 (m, 1H), 7.54 (d, *J* = 5.1 Hz, 1H), 7.31 (dd, *J* = 5.0, 2.9 Hz, 1H), 5.10 (t, *J* = 7.0 Hz, 1H), 2.86 (dd, *J* = 15.3, 5.6 Hz, 1H), 2.65 (dd, *J* = 15.3, 8.2 Hz, 1H), 2.16 (dq, *J* = 13.6, 6.8 Hz, 1H), 2.10 – 1.93 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.46 – 1.35 (m, 1H), 1.34 – 1.22 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 194.9, 143.1, 131.9, 131.7, 127.2, 126.4, 124.5, 47.4, 37.3, 29.8, 25.9, 25.7, 20.1, 17.8; **IR** (Neat) 3104, 2959, 2920, 1719, 1666, 1510, 1452, 1410, 1377, 1280, 1228, 1177, 1072, 1012, 977, 898, 869, 787, 731, 637. **HRMS**: calcd for $C_{14}H_{20}OS^+$: 236.1235 found: 236.1233.



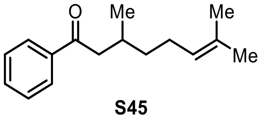
S41

1-(4-chlorophenyl)-3,7-dimethyloct-6-en-1-one (S41): General procedure A1 was employed on 6.48 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 1.35 g (78% over two steps) of **S41** as a yellow oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.90 – 7.86 (m, 2H), 7.44 – 7.41 (m, 2H), 5.11 – 5.07 (m, 1H), 2.93 (dd, *J* = 15.7, 5.5 Hz, 1H), 2.71 (dd, *J* = 15.7, 8.2 Hz, 1H), 2.20 – 2.12 (m, 1H), 2.09 – 1.96 (m, 2H), 1.68 (d, *J* = 0.9 Hz, 3H), 1.60 (s, 3H), 1.41 (ddt, *J* = 13.3, 9.5, 6.1 Hz, 1H), 1.28 (dddd, *J* = 13.5, 9.4, 7.8, 6.0 Hz, 1H), 0.96 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 199.3, 139.4, 135.9, 131.8, 129.7, 129.0, 124.4, 46.0, 37.3, 29.7, 25.9, 25.7, 20.1, 17.8; **IR** (Neat) 2960, 2914, 1683, 1588, 1571, 1487, 1452, 1399, 1376, 1285, 1210, 1175, 1092, 1010, 935, 815, 793, 765. **HRMS**: calcd for $C_{16}H_{22}ClO^+$: 265.1354 found: 265.1350.



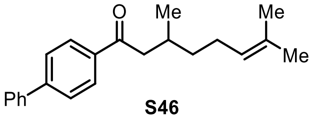
S43

3,7-dimethyl-1-(naphthalen-2-yl)oct-6-en-1-one (S43): General procedure A1 was employed on 3.42 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.67 g (74% over two steps) of **S43** as a white solid. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 8.45 (s, 1H), 8.03 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.97 (d, *J* = 8.1 Hz, 1H), 7.89 (dd, *J* = 11.6, 8.4 Hz, 2H), 7.62 – 7.58 (m, 1H), 7.57 – 7.53 (m, 1H), 5.12 (t, *J* = 7.0 Hz, 1H), 3.09 (dd, *J* = 15.6, 5.6 Hz, 1H), 2.88 (dd, *J* = 15.6, 8.2 Hz, 1H), 2.25 (dq, *J* = 13.7, 6.9 Hz, 1H), 2.13 – 1.99 (m, 2H), 1.68 (s, 3H), 1.61 (s, 3H), 1.50 – 1.44 (m, 1H), 1.33 (dddd, *J*= 13.5, 9.4, 7.8, 6.0 Hz, 1H), 1.01 (d, *J* = 6.7 Hz, 3H);**^{13}C NMR** (175 MHz; CDCl$_3$) δ 200.5, 135.6, 135.0, 132.7, 131.7, 129.8, 129.7, 128.53, 128.47, 127.9, 126.9, 124.6, 124.2, 46.1, 37.4, 29.9, 25.9, 25.7, 20.2, 17.9; **IR** (Neat) 3056, 2958, 2911, 1677, 1627, 1596, 1577, 1506, 1467, 1406, 1374, 1288, 1212, 1185, 1123, 935, 911, 853, 819, 744, 663, 645. **HRMS**: calcd for $C_{20}H_{24}O^+$: 280.1827 found: 280.1828.



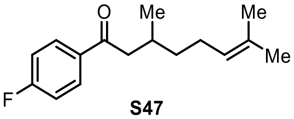
S45

3,7-dimethyl-1-phenyloct-6-en-1-one (S45): General procedure A1 was employed on 16.7 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 3.16 g (82% over two steps) of **S45** as a clear oil. **^{1}H NMR** (400 MHz; CDCl$_3$) δ 7.97 – 7.91 (m, 2H), 7.59 – 7.51 (m, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 5.10 (tt, *J* = 6.9, 1.6 Hz, 1H), 2.96 (dd, *J* = 15.7, 5.5 Hz, 1H), 2.74 (dd, *J* = 15.7, 8.2 Hz, 1H), 2.24 – 2.12 (m, 1H), 2.13 – 1.91 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.42 (ddt, *J* = 12.4, 9.4, 6.1 Hz, 1H), 1.29 (dddd, *J* = 13.6, 9.3, 7.7, 6.2 Hz, 1H), 0.96 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (100 MHz; CDCl$_3$) δ 200.6, 137.6, 133.0, 131.7, 128.7, 128.3, 124.5, 46.1, 37.3, 29.7, 25.9, 25.7, 20.1, 17.8; **IR** (Neat) 2962, 2913, 1682, 1597, 1580, 1448, 1376, 1284, 1211, 1180, 1002, 828, 750, 690. **HRMS**: calcd for $C_{16}H_{22}O^+$: 230.1671 found: 230.1668.



S46

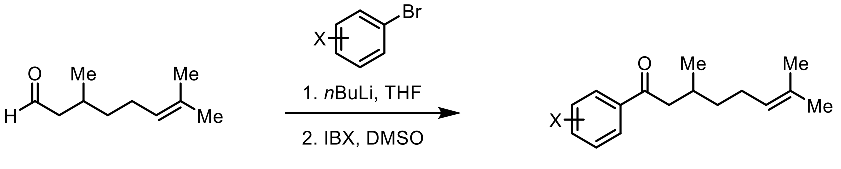
1-([1,1'-biphenyl]-4-yl)-3,7-dimethyloct-6-en-1-one (S46): General procedure A1 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 1.21 g (81% over two steps) of **S46** as a white solid. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 8.02 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.65 – 7.60 (m, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 5.11 (t, *J* = 7.1 Hz, 1H), 3.00 (dd, *J*= 15.6, 5.5 Hz, 1H), 2.77 (dd, *J* = 15.6, 8.2 Hz, 1H), 2.21 (td, *J* = 13.7, 7.1 Hz, 1H), 2.05 (dtt,*J* = 21.7, 14.5, 7.2 Hz, 2H), 1.69 (s, 3H), 1.61 (s, 3H), 1.44 (ddt, *J* = 12.3, 9.5, 6.1 Hz, 1H), 1.38 – 1.26 (m, 1H), 0.99 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (125 MHz; CDCl$_3$) δ 200.2, 145.7, 140.1, 136.3, 131.7, 129.1, 128.9, 128.3, 127.42, 127.35, 124.6, 46.1, 37.4, 29.8, 25.9, 25.7, 20.1, 17.9; **IR** (Neat) 3028, 2962, 2912, 1680, 1603, 1559, 1486, 1449, 1403, 1376, 1285, 1217, 1190, 1112, 1076, 1024, 1004, 828, 762, 736, 696. **HRMS**: calcd for $C_{22}H_{27}O^+$: 307.2056 found: 307.2059.



S47

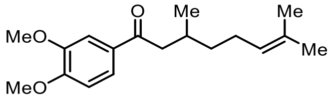
1-(4-fluorophenyl)-3,7-dimethyloct-6-en-1-one (S47): General procedure A1 was employed on 3.20 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.64 g (81% over two steps) of **S47** as a clear oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.99 – 7.95 (m, 2H), 7.15 – 7.09 (m, 2H), 5.11 – 5.08 (m, 1H), 2.93 (dd, *J* = 15.7, 5.5 Hz, 1H), 2.71 (dd, *J*= 15.7, 8.2 Hz, 1H), 2.16 (td, *J* = 13.7, 6.8 Hz, 1H), 2.09 – 1.96 (m, 2H), 1.68 (d, *J* = 0.8 Hz, 3H), 1.60 (s, 3H), 1.41 (ddt, *J* = 13.3, 9.6, 6.0 Hz, 1H), 1.29 (dddd, *J* = 13.5, 9.4, 7.8, 6.0 Hz, 1H), 0.96 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 198.8, 165.7 (d, *J* = 254.4 Hz), 134.0 (d, *J* = 3.1 Hz), 131.7, 130.8 (d, *J* = 9.2 Hz), 124.5, 115.7 (d, *J* = 21.7 Hz), 45.9, 37.3, 29.7, 25.8, 25.7, 20.1, 17.8; **IR** (Neat) 2963, 2914, 1682, 1596, 1506, 1453, 1408, 1376, 1284, 1227, 1155, 1098, 1007, 936, 830, 767, 740. **HRMS**: calcd for $C_{16}H_{22}FO^+$: 249.1649 found: 249.1650.

General Procedure (A2): Lithiation, nucleophilic addition, and IBX oxidation procedure for the synthesis of substrates S26 & S42



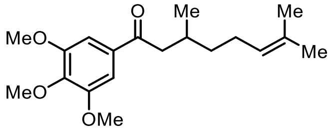
S26 & S42

A flame dried round bottom flask equipped with a magnetic stir bar was charged with dry THF (0.2 M) and aryl bromide (1.1 eq). The reaction flask was then cooled to -78 °C, and n-BuLi (1.3 eq, 1.6 M) was added dropwise. The reaction mixture was stirred for 30 minutes at -78 °C, and citronellal (1.0 eq) was added dropwise. The reaction was stirred until judged complete by TLC analysis. The reaction flask was allowed to warm to room temperature and was then quenched with saturated ammonium chloride, and partitioned between ethyl acetate and water. The aqueous layer was further extracted with ethyl acetate (x2) and the combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude alcohol was used without further purification. A magnetic stir bar and dry DMSO (0.3 M) were added to the flask containing the crude alcohol, followed by IBX (1.3 eq). The resulting mixture was stirred until judged complete by TLC analysis, quenched with water, and filtered through celite eluting with ethyl acetate. The filtrate was then partitioned between ethyl acetate and water. The aqueous layer was further extracted with ethyl acetate (x2) and the combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude ketone was purified by column chromatography eluting with the indicated solvent to give the pure aryl ketone **S26 & S42**.



S26

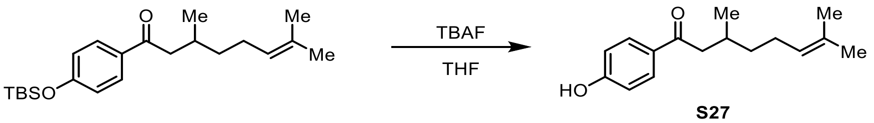
1-(3,4-dimethoxyphenyl)-3,7-dimethyloct-6-en-1-one (S26): General procedure A2 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.36 g (25% over two steps) of **S26** as a clear oil. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.57 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.53 (d, *J* = 1.9 Hz, 1H), 6.88 (d,*J* = 8.4 Hz, 1H), 5.10 (t, *J* = 7.1 Hz, 1H), 3.94 (m, 6H), 2.92 (dd, *J* = 15.4, 5.6 Hz, 1H), 2.70 (dd, *J* = 15.4, 8.2 Hz, 1H), 2.17 (dq, *J* = 13.7, 6.9 Hz, 1H), 2.11 – 1.95 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.46 – 1.38 (m, 1H), 1.33 – 1.23 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 199.2, 153.2, 149.2, 131.6, 130.9, 124.6, 122.9, 110.4, 110.1, 56.2, 56.1, 45.6, 37.4, 30.1, 25.9, 25.7, 20.1, 17.8; **IR** (Neat) 2952, 2922, 2831, 1606, 1493, 1465, 1409, 1384, 1335, 1287, 1234, 1200, 1164, 1064, 1027, 1003, 839, 760. **HRMS**: calcd for $C_{18}H_{26}O_3^+$: 272.1776 found: 272.1779.



S42

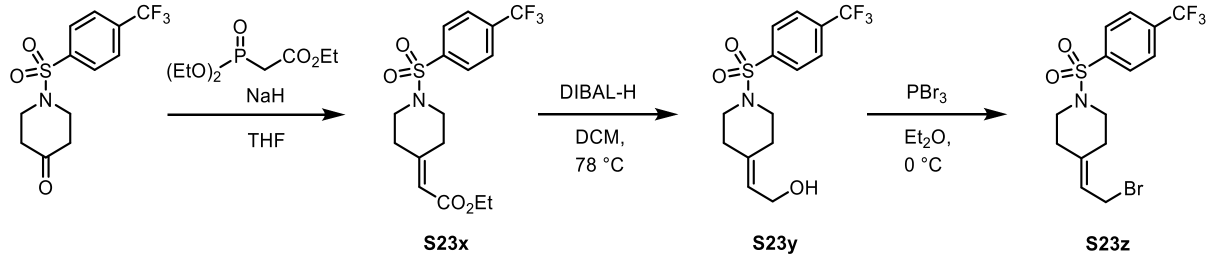
1-(2-methoxyphenyl)-3,7-dimethyloct-6-en-1-one (S42): General procedure A2 was employed on 4.86 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 0.63 g (41% over two steps) of **S42** as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.21 (s, 2H), 5.11 (t, *J* = 7.0 Hz, 1H), 3.92 (m, 9H), 2.92 (dd, *J* = 15.6, 5.5 Hz, 1H), 2.70 (dd, *J* = 15.6, 8.1 Hz, 1H), 2.18 (dq, *J* = 13.6, 6.9 Hz, 1H), 2.04 (pd, *J* = 14.7, 7.0 Hz, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.43 (ddt, *J* = 12.3, 9.5, 6.1 Hz, 1H), 1.33 – 1.24 (m, 1H), 0.97 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 199.2, 153.2, 142.6, 132.9, 131.7, 124.5, 105.8, 61.1, 56.5, 45.8, 37.4, 29.9, 25.9, 25.8, 20.1, 17.8; **IR** (Neat) 2960, 2928, 1676, 1583, 1504, 1454, 1411, 1363, 1329, 1230, 1189, 1151, 1124, 1055, 1003, 924, 884, 823, 781, 714, 668, 617. **HRMS**: calcd for $C_{19}H_{28}O_4^+$: 320.1988 found: 320.1985.

TBS deprotection for the synthesis of substrate S27



1-(4-hydroxyphenyl)-3,7-dimethyloct-6-en-1-one (S27): A flame dried round bottom flask equipped with a magnetic stir bar was charged with dry THF (5 mL) and **S27a** (0.83 mmol). The reaction flask was then cooled to 0 °C, and TBAF (1 mmol, 1M) was added dropwise and stirred until judged complete by TLC analysis (15 min – 1 h). The resulting reaction mixture was quenched with saturated ammonium chloride (15 mL), and then partitioned between ethyl acetate (20 mL) and water (10 mL). The organic layer was washed with water (1 x 15 mL) and saturated sodium chloride (1 x 15 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude ketone was purified by column chromatography eluting with hexanes/EtOAc to provide 0.16 g (77%) of **S27** as a yellow oil. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.90 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 5.09 (t, *J* = 7.0 Hz, 1H), 2.91 (dd, *J* = 15.4, 5.6 Hz, 1H), 2.68 (dd, *J* = 15.4, 8.2 Hz, 1H), 2.15 (td, *J* = 13.8, 6.9 Hz, 1H), 2.09 – 1.92 (m, 2H), 1.67 (s, 3H), 1.59 (s, 3H), 1.41 (ddt, *J* = 12.4, 9.5, 6.1 Hz, 1H), 1.33 – 1.22 (m, 1H), 0.95 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (100 MHz; $CDCl_3$) δ 199.7, 160.2, 131.7, 130.9, 130.7, 124.6, 115.4, 45.8, 37.4, 30.0, 25.9, 25.7, 20.1, 17.8; **IR** (Neat) 3276, 2959, 2916, 2853, 1649, 1598, 1574, 1513, 1438, 1375, 1310, 1284, 1218, 1165, 1107, 1004, 894, 831, 772, 741. **HRMS**: calcd for $C_{16}H_{22}O_2^+$: 246.1620 found: 246.1628.

3-step sequence for the synthesis of bromide S23z

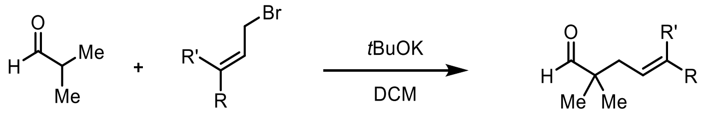


ethyl 2-(1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-ylidene)acetate (S23x): A flame dried round bottom flask equipped with a magnetic stir bar was charged with NaH (472 mg, 60% dispersion in mineral oil, 12.3 mmol) and THF (112 mL). The flask was cooled to 0 °C and Triethyl phosphonoacetate (2.22 mL, 11.2 mmol) was added. After stirring for 10 minutes, 1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-one (1.7 g, 5.6 mmol) was added and the reaction was allowed to slowly warm to room temperature over two hours. Upon completion as judged by TLC analysis, the solution was cooled to 0 °C, diluted with 10 mL Et_2O, and quenched with saturated aqueous $NaHCO_3$ (10 mL). The layers were separated and the organic layer was washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography eluting with hexane/EtOAc to provide 0.85 g (40%) of **S23x** as a white solid. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.92 – 7.86 (m, 2H), 7.80 (d, *J* = 8.3 Hz, 2H), 5.69 – 5.64 (m, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.22 – 3.11 (m, 4H), 3.11 – 3.03 (m, 2H), 2.40 (td, *J* = 5.8, 1.2 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 166.1, 154.7, 140.2, 134.8 (q, *J* = 33.0 Hz), 128.2, 126.4 (q, *J* = 3.7 Hz), 123.3 (q, *J* = 273 Hz), 116.5, 60.1, 47.4, 46.9, 36.0, 28.7, 14.4; **IR** (Neat) 2996, 1710, 1658, 1404, 1321, 1260, 1205, 1169, 1152, 1132, 1106, 1062, 1036, 928, 844, 727, 703. **HRMS**: calcd for $C_{16}H_{18}F_3NO_4SNa^+$: 400.0806 found: 400.0806.

2-(1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-ylidene)ethan-1-ol (S23y): A flame-dried round bottom flask equipped with a magnetic stir bar was charged with **S23x** (1 g, 2.65 mmol) and DCM (27 mL). The flask was cooled to -78 °C, and diisobutylaluminum hydride (8 mL, 1M solution in hexanes, 8 mmol) was added slowly. Subsequently, the reaction was allowed to warm slowly to room temperature over two hours. The reaction was cooled to -78 °C, Rochelle's salt was added and the reaction flask was allowed to slowly warm to room temperature overnight. The next day, the reaction mixture was partitioned between DCM and water, and the layers were separated. The aqueous layer was further extracted with DCM (x2). The combined organic layers were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography eluting with hexanes/EtOAc to provide 370 mg (42%) of **S23y** as a white solid. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 5.46 (t, *J* = 7.0 Hz, 1H), 4.10 (d, *J* = 7.0 Hz, 2H), 3.09 (dt, *J* = 11.1, 5.8 Hz, 4H), 2.40 (t, *J* = 5.8 Hz, 2H), 2.32 (t, *J* = 5.8 Hz, 2H), 1.31 (br s, 1H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 140.2, 137.1, 134.6 (q, *J* = 33.1 Hz), 128.2, 126.4 (q, *J* = 3.6 Hz), 124.1, 123.3 (q, *J* = 273.0 Hz), 58.3, 47.8, 47.2, 35.2, 28.0; **IR** (Neat) 3333, 2944, 2895, 1404, 1265, 1133, 1106, 1062, 1040, 1016, 997, 931, 842. **HRMS**: calcd for $C_{14}H_{16}F_3NO_3SNa^+$: 358.0701 found: 358.0699.

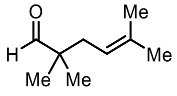
4-(2-bromoethylidene)-1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidine (S23z): A flame dried round bottom flask equipped with a magnetic stir bar was charged with **S23y** (370 mg, 1.1 mmol) and anhydrous Et_2O (11 ml). The flask was cooled to 0 °C and PBr_3 (0.052 mL, 0.55 mmol) was added dropwise. Upon consumption of starting material as judged by TLC analysis (~1.5 hours), water was added to quench the reaction, and the mixture was partitioned between Et_2O and water. The layers were separated, and the aqueous layer was further extracted wither Et_2O (x2). The combined organic layers were washed with saturated sodium chloride, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography eluting with hexanes/EtOAc to provide 220 mg (50%) of **S23z** as a white solid. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.89 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 8.2 Hz, 2H), 5.61 – 5.57 (m, 1H), 3.91 (d, *J* = 8.4 Hz, 2H), 3.15 – 3.09 (m, 4H), 2.46 – 2.41 (m, 2H), 2.35 (t, *J* = 5.8 Hz, 2H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 140.3, 140.0, 134.7 (q, *J* = 33.1 Hz), 128.1, 126.4 (q, *J* = 3.7 Hz), 123.3 (q, *J* = 273.1 Hz), 121.4, 47.5, 46.7, 35.1, 27.7, 27.0; **IR** (Neat) 2956, 2906, 2851, 1405, 1322, 1265, 1166, 1127, 1061, 1039, 1016, 928, 840, 786, 737, 725, 702, 652. **HRMS**: calcd for $C_{14}H_{16}F_3NO_2S^+$: 398.0037 found: 398.0030.

General Procedure (B): Allylation of isobutyraldehyde for the synthesis of aldehydes S18a-S24a



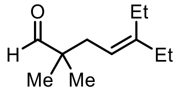
S18a-S24a

A flame dried round bottom flask equipped with a magnetic stir bar was charged with the corresponding allylic bromide (1 eq), DCM (0.2 M), and isobutyraldehyde (1.2 eq). The resulting mixture was cooled to 0°C before solid tBuOK (1.2 eq) was added in a single portion. The reaction was allowed to warm to room temperature and stir until judged complete by TLC analysis. The reaction was then quenched with saturated ammonium chloride and the layers were separated. The organic layer was collected and the aqueous layer was further extracted with DCM (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography or distillation to give pure allylated aldehyde **S18a-S24a**.



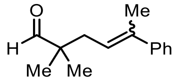
S18a

2,2,5-trimethylhex-4-enal (S18a): General procedure B was employed on a 26.0 mmol scale and purification by distillation provided 2.24 g (62%) of **S18a** as a clear oil. The ^{1}H-NMR data is consistent with literature(*57*) reported data. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 9.47 (s, 1H), 5.05 (dddd, *J* = 7.7, 6.3, 2.9, 1.5 Hz, 1H), 2.19 – 2.10 (m, 2H), 1.70 (s, 3H), 1.60 (s, 3H), 1.04 (s, 6H).



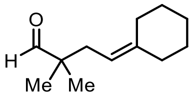
S19a

5-ethyl-2,2-dimethylhept-4-enal (S19a): General procedure B was employed on a 11.3 mmol scale. Purification by distillation under reduced pressure provided 716 mg (38%) of **S19a** as a clear oil. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 9.48 (s, 1H), 4.99 (t, *J* = 7.5 Hz, 1H), 2.19 (d, *J* = 7.5 Hz, 2H), 2.09 – 1.94 (m, 4H), 1.05 (s, 6H), 0.96 (dt, *J* = 10.0, 7.5 Hz, 6H); **^{13}C NMR** (100 MHz; $CDCl_3$) δ 206.7, 146.1, 116.7, 46.5, 35.1, 29.4, 23.2, 21.3, 13.1, 13.1; **IR** (Neat) 2964, 2932, 2876, 2699, 1725, 1464, 1365, 1201, 1080, 1049, 913, 884, 768. **HRMS**: calcd for $C_{11}H_{20}O^+$: 168.1514 found: 168.1493.



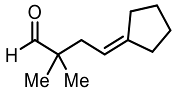
S20a

2,2-dimethyl-5-phenylhex-4-enal (S20a): General procedure B was employed on a 5.23 mmol scale and purification by column chromatography provided 252 mg (24%) of **S20a** (1.3:1 mixture of alkene isomers) as a clear oil. **^{1}H NMR** (for the mixture of isomers; 400 MHz; $CDCl_3$) δ 9.55 (s, 1.3H), 9.35 (s, 1H), 7.38 – 7.20 (m, 9.5H), 7.14 – 7.10 (m, 2H), 5.68 (td, *J* = 7.6, 1.4 Hz, 1.3H), 5.37 (td, *J* = 7.4, 1.5 Hz, 1H), 2.39 (dd, *J* = 7.7, 1.0 Hz, 2.6H), 2.15 (dq, *J* = 7.5, 1.3 Hz, 2H), 2.04 (dt, *J* = 1.6, 0.9 Hz, 3.9H), 2.02 (q, *J* = 1.4 Hz, 3H), 1.13 (s, 7.8H), 0.98 (s, 6H). **^{1}H NMR** (signals corresponding to the major isomer; 400 MHz; $CDCl_3$) δ 9.55 (s, 1H), 5.68 (td, *J* = 7.6, 1.4 Hz, 1H), 2.39 (dd, *J* = 7.7, 1.0 Hz, 2H), 2.04 (dt, *J* = 1.6, 0.9 Hz, 3H), 1.13 (s, 6H); **^{13}C NMR** (for the mixture of isomers; 175 MHz; $CDCl_3$) δ 206.3, 206.1, 143.9, 141.9, 139.9, 138.0, 128.4, 128.3, 128.1, 127.0, 126.8, 125.9, 122.7, 121.5, 46.9, 46.5, 36.3, 36.2, 26.2, 21.5, 21.3, 16.3; **IR** (Neat) 2966, 1723, 1494, 1466, 1445, 1378, 1271, 1165, 1026, 913, 883, 754, 697. **HRMS**: calcd for $C_{14}H_{18}O^+$: 202.1358 found: 202.1355.



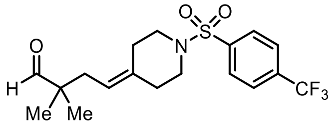
S21a

4-cyclohexylidene-2,2-dimethylbutanal (S21a): General procedure B was employed on a 10.6 mmol scale and purification by column chromatography provided 1.35 g (71%) of **S21a** as a brown oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 9.48 (s, 1H), 5.00 (t, J = 7.8 Hz, 1H), 2.17 (d, J = 7.8 Hz, 2H), 2.11 (t, J = 6.1 Hz, 2H), 2.07 (t, J = 5.9 Hz, 2H), 1.58 – 1.45 (m, 6H), 1.04 (s, 6H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 206.5, 143.0, 115.3, 46.6, 37.5, 34.6, 28.83, 28.75, 27.8, 26.9, 21.2; **IR** (Neat) 2930, 2858, 1712, 1449, 1366, 1155, 1038, 981, 915, 846. **HRMS**: calcd for $C_{12}H_{20}O^+$: 180.1514 found: 180.1510.



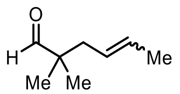
S22a

4-cyclopentylidene-2,2-dimethylbutanal (S22a): General procedure B was employed on a 12.9 mmol scale and purification by distillation provided 707 mg (33%) of **S22a** as a pale yellow oil. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 9.48 (s, 1H), 5.23 – 5.10 (m, 1H), 2.26 – 2.19 (m, 2H), 2.18 – 2.11 (m, 4H), 1.69 – 1.54 (m, 4H), 1.05 (s, 6H). **^{13}C NMR** (125 MHz; $CDCl_3$) δ 206.7, 146.8, 114.3, 46.8, 37.5, 33.9, 29.0, 26.4, 26.4, 21.3; **IR** (Neat) 2955, 2870, 1724, 1467, 1433, 1364, 1106, 1022, 950, 914, 880, 768. **HRMS**: calcd for $C_{11}H_{18}O^+$: 166.1358 found: 166.1360.



S23a

2,2-dimethyl-4-(1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-ylidene)butanal (S23a): General procedure B was employed on a 0.552 mmol scale and purification by column chromatography provided 135 mg (63%) of **S23a** as a white solid. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 9.41 (s, 1H), 7.88 (d, J = 8.2 Hz, 2H), 7.79 (d, J = 8.3 Hz, 2H), 5.13 (t, J = 7.7 Hz, 1H), 3.06 (dt, J = 13.5, 5.8 Hz, 4H), 2.34 (t, J = 5.6 Hz, 2H), 2.28 (t, J = 5.6 Hz, 2H), 2.12 (d, J = 7.7 Hz, 2H), 1.01 (s, 6H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 205.8, 140.6, 135.9, 134.6 (q, J = 32.9 Hz), 128.1, 126.4 (q, J = 3.7 Hz), 123.4 (q, J = 272.8 Hz), 119.9, 48.0, 47.1, 46.4, 35.7, 34.5, 28.0, 21.4; **IR** (Neat) 2967, 2930, 2850, 1722, 1609, 1467, 1404, 1356, 1341, 1320, 1268, 1250, 1166, 1130, 1106, 1092, 1061, 1040, 1015, 982, 932, 879, 844, 786, 738, 725, 701, 688, 657, 629. **HRMS**: calcd for $C_{18}H_{23}F_3NO_3S^+$: 390.1345 found: 390.1342.

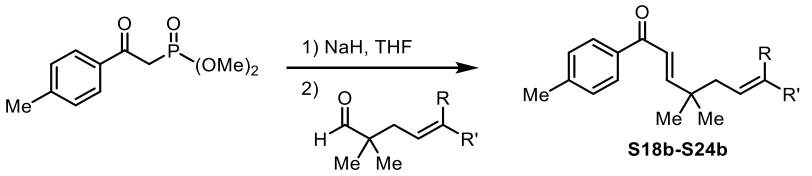


S24a

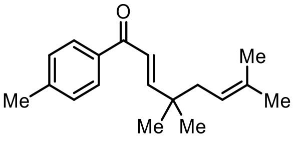
2,2-dimethylhex-4-enal (S24a): General procedure B was employed on a 10.6 mmol scale and purification by column chromatography provided 370 mg (28%) of **S24a** (4:1 mixture of alkene isomers) as a clear oil. The ^{1}H-NMR data is consistent with literature(*58*) reported data. **^{1}H NMR** (for the mixture of alkene isomers; 500 MHz; $CDCl_3$) δ 9.49 (s, 1H), 9.46 (s, 4H), 5.64 – 5.54 (m, 1H), 5.52 – 5.43 (m, 4H), 5.37 – 5.26 (m, 5H), 2.21 (d, J = 7.2 Hz, 2H), 2.13 (d, J = 7.2, 1.2 Hz, 8H), 1.65 (d, J = 6.3, 1.4 Hz, 12H), 1.61 (d, J = 6.8, 2.0, 1.0 Hz, 3H), 1.06 (s, 6H), 1.03 (s, 24H).

^{1}H NMR (signals corresponding to the major isomer; 500 MHz; $CDCl_3$) δ 9.46 (s, 1H), 2.13 (d, *J* = 7.2, 1.2 Hz, 2H), 1.65 (d, *J* = 6.3, 1.4 Hz, 3H), 1.03 (s, 6H).

General Procedure (C): Olefination of allylated aldehydes for the synthesis of enones S18b-S24b

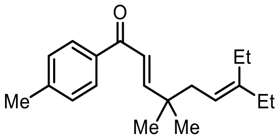


A flame dried round bottom flask equipped with a magnetic stir bar was charged with NaH (1.25 eq) and THF (0.3 M). The reaction was then cooled to 0˚C and dimethyl (2-oxo-2-(*p*-tolyl)ethyl)phosphonate (1.13 eq) was added as a solution in THF (5 mL). After stirring for 0.5 h, the reaction was allowed to warm to room temperature and the corresponding aldehyde was added. Then, the reaction was heated to reflux and stirred until judged complete by TLC. Once complete, the mixture was diluted with saturated ammonium chloride, water, and ethyl acetate after it was allowed to cool to room temperature. The layers were separated and the organic layer was collected. The aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography to give pure enone **S18b-S24b**.



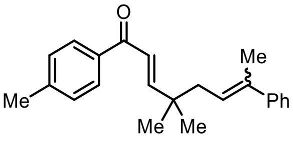
S18b

(*E*)-4,4,7-trimethyl-1-(*p*-tolyl)octa-2,6-dien-1-one (S18b): General procedure C with **S18a** was employed on 3.57 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 897 mg (98%) of **S18b** as a pale yellow oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.85 – 7.81 (m, 2H), 7.28 – 7.24 (m, 2H), 7.00 (d, *J* = 15.7 Hz, 1H), 6.74 (d, *J* = 15.7 Hz, 1H), 5.12 (ddq, *J* = 9.0, 7.6, 1.5 Hz, 1H), 2.42 (s, 3H), 2.10 (d, *J* = 7.6 Hz, 2H), 1.71 (s, 3H), 1.60 (s, 3H), 1.11 (s, 6H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 191.2, 158.5, 143.4, 135.8, 134.1, 129.3, 128.9, 122.2, 120.3, 40.6, 38.2, 26.4, 26.2, 21.8, 18.1; **IR** (Neat) 2963, 2923, 1668, 1616, 1448, 1383, 1328, 1302, 1227, 1180, 1033, 1016, 989, 910, 814, 729, 681. **HRMS**: calcd for $C_{18}H_{25}O^+$: 257.1900 found: 257.1897.



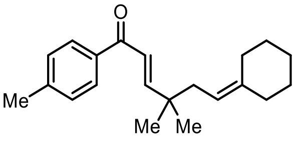
S19b

(*E*)-7-ethyl-4,4-dimethyl-1-(*p*-tolyl)nona-2,6-dien-1-one (S19b): General procedure C with **S19a** was employed on a 4.70 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 774 mg (65%) of **S19b** as a yellow oil. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.83 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 2H), 6.87 (dd, *J* = 107.5, 15.7 Hz, 2H), 5.08 (t, *J* = 7.5 Hz, 1H), 2.42 (s, 3H), 2.14 (d, *J* = 7.5 Hz, 2H), 2.07 – 1.97 (m, 4H), 1.12 (s, *J* = 2.5 Hz, 6H), 0.96 (dt, *J* = 13.9, 7.5 Hz, 6H); **^{13}C NMR** (100 MHz; $CDCl_3$) δ 191.2, 158.6, 145.3, 143.4, 135.8, 129.3, 128.9, 122.3, 118.2, 39.8, 37.9, 29.5, 26.5, 23.2, 21.8, 13.2, 13.1; **IR** (Neat) 2962, 2930, 2873, 1734, 1668, 1650, 1617, 1572, 1459, 1407, 1300, 1226, 1206, 1180, 1116, 1078, 984, 936, 910, 843, 815, 792, 730, 681. **HRMS**: calcd for $C_{20}H_{29}O^+$: 285.2213 found: 285.2210.



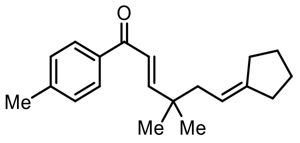
S20b

(2*E*)-4,4-dimethyl-7-phenyl-1-(*p*-tolyl)octa-2,6-dien-1-one (S20b): General procedure C with **S20a** was employed on 1.35 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 245 mg (57%) of **S20b** (3.4:1 mixture of alkene isomers) as a clear oil. **^{1}H NMR** (for the mixture of isomers; 400 MHz; $CDCl_3$) δ δ 7.86 – 7.79 (m, 8.8H), 7.39 – 7.18 (m, 28.8H), 7.15 – 7.10 (m, 2H), 7.07 (d, *J* = 15.7 Hz, 3.4H), 6.95 (d, *J* = 15.8 Hz, 1H), 6.79 (d, *J* = 15.8 Hz, 3.4H), 6.71 (d, *J* = 15.7 Hz, 1H), 5.76 (td, *J* = 7.7, 1.5 Hz, 3.4H), 5.44 (t, *J* = 7.4 Hz, 1H), 2.45 – 2.39 (m, 13.2H), 2.34 (d, *J* = 7.6 Hz, 6.8H), 2.10 (d, *J* = 7.9 Hz, 2H), 2.05 – 2.00 (m, 13.2H), 1.20 (s, 20.4H), 1.06 (s, 6H). **^{1}H NMR** (signals corresponding to the major isomer; 400 MHz; $CDCl_3$) δ 7.07 (d, *J* = 15.7 Hz, 1H), 6.79 (d, *J* = 15.8 Hz, 1H), 5.76 (td, *J* = 7.7, 1.5 Hz, 1H), 2.34 (d, *J* = 7.6 Hz, 2H), 1.20 (s, 6H); **^{13}C NMR** (for the mixture of isomers; 125 MHz; $CDCl_3$) δ 191.1, 158.3, 157.9, 144.1, 143.51, 143.46, 142.3, 139.0, 137.3, 135.8, 135.7, 129.34, 129.32, 128.9, 128.32, 128.25, 128.2, 126.9, 126.6, 125.9, 124.2, 123.0, 122.5, 122.3, 41.23, 41.16, 38.5, 37.8, 26.58, 26.57, 26.2, 21.8, 16.3; **IR** (Neat) 2960, 1722, 1667, 1605, 1446, 1269, 1178, 1105, 754, 734, 700. **HRMS**: calcd for $C_{23}H_{27}O^+$: 319.2056 found: 319.2061.



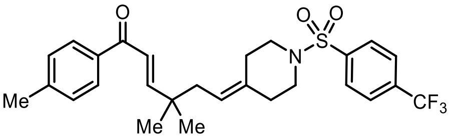
S21b

((*E*)-6-cyclohexylidene-4,4-dimethyl-1-(*p*-tolyl)hex-2-en-1-one (S21b): General procedure C with **S21a** was employed on 2.77 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 487 mg (59%) of **S21b** as a yellow oil. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.83 (d, *J* = 7.9 Hz, 2H), 7.31 – 7.21 (m, 2H), 7.02 (d, *J* = 15.8 Hz, 1H), 6.74 (d, *J* = 15.7 Hz, 1H), 5.07 (t, *J* = 7.8 Hz, 1H), 2.42 (s, 3H), 2.17 – 2.02 (m, 6H), 1.59 – 1.43 (m, 6H), 1.12 (s, 6H); **^{13}C NMR** (100 MHz; $CDCl_3$) δ 191.1, 158.6, 143.4, 142.3, 135.8, 129.3, 128.8, 122.1, 116.8, 39.5, 38.1, 37.7, 29.0, 28.9, 27.8, 27.1, 26.4, 21.8; **IR** (Neat) 2928, 2857, 1721, 1667, 1614, 1446, 1299, 1227, 1179, 1034, 1016, 984, 845, 816, 730. **HRMS**: calcd for $C_{21}H_{29}O^+$: 297.2213 found: 297.2206.



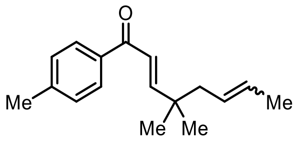
S22b

(*E*)-6-cyclopentylidene-4,4-dimethyl-1-(*p*-tolyl)hex-2-en-1-one (S22b): General procedure C with **S22a** was employed on 3.57 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 996 mg (87%) of **S22b** as a pale yellow oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.28 – 7.24 (m, 2H), 7.01 (d, *J* = 15.7 Hz, 1H), 6.74 (d, *J* = 15.7 Hz, 1H), 5.24 (tq, *J* = 7.1, 2.3 Hz, 1H), 2.42 (s, 3H), 2.26 – 2.20 (m, 2H), 2.17 – 2.13 (m, 2H), 2.09 (dt, *J* = 7.5, 1.4 Hz, 2H), 1.68 – 1.62 (m, 2H), 1.61 – 1.56 (m, 2H), 1.12 (s, 6H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 191.3, 158.6, 146.0, 143.4, 135.8, 129.3, 128.9, 122.2, 115.8, 42.3, 38.2, 33.9, 29.0, 26.5, 26.5, 26.4, 21.8; **IR** (Neat) 2955, 2867, 2835, 1668, 1617, 1450, 1299, 1226, 1180, 1033, 1016, 991, 909, 845, 814, 729, 680. **HRMS**: calcd for $C_{20}H_{27}O^+$: 283.2056 found: 283.2056.



S23b

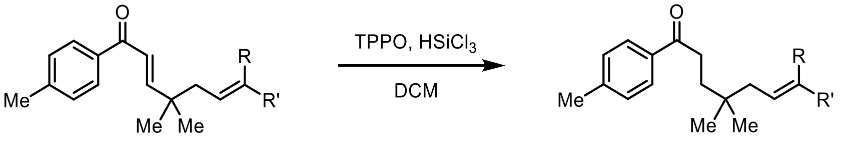
(*E*)-4,4-dimethyl-1-(*p*-tolyl)-6-(1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-ylidene)hex-2-en-1-one (S23b): General procedure C with **S23a** was employed on 0.392 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 144 mg (82%) of **S23b** as a yellow oil. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.78 (dd, *J* = 15.8, 8.1 Hz, 4H), 7.26 (t, *J* = 3.9 Hz, 2H), 6.94 (d, *J* = 15.7 Hz, 1H), 6.72 (d, *J* = 15.7 Hz, 1H), 5.19 (t, *J* = 7.6 Hz, 1H), 3.06 (q, *J* = 5.4 Hz, 4H), 2.42 (s, 3H), 2.30 (dt, *J* = 21.6, 5.5 Hz, 4H), 2.08 (d, *J* = 7.7 Hz, 2H), 1.08 (s, 6H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 190.4, 157.5, 143.8, 140.5, 135.6, 135.3, 134.5 (q, *J* = 33.1 Hz), 129.4, 128.7, 128.1, 126.3 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 273.0 Hz), 122.1, 121.0, 48.1, 47.2, 39.7, 37.9, 35.7, 28.0, 26.4, 21.8; **IR** (Neat) 2962, 2926, 2850, 1667, 1616, 1571, 1465, 1404, 1356, 1321, 1267, 1249, 1231, 1167, 1131, 1106, 1061, 1038, 1015, 985, 933, 843, 817, 786, 737, 726, 701, 684, 656. **HRMS**: calcd for $C_{27}H_{30}F_3NO_3S^+$: 505.1899 found: 505.1891.



S24b

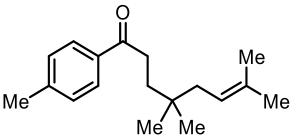
(2*E*)-4,4-dimethyl-1-(*p*-tolyl)octa-2,6-dien-1-one (S24b): General procedure C with **S24a** was employed on 2.82 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 300 mg (44%) of **S24b** (4:1 mixture of alkene isomers) as a clear oil. **^{1}H NMR** (for the mixture of isomers; 400 MHz; CDCl$_3$) δ 7.86 – 7.80 (m, 10H), 7.29 – 7.24 (m, 10H), 7.04 – 6.96 (m, 5H), 6.78 – 6.69 (m, 5H), 5.65 – 5.31 (m, 10H), 2.42 (s, 15H), 2.17 (d, *J* = 7.6 Hz, 2H), 2.09 (d, *J* = 7.0 Hz, 8H), 1.68 – 1.64 (m, 12H), 1.61 (ddt, *J* = 6.8, 1.8, 0.9 Hz, 3H), 1.14 (s, 6H), 1.10 (s, 24H); ^{1}**H NMR** (signals corresponding to the major isomer; 400 MHz; $CDCl_3$) δ 2.09 (d, *J* = 7.0 Hz, 2H), 1.68 – 1.64 (m, 3H), 1.10 (s, 6H); ^{13}**C NMR** (for the mixture of isomers; 100 MHz; $CDCl_3$) δ 191.2, 158.4, 158.1, 143.4, 135.8, 129.3, 128.9, 128.8, 128.5, 126.9, 126.5, 126.2, 122.3, 122.3, 45.5, 39.2, 37.6, 26.4, 26.4, 21.8, 18.2; **IR** (Neat) 2960, 1668, 1616, 1449, 1298, 1226, 1180, 1116, 1033, 1016, 967, 846, 816, 729. 680. **HRMS**: calcd for $C_{17}H_{23}O^{+}$: 243.1749 found: 243.1743.

General procedure (D): 1,4 reduction of enones for the synthesis of substrates 18-24(*59*)



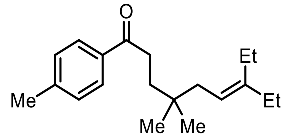
18-24

A flame dried round bottom flask equipped with a magnetic stir bar was charged with triphenylphosphine oxide (0.2 eq), the corresponding enone (1.0 eq), and DCM (0.1 M). The reaction was cooled to 0˚C, trichlorosilane (2.0 eq) was added, and the reaction was then allowed to warm to room temperature. After completion of the reaction as judged by TLC analysis, the mixture was diluted with DCM and slowly quenched with saturated sodium bicarbonate. The layers were separated and the aqueous layer was further extracted with DCM (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography to give pure substrate **18-24**.



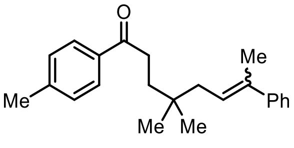
18

4,4,7-trimethyl-1-(*p*-tolyl)oct-6-en-1-one (18): General procedure D with **S18b** was employed on 1.17 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 207 mg (69%) of **18** as a clear oil. ^{1}**H NMR** (700 MHz; C_6D_6) δ 7.92 – 7.89 (m, 2H), 6.94 (d, *J* = 7.8 Hz, 2H), 5.27 (tp, *J* = 7.6, 1.5 Hz, 1H), 2.77 – 2.71 (m, 2H), 2.02 (s, 3H), 1.92 (d, *J* = 7.6 Hz, 2H), 1.79 – 1.73 (m, 2H), 1.67 (s, 3H), 1.54 (s, 3H), 0.84 (s, 6H); ^{13}**C NMR** (175 MHz; C_6D_6) δ 199.0, 143.1, 135.5, 133.0, 129.4, 128.6, 121.6, 40.5, 36.5, 33.9, 33.9, 26.9, 26.2, 21.4, 18.0; **IR** (Neat) 2957, 2923, 1681, 1607, 1449, 1408, 1384, 1364, 1312, 1296, 1180, 977, 818, 767, 724. **HRMS**: calcd for $C_{18}H_{27}O^{+}$: 259.2056 found: 259.2054.



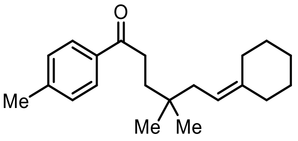
19

7-ethyl-4,4-dimethyl-1-(*p*-tolyl)non-6-en-1-one (19): General procedure D with **S19b** was employed on a 1.05 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 174 mg (58%) of **19** as an orange oil. **^{1}H NMR** (400 MHz; CDCl$_3$) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 6.7 Hz, 2H), 5.15 (t, *J* = 7.4 Hz, 1H), 2.98 – 2.80 (m, 2H), 2.41 (s, 3H), 2.10 – 2.00 (m, 4H), 1.97 (d, *J* = 7.5 Hz, 2H), 1.70 – 1.58 (m, 2H), 0.99 (t, *J* = 7.5 Hz, 3H), 0.97 – 0.91 (m, 9H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 201.0, 144.5, 143.7, 134.7, 129.4, 128.4, 118.8, 39.4, 36.4, 34.0, 33.6, 29.5, 27.0, 23.2, 21.8, 13.2, 13.1; **IR** (Neat) 2960, 2930, 2871, 1681, 1607, 1574, 1462, 1408, 1384, 1364, 1314, 1297, 1221, 1207, 1180, 1116, 1041, 977, 936, 903, 817, 768, 724; **HRMS**: calcd for $C_{20}H_{31}O^+$: 287.2369 found: 287.2368.



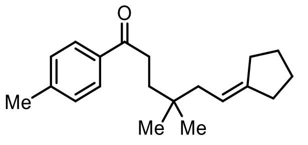
20

4,4-dimethyl-7-phenyl-1-(*p*-tolyl)oct-6-en-1-one (20): General procedure D with **S20b** was employed on 0.729 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 202 mg (86%) of **20** (3.4:1 mixture of alkene isomers) as a clear oil. **^{1}H NMR** (for the mixture of isomers; 400 MHz; CDCl$_3$) δ 7.85 (d, *J* = 8.0 Hz, 7H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 7H), 7.35 – 7.17 (m, 22.5H), 7.13 (d, *J* = 7.6 Hz, 2H), 5.85 (t, *J* = 7.6 Hz, 3.5H), 5.54 (t, *J* = 7.3 Hz, 1H), 2.99 – 2.89 (m, 7H), 2.71 – 2.62 (m, 2H), 2.45 – 2.37 (m, 13.5H), 2.17 (d, *J* = 7.6 Hz, 7H), 2.07 – 2.01 (m, 13.5H), 1.94 (d, *J* = 7.4 Hz, 2H), 1.76 – 1.67 (m, 7H), 1.00 (s, 21H), 0.87 (s, 6H). **^{1}H NMR** (signals corresponding to the major isomer; 400 MHz; CDCl$_3$) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 2H), 5.85 (t, *J* = 7.6 Hz, 1H), 2.99 – 2.89 (m, 2H), 2.17 (d, *J* = 7.6 Hz, 2H), 1.76 – 1.67 (m, 2H), 1.00 (s, 6H); **^{13}C NMR** (for the mixture of isomers; 125 MHz; CDCl$_3$) δ 200.8, 144.4, 143.8, 143.7, 142.5, 138.2, 136.5, 134.7, 134.7, 129.4, 129.3, 128.4, 128.3, 128.3, 128.2, 128.2, 126.7, 126.5, 125.9, 125.1, 123.8, 40.9, 40.3, 36.6, 35.6, 34.4, 34.0, 33.7, 33.5, 27.4, 27.1, 26.3, 21.8, 16.3; **IR** (Neat) 2958, 2918, 1720, 1680, 1606, 1447, 1366, 1266, 1179, 1108, 1063, 816, 761, 700. **HRMS**: calcd for $C_{23}H_{29}O^+$: 321.2213 found: 321.2217.



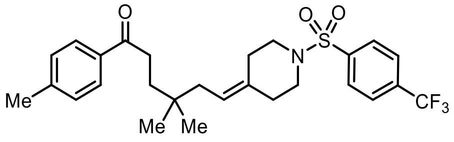
21

6-cyclohexylidene-4,4-dimethyl-1-(*p*-tolyl)hexan-1-one (21): General procedure D with **S21b** was employed on 1.31 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 227 mg (58%) of **21** as a clear oil. **^{1}H NMR** (400 MHz; CDCl$_3$) δ 7.90 – 7.79 (m, 2H), 7.31 – 7.19 (m, 2H), 5.14 (t, *J* = 7.7 Hz, 1H), 2.93 – 2.85 (m, 2H), 2.41 (s, 3H), 2.17 – 2.06 (m, 4H), 1.95 (d, *J* = 7.7 Hz, 2H), 1.68 – 1.59 (m, 2H), 1.58 – 1.43 (m, 6H), 0.91 (s, 6H); **^{13}C NMR** (100 MHz; CDCl$_3$) δ 201.0, 143.7, 141.5, 134.7, 129.4, 128.4, 117.6, 39.1, 37.8, 36.3, 34.0, 33.8, 29.0, 28.9, 27.8, 27.1, 27.0, 21.8; **IR** (Neat) 2924, 2851, 1681, 1607, 1446, 1364, 1296, 1179, 979, 819, 767. **HRMS**: calcd for $C_{21}H_{31}O^+$: 299.2369 found: 299.2373.



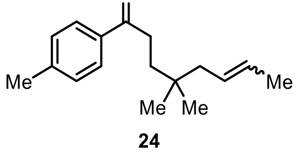
22

6-cyclopentylidene-4,4-dimethyl-1-(*p*-tolyl)hexan-1-one (22): General procedure D with **S22b** was employed on 0.708 mmol scale. 2,6-lutidine (2.0 eq) was added after the reaction was cooled to 0˚C and before the addition of trichlorosilane. Purification by column chromatography eluting with hexanes/EtOAc provided 98 mg (49%) of **22** as a clear oil. ^{1}**H NMR** (700 MHz; $CDCl_3$) δ 7.87 – 7.84 (m, 2H), 7.27 – 7.24 (m, 2H), 5.32 (tt, *J* = 7.4, 2.3 Hz, 1H), 2.92 – 2.85 (m, 2H), 2.41 (s, 3H), 2.25 (tq, *J* = 7.2, 1.6 Hz, 2H), 2.17 (tt, *J* = 7.2, 1.7 Hz, 2H), 1.93 (dt, *J* = 7.5, 1.5 Hz, 2H), 1.68 – 1.56 (m, 6H), 0.92 (s, 6H); ^{13}**C NMR** (175 MHz; $CDCl_3$) δ 201.0, 145.1, 143.7, 134.7, 129.4, 128.4, 116.5, 41.9, 36.4, 34.0, 34.0, 33.9, 29.0, 27.0, 26.5 (two carbons observed by HSQC), 21.8; **IR** (Neat) 2952, 2864, 2834, 1680, 1607, 1573, 1467, 1450, 1408, 1364, 1313, 1295, 1222, 1206, 1180, 999, 976, 897, 817, 768, 723. **HRMS**: calcd for $C_{20}H_{28}ONa^{+}$: 307.2032 found: 307.2030.



23

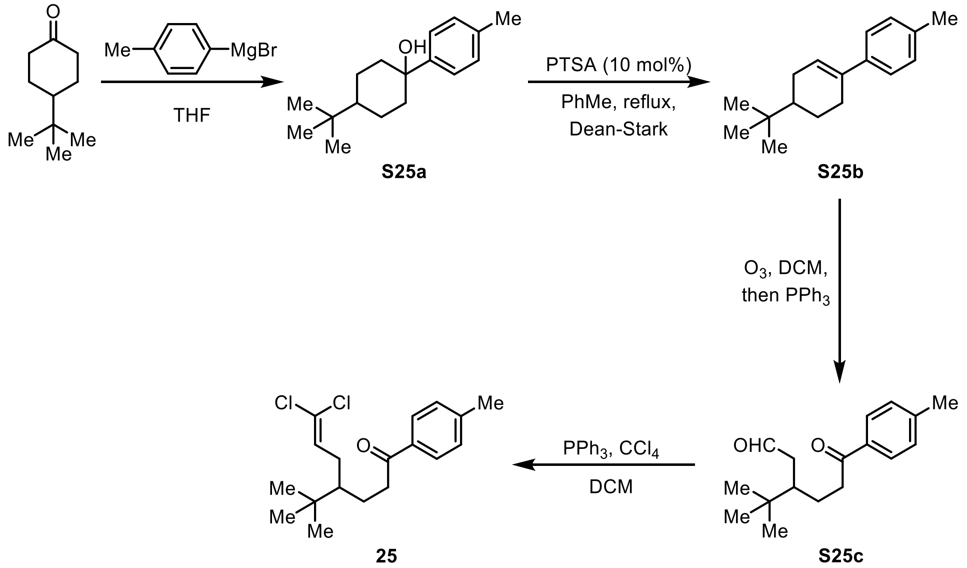
4,4-dimethyl-1-(*p*-tolyl)-6-(1-((4-(trifluoromethyl)phenyl)sulfonyl)piperidin-4-ylidene)hexan-1-one (23): General procedure D with **S23b** was employed on 0.285 mmol scale. 2,6-lutidine (2.0 eq) was added after the reaction was cooled to 0˚C and before the addition of trichlorosilane. Purification by column chromatography eluting with hexanes/EtOAc provided 105 mg (72%) of **23** as a white solid. ^{1}**H NMR** (700 MHz; $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.1 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 5.26 (t, *J* = 7.7 Hz, 1H), 3.06 (dt, *J* = 10.9, 5.7 Hz, 4H), 2.91 – 2.79 (m, 2H), 2.41 (s, 3H), 2.34 (t, *J* = 5.6 Hz, 2H), 2.30 (t, *J* = 5.6 Hz, 2H), 1.90 (d, *J* = 7.7 Hz, 2H), 1.69 – 1.51 (m, 2H), 0.86 (s, 6H); ^{13}**C NMR** (175 MHz; $CDCl_3$) δ 200.5, 143.9, 140.5, 134.6, 134.5 (q, *J* = 32.9 Hz), 134.4, 129.4, 128.3, 128.1, 126.3 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 272.7 Hz), 121.9, 48.1, 47.2, 39.4, 36.0, 35.8, 33.74, 33.68, 28.0, 26.8, 21.8; **IR** (Neat) 2966, 2945, 2901, 2864, 1677, 1607, 1473, 1404, 1388, 1352, 1339, 1321, 1302, 1248, 1168, 1128, 1106, 1075, 1061, 1039, 1016, 999, 978, 938, 861, 823, 785, 774, 738, 726, 700, 660. **HRMS**: calcd for $C_{27}H_{32}F_3NO_3S^{+}$: 507.2055 found: 507.2037.



24

4,4-dimethyl-1-(*p*-tolyl)oct-6-en-1-one (24): General procedure D with **S24b** was employed on 0.99 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 199 mg (82%) of **24** (4.3:1 mixture of alkene isomers) as a clear oil. **^{1}H NMR** (for the mixture of isomers; 400 MHz; $CDCl_3$) δ 7.89 – 7.83 (m, 10.6H), 7.28 – 7.23 (m, 10.6H), 5.44 (dt, *J* = 5.7, 3.3 Hz, 10.6H), 2.95 – 2.84 (m, 10.6H), 2.41 (s, 15.9H), 2.00 (d, *J* = 7.5 Hz, 2H), 1.96 – 1.91 (m, 8.6H), 1.71 – 1.50 (m, 26.5H), 0.97 – 0.87 (m, 31.8H); **^{1}H NMR** (signals corresponding to the major isomer; 400 MHz; $CDCl_3$) δ 1.96 – 1.91 (m, 2H); **^{13}C NMR** (for the mixture of isomers; 125 MHz; $CDCl_3$) δ 200.9, 200.8, 143.7, 134.7, 129.4, 128.4, 128.4, 127.8, 127.6, 127.0, 125.8, 45.2, 38.8, 36.4, 36.3, 33.9, 33.8, 33.8, 33.3, 27.0, 26.9, 21.8, 18.2, 13.1; **IR** (Neat) 2956, 1679, 1607, 1450, 1365, 1314, 1295, 1180, 969, 819, 769. **HRMS**: calcd for $C_{17}H_{25}O^+$: 245.1905 found: 245.1900.

4 step sequence for the synthesis of substrate 25



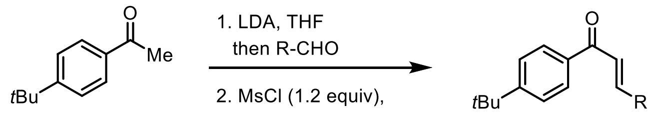
4-(tert-butyl)-1-(p-tolyl)cyclohexan-1-ol (S25a): A flame dried round bottom flask equipped with a magnetic stir bar was charged with freshly ground Mg (706 mg, 29.2 mmol), 4-bromotoluene (9.03 g, 38.9 mmol) and THF (50 mL). The mixture was allowed to stir at room temperature until all of the magnesium dissolved. Then, the mixture was cooled to 0°C and a solution of 4-tert-Butylcyclohexanone (3.0 g, 19.4 mmol) in THF (50 mL) was added. The resulting mixture was allowed to warm to room temperature and stirred until judged complete by TLC. The reaction was quenched with ammonium chloride and portioned between ethyl acetate and water. The layers were separated and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was used without further purification.

4-(tert-butyl)-4'-methyl-2,3,4,5-tetrahydro-1,1'-biphenyl (S25b): A flame dried round bottom flask equipped with a magnetic stir bar was charged with **S25a** (19.4 mmol), PTSA (370 mg, 1.94 mmol) and toluene (70 mL). The reaction was attached to a Dean-Stark apparatus, heated to reflux, and allowed to stir until judged complete by TLC. After cooling to room temperature, the reaction was quenched with saturated sodium bicarbonate and partitioned between water and ethyl acetate. The layers were separated and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes provided 2.85 g (64% over 2 steps) of **S25b** as a white solid. The **^{1}H NMR** data is consistent with literature(*60*) reported data. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.11 (d, J = 7.8 Hz, 2H), 6.13 – 6.05 (m, 1H), 2.55 – 2.46 (m, 1H), 2.46 – 2.35 (m, 1H), 2.33 (s, 3H), 2.28 – 2.19 (m, 1H), 2.01 – 1.91 (m, 2H), 1.33 (dddt, J = 23.9, 19.1, 12.1, 5.8 Hz, 2H), 0.91 (s, 9H).

3-(*tert*-butyl)-6-oxo-6-(*p*-tolyl)hexanal (S25c): A flame dried round bottom flask equipped with a magnetic stir bar was charged with **S25b** (1.0 g, 4.38 mmol) and DCM (22 mL). The resulting mixture was cooled to -78˚C and a stream of ozone was passed through the solution until a blue-violet color was observed. Excess ozone was removed by passing a stream of nitrogen through the solution. The reaction was quenched by addition of PPh_3 (1.4 g, 5.25 mmol) and the mixture was allowed to warm to room temperature overnight. The next day, the mixture was concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 470 mg (41%) of **S25c** as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 9.85 – 9.81 (m, 1H), 7.83 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 7.9 Hz, 2H), 2.98 – 2.85 (m, 2H), 2.67 – 2.61 (m, 1H), 2.40 (s, 3H), 2.26 (ddd, J = 17.6, 6.2, 2.1 Hz, 1H), 2.06 (dddd, J = 13.4, 9.5, 6.3, 3.0 Hz, 1H), 1.90 – 1.84 (m, 1H), 1.45 (dtd, J = 19.6, 9.6, 5.7 Hz, 1H), 0.93 – 0.90 (m, 9H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 203.1, 199.8, 144.0, 134.5, 129.4, 128.3, 46.3, 42.3, 37.8, 33.8, 27.7, 25.9, 21.8; **IR** (Neat) 2960, 2870, 1721, 1680, 1607, 1471, 1408, 1396, 1365, 1286, 1225, 1204, 1181, 1036, 975, 809. **HRMS**: calcd for $C_{17}H_{24}O_2Na^+$: 283.1669 found: 283.1658.

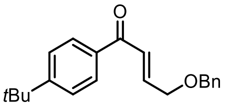
4-(tert-butyl)-7,7-dichloro-1-(p-tolyl)hept-6-en-1-one (25): A flame dried round bottom flask equipped with a magnetic stir bar was charged with PPh_3 (403 mg, 1.54 mmol.) and DCM (0.6 mL). Then, **S25c** (100 mg, 0.31 mmol) and carbon tetrachloride (0.074 mL, 0.76 mmol) were added and the reaction was allowed to stir at room temperature overnight. The next day, the reaction was quenched with water and partitioned between DCM and water. The layers were separated and the aqueous layer was further extracted with DCM (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 86 mg (68%) of **25** as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.86 (d, J = 8.1 Hz, 2H), 7.29 – 7.25 (m, 2H), 5.93 (dd, J = 8.2, 6.6 Hz, 1H), 3.08 – 3.00 (m, 1H), 2.90 (ddd, J = 16.2, 9.8, 6.0 Hz, 1H), 2.41 (s, 3H), 2.38 – 2.32 (m, 1H), 2.17 – 2.08 (m, 1H), 2.00 (dddd, J = 13.7, 9.7, 6.1, 3.1 Hz, 1H), 1.48 (dtd, J = 14.4, 9.3, 5.3 Hz, 1H), 1.30 – 1.24 (m, 1H), 0.93 (s, 9H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 200.0, 143.9, 134.6, 130.7, 129.5, 128.3, 119.6, 48.1, 38.2, 34.2, 31.2, 27.9, 25.4, 21.8; **IR** (Neat) 2960, 2868, 1681, 1607, 1471, 1408, 1396, 1366, 1280, 1225, 1201, 1180, 867, 817. **HRMS**: calcd for $C_{18}H_{24}OCl_2Na^+$: 349.1096 found: 349.1105.

General procedure (E): Aldol condensation for the synthesis of enones S29a & S33a



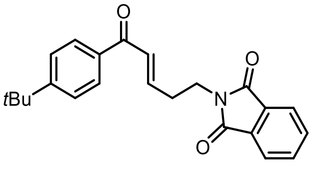
S29a & S33a

A flame dried round bottom flask equipped with a magnetic stir bar was charged with diisopropylamine (1.1 eq) and THF (0.5 M). The flask was cooled to 0˚C and n-butyllithium (1.1 eq, 2.5M in hexanes) was added. The reaction was allowed to stir at 0˚C for 0.5 h before being cooled to -78˚C. At -78˚C, 4'-tert-butylacetophenone (1 eq) was added and the reaction was allowed to stir for another 0.5 h. Then, the corresponding aldehyde (1.1 eq) was added as a solution in THF (5 mL) and the reaction was allowed to stir until judged complete by TLC analysis. The resulting reaction mixture was quenched with water and allowed to warm up to room temperature. The reaction was diluted with saturated ammonium chloride and ethyl acetate. The organic layer was collected and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure to give the crude product, which was used directly without further purification. A magnetic stir bar and DCM (0.2 M) were added to the flask containing the crude product, and the reaction was cooled to 0˚C. Triethylamine (2.5 eq) was added, followed by methanesulfonyl chloride (1.2 eq), and the reaction was allowed to warm temperature. The reaction was diluted with 10% HCl and DCM after completion of the reaction as judged by TLC analysis. The organic layer was collected and the aqueous layer was further extracted with DCM (x2). The combined organics were washed with saturated sodium bicarbonate, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography to give pure enone **S29a & S33a**.



S29a

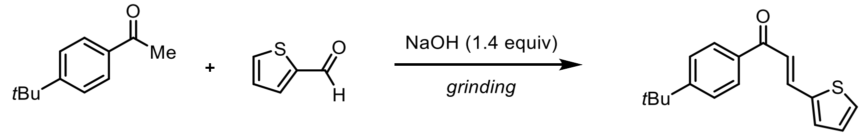
(*E*)-4-(benzyloxy)-1-(4-(*tert*-butyl)phenyl)but-2-en-1-one (S29a): General procedure E with benzyloxyacetaldehyde was employed on a 7.66 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 984 mg (42%) of **S29a** as pale yellow oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.94 – 7.89 (m, 2H), 7.51 – 7.46 (m, 2H), 7.40 – 7.29 (m, 5H), 7.25 – 7.19 (m, 1H), 7.07 (dtd, *J* = 15.5, 4.1, 1.3 Hz, 1H), 4.63 (s, 2H), 4.35 – 4.24 (m, 2H), 1.35 (s, 9H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 190.0, 156.8, 144.1, 137.9, 135.2, 128.8, 128.7, 128.0, 127.8, 125.7, 125.1, 73.0, 69.4, 35.3, 31.3; **IR** (Neat) 2960, 2905, 2867, 1670, 1624, 1604, 1455, 1407, 1362, 1324, 1297, 1283, 1269, 1191, 1109, 1027, 1012, 961, 857, 808, 735, 697. **HRMS**: calcd for $C_{21}H_{25}O^+$: 309.1849 found: 309.1850.



S33a

(*E*)-2-(5-(4-(*tert*-butyl)phenyl)-5-oxopent-3-en-1-yl)isoindoline-1,3-dione (S33a): General procedure E with 3-(1,3-dioxoisoindolin-2-yl)propanal was employed on a 4.75 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 628 mg (37%) of **S33a** as white solid. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.88 – 7.81 (m, 4H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.01 – 6.92 (m, 2H), 3.91 (t, *J* = 7.2 Hz, 2H), 2.73 (q, *J* = 6.8 Hz, 2H), 1.34 (s, 9H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 190.1, 168.3, 156.7, 143.9, 135.0, 134.2, 132.1, 128.7, 128.3, 125.6, 123.5, 36.6, 35.2, 31.8, 31.2; **IR** (Neat) 2958, 2907, 2868, 1772, 1708, 1668, 1620, 1604, 1467, 1435, 1394, 1356, 1334, 1269, 1189, 1109, 1012, 993, 876, 858, 820, 717, 680. **HRMS**: calcd for $C_{23}H_{23}NO_3Na^+$: 384.1570 found: 384.1570.

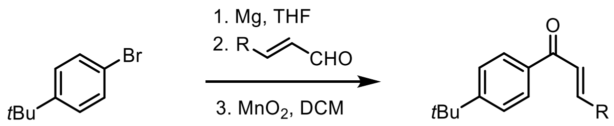
Neat aldol condensation for the synthesis of S35a



S35a

(*E*)-1-(4-(*tert*-butyl)phenyl)-3-(thiophen-2-yl)prop-2-en-1-one (S35a):(*61*) A mixture of 4'-tert-butylacetophenone (0.91 mL, 5.0 mmol), 2-thiophenecarboxaldehyde (0.47 mL, 5.0 mmol), and sodium hydroxide (280 mg, 7.00 mmol) was thoroughly ground with a mortar and pestle at room temperature until the initially melted mixture hardened. Grinding was continued until the reaction was judged complete by TLC analysis. The solid was washed with water and filtered. The precipitate was recrystallized from ethanol to give 472 mg (35%) of **S35a** as yellow crystals. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.98 – 7.92 (m, 3H), 7.54 – 7.50 (m, 2H), 7.42 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.37 – 7.33 (m, 2H), 7.09 (ddd, *J* = 4.9, 3.6, 1.0 Hz, 1H), 1.36 (s, 9H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 189.6, 156.7, 140.7, 136.9, 135.6, 132.1, 128.8, 128.5, 128.5, 125.7, 121.0, 35.3, 31.3; **IR** (Neat) 2960, 2904, 2867, 1655, 1605, 1585, 1560, 1281, 1214, 1190, 1108, 1030, 1009, 969, 818, 705, 688. **HRMS**: calcd for $C_{17}H_{19}OS^+$: 271.1151 found: 271.1153.

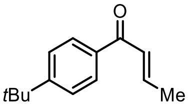
General procedure (F): Grignard addition/oxidation for the synthesis of enones S39a & S44a



S39a & S44a

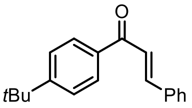
A flame-dried 250 mL round bottom flask equipped with a magnetic stir bar was charged with 1-bromo-4-tert-butylbenzene (1.5 eq) and THF (0.5 M). Magnesium turnings (1.5 eq) were then added, and the reaction was allowed to stir at room temperature until the magnesium dissolved. The reaction was then cooled to 0˚C and the corresponding enal was added. The reaction was allowed to warm up to room temperature and stirred until judged complete by TLC analysis. The resulting reaction mixture was quenched with saturated ammonium chloride and diluted with water and ethyl acetate. The layers were separated and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure to give the crude allylic alcohol, which was used without further purification. A magnetic stir bar and DCM (0.25 M) were added to the flask containing the crude alcohol. Activated manganese dioxide (15 eq) was then added and the reaction was allowed to stir at room temperature. After completion of the reaction as judged complete by

TLC analysis, the reaction was filtered over celite eluting with DCM. The filtrate was then concentrated and purified to give pure enone **S39a & S44a**.



S39a

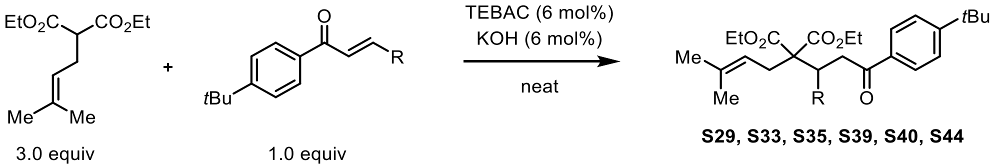
(*E*)-1-(4-(*tert*-butyl)phenyl)but-2-en-1-one (S39a): General procedure F with crotonaldehyde was employed on a 24.3 mmol scale and purification by column chromatography eluting with hexanes/EtOAc provided 2.92 g (60%) of **S39a** as a yellow oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.90 – 7.85 (m, 2H), 7.50 – 7.45 (m, 2H), 7.07 (dq, *J* = 15.4, 6.9 Hz, 1H), 6.92 (dq, *J* = 15.2, 1.7 Hz, 1H), 2.00 (dd, *J* = 6.9, 1.7 Hz, 3H), 1.35 (s, 9H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 190.4, 156.5, 144.6, 135.4, 128.6, 127.6, 125.6, 35.2, 31.3, 18.7; **IR** (Neat) 2962, 2906, 2870, 1668, 1652, 1622, 1604, 1442, 1407, 1364, 1330, 1294, 1268, 1225, 1190, 1113, 1103, 1038, 1014 964, 918, 810, 719, 668. **HRMS**: calcd for $C_{14}H_{19}O^+$: 203.1430 found: 203.1430.



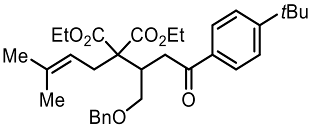
S44a

((*E*)-1-(4-(*tert*-butyl)phenyl)-3-phenylprop-2-en-1-one (S44a): General procedure F with cinnamaldehyde was employed on a 23.8 mmol scale and purification by recrystallization from methanol provided 3.48 g (55%) of **S44a** as yellow crystals. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.98 (d, *J* = 8.1 Hz, 2H), 7.81 (d, *J* = 15.7 Hz, 1H), 7.67 – 7.63 (m, 2H), 7.57 – 7.50 (m, 3H), 7.45 – 7.39 (m, 3H), 1.37 (s, 9H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 190.2, 156.7, 144.5, 135.7, 135.2, 130.5, 129.1, 128.6, 128.5, 125.7, 122.3, 35.3, 31.3; **IR** (Neat) 2962, 2902, 2870, 1661, 1607, 1576, 1449, 1334, 1305, 1286, 1221, 1190, 1109, 1034, 1010, 998, 978, 836, 768, 741, 676. **HRMS**: calcd for $C_{19}H_{20}ONa^+$: 287.1406 found: 287.1403.

General procedure (G): Michael addition for the synthesis of substrates S29, S33, S35, S39, S40, S44

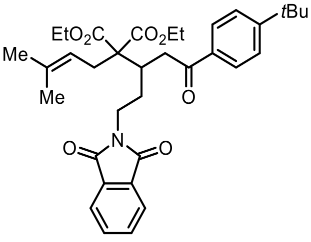


A 20 mL scintillation vial equipped with a magnetic stir bar was charged with the corresponding enone (1 mmol) and diethyl 2-(3-methylbut-2-en-1-yl)malonate (3 mmol). TEBAC (14 mg, 0.06 mmol) and KOH (3.4 mg, 0.06 mmol) were then added at room temperature. After being judged complete by TLC analysis, the reaction was diluted with DCM (20 mL) and water (20 mL). The organic layer was collected, and the aqueous layer was further extracted with DCM (2 x 10 mL). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography afforded pure substrate.



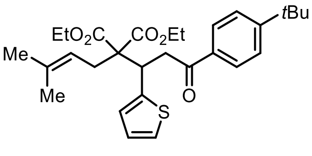
S29

diethyl 2-(1-(benzyloxy)-4-(4-(*tert*-butyl)phenyl)-4-oxobutan-2-yl)-2-(3-methylbut-2-en-1-yl)malonate (S29): General procedure G with **S29a** was employed and purification by column chromatography eluting with hexanes/EtOAc provided 365 mg (68%) of **S29** as a clear oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.91 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.25 – 7.18 (m, 3H), 7.16 (d, *J* = 7.3 Hz, 2H), 5.12 – 5.07 (m, 1H), 4.35 – 4.29 (m, 2H), 4.17 – 4.06 (m, 4H), 3.56 (qd, *J* = 10.1, 4.2 Hz, 2H), 3.38 (dd, *J* = 17.0, 9.6 Hz, 1H), 3.29 – 3.24 (m, 1H), 3.15 (dd, *J* = 17.1, 2.5 Hz, 1H), 2.75 (dd, *J* = 15.4, 6.9 Hz, 1H), 2.69 (dd, *J* = 15.3, 7.7 Hz, 1H), 1.68 (s, 3H), 1.56 (s, 3H), 1.34 (s, 9H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 198.8, 171.14, 171.07, 156.5, 138.3, 135.04, 134.96, 128.21, 128.19, 127.8, 127.5, 125.5, 118.4, 73.2, 69.4, 61.3, 61.1, 59.6, 37.9, 37.8, 35.2, 32.5, 31.3, 26.2, 18.0, 14.19, 14.15; **IR** (Neat) 2962, 2930, 2907, 2873, 1724, 1680, 1605, 1452, 1406, 1364, 1270, 1221, 1180, 1091, 1040, 1026, 1006, 858, 828, 737, 698. **HRMS**: calcd for $C_{33}H_{44}O_6Na^+$: 559.3030 found: 559.3029.



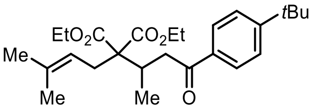
S33

diethyl 2-(1-(4-(*tert*-butyl)phenyl)-5-(1,3-dioxoisoindolin-2-yl)-1-oxopentan-3-yl)-2-(3-methylbut-2-en-1-yl)malonate (S33): General procedure G with **S33a** was employed and purification by column chromatography eluting with hexanes/EtOAc provided 342 mg (58%) of **S33** as a viscous yellow oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.92 (d, *J* = 8.3 Hz, 2H), 7.81 – 7.76 (m, 2H), 7.70 – 7.65 (m, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 5.15 (t, *J* = 7.4 Hz, 1H), 4.21 (qt, *J* = 7.3, 3.7 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.72 (ddd, *J* = 13.5, 11.1, 5.6 Hz, 1H), 3.56 – 3.45 (m, 2H), 3.17 – 3.11 (m, 1H), 2.99 (dd, *J* = 18.4, 6.8 Hz, 1H), 2.71 – 2.62 (m, 2H), 2.01 – 1.92 (m, 1H), 1.69 (s, 3H), 1.61 (s, 3H), 1.58 – 1.49 (m, 1H), 1.34 (s, 9H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 198.0, 171.1, 170.9, 168.2, 156.8, 135.2, 134.5, 133.9, 132.3, 128.2, 125.7, 123.2, 118.6, 62.1, 61.4, 61.4, 41.5, 37.0, 35.2, 34.5, 32.8, 31.7, 31.3, 26.2, 18.1, 14.3, 14.2; **IR** (Neat) 2966, 1772, 1710, 1685, 1605, 1436, 1366, 1268, 1224, 1188, 1108, 1060, 1003, 864, 828, 794, 721. **HRMS**: calcd for $C_{35}H_{43}NO_7Na^+$: 612.2932 found: 612.2933.



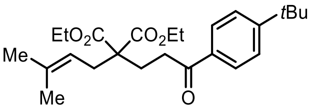
S35

diethyl 2-(3-(4-(*tert*-butyl)phenyl)-3-oxo-1-(thiophen-2-yl)propyl)-2-(3-methylbut-2-en-1-yl)malonate (S35): General procedure G with **S35a** was employed and purification by column chromatography eluting with hexanes/EtOAc provided 171 mg (34%) of **S35** as a clear oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.86 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 5.1 Hz, 1H), 6.87 – 6.85 (m, 1H), 6.85 – 6.83 (m, 1H), 5.19 (t, J = 7.4 Hz, 1H), 4.56 (dd, J = 10.9, 2.1 Hz, 1H), 4.33 (dtd, J = 10.8, 7.6, 6.7 Hz, 1H), 4.27 (ddt, J = 10.9, 7.8, 6.7 Hz, 1H), 4.18 – 4.11 (m, 2H), 3.76 (dd, J = 17.5, 10.7 Hz, 1H), 3.56 (dd, J = 17.4, 2.1 Hz, 1H), 2.64 (dd, J = 15.3, 6.8 Hz, 1H), 2.49 (dd, J = 15.2, 7.6 Hz, 1H), 1.71 (s, 3H), 1.55 (s, 3H), 1.35 (td, J = 7.2, 0.9 Hz, 3H), 1.32 (s, 9H), 1.22 (td, J = 7.1, 0.9 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 197.1, 170.8, 170.7, 156.7, 142.5, 135.2, 134.6, 128.1, 127.1, 126.4, 125.6, 124.4, 118.5, 62.1, 61.55, 61.54, 43.8, 39.9, 35.2, 33.2, 31.2, 26.3, 18.2, 14.3, 14.2; **IR** (Neat) 2960, 2904, 2867, 1655, 1605, 1585, 1406, 1364, 1298, 1281, 1239, 1214, 1190, 1108, 1030, 1009, 969, 818, 705, 688. **HRMS**: calcd for $C_{29}H_{38}O_5SNa^+$: 521.2332 found: 521.2336.



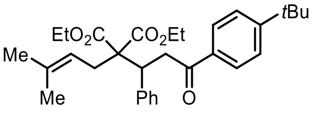
S39

diethyl 2-(4-(4-(*tert*-butyl)phenyl)-4-oxobutan-2-yl)-2-(3-methylbut-2-en-1-yl)malonate (S39): General procedure G with **S39a** was employed and purification by column chromatography eluting with hexanes/EtOAc provided 237 mg (55%) of **S39** as a clear oil. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 7.94 (d, J = 8.2 Hz, 2H), 7.47 (d, J = 8.2 Hz, 2H), 5.10 (t, J = 7.3 Hz, 1H), 4.28 – 4.21 (m, 2H), 4.21 – 4.12 (m, 2H), 3.34 (dd, J = 16.1, 1.9 Hz, 1H), 2.97 (ddt, J = 12.3, 7.8, 3.9 Hz, 1H), 2.82 – 2.63 (m, 3H), 1.69 (s, 3H), 1.62 (s, 3H), 1.38 – 1.28 (m, 12H), 1.28 – 1.19 (m, 3H), 0.95 (d, J = 6.8 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 199.0, 171.3, 170.9, 156.8, 135.0, 134.8, 128.3, 125.6, 118.5, 61.6, 61.2, 61.2, 42.8, 35.2, 32.6, 32.4, 31.3, 26.2, 18.1, 15.8, 14.4, 14.3; **IR** (Neat) 2968, 1723, 1684, 1605, 1457, 1447, 1406, 1365, 1270, 1229, 1179, 1093, 1050, 1025, 994, 857, 827. **HRMS**: calcd for $C_{26}H_{39}O_5^+$: 431.2792 found: 431.2800.



S40

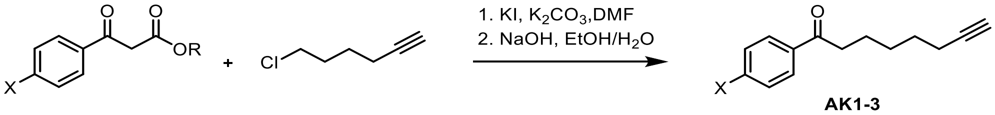
diethyl 2-(3-(4-(*tert*-butyl)phenyl)-3-oxopropyl)-2-(3-methylbut-2-en-1-yl)malonate (S40): General procedure G with 1-(4-(*tert*-butyl)phenyl)prop-2-en-1-one was employed. The reaction was cooled to 0˚C before adding TEBAC and KOH, and it was warmed to room temperature after those reagents were added. Purification by column chromatography eluting with hexanes/EtOAc provided 199 mg (48%) of **S40** as a clear oil. ^{1}**H NMR** (700 MHz; CDCl$_3$) δ 7.90 – 7.86 (m, 2H), 7.48 – 7.44 (m, 2H), 5.01 (tt, *J* = 7.8, 6.4, 2.4 Hz, 1H), 4.18 (qt, *J* = 7.1, 1.3 Hz, 4H), 2.98 – 2.91 (m, 2H), 2.67 (d, *J* = 7.4 Hz, 2H), 2.32 – 2.26 (m, 2H), 1.69 (s, 3H), 1.63 (s, 3H), 1.33 (s, 9H), 1.24 (td, *J* = 7.1, 1.1 Hz, 6H); ^{13}**C NMR** (175 MHz; CDCl$_3$) δ 198.9, 171.5, 156.9, 135.8, 134.3, 128.2, 125.7, 117.7, 61.4, 57.2, 35.3, 33.9, 32.3, 31.2, 27.3, 26.2, 18.2, 14.2; **IR** (Neat) 2963, 1728, 1683, 1606, 1446, 1406, 1366, 1269, 1221, 1181, 1108, 1072, 1046, 1025, 982, 859, 844, 784. **HRMS**: calcd for $C_{25}H_{36}O_5Na^+$: 439.2455 found: 439.2457.



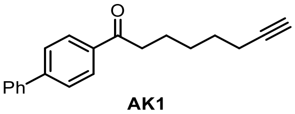
S44

diethyl 2-(3-(4-(*tert*-butyl)phenyl)-3-oxo-1-phenylpropyl)-2-(3-methylbut-2-en-1-yl)malonate (S44): General procedure G with **S44a** was employed and the reaction was run in toluene (1 mL). Purification by column chromatography eluting with hexanes/EtOAc provided 187 mg (38%) of **S44** as a clear oil. ^{1}**H NMR** (700 MHz; CDCl$_3$) δ 7.87 – 7.83 (m, 2H), 7.44 – 7.40 (m, 2H), 7.22 – 7.18 (m, 2H), 7.17 – 7.13 (m, 3H), 5.14 (tt, *J* = 6.5, 5.1, 1.9 Hz, 1H), 4.36 – 4.24 (m, 2H), 4.22 – 4.10 (m, 3H), 3.74 (dd, *J* = 17.5, 10.9 Hz, 1H), 3.64 (dd, *J* = 17.5, 2.4 Hz, 1H), 2.49 (dd, *J* = 15.2, 6.4 Hz, 1H), 2.31 (dd, *J* = 15.2, 7.8 Hz, 1H), 1.70 (s, 3H), 1.48 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.31 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (175 MHz; CDCl$_3$) δ 197.6, 171.2, 171.0, 156.6, 139.5, 135.0, 134.7, 129.4, 128.2, 128.1, 127.2, 125.5, 118.5, 61.8, 61.4, 61.4, 44.2, 42.3, 35.2, 33.2, 31.2, 26.3, 18.1, 14.3, 14.2; **IR** (Neat) 2964, 2906, 2872, 1724, 1684, 1604, 1454, 1406, 1365, 1294, 1270, 1220, 1177, 1108, 1074, 1054, 1023, 989, 859, 843, 826, 753, 701. **HRMS**: calcd for $C_{31}H_{41}O_5^+$: 493.2949 found: 493.2949.

General procedure (H): Alkylation/decarboxylation for the synthesis of terminal alkynes AK1-3

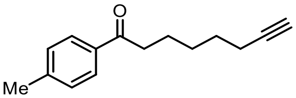


A flame dried round bottom flask equipped with a magnetic stir bar was charged with KI (1.2 eq), K_2CO_3 (2.0 eq), dry DMF (0.5 M), and staring β-keto ester (1.0 eq). 6-chlorohex-1-yne (1.2 eq) was added to the flask last and the resulting mixture was heated to 80°C overnight. The resulting reaction mixture was quenched with saturated ammonium chloride and was partitioned between ethyl acetate and water. The aqueous layer was further extracted with ethyl acetate (x2), and the combined organic layers was washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure to remove all volatiles to give the crude alkylated β-keto ester, which was used without further purification. A round bottom flask equipped with a magnetic stir bar was charged with EtOH:water (1:1, 0.2 M) and crude alkyl β-keto ester (1.0 eq). The reaction flask was charged with NaOH (4.0 eq) and fitted with a reflux condenser. The reaction was allowed to reflux until judged complete by TLC analysis. The resulting reaction mixture was partitioned between ethyl acetate and water. The aqueous layer was further extracted with ethyl acetate (x2), and the combined organic layer was washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure to remove all volatiles. The crude product was purified by column chromatography eluting with the indicated solvent to give the pure alkyne **AK1-3.**



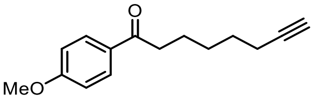
AK1

1-([1,1'-biphenyl]-4-yl)oct-7-yn-1-one (AK1): General procedure H was employed on 20.5 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 1.36 g (24% over two steps) of **AK1** as a white solid. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 8.5 Hz, 2H), 7.66 – 7.61 (m, 2H), 7.48 (t, J = 7.5 Hz, 2H), 7.40 (t, J= 7.3 Hz, 1H), 3.02 (t, J = 7.4 Hz, 2H), 2.23 (td, J = 7.0, 2.6 Hz, 2H), 1.95 (t, J = 2.6 Hz, 1H), 1.84 – 1.74 (m, 2H), 1.61 (dt, J = 13.9, 6.8 Hz, 2H), 1.56 – 1.48 (m, 2H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 200.0, 145.8, 140.1, 135.9, 129.1, 128.8, 128.3, 127.41, 127.38, 84.6, 68.5, 38.6, 28.6, 28.5, 24.0, 18.5; **IR** (Neat) 3295, 2936, 1671, 1602, 1560, 1485, 1466, 1448, 1402, 1336, 1269, 1235, 1193, 1183, 1159, 1084, 1039, 1022, 1006, 974, 844, 818, 766, 750, 734, 723, 688, 645, 632. **HRMS**: calcd for $C_{20}H_{21}O^+$: 277.1587 found: 277.1585.



AK2

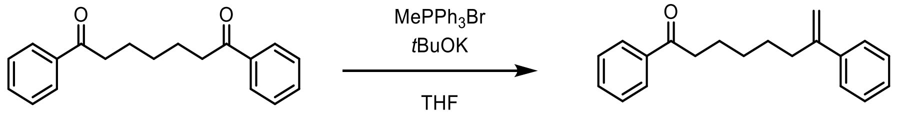
1-(*p*-tolyl)oct-7-yn-1-one (AK2): General procedure H was employed on 8.58 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 1.12 g (61% over two steps) of **AK2** as a white solid. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.86 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 6.8 Hz, 2H), 2.95 (t, J = 7.4 Hz, 2H), 2.41 (s, 3H), 2.21 (td, J = 6.9, 2.6 Hz, 2H), 1.94 (t, J = 2.6 Hz, 1H), 1.80 – 1.69 (m, 2H), 1.63 – 1.54 (m, 2H), 1.54 – 1.43 (m, 2H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 200.1, 143.8, 134.7, 129.4, 128.3, 84.6, 68.4, 38.5, 28.6, 28.5, 24.0, 21.8, 18.5; **IR** (Neat) 3260, 2940, 2853, 1670, 1604, 1573, 1462, 1406, 1376, 1363, 1336, 1300, 1287, 1235, 1199, 1181, 1120, 1086, 1057, 1041, 1011, 968, 936, 852, 841, 799, 763, 749, 727, 684. **HRMS**: calcd for $C_{15}H_{18}O^+$: 214.1358 found: 214.1362.



AK3

1-(4-methoxyphenyl)oct-7-yn-1-one (AK3): General procedure H was employed on 22.5 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 3.25 g (63% over two steps) of **AK3** as a white solid. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.94 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H), 2.93 (t, J = 7.4 Hz, 2H), 2.21 (td, J = 7.0, 2.6 Hz, 2H), 1.94 (t, J = 2.6 Hz, 1H), 1.79 – 1.70 (m, 2H), 1.63 – 1.54 (m, 2H), 1.54 – 1.45 (m, 2H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 199.0, 163.5, 130.4, 130.3, 113.8, 84.6, 68.4, 55.6, 38.2, 28.7, 28.5, 24.1, 18.5; **IR** (Neat) 3283, 3020, 2933, 2857, 1665, 1601, 1575, 1509, 1465, 1417, 1405, 1373, 1360, 1331, 1311, 1253, 1231, 1197, 1174, 1109, 1083, 1056, 1028, 1010, 972, 847, 826, 817, 753, 733, 717, 684, 652, 602. **HRMS**: calcd for $C_{15}H_{19}O_2^+$: 231.1380 found: 231.1379.

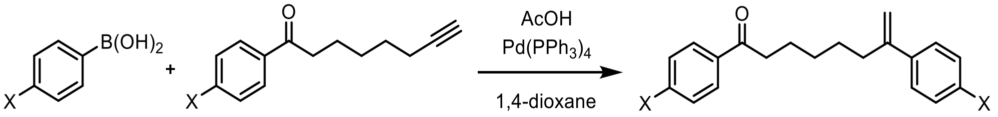
Wittig olefination for the synthesis of S49



S49

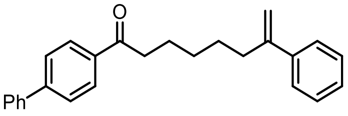
1,7-diphenyloct-7-en-1-one (S49): A flame dried round bottom flask equipped with a magnetic stir bar was charged with THF (12 mL) and methyltriphenylphosphonium bromide (828 mg, 2.32 mmol). The reaction flask was charged with *t*BuOK (240 mg, 2.14 mmol) and the resulting yellow mixture was allowed to stir for 30 minutes. The reaction flask was cooled to 0 °C and charged with 1,7-diphenylheptane-1,7-dione (500 mg, 1.78 mmol). The mixture was allowed to slowly warm to room temperature overnight. The resulting reaction mixture was quenched with saturated ammonium chloride and partitioned between ethyl acetate and water. The aqueous layer was further extracted with ethyl acetate (x2), and the combined organic layers were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 167 mg (34%) of **S49** as a white solid. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.94 (d, *J* = 7.3 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.40 (d, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.28 – 7.23 (m, 1H), 5.26 (s, 1H), 5.05 (d, *J* = 1.0 Hz, 1H), 2.94 (t, *J* = 7.4 Hz, 2H), 2.52 (t, *J* = 7.4 Hz, 2H), 1.80 – 1.68 (m, 2H), 1.51 (dt, *J* = 14.7, 7.2 Hz, 2H), 1.46 – 1.38 (m, 2H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 200.6, 148.7, 141.5, 137.2, 133.0, 128.7, 128.4, 128.2, 127.4, 126.3, 112.4, 38.7, 35.3, 29.1, 28.2, 24.3; **IR** (Neat) 3058, 2938, 2857, 1721, 1708, 1680, 1596, 1580, 1492, 1461, 1447, 1408, 1358, 1274, 1213, 1179, 1074, 1001, 970, 849, 754, 690. **HRMS**: calcd for $C_{20}H_{22}O$: 278.1671 found: 278.1668.

General Procedure (I): Alkyne hydroarylation for the synthesis of 1,1-disubstituted alkenes S48 & S50-53(*62*)



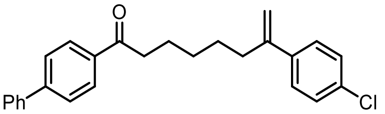
S48 & S50-53

A scintillation vial equipped with a magnetic stir bar was charged with 1,4-dioxane (0.3 M), aryl ketone (1.0 eq), boronic acid (1.2 eq), and Tetrakis(triphenylphosphine)palladium(0) (0.03 eq). Acetic acid (0.1 eq) was added to the vial last and the resulting mixture was heated to 80°C overnight. The resulting reaction mixture was partitioned between ethyl acetate and water. The aqueous layer was further extracted with ethyl acetate (x2), and the combined organic layer was washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure to remove all volatiles. The crude product was purified by column chromatography eluting with the indicated solvent to give the pure substrate **S48 & S50-53**.



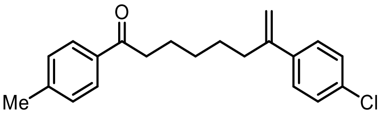
S48

1-([1,1'-biphenyl]-4-yl)-7-phenyloct-7-en-1-one (S48): General procedure I with **AK1** was employed on 1.09 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 232 mg (60%) of **S48** as a white solid. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 8.01 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.43 – 7.37 (m, 3H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.28 – 7.24 (m, 1H), 5.26 (s, 1H), 5.06 (s, 1H), 2.97 (t, *J* = 7.4 Hz, 2H), 2.53 (t, *J* = 7.4 Hz, 2H), 1.83 – 1.69 (m, 2H), 1.56 – 1.48 (m, 2H), 1.48 – 1.39 (m, 2H); **^{13}C NMR** (125 MHz; CDCl$_3$) δ 200.2, 148.6, 145.7, 141.5, 140.1, 135.9, 129.1, 128.8, 128.4, 128.3, 127.42, 127.40, 127.3, 126.3, 112.40, 38.7, 35.3, 29.1, 28.2, 24.3; **IR** (Neat) 3078, 3052, 2936, 2856, 1673, 1630, 1603, 1560, 1486, 1464, 1440, 1403, 1373, 1361, 1336, 1299, 1285, 1233, 1191, 1181, 1156, 1134, 1125, 1078, 1058, 1025, 1110, 1006, 974, 895, 850, 822, 774, 768, 756, 738, 726, 710, 690. **HRMS**: calcd for $C_{26}H_{27}O^+$: 355.2056 found: 355.2056.



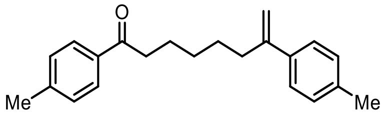
S50

1-([1,1'-biphenyl]-4-yl)-7-(4-chlorophenyl)oct-7-en-1-one (S50): General procedure I with **AK1** was employed on 1.09 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 253 mg (60%) of **S50** as a white solid. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 8.01 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.30 (dd, *J* = 21.4, 8.7 Hz, 4H), 5.25 (s, 1H), 5.07 (s, 1H), 2.97 (t, *J* = 7.3 Hz, 2H), 2.50 (t, *J* = 7.3 Hz, 2H), 1.82 – 1.69 (m, 2H), 1.50 (dt, *J* = 14.6, 7.4 Hz, 2H), 1.46 – 1.38 (m, 2H); **^{13}C NMR** (125 MHz; CDCl$_3$) δ 200.1, 147.5, 145.7, 140.1, 139.9, 135.9, 133.2, 129.1, 128.8, 128.5, 128.3, 127.6, 127.40, 127.36, 113.0, 38.7, 35.2, 29.1, 28.1, 24.3; **IR** (Neat) 2927, 2853, 1675, 1624, 1603, 1561, 1488, 1447, 1402, 1372, 1337, 1282, 1234, 1193, 1117, 1088, 1024, 1012, 1005, 973, 937, 909, 900, 856, 835, 821, 770, 763, 749, 735, 725, 689. **HRMS**: calcd for $C_{26}H_{26}ClO^+$: 389.1667 found: 389.1664.



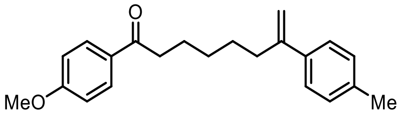
S51

7-(4-chlorophenyl)-1-(*p*-tolyl)oct-7-en-1-one (S51): General procedure I with **AK2** was employed on 1.40 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 249 mg (54%) of **S51** (4.5:1 mixture of alkene isomers) as a white solid. **^{1}H NMR** (for the mixture of isomers; 400 MHz; CDCl$_3$) δ 7.88 – 7.80 (m, 11H), 7.34 – 7.22 (m, 33H), 5.79 – 5.72 (m, 1H), 5.25 – 5.20 (m, 4.5H), 5.08 – 5.03 (m, 4.5H), 2.97 (t, *J* = 7.3 Hz, 2H), 2.91 (t, *J* = 7.4 Hz, 9H), 2.52 – 2.44 (m, 9H), 2.41 (s, 16.5H), 2.28 – 2.20 (m, 2H), 2.02 – 1.98 (m, 2H), 1.86 – 1.66 (m, 11H), 1.60 – 1.32 (m, 20H). **^{1}H NMR** (signals corresponding to the major isomer; 400 MHz; $CDCl_3$) δ 5.25 – 5.20 (m, 1H), 5.08 – 5.03 (m, 1H), 2.91 (t, *J* = 7.4 Hz, 2H), 2.52 – 2.44 (m, 2H); **^{13}C NMR** (for the mixture of isomers; 175 MHz; $CDCl_3$) δ 200.2, 147.5, 143.8, 139.8, 134.7, 133.2, 129.4, 128.5, 128.32, 128.31, 128.29, 127.6, 127.0, 112.9, 38.5, 35.2, 29.4, 29.0, 28.8, 28.1, 24.32, 24.28, 21.8; **IR** (Neat) 2933, 2863, 1673, 1606, 1492, 1407, 1373, 1353, 1259, 1227, 1193, 1181, 1093, 1011, 972, 892, 835, 803. **HRMS**: calcd for $C_{21}H_{23}ClO^+$: 326.1437 found: 326.1436.



S52

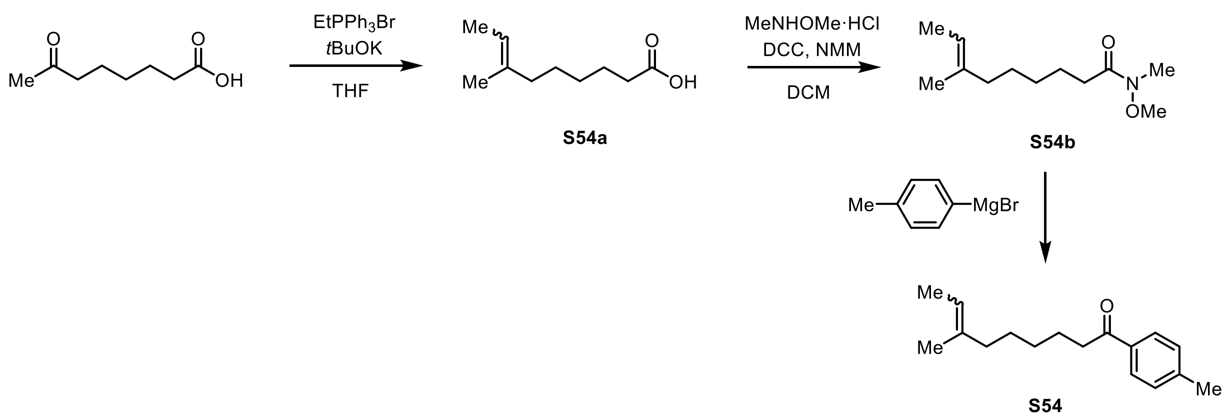
1,7-di-*p*-tolyloct-7-en-1-one (S52): General procedure I with **AK2** was employed on 1.40 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 313 mg (73%) of **S52** as a white solid. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 5.23 (d, *J* = 1.3 Hz, 1H), 5.00 (d, *J* = 1.2 Hz, 1H), 2.93 – 2.88 (m, 2H), 2.50 (t, *J* = 7.5 Hz, 2H), 2.41 (s, 3H), 2.34 (s, 3H), 1.72 (dt, *J* = 15.1, 7.5 Hz, 2H), 1.49 (dt, *J* = 15.2, 7.4 Hz, 2H), 1.43 – 1.38 (m, 2H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 200.3, 148.4, 143.7, 138.5, 137.1, 134.7, 129.4, 129.1, 128.3, 126.1, 111.6, 38.6, 35.3, 29.2, 28.2, 24.4, 21.8, 21.3; **IR** (Neat) 2933, 2858, 1673, 1606, 1574, 1514, 1464, 1406, 1373, 1354, 1302, 1287, 1262, 1226, 1192, 1182, 1126, 1104, 1035, 1017, 971, 889, 880, 846, 834, 823, 802, 759, 734, 727. **HRMS**: calcd for $C_{22}H_{26}ONa^+$: 329.1876 found: 329.1876.



S53

1-(4-methoxyphenyl)-7-(*p*-tolyl)oct-7-en-1-one (S53): General procedure I with **AK3** was employed on 2.17 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 502 mg (72%) of **S53** as a white solid. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.92 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 5.23 (s, 1H), 5.00 (s, 1H), 3.87 (s, 3H), 2.88 (t, *J* = 7.4 Hz, 2H), 2.50 (t, *J* = 7.4 Hz, 2H), 2.34 (s, 3H), 1.75 – 1.68 (m, 2H), 1.50 (dt, *J* = 14.9, 7.3 Hz, 2H), 1.45 – 1.36 (m, 2H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 199.3, 163.5, 148.4, 138.5, 137.1, 130.5, 130.3, 129.1, 126.1, 113.8, 111.6, 55.6, 38.4, 35.3, 29.2, 28.2, 24.5, 21.2; **IR** (Neat) 2932, 1670, 1598, 1509, 1462, 1405, 1373, 1349, 1318, 1306, 1255, 1230, 1197, 1170, 1113, 1024, 977, 897, 851, 823, 812, 757, 736, 715. **HRMS**: calcd for $C_{22}H_{27}O_2^+$: 323.2006 found: 323.2001.

3 step sequence for the synthesis of substrate S54

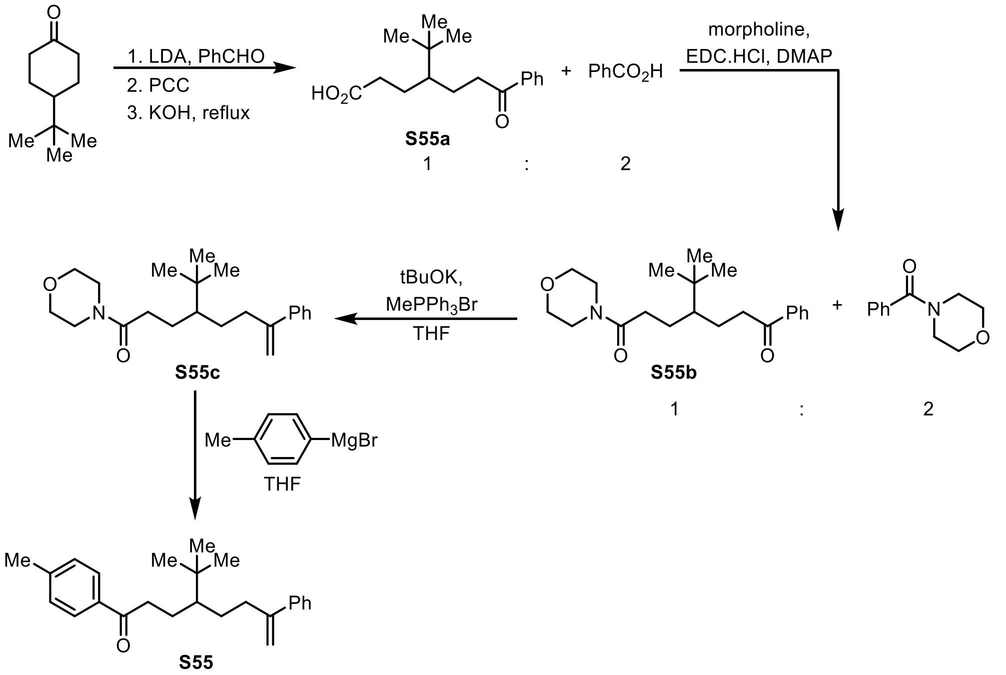


(*Z*)-7-methylnon-7-enoic acid (S54a): A flame-dried round bottom flask equipped with a magnetic stir bar was charged with THF (31 mL) and ethyltriphenylphosphonium bromide (2.93 g, 7.95 mmol). The reaction flask was cooled to 0 °C and was charged with *t*BuOK (1.79 g, 15.9 mmol). The resulting mixture was allowed to stir for 30 minutes at room temperature. The reaction flask was cooled to 0 °C and charged with 7-oxooctanoic acid (968 mg, 6.12 mmol). The mixture was allowed to slowly warm to room temperature overnight. The resulting reaction mixture was quenched with 1 M NaOH and partitioned between ether and water. The aqueous layer was acidified using concentrated HCl at 0 °C until the pH of the solution reached 1. The aqueous layer was extracted with ethyl acetate (x3), and the combined organic layers were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 360 mg (35%) of **S54a** (2.3:1 mixture of E/Z isomers, major isomer shown) as a clear oil. ^{1}**H NMR** (for the mixture of isomers; 700 MHz; CDCl3) δ 5.23 – 5.17 (m, 3.3H), 2.36 (dd, *J* = 14.4, 7.0 Hz, 6.6H), 2.04 – 2.01 (m, 4.6H), 1.97 (t, *J* = 7.6 Hz, 2H), 1.67 – 1.63 (m, 13.2H), 1.59 – 1.54 (m, 13.2H), 1.44 – 1.28 (m, 13.2H); ^{1}**H NMR** (signals corresponding to the major isomer; 700 MHz; CDCl3) δ 2.04 – 2.01 (m, 2H); ^{13}**C NMR** (for the mixture of isomers; 175 MHz; $CDCl_3$) δ 179.7, 136.1, 135.8, 119.2, 118.5, 39.5, 34.1, 31.3, 29.1, 28.8, 27.7, 27.5, 24.8, 24.7, 23.5, 15.7, 13.5, 13.4; **IR** (Neat) 2925, 2857, 1705, 1460, 1412, 1375, 1279, 1229, 1140, 1101, 1062, 1027, 934, 814, 728. **HRMS**: calcd for $C_{10}H_{18}O_2^+$: 170.1307 found: 170.1311.

(*Z*)-*N*-methoxy-*N*,7-dimethylnon-7-enamide (S54b): A flame-dried round bottom flask equipped with a magnetic stir bar was charged with DCM (7 mL) and **S54a** (360 mg, 2.11 mmol). The reaction flask was cooled to 0 °C and was charged with *N,O*-dimethylhydroxylamine hydrochloride (227 mg, 2.33 mmol) and NMM (0.26 mL, 2.33 mmol). DCC (611 mg, 2.96 mmol) was added to the flask last and the resulting mixture was allowed to slowly warm to room temperature overnight. The resulting reaction mixture was filtered through a pad of celite, eluting with DCM. The organic layer was washed with 1 M HCl and saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 367 mg (81%) of **S54b** (2.3:1 mixture of E/Z isomers, major isomer shown) as a clear oil. ^{1}**H NMR** (for the mixture of isomers; 400 MHz; CDCl3) δ 5.27 – 5.12 (m, 1H), 3.68 (s, 3H), 3.18 (s, 3H), 2.42 (t, *J* = 7.3 Hz, 2H), 2.07 – 1.90 (m, 2H), 1.71 – 1.52 (m, 8H), 1.47 – 1.24 (m, 4H); ^{13}**C NMR** (for the mixture of isomers; 125 MHz; $CDCl_3$) δ 174.8, 136.3, 136.0, 119.0, 118.3, 61.3, 39.6, 32.5, 32.1, 31.4, 29.6, 29.3, 27.9, 27.7, 24.8, 24.7, 23.4, 15.7, 13.4, 13.3; **IR** (Neat) 2930, 2857, 1662, 1441, 1411, 1381, 1174, 1151, 1114, 1101, 999, 813, 744, 718. **HRMS**: calcd for $C_{12}H_{24}O_2^+$: 214.1802 found: 214.1803.

(*Z*)-7-methyl-1-(*p*-tolyl)non-7-en-1-one (S54): A flame-dried round bottom flask equipped with a magnetic stir bar was charged with activated magnesium (51 mg, 2.11 mmol). Dry THF (4 mL) was then added, followed by 4-bromotoluene (0.303 mL, 2.46 mmol). The resulting mixture was stirred until the activated magnesium dissolved. The reaction flask was then cooled to 0 °C, and **S54b** (150 mg, 0.703 mmol) dissolved in THF (5 mL) was added dropwise and stirred until judged complete by TLC analysis. The resulting reaction mixture was quenched with saturated ammonium chloride, and then partitioned between ethyl acetate and water. The aqueous layer was further extracted with ethyl acetate (x2) and the combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 112 mg (65%) of **S54** (2.4:1 mixture of E/Z isomers, major isomer shown) as a clear oil. ^{1}**H NMR** (for the mixture of isomers; 700 MHz; $CDCl_3$) δ 7.88 – 7.84 (m, 6.8H), 7.27 – 7.23 (m, 6.8H), 5.22 – 5.17 (m, 3.4H), 2.96 – 2.90 (m, 6.8H), 2.41 (s, 10.2H), 2.03 (t, *J* = 7.5 Hz, 4.8H), 1.98 (t, *J* = 7.6 Hz, 2H), 1.78 – 1.69 (m, 6.8H), 1.67 – 1.65 (m, 7.2H), 1.59 – 1.53 (m, 13.2H), 1.47 – 1.31 (m, 13.6H). ^{1}**H NMR** (signals corresponding to the major isomer; 700 MHz; $CDCl_3$) δ 2.03 (t, *J* = 7.5 Hz, 2H), 1.67 – 1.65 (m, 3H); ^{13}**C NMR** (for the mixture of isomers; 125 MHz; $CDCl_3$) δ 200.4, 200.3, 143.7, 136.3, 136.0, 134.8, 129.4, 128.3, 119.0, 118.4, 39.6, 38.68, 38.65, 31.4, 29.5, 29.2, 27.9, 27.8, 24.63, 24.56, 23.5, 21.8, 15.7, 13.5, 13.4; **IR** (Neat) 2925, 2855, 1681, 1606, 1446, 1407, 1373, 1271, 1224, 1205, 1178, 1135, 1128, 1110, 967, 806. **HRMS**: calcd for $C_{17}H_{25}O^+$: 245.1900 found: 245.1900.

6 step sequence for the synthesis of substrate S55



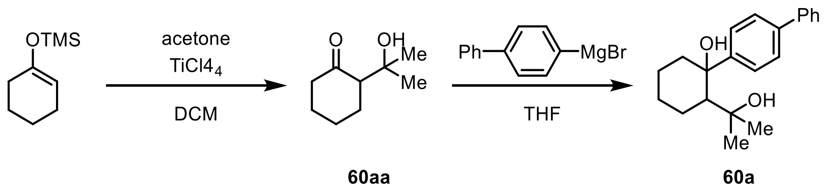
4-(tert-butyl)-7-oxo-7-phenylheptanoic acid (S55a): A flame dried round bottom flask equipped with a magnetic stir bar was charged with DIPA (4.72 mL, 33.7 mmol) and THF (75 mL). The solution was cooled to 0 ˚C, n-Butyllithium (13.5 mL, 33.7 mmol) was added dropwise, and the solution was stirred for 15 minutes. Then, the reaction was cooled to -78 ˚C and a solution of 4-tert-butylcyclohexanone (4 g, 25.9 mmol) in THF (25 mL) was added and the mixture was allowed to stir for 30 minutes before a solution of benzaldehyde (3.44 mL, 33.7 mmol) in THF (25 mL) was added. The resulting mixture was allowed to stir at -78˚C until judged complete by TLC. The reaction was quenched with saturated ammonium chloride, warmed to room temperature, and partitioned between water and ethyl acetate. The layers were separated, and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure to give a crude product that was used without further purification. A suspension of the crude aldol product and celite (24 g) in DCM (125 mL) was charged with PCC (8.39 g, 38.9 mmol). The mixture was allowed to stir overnight at room temperature. The next day, the mixture was filtered over a short pad of silica gel using DCM as the eluent. Concentration of the filtrate under reduced pressure gave a crude product that was contaminated with benzaldehyde, which was removed by heating at 80˚C under vacuum (~1 torr). The resulting yellow solid was then directly used in the next step without further purification. A solution of KOH (2.57 g, 38.9 mmol) in water (60 mL) was added to the crude 1,3-diketone and the suspension was heated to reflux. The mixture was allowed to stir at reflux until the reaction was judged complete by TLC (the mixture had become nearly homogeneous). After cooling to room temperature, the aqueous layer was extracted with ether (x2). The combined organic extracts were extracted with 1M NaOH and then discarded. The combined aqueous layers was cooled to 0˚C and neutralized with concentrated HCl to pH ~1. Ethyl acetate was added, the layers were separated, and the aqueous layer was further extracted with ethyl acetate. The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure provided 2.5 g (56% over 3 steps) of a yellow solid. ^{1}HNMR was used to determine that the crude material contained a 1:2 (molar ratio) mixture of **S55a** and benzoic acid as the two retro-Claisen products. This mixture was used in the next step without further purification. **^{1}H NMR** (signals corresponding to **S55a**; 400 MHz; $CDCl_3$) δ 8.00 – 7.93 (m, 2H), 7.59 – 7.52 (m, 1H), 3.11 (ddd, *J* = 16.0, 10.2, 5.4 Hz, 1H), 2.99 (ddd, *J* = 16.6, 10.0, 5.8 Hz, 1H), 2.57 – 2.37 (m, 2H), 2.03 – 1.85 (m, 2H), 1.58 – 1.42 (m, 2H), 1.08 (tt, *J* = 7.5, 3.8 Hz, 1H), 0.93 (s, 9H).

4-(tert-butyl)-1-morpholino-7-phenylheptane-1,7-dione (S55b): A flame dried round bottom flask equipped with a magnetic stir bar was charged with the crude acid mixture (2.5g, 14.4 mmol), DCM (100 mL), DMAP (352 mg, 2.88 mmol), and morpholine (1.68 mL, 19.2 mmol). The resulting mixture was cooled to 0 ˚C and EDC.HCl (3.68 g, 19.2 mmol) was added. After warming to room temperature overnight and completion was observed as judged by TLC, the reaction was quenched w/ 10% HCl. The layers were separated and the aqueous layer was further extracted with DCM (x2). The combined organics were washed with saturated sodium bicarbonate, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography using DCM/EtOAc as the eluent provided 2.25 g (65%) of a 1:2 (molar ratio) mixture of **S55b** and morpholino(phenyl)methanone as a yellow oil. The purity of the material was measured to be 42 wt. % by ^{1}HNMR using dimethyl terephthalate as an internal standard. This material was used directly in the next step without further purification. **^{1}H NMR** (signals corresponding to **S55b**; 400 MHz; $CDCl_3$) δ 7.98 – 7.93 (m, 2H), 7.59 – 7.54 (m, 1H), 7.50 – 7.44 (m, 2H), 3.13 – 2.93 (m, 2H), 2.42 (ddd, *J* = 15.7, 10.4, 5.5 Hz, 1H), 2.30 (ddd, *J* = 15.5, 10.1, 6.0 Hz, 1H), 2.00 – 1.81 (m, 2H), 1.12 – 1.03 (m, 1H), 0.92 (s, 9H).

4-(tert-butyl)-1-morpholino-7-phenyloct-7-en-1-one (S55c): A flame dried round bottom flask equipped with a magnetic stir bar was charged with methyltriphenylphosphonium bromide (2.89 g, 8.1 mmol) and THF (20 mL). The resulting suspension was cooled to 0 °C and tBuOK (909 mg, 8.1 mmol) was added. After stirring for 0.5h, a solution of the amide mixture (2.25 g) in THF (10 mL) was added. The mixture was allowed to warm to room temperature and stir until judged complete by TLC. The reaction was quenched with saturated ammonium chloride and partitioned between water and ethyl acetate. The layers were separated and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography using hexanes/EtOAc as the eluent provided 876 mg (94%) of **S55c** as a clear oil that contained an unidentified impurity. The purity of the material was measured to be 85 wt. % by ^{1}HNMR using dimethyl terephthalate as an internal standard. This material was used directly in the next step without further purification. **^{1}H NMR** (signals corresponding to **S55c**; 700 MHz; $CDCl_3$) δ 7.40 (dt, *J* = 8.1, 1.2 Hz, 2H), 7.35 – 7.30 (m, 2H), 5.27 (s, 1H), 5.06 (s, 1H), 3.68 – 3.57 (m, 6H), 3.34 (t, *J* = 4.8 Hz, 2H), 2.57 (ddd, *J* = 15.6, 10.3, 5.7 Hz, 1H), 2.50 (ddd, *J* = 15.0, 10.1, 6.1 Hz, 1H), 2.28 (ddd, *J* = 16.0, 11.3, 5.1 Hz, 1H), 2.19 (ddd, *J* = 14.8, 11.1, 5.5 Hz, 1H), 1.87 – 1.80 (m, 1H), 1.23 – 1.16 (m, 1H), 1.02 (tt, *J* = 7.3, 3.5 Hz, 1H), 0.86 (s, 9H).

4-(tert-butyl)-7-phenyl-1-(p-tolyl)oct-7-en-1-one (S55): A flame dried round bottom flask equipped with a magnetic stir bar was charged with freshly ground Mg (66 mg, 7.72 mmol), THF (6 mL) and 4-bromotoluene (0.41 mL, 3.34 mmol). The mixture was allowed to stir at room temperature until all of the magnesium dissolved. Then, the aryl Grignard solution was cooled to 0°C and a solution of **S55c** (500 mg, 1.24 mmol) in THF (6 mL) was added dropwise. The mixture was initially stirred at 0°C for 1.5 h, followed by warming to room temperature and continued stirring until completion as judged by TLC. The reaction was quenched with saturated ammonium chloride and partitioned between water and ethyl acetate. The layers were separated and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography provided 193 mg (45%) of **S55** as a clear oil. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.81 (d, *J* = 8.1 Hz, 2H), 7.42 – 7.38 (m, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.28 – 7.23 (m, 3H), 5.26 (s, 1H), 5.06 (s, 1H), 2.95 (ddd, *J* = 16.0, 10.5, 5.3 Hz, 1H), 2.87 (ddd, *J* = 16.3, 10.3, 5.8 Hz, 1H), 2.60 (ddd, *J* = 15.4, 10.6, 5.4 Hz, 1H), 2.51 (ddt, *J* = 15.0, 10.2, 4.9 Hz, 1H), 2.42 (s, 3H), 2.00 – 1.88 (m, 1H), 1.66 (ddq, *J* = 14.0, 5.9, 3.7 Hz, 1H), 1.51 – 1.40 (m, 1H), 1.32 – 1.19 (m, 1H), 1.08 (tt, *J* = 7.3, 3.6 Hz, 1H), 0.87 (s, 9H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 200.4, 149.1, 143.8, 141.4, 134.7, 129.4, 128.5, 128.3, 127.5, 126.3, 112.5, 48.1, 38.7, 35.9, 34.3, 30.2, 27.9, 26.1, 21.8; **IR** (Neat) 3080, 3056, 3030, 2959, 2868, 1683, 1625, 1607, 1475, 1180, 894, 778. **HRMS**: calcd for $C_{25}H_{32}ONa^+$: 371.2345 found: 371.2346.

2 step sequence for the synthesis of diol 60a

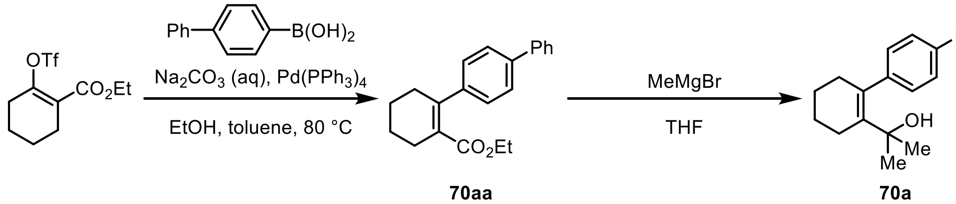


60aa **60a**

2-(2-hydroxypropan-2-yl)cyclohexan-1-one (60aa): A flame dried round bottom flask equipped with a magnetic stir bar was charged with acetone (1.6 mL, 21.1 mmol) and DCM (40 mL). The mixture was cooled to -78˚C and a $TiCl_4$-(2.1 mL, 19.4 mmol was added. Then, a solution of 1-(trimethylsiloxy)cyclohexene (3 g, 17.6 mmol) in DCM (30 mL) was added dropwise. The reaction was allowed to stir at -78˚C until judged complete by TLC. The reaction was quenched by the addition of water. After warming to room temperature, the layers of the biphasic mixture were separated and the aqueous layer was further extracted with DCM (x2). The combined organics were washed with saturated sodium bicarbonate, dried over Na_2SO_4, and concentrated to give 2.17 g (79%) of **60aa** as a light pink oil that was used without further purification.

1-([1,1'-biphenyl]-4-yl)-2-(2-hydroxypropan-2-yl)cyclohexan-1-ol (60a): A flame dried round bottom flask equipped with a magnetic stir bar was charged with 4-bromobiphenyl (8.1 g, 35 mmol), freshly ground Mg (1.69 g, 69.5 mmol) and THF (35 mL). The mixture was allowed to stir at room temperature for 1 h. Then, a solution of **60aa** (2.17 g, 13.9 mmol) in THF (35 mL) was cooled to 0˚C and the solution of aryl Grignard reagent was added via canula. The mixture is allowed to warm to room temperature and stirred until judged complete by TLC. The reaction is quenched with saturated ammonium chloride and partitioned between ethyl acetate and water. The layers were separated and the aqueous layer is further extracted with ethyl acetate (x2). The combined organics are washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 351 mg (8%) of **60a** as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.63 – 7.59 (m, 2H), 7.56 – 7.52 (m, 2H), 7.50 – 7.46 (m, 2H), 7.45 – 7.41 (m, 2H), 7.35 – 7.31 (m, 1H), 2.64 (dt, *J* = 15.0, 5.3 Hz, 1H), 2.25 – 2.18 (m, 1H), 2.05 (s, 1H), 1.95 (ddd, *J* = 14.1, 9.6, 4.7 Hz, 1H), 1.85 – 1.80 (m, 1H), 1.79 – 1.70 (m, 5H), 1.67 – 1.59 (m, 1H), 1.57 – 1.48 (m, 4H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 148.4, 141.1, 139.1, 136.6, 130.1, 128.8, 127.2, 127.1, 126.8, 125.8, 77.3, 41.2, 26.7, 23.0, 22.1, 21.6, 18.0; **IR** (Neat) 3593, 3478, 3055, 3028, 2934, 2864, 1600, 1485, 1448, 1399, 1180, 1077, 1007, 969. **HRMS**: calcd for $C_{21}H_{26}O_2Na^+$: 333.1825 found: 333.1845.

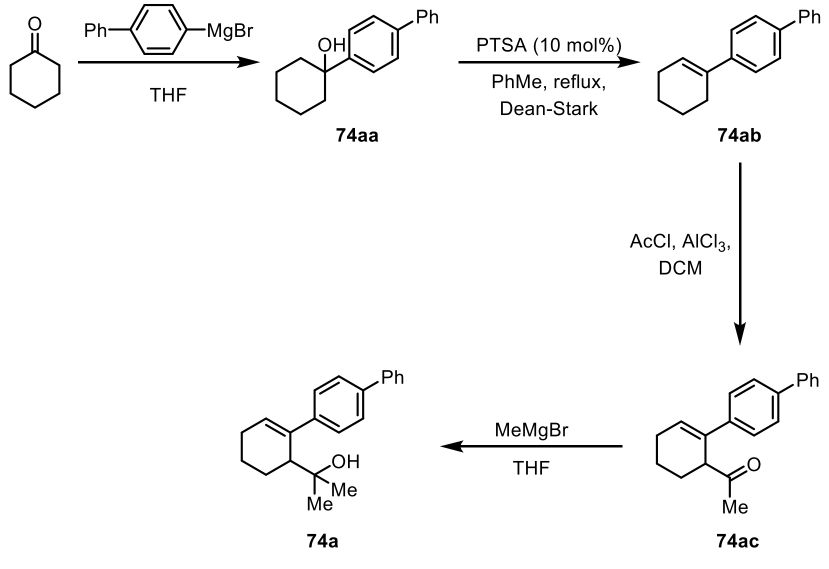
2 step sequence for the synthesis of tetrasubstituted olefin 70a



ethyl 3,4,5,6-tetrahydro-[1,1':4',1''-terphenyl]-2-carboxylate (70aa): A flame dried round bottom flask equipped with a magnetic stir bar was charged with ethyl 2-(((trifluoromethyl)sulfonyl)oxy)cyclohex-1-ene-1-carboxylate (1.39 g, 4.59 mmol), toluene (18 mL), 4-biphenylboronic acid (1 g, 5.05 mmol), aqueous sodium carbonate (6 mL, 12 mmol, 2M), $Pd(PPh_3)_4$ (265 mg, 0.23 mmol), and ethanol (6 mL). The mixture was sparged with N_2 for 5 minutes at room temperature, heated to 80 ˚C, and stirred until judged complete by TLC. The reaction was quenched with saturated ammonium chloride and partitioned between water and ethyl acetate. The layers were separated, and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 758 mg (49%) of **70aa** as a white solid. ^{1}**H NMR** (500 MHz; CDCl$_3$) δ 7.60 (d, *J* = 7.1 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 3.90 (q, *J* = 7.1 Hz, 2H), 2.44 (qd, *J* = 8.4, 6.9, 2.5 Hz, 4H), 1.77 (ttq, *J* = 8.0, 5.5, 2.9, 2.5 Hz, 4H), 0.86 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (125 MHz; CDCl$_3$) δ 170.2, 145.2, 142.7, 141.0, 140.0, 128.9, 128.4, 127.5, 127.4, 127.2, 126.8, 60.3, 32.7, 26.8, 22.7, 22.1, 13.7; **IR** (Neat) 3028, 2979, 2933, 2858, 1703, 1486, 1370, 1283, 1243, 1225, 1137, 1050, 837, 765. **HRMS**: calcd for $C_{21}H_{22}O_2Na^+$: 329.1512 found: 329.1514.

2-(3,4,5,6-tetrahydro-[1,1':4',1''-terphenyl]-2-yl)propan-2-ol (70a): A flame dried round bottom flask equipped with a magnetic stir bar was charged with **70aa** (500 mg, 1.63 mmol) and THF (8 mL). The solution was cooled to 0˚C and MeMgBr (1.6 mL, 4.90 mmol, 3M in ether) was added. The reaction was allowed to warm to room temperature overnight. After being judged complete by TLC, the reaction was quenched with saturated ammonium chloride and partitioned between water and ethyl acetate. The layers were separated and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 308 mg (65%) of **70a** as a white solid. ^{1}**H NMR** (700 MHz; CDCl$_3$) δ 7.60 – 7.57 (m, 2H), 7.57 – 7.54 (m, 2H), 7.45 – 7.41 (m, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.24 – 7.22 (m, 2H), 2.24 – 2.13 (m, 4H), 1.72 – 1.66 (m, 4H), 1.47 (s, 1H), 1.29 (s, 6H); ^{13}**C NMR** (175 MHz; CDCl$_3$) δ 145.0, 141.0, 139.4, 139.3, 131.7, 128.9, 128.7, 127.33, 127.30, 127.2, 75.2, 36.2, 30.6, 27.7, 23.5, 23.4; **IR** (Neat) 3588, 3453, 3026, 2972, 2928, 2857, 1485, 1447, 1360, 1173, 1147, 1109, 939, 835. **HRMS**: calcd for $C_{21}H_{24}ONa^+$: 315.1719 found: 315.1711.

4 step sequence for the synthesis of trisubstituted olefin 74a



1-([1,1'-biphenyl]-4-yl)cyclohexan-1-ol (74aa): A flame dried round bottom flask equipped with a magnetic stir bar was charged with freshly ground Mg (706 mg, 29.0 mmol), 4-bromobiphenyl (9.03 g, 38.7 mmol) and THF (35 mL). The mixture was allowed to stir at room temperature until all of the magnesium dissolved. In a separate round bottom flask, a solution of cyclohexanone (2 mL, 19.4 mmol) in THF (35 mL) was cooled to 0˚C, and the aryl Grignard solution was added via canula. The resulting mixture was allowed to warm to room temperature and stirred until judged complete by TLC. The reaction was quenched with ammonium chloride and portioned between ethyl acetate and water. The layers were separated and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was used without further purification.

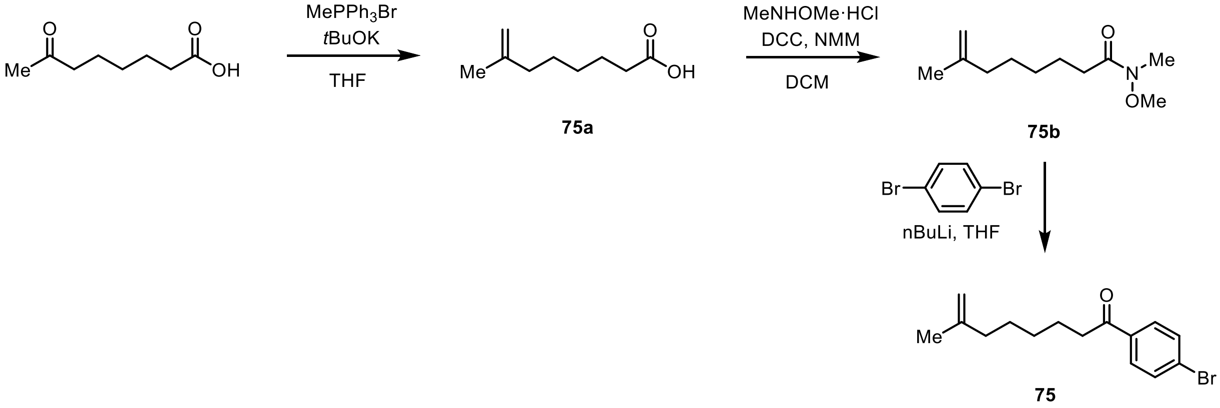
2,3,4,5-tetrahydro-1,1':4',1''-terphenyl (74ab): A flame dried round bottom flask equipped with a magnetic stir bar was charged with **74aa** (19.4 mmol), PTSA (368 mg, 1.94 mmol) and toluene (70 mL). The reaction was attached to a Dean-Stark apparatus, heated to reflux, and allowed to stir until judged complete by TLC. After cooling to room temperature, the reaction was quenched with saturated sodium bicarbonate and partitioned between water and ethyl acetate. The layers were separated and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was used without further purification.

1-(2,3,4,5-tetrahydro-[1,1':4',1''-terphenyl]-2-yl)ethan-1-one (74ac): A flame dried round bottom flask equipped with a magnetic stir bar was charged with aluminum chloride (2.58 g, 19.4 mmol) and dry DCM (100 mL). The mixture was cooled to 0˚C before acetyl chloride (1.4 mL, 19.4 mmol) was added. After stirring for 10 minutes at 0˚C, a solution of **74ab** (19.4 mmol) in dry DCM (100 mL) was added via cannula. The mixture was allowed to stir at 0˚C until judged complete by TLC. The reaction was quenched with ice water. The layers were separated after warming to room temperature and the aqueous layer was further extracted with DCM (x2). The combined organics were washed with saturated sodium bicarbonate, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided **74ac** as a yellow solid. Further purification via recrystallization from hexanes provided 720 mg (14% over 3 steps) of **74ac** as an off-white solid. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.60 – 7.56 (m, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.38 – 7.31 (m, 3H), 6.34 – 6.30 (m, 1H), 3.83 – 3.75 (m, 1H), 2.36 – 2.24 (m, 2H), 2.07 – 1.92 (m, 5H), 1.78 – 1.64 (m, 2H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 211.1, 140.8, 140.8, 139.8, 134.9, 128.9, 128.9, 127.4, 127.3, 127.1, 126.0, 51.8, 28.2, 26.5, 25.9, 19.6; **IR** (Neat) 3032, 2934, 2862, 2829, 1701, 1487, 1448, 1352, 1163, 1150, 1004, 845, 764. **HRMS**: calcd for $C_{20}H_{20}ONa^+$: 299.1406 found: 299.1409.

2-(2,3,4,5-tetrahydro-[1,1':4',1''-terphenyl]-2-yl)propan-2-ol (74a): A flame dried round bottom flask equipped with a magnetic stir bar was charged with **74ac** (200 mg, 0.724 mmol) and THF (7 mL). The solution was cooled to 0˚C, and MeMgBr (0.6 mL, 1.81 mmol, 3M in ether) was added. The reaction was allowed to warm to room temperature overnight. After being judged complete by TLC, the reaction was quenched with saturated ammonium chloride and partitioned between water and ethyl acetate. The layers were separated and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 83 mg (39%) of **74a** as a white solid. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.61 – 7.57 (m, 2H), 7.57 – 7.53 (m, 2H), 7.45 – 7.41 (m, 2H), 7.40 – 7.36 (m, 2H), 7.35 – 7.32 (m, 1H), 6.03 (t, *J* = 4.1 Hz, 1H), 3.00 (t, *J* = 5.6 Hz, 1H), 2.29 – 2.14

(m, 2H), 1.95 – 1.80 (m, 3H), 1.63 – 1.57 (m, 1H), 1.18 (s, 3H), 1.11 (s, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 144.5, 140.9, 139.6, 139.4, 131.9, 128.9, 127.32, 127.30 (two carbons as observed by HSQC), 127.1, 74.7, 46.7, 30.1, 27.7, 26.3, 25.9, 19.7; **IR** (Neat) 3579. 3449, 3027, 2967, 2931, 1600, 1486, 1383, 1369, 1165, 1139, 1076, 1006, 933, 843. **HRMS**: calcd for $C_{21}H_{24}ONa^+$: 315.1719 found: 315.1707.

3 step sequence for the synthesis of substrate 75



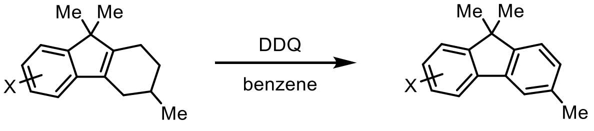
7-methyloct-7-enoic acid (75a): A flame dried round bottom flask equipped with a magnetic stir bar was charged with THF (32 mL) and methyltriphenylphosphonium bromide (2.94 g, 8.22 mmol). The reaction flask was cooled to 0 °C and was charged with tBuOK (1.84 g, 16.4 mmol). The resulting mixture was allowed to stir for 30 minutes at room temperature. The reaction flask was cooled to 0 °C and charged with 7-oxooctanoic acid (1.0 g, 6.32 mmol). The mixture was allowed to slowly warm to room temperature overnight. The resulting reaction mixture was quenched with 1 M NaOH and partitioned between ether and water. The aqueous layer was acidified using concentrated HCl at 0 °C until the pH of the solution reached 1. The aqueous layer was extracted with ethyl acetate (x3). The combined organic layers were washed with saturated sodium chloride, dried over Na$_2$SO$_4$, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 250 mg (25%) of **75a** as a clear oil. **^{1}H NMR** (400 MHz; CDCl$_3$) δ 10.99 (br s, 1H), 4.72 – 4.68 (m, 1H), 4.68 – 4.64 (m, 1H), 2.36 (t, J = 7.5 Hz, 2H), 2.01 (t, J = 7.5 Hz, 2H), 1.74 – 1.60 (m, 5H), 1.51 – 1.40 (m, 2H), 1.39 – 1.29 (m, 2H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 179.5, 146.0, 110.0, 37.7, 34.0, 28.8, 27.3, 24.7, 22.5; **IR** (Neat) 3073, 2932, 2859, 1705, 1649, 1412, 1282, 1223, 934, 884, 730. **HRMS**: calcd for $C_9H_{15}O_2^-$: 155.1078 found: 155.1072.

***N*-methoxy-*N*,7-dimethyloct-7-enamide (75b):** A flame dried round bottom flask equipped with a magnetic stir bar was charged with DCM (5 mL) and **75a** (225 mg, 1.44 mmol). The reaction flask was cooled to 0 °C and was charged with N,O-dimethylhydroxylamine hydrochloride (155 mg, 1.58 mmol) and NMM (0.17 mL, 1.58 mmol). DCC (416 mg, 2.02 mmol) was added to the flask last and the resulting mixture was allowed to slowly warm to room temperature overnight. The resulting reaction mixture was filtered through a pad of celite, eluting with DCM. The organic layer was washed with 1 M HCl and saturated sodium chloride, dried over Na$_2$SO$_4$, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 248 mg (86%) of **75b** as a clear oil. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 4.72

– 4.63 (m, 2H), 3.68 (s, 3H), 3.18 (s, 3H), 2.42 (t, *J* = 7.7 Hz, 2H), 2.01 (t, *J* = 7.6 Hz, 2H), 1.71 (s, 3H), 1.65 (p, *J* = 7.7 Hz, 2H), 1.46 (p, *J* = 7.5 Hz, 2H), 1.38 – 1.30 (m, 2H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 174.8, 146.1, 109.8, 61.3, 37.7, 32.2, 31.9, 29.1, 27.5, 24.6, 22.4; **IR** (Neat) 3073, 2933, 2857, 1664, 1443, 1413, 1383, 1176, 1151, 1109, 996, 884. **HRMS**: calcd for $C_{11}H_{22}NO_2^+$: 200.1645 found: 200.1645.

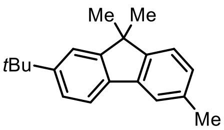
1-(4-bromophenyl)-7-methyloct-7-en-1-one (75): A flame dried round bottom flask equipped with a magnetic stir bar was charged with dry THF (1 mL) and 1,4-dibromobenzene (273 mg, 1.16 mmol). The reaction flask was cooled to -78 °C and was charged with n-BuLi (0.46 mL, 1.16 mmol, 2.5 M). The resulting reaction mixture was stirred at -78 °C for 30 minutes followed by addition of **75b** (210 mg, 1.05 mmol). The reaction was kept at -78 °C for an additional 15 minutes before being quenched with saturated ammonium chloride. The aqueous layer was extracted with ethyl acetate (x3), and the combined organic layers were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 209 mg (67%) of **75** as a white solid. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.85 – 7.78 (m, 2H), 7.63 – 7.57 (m, 2H), 4.72 – 4.63 (m, 2H), 2.96 – 2.90 (m, 2H), 2.02 (t, *J* = 7.5 Hz, 2H), 1.79 – 1.67 (m, 5H), 1.53 – 1.43 (m, 2H), 1.43 – 1.33 (m, 2H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 199.4, 146.0, 135.9, 132.0, 129.7, 128.1, 109.9, 38.7, 37.7, 29.1, 27.5, 24.2, 22.5; **IR** (Neat) 3085, 2970, 2915, 2863, 2824, 1674, 1651, 1583, 1567, 1463, 1396, 1371, 1248, 1190, 1071, 1009, 974, 882, 813. **HRMS**: calcd for $C_{15}H_{19}BrO^+$: 294.0619 found: 294.0614.

General DDQ oxidation procedure for the synthesis of fluorenes F28, F32, F46, 77



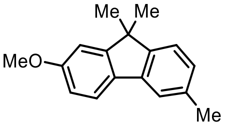
F28, F32, F46, 77

A flame dried round bottom flask equipped with a magnetic stir bar was charged with dry benzene (0.02 M) and indene product (1.0 eq). The reaction flask was charged with DDQ (3.0 eq) and fitted with a reflux condenser. The reaction was allowed to reflux until judged complete by TLC analysis. The resulting reaction mixture was quenched with saturated sodium thiosulfate and 1 M sodium hydroxide solution, and then partitioned between ethyl acetate and water. The aqueous layer was further extracted with ethyl acetate (x2), and the combined organic layer was washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure to remove all volatiles. The crude product was purified by column chromatography eluting with the indicated solvent to give the pure fluorene **F28, F32, F46, 77.**



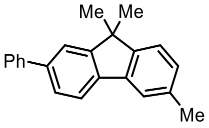
F28

2-(*tert*-butyl)-6,9,9-trimethyl-9*H*-fluorene (F28): The DDQ oxidation procedure was performed on **28** on a 0.186 mmol scale with a total reaction time of 22 h. Purification by column chromatography eluting with hexanes provided 32 mg (65% yield) of **F28** as a clear oil. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 1H), 7.51 (s, 1H), 7.44 (d, *J* = 1.5 Hz, 1H), 7.39 – 7.36 (m, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 2.44 (s, 3H), 1.48 (s, 6H), 1.39 (s, 9H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 154.0, 151.2, 150.6, 139.5, 136.8, 136.6, 128.5, 127.7, 124.2, 122.3, 120.5, 119.4, 46.6, 35.1, 31.8, 27.5, 21.7; **IR** (Neat) 3008, 2958, 2862, 1618, 1488, 1459, 1409, 1392, 1361, 1274, 1242, 1200, 1182, 1092, 1074, 1021, 938, 876, 826, 813, 784, 743, 704, 662, 652, 587. **HRMS**: calcd for $C_{20}H_{24}^+$: 264.1878 found: 264.1875.



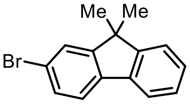
F32

2-methoxy-6,9,9-trimethyl-9*H*-fluorene (F32): The DDQ oxidation procedure was performed on **32** on a 0.124 mmol scale with a total reaction time of 6 h. Purification by column chromatography eluting with hexanes provided 29 mg (99% yield) of **F32** as a white solid. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.60 (d, *J* = 8.3 Hz, 1H), 7.45 (s, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 2.3 Hz, 1H), 6.87 (dd, *J* = 8.3, 2.4 Hz, 1H), 3.87 (s, 3H), 2.42 (s, 3H), 1.45 (s, 6H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 159.7, 156.1, 150.6, 139.4, 136.7, 132.3, 127.1, 122.3, 120.8, 120.0, 112.5, 108.7, 55.7, 46.7, 27.5, 21.7; **IR** (Neat) 2955, 2921, 2852, 1606, 1584, 1494, 1438, 1422, 1378, 1358, 1344, 1296, 1269, 1232, 1218, 1198, 1175, 1132, 1091, 1070, 1035, 1018, 939, 883, 846, 830, 812, 773, 740, 702, 668. **HRMS**: calcd for $C_{17}H_{18}O^+$: 238.1358 found: 238.1358.



F46

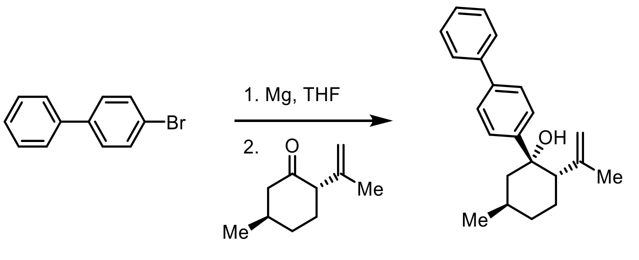
6,9,9-trimethyl-2-phenyl-9*H*-fluorene (F46): The DDQ oxidation procedure was performed on **46** on a 0.201 mmol scale with a total reaction time of 17 h. Purification by column chromatography eluting with hexanes provided 51 mg (89% yield) of **F46** as a white solid. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.76 (d, *J* = 7.8 Hz, 1H), 7.68 – 7.65 (m, 2H), 7.63 (d, *J* = 1.4 Hz, 1H), 7.58 – 7.55 (m, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.37 – 7.33 (m, 2H), 7.15 (d, *J* = 7.6 Hz, 1H), 2.46 (s, 3H), 1.52 (s, 6H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 154.8, 151.3, 141.8, 140.4, 139.1, 138.6, 136.8, 128.9, 128.3, 127.4, 127.2, 126.3, 122.5, 121.6, 120.8, 120.3, 46.8, 27.5, 21.7; **IR** (Neat) 3029, 2956, 2920, 2859, 1617, 1599, 1484, 1447, 1424, 1409, 1380, 1359, 1283, 1265, 1235, 1180, 1142, 1075, 1040, 1016, 934, 914, 888, 832, 815, 781, 757, 742, 722, 696, 673, 588.
HRMS: calcd for $C_{22}H_{20}^+$: 284.1565 found: 284.1563.



77

2-bromo-9,9-dimethyl-9H-fluorene (77): The DDQ oxidation procedure was performed on **76** on a 0.065 mmol scale with a total reaction time of 6 h. Purification by column chromatography eluting with hexanes provided 12 mg (67% yield) of **77** as a white solid. The ^{1}H-NMR data is consistent with literature(*63*) reported data. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.71 – 7.67 (m, 1H), 7.60 – 7.54 (m, 2H), 7.48 – 7.40 (m, 2H), 7.37 – 7.31 (m, 2H), 1.48 (s, 6H).

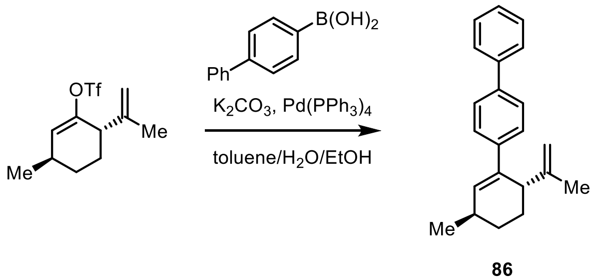
Grignard addition procedure for the synthesis of 85



85

(1*S*,2*S*,5*R*)-1-([1,1'-biphenyl]-4-yl)-5-methyl-2-(prop-1-en-2-yl)cyclohexan-1-ol (85): A flame-dried 100 mL round bottom flask equipped with a magnetic stir bar was charged with activated magnesium (320 mg, 13.1 mmol) and dry THF (35 mL). 4-bromo-1,1'-biphenyl (3.83 g, 16.4 mmol) was added and the resulting mixture was stirred until the activated magnesium dissolved. The reaction flask was then cooled to 0 °C, and (2*S*,5*R*)-isopulegone (1.1 mL, 6.6 mmol) was added dropwise and stirred for 3 hours. The resulting reaction mixture was quenched with saturated ammonium chloride, and then partitioned between ethyl acetate and water. The layers were separated and the aqueous layer was further extracted with ethyl acetate (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography to give 1.2g (58%) of **85** as a white solid. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.63 – 7.59 (m, 2H), 7.58 – 7.53 (m, 2H), 7.50 – 7.45 (m, 2H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.36 – 7.30 (m, 1H), 4.82 (p, *J* = 1.6 Hz, 1H), 4.79 – 4.75 (m, 1H), 2.49 (dd, *J* = 12.8, 3.7 Hz, 1H), 2.32 (br s, 1H), 2.04 – 1.78 (m, 4H), 1.68 – 1.49 (m, 2H), 1.20 (s, 3H), 1.16 – 1.04 (m, 1H), 0.93 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 148.4, 147.6, 140.9, 139.2, 128.9, 127.3, 127.1, 126.7, 125.4, 112.4, 74.6, 52.9, 49.2, 35.1, 28.3, 28.0, 25.7, 22.3. **IR** (Neat) 2923, 1626, 1486, 1447, 1372, 1116, 1070, 1052, 1005, 951, 892, 855, 762, 726, 689. **HRMS**: calcd for $C_{22}H_{26}O^+$: 306.1984 found: 306.1995.

