Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Electrochemically site-selective alkoxylation of twisted 2-arylbenzoic acids *via* spirolactonization

Manel Estruch-Blasco,[a] Irene Bosque,*[a] David Guijarro,[a] and Jose C. Gonzalez-Gomez*[a]

Email: josecarlos.gonzalez@ua.es; irene.bosque@ua.es

CONTENTS

General Remarks

Commercial chemicals were used as obtained from Sigma-Aldrich, TCI Europe or Alfa-Aesar. CH_3CN (for analysis, ACS) was purchased from Panreac 99.7% pure. The preparation of starting materials not obtained from commercial sources is detailed below. TLCs were performed on silica gel 60 F_{254}, using aluminum plates and visualized by exposure to ultraviolet light. Flash chromatographies (FC) were carried out on hand-packed columns of silica gel 60 (230–400 mesh). Melting points (M.P.) were measured in a Riecher Thermovar heating stage microscope and were not corrected. GC yields were determined by GC-FID (6890 Agilent, HP-5 30 m column), using 1,2,4,5-tetramethylbenzene as the internal standard. LRMS were obtained using a mass spectrometer coupled with a gas chromatographer (GC); the mobile phase was helium (2 $mL \cdot min^{-1}$); HP-1 column of 12 m was used; temperature program starts at 80 ºC for 3 min, then up to 270 ºC at a rate of 15 $ºC \cdot min^{-1}$, and 15 min at 300 ºC (unless other conditions are indicated). HPLC analysis was performed in a chiral OD-H column, under a flow rate of 0.5 mL/min in 98:2 hexane:*i*-PrOH media. NMR spectra were recorded at 300 or 400 MHz for ^1H and at 75 or 101 MHz for ^{13}C, using $CDCl_3$ as solvent (unless otherwise stated). For ^1H-NMR, TMS was used as an internal standard (0.00 ppm). The data are reported as (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, brs = broad signal, coupling constant(s) in Hz, integration). ^{13}C-NMR spectra were recorded with ^1H-decoupling at 101 MHz and referenced to $CDCl_3$ at 77.16 ppm. Exact masses were determined by HRMS (Agilent 7200 de Quadrupole-Time of Flight(Q-TOF)). Cyclic voltammograms were performed using a EmStat3 blue+ potentiostat (PalmSens). Electrochemical ECDC was performed using a programmable power supply FA-405 (Promax).

Materials and set-up of the ECDC:

Small scale:

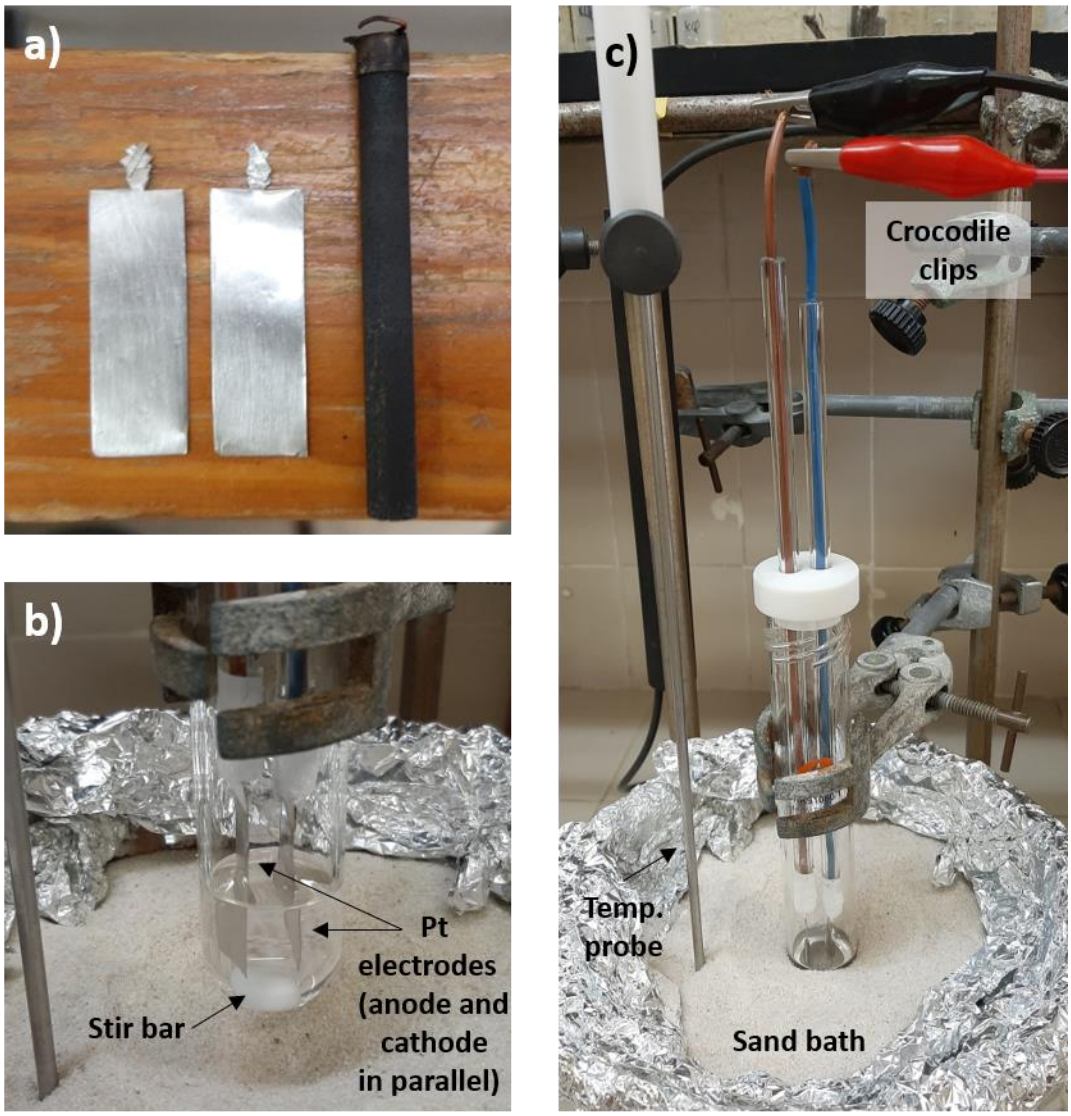


Figure S1: a) Set of electrodes used in this work: Pt foil (1 x 2.5 cm^2) and graphite bar (0.3 cm diameter). b) reaction vessel with both electrodes and a stir bar. c) complete set-up with a sand bath and a temperature probe to control the reaction temperature, and the electrical connections.

Large scale:

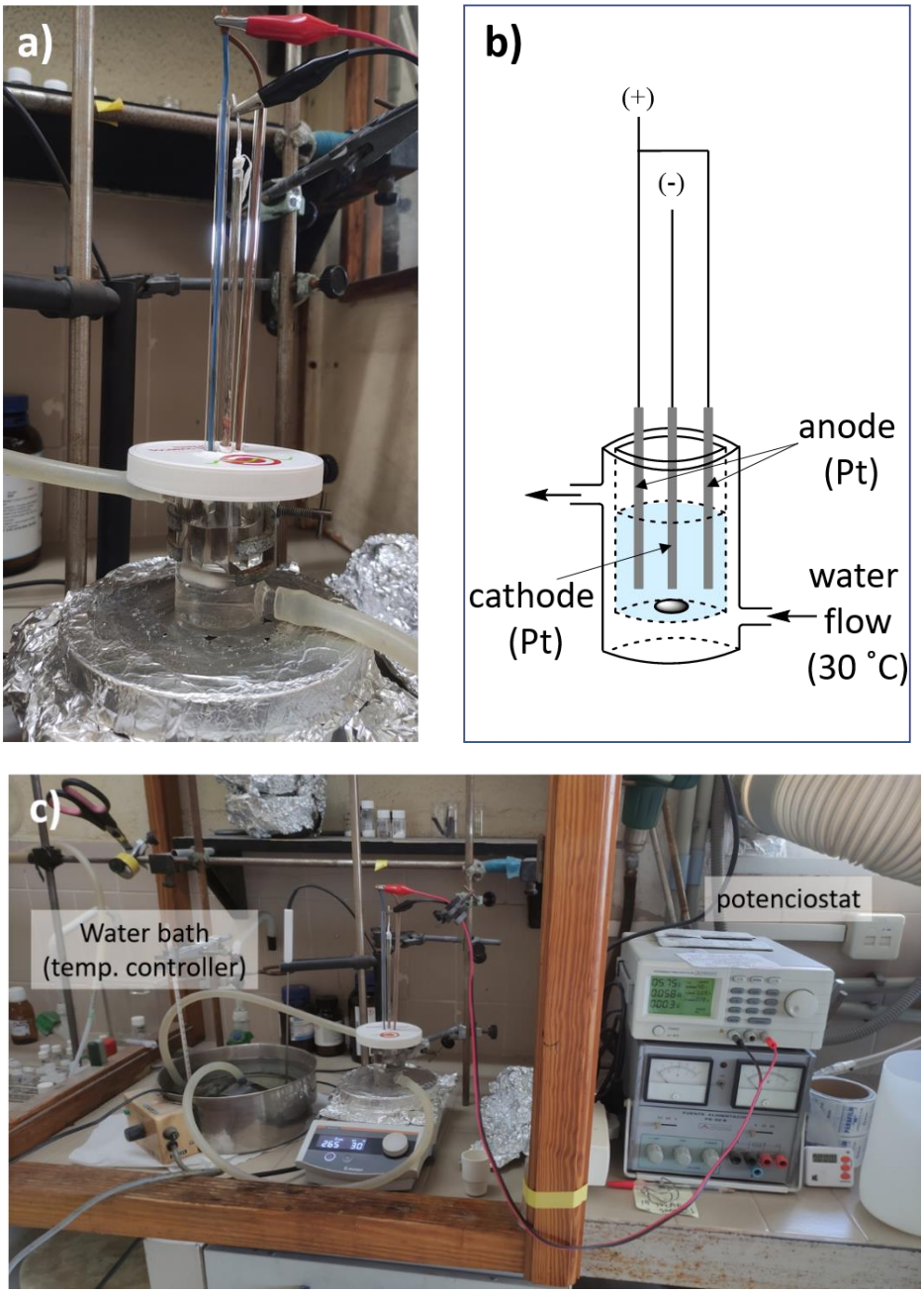
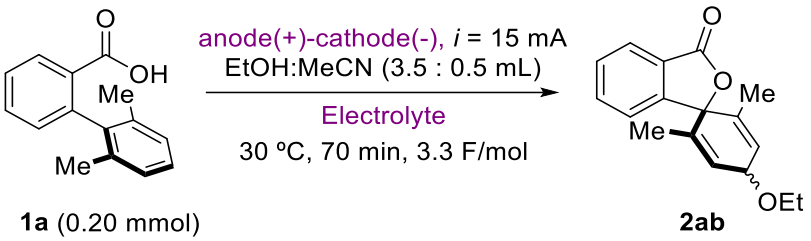


Figure S2: a) Set-up of the reaction. Anode Pt foil (1 x 2 cm^2 each) and cathode Pt electrode (2.5 x 2 cm^2) b) Schematic representation of the set-up. c) complete set-up with the temperature controller and the potentiostat.

Further optimization of the ECDC

Electrodes

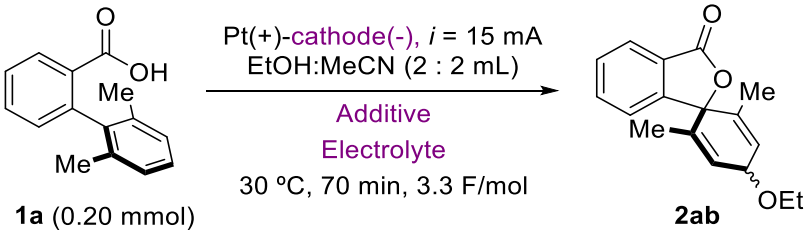


1a (0.20 mmol) **2ab**

Anode	Cathode	Electrolyte (eq.)	GC yield recovered of 1a [a] (%)	GC yield 2aa[a] (isolated) (%)
Pt	**C fiber**	Bu_4NPF_6 (1)	-	**48 (50)**
C fiber	**Pt**	Bu_4NPF_6 (1)	-	**18**
Pt	**Pt**	Bu_4NPF_6 (1)	-	**34**
C fiber	**C fiber**	Bu_4NPF_6 (1)	-	**9**
Pt	**Graph2**	KPF_6 (0.2)	-	**nr**

[a] Yield was determined by GC using durene as internal standard.

Electrolytes

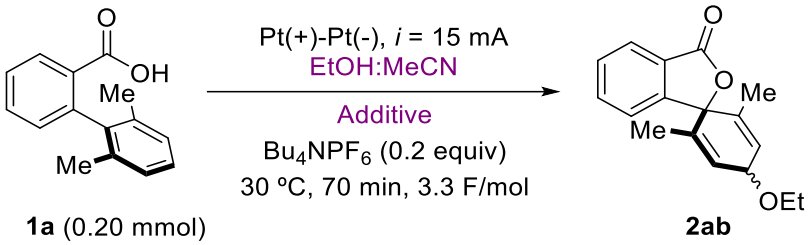


1a (0.20 mmol) **2ab**

Cathode	Electrolyte (eq.)	Add. (eq.)	CH_3CN : EtOH	GC yield recovered of 1a [a] (%)	GC yield 2aa[a] (isolated) (%)
C fiber	KOH (0.3)	-	3:1	-	**nr**
C fiber	KPF_6 (1)	-	3:1	-	**51**
Pt	Bu_4NPF_6 (0.2)	2,6-lut. (0.5)	1:1	3	**81 (69)**
Pt	$NaClO_4$(0.2)	2,6-lut. (0.5)	1:1	-	**70**
Pt	$NaBF_4$(0.2)	2,6-lut. (0.5)	1:1	-	**78**
Pt	Bu_4NBr (0.2)	2,6-lut. (0.5), hv	1:1	-	**nr**

[a] Yield was determined by GC using durene as internal standard.

Additives

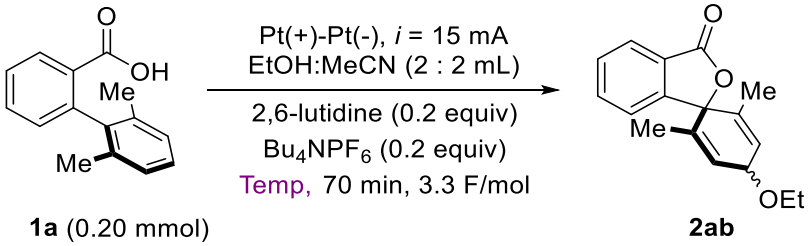


1a (0.20 mmol) **2ab**

Add. (eq.)	CH_3CN : EtOH	GC yield recovered of 1a [a] (%)	GC yield 2aa[a] (isolated) (%)
2,6-lut. (0.5)	12.3:1	**10**	**76**
2,6-lut. (0.5), NaBr	1:1	-	**nr**
2,6-lut. (0.2)	1:1	-	**85**
HFIP (10)	10 eq EtOH	-	**nr**
-	29 eq EtOH	22	**23**
2,6-lut. (0.2)	29 eq EtOH	20	**34**
2,6-lut. (1)	25 eq EtOH	24	**47**

[a] Yield was determined by GC using durene as internal standard.

Temperature



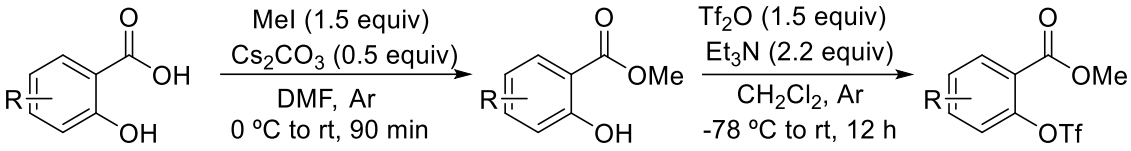
1a (0.20 mmol) **2ab**

Temperature[a]	GC yield recovered of 1a [b] (%)	GC yield 2aa[b] (isolated) (%)
0 ˚C	**19**	**45**
15 ˚C	**11**	**56**
25 ˚C	**5**	**59**
(rT) 30 ˚C	-	**81 (74)**
40 ˚C	**2**	**55**

[a] A sand bath was used to control the external temperature. [b] Yield was determined by GC using durene as internal standard.

General synthetic procedures

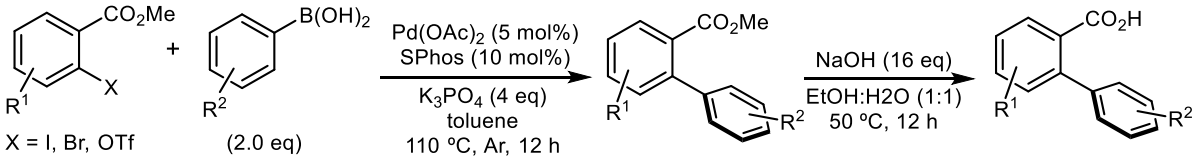
General for the synthesis of *o*-triflatemethylbenzoates (**Procedure A**):



The procedure is a slightly modified protocol previously described in the literature:[1] To a solution of the corresponding acid (3 mmol) in dry DMF (30 mL) was added Cs_2CO_3 (489 mg, 1.5 mmol) under Ar atmosphere, followed by MeI (196 µL, 3.15 mmol). This mixture was stirred for 90 minutes under Ar atmosphere at room temperature. At this time, the rxm was distributed between phases using a EtOAc/H_2O mixture (30 mL:30 mL). The aqueous layer was extracted with EtOAc (4 × 20 mL). The combined layers were washed with H_2O (2 × 10 mL), $NaHCO_3$ (aq. sat.) (2 × 10 mL) and brine (1 × 5 mL), dried over $MgSO_4$, filtered and concentrated to afford the desired hydroxiester intermediate.

The hydroxiester previously obtained was dissolved in dry CH_2Cl_2 (30 mL). This rxm was cooled to -78 ºC under Ar atmosphere and then Et_3N (6.6 mmol, 921 µL), followed by Tf_2O (4.5 mmol, 760 µL) were both added dropwise. After complete addition, the rxm was stirred for 30 minutes at -78 ºC and allowed to reach room temperature for 12 h under Ar atmosphere. The reaction mixture was extracted with Et_2O (4 × 25 mL). The combined layers were washed with HCl 1M (4 × 25 mL) and brine (1 × 5 mL), then dried over $MgSO_4$, filtered and concentrated. The obtained residue was purified by FC.

General procedure for the synthesis of other o-*arylbenzoic acids* (**Procedure B):**

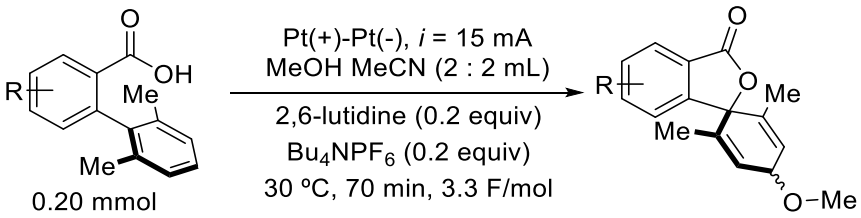


In a pressure tube with a Teflon cap, the corresponding methyl benzoate (1.30 mmol) and the corresponding phenyl boronic acid (2.60 mmol, 2 equiv) were added, followed by $Pd(OAc)_2$ (13.5 mg, 5 mol%) and SPhos (54 mg, 10 mol%). Then, dry toluene (7 mL) was added and the solution was vigorously stirred before the addition of K_3PO_4 (1.10 g, 4 equiv). The pressure tube was flushed with Ar, capped and place in an oil bath at 110 ºC for 12-15 h. After this time, the reaction was allowed to

reach room temperature, diluted with water and poured into a separation funnel. The mixture was extracted with EtOAc (4x15 mL), and the collected organics were washed with water (20 mL) and brine (10 mL), then dried over $MgSO_4$, filtered and concentrated. The obtained residue was purified by FC and its identity was confirmed by GC-MS analysis in all cases.

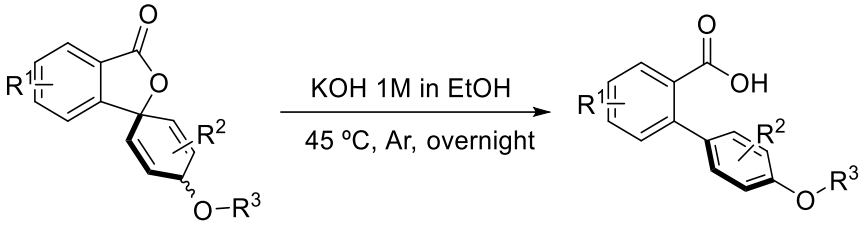
The purified intermediate ester was hydrolyzed by adding EtOH (8 mL/mmol ester) and a 2 M NaOH (8 mL/mmol ester, 16 equiv). The mixture was heated at 50 ºC for 12 h, using a reflux condenser. Then, it was cooled down to 0 ºC and 1 M HCl solution was added dropwise until pH 3 (around 8 mL/mmol ester). A precipitate crushed out and was filtered off under vacuum and dried under vacuum. Further purification was not necessary unless otherwise noted.

General procedure for the synthesis of spiro compounds through ECDC reaction (**Procedure C):**



The corresponding acid (0.20 - 0.30 mmol) and the electrolyte (0.2 equiv) were added to a glass tube used as undivided cell (15 x 2 cm, large x internal diameter), and the mixture was flushed with Ar. Then 0.02 M solution of 2,6-lutidine in MeCN was added (2 - 3 mL, 0.2 equiv), followed by the alcohol (2 - 3 mL). After complete dissolution, the electrodes were placed in the reaction media (immersed area = 1 - 1.5 cm^2) and the current was circulated for 70 - 80 min in a galvanostatic manner (15 - 20 mA, 3.3 F/mmol). Then the solvent was removed under reduced pressure and the product purified by FC.

General Procedure for the isomerization of spiro compounds (**Procedure D**)

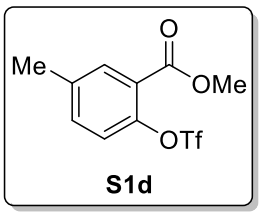


The corresponding spiro compound (0.10 mmol) was placed in a 10 mL pressure tube and dissolved in a solution of KOH in EtOH (1 M, 1 mL). The rxm was flushed with Ar, closed with a teflon cap, placed in an oil bath at 45 ºC, and stirred overnight at the same temperature. Then the rxm was cooled down to room temperature, placed in an ice-water bath for 10 min, and quenched with HCl 1M (≈ 1 mL) until pH ≈ 1, observing the formation of a precipitate. The solid was filtered off, and dried under vacuum, with no further purification unless otherwise noted.

Synthesis of compounds

Synthesis of *o*-triflatemethylbenzoates **S1d**, **S1e**, **S1f** and **S1i**

Methyl 5-methyl-2-(((trifluoromethyl)sulfonyl)oxy)benzoate (**S1d**):



S1d

Following the procedure A, compound **S1d** was obtained from *5-methylsalicylic acid* (456 mg, 3 mmol) as a yellow liquid (486 mg, 54% over two steps), after FC (98:2-95:5 hexane/EtOAc).

TLC (95:5 hexane/EtOAc): R_f 0.15.

IR ν cm^{-1} 1732, 1423, 1296, 1207, 11381076, 903, 868.

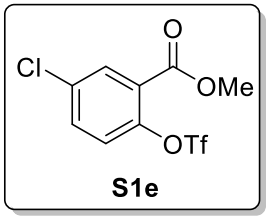
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 2.1 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.18 (br d, J = 8.4 Hz, 1H), 3.96 (s, 3H), 2.42 (s, 1H) ppm.

^{13}C NMR {H^1} (75 MHz, $CDCl_3$): δ 164.5, 146.4, 138.9, 134.9, 133.2, 124.0, 122.6, 118.8 (q, J = 320.7 Hz), 52.7, 20.9 ppm.

LRMS (EI): *m/z* (%) 298 (M^+, 100), 267 (49), 203 (46), 165 (88), 134 (39).

HRMS (EI-TOF): *m/z* calcd for $C_{10}H_9F_3O_5S$ 298.0123, found 298.0127.

Methyl 5-chloro-2-(((trifluoromethyl)sulfonyl)oxy)benzoate (**S1e**):



S1e

Following the procedure A, the desired product **S1e** was obtained from *5-chlorosalicylic acid* (520 mg, 3 mmol) after FC (97:3 Hex:EtOAc) as an off-white solid (615 mg, 64% over two steps).

TLC (95:5 hexane/EtOAc): R_f 0.32.

IR ν 1735, 1477, 1427, 1388, 1261, 1207, 1137, 890, 840 cm^{-1}

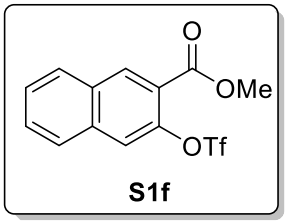
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 2.6 Hz, 1H), 7.58 (dd, J = 8.8, 2.6 Hz, 1H), 7.25 (d, J = 8.8 Hz, 1H), 3.97 (s, 3H) ppm**.**

^{13}C NMR {H^1} (75 MHz, $CDCl_3$) δ 163.2, 146.7, 134.2, 132.7, 125.8, 124.3, 118.7 (q, J = 320.6 Hz), 53.2 ppm.

LRMS (EI) *m/z* (%) 320 (26), 318 (M^+, 75), 289 (16), 287 (47), 225 (34), 223 (100), 185 (49), 169 (21), 157 (28), 154 (38), 129 (32), 126 (24).

HRMS (EI-TOF): *m/z* calcd for $C_9H_6ClF_3O_5S$ 317.9577, found 317.9581.

Methyl 3-(trifluoromethylsulfonyloxy)-2-naphthoate (**S1f**):



S1f

Following the procedure A, the desired product **S1f** was obtained from *3-hydroxy-2-naphthoic acid* (564 mg, 3 mmol) after FC (95:5 Hex:EtOAc) as an off-green solid (585 mg, 58% over two steps).

TLC (95:5 hexane/EtOAc): R_f 0.23.

IR: ν 3065, 1712, 1415, 1230, 1218, 848, 763 cm^{-1}.

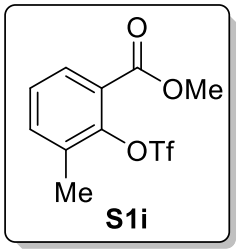
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.66 (s, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.74 (s, 1H), 7.71 – 7.59 (m, 2H), 4.02 (s, 3H) ppm.

^{13}C NMR {H^1} (75 MHz, $CDCl_3$): δ 164.5, 144.9, 135.09, 134.99, 131.5, 129,9, 129.2, 128.2, 127.8, 122,1, 121.2, 118.82 (q, J = 320.7 Hz), 52.8 ppm.

LRMS (EI) *m/z* (%) 334 (M^+, 100), 303 (23), 239 (8), 201 (74), 173 (38), 170 (26), 143 (89), 115 (42), 114 (48).

HRMS (EI-TOF) calcd for $C_{13}H_9F_3O_5S$ 334.0123, found 334.0124.

Methyl 3-methyl-2-(trifluoromethylsulfonyloxy)benzoate (**S1i**):



S1i

Following the procedure A, the desired product **S1i** was obtained from *3-methylsalicylic acid* (456 mg, 3 mmol) after FC (98:2 to 95:5 Hex:EtOAc) as an off-yellow oil (588 mg, 66% over two steps).

TLC (8:2 hexane/EtOAc): R_f 0.26.

IR: ν 2958, 1731, 1423, 1295, 1207, 1137, 887 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81 (dd, J = 7.6, 1.8 Hz, 1H), 7.47 (ddd, J = 7.7, 1.9, 0.8 Hz, 1H), 7.34 (t, J = 7.7 Hz, 1H), 3.93 (s, 3H), 2.42 (s, 3H) ppm.

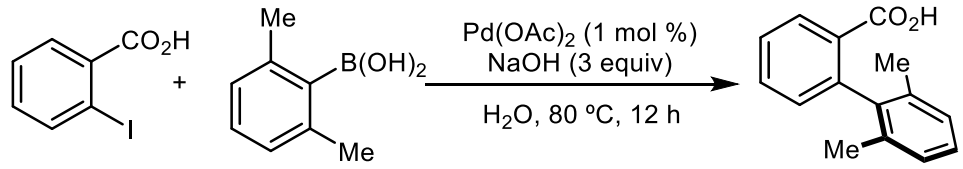
^{13}C NMR {H^1} (75 MHz, $CDCl_3$): δ 165.3, 146.2, 136.2, 132.2, 130.2, 127.9, 125.6, 118.7 (q, J = 320.7 Hz), 52.8, 16.6 ppm.

LRMS (EI): *m/z* (%) 298 (M^+, 22), 267 (26), 203 (22), 165 (25), 133 (100), 105 (23).

HRMS (EI-TOF): *m/z* calcd for $C_{10}H_9F_3O_5S$ 298.0123, found 298.0128.

Synthesis of *o*-arylbenzoic acids **1**

2',6'-Dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**1a**)



(1.05 equiv) **1a**

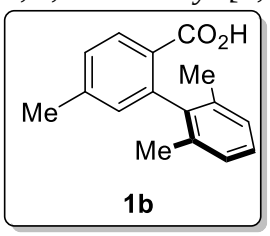
Acid **1a** was prepared from *2-iodobenzoic acid* (1290 mg, 5.2 mmol) and *2,6-dimethylphenyl boronic acid* (820 mg, 5.46 mmol) following a procedure described in the literature.[2] After FC (8:2, hexane:(3:1:0.1, EtOAc, EtOH, AcOH), the desired acid was obtained as a white solid in a range of 54-56% yield, with a characterization data that matched the one described in the literature.

TLC (8:2 hexane/EtOAc): R_f 0.26; (8:2, hexane:(3:1:0.1, EtOAc, EtOH, AcOH): R_f 0.35.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.39 (br s, 1H), 8.10 (dd, J = 7.9, 1.1 Hz, 1H), 7.61 (td, J = 7.5, 1.4 Hz, 1H), 7.44 (td, J = 7.7, 1.3 Hz, 1H), 7.20 – 7.12 (m, 2H), 7.12 – 7.02 (m, 2H), 1.94 (s, 6H) ppm.

^{13}C NMR {H^1} (75 MHz, $CDCl_3$): δ 172.0 (C=O), 143.0 (C), 140.9 (C), 135.3 (2xC), 133.2 (CH), 131.4 (CH), 131.0 (CH), 129.0 (C), 127.3 (CH), 127.1 (2xCH), 20.7 (2xCH_3) ppm.

2',6', 5-Trimethyl-[1,1'-biphenyl]-2-carboxylic acid (**1b**):



Following procedure B, from *methyl 2-bromo-4-methylbenzoate* (300 mg, 1.3 mmol) and *2,6-dimethylphenylboronic acid* (390 mg, 2.6 mmol) the intermediate ester was obtained after FC (98:2 Hex:EtOAc) as a colorless oil (298 mg, 90%). GC-MS analysis showed a single peak with *m/z* = 254. The hydrolysis of the ester gave the corresponding acid **1b** as a white solid (201 mg, 72%).

TLC (8:2 hexane/EtOAc): R_f 0.25.

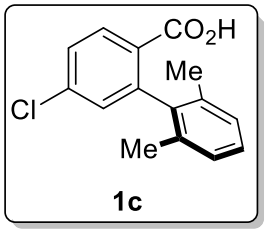
IR: ν 3020, 2924, 1689, 1608, 1412, 1288, 910, 775, 732 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.31 (br s, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.24 (dd, J = 8.1, 1.2 Hz, 1H), 7.15 (dd, J = 8.3, 6.6 Hz, 1H), 7.07 (d, J = 7.7 Hz, 2H), 6.98 – 6.94 (m, 1H), 2.42 (s, 3H), 1.95 (s, 6H) ppm.

^{13}C NMR {H^1} (75 MHz, $CDCl_3$): δ 172.1, 144.0, 143.2, 141.2, 135.2, 131.63, 131.59, 128.0, 127.04, 126.92, 126.0, 21.7, 20.7 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{16}H_{16}O_2$ 240.1150, found 240.1155.

5-chloro-2',6'-dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**1c**):



Following procedure B, from *methyl 4-chloro-2-iodobenzoate* (200 mg, 0.67 mmol) and *2,6-dimethylphenylboronic acid* (201 mg, 1.34 mmol) the intermediate ester was obtained after FC (98:2 Hex:EtOAc) as a colorless oil (136 mg, 74%). GC-MS analysis showed two peaks, the major one with *m/z* = 274, corresponding to the product, and another with *m/z* = 344, corresponding to the disubstituted product. The hydrolysis of the ester gave the corresponding acid **1c** as a yellow solid (115 mg, 88%).

TLC (8:2 hexane:(3:1:0.1, EtOAc, EtOH, AcOH): R_f 0.47

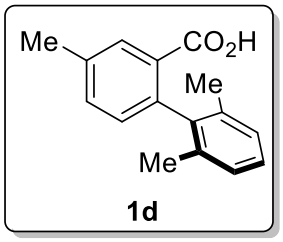
IR: ν 2650, 2557, 1685, 1585, 1423, 1288, 937, 841, 771 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04 (dd, *J* = 8.5, 0.4 Hz, 1H), 7.42 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.19 – 7.13 (m, 2H), 7.09 – 7.04 (m, 2H), 1.94 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 171.1, 145.0, 139.6, 139.5, 135.0, 132.9, 131.1, 127.6, 127.5, 127.4, 127.2, 20.7 ppm.

HRMS (EI-TOF) *m/z* calcd for $C_{15}H_{13}ClO_2$ 260.0604, found 260.0579.

2',4,6'-trimethyl-[1,1'-biphenyl]-2-carboxylic acid (**1d**):



Following procedure B, from *methyl 2-triflate-5-methylbenzoate* (**S1d**) (387 mg, 1.3 mmol) and *2,6-dimethylphenylboronic acid* (390 mg, 2.6 mmol) the intermediate ester was obtained after FC (98:2 Hex:EtOAc) as a white solid (256 mg, 77%). GC-MS analysis showed a single peak with *m/z* = 254 The hydrolysis of the ester gave the corresponding acid **1d** as a white solid (238 mg, 99%).

TLC (8:2 hexane/EtOAc): R_f 0.38.

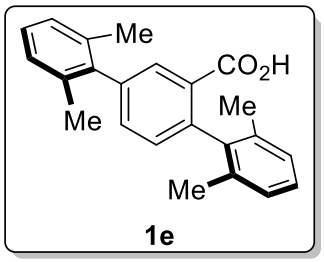
IR: ν cm^{-1} 2920, 1689, 1423, 1292, 1261, 1211, 768.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93 – 7.89 (m, 1H), 7.54 – 7.35 (m, 1H), 7.14 (dd, *J* = 8.6, 6.2 Hz, 1H), 7.09 – 6.99 (m, 3H), 2.44 (s, 3H), 1.93 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.4, 141.1, 139.7, 136.9, 135.5, 133.7, 131.6, 130.7, 129.4, 127.0, 126.9, 21.1, 20.7 ppm.

HRMS (EI-TOF) calcd for $C_{16}H_{16}O_2$ 240.115, found 240.1142.

2',2'',6',6''-Tetramethyl-[1',1:4,1''-terphenyl]-2-carboxylic acid (**1e**):



1e

Following procedure B, from methyl 5-chloro-2-(trifluoromethylsulfonyloxy)benzoate (**S1e**) (413 mg, 1.3 mmol) and 2,6-dimethylphenylboronic acid (390 mg, 2.6 mmol) the double substituted intermediate ester was obtained as major product after column chromatography (97:3 Hex:EtOAc) as a white solid (300 mg, 67%). GC-MS analysis showed a single peak with *m/z* = 344. The hydrolysis of the ester gave the corresponding acid **1e** as a white solid (237 mg, 82%).

TLC (8:2 hexane/EtOAc): R_f 0.29

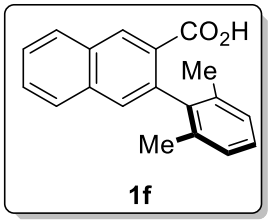
IR: ν 3019, 2958, 2919, 1685, 1461, 1427, 1299, 1261, 933, 767 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.22 – 7.06 (m, 7H), 2.09 (s, 6H), 2.00 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.2, 141.4, 140.8, 140.4, 140.2, 136.1, 135.4, 134.5, 133.9, 132.0, 131.2, 129.1, 127.6, 127.5, 127.1, 21.0, 20.7 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{23}H_{22}O_2$ 330.1620, found 330.1610.

3-(2,6-Dimethylphenyl)-2-naphthoic acid (**1f**):



1f

Following procedure B, from *methyl 3-(trifluoromethylsulfonyloxy)-2-naphthoate* (**S1f**) (434 mg, 1.30 mmol) and *2,6-dimethylphenylboronic acid* (390 mg, 2.6 mmol) the intermediate ester was obtained after column chromatography (97:3 Hex:EtOAc) as a white solid (369 mg, 98%). GC-MS analysis showed a single peak with *m/z* = 290. The hydrolysis of the ester gave the corresponding acid **1f** as a white solid (311 mg, 89%).

TLC (8:2 hexane/EtOAc): R_f 0.28.

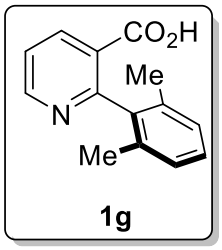
IR: ν 3050, 2919, 2881, 1681, 1457, 1407, 1284, 910, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.66 – 7.55 (m, 3H), 7.24 – 7.18 (m, 1H), 7.16 – 7.11 (m, 2H), 1.99 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.1, 140.9, 138.4, 135.8, 135.6, 133.2, 131.6, 129.9, 129.2, 128.8, 127.7, 127.2, 127.1, 127.1, 126.8, 20.9 ppm.

HRMS (EI-TOF): calcd for $C_{19}H_{16}O_2$ 276.1150, found 276.1146.

2-(2,6-dimethylphenyl)Nicotinic acid (**1g**):



Following procedure B, from *methyl 2-chloronicotinate* (222 mg, 1.3 mmol) and *2,6-dimethylphenylboronic acid* (390 mg, 2.6 mmol) the intermediate ester was obtained after FC (8:2 Hex:EtOAc) as a colorless oil (288 mg, 87%). GC-MS analysis showed a single peak with *m/z* = 257. The crystallization of the acid directly from the reaction media gave pure acid **1g** as a white solid (156 mg, 67% yield). When the precipitation was not successful, extraction with EtOAc (x3) gave the title pure product after drying, filtration and concentration of the organic phase (219 mg, 80%).

TLC (7:3 hexane/(3:1:0.1 EtOAc:EtOH:AcOH): R_f 0.29.

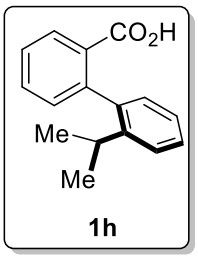
IR: ν 2923, 1701, 1574, 1446, 1265, 1068, 764 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.96 (brs, 1H), 8.81 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.26 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.52 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.14 (dd, *J* = 8.4, 6.4 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 2H), 1.85 (s, 6H) ppm.

^{13}C NMR {H^1} (75 MHz, DMSO-d_6): δ 167.4, 158.4, 151.9, 140.6, 137.6, 134.6, 128.1, 127.2, 126.8, 122.3, 19.6 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{14}H_{12}NO$ [M^+-OH] 210.0919, found 210.0911.

2'-Isopropyl-[1,1'-biphenyl]-2-carboxylic acid (**1h**):



Following procedure B, from *methyl 2-iodobenzoate* (280 mg, 1.3 mmol) and *2-isopropylphenylboronic acid* (434 mg, 2.6 mmol) the intermediate ester was obtained after FC (95:5 Hex:EtOAc) as a colorless oil (288 mg, 87%). GC-MS analysis showed a single peak with *m/z* = 254. The crystallization of the acid directly from the reaction media after hydrolysis of the ester was not successful. Extraction using EtOAc (3x10 mL) was performed to the whole sample obtaining pure acid **1h** as a white solid (270 mg, quant.).

TLC (8:2 hexane/EtOAc): R_f 0.29.

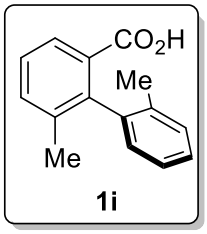
IR: ν 3058, 2962, 2923, 1689, 1596, 1296, 1107, 937, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.34 (brs, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.25 (d, *J* = 7.8 Hz, 1H), 7.17 (td, *J* = 8.0, 4.0 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 2.69 (hept, *J* = 6.8 Hz, 1H), 1.11 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 6.8 Hz, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.6, 146.1, 143.7, 140.1, 132.2, 131.6, 130.8, 129.3, 128.7, 127.8, 127.2, 125.2, 125.0, 30.3, 24.7, 23.2 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{16}H_{16}O_2$ 240.1150, found 240.1147.

2',6-dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**1i**):



Following procedure B, from *3-methyl-2-(trifluoromethylsulfonyloxy)benzoate* (**S1i**) (387 mg, 1.3 mmol) and *2-methylphenylboronic acid* (354 mg, 2.6 mmol), the intermediate ester was obtained after FC (95:5 Hex:EtOAc). The product was contaminated with some *2,2'-dimethyl-1,1'-biphenyl* that was removed in *vacuo* (7 h at 1-5 mmBar, 80 ºC), obtaining the desired ester as a colorless oil (143 mg, 45%). GC-MS analysis showed a major peak with *m/z* = 240. The hydrolysis of the ester in basic media followed by acidic quench favored the crystallization of the acid **1i** from the reaction media as a white solid (98 mg, 72%.).

TLC (8:2 hexane/EtOAc): R_f 0.20.

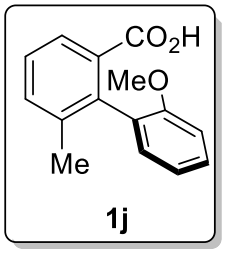
IR: ν 2919, 2865, 1681, 1577, 1276, 929, 759, 721 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.78 (brs, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.27 – 7.18 (m, 3H), 6.95 (d, *J* = 7.2 Hz, 1H), 1.99 (s, 3H), 1.98 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.8, 142.5, 139.7, 137.7, 135.6, 134.3, 129.7, 129.6, 128.4, 128.1, 127.3, 127.2, 125.7, 20.4, 19.8 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{15}H_{14}O_2$ 226.0994, found 226.0990.

2'-Methoxy-6-methyl-[1,1'-biphenyl]-2-carboxylic acid (**1j**):



Following procedure B, from *methyl 3-methyl-2-(trifluoromethylsulfonyloxy)benzoate* (**S1i**) (387 mg, 1.3 mmol) and *2-methoxyphenylboronic acid* (395 mg, 2.6 mmol) the intermediate ester was obtained after FC (97:3 to 95:5 Hex:EtOAc) as a white solid (293 mg, 88%). GC-MS analysis showed a single peak with *m/z* = 256. The hydrolysis of the ester gave the corresponding acid **1j** as a white solid (198 mg, 72%)

TLC (7:3 hexane/EtOAc): R_f 0.12.

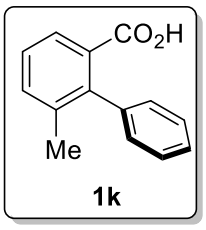
IR: ν 2962, 2915, 1681, 1461, 1430, 1288, 1230, 1014, 948, 755 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.38 – 7.28 (m, 2H), 7.03 – 6.96 (m, 2H), 6.93 (d, *J* = 8.2 Hz, 1H), 3.70 (s, 3H), 2.08 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 173.2, 156.4, 139.2, 138.2, 134.1, 130.5, 129.9, 128.9, 128.8, 128.0, 127.1, 120.6, 110.8, 55.6, 20.5 ppm.

HRMS (EI) calcd for $C_{15}H_{14}O_3$ 242.0943, found 242.0944.

6-Methyl-[1,1'-biphenyl]-2-carboxylic acid (**1k**):



Following procedure B, from *methyl 2-chlorobenzoate* (222 mg, 1.3 mmol) and *phenylboronic acid* (320 mg, 2.6 mmol) the intermediate ester was obtained after FC (97:3 Hex:EtOAc) as a colorless oil (261 mg, 89%). GC-MS analysis showed a single peak with *m/z* = 226. The crystallization of the acid directly from the reaction media after hydrolysis of the ester provided the corresponding acid **1k** as a white solid (215 mg, 88%.).

TLC (7:3 hexane/EtOAc): R_f 0.11.

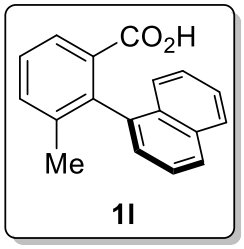
IR: ν 3058, 3019, 2915, 1685, 1446, 1411, 1299, 763 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.68 (s, 1H), 7.78 (d, J = 7.7 Hz, 1H), 7.46 – 7.28 (m, 5H), 7.18 – 7.12 (m, 2H), 2.08 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 173.3, 142.6, 140.0, 137.6, 134.0, 130.2, 128.6, 128.1, 128.0, 127.2, 127.0, 20.9 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{14}H_{12}O_2$ 212.0837, found 212.0834.

3-methyl-2-(naphthalen-1-yl)benzoic acid (**1l**):



Following procedure B, from *methyl 3-methyl-2-(trifluoromethylsulfonyloxy)benzoate* (**S1i**) (201 mg, 0.67 mmol) and *1-naphtylboronic acid* (230 mg, 1.34 mmol) the intermediate ester was obtained after FC (99:1 to 98:2 Hex:EtOAc) as a colorless oil (183 mg, quant.). GC-MS analysis showed a single peak with *m/z* = 276. The hydrolysis of the ester gave the corresponding acid **1l** as a white solid (151 mg, 82%).

TLC (8:2 hexane/EtOAc): R_f 0.27.

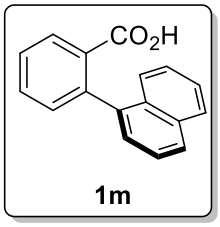
IR: ν 3051, 2924, 2854, 1689, 1581, 1404, 1269, 910, 767, 734 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (d, J = 8.2 Hz, 1H), 7.83 (t, J = 8.7 Hz, 2H), 7.52 – 7.43 (m, 3H), 7.39 (t, J = 7.7 Hz, 1H), 7.32 (ddd, J = 8.0, 6.7, 1.2 Hz, 1H), 7.26 (d, J = 8.4 Hz, 1H), 7.17 (dd, J = 7.0, 1.1 Hz, 1H), 1.89 (s, 3H) ppm.

^{13}C NMR {H^1} (75 MHz, $CDCl_3$): δ 172.3, 141.0, 138.7, 138.0, 134.2, 133.4, 132.0, 130.6, 128.5, 128., 127.5, 126.1, 125.9, 125.7, 125.44, 125.38, 20.4 ppm.

HRMS (EI-TOF) *m/z* calcd for $C_{18}H_{14}O_2$ 262.0994, found 262.0970.

2-(Naphthalen-1-yl)benzoic acid (**1m**):



Following procedure B, from *methyl 2-iodobenzoate* (280 mg, 1.3 mmol) and *(naphthalen-1-yl)boronic acid* (447, 2.6 mmol) the intermediate ester was obtained after FC (97:3 Hex:EtOAc) as a white solid (312 mg, 92%). GC-MS analysis showed a single peak with *m/z* = 262. The hydrolysis of the ester gave the corresponding acid **1m** as a white solid (270 mg, 91%)

TLC (8:2 hexane/EtOAc): R_f 0.12.

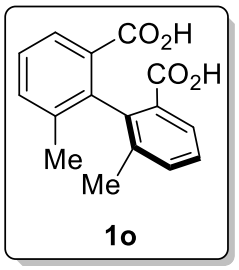
IR: ν 3008, 2869, 1689, 1407, 1292, 1272, 925, 767 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.07 (brs, 1H), 8.04 (d, J = 7.8 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.2 Hz, 1H), 7.60 (t, J = 7.5 Hz, 1H), 7.52 – 7.45 (m, 3H), 7.43 (s, 1H), 7.39 – 7.31 (m, 2H), 7.28 (d, J = 7.0 Hz, 1H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.1, 142.1, 139.3, 133.4, 132.29, 132.27, 132.1, 131.0, 130.3, 128.3, 127.7, 127.6, 126.1, 125.67, 125.61, 125.2 ppm.

HRMS (EI) calcd for $C_{17}H_{12}O_2$ 248.0837, found 248.0832.

6,6'-dimethyldiphenic acid (**1o**):



The title compound was obtained from *2-amino-3-methylbenzoic acid* (3.02 g, 20 mmol), following a reported procedure.[3] The bright yellow diazocompound was removed by filtration after stirring in boiling EtOH (40 mL) over 10-15 min. After adding water (90 mL) to the filtrate, the mixture was heated to reflux for 10 min and left cooling first to room temperature, then in the fridge (5 ºC approx.) overnight. The desired compound **1o** was obtained as light brown crystals (860 mg, 44%), which were filtered out and dried to air. The spectroscopic data is in accordance to the one previously reported.[4]

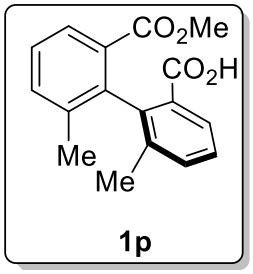
TLC (7:3 hexane/(3:1:0.1 EtOAc:EtOH:AcOH): R_f .0.26.

IR: ν 3062, 2962, 2920, 1689, 1585, 1415, 1277, 1184, 1157, 929, 756 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ 12.26 (bs, 2H), 7.72 (d, J = 7.5 Hz, 2H), 7.44 (d, J = 7.5 Hz, 2H), 7.31 (t, J = 7.5 Hz, 2H), 1.82 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, DMSO-d_6): δ 168.1, 140.7, 136.0, 132.9, 130.4, 127.3, 126.6, 19.8 ppm.

2'-(methoxycarbonyl)-6,6'-dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**1p**)



Following the protocol previously described in the literature:[5] To a solution of *6,6'-dimethyldiphenic acid* (0.6 mmol) and Ag_2CO_3 (83 mg, 0.3 mmol) in acetone (8.3 mL) at room temperature, was added MeI (114 µL, 1.8 mmol). This mixture was stirred for 12 hours at 40 ºC. At this time, the reaction mixture was quenched with HCl 2M (≈ 10 mL), distributed between phases using a EtOAc (40 mL) and separated. The aqueous layer was extracted with EtOAc (2 × 20 mL). The combined layers were washed with brine (1 × 20 mL), dried over $MgSO_4$, filtered, and concentrated to afford the desired methyl ester **1p** as an orange solid (114 mg, 67%), after FC (8:2 hexane/EtOAc).

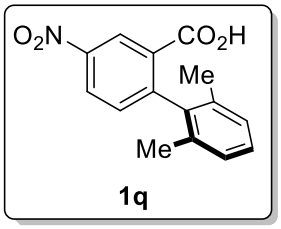
TLC (8:2 hexane/EtOAc): R_f 0.18.

IR ν cm^{-1}1720, 1659, 1435, 1259, 1188, 1142, 760 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 7.8 Hz, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.48 – 7.39 (m, 2H), 7.32 (td, J = 7.7, 3.3 Hz, 2H), 3.60 (s, 2H), 1.89 (s, 3H), 1.86 (s, 3H) ppm.

^{13}C NMR {H^1} (75 MHz, $CDCl_3$): δ 171.8, 168.4, 141.1, 140.7, 136.8, 136.6, 134.3, 133.9, 129.4, 129.3, 128.3, 127.7, 127.22, 127.18, 52.1, 20.11, 20.09 ppm.

2',6'-Dimethyl-4-nitro-[1,1'-biphenyl]-2-carboxylic acid (**1q**):



Following procedure B, from *methyl 2-iodo-5-nitrobenzoate* (200 mg, 0.66 mmol) and 2,6-dimethylphenylboronic acid (200 mg, 1.32 mmol) the intermediate ester was obtained after FC (98:2 Hex:EtOAc) as a white solid (150 mg, 80%). GC-MS analysis showed a single peak with *m/z* = 285. The hydrolysis of the ester gave the corresponding acid **1q** as white solid (130 mg, 90%).

TLC (7:3 hexane/EtOAc): R_f 0.20; (8:2 hexane/EtOAc): R_f 0.09

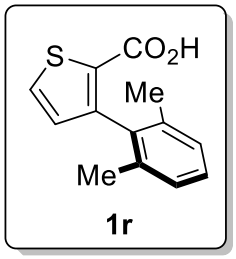
IR: ν cm^{-1} 2924, 1701, 1604, 1523, 1458, 1346, 1273, 914, 740.

^{1}H NMR (400 MHz, CD_3OD): δ 8.77 (dd, J = 2.5, 0.4 Hz, 1H), 8.43 (dd, J = 8.4, 2.5 Hz, 1H), 7.37 (dd, J = 8.4, 0.5 Hz, 1H), 7.13 (dd, J = 8.5, 6.6 Hz, 1H), 7.08 – 7.03 (m, 2H), 1.92 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 169.6, 149.8, 147.0, 138.8, 134.6, 132.6, 130.7, 128.0, 127.4, 127.4, 126.5, 20.6 ppm.

HRMS (EI-TOF) *m/z* calcd for $C_{15}H_{13}NO_4$ 271.0845, found 271.0848.

3-(2,6-dimethylphenyl)Thiophene-2-carboxylic acid (**1r**):



Following procedure B, from *methyl 3-iodothiophene-2-carboxylate* (348 mg, 1.3 mmol) and *2,6-dimethylphenylboronic acid* (388 mg, 2.6 mmol) the intermediate ester was obtained after FC (95:5 Hex:EtOAc) as a colorless oil (287 mg, 90%). GC-MS analysis showed a single peak with *m/z* = 246. The hydrolysis of the ester gave the corresponding acid **1r** as a white solid (216 mg, 75%).

TLC (8:2 hexane/EtOAc): R_f 0.26.

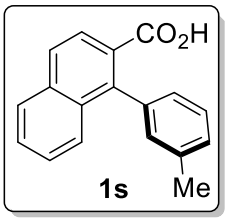
IR: ν 2931, 1658, 1439, 1288, 1107, 902, 771, 729 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 5.0 Hz, 1H), 7.17 (dd, *J* = 8.2, 6.8 Hz, 1H), 7.07 (d, *J* = 7.7 Hz, 2H), 6.88 (d, *J* = 5.0 Hz, 1H), 2.00 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 167.1, 148.8, 136.0, 135.7, 132.6, 131.2, 128.0, 127.7, 127.2, 20.5 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{13}H_{12}O_2S$ 232.0558, found 232.0563.

1-(m-tolyl)-2-Naphthoic acid (**1s**):



Following procedure B, from *methyl 1-hydroxy-2-naphthoate* (202 mg, 1.00 mmol) and 3-*methylphenylboronic acid* (270 mg, 2.00 mmol) the intermediate ester was obtained after FC (97:3 Hex:EtOAc) as a colorless oil (115 mg, 42%). GC-MS analysis showed a single peak with *m/z* = 276. The crystallization of the acid directly from the reaction media after hydrolysis of the ester was not successful. Extraction using EtOAc (3x10 mL) was performed to the whole sample obtaining pure acid **1s** as a white solid (103 mg, 89%).

TLC (7:3 hexane/(3:1:0.1 EtOAc:EtOH:AcOH): R_f 0.32.

IR: ν 2919, 1685, 1407, 1284, 1253, 1153, 767 cm^{-1}.

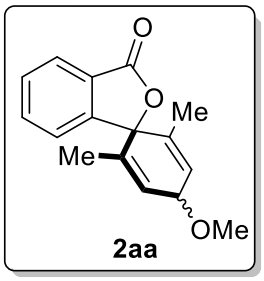
^{1}H NMR (300 MHz, $CDCl_3$): δ 10.85 (brs, 1H), 8.03 (d, *J* = 8.7 Hz, 1H), 7.92 (d, *J* = 8.3 Hz, 2H), 7.59 (dd, *J* = 15.5, 8.2 Hz, 2H), 7.40 (dt, *J* = 15.9, 8.2 Hz, 2H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.18 – 7.10 (m, 2H), 2.45 (s, 3H) ppm.

^{13}C NMR {H^1} (75 MHz, $CDCl_3$): δ 173.7, 143.0, 138.6, 137.5, 135.2, 132.9, 130.3, 128.3, 128.3, 127.9, 127.7, 126.8, 126.7, 126.6, 125.9, 21.6 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{18}H_{14}O_2$ 262.0994, found 262.0992.

Synthesis of spiro compounds **2** using ECDC

4-Methoxy-2,6-dimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2aa**):



2aa

From the corresponding acid **1a** (68 mg, 0.30 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as a colorless wax (60 mg, 78%) in a 57:43 dr (diastereomeric ratio according ^{1}H-NMR).

TLC (9:1 hexane/EtOAc): R_f 0.13 for both diastereoisomers.

IR: ν 2927, 2823, 1762, 1457, 1245, 1083, 929, 728 cm^{-1}.

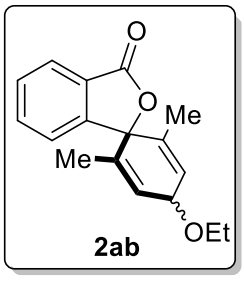
^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture: δ 7.88 (dt, J = 7.6, 0.9 Hz, 1H), 7.63 (tdd, J = 7.5, 2.8, 1.2 Hz, 1H), 7.52 (tt, J = 7.4, 1.0 Hz, 1H), 7.27 (dt, J = 7.6, 0.9 Hz, 0.57H), 7.09 (dt, J = 7.7, 0.9 Hz, 0.43H), 6.02 (d, J = 3.7 Hz, 1.14H), 5.93 (d, J = 3.0 Hz, 0.86H), 4.57 (ddq, J = 4.8, 3.3, 1.7 Hz, 0.43H), 4.37 (dqd, J = 4.0, 2.7, 1.3 Hz, 0.57H), 3.46 (s, 1.71H), 3.32 (s, 1.29H), 1.42 (t, J = 1.5 Hz, 2.58H), 1.40 (t, J = 1.2 Hz, 3.42H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) of the diastereoisomeric mixture: δ170.80, 170.75, 150.99, 150.84, 136.4, 134.77, 134.72, 134.65, 129.5, 126.7, 126.4, 125.2, 122.2, 121.6, 85.9, 85.6, 71.2, 70.0, 55.1, 53.6, 16.8, 16.7 ppm.

LRMS (EI): *m/z* (%) 256 (M^+,10), 541 (33), 255 (31), 209 (46), 197 (100), 181 (45), 165 (49).

HRMS (EI): calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1097.

4-Ethoxy-2,6-dimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2ab**):



2ab

From the corresponding acid **1a** (68 mg, 0.3 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as a colorless wax (60 mg, 74%) in a 1:1 dr.

TLC (9:1 hexane/EtOAc): R_f 0.22 for both diastereoisomers.

IR: ν 2977, 1762, 1457, 1083, 995, 933, 732 cm^{-1}.

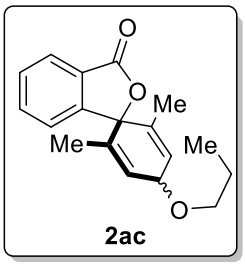
^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture: δ 7.89 (d, J = 7.6 Hz, 1H), 7.64 (tdd, J = 7.5, 4.3, 1.0 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.30 (d, J = 7.6 Hz, 0.5H), 7.10 (d, J = 7.6 Hz, 0.5H), 6.04 (d, J = 3.6 Hz, 1H), 5.97 (d, J = 2.7 Hz, 1H), 4.64 – 4.56 (m, 0.5H), 4.44 (s, 0.5H), 3.69 (q, J = 7.0 Hz, 1H), 3.56 (q, J = 7.0 Hz, 1H), 1.43 (s, 3H), 1.40 (s, 3H), 1.29 (t, J = 7.0 Hz, 1.5H), 1.23 (t, J = 7.0 Hz, 1.5H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) of the diastereomeric mixture: δ170.88, 170.81, 151.13, 150.94, 136.0, 134.79, 134.73, 134.3, 129.6, 127.5, 127.00, 126.95, 125.4, 122.4, 121.8, 86.1, 85.7, 70.1, 69.4, 63.2, 61.9, 16.9, 16.7, 15.94, 15.89 ppm.

LRMS (EI) *m/z* (%) 270 (M^+, 63), 255 (23), 226 (72), 225 (100), 211 (75), 197 (45), 183 (50), 181 (69), 165 (68), 152 (29).

HRMS (EI-TOF): *m/z* calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1250.

4-Propoxy-2,6-dimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2ac**):



From the corresponding acid **1a** (68 mg, 0.30 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as a colorless oil (58 mg, 68%) in a 1:1 dr.

TLC (9:1 hexane/EtOAc): R_f 0.29, 0.31 for each diastereoisomer

IR: ν 2962, 2927, 2873, 1762, 1461, 1245, 1083, 933, 728 cm^{-1}.

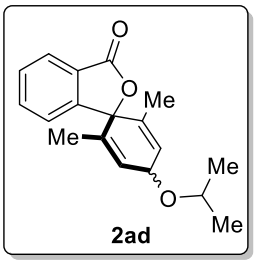
^{1}H NMR (400 MHz, $CDCl_3$) of the diastereomeric mixture: δ 7.88 (d, *J* = 7.6 Hz, 1H), 7.63 (tdd, *J* = 7.6, 4.6, 1.1 Hz, 1H), 7.51 (dt, *J* = 15.0, 1.0 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 0.5H), 7.09 (d, *J* = 7.7 Hz, 0.5H), 6.03 (d, *J* = 3.7 Hz, 1H), 5.95 (d, *J* = 2.9 Hz, 1H), 4.59 (ddd, *J* = 4.7, 3.1, 1.6 Hz, 0.5H), 4.42 (dtd, *J* = 3.8, 2.7, 1.4 Hz, 0.5H), 3.57 (t, *J* = 6.7 Hz, 1H), 3.44 (t, *J* = 6.7 Hz, 1H), 1.66 (dd, *J* = 15.4, 8.0 Hz, 1H), 1.61 (dd, *J* = 15.4, 8.0 Hz, 1H), 1.42 (s, 3H), 1.40 (s, 3H), 0.98 (t, *J* = 7.3 Hz, 1.5H), 0.94 (t, *J* = 7.3 Hz, 1.5H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) of the diastereomeric mixture: δ 170.86, 170.79, 151.1, 150.9, 135.9, 134.76, 134.72, 134.2, 129.61, 129.59, 127.5, 127.0, 126.9, 125.3, 122.4, 121.8, 86.1, 85.7, 70.2, 69.6, 69.4, 68.2, 23.6, 16.9, 16.6, 10.81, 10.76 ppm.

LRMS (EI): *m/z* (%) 284 (M^+,5), 269 (11), 240 (34), 255 (100), 183 (71), 165 (53).

HRMS (EI-TOF): *m/z* calcd for $C_{18}H_{20}O_3$ 284.1412, found 284.1414.

4-Isopropoxy-2,6-dimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2ad**):



From the corresponding acid **1a** (45.2 mg, 0.20 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as colorless wax (30 mg, 53 %) in a 1:1 dr.

TLC (9:1 hexane/EtOAc): R_f 0.45.

IR: ν 2974, 1766, 1462, 1377, 1246, 1030, 999, 937 cm^{-1}.

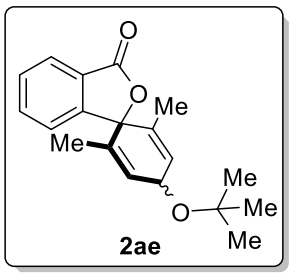
^{1}H NMR (400 MHz, $CDCl_3$) of the diastereomeric mixture: δ 7.89 (d, *J* = 1.2 Hz, 0.50H), 7.87 (d, *J* = 1.2 Hz, 0.50H), 7.67 – 7.59 (m, 1H), 7.52 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.33 (d, *J* = 7.7 Hz, 0.50H), 7.09 (d, *J* = 7.7 Hz, 0.50H), 6.00 (d, *J* = 3.8 Hz, 1H), 5.97 – 5.91 (m, 1H), 4.55 (tp, *J* = 3.4, 1.7 Hz, 0.50H), 4.43 (tp, *J* = 4.0, 1.4 Hz, 0.50H), 3.93 (h, *J* = 12.2, 6.1 Hz, 0.50H), 3.84 (h, *J* = 6.1 Hz, 0.50H), 1.42 (s, 3H), 1.39 (s, 3H), 1.25 (d, *J* = 6.1 Hz, 3H), 1.21 (d, *J* = 6.1 Hz, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) of the diastereomeric mixture: δ 171.0, 170.8, 151.2, 150.9, 135.4, 134.75, 134.67, 133.3, 129.58, 129.55, 128.0, 127.4, 126.9, 126.8, 125.3, 125.2, 122.6, 121.7, 86.2, 85.7, 69.9, 69.6, 68.0, 67.9, 23.4, 23.2, 16.9, 16.6 ppm.

LRMS (EI): *m/z* (%) 242 (33), 225 (66), 197 (34), 183 (100), 181 (39), 165 (51).

HRMS (EI-TOF): calcd for $C_{18}H_{20}O_3$ 284.1412, found 284.1413.

4-tert-*Butoxy-2,6-dimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one* (**2ae**):



2ae

From the corresponding acid **1a** (45 mg, 0.20 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as a colorless wax (22 mg, 37%) in a 55:45 dr.

TLC (9:1 hexane/EtOAc): R_f 0.31 for both diastereoisomers.

IR: ν 2973, 2923, 2873, 1762, 1461, 1369, 1241, 998, 933, 763 cm^{-1}.

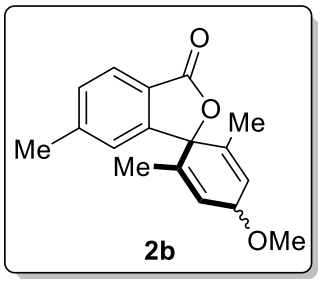
^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture: δ 7.89 (q, J = 1.1 Hz, 0.55H), 7.86 (q, J = 1.1 Hz, 0.45H), 7.63 (tdd, J = 7.5, 3.7, 1.2 Hz, 1.1H), 7.51 (td, J = 7.5, 1.0 Hz, 0.9H), 7.37 (dt, J = 7.6, 0.9 Hz, 0.55H), 7.12 (dt, J = 7.6, 0.9 Hz, 0.45H), 5.88 (d, J = 3.8 Hz, 1.1H), 5.82 (d, J = 2.9 Hz, 0.9H), 4.57 (tq, J = 3.2, 1.6 Hz, 0.45H), 4.50 (ddq, J = 4.0, 2.7, 1.4 Hz, 0.55H), 1.41 (t, *J* = 1.5 Hz, 2.7H), 1.37 (t, *J* = 1.3 Hz, 3.3H), 1.31 (s, 9H).ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) of the diastereomeric mixture: δ171.1, 171.0, 151.3, 151.0, 134.5, 134.4, 134.1, 132.5, 129.9, 129.3, 128.4, 126.9, 126.7, 125.1, 125.0, 122.7, 121.6, 86.3, 85.4, 74.8, 74.7, 63.1, 62.6, 28.5, 28.2, 16.9, 16.6 ppm.

LRMS (EI): *m/z* (%) 298 (M^+,1), 242 (100), 225 (72), 224 (44), 183 (75), 181 (48), 165 (38).

HRMS (EI-TOF): *m/z* calcd for $C_{19}H_{22}O_3$ 298.1569, found 298.1560.

4-Methoxy-2,6,6'-trimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2b**):



2b

From the corresponding acid **1b** (45 mg, 0.20 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as a colorless wax (38 mg, 70%) in a 52:48 dr.

TLC (8:2 hexane/EtOAc): R_f 0.32 for both diastereoisomers.

IR: ν 2981, 1766, 1373, 1240, 1087, 1045, 732 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture: δ 7.77 (s, 0.48H), 7.75 (s, 0.52H), 7.32 (td, J = 1.4, 0.7 Hz, 0.52H), 7.30 (td, J = 1.4, 0.7 Hz, 0.48H), 7.03 (s, 0.52H), 6.85 (s, 0.48H), 6.02 (d, *J* = 3.7 Hz, 1.04H), 5.95 – 5.88 (m, 0.96H), 4.58 (tp, *J* = 3.4, 1.7 Hz,

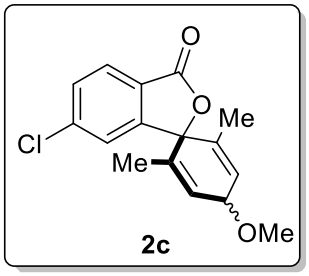
0.48H), 4.35 (tp, *J* = 4.1, 1.4 Hz, 0.52H), 3.48 (s, 1.56H), 3.32 (s, 1.44H), 2.43 (s, 3H), 1.44 (s, 2.88H), 1.41 (s, 3.12H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) of the diasteromeric mixture: δ 170.88, 170.84, 151.5, 151.3, 146.2, 146.1, 136.6, 135.1, 130.8, 126.6, 126.3, 125.1, 124.42, 124.35, 122.4, 121.9, 85.6, 85.3, 71.3, 70.0, 55.4, 53.6, 22.2, 16.9, 16.7 ppm.

LRMS (EI): *m/z* (%) 270 (M^+, 36), 255 (31), 239 (19), 225 (20), 211 (100), 195 (35), 165 (34).

HRMS (EI-TOF): *m/z* calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1255.

4-Methoxy-6'-chloro-2,6-dimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2c**):



2c

From the corresponding acid **2c** (52 mg, 0.20 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as a yellow wax (34 mg, 60 %) with a 47:53 dr.

TLC (9:1 hexane/EtOAc): R_f 0.23 for both diasteroisomers.

IR ν cm^{-1} 2924, 1766, 1601, 1454, 1261, 1234, 1080, 945, 841, 690.

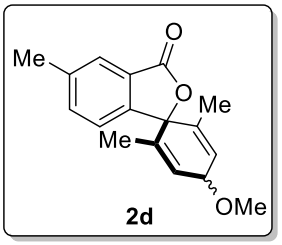
^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture: δ 7.83 (dd, *J* = 1.1, 0.6 Hz, 0.47H), 7.81 (dd, *J* = 1.1, 0.6 Hz, 0.53H), 7.51 (dd, J = 1.7, 0.8 Hz, 0.53H), 7.49 (dd, J = 1.7, 0.8 Hz, 0.47H),7.26 (dd, *J* = 1.7, 0.6 Hz, 0.47H), 7.06 (dd, *J* = 1.7, 0.6 Hz, 1H), 6.06 (dq, *J* = 4.5, 1.1 Hz, 1.06H), 5.99 – 5.96 (m, 0.94H), 4.57 (tp, *J* = 3.4, 1.7 Hz, 0.47H), 4.35 (tp, *J* = 4.0, 1.4 Hz, 0.53H), 3.48 (s, 1.59H), 3.33 (s, 1.41H), 1.46 (t, *J* = 1.5 Hz, 2.82H), 1.43 (t, *J* = 1.3 Hz, 3.18H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) δ of the diastereomeric mixture: 169.6, 169.5, 152.7, 152.6, 141.7, 141.5, 135.9, 134.2, 130.52, 130.50, 127.3, 127.1, 126.59, 126.56, 125.35, 125.35, 122.7, 122.2, 85.5, 71.1, 69.9, 55.5, 53.8, 16.9, 16.7 ppm.

LRMS (EI) *m/z* (%) 290 (M^+, 36), 275 (54), 259 (53), 246 (54), 245 (40), 231 (82), 211 (63), 196 (100), 181 (32) 180 (38), 179 (48), 165 (68), 152 (52), 123 (29).

HRMS (EI-TOF): *m/z* calcd for $C_{16}H_{15}ClO_3$ 290.0710, found 290.0711.

4-Methoxy-2,5',6-trimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2d**):



2d

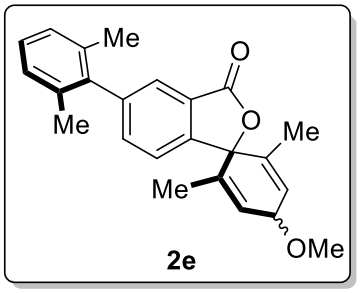
From the corresponding acid **1d** (73 mg, 0.20 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as a white wax (30 mg, 37%) in a 55:45 dr.

TLC (95:5 hexane/EtOAc): R_f 0.17 for both diasteroisomers.

IR: ν 2924, 1763, 1446, 1254, 1165, 1080, 937 cm^{-1}.

