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Supplementary Information

Mechanism and regioselectivity of the anionic oxidative rearrangement of 1,3-diketones towards all-carbon quaternary carboxylates

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1 General experimental

NMR Characterization raw data can be download from Zenodo DOI: 10.5281/zenodo.3234375

Materials. All reactions were carried out under air atmosphere. In order to ensure high degree of reproducibility, the experiments performed were carried out in anhydrous solvents (> 99.8%). All reagents and solvents were purchased from commercially available suppliers and used without further purification and used as received.

Chromatography. Flash chromatography was performed on GRACE Reveleris X2 automated flash systems from Büchi equipped with ELS and UV detection. The columns used were prepacked silica gel columns supplied by Biotage (SNAP Cartridge KP-Sil, 50 µm silica particles with a surface area of 500 m^2/g). Silica columns with 50 g or 100 g silica were used. HPLC solvents purity >99.9%. Preparative HPLC was performed on a Kromasil C18 column (10 µm 250 x 50 ID mm) using a gradient of acetonitrile in H_2O/CH_3CN/formic acid 95/5/0.2 buffer over 20 min with a flow of 100 mL/min. The instrument was connected to an UV/VIS detector 155 from Gilson. Analytical UHPLC/MS was obtained on a Waters Aquity system with a Waters SQD mass spectrometer equipped with a BEH C18 column (1.7 µm 2.1 × 50 mm) using a 46 mM ammonium carbonate/NH_3 buffer at pH 10 and a HSS C18 column (1.8 µm 2.1× 50 mm) using a 11 mM ammonium formate buffer at pH 3 with a flow rate of 1 mL/min. The obtained HPLC fractions were evaporated under reduced pressure (rotavapor and vacuum line).

Characterization. NMR spectra for the characterization of compounds were recorded at room temperature on a Bruker instruments 400 MHz (^{1}H) and at 100 MHz (^{13}C), 500 MHz (^{1}H) and at 125 MHz (^{13}C) or 600 MHz (^{1}H) and at 150 MHZ (^{13}C). The 600 MHz and 500 MHz instruments were equipped with a Bruker cryo probe. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (δH = 7.26 and δC = 77.16 ppm), MeOD (δH = 4.87 and δC = 49.0 ppm), (as internal reference, and coupling constants (nJ) are given in hertz (Hz). ^{19}F-NMR shifts were given by using TFA (trifluoroacetic acid) as reference. Data are reported as follows: chemical shift, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, hex: hexet; br: broad, m: multiplet), coupling constants (J in Hz) and integration. Carbon multiplicities were assigned by DEPT and edited HSQC techniques. High-resolution mass spectra (HRMS) were determined at AstraZeneca (Mölndal) Mass Spectrometry Division. The mass spectrometer used electrospray ionization (ESI) in both positive and negative mode.

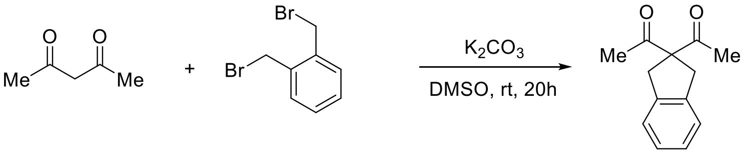
Experimental details. Reactions were performed in common pyrex round bottom flasks, microwave vials 0.5 - 2 ml (VWR), or 5 - 20 ml flat bottom vials (Cronus, SMI-LabHut Ltd.) crimped on top with 20 mm Sil/PTFE Septa. When needed, pH values were determined by using pH indicator strips (pH 0 - 14 Universal indicator paper, Merck MColorpHaspt). Kinetic experiments concentrations are expressed as percentage of the starting concentration of the limiting reagent (100% = 0.05 M).

2 Experimental procedures

2.1 Synthesis of starting materials

The synthesis of diketones **4c – k** was carried out according to previously described procedures.[1]

1,1'-(2,3-Dihydro-1H-indene-2,2-diyl)diethanone (4c)[1]



S1c **S2** **4c**

Dimethylsulfoxide DMSO (17 ml) was added to anhydrous potassium carbonate (3.04 g, 21.97 mmol, 2.2 equiv.) followed by pentane-2,4-dione (1.03 ml, 9.99 mmol, 1.0 equiv.). The mixture was allowed to stir under nitrogen atmosphere. Then, 1,2-bis(bromomethyl)benzene (2.64 g, 9.99 mmol, 1.0 equiv.) dissolved in DMSO (6 ml) was added dropwise during 10 min using a syringe pump. The reaction mixture was then left to stir over night at rt. The mixture was filtered. Water and diethyl ether was added to the filtrate. The water phase was extracted two times with ether. The combined organics were washed with water and dried using Na_2SO_4, filtered and evaporated. The crude was purified by flash chromatography (GRACE system, 100 g SiO_2-column) using a gradient of ethyl acetate/heptane 0 – 20 %, 18 CV, 254 nm. Gave 1,1'-(2,3-dihydro-1*H*-indene-2,2-diyl)diethanone **4c** (0.591 g, 2.93 mmol, 29.3 %) as a colorless oil. Measured experimental NMR data is in full agreement with previously described spectra in the literature.[1]

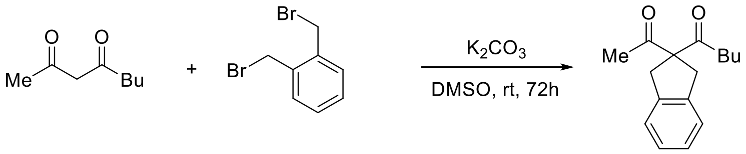
Appearance: Colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.13 - 7.23 (m, 4H), 3.51 (s, 4H), 2.17 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 205.0, 139.8, 127.2, 124.6, 37.8, 26.7.

HRMS: m/z $[M+H]^+$ calculated for $[C_{13}H_{14}O_2+H]^+$, 203.1072; found 203.1066.

1-(2-Acetyl-2,3-dihydro-1H-inden-2-yl)pentan-1-one (4d)



S1d **S2** **4d**

DMSO (13 ml) was added to anhydrous potassium carbonate (2.14 g, 15.47 mmol, 2.2 equiv.) followed by octane-2,4-dione (1.00 g, 7.03 mmol, 1.0 equiv.). The mixture was stirred under nitrogen atmosphere. Then, 1,2-Bis(bromomethyl)benzene (1.86 g, 7.03 mmol, 1.0 equiv.) dissolved in DMSO (6 ml) was added dropwise during 20 min using a syringe pump. The reaction mixture was then left to stir over the weekend at rt.

Water and diethyl ether was added and the phases were separated, the water phase was extracted twice with diethyl ether. The combined organics was dried using Na_2SO_4, filtered and evaporated. The crude was further purified by flash chromatography (GRACE system, 50 g Si-column) using a gradient of 0-20 % EtOAc in heptane, ELS-detection, 254 / 280 nm, 18 CV. Gave 1-(2-acetyl-2,3-dihydro-1*H*-inden-2-yl)pentan-1-one **4d** (0.905 g, 3.70 mmol, 52.7 %) as a colorless oil after evaporation of solvents.

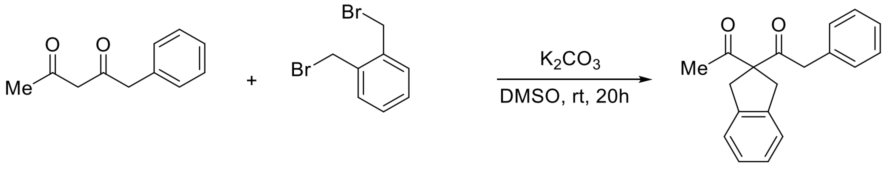
Appearance: Colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.1 – 7.2 (m, 4H), 3.5 (s, 4H), 2.4 (t, *J* = 7.31 Hz, 2H), 2.2 (s, 3H), 1.5 – 1.6 (m, 2H), 1.2 – 1.3 (m, 2H), 0.9 (t, *J* = 7.34 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 207.2, 205.0, 139.9, 127.2, 124.5, 75.0, 38.8, 37.7, 26.7, 26.2, 22.4, 14.0.

HRMS m/z $[M+H]^+$ calculated for $[C_{16}H_{20}O_2+H]^+$, 245.1541; found 245.1541.

1-(2-Acetyl-2,3-dihydro-1H-inden-2-yl)-2-phenylethanone (4e)



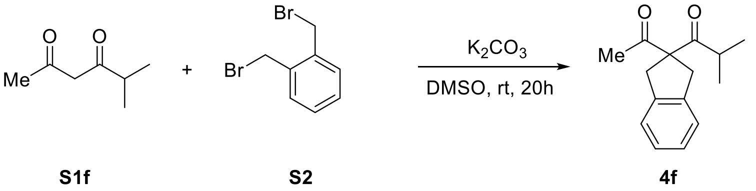
S1e **S2** **4e**

DMSO (13 ml) was added to anhydrous potassium carbonate (1.73 g, 12.48 mmol, 2.2 equiv.) followed by 1-phenylpentane-2,4-dione (1.00 g, 5.67 mmol, 1.0 equiv.). The mixture was stirred under nitrogen atmosphere. Then, 1,2-bis(bromomethyl)benzene (1.50 g, 5.67 mmol, 1.0 equiv.) dissolved in DMSO (6 ml) was added dropwise during 20 min using a syringe pump. The reaction mixture was then left to stir over night at rt. Water and diethyl ether was added, the phases were separated and the water phase was extracted twice with ether. The combined organics were dried using Na_2SO_4, filtered and evaporated. The crude was further purified by flash chromatography (GRACE system, 50 g SiO_2-column) using a gradient of 0 - 10 % EtOAc in heptane, ELS-detection and UV detection at 254 / 280 nm, 18 CV. Gave 1-(2-acetyl-2,3-dihydro-1*H*-inden-2-yl)-2-phenylethanone **4e** (0.52 g, 1.89 mmol, 33.3 %) as a colorless oil.

Appearance: Colorless oil

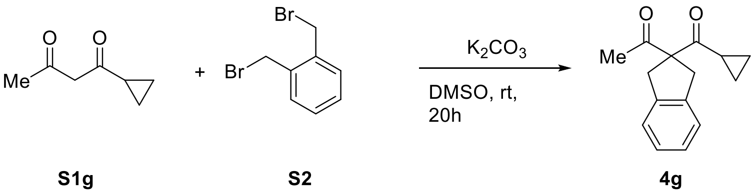
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.28 - 7.35 (m, 3H), 7.15 - 7.23 (m, 6H), 3.78 (s, 2H), 3.51 - 3.64 (m, 4H), 2.10 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 204.8, 204.2, 139.6, 133.4, 129.5, 128.6, 128.2, 127.1, 127.1, 124.4, 74.9, 45.5, 37.6, 26.6.
HRMS m/z $[M+H]^+$ calculated for $[C_{19}H_{18}O_2+H]^+$, 279.1385; found 279.1372.

1-(2-Acetyl-2,3-dihydro-1H-inden-2-yl)-2-methylpropan-1-one (4f)



DMSO (13 ml) was added to anhydrous potassium carbonate (2.372 g, 17.16 mmol, 2.2 equiv.) followed by 5-methylhexane-2,4-dione (1 g, 7.80 mmol, 1.0 equiv.). The mixture was stirred under nitrogen atmosphere. Then, 1,2-bis(bromomethyl)benzene (2.06 g, 7.80 mmol, 1.0 equiv.) dissolved in DMSO (6 ml) was added dropwise during 10 min using a syringe pump. The reaction mixture was then left to stir over night at rt. The mixtured was filtered. Water and diethyl ether was added to the filtrate and the water phase was extracted twice with ether. The combined organics were dried using Na2SO4, filtered and evaporated. The crude was further purified by flash chromatography (GRACE system, 50 g SiO_2-column) using a gradient of 0 - 20 % EtOAc in heptane, ELS-detection and UV detection at 254 / 280 nm, 15 CV. Gave 1-(2-acetyl-2,3-dihydro-1*H*-inden-2-yl)-2-methylpropan-1-one **4f** (0.812 g, 3.53 mmol, 45.2 %) as a colorless oil.
Appearance: Colorless oil
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.12 - 7.22 (m, 4H), 3.43 - 3.65 (m, 4H), 2.89 - 3.04 (m, 1H), 2.17 (s, 3H), 1.06 (d, *J* = 6.71 Hz, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 211.7, 204.8, 139.9, 127.1, 124.5, 75.7, 37.6, 37.2, 26.9, 20.3.
HRMS: m/z $[M+H]^+$ calculated for $[C_{15}H_{18}O_2+H]^+$, 231.1385; found 231.1397

1-(2-(Cyclopropanecarbonyl)-2,3-dihydro-1H-inden-2-yl)ethanone (4g)



DMSO (13 ml) was added to anhydrous potassium carbonate (2.41 g, 17.44 mmol, 2.2 equiv.) followed by 1-cyclopropylbutane-1,3-dione (1 g, 7.93 mmol, 1.0 equiv.). The mixture was stirred under nitrogen atmosphere. Then, 1,2-bis(bromomethyl)benzene (2.09 g, 7.93 mmol, 1.0 equiv.) dissolved in DMSO (6 ml) was added dropwise during 20 min using a syringe pump. The reaction mixture was then left to stir over night at rt. Water and diethyl ether was added, the phases were separated and the water phase was extracted twice with ether. The combined organics were dried using Na_2SO_4, filtered and evaporated. The crude was further purified by flash chromatography (GRACE system, 50 g SiO_2-column) using a gradient of 0 - 10 % EtOAc in heptane, ELS-detection and UV detection at 254 / 280 nm, 18 CV. Gave 1-(2-(cyclopropanecarbonyl)-2,3-dihydro-1*H*-inden-2-yl)ethenone **4g** (0.911 g, 3.99 mmol, 50.3 %) as a colorless oil.

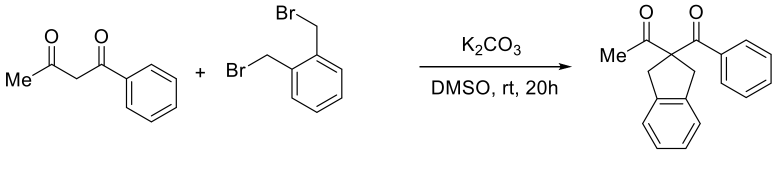
Appearance: Colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.22 - 7.35 (m, 4H), 3.59 - 3.84 (m, 4H), 2.31 (s, 3H), 1.98 - 2.13 (m, 1H), 1.13 - 1.26 (m, 2H), 0.99 - 1.13 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 206.8, 204.5, 139.8, 126.9, 124.4, 74.4, 37.3, 26.7, 18.1, 12.3.

HRMS m/z $[M+H]^+$ calculated for $[C_{15}H_{16}O_2+H]^+$, 229.1228; found 229.1219.

1-(2-Benzoyl-2,3-dihydro-1H-inden-2-yl)ethanone (4h)[1]



S1h **S2** **4h**

DMSO (13 ml) was added to anhydrous potassium carbonate (1.88 g, 13.56 mmol, 2.2 equiv.) followed by 1-phenylbutane-1,3-dione (1 g, 6.17 mmol, 1.0 equiv.). The mixture was stirred under nitrogen atmosphere. Then, 1,2-bis(bromomethyl)benzene (1.63 g, 6.17 mmol, 1.0 equiv.) dissolved in DMSO (6 ml) was added dropwise during 20 min using a syringe pump. The reaction mixture was then left to stir over night at rt. Water and diethyl ether was added. The phases were separated and the water phase was extracted twice with ether. The combined organics were dried using Na_2SO_4, filtered and evaporated. The crude was further purified by flash chromatography (GRACE system, 50 g SiO_2-column) using a gradient of 0 → 20 % EtOAc in heptane, ELS-detection and UV detection at 254 / 280 nm, 18 CV. Gave 1-(2-benzoyl-2,3-dihydro-1*H*-inden-2-yl)ethanone **4h** (0.54 g, 2,04 mmol, 33.1 %) as a colorless oil. The purity was determined to be 74 % using NMR with trimetoxybenzene as internal standard and used in the rearrangement reaction. Measured experimental NMR data is in full agreement with previously described spectra in the literature.[1]

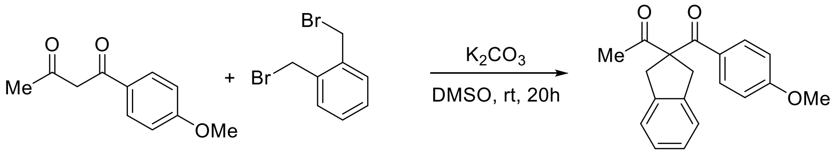
Appearance: Colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.86 - 7.92 (m, 2H), 7.45 - 7.5 (m, 2H), 7.14 - 7.22 (m, 4H), 3.63 - 3.88 (m, 5H), 2.15 (s, 3H).

^{13}C NMR (126 MHz, CD_3OD) δ (ppm) = 206.7, 198.4, 141.0, 134.6, 134.0, 130.2, 130.0, 128.0, 125.3, 73.2, 40.4, 26.9.

HRMS m/z $[M+H]^+$ calculated for $[C_{18}H_{16}O_2+H]^+$, 265.1228; found 265.1223.

1-(2-(4-Methoxybenzoyl)-2,3-dihydro-1H-inden-2-yl)ethan-1-one (4i)



S1i **S2** **4i**

DMSO (12 ml) was added to anhydrous potassium carbonate (1.60 g, 11.58 mmol, 2.2 equiv.) followed by 1-(4-methoxyphenyl)butane-1,3-dione (1.01 g, 5.25 mmol, 1.0 equiv.). The mixture was stirred under nitrogen atmosphere. Then, 1,2-bis(bromomethyl)benzene (1.39 g, 5.27 mmol, 1.0 equiv.) dissolved in DMSO (5.52 ml) was added dropwise during 20 min using a syringe pump. The reaction mixture was then left to stir over night at rt. Water and diethyl ether was added, the phases were separated and the water phase was extracted twice with ether. The combined organics were dried using Na_2SO_4, filtered and evaporated. The crude was further purified by flash chromatography (GRACE system, 100 g SiO_2-column) using a gradient of 0 - 12 % EtOAc in heptane, 254 / 280 nm and ELS-detection , 14 CV, then 12 - 20 % for 4 CV. Gave 1-(2-(4-methoxybenzoyl)-2,3-dihydro-1*H*-inden-2-yl)ethan-1-one **4i** (0.36 g, 1.22 mmol, 23.1 %) as a white solid after evaporation of solvents.

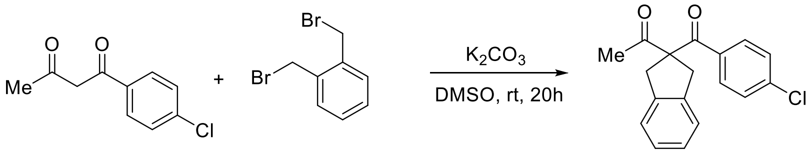
Appearance: White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.84 - 7.92 (m, 2H), 7.12 - 7.23 (m, 4H), 6.88 - 6.98 (m, 2H), 3.88 (s, 3H), 3.63 - 3.86 (m, 4H), 2.13 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 205.0, 194.9, 163.6, 139.7, 131.7, 127.8, 126.9, 124.3, 114.0, 72.0, 55.5, 39.2, 26.8.

HRMS m/z $[M+H]^+$ calculated for $[C_{19}H_{18}O_3+H]^+$, 295.1334; found 295.1337.

1-(2-(4-Chlorobenzoyl)-2,3-dihydro-1H-inden-2-yl)ethan-1-one (4j)



S1j **S2** **4j**

DMSO (12 ml) was added to anhydrous potassium carbonate (1.72 g, 12.45 mmol, 2.37 equiv.) followed by 1-(4-chlorophenyl)butane-1,3-dione (1.07 g, 5.44 mmol, 1.04 equiv.). The mixture was stirred under nitrogen atmosphere. Then, 1,2-bis(bromomethyl)benzene (1.39 g, 5.25 mmol, 1.00 equiv.) dissolved in DMSO (5.7 ml) was added dropwise during 20 min using a syringe pump. The reaction mixture was then left to stir over night at rt. The mixture was filtered, the solid was washed with diethyl ether. Water was added to the organics, the phases were separated and the water phase was extracted twice with ether. The combined organics were dried using Na_2SO_4, filtered and evaporated. The crude was further purified by flash chromatography (GRACE system, 100 g SiO_2-column) using a gradient of 0 - 15 % EtOAc in heptane, 240 / 260 nm and ELS-detection, 18 CV. Gave 1-(2-(4-chlorobenzoyl)-2,3-dihydro-1*H*-inden-2-yl)ethan-1-one **4j** (0.45 g, 1.69 mmol, 31 %) as a white solid after evaporation of solvents.

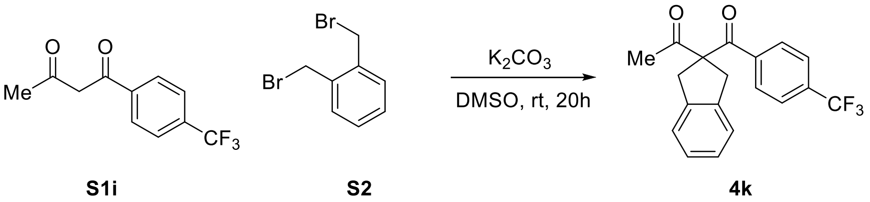
Appearance: White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.89 - 7.95 (m, 2H), 7.5 - 7.57 (m, 2H), 7.23 - 7.33 (m, 4H), 3.85 (d, *J* =16.5 2H), 3.81 (d, *J* =16.5 Hz, 2H), 2.24 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) = 204.5, 195.4, 140.0, 139.4, 133.3, 130.7, 129.2, 127.1, 124.3, 72.3, 39.1, 26.9.

HRMS m/z $[M+H]^+$ calculated for $[C_{18}H_{15}ClO_2+H]^+$, 299.0839; found 299.0852.

1-(2-(4-(Trifluoromethyl)benzoyl)-2,3-dihydro-1H-inden-2-yl)ethan-1-one (4k)



DMSO (10 ml) was added to anhydrous potassium carbonate (1.56 g, 11.29 mmol, 2.6 equiv.) followed by 1-(4-(trifluoromethyl)phenyl)butane-1,3-dione (1 g, 4.34 mmol, 1.0 equiv.). The mixture was stirred under nitrogen atmosphere. Then, 1,2-bis(bromomethyl)benzene (1.2 g, 4.55 mmol, 1.05 equiv.) dissolved in DMSO (5 ml) was added dropwise during 20 min using a syringe pump. The reaction mixture was then left to stir over night at rt. Water and diethyl ether was added, the phases were separated and the water phase was extracted twice with ether. The combined organics were dried using Na_2SO_4, filtered and evaporated. The crude was further purified by flash chromatography (GRACE system, 100 g SiO_2-column) using a gradient of 0 - 20 % EtOAc in heptane, 240 and 260 nm and ELS-detection, 18 CV. Gave 1-(2-(4-(trifluoromethyl)benzoyl)-2,3-dihydro-1*H*-inden-2-yl)ethan-1-one **4k** (0.48 g, 1.45 mmol, 33.3 %) as a white solid after evaporation of solvents (purity 91 %).

Appearance: White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 8.07 (d, *J*=8.2 Hz, 2H), 7.75 - 7.89 (m, 2H), 7.38 - 7.44 (m, 1H), 7.24 - 7.32 (m, 3H), 3.74 - 3.98 (m, 4H), 2.25 (s, 3H).

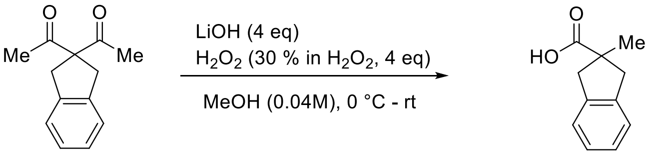
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 204.4, 196.1, 139.4, 138.0, 134.8 (q, *J* = 32.8), 129.8, 127.3, 126.8, 126.0 (q, *J* = 3.7), 124.6, 124.5, 122.5, 120.3, 72.6, 39.3, 27.0.

^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -63.26 (s).

HRMS m/z $[M+H]^+$ calculated for $[C_{19}H_{15}F_3O_2+H]^+$, 333.1102; found 333.1114.

2.2 Study of the effect substituents and characterization of all-carbon quaternary carboxylates

2-Methyl-2,3-dihydro-1H-indene-2-carboxylic acid (1c)



4c **1c**

LiOH (95 mg, 3.96 mmol, 4.0 equiv.) and 30% H_2O_2 in water (0.40 ml, 3.96 mmol, 4.0 equiv.) were mixed in MeOH (8 ml) at 0 °C for 20 min. 1,1'-(2,3-dihydro-1*H*-indene-2,2-diyl)bis(ethan-1-one) **4c** (0.2 g, 0.99 mmol, 1.0 equiv.) in MeOH (19 ml) cooled to 0 °C was added. The reaction was left at 0 °C for 30 min. The ice bath was removed and the stirring was continued for 30 min at rt. Water and NaOH (10% aq solution) was added followed by diethyl ether. The water phase was extracted twice with diethyl ether. The water phase was made acidic with 3.8 M HCl. The suspension was extracted with diethyl ether four times. The pooled organics were dried (Na_2SO_4), filtered and evaporated. Gave 2-methyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1c** (150 mg, 0.85 mmol, 85 %) as a white solid.

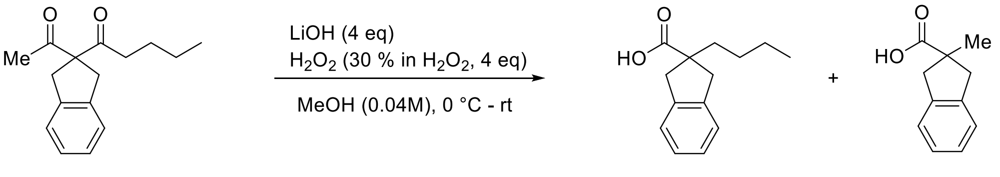
Appearance: White solid

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 1.34 (s, 3H), 2.79 (d, *J* = 15.6 Hz, 2H), 3.44 (d, *J* = 15.7 Hz, 2H), 7.07 - 7.25 (m, 4H).

^{13}C NMR (101 MHz, CD_3OD) δ (ppm) = 181.4, 142.6, 127.6, 125.5, 50.7, 45.0, 25.3.

HRMS m/z $[M-H]^-$ calculated for $[C_{11}H_{12}O_2-H]^-$, 175.0759; found 175.0742.

2-Butyl-2,3-dihydro-1H-indene-2-carboxylic acid (1d)



4d **1d** **1c**

LiOH (0.24 g, 10.19 mmol, 4.0 equiv) was dissolved in MeOH (19 ml) and 30% H_2O_2 in water (1.02 ml, 9.95 mmol, 4.0 equiv.) was added at 0 °C under nitrogen. The mixture was left at 0 °C for 30 min. A white solid was formed. The mixture was cooled to 0 °C and 1-(2-acetyl-2,3-dihydro-1*H*-inden-2-yl)pentan-1-one **4d** (0.61 g, 2.49 mmol, 1.0 equiv.) in MeOH (49 ml) cooled to 0 °C was added (the solid went into solution). The reaction was left at 0 °C for 1h, then at room temperature for 1h and then cooled again to 0 °C. Water was added dropwise followed by diethyl ether. The water phase was extracted twice with diethyl ether. The water phase was made acidic with 3.8 M HCl. The suspension was extracted twice with diethyl ether. The pooled organics were dried (Na_2SO_4), filtered and evaporated. The crude solid was purified by preparative HPLC on a Kromasil C8 column (10 µm 250 x

50 ID mm) using a gradient of 25 - 65 % acetonitrile in H_2O/ACN/FA 95/5/0.2 buffer over 20 minutes with a flow of 100 mL/min. The compounds were detected by UV at 265 nm. Gave 2-butyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1d** (110 mg, 0.50 mmol, 20 %) and 2-methyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1c** (210 mg, 1.20 mmol, 48 %) as white solids. NMR data of **1c** was in full agreement with spectra reported above, characterization data of **1d** as follows:

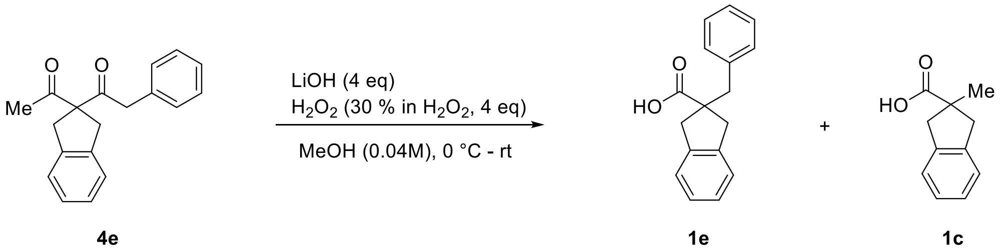
Appearance: White solid

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 7.05 - 7.2 (m, 4H), 3.42 (d, *J* =15.9 Hz, 2H), 2.87 (d, *J* =15.9 Hz, 2H), 1.68 - 1.8 (m, 2H), 1.24 - 1.38 (m, 4H), 0.84 - 0.97 (m, 3H).

^{13}C NMR (101 MHz, CD_3OD) δ (ppm) = 180.7, 142.7, 127.5, 125.3, 55.5, 43.2, 39.6, 29.0, 24.2, 14.3.

HRMS m/z $[M+NH_4]^+$ calculated for $[C_{14}H_{18}O_2+ NH_4]^+$, 236.1651; found 236.1647.

2-Benzyl-2,3-dihydro-1H-indene-2-carboxylic acid (1e)



LiOH (0.16 g, 6.68 mmol, 4.0 equiv.) was dissolved in MeOH (13 ml) and 30% H_2O_2 in water (0.68 ml, 6.61 mmol, 4.0 equiv.) was added at 0 °C. The mixture was left at 0 °C for 30 min. 1-(2-acetyl-2,3-dihydro-1*H*-inden-2-yl)-2-phenylethan-1-one **4e** (0.46 g, 1.65 mmol, 1.0 equiv.) in MeOH (32 ml) cooled to 0 °C was added. The reaction was left at 0 °C for 50 min. The ice bath was removed and the reaction was continued for 1h at rt and then cooled again to 0 °C. Water was added dropwise followed by diethyl ether. The water phase was extracted twice with diethyl ether. The water phase was made acidic with 3.8 M HCl. The suspension was extracted with diethyl ether two times. The pooled organics were dried (Na_2SO_4), filtered and evaporated. The crude was further purified by preparative HPLC on a Kromasil C8 column (10 µm 250 x 50 ID mm) using a gradient of 30 - 75 % acetonitrile in H_2O/ACN/FA 95/5/0.2 buffer over 20 minutes with a flow of 100 mL/min. The compounds were detected by UV at 265 nm. Gave 2-benzyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1e** (100 mg, 0.40 mmol, 24 %) and 2-methyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1c** (120 mg, 0.69 mmol, 42 %) after evaporation of solvents as white solids. NMR data of **1c** was in full agreement with spectra reported above, characterization data of **1e** as follows:

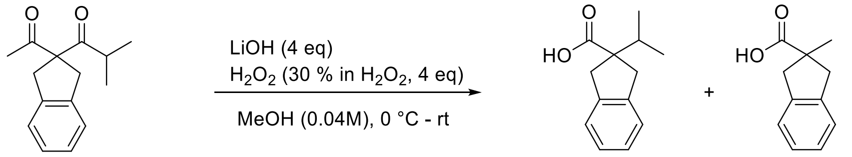
Appearance: White solid

^{1}H NMR (500 MHz, CD_3OD) δ (ppm) = 7.09 - 7.28 (m, 9H), 3.34 (s, 1H), 3.03 (s, 2H), 2.98 (d, *J* = 15.8 Hz, 2H).