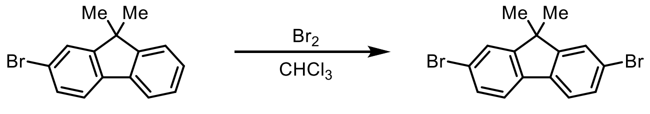
Suzuki Cross coupling procedure for the synthesis of 86



86

(2*S*,5*R*)-5-methyl-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1,1':4',1''-terphenyl (86): A scintillation vial equipped with a magnetic stir bar was charged with (3*R*,6*S*)-3-methyl-6-(prop-1-en-2-yl)cyclohex-1-en-1-yl trifluoromethanesulfonate (70 mg, 0.246 mmol), boronic acid (73 mg, 0.369 mmol), K_2CO_3 (136 mg, 0.985 mmol), 5:2:1 Toluene:Water:Ethanol (5 mL), and Tetrakis(triphenylphosphine)palladium(0) (29 mg, 0.025 mmol). The mixture was heated to 80°C for 2 days. The resulting reaction mixture was partitioned between ethyl acetate and water. The aqueous layer was further extracted with DCM (x2), and the combined organic layers was washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes provided 40 mg (21% yield) of **86** as a white solid. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.60 – 7.57 (m, 2H), 7.52 – 7.49 (m, 2H), 7.44 – 7.38 (m, 4H), 7.31 (tt, *J* = 7.3, 1.1 Hz, 1H), 6.06 – 6.05 (m, 1H), 4.79 – 4.77 (m, 1H), 4.75 – 4.73 (m, 1H), 3.41 – 3.36 (m, 1H), 2.39 (tt, *J* = 8.2, 2.6 Hz, 1H), 1.90 (ddddd, *J* = 30.3, 11.8, 8.6, 5.7, 2.8 Hz, 2H), 1.73 – 1.66 (m, 1H), 1.65 – 1.61 (m, 3H), 1.28 (dddd, *J* = 18.5, 15.6, 7.5, 4.0 Hz, 1H), 1.07 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (175 MHz; $CDCl_3$) δ 147.4, 141.5, 141.1, 139.2, 137.8, 134.1, 128.8, 127.14, 127.05, 126.8, 126.5, 113.1, 44.9, 30.7, 28.0, 26.7, 21.8, 20.7. **IR** (Neat) 3027, 2925, 2863, 2359, 2337, 1485, 1447, 1371, 1132, 1073, 1006, 890, 837, 760, 733, 695. **HRMS**: calcd for $C_{22}H_{24}^+$: 288.1878 found: 288.1874.

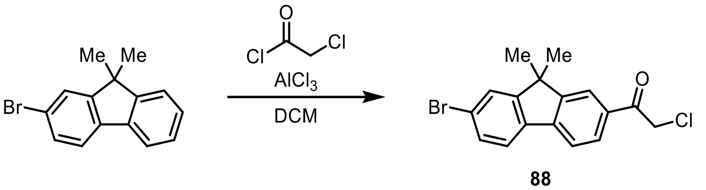
Bromination of 77 for the synthesis of 87



87

2,7-dibromo-9,9-dimethyl-9H-fluorene (87): A flame dried round bottom flask equipped with a magnetic stir bar was charged with **77** (450 mg, 1.65 mmol) and $CHCl_3$ (8 mL). The solution was cooled to 0°C and bromine (0.1 mL, 1.98 mmol) was slowly added. The reaction was allowed to warm to room temperature and stirred until judged complete by TLC. The mixture was quenched with saturated sodium thiosulfate and diluted with water and DCM. The layers were separated and the aqueous layer was further extracted with DCM (x2). The combined organics were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes provided 384 mg of **87** as an off-white solid. The **^{1}H NMR** data is consistent with literature(*64*) reported data. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.57 – 7.52 (m, 4H), 7.46 (dd, J = 8.2, 1.7 Hz, 2H), 1.47 (s, 6H).

Friedel-Crafts acylation of 77 for the synthesis of 88

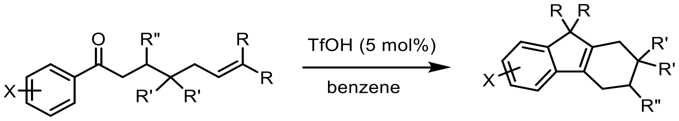


88

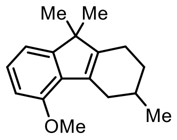
1-(7-bromo-9,9-dimethyl-9H-fluoren-2-yl)-2-chloroethan-1-one (88): A flame dried scintillation vial equipped with a magnetic stir bar was charged with DCM (1.8 mL) and $AlCl_3$ (98 mg, 0.73 mmol). The reaction vial was cooled to 0 °C and was charged with 2-

chloroacetyl chloride (0.06 mL, 0.73 mmol), followed by **77** (100 mg, 0.37 mmol). The resulting reaction mixture was stirred at room temperature overnight. The reaction mixture was quenched with water and the aqueous layer was extracted with DCM (x3). The combined organic layers were washed with saturated sodium chloride, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography eluting with hexanes/EtOAc provided 103 mg (80%) of **88** as a white solid. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 8.04 (s, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.61 (s, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 4.77 – 4.73 (m, 2H), 1.52 (s, 6H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 190.9, 156.9, 153.9, 144.1, 136.7, 133.5, 130.8, 128.6, 126.7, 123.3, 123.1, 122.6, 120.3, 47.5, 46.1, 26.9; **IR** (Neat) 2963, 2924, 2857, 1678, 1606, 1463, 1425, 1404, 1302, 1250, 1187, 1060, 1022, 804, 786, 734. **HRMS**: calcd for $C_{17}H_{14}BrClO^+$: 347.9917 found: 347.9905.

General interrupted carbonyl-olefin metathesis procedure

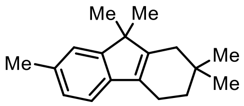


A 20 mL scintillation vial equipped with a magnetic stir bar was charged with the respective aryl ketone substrate (1.0 eq) and degassed benzene (sparged with N_2 for 30 min prior to use) (0.02 M). To this solution was added TfOH (0.05 eq) *via* a micro-syringe, and the resultant mixture was stirred for the indicated time (as determined by TLC analysis) at 80 °C. Upon completion, the reaction mixture was filtered through a silica plug eluting with DCM. The filtrate was concentrated under reduced pressure to remove all volatiles, and the crude product was purified by column chromatography eluting with the indicated solvent to give the pure product.



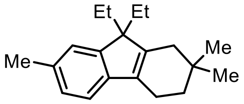
17

5-methoxy-3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (17): The cyclization of **14** was performed on 0.189 mmol scale with a total reaction time of 1 h. Purification by column chromatography eluting with hexanes/EtOAc provided 22 mg (48%) of **17** as a yellow oil. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.09 (t, *J* = 7.7 Hz, 1H), 6.94 (d, *J* = 7.3 Hz, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 3.84 (s, 3H), 3.01 – 2.82 (m, 1H), 2.29 – 2.10 (m, 3H), 1.92 – 1.73 (m, 2H), 1.47 – 1.30 (m, 1H), 1.20 – 1.15 (m, 6H), 1.08 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 156.4, 154.0, 148.2, 131.7, 131.2, 125.2, 114.3, 109.3, 55.5, 48.8, 33.6, 31.2, 29.6, 24.3, 24.2, 21.9, 21.5; **IR** (Neat) 2952, 2920, 2865, 2831, 1630, 1581, 1478, 1459, 1438, 1374, 1356, 1278, 1262, 1252, 1238, 1177, 1144, 1128, 1080, 1056, 940, 866, 786, 740, 678, 649, 630, 615. **HRMS**: calcd for $C_{17}H_{22}O^+$: 242.1671 found: 242.1674.



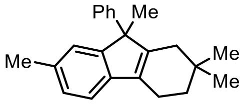
P18

2,2,7,9,9-pentamethyl-2,3,4,9-tetrahydro-1*H*-fluorene (P18): The cyclization of **18** was performed on a 0.22 mmol scale with a total reaction time of 2.5 h. Purification by column chromatography eluting with hexanes/EtOAc provided 46 mg (85%) of **P18** as a clear oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.13 (s, 1H), 7.06 (d, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.7 Hz, 1H), 2.42 – 2.37 (m, 5H), 1.96 (d, *J* = 2.2 Hz, 2H), 1.57 – 1.53 (m, 2H), 1.17 (s, 6H), 0.99 (s, 6H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 154.3, 148.9, 141.0, 133.6, 130.6, 126.9, 122.1, 117.6, 48.4, 35.9, 35.8, 30.1, 28.5, 24.0, 21.7, 20.0; **IR** (Neat) 2951, 2921, 2864, 1636, 1460, 1383, 1363, 1284, 1253, 1126, 939, 879, 810. **HRMS**: calcd for $C_{18}H_{24}^+$: 240.1878 found: 242.1884.



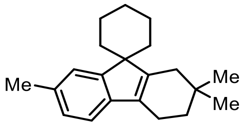
P19

9,9-diethyl-2,2,7-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (P19): The cyclization of **19** was performed on 0.175 mmol scale with a total reaction time of 3 h. Purification by column chromatography eluting with hexanes/EtOAc provided 40 mg (86%) of **P19** as a yellow oil. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 7.02 – 6.97 (m, 3H), 2.44 – 2.39 (m, 2H), 2.37 (s, 3H), 1.82 (s, 2H), 1.78 (dt, *J* = 14.7, 7.3 Hz, 2H), 1.61 (dq, *J* = 14.5, 7.3 Hz, 2H), 1.55 – 1.51 (m, 2H), 1.01 (s, 6H), 0.30 (t, *J* = 7.4 Hz, 6H); **^{13}C NMR** (125 MHz; CDCl$_3$) δ 150.0, 144.3, 143.6, 134.3, 133.2, 126.7, 122.3, 117.0, 57.3, 36.3, 36.1, 30.3, 30.0, 28.8, 21.8, 20.0, 8.3; **IR** (Neat) 2960, 2915, 2866, 2820, 1638, 1452, 1375, 1362, 1280, 1261, 1212, 1168, 1140, 1126, 1084, 1035, 938, 878, 814, 797, 732, 716, 676. **HRMS**: calcd for $C_{20}H_{28}^+$: 268.2191 found: 268.2192.



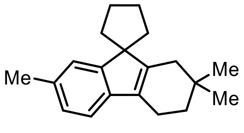
P20

2,2,7,9-tetramethyl-9-phenyl-2,3,4,9-tetrahydro-1*H*-fluorene (P20): The cyclization of **20** was performed on a 0.23 mmol scale with a total reaction time of 18 h. Purification by column chromatography eluting with hexanes/EtOAc provided 48 mg (68%) of **P20** as a yellow oil. **^{1}H NMR** (400 MHz; CDCl$_3$) δ 7.25 – 7.19 (m, 2H), 7.19 – 7.13 (m, 1H), 7.13 – 7.00 (m, 4H), 6.88 (s, 1H), 2.56 – 2.39 (m, 2H), 2.28 (s, 3H), 1.89 (dt, *J* = 17.6, 2.4 Hz, 1H), 1.66 – 1.51 (m, 6H), 0.94 (s, 3H), 0.89 (s, 3H); **^{13}C NMR** (100 MHz; CDCl$_3$) δ 155.0, 149.4, 143.5, 141.4, 134.3, 132.6, 128.3, 127.2, 126.5, 126.1, 123.4, 117.8, 56.2, 36.0, 35.8, 30.1, 28.6, 28.1, 21.6, 21.4, 20.1; **IR** (Neat) 2949, 2914, 2863, 1598, 1494, 1444, 1364, 1125, 1027, 908, 815, 734, 698. **HRMS**: calcd for $C_{23}H_{26}^+$: 302.2035 found: 302.2036.



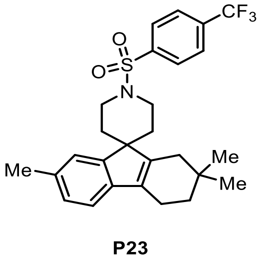
P21

2',2',7'-trimethyl-1',2',3',4'-tetrahydrospiro[cyclohexane-1,9'-fluorene] (P21): The cyclization of **21** was performed on a 0.23 mmol scale with a total reaction time of 5 h. Purification by column chromatography eluting with hexanes/EtOAc provided 49 mg (77%) of **P21** as a white solid. **^{1}H NMR** (400 MHz; CDCl$_3$) δ ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (s, 1H), 7.08 (s, 2H), 2.45 – 2.35 (m, 5H), 2.04 – 1.86 (m, 5H), 1.82 – 1.69 (m, 2H), 1.65 (td, *J* = 13.0, 4.2 Hz, 2H), 1.58 – 1.50 (m, 2H), 1.48 – 1.33 (m, 1H), 1.27 – 1.13 (m, 2H), 0.98 (s, 6H); **^{13}C NMR** (100 MHz; CDCl$_3$) δ 153.3, 149.1, 141.8, 132.6, 131.0, 126.9, 125.4, 117.5, 52.0, 36.6, 35.8, 32.0, 30.3, 28.4, 25.8, 22.8, 21.9, 20.0; **IR** (Neat) 2923, 2860, 1652, 1470, 1448, 1362, 1127, 1031, 982, 883, 814, 804. **HRMS**: calcd for $C_{21}H_{28}^+$: 280.2191 found: 280.2196.



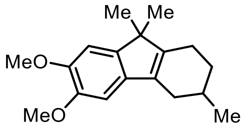
P22

2',2',7'-trimethyl-1',2',3',4'-tetrahydrospiro[cyclopentane-1,9'-fluorene] (P22): The cyclization of **22** was performed on a 0.22 mmol scale with a total reaction time of 1.5 h. Purification by column chromatography eluting with hexanes/EtOAc provided 43 mg (75%) of **P22** as a white solid. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.14 – 7.12 (m, 1H), 7.04 – 7.00 (m, 2H), 2.41 – 2.36 (m, 5H), 2.05 – 1.96 (m, 4H), 1.93 – 1.87 (m, 2H), 1.83 – 1.78 (m, 2H), 1.76 – 1.71 (m, 2H), 1.55 – 1.52 (m, 2H), 0.99 (s, 6H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 156.0, 147.7, 141.2, 133.8, 130.9, 126.6, 122.3, 117.2, 59.3, 36.4, 35.8, 35.2, 30.2, 28.5, 27.5, 21.8, 20.0; **IR** (Neat) 2948, 2910, 2862, 1636, 1581, 1482, 1449, 1383, 1362, 1281, 1218, 1147, 1127, 1034, 932, 877, 810. **HRMS**: calcd for $C_{20}H_{26}^+$: 266.2035 found: 266.2038.



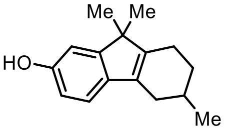
P23

2,2,7-trimethyl-1'-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,4-tetrahydrospiro[fluorene-9,4'-piperidine] (P23): The cyclization of **23** was performed on 0.108 mmol scale. Purification by column chromatography eluting with hexanes/EtOAc provided 46 mg (87%) of **P23** as a white solid. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 8.04 (d, *J* = 8.1 Hz, 2H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.04 (q, *J* = 7.6 Hz, 2H), 6.70 (s, 1H), 3.83 (dt, *J* = 12.2, 3.7 Hz, 2H), 3.13 (td, *J* = 12.3, 2.9 Hz, 2H), 2.36 (t, *J* = 6.3 Hz, 2H), 2.14 (s, 3H), 2.00 (td, *J* = 13.3, 4.9 Hz, 2H), 1.85 (s, 2H), 1.51 (t, *J* = 6.4 Hz, 2H), 1.25 (d, *J* = 13.4 Hz, 2H), 0.95 (s, 6H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 150.5, 146.3, 141.7, 140.4, 134.8 (q, *J* = 33.2 Hz), 133.0, 132.9, 128.4, 127.6, 126.4 (q, *J* = 3.6 Hz), 124.7, 123.4 (q, *J* = 272.8 Hz), 118.3, 48.9, 43.2, 36.3, 35.5, 30.8, 30.3, 28.3, 21.6, 19.9; **IR** (Neat) 3054, 2953, 2922, 1472, 1423, 1404, 1386, 1357, 1323, 1265, 1171, 1137, 1108, 1093, 1062, 1016, 992, 939, 922, 906, 895, 846, 819, 786, 732, 703. **HRMS**: calcd for $C_{27}H_{30}F_3NO_2S^+$: 489.1949 found: 489.1960.



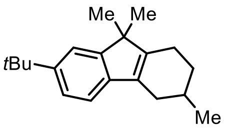
26

6,7-dimethoxy-3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (26): The cyclization of **S26** was performed on 0.170 mmol scale with a total reaction time of 3 h. Purification by column chromatography eluting with hexanes/EtOAc provided 36 mg (78%) of **26** as a yellow oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 6.90 (s, 1H), 6.74 (s, 1H), 3.91 (d, *J* = 2.6 Hz, 6H), 2.51 (dd, *J* = 16.3, 4.1 Hz, 1H), 2.28 – 2.15 (m, 2H), 2.00 – 1.92 (m, 1H), 1.91 – 1.81 (m, 2H), 1.42 – 1.34 (m, 1H), 1.20 – 1.15 (m, 6H), 1.09 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 149.0, 148.2, 146.6, 146.3, 136.4, 131.5, 106.1, 102.1, 56.7, 56.3, 48.6, 31.5, 30.7, 29.3, 24.4, 24.3, 21.9, 21.4; **IR** (Neat) 2952, 2922, 2831, 1606, 1493, 1465, 1409, 1384, 1335, 1287, 1234, 1200, 1164, 1064, 1027, 1003, 839, 760, 626. **HRMS**: calcd for $C_{18}H_{24}O_2^+$: 272.1776 found: 272.1779.



27

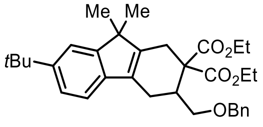
3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluoren-7-ol (27): The cyclization was performed on TBS protected phenolic substrate **S27a** on 0.136 mmol scale with a total reaction time of 23 h. Purification by column chromatography eluting with hexanes/EtOAc provided 29 mg (92% yield) of **27** as a yellow oil. The interrupted carbonyl-olefin metathesis procedure was performed on unprotected phenolic substrate **S27** on 0.206 mmol scale with a total reaction time of 3 h. Purification by column chromatography eluting with hexanes/EtOAc provided 33 mg (71%) of **27** as a yellow oil. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 6.98 (d, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.67 (dd, *J* = 7.9, 2.3 Hz, 1H), 4.49 (brs, 1H), 2.48 (dd, *J*= 16.3, 3.6 Hz, 1H), 2.31 – 2.09 (m, 2H), 2.02 – 1.73 (m, 3H), 1.43 – 1.31 (m, 1H), 1.20 – 1.14 (m, 6H), 1.07 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 156.2, 153.2, 148.0, 137.0, 131.5, 118.1, 112.7, 109.5, 48.5, 31.5, 30.6, 29.2, 24.2, 24.1, 21.9, 21.3; **IR** (Neat) 3308, 2952, 2921, 1611, 1589, 1455, 1376, 1355, 1290, 1272, 1192, 1139, 1059, 934, 888, 815. **HRMS**: calcd for $C_{16}H_{20}O^+$: 228.1514 found: 228.1507.



28

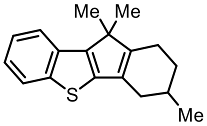
7-(*tert*-butyl)-3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (28): The cyclization of **S28** was performed on 0.180 mmol scale with a total reaction time of 1.5 h. Purification by column chromatography eluting with hexanes/EtOAc provided 44 mg (90%) of **28** as a clear oil. **^{1}H NMR**

(400 MHz; $CDCl_3$) δ 7.38 – 7.32 (m, 1H), 7.29 – 7.24 (m, 1H), 7.09 (d, *J* = 7.8 Hz, 1H), 2.52 (dd, *J* = 16.4, 3.8 Hz, 1H), 2.32 – 2.10 (m, 2H), 2.01 – 1.77 (m, 3H), 1.45 – 1.33 (m, 10H), 1.23 – 1.17 (m, 6H), 1.08 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 153.8, 149.6, 147.3, 141.2, 131.8, 123.2, 118.2, 117.1, 48.6, 34.9, 31.9, 31.5, 30.6, 29.2, 24.3, 24.2, 21.8, 21.3; **IR** (Neat) 2952, 2905, 2867, 2829, 1637, 1576, 1481, 1456, 1374, 1361, 1251, 1236, 1202, 1143, 1104, 1035, 972, 908, 884, 866, 821, 768, 732, 702, 649. **HRMS**: calcd for $C_{20}H_{28}^+$: 268.2191 found: 268.2189.



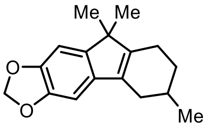
29

diethyl 3-((benzyloxy)methyl)-7-(*tert*-butyl)-9,9-dimethyl-1,3,4,9-tetrahydro-2*H*-fluorene-2,2-dicarboxylate (29): The cyclization of **S29** was performed on a 0.23 mmol scale with a total reaction time of 1.5 h. The yield was determined to be 54% by ^{1}H-NMR using dimethyl terephthalate as an internal standard. An analytically pure sample of **29** was obtained as a clear oil.**^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.34 (d, *J* = 1.7 Hz, 1H), 7.31 – 7.22 (m, 6H), 7.09 (d, *J* = 7.8 Hz, 1H), 4.48 – 4.42 (m, 2H), 4.12 – 4.04 (m, 4H), 3.58 (dd, *J* = 9.6, 6.4 Hz, 1H), 3.51 (dd, *J* = 9.6, 7.4 Hz, 1H), 3.07 (p, *J* = 6.3 Hz, 1H), 2.95 – 2.82 (m, 2H), 2.77 (dt, *J* = 17.7, 2.3 Hz, 1H), 2.49 (dd, *J* = 17.5, 4.5 Hz, 1H), 1.34 (s, 9H), 1.23 – 1.15 (m, 12H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 170.9, 170.6, 153.6, 148.0, 145.9, 140.3, 138.3, 130.6, 128.4, 127.9, 127.7, 123.4, 118.2, 117.7, 73.2, 71.3, 61.6, 61.5, 56.6, 48.9, 38.3, 34.9, 31.9, 26.2 (observed by HSQC), 23.82, 23.77, 23.7, 14.10, 14.08; **IR** (Neat) 2960, 2859, 1729, 1482, 1462, 1364, 1244, 1205, 1178, 1094, 1028, 824, 736, 698. **HRMS**: calcd for $C_{33}H_{42}O_5Na^+$: 541.2924 found: 541.2926.



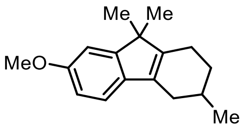
30

3,10,10-trimethyl-2,3,4,10-tetrahydro-1*H*-benzo[*b*]indeno[2,1-*d*]thiophene (30): The cyclization of **S30** was performed on 0.175 mmol scale with a total reaction time of 1 h. Purification by column chromatography eluting with hexanes/EtOAc provided 34 mg (73%) of **30** as a yellow oil. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.84 (d, *J* = 8.1 Hz, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 2.55 (dd, *J* = 16.7, 3.0 Hz, 1H), 2.39 – 2.24 (m, 2H), 2.12 – 2.02 (m, 1H), 1.98 – 1.83 (m, 2H), 1.48 – 1.30 (m, 7H), 1.09 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 153.8, 148.3, 144.2, 143.1, 134.3, 129.8, 124.3, 124.2, 121.8, 119.9, 48.3, 31.8, 31.1, 29.2, 23.1, 23.0, 21.7, 21.5; **IR** (Neat) 3054, 2958, 2922, 2865, 1706, 1457, 1428, 1374, 1263, 1156, 1060, 1018, 943, 817, 761, 730, 702. **HRMS**: calcd for $C_{18}H_{20}S^+$: 268.1286 found: 268.1283.



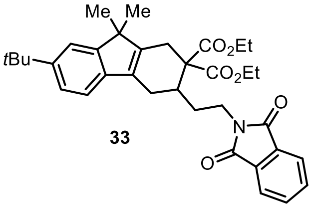
31

6,9,9-trimethyl-6,7,8,9-tetrahydro-5*H*-fluoreno[2,3-*d*][1,3]dioxole (31): The cyclization of **S31** was performed on a 0.19 mmol scale with a total reaction time of 2 h. Purification by column chromatography eluting with hexanes/EtOAc provided 37 mg (76%) of **31** as a white solid. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 6.84 (s, 1H), 6.67 (s, 1H), 5.92 (d, *J* = 1.1 Hz, 2H), 2.50 – 2.41 (m, 1H), 2.28 – 2.11 (m, 2H), 1.98 – 1.76 (m, 3H), 1.38 (dtd, *J* = 12.5, 10.1, 6.3 Hz, 1H), 1.21 – 1.13 (m, 6H), 1.08 (d, *J* = 6.3 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 149.1, 147.9, 146.2, 145.0, 137.6, 131.5, 103.2, 100.8, 99.5, 48.4, 31.5, 30.6, 29.2, 24.3, 24.2, 21.9, 21.4; **IR** (Neat) 2952, 2920, 2867, 2828, 1634, 1599, 1471, 1455, 1416, 1374, 1356, 1254, 1231, 1144, 1075, 1034, 911, 887, 825, 769, 755, 696. **HRMS**: calcd for $C_{17}H_{21}O_2^+$: 257.1536 found: 257.1540.



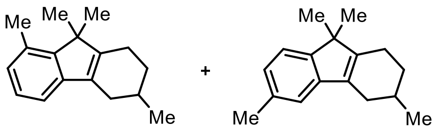
32

7-methoxy-3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (32): The cyclization of **S32** was performed on a 0.20 mmol scale with a total reaction time of 2.5 h. Purification by column chromatography eluting with hexanes/EtOAc provided 41 mg (85%) of **32** as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.04 (d, *J* = 8.1 Hz, 1H), 6.90 (d, *J* = 2.3 Hz, 1H), 6.76 (dd, *J* = 8.2, 2.4 Hz, 1H), 3.83 (s, 3H), 2.54 – 2.46 (m, 1H), 2.27 – 2.15 (m, 2H), 1.95 (ddd, *J* = 16.4, 9.4, 2.9 Hz, 1H), 1.91 – 1.81 (m, 2H), 1.38 (dtd, *J* = 12.1, 10.3, 5.8 Hz, 1H), 1.21 – 1.16 (m, 6H), 1.08 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 157.6, 155.9, 148.1, 137.0, 131.5, 117.9, 110.8, 108.7, 55.8, 48.8, 31.5, 30.6, 29.2, 24.3, 24.2, 21.9, 21.3; **IR** (Neat) 2949, 2906, 2829, 1608, 1583, 1475, 1426, 1374, 1308, 1279, 1204, 1178, 1140, 1063, 1042, 1029, 868, 848, 804. **HRMS**: calcd for $C_{17}H_{23}O^+$: 243.1743 found: 243.1744.



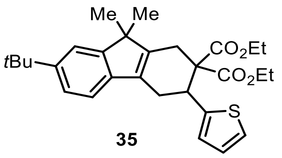
33

diethyl 7-(*tert*-butyl)-3-(2-(1,3-dioxoisoindolin-2-yl)ethyl)-9,9-dimethyl-1,3,4,9-tetrahydro-2*H*-fluorene-2,2-dicarboxylate (33): The cyclization of **S33** was performed on a 0.23 mmol scale with a total reaction time of 9 h. Purification by column chromatography eluting with hexanes/EtOAc provided 76 mg (59%) of **33** as a white foam. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.86 – 7.81 (m, 2H), 7.73 – 7.69 (m, 2H), 7.34 (s, 1H), 7.30 (d, *J* = 7.7 Hz, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 4.15 – 4.05 (m, 4H), 3.84 (dt, *J* = 15.5, 8.0 Hz, 1H), 3.76 (ddd, *J* = 13.4, 7.9, 4.3 Hz, 1H), 2.93 – 2.83 (m, 2H), 2.74 (d, *J* = 17.6 Hz, 1H), 2.64 – 2.58 (m, 1H), 2.58 – 2.52 (m, 1H), 1.86 (dt, *J* = 16.3, 8.4 Hz, 1H), 1.76 – 1.67 (m, 1H), 1.35 (s, 9H), 1.23 – 1.20 (m, 6H), 1.19 – 1.14 (m, 6H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 170.9, 170.4, 168.4, 153.7, 148.0, 146.1, 140.3, 134.0, 132.3, 130.4, 123.5, 123.4, 118.3, 117.7, 61.7, 61.6, 58.7, 48.9, 36.5, 35.3, 35.0, 31.9, 30.0, 26.3 (observed by HSQC), 24.7, 23.9, 23.8, 14.10, 14.07; **IR** (Neat) 2960, 1772, 1711, 1466, 1437, 1396, 1363, 1247, 1181, 1076, 1052, 1023, 866, 826, 721. **HRMS**: calcd for $C_{35}H_{42}NO_7^+$: 572.3007 found: 572.3007.



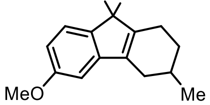
34

3,6,9,9-tetramethyl-2,3,4,9-tetrahydro-1*H*-fluorene + 3,8,9,9-tetramethyl-2,3,4,9-tetrahydro-1*H*-fluorene (2:1) (34): The cyclization of **S34** was performed on 0.209 mmol scale with a total reaction time of 3.5 h. The yield was determined to be 86% of **34** (1:1 mixture of regioisomers) by ^{1}H-NMR using dimethyl terephthalate as an internal standard. An analytically pure sample of **34** (2:1 mixture of regioisomers) was obtained as a white solid. **^{1}H NMR** (for the mixture of regioisomers; 700 MHz; $CDCl_3$) δ 7.18 (d, *J* = 7.4 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 2H), 7.01 – 6.97 (m, 3H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.88 (d, *J*= 7.6 Hz, 2H), 2.55 – 2.47 (m, 9H), 2.37 (s, 3H), 2.28 – 2.15 (m, 7H), 1.99 – 1.82 (m, 10H), 1.45 – 1.35 (m, 3H), 1.30 – 1.27 (m, 12H), 1.19 – 1.17 (m, 6H), 1.08 (d, *J* = 6.6 Hz, 9H); **^{1}H NMR** (signals corresponding to the major regioisomer; 700 MHz; $CDCl_3$) δ 7.13 (t, *J* = 7.4 Hz, 1H), 6.88 (d, *J*= 7.6 Hz, 1H), 1.30 – 1.27 (m, 6H); **^{13}C NMR** (for the mixture of regioisomers; 175 MHz; $CDCl_3$) δ 151.2, 150.51, 150.45, 150.3, 144.3, 144.0, 135.9, 132.4, 131.9, 131.8, 126.8, 126.5, 124.7, 120.7, 118.7, 115.5, 49.7, 48.2, 31.6, 31.5, 30.54, 30.49, 29.19, 29.16, 24.2, 24.1, 21.9, 21.8, 21.7, 21.5, 21.4, 21.3, 21.0, 18.9; **IR** (Neat) 3037, 2953, 2920, 2867, 2830, 1692, 1644, 1596, 1457, 1375, 1356, 1306, 1255, 1143, 1076, 1051, 946, 888, 870, 811, 782, 752, 725, 680, 637, 615, 606. **HRMS**: calcd for $C_{17}H_{22}^+$: 226.1722 found: 226.1717.



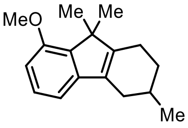
35

diethyl 7-(*tert*-butyl)-9,9-dimethyl-3-(thiophen-2-yl)-1,3,4,9-tetrahydro-2*H*-fluorene-2,2-dicarboxylate (35): The cyclization of **S35** was performed on a 0.23 mmol scale with a total reaction time of 2.5 h. Purification by column chromatography eluting with hexanes/EtOAc provided 53 mg (49%) of **35** as a white foam.**^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.40 – 7.38 (m, 1H), 7.31 – 7.27 (m, 1H), 7.11 – 7.06 (m, 2H), 6.84 – 6.80 (m, 2H), 4.39 (d, *J* = 6.7 Hz, 1H), 4.20 – 4.10 (m, 2H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.31 – 3.25 (m, 1H), 3.03 (d, *J* = 18.1 Hz, 1H), 2.93 – 2.88 (m, 1H), 2.79 (d, *J* = 17.5 Hz, 1H), 1.36 (s, 9H), 1.30 (s, 3H), 1.26 – 1.22 (m, 6H), 1.15 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 170.2, 169.9, 153.8, 148.1, 146.3, 144.1, 140.0, 130.7, 126.2, 126.1, 124.4, 123.5, 118.3, 117.8, 61.8, 61.7, 58.8, 49.2, 38.8, 35.0, 31.9, 28.6, 25.0, 23.8, 23.6, 14.15, 14.08; **IR** (Neat) 2959, 2906, 2870, 1732, 1464, 1436, 1363, 1249, 1216, 1178, 1096, 1077, 1065, 1052, 864, 825, 702. **HRMS**: calcd for $C_{29}H_{36}O_4SNa^+$: 503.2227 found: 503.2225.



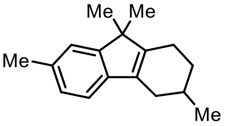
36 major

6-methoxy-3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (36 major): The cyclization of **S36** was performed on a 0.20 mmol scale with a total reaction time of 2 h. Purification by column chromatography eluting with hexanes/EtOAc provided 23 mg (48%) of the yellow oil **36 major** as one of two regioisomers. ^{1}**H NMR** (500 MHz; CDCl$_3$) δ 7.18 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 2.4 Hz, 1H), 6.68 (dd, *J* = 8.0, 2.4 Hz, 1H), 3.83 (s, 3H), 2.51 (dddt, *J* = 16.4, 5.0, 2.6, 1.3 Hz, 1H), 2.31 – 2.14 (m, 2H), 2.00 – 1.79 (m, 3H), 1.40 (dtd, *J* = 12.5, 10.2, 5.9 Hz, 1H), 1.21 – 1.14 (m, 6H), 1.09 (d, *J* = 6.5 Hz, 3H); ^{13}**C NMR** (125 MHz; CDCl$_3$) δ 159.1, 151.7, 146.3, 145.2, 131.7, 121.3, 109.1, 104.1, 55.6, 48.0, 31.5, 30.5, 29.2, 24.3, 24.2, 21.9, 21.4; **IR** (Neat) 2951, 2920, 2829, 1606, 1584, 1476, 1432, 1280, 1206, 1173, 1137, 1029, 800, 725. **HRMS**: calcd for $C_{17}H_{23}O^{+}$: 243.1743 found: 243.2744.



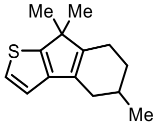
36 minor

8-methoxy-3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (36 minor): The cyclization of **S36** was performed on a 0.20 mmol scale with a total reaction time of 2 h. Purification by column chromatography eluting with hexanes/EtOAc provided 5 mg (10%) of the brown solid **36 minor** as one of two regioisomers. ^{1}**H NMR** (700 MHz; CDCl$_3$) δ 7.20 (t, *J* = 7.8 Hz, 1H), 6.80 (d, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 1H), 3.86 (s, 3H), 2.55 – 2.47 (m, 1H), 2.29 – 2.14 (m, 2H), 2.00 – 1.79 (m, 3H), 1.39 (dtd, *J* = 12.2, 10.3, 5.8 Hz, 1H), 1.31 – 1.24 (m, 6H), 1.08 (d, *J* = 6.6 Hz, 3H); ^{13}**C NMR** (175 MHz; CDCl$_3$) δ 155.5, 151.3, 145.7, 139.3, 131.5, 127.8, 111.0, 107.5, 55.3, 49.4, 31.5, 30.7, 29.2, 21.9, 21.5, 21.5, 21.0; **IR** (Neat) 2951, 2922, 2832, 1603, 1583, 1478, 1456, 1262, 1100, 1037, 788, 737. **HRMS**: calcd for $C_{17}H_{23}O^{+}$: 243.1743 found: 243.1738.



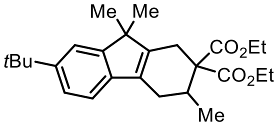
37

3,7,9,9-tetramethyl-2,3,4,9-tetrahydro-1*H*-fluorene (37): The cyclization of **S37** was performed on a 10.2 mmol scale at a concentration of 0.1M and a total reaction time of 6 h. Purification by column chromatography eluting with hexanes/EtOAc provided 2.14 g (92%) of **37** as a clear oil. ^{1}**H NMR** (500 MHz; CDCl$_3$) δ 7.12 (s, 1H), 7.07 – 6.99 (m, 2H), 2.51 (dd, *J* = 16.1, 4.3 Hz, 1H), 2.38 (s, 3H), 2.29 – 2.12 (m, 2H), 2.01 – 1.78 (m, 3H), 1.48 – 1.33 (m, 1H), 1.21 – 1.16 (m, 6H), 1.08 (d, *J* = 6.5 Hz, 3H); ^{13}**C NMR** (175 MHz; CDCl$_3$) δ 154.3, 149.1, 141.2, 133.6, 131.9, 126.9, 122.1, 117.5, 48.4, 31.5, 30.6, 29.2, 24.2, 24.1, 21.9, 21.7, 21.3; **IR** (Neat) 2952, 2921, 2830, 1636, 1484, 1455, 1374, 1356, 1283, 1254, 1192, 1143, 1126, 1036, 931, 878, 812, 723. **HRMS**: calcd for $C_{17}H_{22}^{+}$: 226.1722 found: 226.1722.



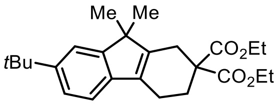
38

5,8,8-trimethyl-5,6,7,8-tetrahydro-4*H*-indeno[2,1-*b*]thiophene (38): The cyclization of **S38** was performed on 0.212 mmol scale with a total reaction time of 2 h. Purification by column chromatography eluting with hexanes/EtOAc provided 26 mg (57%) of **38** as a yellow oil. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.21 (d, *J* = 4.8 Hz, 1H), 6.86 (d, *J* = 4.8 Hz, 1H), 2.51 (dd, *J* = 17.4, 5.4 Hz, 1H), 2.27 – 2.12 (m, 2H), 2.07 – 1.94 (m, 1H), 1.90 – 1.77 (m, 2H), 1.43 – 1.31 (m, 1H), 1.26 – 1.21 (m, 6H), 1.06 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (100 MHz; $CDCl_3$) δ 152.8, 150.6, 147.1, 129.9, 126.1, 117.8, 48.4, 31.9, 31.4, 29.2, 25.2, 25.1, 21.8, 21.6; **IR** (Neat) 2953, 2921, 2867, 1695, 1645, 1456, 1378, 1356, 1263, 1140, 1075, 1025, 863, 814, 735, 720, 703, 661. **HRMS**: calcd for $C_{14}H_{18}S^+$: 218.1129 found: 218.1129.



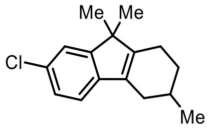
39

diethyl 7-(*tert*-butyl)-3,9,9-trimethyl-1,3,4,9-tetrahydro-2*H*-fluorene-2,2-dicarboxylate (39): The cyclization of **S39** was performed on a 0.23 mmol scale with a total reaction time of 1 h. Purification by column chromatography eluting with hexanes/EtOAc provided 56 mg (60%) of **39** as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.34 (d, *J* = 1.7 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 4.25 – 4.13 (m, 2H), 4.11 (qd, *J* = 7.1, 1.3 Hz, 2H), 2.92 – 2.77 (m, 4H), 2.30 (d, *J* = 14.4 Hz, 1H), 1.34 (s, 9H), 1.27 – 1.18 (m, 12H), 1.05 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 171.2, 170.9, 153.7, 147.9, 145.7, 140.5, 130.5, 123.4, 118.3, 117.5, 61.43, 61.38, 58.3, 48.9, 34.9, 32.5, 31.9, 28.0, 25.5, 23.9, 23.8, 17.0, 14.22, 14.18; **IR** (Neat) 2960, 1730, 1483, 1464, 1364, 1245, 1209, 1179, 1095, 1035, 886, 864, 824. **HRMS**: calcd for $C_{26}H_{37}O_4^+$: 413.2686 found: 413.2687.



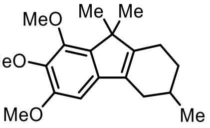
40

diethyl 7-(*tert*-butyl)-9,9-dimethyl-1,3,4,9-tetrahydro-2*H*-fluorene-2,2-dicarboxylate (40): The cyclization of **S40** was performed on a 0.23 mmol scale with a total reaction time of 3.5 h. The yield was determined to be 65% by ^{1}H-NMR using dimethyl terephthalate as an internal standard. An analytically pure sample of **40** was obtained as a clear oil. **^{1}H NMR** (700 MHz; $CDCl_3$) δ 7.34 (d, *J* = 1.7 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 4.16 (p, *J* = 7.1 Hz, 4H), 2.80 – 2.76 (m, 2H), 2.51 (td, *J* = 6.1, 2.9 Hz, 2H), 2.33 (t, *J* = 6.4 Hz, 2H), 1.34 (s, 9H), 1.26 – 1.22 (m, 12H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 171.7, 153.6, 147.9, 146.5, 140.2, 131.2, 123.3, 118.2, 117.5, 61.5, 54.3, 49.0, 34.9, 31.9, 28.3, 28.0, 23.9, 19.7, 14.2; **IR** (Neat) 2960, 1732, 1482, 1463, 1364, 1291, 1249, 1228, 1174, 1092, 1074, 1062, 1032, 867, 820, 767. **HRMS**: calcd for $C_{25}H_{34}O_4Na^+$: 421.2349 found: 421.2350.



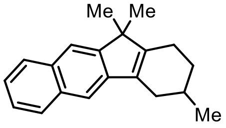
41

7-chloro-3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (41): The cyclization of **S41** was performed on 0.187 mmol scale with a total reaction time of 3.5 h. The yield was determined to be 66% of **41** by ^{1}H-NMR using dimethyl terephthalate as an internal standard. An analytically pure sample of **41** was obtained as a clear oil. **^{1}H NMR** (400 MHz; CDCl$_3$) δ 7.25 (d, *J* = 2.0 Hz, 1H), 7.18 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.04 (d, *J* = 7.9 Hz, 1H), 2.49 (dd, *J* = 16.2, 4.4 Hz, 1H), 2.29 – 2.13 (m, 2H), 1.98 – 1.77 (m, 3H), 1.45 – 1.32 (m, 1H), 1.21 – 1.15 (m, 6H), 1.08 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (100 MHz; CDCl$_3$) δ 155.8, 150.7, 142.2, 131.6, 130.0, 126.4, 121.8, 118.6, 48.9, 31.3, 30.5, 29.1, 24.0, 23.9, 21.8, 21.4; **IR** (Neat) 2953, 2921, 2868, 2830, 1862, 1743, 1635, 1573, 1455, 1410, 1375, 1357, 1254, 1238, 1142, 1126, 1089, 1078, 1062, 1036, 1012, 970, 941, 925, 908, 874, 814, 793, 759, 732, 696, 671, 648. **HRMS**: calcd for $C_{16}H_{19}Cl^+$: 246.1175 found: 246.1178.



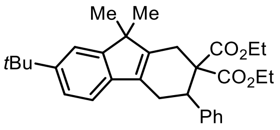
42

6,7,8-trimethoxy-3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (42): The cyclization of **S42** was performed on 0.161 mmol scale with a total reaction time of 1 h. Purification by column chromatography eluting with hexanes/EtOAc provided 44 mg (90%) of **42** as a yellow oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 6.52 (s, 1H), 3.97 (s, 3H), 3.88 (s, 3H), 3.86 (s, 3H), 2.47 (dd, *J* = 15.7, 4.5 Hz, 1H), 2.26 – 2.12 (m, 2H), 1.95 – 1.79 (m, 3H), 1.37 (dtd, *J* = 12.7, 10.4, 5.7 Hz, 1H), 1.29 – 1.26 (m, 6H), 1.08 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 153.2, 151.2, 149.9, 139.8, 139.6, 136.7, 131.2, 97.8, 61.03, 60.95, 56.4, 49.4, 31.4, 30.6, 29.2, 22.63, 22.58, 21.8, 21.0; **IR** (Neat) 2930, 2831, 1640, 1602, 1581, 1456, 1411, 1388, 1373, 1345, 1290, 1263, 1228, 1197, 1160, 1104, 1023, 926, 825, 786, 733, 703. **HRMS**: calcd for $C_{19}H_{26}O_3^+$: 302.1882 found: 302.1889.



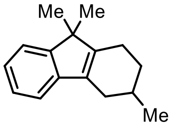
43

3,11,11-trimethyl-2,3,4,11-tetrahydro-1*H*-benzo[*b*]fluorine (43): The cyclization of **S43** was performed on 0.175 mmol scale with a total reaction time of 2 h. Purification by column chromatography eluting with hexanes/EtOAc provided 42 mg (91%) of **43** as a yellow oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 8.12 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.51 (ddd, *J* = 8.3, 6.7, 1.3 Hz, 1H), 7.44 (d, *J* = 8.2 Hz, 1H), 7.38 (ddd, *J* = 8.0, 6.8, 1.0 Hz, 1H), 2.70 – 2.64 (m, 1H), 2.42 – 2.30 (m, 2H), 2.12 – 2.06 (m, 1H), 1.99 – 1.89 (m, 2H), 1.50 – 1.43 (m, 7H), 1.14 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 152.0, 147.3, 141.1, 132.2, 132.0, 129.7, 129.0, 127.6, 125.6, 123.4, 123.3, 118.1, 50.3, 31.6, 30.7, 29.3, 23.9, 23.7, 21.9, 21.2; **IR** (Neat) 3055, 2958, 2925, 2869, 1644, 1584, 1516, 1456, 1435, 1359, 1264, 1209, 1142, 1020, 949, 891, 862, 815, 736, 702, 658. **HRMS**: calcd for $C_{20}H_{22}^+$: 262.1722 found: 262.1725.



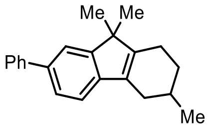
44

diethyl 7-(*tert*-butyl)-9,9-dimethyl-3-phenyl-1,3,4,9-tetrahydro-2*H*-fluorene-2,2-dicarboxylate (44): The cyclization of **S44** was performed on a 0.23 mmol scale with a total reaction time of 2.5 h. Purification by column chromatography eluting with hexanes/EtOAc provided 65 mg (60%) of **44** as a white foam.^{1}**H NMR** (700 MHz; CDCl$_3$) δ 7.41 (d, *J* = 1.8 Hz, 1H), 7.31 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.20 – 7.17 (m, 3H), 7.16 – 7.12 (m, 3H), 4.15 – 4.00 (m, 5H), 3.38 – 3.31 (m, 1H), 2.97 (d, *J* = 17.8 Hz, 1H), 2.78 – 2.72 (m, 2H), 1.37 (s, 9H), 1.31 (s, 3H), 1.25 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}**C NMR** (175 MHz; CDCl$_3$) δ 170.5, 170.3, 153.7, 148.2, 146.5, 142.3, 140.1, 132.0, 128.5, 128.4, 127.3, 123.5, 118.4, 117.9, 61.6, 61.5, 58.9, 49.2, 42.6, 35.0, 31.9, 27.5, 24.3, 23.8, 23.7, 14.14, 14.08; **IR** (Neat) 2955, 2904, 1733, 1483, 1462, 1453, 1363, 1269, 1246, 1209, 1177, 1085, 1056, 1026, 865, 825, 702. **HRMS**: calcd for $C_{31}H_{38}O_4Na^+$: 497.2662 found: 497.2661.



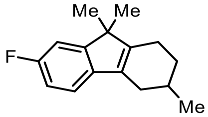
45

3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (45): The cyclization of **S45** was performed on a 0.22 mmol scale with a total reaction time of 2.5 h. Purification by column chromatography eluting with hexanes/EtOAc provided 26 mg (55%) of **45** as a clear oil. ^{1}**H NMR** (400 MHz; CDCl$_3$) δ 7.31 (dt, *J* = 7.2, 1.0 Hz, 1H), 7.26 – 7.20 (m, 1H), 7.20 – 7.10 (m, 2H), 2.61 – 2.50 (m, 1H), 2.33 – 2.16 (m, 2H), 2.05 – 1.79 (m, 3H), 1.50 – 1.34 (m, 1H), 1.25 – 1.19 (m, 6H), 1.11 (d, *J* = 6.5 Hz, 3H); ^{13}**C NMR** (100 MHz; CDCl$_3$) δ 154.0, 150.2, 143.8, 132.1, 126.4, 124.1, 121.0, 117.8, 48.6, 31.5, 30.5, 29.2, 24.1, 24.0, 21.9, 21.3; **IR** (Neat) 2952, 2919, 2867, 2829, 1636, 1602, 1470, 1453, 1375, 1356, 1253, 1141, 1018, 927, 747. **HRMS**: calcd for $C_{16}H_{20}^+$: 212.1565 found: 212.1567.



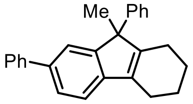
46

3,9,9-trimethyl-7-phenyl-2,3,4,9-tetrahydro-1*H*-fluorene (46): The cyclization of **S46** was performed on a 0.17 mmol scale with a total reaction time of 1.5 h. Purification by column chromatography eluting with hexanes/EtOAc provided 42 mg (87%) of **46** as a white solid. ^{1}**H NMR** (400 MHz; CDCl$_3$) δ 7.67 – 7.61 (m, 2H), 7.56 – 7.52 (m, 1H), 7.50 – 7.41 (m, 3H), 7.35 – 7.29 (m, 1H), 7.23 (d, *J* = 7.7 Hz, 1H), 2.62 – 2.53 (m, 1H), 2.35 – 2.18 (m, 2H), 2.07 – 1.96 (m, 1H), 1.96 – 1.83 (m, 2H), 1.49 – 1.37 (m, 1H), 1.31 – 1.21 (m, 6H), 1.11 (d, *J* = 6.5 Hz, 3H); ^{13}**C NMR** (175 MHz; CDCl$_3$) δ 154.7, 150.9, 143.1, 142.4, 137.4, 131.9, 128.8, 127.3, 126.8, 125.6, 120.1, 118.0, 48.8, 31.5, 30.6, 29.2, 24.2, 24.1, 21.9, 21.4; **IR** (Neat) 2952, 2921, 2866, 2829, 1599, 1471, 1456, 1375, 1356, 1230, 1144, 1033, 887, 825, 769, 754, 696. **HRMS**: calcd for $C_{22}H_{24}^{+}$: 288.1878 found: 288.1876.



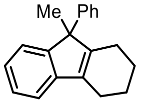
47

7-fluoro-3,9,9-trimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (47): The cyclization of **S47** was performed on 0.207 mmol scale with a total reaction time of 2 h. Purification by column chromatography eluting with hexanes/EtOAc provided 42 mg (88%) of **47** as a clear oil. **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.02 (ddd, *J* = 11.3, 8.5, 3.7 Hz, 2H), 6.93 – 6.86 (m, 1H), 2.50 (dd, *J* = 16.3, 3.5 Hz, 1H), 2.30 – 2.12 (m, 2H), 2.00 – 1.78 (m, 3H), 1.44 – 1.32 (m, 1H), 1.21 – 1.15 (m, 6H), 1.08 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (100 MHz; $CDCl_3$) δ 161.3 (d, *J* = 241.6 Hz), 156.2 (d, *J* = 7.4 Hz), 149.8 (d, *J* = 3.9 Hz), 139.5 (d, *J* = 2.2 Hz), 131.4 (d, *J* = 0.5 Hz), 118.1 (d, *J* = 8.5 Hz), 112.7 (d, *J* = 22.5 Hz), 109.1 (d, *J* = 22.8 Hz), 48.8 (d, *J* = 2.1 Hz), 31.4, 30.6, 29.1, 24.1, 24.0, 21.9, 21.3; **IR** (Neat) 2952, 2924, 2830, 1637, 1592, 1508, 1481, 1469, 1430, 1376, 1358, 1345, 1267, 1253, 1231, 1185, 1135, 1055, 973, 934, 884, 863, 814, 795, 725, 682, 668. **HRMS**: calcd for $C_{16}H_{19}F^{+}$: 230.1471 found: 230.1473.



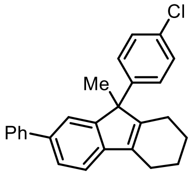
48

9-methyl-7,9-diphenyl-2,3,4,9-tetrahydro-1*H*-fluorene (48): The cyclization of **S48** was performed on 0.141 mmol scale with a total reaction time of 44 h. Purification by column chromatography eluting with hexanes/EtOAc provided 36 mg (76%) of **48** as a white solid. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.55 – 7.52 (m, 2H), 7.48 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.32 – 7.21 (m, 5H), 7.18 – 7.11 (m, 3H), 2.59 – 2.45 (m, 2H), 2.23 – 2.11 (m, 1H), 1.96 – 1.69 (m, 5H), 1.66 (s, 3H); **^{13}C NMR** (175 MHz; $CDCl_3$) δ 155.1, 151.6, 143.7, 143.3, 142.0, 137.8, 133.9, 128.7, 128.5, 127.2, 126.8, 126.4, 126.3, 125.7, 121.4, 118.2, 56.8, 23.2, 22.8, 22.3, 22.1, 21.5; **IR** (Neat) 3027, 2927, 1636, 1598, 1491, 1472, 1443, 1264, 1158, 1131, 1074, 1027, 890, 832, 761, 735, 695, 634. **HRMS**: calcd for $C_{26}H_{24}^{+}$: 336.1878 found: 336.1876.



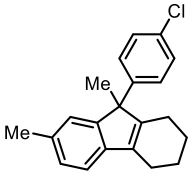
49

9-methyl-9-phenyl-2,3,4,9-tetrahydro-1*H*-fluorene (49): The cyclization of **S49** was performed on 0.180 mmol scale with a total reaction time of 21 h. Purification by column chromatography eluting with hexanes/EtOAc provided 21 mg (45%) of **49** as a clear oil. **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.25 – 7.19 (m, 4H), 7.18 – 7.12 (m, 1H), 7.11 – 7.04 (m, 4H), 2.56 – 2.41 (m, 2H), 2.21 – 2.07 (m, 1H), 1.93 – 1.66 (m, 5H), 1.61 (s, 3H); **^{13}C NMR** (125 MHz; $CDCl_3$) δ 154.5, 150.9, 144.4, 143.5, 134.1, 128.4, 126.5, 126.4, 126.2, 124.7, 122.4, 118.0, 56.6, 23.2, 22.8, 22.3, 22.0, 21.3; **IR** (Neat) 3014, 2926, 2853, 1953, 1899, 1803, 1743, 1680, 1637, 1596, 1492, 1468, 1443, 1367, 1272, 1235, 1152, 1130, 1103, 1059, 1027, 950, 931, 911, 853, 821, 777, 741, 696, 683, 653, 632. **HRMS**: calcd for $C_{20}H_{20}^{+}$: 260.1565 found: 260.1565.



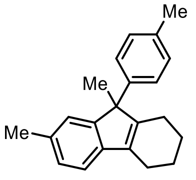
50

9-(4-chlorophenyl)-9-methyl-7-phenyl-2,3,4,9-tetrahydro-1*H*-fluorene (50): The cyclization of **S50** was performed on 0.129 mmol scale with a total reaction time of 62 h. Purification by column chromatography eluting with hexanes/EtOAc provided 33 mg (70%) of **50** as a yellow solid. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 7.53 (d, *J* = 7.3 Hz, 2H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.30 – 7.24 (m, 3H), 7.11 (dd, *J* = 71.7, 8.5 Hz, 4H), 2.60 – 2.42 (m, 2H), 2.21 – 2.10 (m, 1H), 1.91 – 1.66 (m, 5H), 1.63 (s, 3H); **^{13}C NMR** (125 MHz; CDCl$_3$) δ 154.7, 151.1, 143.6, 142.0, 141.8, 138.1, 134.3, 132.1, 128.8, 128.6, 127.9, 127.2, 126.9, 125.9, 121.3, 118.4, 56.4, 23.2, 22.8, 22.3, 22.0, 21.4; **IR** (Neat) 2926, 1649, 1637, 1598, 1489, 1472, 1389, 1178, 1132, 1124, 1092, 1076, 1037, 1011, 924, 889, 814, 769, 755, 716, 696. **HRMS**: calcd for $C_{26}H_{23}Cl^{+}$: 370.1488 found: 370.1486.



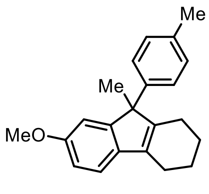
51

9-(4-chlorophenyl)-7,9-dimethyl-2,3,4,9-tetrahydro-1H-fluorene (51): The cyclization of **S51** was performed on 0.214 mmol scale with a total reaction time of 84 h. Purification by column chromatography eluting with hexanes/EtOAc provided 30 mg (47%) of **51** as a yellow oil. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 7.21 – 7.16 (m, 2H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.06 – 7.03 (m, 1H), 7.03 – 6.99 (m, 2H), 6.88 – 6.86 (m, 1H), 2.54 – 2.40 (m, 2H), 2.30 (s, 3H), 2.15 – 2.07 (m, 1H), 1.87 – 1.65 (m, 5H), 1.58 (s, 3H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ 154.3, 149.4, 142.4, 141.6, 134.5, 134.3, 131.9, 128.5, 127.9, 127.3, 123.3, 117.9, 56.0, 23.2, 22.8, 22.3, 21.8, 21.6, 21.3; **IR** (neat) 2923, 1489, 1456, 1263, 1092, 1012, 812, 735. **HRMS**: calcd for $C_{21}H_{21}Cl^{+}$: 308.1332 found: 308.1339.



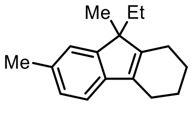
52

7,9-dimethyl-9-(*p*-tolyl)-2,3,4,9-tetrahydro-1*H*-fluorene (52): The cyclization of **S52** was performed on 0.228 mmol scale with a total reaction time of 84 h. Purification by column chromatography eluting with hexanes/EtOAc provided 28 mg (45%) of **52** as a yellow oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.09 (d, *J* = 7.5 Hz, 1H), 7.03 (t, *J* = 8.9 Hz, 3H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.90 (s, 1H), 2.54 – 2.40 (m, 2H), 2.29 (s, 6H), 2.16 – 2.07 (m, 1H), 1.90 – 1.65 (m, 5H), 1.58 (s, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 154.8, 149.9, 141.7, 140.7, 135.6, 134.3, 133.8, 129.1, 127.1, 126.3, 123.3, 117.6, 56.1, 23.3, 22.9, 22.3, 21.9, 21.7, 21.5, 21.1; **IR** (Neat) 2922, 2855, 1699, 1684, 1652, 1635, 1616, 1575, 1558, 1539, 1509, 1456, 1380, 1310, 1265, 1187, 1126, 1056, 1037, 1018, 921, 812, 762, 736 702. **HRMS**: calcd for $C_{22}H_{24}^+$: 288.1878 found: 288.1873.



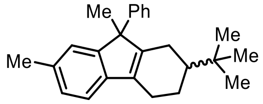
53

7-methoxy-9-methyl-9-(*p*-tolyl)-2,3,4,9-tetrahydro-1*H*-fluorene (53): The cyclization of **S53** was performed on 0.217 mmol scale with a total reaction time of 48 h. Purification by column chromatography eluting with hexanes/EtOAc provided 44 mg (67%) of **53** as a yellow oil. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 7.09 (d, *J* = 8.1 Hz, 1H), 7.00 (dd, *J* = 26.5, 8.1 Hz, 4H), 6.75 (dd, *J* = 8.1, 2.3 Hz, 1H), 6.68 (d, *J* = 2.3 Hz, 1H), 3.73 (s, 3H), 2.53 – 2.36 (m, 2H), 2.28 (s, 3H), 2.16 – 2.07 (m, 1H), 1.89 – 1.64 (m, 5H), 1.57 (s, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 157.9, 156.3, 148.8, 140.6, 137.5, 135.6, 133.4, 129.1, 126.3, 118.2, 111.3, 109.6, 56.3, 55.6, 23.3, 22.9, 22.4, 21.9, 21.6, 21.1; **IR** (Neat) 2930, 2830, 1606, 1582, 1558, 1539, 1509, 1477, 1456, 1380, 1269, 1235, 1187, 1159, 1129, 1091, 1033, 1019, 897, 871, 813, 778, 757, 733, 702. **HRMS**: calcd for $C_{22}H_{25}O^+$: 305.1900 found: 305.1899.



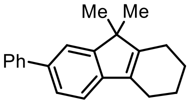
54

9-ethyl-7,9-dimethyl-2,3,4,9-tetrahydro-1*H*-fluorene (54): The cyclization of **S54** was performed on 0.225 mmol scale with a total reaction time of 6 days. Purification by column chromatography eluting with hexanes/EtOAc provided 37 mg (72%) of **54** as a yellow oil. **^{1}H NMR** (700 MHz; CDCl$_3$) δ 7.06 (s, 1H), 7.05 – 7.01 (m, 2H), 2.45 – 2.34 (m, 5H), 2.19 – 2.02 (m, 2H), 1.84 – 1.75 (m, 5H), 1.66 (dq,*J* = 14.6, 7.4 Hz, 1H), 1.17 (s, 3H), 0.32 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 151.9, 147.1, 142.6, 133.8, 133.4, 126.8, 122.1, 117.2, 52.8, 30.3, 23.8, 23.3, 23.0, 22.2, 21.82, 21.75, 8.7; **IR** (Neat) 2959, 2926, 2860, 1722, 1713, 1686, 1642, 1608, 1452, 1379, 1265, 1171, 1162, 1153, 1129, 1107, 1090, 1084, 1072, 1054, 1000, 922, 812, 737, 704. **HRMS**: calcd for $C_{17}H_{22}^+$: 226.1722 found: 226.1719.



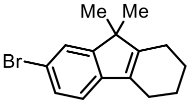
55

2-(tert-butyl)-7,9-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-fluorene (55): The cyclization of **S55** was performed on 0.226 mmol scale with a total reaction time of 1.5 h. The yield was determined to be 55% by ^{1}H NMR using dimethyl terephthalate as an internal standard, and the crude diastereomeric ratio was estimated to be 1.5:1 by ^{1}H-NMR. An analytically pure sample of **55** was obtained as a clear oil. ^{1}**H NMR** (for the mixture of diastereomers; 700 MHz; C_6D_6) δ 7.24 – 7.17 (m, 3H), 7.11 (t, *J* = 7.6 Hz, 2H), 7.08 – 7.05 (m, 1H), 7.04 – 7.01 (m, 1H), 6.99 – 6.97 (m, 1H), 2.64 – 2.53 (m, 1H), 2.41 – 2.26 (m, 1H), 2.24 – 2.18 (m, 0.4H), 2.16 – 2.12 (m, 3H), 2.06 – 2.00 (m, 0.6H), 1.98 – 1.92 (m, 0.6H), 1.91 – 1.85 (m, 1H), 1.80 – 1.72 (m, 0.4H), 1.65 – 1.61 (m, 3H), 1.44 – 1.30 (m, 1H), 1.29 – 1.19 (m, 1H), 0.77 (s, 9H); ^{13}**C NMR** (for the mixture of diastereomers; 175 MHz; C_6D_6) δ 155.7, 155.6, 150.34, 150.28, 144.2, 143.9, 141.8, 141.7, 134.62, 134.59, 134.47, 134.45, 128.76, 128.74, 128.5, 127.6, 126.73, 126.70, 126.5, 123.85, 123.83, 118.29, 118.28, 56.9, 56.6, 45.7, 45.4, 32.5, 32.4, 27.4, 24.68, 24.65, 23.72, 23.67, 23.66, 23.5, 21.8, 21.6, 21.5; **IR** (Neat) 3084, 3058, 3021, 2961, 2916, 2869, 2836, 1599, 1494, 1476, 1365, 1028, 910, 814, 698. **HRMS**: calcd for $C_{25}H_{30}^+$: 330.2348 found: 330.2361.



74

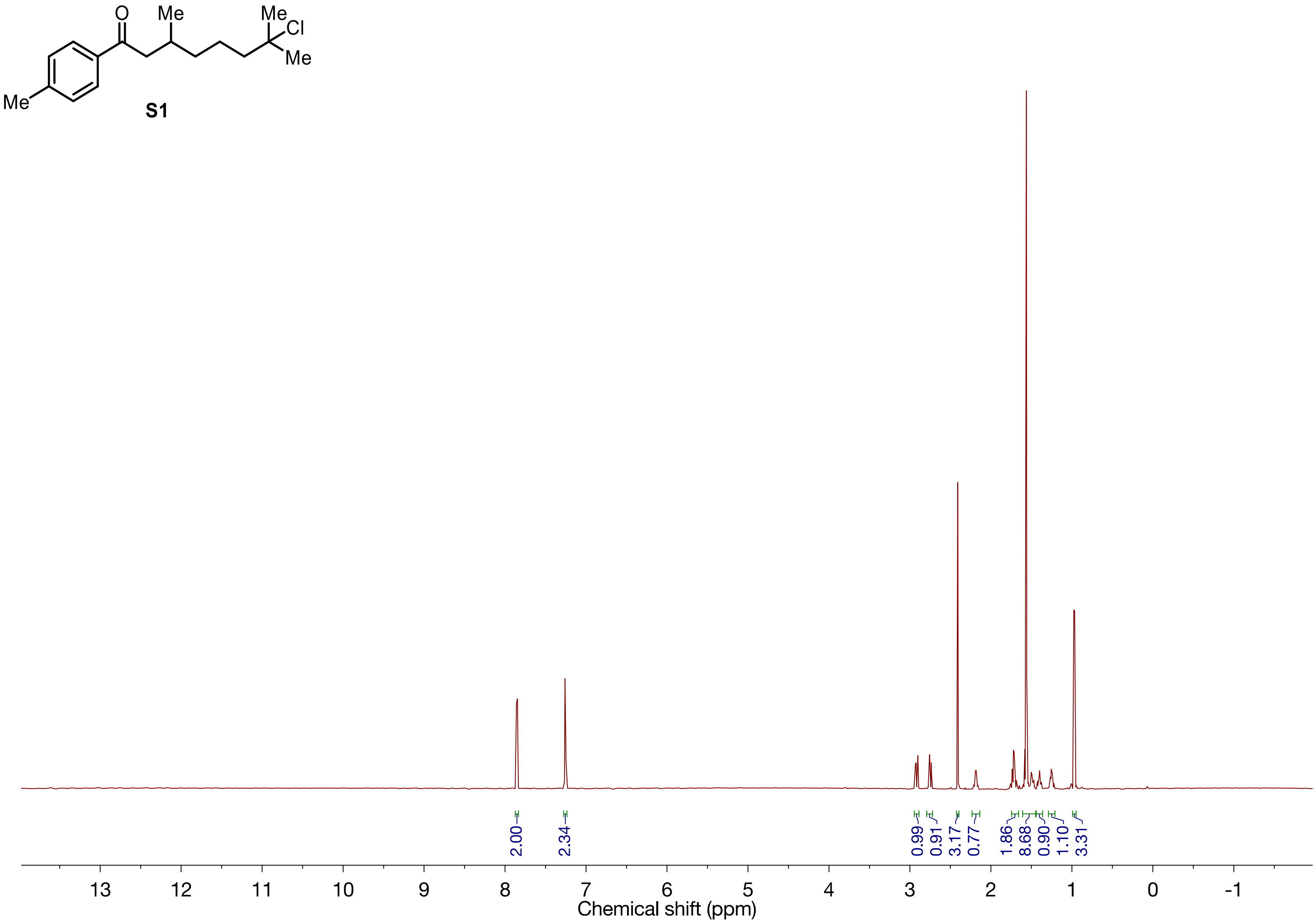
9,9-dimethyl-7-phenyl-2,3,4,9-tetrahydro-1H-fluorene (74): The cyclization of **60a** was performed on 0.226 mmol scale with a total reaction time of 2 h. Purification by column chromatography eluting with hexanes/EtOAc provided 45 mg (73%) of **74** as a yellow oil. The cyclization of **70a** was performed on 0.226 mmol scale with a total reaction time of 2 h. Purification by column chromatography eluting with hexanes/EtOAc provided 39 mg (63%) of **74** as a yellow oil. The cyclization of **74a** was performed on 0.226 mmol scale with a total reaction time of 2 h. Purification by column chromatography eluting with hexanes/EtOAc provided 40 mg (65%) of **74** as a yellow oil. ^{1}**H NMR** (700 MHz; $CDCl_3$) δ 7.65 – 7.61 (m, 2H), 7.54 – 7.51 (m, 1H), 7.47 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.43 (td, *J* = 7.8, 1.4 Hz, 2H), 7.31 (td, *J* = 7.3, 1.4 Hz, 1H), 7.22 (d, *J* = 7.7 Hz, 1H), 2.46 – 2.40 (m, 2H), 2.26 – 2.20 (m, 2H), 1.85 – 1.77 (m, 4H), 1.25 (s, 6H); ^{13}**C NMR** (175 MHz; $CDCl_3$) δ 154.4, 151.2, 143.2, 142.4, 137.4, 132.1, 128.8, 127.3, 126.8, 125.6, 120.1, 118.0, 49.0, 24.1, 23.2, 23.0, 22.2, 21.7; **IR** (Neat) 3059, 3028, 2954, 2925, 2857, 2829, 1599, 1472, 1147, 1074, 833, 769, 756, 710. **HRMS**: calcd for $C_{21}H_{22}^+$: 274.1722 found: 274.1715.

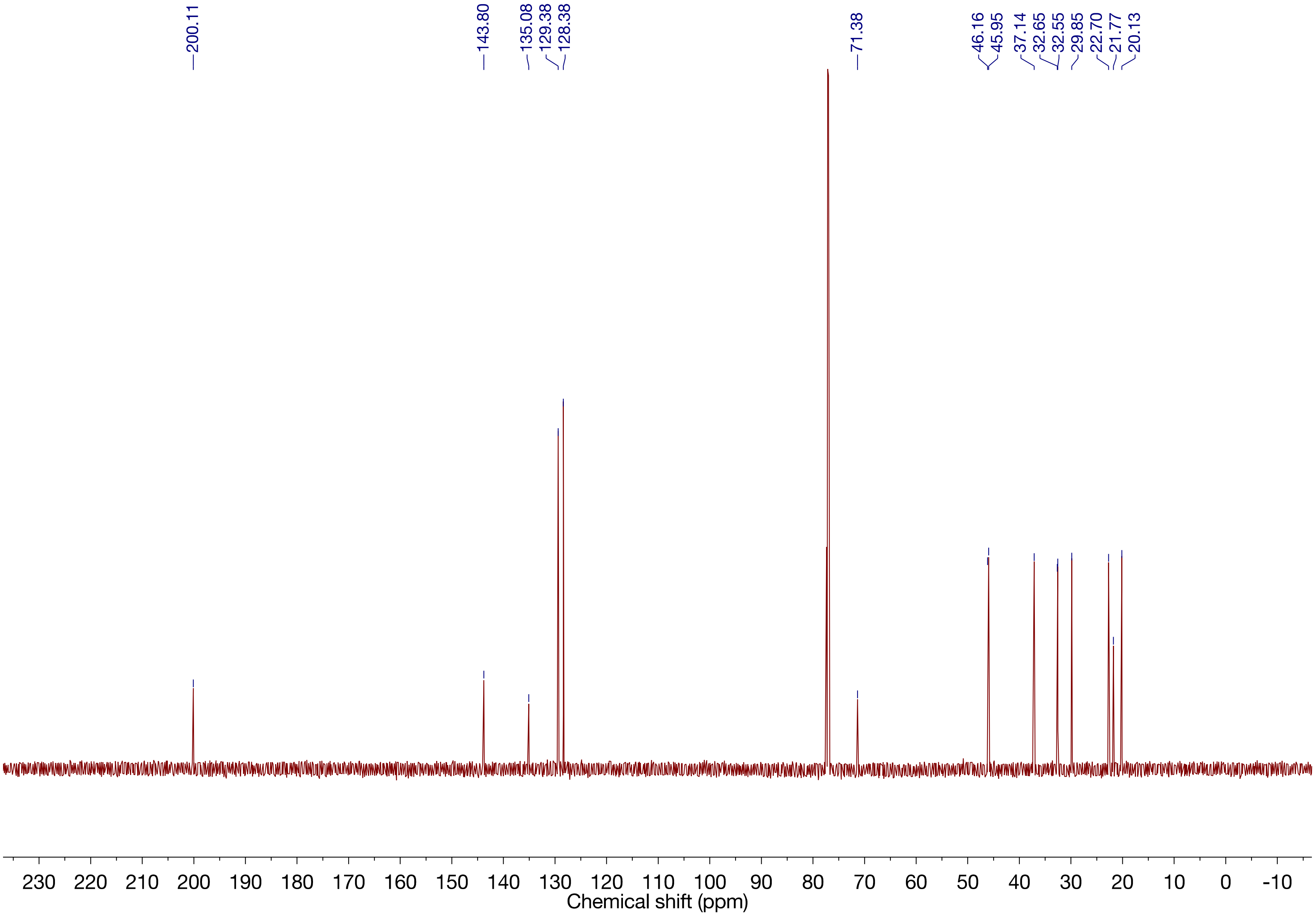


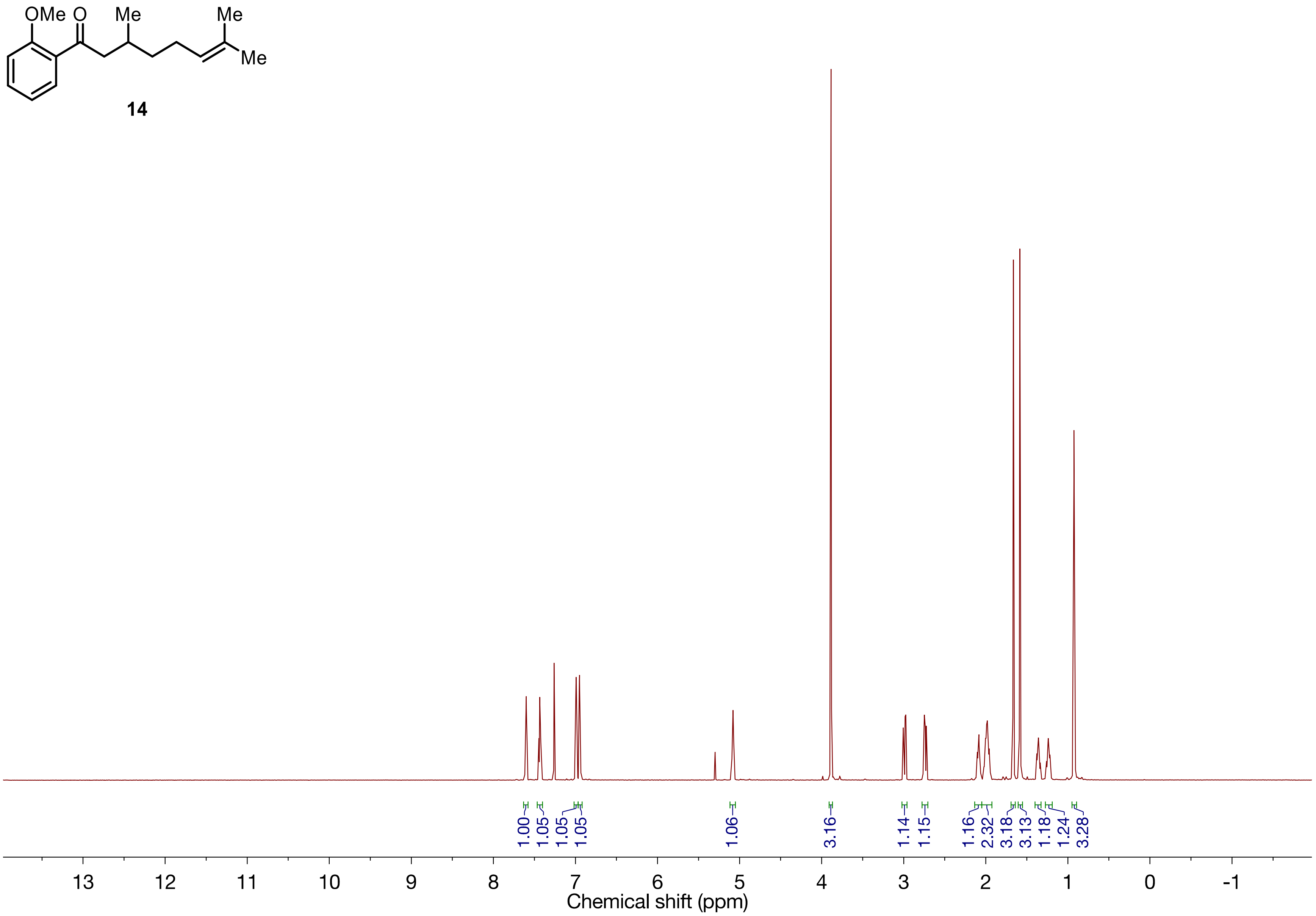
76

7-bromo-9,9-dimethyl-2,3,4,9-tetrahydro-1H-fluorene (76): The cyclization of **75** was performed on 0.227 mmol scale with a total reaction time of 7 days. The yield was determined to be 48% by ^{1}H-NMR using dimethyl terephthalate as an internal standard. An analytically pure sample of **76** was obtained as a clear oil. **^{1}H NMR** (500 MHz; CDCl$_3$) δ 7.40 (d, *J* = 1.8 Hz, 1H), 7.33 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.00 (d, *J* = 7.9 Hz, 1H), 2.39 – 2.33 (m, 2H), 2.20 – 2.14 (m, 2H), 1.82 – 1.75 (m, 4H), 1.18 (s, 6H); **^{13}C NMR** (175 MHz; CDCl$_3$) δ 155.9, 151.1, 142.8, 131.7, 129.3, 124.6, 119.1, 118.1, 49.2, 23.8, 23.0, 22.8, 22.0, 21.6; **IR** (Neat) 2930, 2864, 1635, 1454, 1394, 1264, 1070, 1010, 813, 735. **HRMS**: calcd for $C_{15}H_{17}Br^+$: 276.0514 found: 276.0515.

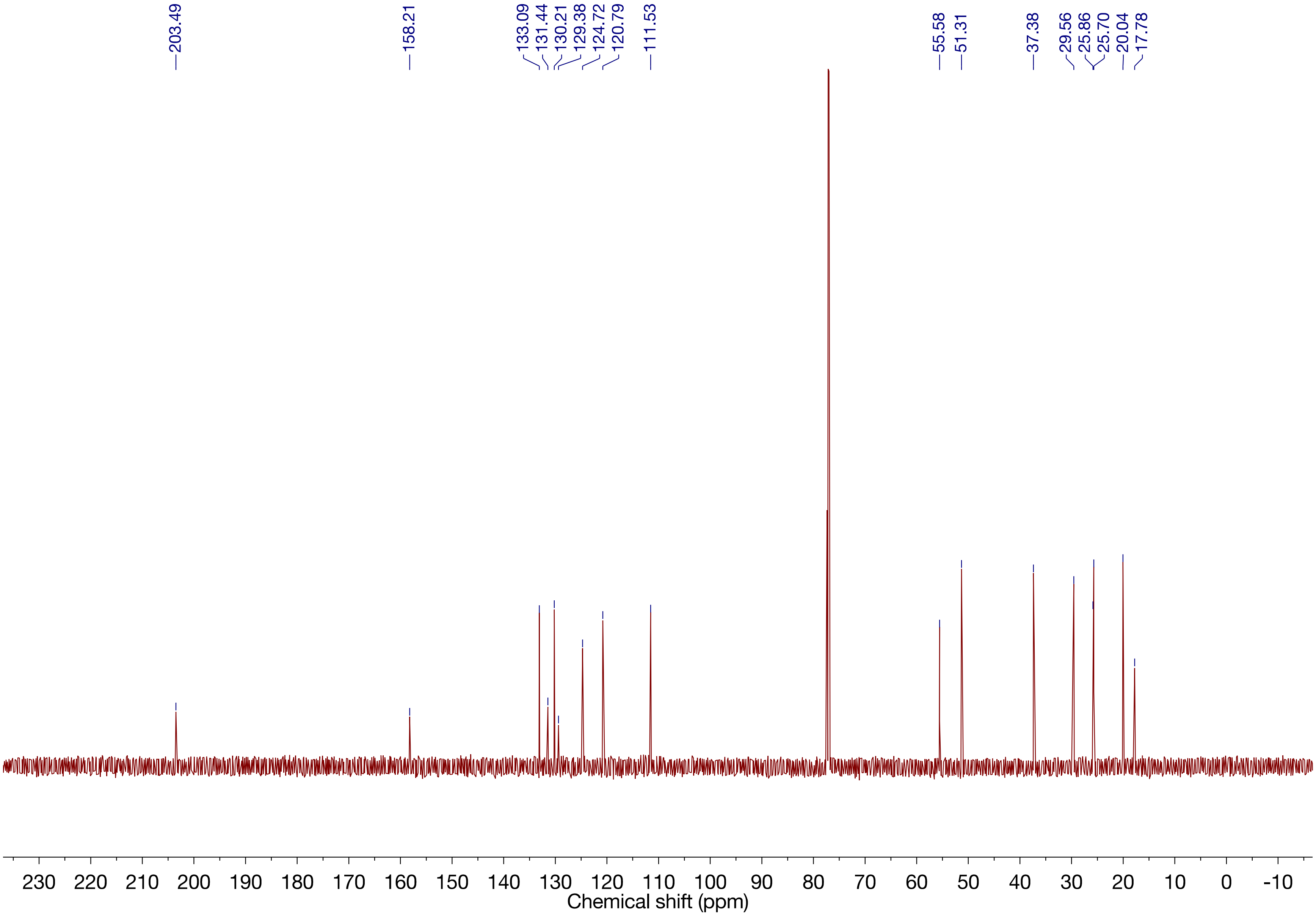
10. ^{1}H & ^{13}C NMR Spectra

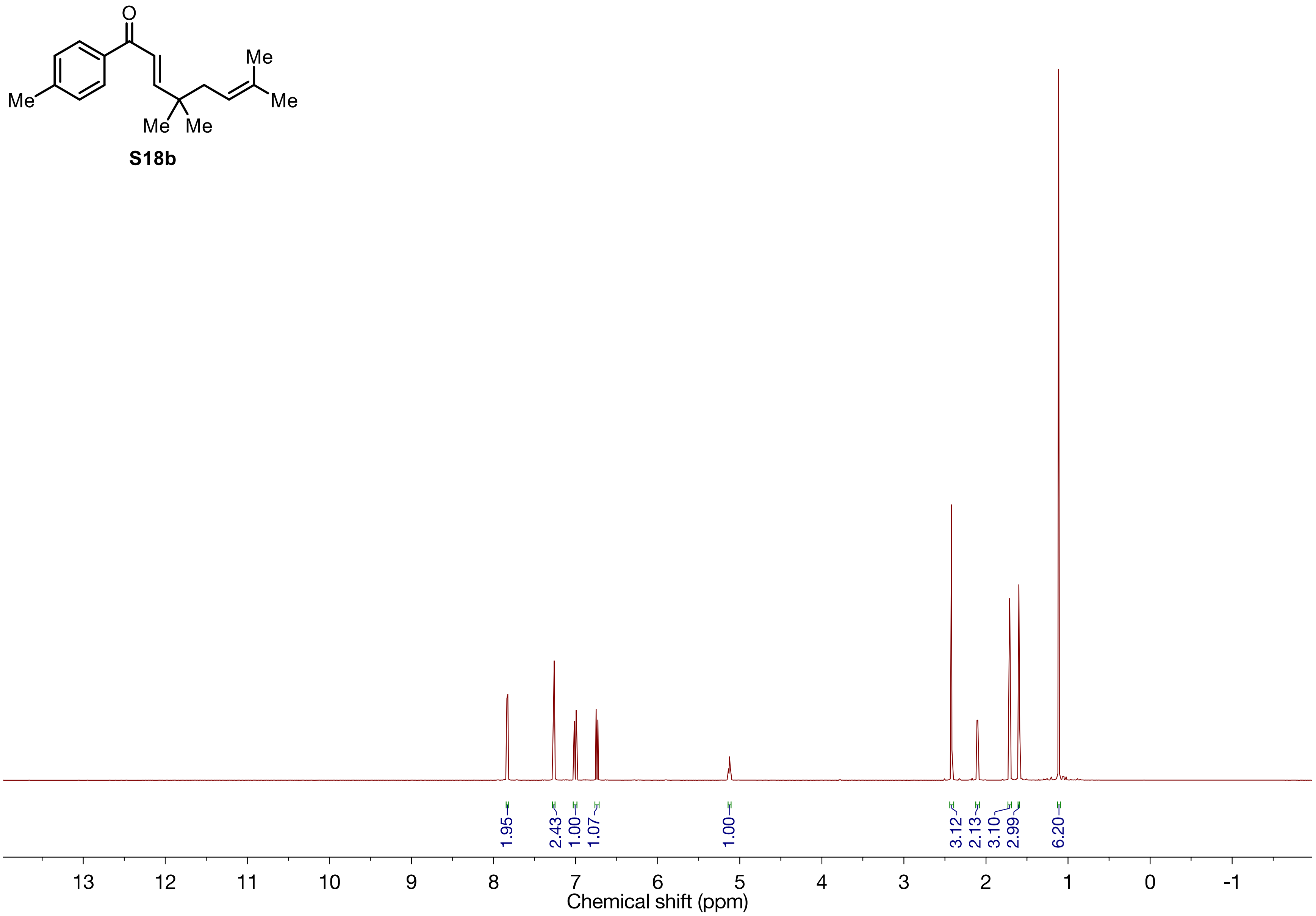

S1


200.11
143.80
135.08
129.38
128.38
71.38
46.16
45.95
37.14
32.65
32.55
29.85
22.70
21.77
20.13
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


OMe
O
Me
Me
Me
1.00
1.05
1.05
1.05
1.06
3.16
1.14
1.15
1.16
2.32
3.18
3.13
1.18
1.24
3.28
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

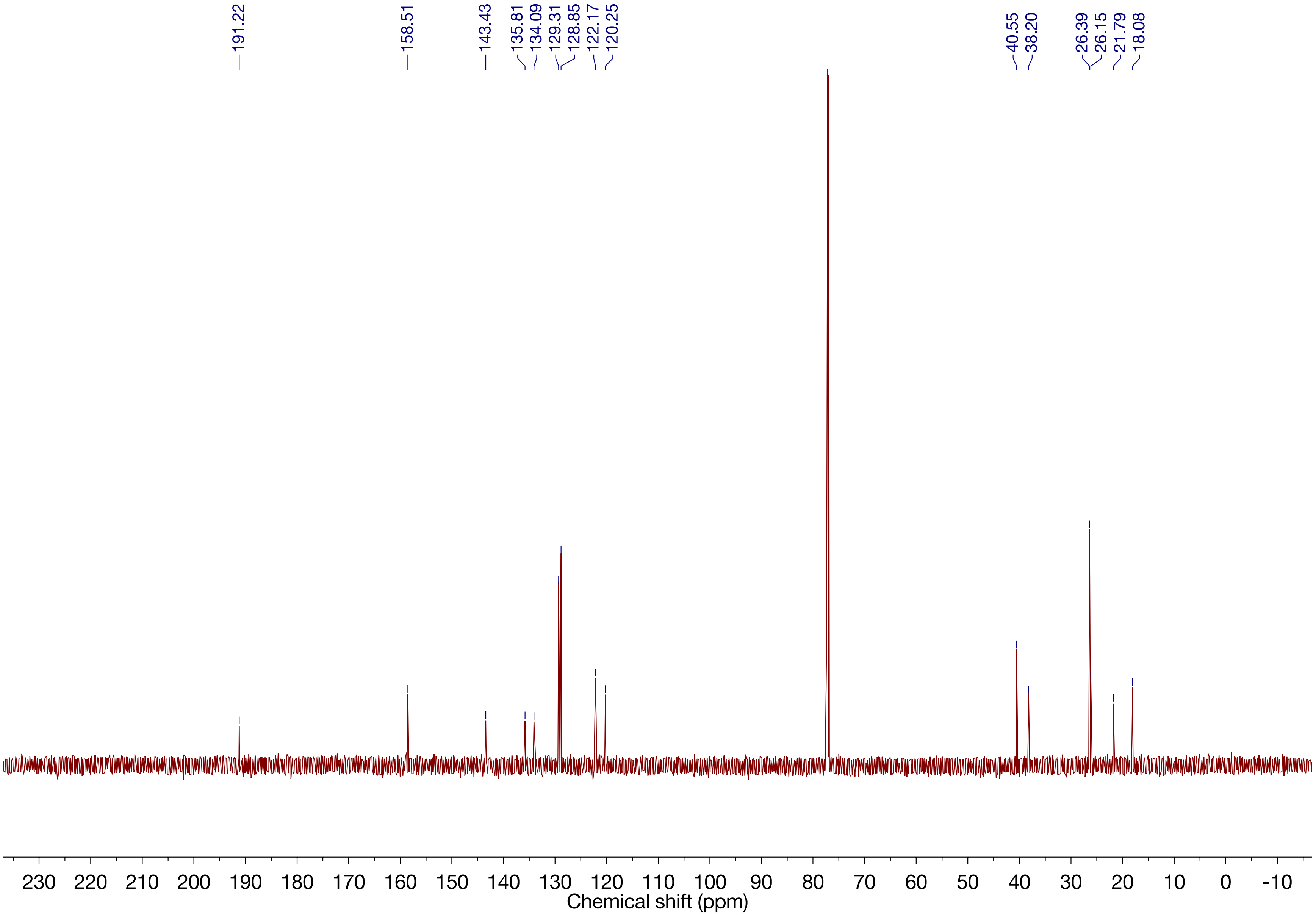
14

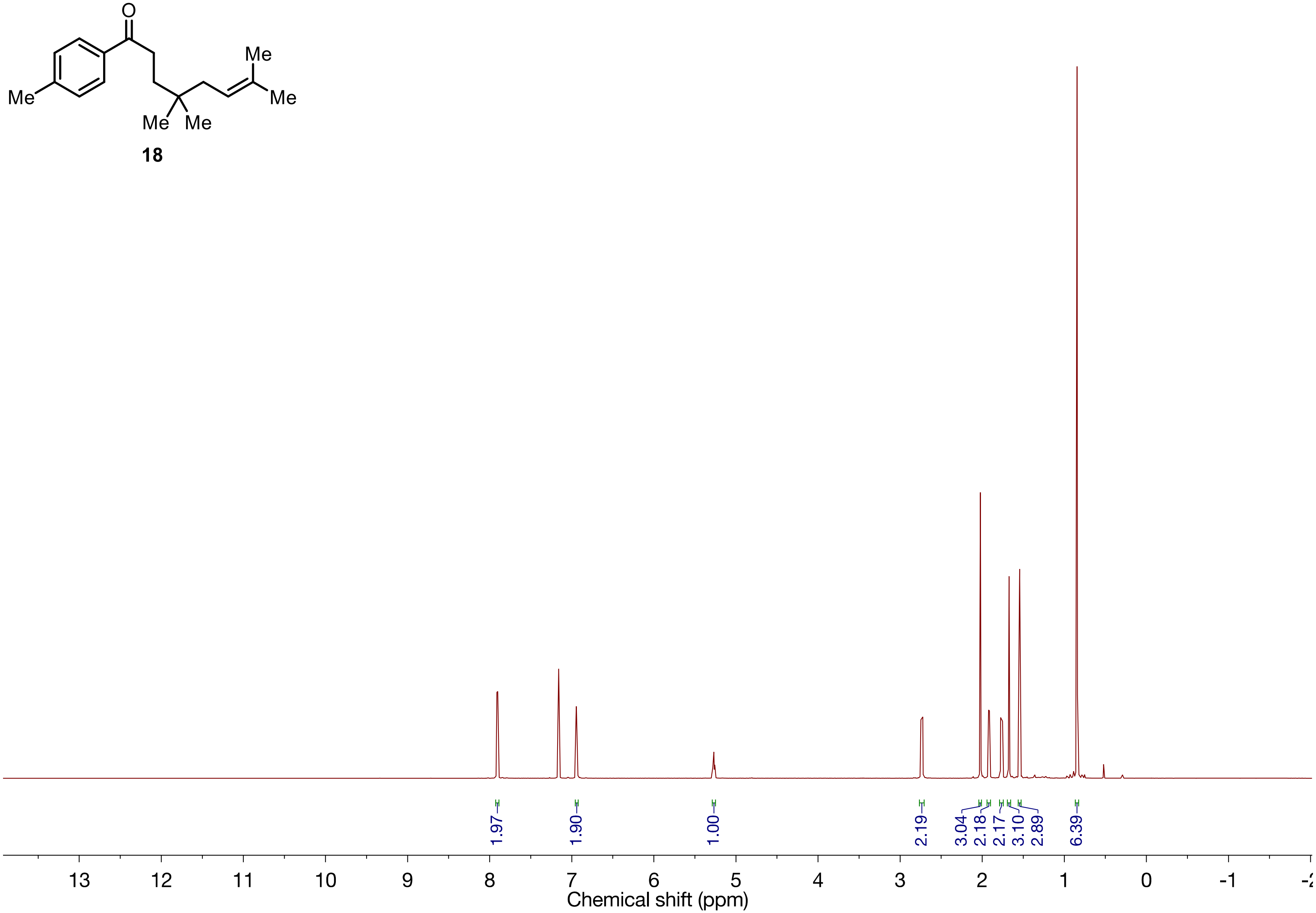

203.49
158.21
133.09
131.44
130.21
129.38
124.72
120.79
111.53
55.58
51.31
37.38
29.56
25.86
25.70
20.04
17.78
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



S18b

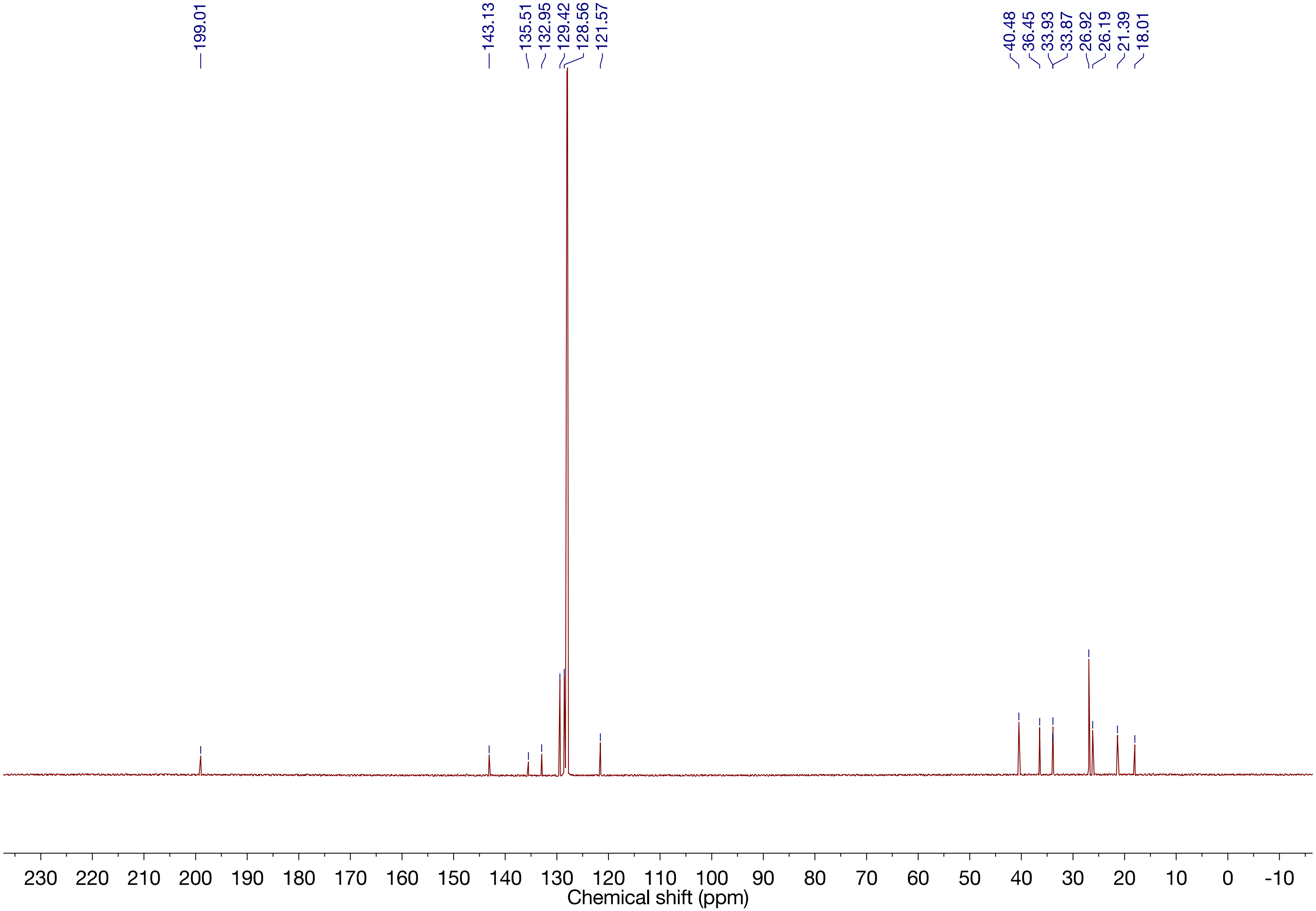
O
Me
Me
Me
Me
Me
1.95
2.43
1.00
1.07
1.00
3.12
2.13
3.10
2.99
6.20
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

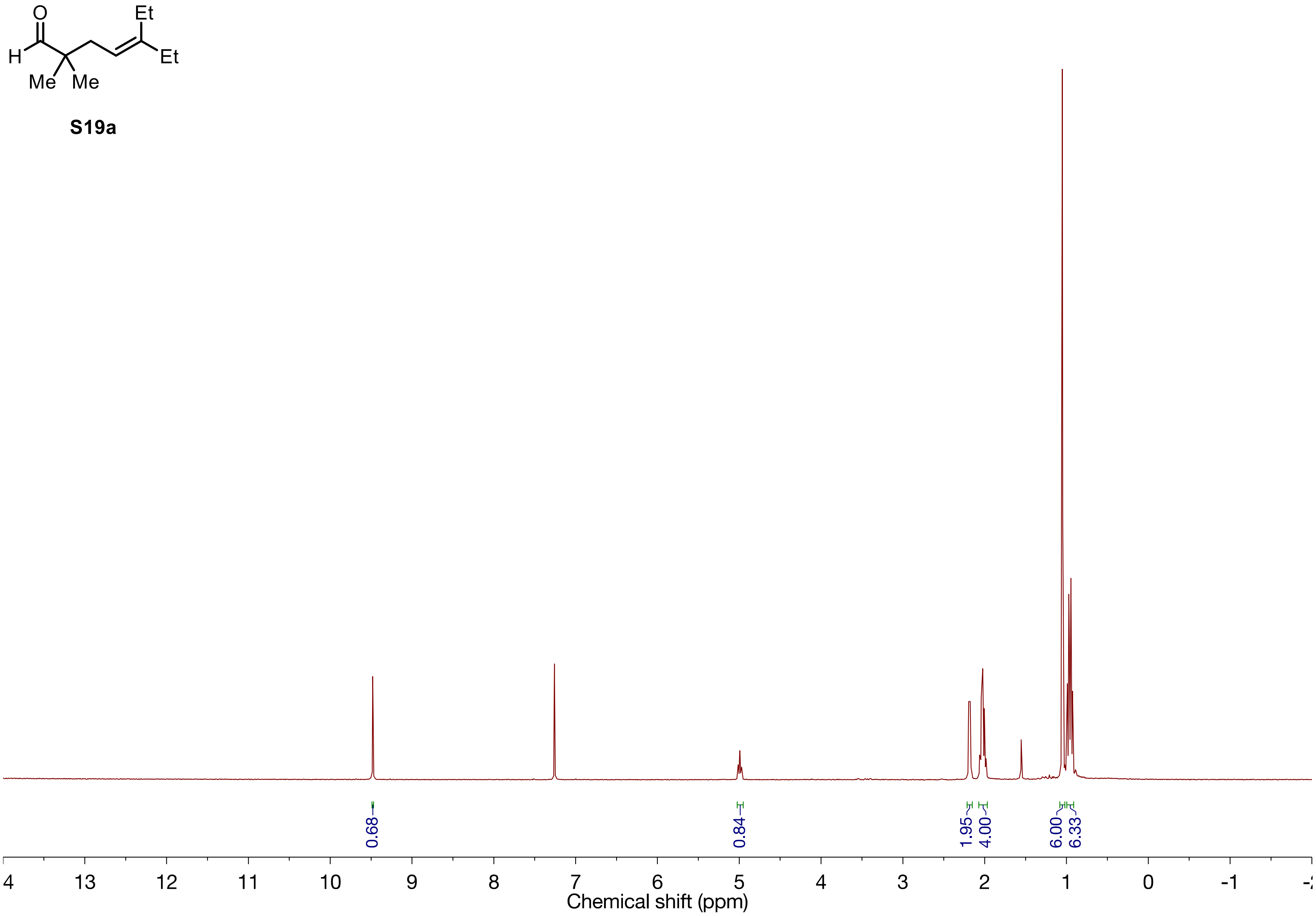

191.22
158.51
143.43
135.81
134.09
129.31
128.85
122.17
120.25
40.55
38.20
26.39
26.15
21.79
18.08
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



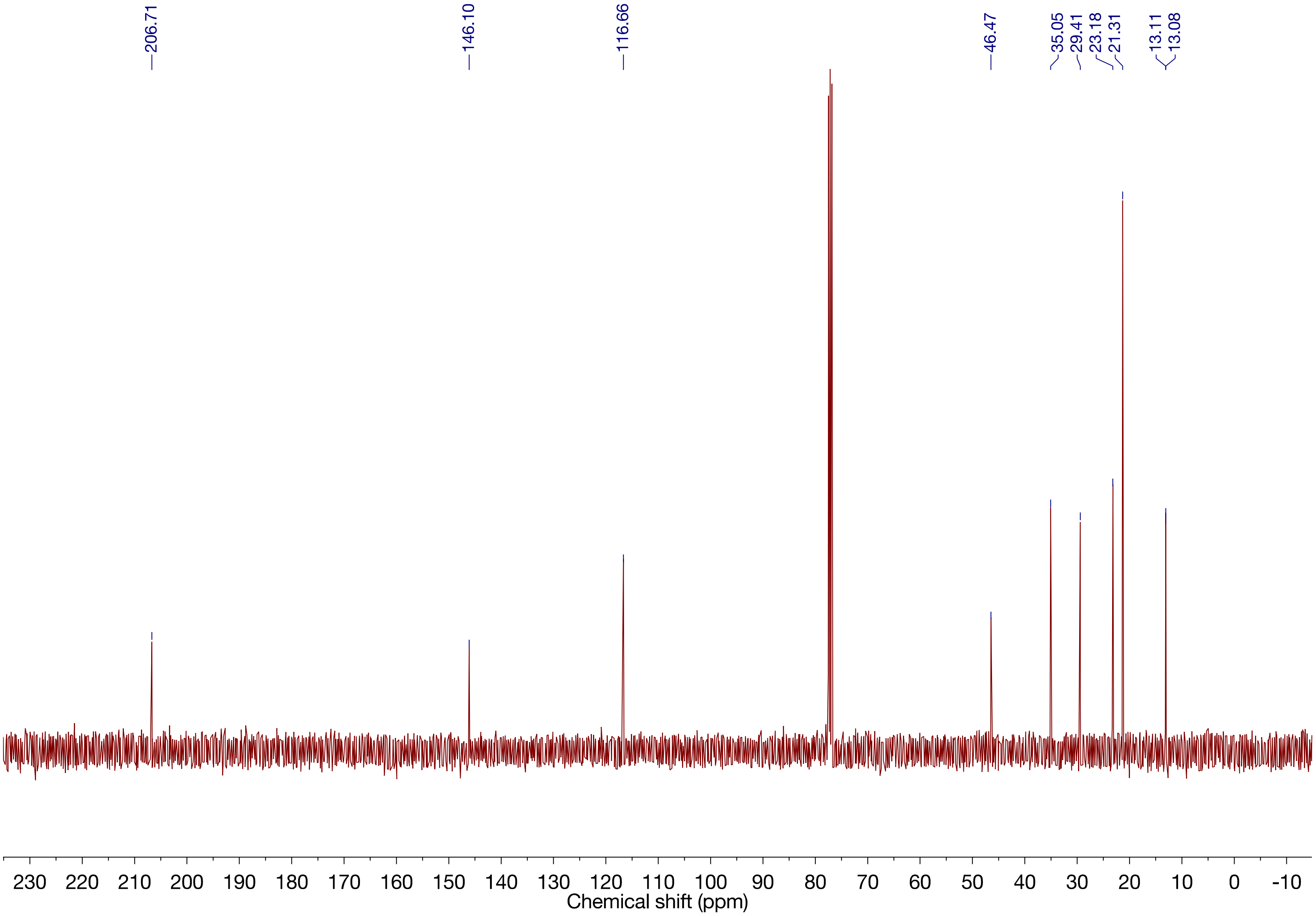
18

1.97
1.90
1.00
2.19
3.04
2.18
2.17
3.10
2.89
6.39
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
Chemical shift (ppm)

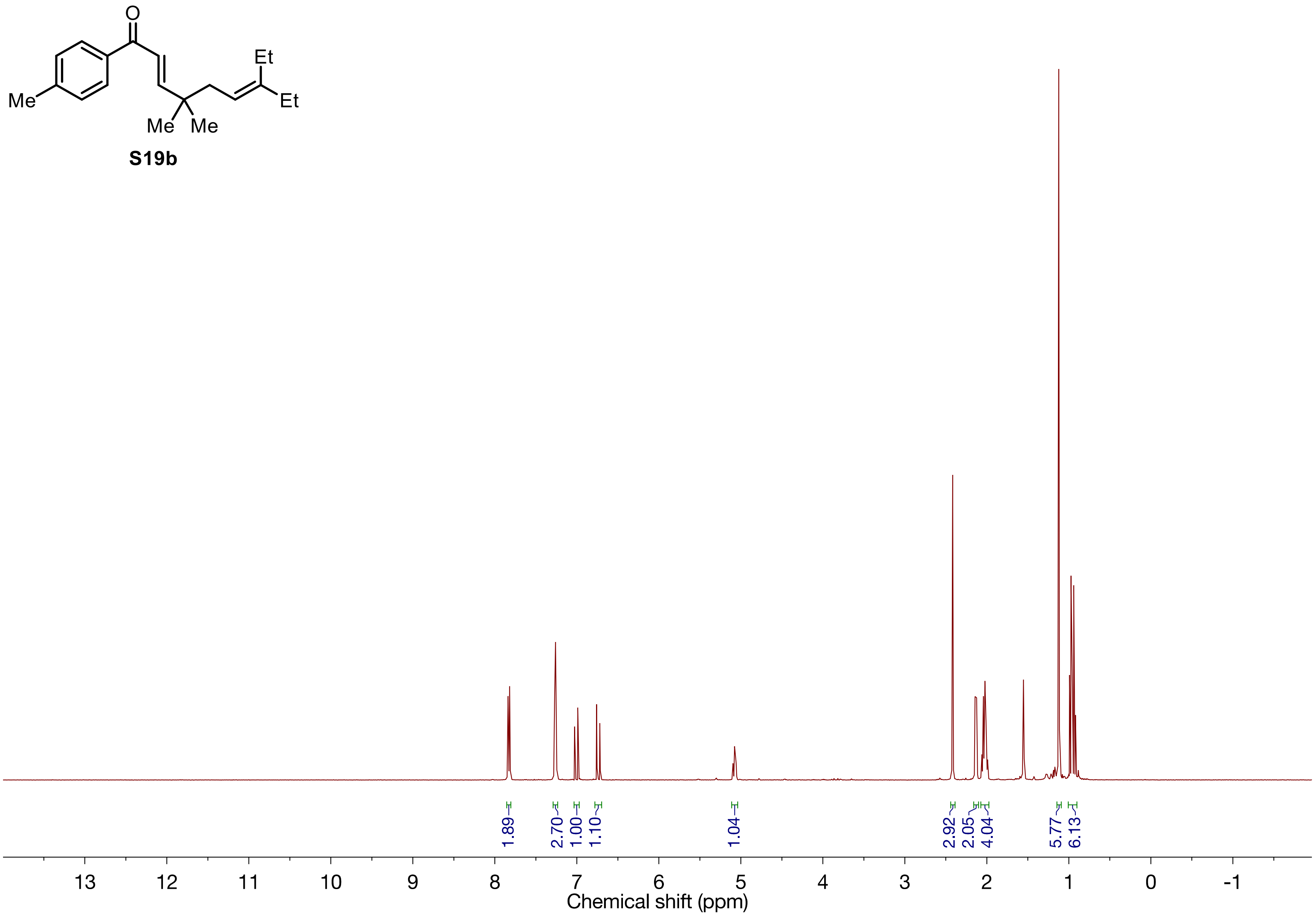

199.01
143.13
135.51
132.95
129.42
128.56
121.57
40.48
36.45
33.93
33.87
26.92
26.19
21.39
18.01
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)

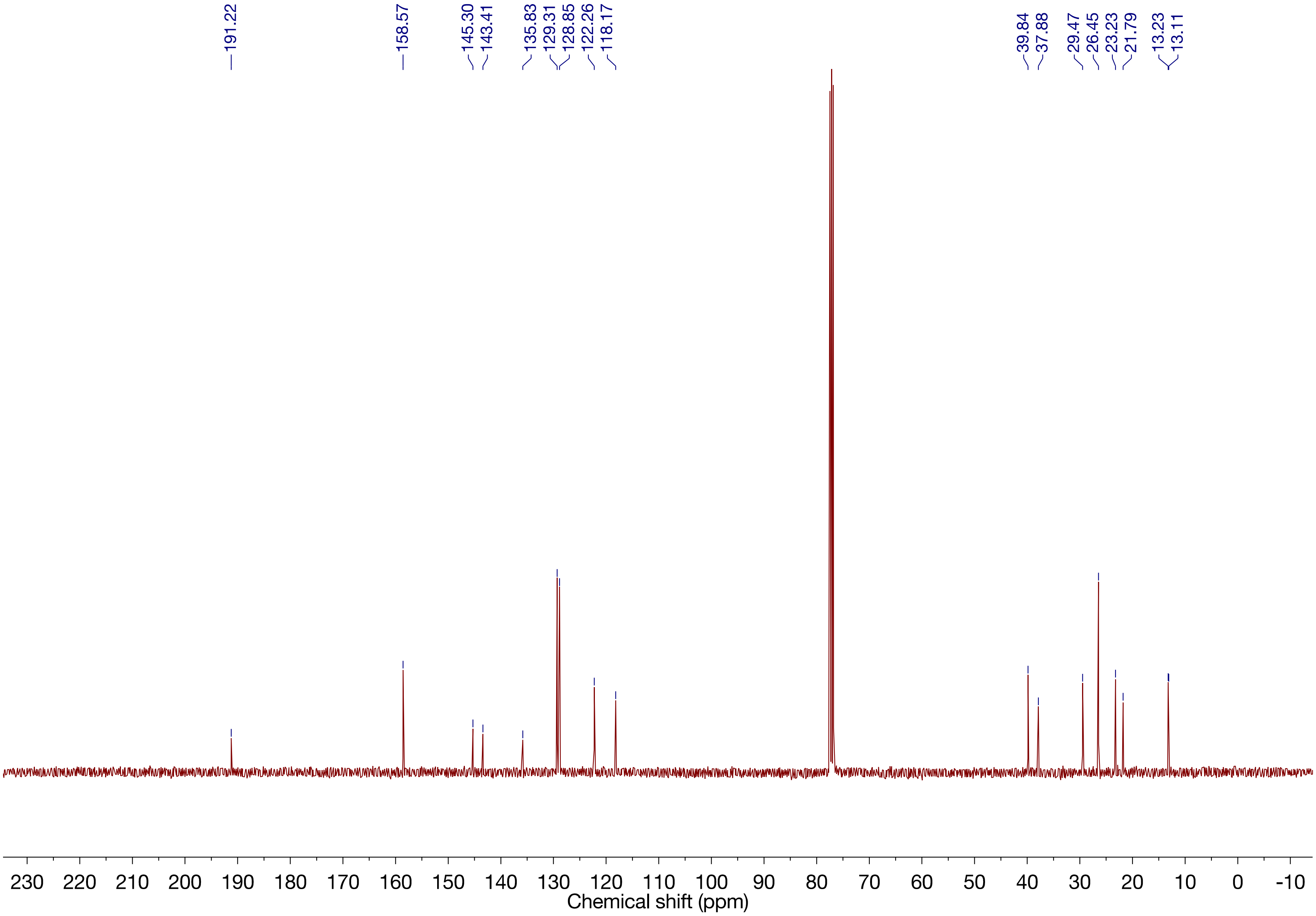

O
Et
H
Et
Me
Me
0.68
0.84
1.95
4.00
6.00
6.33
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-
Chemical shift (ppm)

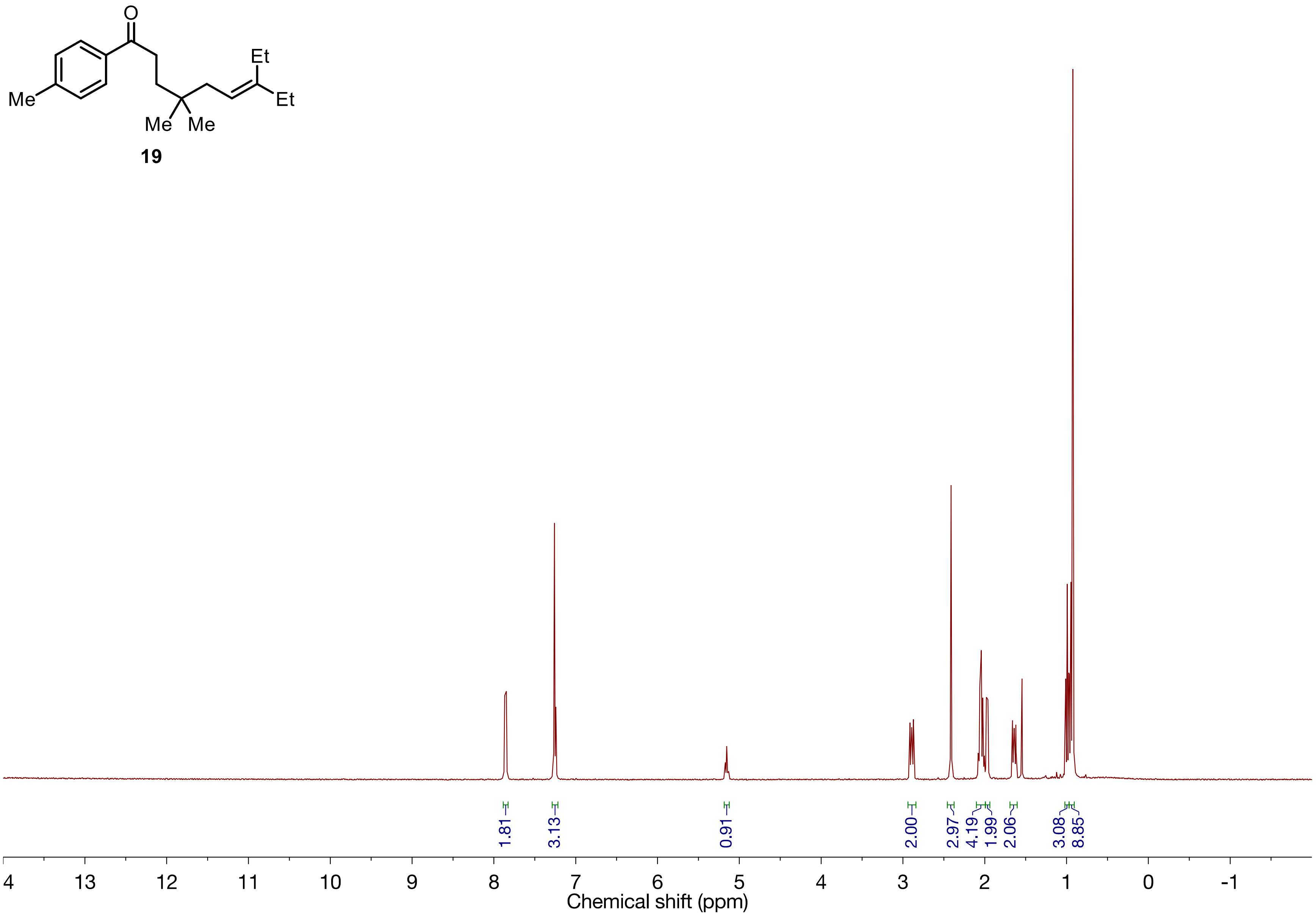
S19a



206.71
146.10
116.66
46.47
35.05
29.41
23.18
21.31
13.11
13.08
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

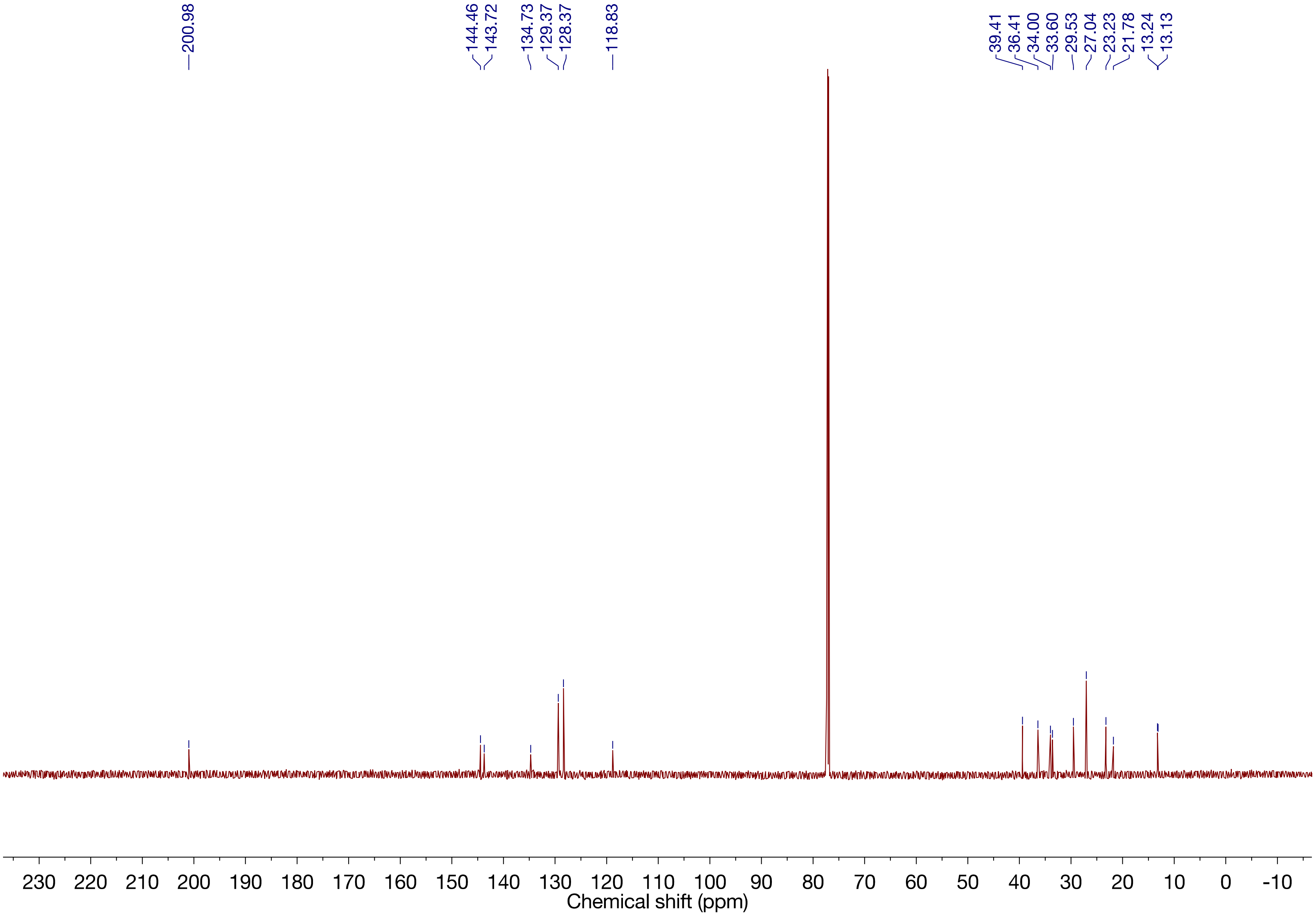

S19b
O
Et
Et
Me
Me
Me
1.89
2.70
1.00
1.10
1.04
2.92
2.05
4.04
5.77
6.13
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

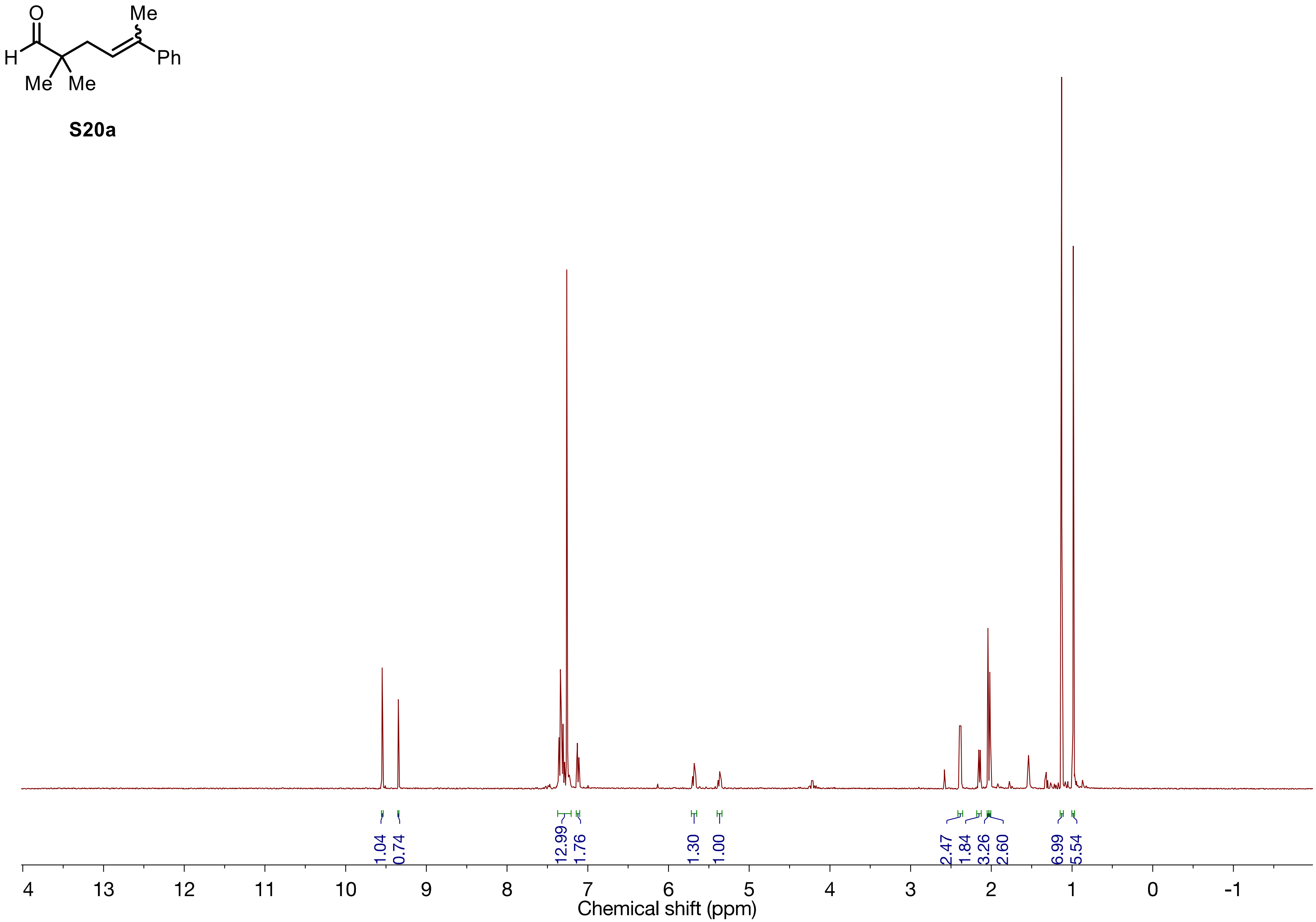

191.22
158.57
145.30
143.41
135.83
129.31
128.85
122.26
118.17
39.84
37.88
29.47
26.45
23.23
21.79
13.23
13.11
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)



19

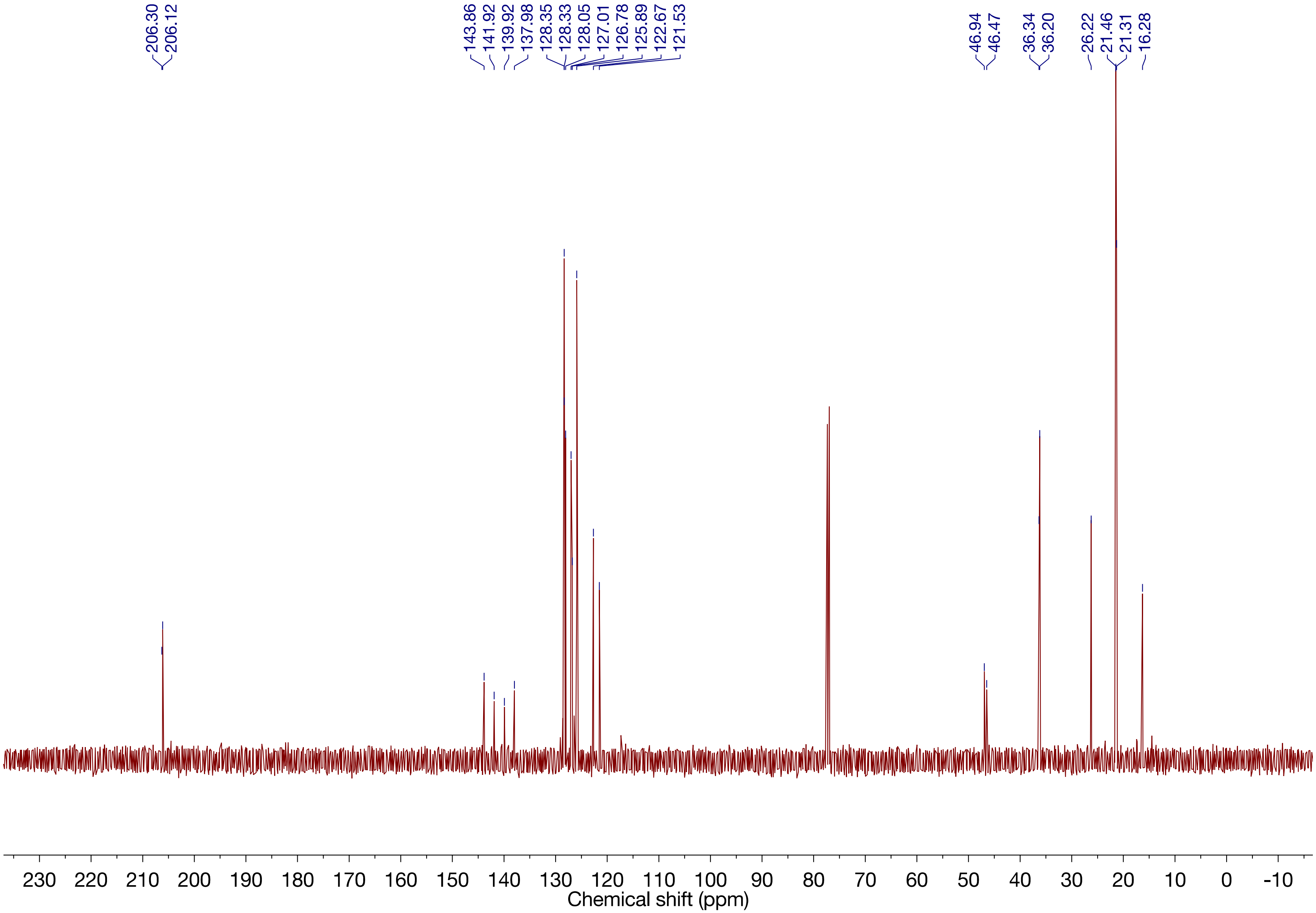
O
Me
Et
Et
Me
Me
1.81
3.13
0.91
2.00
2.97
4.19
1.99
2.06
3.08
8.85
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

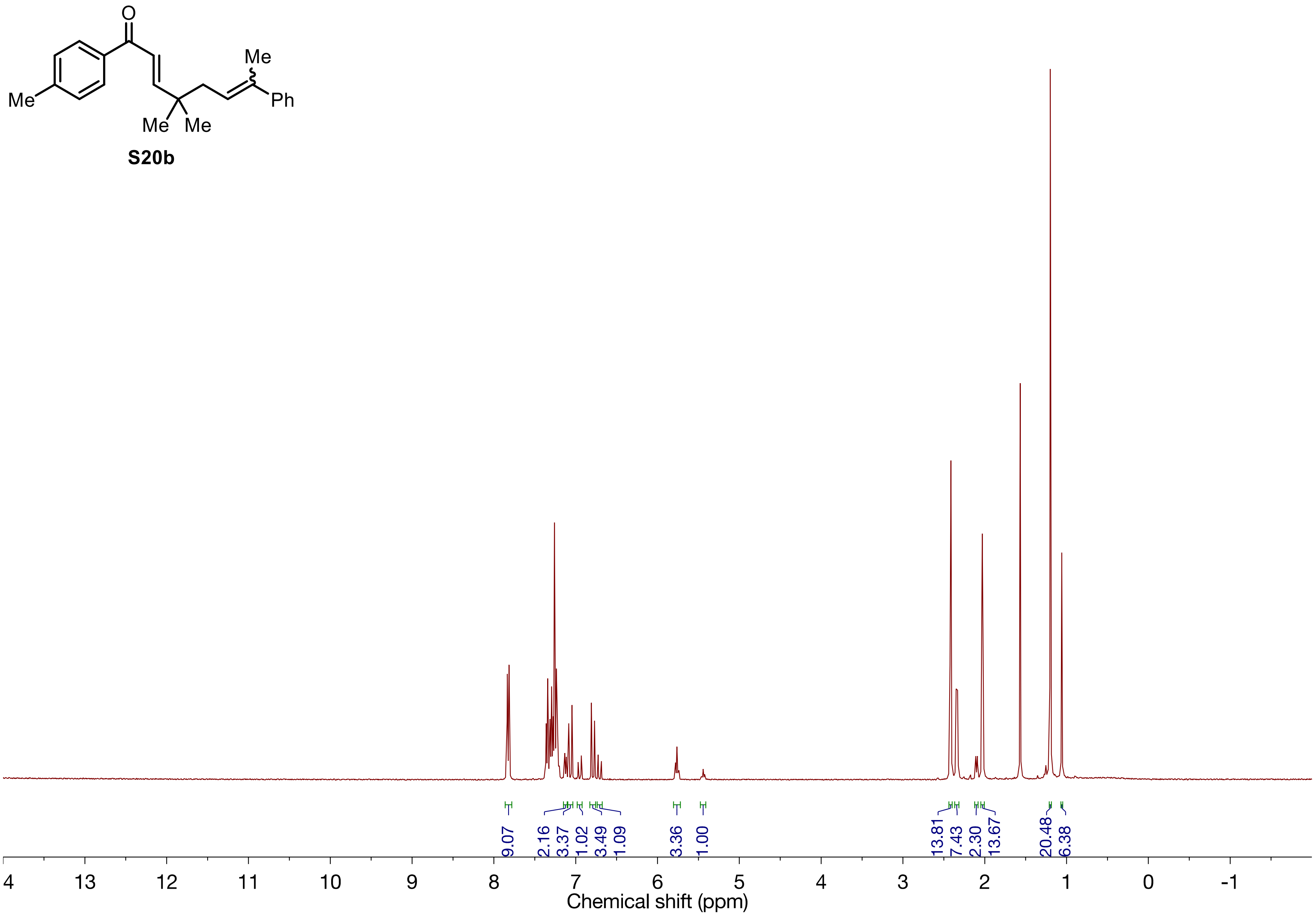

200.98
144.46
143.72
134.73
129.37
128.37
118.83
39.41
36.41
34.00
33.60
29.53
27.04
23.23
21.78
13.24
13.13
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)



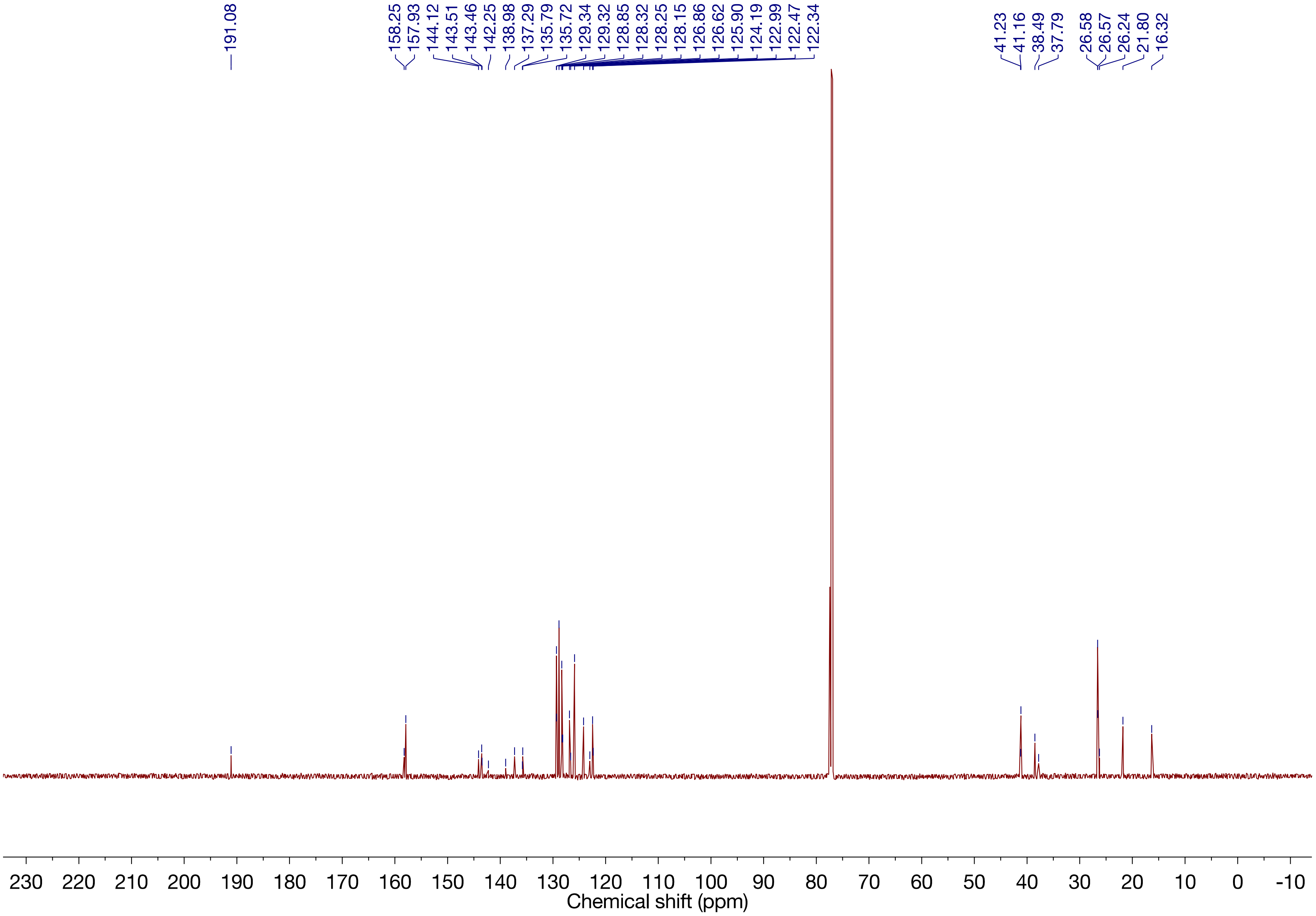
O
H
Me
Me
Me
Ph
1.04
0.74
12.99
1.76
1.30
1.00
2.47
1.84
3.26
2.60
6.99
5.54
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

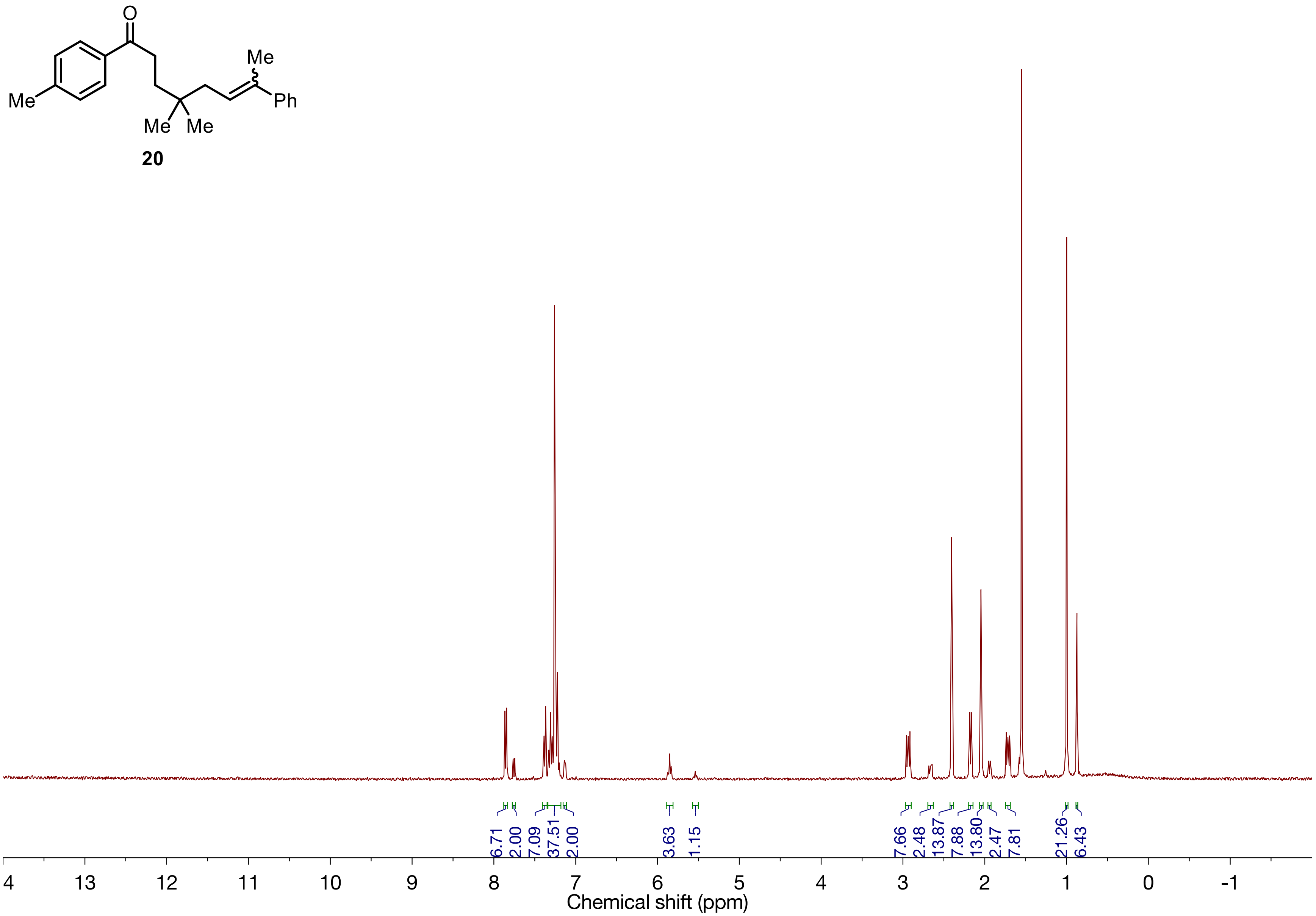
S20a


206.30
206.12
143.86
141.92
139.92
137.98
128.35
128.33
128.05
127.01
126.78
125.89
122.67
121.53
46.94
46.47
36.34
36.20
26.22
21.46
21.31
16.28
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

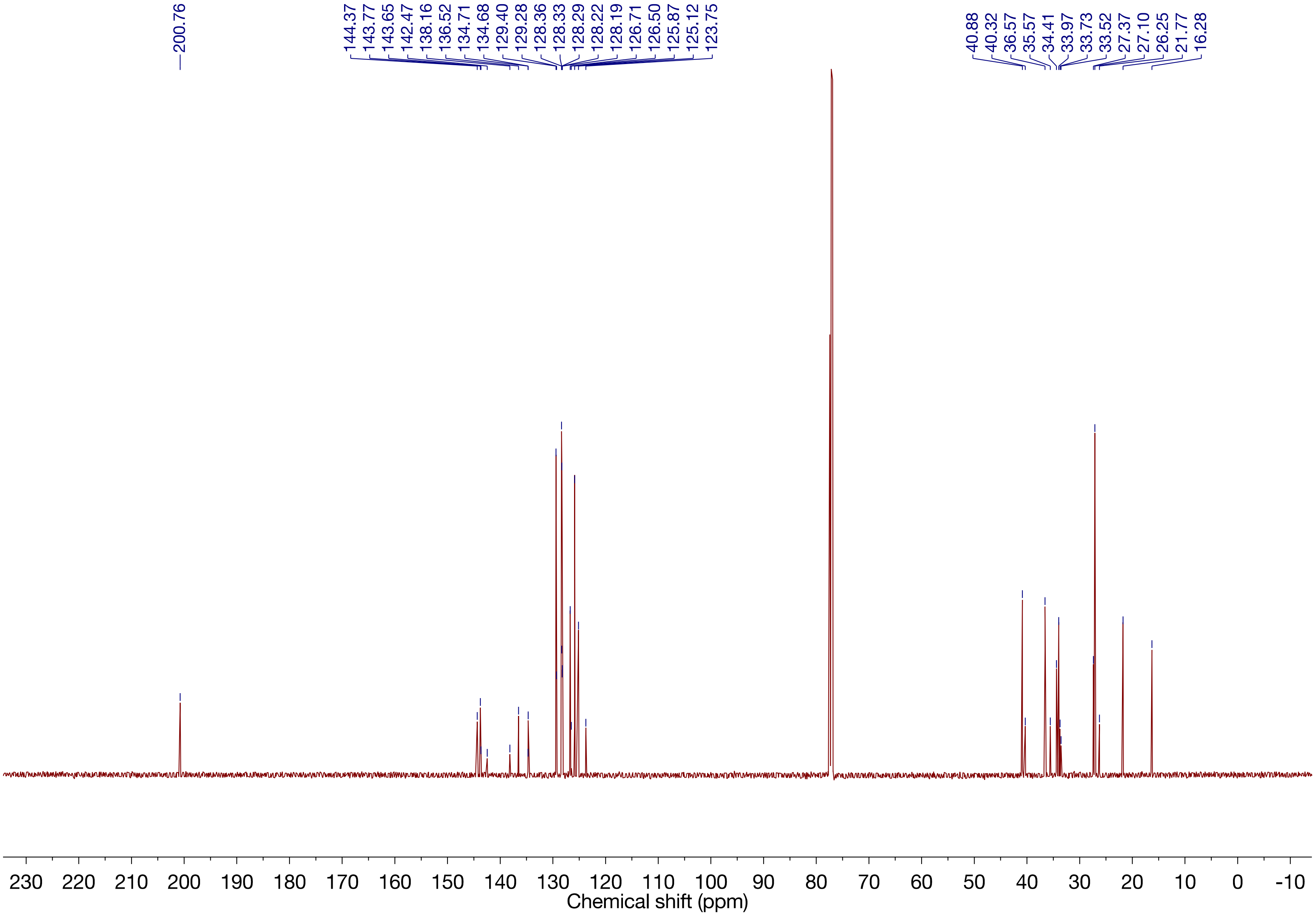

O
Me
Me
Ph
Me
Me
9.07
2.16
3.37
1.02
3.49
1.09
3.36
1.00
13.81
7.43
2.30
13.67
20.48
6.38
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

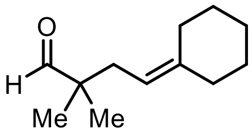
S20b


191.08
158.25
157.93
144.12
143.51
143.46
142.25
138.98
137.29
135.79
135.72
129.34
129.32
128.85
128.32
128.25
128.15
126.86
126.62
125.90
124.19
122.99
122.47
122.34
41.23
41.16
38.49
37.79
26.58
26.57
26.24
21.80
16.32
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

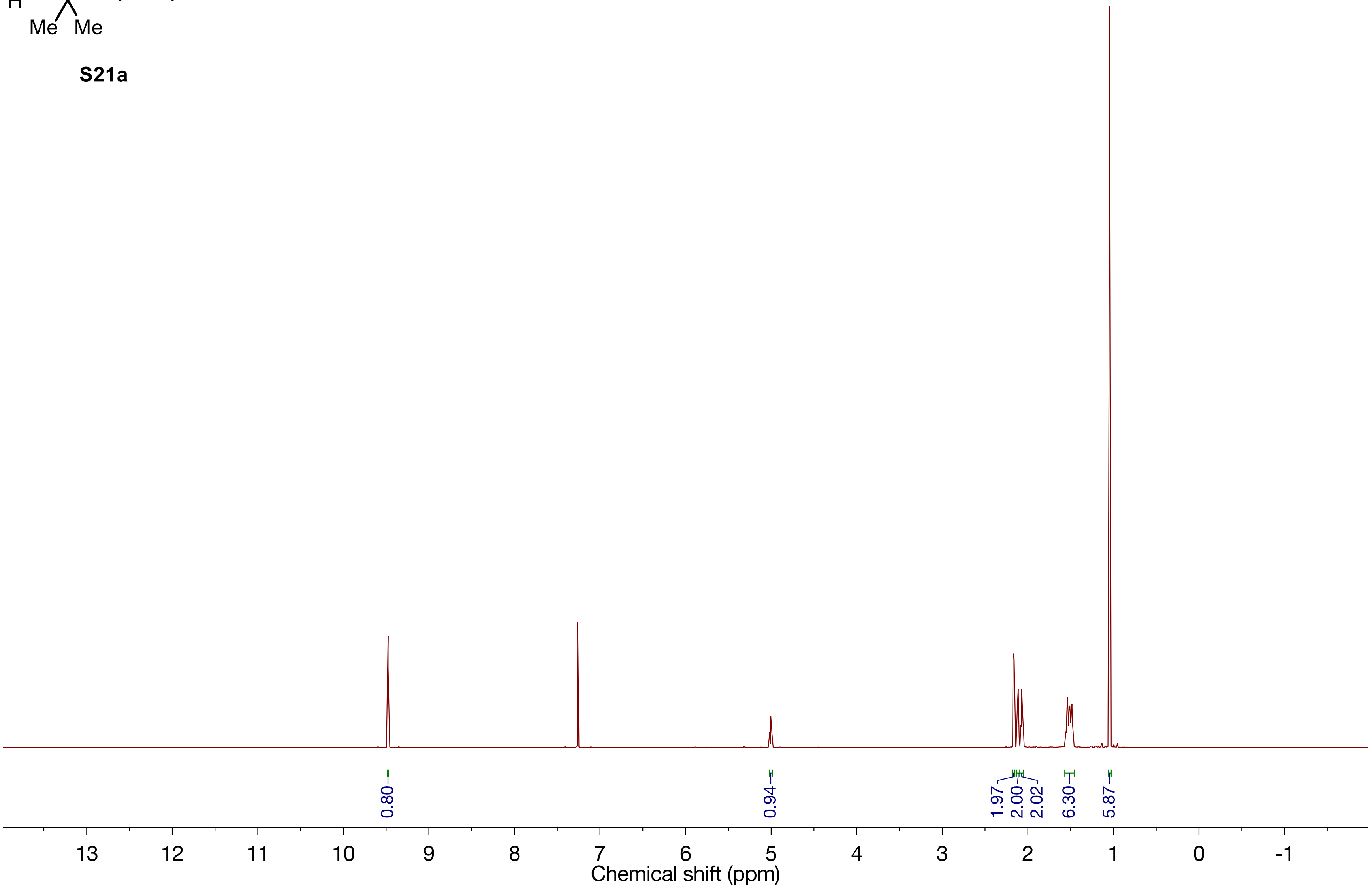

20

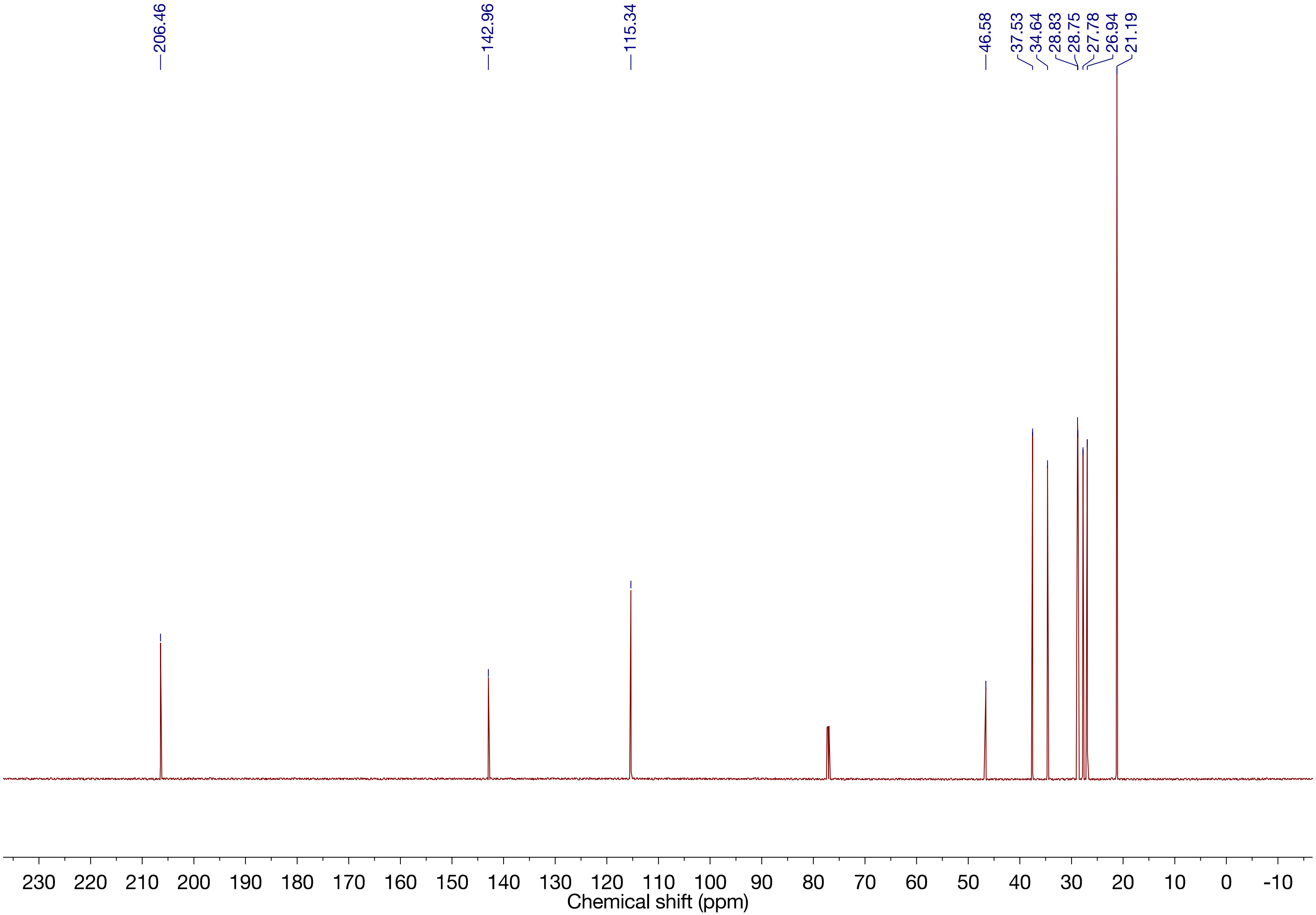
O
Me
Me
Ph
Me
Me
6.71
2.00
7.09
37.51
2.00
3.63
1.15
7.66
2.48
13.87
7.88
13.80
2.47
7.81
21.26
6.43
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