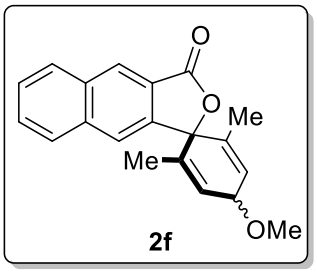
^{1}H NMR (300 MHz, $CDCl_3$) for the diastereomeric mixture: δ 7.67 (d, J = 0.8 Hz, 1H), 7.46 – 7.43 (m, 0.45H), 7.43 – 7.41 (m, 0.55H), 7.14 (d, J = 7.8 Hz, 0.45H), 6.97 (d, J = 7.8 Hz, 0.55H), 6.01 (d, J = 3.6 Hz, 0.90H), 5.92 (d, J = 2.9 Hz, 1.1H), 4.56 (tp, J = 3.3, 1.7 Hz, 0.55H), 4.37 (ddp, J = 3.9, 2.7, 1.4 Hz, 0.45H), 3.46 (s, 1.35H), 3.31 (s, 1.65H), 2.45 (s, 3H), 1.43 (s, 3.30H), 1.40 (s, 2.70H) ppm.
^{13}C NMR {H^1} (75 MHz, $CDCl_3$) for the diastereomeric mixture: δ 170.9, 148.4, 148.2, 140.02, 140.00, 136.7, 136.0, 135.9, 135.1, 127.2, 127.1, 126.7, 126.4, 125.38, 125.35, 122.0, 1215, 85.8, 85.5, 71.2, 70.0, 55.1, 53.6, 21.4, 21.4, 16.9, 16.7 ppm.
LRMS (EI) *m/z* (%) 270 (M^+,12), 255 (27), 239 (16), 226 (21), 225 (16), 212 (16), 211 (100), 196 (28), 195 (29), 180 (21), 179 (23), 165 (30), 152 (15).
HRMS (EI-TOF) calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1256

5'-(2,6-dimethylphenyl)-4-methoxy-2,6-dimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2e**):



From the corresponding acid **1e** (99 mg, 0.30 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as a white solid (58 mg, 54%) in a 55:45 dr.
TLC (9:1 hexane/EtOAc): R_f 0.23 for both diasteroisomers.
IR: ν 3054, 2981, 2923, 1766, 1454, 1191, 1083, 937, 775, 732 cm^{-1}.
^{1}H NMR (300 MHz, $CDCl_3$) for the diastereomeric mixture: δ 7.69 (d, J = 0.6 Hz, 1H), 7.44 (d, J = 13.2 Hz, 1H), 7.36 (d, J = 7.8 Hz, 0.55H), 7.23 – 7.16 (m, 1.45H), 7.15 – 7.11 (m, 2H), 6.07 (d, J = 3.6 Hz, 1.10H), 5.99 (d, J = 2.7 Hz, 0.90H), 4.64 – 4.59 (m, 0.45H), 4.45 – 4.40 (m, 0.55H), 3.49 (s, 1.65H), 3.35 (s, 1.35H), 1.99 (s, 6H), 1.52 (s, 2.7H), 1.50 (s, 3.3H).
^{13}C NMR {H^1} (101 MHz, $CDCl_3$) of the diastereomeric mixture: 170.80, 170.75, 149.5, 149.3, 143.08, 143.05, 139.87, 139.81, 136.6, 136.1, 136.0, 135.8, 134.9, 127.91, 127.88, 127.7, 127.28, 127.24, 126.9, 126.6, 125.7, 122.4, 121.9, 86.0, 85.6, 71.2, 70.0, 55.1, 53.6, 20.9, 17.0, 16.8 ppm.
LRMS (EI) *m/z* (%) 341 (1), 313 (23), 284 (27), 282 (33), 268 (25), 240 (12), 140 (43), 96 (53), 82 (100), 83 (100).
HRMS (EI-TOF) calcd for $C_{24}H_{24}O_3$ 360.1725, found 360.1432.

4-methoxy-2,6-dimethyl-3'H-spiro(cyclohexane-1,1'-naphtho[2,3-c]furan)-2,5-dien-3'-one (**2f**):



From the corresponding acid **1f** (82.8 mg, 0.30 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as a yellow wax (52 mg, 59 %) with a 56:44 dr.

TLC (8:2 hexane/EtOAc): R_f 0.35 for both diasteroisomers.

IR ν 2981, 2927, 1766, 1450, 1373, 1245, 1083, 1045, 937 cm^{-1}

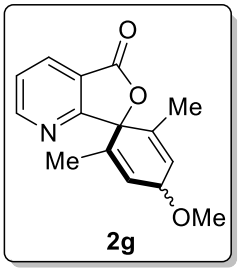
^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture: δ 8.49 (s, 1H), 8.06 (d, *J* = 8.1 Hz, 1H), 7.92 – 7.86 (m, 1H), 7.69 (s, 0.44H), 7.68 – 7.57 (m, 2H), 7.53 (s, 0.56H), 6.08 (d, *J* = 3.6 Hz, 0.88H), 5.98 (d, *J* = 2.9 Hz, 1.12H), 4.72 – 4.66 (m, 0.56H), 4.44 – 4.37 (m, 0.44H), 3.56 (s, 1.32H), 3.36 (s, 1.68H), 1.47 (s, 3H), 1.44 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) δ of the diastereomeric mixture: 170.69, 170.65, 144.9, 144.6, 136.9, 136.71, 136.66, 135.6, 133.5, 130.1, 130.0, 129.3, 129.2, 128.6, 128.4, 127.3, 126.9, 126.8, 126.6, 126.3, 124.6, 124.5, 121.3, 120.8, 86.1, 85.8, 71.4, 70.1, 55.5, 53.6, 17.1, 17.0 ppm.

LRMS (EI) *m/z* (%) 306 (M^+,100), 281 (9), 279 (36), 249 (27), 232 (50), 231 (90), 207 (35).

HRMS (EI-TOF): *m/z* calcd for $C_{20}H_{18}O_3$ 306.1256, found 306.1254.

4-Methoxy-2,6-dimethyl-5'H-spiro[cyclohexane-1,7'-furo[3,4-b]pyridine]-2,5-dien-5'-one (**2g**):



From the corresponding acid **1g** (72 mg, 0.30 mmol), following Procedure C. Crude ^{1}H NMR submitted using durene as internal standard revealed a 51% yield with a 71:29 dr mixture. Unfortunately, the likely instability of this product under silica made possible the isolation of only one of the diastereoisomers after FC (7:3 hexane/EtOAc) as a yellow wax (11 mg, 14 %).

TLC (7:3 hexane/EtOAc): R_f 0.23 for the isolated diastereoisomer.

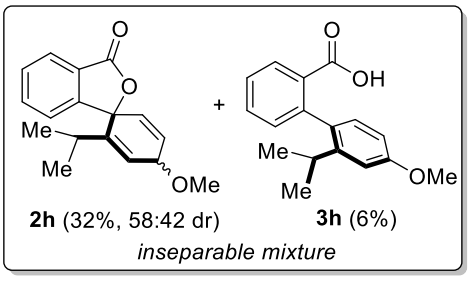
IR ν 2931, 1763, 1593, 1442, 1122, 1068, 926, 791 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$) of a single diastereoisomer: δ 8.88 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.22 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.48 (dd, *J* = 7.7, 4.9 Hz, 1H), 6.12 (d, *J* = 3.5 Hz, 2H), 4.49 (ddd, *J* = 5.0, 3.5, 1.6 Hz, 1H), 3.44 (s, 3H), 1.40 (s, 6H) ppm.

^{13}C NMR {H^1} (75 MHz, $CDCl_3$) of a single diastereoisomer: δ 169.3, 168.8, 156.3, 134.0, 133.9, 129.3, 124.3, 121.2, 87.0, 70.8, 54.4, 17.1 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{15}H_{15}NO_3$ 257.1052, found 257.1057.

2-Isopropyl-4-methoxy-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2h**):



From the corresponding acid **1h** (72 mg, 0.30 mmol), following Procedure C, after FC (95:5 to 8:2 hexane:EtOAc) the desired product was obtained together with the isomerized compound in an 84:16 inseparable mixture **2h:3h** (31 mg, 38% overall) with a 58:42 dr for the spiro compound. Due to the possible instability of the spirocompounds under acidic conditions such as the $CDCl_3$ used to perform the NMR analysis and, since the isomerized compound has a significantly different R_f, we attributed the observed isomerized compound to isomerization during the acquisition of the NMR spectra. Additionally, benzo-3,4-coumarin (**2h'**) was obtained and isolated as a white solid (18 mg, 31%). Characterization data for benzo-3,4-coumarin (**2h'**) matches literature data.[1] Characterization data for the pure isomerized compound **3h** is given further down (*vide infra*). Characterization data for the diasteromeric mixture of the spiro compound **2h** is given below:

TLC (8:2 hexane/EtOAc): R_f 0.33 for both diastereoisomers.

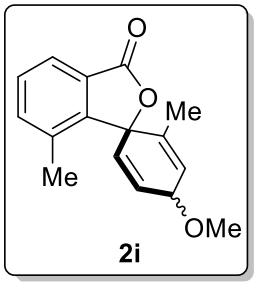
^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture: δ 7.90 (d, J = 7.5 Hz, 1H), 7.63 (tdd, J = 7.5, 2.8, 1.2 Hz, 1H), 7.52 (tdd, J = 7.4, 2.2, 1.0 Hz, 1H), 7.28 (d, J = 7.6 Hz, 0.42H), 7.12 (d, J = 7.6 Hz, 0.58H), 6.24 (ddd, J = 10.0, 3.5, 1.9 Hz, 0.42H), 6.19 – 6.11 (m, 1H), 6.07 (dd, J = 2.8, 2.1 Hz, 0.58H), 5.72 (ddd, J = 10.0, 3.5, 1.6 Hz, 1H), 4.67 (dd, J = 4.6, 2.8 Hz, 0.58H), 4.50 (td, J = 3.6, 1.4 Hz, 0.42H), 3.47 (s, 1.26H), 3.33 (s, 1.74H), 1.78 (h, J = 6.9 Hz, 0.58H), 1.69 (h, J = 6.9 Hz, 0.42H), 1.10 (d, J = 6.9 Hz, 1.74H), 1.07 (d, J = 6.9 Hz, 1.26H), 0.74 (d, J = 6.9 Hz, 1.26H), 0.7 (d, J = 6.9 Hz, 1.74H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) of the diastereomeric mixture: δ 170.6, 159.3, 151.5, 151.1, 146.9, 145.5, 143.1, 134.5, 132.0, 130.8, 129.74, 129.67, 129.5, 129.0, 127.2, 126.7, 126.5, 125.73, 125.68, 125.1, 124.5, 123.0, 122.6, 84.0, 83.5, 70.8, 69.6, 54.9, 53.4, 27.7, 27.5, 24.6, 24.2, 24.1, 23.7 ppm.

LRMS (EI): *m/z* (%) 270 (M^+,12), 211 (12), 197 (15), 165 (11).

HRMS (EI-TOF): *m/z* calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1257.

4-Methoxy-2,7'-dimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2i**):



From the corresponding acid **1i** (45 mg, 0.20 mmol), following Procedure C, the desired product was obtained after FC (9:1 hexane/EtOAc) as a yellow wax (32 mg, 62 %) with a 65:35 dr.

TLC (8:2 hexane/EtOAc): R_f 0.29 for both diasteroisomers.

IR ν 2985, 2931, 1762, 1450, 1272, 1126, 1380, 937, 764 cm^{-1}

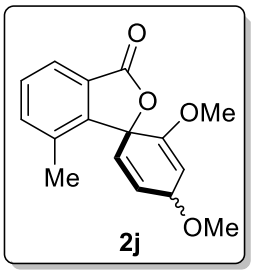
^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture: δ 7.75 (t, *J* = 6.6 Hz, 1H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.42 – 7.38 (m, 1H), 6.40 (ddd, *J* = 10.0, 3.2, 2.0 Hz, 0.35H), 6.22 (ddd, *J* = 10.0, 3.0, 2.0 Hz, 0.65H), 6.18 (dt, *J* = 3.2, 1.7 Hz, 0.35H), 6.01 (dt, *J* = 3.2, 1.7 Hz, 0.65H), 5.66 (td, *J* = 9.9, 1.8 Hz, 1H), 4.51 (ddd, *J* = 4.8, 3.2, 1.7 Hz, 0.65H), 4.38 (dq, *J* = 4.9, 1.7 Hz, 0.35H), 3.47 (s, 1.05H), 3.34 (s, 1.95H), 2.22 (s, 1.05H), 2.11 (s, 1.95H), 1.44 (t, *J* = 1.5 Hz, 1.95H), 1.40 (t, *J* = 1.5 Hz, 1.05H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) δ of the diastereomeric mixture: 170.54, 170.50, 147.8, 136.3, 136.2, 134.1, 133.6, 133.4, 132.9, 131.9, 130.4, 130.0, 129.3, 127.7, 127.5, 127.1, 126.8, 126.7, 123.6, 123.5, 82.8, 82.6, 71.4, 70.2, 56.3, 53.7, 17.2, 16.86, 16.81, 16.3 ppm.

LRMS (EI) *m/z* (%) 256 (M^+, 94), 242 (23), 223 (25), 197 (100), 182 (49), 165 (91).

HRMS (EI-TOF): *m/z* calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1095.

2,4-Dimethoxy-7'-methyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2j**):



2j

From the corresponding acid **1j** (72.6 mg, 0.30 mmol), following Procedure C, the desired product was obtained after FC (8:2 hexane/EtOAc) as a colorless wax (51 mg, 63%) with a 81:19 dr.

TLC (7:3 hexane/EtOAc): R_f 0.23 for both diasteroisomers.

IR ν 2931, 2827, 1762, 1457, 1272, 1068, 941, 767 cm^{-1}

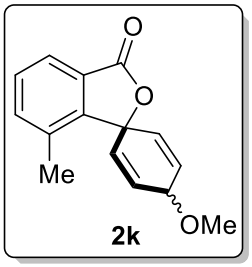
^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture: δ 7.74 – 7.68 (m, 1H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.36 (d, *J* = 7.4 Hz, 1H), 6.38 (ddd, *J* = 9.9, 3.2, 1.6 Hz, 0.19H), 6.21 (ddd, *J* = 9.9, 3.2, 1.5 Hz, 0.81H), 5.64 (dd, *J* = 9.9, 1.4 Hz, 0.81H), 5.59 (dd, *J* = 9.9, 1.7 Hz, 0.19H), 5.33 (dd, *J* = 3.5, 1.5 Hz, 0.19H), 5.16 (dd, *J* = 3.8, 1.5 Hz, 0.81H), 4.80 (td, *J* = 3.7, 1.3 Hz, 0.81H), 4.61 (td, *J* = 3.3, 1.7 Hz, 0.19H), 3.47 (s, 3H), 3.46 (s, 0.57H), 3.30 (s, 2.43H), 2.23 (s, 0.57H), 2.13 (s, 2.43H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) δ of the diastereomeric mixture: 170.4, 170.3, 152.2, 150.0, 147.0, 136.0, 135.9, 133.8, 133.3, 132.2, 131.2, 129.91, 129.87, 126.9, 126.8, 126.0, 123.2, 123.1, 100.2, 98.5, 80.9, 80.8, 72.8, 71.3, 55.9, 55.1, 55.0, 52.7, 17.0, 16.3 ppm.

LRMS (EI) *m/z* (%) 272 (M^+, 9), 257 (10), 241 (100), 240 (54), 213 (61), 197 (43), 182 (50), 181 (44), 165 (20), 153 (31).

HRMS (EI-TOF): *m/z* calcd for $C_{16}H_{16}O_4$ 272.1049, found 272.1043.

4-Methoxy-7'-methyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-3'-one (**2k**):



From the corresponding acid **1k** (64 mg, 0.30 mmol), following Procedure C, the desired product was obtained after FC (9:1 to 8:2 hexane/EtOAc) as a colorless wax (23 mg, 32%) with a 55:45 dr, accompanied with a small amount of the corresponding 10-methyl-*6H*-benzo[*c*]chromen-6-one **2k'** (8 mg, 13%). Characterization data for 10-methyl-*6H*-benzo[*c*]chromen-6-one (**2k'**) matches literature data.[6] Characterization for **2k** is given:

TLC (8:2 hexane/EtOAc): R_f 0.23 for both diasteroisomers.

IR ν 2931, 1762, 1272, 1130, 1084, 937 768 cm^{-1}.

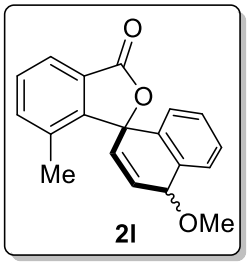
^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture: δ 7.76 (t, *J* = 7.7 Hz, 1H), 7.45 (td, *J* = 7.4, 1.8 Hz, 1H), 7.40 (d, *J* = 7.4 Hz, 1H), 6.45 (dd, *J* = 10.2, 3.1 Hz, 0.9H), 6.27 (dd, *J* = 10.2, 3.0 Hz, 1.1H), 5.76 – 5.71 (m, 2H), 4.53 – 4.48 (m, 0.55H), 4.41 – 4.35 (m, 0.45H), 3.50 (s, 1.35H), 3.37 (s, 1.65H), 2.27 (s, 1.35H), 2.14 (s, 1.65H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) δ 170.2, 148.2, 148.0, 136.3, 136.3, 134.3, 134.0, 132.7, 130.9, 130.2, 127.4, 127.0, 126.2, 126.1, 123.7, 123.5, 80.4, 80.3, 70.2, 69.1, 56.4, 53.9, 17.1, 16.4 ppm.

LRMS (EI) *m/z* (%) 242 (M^+, 63), 211 (30), 198 (68), 183 (76), 165 (100), 152 (77), 128 (55), 115 (43).

HRMS (EI-TOF): *m/z* calcd for $C_{15}H_{14}O_3$ 242.0943, found 242.0943.

4'-Methoxy-7-methyl-3H,4'H-spiro[isobenzofuran-1,1'-naphthalen]-3-one (**2l**):



From the corresponding acid **1l** (45 mg, 0.20 mmol), following Procedure C, the desired product was obtained after FC (9:1 to 85:15 hexane/EtOAc) as a white solid (41 mg, 71%) in a 63:37 dr.

TLC (8:2 hexane/EtOAc): R_f 0.28 for both diasteroisomers.

IR: ν 2981, 2935, 1762, 1272, 1241, 1068, 963 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) for the diastereomeric mixture: δ 7.83 (dd, *J* = 7.6, 0.5 Hz, 1H), 7.67 (d, *J* = 7.9 Hz, 0.37H), 7.62 (dd, *J* = 7.8, 0.6 Hz, 0.63H), 7.52 – 7.44 (m, 1H), 7.42 – 7.33 (m, 2H), 7.24 – 7.16 (m, 1H), 6.80 (dd, *J* = 8.0, 1.1 Hz, 0.67H), 6.70 (dd, *J* = 7.9, 1.1 Hz, 0.37H), 6.62 (dd, *J* = 10.2, 3.0 Hz, 0.37H), 6.40 (dd, *J* = 10.2, 3.2 Hz, 0.63H), 5.92 – 5.86 (m, 1H), 5.23 (t, *J* = 2.4 Hz, 0.63H), 5.13 (t, *J* = 2.4 Hz, 0.37H), 3.44 (s, 1.1H), 3.16 (s, 1.9H), 1.90 (s, 1.1H), 1.81 (s, 1.9H) ppm.

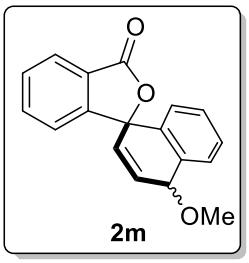
^{13}C NMR {H^1} (126 MHz, $CDCl_3$) for the diastereomeric mixture: δ 170.6, 150.6, 150.1, 136.9, 136.47, 136.42, 134.0, 133.9, 133.5, 133.1, 132.4, 132.3, 130.9, 130.2, 130.1, 129.3, 129.1, 128.64,

128.56, 128.53, 128.2, 128.0, 127.5, 127.0, 126.8, 126.5, 125.9, 123.4, 123.2, 98.0, 82.6, 82.0, 71.9, 70.5, 55.0, 52.1, 17.4, 16.6 ppm.

LRMS (EI): *m/z* (%) 292 (M^+,100), 261 (77), 249 (50), 233 (71), 217 (79), 202 (100).

HRMS (EI-TOF): *m/z* calcd for $C_{19}H_{16}O_3$ 292.1099, found 292.1100.

4'-Methoxy-3H,4'H-spiro[isobenzofuran-1,1'-naphthalen]-3-one (**2m**):



From the corresponding acid **1m** (74 mg, 0.30 mmol), following Procedure C, the desired product was obtained after FC (85:15 hexane/EtOAc) as a white wax (45 mg, 54%) in a 54:46 dr.

TLC (8:2 hexane/EtOAc): R_f 0.28 for both diasteroisomers.

IR: ν 2931, 2823, 1762, 1461, 1241, 1079, 929, 759 cm^{-1}.

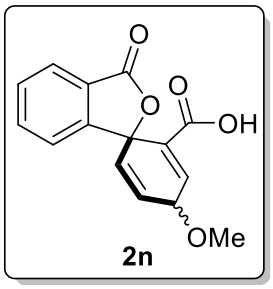
^{1}H NMR (500 MHz, $CDCl_3$) for the diastereomeric mixture: δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 0.46H), 7.61 – 7.49 (m, 2.54H), 7.40 – 7.33 (m, 1H), 7.27 – 7.19 (m, 1.54H), 7.01 – 6.97 (m, 0.46H), 6.89 (dd, *J* = 5.4, 1.0 Hz, 0.54H), 6.87 (dd, *J* = 5.5, 1.1 Hz, 0.46H), 6.49 (dd, *J* = 10.1, 4.0 Hz, 0.54H), 6.37 (dd, *J* = 10.2, 3.0 Hz, 0.46H), 6.02 (dd, *J* = 10.2, 1.2 Hz, 0.54H), 6.00 (dd, *J* = 10.2, 1.9 Hz, 0.46H), 5.32 (s, 0.46H), 5.06 (d, *J* = 3.8 Hz, 0.54H), 3.46 (s, 1.62H), 3.18 (s, 1.38H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) for the diastereomeric mixture: δ 170.49, 170.44, 153.8, 153.0, 134.95, 134.92, 134.85, 133.5, 133.2, 131.5, 130.4, 130.0, 129.9, 129.59, 129.57, 129.0, 128.9, 128.63, 128.56, 128.2, 126.6, 126.5, 125.7, 125.6, 125.3, 125.1, 123.4, 122.6, 83.1, 82.4, 72.0, 70.3, 54.8, 52.2 ppm.

LRMS (EI): *m/z* (%) 278 (M^+,100), 247 (81), 234 (76), 203 (95), 202 (93), 189 (80).

HRMS (EI-TOF): *m/z* calcd for $C_{18}H_{14}O_3$ 278.0943, found 278.0944.

4-Methoxy-3'-oxo-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-2-carboxylic acid (**2n**):



From diphenic acid (**1n**) (72 mg, 0.30 mmol), following Procedure C, the desired product was obtained after FC (8:2 hexane/(3:1:0.1 EtOAc:EtOH:AcOH)) as a yellow wax (51 mg, 63 %) with a 57:43 dr.

TLC (7:3 hexane/(3:1:0.1 EtOAc:EtOH:AcOH)): R_f 0.16 for both diasteroisomers.

IR ν 2989, 2938, 1762, 1724, 1388, 1245, 1083, 944, 759, 690 cm^{-1}

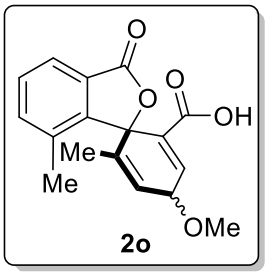
^{1}H NMR (400 MHz, $CDCl_3$) of the diastereomeric mixture: δ 7.87 (d, *J* = 7.6 Hz, 1H), 7.59 (td, *J* = 7.4, 2.2 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.18 (d, *J* = 7.5 Hz, 0.57H), 7.07 (d, *J* = 7.6 Hz, 0.43H), 6.23 (ddd, *J* = 10.1, 3.3, 2.0 Hz, 0.57H), 6.16 (dt, *J* = 10.0, 2.4 Hz, 0.43H), 5.70 (dd, *J* = 10.1, 1.9 Hz,

0.43H), 5.67 (dd, *J* = 10.1, 1.7 Hz, 0.57H), 4.78 (dd, *J* = 4.9, 2.8 Hz, 0.43H), 4.61 (td, *J* = 3.4, 1.8 Hz, 0.57H), 3.51 (s, 1.71H), 3.38 (s, 1.29H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) δ of the diastereomeric mixture: 170.41, 170.36, 168.2, 167.9, 150.6, 150.5, 144.3, 143.8, 134.4, 134.3, 132.4, 131.1, 130.3, 130.2, 129.7, 129.6, 129.2, 128.2, 127.4, 126.9, 125.8, 125.7, 121.9, 121.6, 79.7, 79.4, 70.4, 69.6, 56.0, 54.8 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{15}H_{12}O_5$ 272.0685, found 272.0690.

4-Methoxy-6,7'-dimethyl-3'-oxo-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-2-carboxylic acid (**2o**):



From the corresponding acid **1o** (80 mg, 0.30 mmol), following Procedure C, the desired product was obtained after FC (8:2 hexane/(3:1:0.1 EtOAc:EtOH:AcOH)) as a yellow wax (59 mg, 67 %) with a 52:48 dr.

TLC (8:2 hexane/(3:1:0.1 EtOAc:EtOH:AcOH): R_f 0.21 for both diasteroisomers.

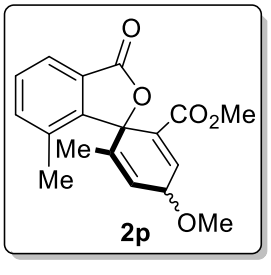
IR ν 2985, 2935, 1763, 1728, 1273, 949, 734 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$) of the diasteromeric mixture: δ 10.04 (brs, 1H), 7.71 (t, *J* = 6.7 Hz, 1H), 7.60 (dd, *J* = 3.0, 2.0 Hz, 0.48H), 7.48 – 7.45 (m, 0.52H), 7.40 (td, *J* = 7.4, 2.4 Hz, 1H), 7.33 (dd, *J* = 7.4, 3.2 Hz, 1H), 6.15 – 6.08 (m, 0.48H), 6.00 – 5.93 (m, 0.52H), 4.60 (dd, *J* = 4.7, 2.9 Hz, 0.52H), 4.48 (dt, *J* = 4.9, 1.7 Hz, 0.48H), 3.51 (s, 1.44H), 3.36 (s, 1.56H), 2.11 (s, 1.44H), 2.01 (s, 1.56H), 1.38 (s, 1.56H), 1.32 (s, 1.44H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) δ of the diastereomeric mixture: 177.5, 171.1, 168.2, 167.9, 146.7, 146.5, 144.3, 143.6, 136.0, 136.0, 134.3, 134.0, 132.8, 132.3, 129.8, 128.3, 127.0, 125.2, 123.2, 123.1, 81.4, 81.3, 71.3, 70.2, 57.0, 54.7, 17.0, 16.6, 16.5, 16.3 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{16}H_{15}O_3$ [M^+-CO_2H] 255.1021, found 255.1009.

Methyl-4-methoxy-6,7'-dimethyl-3'-oxo-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-2-carboxylate (**2p**):



From the corresponding acid **1p** (GC purity of 97%) (88 mg, 0.3 mmol), following Procedure C, the desired product was obtained after FC (8:2 hexane/EtOAc) as a yellow wax (32 mg, 34%) in a 42:58 dr.

TLC (7:3 hexane/EtOAc): R_f 0.28 for both diastereoisomers.

IR: ν 2927, 2357, 1766, 1724, 1442, 1261, 1126, 1072, 945, 733 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture: δ 7.78 (t, *J* = 6.9 Hz, 1H), 7.55 (dd, *J* = 3.4, 2.0 Hz, 0.42H), 7.49 – 7.37 (m, 1H), 7.49 – 7.37 (m, 0.58H), 7.40 – 7.32 (m, 0.58H), 7.37 – 7.30 (m, 0.42H), 6.15 (ddd, *J* = 3.3, 2.0, 1.4 Hz, 0.42H), 6.00 (ddd, *J* = 3.3, 2.0, 1.4 Hz, 0.58H), 4.61 (tq, *J* = 3.6, 1.8 Hz, 0.58H), 4.49 (tq, *J* = 3.4, 1.7 Hz, 0.42H), 3.54 (s, 3H), 3.49 (s, 1.26H), 3.39 (s, 1.74H), 2.15 (s, 1.26H), 2.04 (s, 1.74H), 1.43 (t, *J* = 1.6 Hz, 1.74H), 1.37 (t, *J* = 1.5 Hz, 1.26H) ppm.

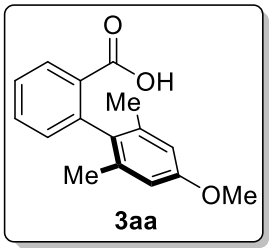
^{13}C NMR {H^1} (75 MHz, $CDCl_3$) of the diastereomeric mixture: δ171.0, 164.2, 163.8, 147.1, 146.9, 142.4, 141.7, 135.94, 135.89, 134.3, 134.0, 133.0, 132.4, 129.9, 129.8, 129.1, 129.0, 128.51, 128.48, 127.2, 125.5, 123.2, 123.0, 81.6, 81.5, 71.5, 70.3, 57.0, 54.7, 52.1, 52.0, 17.1, 16.72, 16.66, 16.32ppm.

LRMS (EI) *m/z* (%) 315 (M^++1,20), 314 (M^+,100), 255 (56), 223 (20), 177 (46).

HRMS (EI-TOF): *m/z* calcd for $C_{18}H_{18}O_5$ 314.1154, found 314.1156.

Synthesis of acids **3** through isomerization of spirolactones **2**

4'-Methoxy-2',6'-dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**3aa**):



3aa

Following procedure D from the corresponding spiro compound **2aa** (52 mg, 0.20 mmol), the desired product was obtained as a white solid (48 mg, 92%).

TLC (8:2 hexane/EtOAc): R_f 0.22.

IR: ν 3058, 2965, 2915, 1685, 1604, 1299, 1153, 767, 736 cm^{-1}.

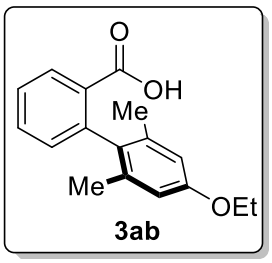
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.31 (br s, 1H), 8.08 (d, J = 7.7 Hz, 1H), 7.59 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.14 (d, J = 7.5 Hz, 1H), 6.65 (s, 2H), 3.83 (s, 3H), 1.93 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.0, 158.4, 142.7, 136.7, 133.4, 133.0, 131.6, 131.3, 129.6, 127.2, 112.5, 55.2, 21.0 ppm.

LRMS (EI): *m/z* (%) 256 (M^+,100), 238 (35), 223 (21), 195 (33), 165 (26), 152 (24).

HRMS (EI-TOF): *m/z* calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1103.

4'-Ethoxy-2',6'-dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**3ab**):



3ab

Following procedure D from the corresponding spiro compound **2ab** (54 mg, 0.20 mmol), the desired product was obtained as a white solid (53 mg, quantitative).

TLC (8:2 hexane/EtOAc): R_f 0.23.

IR: ν 3073, 2973, 2923, 1693, 1600, 1307, 1284, 1157, 763 cm^{-1}.

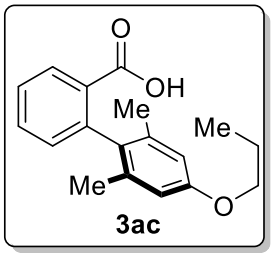
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.08 (dd, J = 7.9, 1.3 Hz, 1H), 7.58 (td, J = 7.5, 1.5 Hz, 1H), 7.43 (td, J = 7.7, 1.3 Hz, 1H), 7.13 (dd, J = 7.6, 1.0 Hz, 1H), 6.63 (s, 2H), 4.05 (q, J = 7.0 Hz, 2H), 1.91 (s, 6H), 1.43 (t, J = 7.0 Hz, 3H) ppm.

^{13}C NMR {H^1} (75 MHz, $CDCl_3$): δ 171.8, 157.9, 142.7, 136.7, 133.2, 132.9, 131.7, 131.3, 129.6, 127.2, 113.1, 63.3, 21.0, 15.1 ppm.

LRMS (EI): *m/z* (%) 270 (M^+,100), 224 (51), 181 (47), 152 (28).

HRMS (EI-TOF): calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1247.

2',6'-Dimethyl-4'-propoxy-[1,1'-biphenyl]-2-carboxylic acid (**3ac**):



Following procedure D from the corresponding spiro compound **2ac** (34 mg, 0.12 mmol), the desired product was obtained as a white solid (34 mg, quantitative).

TLC (8:2 hexane/EtOAc): R_f 0.28.

IR: ν 2962, 2927, 2873, 1662, 1461, 1245, 1083, 933, 729 cm^{-1}.

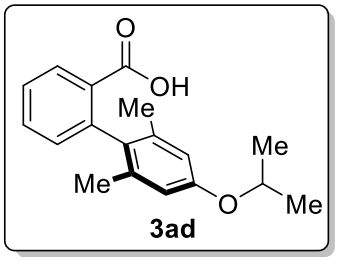
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.58 (td, *J* = 7.5, 1.3 Hz, 1H), 7.42 (td, *J* = 7.7, 1.2 Hz, 1H), 7.14 (dd, *J* = 7.6, 0.9 Hz, 1H), 6.65 (s, 2H), 3.95 (t, *J* = 6.5 Hz, 2H), 1.92 (s, 6H), 1.90 – 1.78 (m, 2H), 1.07 (t, *J* = 7.4 Hz, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.0, 158.1, 142.7, 136.7, 133.1, 132.9, 131.7, 131.2, 129.7, 127.2, 113.1, 69.4, 22.9, 21.0, 10.8 ppm.

LRMS (EI) *m/z* (%) 284 (M^+,100), 242 (27), 224 (81), 209 (11), 196 (26), 181 (49), 165 (25), 152 (20).

HRMS (EI-TOF): calcd for $C_{18}H_{20}O_3$ 284.1412, found 284.1396.

4'-Isopropoxy-2',6'-dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**3ad**):



Following procedure D from the corresponding spiro compound **2ad** (25 mg, 0.088 mmol), the desired product was obtained as a white solid (23 mg, 92%).

TLC (8:2 hexane/EtOAc): R_f 0.28.

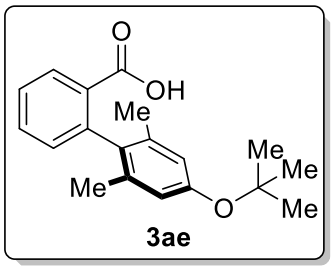
IR: ν 3059, 2978, 2924, 1693, 1604, 1304, 1149, 1119, 768 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.58 (td, *J* = 7.5, 1.4 Hz, 1H), 7.43 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.14 (dd, *J* = 7.6, 1.0 Hz, 1H), 6.62 (s, 2H), 4.57 (p, *J* = 6.0 Hz, 1H), 1.90 (s, 6H), 1.36 (d, *J* = 6.1 Hz, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 171.6, 156.8, 142.7, 136.8, 133.0, 132.9, 131.7, 131.3, 129.7, 127.2, 114.5, 69.7, 22.4, 21.0 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{18}H_{20}O_3$ 284.1412, found 284.1409.

*(4'-(*tert*-butoxy)-2',6'-Dimethyl-[1,1'-biphenyl]-2-carboxylic acid* (**3ae**):



Following procedure D from the corresponding spiro compound **2ae** (17 mg, 0.07 mmol), the desired product was obtained as a white solid (17 mg, quantitative).

TLC (8:2 hexane/EtOAc): R_f 0.31.

IR: ν 3058, 2977, 2927, 1693, 1601, 1299, 1261, 1151, 890, 763 cm^{-1}.

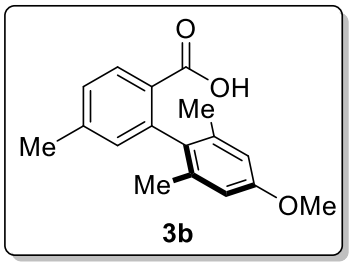
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.05 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.58 (td, *J* = 7.5, 1.4 Hz, 1H), 7.42 (td, *J* = 7.7, 1.2 Hz, 1H), 7.16 (dd, *J* = 7.6, 0.9 Hz, 1H), 6.70 (s, 2H), 1.88 (s, 6H), 1.38 (s, 9H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 171.8, 154.0, 142.8, 135.9, 132.9, 131.3, 131.2, 129.5, 127.2, 122.7, 114.3, 78.3, 29.1, 20.8 ppm.

LRMS (EI) *m/z* (%) 298 (M^+, 3), 242 (100), 224 (68), 209 (10), 196 (19), 181 (32), 165 (21), 152 (20).

HRMS (EI): *m/z* calcd for $C_{19}H_{22}O_3$ 298.1569, found 298.1561.

4'-Methoxy-2',5,6'-trimethyl-[1,1'-biphenyl]-2-carboxylic acid (**3b**):



Following procedure D from the corresponding spiro compound **2b** (28 mg, 0.10 mmol), the desired product was obtained as a white solid (25 mg, 90%).

TLC (8:2 hexane/EtOAc): R_f 0.26.

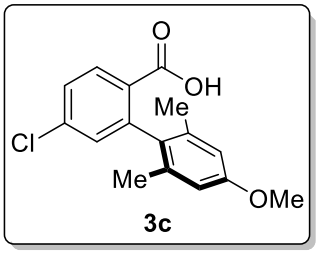
IR: ν 2919, 1689, 1604, 1465, 1415, 1288, 1149, 840, 755 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8.0 Hz, 1H), 7.22 (dd, *J* = 8.0, 0.9 Hz, 1H), 6.94 (s, 1H), 6.63 (s, 2H), 3.82 (s, 3H), 2.41 (s, 3H), 1.92 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 171.8, 158.3, 143.8, 142.9, 136.7, 133.6, 132.3, 131.6, 128.0, 126.5, 112.5, 55.2, 21.6, 21.0 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1262.

5-Chloro-4'-methoxy-2',6'-dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**3c**):



Following procedure D from the corresponding spiro compound **2c** (50 mg, 0.17 mmol), the desired product was obtained as a white solid (33 mg, 66% yield).

TLC (8:2 hexane/EtOAc): R_f 0.12.

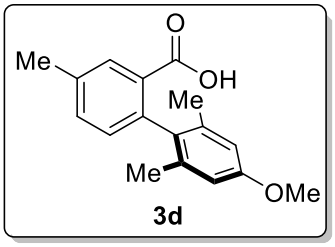
IR: ν 2954, 1693, 1593, 1277, 1153, 1088, 833, 737 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8.5 Hz, 1H), 7.41 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.15 (d, *J* = 2.1 Hz, 1H), 6.63 (s, 2H), 3.82 (s, 3H), 1.92 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 170.8, 158.7, 144.7, 139.3, 136.6, 132.8, 132.11, 131.7, 127.9, 127.6, 55.2, 21.0 ppm.

HRMS (EI): *m/z* calcd for $C_{16}H_{15}ClO_3$ 290.071, found 290.0718.

4'-Methoxy-2',4,6'-trimethyl-[1,1'-biphenyl]-2-carboxylic acid (**3d**):



3d

Following procedure D from the corresponding spiro compound **2d** (28 mg, 0.10 mmol), the desired product was obtained as an orange solid (22 mg, 79% yield).

TLC (8:2 hexane/(3:1:0.1 EtOAc: EtOH: AcOH): R_f 0.48.

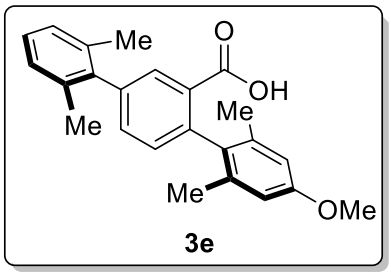
IR: ν 2924, 1689, 1604, 1469, 1307, 1153, 833, 737 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.39 (d, J = 7.7 Hz, 1H), 7.01 (d, J = 7.7 Hz, 1H), 6.63 (s, 2H), 3.82 (s, 3H), 2.43 (s, 3H), 1.92 (s, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ 171.9, 158.4, 139.6, 137.0, 133.9, 133.3, 131.8, 131.5, 129.2, 112.6, 55.2, 21.09, 21.04.

HRMS (EI): *m/z* calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1243.

4-methoxy-2,2'',6,6''-tetramethyl-[1,1':4',1''-terphenyl]-2'-carboxylic acid (**3e**):



3e

Following procedure D, from the corresponding spiro compound **2e** (44 mg, 1.12 mmol) the desired product was obtained as a white solid (41 mg, 93%).

TLC (8:2 hexane/EtOAc): R_f 0.26.

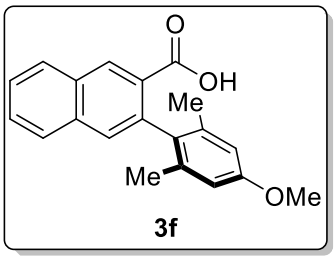
IR: ν 3016, 29.19, 2858, 1685, 1604, 1461, 1307, 1257, 1149, 852, 771 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, *J* = 1.8 Hz, 1H), 7.40 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.23 – 7.18 (m, 2H), 7.18 – 7.12 (m, 2H), 6.67 (s, 2H), 3.83 (s, 3H), 2.09 (s, 6H), 2.00 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.2, 158.4, 141.1, 140.5, 140.1, 136.8, 136.1, 133.8, 133.2, 131.9, 131.8, 129.7, 127.53, 127.5, 112.51, 55.2, 21.0, 21.0 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{24}H_{24}O_3$ 360.1725, found 360.1735.

3-(2,6-Dimethylphenyl)-2-naphthoic acid (**3f**):



3f

Following procedure D, from the corresponding spiro compound **2f** (35 mg, 0.11 mmol) the desired product was obtained as a white solid (31 mg, 89%).

TLC (8:2 hexane/EtOAc): R_f 0.12.

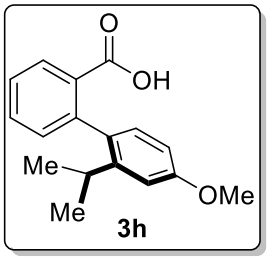
IR: ν 2923, 2857, 1689, 1454, 1280, 1149, 902, 736 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.70 (s, 1H), 7.97 (d, J = 7.9 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.70 – 7.53 (m, 3H), 6.69 (s, 2H), 3.86 (s, 3H), 1.97 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 171.5, 158.5, 138.1, 137.3, 135.5, 135.4, 133.3, 133.1, 131.7, 130.5, 129.2, 128.7, 127.7, 126.8, 112.6, 55.2, 21.2 ppm.

HRMS (EI-TOF): calcd for $C_{20}H_{18}O_3$ 306.1256, found 306.1248.

2'-Isopropyl-4'-methoxy-[1,1'-biphenyl]-2-carboxylic acid (**3h**):



3h

Following procedure D, from the corresponding spiro compound **2h** (31 mg, 0.11 mmol), the desired product was obtained as a white solid (26 mg, 84% yield).

TLC (8:2 hexane/EtOAc): R_f 0.18.

IR: ν 2962, 1689, 1608, 1465, 1288, 1226, 1041, 759 cm^{-1}.

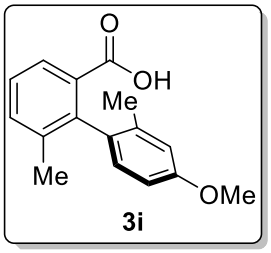
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, J = 7.8, 1.3 Hz, 1H), 7.54 (td, J = 7.5, 1.3 Hz, 1H), 7.42 (td, J = 7.6, 1.1 Hz, 1H), 7.22 (dd, J = 7.5, 0.8 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 6.87 (d, J = 2.6 Hz, 1H), 6.73 (dd, J = 8.4, 2.6 Hz, 1H), 3.86 (s, 3H), 2.68 (hept, J = 6.8 Hz, 1H), 1.09 (d, J = 6.8 Hz, 3H), 1.05 (d, J = 6.8 Hz, 3H). ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.6, 159.2, 147.8, 143.3, 132.7, 132.2, 132.1, 130.8, 129.7, 127.2, 111.2, 110.0, 55.3, 30.4, 24.6, 23.1ppm.

LRMS (EI) *m/z* (%) 270 (M^+, 100), 252 (18), 237 (45), 227 (37), 211 (38), 209 (40), 196 (19), 179 (22), 165 (42), 152 (22).

HRMS (EI-TOF): *m/z* calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1266.

2',6-dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**3i**):



3i

Following procedure D from the corresponding spiro compound **2i** (24 mg, 0.09 mmol), the desired product was obtained as a white solid (24 mg, quantitative).

TLC (8:2 hexane/EtOAc): R_f 0.15

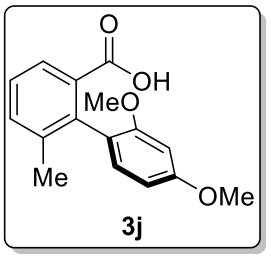
IR: ν 2977, 2927, 1697, 1457, 1292, 1238, 1045, 767 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 7.8 Hz, 1H), 7.44 (d, J = 7.5 Hz, 1H), 7.32 (t, J = 7.7 Hz, 1H), 6.88 (d, J = 8.3 Hz, 1H), 6.80 (d, J = 2.5 Hz, 1H), 6.75 (dd, J = 8.3, 2.5 Hz, 1H), 3.84 (s, 3H), 1.98 (s, 3H), 1.96 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.5, 158.8, 142.1, 138.3, 137.2, 134.1, 132.1, 130.19, 129.18, 128.3, 127.1, 115.3, 110.9, 55.2, 20.4, 20.1 ppm.

HRMS (EI-TOF) *m/z* calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1096.

2',4'-Dimethoxy-6-methyl-[1,1'-biphenyl]-2-carboxylic acid (**3j**):



3j

Following procedure D from spiro compound **3j** (46 mg, 0.17 mmol) precipitation of the product was incomplete. The product was then extracted with EtOAc after acidification, dried over MgSO4, filtered and dried. The dried crude was then dissolved in 0.1 mL of EtOAc and 1 mL of hexane. The precipitate was allowed to settle, and the upper phase was decanted. The solid was then dried obtaining the corresponding acid as white solid, the desired product was obtained as a white solid (31 mg, 67%).

TLC (7:3 hexane/EtOAc): R_f 0.26.

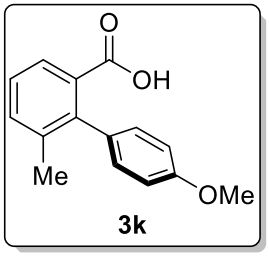
IR: ν 2950, 1689, 1457, 1295, 1207, 1157, 1037, 759 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): 7.79 (d, J = 7.7 Hz, 1H), 7.44 (d, J = 7.2 Hz, 1H), 7.29 (dd, J = 15.0, 7.3 Hz, 1H), 6.93 – 6.89 (m, 1H), 6.64 – 6.48 (m, 2H), 3.86 (s, 3H), 3.68 (s, 3H), 2.09 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 173.4, 160.4, 157.5, 138.8, 138.6, 134.0, 130.9, 130.3, 127.9, 127.0, 121.4, 104.3, 98.8, 55.6, 55.4, 20.6 ppm.

HRMS (EI) calcd for $C_{16}H_{16}O_4$ 272.1053, found 272.1048.

4'-Methoxy-6-methyl-[1,1'-biphenyl]-2-carboxylic acid (**3k**):



Following procedure D from spiro compound **2k** (16 mg, 0.07 mmol) precipitation of the product was incomplete. The product was then extracted with EtOAc after acidification, dried over $MgSO_4$, filtered and dried obtaining the desired product as a pale yellow solid (16 mg, quantitative).

TLC (8:2 hexane/EtOAc): R_f 0.13.

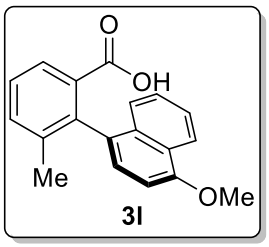
IR: ν 2924, 1689, 1288, 1242, 817, 763 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): 7.76 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.42 (dd, *J* = 7.5, 0.6 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.07 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 2.10 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 173.2, 158.7, 142.2, 138.0, 133.9, 132.2, 130.6, 129.8, 128.0, 127.1, 113.6, 55.3, 20.9 ppm.

HRMS (EI) calcd for $C_{15}H_{14}O_3$ 242.0943, found 242.0953.

2-(4-Methoxynaphthalen-1-yl)-3-methylbenzoic acid (**3l**):



Following procedure D from the corresponding spiro compound **2l** (38 mg, 0.13 mmol), the desired product was obtained as a white solid (31 mg, 82%).

TLC (8:2 hexane/EtOAc): R_f 0.27.

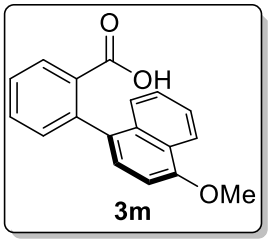
IR: ν 3062, 3004, 2954, 1689, 1585, 1288, 1234, 763, 728 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 7.7 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.39 – 7.31 (m, 2H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 4.04 (s, 3H), 1.91 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.4, 155.0, 140.9, 139.2, 134.0, 132.9, 131.2, 130.0, 128.34, 127.4, 126.6, 125.9, 125.6, 125.2, 125.0, 122.3, 103.5, 55.6, 20.4ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{19}H_{16}O_3$ 292.1099, found 292.1085.

2-(4-Methoxynaphthalen-1-yl)-benzoic acid (**3m**):



Following procedure D from the corresponding spiro compound **2m** (42 mg, 0.15 mmol), the desired product was obtained as a white solid (36 mg, 86%).

TLC (8:2 hexane/EtOAc): R_f 0.24.

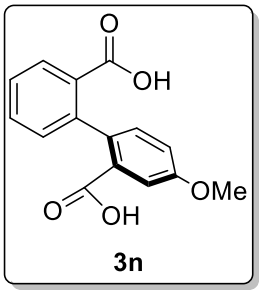
IR: ν 2954, 1689, 1585, 1292, 1234, 1079, 759 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.4 Hz, 1H), 8.02 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.59 (td, *J* = 7.5, 1.4 Hz, 1H), 7.51 – 7.36 (m, 5H), 7.19 (d, *J* = 7.8 Hz, 1H), 6.82 (d, *J* = 7.9 Hz, 1H), 4.04 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 172.2, 155.1, 142.1, 133.0, 132.7, 132.3, 131.5, 130.9, 130.6, 127.4, 126.6, 126.1, 125.4, 125.3, 125.1, 122.2, 103.3, 55.6 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{18}H_{14}O_3$ 278.0943, found 278.0933.

4-Methoxydiphenic acid (**3n**):



3n

Following procedure D from the corresponding spiro compound **2n** (53 mg, 0.19 mmol), the desired product was obtained as a white solid (48 mg, 91%).

TLC (7:3 hexane/(3:1:0.1 EtOAc:EtOH:AcOH): R_f 0.16

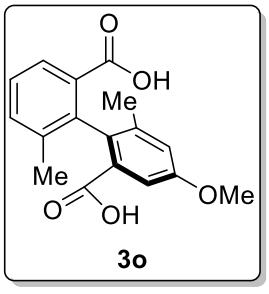
IR: ν 2920, 2854, 1674, 1450, 1412, 1284, 1230, 768 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.85 (d, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.38 (s, 1H), 7.17 – 7.14 (m, 3H), 3.82 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, DMSO-d_6): δ 168.1, 167.7, 157.9, 142.7, 135.2, 131.7, 131.5, 131.0, 130.7, 130.7, 129.5, 126.7, 116.7, 114.4, 55.3 ppm.

HRMS (EI-TOF) *m/z* calcd for $C_{15}H_{12}O_5$ 272.0685, found 272.0684.

4-Methoxy-6,6'-dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylic acid (**3o**):



3o

Following procedure D from the corresponding spiro compound **2o** (48 mg, 0.16 mmol), the desired product was obtained as a white solid (44 mg, 92%).

TLC (7:3 hexane/(3:1:0.1 EtOAc:EtOH:AcOH): R_f 0.19.

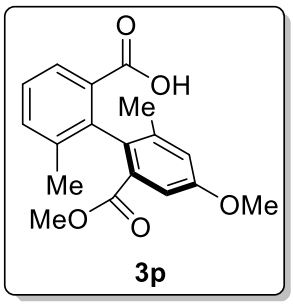
IR: ν 2924, 1685, 1427, 1269, 1234, 764 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.25 (s, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.42 (d, *J* = 7.1 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 2.5 Hz, 1H), 7.05 (d, *J* = 2.6 Hz, 1H), 3.81 (s, 3H), 1.83 (s, 3H), 1.79 (s, 3H) ppm.

^{13}C NMR {H^1} (101 MHz, DMSO-d_6): δ 168.4, 167.9, 157.4, 140.4, 137.7, 136.7, 132.9, 132.6, 131.5, 131.1, 127.1, 126.5, 118.8, 111.8, 55.1, 20.0, 19.9 ppm.

HRMS (EI-TOF) *m/z* calcd for $C_{17}H_{15}O_4$ [M^+-OH] 283.0970, found 283.0958.

4'-Methoxy-2'-(methoxycarbonyl)-6,6'-dimethyl-[1,1'-biphenyl]-2-carboxylic acid (**3p**):



3p

Following procedure D from the corresponding spiro compound **2p** (30 mg, 0.1 mmol precipitation of the product was incomplete. The product was then extracted with EtOAc after acidification, dried over $MgSO_4$, filtered and dried obtaining the desired product as a pale yellow solid (25 mg, 83%).

TLC (8:2 hexane/(3:1:0.1 EtOAc:EtOH:AcOH): R_f 0.16.

IR: ν cm^{-1} 2924, 1685, 1601, 1427, 1269, 1234, 1061, 864, 764, 714.

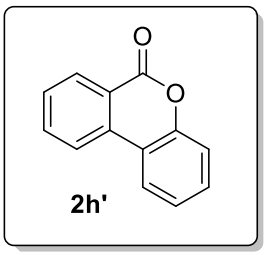
^{1}H NMR (400 MHz, MeOD): 7.66 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 2.7 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.91 (d, *J* = 2.7 Hz, 1H), 3.73 (s, 3H), 3.23 (s, 3H), 1.78 (s, 3H), 1.73 (s, 3H). δ ppm.

^{13}C NMR {H^1} (101 MHz, MeOD): 171.1, 170.7, 159.6, 142.2, 139.4, 138.4, 134.7, 134.3, 132.3, 132.0, 128.7, 127.8, 120.4, 113.4, 55.8, 49.8, 20.5, 20.3. δ ppm.

HRMS (EI-TOF) *m/z* calcd for $C_{18}H_{18}O_5$ 314.1154, found 314.1144.

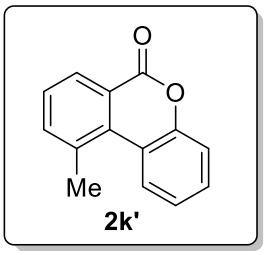
Synthesis of benzocoumarins **2h'**, **2k'** and **2s'**

Benzo-3,4-coumarin (**2h'**)



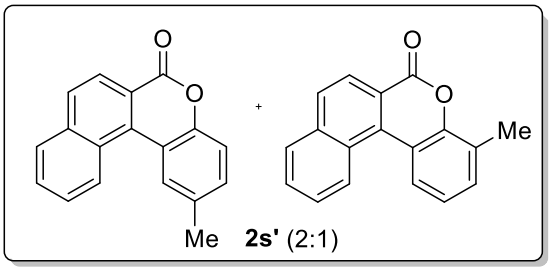
From acid **1h** (72 mg, 0.30 mmol), following Procedure C, byproduct benzo-3,4-coumarin (**2h'**) (8 mg, 13%) was obtained as a white solid (18 mg, 31%) and the characterization data matches literature.[1]

10-Methyl-6H-benzo[c]chromen-6-one (**2k'**)



From acid **1k** (64 mg, 0.30 mmol), following Procedure C, byproduct 10-methyl-*6H*-benzo[*c*]chromen-6-one **2k'** (8 mg, 13%) was obtained and the characterization data matches literature.[6]

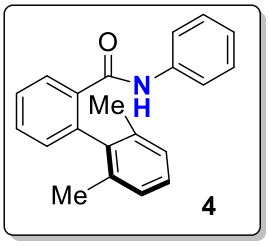
2-Methyl-6H-naphtho[2,1-c]chromen-6-one and its *4-methyl isomer* (**2s'**)



From the corresponding acid **1s** (79 mg, 0.30 mmol), following Procedure C, the desired product was not obtained. Instead, after FC (95:5 to 8:2 hexane/EtOAc) a white solid was isolated and identified as 2:1 mixture of benzocoumarins **2s'** (22 mg, 28%). Characterization data matches literature. [6]

Synthesis of amide **4,** alcohol **6** and their corresponding spiro compounds **5** and **7**

2',6'-Dimethyl-N-phenyl-[1,1'-biphenyl]-2-carboxamide (**4**):



Following a reported procedure,[7] a solution of acid **1a** (226 mg, 1 mmol) in dry CH_2Cl_2 (0.75 mL) was prepared in a dry flask refilled with Ar. The solution was cooled to 0 ºC before adding a drop of DMF, followed by thionyl chloride (88 µL, 1.2 mmol). The reaction mixture was stirred at the same temperature for 30 min and then left stirring while warming to room temperature for additional 3 h. The volatiles were carefully removed *in vacuo* and dissolved in dry CH_2Cl_2 (2 mL). This solution was added dropwise over a solution of aniline (137 µL, 1.5 mmol) and Et_3N (209 µL, 1.5 mmol) at 0 ºC. The reaction mixture was stirred at this temperature for 30 min and then stirred overnight while warming to room temperature. Quenching with aqueous NH_4Cl (1x 5 mL) was followed by extraction with EtOAc (3x 15 mL). The combined organic layers were washed with brine (1x 5 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Purification by FC (100% Hexane to 9:1 Hex/EtOAc) furnished pure amide **4** as a pale yellow solid (270 mg, 0.90 mmol, 90%).

TLC (9:1 hexane/EtOAc): R_f 0.35.

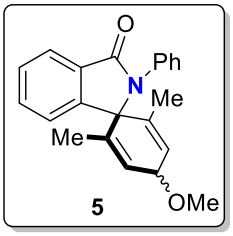
IR: ν 3421, 2920, 1666, 1597, 1523, 1439, 1319, 760 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (dd, J = 7.9, 1.4 Hz, 1H), 7.60 (td, J = 7.4, 1.6 Hz, 1H), 7.55 (td, J = 7.6, 1.5 Hz, 1H), 7.45 (br s, 1H), 7.36 (dd, J = 8.3, 6.8 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.25 – 7.16 (m, 3H), 7.09 – 7.00 (m, 3H), 2.07 (s, 6H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 164.9, 139.6, 138.3, 137.9, 136.7, 133.1, 131.8, 131.9, 130.3, 128.9, 128.8, 128.6, 128.1, 124.2, 119.9, 20.7 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{21}H_{19}NO$ 301.1467, found 301.1477.

4-Methoxy-2,6-dimethyl-2'-phenylspiro[cyclohexane-1,1'-isoindoline]-2,5-dien-3'-one (**5**):



From carboxamide **4** (60 mg, 0.20 mmol), following General Procedure C for the synthesis of spiro compounds, the desired product was obtained after FC (95:5 to 9:1 hexane/EtOAc) as a colorless wax (41 mg, 0.12 mmol, 60%) in a 55:45 dr (diastereomeric ratio according ^{1}H-NMR).

TLC (9:1 hexane/EtOAc): R_f 0.38 for both diastereoisomers.

IR: ν 2924, 1697, 1496, 1323, 1072, 941, 756, 694 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture: δ 7.94 – 7.89 (m, 1H), 7.78 – 7.72 (m, 0.90H), 7.64 – 7.45 (m, 3.10H), 7.38 – 7.29 (m, 2.55H), 7.22 – 7.13 (m, 1H), 7.09 (d, J = 7.2 Hz,

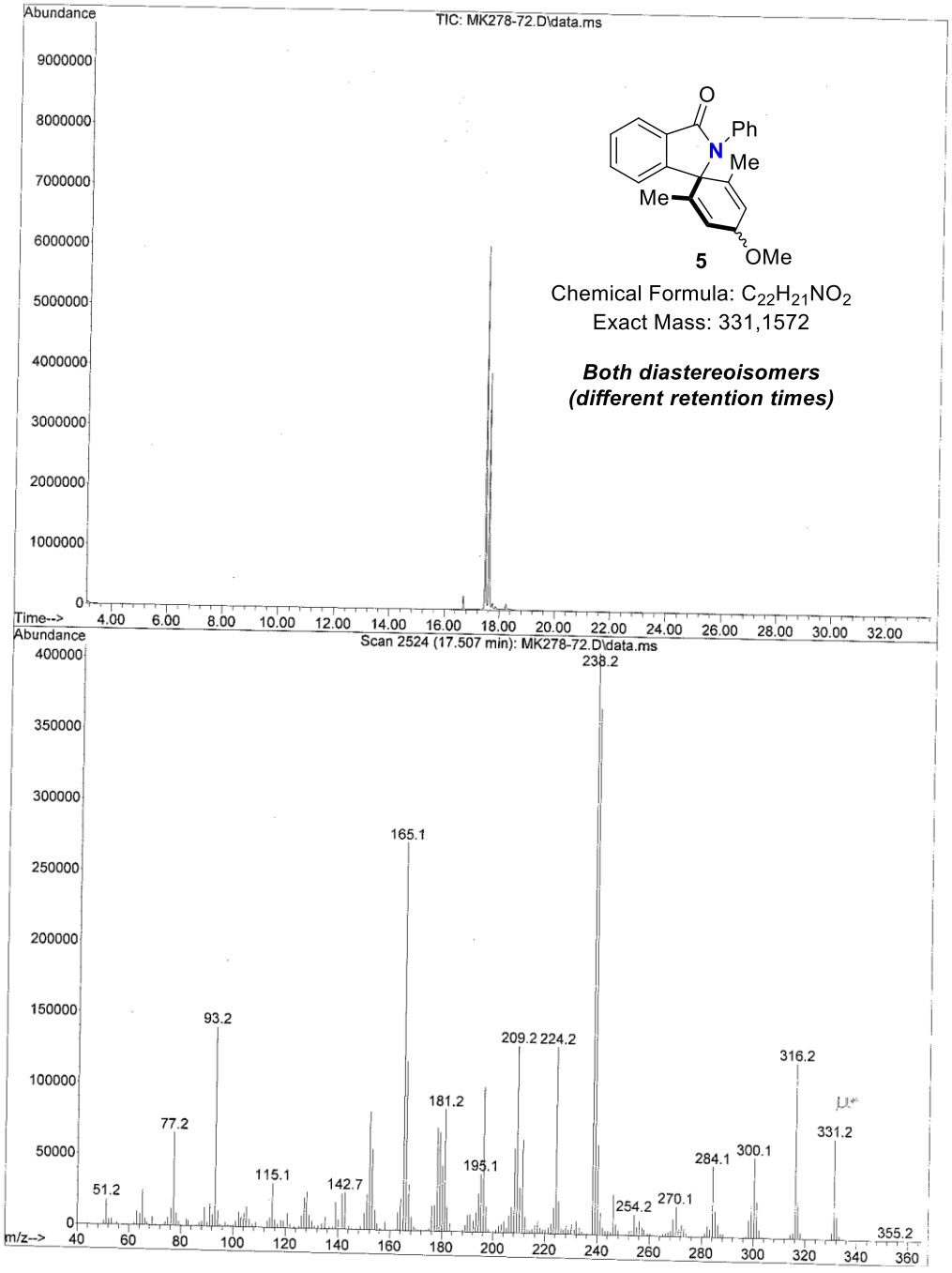
0.45H), 6.03 (d, *J* = 3.6 Hz, 1.10H), 5.96 (d, *J* = 3.2 Hz, 0.90H), 4.67 (dt, *J* = 3.2, 1.6 Hz, 0.45H), 4.34 (tt, *J* = 2.2, 1.2 Hz, 0.55H), 3.50 (s, 1.65H), 3.30 (s, 1.35H), 1.35 (s, 2.70H), 1.34 (s, 3.30H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) of the diastereoisomeric mixture: δ 168.8, 168.7, 146.7, 138.3, 137.8, 137.1, 133.1, 133.0, 132.3, 132.2, 129.0, 129.0, 128.9, 128.9,128.8, 126.6, 126.5, 126.2, 125.7, 125.5, 123.9, 122.6, 122.5, 122.4, 122.3, 121.7, 71.5, 71.3, 71.2, 70.5, 55.3, 54.2, 17.6, 17.4 ppm.

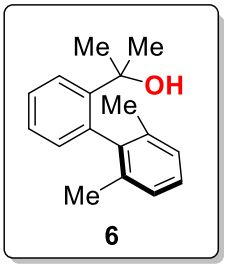
HRMS (EI): calcd for $C_{22}H_{21}NO_2$ 331.1572, found 331.1568.

LRMS (EI): *m/z* (%) 331 (M^+,16), 316 (29), 300 (14), 239 (92), 238 (100), 224 (32), 209 (36). 165 (73), 93 (39).

GC-LRMS copy:



2-(2',6'-Dimethyl-[1,1'-biphenyl]-2-yl)propan-2-ol (**6**):



A solution of **1a-Et-ester** (127 mg, 0.50 mmol) in dry THF (5 mL) was cooled down to – 78 ºC, followed by the dropwise addition of a solution of MeLi in THF (1.6 M, 1 mL). The reaction mixture was stirred at the same temperature for 1 h, the cooling bath was removed and the stirring continued overnight at room temperature. Quenching with aqueous NH_4Cl (10 mL) was followed by extraction with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (1x 5 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Purification by FC (100% Hexane to 95:5 Hex/EtOAc) furnished pure alcohol **6** as a pale yellow solid (84 mg, 0.35 mmol, 70%).

TLC (95:5 hexane/EtOAc): R_f 0.30.

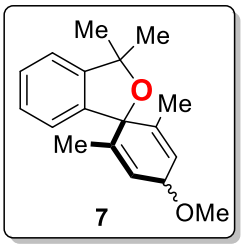
IR: ν 3348, 2981, 1458, 1369, 1161, 953, 764, 717cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (dd, J = 7.9, 1.5 Hz, 1H), 7.36 (ddd, J = 8.0, 7.3, 1.6 Hz, 1H), 7.29 (td, J = 7.4, 1.4 Hz, 1H), 7.19 (dd, J = 8.5, 6.5 Hz, 1H), 7.15 – 7.08 (m, 2H), 6.91 (dd, J = 7.6, 1.5 Hz, 1H), 2.04 (s, 6H), 1.81 (s, 1H), 1.48 (s, 6H) ppm.

^{13}C NMR {H^1} (75 MHz, $CDCl_3$): δ 145.7, 142.4, 137.4, 136.4, 131.2, 127.6, 127.6, 127.5, 127.3, 127.0, 74.4, 32.1, 21.4 ppm.

HRMS (EI-TOF): *m/z* calcd for $C_{17}H_{20}O$ 240.1514, found 240.1524.

4-Methoxy-2,3',3',6-tetramethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene (**7**):



From alcohol **6** (48 mg, 0.20 mmol), following General Procedure C for the synthesis of spiro compounds, the desired product was obtained after FC (95:5 to 9:1 hexane/EtOAc) as a colorless oil (26 mg, 0.10 mmol, 50%) in a 54:46 dr (diastereomeric ratio according ^{1}H-NMR).

TLC (9:1 hexane/EtOAc): R_f 0.43 for both diastereoisomers.

IR: ν 2974, 2927, 1450, 1373, 1068, 1003, 645, 868, 760 cm^{-1}.

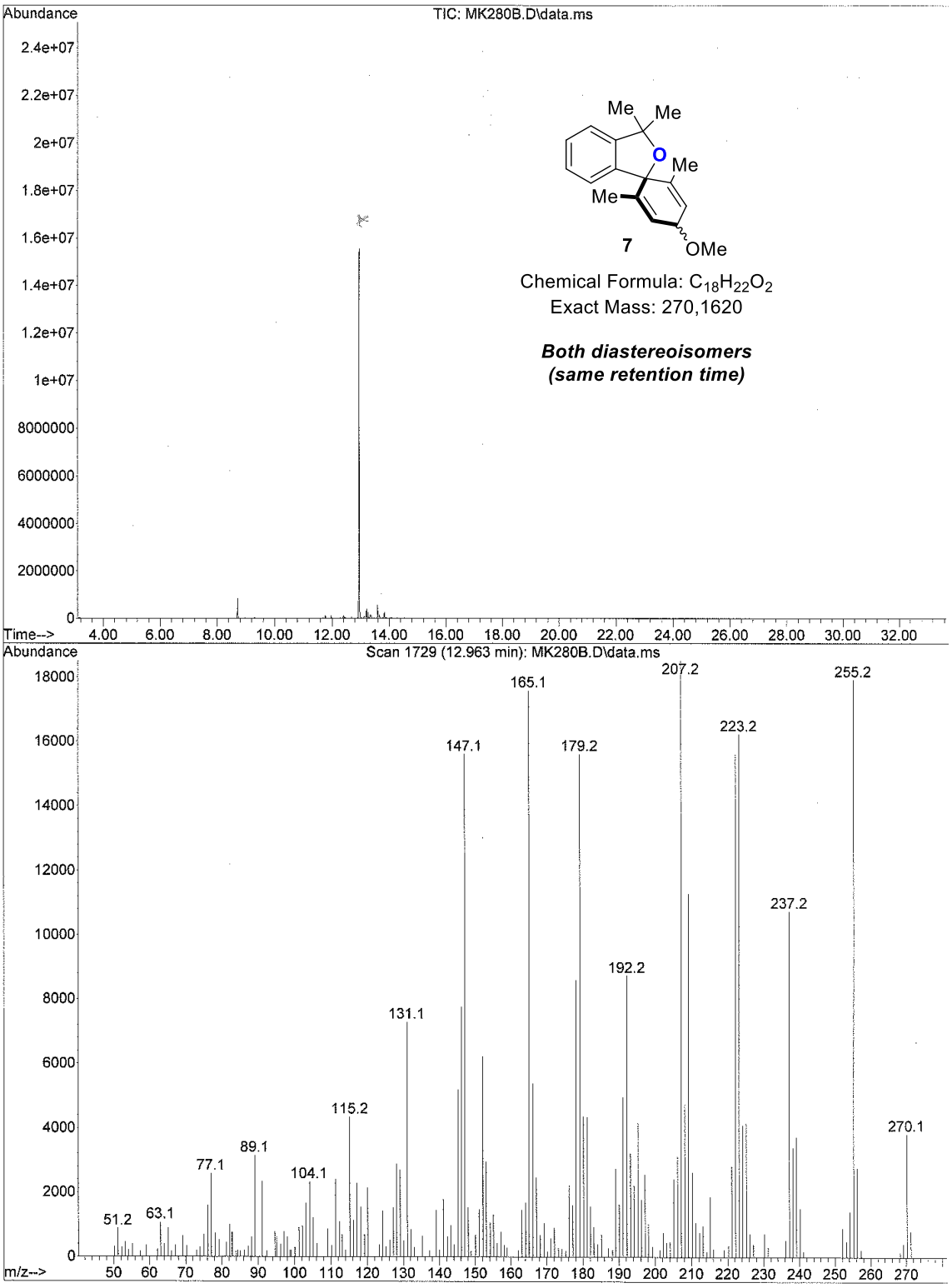
^{1}H NMR (400 MHz, $CDCl_3$) of the diastereomeric mixture: δ 7.34 – 7.22 (m, 2H), 7.15 – 7.10 (m, 1H), 6.97 (ddd, J = 7.5, 1.2, 0.7 Hz, 0.54H), 6.79 (dt, J = 7.5, 0.9 Hz, 0.46H), 5.87 (d, J = 3.7 Hz, 1.08H), 5.76 (d, J = 3.1 Hz, 0.92H), 4.56 (tt, J = 3.2, 1.7 Hz, 0.46H), 4.34 (ddt, J = 5.1, 3.6, 1.5 Hz, 0.54H), 3.44 (s, 1.62H), 3.31 (s, 1.38H), 1.68 (s, 2.76H), 1.66 (s, 3.24H), 1.64 (s, 2.76H), 1.60 (s, 3.24H) ppm.

^{13}C NMR {H^1} (101 MHz, $CDCl_3$) of the diastereoisomeric mixture: δ 147.2, 146.8, 141.8, 141.3, 141.1, 140.5, 128.4, 128.4, 128.1, 128.0, 124.7, 123.8, 122.2, 121.7, 120.6, 120.5, 87.7, 87.5, 86.4, 86.2, 71.3, 70.1, 54.3, 52.9, 30.3, 30.2, 20.4, 20.4 ppm.

HRMS (EI): calcd for $C_{18}H_{28}O_2$ 270.1620, found 270.1619.

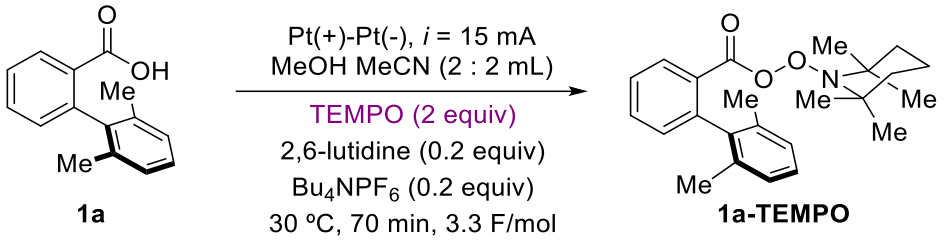
LRMS (EI): *m/z* (%) 270 (M^+,8), 255 (70), 222 (57), 207 (100), 192 (54), 165 (76), 147 (98), 146 (53), 131 (60).

GC-LRMS copy:



Synthesis of **1a-TEMPO**

2,2,6,6-Tetramethylpiperidin-1-yl -2',6'-dimethyl-[1,1'-biphenyl]-2-carboperoxoate (**1a-TEMPO**):



Following Procedure C, the electrolysis of substrate **1a** (45.2 mg, 0.2 mmol) in the presence of TEMPO (65 mg, 0.4 mmol, 2 equiv), afforded product **1a-TEMPO**, which was isolated as a white solid (77 mg, quant.) after FC (9:1 hexane/EtOAc).

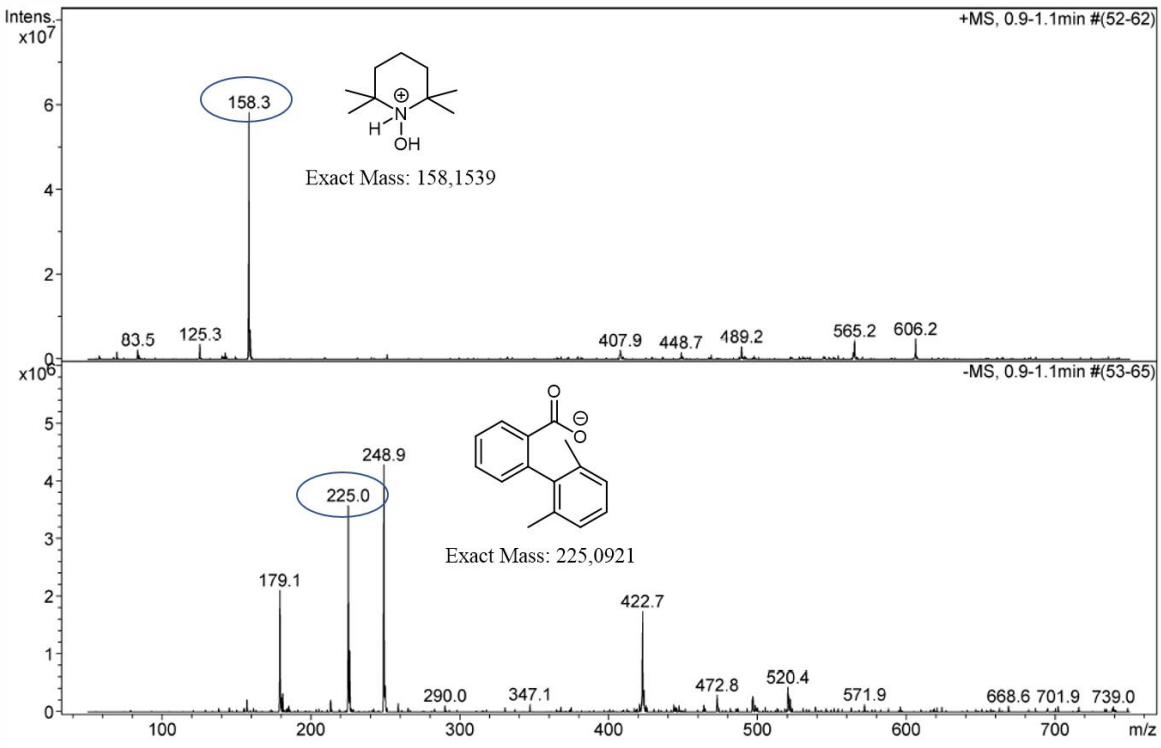
TLC (8:2 hexane/EtOAc): R_f 0.22.