^{13}C NMR (126 MHz, CD_3OD) δ (ppm) = 179.9, 142.5, 139.4, 130.8, 129.2, 127.6, 127.6, 125.5, 56.9, 44.2, 42.6.

HRMS m/z $[M+NH_4]^+$ calculated for $[C_{17}H_{16}O_2+NH_4]^+$, 270.1494; found 270.1495.

2-Isopropyl-2,3-dihydro-1H-indene-2-carboxylic acid (1f)



4f **1f** **1c**

LiOH (0.21 g, 8.68 mmol, 4.0 equiv.) was dissolved in MeOH (17 ml) and 30 % H_2O_2 in water (0.89 ml, 8.68 mmol, 4.0 equiv.) was added at 0 °C. The mixture was stirred for 30 min. 1-(2-acetyl-2,3-dihydro-1*H*-inden-2-yl)-2-methylpropan-1-one **4f** (0.5 g, 2.17 mmol, 1.0 equiv.) in MeOH (42 ml) cooled to 0 °C was added. The reaction was left at 0 °C for 30 min. The ice bath was removed and the stirring was continued for 45 min at rt, then cooled again to 0 °C. Water was added dropwise followed by diethyl ether. The water phase was extracted twice with diethyl ether. The water phase was made acidic with 3.8 M HCl. The suspension was extracted with diethyl ether two times. The pooled organics were dried (Na_2SO_4), filtered and evaporated. The crude product was purified by preparative HPLC on a Kromasil C8 column (10 µm 250 x 50 ID mm) using a gradient of 15 - 65 % acetonitrile in H_2O/ACN/FA 95/5/0.2 buffer over 25 minutes with a flow of 100 mL/min. The compounds were detected by UV at 265 nm. Gave 2-isopropyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1f** (120 mg, 0.61 mmol, 28 %) and 2-methyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1c** (110 mg, 0.63 mmol, 29 %) after evaporation of solvents. NMR data of **1c** was in full agreement with spectra reported above, characterization data of **1f** as follows:

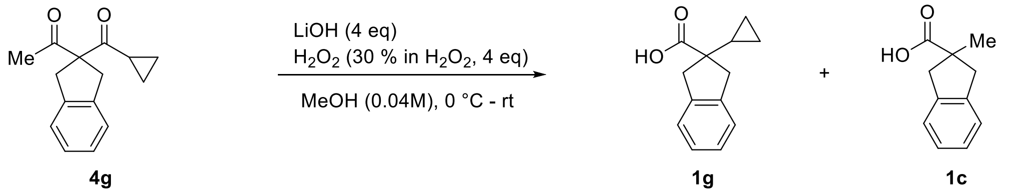
Appearance: White solid

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 7.04 - 7.19 (m, 4H), 3.44 (d, *J* = 16.1 Hz, 2H), 2.94 (d, *J* = 16.1 Hz, 2H), 2.1 - 2.23 (m, 1H), 0.92 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (101 MHz, CD_3OD) δ (ppm) = 180.4, 143.1, 127.4, 124.9, 59.7, 40.9, 36.64, 18.8.

HRMS m/z $[M+NH_4]^+$ calculated for $[C_{13}H_{16}O_2+NH_4]^+$, 222.1494; found 222.1492.

2-Cyclopropyl-2,3-dihydro-1H-indene-2-carboxylic acid (1g)



4g **1g** **1c**

LiOH (0.23 g, 9.41 mmol, 4.0 equiv.) was dissolved in MeOH (18 ml) and 30% H_2O_2 in water (0.96 ml, 9.41 mmol, 4.0 equiv.) was added at 0 °C. The mixture was stirred for 30 min. 1-(2-

(cyclopropanecarbonyl)-2,3-dihydro-1*H*-inden-2-yl)ethan-1-one **4g** (0.54 g, 2.35 mmol, 1.0 equiv.) in MeOH (46 ml) cooled to 0 °C were added. The reaction was left at 0 °C for 30 min. The ice bath was removed and the stirring was continued for 45 min at rt and then cooled again to 0 °C. Water was added dropwise followed by diethyl ether. The water phase was extracted twice with diethyl ether. The water phase was made acidic with 3.8 M HCl. The suspension was extracted two times with diethyl ether. The pooled organics were dried (Na_2SO_4), filtered and evaporated. The crude was purified by preparative HPLC on a Kromasil C8 column (10 µm 250x50 ID mm) using a gradient of 15 - 65 % acetonitrile in H_2O/ACN/FA 95/5/0.2 buffer over 25 minutes with a flow of 100 mL/min. The compounds were detected by UV at 265nm. Gave 2-cyclopropyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1g** (105 mg, 0.52 mmol, 22 %) and 2-methyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1g** (243 mg, 1.39 mmol, 59 %) after evaporation of solvents. NMR data of **1c** was in full agreement with spectra reported above, characterization data of **1g** as follows:

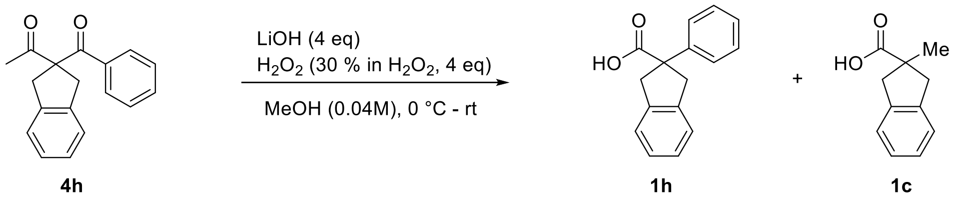
Appearance: White solid

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 7 - 7.23 (m, 4H), 3.35 (d, *J* = 15.9 Hz, 2H), 2.78 (d, *J* = 15.9 Hz, 2H), 1.17 - 1.28 (m, 1H), 0.26 - 0.46 (m, 4H).

^{13}C NMR (101 MHz, CD_3OD) δ (ppm) 180.5, 142.7, 127.5, 125.1, 55.1, 41.2, 18.9, 2.0.

HRMS m/z $[M+NH_4]^+$ calculated for $[C_{13}H_{14}O_2+NH_4]^+$, 220.1338; found 220.1317.

2-Phenyl-2,3-dihydro-1H-indene-2-carboxylic acid (1h)



LiOH (0.16 g, 6.76 mmol, 4.0 equiv.) was dissolved in MeOH (13 ml) and 30% H_2O_2 in water (0.69 ml, 6.72 mmol, 4.0 equiv.) was added at 0 °C. The mixture was left at 0 °C for 30 min. A white solid was formed. 1-(2-benzoyl-2,3-dihydro-1*H*-inden-2-yl)ethan-1-one **4h** (0.6 g, 1.68 mmol, 1.0 equiv.) in MeOH (33 ml) cooled to 0 °C was added (the solid went into solution). The reaction was left at 0 °C and stirred for 30 min, at rt for 2h and then cooled again to 0 °C. Water was added dropwise followed by diethyl ether. The water phase was extracted twice with diethyl ether. The water phase was made acidic with 3.8 M HCl. The suspension was extracted with diethyl ether two times. The pooled organics were dried (Na_2SO_4), filtered and evaporated. The crude solid was purified by preparative HPLC on a Kromasil C8 column (10 µm 250 x 50 ID mm) using a gradient of 15 - 65 % acetonitrile in H_2O/ACN/FA 95/5/0.2 buffer over 25 minutes with a flow of 100 mL/min. The compounds were detected by UV at 265nm. Gave 2-phenyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1h** (34 mg, 0.13 mmol, 8 %) and 2-methyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **4h** (190 mg, 1.08 mmol, 64 %) as white solids after evaporation of solvents. NMR data of **1c** was in full agreement with spectra reported above, characterization data of **1h** as follows:

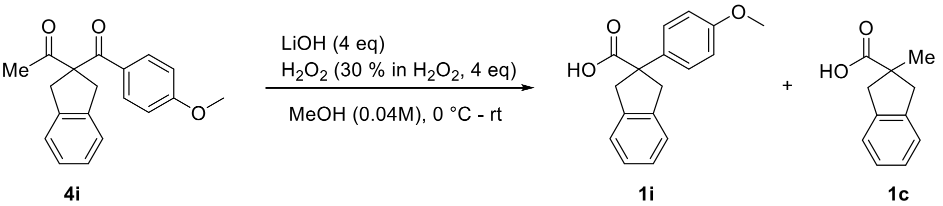
Appearance: White solid

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 7.41 - 7.49 (m, 2H), 7.28 - 7.36 (m, 2H), 7.2 - 7.28 (m, 3H), 7.08 - 7.18 (m, 2H), 3.94 (d, *J* = 15.5, 2H), 3.27 (d, *J* = 15.5, 2H).

^{13}C NMR (101 MHz, CD_3OD) δ (ppm) = 179.0, 144.4, 142.6, 129.4, 128.0, 127.9, 127.7, 125.1, 60.8, 43.7.

HRMS m/z $[M+NH_4]^+$ calculated for $[C_{16}H_{14}O_2+NH_4]^+$, 256.1338; found 256.1299.

2-(4-Methoxyphenyl)-2,3-dihydro-1H-indene-2-carboxylic acid (1i)



LiOH (77 mg, 3.23 mmol, 4.0 equiv.) was dissolved in MeOH (6 ml) and 30% H_2O_2 in water (0.33 ml, 3.23 mmol, 4.0 equiv.) was added at 0 °C. The mixture was stirred for 30 min (a solid was formed). A slurry of 1-(2-(4-methoxybenzoyl)-2,3-dihydro-1*H*-inden-2-yl)ethan-1-one **4i** (0.24 g, 0.81 mmol, 1.0 equiv.) in MeOH (16 ml) cooled to 0 °C were added. The reaction was left at 0 °C for 30 min, everything went into solution. The ice bath was removed and the stirring was continued for 45 min at rt and then cooled again to 0 °C. Water was added dropwise followed by diethyl ether. The water phase was extracted twice with diethyl ether. The water phase was made acidic with 3.8 M HCl. The suspension was extracted two times with diethyl ether. The pooled organics were dried (Na_2SO_4), filtered and evaporated. The crude (217 mg) was purified by preparative HPLC on a Kromasil C8 column (10 µm 250 x 50 ID mm) using a gradient of 15 - 65 % acetonitrile in H_2O/ACN/FA 95/5/0.2 buffer over 25 minutes with a flow of 100 mL/min. The compounds were detected by UV at 270 nm. Gave 2-(4-methoxyphenyl)-2,3-dihydro-1H-indene-2-carboxylic acid **1i** (14 mg, 0.066 mmol, 7 %) and 2-methyl-2,3-dihydro-1H-indene-2-carboxylic acid (81 mg, 0.46 mmol, 57 %) **1c** as white solids after evaporation of solvents. NMR data of **1c** was in full agreement with spectra reported above, characterization data of **1i** as follows:

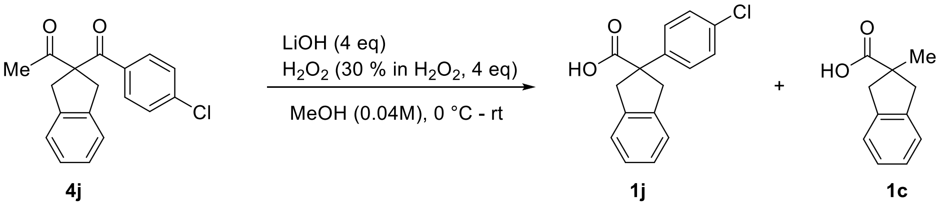
Appearance: White solid

^{1}H NMR (400 MHz, CD_3OD δ (ppm) = 7.31 - 7.4 (m, 2H), 7.18 - 7.26 (m, 2H), 7.08 - 7.17 (m, 2H), 6.84 - 6.92 (m, 2H), 3.91 (d, *J* = 15.4 Hz, 2H), 3.77 (s, 3H), 3.23 (d, *J* = 15.4 Hz, 2H).

^{13}C NMR (101 MHz, CD_3OD) δ (ppm) = 179.3, 160.1, 142.8, 136.3, 129.0, 127.6, 125.1, 114.7, 60.2, 55.7, 43.8.

HRMS m/z $[M+H]^+$ calculated for $[C_{17}H_{16}O_3+H]^+$, 269.1178; found 269.1159.

2-(4-Chlorophenyl)-2,3-dihydro-1H-indene-2-carboxylic acid (1j)



LiOH (0.17 g, 7.24 mmol, 4.0 equiv.) was dissolved in MeOH (14 ml) and 30% H_2O_2 in water (0.74 ml, 7.24 mmol, 4.0 equiv.) was added at 0 °C. The mixture was stirred for 30 min, a solid was formed. 1-(2-(4-chlorobenzoyl)-2,3-dihydro-1*H*-inden-2-yl)ethan-1-one **4j** (0.54 g, 1.81 mmol, 1.0 equiv.) in MeOH (35 ml) cooled to 0 °C were added (a slurry). The reaction was left at 0 °C for 30 min, everything went into solution. The ice bath was removed and the stirring was continued for 45 min at rt and then cooled again to 0 °C.

Water was added dropwise followed by diethyl ether. The water phase was extracted with diethyl ether twice. The water phase was made acidic with 3.8 M HCl. The suspension was extracted two times with diethyl ether. The pooled organics were dried (Na_2SO_4), filtered and evaporated. The crude (389 mg) was purified by preparative HPLC on a Kromasil C8 column (10 µm 250 x 50 ID mm) using a gradient of 15 - 75 % acetonitrile in H_2O/ACN/FA 95/5/0.2 buffer over 25 minutes with a flow of 100 mL/min. The compounds were detected by UV at 240 /270 nm. Gave 2-(4-chlorophenyl)-2,3-dihydro-1*H*-indene-2-carboxylic acid (18 mg, 0.065 mmol, 3.6 %) **1j** and 2-methyl-2,3-dihydro-1*H*-indene-2-carboxylic acid (165 mg, 0.92 mmol, 51 %) **1c** as white solids. NMR data of **1c** was in full agreement with spectra reported above, characterization data of **1j** as follows:

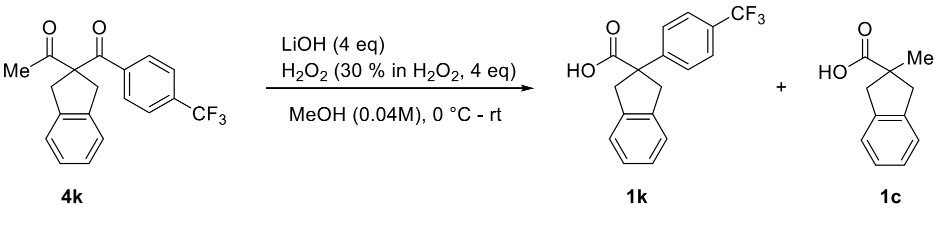
Appearance: White solid

^{1}H NMR (400 MHz, CD_3OD) δ (ppm) = 7.4 - 7.48 (m, 2H), 7.29 - 7.37 (m, 2H), 7.19 - 7.28 (m, 2H), 7.09 - 7.19 (m, 2H), 3.93 (d, *J* = 15.5 Hz, 2H), 3.26 (d, *J* = 15.5 Hz, 2H).

^{13}C NMR (126 MHz, CD_3OD) δ (pmm) = 178.5, 143.2, 142.4, 133.9, 129.6, 129.4, 127.8, 125.2, 60.4, 43.7.

HRMS m/z $[M+NH_4]^+$ calculated for $[C_{16}H_{13}ClO_2+NH_4]^+$, 290.0947; found 290.0941.

2-(4-(Trifluoromethyl)phenyl)-2,3-dihydro-1H-indene-2-carboxylic acid (1k)



LiOH (0.125 g, 5.21 mmol, 4.0 equiv.) was dissolved in MeOH (10 ml) and 30% H_2O_2 in water (0.53 ml, 5.21 mmol, 4.0 equiv.) was added at 0 °C. The mixture was stirred for 30 min (a solid was formed). 1-(2-(4-(trifluoromethyl)benzoyl)-2,3-dihydro-1*H*-inden-2-yl)ethan-1-one **4k** (0.48 g, 1.30 mmol, 1.0 equiv.) in MeOH (26 ml) cooled to 0 °C were added (a slurry). The reaction was left at 0 °C for 30 min (everything went into solution). The ice bath was removed and the stirring was continued for 45 min at rt and then cooled again to 0 °C. Water was added dropwise followed by diethyl ether. The water phase was extracted twice with diethyl ether. The water phase was made acidic with 3.8 M HCl. The suspension was extracted with diethyl ether two times. The pooled organics were dried (Na_2SO_4), filtered and evaporated. The crude (369 mg) was purified by preparative HPLC on a Kromasil C8 column (10 µm 250 x 50 ID mm) using a gradient of 15 - 75 % acetonitrile in H_2O/ACN/FA 95/5/0.2 buffer over 25 minutes with a flow of 100 mL/min. The compounds were detected by UV at 240 nm. Gave 2-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-indene-2-carboxylic acid **1k** (8 mg, 0.026 mmol, 2 %) as a white solid. The other carboxylic acid was not pure after the preparative HPLC. The compound was purified again on the Kromasil C8 column (10 µm 250 x 50 ID mm) using a gradient of 15-55 % acetonitrile in H_2O/ACN/FA 95/5/0.2 buffer over 20 minutes with a flow of 100 mL/min. The compound was detected by UV at 270 nm. Still some impurity left. The amount of 2-methyl-2,3-dihydro-1*H*-indene-2-carboxylic acid (0.14 g, 0.81 mmol, 62 %) **1c** was calculated from ^1H NMR using dichloroethane as internal standard. NMR data of **1c** was in full agreement with spectra reported above, characterization data of **1k** as follows:

Appearance: White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.45 - 7.69 (m, 4H), 7.16 - 7.27 (m, 4H), 3.99 (d, *J* = 15.5 Hz, 2H), 3.33 (d, *J* = 15.5 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 179.6, 145.9, 140.5, 129.8 (q, *J* = 32.69), 127.6, 127.2, 125.7 (q, *J* = 3.78), 125.2, 124.5, 123.1, 59.4, 42.6.

^{19}F NMR (472 MHz, $CDCl_3$) δ (ppm) = -63.26.

HRMS m/z unable to be determined due to possible fast decomposition during the ionization process.

3 Mechanistic experiments

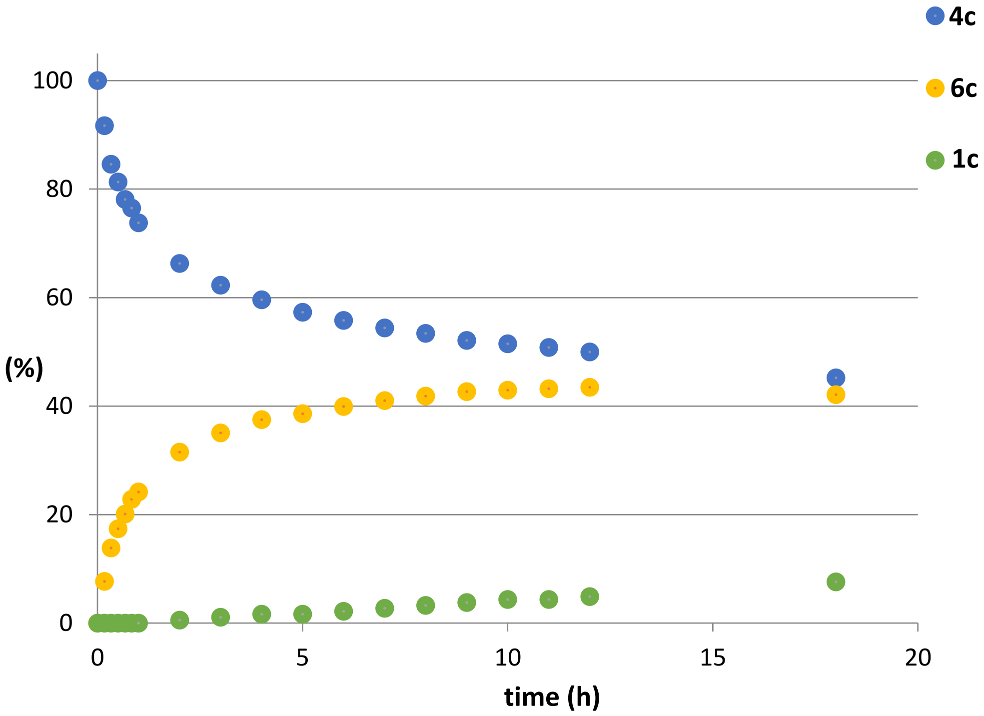
3.1 Diketone 4c and H_2O_2 in neutral media

Procedure

Diketone 1,1'-(2,3-Dihydro-1*H*-indene-2,2-diyl)diethanone **4c** (5.2 mg, 0.03 mmol) and 1,1,2,2-tetrachloroethane as internal standard (5.6 mg, 0.03 mmol) were dissolved in MeOD (0.5 mL) in a

NMR vial at rt. Then, water peroxide H_2O_2 (30 % in water, 10.51 µL, 0.10 mmol) was added and the reaction was monitored by ^{1}H-NMR for 18 h.

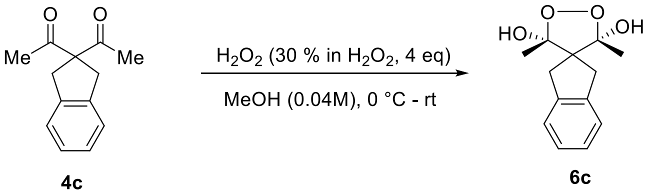
Time-profile data



Time (h)	Conversion (%)	% 4c	% 6c	% 1c
0	0	100	0	0
0,17	8	92	8	0
0,33	15	85	14	0
0,5	19	81	17	0
0,67	22	78	20	0
0,83	24	77	23	0
1	26	74	24	0
2	34	66	32	1
3	38	62	35	1
4	40	60	38	2
5	43	57	39	2
6	44	56	40	2
7	46	54	41	3
8	47	53	42	3
9	48	52	43	4
10	49	52	43	4
11	49	51	43	4
12	50	50	43	5
18	55	45	42	8

Characterization of intermediates 6c:

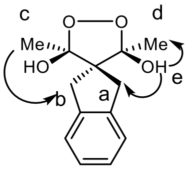
(3'R*,5'S*)-3',5'-dimethyl-1,3-dihydrospiro[indene-2,4'-[1,2]dioxolane]-3',5'-diol (meso-6c)



4c **6c**

Characterization of endoperoxide **6c** was carried out by NMR monitorization of the reaction in neutral conditions according to the general procedure described above. Diketone 1,1'-(2,3-Dihydro-1*H*-indene-2,2-diyl)diethanone **4c** (5.2 mg, 0.025 mmol, 1.0 equiv.) was dissolved in CD_3OD (0.5 mL) in a NMR vial at rt. Then, water peroxide H_2O_2 (30 % in water, 10.51 µL, 0.10 mmol, 4.0 equiv) was added and the reaction was monitored by ^{1}H-NMR. After 8h NMR showed appearance of intermediate **6c** in 42% according to the profile experiment, (*meso*-**6c**, *rac*-**6c** 10:1 ratio).

NOE



meso-**6c**

^{1}H NMR (600 MHz, CD_3OD) δ (ppm) 7.23 – 7.10 (m, 5H), 3.22 (s, 2H), 3.05 (s, 2H), 1.27 (s, 6H).

^{1}H NMR (400 MHz, DMSO*d6*) δ (ppm) 7.29 – 7.05 (m, 4H), 6.91 (s, 2H), 3.13 (s, 2H), 2.96 (s, 2H), 1.20 (s, 6H).

^{13}C NMR (151 MHz, CD_3OD) δ (pmm) = 141.2, 140.6, 126.5, 126.4, 123.9, 123.5, 107.1, 67.9, 37.9, 34.7, 18.0, 17.9.

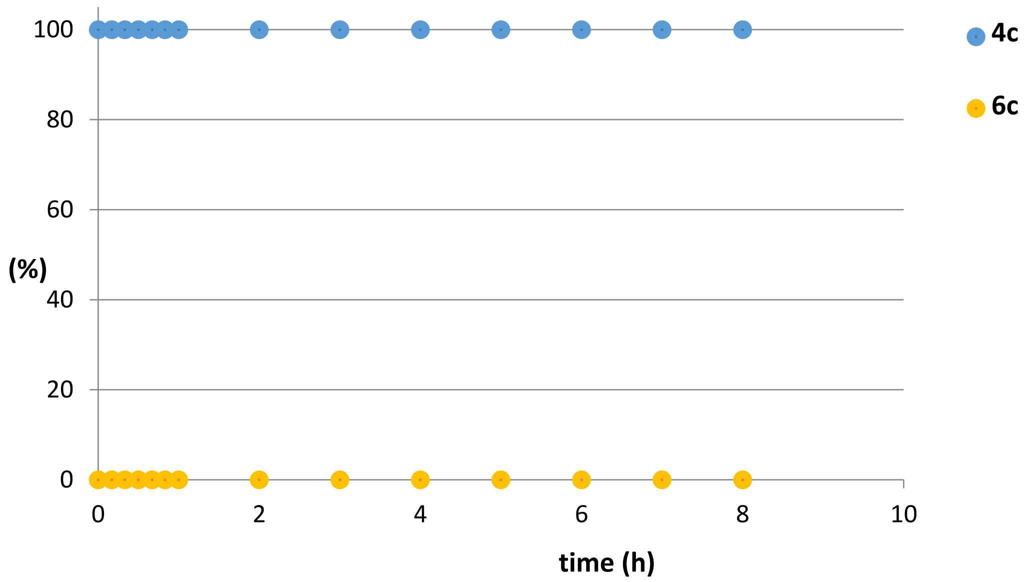
HRMS m/z unable to be determined due to possible fast decomposition during the ionization process.

3.2 Diketone 4c and H_2O_2 and AcOH as additive

Procedure

Diketone 1,1'-(2,3-Dihydro-1*H*-indene-2,2-diyl)diethanone **4c** (5.0 mg, 0.02 mmol), acetic acid (1.41 µL, 0.02 mmol, 1.0 equiv.) and 1,1,2,2-tetrachloroethane as internal standard (5.1 mg, 0.03 mmol) were dissolved in CD_3OD (0.5 mL) in a NMR vial at rt. Then, water peroxide H_2O_2 (30 % in water, 10.10 µL, 0.10 mmol, 4.0 equiv.) was added and the reaction was monitored by ^{1}H-NMR for 20 h.

Time-profile data



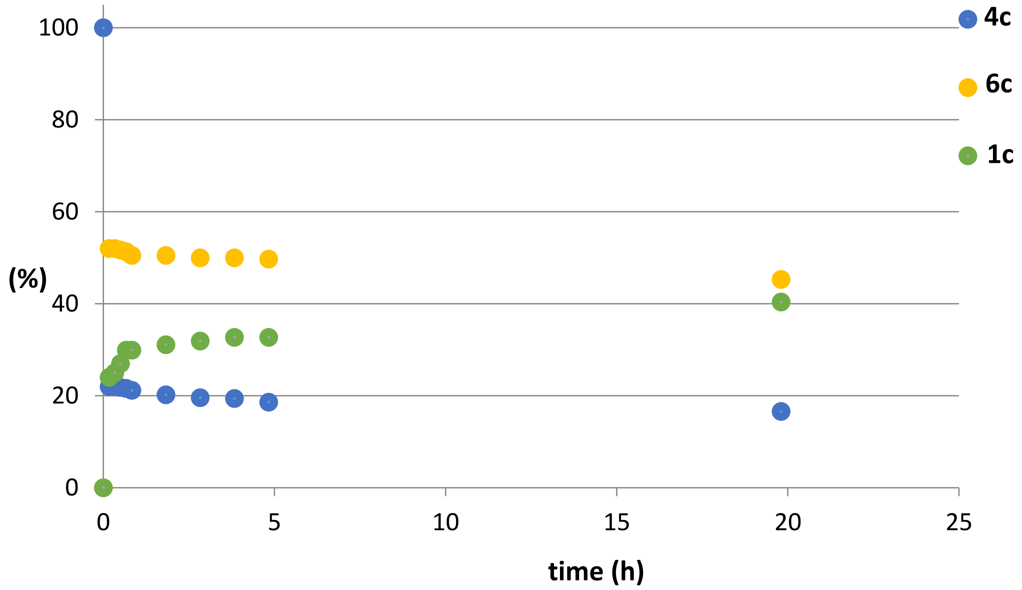
Time (h)	% 4c	% 6c
0	100	0
0,17	100	0
0,33	100	0
0,5	100	0
0,67	100	0
0,83	100	0
1	100	0
2	100	0
3	100	0
4	100	0
5	100	0
6	100	0
7	100	0
8	100	0

3.3 Diketone 4c with H_2O_2 and LiOH as additive

Procedure for the study of amount of base

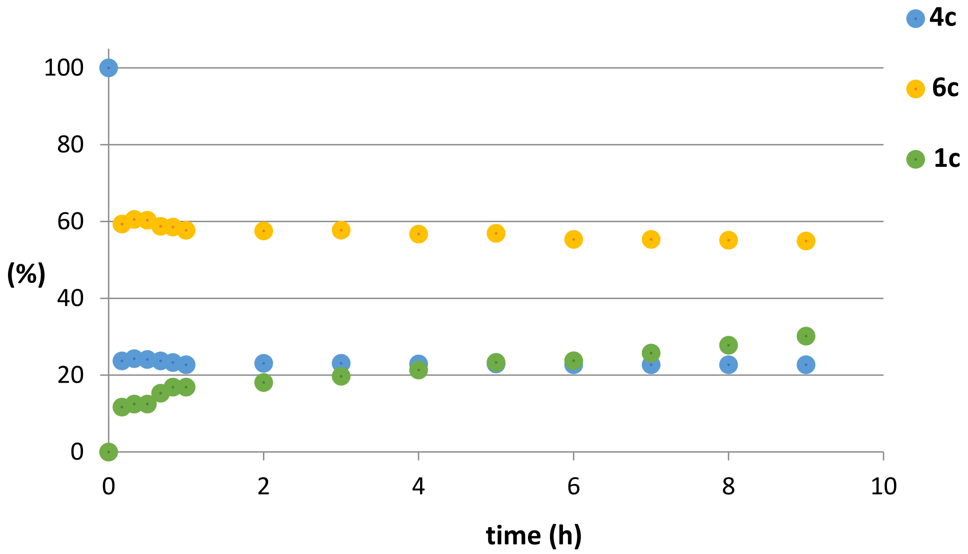
Diketone 1,1'-(2,3-Dihydro-1*H*-indene-2,2-diyl)bis(ethan-1-one) **4c** (5.1 mg, 0.025 mmol) and mesitylene (3.00 µL, 0.02 mmol) as internal standard were dissolved in CD_3OD (0.5 mL) in a NMR vial. Then, water peroxide H_2O_2 (30 % in water, 10.30 µL, 0.10 mmol, 4.0 equiv.) was added, followed by the base and the reaction was monitored by ^{1}H-NMR at rt for 20h.