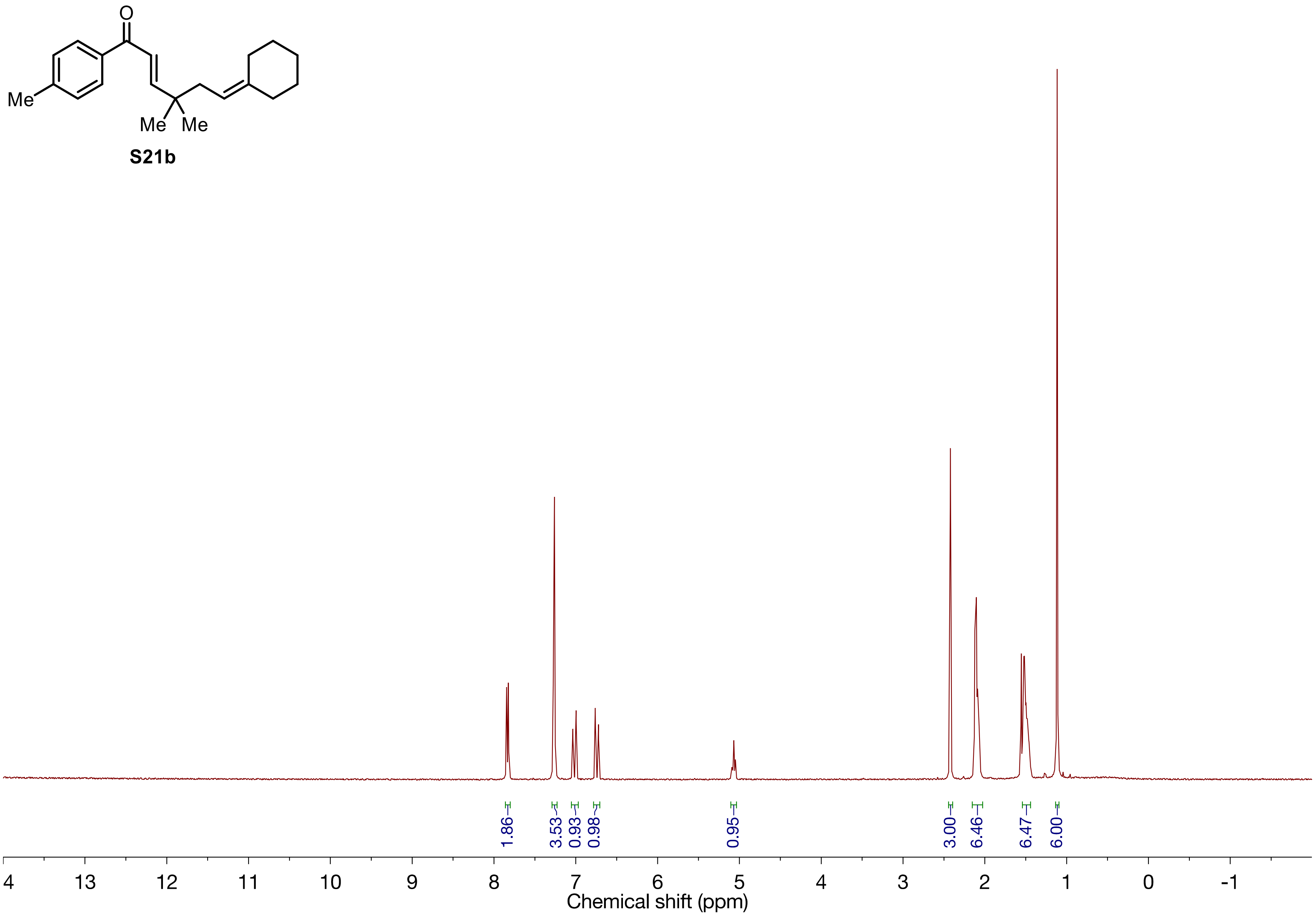

200.76
144.37
143.77
143.65
142.47
138.16
136.52
134.71
134.68
129.40
129.28
128.36
128.33
128.29
128.22
128.19
126.71
126.50
125.87
125.12
123.75
40.88
40.32
36.57
35.57
34.41
33.97
33.73
33.52
27.37
27.10
26.25
21.77
16.28
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


O
H
Me
Me

S21a

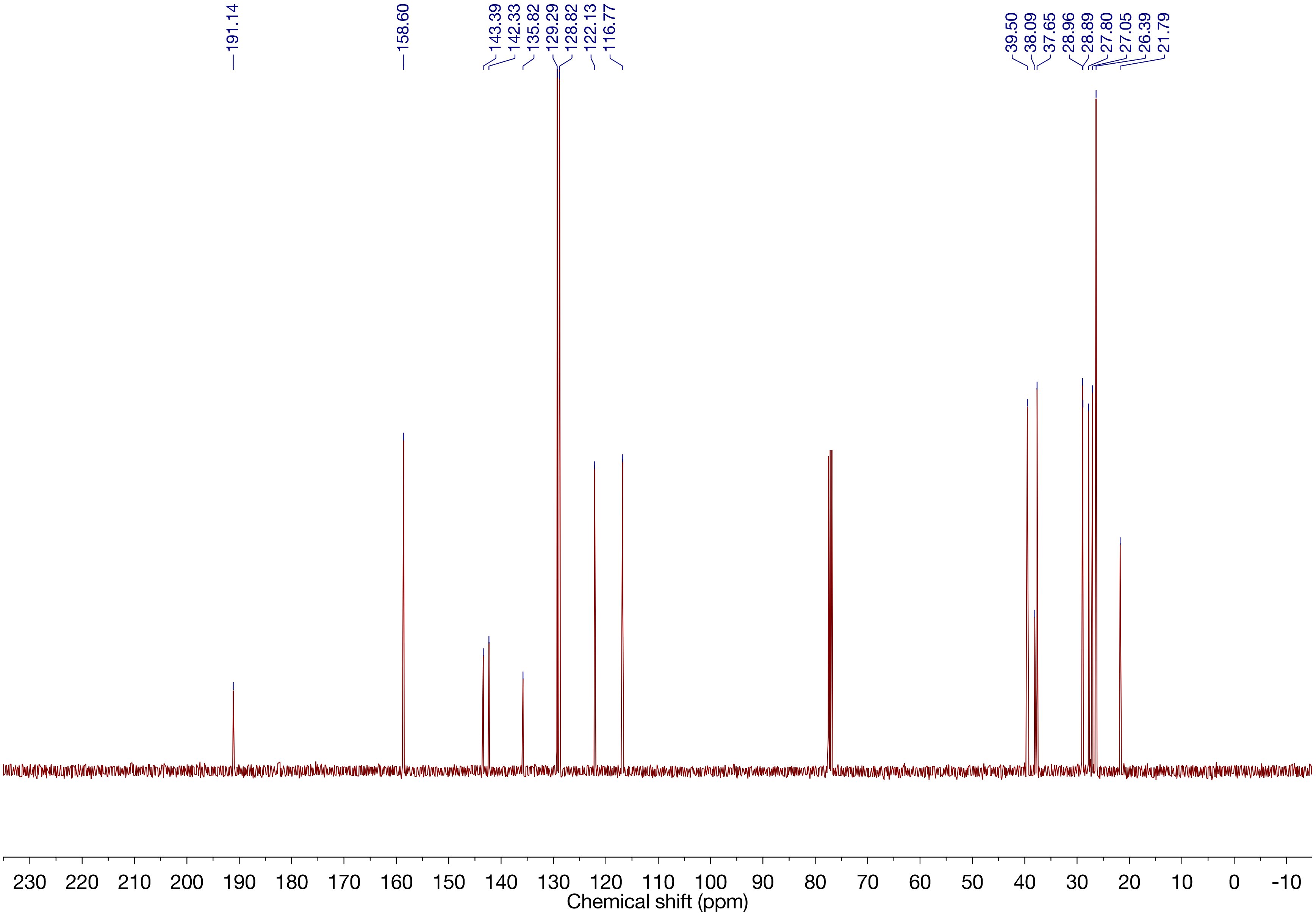

0.80
0.94
1.97
2.00
2.02
6.30
5.87
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

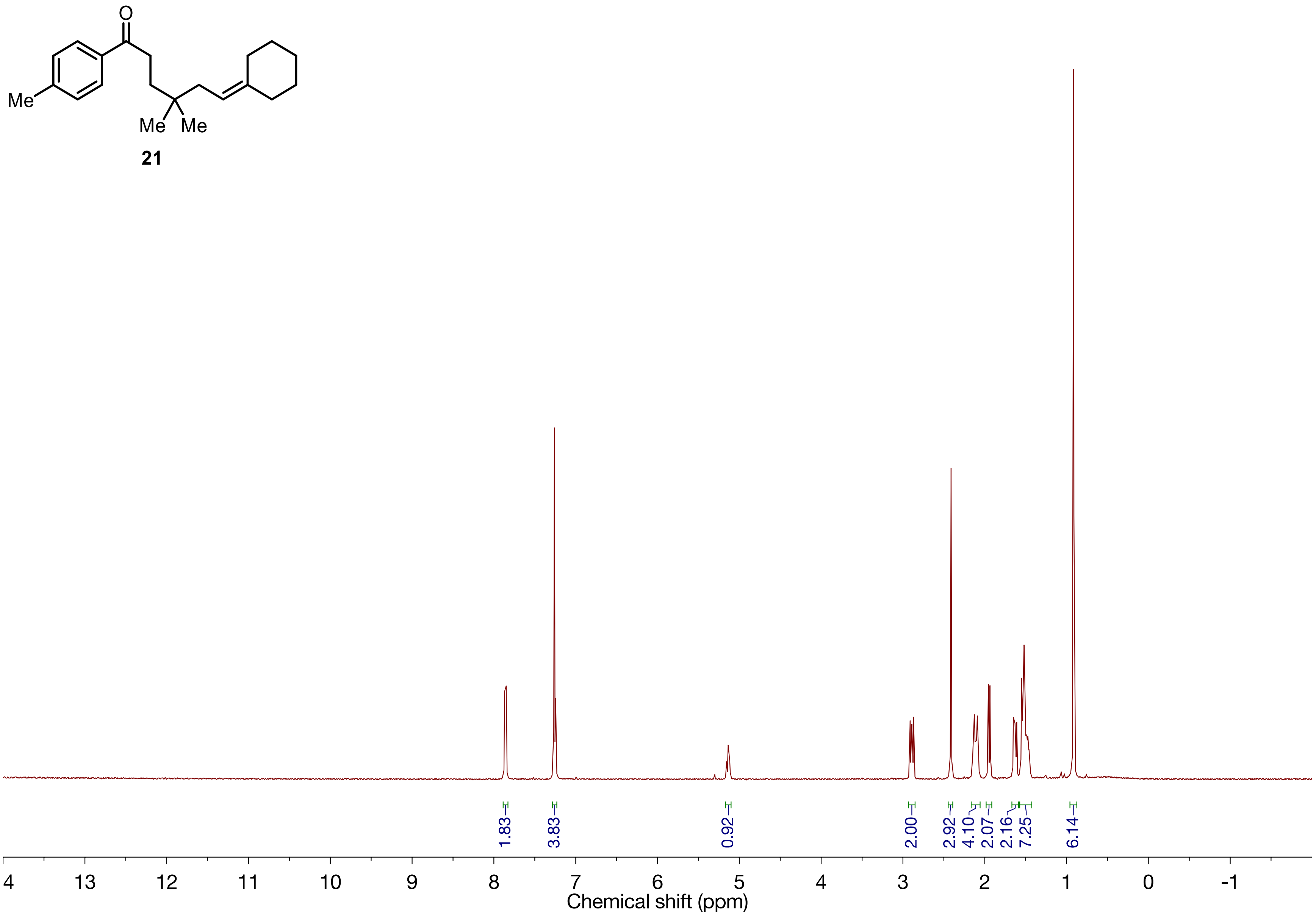

206.46
142.96
115.34
46.58
37.53
34.64
28.83
28.75
27.78
26.94
21.19
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)



S21b

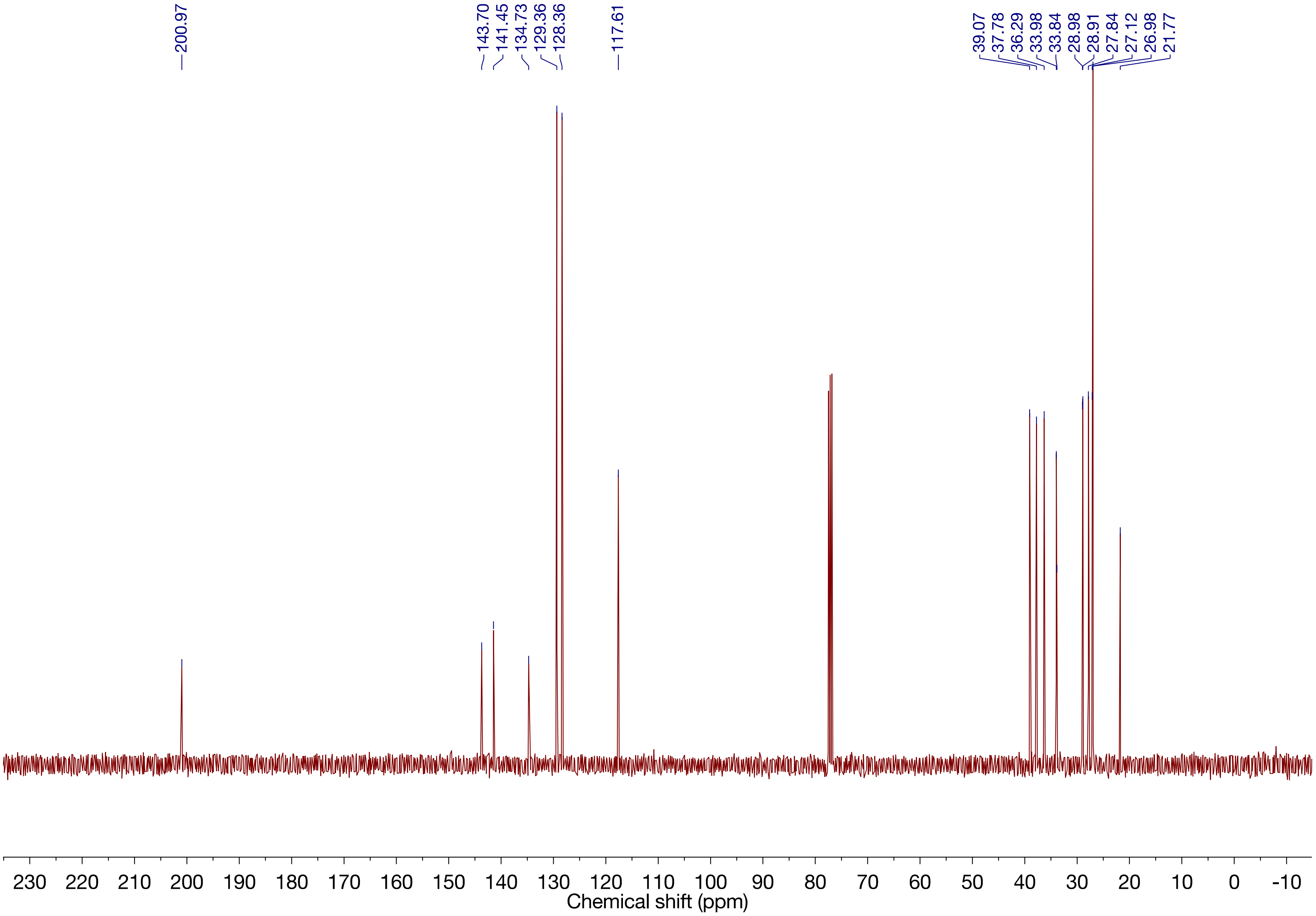
O
Me
Me
Me
1.86
3.53
0.93
0.98
0.95
3.00
6.46
6.47
6.00
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

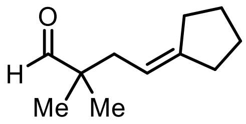

191.14
158.60
143.39
142.33
135.82
129.29
128.82
122.13
116.77
39.50
38.09
37.65
28.96
28.89
27.80
27.05
26.39
21.79
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



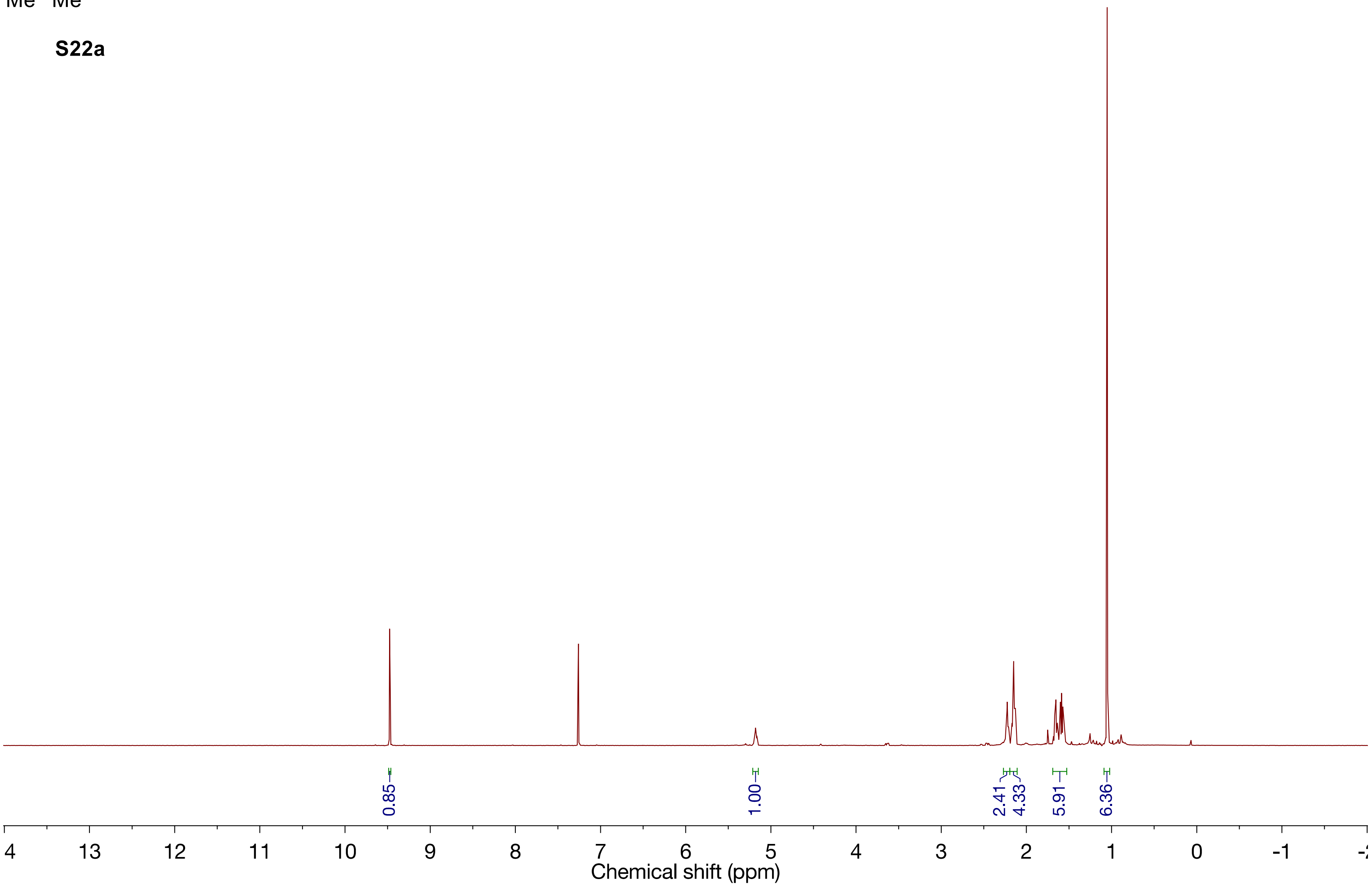
21

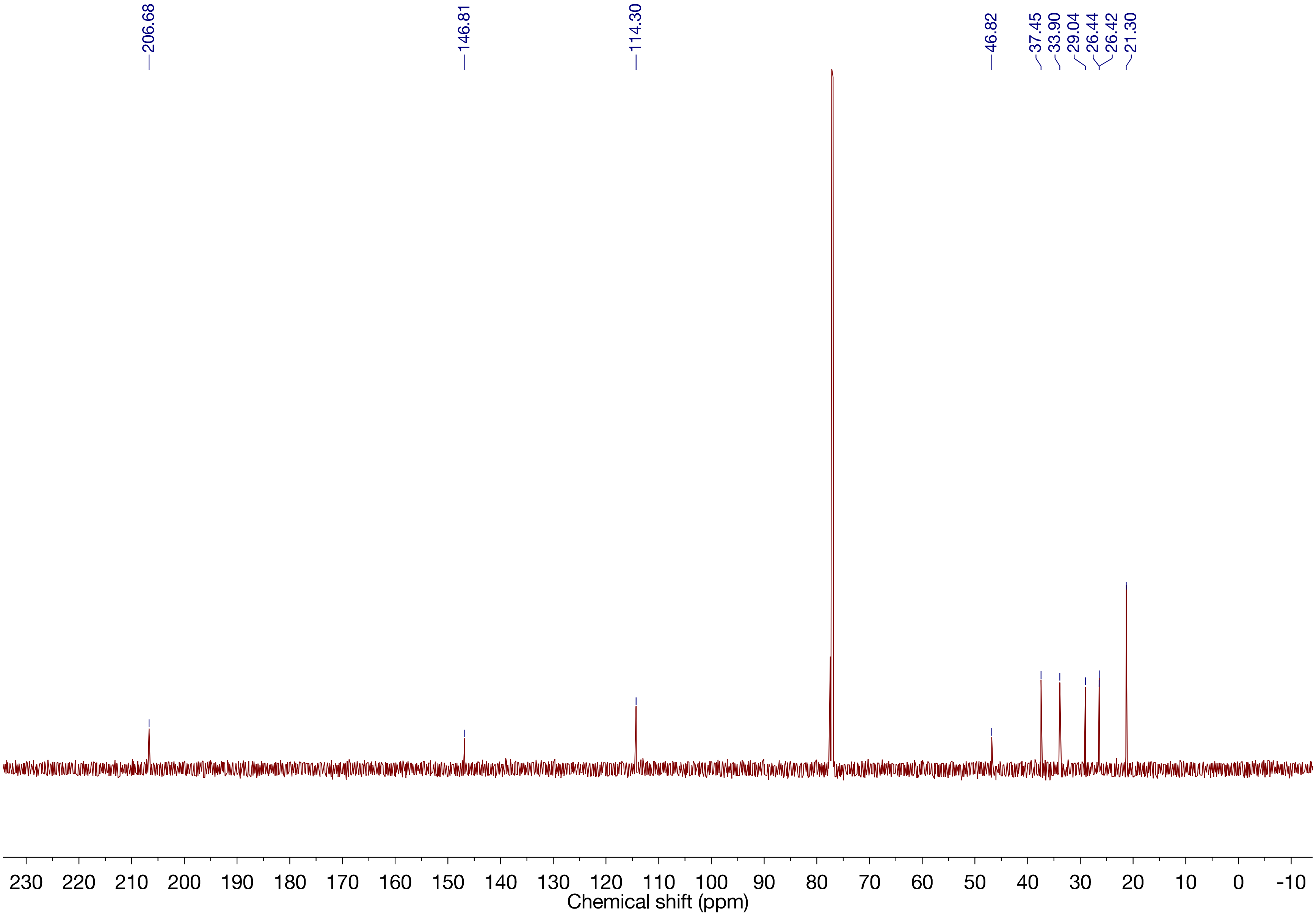
O
Me
Me
Me
1.83
3.83
0.92
2.00
2.92
4.10
2.07
2.16
7.25
6.14
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

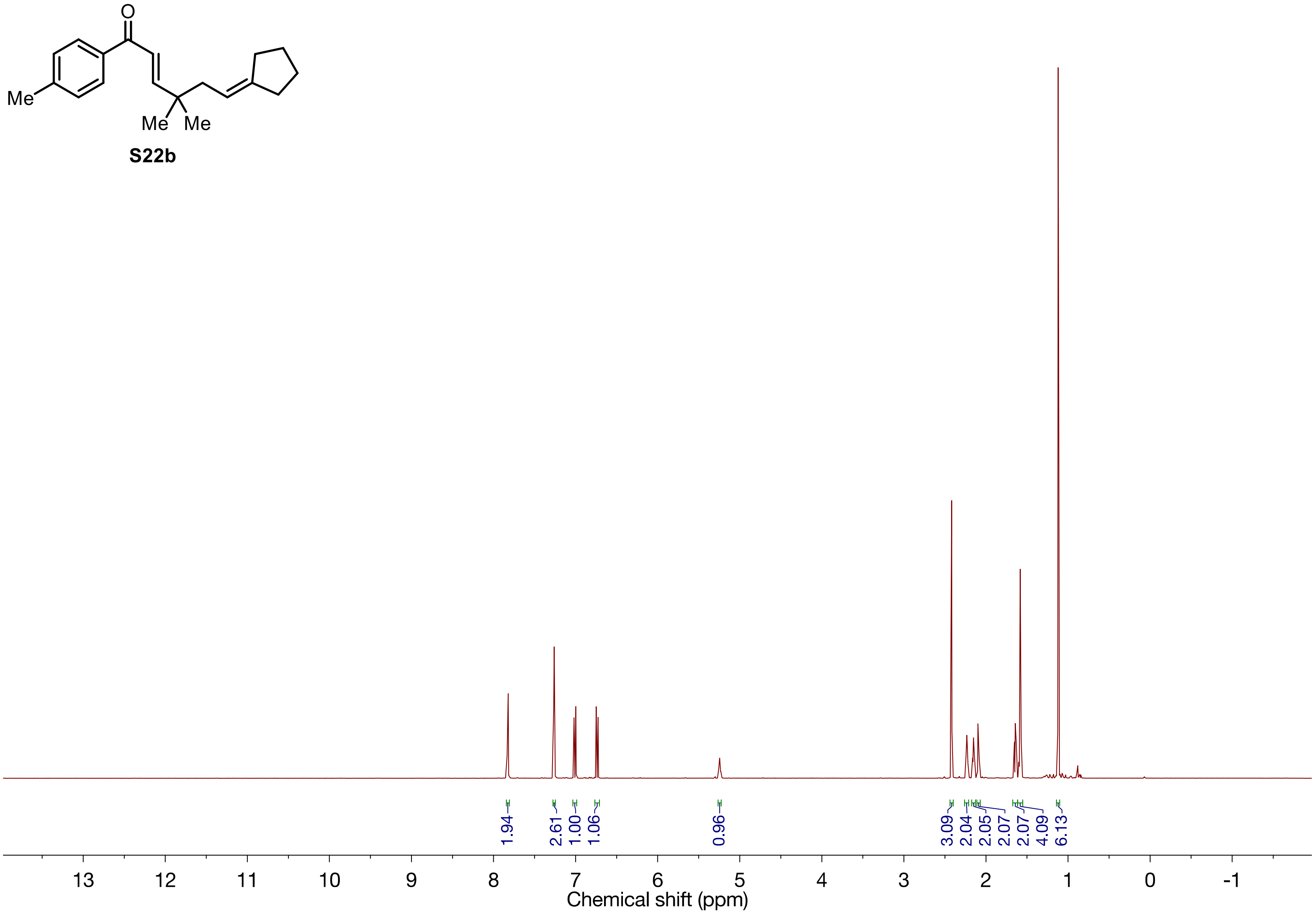

200.97
143.70
141.45
134.73
129.36
128.36
117.61
39.07
37.78
36.29
33.98
33.84
28.98
28.91
27.84
27.12
26.98
21.77
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


O
H
Me
Me

S22a

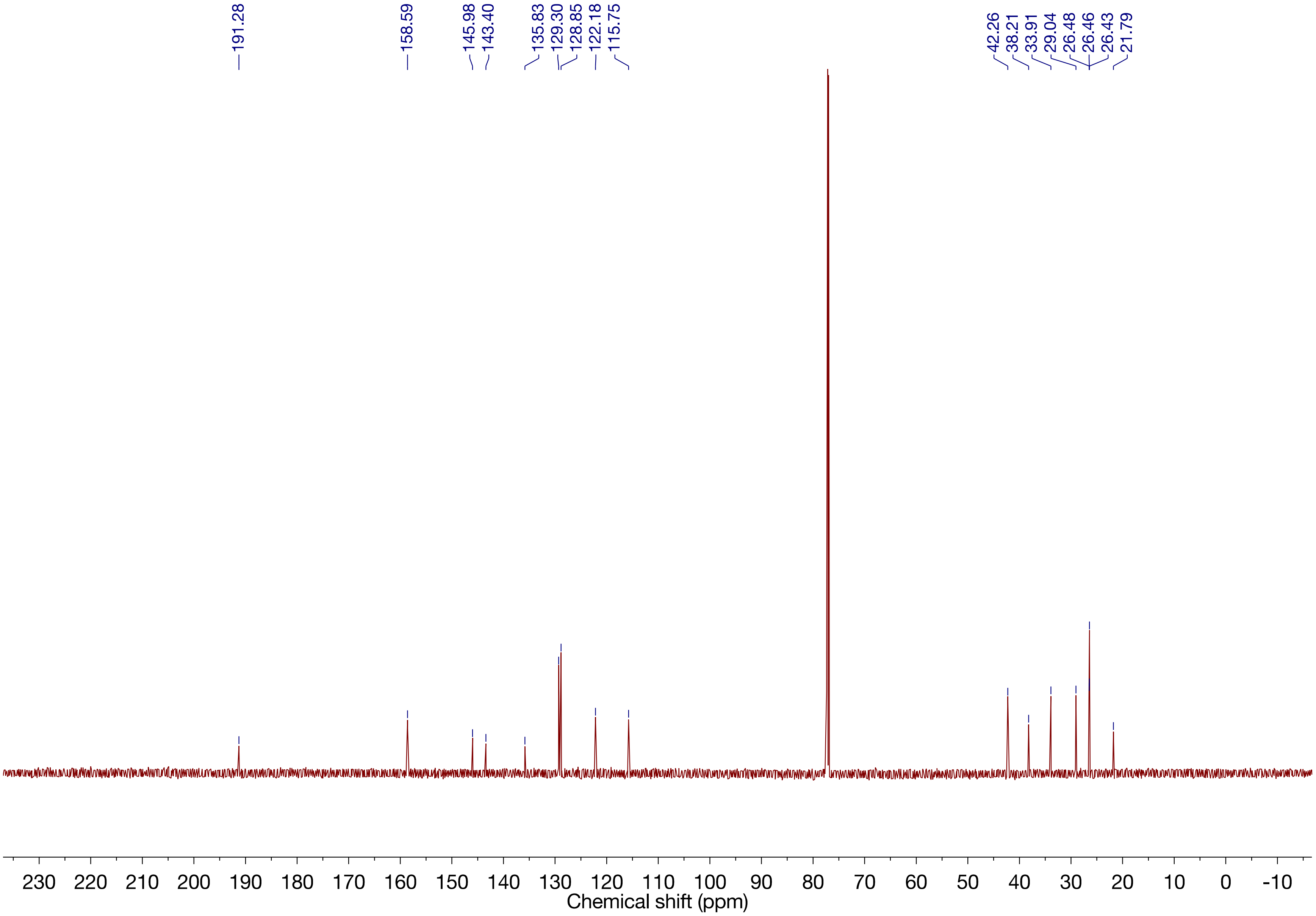

0.85
1.00
2.41
4.33
5.91
6.36
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-
Chemical shift (ppm)

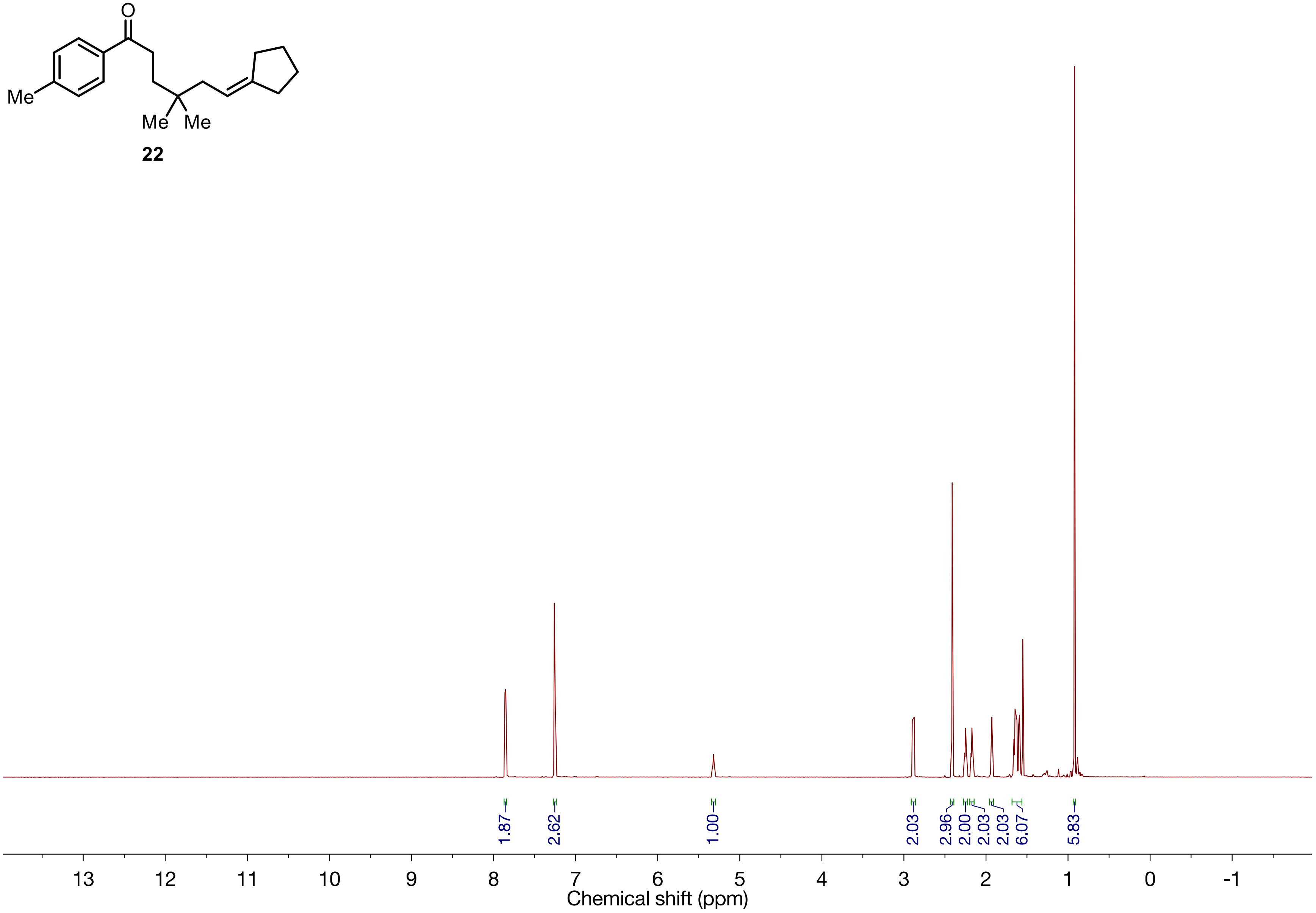

206.68
146.81
114.30
46.82
37.45
33.90
29.04
26.44
26.42
21.30
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


O
Me
Me
Me

S22b

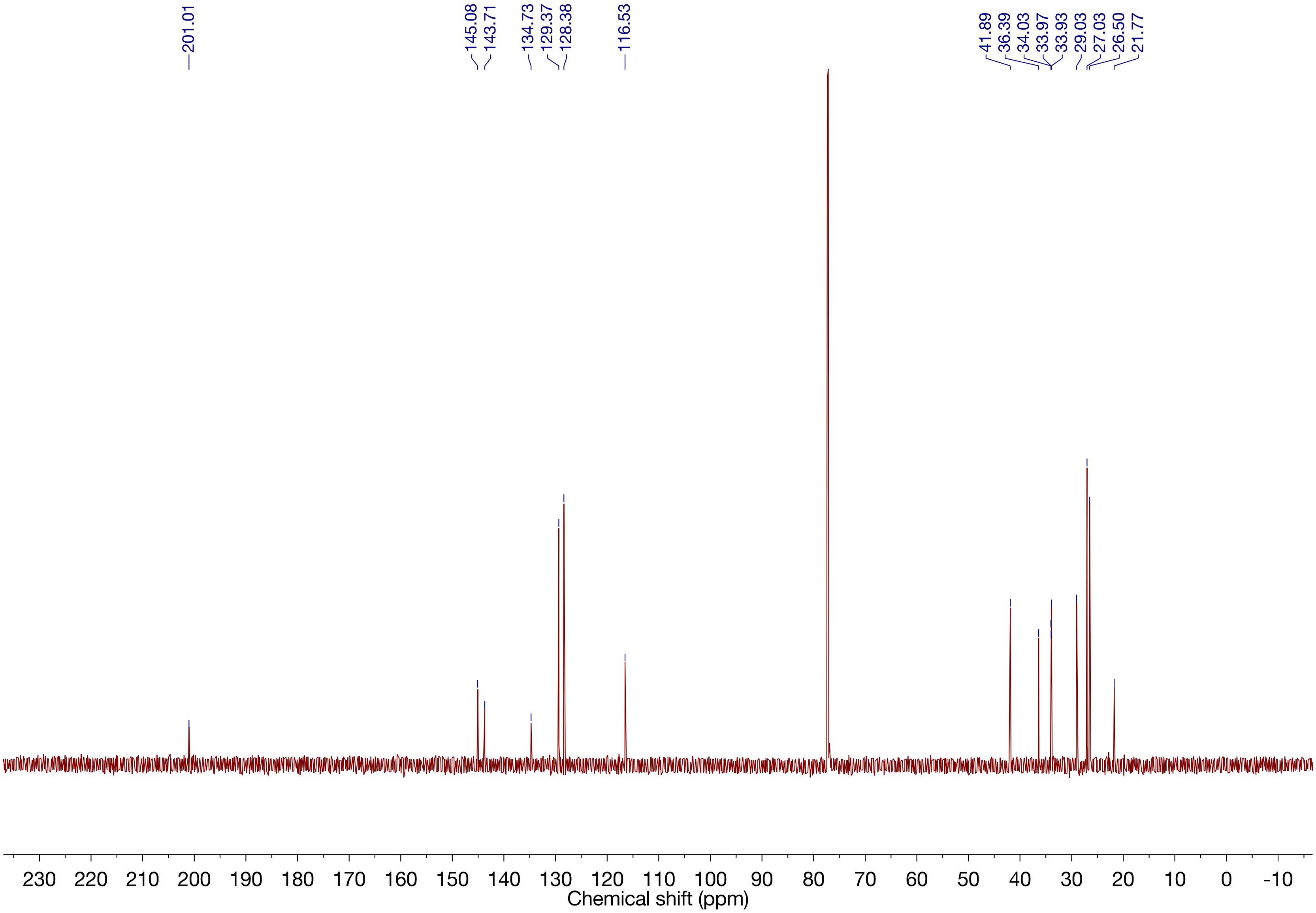
1.94
2.61
1.00
1.06
0.96
3.09
2.04
2.05
2.07
2.07
4.09
6.13
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

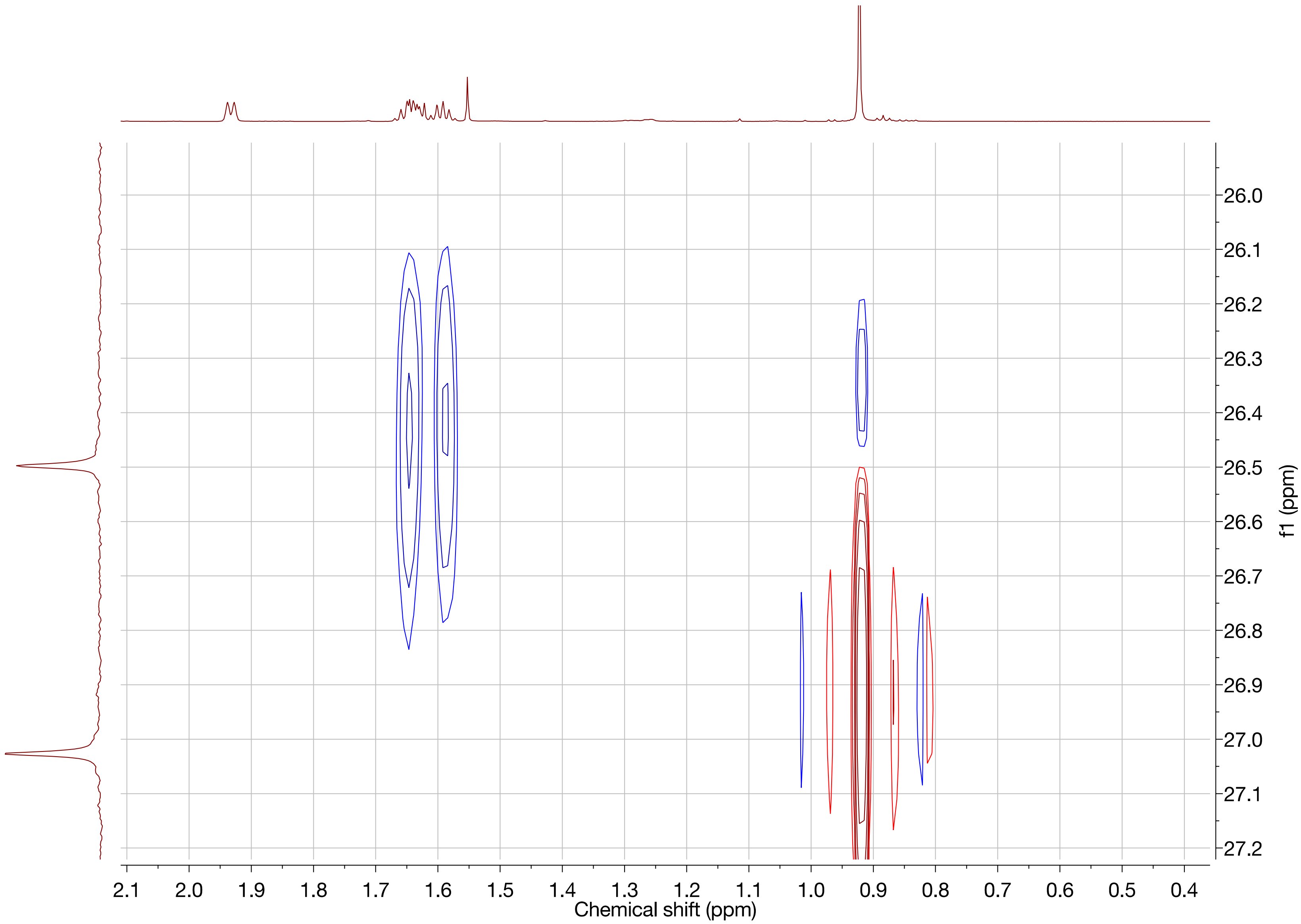

191.28
158.59
145.98
143.40
135.83
129.30
128.85
122.18
115.75
42.26
38.21
33.91
29.04
26.48
26.46
26.43
21.79
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



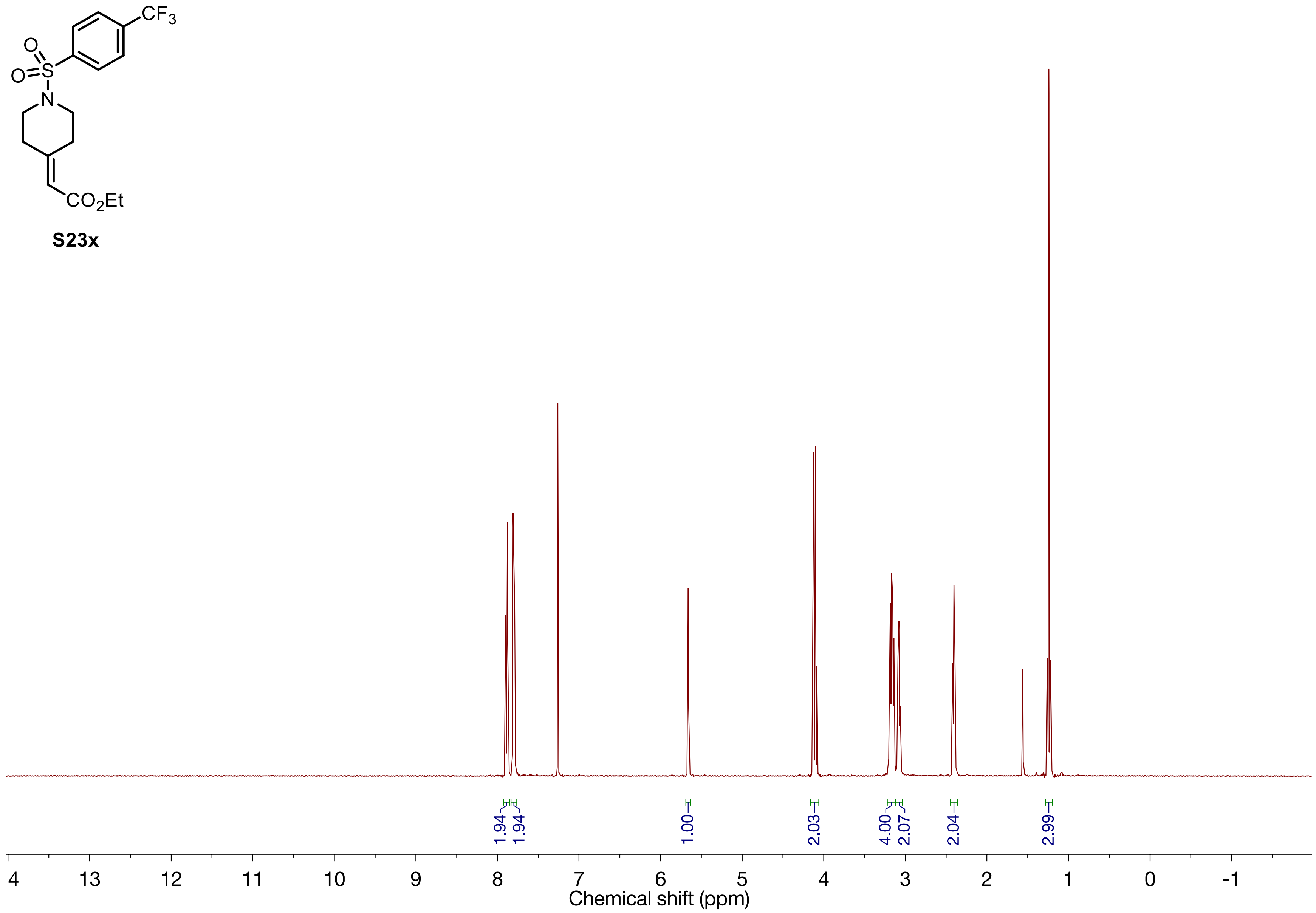
22

1.87
2.62
1.00
2.03
2.96
2.00
2.03
2.03
6.07
5.83
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


201.01
145.08
143.71
134.73
129.37
128.38
116.53
41.89
36.39
34.03
33.97
33.93
29.03
27.03
26.50
21.77
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)

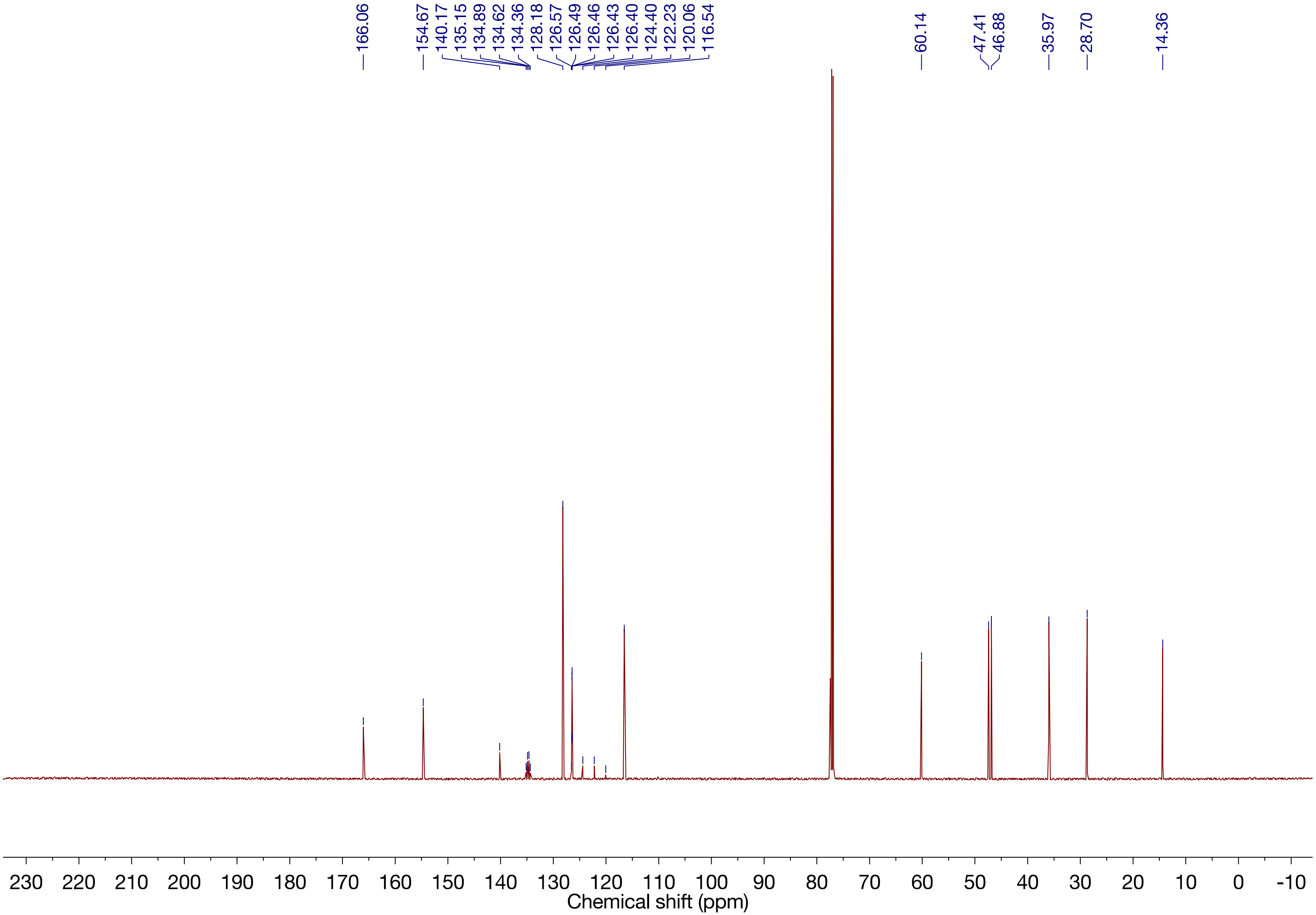


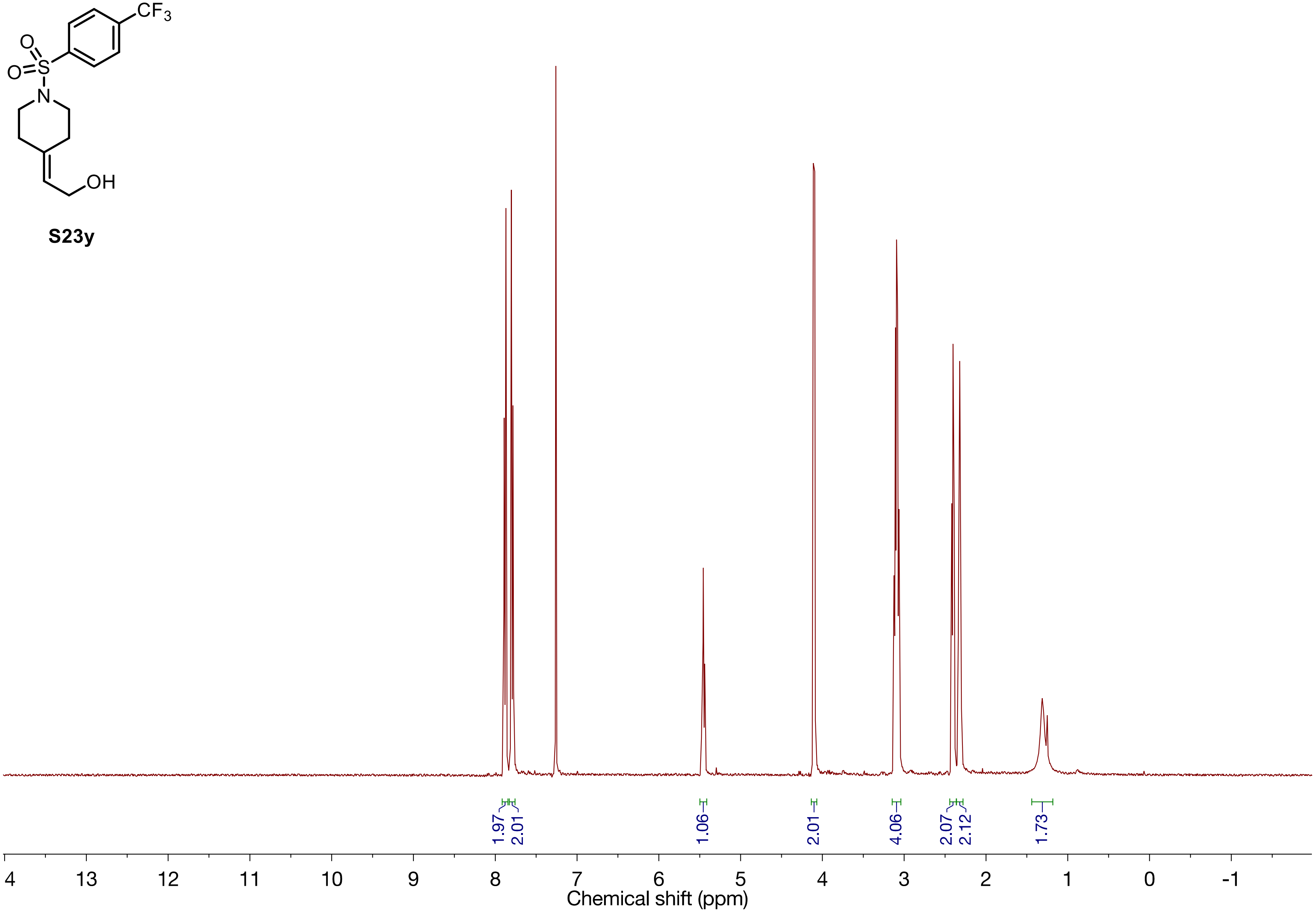
26.0
26.1
26.2
26.3
26.4
26.5
26.6
26.7
26.8
26.9
27.0
27.1
27.2
f1 (ppm)
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
Chemical shift (ppm)

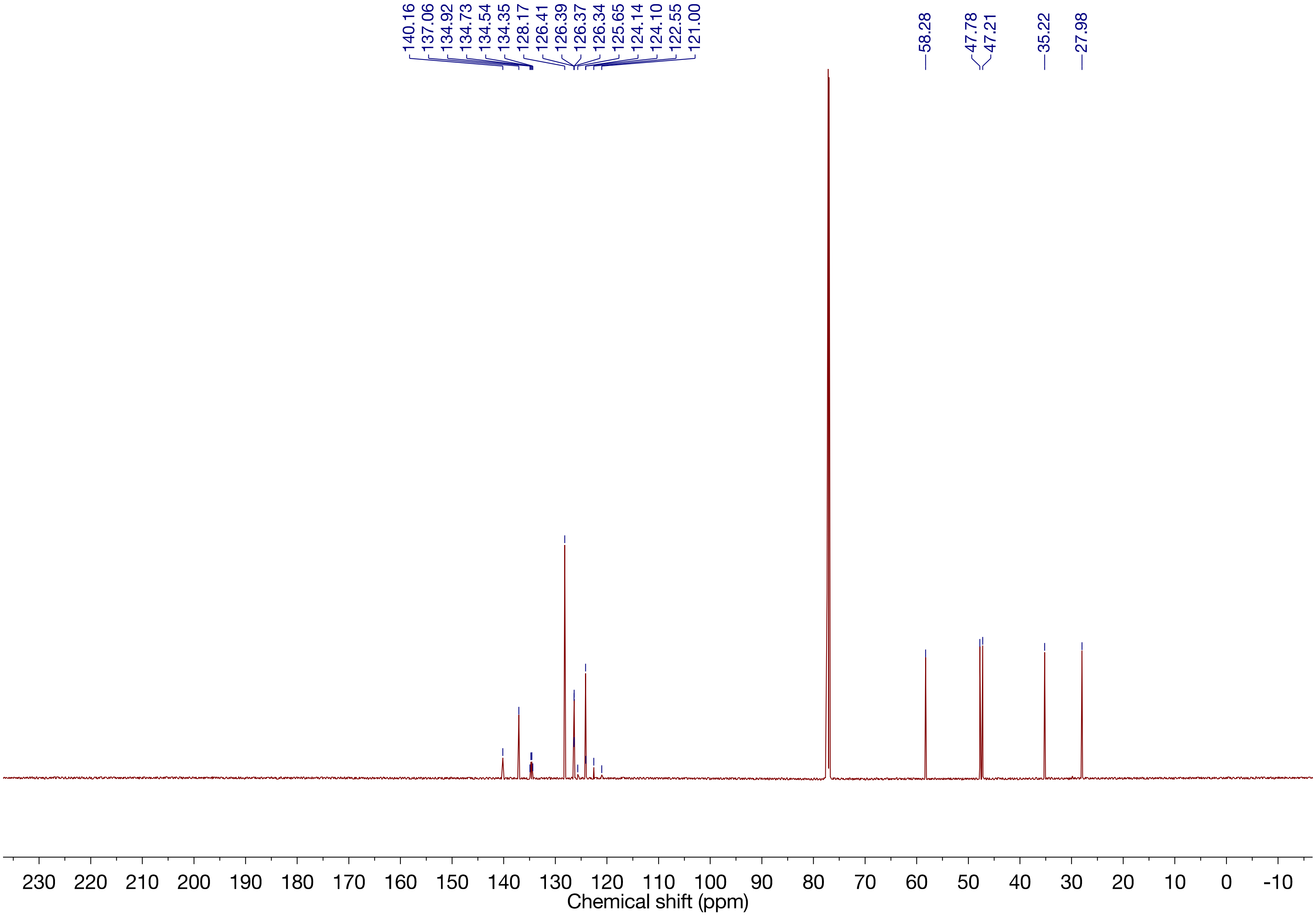


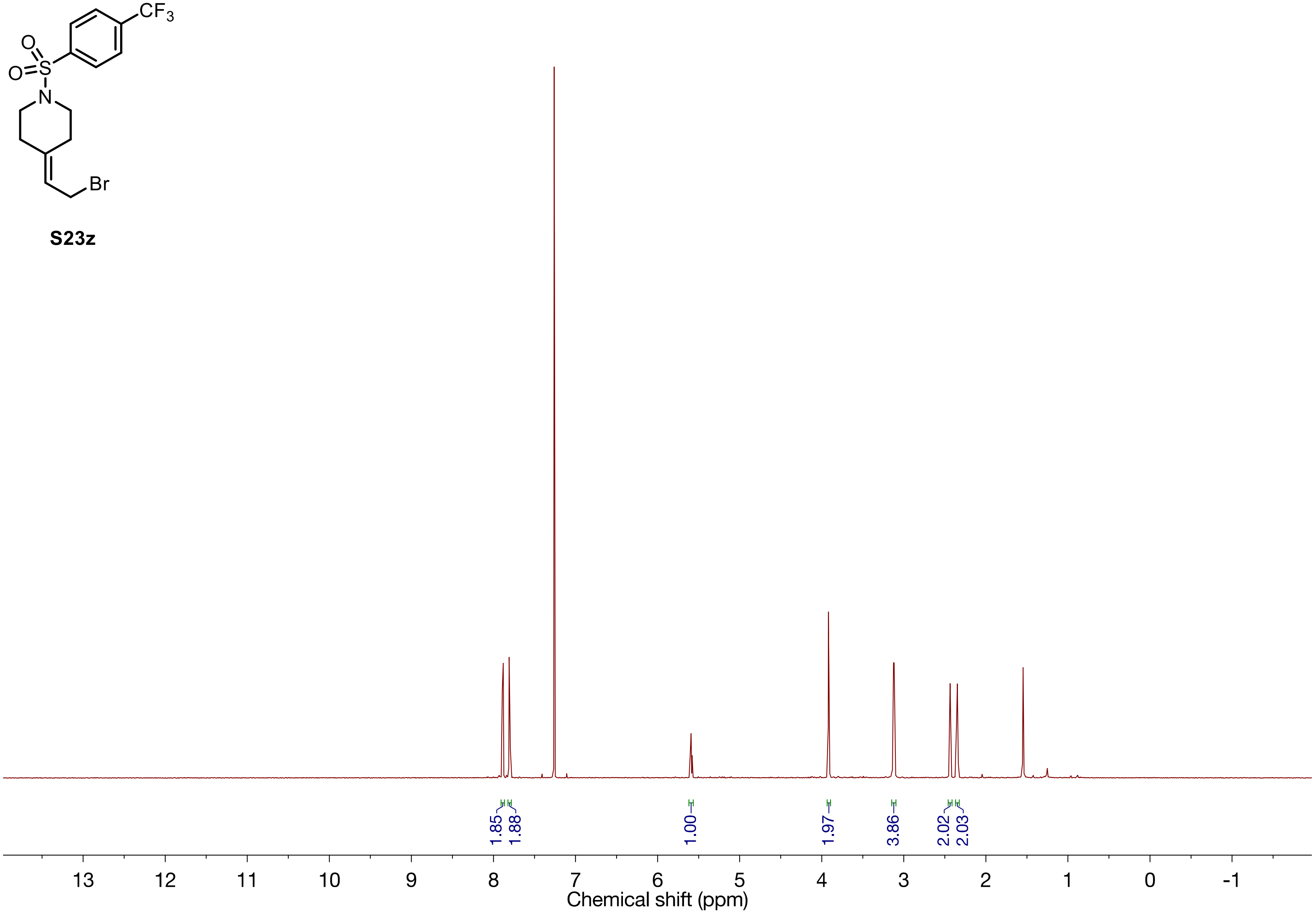
S23x

CF3
O
O=S
N
CO2Et
1.94
1.94
1.00
2.03
4.00
2.07
2.04
2.99
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

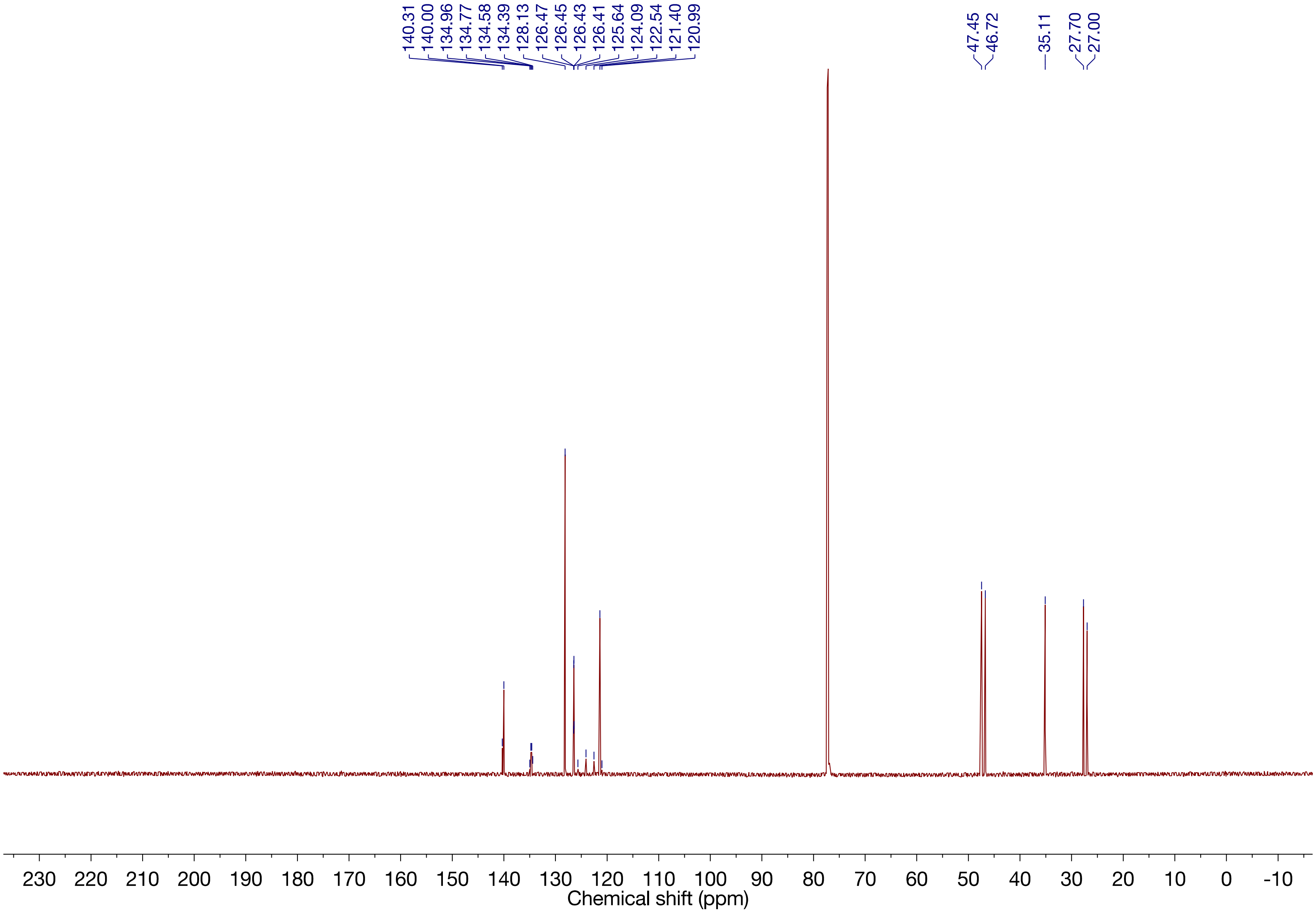

166.06
154.67
140.17
135.15
134.89
134.62
134.36
128.18
126.57
126.49
126.46
126.43
126.40
124.40
122.23
120.06
116.54
60.14
47.41
46.88
35.97
28.70
14.36
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

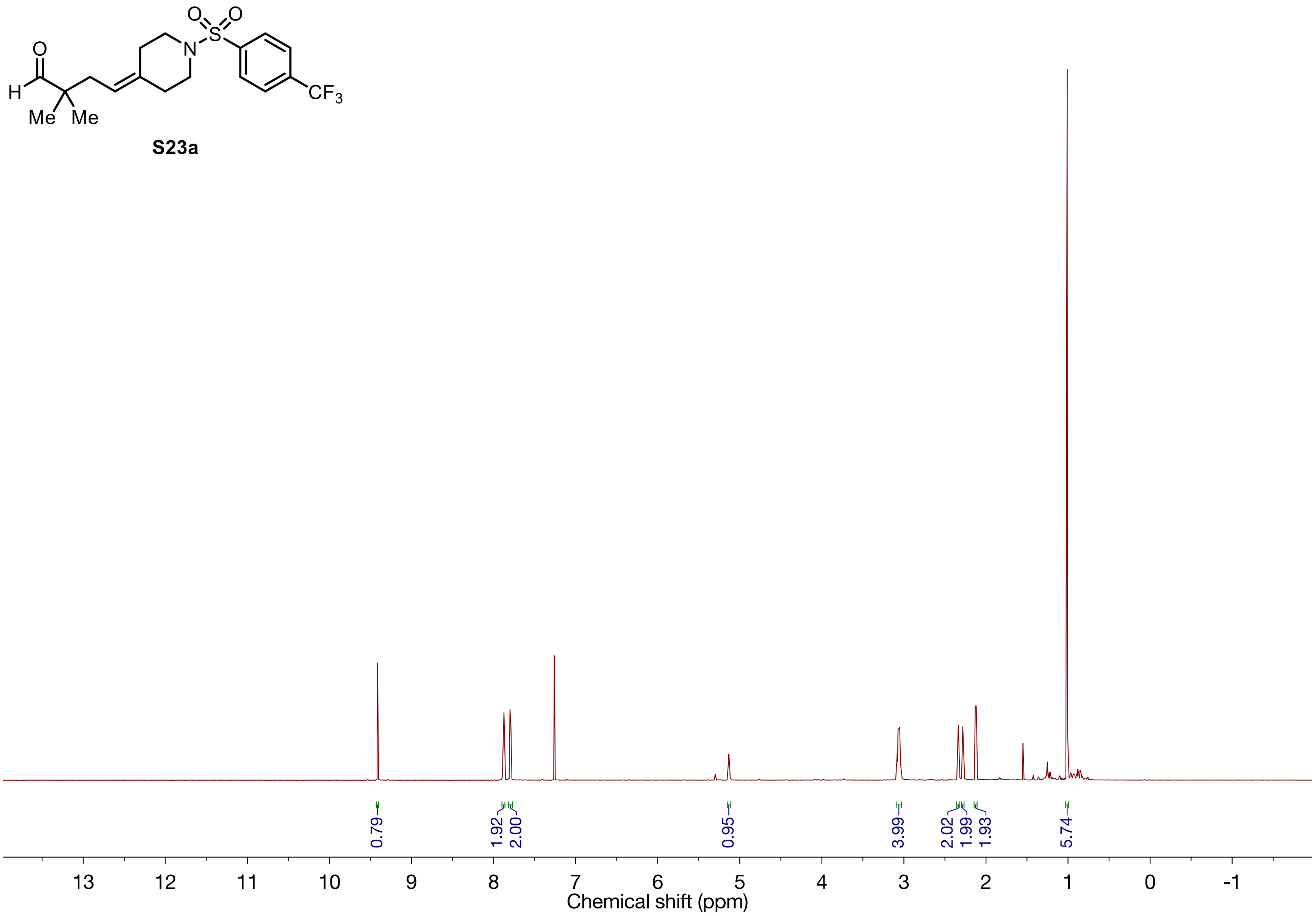

CF3
O
O
S
N
OH
S23y
1.97
2.01
1.06
2.01
4.06
2.07
2.12
1.73
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


140.16
137.06
134.92
134.73
134.54
134.35
128.17
126.41
126.39
126.37
126.34
125.65
124.14
124.10
122.55
121.00
58.28
47.78
47.21
35.22
27.98
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

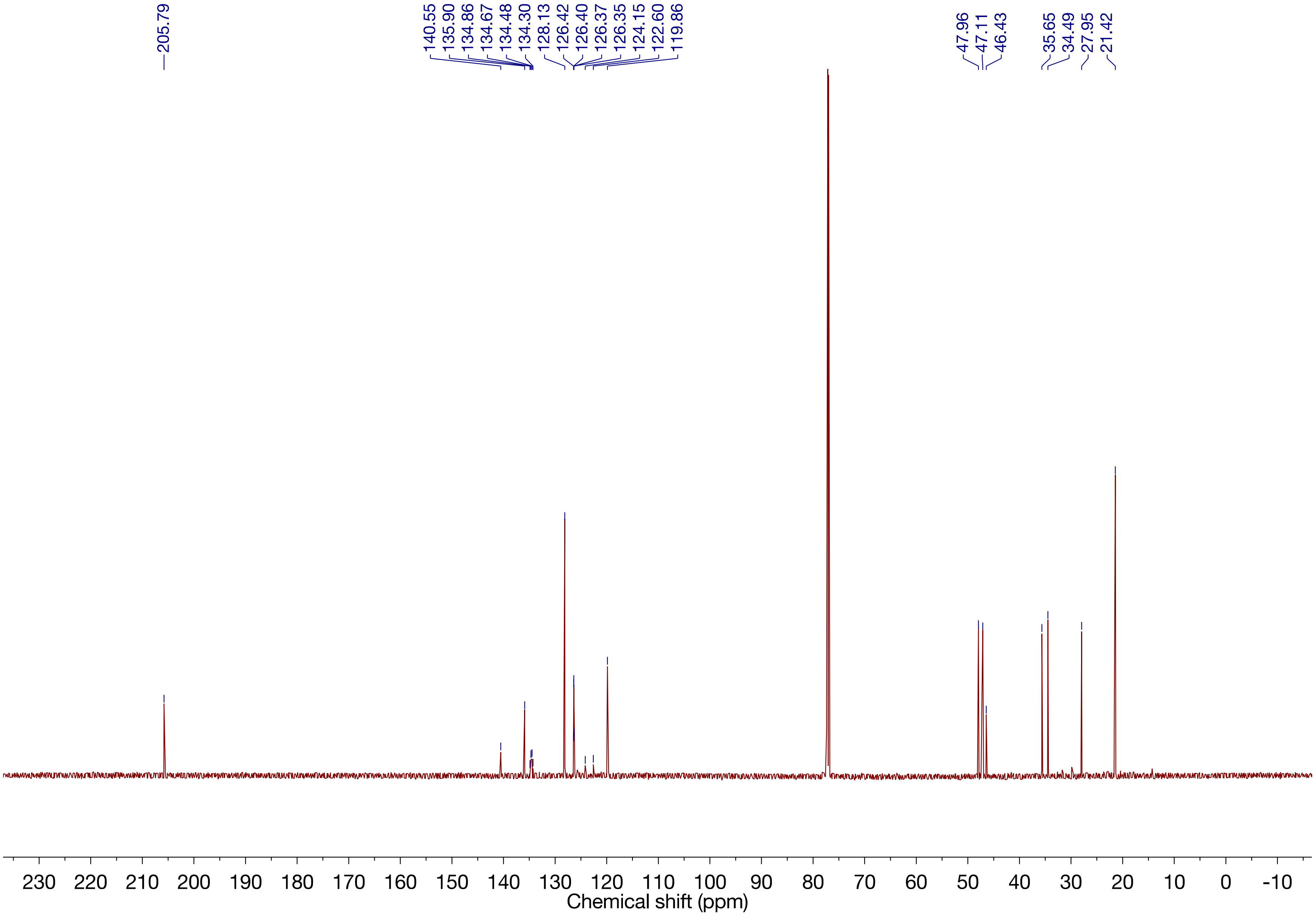

CF3
O
O
S
N
Br
1.85
1.88
1.00
1.97
3.86
2.02
2.03
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

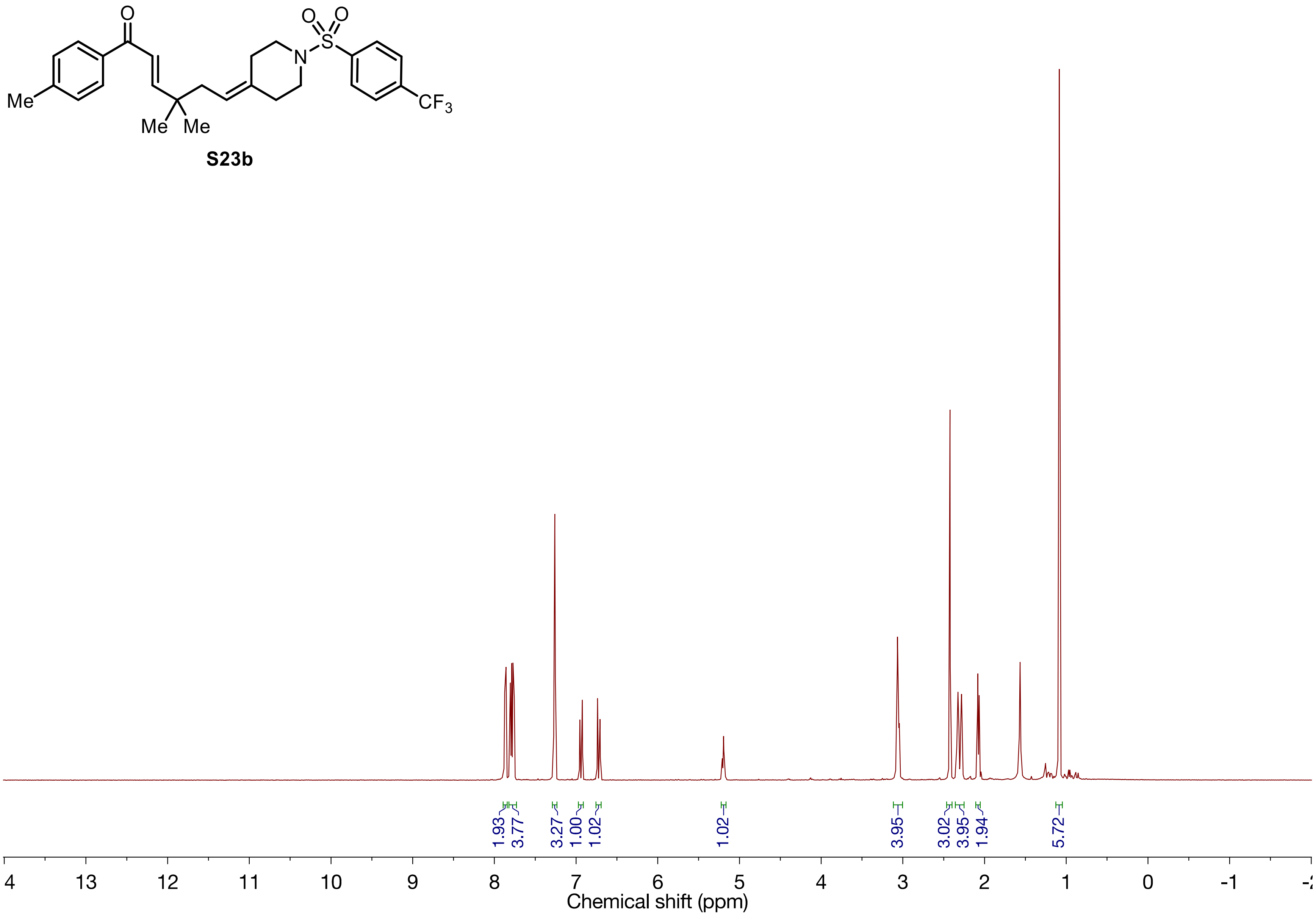
S23z


140.31
140.00
134.96
134.77
134.58
134.39
128.13
126.47
126.45
126.43
126.41
125.64
124.09
122.54
121.40
120.99
47.45
46.72
35.11
27.70
27.00
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


S23a

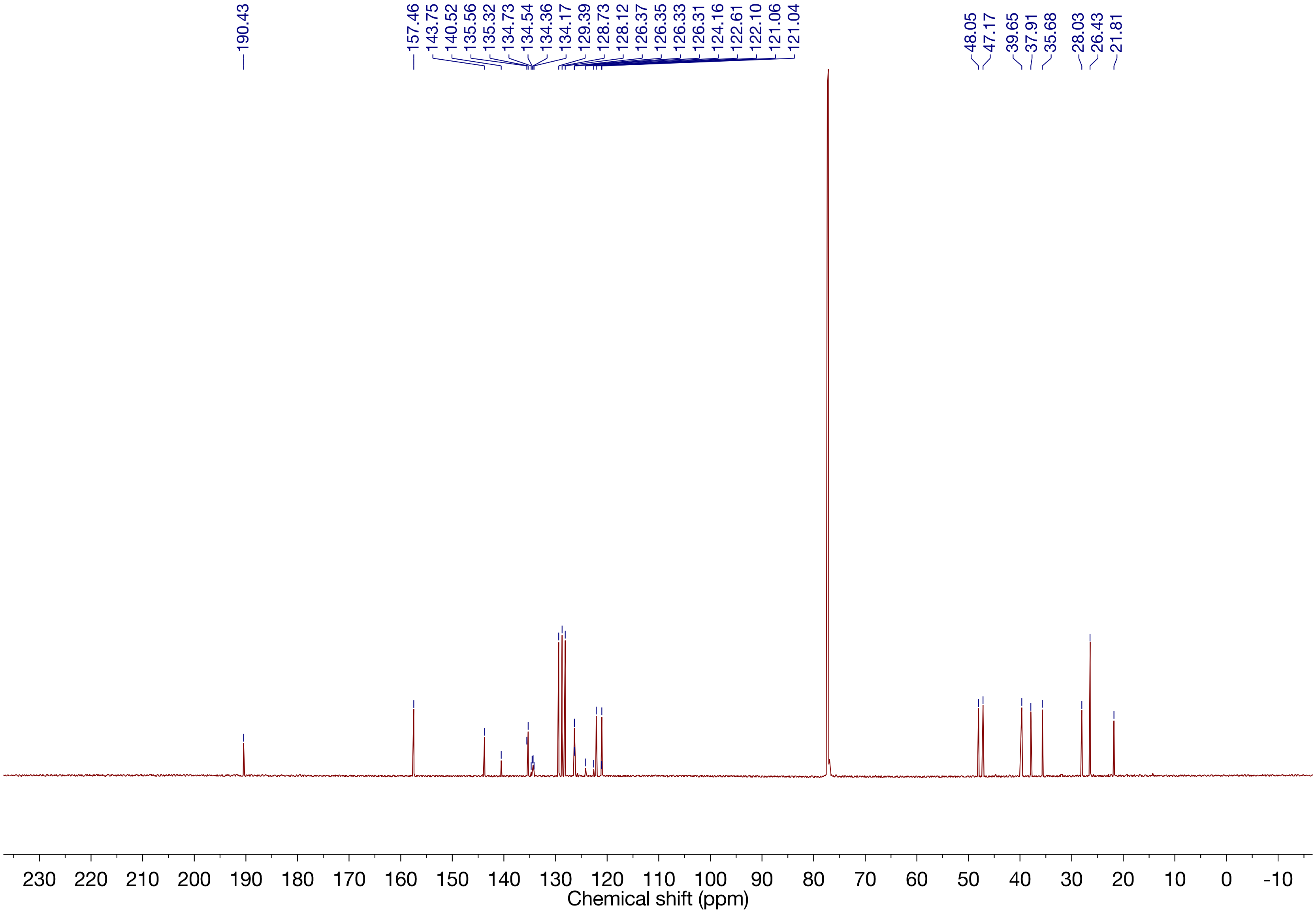
O
H
Me
Me
N
S
O
O
CF3
0.79
1.92
2.00
0.95
3.99
2.02
1.99
1.93
5.74
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


205.79
140.55
135.90
134.86
134.67
134.48
134.30
128.13
126.42
126.40
126.37
126.35
124.15
122.60
119.86
47.96
47.11
46.43
35.65
34.49
27.95
21.42
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

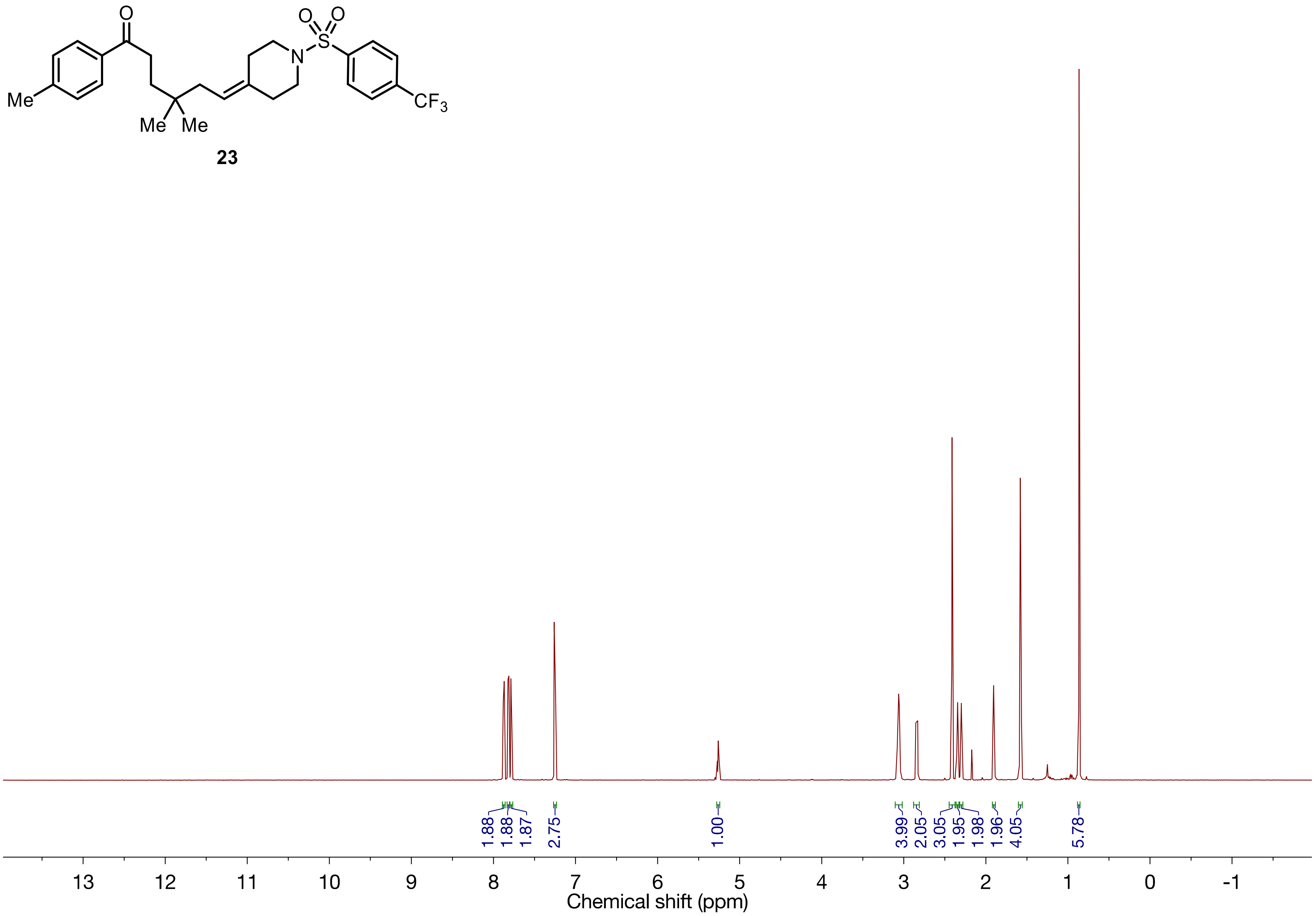


S23b

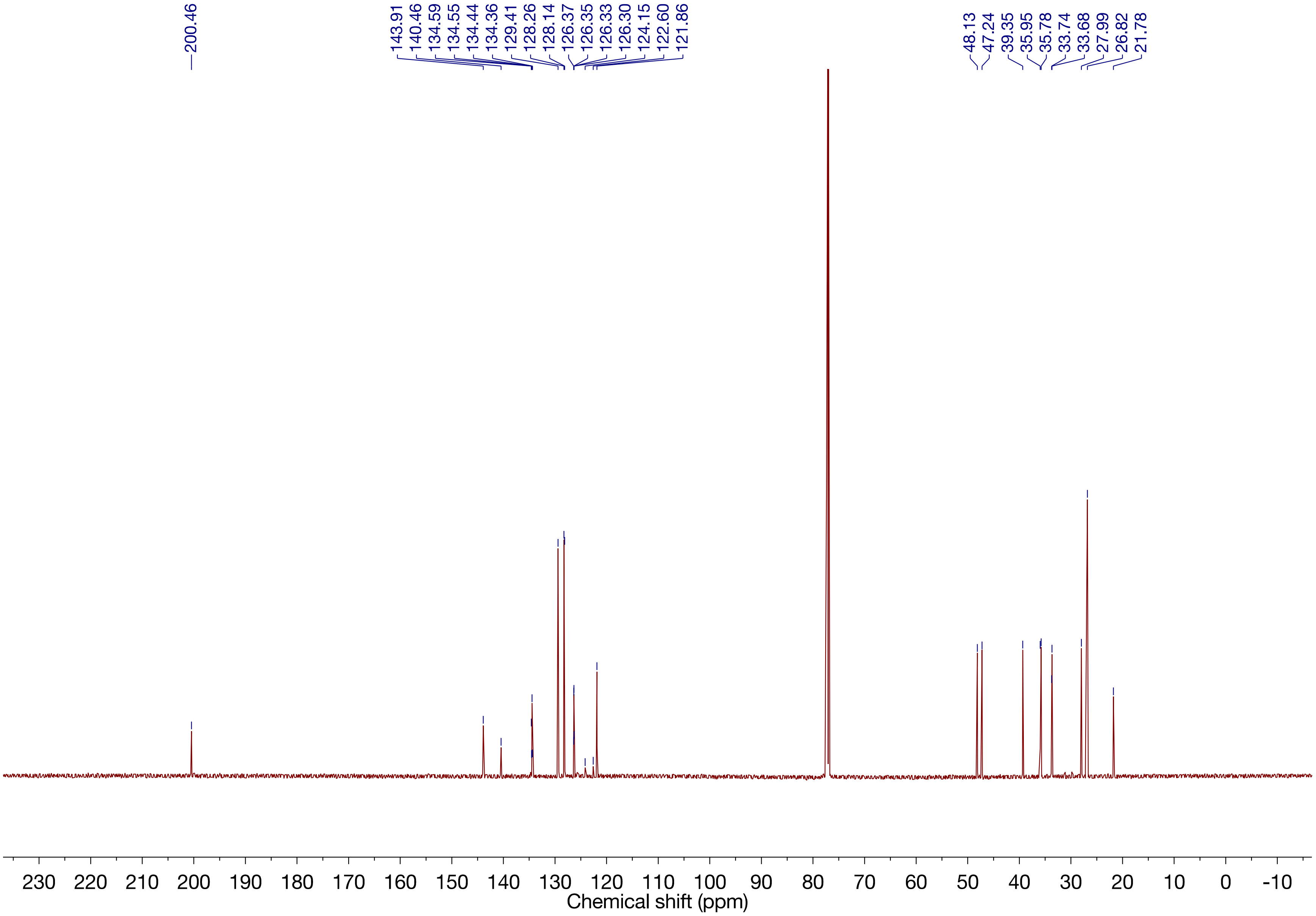
O
O
O
S
N
Me
Me
Me
CF3
1.93
3.77
3.27
1.00
1.02
1.02
3.95
3.02
3.95
1.94
5.72
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-
Chemical shift (ppm)

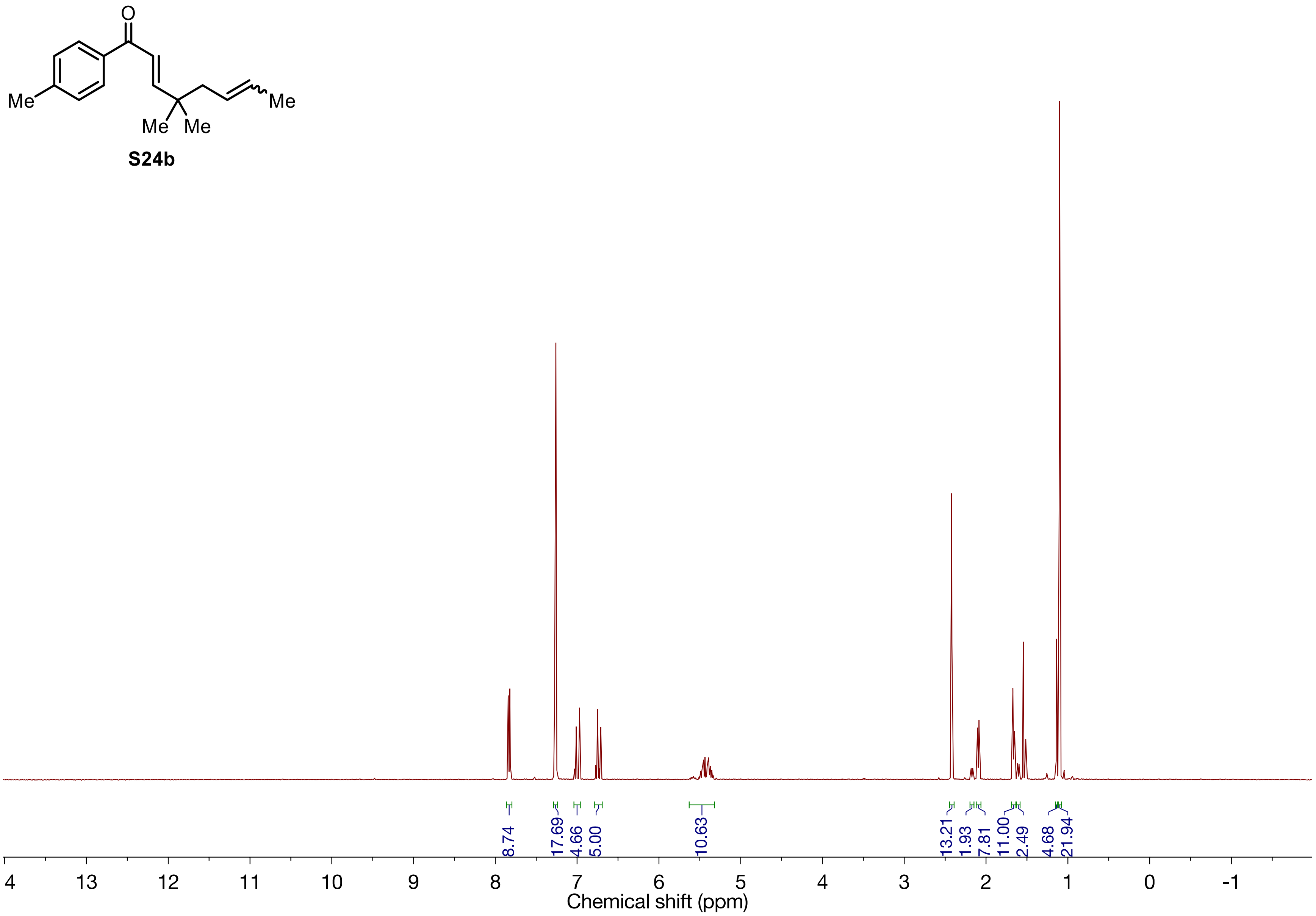


190.43
157.46
143.75
140.52
135.56
135.32
134.73
134.54
134.36
134.17
129.39
128.73
128.12
126.37
126.35
126.33
126.31
124.16
122.61
122.10
121.06
121.04
48.05
47.17
39.65
37.91
35.68
28.03
26.43
21.81
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)

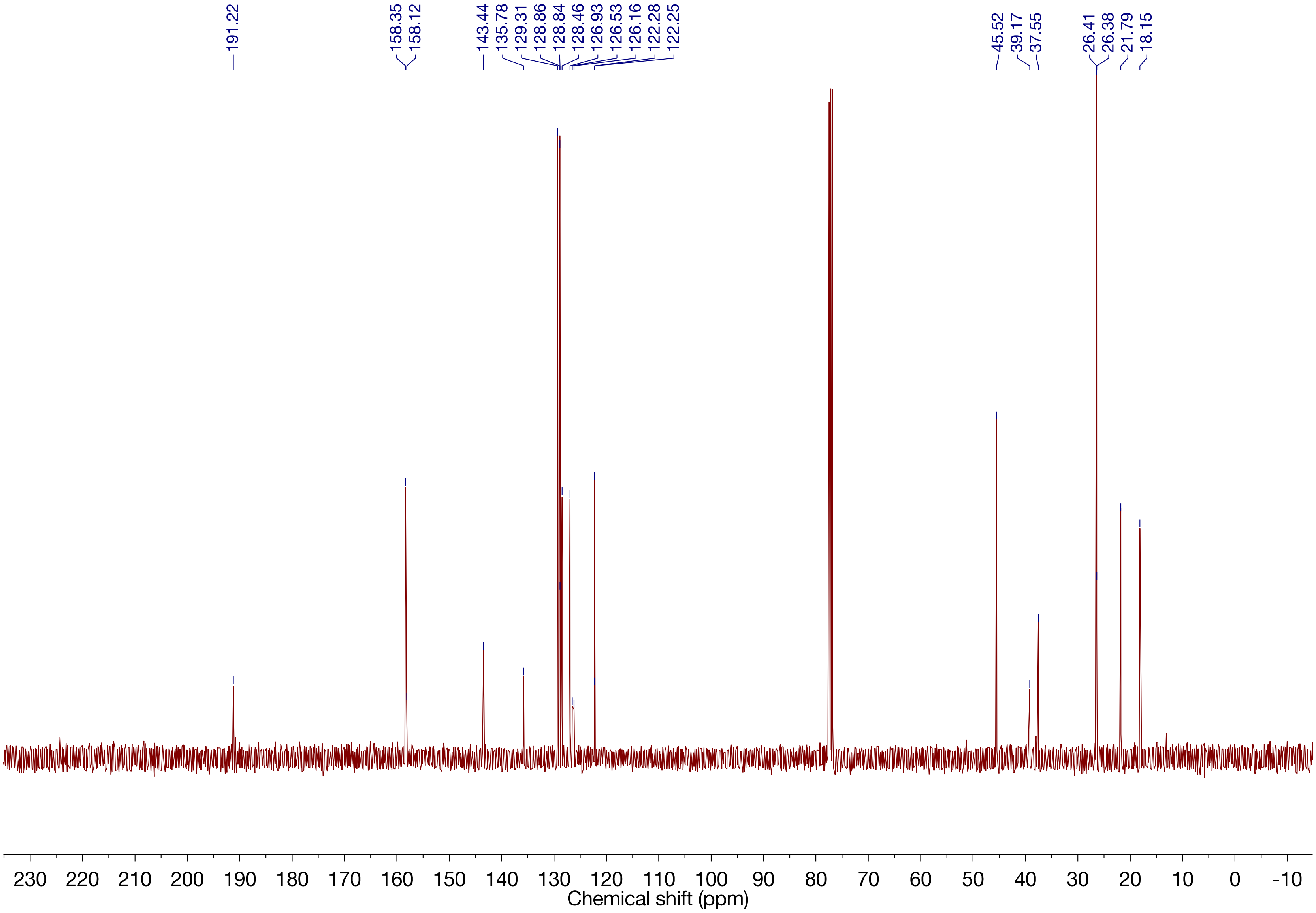

O
O
O
N
S
Me
Me
Me
CF3
1.88
1.88
1.87
2.75
1.00
3.99
2.05
3.05
1.95
1.98
1.96
4.05
5.78
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

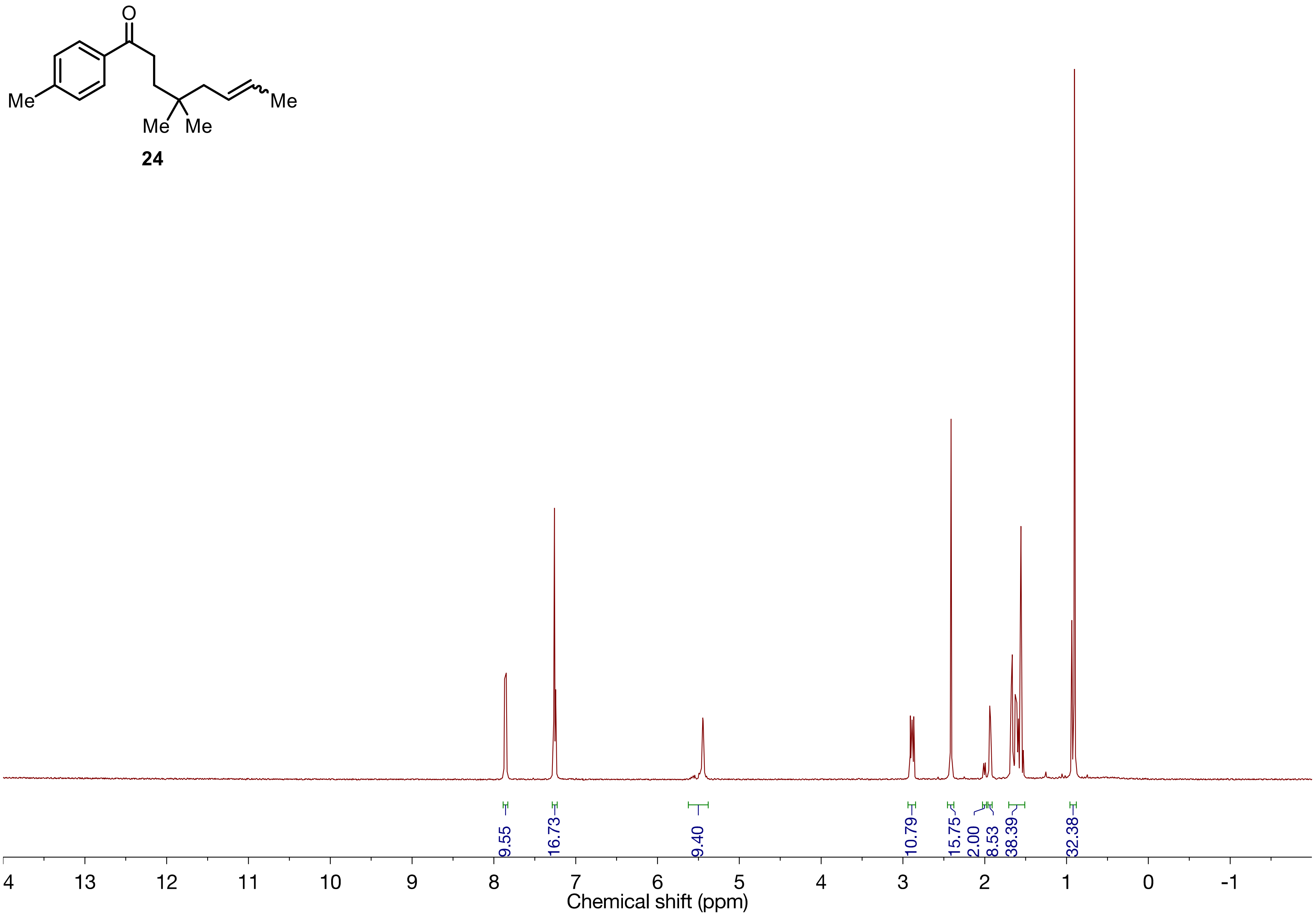
23


200.46
143.91
140.46
134.59
134.55
134.44
134.36
129.41
128.26
128.14
126.37
126.35
126.33
126.30
124.15
122.60
121.86
48.13
47.24
39.35
35.95
35.78
33.74
33.68
27.99
26.82
21.78
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

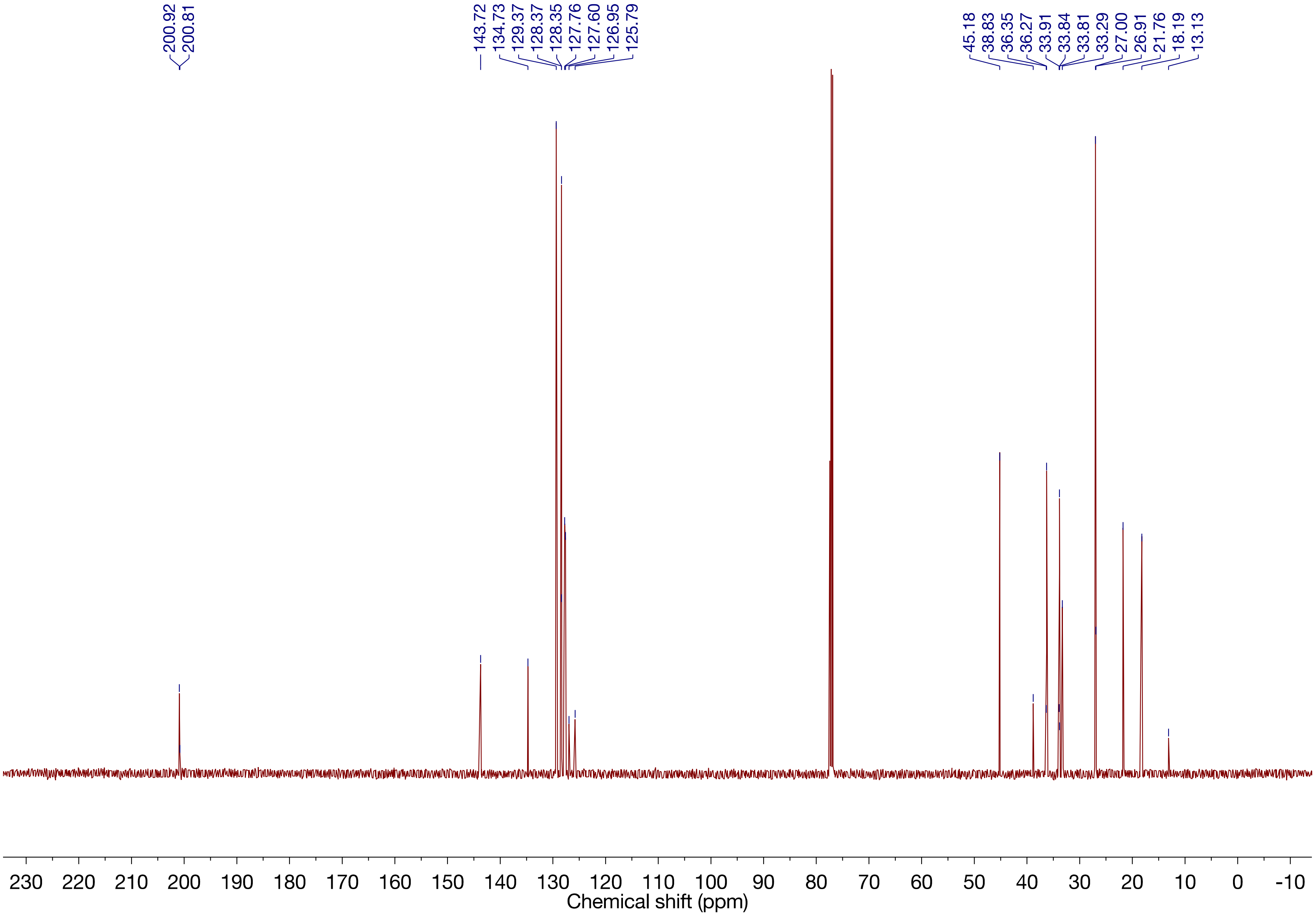

S24b

O
Me
Me
Me
Me
8.74
17.69
4.66
5.00
10.63
13.21
1.93
7.81
11.00
2.49
4.68
21.94
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

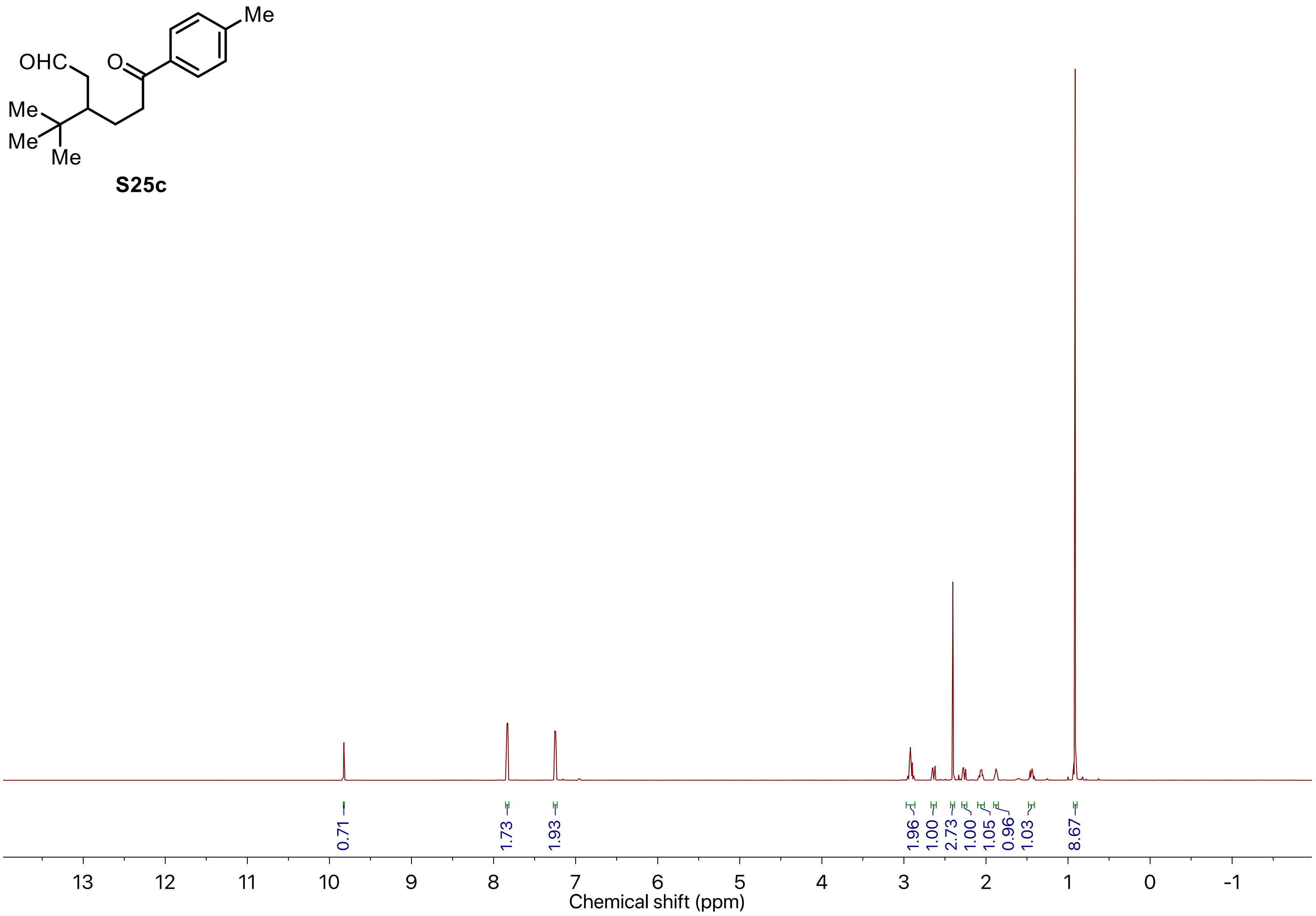

191.22
158.35
158.12
143.44
135.78
129.31
128.86
128.84
128.46
126.93
126.53
126.16
122.28
122.25
45.52
39.17
37.55
26.41
26.38
21.79
18.15
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


24

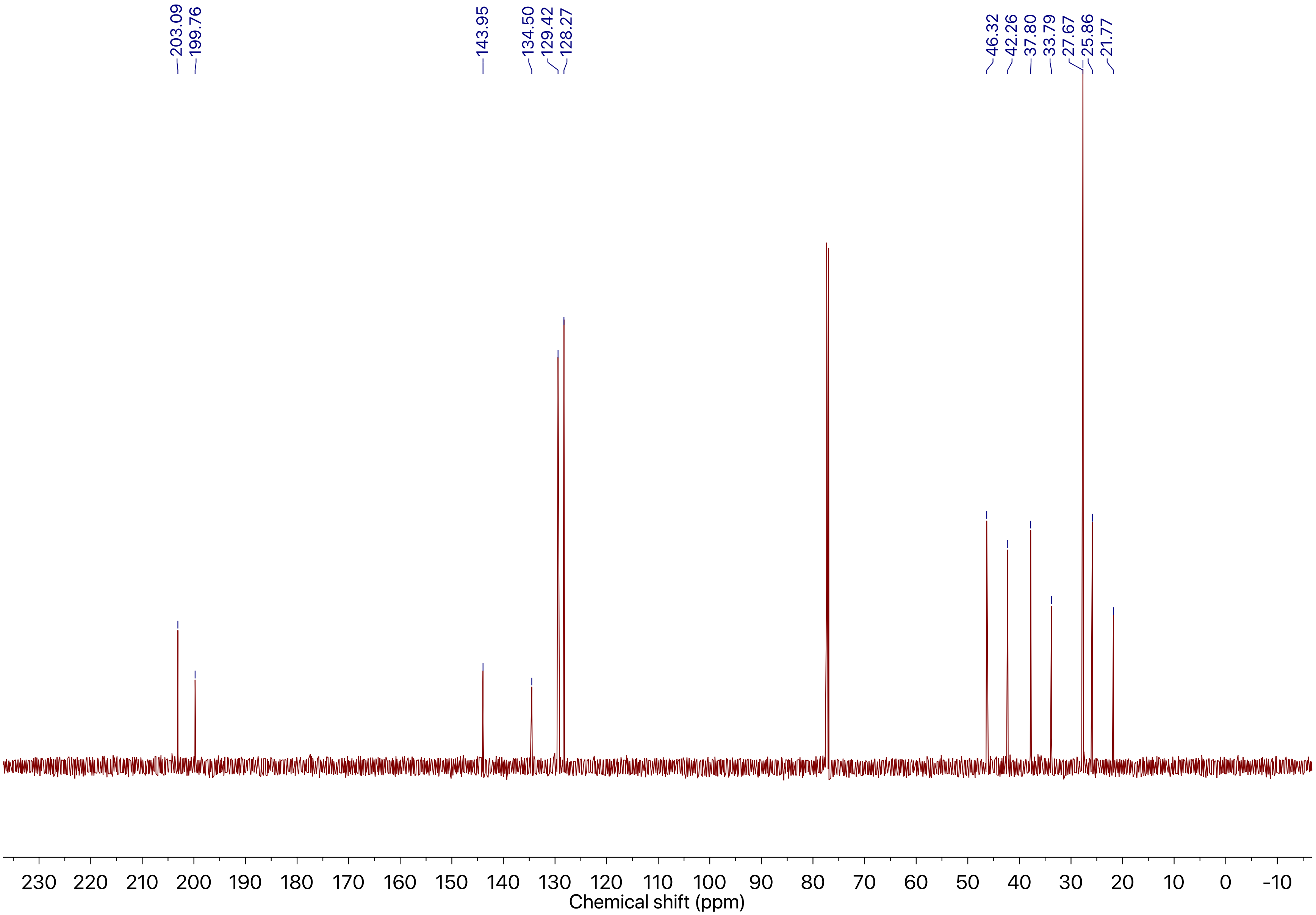
O
Me
Me
Me
Me
9.55
16.73
9.40
10.79
15.75
2.00
8.53
38.39
32.38
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)



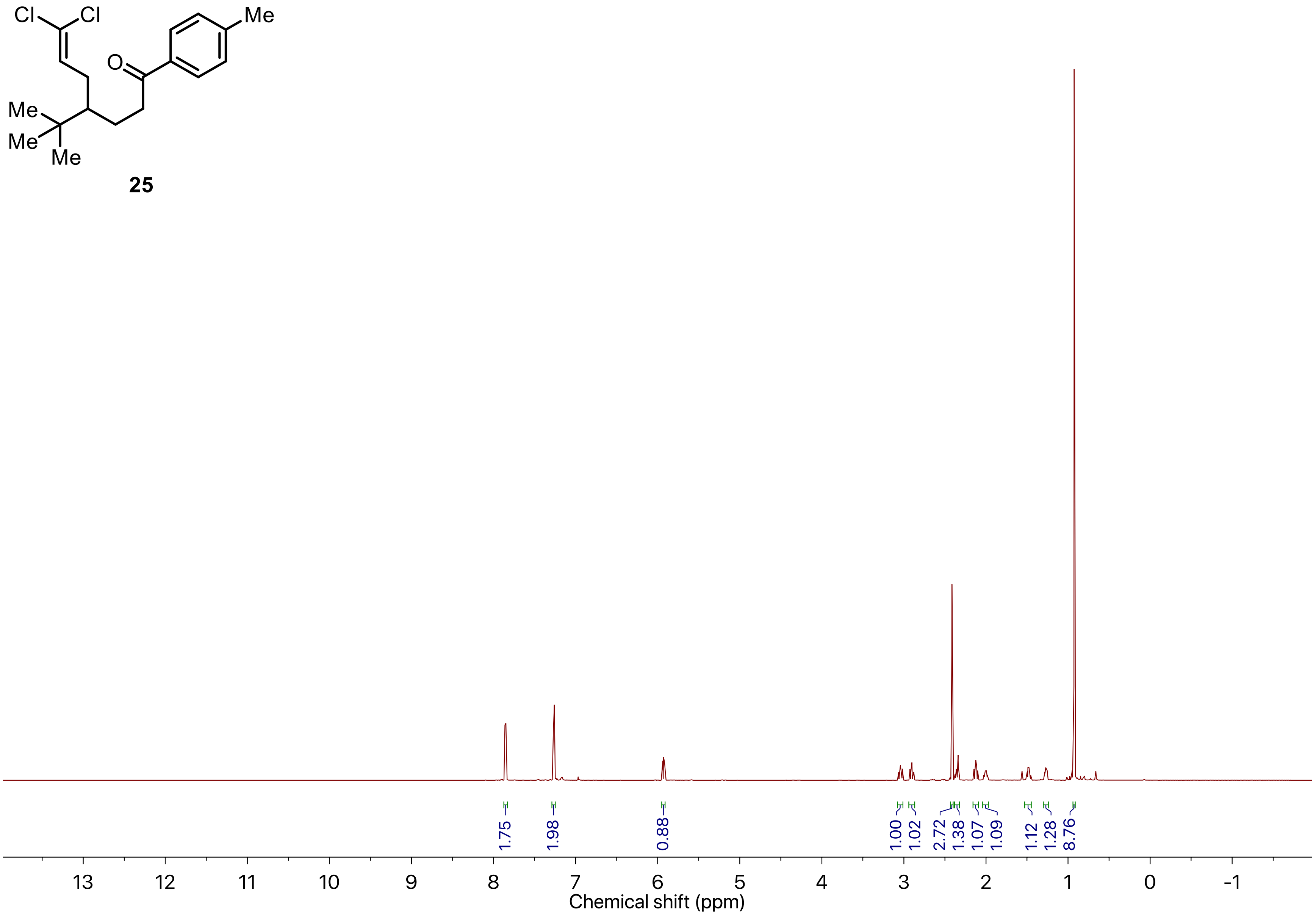
200.92
200.81
143.72
134.73
129.37
128.37
128.35
127.76
127.60
126.95
125.79
45.18
38.83
36.35
36.27
33.91
33.84
33.81
33.29
27.00
26.91
21.76
18.19
13.13
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


OHC
O
Me
Me
Me
Me
0.71
1.73
1.93
1.96
1.00
2.73
1.00
1.05
0.96
1.03
8.67
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

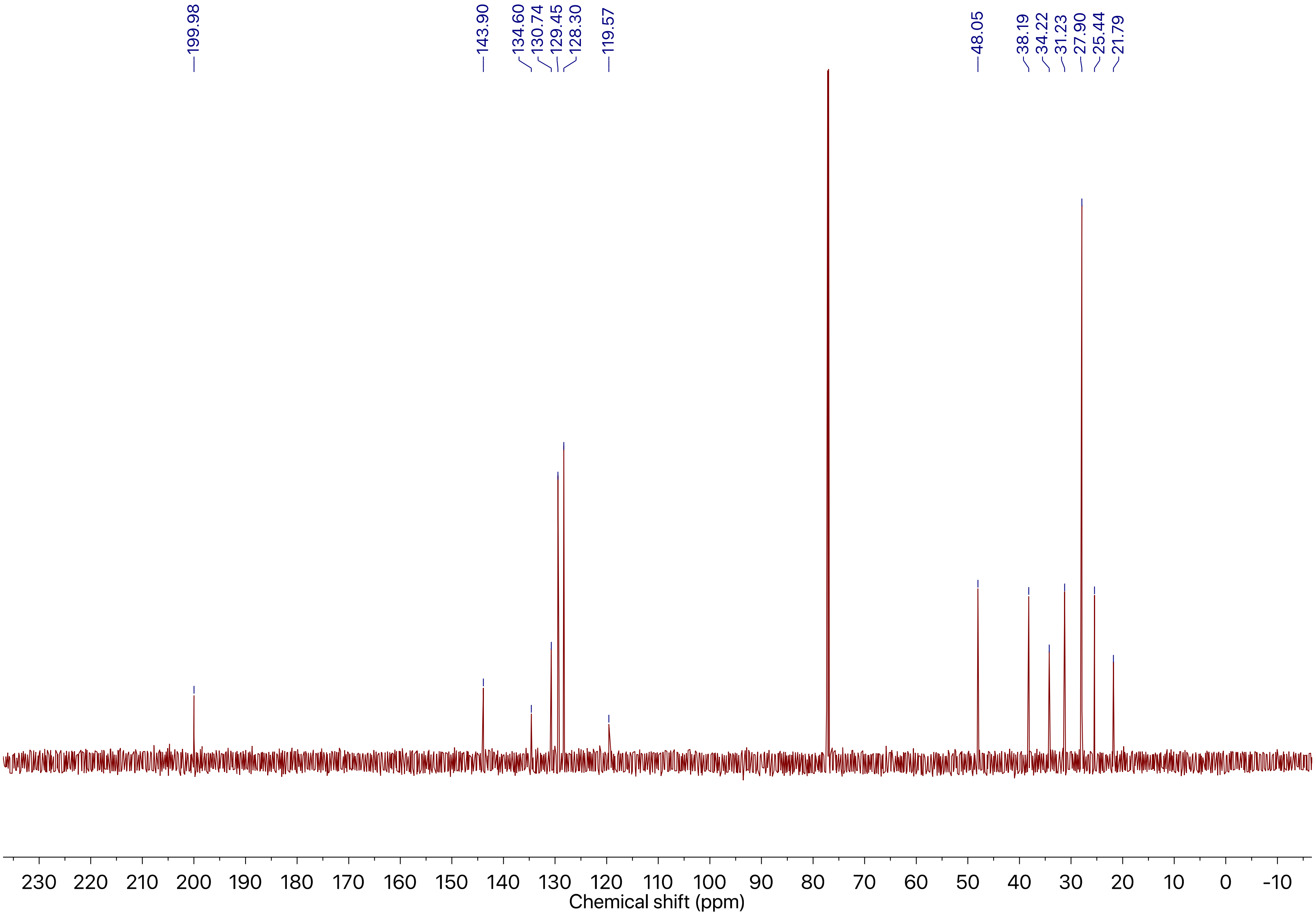
S25c



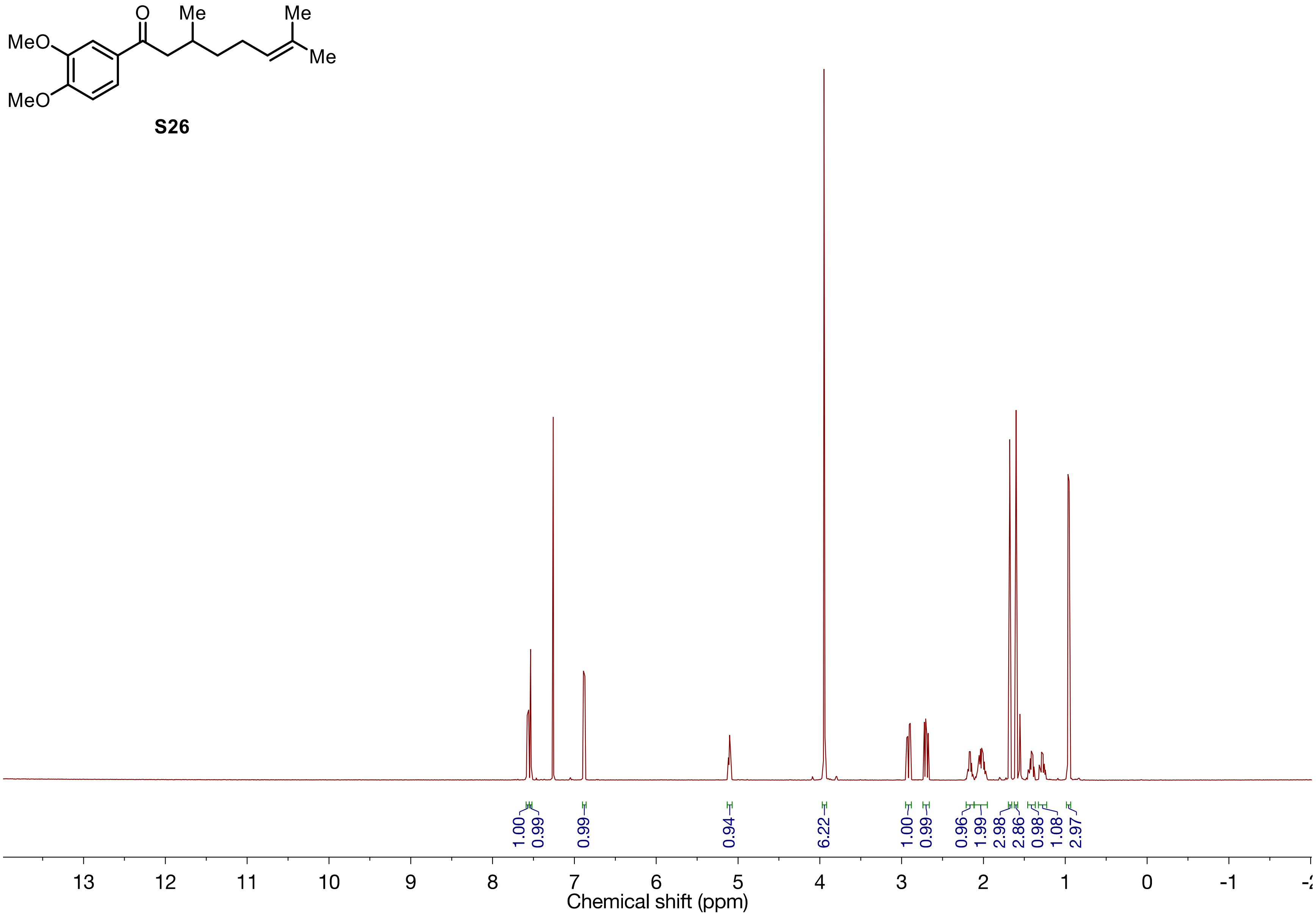
203.09
199.76
143.95
134.50
129.42
128.27
46.32
42.26
37.80
33.79
27.67
25.86
21.77
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


25

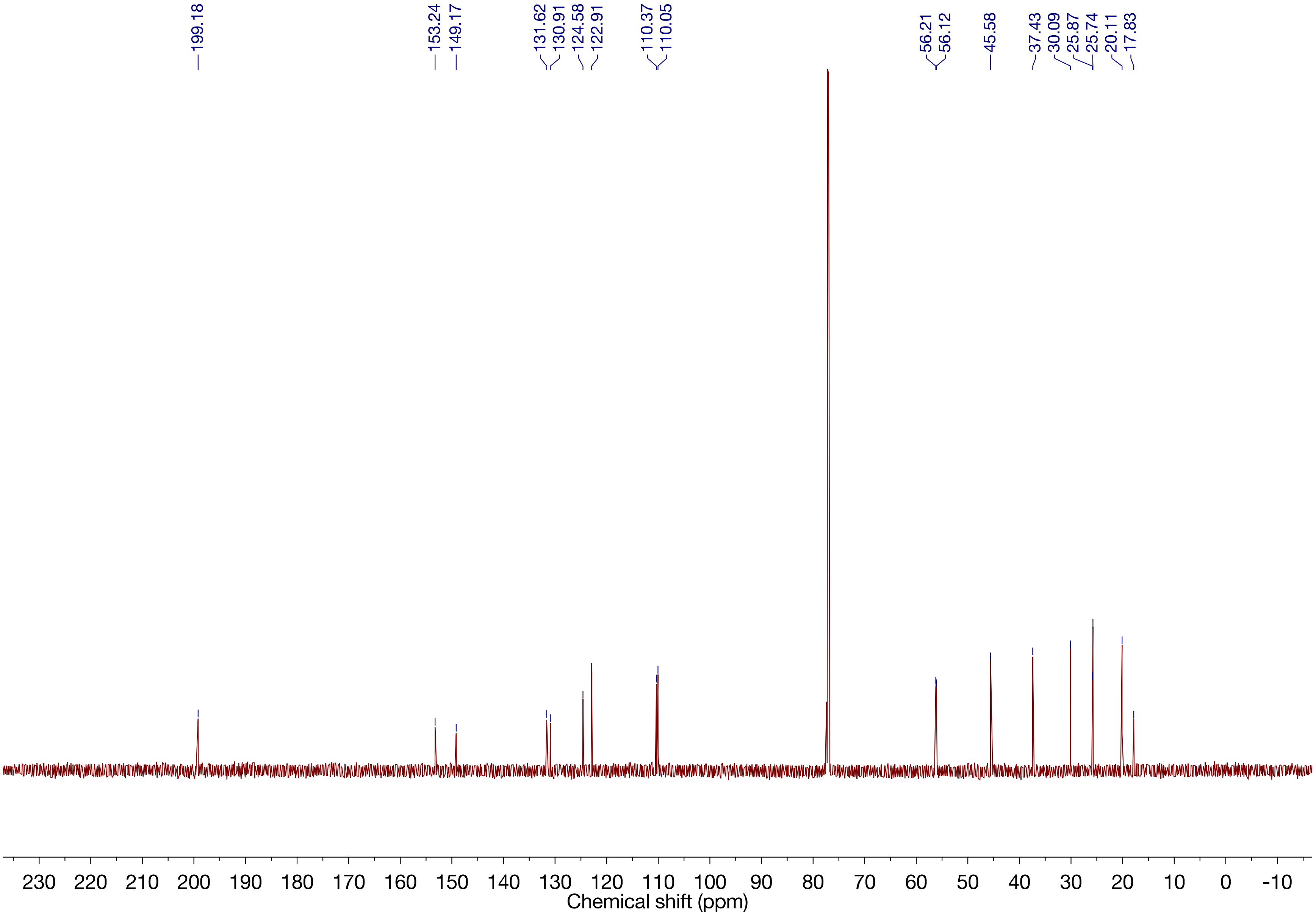
Cl
Cl
O
Me
Me
Me
Me
1.75
1.98
0.88
1.00
1.02
2.72
1.38
1.07
1.09
1.12
1.28
8.76
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)



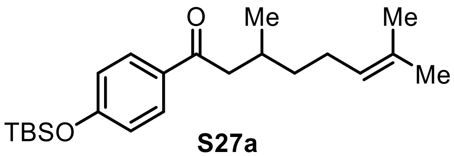
199.98
143.90
134.60
130.74
129.45
128.30
119.57
48.05
38.19
34.22
31.23
27.90
25.44
21.79
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


MeO
MeO
O
Me
Me
Me
1.00
0.99
0.99
0.94
6.22
1.00
0.99
0.96
1.99
2.98
2.86
0.98
1.08
2.97
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-
Chemical shift (ppm)

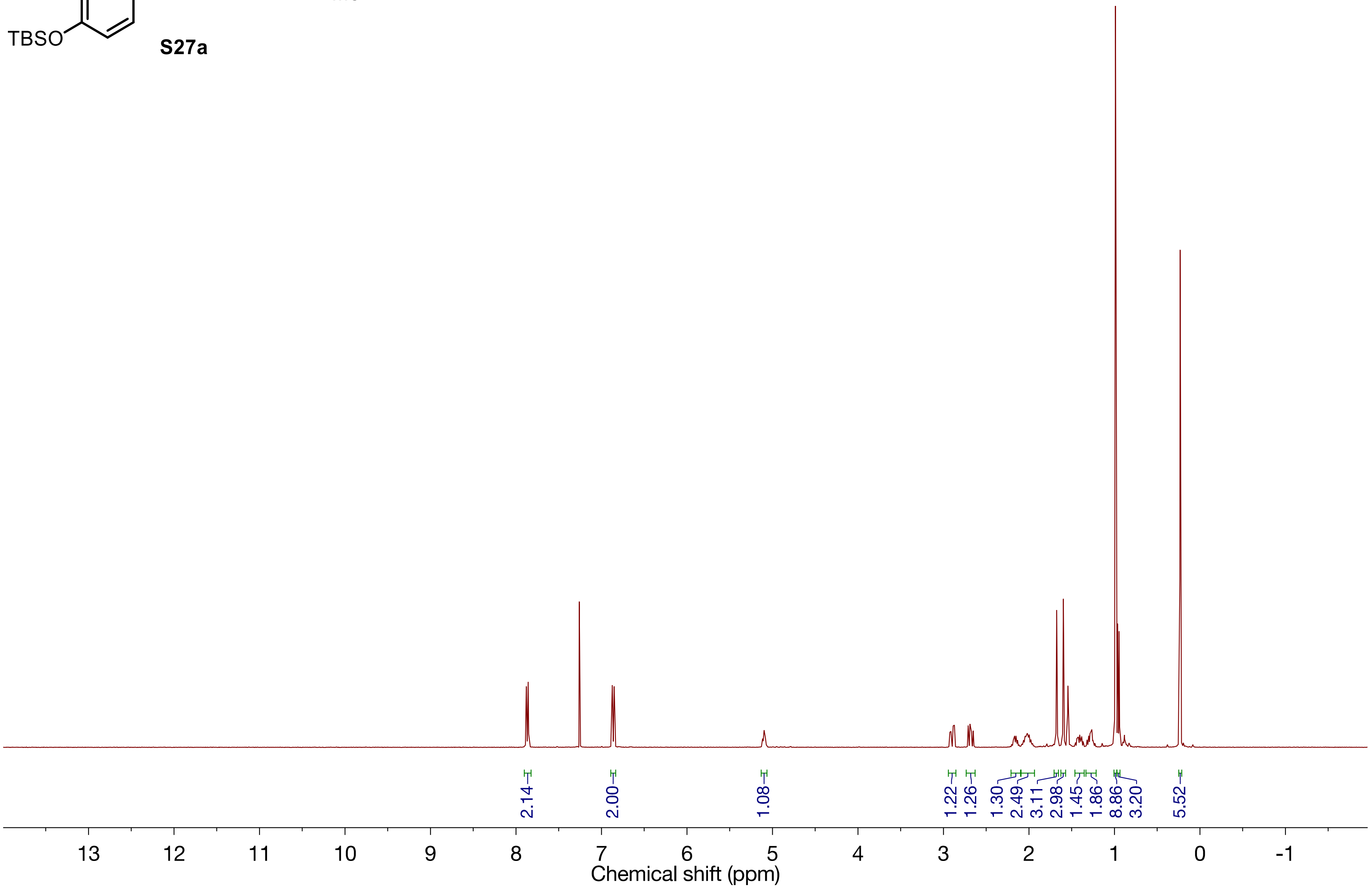
S26

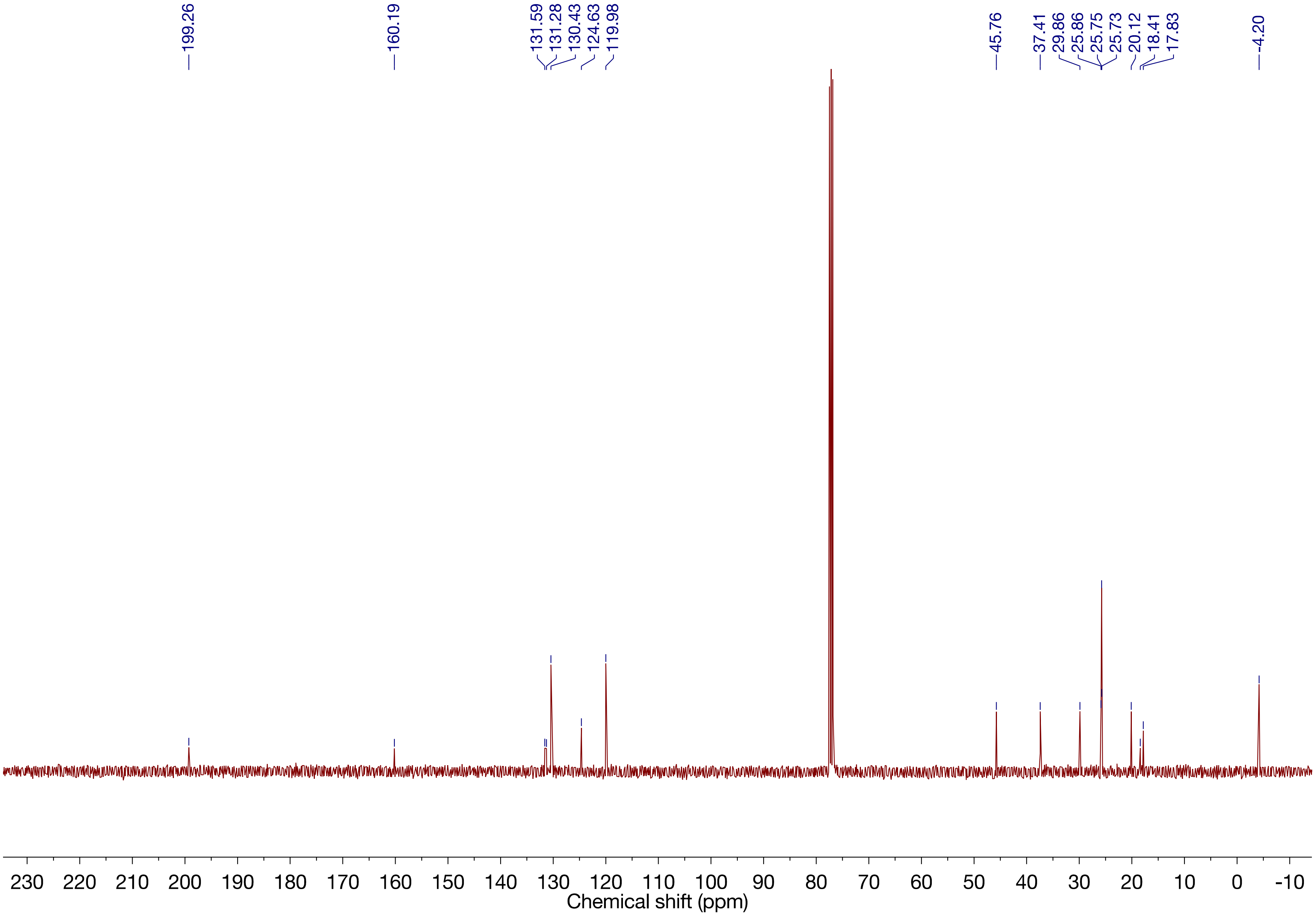


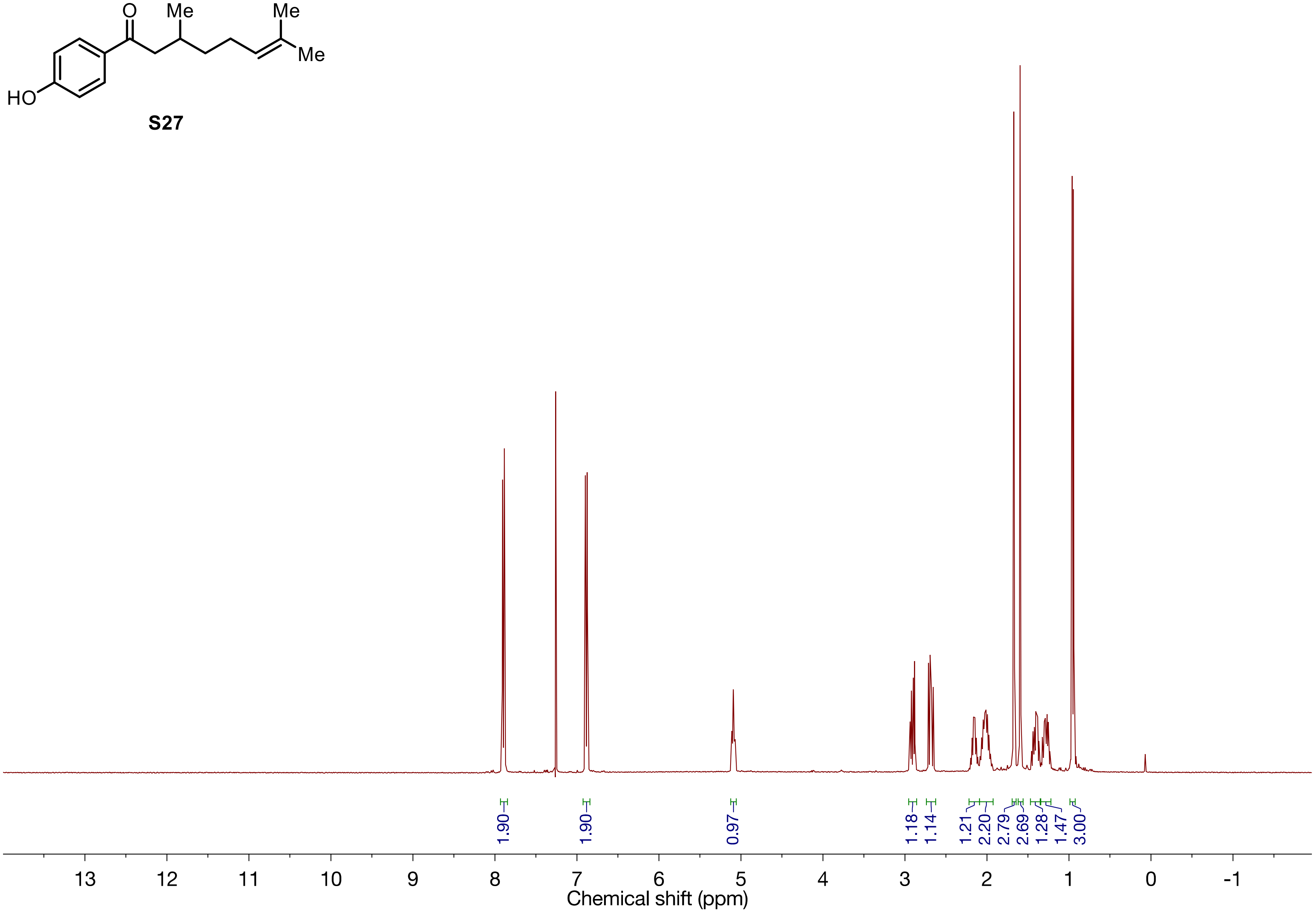
199.18
153.24
149.17
131.62
130.91
124.58
122.91
110.37
110.05
56.21
56.12
45.58
37.43
30.09
25.87
25.74
20.11
17.83
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


O
Me
Me
Me
TBSO

S27a

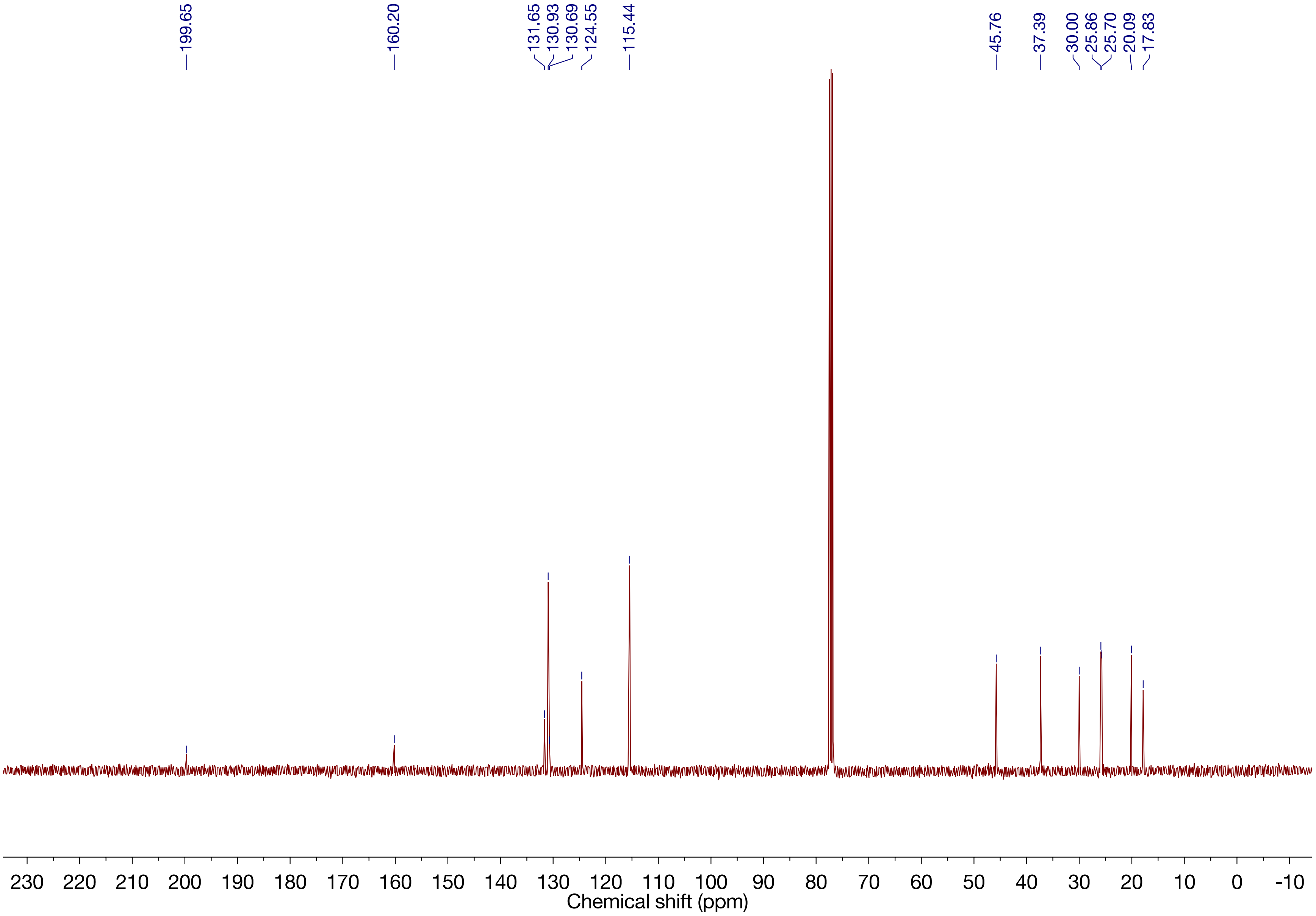

2.14
2.00
1.08
1.22
1.26
1.30
2.49
3.11
2.98
1.45
1.86
8.86
3.20
5.52
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