IR: ν 3025, 2981, 2569, 1708, 1454, 1384, 1249, 763, 728 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (dd, J = 7.5, 0.8 Hz, 1H), 7.48 (t, J = 7.4 Hz, 1H), 7.40 (t, J = 7.4 Hz, 1H), 7.13 – 7.07 (m, 2H), 7.05 – 7.01 (m, 2H), 2.02 (s, 6H), 1.79 – 1.58 (m, 5H), 1.56– 1.48 (m, 1H), 1.28 (s, 6H), 1.15 (s, 6H) ppm.

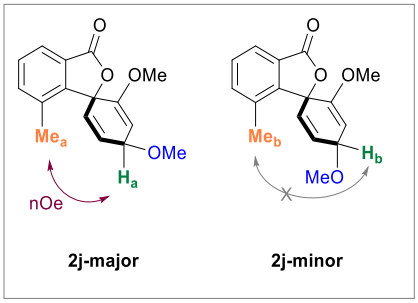
^{13}C NMR {H^1} (101 MHz, $CDCl_3$): δ 173.8, 141.2, 139.7, 135.4, 135.1, 129.5, 129.2, 128.3, 126.3, 126.0, 125.9, 64.7, 36.4, 26.9, 20.2, 19.6, 15.4 ppm.

LRMS (ESI) (positive and negative modes):

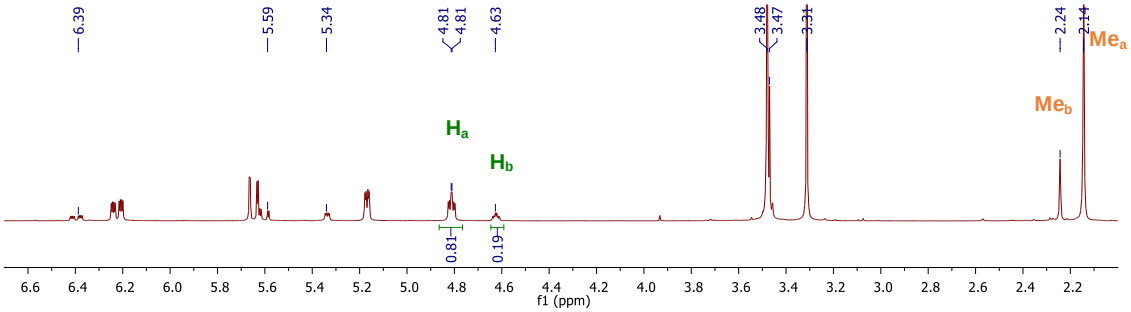


nOe-d_1 experiments performed for spirolactone **2j**:

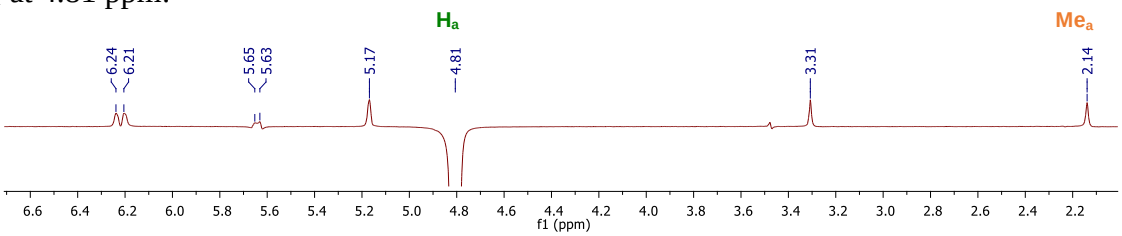
To elucidate the major diastereoisomer of spirolactone **2j**, differential nOe experiments were performed selectively irradiating the C-4´-H of the molecule, named H_a and H_b for the major and minor diastereoisomers respectively. nOe between H_a (4.81 ppm) and the C-6-Me_a (2.14 ppm) was observed for the major component, whereas no nOe was detected between H_b (4.63 ppm) and the C-6-Me_b (2.24 ppm).



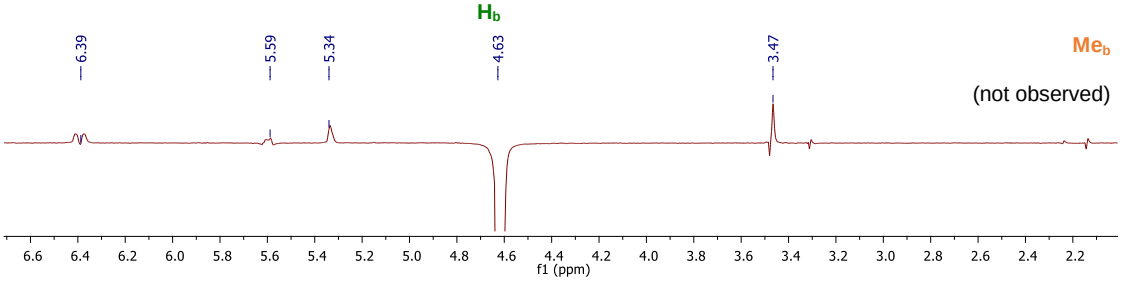
^{1}H-NMR section of **2j:**



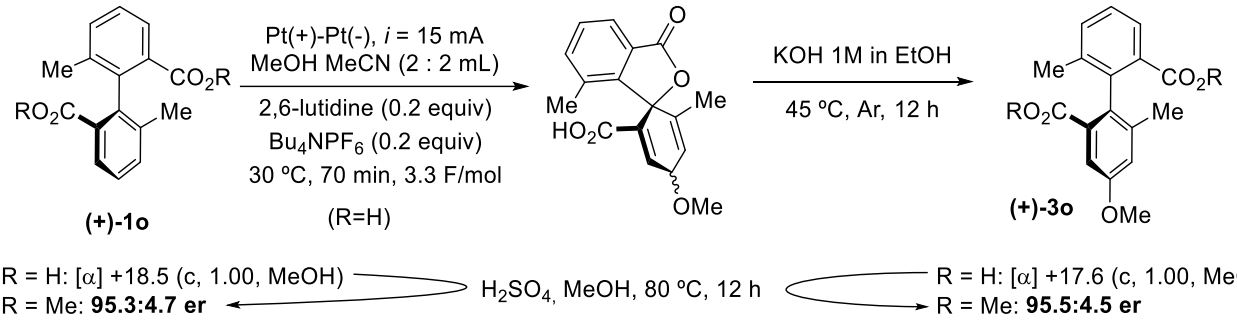
nOe-d_1 at 4.81 ppm:



nOe-d_1 at 4.63 ppm:

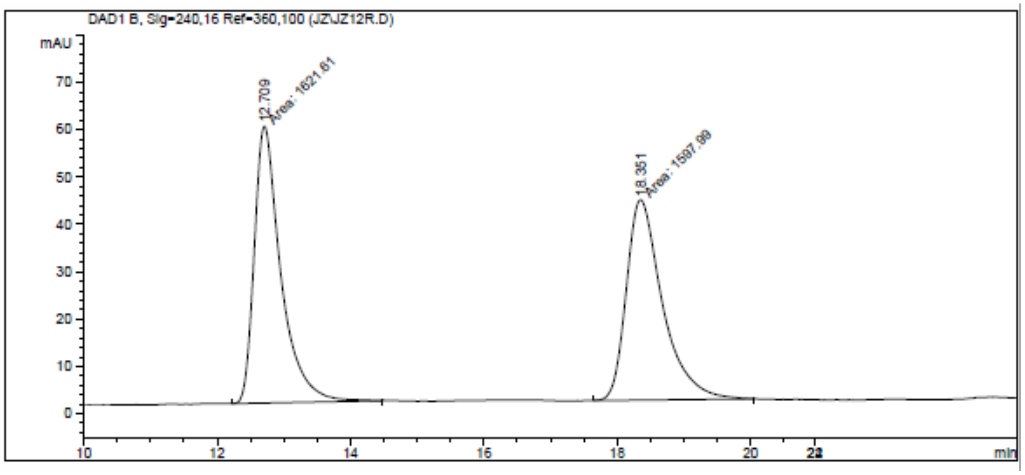


HPLC and MS data for enantioenriched **(+)-3o**



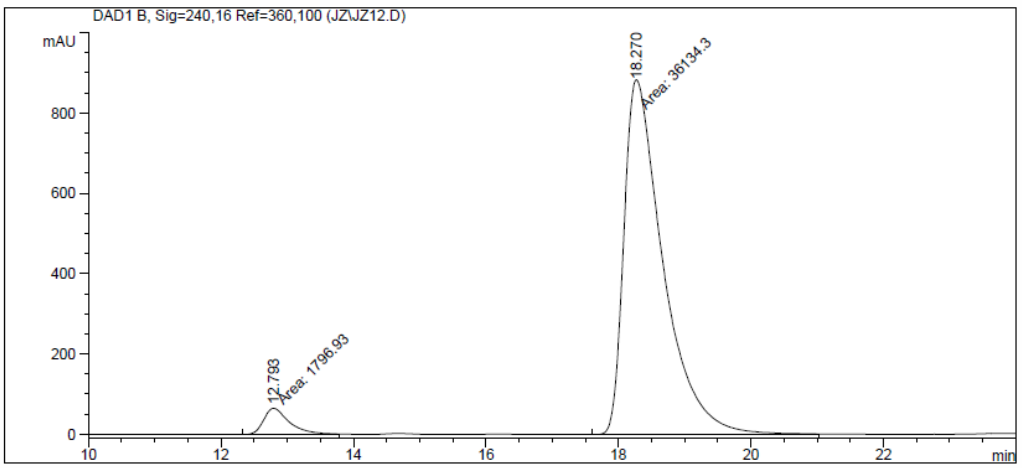
Resolution of **rac-1o** was performed with quinine, following a reported procedure.[8] By comparison of spectroscopic data and optical rotation, the enantiomer obtained after crystallization was **(+)-1o**, with *P*-configuration at the biphenyl moiety. For HPLC analysis (shown below), the corresponding dimethyl esters were prepared using MeOH and H_2SO_4 as the catalyst (Fisher method).

***rac*-1o**-dimethyl ester



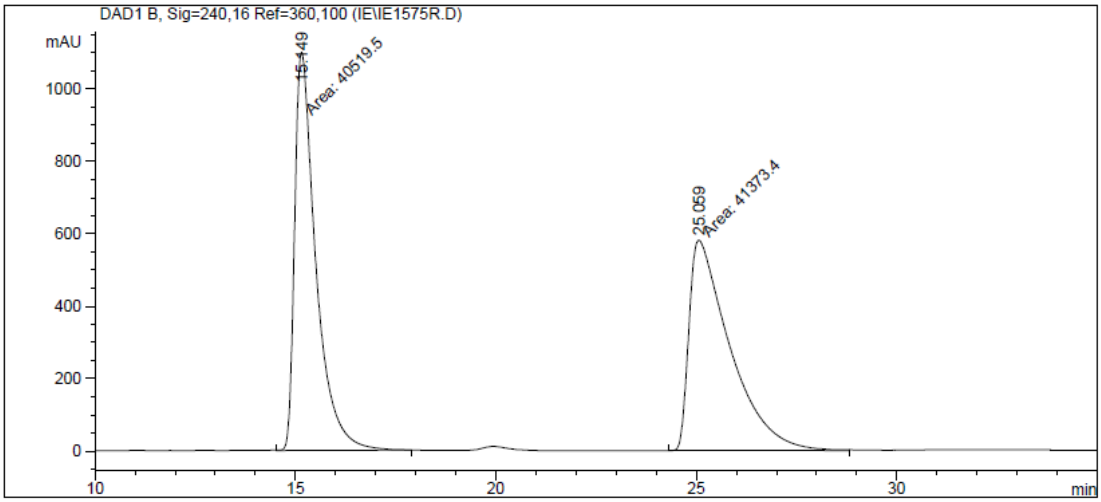
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.709	MM	0.4622	1621.61121	58.47356	50.3669
2	18.351	MM	0.6289	1597.98828	42.34860	49.6331

(+)-1o-dimethyl ester



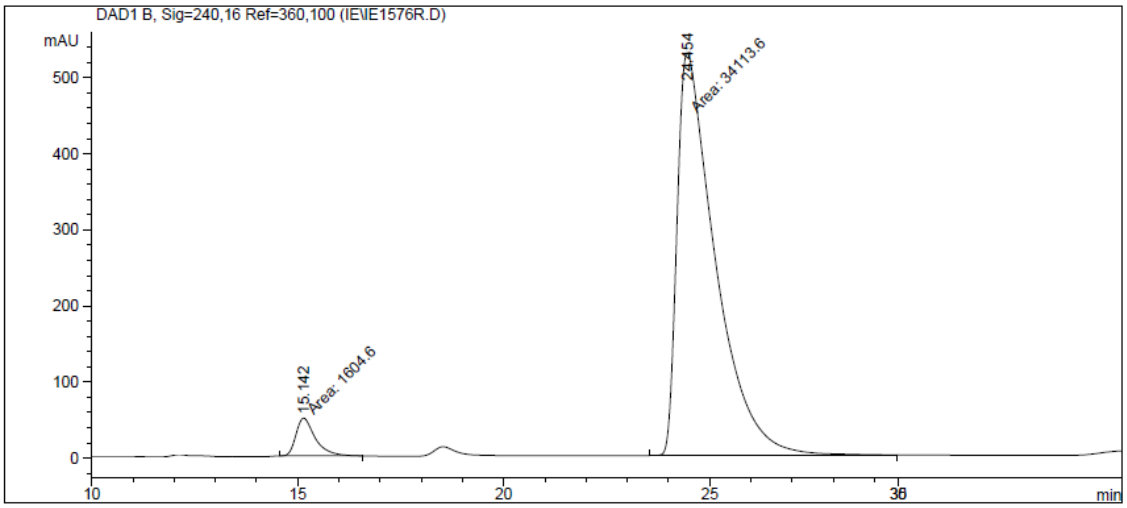
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.793	MM	0.4563	1796.92664	65.63340	4.7373
2	18.270	MM	0.6822	3.61343e4	882.81482	95.2627

***rac*-3o**-dimethyl ester



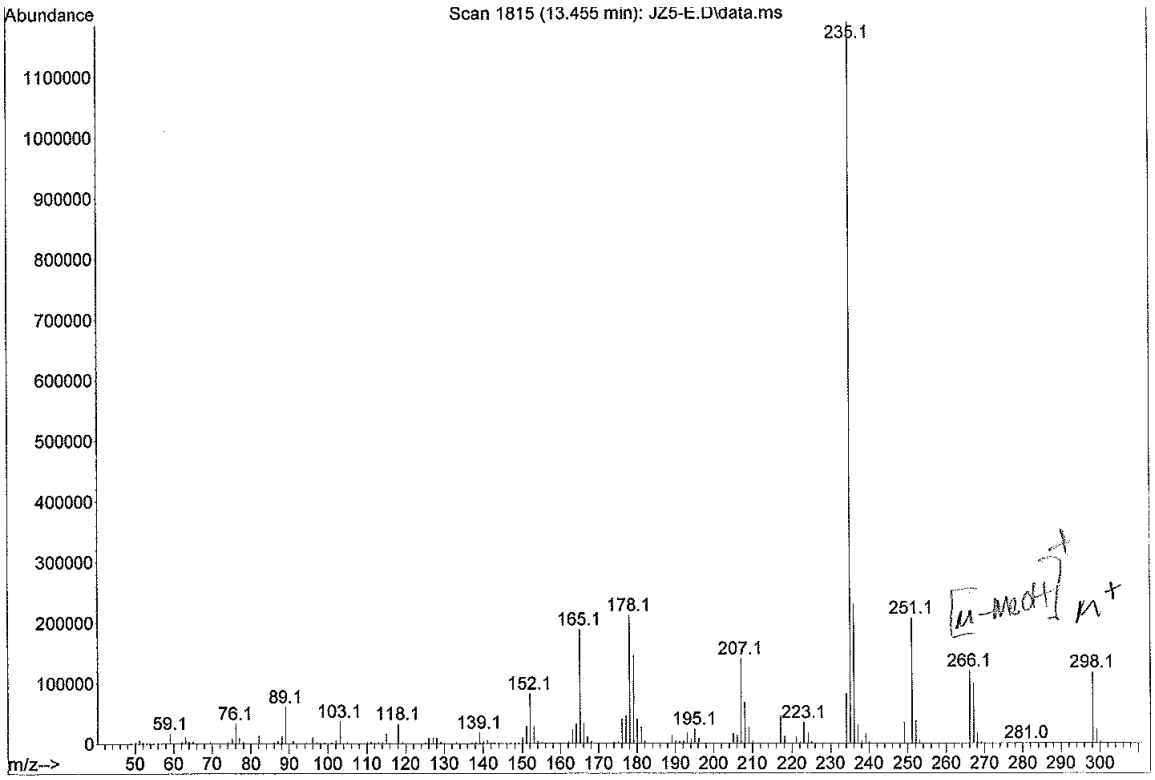
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.149	MM	0.6135	4.05195e4	1100.71777	49.4787
2	25.059	MM	1.1866	4.13734e4	581.10028	50.5213

(+)-3o-dimethyl ester

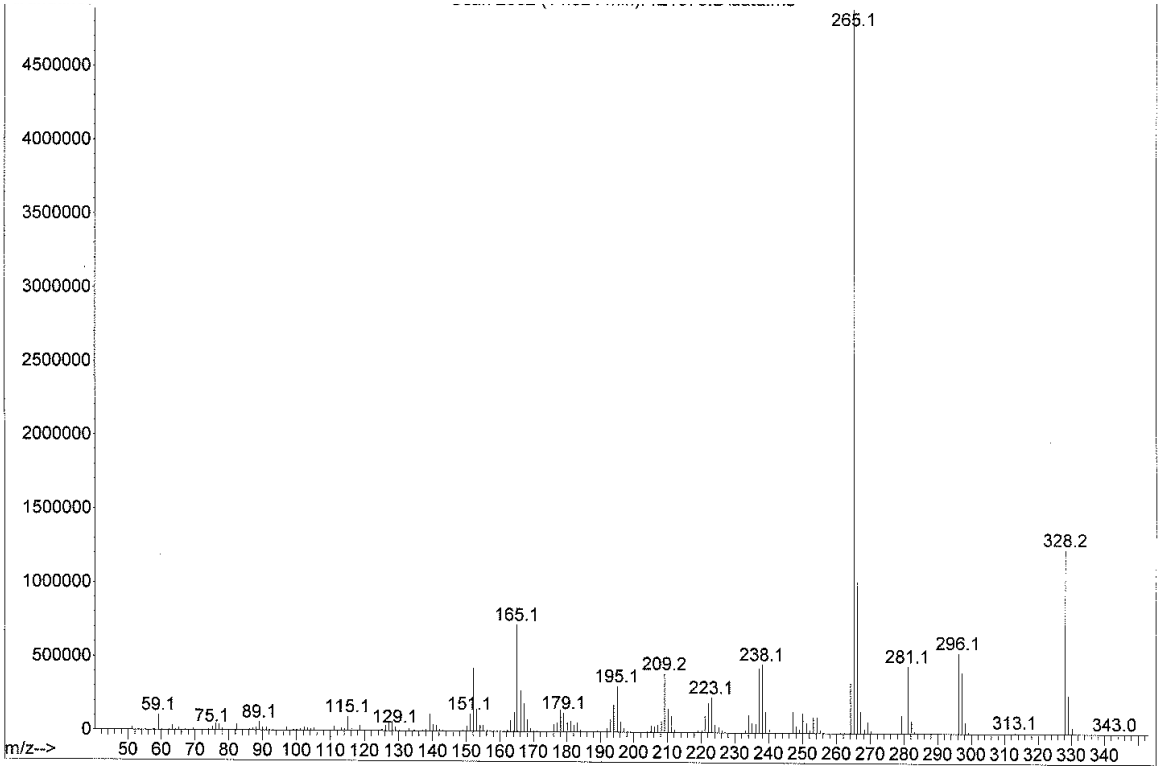


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.142	MM	0.5402	1604.59875	49.50425	4.4924
2	24.454	MM	1.0745	3.41136e4	529.15594	95.5076

MS for ***rac*-1o**-dimethyl ester (M^+ = 298)



MS for ***rac*-3o**-dimethyl ester (M^+ = 328)



Cyclic voltammetry studies

Summary of onset potential and $E_{p/2}$ potential of starting acids **1** and compounds **1a-Et-ester**, **2ab**, **3ab**, biphenyl, sodium benzoate

Table S1:

Compound	Onset potential (vs Ag/AgCl)	$E_{p/2}$ (vs Ag/AgCl)	Onset potential (vs Ag/AgCl) **with 2,6-lutidine**	$E_{p/2}$ (vs Ag/AgCl) **with 2,6-lutidine**
1a	1.60 V	> 1.80 V	1.05 V	1.55 V
1b	1.30 V	1.70 V	1.00 V	1.55 V
1c	1.60 V	> 1.80 V	0.95 V	1.45 V
1d	1.50 V	> 1.80 V	1.0 V	1.55 V
1e	1.60 V	1.75 V	1.00 V	1.50 V
1f	1.50 V	> 1.80 V	1.15 V	1.40 V
1g	1.45 V	1.65 V	1.00 V	1.45 V
1h	1.60 V	> 1.80 V	1.10 V	1.35 V
1i	1.50 V	1.80 V	1.05 V	1.50 V
1j	1.40 V	1.55V	0.90 V	1.30 V
1k	1.70 V	> 1.80 V	1.10 V	1.40 V
1l	1.30 V	> 1.80 V	0.90 V	1.25 V
1m	1.35 V	1.45 V	0.80 V	1.15 V
1n (diphenic acid)	1.00 V	1.10 V	0.70 V	0.75 V
1o	1.00 V	1.05 V	0.60 V	0.65 V
1p	1.00 V	1.10 V	0.60 V	0.70 V
1q	1.45 V	1.55 V	1.10 V	1.20 V
1r	1.65 V	> 1.80 V	1.20 V	1.45 V
1s	1.60 V	1.70 V	1.05 V	1.45 V
1a-Et ester	1.70 V	> 1.80 V	1.10 V	1.50 V
2ab	1.70 V	> 1.80 V	1.70 V	> 1.80 V
3ab	1.30 V	1.35 V	0.80 V	1.10 V
2,6-lutidine	1.60 V	> 1.80 V	-	-
biphenyl	1.65 V	>1.80 V	1.65 V	>1.80 V
Sodium benzoate	1.20 V	1.55 V	-	-

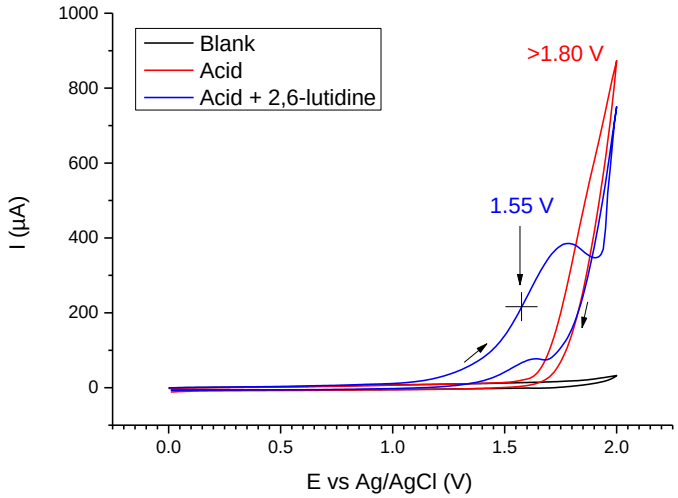
Summary of onset potential and $E_{p/2}$ potential of amide **4**, benzanilide and alcohol **6**

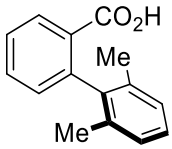
Table S2:

Compound	Onset potential (vs Ag/AgCl)	$E_{p/2}$ (vs Ag/AgCl)	Onset potential (vs Ag/AgCl) **with 2,6-lutidine**	$E_{p/2}$ (vs Ag/AgCl) **with 2,6-lutidine**
4	1.45 V	1.70 V	1.40 V	1.55 V
Benzanilide	1.50 V	1.70 V	1.35 V	1.50 V
6	1.40 V	1.70 V	1.40 V	1.65 V

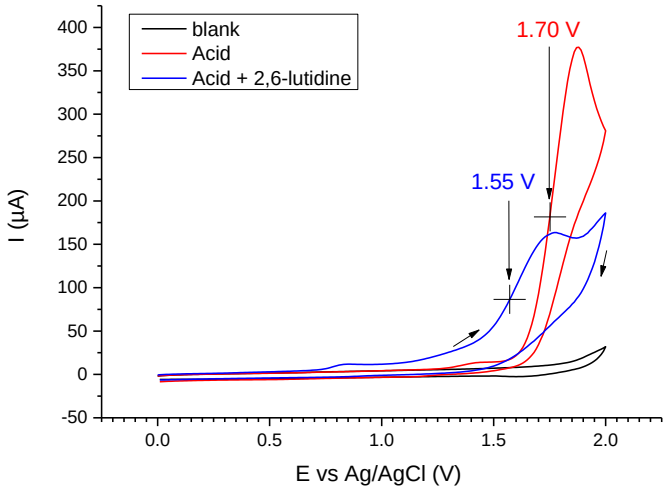
Cyclic voltammograms (CV) of products **1**, **1a-Et-ester**, **2ab**, **3ab**, 2,6-lutidine, biphenyl, sodium benzoate, **4**, benzanilide and **6**.

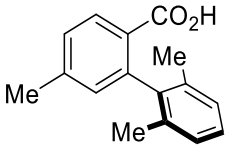
Measurements were performed using EmStatblue+ potentiostat at a scan rate of 100 mV/s. A glassy carbon electrode of 3 mm diameter was used as a working electrode, a platinum wire as a counter electrode and a Ag/AgCl (aq., 0.1 M KCl) as a reference electrode. Measurements were performed in 3 mL of blank solution (0.1 M Bu_4NPF_6 in MeCN, black line) with the corresponding compound (0.05 M, red line) and adding 2,6-lutidine (0.05 M, blue line). Ferrocene was used as an internal standard. The first half-peak potential ($E_{p/2}$) in V vs Ag/AgCl is indicated in each case in the absence (red) and in the presence (blue) of 2,6-lutidine.



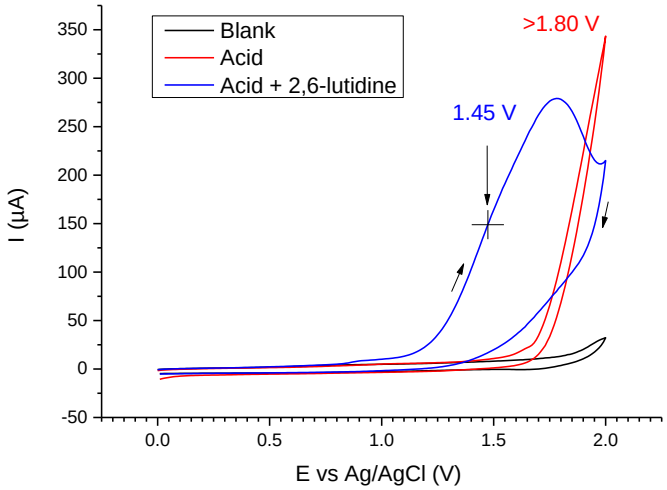


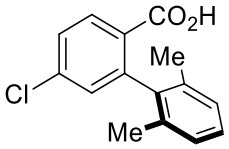
1a



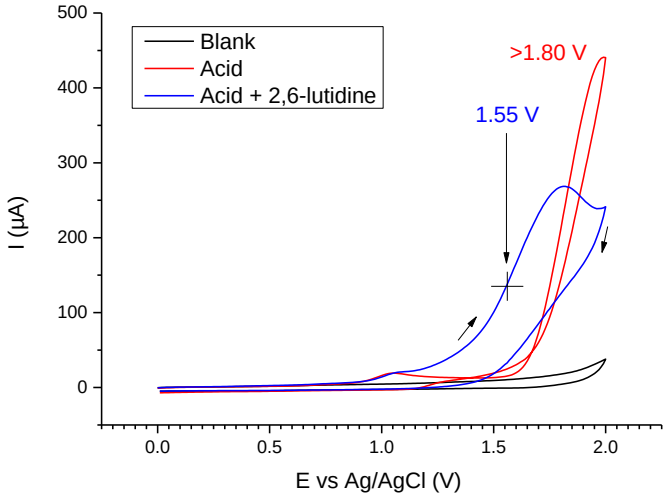


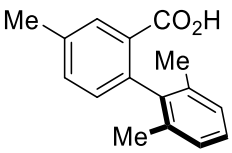
1b


Blank
Acid
Acid + 2,6-lutidine
>1.80 V
1.45 V
I (µA)
E vs Ag/AgCl (V)

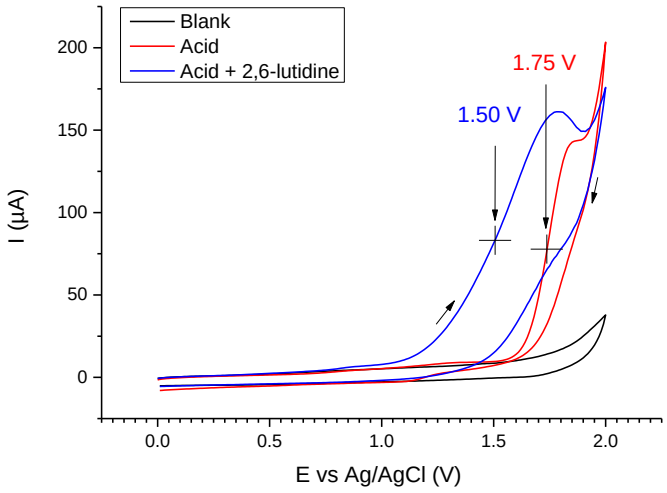

CO2H
Me
Cl
Me

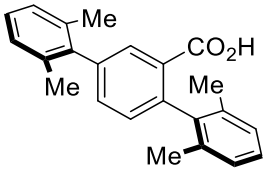
1c


Blank
Acid
Acid + 2,6-lutidine
>1.80 V
1.55 V
I (µA)
E vs Ag/AgCl (V)

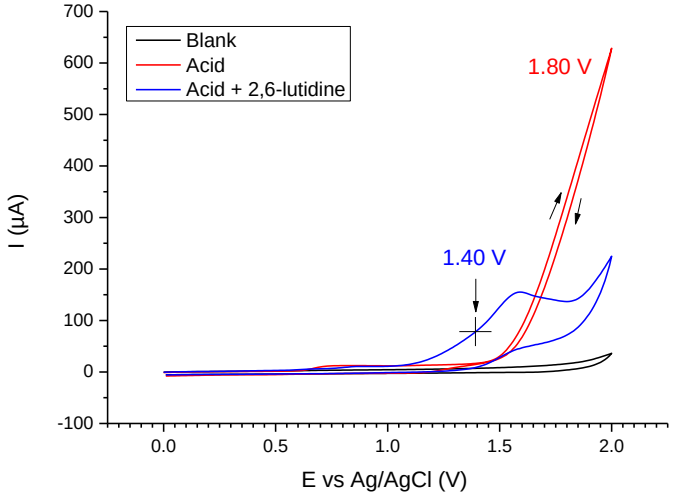

Me
CO2H
Me
Me

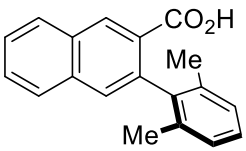
1d


Blank
Acid
Acid + 2,6-lutidine
1.75 V
1.50 V
I (µA)
E vs Ag/AgCl (V)

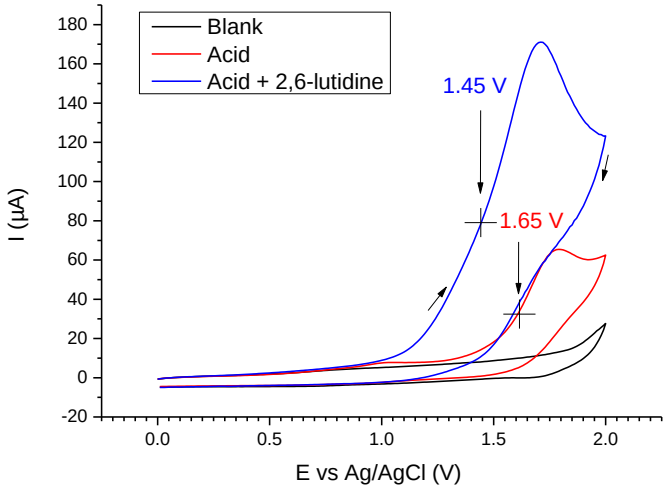

Me
Me
CO2H
Me
Me

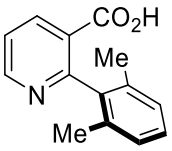
1e


Blank
Acid
Acid + 2,6-lutidine
1.80 V
1.40 V
I (μA)
E vs Ag/AgCl (V)

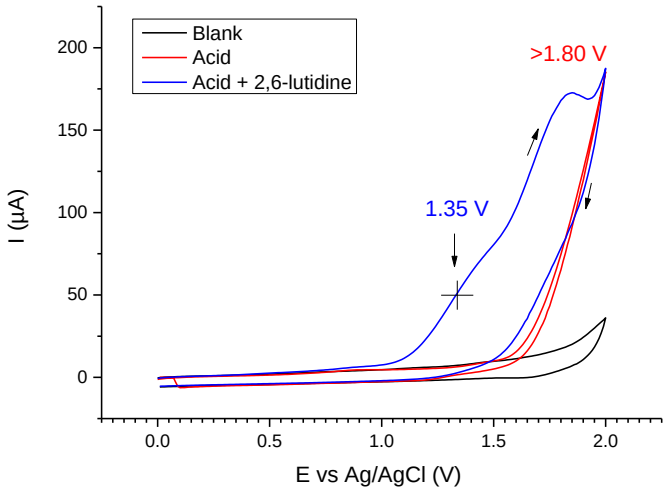

CO2H
Me
Me

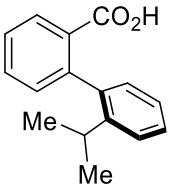
1f


Blank
Acid
Acid + 2,6-lutidine
1.45 V
1.65 V
I (μA)
E vs Ag/AgCl (V)

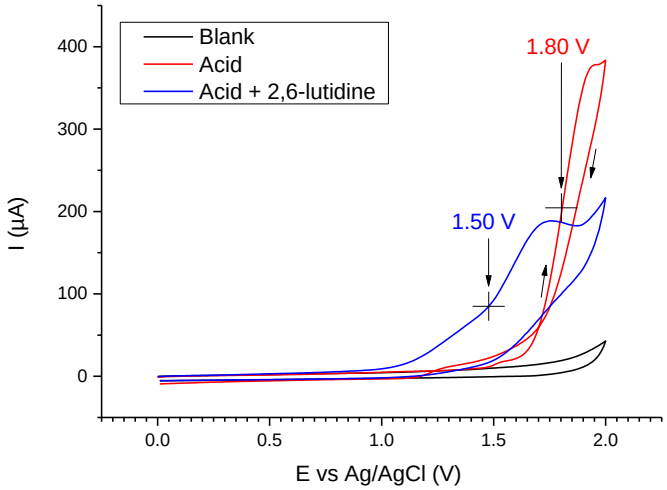

CO2H
Me
N
Me

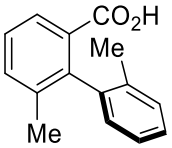
1g


Blank
Acid
Acid + 2,6-lutidine
>1.80 V
1.35 V
I (μA)
E vs Ag/AgCl (V)

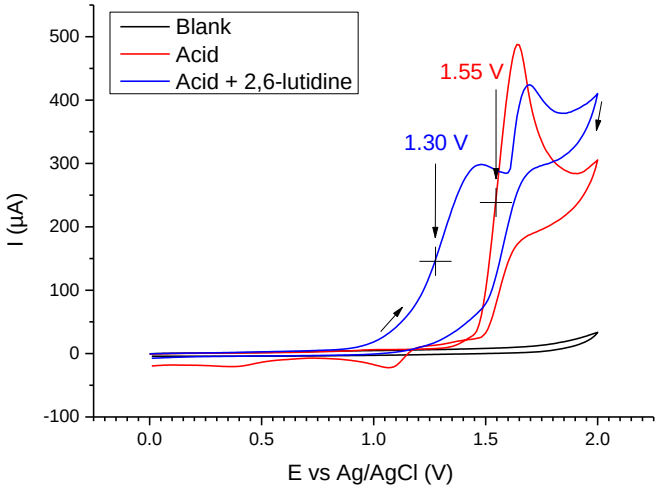

CO2H
Me
Me

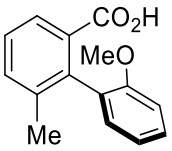
1h


Blank
Acid
Acid + 2,6-lutidine
1.80 V
1.50 V
I (μA)
E vs Ag/AgCl (V)

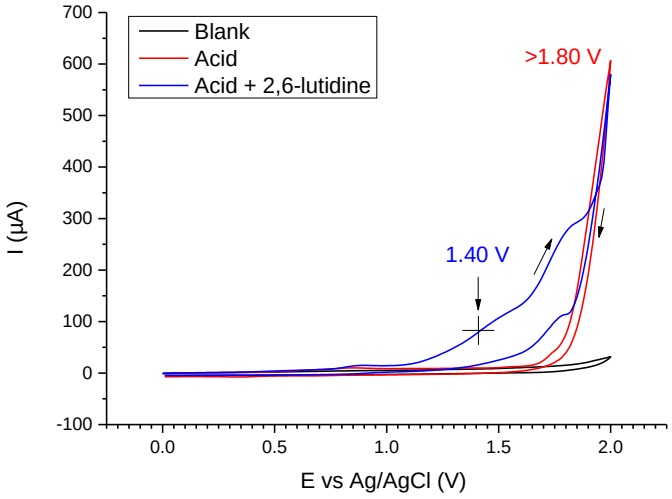

CO2H
Me
Me

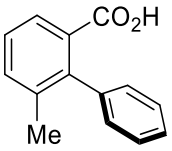
1i


Blank
Acid
Acid + 2,6-lutidine
1.55 V
1.30 V
I (μA)
E vs Ag/AgCl (V)

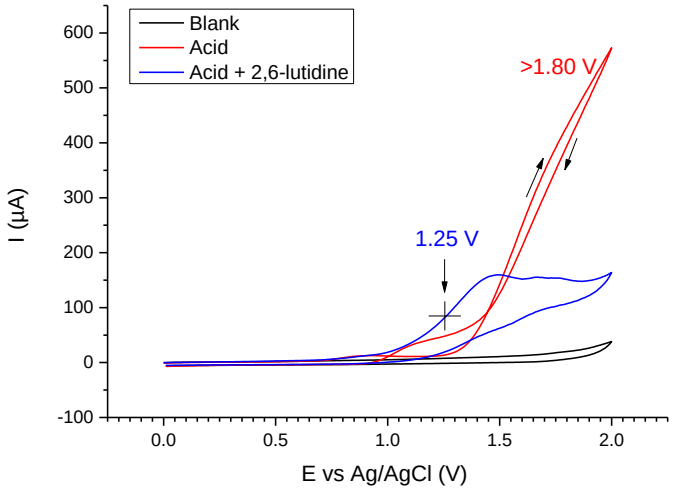

CO2H
MeO
Me

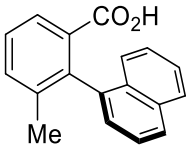
1j


Blank
Acid
Acid + 2,6-lutidine
>1.80 V
1.40 V
I (μA)
E vs Ag/AgCl (V)

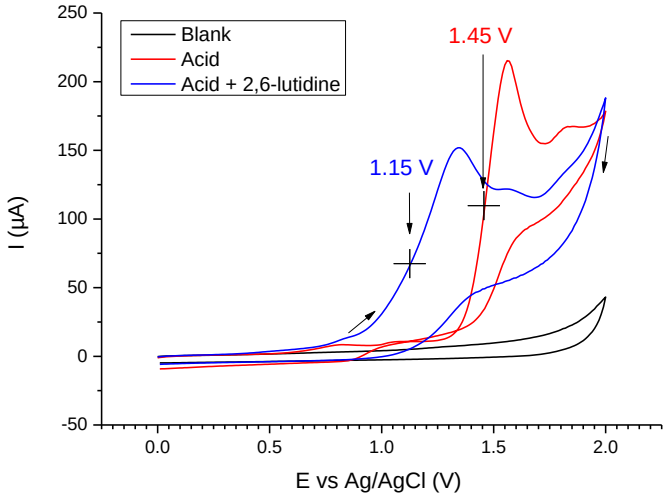

CO2H
Me

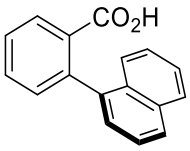
1k



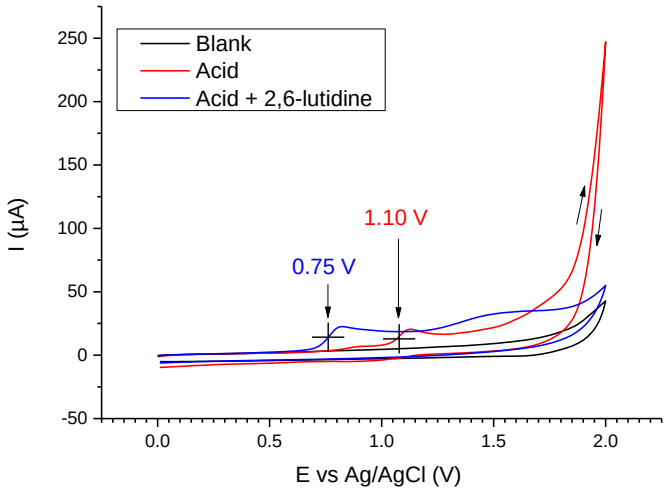


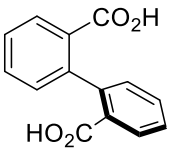
1l



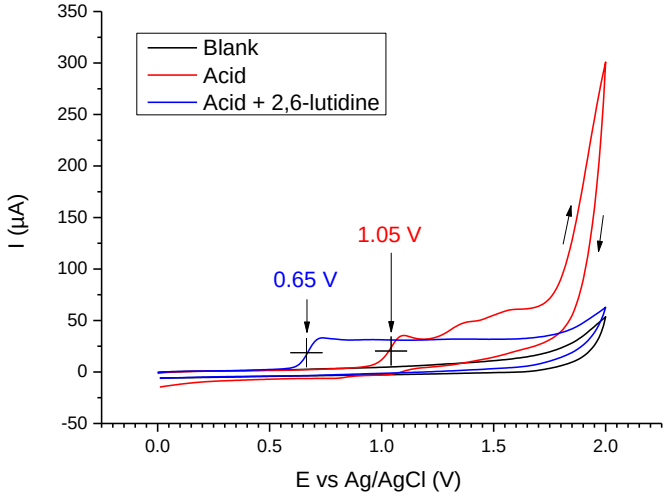


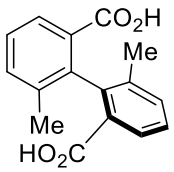
1m



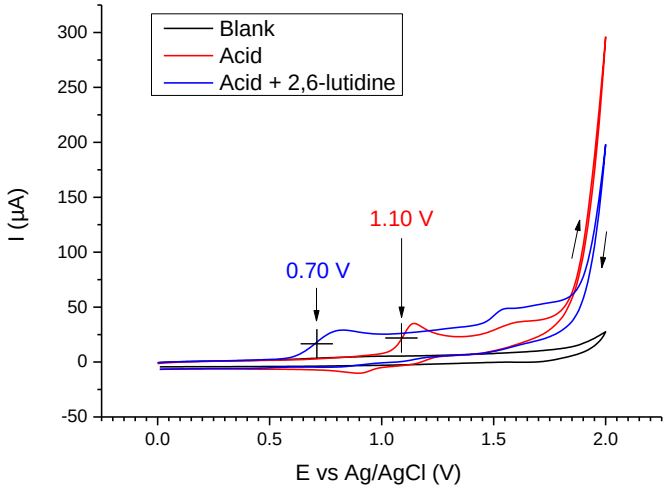


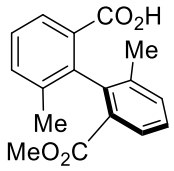
1n
(diphenic acid)


Blank
Acid
Acid + 2,6-lutidine
I (μA)
E vs Ag/AgCl (V)
0.65 V
1.05 V

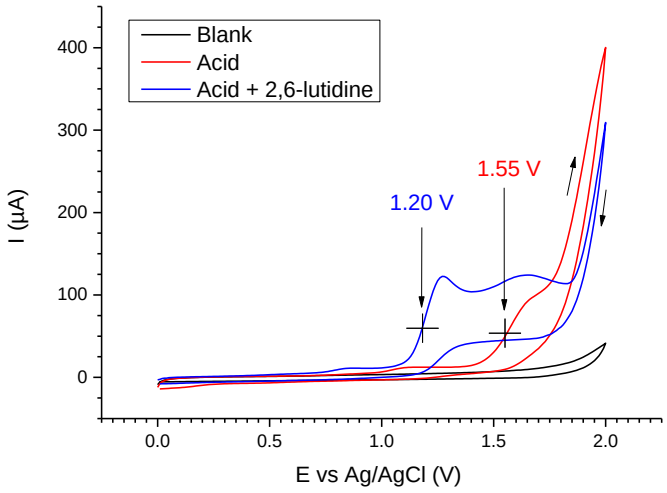

CO2H
Me
Me
HO2C

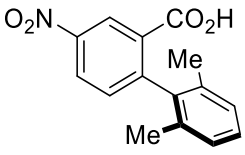
1o


Blank
Acid
Acid + 2,6-lutidine
I (μA)
E vs Ag/AgCl (V)
0.70 V
1.10 V

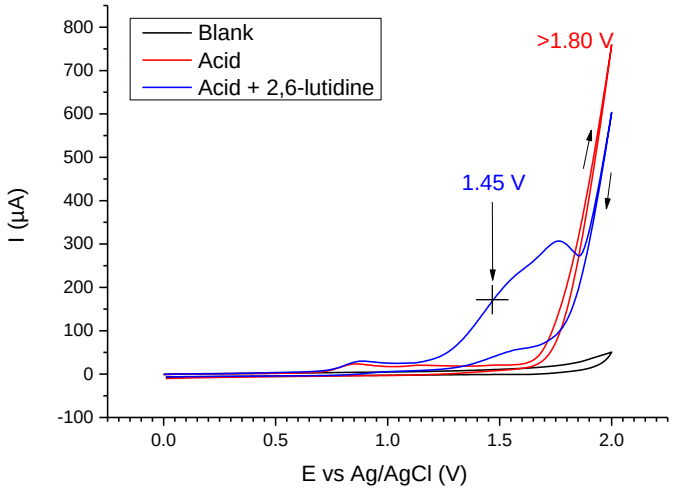

CO2H
Me
Me
MeO2C

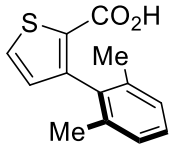
1p


Blank
Acid
Acid + 2,6-lutidine
I (μA)
E vs Ag/AgCl (V)
1.20 V
1.55 V

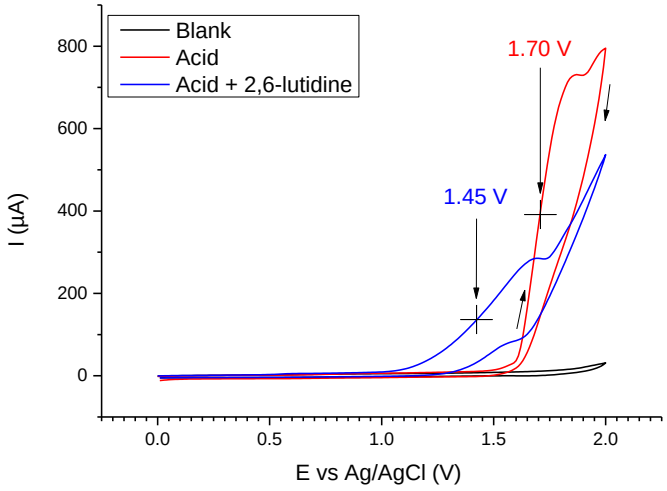

O2N
CO2H
Me
Me

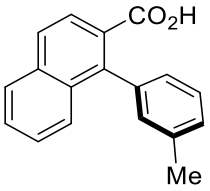
1q



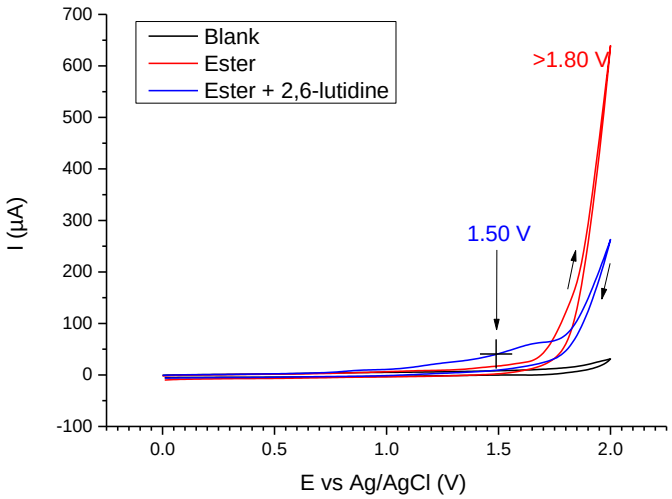


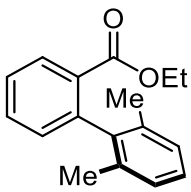
1r





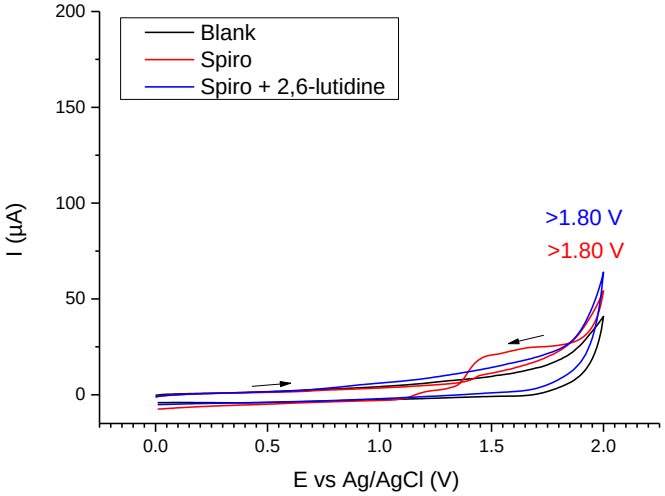
1s

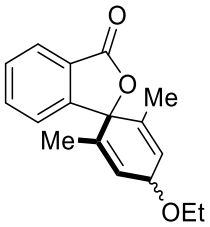




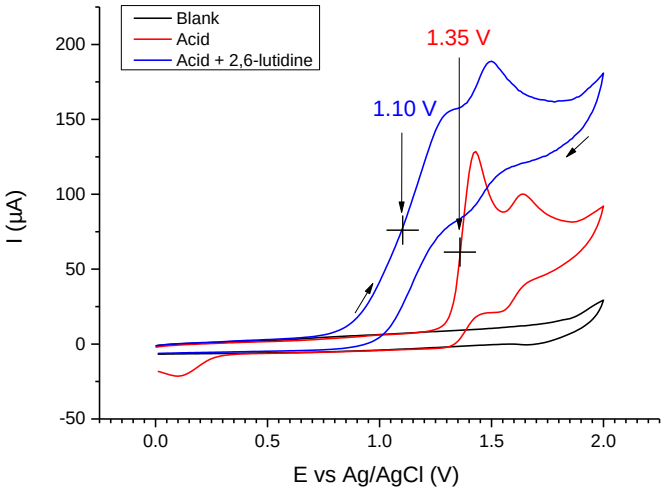
1a-Et ester

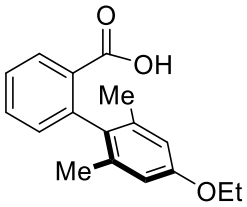
Eventhough a shift in the presence of 2,6-lutidine is observed, the ECDC under the optimized conditions gave no product and only partial decomposition of the ester. The formation of a charge transfer complex might promote the observed shift.



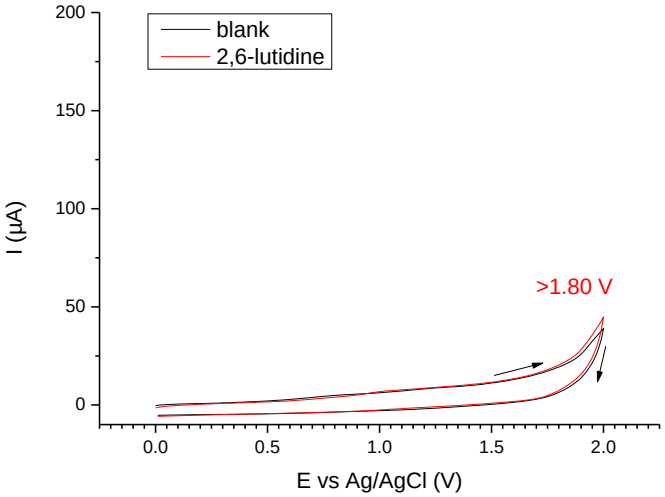


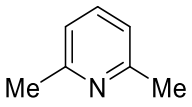
2ab



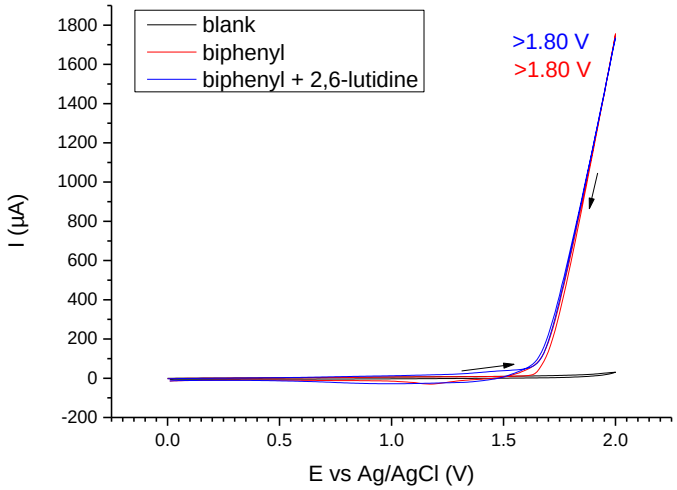


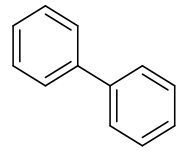
3ab



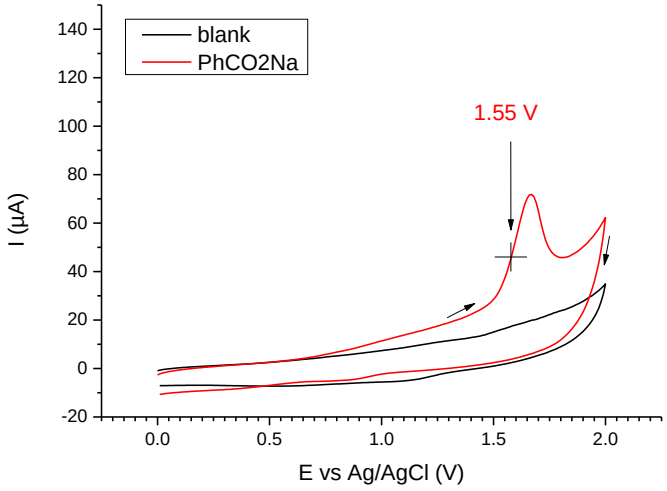


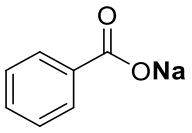
2,6-lutidine





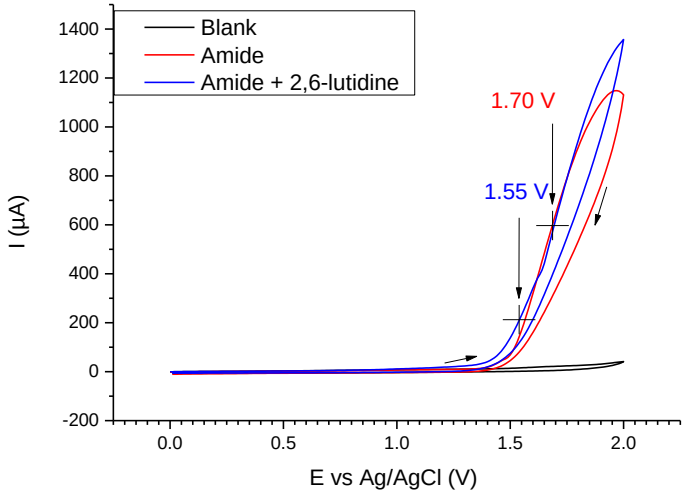
biphenyl

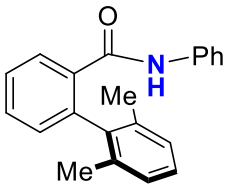




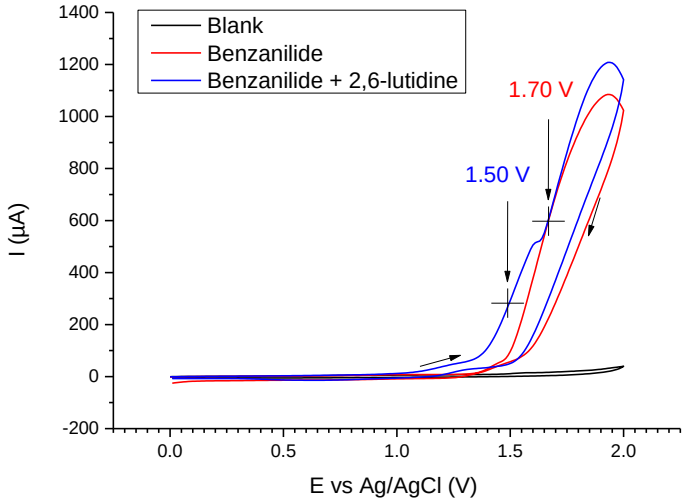
Sodium benzoate

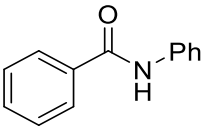
(50 µL of water were added to facilitate the solubility of the salt)



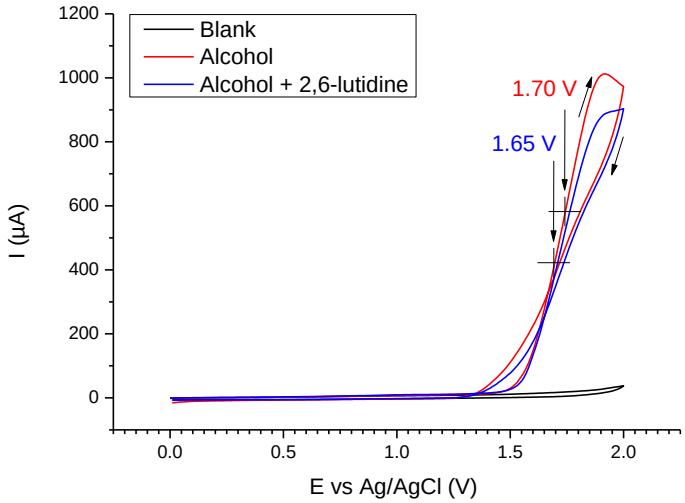


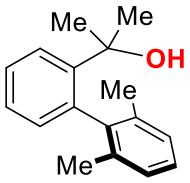
4





Benzanilide





6

Cyclic voltammogram (CV) of ferrocene (reference).

Measurements were performed using EmStatblue+ potentiostat at a scan rate of 100 mV/s. A glassy carbon electrode of 3 mm diameter was used as a working electrode, a platinum wire as a counter electrode and a Ag/AgCl (aq., 0.01 M) as a reference electrode. Measurements were performed in 3 mL of blank solution (0.1 M Bu_4NPF_6 in MeCN, black line) with ferrocene (orange line, Figure S3).

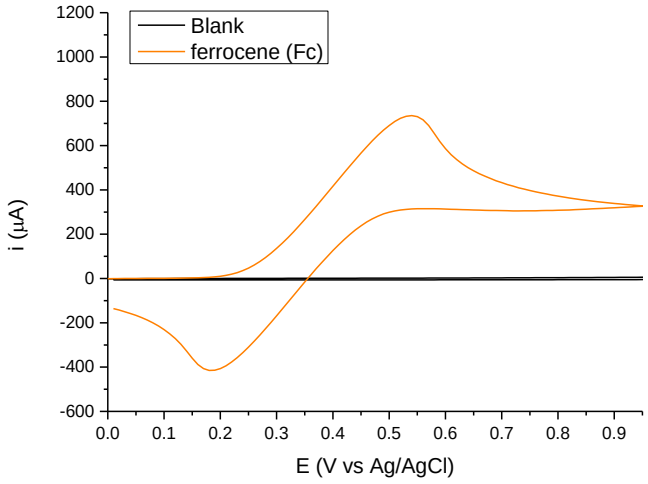


Figure S3

Working electrode characterization using cyclic voltammogram (CV):

Typical profile of a **Pt-poly electrode** (Figure S4). This electrode was used in the electrochemical experiments. The measurement was performed under strict N_2 atmosphere in an aqueous 0.1 M solution of $HClO_4$, using a Pt wire as counter electrode and a RHE as reference electrode. The electrode was cleaned using a torch until incandescence observed and cooled down under H_2 atmosphere prior to the measurement.

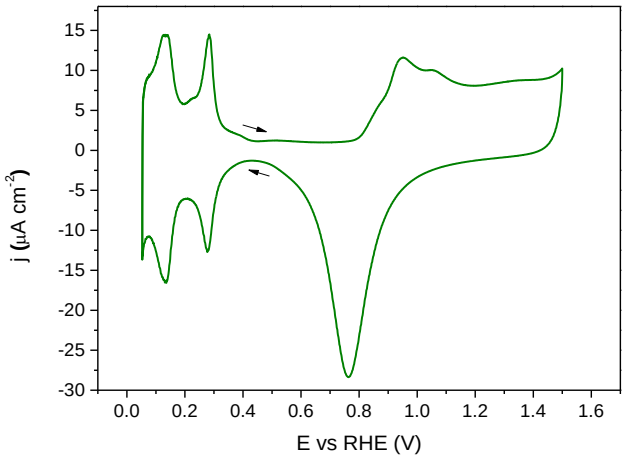


Figure S4

DFT calculations

The geometry optimizations were performed by DFT calculations with the program package Gaussian 16, revision C.01,[9] using the B3LYP functional[10] with D3 dispersion correction[11] and the 6-311G(d,p) basis set.[12] The effect of the bulk solvent acetonitrile (ε = 37.5) was estimated by using the Solvation Model based on Density (SMD).[13] Vibrational frequency calculations were carried out at the same level of theory and they confirmed that the optimized structures were either minima (no imaginary frequencies) or transition states (only one imaginary frequency) on the potential energy surfaces (PES). For each transition state structure, the intrinsic reaction coordinate (IRC) routes towards the corresponding minima were calculated and, if the IRC calculations failed to reach the energy minima, geometry optimizations were performed from the final point of the IRC analysis. Gibbs free energies at 298.15 K were obtained from the vibrational frequency calculations and a correction term of 1.89 kcal/mol was added to them in order to consider the change in the standard state from 1 atm to 1 M.

Study of possible reaction pathways for the cyclization of radical **II** derived from acid **1a**

We studied two reaction pathways for the cyclization of radical **II** and the calculated energy profiles are shown in Figure S5. The formation of cyclohexadienyl radical **III** by spirocyclization of radical **II** via transition state **TS1** is a thermodynamically spontaneous process with a low activation barrier of 2.2 kcal/mol, which suggests that this transformation should be very fast. The alternative intramolecular reaction of radical **II** with the C6' atom (see Figures S6 and S7 for labels) to give a six-membered lactone ring has a higher energy barrier of 8.1 kcal/mol to reach **TS2**. Moreover, radical **V** is thermodynamically less stable than the starting radical **II**, which makes the transformation of **II** to **V** non-spontaneous. According to these observations, formation of **III** should be highly favored and that has been observed experimentally, since spirolactones **2a**-**2g** were the only products detected when acid **1a** was used as starting material.

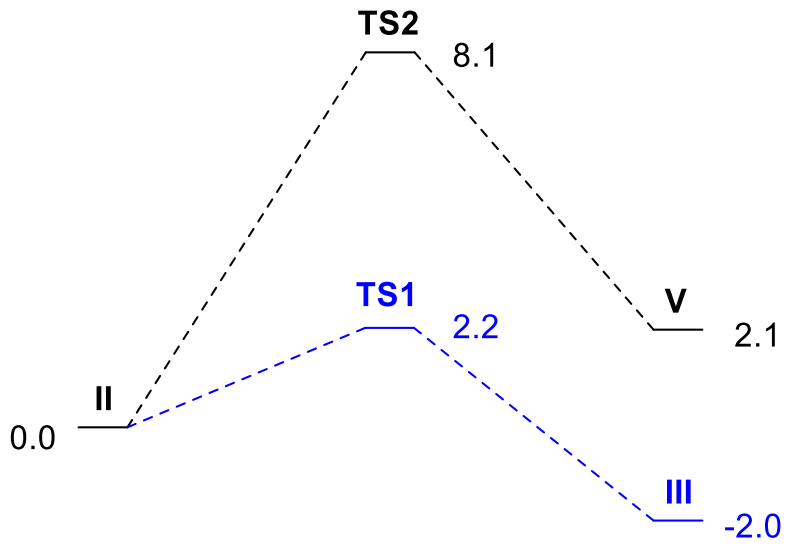
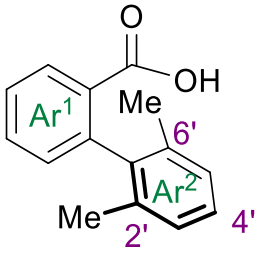


Figure S5: Gibbs free energy profile for two possible reaction pathways for the cyclization of radical **II**, obtained from DFT calculations at the B3LYP-D3/6-311G(d,p) level with acetonitrile as solvent using the SMD model. Energies are given in kcal/mol.

The optimized structures of species **II**, **TS1**, **III**, **TS2** and **V** are shown in Figure S7. Structures **II**, **TS1** and **III** have a plane of symmetry that contains ring Ar^1, the COO group, carbon atoms C1' and C4'and the hydrogen atom bonded to the latter. The two methyl groups are pointing away from that plane and do not cause important steric repulsions. For the other reaction path, in order to create the C6'-O1 bond, ring Ar^2 needs to rotate, the dihedral angle C2'-C1'-C2-C1 being 122.5º for **TS2** and 146.7º for **V**. This twist of the biaryl system approaches the methyl group bonded to C2' to the ring

Ar^1, increasing the steric hindrance. This, together with the change to a less stable conformation of the biaryl system, may account for the differences in energy observed between **TS1** and **TS2** and between **III** and **V**.



1a

Figure S6: definition of Ar^1 and Ar^2 for substrates **1**, showing **1a** as example.

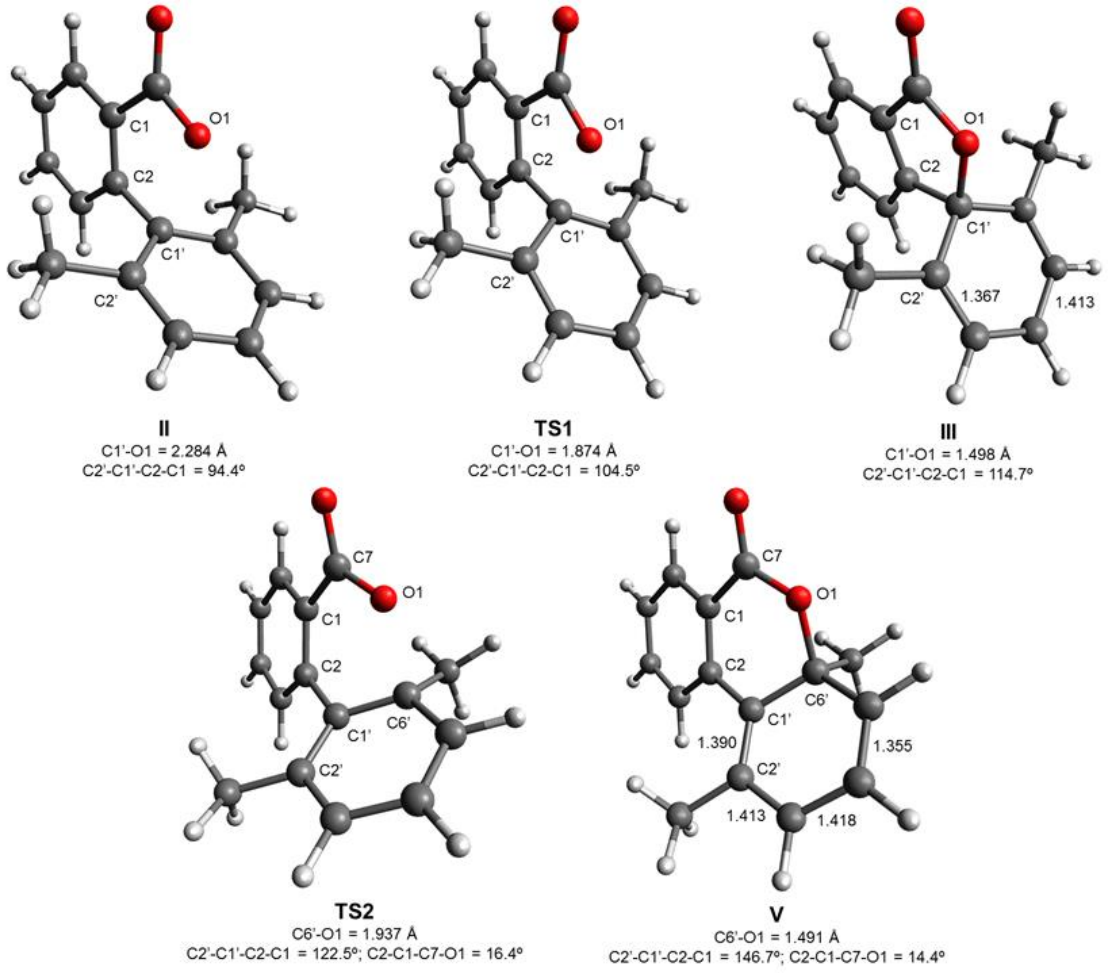
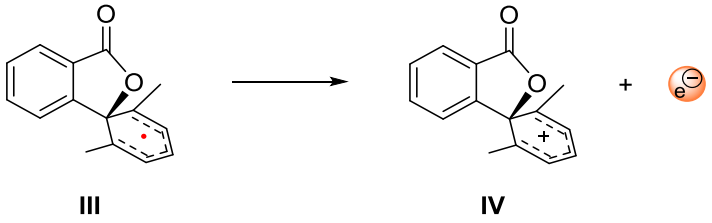


Figure S7: Optimized structures of species **II**, **TS1**, **III**, **TS2** and **V** at the B3LYP-D3/6-311G(d,p) level with acetonitrile as solvent using the SMD model. Bond distances are in Å. (Color of atoms: C, grey; H, white; O, red).

Estimation of the oxidation potential of radical **III** to carbocation **IV**

In our mechanistic proposal, we assume that radical **III** undergoes an electrochemical oxidation at the anode to give carbocation **IV** (Scheme S1). In order to study the feasibility of this oxidation step, we estimated its electrochemical potential from the change in the Gibbs free energy between the cation and the radical.[14]



Scheme S1: Electrochemical oxidation of radical **III** to carbocation **IV**.