Time-profile data LiOH (0.5 equivalents, 0.025 M)



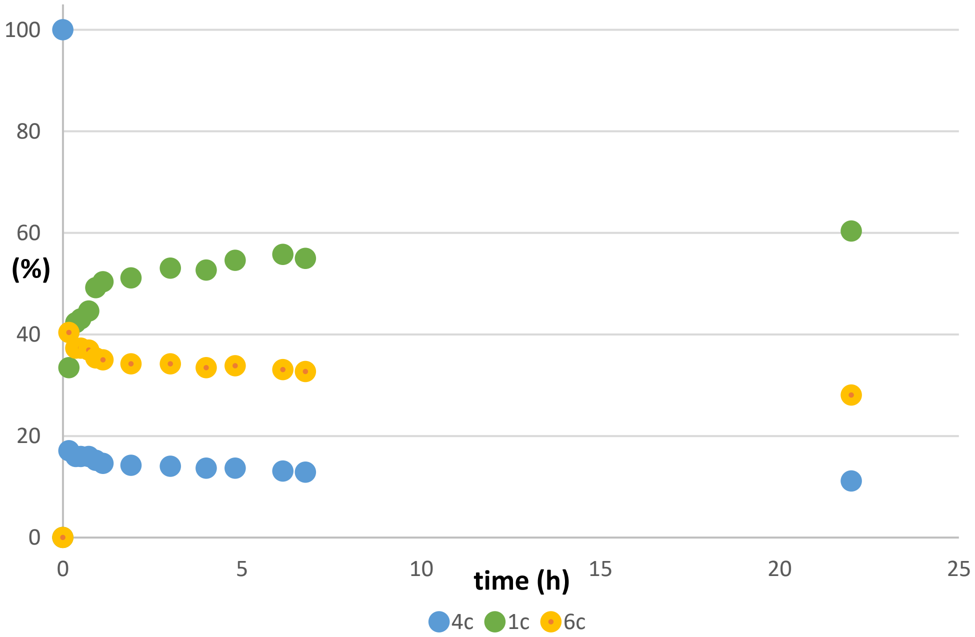
Time (h)	% 4c	% 6c	% 1c
0	100	0	0
0,17	22	52	24
0,33	22	52	25
0,5	22	52	27
0,67	22	51	30
0,83	21	51	30
1,83	20	51	31
2,83	20	50	32
3,83	19	50	33
4,83	19	50	33
19,8	17	45	40

Time-profile data LiOH (1 equivalent, 0.05 M)



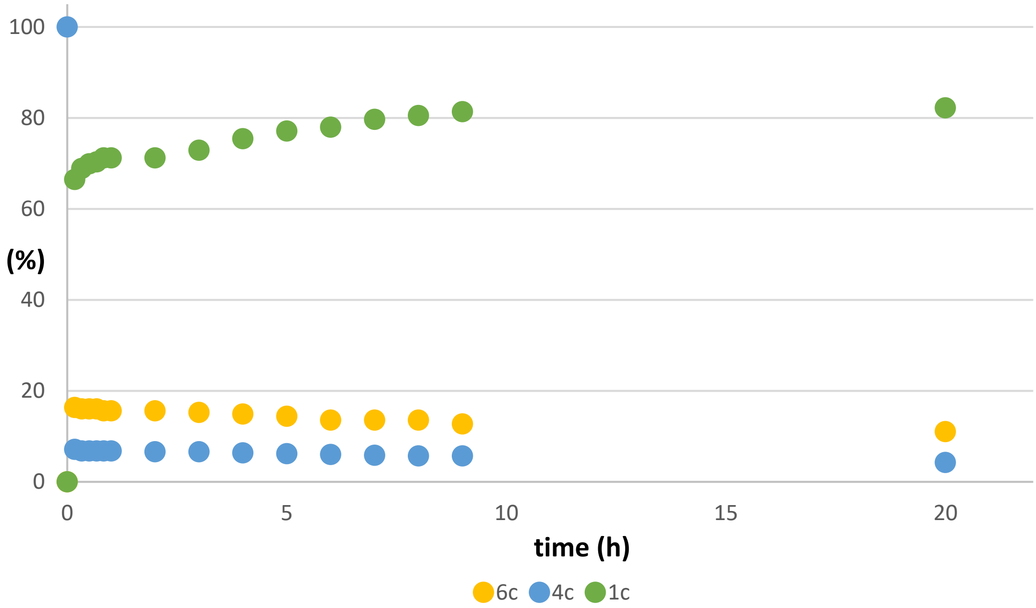
Time (h)	% 4c	% 6c	% 1c
0	100	0	0
0,17	22	59	12
0,33	22	61	12
0,5	22	60	12
0,67	22	59	15
0,83	21	59	17
1	21	58	17
2	21	58	18
3	21	58	20
4	21	57	21
5	21	57	23
6	21	55	24
7	21	55	26
8	21	55	28
9	21	54	29

Time-profile data LiOH (2 equivalents, 0.10 M)



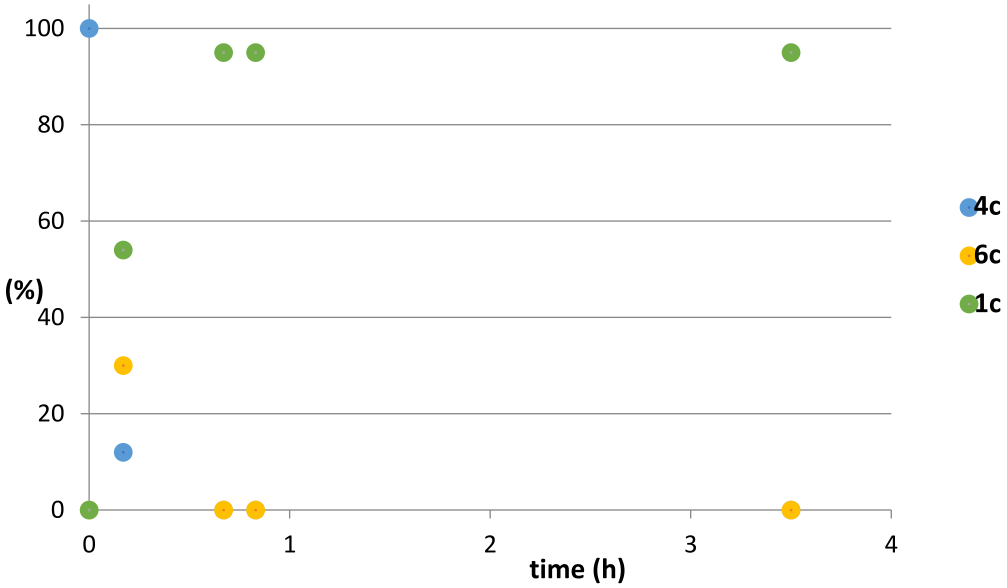
Time (h)	% 4c	% 6c	% 1c
0	100	0	0
0,17	17	40	33
0,36	16	37	42
0,5	16	37	43
0,72	16	37	45
0,92	15	35	49
1,12	15	35	50
1,9	14	34	51
3	14	34	53
4	14	33	53
4,81	14	34	55
6,14	13	33	56
6,77	13	33	55
22	11	28	60

Time-profile data LiOH (3 equivalents, 0.15 M)



Time (h)	% 4c	% 6c	% 1c
0	100	0	0
0,17	7	16	66
0,33	7	16	69
0,5	7	16	70
0,67	7	16	70
0,83	7	16	71
1	7	16	71
2	7	16	71
3	7	15	73
4	6	15	75
5	6	14	77
6	6	14	78
7	6	14	80
8	6	14	81
9	6	13	81
20	4	11	82

Time-profile data LiOH (4 equivalents, 0.20 M)



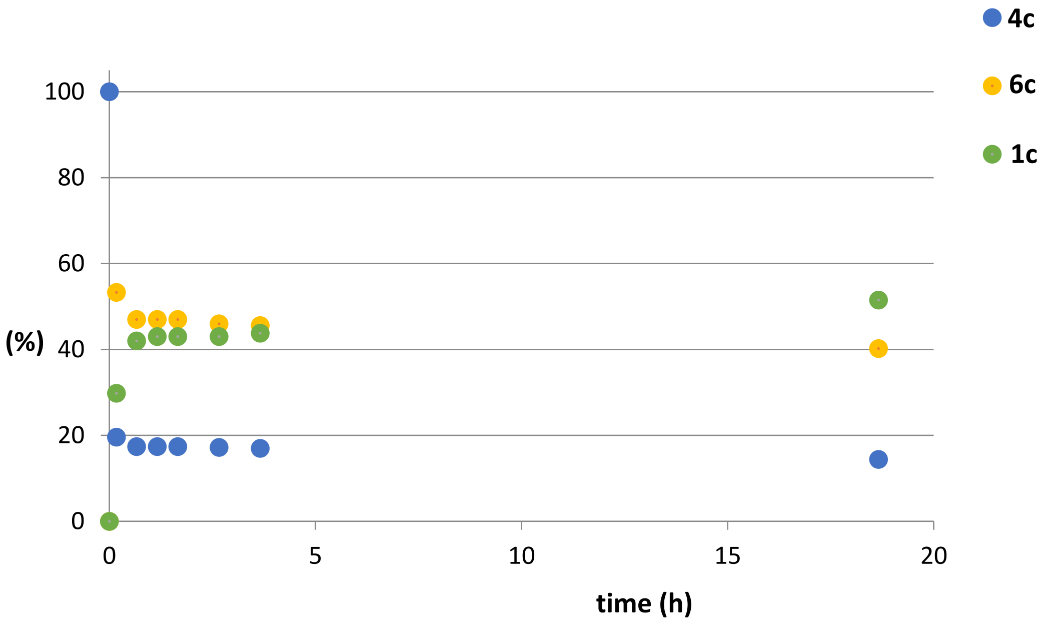
Time (h)	% 4c	% 6c	% 1c
0	100	0	0
0,17	12	30	54
0,67	0	0	95
0,83	0	0	95
3,5	0	0	95

3.4 Diketone 4c with H_2O_2 and other bases

Procedure

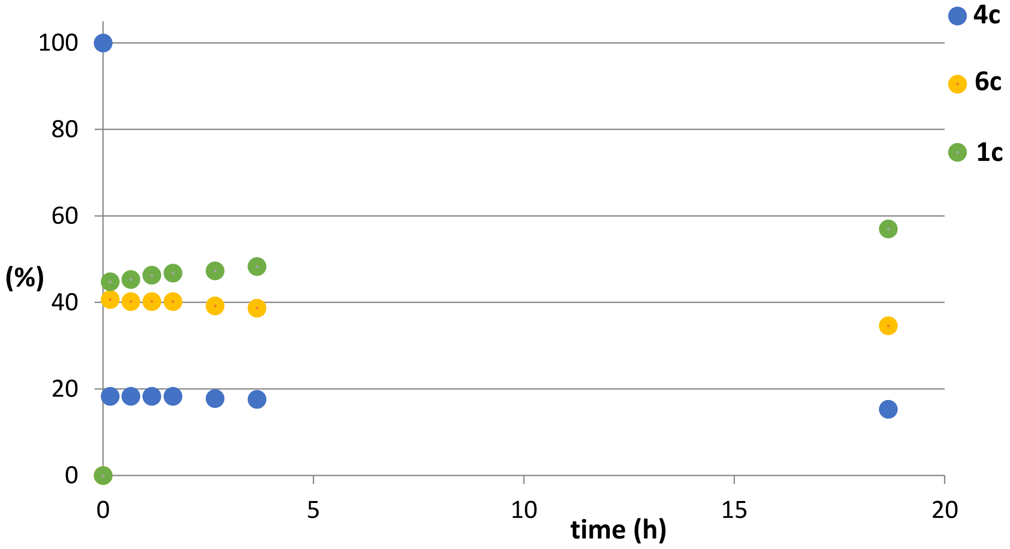
Diketone 1,1'-(2,3-Dihydro-1H-indene-2,2-diyl)diethanone **4c** (5.3 mg, 0.03 mmol) and mesitylene (3.00 µL, 0.02 mmol) as internal standard were dissolved in CD_3OD (0.5 mL) in a NMR vial. Then, H_2O_2 (10.71 µL, 0.10 mmol, 4.0 equiv.) was added, followed by NaOH (4.3 mg, 0.11 mmol, 4.0 equiv.) or KOH (6.2 mg, 011 mmol, 4.0 equiv.) and the reaction was monitored by ^{1}H-NMR at rt for 18 h.

Time-profile data NaOH as base (1 equivalent, 0.05 M)



Time (h)	CONVERSION	% 4c	% 6c	% 1c
0	0	100	0	0
0,17	80	20	52	28
0,67	85	15	44	40
1,16	85	15	43	41
1,66	85	15	43	41
2,66	85	15	42	41
3,66	85	15	42	42
18,66	88	12	39	50

Time-profile data KOH as base (1 equivalent, 0.05 M)



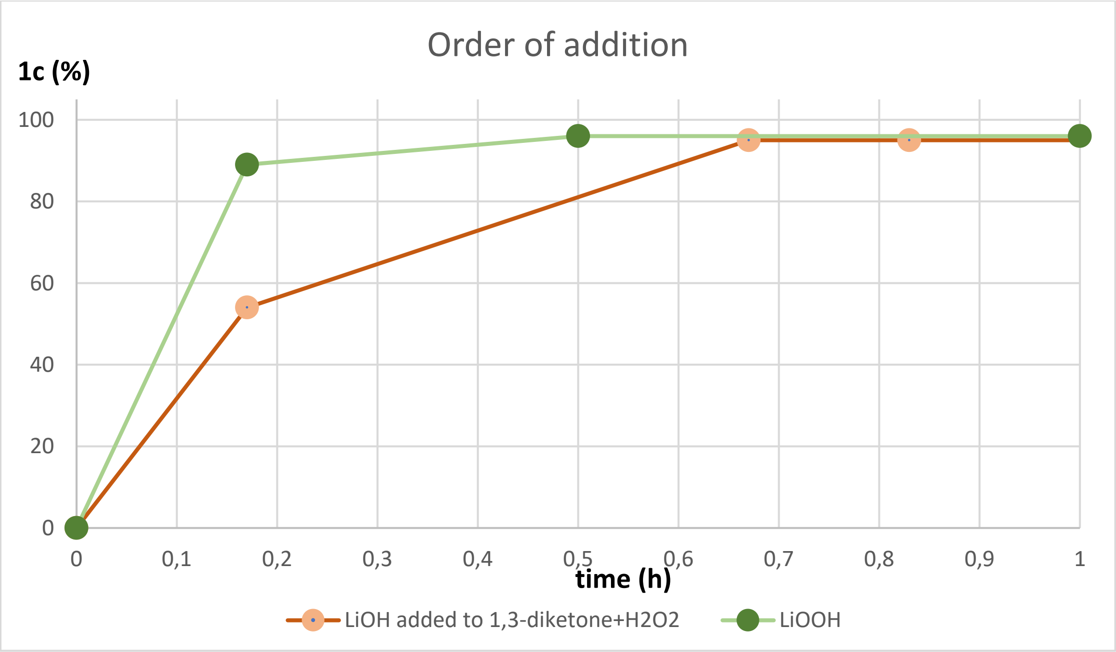
Time (h)	CONVERSION	% 4c	% 6c	% 1c
0	0	100	0	0
0,17	82	18	40	43
0,67	83	18	40	44
1,16	83	17	40	44
1,66	83	17	39	45
2,66	83	17	39	45
3,66	84	16	37	47
18,66	86	14	33	54

3.5 Diketone 4c with LiOOH

Procedure

LiOH (2.6 mg, 0.11 mmol) and H_2O_2 (30 % in water,10.51 µL, 0.10 mmol) were mixed in an NMR tube with 0.2 ml CD_3OD at 0 °C for 20 min. Then, 1,1'-(2,3-dihydro-1*H*-indene-2,2-diyl)diethanone **4c** (5.2 mg, 0.025 mmol) and mesitylene (2.78 µL, 0.02 mmol) as internal standard in CD_3OD (0.5 mL) were added at 0 °C. The reaction was left at 0 °C for 10 min. Then, the reaction was allowed to reach rt. The reaction was monitored by ^{1}H-NMR and a spectrum was recorded every 10 min for 40 min. Desired product 2-methyl-2,3-dihydro-1*H*-indene-2-carboxylic acid **1c** was obtained in 96 % yield calculated from the internal standard.

Time-profile data LiOOH vs LiOH



4eq LiOH, rt

Time (h)	% 4c	% 6c	% 1c
0	100	0	0
0,17	12	30	54
0,67	0	0	95
0,83	0	0	95
3,5	0	0	95

4eq LiOH, rt, LiHO2-salt pre-formed first before addition of 4c

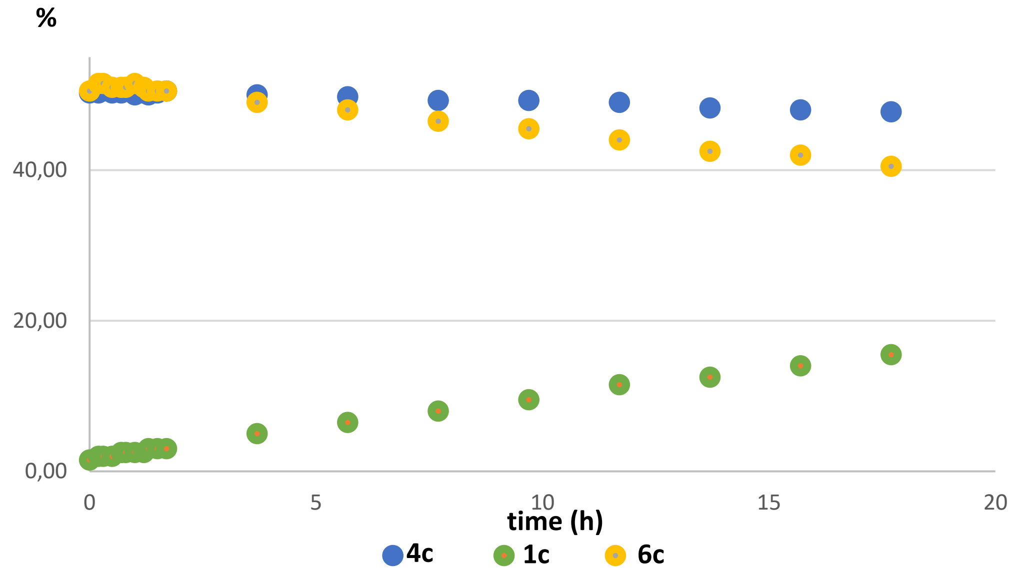
Time (h)	% 4c	% 6c	% 1c
0	100	0	0
0,17	3	5	89
0,5	0	0	96
1	0	0	96
4,5	0	0	96

3.6 Endoperoxide 6c with AcOH

Procedure

To a mixture 1:1 of endoperoxide **6c** and diketone **4c** prepared in neutral conditions as stated above (see section **3.1**), was added acetic acid (2.1 µL, 0.03 mmol, 1.0 equiv.) The reaction was monitored by ^{1}H-NMR.

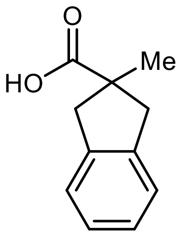
Time-profile data



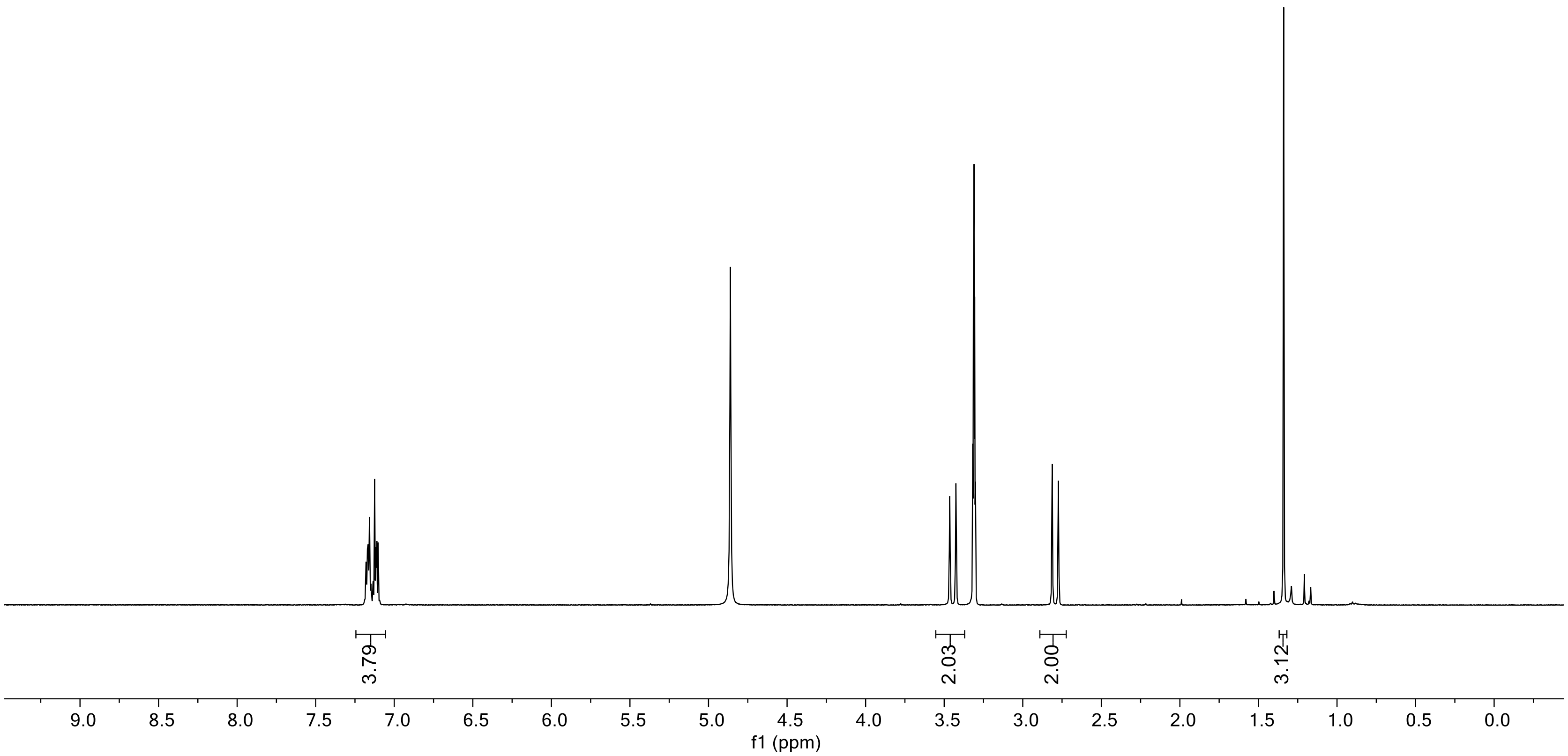
Time (h)	4c	1c	6c
0	50,25	1,50	50,50
0,2	50,25	2,00	51,50
0,3	50,50	2,00	51,50
0,5	50,25	2,00	51,00
0,7	50,25	2,50	51,00
0,8	50,50	2,50	51,00
1	50,00	2,50	51,50
1,2	50,25	2,50	51,00
1,3	50,00	3,00	50,50
1,5	50,25	3,00	50,50
1,7	50,50	3,00	50,50
3,7	50,00	5,00	49,00
5,7	49,75	6,50	48,00
7,7	49,25	8,00	46,50
9,7	49,25	9,50	45,50
11,7	49,00	11,50	44,00
13,7	48,25	12,50	42,50
15,7	48,00	13,50	42,00
17,7	47,75	14,50	40,00

4 Spectroscopic characterization of synthesized compounds

^{1}H-NMR of compound 1c (500MHz, CD$_3$OD)

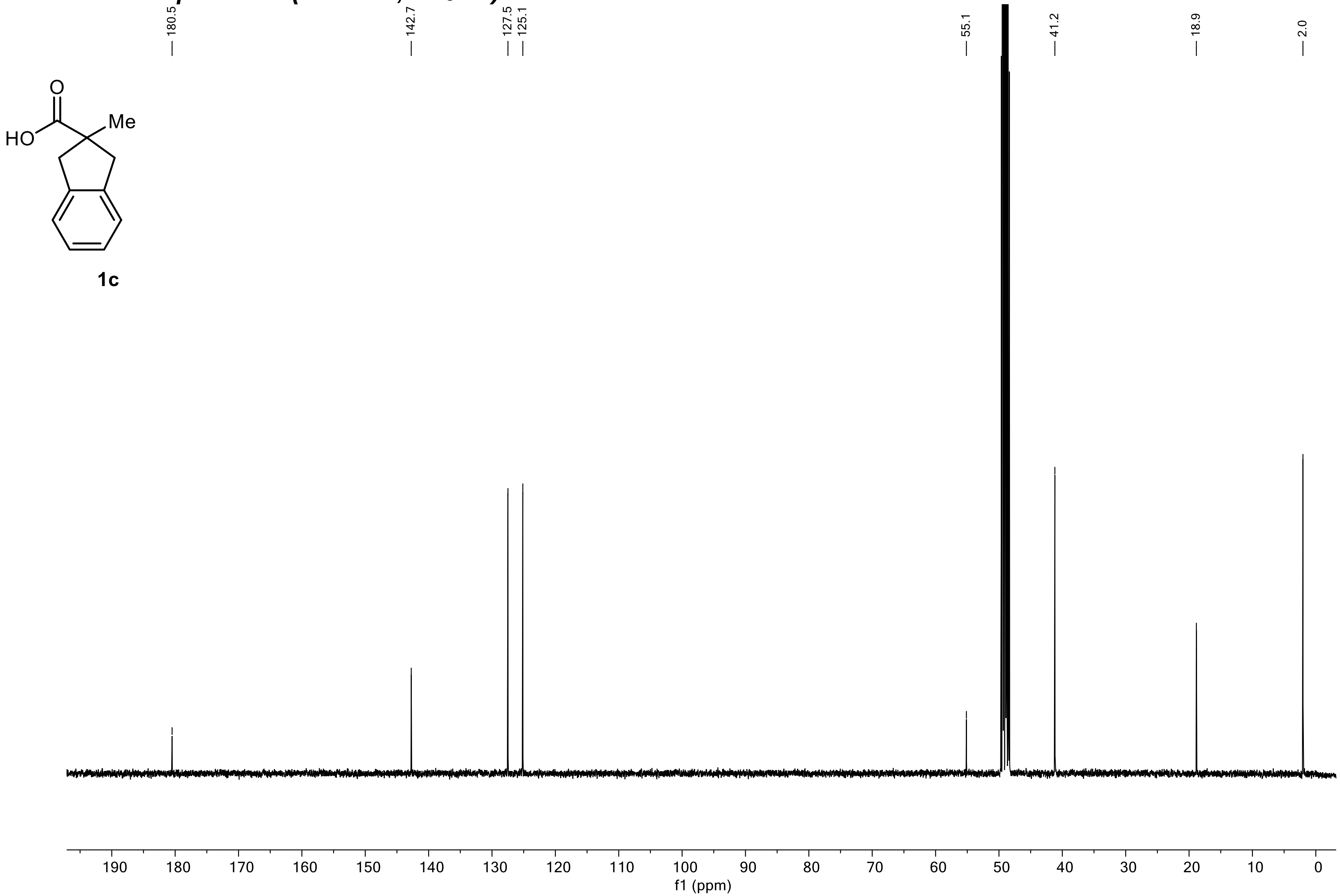


1c

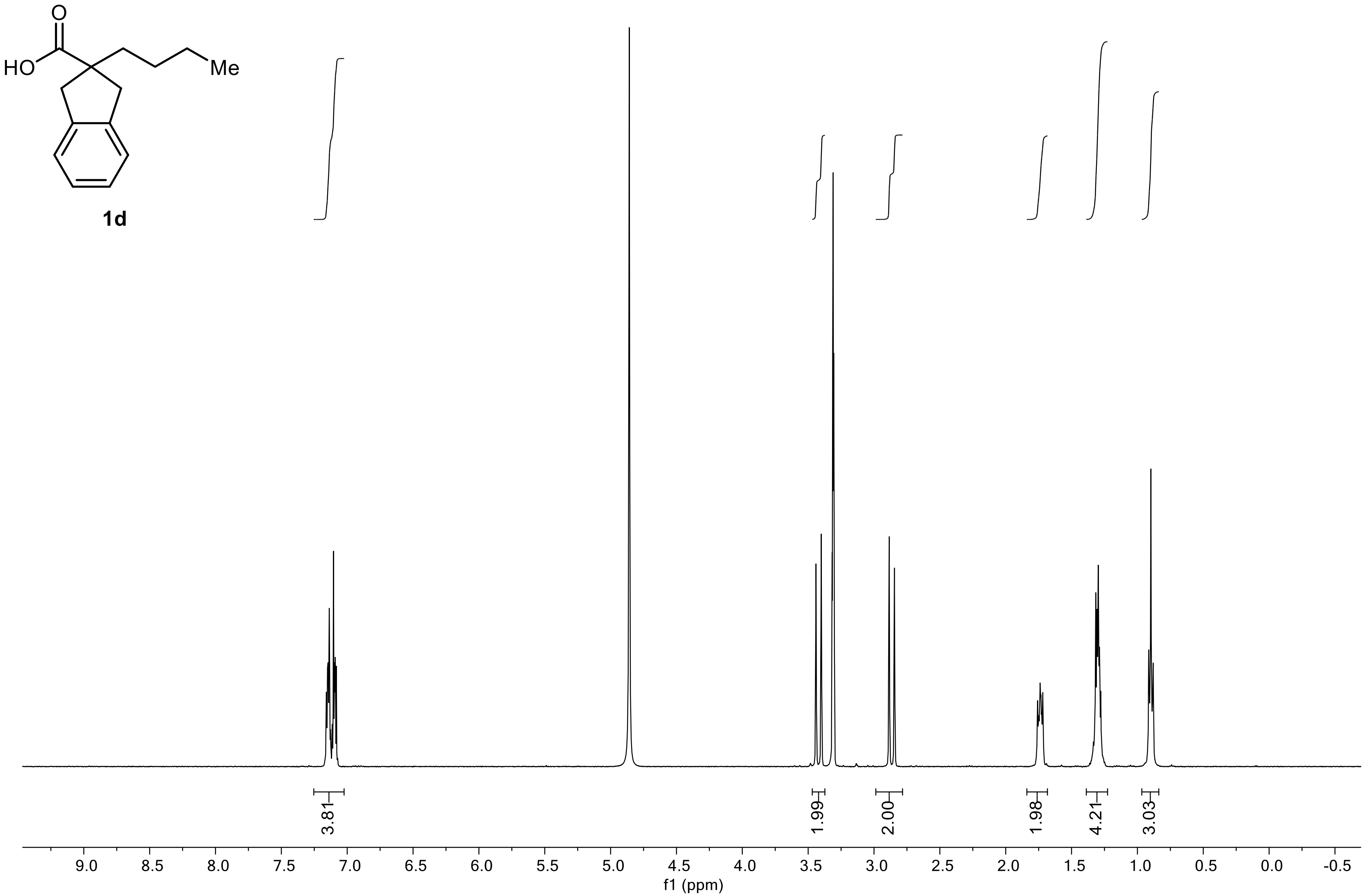


^{13}C-NMR of compound 1c (125 MHz, CD_3OD)