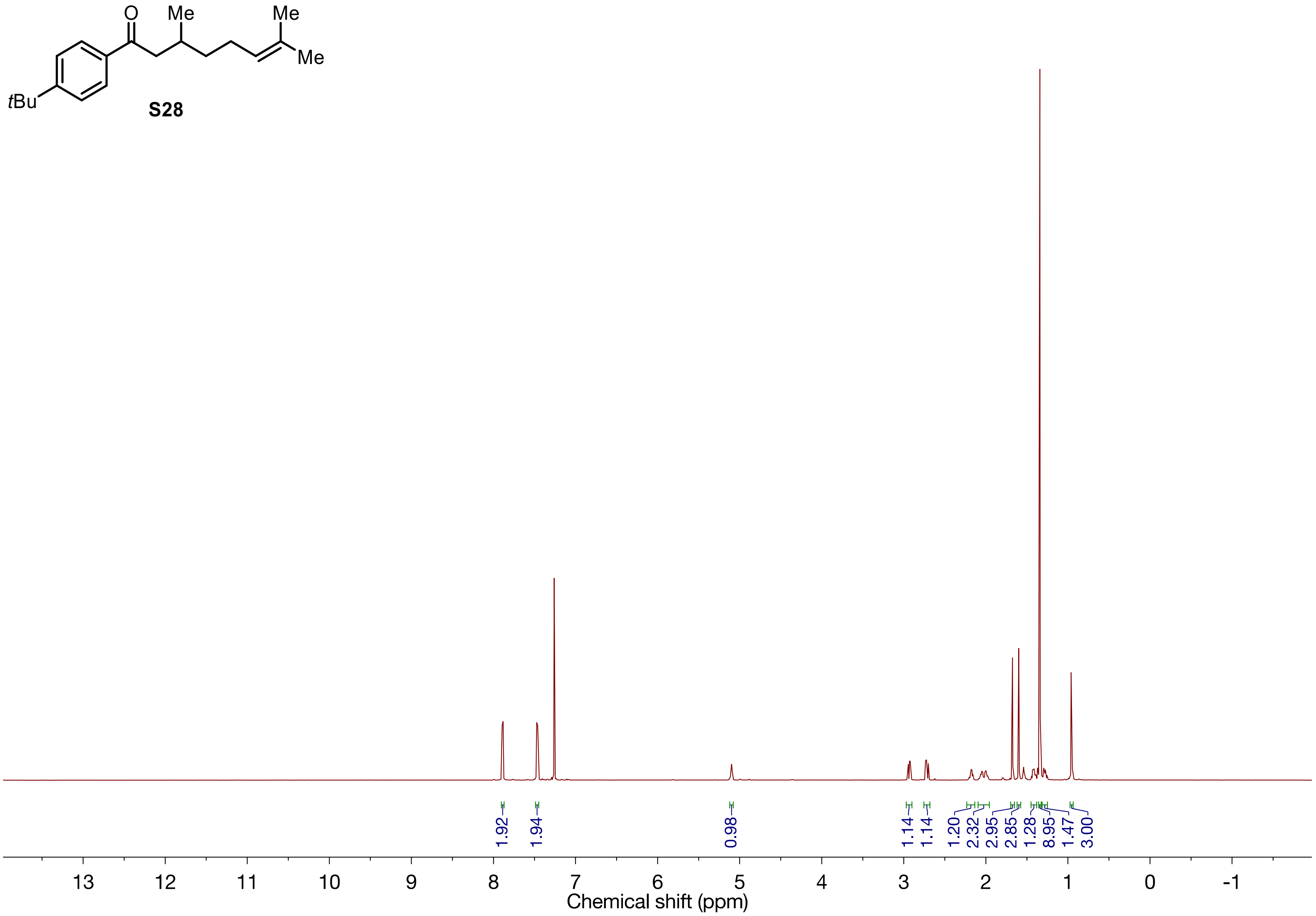

199.26
160.19
131.59
131.28
130.43
124.63
119.98
45.76
37.41
29.86
25.86
25.75
25.73
20.12
18.41
17.83
-4.20
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



S27

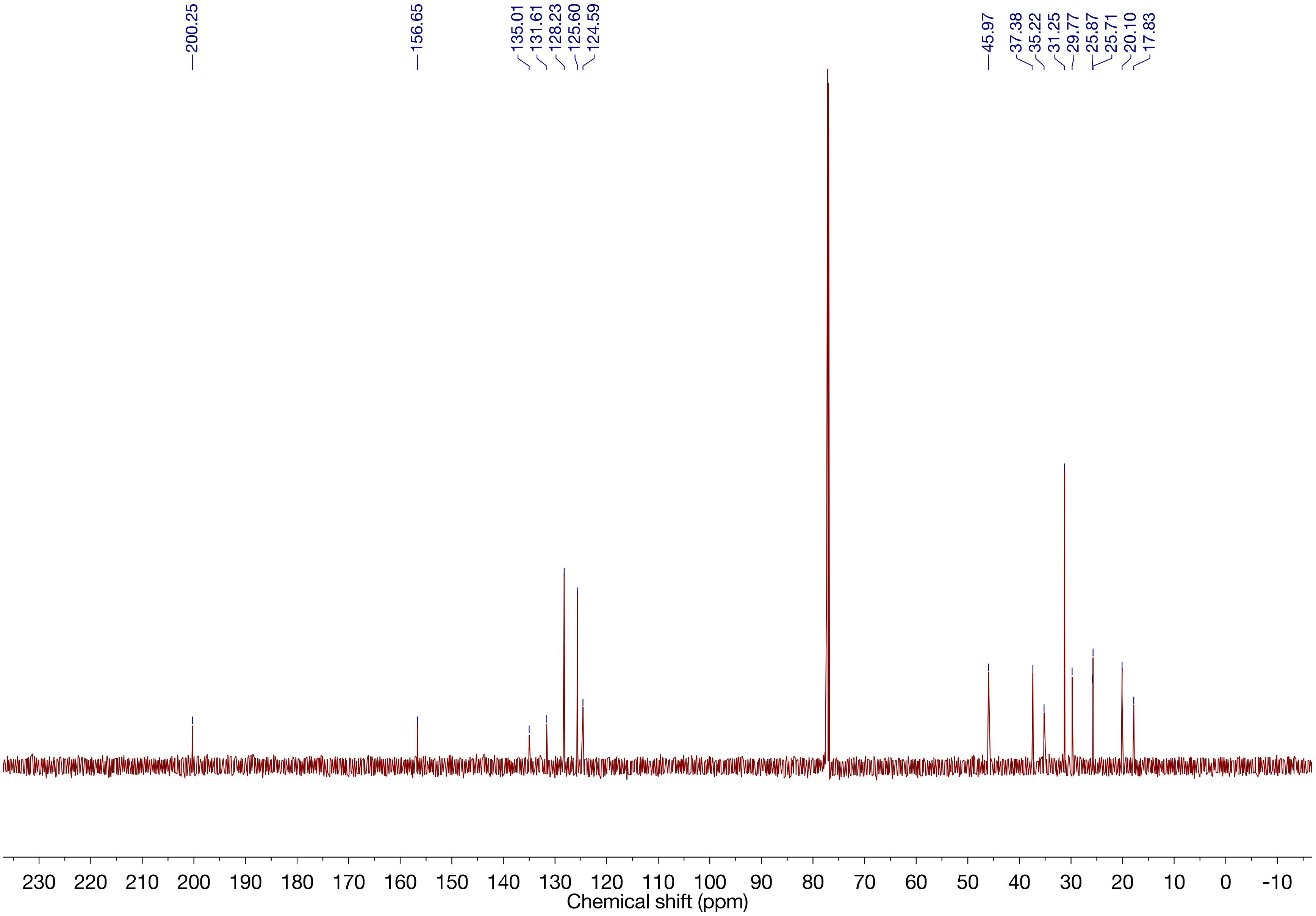
O
Me
Me
Me
HO
1.90
1.90
0.97
1.18
1.14
1.21
2.20
2.79
2.69
1.28
1.47
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

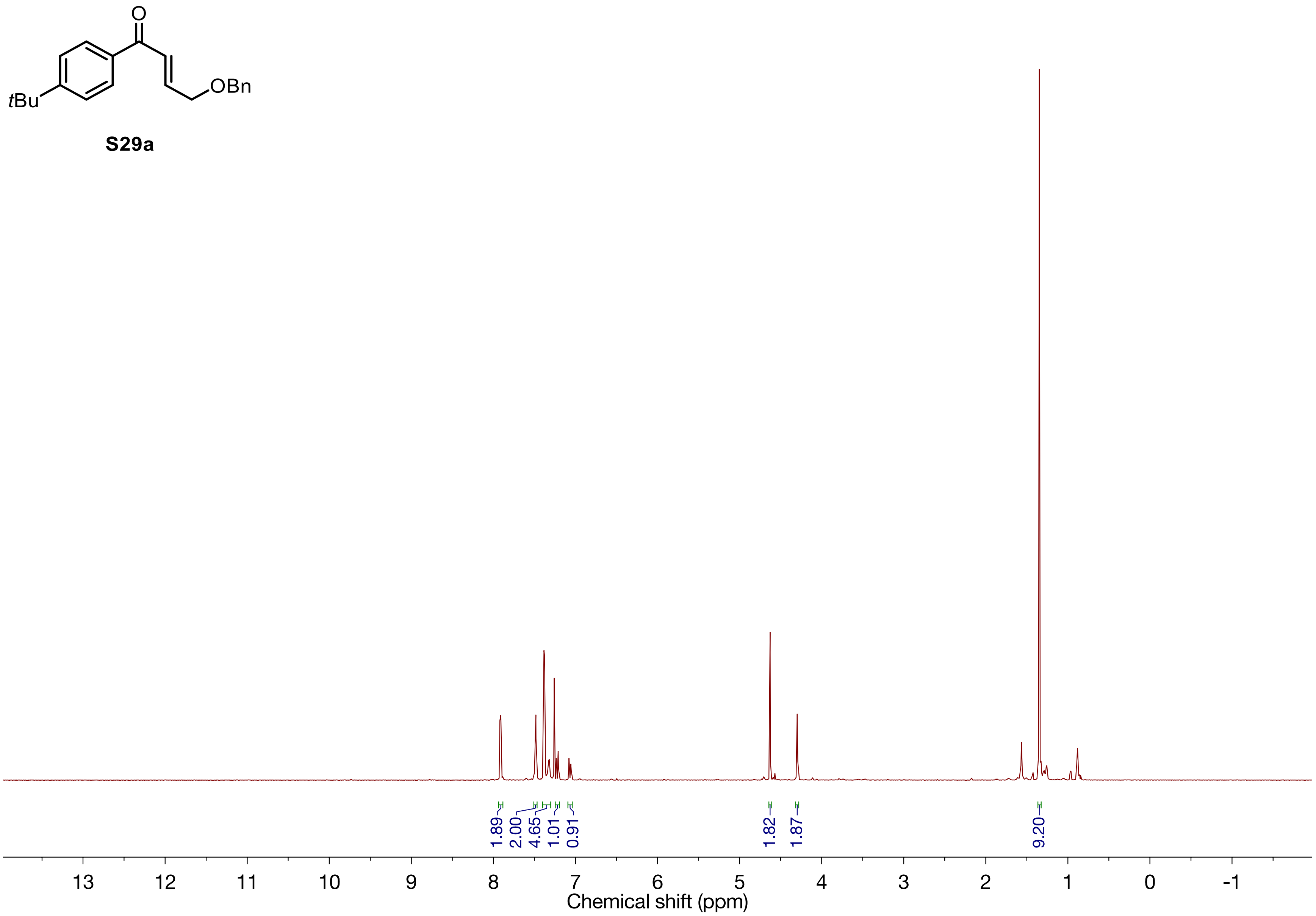

199.65
160.20
131.65
130.93
130.69
124.55
115.44
45.76
37.39
30.00
25.86
25.70
20.09
17.83
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



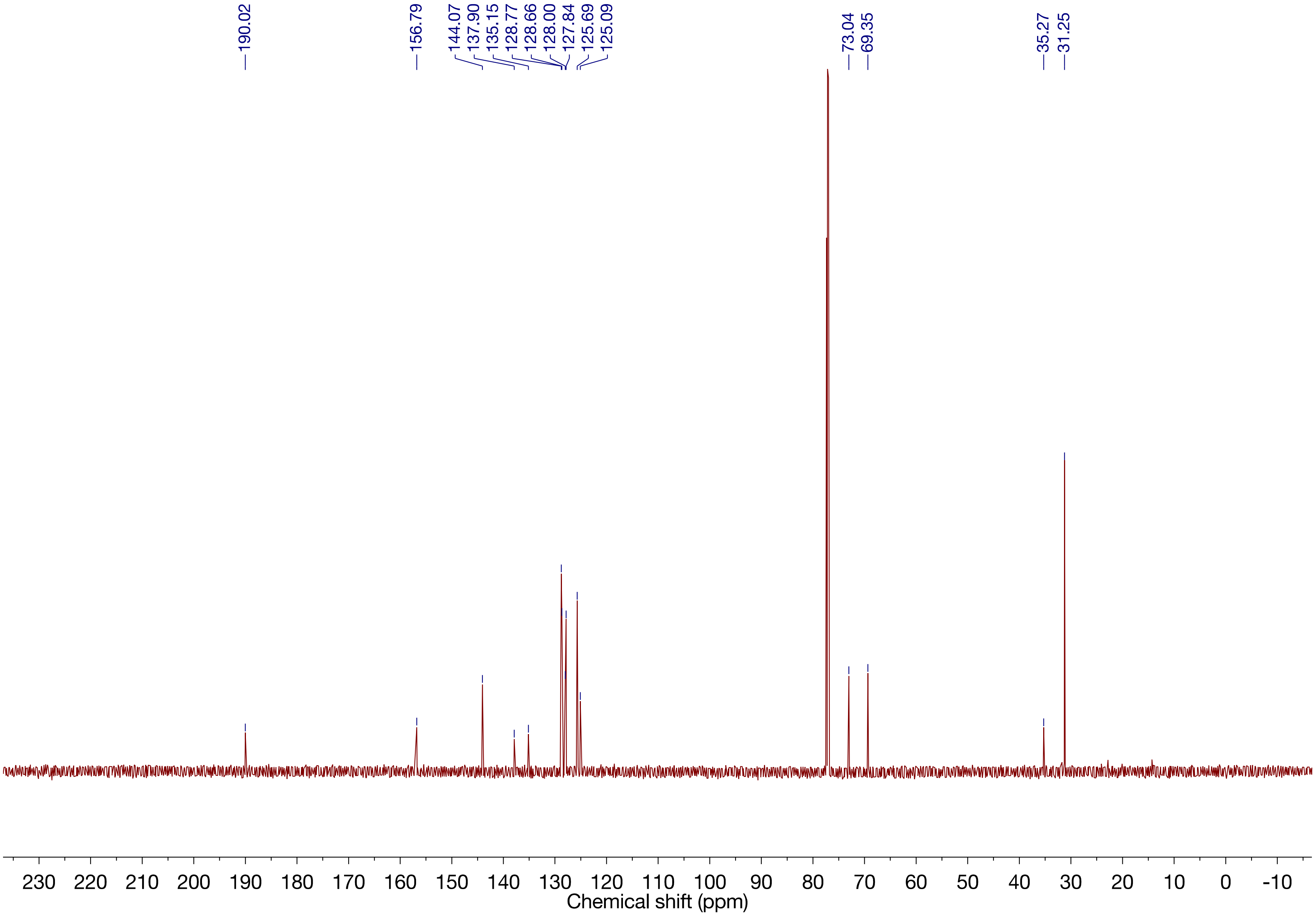
S28

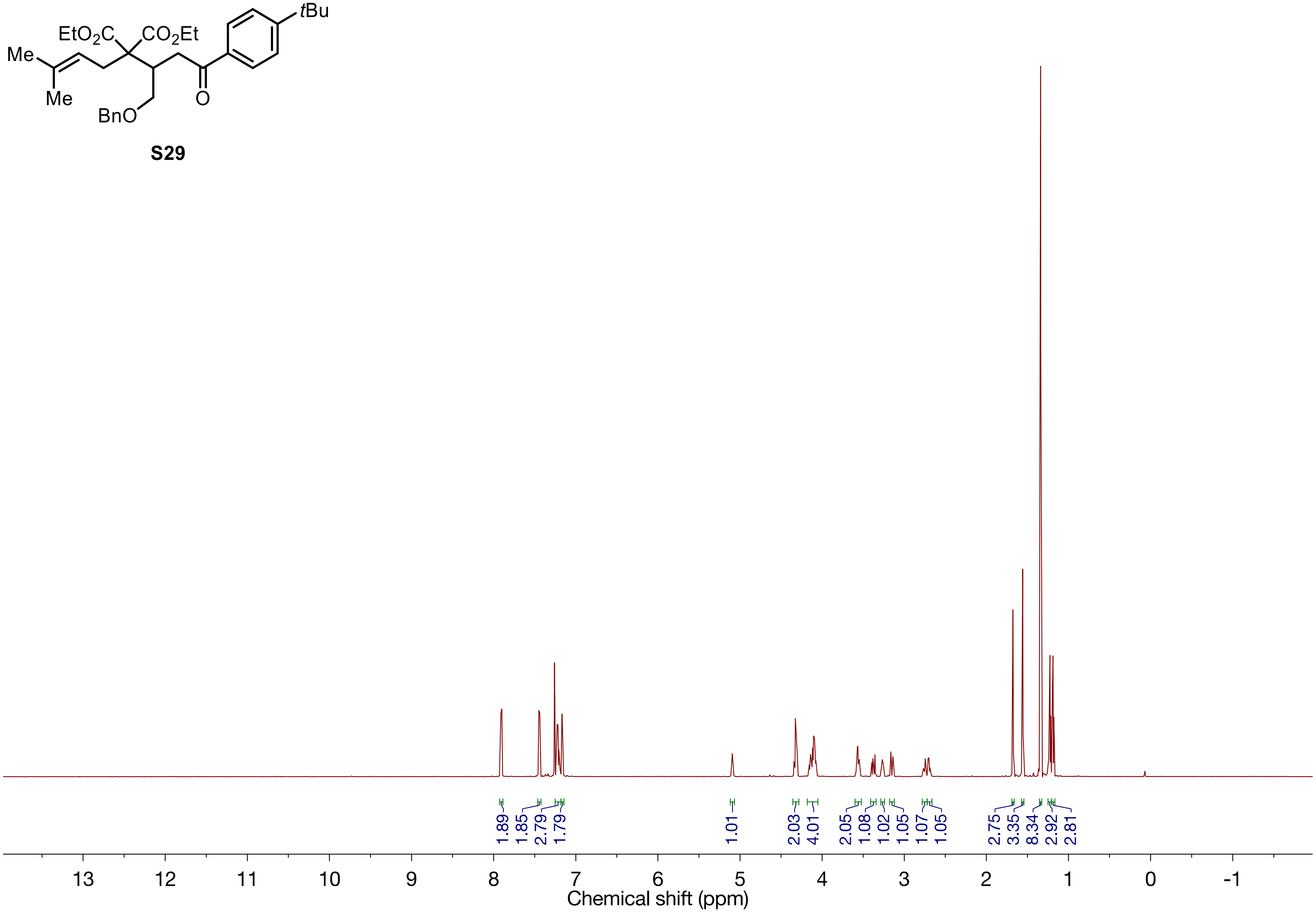
O
Me
Me
Me
tBu
1.92
1.94
0.98
1.14
1.14
1.20
2.32
2.95
2.85
1.28
8.95
1.47
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

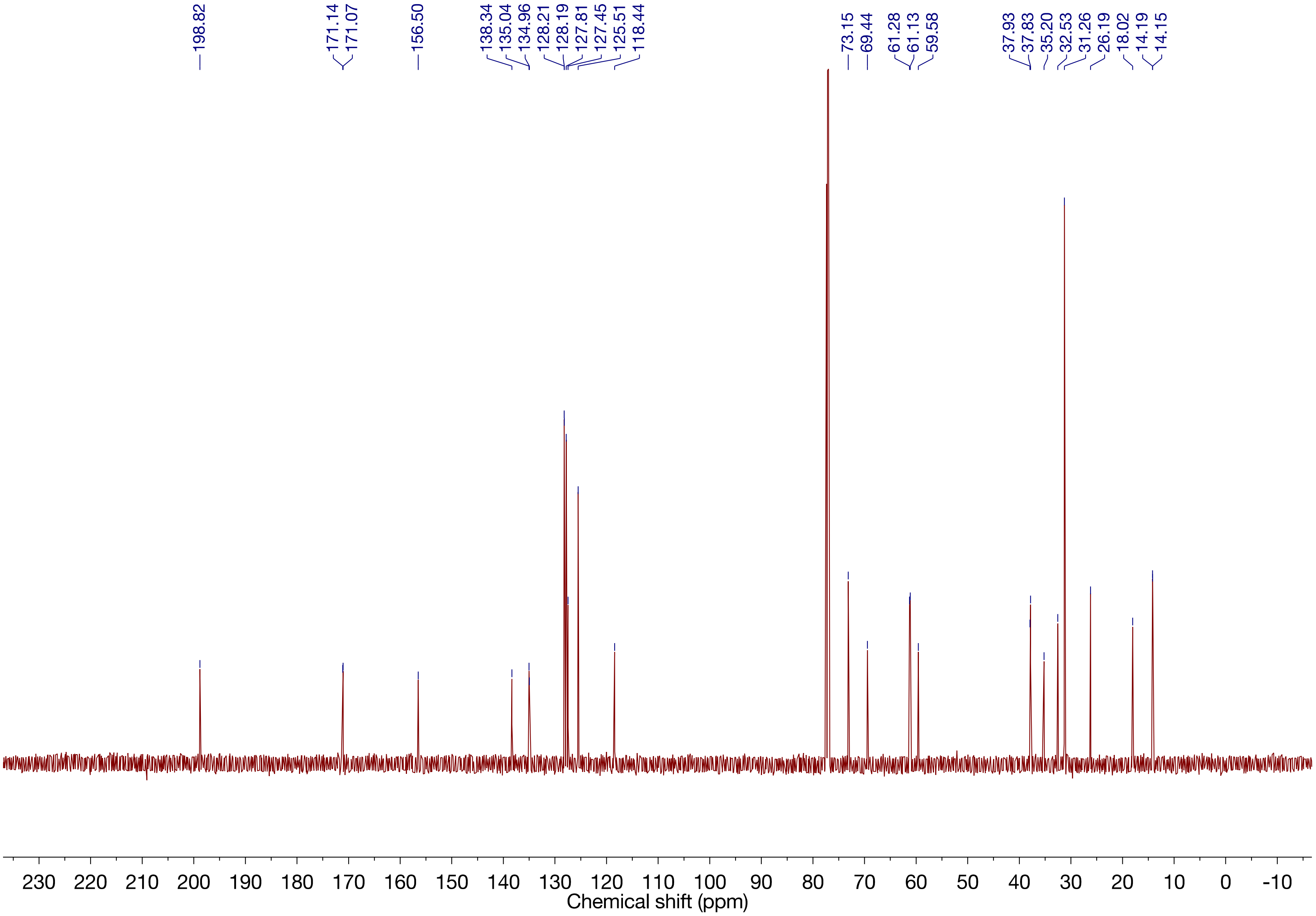

200.25
156.65
135.01
131.61
128.23
125.60
124.59
45.97
37.38
35.22
31.25
29.77
25.87
25.71
20.10
17.83
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

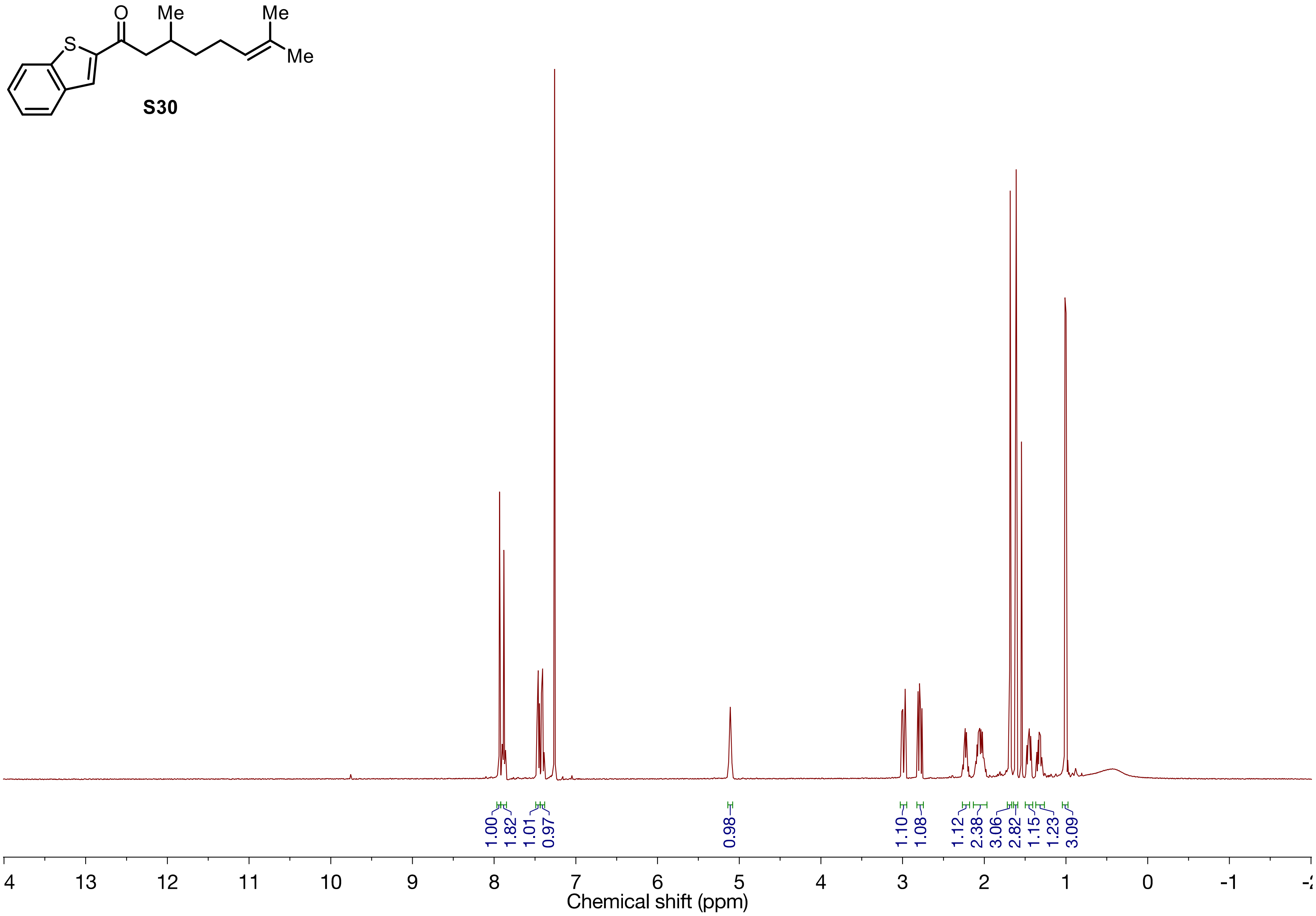

O
tBu
OBn
1.89
2.00
4.65
1.01
0.91
1.82
1.87
9.20
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

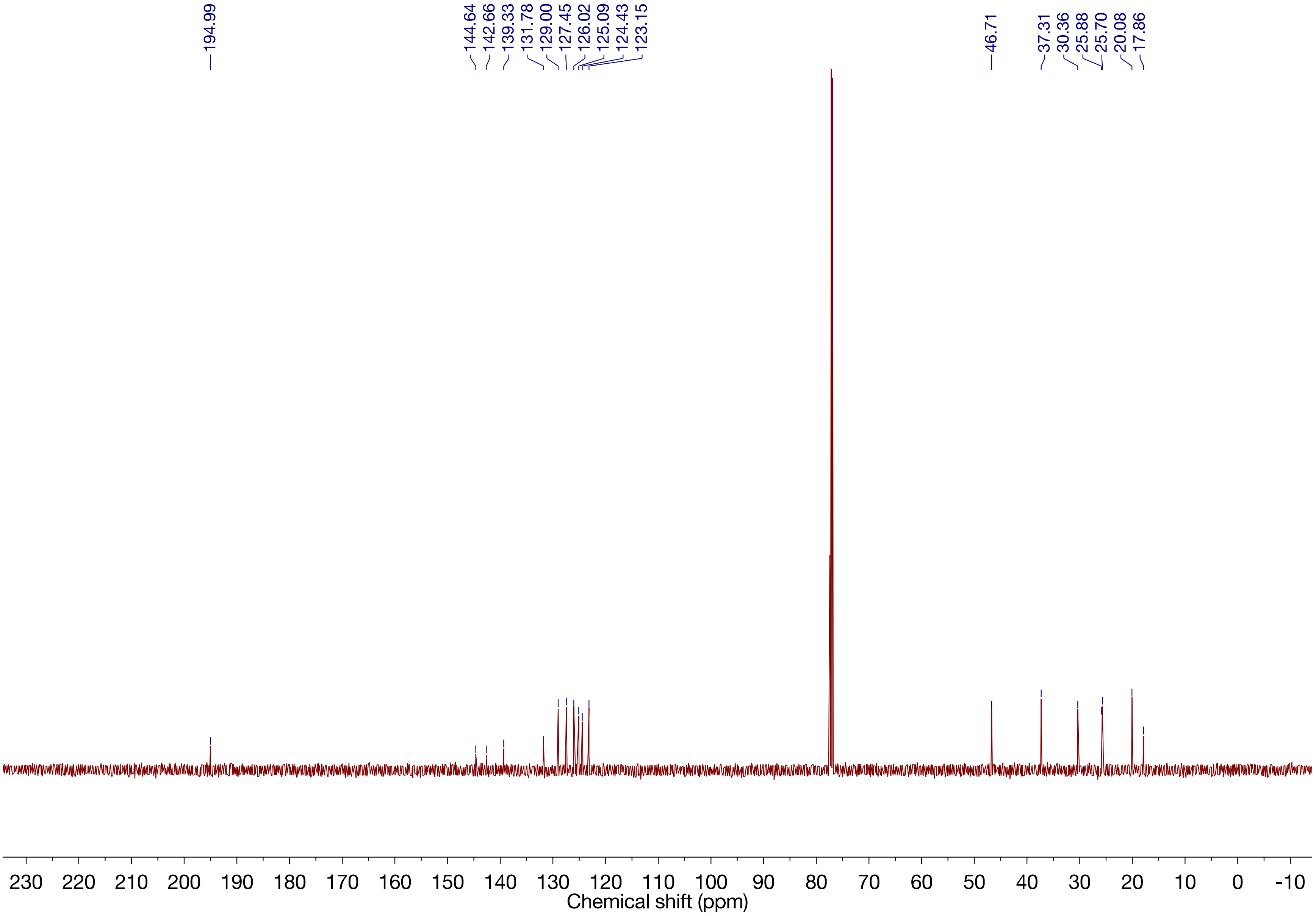
S29a

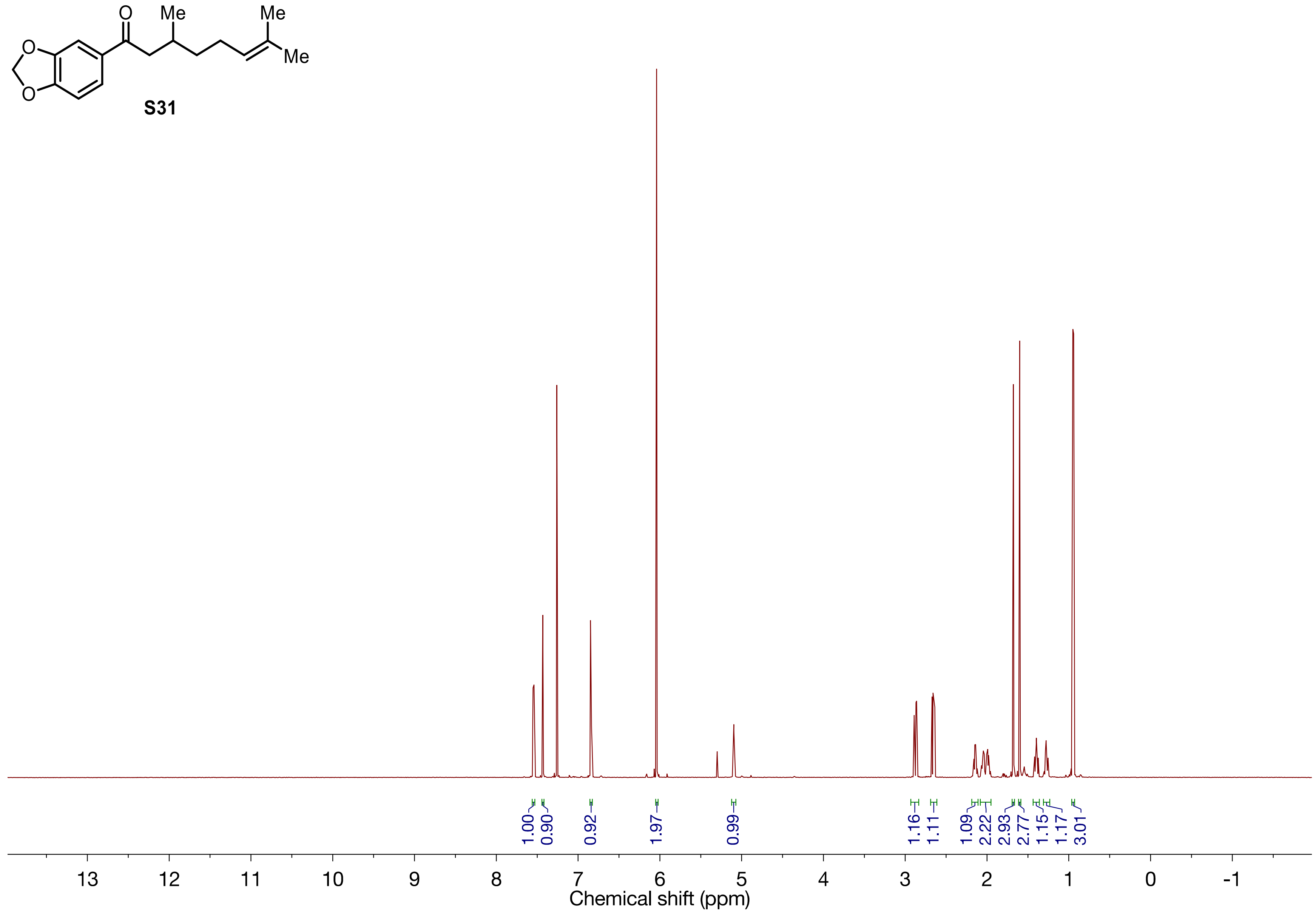

190.02
156.79
144.07
137.90
135.15
128.77
128.66
128.00
127.84
125.69
125.09
73.04
69.35
35.27
31.25
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


EtO2C
CO2Et
tBu
Me
Me
BnO
O
S29
1.89
1.85
2.79
1.79
1.01
2.03
4.01
2.05
1.08
1.02
1.05
1.07
1.05
2.75
3.35
8.34
2.92
2.81
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

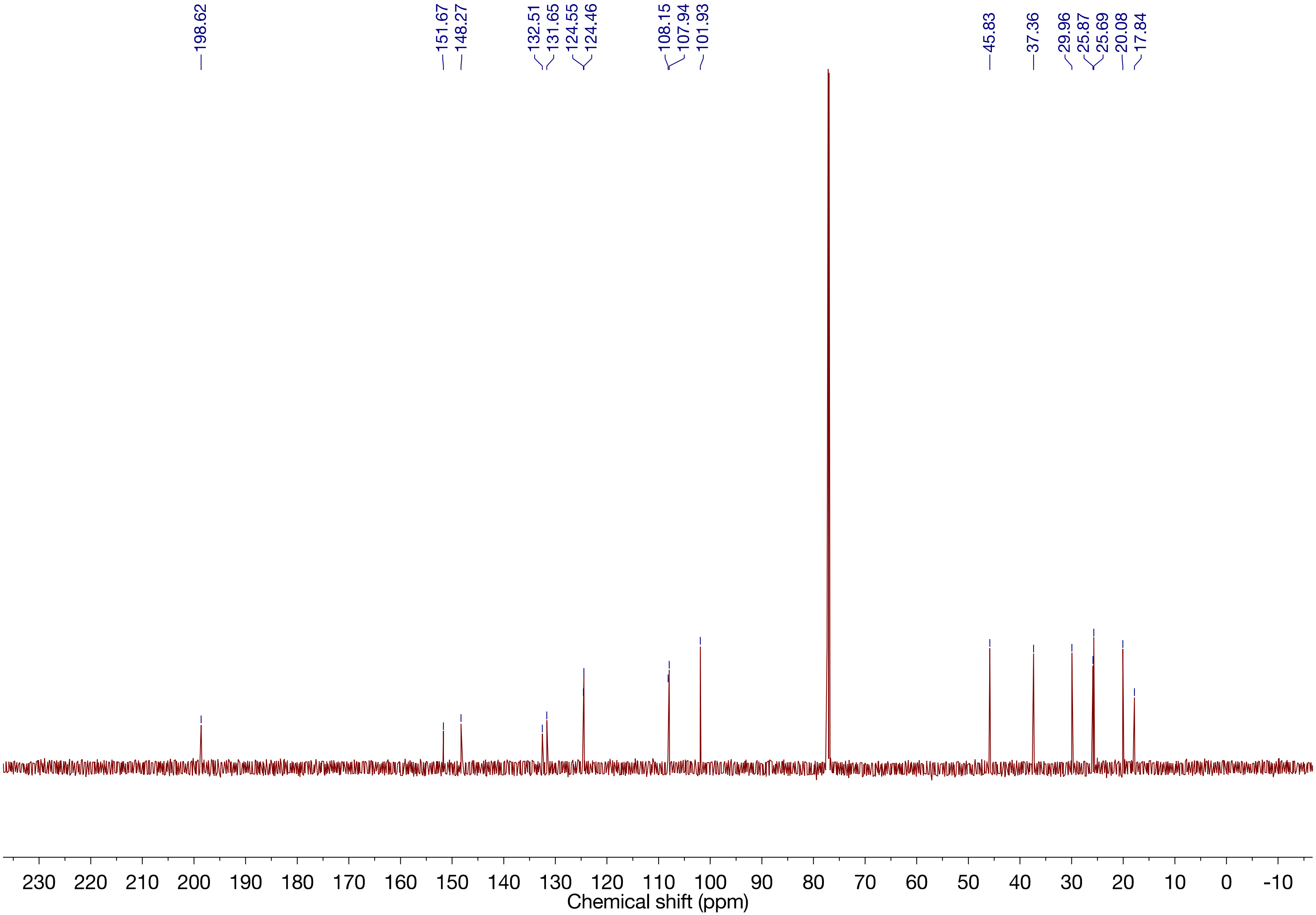

198.82
171.14
171.07
156.50
138.34
135.04
134.96
128.21
128.19
127.81
127.45
125.51
118.44
73.15
69.44
61.28
61.13
59.58
37.93
37.83
35.20
32.53
31.26
26.19
18.02
14.19
14.15
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

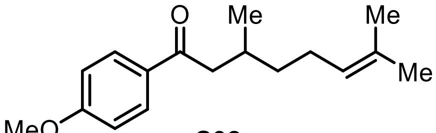

O
Me
Me
S
Me
S30
1.00
1.82
1.01
0.97
0.98
1.10
1.08
1.12
2.38
3.06
2.82
1.15
1.23
3.09
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


194.99
144.64
142.66
139.33
131.78
129.00
127.45
126.02
125.09
124.43
123.15
46.71
37.31
30.36
25.88
25.70
20.08
17.86
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

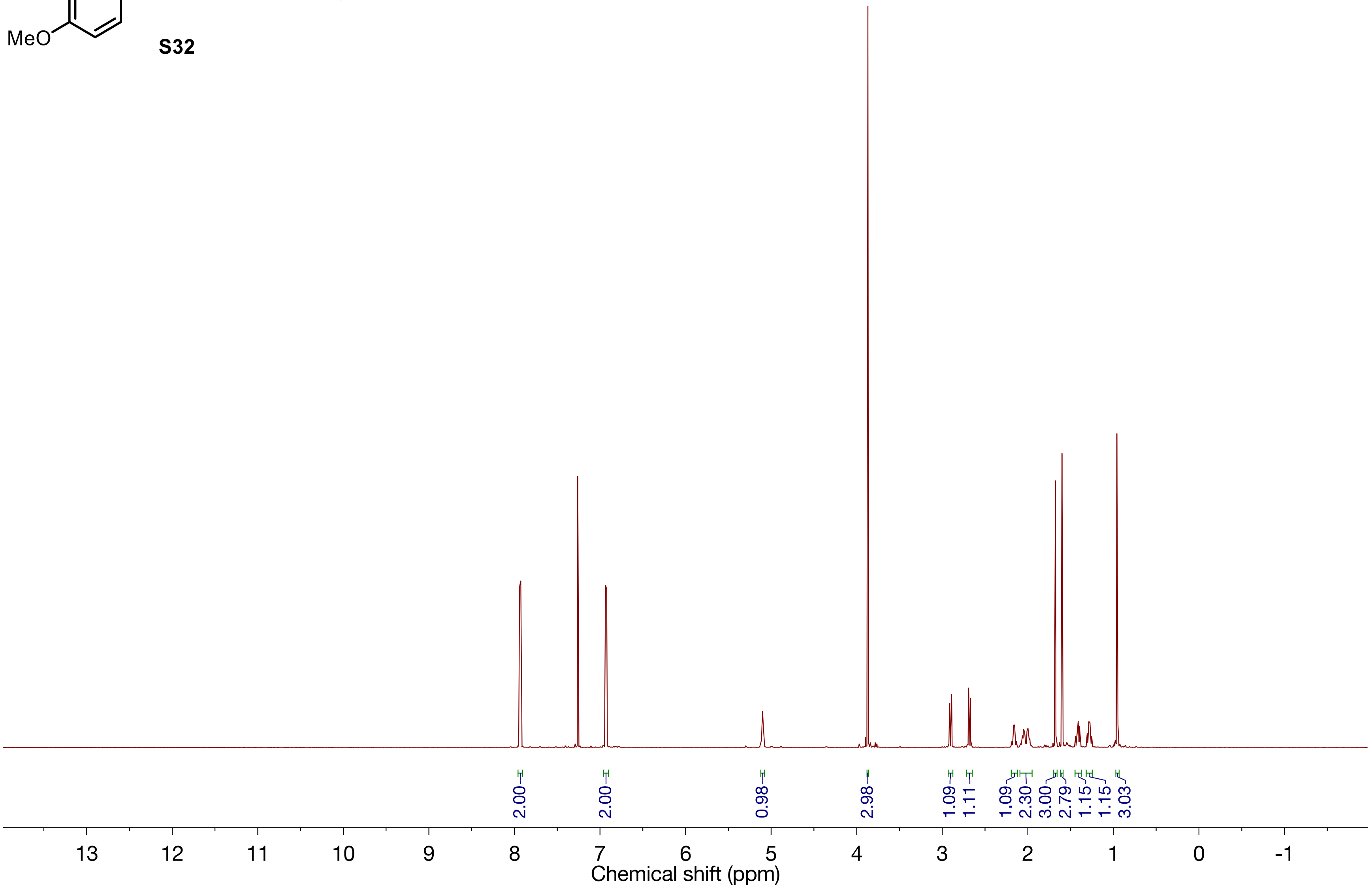

O
Me
Me
Me
O
O
1.00
0.90
0.92
1.97
0.99
1.16
1.11
1.09
2.22
2.93
2.77
1.15
1.17
3.01
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

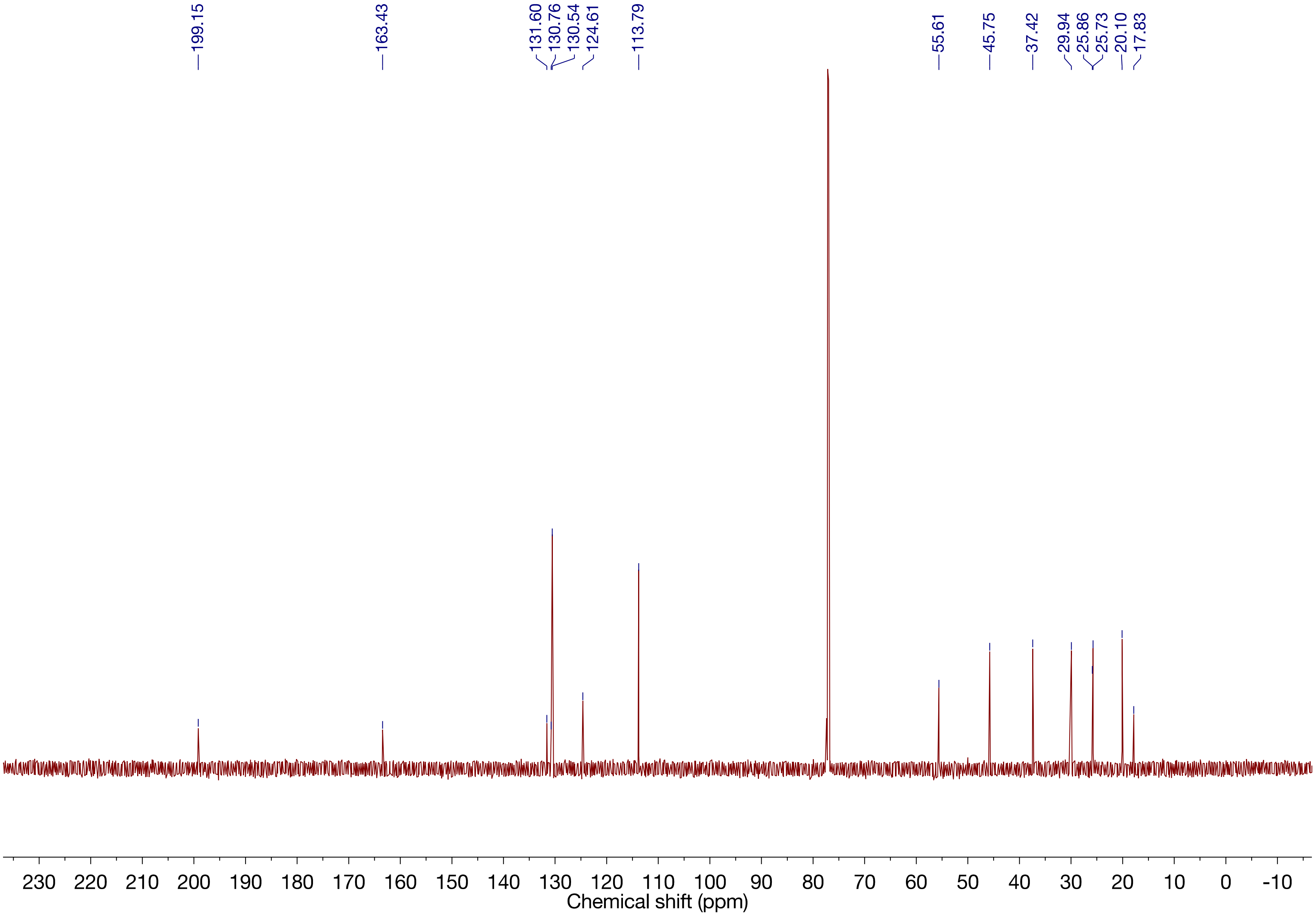
S31

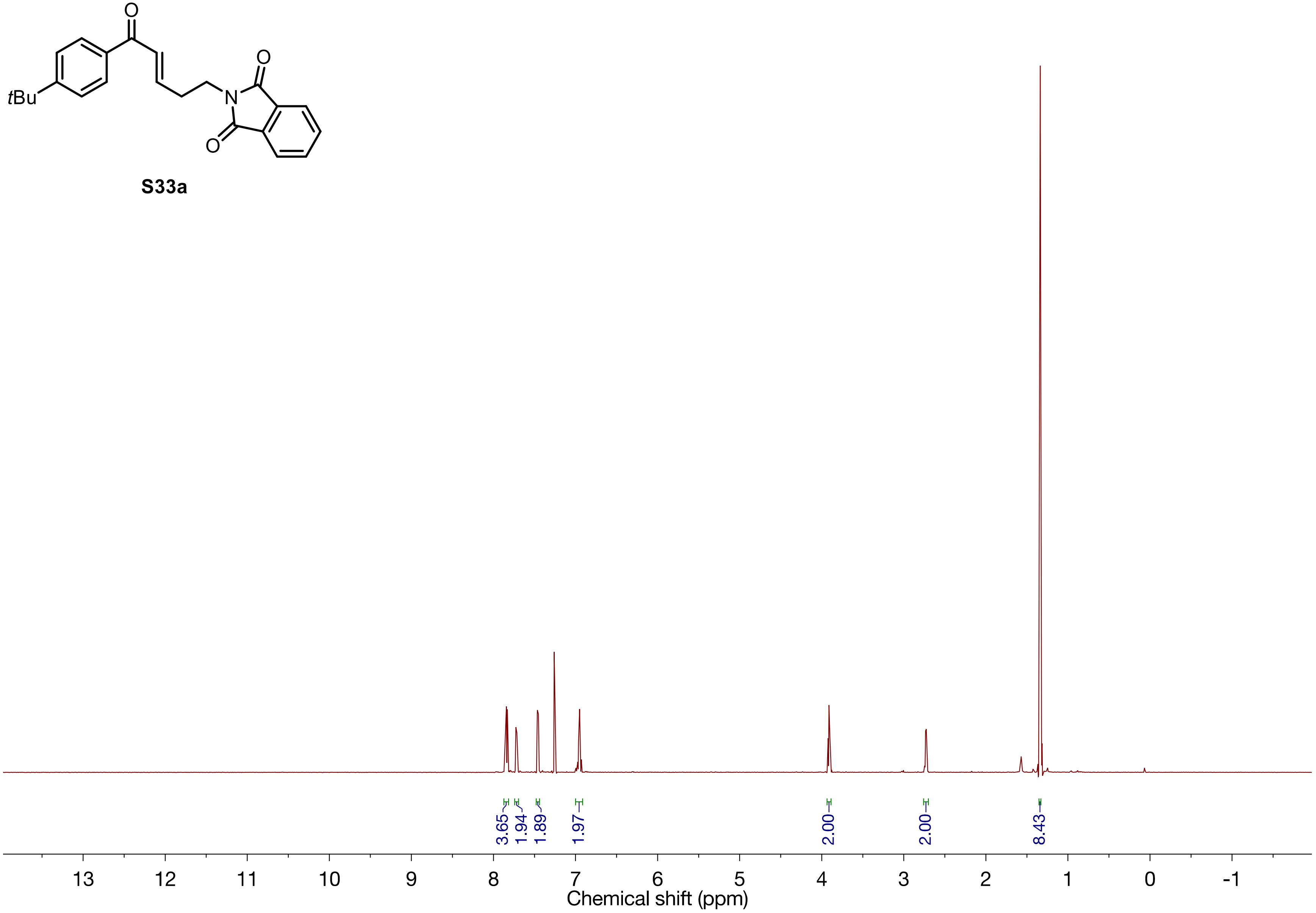

198.62
151.67
148.27
132.51
131.65
124.55
124.46
108.15
107.94
101.93
45.83
37.36
29.96
25.87
25.69
20.08
17.84
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


O
Me
Me
Me
MeO

S32

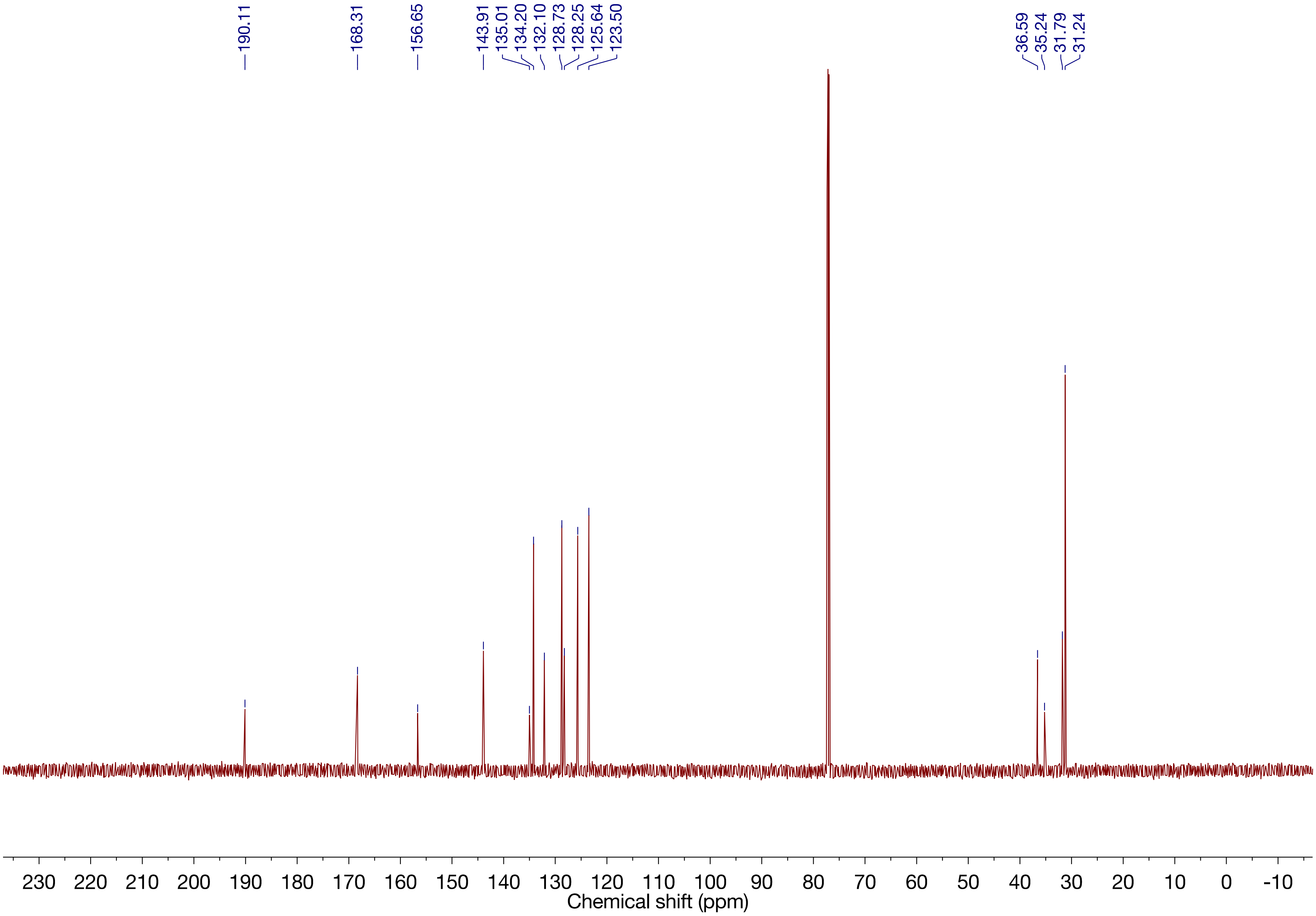

2.00
2.00
0.98
2.98
1.09
1.11
1.09
2.30
3.00
2.79
1.15
1.15
3.03
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

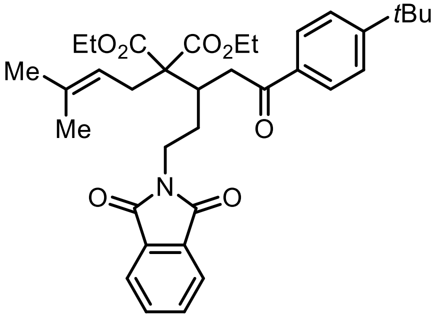

199.15
163.43
131.60
130.76
130.54
124.61
113.79
55.61
45.75
37.42
29.94
25.86
25.73
20.10
17.83
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


O
O
O
N
tBu

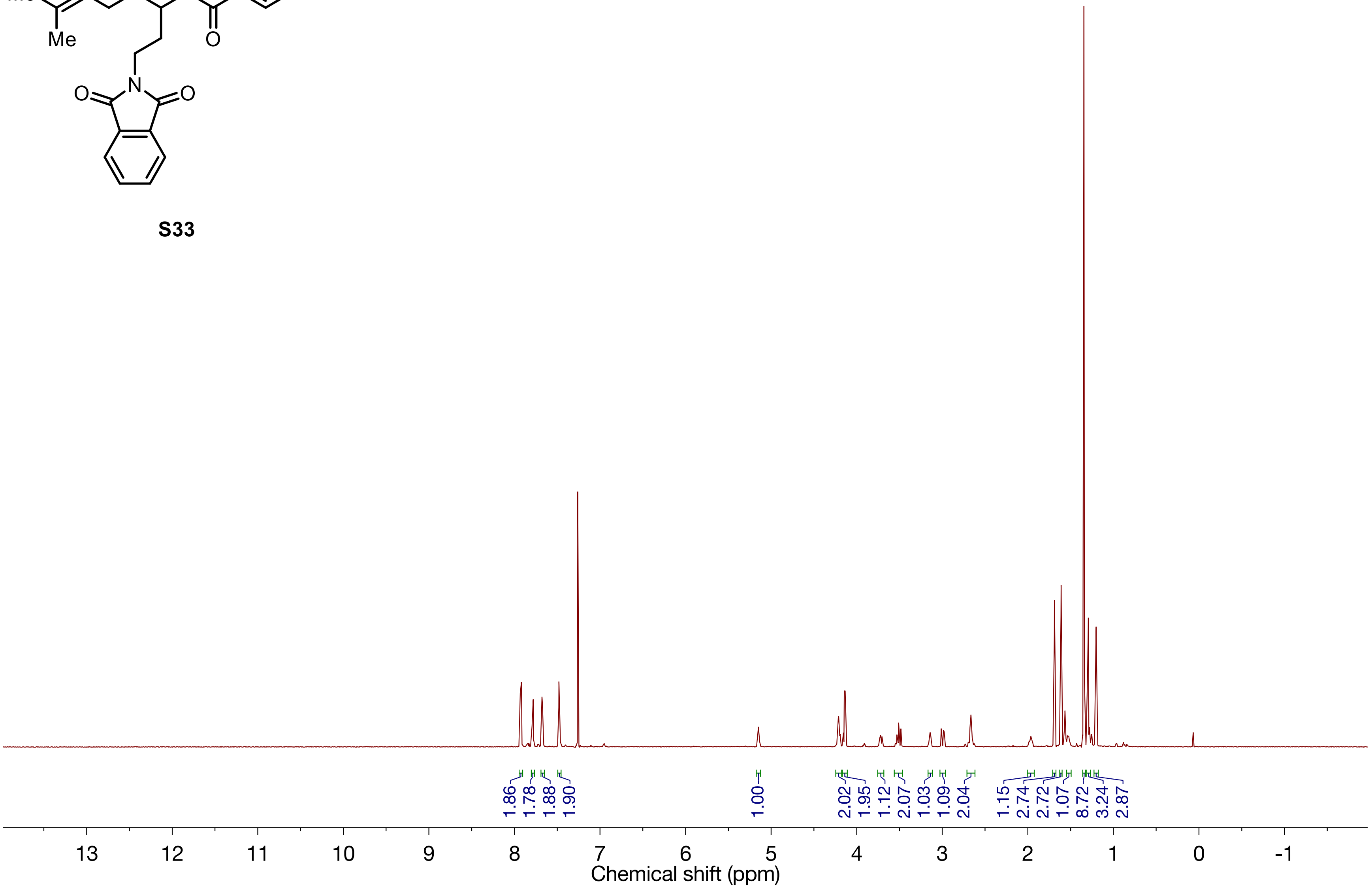
S33a

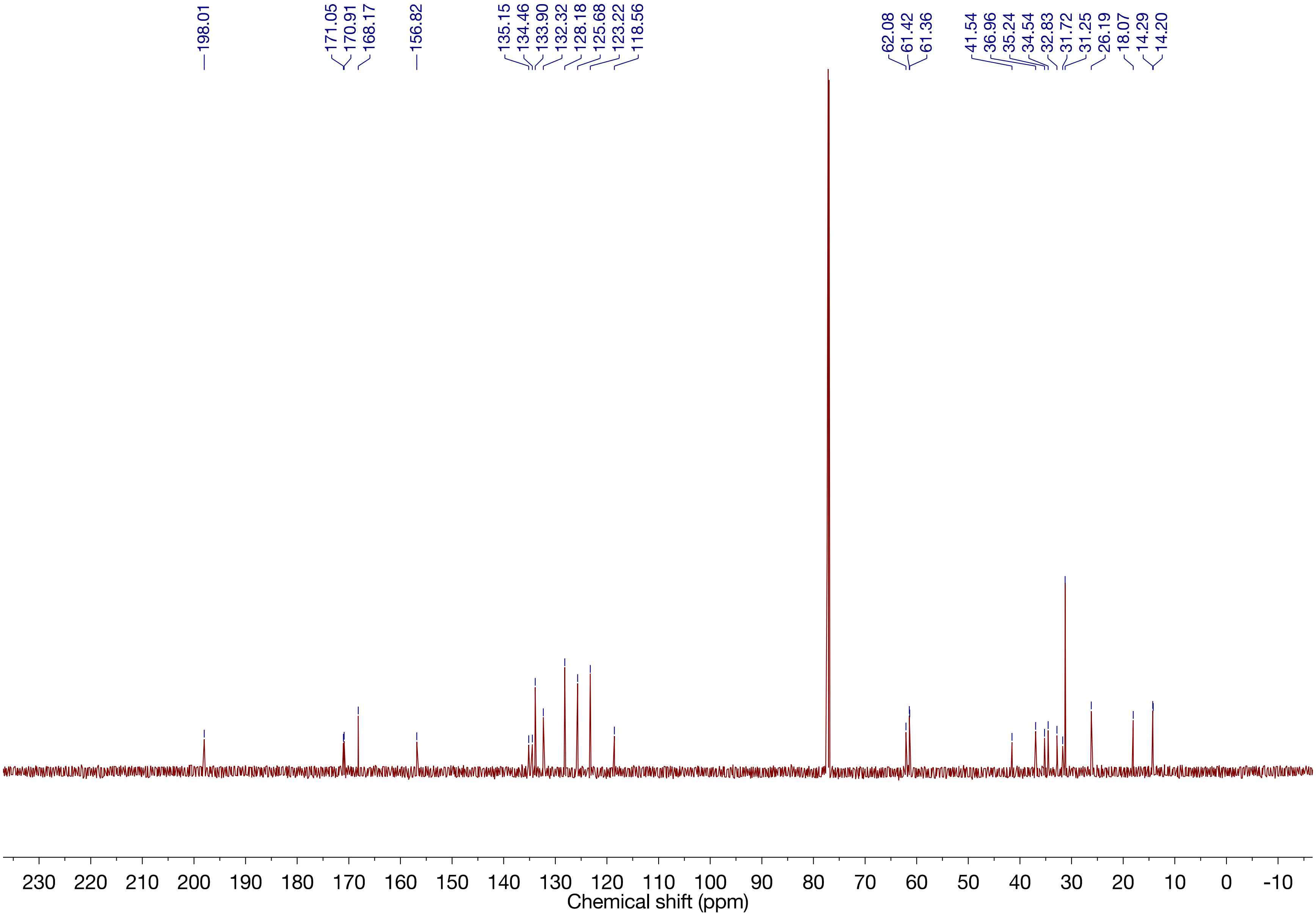
3.65
1.94
1.89
1.97
2.00
2.00
8.43
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

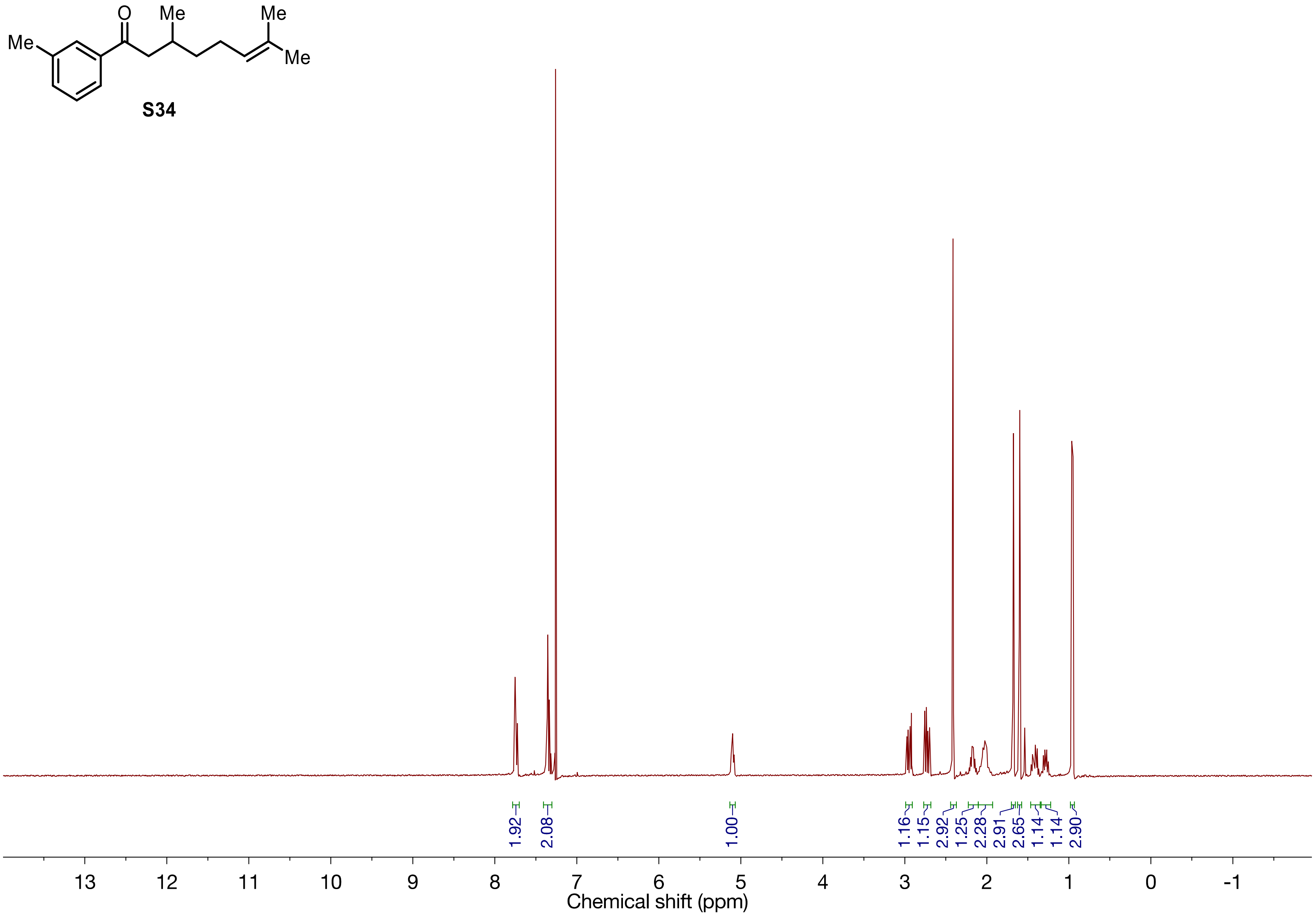

190.11
168.31
156.65
143.91
135.01
134.20
132.10
128.73
128.25
125.64
123.50
36.59
35.24
31.79
31.24
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


EtO2C
CO2Et
tBu
Me
Me
O
N
O
O

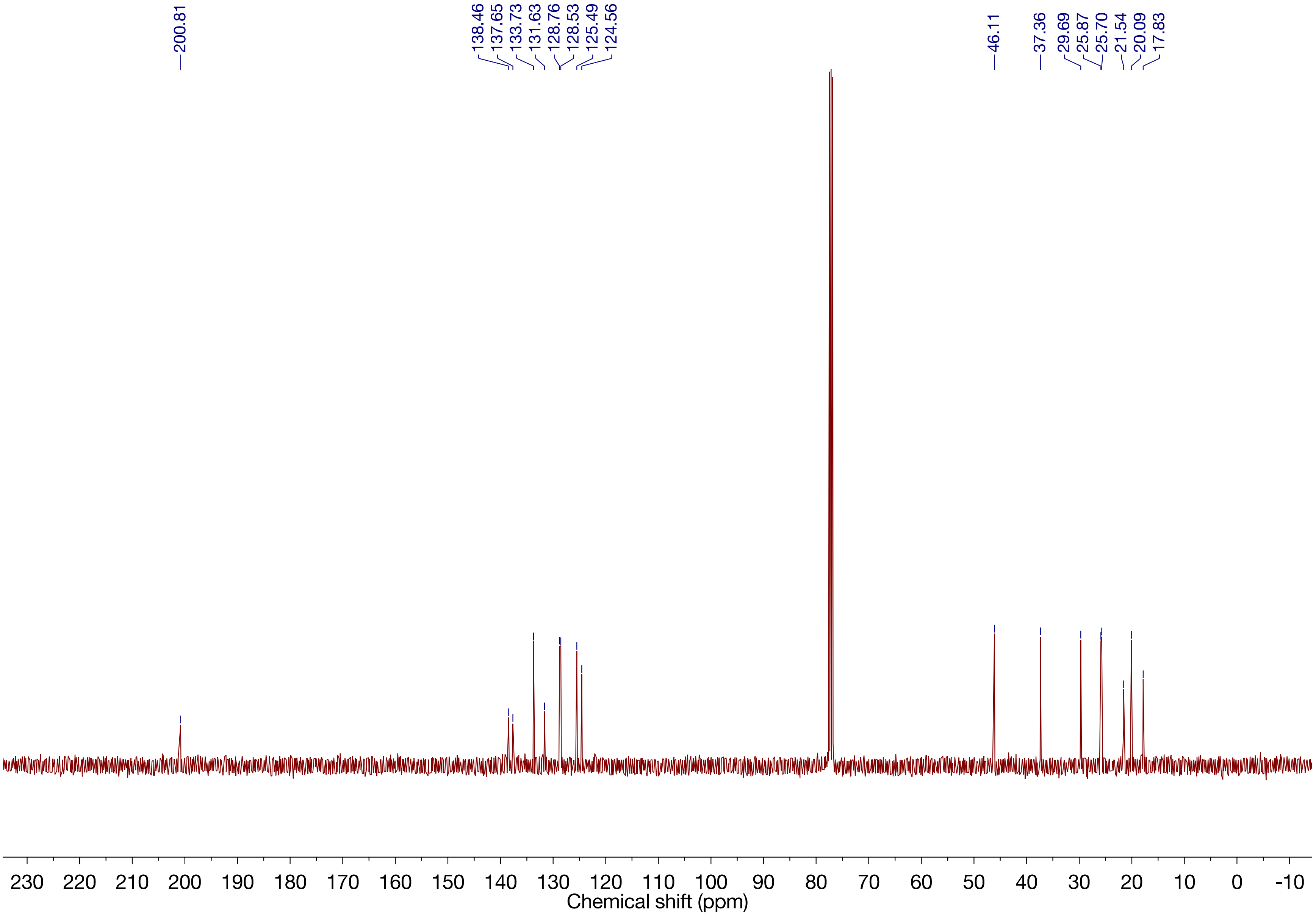
S33

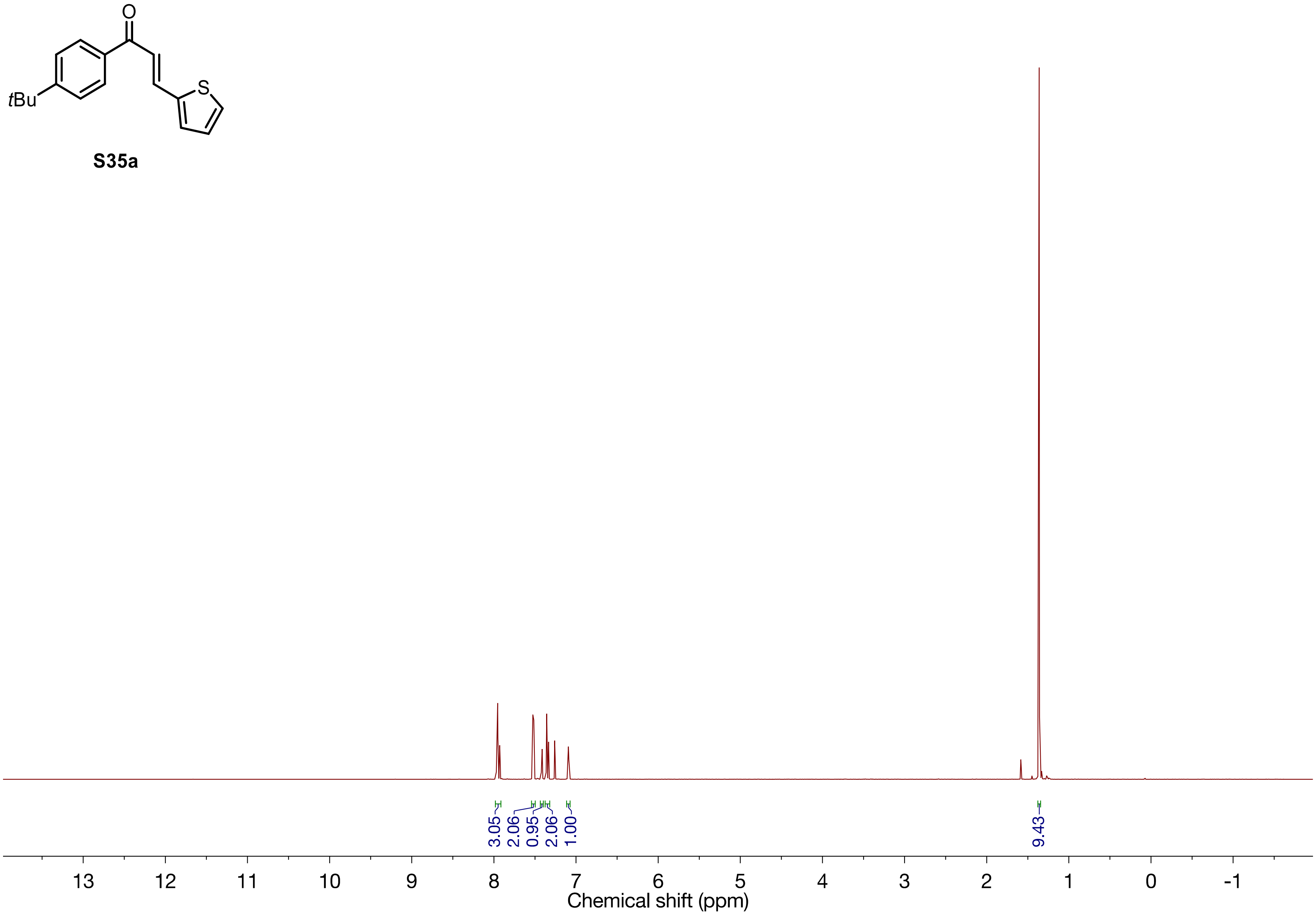

1.86
1.78
1.88
1.90
1.00
2.02
1.95
1.12
2.07
1.03
1.09
2.04
1.15
2.74
2.72
1.07
8.72
3.24
2.87
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


198.01
171.05
170.91
168.17
156.82
135.15
134.46
133.90
132.32
128.18
125.68
123.22
118.56
62.08
61.42
61.36
41.54
36.96
35.24
34.54
32.83
31.72
31.25
26.19
18.07
14.29
14.20
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


S34

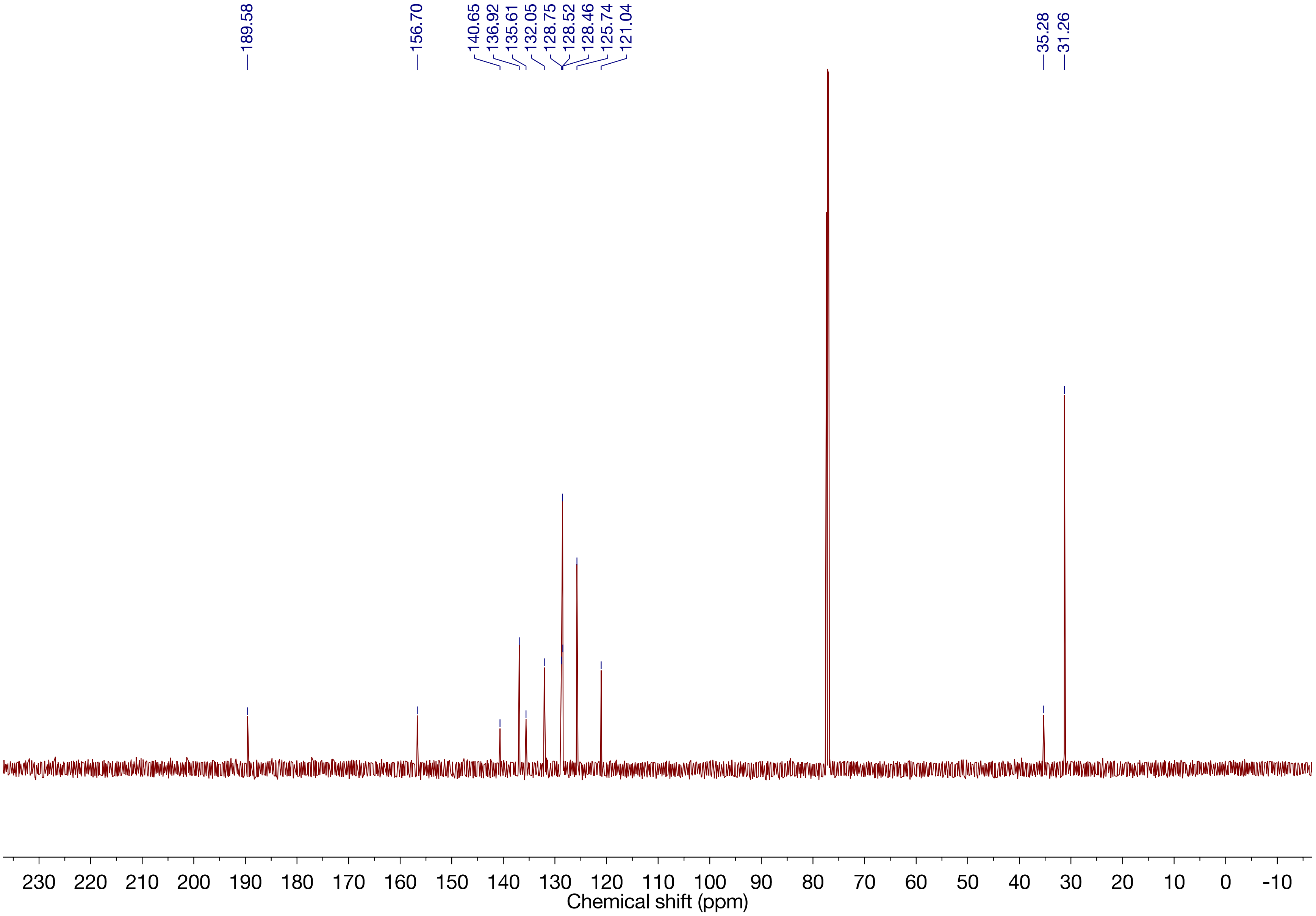
Me
O
Me
Me
Me
1.92
2.08
1.00
1.16
1.15
2.92
1.25
2.28
2.91
2.65
1.14
1.14
2.90
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

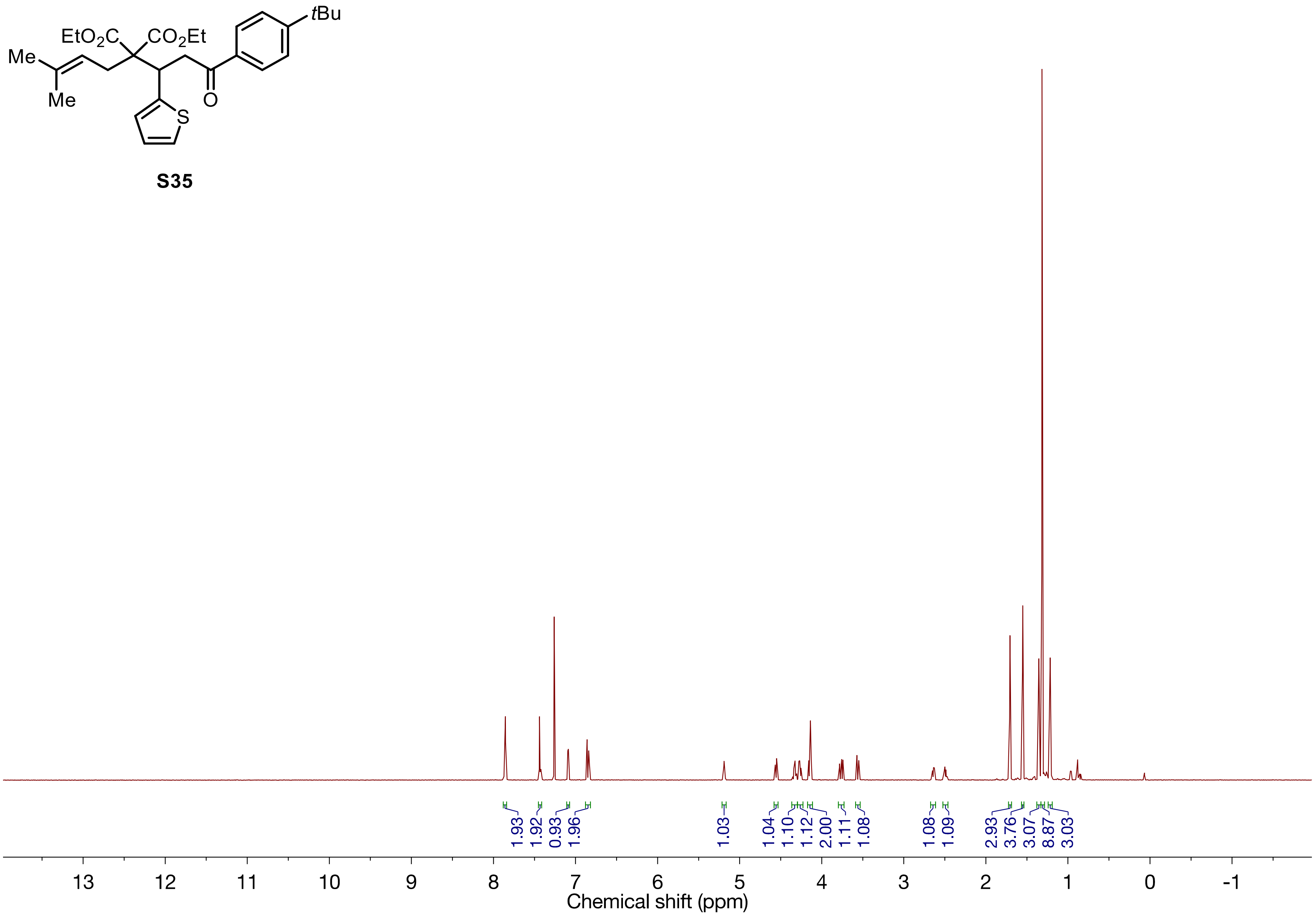

200.81
138.46
137.65
133.73
131.63
128.76
128.53
125.49
124.56
46.11
37.36
29.69
25.87
25.70
21.54
20.09
17.83
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


O
S
tBu

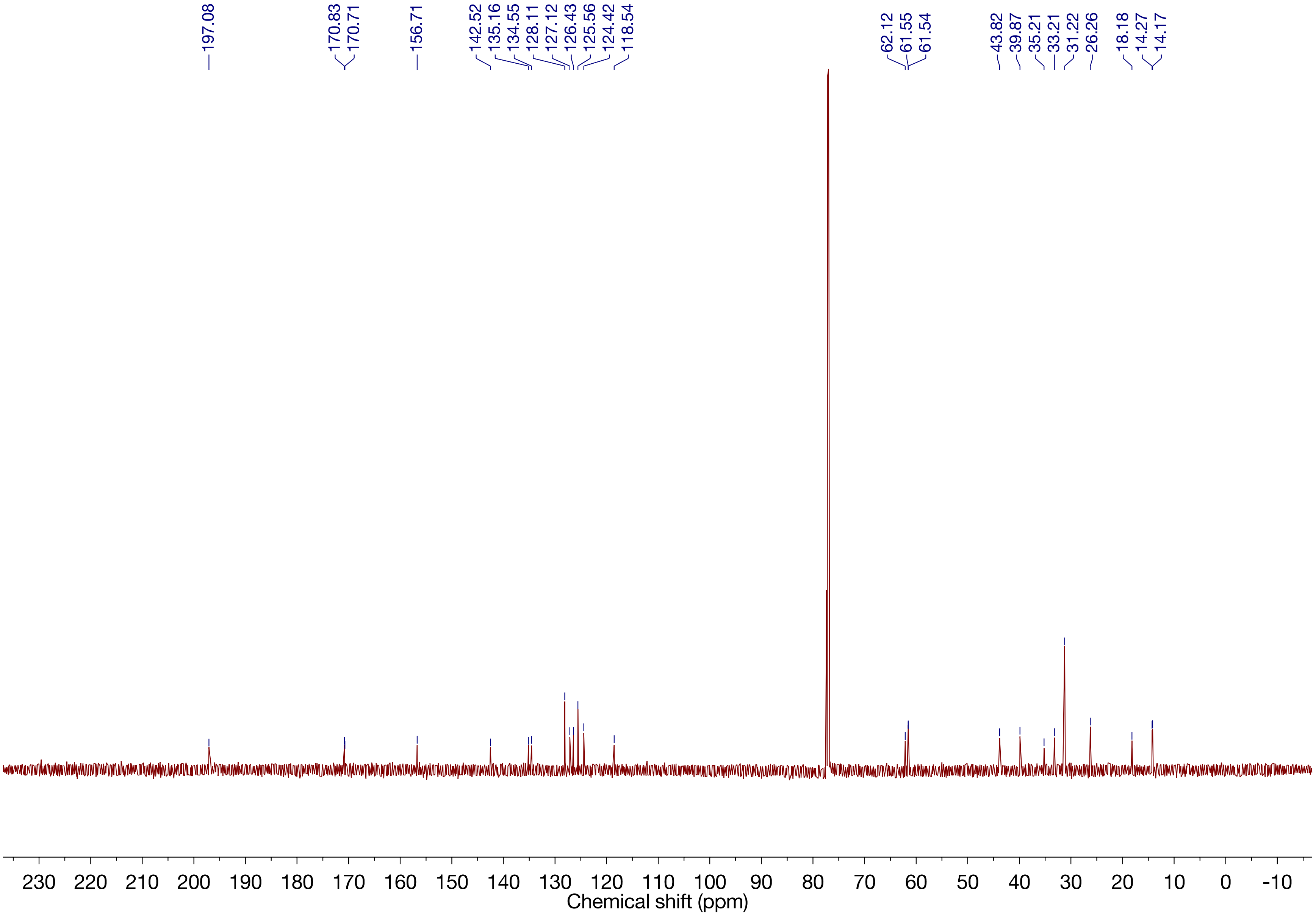
S35a

3.05
2.06
0.95
2.06
1.00
9.43
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

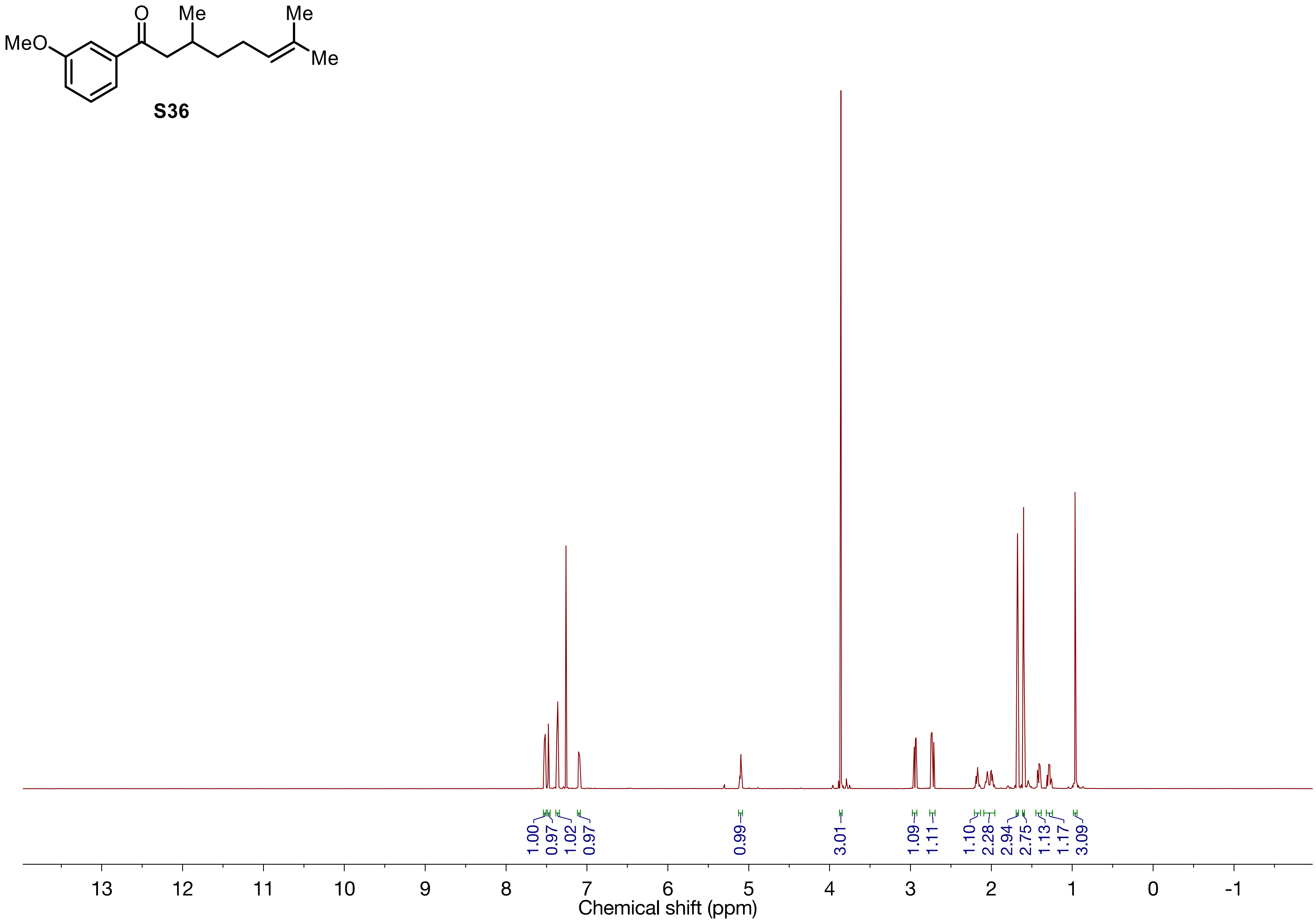

189.58
156.70
140.65
136.92
135.61
132.05
128.75
128.52
128.46
125.74
121.04
35.28
31.26
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


EtO2C
CO2Et
tBu
Me
Me
S
O
1.93
1.92
0.93
1.96
1.03
1.04
1.10
1.12
2.00
1.11
1.08
1.08
1.09
2.93
3.76
3.07
8.87
3.03
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

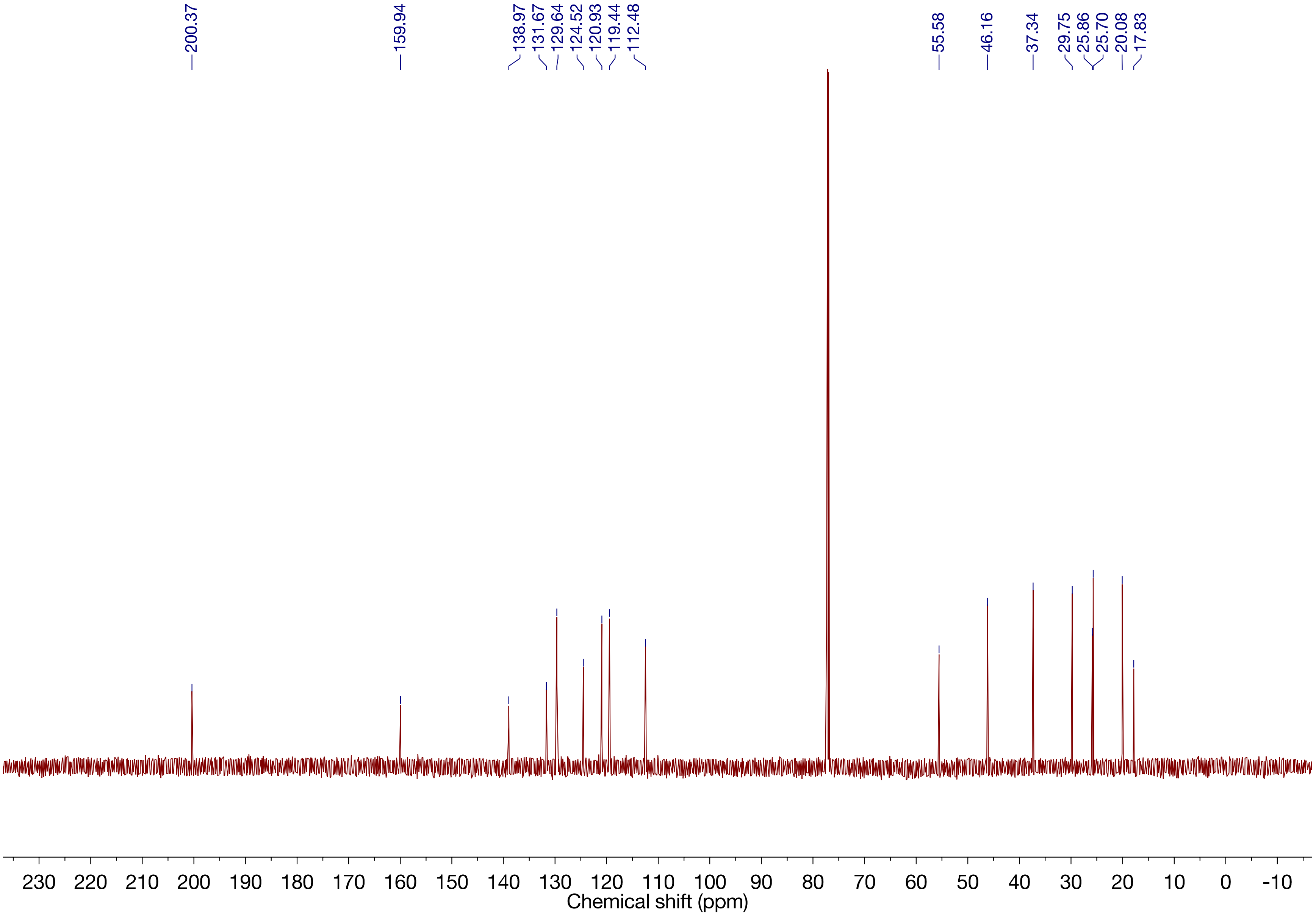
S35

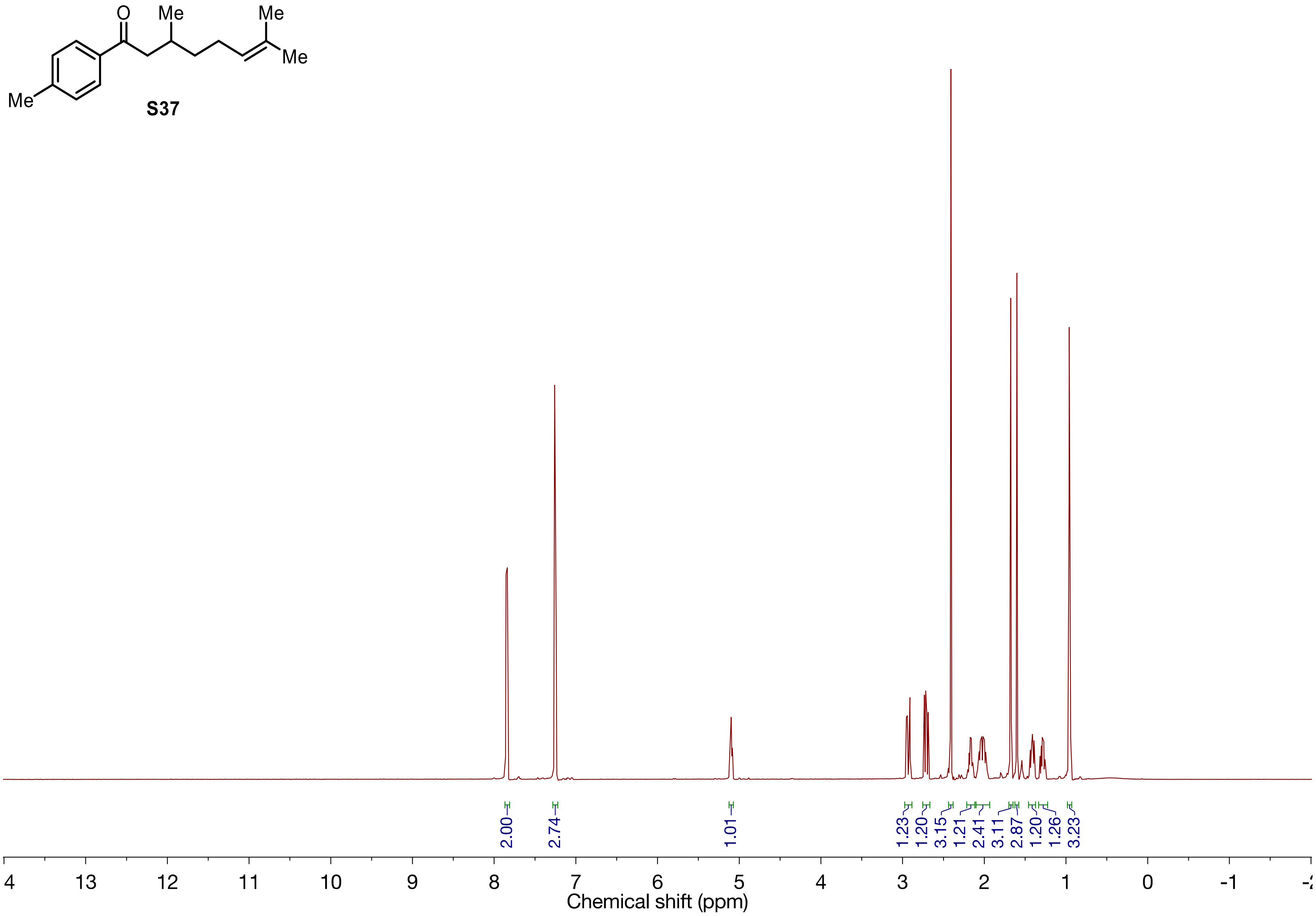


197.08
170.83
170.71
156.71
142.52
135.16
134.55
128.11
127.12
126.43
125.56
124.42
118.54
62.12
61.55
61.54
43.82
39.87
35.21
33.21
31.22
26.26
18.18
14.27
14.17
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

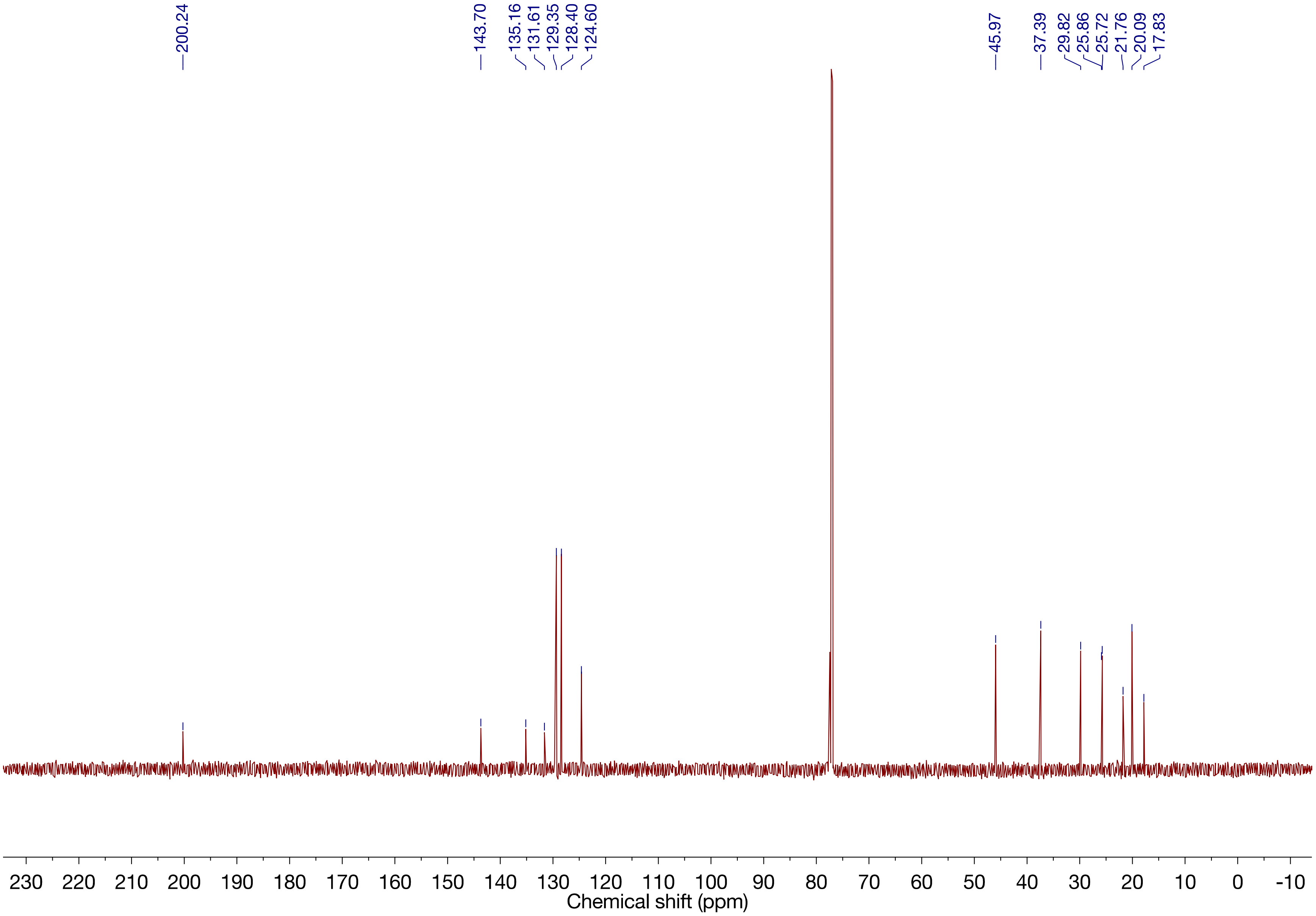

MeO
O
Me
Me
Me
1.00
0.97
1.02
0.97
0.99
3.01
1.09
1.11
1.10
2.28
2.94
2.75
1.13
1.17
3.09
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

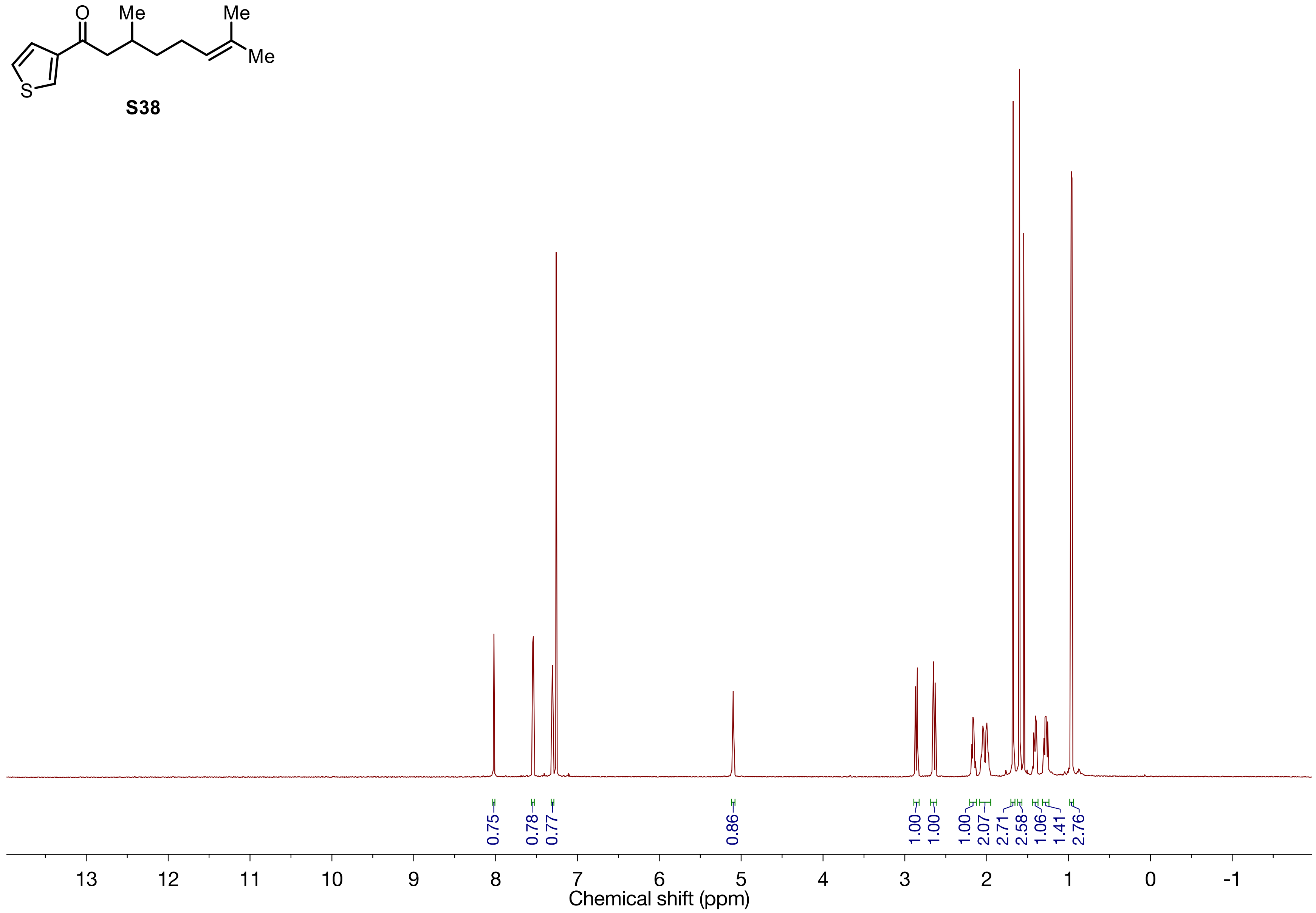
S36

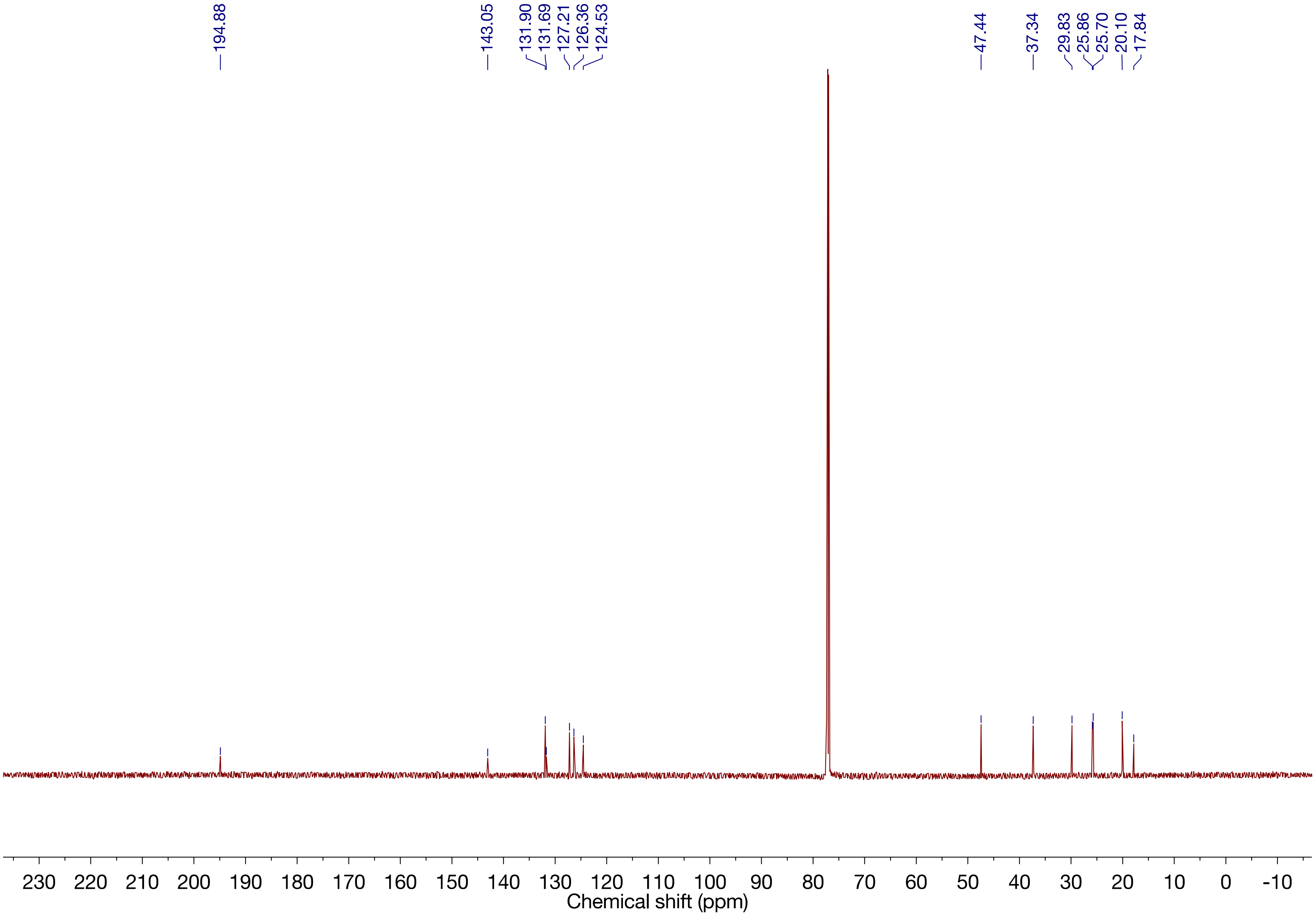

200.37
159.94
138.97
131.67
129.64
124.52
120.93
119.44
112.48
55.58
46.16
37.34
29.75
25.86
25.70
20.08
17.83
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

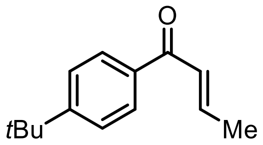

O
Me
Me
Me
Me
2.00
2.74
1.01
1.23
1.20
3.15
1.21
2.41
3.11
2.87
1.20
1.26
3.23
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-
Chemical shift (ppm)

S37

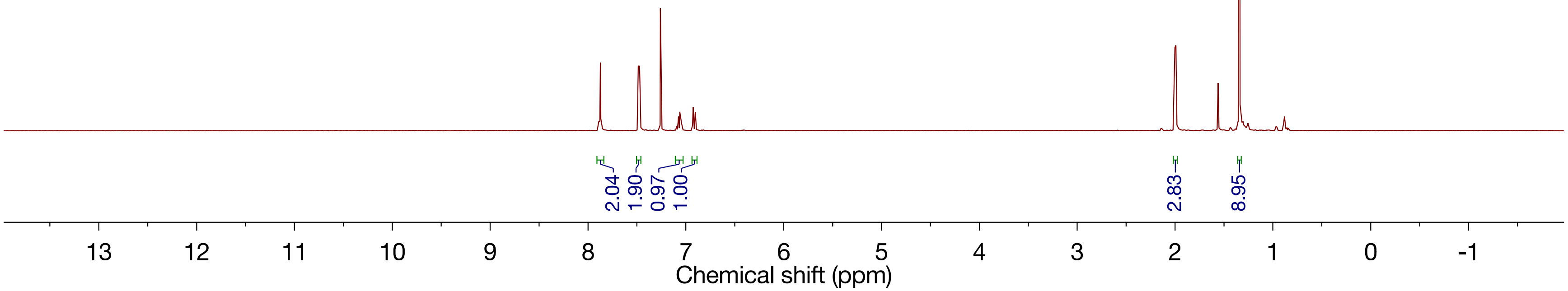

200.24
143.70
135.16
131.61
129.35
128.40
124.60
45.97
37.39
29.82
25.86
25.72
21.76
20.09
17.83
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

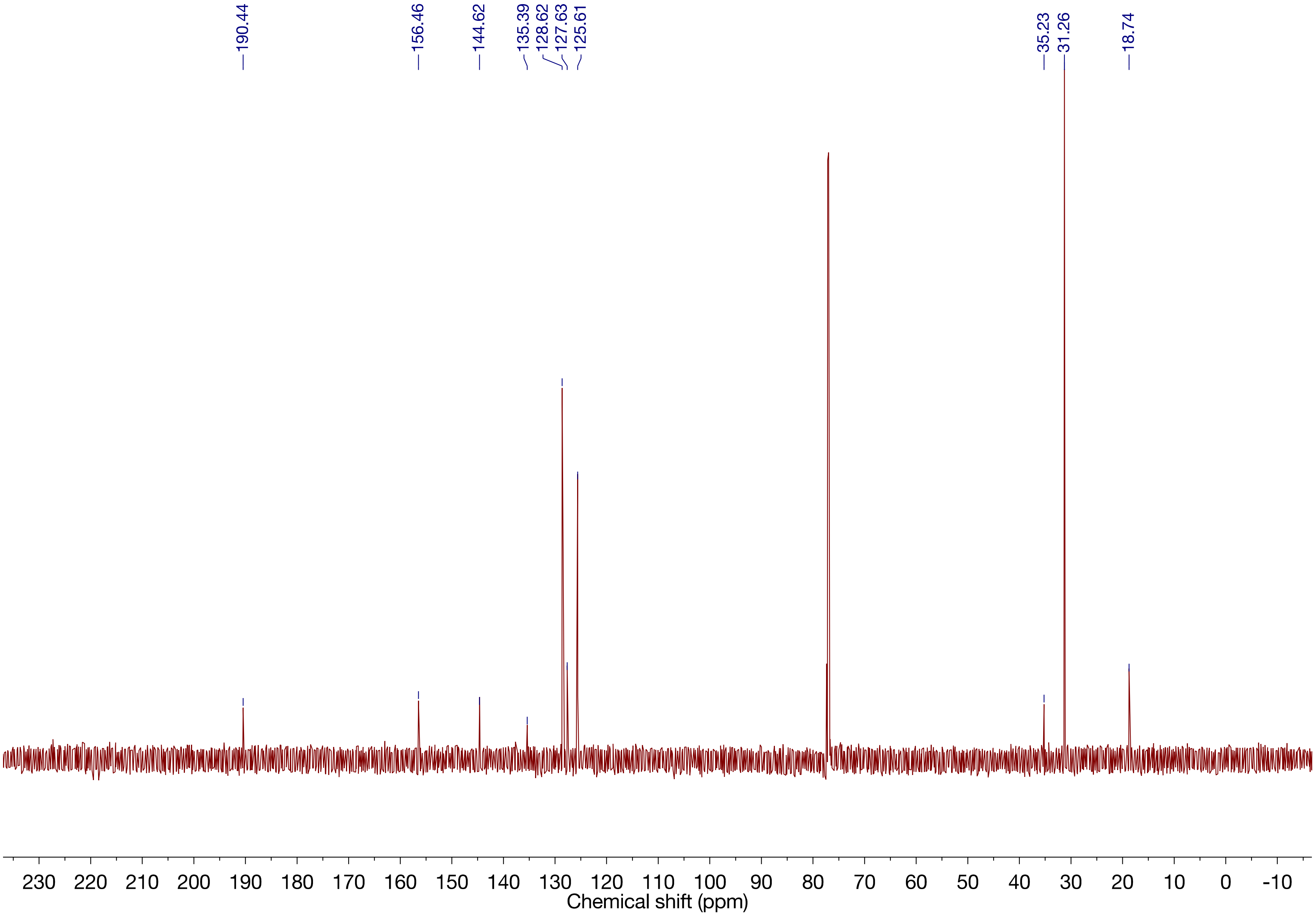

S38
O
Me
Me
Me
S
0.75
0.78
0.77
0.86
1.00
1.00
1.00
2.07
2.71
2.58
1.06
1.41
2.76
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

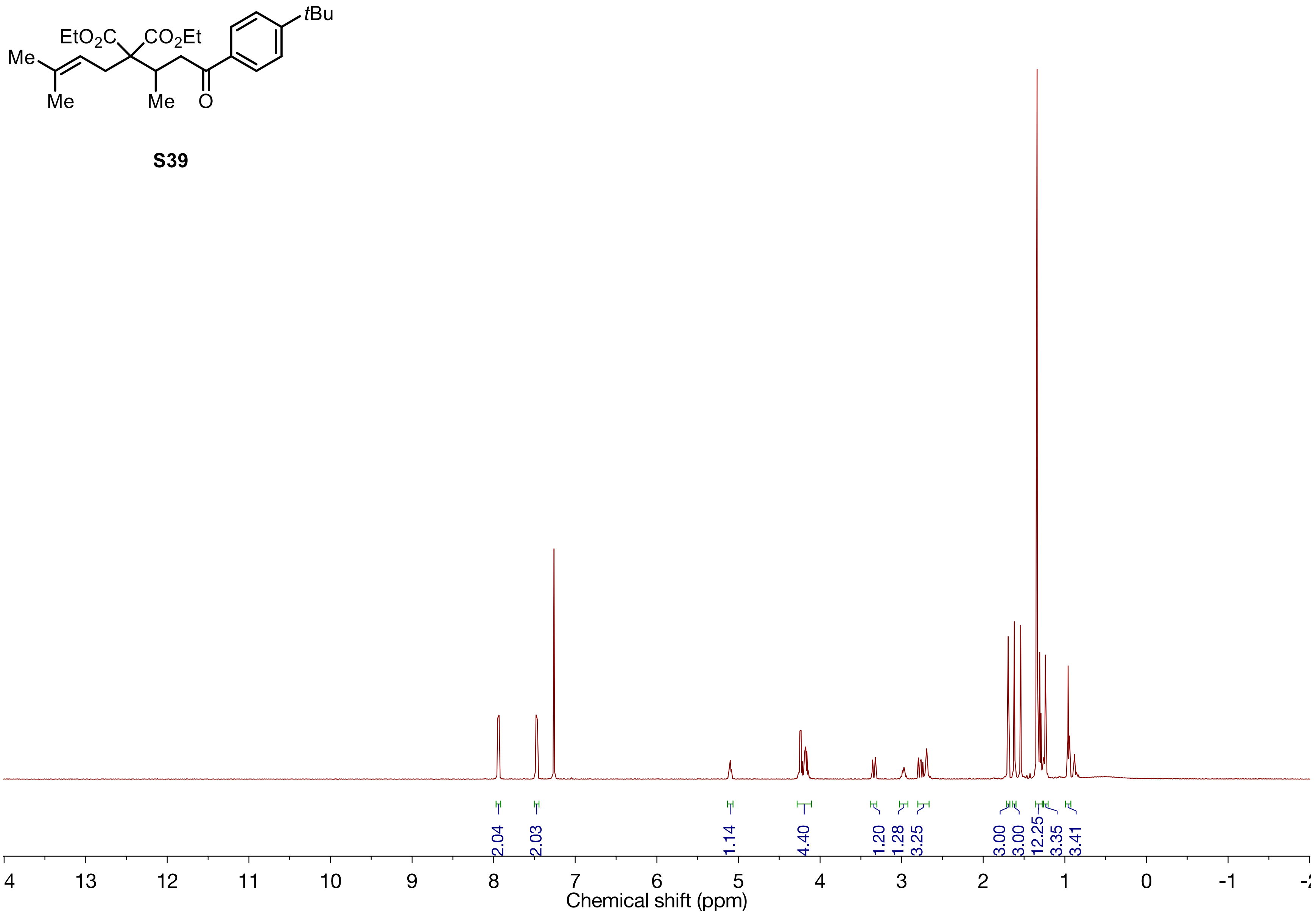

194.88
143.05
131.90
131.69
127.21
126.36
124.53
47.44
37.34
29.83
25.86
25.70
20.10
17.84
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


O
tBu
Me

S39a

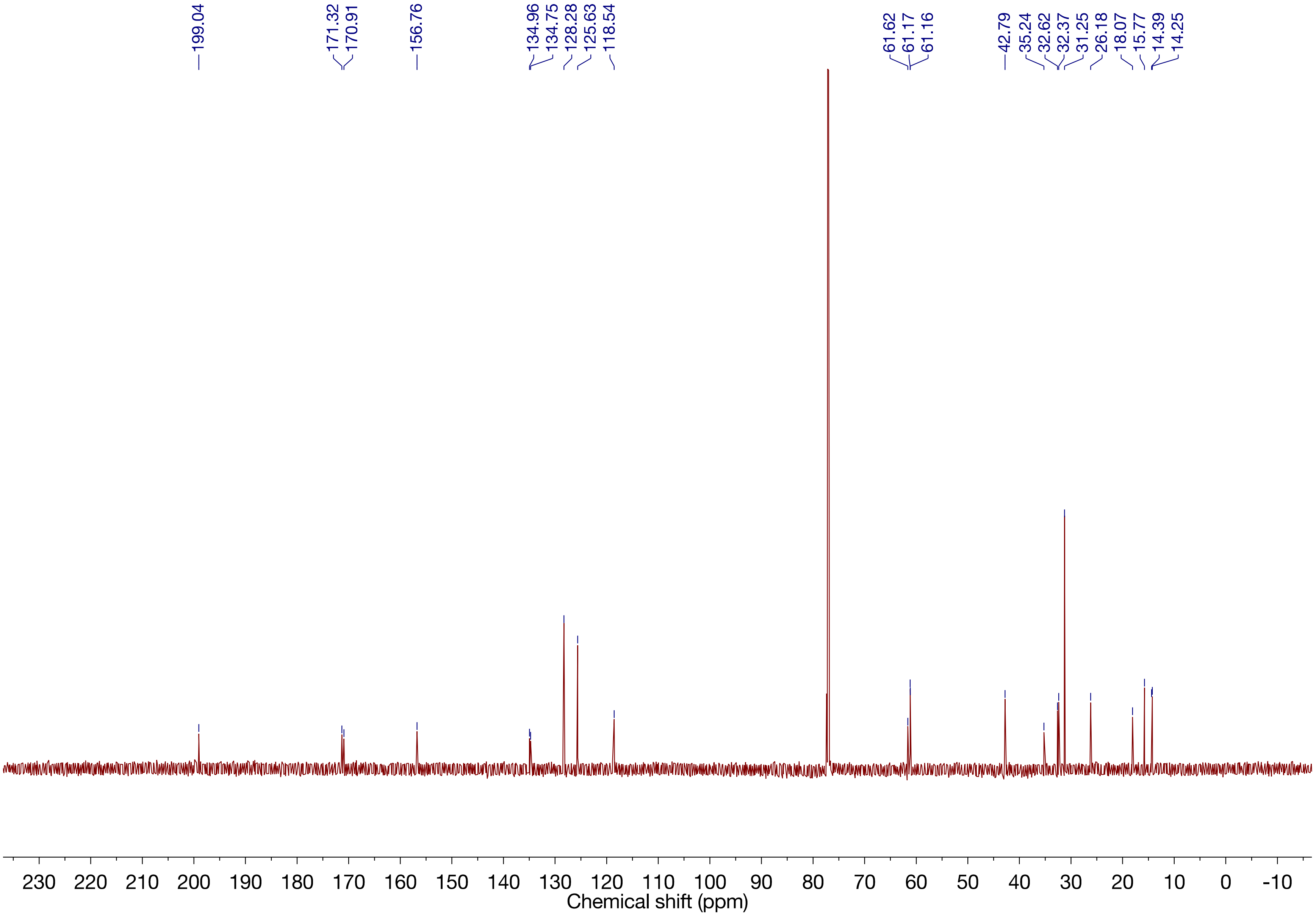

2.04
1.90
0.97
1.00
2.83
8.95
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


190.44
156.46
144.62
135.39
128.62
127.63
125.61
35.23
31.26
18.74
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)

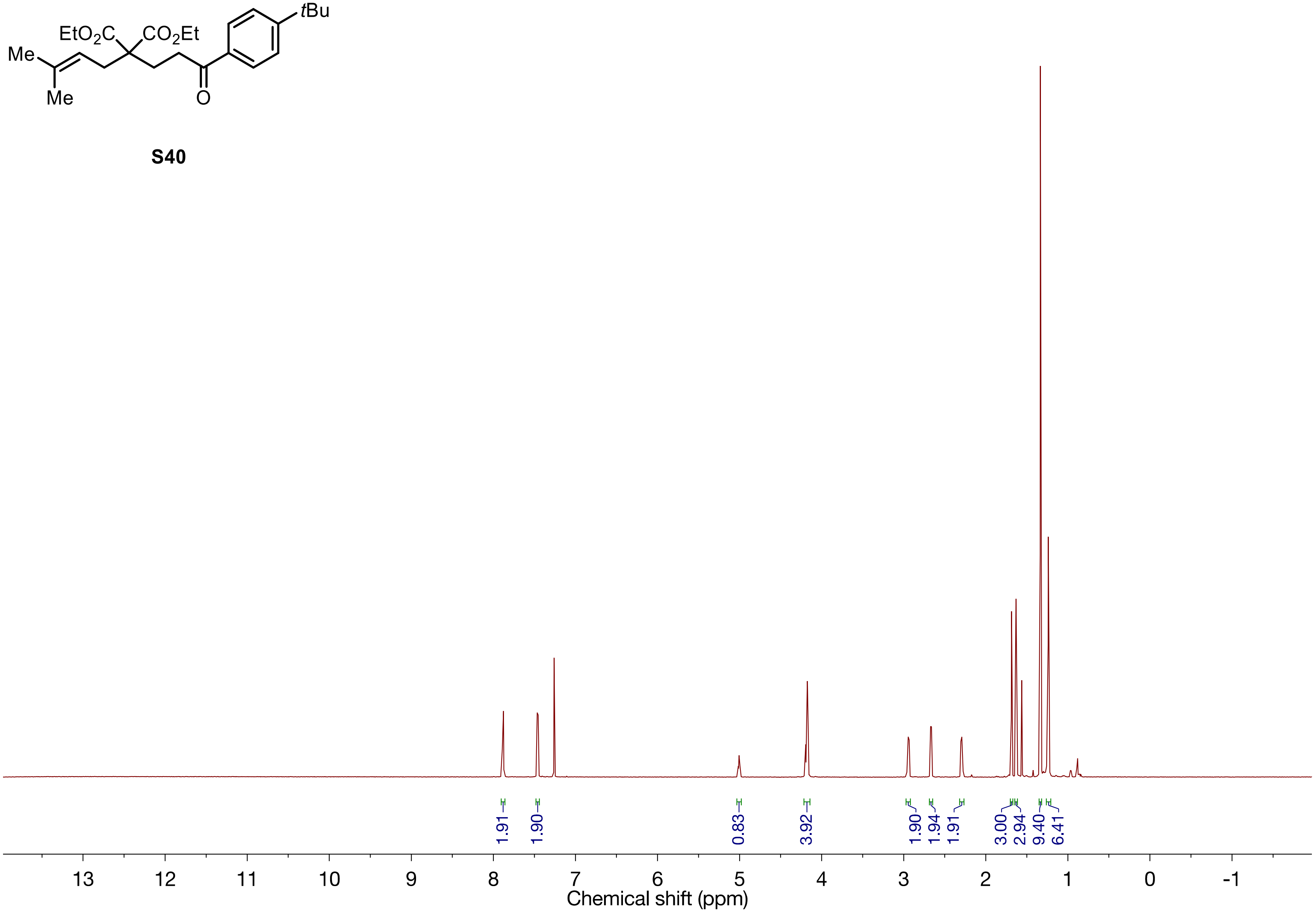


S39

tBu
EtO2C
CO2Et
Me
Me
Me
O
2.04
2.03
1.14
4.40
1.20
1.28
3.25
3.00
3.00
12.25
3.35
3.41
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

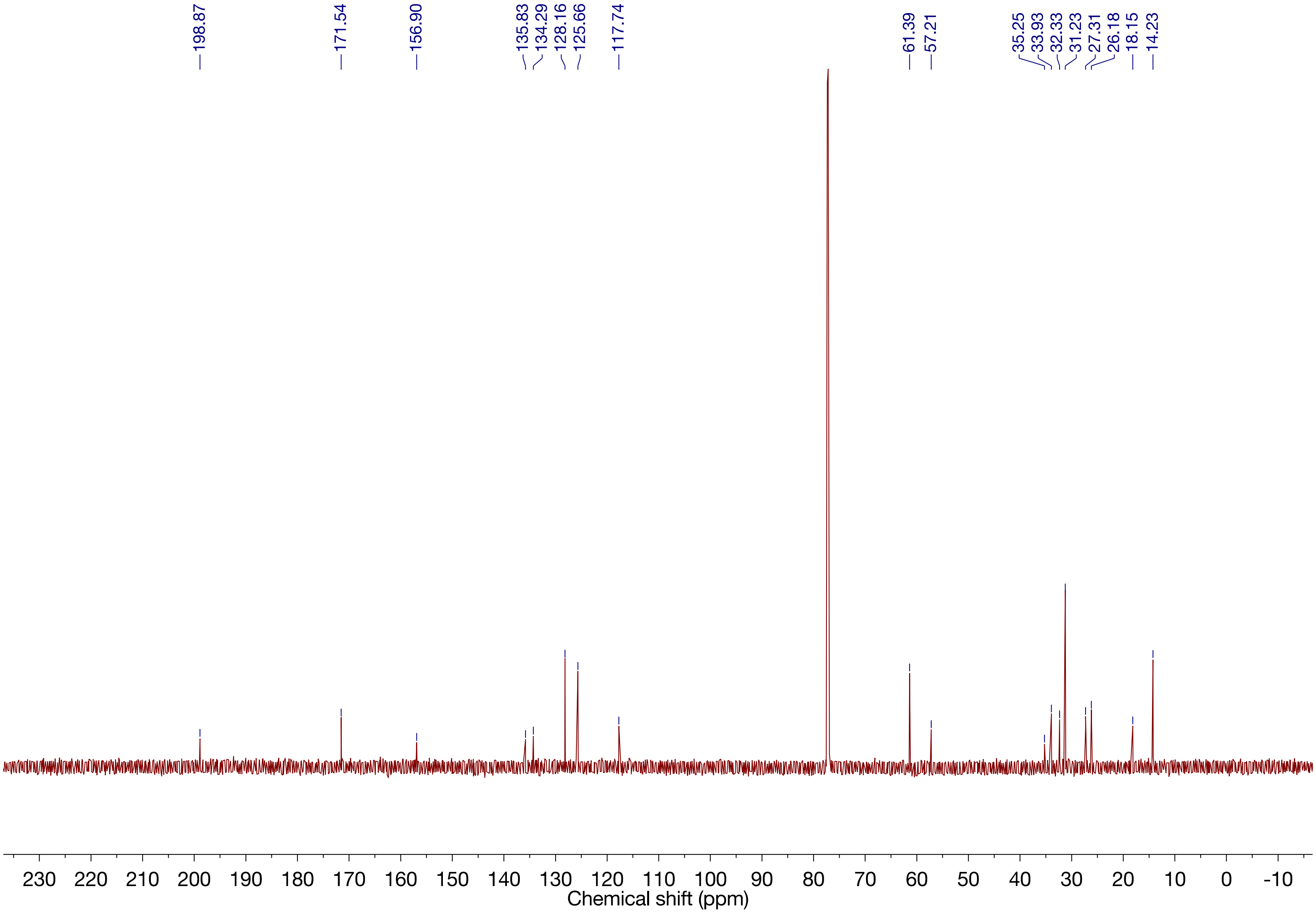


199.04
171.32
170.91
156.76
134.96
134.75
128.28
125.63
118.54
61.62
61.17
61.16
42.79
35.24
32.62
32.37
31.25
26.18
18.07
15.77
14.39
14.25
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

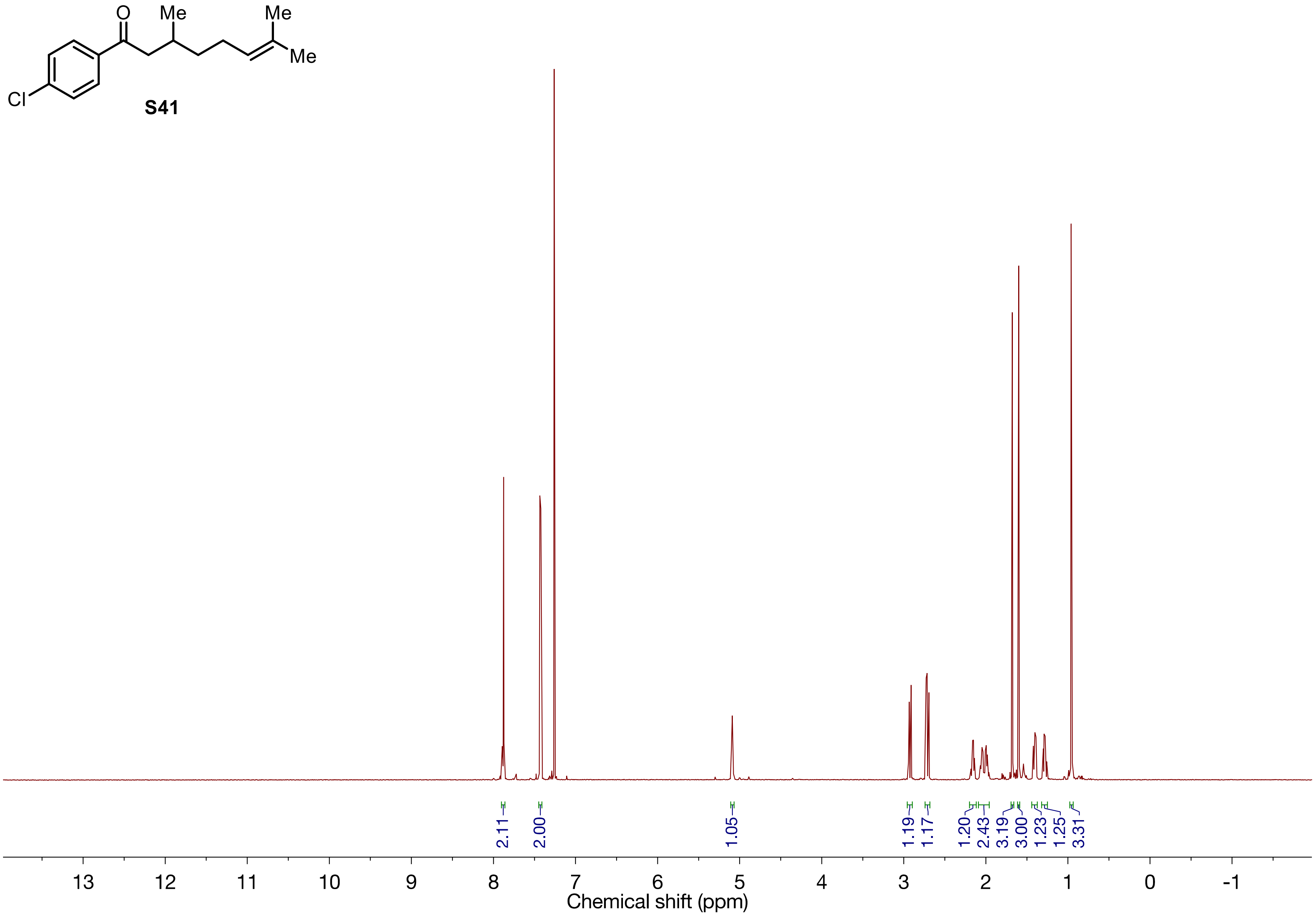


S40

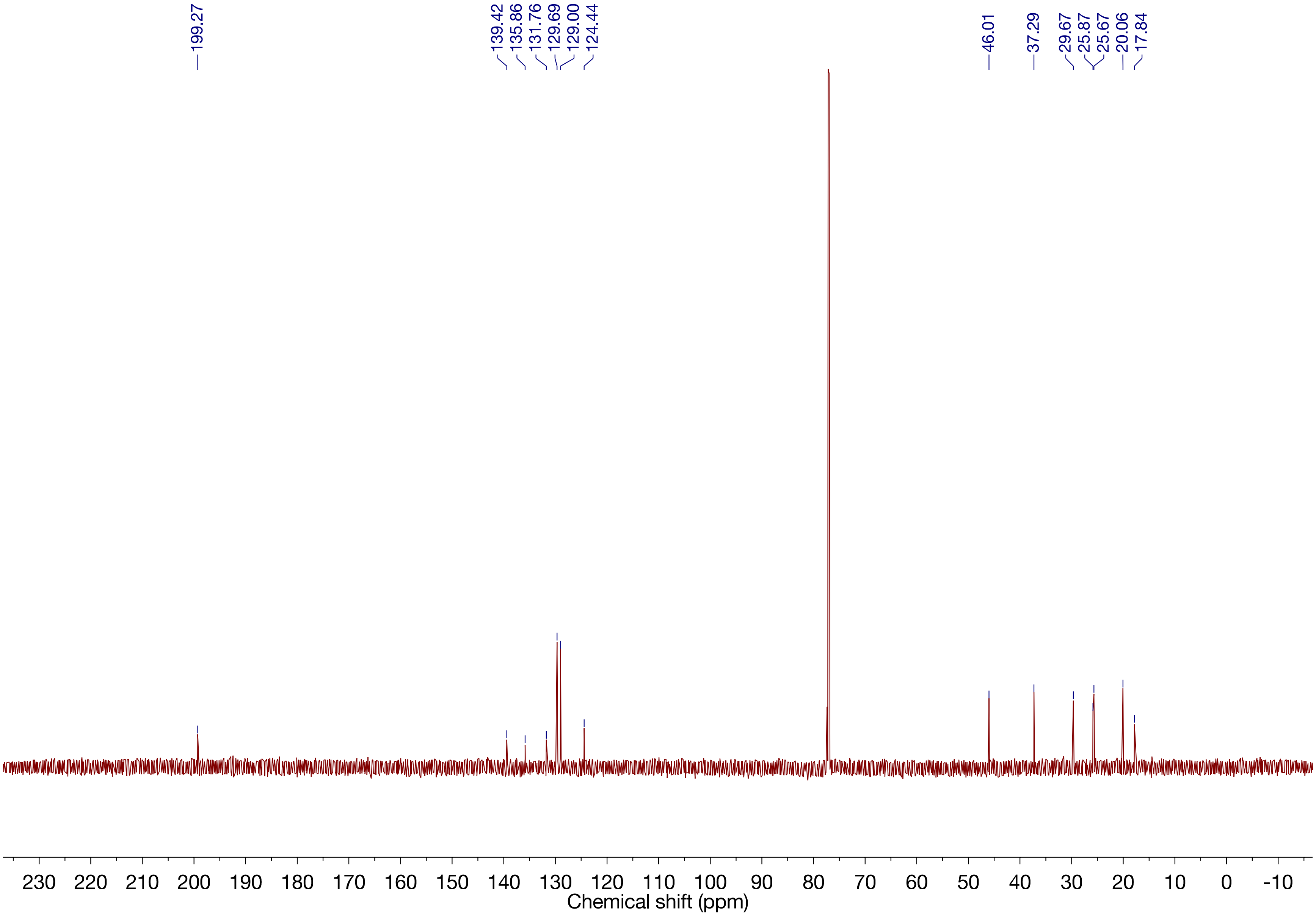
EtO2C
CO2Et
tBu
Me
Me
O
1.91
1.90
0.83
3.92
1.90
1.94
1.91
3.00
2.94
9.40
6.41
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)



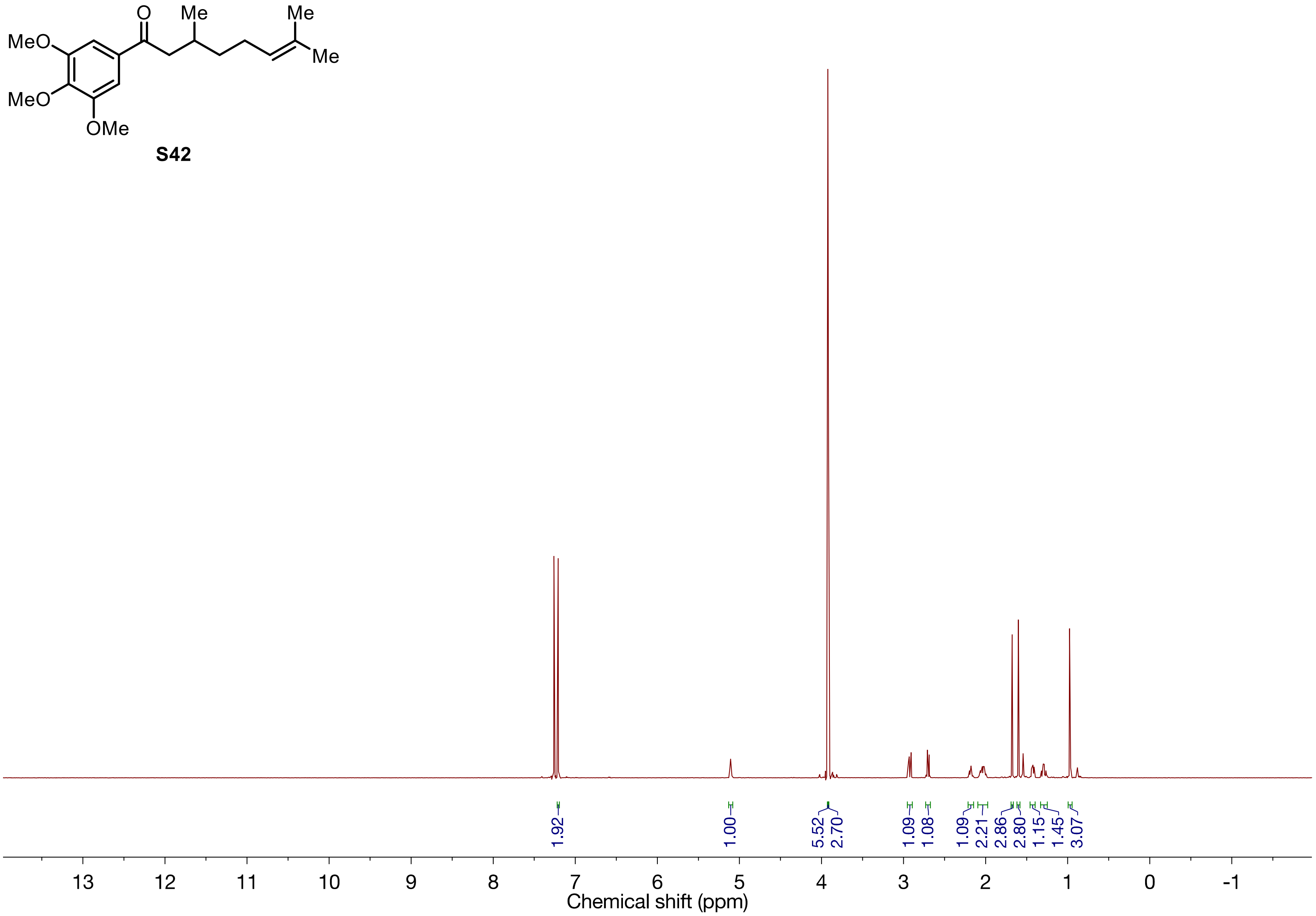
198.87
171.54
156.90
135.83
134.29
128.16
125.66
117.74
61.39
57.21
35.25
33.93
32.33
31.23
27.31
26.18
18.15
14.23
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


S41

O
Me
Me
Me
Cl
2.11
2.00
1.05
1.19
1.17
1.20
2.43
3.19
3.00
1.23
1.25
3.31
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

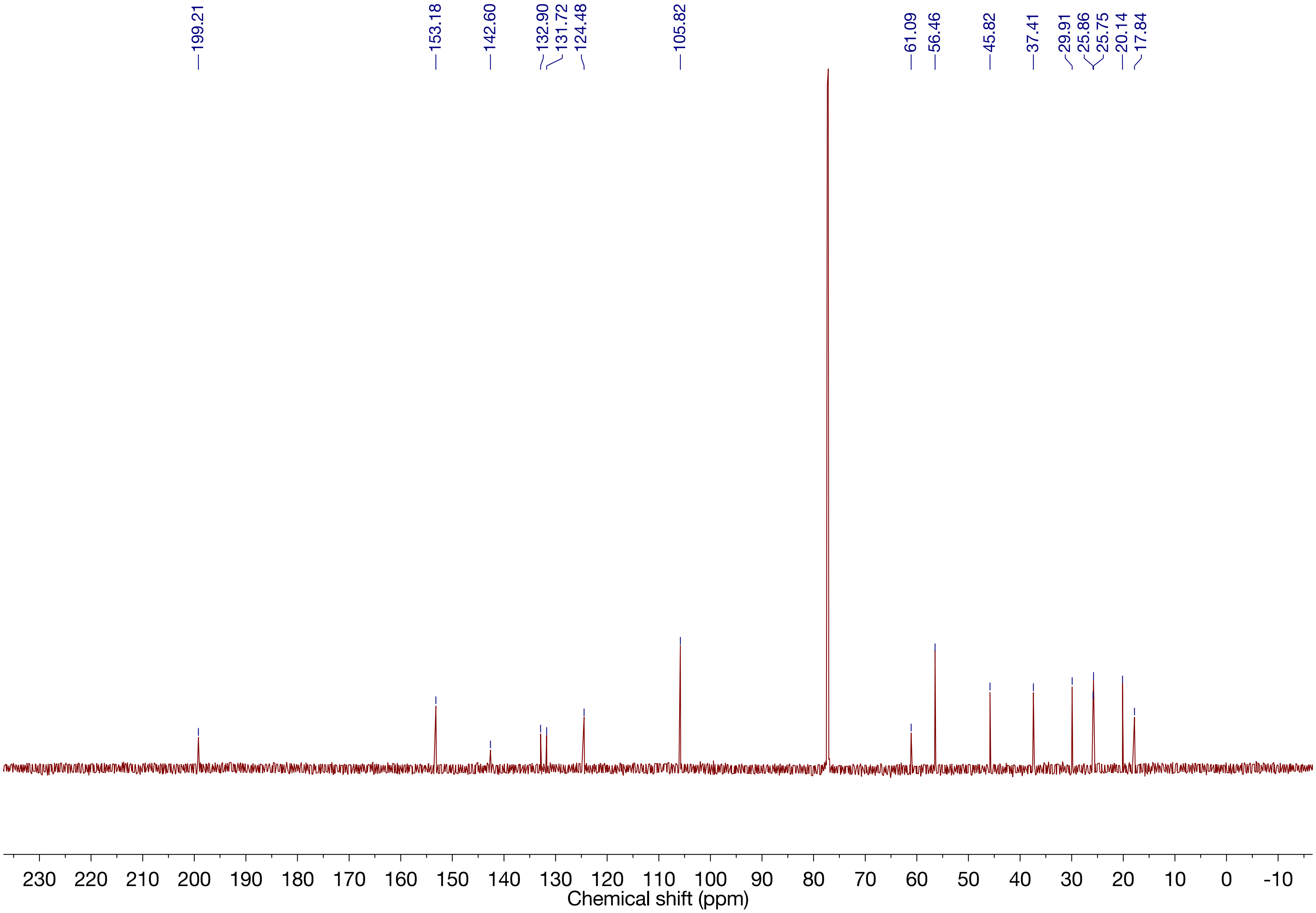


199.27
139.42
135.86
131.76
129.69
129.00
124.44
46.01
37.29
29.67
25.87
25.67
20.06
17.84
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

