# Electronic Supplementary Information (ESI)

# $I_2$-$PPh_3$ mediated spiroannulation of unsaturated β-dicarbonyl compounds. First synthesis of (±)-negundoin A.

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## General Procedures

Unless stated otherwise, reactions were performed in oven-dried glassware under an argon atmosphere using dry solvents. Solvents were dried as follows: THF and MeOtBu over Na–benzophenone, benzene over Na, DCM and MeOH over $CaH_2$. Dimethylformamide (DMF) was dried over 4Å molecular sieves.

Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching and phosphomolybdic acid solution staining. Flash chromatography was performed on silica gel (Merck Kieselgel 60, 230-400 mesh) Chromatography separations were carried out by conventional column on silica gel 60 (230-400 Mesh), using Hexanes-MeOtBu (H-E) mixtures of increasing polarity.

$^{1}H$ and $^{13}C$ NMR spectra were recorded on a Varian instrument (at 500 MHz and 125 MHz, respectively). $CDCl_3$ was treated with $K_2CO_3$. Chemical shifts (δ H) are quoted in parts per million (ppm) referenced to the appropriate residual solvent peak and tetramethylsilane. Data for $^{1}H$ NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration), with the abbreviations s, br s, d, br d, t, q, and m denoting singlet, broad singlet, doublet, broad doublet, triplet, quartet and multiplet respectively. J = coupling constant in Hertz (Hz). Data for $^{13}C$ NMR spectra are reported in terms of chemical shift relative to $Me_4Si$ (δ 0.0) and the signals were assigned utilizing DEPT experiments and on the basis of heteronuclear correlations.

Infrared spectra (IR) were recorded as thin films or as solids on a Mattson model Satellite FTIR spectrophotometer with samples between sodium chloride plates or as potassium bromide pellets and are reported in frequency of absorption ($cm^{-1}$). Only selected absorbances ($\nu_{max}$) are reported.

($[\alpha]^{D}$) measurements were carried out in a PERKIN-ELMER 341 polarimeter; utilizing a 1dm length cell and $CHCl_3$ as a solvent. Concentration is expressed in mg/mL.

Mass spectra: HRMS were recorded on a AutoSpecQ VG-Analytical (Fisons) spectrometer, using FAB with thioglicerol or glycerol matrix doped in NaI 1%.

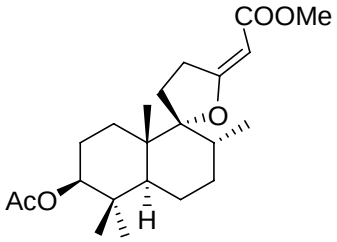
Melting points were determined with a Kofler hot stage melting point apparatus and are uncorrected.

## Experimental Procedures

### General procedure for the preparation of spiro enol ether derivatives.

To a solution of triphenylphosphine (0.1 mmol) in dry $CH_2Cl_2$ (10 mL) was added iodine (0.1 mmol) and the mixture was stirred at room temperature for 5 min. Then, a solution of compounds **9-20** (1 mmol) in dry $CH_2Cl_2$ (5 mL) was added and the resulting mixture was stirred at room temperature for the specified time, and the course of the reaction was monitored by TLC. When the starting material was consumed, the solvent was removed under vacuum and the crude product was directly purified by flash chromatography on silica gel (ether/hexanes mixture) to give the desired spiro enol ether **21-28** and pyran derivatives **29, 30,** respectively.

### Negundoin A (4).



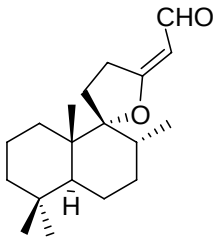

**4**

To a solution of **35** (120 mg, 0.36 mmol) in $CH_2Cl_2$ (3 ml) at 0 ºC were added pyridine (0.5 mL) and acetic anhydride (0.2 mL), and the reaction mixture was stirred at room temperature for 1 h, at which time TLC showed no starting material. Then, the reaction mixture was cooled at 0 ºC, water (0.5 mL) was added to quench the reaction and the mixture was stirred for an additional 5 min. Then, it was diluted with ether (20 mL) and

washed with water (5 mL), 2N HCl (3 x 5 mL), again water (5 mL), sat. aq. $NaHCO_3$ (5 mL) and brine, and the organic phase was dried over $Na_2SO_4$. Removal of the solvent under vacuum afforded a crude product which was purified by flash chromatography on silica gel (15 % ether/hexanes) to yield **4** (130 mg, 96%) as a colourless syrup. $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.77 (d, *J* = 6.6 Hz, 3H), 0.86 (s, 3H), 0.89 (s, 3H), 0.95 (s, 3H), 1.34 - 1.44 (m, 4H), 1.54 - 1.73 (m, 5H), 1.75 - 1.83 (m, 2H), 2.04 (s, 3H), 2.08 (m, 1H), 3.07 (m, 2H), 3.65 (s, 3H), 4.47 (dd, *J* = 11.7, 4.5 Hz, 1H), 5.29 (t, *J* = 1.8 Hz, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 15.5 ($CH_3$), 16.6 ($CH_3$), 16.8 ($CH_3$), 20.9 ($CH_2$), 21.3 ($CH_3$), 23.3 ($CH_2$), 26.7 ($CH_2$), 28.0 ($CH_3$), 29.3 ($CH_2$), 31.0 ($CH_2$), 31.6 ($CH_2$), 36.5 (CH), 37.7 (C), 42.0 (C), 46.2 (CH), 50.5 ($CH_3$), 80.2 (CH), 87.3 (CH), 97.7 (C), 169.5 (C), 170.8 (C), 178.5 (C). IR (film): 1735, 1707, 1633, 1365, 1244, 1127, 1033, 794, 755 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{22}H_{34}O_5Na$ ($M+Na^+$) 401.2304, found: 401.2299.

NMR data for natural negundoin A (**4**):[1] $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.77 (d, *J* = 6.5 Hz, 3H), 0.86 (s, 3H), 0.89 (s, 3H), 0.95 (s, 3H), 1.37 (m, 1H), 1.38 (m, 1H), 1.38 (m, 2H), 1.55 (m, 1H), 1.58 (m, 1H), 1.63 (m, 1H), 1.71 (m, 2H), 1.78 (m, 1H), 1.80 (m, 1H), 2.04 (s, 3H), 2.08 (m, 1H), 3.04 (m, 1H), 3.12 (m, 1H), 3.65 (s, 3H), 4.47 (dd, *J* = 11.6, 4.6 Hz, 1H), 5.30 (s, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 15.5 ($CH_3$), 16.5 ($CH_3$), 16.8 ($CH_3$), 20.9 ($CH_2$), 21.3 ($CH_3$), 23.3 ($CH_2$), 26.7 ($CH_2$), 27.9 ($CH_3$), 29.3 ($CH_2$), 31.0 ($CH_2$), 31.5 ($CH_2$), 36.5 (CH), 37.7 (C), 42.0 (C), 46.2 (CH), 50.5 ($CH_3$), 80.2 (CH), 87.3 (CH), 97.7 (C), 169.3 (C), 170.8 (C), 178.5 (C).

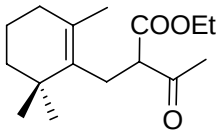
**3-Deacetoxynegundoin C (5).**




**5**

(10% ether/hexanes) (82 %) yellow syrup. $[\alpha]_D^{25}$= + 1.2 (c = 8.6 $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.78 (d, *J* = 6.6 Hz, 3H), 0.82 (s, 3H), 0.89 (s, 3H), 0.94 (s, 3H), 1.05 - 1.19 (m, 2H), 1.29 - 1.40 (m, 4H), 1.42 - 1.66 (m, 5H), 1.80 - 1.89 (m, 2H), 2.17 (ddd, *J* = 13.4, 11.5, 7.8 Hz, 1H), 3.00 - 3.15 (m, 2H), 5.60 (d, *J* = 7.8 Hz, 1H), 9.55 (d, *J* = 7.8 Hz, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 15.7 ($CH_3$), 16.8 ($CH_3$), 18.2 ($CH_2$), 21.3 ($CH_2$), 21.8 ($CH_3$), 26.0 ($CH_2$), 30.1 ($CH_2$), 31.2 ($CH_2$), 31.3 ($CH_2$), 33.2 ($CH_3$), 33.3 (C), 36.6 (CH), 41.4 ($CH_2$), 42.5 (C), 46.8 (CH), 100.0 (CH), 100.6 (C), 182.6 (C), 190.3 (CH). IR (film): 1656, 1625, 1577, 1354, 1213, 1154, 877 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{19}H_{30}O_2Na$ ($M+Na^+$) 313.2143, found: 313.2136.

**Ethyl 3-oxo-2-((2,6,6-trimethylcyclohex-1-enyl)methyl)butanoate (11).**

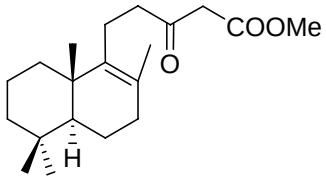



**11**

$^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.938 (s, 3H), 0.942 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.37 - 1.42 (m, 2H), 1.50 (s, 3H), 1.52 - 1.58 (m, 4H), 1.90 (t, *J* = 6.4 Hz, 1H), 2.21 (s, 3H), 2.65 (t, *J* = 6.0 Hz, 1H), 3.55 (t, *J* = 6.0 Hz, 1H), 4.10 - 4.20 (m, 2H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 14.0 ($CH_3$), 19.2 ($CH_2$), 20.5 ($CH_3$), 26.4 ($CH_2$), 28.5 ($CH_3$), 28.7 ($CH_3$), 29.3 ($CH_3$), 32.9 ($CH_2$), 34.8 (C), 40.0 ($CH_2$), 60.7 (CH), 61.3 ($CH_2$), 130.1 (C),

134.6 (C), 170.2 (C), 203.0 (C). IR (film): 1739, 1718, 1462, 1360, 1190, 1150, 1051, 1025 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{16}H_{26}O_3Na$ ($M+Na^+$) 289.1780, found: 289.1772.