The Gibbs free energy values obtained from our DFT calculations are:

$$G\ (\boldsymbol{IV}) = -729.7085352\ a.u.$$

$$G\ (\boldsymbol{III}) = -729.8799172\ a.u.$$

$$\Delta G = G\ (\boldsymbol{III}) - G\ (\boldsymbol{IV}) = -0.171382\ a.u. = -107.5\ kcal/mol\ = -450264.1618\ J/mol$$

$$E_{abs}\ (\boldsymbol{IV} \rightarrow \boldsymbol{III}) = -\frac{\Delta G}{nF} = 4.67\ V$$

where *F* is the Faraday constant (23.06 kcal/mol·V) and *n* equals 1. Is it possible to correlate the redox potential with the Gibbs free energy change obtained from the DFT calculations :

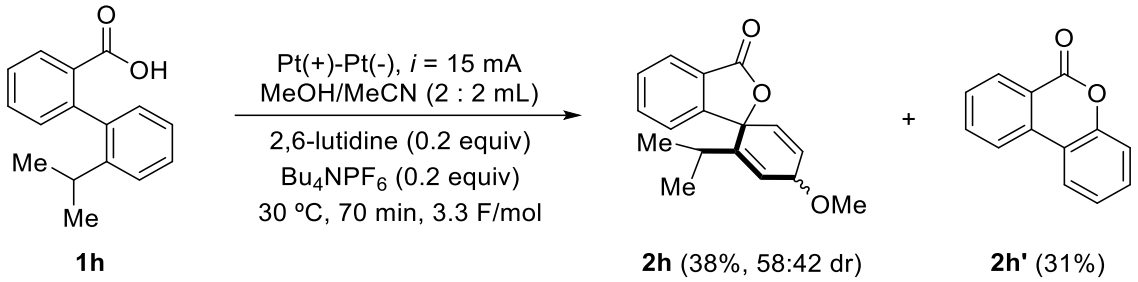
$$E^o(vs\ SHE) = -\frac{\Delta G^o}{nF} - E_{abs}(SHE)$$

where $E_{abs}(SHE) = E^0(H^+ / H_2) = 4.43\ V$.[15] Thus,

$$\boldsymbol{E^o(IV \rightarrow III)} = -\frac{(-107.5)}{23.06} - 4.43\ \text{V} = 0.23\ V\ vs\ SHE = \boldsymbol{-0.06\ V\ vs\ Ag/AgCl}$$

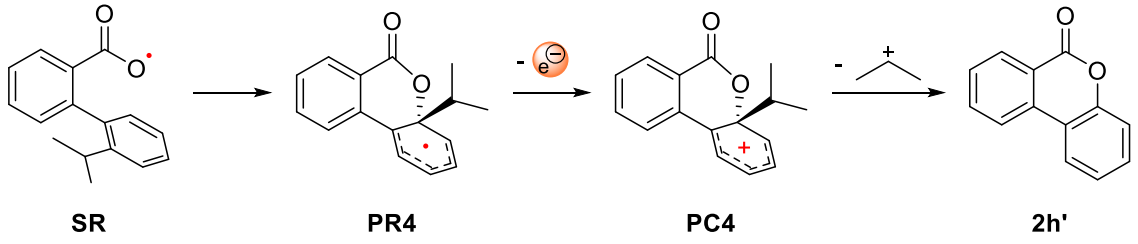
Study of possible reaction pathways for the cyclization of radical **SR** derived from acid **1h**

When acid **1h**, having an isopropyl group at the C2' atom, was used as starting material, a mixture of spirolactones **2h** and benzo-3,4-coumarin **2h'** was obtained (Scheme S2).



Scheme S2: Products obtained for the reaction with substrate **1h**.

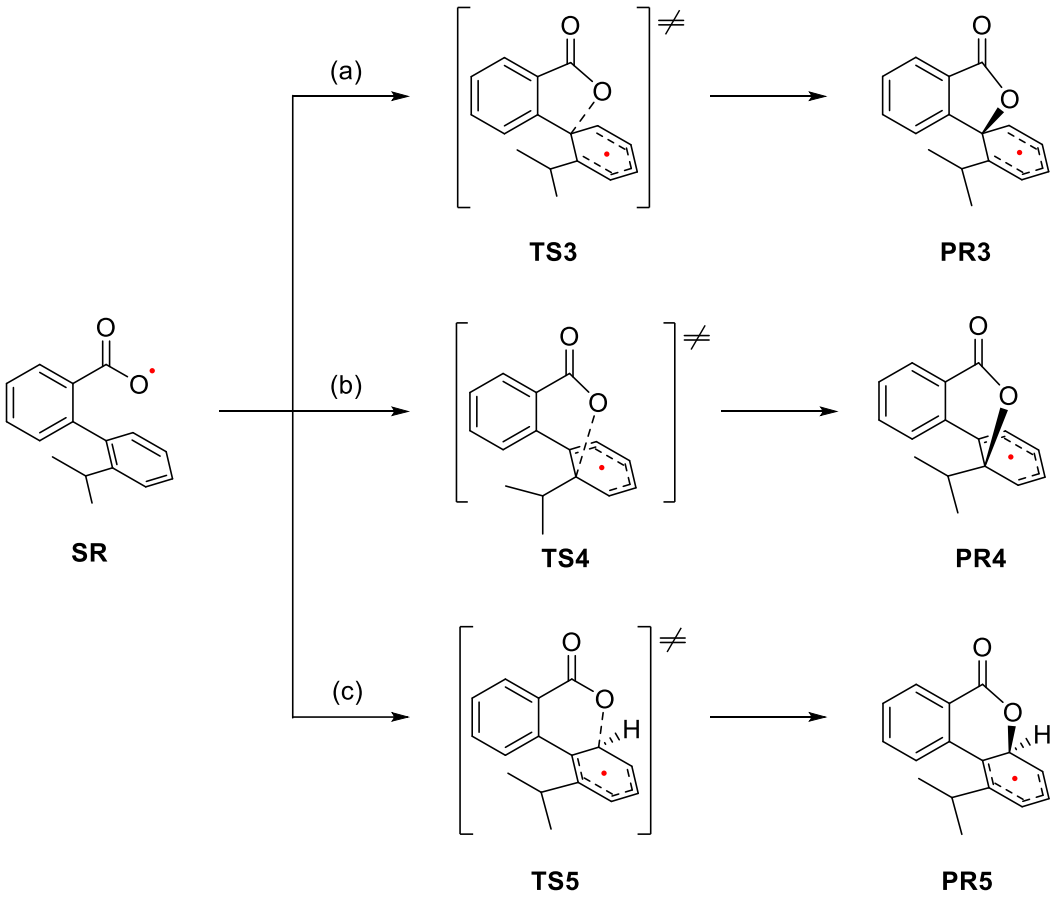
We supposed that product **2h'** resulted from the cyclization of the generated oxygen radical **SR** (Scheme S3) at the C2' atom of the Ar^2 ring. This reaction would give the cyclohexadienyl radical **PR4**, which could be electrochemically oxidized to **PC4**. Loss of the isopropyl cation would rearomatize Ar^2, giving the obtained coumarin **2h'**. The isopropyl cation could be trapped by a molecule of methanol, giving, after deprotonation, isopropyl methyl ether. Another possibility would be the deprotonation of the isopropyl cation by 2,6-lutidine to give propene. Both isopropyl methyl ether and propene are volatile compounds and would not be detected after the reaction work-up. Another possible reaction pathway for **PC4** could be the deprotonation of a methyl group by 2,6-luditine leading to elimination of product **2h'** through an E2 process.



Scheme S3: Reaction of radical **SR** at the C2' atom of the Ar^2 ring.

After seeing the products that were obtained from acid **1h**, it was apparent that the cyclization processes to give either a five-membered ring or a six-membered ring lactone were taking place in this case. Thus, we decided to study the possible reaction pathways for the cyclization of radical **SR** by DFT calculations, looking for an explanation for its different behavior in comparison with radical **II**,

which yielded only the spirocyclization product. The three reaction pathways that we have envisioned are shown in Scheme S4. Route (a) corresponds to the spirocyclization process, which would give radical **PR3** via transition state **TS3**. The other two paths represent the reactions of the oxygen radical with carbon atoms C2' (route (b), giving radical **PR4** via transition state **TS4**) and C6' (route (c), affording radical **PR5** via transition state **TS5**), that would result in the formation of six-membered ring lactones.



Scheme S4: Possible reaction pathways for the cyclization of radical **SR**.

The calculated Gibbs free energy profiles for the three routes are presented in Figure S8. As it was the case for the cyclization of radical **II**, the spirocyclization path is the most favored kinetically, its activation barrier being only 1.7 kcal/mol. The difference between the barriers to reach **TS4** and **TS3** is 3.8 kcal/mol, which is lower than the difference observed between the two reaction pathways studied above for the cyclization of radical **II** (5.9 kcal/mol). Moreover, radical **PR4** is thermodynamically more stable than radical **PR3** (difference of 1.7 kcal/mol between them). The transformation **SR**$^{\cdot}$**→PR3** could also be partially reversible, since the energy barrier from **PR3** to **TS3** is 2.8 kcal/mol. These observations led us to consider that, for the cyclization of radical **SR**, the system could evolve towards

a compromise between the radical that forms faster (**PR3**) and the one that is more stable (**PR4**), being routes (a) and (b) feasible in this case. This is in agreement with the experimental results, since products **2h** and **2h'** were both isolated in the reaction with acid **1h**. Concerning route (c), which involves the generation of an O-C6' bond, its activation barrier is 7.0 kcal/mol and, therefore, it is kinetically less favored than the other two routes. Moreover, formation of radical **PR5** is thermodynamically non spontaneous. According to these observations, we consider that route (c) can initially be discarded. In fact, when acid **1h** was used as starting material, no products that could arise from route (c) were detected.

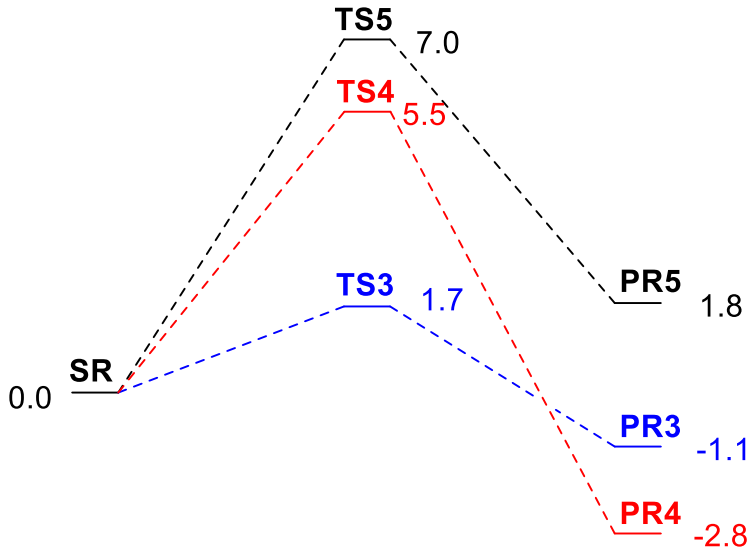


Figure S8: Gibbs free energy profile for three possible reaction pathways for the cyclization of radical **SR**, obtained from DFT calculations at the B3LYP-D3/6-311G(d,p) level with acetonitrile as solvent using the SMD model. Energies are given in kcal/mol.

The optimized structures of radicals **PR3**, **PR4** and **PR5** are shown in Figure S9. Some relevant interatomic distances are collected in Table S2. The dihedral angle between the Ar^1 ring and the cyclohexadienyl ring in **PR5** is quite small (32.3º) and the isopropyl group is, therefore, quite close to the Ar^1 ring, causing important repulsive interactions with it (distance H25-H8 2.152 Å; distance H31-H8 2.347 Å). There is also a short distance between H28 of the isopropyl group and H22 of the cyclohexadienyl ring (2.223 Å). The three-ring system of **PR4** is quite close to planarity (the dihedral angle between the Ar^1 ring and the cyclohexadienyl ring is 24.6º) and this places the isopropyl group pointing away from that ring system, not having important steric hindrance between them (the hydrogen atoms that are closest in space are H28 and H22, the distance being 2.388 Å). As it can be seen in Figure S8, **PR4** is the most stable radical. On the other hand, the benzolactone skeleton and

the cyclohexadienyl ring of **PR3** are in perpendicular planes. Because of that, the isopropyl group is not causing a relevant steric congestion with the benzolactone substructure, but there are some repulsive interactions between the isopropyl group and H22 of the cyclohexadienyl ring (distance H22-H32 2.378 Å; distance H28-H22 2.505 Å). All the observations commented above could help to understand the differences in stability between radicals **PR3**, **PR4** and **PR5**.

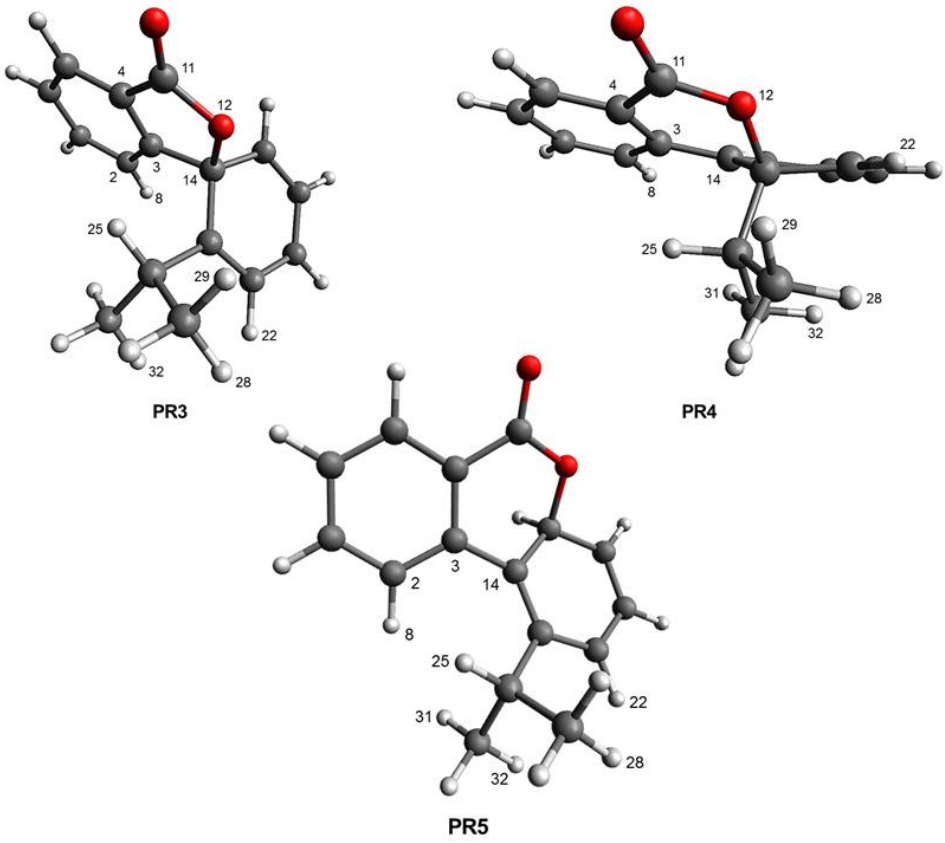


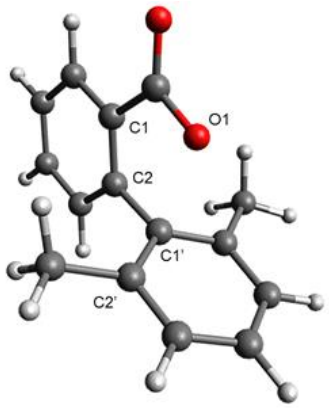
Figure S9: Optimized structures of species **PR3**, **PR4** and **PR5** at the B3LYP-D3/6-311G(d,p) level with acetonitrile as solvent using the SMD model. (Color of atoms: C, grey; H, white; O, red).

Table S2: Selected interatomic distances (Å) in optimized structures **PR3**, **PR4** and **PR5**

Pair of atoms	**PR3**	**PR4**	**PR5**
H25-C3	2.679	2.751	2.664
H25-C4	2.840	2.728	>3
H28-H22	2.505	2.388	2.223
H25-C14	2.575	2.701	2.641
H25-H8	>3	>3	2.152
H25-C2	>3	>3	2.486
H31-H8	>3	>3	2.347
H25-O12	2.635	2.625	>3
H22-H32	2.378	>3	2.500
H22-H29	>3	2.893	>3
H31-C14	>3	2.696	>3
H29-O12	>3	2.496	>3
H25-C11	2.818	2.779	>3

Cartesian coordinates and energies of the optimized geometries

Gibbs free energies at 298.15 K were obtained from the vibrational frequency calculations (Sum of electronic and thermal Free Energies) and a correction term of 0.003019831 a.u. (corresponding to 1.89 kcal/mol) was added to them in order to consider the change in the standard state from 1 atm to 1 M. All Gibbs free energy values are given in a.u.



II

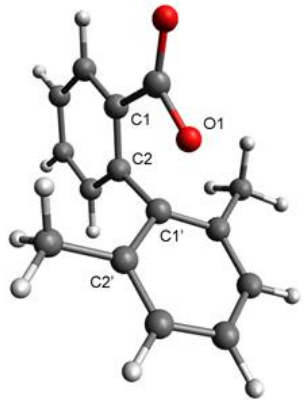
II

Gibbs free energy = -729,8766832

Cartesian coordinates:

C	-2.87487	-0.23125	1.21556
C	-1.49092	-0.32158	1.24287
C	-0.78144	-0.34058	0.00001
C	-1.49092	-0.32163	-1.24286
C	-2.87487	-0.23129	-1.21555
C	-3.56263	-0.18515	0.00000
H	-3.42621	-0.20013	2.14849
H	-3.42621	-0.20021	-2.14848
H	-4.64488	-0.11586	0.00000
C	0.69189	-0.57900	0.00001
C	1.55144	0.52294	-0.00001
C	1.22957	-1.86747	0.00003
C	2.93489	0.35115	-0.00001
C	2.61347	-2.04012	0.00003
H	0.57000	-2.72773	0.00005
C	3.46733	-0.93428	0.00002
H	3.57327	1.22726	-0.00002
H	3.02718	-3.04235	0.00005
H	4.54164	-1.07832	0.00002
C	-0.73800	-0.37035	-2.54034
H	-0.03410	0.46495	-2.60860
H	-0.14798	-1.28846	-2.61986

H	-1.41955	-0.31986	-3.39035
C	-0.73800	-0.37026	2.54035
H	-0.14798	-1.28836	2.61990
H	-0.03411	0.46505	2.60858
H	-1.41955	-0.31974	3.39036
C	0.93362	1.88261	-0.00003
O	1.58681	2.92523	-0.00005
O	-0.36617	1.90493	-0.00003



TS1

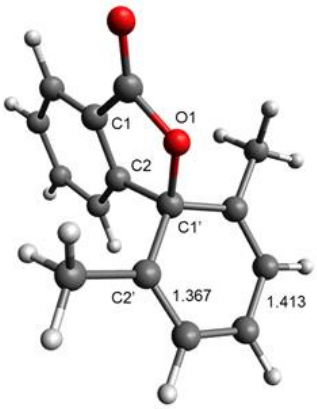
TS1

Gibbs free energy = -729,8732382

Cartesian coordinates:

C	-2.85389	-0.30741	1.22037
C	-1.47944	-0.22471	1.25795
C	-0.74225	-0.10489	-0.00000
C	-1.47943	-0.22455	-1.25798
C	-2.85387	-0.30726	-1.22043
C	-3.54773	-0.34134	-0.00003
H	-3.40795	-0.35963	2.15123
H	-3.40792	-0.35936	-2.15130
H	-4.62965	-0.40743	-0.00005
C	0.69751	-0.53378	-0.00002
C	1.61707	0.50792	0.00003
C	1.13432	-1.85607	-0.00010
C	2.98765	0.26606	0.00002
C	2.50735	-2.10632	-0.00011
H	0.42206	-2.67318	-0.00014
C	3.43051	-1.05415	-0.00006
H	3.68247	1.09821	0.00006
H	2.86275	-3.13062	-0.00017
H	4.49262	-1.27077	-0.00007
C	-0.72010	-0.19189	-2.54947
H	-0.08690	0.69965	-2.60143
H	-0.05559	-1.05719	-2.64068

H	-1.39987	-0.18636	-3.40259
C	-0.72014	-0.19221	2.54945
H	-0.05564	-1.05753	2.64057
H	-0.08693	0.69932	2.60153
H	-1.39991	-0.18678	3.40257
C	0.95828	1.84149	0.00011
O	1.53769	2.91683	0.00016
O	-0.35575	1.72897	0.00011



III

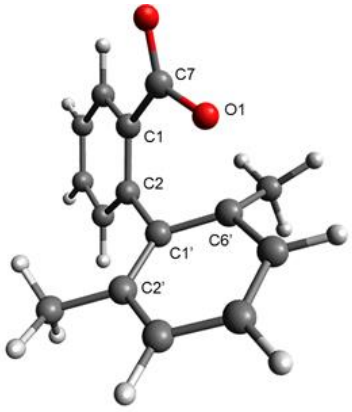
III

Gibbs free energy = -729,8799172

Cartesian coordinates:

C	2.74309	-0.46603	-1.22405
C	1.47089	0.03137	-1.27844
C	0.68985	0.25134	0.00002
C	1.47090	0.03106	1.27843
C	2.74309	-0.46633	1.22391
C	3.39254	-0.74241	-0.00011
H	3.27437	-0.64244	-2.15431
H	3.27438	-0.64296	2.15412
H	4.40160	-1.13628	-0.00016
C	-0.62346	-0.52421	-0.00006
C	-1.68726	0.36381	0.00005
C	-0.83723	-1.89572	-0.00022
C	-3.00988	-0.07185	0.00001
C	-2.15896	-2.34530	-0.00027
H	-0.00777	-2.59321	-0.00031
C	-3.23532	-1.44567	-0.00015
H	-3.82872	0.63832	0.00010
H	-2.35909	-3.41094	-0.00039
H	-4.24973	-1.82711	-0.00019
C	0.78286	0.36696	2.56681
H	0.49978	1.42457	2.59471
H	-0.14074	-0.20929	2.69157

H	1.43206	0.16276	3.41983
C	0.78285	0.36758	-2.56674
H	-0.14077	-0.20862	-2.69163
H	0.49979	1.42521	-2.59438
H	1.43204	0.16359	-3.41981
C	-1.15566	1.73923	0.00022
O	-1.74250	2.79310	0.00035
O	0.20537	1.66856	0.00019



TS2

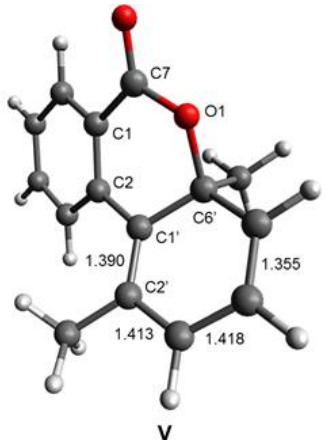
TS2

Gibbs free energy = -729,8637302

Cartesian coordinates:

C	2.69920	-0.97429	0.56936
C	1.29049	-0.73717	0.76216
C	0.73073	0.49391	0.22069
C	1.54273	1.41830	-0.44107
C	2.91219	1.13418	-0.57588
C	3.47806	-0.05878	-0.08406
H	3.12481	-1.88223	0.97988
H	3.54310	1.83973	-1.10485
H	4.53914	-0.23852	-0.21566
C	-0.74279	0.58391	0.23693
C	-1.47142	-0.51780	-0.25540
C	-1.43537	1.70514	0.70805
C	-2.86685	-0.47504	-0.27378
C	-2.82727	1.72803	0.70378
H	-0.88106	2.55051	1.09607
C	-3.54639	0.63813	0.21073
H	-3.40594	-1.32424	-0.67564
H	-3.35076	2.59708	1.08632
H	-4.63018	0.65892	0.20161
C	0.99803	2.68326	-1.06106
H	0.03956	2.51067	-1.55506
H	0.83934	3.45824	-0.30556

H	1.69976	3.07817	-1.79772
C	0.69913	-1.36193	2.00538
H	-0.38813	-1.31730	2.02709
H	1.01790	-2.40196	2.08756
H	1.07762	-0.81822	2.87779
C	-0.78197	-1.74039	-0.80535
O	-1.39770	-2.55100	-1.49125
O	0.48568	-1.92746	-0.53686



V

V

Gibbs free energy = -729,8732962

Cartesian coordinates:

C	2.59576	-1.20904	0.17412
C	1.15392	-0.92384	0.44643
C	0.70062	0.47120	0.05664
C	1.62437	1.44023	-0.31778
C	2.99397	1.10090	-0.39008
C	3.45724	-0.22144	-0.17003
H	2.91571	-2.23467	0.31709
H	3.70251	1.86326	-0.69226
H	4.51034	-0.44129	-0.30966
C	-0.75235	0.62536	0.09346
C	-1.53919	-0.51188	-0.21199
C	-1.42557	1.80987	0.44615
C	-2.93409	-0.44442	-0.20022
C	-2.81418	1.86154	0.47199
H	-0.86236	2.68318	0.74025
C	-3.57701	0.73862	0.14094
H	-3.49958	-1.33099	-0.45950
H	-3.30629	2.78331	0.76193
H	-4.65947	0.78670	0.15794
C	1.24282	2.84558	-0.72727
H	0.31439	2.86668	-1.30124
H	1.10729	3.49481	0.14312
H	2.03167	3.28387	-1.34146

C	0.85522	-1.22123	1.93028
H	-0.20730	-1.09858	2.14965
H	1.15030	-2.24692	2.16309
H	1.42380	-0.53607	2.56286
C	-0.90339	-1.79921	-0.59342
O	-1.50119	-2.71522	-1.11802
O	0.41495	-1.94062	-0.35536

Cation IV

Gibbs free energy = -729,7085352

Cartesian coordinates:

C	-2.54651	0.58591	-1.23876
C	-1.43022	-0.20650	-1.28600
C	-0.69254	-0.46280	0.00004
C	-1.43023	-0.20620	1.28601
C	-2.54651	0.58620	1.23858
C	-3.07606	0.98676	-0.00014
H	-3.05425	0.86354	-2.15360
H	-3.05427	0.86405	2.15335
H	-3.97211	1.59848	-0.00022
C	0.51212	0.53073	-0.00007
C	1.66502	-0.23789	0.00006
C	0.55035	1.91351	-0.00026
C	2.92518	0.35544	0.00001
C	1.81130	2.51284	-0.00030
H	-0.35883	2.50258	-0.00036
C	2.98445	1.74554	-0.00017
H	3.82075	-0.25419	0.00011
H	1.88212	3.59413	-0.00044
H	3.94640	2.24363	-0.00020
C	-0.87441	-0.76929	2.53650
H	-0.93741	-1.86309	2.49478
H	0.18908	-0.52787	2.63896
H	-1.41637	-0.40589	3.40801
C	-0.87440	-0.76989	-2.53635
H	0.18909	-0.52848	-2.63888
H	-0.93738	-1.86368	-2.49436
H	-1.41636	-0.40671	-3.40794
C	1.31406	-1.66494	0.00022
O	1.99457	-2.64881	0.00037
O	-0.07333	-1.75282	0.00019

SR

Gibbs free energy = -769,1720132

Cartesian coordinates:

C	2.80574	0.20254	-2.05882
C	1.45707	-0.12581	-1.92136
C	0.91851	-0.34280	-0.65165
C	1.74964	-0.23862	0.47017
C	3.09820	0.08885	0.33190
C	3.62751	0.31219	-0.93520
H	3.21610	0.37367	-3.04772
H	0.82140	-0.20647	-2.79556
H	3.71491	0.16024	1.22046
H	4.67474	0.56684	-1.04999
C	1.16316	-0.48746	1.81805
O	-0.10656	-0.76040	1.85851
O	1.81105	-0.44869	2.86445
C	-0.51943	-0.69546	-0.46914
C	-0.91762	-2.03278	-0.70413
C	-1.50424	0.30213	-0.19422
C	-2.24661	-2.39432	-0.63450
H	-0.15550	-2.76976	-0.92776
C	-2.84314	-0.09564	-0.13670
C	-3.21513	-1.41722	-0.34913
H	-2.54394	-3.42265	-0.80338
H	-3.60783	0.64340	0.07094
H	-4.26185	-1.69580	-0.29925
C	-1.12549	1.75420	0.02151
H	-0.03630	1.82295	0.02352
C	-1.62532	2.27845	1.37828
H	-1.25714	3.29544	1.54187
H	-2.71783	2.30805	1.41914
H	-1.26745	1.64482	2.19287
C	-1.64077	2.62572	-1.13907
H	-1.25264	2.27572	-2.09969
H	-2.73360	2.60967	-1.18636
H	-1.32164	3.66267	-0.99880

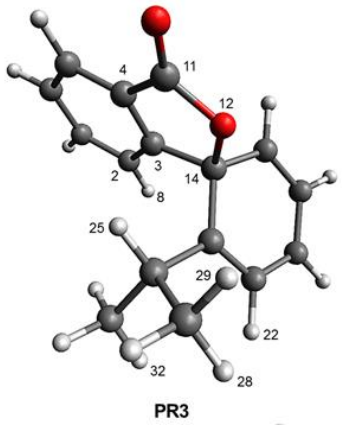
TS3

Gibbs free energy = -769,1693042

Cartesian coordinates:

C	2.66601	0.66763	-2.01665
C	1.33370	0.28194	-1.85688
C	0.92746	-0.21113	-0.61975
C	1.83612	-0.31533	0.42713
C	3.16554	0.06607	0.27447
C	3.57789	0.56103	-0.96056

H	2.99776	1.05503	-2.97341
H	0.62955	0.36572	-2.67641
H	3.85239	-0.02322	1.10844
H	4.60769	0.86623	-1.10654
C	1.20758	-0.84178	1.66736
O	-0.07479	-1.09904	1.48639
O	1.77804	-1.01821	2.73226
C	-0.46466	-0.67310	-0.29513
C	-0.85092	-1.96234	-0.83805
C	-1.51260	0.32588	-0.09317
C	-2.16625	-2.27271	-1.05342
H	-0.06248	-2.67531	-1.04609
C	-2.82580	-0.03556	-0.33136
C	-3.16734	-1.31158	-0.79717
H	-2.44055	-3.24819	-1.43813
H	-3.61354	0.68908	-0.15970
H	-4.20812	-1.55857	-0.97158
C	-1.15458	1.69859	0.43811
H	-0.07449	1.72788	0.59546
C	-1.82590	1.95857	1.79864
H	-1.49014	2.91755	2.20420
H	-2.91490	1.99481	1.70375
H	-1.56882	1.17245	2.51278
C	-1.50608	2.79949	-0.57842
H	-0.99545	2.63469	-1.53117
H	-2.58292	2.82835	-0.76890
H	-1.20303	3.77738	-0.19270



PR3

PR3

Gibbs free energy = -769,1737172

Cartesian coordinates:

C	-2.51052	-1.12483	1.88497
C	-1.20908	-1.23553	1.39206
C	-0.91001	-0.57423	0.20799

C	-1.87329	0.16789	-0.45782
C	-3.17480	0.28499	0.02339
C	-3.48458	-0.37435	1.20982
H	-2.77463	-1.62794	2.80839
H	-0.45803	-1.81458	1.91627
H	-3.91328	0.87217	-0.51007
H	-4.48583	-0.30809	1.61929
C	-1.26413	0.76587	-1.66084
O	0.04251	0.38167	-1.71166
O	-1.75517	1.48109	-2.49891
C	0.40341	-0.51327	-0.56046
C	0.76599	-1.85287	-1.12665
C	1.50721	0.15992	0.22042
C	1.96691	-2.44080	-0.87696
H	0.00602	-2.33387	-1.73159
C	2.69078	-0.49960	0.42963
C	2.94553	-1.78785	-0.08570
H	2.18243	-3.41920	-1.29316
H	3.46917	-0.00660	1.00308
H	3.89778	-2.26787	0.10446
C	1.25460	1.56492	0.73118
H	0.22622	1.83652	0.47793
C	2.17981	2.57940	0.03448
H	1.94662	3.59638	0.36471
H	3.22874	2.37735	0.27087
H	2.05955	2.53454	-1.05107
C	1.38776	1.65132	2.26159
H	0.70822	0.95117	2.75512
H	2.40761	1.42023	2.58231
H	1.14710	2.66192	2.60549

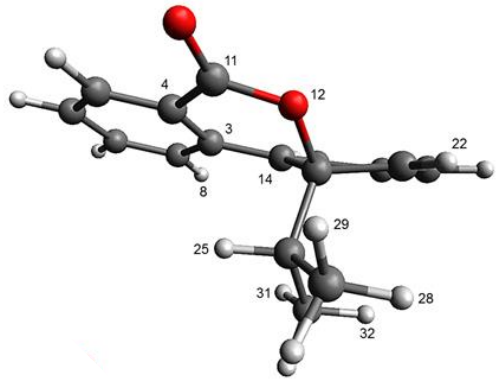
TS4

Gibbs free energy = -769,1631932

Cartesian coordinates:

C	3.15960	1.51162	0.91949
C	1.79918	1.73550	0.72955
C	1.01088	0.78194	0.07428
C	1.61271	-0.39143	-0.42321
C	2.98039	-0.59849	-0.23601
C	3.75172	0.34079	0.44193
H	3.75762	2.24873	1.44349
H	1.33530	2.63933	1.10732
H	3.42866	-1.49732	-0.64128
H	4.81153	0.16727	0.58923
C	0.83134	-1.39980	-1.22739

O	-0.47492	-1.31755	-1.25405
O	1.41038	-2.27655	-1.86206
C	-0.42789	0.98012	-0.15471
C	-0.91373	2.15200	-0.71662
C	-1.31532	-0.14999	0.07756
C	-2.24593	2.25125	-1.12097
H	-0.23223	2.97617	-0.89292
C	-2.66782	-0.01690	-0.40124
C	-3.10975	1.14440	-0.98263
H	-2.60718	3.16691	-1.57375
H	-3.35058	-0.84425	-0.26116
H	-4.13775	1.22324	-1.31775
C	-1.08987	-1.02582	1.31555
H	-0.01720	-1.20497	1.40276
C	-1.79394	-2.38513	1.25527
H	-1.46133	-2.99920	2.09662
H	-2.88004	-2.28635	1.33307
H	-1.55635	-2.91083	0.32935
C	-1.52614	-0.23157	2.56192
H	-0.98096	0.71211	2.64768
H	-2.59641	-0.00725	2.52847
H	-1.32926	-0.82188	3.46116



PR4

PR4

Gibbs free energy = -769,1764532

Cartesian coordinates:

C	-3.28068	-1.60864	0.62458
C	-1.92874	-1.83145	0.40632
C	-1.09502	-0.79127	-0.04768
C	-1.67634	0.47575	-0.28986
C	-3.04068	0.68596	-0.07239
C	-3.84373	-0.34815	0.39036
H	-3.90325	-2.41817	0.98907
H	-1.50678	-2.80699	0.61403

H	-3.45708	1.66399	-0.27975
H	-4.89985	-0.18108	0.56620
C	-0.87003	1.58229	-0.86545
O	0.46650	1.40957	-0.95482
O	-1.35033	2.60802	-1.29863
C	0.32728	-0.94621	-0.28548
C	0.94951	-2.15162	-0.55454
C	1.13986	0.32523	-0.20351
C	2.30018	-2.21443	-0.91248
H	0.36617	-3.06539	-0.54888
C	2.49693	0.19667	-0.82489
C	3.04601	-1.01364	-1.09469
H	2.75702	-3.17183	-1.13128
H	3.04005	1.11704	-0.99797
H	4.05626	-1.07328	-1.48524
C	1.24512	0.82193	1.29214
H	0.20987	0.96531	1.61949
C	1.96989	2.16861	1.40286
H	1.86764	2.55235	2.42174
H	3.03818	2.06660	1.19279
H	1.55287	2.90953	0.71817
C	1.89025	-0.22568	2.20399
H	1.33475	-1.16568	2.20590
H	2.91881	-0.43554	1.89734
H	1.91704	0.15041	3.23028

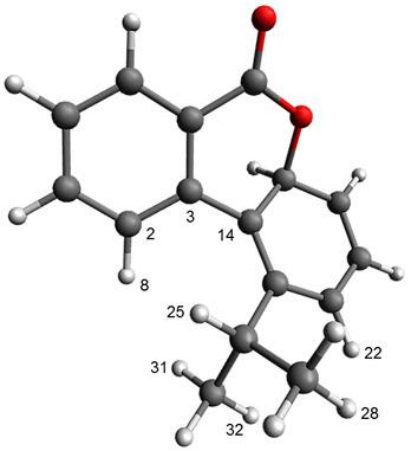
TS5

Gibbs free energy = -769,1609042

Cartesian coordinates:

C	-2.17702	-2.45283	-0.84474
C	-0.94947	-1.80038	-0.90421
C	-0.81839	-0.48805	-0.43127
C	-1.94619	0.16155	0.11234
C	-3.16865	-0.51124	0.18327
C	-3.29000	-1.80959	-0.29969
H	-2.26634	-3.46321	-1.22776
H	-0.09220	-2.29680	-1.34211
H	-4.01536	-0.00329	0.62869
H	-4.24458	-2.32059	-0.24926
C	-1.85870	1.54631	0.69917
O	-0.82432	2.30072	0.40541
O	-2.72757	1.96836	1.45369
C	0.44004	0.27775	-0.51271
C	0.26062	1.62481	-1.00672
C	1.68281	-0.13258	-0.03094
C	1.38375	2.50736	-1.08916
H	-0.53714	1.78246	-1.72378

C	2.75646	0.77701	-0.12179
C	2.60766	2.07669	-0.64244
H	1.24689	3.49599	-1.50939
H	3.73278	0.47343	0.23657
H	3.47319	2.72692	-0.70078
C	1.92265	-1.49131	0.61424
H	0.95646	-1.98043	0.74238
C	2.54248	-1.35608	2.01583
H	2.60955	-2.34065	2.48797
H	3.55242	-0.93840	1.97625
H	1.93236	-0.71279	2.65627
C	2.78639	-2.38537	-0.29079
H	2.32264	-2.52227	-1.27164
H	3.77728	-1.94612	-0.44332
H	2.92054	-3.37108	0.16474



PR5

PR5

Gibbs free energy = -769,1691862

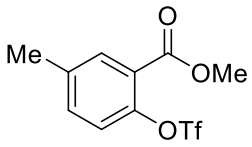
Cartesian coordinates:

C	-2.01094	-2.64318	-0.63199
C	-0.82073	-1.92556	-0.66500
C	-0.78648	-0.57179	-0.28799
C	-2.00245	0.03976	0.10049
C	-3.19013	-0.69510	0.14647
C	-3.19968	-2.03475	-0.21972
H	-2.01427	-3.68230	-0.94166
H	0.07784	-2.40674	-1.02574
H	-4.09689	-0.20021	0.47221
H	-4.12329	-2.60093	-0.19329
C	-2.03389	1.46161	0.54107
O	-0.97265	2.23233	0.22711
O	-2.94246	1.94790	1.17974

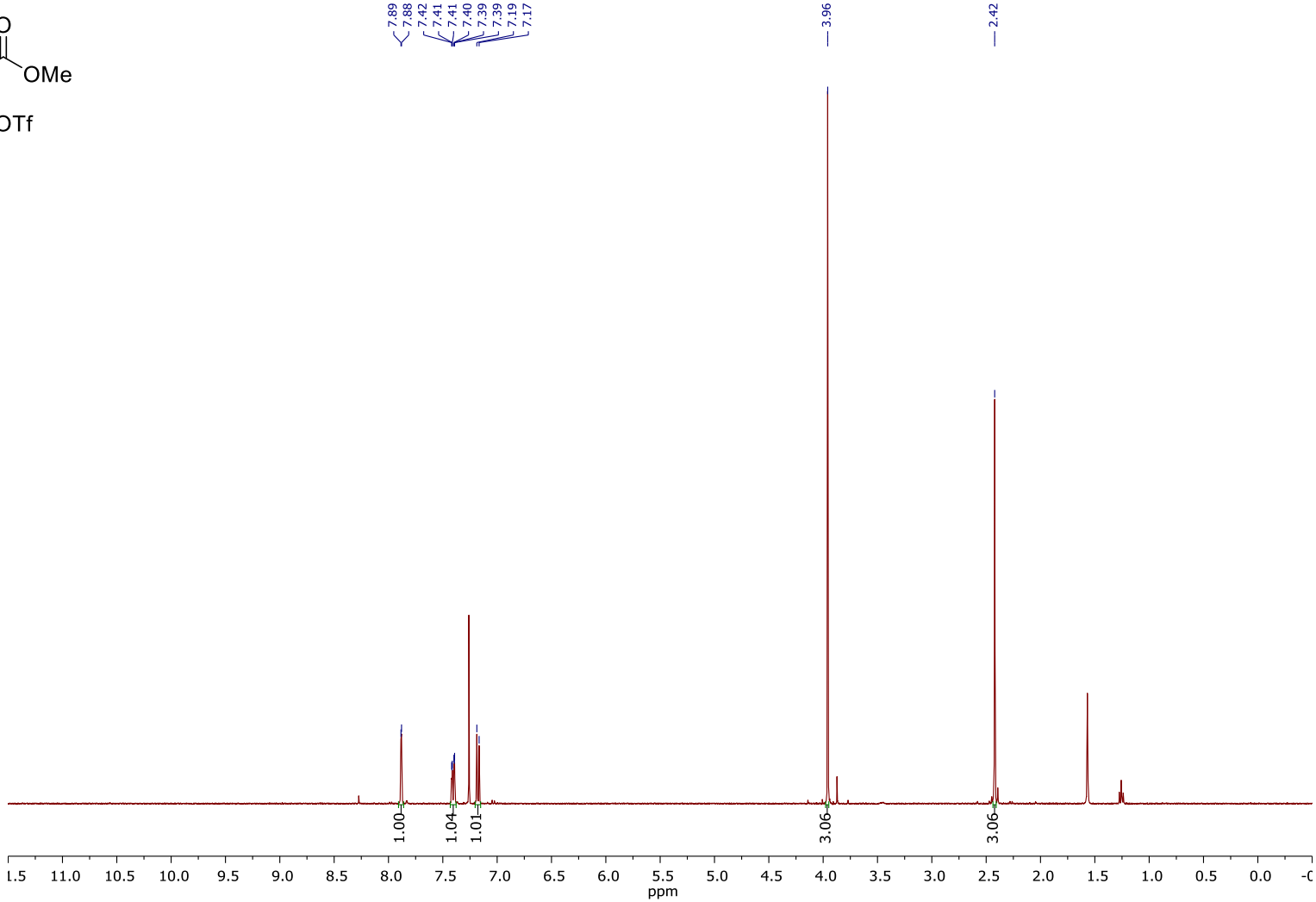
C	0.40108	0.28452	-0.34172
C	0.02816	1.68844	-0.73767
C	1.71011	-0.04584	-0.02998
C	1.14198	2.66769	-0.80291
H	-0.50226	1.66711	-1.70044
C	2.71533	0.94336	-0.17858
C	2.42012	2.27507	-0.56227
H	0.88923	3.68839	-1.06422
H	3.74370	0.68391	0.03819
H	3.23217	2.99005	-0.64218
C	2.12982	-1.40821	0.51330
H	1.22886	-1.97761	0.74150
C	2.90831	-1.27903	1.83493
H	3.09473	-2.27345	2.25156
H	3.87728	-0.79234	1.69479
H	2.34139	-0.70337	2.57221
C	2.94230	-2.19704	-0.52723
H	2.38283	-2.32570	-1.45803
H	3.87654	-1.67933	-0.76582
H	3.19559	-3.18902	-0.14107

^{1}H NMR and ^{13}C NMR spectra of the synthetized compounds

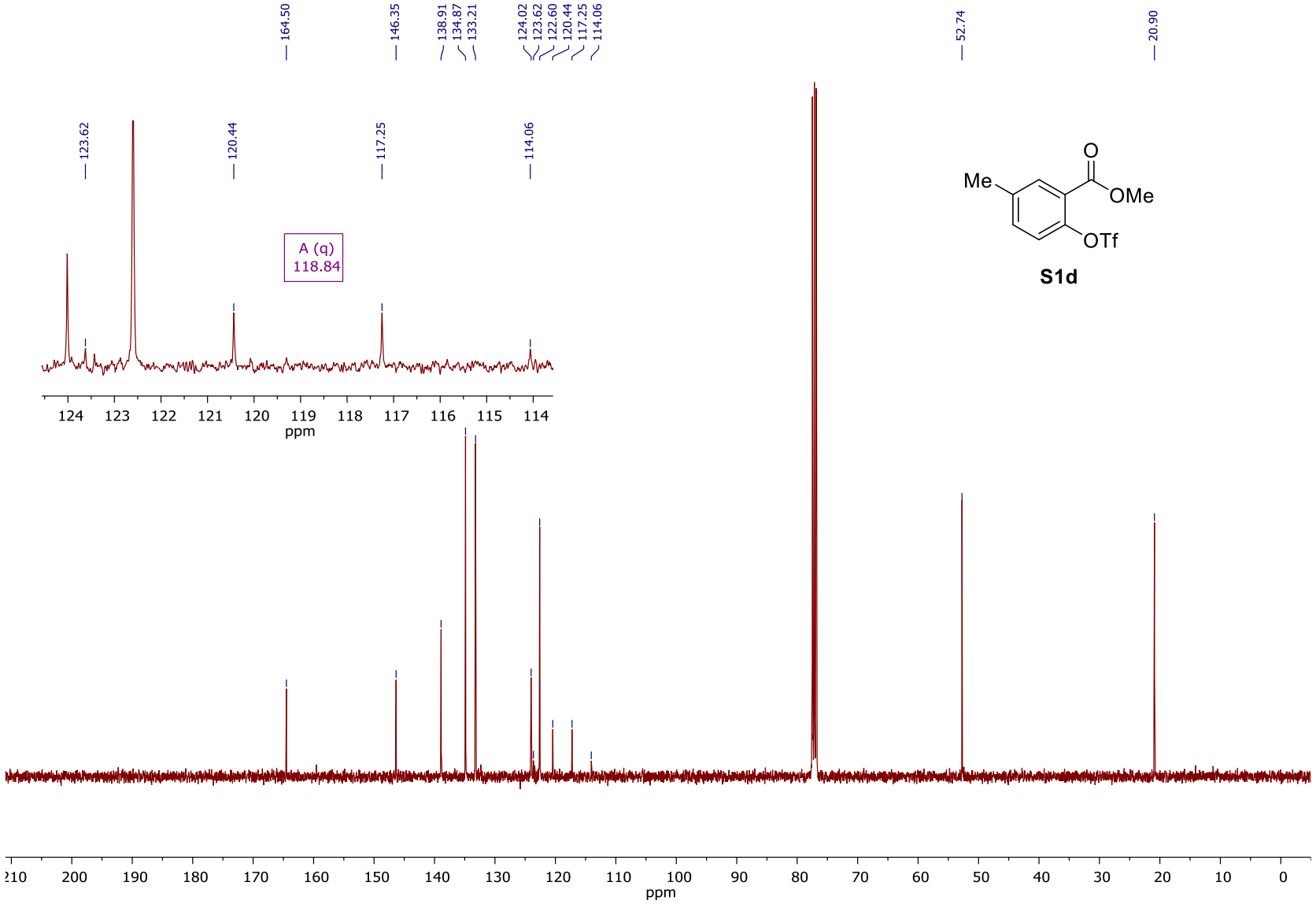
^{1}H-NMR (400 MHz, $CDCl_3$) **S1d**



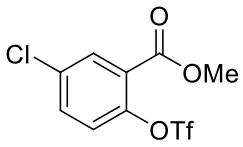
S1d



^{13}C NMR (75 MHz, $CDCl_3$)

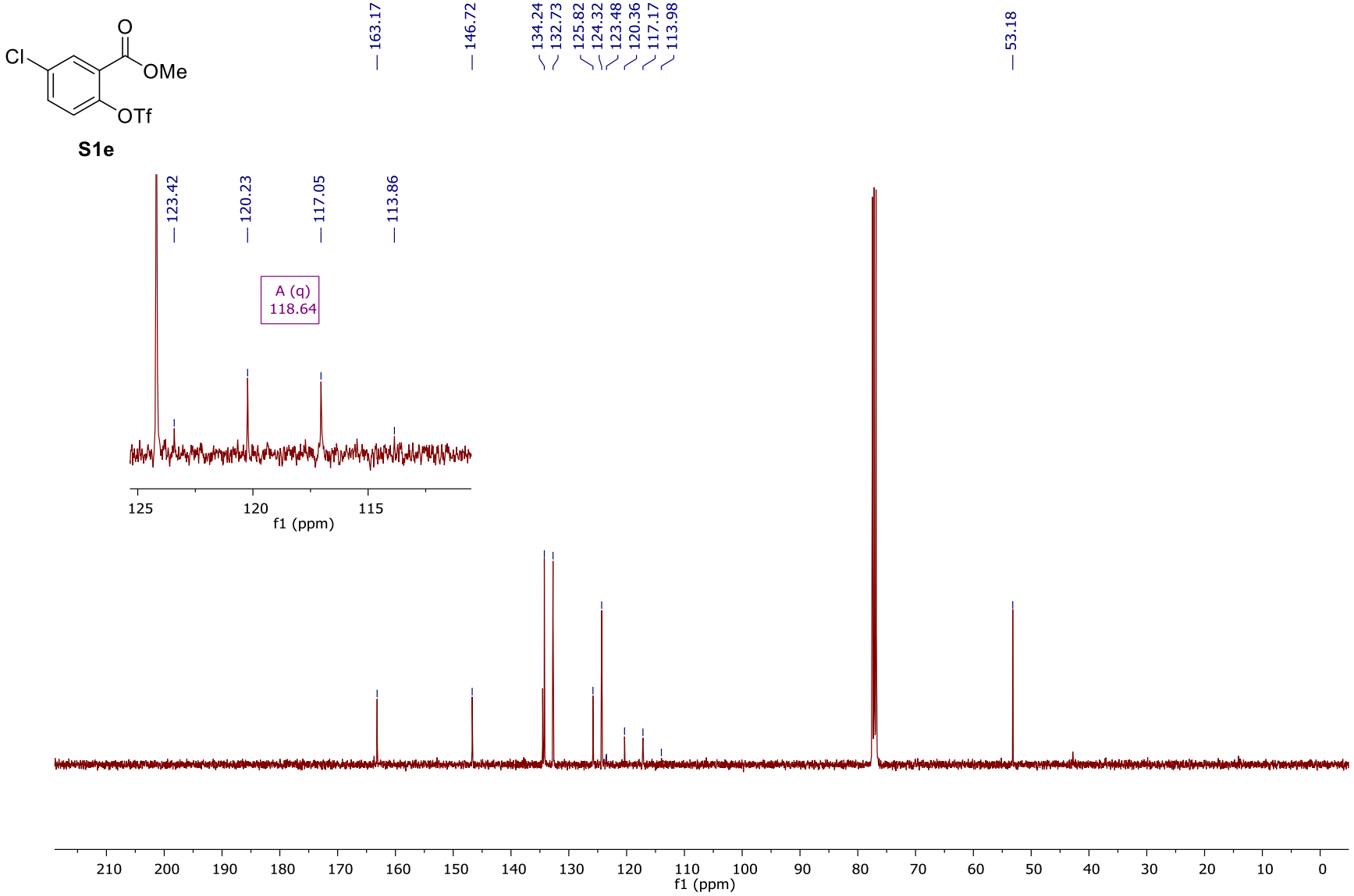


^{1}H NMR (300 MHz, $CDCl_3$) **S1e**

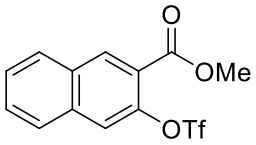


S1e

^{13}C NMR (75 MHz, $CDCl_3$)

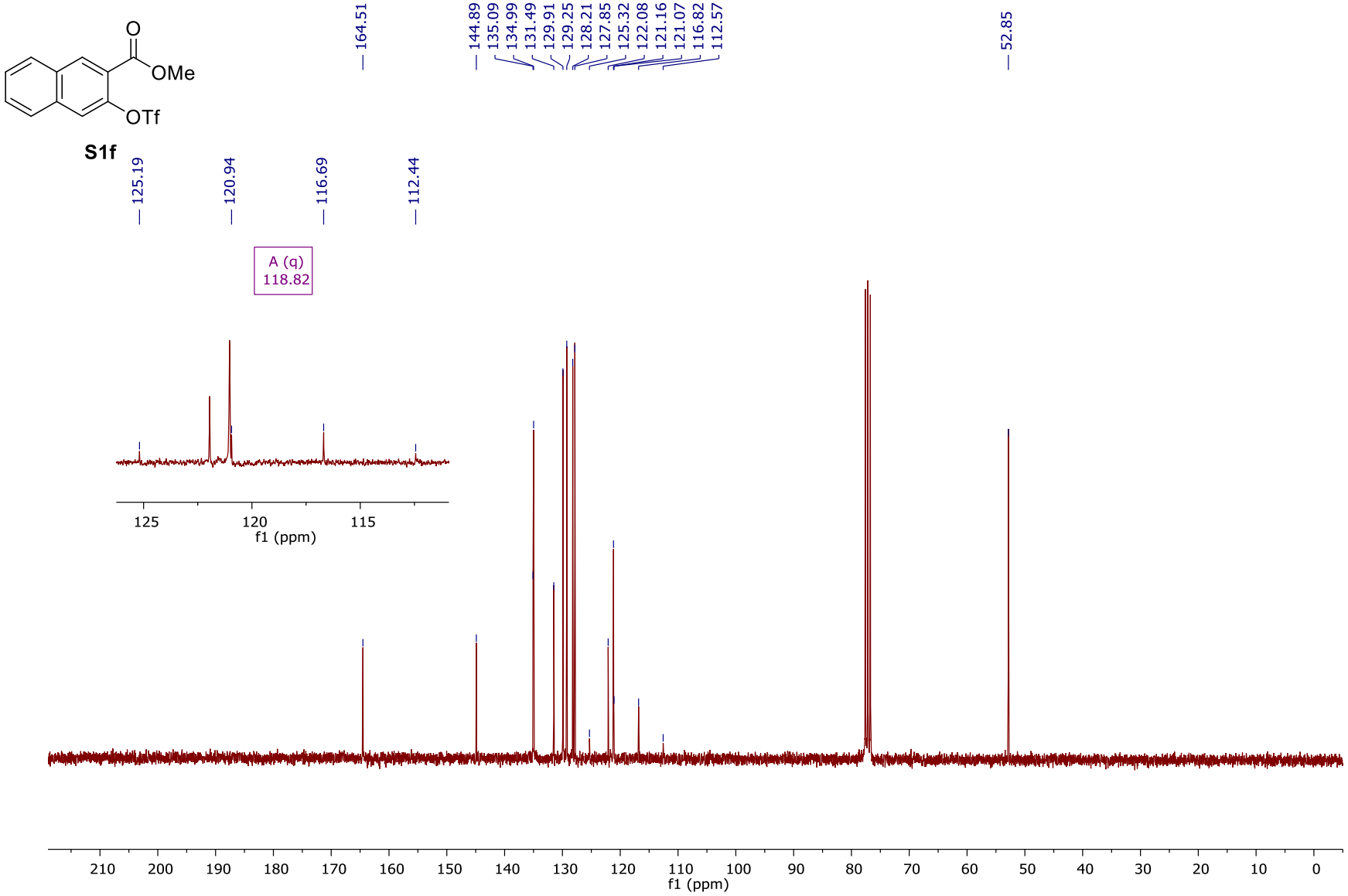


^{1}H NMR (300 MHz, $CDCl_3$) **S1f**

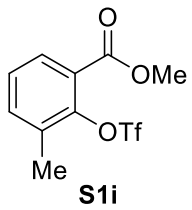


S1f

^{13}C NMR (75 MHz, $CDCl_3$)

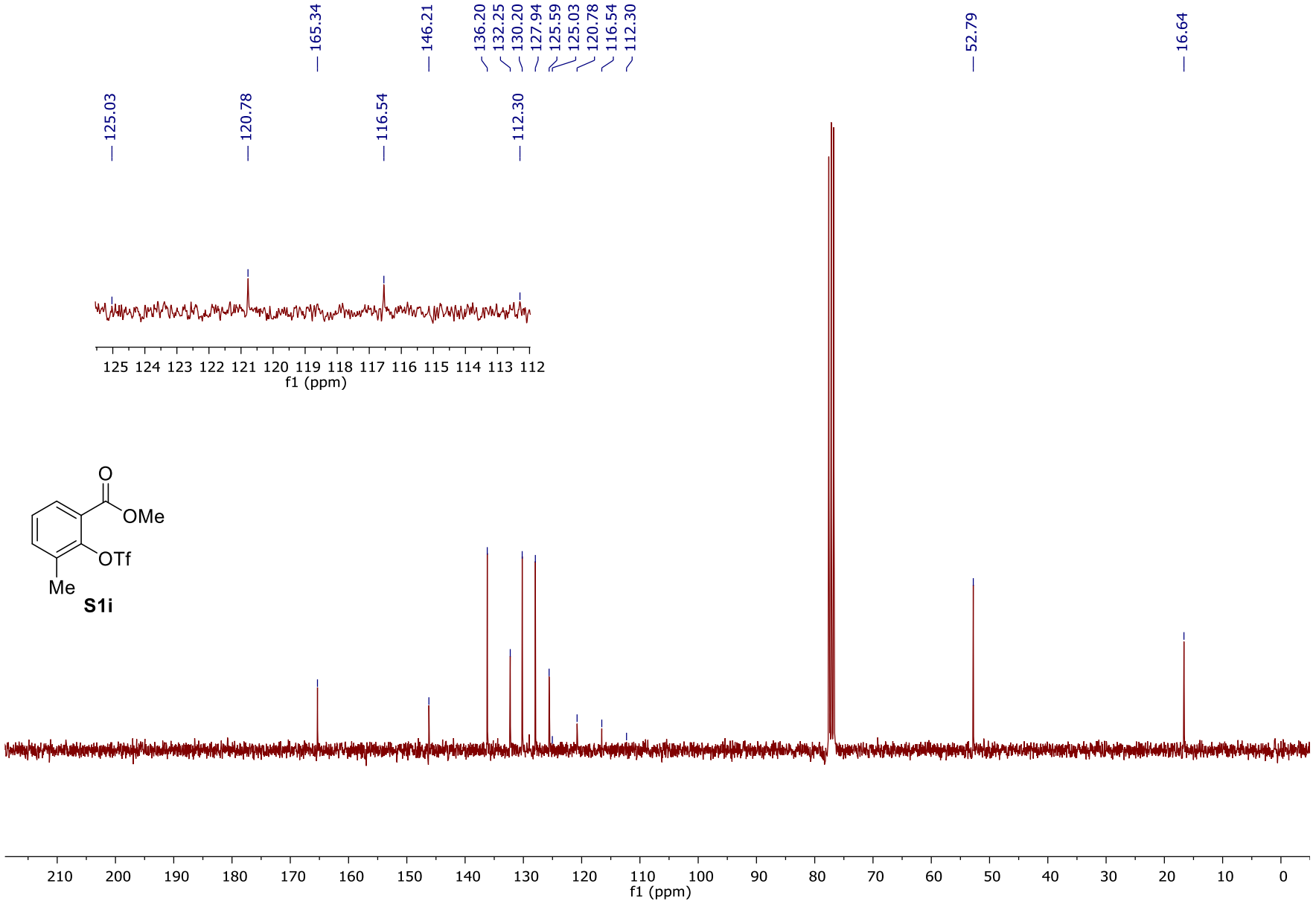


^{1}H NMR (300 MHz, $CDCl_3$) **S1i**

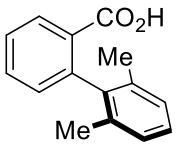


S1i

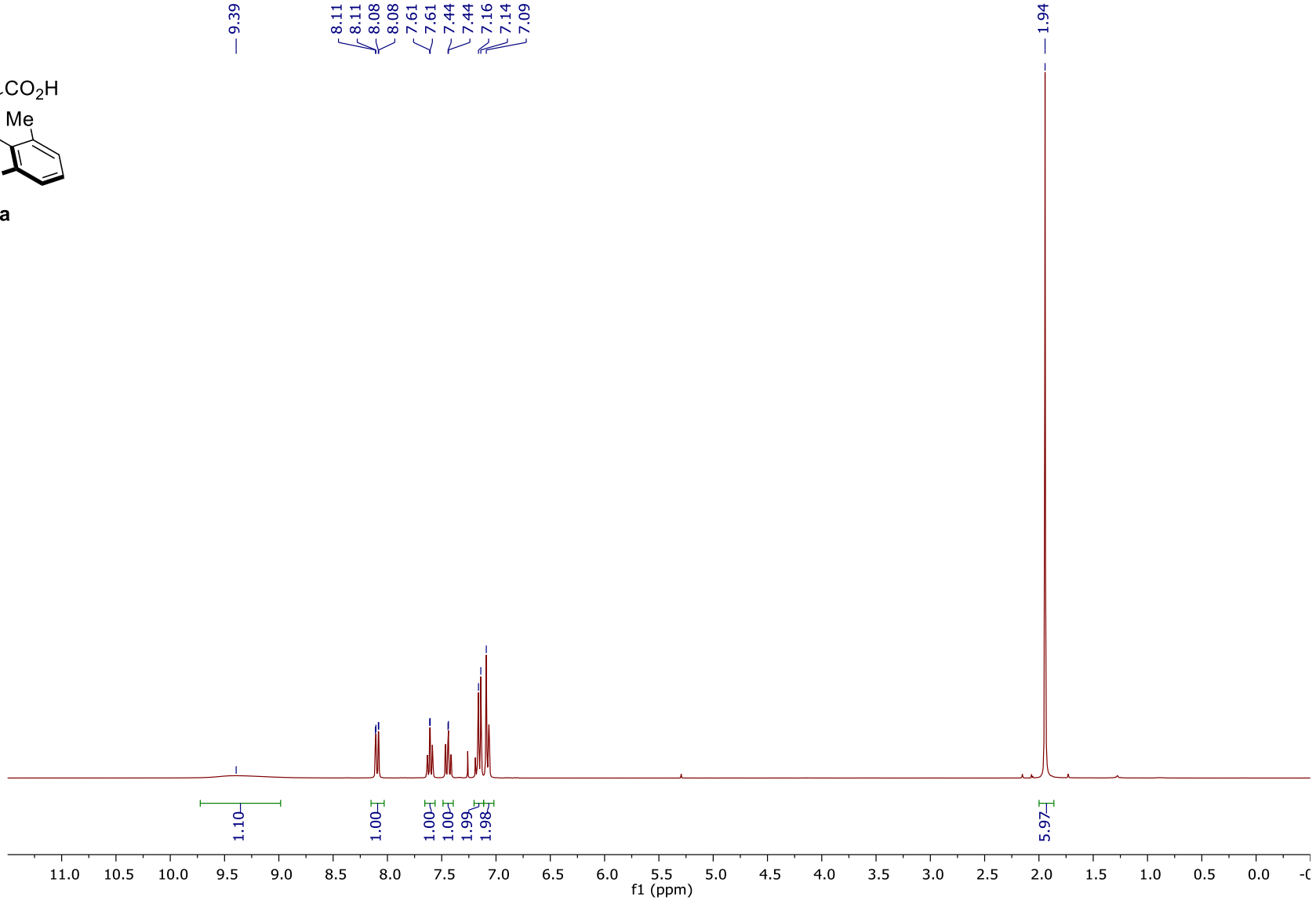
^{13}C NMR (75 MHz, $CDCl_3$)



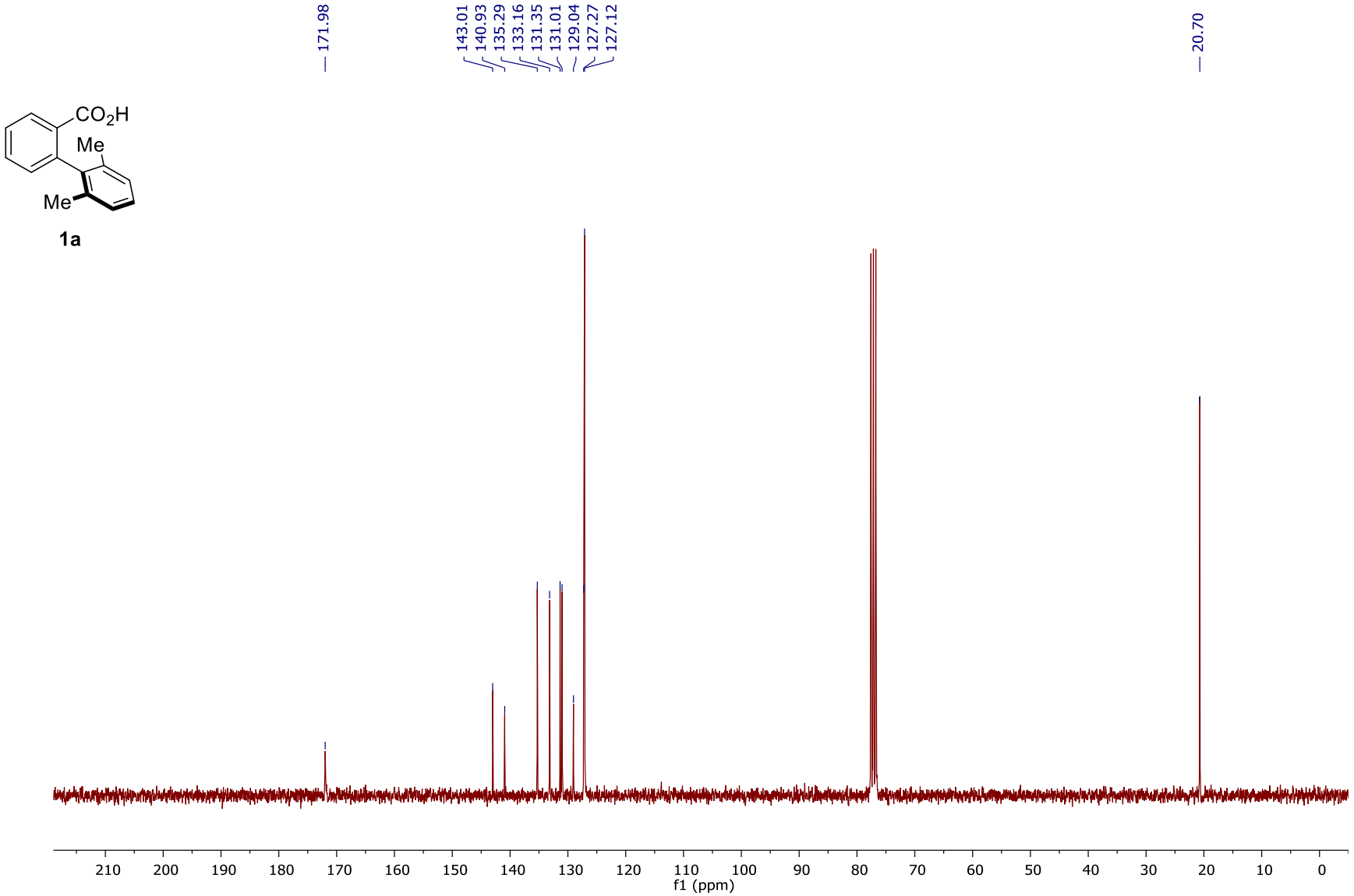
^{1}H NMR (300 MHz, $CDCl_3$) **1a**



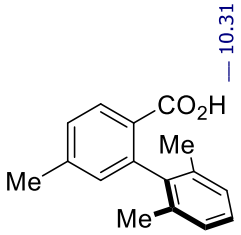
1a



^{13}C NMR (75 MHz, $CDCl_3$)

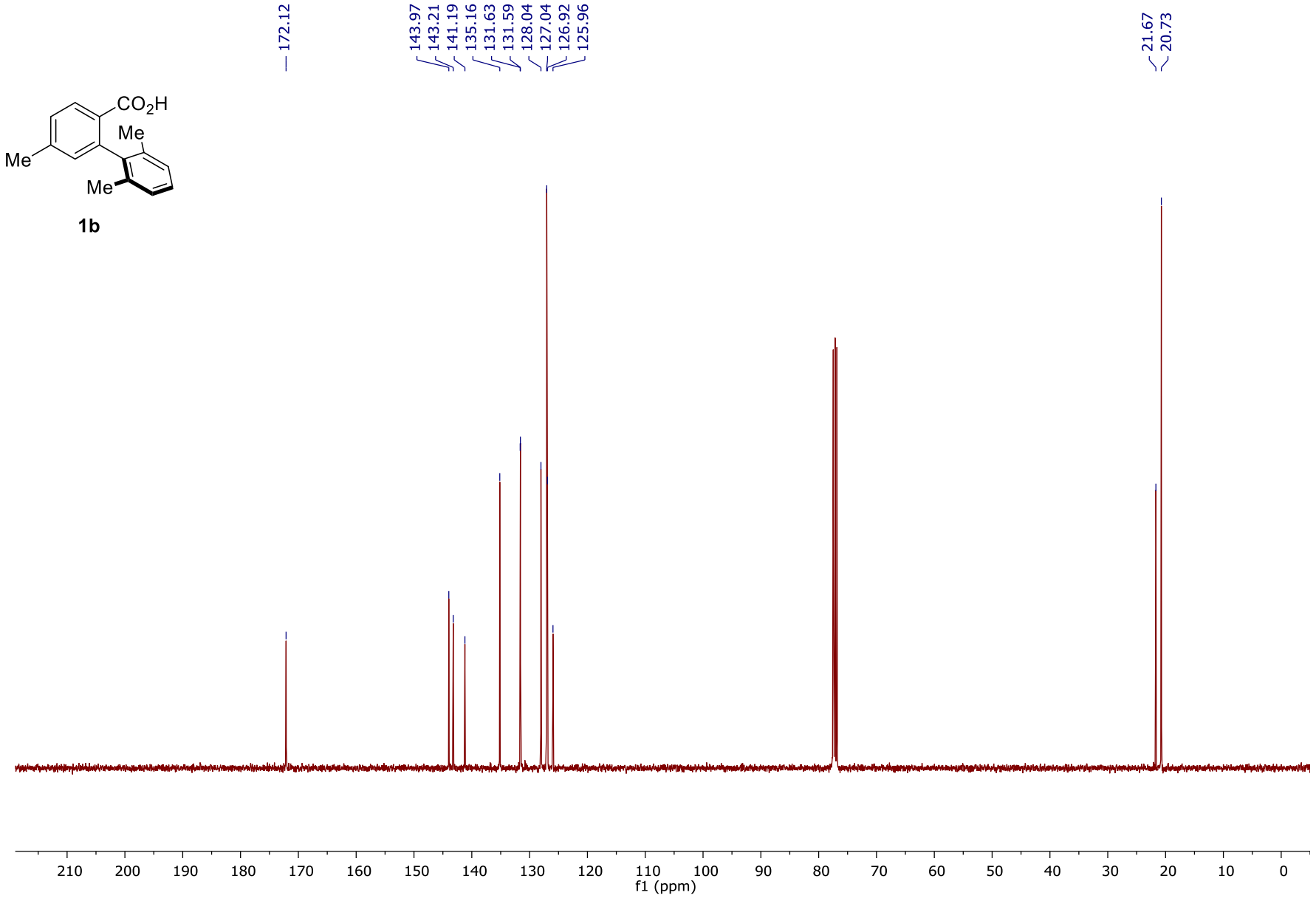


^{1}H NMR (300 MHz, $CDCl_3$) **1b**

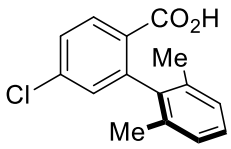


1b

^{13}C NMR (75 MHz, $CDCl_3$)

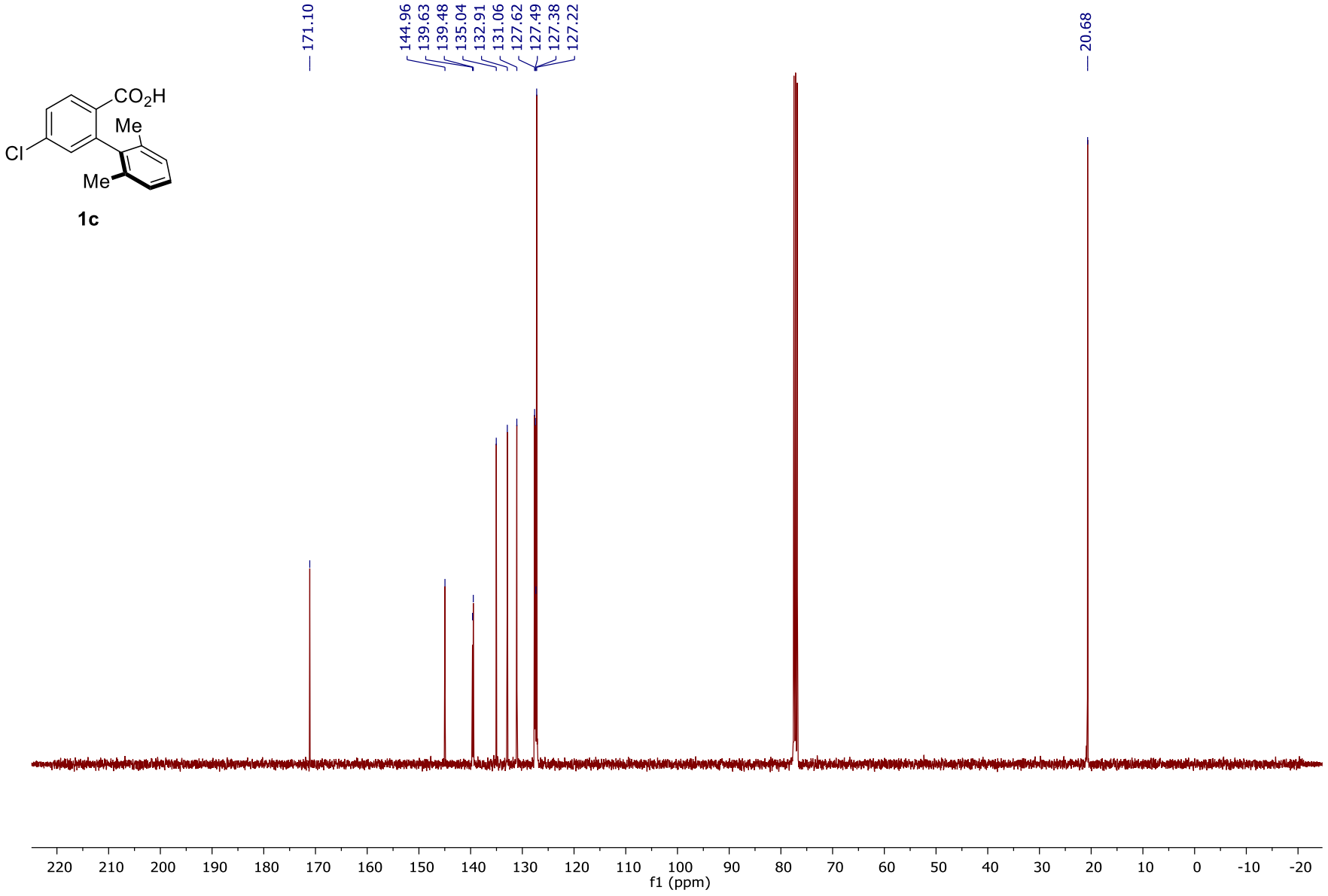


^{1}H NMR (300 MHz, $CDCl_3$) **1c**

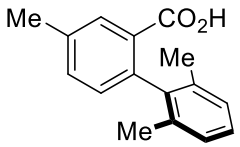


1c

^{13}C NMR (101 MHz, $CDCl_3$)