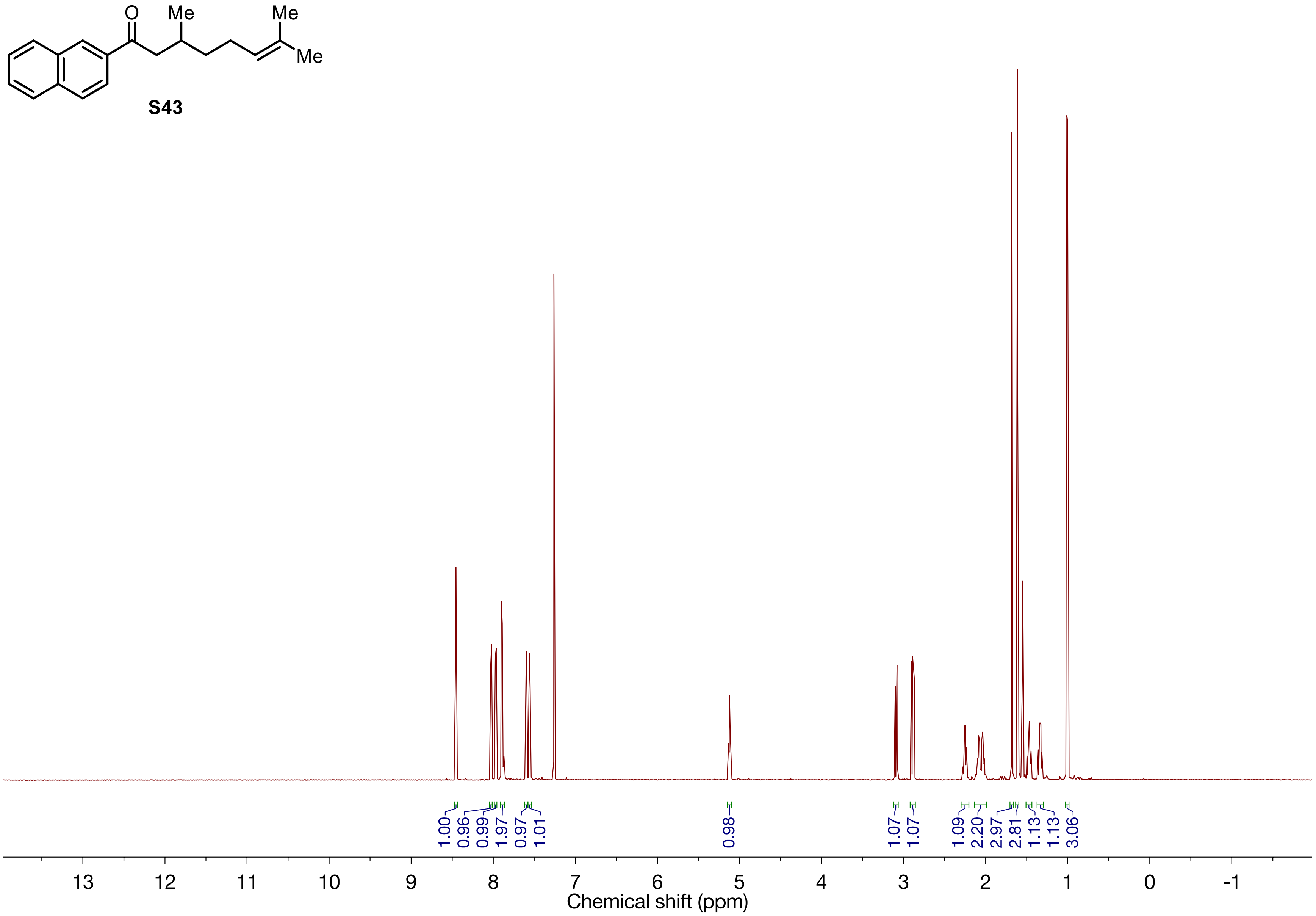


S42

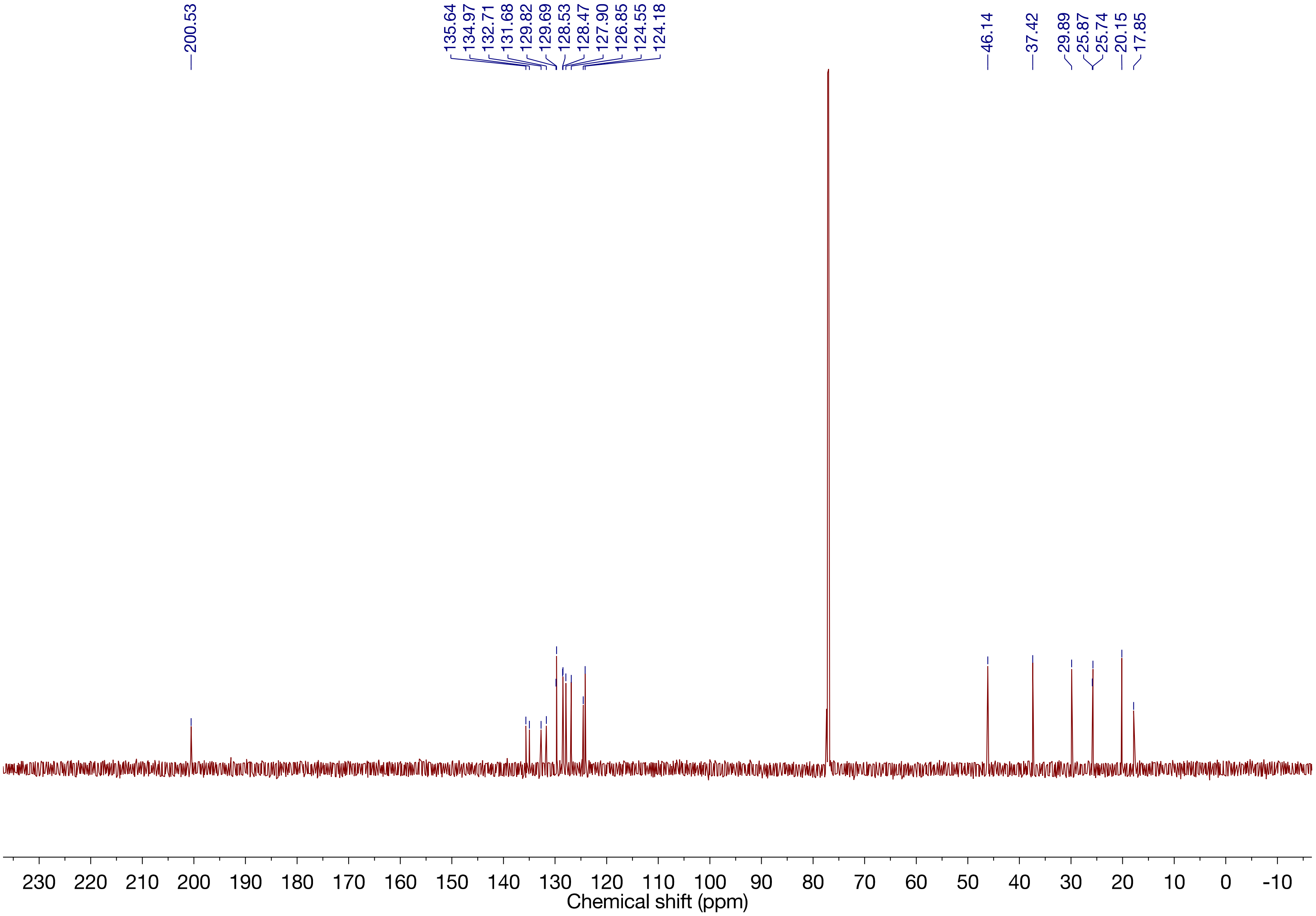
O
Me
Me
MeO
Me
MeO
OMe
1.92
1.00
5.52
2.70
1.09
1.08
1.09
2.21
2.86
2.80
1.15
1.45
3.07
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

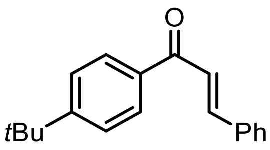


199.21
153.18
142.60
132.90
131.72
124.48
105.82
61.09
56.46
45.82
37.41
29.91
25.86
25.75
20.14
17.84
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

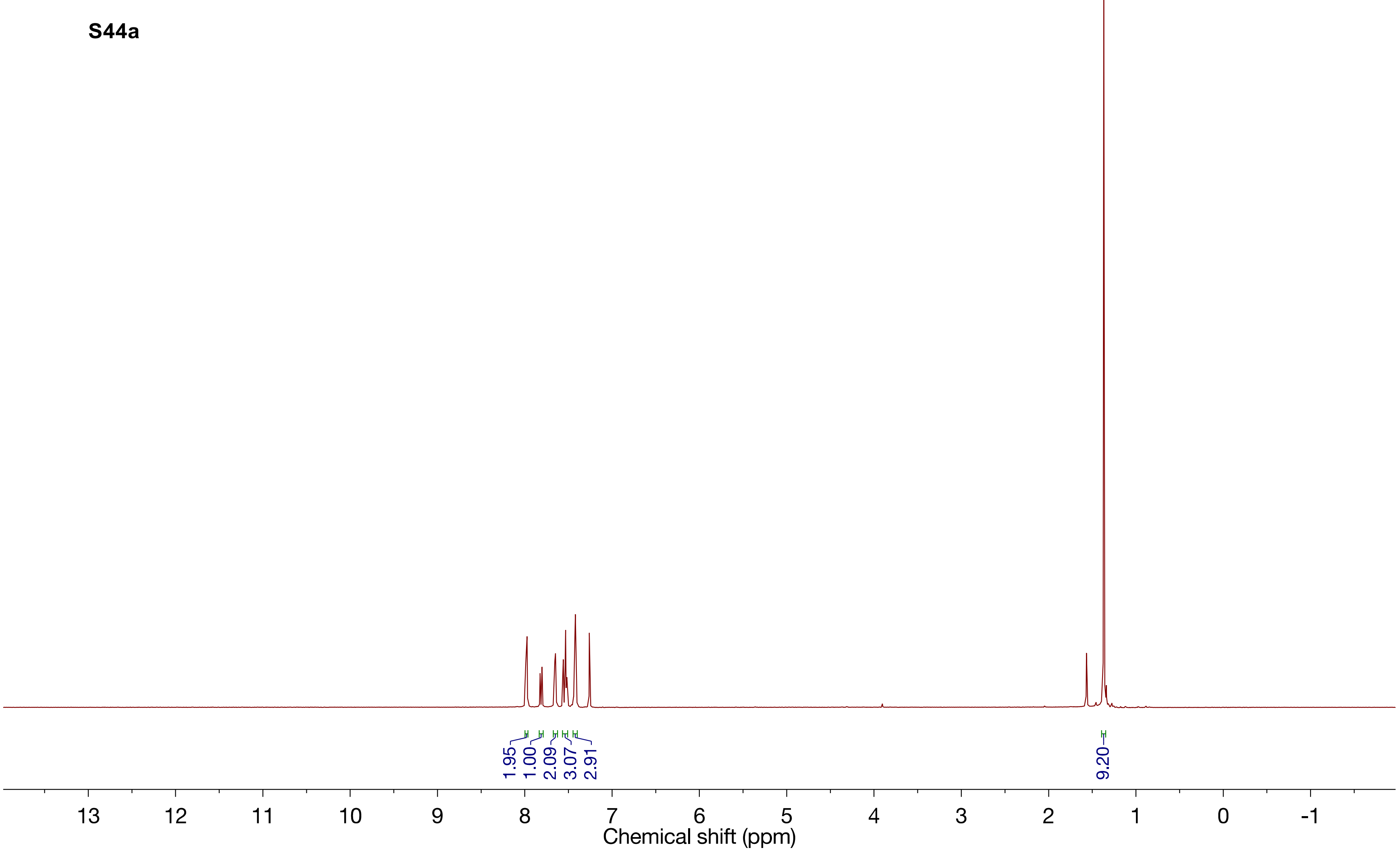

S43

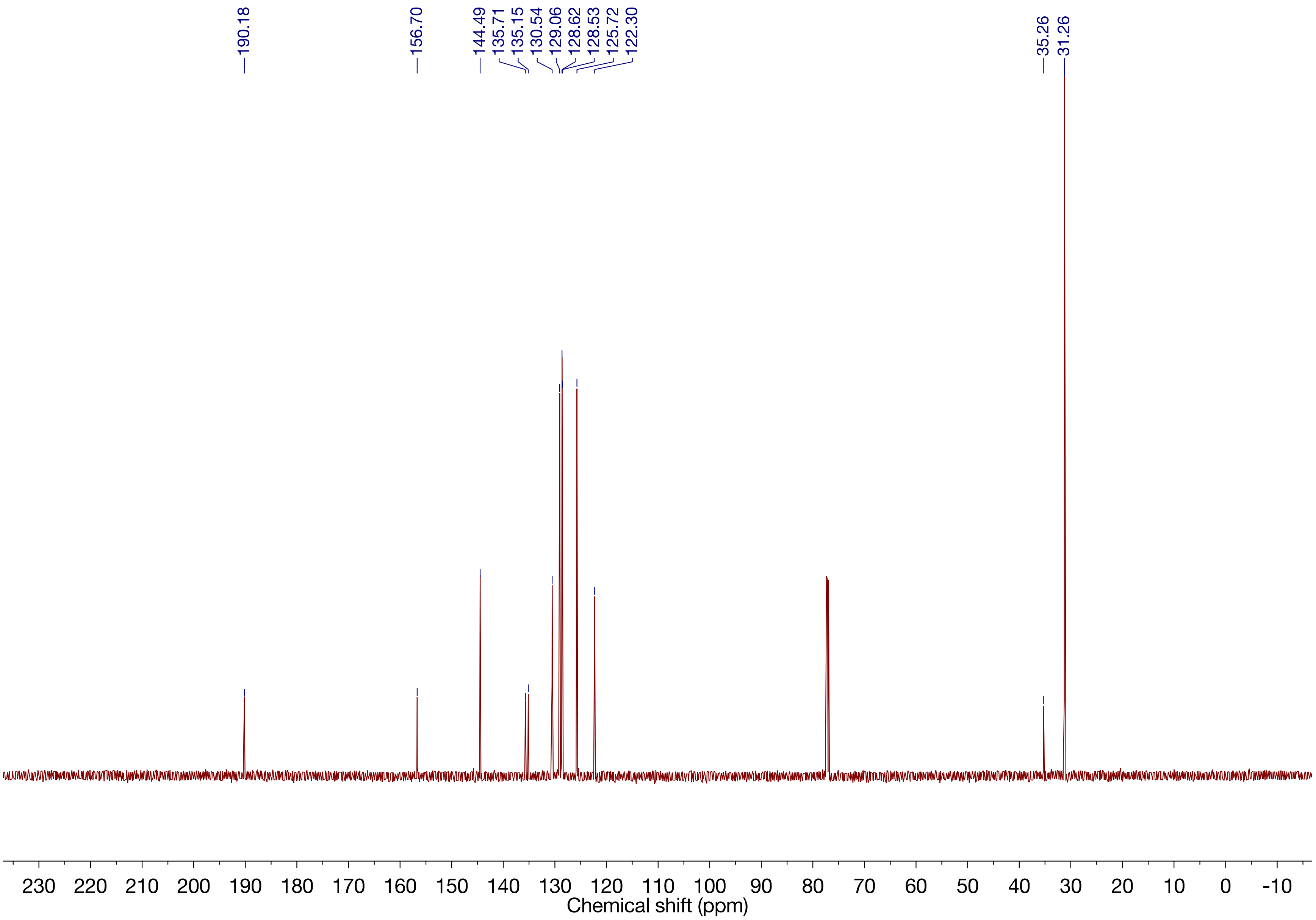
O
Me
Me
Me
1.00
0.96
0.99
1.97
0.97
1.01
0.98
1.07
1.07
1.09
2.20
2.97
2.81
1.13
1.13
3.06
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


200.53
135.64
134.97
132.71
131.68
129.82
129.69
128.53
128.47
127.90
126.85
124.55
124.18
46.14
37.42
29.89
25.87
25.74
20.15
17.85
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

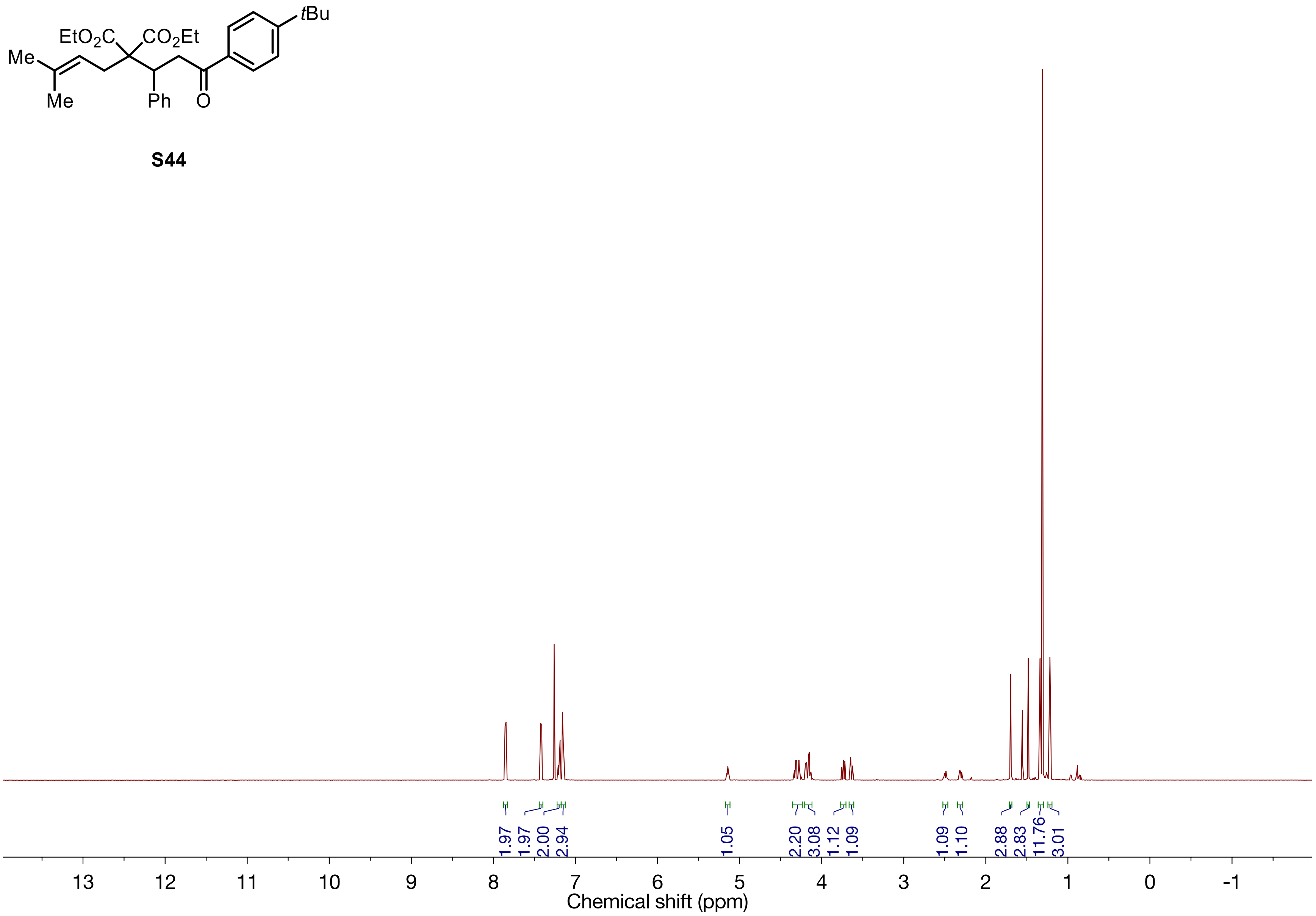

O
tBu
Ph

S44a

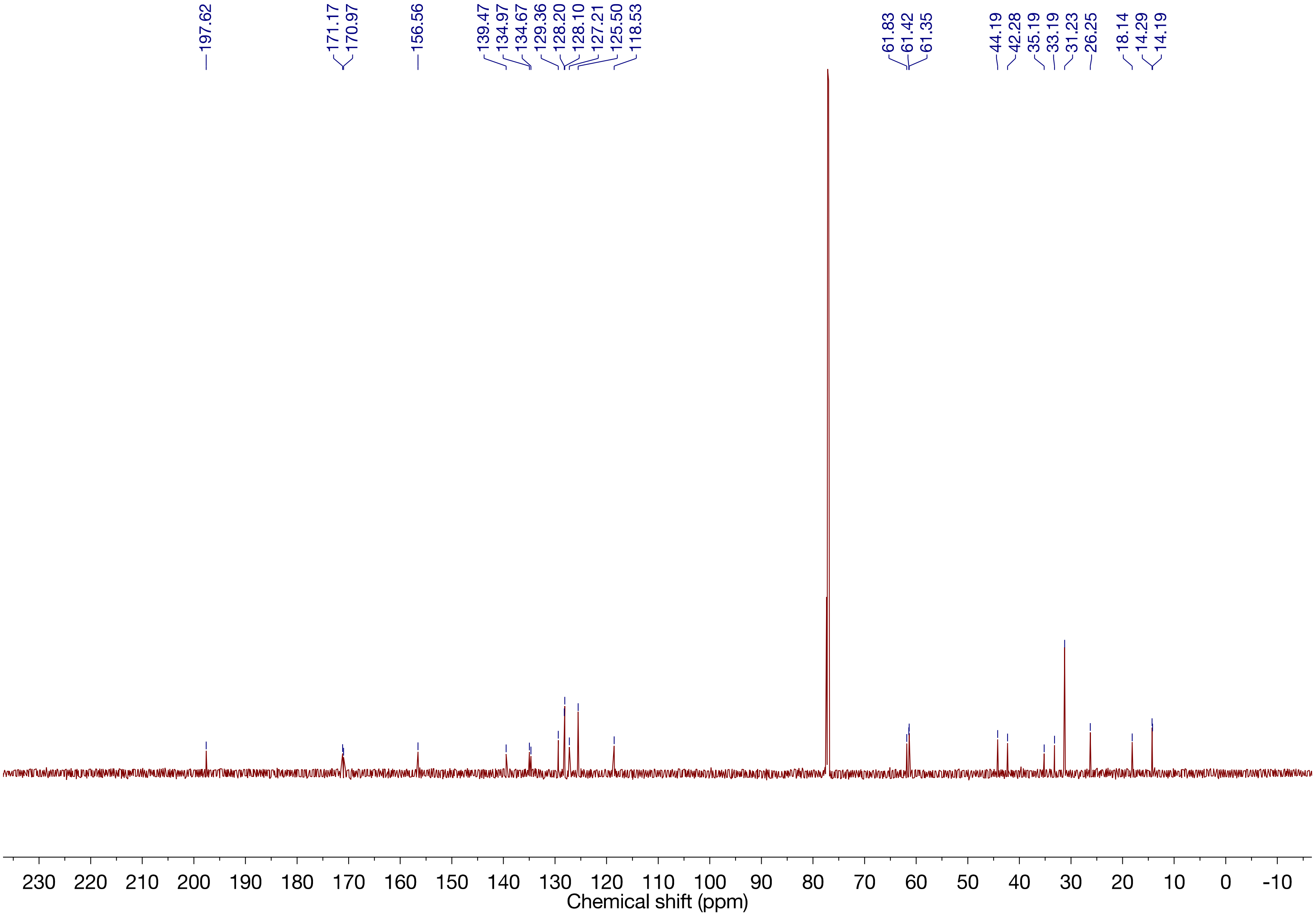

1.95
1.00
2.09
3.07
2.91
9.20
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

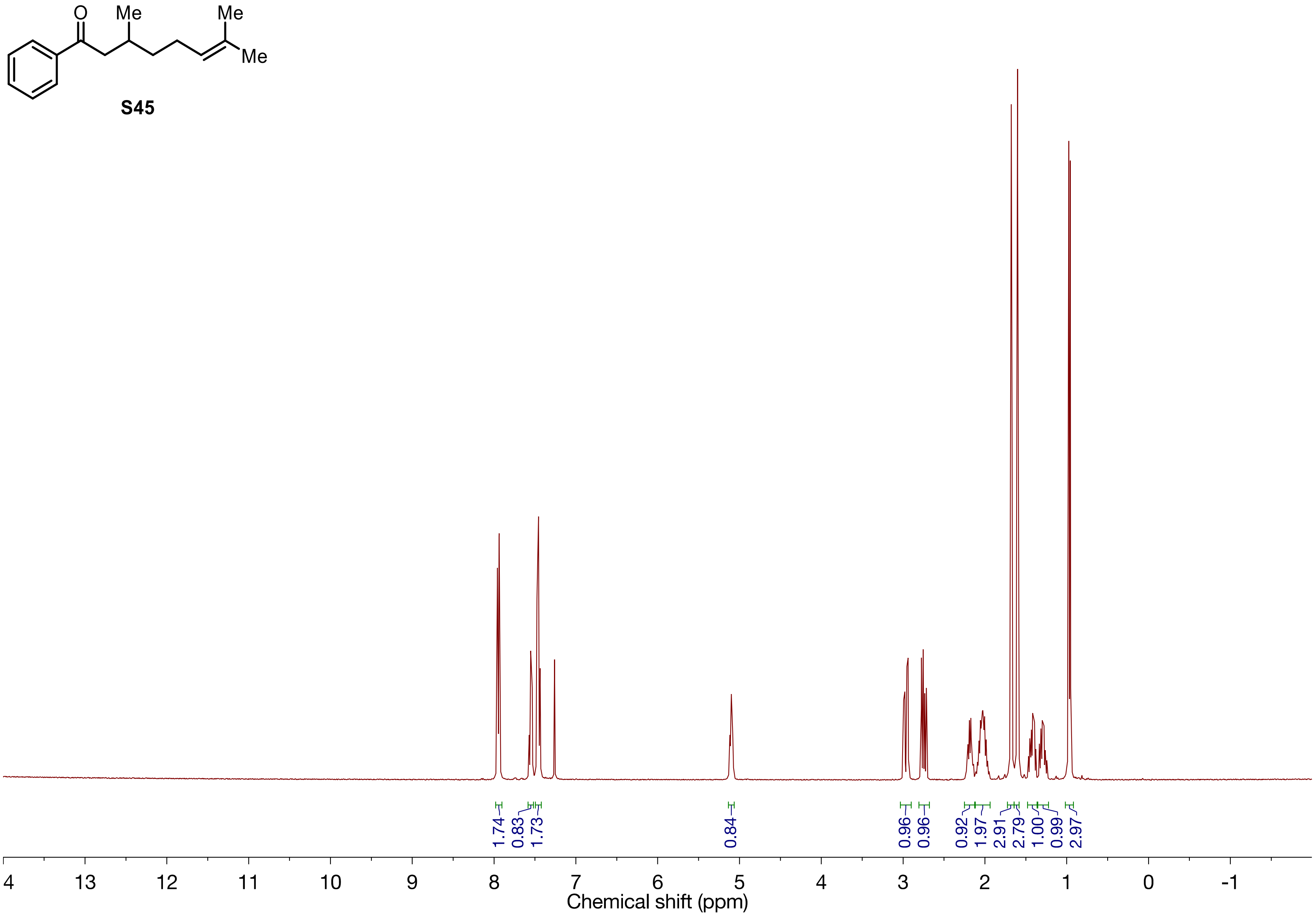


190.18
156.70
144.49
135.71
135.15
130.54
129.06
128.62
128.53
125.72
122.30
35.26
31.26
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


EtO2C
CO2Et
tBu
Me
Me
Ph
O
1.97
1.97
2.00
2.94
1.05
2.20
3.08
1.12
1.09
1.09
1.10
2.88
2.83
11.76
3.01
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

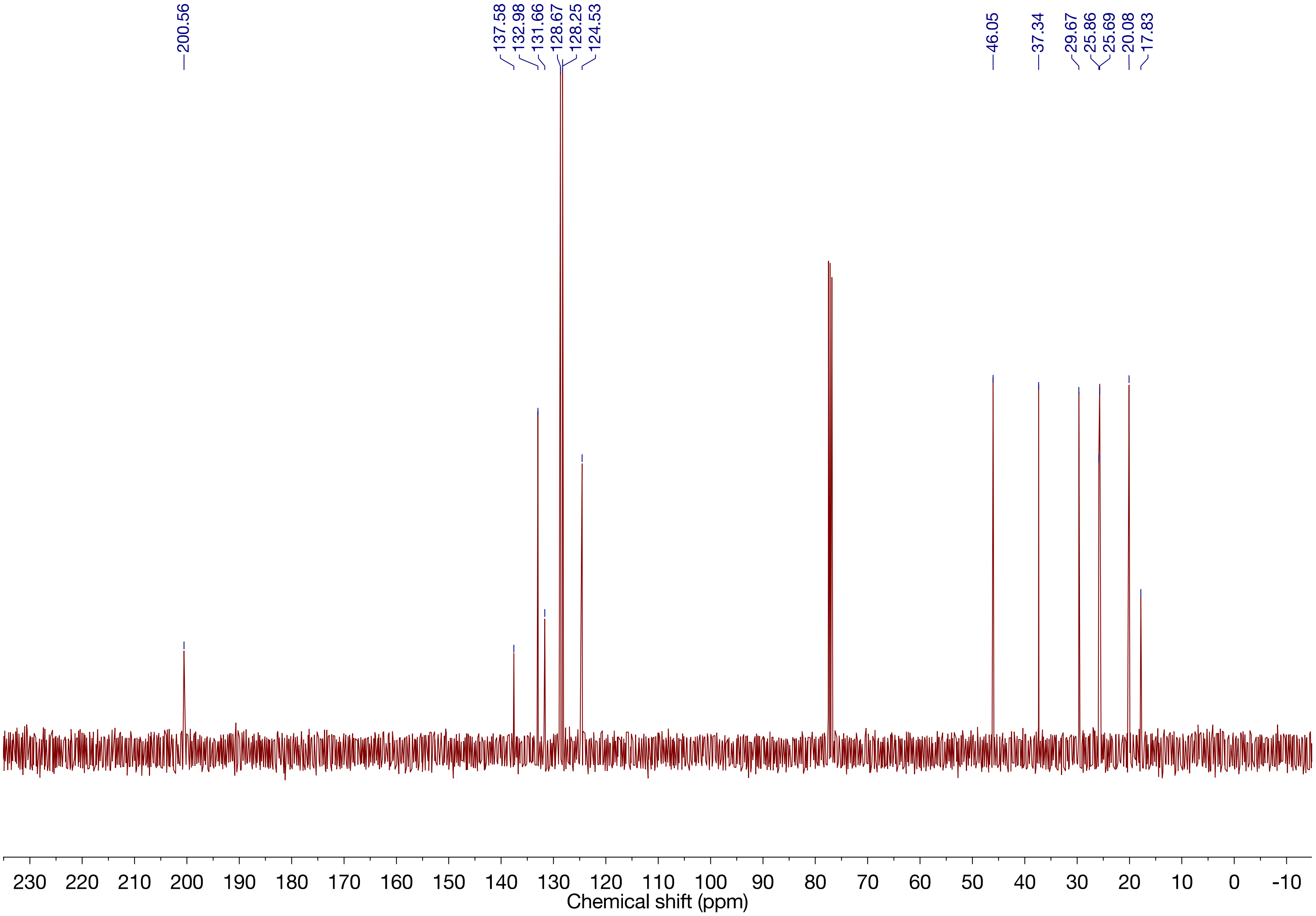
S44


197.62
171.17
170.97
156.56
139.47
134.97
134.67
129.36
128.20
128.10
127.21
125.50
118.53
61.83
61.42
61.35
44.19
42.28
35.19
33.19
31.23
26.25
18.14
14.29
14.19
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

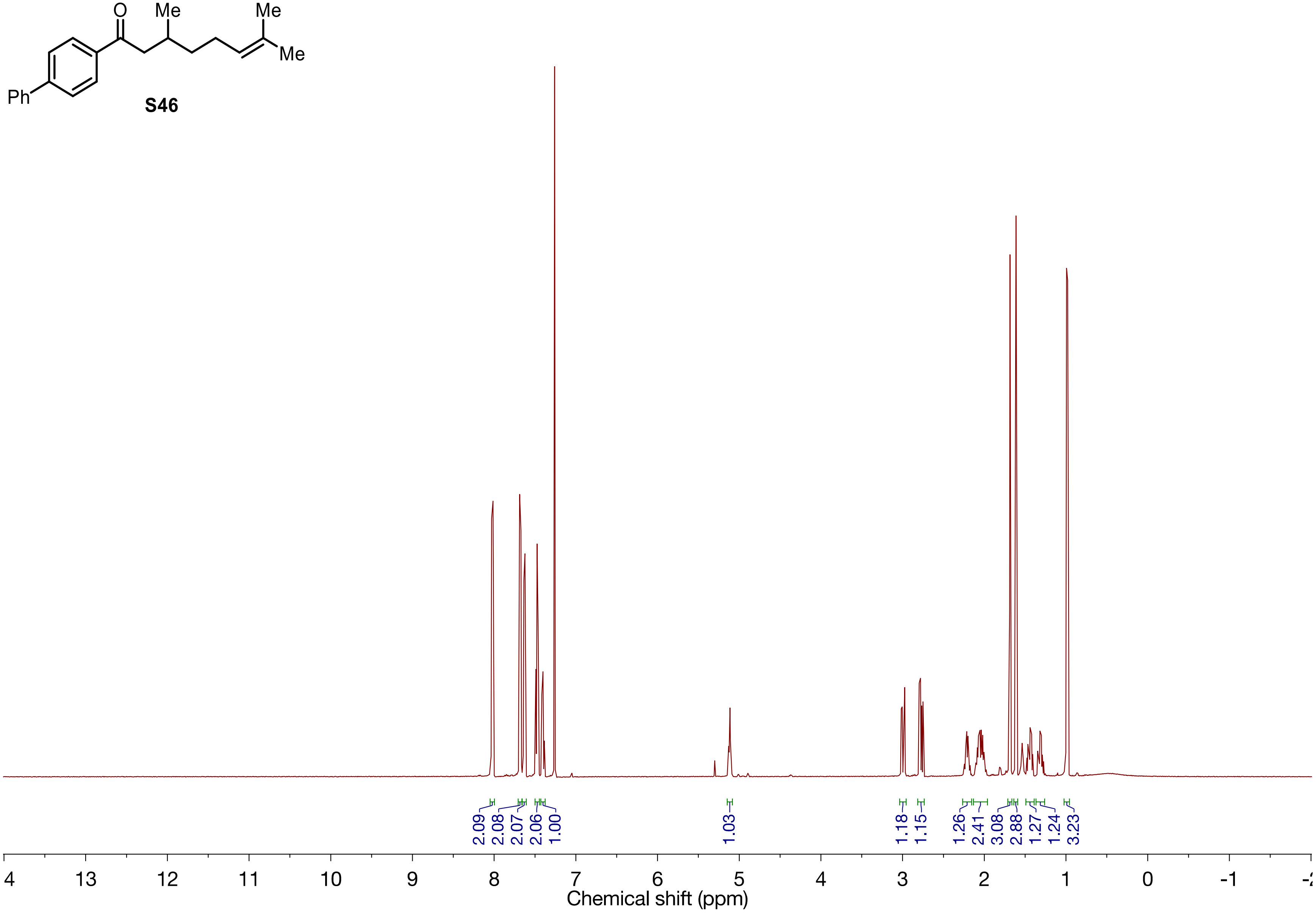


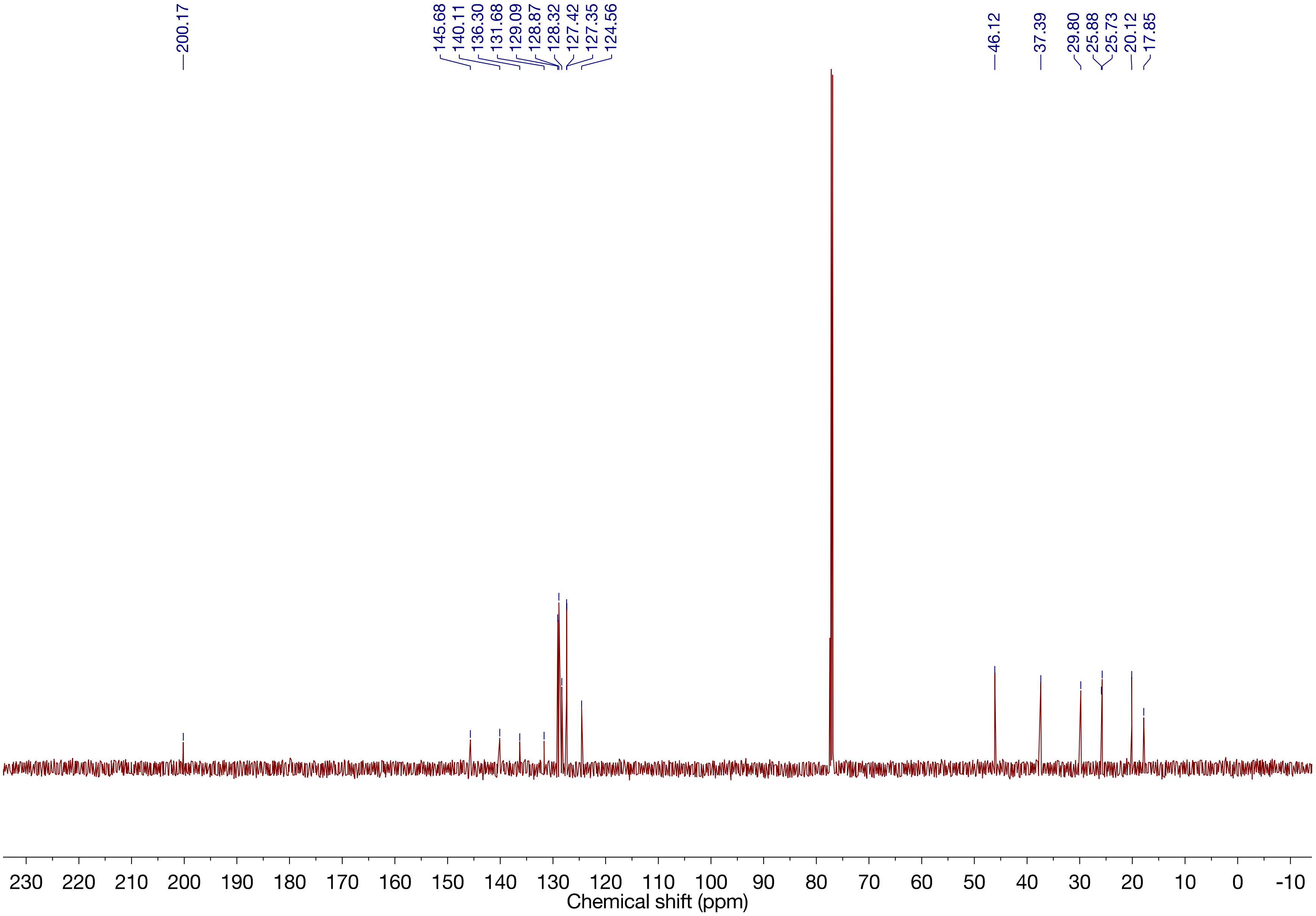
S45

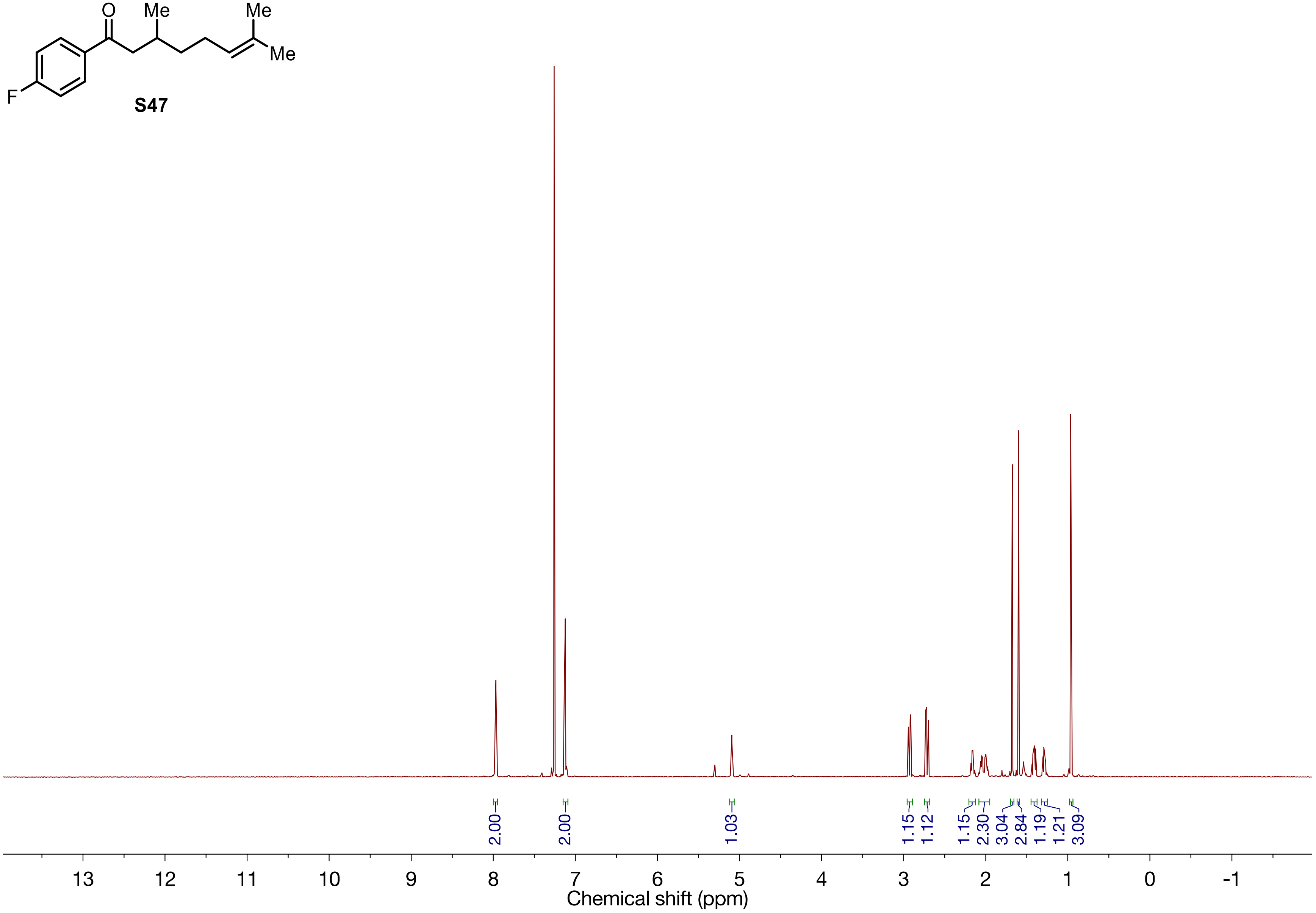
O
Me
Me
Me
1.74
0.83
1.73
0.84
0.96
0.96
0.92
1.97
2.91
2.79
1.00
0.99
2.97
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

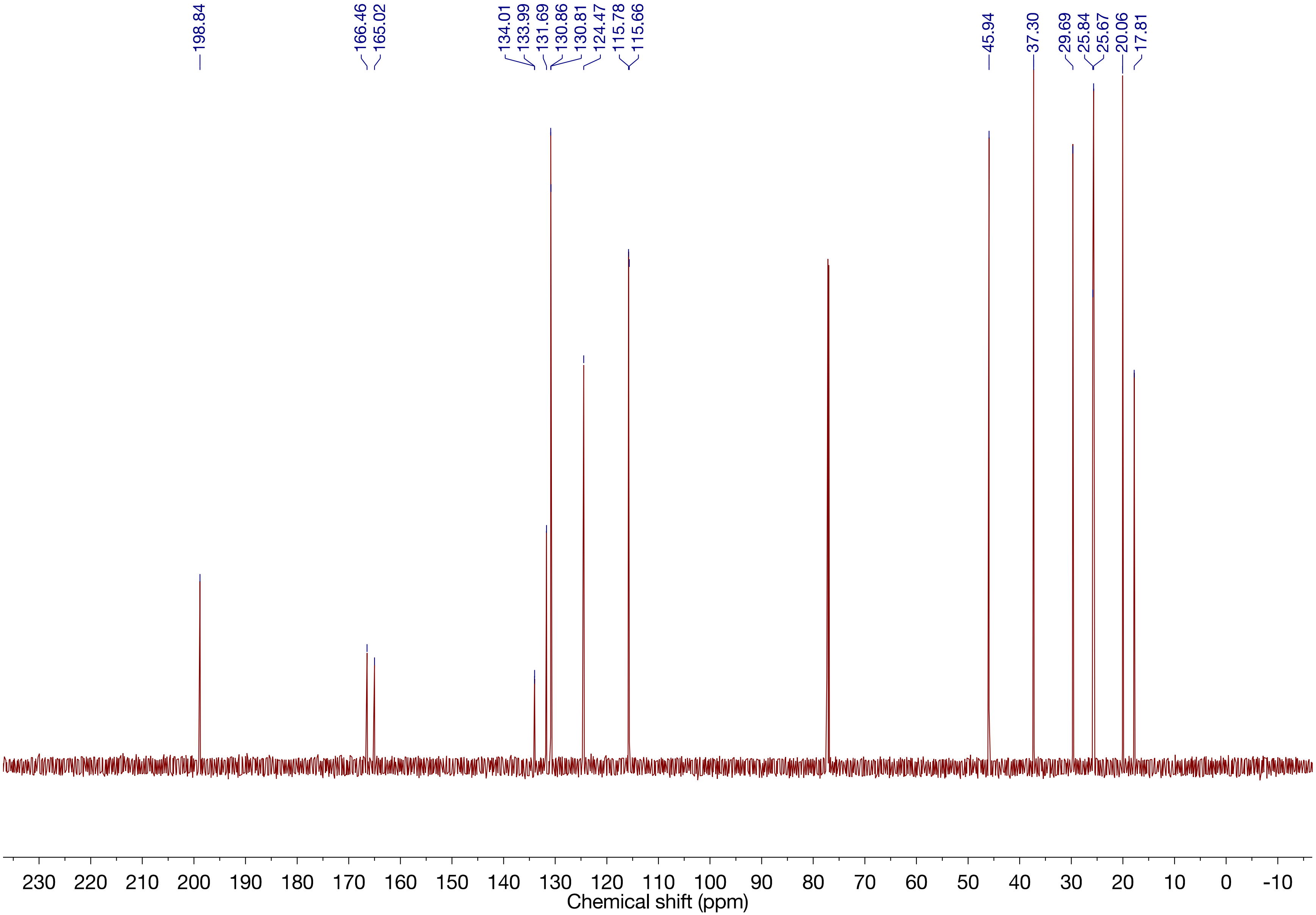


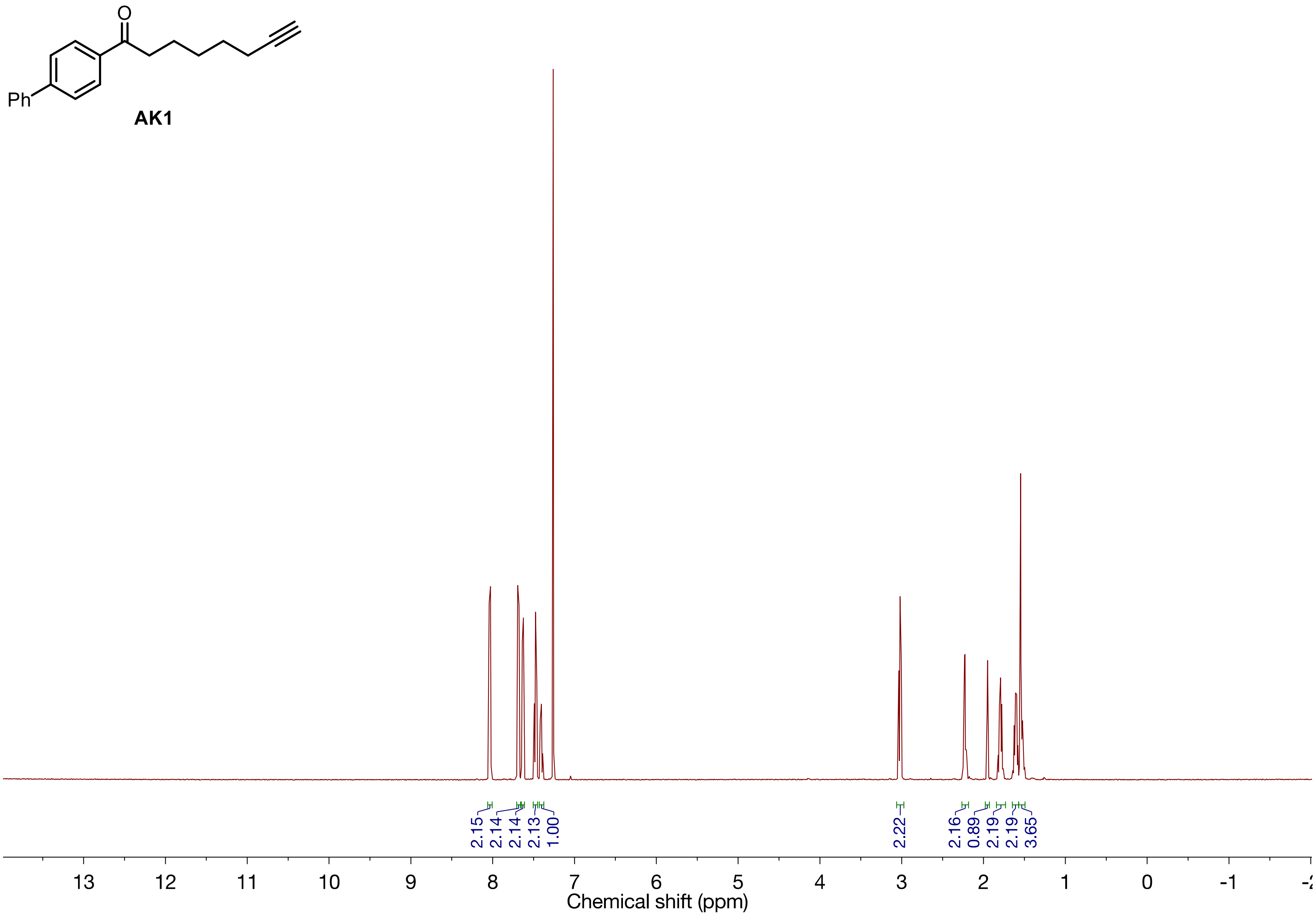
200.56
137.58
132.98
131.66
128.67
128.25
124.53
46.05
37.34
29.67
25.86
25.69
20.08
17.83
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


S46
O
Me
Me
Me
Ph
2.09
2.08
2.07
2.06
1.00
1.03
1.18
1.15
1.26
2.41
3.08
2.88
1.27
1.24
3.23
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

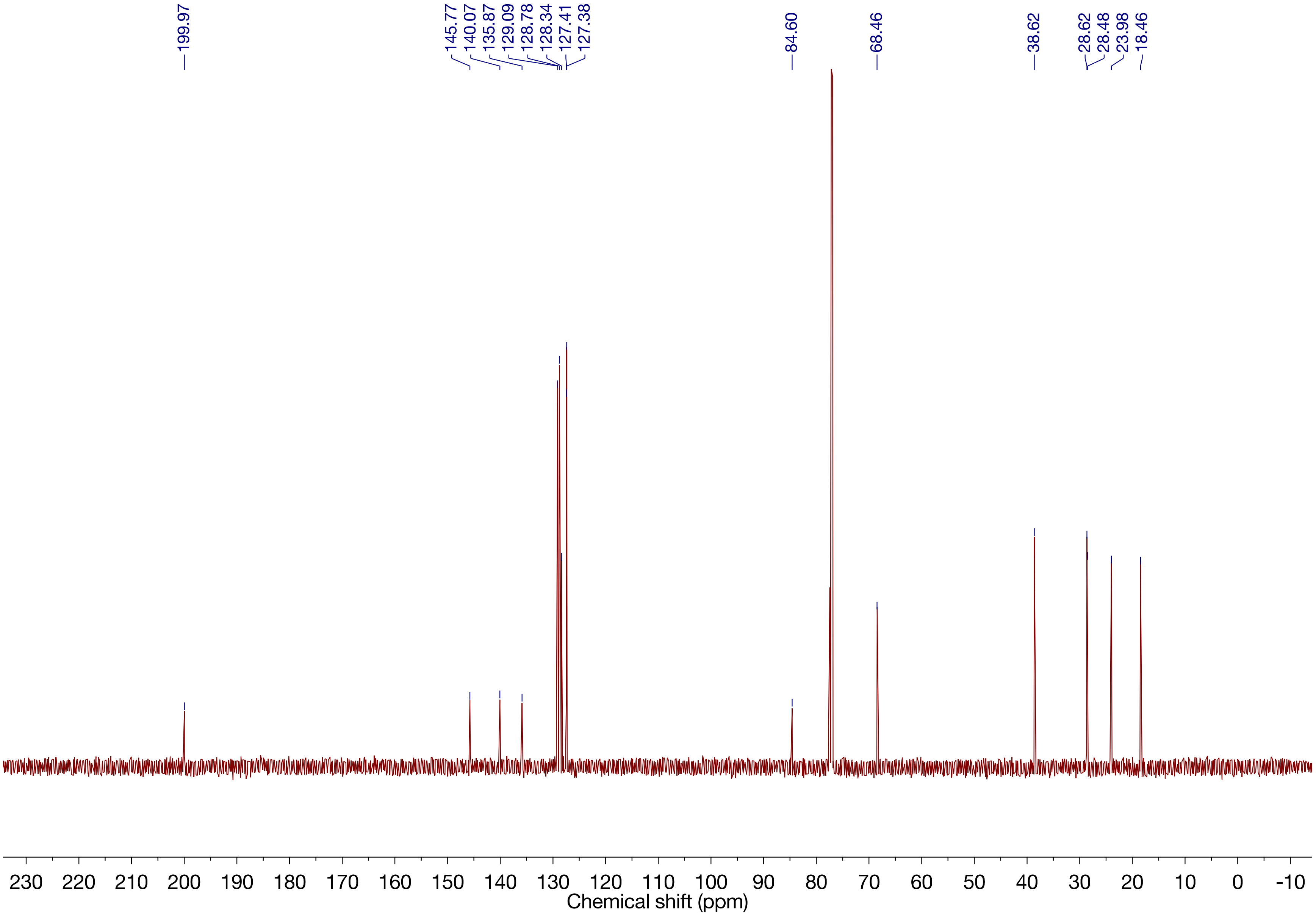

200.17
145.68
140.11
136.30
131.68
129.09
128.87
128.32
127.42
127.35
124.56
46.12
37.39
29.80
25.88
25.73
20.12
17.85
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

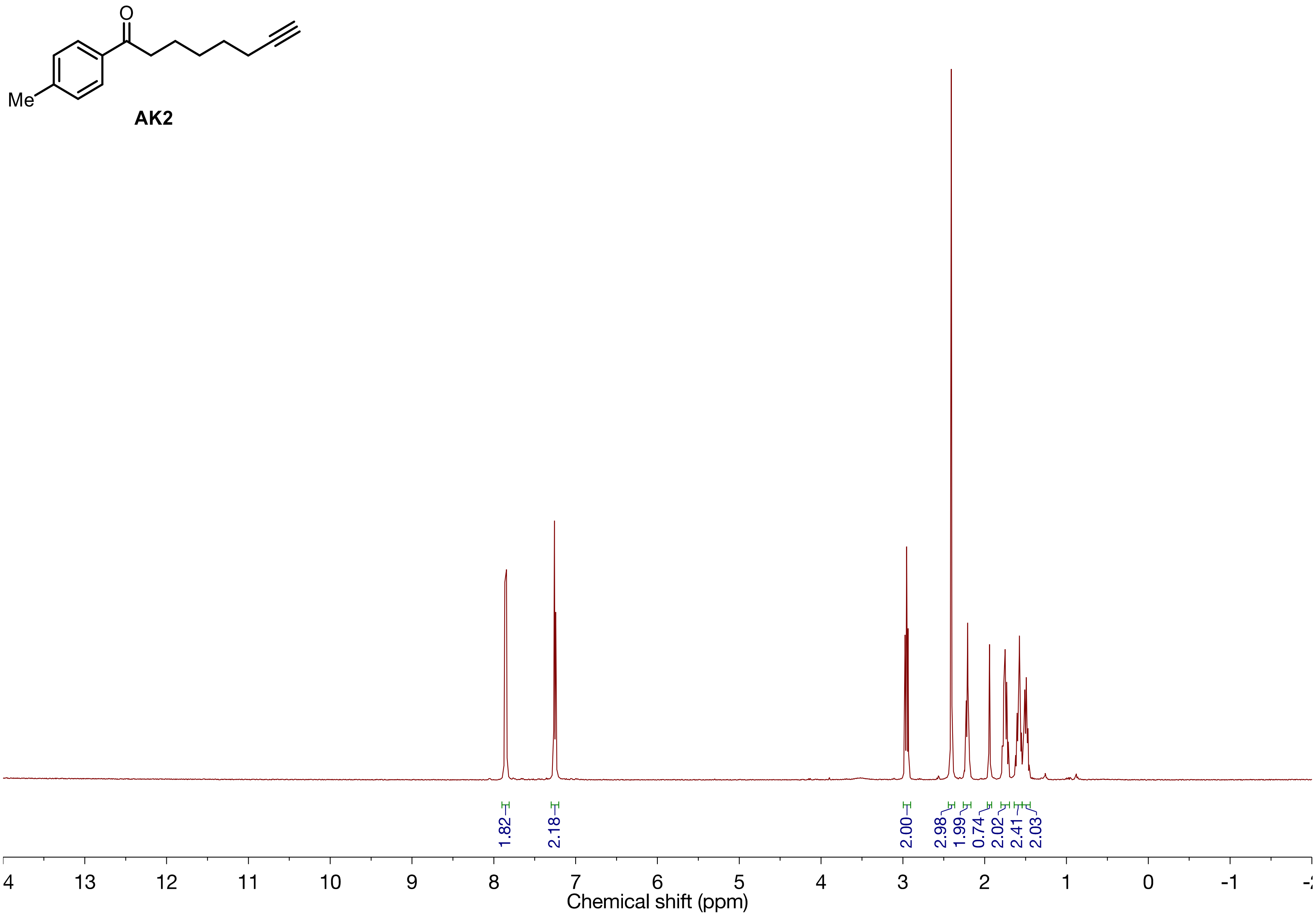

O
Me
Me
Me
F
S47
2.00
2.00
1.03
1.15
1.12
1.15
2.30
3.04
2.84
1.19
1.21
3.09
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


198.84
166.46
165.02
134.01
133.99
131.69
130.86
130.81
124.47
115.78
115.66
45.94
37.30
29.69
25.84
25.67
20.06
17.81
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

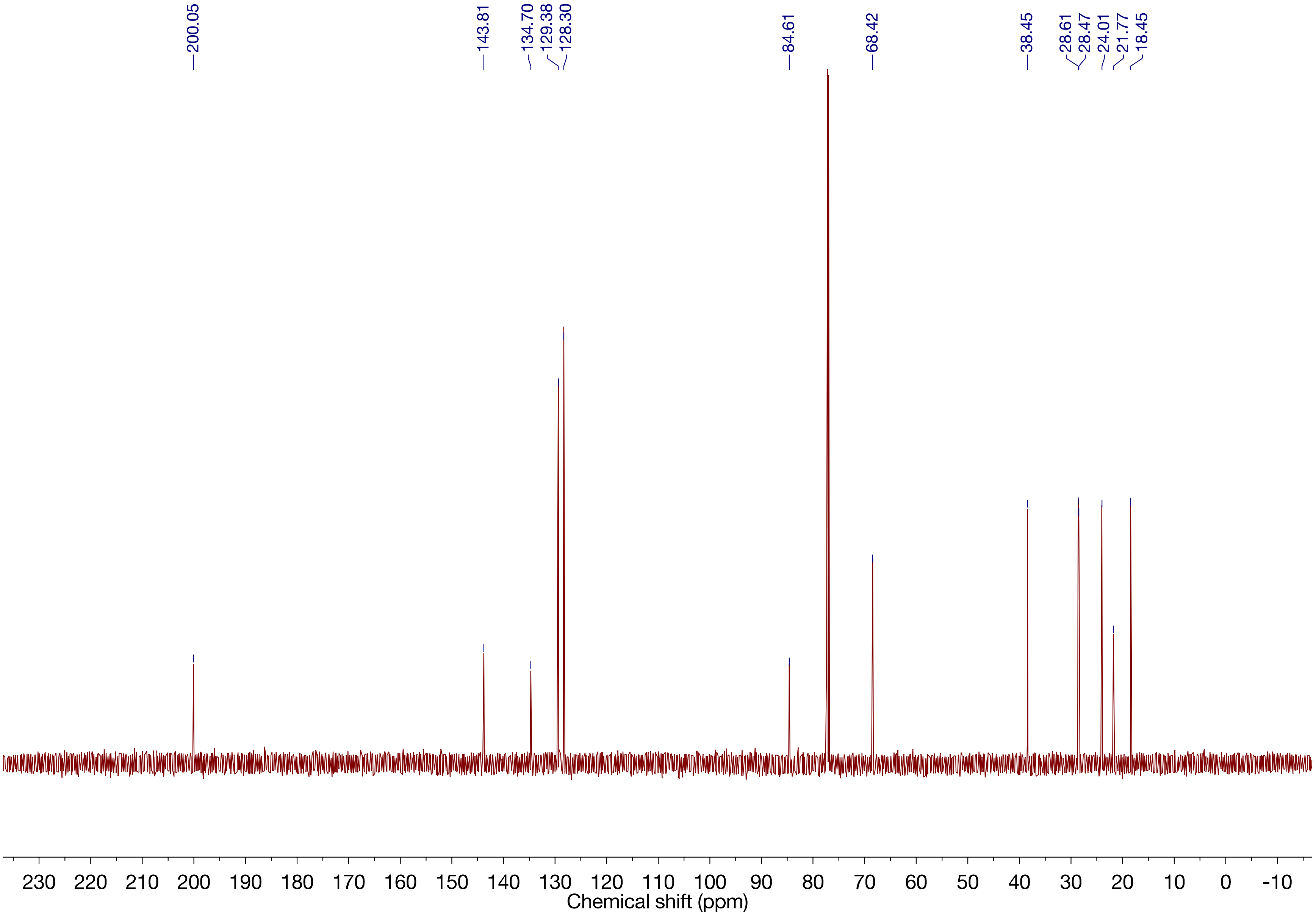

O
Ph
2.15
2.14
2.14
2.13
1.00
2.22
2.16
0.89
2.19
2.19
3.65
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

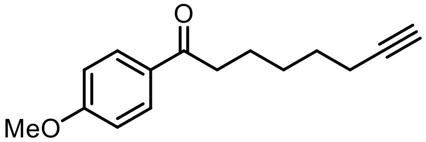
AK1


199.97
145.77
140.07
135.87
129.09
128.78
128.34
127.41
127.38
84.60
68.46
38.62
28.62
28.48
23.98
18.46
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

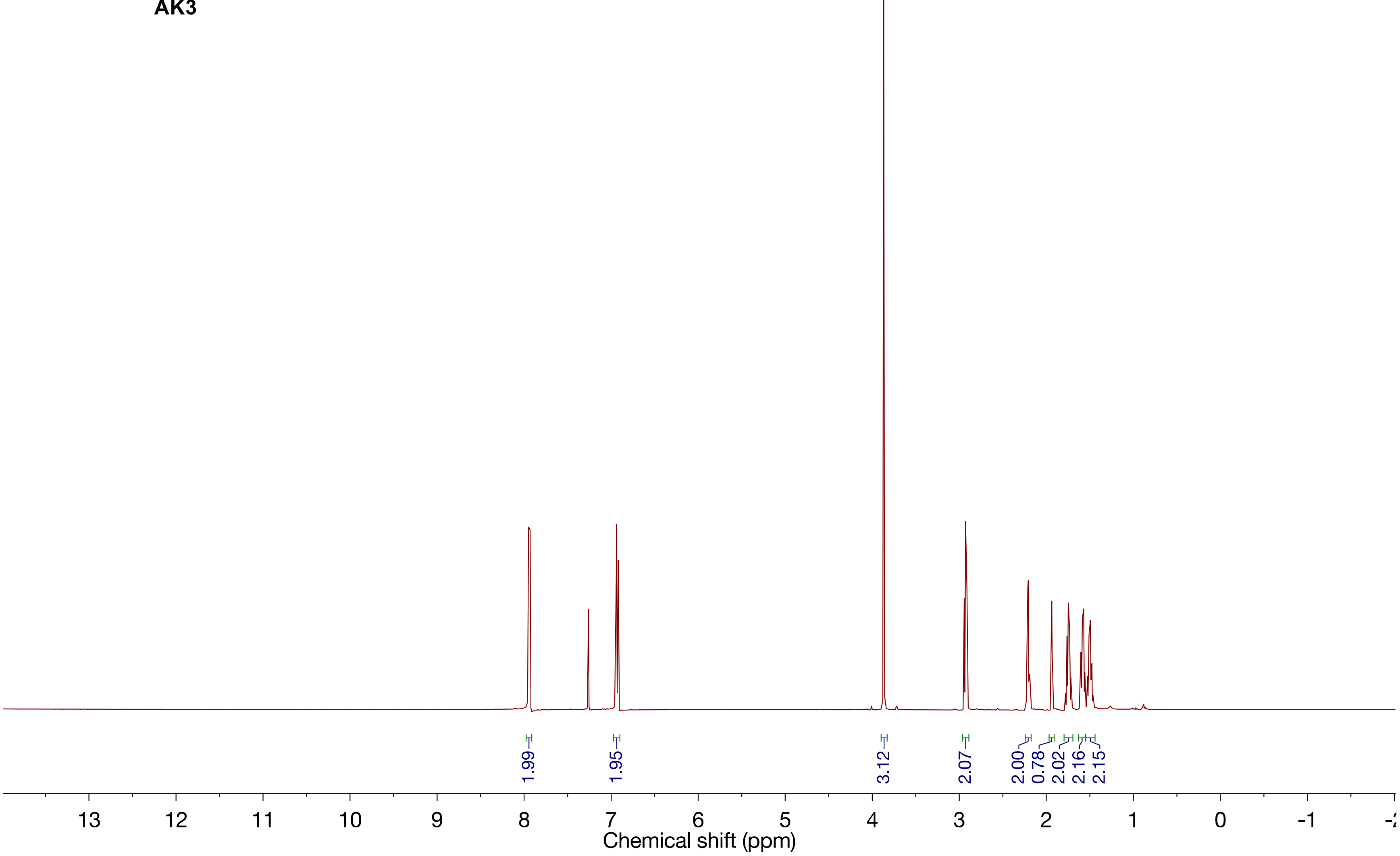

AK2

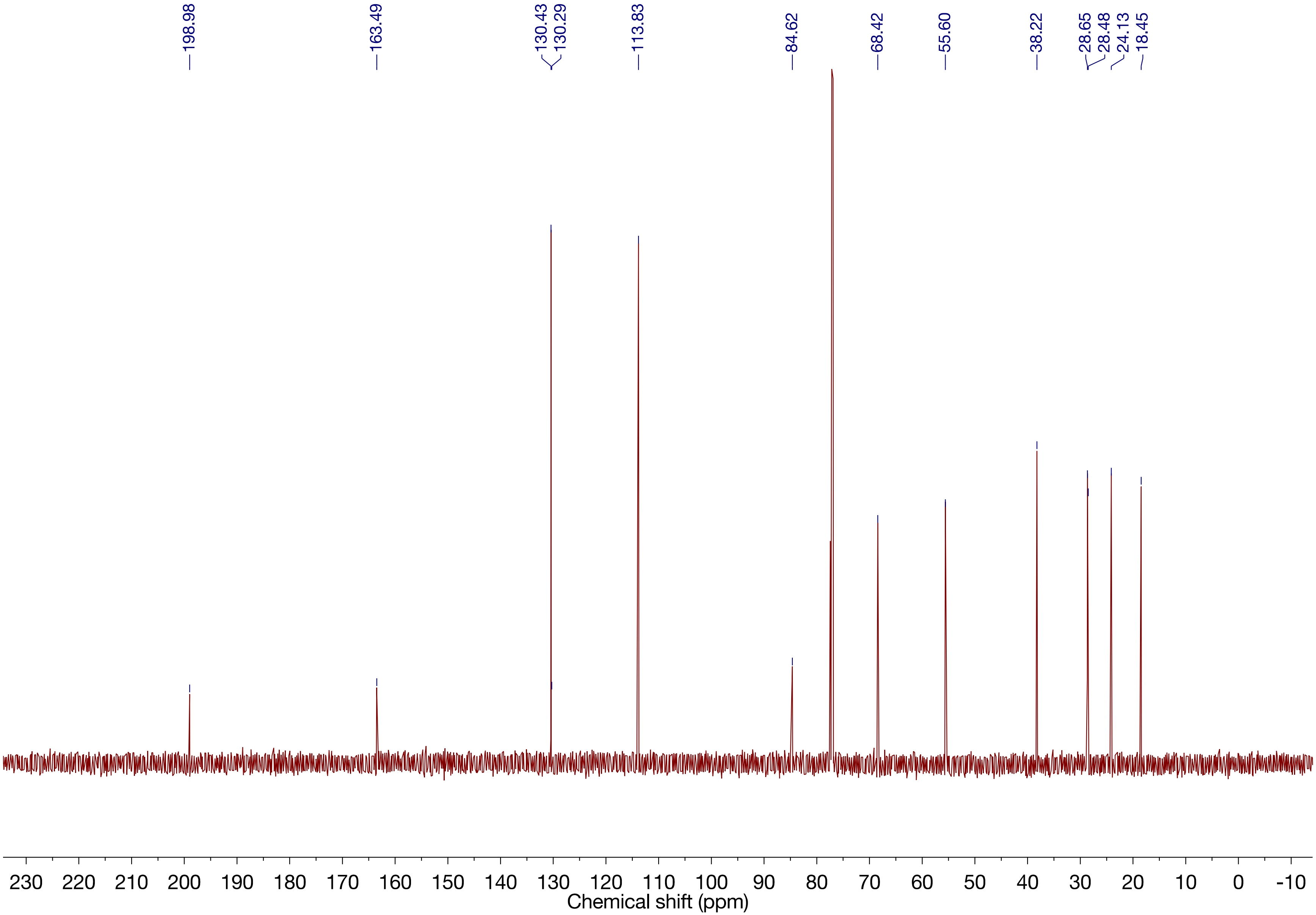
O
Me
1.82
2.18
2.00
2.98
1.99
0.74
2.02
2.41
2.03
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

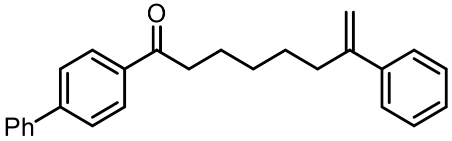

200.05
143.81
134.70
129.38
128.30
84.61
68.42
38.45
28.61
28.47
24.01
21.77
18.45
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)


O
MeO

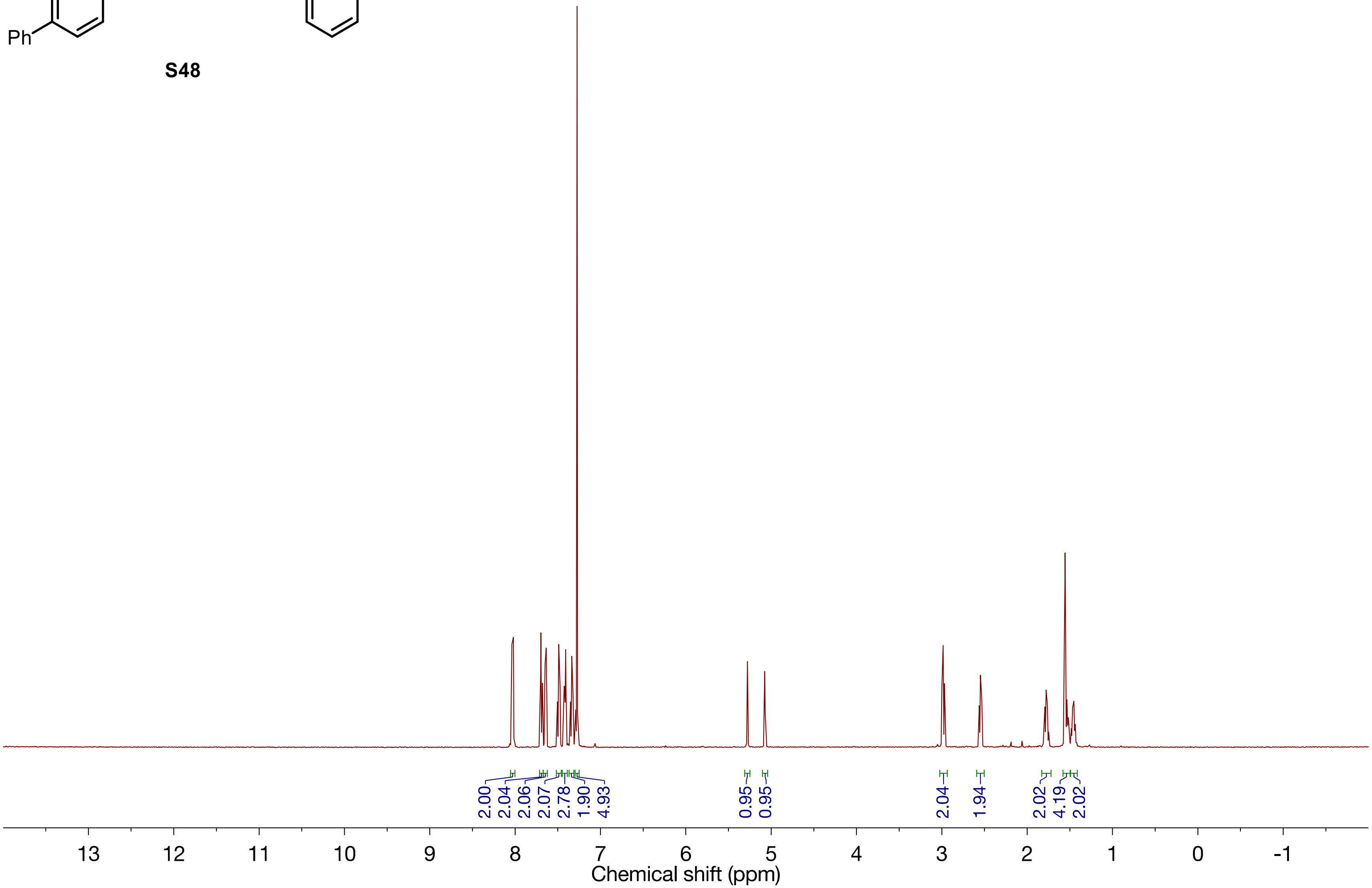
AK3

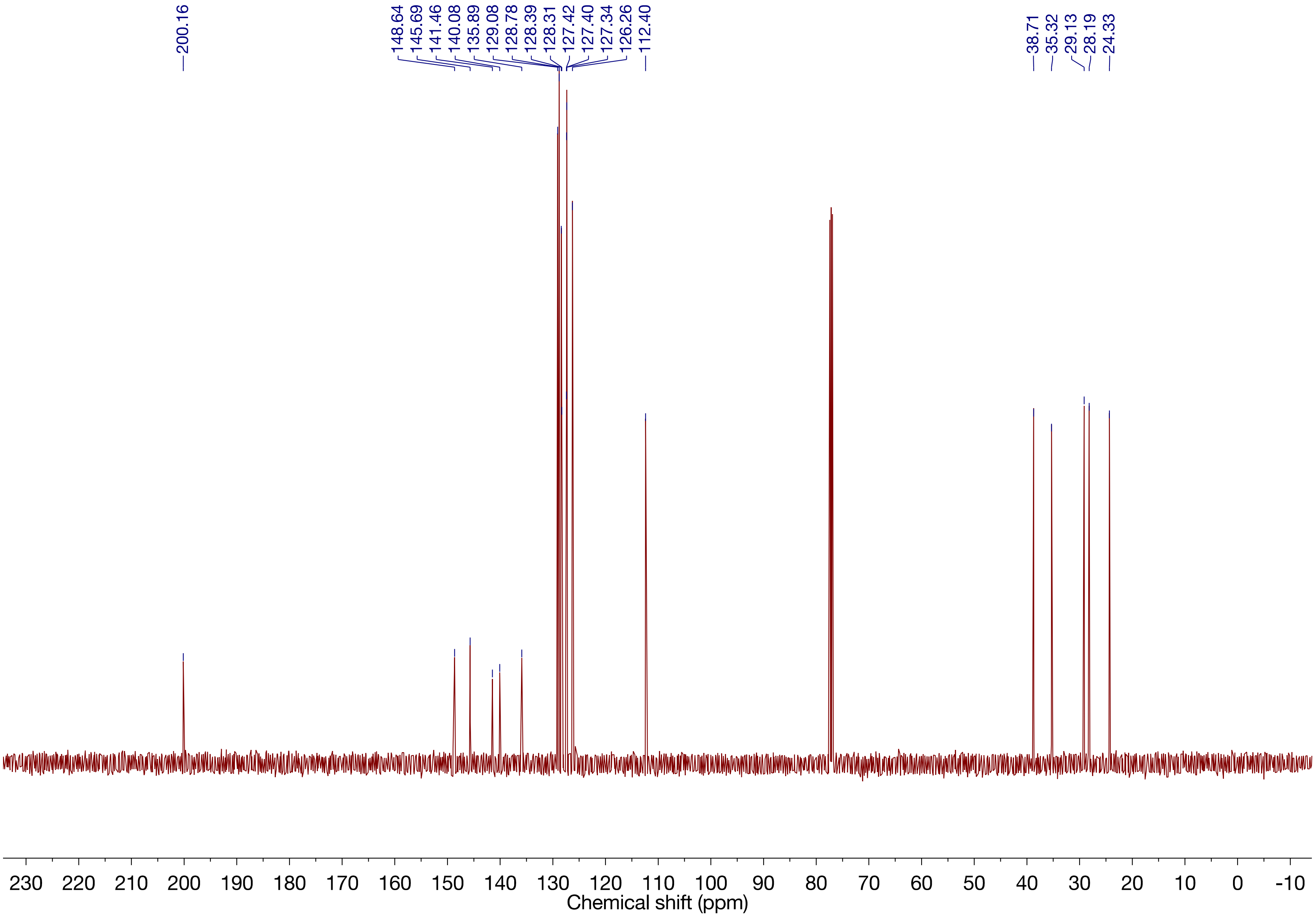

1.99
1.95
3.12
2.07
2.00
0.78
2.02
2.16
2.15
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

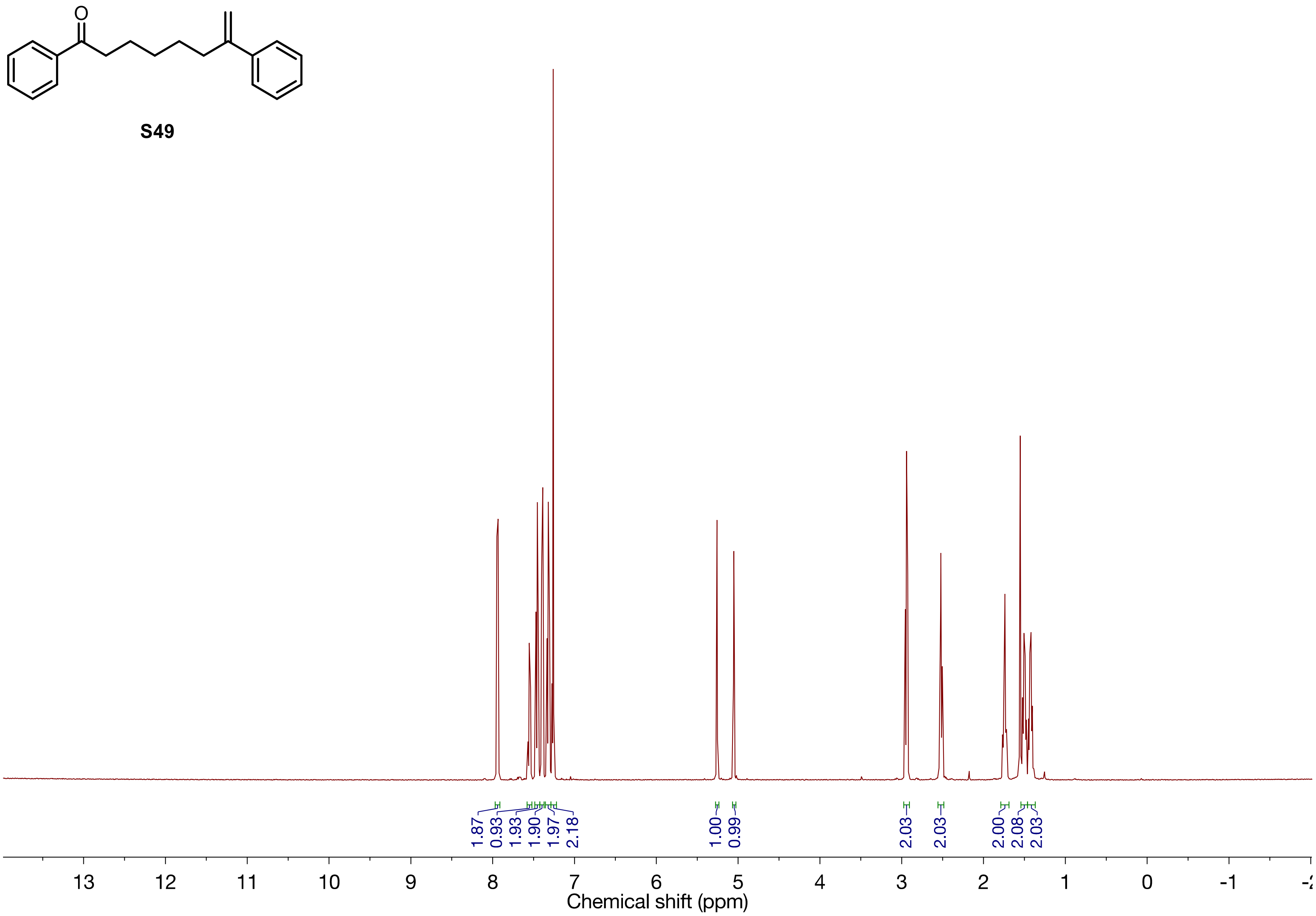

198.98
163.49
130.43
130.29
113.83
84.62
68.42
55.60
38.22
28.65
28.48
24.13
18.45
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)


O
Ph

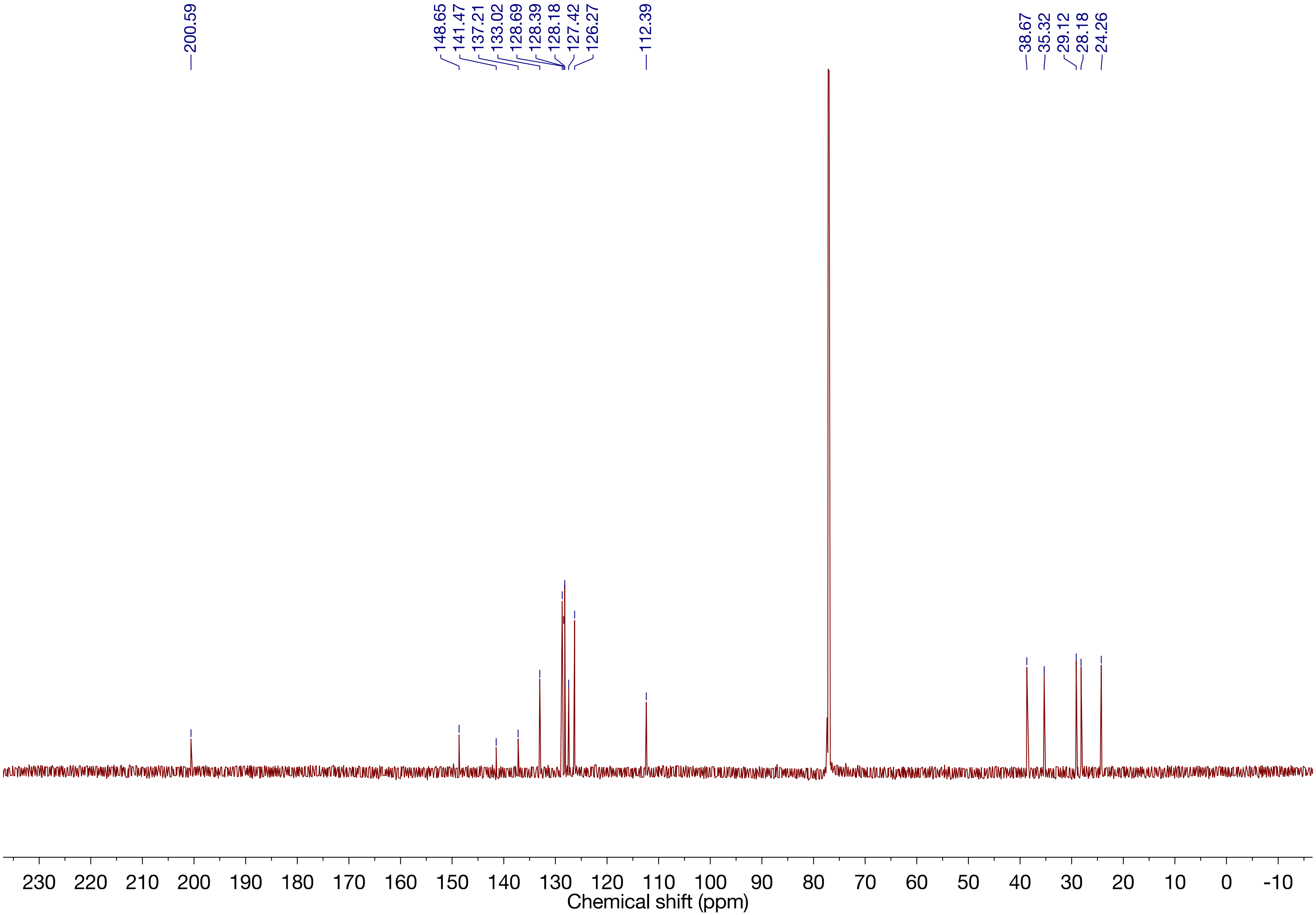
S48

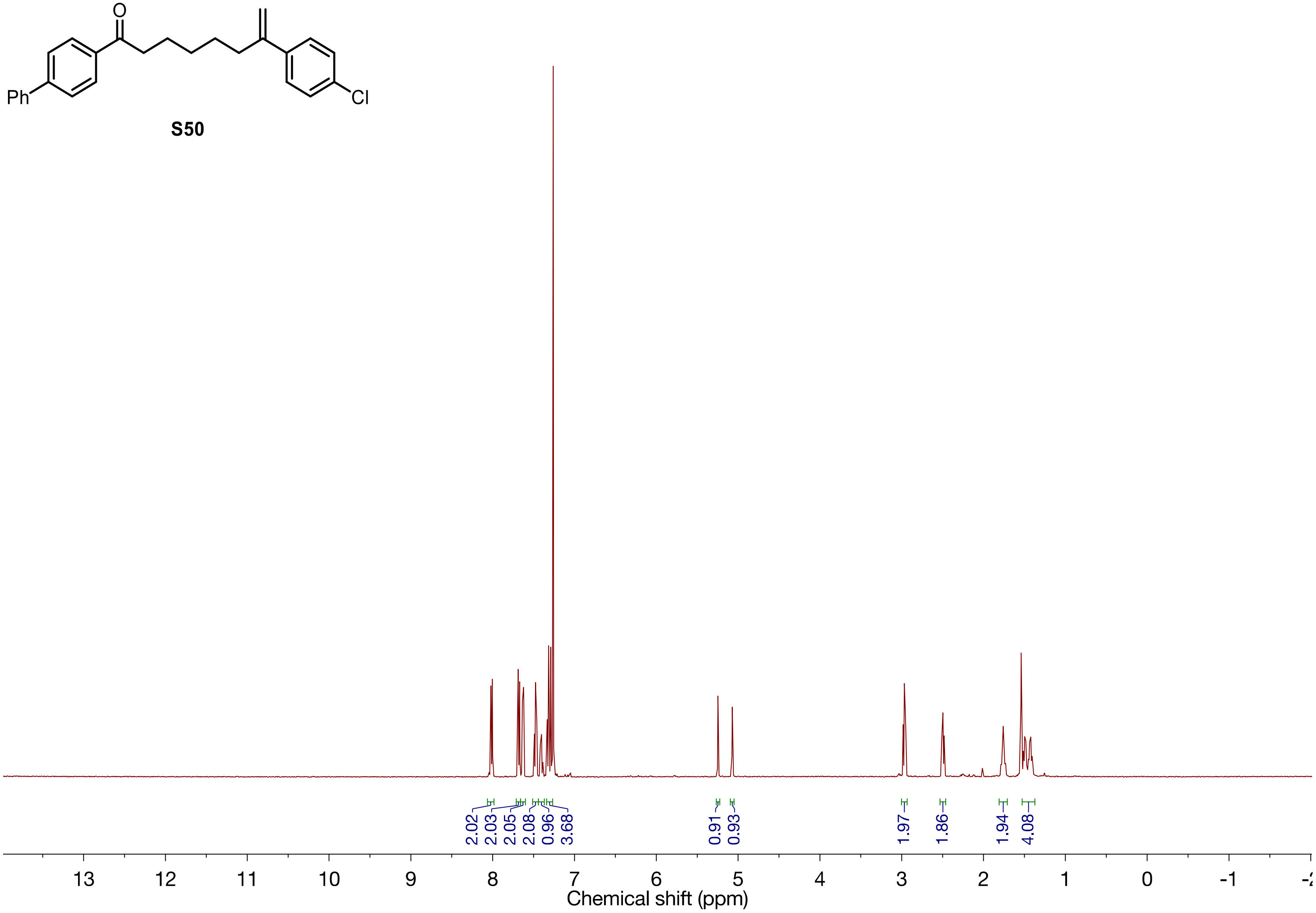

2.00
2.04
2.06
2.07
2.78
1.90
4.93
0.95
0.95
2.04
1.94
2.02
4.19
2.02
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

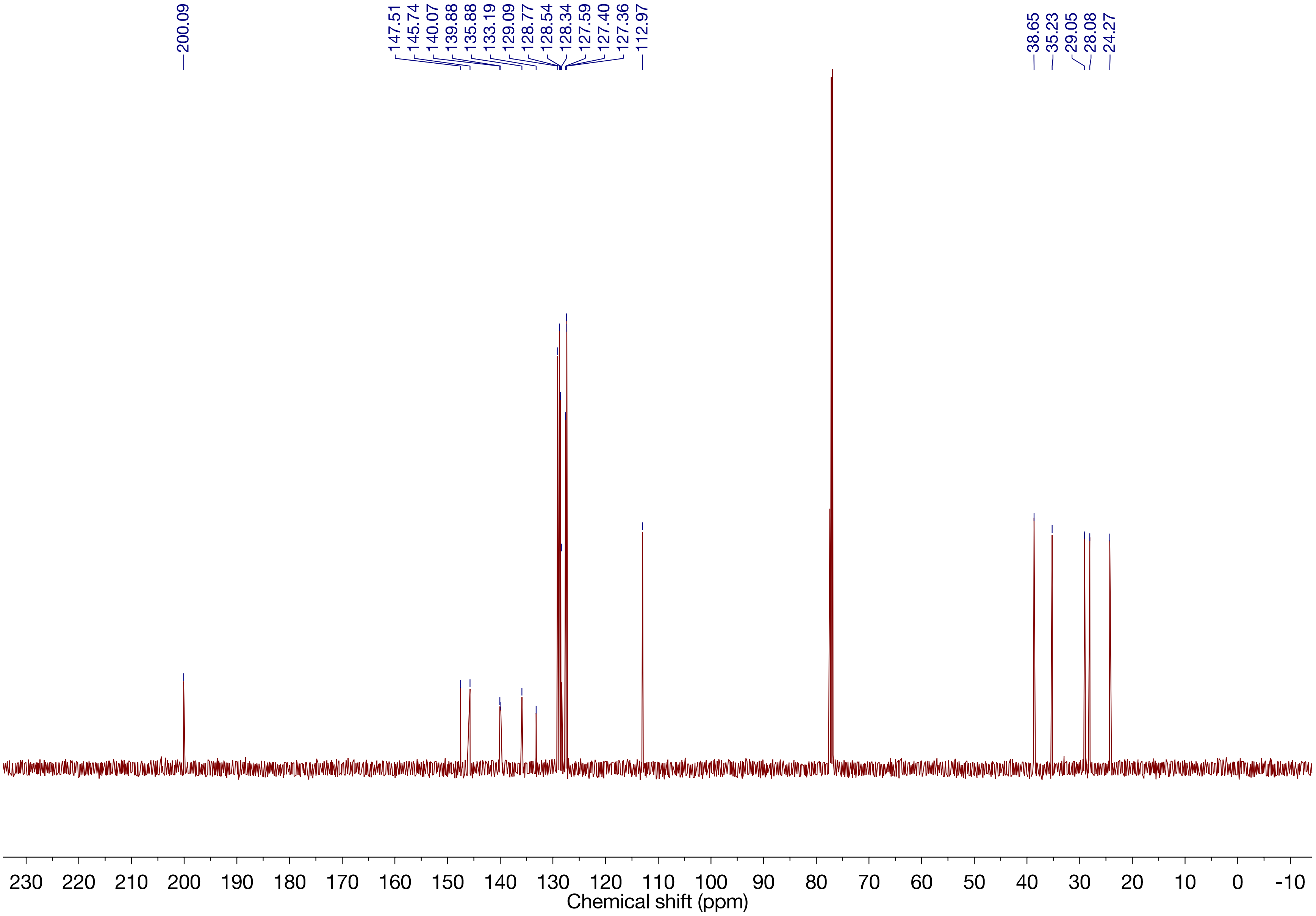

200.16
148.64
145.69
141.46
140.08
135.89
129.08
128.78
128.39
128.31
127.42
127.40
127.34
126.26
112.40
38.71
35.32
29.13
28.19
24.33
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

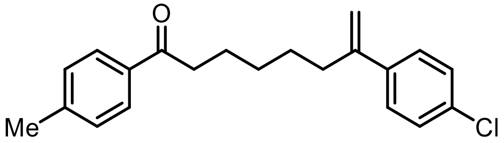

O
1.87
0.93
1.93
1.90
1.97
2.18
1.00
0.99
2.03
2.03
2.00
2.08
2.03
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
Chemical shift (ppm)

S49

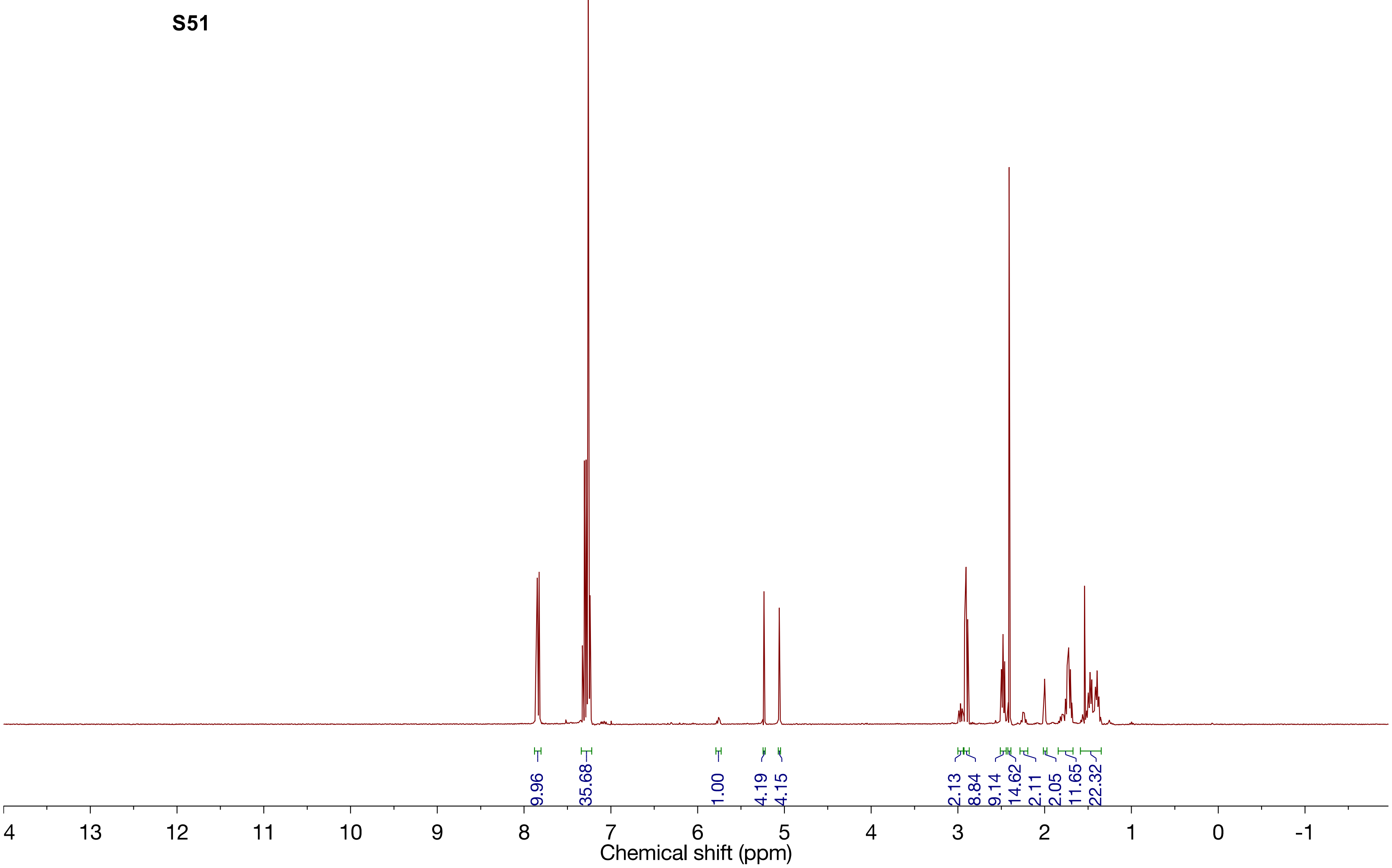

200.59
148.65
141.47
137.21
133.02
128.69
128.39
128.18
127.42
126.27
112.39
38.67
35.32
29.12
28.18
24.26
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)

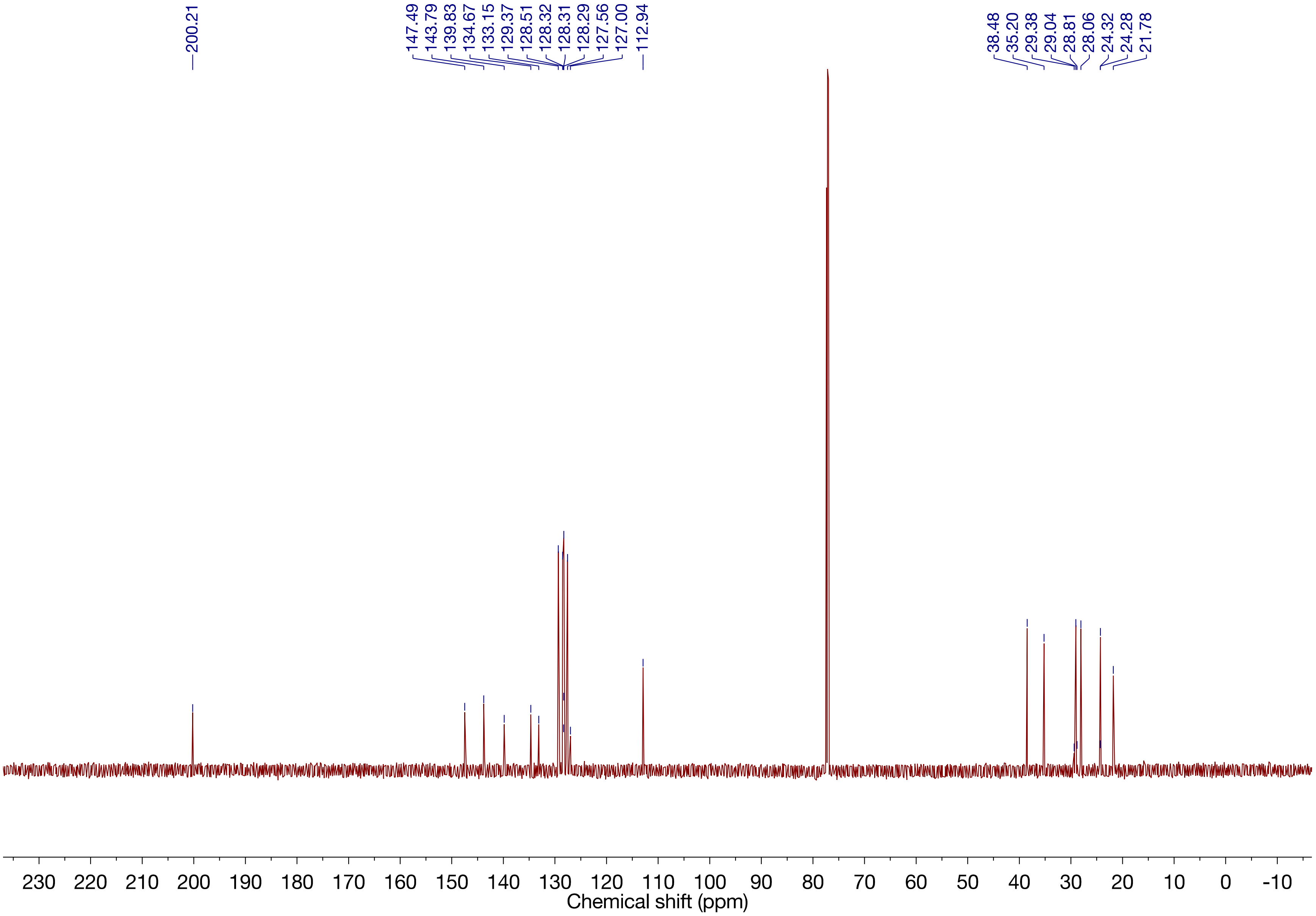

O
Ph
Cl
S50
2.02
2.03
2.05
2.08
0.96
3.68
0.91
0.93
1.97
1.86
1.94
4.08
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
Chemical shift (ppm)

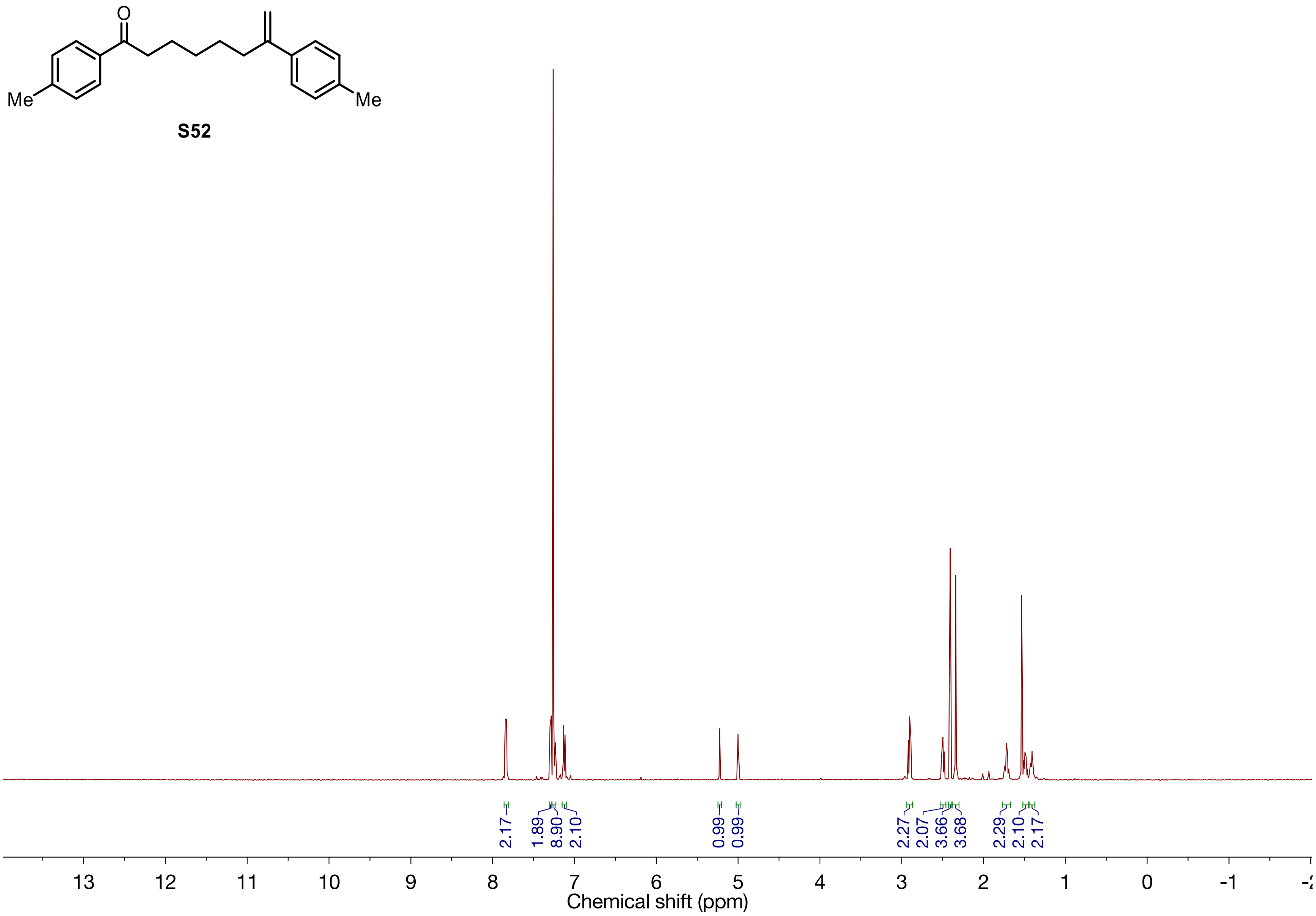

200.09
147.51
145.74
140.07
139.88
135.88
133.19
129.09
128.77
128.54
128.34
127.59
127.40
127.36
112.97
38.65
35.23
29.05
28.08
24.27
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


O
Me
Cl

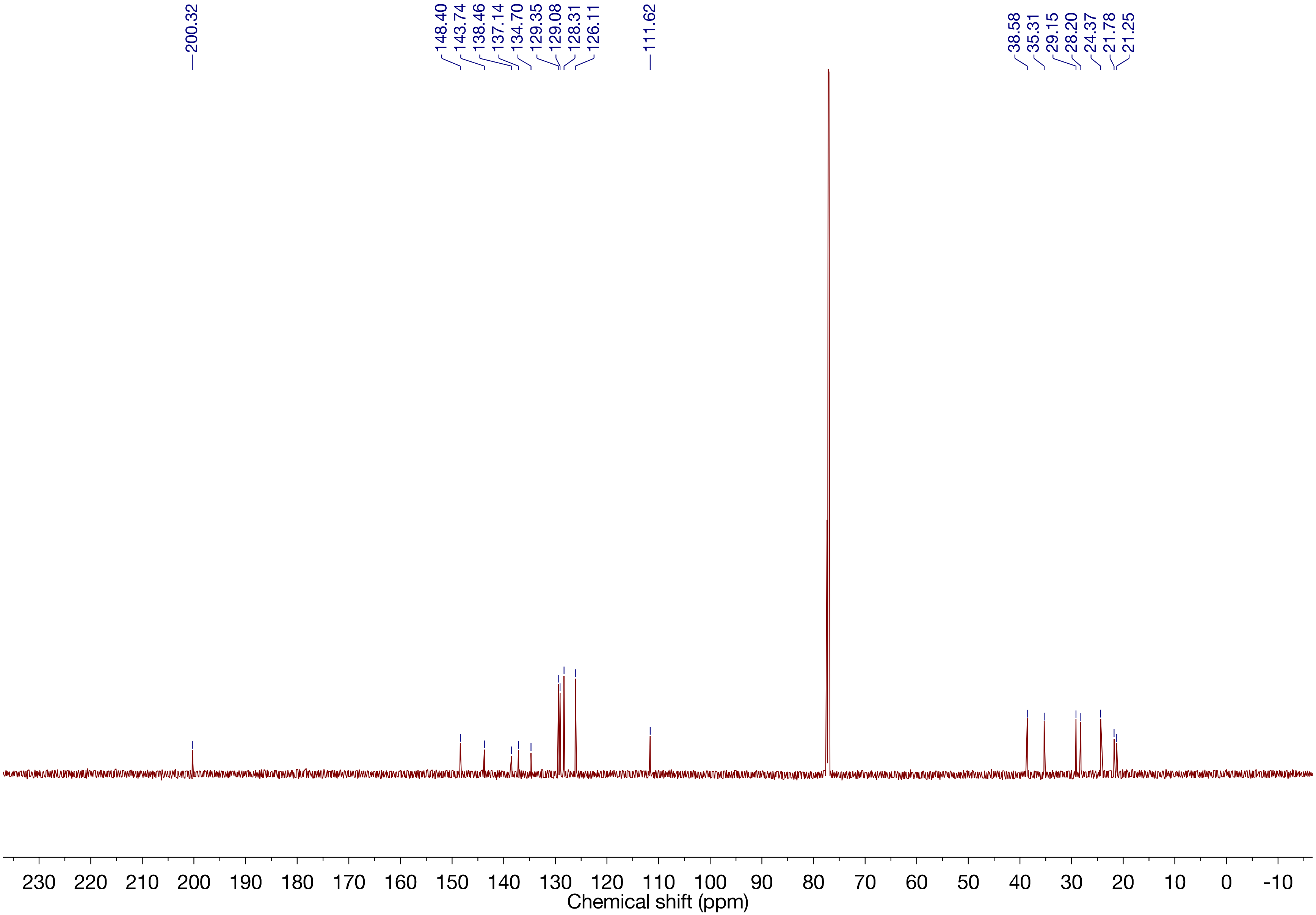
S51

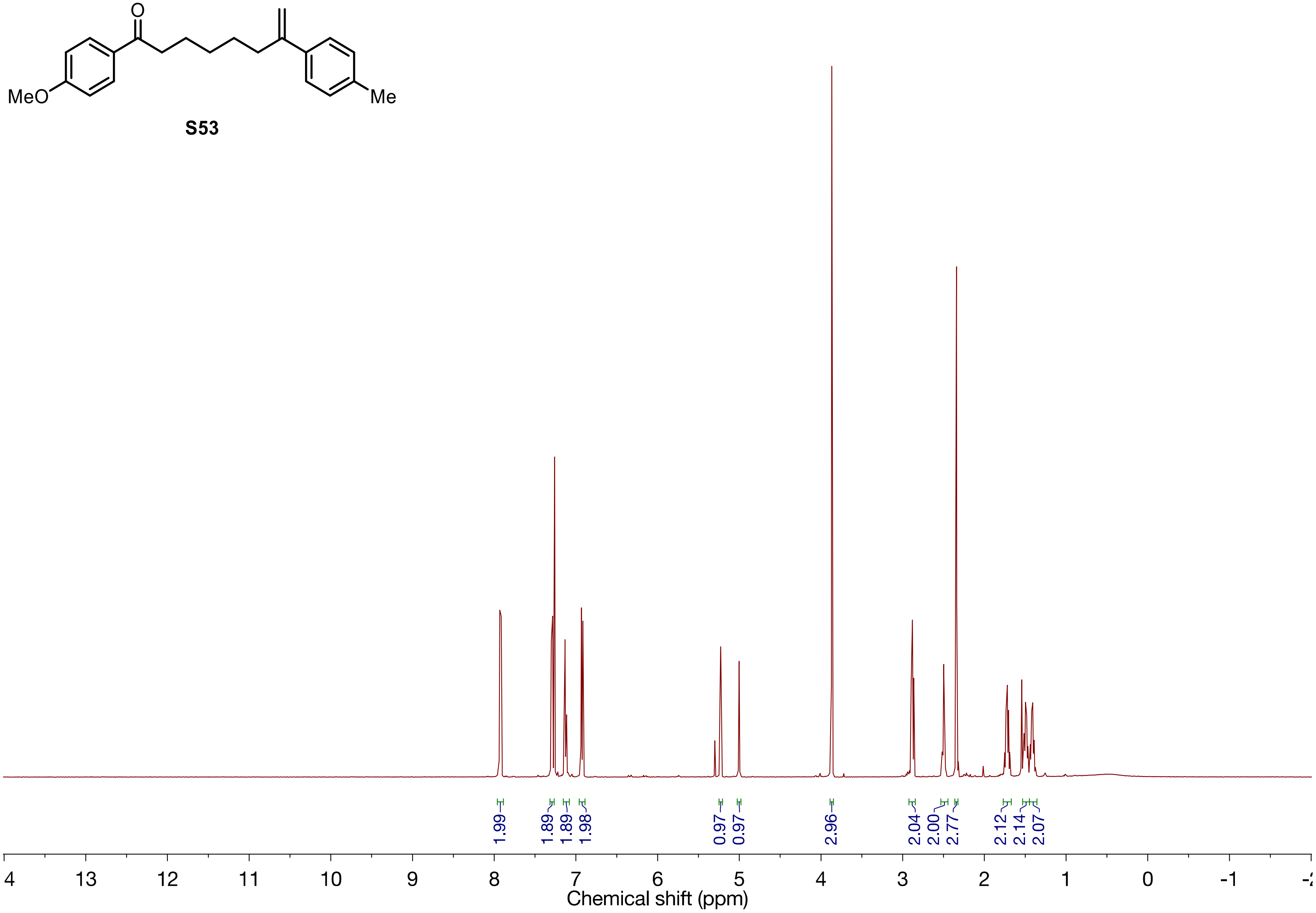

9.96
35.68
1.00
4.19
4.15
2.13
8.84
9.14
14.62
2.11
2.05
11.65
22.32
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


200.21
147.49
143.79
139.83
134.67
133.15
129.37
128.51
128.32
128.31
128.29
127.56
127.00
112.94
38.48
35.20
29.38
29.04
28.81
28.06
24.32
24.28
21.78
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


O
Me
Me
2.17
1.89
8.90
2.10
0.99
0.99
2.27
2.07
3.66
3.68
2.29
2.10
2.17
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

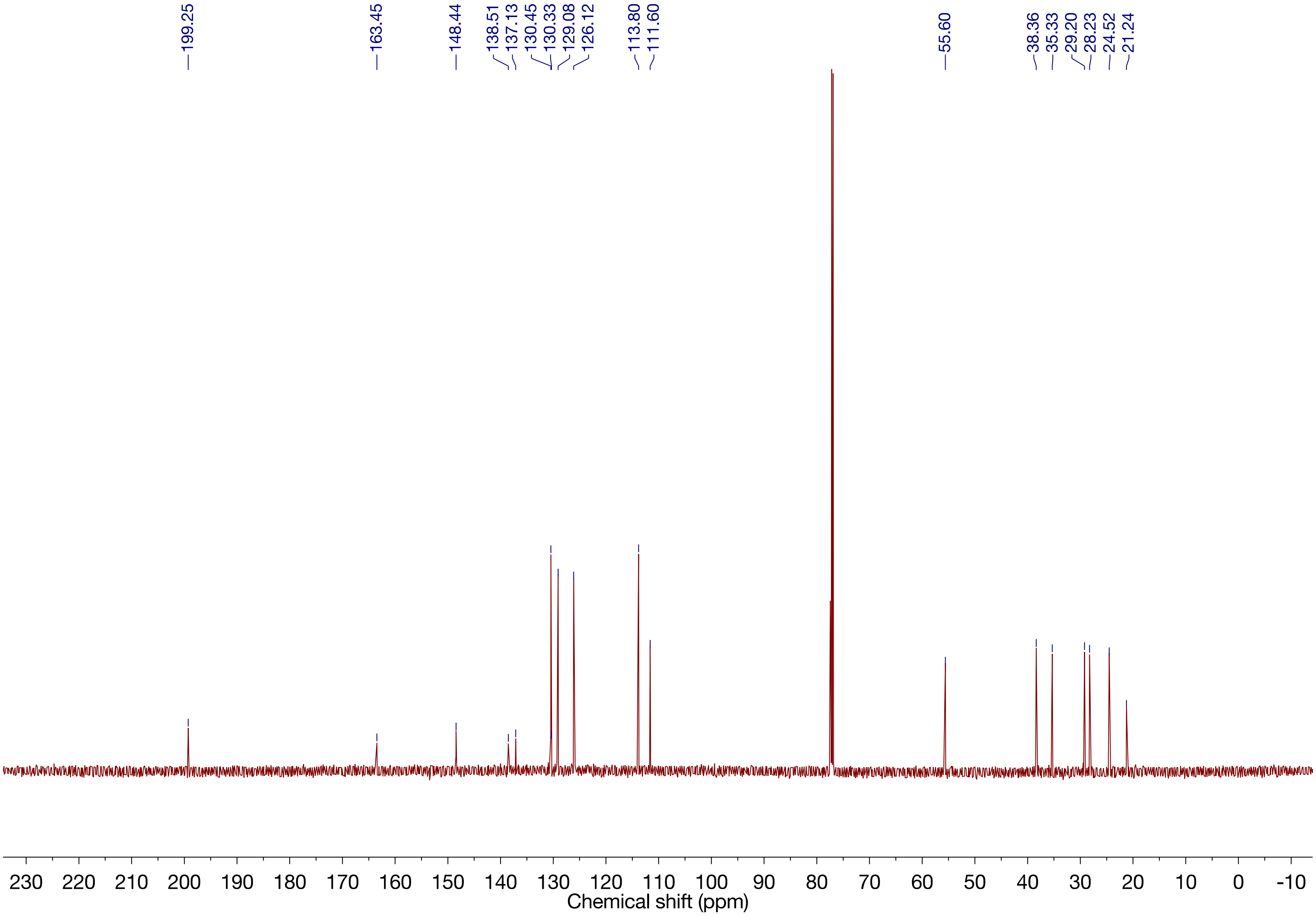
S52


200.32
148.40
143.74
138.46
137.14
134.70
129.35
129.08
128.31
126.11
111.62
38.58
35.31
29.15
28.20
24.37
21.78
21.25
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

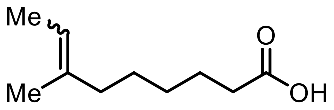


S53

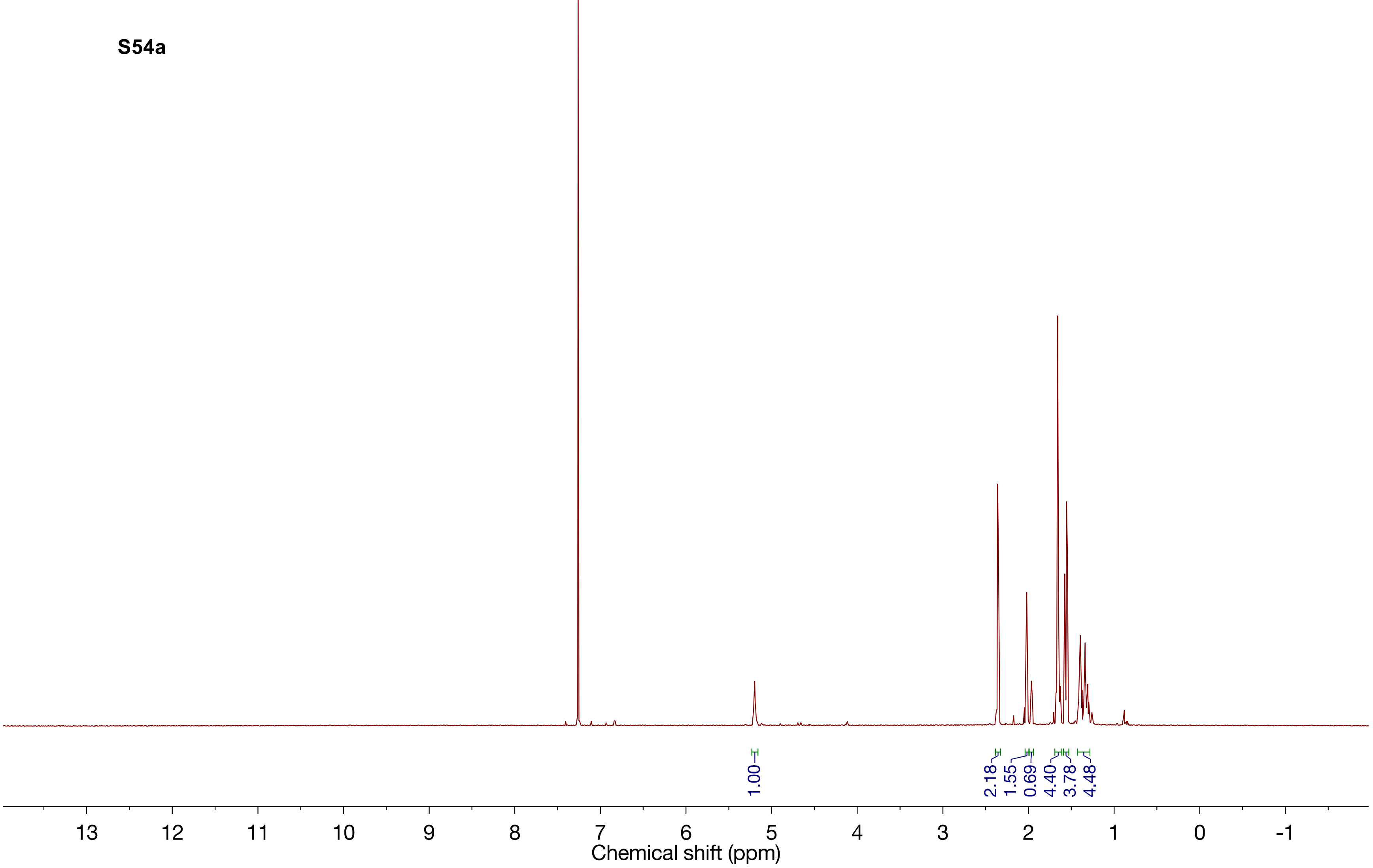
MeO
O
Me
1.99
1.89
1.89
1.98
0.97
0.97
2.96
2.04
2.00
2.77
2.12
2.14
2.07
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

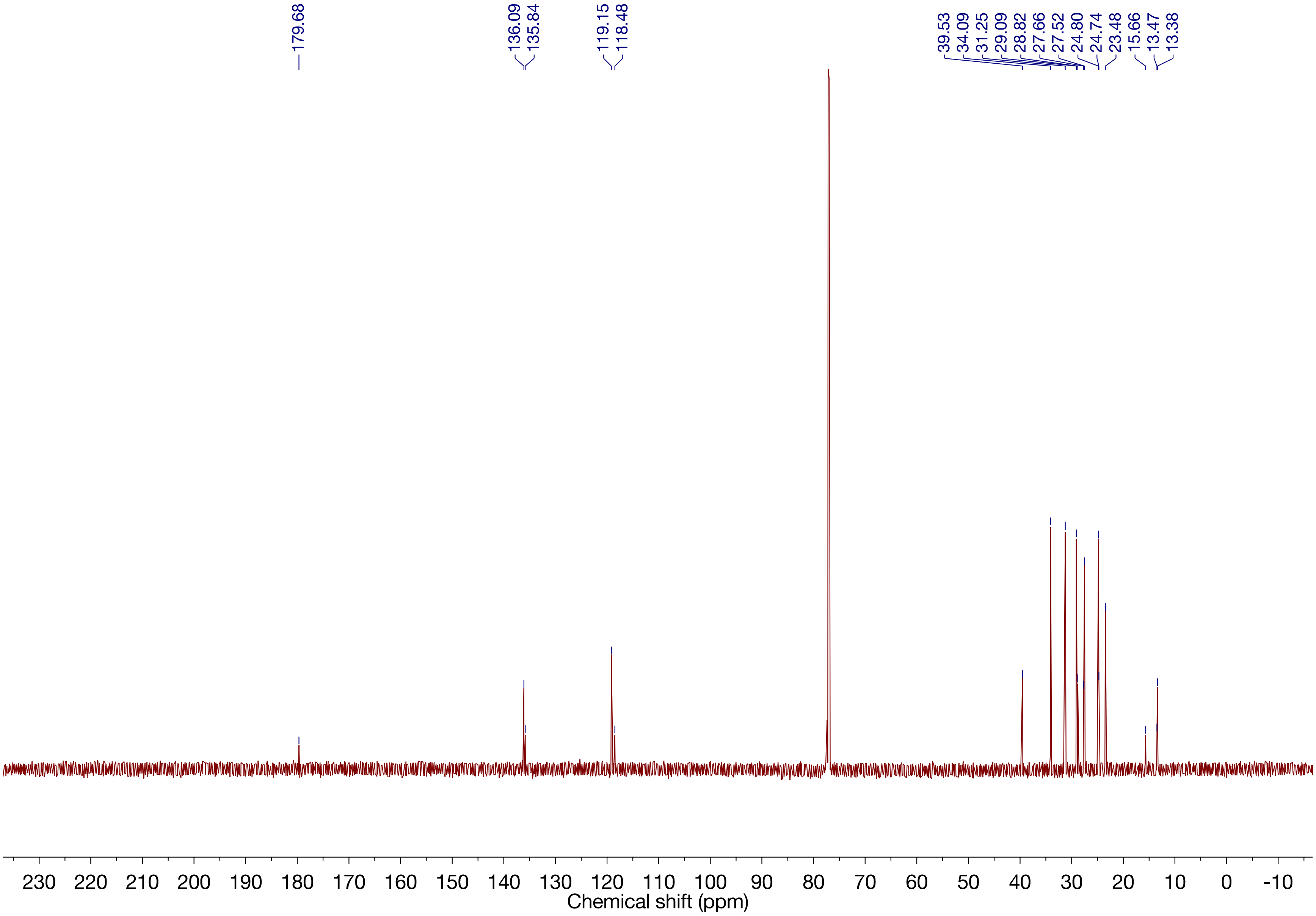


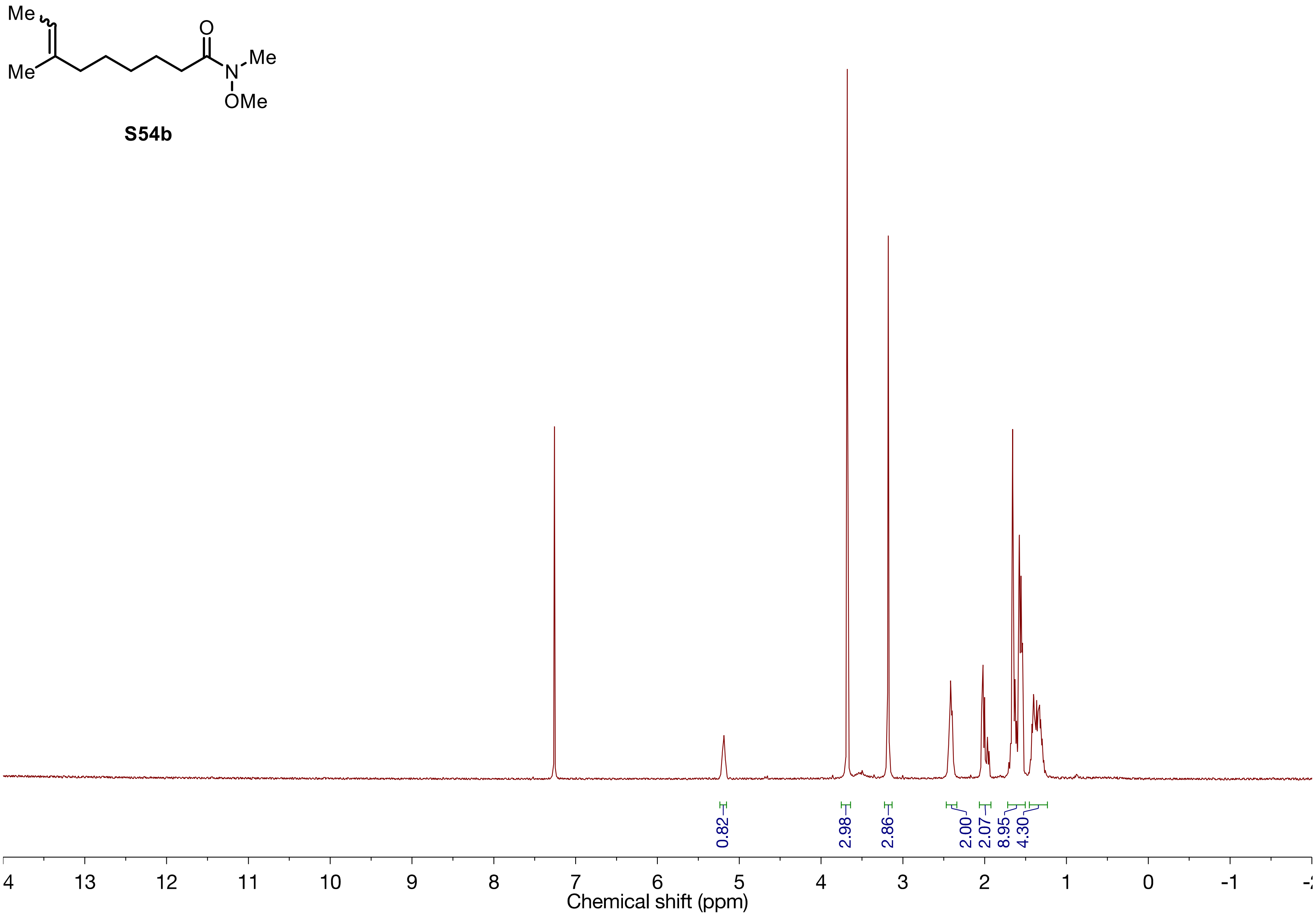
199.25
163.45
148.44
138.51
137.13
130.45
130.33
129.08
126.12
113.80
111.60
55.60
38.36
35.33
29.20
28.23
24.52
21.24
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

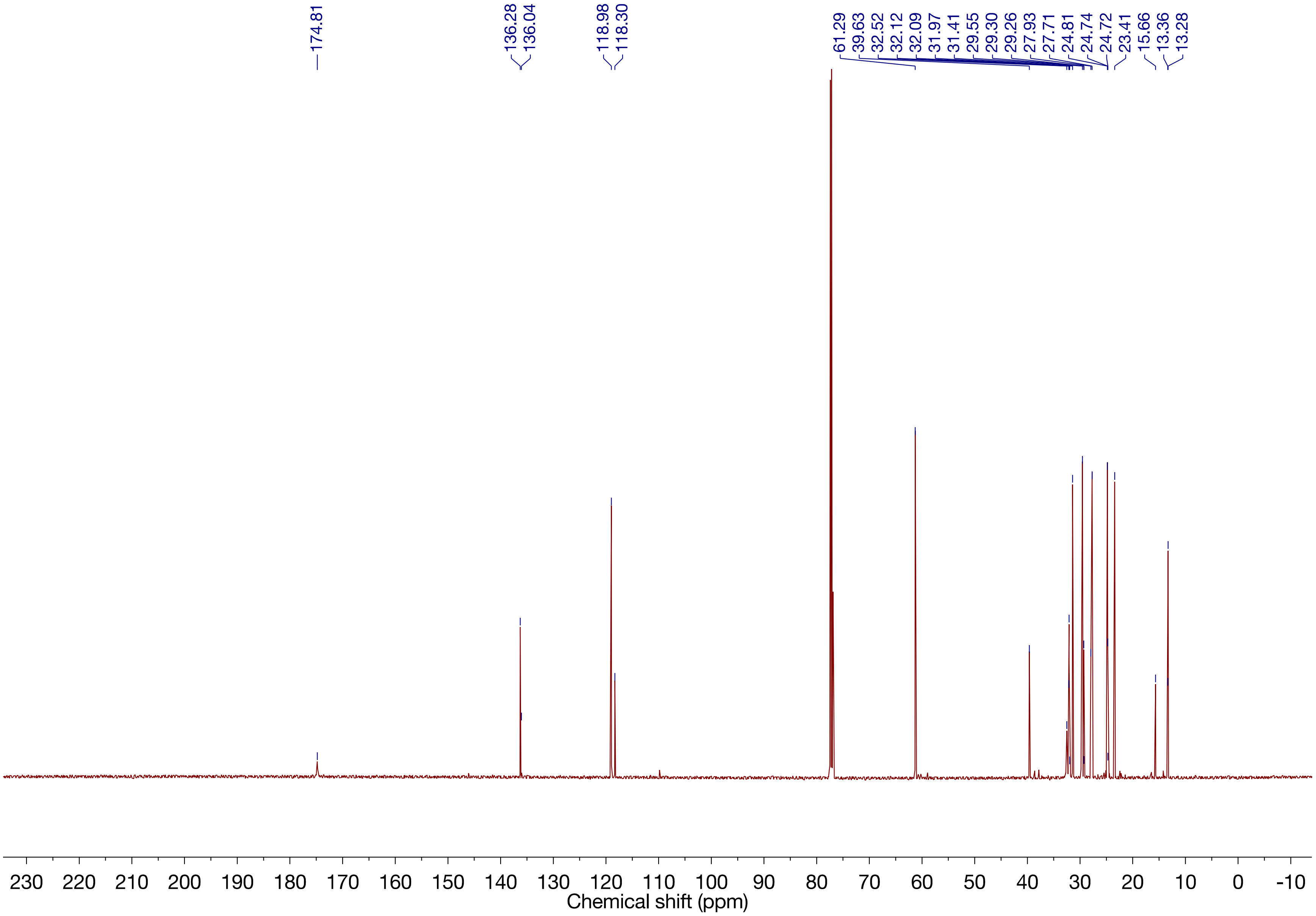

Me
Me
O
OH

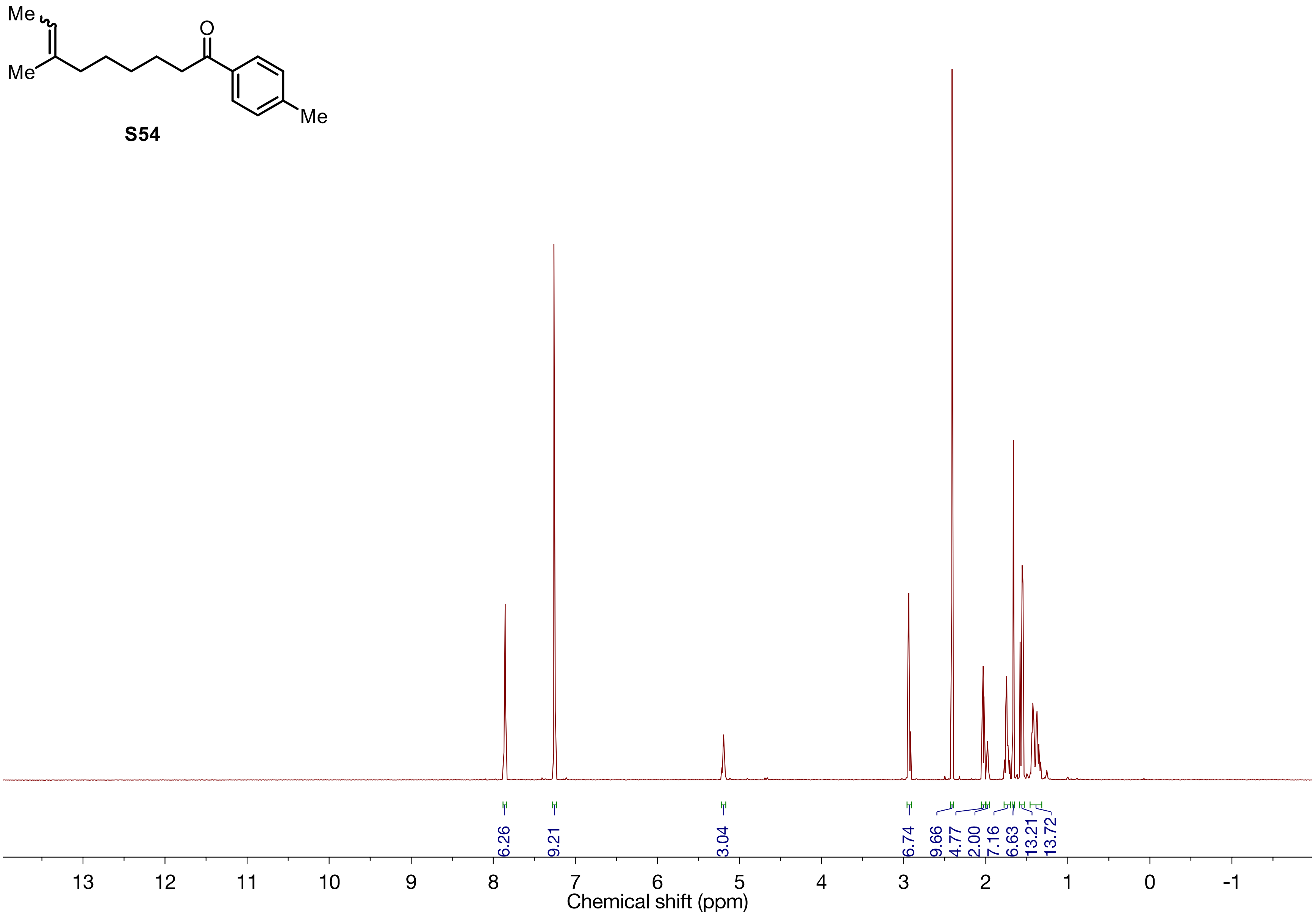
S54a

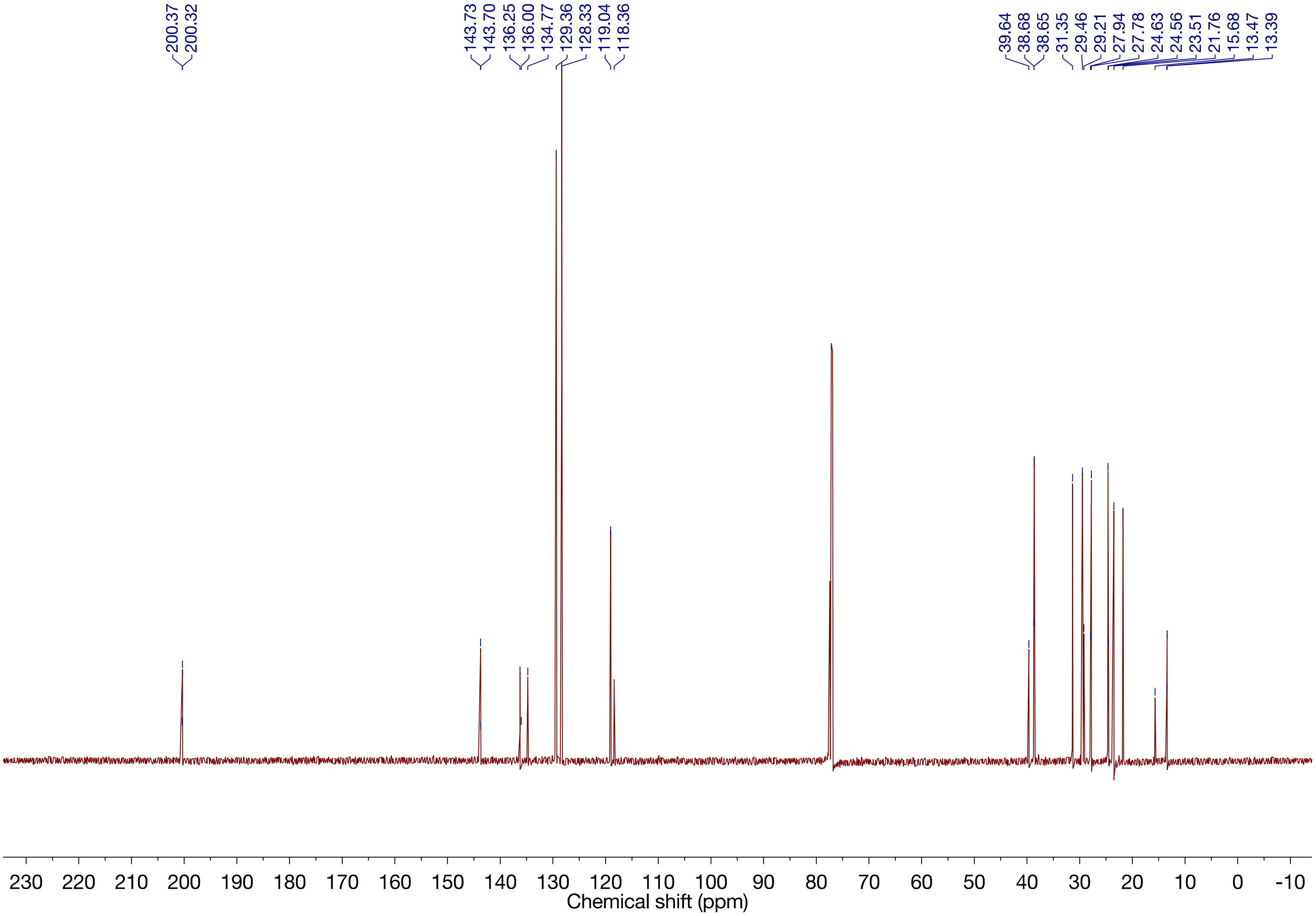

1.00
2.18
1.55
0.69
4.40
3.78
4.48
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

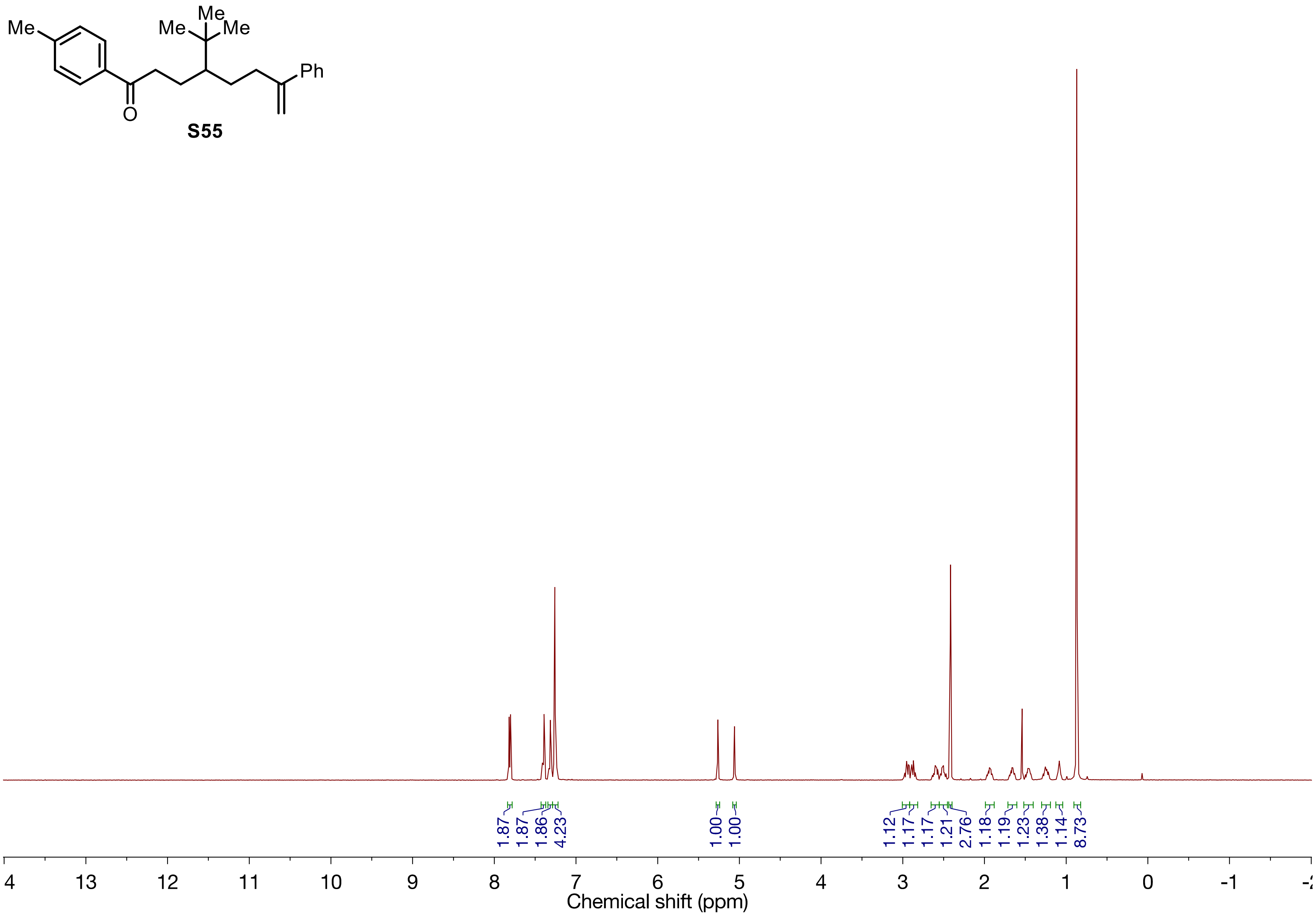

179.68
136.09
135.84
119.15
118.48
39.53
34.09
31.25
29.09
28.82
27.66
27.52
24.80
24.74
23.48
15.66
13.47
13.38
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)


Me
Me
O
N
Me
OMe
S54b
0.82
2.98
2.86
2.00
2.07
8.95
4.30
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

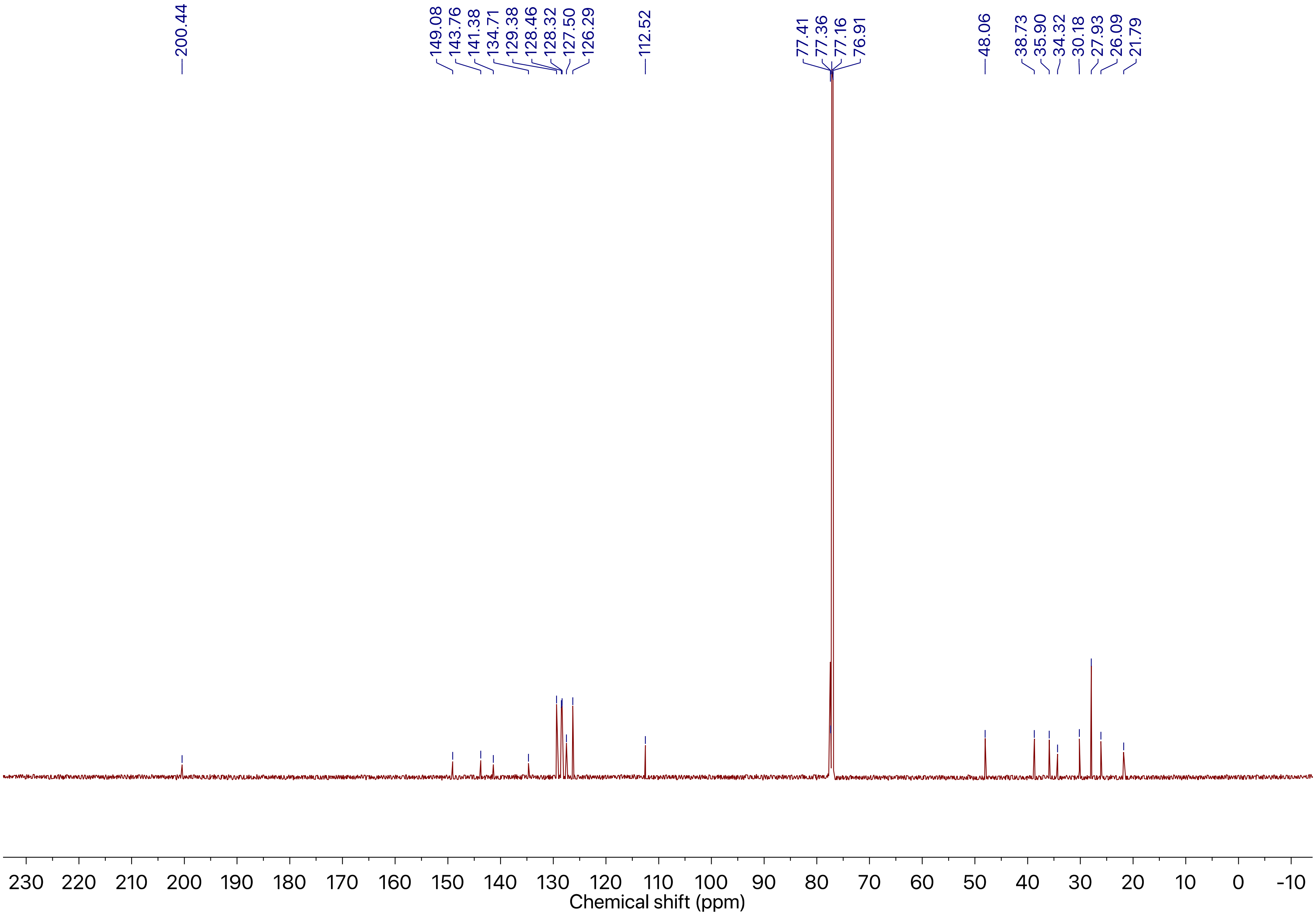

174.81
136.28
136.04
118.98
118.30
61.29
39.63
32.52
32.12
32.09
31.97
31.41
29.55
29.30
29.26
27.93
27.71
24.81
24.74
24.72
23.41
15.66
13.36
13.28
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

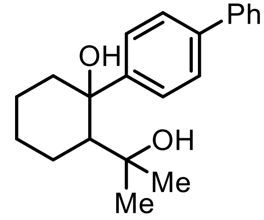

S54
Me
Me
O
Me
6.26
9.21
3.04
6.74
9.66
4.77
2.00
7.16
6.63
13.21
13.72
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


200.37
200.32
143.73
143.70
136.25
136.00
134.77
129.36
128.33
119.04
118.36
39.64
38.68
38.65
31.35
29.46
29.21
27.94
27.78
24.63
24.56
23.51
21.76
15.68
13.47
13.39
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)

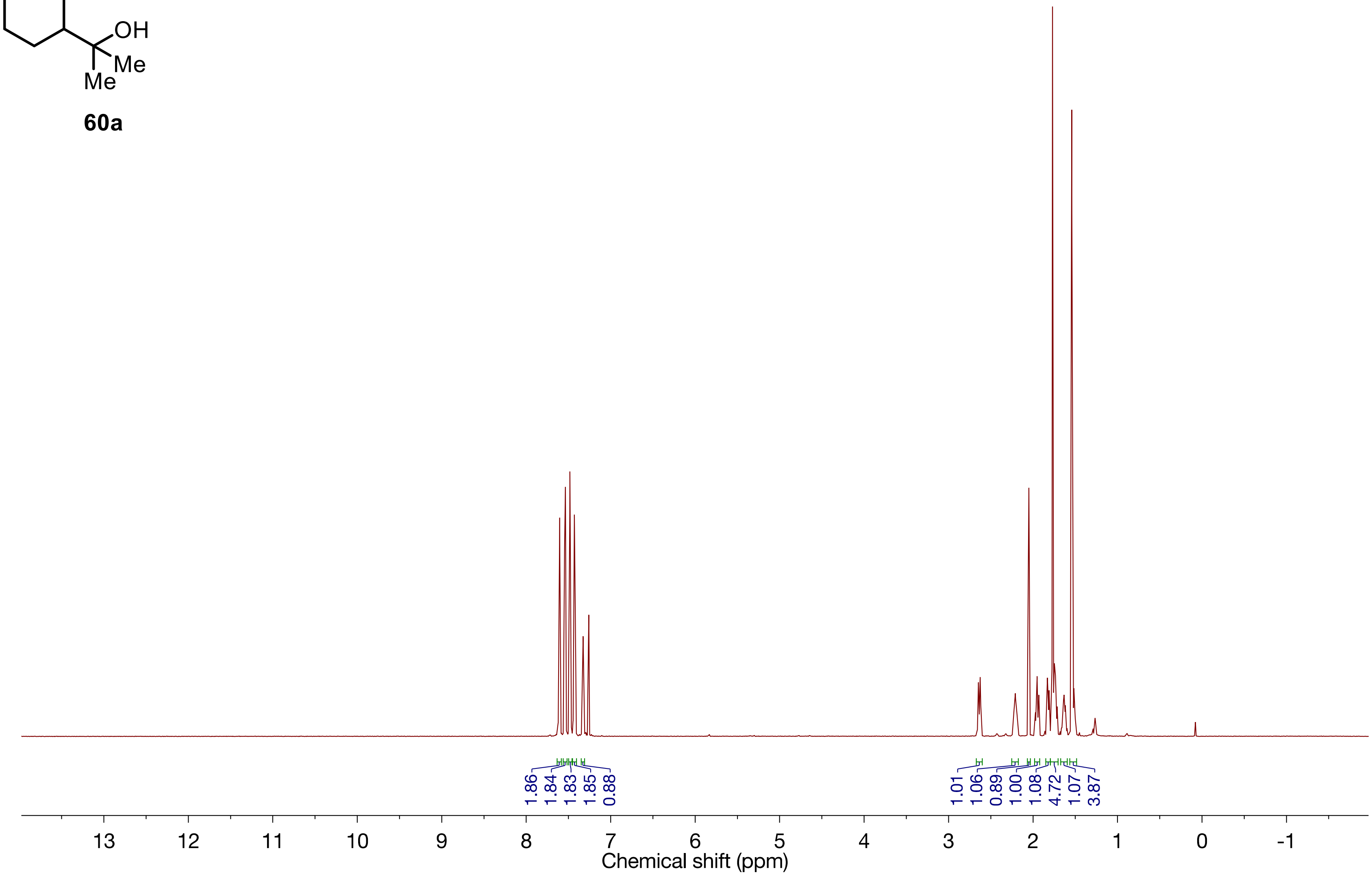

Me
Me
Me
Me
O
Ph
1.87
1.87
1.86
4.23
1.00
1.00
1.12
1.17
1.17
1.21
2.76
1.18
1.19
1.23
1.38
1.14
8.73
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-
Chemical shift (ppm)

