Supporting Information for

A Pd-Catalysed One-Pot Three-Step Reaction in the Synthesis of Naphthalenes and 1,2-Naphthoquinones

Anton A. Nechaev,[a] Pratap R. Jagtap,[a] Ema Bažíková,[a] Johana Neumannová,[a] Ivana Císařová,[b] and Eliška Matoušová[a,*]

[a] *Department of Organic Chemistry, Faculty of Science, Charles University, Hlavova 8, 128 00 Praha 2, Czech Republic*

[b] *Department of Inorganic Chemistry, Faculty of Science, Charles University, Hlavova 8, 128 00 Praha 2, Czech Republic*

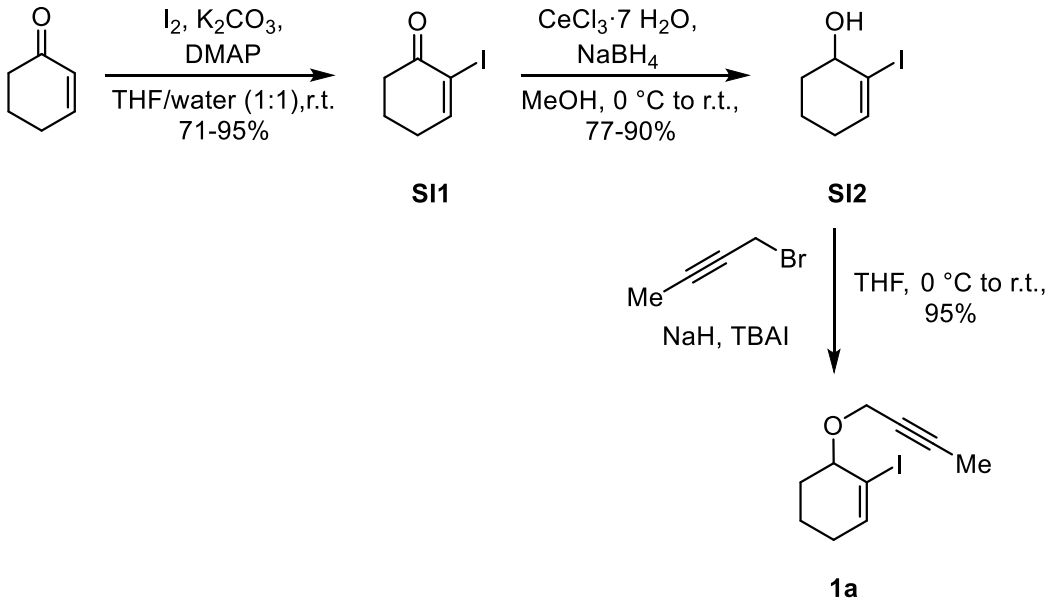
Contents

1. General experimental procedures

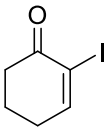
Unless otherwise specified, the following general procedures were used in all reactions. Commercially available compounds were used without further purification unless otherwise stated. Levoglucosenone was kindly donated by the Circa Group Pty Ltd (Australia). Tetrahydrofuran (THF) purified and dried by distillation from sodium/benzophenone. Dry dichloromethane was purchased from Acros and used without purification. Analytical thin layer chromatography (TLC) was performed on Merck Silica gel 60- F254 coated aluminum plates. Eluated plates were checked using a UV lamp (254 nm) and/or by treatment with a suitable dip followed by heating. Followed dips were used: phosphomolybdate dip: [$Ce(SO_4)_2 \cdot 4H_2O$ (2 g), $H_3[P(Mo_3O_{10})_4]$ (4g), H_2SO_4 (10 mL), H_2O (200 mL)]; anisaldehyde dip: [CH_3COOH (99%) (6 mL), anisaldehyde (8 mL), CH_3CH_2OH (400 mL), H_2SO_4 (20 mL)]. Flash chromatography was performed on Acros Silica gel 60A (35–70 μm). Proton (^1H) and carbon (^{13}C) NMR spectra were recorded on a Bruker AVANCE III HD 400 instrument using the residual signals from $CHCl_3$, δ 7.26 ppm and δ 77.16 ppm; DMSO, δ 2.50 ppm and δ 39.52 ppm; THF δ 3.58 and 1.73 ppm, δ 67.57 and δ 25.37 ppm; MeOH δ 3.31 and δ 49.00 ppm, as internal references for ^1H and ^{13}C chemical shifts, respectively. IR spectra were measured on Thermo Nicolet AVATAR 370 FT-IR spectrometer on KBr tablets of the compounds via DRIFT method. EI and CI mass spectra were measured using orthogonal acceleration time-of-flight mass spectrometer GCT Premier (Waters) coupled to a 7890A gas chromatograph (Agilent). ESI mass spectra (low resolution) were recorded using Q-Tof micro (Waters) mass spectrometer. ESI or APCI mass spectra (high resolution) was measured using LTQ Orbitrap XL hybrid mass spectrometer (Thermo Fisher Scientific) equipped with an electrospray ion source. Melting points were measured on Büchi Melting Point B-545 using capillary method and are uncorrected. Optical rotations measured on AUTOMATIC POLARIMETR, Autopol III are given in $deg \cdot mL \cdot g^{-1} \cdot dm^{-1}$ with accuracy ±2 and the mass concentrations (marked as *c* are given in g/100 mL). The cytotoxic activity screening was performed by our collaborators from the group of Dr. Hana Mertlikova-Kaiserova at the Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences.

2. Synthesis of starting materials

2.1 Synthesis of compound **1a**



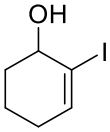
2-Iodocyclohex-2-en-1-one (SI1)



Applying modified procedure from the literature source,[1] to a solution of cyclohex-2-en-1-one (1.936 mL, 20.0mmol) in THF/H_2O (50/50 mL) K_2CO_3 (3.317 g, 24.0 mmol), I_2 (7.594 g, 30.0 mmol) and 4-dimethylaminopyridine (0.49 g, 4.0 mmol) were added subsequently. The reaction mixture was allowed to stir at room temperature and after 3 h was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (15 ml) and extracted between brine (50 ml) and EtOAc (2 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified on a silica gel column using hexanes/EtOAc (85/15) as eluent to obtain the target iodinated compound **SI1** as a yellow amorphous solid (4.22 g, 95%). The iodination reaction was performed several times and the isolated yields were in the range of 75–95%. The recorded spectral data were in agreement with previously reported values.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (t, *J* = 4.4 Hz, 1H), 2.69–2.63 (m, 2H), 2.44 (td, *J* = 6.0, 4.4 Hz, 2H), 2.13–2.05 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.3, 159.5, 104.0, 37.4, 30.1, 23.0.

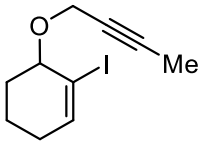
2-Iodocyclohex-2-en-1-ol (SI2)



Applying modified Luche reduction conditions,[3] 2-iodocyclohex-2-en-1-one **SI1** (3.363 g, 15.15 mmol) and $CeCl_3 \cdot 7H_2O$ (12.7 g, 34.09 mmol) were diluted with MeOH (140 mL) and cooled to 0 °C. $NaBH_4$ (0.716 g, 18.94 mmol) was added portionwise and the reaction was allowed to stir at 0 °C for 1.5 h. Then the reaction mixture was quenched with H_2O (15 mL) and stirred for additional 10-15 min. After evaporation of MeOH, extraction between H_2O (40 mL) and EtOAc (3 × 50 mL) the organic layers were separated, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting colorless solid compound **SI2** was obtained in (3.06 g, 90%) and applied to the next step without purification. The reaction was performed several times and the yields were in the range of 77–90%. The recorded spectral data were in agreement with previously reported values.[4]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.50 (t, *J* = 4.1 Hz, 1H), 4.24–4.15 (m, 1H), 2.18–1.95 (m, 4H), 1.91–1.84 (m, 1H), 1.82–1.63 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.2, 103.8, 72.2, 32.1, 29.5, 17.9.

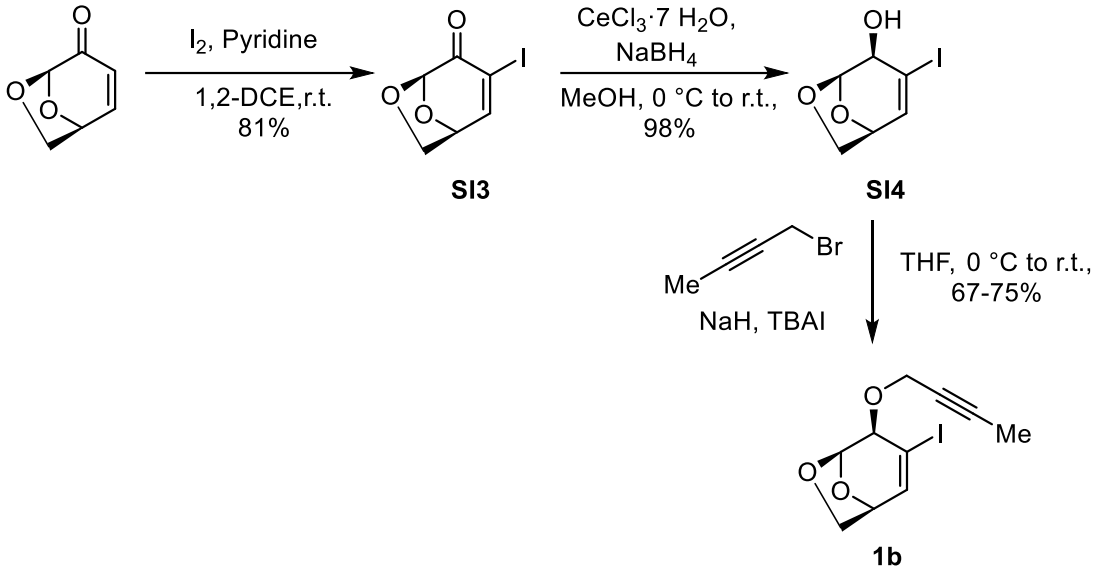
6-(But-2-yn-1-yloxy)-1-iodocyclohex-1-ene (1a)



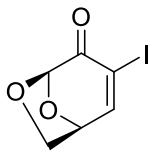
2-Iodocyclohex-2-en-1-ol **SI2** (0.493 g, 2.2 mmol) and tetrabutyl-ammonium iodide (TBAI) (0.082 g, 0.22 mmol) were dissolved in dry THF (6.6 mL) under argon atmosphere. 1-Bromobut-2-yne (0.347 mL, 3.96 mmol) was added and the reaction mixture cooled to 0 °C. NaH (0.159 g, 60% dispersion in mineral oil, 3.96 mmol) was added portionwise and the reaction was stirred at 0 °C. After 20 min it was allowed to warm to room temperature and the stirring was continued overnight. Reaction mixture was quenched with saturated NH_4Cl (10 mL) and extracted between brine (30 mL) and EtOAc (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Column chromatography on silica gel using hexanes/diethyl ether (90/10) as eluent delivered desired product **1a** as a yellow oil (0.590 g, 97%). Compound **1a** is relatively stable in a refrigerator under argon atmosphere within 4 days, after that it starts to decompose slowly.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56–6.53 (m, 1H), 4.30–4.17 (m, 2H), 4.06–4.01 (m, 1H), 2.19–1.92 (m, 3H), 1.86 (t, *J* = 2.3 Hz, 3H), 1.85–1.58 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.2, 98.8, 82.7, 78.1, 75.5, 57.7, 29.5, 29.3, 17.2, 3.8; **IR** (KBr) ν_{max} 2941, 2848, 2295, 2229, 1138, 1063, 988, 940, 806 cm^{-1}; **MS** (EI) *m/z* (%) 276.0 (10, $M^{+\bullet}$), 246.0 (48), 223.0 (70), 205.9 (95), 149.1 (35), 119.1 (100), 97.1 (48), 79.0 (85), 77.0 (60), 53.0 (40); **HRMS** (EI) *m/z* calcd for $C_{10}H_{13}IO$ 276.0011, found 276.0014.

2.2 Synthesis of compound **1b**



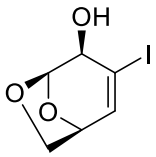
(1*S*,5*R*)-3-Iodo-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (SI3)



According to a literature procedure[5] to a solution of levoglucosenone (1.5 g, 11.9 mmol) in dry 1,2-dichloroethane (20 mL) iodine (4.2 g,16.5 mmol) and pyridine (1.08 mL, 13.4 mmol) were added subsequently. The reaction mixture was allowed to stir at room temperature and after 15 min toluene (20 ml) was added. The resulting media was poured onto a 5 cm plug of silica and the product eluted with toluene. Concentration on a rotary evaporator provided the target iodinated levoglucosenone **SI3** as a yellow crystalline solid (2.45 g, 81%). The recorded spectral data were in agreement with previously reported values.[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 5.0 Hz, 1H), 5.57 (s, 1H), 4.93 (ddd, *J* = 5.1, 4.5, 0.7 Hz, 1H), 3.87 (dd, *J* = 7.0, 4.5 Hz, 1H), 3.81 (d, *J* = 7.1 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 183.2, 155.7, 101.1, 100.0, 74.4, 66.7.

(1*S*,4*R*,5*R*)-3-Iodo-6,8-dioxabicyclo[3.2.1]oct-2-en-4-ol (SI4)

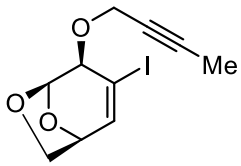


Using reaction conditions for **SI2**, the compound **SI4** was obtained as brownish oil in (2.431 g, 98%) and applied to the next step without purification. The recorded spectral data were in agreement with previously reported values.[6]

Reagent	n [mmol]	m [g]	V [mL]
MeOH			98
SI3	9.7	2.45	
$NaBH_4$	12.2	0.5	
$CeCl_3 \cdot 7H_2O$	21.9	8.14	

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (dd, *J* = 4.8, 0.8 Hz, 1H), 5.55 (d, *J* = 2.8 Hz, 1H), 4.53 (t, *J* = 4.5 Hz, 1H), 4.22 (dd, *J* = 11.8, 3.0 Hz, 1H), 3.86 (d, *J* = 6.9 Hz, 1H), 3.69 (ddd, *J* = 6.9, 4.1, 1.1 Hz, 1H), 2.38 (d, *J* = 11.8 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.5, 103.6, 100.8, 74.3, 73.7, 70.6; **Specific rotation** $[\alpha]_D$ = –51.0° (c 0.5, $CHCl_3$) [lit.[6] $[\alpha]_D$ = –56.7 (0.2, $CHCl_3$)].

(1*S*,4*R*,5*R*)-4-(But-2-yn-1-yloxy)-3-iodo-6,8-dioxabicyclo[3.2.1]oct-2-ene (1b)



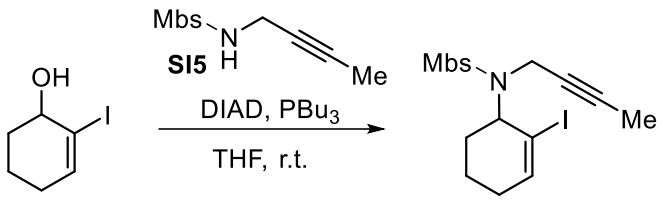
Reaction conditions for **1** were applied. Column chromatography on silica gel with hexanes/diethyl ether (80/20) as eluent delivered desired product **1b** as a viscous yellowish oil (1.21 g, 67%).

Reagent	n [mmol]	m [g]	V [mL]
THF			17.8
SI4	5.93	1.506	
TBAI	0.59	0.219	
1-bromobut-2-yne	10.67		0.9
NaH (60% dispersion in mineral oil)	10.67	0.256	

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (dd, *J* = 4.7, 1.3 Hz, 1H), 5.68 (d, *J* = 2.6 Hz, 1H), 4.51 (t, *J* = 4.4 Hz, 1H), 4.44–4.29 (m, 3H), 3.95 (d, *J* = 6.8 Hz, 1H), 3.71 (ddd, *J* = 6.9,

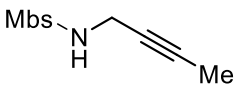
4.0, 1.3 Hz, 1H), 1.86 (t, *J* = 2.3 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.0, 100.4, 99.7, 83.8, 80.0, 74.9, 73.7, 71.0, 59.1, 3.8; **IR** (KBr) ν_{max} 3485, 3354, 2887, 1625, 1329, 1129, 1087, 985 cm^{-1}; **MS** (EI) *m/z* (%) 306.0 (18, $M^{+\bullet}$), 253.8 (55), 207.9 (100), 206.9 (40), 179.9 (17), 133.1 (30), 97.0 (18); **HRMS** (EI) *m/z* calcd for $C_{10}H_{11}IO_3$ 305.9753, found 305.9754; **Specific rotation** $[\alpha]_D$ = –39.3° (c 1, $CHCl_3$).

2.3 Synthesis of compound **1c**



SI2 **1c**

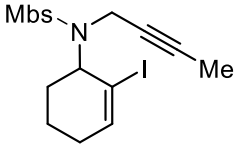
***N*-(But-2-yn-1-yl)-4-methoxybenzenesulfonamide (SI5)**



Applying modified procedure from the literature source,[7] 4-methoxybenzenesulfonamide (2.25 g, 12 mmol) was dissolved in dry MeCN (10 mL) under an argon atmosphere, then K_2CO_3 (829 mg, 6 mmol) and 1-bromobut-2-yne (0.53 mL, 6 mmol) were added. The resulting mixture was heated at reflux for 2 h, before being cooled down and extracted with water (25 mL) and EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Column chromatography on silica gel using hexanes/EtOAc (80/20 → 70/30 → 60/40) as eluent delivered desired product **SI5** as a yellowish powder (0.613 g, 43%). The recorded spectral data were in agreement with previously reported values.[8]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 – 7.78 (m, 2H), 7.02 – 6.94 (m, 2H), 4.52 (bt, *J* = 6.0 Hz, 1H), 3.87 (s, 3H), 3.75 (dq, *J* = 6.1, 2.4 Hz, 2H), 1.61 (t, *J* = 2.4 Hz, 3H).

***N*-(But-2-yn-1-yl)-*N*-(2-iodocyclohex-2-en-1-yl)-4-methoxybenzenesulfonamide (1c)**

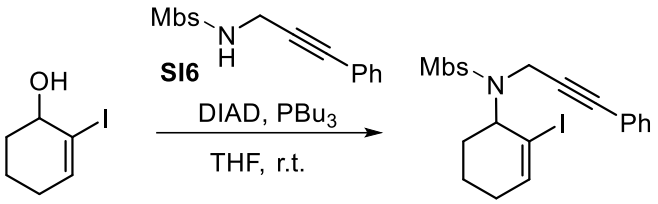


Alcohol **SI2** (500 mg, 2.23 mmol) was dissolved in dry THF (12 mL) under an argon atmosphere, then tributylphosphine (542 mg, 2.68 mmol) and sulfonamide **SI5** (588 mg, 2.46 mmol) were added, and

the mixture was stirred until clear solution was formed. Then the reaction mixture was cooled to 0 °C, and DIAD (541 mg, 2.68 mmol) was added. After 5 min the reaction mixture was warmed to room temperature and stirred for 1 h. Silica gel (1.5 g) was added to the mixture, concentrated under reduced pressure and used directly to column chromatography on silicagel with hexanes/EtOAc (85/15 → 80/20 → 70/30) (to provide the title compound as a white crystalline solid (812 g, 82%), m.p. = 141.3 °C (recrystallized from hexanes/DCM).

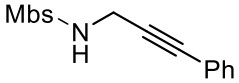
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 – 7.85 (m, 2H), 6.98 – 6.91 (m, 2H), 6.73 (ddd, *J* = 5.2, 3.4, 2.0 Hz, 1H), 4.59 – 4.51 (m, 1H), 4.26 (dq, *J* = 18.4, 2.4 Hz, 1H), 3.86 (s, 3H), 3.60 (dq, *J* = 18.2, 2.3 Hz, 1H), 2.20 – 1.78 (m, 5H), 1.68 (t, *J* = 2.4 Hz, 3H), 1.67 – 1.55 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.9, 145.4, 133.1, 130.1, 113.7, 100.1, 80.5, 75.5, 61.6, 55.7, 33.9, 29.6, 29.0, 20.6, 3.7; **IR** (KBr) ν_{max} 2947, 2870, 2220, 1593, 1496, 1338, 1261, 1151, 1099, 1026, 833, 669, 577 cm^{-1}; **MS** (ESI) *m/z* (%) 469.0 (15), 468.0 (100, $[M+Na]^+$), 446.0 (5, $[M+H]^+$), 240.1 (7); **HRMS** (ESI) *m/z* calcd for $C_{17}H_{20}O_3NISNa$ 468.0101, found 468.0096.

2.4 Synthesis of compound **1d**



SI2 **1d**

4-Methoxy-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (SI6)

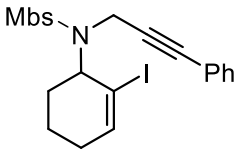


The product was prepared from Mbs-protected propargylamine[9] and iodobenzene using procedure from the literature source.[10] Column chromatography on silica gel with hexanes/EtOAc (80/20 → 70/30 → 1/1) as eluent delivered the desired product **SI6** (86% yield) as a white crystalline solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.83 (m, 2H), 7.32 – 7.21 (m, 3H), 7.18 – 7.13 (m, 2H), 6.97 – 6.91 (m, 2H), 4.54 (bs, 1H), 4.07 (d, *J* = 5.9 Hz, 2H), 3.78 (s, 3H); **^{13}C NMR**

(101 MHz, $CDCl_3$) δ 163.2, 131.7, 131.5, 129.8, 128.7, 128.3, 122.2, 114.4, 84.9, 83.5, 55.7, 33.9; **IR** (KBr) ν_{max} 3273, 1598, 1497, 1425, 1329, 1263, 1159, 1027, 836, 755, 692 cm^{-1}; **MS** (EI) *m/z* (%) 302.1 (12), 301.1 (58, $M^{+\bullet}$), 238.1 (82), 236.1 (80), 208.1 (60), 155.0 (80), 130.1 (100); **HRMS** (ESI) *m/z* calcd for $C_{16}H_{15}O_3NS$ 301.0773, found 301.0775.

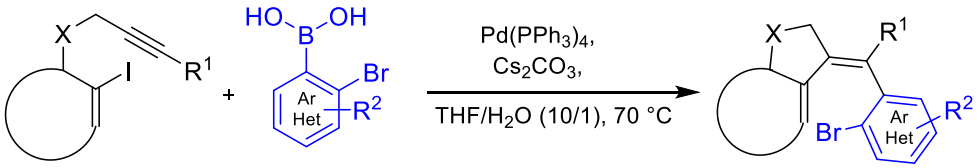
N-(2-Iodocyclohex-2-en-1-yl)-4-methoxy-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (1d)



Alcohol **SI2** (448 mg, 2 mmol) was dissolved in dry THF (12 mL) under an argon atmosphere, then tributylphosphine (0.6 mL, 2.4 mmol) and sulfonamide **SI6** (723 mg, 2.4 mmol) were added, and the mixture was stirred until clear solution was formed. Then the reaction mixture was cooled to 0 °C, and DIAD (0.47 mL, 2.4 mmol) was added. After 5 min the reaction mixture was warmed to room temperature and stirred for 3 h. Silica gel (1.5 g) was added to the mixture, concentrated under reduced pressure and used directly to column chromatography on silicagel with hexanes/EtOAc (85/15 → 80/20 → 70/30 as eluent delivered the desired product **1d** as a colourless oil (0.800 g, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.87 (m, 2H), 7.34 – 7.18 (m, 5H), 6.90 – 6.83 (m, 2H), 6.78 (ddd, *J* = 5.3, 3.4, 1.9 Hz, 1H), 4.69 – 4.61 (m, 1H), 4.55 (d, *J* = 18.7 Hz, 1H), 3.90 (d, *J* = 18.7 Hz, 1H), 3.76 (s, 3H), 2.22 – 2.06 (m, 2H), 2.03 – 1.79 (m, 3H), 1.65 – 1.59 (m, 1H); **^{13}C NMR** (101 MHz, CDCl3) δ 162.9,145.6, 133.1, 131.6, 130.1, 128.4, 128.3, 122.8, 113.9, 100.0, 85.7, 84.6, 61.6, 55.6, 34.3, 29.6, 29.0, 20.5; **IR** (KBr) ν_{max} 2947, 2917, 2869, 2851, 1736, 1595, 1503, 1341, 1302, 1263, 1153, 1099, 1027, 833, 761, 665, 588 cm^{-1}; **MS** (ESI) *m/z* (%) 1037.1 (50, $[2M+Na]^+$), 531.0 (26), 530.0 (100, $[M+Na]^+$), 448.3 (6), 447.3 (22), 433.1 (10), 365.1 (10); **HRMS** (ESI) *m/z* calcd for $C_{22}H_{22}O_3NISNa$ 530.0257, found 530.0256.

3. Tandem cyclisation/Suzuki cross-coupling reaction

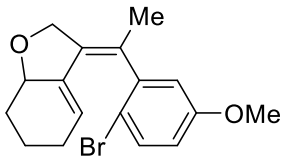


1 X = O, N-Mbs
R^1 = Me, Ph

2

General procedure for the tandem reaction: The iodinated propargylic starting material **1** (1 mmol) was dissolved in (9.1 mL) of THF or DMF followed by addition of 2-bromo-(hetero)arylboronic acid (1.5 mmol), Cs_2CO_3 (2.0 mmol) and water (0.9 mL). The reaction mixture was degassed and backfilled with argon (2×), then $Pd(PPh_3)_4$ (4 mol%) was added and the degassing procedure was repeated again (2×). Reaction was stirred at 70 °C (80 °C for DMF) until the full conversion of the starting material was observed by TLC, cooled down and extracted with water (25 mL) and EtOAc (2 × 25 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude mixture was subjected to column chromatography on silica gel delivering desired Heck/Suzuki product **2**. Reaction and purification details are specified for the each substrate below.

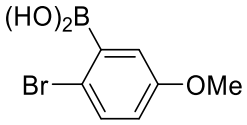
(*E*)-3-(1-(2-Bromo-5-methoxyphenyl)ethylidene)-2,3,5,6,7,7a-hexahydrobenzofuran (2aa)



Reaction time: 9 h; Column chromatography: (98/2) hexanes/diethyl ether

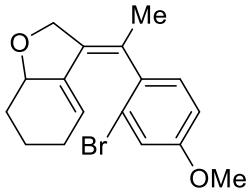
Yield: 80% (0.504 g); pale yellow solid, mp = 59.6 °C (recrystallized from $CHCl_3$)

Reagent	n [mmol]	m [mg]	V [mL]
THF			17.1
Water			1.7
1a	1.88	519	

	2.82	651	
$Pd(PPh_3)_4$	0.075	87	
Cs_2CO_3	3.76	1225	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.47 (d, *J* = 0.7 Hz, 1H), 7.45 (d, *J* = 0.8 Hz, 1H$^{\#}$), 6.75 (d, *J* = 3.0 Hz, 1H), 6.71 (d, *J* = 3.3 Hz, 1H$^{\#}$), 6.69 (d, *J* = 3.3 Hz, 1H$^{\#}$), 6.67 (d, *J* = 3.0 Hz, 1H), 4.80–4.73 (m, 1H, 1H$^{\#}$), 4.62 (d, *J* = 12.9 Hz, 1H), 4.60 (d, *J* = 12.7 Hz, 1H$^{\#}$), 4.49–4.41 (m, 1H, 1H$^{\#}$), 4.22–4.13 (m, 1H, 1H$^{\#}$), 3.79 (s, 3H), 3.77 (s, 3H$^{\#}$), 2.21–2.11 (m, 1H, 1H$^{\#}$), 1.95–1.84 (m, 2H, 2H$^{\#}$), 1.91 (s, 3H), 1.89 (s, 3H$^{\#}$), 1.79–1.70 (m, 1H, 1H$^{\#}$), 1.50–1.23 (m, 2H, 2H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 159.7, 159.2$^{\#}$, 145.1, 144.5$^{\#}$, 137.6, 136.9$^{\#}$, 134.0, 133.5, 133.4$^{\#}$, 127.1, 126.7$^{\#}$, 121.6, 120.7$^{\#}$, 115.1, 114.8$^{\#}$, 114.5, 114.4$^{\#}$, 113.5, 112.3$^{\#}$, 79.2, 79.1$^{\#}$, 70.5, 70.4$^{\#}$, 55.7 (1C, 1C$^{\#}$), 28.7, 28.6$^{\#}$, 25.8, 25.7$^{\#}$, 21.8, 21.5$^{\#}$, 19.4, 19.3$^{\#}$, one aromatic signal is overlapped ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 3425, 2944, 2857, 2833, 1592, 1565, 1467, 1296, 1234, 1069, 1048, 1018 cm^{-1}; **MS** (EI) *m/z* (%) 336.1 (9, $M^{+\bullet}$), 334.1 (10, $M^{+\bullet}$), 255.1 (75), 237.1 (22), 226.1 (25), 225.1 (100), 212.1 (15), 199.1 (22), 171.1 (25); **HRMS** (EI) *m/z* calcd for $C_{17}H_{19}O_2Br$ 334.0568, found 334.0566.

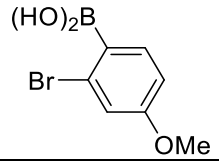
(*E*)-3-(1-(2-Bromo-4-methoxyphenyl)ethylidene)-2,3,5,6,7,7a-hexahydrobenzofuran (2ab)



Reaction time: 7 h; Column chromatography: (90/10) hexanes/ diethyl ether

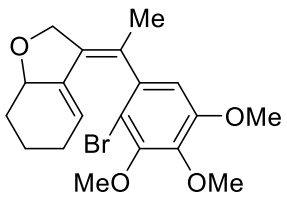
The boronic acid was synthesised according to a literature procedure.[11]

Yield: 81% (0.368 g); colourless oil

Reagent	n [mmol]	m [mg]	V [mL]
THF			13.7
Water			1.3
1a	1.50	414	
	2.25	519	
$Pd(PPh_3)_4$	0.06	69	
Cs_2CO_3	3.00	977	

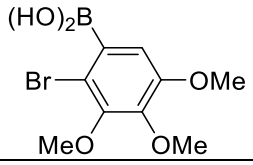
^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.14 (s, 1H), 7.14 (s, 1H$^{\#}$), 7.09 (d, *J* = 8.5 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 1H$^{\#}$), 6.87 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.85 (dd, *J* = 8.6, 2.6 Hz, 1H$^{\#}$), 4.76–4.69 (m, 1H, 1H$^{\#}$), 4.61 (d, *J* = 12.5 Hz, 1H), 4.59 (d, *J* = 12.3 Hz, 1H$^{\#}$), 4.48–4.40 (m, 1H, 1H$^{\#}$), 4.22–4.12 (m, 1H, 1H$^{\#}$), 3.81 (s, 3H, 3H$^{\#}$), 2.20–2.11 (m, 1H, 1H$^{\#}$), 1.98–1.83 (m, 2H, 2H$^{\#}$), 1.90 (s, 3H), 1.87 (s, 3H$^{\#}$), 1.80–1.68 (m, 1H, 1H$^{\#}$), 1.51–1.23 (m, 2H, 2H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 159.1, 159.0$^{\#}$, 137.8, 137.2$^{\#}$, 136.5, 135.9$^{\#}$, 133.9, 133.8$^{\#}$, 130.4, 130.0$^{\#}$, 127.0, 126.5$^{\#}$, 123.3, 122.2$^{\#}$, 121.3, 120.4$^{\#}$, 118.4, 117.7$^{\#}$, 114.7, 113.9$^{\#}$, 79.2, 79.1$^{\#}$, 70.5, 70.5$^{\#}$, 55.7 (1C, 1C$^{\#}$), 28.7, 28.7$^{\#}$, 25.7, 25.6$^{\#}$, 22.1, 21.7$^{\#}$, 19.4, 19.3$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 2938, 2833, 1598, 1488, 1281, 1228, 1075, 1039 cm^{-1}; **MS** (EI) *m/z* (%) 334.1 (32, $M^{+\bullet}$), 334.1 (34, $M^{+\bullet}$), 316.0 (100), 255.1 (45), 235.1 (28), 222.1 (20), 199.0 (13), 165.1 (13); **HRMS** (EI) *m/z* calcd for $C_{17}H_{19}O_2Br$ 334.0568, found 334.0568.

(*E*)-3-(1-(2-Bromo-3,4,5-trimethoxyphenyl)ethylidene)-2,3,5,6,7,7a-hexahydro-benzofuran (2ac)



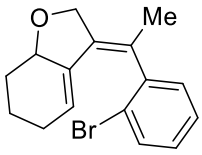
Reaction time: 5 h; Column chromatography: (90/10 → 85/15) hexanes/EtOAc

Yield: 93% (0.368 g); dark orange oil

Reagent	n [mmol]	m [mg]	V [mL]
THF			9.1
Water			0.9
1a	1.00	276	
	1.50	436	
$Pd(PPh_3)_4$	0.04	46	
Cs_2CO_3	2.00	652	

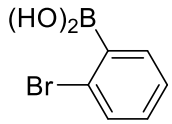
^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 6.56 (s, 1H), 6.47 (s, 1H$^{\#}$), 4.80–4.72 (m, 1H, 1H$^{\#}$), 4.62 (d, *J* = 12.9 Hz, 1H), 4.59 (d, *J* = 12.3 Hz, 1H$^{\#}$), 4.48–4.40 (m, 1H, 1H$^{\#}$), 4.21–4.13 (m, 1H, 1H$^{\#}$), 3.92 (s, 3H), 3.91 (s, 3H), 3.91 (s, 3H$^{\#}$), 3.89 (s, 3H$^{\#}$), 3.84 (s, 3H), 3.82 (s, 3H$^{\#}$), 2.21–2.11 (m, 1H, 1H$^{\#}$), 1.95–1.84 (m, 2H, 2H$^{\#}$), 1.90 (s, 3H), 1.89 (s, 3H$^{\#}$), 1.80–1.69 (m, 1H, 1H$^{\#}$), 1.52–1.19 (m, 2H, 2H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 153.6, 153.1$^{\#}$, 151.8, 151.2$^{\#}$, 142.1, 142.0$^{\#}$, 139.7, 139.2$^{\#}$, 137.6, 136.9$^{\#}$, 133.6, 133.3$^{\#}$, 127.1, 126.7$^{\#}$, 121.4, 120.5$^{\#}$, 109.1, 108.3, 108.0$^{\#}$, 107.8$^{\#}$, 79.3, 79.1$^{\#}$, 70.5, 70.4$^{\#}$, 61.4, 61.4$^{\#}$, 61.2 (1C, 1C$^{\#}$), 56.4, 56.3$^{\#}$, 28.7, 28.6$^{\#}$, 25.8, 25.7$^{\#}$, 21.8, 21.6$^{\#}$, 19.4, 19.3$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 2938, 2845, 1559, 1482, 1386, 1105, 1006 cm^{-1}; **MS** (APCI) *m/z* (%) 397.1 (44, $[M+H]^+$), 395.1 (45, $[M+H]^+$), 317.2 (15), 316.2 (100), 315.2 (20), 285.1 (40), 279.1 (22); **HRMS** (ESI) *m/z* calcd for $C_{19}H_{24}O_4Br$ 395.0853, found 395.0849.

(*E*)-3-(1-(2-Bromophenyl)ethylidene)-2,3,5,6,7,7a-hexahydrobenzofuran (2ad)



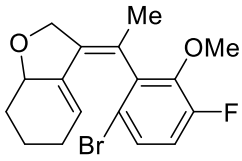
Reaction time: 9 h; Column chromatography: (95/5) hexanes/EtOAc

Yield: 77% (0.234 g); yellow crystalline solid, mp = 54.5 °C (recrystallized from $CHCl_3$)

Reagent	n [mmol]	m [mg]	V [mL]
THF			9.1
Water			0.9
1a	1.00	276	
	1.50	301	
$Pd(PPh_3)_4$	0.04	46	
Cs_2CO_3	2.00	651	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.61–7.55 (m, 1H, 1H$^{\#}$), 7.34–7.25 (m, 1H, 1H$^{\#}$), 7.21–7.10 (m, 2H, 2H$^{\#}$), 4.69–4.58 (m, 2H, 2H$^{\#}$), 4.50–4.42 (m, 1H, 1H$^{\#}$), 4.22–4.14 (m, 1H, 1H$^{\#}$), 2.21–2.11 (m, 1H, 1H$^{\#}$), 1.96–1.82 (m, 2H, 2H$^{\#}$), 1.93 (s, 3H), 1.90 (s, 3H$^{\#}$), 1.78–1.68 (m, 1H, 1H$^{\#}$), 1.50–1.22 (m, 2H, 2H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 144.2, 143.6$^{\#}$, 137.7, 137.1$^{\#}$, 133.6, 133.5$^{\#}$, 133.4, 132.7$^{\#}$, 130.1, 129.6$^{\#}$, 128.6, 128.5$^{\#}$, 128.3, 127.6$^{\#}$, 127.3, 126.8$^{\#}$, 123.0, 121.9$^{\#}$, 121.5, 120.6$^{\#}$, 79.2, 79.1$^{\#}$, 70.5, 70.4$^{\#}$, 28.7, 28.6$^{\#}$, 25.7, 25.6$^{\#}$, 21.8, 21.4$^{\#}$, 19.3, 19.3$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 2944, 2866, 2830, 1473, 1431, 1102, 1075, 1021, 755 cm^{-1}; **MS** (EI) *m/z* (%) 306.0 (92, $M^{+\bullet}$), 304.0 (100, $M^{+\bullet}$), 250 (29), 248 (29), 225.1 (52), 222.0 (70), 169.1 (55), 165.1 (45), 141.1 (67), 128.1 (25), 115.1 (25); **HRMS** (EI) *m/z* calcd for $C_{16}H_{17}OBr$ 304.0463, found 304.0464.

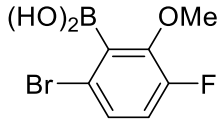
(*E*)-3-(1-(6-Bromo-3-fluoro-2-methoxyphenyl)ethylidene)-2,3,5,6,7,7a-hexahydro-benzofuran (2ae)



Reaction time: 9 h; Column chromatography: (90/10) hexanes/diethyl ether

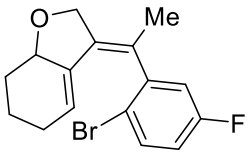
Yield: 67% (0.282 g); yellow amorphous solid

Reagent	n [mmol]	m [mg]	V [mL]
THF			10.8

Water			1.1
1a	1.19	3304	
	1.79	445	
$Pd(PPh_3)_4$	0.05	55	
Cs_2CO_3	3	775	

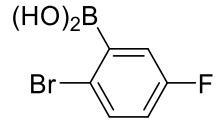
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (dd, *J* = 7.1, 2.4 Hz, 1H), 6.90 (dd, *J* = 5.4, 2.3 Hz, 1H), 5.06–4.99 (m, 1H), 4.59 (d, *J* = 13.0 Hz, 1H), 4.44 (d, *J* = 13.2 Hz, 1H), 4.22–4.14 (m, 1H), 3.88 (s, 3H), 2.21–2.13 (m, 1H), 1.98–1.92 (m, 2H), 1.90 (s, 3H), 1.81–1.71 (m, 1H), 1.50–1.36 (m, 1H), 1.34–1.22 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.0 (d, *J* = 12.2 Hz), 137.1, 135.2, 132.9 (d, *J* = 15.8 Hz), 124.1 (d, *J* = 2.5 Hz), 121.8, 119.9, 116.2 (d, *J* = 4.3 Hz), 115.3 (d, *J* = 1.8 Hz), 79.1, 70.7, 56.6, 28.7, 25.7, 21.7, 19.2 (C–F signal is not clearly visible in the spectrum even when measured in high concentration, it is probably around 148 ppm and splitted); **IR** (KBr) ν_{max} 2944, 2857, 2830, 1601, 1568, 1479, 1410, 1326, 1257, 1213, 1069, 1045 cm^{-1}; **MS** (EI) *m/z* (%) 354.0 (9, $M^{+\bullet}$), 352.0 (10, $M^{+\bullet}$), 338.1 (15), 334.0 (100), 332.0 (80), 319.0 (20), 291.0 (20), 253.1 (13), 209.1 (13), 183.1 (10); **HRMS** (EI) *m/z* calcd for $C_{17}H_{18}O_2BrF$ 352.0474, found 352.0468.

(*E*)-3-(1-(2-Bromo-5-fluorophenyl)ethylidene)-2,3,5,6,7,7a-hexahydrobenzofuran (2af)



Reaction time: 8 h; Column chromatography: (96/4) hexanes/EtOAc

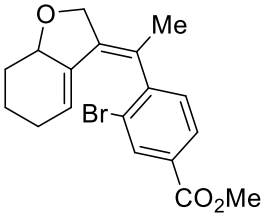
Yield: 85% (0.274 g); yellow crystalline solid, mp = 92.2 °C (recrystallized from $CHCl_3$)

Reagent	n [mmol]	m [mg]	V [mL]
THF			9.1
Water			0.9
1a	1.00	276	
	1.50	328	

$Pd(PPh_3)_4$	0.04	46	
Cs_2CO_3	2.00	652	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.57–7.51 (m, 1H, 1H$^{\#}$), 6.98–6.82 (m, 2H, 2H$^{\#}$), 4.77–4.70 (m, 1H, 1H$^{\#}$), 4.62 (d, *J* = 12.5 Hz, 1H), 4.60 (d, *J* = 12.4 Hz, 1H$^{\#}$), 4.48–4.41 (m, 1H, 1H$^{\#}$), 4.21–4.13 (m, 1H, 1H$^{\#}$), 2.21–2.12 (m, 1H, 1H$^{\#}$), 1.96–1.84 (m, 2H, 2H$^{\#}$), 1.91 (s, 3H), 1.89 (s, 3H$^{\#}$), 1.80–1.71 (m, 1H, 1H$^{\#}$), 1.51–1.23 (m, 2H, 2H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 162.5 (d, *J* = 247.8 Hz), 162.1$^{\#}$ (d, *J* = 248.0 Hz), 146.0 (d, *J* = 7.7 Hz), 145.4$^{\#}$ (d, *J* = 7.7 Hz), 137.5, 136.9$^{\#}$, 134.7 (d, *J* = 8.2 Hz), 134.2, 134.1$^{\#}$, 134.0$^{\#}$ (d, *J* = 8.2 Hz), 126.1 (d, *J* = 1.2 Hz), 125.6$^{\#}$ (d, *J* = 1.3 Hz), 122.0, 121.1$^{\#}$, 117.3 (d, *J* = 3.2 Hz), 117.1 (d, *J* = 21.8 Hz), 116.6$^{\#}$ (d, *J* = 22.0 Hz), 116.2$^{\#}$ (d, *J* = 3.2 Hz), 115.8 (d, *J* = 22.5 Hz), 115.7$^{\#}$ (d, *J* = 22.4 Hz), 79.1, 79.1$^{\#}$, 70.4, 70.4$^{\#}$, 28.6, 28.6$^{\#}$, 25.8, 25.6$^{\#}$, 21.5, 21.1$^{\#}$, 19.3, 19.2$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 3055, 2938, 2869, 2839, 1574, 1461, 1305, 1198, 1069, 1003 cm^{-1}; **MS** (EI) *m/z* (%) 324.0 (92, $M^{+\bullet}$), 322.0 (100, $M^{+\bullet}$), 266.0 (33), 268 (29), 240.0 (70), 238.0 (66), 187.1 (55), 159.1 (75), 146.1 (25), 133.0 (20); **HRMS** (EI) *m/z* calcd for $C_{16}H_{16}OBrF$ 322.0369, found 322.0368.

Methyl (*E*)-3-bromo-4-(1-(5,6,7,7a-tetrahydrobenzofuran-3(2*H*)-ylidene)ethyl)-benzoate (2ai)

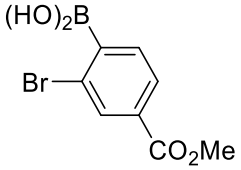


Reaction time: 4 h; Column chromatography: (95/5 → 90/10) hexanes/EtOAc

The boronic acid was synthesised according to a literature procedure.[11]

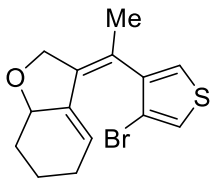
Yield: 60% (0.087 g); yellowish oil

Reagent	n [mmol]	m [mg]	V [mL]
THF			3.6
Water			0.4

1a	0.40	110	
	0.52	134	
$Pd(PPh_3)_4$	0.016	18	
Cs_2CO_3	0.8	261	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 8.26 (d, *J* = 1.7 Hz, 1H), 8.25 (d, *J* = 1.7 Hz, 1H$^{\#}$), 7.97 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.93 (dd, *J* = 7.9, 1.7 Hz, 1H$^{\#}$), 7.27 (d, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 1H$^{\#}$), 4.68 – 4.57 (m, 2H, 2H$^{\#}$), 4.48 – 4.45 (m, 1H), 4.44 – 4.41 (m, 1H$^{\#}$), 4.20 – 4.12 (m, 1H, 1H$^{\#}$), 3.92 (s, 3H, 3H$^{\#}$), 2.19 – 2.10 (m, 1H, 1H$^{\#}$), 1.92 (s, 3H), 1.89 (s, 3H$^{\#}$), 1.88 – 1.82 (m, 2H, 2H$^{\#}$), 1.77 – 1.68 (m, 1H, 1H$^{\#}$), 1.48 – 1.19 (m, 2H, 2H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 165.8 (1C, 1C$^{\#}$), 149.0, 148.4$^{\#}$, 137.5, 136.9$^{\#}$, 134.6, 134.1, 134.0$^{\#}$, 133.95$^{\#}$, 130.5, 130.4$^{\#}$, 130.2, 129.7$^{\#}$, 129.4, 128.7$^{\#}$, 126.3, 125.8$^{\#}$, 123.2, 122.12, 122.10$^{\#}$, 121.1$^{\#}$, 79.1, 79.0$^{\#}$, 70.4, 70.3$^{\#}$, 52.5 (1C, 1C$^{\#}$), 28.6, 28.5$^{\#}$, 25.7, 25.6$^{\#}$, 21.4, 21.0$^{\#}$, 19.22, 19.17$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 2949, 2829, 1727, 1549, 1435, 1379, 1282, 1238, 1113, 774 cm^{-1}; **MS** (APCI) *m/z* (%) 365.1 (68, $[M+H]^+$), 363.1 (63, $[M+H]^+$), 347.0 (99), 345.0 (100), 284.1 (49), 266.1 (96), 253.1 (67); **HRMS** (APCI) *m/z* calcd for $C_{18}H_{20}O_3Br$ 363.0590, found 363.0586.

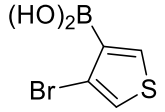
(*E*)-3-(1-(4-Bromothiophen-3-yl)ethylidene)-2,3,5,6,7,7a-hexahydrobenzofuran (2aj)



Reaction time: 3.5 h; Column chromatography: (99/1) hexanes/EtOAc

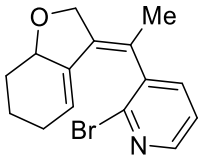
Yield: 79% (0.173 g); yellow oil

Reagent	n [mmol]	m [mg]	V [mL]
THF			6.4
Water			0.6

1a	0.70	193	
	1.05	217	
$Pd(PPh_3)_4$	0.03	32	
Cs_2CO_3	1.40	456	

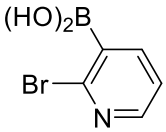
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, *J* = 3.4 Hz, 1H), 7.39 (bs, 1H), 4.76–4.70 (m, 1H), 4.54 (dd, *J* = 13.3, 1.1 Hz, 1H), 4.33 (dd, *J* = 13.3, 1.1 Hz, 1H), 4.13–4.03 (m, 1H), 2.09–2.01 (m, 1H), 1.93–1.85 (m, 2H), 1.84 (s, 3H), 1.74–1.65 (m, 1H), 1.41–1.27 (m, 1H), 1.22–1.10 (m, 1H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 142.5, 137.6, 135.1, 124.6, 123.1, 120.9, 119.9, 78.2, 69.6, 28.1, 25.0, 22.0, 18.7, one aromatic signal was not found; **IR** (KBr) ν_{max} 3506, 3270, 2944, 2866, 2827, 1335, 1075, 1006, 794 cm^{-1}; **MS** (EI) *m/z* (%) 312.0 (28, $M^{+\bullet}$), 310.0 (30, $M^{+\bullet}$), 231.1 (100), 216.1 (13), 203.1 (18), 187.1 (12), 161.0 (8), 147.0 (8); **HRMS** (EI) *m/z* calcd for $C_{14}H_{15}OSBr$ 310.0027, found 310.0027.

(*E*)-2-Bromo-3-(1-(5,6,7,7a-tetrahydrobenzofuran-3(2H)-ylidene)ethyl)pyridine (2ak)



Reaction time: 7 h; Column chromatography: (85/15) hexanes/EtOAc

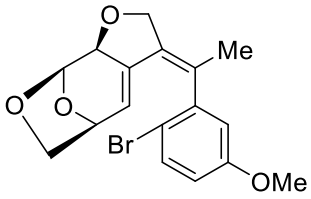
Yield: 43% (0.218 g); pale yellow crystalline solid; mp = 69.1 °C (recrystallized from $CHCl_3$)

Reagent	n [mmol]	m [mg]	V [mL]
DMF			9.1
Water			0.9
1a	1.64	453	
	2.46	496	
$Pd(PPh_3)_4$	0.065	6	
Cs_2CO_3	3.28	1069	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 8.34–8.28 (m, 1H, 1H$^{\#}$), 7.48 (ddd, *J* = 26.0, 7.5, 2.0 Hz, 1H, 1H$^{\#}$), 7.32–7.22

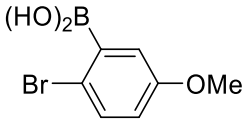
(m, 1H, 1H[#]), 4.75–4.70 (m, 1H), 4.69–4.64 (m, 1H[#]), 4.66–4.57 (m, 1H, 1H[#]), 4.50–4.40 (m, 1H, 1H[#]), 4.24–4.13 (m, 1H, 1H[#]), 2.23–2.12 (m, 1H, 1H[#]), 2.00–1.81 (m, 2H, 2H[#]), 1.95 (s, 3H), 1.93 (s, 3H[#]), 1.80–1.71 (m, 1H, 1H[#]), 1.51–1.21 (m, 2H, 2H[#]); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 148.7, 148.6[#], 142.9, 142.0[#], 141.3, 140.6[#], 138.8, 138.3[#], 137.8, 137.0, 135.2[#], 124.7, 124.2[#], 123.6, 122.8[#], 122.8, 121.5[#], 79.1, 79.0[#], 70.5 (1C, 1C[#]), 28.6, 28.5[#], 25.8, 25.6[#], 21.0, 21.0[#], 19.2, 19.2[#], one aromatic signal is overlapped ([#]atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by [#]); **IR** (KBr) ν_{max} 3369, 2935, 2863, 2833, 1545, 1389, 1051, 1009 cm^{-1}; **MS** (EI) *m/z* (%) 307.0 (43, $M^{+\bullet}$), 305.0 (45, $M^{+\bullet}$), 226.1 (100), 211.1 (13), 198.1 (23), 182.1 (10); **HRMS** (EI) *m/z* calcd for $C_{15}H_{16}NOBr$ 305.0415, found 305.0416.

(5*S*,8*R*,8a*S*,*E*)-3-(1-(2-Bromo-5-methoxyphenyl)ethylidene)-2,3,5,6,8,8a-hexahydro-5,8-epoxyfuro[2,3-*c*]oxepine (2ba)



Reaction time: 5 h; Column chromatography: (99/1 → 95/5) dichloromethane/diethyl ether

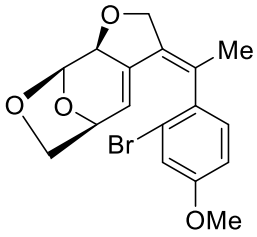
Yield: 70% (0.256 g); brownish amorphous solid

Reagent	n [mmol]	m [mg]	V [mL]
THF			9.1
Water			0.9
1b	1.0	306	
	1.50	346	
$Pd(PPh_3)_4$	0.04	46	
Cs_2CO_3	2.0	651	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.50–7.42 (m, 1H, 1H[#]), 6.75–6.62 (m, 2H, 2H[#]), 5.72 (s, 1H), 5.71 (s, 1H[#]), 4.86–4.80 (m, 1H, 1H[#]), 4.76–4.67 (m, 1H, 1H[#]), 4.60–4.55 (m, 1H, 1H[#]), 4.54–4.44 (m,

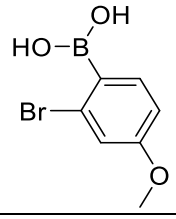
2H, 2H$^{\#}$), 3.88 (d, *J* = 6.5 Hz, 1H), 3.81 (d, *J* = 6.6 Hz, 1H$^{\#}$), 3.79 (s, 3H), 3.78 (s, 3H$^{\#}$) 3.77–3.71 (m, 1H, 1H$^{\#}$), 1.92 (s, 3H), 1.90 (s, 3H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 159.8, 159.1$^{\#}$, 144.2, 143.7$^{\#}$, 135.2, 134.5$^{\#}$, 134.3, 133.4$^{\#}$, 131.8, 131.5$^{\#}$, 130.5, 129.9$^{\#}$, 120.3, 119.4$^{\#}$, 114.9, 114.9$^{\#}$, 114.5 (1C, 1C$^{\#}$), 112.8, 112.1$^{\#}$, 100.1, 100.0$^{\#}$, 80.3, 80.3$^{\#}$, 74.2 (1C, 1C$^{\#}$), 72.7 (1C, 1C$^{\#}$), 71.4, 71.3$^{\#}$, 55.7 (1C, 1C$^{\#}$), 21.6, 21.3$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 3557, 3482, 3416, 2920, 2851, 1712, 1619, 1464, 1299, 1225, 1066, 1024 cm^{-1}; **MS** (EI) *m/z* (%) 366.0 (8, M$^{+\bullet}$), 364.0 (10, M$^{+\bullet}$), 302.0 (12), 277.1 (100), 239.1 (18), 201.1 (17), 199.0 (20), 183.0 (18), 152.1 (17); **HRMS** (EI) *m/z* calcd for $C_{17}H_{17}O_4Br$ 364.0310, found 364.0319; **Specific rotation** $[\alpha]_D$ = –32° (c 1, $CHCl_3$).

(5*S*,8*R*,8a*S*,*E*)-3-(1-(2-Bromo-4-methoxyphenyl)ethylidene)-2,3,5,6,8,8a-hexahydro-5,8-epoxyfuro[2,3-*c*]oxepine (2bb)



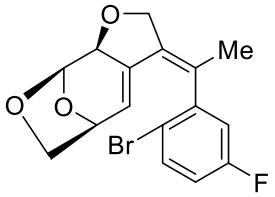
Reaction time: 10 h; Column chromatography: (97/3) dichloromethane/EtOAc

Yield: 88% (0.546 g); brownish amorphous solid

Reagent	n [mmol]	m [mg]	V [mL]
THF			15.5
Water			1.5
1b	1.70	520	
	2.55	589	
$Pd(PPh_3)_4$	0.07	79	
Cs_2CO_3	3.40	1108	

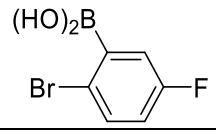
^{1}H NMR (400 MHz, THF-d_8; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.19 (d, *J* = 2.6 Hz, 1H), 7.17 (d, *J* = 2.5 Hz, 1H$^{\#}$), 7.12 (d, *J* = 8.5 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H$^{\#}$), 6.92 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.90 (dd, *J* = 8.5, 2.5 Hz, 1H$^{\#}$), 5.52–5.50 (m, 1H, 1H$^{\#}$), 4.81–4.76 (m, 1H, 1H$^{\#}$), 4.62–4.53 (m, 1H, 1H$^{\#}$), 4.51–4.46 (m, 1H, 1H$^{\#}$), 4.43–4.40 (m, 1H), 4.39–4.36 (m, 1H$^{\#}$), 4.35–4.32 (m, 1H, 1H$^{\#}$), 3.79 (s, 3H), 3.78 (s, 3H$^{\#}$), 3.69 (d, *J* = 6.4 Hz, 1H), 3.64 (d, *J* = 6.4 Hz, 1H$^{\#}$), 3.61–3.54 (m, 1H, 1H$^{\#}$, signal overlapped by the solvent signal), 1.90 (s, 3H), 1.87 (s, 3H$^{\#}$); **^{13}C NMR** (101 MHz, THF-d_8; mixture of atropoisomers, signals of both atropoisomers are listed) δ 160.8, 160.6$^{\#}$, 136.6, 136.6$^{\#}$, 136.2, 136.1$^{\#}$, 134.0, 133.9$^{\#}$, 131.0, 131.0$^{\#}$, 130.4, 129.8$^{\#}$, 123.5, 122.9$^{\#}$, 121.4, 120.5$^{\#}$, 119.4, 118.6$^{\#}$, 115.5, 114.6$^{\#}$, 101.2, 101.2$^{\#}$, 81.7, 81.6$^{\#}$, 74.7 (1C, 1C$^{\#}$), 73.6, 73.6$^{\#}$, 71.7, 71.7$^{\#}$, 56.0 (1C, 1C$^{\#}$), 21.9, 21.7$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 2950, 2836, 1604, 1491, 1284, 1228, 1129, 1081, 1033, 976 cm^{-1}; **MS** (EI) *m/z* (%) 366.0 (95, M$^{+\bullet}$), 364.0 (100, M$^{+\bullet}$), 318.0 (30), 285.1 (32), 239.1 (60), 211.1 (48), 196.1 (50), 179.1 (15), 165.1 (20); **HRMS** (EI) *m/z* calcd for $C_{17}H_{17}O_4Br$ 364.0310, found 364.0309; **Specific rotation** $[\alpha]_D$ = –42° (c 1, $CHCl_3$).

(5*S*,8*R*,8a*S*,*E*)-3-(1-(2-bromo-5-fluorophenyl)ethylidene)-2,3,5,6,8,8a-hexahydro-5,8-epoxyfuro[2,3-*c*]oxepine (2bf)



Reaction time: 18 h; Column chromatography: (95/5 → 80/20) hexanes/EtOAc

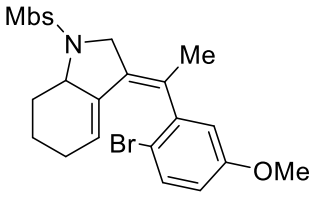
Yield: 62% (0.110 g); brown foam

Reagent	n [mmol]	m [mg]	V [mL]
THF			4.5
Water			0.5
1b	0.50	153	
	0.75	164	
$Pd(PPh_3)_4$	0.02	23	

Cs_2CO_3	1.00	325	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.58 – 7.54 (m, 1H$^{\#}$); 7.53 (dd, *J* = 8.7, 5.2 Hz, 1H), 6.93 – 6.83 (m, 2H, 2H$^{\#}$), 5.71 (s, 1H$^{\#}$), 5.70 (s, 1H), 4.82 – 4.79 (m, 1H, 1H$^{\#}$), 4.75 – 4.66 (m, 1H, 1H$^{\#}$), 4.61 – 4.55 (m, 1H, 1H$^{\#}$), 4.53 – 4.45 (m, 2H, 2H$^{\#}$), 3.86 (d, *J* = 6.6 Hz, 1H), 3.82 (d, *J* = 6.6 Hz, 1H$^{\#}$), 3.76 – 3.71 (m, 1H, 1H$^{\#}$), 1.92 (s, 3H), 1.92 (s, 3H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 162.5 (d, *J* = 248.5 Hz), 161.9$^{\#}$ (d, *J* = 248.5 Hz), 145.0 (d, *J* = 7.7 Hz), 144.5$^{\#}$ (d, *J* = 7.7 Hz), 135.1$^{\#}$, 135.0$^{\#}$ (d, *J* = 8.3 Hz), 134.4, 134.0 (d, *J* = 8.4 Hz), 132.4$^{\#}$, 132.2, 129.4 (d, *J* = 1.4 Hz), 128.7$^{\#}$ (d, *J* = 1.3 Hz), 120.6, 119.7$^{\#}$, 116.7 (d, *J* = 3.1 Hz), 116.58 (d, *J* = 22.4 Hz), 116.55$^{\#}$ (d, *J* = 22.0 Hz), 116.2 (d, *J* = 22.4 Hz), 116.1$^{\#}$ (d, *J* = 22.3 Hz), 116.0$^{\#}$ (d, *J* = 3.1 Hz), 100.0, 99.9$^{\#}$, 80.2, 80.1$^{\#}$, 74.1$^{\#}$, 74.0, 72.61$^{\#}$, 72.59, 71.3, 71.2$^{\#}$, 21.3$^{\#}$, 21.0; **IR** (KBr) ν_{max} 3062, 2949, 2885, 2843, 1712, 1601, 1574, 1462, 1402, 1300, 1213, 1176, 1131, 1087, 1074, 1055, 1028, 989, 979, 916, 889, 847, 814, 679, 623, 611, 461 cm^{-1}; **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}O_3BrFNa$ 375.0003, found 374.9998.

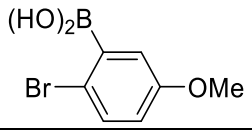
(*E*)-3-(1-(2-bromo-5-methoxyphenyl)ethylidene)-1-((4-methoxyphenyl)sulfonyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole (2ca)



Reaction time: 23 h; Column chromatography: (85/15 → 80/20) hexanes/EtOAc

Yield: 59% (0.149 g); yellowish foam

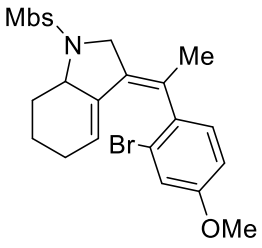
(27% of unreacted starting material was isolated)

Reagent	n [mmol]	m [mg]	V [mL]
THF			4.5
Water			0.5
1c	0.50	223	
	0.75	173	
$Pd(PPh_3)_4$	0.02	23	

Cs_2CO_3	1.00	326	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.85 – 7.77 (m, 2H, 2H$^{\#}$), 7.44 (d, *J* = 8.8 Hz, 1H), 7.38 (d, *J* = 8.7 Hz, 1H$^{\#}$), 7.08 – 7.00 (m, 2H, 2H$^{\#}$), 6.71 – 6.64 (m, 2H, 1H$^{\#}$), 6.47 (d, *J* = 3.0 Hz, 1H$^{\#}$), 4.90 – 4.82 (m, 1H, 1H$^{\#}$), 4.26 – 4.19 (m, 1H, 1H$^{\#}$), 3.90 (s, 3H), 3.89 (s, 3H$^{\#}$), 3.78 (s, 3H), 3.78 – 3.73 (m, 1H, 1H$^{\#}$), 3.72 (s, 3H$^{\#}$), 3.47 – 3.37 (m, 1H, 1H$^{\#}$), 2.59 – 2.51 (m, 1H, 1H$^{\#}$), 1.89 (s, 3H), 1.87 (s, 3H$^{\#}$), 1.88 – 1.70 (m, 3H, 3H$^{\#}$), 1.49 – 1.23 (m, 2H, 2H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 163.3, 163.2$^{\#}$, 159.6, 159.3$^{\#}$, 144.8, 144.2$^{\#}$, 135.3, 134.5$^{\#}$, 134.0, 133.5$^{\#}$, 130.3, 130.3$^{\#}$, 129.3, 129.0$^{\#}$, 128.9, 128.3$^{\#}$, 127.8, 127.4$^{\#}$, 124.7, 123.7$^{\#}$, 115.0, 114.6$^{\#}$, 114.6, 114.4$^{\#}$, 114.36 (1C, 1C$^{\#}$), 113.4, 112.0$^{\#}$, 60.9, 60.7$^{\#}$, 55.8 (1C, 1C$^{\#}$), 55.6, 55.6$^{\#}$, 52.6, 52.6$^{\#}$, 29.5, 29.5$^{\#}$, 25.2, 25.1$^{\#}$, 22.2, 21.8$^{\#}$, 19.8, 19.7$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 2939, 2837, 1595, 1496, 1464, 1346, 1261, 1161, 1093, 1041, 814, 671, 594, 561 cm^{-1}; **MS** (ESI) *m/z* (%) 1031.1 (23, [2M+Na]$^+$), 528.1 (94, [M+Na]$^+$), 526.1 (100, [M+Na]$^+$), 506.1 (4, [M+H]$^+$); **HRMS** (ESI) *m/z* calcd for $C_{24}H_{27}O_4NBrS$ 504.0839, found 504.0843.