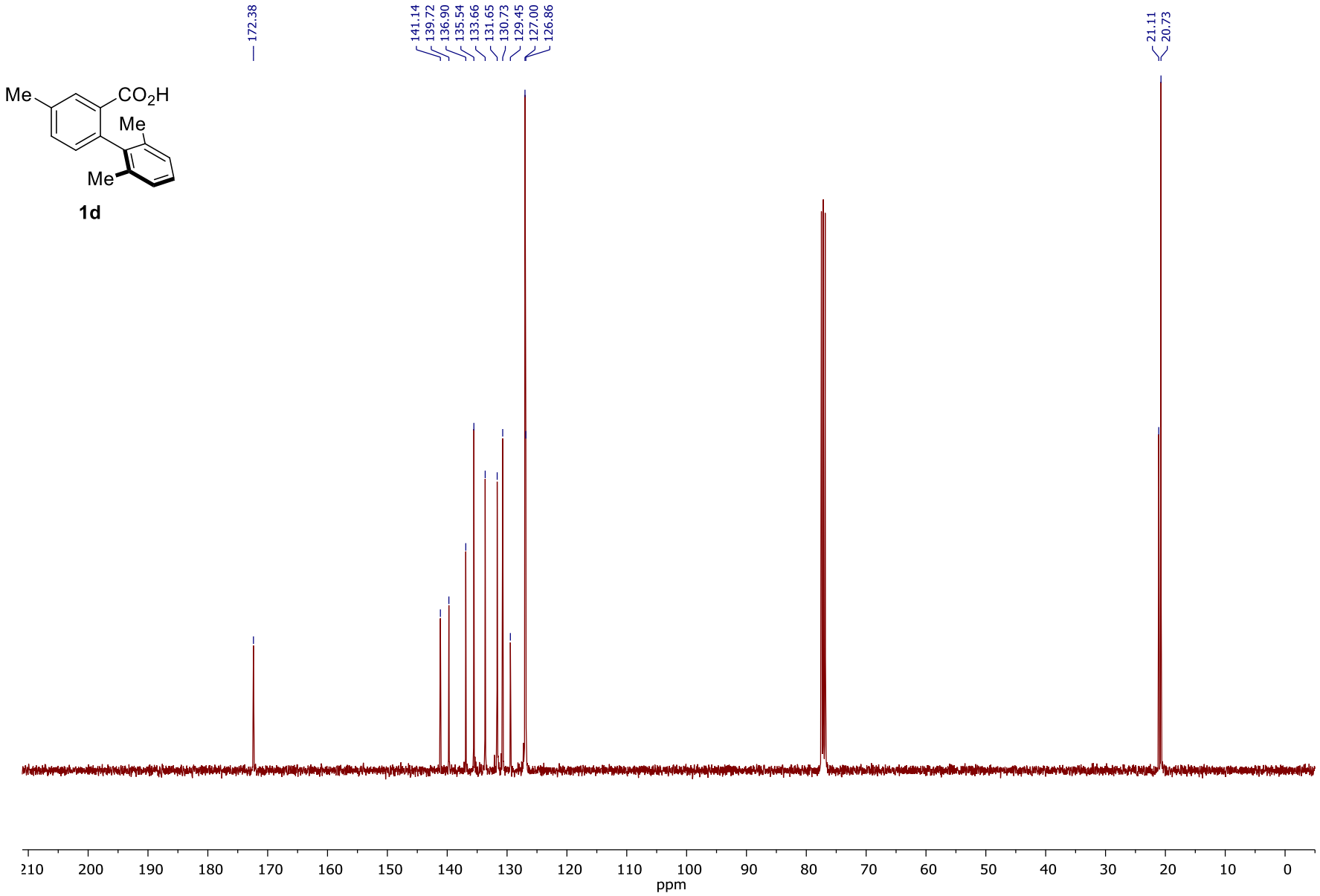


^{1}H NMR (300 MHz, $CDCl_3$) **1d**

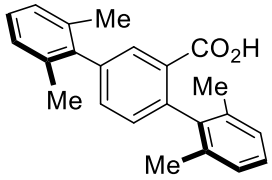


1d

^{13}C NMR (101 MHz, $CDCl_3$)

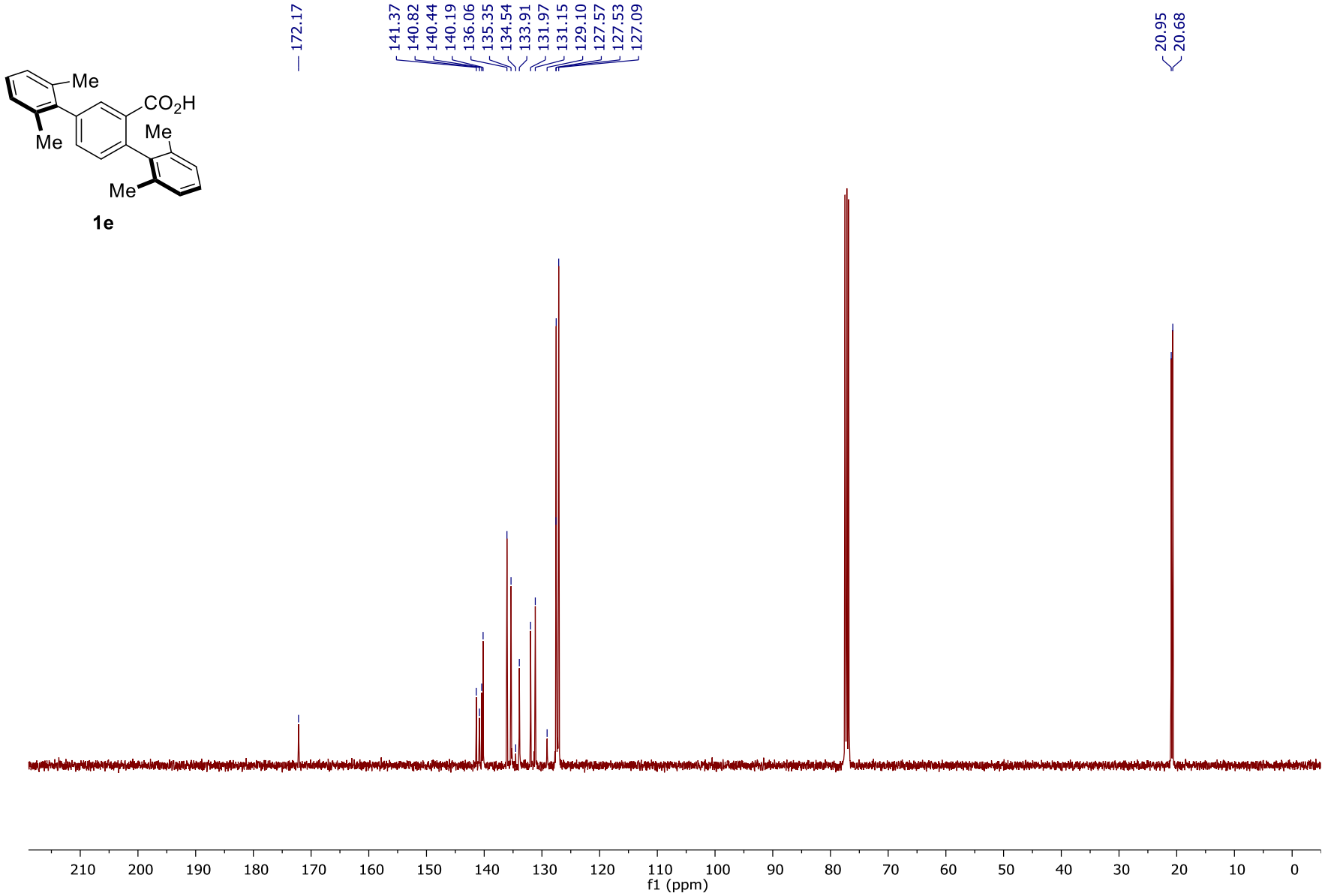


^{1}H NMR (400 MHz, $CDCl_3$) **1e**

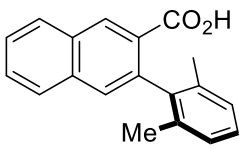


1e

^{13}C NMR (101 MHz, $CDCl_3$)

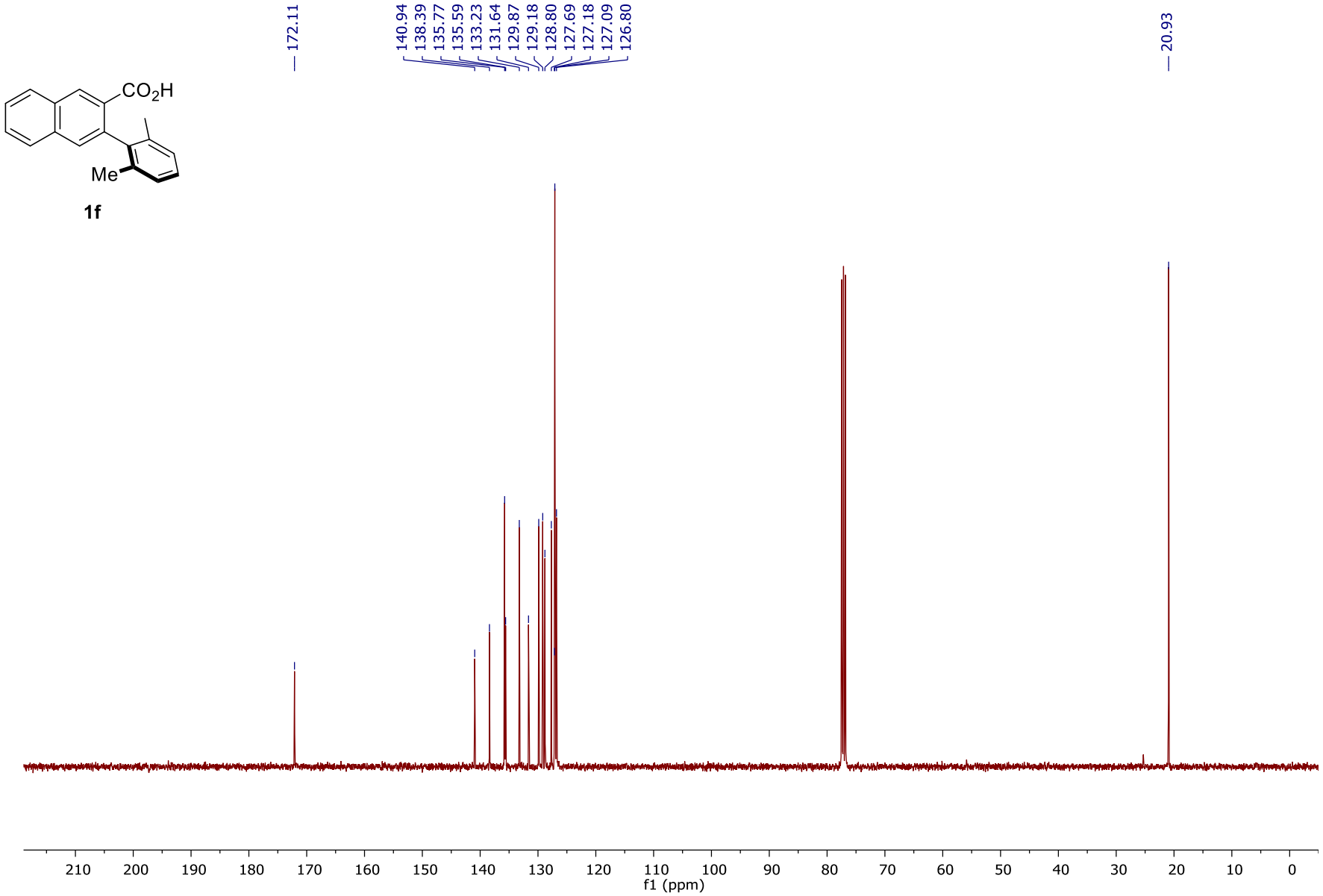


^{1}H NMR (400 MHz, $CDCl_3$) **1f**

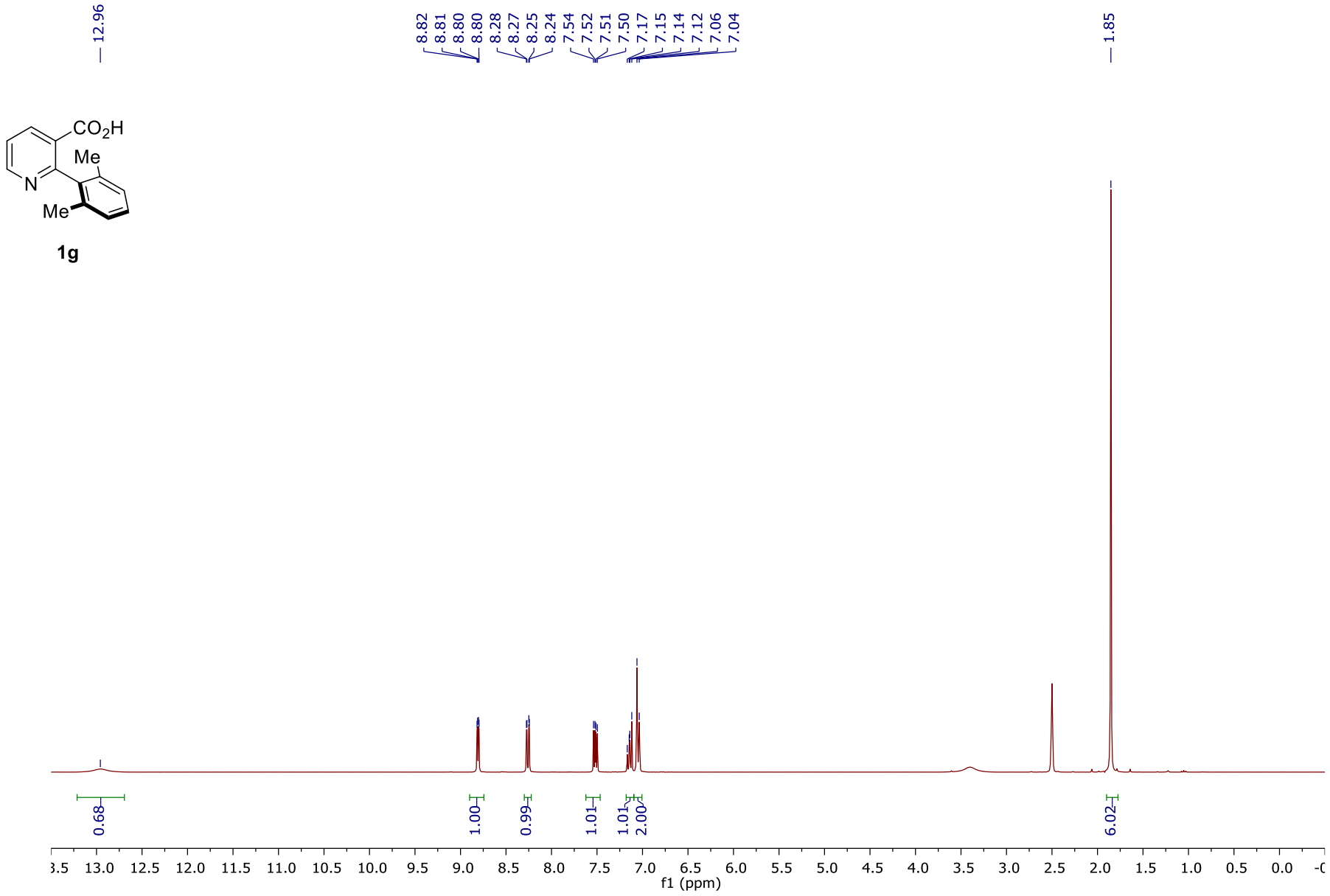


1f

^{13}C NMR (101 MHz, $CDCl_3$)

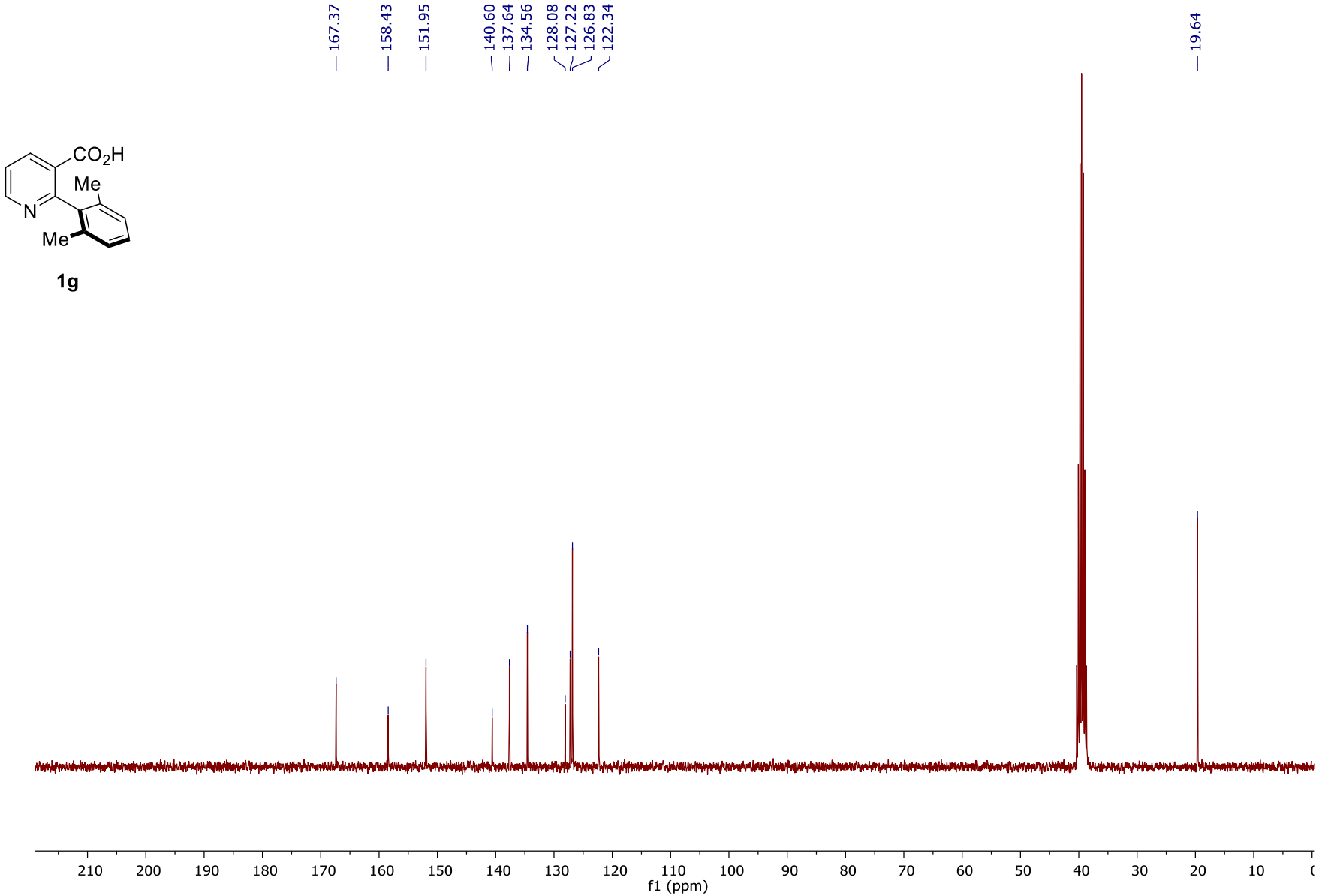


^{1}H NMR (300 MHz, DMSO-d_6) **1g**



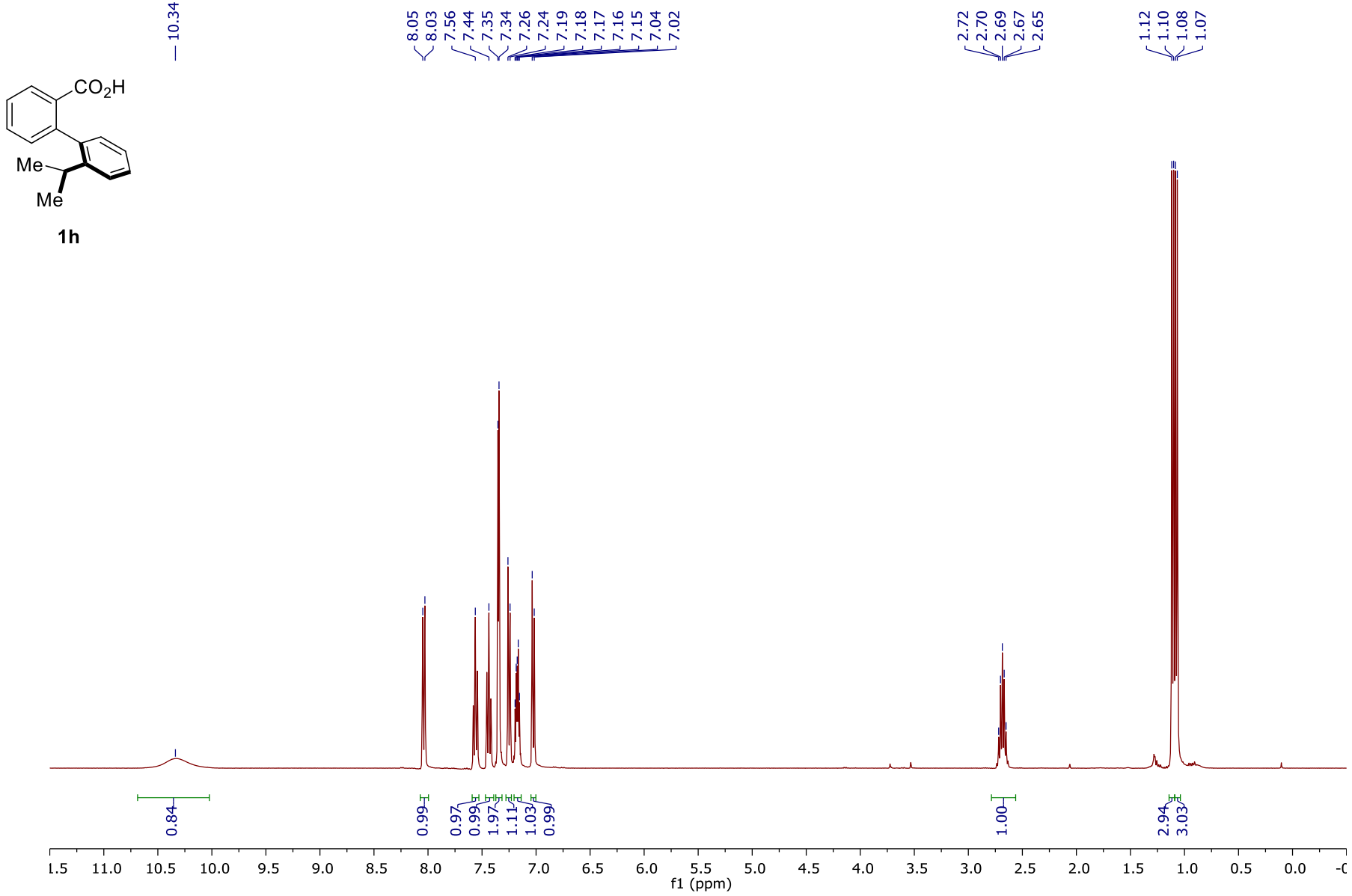
1g

^{13}C NMR (75 MHz, DMSO-d_6)



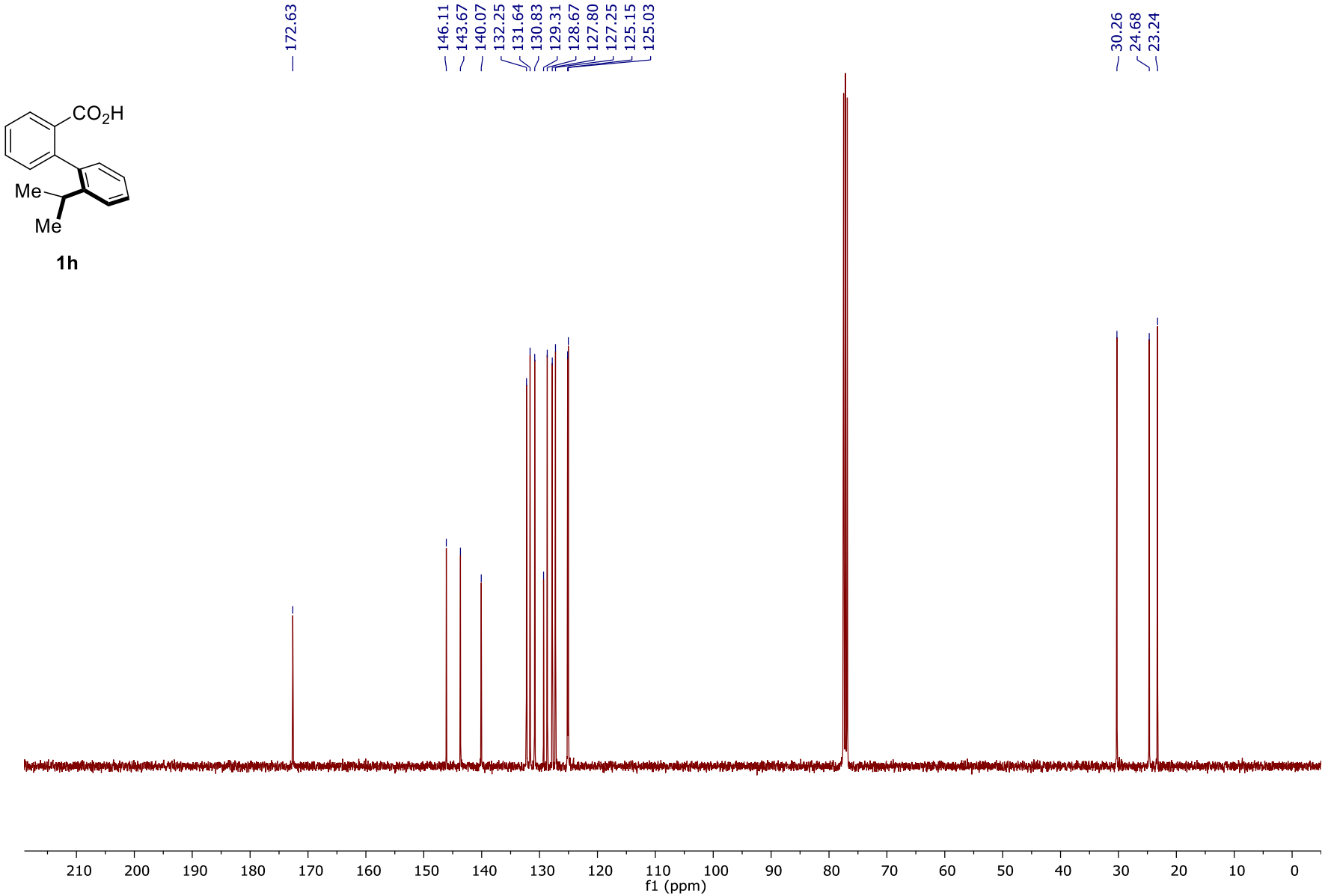
1g

^{1}H NMR (400 MHz, $CDCl_3$) **1h**

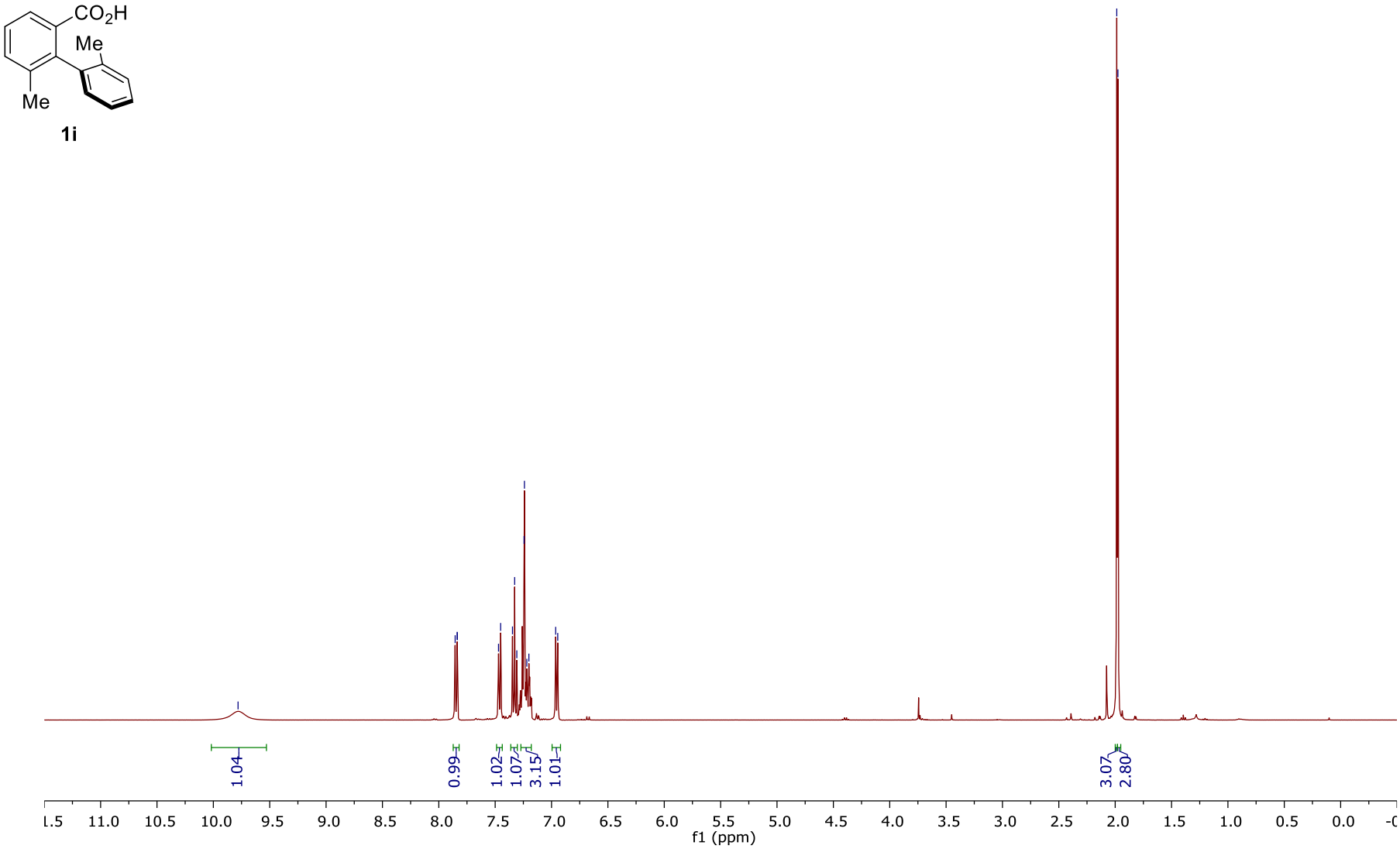


1h

^{13}C NMR (101 MHz, $CDCl_3$)

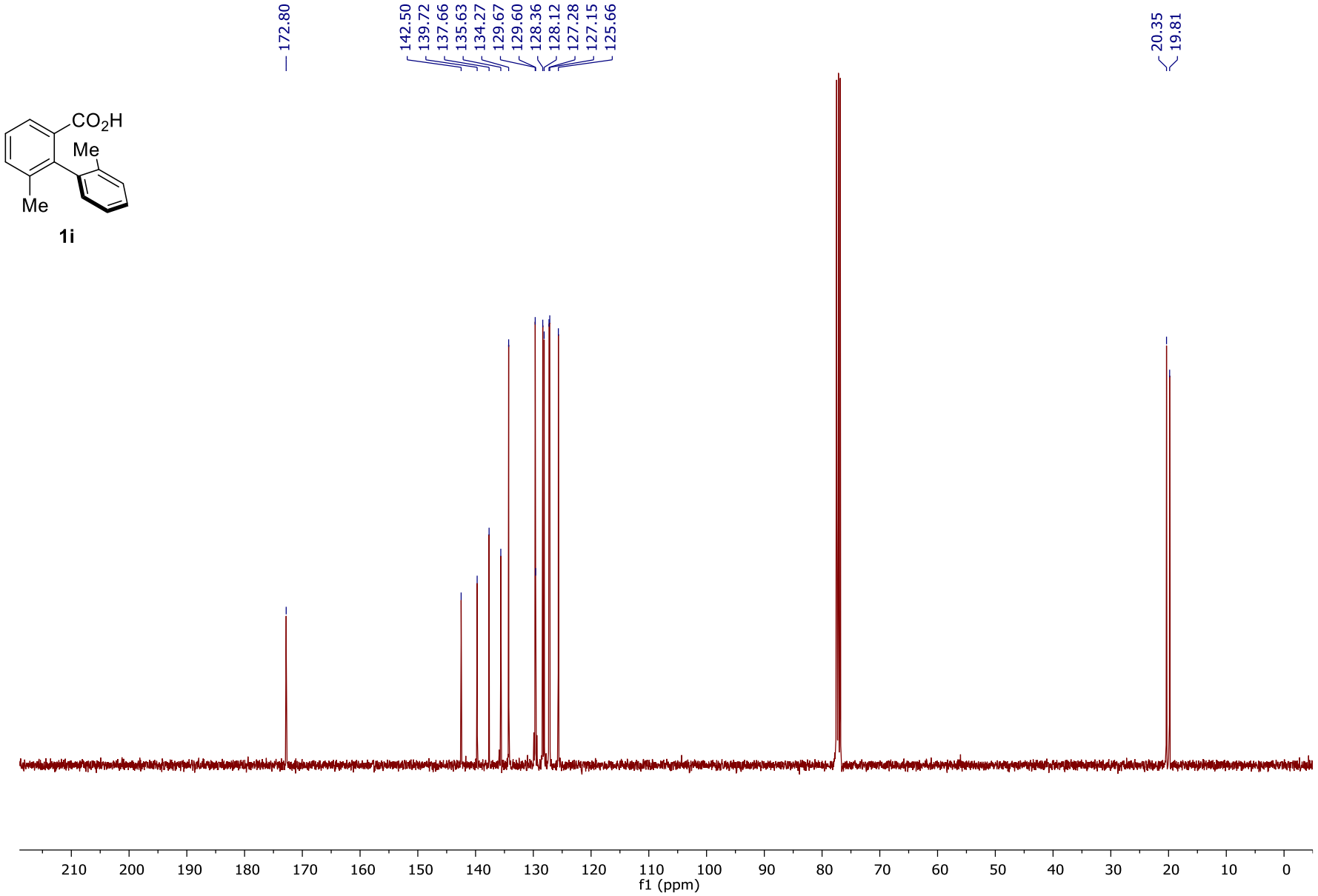


^{1}H NMR (400 MHz, $CDCl_3$) **1i**

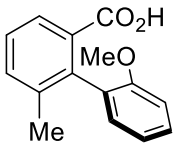


1i

^{13}C NMR (101 MHz, $CDCl_3$)

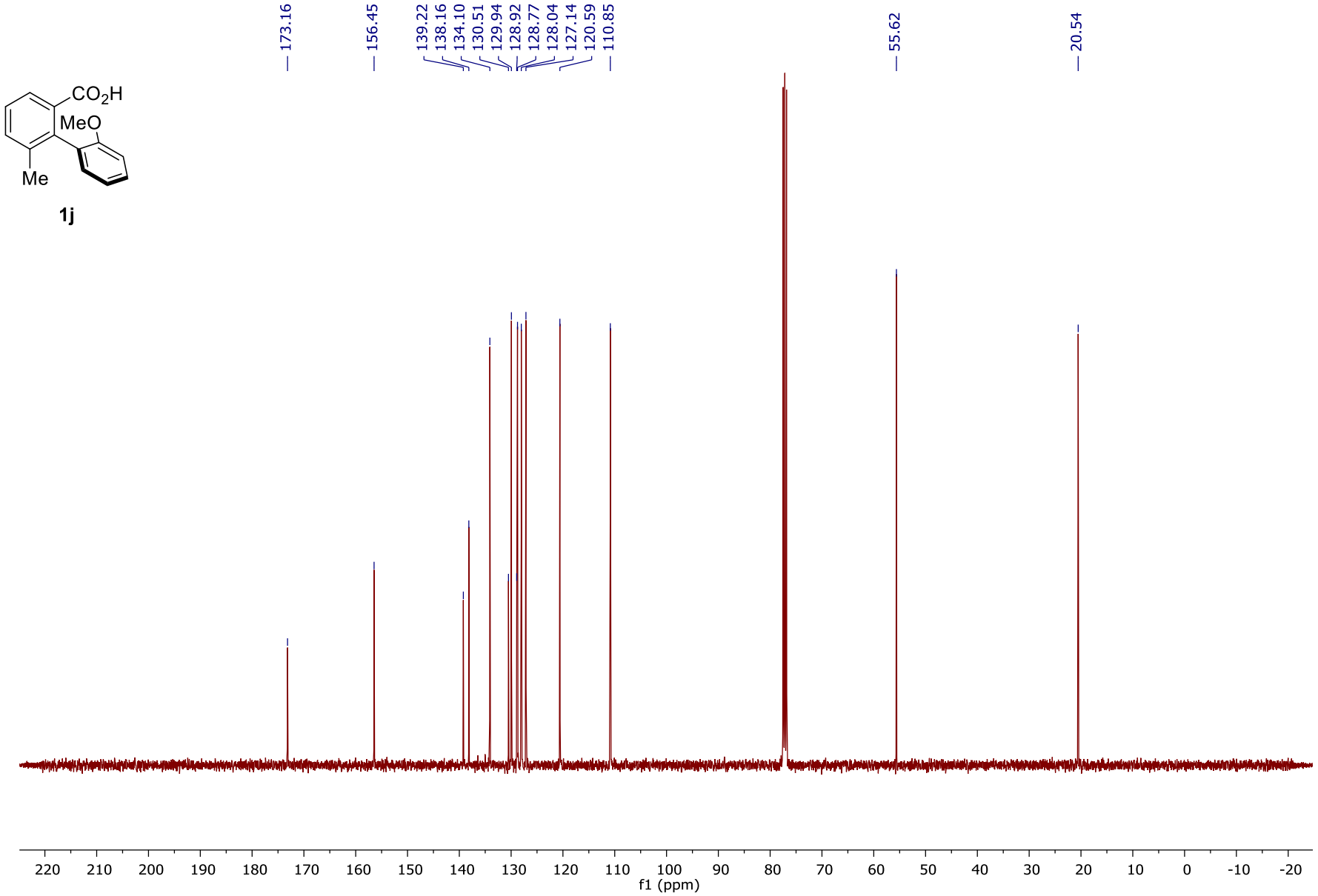


^{1}H NMR (300 MHz, $CDCl_3$) **1j**

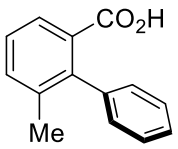


1j

^{13}C NMR (101 MHz, $CDCl_3$)

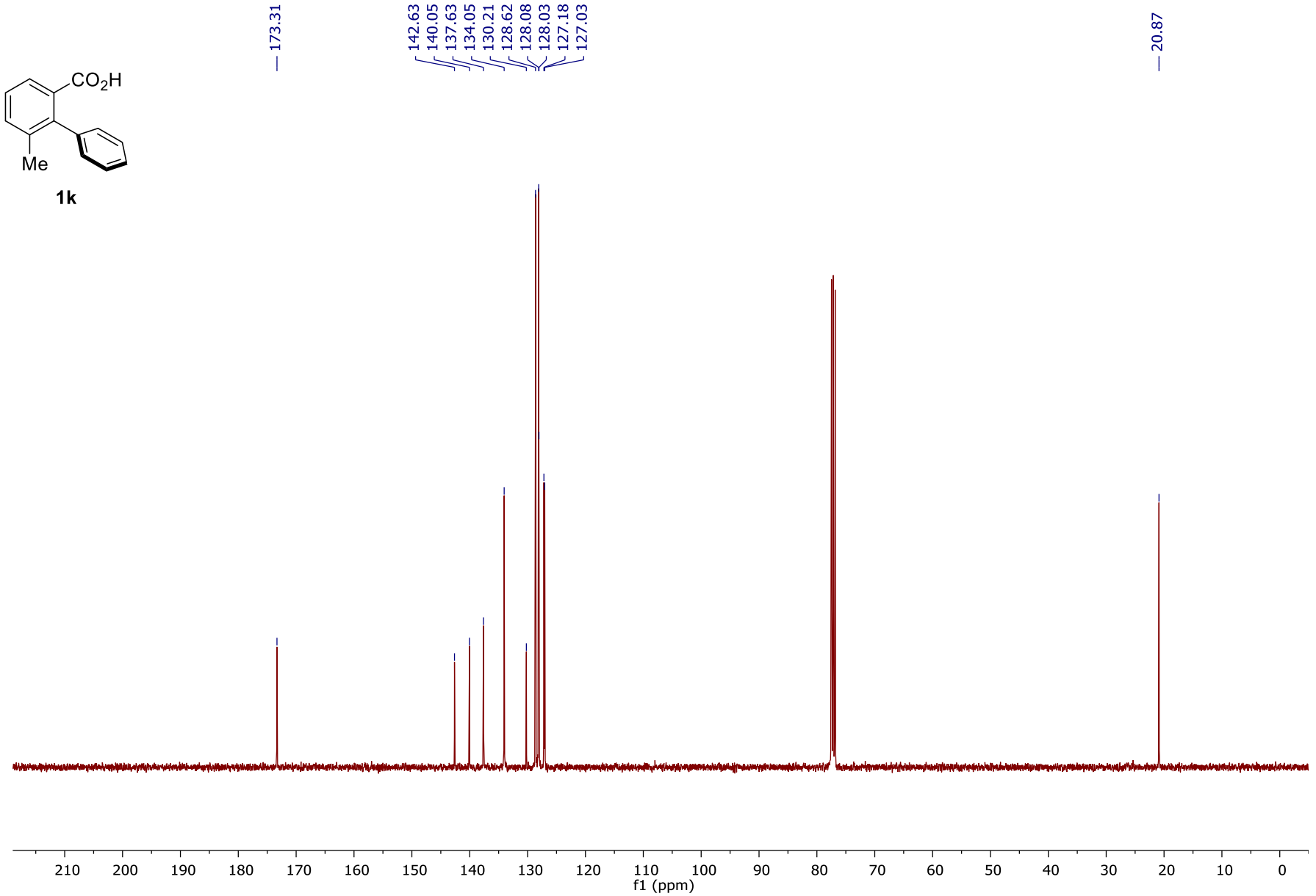


^{1}H NMR (400 MHz, $CDCl_3$) **1k**

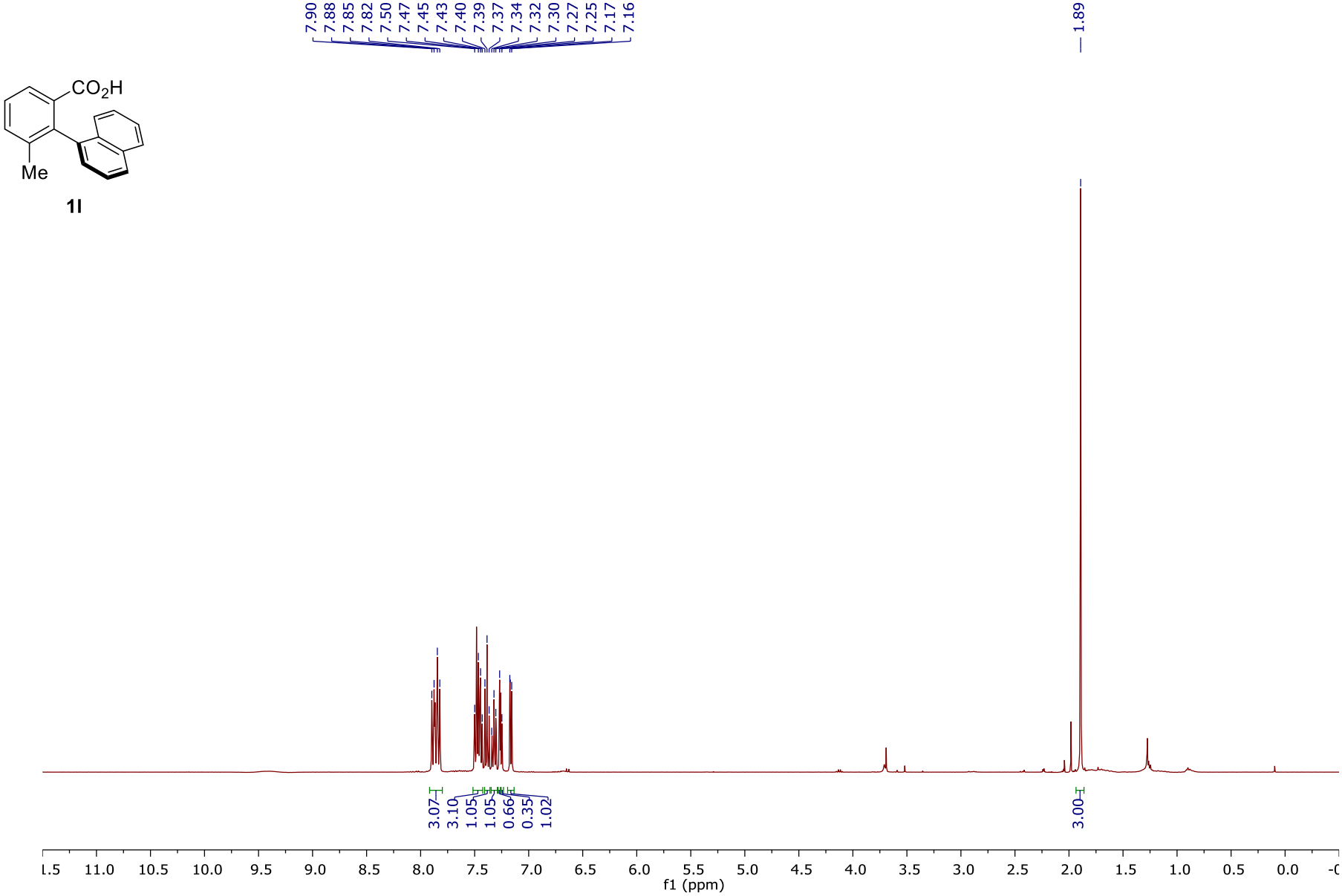


1k

^{13}C NMR (101 MHz, $CDCl_3$)

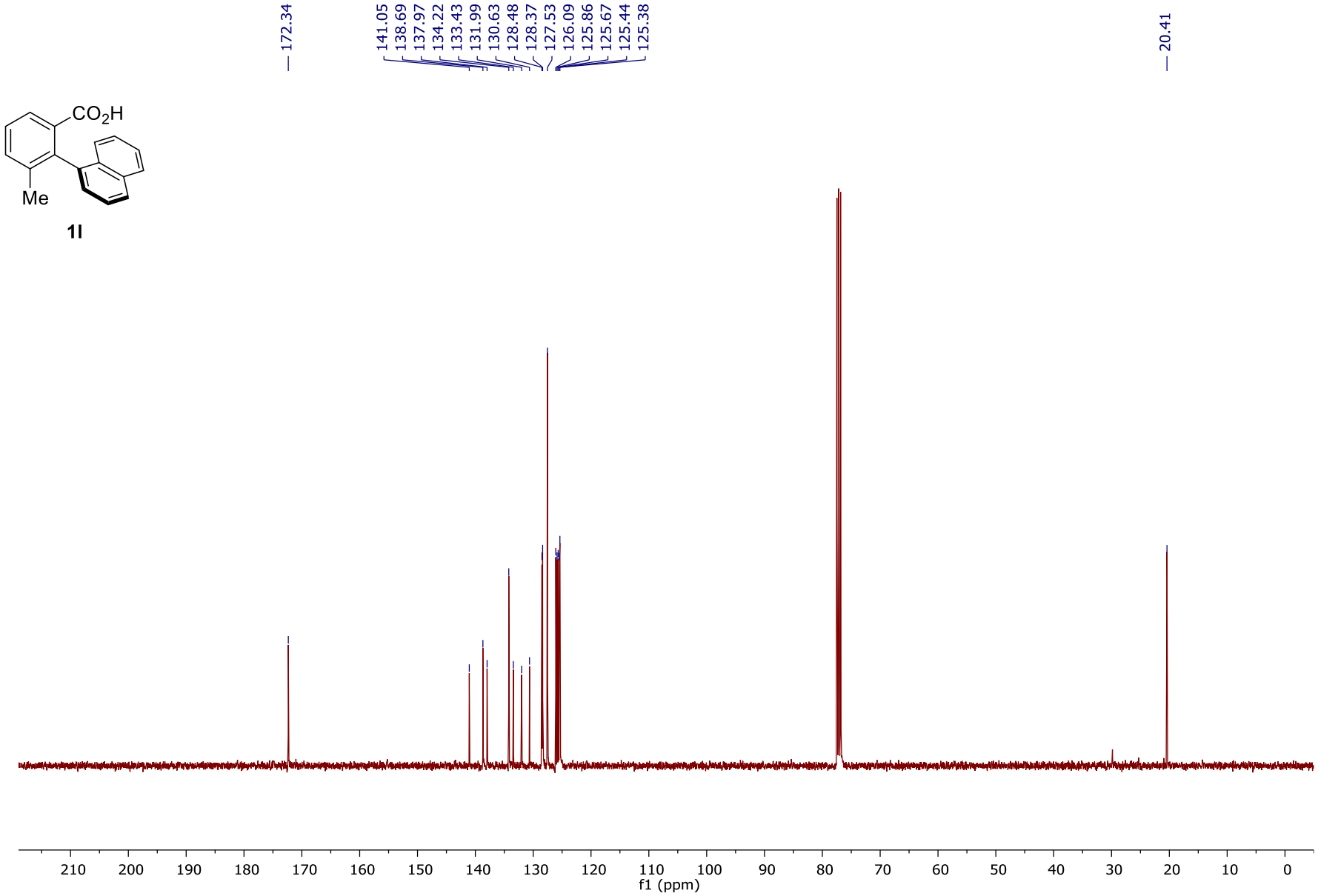


^{1}H NMR (300 MHz, $CDCl_3$) **1l**

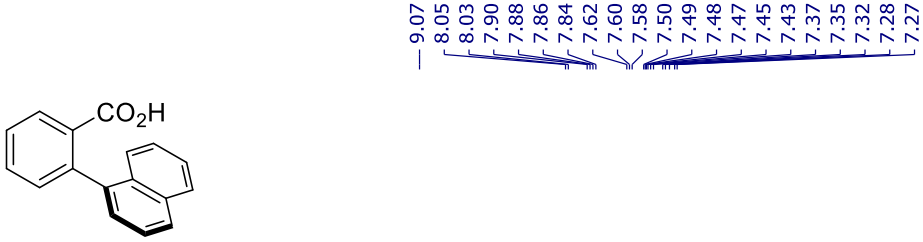


1l

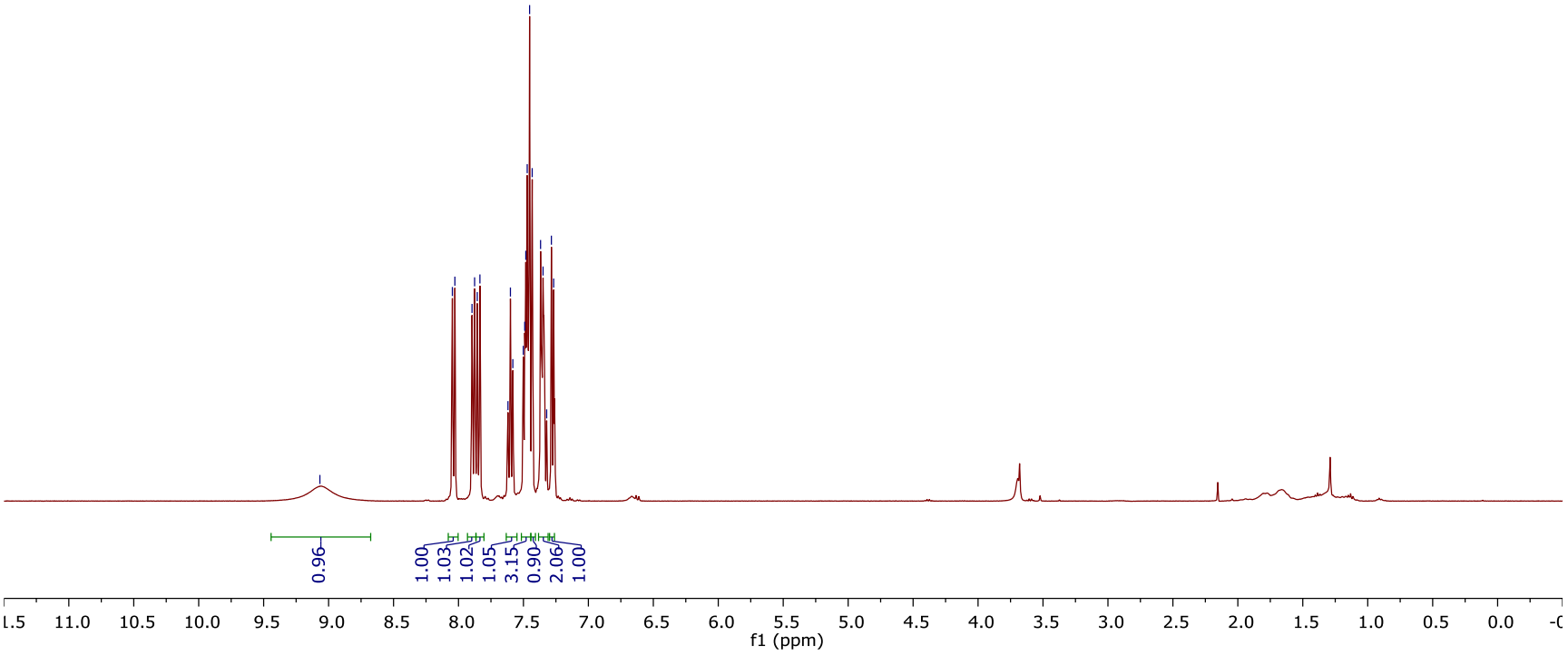
^{13}C NMR (75 MHz, $CDCl_3$)



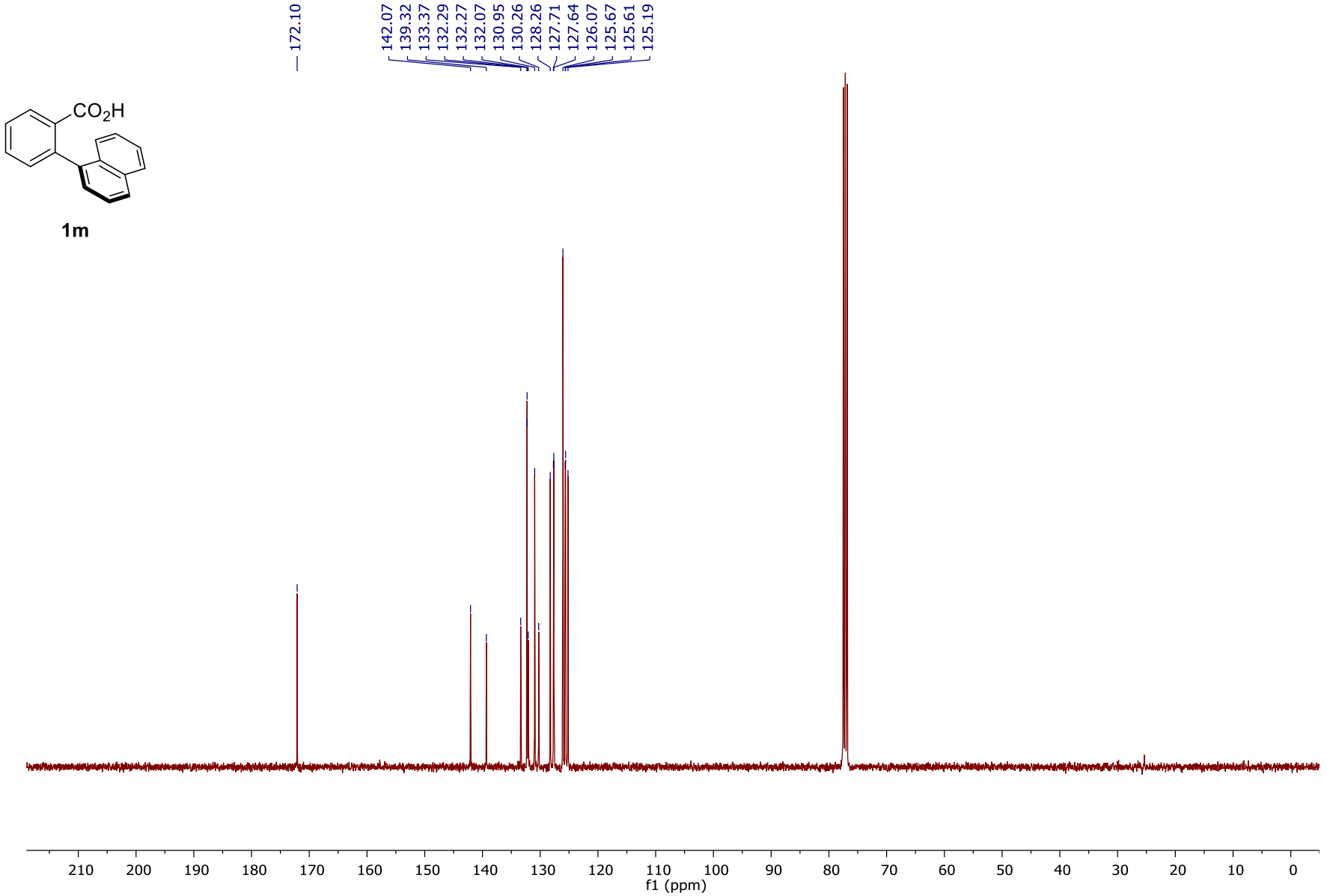
^{1}H NMR (400 MHz, $CDCl_3$) **1m**



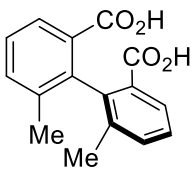
1m



^{13}C NMR (101 MHz, $CDCl_3$)

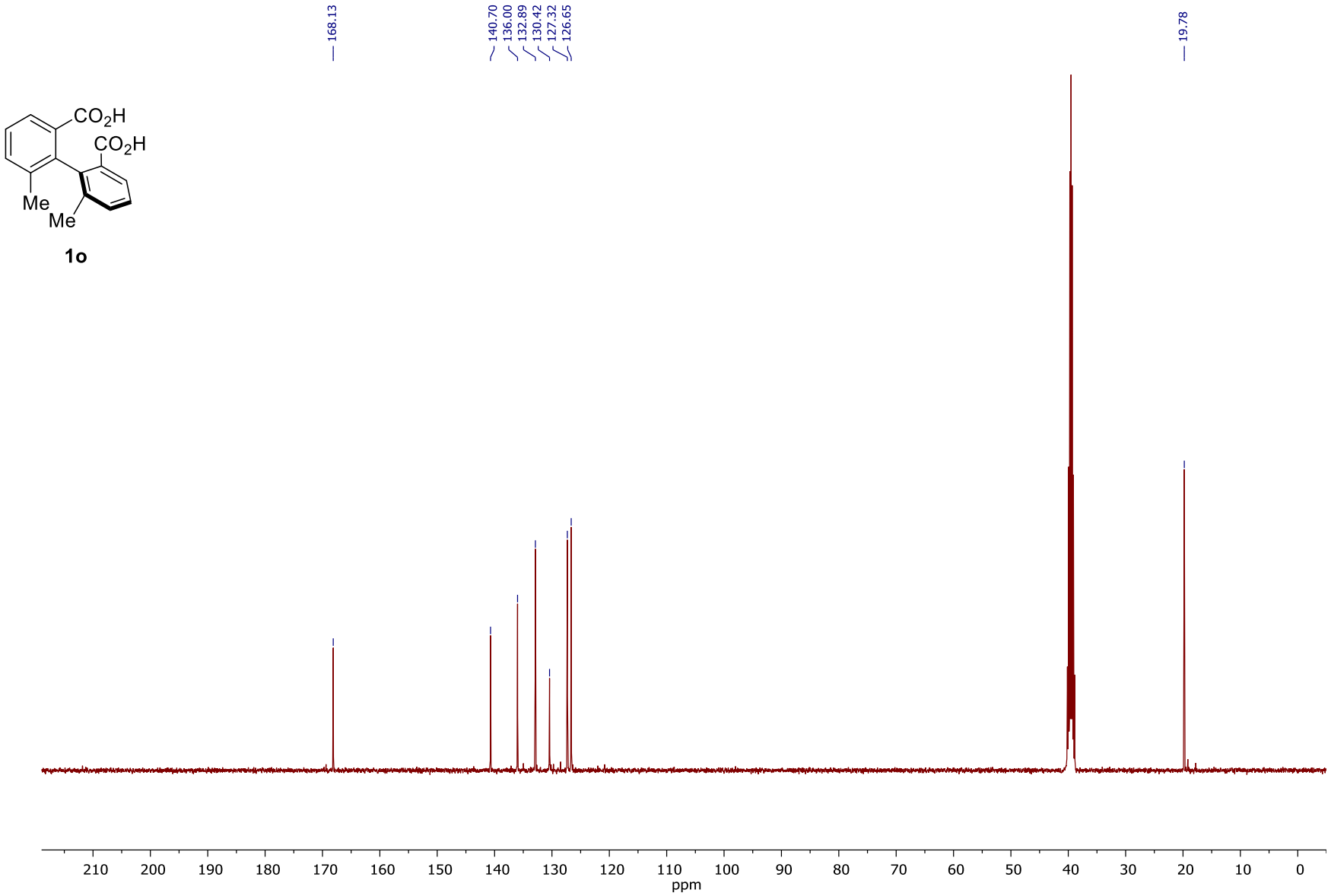


^{1}H NMR (300 MHz, DMSO-d_6) **1o**



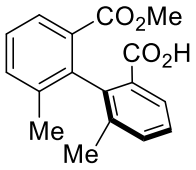
1o

^{13}C NMR {H^1} (101 MHz, DMSO-d_6)



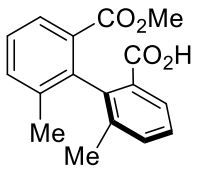
1o

^{1}H NMR (400 MHz, $CDCl_3$) **1p**



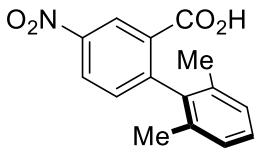
1p

^{13}C NMR (101 MHz, $CDCl_3$)



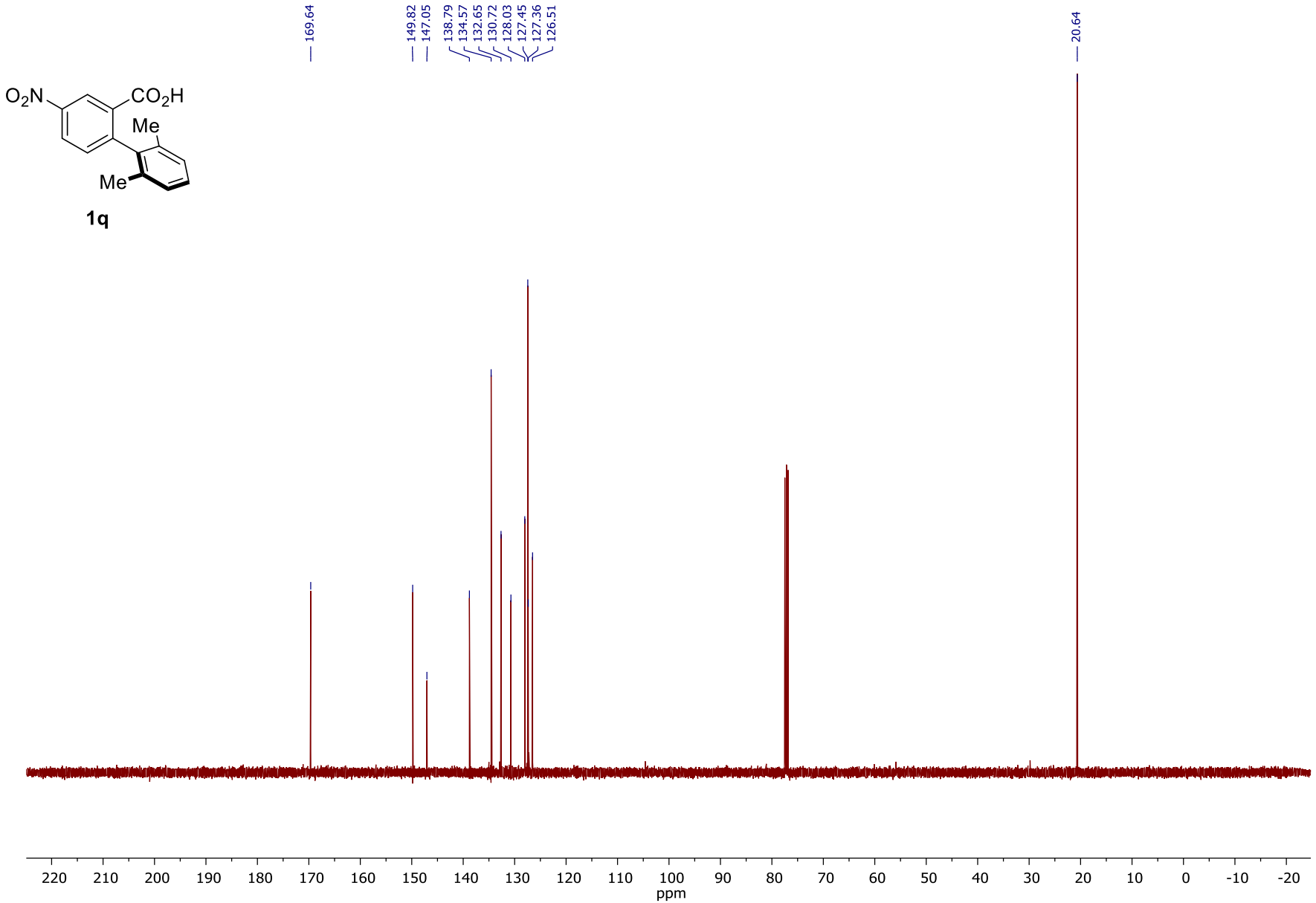
1p

^{1}H NMR (400 MHz, CD_3OD) **1q**

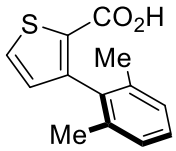


1q

^{13}C NMR (101 MHz, $CDCl_3$)

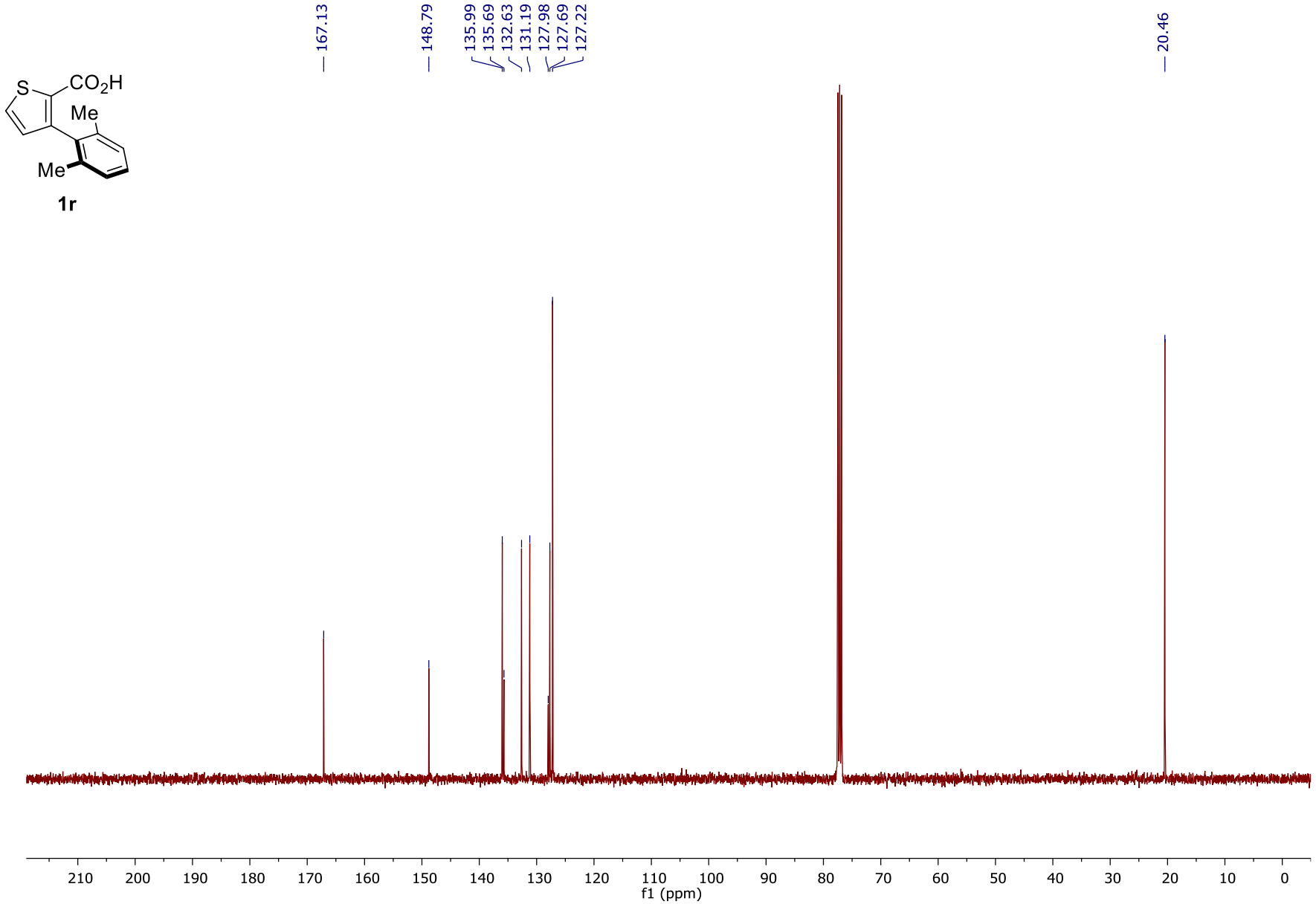


^{1}H NMR (400 MHz, $CDCl_3$) **1r**

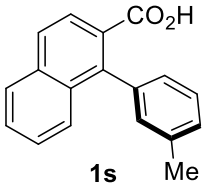


1r

^{13}C NMR (101 MHz, $CDCl_3$)

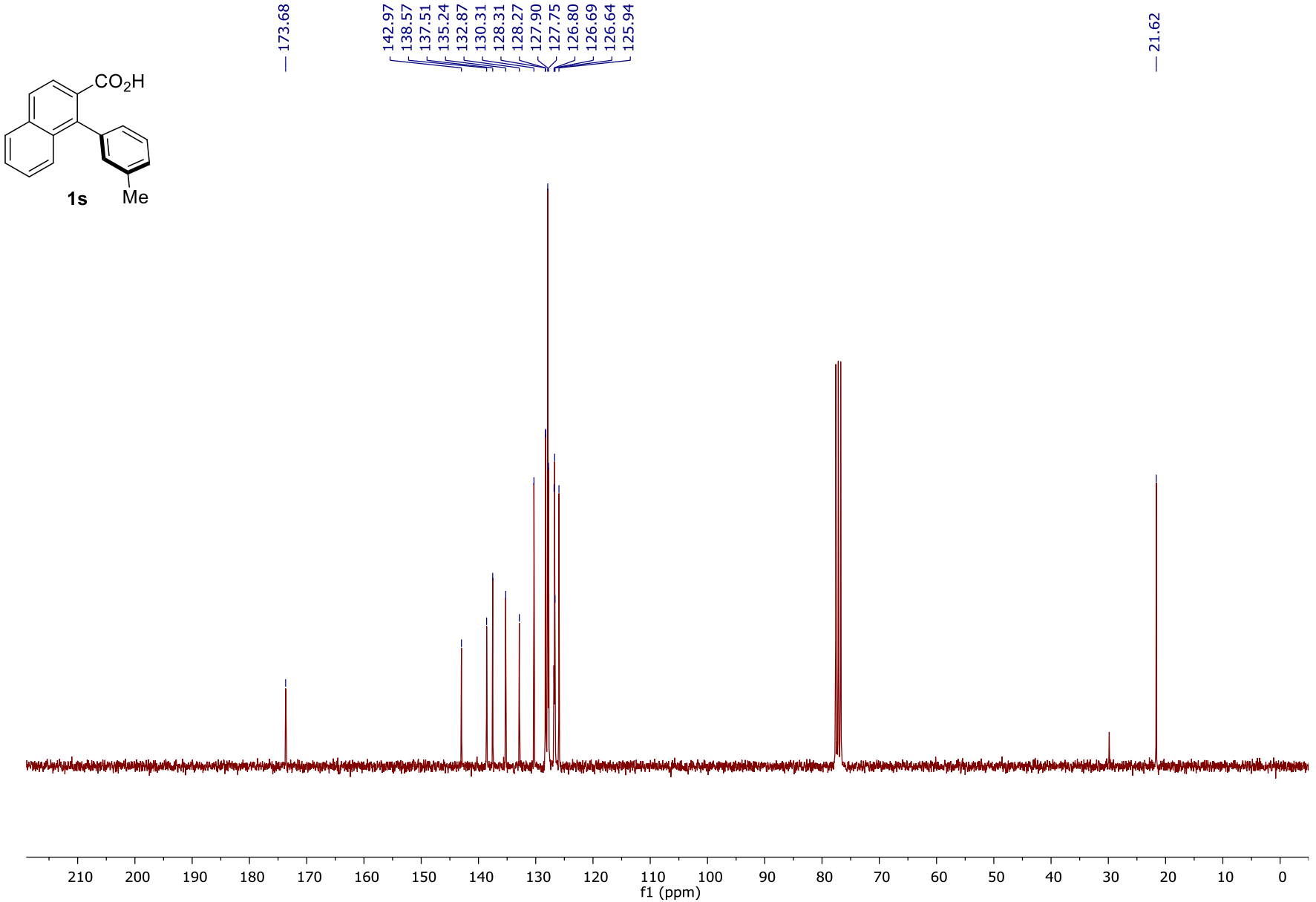


^{1}H NMR (300 MHz, $CDCl_3$) **1s**

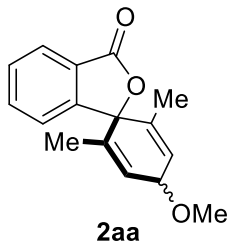


1s

^{13}C NMR (75 MHz, $CDCl_3$)