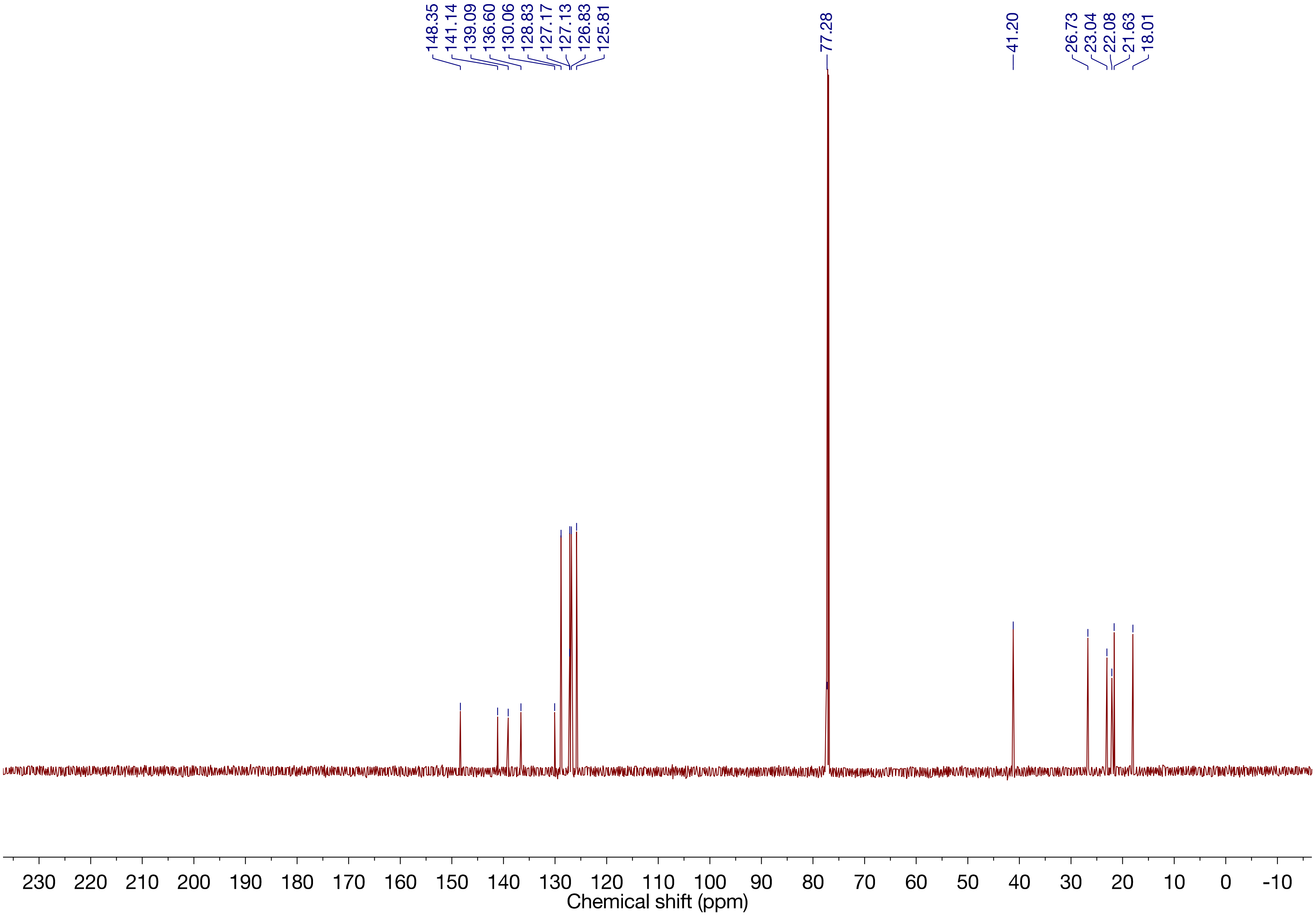
S55

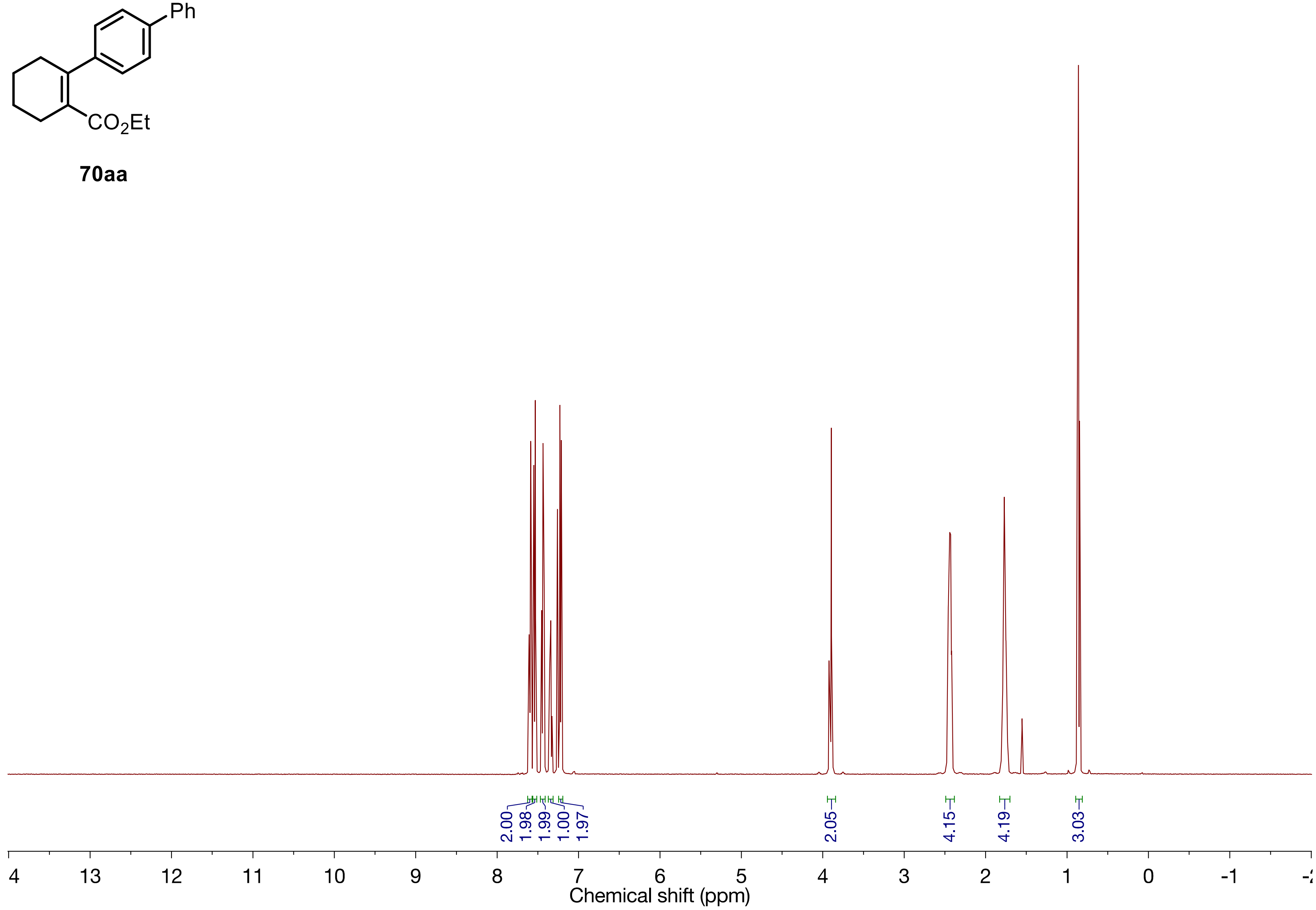

200.44
149.08
143.76
141.38
134.71
129.38
128.46
128.32
127.50
126.29
112.52
77.41
77.36
77.16
76.91
48.06
38.73
35.90
34.32
30.18
27.93
26.09
21.79
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Ph
OH
OH
Me
Me

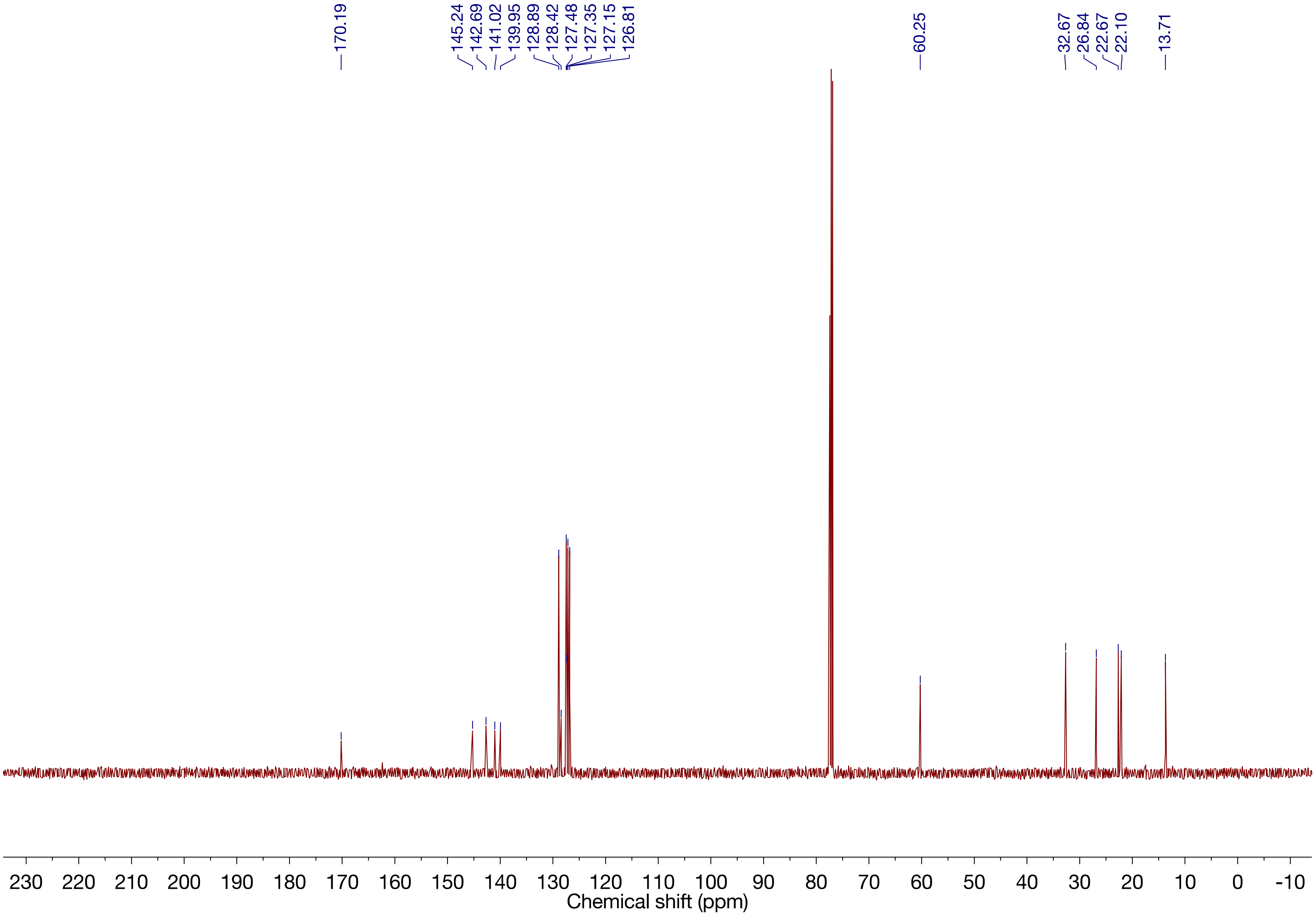
60a

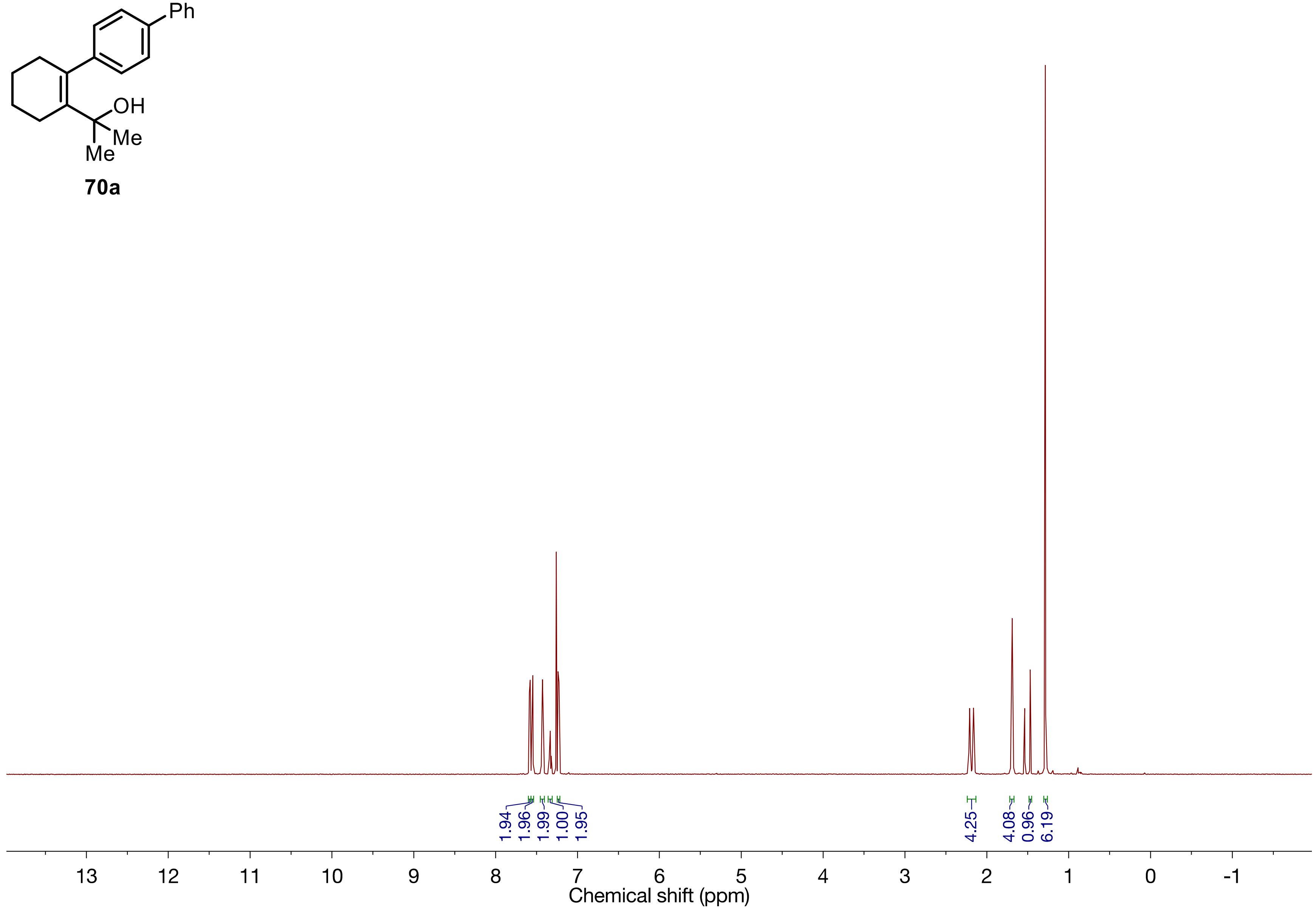

1.86
1.84
1.83
1.85
0.88
1.01
1.06
0.89
1.00
1.08
4.72
1.07
3.87
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


148.35
141.14
139.09
136.60
130.06
128.83
127.17
127.13
126.83
125.81
77.28
41.20
26.73
23.04
22.08
21.63
18.01
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

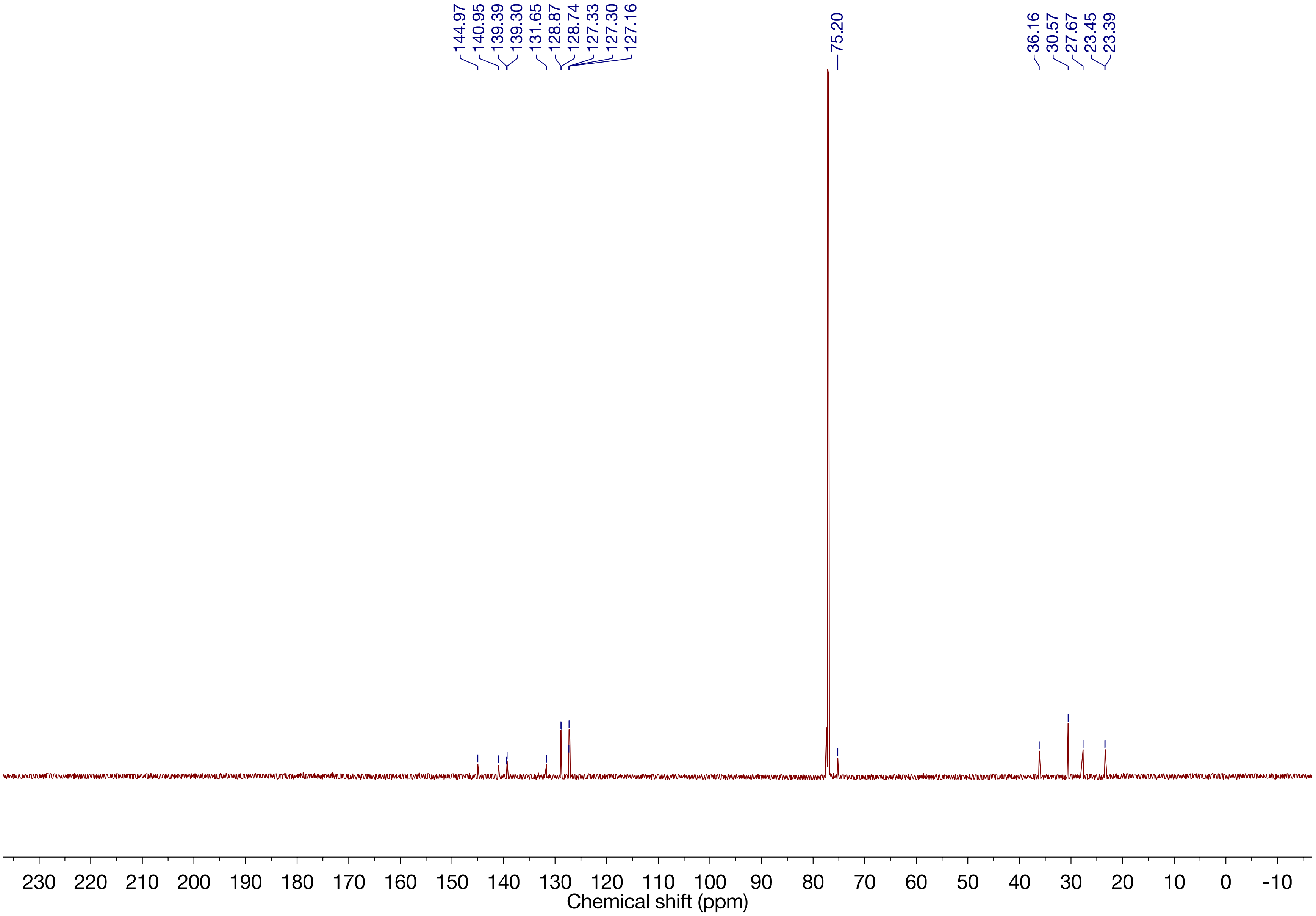

Ph
CO2Et
2.00
1.98
1.99
1.00
1.97
2.05
4.15
4.19
3.03
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-
Chemical shift (ppm)

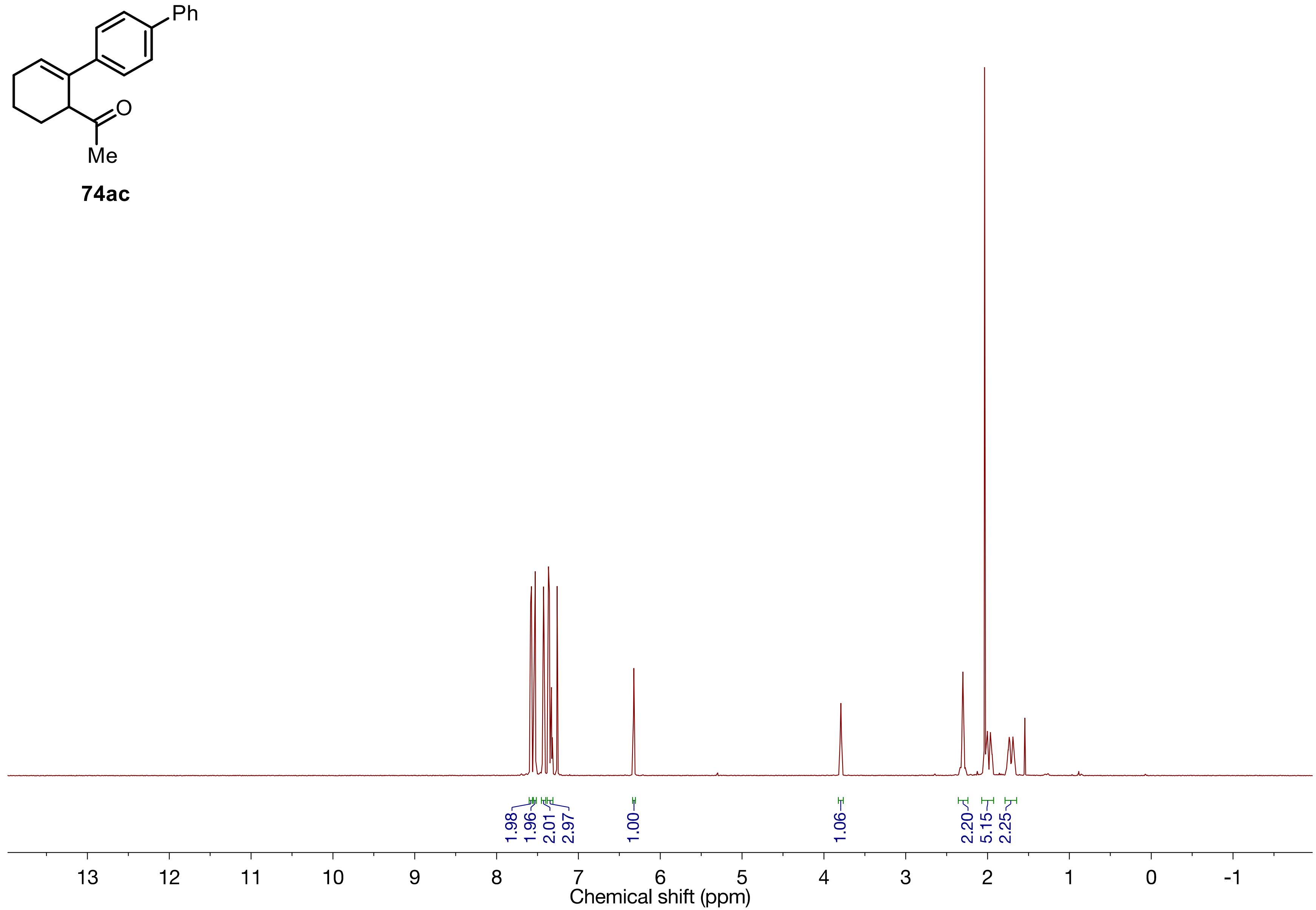
70aa


170.19
145.24
142.69
141.02
139.95
128.89
128.42
127.48
127.35
127.15
126.81
60.25
32.67
26.84
22.67
22.10
13.71
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Ph
OH
Me
Me
1.94
1.96
1.99
1.00
1.95
4.25
4.08
0.96
6.19
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

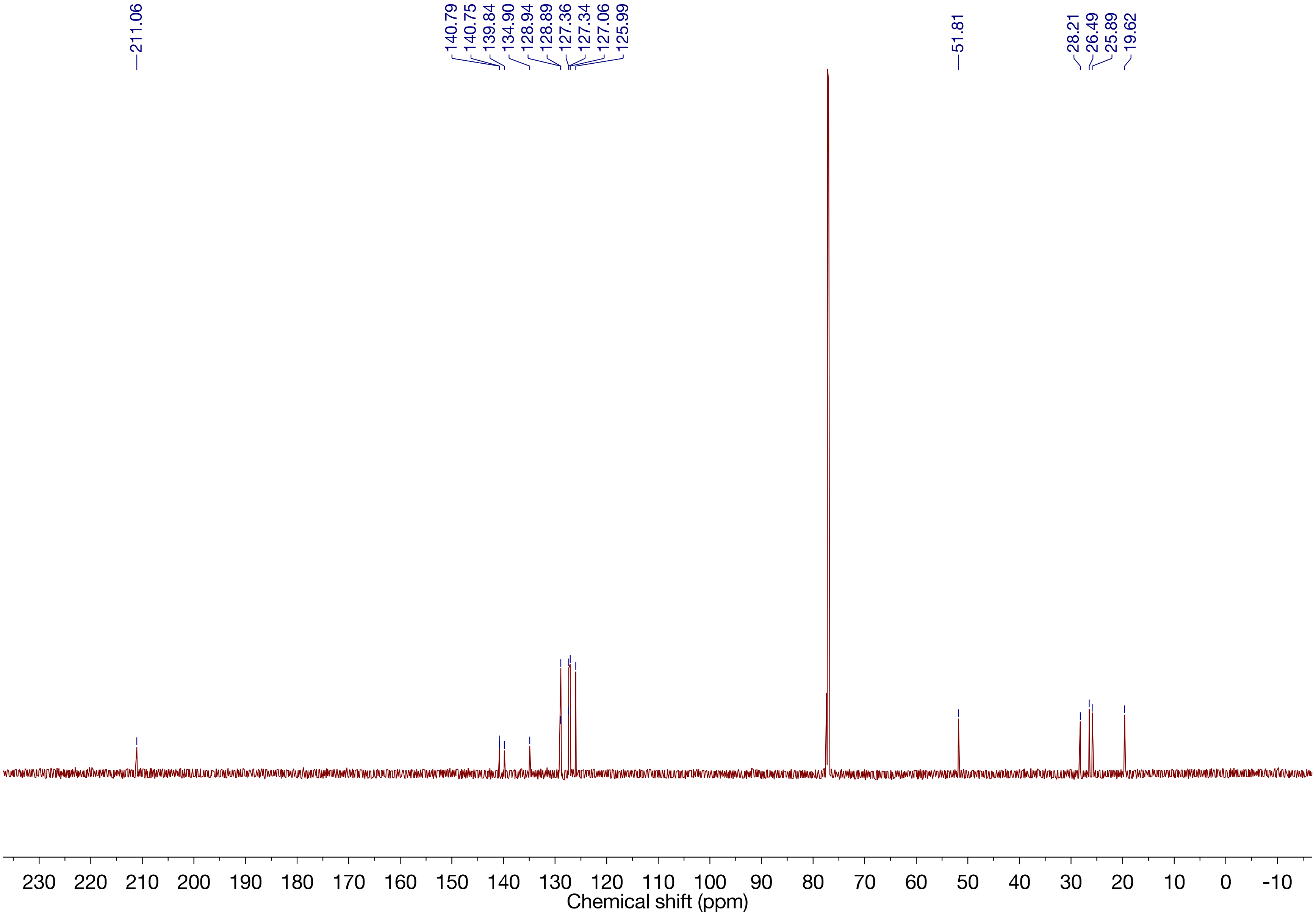
70a

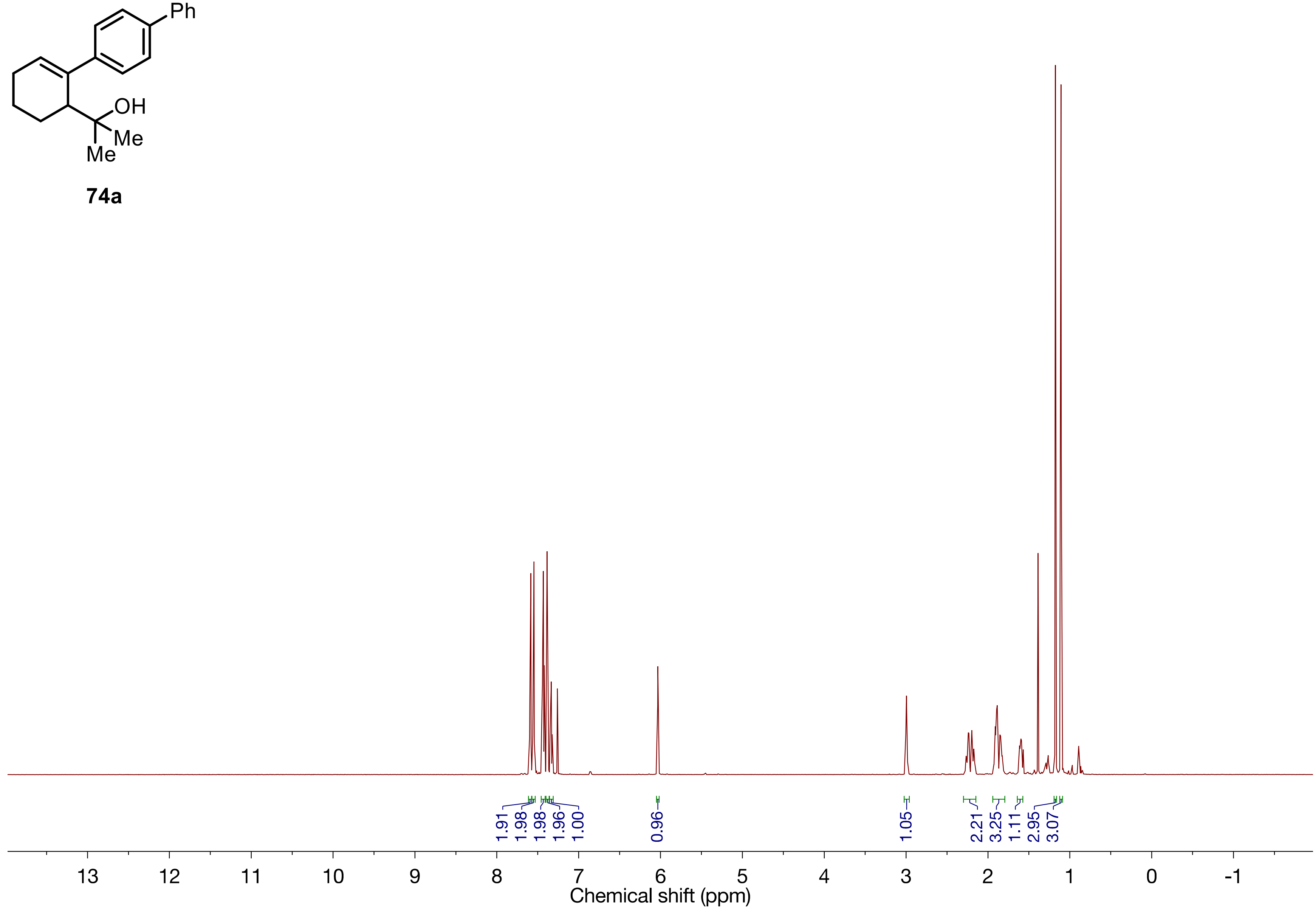

144.97
140.95
139.39
139.30
131.65
128.87
128.74
127.33
127.30
127.16
75.20
36.16
30.57
27.67
23.45
23.39
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Ph
O
Me

74ac

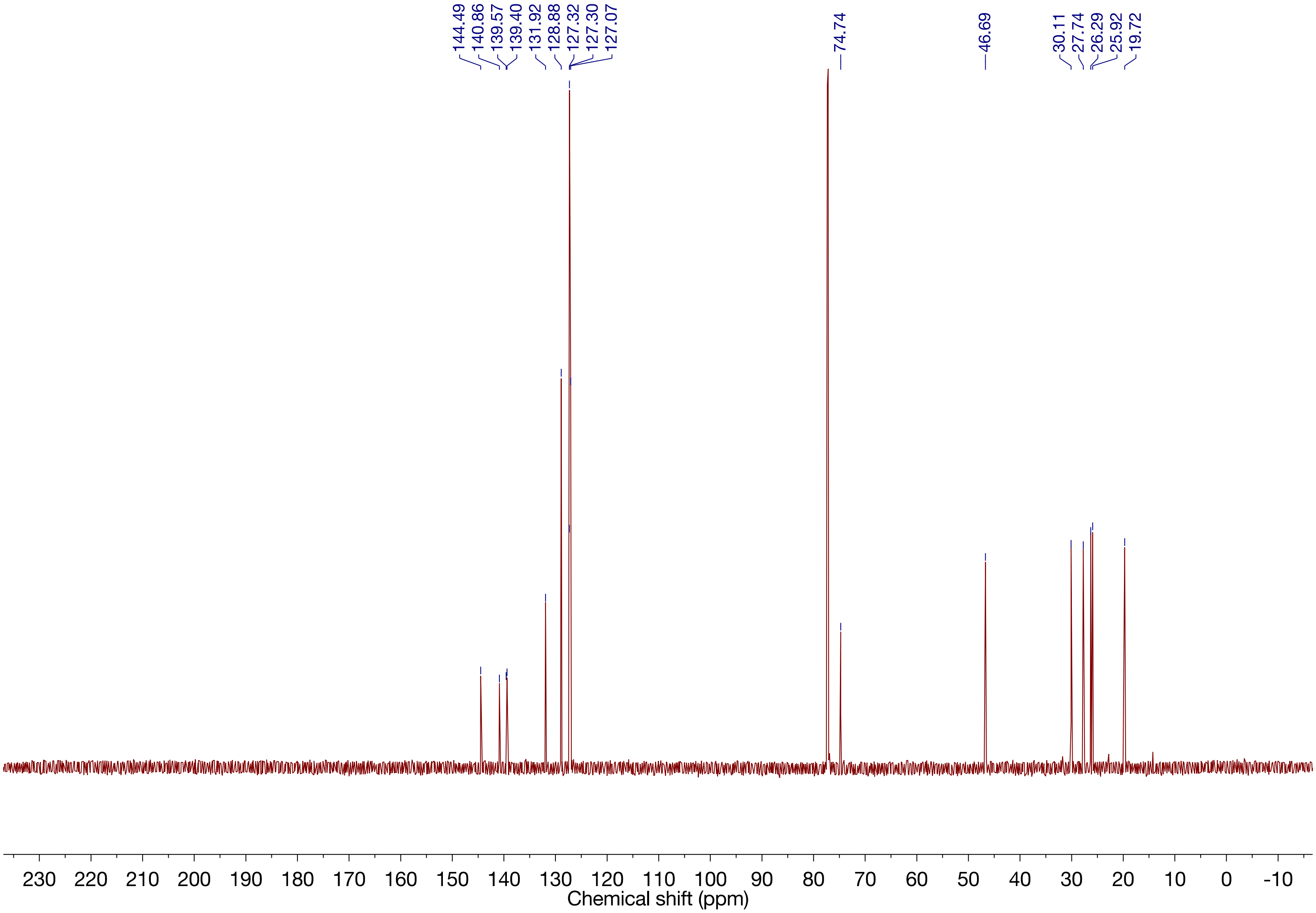
1.98
1.96
2.01
2.97
1.00
1.06
2.20
5.15
2.25
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

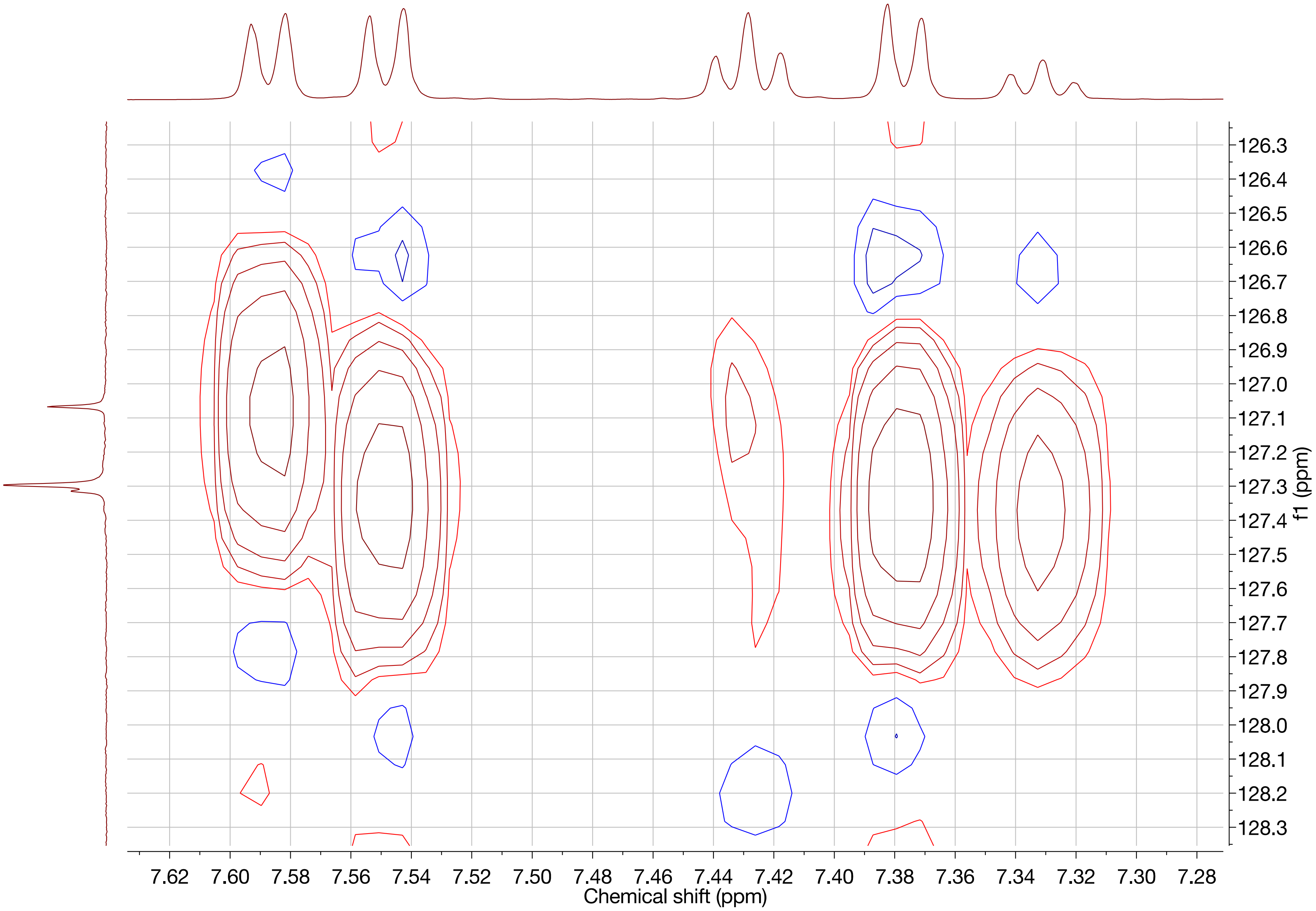

211.06
140.79
140.75
139.84
134.90
128.94
128.89
127.36
127.34
127.06
125.99
51.81
28.21
26.49
25.89
19.62
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

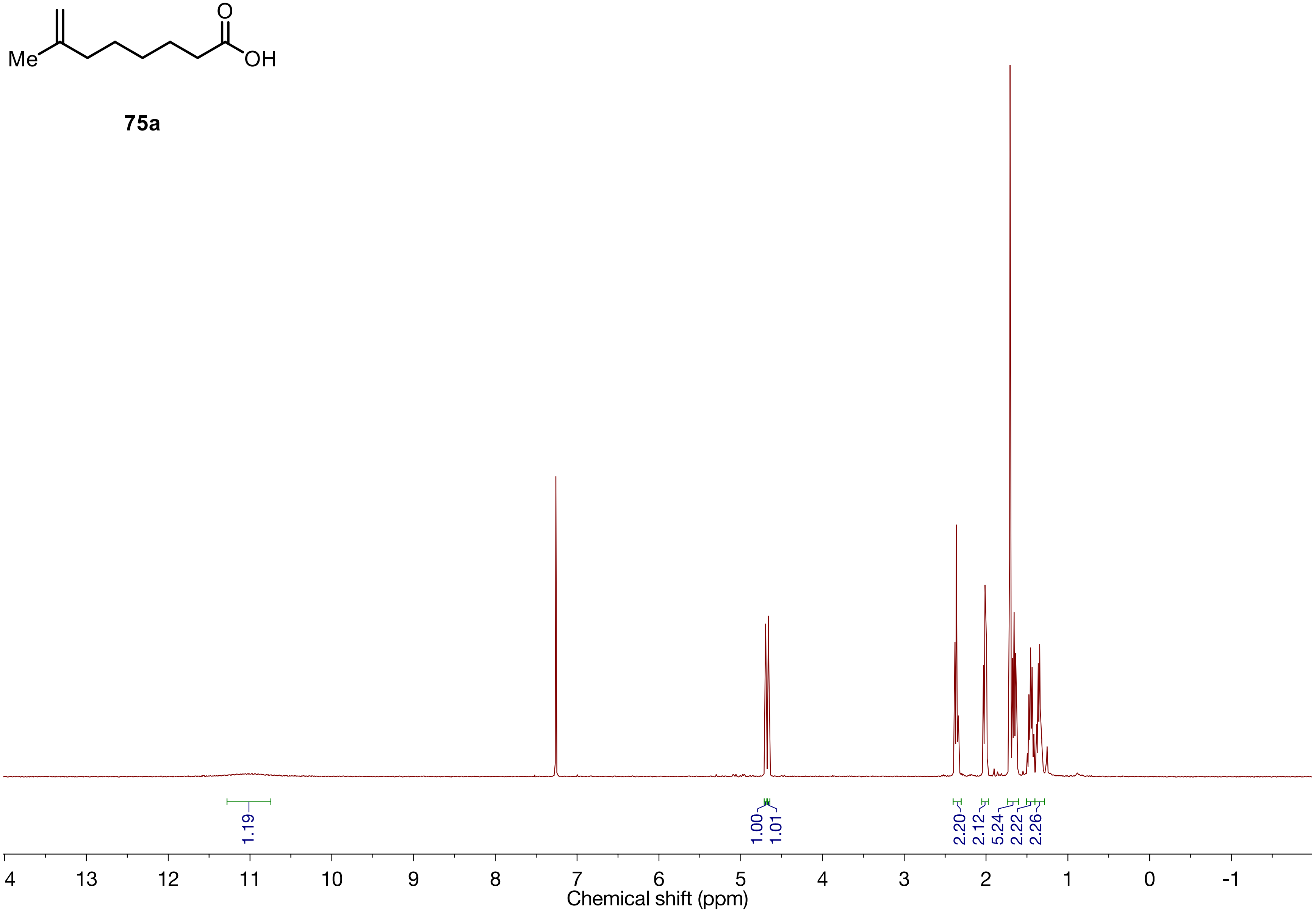

Ph
OH
Me
Me

74a

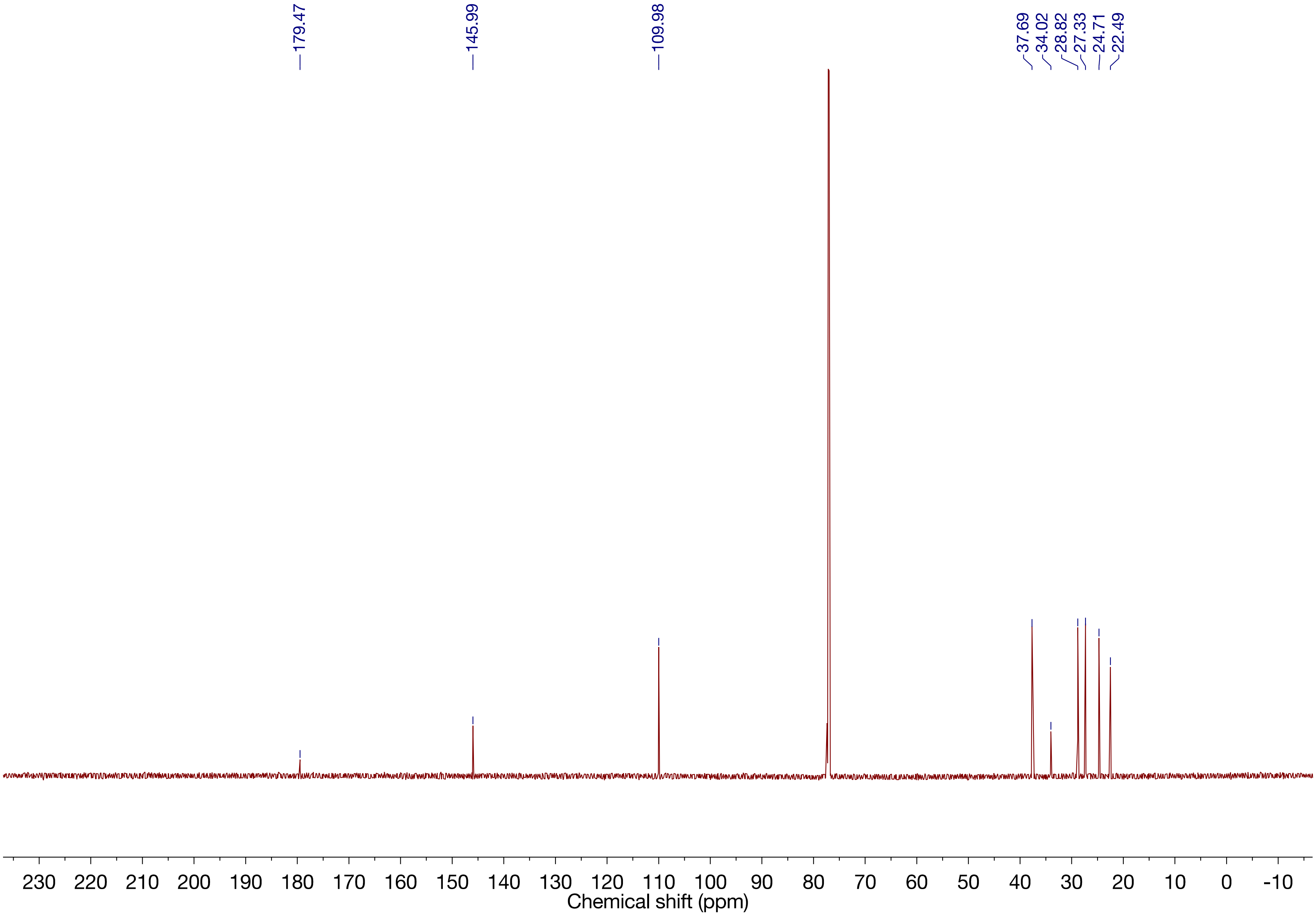
1.91
1.98
1.98
1.96
1.00
0.96
1.05
2.21
3.25
1.11
2.95
3.07
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

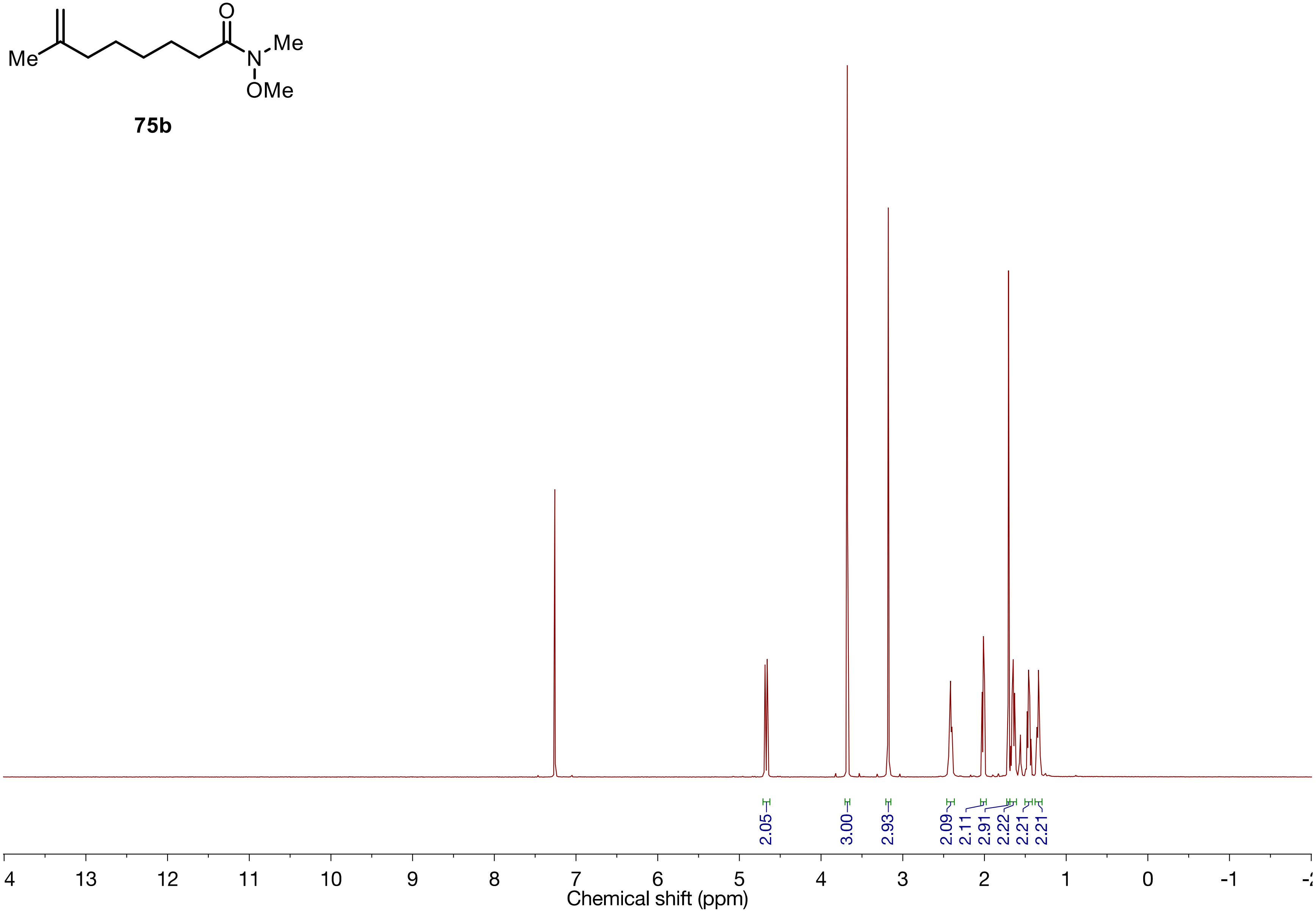

144.49
140.86
139.57
139.40
131.92
128.88
127.32
127.30
127.07
74.74
46.69
30.11
27.74
26.29
25.92
19.72
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


7.62
7.60
7.58
7.56
7.54
7.52
7.50
7.48
7.46
7.44
7.42
7.40
7.38
7.36
7.34
7.32
7.30
7.28
Chemical shift (ppm)
126.3
126.4
126.5
126.6
126.7
126.8
126.9
127.0
127.1
127.2
127.3
127.4
127.5
127.6
127.7
127.8
127.9
128.0
128.1
128.2
128.3
f1 (ppm)

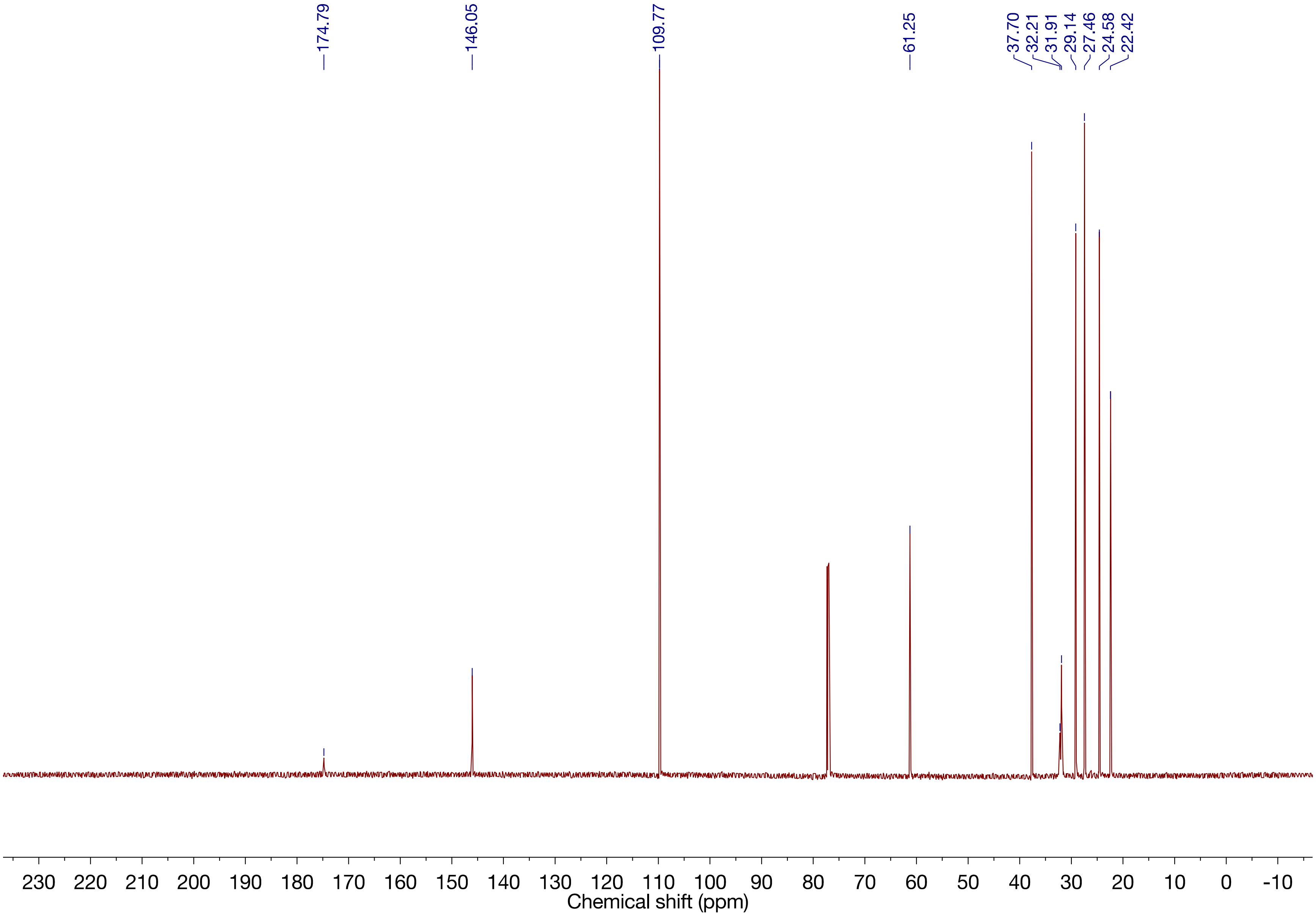

Me
O
OH
1.19
1.00
1.01
2.20
2.12
5.24
2.22
2.26
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

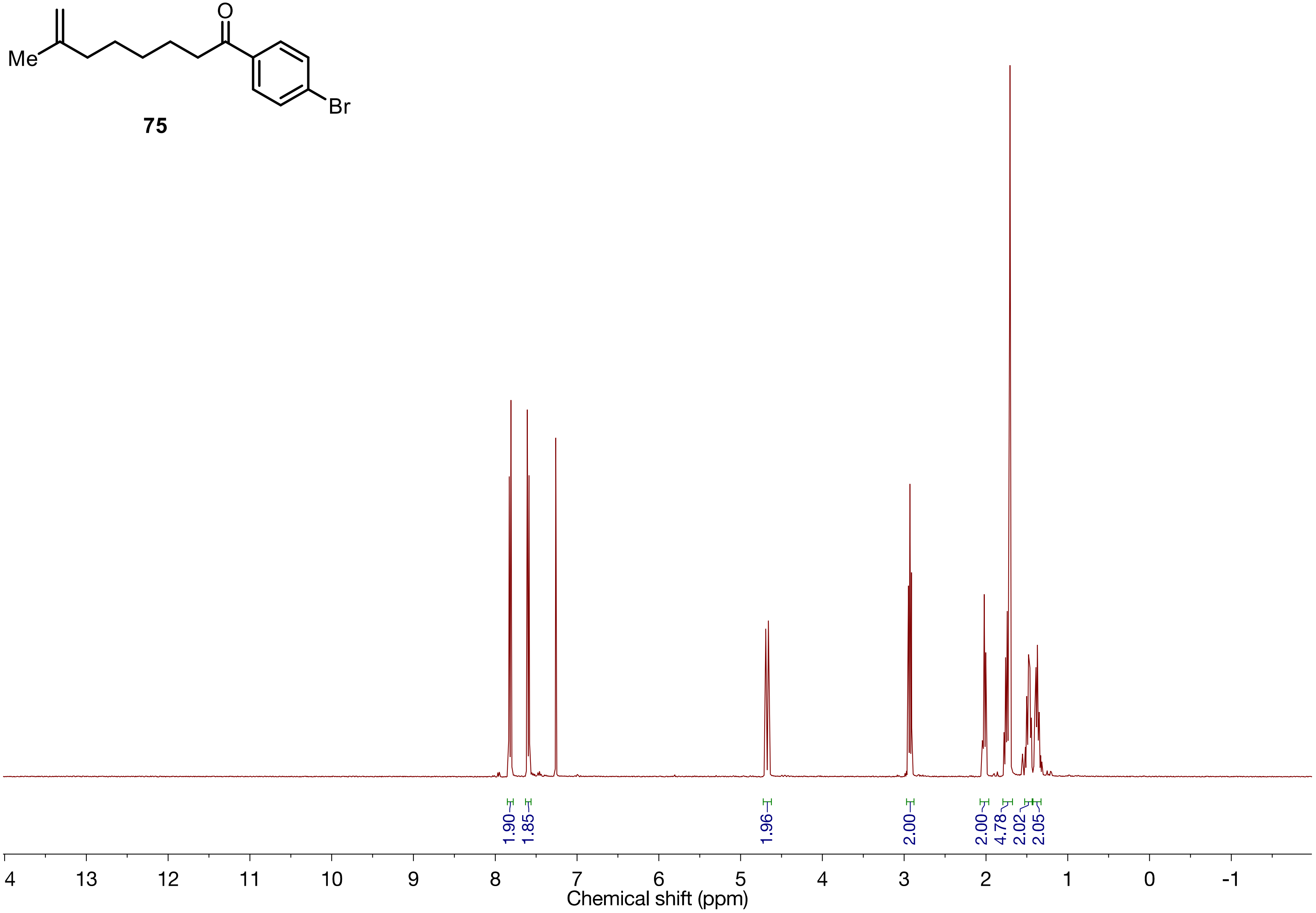
75a


179.47
145.99
109.98
37.69
34.02
28.82
27.33
24.71
22.49
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



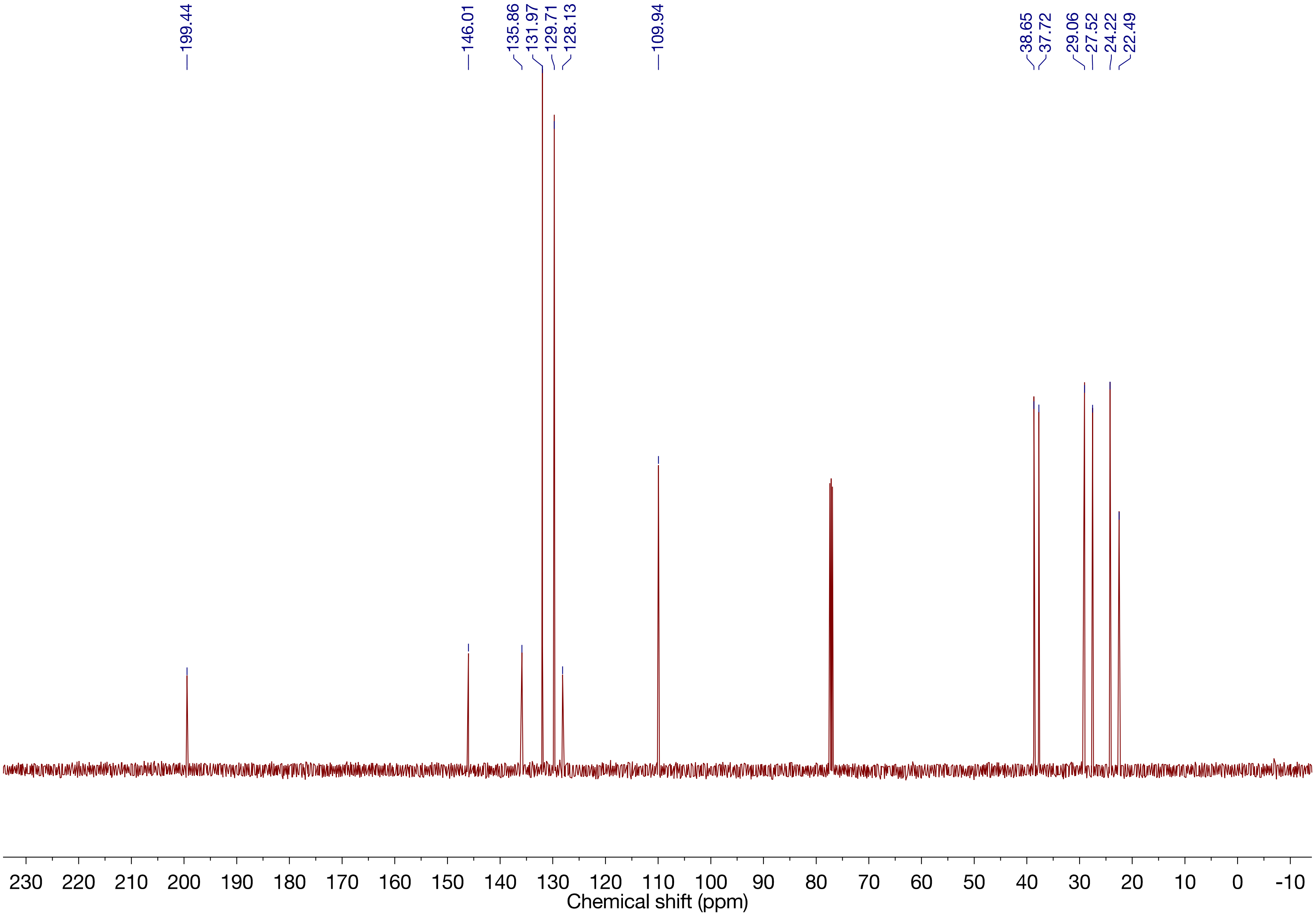
O
N
Me
Me
OMe
75b
2.05
3.00
2.93
2.09
2.11
2.91
2.22
2.21
2.21
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

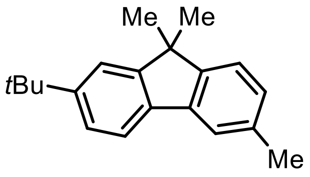

174.79
146.05
109.77
61.25
37.70
32.21
31.91
29.14
27.46
24.58
22.42
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



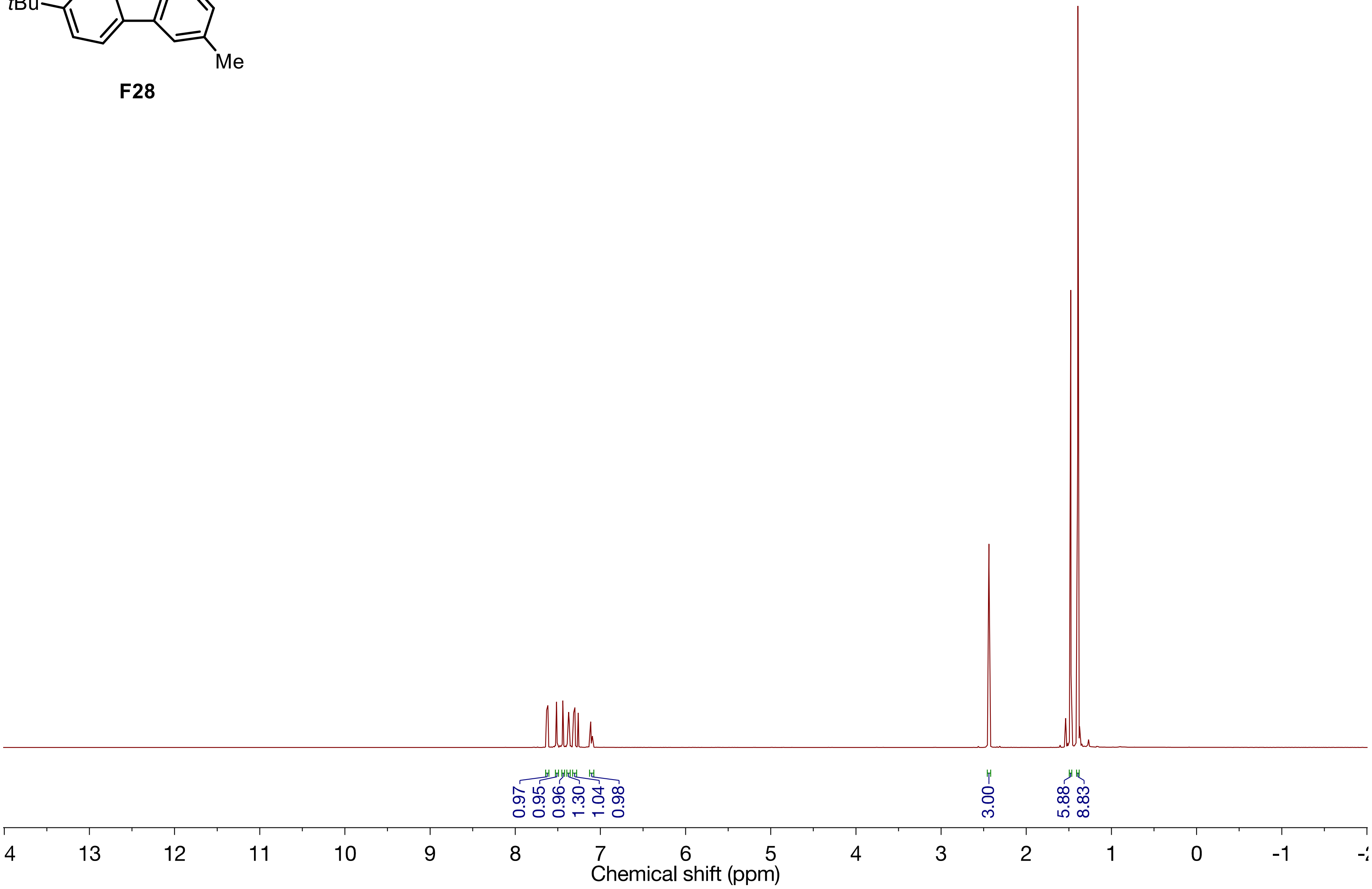
75

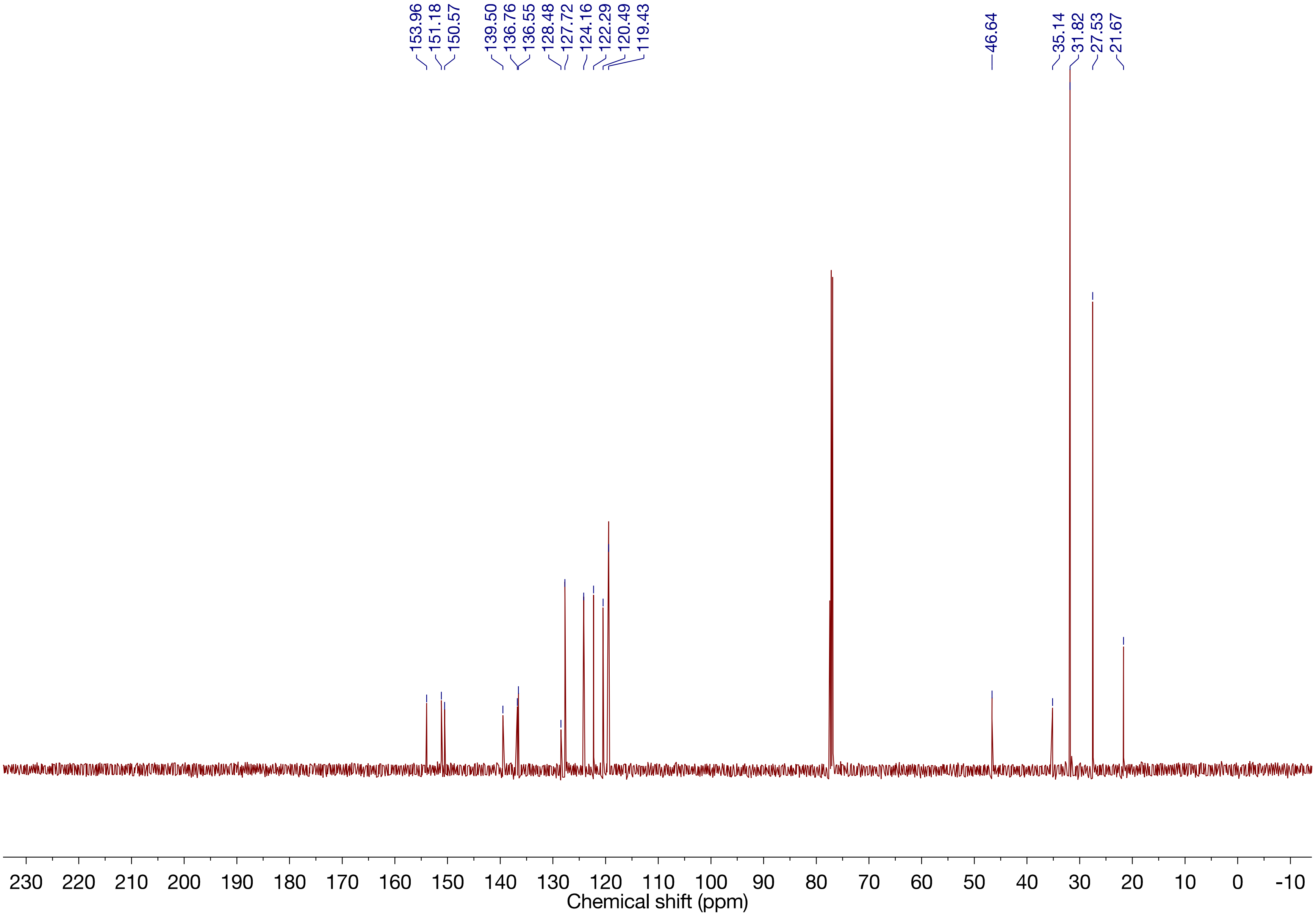
Me
O
Br
1.90
1.85
1.96
2.00
2.00
4.78
2.02
2.05
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


199.44
146.01
135.86
131.97
129.71
128.13
109.94
38.65
37.72
29.06
27.52
24.22
22.49
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

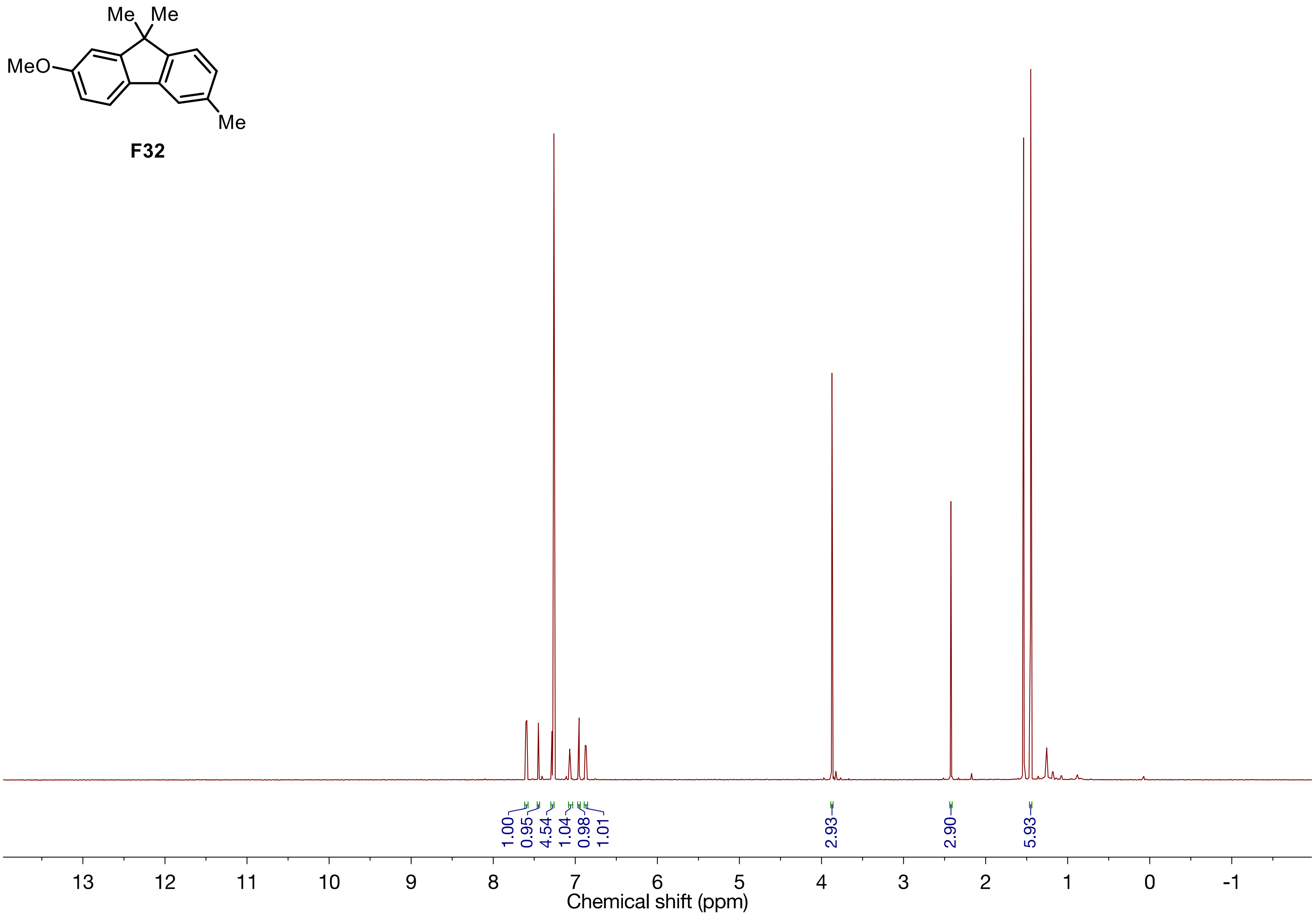

Me
Me
tBu
Me

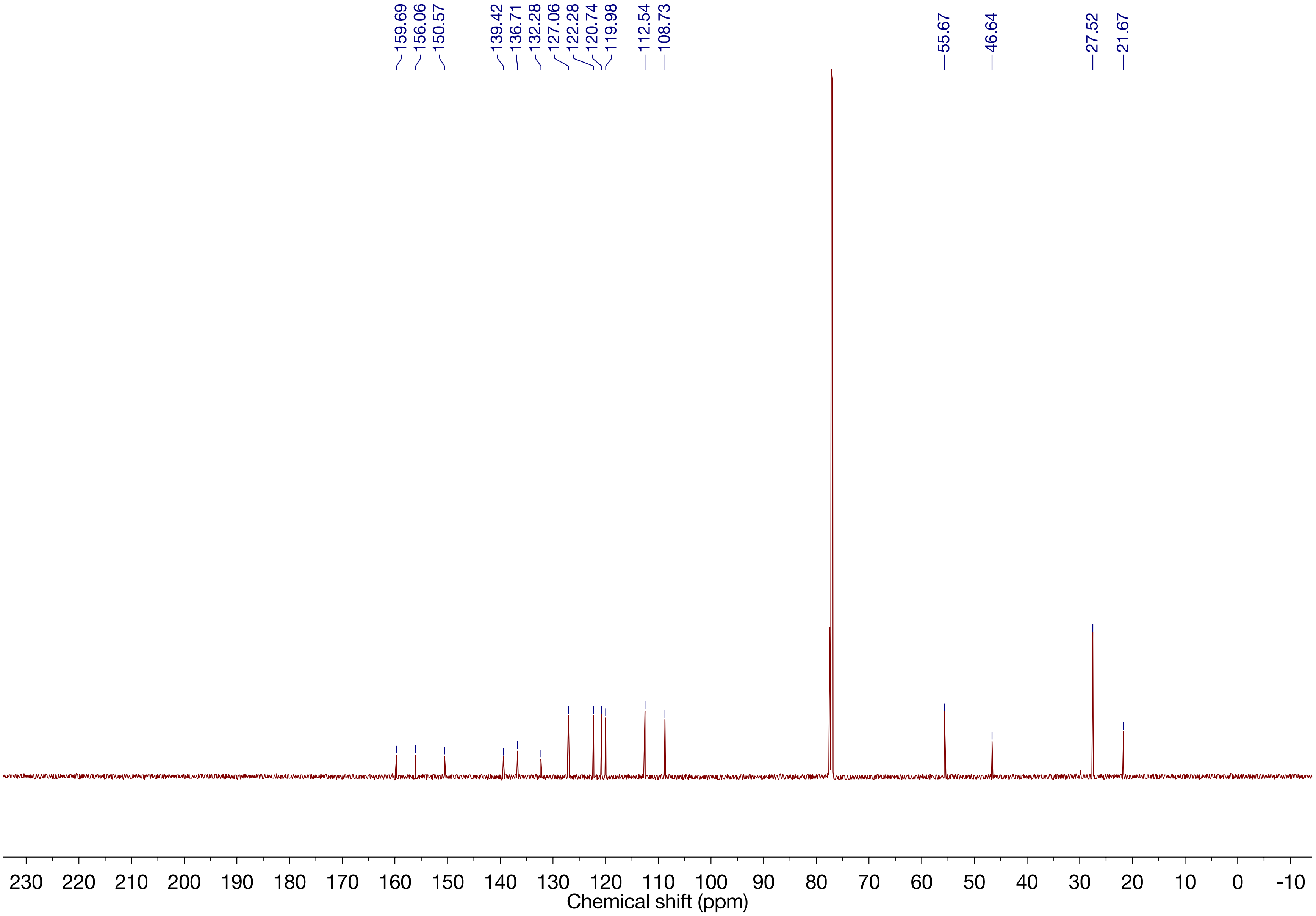
F28


0.97
0.95
0.96
1.30
1.04
0.98
3.00
5.88
8.83
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-
Chemical shift (ppm)

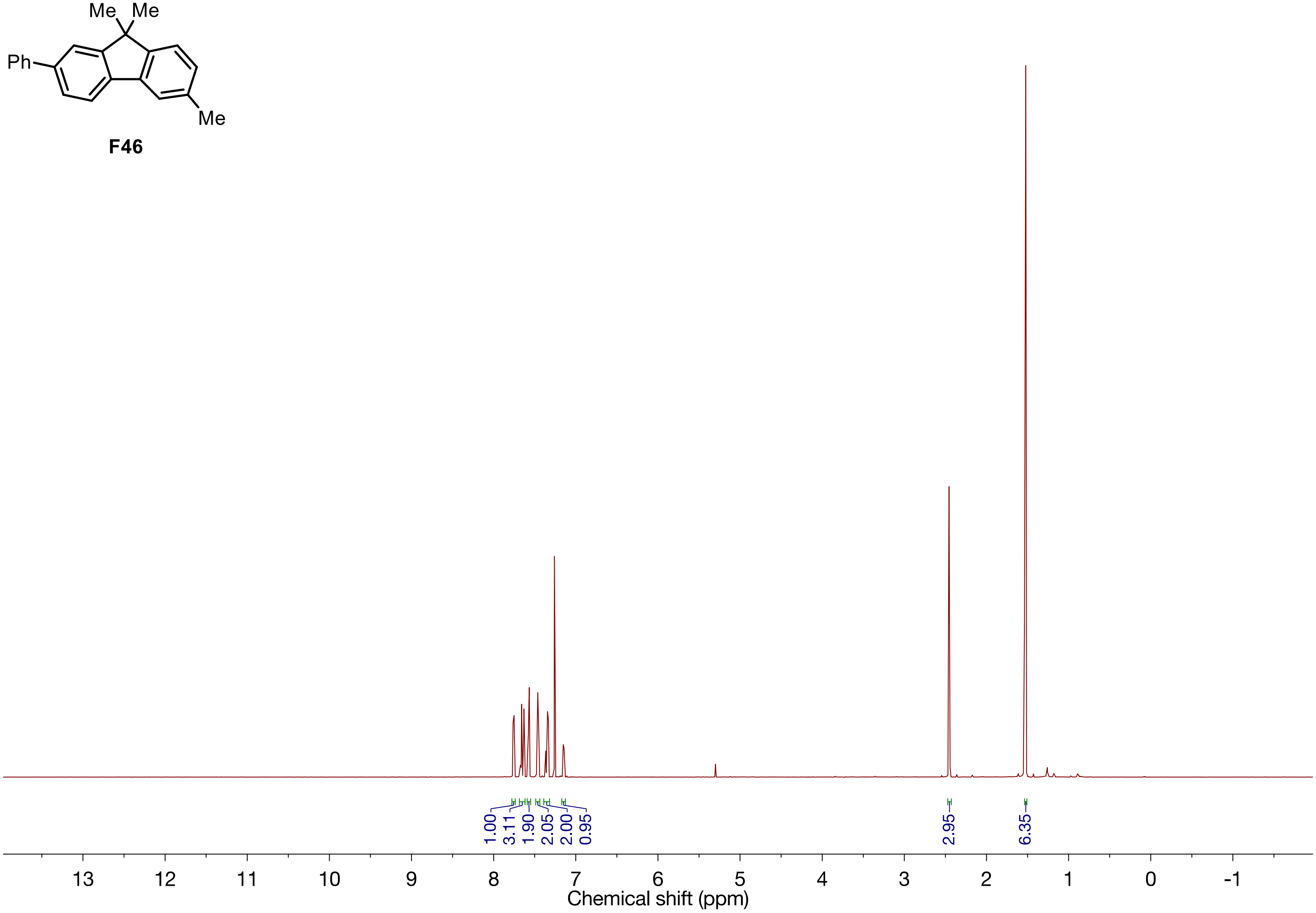


153.96
151.18
150.57
139.50
136.76
136.55
128.48
127.72
124.16
122.29
120.49
119.43
46.64
35.14
31.82
27.53
21.67
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

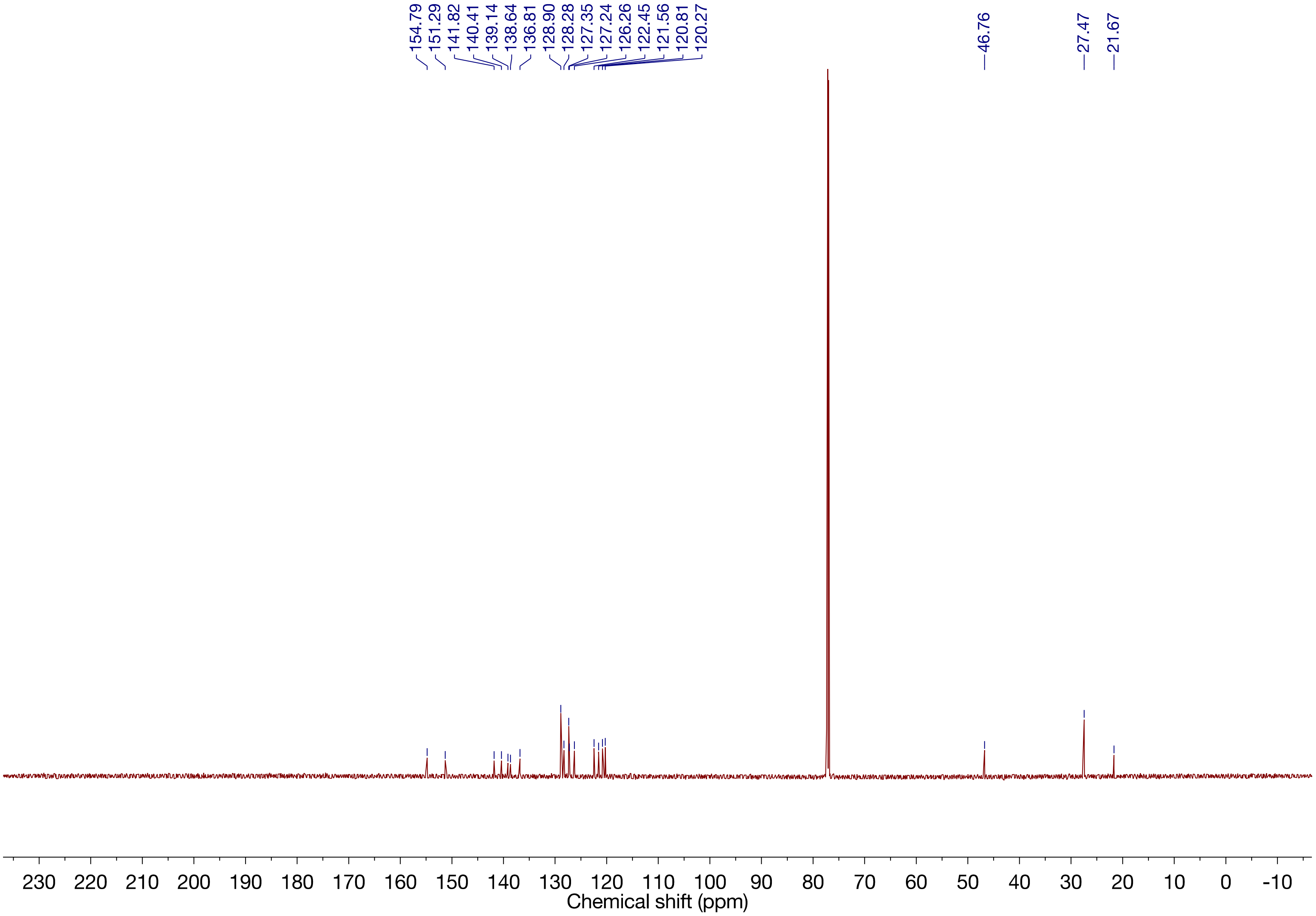

F32
Me
Me
MeO
Me
1.00
0.95
4.54
1.04
0.98
1.01
2.93
2.90
5.93
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

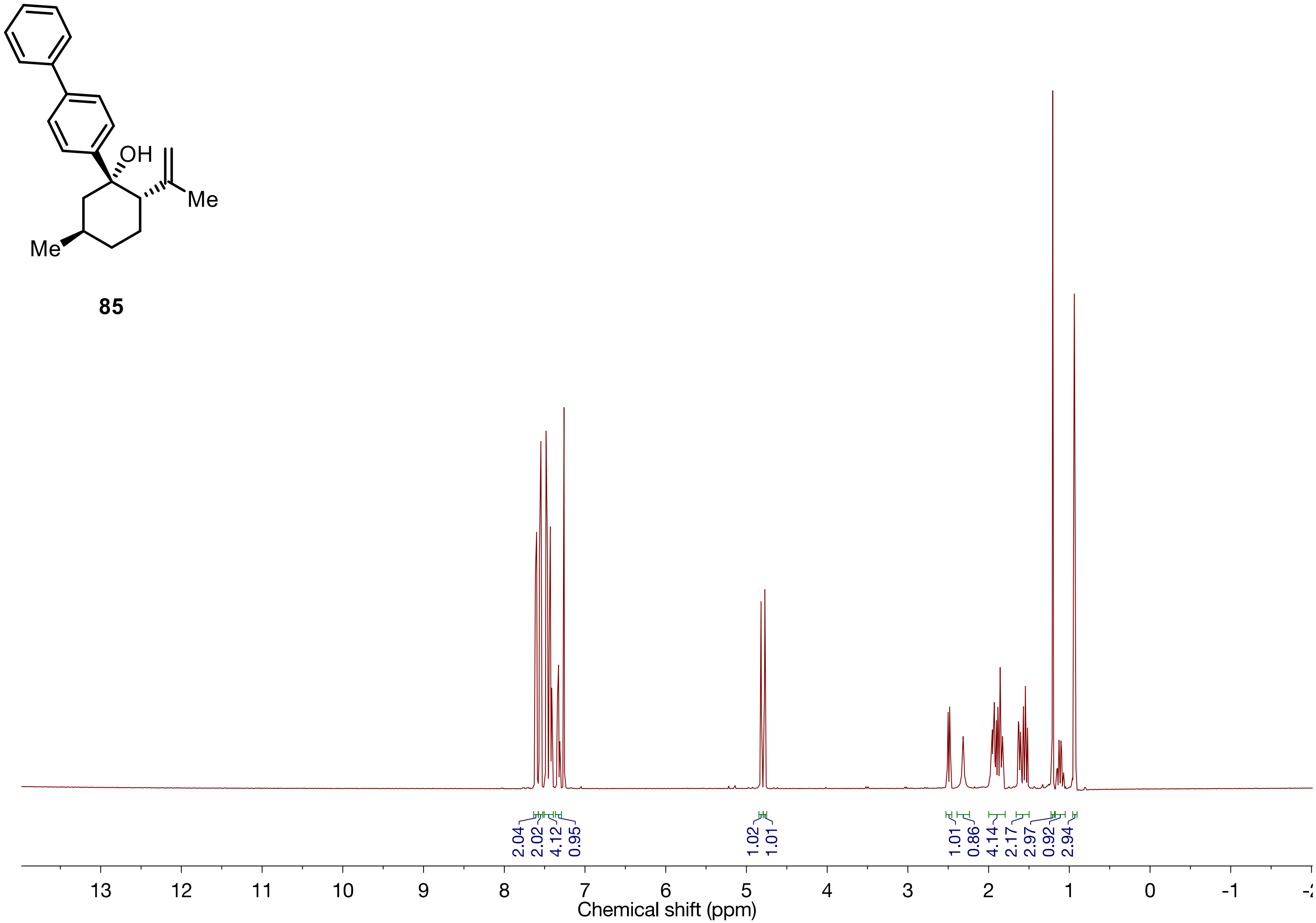


159.69
156.06
150.57
139.42
136.71
132.28
127.06
122.28
120.74
119.98
112.54
108.73
55.67
46.64
27.52
21.67
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
Ph
Me
1.00
3.11
1.90
2.05
2.00
0.95
2.95
6.35
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

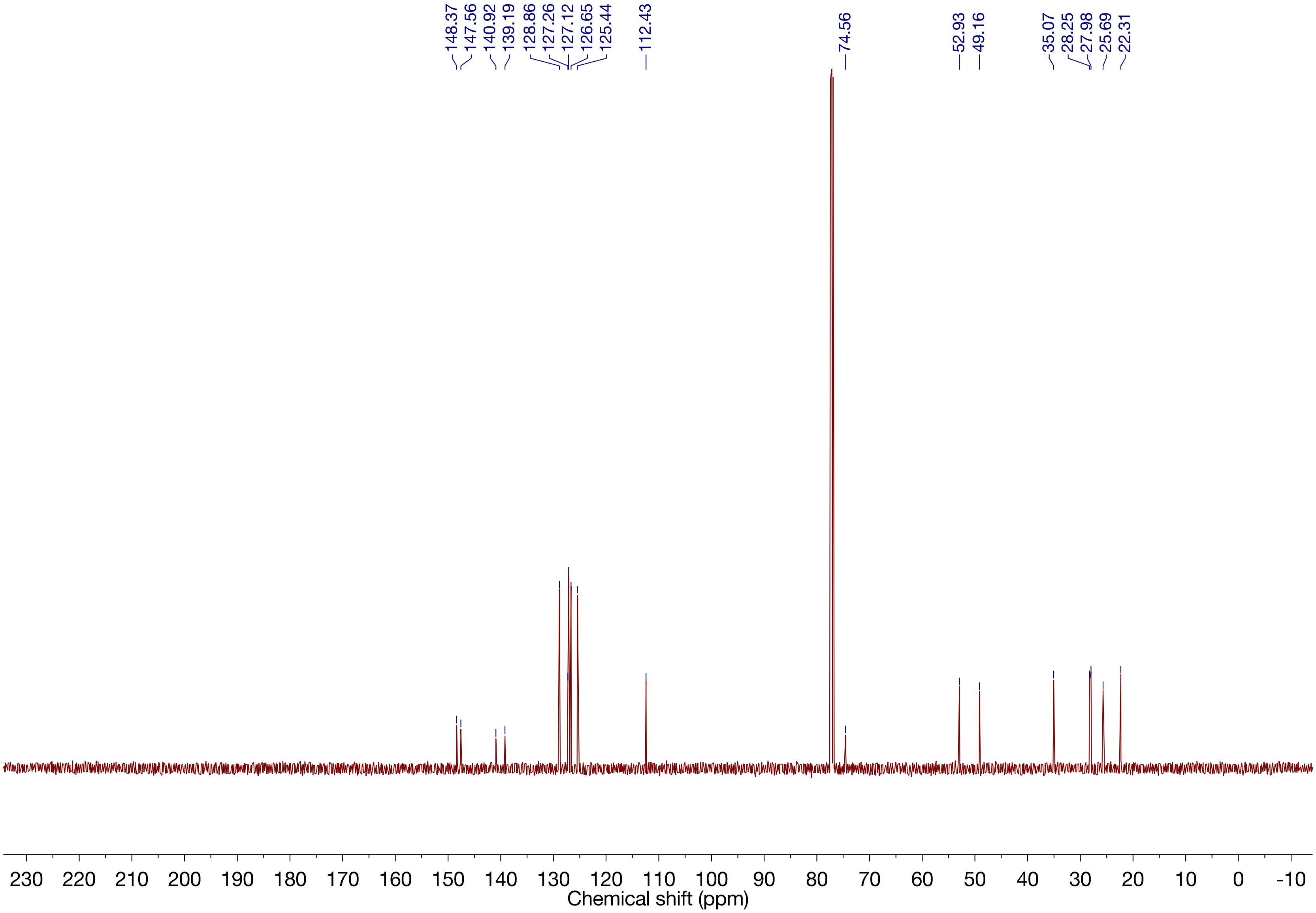
F46

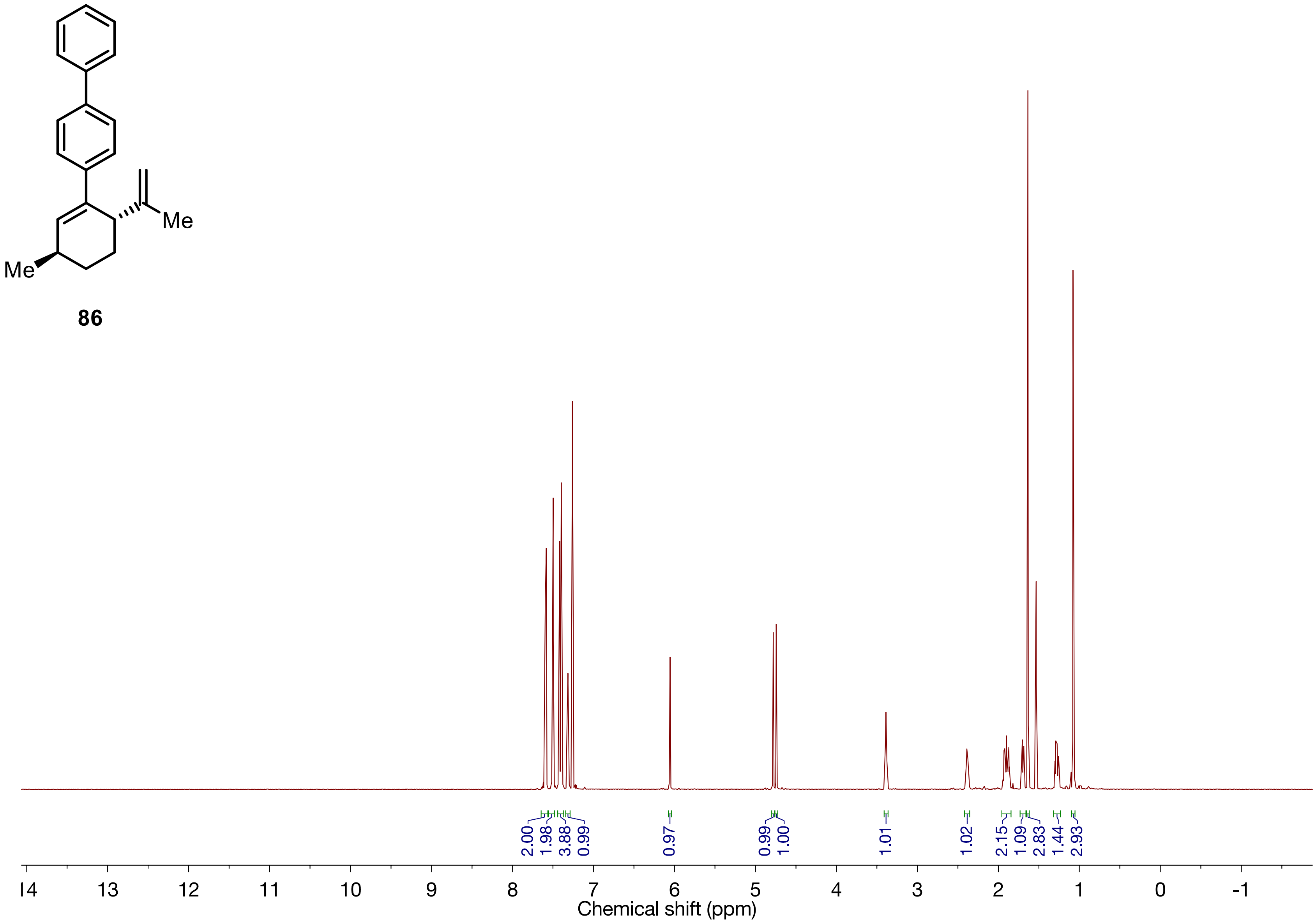

154.79
151.29
141.82
140.41
139.14
138.64
136.81
128.90
128.28
127.35
127.24
126.26
122.45
121.56
120.81
120.27
46.76
27.47
21.67
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)


OH
Me
Me

85

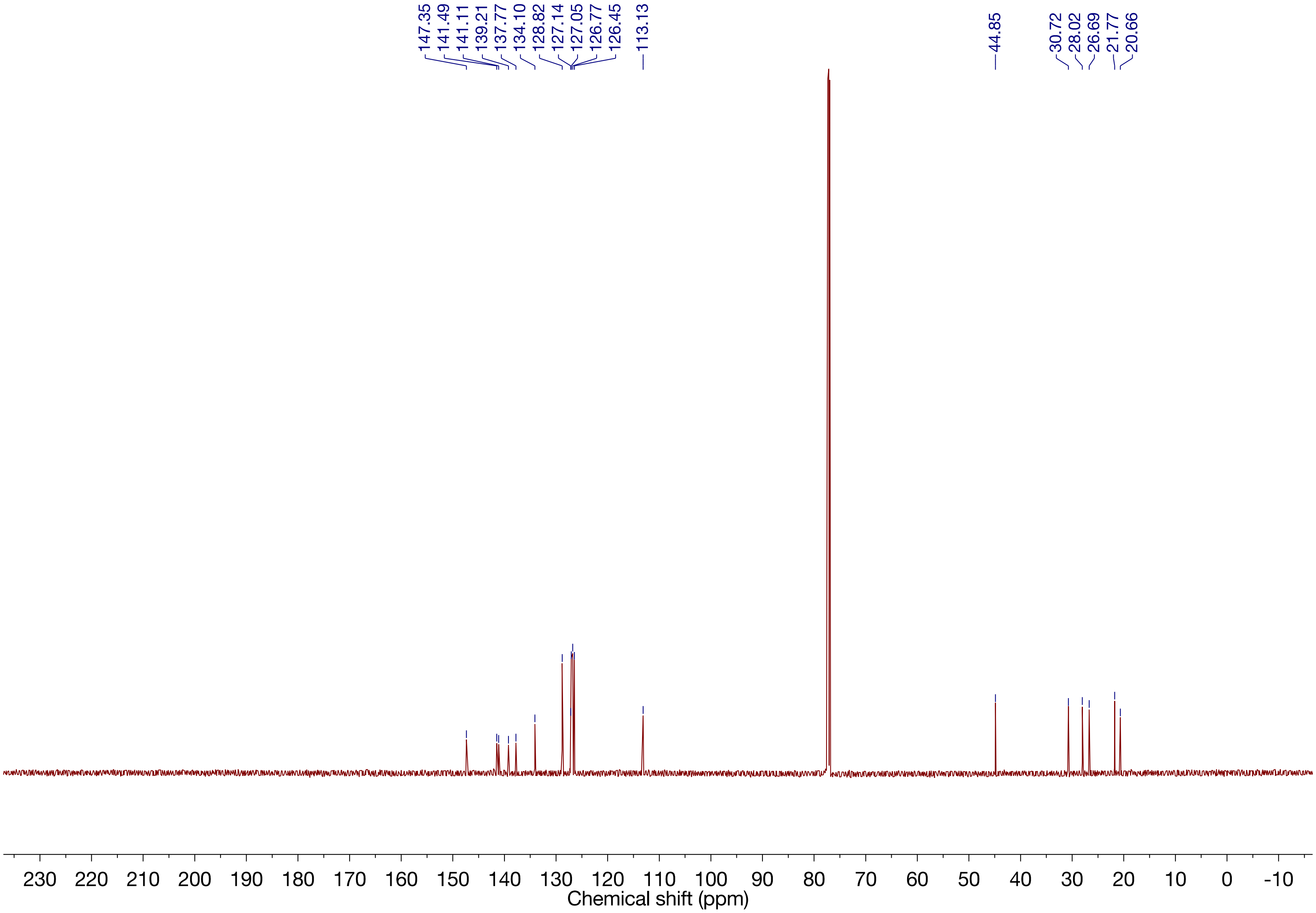
2.04
2.02
4.12
0.95
1.02
1.01
1.01
0.86
4.14
2.17
2.97
0.92
2.94
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

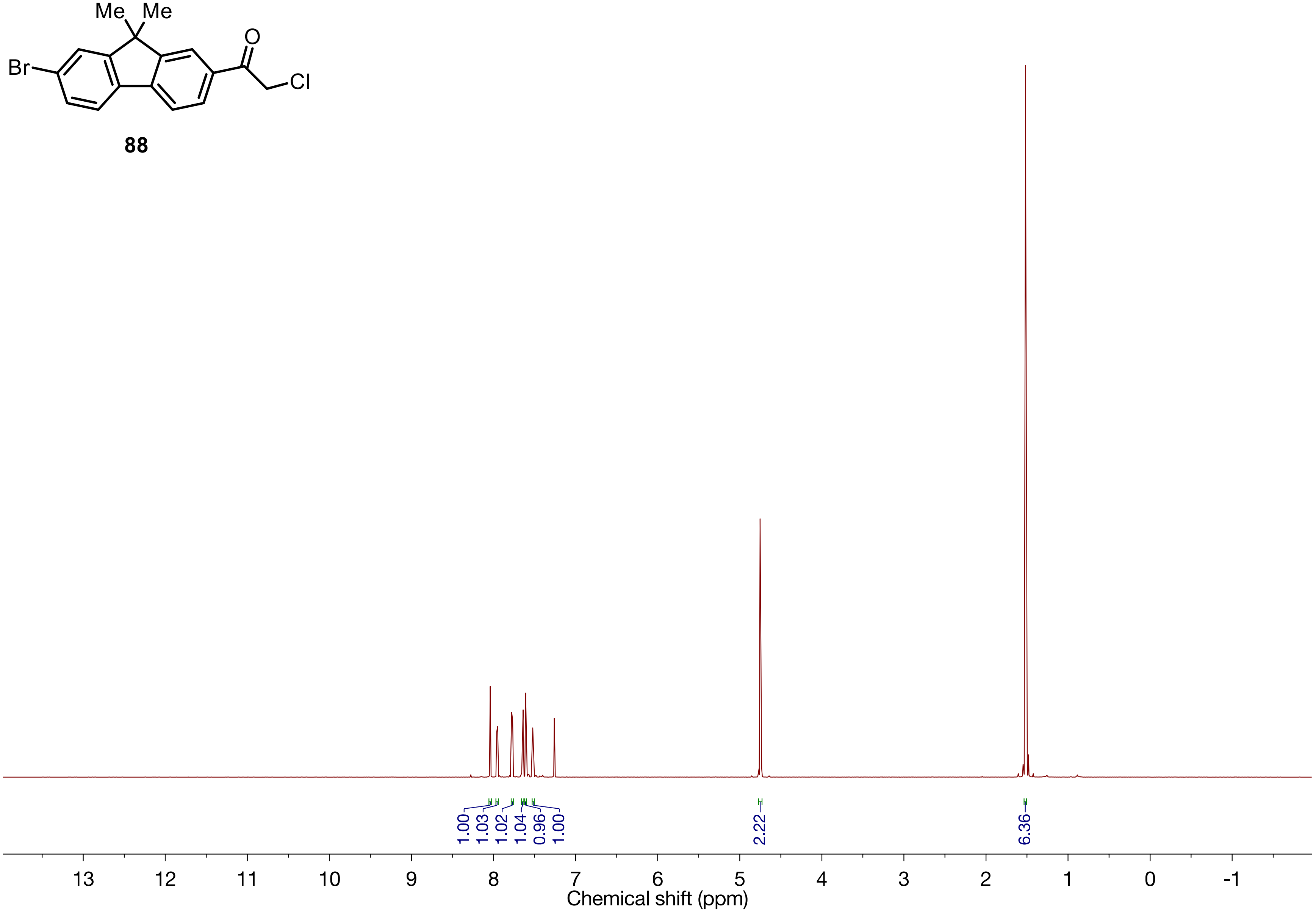

148.37
147.56
140.92
139.19
128.86
127.26
127.12
126.65
125.44
112.43
74.56
52.93
49.16
35.07
28.25
27.98
25.69
22.31
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

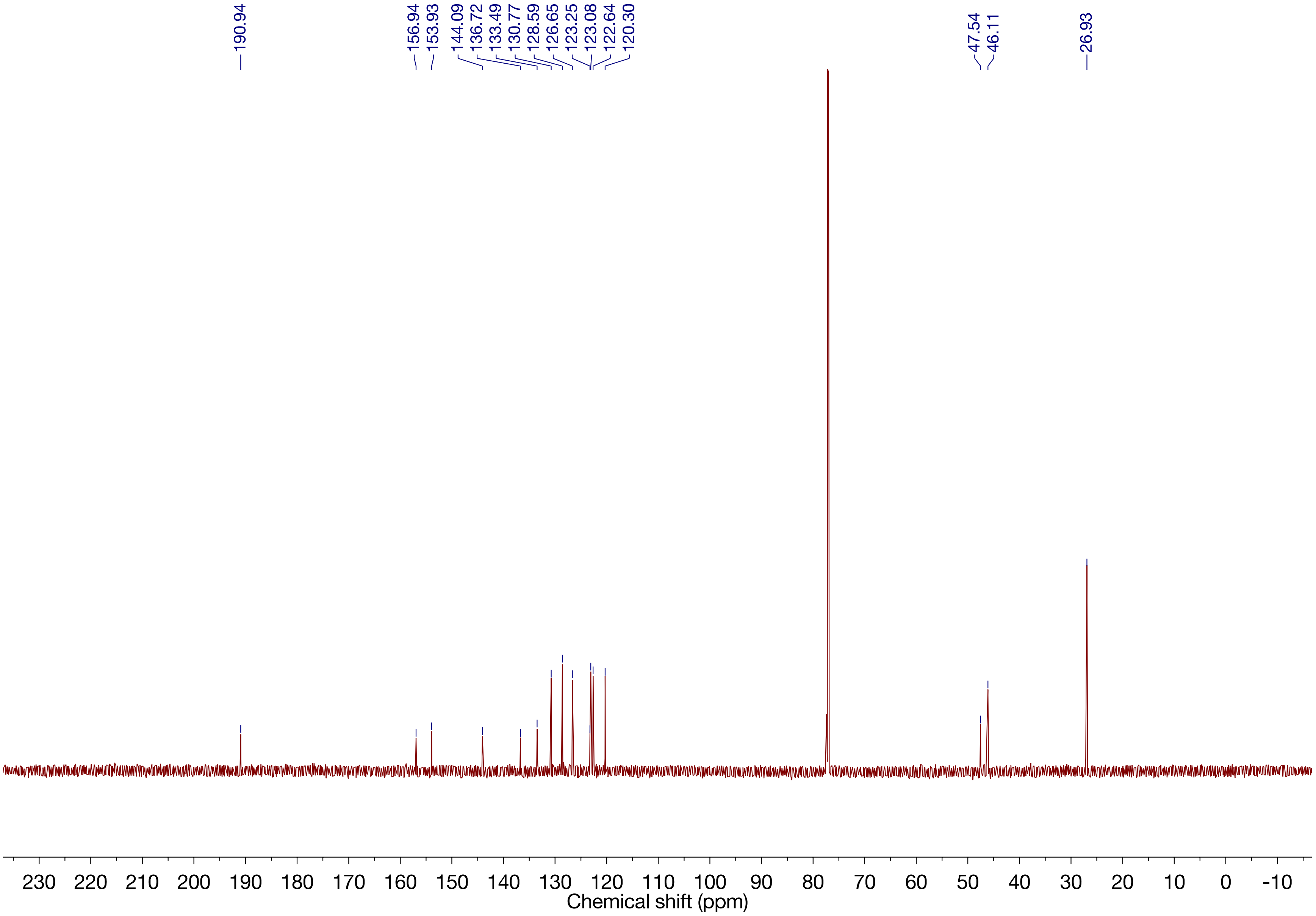

Me
Me

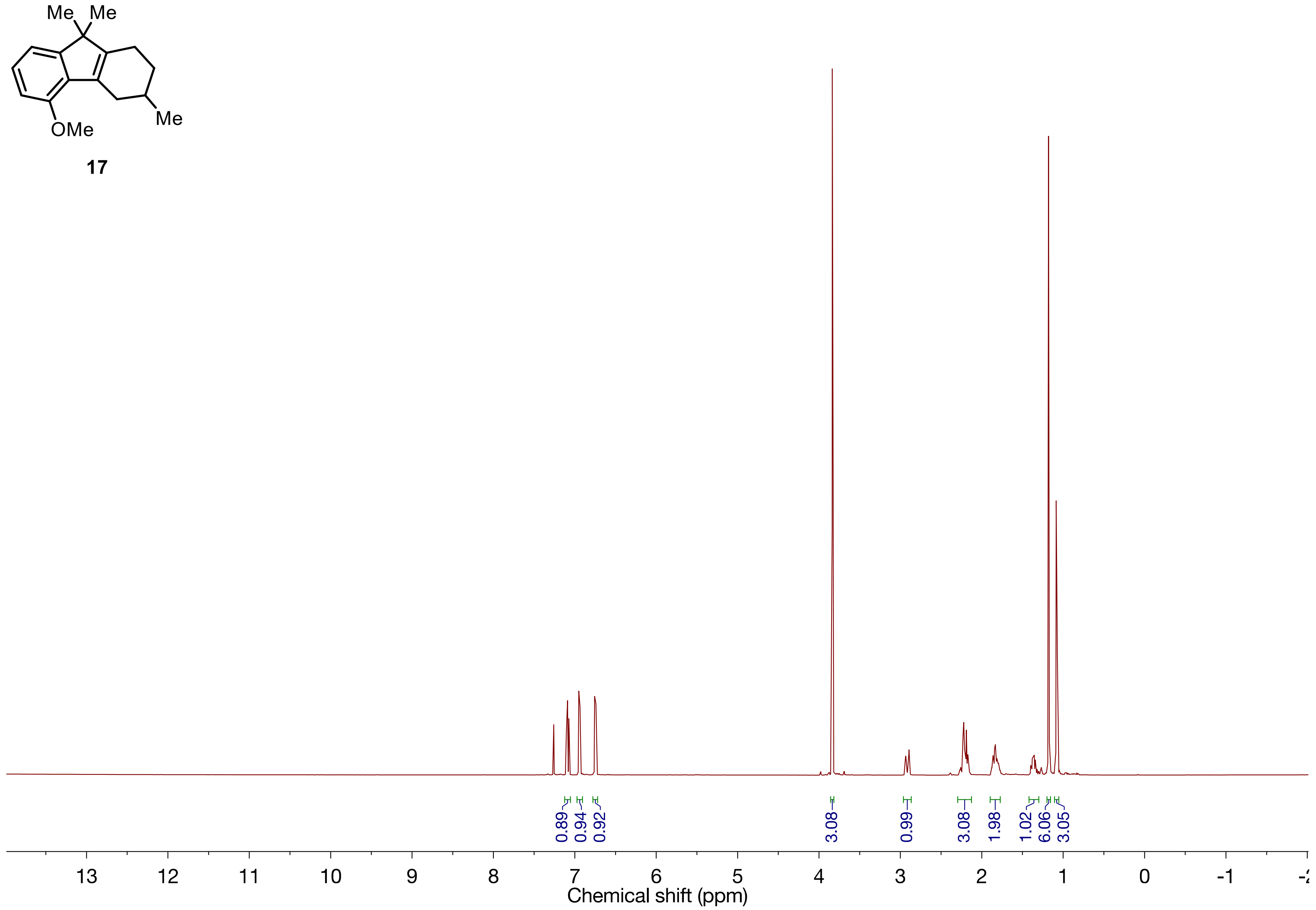
86

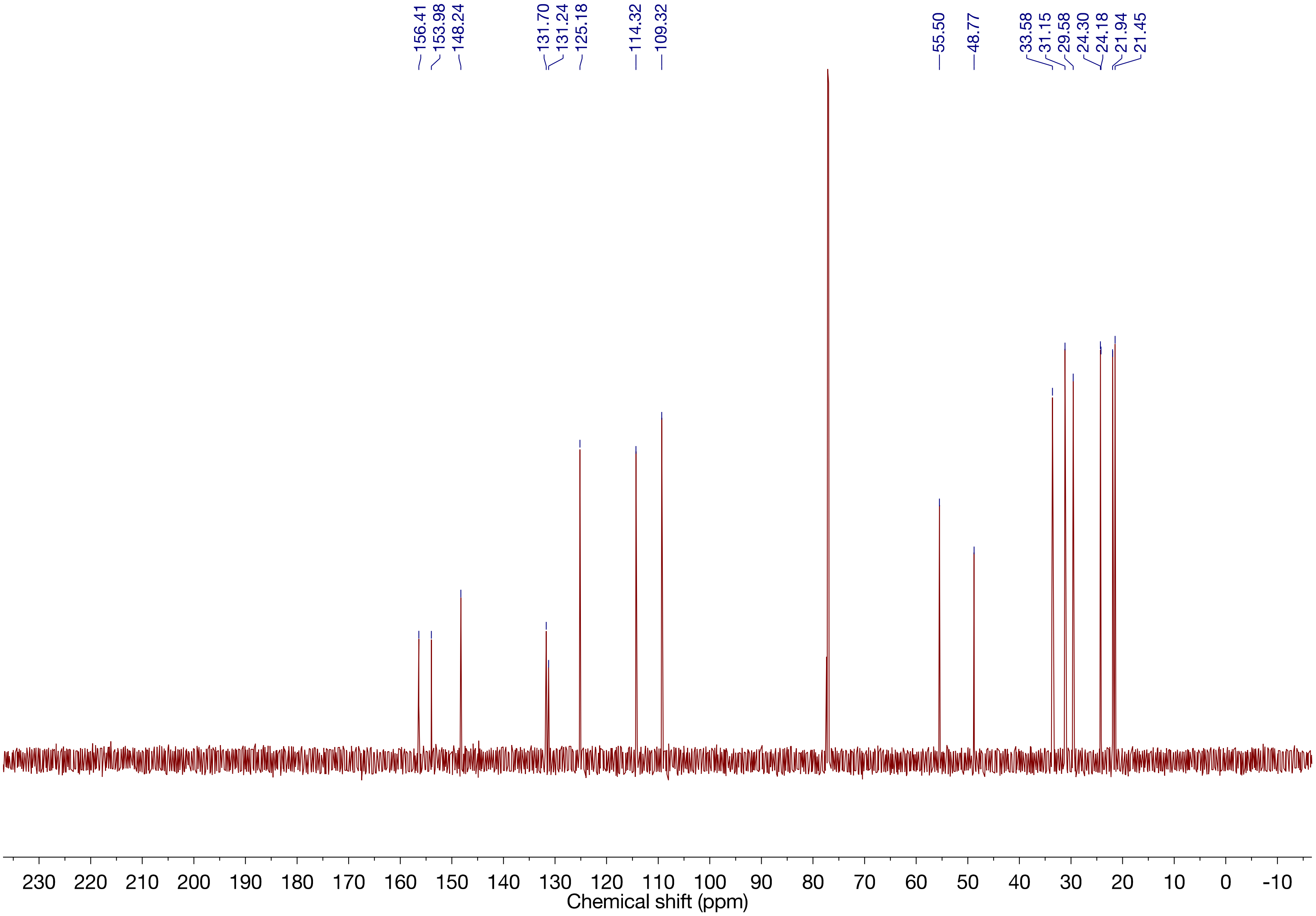
2.00
1.98
3.88
0.99
0.97
0.99
1.00
1.01
1.02
2.15
1.09
2.83
1.44
2.93
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

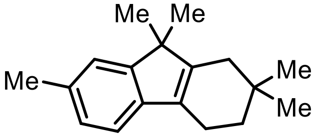

147.35
141.49
141.11
139.21
137.77
134.10
128.82
127.14
127.05
126.77
126.45
113.13
44.85
30.72
28.02
26.69
21.77
20.66
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
O
Br
Cl
88
1.00
1.03
1.02
1.04
0.96
1.00
2.22
6.36
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

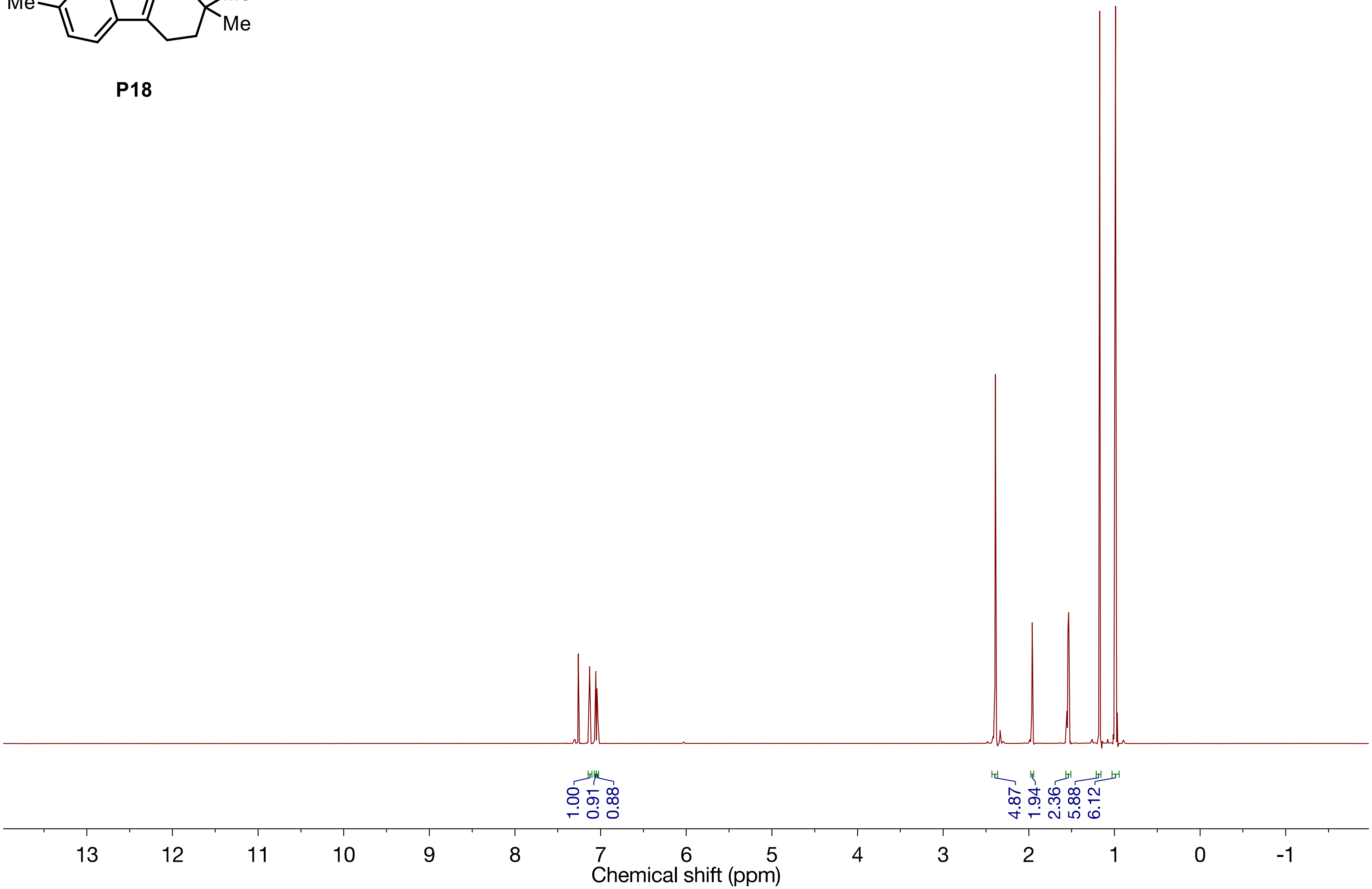

190.94
156.94
153.93
144.09
136.72
133.49
130.77
128.59
126.65
123.25
123.08
122.64
120.30
47.54
46.11
26.93
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

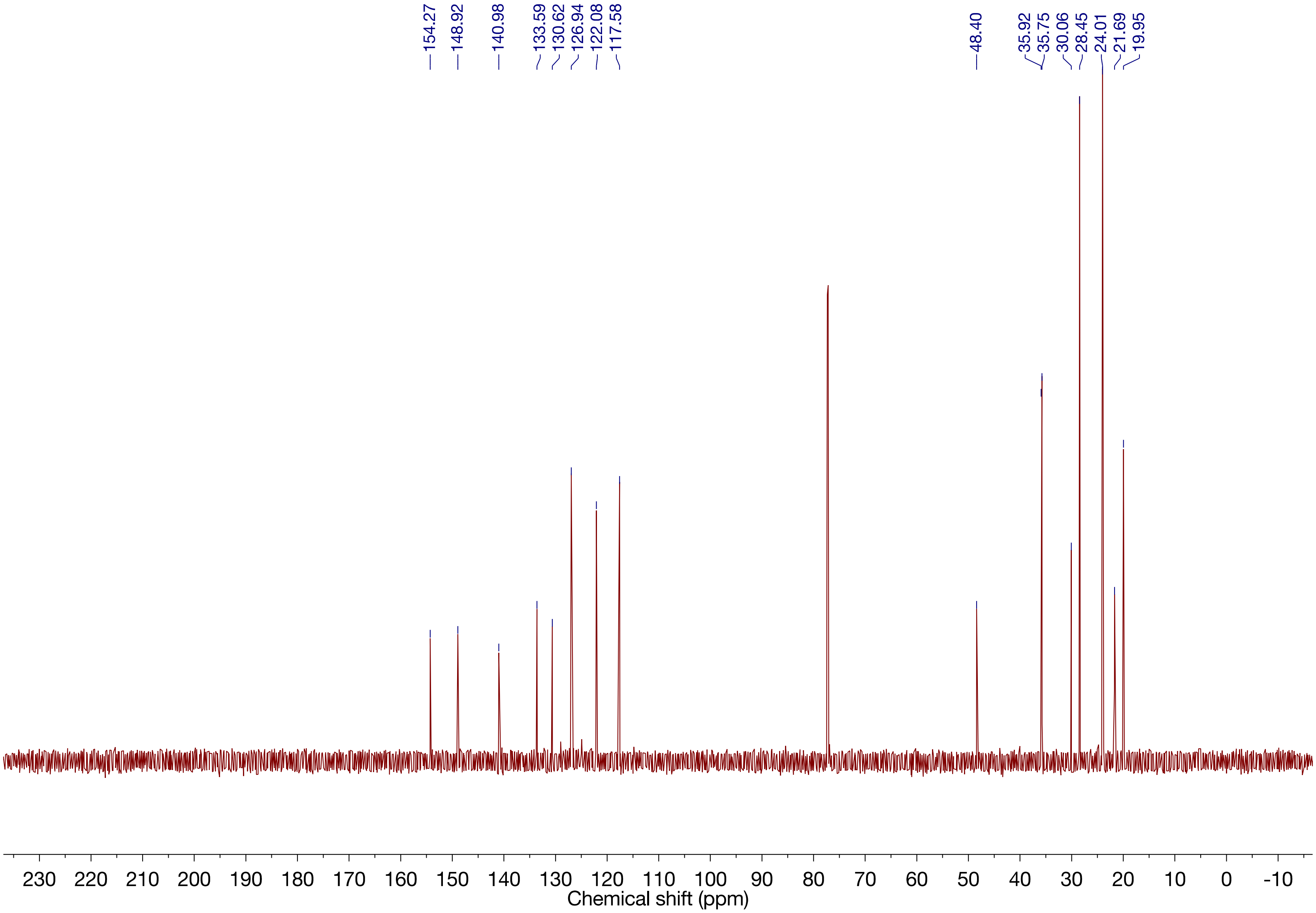

Me
Me
OMe
Me
17
0.89
0.94
0.92
3.08
0.99
3.08
1.98
1.02
6.06
3.05
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

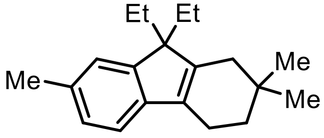

156.41
153.98
148.24
131.70
131.24
125.18
114.32
109.32
55.50
48.77
33.58
31.15
29.58
24.30
24.18
21.94
21.45
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
Me
Me
Me

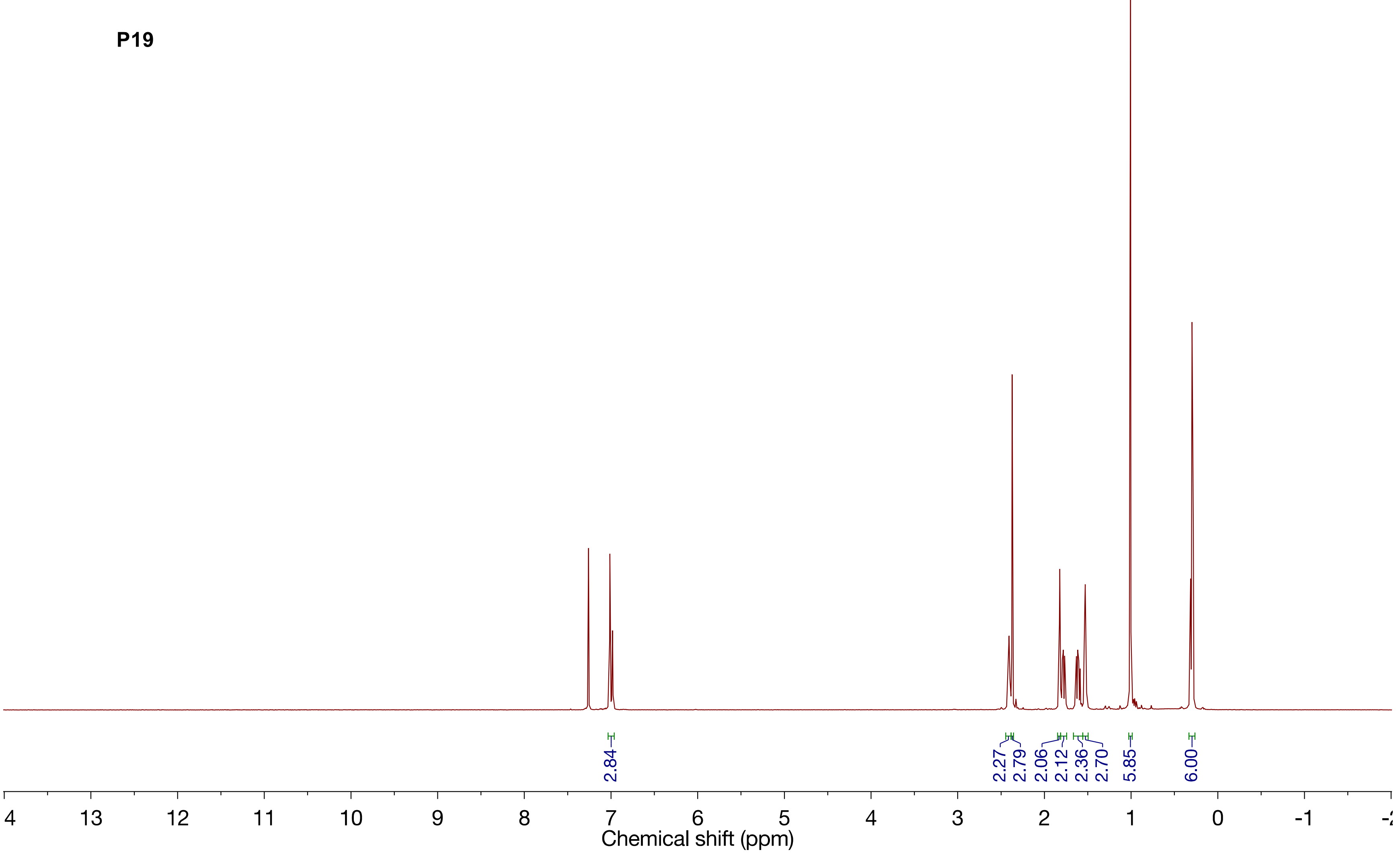
P18

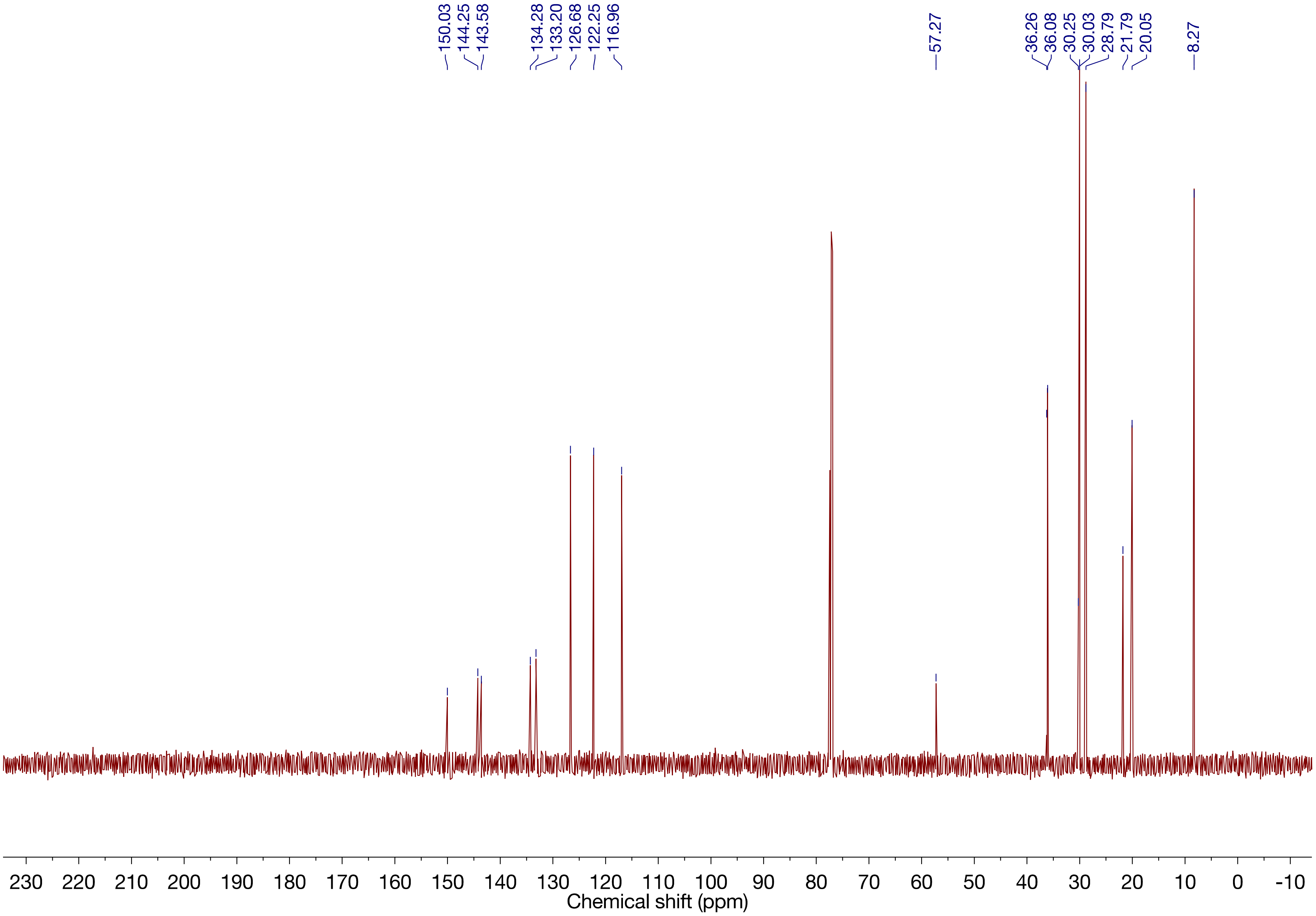

1.00
0.91
0.88
4.87
1.94
2.36
5.88
6.12
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

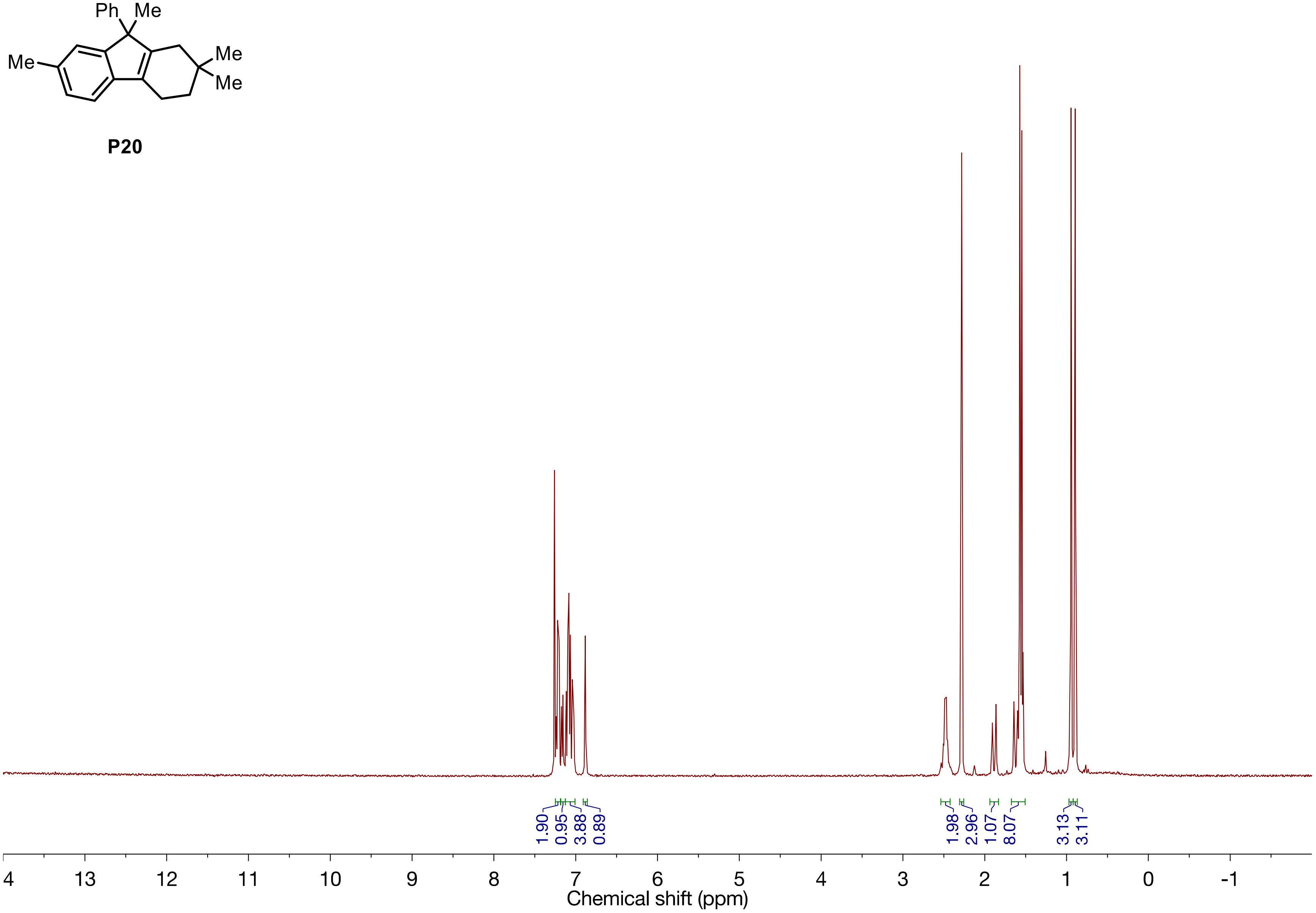

154.27
148.92
140.98
133.59
130.62
126.94
122.08
117.58
48.40
35.92
35.75
30.06
28.45
24.01
21.69
19.95
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

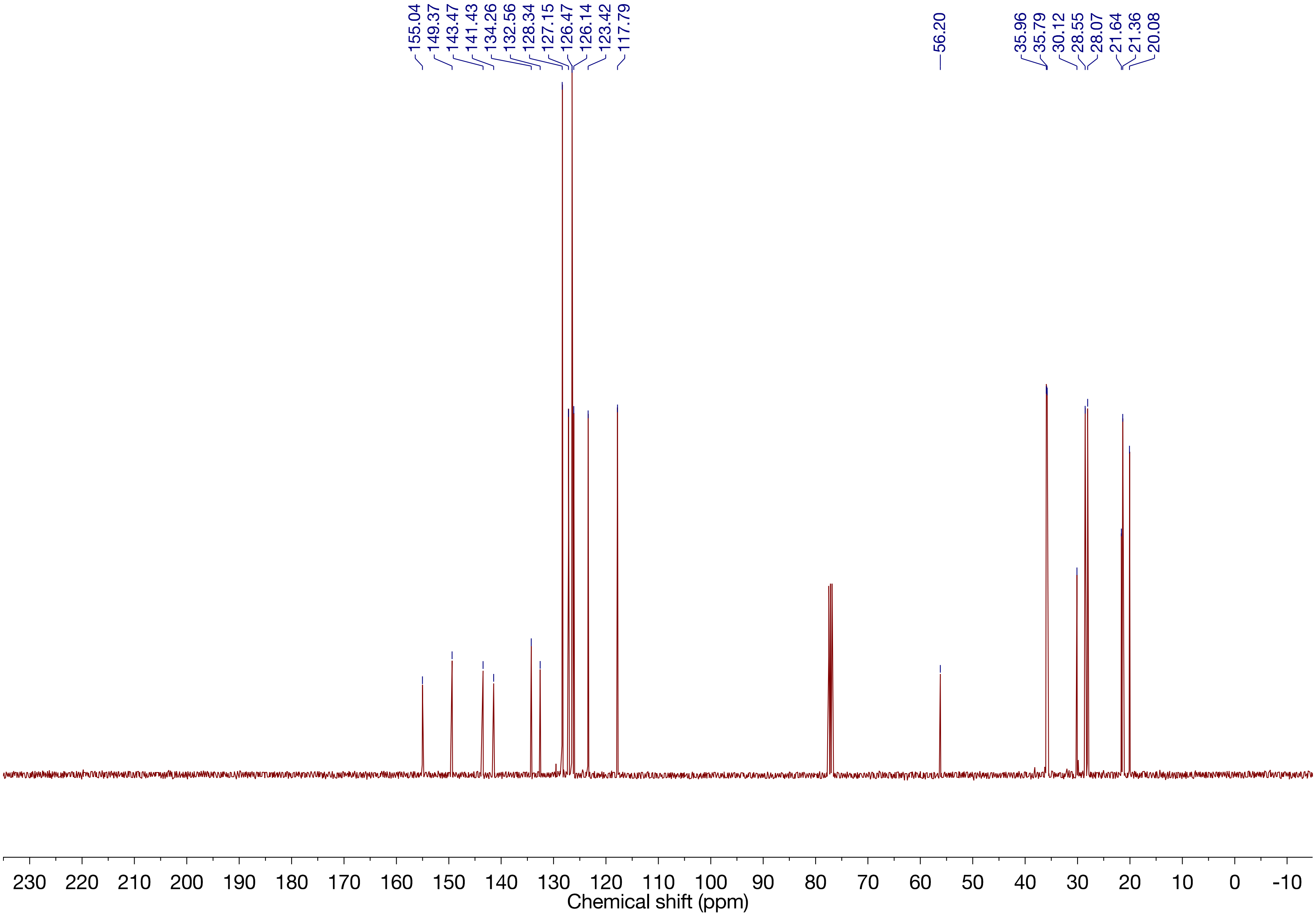

Et
Et
Me
Me
Me

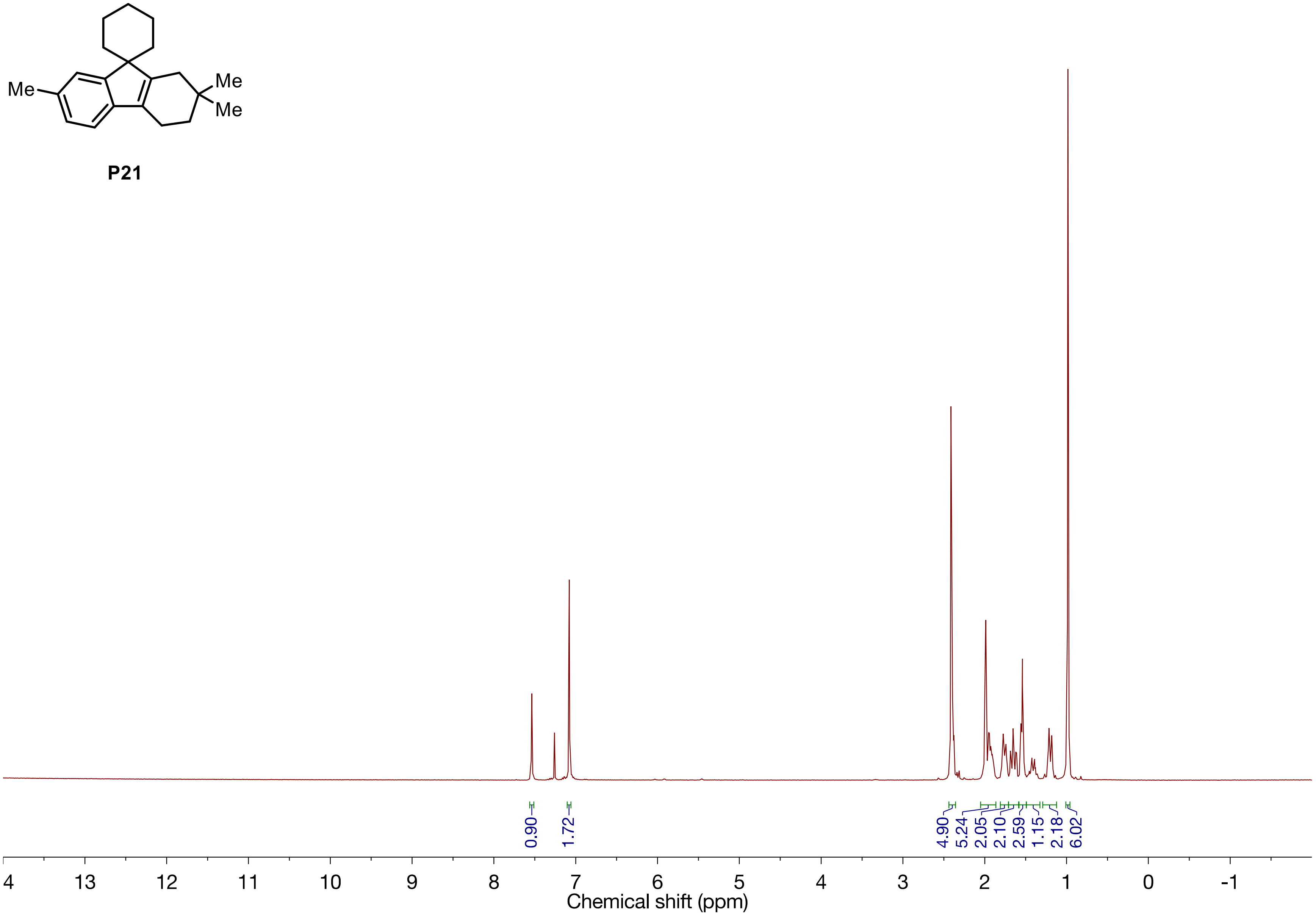
P19


2.84
2.27
2.79
2.06
2.12
2.36
2.70
5.85
6.00
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

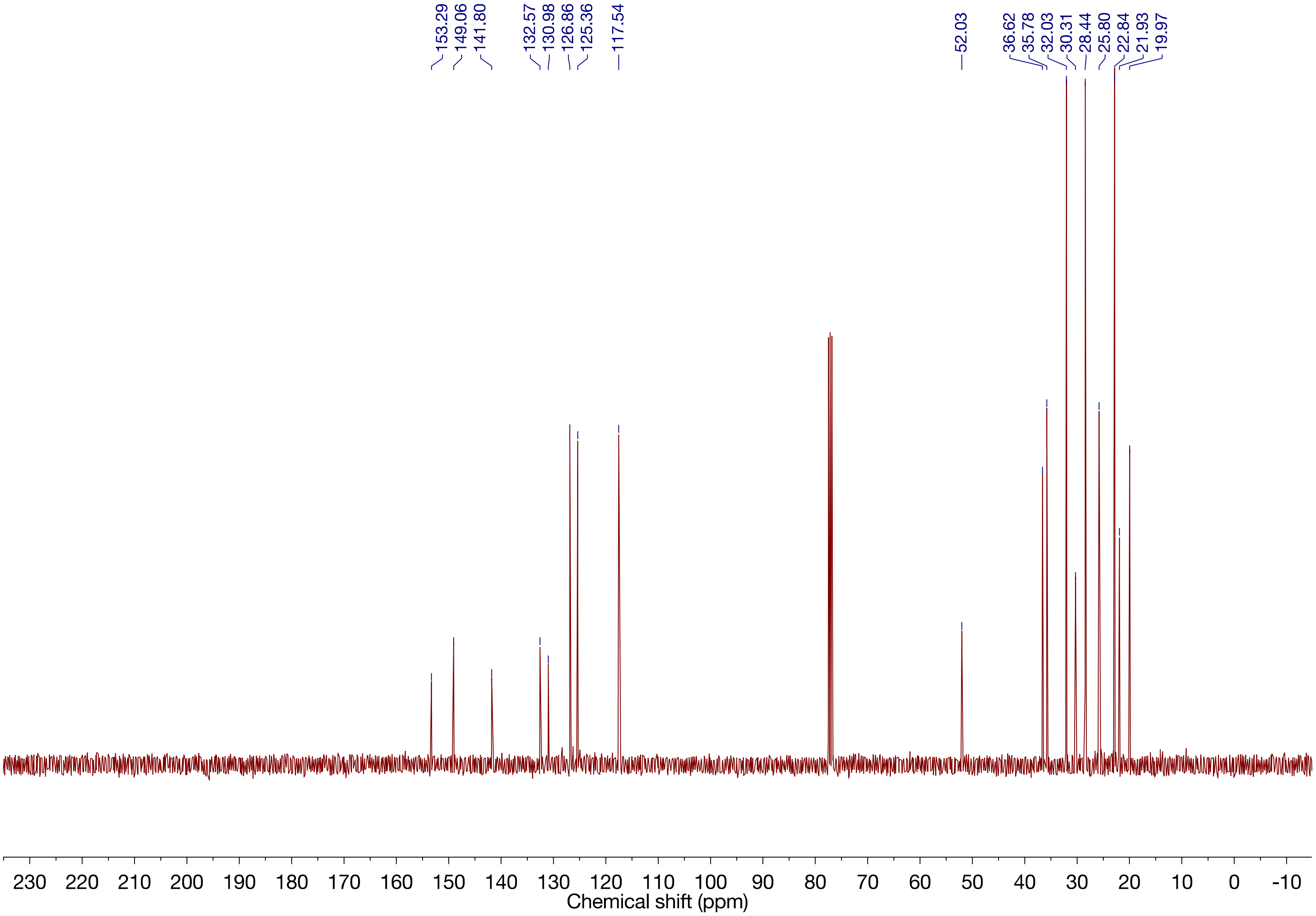

150.03
144.25
143.58
134.28
133.20
126.68
122.25
116.96
57.27
36.26
36.08
30.25
30.03
28.79
21.79
20.05
8.27
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