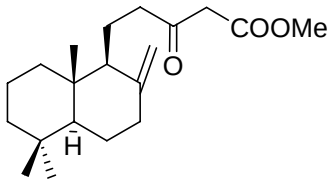
**Methyl 3-oxo-5-((4a*S*,8a*S*)-2,5,5,8a-tetramethyl-3,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)pentanoate (12).**




**12**

$[\alpha]_D^{25}$= +55.7 (c = 38.0, $CHCl_3$). $^1H$ NMR ($CDCl_3$, 500 MHz) δ: 0.81 (s, 3H), 0.87 (s, 3H), 0.92 (s, 3H), 1.00 - 1.18 (m, 3H), 1.32 - 1.68 (m, 5H), 1.52 (s, 3H), 1.75 (br d, *J* = 12.3 Hz, 1H), 1.88 - 2.06 (m, 2H), 2.18 (m, 1H), 2.30 (m, 1H), 2.58 (m, 2H), 3.43 (s, 2H), 3.72 (s, 3H). $^{13}C$ RMN ($CDCl_3$, 125 MHz) δ: 18.95 ($CH_2$), 18.97 ($CH_2$), 19.4 ($CH_3$), 19.9 ($CH_3$), 21.3 ($CH_2$), 21.6 ($CH_3$), 33.3 ($CH_3$), 33.3 (C), 33.6 ($CH_2$), 36.9 ($CH_2$), 39.0 (C), 41.7 ($CH_2$), 43.9 ($CH_2$), 48.9 ($CH_2$), 51.9 ($CH_3$), 52.3 (CH), 126.9 (C), 138.8 (C), 167.6 (C), 202.5 (C). IR (film): 1750, 1719, 1654, 1672, 1447, 1319, 1238, 1151 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{20}H_{32}O_3Na$ ($M+Na^+$) 343.2249, found: 343.2256.

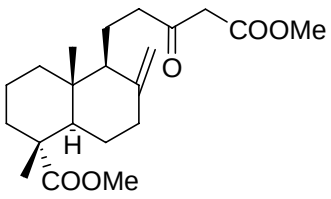
**Methyl 3-oxo-5-((1*S*,4a*S*,8a*S*)-5,5,8a-trimethyl-2-methylene-decahydronaphthalen-1-yl)pentanoate (13).**




**13**

$[\alpha]_D^{25}$= + 18.0 (c = 1.3, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.67 (s, 3H), 0.79 (s, 3H), 0.85 (s, 3H), 1.03 - 1.11 (m, 2H), 1.16 (ddd, *J* = 13.4, 13.4, 4.2 Hz, 1H), 1.31 (ddd, *J* = 25.9, 13.0, 4.3 Hz, 1H), 1.38 (br d, *J* = 13.1 Hz, 1H), 1.43 - 1.66 (m, 4H), 1.71 (m, 1H), 1.77 (br d, *J* = 12.7 Hz, 1H), 1.84 - 1.99 (m, 2H), 2.33 - 2.46 (m, 2H), 2.63 - 2.72 (m, 1H), 3.40 (s, 2H), 3.72 (s, 3H), 4.41 (s, 1H), 4.81 (d, *J* = 0.86 Hz, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 14.3 ($CH_3$), 17.3 ($CH_2$), 19.4 ($CH_2$), 21.7 ($CH_3$), 24.5 ($CH_2$), 33.63 (C), 33.67 ($CH_3$), 38.3 ($CH_2$), 39.0 ($CH_2$), 39.8 (C), 42.1 ($CH_2$), 42.2 ($CH_2$), 49.2 ($CH_2$), 52.3 ($CH_3$), 55.5 (CH), 56.1 (CH), 106.3 ($CH_2$), 148.3 (C), 167.7 (C), 203.1 (C). IR (film): 1749, 1717, 1646, 1457, 1437, 1318, 1236, 889, 667 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{20}H_{32}O_3Na$ ($M+Na^+$) 343.2249, found: 343.2250.

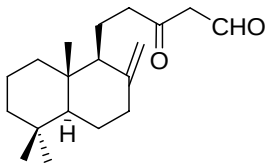
**(1*R*,4a*R*,5*S*,8a*R*)-Methyl-5-(5-methoxy-3,5-dioxopentyl)-1,4a-dimethyl-6-methylene-decahydronaphthalene-1-carboxylate (14).**




**14**

$[\alpha]_D^{25}$= +27.9 (c = 10.2, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.70 (s, 3H), 1.13 (s, 3H), 1.20 (m, 2H), 1.43 (ddd, *J* = 25.8, 12.9, 4.4 Hz, 1H), 1.49 - 1.78 (m, 4H), 1.62 - 1.77 (m, 2H), 1.80 (br d, *J* = 12.4 Hz, 1H), 1.89 (m, 1H), 1.93 (dd, *J* = 12.6, 2.7 Hz, 1H), 1.99 (ddd, *J* = 13.2, 13.2, 5.3 Hz, 1H), 2.32 (ddd, *J* = 12.7, 4.2, 2.2 Hz, 1H), 2.43 (ddd, *J* = 18.5, 7.5, 7.5 Hz, 1H), 2.68 (ddd, *J* = 18.2, 8.7, 4.7 Hz, 1H), 3.41 (s, 2H), 3.65 (s, 3H), 3.73 (s, 3H), 4.43 (s, 1H), 4.82 (s, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 14.5 ($CH_3$), 16.5 ($CH_3$), 17.0 ($CH_2$), 18.4 ($CH_2$), 26.8 ($CH_2$), 37.0 ($CH_2$), 37.7 ($CH_2$), 37.9 ($CH_2$), 39.1 (C), 42.0 ($CH_2$), 47.7 (C), 49.1 ($CH_2$), 49.7 ($CH_3$), 51.9 ($CH_3$), 52.3 (CH), 55.9 (CH), 106.9 ($CH_2$), 147.5 (C), 167.6 (C), 179.2 (C), 202.9 (C). IR (film): 1748, 1723, 1644, 1437, 1245, 1173, 1130, 893 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{21}H_{32}O_5Na$ ($M+Na^+$) 387.2147, found: 387.2151.

**3-Oxo-5-((1*S*,4a*S*,8a*S*)-5,5,8a-trimethyl-2-methylene-decahydronaphthalen-1-yl)pentanal (16):**

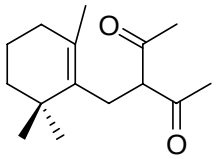



**16**

$[\alpha]_D^{25}$= + 42.6 (c = 17.0, $CHCl_3$).$^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.69 (s, 3H), 0.80 (s, 3H), 0.87 (s, 3H), 1.00 - 1.13 (m, 2H), 1.18 (ddd, *J* = 13.2, 13.2, 4.2 Hz, 1H), 1.32 (m, 1H), 1.39 (br d, *J* = 13.0 Hz, 1H), 1.44 - 1.67 (m, 4H), 1.67 - 2.05 (m, 4H), 2.19 (m, 1H), 2.39 (m, 2H), 2.52 (m, 1H), 4.49 (s, 1H), 4.85 (s, 1H), 5.50 (d, *J* = 4.3 Hz, 1H), 7.88 (d, *J* = 4.3 Hz, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 14.3 ($CH_3$), 19.1 ($CH_2$), 19.3 ($CH_2$), 21.7 ($CH_3$), 24.4 ($CH_2$), 33.63 (C), 33.64 ($CH_3$), 38.2 ($CH_2$), 38.5 ($CH_2$), 39.0 ($CH_2$), 39.8 (C), 42.1 ($CH_2$), 55.5 (CH), 56.2 (CH), 101.9 (CH), 106.4 ($CH_2$), 148.1 (C),

175.2 (CH), 196.4 (C). IR (film): 1639, 1598, 1459, 1387, 1365, 1249, 890 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{19}H_{30}O_2Na$ ($M+Na^+$) 313.2143, found: 313.2136.

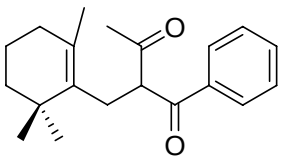
**3-((2,6,6-Trimethylcyclohex-1-enyl)methyl)pentane-2,4-dione (17).**



**17**

$^1H$ NMR ($CDCl_3$, 500 MHz) δ: 0.91 (s, 6H), 1.38 (m, 2H), 1.46 (s, 3H), 1.54 (m, 2H), 1.89 (t, *J* = 6.2 Hz, 1H), 2.15 (s, 6H), 2.59 (d, *J* = 6.0 Hz, 1H), 3.77 (t, *J* = 6.0 Hz, 1H). $^{13}C$ RMN ($CDCl_3$, 125 MHz) δ: 26.9 ($CH_2$), 20.6 ($CH_3$), 26.9 ($CH_2$), 28.6 ($CH_3$), 28.6 ($CH_3$), 29.6 ($CH_3$), 29.6 ($CH_3$), 32.9 ($CH_2$), 34.7 (C), 40.0 ($CH_2$), 70.0 (CH), 130.2 (C), 135.0 (C), 204.3 (C), 204.3 (C). IR (film): 1726, 1700, 1579, 1473, 1358, 1260, 1150, 953 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{15}H_{24}O_2Na$ ($M+Na^+$) 259.1674, found: 259.1668.