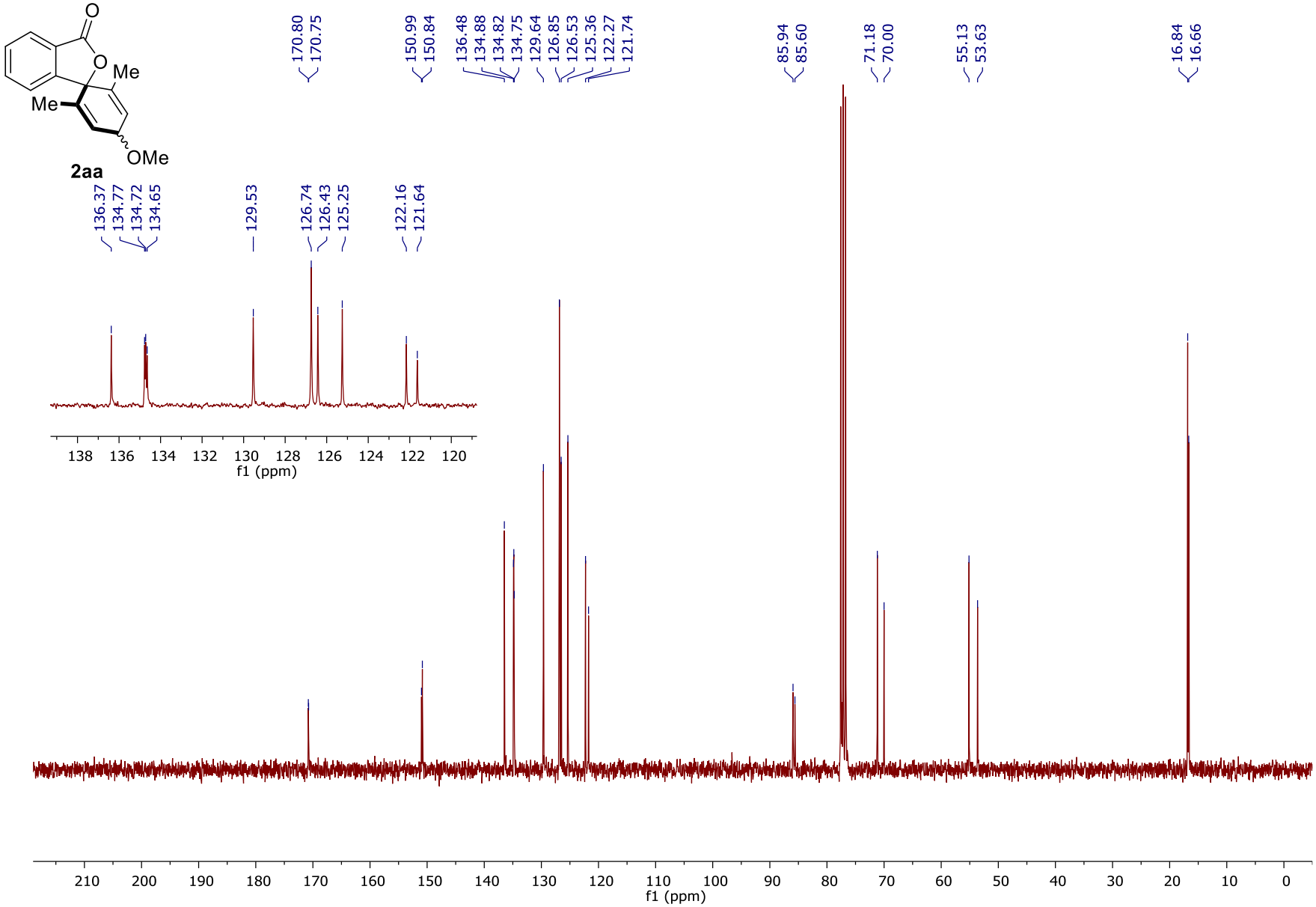


^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture **2aa**

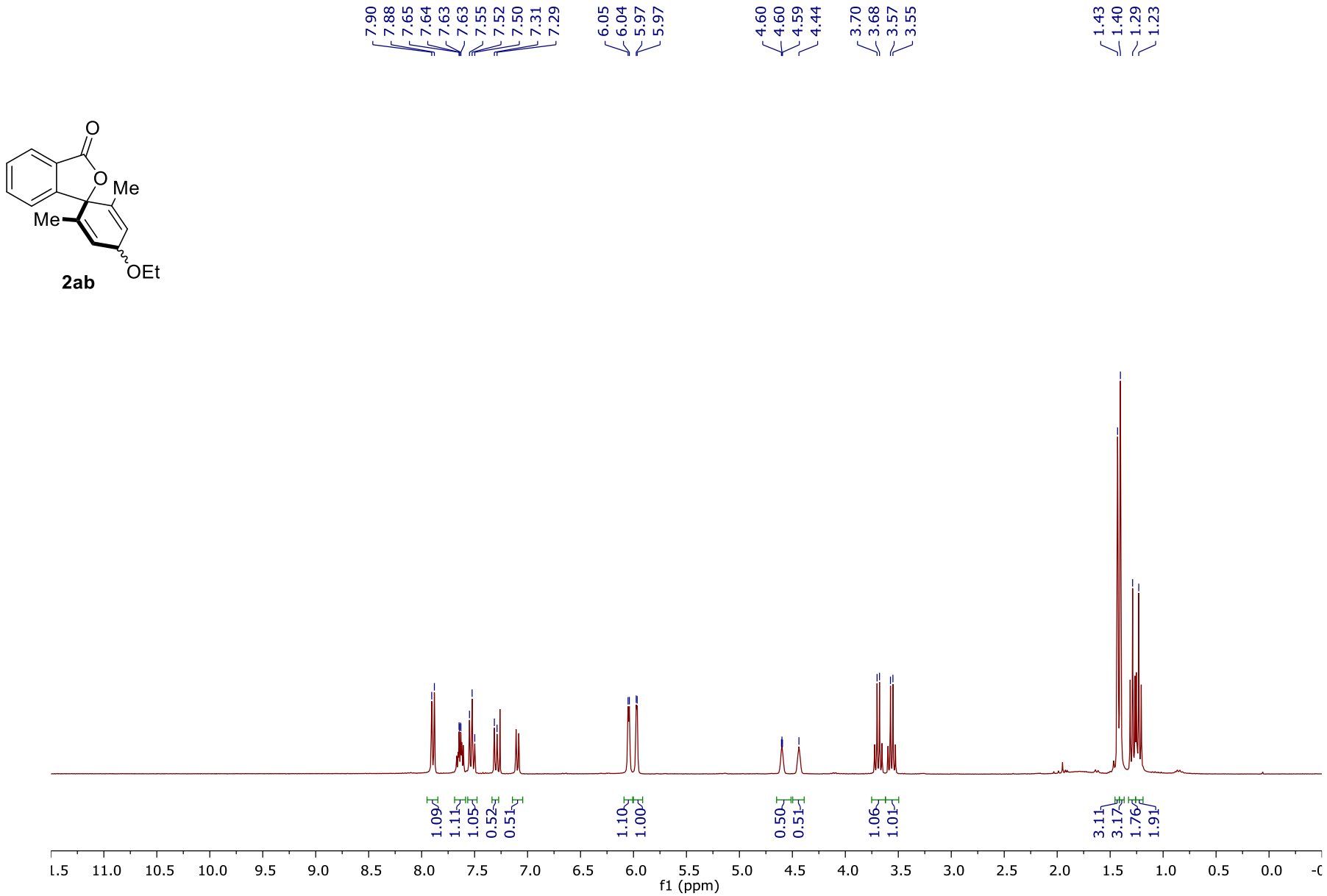


2aa

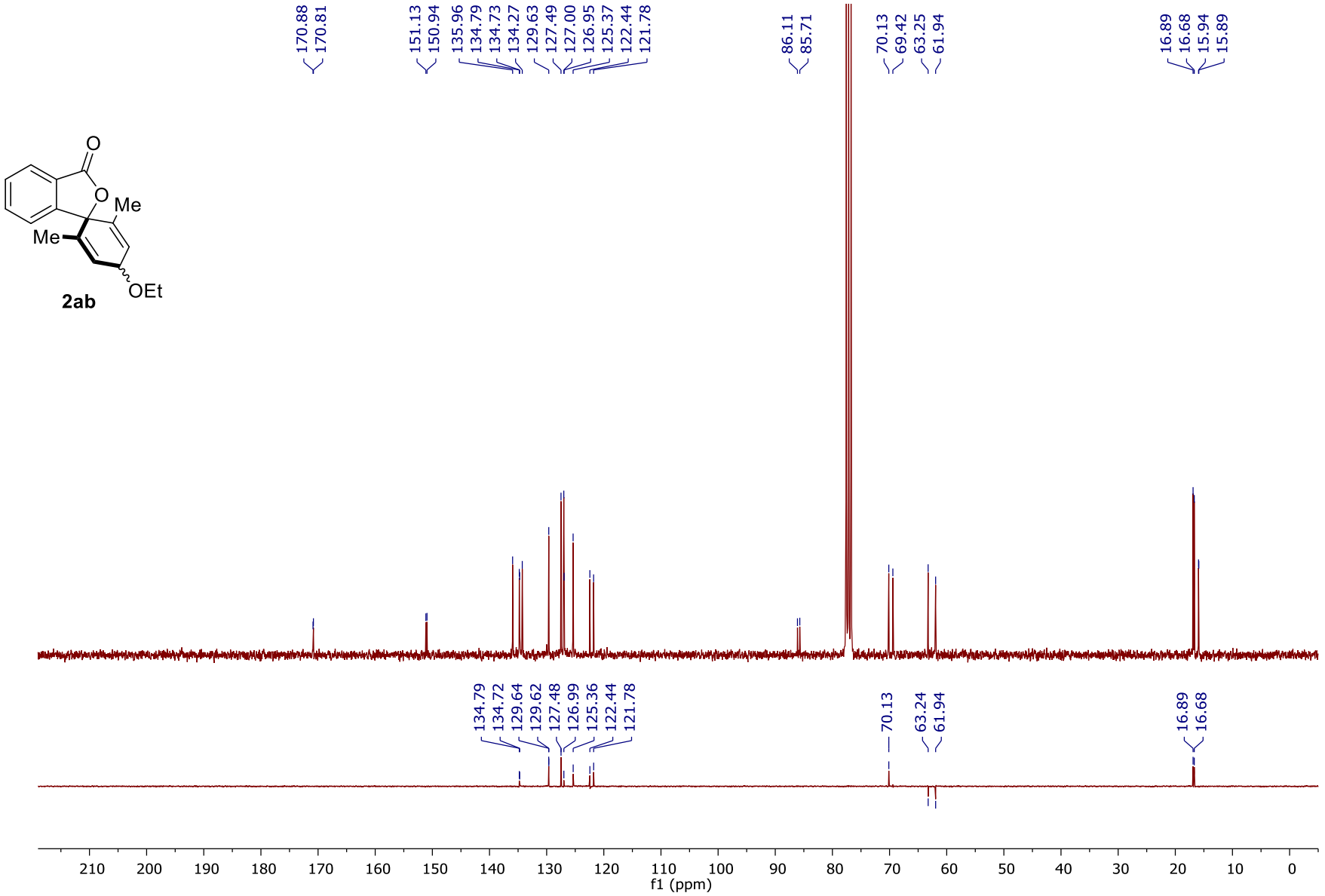
^{13}C NMR (101 MHz, $CDCl_3$) of the diastereoisomeric mixture



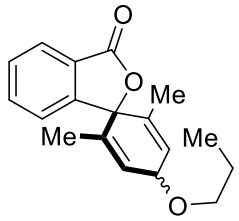
^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture **2ab**



^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture

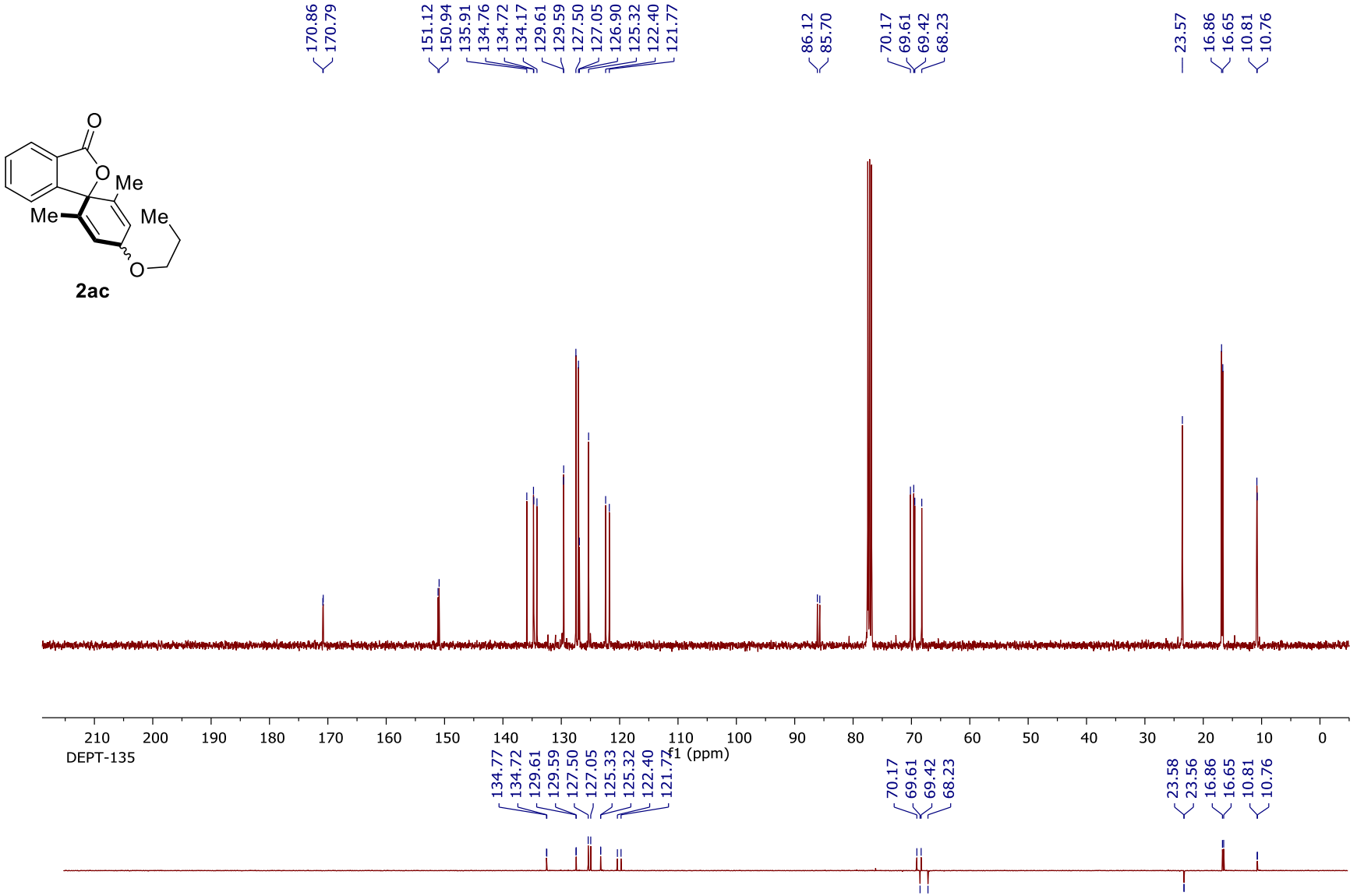


^{1}H NMR (400 MHz, $CDCl_3$) of the diastereomeric mixture **2ac**

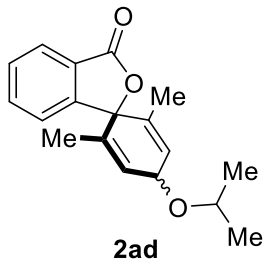


2ac

^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture

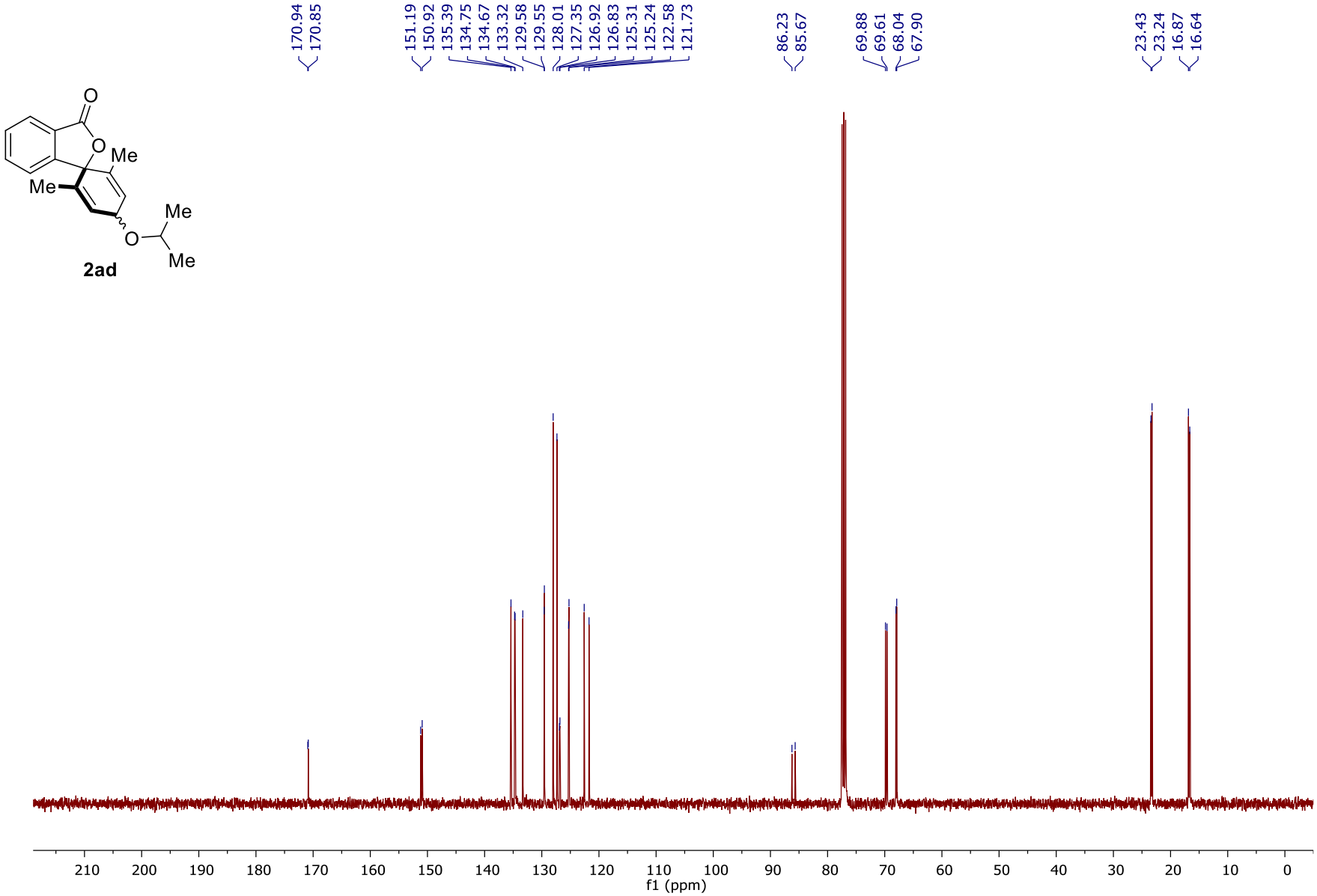


^{1}H NMR (400 MHz, $CDCl_3$) of the diastereomeric mixture **2ad**

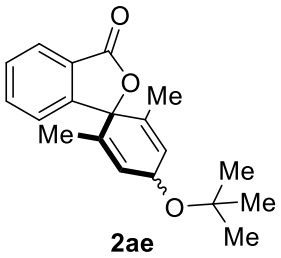


2ad

^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture

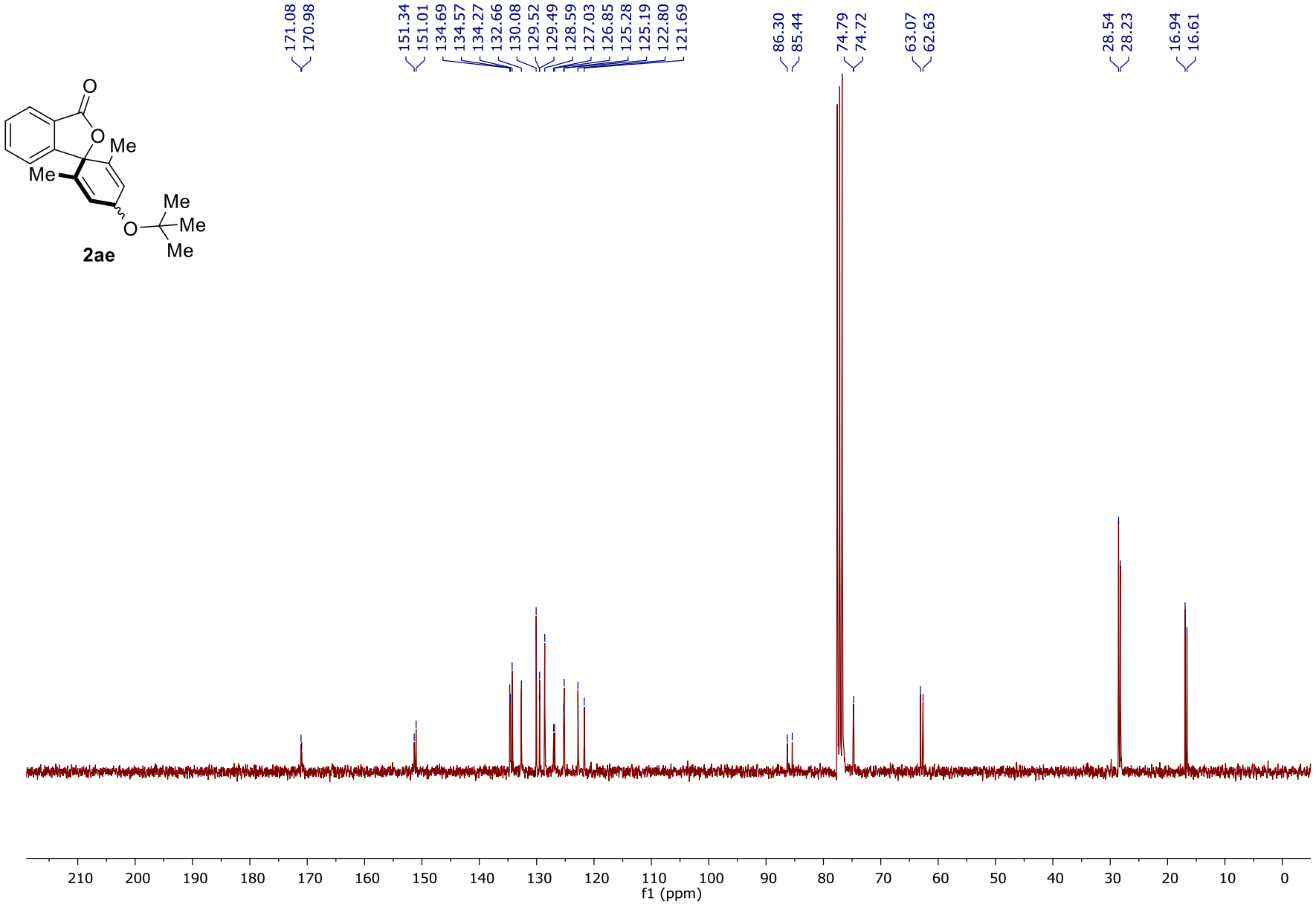


^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture **2ae**

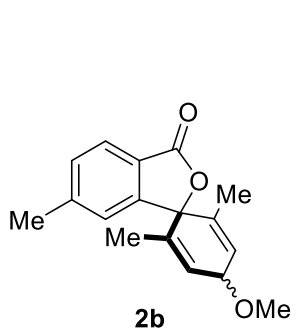


2ae

^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture

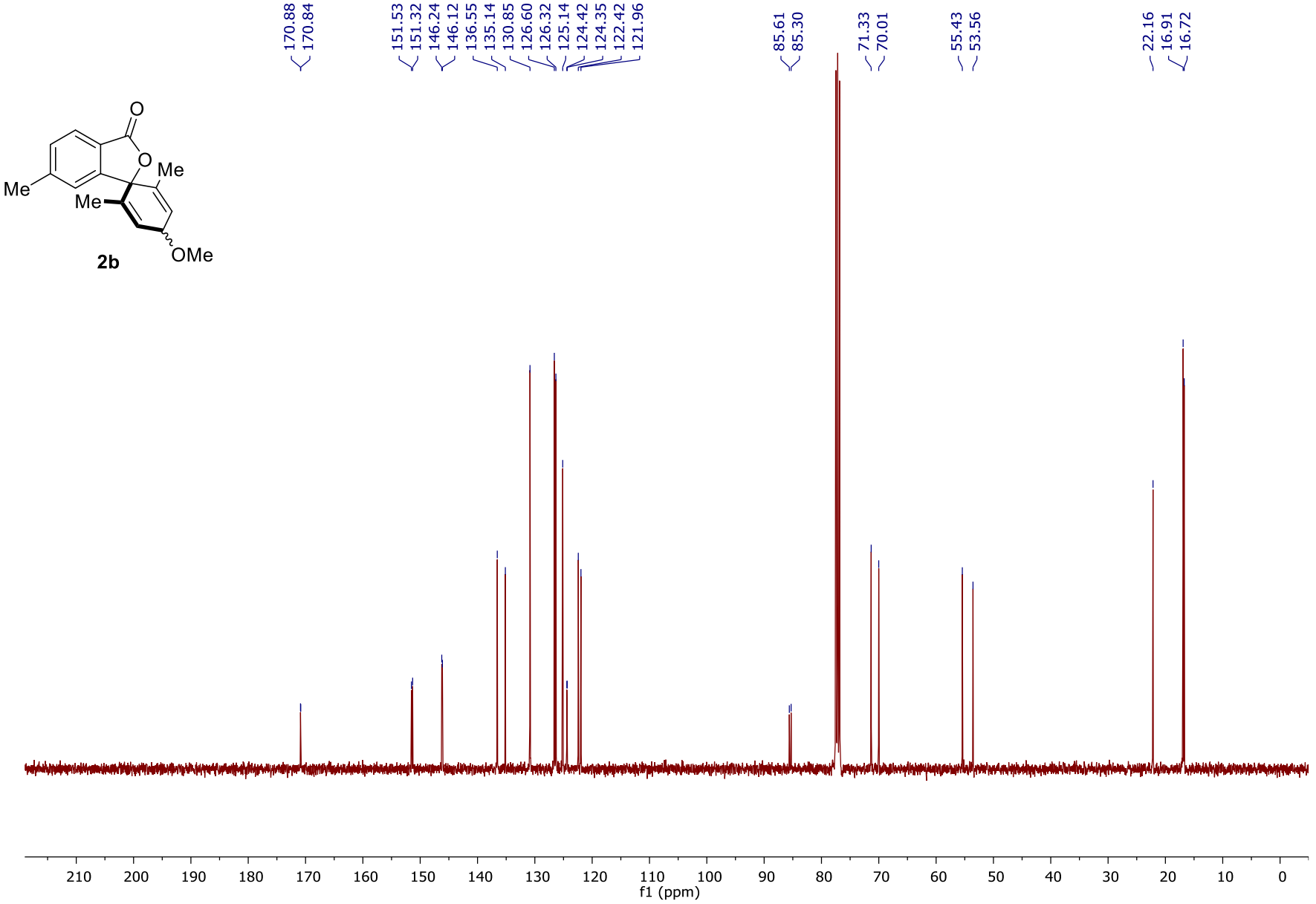


^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture **2b**

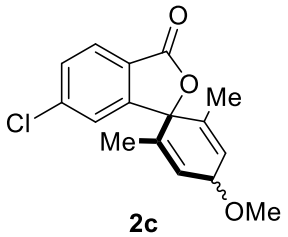


2b

^{13}C NMR (101 MHz, $CDCl_3$) of the diasteromeric mixture:

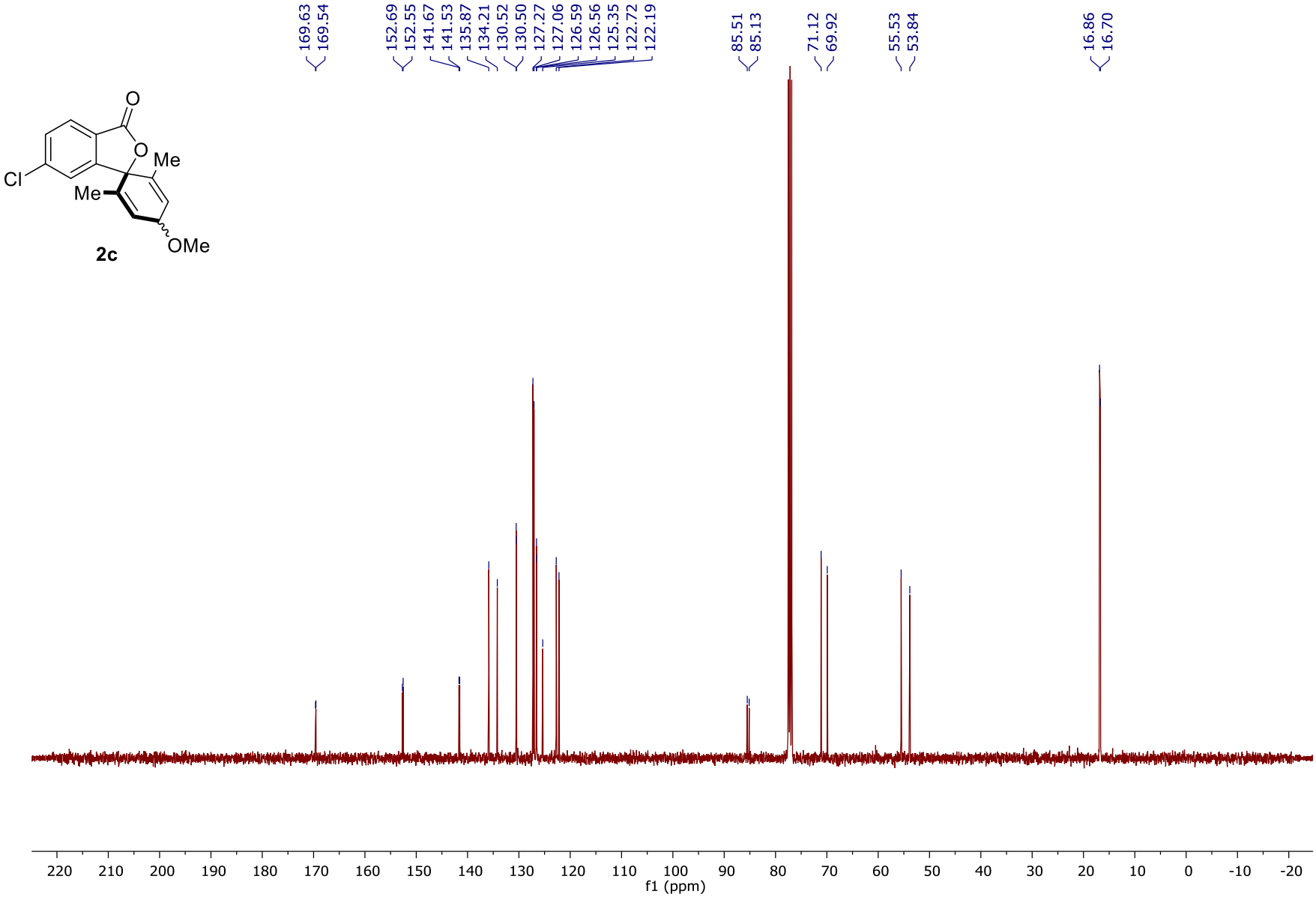


^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture **2c**

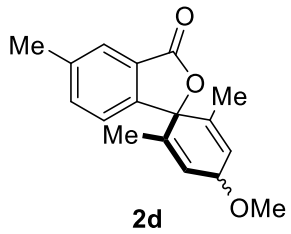


2c

^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture

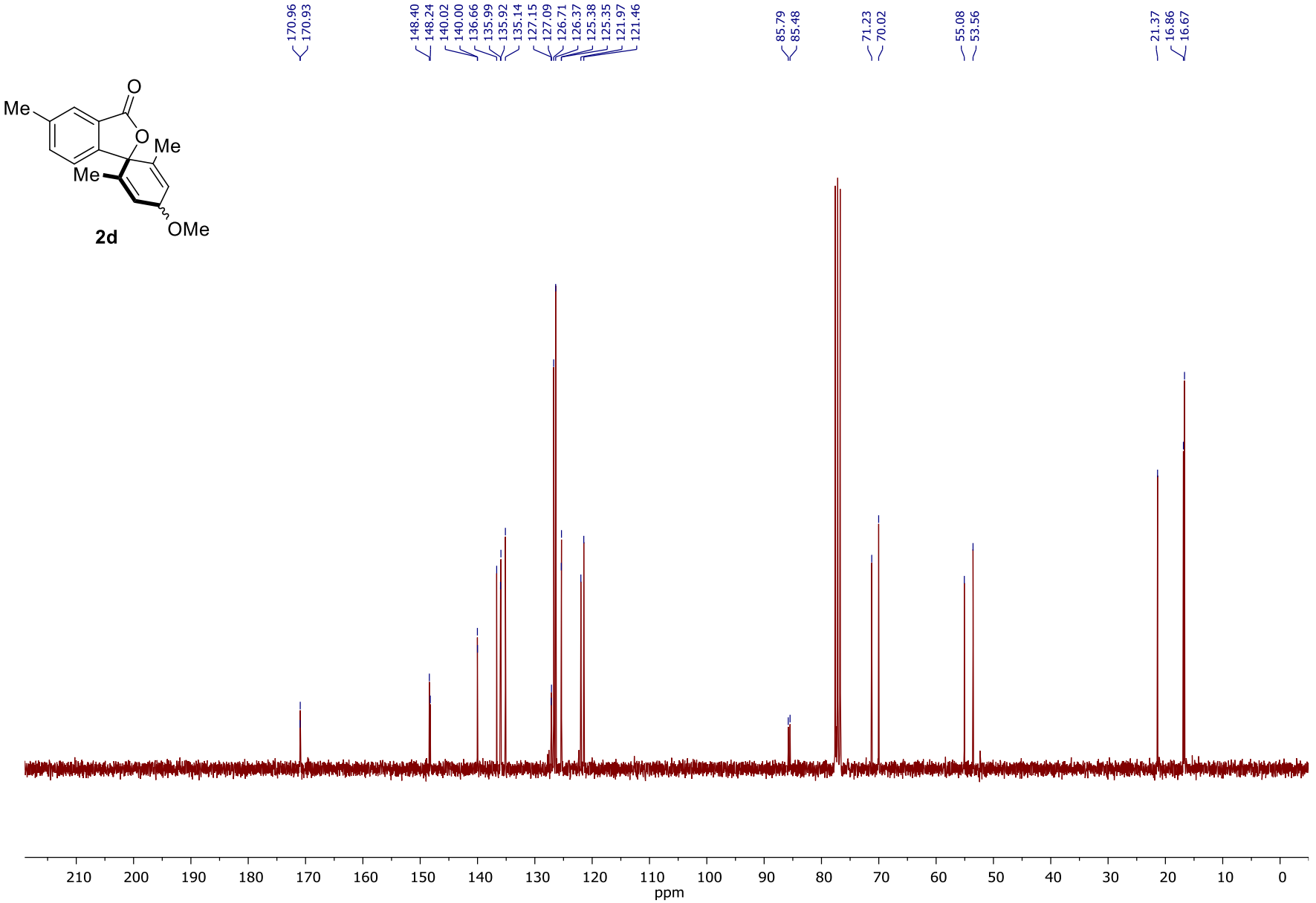


^{1}H NMR (300 MHz, $CDCl_3$) for the diastereomeric mixture **2d**

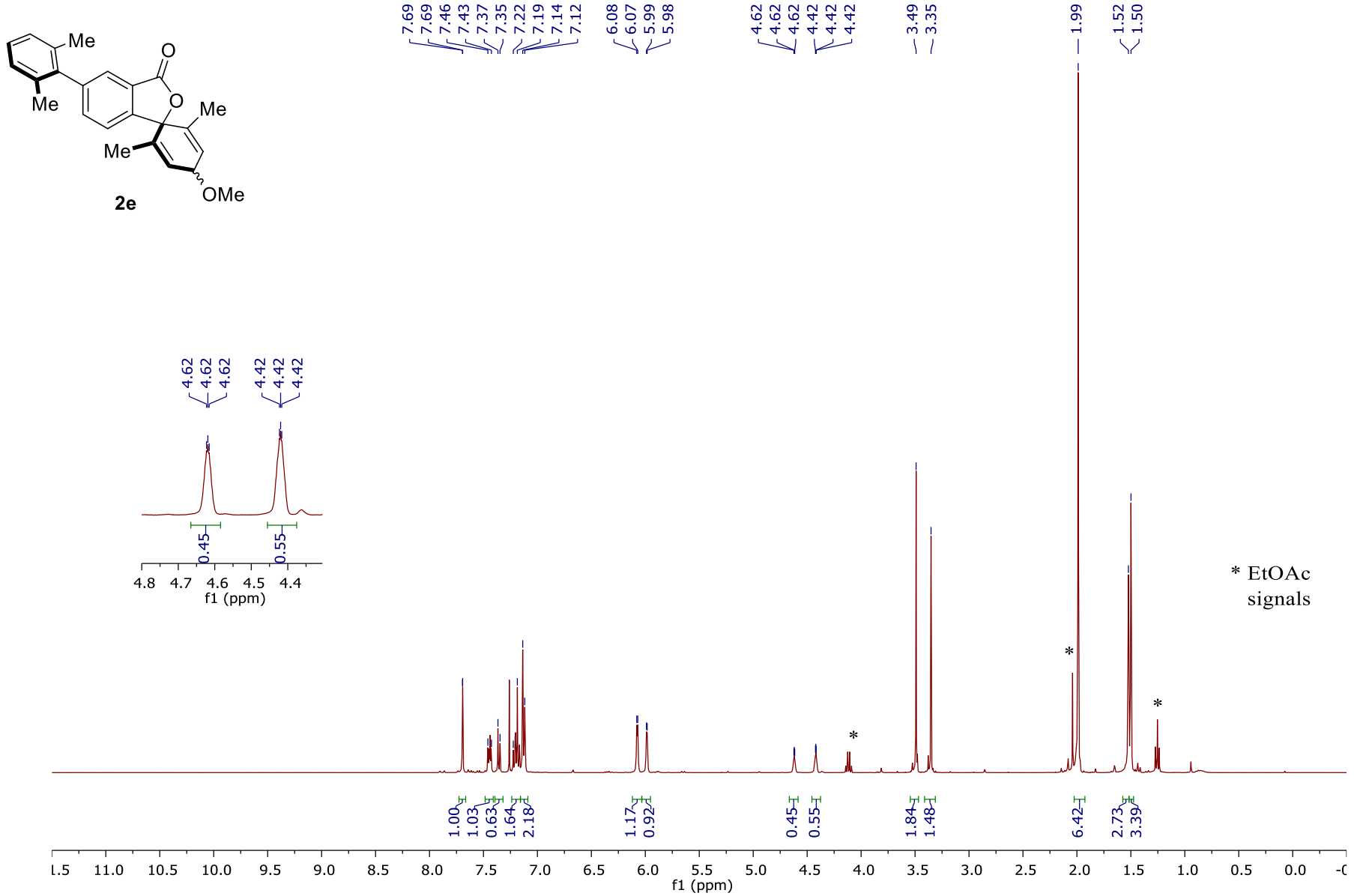


2d

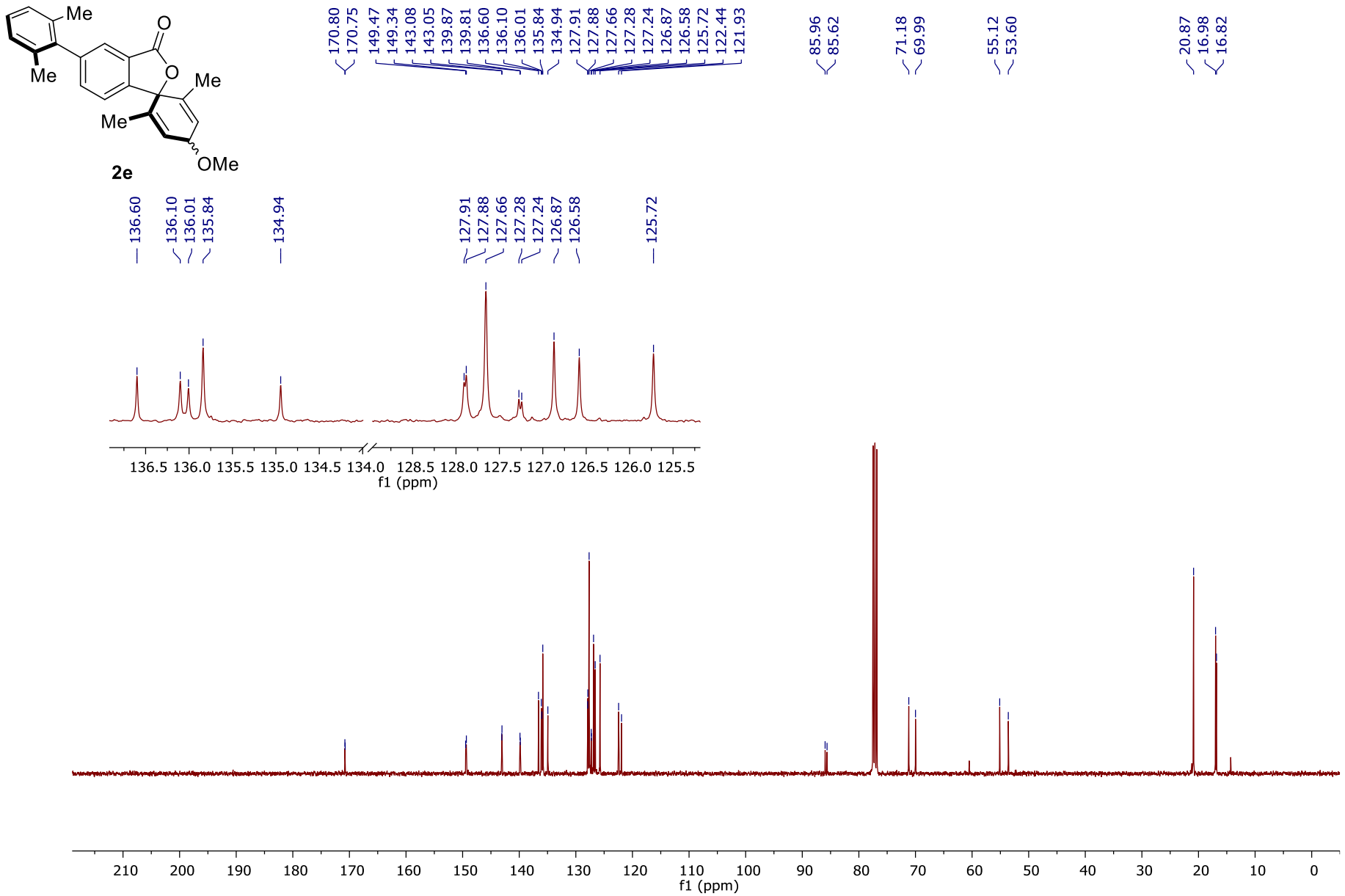
^{13}C NMR (75 MHz, $CDCl_3$) for the diastereomeric mixture



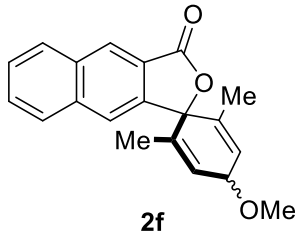
^{1}H NMR (300 MHz, $CDCl_3$) for the diastereomeric mixture **2e**



^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture

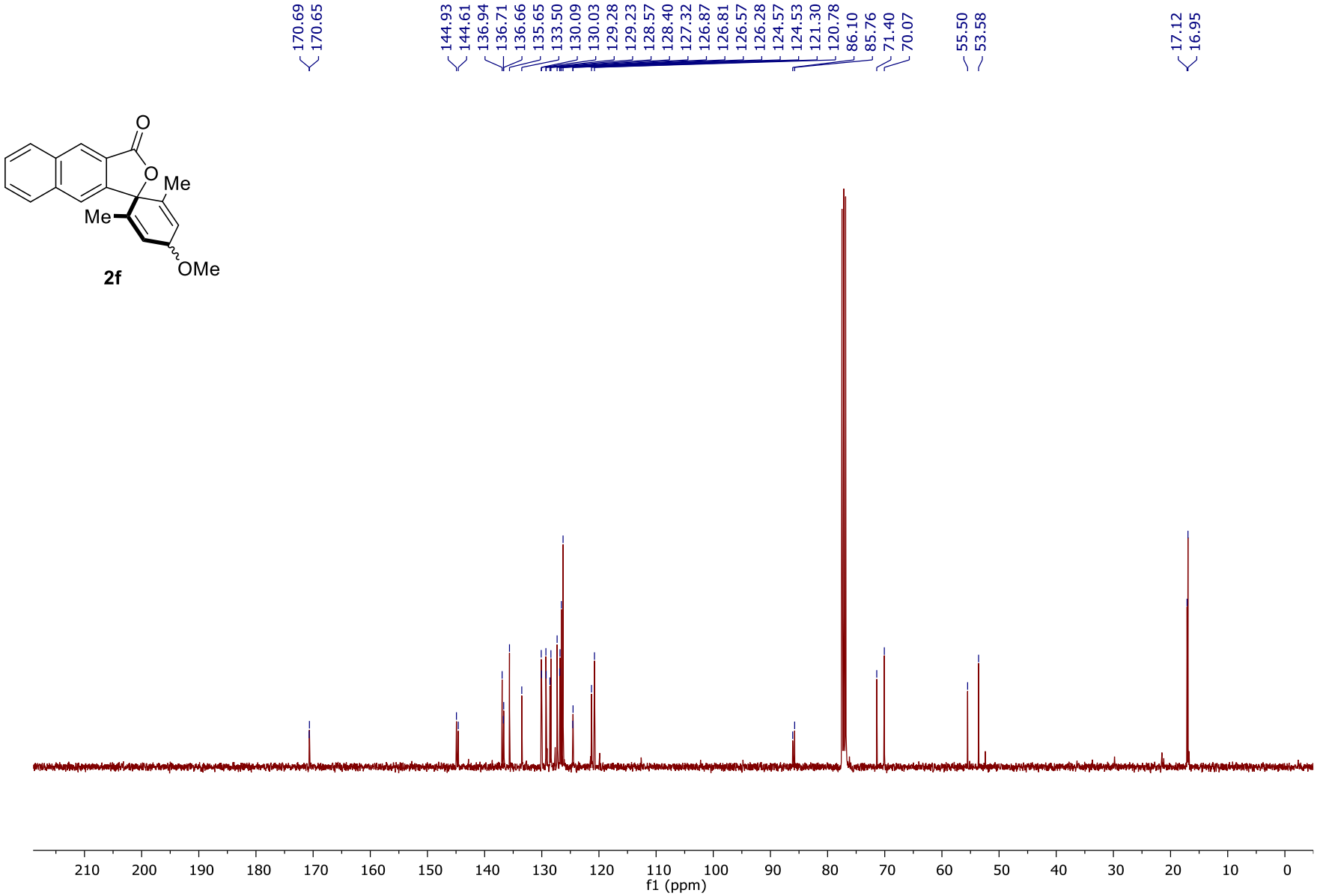


^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture **2f**

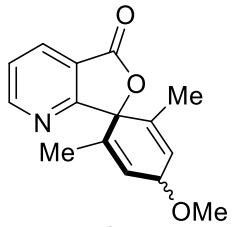


2f

^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture

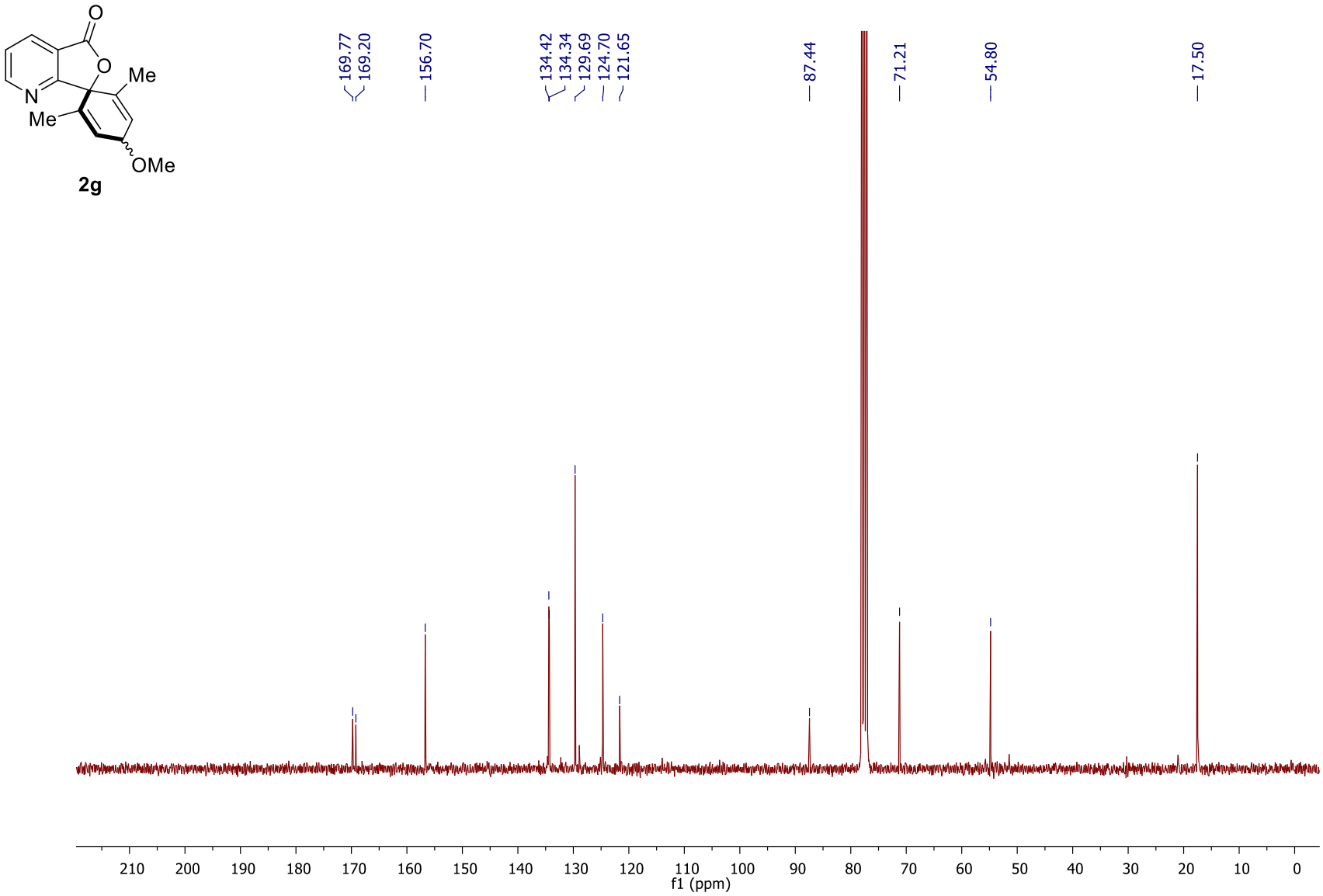


^{1}H NMR (300 MHz, $CDCl_3$) of a single dias **2g**

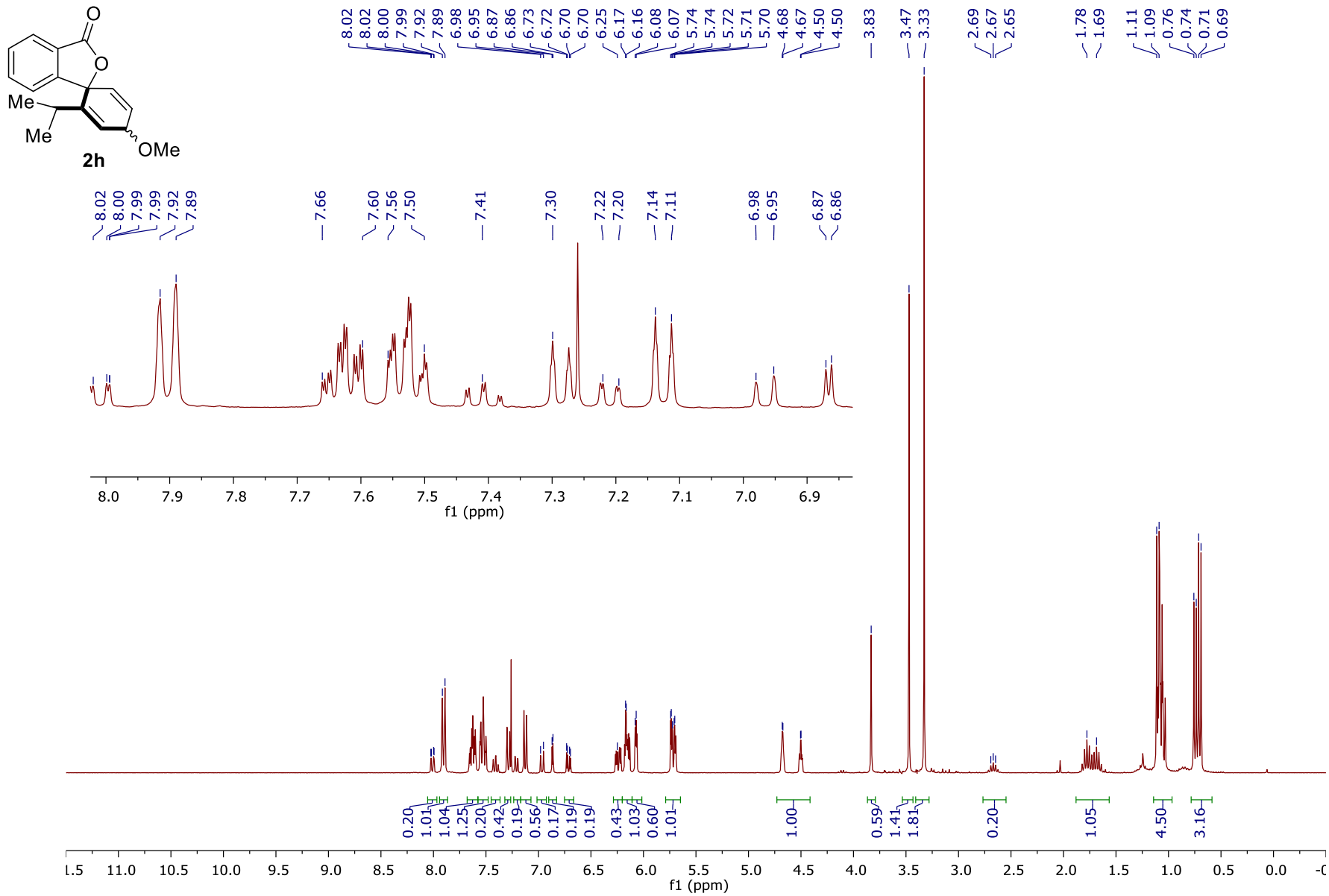


2g

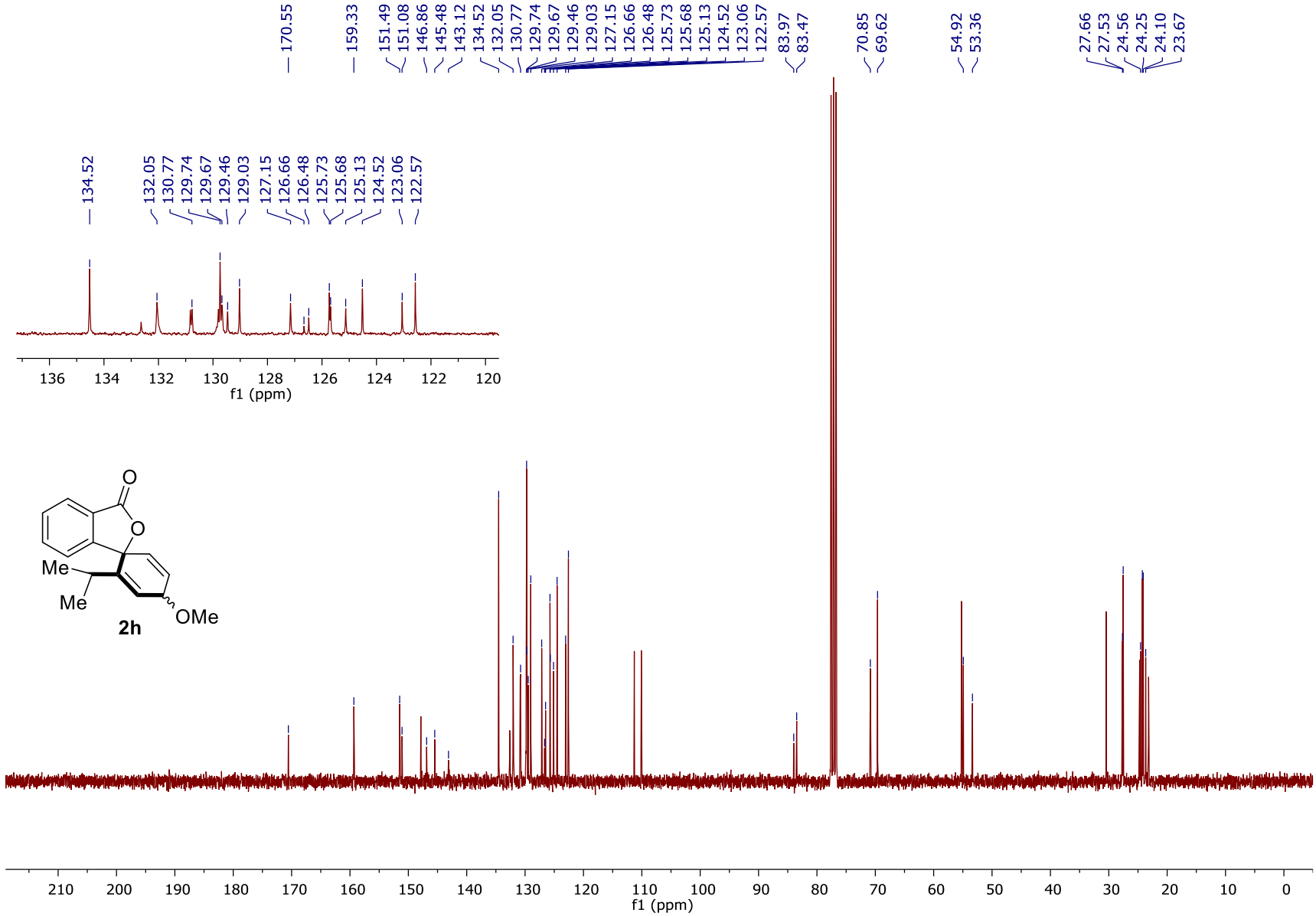
^{13}C NMR (75 MHz, $CDCl_3$) of the diastereomeric mixture



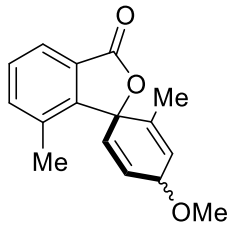
^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture **2h**



^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture

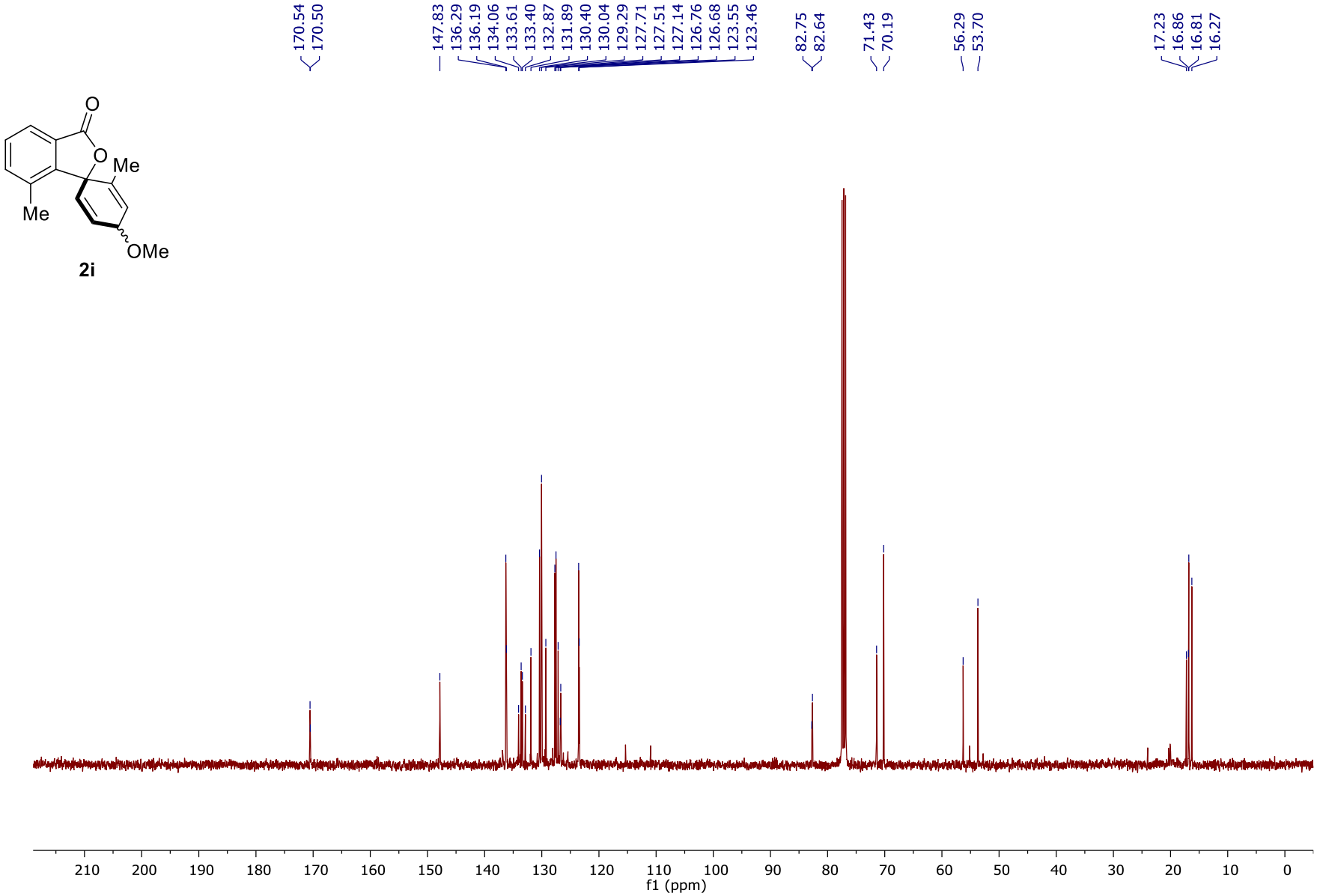


^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture **2i**

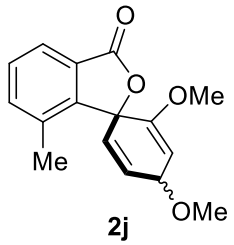


2i

^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture

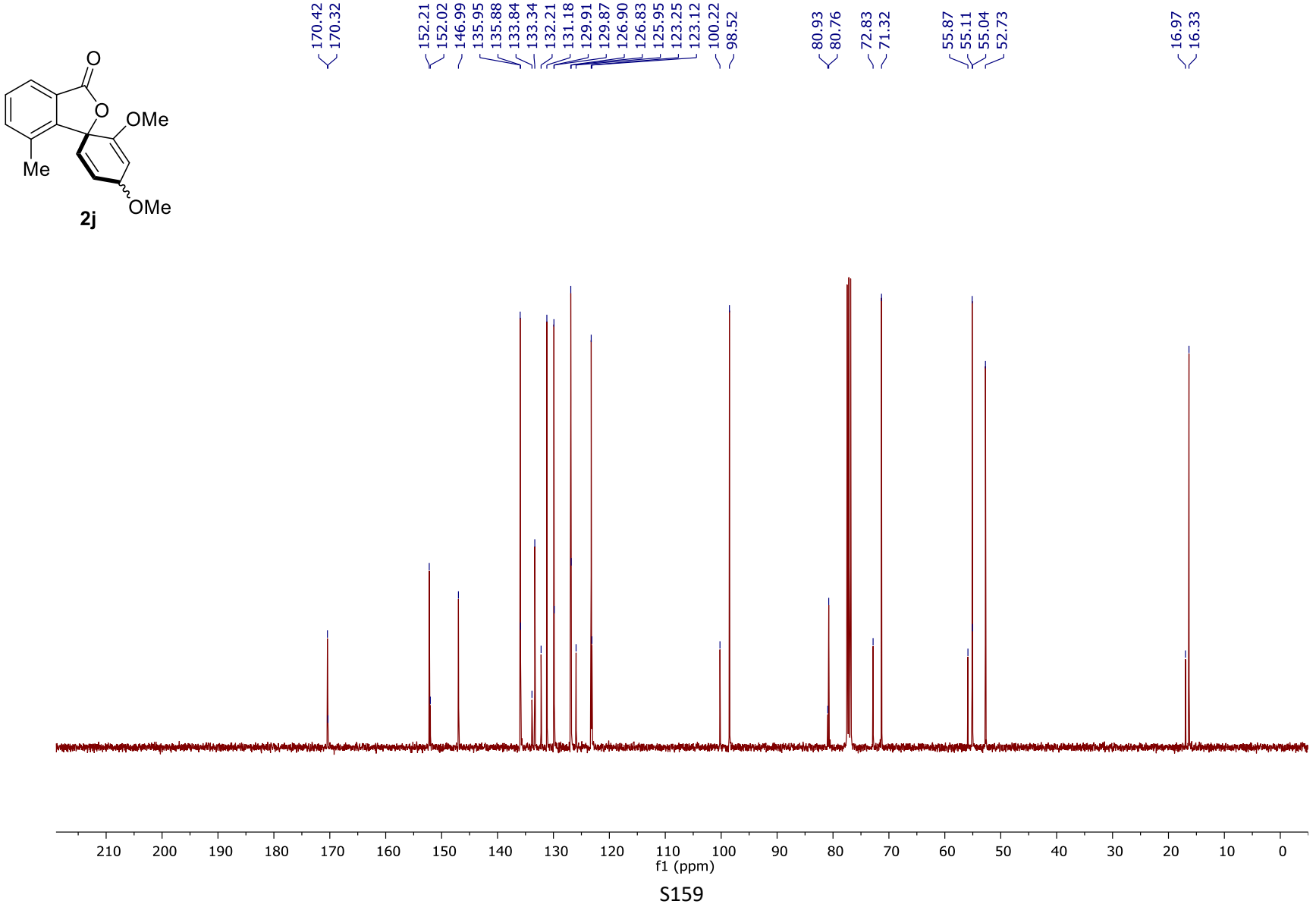


^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture **2j**

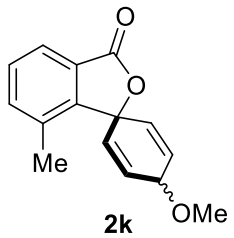


2j

^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture

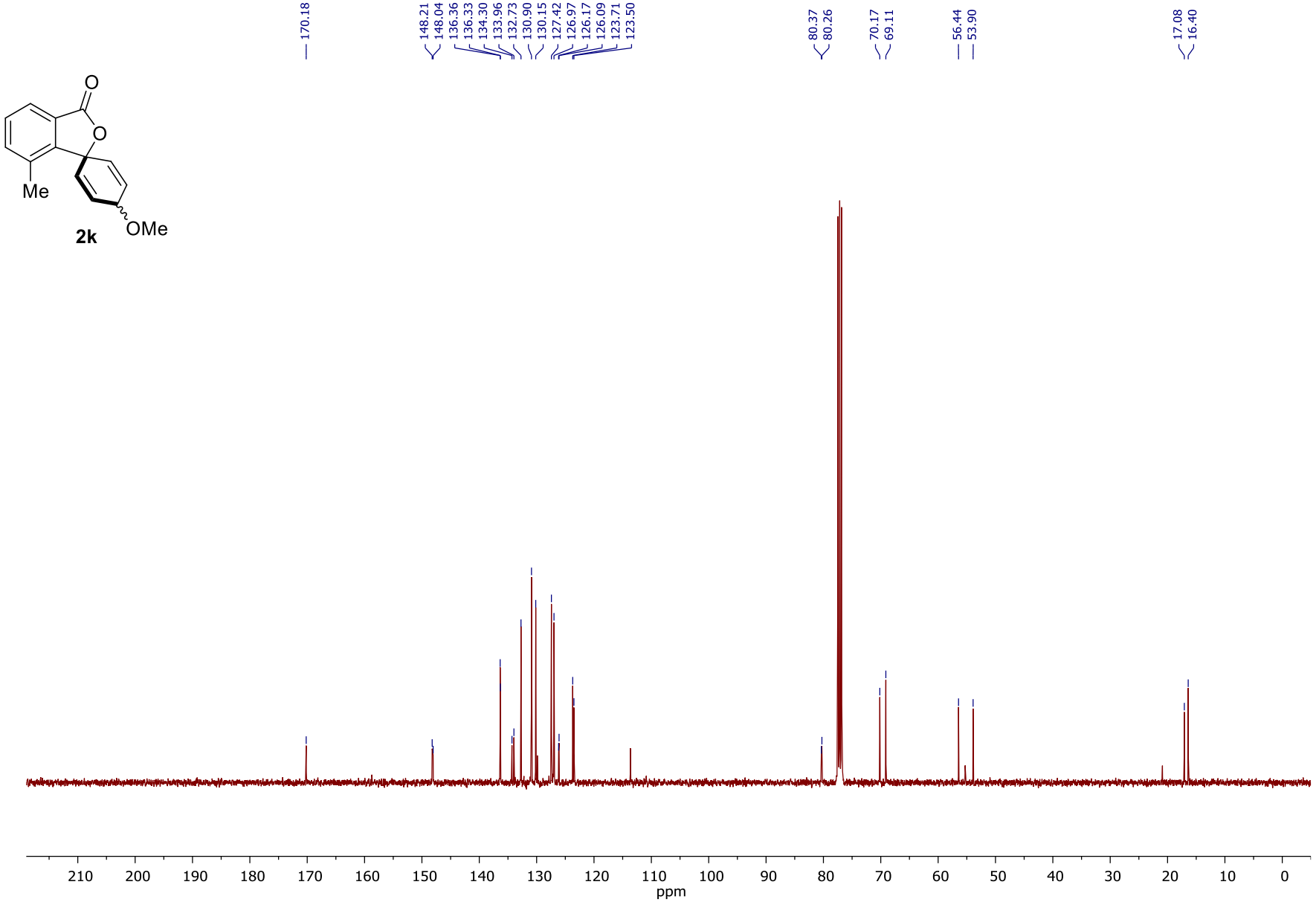


^{1}H NMR (400 MHz, $CDCl_3$) of the diasteromeric mixture **2k**

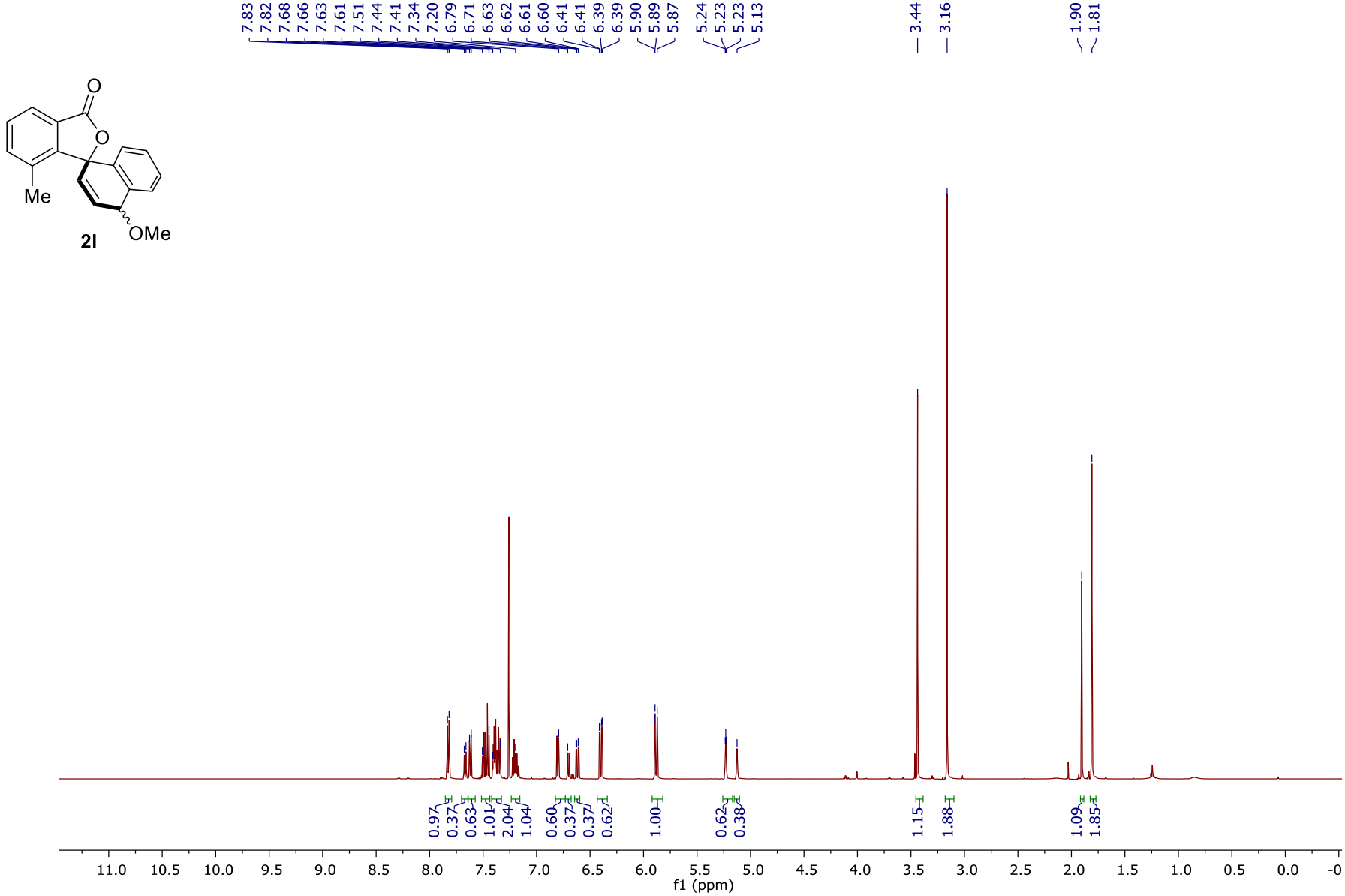


2k

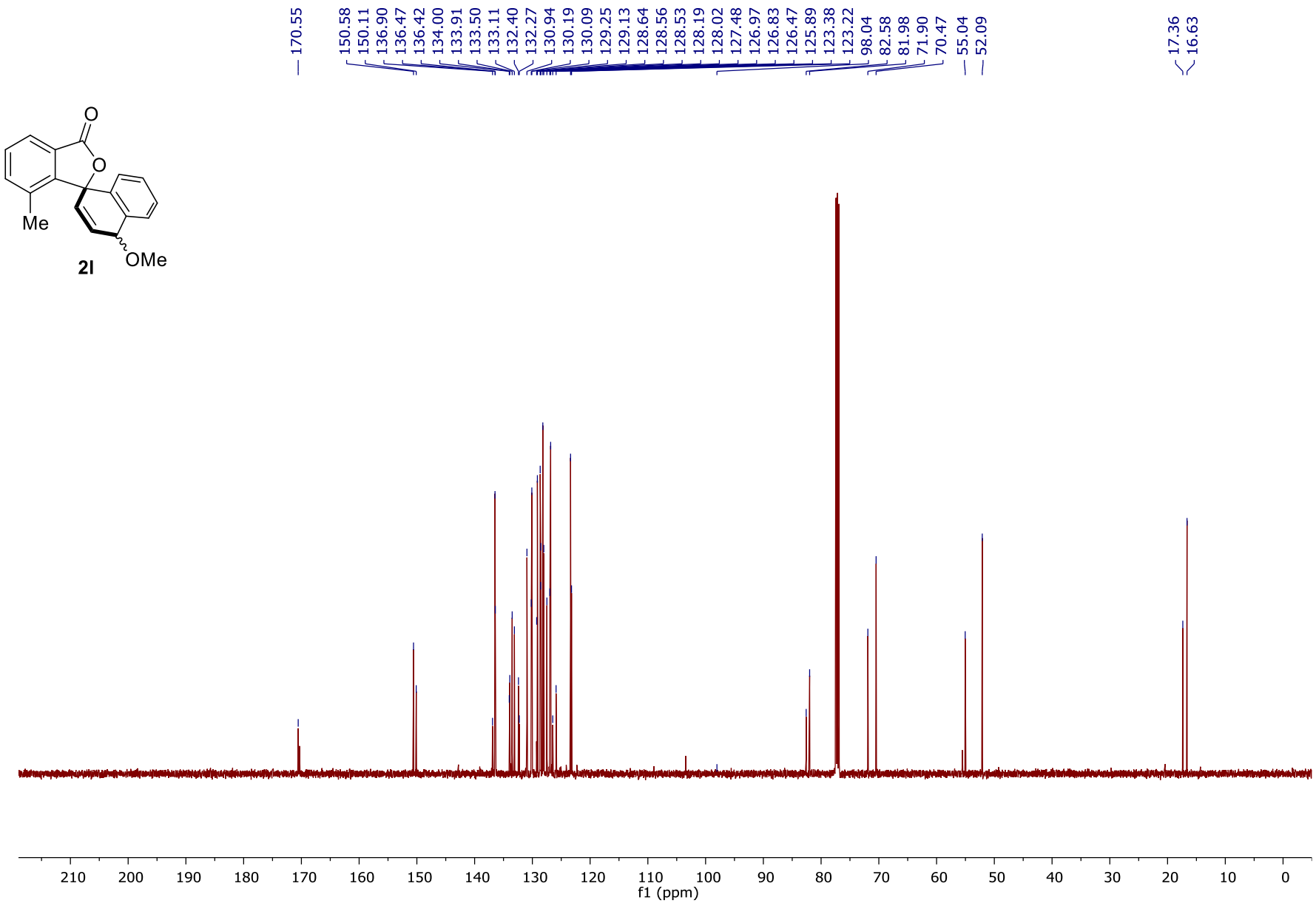
^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture **2k**