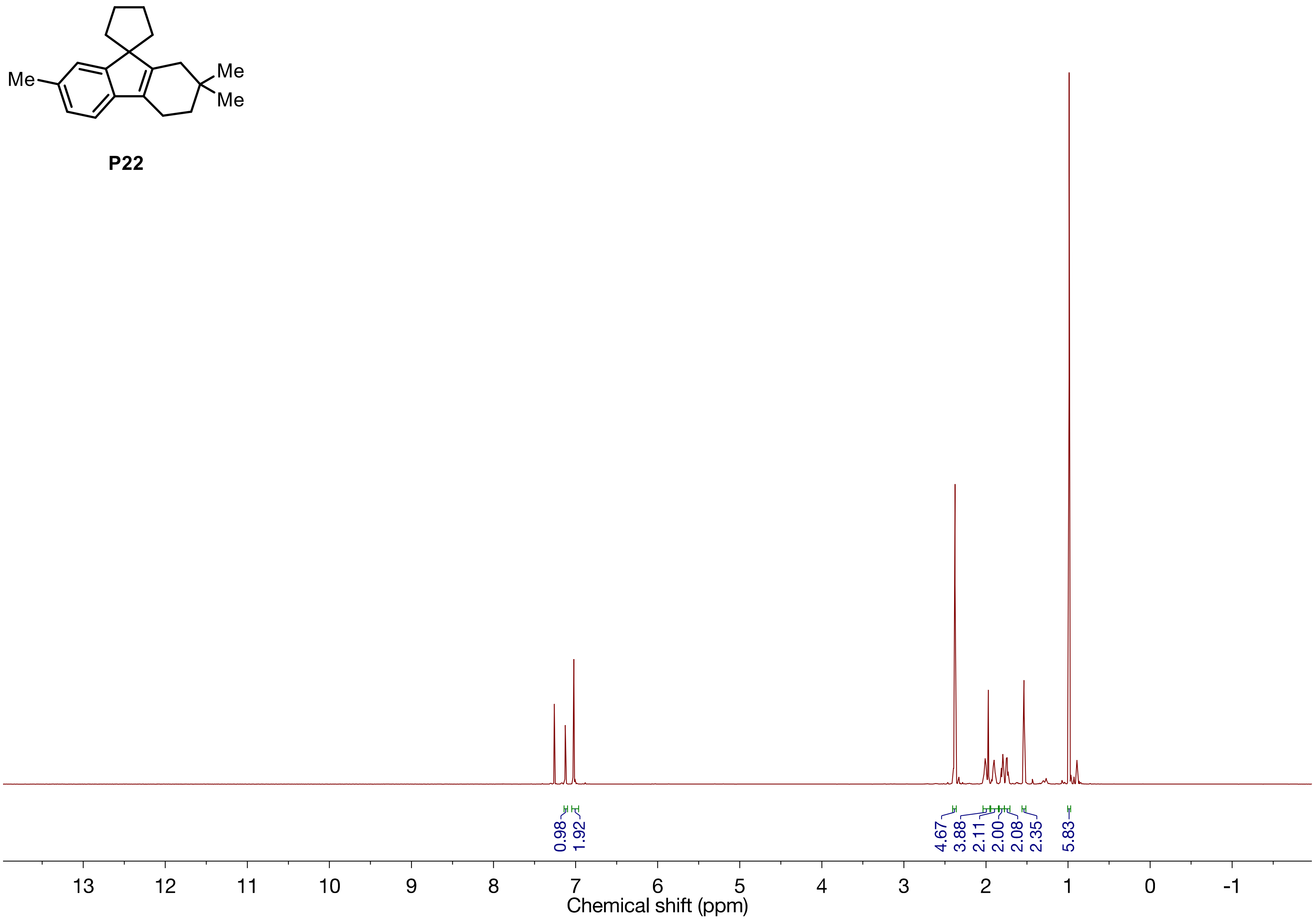

Ph
Me
Me
Me
Me
P20
1.90
0.95
3.88
0.89
1.98
2.96
1.07
8.07
3.13
3.11
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


155.04
149.37
143.47
141.43
134.26
132.56
128.34
127.15
126.47
126.14
123.42
117.79
56.20
35.96
35.79
30.12
28.55
28.07
21.64
21.36
20.08
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
Me
0.90
1.72
4.90
5.24
2.05
2.10
2.59
1.15
2.18
6.02
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

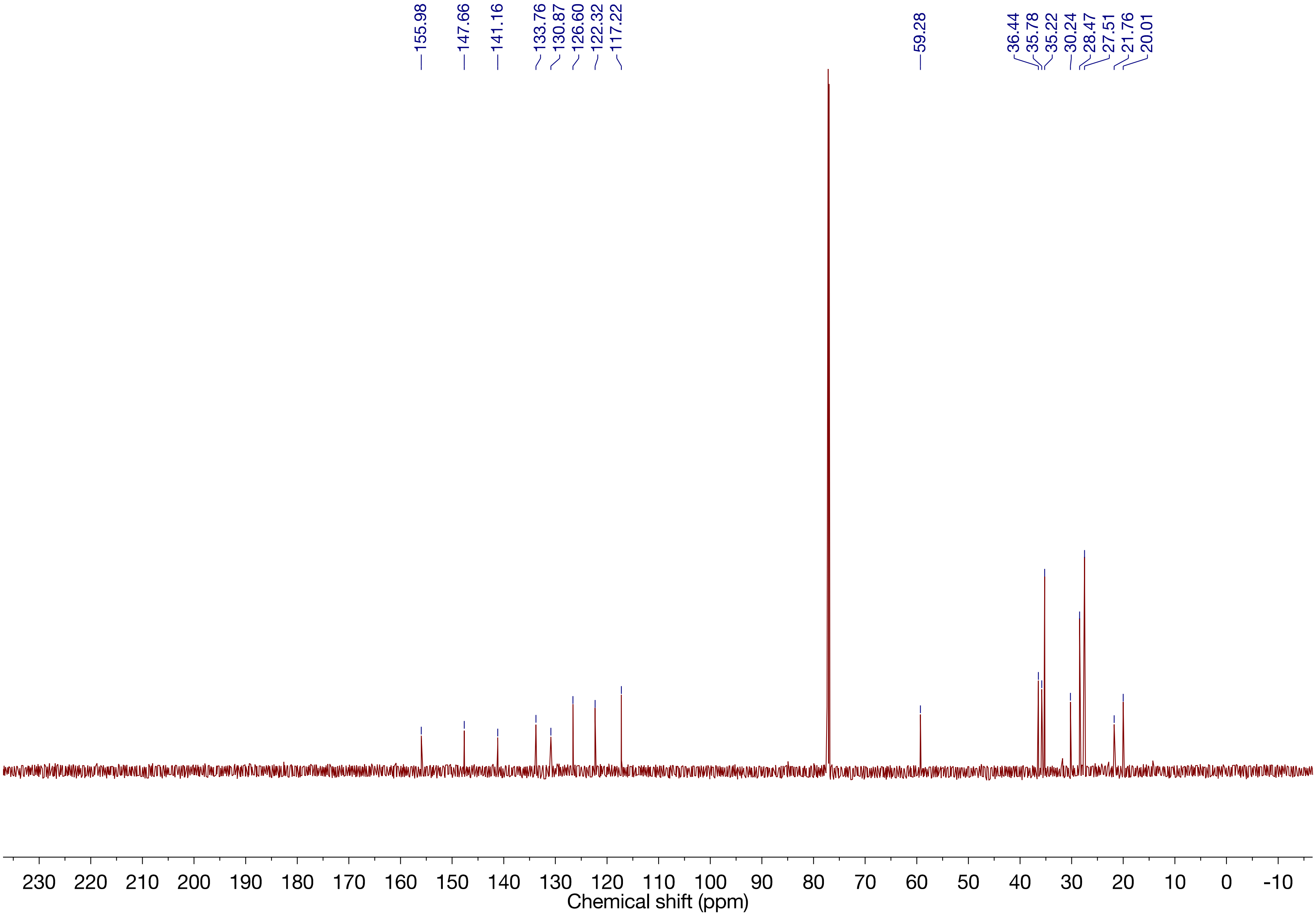
P21

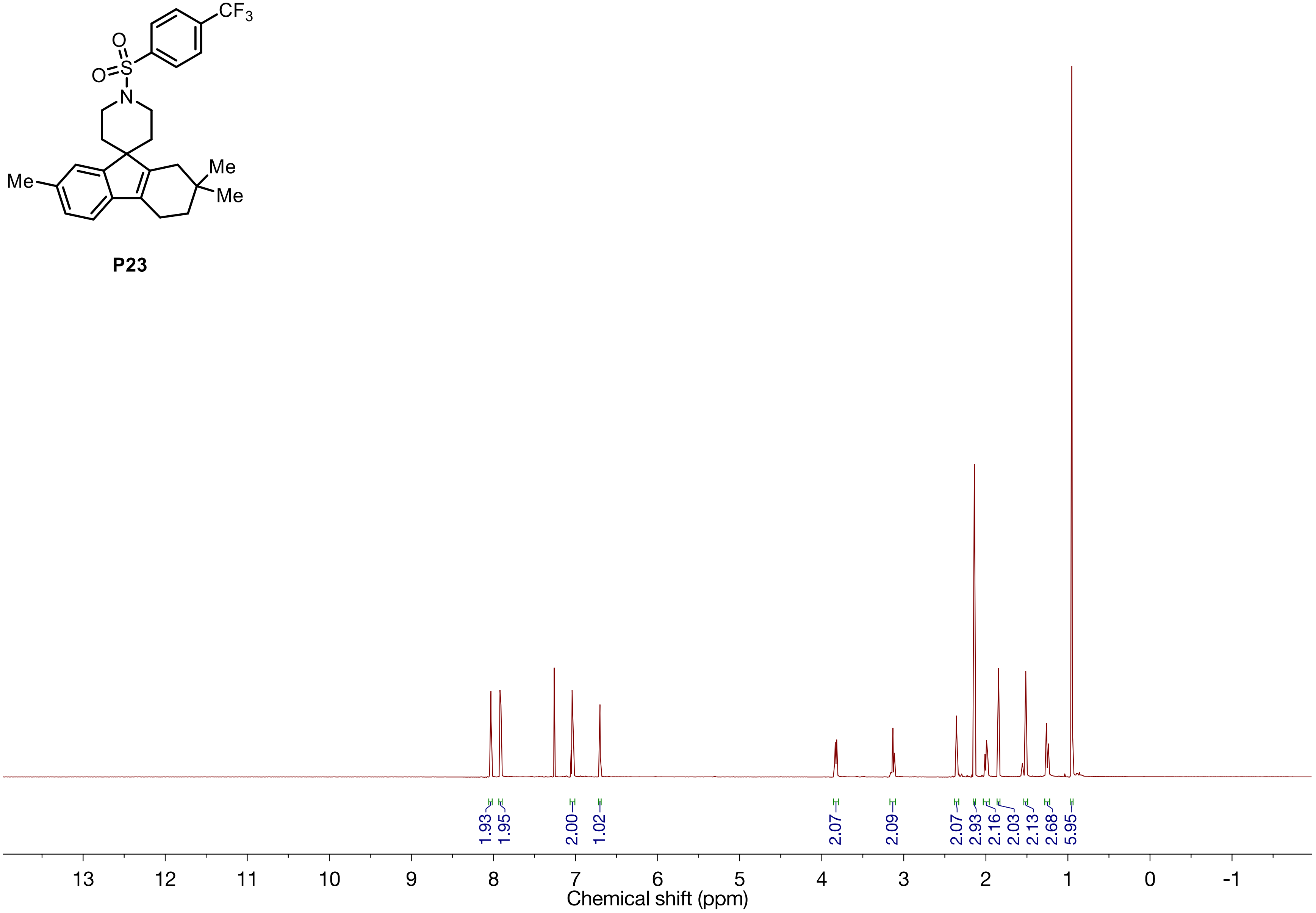

153.29
149.06
141.80
132.57
130.98
126.86
125.36
117.54
52.03
36.62
35.78
32.03
30.31
28.44
25.80
22.84
21.93
19.97
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)



Me
Me
Me
0.98
1.92
4.67
3.88
2.11
2.00
2.08
2.35
5.83
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

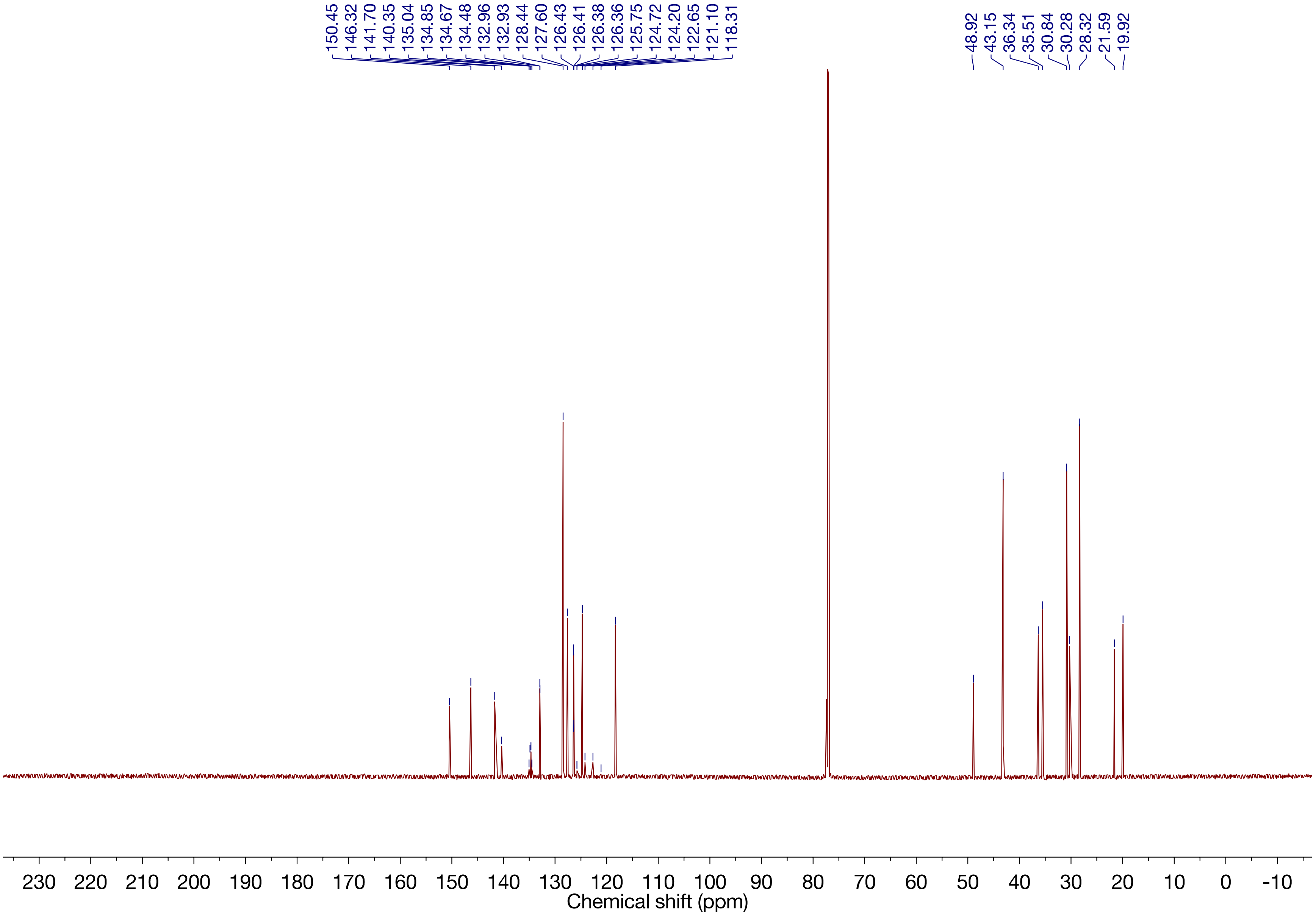
P22


155.98
147.66
141.16
133.76
130.87
126.60
122.32
117.22
59.28
36.44
35.78
35.22
30.24
28.47
27.51
21.76
20.01
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

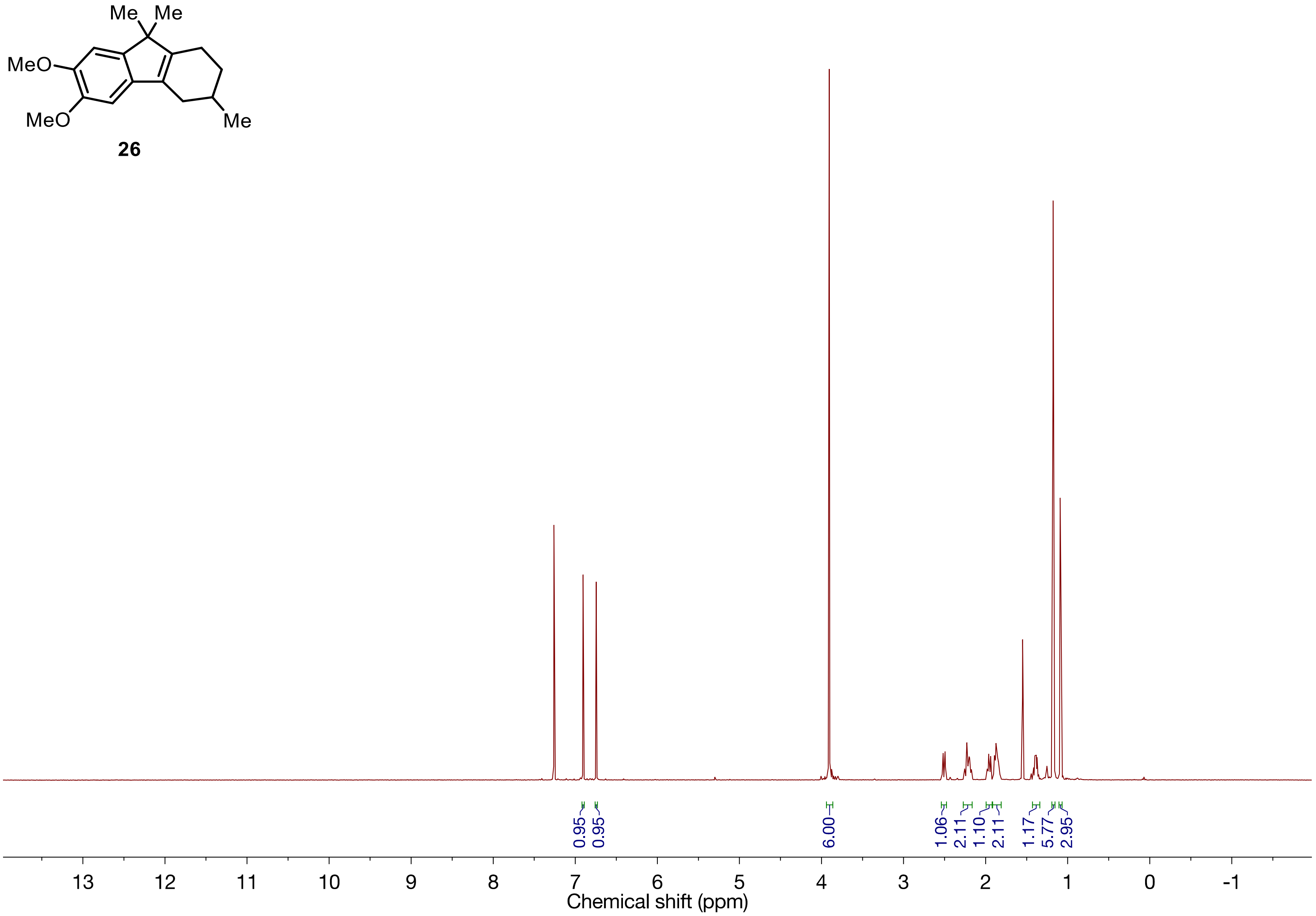

CF3
O
O=S
N
Me
Me
Me

P23

1.93
1.95
2.00
1.02
2.07
2.09
2.07
2.93
2.16
2.03
2.13
2.68
5.95
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

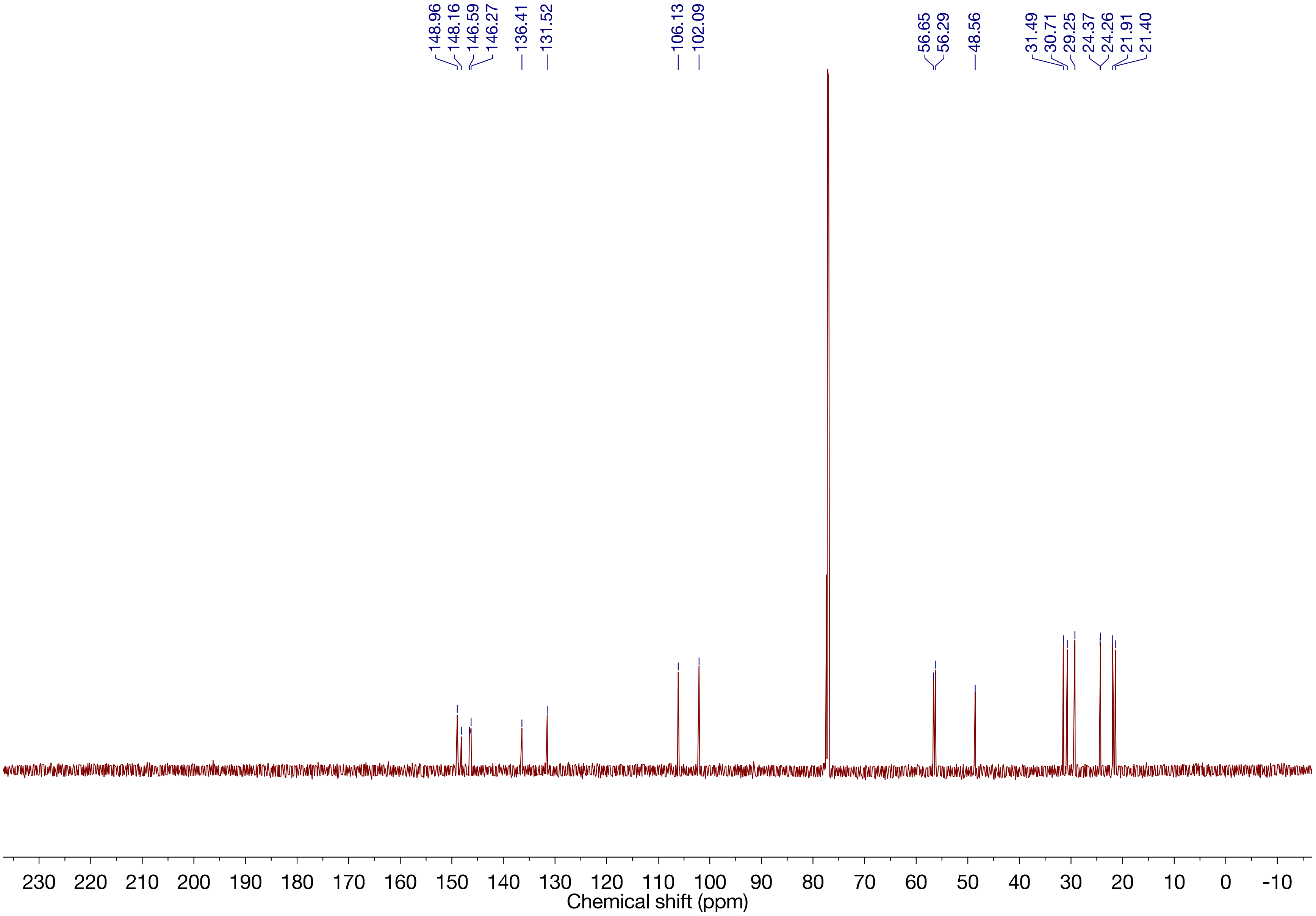


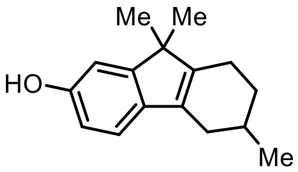
150.45
146.32
141.70
140.35
135.04
134.85
134.67
134.48
132.96
132.93
128.44
127.60
126.43
126.41
126.38
126.36
125.75
124.72
124.20
122.65
121.10
118.31
48.92
43.15
36.34
35.51
30.84
30.28
28.32
21.59
19.92
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



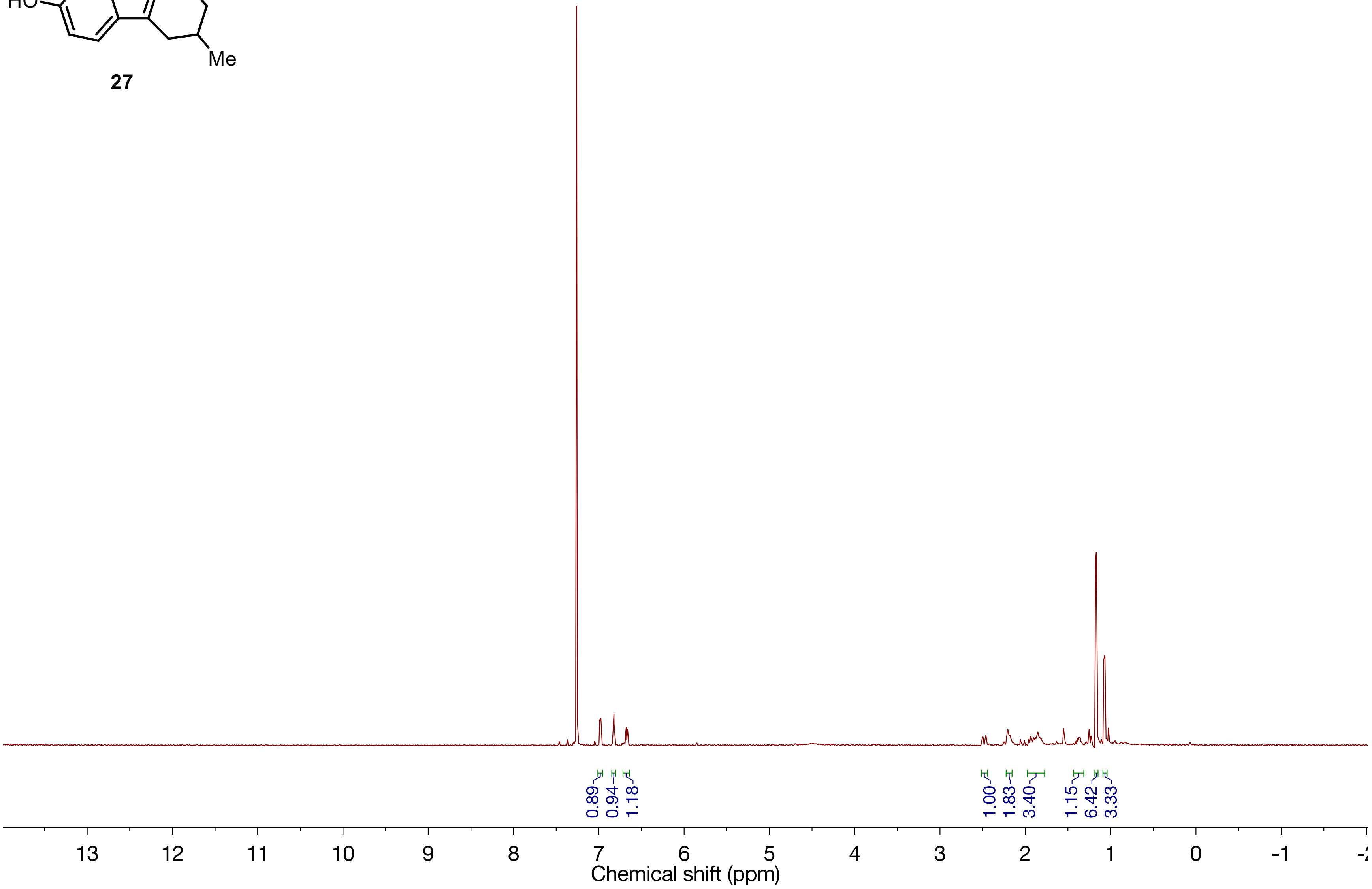
26

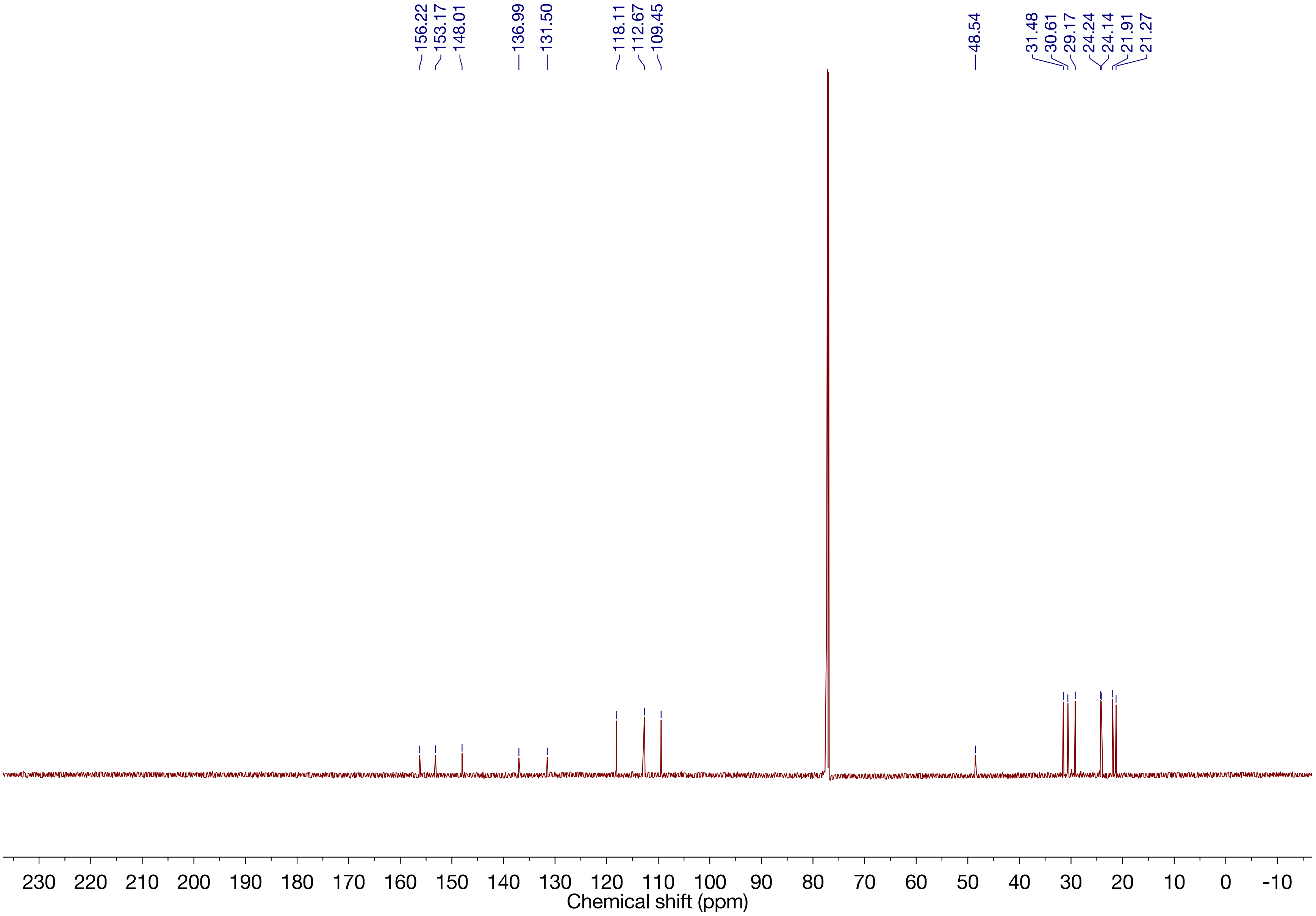
Me
Me
MeO
MeO
Me
0.95
0.95
6.00
1.06
2.11
1.10
2.11
1.17
5.77
2.95
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

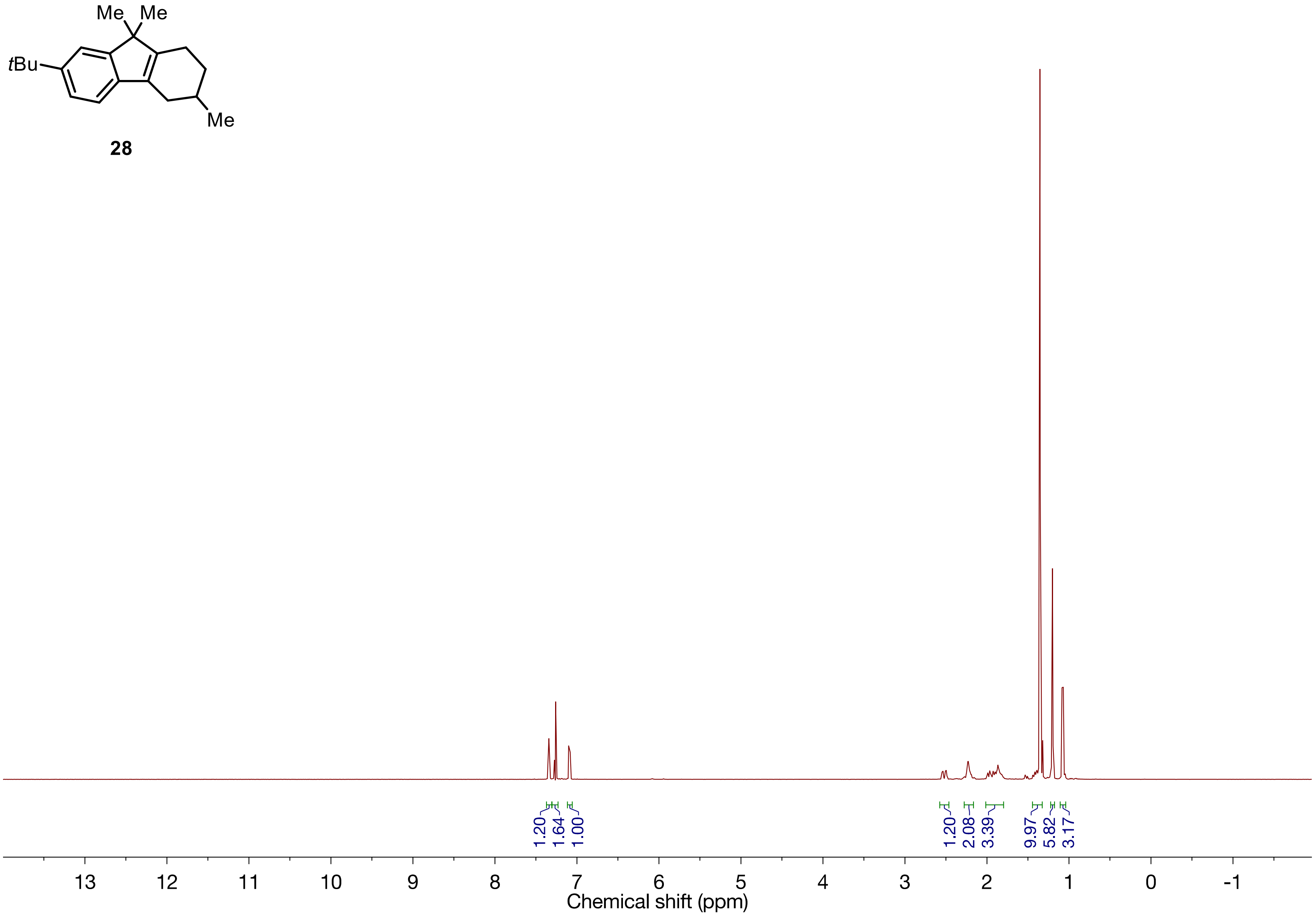

148.96
148.16
146.59
146.27
136.41
131.52
106.13
102.09
56.65
56.29
48.56
31.49
30.71
29.25
24.37
24.26
21.91
21.40
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
HO
Me

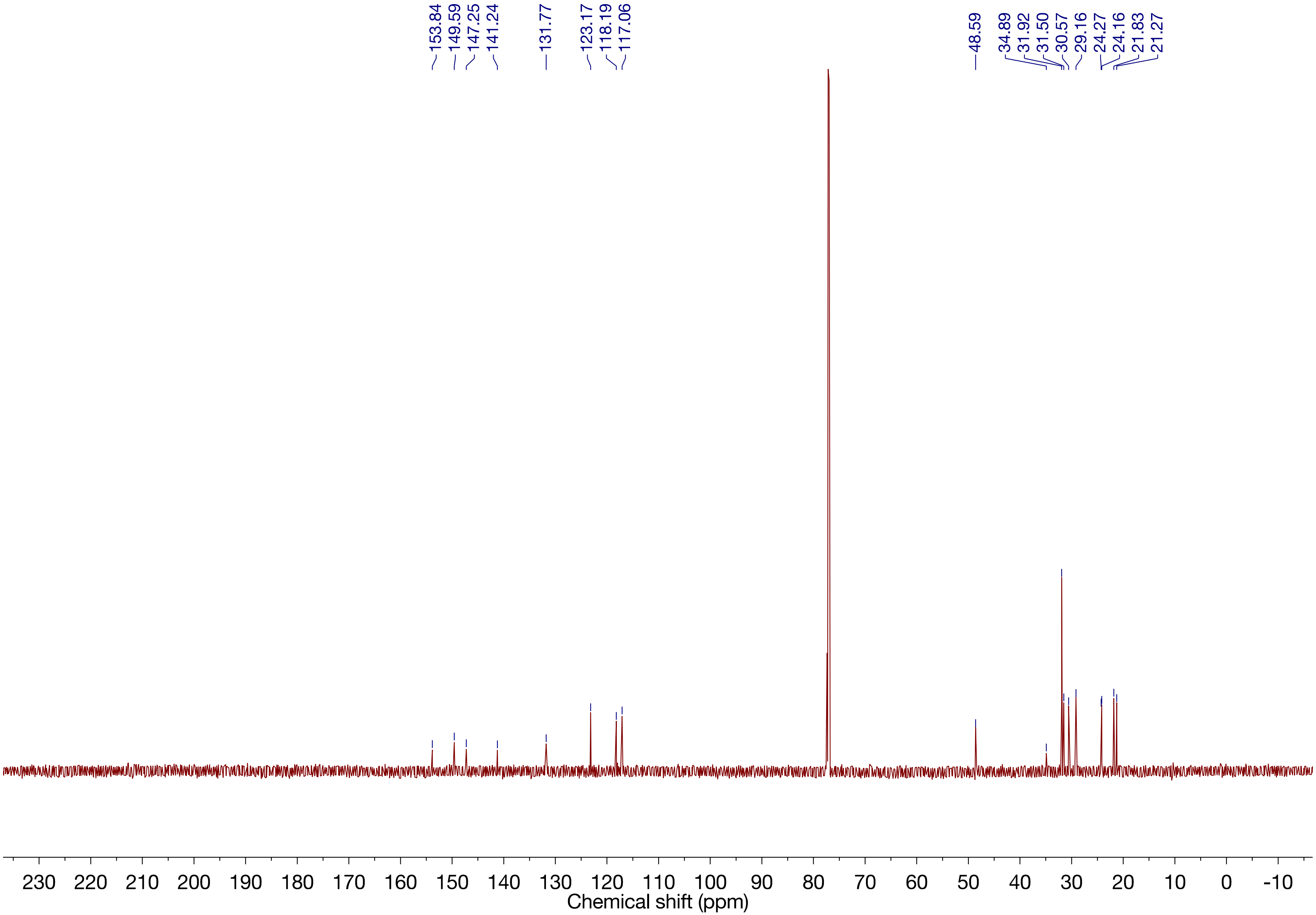
27

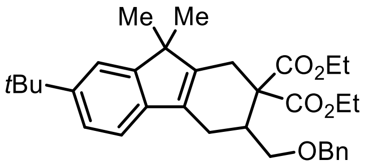

0.89
0.94
1.18
1.00
1.83
3.40
1.15
6.42
3.33
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


156.22
153.17
148.01
136.99
131.50
118.11
112.67
109.45
48.54
31.48
30.61
29.17
24.24
24.14
21.91
21.27
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
*t*Bu
Me
1.20
1.64
1.00
1.20
2.08
3.39
9.97
5.82
3.17
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

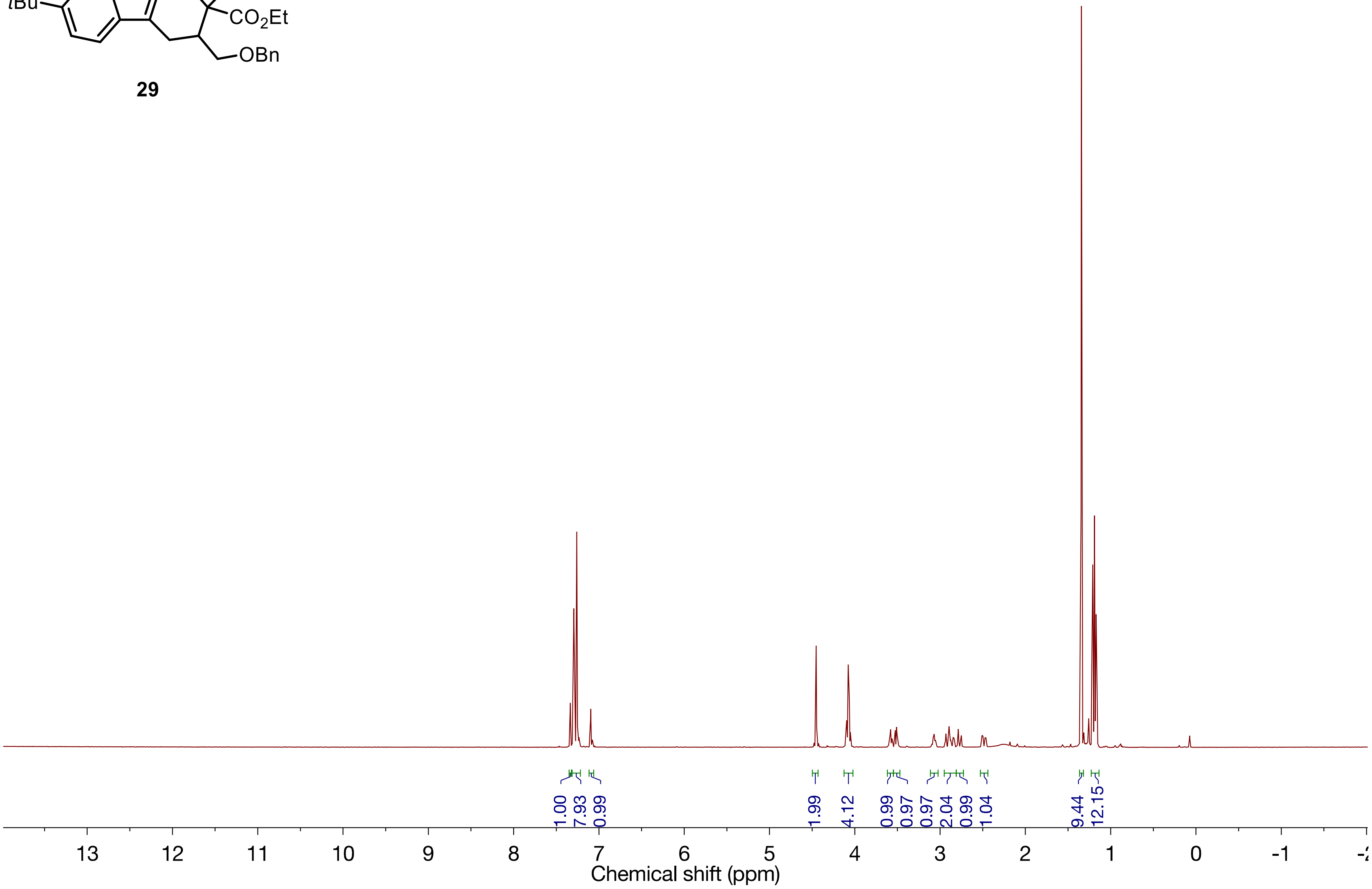
28


153.84
149.59
147.25
141.24
131.77
123.17
118.19
117.06
48.59
34.89
31.92
31.50
30.57
29.16
24.27
24.16
21.83
21.27
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

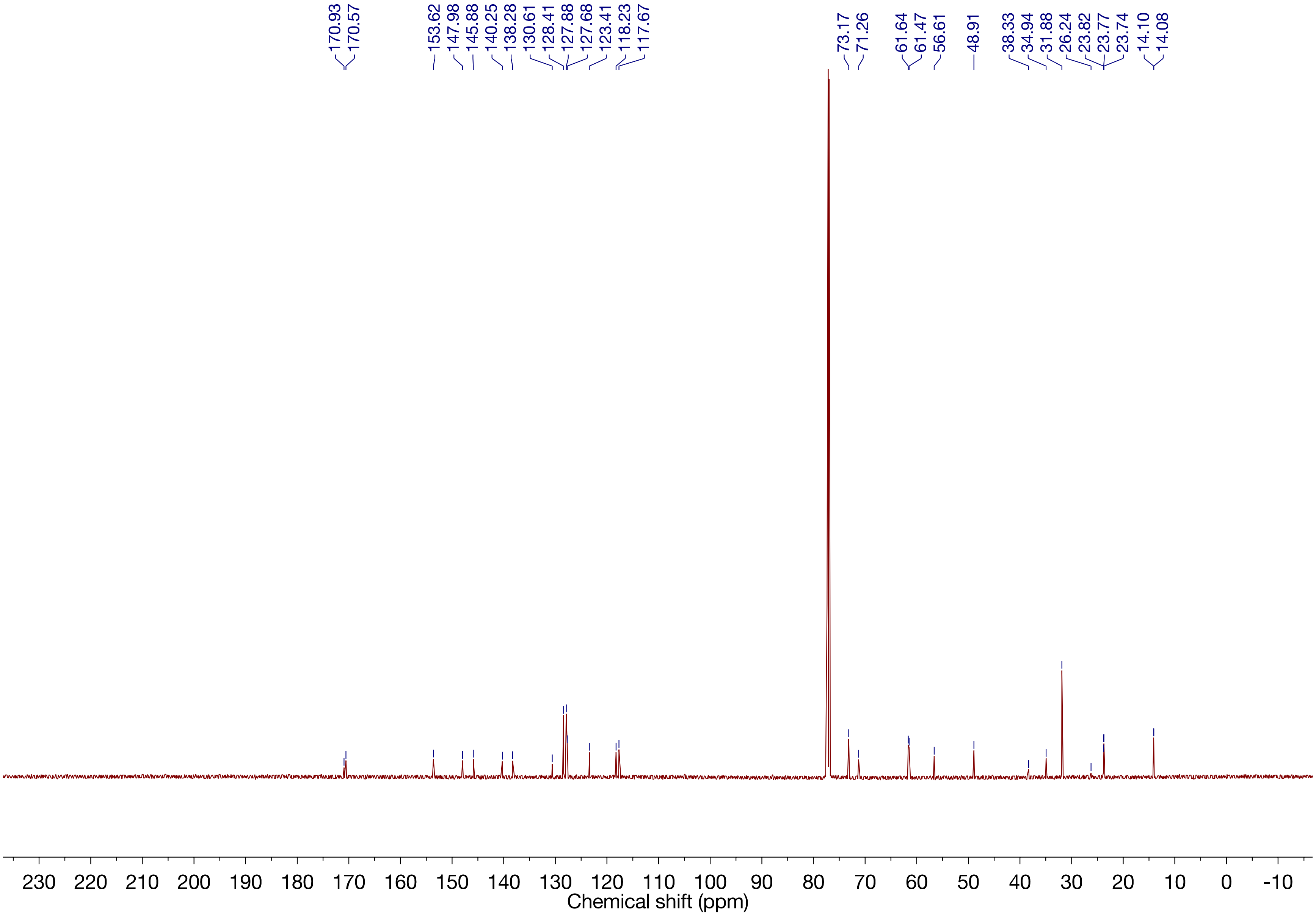


Me
Me
tBu
CO2Et
CO2Et
OBn

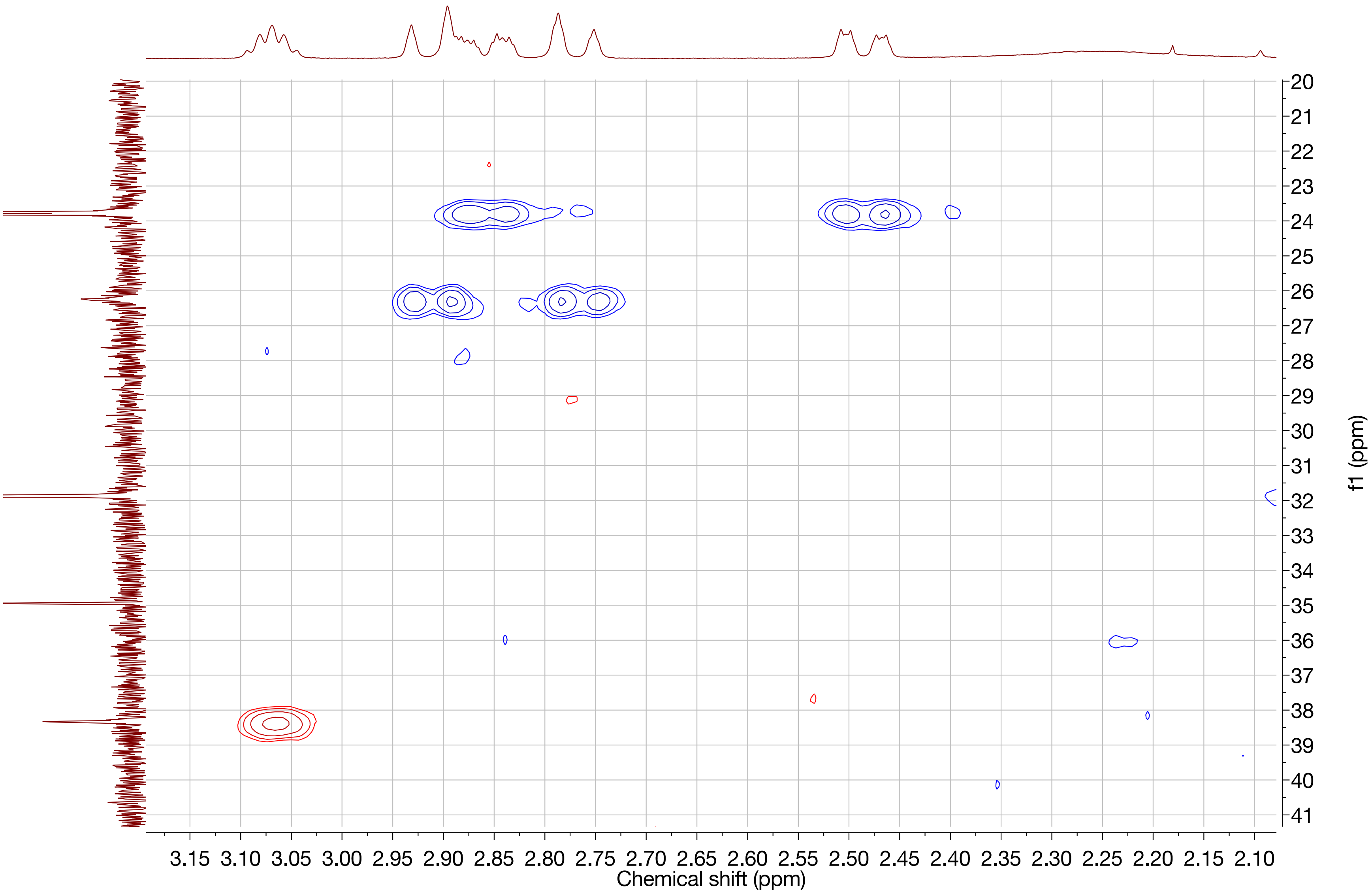
29

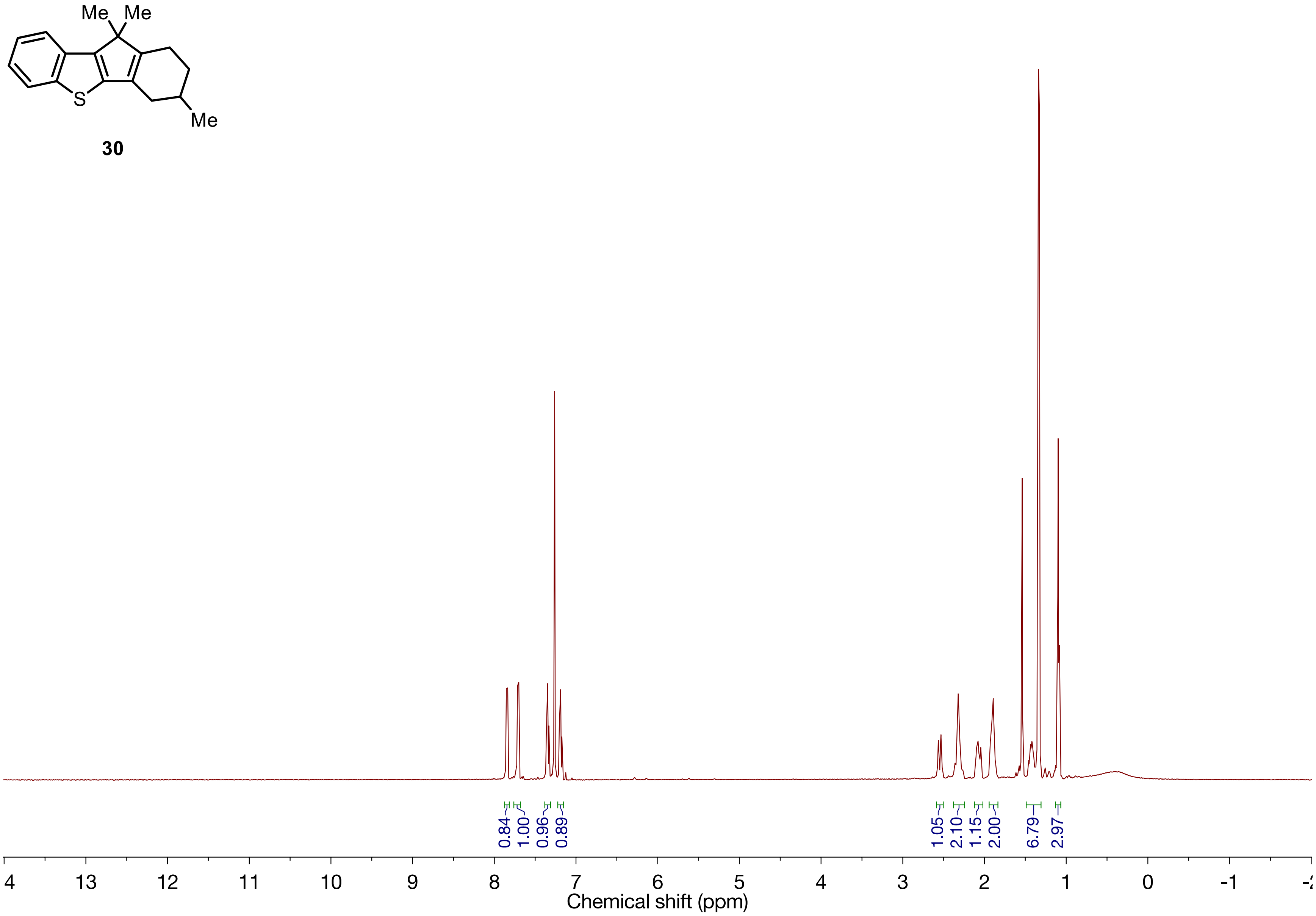


1.00
7.93
0.99
1.99
4.12
0.99
0.97
0.97
2.04
0.99
1.04
9.44
12.15
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

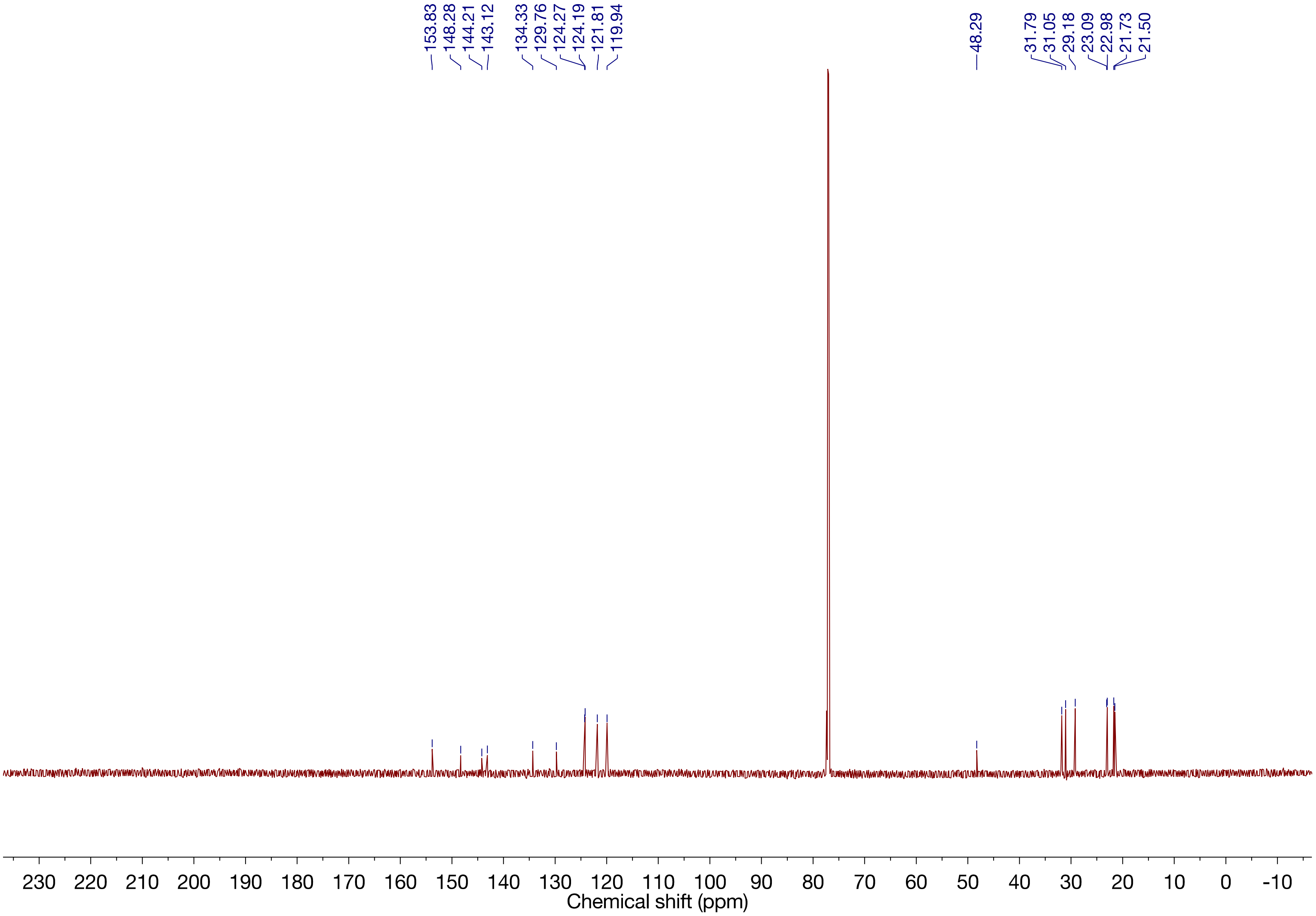


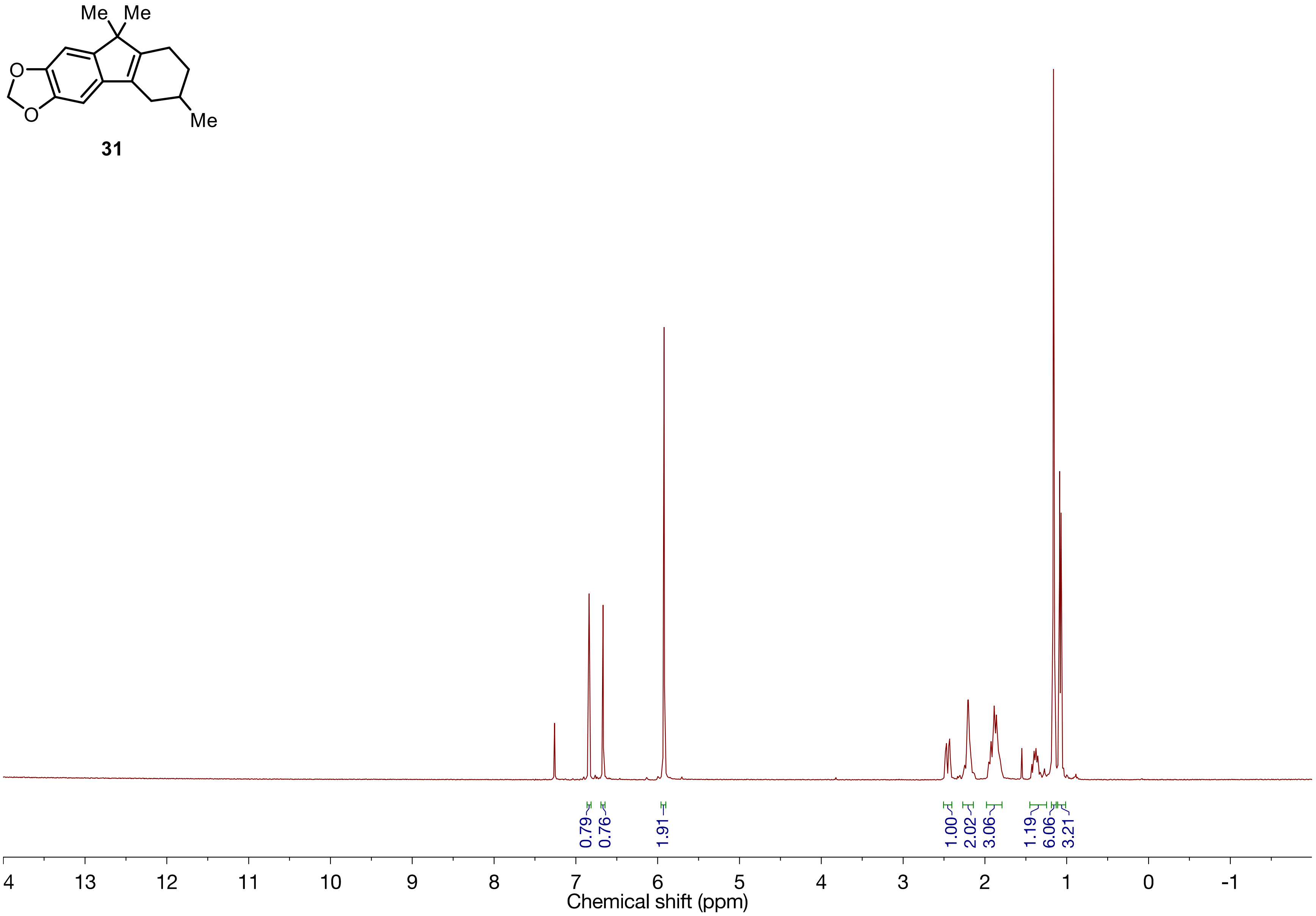
170.93
170.57
153.62
147.98
145.88
140.25
138.28
130.61
128.41
127.88
127.68
123.41
118.23
117.67
73.17
71.26
61.64
61.47
56.61
48.91
38.33
34.94
31.88
26.24
23.82
23.77
23.74
14.10
14.08
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

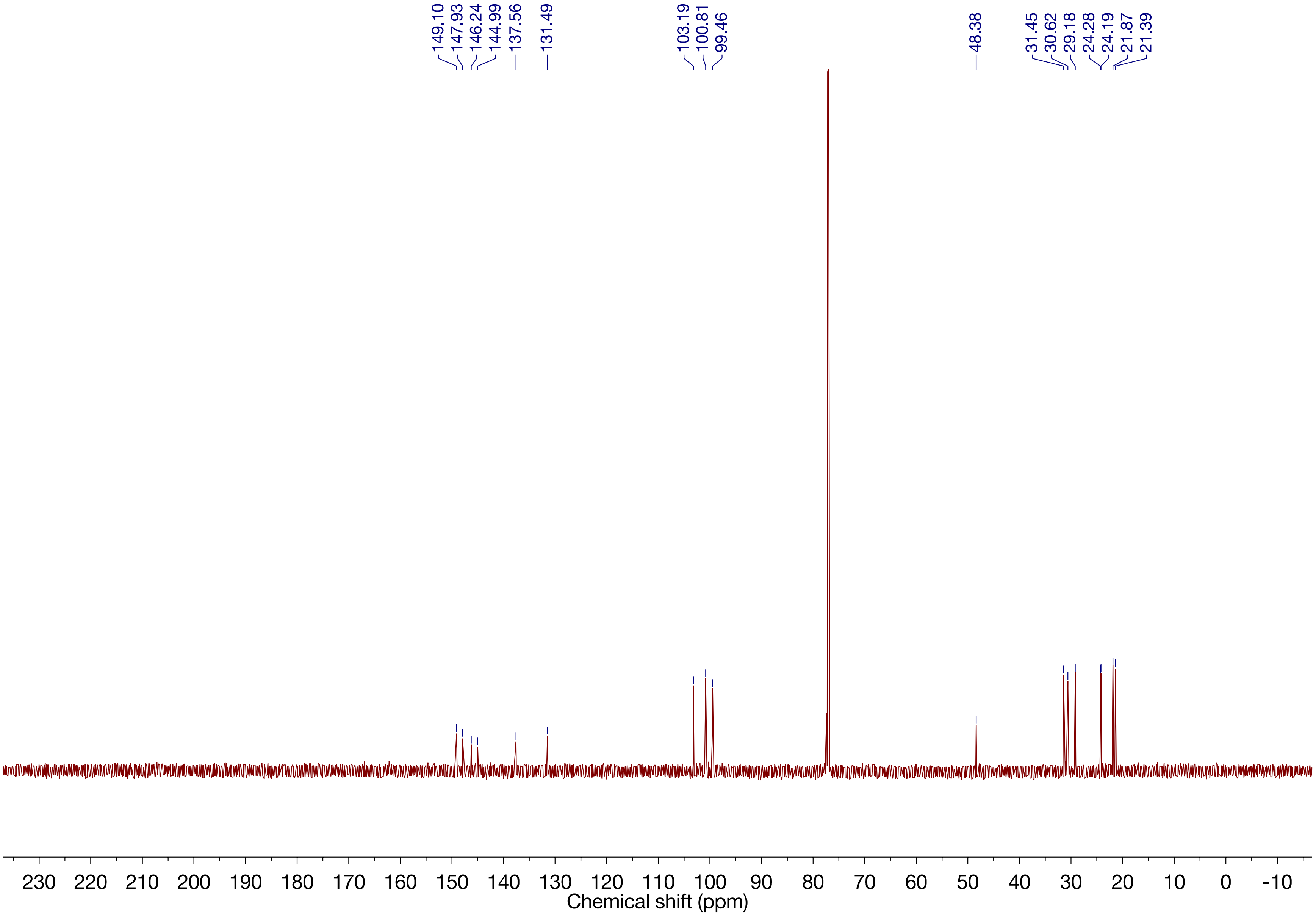

3.15
3.10
3.05
3.00
2.95
2.90
2.85
2.80
2.75
2.70
2.65
2.60
2.55
2.50
2.45
2.40
2.35
2.30
2.25
2.20
2.15
2.10
Chemical shift (ppm)
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
f1 (ppm)

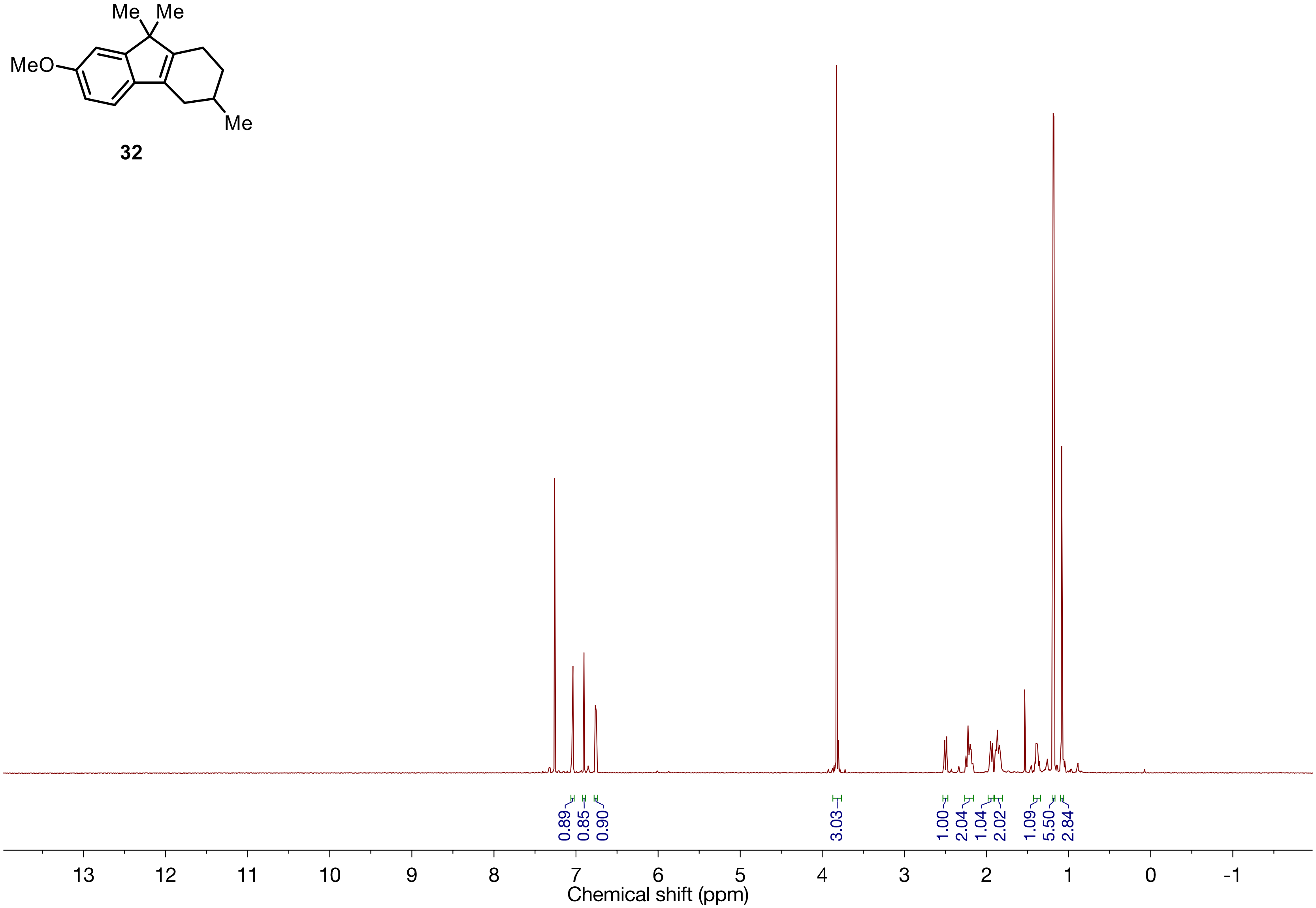

Me
Me
Me
S
0.84
1.00
0.96
0.89
1.05
2.10
1.15
2.00
6.79
2.97
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

30

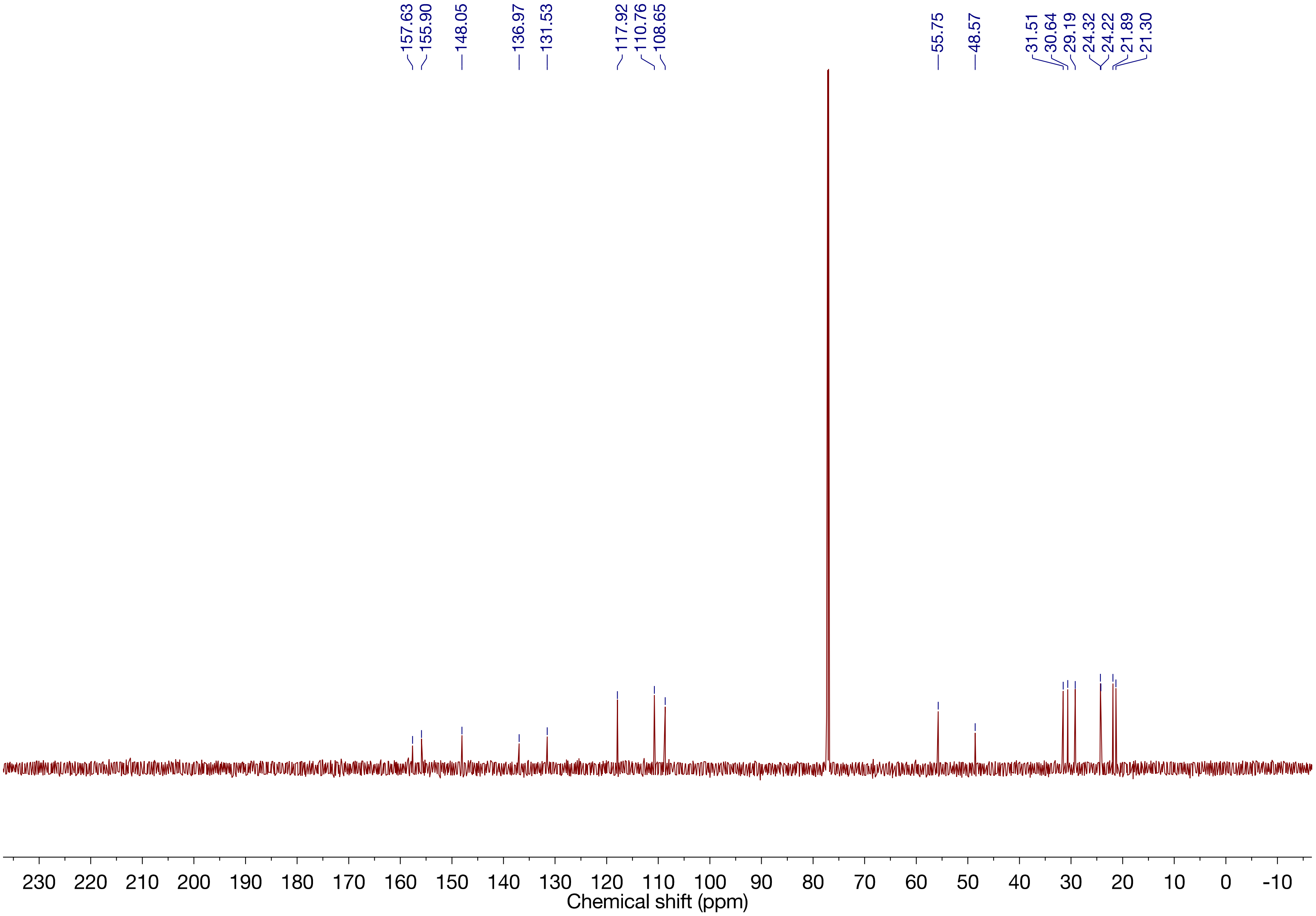

153.83
148.28
144.21
143.12
134.33
129.76
124.27
124.19
121.81
119.94
48.29
31.79
31.05
29.18
23.09
22.98
21.73
21.50
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

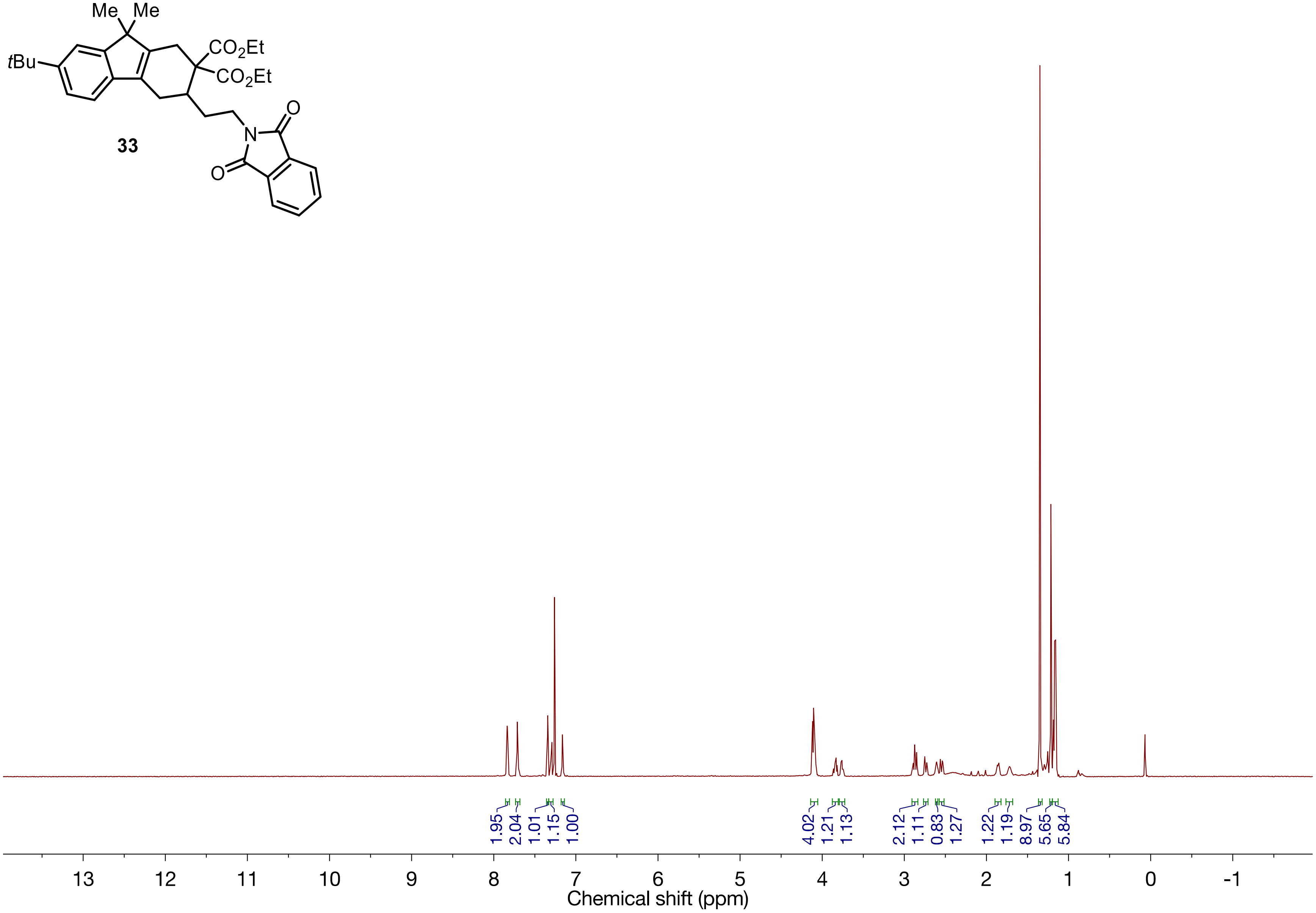

Me
Me
O
O
Me
31
0.79
0.76
1.91
1.00
2.02
3.06
1.19
6.06
3.21
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


149.10
147.93
146.24
144.99
137.56
131.49
103.19
100.81
99.46
48.38
31.45
30.62
29.18
24.28
24.19
21.87
21.39
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


32

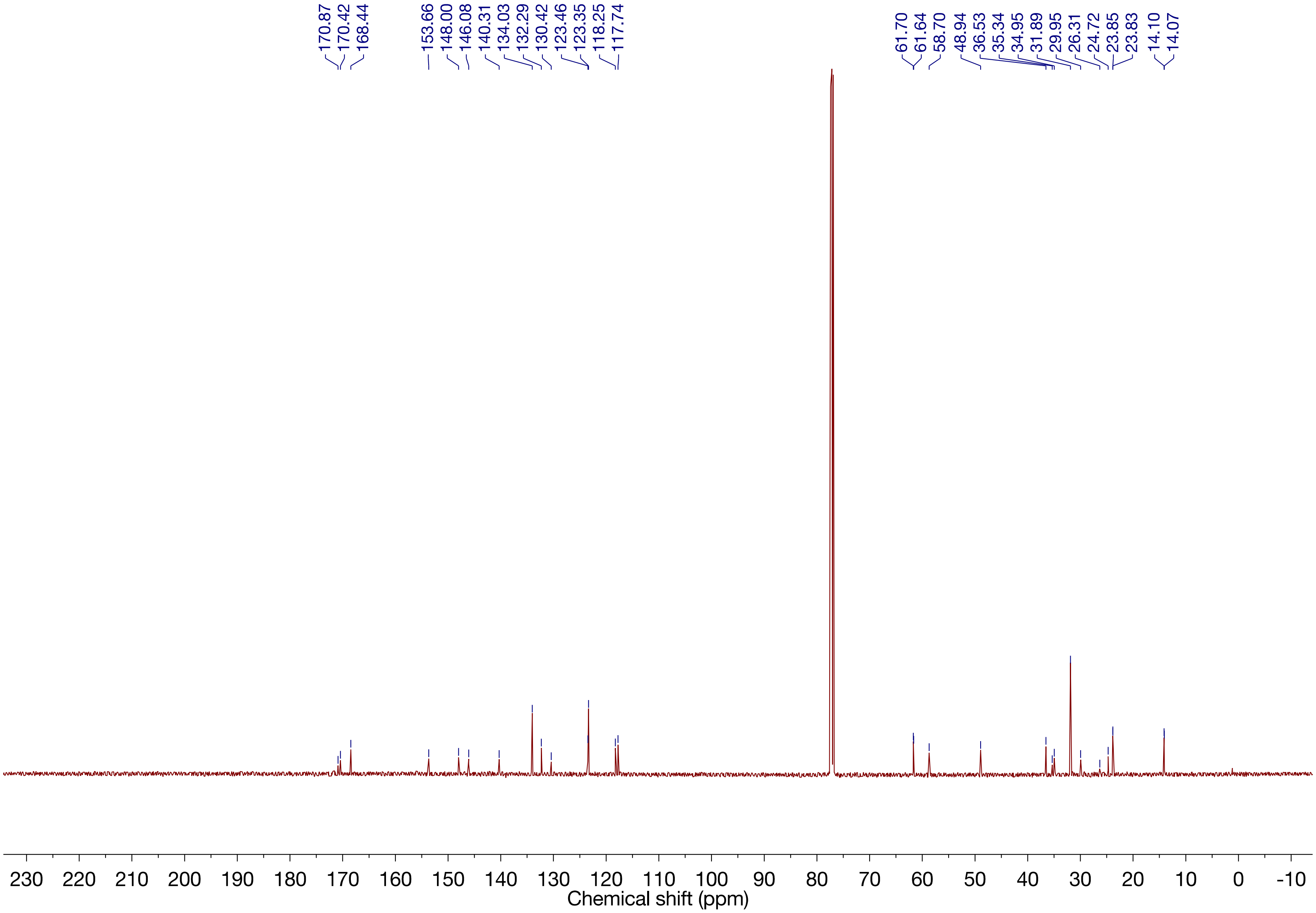
Me
Me
MeO
Me
0.89
0.85
0.90
3.03
1.00
2.04
1.04
2.02
1.09
5.50
2.84
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

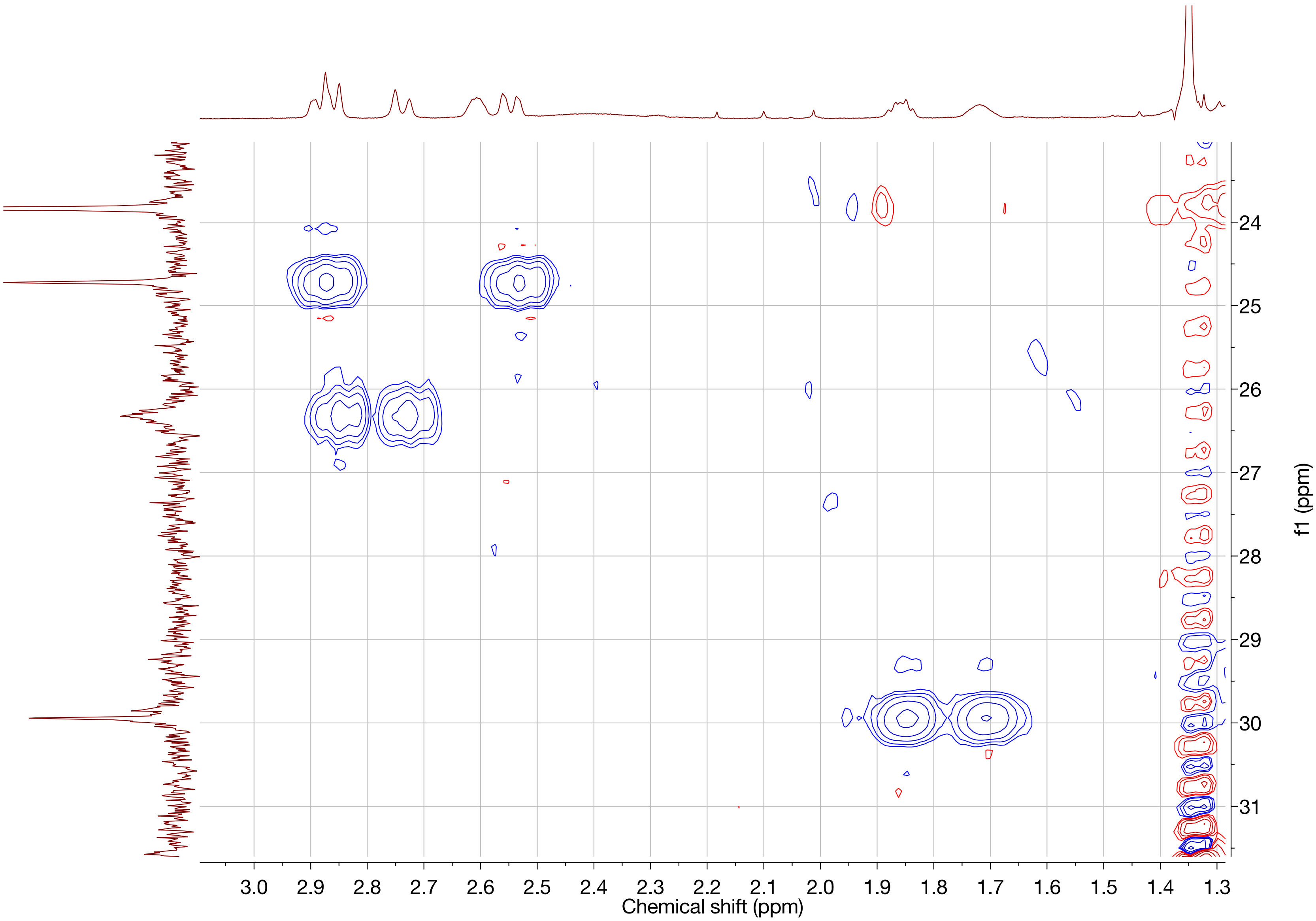

157.63
155.90
148.05
136.97
131.53
117.92
110.76
108.65
55.75
48.57
31.51
30.64
29.19
24.32
24.22
21.89
21.30
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

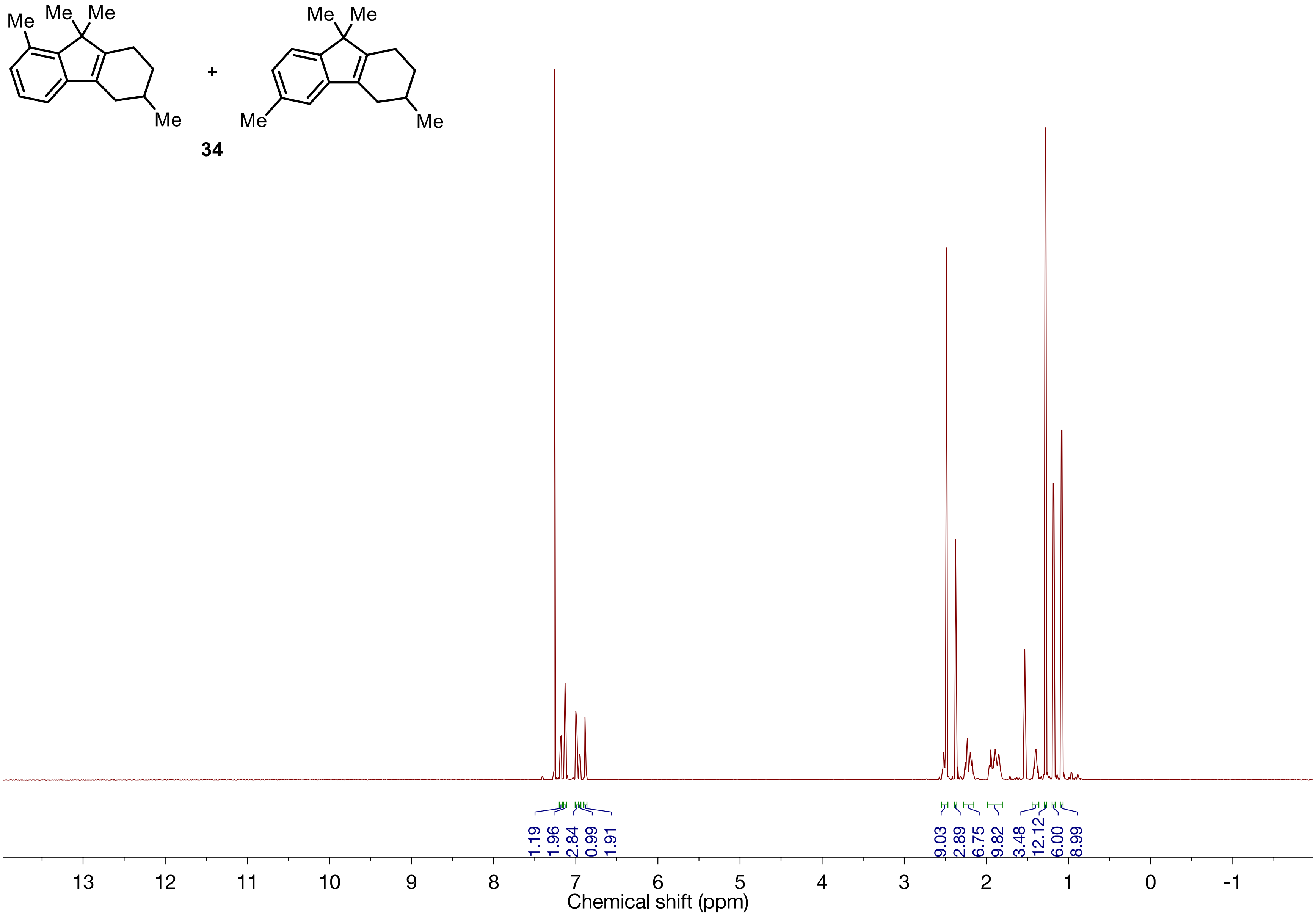

Me
Me
tBu
CO2Et
CO2Et
N
O
O

33

1.95
2.04
1.01
1.15
1.00
4.02
1.21
1.13
2.12
1.11
0.83
1.27
1.22
1.19
8.97
5.65
5.84
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

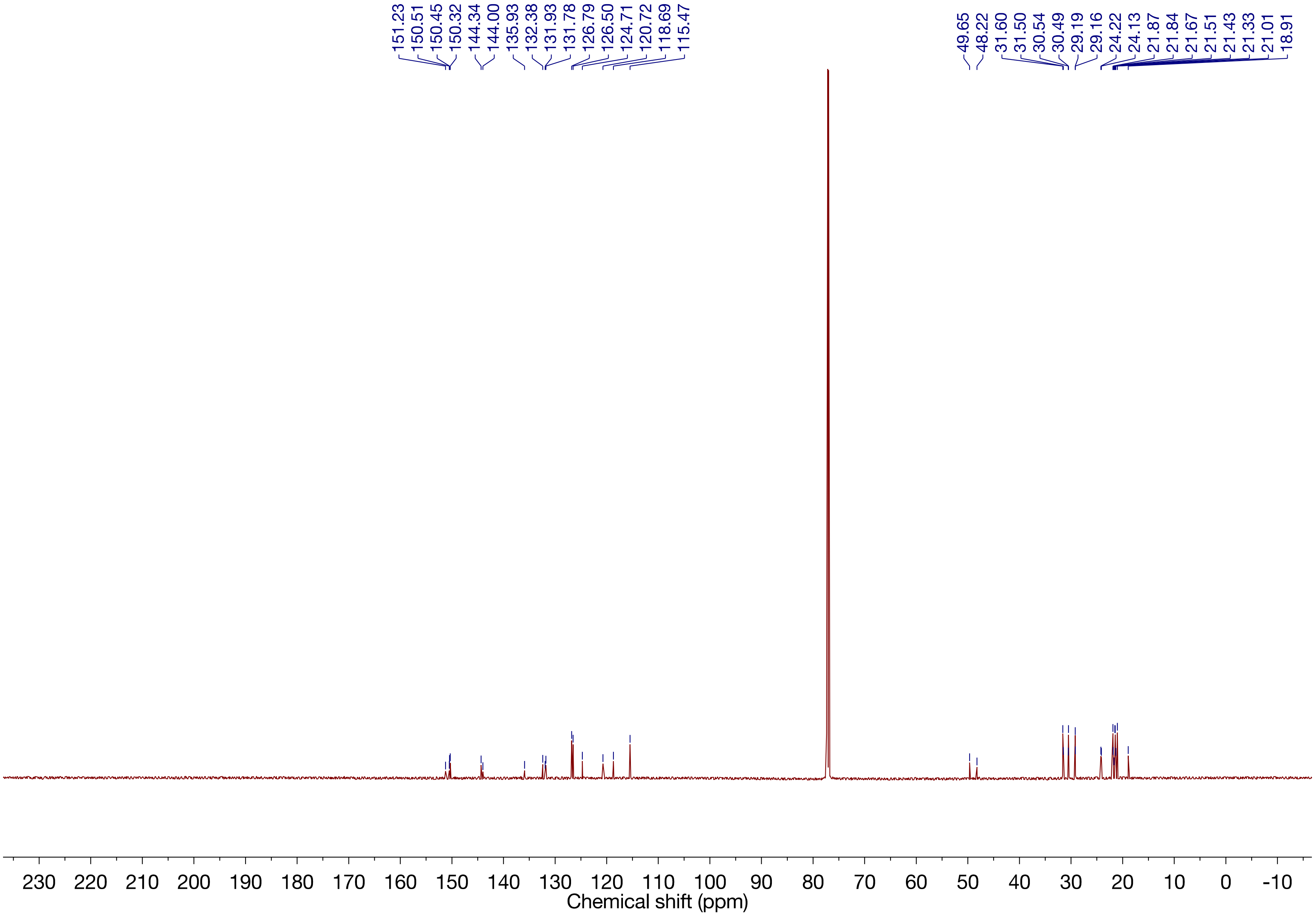

170.87
170.42
168.44
153.66
148.00
146.08
140.31
134.03
132.29
130.42
123.46
123.35
118.25
117.74
61.70
61.64
58.70
48.94
36.53
35.34
34.95
31.89
29.95
26.31
24.72
23.85
23.83
14.10
14.07
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

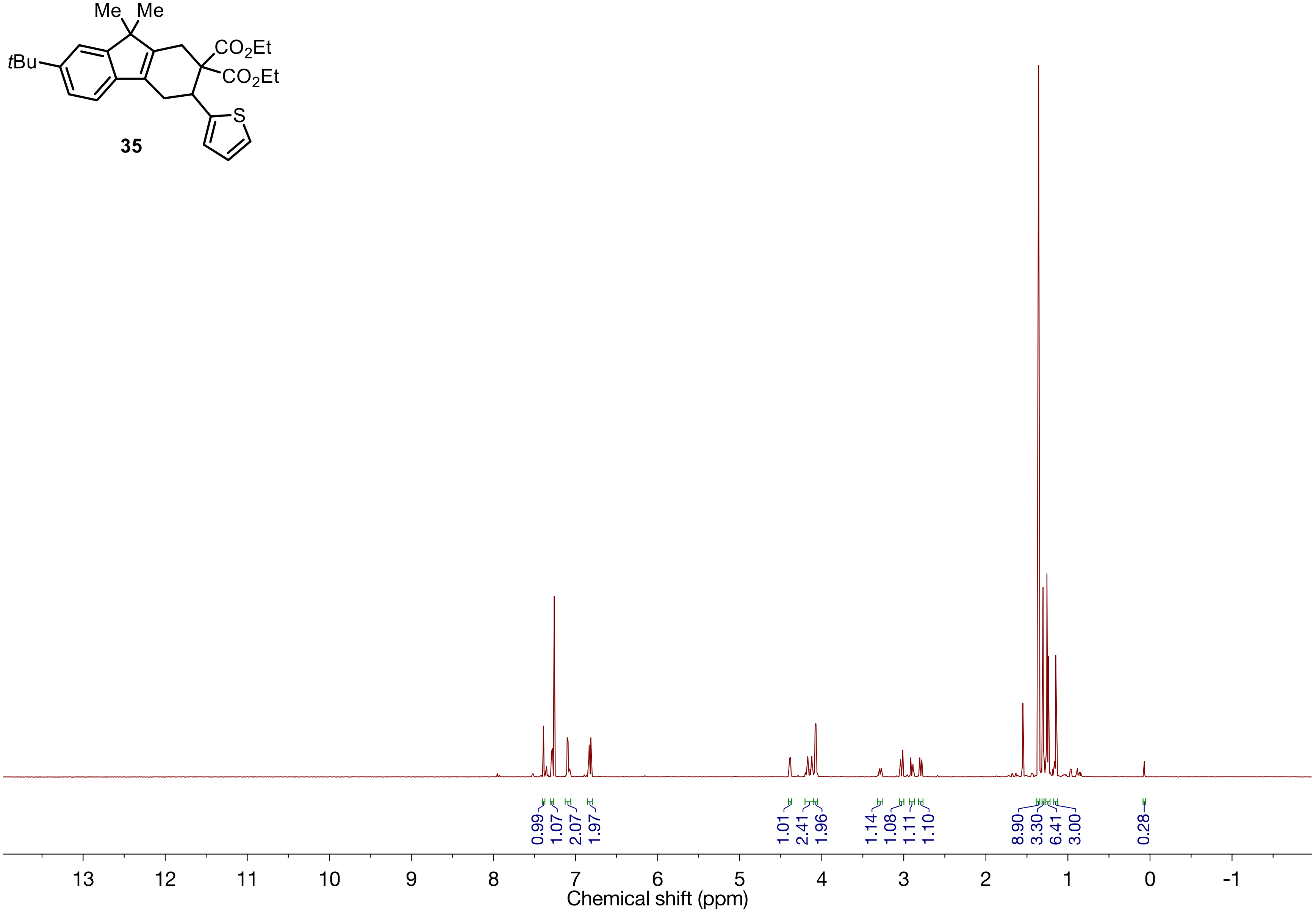

3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
Chemical shift (ppm)
24
25
26
27
28
29
30
31
f1 (ppm)


Me
Me
Me
Me
+
Me
Me
Me
Me
Me

34

1.19
1.96
2.84
0.99
1.91
9.03
2.89
6.75
9.82
3.48
12.12
6.00
8.99
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

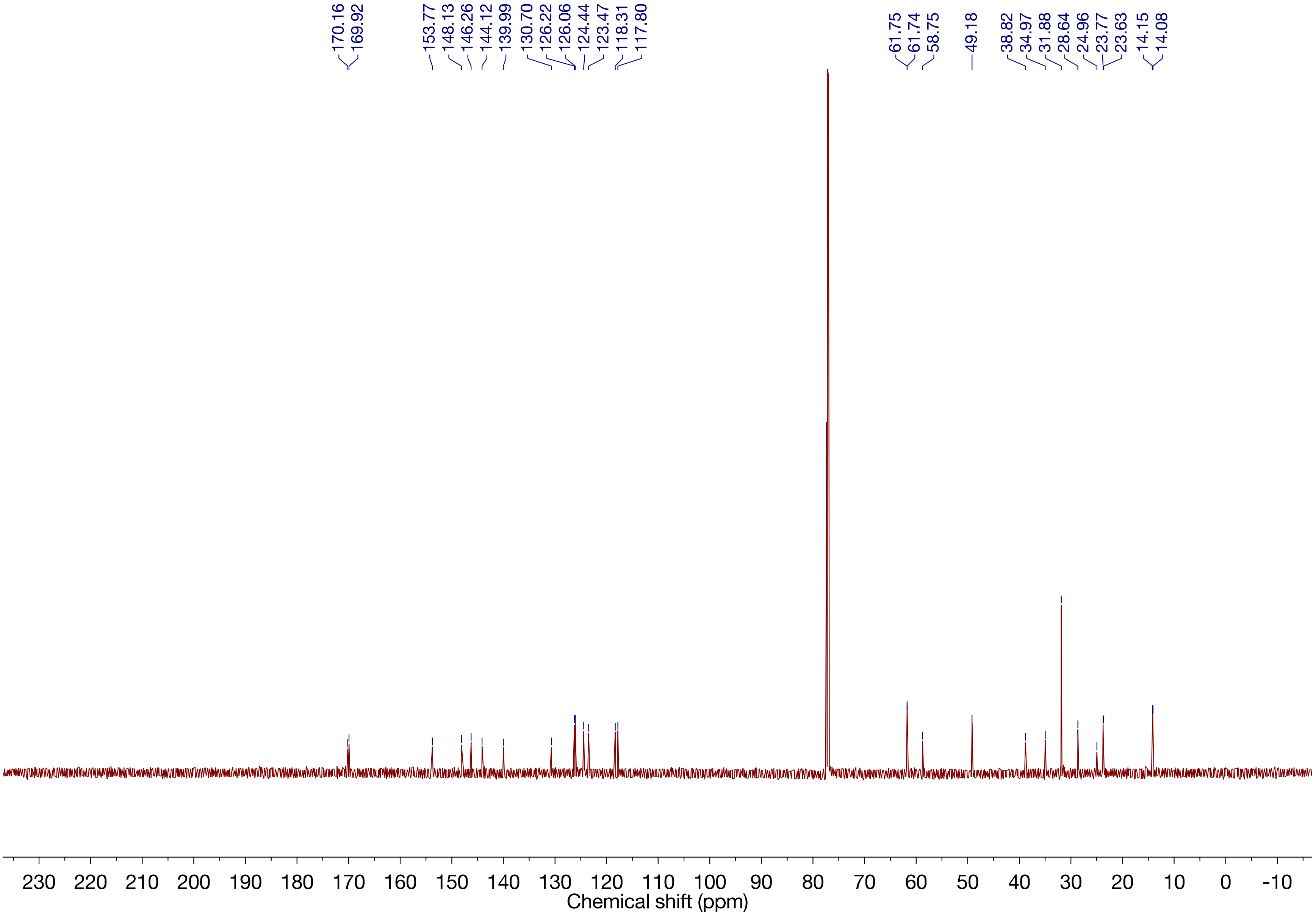

151.23
150.51
150.45
150.32
144.34
144.00
135.93
132.38
131.93
131.78
126.79
126.50
124.71
120.72
118.69
115.47
49.65
48.22
31.60
31.50
30.54
30.49
29.19
29.16
24.22
24.13
21.87
21.84
21.67
21.51
21.43
21.33
21.01
18.91
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

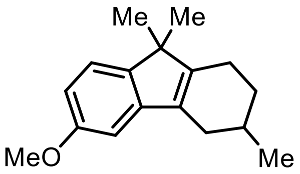


Me
Me
tBu
CO2Et
CO2Et
S

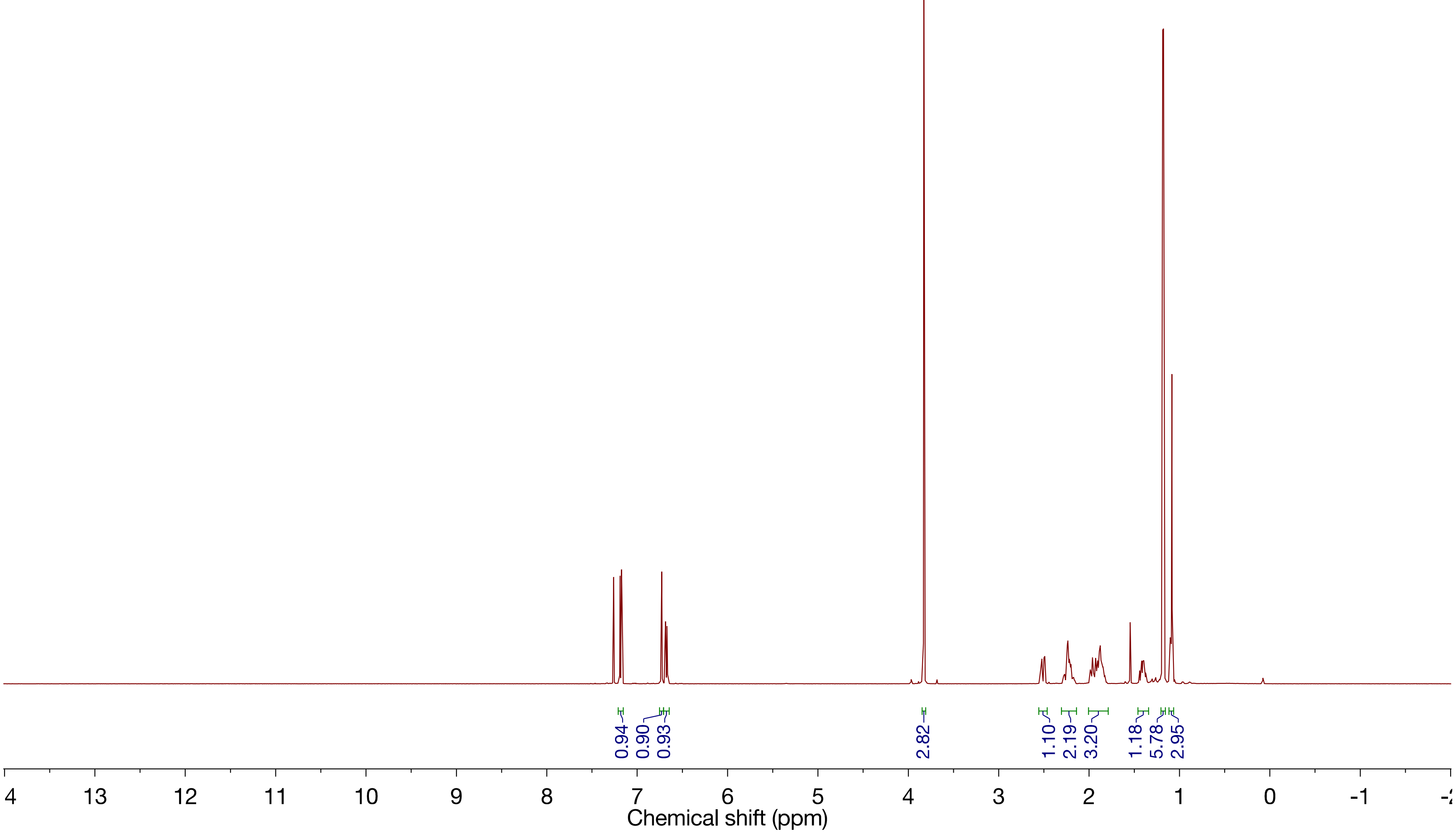
35

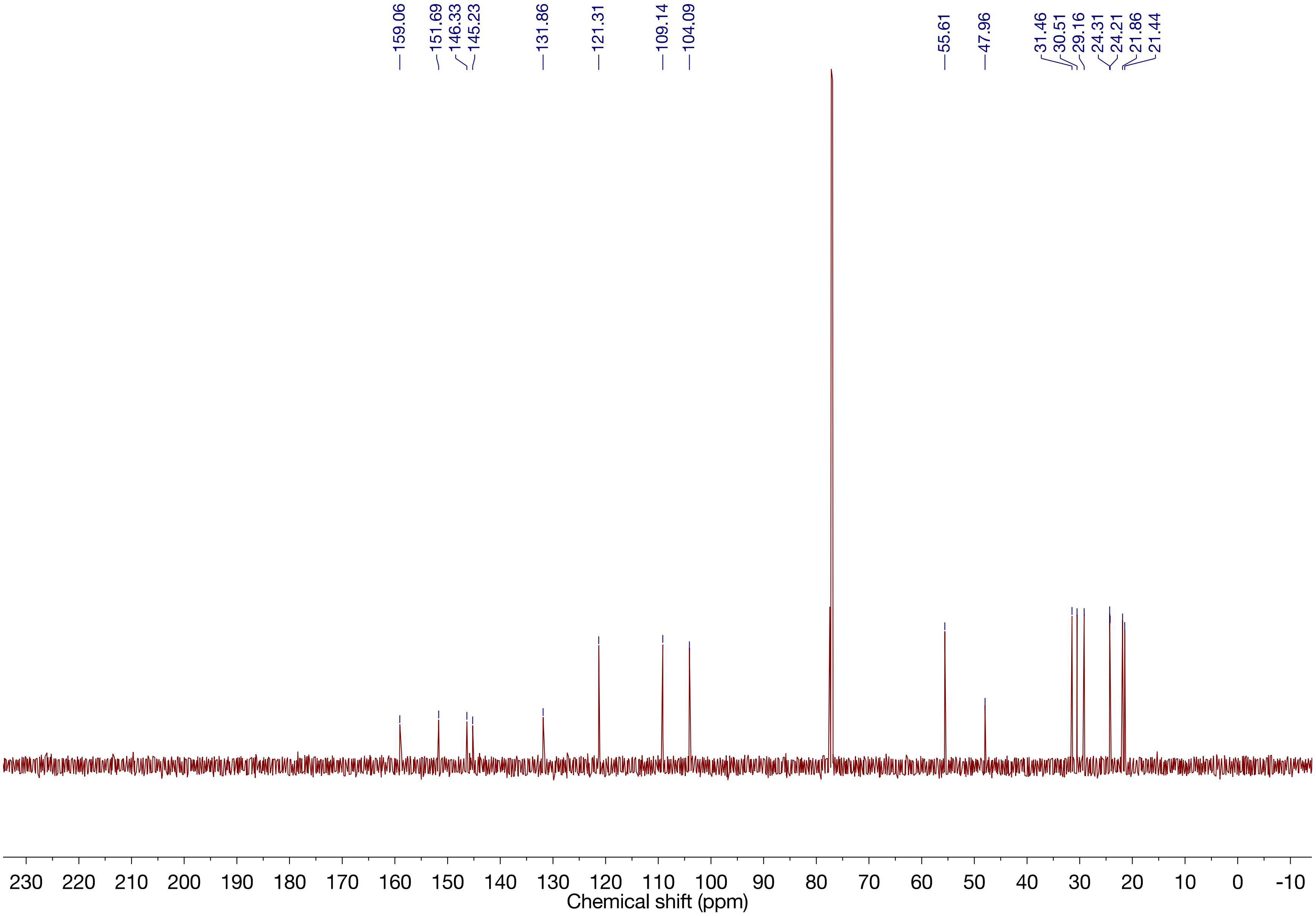
0.99
1.07
2.07
1.97
1.01
2.41
1.96
1.14
1.08
1.11
1.10
8.90
3.30
6.41
3.00
0.28
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


170.16
169.92
153.77
148.13
146.26
144.12
139.99
130.70
126.22
126.06
124.44
123.47
118.31
117.80
61.75
61.74
58.75
49.18
38.82
34.97
31.88
28.64
24.96
23.77
23.63
14.15
14.08
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
MeO
Me

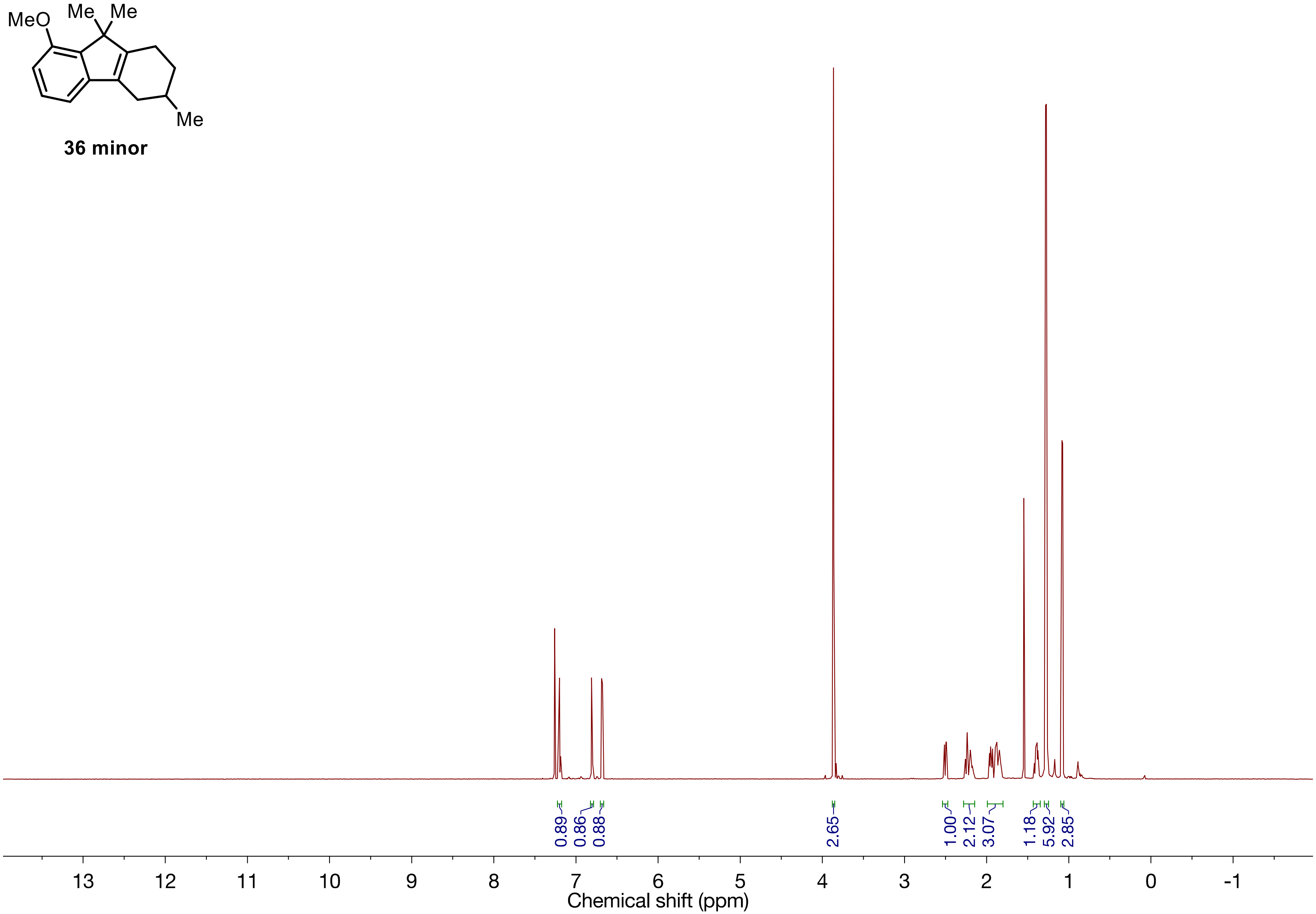
36 major

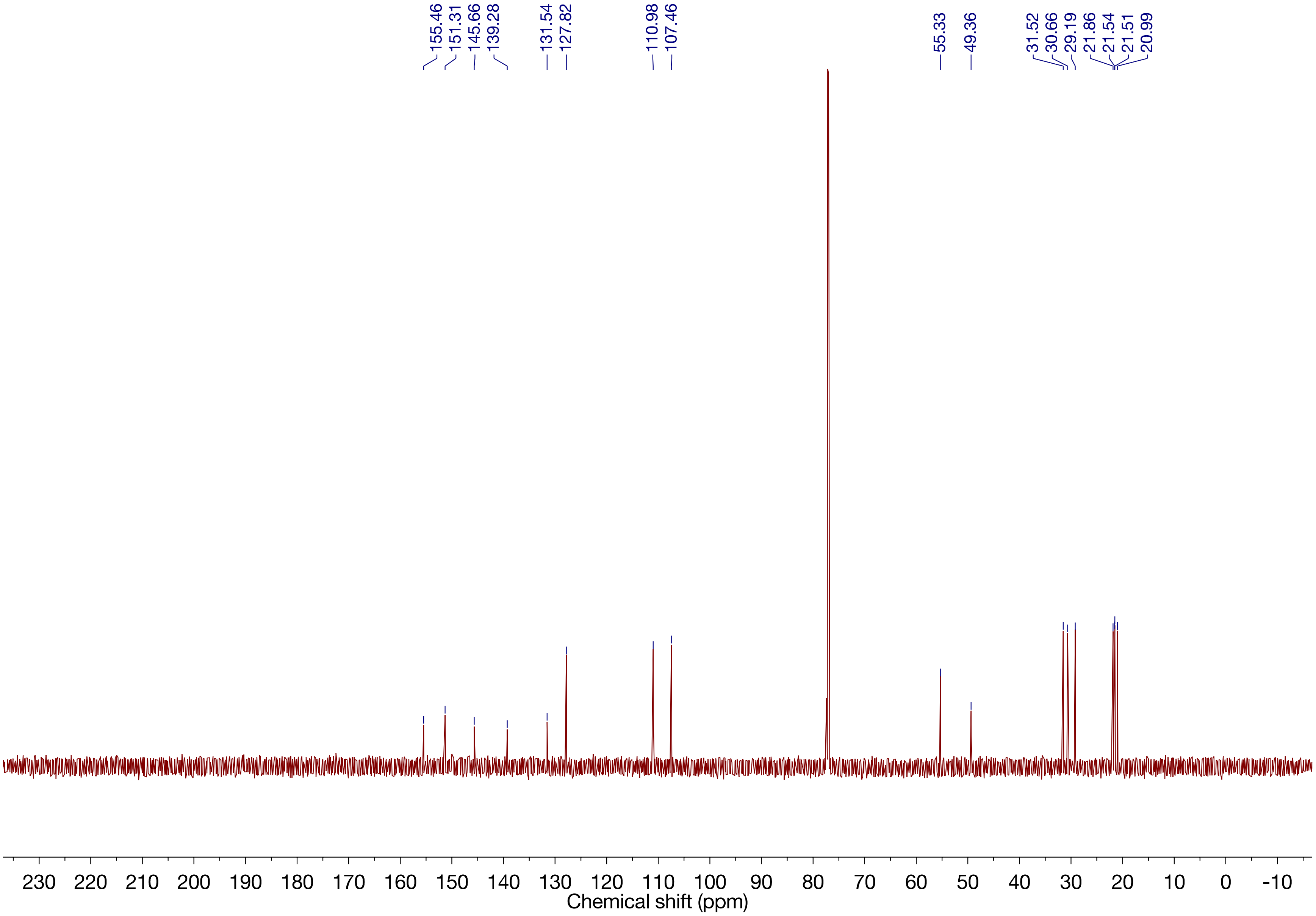

0.94
0.90
0.93
2.82
1.10
2.19
3.20
1.18
5.78
2.95
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

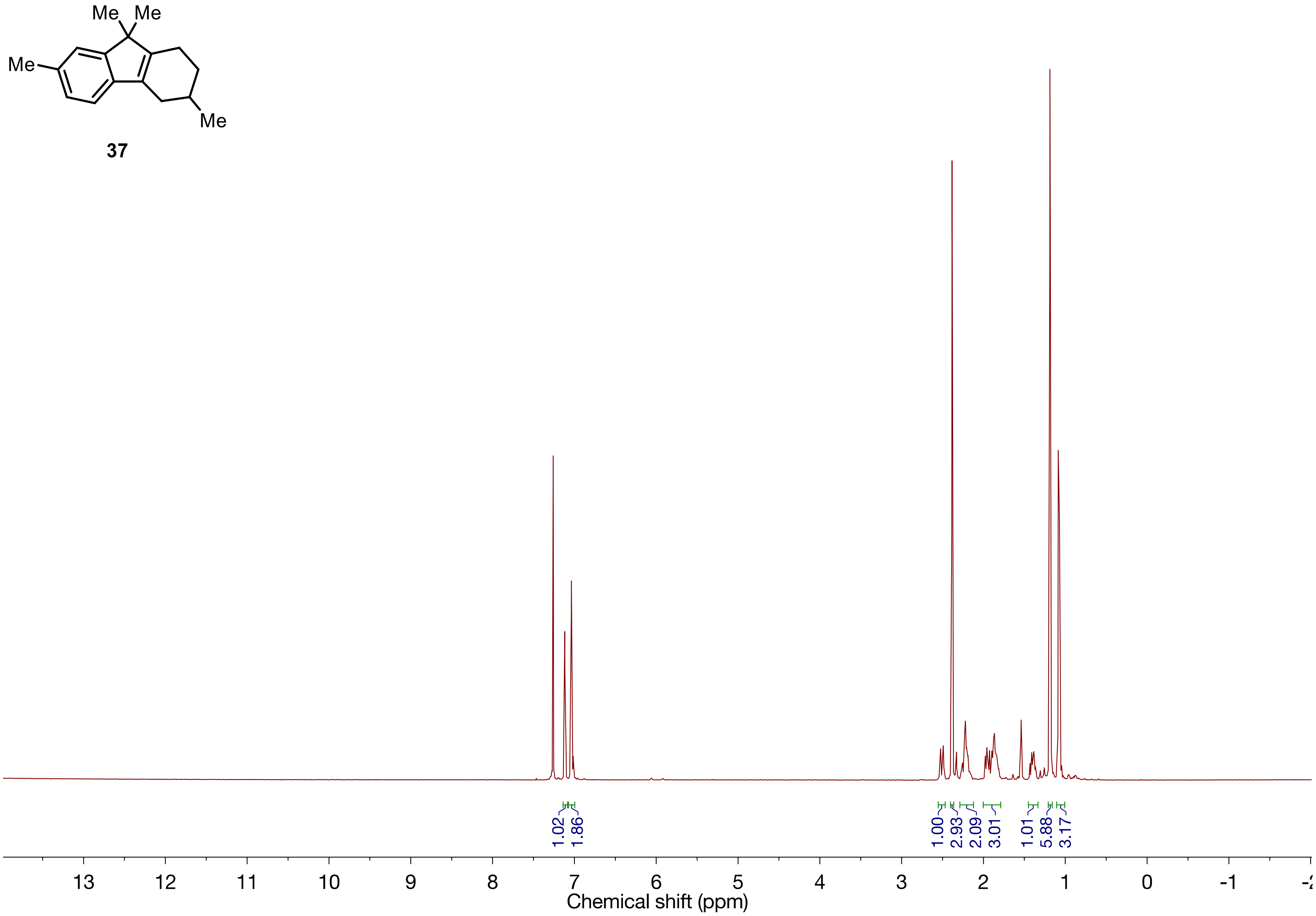

159.06
151.69
146.33
145.23
131.86
121.31
109.14
104.09
55.61
47.96
31.46
30.51
29.16
24.31
24.21
21.86
21.44
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

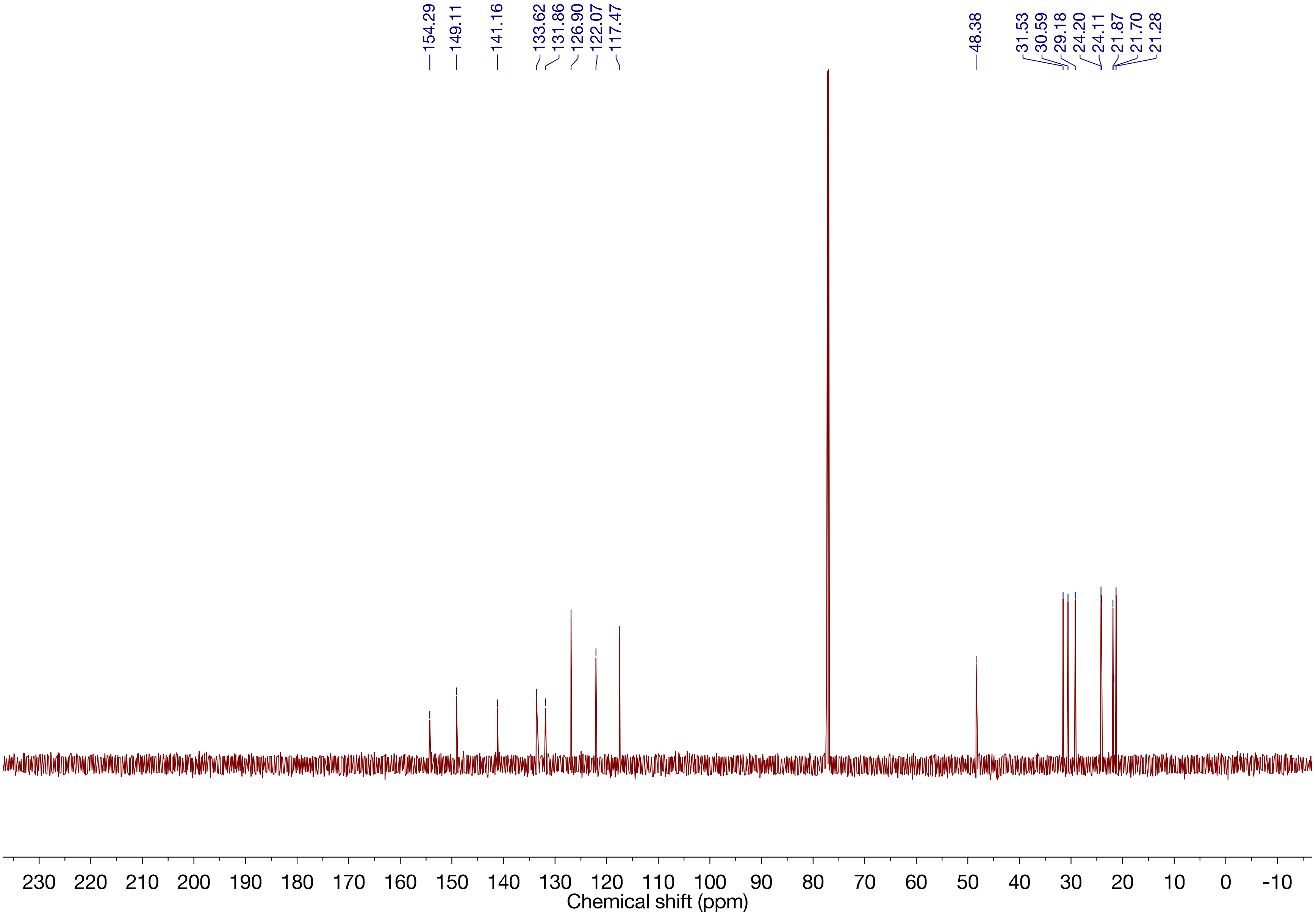
MeO
Me
Me
Me

36 minor

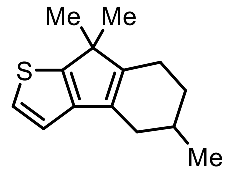

0.89
0.86
0.88
2.65
1.00
2.12
3.07
1.18
5.92
2.85
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


155.46
151.31
145.66
139.28
131.54
127.82
110.98
107.46
55.33
49.36
31.52
30.66
29.19
21.86
21.54
21.51
20.99
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical shift (ppm)

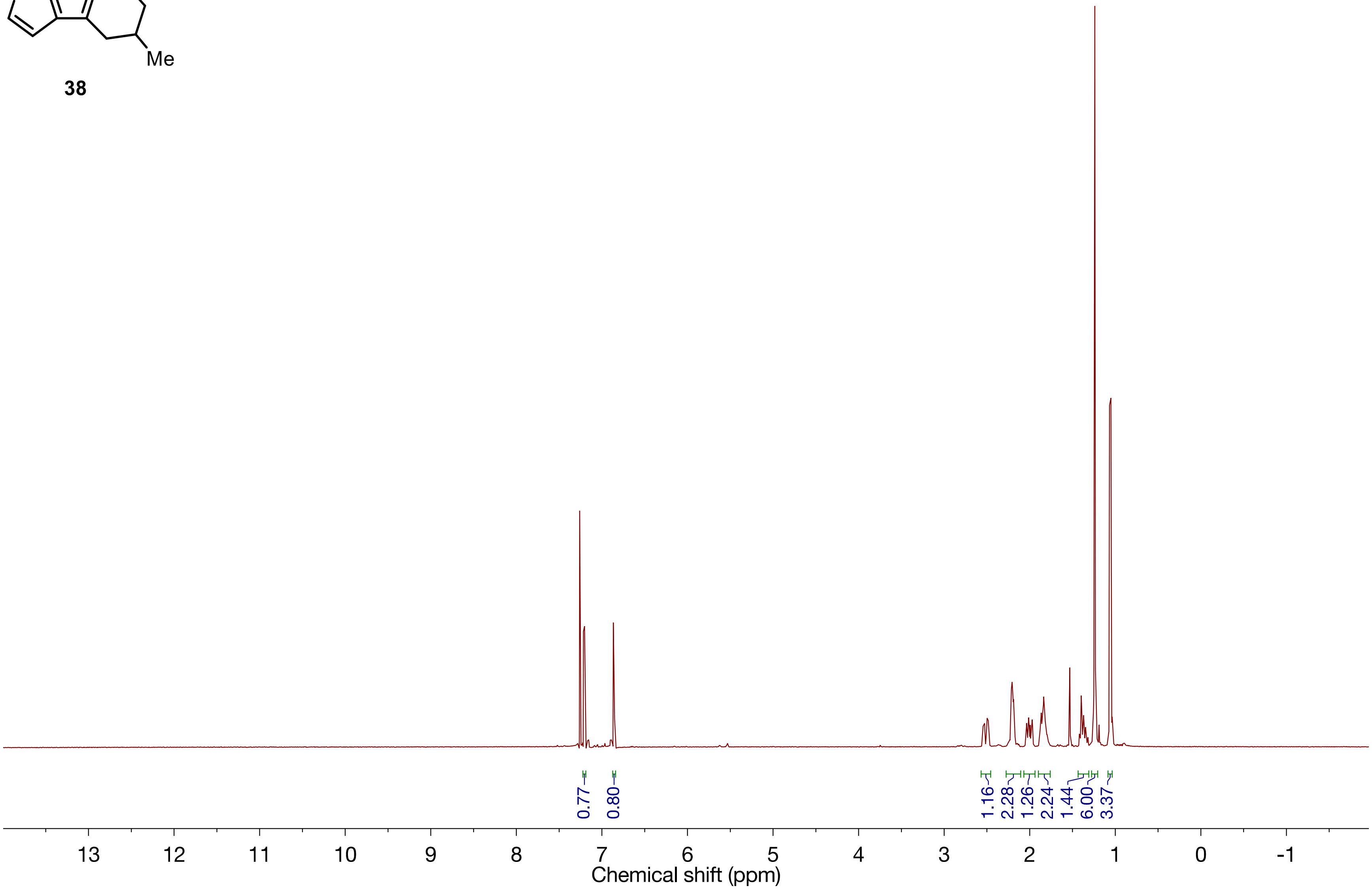
Me
Me
Me
Me
37
1.02
1.86
1.00
2.93
2.09
3.01
1.01
5.88
3.17
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

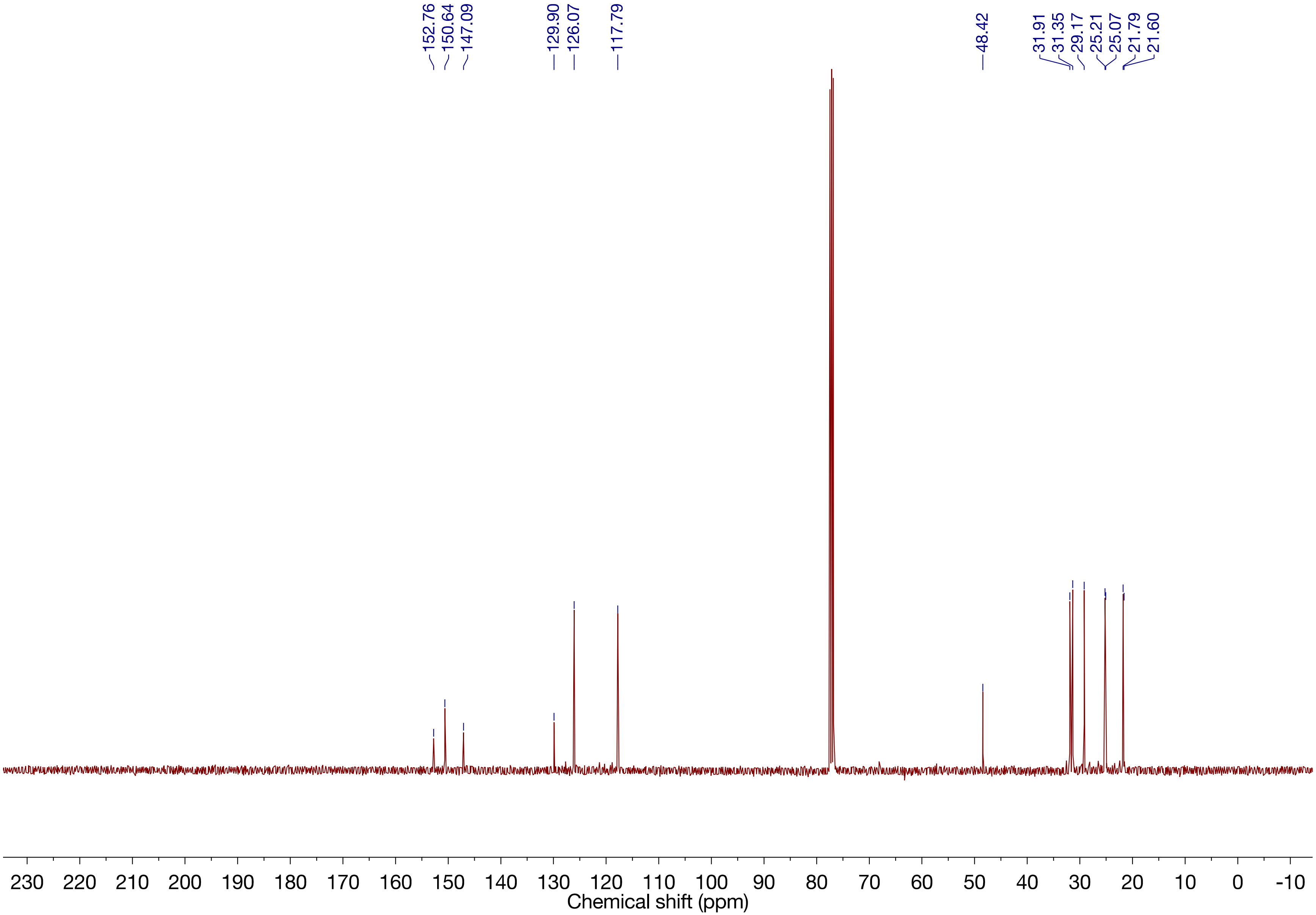


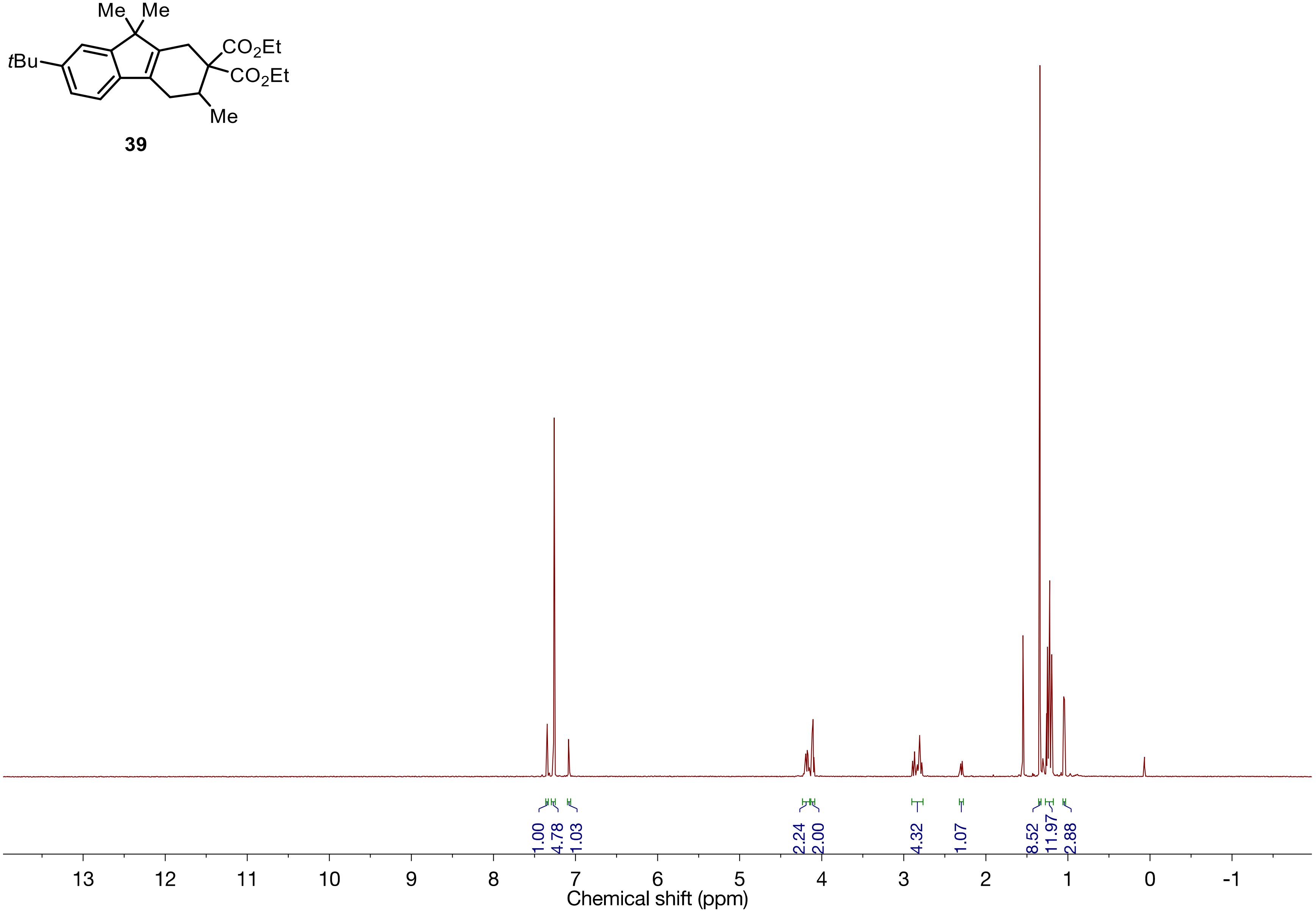
154.29
149.11
141.16
133.62
131.86
126.90
122.07
117.47
48.38
31.53
30.59
29.18
24.20
24.11
21.87
21.70
21.28
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
S
Me

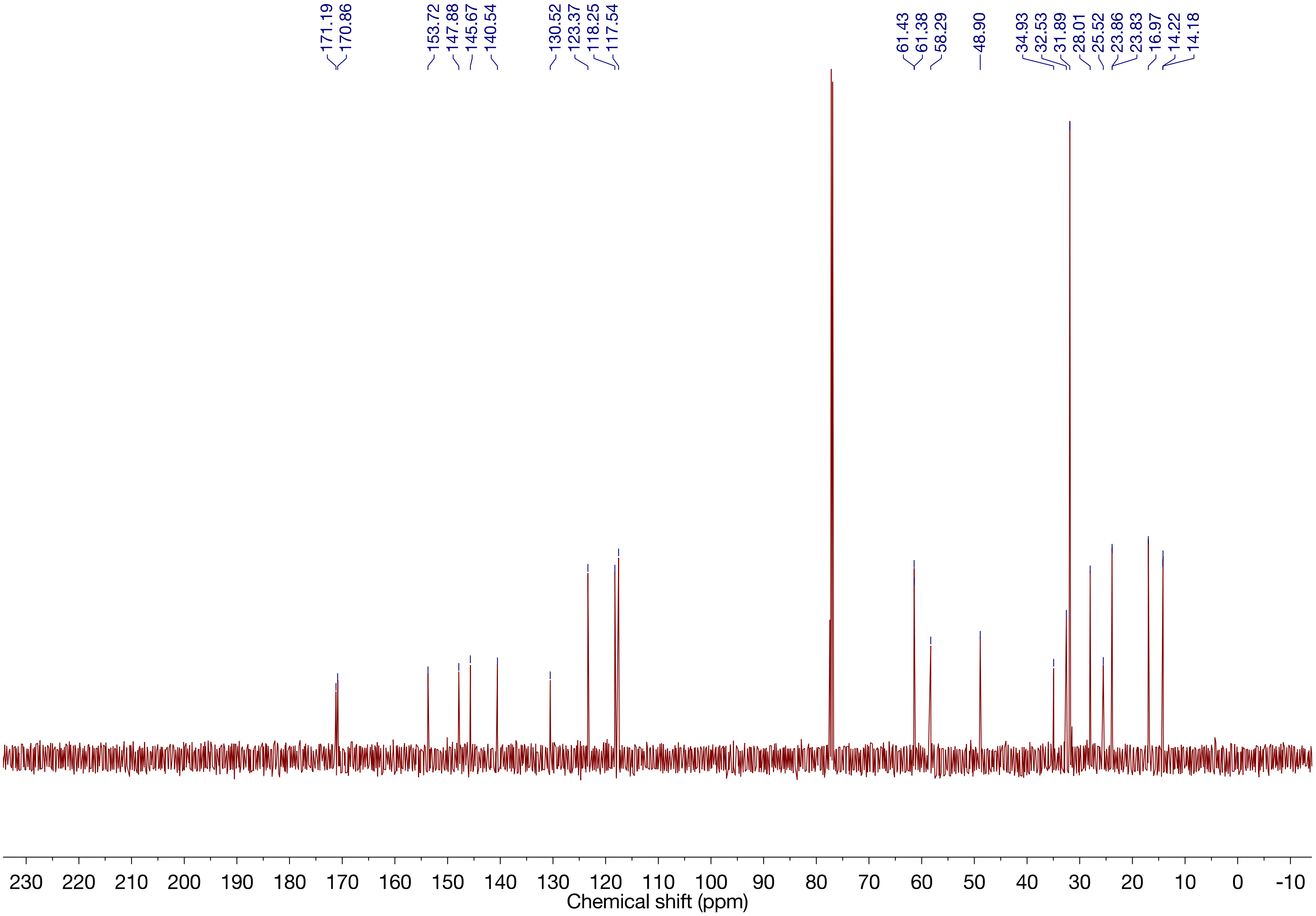
38

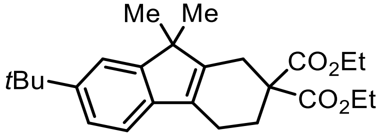

0.77
0.80
1.16
2.28
1.26
2.24
1.44
6.00
3.37
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


152.76
150.64
147.09
129.90
126.07
117.79
48.42
31.91
31.35
29.17
25.21
25.07
21.79
21.60
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

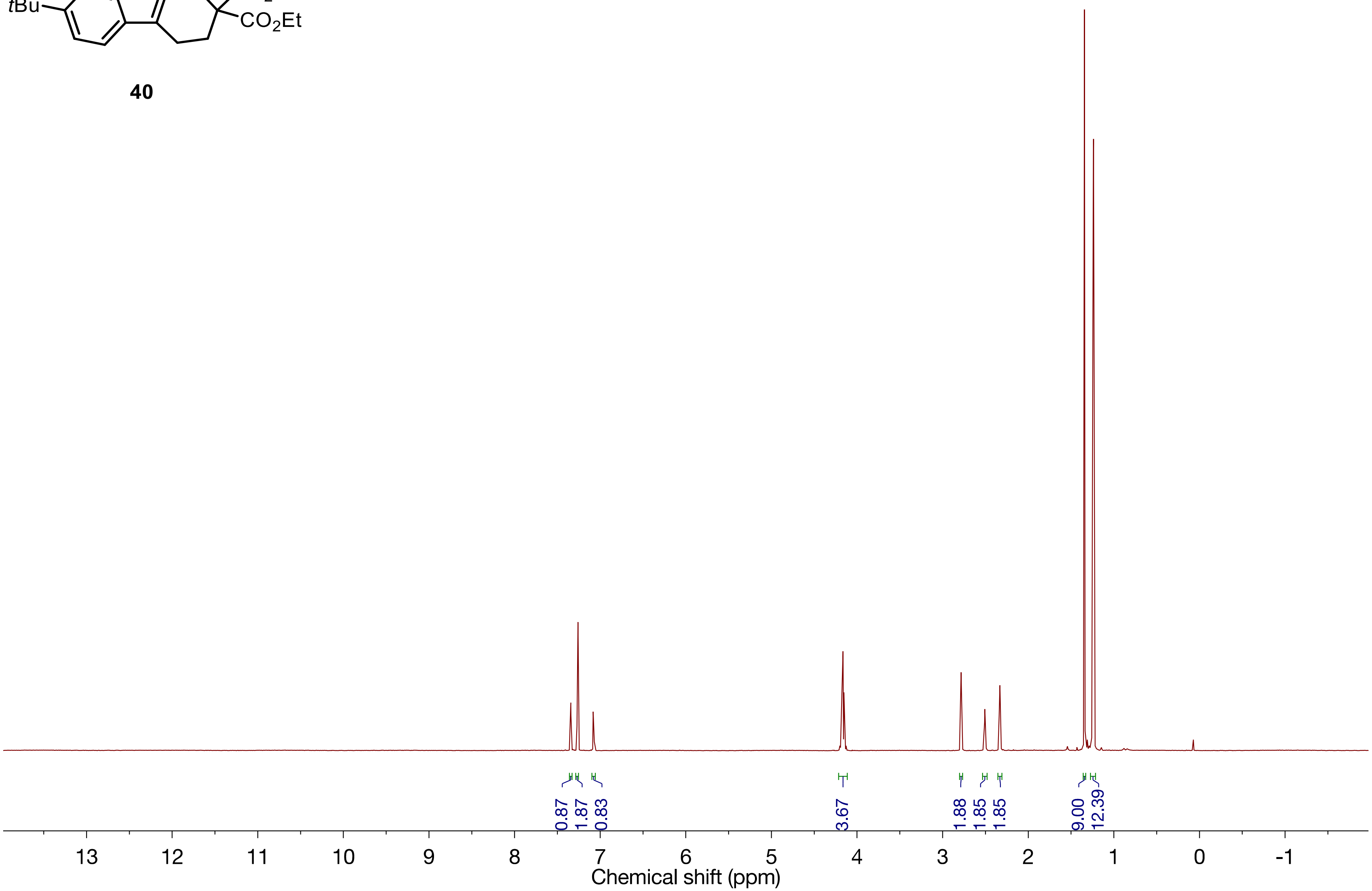

Me
Me
tBu
CO2Et
CO2Et
Me
1.00
4.78
1.03
2.24
2.00
4.32
1.07
8.52
11.97
2.88
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