1c

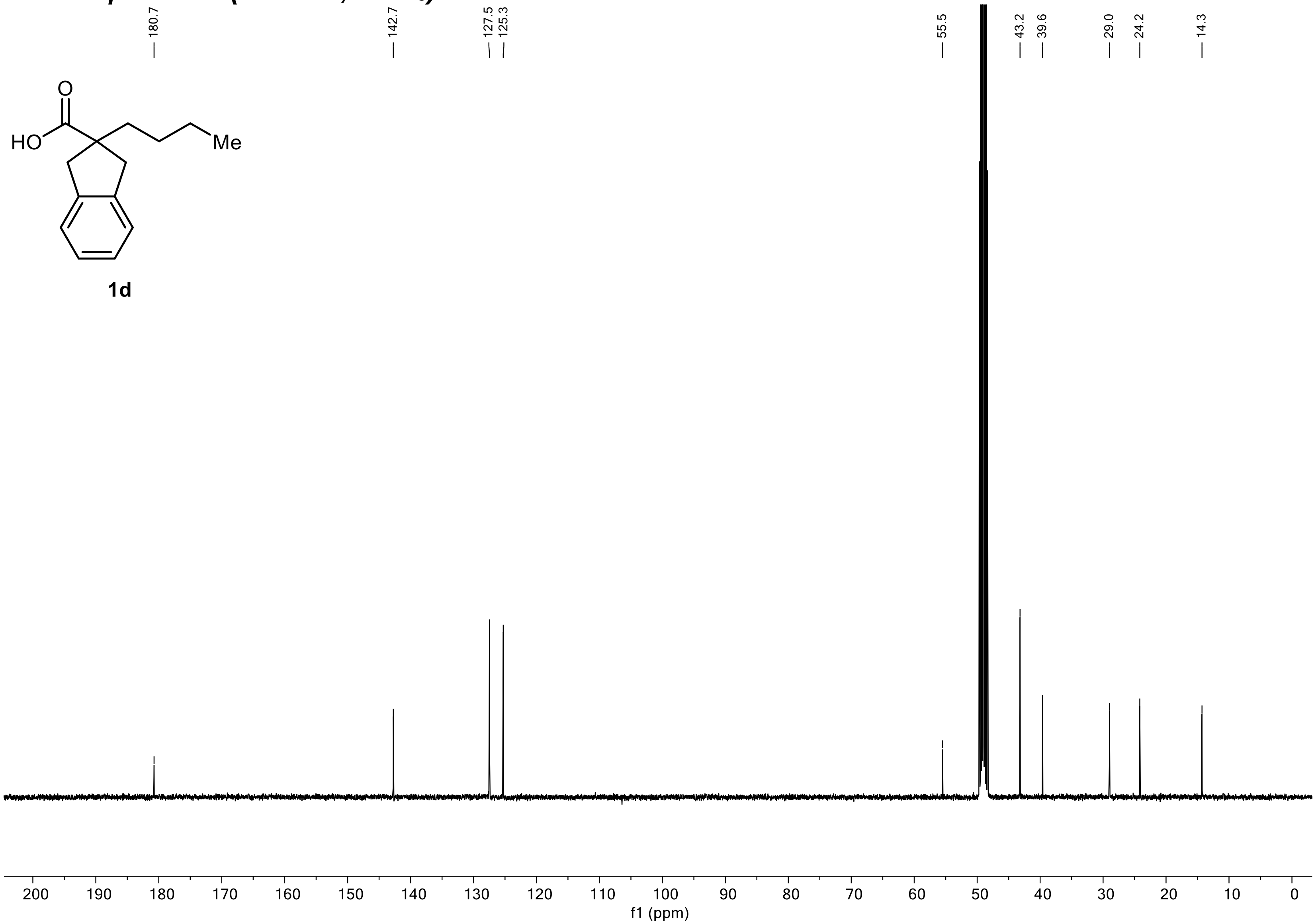


^{1}H-NMR of compound 1d (400MHz, CD_3OD)



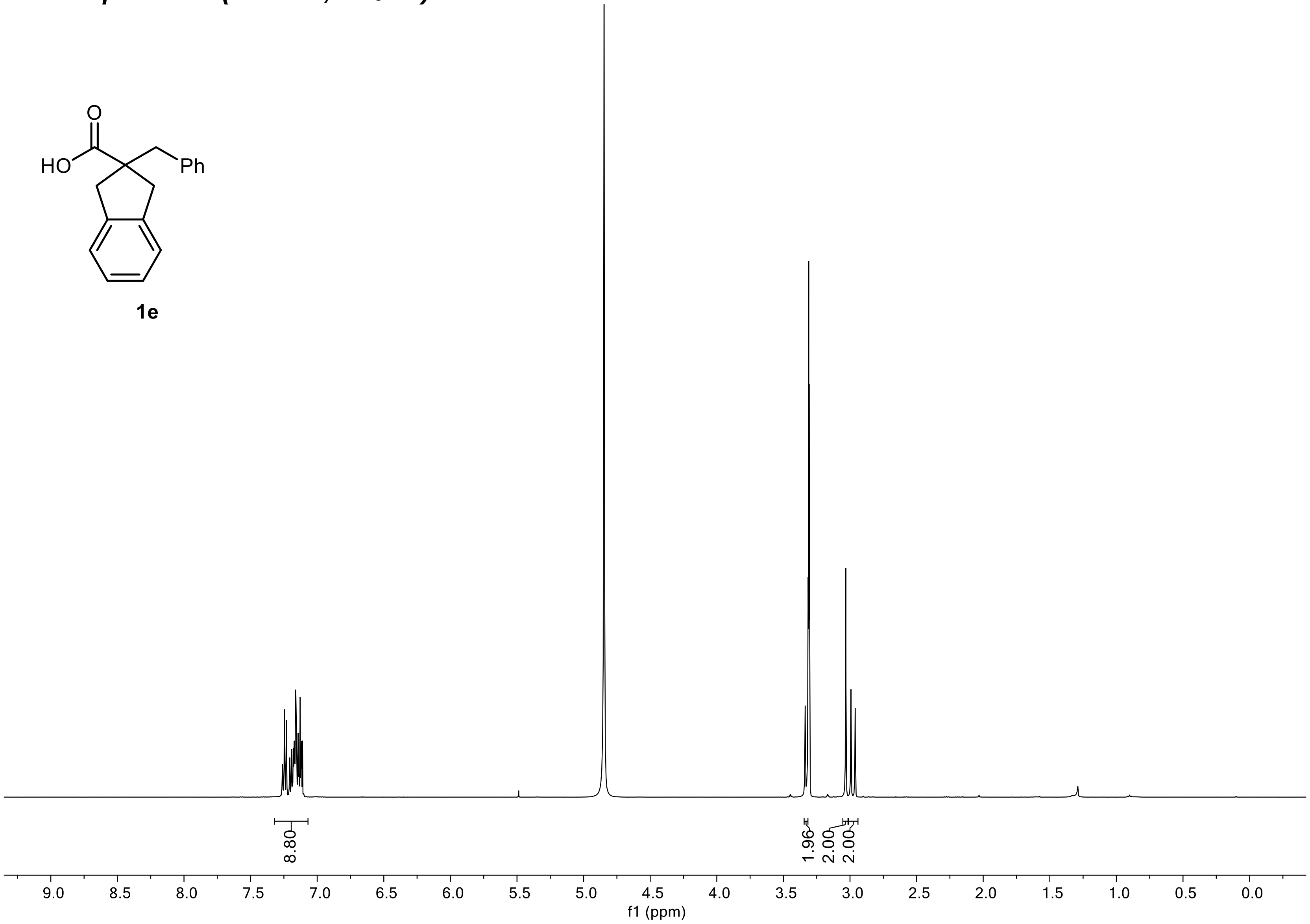
1d

^{13}C-NMR of compound 1d (100 MHz, $CDCl_3$)



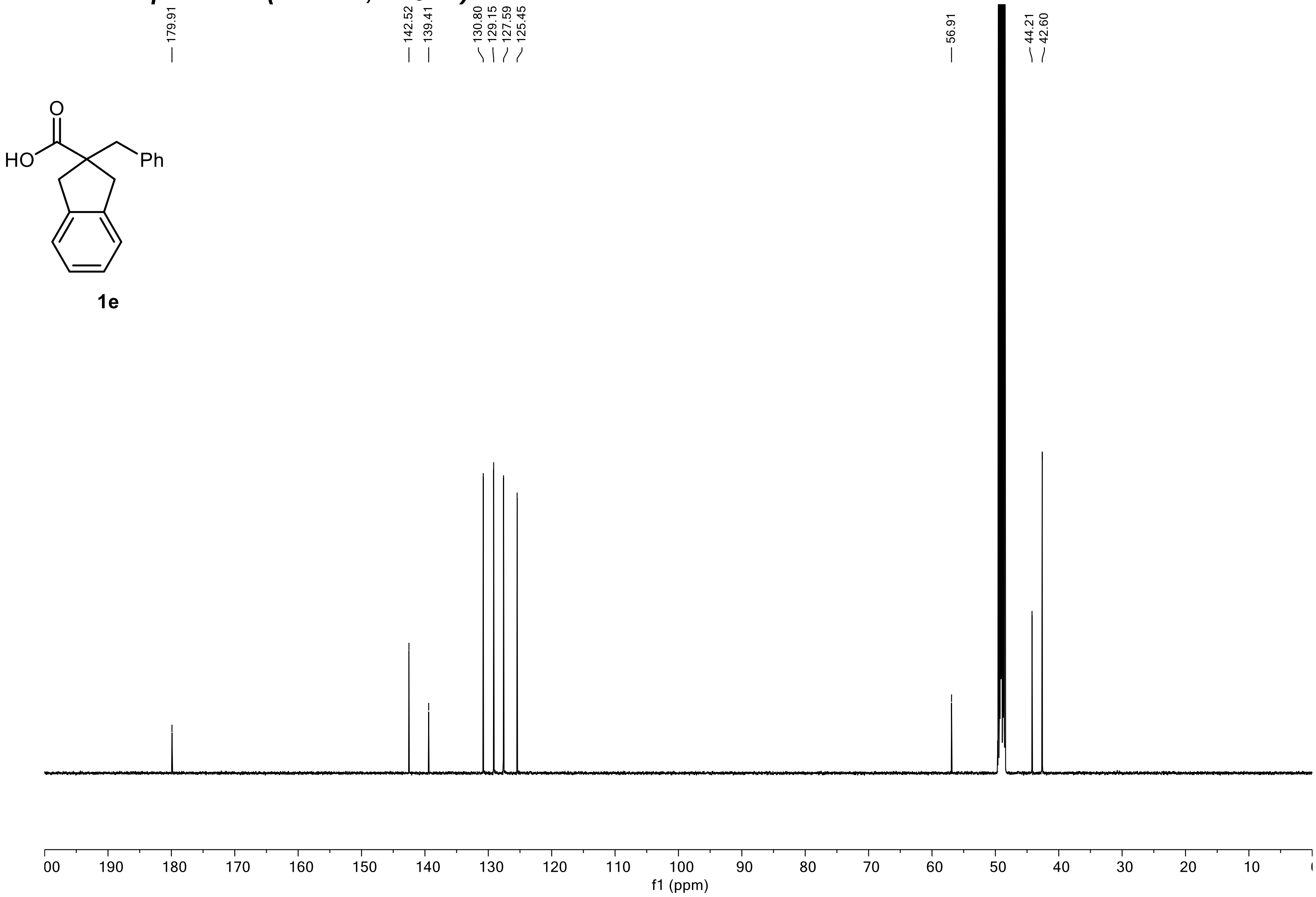
1d

^{1}H-NMR of compound 1e (500MHz, CD_3OD)



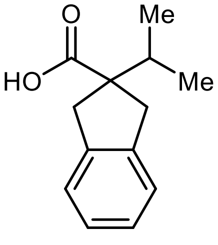
1e

^{13}C-NMR of compound 1e (126MHz, CD$_3$OD)

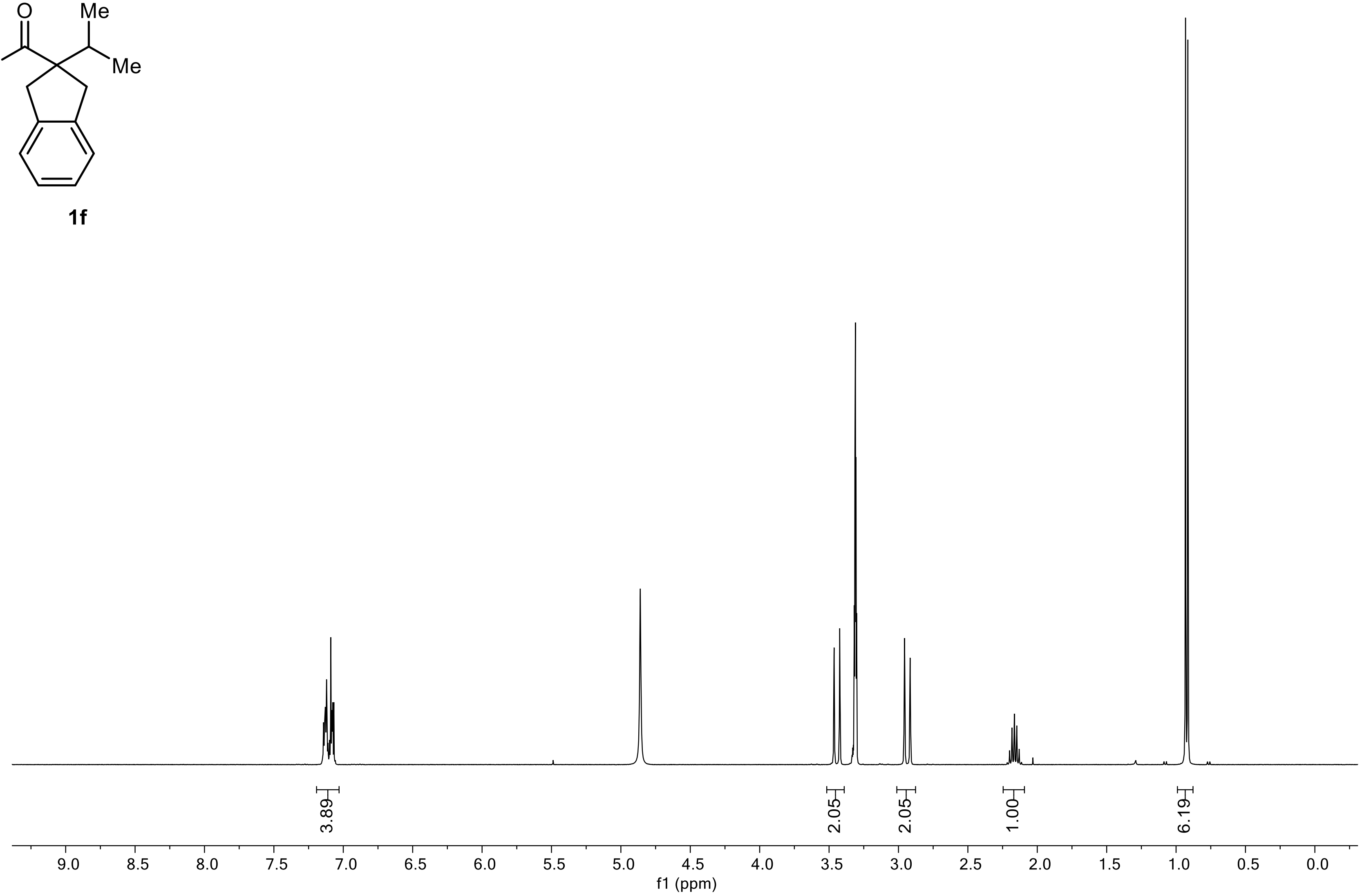


1e

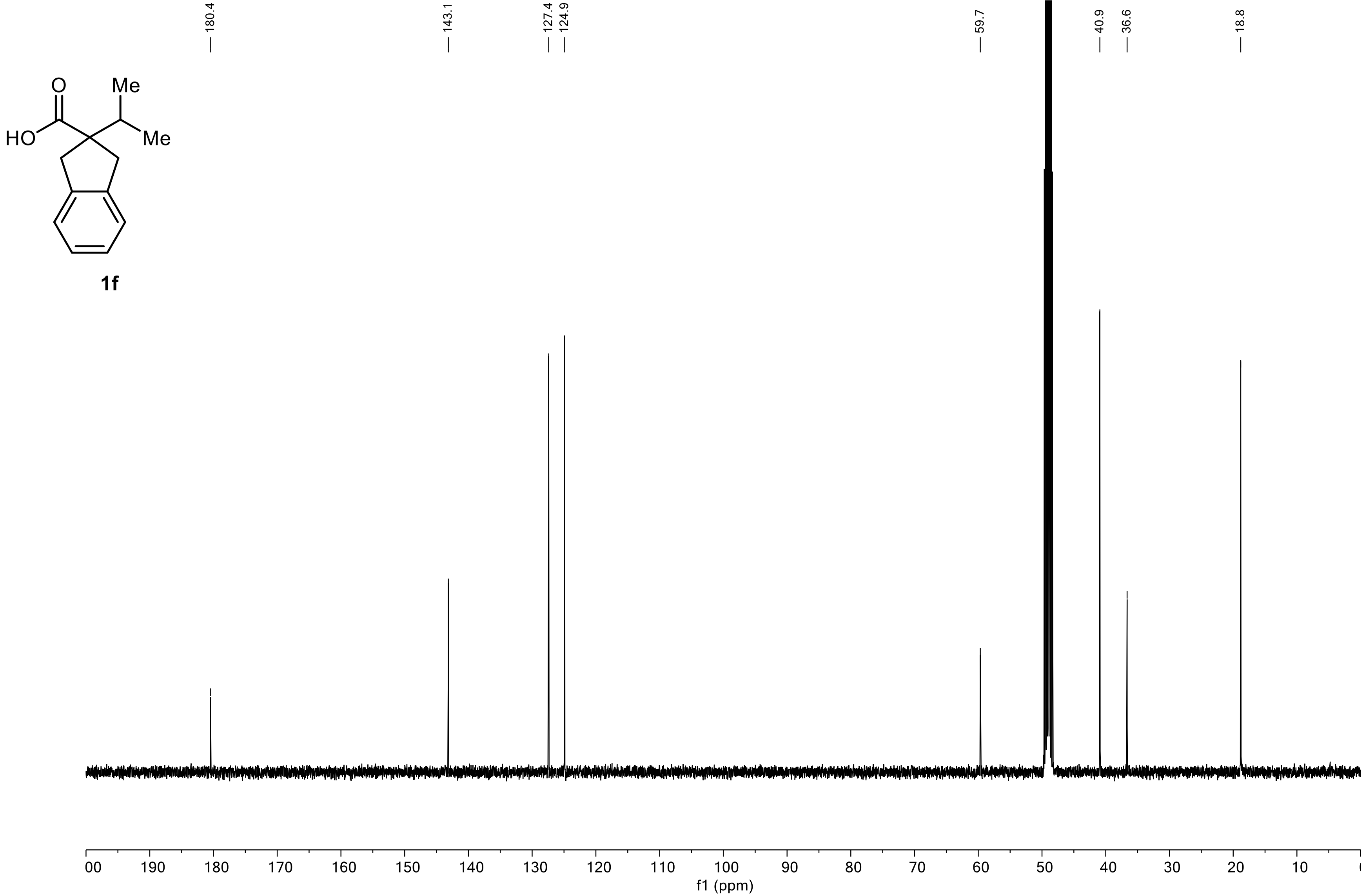
^{1}H-NMR of compound 1f (400MHz, CD_3OD)



1f

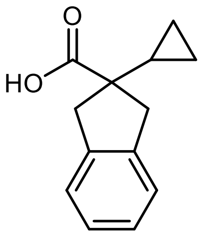


^{13}C-NMR of compound 1f (100MHz, CD$_3$OD)

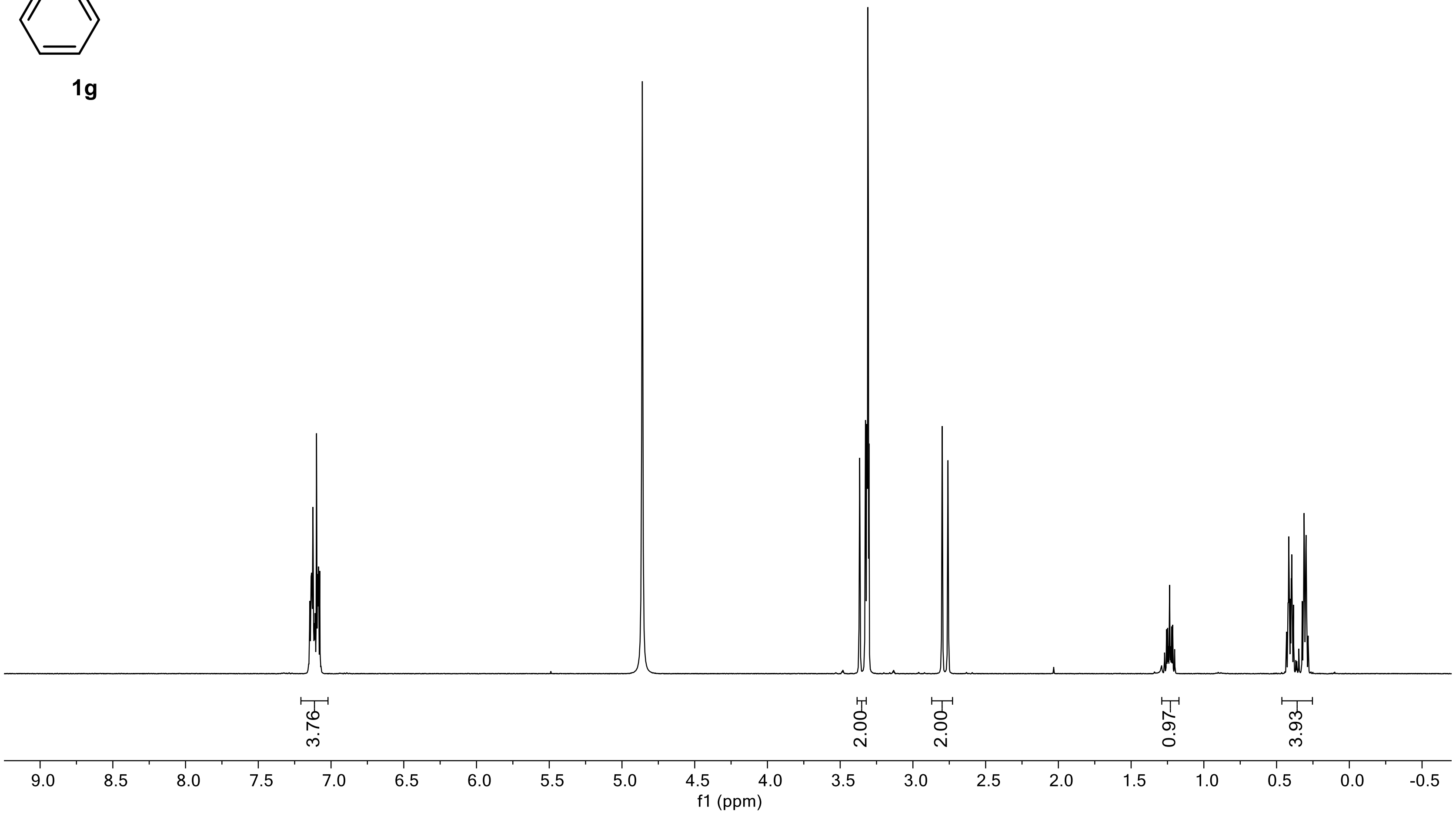


1f

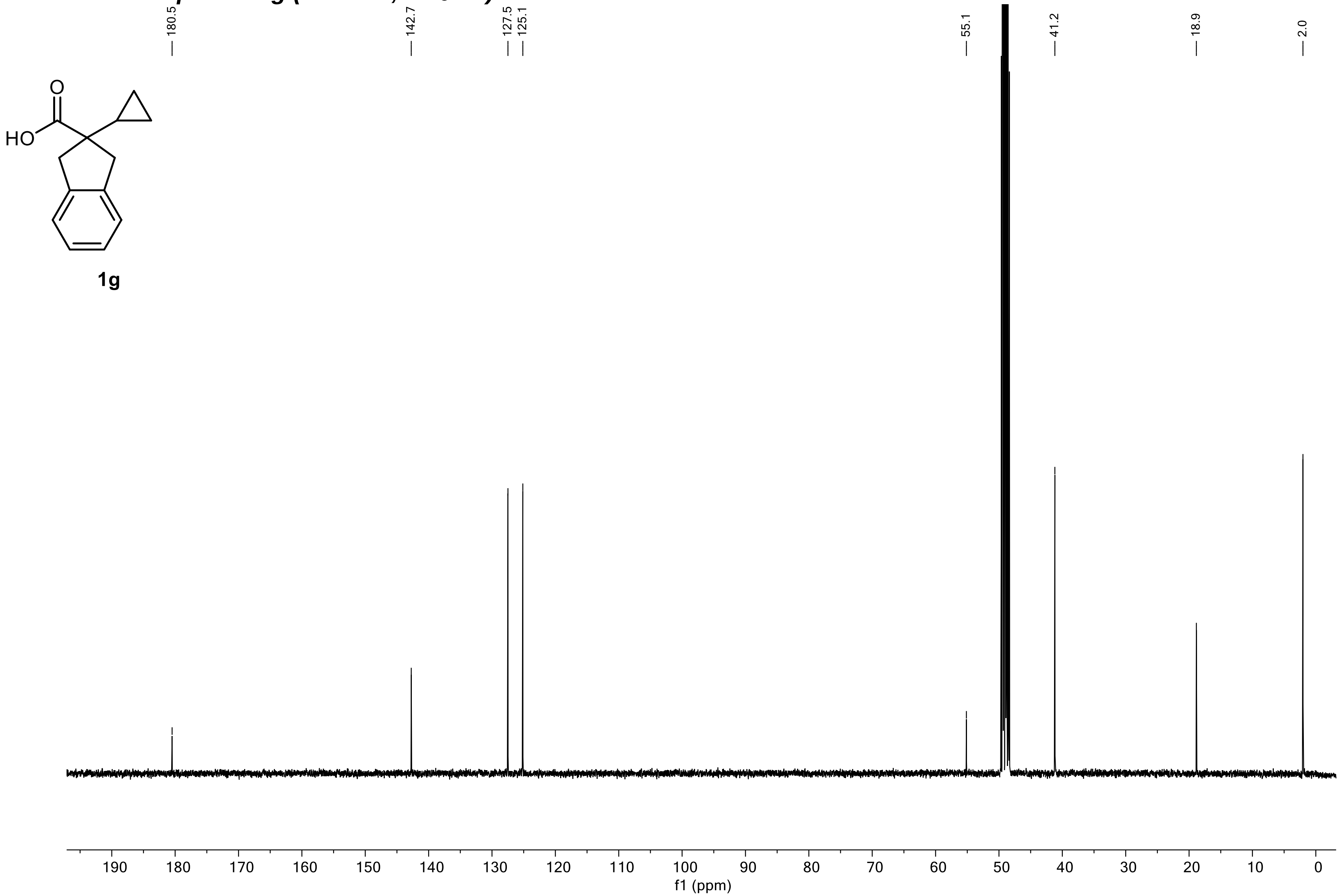
^{1}H-NMR of compound 1g (400MHz, CD$_3$OD)



1g

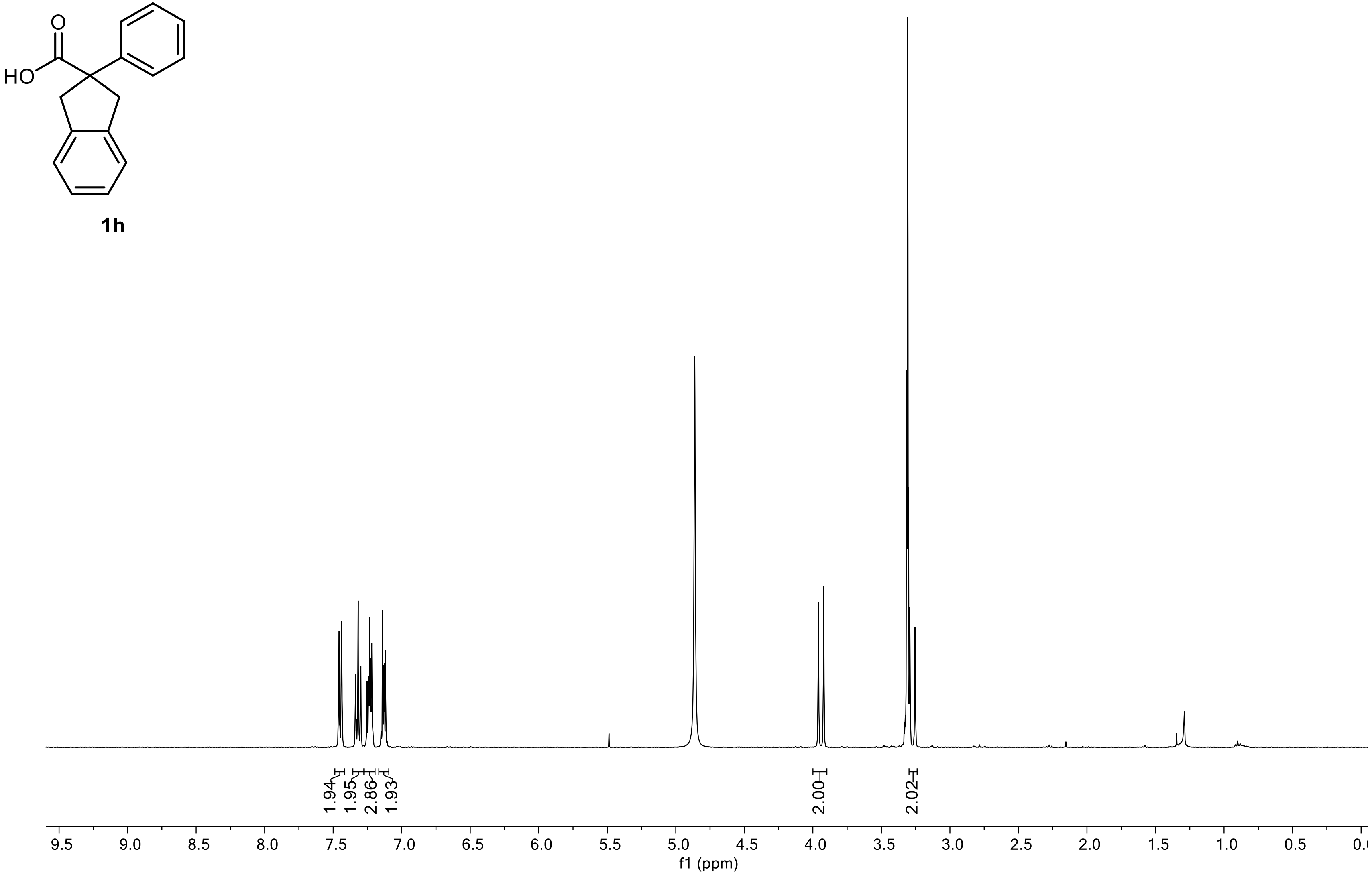


^{13}C-NMR of compound 1g (100MHz, CD_3OD)

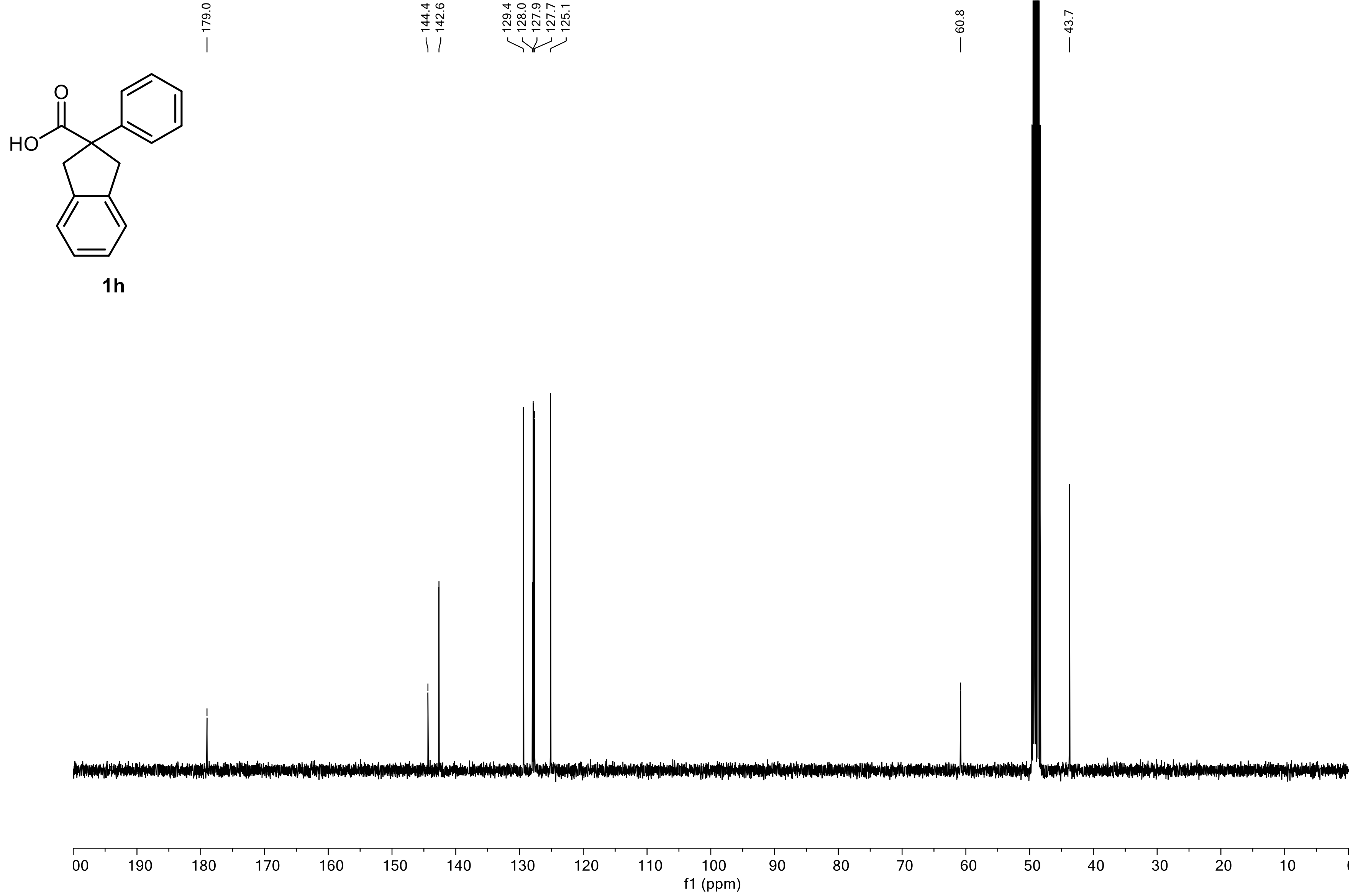


1g

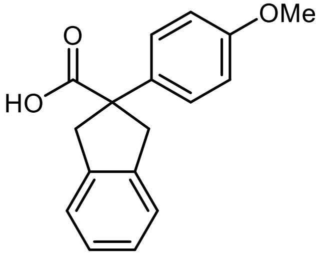
^{1}H-NMR of compound 1h (400MHz, CD_3OD)