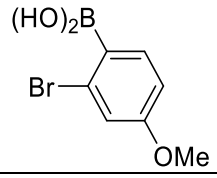
(*E*)-3-(1-(2-bromo-4-methoxyphenyl)ethylidene)-1-((4-methoxyphenyl)sulfonyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole (2cb)



Reaction time: 16 h; Column chromatography: (95/5 → 80/20) hexanes/EtOAc

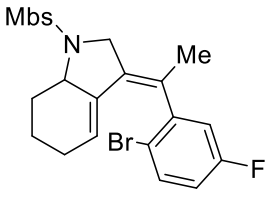
Yield: 62% (0.079 g) as a mixture of *E*/*Z* isomers (9.7:1); yellowish foam

Reagent	n [mmol]	m [mg]	V [mL]
THF			2.3
Water			0.3
1c	0.25	111	

	0.37	87	
$Pd(PPh_3)_4$	0.02	12	
Cs_2CO_3	1.00	163	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.84 – 7.77 (m, 2H, 2H$^{\#}$), 7.11 (d, *J* = 2.5 Hz, 1H), 7.06 (d, *J* = 2.5 Hz, 1H$^{\#}$), 7.06 – 7.01 (m, 2H, 3H$^{\#}$), 6.85 (dd, *J* = 8.5, 2.5 Hz, 1H$^{\#}$), 6.81 (d, *J* = 8.5, 2.5 Hz, 1H), 6.76 (dd, *J* = 8.8, 2.5 Hz, 1H), 4.85 – 4.78 (m, 1H, 1H$^{\#}$), 4.26 – 4.18 (m, 1H, 1H$^{\#}$), 3.89 (s, 3H), 3.88 (s, 3H$^{\#}$), 3.78 (m, 3H, 3H$^{\#}$), 3.78 – 3.71 (m, 1H, 1H$^{\#}$), 3.46 – 3.37 (m, 1H, 1H$^{\#}$), 2.60 – 2.50 (m, 1H, 1H$^{\#}$), 1.88 (s, 3H$^{\#}$), 1.85 (s, 3H), 1.88 – 1.77 (m, 1H, 3H$^{\#}$), 1.78 – 1.70 (m, 1H, 1H$^{\#}$), 1.53 – 1.27 (m, 3H, 1H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 163.24$^{\#}$, 163.22, 159.1, 159.0$^{\#}$, 136.1$^{\#}$, 135.5$^{\#}$, 135.4, 134.7, 130.31, 130.27, 130.25, 129.7$^{\#}$, 129.6, 129.3$^{\#}$, 128.9$^{\#}$, 128.2$^{\#}$, 127.6$^{\#}$, 127.4$^{\#}$, 124.4, 123.4, 123.2$^{\#}$, 121.9$^{\#}$, 118.4, 117.8, 114.6$^{\#}$, 114.36, 114.34, 113.9$^{\#}$, 60.9, 60.7$^{\#}$, 55.8 (1C, 1C$^{\#}$), 55.6 (1C, 1C$^{\#}$), 52.7, 52.6$^{\#}$, 29.5 (1C, 1C$^{\#}$), 25.2, 25.0$^{\#}$, 22.5$^{\#}$, 22.1, 19.8, 19.7$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 2968, 2939, 2837, 1597, 1495, 1460, 1346, 1261, 1225, 1161, 1034, 835, 818, 669, 579, 558 cm^{-1}; **MS** (ESI) *m/z* (%) 1031.2 (12, [2M+Na]$^+$), 528.1 (97, [M+Na]$^+$), 526.1 (100, [M+Na]$^+$), 507.1 (4), 506.1 (11, [M+H]$^+$), 505.1 (4), 504.1 (12, [M+H]$^+$); **HRMS** (ESI) *m/z* calcd for $C_{24}H_{27}O_4NBrS$ 504.0839, found 504.0839.

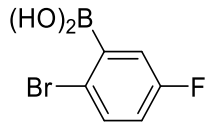
(*E*)-3-(1-(2-bromo-4-fluorophenyl)ethylidene)-1-((4-methoxyphenyl)sulfonyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole (2cf)



Reaction time: 48 h; Column chromatography: (95/5 → 83/17) hexanes/EtOAc

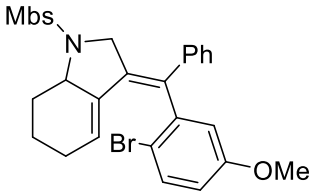
Yield: 53% (0.131 g); white foam

(27% of unreacted starting material was isolated)

Reagent	n [mmol]		m [mg]	V [mL]
THF				4.5
Water				0.5
1c	0.50		223	
	0.75		164	
$Pd(PPh_3)_4$	0.02		23	
Cs_2CO_3	1.00		326	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.85 – 7.78 (m, 2H, 2H$^{\#}$), 7.51 (dd, *J* = 8.7, 5.3 Hz, 1H), 7.46 (dd, *J* = 8.8, 5.3 Hz, 1H$^{\#}$), 7.08 – 7.00 (m, 2H, 2H$^{\#}$), 6.89 (dd, *J* = 8.8, 3.0 Hz, 1H$^{\#}$), 6.87 – 6.80 (m, 1H, 1H$^{\#}$), 6.65 (dd, *J* = 8.9, 3.1 Hz, 1H), 4.85 – 4.80 (m, 1H, 1H$^{\#}$), 4.26 – 4.18 (m, 1H, 1H$^{\#}$), 3.90 (s, 3H), 3.89 (s, 3H$^{\#}$), 3.81 – 3.71 (m, 1H, 1H$^{\#}$), 3.46 – 3.38 (m, 1H, 1H$^{\#}$), 2.61 – 2.51 (m, 1H, 1H$^{\#}$), 1.89 (s, 3H), 1.86 (s, 3H$^{\#}$), 1.88 – 1.80 (m, 1H, 3H$^{\#}$), 1.80 – 1.71 (m, 1H, 1H$^{\#}$), 1.48 – 1.30 (m, 3H, 1H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 163.3 (1C, 1C$^{\#}$), 162.4 (d, *J* = 247.8 Hz), 162.2$^{\#}$ (d, *J* = 248.5 Hz), 145.7 (d, *J* = 7.8 Hz), 145.1$^{\#}$ (d, *J* = 7.6 Hz), 135.2$^{\#}$, 134.6$^{\#}$ (d, *J* = 8.3 Hz), 134.4, 134.2 (d, *J* = 8.4 Hz), 130.3, 130.2$^{\#}$, 130.1$^{\#}$, 129.7, 128.0 (d, *J* = 1.2 Hz),127.51, 127.49$^{\#}$, 127.2$^{\#}$ (d, *J* = 1.5 Hz), 125.1, 124.1$^{\#}$, 117.3 (d, *J* = 3.1 Hz), 117.0$^{\#}$ (d, *J* = 22.1 Hz), 116.3 (d, *J* = 22.4 Hz), 115.96$^{\#}$ (d, *J* = 3.1 Hz), 115.95 (d, *J* = 22.4 Hz), 115.8$^{\#}$ (d, *J* = 22.2 Hz), 114.39, 114.38$^{\#}$, 60.8, 60.6$^{\#}$, 55.8 (1C, 1C$^{\#}$), 52.6, 52.5$^{\#}$, 29.50, 29.47$^{\#}$, 25.2, 25.1$^{\#}$, 21.9$^{\#}$, 21.5, 19.71, 19.66$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 2941, 2839, 1597, 1576, 1496, 1462, 1346, 1306, 1261, 1161, 1093, 1026, 835, 816, 671, 594, 561 cm^{-1}; **MS** (ESI) *m/z* (%) 1007.2 (9, $[2M+Na]^+$), 532.1 (23, $[M+K]^+$), 530.1 (22, $[M+K]^+$), 516.1 (100, $[M+Na]^+$), 514.1 (98, $[M+Na]^+$), 494.1 (37, $[M+H]^+$), 492.1 (36, $[M+H]^+$), 342.1 (6); **HRMS** (ESI) *m/z* calcd for $C_{23}H_{24}O_3NBrFS$ 492.0639, found 492.0640.

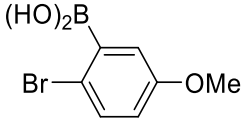
(*E*)-3-((2-bromo-5-methoxyphenyl)(phenyl)methylene)-1-((4-methoxyphenyl)sulfonyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole (2da)



Reaction time: 23 h; Column chromatography: (85/15 → 80/20) hexanes/EtOAc

Yield: 72% (0.081 g); white foam

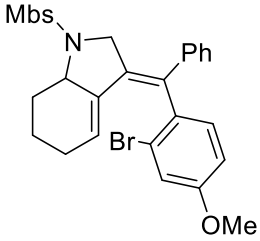
(33% of unreacted starting material was isolated)

Reagent	n [mmol]	m [mg]	V [mL]
THF			1.8
Water			0.2
1d	0.20	102	
	0.30	69	
$Pd(PPh_3)_4$	0.008	9.2	
Cs_2CO_3	0.40	130	

^{1}H NMR (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.66 – 7.60 (m, 2H, 2H$^{\#}$), 7.40 – 7.35 (m, 1H, 1H$^{\#}$), 7.33 – 7.22 (m, 3H, 3H$^{\#}$), 7.12 – 7.05 (m, 2H, 2H$^{\#}$), 6.96 – 6.88 (m, 2H, 2H$^{\#}$), 6.70 – 6.62 (m, 2H, 1H$^{\#}$), 6.37 (d, *J* = 3.1 Hz, 1H$^{\#}$), 5.17 – 5.13 (m, 1H), 5.06 – 5.01 (m, 1H$^{\#}$), 4.40 (d, *J* = 14.8 Hz, 1H), 4.40 (d, *J* = 14.7 Hz, 1H$^{\#}$), 3.92 (d, *J* = 14.8 Hz, 1H), 3.88 (d, *J* = 14.7 Hz, 1H$^{\#}$), 3.86 (s, 3H), 3.84 (s, 3H$^{\#}$), 3.73 (s, 3H), 3.70 (s, 3H$^{\#}$), 3.65 – 3.58 (m, 1H), 3.58 – 3.51 (m, 1H$^{\#}$), 2.57 – 2.44 (m, 1H, 1H$^{\#}$), 2.02 – 1.63 (m, 3H, 3H$^{\#}$), 1.52 – 1.34 (m, 2H, 2H$^{\#}$); **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 163.2, 163.1$^{\#}$, 159.2, 159.0$^{\#}$, 142.9, 142.9$^{\#}$, 140.3, 139.6$^{\#}$, 136.5, 136.0$^{\#}$, 133.9, 133.9$^{\#}$, 133.5, 132.8$^{\#}$, 132.7, 132.0$^{\#}$, 130.1, 130.0$^{\#}$, 129.1, 128.8$^{\#}$, 128.4, 128.3$^{\#}$, 128.2, 127.8$^{\#}$, 127.7, 127.6$^{\#}$, 126.7, 126.0$^{\#}$, 116.8, 116.6$^{\#}$, 115.2, 114.7$^{\#}$, 114.4, 114.3$^{\#}$, 114.28, 113.5$^{\#}$, 59.9, 59.6$^{\#}$, 55.7, 55.7$^{\#}$, 55.6, 55.5$^{\#}$, 52.8, 52.7$^{\#}$, 29.9, 29.6$^{\#}$, 25.2, 25.1$^{\#}$, 19.9, 19.8$^{\#}$ ($^{\#}$atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$); **IR** (KBr) ν_{max} 2935, 2837, 1595, 1496, 1464, 1343, 1261, 1159, 1093, 1018, 835, 669, 598, 565 cm^{-1};

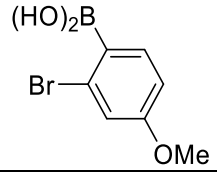
MS (APCI) *m/z* (%) 568.1 (100, $[M+H]^+$), 566.1 (97, $[M+H]^+$), 486.2 (50), 379.1 (9), 300.2 (46); **HRMS** (APCI) *m/z* calcd for $C_{29}H_{29}O_4NBrS$ 566.0995, found 566.0999.

(*E*)-3-((2-bromo-4-methoxyphenyl)(phenyl)methylene)-1-((4-methoxyphenyl)-sulfonyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole (2db)



Reaction time: 72 h; Column chromatography: (95/5 → 80/20) hexanes/EtOAc

Yield: 82% (0.092 g) as a mixture of *E*/*Z* isomers (2.4:1); brown foam

Reagent	n [mmol]	m [mg]	V [mL]
THF			1.8
Water			0.2
1d	0.20	100	
	0.30	68	
$Pd(PPh_3)_4$	0.008	9	
Cs_2CO_3	0.39	128	

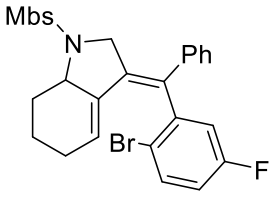
(*E*)-2db (major): **^{1}H NMR** (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.67 – 7.60 (m, 2H, 2H$^{\#}$), 7.32 – 7.21 (m, 4H, 4H$^{\#}$), 7.09 – 7.04 (m, 3H, 3H$^{\#}$), 6.95 – 6.89 (m, 2H, 2H$^{\#}$), 6.81 – 6.73 (m, 1H, 1H$^{\#}$), 5.13 – 5.07 (m, 1H$^{\#}$), 5.01 – 4.96 (m, 1H), 4.42 (d, *J* = 14.7 Hz, 1H$^{\#}$), 4.34 (d, *J* = 14.7 Hz, 1H), 3.91 – 3.86 (m, 1H, 1H$^{\#}$), 3.86 (s, 3H), 3.81 (s, 3H$^{\#}$), 3.78 (s, 3H$^{\#}$), 3.77 (s, 3H), 3.65 – 3.47 (m, 1H, 1H$^{\#}$), 2.62 – 2.46 (m, 1H, 1H$^{\#}$), 2.03 – 1.84 (m, 2H, 2H$^{\#}$), 1.84 – 1.70 (m, 1H, 1H$^{\#}$), 1.52 – 1.36 (m, 2H, 2H$^{\#}$);

(*Z*)-2db (minor): **^{1}H NMR** (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.75 – 7.71 (m, 2H), 7.71 – 7.67 (m, 2H$^{\#}$), 7.32 – 7.15 (m, 4H, 4H$^{\#}$), 7.09 – 7.04 (m, 2H, 2H$^{\#}$), 7.04 – 6.98 (m, 2H, 2H$^{\#}$), 6.92 – 6.87 (m, 1H$^{\#}$), 6.81 – 6.73 (m, 2H, 1H$^{\#}$), 5.50 – 5.45 (m, 1H$^{\#}$), 5.43 – 5.38 (m, 1H), 4.02 (d, *J* = 14.9 Hz,

1H$^{\#}$), 3.93 (d, *J* = 14.9 Hz, 1H), 3.90 (s, 3H$^{\#}$), 3.89 (s, 3H, 3H$^{\#}$), 3.87 (s, 3H), 3.65 – 3.47 (m, 1H, 1H$^{\#}$), 3.57 (d, *J* = 14.9 Hz, 1H), 3.48 (d, *J* = 14.9 Hz, 1H$^{\#}$), 2.62 – 2.46 (m, 1H, 1H$^{\#}$), 2.03 – 1.84 (m, 2H, 2H$^{\#}$), 1.84 – 1.70 (m, 1H, 1H$^{\#}$), 1.52 – 1.35 (m, 2H, 2H$^{\#}$) ($^{\#}$ atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$);

Mixture of *E*/*Z* isomers of **2db**: **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 163.3^{Z}, 163.2^{E}, 163.13$^{Z\#}$, 163.09$^{E\#}$, 159.5, 159.4, 159.1, 140.9, 140.4, 139.8 136.8, 136.2, 134.8, 134.53, 134.46, 134.41, 133.95, 133.1, 132.6, 132.3, 132.1, 131.5, 131.0, 130.4, 130.3, 130.12, 130.07, 129.99, 129.1, 128.8, 128.7, 128.6, 128.5, 128.42, 128.40, 128.2, 127.9, 127.6, 127.4, 127.3, 126.9, 126.7, 126.6, 125.7, 125.0, 123.4, 118.7^{Z}, 118.4^{E}, 117.94$^{Z\#}$, 117.90$^{E\#}$, 114.7, 114.4, 114.30, 114.29, 114.0, 113.8, 60.89^{Z}, 60.73$^{Z\#}$, 59.95$^{E\#}$, 59.63^{E}, 55.76^{E}, 55.75, 55.70, 55.61, 55.59^{E}, 53.67^{Z}, 53.43$^{Z\#}$, 52.92^{E}, 52.76$^{E\#}$, 29.93^{Z}, 29.89^{E}, 29.78$^{Z\#}$, 29.68$^{E\#}$, 25.23$^{E\#}$, 25.16 (1C^{E},1C^{Z}), 25.08$^{Z\#}$, 19.94$^{E\#}$, 19.87^{E}, 19.85$^{Z\#}$, 19.78^{Z} (^{E} signal could be assigned to the major *E* isomer; ^{Z} signal could be assigned to the minor *Z* isomer); **IR** (KBr) ν_{max} 2939, 2837, 1597, 1493, 1441, 1346, 1284, 1261, 1225, 1159, 1093, 1036, 835, 700, 669, 558 cm^{-1}; **MS** (APCI) *m/z* (%) 590.1 (8, [M+Na]$^{+}$), 588.1 (6, [M+Na]$^{+}$), 568.1 (97, [M+H]$^{+}$), 566.1 (100, [M+H]$^{+}$), 381.1 (12), 379.1 (13), 300.2 (89); **HRMS** (ESI) *m/z* calcd for $C_{29}H_{29}O_4NBrS$ 566.0995, found 566.0997.

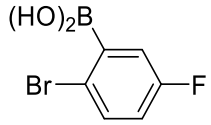
(*E*)-3-((2-bromo-5-fluorophenyl)(phenyl)methylene)-1-((4-methoxyphenyl)sulfonyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole (2df)



Reaction time: 7 h, 80 °C; Column chromatography: (95/5 → 80/20) hexanes/EtOAc

Yield: 75% (0.104 g) as a mixture of *E*/*Z* isomers (2.5:1); white foam

Reagent	n [mmol]	m [mg]	V [mL]
THF			2.3
Water			0.2
1d	0.25	127	

	0.33	72	
$Pd(PPh_3)_4$	0.01	12	
Cs_2CO_3	0.50	163	

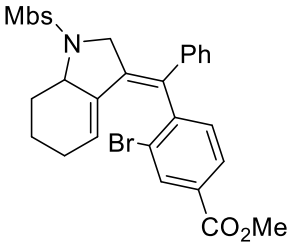
(*E*)-2df (major): **^{1}H NMR** (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.66 – 7.59 (m, 2H, 2H$^{\#}$), 7.48 – 7.41 (m, 1H, 1H$^{\#}$), 7.34 – 7.22 (m, 4H, 4H$^{\#}$), 7.11 – 7.06 (m, 1H, 1H$^{\#}$), 7.04 – 6.98 (m, 4H, 3H$^{\#}$), 6.49 (dd, *J* = 8.8, 3.1 Hz, 1H$^{\#}$), 5.15 – 5.09 (m, 1H$^{\#}$), 5.06 – 4.99 (m, 1H), 4.41 (d, *J* = 15.0 Hz, 1H$^{\#}$), 4.34 (d, *J* = 14.9 Hz, 1H), 3.94 – 3.89 (m, 1H, 1H$^{\#}$), 3.88 (s, 3H$^{\#}$), 3.85 (s, 3H), 3.67 – 3.52 (m, 1H, 1H$^{\#}$), 2.61 – 2.44 (m, 1H, 1H$^{\#}$), 2.03 – 1.85 (m, 2H, 2H$^{\#}$), 1.85 – 1.74 (m, 1H, 1H$^{\#}$), 1.53 – 1.39 (m, 2H, 2H$^{\#}$);

(*Z*)-2df (minor): **^{1}H NMR** (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 7.76 – 7.71 (m, 2H), 7.71 – 7.68 (m, 2H$^{\#}$), 7.50 – 7.41 (m, 1H, 1H$^{\#}$), 7.34 – 7.22 (m, 4H, 4H$^{\#}$), 7.11 – 7.06 (m, 1H, 1H$^{\#}$), 7.04 – 6.98 (m, 4H, 3H$^{\#}$), 6.56 (dd, *J* = 8.8, 3.1 Hz, 1H$^{\#}$), 5.52 – 5.47 (m, 1H$^{\#}$), 5.45 – 5.40 (m, 1H), 4.01 (d, *J* = 14.9 Hz, 1H$^{\#}$), 3.94 – 3.91(m, 1H), 3.90 (s, 3H$^{\#}$), 3.89 (s, 3H), 3.60 – 3.52 (m, 1H), 3.58 (d, *J* = 14.9 Hz, 1H), 3,52 – 3.48 (m, 1H$^{\#}$), 3.44 (d, *J* = 14.9 Hz, 1H$^{\#}$), 2.61 – 2.44 (m, 1H, 1H$^{\#}$), 2.03 – 1.85 (m, 2H, 2H$^{\#}$), 1.85 – 1.74 (m, 1H, 1H$^{\#}$), 1.53 – 1.39 (m, 2H, 2H$^{\#}$) ($^{\#}$ atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$);

Mixture of *E*/*Z* isomers of **2df**: **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 163.3, 163.2, 162.1 (d, *J* = 247.9 Hz), 162.04 (d, *J* = 247.9 Hz), 161.99 (d, *J* = 248.7 Hz), 143.9 (d, *J* = 7.8 Hz), 143.8 (d, *J* = 7.8 Hz), 139.9, 139.8, 139.1, 136.5, 136.1, 134.8 (d, *J* = 8.4 Hz), 134.7 (d, *J* = 8.4 Hz), 134.6 (d, *J* = 8.2 Hz), 134.3 (d, *J* = 8.2 Hz), 133.6, 133.2 (d, *J* = 1.3 Hz), 132.9, 131.8 (d, *J* = 1.5 Hz), 131.6, 130.3, 130.09, 130.06, 130.0, 129.1, 128.9, 128.8, 128.34, 128.32, 128.30, 127.95, 127.93, 127.80, 127.75, 127.66, 127.61, 127.5, 127.3, 126.4, 119.1 (d, *J* = 3.1 Hz), 118.7 (d, *J* = 22.1 Hz), 118.0 (d, *J* = 22.1 Hz), 117.4 (d, *J* = 3.1 Hz), 116.3 (d, *J* = 22.3 Hz), 116.1 (d, *J* = 22.3 Hz), 114.42, 114.39, 114.35, 114.30, 60.8, 60.7, 59.8, 59.5, 55.8, 55.7, 55.6, 53.4, 53.1, 52.7, 52.6, 29.9, 29.8, 29.6, 29.5, 25.24, 25.17, 25,1, 20.5,

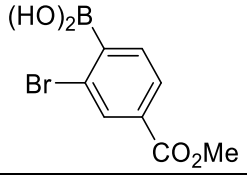
19.9, 19.8, 19.7 (distinguishing between signals of *E*/*Z* isomers was not possible); **IR** (KBr) ν_{max} 2933, 2862, 2839, 2825, 1597, 1576, 1498, 1464, 1348, 1269, 1157, 1097, 1032, 827, 702, 671, 598, 561 cm^{-1}; **MS** (ESI) *m/z* (%) 1131.1 (12, $[2M+Na]^+$), 578.1 (97, $[M+Na]^+$), 576.1 (100, $[M+Na]^+$), 530.0 (39), 301.1 (13); **HRMS** (ESI) *m/z* calcd for $C_{28}H_{25}O_3NBrFSNa$ 576.0615, found 576.0614.

Methyl (*E*)-3-bromo-4-((1-((4-methoxyphenyl)sulfonyl)-1,2,5,6,7,7a-hexahydro-3*H*-indol-3-ylidene)(phenyl)methyl)benzoate (2di)



Reaction time: 72 h; Column chromatography: (95/5 → 80/20) hexanes/EtOAc

Yield: 63% (0.093 g) as a mixture of *E*/*Z* isomers (3.2:1); yellowish foam

Reagent	n [mmol]	m [mg]	V [mL]
THF			2.3
Water			0.3
1d	0.25	127	
	0.38	97	
$Pd(PPh_3)_4$	0.01	12	
Cs_2CO_3	0.50	163	

(*E*)-2di (major): **^{1}H NMR** (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 8.18 (d, *J* = 1.6 Hz, 1H, 1H$^{\#}$), 7.90 – 7.86 (m, 1H, 1H$^{\#}$), 7.72 – 7.76 (m, 2H, 2H$^{\#}$), 7.33 – 7.19 (m, 4H, 4H$^{\#}$), 7.06 – 6.99 (m, 2H, 2H$^{\#}$), 6.98 – 6.89 (m, 2H, 2H$^{\#}$), 5.08 – 5.04 (m, 1H$^{\#}$), 4.96 – 4.91 (m, 1H), 4.43 (d, *J* = 14.9 Hz, 1H$^{\#}$), 4.35 (d, *J* = 14.9 Hz, 1H), 3.95 – 3.82 (m, 7H, 7H$^{\#}$), 3.67 – 3.48 (m, 1H, 1H$^{\#}$), 2.63 – 2.45 (m, 1H, 1H$^{\#}$), 2.00 – 1.71 (m, 3H, 3H$^{\#}$), 1.49 – 1.36 (m, 2H, 2H$^{\#}$);

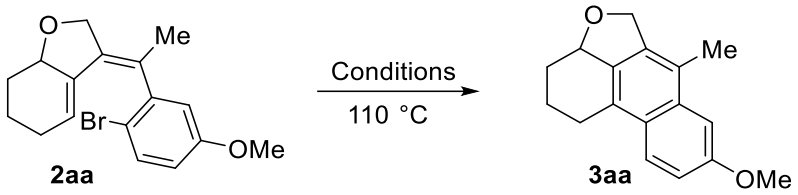
(*Z*)-2di (minor): **^{1}H NMR** (400 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 8.30 (d, *J* = 1.7 Hz, 1H$^{\#}$), 8.21 (d, *J* = 1.7 Hz, 1H), 8.01 (dd, *J*

= 8.0, 1.7 Hz, 1H), 7.90 – 7.86 (m, 1H$^{\#}$), 7.72 – 7.76 (m, 2H, 2H$^{\#}$), 7.44 (d, *J* = 8.0 Hz, 1H), 7.33 – 7.19 (m, 3H, 4H$^{\#}$), 7.06 – 6.99 (m, 2H, 2H$^{\#}$), 6.98 – 6.89 (m, 2H, 2H$^{\#}$), 5.54 – 5.50 (m, 1H$^{\#}$), 5.48 – 5.43 (m, 1H), 3.98 (d, *J* = 14.9 Hz, 1H$^{\#}$), 3.95 – 3.82 (m, 7H, 6H$^{\#}$), 3.67 – 3.48 (m, 2H, 1H$^{\#}$), 3.40 (d, *J* = 14.9 Hz, 1H$^{\#}$), 2.63 – 2.45 (m, 2H, 1H$^{\#}$), 2.00 – 1.71 (m, 2H, 3H$^{\#}$), 1.49 – 1.36 (m, 2H, 2H$^{\#}$) ($^{\#}$ atropoisomer signals – the signals are in pairs but could not be assigned to the particular atropoisomer, one signal of the pair is always marked by $^{\#}$);

Mixture of *E*/*Z* isomers of **2di**: **^{13}C NMR** (101 MHz, $CDCl_3$; mixture of atropoisomers, signals of both atropoisomers are listed) δ 165.67^{E}, 165.66 (1C$^{E\#}$, 1C$^{Z\#}$), 165.5^{Z}, 163.3^{Z}, 163.23^{E}, 163.18$^{Z\#}$, 163.1$^{E\#}$, 147.4, 146.9, 146.84, 146.80, 139.8, 139.0, 138.5, 136.5, 136.0, 134.63, 134.61, 134.51, 134.48, 134.2, 134.1, 133.6, 133.4, 132.8, 132.7, 132.03, 132.00, 131.89, 131.88, 131.1, 130.9, 130.51, 130.49, 130.2, 130.1, 130.04, 130.01, 129.9, 129.19, 129.16, 129.0, 128.93, 128.88, 128.8, 128.59, 128.57, 128.4, 128.3, 128.0, 127.83, 127.80, 127.77, 127.68, 127.66, 127.5, 127.4, 126.9, 126.6, 124.9, 123.3, 123.2, 122.6, 114.4, 114.33, 114.30, 60.8^{Z}, 60.7$^{Z\#}$, 59.8$^{E\#}$, 59.4^{E}, 55.8$^{E,Z\#}$, 53.3^{Z}, 53.2$^{Z\#}$, 52.7^{E}, 52.6$^{E\#}$, 52.53$^{E\#}$, 52.52^{Z}, 29.9^{Z}, 29.8^{E}, 29.7$^{Z\#}$, 29.6$^{E\#}$, 25.19$^{E\#}$, 25.17^{Z}, 25.1$^{E,Z\#}$, 19.8$^{E\#}$, 19.73$^{E,Z\#}$, 19.68^{Z} (^{E} signal could be assigned to the major *E* isomer; ^{Z} signal could be assigned to the minor *Z* isomer); **IR** (KBr) ν_{max} 2947, 2868, 2839, 1726, 1597, 1496, 1435, 1346, 1284, 1261, 1244, 1159, 1111, 1093, 1024, 835, 764, 700, 669, 606, 563 cm^{-1}; **MS** (ESI) *m/z* (%) 1211.2 (11, [2M+Na]$^{+}$), 618.1 (98, [M+Na]$^{+}$), 616.1 (100, [M+Na]$^{+}$), 596.1 (12, [M+H]$^{+}$), 594.1 (14, [M+H]$^{+}$), 279.1 (10); **HRMS** (ESI) *m/z* calcd for $C_{30}H_{29}O_5NBrS$ 594.0944, found 594.0945.

4. Synthesis of naphthalenes

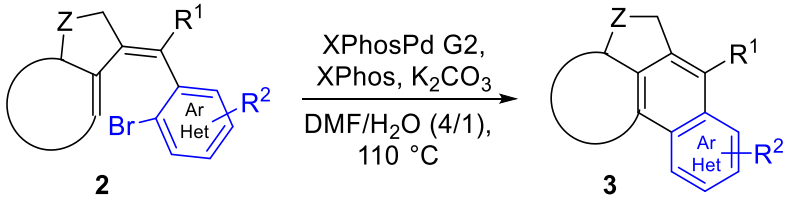
*Table S1. Optimisation of the conditions of the Heck reaction of **2aa***



Entry	Catalyst (mol%)	Ligand (mol%)	Base (eq)	Solvent	Time [h]	Yield[a] [%]
1	$Pd_2(dba)_3$ (10)	XPhos (20)	K_2CO_3 (4)	DMF/H_2O (4:1)	2	63 (60)
2	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (4)	DMF/H_2O (4:1)	48	15
3	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (4)	DMF/H_2O (4:1)	4.5	68 (61)
4	$Pd(PPh_3)_4$ (10)	XPhos (20)	K_2CO_3 (4)	DMF/H_2O (4:1)	2	65
5	$PdCl_2(CH_3CN)_2$ (10)	XPhos (20)	K_2CO_3 (2)	DMF/H_2O (4:1)	4	27
6	$Pd(TFA)_2$ (10)	XPhos (20)	K_2CO_3 (2)	DMF/H_2O (4:1)	2	29
7	$Pd(PPh_3)_2Cl_2$ (10)	XPhos (20)	K_2CO_3 (2)	DMF/H_2O (4:1)	3.5	64
8	Hermann-Beller Pd (10)	XPhos (20)	K_2CO_3 (2)	DMF/H_2O (4:1)	2	66
9	XPhosPd G2	XPhos (20)	K_2CO_3 (4)	DMF/H_2O (4:1)	2	70
10	XPhosPd G2	–	K_2CO_3 (2)	DMF/H_2O (4:1)	6	48
11	$Pd(OAc)_2$ (10)	BINAP (20)	K_2CO_3 (4)	DMF/H_2O (4:1)	5	0
12	$Pd(OAc)_2$ (10)	dppf (20)	K_2CO_3 (4)	DMF/H_2O (4:1)	5	68
13	$Pd(OAc)_2$ (10)	TTBP.HBF_4 (20)	K_2CO_3 (4)	DMF/H_2O (4:1)	23	63
14	$Pd(OAc)_2$ (10)	SPhos (20)	K_2CO_3 (4)	DMF/H_2O (4:1)	4.5	66
15	$Pd(OAc)_2$ (10)	–	K_2CO_3 (4)[b]	DMF	27	0
16	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (4)	Toluene/H_2O (4:1)	2	0
17	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (4)	Ethanol/H_2O (4:1)	2	5
18	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (4)	DMF	12	43
19	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (4)[c]	DMF	4.5	65
20	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (4)	dioxane/H_2O (4:1)	3	11

21	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (4)	DMSO/H_2O (4:1)	6.5	10
22	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (4)	DMA/H_2O (4:1)	3	61
23	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (4)	*i*PrOH/H_2O (4:1)	5	12
24	$Pd(OAc)_2$ (10)	XPhos (20)	Ag_2CO_3 (4)	DMF	5	4
25	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (0.5)	DMF/H_2O (4:1)	2	29
26	$Pd(OAc)_2$ (10)	XPhos (20)	Na_2CO_3 (4)	DMF/H_2O (4:1)	23	39
27	$Pd(OAc)_2$ (10)	XPhos (20)	Cs_2CO_3 (4)	DMF/H_2O (4:1)	5	51
28	$Pd(OAc)_2$ (10)	XPhos (20)	K_3PO_4 (4)	DMF/H_2O (4:1)	5	63
29	$Pd(OAc)_2$ (10)	XPhos (20)	DIPEA (4)	DMF/H_2O (4:1)	5	19
30	$Pd(OAc)_2$ (10)	XPhos (20)	KOtBu (2)	DMF/H_2O (4:1)	2	0
31	$Pd(OAc)_2$ (10)	XPhos (20)	Li_2CO_3 (2)	DMF/H_2O (4:1)	19	12
32	$Pd(OAc)_2$ (10)	XPhos (20)	KF (2)	DMF/H_2O (4:1)	18	27
33	$Pd(OAc)_2$ (10)	XPhos (20)	$NaHCO_3$ (2)	DMF/H_2O (4:1)	12	30
34	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (2)	DMF/H_2O (2:1)	4	11
35	$Pd(OAc)_2$ (10)	XPhos (20)	K_2CO_3 (2)	DMF/H_2O (9:1)	2	63
36	$Pd(OAc)_2$ (5)	XPhos (10)	K_2CO_3 (2)	DMF/H_2O (4:1)	4	7
37	$Pd(OAc)_2$ (10)	XPhos (10)	K_2CO_3 (2)	DMF/H_2O (4:1)	2	16

[a] ^{1}H NMR yield; 3,4,5-trimethoxybenzaldehyde was used as internal standard. [b] 2 equiv. of *n*Bu_4NOAc were used as additive. [c] 2 equiv. of *n*Bu_4NCl were used as additive.



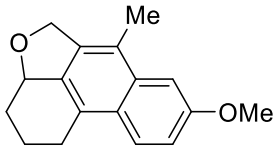
2 **3**

General procedure 1 for the Heck reaction: Compound **2** (1.0 mmol), K_2CO_3 (2.0 mmol), XPhos (20 mol%) and XPhosPd G2 (10 mol%) were dissolved in DMF (8 mL) and stirred for 5 minutes followed by addition of water (2 mL). The reaction mixture was degassed and backfilled with argon (3×) and stirred at 110 °C for an indicated time. Upon completion, it was cooled down, filtrated through the sand/cotton layer and

extracted between brine (2 × 20 mL) and EtOAc (20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude mixture was subjected to column chromatography on silica gel providing desired naphthalene product **3**. Reaction and purification details are specified for the each substrate below.

General procedure 2 for the Heck reaction: Compound **2** (0.2 mmol) and Cs_2CO_3 (0.4 mmol) were dissolved in DMF (1.8 mL) and water (0.18 mL). The reaction mixture was degassed and backfilled with argon (3×), or degassed by bubbling Ar through the mixture for 5 minutes. Then $Pd_2(dba)_3$ (0.02 mmol) and P(o-tol)$_3$ (0.04 mmol) were added, the mixture was degassed again and stirred at 130 °C for an indicated time. Upon completion, it was cooled down, diluted with toluene and concentrated under reduced pressure. Crude mixture was subjected to column chromatography on silica gel providing desired naphthalene product **3**. Reaction and purification details are specified for the each substrate below.

8-Methoxy-6-methyl-2,3,3a,5-tetrahydro-1*H*-phenanthro[1,10-*bc*]furan (3aa)



General procedure 1; Reaction time: 2 h; Column chromatography: (97/3) hexanes/ acetone

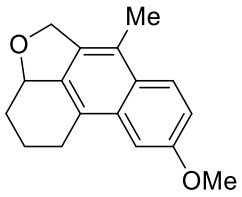
Yield: 61% (0.070 g); white crystalline solid; mp = 135.1 °C (recrystallized from $CHCl_3$)

Reagent	n [mmol]	m [mg]	V [mL]
DMF			3.6
Water			0.9
2aa	0.45	151	
XPhosPd G2	0.045	52	
XPhos	0.09	43	
K_2CO_3	0.90	124	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 9.0 Hz, 1H), 7.29 (d, *J* = 2.6 Hz, 1H), 7.18 (dd, *J* = 9.0, 2.6 Hz, 1H), 5.11 (d, *J* = 12.4 Hz, 1H), 5.06 (d, *J* = 12.3 Hz, 1H), 4.96–5.90 (m,

1H), 3.96 (s, 3H), 3.14 (dd, *J* = 17.5, 6.9 Hz, 1H), 2.91–2.79 (m, 1H), 2.50 (s, 3H), 2.46–2.38 (m, 1H), 2.32–2.23 (m, 1H), 1.96–1.82 (m, 1H), 1.50 (dtd, *J* = 13.9, 11.0, 3.0 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.4, 137.2, 136.3, 134.6, 127.0, 125.8, 125.2, 122.9, 116.8, 104.1, 79.9, 71.4, 55.43 29.5, 23.5, 20.9, 15.8; **IR** (KBr) ν_{max} 3422, 2938, 2917, 2851, 1458, 1228, 1030 cm^{-1}; **MS** (EI) *m/z* (%) 255.1 (10), 254.1 (90, $M^{+\bullet}$), 226.1 (100), 211.1 (22), 198.1 (20), 183.1 (22), 168.1 (7), 155.1 (3); **HRMS** (EI) *m/z* calcd for $C_{17}H_{18}O_2$ 254.1307, found 254.1308.

9-Methoxy-6-methyl-2,3,3a,5-tetrahydro-1*H*-phenanthro[1,10-*bc*]furan (3ab)



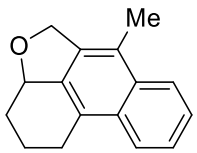
General procedure 1; Reaction time: 2 h; Column chromatography: (97/2) hexanes/acetone

Yield: 55% (0.154 g); white crystalline solid; mp = 130.3 °C (recrystallized from $CHCl_3$)

Reagent	n [mmol]	m [mg]	V [mL]
DMF			8.8
Water			2.2
2ab	1.10	354	
XPhosPd G2	0.11	87	
XPhos	0.22	105	
K_2CO_3	2.20	304	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.89 (m, 1H), 7.21–7.14 (m, 2H), 5.10 (d, *J* = 12.1 Hz, 1H), 5.05 (d, *J* = 12.0 Hz, 1H), 4.98–4.91 (m, 1H), 3.94 (s, 3H), 3.10 (dd, *J* = 17.3, 7.0 Hz, 1H), 2.88–2.77 (m, 1H), 2.52 (s, 3H), 2.47–2.39 (m, 1H), 2.35–2.26 (m, 1H), 1.99–1.85 (m, 1H), 1.52 (dtd, *J* = 13.9, 11.0, 3.0 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.4, 139.0, 134.4, 133.2, 128.4, 126.0, 124.7, 124.2, 116.7, 103.1, 80.0, 71.3, 55.4, 29.4, 23.6, 20.9, 15.7; **IR** (KBr) ν_{max} 3411, 2947, 2842, 1616, 1431, 1234, 1048, 815 cm^{-1}; **MS** (EI) *m/z* (%) 255.1 (8), 254.1 (55, $M^{+\bullet}$), 236.1 (100), 226.1 (34), 223.1 (52), 211.1 (25), 193.1 (20), 178.1 (35), 165.1 (23), 152.1 (12); **HRMS** (EI) *m/z* calcd for $C_{17}H_{18}O_2$ 254.1307, found 254.1308.

6-Methyl-2,3,3a,5-tetrahydro-1*H*-phenanthro[1,10-*bc*]furan (3ad)



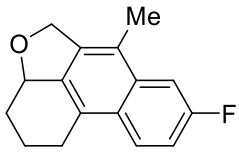
General procedure 1; Reaction time: 4 h; Column chromatography: (97/2) hexanes/acetone

Yield: 70% (0.063 g); yellow crystalline solid, mp = 119.6 °C (recrystallized from $CHCl_3$)

Reagent	n [mmol]	m [mg]	V [mL]
DMF			3.2
Water			0.8
2ad	0.40	122	
XPhosPd G2	0.04	31	
XPhos	0.08	38	
K_2CO_3	0.80	110	

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05–7.99 (m, 1H), 7.93–7.87 (m, 1H), 7.56–7.48 (m, 2H), 5.13 (d, *J* = 12.4 Hz, 1H), 5.08 (d, *J* = 12.3 Hz, 1H), 5.00–4.92 (m, 1H), 3.18 (dd, *J* = 17.5, 7.0 Hz, 1H), 2.95–2.82 (m, 1H), 2.55 (s, 3H), 2.48–2.41 (m, 1H), 2.35–2.26 (m, 1H), 1.99–1.85 (m, 1H), 1.52 (dtd, *J* = 13.9, 11.0, 3.1 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.3, 136.6, 133.3, 131.9, 125.8, 125.3, 125.2, 124.5, 124.2, 123.7, 80.0, 71.4, 29.4, 23.47, 20.9, 15.7; **IR** (KBr) ν_{max} 2941, 2926, 2860, 2836, 1512, 1443, 1332, 1045, 964, 749 cm^{-1}; **MS** (EI) *m/z* (%) 225.1 (10), 224.1 (93, $M^{+\bullet}$), 220.1 (20), 205.1 (25), 196.1 (100), 181.1 (22), 168.1 (17), 153.1 (15); **HRMS** (EI) *m/z* calcd for $C_{16}H_{16}O$ 224.1201, found 224.1203.

8-Fluoro-6-methyl-2,3,3a,5-tetrahydro-1*H*-phenanthro[1,10-*bc*]furan (3af)



General procedure 1; Reaction time: 4 h; Column chromatography: (97/2) hexanes/ acetone

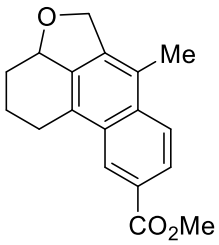
Yield: 67% (0.074 g); yellow crystalline solid, mp = 112.4 °C (recrystallized from $CHCl_3$)

Reagent	n [mmol]	m [mg]	V [mL]
DMF			3.6

Water			0.9
2af	0.45	145	
XPhosPd G2	0.045	35	
XPhos	0.09	43	
K_2CO_3	0.90	124	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 9.1, 5.9 Hz, 1H), 7.60 (dd, *J* = 11.3, 2.6 Hz, 1H), 7.27 (ddd, *J* = 9.1, 8.0, 2.6 Hz, 1H), 5.11 (d, *J* = 12.5 Hz, 1H), 5.06 (d, *J* = 12.5 Hz, 1H), 4.97–4.89 (m, 1H), 3.15 (dd, *J* = 17.5, 7.0 Hz, 1H), 2.92–2.80 (m, 1H), 2.49 (s, 3H), 2.47–2.39 (m, 1H), 2.34–2.25 (m, 1H), 1.98–1.84 (m, 1H), 1.51 (dtd, *J* = 14.0, 11.1, 3.0 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.7 (d, *J* = 244.2 Hz), 137.9, 137.8 (d, *J* = 2.4 Hz), 134.6 (d, *J* = 8.1 Hz), 128.9 (d, *J* = 0.8 Hz), 126.0 (d, *J* = 0.8 Hz), 125.9 (d, *J* = 9.1 Hz), 123.7 (d, *J* = 5.4 Hz), 115.0 (d, *J* = 24.5 Hz), 108.5 (d, *J* = 21.1 Hz), 79.8, 71.3, 29.3, 23.6, 20.8, 15.7; **IR** (KBr) ν_{max} 2965, 2935, 2878, 2839, 1619, 1530, 1446, 1329, 1222, 1186, 1039, 964 cm^{-1}; **MS** (EI) *m/z* (%) 243.1 (15), 242.1 (85, $M^{+\bullet}$), 224.1 (22), 214.1 (100), 209.1 (22), 199.1 (30), 183.1 (28), 171.1 (33); **HRMS** (EI) *m/z* calcd for $C_{16}H_{15}OF$ 242.1107, found 242.1104.

Methyl 6-methyl-2,3,3a,5-tetrahydro-1*H*-phenanthro[1,10-*bc*]furan-9-carboxylate (3ai)



General procedure 2; Reaction time: 4 h; Column chromatography: (95/5 → 90/10) hexanes/EtOAc

Yield: 16% (9 mg); yellowish oil

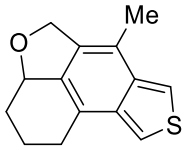
(ester partially hydrolysed in the reaction)

Reagent	n [mmol]	m [mg]	V [mL]
DMF			1.8
Water			0.18
2ai	0.20	74	
$Pd_2(dba)_3$	0.02	9	
P(o-tol)$_3$	0.04	12	

Cs_2CO_3	0.40	129	

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 1.5 Hz, 1H), 8.08 (dd, *J* = 8.8, 1.7 Hz, 1H), 8.03 (d, *J* = 8.8 Hz, 1H), 5.12 (d, *J* = 12.8 Hz, 1H), 5.07 (d, *J* = 12.7 Hz, 1H), 4.99 – 4.92 (m, 1H), 3.99 (s, 3H), 3.26 (dd, *J* = 17.7, 6.9 Hz, 1H), 3.00 – 2.87 (m, 1H), 2.55 (s, 3H), 2.48 – 2.41 (m, 1H), 2.36 – 2.28 (m, 1H), 2.00 – 1.85 (m, 1H), 1.52 (dtd, *J* = 13.9, 11.0, 3.0 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.6, 139.3, 139.2, 135.8, 131.3, 127.5, 126.64, 126.63, 124.8, 124.7, 124.3, 79.9, 71.4, 52.3, 29.2, 23.5, 20.8, 15.7; **IR** (KBr) ν_{max} 2949, 2835, 1716, 1448, 1315, 1277, 1255, 1219, 1107, 1043, 1005, 964, 754 cm^{-1}; **MS** (APCI) *m/z* (%) 284.1 (17), 283.1 (100, $[M+H]^+$), 265.1 (6), 253.1 (5); **HRMS** (APCI) *m/z* calcd for $C_{18}H_{19}O_3$ 283.1329, found 283.1326.

6-Methyl-1,2,3,3a-tetrahydro-5*H*-thieno[3',4':5,6]naphtho[1,8-*bc*]furan (3aj)



General procedure 1; Reaction time: 2 h; Column chromatography: (97/2) hexanes/acetone

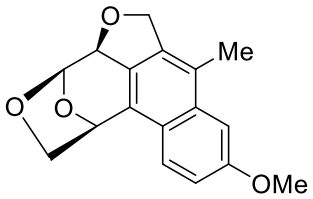
Yield: 30% (0.031 g); pale brown amorphous solid

Reagent	n [mmol]	m [mg]	V [mL]
DMF			3.6
Water			0.9
2aj	0.45	139	
XPhosPd G2	0.045	35	
XPhos	0.09	43	
K_2CO_3	0.90	124	

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (d, *J* = 3.2 Hz, 1H), 7.77 (d, *J* = 3.2 Hz, 1H), 4.85 (d, *J* = 12.6 Hz, 1H), 4.77 (d, *J* = 12.7 Hz, 1H), 4.70–4.63 (m, 1H), 2.86 (dd, *J* = 17.9, 6.8 Hz, 1H), 2.68–2.56 (m, 1H), 2.34 (s, 3H), 2.29–2.20 (m, 1H), 2.17–2.07 (m, 1H), 1.86–1.71 (m, 1H), 1.30 (dtd, *J* = 13.9, 10.9, 3.1 Hz, 1H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 140.3, 138.1, 136.9, 134.1, 120.8, 119.3, 115.9, 114.6, 77.6, 69.0, 28.9, 23.2, 19.9, 15.4; **IR** (KBr) ν_{max} 3560, 2929, 2839, 1715, 1518, 1458, 1386, 1329, 1051, 755 cm^{-1}; **MS** (EI) *m/z* (%) 231.1 (15), 230.1 (100, $M^{+\bullet}$), 212.1 (30), 202.1 (65), 197.0 (27), 187.1

(28), 174.1 (30), 165.1 (5), 152.1 (8); **HRMS** (EI) *m/z* calcd for $C_{14}H_{14}OS$ 230.0765, found 230.0768.

(1*S*,4*R*,4a*S*)-9-Methoxy-7-methyl-1,2,4a,6-tetrahydro-4*H*-1,4-epoxybenzo[*f*]oxepino[3,4,5-*cd*]isobenzofuran (3ba)



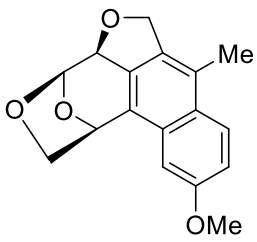
General procedure 1; Reaction time: 3 h; Column chromatography: (97/3) dichloromethane/diethyl ether

Yield: 64% (0.091 g); white amorphous solid

Reagent	n [mmol]	m [mg]	V [mL]
DMF			3.6
Water			0.9
2ba	0.50	183	
XPhosPd G2	0.05	39	
XPhos	0.10	48	
K_2CO_3	1.0	138	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 9.0 Hz, 1H), 7.29 (d, *J* = 2.5 Hz, 1H), 7.19 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.02–6.00 (m, 1H), 5.92 (d, *J* = 3.7 Hz, 1H), 5.27 (s, 1H), 5.15 (d, *J* = 12.2 Hz, 1H), 5.07 (d, *J* = 12.2 Hz, 1H), 4.06 (ddd, *J* = 6.7, 3.8, 1.1 Hz, 1H), 3.95 (s, 3H), 3.62 (d, *J* = 6.7 Hz, 1H), 2.50 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.6, 138.0, 135.4, 132.1, 126.8, 125.8, 124.2, 123.3, 117.8, 104.6, 101.1, 81.1, 76.3, 72.6, 72.5, 55.5, 16.3; **IR** (KBr) ν_{max} 3422, 2968, 2884, 2842, 1622, 1431, 1231, 1048, 934 cm^{-1}; **MS** (ESI) *m/z* (%) 308.1 (18), 307.1 (100, $[M+Na]^+$), 285.1 (25, $[M+H]^+$), 267.1 (8); **HRMS** (ESI) *m/z* calcd for $C_{17}H_{16}O_4Na$ 307.0941, found 307.0939; **Specific rotation** $[\alpha]_D$ = +119.7° (c 1, $CHCl_3$).

(1*S*,4*R*,4a*S*)-10-Methoxy-7-methyl-1,2,4a,6-tetrahydro-4*H*-1,4-epoxybenzo[*f*]oxepino[3,4,5-*cd*]isobenzofuran (3bb)



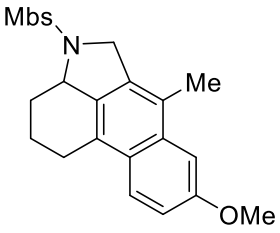
General procedure 1; Reaction time: 3 h; Column chromatography: (97/3) dichloromethane/ acetone; Compound was additionally washed with n-pentane.

Yield: 36% (0.092 g); pale brown amorphous solid

Reagent	n [mmol]	m [mg]	V [mL]
DMF			8.0
Water			2.0
2bb	1.0	365	
XPhosPd G2	0.10	79	
XPhos	0.20	95	
K_2CO_3	2.0	276	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 9.2 Hz, 1H), 7.19 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.04 (d, *J* = 2.6 Hz, 1H), 6.02–6.00 (m, 1H), 5.91 (d, *J* = 3.6 Hz, 1H), 5.26 (s, 1H), 5.13 (d, *J* = 12.0 Hz, 1H), 5.06 (d, *J* = 12.0 Hz, 1H), 4.08 (ddd, *J* = 6.7, 3.7, 1.0 Hz, 1H), 3.93 (s, 3H), 3.66 (d, *J* = 6.7 Hz, 1H), 2.51 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.9, 135.2, 135.1, 129.4, 129.2, 127.4, 126.6, 125.6, 117.2, 102.2, 101.1, 81.3, 76.2, 72.6, 72.4, 55.5, 16.2; **IR** (KBr) ν_{max} 3602, 3249, 1619, 1461, 1428, 1228, 1048 cm^{-1}; **MS** (APCI) *m/z* (%) 286.1 (17), 285.1 (100, $[M+H]^+$), 267.1 (47), 257.1 (6), 239.1 (40), 227.1 (27), 211.1 (16); **HRMS** (APCI) *m/z* calcd for $C_{17}H_{17}O_4$ 285.1121, found 285.1118; **Specific rotation** $[\alpha]_D$ = +156.1° (c 1, $CHCl_3$).

8-Methoxy-4-((4-methoxyphenyl)sulfonyl)-6-methyl-1,2,3,3a,4,5-hexahydro-naphtho[3,2,1-*cd*]indole (3ca)



General procedure 2; Reaction time: 6 h; Column chromatography: (85/15 → 80/20 → 70/30) hexanes/EtOAc

Yield: 62% (76 mg); brownish powder

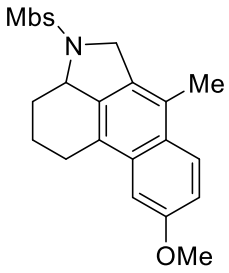
(21% of unreacted starting material was isolated)

Reagent	n [mmol]	m [mg]	V [mL]
DMF			2.6
Water			0.26
2ca	0.29	146	

$Pd_2(dba)_3$	0.03	13	
$P(o\text{-}tol)_3$	0.06	17	
Cs_2CO_3	0.58	188	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.86 (m, 2H), 7.77 (d, *J* = 9.1 Hz, 1H), 7.22 (d, *J* = 2.6 Hz, 1H), 7.15 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.07 – 7.01 (m, 2H), 4.72 (d, *J* = 13.0 Hz, 1H), 4.36 (d, *J* = 13.0 Hz, 1H), 4.18 (dd, *J* = 10.9, 4.4 Hz, 1H), 3.93 (s, 3H), 3.86 (s, 3H), 3.08 (dd, *J* = 17.6, 7.0 Hz, 1H), 2.90 – 2.75 (m, 2H), 2.45 (s, 3H), 2.33 – 2.24 (m, 1H), 1.92 – 1.78 (m, 1H), 1.71 – 1.59 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.3, 157.4, 134.4, 133.0, 132.0, 130.6, 127. 5, 127.3, 127.1, 125.1, 124.1, 117.1, 114.5, 103.8, 62.4, 55.8, 55.4, 53.9, 30.1, 23.4, 21.5, 15.5; **IR** (KBr) ν_{max} 2931, 2837, 1595, 1496, 1456, 1346, 1259, 1230, 1159, 1095, 1032, 837, 804, 667, 596, 561 cm^{-1}; **MS** (ESI) *m/z* (%) 869.3 (12, $[2M+Na]^+$), 446.1 (100, $[M+Na]^+$), 424.2 (6, $[M+H]^+$); **HRMS** (ESI) *m/z* calcd for $C_{24}H_{25}O_4NSNa$ 446.1397, found 446.1402.

9-Methoxy-4-((4-methoxyphenyl)sulfonyl)-6-methyl-1,2,3,3a,4,5-hexahydro-naphtho[3,2,1-*cd*]indole (3cb)



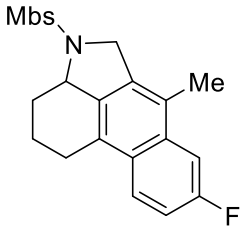
General procedure 2; Reaction time: 16 h; Column chromatography: (95/5 → 60/40) hexanes/EtOAc

Yield: 74% (25 mg); white foam

Reagent	n [mmol]	m [mg]	V [mL]
DMF			0.8
Water			0.08
2cb	0.08	40	
$Pd_2(dba)_3$	0.008	7.2	
$P(o\text{-}tol)_3$	0.016	5.4	
Cs_2CO_3	0.16	52	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.86 (m, 3H), 7.15 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.12 (d, *J* = 2.2 Hz, 1H), 7.06 – 7.02 (m, 2H), 4.72 (d, *J* = 12.7 Hz, 1H), 4.35 (d, *J* = 12.7 Hz, 1H), 4.23 – 4.16 (m, 1H), 3.92 (s, 3H), 3.87 (s, 3H), 3.05 (dd, *J* = 17.5, 7.0 Hz, 1H), 2.98 – 2.76 (m, 2H), 2.47 (s, 3H), 2.36 – 2.26 (m, 1H), 1.95 – 1.81 (m, 1H), 1.75 – 1.60 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.3, 157.5, 135.8, 133.3, 130.5, 129.1, 128.2, 127.5, 126.1, 126.0, 125.5, 117.2, 114.5, 102.8, 62.6, 55.8, 55.4, 53.8, 30.0, 23.5, 21.5, 15.4; **IR** (KBr) ν_{max} 2949, 2925, 2843, 1597, 1495, 1460, 1425, 1344, 1265, 1232, 1153, 1095, 1028, 839, 669, 571, 559 cm^{-1}; **MS** (ESI) *m/z* (%) 446.1 (4, $[M+Na]^+$), 425.2 (18), 424.2 (100, $[M+H]^+$), 321.1 (18), 237.1 (5); **HRMS** (ESI) *m/z* calcd for $C_{24}H_{26}O_4NS$ 424.1577, found 424.1576.

8-Fluoro-4-((4-methoxyphenyl)sulfonyl)-6-methyl-1,2,3,3a,4,5-hexahydro-naphtho[3,2,1-*cd*]indole (3cf)



General procedure 2; Reaction time: 15 h; Column chromatography: (95/5 → 83/17) hexanes/EtOAc

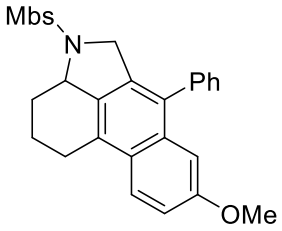
Yield: 85% (25 mg); brownish foam

Reagent	n [mmol]	m [mg]	V [mL]
DMF			0.65
Water			0.06
2cf	0.07	35	
$Pd_2(dba)_3$	0.007	6.5	
$P(o\text{-}tol)_3$	0.014	4.3	
Cs_2CO_3	0.14	47	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.81 (m, 3H), 7.55 (dd, *J* = 11.2, 2.6 Hz, 1H), 7.28 (m, 1H), 7.08 – 7.02 (m, 2H), 4.72 (d, *J* = 13.2 Hz, 1H), 4.36 (d, *J* = 13.2 Hz, 1H), 4.18 (dd, *J* = 11.2, 4.4 Hz, 1H), 3.87 (s, 3H), 3.10 (dd, *J* = 17.7, 7.1 Hz, 1H), 2.92 – 2.76 (m, 2H), 2.44 (s, 3H), 2.35 – 2.25 (m, 1H), 1.86 (tddd, *J* = 13.9, 10.4, 7.1, 2.9 Hz, 1H), 1.73 – 1.60 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.4, 160.78 (d, *J* = 244.9 Hz), 134.6 (d, *J* = 2.4 Hz), 134.3 (d, *J* = 8.4 Hz), 132.6, 130.5, 128.9, 127.5, 127.3, 125.9 (d, *J* = 9.0 Hz),

124.9 (d, *J* = 5.4 Hz), 115.3 (d, *J* = 24.6 Hz), 114.5, 108.3 (d, *J* = 21.2 Hz), 62.3, 55.8, 53.8, 30.0, 23.4, 21.4, 15.4; **IR** (KBr) ν_{max} 2962, 2972, 2898, 2843, 1597, 1523, 1496, 1444, 1344, 1267, 1178, 1155, 1093, 1051, 841, 804, 667, 592, 561 cm^{-1}; **MS** (ESI) *m/z* (%) 845.2 (8, $[2M+Na]^+$), 823.3 (7, $[2M+H]^+$), 434.1 (6, $[M+Na]^+$), 413.1 (21), 412.1 (100, $[M+H]^+$); **HRMS** (ESI) *m/z* calcd for $C_{23}H_{23}O_3NFS$ 412.1377, found 412.1378.

8-Methoxy-4-((4-methoxyphenyl)sulfonyl)-6-phenyl-1,2,3,3a,4,5-hexahydro-naphtho[3,2,1-*cd*]indole (3da)



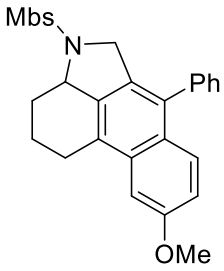
General procedure 2; Reaction time: 7 h; Column chromatography: (85/15) hexanes/EtOAc

Yield: 91% (51 mg); brownish foam

Reagent	n [mmol]	m [mg]	V [mL]
DMF			1.0
Water			0.1
2da	0.12	65	
$Pd_2(dba)_3$	0.01	5	
$P(o\text{-}tol)_3$	0.02	7	
Cs_2CO_3	0.23	74	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.79 (m, 2H), 7.82 (d, *J* = 9.1 Hz, 1H), 7.53 – 7.39 (m, 3H), 7.35 – 7.27 (m, 2H), 7.15 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.06 – 7.01 (m, 2H), 6.99 (d, *J* = 2.6 Hz, 1H), 4.37 (d, *J* = 13.4 Hz, 1H), 4.26 (d, *J* = 13.3 Hz, 1H), 4.26 – 4.20 (m, 1H), 3.87 (s, 3H), 3.70 (s, 3H), 3.17 (dd, *J* = 17.8, 7.0 Hz, 1H), 2.98 – 2.86 (m, 1H), 2.85 – 2.77 (m, 1H), 2.38 – 2.28 (m, 1H), 1.96 – 1.82 (m, 1H), 1.76 – 1.64 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.3, 157.6, 138.1, 134.0, 133.1, 132.2, 131.0, 130.4, 129.9, 129.7, 129.0, 128.9, 128.8, 127.8, 127.4, 127.3 124.7, 117.5, 114.4, 106.0, 62.3, 55.7, 55.2, 54.1, 23.0, 23.6, 21.5; **IR** (KBr) ν_{max} 2937, 2835, 1595, 1496, 1458, 1343, 1259, 1228, 1159, 1095, 1055, 1024, 806, 667, 584, 561 cm^{-1}; **MS** (ESI) *m/z* (%) 993.3 (21, $[2M+Na]^+$), 509.2 (8), 508.2 (100, $[M+Na]^+$), 486.2 (7, $[M+H]^+$); **HRMS** (ESI) *m/z* calcd for $C_{29}H_{28}O_4NS$ 486.1734, found 486.1738.