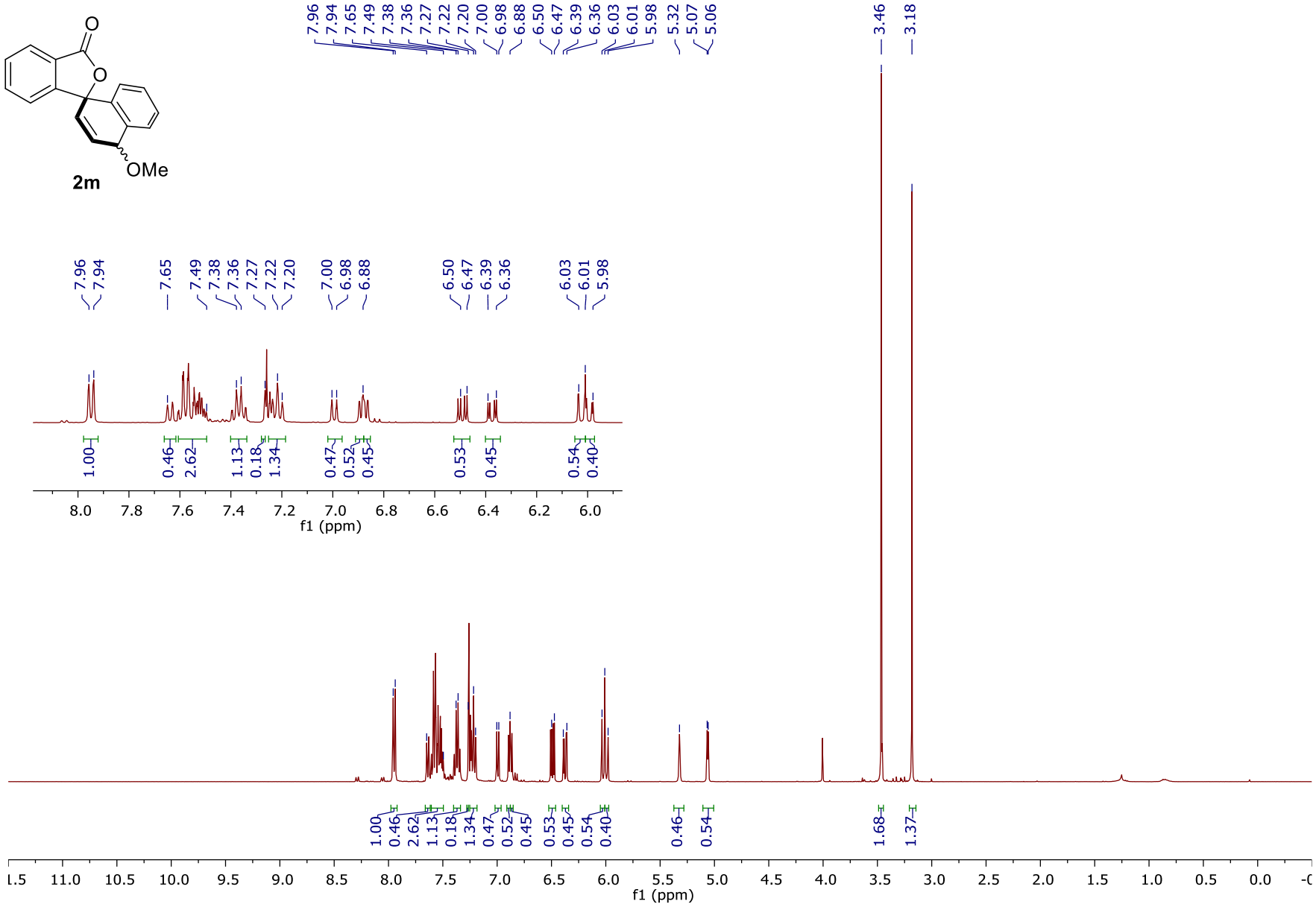
^{1}H NMR (500 MHz, $CDCl_3$) for the diastereomeric mixture **2l**



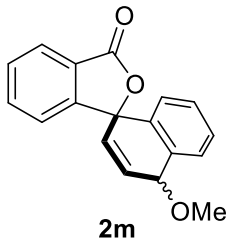
^{13}C NMR (126 MHz, $CDCl_3$) for the diastereomeric mixture



^{1}H NMR (500 MHz, $CDCl_3$) for the diastereomeric mixture **2m**

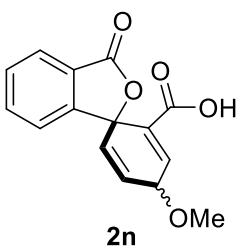


^{13}C NMR (101 MHz, $CDCl_3$) for the diastereomeric mixture



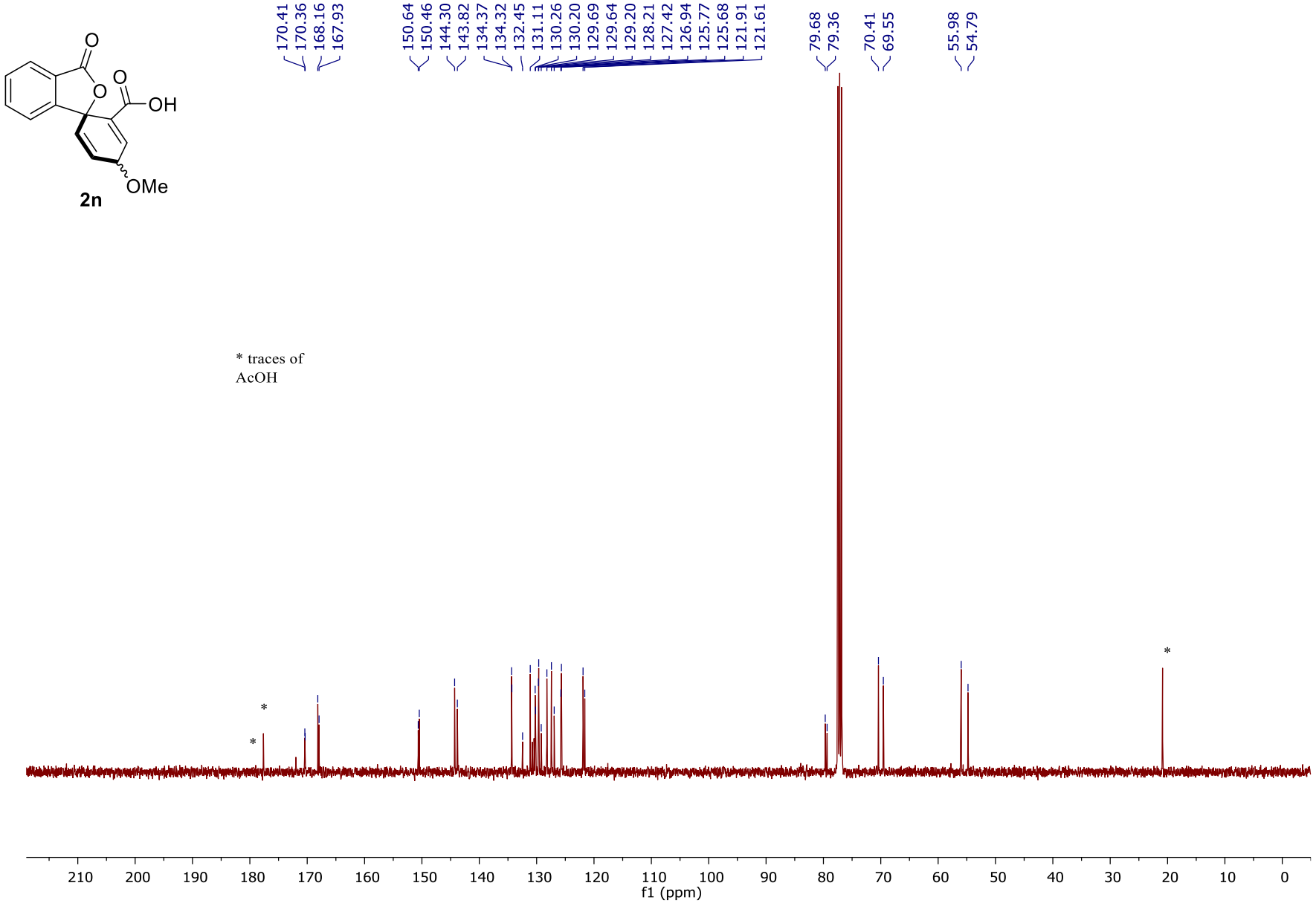
2m

^{1}H NMR (400 MHz, $CDCl_3$) of the diastereomeric mixture **2n**

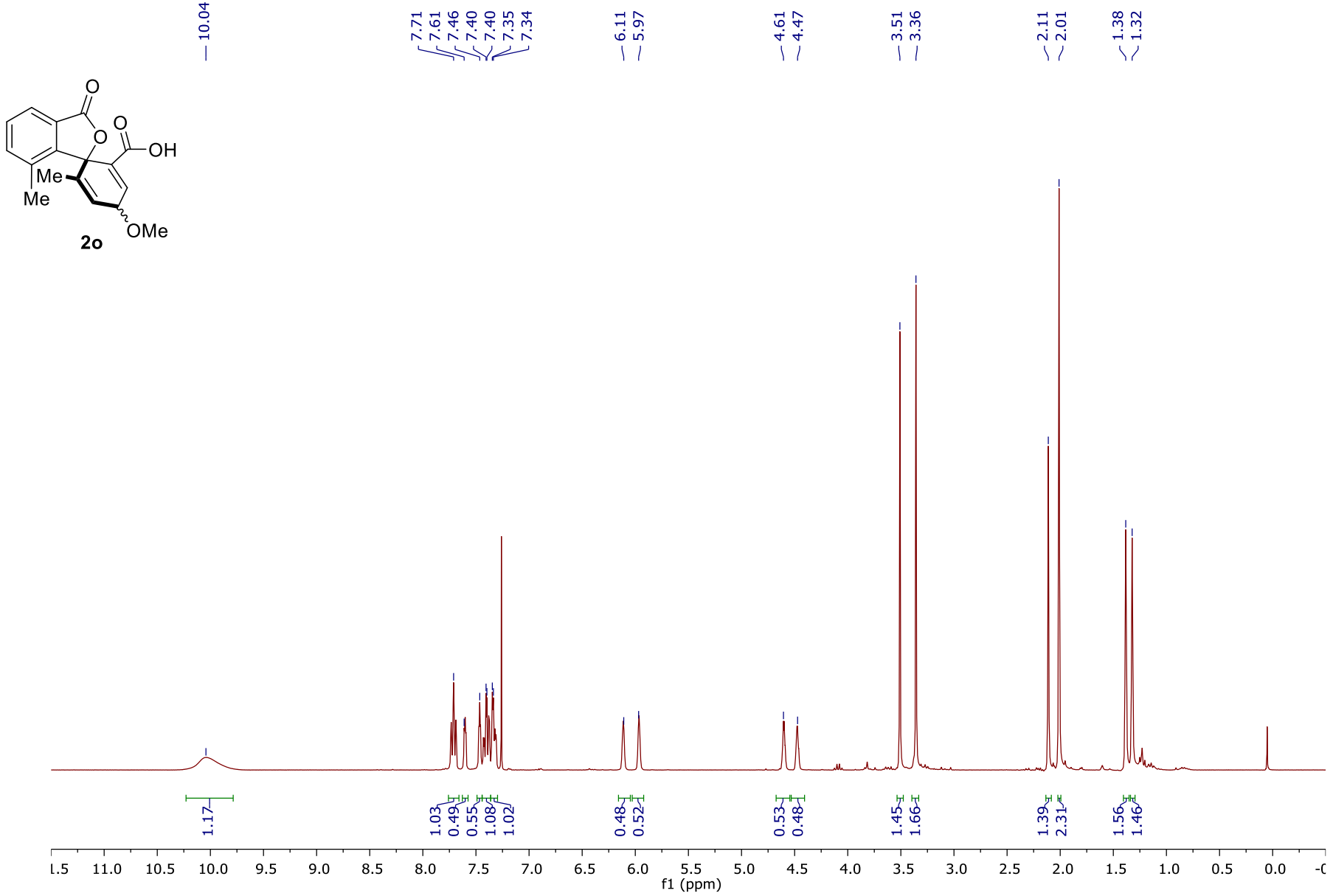


2n

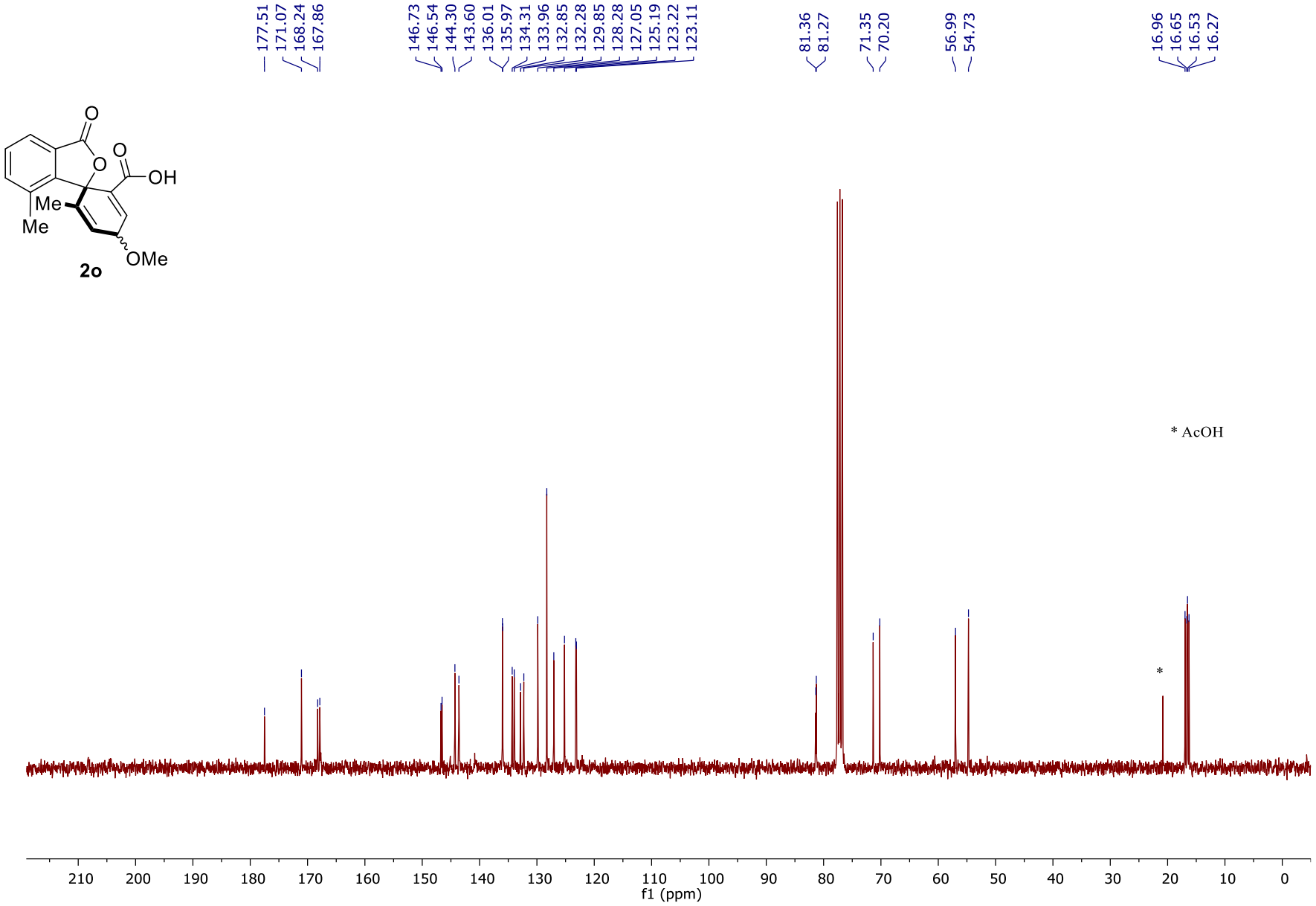
^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture



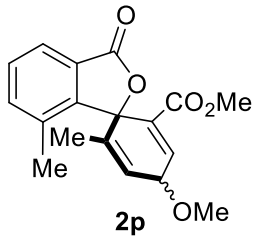
^{1}H NMR (300 MHz, $CDCl_3$) of the diasteromeric mixture: **2o**



^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture:

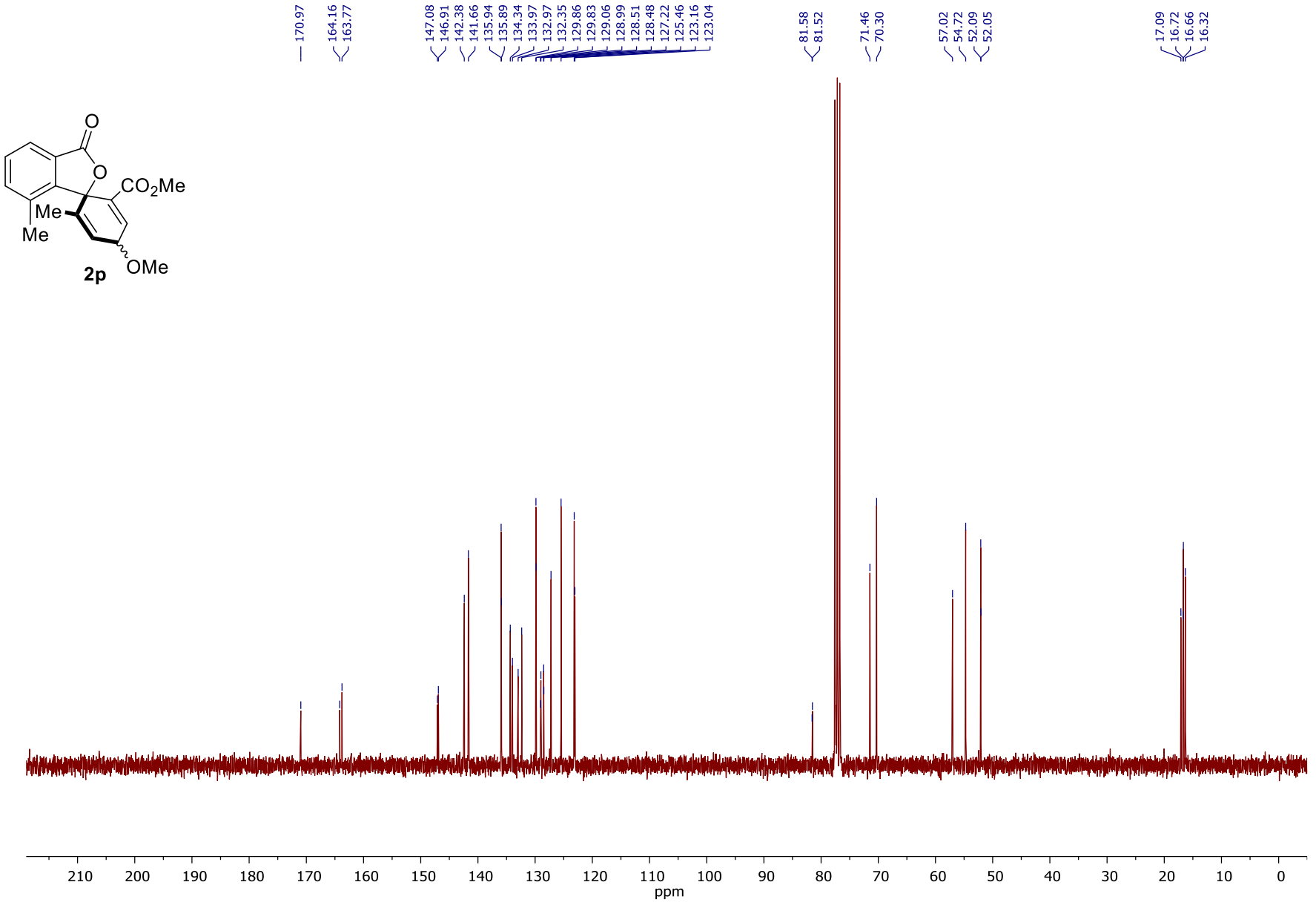


^{1}H NMR (300 MHz, $CDCl_3$) of the diastereomeric mixture **2p**

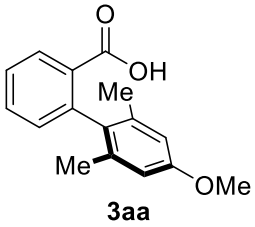


2p

^{13}C NMR (101 MHz, $CDCl_3$) of the diastereomeric mixture:

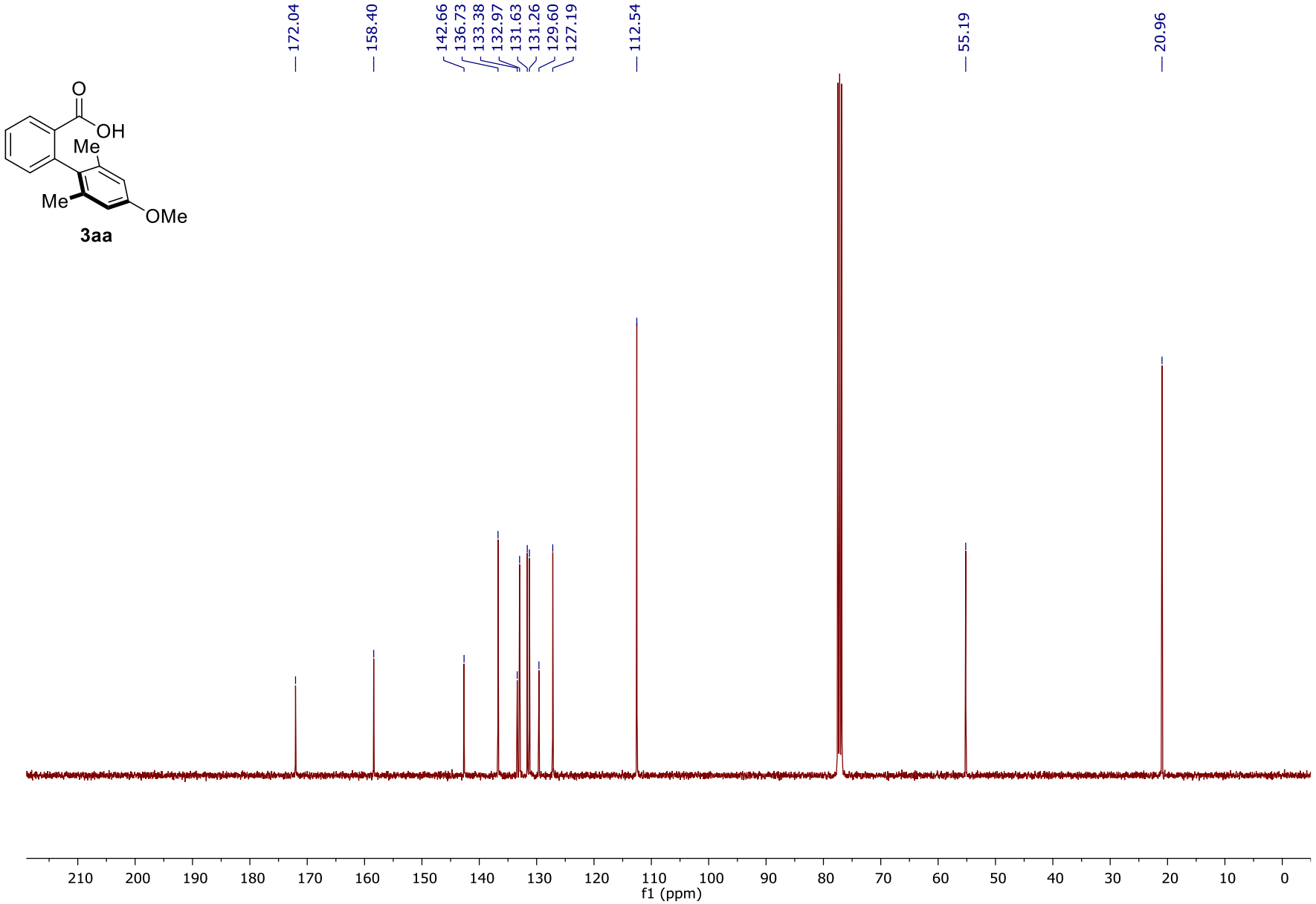


^{1}H NMR (400 MHz, $CDCl_3$) **3aa**

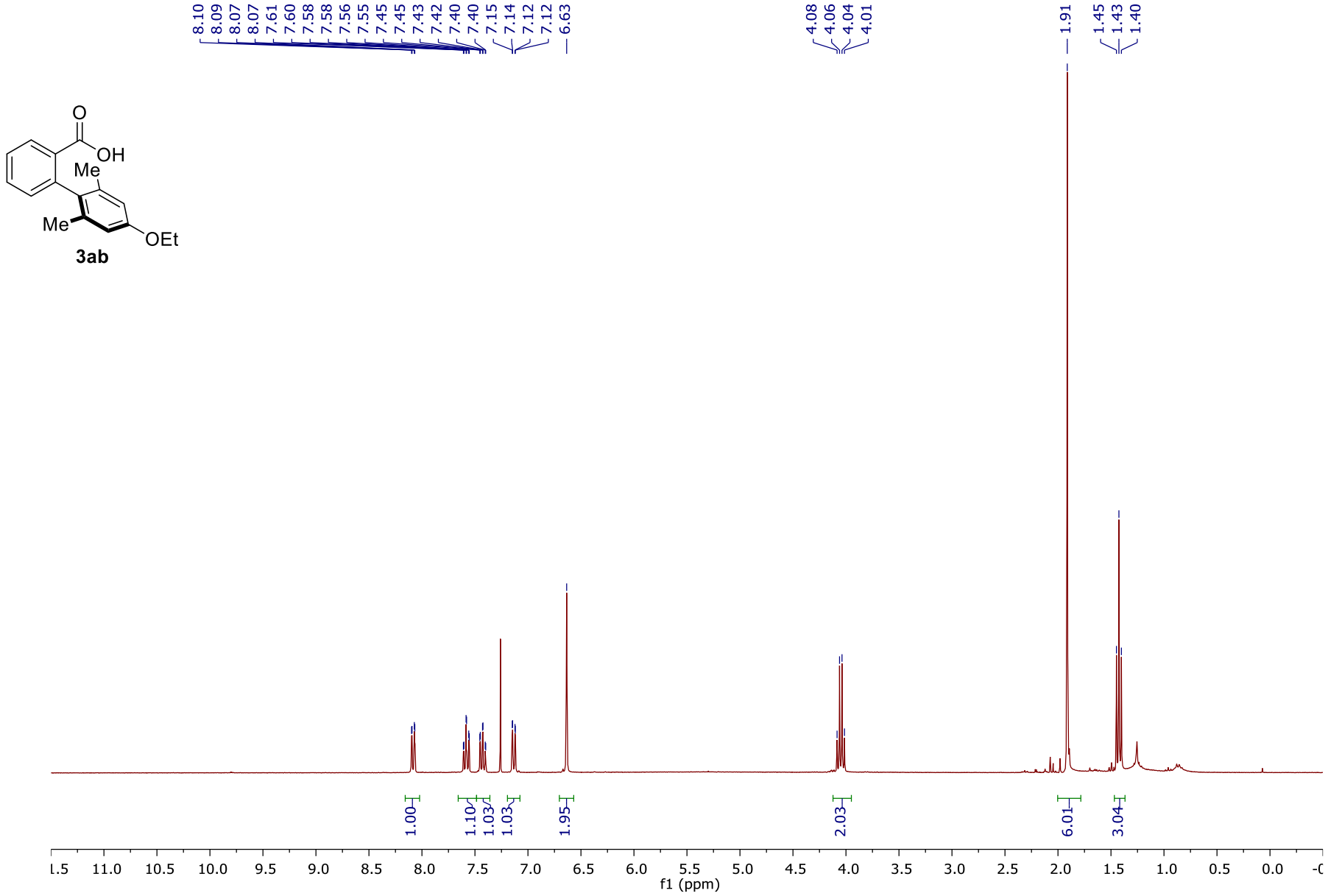


3aa

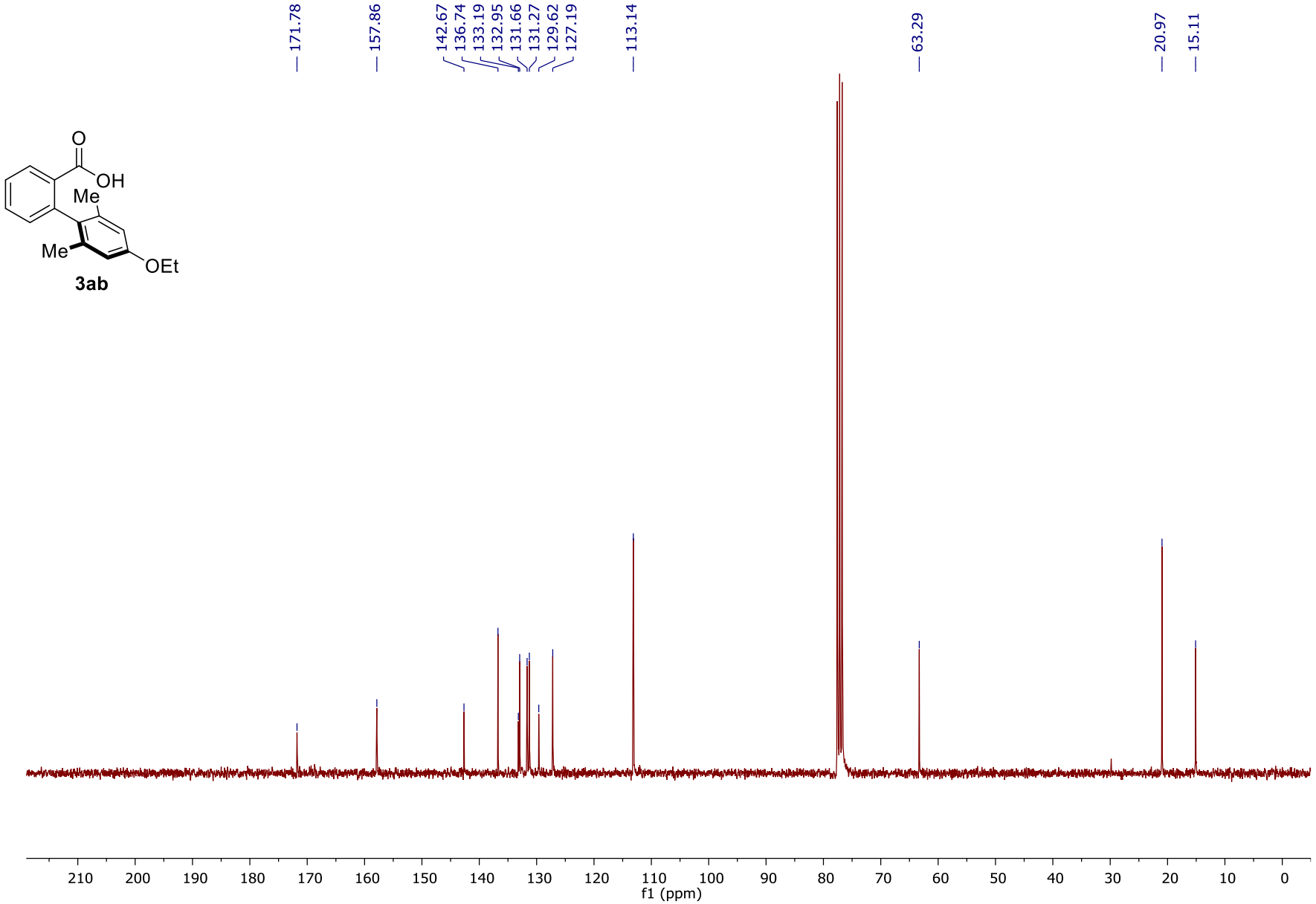
^{13}C NMR (101 MHz, $CDCl_3$)



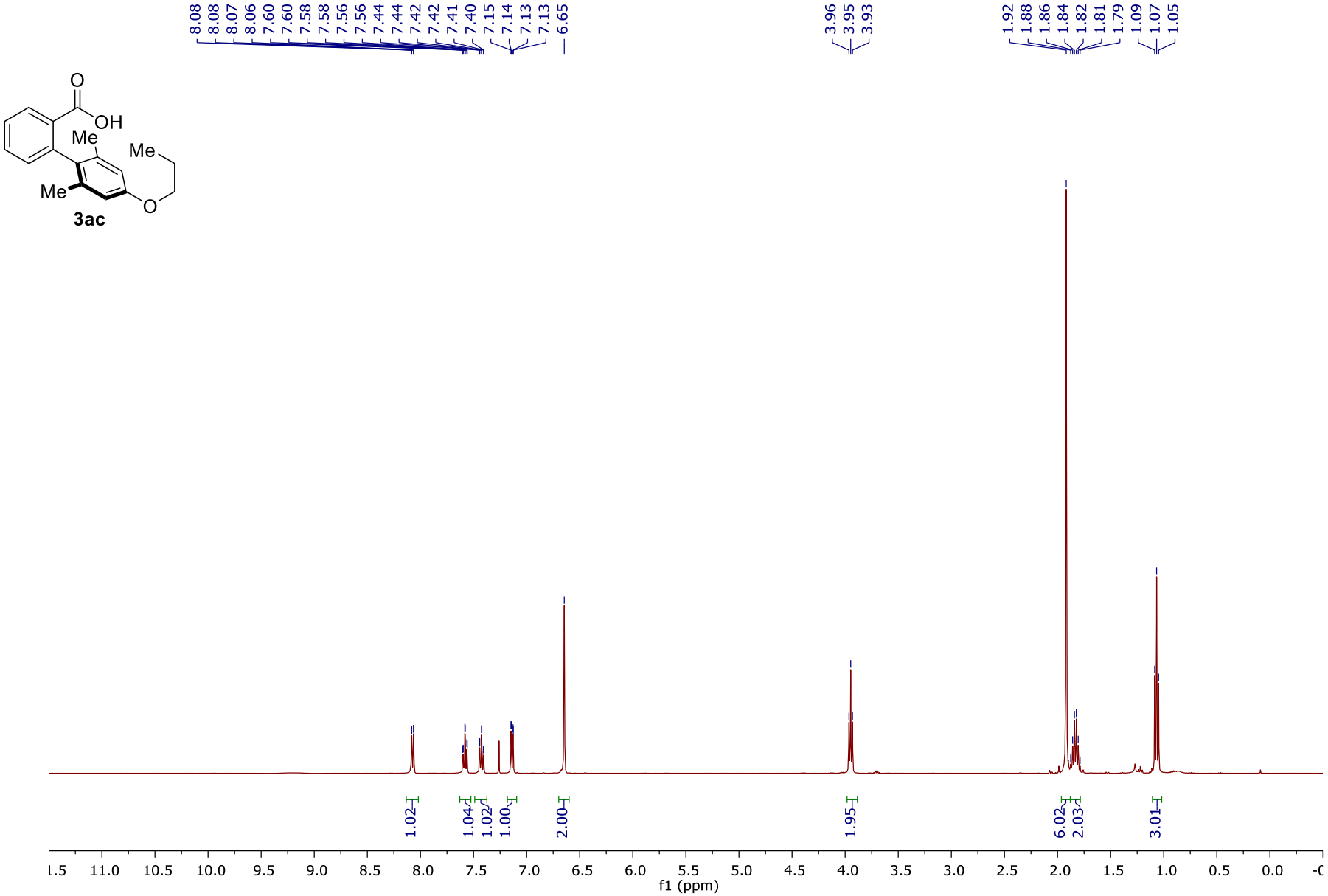
^{1}H NMR (300 MHz, $CDCl_3$) **3ab**



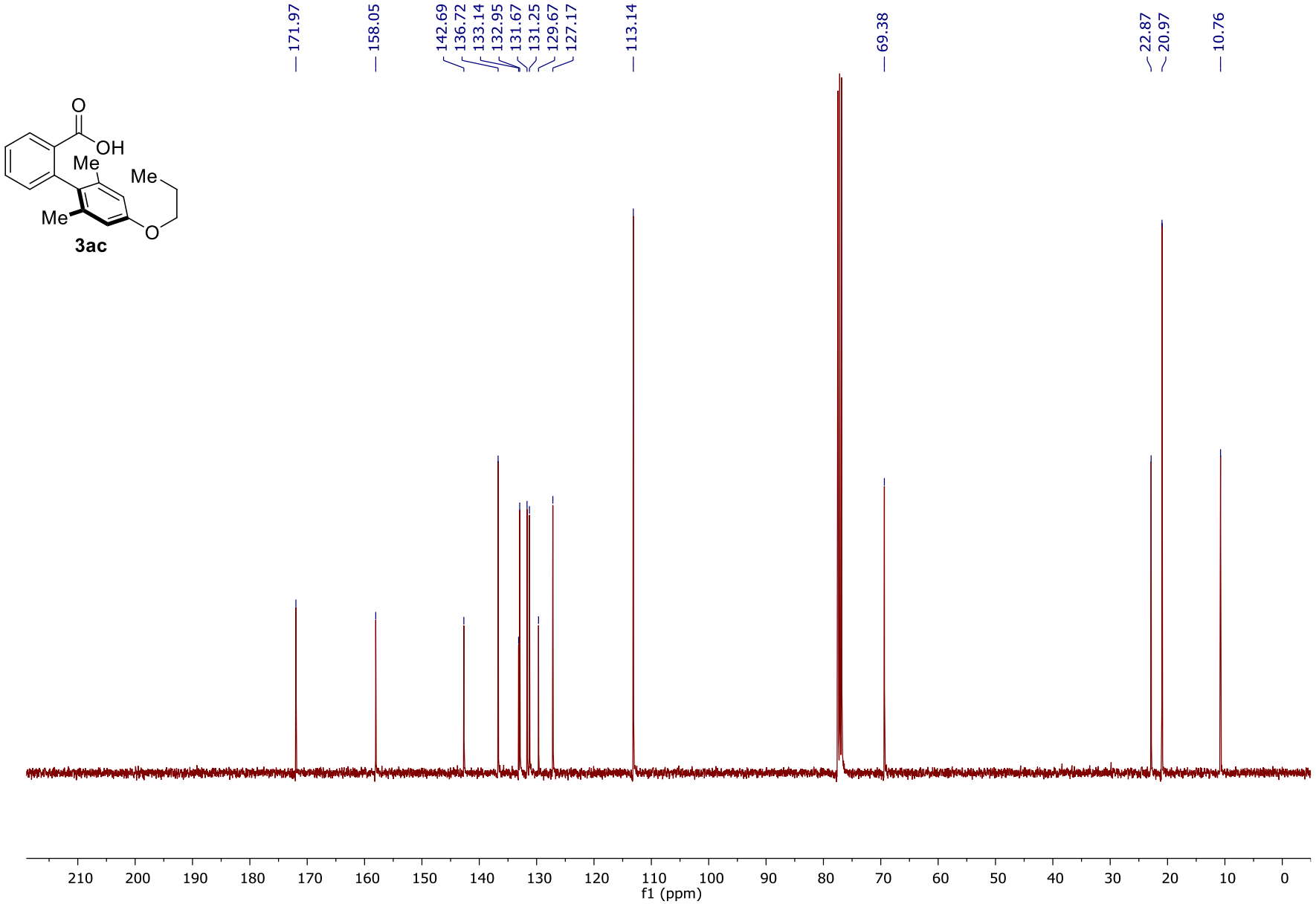
^{13}C NMR (75 MHz, $CDCl_3$)



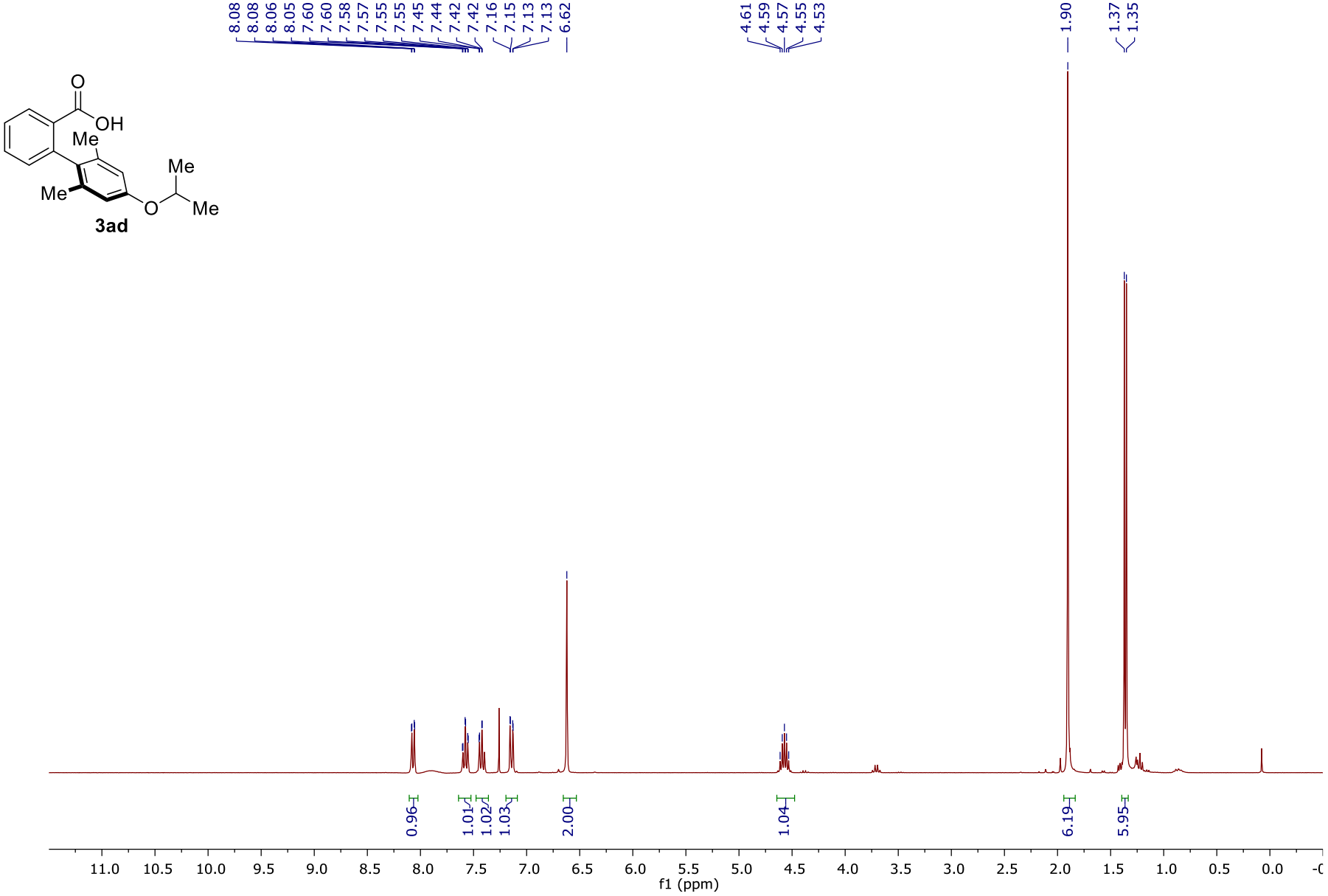
^{1}H NMR (400 MHz, $CDCl_3$) **3ac**



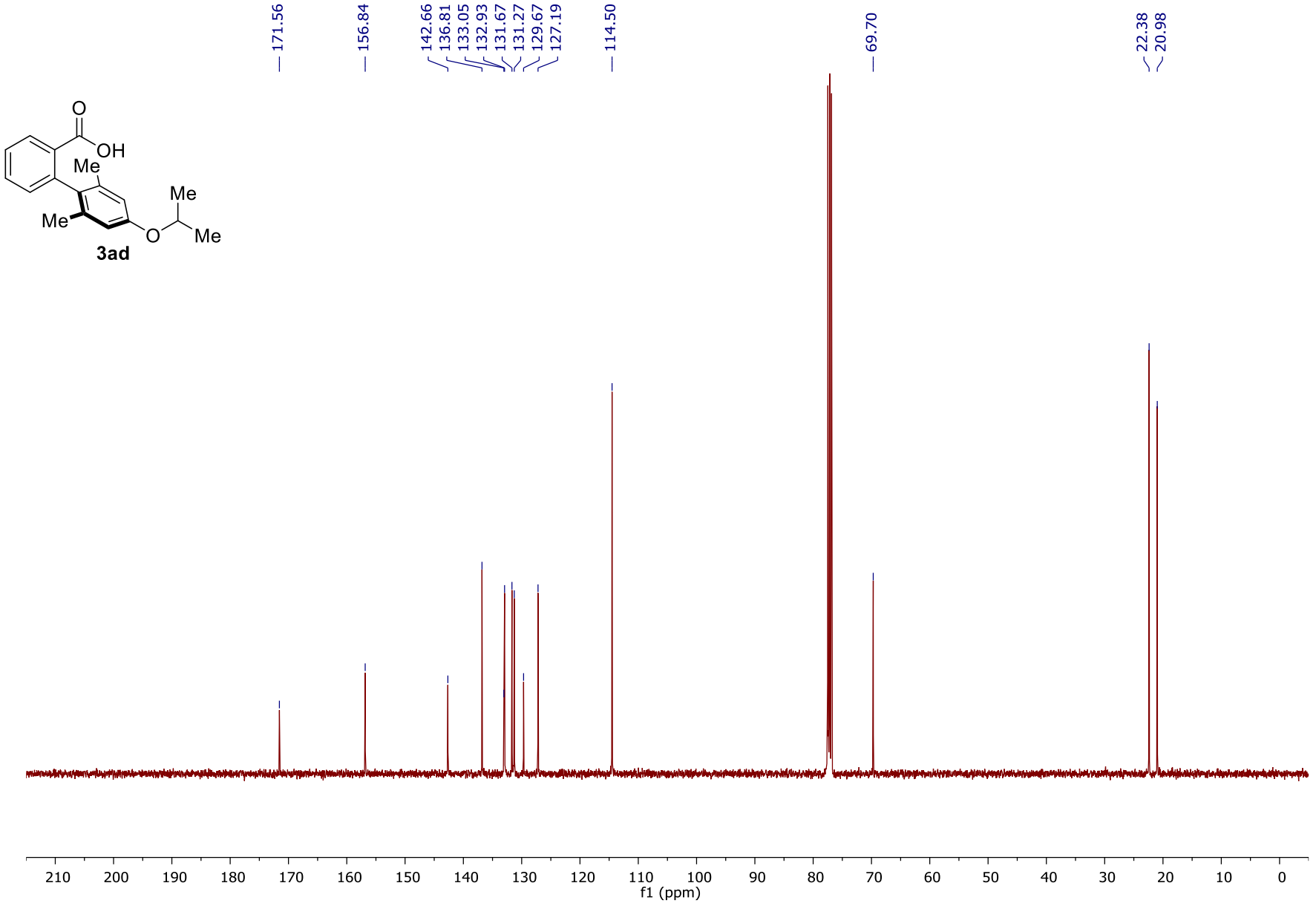
^{13}C NMR (101 MHz, $CDCl_3$)



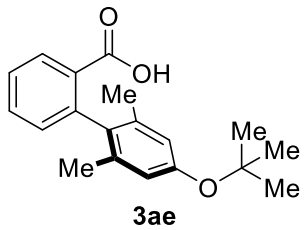
^{1}H NMR (300 MHz, $CDCl_3$) **3ad**



^{13}C NMR (101 MHz, $CDCl_3$)

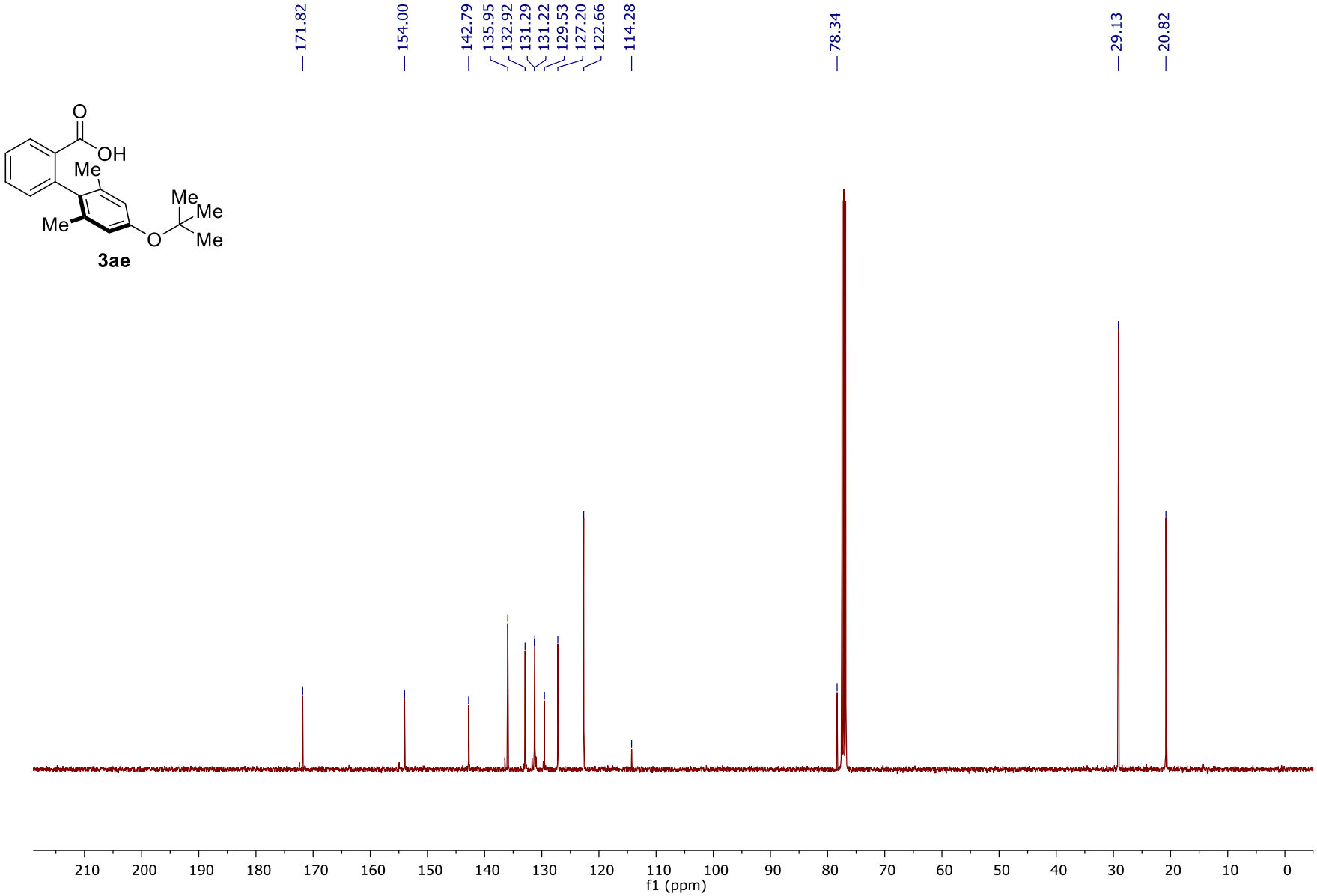


^{1}H NMR (300 MHz, $CDCl_3$) **3ae**

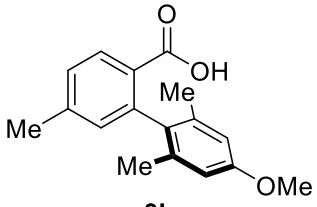


3ae

^{13}C NMR {H^1} (101 MHz, $CDCl_3$)

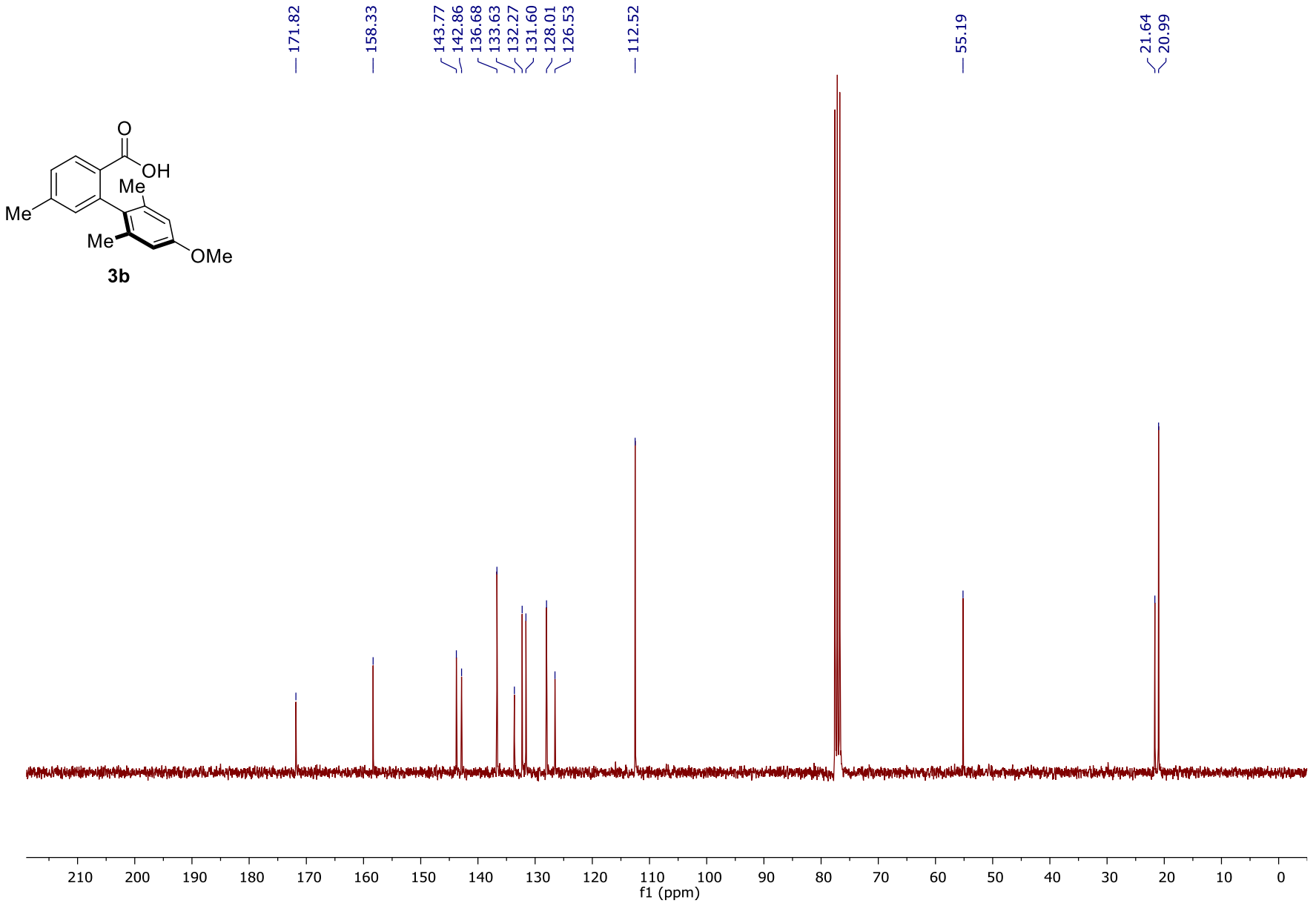


^{1}H NMR (300 MHz, $CDCl_3$) **3b**

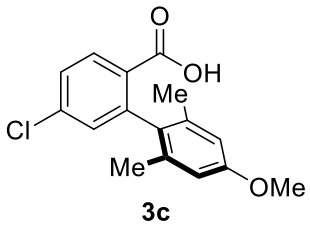


3b

^{13}C NMR (101 MHz, $CDCl_3$)

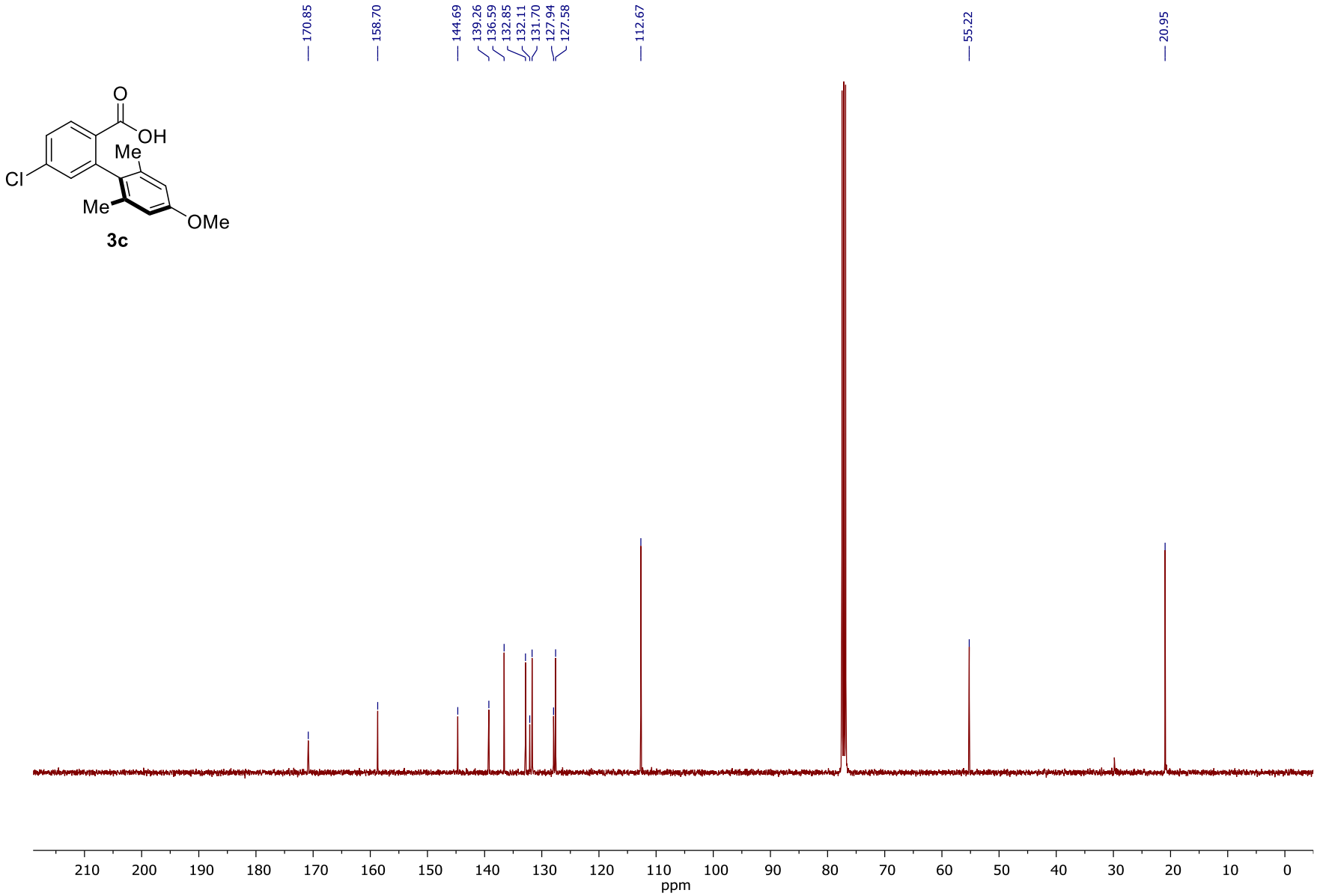


^{1}H NMR (300 MHz, $CDCl_3$) **3c**

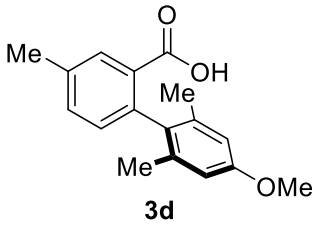


3c

^{13}C NMR (101 MHz, $CDCl_3$)

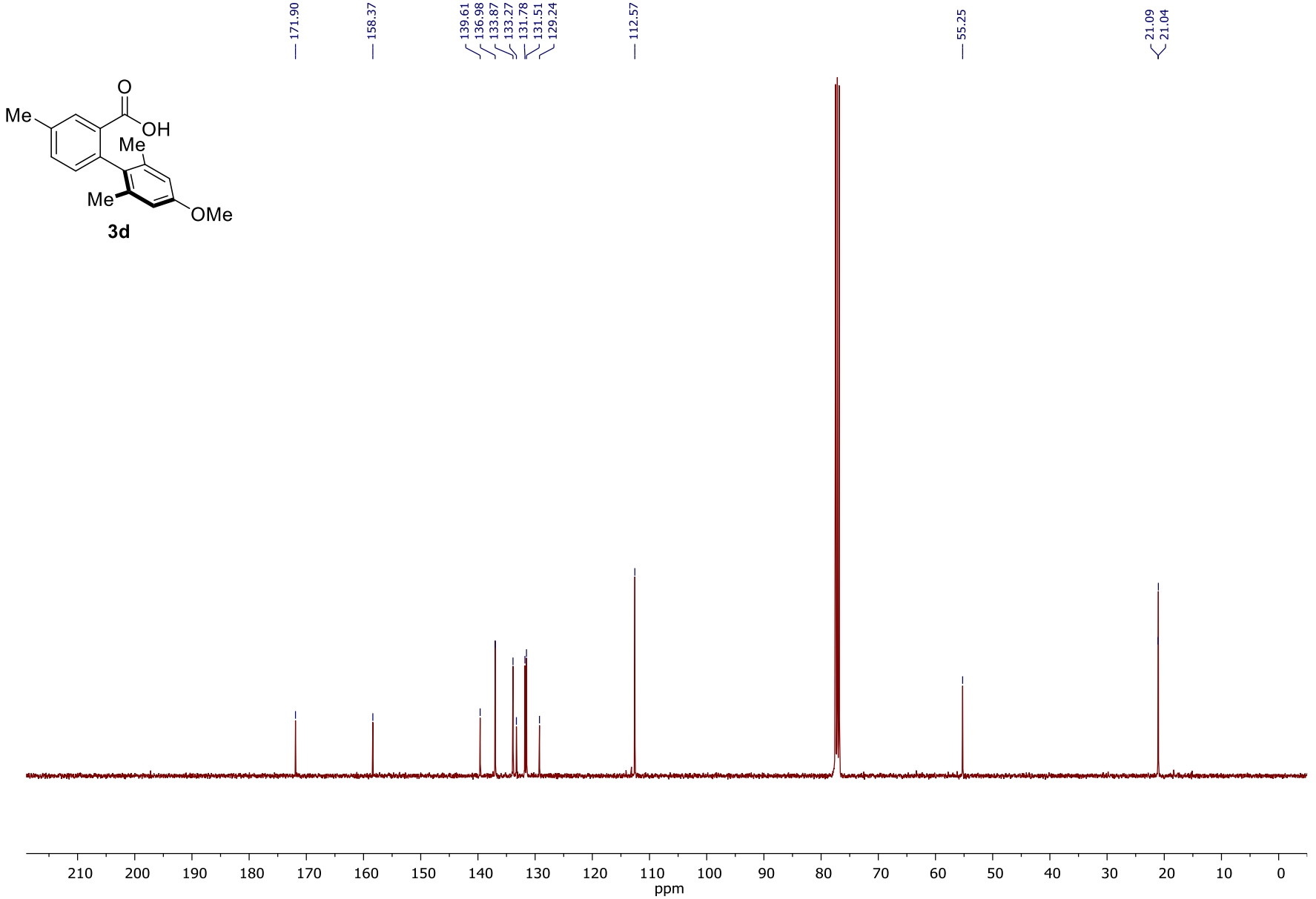


^{1}H NMR (400 MHz, $CDCl_3$) **3d**

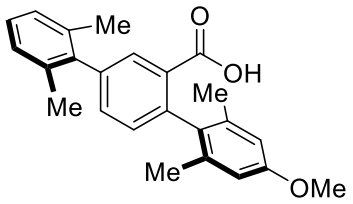


3d

^{13}C NMR (101 MHz, $CDCl_3$)

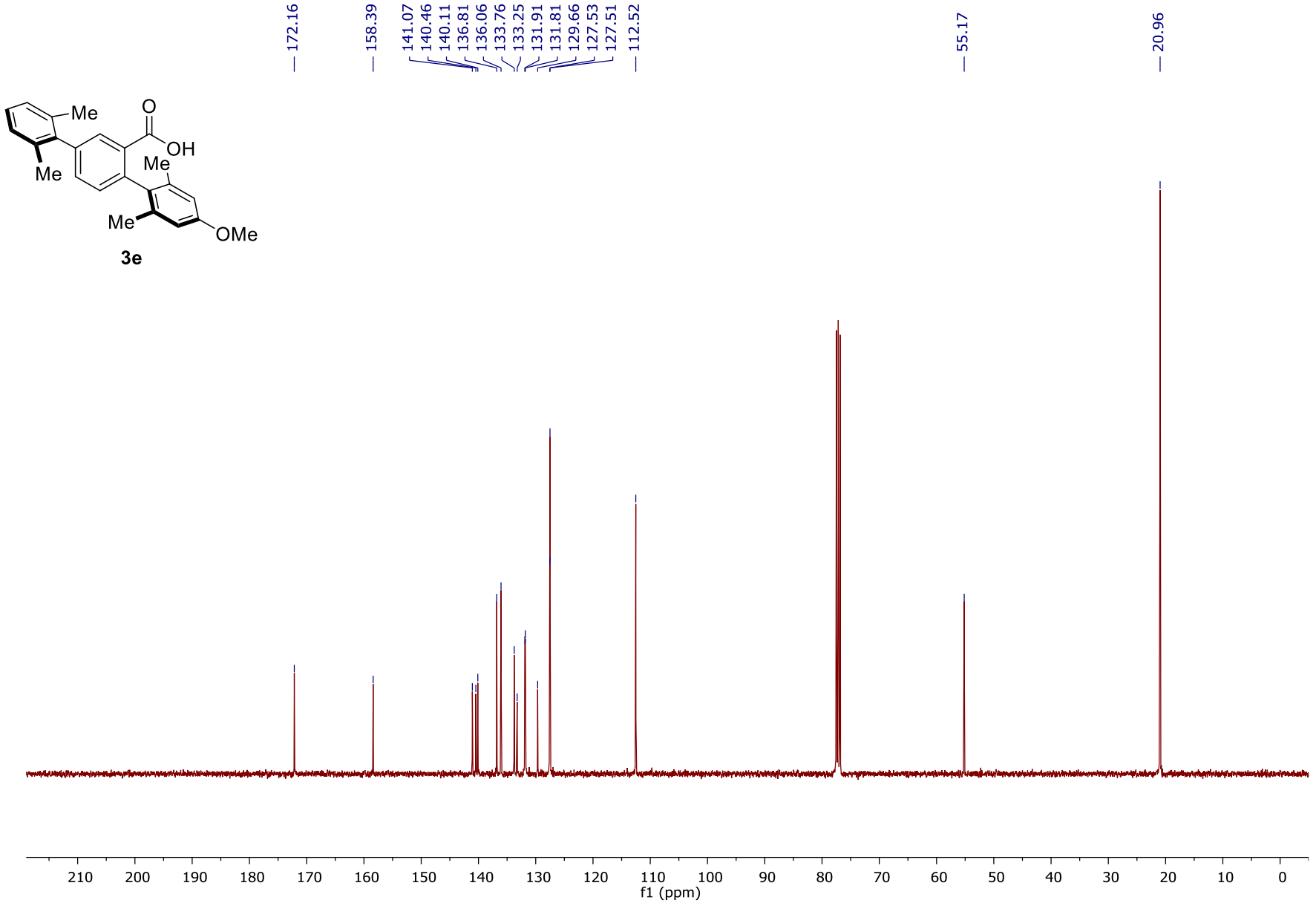


^{1}H NMR (400 MHz, $CDCl_3$) **3e**

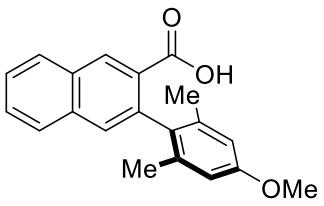


3e

^{13}C NMR (101 MHz, $CDCl_3$)