**1-Phenyl-2-((2,6,6-trimethylcyclohex-1-enyl)methyl)butane-1,3-dione (18).**

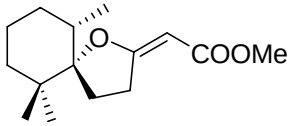


**18**

$^1H$ NMR ($CDCl_3$, 500 MHz) δ: 0.87 (s, 3H), 0.97 (s, 3H), 1.39 (m, 2H), 1.46 (s, 3H), 1.53 (m, 2H), 1.88 (m, 2H), 2.15 (s, 3H), 2.82 (dq, *J* = 15.1, 5.6 Hz, 2H), 4.56 (t, *J* = 5.0 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.95 (d, *J* = 7.2 Hz, 2H). $^{13}C$ RMN ($CDCl_3$, 125 MHz) δ: 19.3 ($CH_2$), 20.8 ($CH_3$), 27.4 ($CH_2$), 28.2 ($CH_3$), 28.68 ($CH_3$), 28.73 ($CH_3$), 32.9 ($CH_2$), 34.8 (C), 39.9 ($CH_2$), 65.3 (CH), 128.7 (CH), 128.8

(CH), 130.2 (C), 133.5 (CH), 135.4 (C), 136.9 (C), 197.3 (C), 203.6 (C). IR (film): 1719, 1675, 1596, 1448, 1359, 1203, 703 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{20}H_{26}O_2Na$ ($M+Na^+$) 321.1830, found: 321.1832.

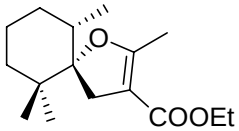
**Methyl (*E*)-3,4-dihydro-2´,2´,6´-trimethyl-spiro[furan-2,1´-cyclohexane]-2-yliden acetate (21).**




**21**

(10% ether/hexanes) (65 %) colourless oil. $^1H$ NMR ($CDCl_3$, 500 MHz) δ: 0.77 (d, *J* = 5.5 Hz, 3H), 0.78 (s, 3H), 0.93 (s, 3H), 1.17 - 1.71 (m, 5H), 1.74 - 1.85 (m, 2H), 2.07 (m, 1H), 2.50 (m, 1H), 3.01 (m, 1H), 3.18 (m, 1H), 3.63 (s, 3H), 5.24 (t, *J* = 1.6 Hz, 1H). $^{13}C$ RMN ($CDCl_3$, 125 MHz) δ: 15.7 ($CH_3$), 21.3 ($CH_2$), 23.0 ($CH_3$), 24.7 ($CH_3$), 27.0 ($CH_2$), 30.8 ($CH_2$), 32.1 ($CH_2$), 32.7 (C), 36.4 ($CH_2$), 36.7 (CH), 50.4 ($CH_3$), 86.6 (CH), 96.8 (C), 169.6 (C), 178.9 (C). IR (film): 1750, 1706, 1633, 1436, 1362, 1127, 1106, 1043, 958, 817 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{15}H_{24}O_3Na$ ($M+Na^+$) 275.1623, found: 275.1615.

**4-Methoxycarbonyl-2´,2´,5,6´-tetramethyl-spiro[furan-2(3H),1´-cyclohexane] (22).**

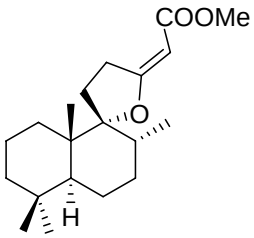



**22**

(10% ether/hexanes) (81%) colourless oil. $^1H$ NMR ($CDCl_3$, 500 MHz) δ: 0.79 (d, *J* = 6.6 Hz, 1H), 0.82 (s, 3H), 0.93 (s, 3H), 1.14 - 1.23 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H),

1.32 - 1.44 (m, 3H), 1.45 - 1.56 (m, 2H), 1.56 - 1.72 (m, 2H), 2.18 (s, 3H), 2.50 (d, *J* = 14.9 Hz, 1H), 2.80 (d, *J* = 14.9 Hz, 1H), 4.10 - 4.21 (m, 2H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 13.8 ($CH_3$), 14.5 ($CH_3$), 15.4 ($CH_3$), 21.3 ($CH_2$), 21.9 ($CH_3$), 24.6 ($CH_3$), 30.4 ($CH_2$), 34.6 ($CH_2$), 36.0 ($CH_2$), 36.7 (CH), 37.8 (C), 59.3 ($CH_2$), 94.0 (C), 101.9 (C), 166.4 (C), 168.3 (C). IR (film): 1701, 1648, 1384, 1241, 1247, 1074, 770 cm$^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{16}H_{26}O_3Na$ ($M+Na^+$) 289.1780, found: 289.1772.

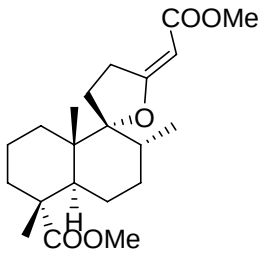
**3-Deacetoxynegundoin A (23).**




**23**

(10% ether/hexanes) (90 %) colourless syrup. $[\alpha]_D^{25}$= + 16.0 (c = 1.0, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.76 (d, *J* = 6.5 Hz, 3H), 0.81 (s, 3H), 0.88 (s, 3H), 0.91 (s, 3H), 1.08 - 1.18 (m, 2H), 1.27 - 1.67 (m, 9H), 1.72 - 1.83 (m, 2H), 2.09 (m, 1H), 2.96 - 3.17 (m, 2H), 3.64 (s, 3H), 5.27 (t, *J* = 1.7 Hz, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 15.7 ($CH_3$), 16.7 ($CH_3$), 18.3 ($CH_2$), 21.4 ($CH_2$), 21.9 ($CH_3$), 26.5 ($CH_2$), 31.3 (2 $CH_2$), 31.8 ($CH_2$), 33.28 ($CH_3$), 33.30 (C), 36.7 (CH), 41.6 ($CH_2$), 42.4 (C), 46.8 (CH), 50.4 ($CH_3$), 86.7 (CH), 98.4 (C), 169.6 (C), 179.1 (C). IR (film): 1706, 1635, 1458, 1362, 1129, 1114, 1044, 964 cm$^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{20}H_{32}O_3Na$ ($M+Na^+$) 343.2249, found: 343.2254.

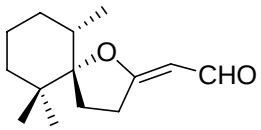
**3-Deacetoxy-17-methoxycarbonylnegundoin A (24).**




**24**

(15% ether/hexanes) (87%) colourless syrup. $[\alpha]_D^{25}$= + 56.4 (c = 10.5, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.76 (d, *J* = 6.6 Hz, 3H), 0.94 (s, 3H), 1.15 (s, 3H), 1.08 - 1.30 (m, 3H), 1.31 - 1.62 (m, 7H), 1.65 - 1.84 (m, 3H), 2.09 (m, 1H), 2.96 - 3.18 (m, 2H), 3.65 (s, 3H), 3.66 (s, 3H), 5.35 (t, *J* = 1.7 Hz, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 15.6 ($CH_3$), 16.7 ($CH_3$), 17.0 ($CH_3$), 17.6 ($CH_2$), 23.9 ($CH_2$), 26.5 ($CH_2$), 30.4 ($CH_2$), 30.8 ($CH_2$), 31.6 ($CH_2$), 33.1 (C), 36.4 ($CH_2$), 36.7 (CH), 42.0 (CH), 47.5 (C), 50.5 ($CH_3$), 51.9 ($CH_3$), 87.1 (CH), 97.9 (C), 169.6 (C), 178.7 (C), 179.0 (C). IR (film): 1725, 1706, 1633, 1434, 1363, 1249, 1125, 957, 772 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{21}H_{32}O_5Na$ ($M+Na^+$) 387.2147, found: 387.2143.

**(*E*)-3,4-Dihydro-2',2',6'-trimethylspiro[furan-2,1'-cyclohexan]-2-yliden acetaldehyde (25a).**

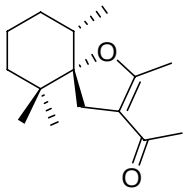



**25a**

A 4:1 mixture of *E* and *Z* isomers was obtained. (15% ether/hexanes) (80%) colourless oil. After successives column chromatographies, the major *E* isomer **25a** was isolated. $^1$H NMR ($CD_3COCD_3$, 500 MHz) δ: 0.83 (s, 3H), 0.84 (d, *J* = 5.9 Hz, 3H), 1.02 (s, 3H),

1.27-1.43 (m, 2H), 1.46-1.55 (m, 2H), 1.57-1.71 (m, 2H), 1.99 (m, 1H), 2.27 (m, 1H), 3.17 (m, 1H), 3.29 (m, 1H), 5.40 (d, $J$ = 7.9 Hz, 1H), 9.56 (d, $J$ = 7.9 Hz, 1H). $^{13}$C RMN ($CD_3COCD_3$, 125 MHz) δ: 17.8 ($CH_3$), 23.7 ($CH_2$), 25.0 ($CH_3$), 26.7 ($CH_3$), 29.1 ($CH_2$), 31.8 ($CH_3$), 32.1 ($CH_2$), 33.4 ($CH_2$), 39.05 ($CH_2$), 39.11 ($CH_3$), 40.8 (C), 100.5 (C), 102.6 (CH), 184.9 (C), 191.7 (CH). IR (film): 1659, 1625, 1462, 1353, 1208, 1153, 878 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{14}H_{22}O_2Na$ ($M+Na^+$) 245.1517, found: 245.1516.