9-Methoxy-4-((4-methoxyphenyl)sulfonyl)-6-phenyl-1,2,3,3a,4,5-hexahydro-naphtho[3,2,1-*cd*]indole (3db)



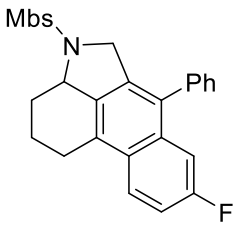
General procedure 2; Reaction time: 6 h; Column chromatography: (85/15) hexanes/EtOAc

Yield: 63% (27 mg); brownish foam

Reagent	n [mmol]	m [mg]	V [mL]
DMF			0.8
Water			0.8
2db	0.09	50	
$Pd_2(dba)_3$	0.009	8	
$P(o\text{-}tol)_3$	0.018	5.4	
Cs_2CO_3	0.18	58	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.80 (m, 2H), 7.57 (d, *J* = 9.2 Hz, 1H), 7.52 – 7.40 (m, 3H), 7.30 – 7.24 (m, 2H), 7.16 (d, *J* = 2.6 Hz, 1H), 7.06 – 7.00 (m, 3H), 4.38 (d, *J* = 13.1 Hz, 1H), 4.26 (d, *J* = 13.1 Hz, 1H), 4.27 – 4.22 (m, 1H), 3.92 (s, 3H), 3.87 (s, 3H), 3.13 (dd, *J* = 17.6, 7.0 Hz, 1H), 2.96 – 2.80 (m, 2H), 2.40 – 2.31 (m, 1H), 1.99 – 1.85 (m, 1H), 1.78 – 1.65 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.3, 157.7, 138.1, 135.9, 133.3, 132.2, 130.4, 130.1, 129.7, 129.2, 128.73, 128.66, 128.32, 127.80, 127.76, 127.66, 127.4, 117.5, 114.5, 102.3, 62.5, 55.8, 55.4, 54.0, 29.9, 23.7, 21.5; **IR** (KBr) ν_{max} 2949, 2929, 2841, 1616, 1595, 1496, 1458, 1425, 1348, 1303, 1261, 1227, 1161, 1151, 1093, 1057, 1034, 833, 764, 673, 619, 580, 550 cm^{-1}; **MS** (ESI) *m/z* (%) 1010.3 (5, $[2M+K]^+$), 993.3 (26, $[2M+Na]^+$), 524.1 (18, $[M+K]^+$), 509.2 (31), 508.2 (100, $[M+Na]^+$), 486.2 (23, $[M+H]^+$), 343.1 (12); **HRMS** (ESI) *m/z* calcd for $C_{29}H_{28}O_4NS$ 486.1734, found 486.1734.

8-Fluoro-4-((4-methoxyphenyl)sulfonyl)-6-phenyl-1,2,3,3a,4,5-hexahydro-naphtho[3,2,1-*cd*]indole (3df)



General procedure 2; Reaction time: 5 h; Column chromatography: (95/15 → 80/20) hexanes/EtOAc

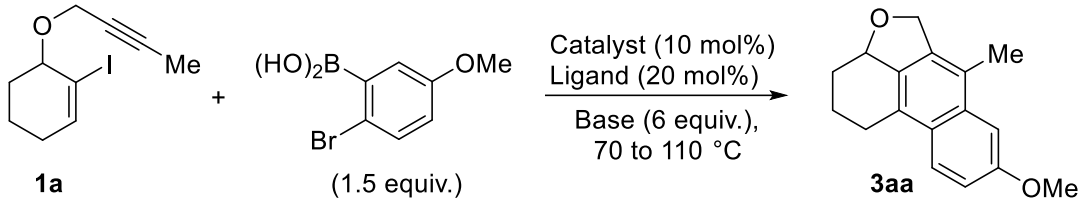
Yield: 77% (18 mg); brownish foam

Reagent	n [mmol]	m [mg]	V [mL]
DMF			0.45
Water			0.05
2df	0.05	27	
$Pd_2(dba)_3$	0.005	4.9	
$P(o\text{-}tol)_3$	0.01	3.3	
Cs_2CO_3	0.1	35	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (ddd, *J* = 8.6, 5.8, 1.0 Hz, 1H), 7.86 – 7.80 (m, 2H), 7.53 – 7.42 (m, 3H), 7.32 – 7.21 (m, 4H), 7.07 – 7.00 (m, 2H), 4.39 (d, *J* = 13.4 Hz, 1H), 4.26 (d, *J* = 13.6 Hz, 1H), 4.26 – 4.19 (m, 1H), 3.87 (s, 3H), 3.19 (dd, *J* = 17.8, 7.0 Hz, 1H), 2.99 – 2.88 (m, 1H), 2.84 (dtd, *J* = 11.9, 4.3, 3.0 Hz, 1H), 2.40 – 2.30 (m, 1H), 1.98 – 1.84 (m, 1H), 1.78 – 1.65 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.4, 160.9 (d, *J* = 245.1 Hz), 137.4, 134.7 (d, *J* = 2.4 Hz), 133.9 (d, *J* = 8.7 Hz), 132.9, 131.6 (d, *J* = 5.3 Hz), 130.4, 129.9, 129.6, 129.2, 129.0, 128.94, 128.90, 128.1, 127.3, 125.5 (d, *J* = 8.9 Hz), 115.7 (d, *J* = 24.9 Hz), 114.5, 110.4 (d, *J* = 22.0 Hz), 62.3, 55.8, 54.0, 29.9, 23.7, 21.4; **IR** (KBr) ν_{max} 2966, 2939, 2839, 1712, 1595, 1496, 1456, 1350, 1309, 1261, 1163, 1093, 1053, 1026, 806, 737, 667, 582, 558 cm^{-1}; **MS** (ESI) *m/z* (%) 947.3 (5, $[2M+H]^+$), 496.1 (4, $[M+Na]^+$), 475.2 (27), 474.2 (100, $[M+H]^+$), 287.1 (6); **HRMS** (ESI) *m/z* calcd for $C_{28}H_{25}O_3NFS$ 474.1534, found 474.1533.

5. Optimisation of the one-pot procedure

*Table S2. Optimisation of the one-pot cyclisation/Suzuki/Heck reaction of **1a** (additional experiments, see Table 2 for the best results)*



Entry	Catalyst	Ligand	Base	Solvent	Time at 70 °C [h]	Time at 110 °C [h]	Yield[a] of **2aa** [%]	Yield[a] of **3aa** [%]
1	$Pd(PPh_3)_4$	–	Cs_2CO_3	dioxane/H_2O (10:1)	3.5	2	17	20
2	$Pd(PPh_3)_4$	–	Cs_2CO_3	dioxane/H_2O/HMPA (10:1:2)	3.5	2	13	24
3	$Pd(PPh_3)_4$	–	Cs_2CO_3	dioxane/H_2O (10:1)	2.3	3	12	16
4	$Pd(PPh_3)_4$	XPhos	Cs_2CO_3	dioxane/H_2O (10:1)	2.3	3	14	14
5	$Pd(PPh_3)_4$	XPhos	Cs_2CO_3	DMF/H_2O (10:1)	2	3	0	26
6	$Pd(PPh_3)_4$	XPhos	K_2CO_3	DMF	2	3[b]	19	15
7	XPhosPd G2	–	K_2CO_3	DMF	2	3[b]	traces	traces
8	XPhosPd G2	XPhos	K_2CO_3	DMF	2	3[b]	traces	traces
9	$Pd(PPh_3)_4$	XPhos	K_2CO_3	DMF/H_2O (10:1)	2	3[b]	17	16
10	$Pd(PPh_3)_4$	SPhos	K_2CO_3	DMF/H_2O (10:1)	2	3[b]	16	14
11	XPhosPd G2	XPhos	K_2CO_3	DMF/H_2O (10:1)	2	3[b]	11	7
12	$Pd(PPh_3)_4$	XPhos	K_2CO_3	DMF	1.5	5[b]	20	18
13	$Pd(OAc)_2$	XPhos	K_2CO_3	DMF	1.5	5[b]	0	3
14	$Pd(dba)_2$	XPhos	K_3PO_4	DMF	1.5	5[b]	0	6
15	$Pd(PPh_3)_4$	–	K_2CO_3	dioxane/H_2O (15:1)	2	16[b]	54	5
16	$Pd(PPh_3)_4$	XPhos	K_2CO_3	dioxane/H_2O (15:1)	2	16[b]	10	22
17	$Pd(PPh_3)_4$	–	K_2CO_3	DMF/H_2O (15:1)	1.6	3[b]	24	13

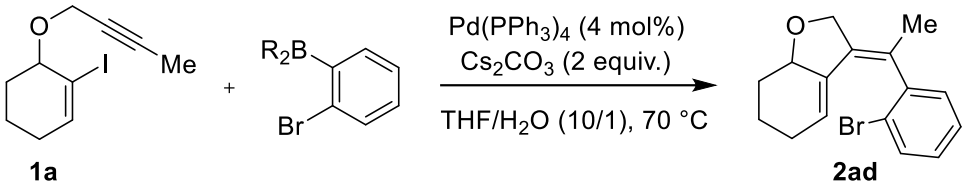
18	$Pd(PPh_3)_4$	–	K_2CO_3	DMF/H_2O (15:1)[c]	1.6	3[b]	70	1
19	$Pd(PPh_3)_4$	–	K_2CO_3	dioxane/H_2O (15:1)	1.6	24[b]	19	16
20	$Pd(PPh_3)_4$	–	K_2CO_3	dioxane/H_2O (15:1)[c]	1.6	24[b]	61	traces
21	$Pd(PPh_3)_4$	XPhos	K_2CO_3	toluene/H_2O (10:1)	2	3	30	4
22	$Pd(PPh_3)_4$	–	AcOK	DMF-d_7/D_2O (10:1)	1.5	3	30	18
23	SPhosPd G3	–	Cs_2CO_3	DMF-d_7/D_2O (10:1)	1.5	3	traces	20
24	$Pd_2(dba)_3$	P(*o*-tol)$_3$	Cs_2CO_3	toluene/H_2O (10:1)	2	4	15	1
25	$Pd_2(dba)_3$	PCy_3	Cs_2CO_3	toluene/H_2O (10:1)	2	4	9	36
26	$Pd_2(dba)_3$	P(*o*-tol)$_3$	AcOK[d]	toluene/H_2O (10:1)	2	4	traces	traces
27	$Pd_2(dba)_3$	TFP[e]	Cs_2CO_3	DMF-d_7/D_2O (10:1)	1.5	4	62	traces
28	$Pd_2(dba)_3$	P(*o*-tol)$_3$	Et_3N	DMF-d_7/D_2O (10:1)	1.5	4	0	0

[a] ^{1}H NMR yield; 3,4,5-trichloropyridine was used as internal standard. [b] At 100 °C. [c] Reaction was conducted without inert atmosphere and without degassing the solvents. [d] 0.5 equiv. of CsOPiv was added. [e] Tri(2-furyl)phosphine.

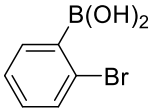
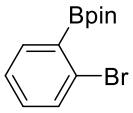
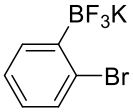
Optimised procedure for the one-pot reaction: Compound **1** (0.2 mmol), arylboronic acid (0.3 mmol) and Cs_2CO_3 (1.2 mmol) were dissolved in DMF (1.8 mL) and water (0.18 mL). The reaction mixture was degassed and backfilled with argon (3×), or degassed by bubbling Ar through the mixture for 5 minutes. Then $Pd_2(dba)_3$ (0.02 mmol) and P(o-tol)$_3$ (0.04 mmol) were added, the mixture was degassed again and stirred for an indicated time at 70 or 80 °C, and then at 110 or 130 °C. Upon completion, it was cooled down, diluted with toluene and concentrated under reduced pressure. The crude mixture was subjected to column chromatography on silica gel providing desired naphthalene product **3**.

6. Reactions with boronic acid derivatives

*Table S3. Cyclisation/Suzuki cross-coupling reaction of **1a** with boronic acid derivatives*

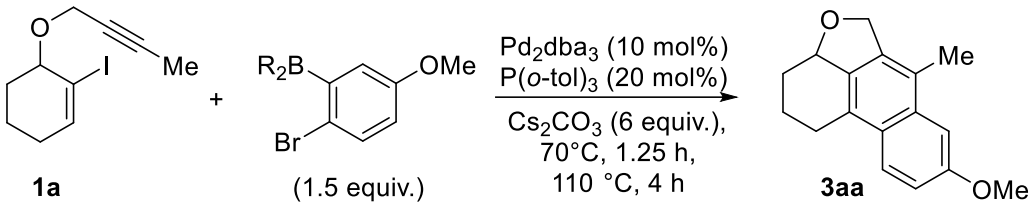


1a **2ad**

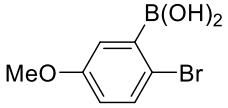
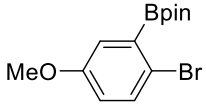
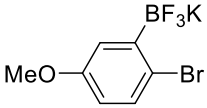
Entry	Boronic acid derivative	Time [h]	Yield of **2ad** [%]
1		9	77[a]
2		4.5	62[b]
3		24	traces

[a] Isolated yield. [b] ^{1}H NMR yield; 3,4,5-trichloropyridine was used as internal standard.

*Table S4. One-pot cyclisation/Suzuki/Heck reaction of **1a** with boronic acid derivatives*

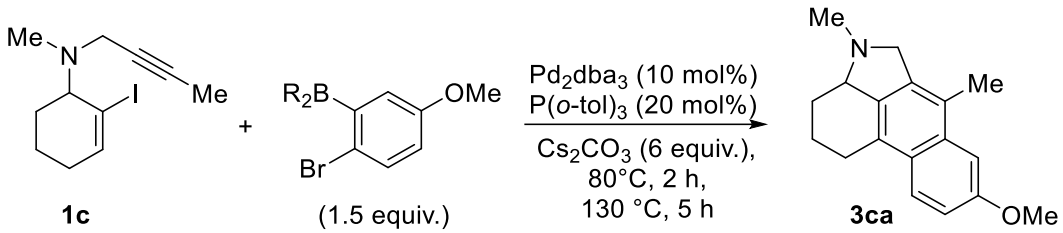


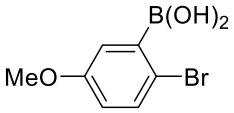
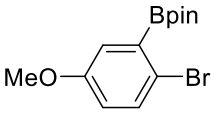
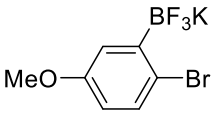
1a (1.5 equiv.) **3aa**

Entry	Boronic acid derivative	Yield of **3aa** [%]
1		61[a]
2		60[b]
3		traces

[a] Isolated yield. [b] ^{1}H NMR yield; 3,4,5-trichloropyridine was used as internal standard.

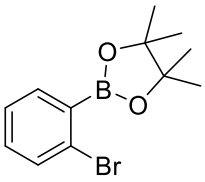
*Table S5. One-pot cyclisation/Suzuki/Heck reaction of **1c** with boronic acid derivatives*



Entry	Boronic acid derivative	Yield of **3ca** [%]
1		76[a]
2		63[b]
3		traces

[a] Isolated yield. [b] ^{1}H NMR yield; 3,4,5-trichloropyridine was used as internal standard.

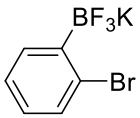
2-(2-Bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



The pinacol ester was synthesised from 2-bromophenylboronic acid using a literature procedure.[12] The recorded spectral data were in agreement with previously reported values.[13]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.60 (m, 1H), 7.56 – 7.51 (m, 1H), 7.30 – 7.21 (m, 2H), 1.38 (s, 12H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.5, 132.7, 132.0, 128.1, 126.4, 84.4, 24.9, signal of a boron-bonded carbon was not found; **^{11}B NMR** (128 MHz, $CDCl_3$) δ 30.86.

Potassium (2-bromophenyl)trifluoroborate

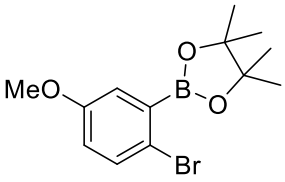


The trifluoroborate salt was synthesised from 2-bromophenylboronic acid using a literature procedure.[14] The recorded spectral data were in agreement with previously reported values.[15]

^{1}H NMR (400 MHz, CD_3OD) δ 7.59 – 7.51 (m, 1H), 7.41 – 7.35 (m, 1H), 7.17 – 7.10 (m, 1H), 7.04 – 6.96 (m, 1H); **^{13}C NMR** (101 MHz, CD_3OD) δ 135.2 (q, *J* = 3.2 Hz), 132.9,

129.0, 128.8, 126.6, signal of a boron-bonded carbon was not found; **^{11}B NMR** (128 MHz, CD_3OD) δ 3.03 (q, *J* = 52.5 Hz); **^{19}F NMR** (376 MHz, CD_3OD) δ -142.68 – -143.43 (m).

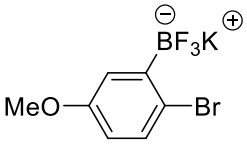
2-(2-Bromo-5-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



The pinacol ester was synthesised from 2-bromophenylboronic acid using a literature procedure.[12] The recorded spectral data were in agreement with previously reported values.[16]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.7 Hz, 1H), 7.13 (d, *J* = 3.2 Hz, 1H), 6.80 (dd, *J* = 8.8, 3.2 Hz, 1H), 3.79 (s, 3H), 1.37 (s, 12H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2, 133.7, 121.2, 118.5, 118.2, 84.5, 55.6, 24.9, signal of a boron-bonded carbon was not found; **^{11}B NMR** (128 MHz, $CDCl_3$) δ 30.72; **MS** (APCI) *m/z* (%) 314.1 (96, M^+), 313.1 (24), 312.1 (100, M^+), 311.1 (15), 233.1 (36); **HRMS** (ESI) *m/z* calcd for $C_{13}H_{18}O_3BBr$ 312.0527, found 312.0528.

Potassium (2-bromo-5-methoxyphenyl)trifluoroborate



The trifluoroborate salt was synthesised from 2-bromophenylboronic acid using a modified literature procedure,[17] using dry THF instead of Et_2O.

^{1}H NMR (400 MHz, CD_3OD) δ 7.26 (d, *J* = 8.6 Hz, 1H), 7.12 (d, *J* = 3.3 Hz, 1H), 6.59 (dd, *J* = 8.6, 3.3 Hz, 1H), 3.74 (s, 3H); **^{13}C NMR** (101 MHz, CD_3OD) δ 159.4, 133.6, 120.4 (q, *J* = 3.2 Hz), 119.3, 114.7, 55.6, signal of a boron-bonded carbon was not found; **^{11}B NMR** (128 MHz, CD_3OD) δ 3.03 (q, *J* = 52.8, 52.1 Hz); **MS** (ESI) *m/z* (%) 255.0 (99, M^-), 254.0 (29), 253.0 (100, M^-), 252.0 (23), 80.9 (11); **HRMS** (ESI) *m/z* calcd for $C_7H_6OBBrF_3$ 252.9653, found 252.9656.

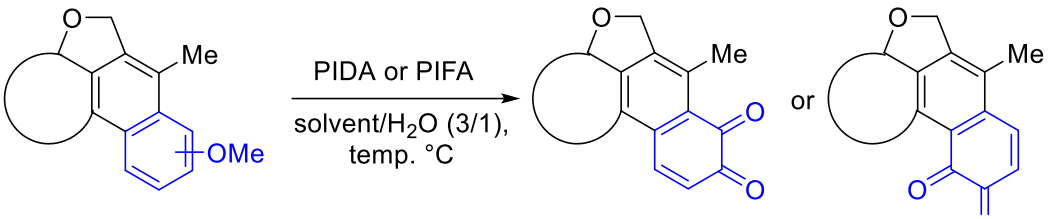
7. Synthesis of 1,2-naphthoquinones

*Table S6. Optimisation of the oxidation reaction of **3aa** (additional experiments, see Table 3 for the best results)*

Entry	Starting material	Oxidant (equiv.)	Additive (equiv.)	Solvent	Temp. [°C]	Time [min]	Yield[a] of product **4a** [%]
1	**3aa**	CAN[b] (3)	KH_2PO_4 (0.62)	MeCN/H_2O (4:1)	0 to rt	240	10
2	**3aa**	CAN (3)		Acetone	0	240	8
3	**3aa**	IBX[c] (2)	-	TFE/H_2O (1:1)	r.t.	1440	0[d]
4	**3aa**	PIFA[e] (2)	-	TFE/H_2O (1:1)	0	1080	12
5	**3aa**	PIFA (2)	$NaHCO_3$ (2)	TFE/H_2O (1:1)	0	120	22
6	**3aa**	PIFA (4)	$NaHCO_3$ (4)	TFE/H_2O (1:1)	0	120	15
7	**3aa**	PIDA[f] (2)	$NaHCO_3$ (2)	TFE/H_2O (1:1)	0	60	0[g]
8	**3aa**	PIFA (2)	$NaHCO_3$ (2)	HFIP/H_2O (1:1)	0	15	15
9	**3aa**	CAN (2)	$NaHCO_3$ (2)	TFE/H_2O (1:1)	0	40	4
10	**3aa**	HTIB[h] (2)	$NaHCO_3$ (2)	TFE/H_2O (1:1)	0	180	0[i]
11	**3aa**	AgO (10)	HNO_3 (excess)	Dioxane	rt	150	23[j]
12	**3aa**	PIFA (2)	$NaHCO_3$ (2)	$MeNO_2$/H_2O (2:1)	0 to rt	270	12
13	**3aa**	PIFA (2)	$NaHCO_3$ (2)	MeOH/H_2O (1:1)	0 to rt	150	0[g]
14	**3aa**	PIFA (2)	TFA (1)	TFE/H_2O (1:1)	0	20	17
15	**3aa**	PIFA (2)	$BF_3{\cdot}Et_2O$ (2)	TFE/H_2O (5:1)	0	30	18
16	**3aa**	$PhI(OPiv)_2$ (2)	$BF_3{\cdot}Et_2O$ (3)	TFE/H_2O (3:1)	0	5	36
17	**3aa**	PIDA (2)	$BF_3{\cdot}Et_2O$ (3)	TFE/H_2O (3:1)	0	5	34
18	**3aa**	HTIB (2)	$BF_3{\cdot}Et_2O$ (3)	TFE/H_2O (3/1	0	5	21
19	**3aa**	IBX (2)	$BF_3{\cdot}Et_2O$ (3)	TFE/H_2O (3:1)	0	90	0[g]
20	**3aa**	$PhI(OPiv)_2$ (2)	$BF_3{\cdot}Et_2O$ (6)	TFE/H_2O (3:1)	0	5	38

21	**3aa**	$PhI(OPiv)_2$ (2)	$BF_3{\cdot}Et_2O$ (6)	TFE/H_2O (3:1)	-35 to -15	15	33
22	**3aa**	$PhI(OPiv)_2$ (2)	$B(C_6F_5)_3$ (6)	TFE/H_2O (3:1)	-15	15	9
23	**3aa**	$PhI(OPiv)_2$ (2)	PTSA[k] (6)	TFE/H_2O (3:1)	-15	5	19
24	**3aa**	$PhI(OPiv)_2$ (2)	TFA[l] (6) $BF_3{\cdot}Et_2O$ (6)	TFE/H_2O (3:1)	-15 to 10	5	16
25	**3aa**	$PhI(OPiv)_2$ (2)	H_2SO_4 (10)	TFE/H_2O (3:1)	-15	5	82
26	**3aa**	$PhI(OPiv)_2$ (2)	H_2SO_4 (6)	MeCN/H_2O (4:1)	-15 to 0	30	82
27	**3aa**	$PhI(OPiv)_2$ (1.2)	H_2SO_4 (6)	TFE/H_2O (3:1)	-15	5	44
28	**3aa**	$PhI(OPiv)_2$ (2)	H_2SO_4 (6)	Acetone/H_2O (6:1)	-15 to 0	30	18
29	**3aa**	PIDA (2)	H_2SO_4 (6)	HFIP/H_2O (3:1)	-15	30	41

[a] ^1H NMR yield; 3,4,5-trimethoxybenzaldehyde was used as internal standard. [b] CAN = ammonium cerium(IV) nitrate. [c] IBX = 2-iodoxybenzoic acid. [d] 92% of starting material remained unreacted. [e] PIFA = [bis(trifluoroacetoxy)iodo]benzene. [f] PIDA = (diacetoxyiodo)benzene. [g] Starting material remained unreacted. [h] HTIB = [hydroxy(tosyloxy)iodo]benzene. [i] Starting material decomposed. [j] Product of nitration was formed. [k] PTSA = *p*-toluenesulfonic acid. [l] TFA = Trifluoroacetic acid.

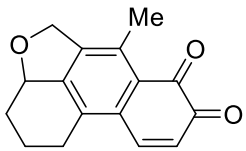


3 4 5

General procedure for the oxidation: Naphthalene **3** (0.3 mmol), bearing methoxy group was suspended in of 2,2,2-trifluoroethanol (TFE) or MeCN (1.8 mL) under argon atmosphere and cooled down to an indicated temperature. Sulphuric acid (1.8 mmol) preliminary mixed with water (0.6 mL) followed by of (diacetoxyiodo)benzene (PIDA) or (bis(trifluoroacetoxy)iodo)benzene (PIFA) (0.6 mmol) were added to a mixture and kept with a vigorous stirring at indicated time and temperature. Upon completion, the reaction was quenched at 0 °C by the slow addition of saturated aqueous $NaHCO_3$ and the mixture extracted between water (15 mL) and EtOAc (2 × 15 mL). The combined organic

layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography yielding desired 1,2-naphthoquinone **4** or **5**. Reaction and purification details are specified for the each substrate below.

6-Methyl-2,3,3a,5-tetrahydro-1*H*-phenanthro[1,10-*bc*]furan-7,8-dione (4a)

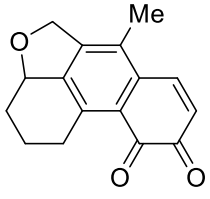


Reaction time: 5 min; Reaction temperature: -15°C;
Column chromatography: (70/30) hexanes/EtOAc;
Yield: 84% (0.065 g); purple amorphous solid

Reagent	n [mmol]	m [mg]	V [mL]
TFE			1.8
Water			0.6
3aa	0.3	76	
PIDA	0.6	193	
H_2SO_4	1.8	176	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 10.3 Hz, 1H), 6.40 (d, *J* = 10.3 Hz, 1H), 5.08–4.97 (m, 2H), 4.92–4.85 (m, 1H), 3.00 (dd, *J* = 17.6, 7.0 Hz, 1H), 2.68 (ddd, *J* = 17.8, 11.0, 7.0 Hz, 1H), 2.54 (s, 3H), 2.44–2.37 (m, 1H), 2.29–2.19 (m, 1H), 1.89–1.75 (m, 1H), 1.48 (dtd, *J* = 14.2, 11.4, 3.1 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.7, 181.5, 147.6, 143.3, 141.7, 137.0, 133.3, 130.9, 130.5, 126.5, 80.7 71.8, 28.6, 23.5, 20.6, 19.2; **IR** (KBr) ν_{max} 2941, 2872, 2815, 1718, 1682, 1658, 1452, 1296, 1045 cm^{-1}; **MS** (ESI) *m/z* (%) 278.1 (18), 277.1 (100, $[M+Na]^+$), 255.1 (28, $[M+H]^+$), 227.1 (3); **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}O_3Na$ 277.0835, found 277.0833.

6-Methyl-2,3,3a,5-tetrahydro-1*H*-phenanthro[1,10-*bc*]furan-9,10-dione (5a)

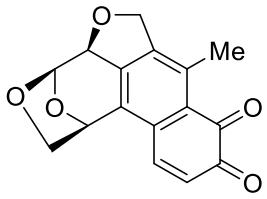


Reaction time: 40 min; Reaction temperature: -35°C → r.t (slowly warmed up);
Column chromatography: (97/3) dichloromethane/diethyl ether;
Yield: 71% (0.055 g); bright orange amorphous solid

Reagent	n [mmol]	m [mg]	V [mL]
MeCN			1.8
Water			0.6
3ab	0.3	76	
PIDA	0.6	193	
H_2SO_4	1.8	176	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 10.5 Hz, 1H), 6.39 (d, *J* = 10.4 Hz, 1H), 5.06–4.94 (m, 2H), 4.92–4.83 (m, 1H), 3.37 (dd, *J* = 20.3, 6.8 Hz, 1H), 2.92 (ddd, *J* = 19.5, 11.1, 7.1 Hz, 1H), 2.41–2.28 (m, 1H), 2.35 (s, 3H), 2.24–2.11 (m, 1H), 1.80–1.66 (m, 1H), 1.44 (dtd, *J* = 14.1, 11.3, 3.1 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.2, 181.0, 146.6, 144.4, 142.2, 138.9, 134.2, 129.3, 129.0, 126.3, 80.8, 71.8, 28.7, 27.3, 20.7, 15.5; **IR** (KBr) ν_{max} 3554, 3479, 3419, 2956, 2935, 2845, 1682, 1658, 1622, 1577, 1287 cm^{-1}; **MS** (ESI) *m/z* (%) 278.1 (17), 277.1 (100, $[M+Na]^+$), 255.1 (16, $[M+H]^+$); **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}O_3Na$ 277.0835, found 277.0836.

(1*S*,4*R*,4a*S*)-7-Methyl-1,2,4a,6-tetrahydro-4*H*-1,4-epoxybenzo[*f*]oxepino[3,4,5-*cd*]-isobenzofuran-8,9-dione (4b)



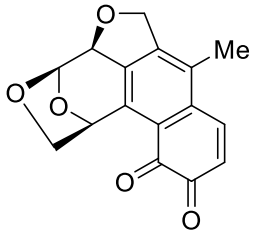
Reaction time: 20 min; Reaction temperature: -15°C → r.t. (placed at r.t. after 5 minutes);
Column chromatography: (96/4) dichloromethane/diethyl ether;
Yield: 52% (0.033 g); bright orange amorphous solid

Reagent	n [mmol]	m [mg]	V [mL]
TFE			1.35
Water			0.45
3ba	0.22	62	
PIFA	0.44	190	
H_2SO_4	1.32	130	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 10.2 Hz, 1H), 6.47 (d, *J* = 10.2 Hz, 1H), 5.97–5.95 (m, 1H), 5.73 (d, *J* = 3.8 Hz, 1H), 5.19–5.15 (m, 1H), 5.10 (dd, *J* = 13.0, 3.0 Hz,

1H), 5.03 (dd, *J* = 13.0, 1.8 Hz, 1H), 4.09 (dd, *J* = 6.9, 3.9 Hz, 1H), 3.72 (d, *J* = 7.1 Hz, 1H), 2.57 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.0, 181.0, 145.1, 144.1, 140.0, 139.7, 131.9, 130.9, 129.4, 127.8, 101.2, 82.0, 76.5, 72.8, 71.9, 19.6; **IR** (KBr) ν_{max} 2920, 2860, 1670, 1293, 1141, 1060, 964 cm^{-1}; **MS** (ESI) *m/z* (%) 308.0 (20), 307.0 (100, $[M+Na]^+$), 285.0 (22, $[M+H]^+$), 239.0 (5); **HRMS** (ESI) *m/z* calcd for $C_{16}H_{12}O_5Na$ 307.0577, found 307.0576; **Specific rotation** $[\alpha]_D$ = –241.5° (c 1, $CHCl_3$).

(1*S*,4*R*,4a*S*)-7-Methyl-1,2,4a,6-tetrahydro-4*H*-1,4-epoxybenzo[*f*]oxepino[3,4,5-*cd*]-isobenzofuran-10,11-dione (5b)



Reaction time: 40 min; Reaction temperature: -15°C → 5°C (slowly warmed up);

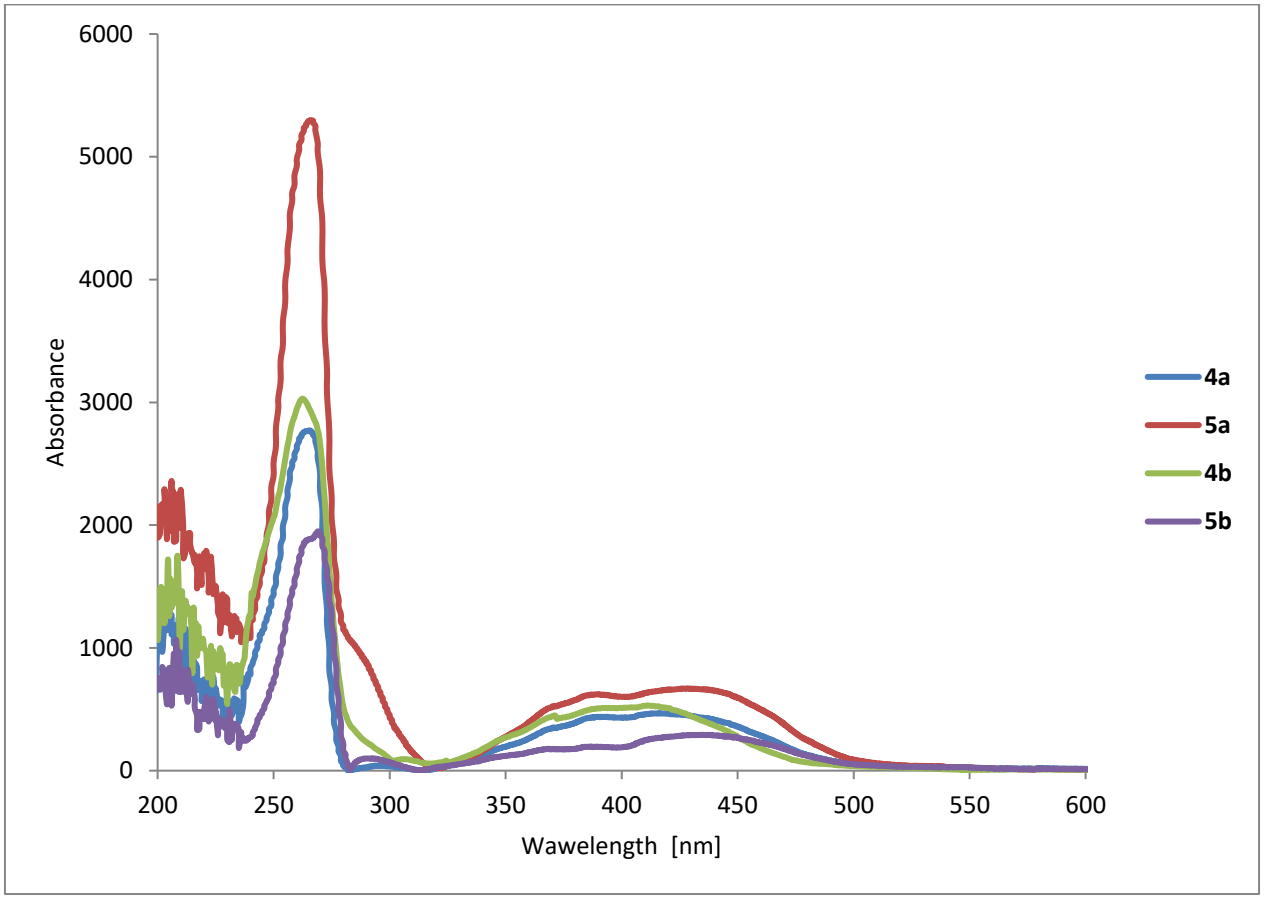
Column chromatography: (40/60) hexanes/EtOAc;

Yield – 24% (0.011 g); bright orange amorphous solid

Reagent	n [mmol]	m [mg]	V [mL]
TFE			1.0
Water			0.2
3bb	0.161	46	
PIFA	0.323	139	
H_2SO_4	0.966	95	

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 10.5 Hz, 1H), 6.43 (d, *J* = 10.5 Hz, 1H), 6.33 (d, *J* = 4.1 Hz, 1H), 5.93–5.91 (m, 1H), 5.19–5.14 (m, 1H), 5.07 (dd, *J* = 13.5, 3.1 Hz, 1H), 4.99 (dd, *J* = 13.4, 1.6 Hz, 1H), 4.16 (dd, *J* = 7.3, 4.1 Hz, 1H), 3.67 (d, *J* = 7.4 Hz, 1H), 2.37 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.5, 180.6, 148.7, 141.7, 140.8, 138.1, 134.3, 131.7, 126.7, 126.2, 100.5, 81.8, 76.7, 73.9, 72.8, 15.7; **IR** (KBr) ν_{max} 2950, 2920, 2890, 2842, 1667, 1302, 1272, 1165, 1132, 1087, 1051, 1006, 964 cm^{-1}; **MS** (ESI) *m/z* (%) 308.1 (18), 307.1 (100, $[M+Na]^+$), 285.1 (19, $[M+H]^+$); **HRMS** (APCI) *m/z* calcd for $C_{16}H_{13}O_5$ 285.0758, found 285.0755; **Specific rotation** $[\alpha]_D$ = +916.7° (c 0.4, $CHCl_3$).

8. UV/Vis spectroscopy data



UV/Vis spectroscopy data for 1,2-naphthoquinones **4a**, **5a**, **4b**, **5b**

Concentration: 1×10^{-5} M in $CHCl_3$

4a: λ_{max} = 265.5 nm

5a: λ_{max} = 266.5 nm

4b: λ_{max} = 262.5 nm

5b: λ_{max} = 269.5 nm

9. X-ray structure data for compound **5a**

Crystallographic data for naphthoquinone **5a** (Figure 1) were collected on Bruker D8 VENTURE Kappa Duo PHOTONIII by IμS micro-focus sealed tube CuKα radiation (λ = 1.54178 Å). The measurement was performed at low temperature at 150K. The structure was solved by direct methods (SHELXT 2014/5)[18] and refined by full matrix least squares based on F^2 (SHELXL2018/1).[19] The hydrogen atoms on carbon were fixed into idealised positions (riding model) and assigned temperature factors either $H_{iso}(H) = 1.2\ U_{eq}$ (pivot atom) or $H_{iso}(H) = 1.5\ U_{eq}$ (pivot atom) for methyl moiety. The position of molecule **5a** on the mirror of space group *Pnma* is causing a disorder of several atoms.

Crystal data for **5a**: $C_{17}H_{14}Cl_3O_3$, M_r = 372.63; Orthorhombic, *Pnma* (No.62), a = 21.5473 (6) Å, b = 6.9275 (2) Å, c = 10.8993 (3) Å, V = 1626.93 (8) Å^3 , Z = 4, D_x = 1.521 Mg m^{-3}, orange-red bar of dimensions 0.39 × 0.17 × 0.15 mm, multi-scan absorption correction (μ = 5.21 mm^{-1}), T_{min} =0.32, T_{max} = 0.51; a 26286 total of measured reflections (θ_{max}= 72.3˚), from which 1738 were unique (R_{int} = 0.029) and 1696 observed according to the $I > 2\sigma(I)$ criterion. The refinement converged (Δ/σ_{max}= 0.001) to R = 0.049 for observed reflections and w$R(F^2)$ = 0.135, *GOF* = 1.17 for 149 parameters and all 1738 reflections. The final difference Fourier map displayed no peaks of chemical significance ($\Delta\rho_{max}$ = 0.37 , $\Delta\rho_{min}$ = -0.31 e.Å^{-3}).

Crystallographic data have been deposited with Cambridge Crystallographic Data Centre: CCDC number: 1985309. Copies of the data can be obtained free of harge via https://www.ccdc.cam.ac.uk/structures/ (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

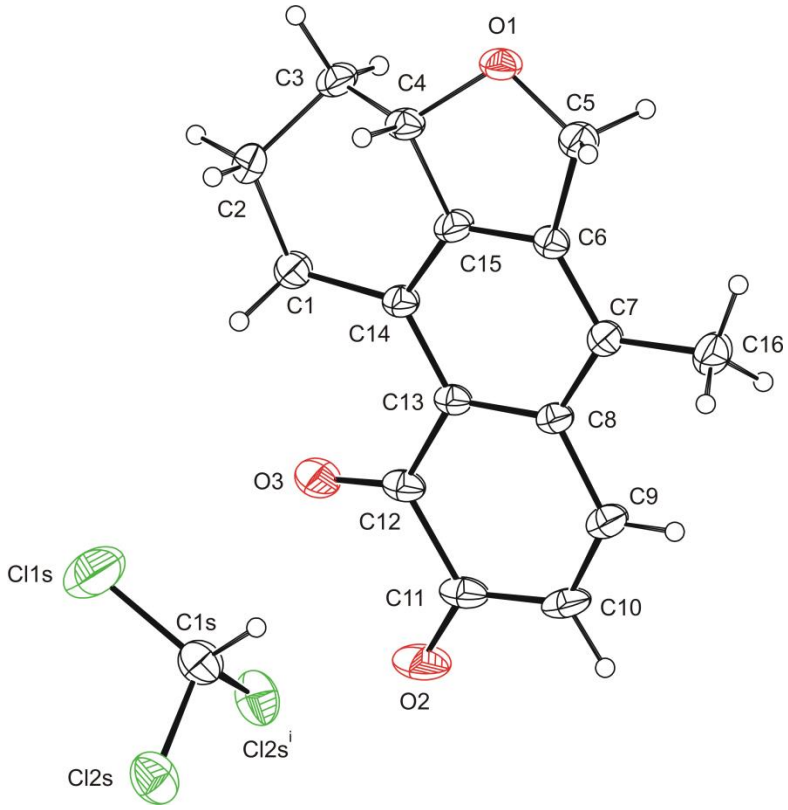


*Figure 1. Platon plot of the molecular structure of **5a** showing the atom-labelling scheme, the displacement ellipsoids are drawn at 30% probability level.*
Symmetry code: (i) x, -y+1/2, z. The disordered atoms are omitted for clarity.

10. Cytotoxicity screening

Cell lines:

CCRF-CEM - human T-lymhpoblastic leukemia (suspension)

HL-60 - human promyelocytic leukemia (suspension)

HeLa - human cervical carcinoma (adherent)

HepG2 - human hepatocellular carcinoma (adherent)

NHDF - human normal dermal fibroblasts (adherent)

Results:

	CEM				HL60				HeLa			
	% of ctrl*	SD	IC_{50}**	SD	% of ctrl	SD	IC_{50}	SD	% of ctrl	SD	IC_{50}	SD
3ba	97	1	n.d.		96	8	n.d.		89	5	n.d.	
4b	4	0	1.80	0.09	14	3	4.65	0.06	24	5	4.32	0.15
5a	4	1	1.54	0.04	2	1	3.79	0.02	11	4	5.33	0.09
4a	3	1	1.66	0.03	4	2	4.38	0.11	39	7	6.28	0.24

	HepG2				NHDF			
	% of ctrl	SD	IC_{50}	SD	% of ctrl	SD	IC_{50}	SD
3ba	96	7	n.d.		91	7	n.d.	
4b	61	9	n.d.		6	2	1.97	0.08
5a	64	4	n.d.		15	3	2.82	0.28
4a	82	4	n.d.		7	2	3.06	0.49

*percentage of viability of compound-treated cells (10 µM) vs. untreated cells

**only compounds with >50% decrease in cell viability in the 10 µM screening test were subjected to IC_{50} determination, values are in µmol/L

Method:

Cytotoxicity of compounds **3ba**, **4a**, **4b** and **5a** was evaluated in four cancer cell lines (CCRF-CEM, HepG2, Hela S3, HL-60) and non-tumour human dermal fibroblasts (NHDF). All cell lines were from ATCC (Manassas, VA, USA). The cells were maintained in RPMI-1640 or DMEM culture medium containing 10% FBS and 1% GlutaMax without antibiotics. Cells were seeded in 384-well white plates (Thermo Fisher Scientific, Waltham, USA) at a concentration between 2,000 – 50,000 cells per well and left to rest overnight. The next day, indicated concentrations of the test compounds were added, the cells were incubated at 37 °C, 5% CO_2 for 72 h after which CellTiter-Glo® 2.0 detection reagent (Promega, Madison, USA) was added. The plate was left on a shaker (350 rpm) for 20 min at room temperature. Luminescence was measured by a multimode plate reader. The signal of the compound-treated cells was related to the value of untreated control which was arbitrarily set to 100% viability. IC_{50} values were calculated from dose-response curves using non-linear regression method using GraphPad Prism software.

11. References

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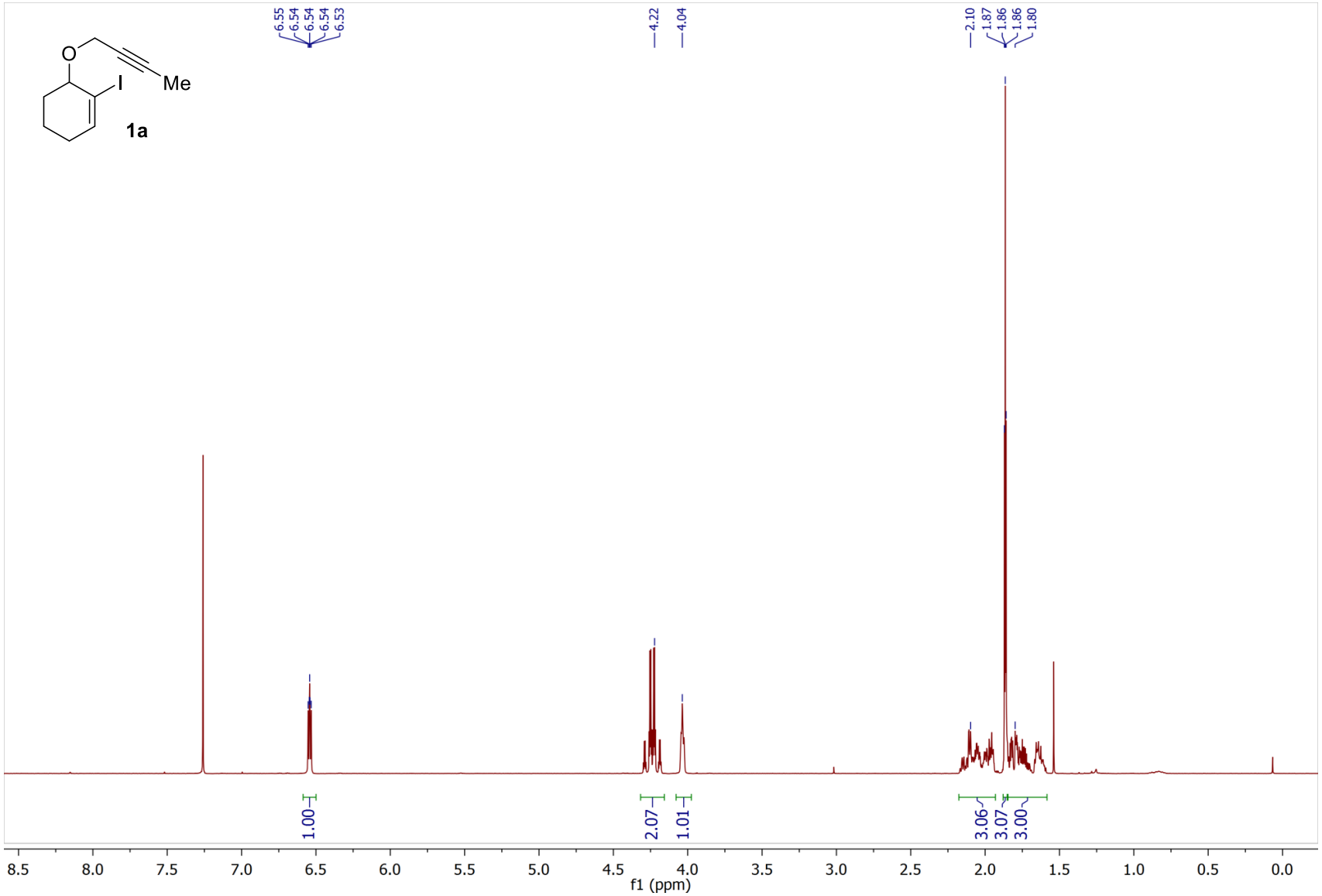
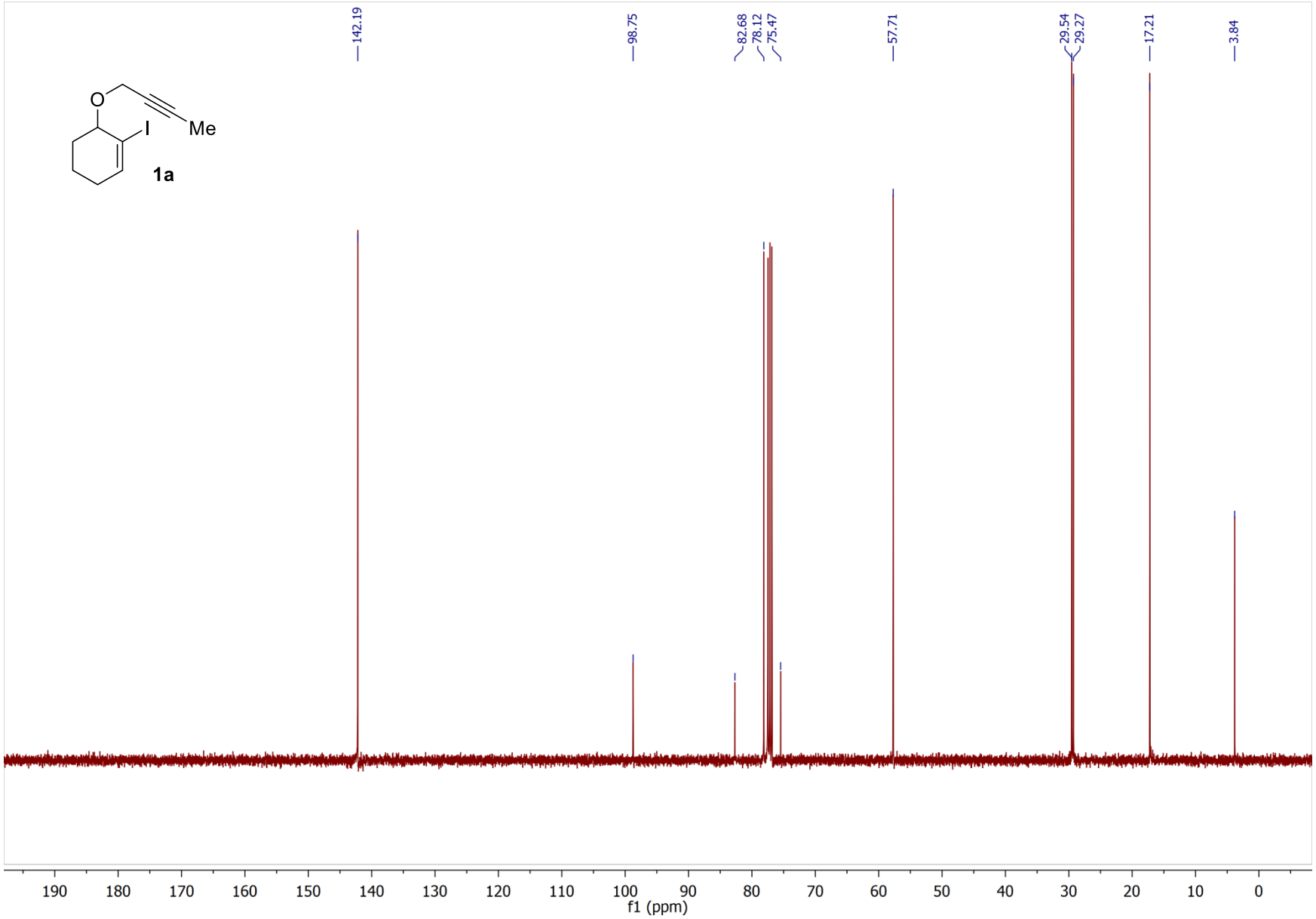
12. Copies of ^{1}H and ^{13}C NMR spectra