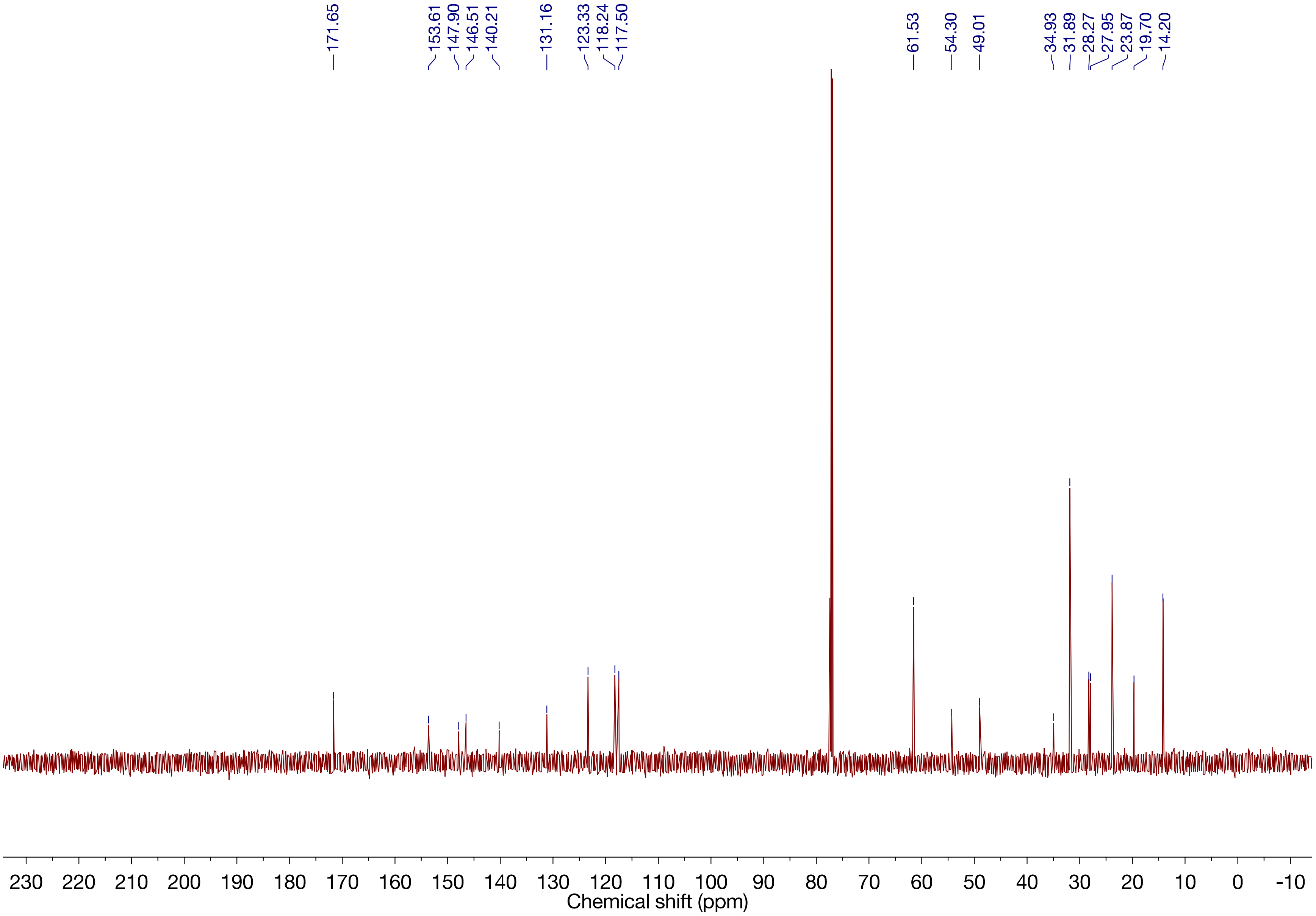
39

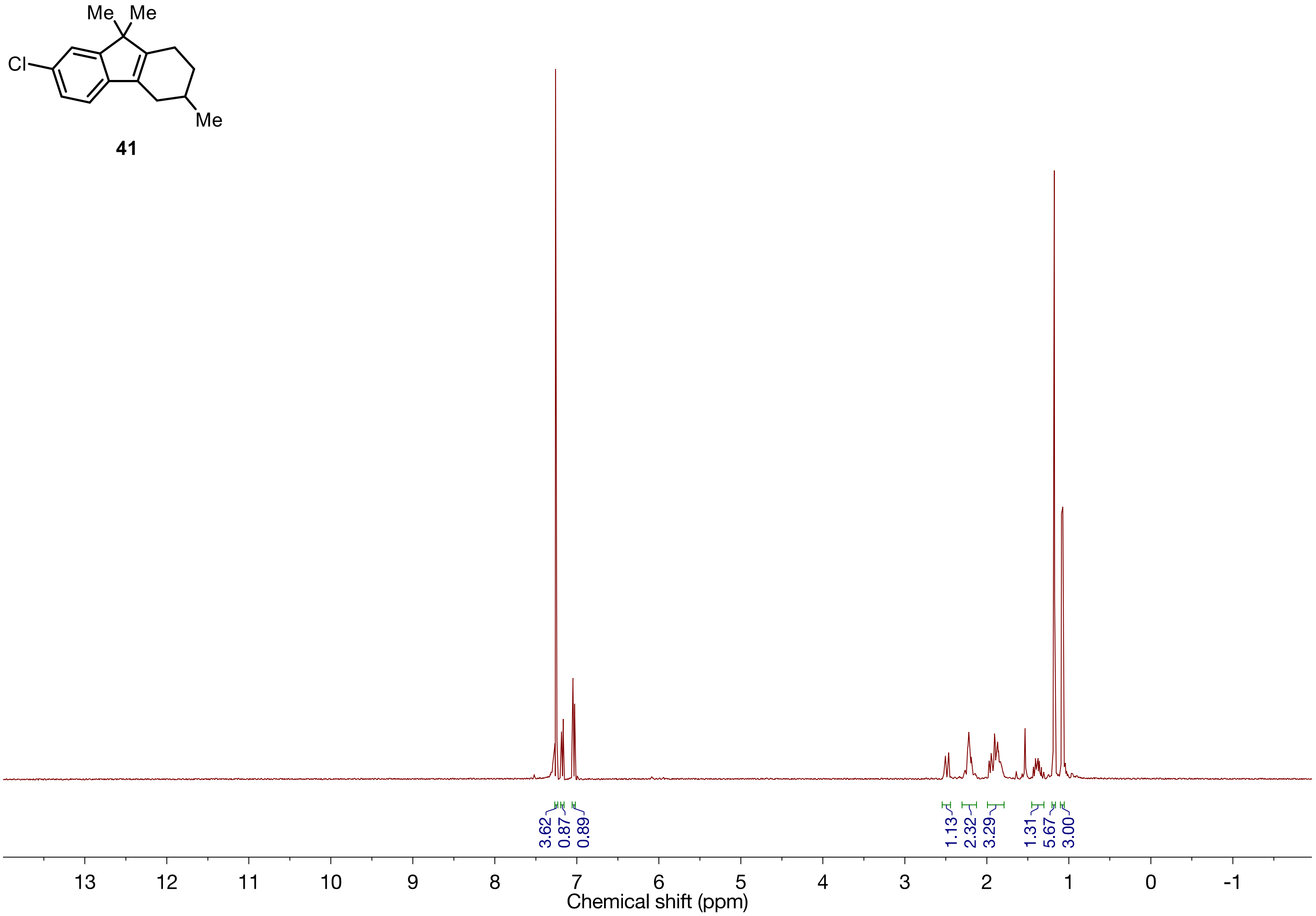

171.19
170.86
153.72
147.88
145.67
140.54
130.52
123.37
118.25
117.54
61.43
61.38
58.29
48.90
34.93
32.53
31.89
28.01
25.52
23.86
23.83
16.97
14.22
14.18
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
tBu
CO2Et
CO2Et

40

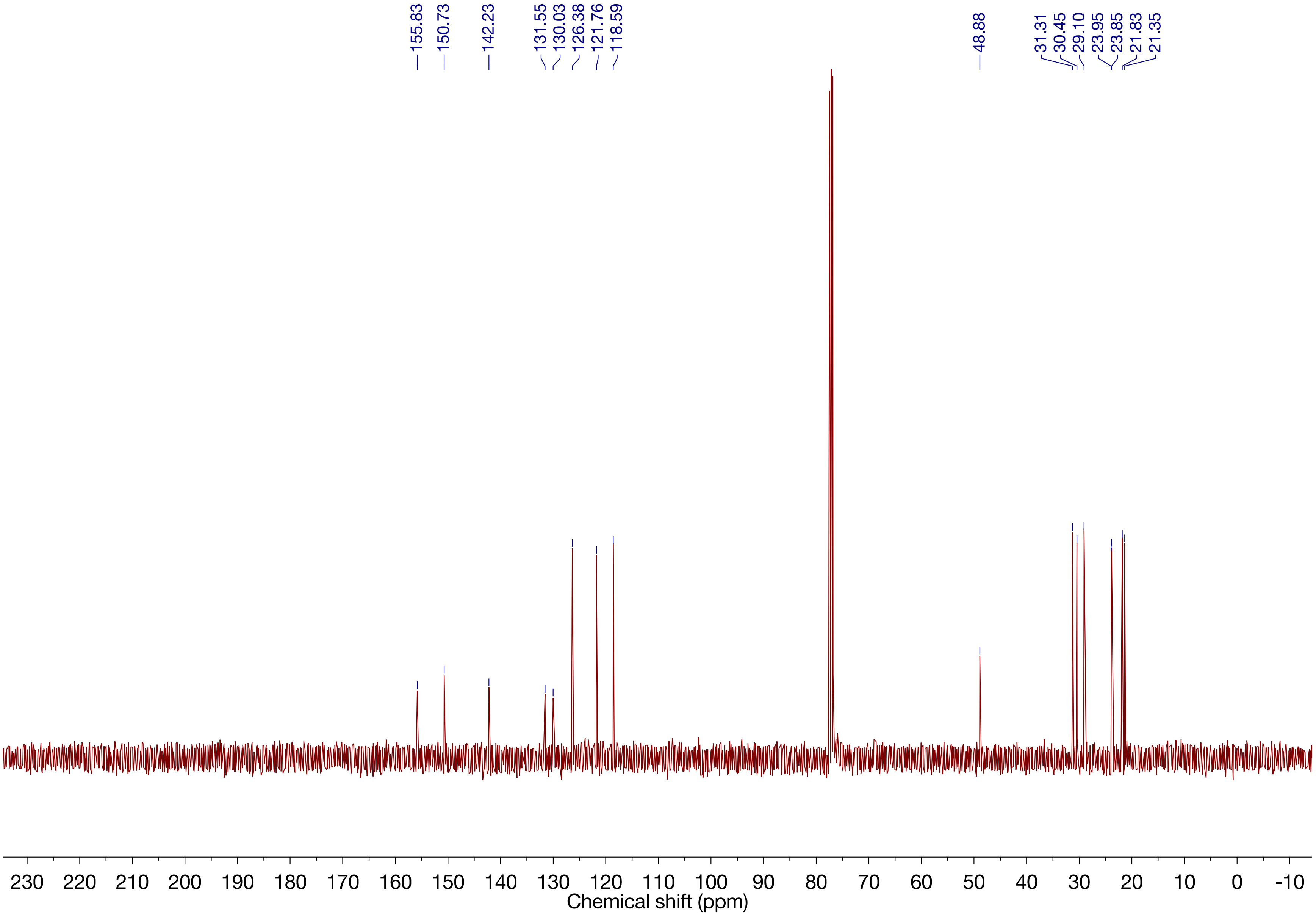

0.87
1.87
0.83
3.67
1.88
1.85
1.85
9.00
12.39
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

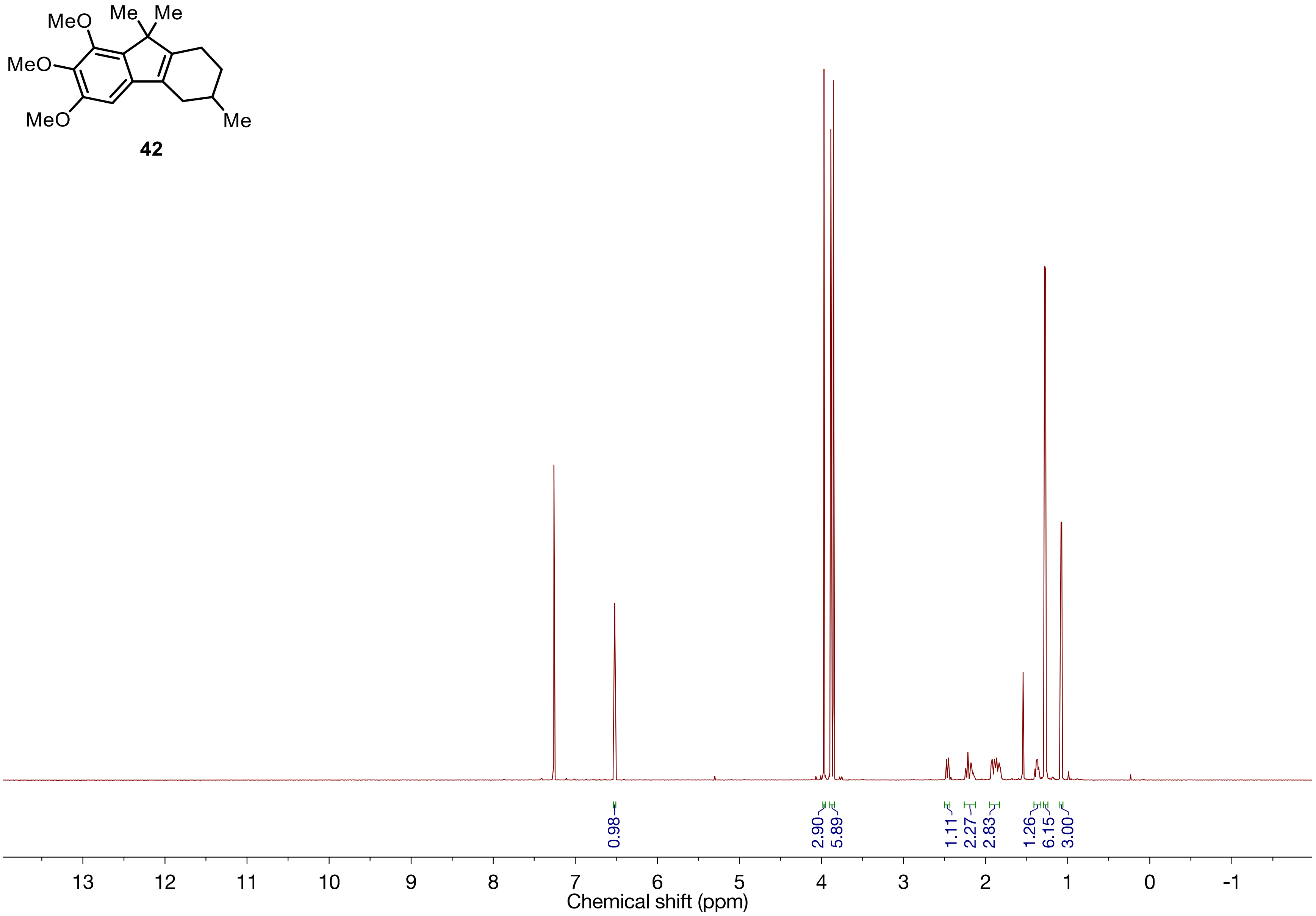

171.65
153.61
147.90
146.51
140.21
131.16
123.33
118.24
117.50
61.53
54.30
49.01
34.93
31.89
28.27
27.95
23.87
19.70
14.20
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
Cl
Me

41

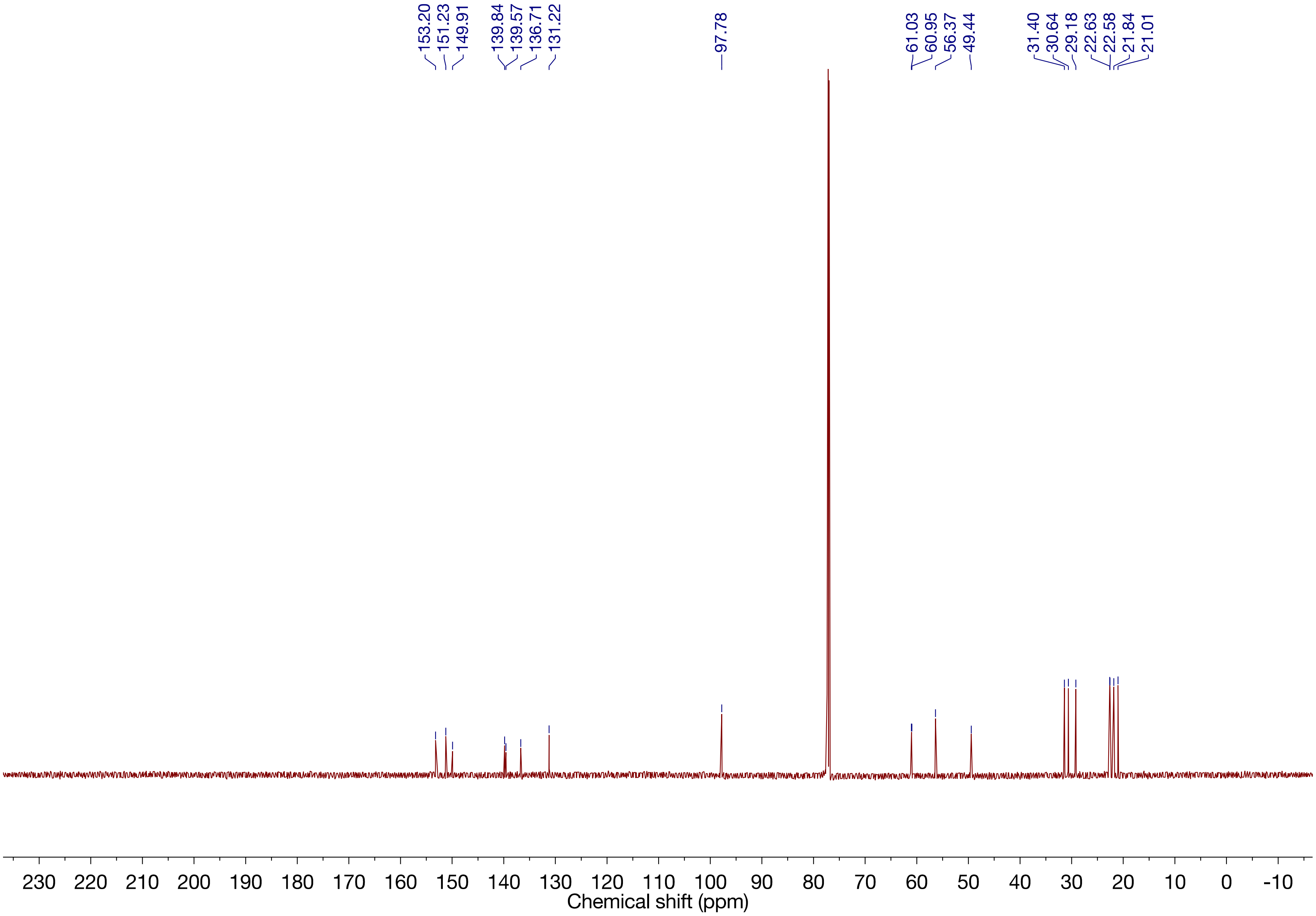
3.62
0.87
0.89
1.13
2.32
3.29
1.31
5.67
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

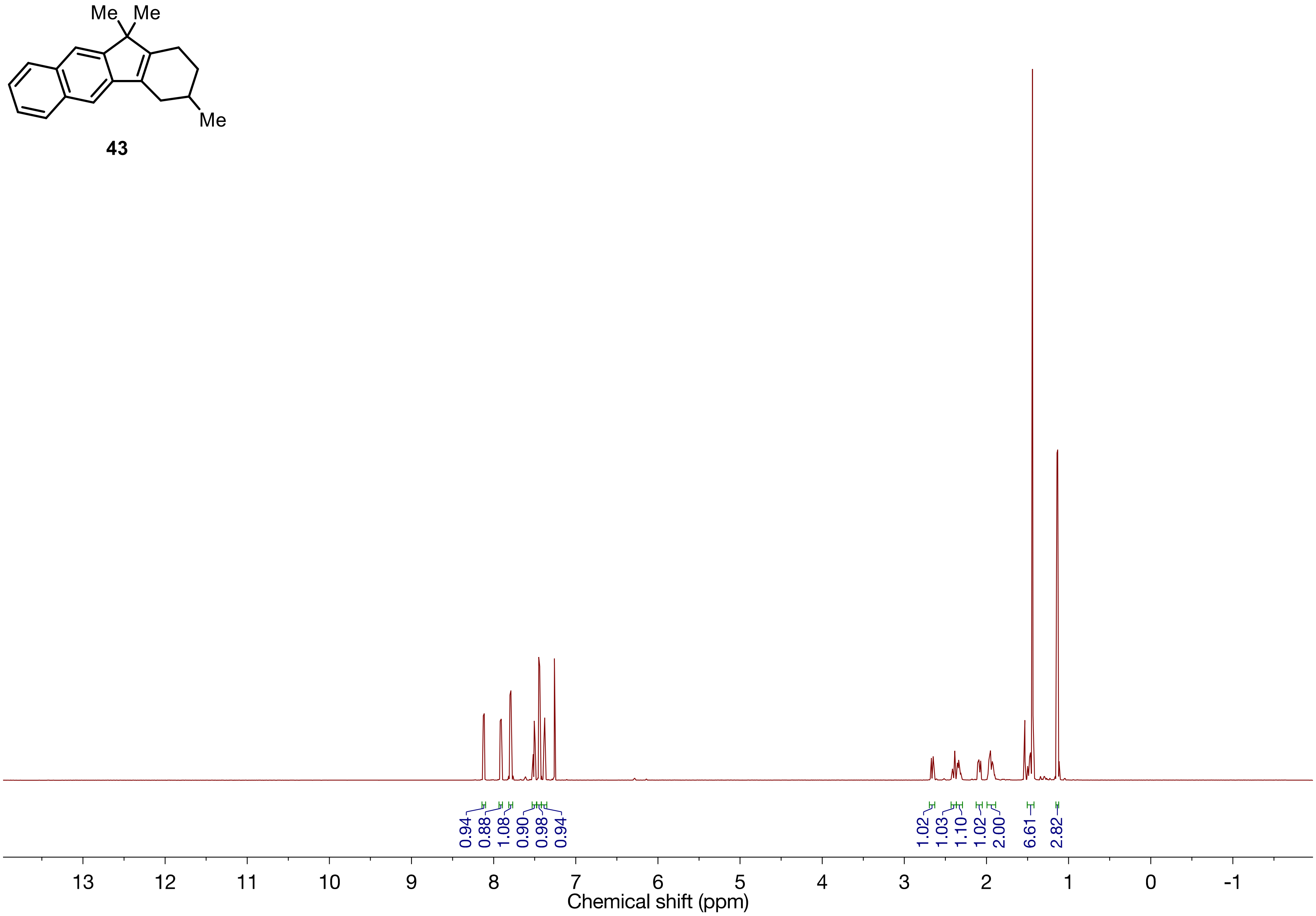

155.83
150.73
142.23
131.55
130.03
126.38
121.76
118.59
48.88
31.31
30.45
29.10
23.95
23.85
21.83
21.35
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



42

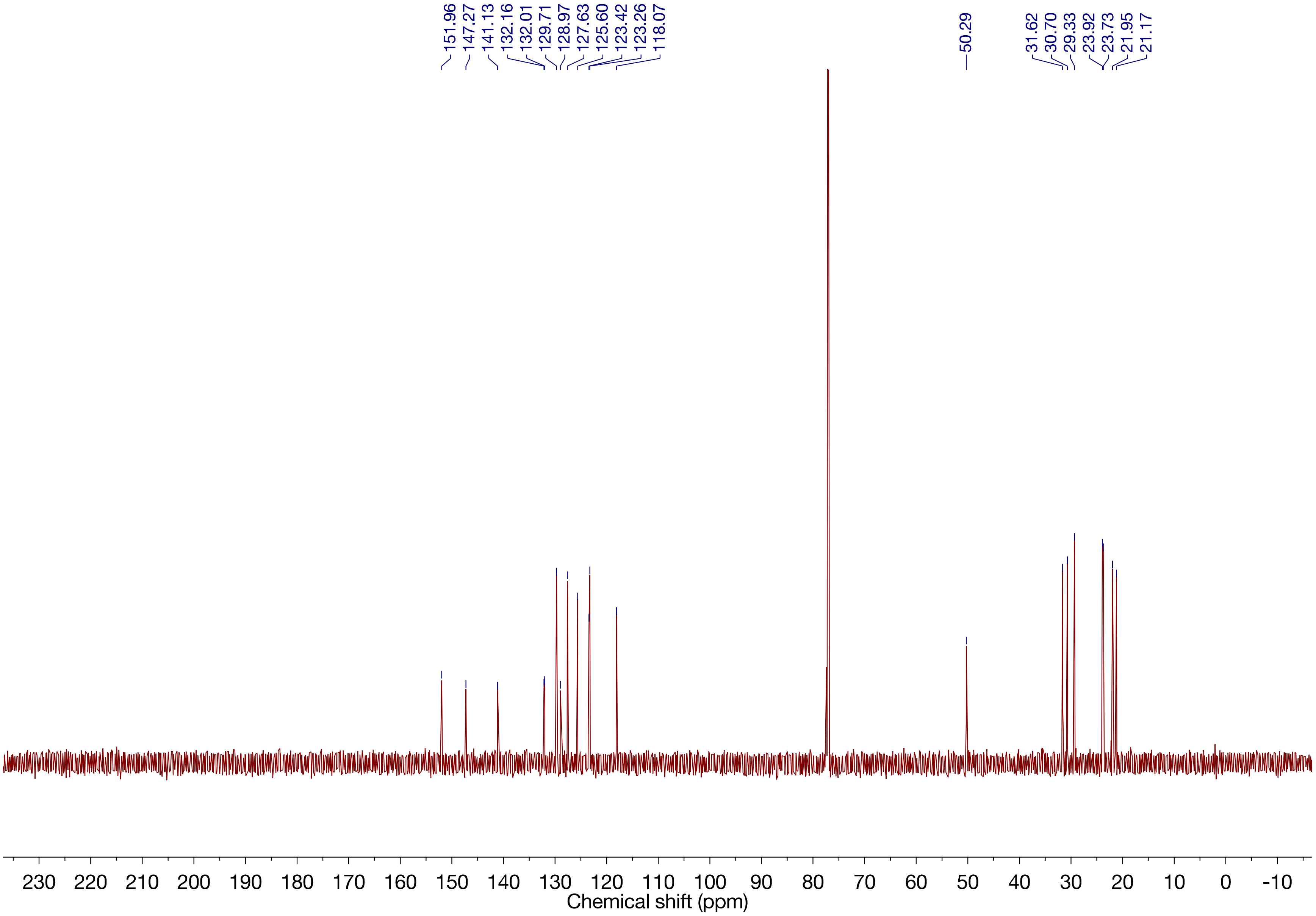
MeO
MeO
MeO
Me
Me
Me
0.98
2.90
5.89
1.11
2.27
2.83
1.26
6.15
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


153.20
151.23
149.91
139.84
139.57
136.71
131.22
97.78
61.03
60.95
56.37
49.44
31.40
30.64
29.18
22.63
22.58
21.84
21.01
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

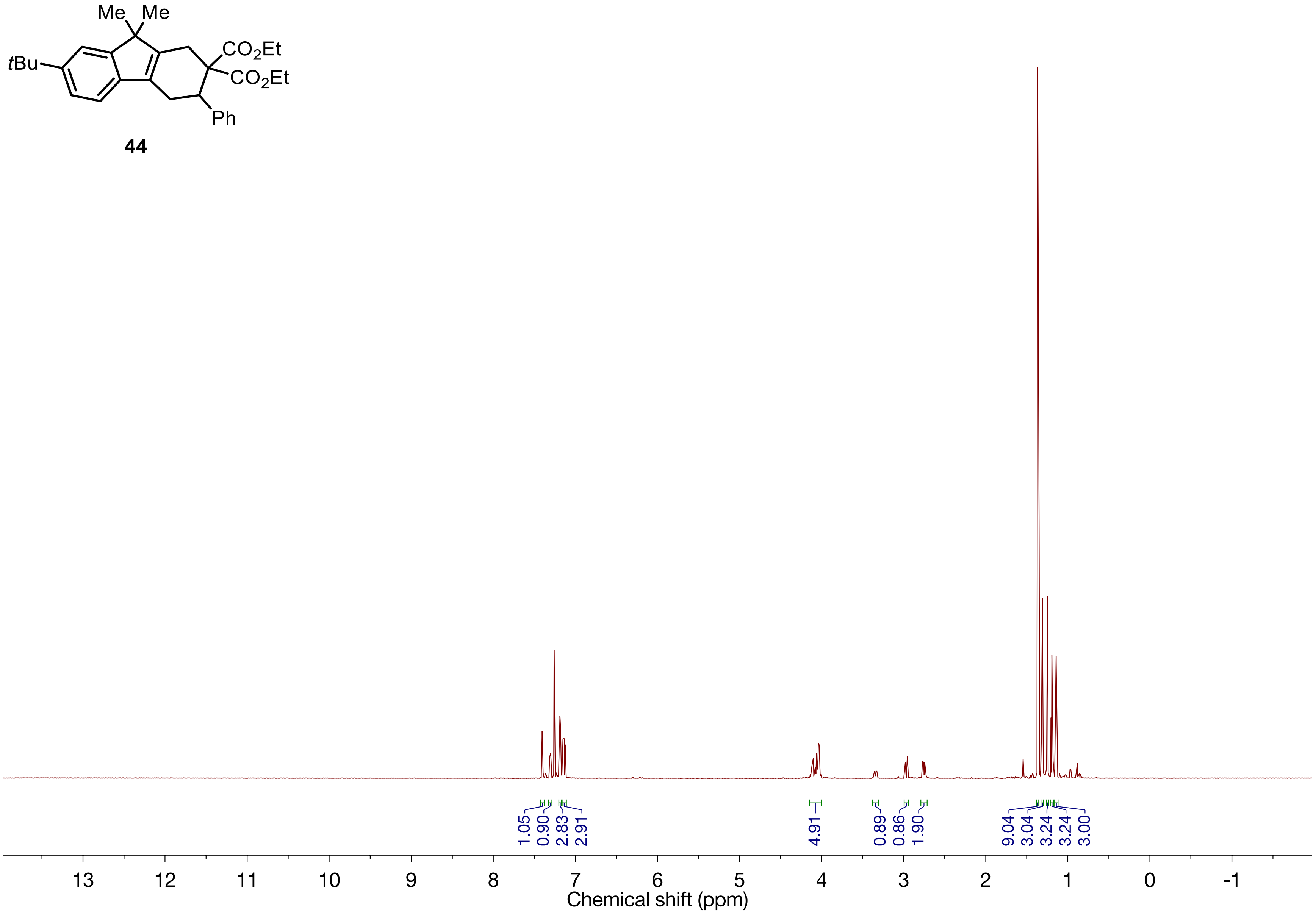

Me
Me
Me

43

0.94
0.88
1.08
0.90
0.98
0.94
1.02
1.03
1.10
1.02
2.00
6.61
2.82
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

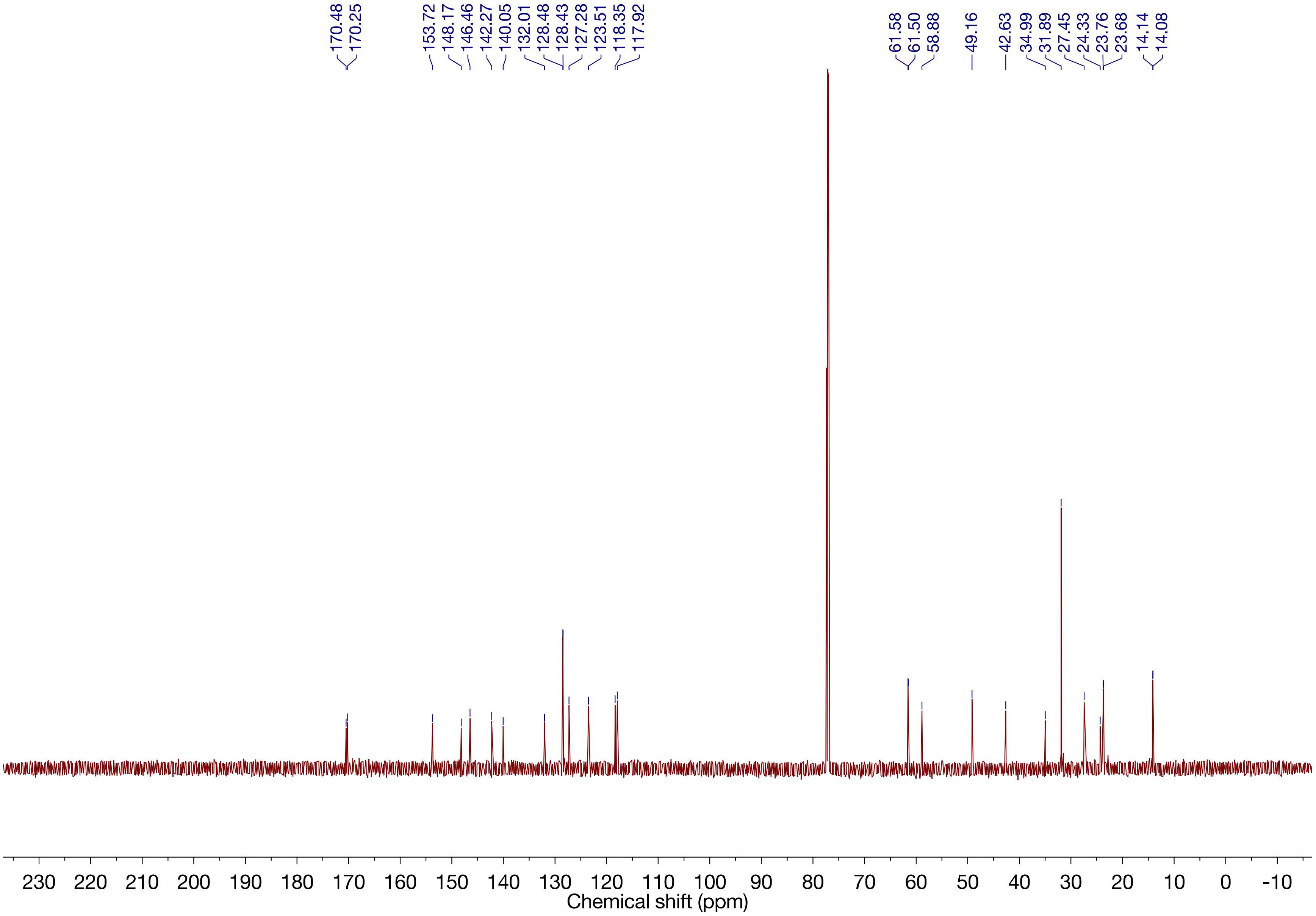


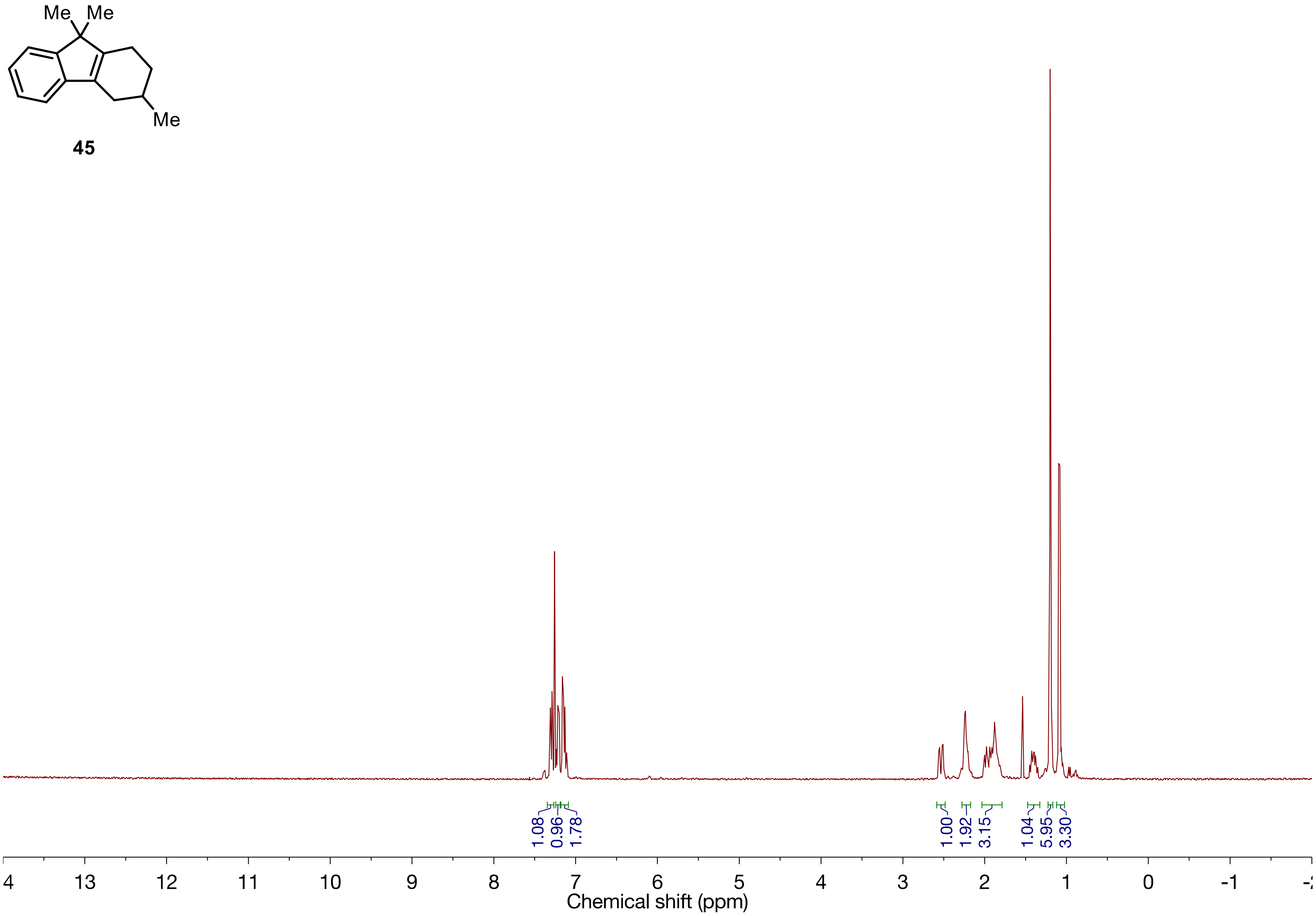
151.96
147.27
141.13
132.16
132.01
129.71
128.97
127.63
125.60
123.42
123.26
118.07
50.29
31.62
30.70
29.33
23.92
23.73
21.95
21.17
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Me
tBu
CO_2Et
CO_2Et
Ph

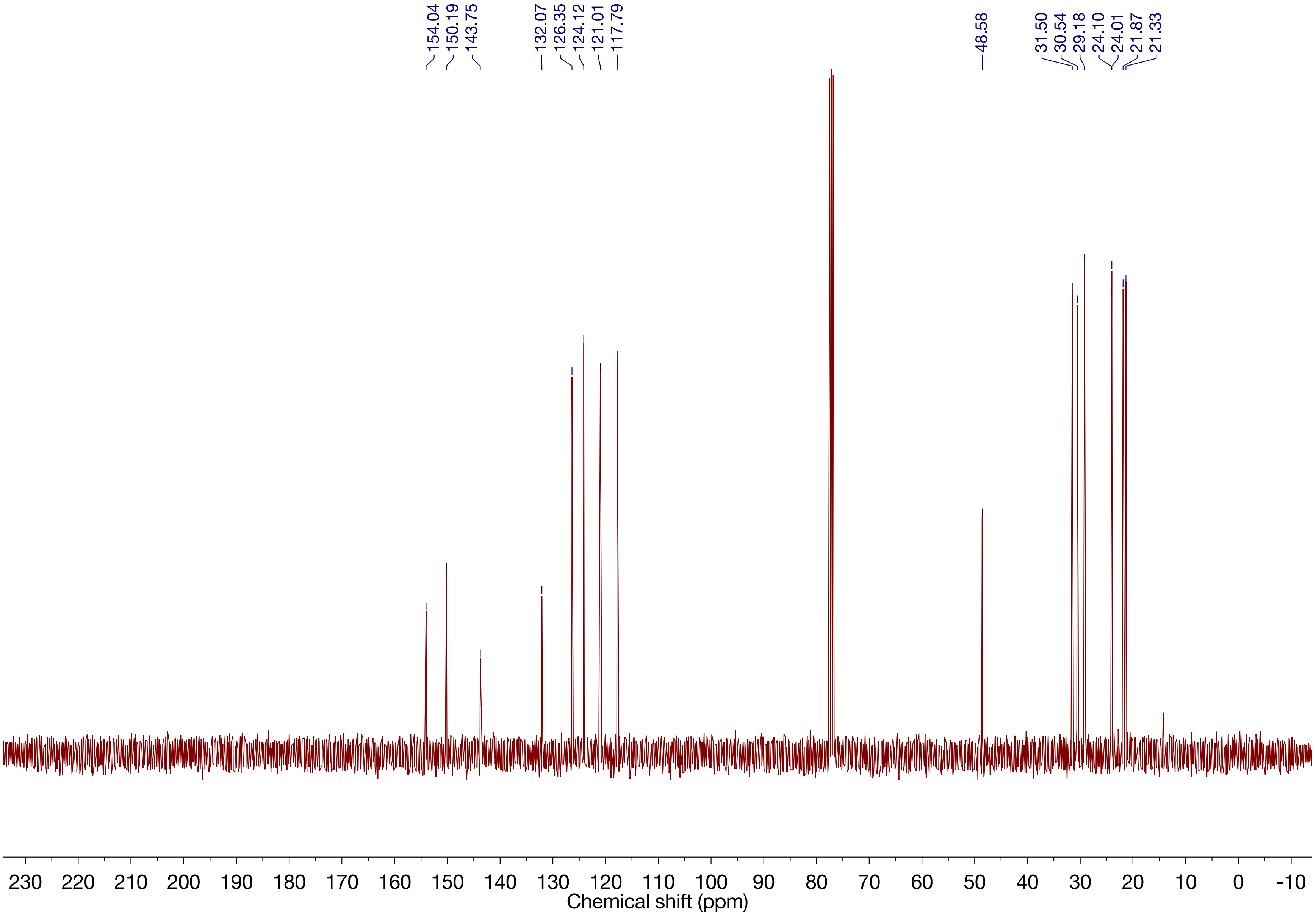
44

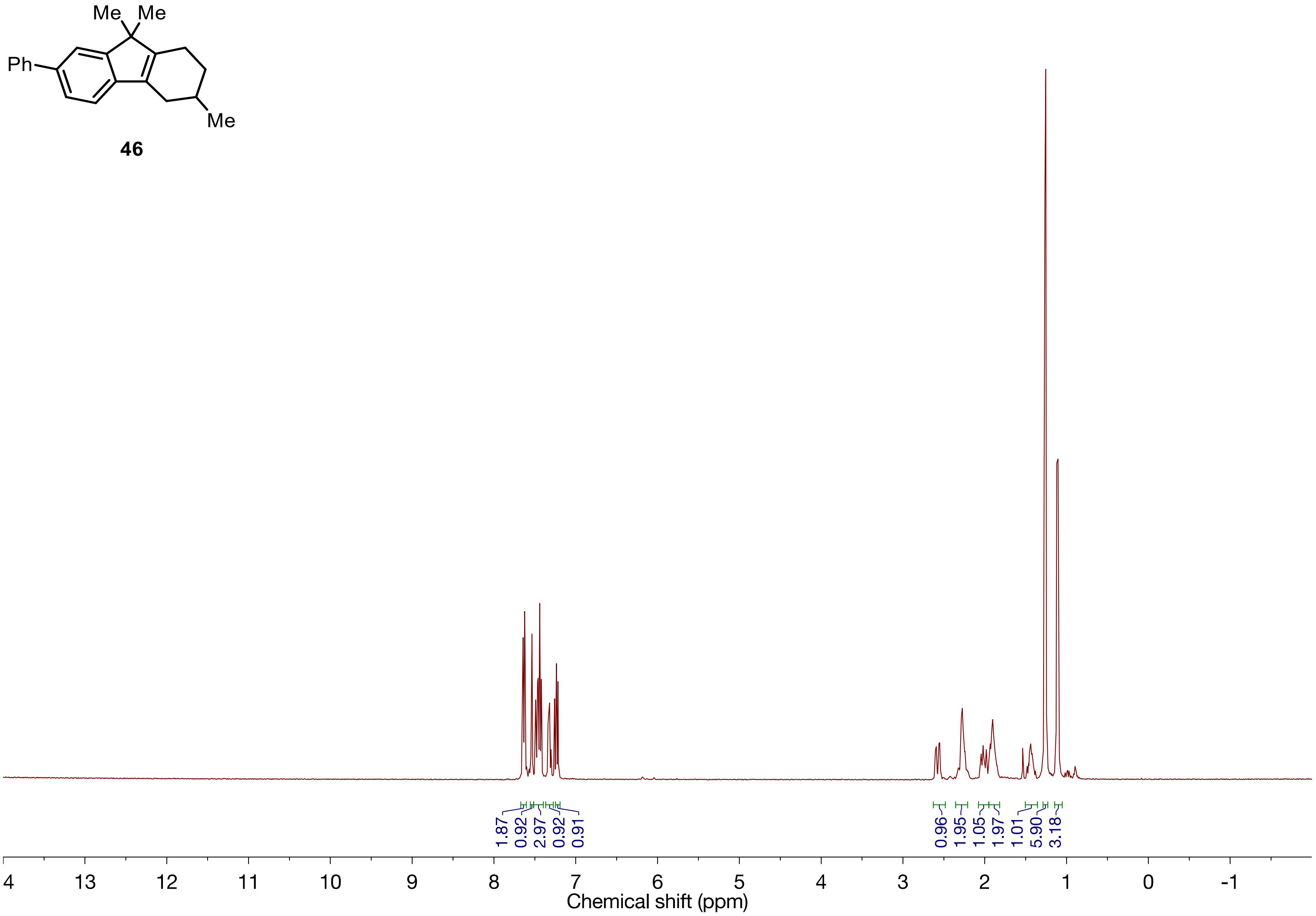
1.05
0.90
2.83
2.91
4.91
0.89
0.86
1.90
9.04
3.04
3.24
3.24
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


170.48
170.25
153.72
148.17
146.46
142.27
140.05
132.01
128.48
128.43
127.28
123.51
118.35
117.92
61.58
61.50
58.88
49.16
42.63
34.99
31.89
27.45
24.33
23.76
23.68
14.14
14.08
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

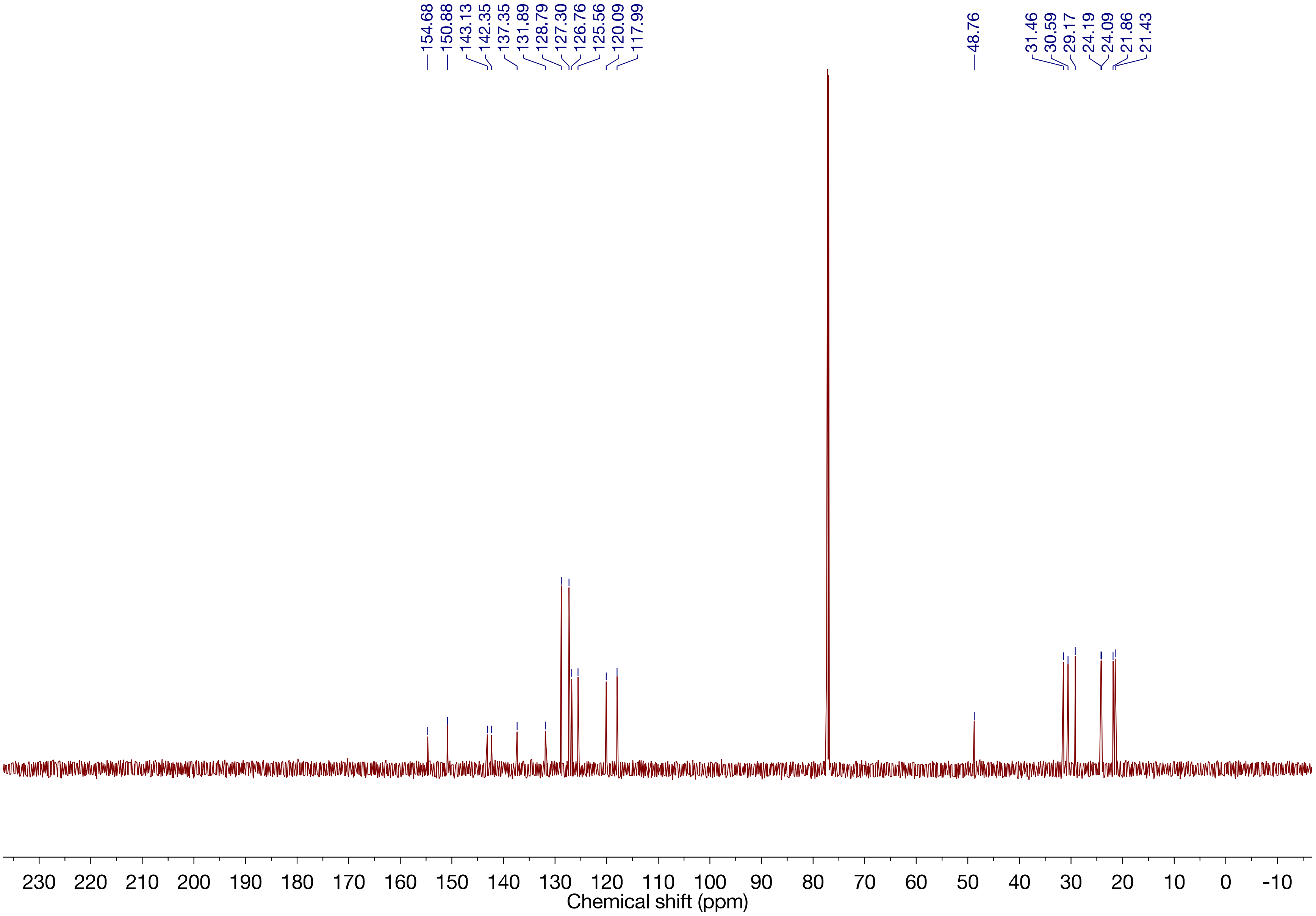

Me
Me
Me
1.08
0.96
1.78
1.00
1.92
3.15
1.04
5.95
3.30
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

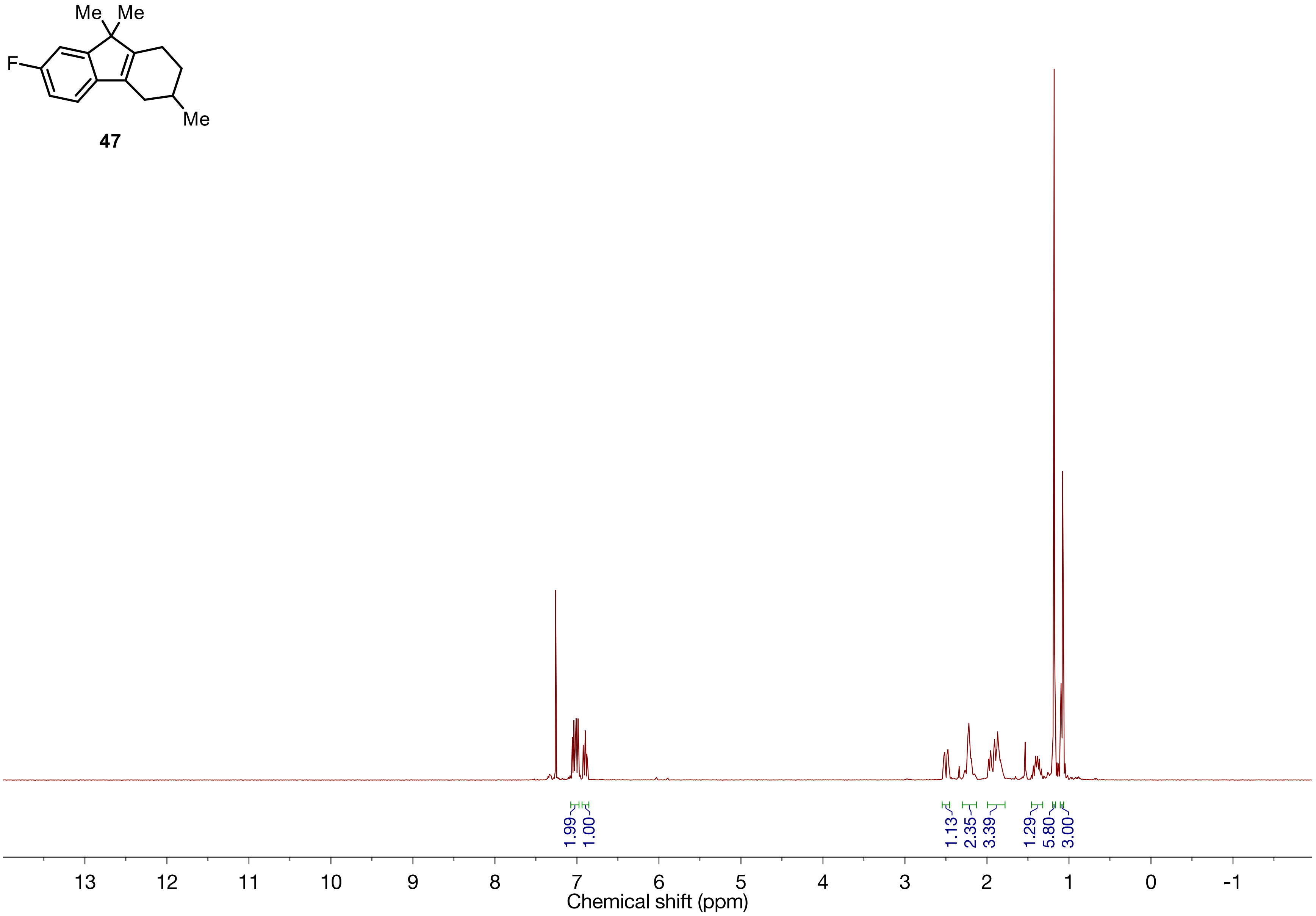
45

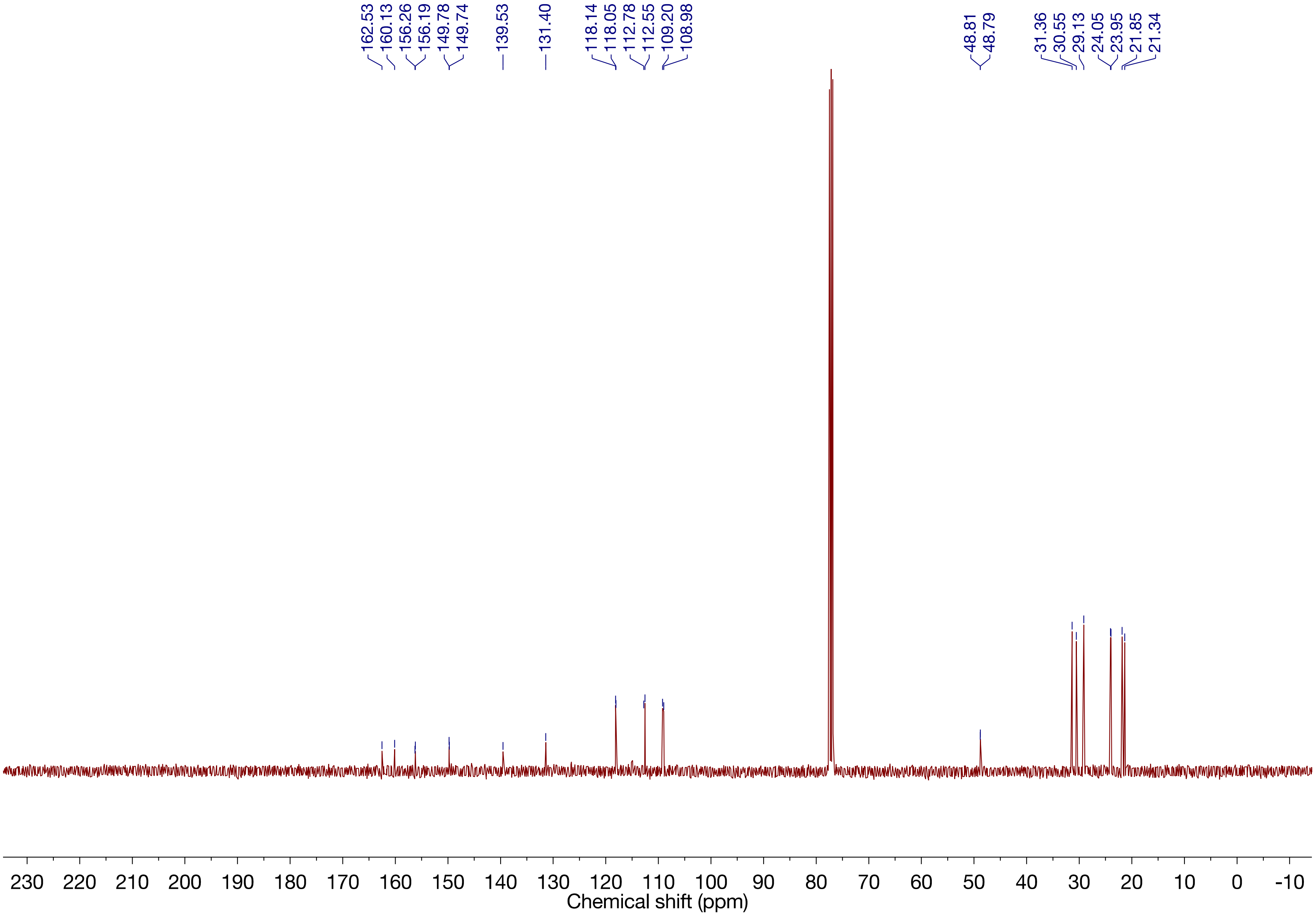

154.04
150.19
143.75
132.07
126.35
124.12
121.01
117.79
48.58
31.50
30.54
29.18
24.10
24.01
21.87
21.33
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

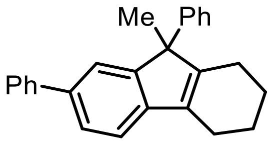

Me
Me
Ph
Me
1.87
0.92
2.97
0.92
0.91
0.96
1.95
1.05
1.97
1.01
5.90
3.18
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

46

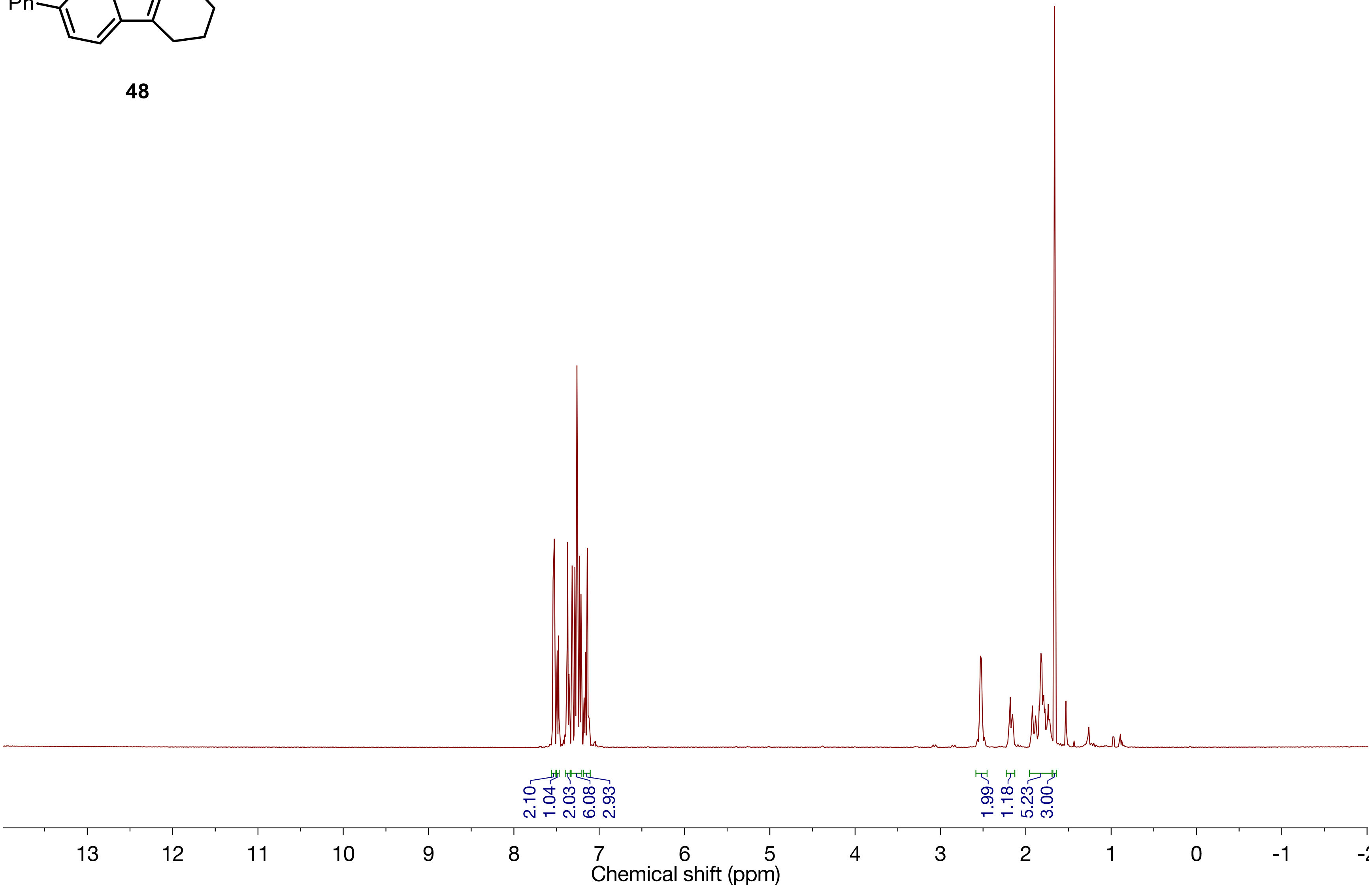

154.68
150.88
143.13
142.35
137.35
131.89
128.79
127.30
126.76
125.56
120.09
117.99
48.76
31.46
30.59
29.17
24.19
24.09
21.86
21.43
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

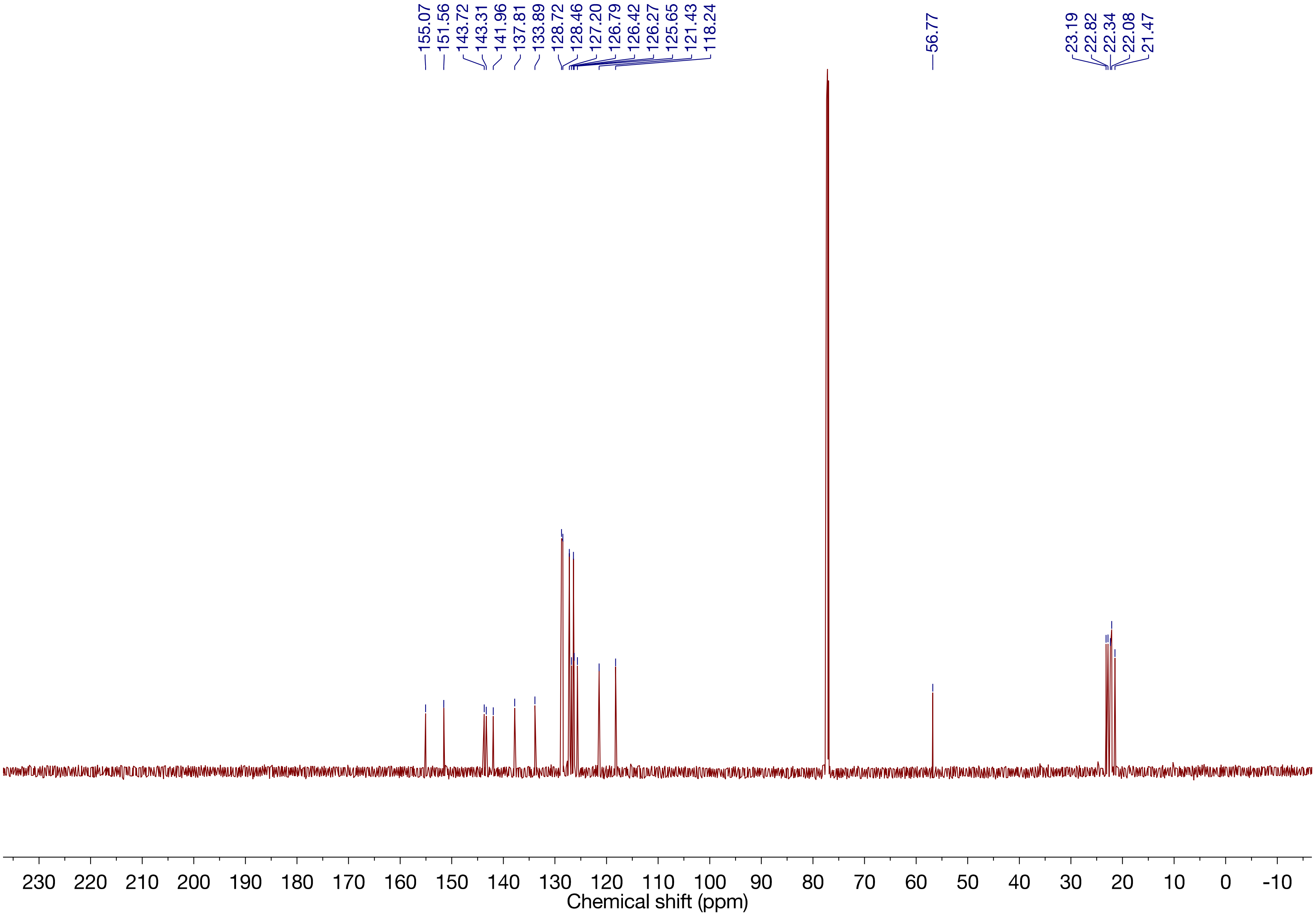

Me
Me
F
Me
47
1.99
1.00
1.13
2.35
3.39
1.29
5.80
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

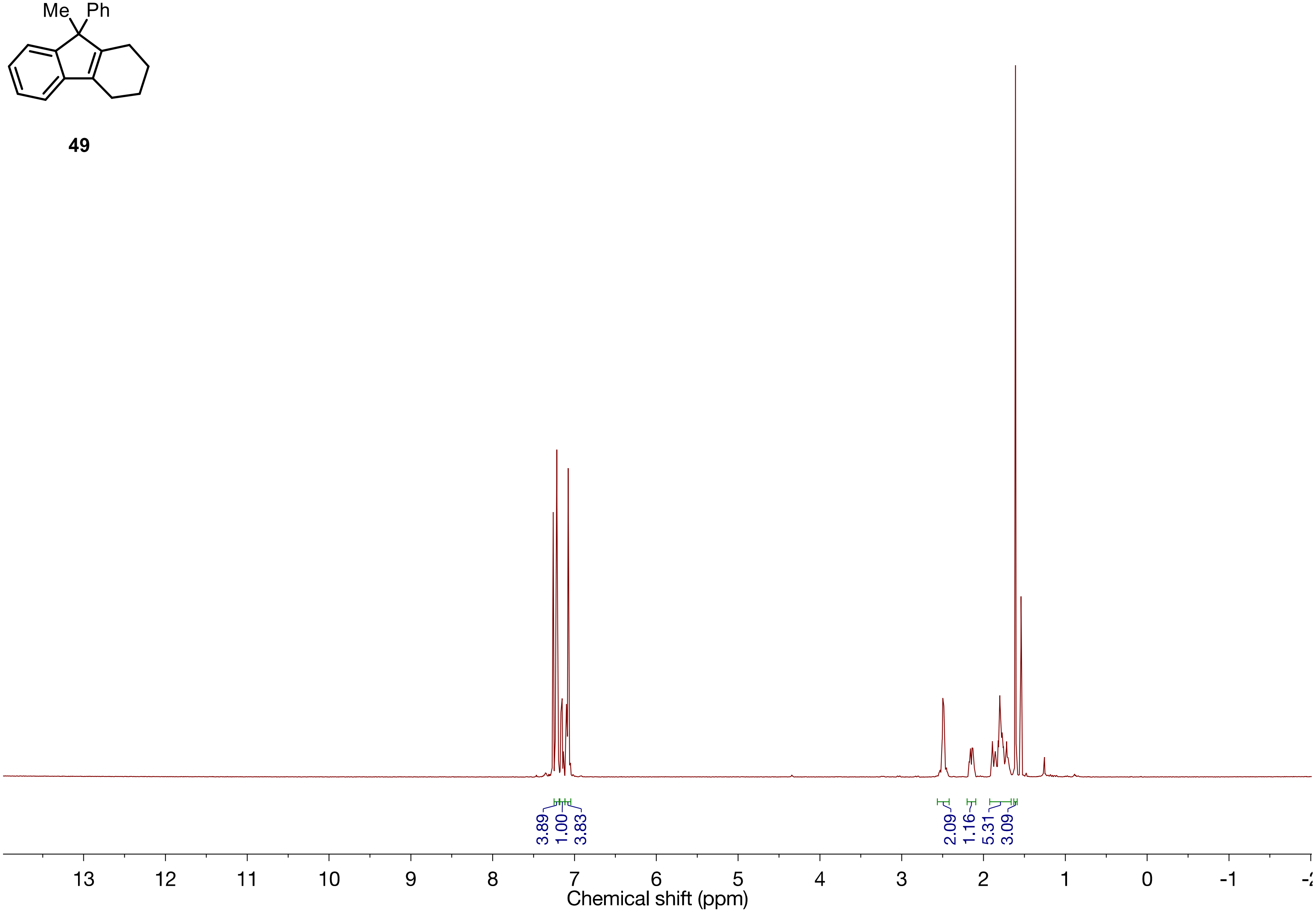

162.53
160.13
156.26
156.19
149.78
149.74
139.53
131.40
118.14
118.05
112.78
112.55
109.20
108.98
48.81
48.79
31.36
30.55
29.13
24.05
23.95
21.85
21.34
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Ph
Ph

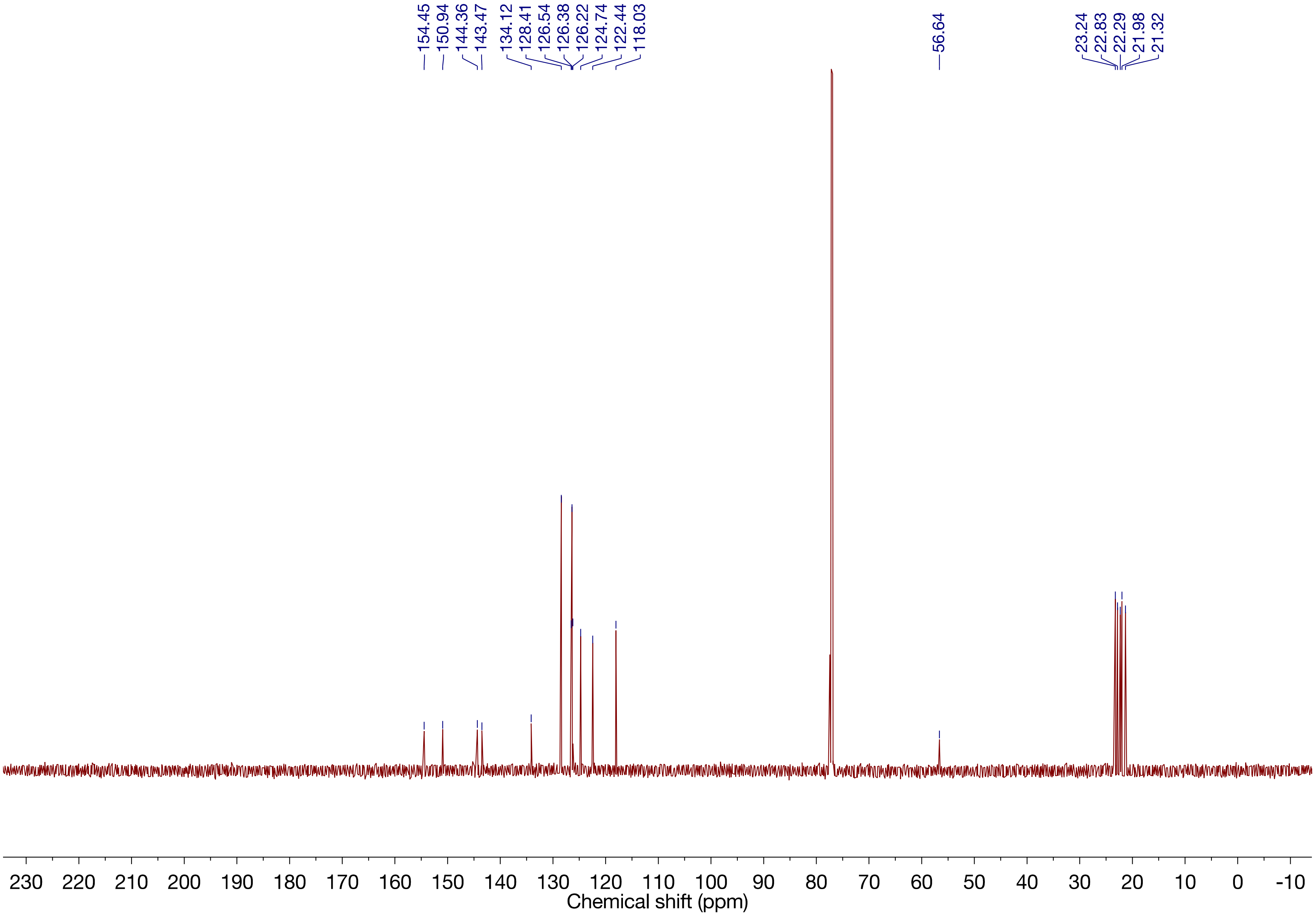
48

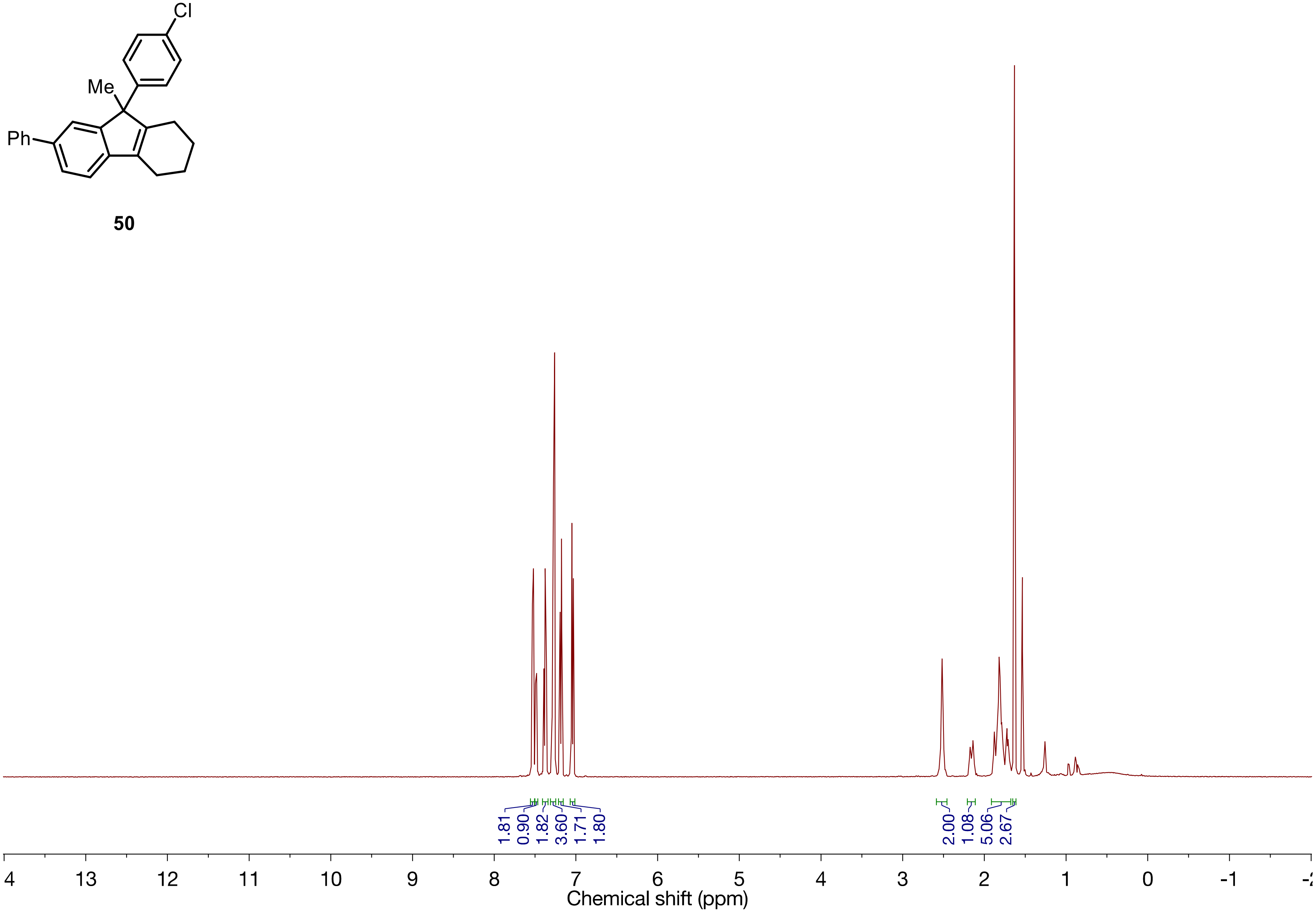

2.10
1.04
2.03
6.08
2.93
1.99
1.18
5.23
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


155.07
151.56
143.72
143.31
141.96
137.81
133.89
128.72
128.46
127.20
126.79
126.42
126.27
125.65
121.43
118.24
56.77
23.19
22.82
22.34
22.08
21.47
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

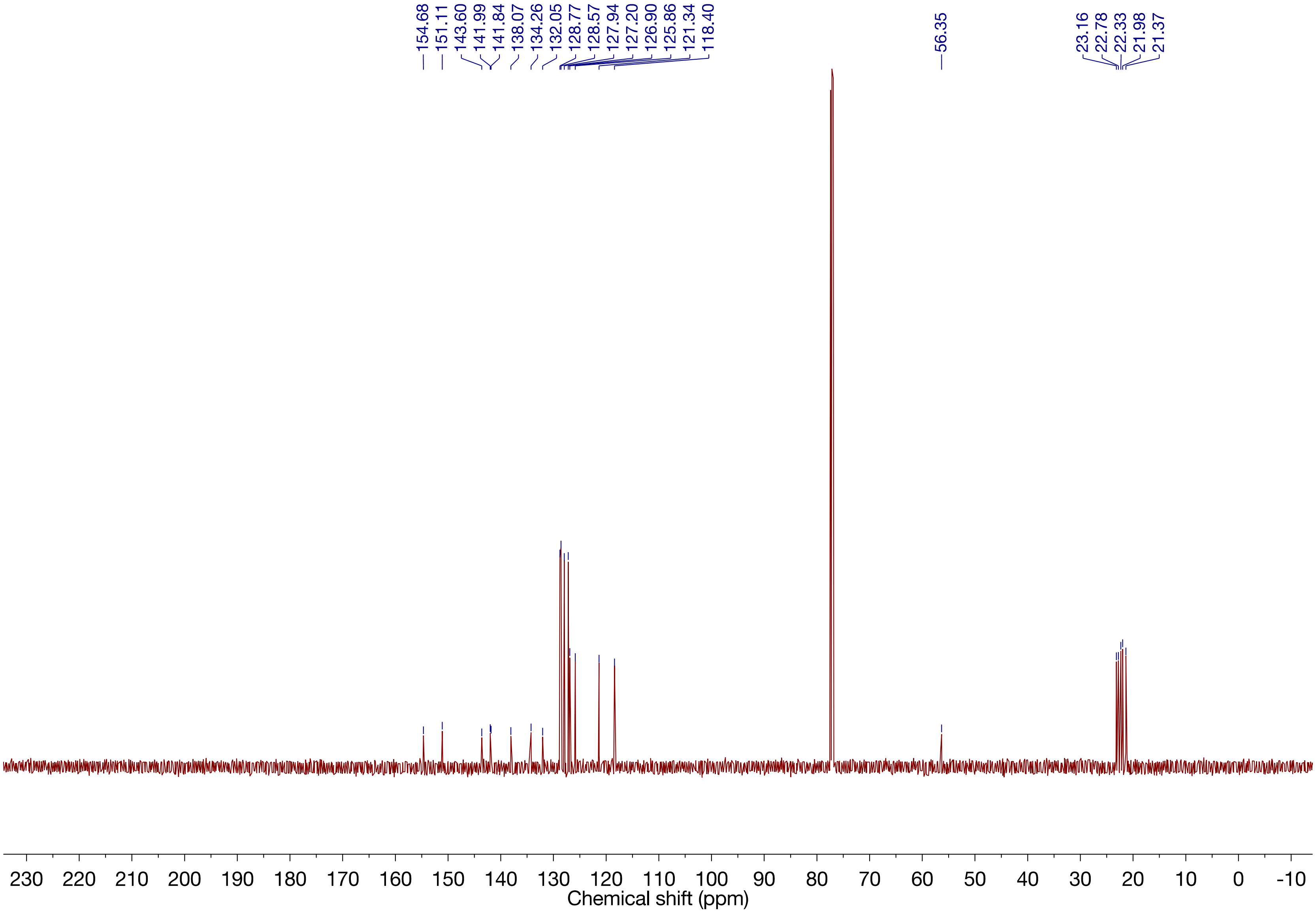

Me
Ph
3.89
1.00
3.83
2.09
1.16
5.31
3.09
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
Chemical shift (ppm)

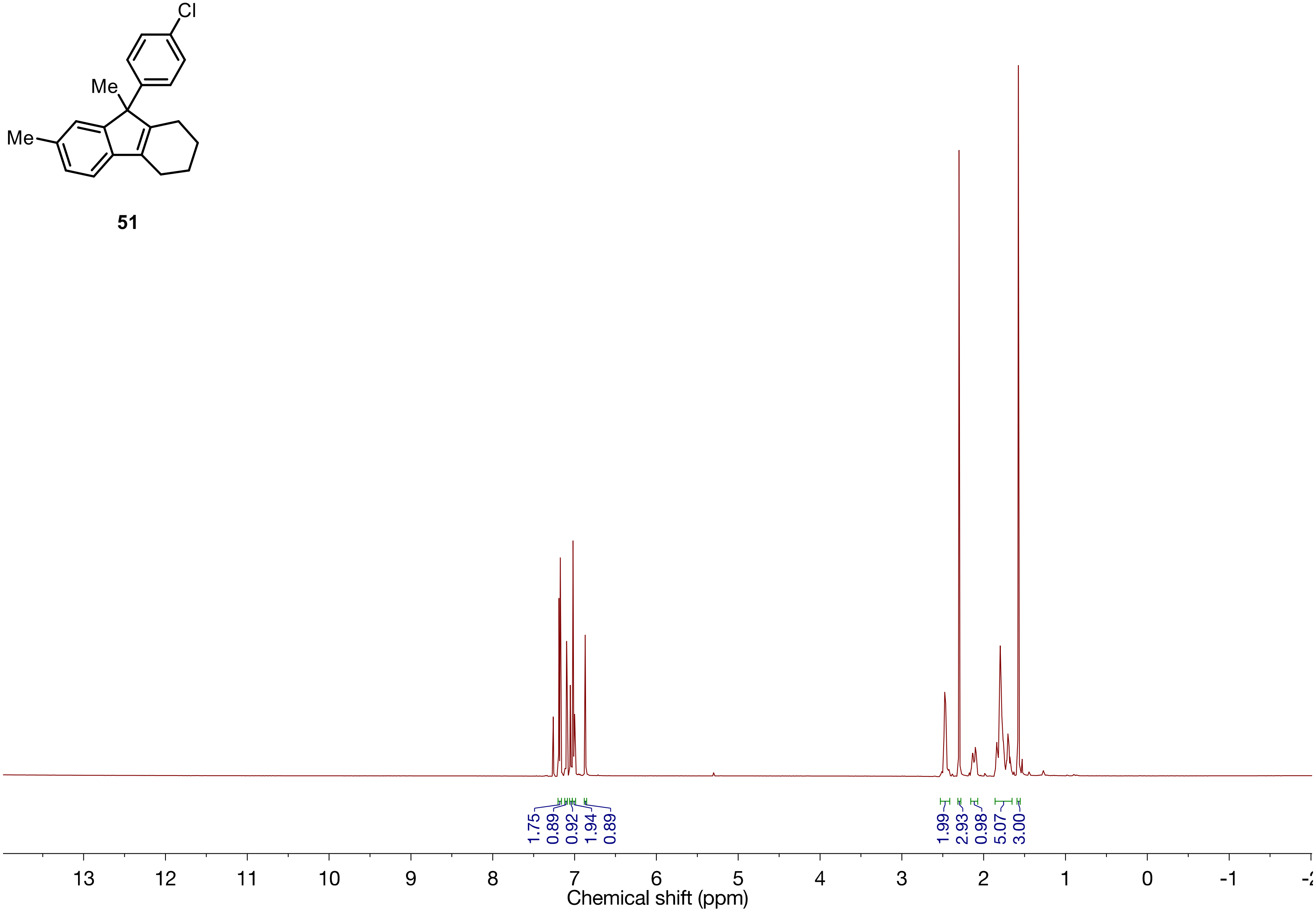
49


154.45
150.94
144.36
143.47
134.12
128.41
126.54
126.38
126.22
124.74
122.44
118.03
56.64
23.24
22.83
22.29
21.98
21.32
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

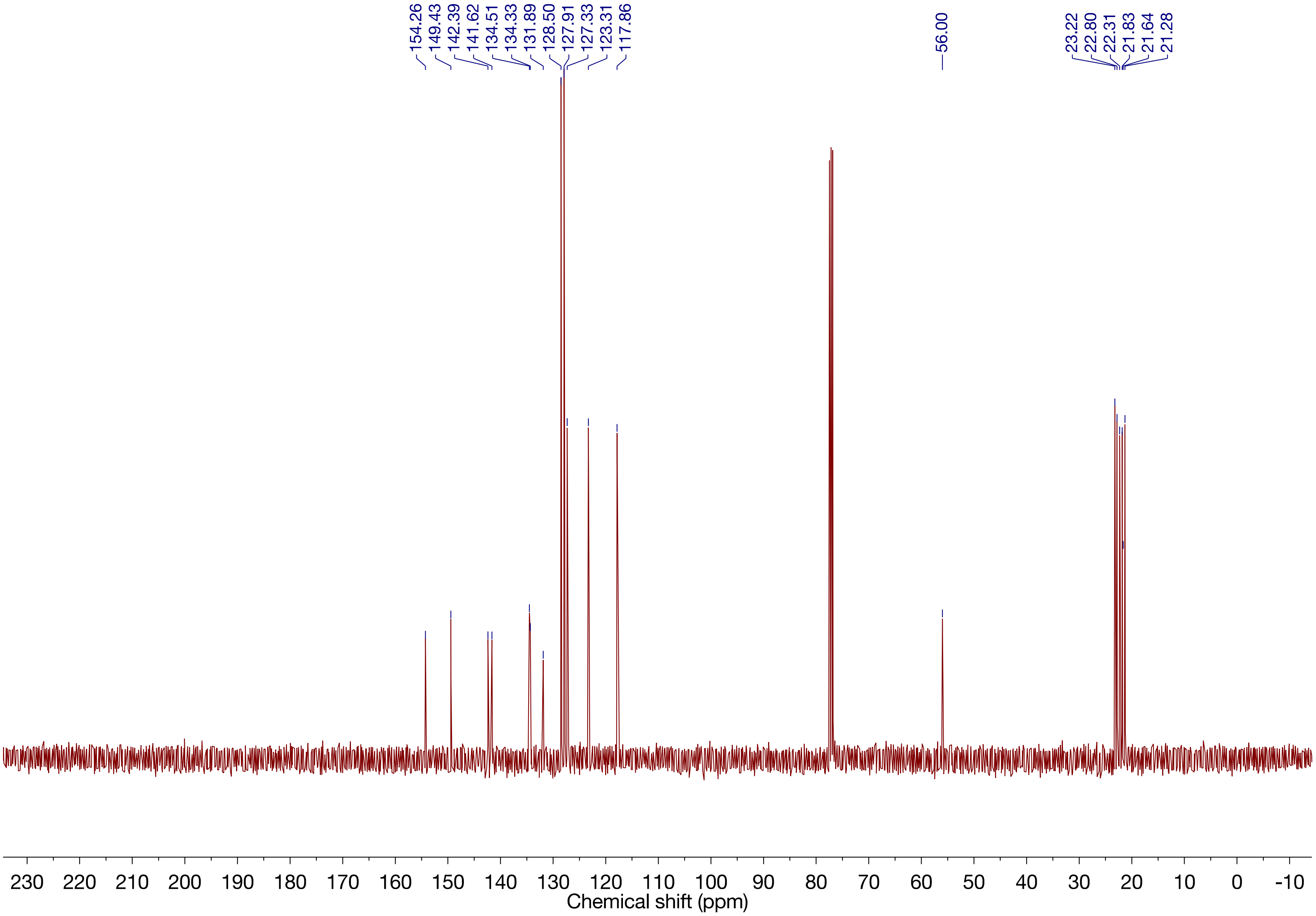

50

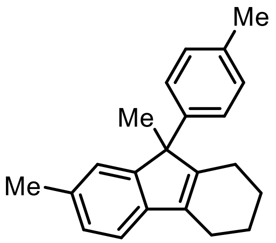
Cl
Me
Ph
1.81
0.90
1.82
3.60
1.71
1.80
2.00
1.08
5.06
2.67
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-
Chemical shift (ppm)


154.68
151.11
143.60
141.99
141.84
138.07
134.26
132.05
128.77
128.57
127.94
127.20
126.90
125.86
121.34
118.40
56.35
23.16
22.78
22.33
21.98
21.37
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

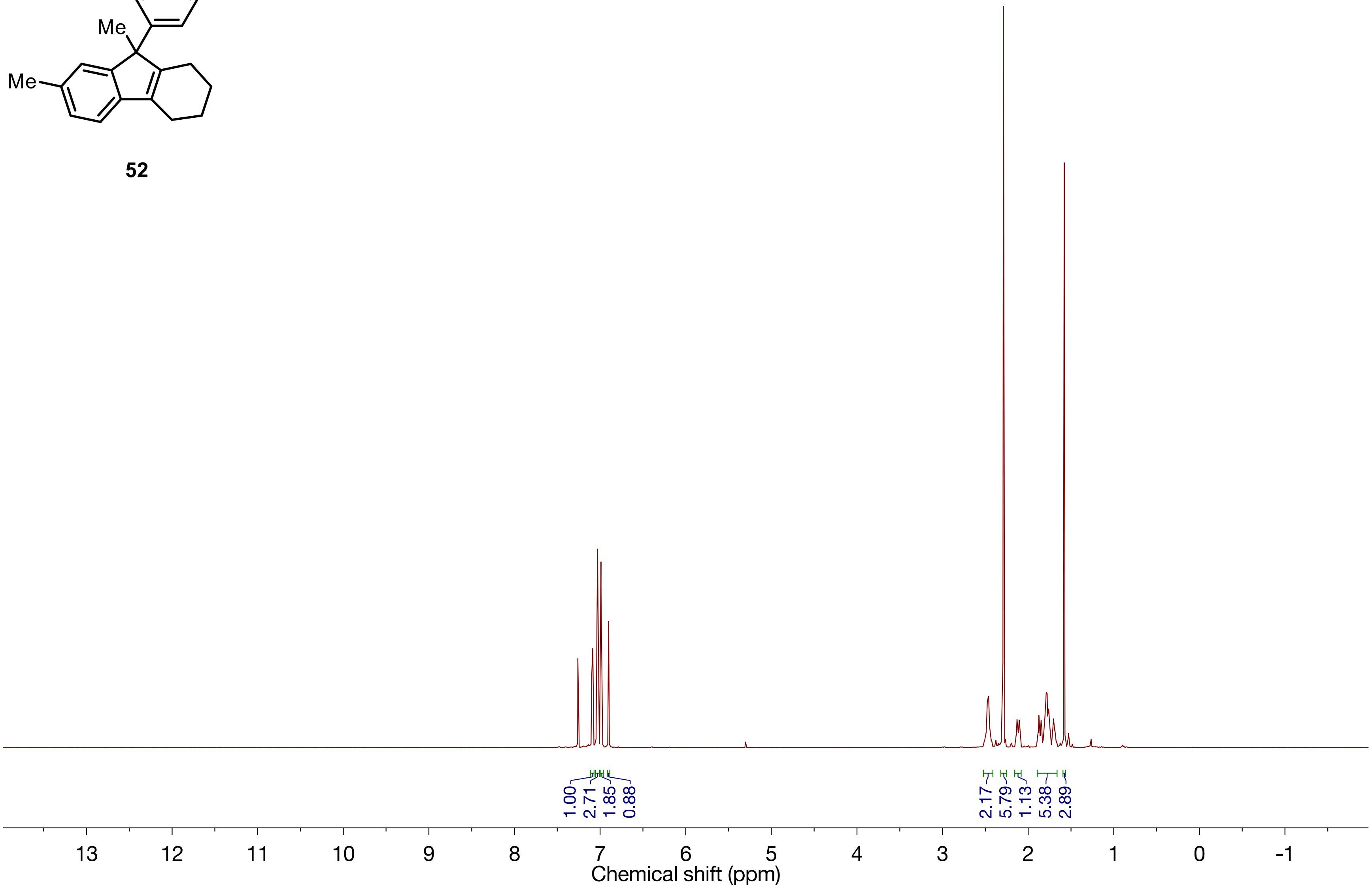

Cl
Me
Me
1.75
0.89
0.92
1.94
0.89
1.99
2.93
0.98
5.07
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

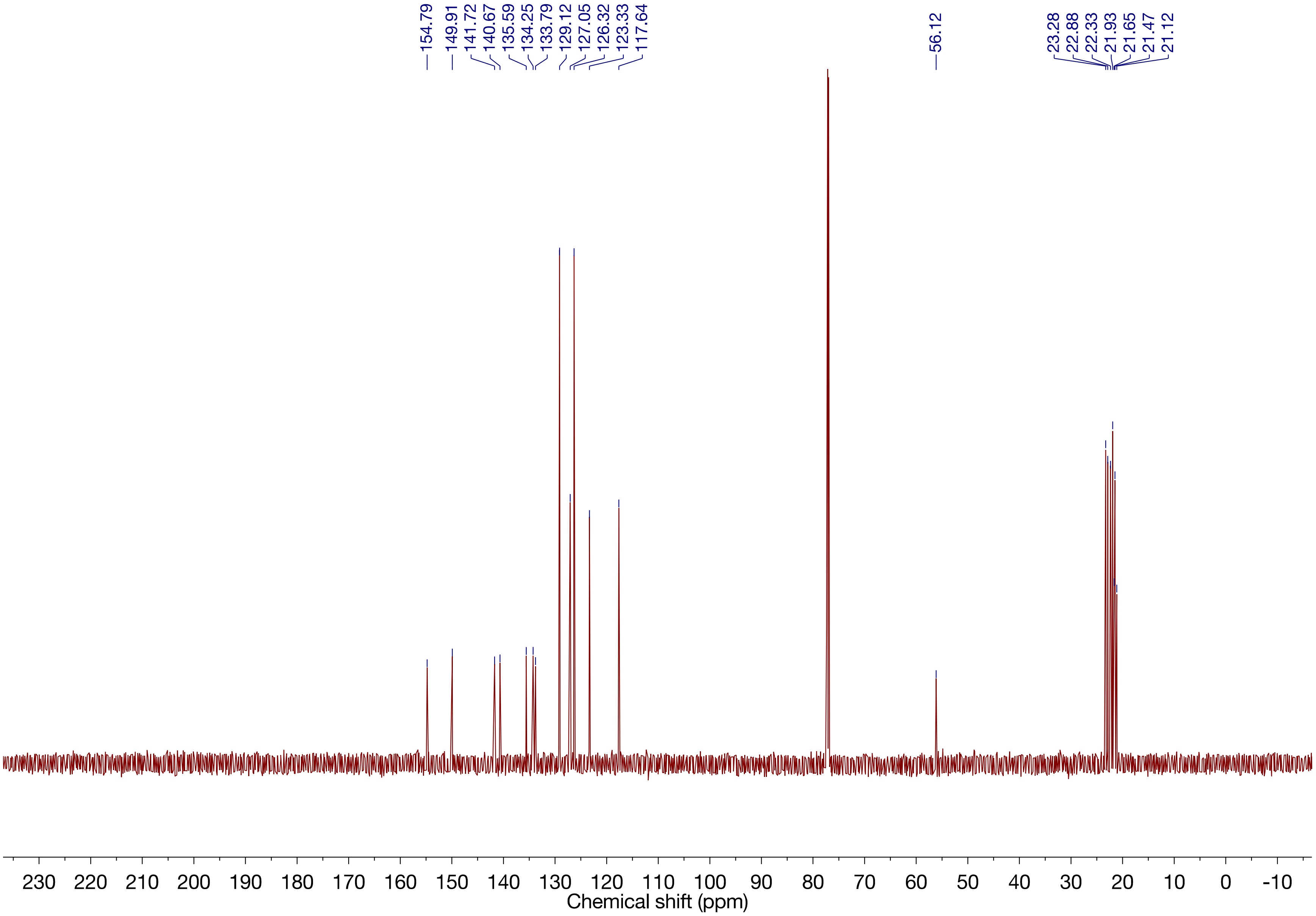
51


154.26
149.43
142.39
141.62
134.51
134.33
131.89
128.50
127.91
127.33
123.31
117.86
56.00
23.22
22.80
22.31
21.83
21.64
21.28
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

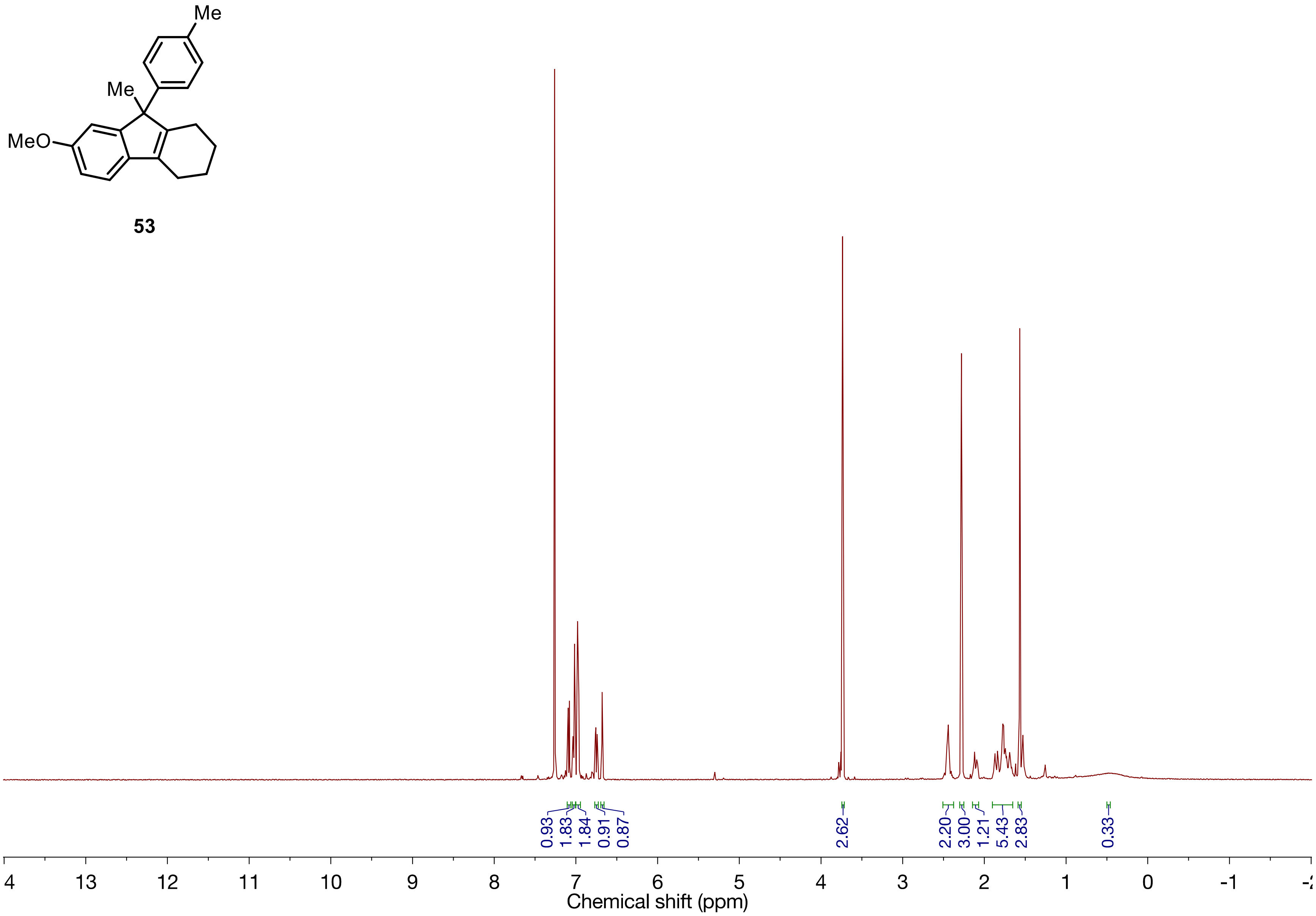

Me
Me
Me

52


1.00
2.71
1.85
0.88
2.17
5.79
1.13
5.38
2.89
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

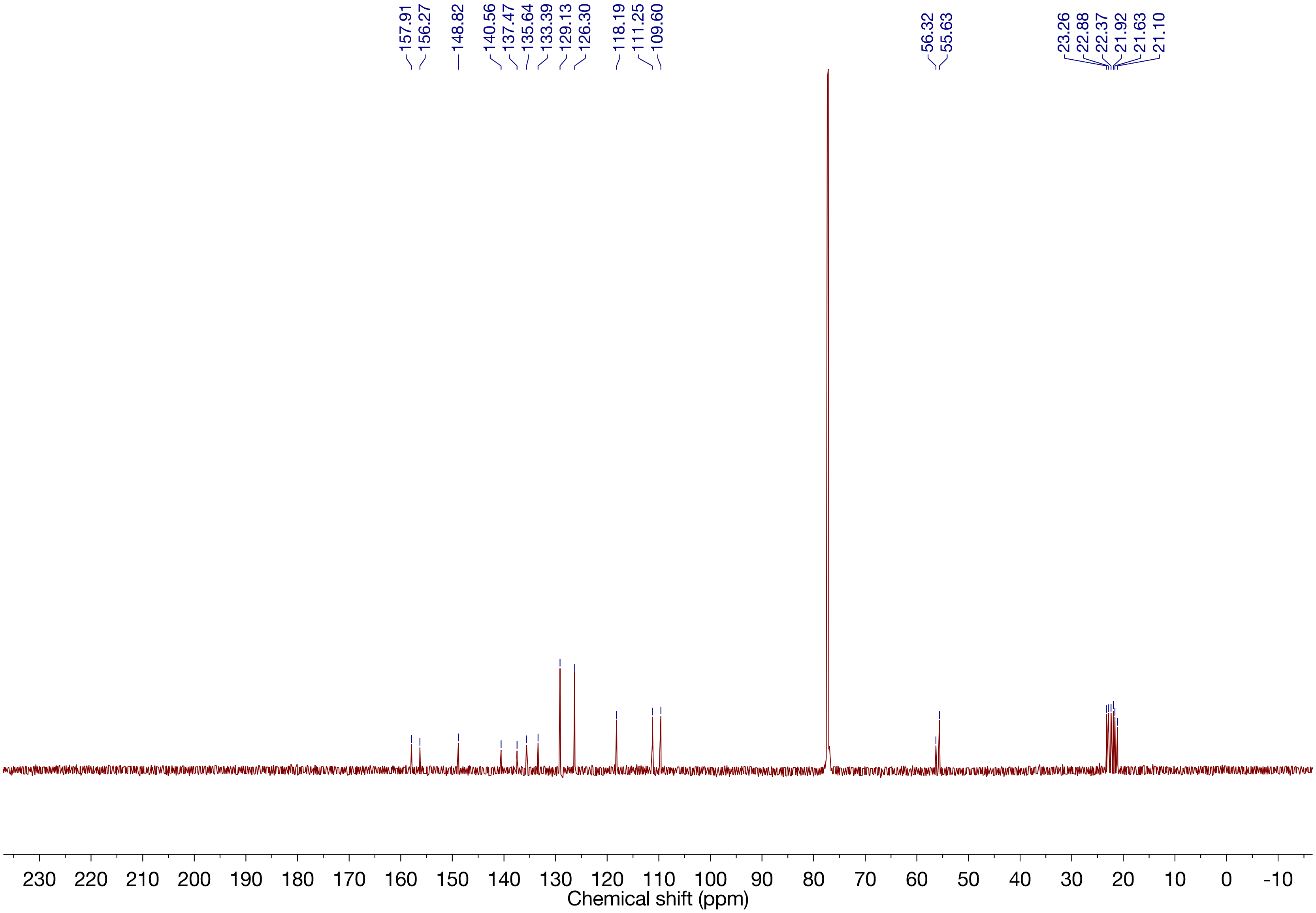


154.79
149.91
141.72
140.67
135.59
134.25
133.79
129.12
127.05
126.32
123.33
117.64
56.12
23.28
22.88
22.33
21.93
21.65
21.47
21.12
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

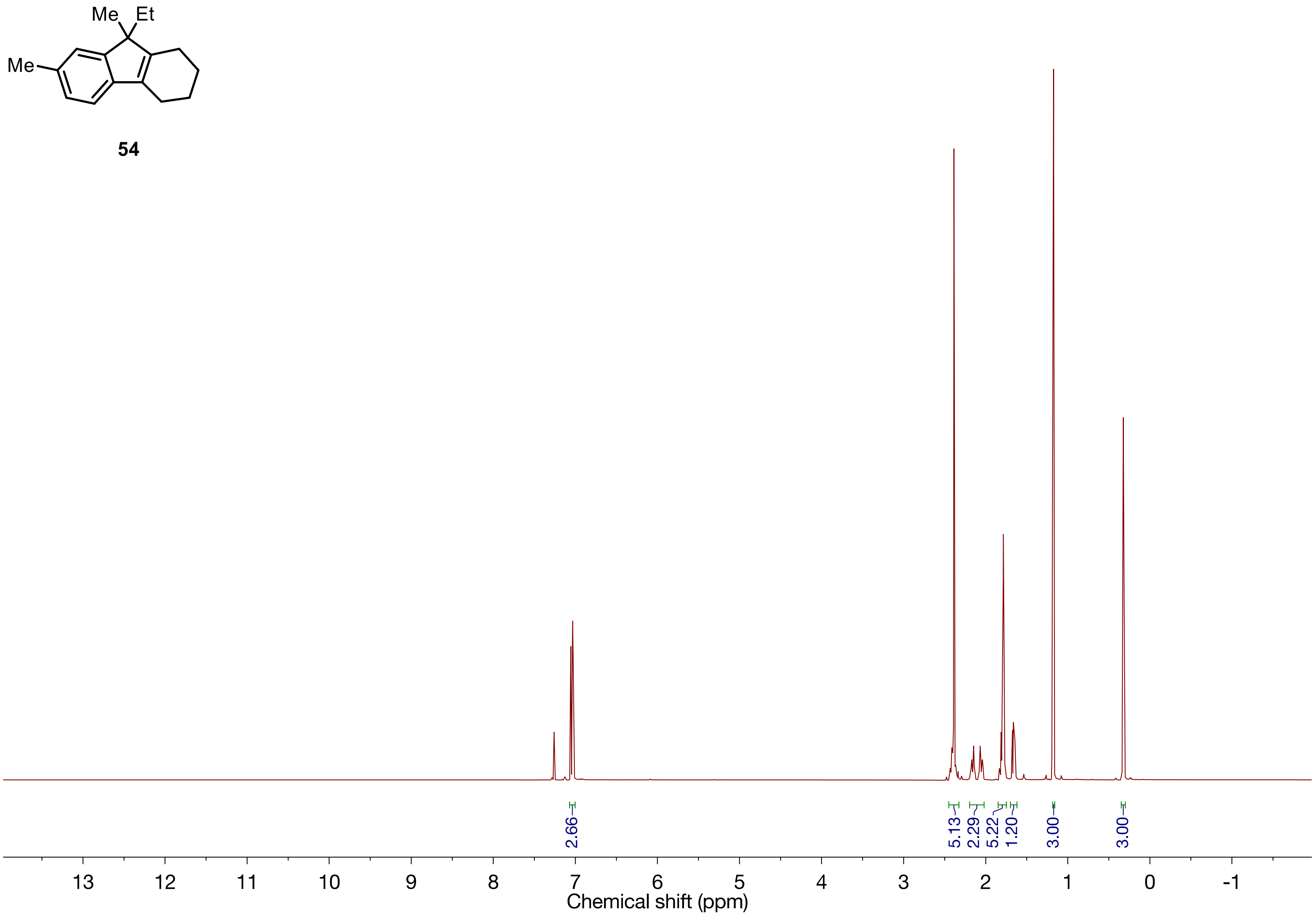


53

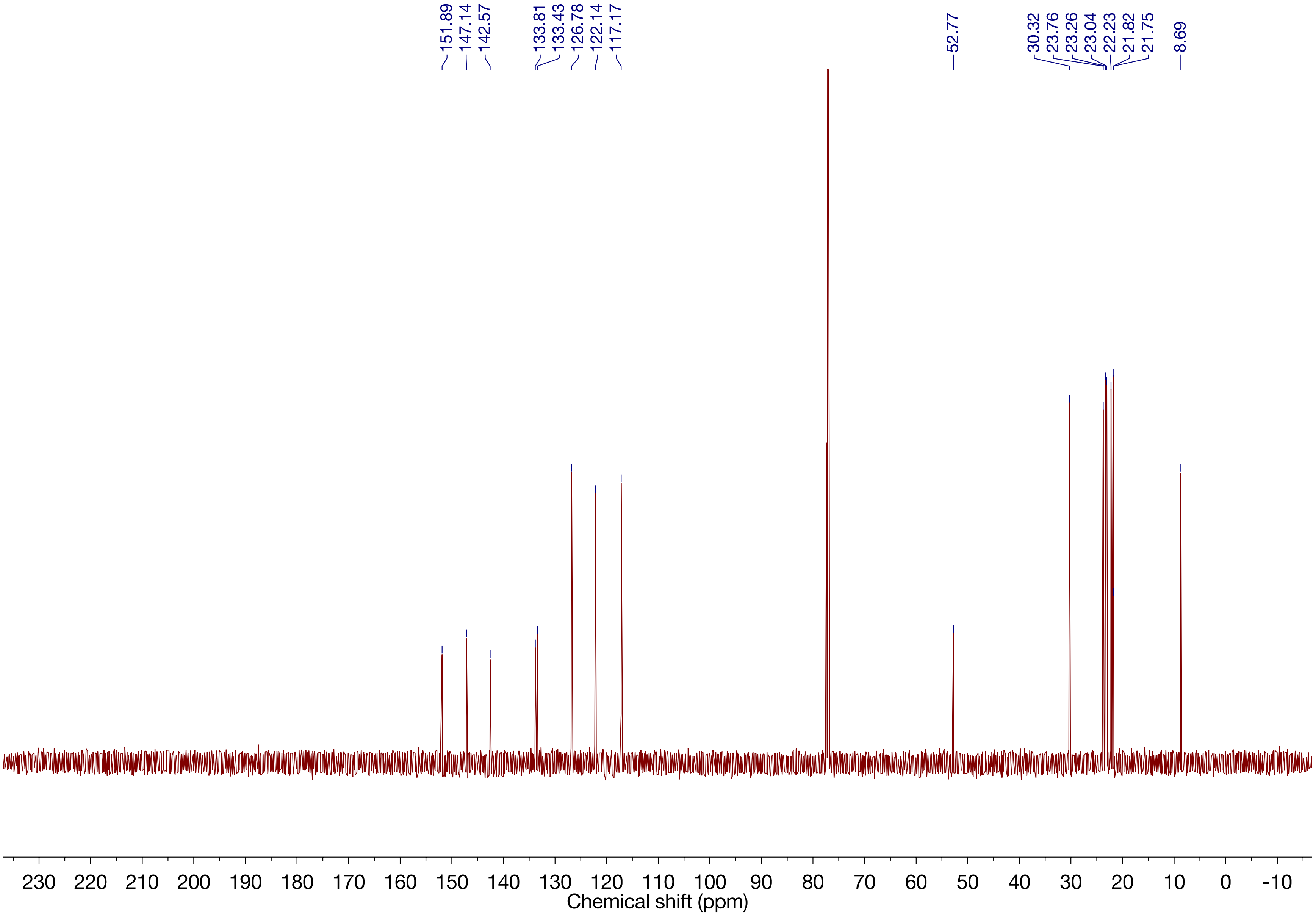
Me
Me
MeO
0.93
1.83
1.84
0.91
0.87
2.62
2.20
3.00
1.21
5.43
2.83
0.33
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-
Chemical shift (ppm)

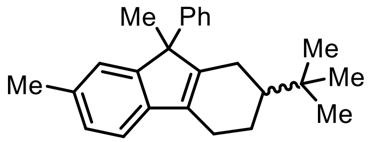


157.91
156.27
148.82
140.56
137.47
135.64
133.39
129.13
126.30
118.19
111.25
109.60
56.32
55.63
23.26
22.88
22.37
21.92
21.63
21.10
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

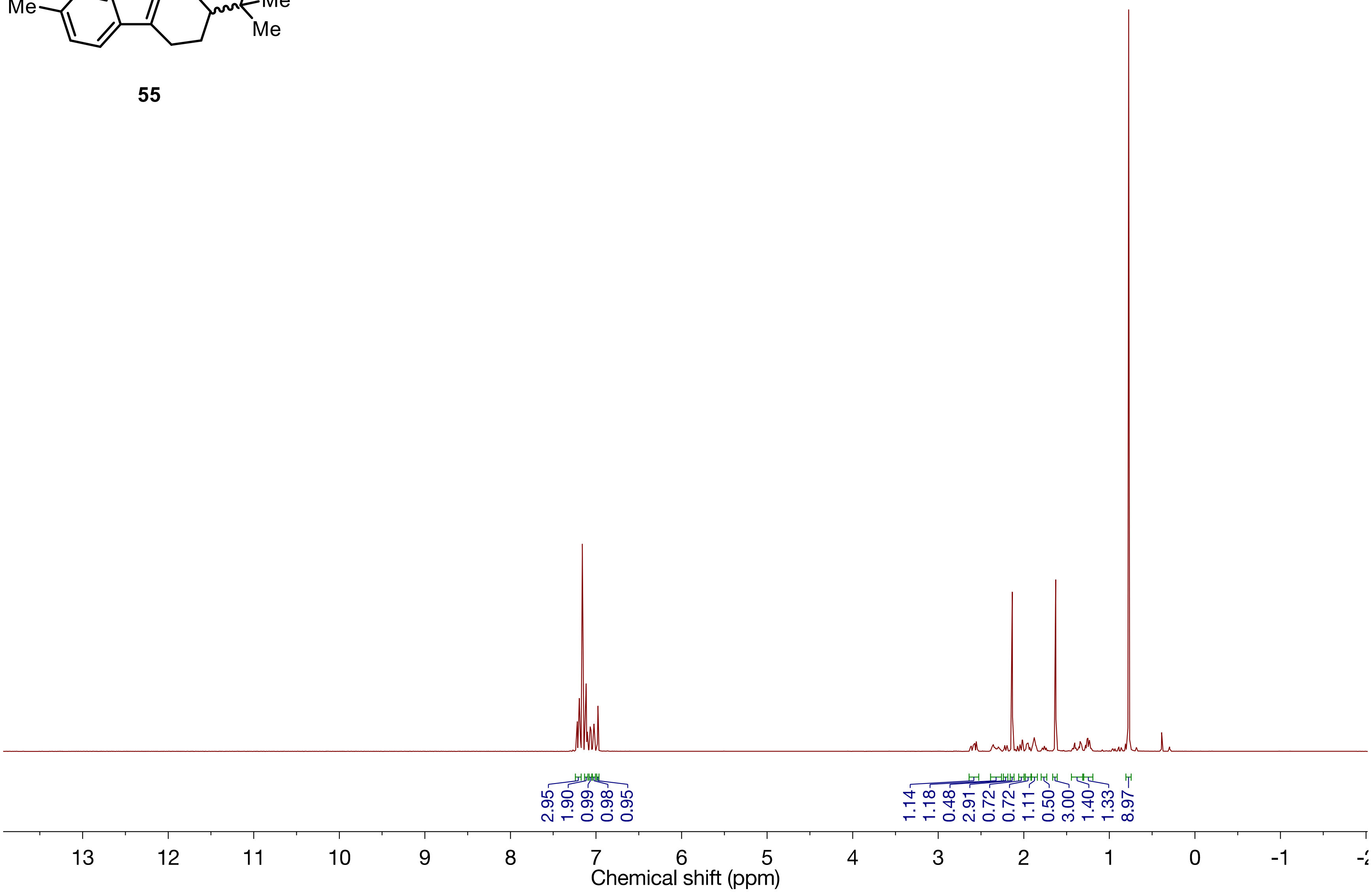

Me
Et
Me
2.66
5.13
2.29
5.22
1.20
3.00
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

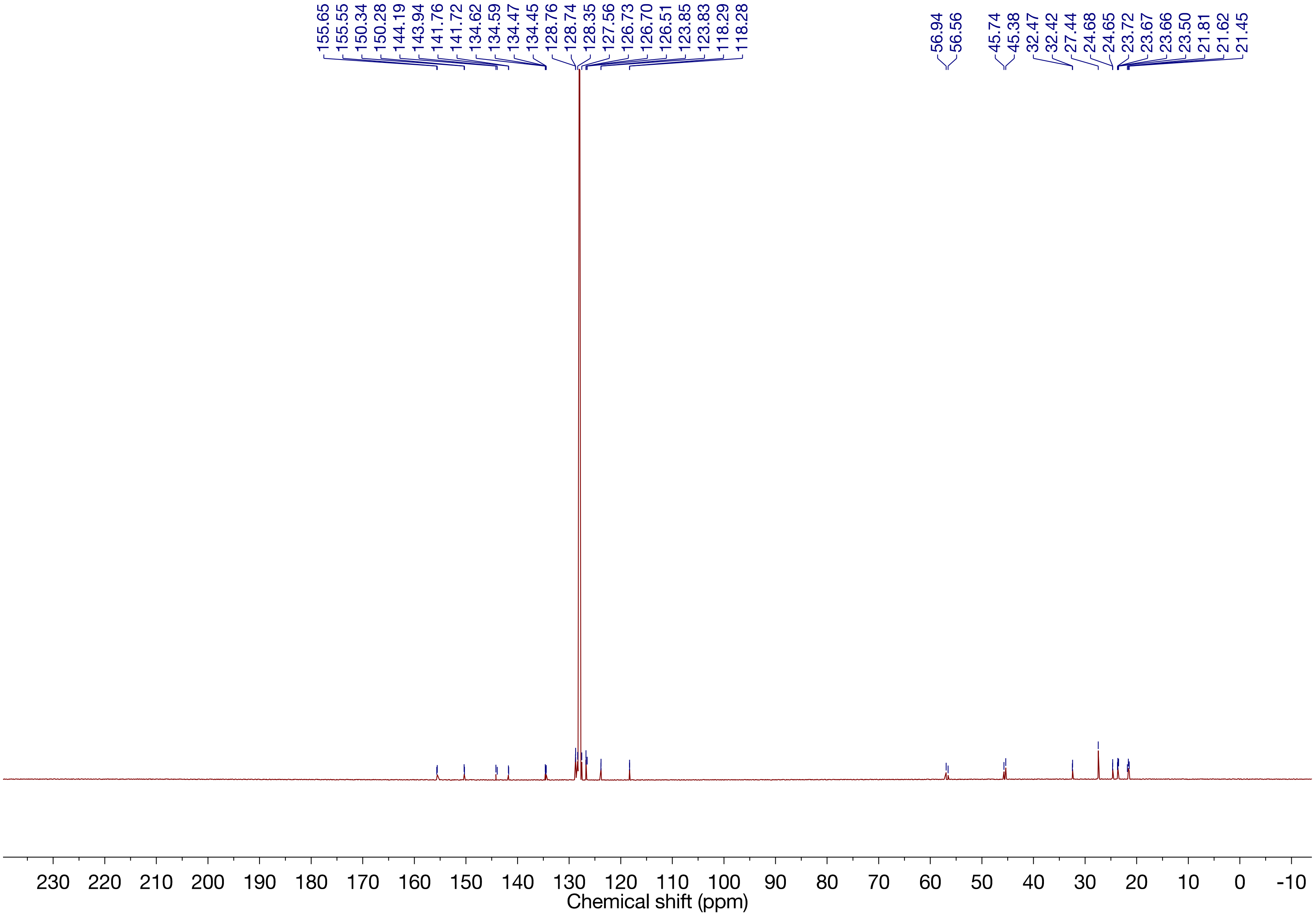
54

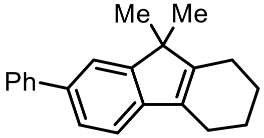

151.89
147.14
142.57
133.81
133.43
126.78
122.14
117.17
52.77
30.32
23.76
23.26
23.04
22.23
21.82
21.75
8.69
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


Me
Ph
Me
Me
Me
Me
Me

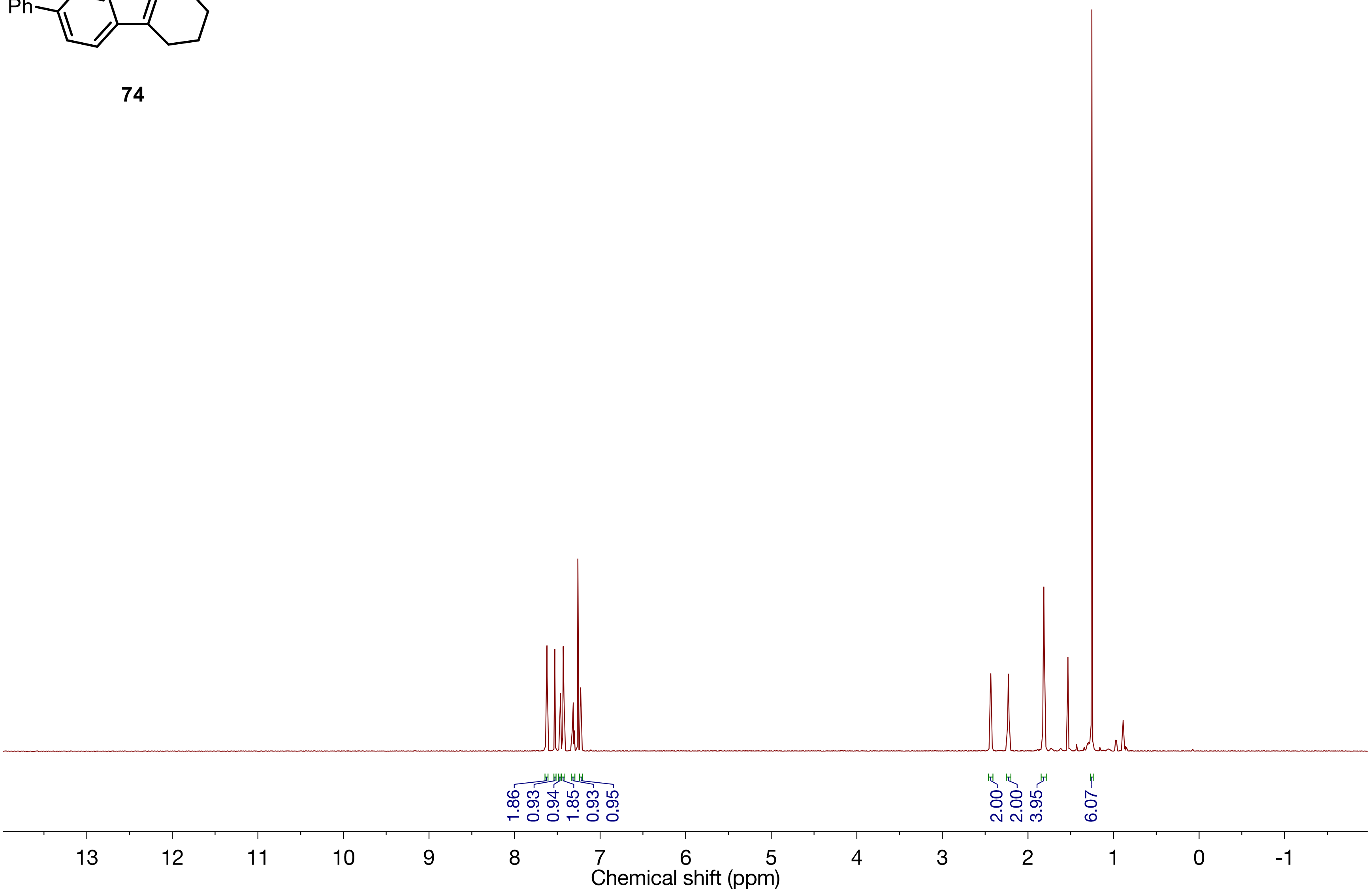
55

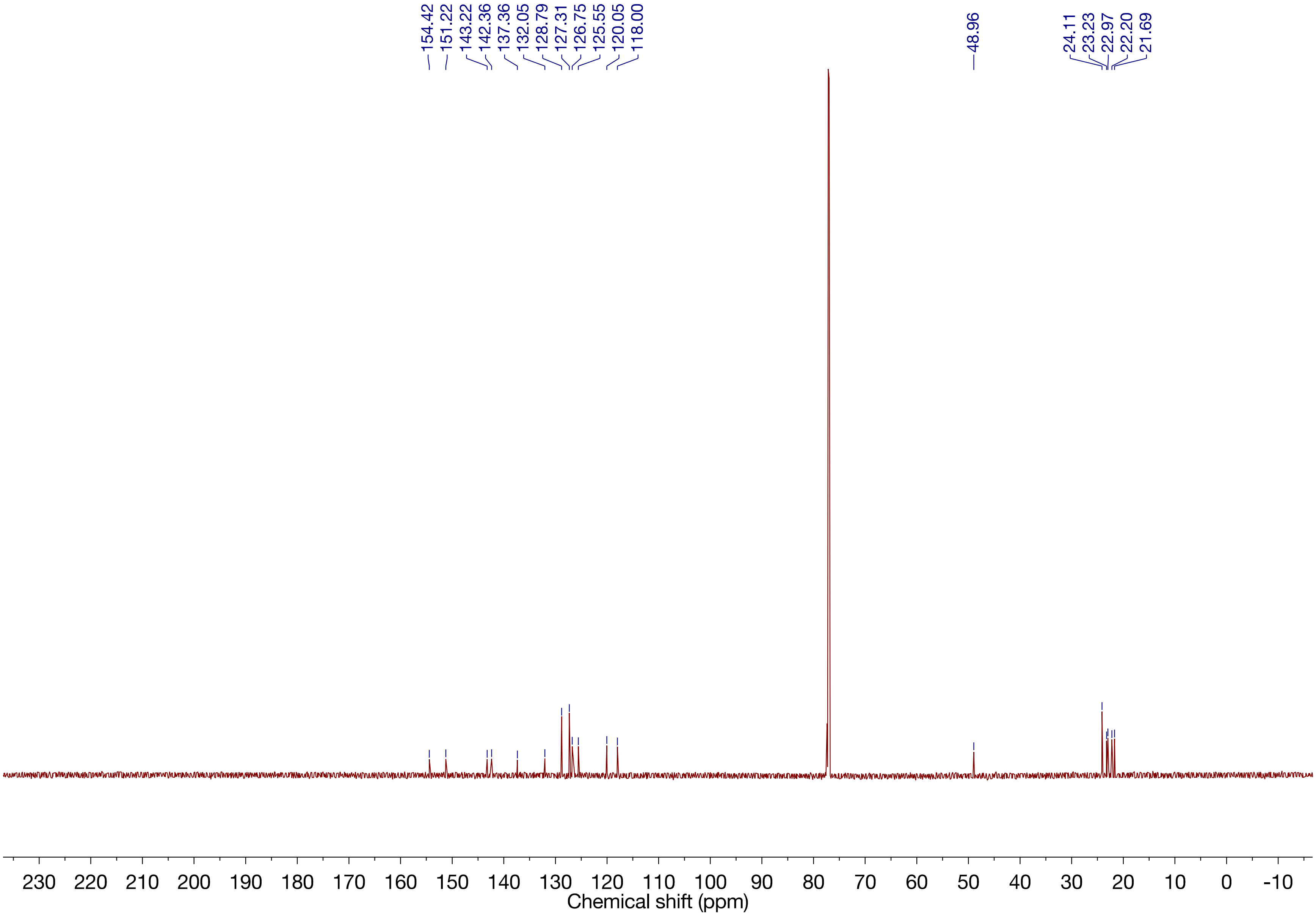

2.95
1.90
0.99
0.98
0.95
1.14
1.18
0.48
2.91
0.72
0.72
1.11
0.50
3.00
1.40
1.33
8.97
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


155.65
155.55
150.34
150.28
144.19
143.94
141.76
141.72
134.62
134.59
134.47
134.45
128.76
128.74
128.35
127.56
126.73
126.70
126.51
123.85
123.83
118.29
118.28
56.94
56.56
45.74
45.38
32.47
32.42
27.44
24.68
24.65
23.72
23.67
23.66
23.50
21.81
21.62
21.45
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

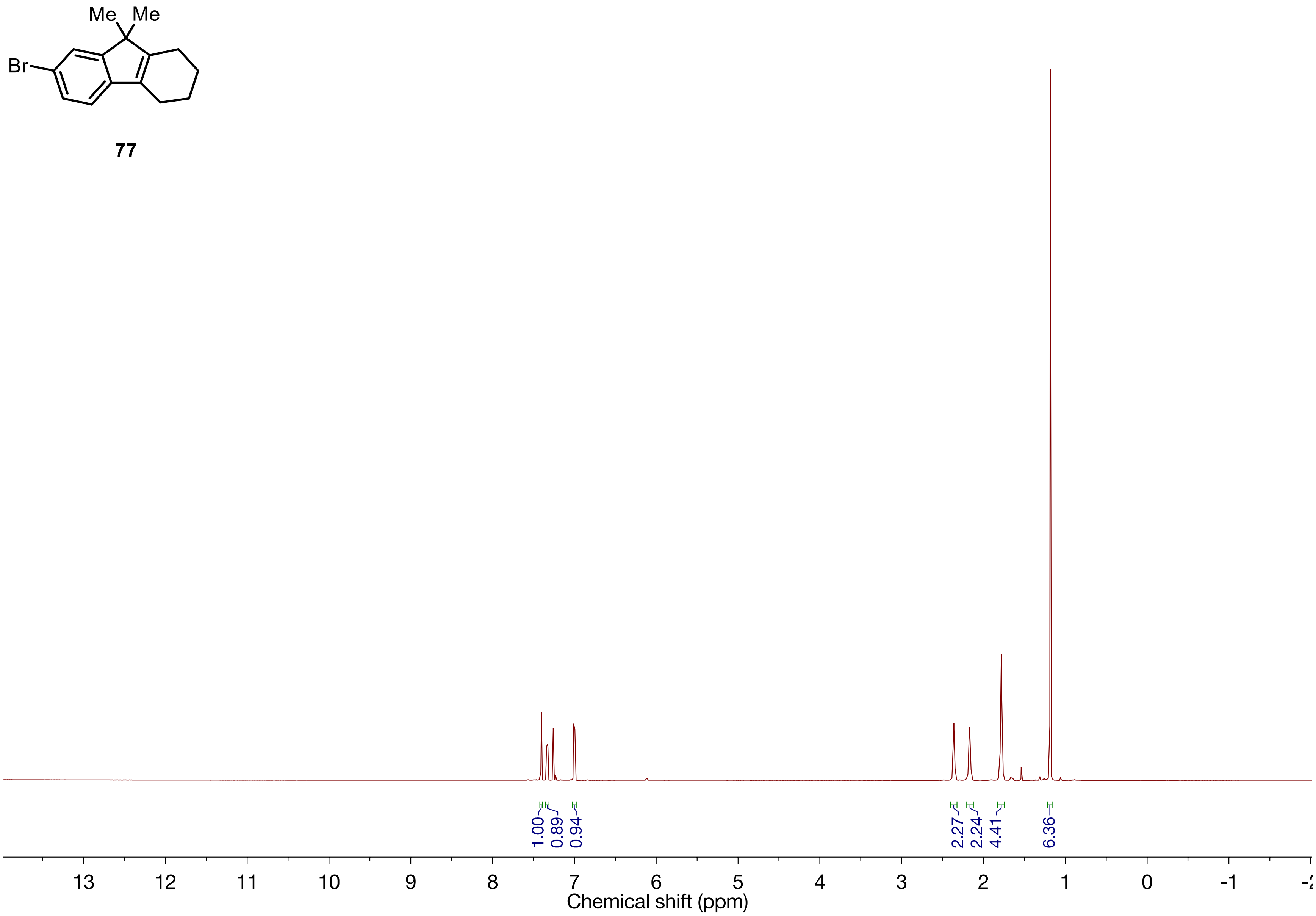

Me
Me
Ph

74


1.86
0.93
0.94
1.85
0.93
0.95
2.00
2.00
3.95
6.07
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)

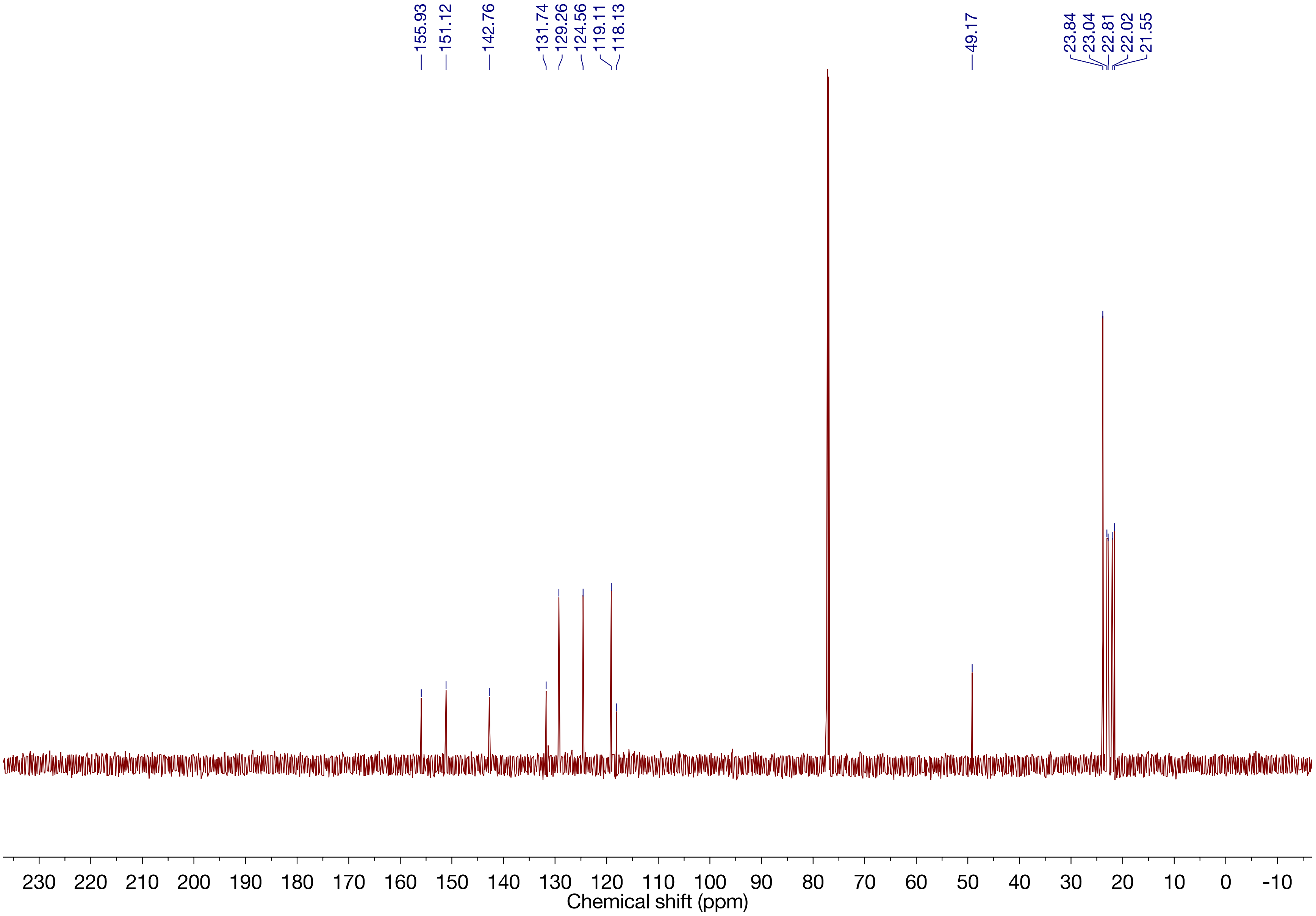


154.42
151.22
143.22
142.36
137.36
132.05
128.79
127.31
126.75
125.55
120.05
118.00
48.96
24.11
23.23
22.97
22.20
21.69
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)



77

Me
Me
Br
1.00
0.89
0.94
2.27
2.24
4.41
6.36
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
Chemical shift (ppm)


155.93
151.12
142.76
131.74
129.26
124.56
119.11
118.13
49.17
23.84
23.04
22.81
22.02
21.55
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)

11. References

1. K. Alder, F. Pascher, A. Schmitz, Über die Anlagerung von Maleinsäure-anhydrid und Azodicarbonsäure-ester an einfach ungesättigte Koh an einfach ungesättigte Kohlenwasserstoffe. Zur Kenntnis von Substitutionsvorgängen in der Allyl-Stellung. *Berichte Dtsch. Chem. Ges. B Ser.* **76**, 27–53 (1943).

2. M. L. Clarke, M. B. France, The carbonyl ene reaction. *Tetrahedron*. **64**, 9003–9031 (2008).

3. K. Mikami, M. Shimizu, Asymmetric ene reactions in organic synthesis. *Chem. Rev.* **92**, 1021–1050 (1992).

4. C.-Y. Ho, K. D. Schleicher, C.-W. Chan, T. F. Jamison, Catalytic Addition of Simple Alkenes to Carbonyl Compounds by Use of Group 10 Metals. *Synlett*. **2009**, 2565–2582 (2009).

5. B. B. Snider, in *Comp. Org. Synth.*, B. M. Trost, I. Fleming, Eds. (Pergamon, Oxford, 1991), vol. 2, pp. 527-562.

6. O. Kriewitz, Additive compounds of formaldehyde with terpenes. *Ber*. **32**, 57-60 (1899).

7. H. J. Prins, The reciprocal condensation of unsaturated organic compounds. *Chem. Weekblad*. **16**, 1510-1526 (1919).

8. E. Arundale, L. A. Mikeska, The Olefin-Aldehyde Condensation. The Prins Reaction. *Chem. Rev.* **51**, 505–555 (1952).

9. C. Olier, M. Kaafarani, S. Gastaldi, M. P. Bertrand, Synthesis of tetrahydropyrans and related heterocycles via prins cyclization; extension to aza-prins cyclization. *Tetrahedron*. **66**, 413–445 (2010).

10. L. M. Pastor, M. Yus, The Prins Reaction: Advances and Applications. *Curr. Org. Chem.* **11**, 925-957 (2007).

11. L. M. Stephenson, M. Orfanopoulos, Changes in ene reaction mechanisms with Lewis acid catalysis. *J. Org. Chem.* **46**, 2200–2201 (1981).

12. H. Kwart, M. Brechbiel, Observations on the mechanism of the Lewis acid catalyzed ene reaction. *J. Org. Chem.* **47**, 5409–5411 (1982).

13. B. B. Snider, E. Ron, The mechanism of Lewis acid catalyzed ene reactions. *J. Am. Chem. Soc.* **107**, 8160–8164 (1985).

14. D. A. Singleton, C. Hang, 13C and 2H Kinetic Isotope Effects and the Mechanism of Lewis Acid-Catalyzed Ene Reactions of Formaldehyde. *J. Org. Chem.* **65**, 895–899 (2000).

15. J. R. Ludwig, P. M. Zimmerman, J. B. Gianino, C. S. Schindler, Iron(III)-catalysed carbonyl–olefin metathesis. *Nature*. **533**, 374–379 (2016).

16. J. R. Ludwig *et al.*, Mechanistic Investigations of the Iron(III)-Catalyzed Carbonyl-Olefin Metathesis Reaction. *J. Am. Chem. Soc.* **139**, 10832–10842 (2017).

17. E. Paternò, Organic Syntheses Induced by Light. Introductory Note. *Gazz. Chim. Ital.* **39**, 237-250 (1909).

18. G. Büchi, C. G. Inman, E. S. Lipinsky, Light-catalyzed Organic Reactions. I. The Reaction of Carbonyl Compounds with 2-Methyl-2-butene in the Presence of Ultraviolet Light. *J. Am. Chem. Soc.* **76**, 4327–4331 (1954).

19. J. A. Porco Jr., S. L. Schreiber, in *Comp. Org. Synth.*, B. M. Trost, I. Fleming, Eds. (Pergamon, Oxford, 1991). vol. 5, pp. 151-192.

20. The formation of a related tetrahydrofluorene has previously been described as a byproduct in 38% yield using catalytic $Bi(OTf)_3$. However, the reaction was assumed to proceed following a carbonyl-ene reaction path and subsequent Friedel-Crafts alkylation. See (21)

21. P. Tremel *et al.*, Catalytic intramolecular carbonyl–ene reaction with ketones: evidence for a retro–ene process. *New J. Chem.* **39**, 7453–7458 (2015).

22. B. B. Snider, Lewis-acid catalyzed ene reactions. *Acc. Chem. Res.* **13**, 426–432 (1980).

23. G. Lemière *et al.*, Gold(I)- and Gold(III)-Catalyzed Cycloisomerization of Allenynes: A Remarkable Halide Effect. *Angew. Chem. Int. Ed.* **45**, 7596–7599 (2006).

24. S. M. Wilkerson-Hill, C. M. Lavados, R. Sarpong, The Diels–Alder reactivity of 2-vinylindenes: synthesis of functionalized tetrahydrofluorenes. *Tetrahedron*. **72**, 3635–3640 (2016).

25. A.-H. Zhou, F. Pan, C. Zhu, L.-W. Ye, Recent Progress towards Transition-Metal-Catalyzed Synthesis of Fluorenes. *Chem. – Eur. J.* **21**, 10278–10288 (2015).

26. Z. Lu, M. Yang, P. Chen, X. Xiong, A. Li, Total Synthesis of Hapalindole-Type Natural Products. *Angew. Chem. Int. Ed.* **53**, 13840–13844 (2014).

27. M. L. Maddess *et al.*, Enantioselective Synthesis of a Highly Substituted Tetrahydrofluorene Derivative as a Potent and Selective Estrogen Receptor Beta Agonist. *Org. Process Res. Dev.* **18**, 528–538 (2014).

28. J. O. Link *et al.*, Discovery of Ledipasvir (GS-5885): A Potent, Once-Daily Oral NS5A Inhibitor for the Treatment of Hepatitis C Virus Infection. *J. Med. Chem.* **57**, 2033–2046 (2014).

29. P. M. Zimmerman, Single-ended transition state finding with the growing string method. *J. Comput. Chem.* **36**, 601–611 (2015).

30. Attempts to probe the Prins reaction pathway computationally did not support a tertiary carbocation, but instead implicated benzylic carbocation **81** via a transition state resembling an oxetane (**79**).

31. Z. Lu, M. Shen, T. P. Yoon, [3+2] Cycloadditions of Aryl Cyclopropyl Ketones by Visible Light Photocatalysis. *J. Am. Chem. Soc.* **133**, 1162–1164 (2011).

32. D. Kurauchi *et al.*, Dialkylzinc-mediated allylic polyfluoroarylation reaction. *Tetrahedron*. **71**, 5849–5857 (2015).

33. L. Xu *et al.*, Copper-free arylation of 3,3-disubstituted allylic halides with triazene-softened aryl Grignard reagents. *Org. Biomol. Chem.* **13**, 6333–6337 (2015).

34. R. J. Comito, F. G. Finelli, D. W. C. MacMillan, Enantioselective Intramolecular Aldehyde α-Alkylation with Simple Olefins: Direct Access to Homo-Ene Products. *J. Am. Chem. Soc.* **135**, 9358–9361 (2013).

35. G. L. Ellis *et al.*, Two-Step Synthesis of Achiral Dispiro-1,2,4,5-tetraoxanes with Outstanding Antimalarial Activity, Low Toxicity, and High-Stability Profiles. *J. Med. Chem.* **51**, 2170–2177 (2008).

36. X. Tao, W. Li, X. Li, X. Xie, Z. Zhang, Diastereo- and Enantioselective Asymmetric Hydrogenation of α-Amido-β-keto Phosphonates via Dynamic Kinetic Resolution. *Org. Lett.* **15**, 72–75 (2013).

37. M. P. Storz, G. Allegretta, B. Kirsch, M. Empting, R. W. Hartmann, From in vitro to in cellulo: structure–activity relationship of (2-nitrophenyl)methanol derivatives as inhibitors of PqsD in Pseudomonas aeruginosa. *Org. Biomol. Chem.* **12**, 6094–6104 (2014).

38. H.-Y. Lee, Y. Jung, Y. Yoon, B. G. Kim, Y. Kim, Angularly Fused Triquinanes from Linear Substrates through Trimethylenemethane Diyl [2 + 3] Cycloaddition Reaction. *Org. Lett.* **12**, 2672–2674 (2010).

39. D. Wang, Y. Zhao, C. Yang, W. Xia, Regioselective synthesis of α-bromo-α,β-unsaturated carbonyl compounds via photocatalytic α-bromination reactions. *Sci. China Chem.* **59**, 190–194 (2016).

40. S. V. Gagnier, R. C. Larock, Palladium-Catalyzed Carbonylative Cyclization of Unsaturated Aryl Iodides and Dienyl Triflates, Iodides, and Bromides to Indanones and 2-Cyclopentenones. *J. Am. Chem. Soc.* **125**, 4804–4807 (2003).

41. T. Okitsu *et al.*, Replacement of the hydrophobic part of 9-cis-retinoic acid with cyclic terpenoid moiety results in RXR-selective agonistic activity. *Bioorg. Med. Chem.* **19**, 2939–2949 (2011).

42. J. March, *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure* (John Wiley & Sons, England, 3rd Edition, 1985).

43. F. G. Bordwell, Equilibrium acidities in dimethyl sulfoxide solution. *Acc. Chem. Res.* **21**, 456–463 (1988).

44. E. Raamat *et al.*, Acidities of strong neutral Brønsted acids in different media. *J. Phys. Org. Chem.* **26**, 162–170.

45. Y. Shao *et al.*, Advances in molecular quantum chemistry contained in the Q-Chem 4 program package. *Mol. Phys.* **113**, 184–215 (2015).

46. S. Grimme, Semiempirical GGA-type density functional constructed with a long-range dispersion correction. *J. Comput. Chem.* **27**, 1787–1799 (2006).

47. R. Ditchfield, W. J. Hehre, J. A. Pople, Self-Consistent Molecular-Orbital Methods. IX. An Extended Gaussian-Type Basis for Molecular-Orbital Studies of Organic Molecules. *J. Chem. Phys.* **54**, 724–728 (1971).

48. P. M. Zimmerman, Growing string method with interpolation and optimization in internal coordinates: Method and examples. *J. Chem. Phys.* **138**, 184102 (2013).

49. P. Zimmerman, Reliable Transition State Searches Integrated with the Growing String Method. *J. Chem. Theory Comput.* **9**, 3043–3050 (2013).

50. M. Jafari, P. M. Zimmerman, Reliable and efficient reaction path and transition state finding for surface reactions with the growing string method. *J. Comput. Chem.* **38**, 645–658 (2017).

51. J.-D. Chai, M. Head-Gordon, Long-range corrected hybrid density functionals with damped atom–atom dispersion corrections. *Phys. Chem. Chem. Phys.* **10**, 6615–6620 (2008).

52. A. V. Marenich, C. J. Cramer, D. G. Truhlar, Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B*. **113**, 6378–6396 (2009).

53. F. Neese, The ORCA program system. *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **2**, 73–78 (2012).

54. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Crystallogr.* **42**, 339–341 (2009).

55. G. M. Sheldrick, SHELXT – Integrated space-group and crystal-structure determination. *Acta Crystallogr. Sect. Found. Adv.* **71**, 3–8 (2015).

56. G. M. Sheldrick, Crystal structure refinement with SHELXL. *Acta Crystallogr. Sect. C Struct. Chem.* **71**, 3–8 (2015).

57. B. M. Trost, F. D. Toste, Mechanistic Dichotomy in CpRu(CH3CN)3PF6 Catalyzed Enyne Cycloisomerizations. *J. Am. Chem. Soc.* **124**, 5025–5036 (2002).

58. M. Noack, R. Göttlich, Iodide-Catalysed Cyclization of Unsaturated N-Chloroamines: A New Way to Synthesise 3-Chloropiperidines. *Eur. J. Org. Chem.* **2002**, 3171–3178 (2002).

59. M. Sugiura, N. Sato, S. Kotani, M. Nakajima, Lewis base-catalyzed conjugate reduction and reductive aldol reaction of α,β-unsaturated ketones using trichlorosilane. *Chem. Commun.*, 4309–4311 (2008).

60. D. Gauthier, S. Beckendorf, T. M. Gøgsig, A. T. Lindhardt, T. Skrydstrup, A Ligand Free and Room Temperature Protocol for Pd-Catalyzed Kumada−Corriu Couplings of Unactivated Alkenyl Phosphates. *J. Org. Chem.* **74**, 3536–3539 (2009).

61. N. M. Rateb, H. F. Zohdi, Atom-Efficient, Solvent-Free, Green Synthesis of Chalcones by Grinding. *Synth. Commun.* **39**, 2789–2794 (2009).

62. C. H. Oh, H. H. Jung, K. S. Kim, N. Kim, The Palladium-Catalyzed Addition of Organoboronic Acids to Alkynes. *Angew. Chem. Int. Ed.* **42**, 805–808 (2003).

63. C.-S. Li, Y.-H. Tsai, W.-C. Lee, W.-J. Kuo, Synthesis and Photophysical Properties of Pyrrole/Polycyclic Aromatic Units Hybrid Fluorophores. *J. Org. Chem.* **75**, 4004–4013 (2010).

64. A. M. Johnson *et al.*, Narcissistic Self-Sorting in Self-Assembled Cages of Rare Earth Metals and Rigid Ligands. *Angew. Chem. Int. Ed.* **54**, 5641–5645 (2015).