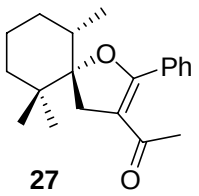
**2',2',5,6'-Tetramethylspiro[furan-2(3H)-1'-cyclohexan]4-methylketone (26).**



**26**

(10% ether/hexanes) (90%) colourless oil. $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.78 (d, $J$ = 6.6 Hz, 3H), 0.80 (s, 3H), 0.94 (s, 3H), 1.2 (m, 1H), 1.40 (m, 2H), 1.50 (m, 2H), 1.67 (m, 2H), 2.19 (s, 3H), 2.21 (s, 3H), 2.56 (dd, $J$ = 14.7, 1.2 Hz, 1H), 2.86 (dd, $J$ = 14.7, 1.3 Hz, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 14.7 ($CH_3$), 15.4 ($CH_3$), 21.2 ($CH_2$), 21.9 ($CH_3$), 24.6 ($CH_3$), 29.3 ($CH_3$), 30.4 ($CH_2$), 35.4 ($CH_2$), 36.0 ($CH_2$), 36.8 (CH), 37.8 (C), 94.3 (C), 112.8 (C), 168.2 (C), 194.2 (C). IR (film): 1672, 1601, 1381, 1269, 1242, 932 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{15}H_{24}O_2Na$ ($M+Na^+$) 259.1674, found: 259.1680.

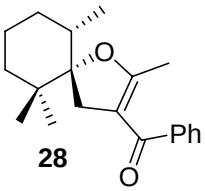
**2',2',6'-Trimethyl- 5-phenylspiro[furan-2(3H)-1'-cyclohexan]4-methylketone (27).**




**27**

(10% ether/hexanes) colourless oil. $^{1}$H NMR ($CDCl_3$, 500 MHz) δ: 0.87 (s, 3H), 0.88 (d, *J* = 6.1 Hz, 3H), 0.96 (s, 3H), 1.24 (d, *J* = 11.5 Hz, 1H), 1.33-1.78 (m, 6H), 1.76 (s, 3H), 2.70 (d, *J* = 15.0 Hz, 1H), 3.04 (d, *J* = 15.1 Hz, 1H), 7.35-7.47 (m, 3H), 7.50 (d, *J* = 6.9 Hz, 2H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 15.2 ($CH_3$), 15.6 ($CH_3$), 21.3 ($CH_2$), 21.9 ($CH_3$), 24.7 ($CH_3$), 30.4 ($CH_2$), 35.8 ($CH_2$), 36.0 ($CH_2$), 36.7 (CH), 37.8 (C), 94.5 (C), 113.3 (C), 127.6 (CH), 127.6 (CH), 128.2 (CH), 128.2 (CH), 130.6 (CH), 141.5 (C), 169.4 (C), 193.1 (C). IR (film): 1612, 1575, 1386, 1365, 1271, 1241, 902, 702 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{20}H_{26}O_2Na$ ($M+Na^+$) 321.1830, found: 321.1821.

**2',2',5,6'-Tetramethylspiro[furan-2(3H)-1'-cyclohexan]4-phenylketone (28).**

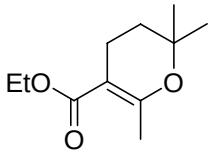



**28**

(15% ether/hexanes) colourless oil. $^{1}$H NMR ($CDCl_3$, 500 MHz) δ: 0.94 (d, *J* = 4.8 Hz, 3H), 0.95 (s, 3H), 0.99 (s, 3H), 1.17-1.55 (m, 5H), 1.65 (m, 1H), 1.78 (m, 1H), 1.88 (s, 3H), 2.77 (d, *J* = 15.7 Hz, 1H), 3.07 (d, *J* = 15.5 Hz, 1H), 7.48 (m, 5H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 15.5 ($CH_3$), 21.3 ($CH_2$), 21.9 ($CH_3$), 24.6 ($CH_3$), 28.7 ($CH_3$), 30.4 ($CH_2$), 35.95 ($CH_2$), 36.02 ($CH_2$), 37.0 (CH), 38.1 (C), 94.5 (C), 115.8 (C), 128.3 (CH),

128.3 (CH), 128.9 (CH), 128.9 (CH), 130.2 (CH), 131.8 (C), 167.2 (C), 194.4 (C).IR (film): 1629, 1592, 1379, 1246, 1077, 900, 696 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{20}H_{26}O_2Na$ ($M+Na^+$) 321.1830, found: 321.1839.

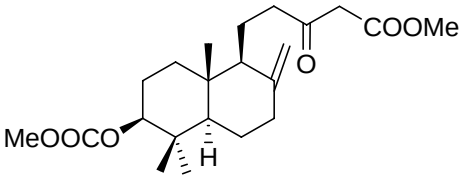
**Ethyl 2,6,6-trimethyl-5,6-dihydro-4H-pyran-3-carboxylate (29).**




**29**

(15% ether/hexanes) (85%) colourless oil. $^1H$ NMR ($CDCl_3$, 500 MHz) δ: 1.24 (s, 6H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.61 (t, *J* = 6.6 Hz, 2H), 2.21 (s, 3H), 2.30 (t, *J* = 6.7 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H).$^{13}C$ RMN ($CDCl_3$, 125 MHz) δ: 14.4 ($CH_3$), 19.4 ($CH_2$), 20.8 ($CH_3$), 26.52 ($CH_3$), 26.52 ($CH_3$), 32.3 ($CH_2$), 59.4 ($CH_2$), 75.4 (C), 99.4 (C), 163.6 (C), 168.8 (C). IR (film): 1705, 1617, 1371, 1279, 1160, 1115, 1073, 1021 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{11}H_{18}O_3Na$ ($M+Na^+$) 221.1154, found: 221.1154.

**Methyl 5-((1S,4aR,6S,8aR)-6-(methoxycarbonyloxy)-5,5,8a-trimethyl-2-methylene-decahydronaphthalen-1-yl)-3-oxopentanoate (33).**

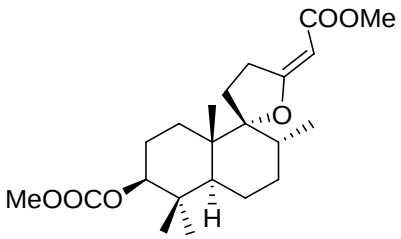



**33**

HNa (60%, 112 mg, 2.8 mmol) and dimethyl carbonate (1.01 mg, 11.2 mmol) were added to a stirred solution of **32** (160 mg, 0.56 mmol) in benzene (15 mL) and the mixture was kept stirring at reflux under argon atmosphere overnight, at which time

TLC showed no remaining starting material. Then, water (1 mL) was slowly added at 0 °C and ether –water (50 : 20 mL) was added, and the phases were shaken and separated. The organic phase was washed with water and brine, and dried over anhydrous $Na_2SO_4$. Removal of the solvent under vacuum afforded a crude product which was directly purified by flash chromatography on silica gel (15% ether/hexanes) to give pure **33** (188 mg, 83%) as a colourless syrup. $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.71 (s, 3H), 0.85 (s, 3H), 0.93 (s, 3H), 1.13 - 1.46 (m, 3H), 1.51 - 175 (m, 3H), 1.80 - 2.02 (m, 4H), 2.36 - 2.48 (m, 2H), 2.64 - 2.80 (m, 2H), 3.41 (s, 2H), 3.73 (s, 3H), 3.77 (s, 3H), 4.36 (dd, *J* = 12.0, 4.2 Hz, 1H), 4.45 (brs, 1H), 4.85 (brs, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 14.3 ($CH_3$), 16.4 ($CH_3$), 17.4 ($CH_2$), 23.7 ($CH_2$), 24.2 ($CH_2$), 28.1 ($CH_3$), 36.5 ($CH_2$), 37.9 ($CH_2$), 38.2 (C), 39.3 (C), 42.0 ($CH_2$), 49.1 ($CH_2$), 52.3 ($CH_3$), 54.5 ($CH_3$), 54.6 (CH), 55.5 (CH), 85.1 (CH), 107.0 ($CH_2$), 147.2 (C), 155.7 (C), 167.6 (C), 202.8 (C). IR (film): 1745, 1718, 1442, 1271, 974, 793 cm$^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{22}H_{34}O_6Na$ ($M+Na^+$) 417.2253, found: 417.2249.