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3.84
O
I
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1a
190
180
170
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50
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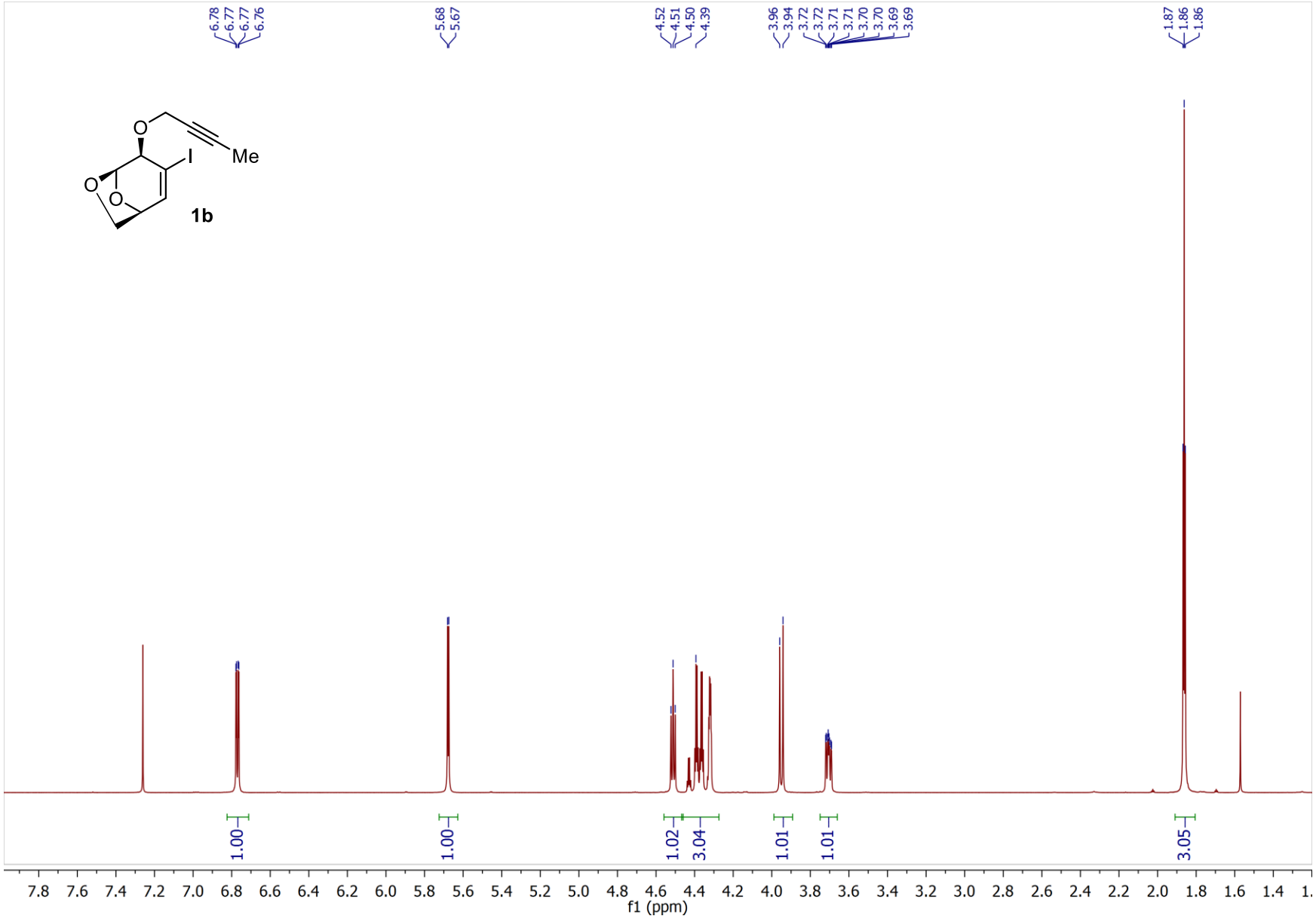
f1 (ppm)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3.72
3.71
3.71
3.70
3.70
3.69
3.69
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1.86
1.86
O
O
O
I
Me
1b
1.00
1.00
1.02
3.04
1.01
1.01
3.05
7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
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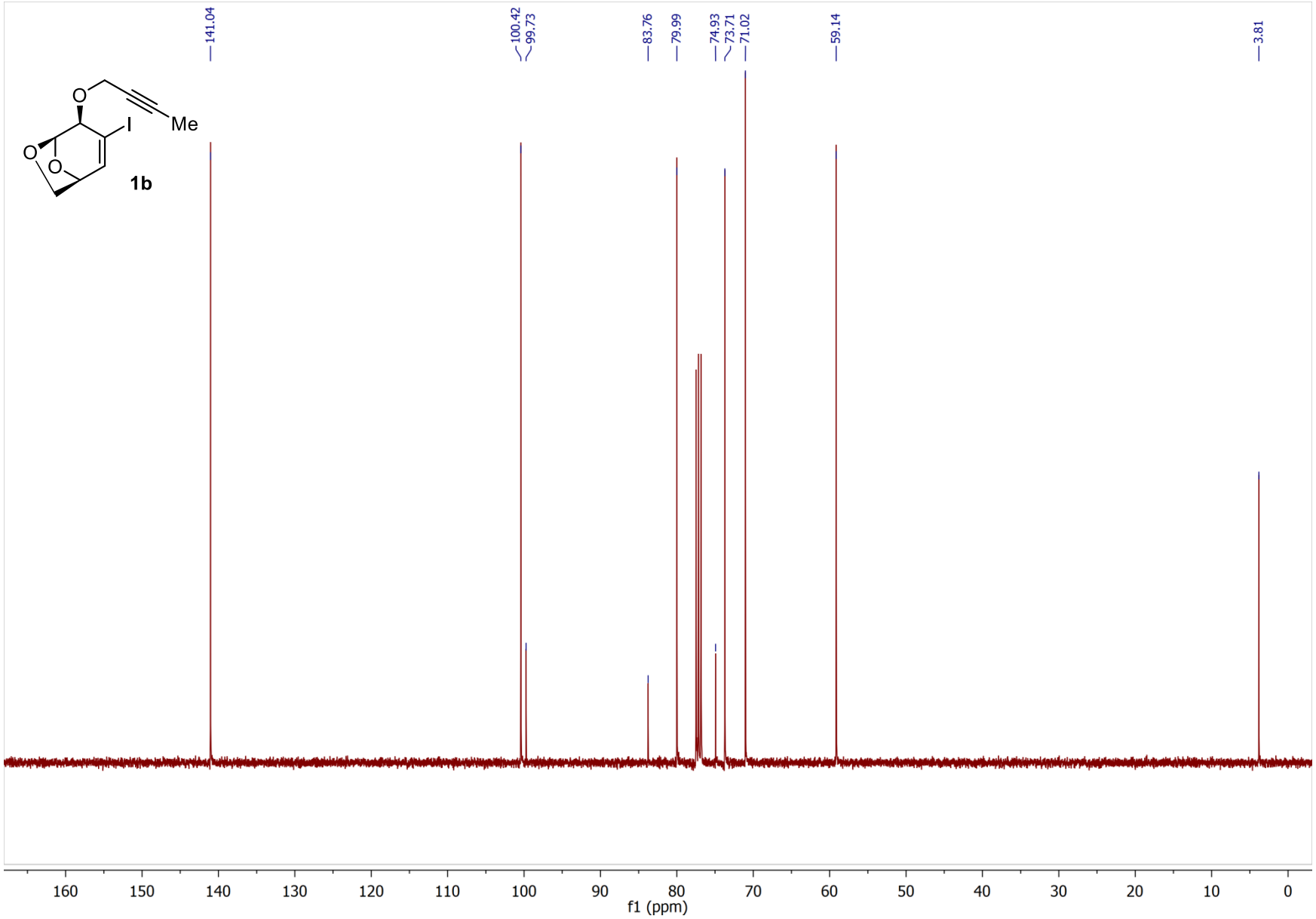
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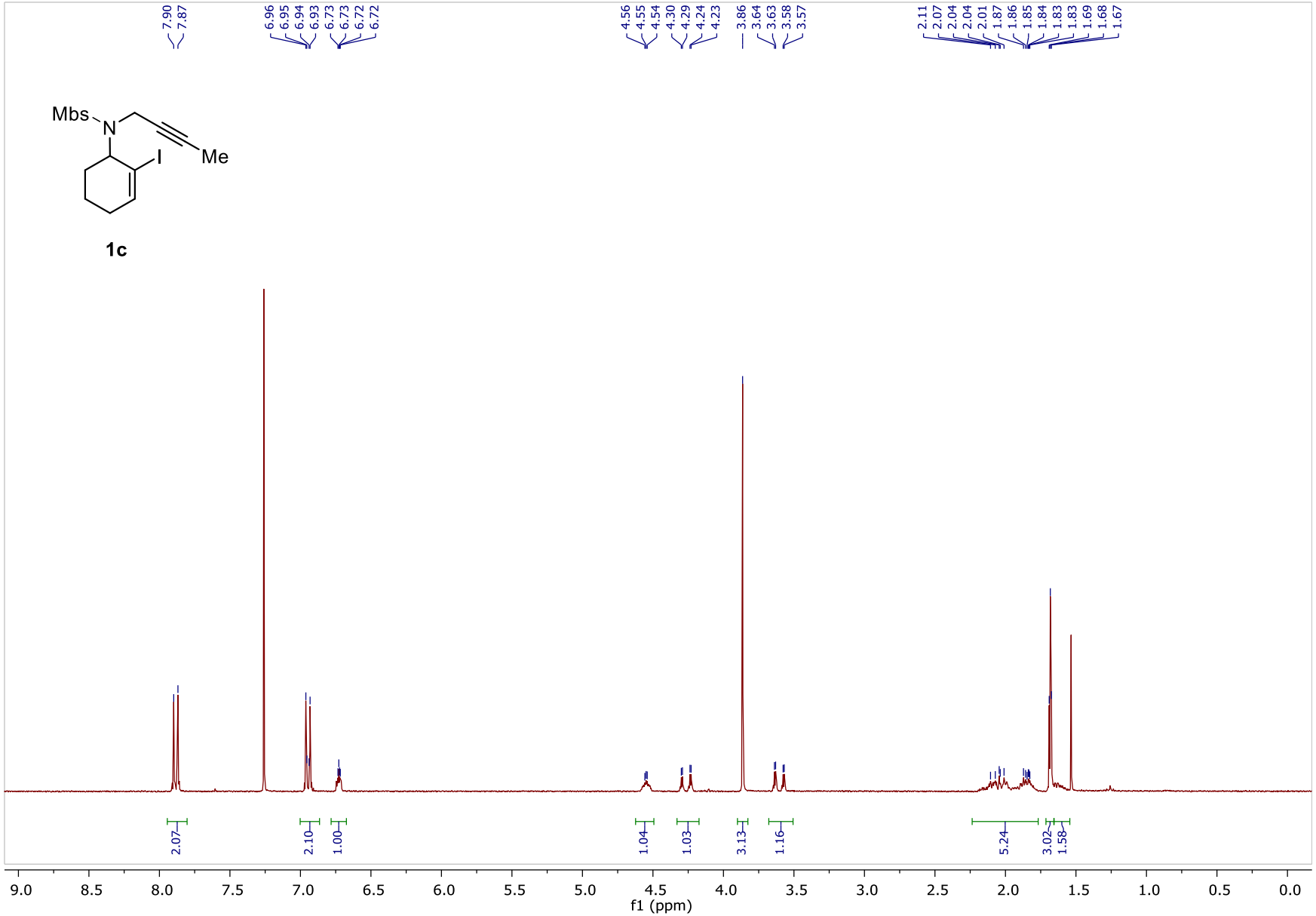
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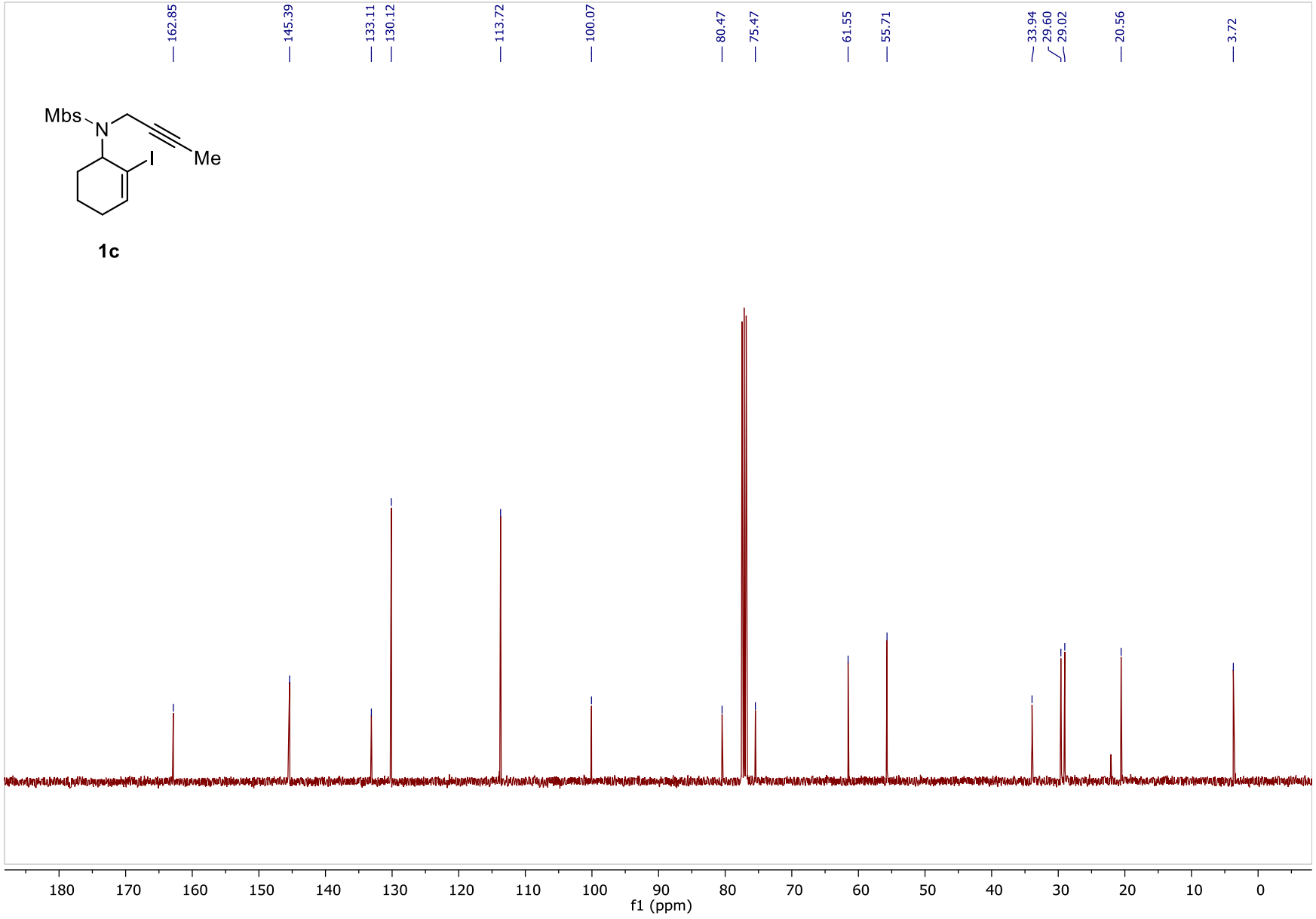
f1 (ppm)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Me
1c
180
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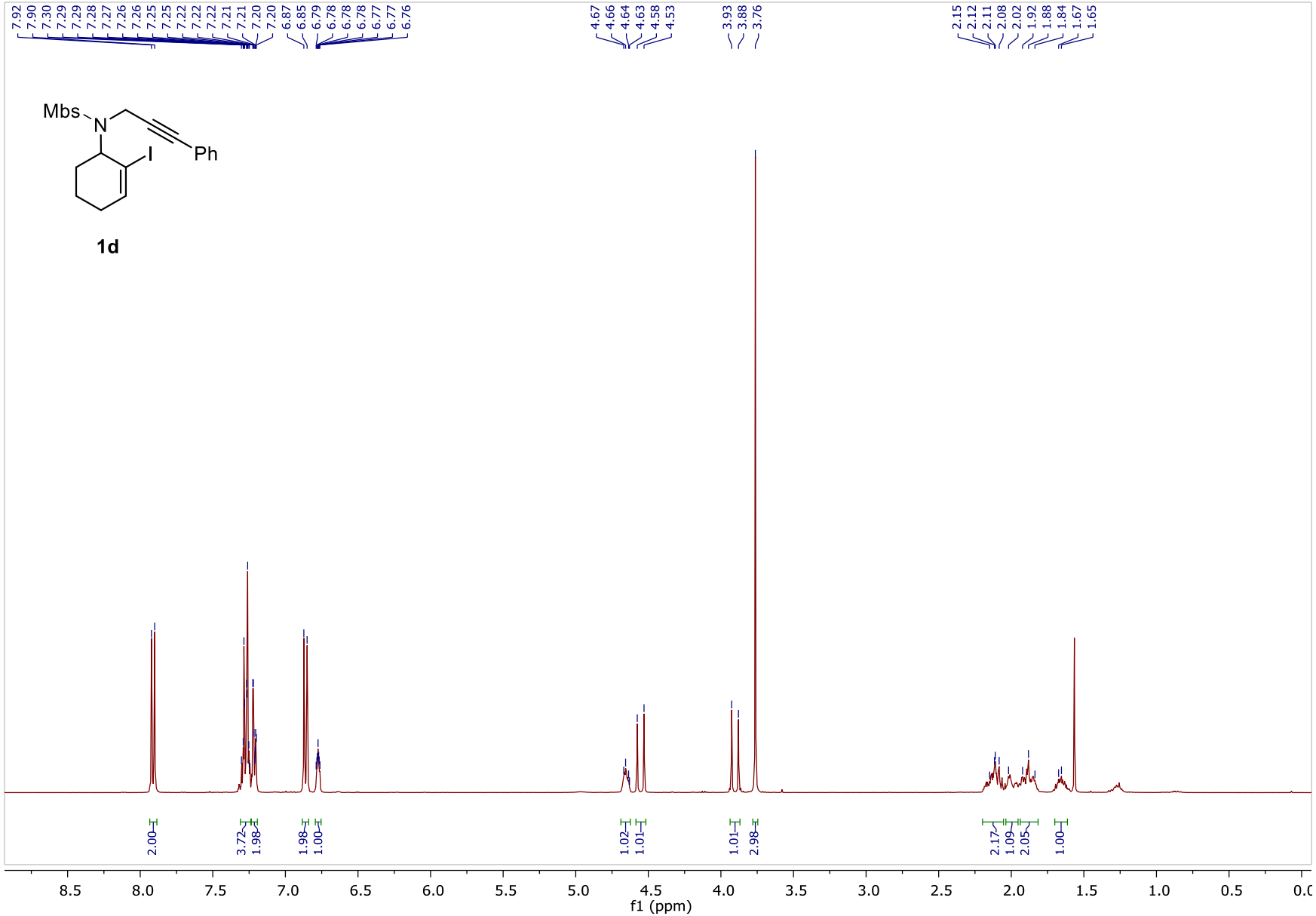
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4.67 4.66 4.64 4.63 4.58 4.53
3.93 3.88 3.76
2.15 2.12 2.11 2.08 2.02 1.92 1.88 1.84 1.67 1.65
Mbs
N
I
Ph
1d
2.00 3.72 1.98 1.98 1.00 1.02 1.01 1.01 2.98 2.17 1.09 2.05 1.00
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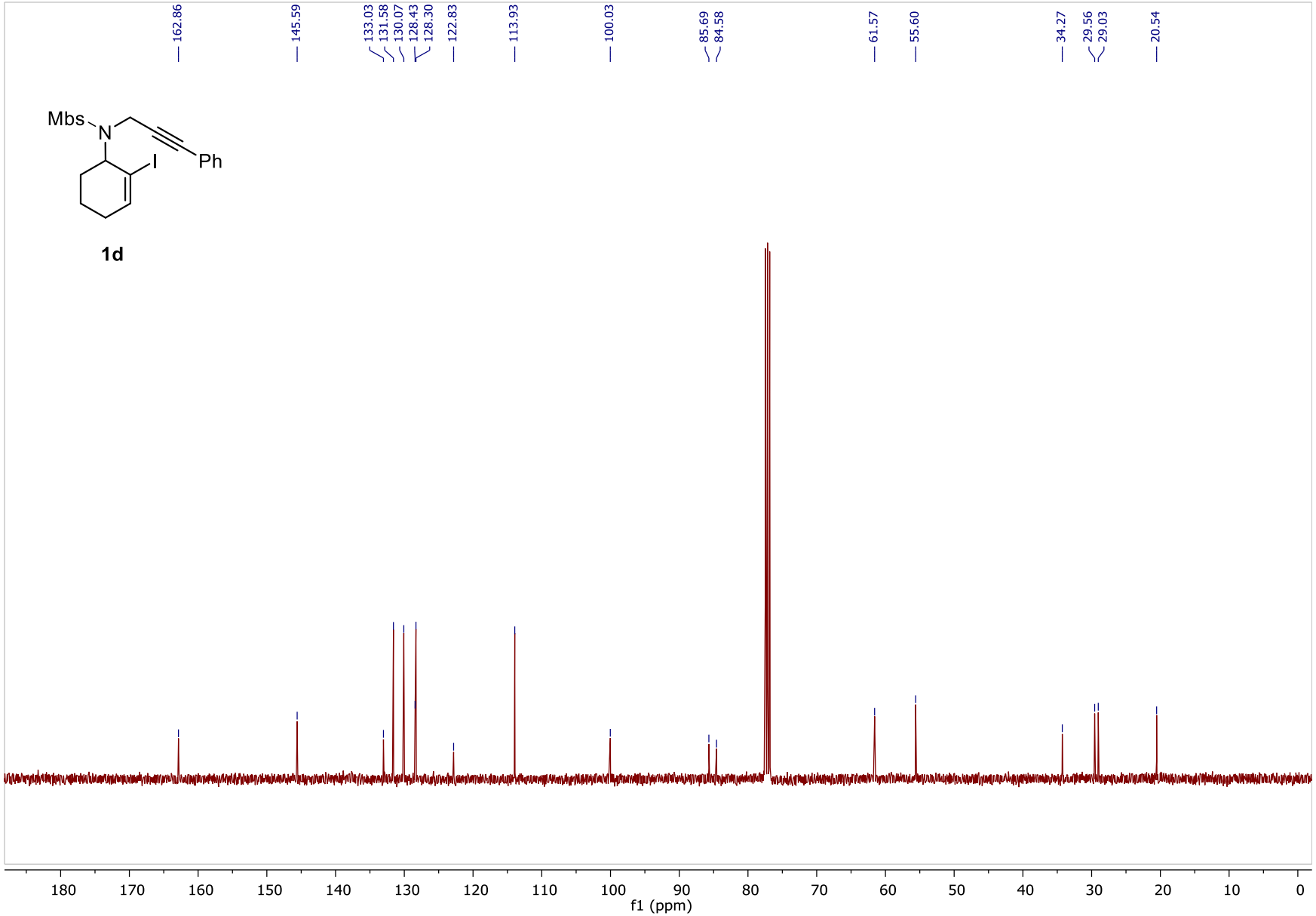
f1 (ppm)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122.83
113.93
100.03
85.69
84.58
61.57
55.60
34.27
29.56
29.03
20.54
Mbs
N
I
Ph
1d
180
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90
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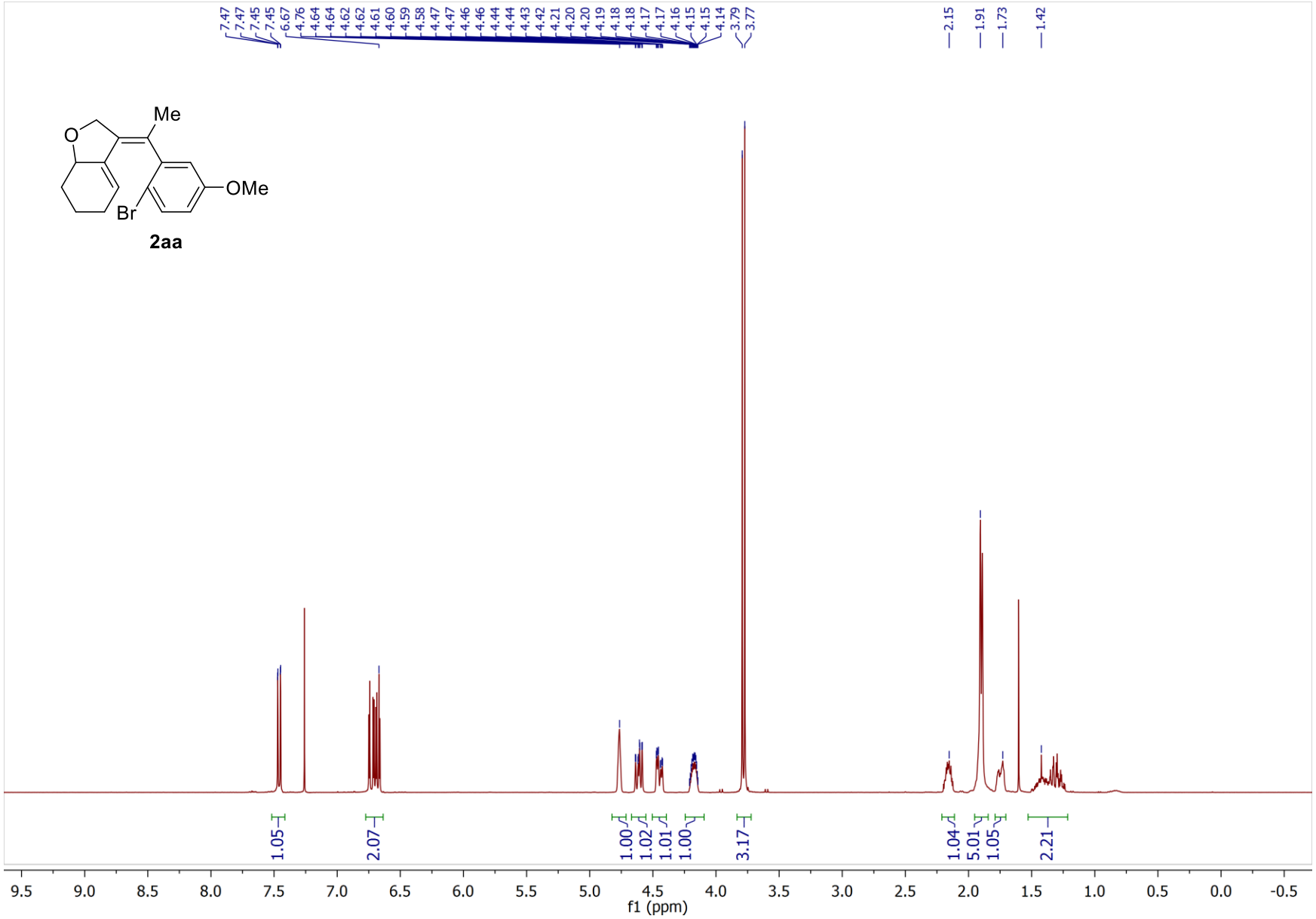
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4.60
4.59
4.58
4.47
4.47
4.46
4.46
4.44
4.44
4.43
4.42
4.21
4.20
4.20
4.19
4.18
4.18
4.17
4.17
4.16
4.15
4.15
4.14
3.79
3.77
2.15
1.91
1.73
1.42
Me
O
OMe
Br
2aa
1.05
2.07
1.00
1.02
1.01
1.00
3.17
1.04
5.01
1.05
2.21
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.0
2.5
2.0
1.5
1.0
0.5
0.0
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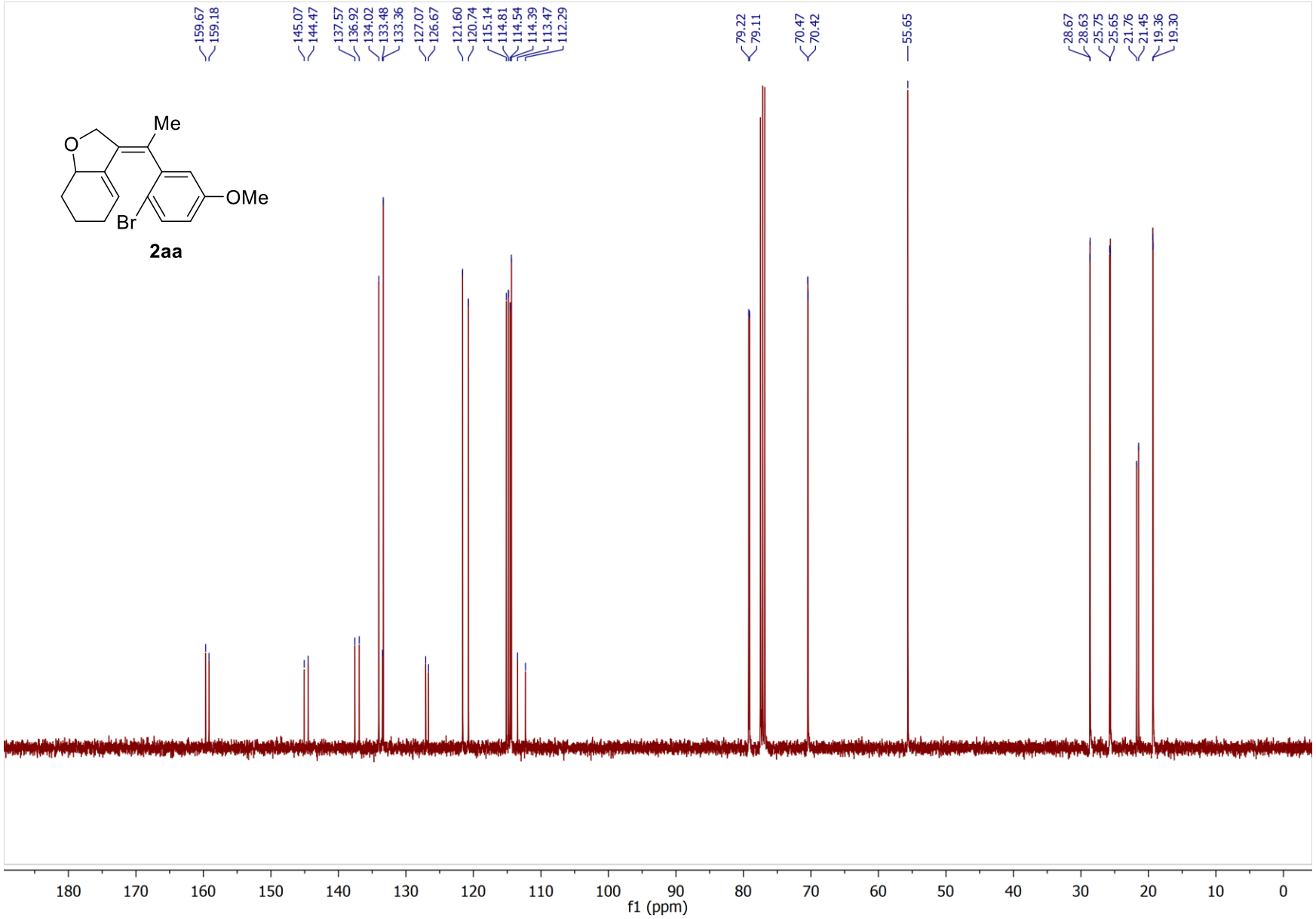
f1 (ppm)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121.60
120.74
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114.81
114.54
114.39
113.47
112.29
79.22
79.11
70.47
70.42
55.65
28.67
28.63
25.75
25.65
21.76
21.45
19.36
19.30
Me
O
OMe
Br
2aa
180
170
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150
140
130
120
110
100
90
80
70
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50
40
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10
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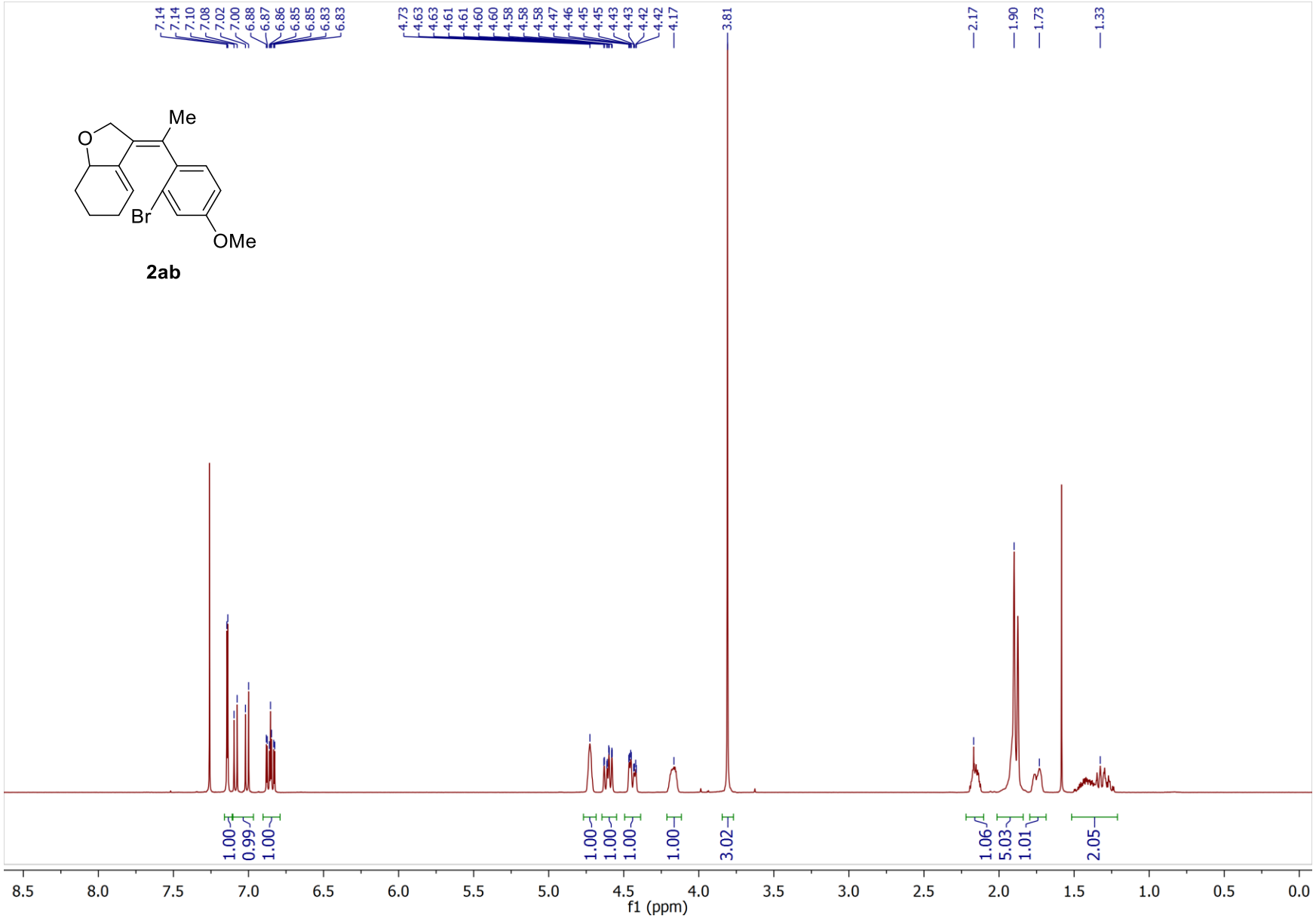
f1 (ppm)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6.87
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6.83
6.83
4.73
4.63
4.63
4.61
4.61
4.60
4.60
4.58
4.58
4.58
4.47
4.46
4.45
4.45
4.43
4.43
4.42
4.42
4.17
3.81
2.17
1.90
1.73
1.33
Me
O
Br
OMe
2ab
1.00
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1.00
1.00
1.00
1.00
1.00
3.02
1.06
5.03
1.01
2.05
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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2.5
2.0
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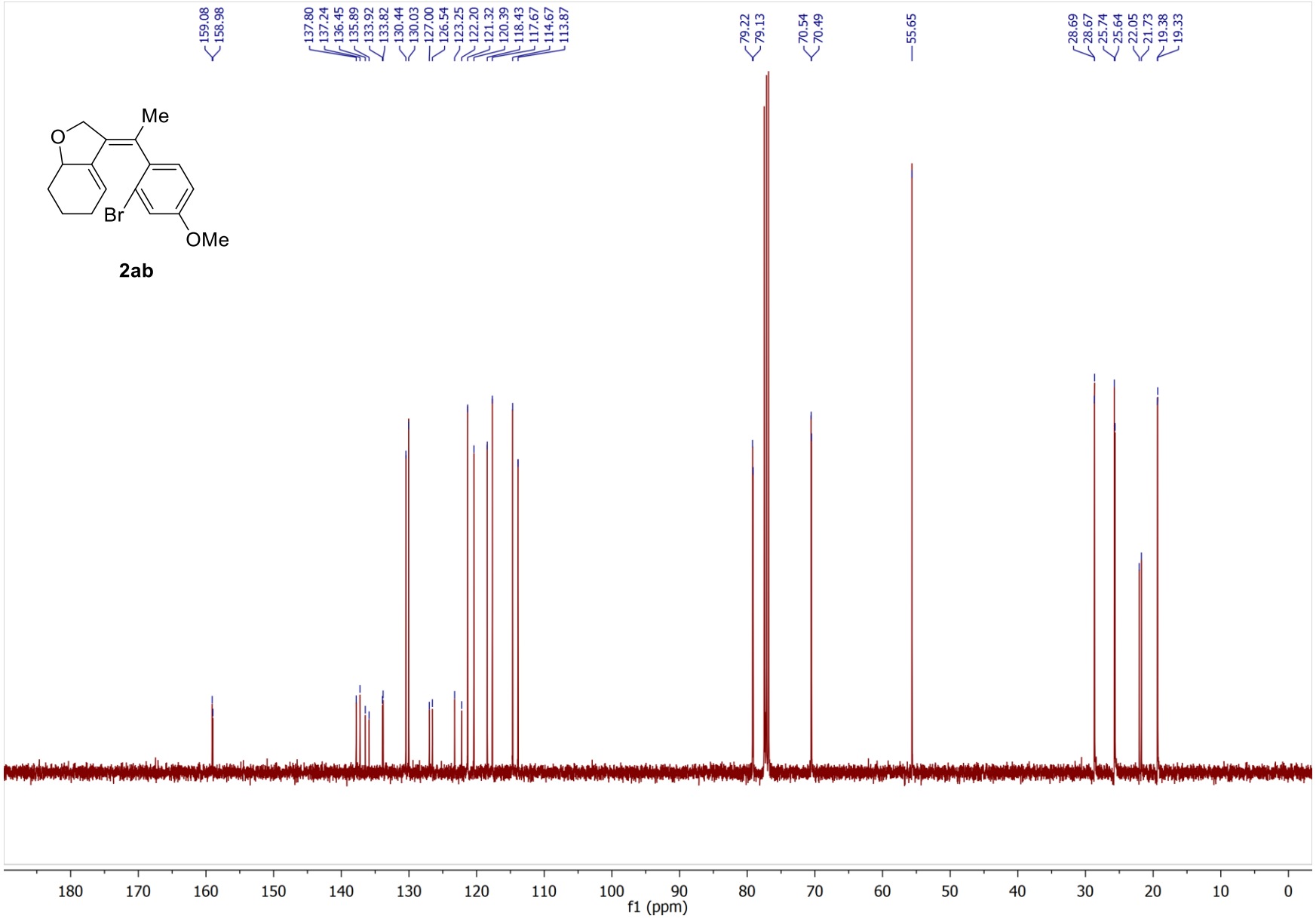
0.0
f1 (ppm)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133.82
130.44
130.03
127.00
126.54
123.25
122.20
121.32
120.39
118.43
117.67
114.67
113.87
79.22
79.13
70.54
70.49
55.65
28.69
28.67
25.74
25.64
22.05
21.73
19.38
19.33
Me
O
Br
OMe
2ab
180
170
160
150
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130
120
110
100
90
80
70
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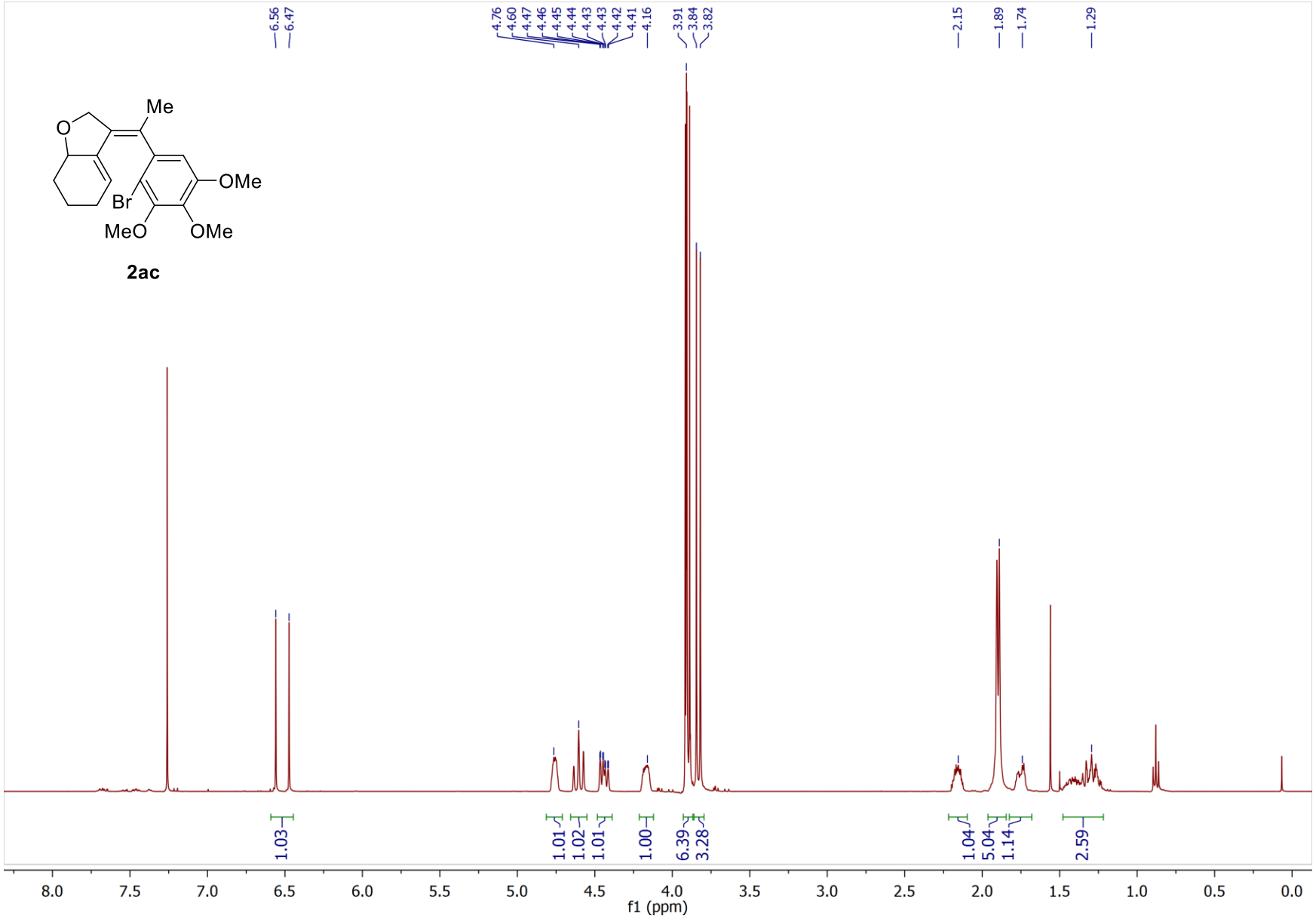
50
40
30
20
10
0
f1 (ppm)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6.47
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4.60
4.47
4.46
4.45
4.44
4.43
4.43
4.42
4.41
4.16
3.91
3.84
3.82
2.15
1.89
1.74
1.29
Me
O
OMe
Br
MeO
OMe
2ac
1.03
1.01
1.02
1.01
1.00
6.39
3.28
1.04
5.04
1.14
2.59
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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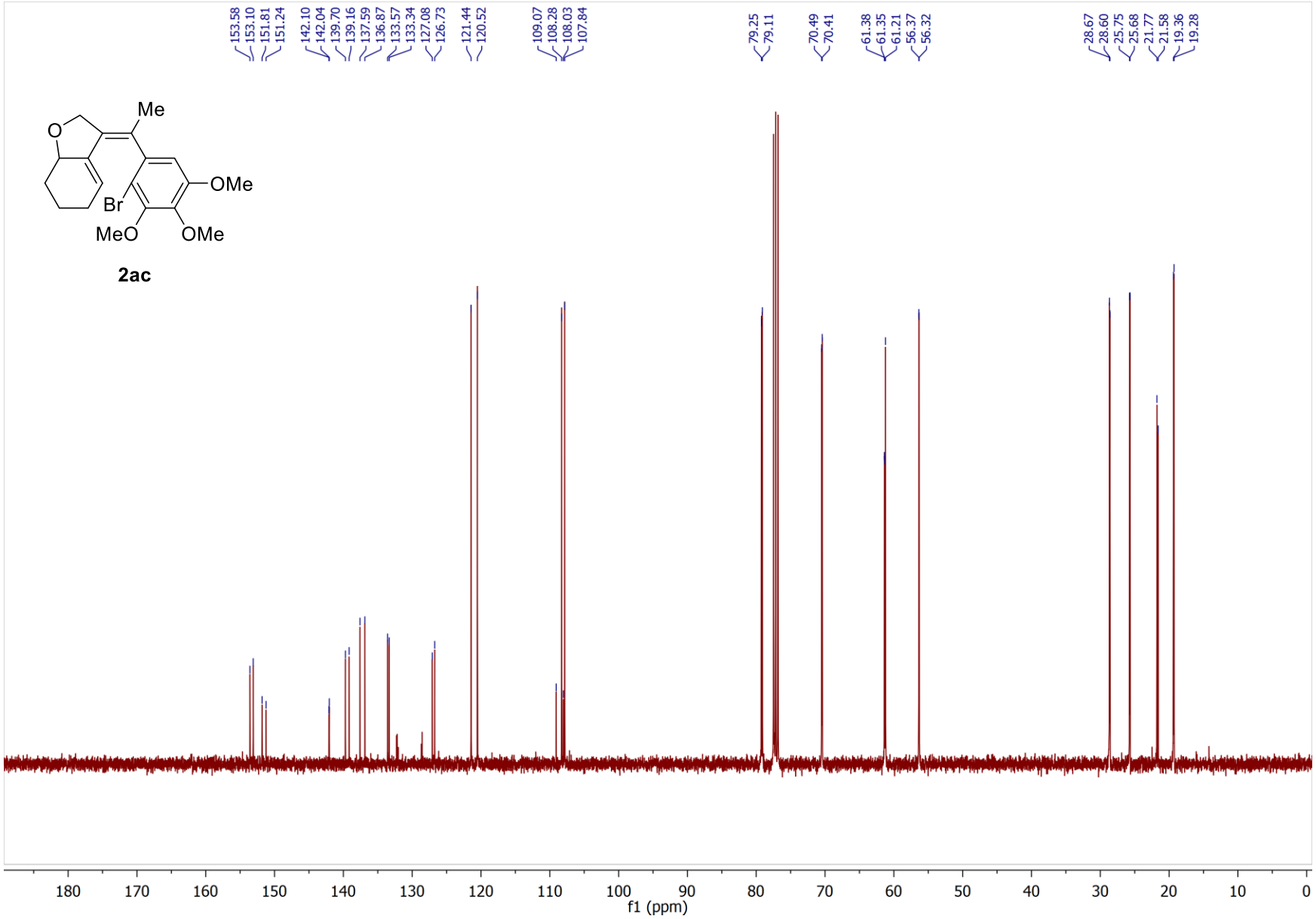
0.0
f1 (ppm)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151.24
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142.04
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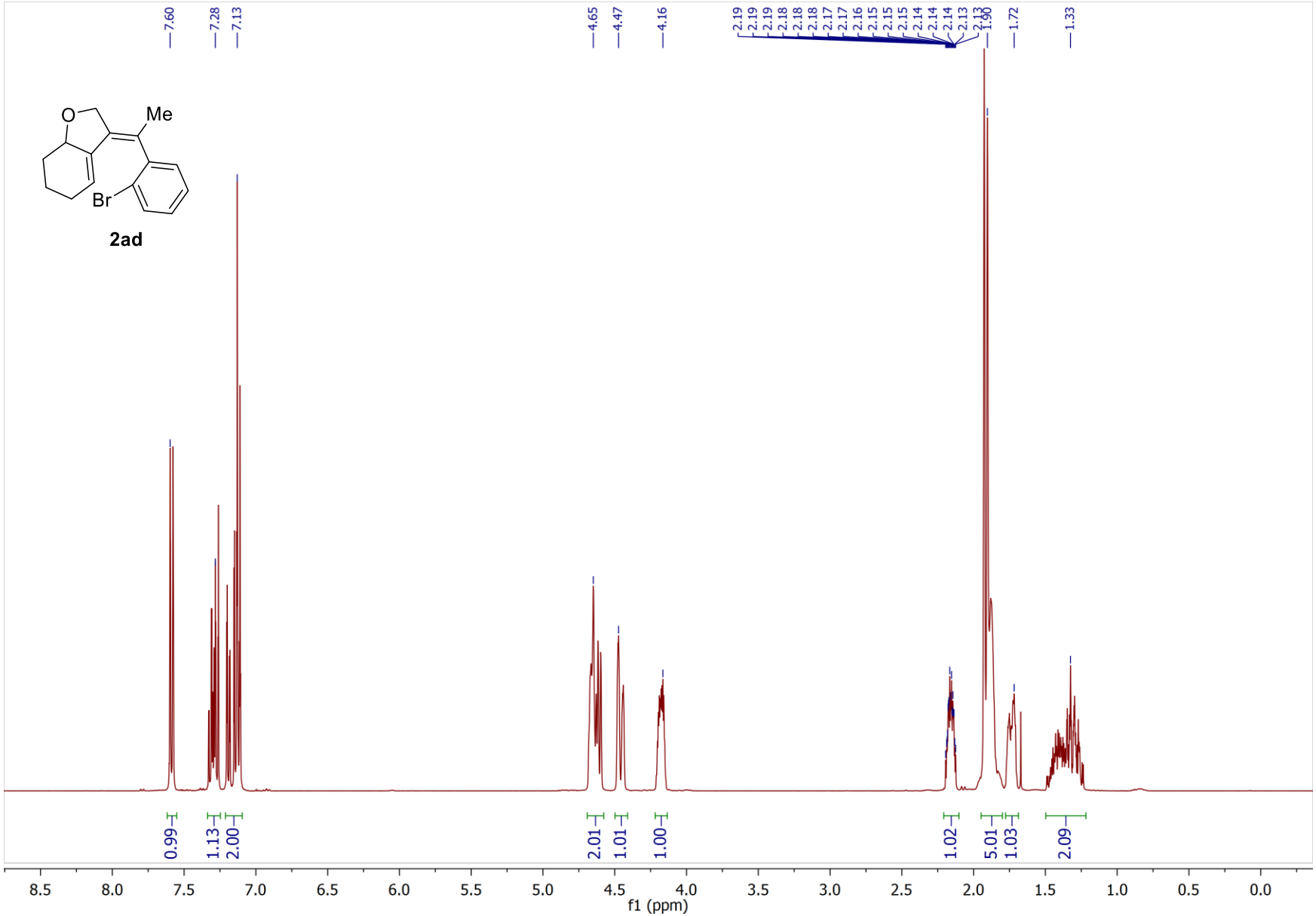
139.16
137.59
136.87
133.57
133.34
127.08
126.73
121.44
120.52
109.07
108.28
108.03
107.84
79.25
79.11
70.49
70.41
61.38
61.35
61.21
56.37
56.32
28.67
28.60
25.75
25.68
21.77
21.58
19.36
19.28
Me
O
OMe
Br
MeO
OMe
2ac
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.28
7.13
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4.47
4.16
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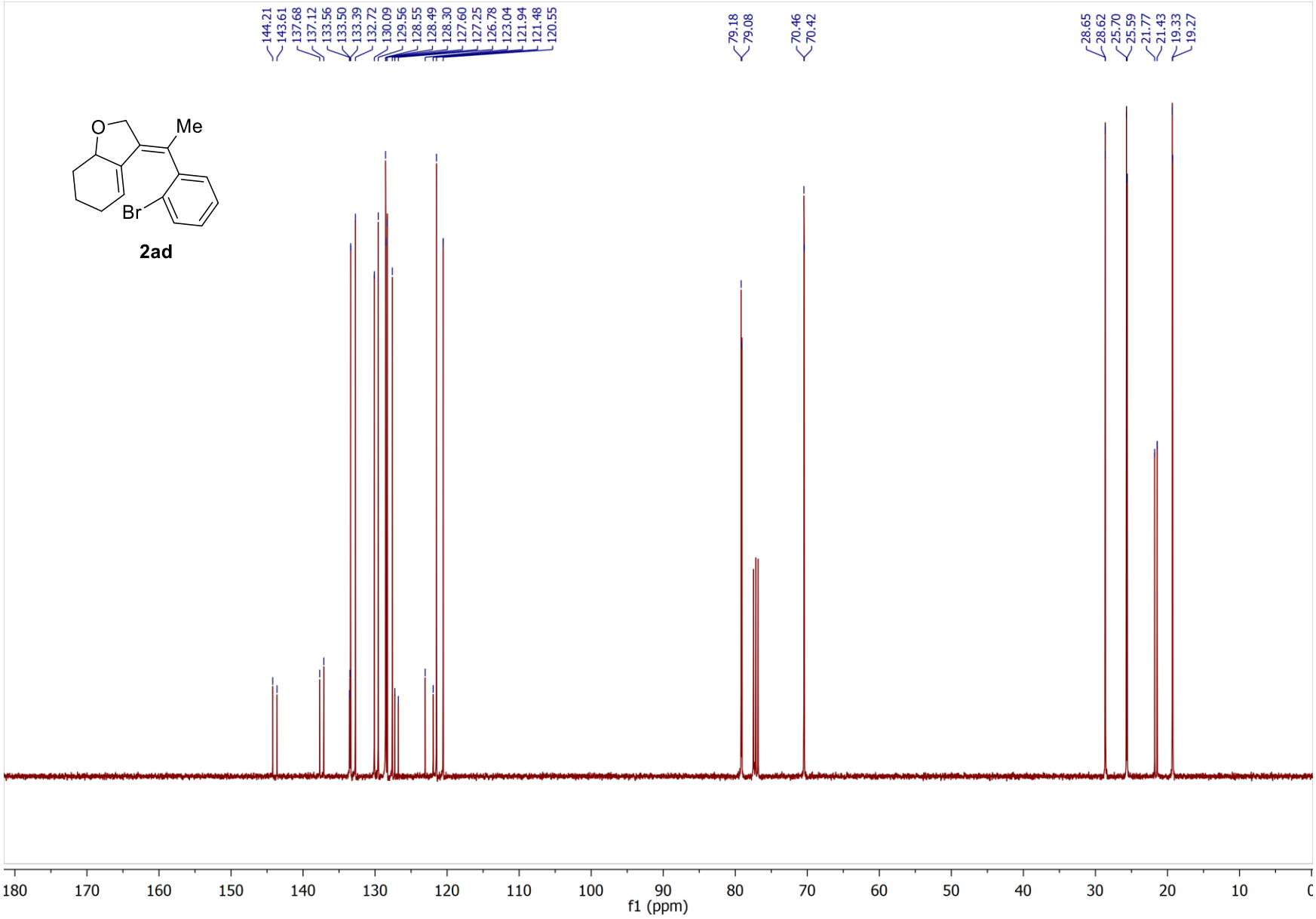
2.19
2.19
2.18
2.18
2.18
2.17
2.17
2.16
2.15
2.15
2.15
2.14
2.14
2.14
2.13
1.90
1.72
1.33
O
Me
Br
2ad
0.99
1.13
2.00
2.01
1.01
1.00
1.02
5.01
1.03
2.09
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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143.61
137.68
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133.50
133.39
132.72
130.09
129.56
128.55
128.49
128.30
127.60
127.25
126.78
123.04
121.94
121.48
120.55
79.18
79.08
70.46
70.42
28.65
28.62
25.70
25.59
21.77
21.43
19.33
19.27
O
Me
Br
2ad
180
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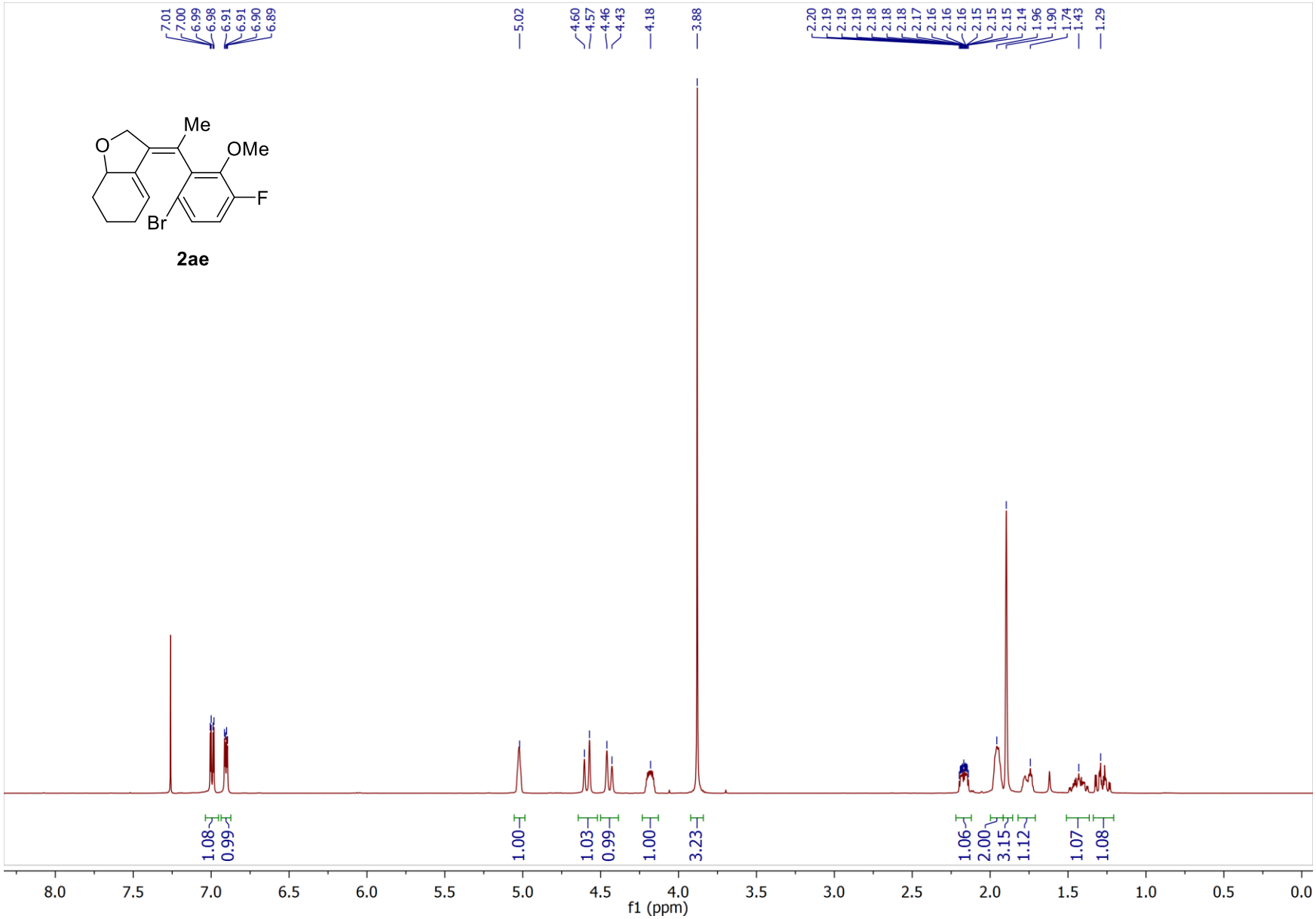
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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6.98
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6.90
6.89
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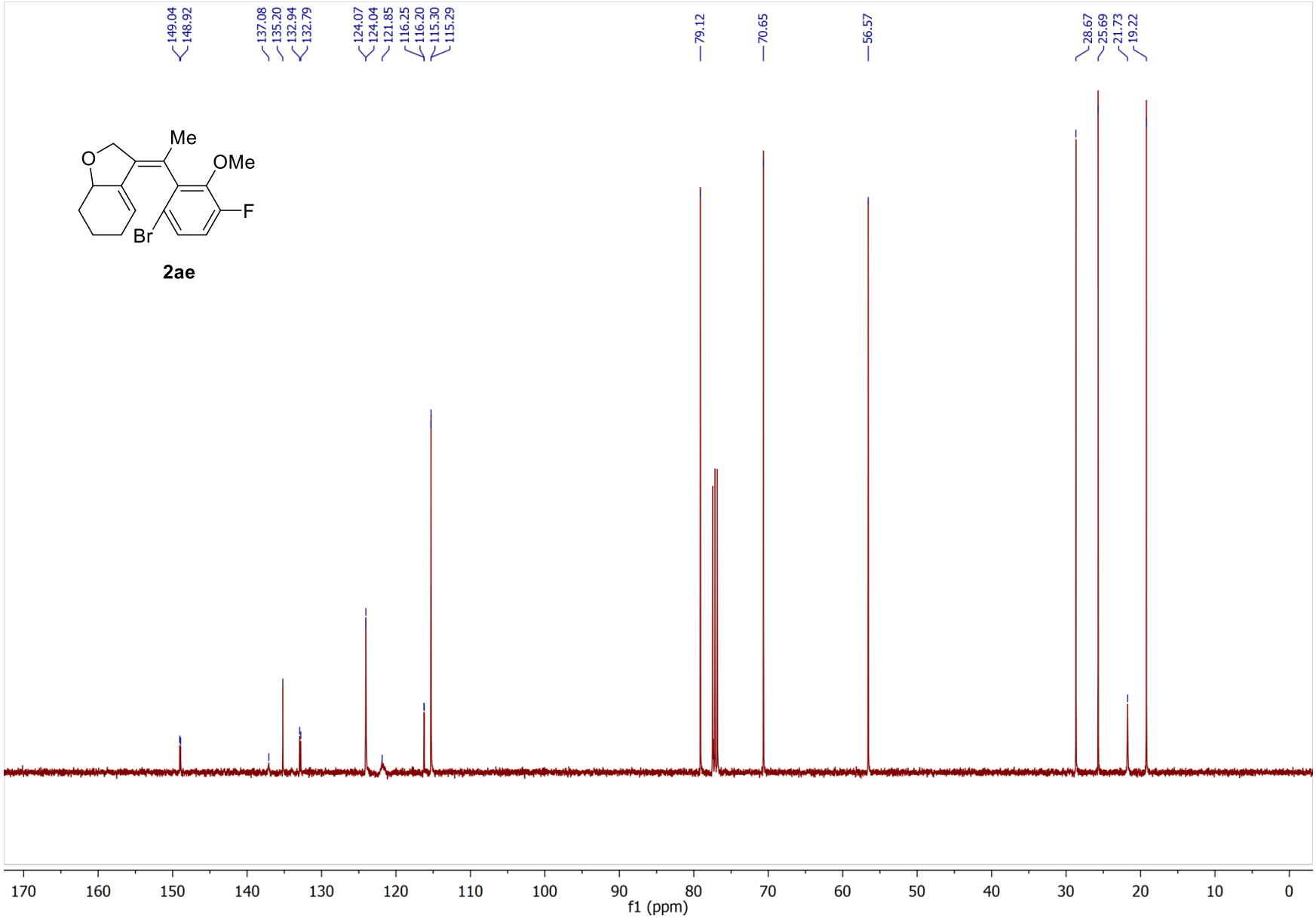
4.57
4.46
4.43
4.18
3.88
2.20
2.19
2.19
2.19
2.18
2.18
2.18
2.17
2.16
2.16
2.16
2.15
2.15
2.15
2.14
1.96
1.90
1.74
1.43
1.29
Me
OMe
F
Br
O
2ae
1.08
0.99
1.00
1.03
0.99
1.00
3.23
1.06
2.00
3.15
1.12
1.07
1.08
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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132.79
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124.04
121.85
116.25
116.20
115.30
115.29
79.12
70.65
56.57
28.67
25.69
21.73
19.22
Me
OMe
O
F
Br
2ae
170
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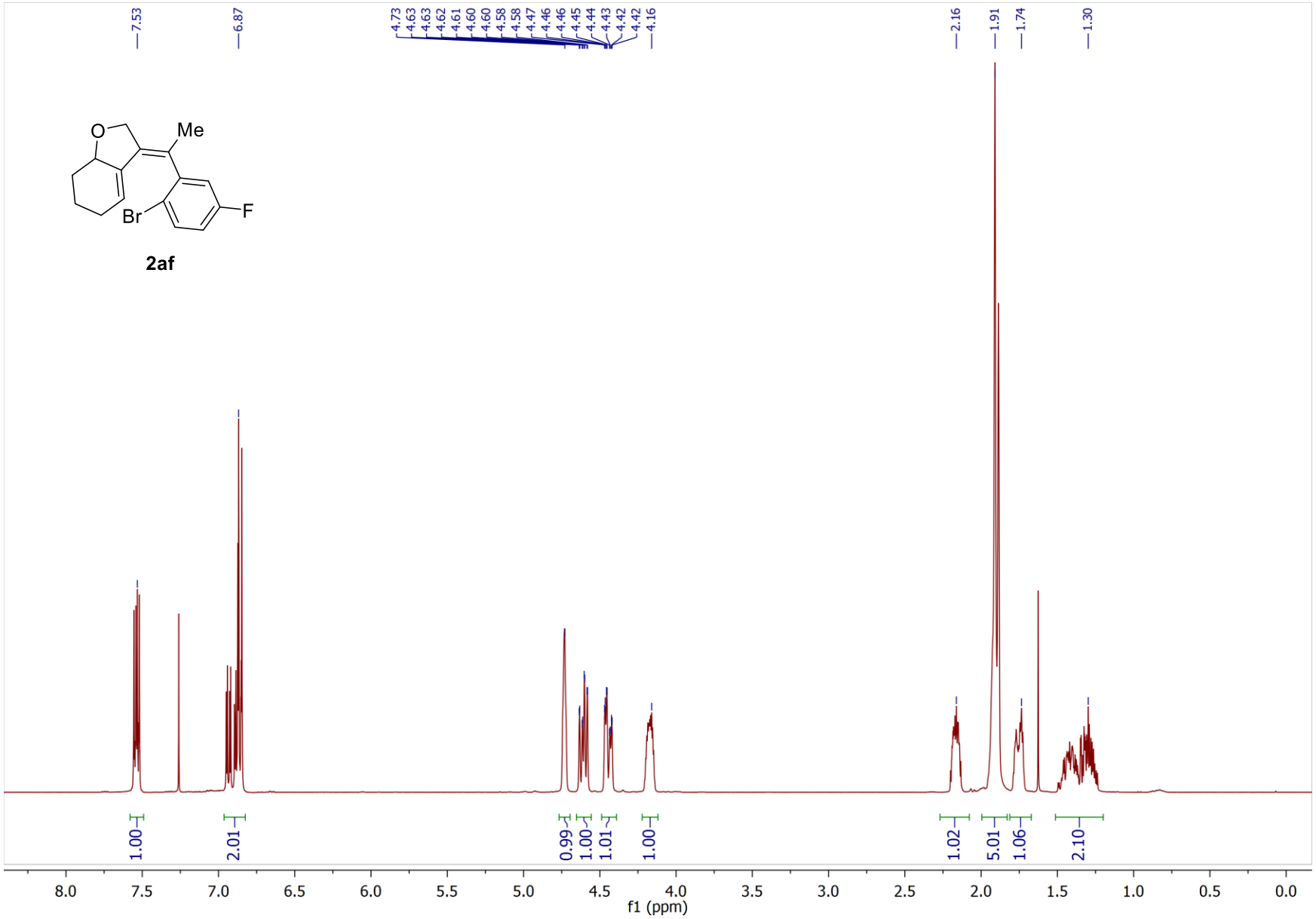
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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4.60