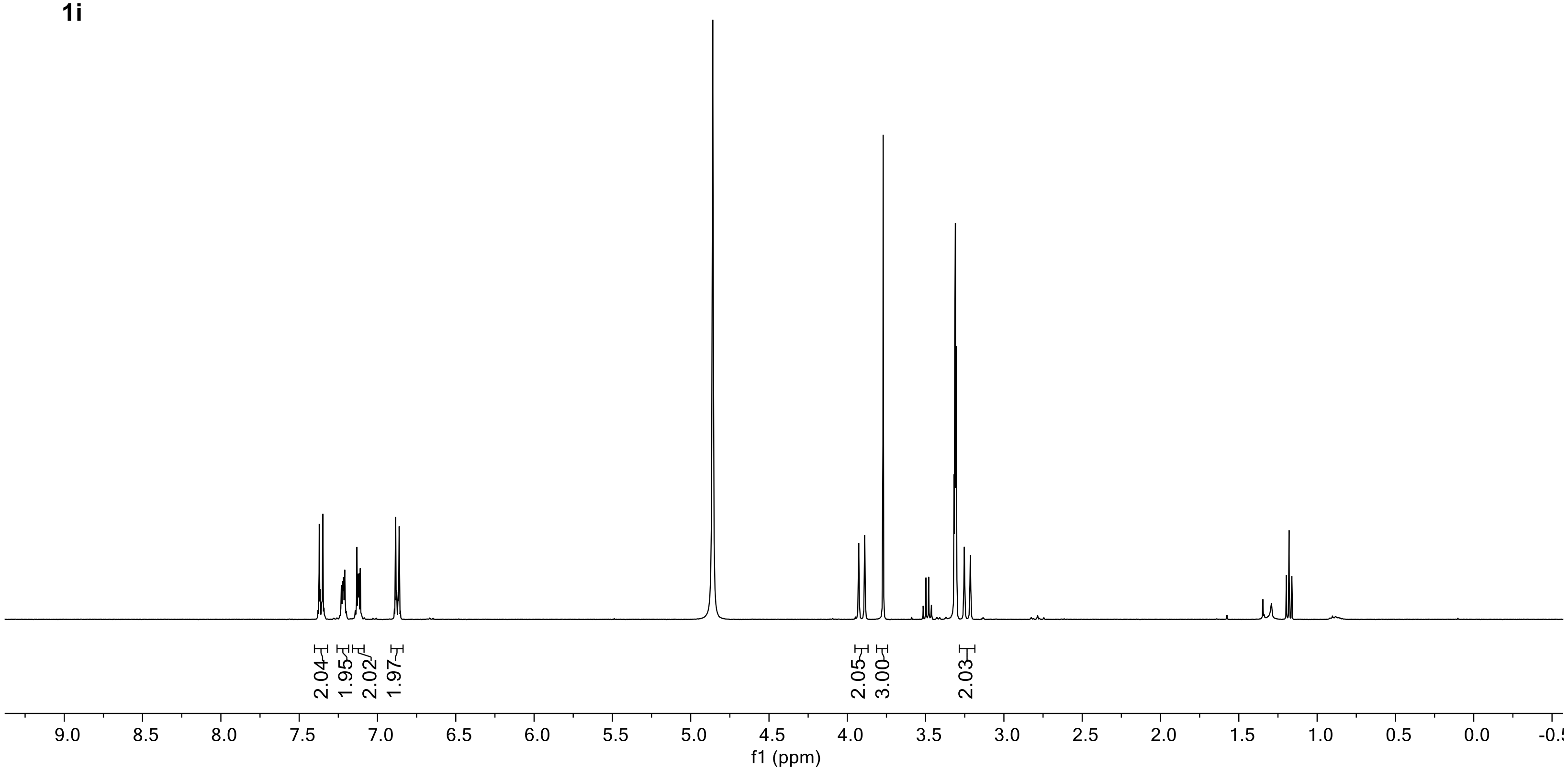
^{13}C-NMR of compound 1h (100MHz, CD$_3$OD)



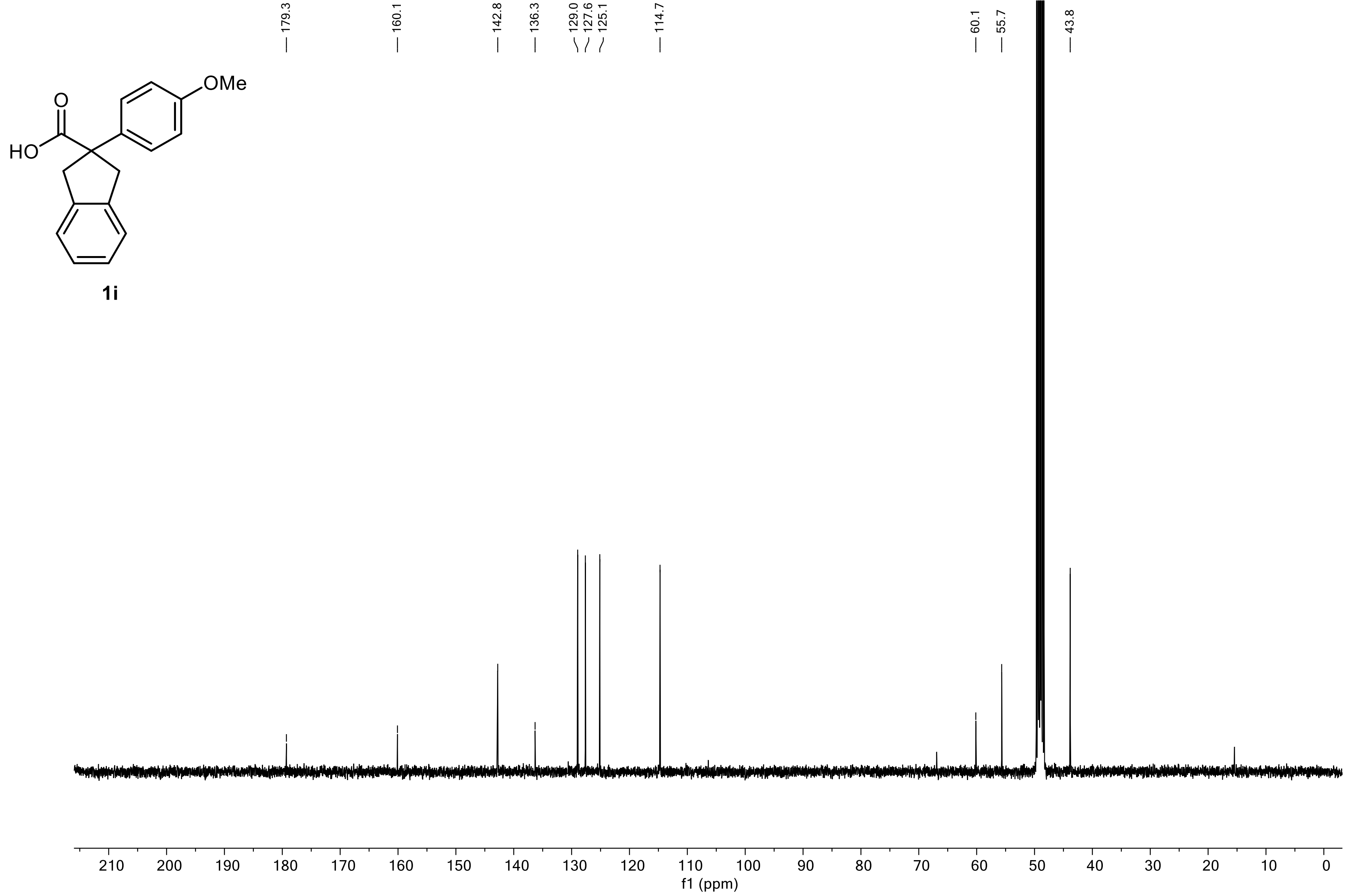
^{1}H-NMR of compound 1i (400MHz, CD_3OD)



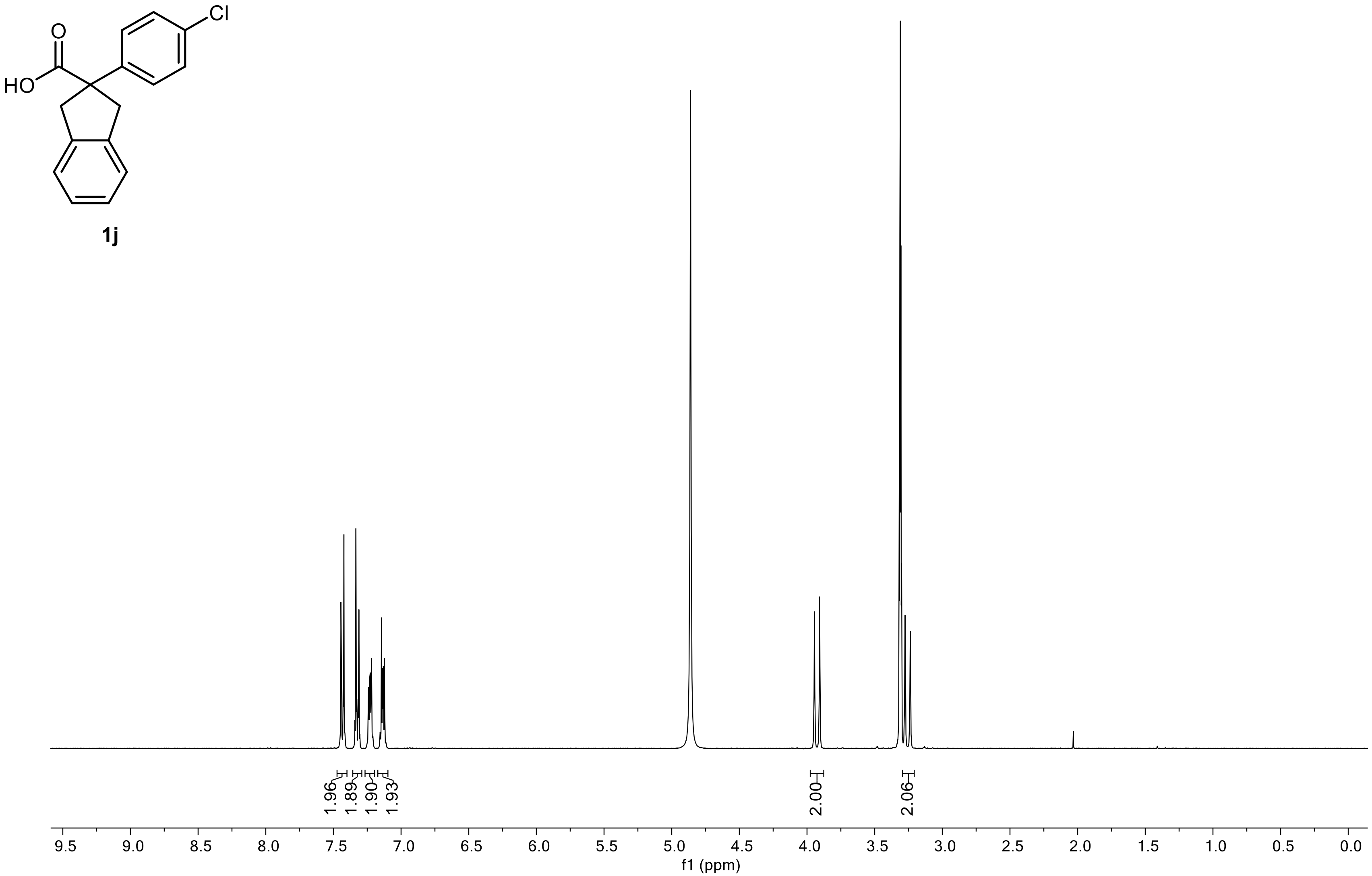
1i



^{13}C-NMR of compound 1i (101MHz, CD_3OD)

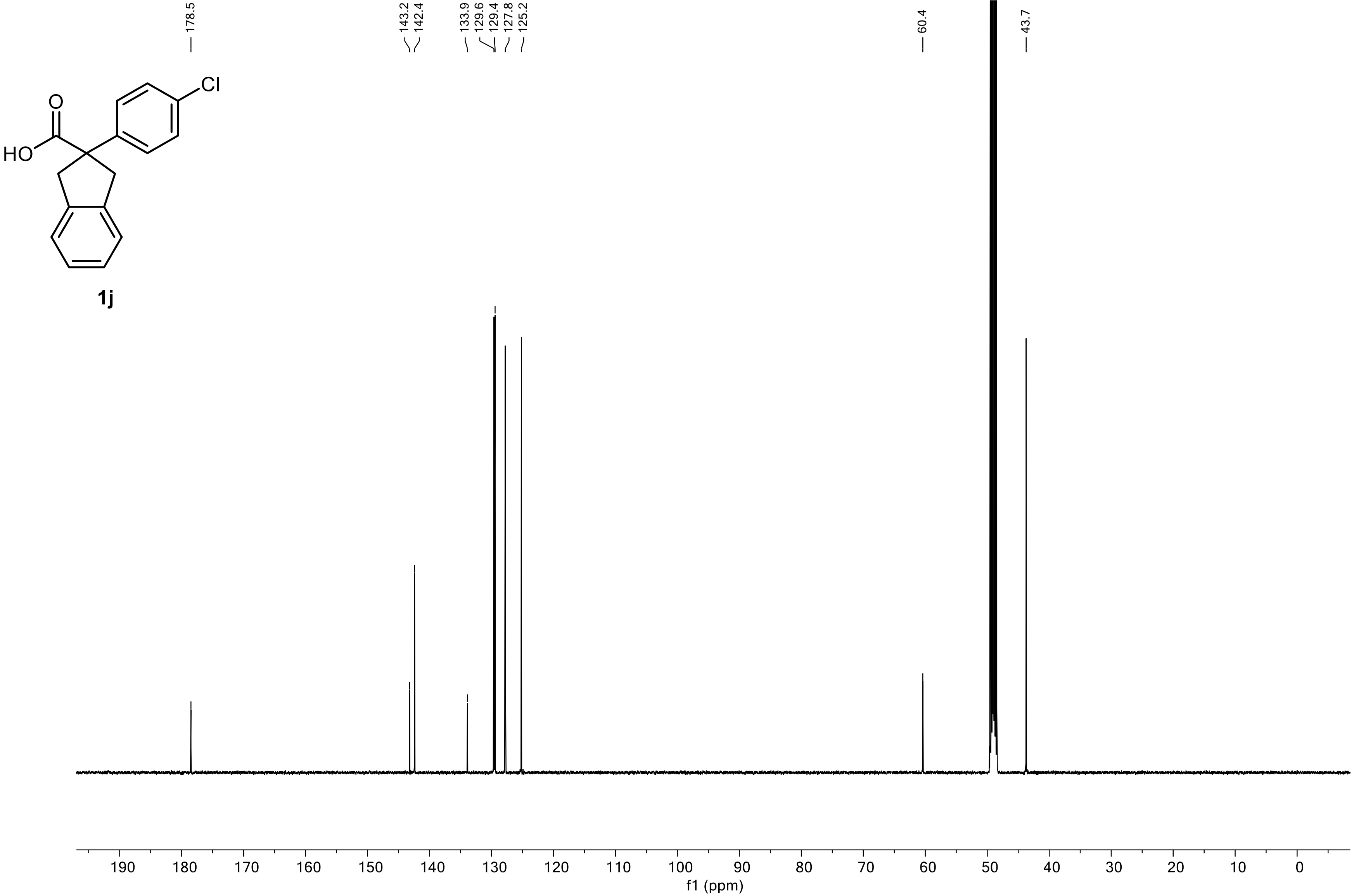


^{1}H-NMR of compound 1j (400MHz, CD$_3$OD)



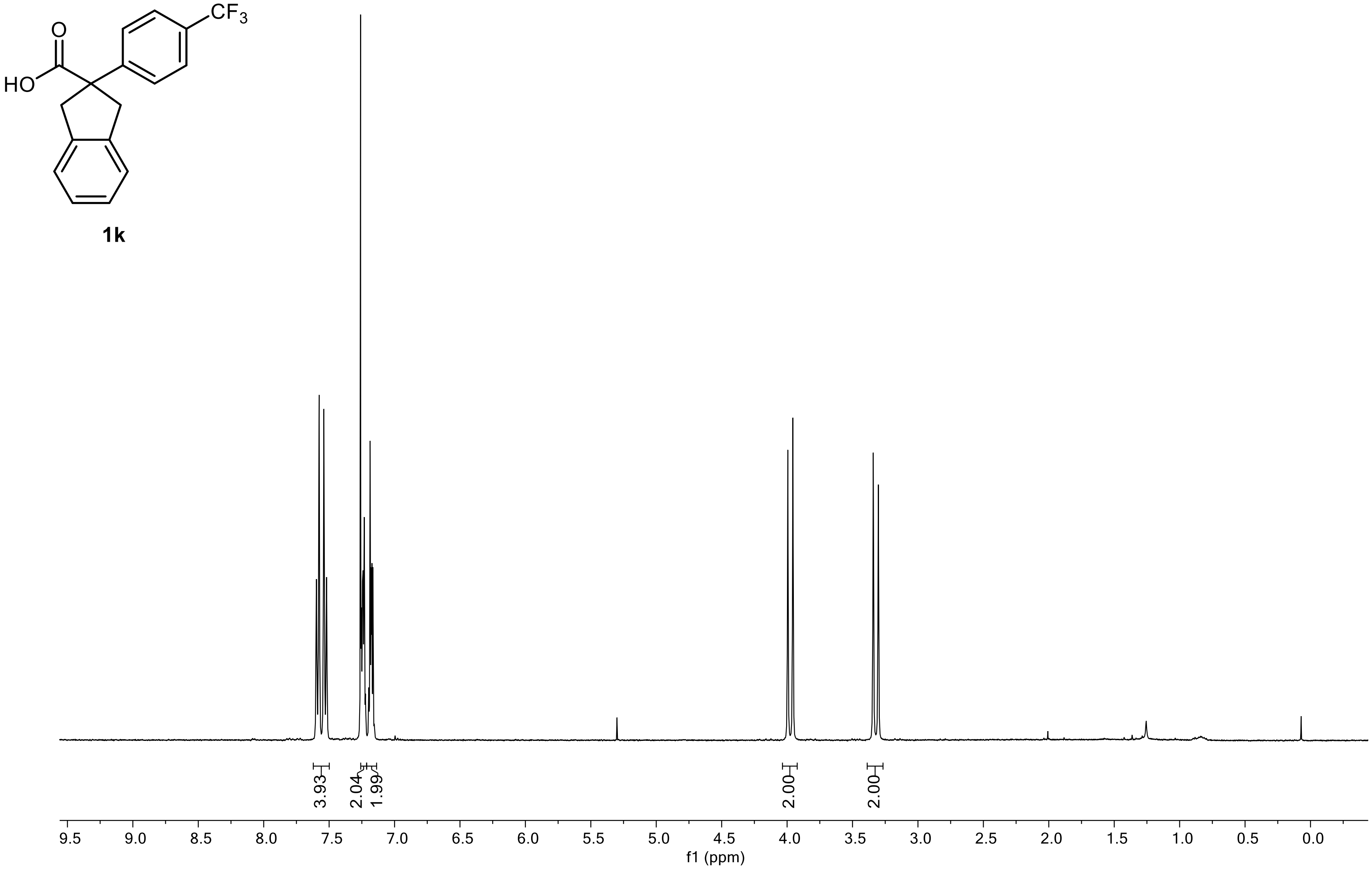
1j

^{13}C-NMR of compound 1j (126MHz, CD_3OD)



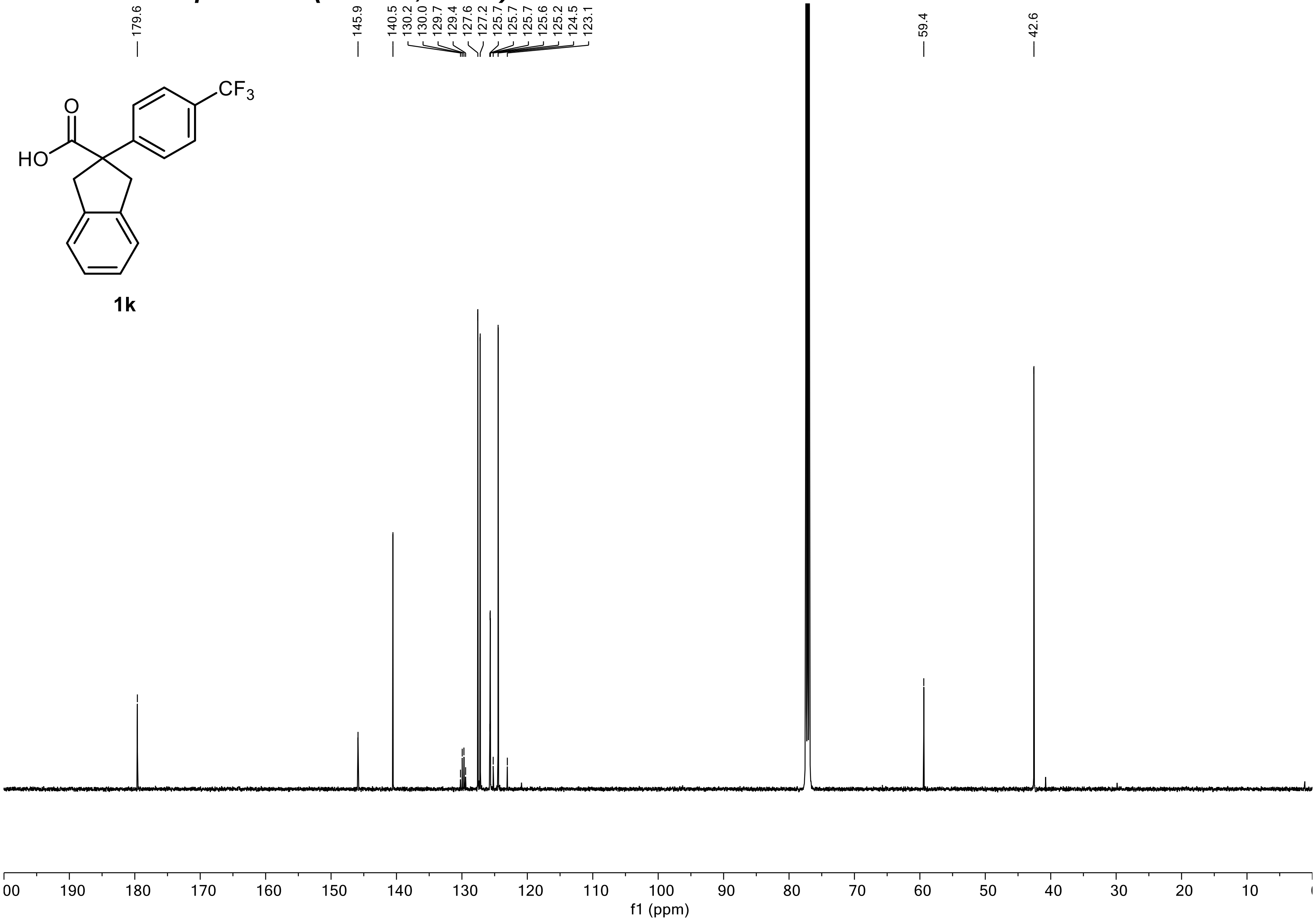
1j

^{1}H-NMR of compound 1k (400MHz, CDCl$_3$)



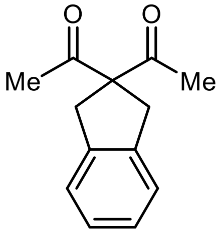
1k

^{13}C-NMR of compound 1k (100MHz, $CDCl_3$)

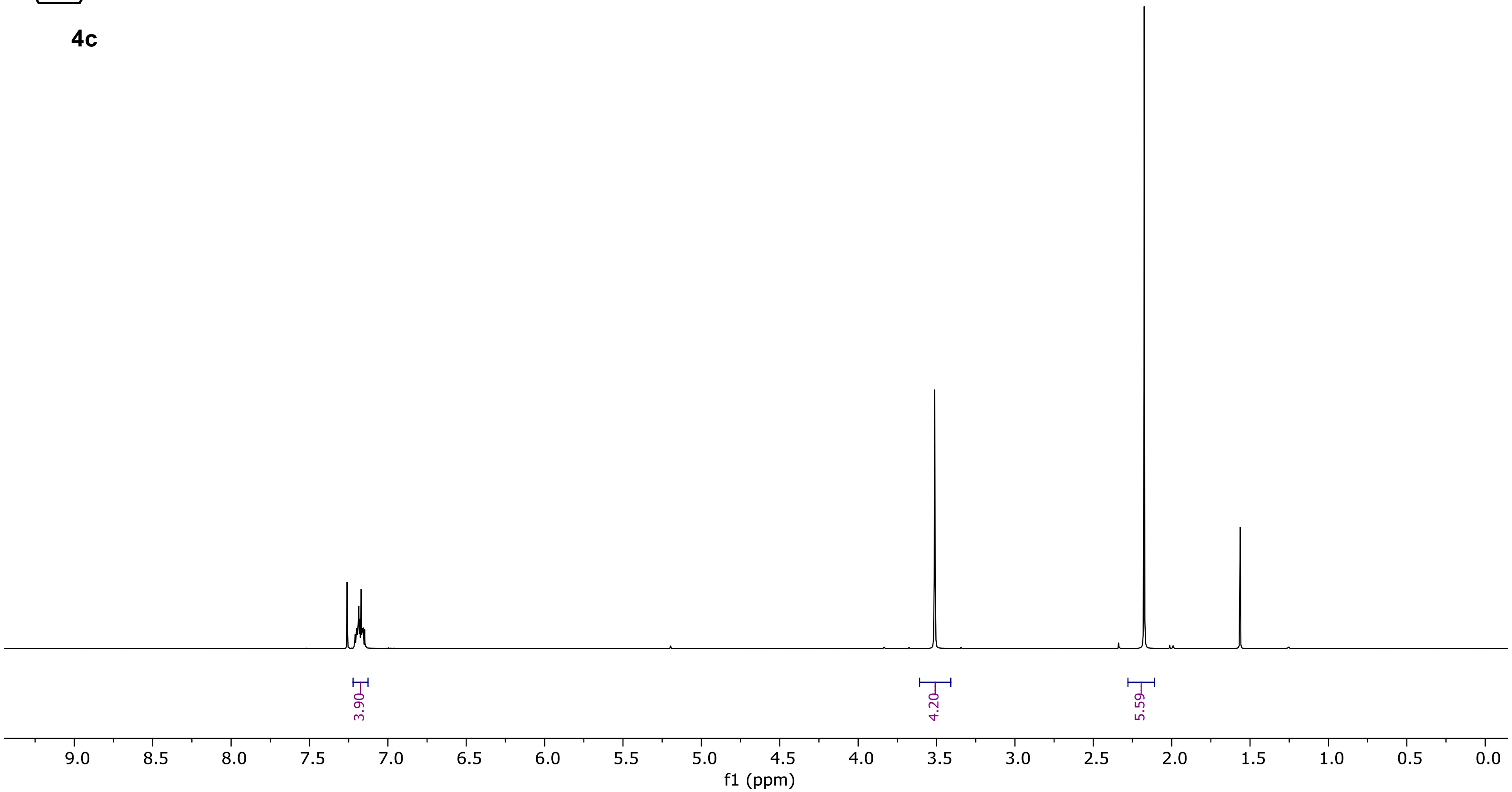


1k

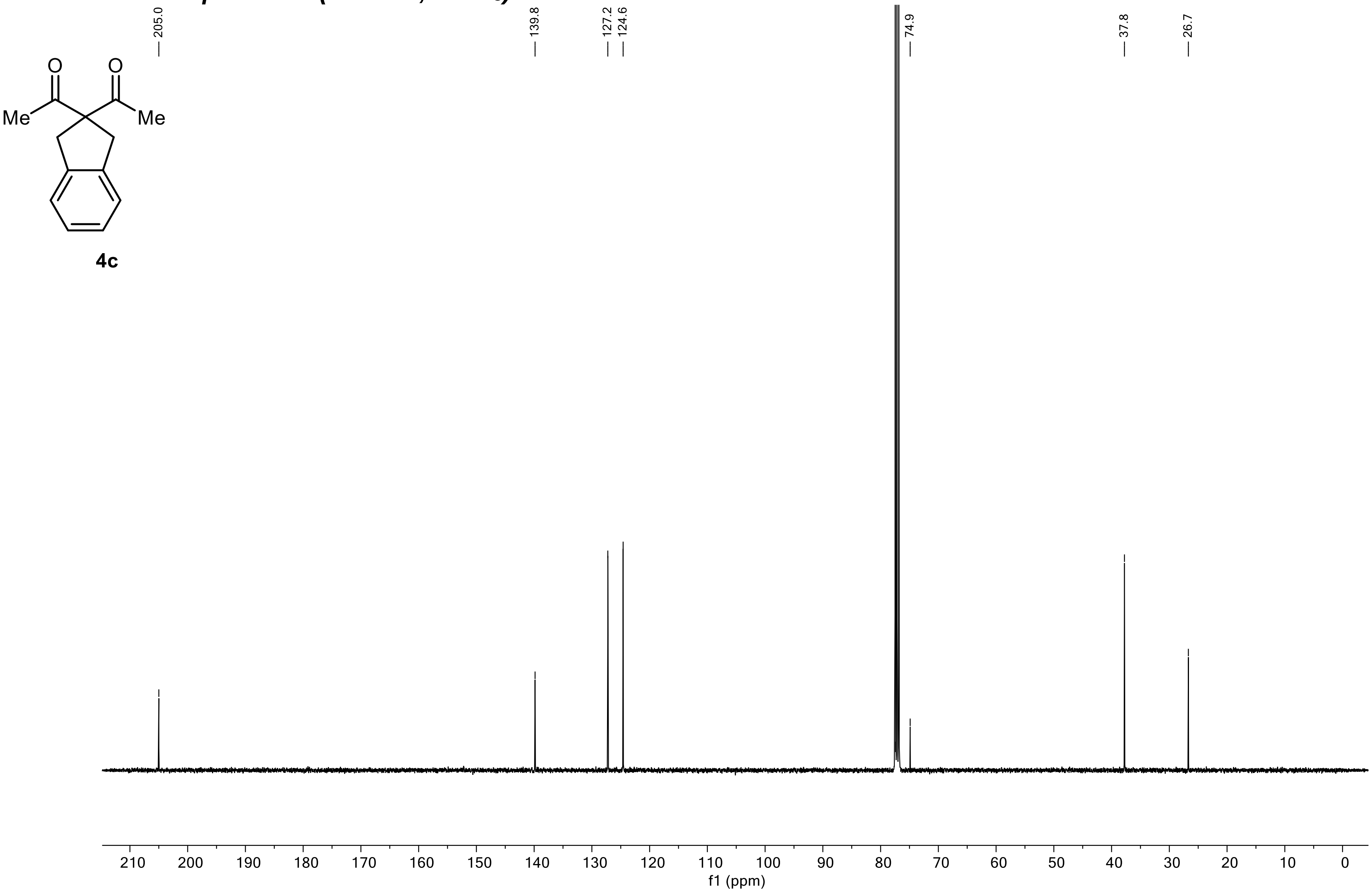
^{1}H-NMR of compound 4c (400MHz, $CDCl_3$)