**3-De-*O*-acetyl-3-*O*-methoxycarbonyl-negundoin A (34).**

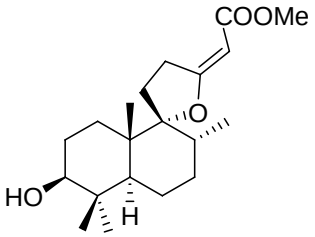



**34**

(15% ether/hexanes) (90%) colourless syrup. $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.77 (d, *J* = 6.6 Hz, 3H), 0.87 (s, 3H), 0.95 (s, 3H), 0.96 (s, 3H), 1.30 - 1.46 (m, 4H), 1.51 - 1.74 (m, 5H), 1.75 - 1.85 (m, 2H), 2.08 (ddd, *J* = 13.5, 11.8, 7.6 Hz, 1H), 3.02 (m, 1H), 3.13 (m, 1H), 3.65 (s, 3H), 3.77 (s, 3H), 4.31 (dd, *J* = 11.9, 4.5 Hz, 1H), 5.30 (t, *J* = 1.8 Hz, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 15.5 ($CH_3$), 16.4 ($CH_3$), 16.8 ($CH_3$), 20.8 ($CH_2$),

23.2 ($CH_2$), 26.7 ($CH_2$), 27.9 ($CH_3$), 29.3 ($CH_2$), 31.0 ($CH_2$), 31.5 ($CH_2$), 36.5 (CH), 37.9 (C), 41.9 (C), 46.2 (CH), 50.5 ($CH_3$), 54.6 ($CH_3$), 84.6 (CH), 87.3 (CH), 97.7 (C), 155.7 (C), 169.5 (C), 178.4 (C). IR (film): 1746, 1706, 1633, 1441, 1273, 1128, 1108, 968, 956, $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{22}H_{34}O_6Na$ ($M+Na^+$) 417.2253, found: 417.2253.

**3-De-*O*-acetyl negundoin A (35).**




**35**

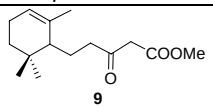
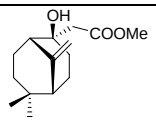
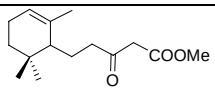
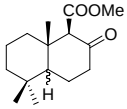
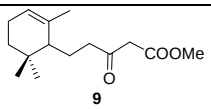
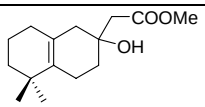
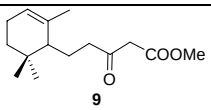
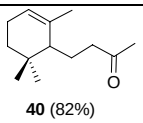
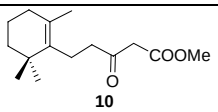
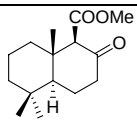
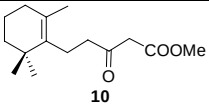
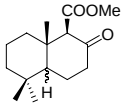
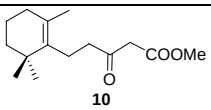
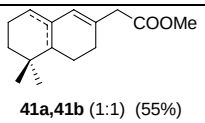
2N KOH in MeOH (1 mL) was added to a solution of **34** (132 mg, 0.34 mmol) in MeOH (10 mL) and the mixture was stirred at room temperature for 18 h, at which time TLC showed no remaining starting material. Then, the solvent was removed in vacuum and ether – water (50 : 15 mL) was added, and the phases were shaken and separated. The organic phase was washed with water and brine, dried over $Na_2SO_4$ and concentrated to afford a crude product which was directly purified by flash chromatography on silica gel (25% ether/hexanes) to give **35** (100 mg, 90 %) as a colourless syrup. $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.77 (d, *J* = 6.6 Hz, 3H), 0.79 (s, 3H), 0.93 (s, 3H), 1.01 (s, 3H), 1.25 - 1.50 (m, 4H), 1.52 - 1.69 (m, 4H), 1.79 (ddd, *J* = 13.5, 11.3, 4.6 Hz, 1H), 2.09 (ddd, *J* = 13.4, 11.7, 7.5 Hz, 1H), 3.00 (ddd, *J* = 11.4, 7.5, 2.0 Hz, 1H) 3.03 (ddd, *J* = 11.5, 7.6, 2.0 Hz, 1H), 3.11 (ddd, *J* = 11.7, 4.6, 1.7 Hz, 1H), 3.14 (ddd, *J* = 11.8, 4.6, 1.7 Hz, 1H), 3.21 (dd, *J* = 11.6, 4.5 Hz, 1H), 3.65 (s, 3H), 5.28 (t, *J* = 1.8 Hz, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 15.4 ($CH_3$), 15.5 ($CH_3$), 16.8 ($CH_3$), 21.1 ($CH_2$), 26.6 ($CH_2$), 26.8 ($CH_2$), 28.0 ($CH_3$), 29.5 ($CH_2$), 31.1 ($CH_2$), 31.6 ($CH_2$),

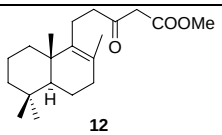
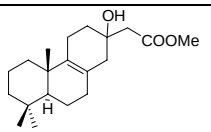
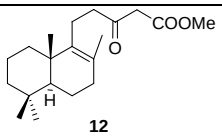
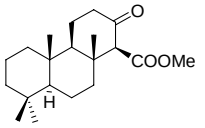
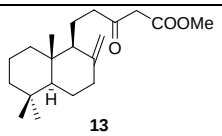
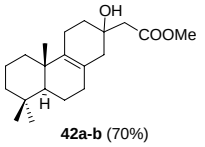
36.5 (CH), 38.8 (C), 42.1 (C), 46.0 (CH), 50.5 ($CH_3$), 78.3 (CH), 87.0 (CH), 98.0 (C), 169.5 (C), 178.8 (C). IR (film): 1667, 1630, 1364, 1126, 1045, 961, 815, 756 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{20}H_{32}O_4Na$ ($M+Na^+$) 359.2198, found: 359.2205.

**Treatment of β-ketoesters 9, 10, 12 and 13 with different cyclizing reagents.**

The behaviour of some unsaturated β-ketoesters under different conditions has been studied. In the Table are shown the results obtained in our laboratory and other related previously described.

**Table.** Treatment of some β-ketoesters with different cyclizing reagents.

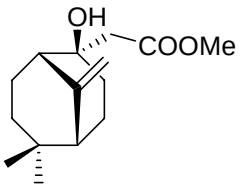
| Entry | β-Ketoester | Reaction conditions | Product |
|---|---|---|---|
| 1 |  **9** | $BF_3$, $CH_2Cl_2$, -30 ºC, 2.5 h |  **36** (42%) |
| 2 |  **9** | $SnCl_4$, $CH_2Cl_2$, rt, 45 min |  **37** (α-H) **38** (β-H) (1:1) (54%)[2] |
| 3 |  **9** | TsOH, benzene, 60 ºC, 12 h |  **39** (40 %) |
| 4 |  **9** | $Pd(OAc)_2$, DMF, 100 ºC, 2 h |  **40** (82%) |
| 5 |  **10** | $SnCl_4$, $CH_2Cl_2$, 30 ºC, 2 h |  **37** (71%)[4] |
| 6 |  **10** | $I_2$, $CH_2Cl_2$, rt, 7 h |  **37** (α-H) **38** (β-H) (3:2) (71%) |
| 7 |  **10** | Amberlyst A-15, $CH_2Cl_2$, reflux, 27 h |  **41a,41b** (1:1) (55%) |

| | | | |
|---|---|---|---|
| 8 |  **12** | Amberlyst A-15, $CH_2Cl_2$, rt, 8 h |  **42a-b** (20%) |
| 9 |  **12** | $SnCl_4$, $CH_2Cl_2$, rt, 20 h |  **43** (66%)[5] |
| 10 |  **13** | $Bi(TfO)_3$,$CH_2Cl_2$, rt, 30 min |  **42a-b** (70%) |

After treatment with boron trifluoride etherate in dichloromethane at -30 ºC for 2.5 h β-ketoester **9** gave the bicyclic hydroxy ester **36**, with approximately 50% of unaltered starting material being recovered. A complex mixture resulted when the reaction time was prolonged or the temperature increased. The treatment of compound **9** with $SnCl_4$ in dichloromethane at room temperature for 45 min afforded a 1:1 mixture of *trans*- and *cis*-fused bicyclic ketoesters, **37** and **38,** respectively.[2] When compound **9** was treated with *p*-toluenesulfonic acid in benzene at room temperature, no reaction was observed after 12 h. Hydroxy ester **39** was obtained in moderate yield when the reaction was carried out at 60 ºC. Treating of ketoester **9** with $Pd(OAc)_2$ in dimethylformamide at 100 ºC led to methylketone **40** together with small amounts of the corresponding α,β-unsaturated ketone; however no reaction took place at room temperature, after 12 h.[3] On the other hand, β-ketoester **10** was transformed into the bicyclic ketoester **37** after treatment with $SnCl_4$ in dichloromethane at 30 ºC.[4] A mixture of diastereomeric ketoesters **37** and **38** resulted after the reaction of compound **10** with iodine in dichloromethane at room temperature. Bicyclic regioisomer esters **41a-b** were obtained when compound **10** was treated with cationic resin in dichloromethane under reflux. Utilizing the same reagent, ketoester **12** led to a complex mixture of compounds, including hydroxy

esters **42a-b**, after 8 h at room temperature. The bicyclic ketoester **12** showed a similar behaviour to that of compound **10**; thus, treatment with $SnCl_4$ led to the corresponding tricyclic β-ketoester **43**.[5] On the other hand, the treatment of ketoester **13** with $Bi(TfO)_3$ gave hydroxy ester **42a-b.**