4.60
4.58
4.58
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4.46
4.46
4.45
4.44
4.43
4.42
4.42
4.16
2.16
1.91
1.74
1.30
O
Me
Br
F
2af
1.00
2.01
0.99
1.00
1.01
1.00
1.02
5.01
1.06
2.10
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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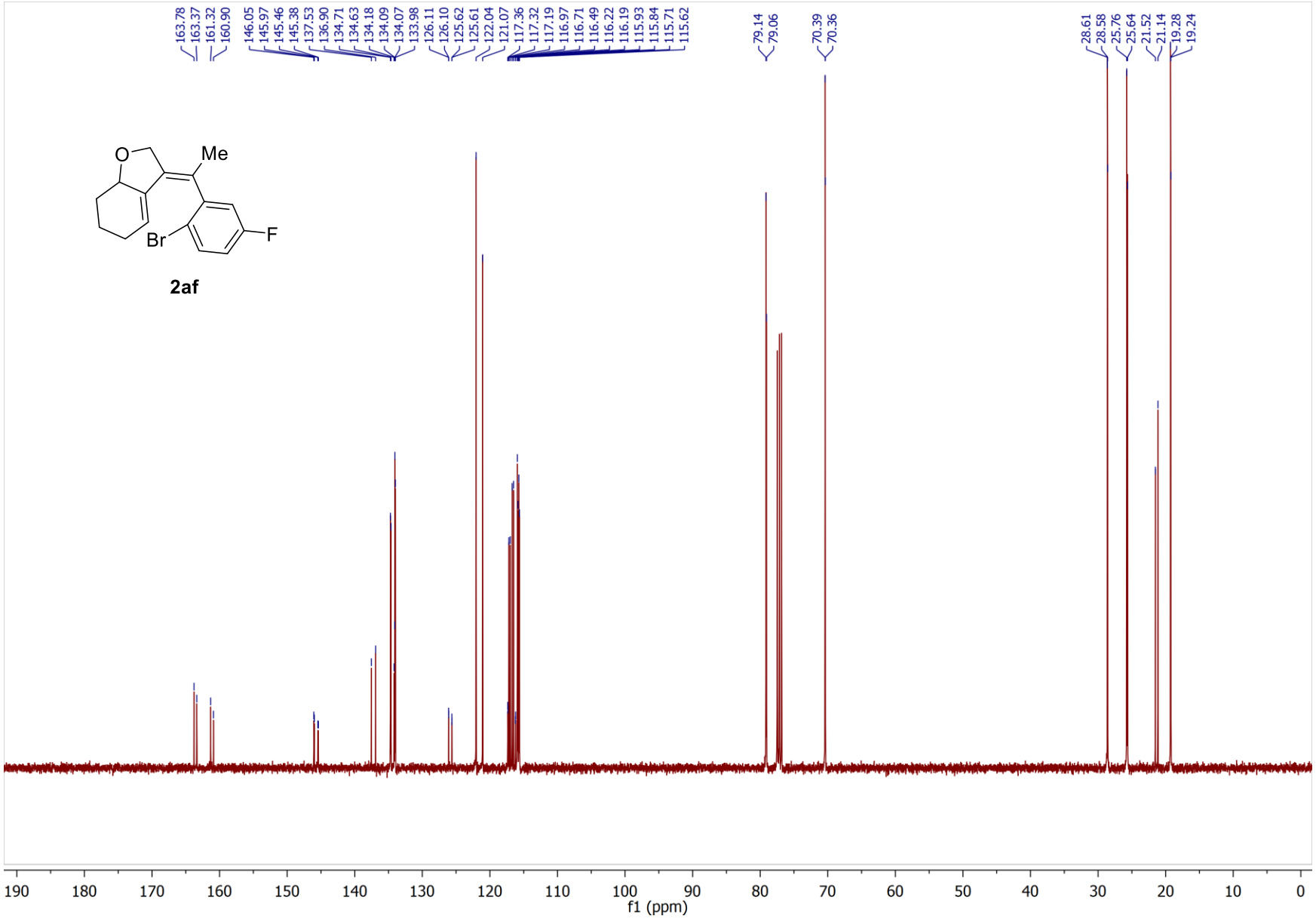
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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134.09
134.07
133.98
126.11
126.10
125.62
125.61
122.04
121.07
117.36
117.32
117.19
116.97
116.71
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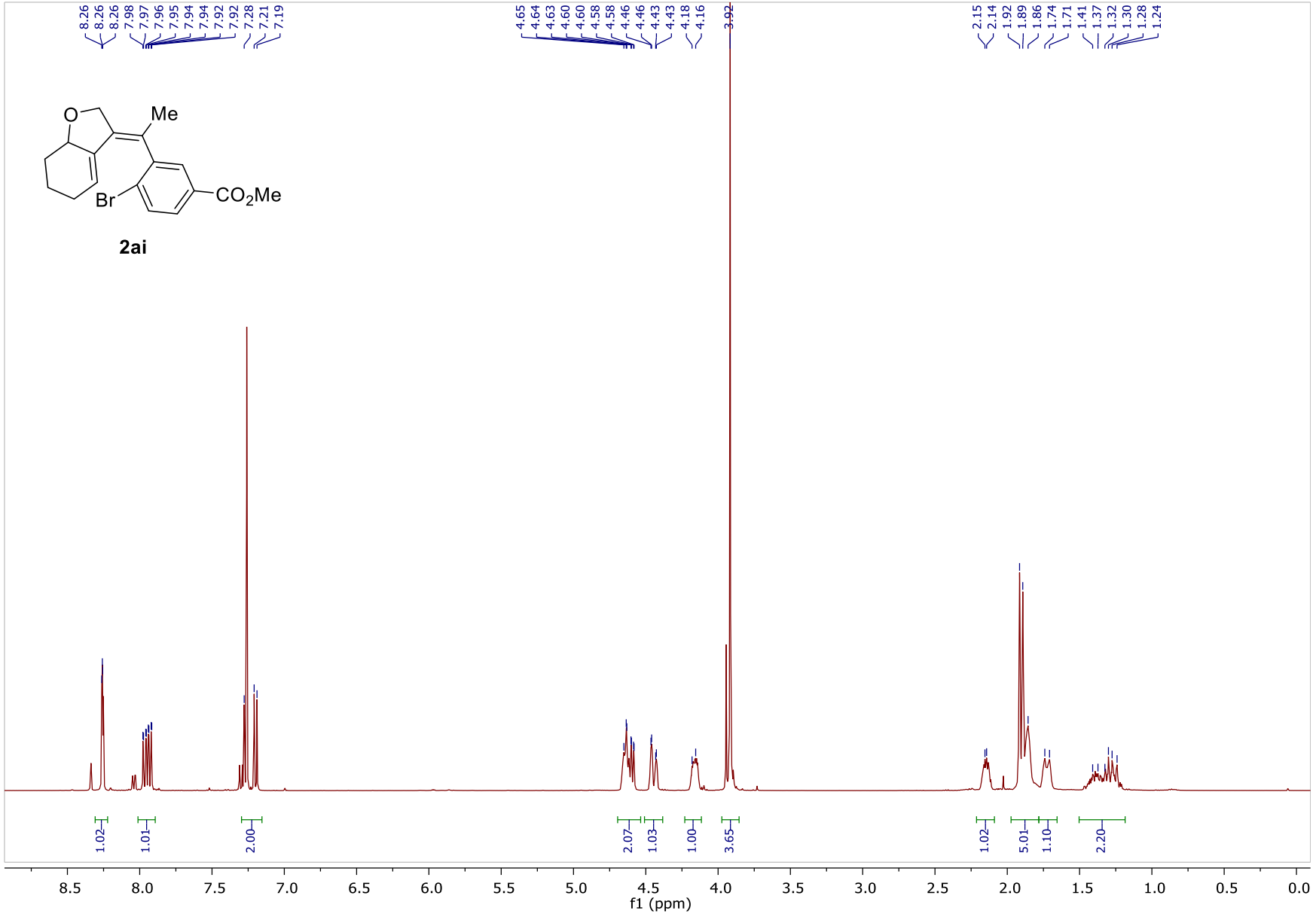
116.22
116.19
115.93
115.84
115.71
115.62
79.14
79.06
70.39
70.36
28.61
28.58
25.76
25.64
21.52
21.14
19.28
19.24
O
Me
Br
F
2af
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.96
7.95
7.94
7.94
7.92
7.92
7.28
7.21
7.19
4.65
4.64
4.63
4.60
4.60
4.58
4.58
4.46
4.46
4.43
4.43
4.18
4.16
3.92
2.15
2.14
1.92
1.89
1.86
1.74
1.71
1.41
1.37
1.32
1.30
1.28
1.24
O
Me
Br
CO2Me
2ai
1.02
1.01
2.00
2.07
1.03
1.00
3.65
1.02
5.01
1.10
2.20
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
3.0
2.5
2.0
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1.0
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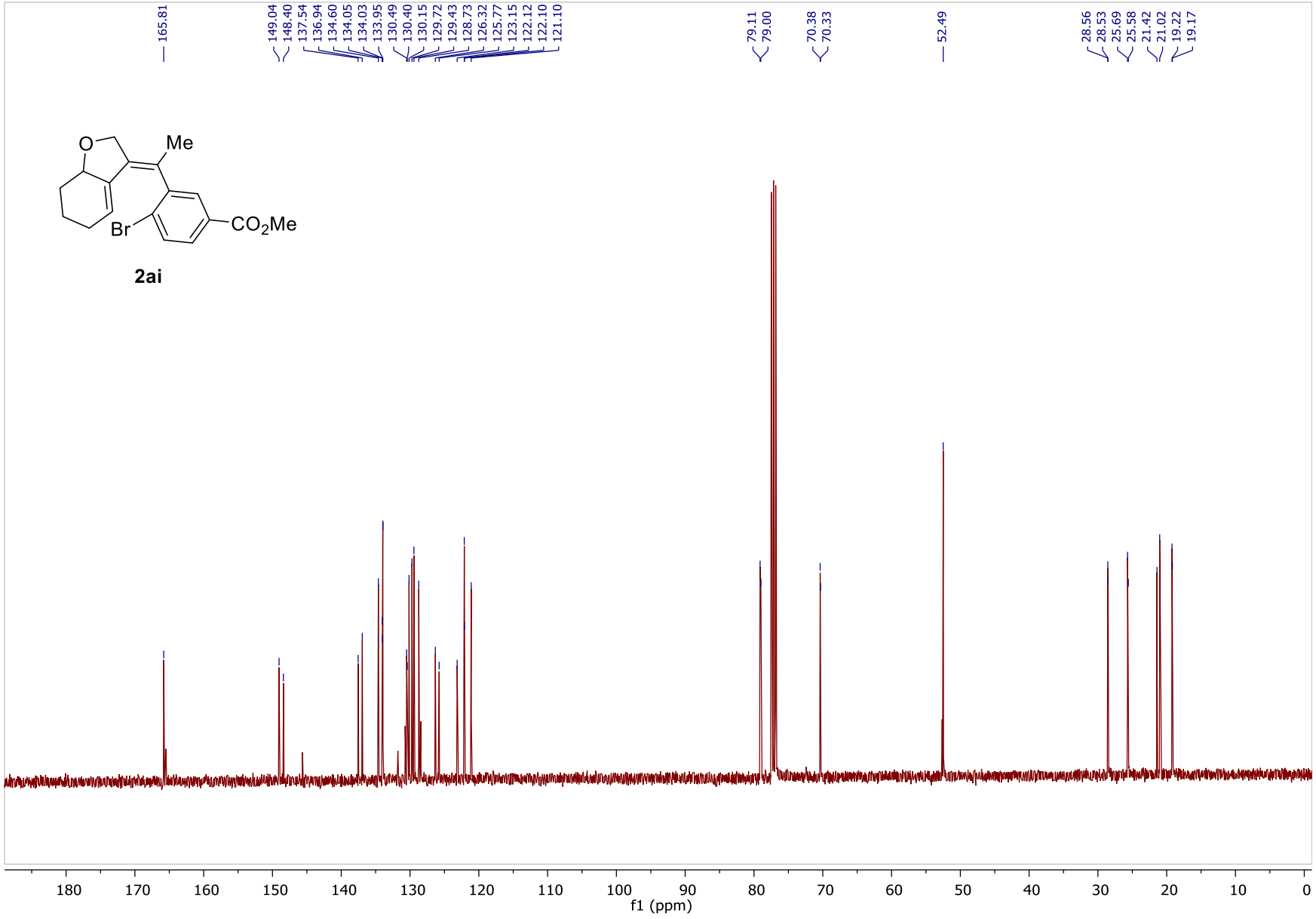
0.0
f1 (ppm)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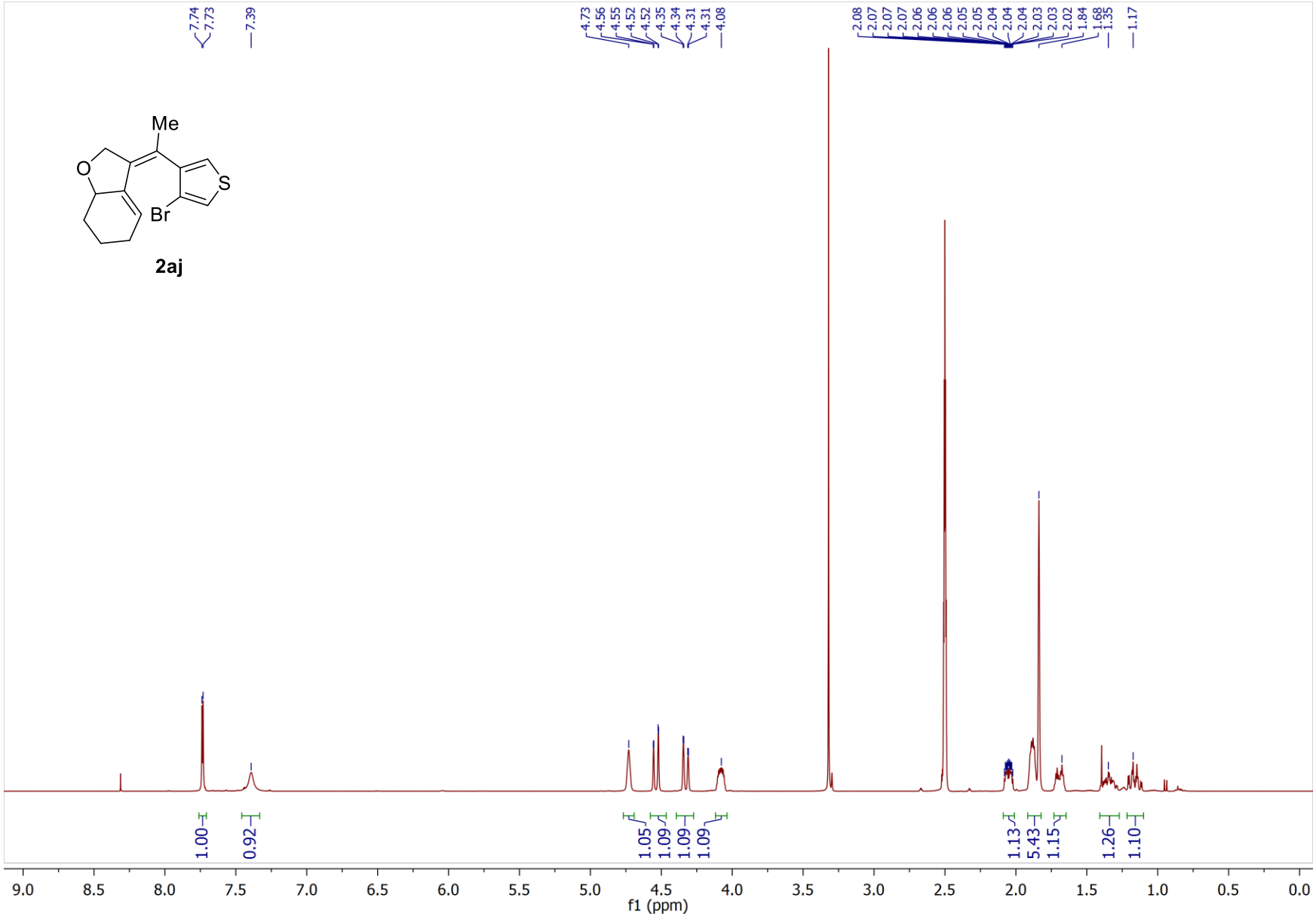
129.43
128.73
126.32
125.77
123.15
122.12
122.10
121.10
79.11
79.00
70.38
70.33
52.49
28.56
28.53
25.69
25.58
21.42
21.02
19.22
19.17
O
Me
Br
CO2Me
2ai
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Me
O
S
Br
2aj
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7.39
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4.56
4.55
4.52
4.52
4.35
4.34
4.31
4.31
4.08
2.08
2.07
2.07
2.07
2.06
2.06
2.06
2.05
2.05
2.04
2.04
2.04
2.03
2.03
2.02
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1.68
1.35
1.17
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1.05
1.09
1.09
1.09
1.13
5.43
1.15
1.26
1.10
9.0
8.5
8.0
7.5
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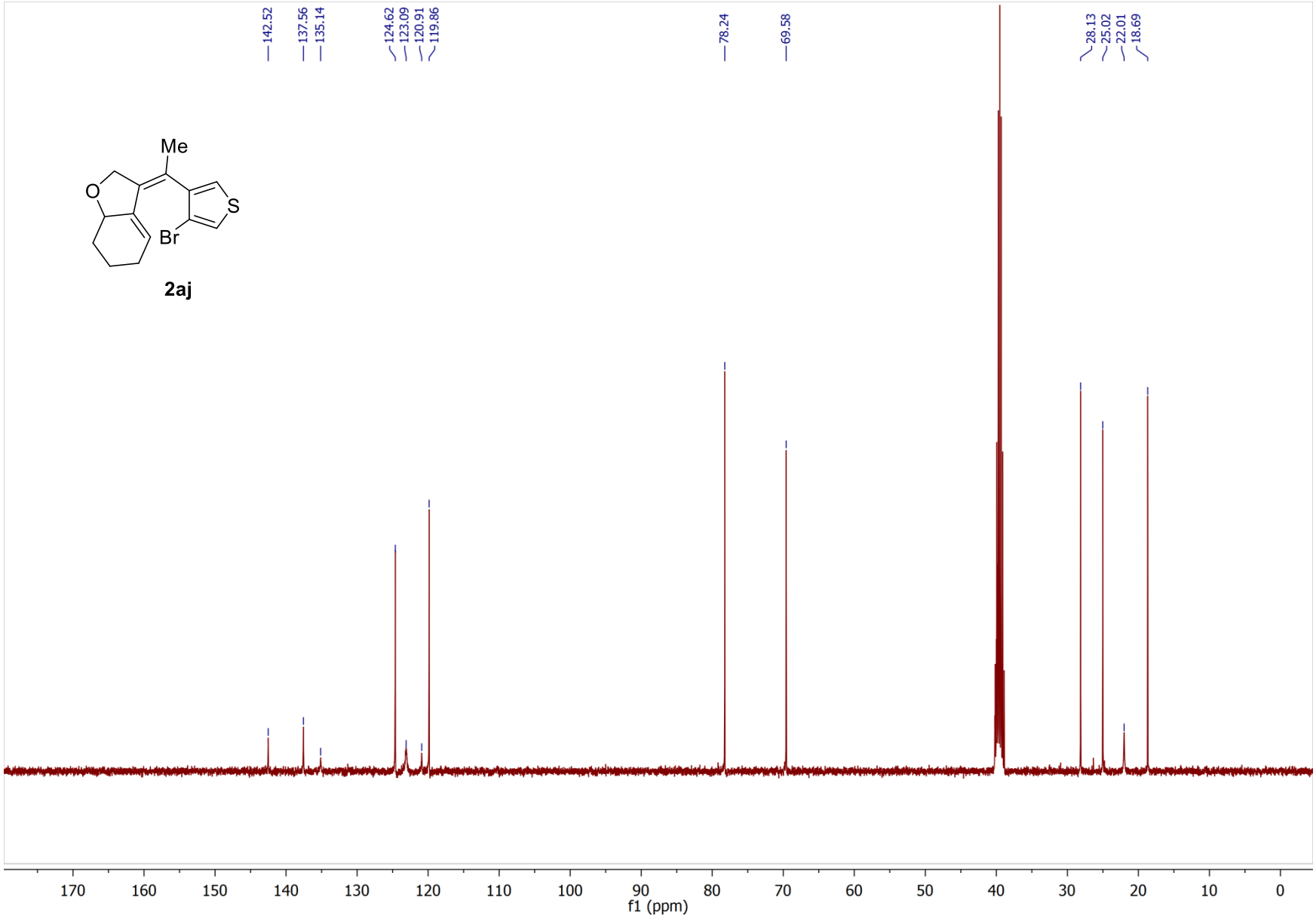
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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135.14
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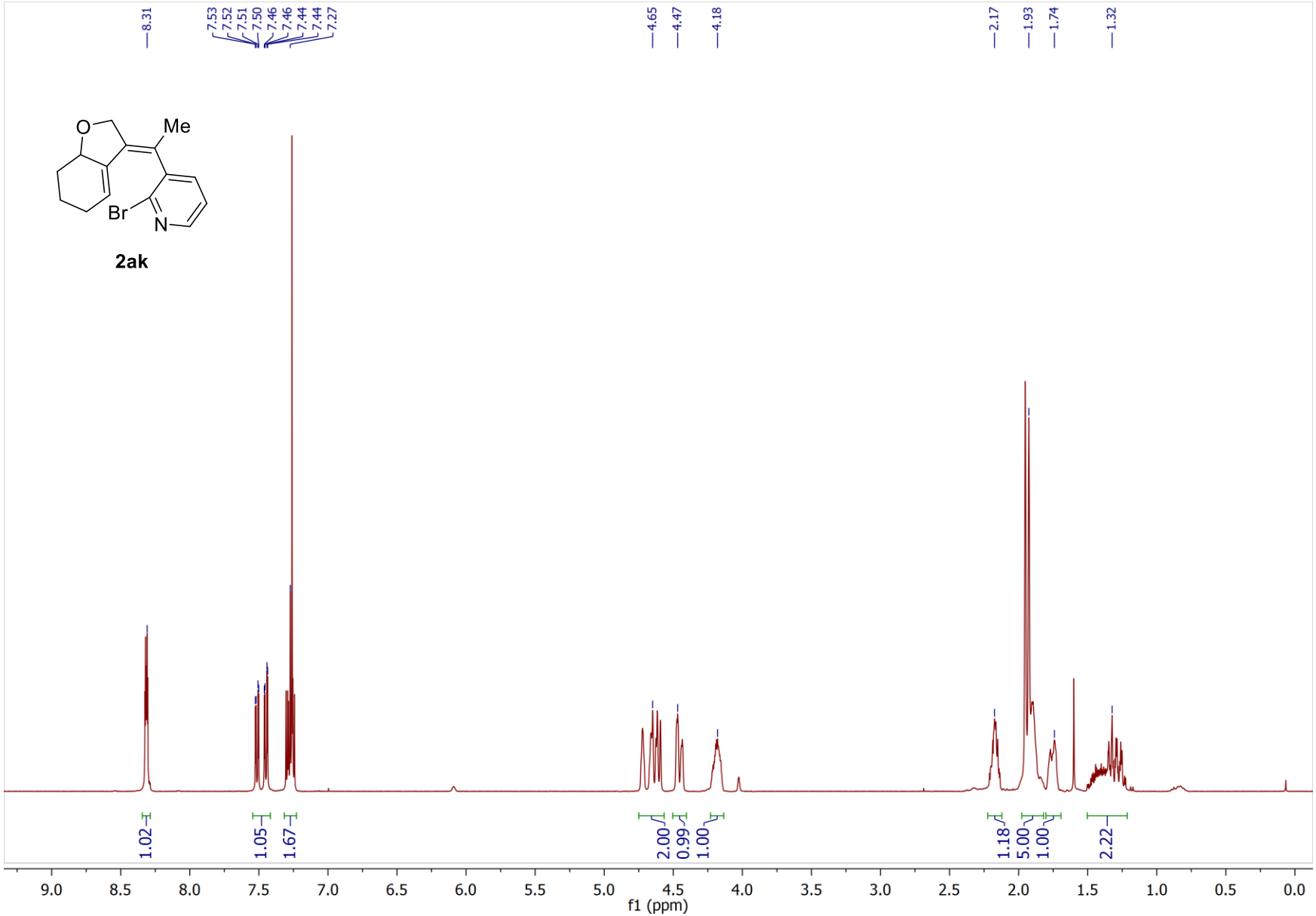
123.09
120.91
119.86
78.24
69.58
28.13
25.02
22.01
18.69
Me
O
S
Br
2aj
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.46
7.46
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7.44
7.27
4.65
4.47
4.18
2.17
1.93
1.74
1.32
O
Me
Br
N
2ak
1.02
1.05
1.67
2.00
0.99
1.00
1.18
5.00
1.00
2.22
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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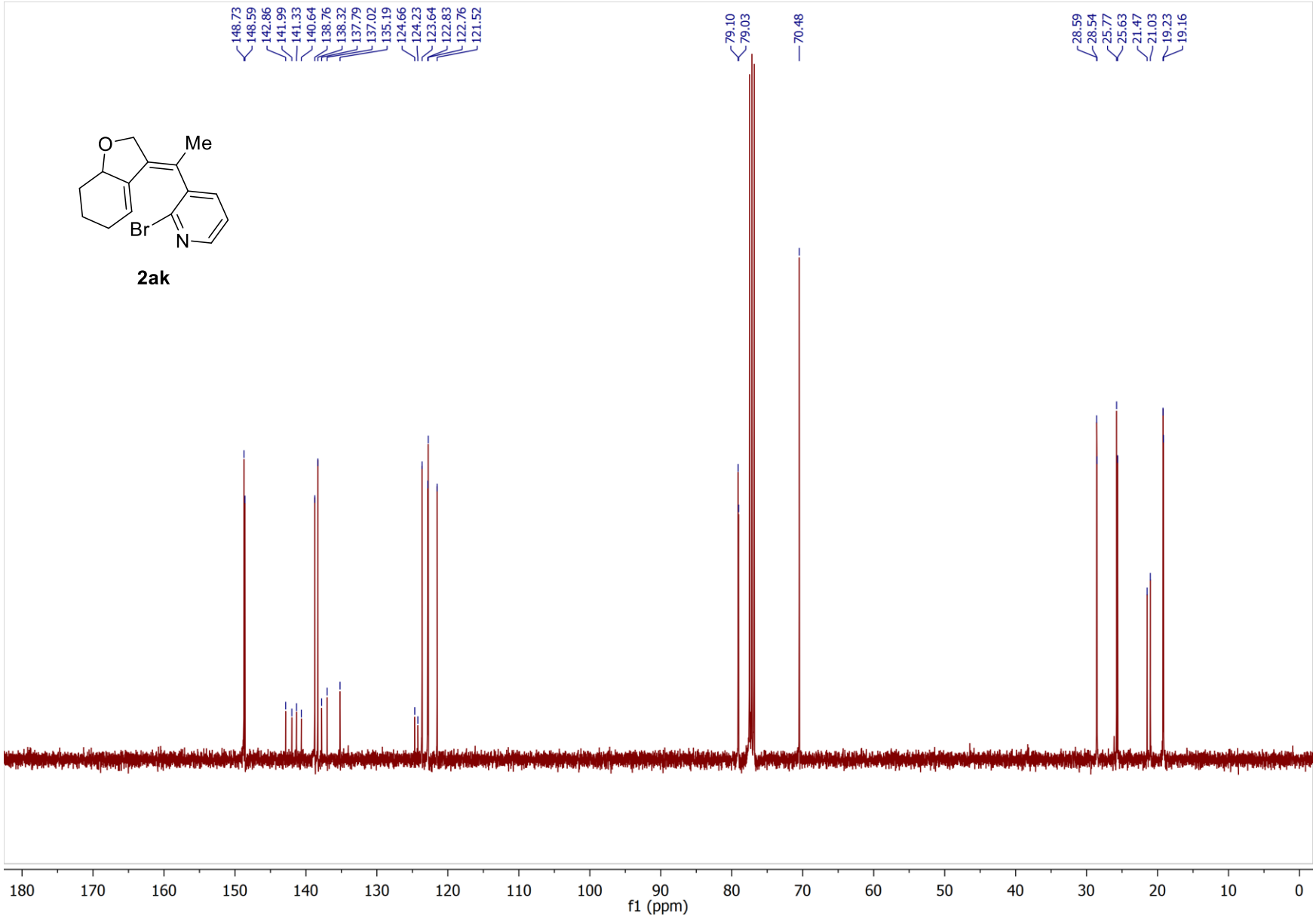
0.0
f1 (ppm)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148.59
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141.99
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140.64
138.76
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137.02
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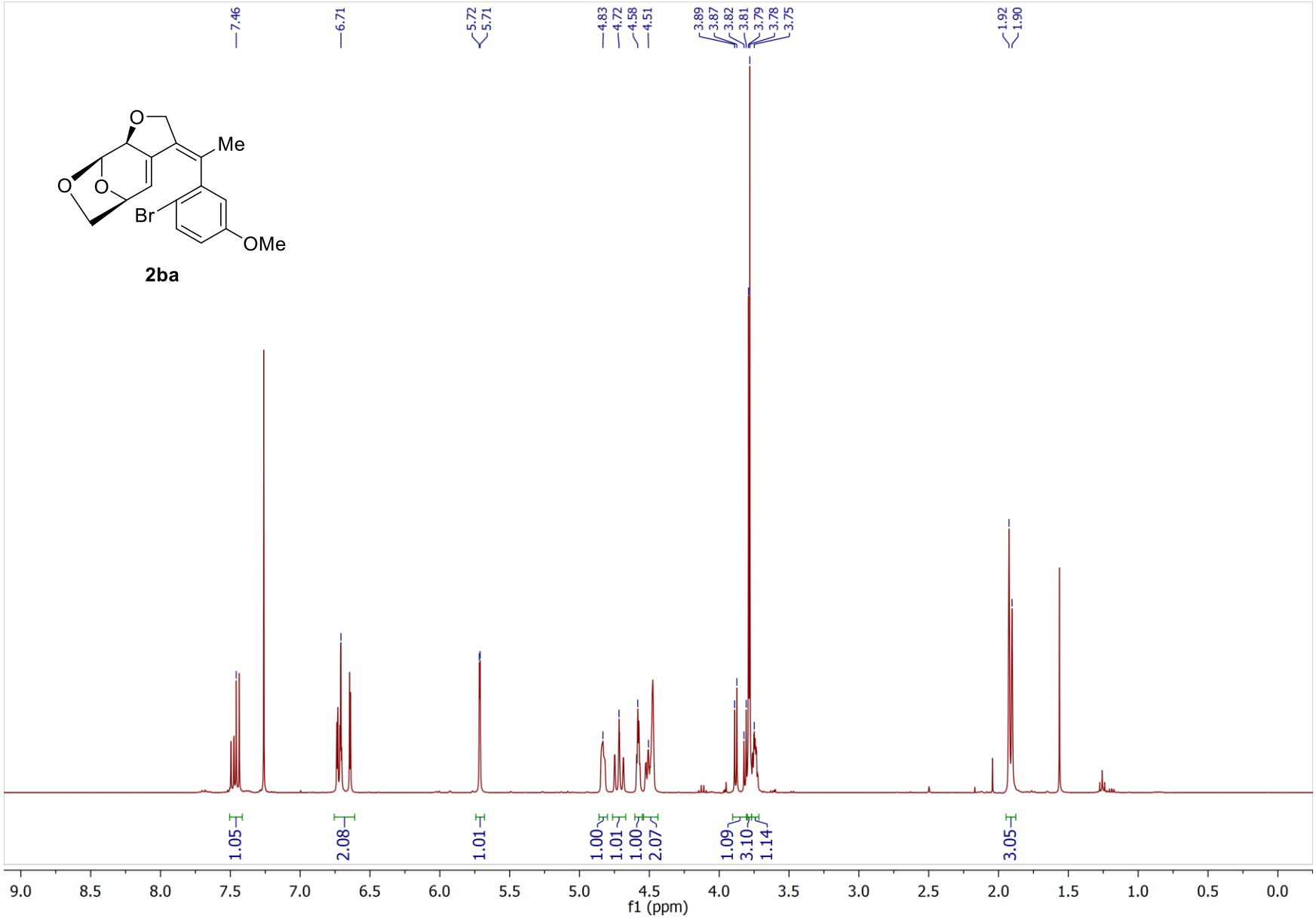
124.66
124.23
123.64
122.83
122.76
121.52
79.10
79.03
70.48
28.59
28.54
25.77
25.63
21.47
21.03
19.23
19.16
O
Me
Br
N
2ak
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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3.79
3.78
3.75
1.92
1.90
O
O
O
Me
Br
OMe
2ba
1.05
2.08
1.01
1.00
1.01
1.00
2.07
1.09
3.10
1.14
3.05
9.0
8.5
8.0
7.5
7.0
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6.0
5.5
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3.0
2.5
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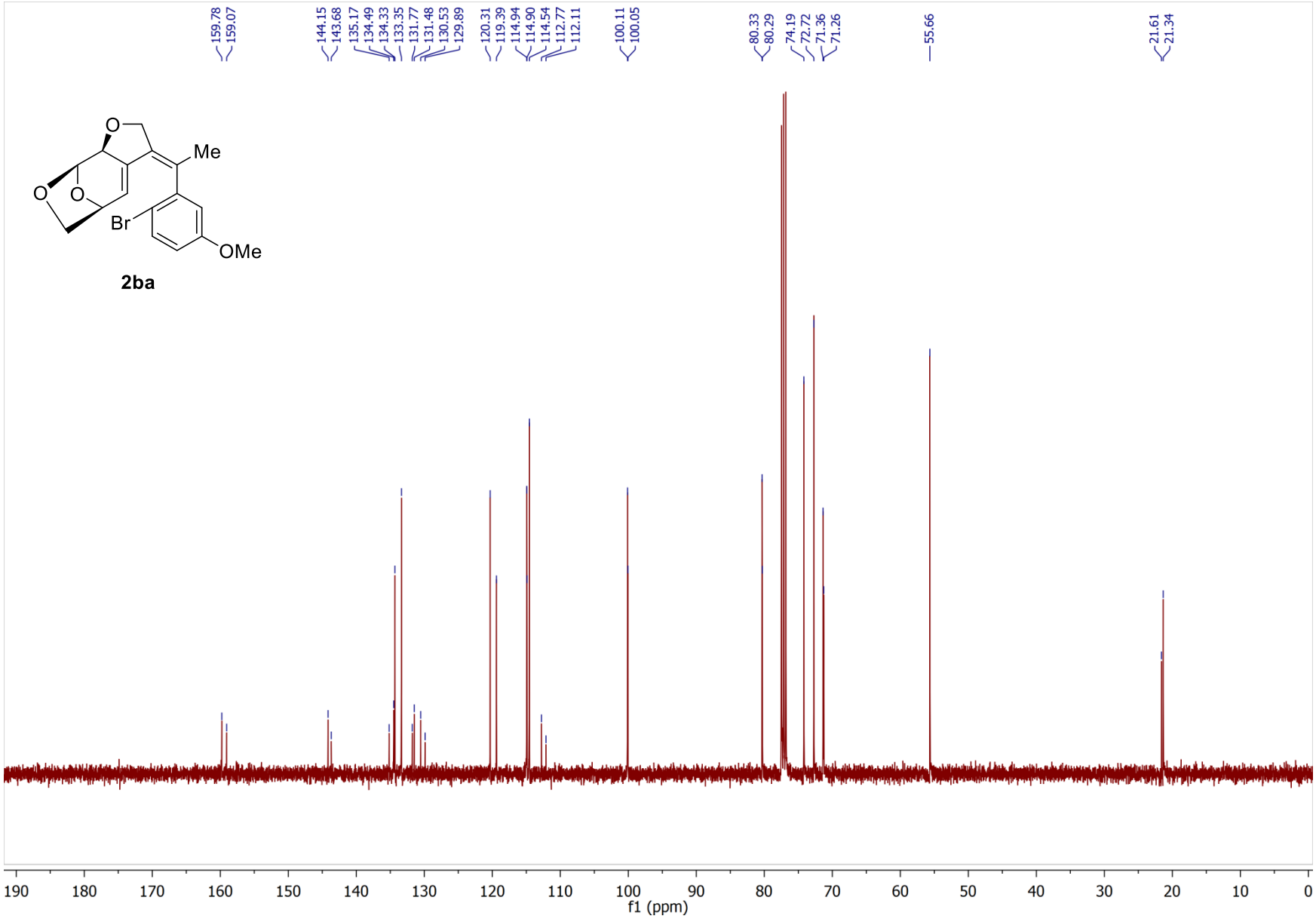
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114.94
114.90
114.54
112.77
112.11
100.11
100.05
80.33
80.29
74.19
72.72
71.36
71.26
55.66
21.61
21.34
O
O
O
Me
Br
OMe
2ba
190
180
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100
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70
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50
40
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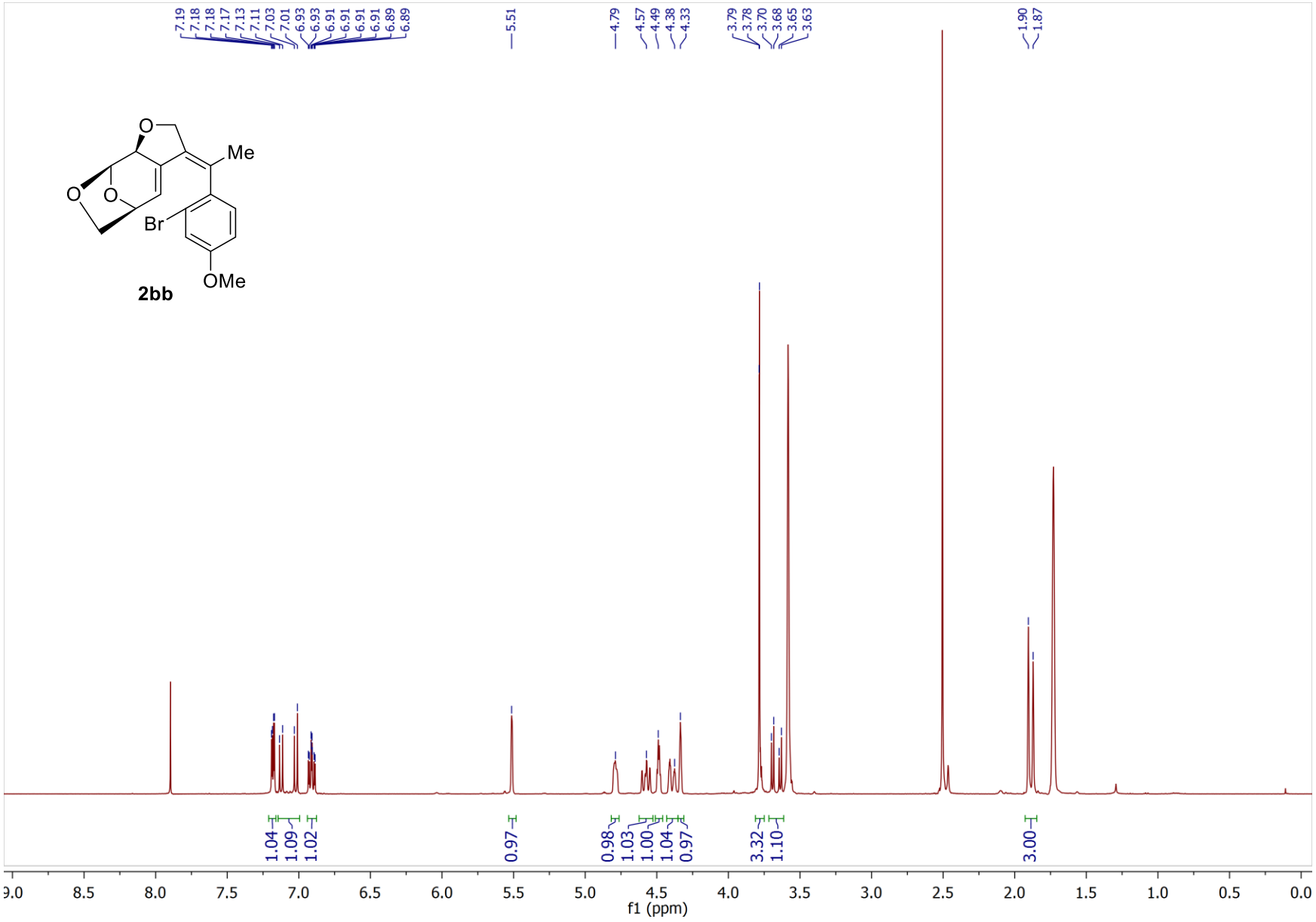
10
0
f1 (ppm)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6.91
6.91
6.89
6.89
5.51
4.79
4.57
4.49
4.38
4.33
3.79
3.78
3.70
3.68
3.65
3.63
1.90
1.87
O
O
O
Me
Br
OMe
2bb
1.04
1.09
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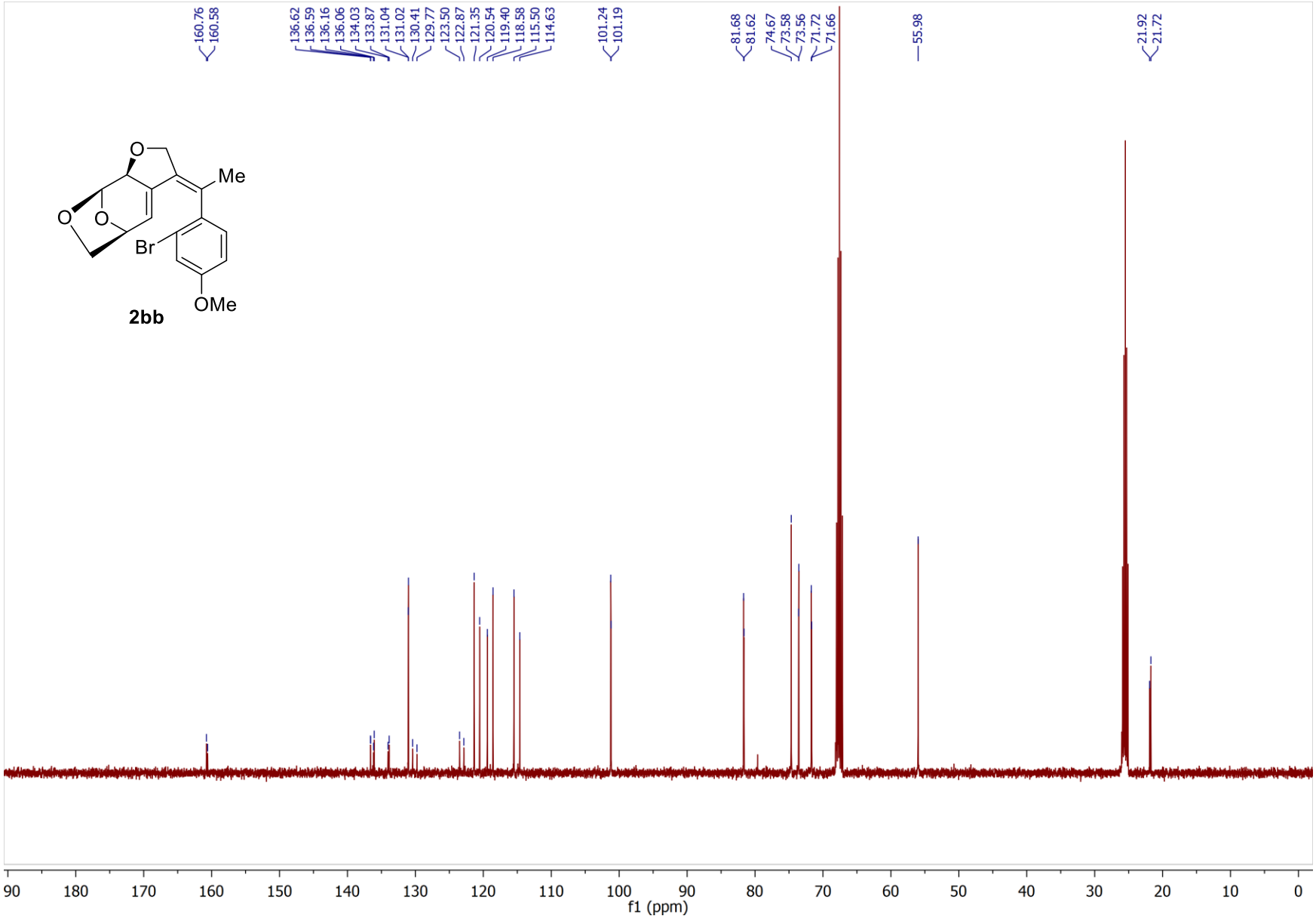
0.98
1.03
1.00
1.04
0.97
3.32
1.10
3.00
f1 (ppm)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114.63
101.24
101.19
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81.62
74.67
73.58
73.56
71.72
71.66
55.98
21.92
21.72
O
O
O
Me
Br
OMe
2bb
90
180
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90
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70
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50
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30
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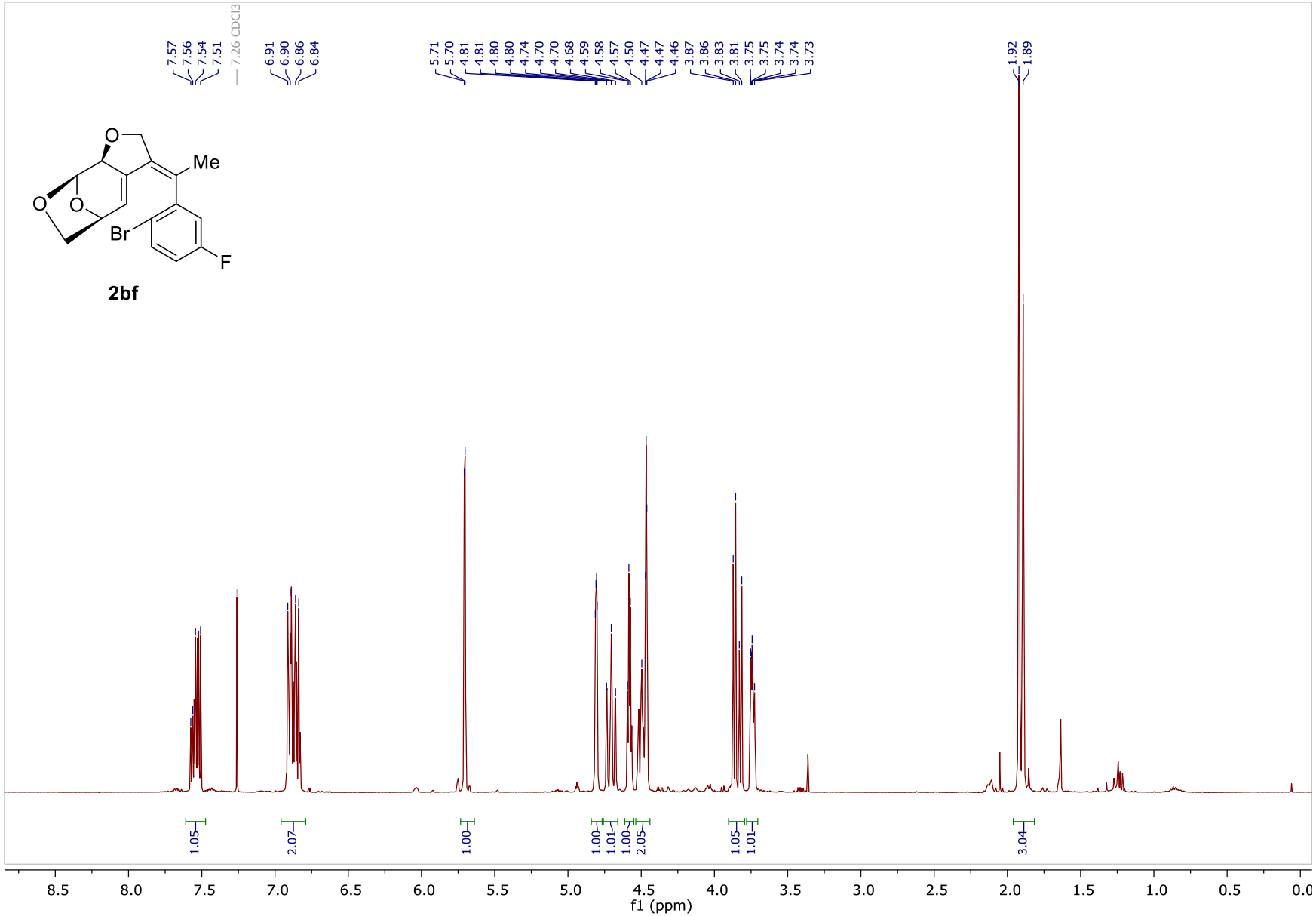
f1 (ppm)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4.80
4.80
4.74
4.70
4.70
4.68
4.59
4.58
4.57
4.50
4.47
4.47
4.46
3.87
3.86
3.83
3.81
3.75
3.75
3.74
3.74
3.73
1.92
1.89
O
O
O
Me
Br
F
2bf
1.05
2.07
1.00
1.00
1.01
1.00
2.05
1.05
1.01
3.04
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7.5
7.0
6.5
6.0
5.5
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2.5
2.0
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1.0
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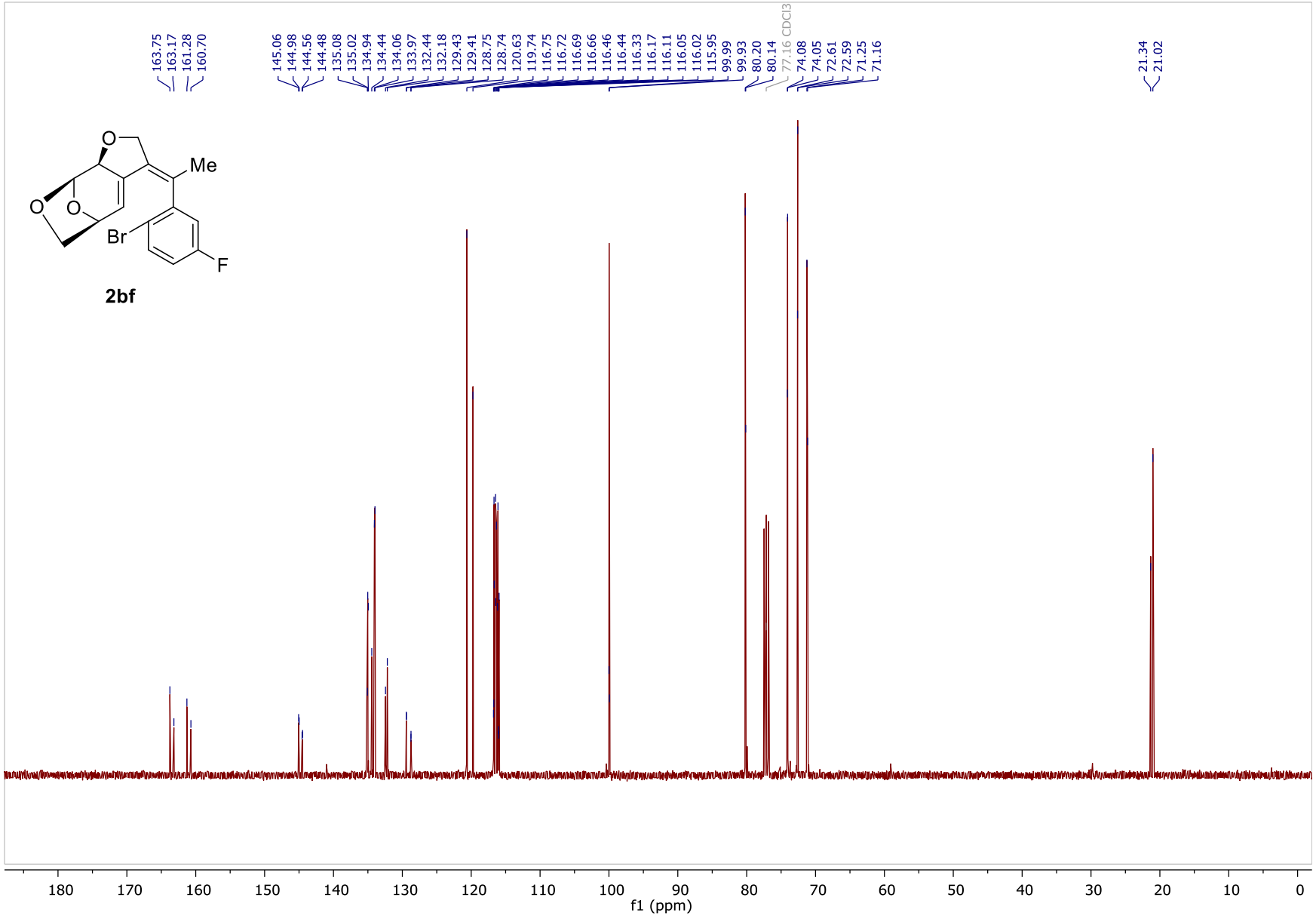
0.0
f1 (ppm)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134.06
133.97
132.44
132.18
129.43
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128.75
128.74
120.63
119.74
116.75
116.72
116.69
116.66
116.46
116.44
116.33
116.17
116.11
116.05
116.02
115.95
99.99
99.93
80.20
80.14
77.16 CDCl3
74.08
74.05
72.61
72.59
71.25
71.16
21.34
21.02
O
O
O
Me
Br
F
2bf
180
170
160
150
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130
120
110
100
90
80
70
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50
40
30
20
10
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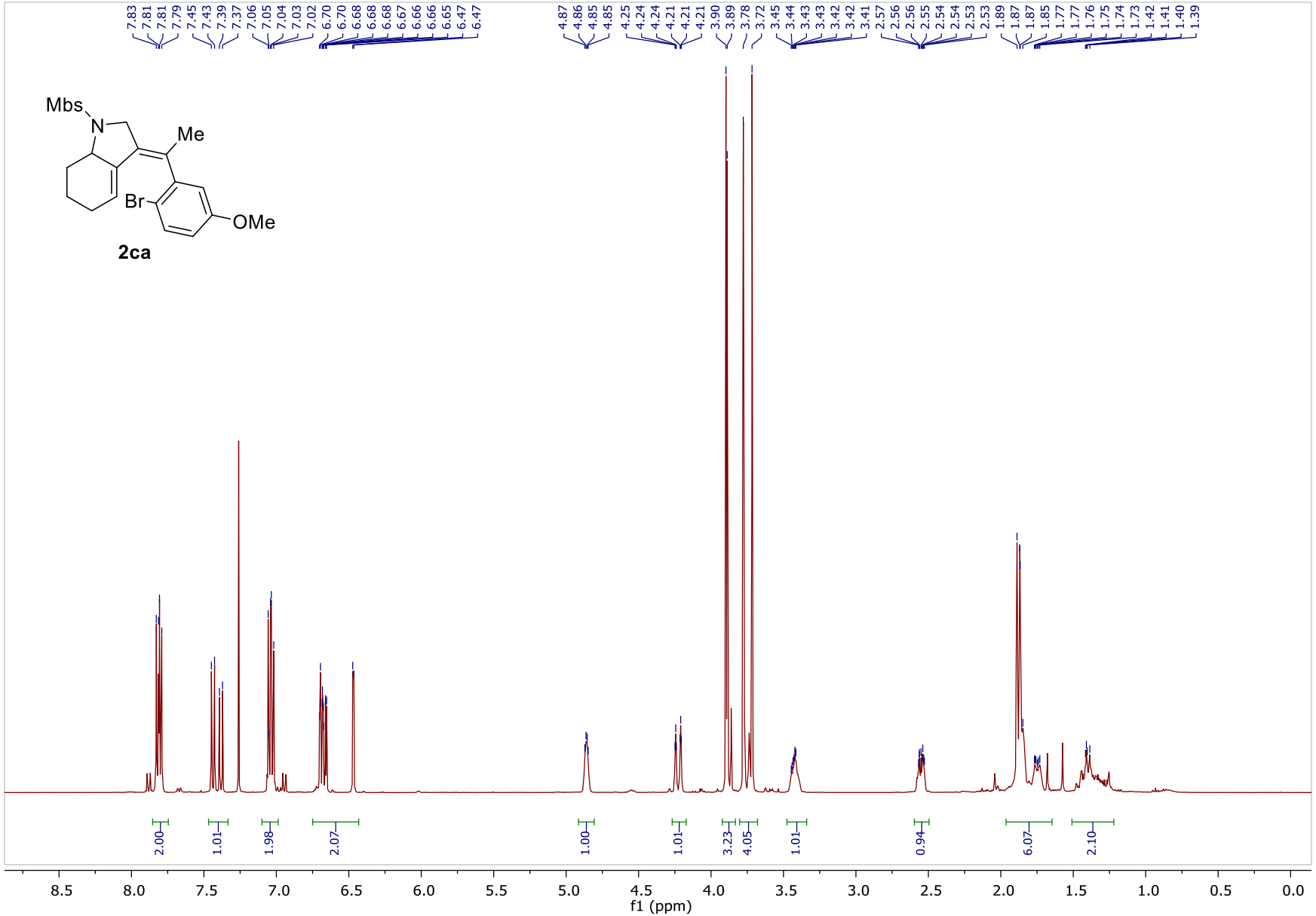
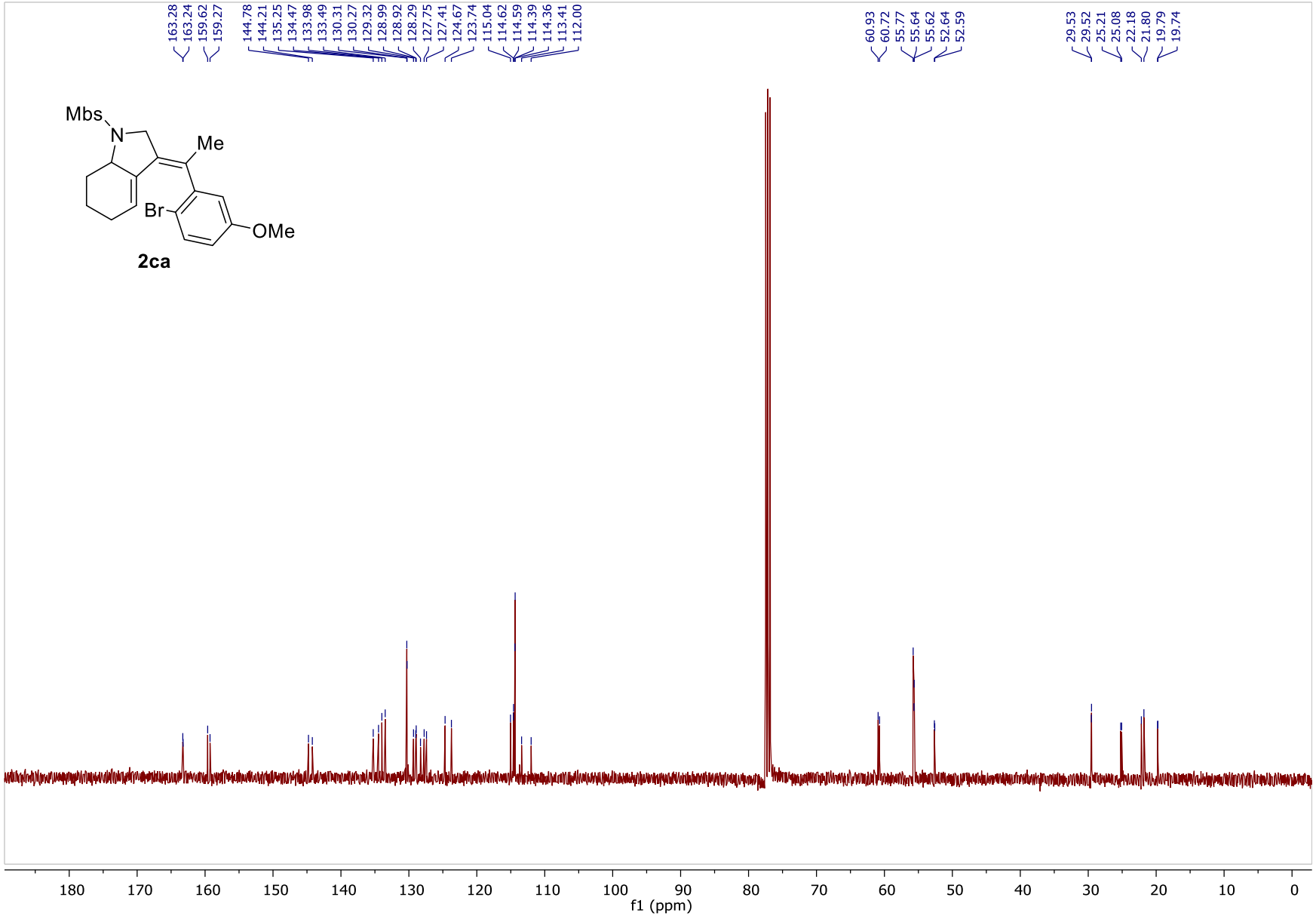
f1 (ppm)