4c

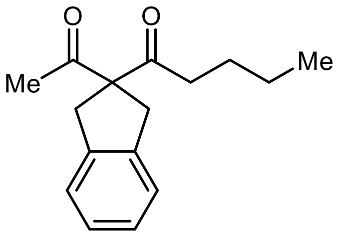


^{13}C-NMR of compound 4c (101MHz, CDCl$_3$)

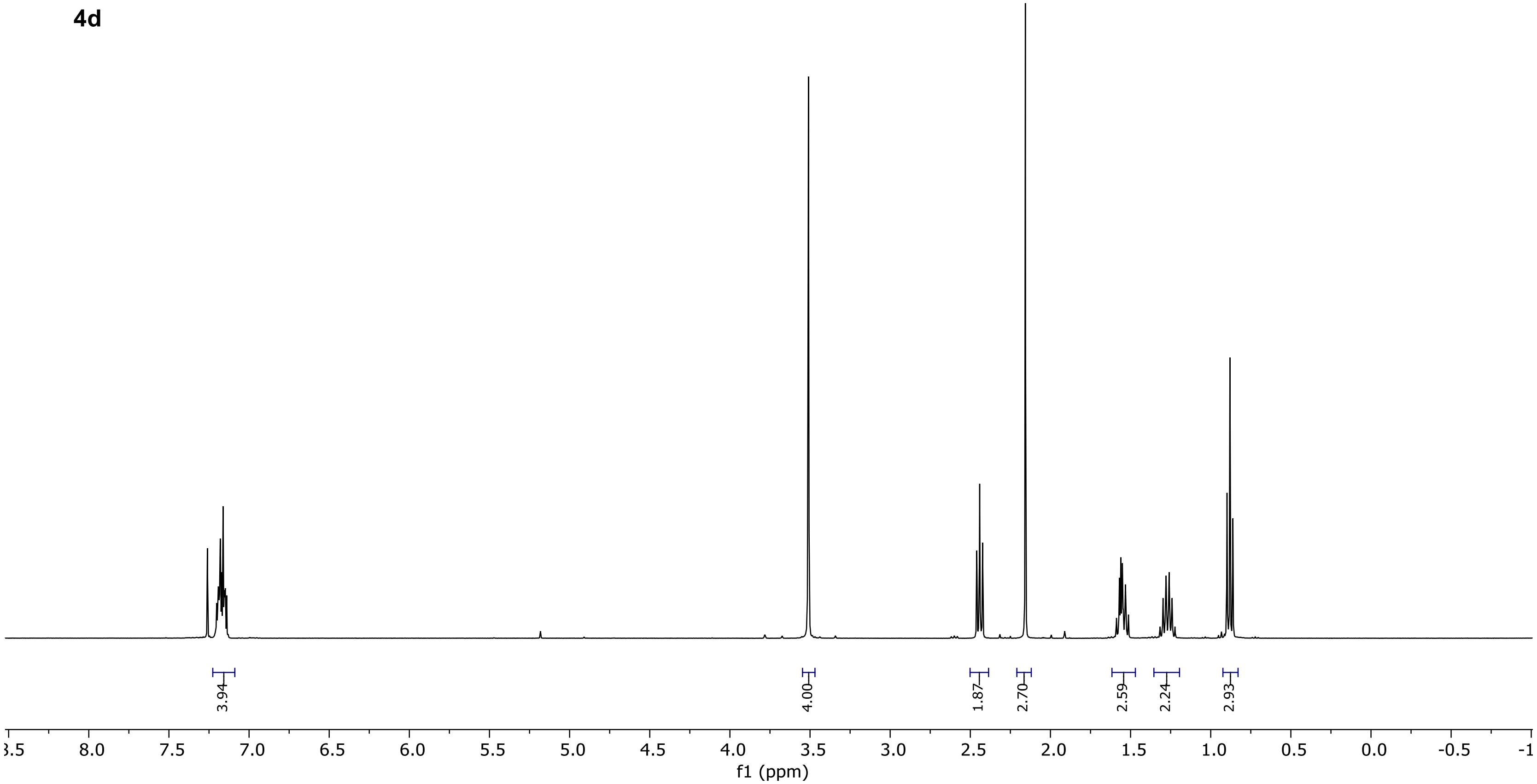


4c

^{1}H-NMR of compound 4d (400MHz, CDCl$_3$)



4d



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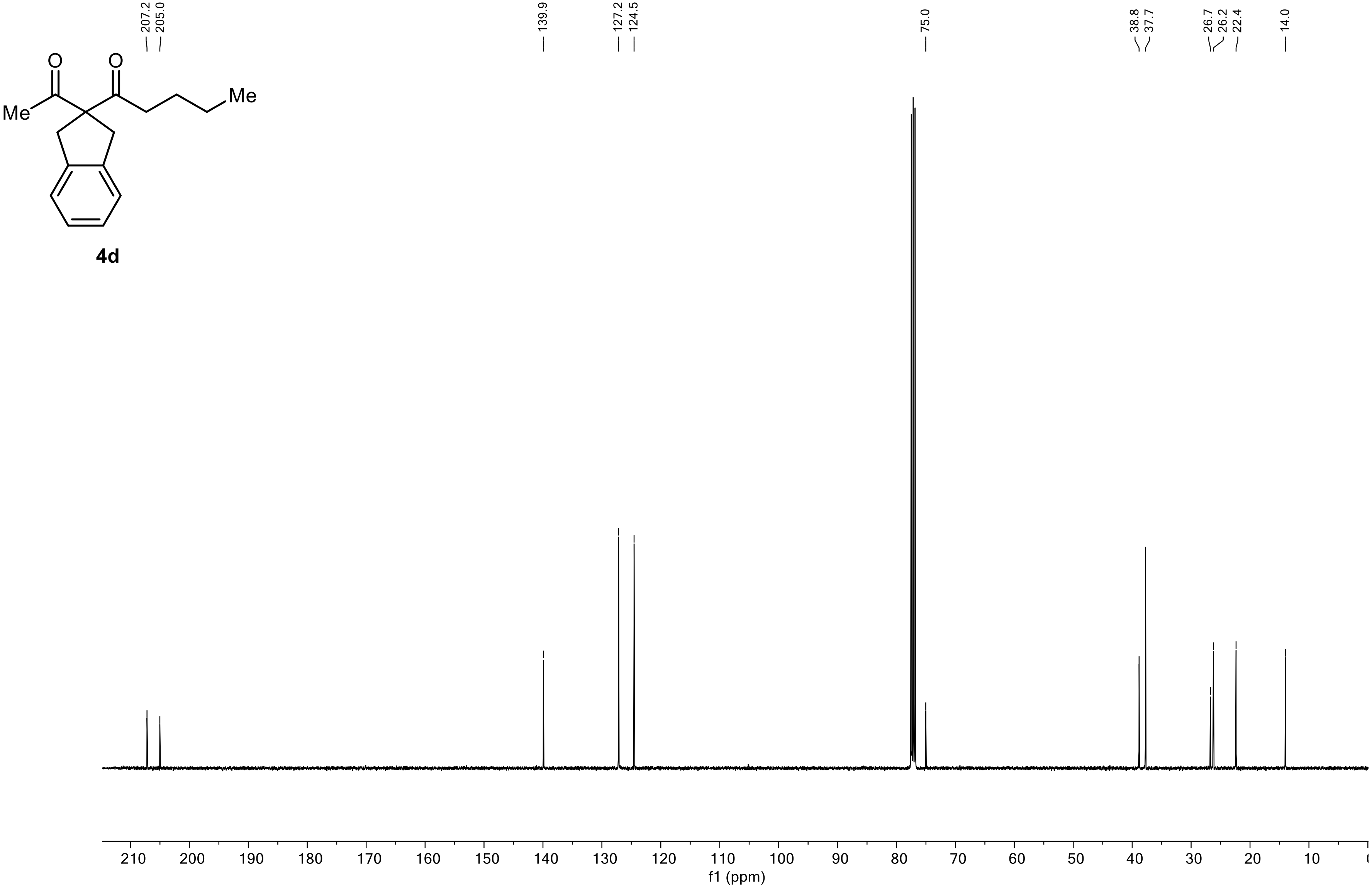
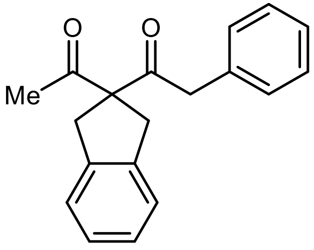
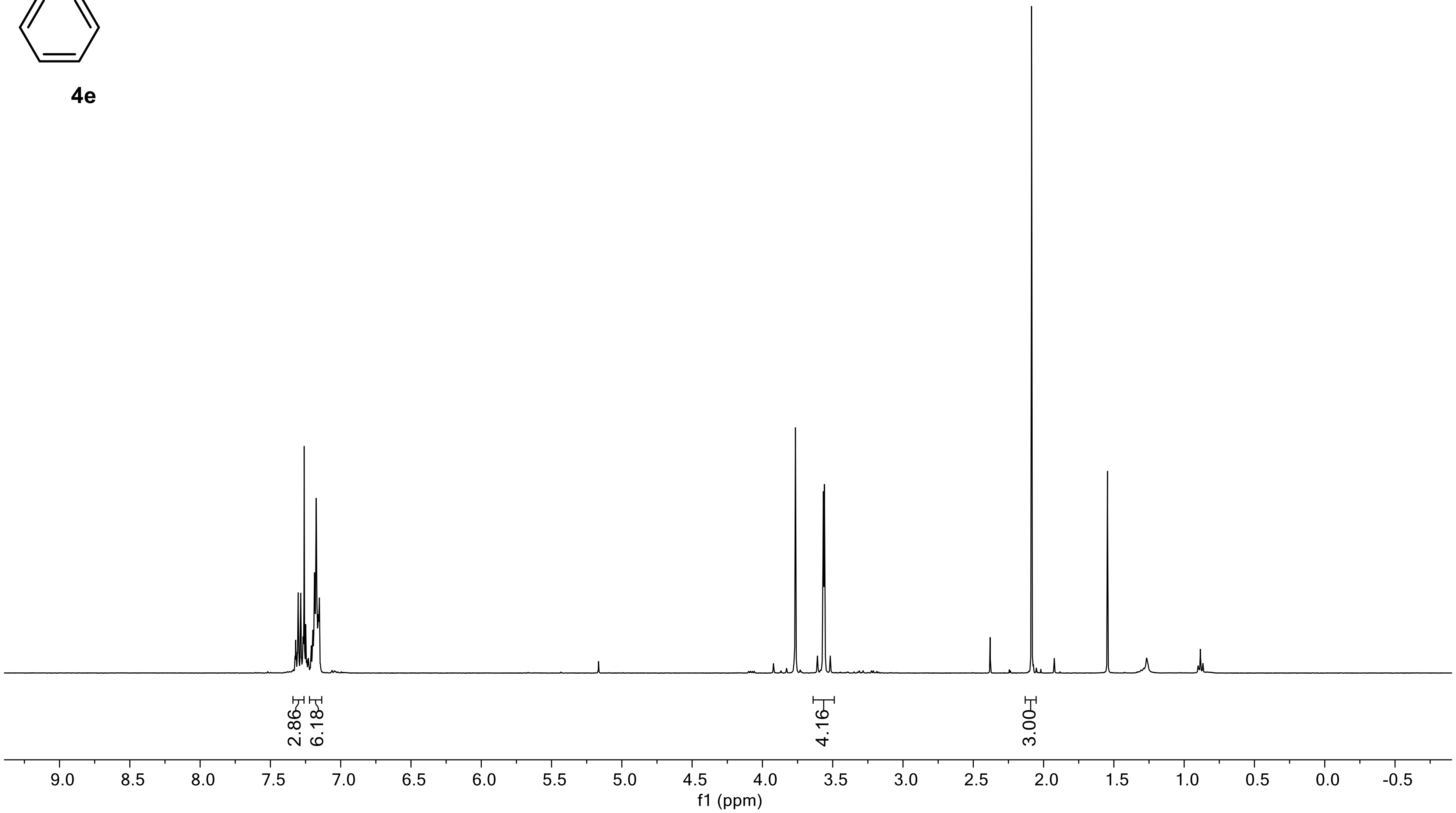


4d

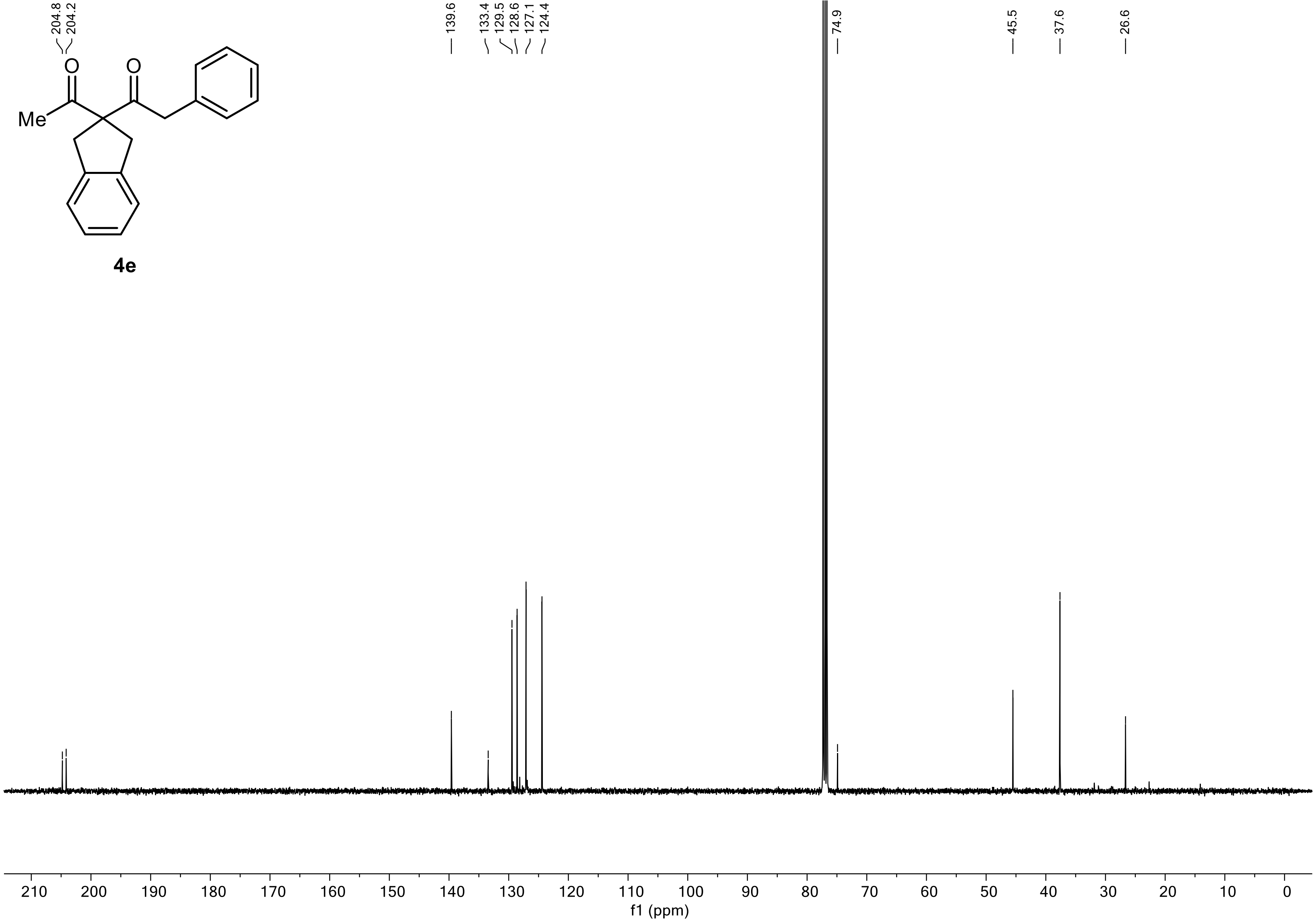
^{1}H-NMR of compound 4e (400MHz, $CDCl_3$)



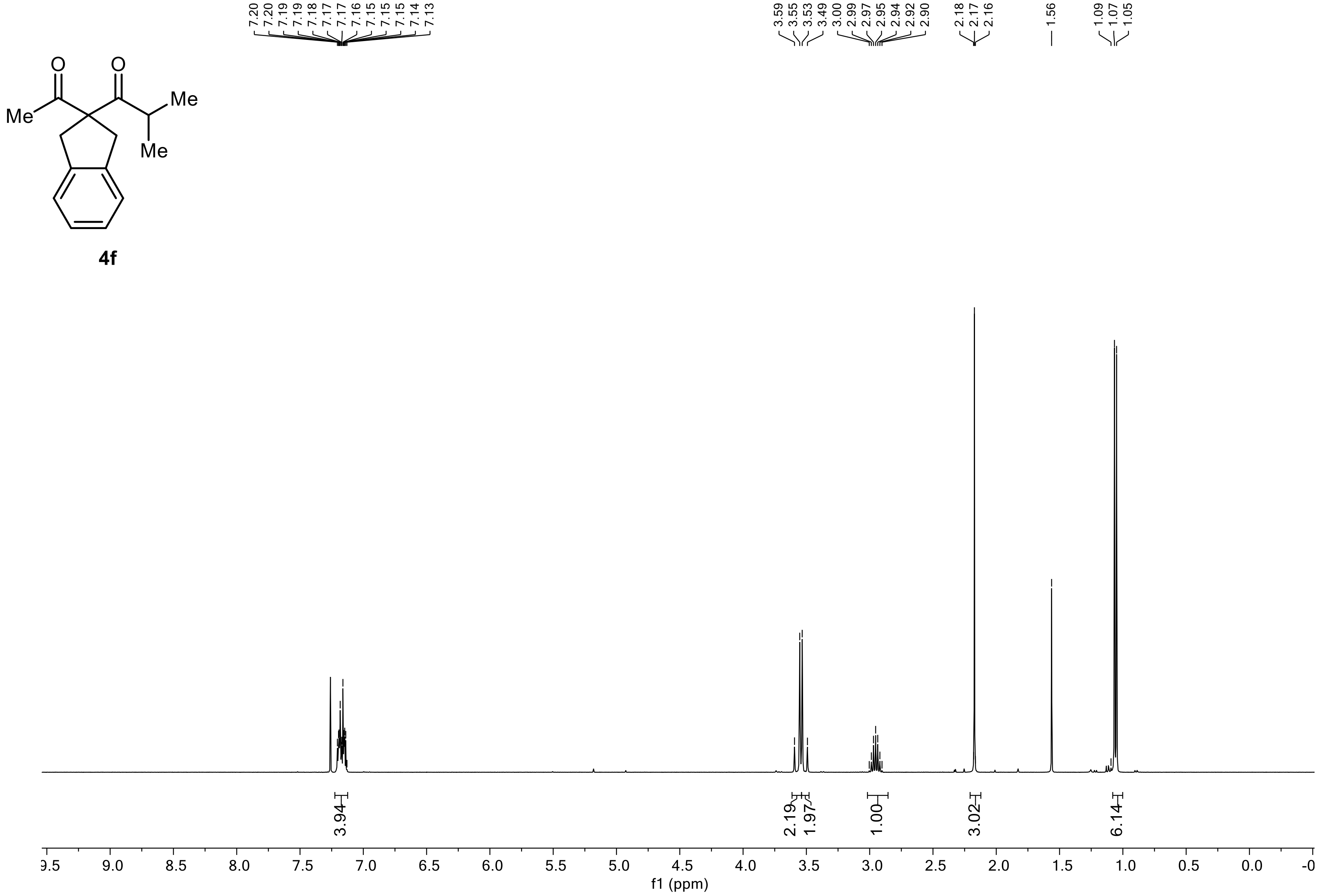
4e



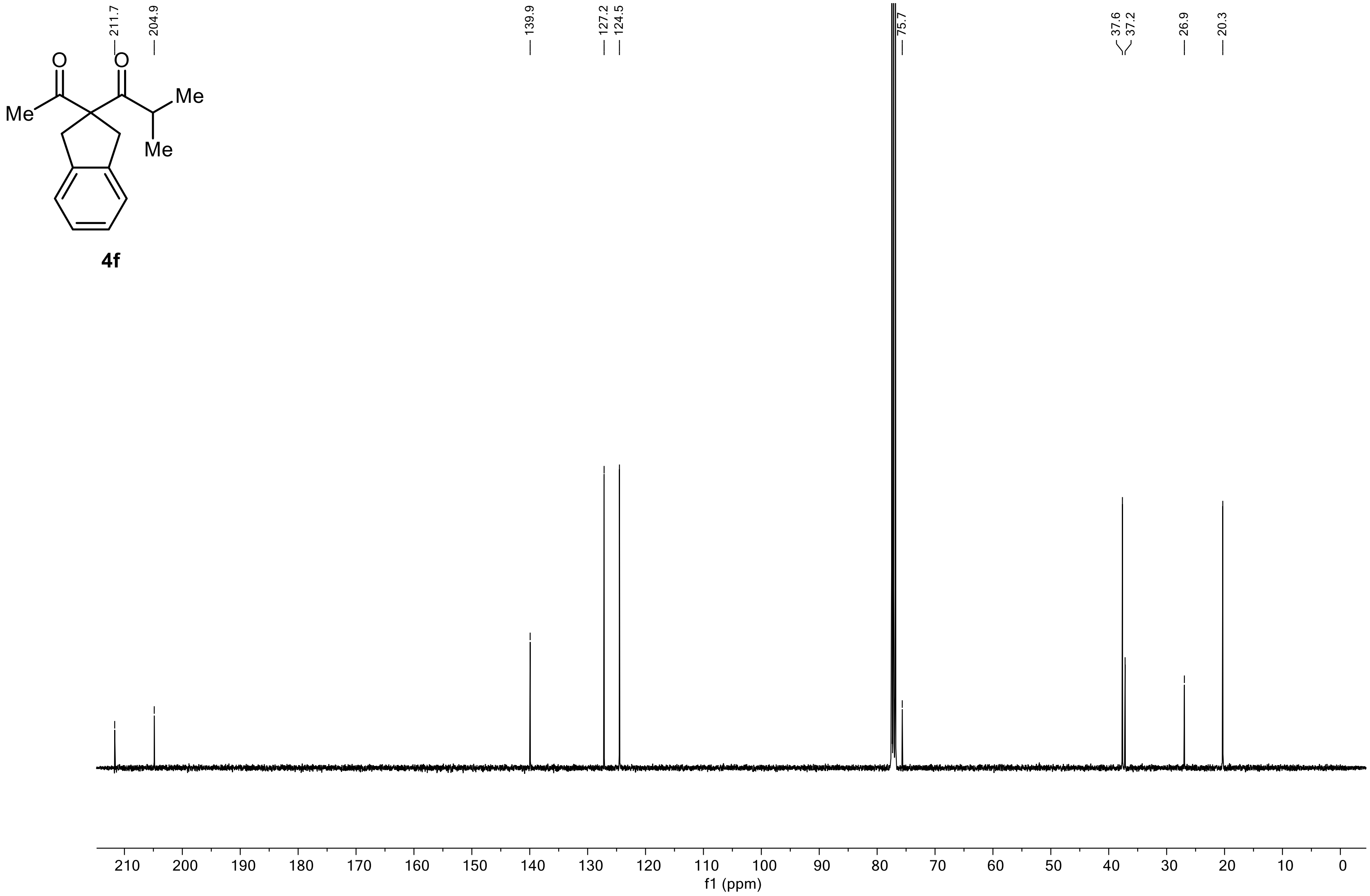
^{13}C-NMR of compound 4e (101MHz, $CDCl_3$)



^{1}H-NMR of compound 4f (400MHz, CD_3Cl)

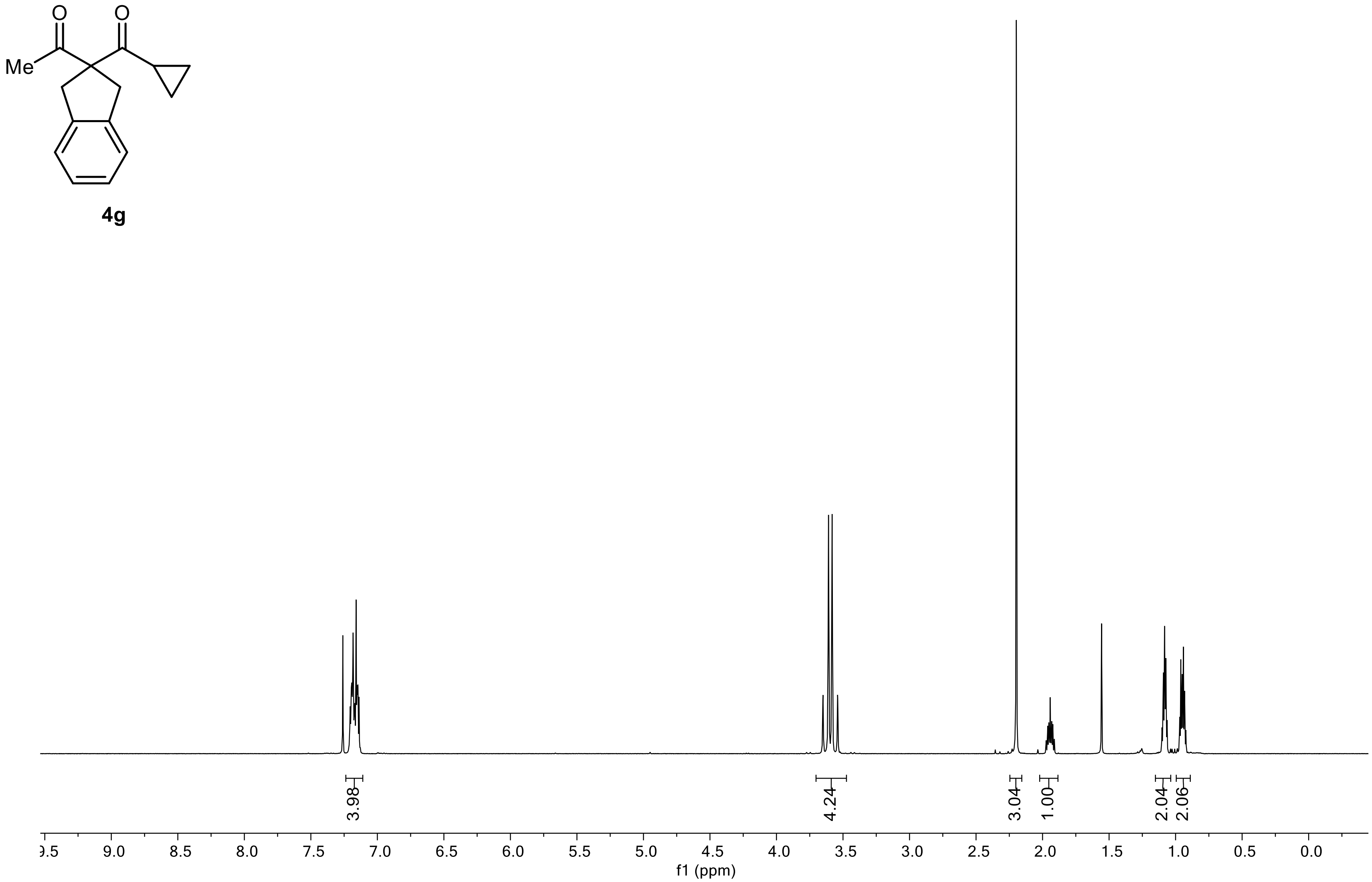


^{13}C-NMR of compound 4f (100MHz, CD_3Cl)



4f

^{1}H-NMR of compound 4g (400MHz, $CDCl_3$)