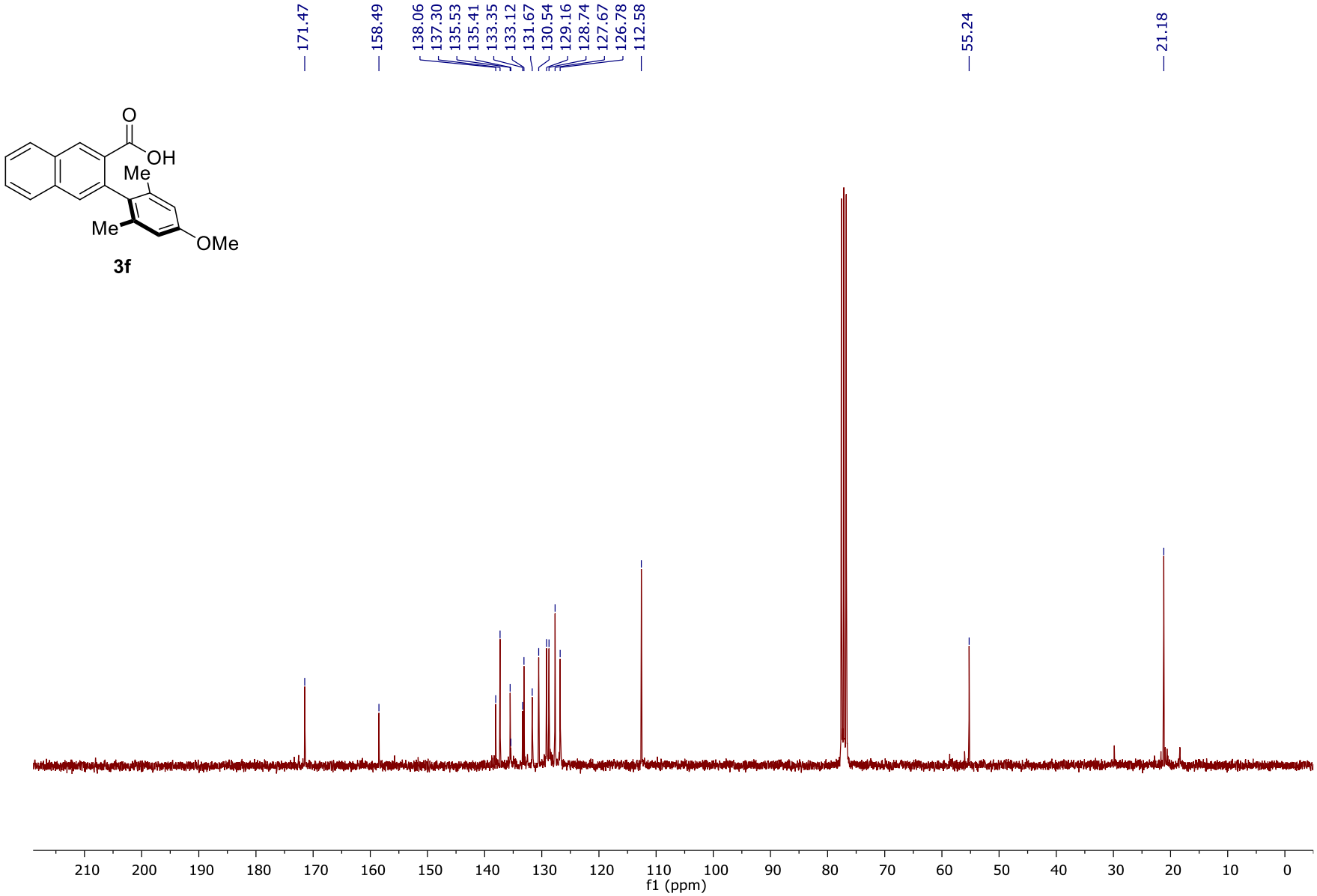


^{1}H NMR (300 MHz, $CDCl_3$) **3f**

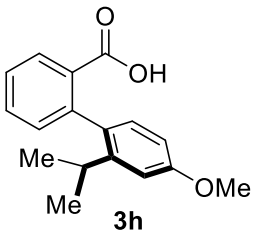


3f

^{13}C NMR (101 MHz, $CDCl_3$)

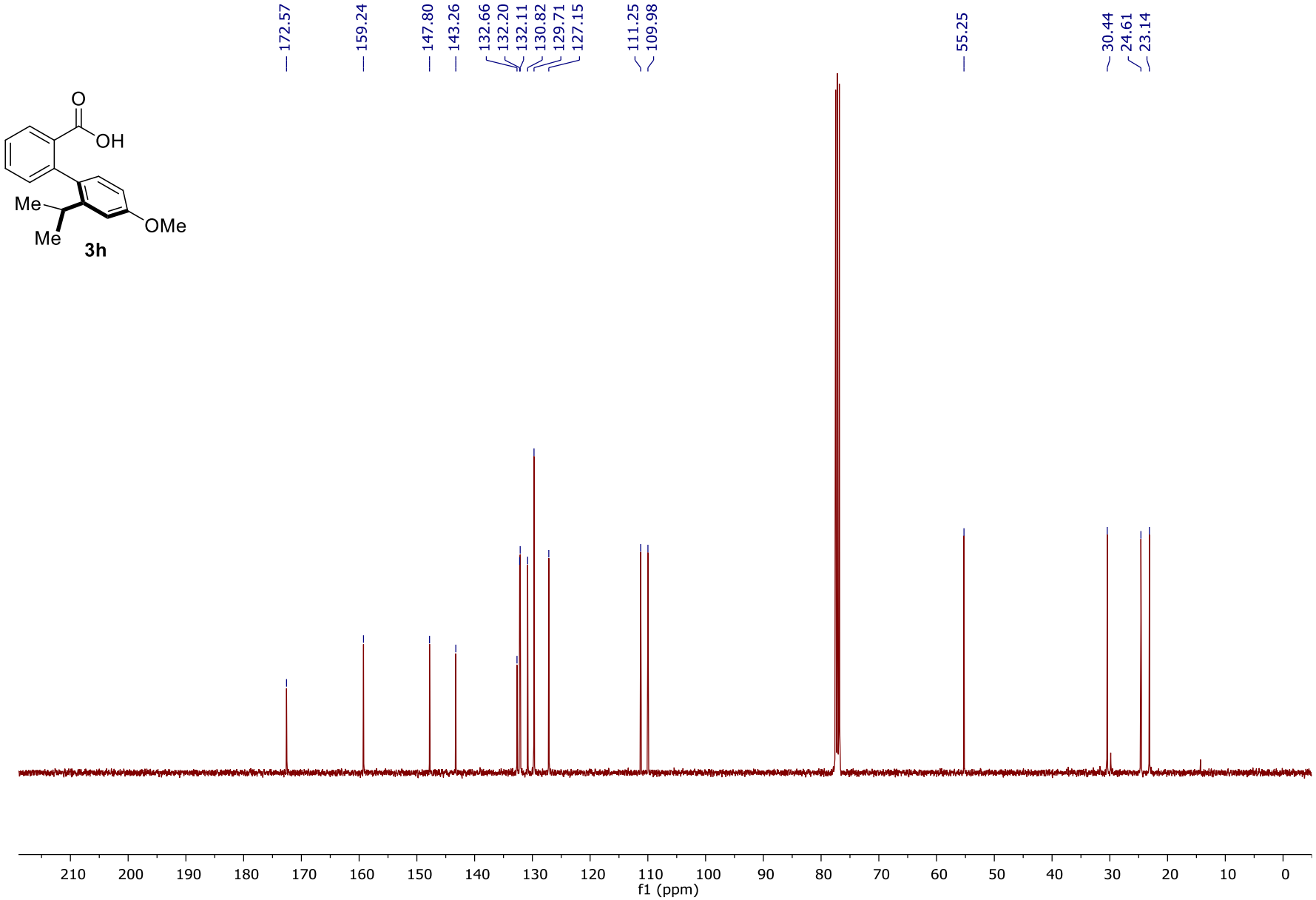


^{1}H NMR (400 MHz, $CDCl_3$) **3h**

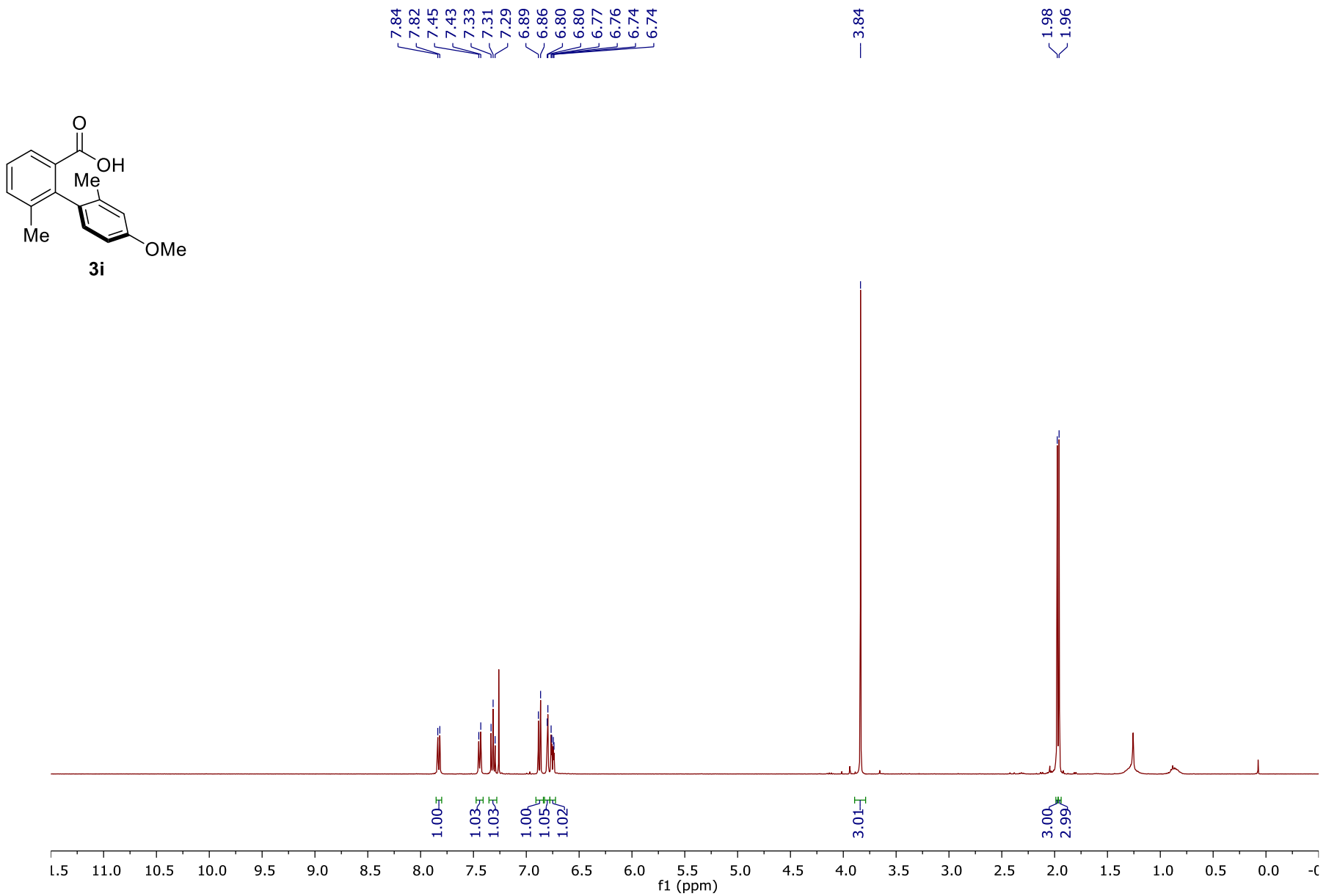


3h

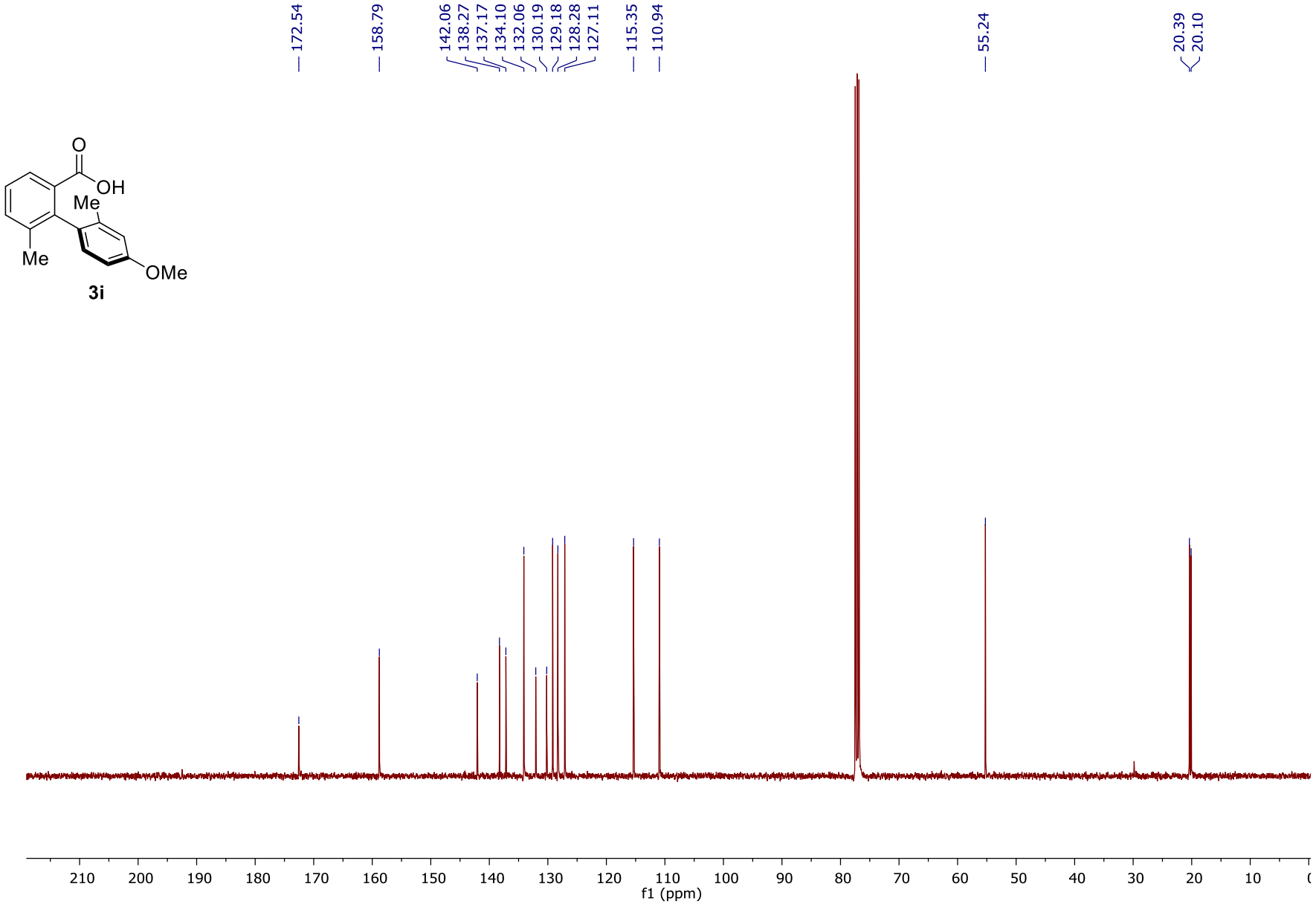
^{13}C NMR (101 MHz, $CDCl_3$)



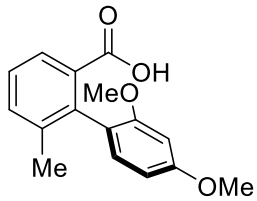
^{1}H NMR (400 MHz, $CDCl_3$) **3i**



^{13}C NMR (101 MHz, $CDCl_3$)

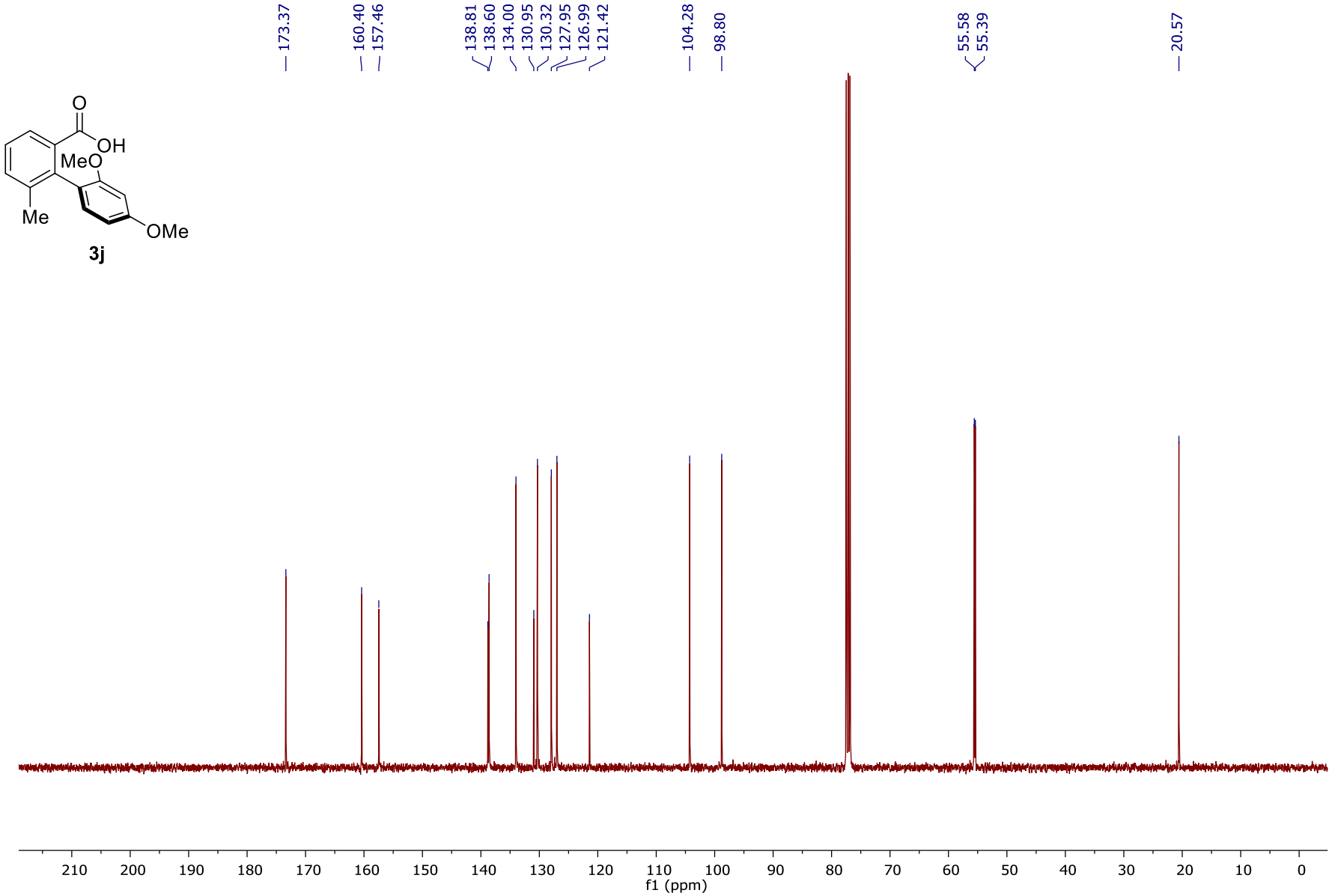


^{1}H NMR (400 MHz, $CDCl_3$) **3j**

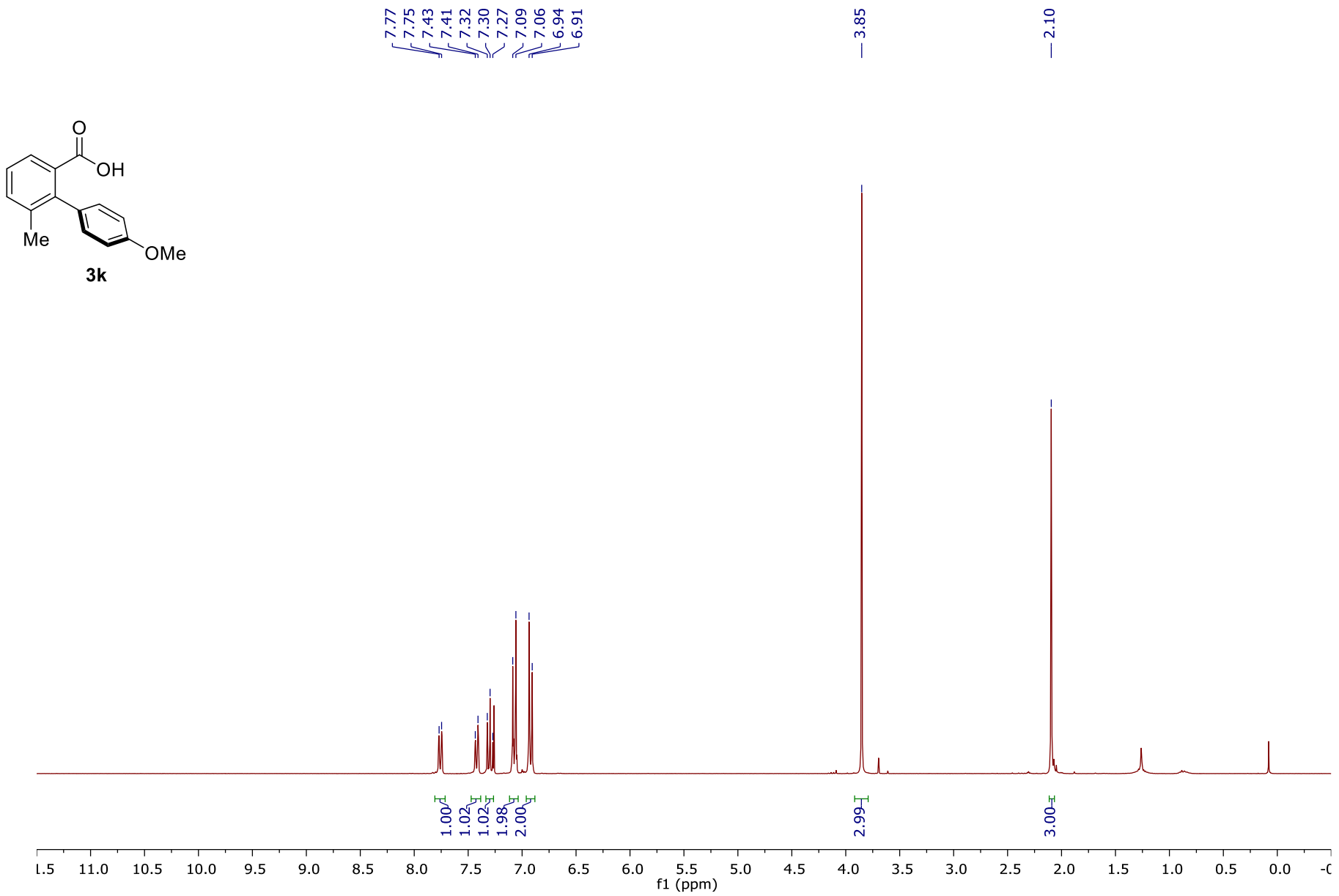


3j

^{13}C NMR (101 MHz, $CDCl_3$)

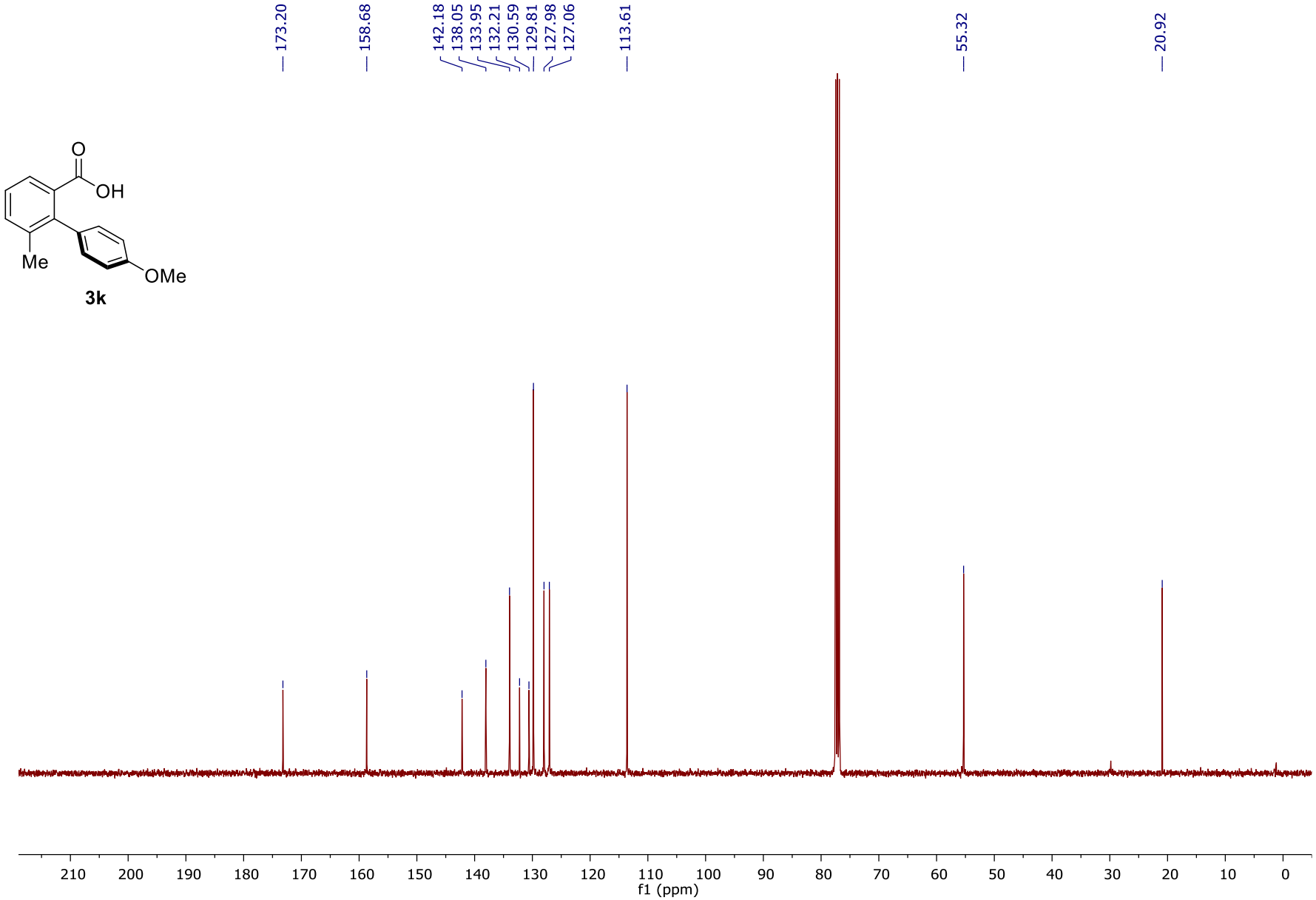


^{1}H NMR (300 MHz, $CDCl_3$) **3k**

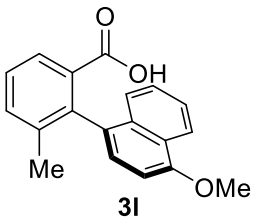


3k

^{13}C NMR (101 MHz, $CDCl_3$)

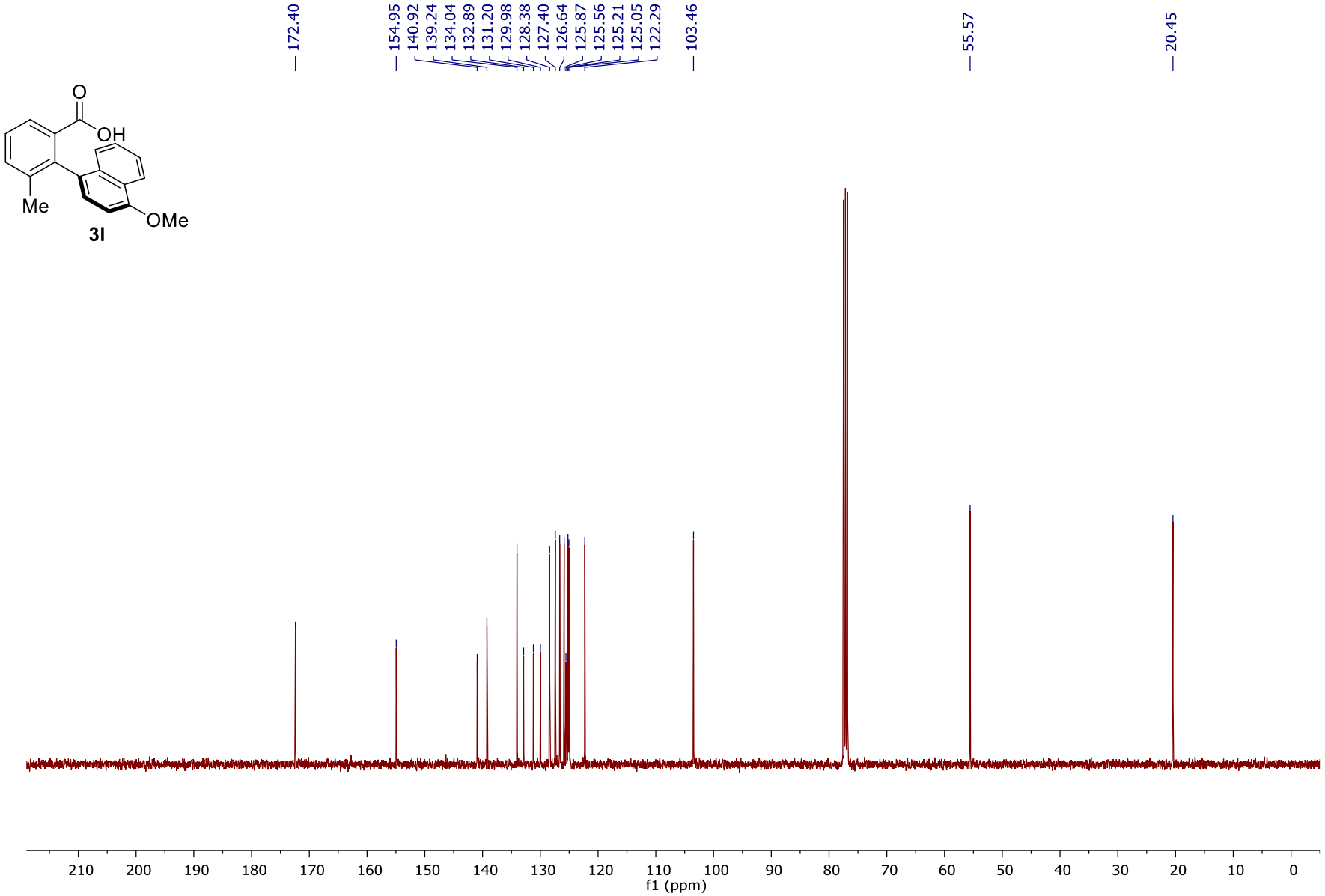


^{1}H NMR (400 MHz, $CDCl_3$) **3l**

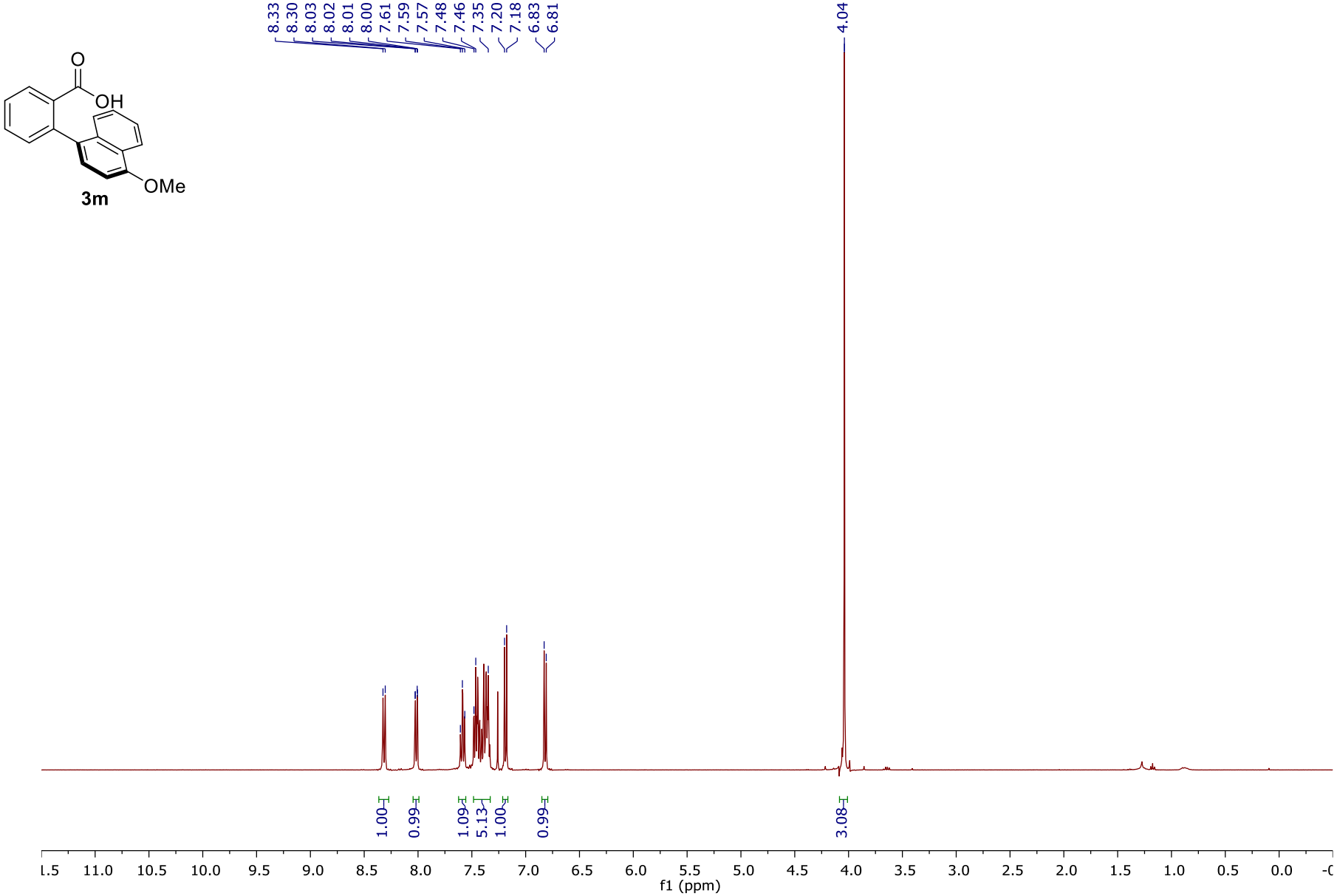


3l

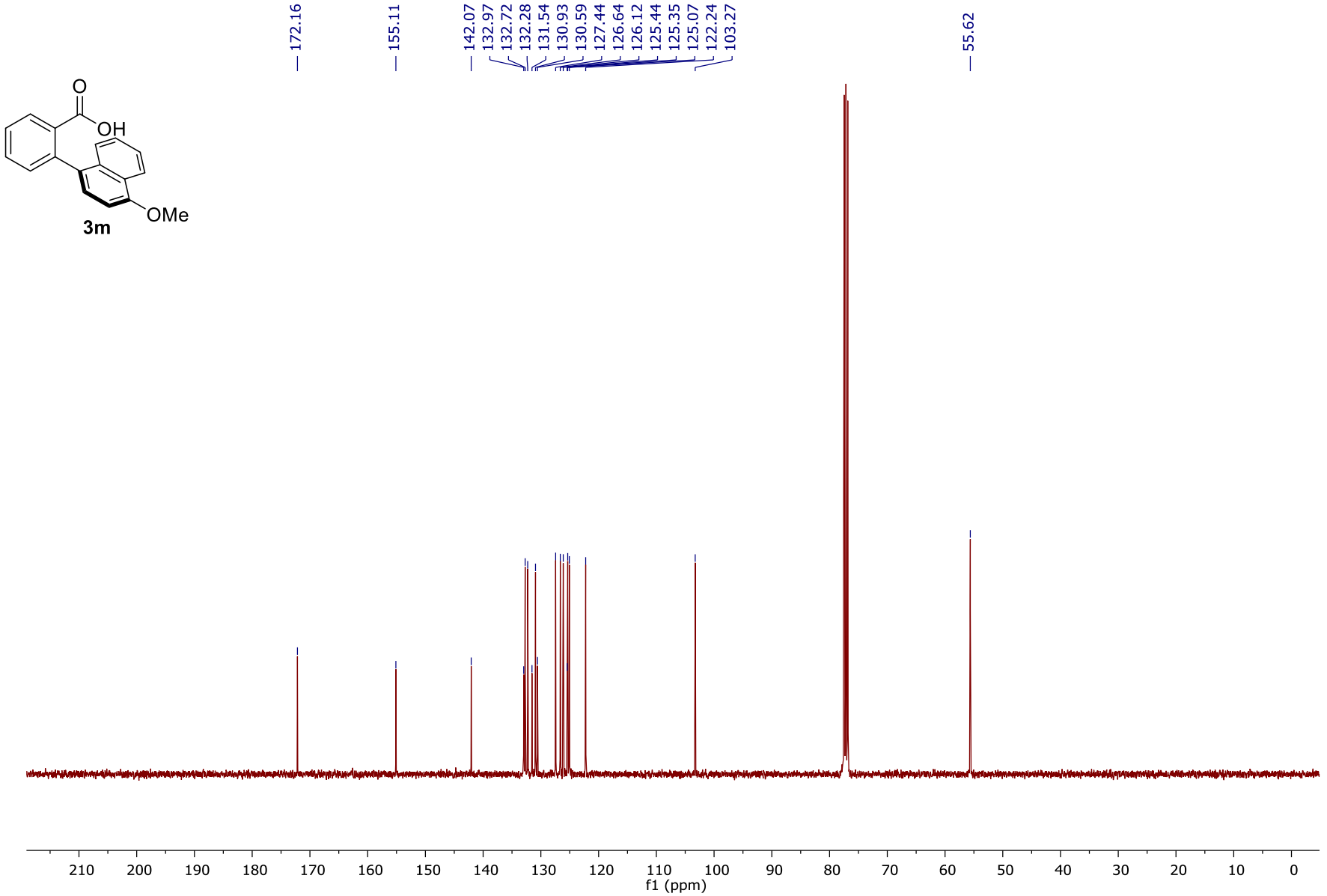
^{13}C NMR (101 MHz, $CDCl_3$)



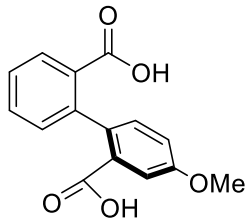
^{1}H NMR (400 MHz, $CDCl_3$) **3m**



^{13}C NMR (101 MHz, $CDCl_3$)

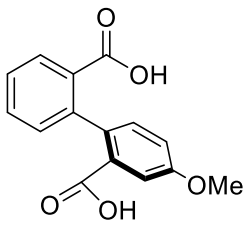


^{1}H NMR (400 MHz, DMSO-d_6) **3n**



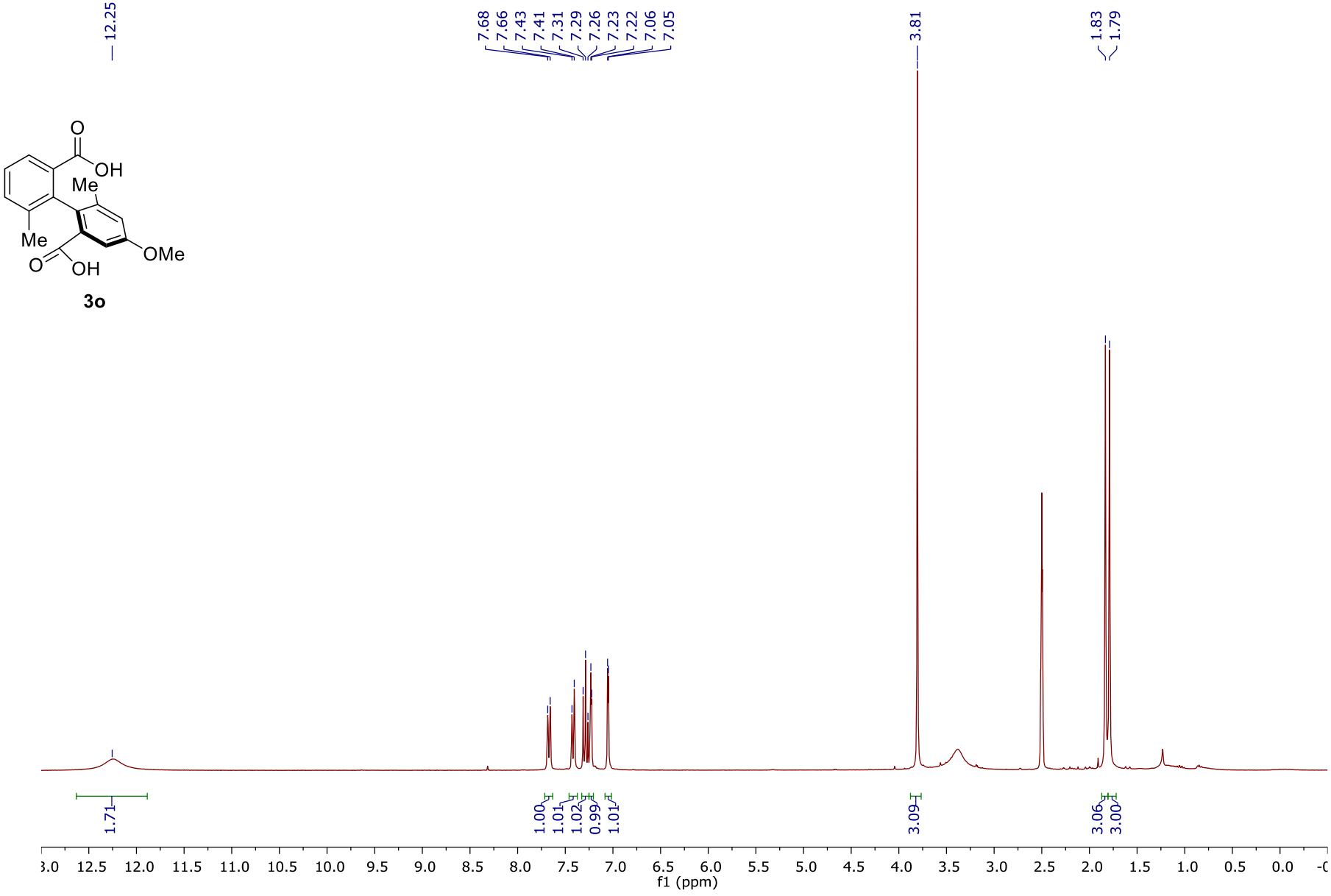
3n

^{13}C NMR (101 MHz, DMSO-d_6)



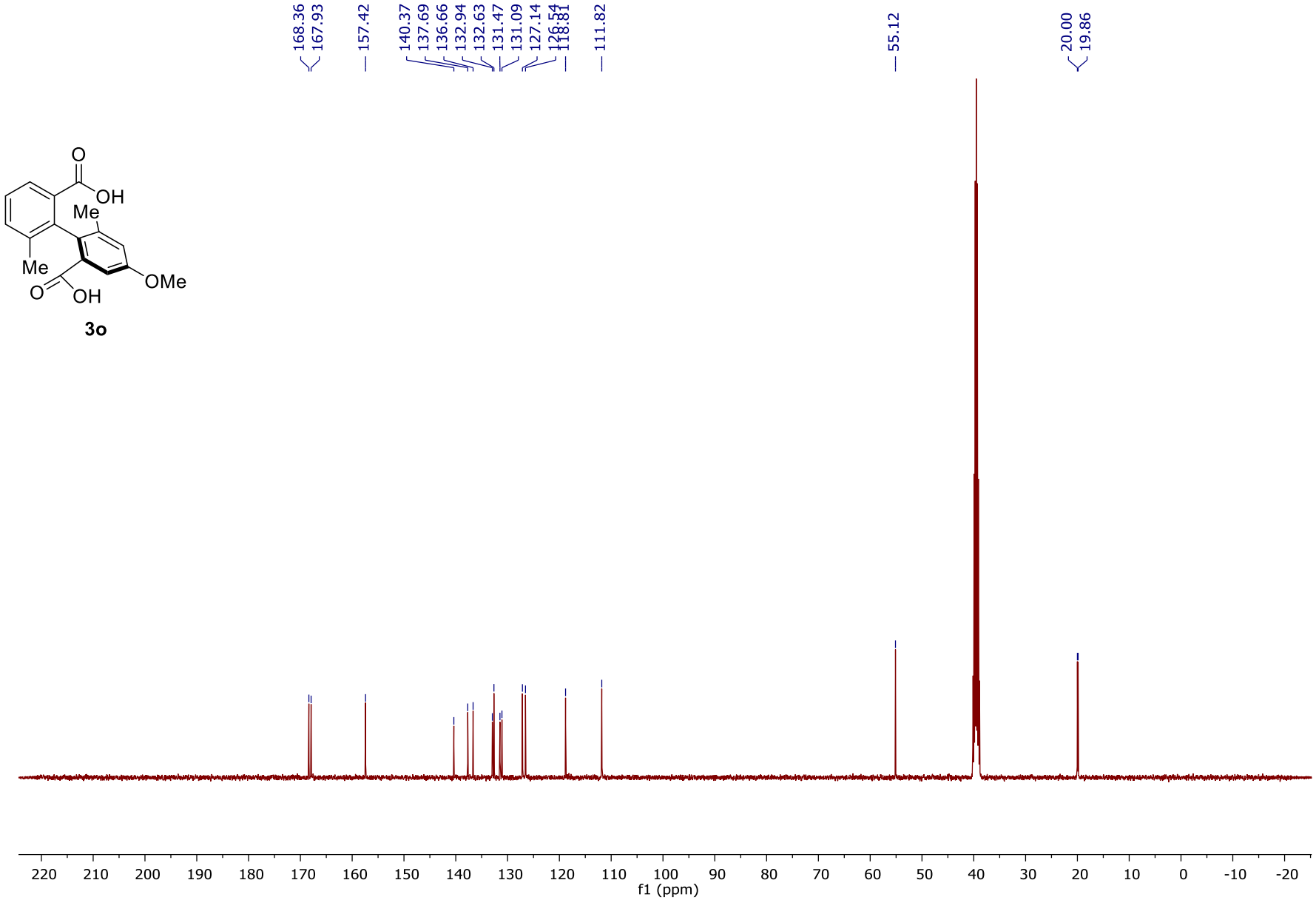
3n

^{1}H NMR (300 MHz, DMSO-d_6) **3o**



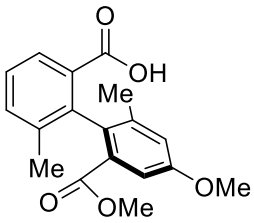
3o

^{13}C NMR (101 MHz, DMSO-d_6)



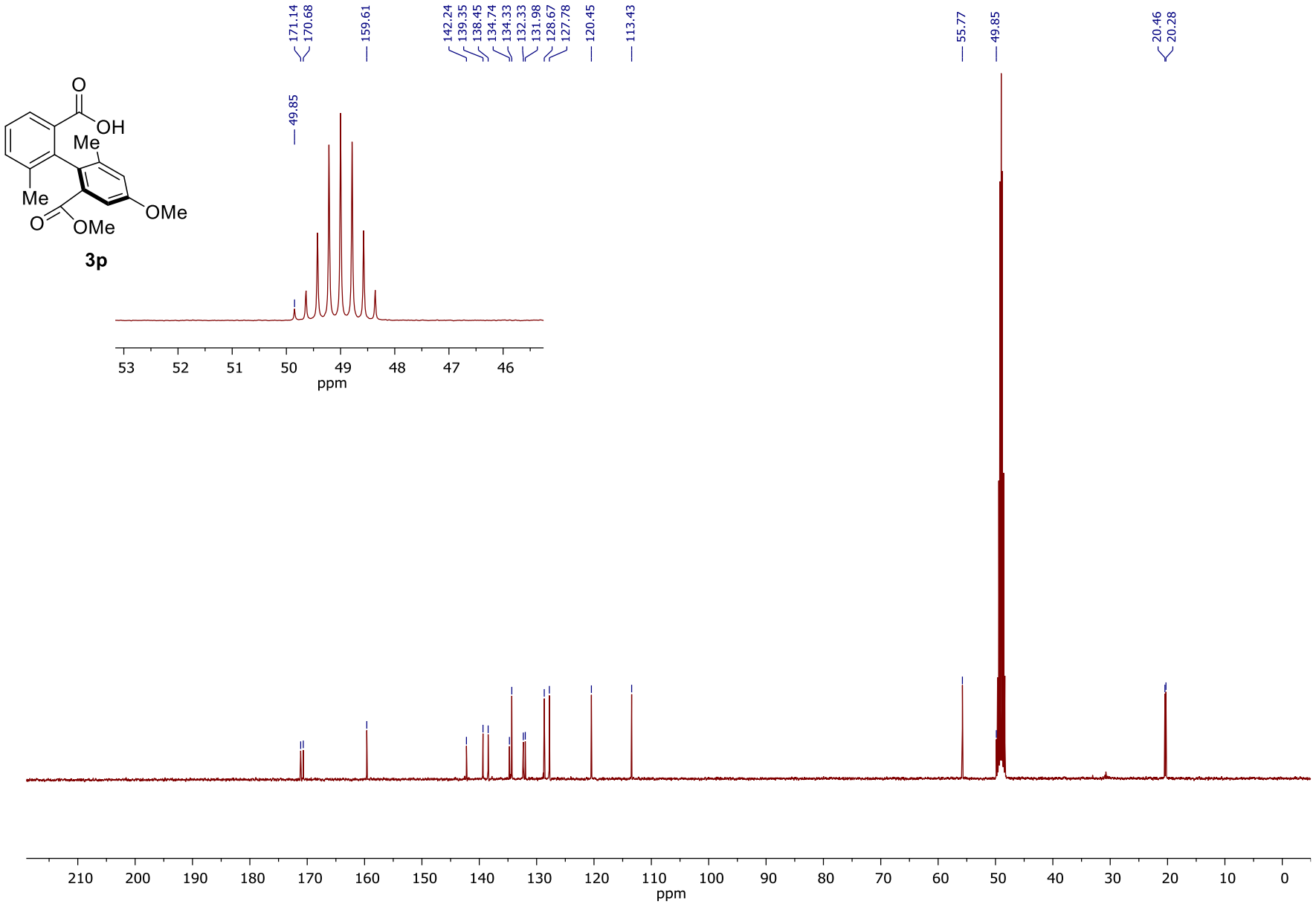
3o

^{1}H NMR (400 MHz, CD_3OD) **3p**

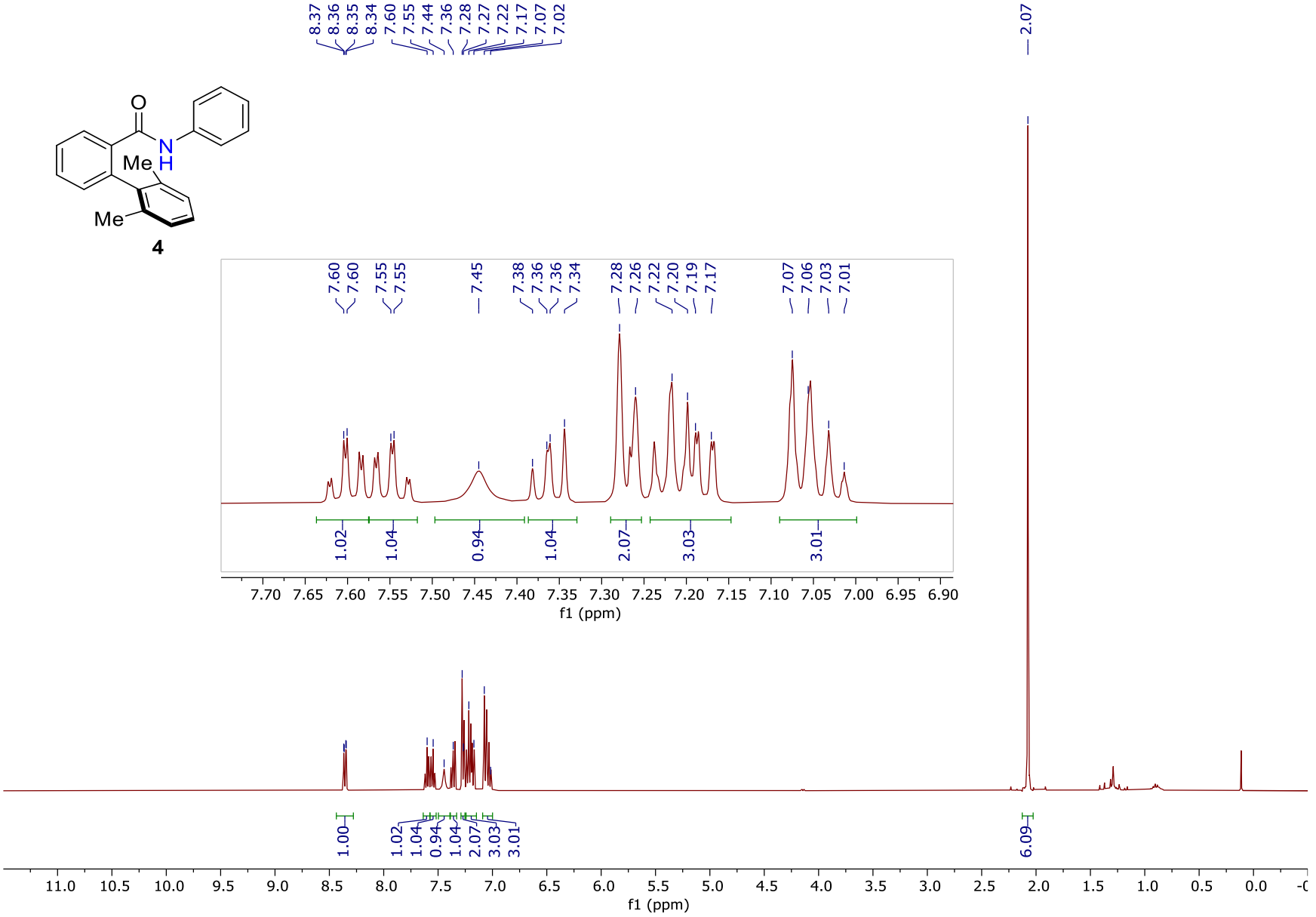


3p

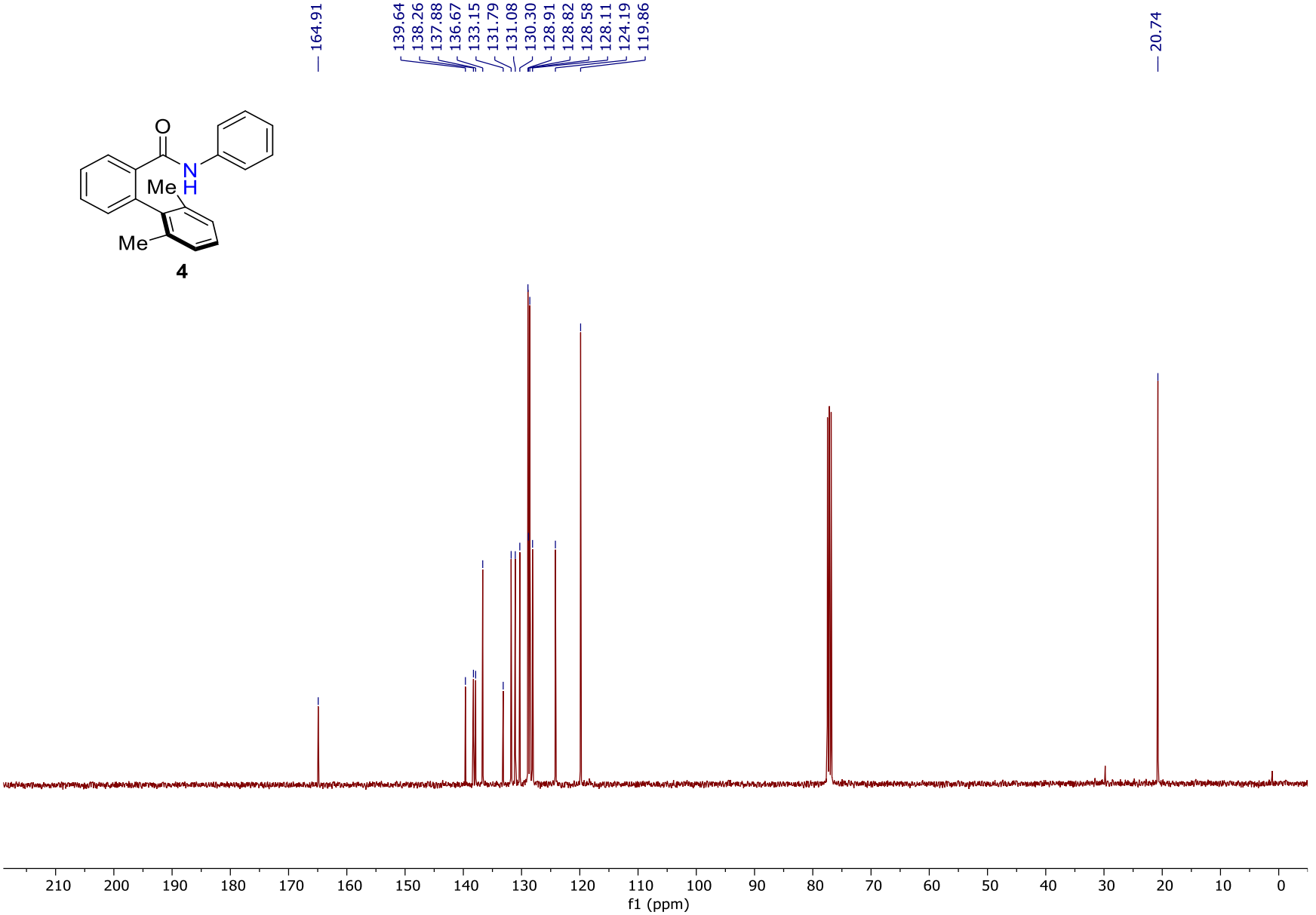
^{13}C NMR (101 MHz, CD_3OD)



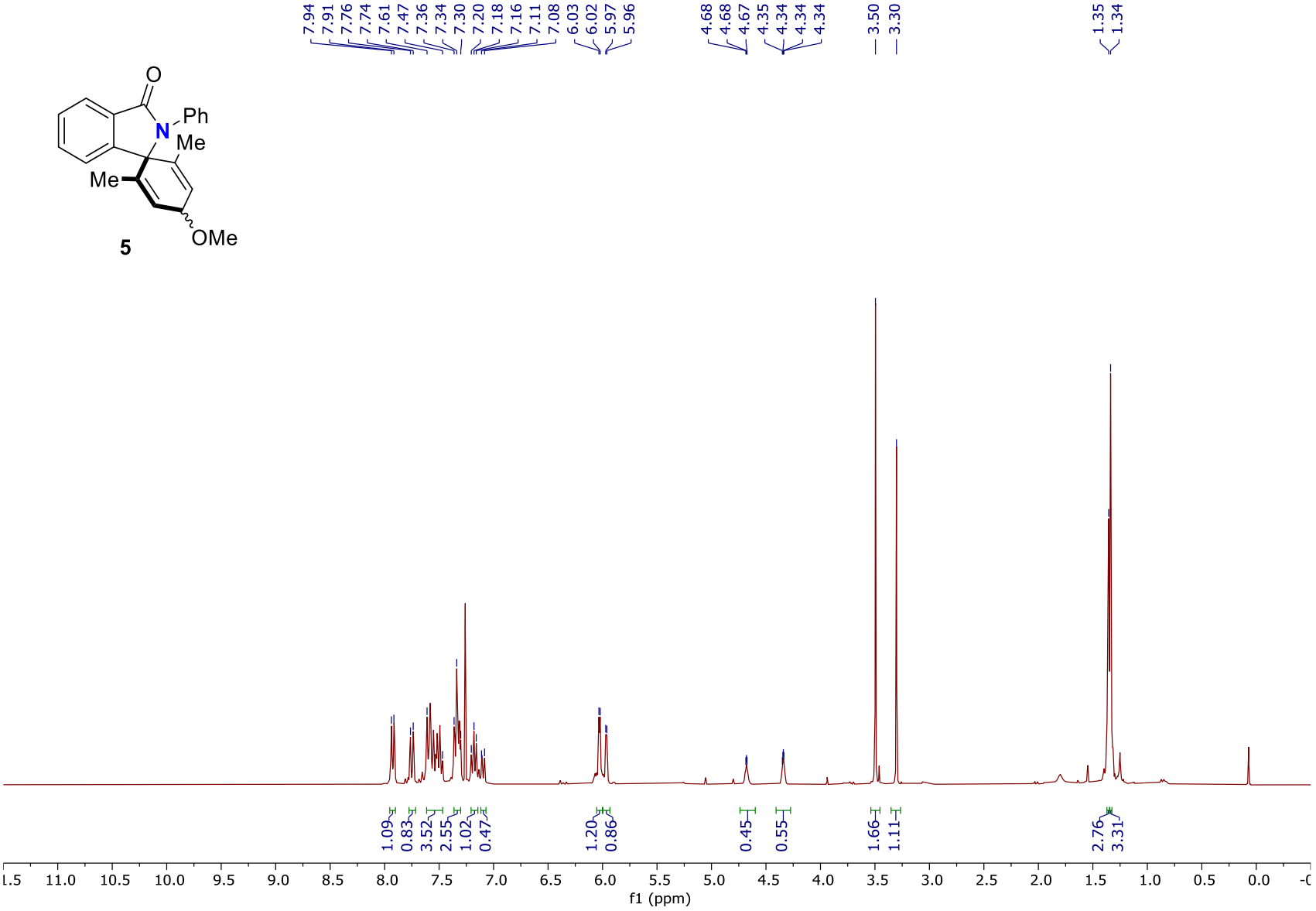
^{1}H NMR (400 MHz, $CDCl_3$) **4**



^{13}C NMR (101 MHz, $CDCl_3$) **4**

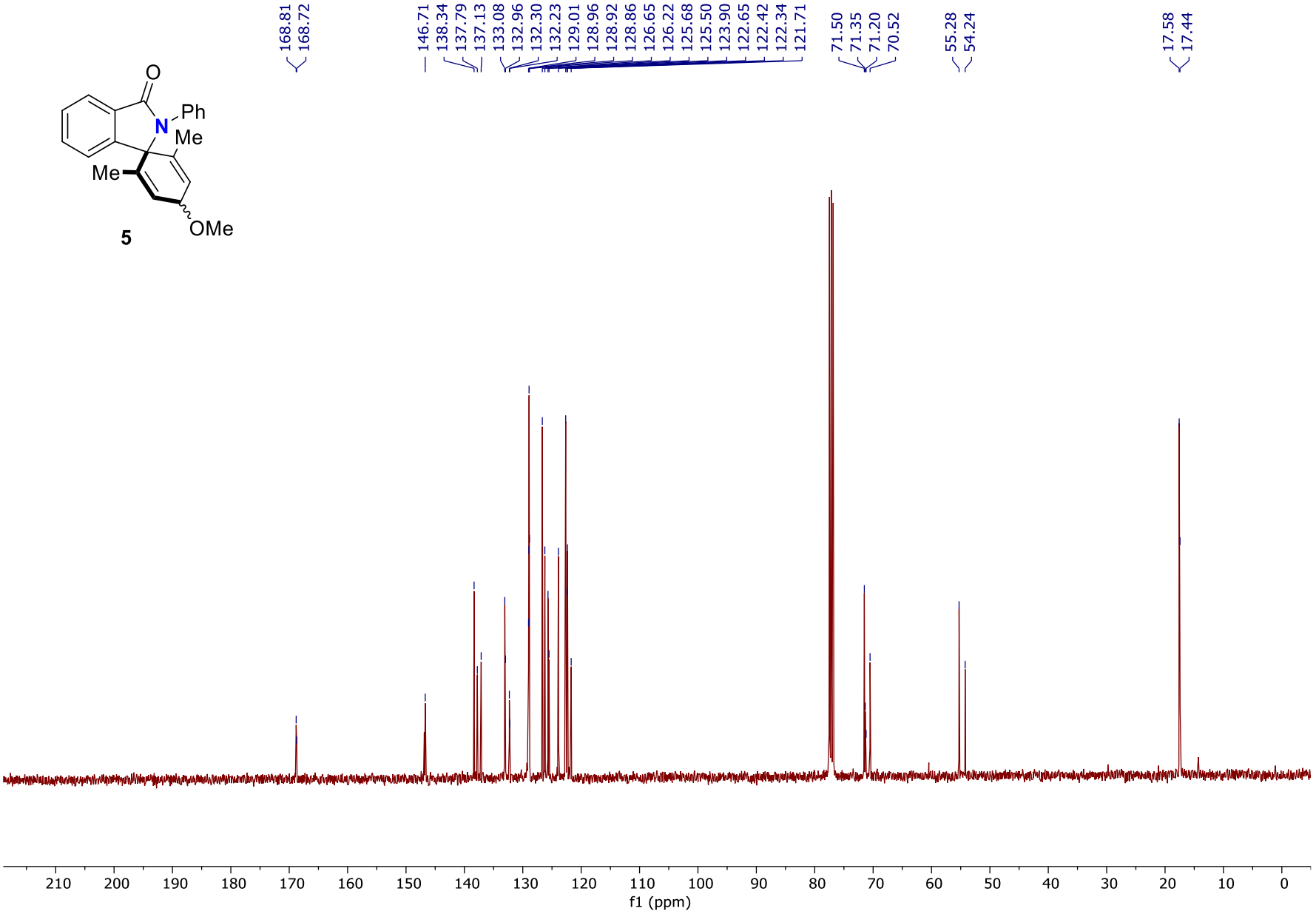


^{1}H NMR (300 MHz, $CDCl_3$) **5**

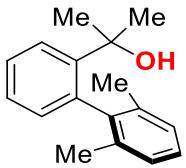


5

^{13}C NMR (101 MHz, $CDCl_3$) **5**

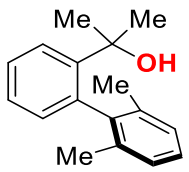


^{1}H NMR (400 MHz, $CDCl_3$) **6**



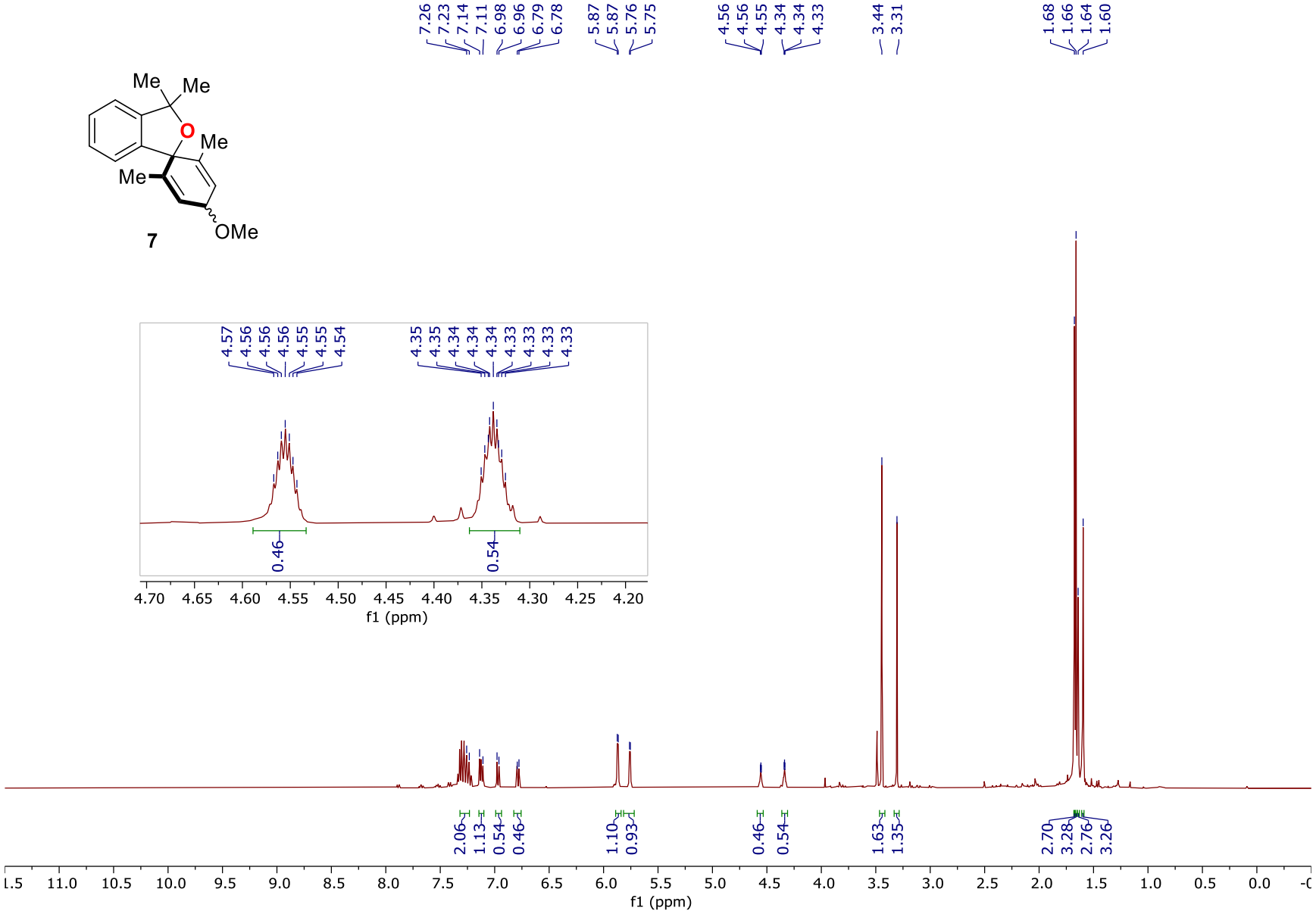
6

^{13}C NMR (101 MHz, $CDCl_3$) **6**

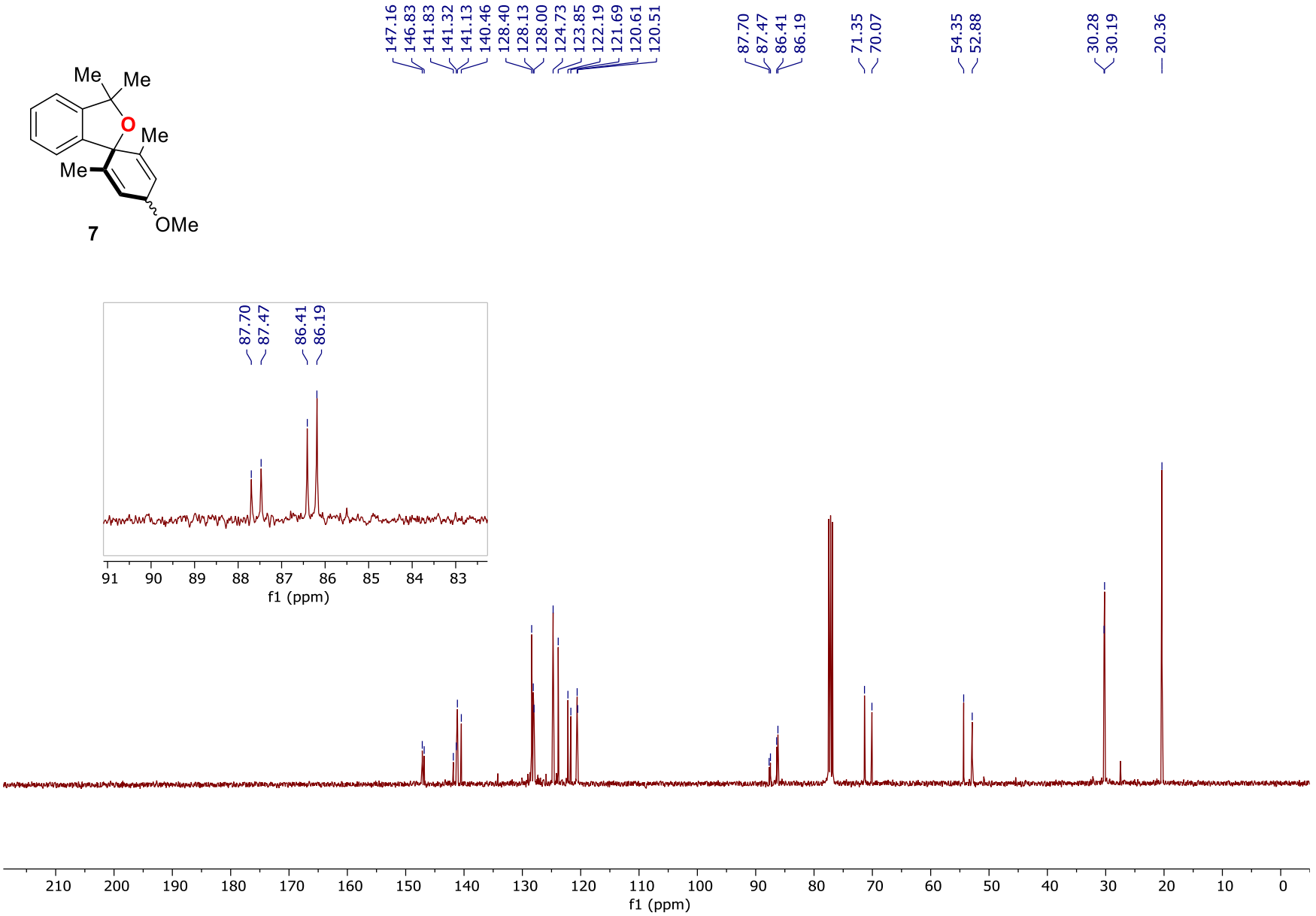


6

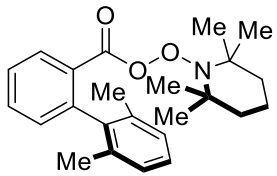
^{1}H NMR (400 MHz, $CDCl_3$) **7**



^{13}C NMR (101 MHz, $CDCl_3$) **7**

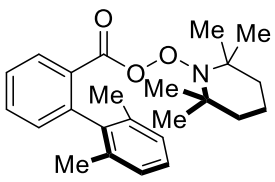


^{1}H NMR (400 MHz, $CDCl_3$) **1a-TEMPO**



1a-TEMPO

^{13}C NMR (101 MHz, $CDCl_3$)



1a-TEMPO

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[1] N. P. Ramirez, I. Bosque and J. C. Gonzalez-Gomez, Photocatalytic Dehydrogenative Lactonization of 2-Arylbenzoic Acids, *Org. Lett.*, 2015, **17**, 4550.

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