Mbs
N
Me
Br
OMe
2ca
f1 (ppm)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129.32
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128.92
128.29
127.75
127.41
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123.74
115.04
114.62
114.59
114.39
114.36
113.41
112.00
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60.72
55.77
55.64
55.62
52.64
52.59
29.53
29.52
25.21
25.08
22.18
21.80
19.79
19.74
Mbs
N
Me
Br
OMe
2ca
180
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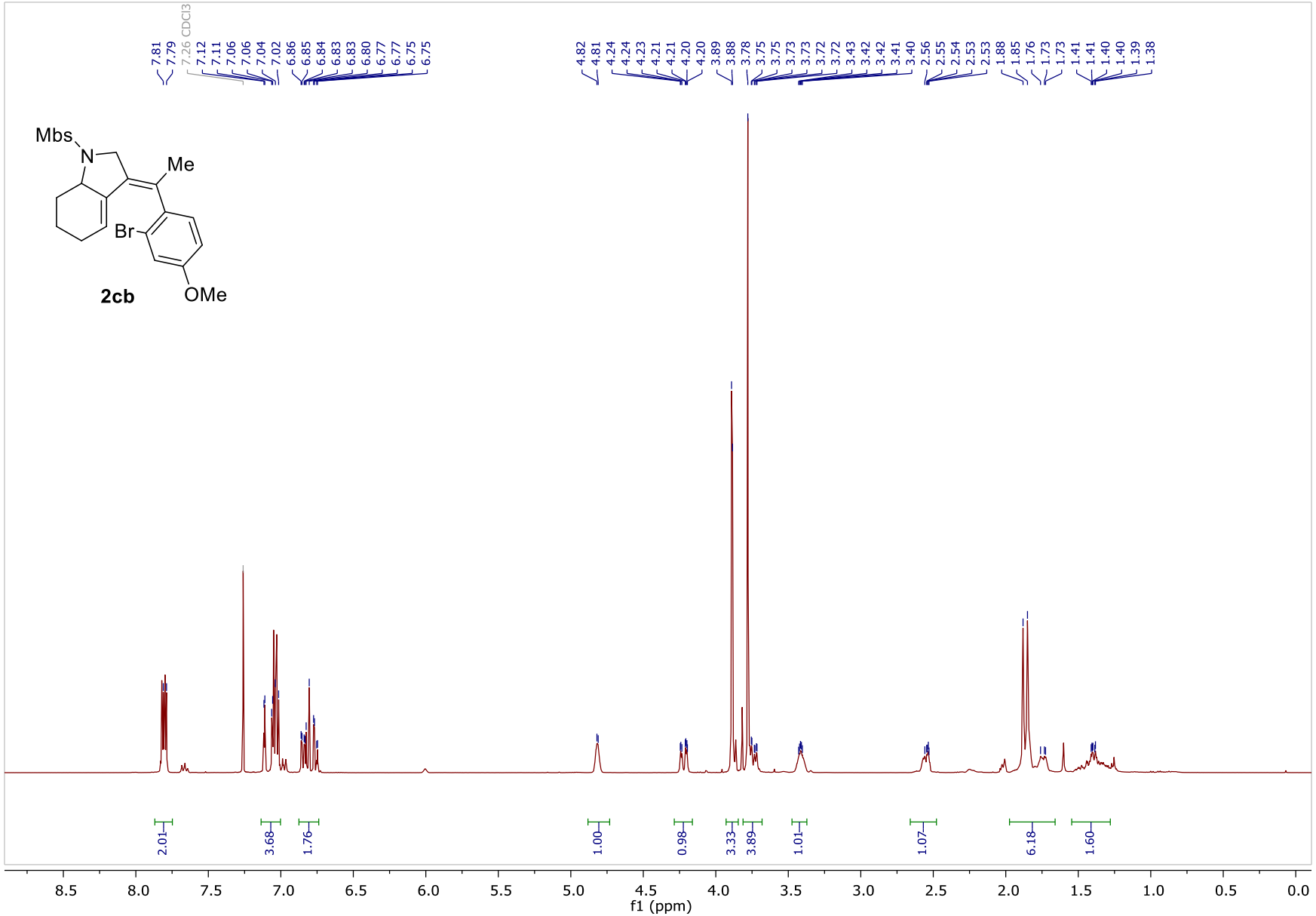
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.02
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6.83
6.80
6.77
6.75
6.75
4.82
4.81
4.24
4.24
4.23
4.21
4.21
4.20
4.20
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3.78
3.75
3.75
3.73
3.73
3.72
3.72
3.43
3.42
3.42
3.41
3.40
2.56
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2.54
2.53
2.53
1.88
1.85
1.76
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1.73
1.41
1.41
1.40
1.40
1.39
1.38
Mbs
N
Me
Br
OMe
2cb
2.01
3.68
1.76
1.00
0.98
3.33
3.89
1.01
1.07
6.18
1.60
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.0
2.5
2.0
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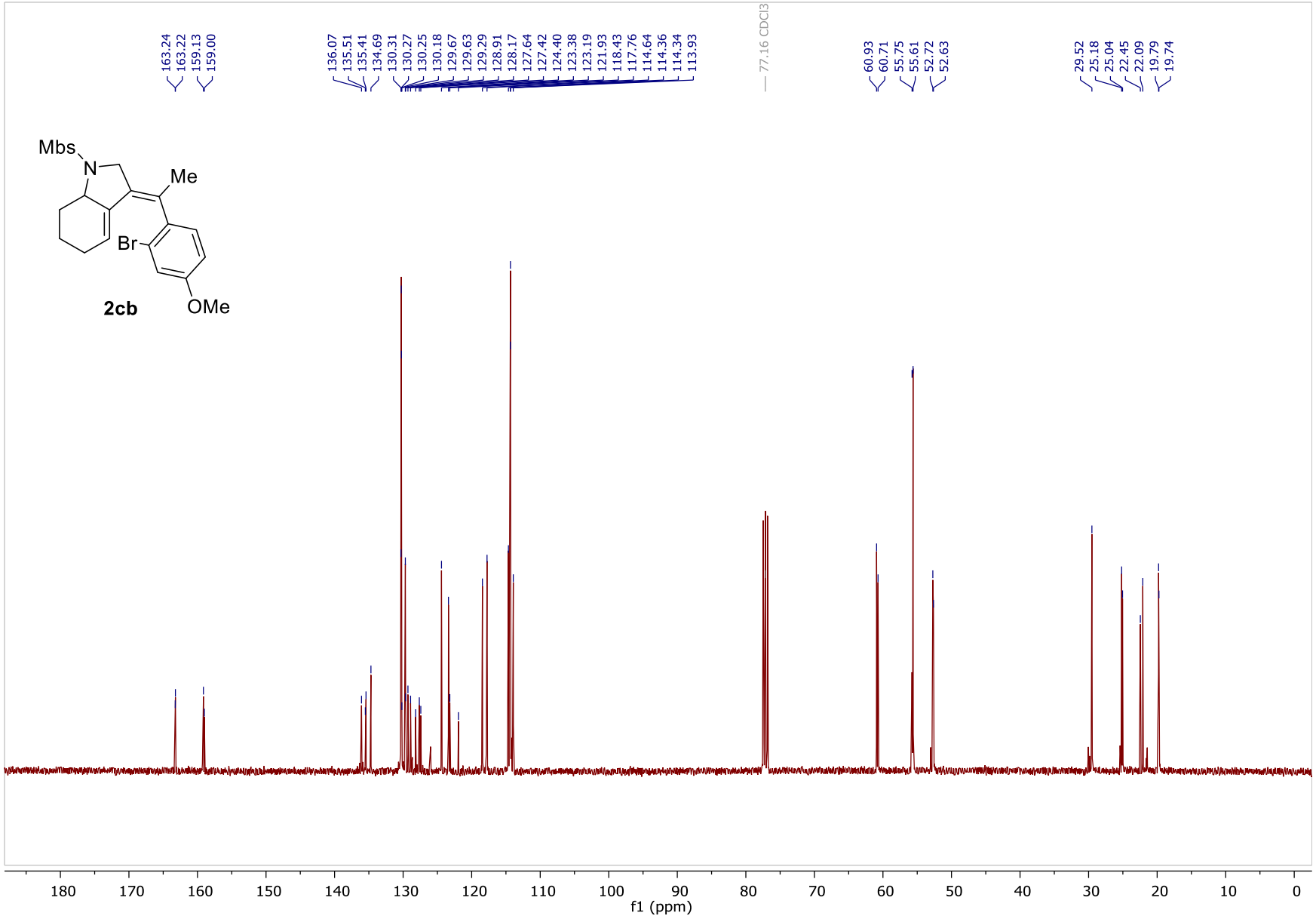
1.0
0.5
0.0
f1 (ppm)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130.18
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129.29
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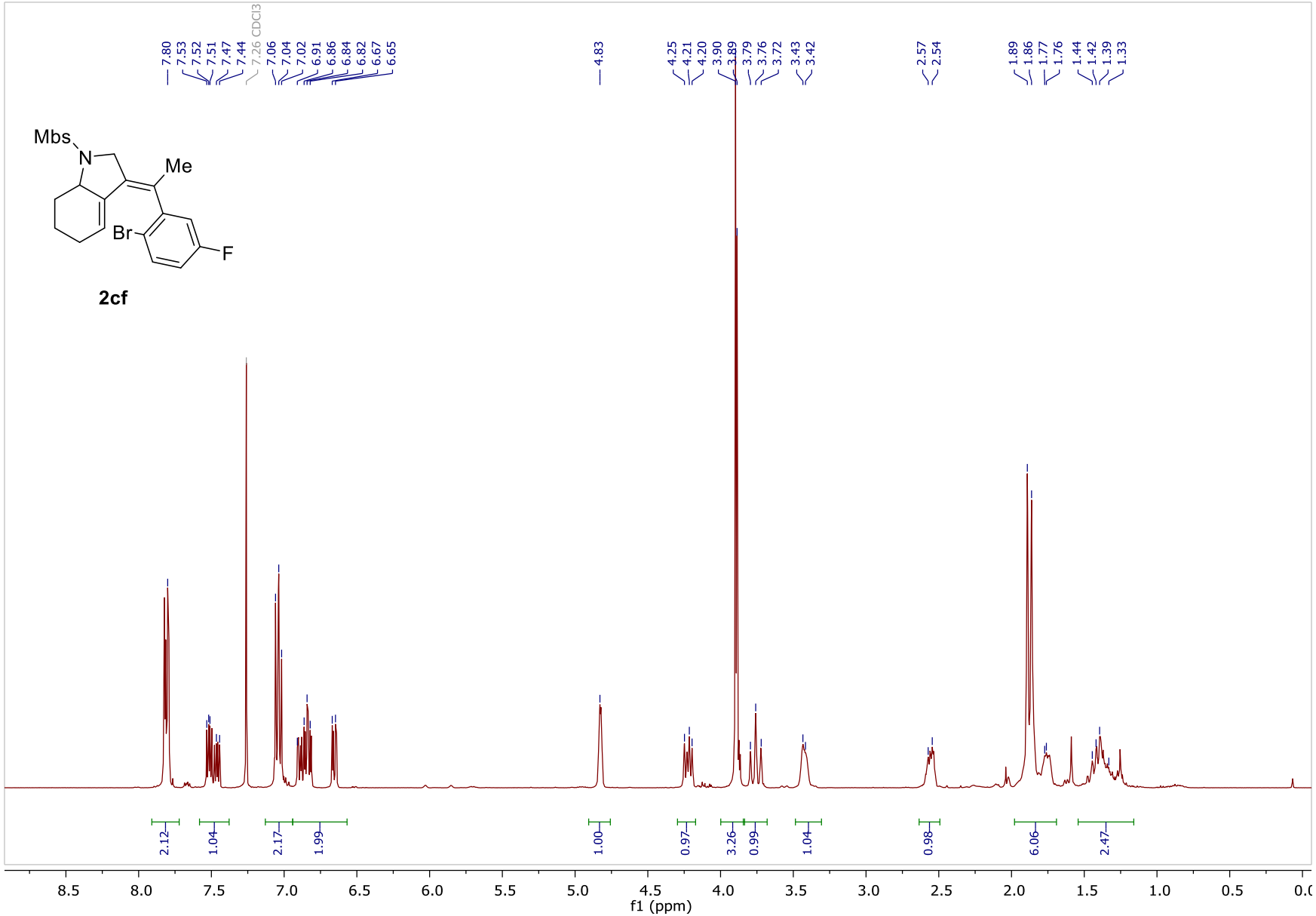
128.17
127.64
127.42
124.40
123.38
123.19
121.93
118.43
117.76
114.64
114.36
114.34
113.93
77.16 CDCl3
60.93
60.71
55.75
55.61
52.72
52.63
29.52
25.18
25.04
22.45
22.09
19.79
19.74
Mbs
N
Me
Br
OMe
2cb
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.53
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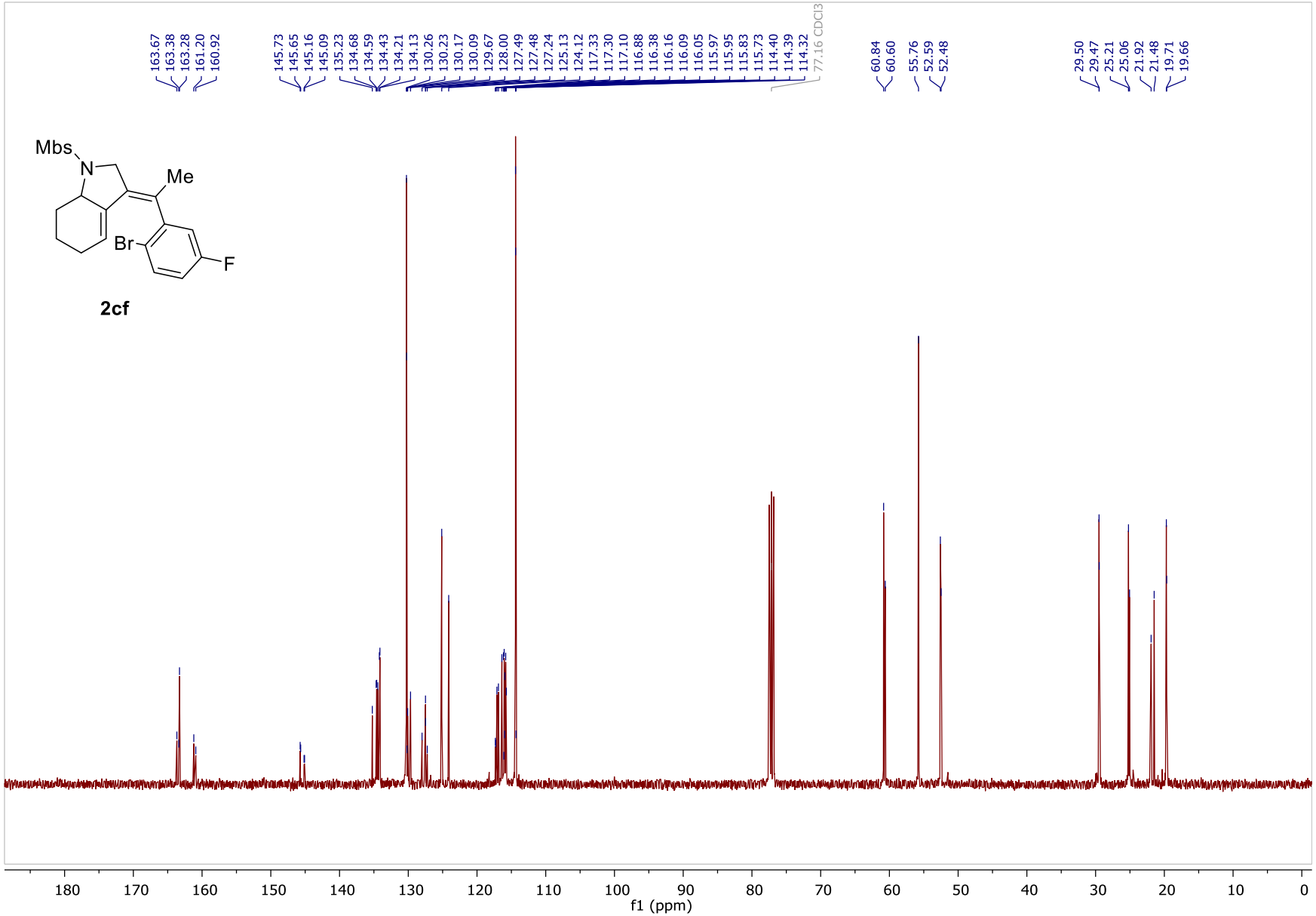
7.04
7.02
6.91
6.86
6.84
6.82
6.67
6.65
4.83
4.25
4.21
4.20
3.90
3.89
3.79
3.76
3.72
3.43
3.42
2.57
2.54
1.89
1.86
1.77
1.76
1.44
1.42
1.39
1.33
Mbs
N
Me
Br
F
2cf
2.12
1.04
2.17
1.99
1.00
0.97
3.26
0.99
1.04
0.98
6.06
2.47
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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130.26
130.23
130.17
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127.48
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124.12
117.33
117.30
117.10
116.88
116.38
116.16
116.09
116.05
115.97
115.95
115.83
115.73
114.40
114.39
114.32
77.16 CDCl3
60.84
60.60
55.76
52.59
52.48
29.50
29.47
25.21
25.06
21.92
21.48
19.71
19.66
Mbs
N
Me
Br
F
2cf
180
170
160
150
140
130
120
110
100
90
80
70
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50
40
30
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10
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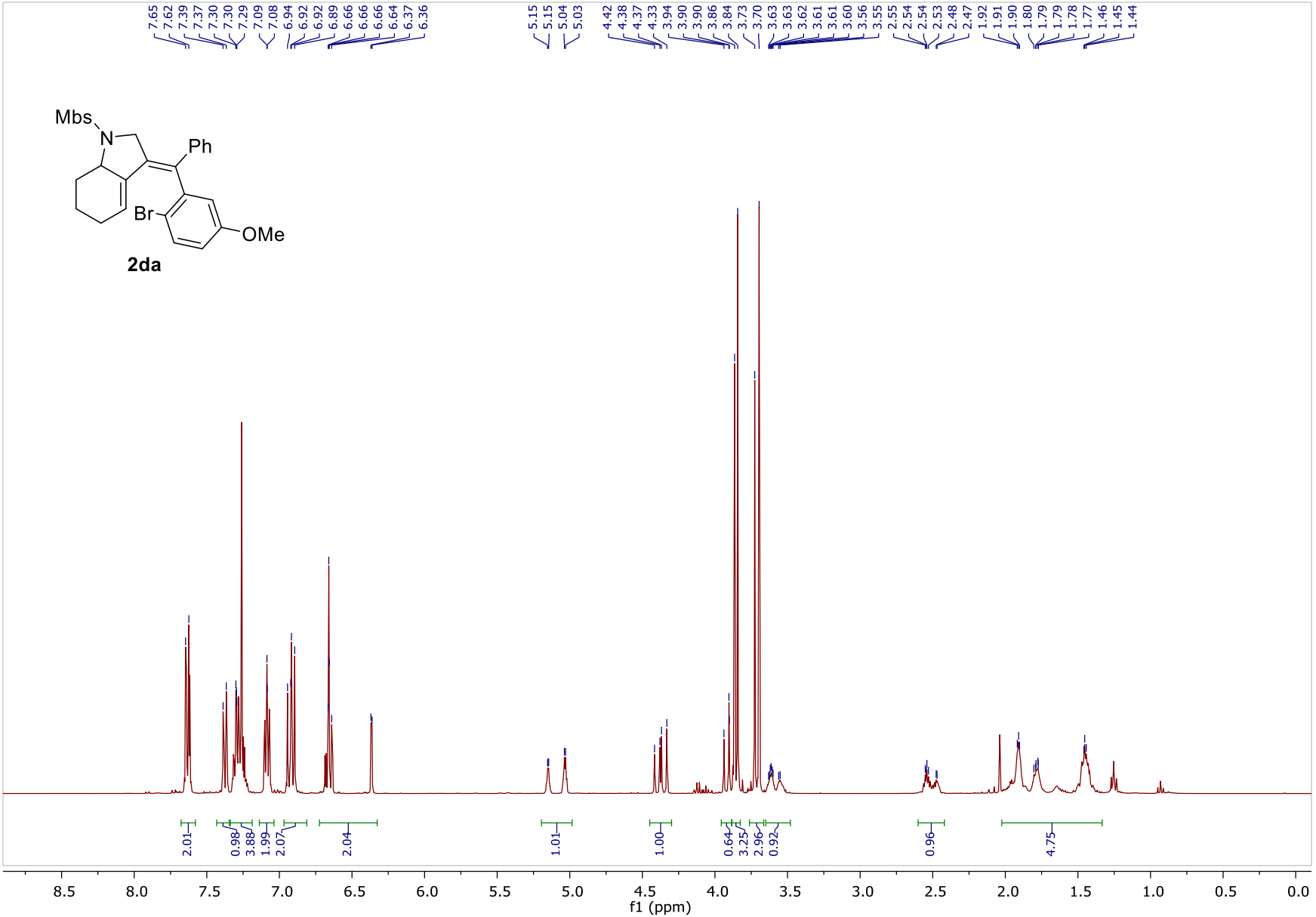
f1 (ppm)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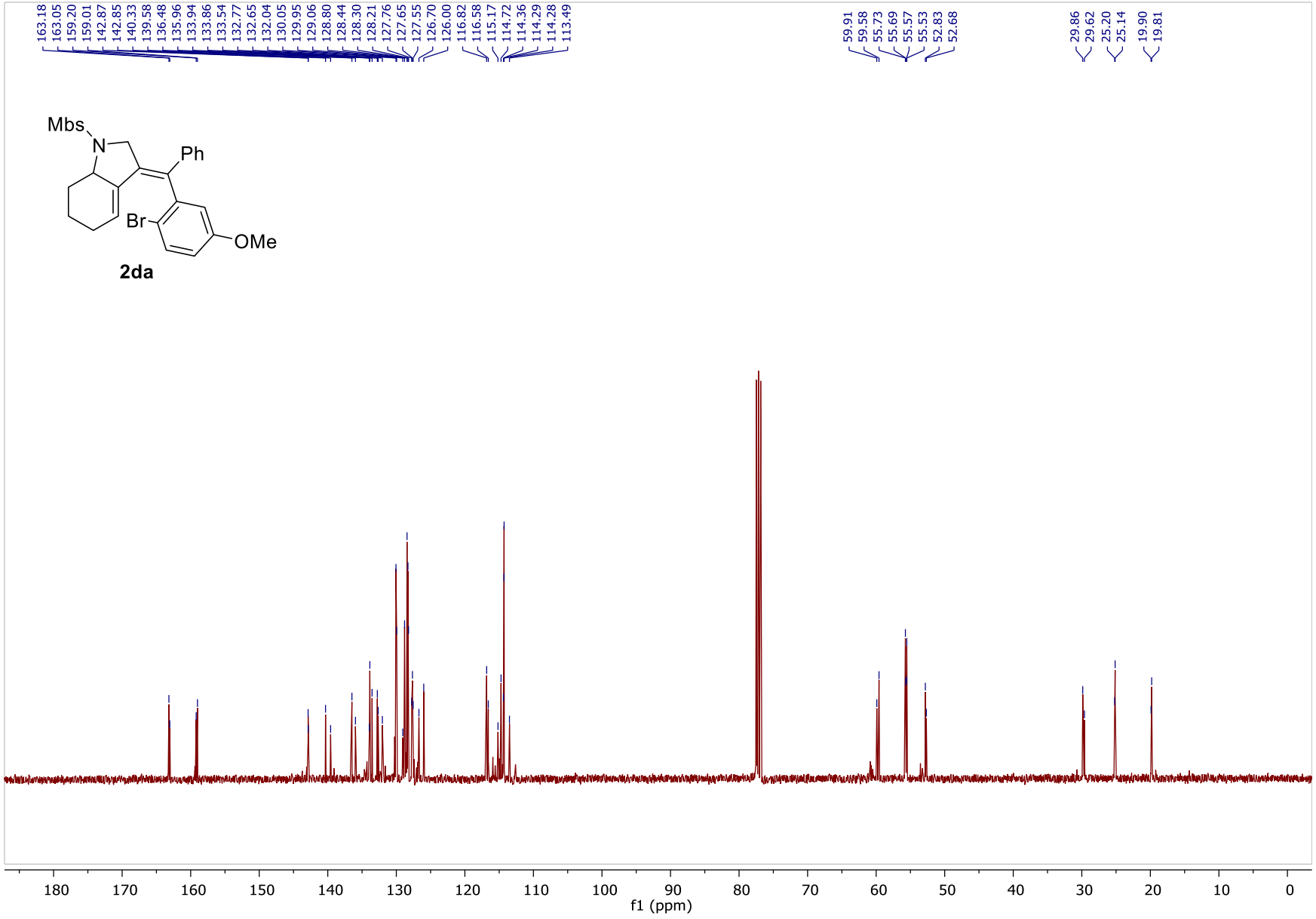
5.15 5.15 5.04 5.03
4.42 4.38 4.37 4.33 3.94 3.90 3.90 3.86 3.84 3.73 3.70 3.63 3.63 3.62 3.61 3.61 3.60 3.56 3.55
2.55 2.54 2.54 2.53 2.48 2.47
1.92 1.91 1.90 1.80 1.79 1.79 1.78 1.77 1.46 1.45 1.44
Mbs
N
Ph
Br
OMe
2da
2.01 0.98 3.88 1.99 2.07 2.04 1.01 1.00 0.64 3.25 2.96 0.92 0.96 4.75
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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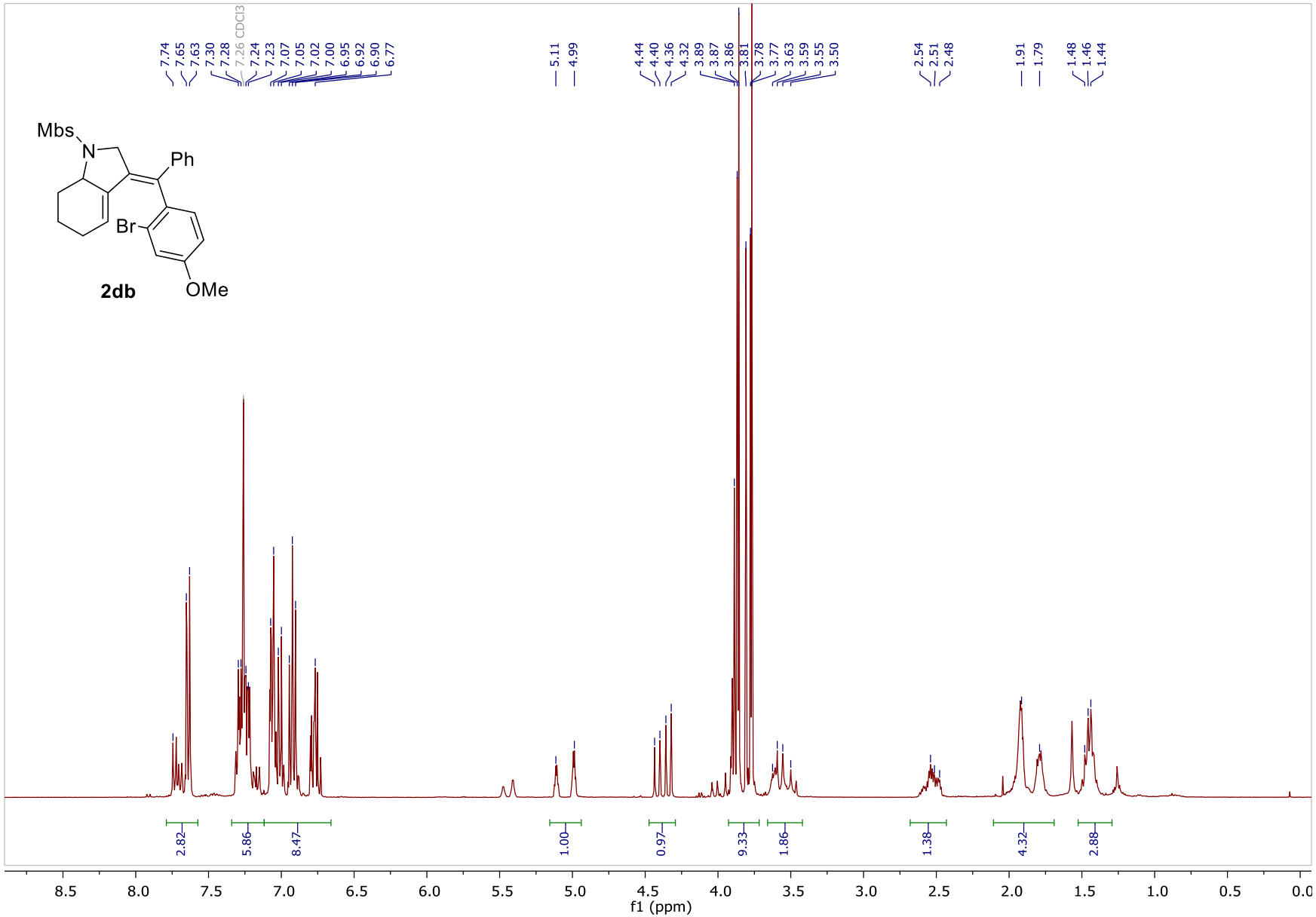
135.96
133.94
133.86
133.54
132.77
132.65
132.04
130.05
129.95
129.06
128.80
128.44
128.30
128.21
127.76
127.65
127.55
126.70
126.00
116.82
116.58
115.17
114.72
114.36
114.29
114.28
113.49
59.91
59.58
55.73
55.69
55.57
55.53
52.83
52.68
29.86
29.62
25.20
25.14
19.90
19.81
Mbs
N
Ph
Br
OMe
2da
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.30
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7.23
7.07
7.05
7.02
7.00
6.95
6.92
6.90
6.77
5.11
4.99
4.44
4.40
4.36
4.32
3.89
3.87
3.86
3.81
3.78
3.77
3.63
3.59
3.55
3.50
2.54
2.51
2.48
1.91
1.79
1.48
1.46
1.44
Mbs
N
Ph
Br
OMe
2db
2.82
5.86
8.47
1.00
0.97
9.33
1.86
1.38
4.32
2.88
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
2.5
2.0
1.5
1.0
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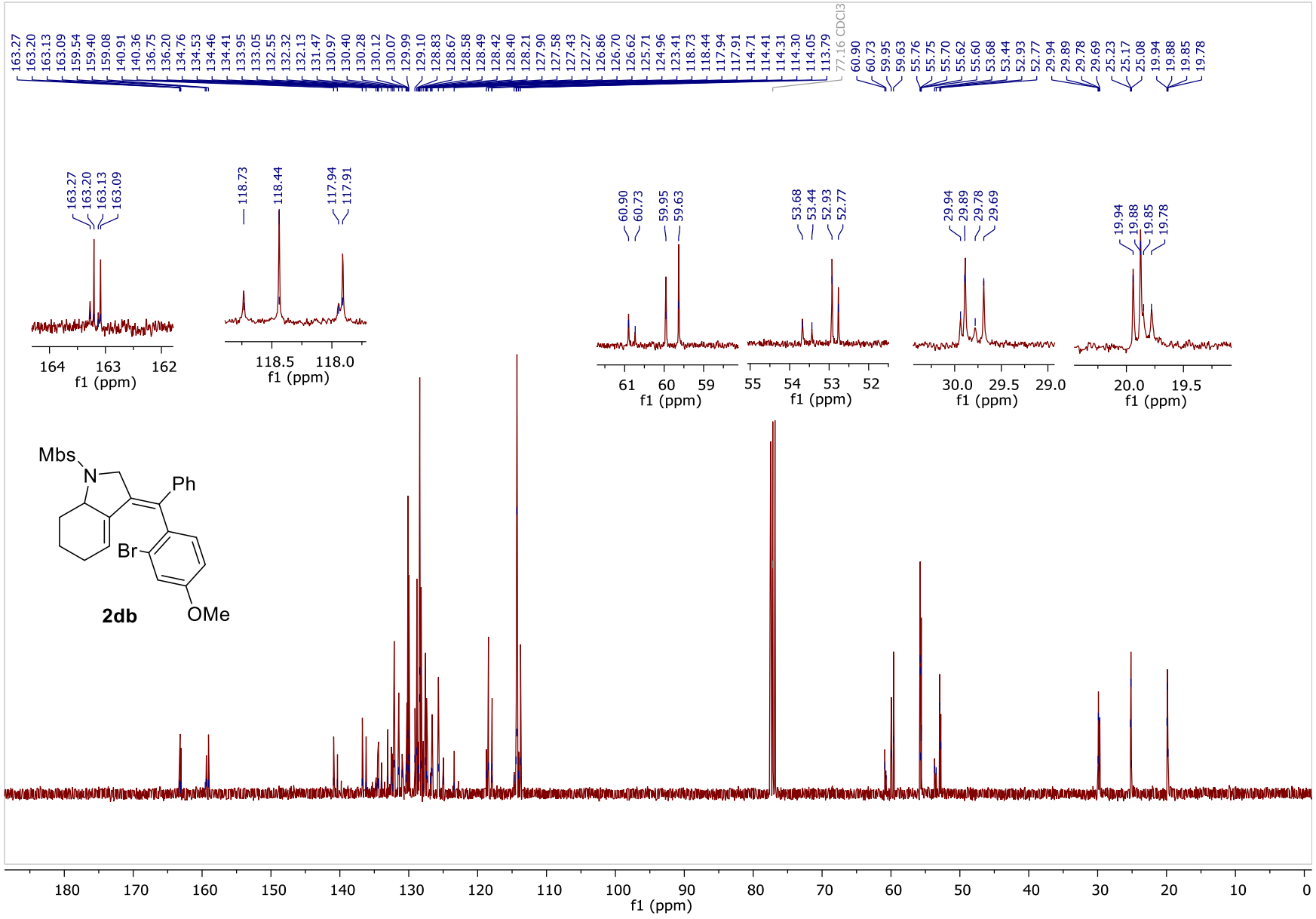
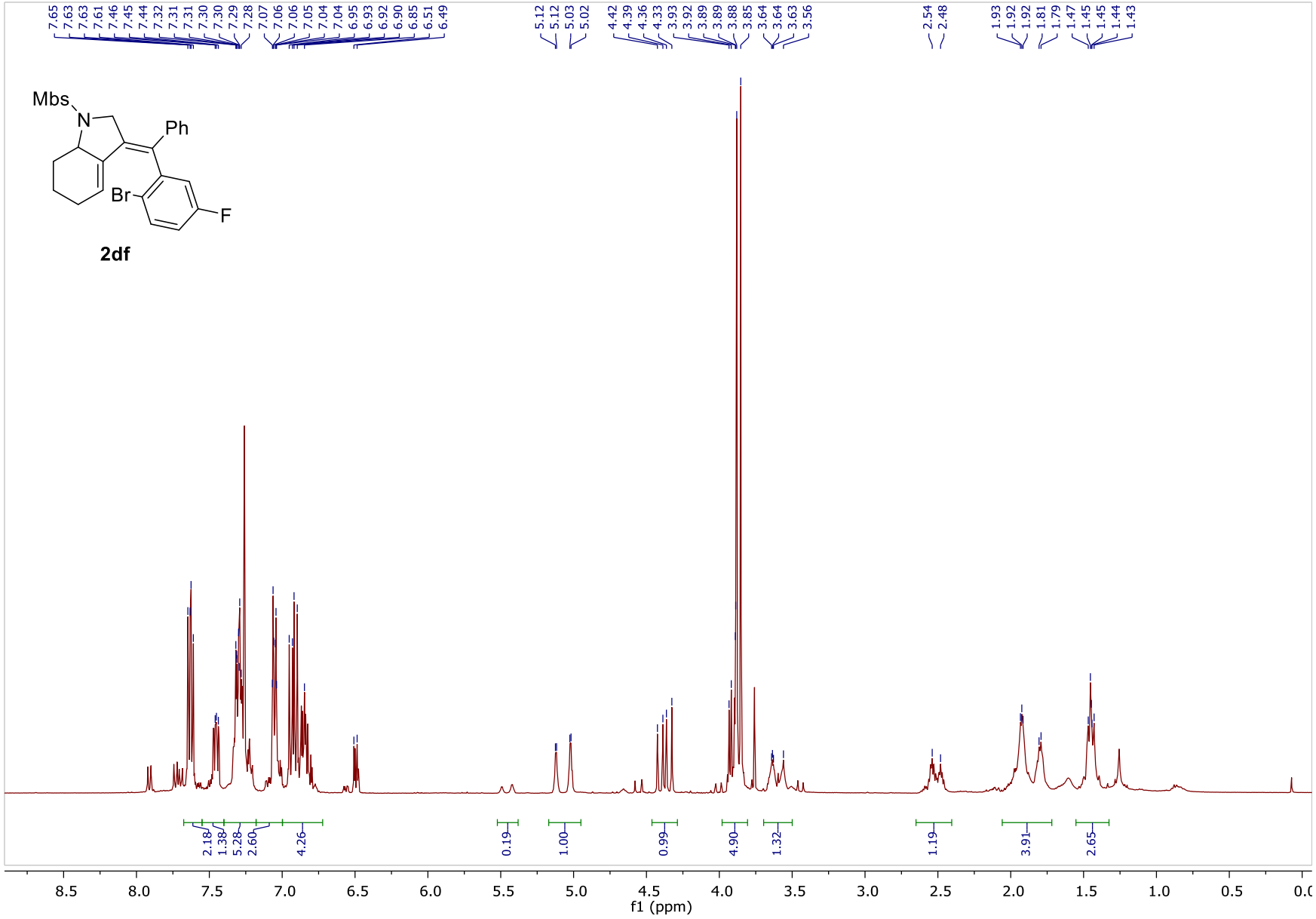
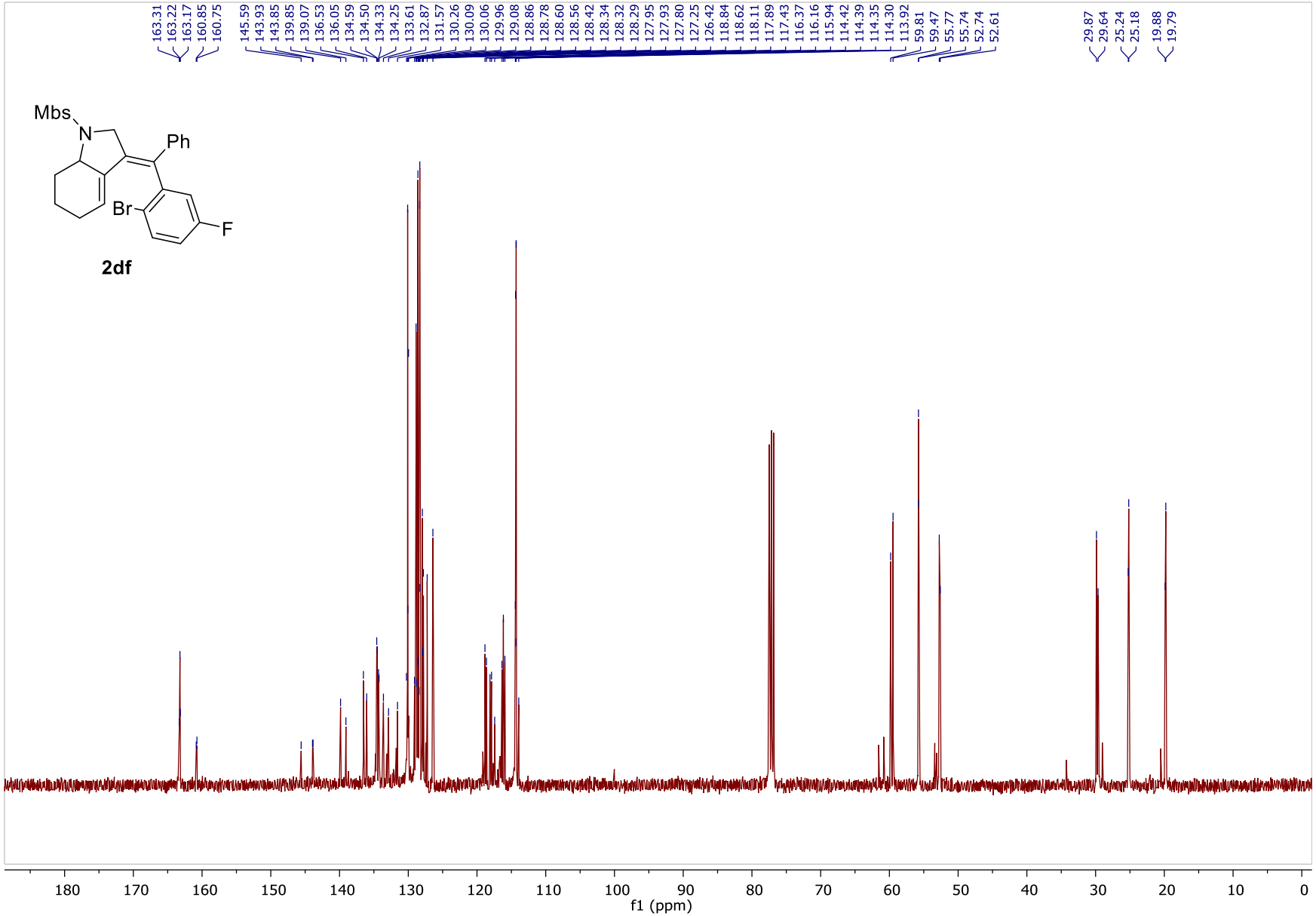
0.0
f1 (ppm)