**Methyl 2-((1S,2R,5R)-2-hydroxy-6,6-dimethyl-9-methylenebicyclo[3.3.1]nonan-2-yl)acetate (36).**

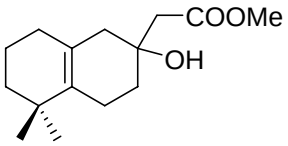



**36**

$BF_3.OEt_2$ (58 mg, 0.85 mmol) was added slowly to a solution of **9** (110 mg, 0.44 mmol) in dry $CH_2Cl_2$ (8 mL) at -30 ºC and the reaction mixture was stirred at this temperature under argon atmosphere for 2.5 h. Then the reaction was quenched with sat. aq. $NaHCO_3$ (1 mL) and the cooling bath was removed. The mixture was poured into ether-water (40: 10 mL) and the phases were shaken and separated. The organic phase was washed with water, brine and dried over $Na_2SO_4$. Removal of the solvent under vacuum afforded a crude product with was directly purified by flash chromatography on silica gel (10% ether/hexanes) to yield **36** (46 mg, 42%) as yellow syrup and recovered starting material (52 mg, 47%). $^1$H RMN ($CDCl_3$, 500 MHz) δ: 0.92 (s, 3H), 0.99 (s, 3H), 1.23 (dd, *J* = 13.3, 6.6 Hz, 1H), 1.64 - 1.98 (m, 9H), 2.33 (br s, 1H), 2.56 (dd, *J* = 32.1, 14.7 Hz, 2H), 3.71 (s, 3H), 4.80 (dd, *J* = 14.6, 2.3 Hz, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 25.3 ($CH_2$), 25.4 ($CH_2$), 28.91 ($CH_3$), 28.95 ($CH_3$), 33.96 ($CH_2$), 33.96 ($CH_2$), 35.3 (C), 43.9 ($CH_2$), 49.0 (CH), 49.2 (CH), 51.6 ($CH_3$), 74.4 (C), 108.4 ($CH_2$), 150.8

(C), 172.1 (C). IR (film): 3523, 1735, 1483, 1204, 1169, 980, 883 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{15}H_{24}O_3Na$ ($M+Na^+$) 275.1623, found: 275.1615.

**Methyl 2-(2-hydroxy-5,5-dimethyl-1,2,3,4,5,6,7,8-octahydronaphthalen-2-yl)acetate (39).**



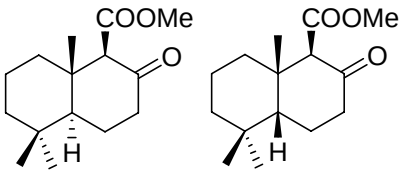

**39**

*p*-Toluenesulfonic acid monohydrate (124 mg, 0.65 mmol) was added to a solution of **9** (127 mg, 0.50 mmol) in benzene (10 mL) and the reaction mixture was stirred at 60ºC for 12 h, at which time TLC showed no **9**. The solvent was removed under vacuum and the crude product was directly purified by flash chromatography on silica gel (20% ether/hexanes) to afford pure **39** (50 mg, 40%) as a colourless syrup. $^1H$ RMN ($CDCl_3$, 500 MHz) δ: 0.97 (s, 3H), 0.99 (s, 3H), 1.38 - 1.50 (m, 2H), 1.55 - 1.64 (m, 3H), 1.69 - 1.90 (m, 3H), 1.97 (m, 1H), 2.02 (dd, *J* = 39.1, 16.4 Hz, 2H), 2.20 (m, 1H), 2.49 (d, *J* = 2.1 Hz, 2H), 3.71 (s, 3H). $^{13}C$ RMN ($CDCl_3$, 125 MHz) δ: 19.2 ($CH_2$), 21.9 ($CH_2$), 27.8 ($CH_3$), 27.9 ($CH_3$), 31.3 ($CH_2$), 33.5 (C), 34.2 ($CH_2$), 39.5 ($CH_2$), 43.4 ($CH_2$), 43.7 ($CH_2$), 51.6 ($CH_3$), 69.2 (C), 124.5 (C), 133.9 (C), 173.2 (C). IR (film): 3505, 1729, 1450, 1359, 1200, 1166, 1071, 1011 $cm^{-1}$. HRMS (FAB) *m/z*: calcd for $C_{15}H_{24}O_3Na$ ($M+Na^+$) 275.1623, found: 275.1622.

**Treatment of ketoester 9 with $Pd(OAc)_2$.**

To a solution of **9** (74 mg, 0.29 mmol). in DMF (7 mL), was added $Pd(OAc)_2$ (30 mg, 0.132 mmol) and the reaction mixture was stirred at 100 ºC for 2 h, at which time TLC showed no starting material. Then the mixture was diluted with ether – water (25 : 10 mL), the phases were shaken and separated. The organic phase was washed with water (4 x 10 mL), brine, dried over anhydrous $Na_2SO_4$ and evaporated to give a crude product which was chromatographed on sílica gel (7% ether/hexanes) to afford **40** (46 mg, 82%) as a colourless oil.

**(1*R*,4a*S*,8a*S*)-Methyl 5,5,8a-trimethyl-2-oxo-decahydronaphthalene-1-carboxylate (37) and (1*R*,4a*R*,8a*S*)-methyl 5,5,8a-trimethyl-2-oxo-decahydronaphthalene-1-carboxylate (38) as racemic mixture.**

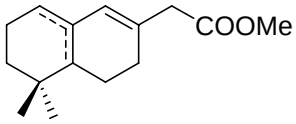



**37** **38**

To a solution of **10** (85 mg, 0.34 mmol) in dry $CH_2Cl_2$ (5 mL) was added iodine (104 mg, 0.41 mmol) and the mixture was stirred at room temperature for 7 h, at this time TLC showed no **10**. Then, aq. 5% $NaHSO_3$ (0.5 ml) was added and the mixture was stirred for an additional 5 min. The reaction mixture was diluted with ether – water (20 – 5 mL) and the phases were shaken and separated. The organic phase was washed with water, brine and dried over anhydrous $Na_2SO_4$. Removal of the solvent under vacuum afforded a crude product which was directly purified by flash chromatography on silica

gel (10% ether/hexanes) to give a mixture of **37** and **38** (ratio 3:2) (42 mg, 50%). Signals assignables to **37**: $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.90 (s, 3H), 0.97 (s, 3H), 1.16 (s, 3H), 1.68 (br d, *J* = 7.1 Hz, 1H), 1.75 (ddd, *J* = 26.1, 12.9, 5.3 Hz, 1H), 2.33 (m, 1H), 3.22 (s, 1H), 3.69 (s, 3H). Signals assignables to **38**: $^1$H NMR ($CDCl_3$, 500 MHz) δ: 1.04 (s, 3H), 1.16 (s, 3H), 1.19 (s, 3H), 2.15 (m, 1H), 3.70 (m, 3H), 3.86 (s, 1H). HRMS (FAB) *m/z*: calcd for $C_{15}H_{24}O_3Na$ ($M+Na^+$) 275.1623, found: 275.1634.

**Methyl 2-(5,5-dimethyl-3,4,4a,5,6,7-hexahydronaphthalen-2-yl)acetate (41a) and methyl 2-(5,5-dimethyl-3,4,5,6,7,8-hexahydronaphthalen-2-yl)acetate (41b).**

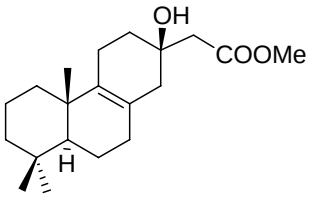



**41a, 41b**

To a solution of **10** (97 mg, 0.38 mmol) in dry $CH_2Cl_2$ (5 mL) was added Amberlyst A-15 (100 mg) and the mixture was stirred under reflux for 27 h, at which time TLC indicated no starting material remaining. Then, the reaction mixture was filtered and the filtrate was evaporated to yield a crude product which was chromatographed on silica gel (5% ether/hexanes) affording the mixture **41a** and **41b** (ratio 1:1) (49 mg, 55%). $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.76 (s, 3H), 0.99 (s, 9H), 1.40 (m, 2H), 1.48 (m, 2H), 1.55 (m, 1H), 1.64 (m, 2H), 1.84 - 1.94 (m, 4H), 1.97 - 2.28 (m, 4H), 2.53 (dd, *J* = 7.5 Hz, 2H), 2.70 (m, 2H), 2.99 (s, 2H), 3.04 (s, 2H), 3.677 (s, 3H), 3.682 (s, 3H), 5.45 (br s, 1H), 5.62 (br s, 1H), 5.91 (s, 1H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 19.1 ($CH_2$), 19.4 ($CH_3$), 23.1 ($CH_2$), 23.3 ($CH_2$), 26.3 ($CH_2$), 27.8 ($CH_3$), 27.8 ($CH_3$), 29.3 ($CH_3$), 29.9 ($CH_2$), 30.8 ($CH_2$), 31.1 (C), 33.2 (C), 35.5 ($CH_2$), 37.8 ($CH_2$), 39.7 ($CH_2$), 42.5 ($CH_2$),

42.9 ($CH_2$), 44.3 (CH), 51.73($CH_3$), 51.75 ($CH_3$), 123.5 (CH), 123.8 (CH), 124.7 (C), 127.7 (C), 129.2 (CH), 131.2 (C), 131.6 (C), 135.5 (C), 172.0 (C), 172.2 (C). HRMS (FAB) *m/z*: calcd for $C_{15}H_{21}O_2Na$ ($M+Na^+$) 256.1439, found: 256.1445.

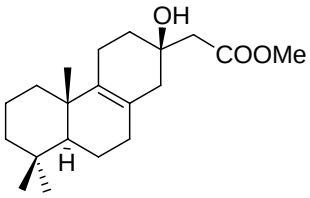
**Treatment of ketoester 12 with Amberlyst A-15.**




**42a**

To a solution of **12** (160 mg, 0.50 mmol) in dry $CH_2Cl_2$ (8 mL) was added Amberlyst A-15 (140 mg) and the mixture was stirred at room temperature for 8 h, at which time TLC indicated no starting material remaining. Then, the reaction mixture was filtered and the filtrate was evaporated to yield a crude product which was chromatographed on silica gel (30% ether/hexanes) to afford a mixture of distereomers **42a-b** (32 mg, 20%) as a colourless syrup. After successive column chromatographies, the major stereoisomer **42a** was isolated.