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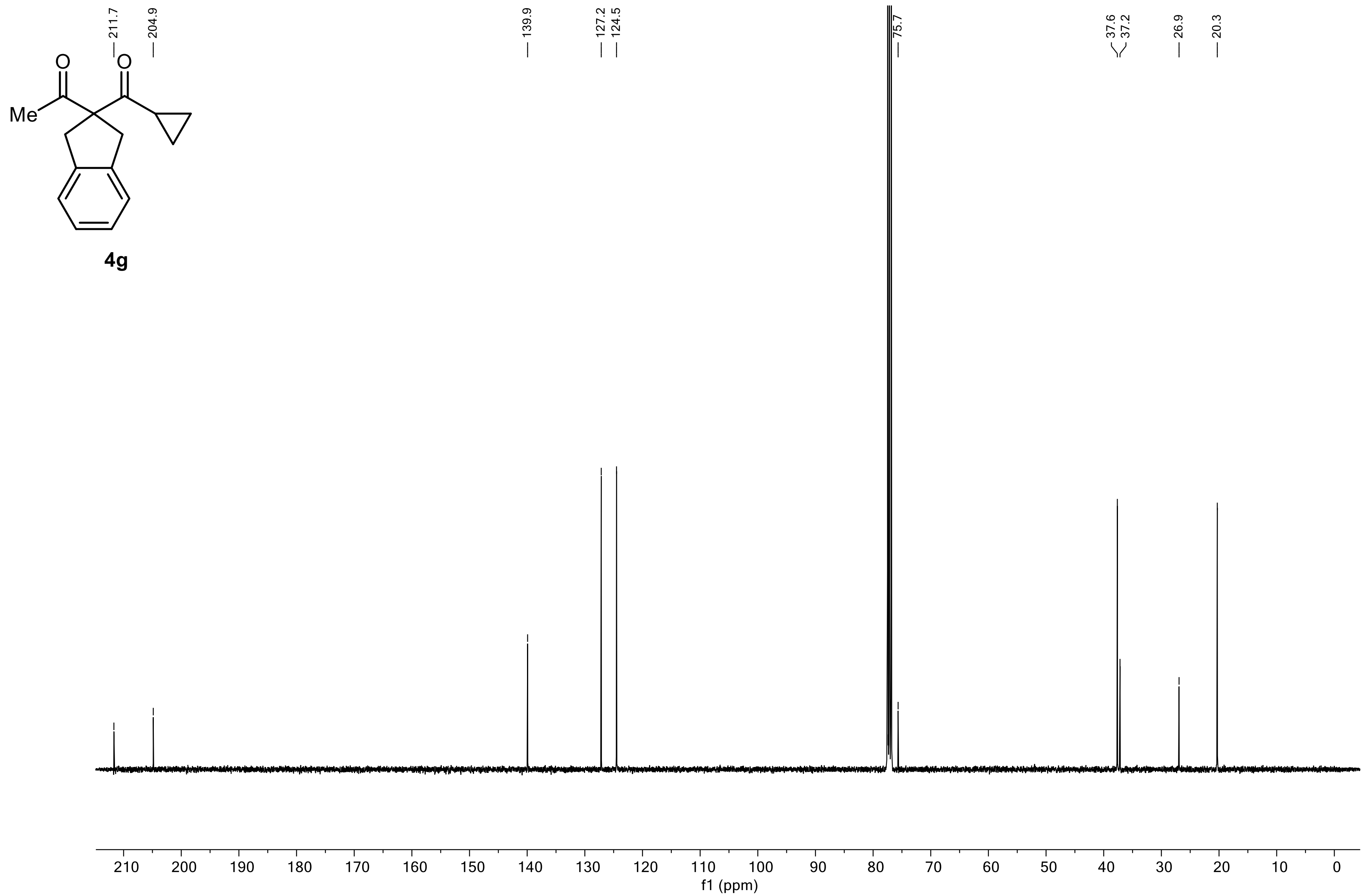
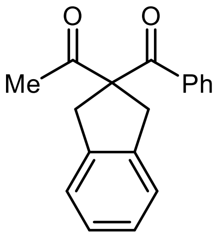
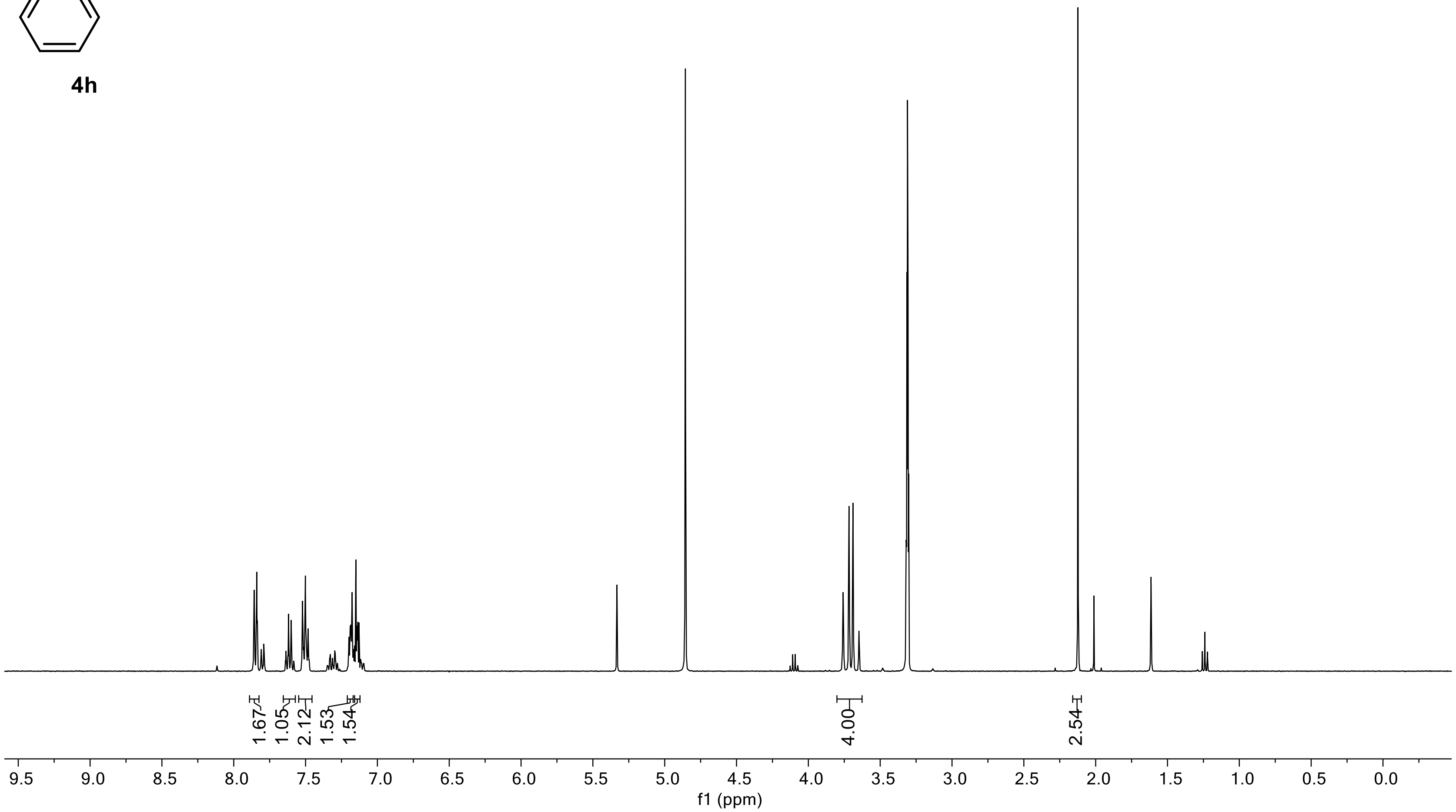


4g

^{1}H-NMR of compound 4h (400MHz, CD_3OD)



4h



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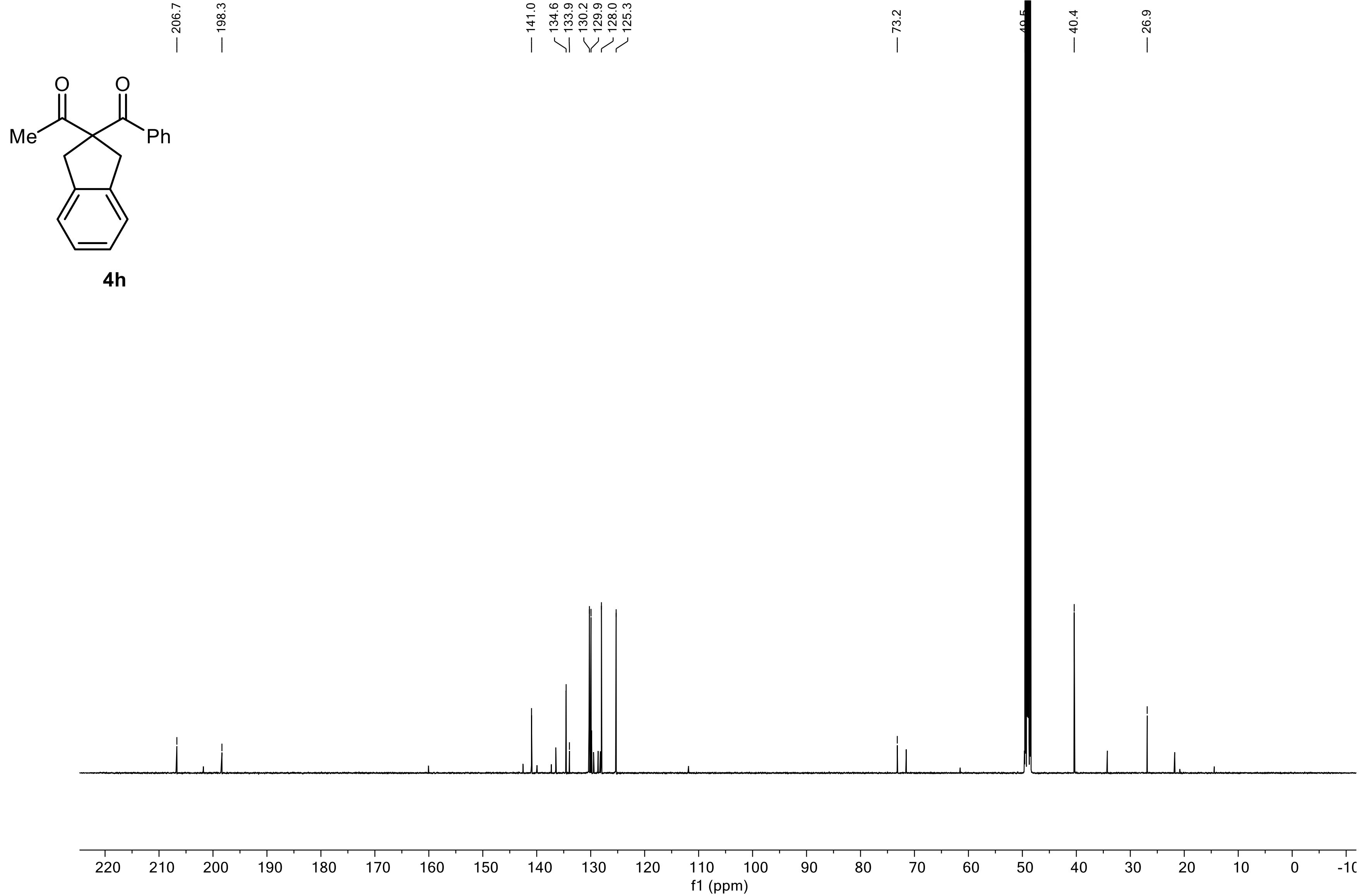
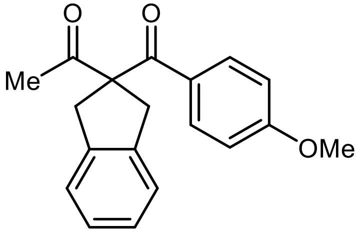
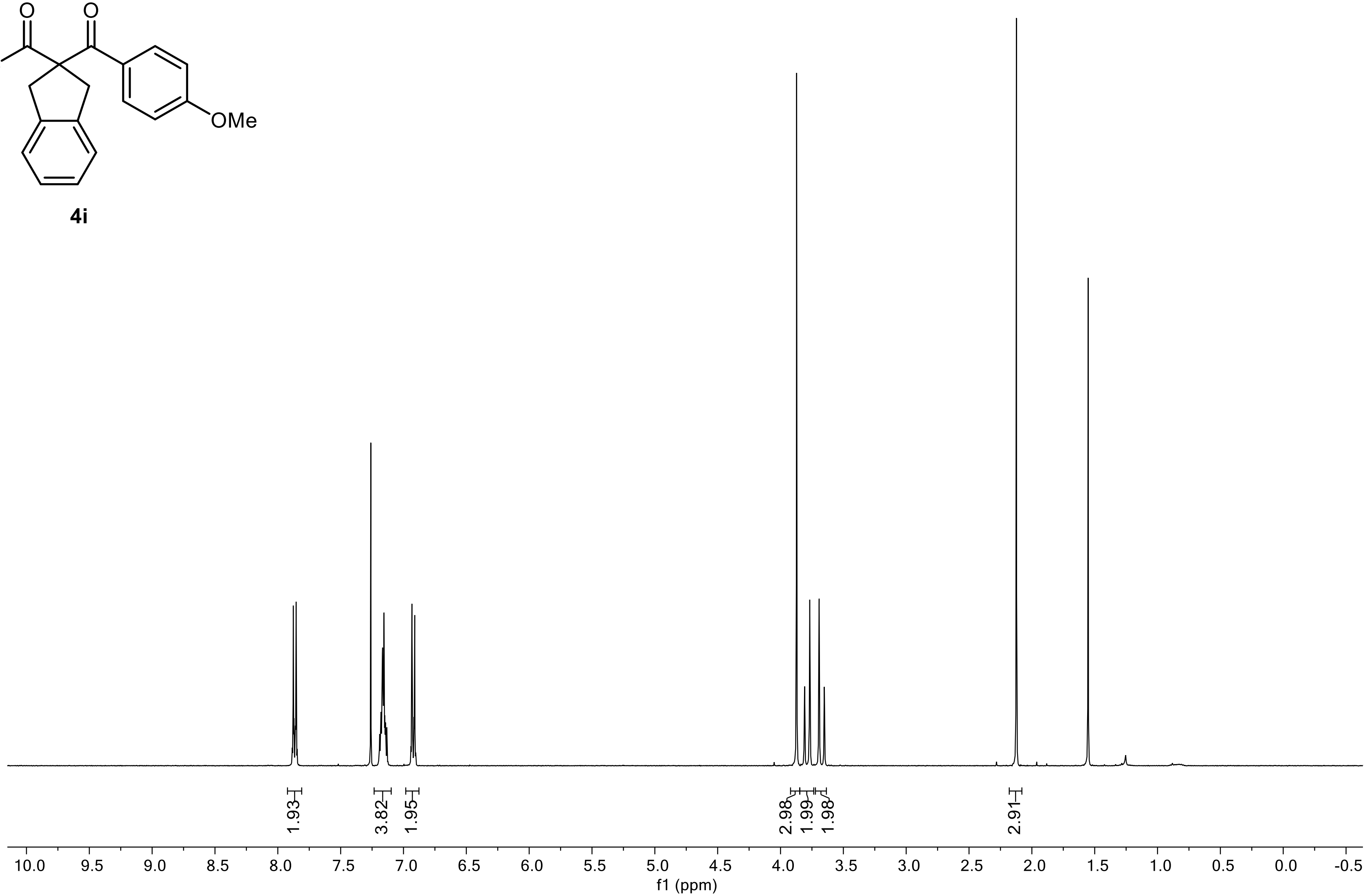


4h

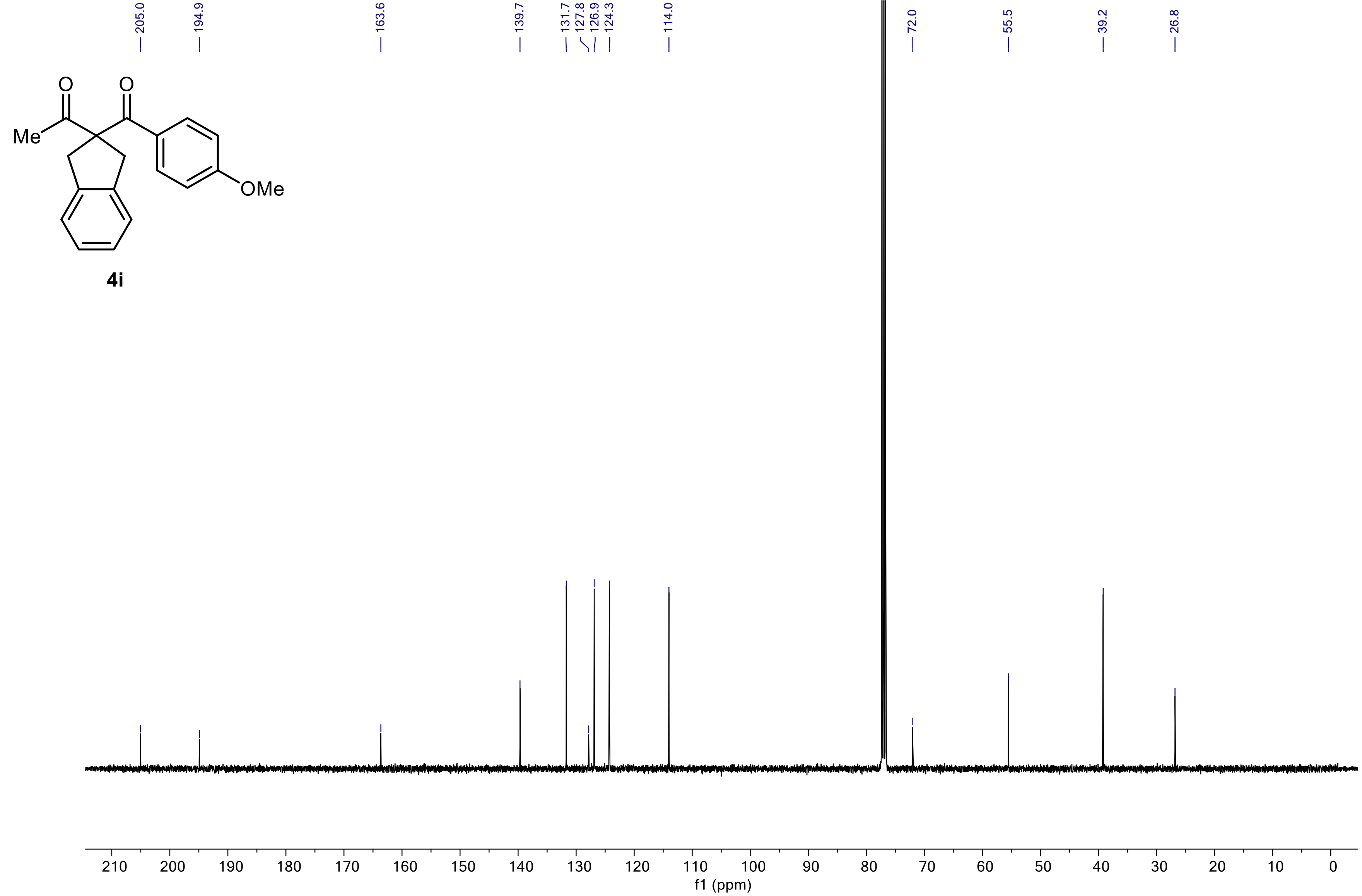
^{1}H-NMR of compound 4i (400MHz, $CDCl_3$)



4i

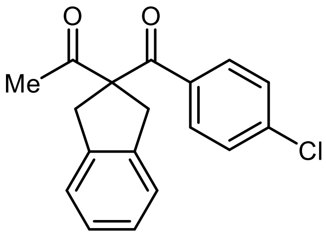


^{13}C-NMR of compound 4i (100MHz, $CDCl_3$)

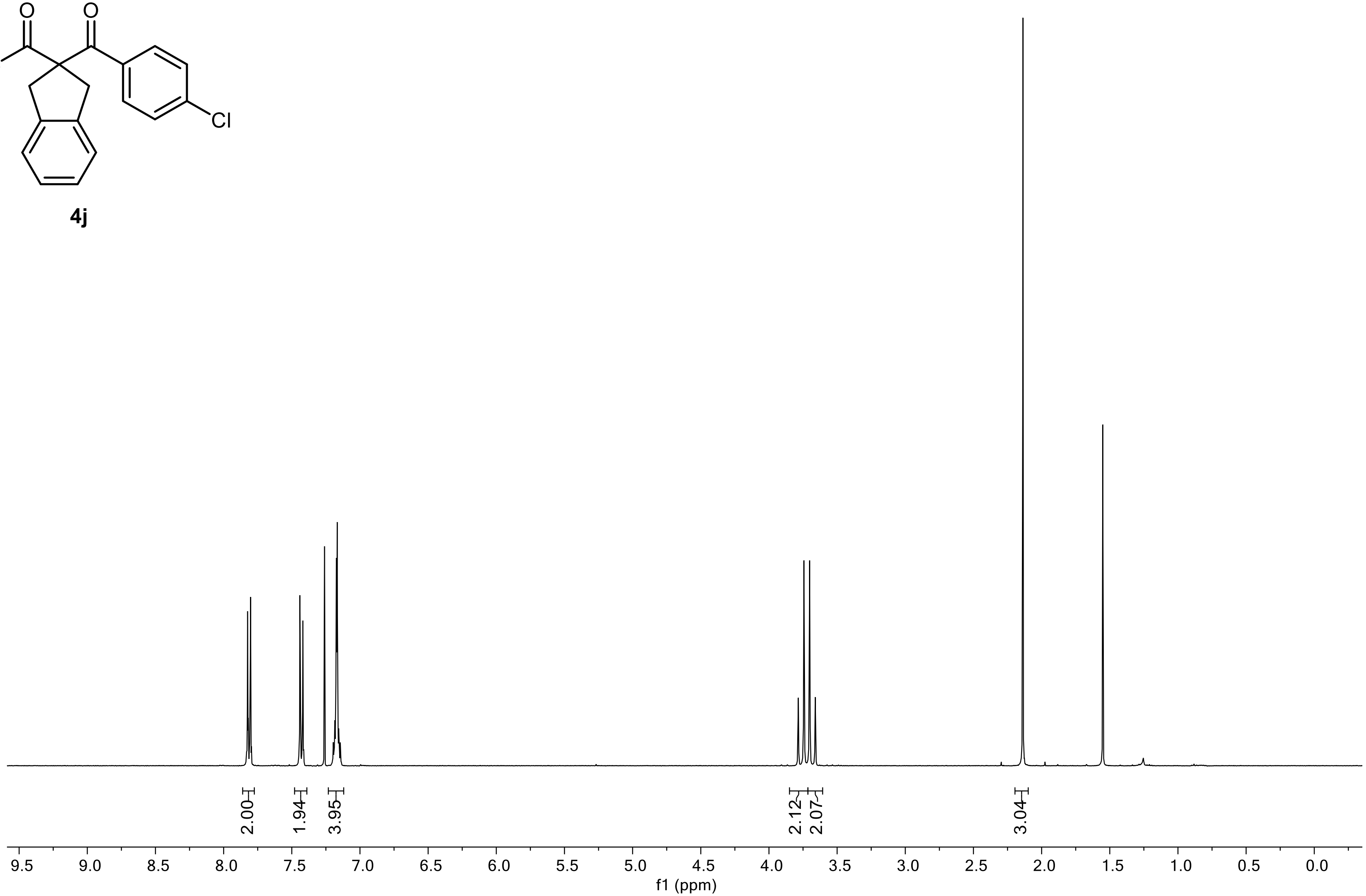


4i

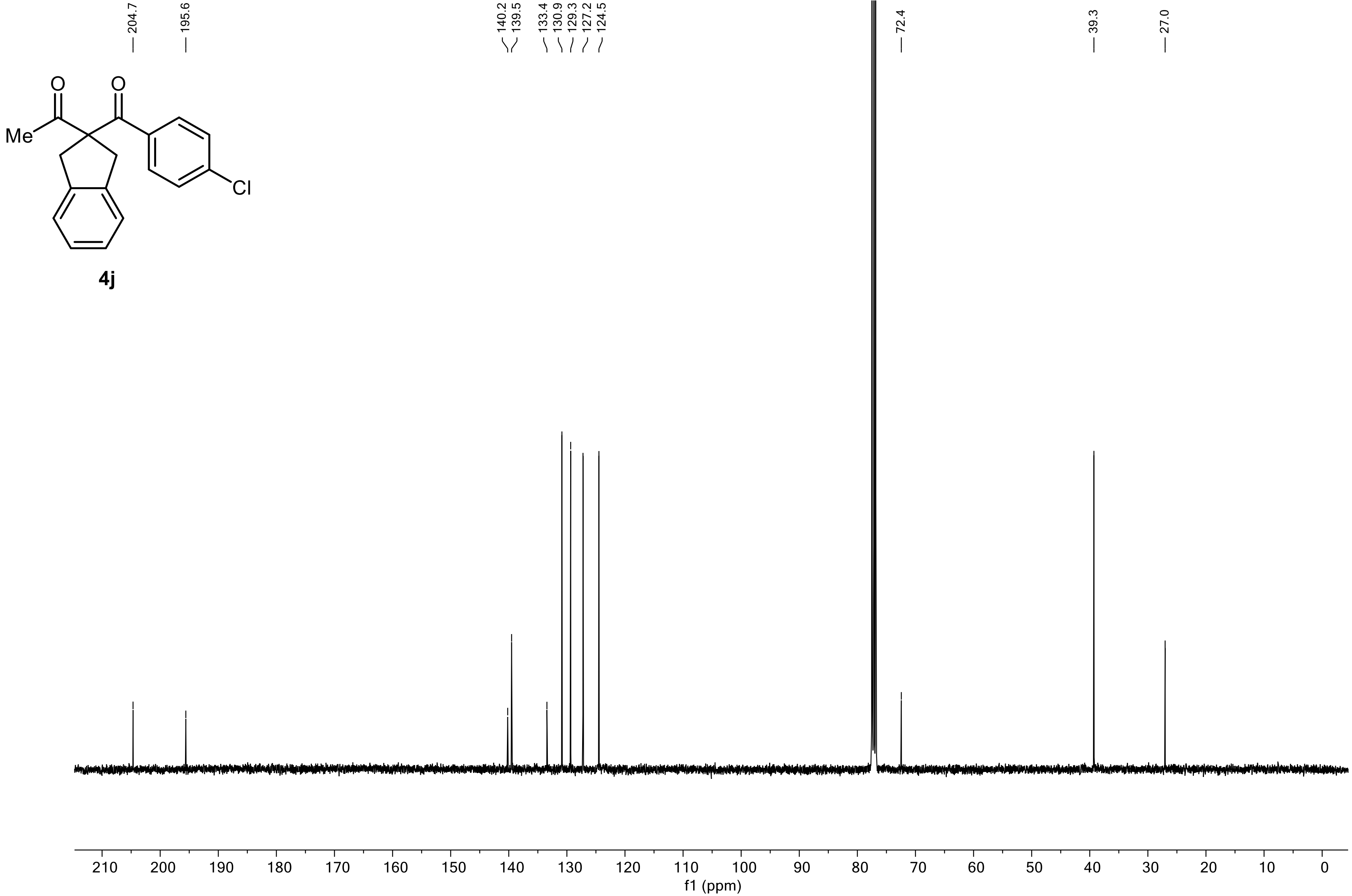
^{1}H-NMR of compound 4j (400MHz, $CDCl_3$)



4j



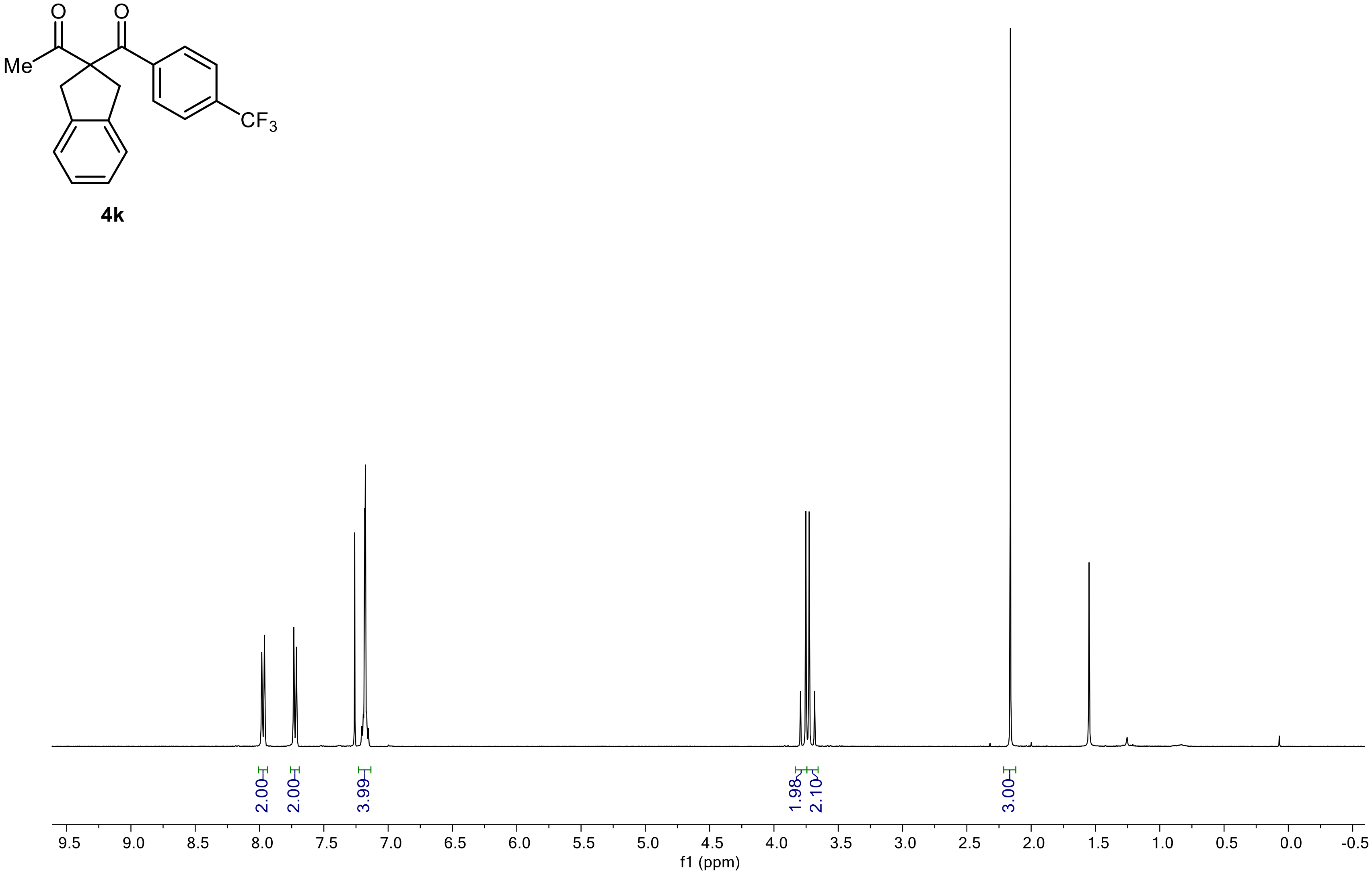
^{13}C-NMR of compound 4j (100MHz, CDCl$_3$)



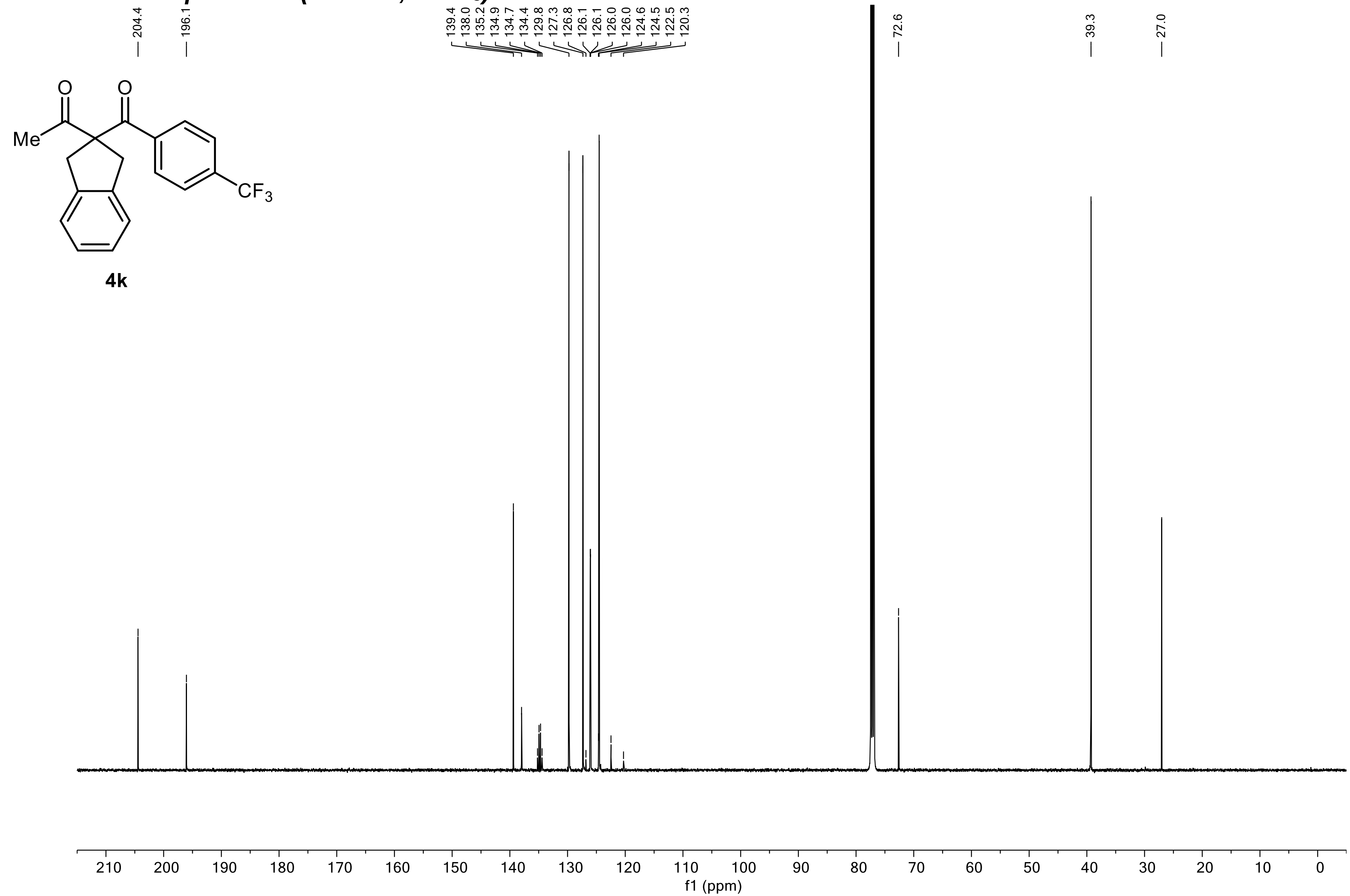
4j

^{1}H-NMR of compound 4k (400MHz, CDCl$_3$)