163.27 163.20 163.13 163.09 159.54 159.40 159.08 140.91 140.36 136.75 136.20 134.76 134.53 134.46 134.41 133.95 133.05 132.55 132.32 132.13 131.47 130.97 130.40 130.28 130.12 130.07 129.99 129.10 128.83 128.67 128.58 128.49 128.42 128.40 128.21 127.90 127.58 127.43 127.27 126.86 126.70 126.62 125.71 124.96 123.41 118.73 118.44 117.94 117.91 114.71 114.41 114.31 114.30 114.05 113.79 77.16 CDCl3 60.90 60.73 59.95 59.63 55.76 55.75 55.70 55.62 55.60 53.68 53.44 52.93 52.77 29.94 29.89 29.78 29.69 25.23 25.17 25.08 19.94 19.88 19.85 19.78
f1 (ppm)
Mbs
N
Ph
Br
OMe
2db


7.65 7.63 7.63 7.61 7.46 7.45 7.44 7.32 7.31 7.31 7.30 7.30 7.29 7.28 7.07 7.06 7.06 7.05 7.04 7.04 6.95 6.93 6.92 6.90 6.85 6.51 6.49
5.12 5.12 5.03 5.02
4.42 4.39 4.36 4.33 3.93 3.92 3.89 3.89 3.88 3.85 3.64 3.64 3.63 3.56
2.54 2.48
1.93 1.92 1.92 1.81 1.79 1.47 1.45 1.45 1.44 1.43
Mbs
N
Ph
Br
F
2df
2.18 1.38 5.28 2.60 4.26 0.19 1.00 0.99 4.90 1.32 1.19 3.91 2.65
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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134.59
134.50
134.33
134.25
133.61
132.87
131.57
130.26
130.09
130.06
129.96
129.08
128.86
128.78
128.60
128.56
128.42
128.34
128.32
128.29
127.95
127.93
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127.25
126.42
118.84
118.62
118.11
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117.43
116.37
116.16
115.94
114.42
114.39
114.35
114.30
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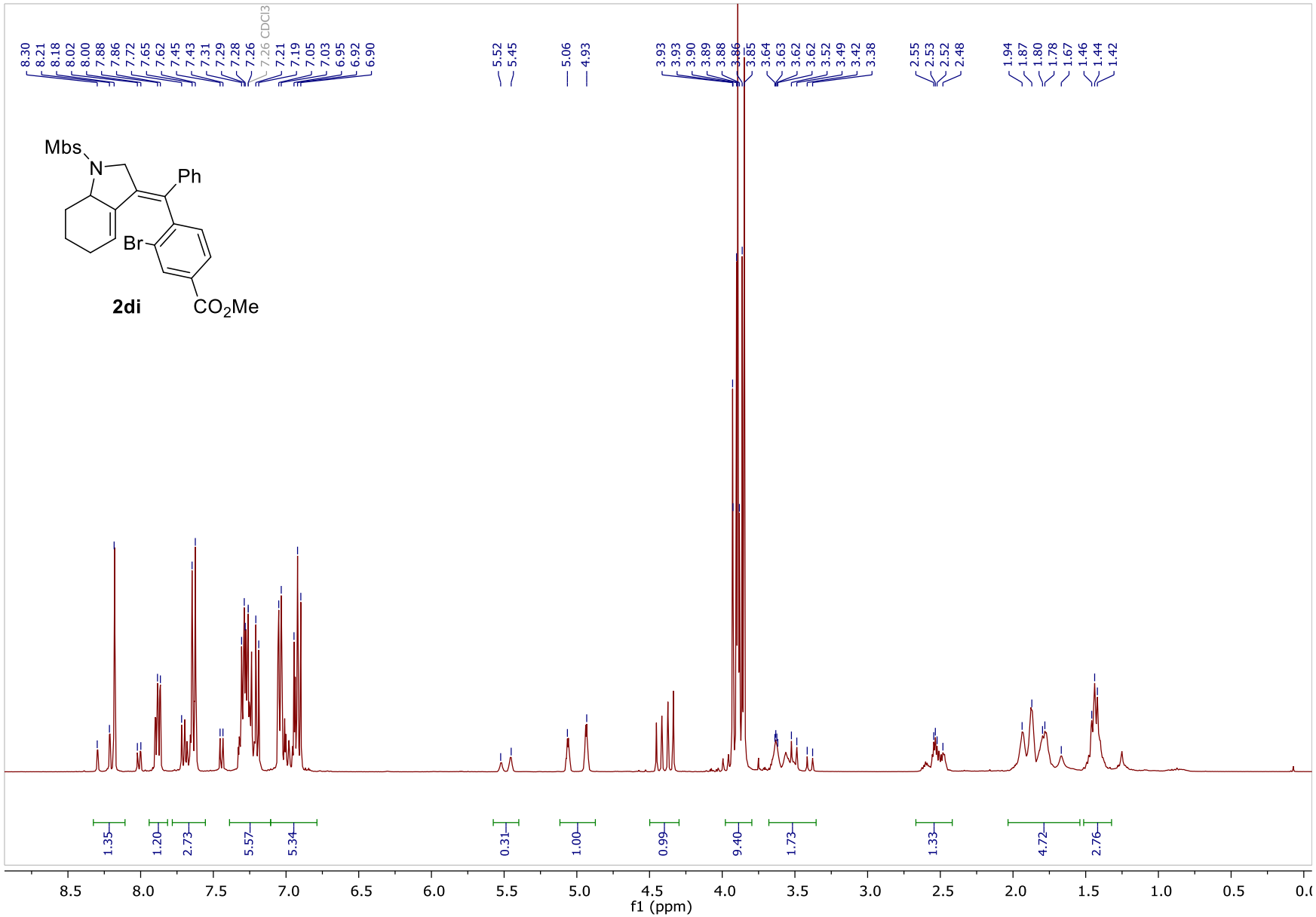
29.64
25.24
25.18
19.88
19.79
Mbs
N
Ph
Br
F
2df
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.86
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7.62
7.45
7.43
7.31
7.29
7.28
7.26
CDCl3
7.21
7.19
7.05
7.03
6.95
6.92
6.90
5.52
5.45
5.06
4.93
3.93
3.93
3.90
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3.86
3.85
3.64
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3.62
3.62
3.52
3.49
3.42
3.38
2.55
2.53
2.52
2.48
1.94
1.87
1.80
1.78
1.67
1.46
1.44
1.42
Mbs
N
Ph
Br
2di
CO2Me
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1.20
2.73
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5.34
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1.00
0.99
9.40
1.73
1.33
4.72
2.76
8.5
8.0
7.5
7.0
6.5
6.0
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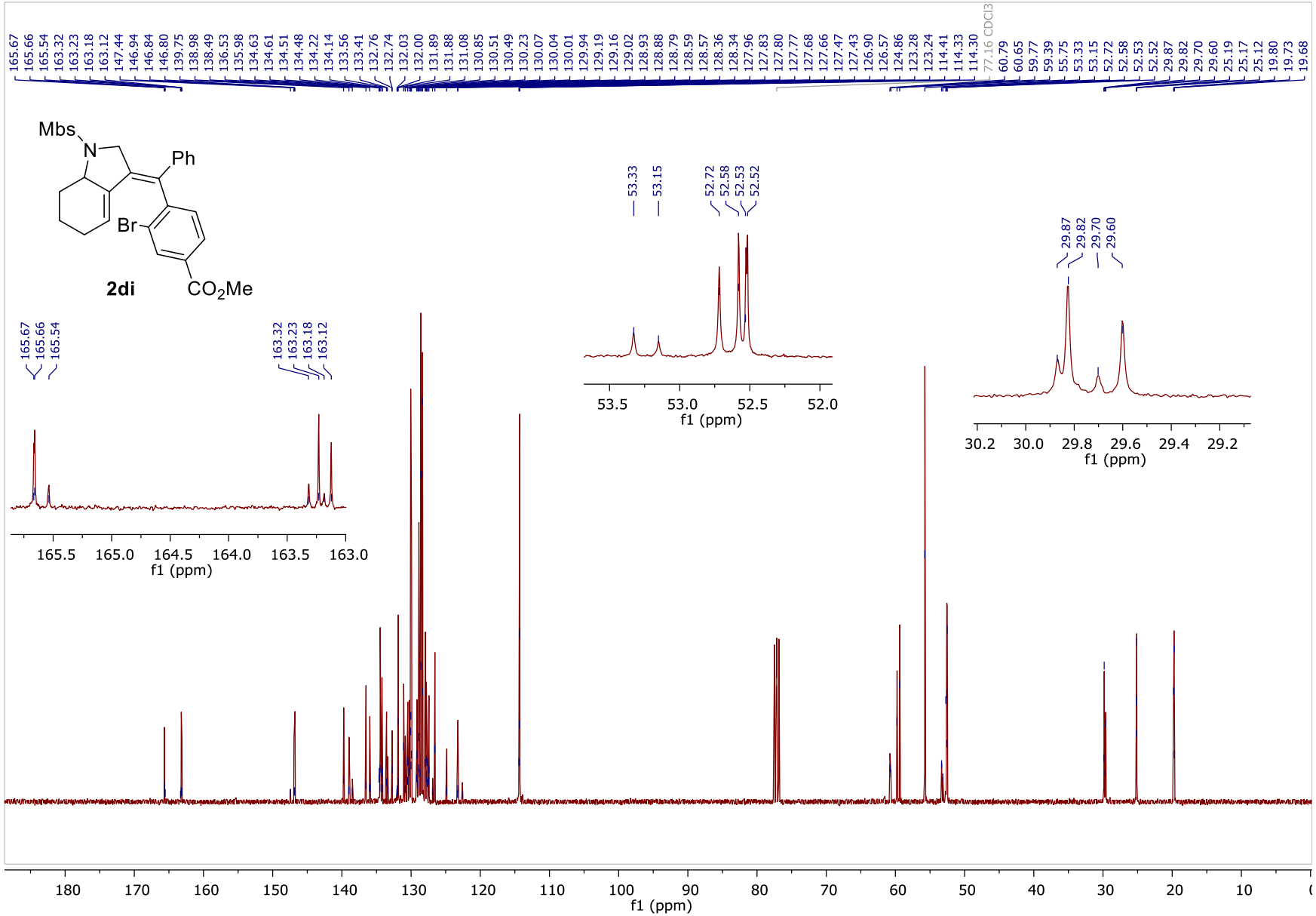
f1 (ppm)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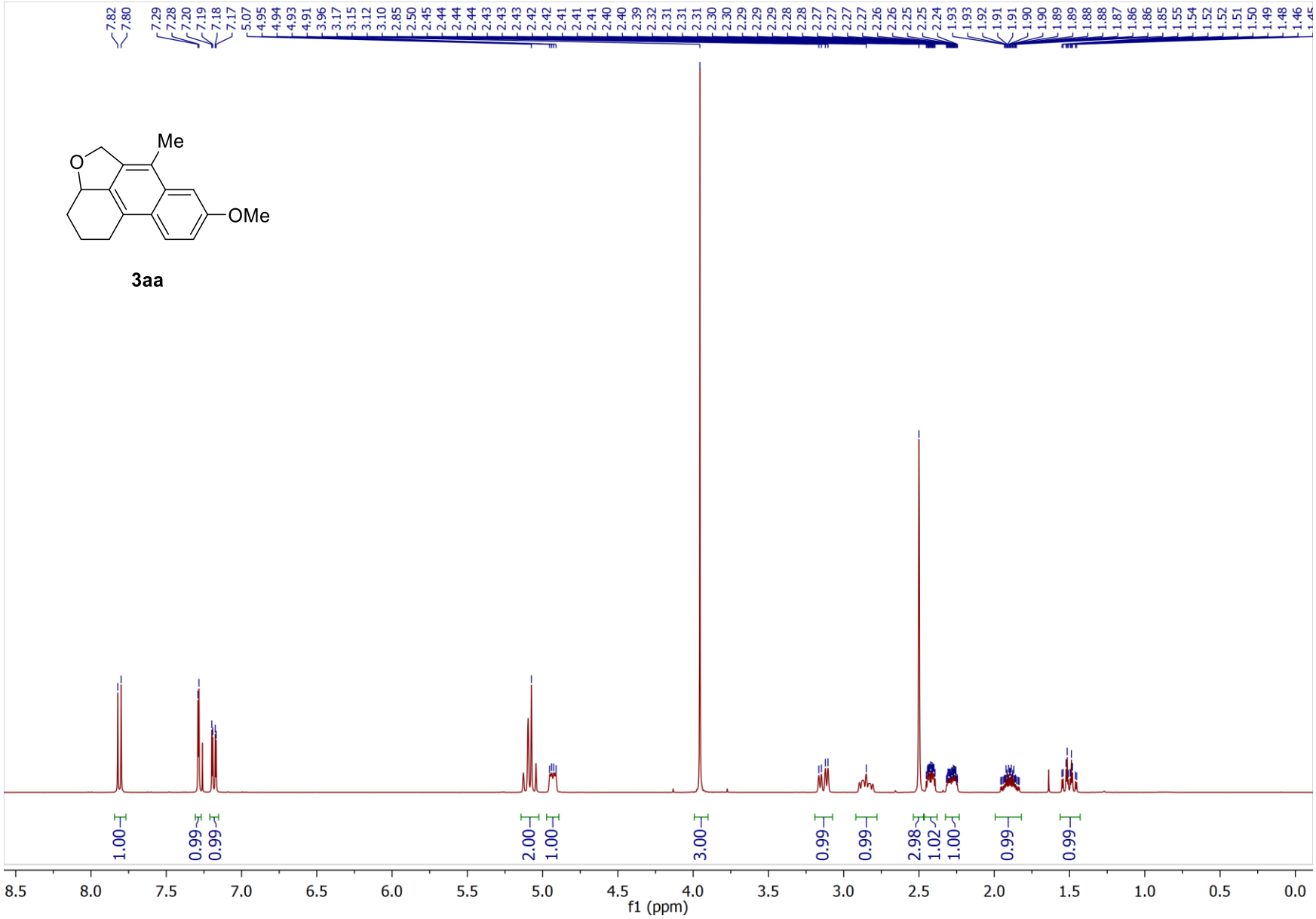
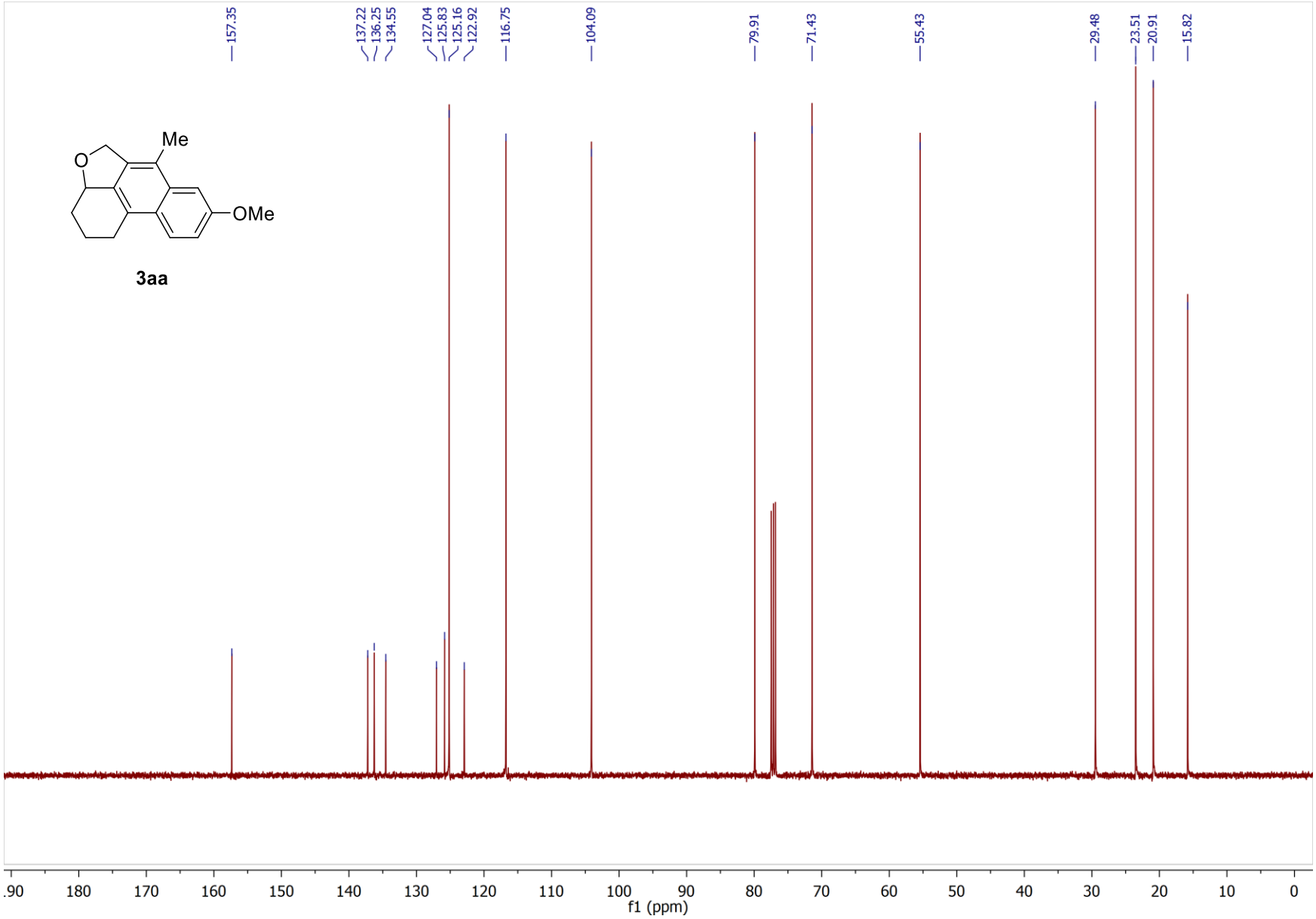
Ph
Br
2di
CO2Me
f1 (ppm)


Me
O
OMe
3aa
f1 (ppm)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122.92
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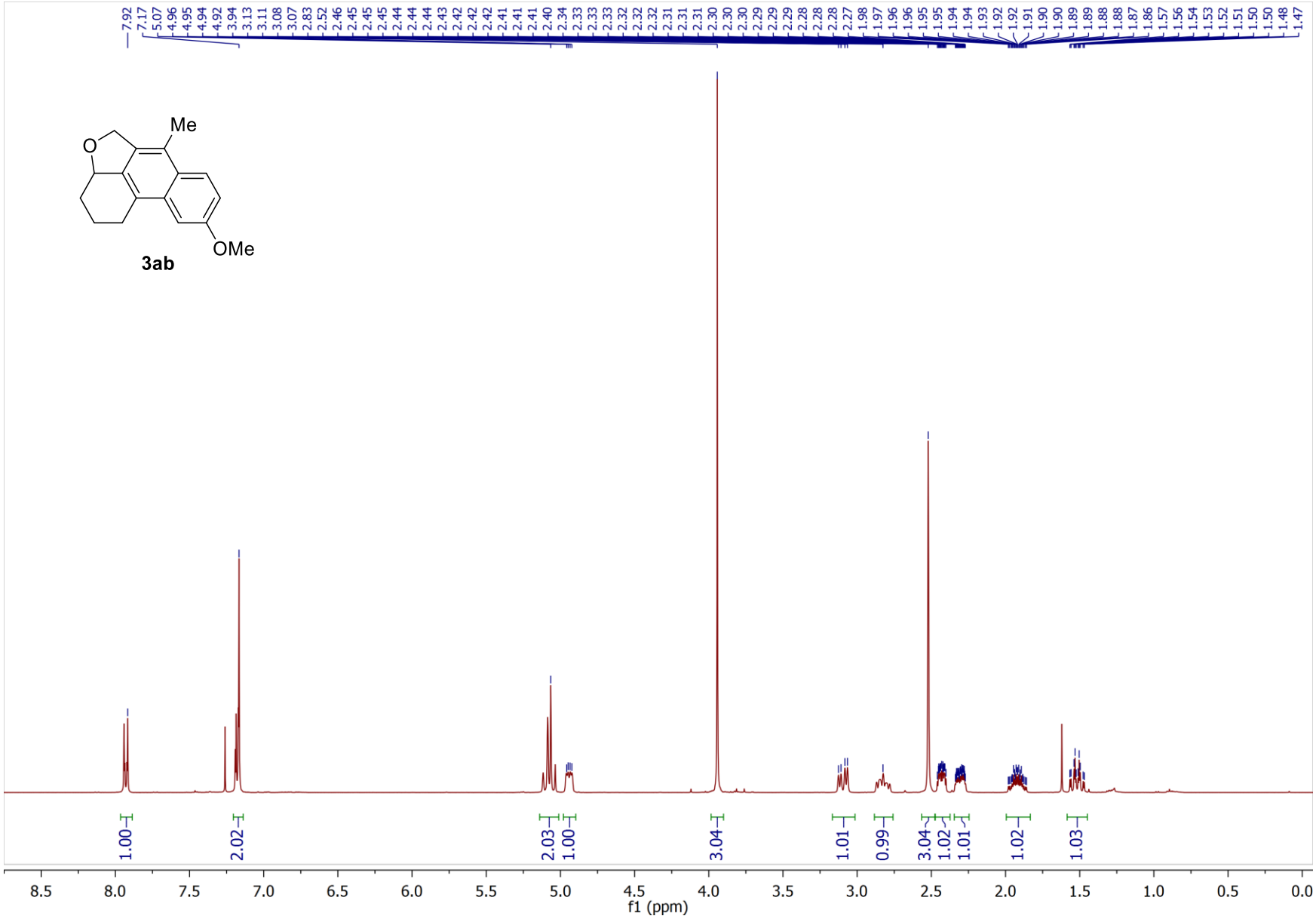
23.51
20.91
15.82
Me
O
OMe
3aa
f1 (ppm)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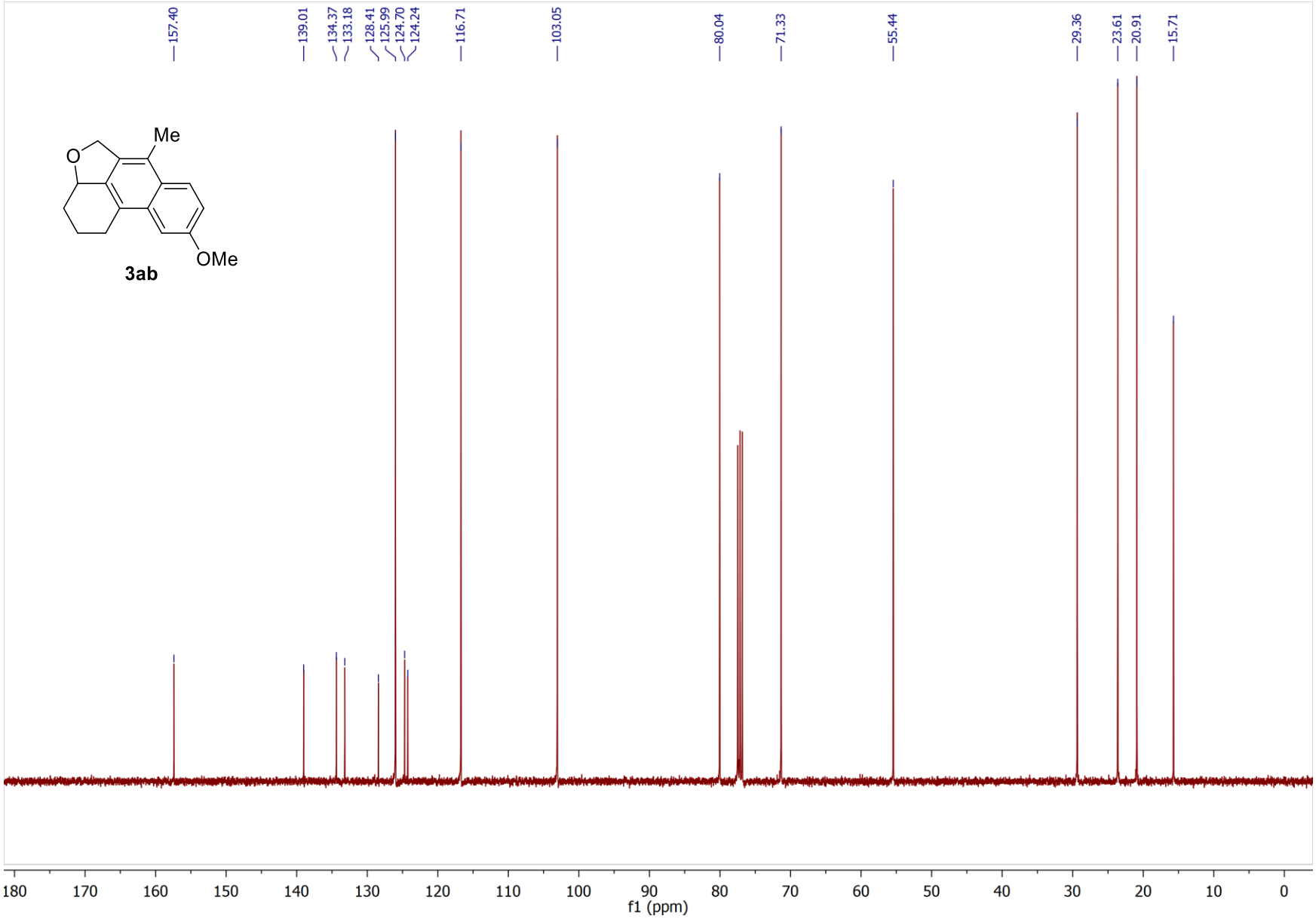
f1 (ppm)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124.70
124.24
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103.05
80.04
71.33
55.44
29.36
23.61
20.91
15.71
Me
O
OMe
3ab
180
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130
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110
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90
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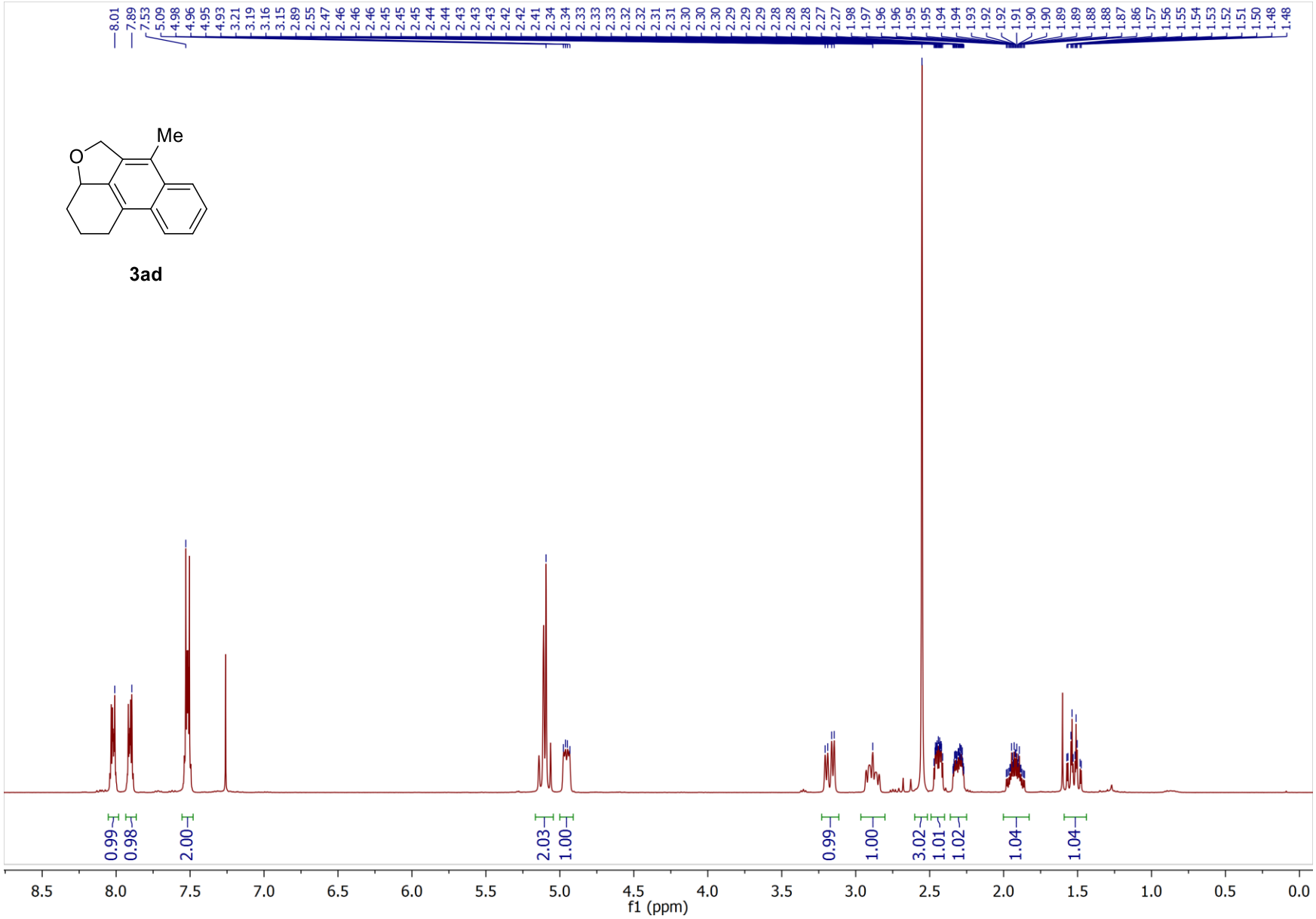
f1 (ppm)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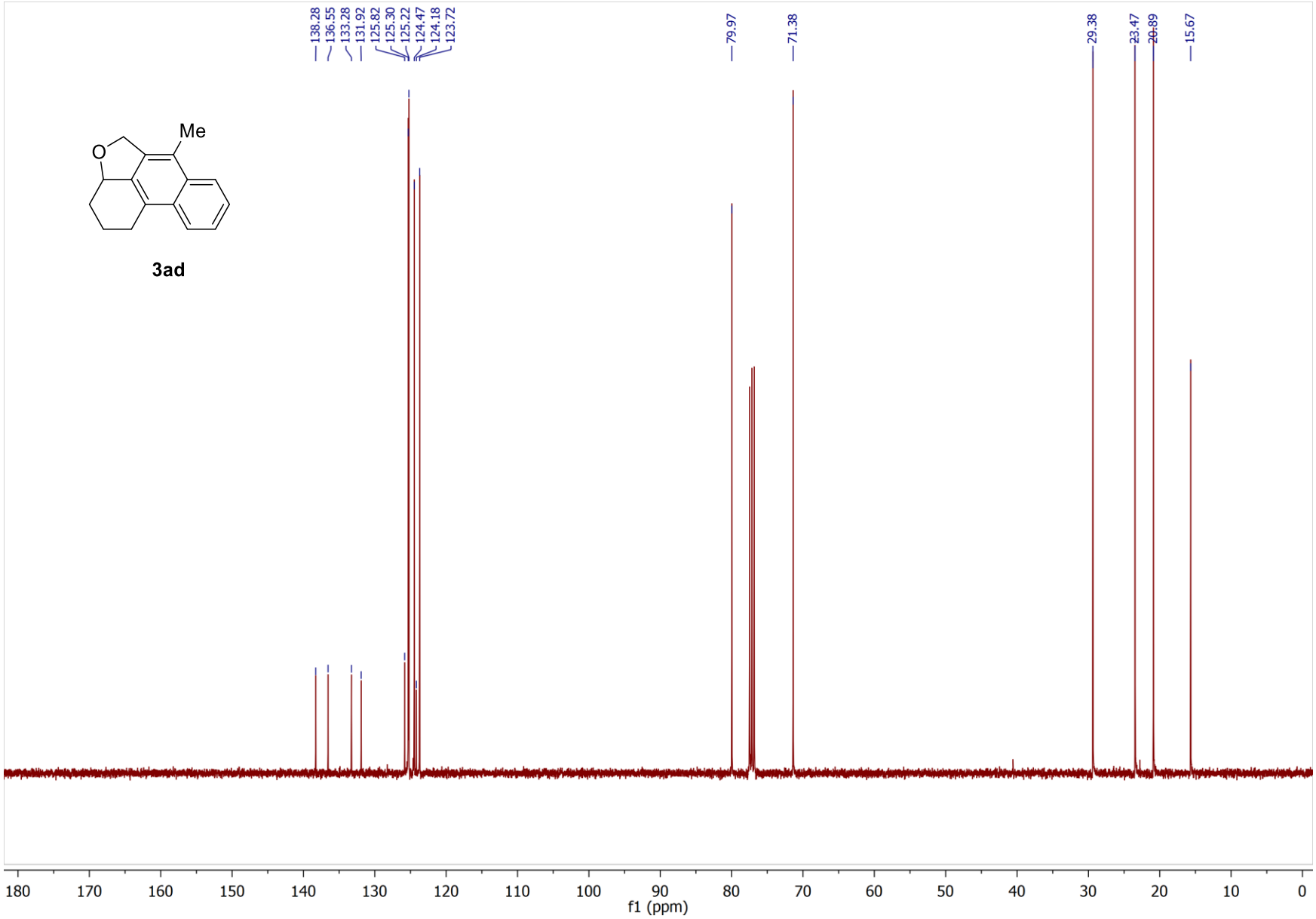
3ad
f1 (ppm)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123.72
79.97
71.38
29.38
23.47
20.89
15.67
Me
O
3ad
180
170
160
150
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130
120
110
100
90
80
70
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50
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30
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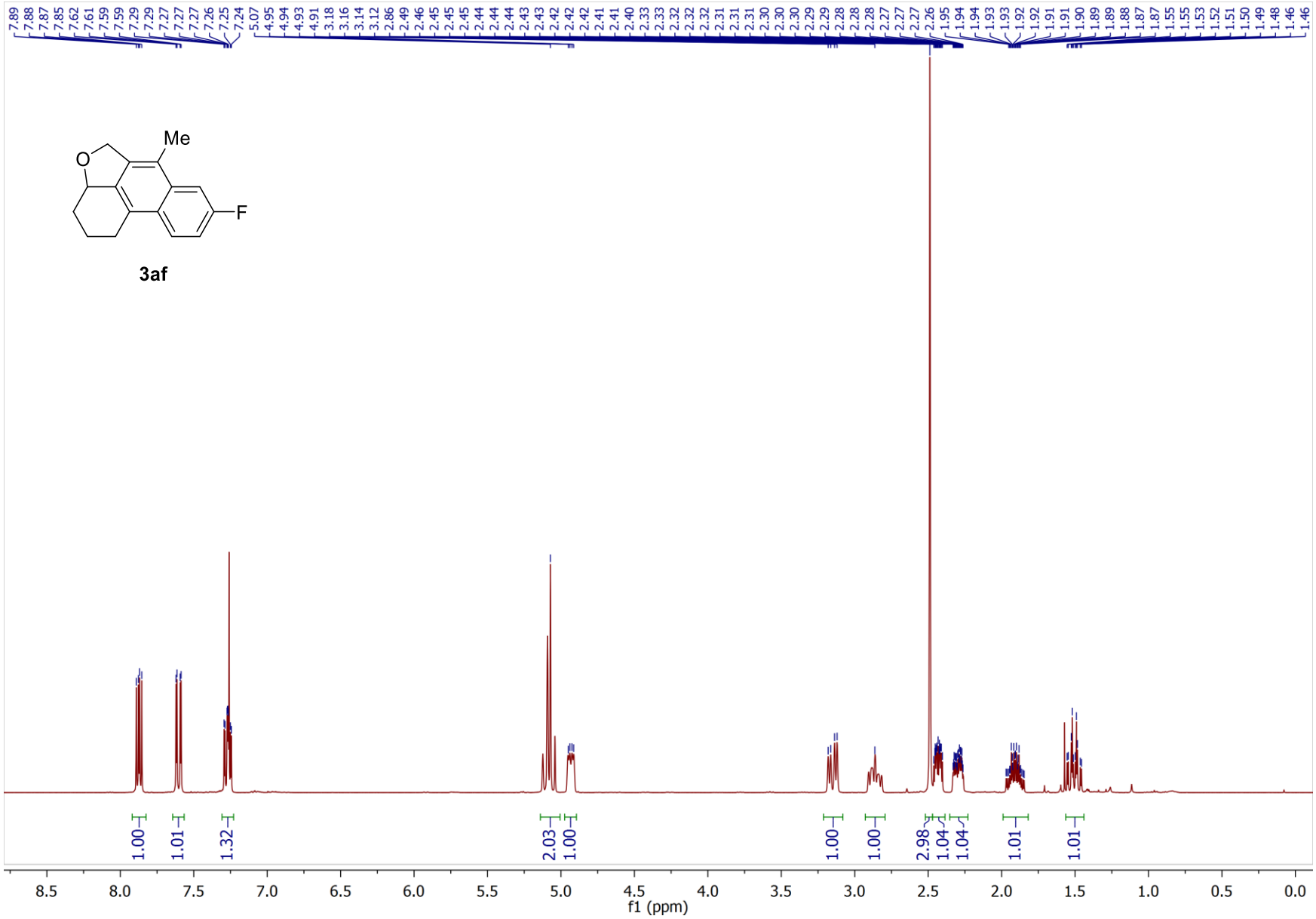
10
0
f1 (ppm)