**Treatment of ketoester 13 with $Bi(TfO)_3$.**




**42a**

To a solution of **13** (114 mg, 0.356 mmol) in $CH_2Cl_2$ ( 8 mL**)** was added at 0ºC bismuth (III) trifluoromethanesulfonate (40 mg, 0.06 mmol) and the reaction mixture was stirred at room temperature for 30 min, at which time TLC showed no starting material. Then

the reaction was quenched by sat. $NaHCO_3$ (1 mL) and the mixture was diluted with ether – water ( 30 : 10 mL) and the phases were shaken and separated. The organic phase was washed with water, brine, dried over anhydrous $Na_2SO_4$ and evaporated to give a crude product which was chromatographed on sílica gel (30% ether/hexanes) to afford a mixture of distereomers **42a-b** (80 mg, 70%) as a colourless syrup. After successive column chromatographies, the major stereoisomer **42a** was isolated. $^1$H NMR ($CDCl_3$, 500 MHz) δ: 0.84 (s, 3H) 0.88 (s, 3H), 0.97 (s, 3H), 1.03 (ddd, *J* = 12.9, 12.9, 3.8 Hz, 1H), 1.09-1.19 (m, 2H), 1.37-1.50 (m, 3H), 1.53-1.77 (m, 5H), 1.80-2.00 (m, 4H), 2.05-2.16 (m, 2H), 2.48 (dd, *J* = 45.4, 15.8 Hz, 2H), 3.72 (s, 3H). $^{13}$C RMN ($CDCl_3$, 125 MHz) δ: 18.7 ($CH_2$), 19.0 ($CH_2$), 19.5 ($CH_3$), 21.6 ($CH_3$), 22.3 ($CH_2$), 32.3 ($CH_2$), 33.2 ($CH_3$), 33.3 (C), 34.6 ($CH_2$), 36.8 ($CH_2$), 37.5 (C), 41.6 ($CH_2$), 41.8 ($CH_2$), 43.6 ($CH_2$), 51.66 (CH), 51.73 ($CH_3$), 69.4 (C), 124.1 (C), 136.7 (C), 173.5 (C). IR (film): 3513, 1728, 1437, 1374, 1203, 1166, $cm^{-1}$.

## References

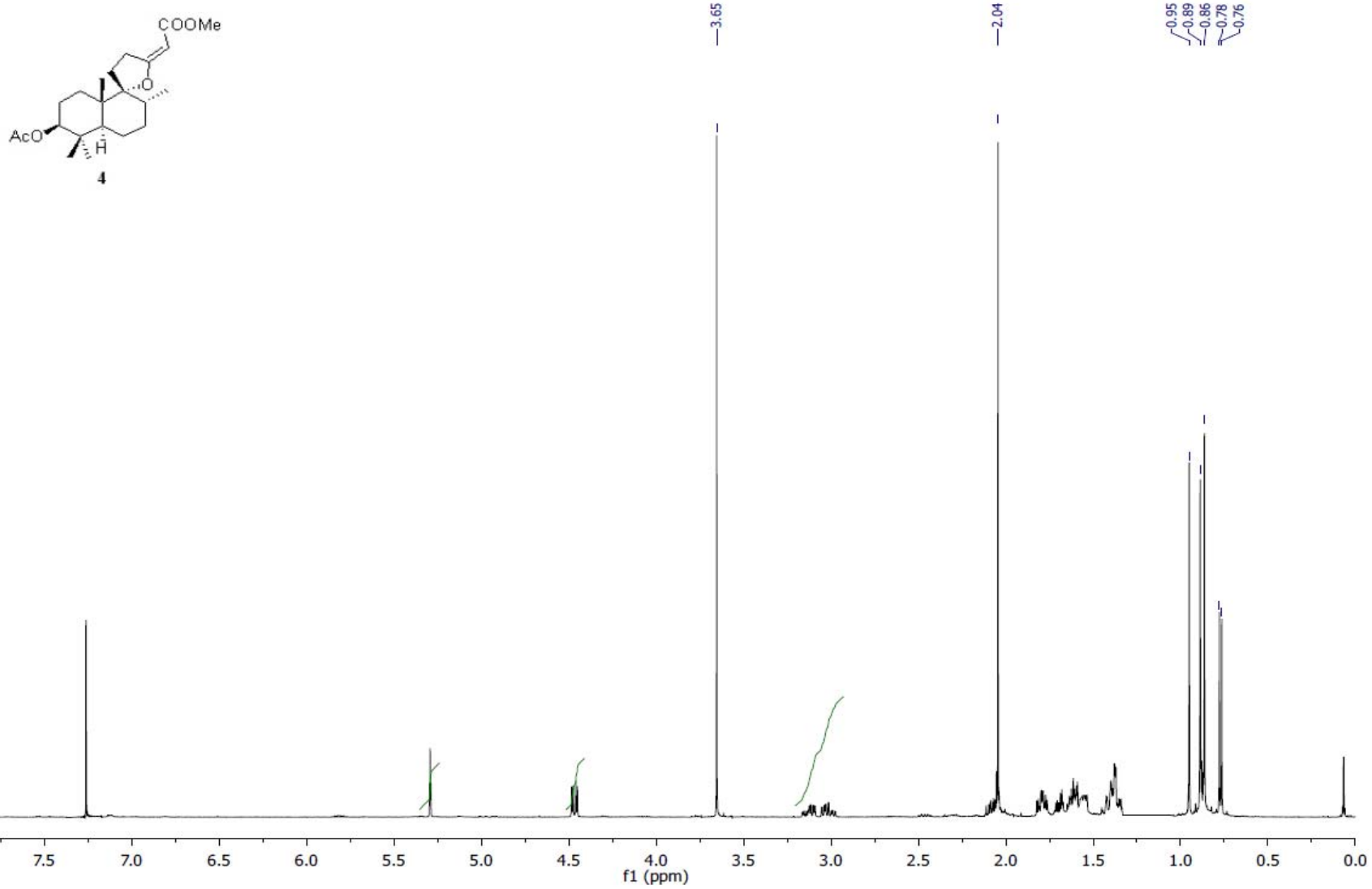
1.- C. – J. Zheng, B. – K. Huang, Y. Wang, Q. Ye, T. Han, T. And Q. – Y. Zhang, *Bioorg. Med. Chem.* 2010, **18**, 175.

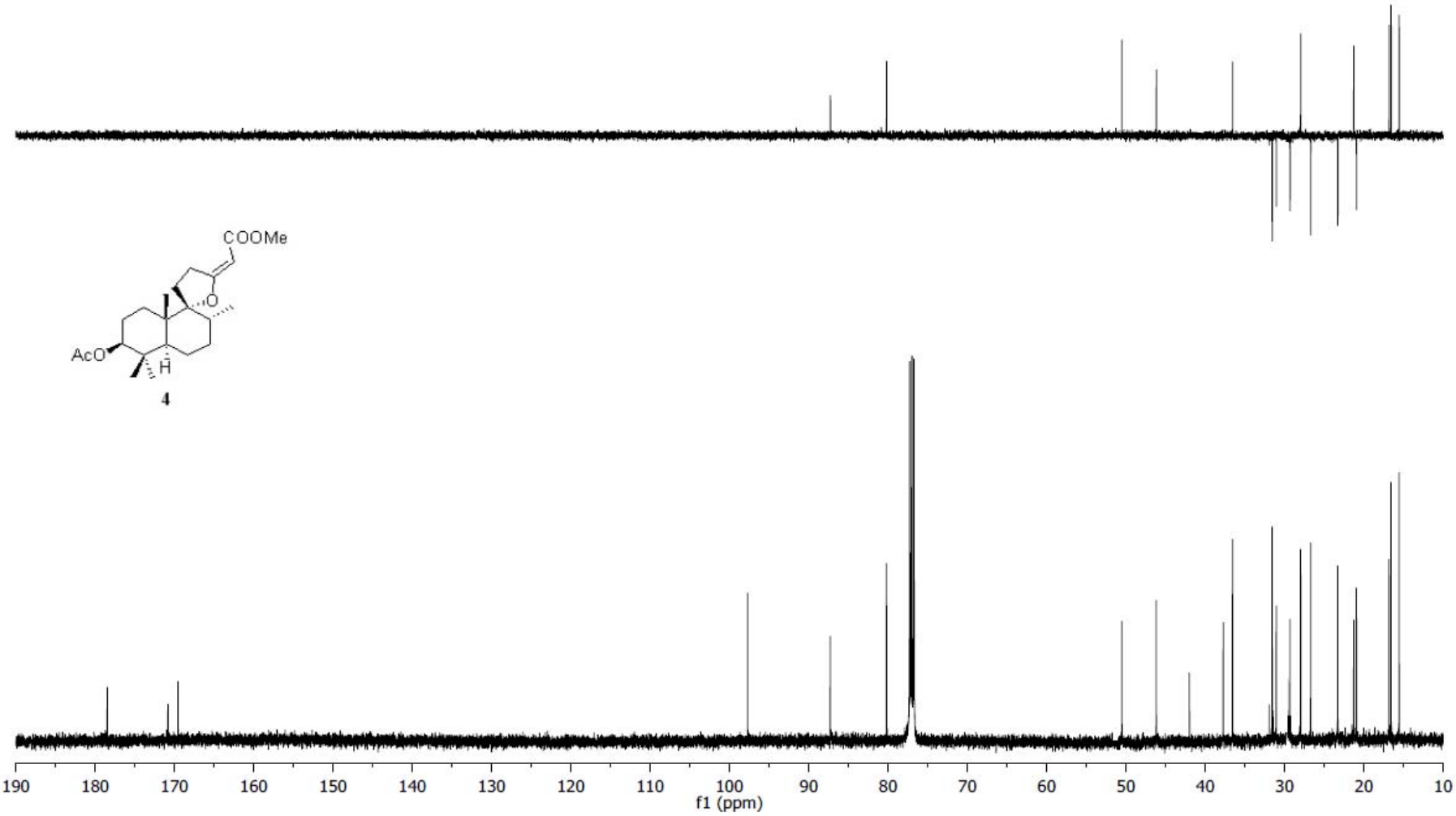
2.- (a) S. Escher, W. Giersch, Y. Niclass, G. Bernardinelli and G. Ohloff, *Helv. Chim. Acta* 1990, **73**, 1935. (b) K. Mori, S. Aki and M. Kido, *Liebigs Ann. Chem.* 1994, 319.