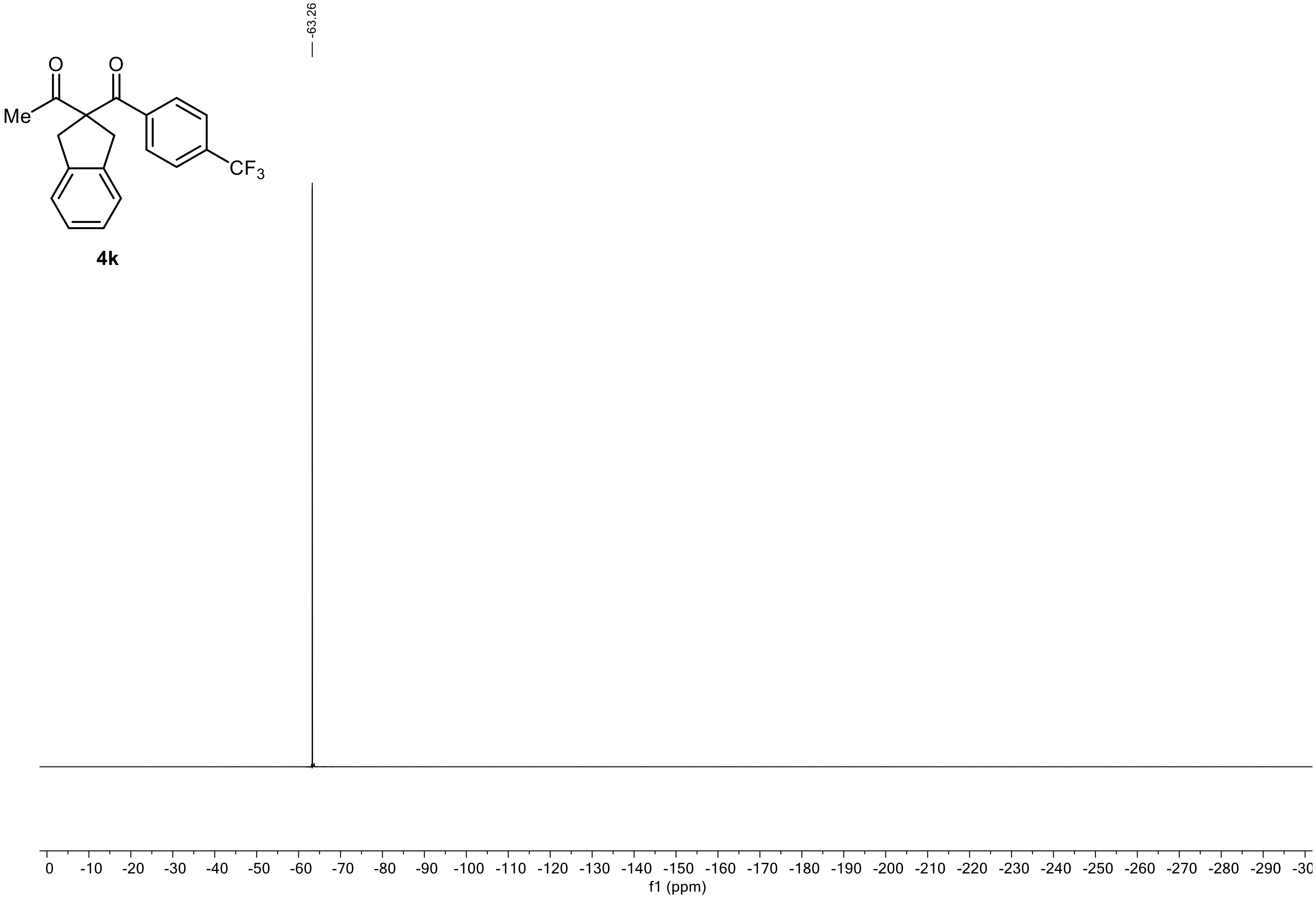
4k



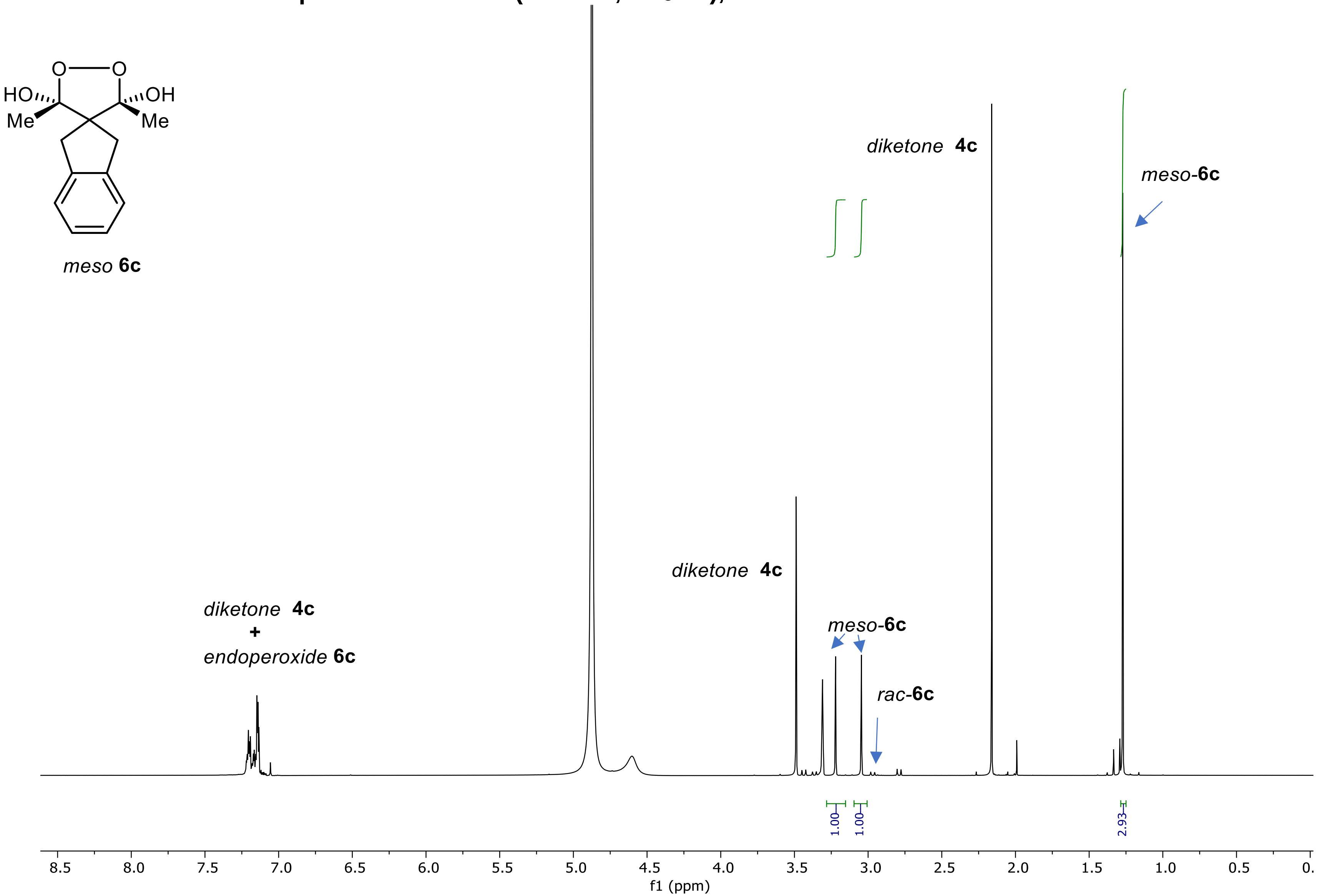
^{13}C-NMR of compound 4k (126MHz, $CDCl_3$)



^{19}F-NMR of compound 4k (472MHz, $CDCl_3$)

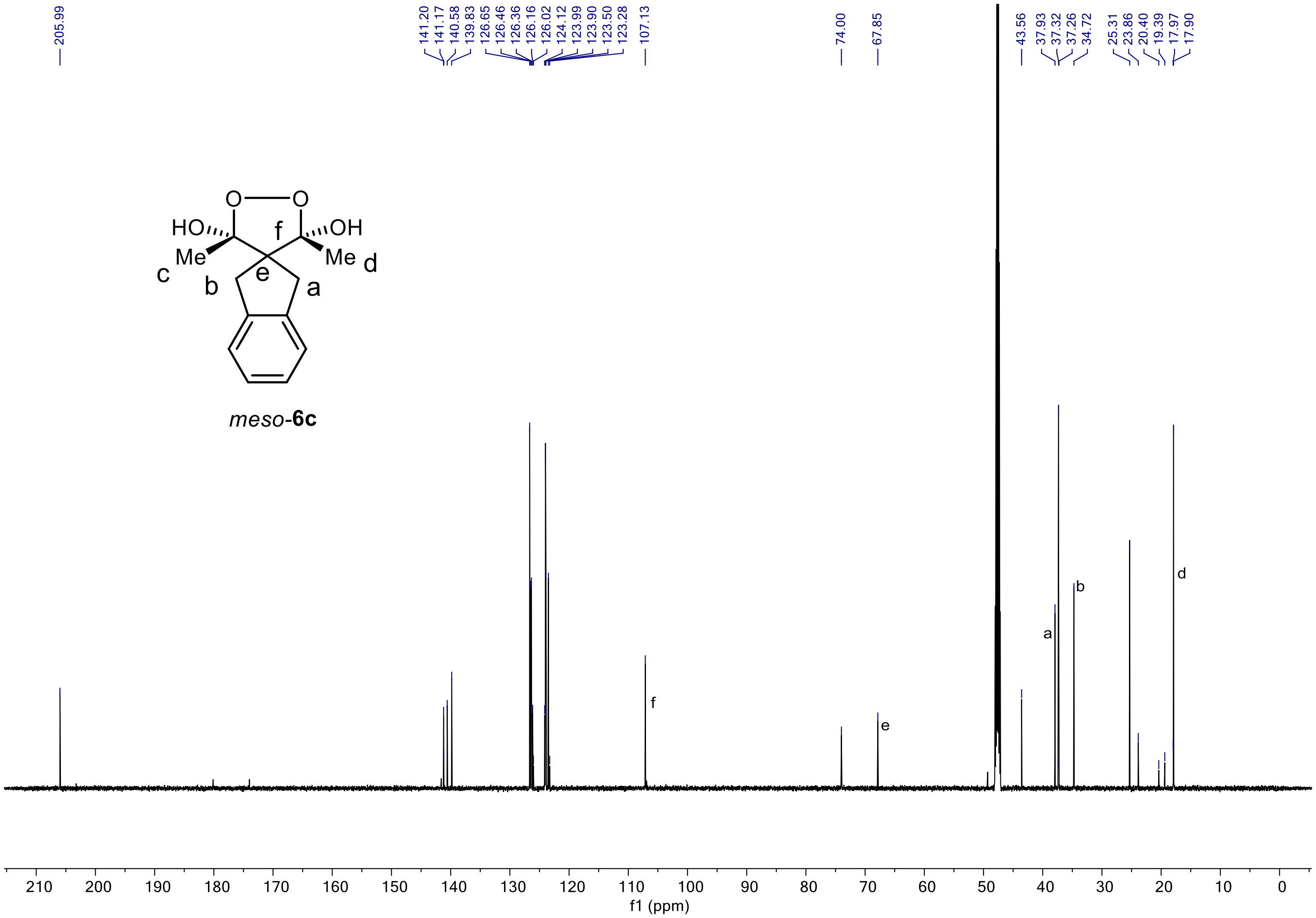


^{1}H-NMR of intermediate endoperoxide meso-6c (600MHz, CD_3OD),



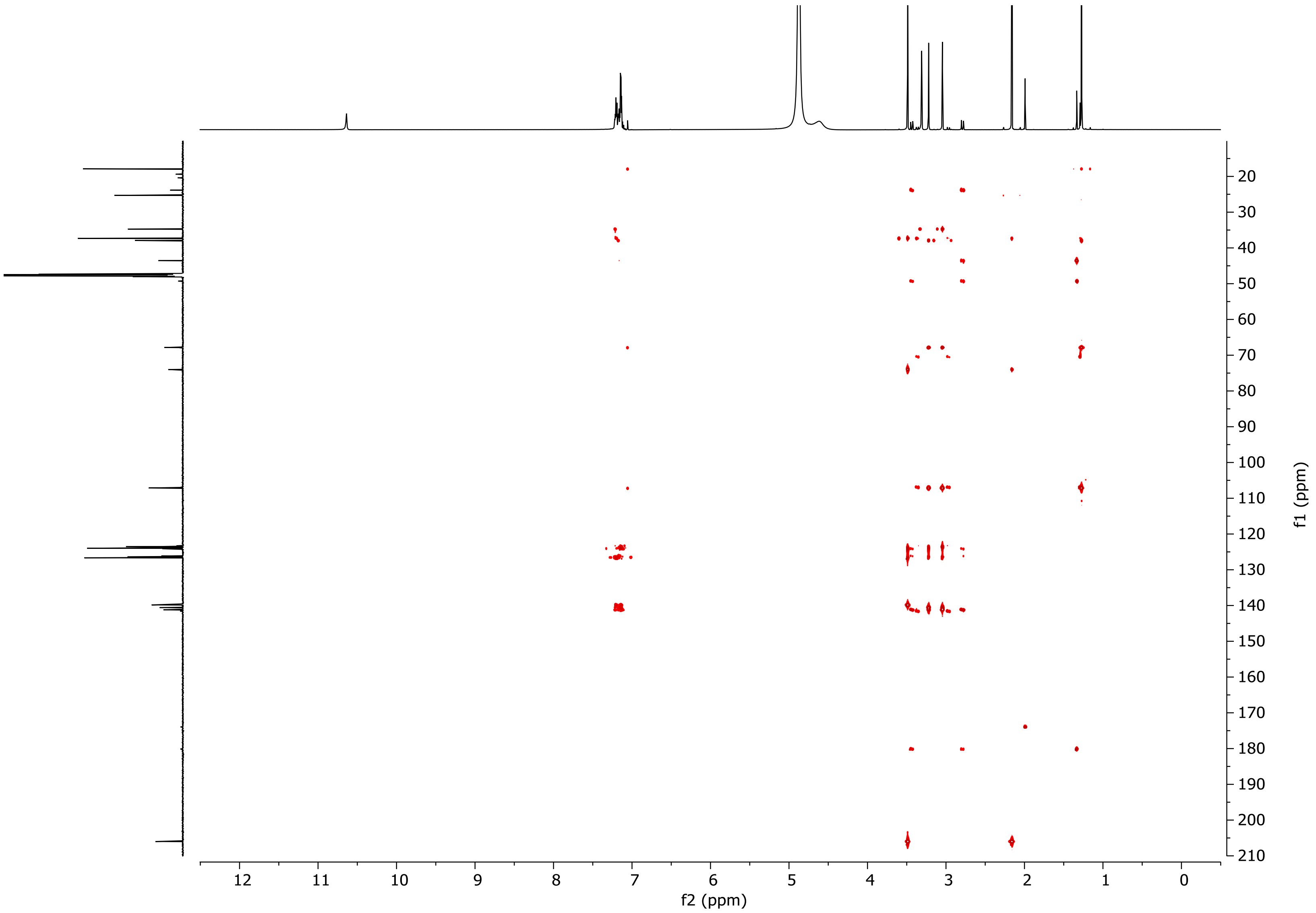
meso **6c**

^{13}C-NMR of compound 6c (151MHz, CD_3OD)

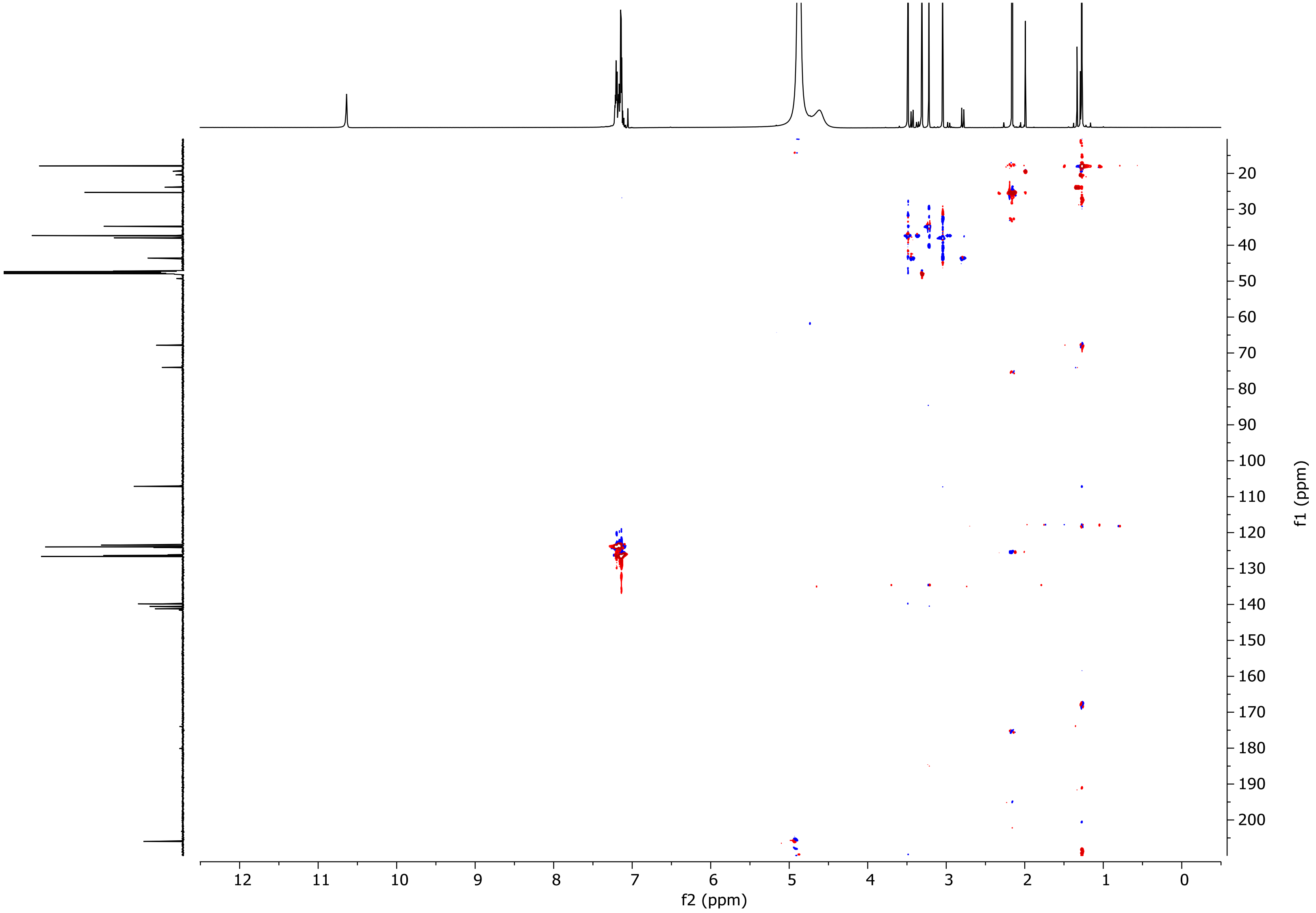


meso-**6c**

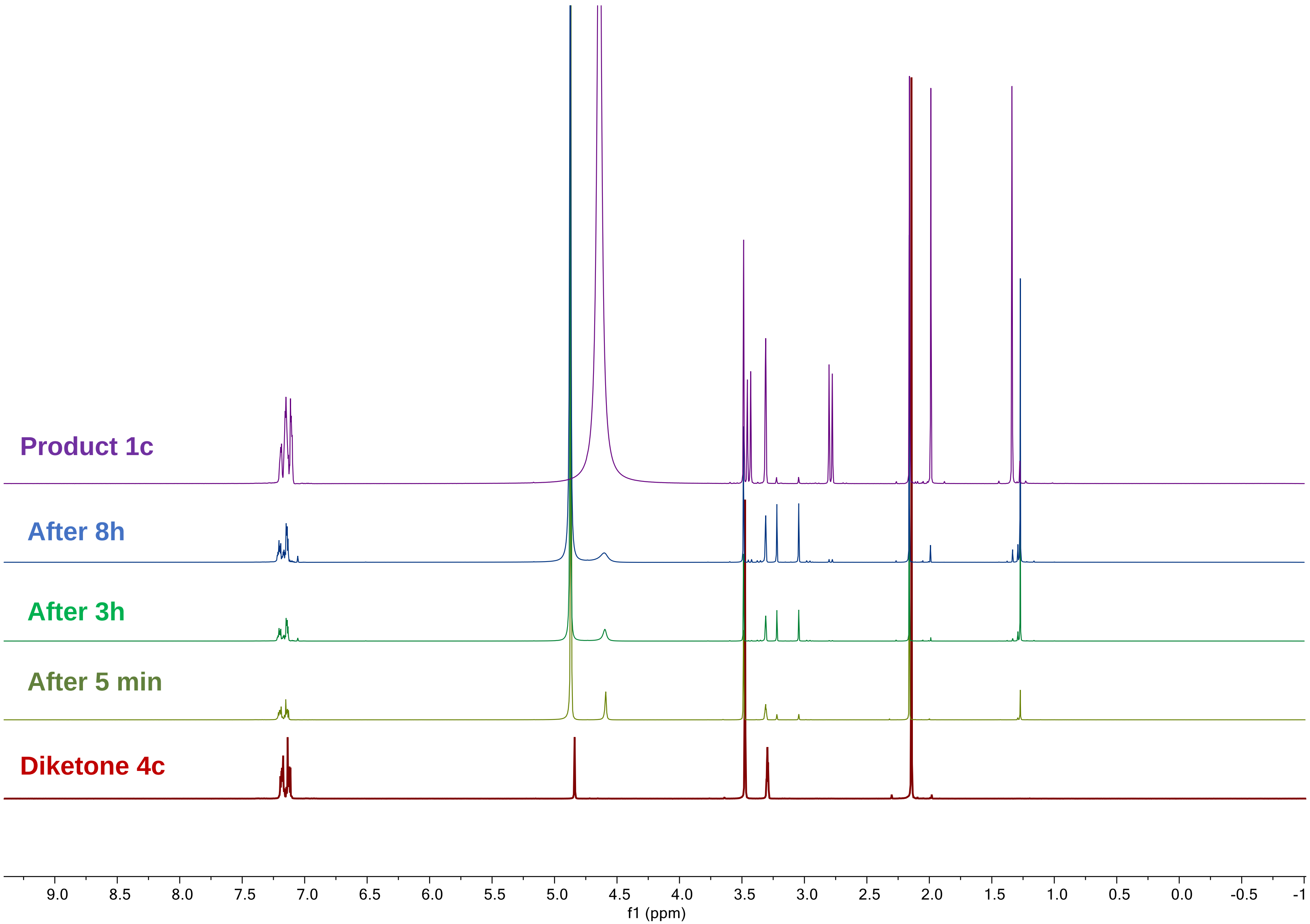
HMBC of compound 6c (CD$_3$OD)



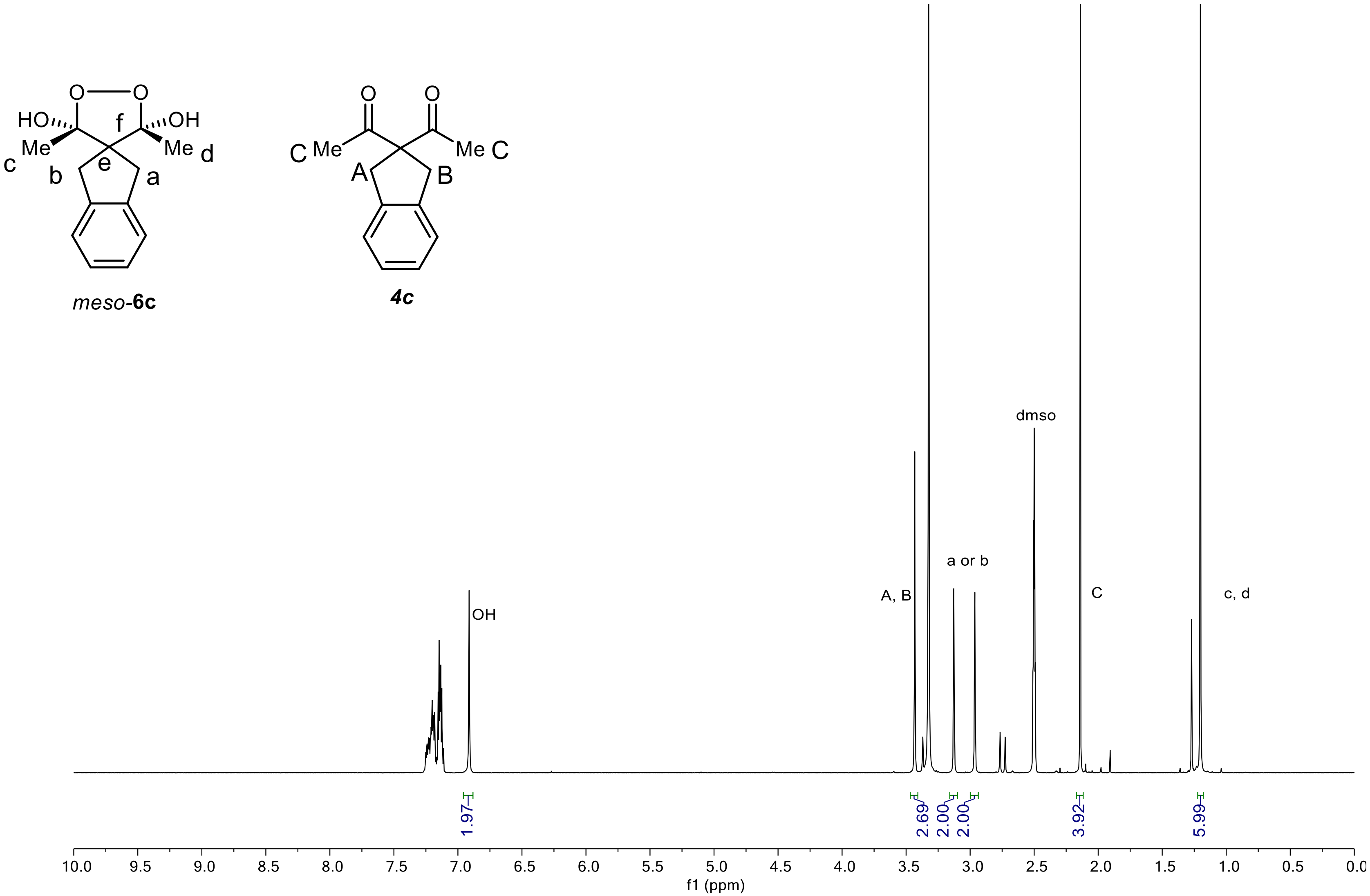
HSQC of compound 6c (CD_3OD)



^{1}H-NMR reaction profile (600MHz, CD_3OD),



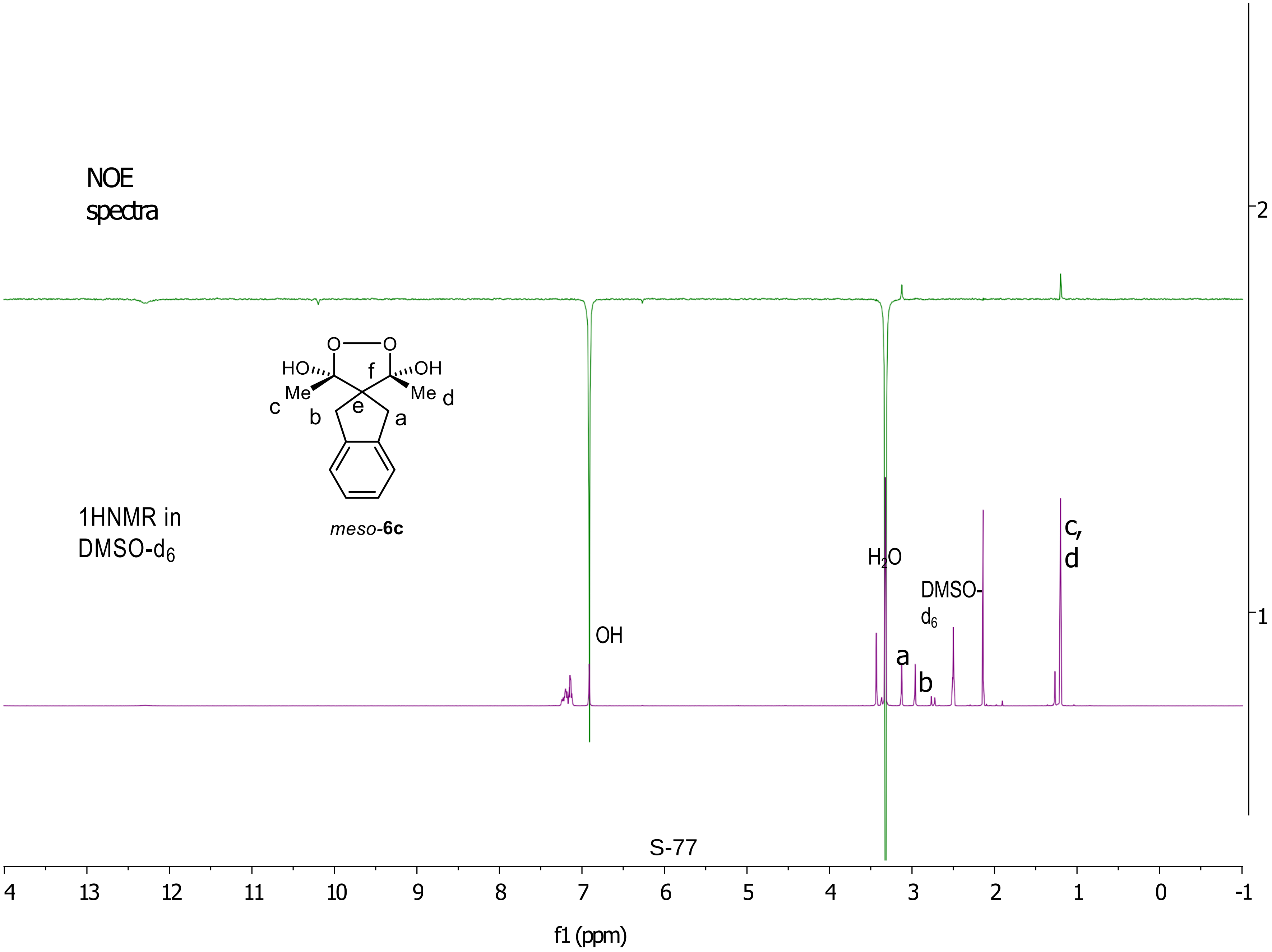
^{1}H-NMR of intermediate endoperoxide meso 6c (400MHz, DMSO$_{d6}$)



meso-**6c**

4c

NOE 1D 6c (400MHz, DMSO$_{d6}$)



5 References

[1] G. Bose, E. Ullah, P. Langer, *Chem. Eur. J.* **2004**, *10*, 6015–6028.