Me
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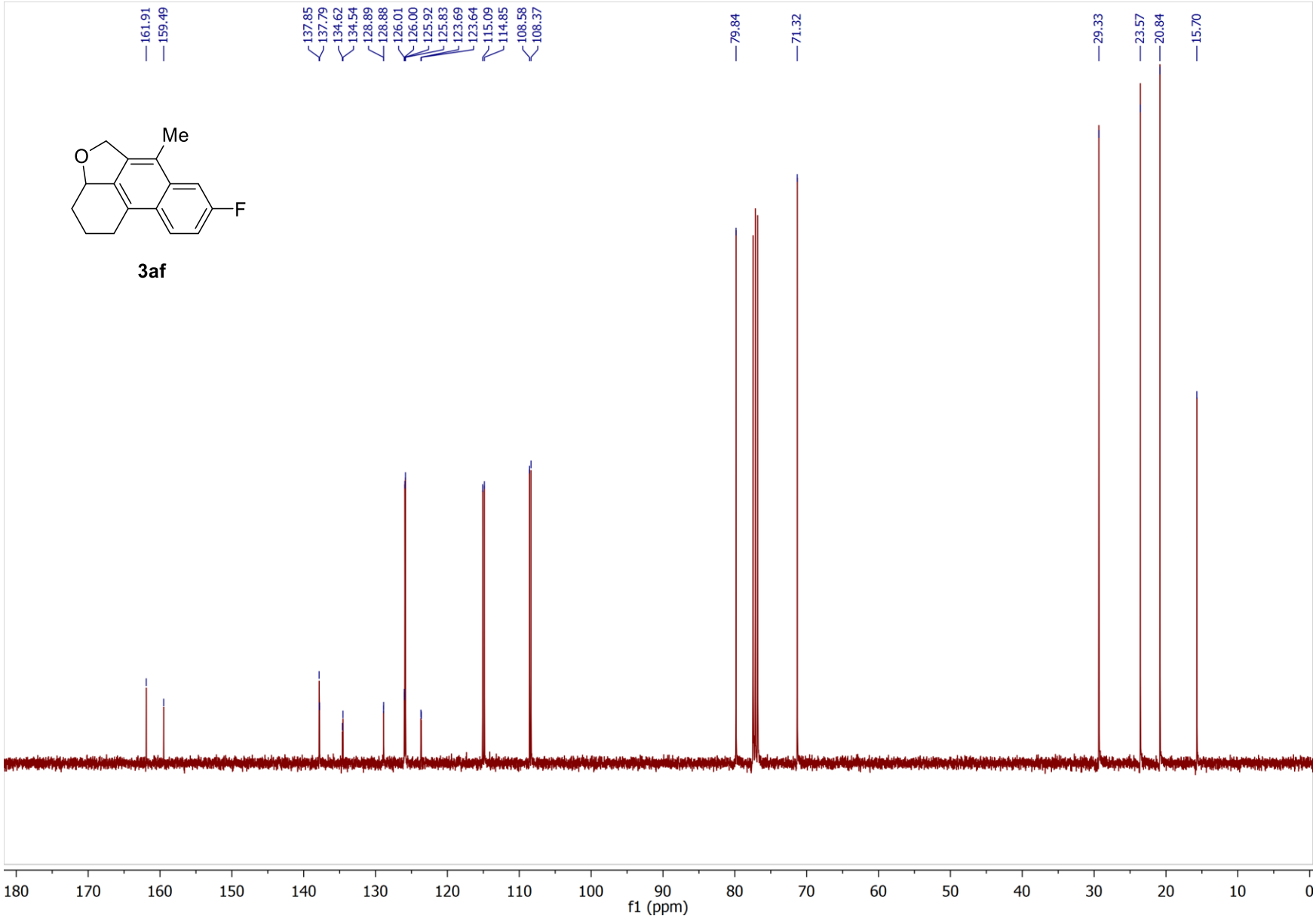
F
3af
f1 (ppm)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125.92
125.83
123.69
123.64
115.09
114.85
108.58
108.37
79.84
71.32
29.33
23.57
20.84
15.70
Me
O
F
3af
180
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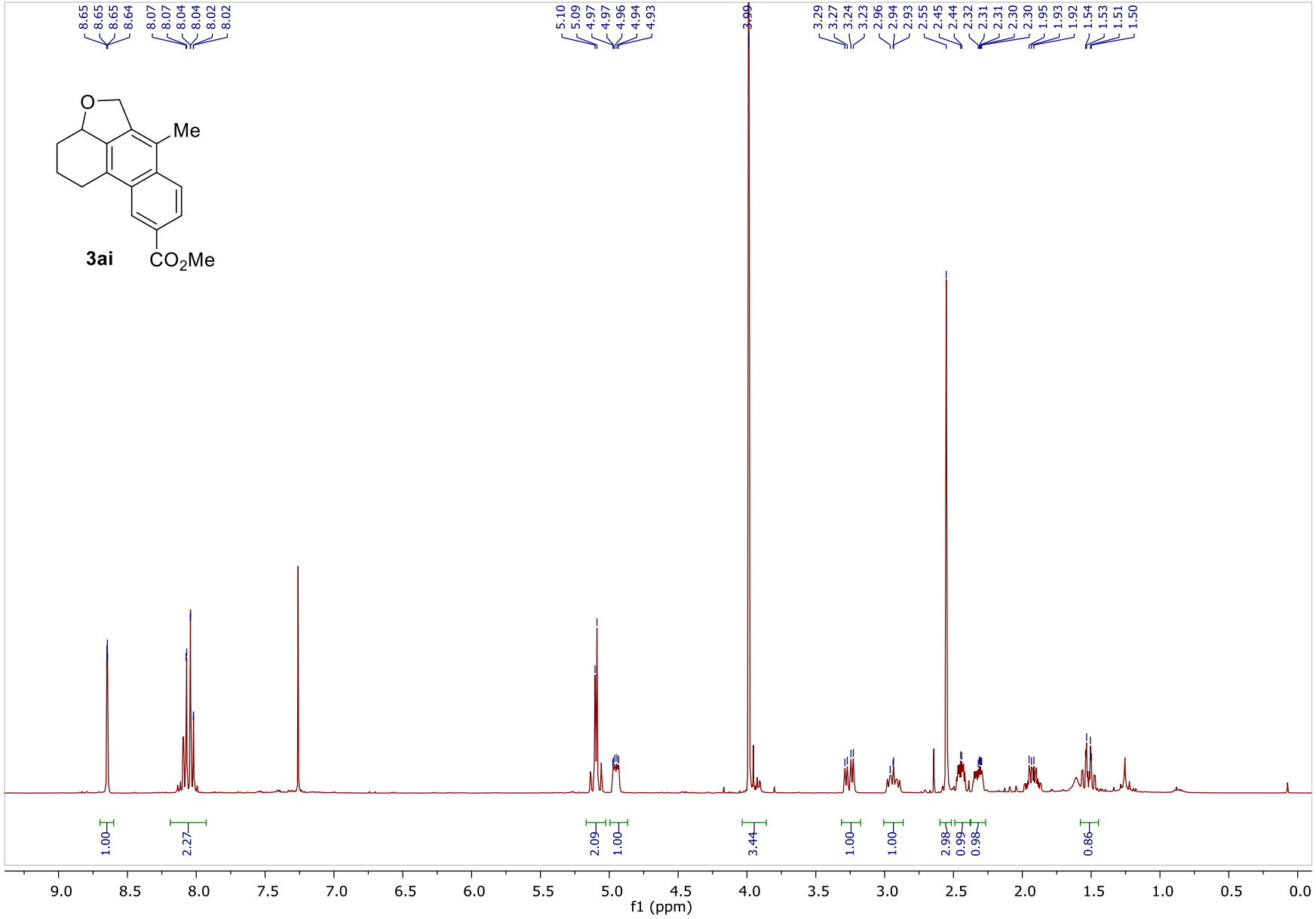
f1 (ppm)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8.07
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8.04
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8.02
5.10
5.09
4.97
4.97
4.96
4.94
4.93
3.99
3.29
3.27
3.24
3.23
2.96
2.94
2.93
2.55
2.45
2.44
2.32
2.31
2.31
2.30
2.30
1.95
1.93
1.92
1.54
1.53
1.51
1.50
O
Me
3ai
CO2Me
1.00
2.27
2.09
1.00
3.44
1.00
1.00
2.98
0.99
0.98
0.86
9.0
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8.0
7.5
7.0
6.5
6.0
5.5
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2.5
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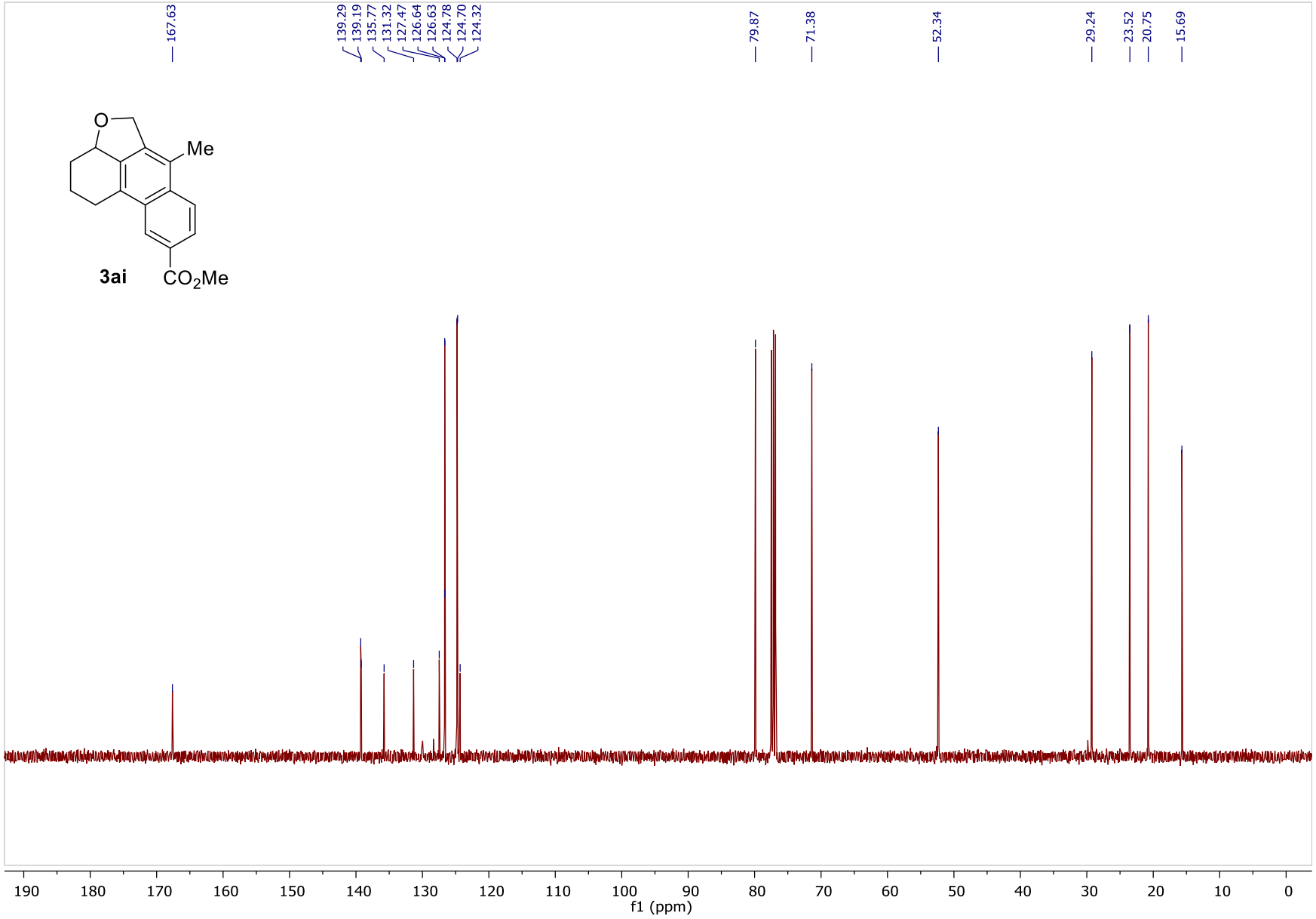
0.0
f1 (ppm)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126.64
126.63
124.78
124.70
124.32
79.87
71.38
52.34
29.24
23.52
20.75
15.69
O
Me
3ai
CO2Me
190
180
170
160
150
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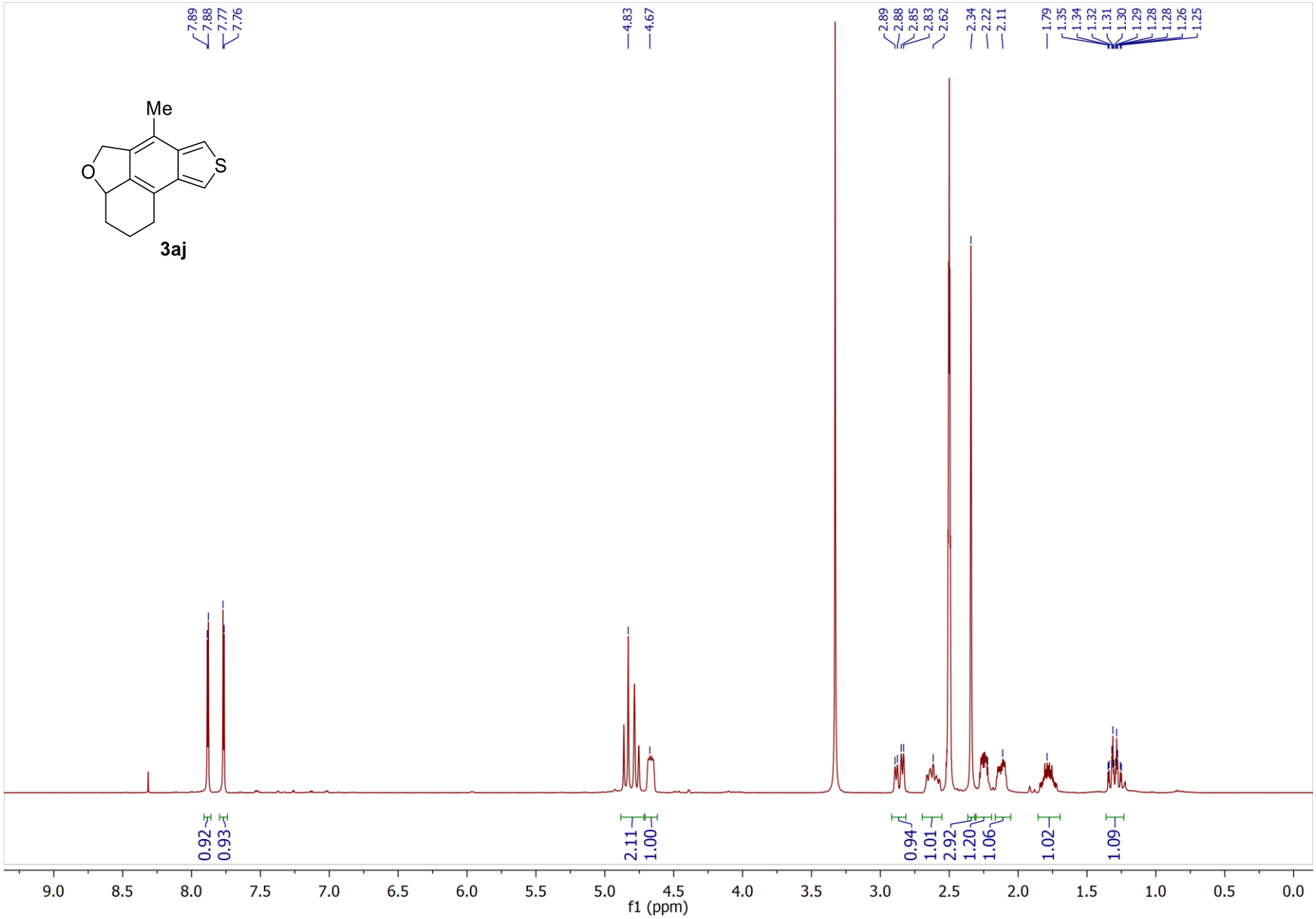
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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2.88
2.85
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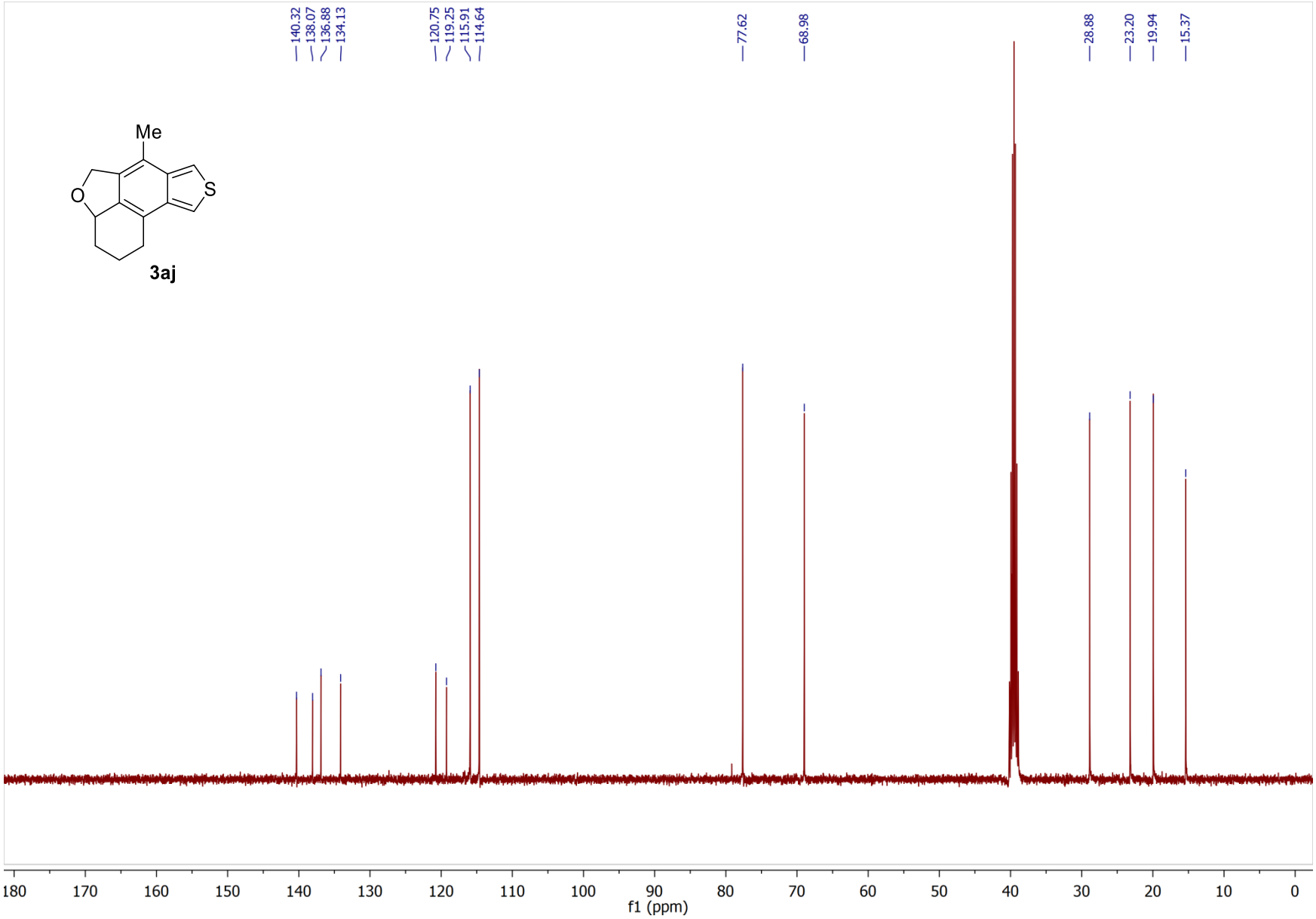
2.62
2.34
2.22
2.11
1.79
1.35
1.34
1.32
1.31
1.30
1.29
1.28
1.28
1.26
1.25
0.92
0.93
2.11
1.00
0.94
1.01
2.92
1.20
1.06
1.02
1.09
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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68.98
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23.20
19.94
15.37
Me
O
S
3aj
180
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160
150
140
130
120
110
100
90
80
70
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50
40
30
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10
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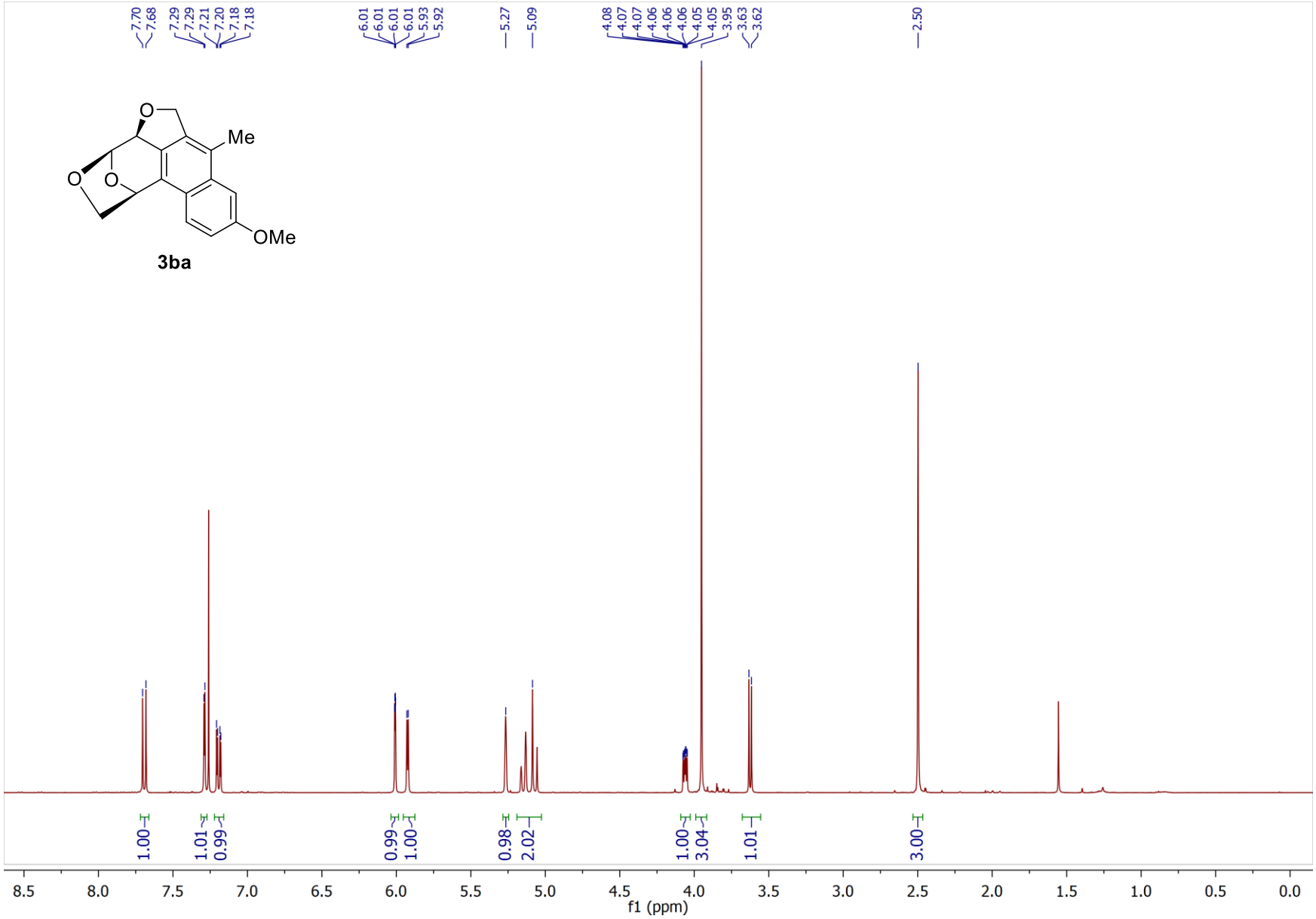
f1 (ppm)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6.01
6.01
6.01
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5.92
5.27
5.09
4.08
4.07
4.07
4.06
4.06
4.06
4.05
4.05
3.95
3.63
3.62
2.50
O
Me
O
O
OMe
3ba
1.00
1.01
0.99
0.99
1.00
0.98
2.02
1.00
3.04
1.01
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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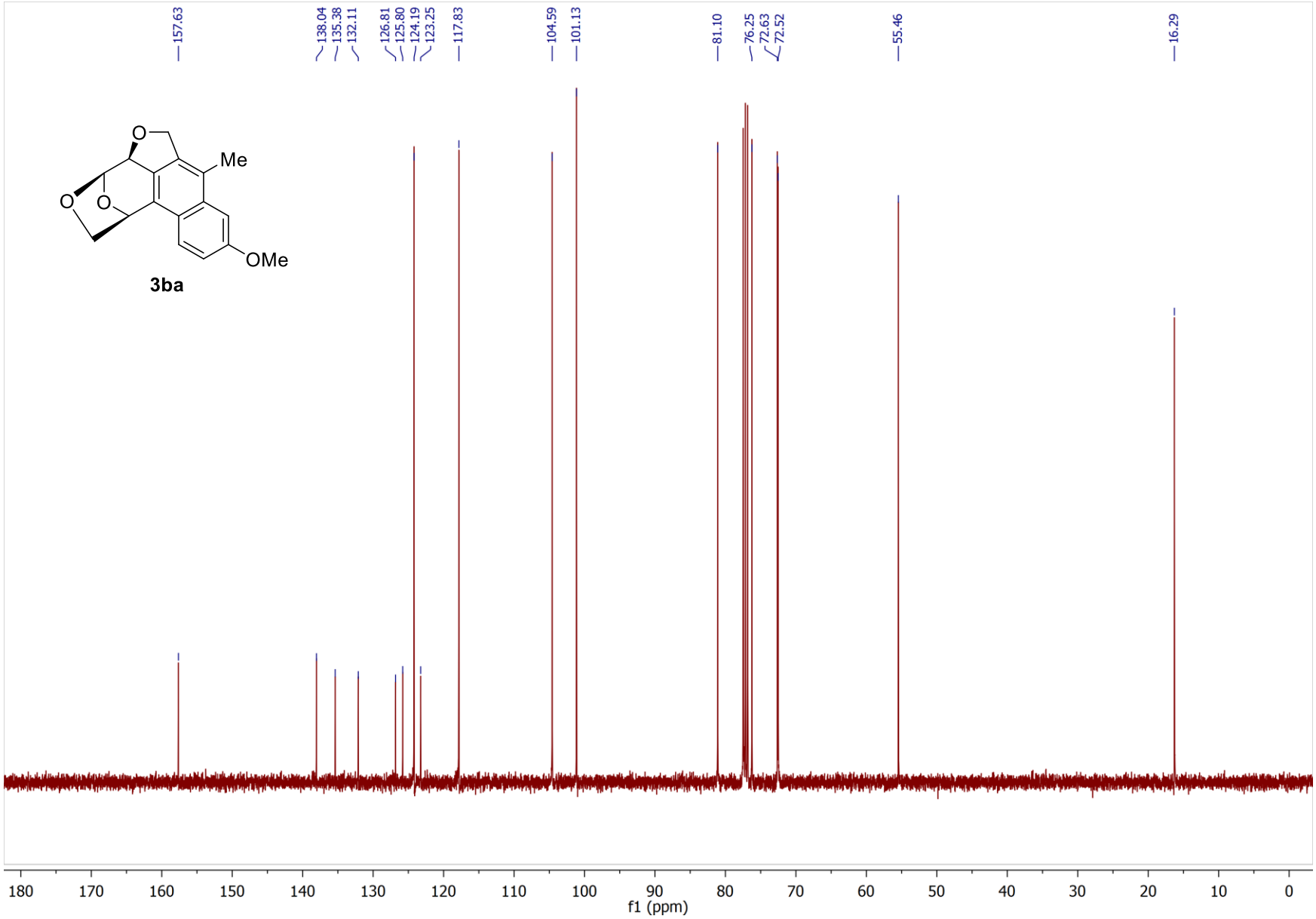
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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123.25
117.83
104.59
101.13
81.10
76.25
72.63
72.52
55.46
16.29
O
O
O
Me
OMe
3ba
180
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130
120
110
100
90
80
70
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50
40
30
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10
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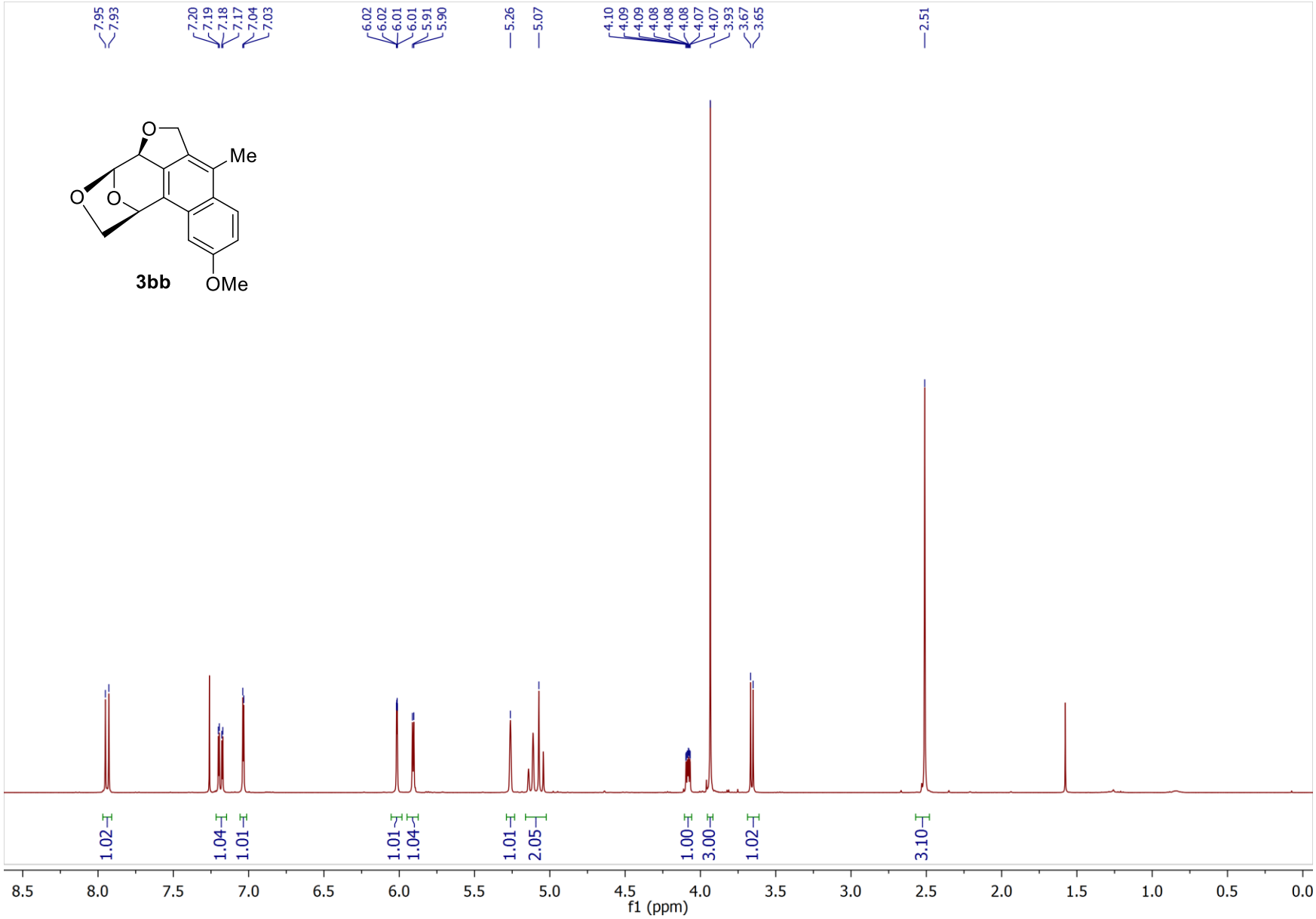
f1 (ppm)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6.02
6.02
6.01
6.01
5.91
5.90
5.26
5.07
4.10
4.09
4.09
4.08
4.08
4.08
4.07
4.07
3.93
3.67
3.65
2.51
O
Me
O
O
3bb
OMe
1.02
1.04
1.01
1.01
1.04
1.01
2.05
1.00
3.00
1.02
3.10
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.0
2.5
2.0
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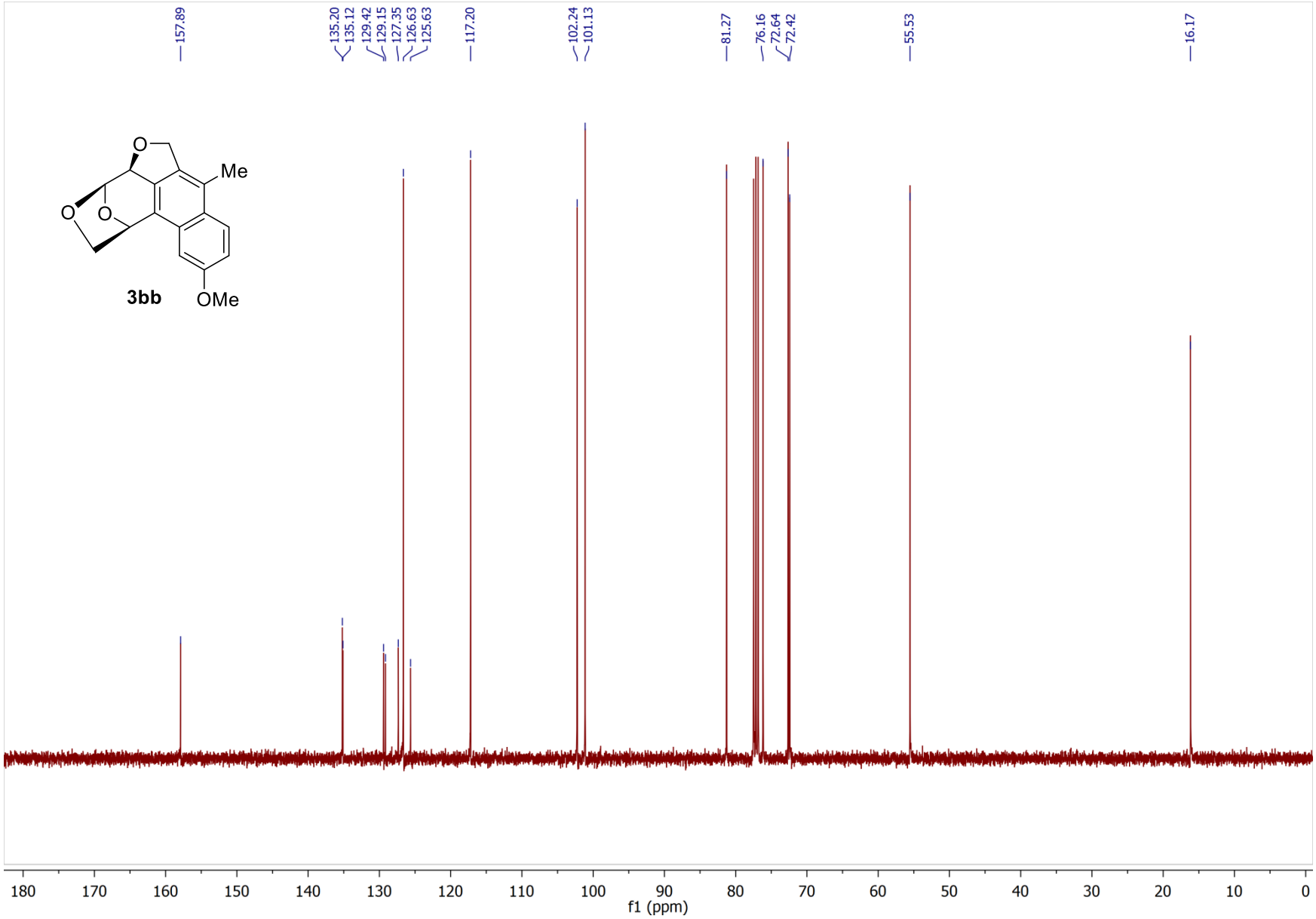
f1 (ppm)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125.63
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102.24
101.13
81.27
76.16
72.64
72.42
55.53
16.17
O
O
O
Me
OMe
3bb
180
170
160
150
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130
120
110
100
90
80
70
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50
40
30
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10
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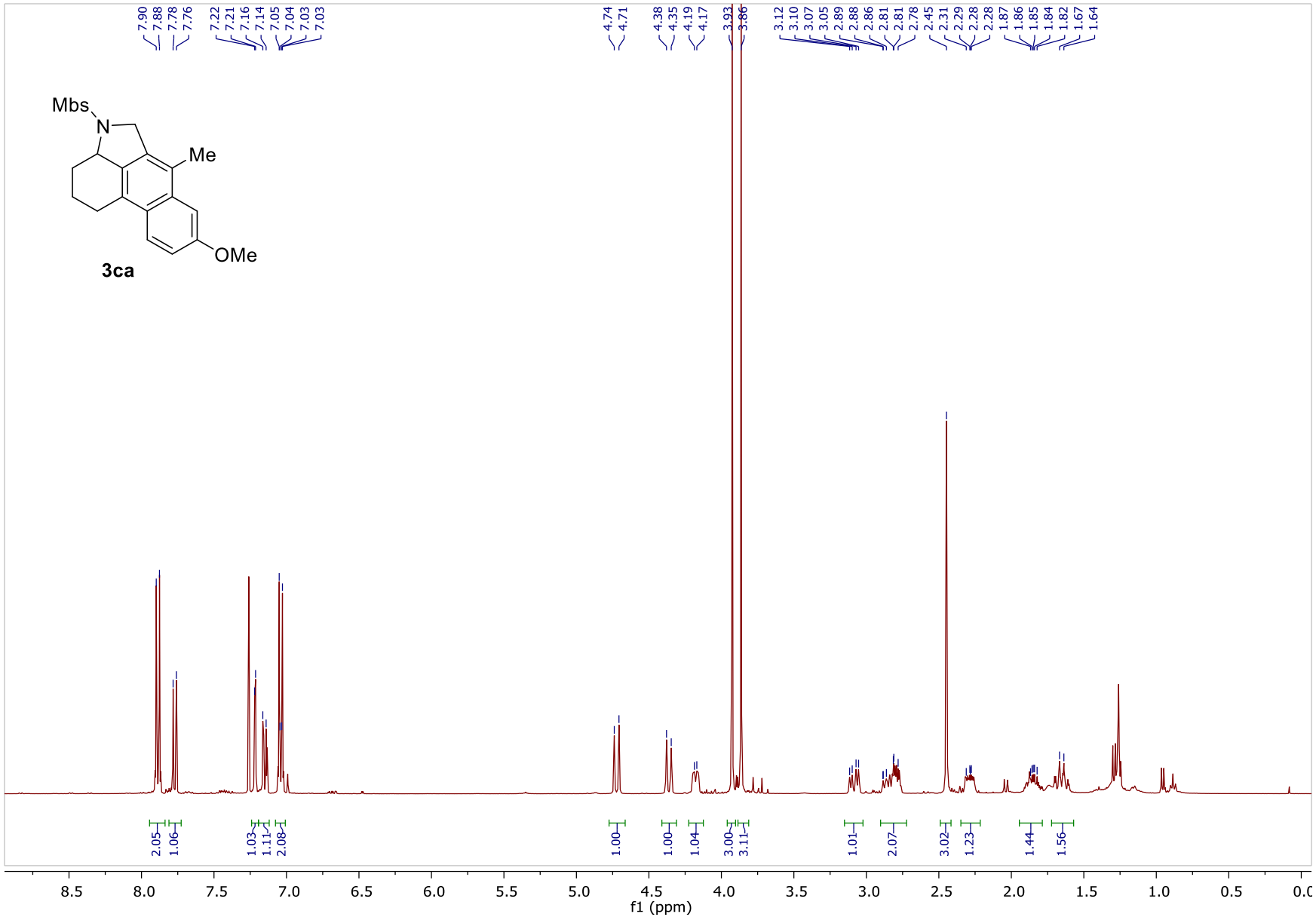
f1 (ppm)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7.03
7.03
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4.38
4.35
4.19
4.17
3.93
3.86
3.12
3.10
3.07
3.05
2.89
2.88
2.86
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2.81
2.78
2.45
2.31
2.29
2.28
2.28
1.87
1.86
1.85
1.84
1.82
1.67
1.64
Mbs
N
Me
OMe
3ca
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1.06
1.03
1.11
2.08
1.00
1.00
1.04
3.00
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1.01
2.07
3.02
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1.44
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6.0
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3.0
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1.5
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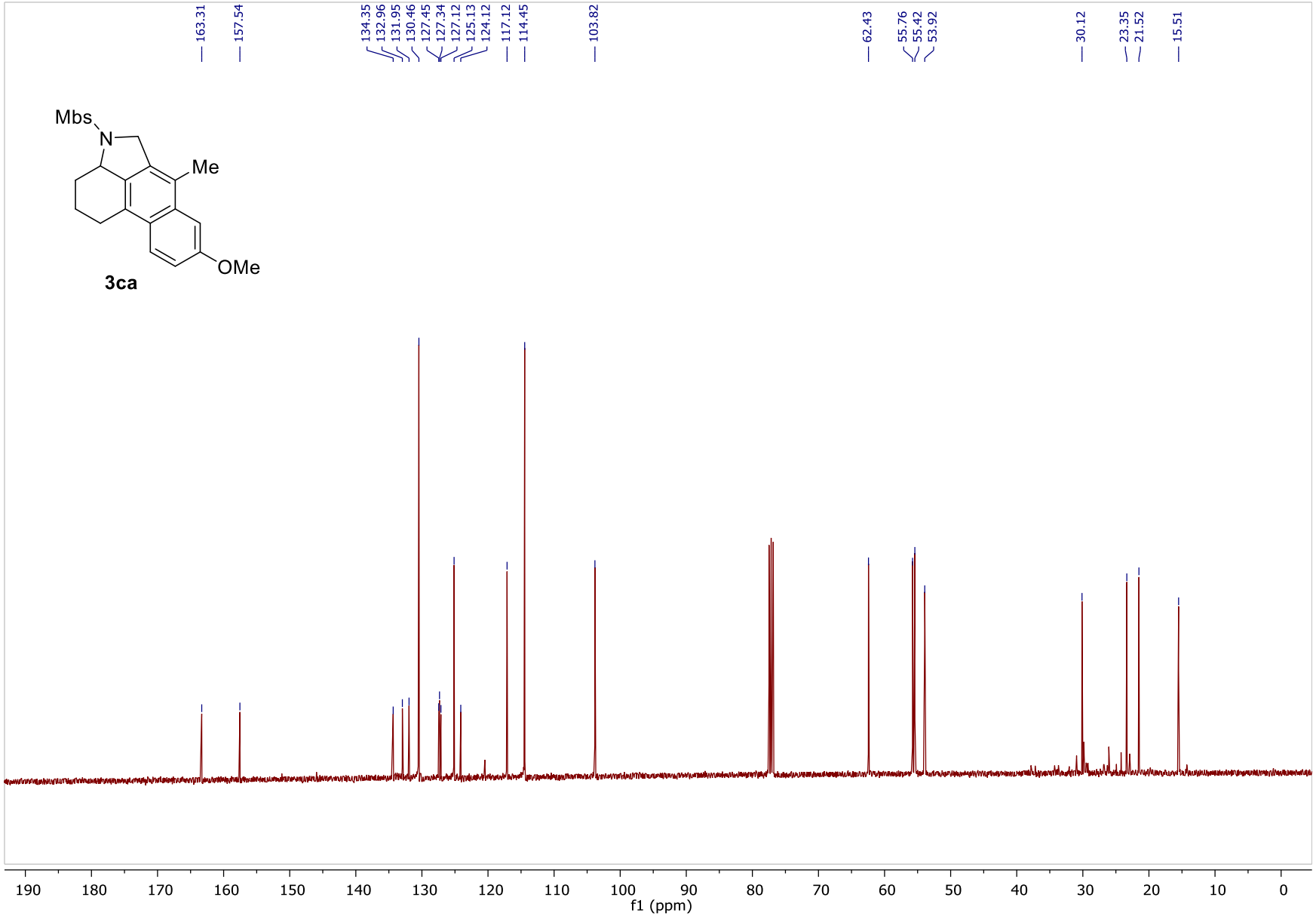
0.5
f1 (ppm)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127.34
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125.13
124.12
117.12
114.45
103.82
62.43
55.76
55.42
53.92
30.12
23.35
21.52
15.51
Mbs
N
Me
OMe
3ca
190
180
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100
90
80
70
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50
40
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10
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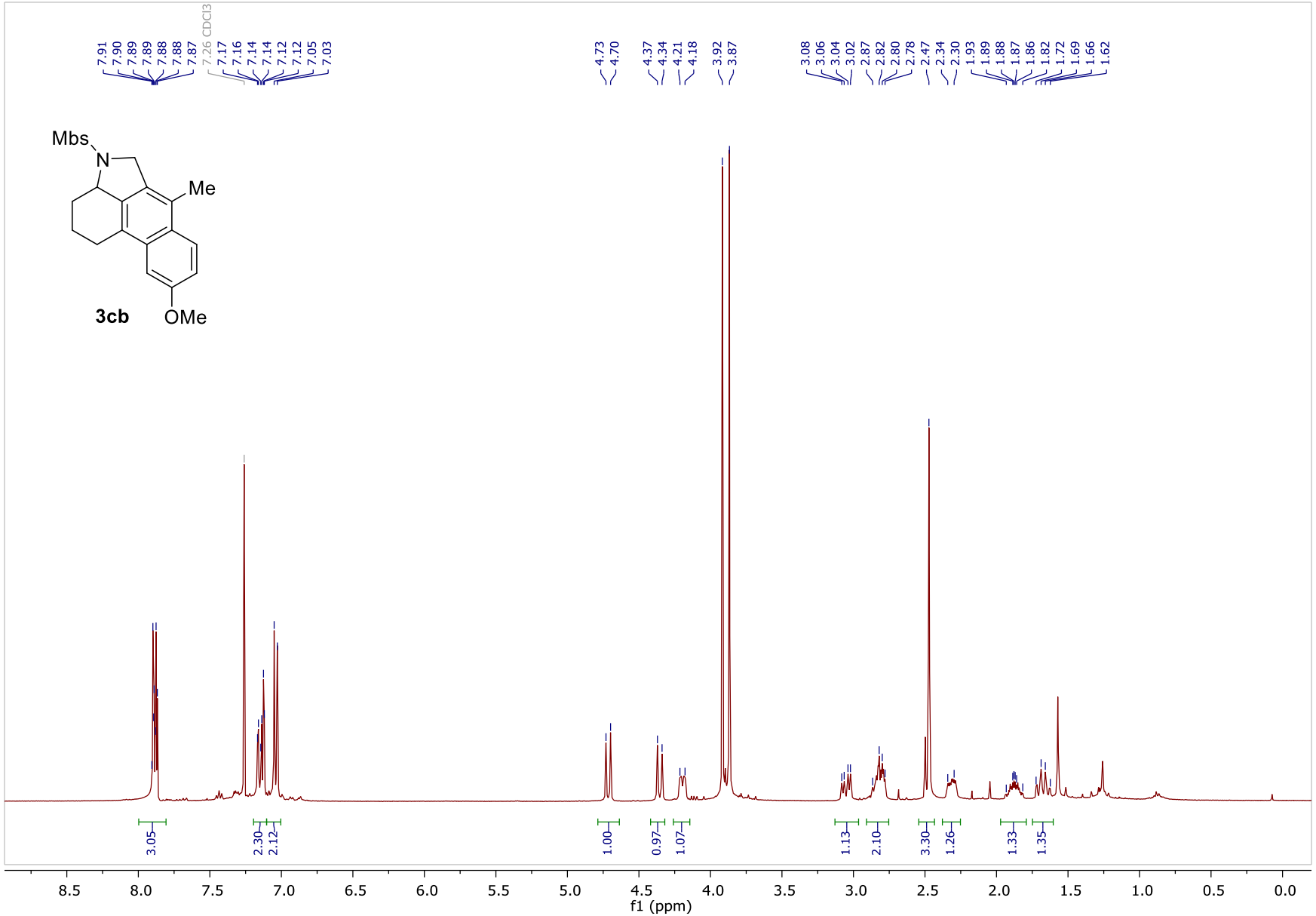
f1 (ppm)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7.89
7.89
7.88
7.88
7.87
7.26 CDCl3
7.17
7.16
7.14
7.14
7.12
7.12
7.05
7.03
4.73
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4.37
4.34
4.21
4.18
3.92
3.87
3.08
3.06
3.04
3.02
2.87
2.82
2.80
2.78
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2.34
2.30
1.93
1.89
1.88
1.87
1.86
1.82
1.72
1.69
1.66
1.62
Mbs
N
Me
OMe
3cb
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2.30
2.12
1.00
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1.07
1.13
2.10
3.30
1.26
1.33
1.35
8.5
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7.5
7.0
6.5
6.0
5.5
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3.0
2.5
2.0
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1.0
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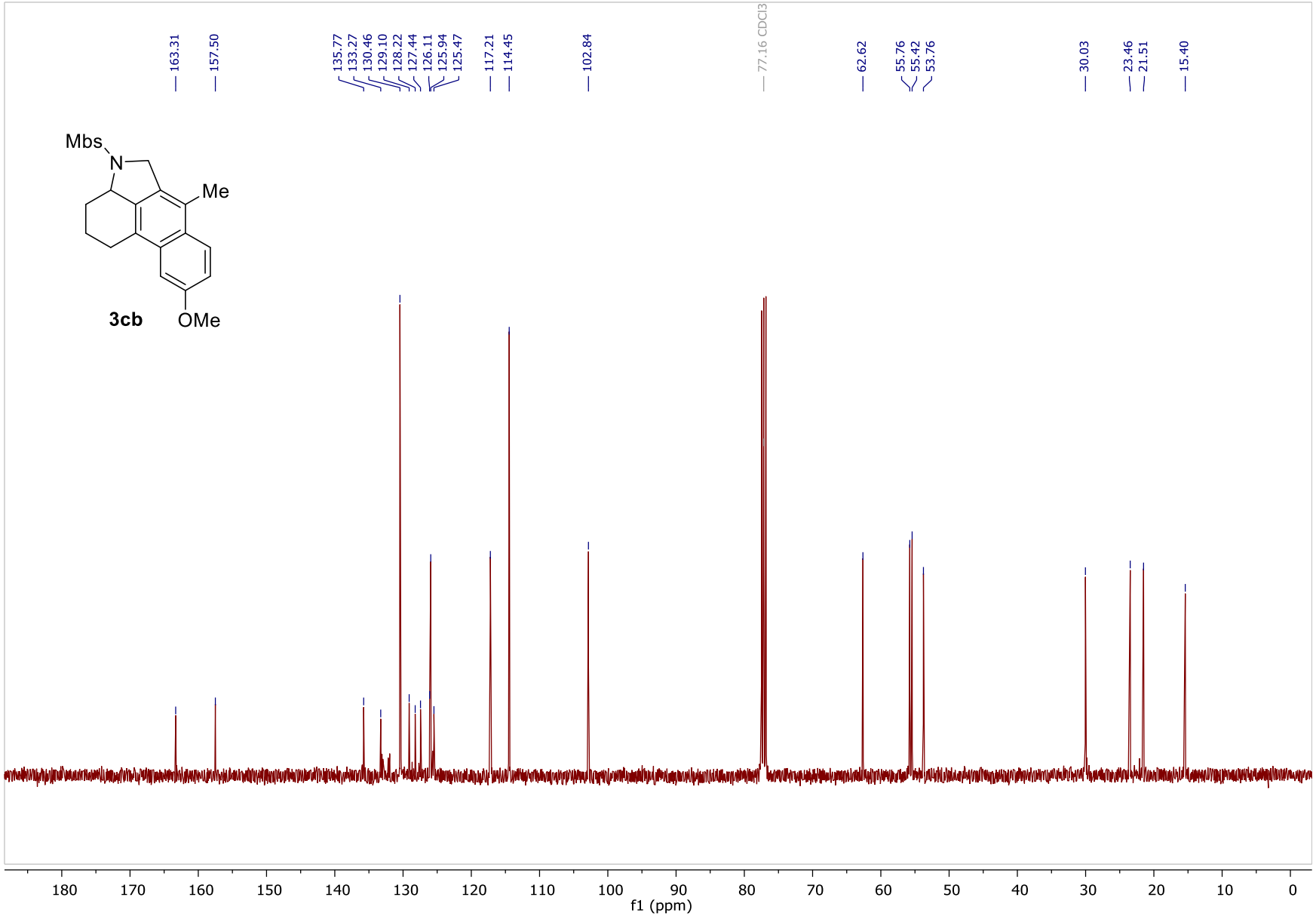
0.0
f1 (ppm)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125.94
125.47
117.21
114.45
102.84
77.16 CDCl3
62.62
55.76
55.42
53.76
30.03
23.46
21.51
15.40
Mbs
N
Me
OMe
3cb
180
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110
100
90
80
70
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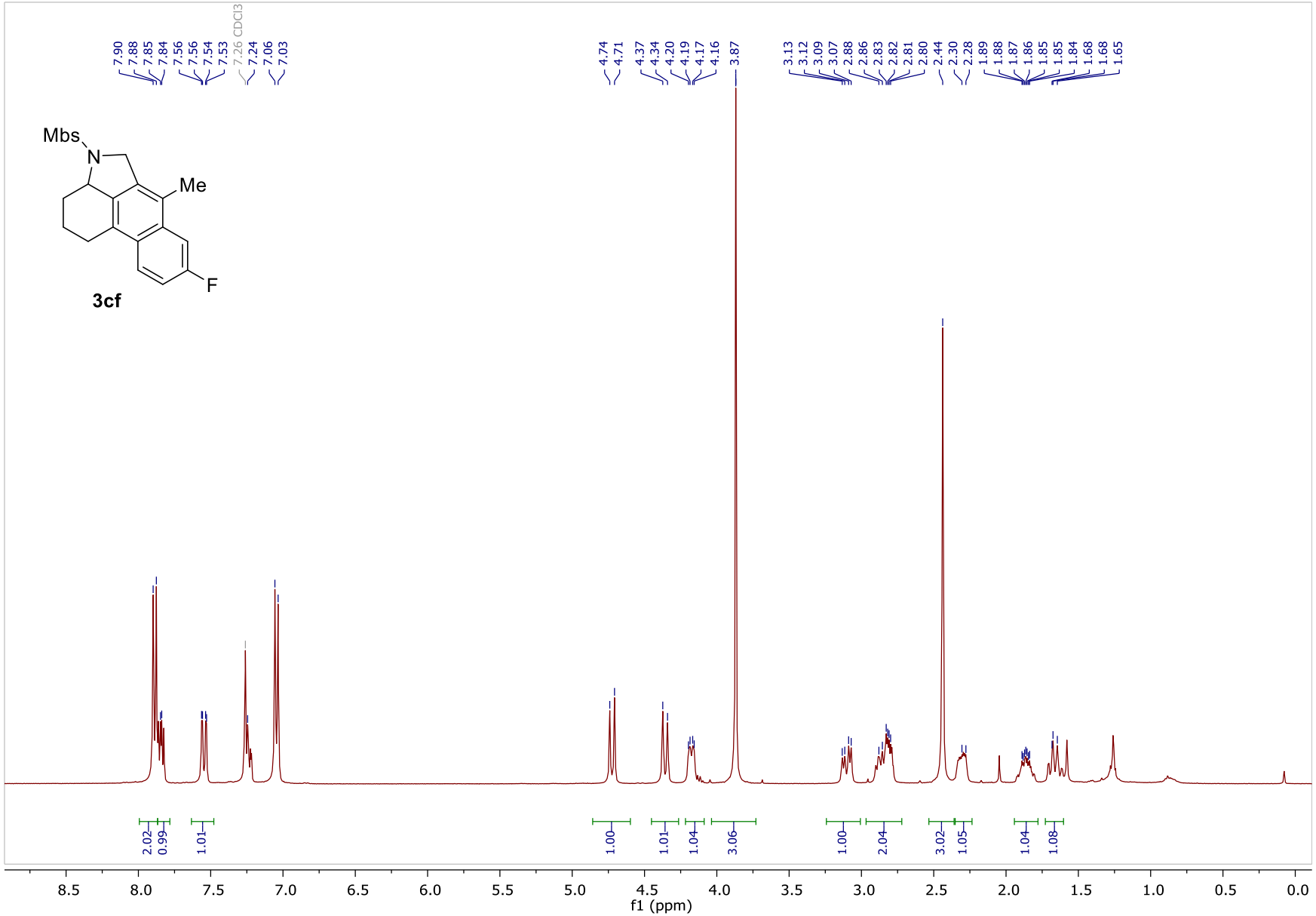
50
40
30
20
10
0
f1 (ppm)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7.56
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7.53
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7.24
7.06
7.03
4.74
4.71
4.37
4.34
4.20
4.19
4.17
4.16
3.87
3.13
3.12
3.09
3.07
2.88
2.86
2.83
2.82
2.81
2.80
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2.28
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1.88
1.87
1.86
1.85
1.85
1.84
1.68
1.68
1.65
Mbs
N
Me
F
3cf
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0.99
1.01
1.00
1.01
1.04
3.06
1.00
2.04
3.02
1.05
1.04
1.08
8.5
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7.5
7.0
6.5
6.0
5.5
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2.0
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1.0
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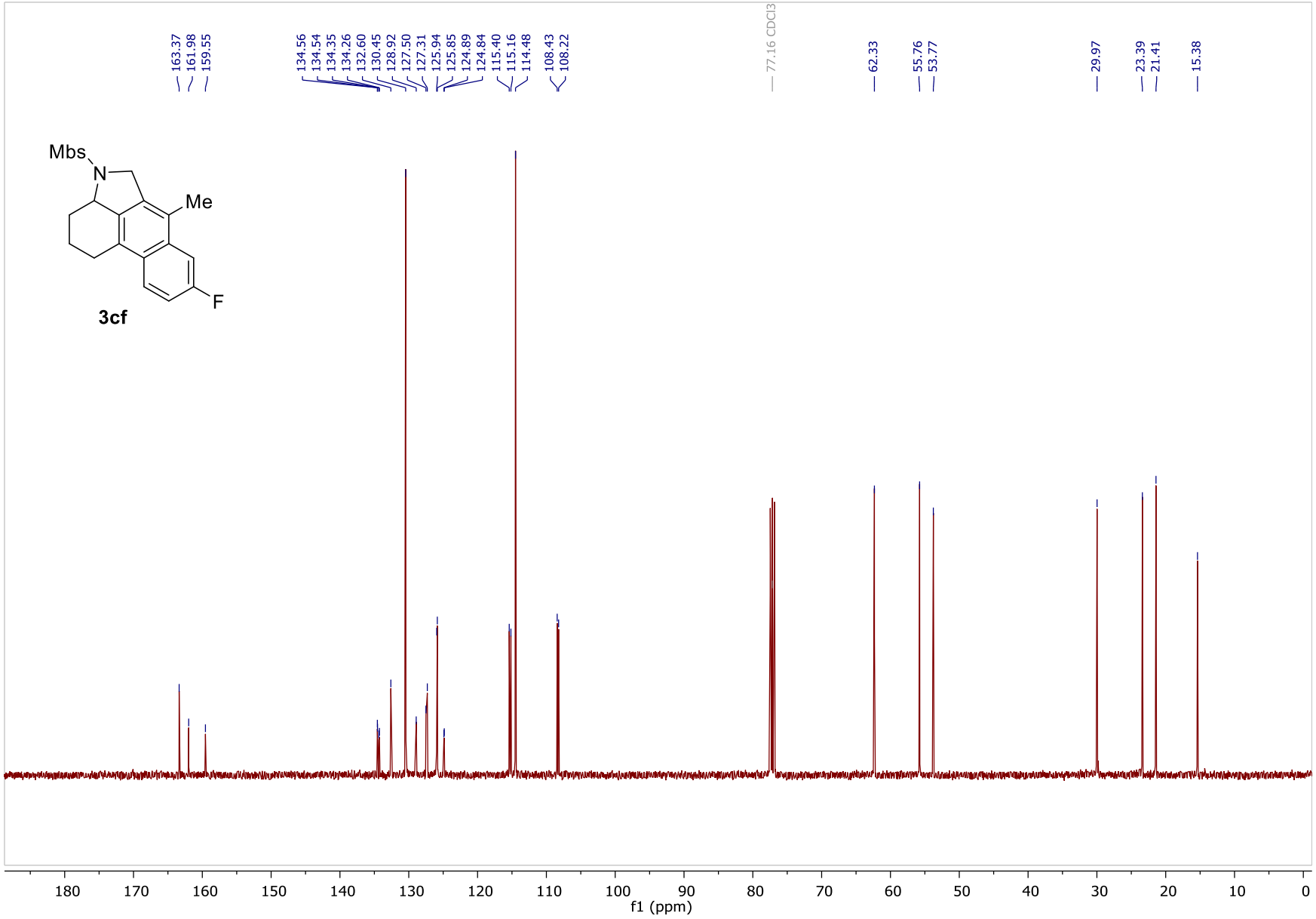
f1 (ppm)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127.50
127.31
125.94
125.85
124.89
124.84
115.40
115.16
114.48
108.43
108.22
77.16 CDCl3
62.33
55.76
53.77
29.97
23.39
21.41
15.38
Mbs
N
Me
F
3cf
180
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130
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110
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90
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50
40
30
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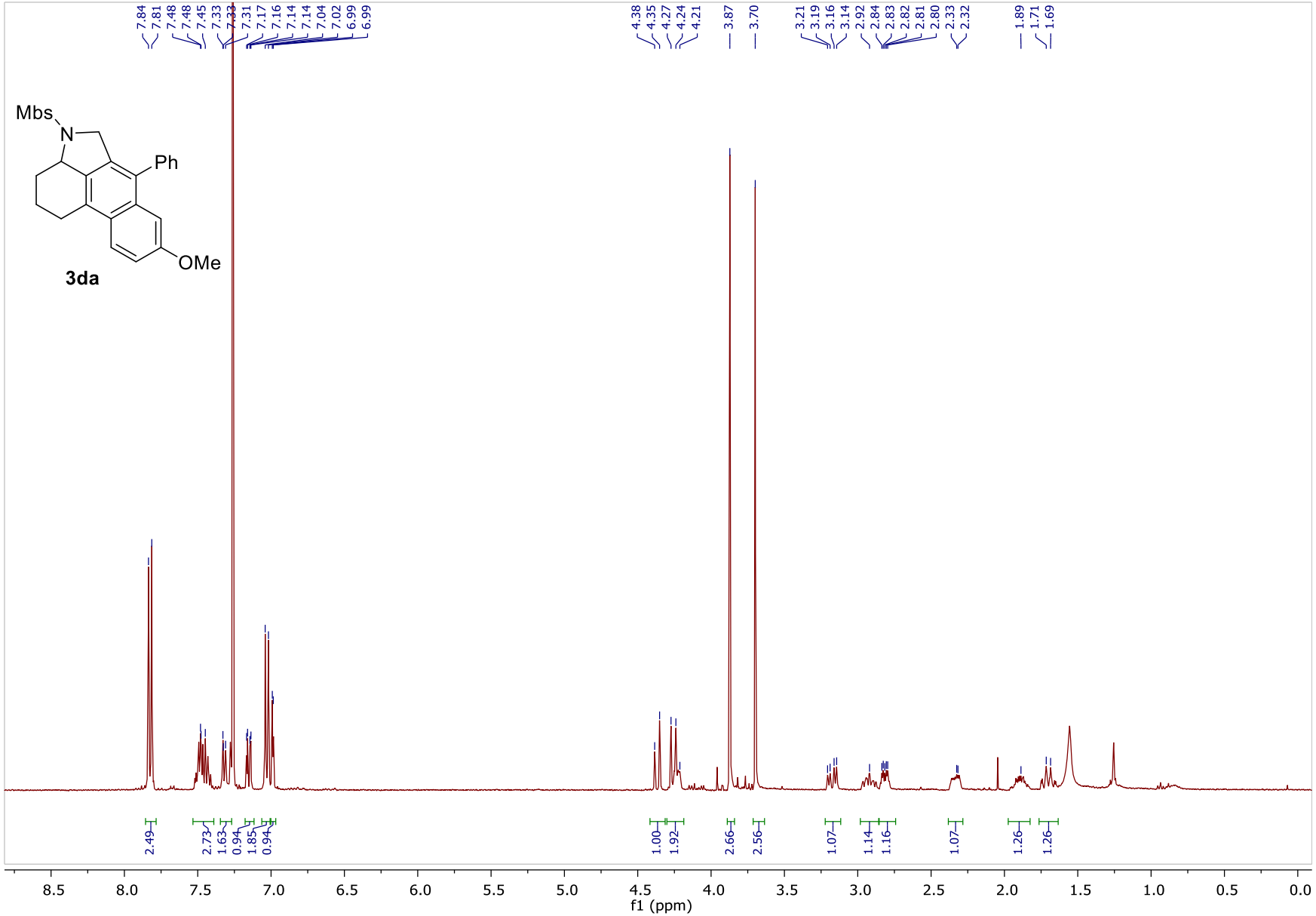
10
0
f1 (ppm)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7.31
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7.14
7.04
7.02
6.99
6.99
4.38
4.35
4.27
4.24
4.21
3.87
3.70
3.21
3.19
3.16
3.14
2.92
2.84
2.83
2.82
2.81
2.80
2.33
2.32
1.89
1.71
1.69
Mbs
N
Ph
OMe
3da
2.49
2.73
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1.85
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1.00
1.92
2.66
2.56
1.07
1.14
1.16
1.07
1.26
1.26
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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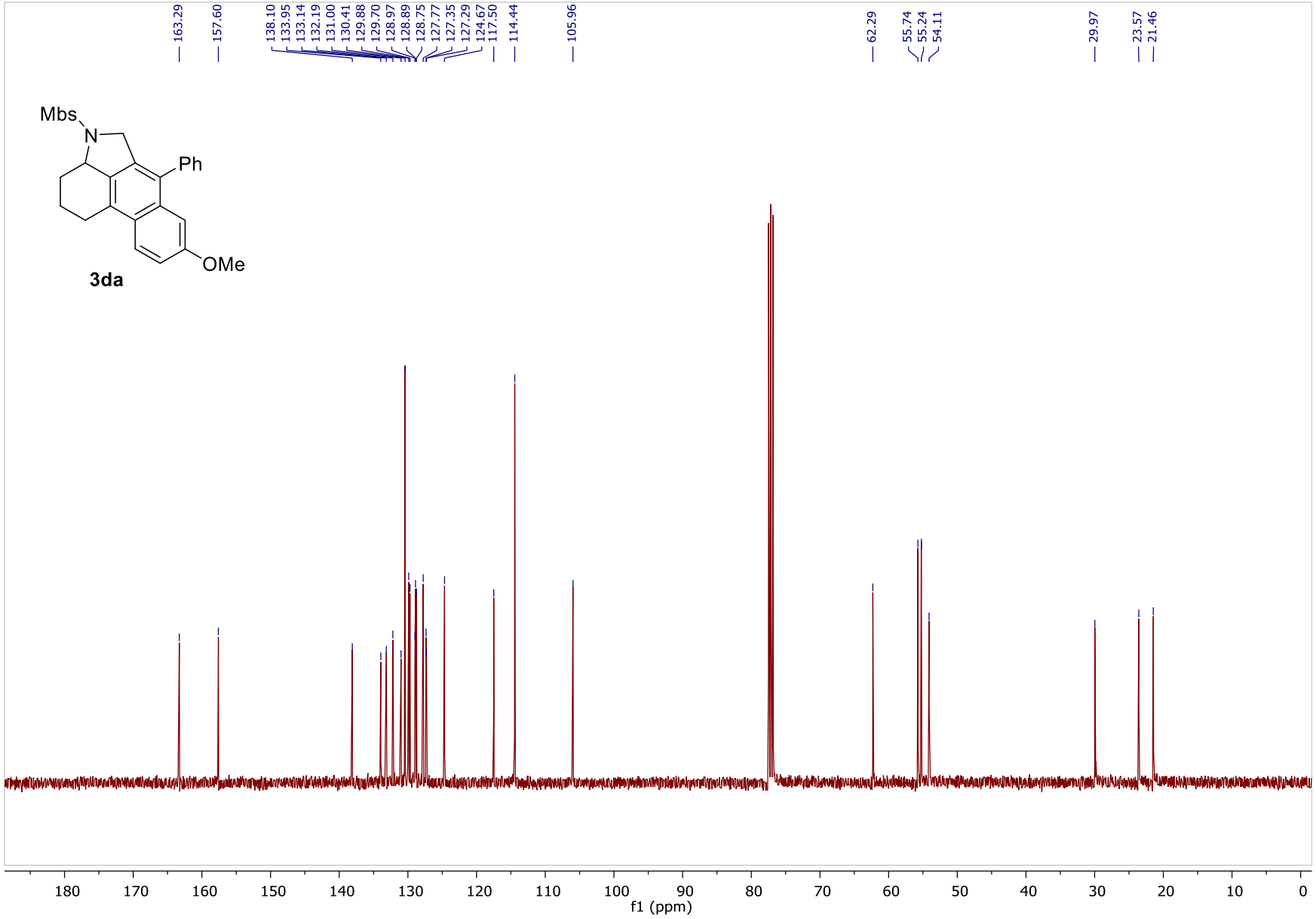
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132.19
131.00
130.41
129.88
129.70
128.97
128.89
128.75
127.77
127.35
127.29
124.67
117.50
114.44
105.96
62.29
55.74
55.24
54.11
29.97
23.57
21.46
Mbs
N
Ph
OMe
3da
180
170
160
150
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130
120
110
100
90
80
70
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50
40
30
20
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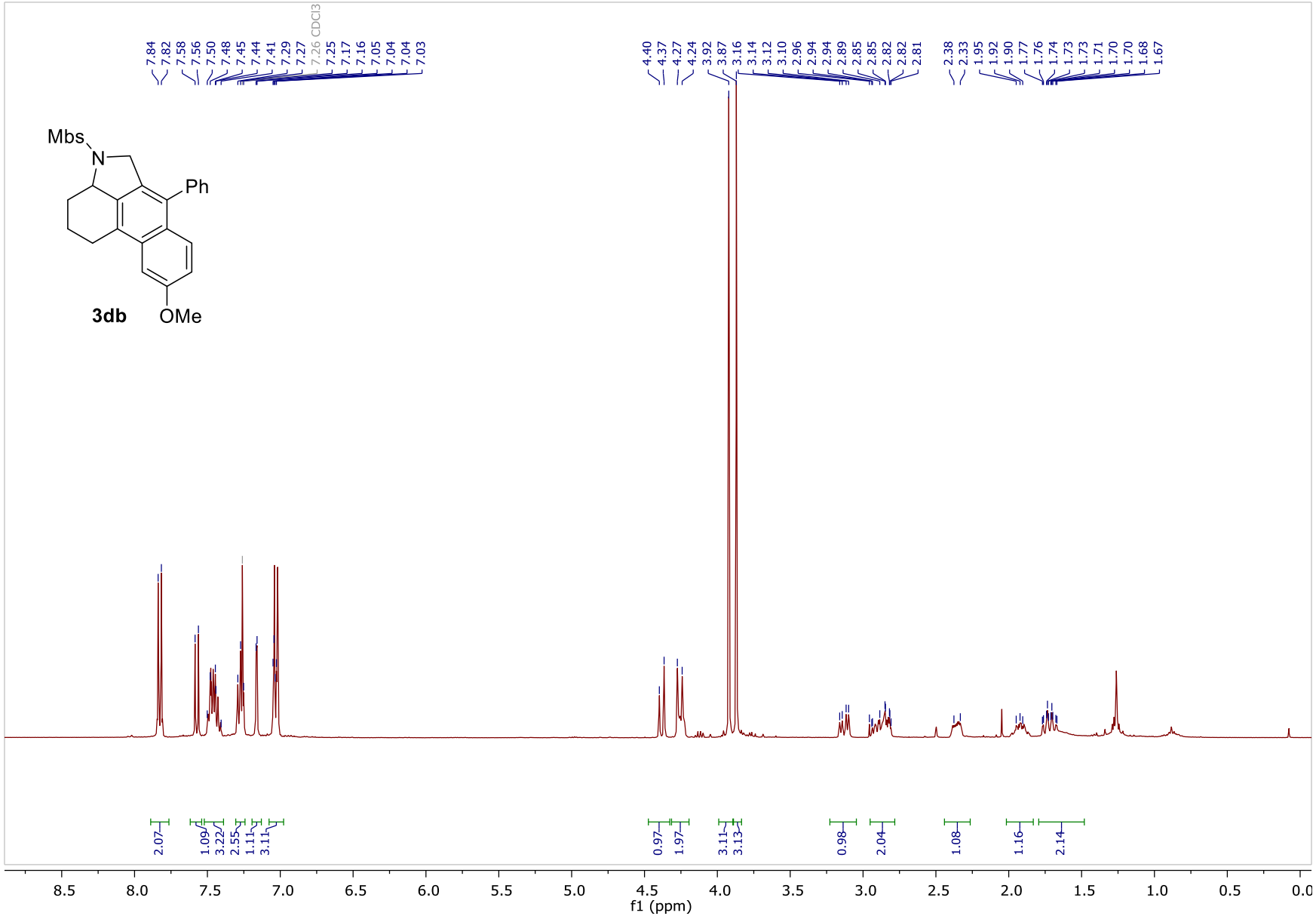
f1 (ppm)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7.45
7.44
7.41
7.29
7.27
7.26 CDCl3
7.25
7.17
7.16
7.05
7.04
7.04
7.03
4.40
4.37
4.27
4.24
3.92
3.87
3.16
3.14
3.12
3.10
2.96
2.94
2.94
2.89
2.85
2.85
2.82
2.82
2.81
2.38
2.33
1.95
1.92
1.90
1.77
1.76
1.74
1.73
1.73
1.71
1.70
1.70
1.68
1.67
Mbs
N
Ph
OMe
3db
2.07
1.09
3.22
2.55
1.11
3.11
0.97
1.97
3.11
3.13
0.98
2.04
1.08
1.16
2.14
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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2.5
2.0
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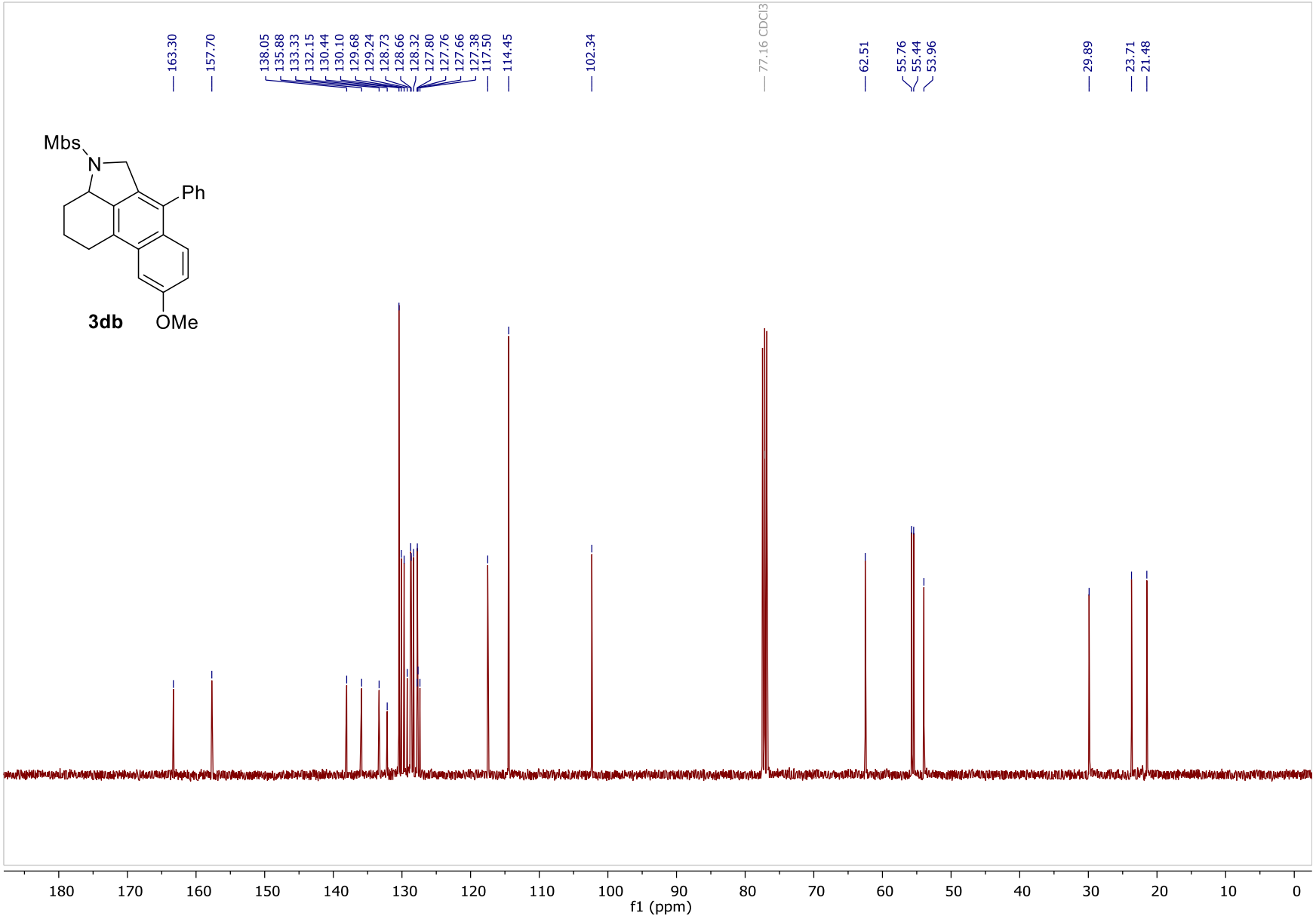
f1 (ppm)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132.15
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130.10
129.68
129.24
128.73
128.66
128.32
127.80
127.76
127.66
127.38
117.50
114.45
102.34
77.16 CDCl3
62.51
55.76
55.44
53.96
29.89
23.71
21.48
Mbs
N
Ph
OMe
3db
180
170
160
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130
120
110
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90
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70
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50
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30
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10
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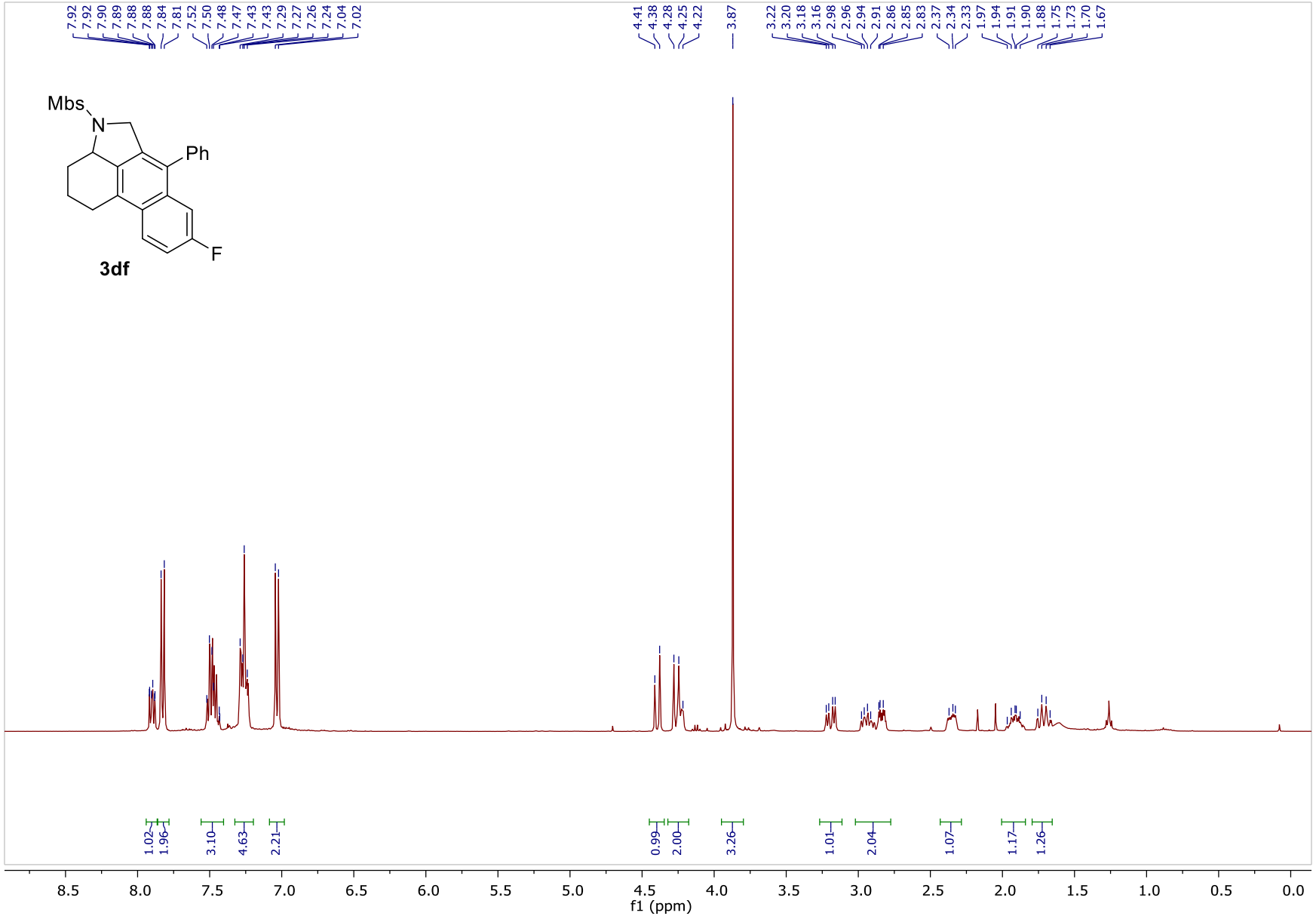
f1 (ppm)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7.92
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7.89
7.88
7.88
7.84
7.81
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7.50
7.48
7.47
7.43
7.43
7.29
7.27
7.26
7.24
7.04
7.02
4.41
4.38
4.28
4.25
4.22
3.87
3.22
3.20
3.18
3.16
2.98
2.96
2.94
2.91
2.86
2.85
2.83
2.37
2.34
2.33
1.97
1.94
1.91
1.90
1.88
1.75
1.73
1.70
1.67
Mbs
N
Ph
F
3df
1.02
1.96
3.10
4.63
2.21
0.99
2.00
3.26
1.01
2.04
1.07
1.17
1.26
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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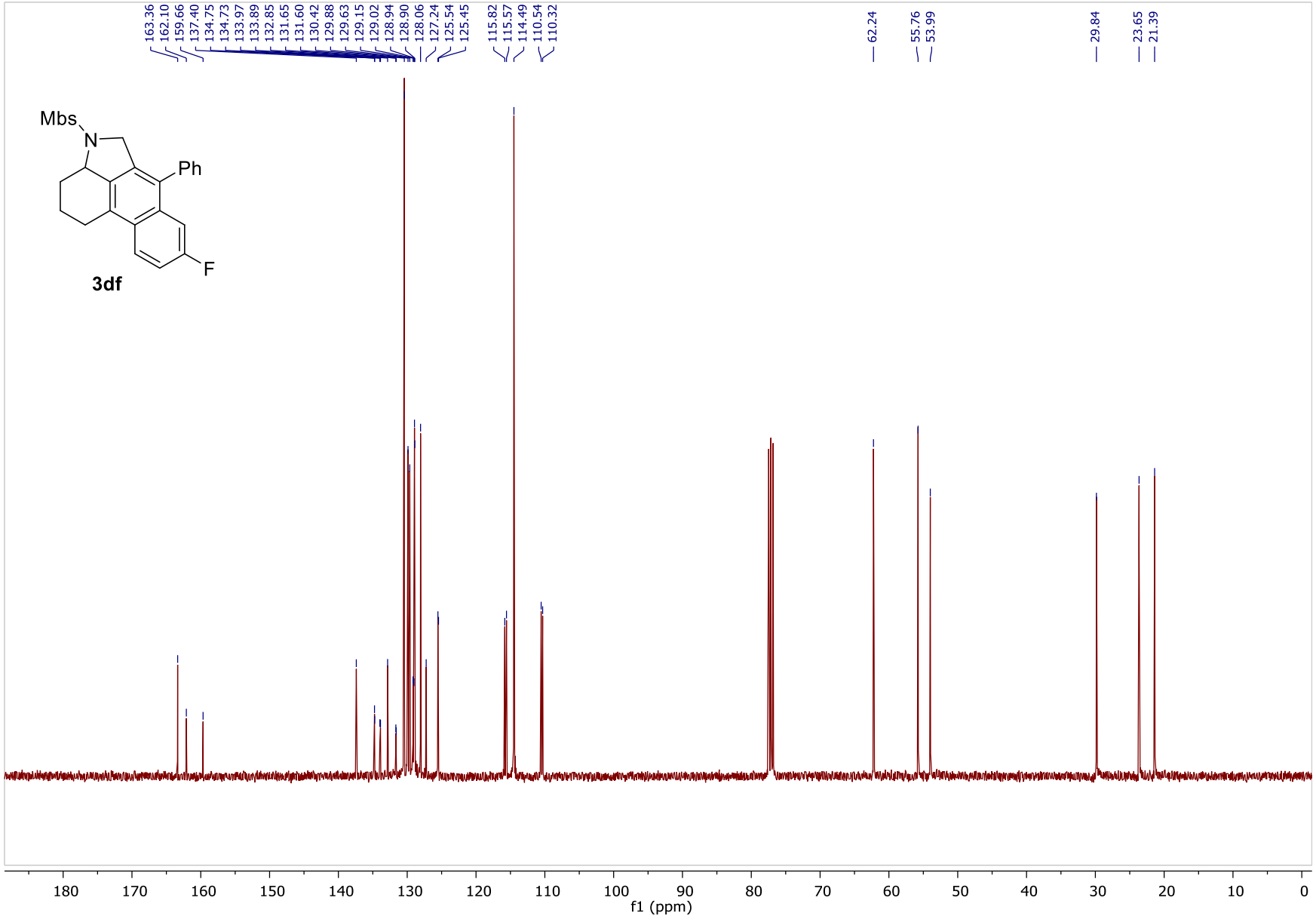
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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131.60
130.42
129.88
129.63
129.15
129.02
128.94
128.90
128.06
127.24
125.54
125.45
115.82
115.57
114.49
110.54
110.32
62.24
55.76
53.99
29.84
23.65
21.39
Mbs
N
Ph
F
3df
180
170
160
150
140
130
120
110
100
90
80
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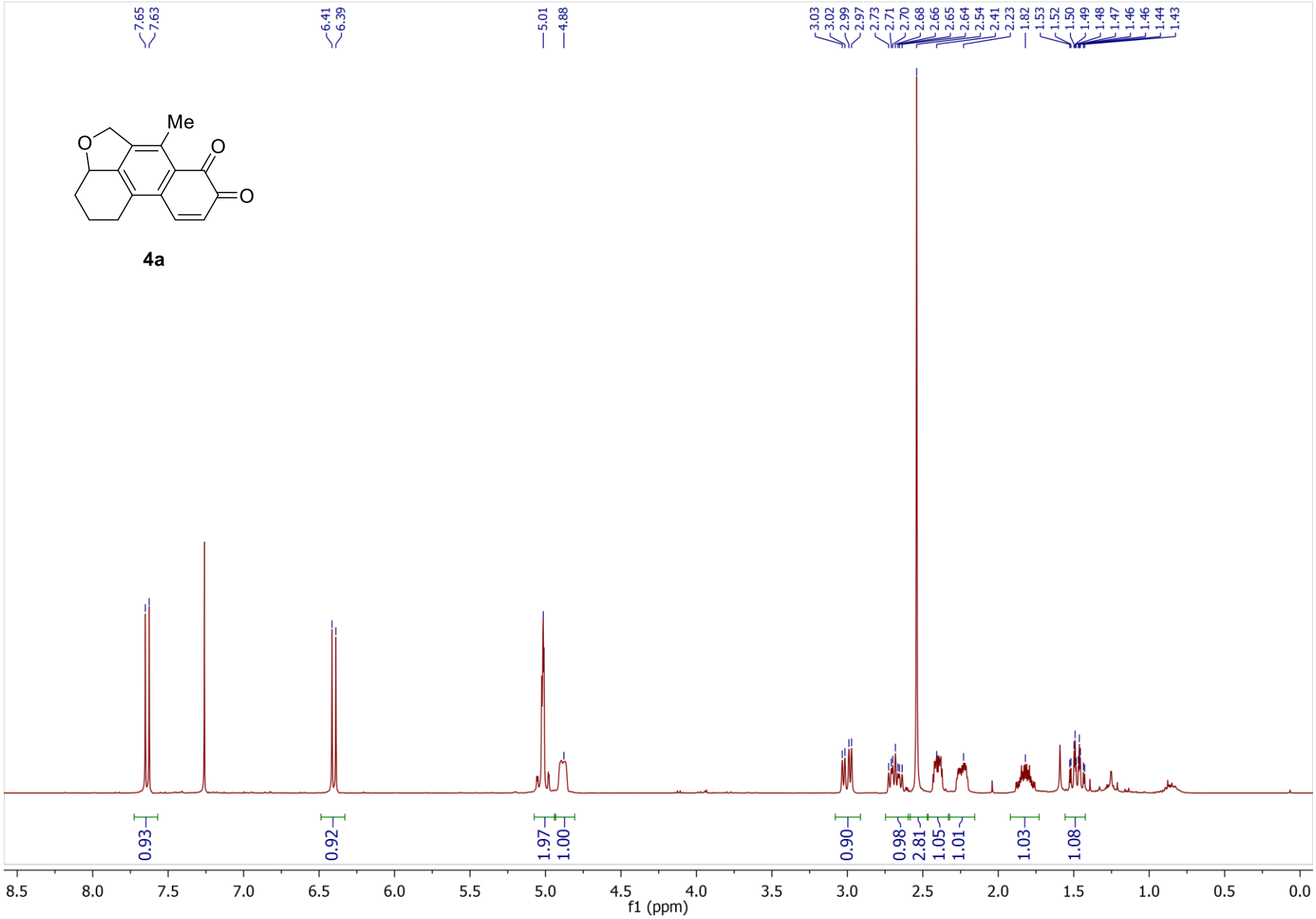
50
40
30
20
10
0
f1 (ppm)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7.63
6.41
6.39
5.01
4.88
3.03
3.02
2.99
2.97
2.73
2.71
2.70
2.68
2.66
2.65
2.64
2.54
2.41
2.23
1.82
1.53
1.52
1.50
1.49
1.48
1.47
1.46
1.46
1.44
1.43
Me
O
O
O
4a
0.93
0.92
1.97
1.00
0.90
0.98
2.81
1.05
1.01
1.03
1.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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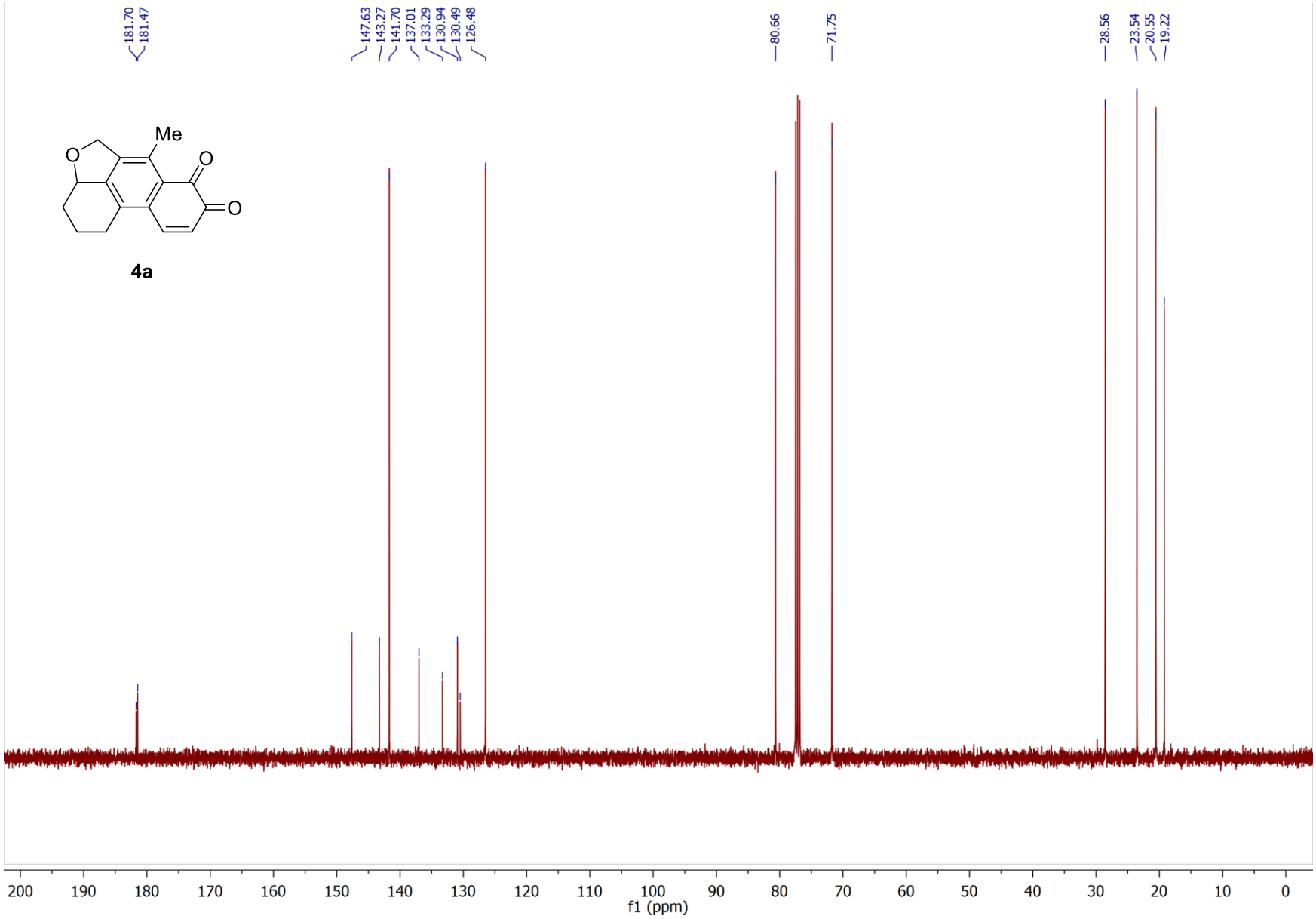
0.0
f1 (ppm)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137.01
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130.94
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126.48
80.66
71.75
28.56
23.54
20.55
19.22
Me
O
O
O
4a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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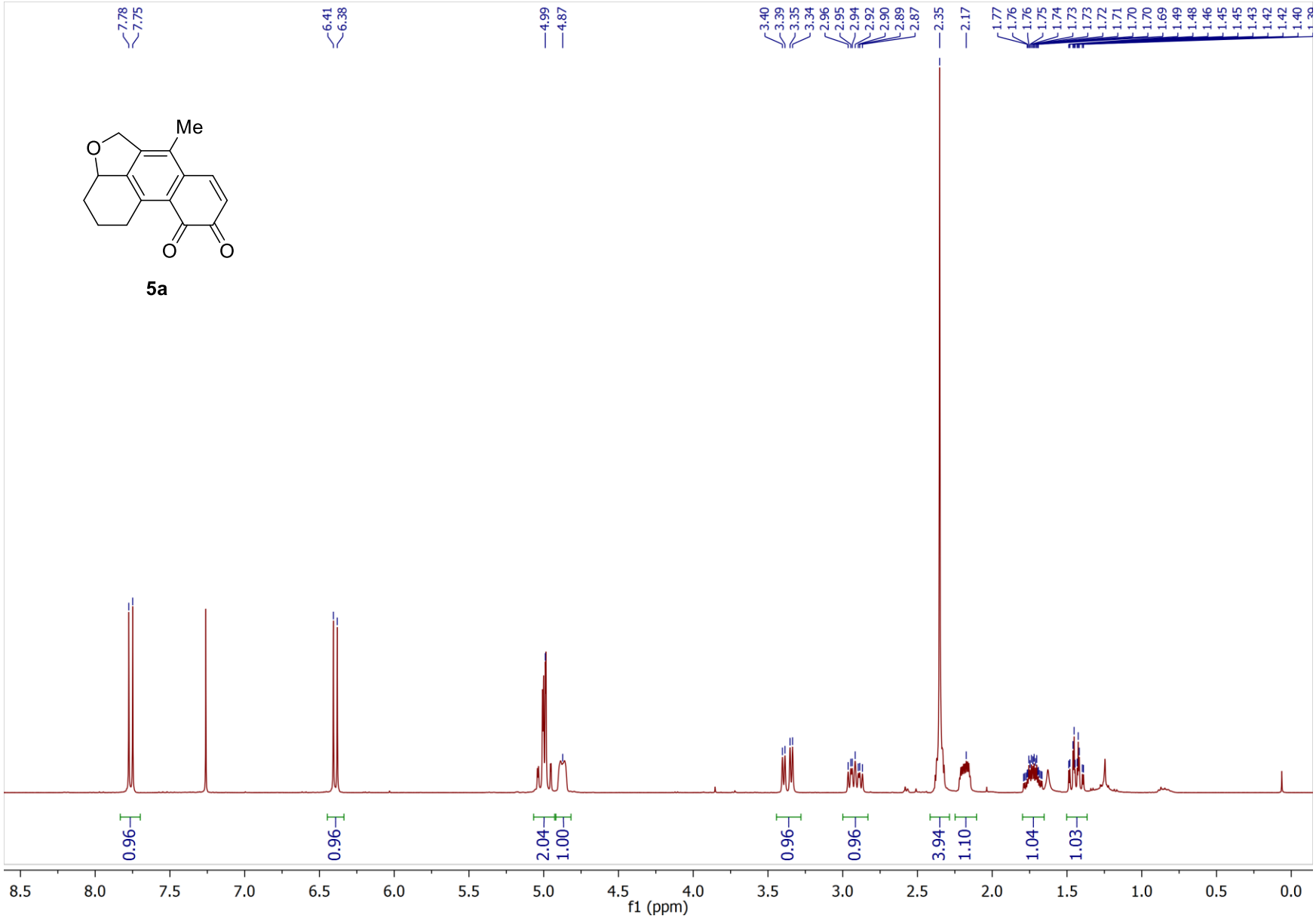
50
40
30
20
10
0
f1 (ppm)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4.87
3.40
3.39
3.35
3.34
2.96
2.95
2.94
2.92
2.90
2.89
2.87
2.35
2.17
1.77
1.76
1.76
1.75
1.74
1.73
1.73
1.72
1.71
1.70
1.70
1.69
1.49
1.48
1.46
1.45
1.45
1.43
1.42
1.42
1.40
Me
O
O
O
5a
0.96
0.96
2.04
1.00
0.96
0.96
3.94
1.10
1.04
1.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.5
3.0
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2.0
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1.0
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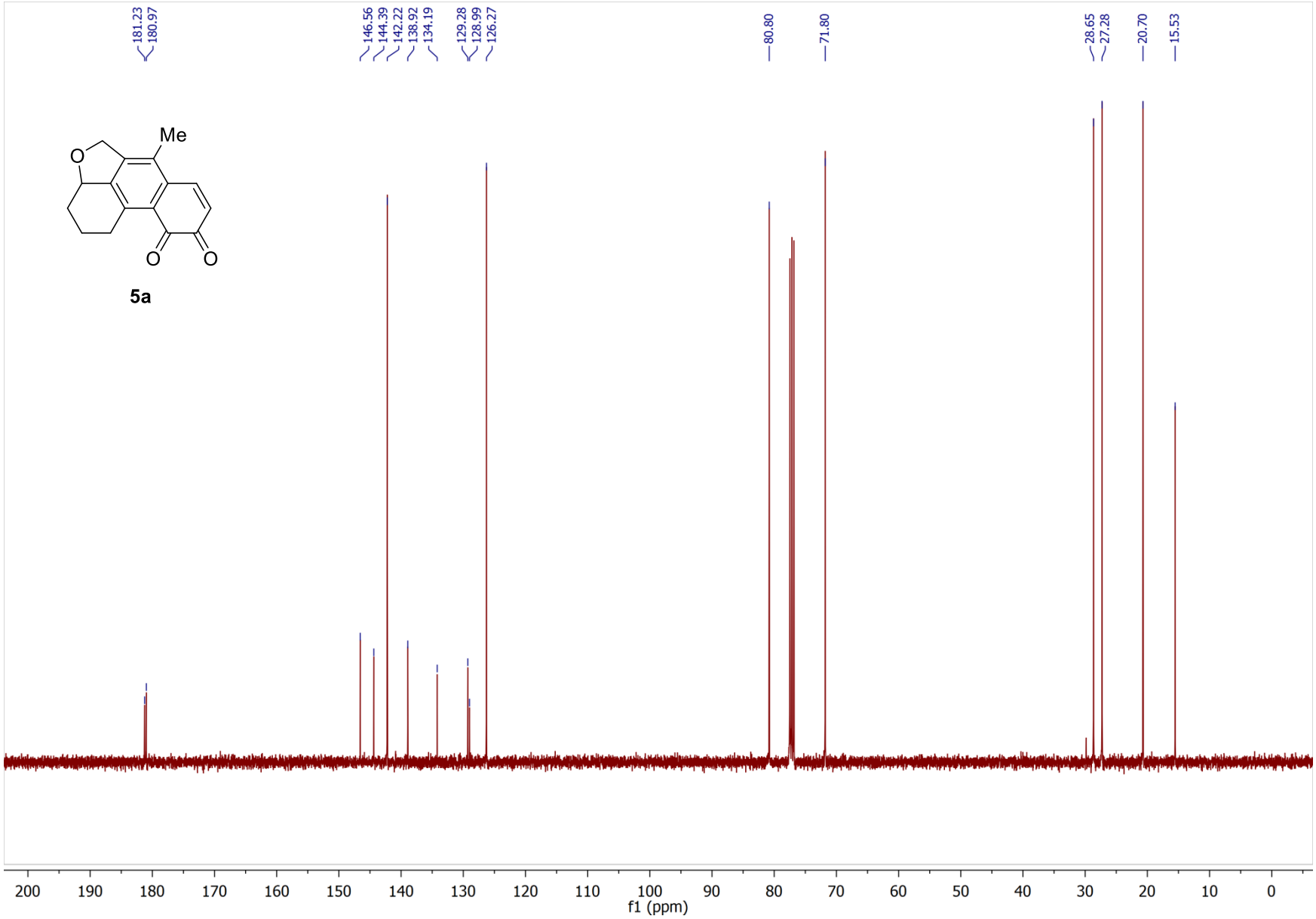
0.0
f1 (ppm)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142.22
138.92
134.19
129.28
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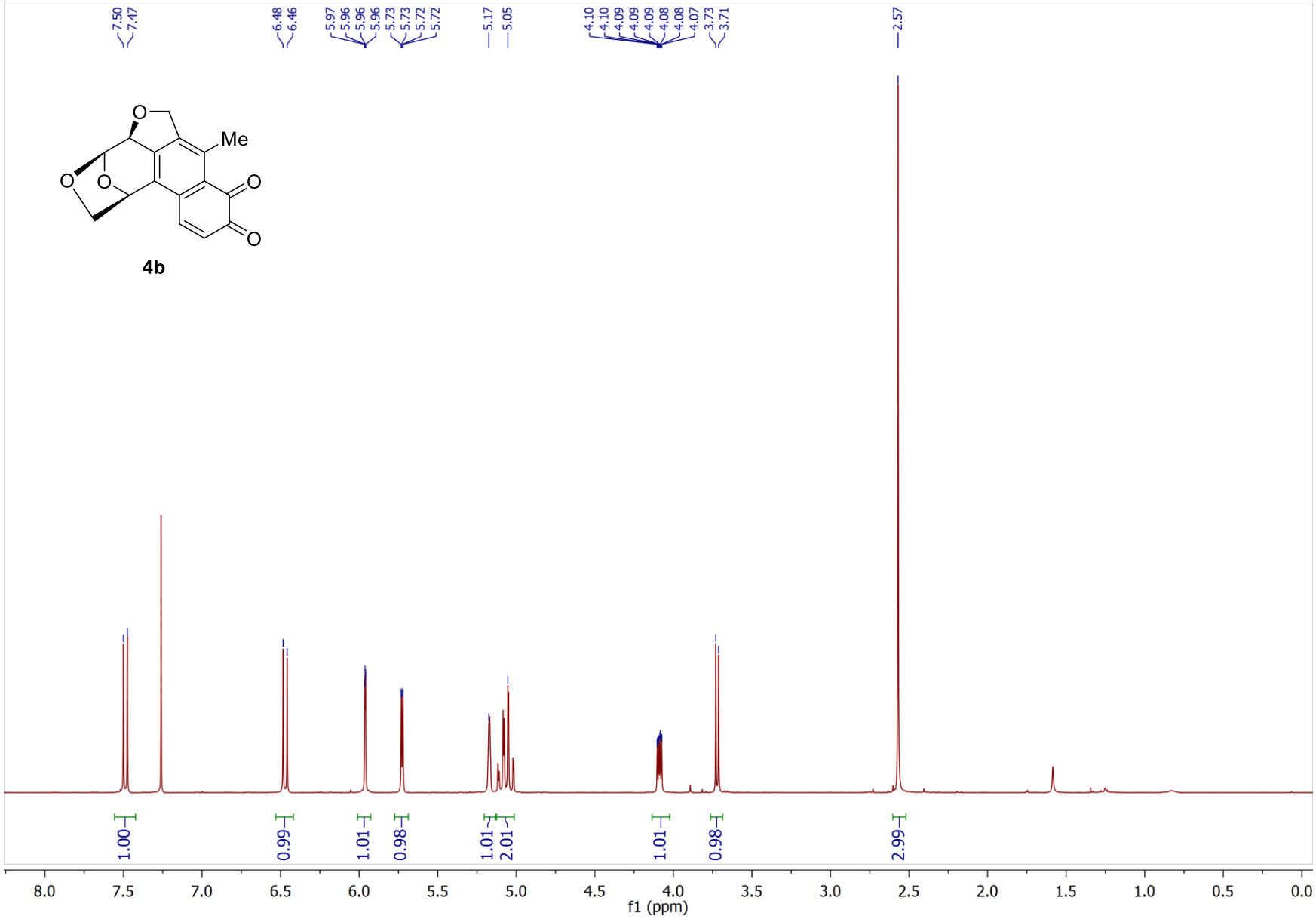
126.27
80.80
71.80
28.65
27.28
20.70
15.53
Me
O
O
O
5a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.47
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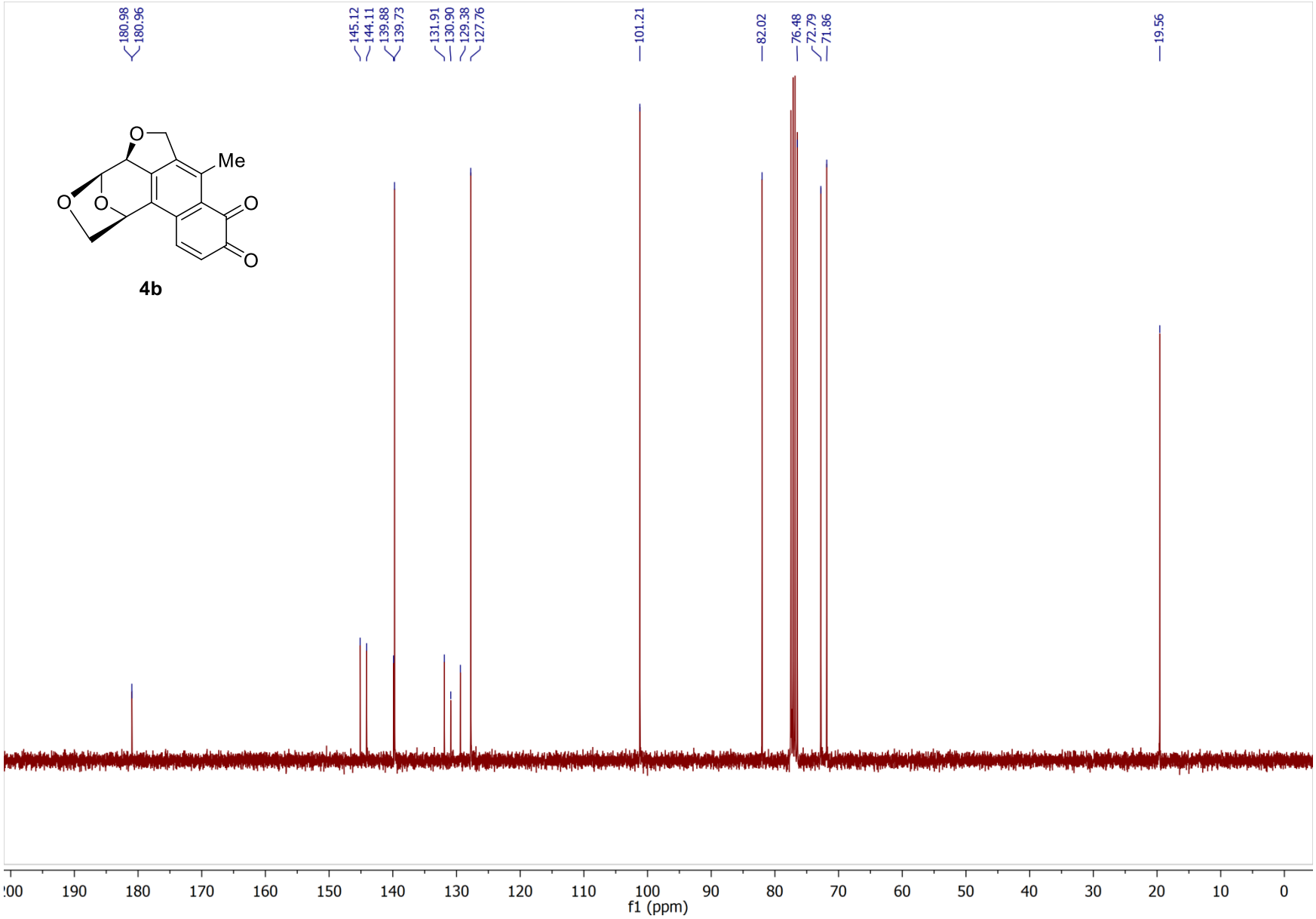
5.96
5.96
5.73
5.73
5.72
5.72
5.17
5.05
4.10
4.10
4.09
4.09
4.09
4.08
4.08
4.07
3.73
3.71
2.57
Me
O
O
O
O
O
4b
1.00
0.99
1.01
0.98
1.01
2.01
1.01
0.98
2.99
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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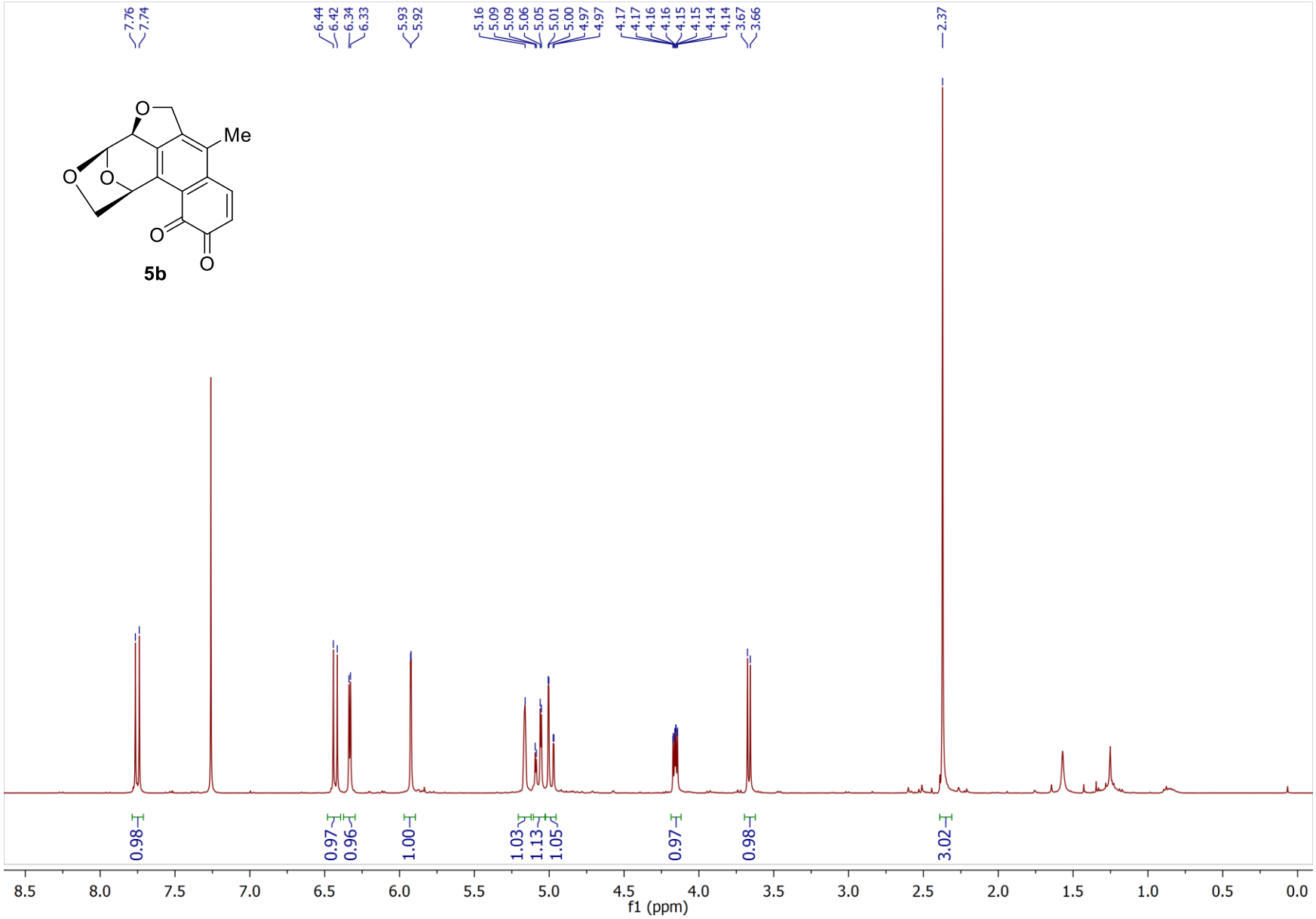
131.91
130.90
129.38
127.76
101.21
82.02
76.48
72.79
71.86
19.56
Me
O
O
O
O
O
4b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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5.06
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5.01
5.00
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4.97
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4.17
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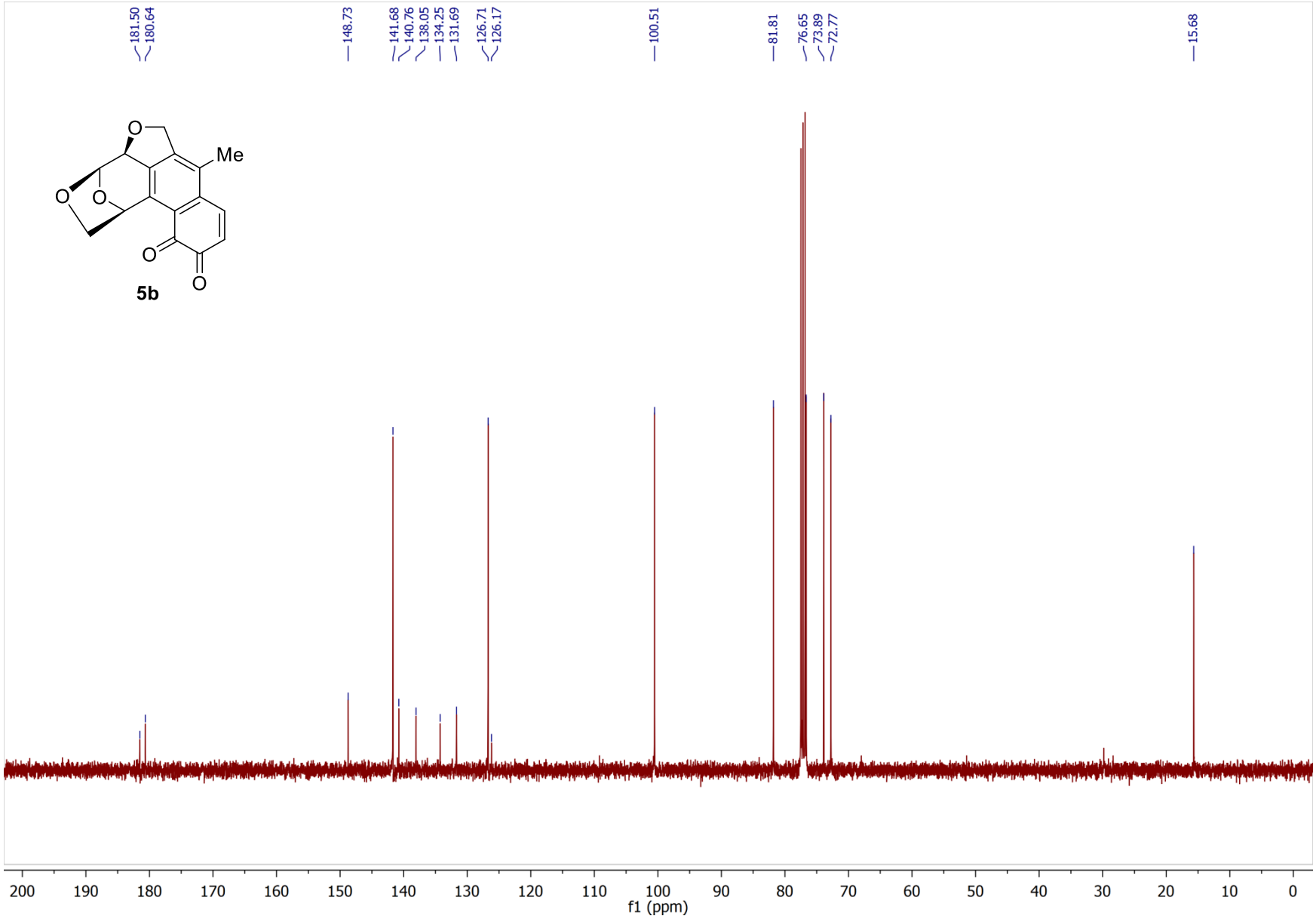
4.16
4.15
4.15
4.14
4.14
3.67
3.66
2.37
O
Me
O
O
O
O
5b
0.98
0.97
0.96
1.00
1.03
1.13
1.05
0.97
0.98
3.02
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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140.76
138.05
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131.69
126.71
126.17
100.51
81.81
76.65
73.89
72.77
15.68
O
O
O
O
O
Me
5b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)