3.- For recent examples of β-ketoesters decarboxylation mediated by palladium see: S. C. Marinescu, T. Nishimata, J. T. Mohr and B. M. Stoltz, *Org. Lett.* 2008**, 10**, 1039.

4.- A. Abad, C. Agulló, A. C. Cuñat, A. González-Coloma and A. Pardo, *Eur. J. Org. Chem.* 2010, 2182.

5.- K. Mori and Y. Koga, *Liebig Ann. Chem.* 1991, 769.



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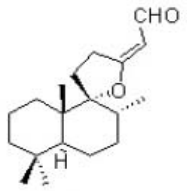


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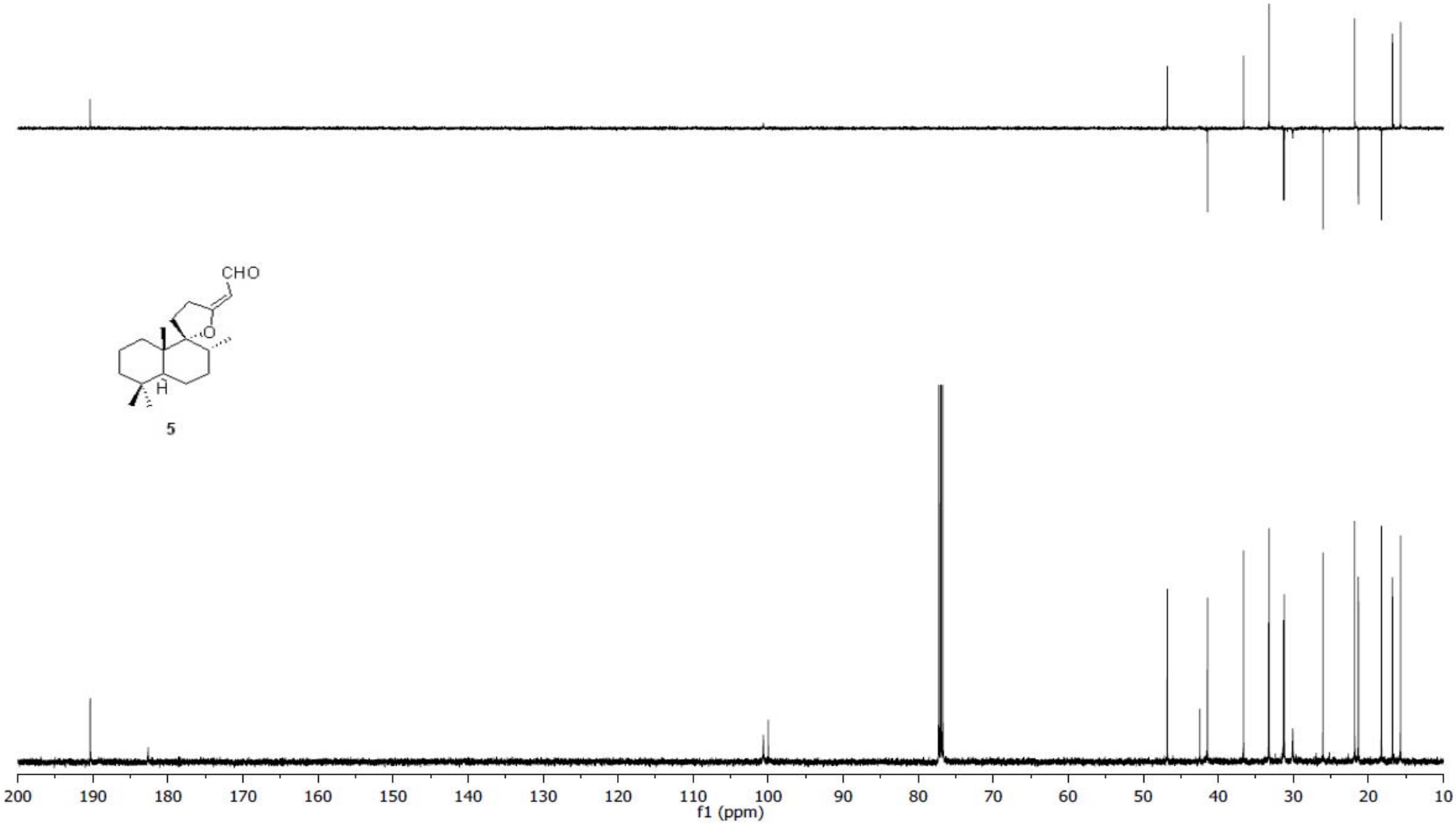


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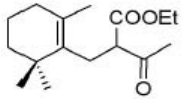
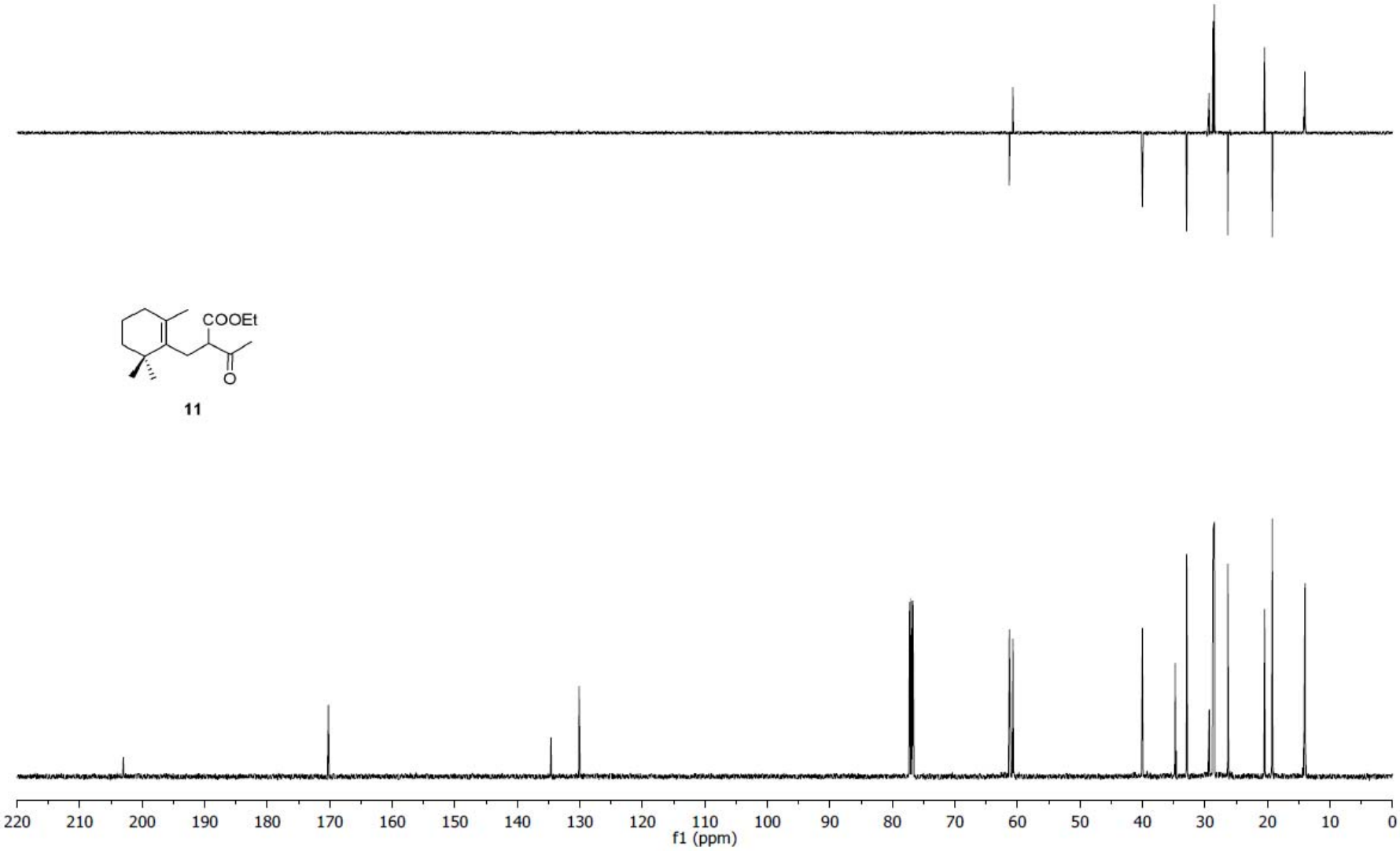
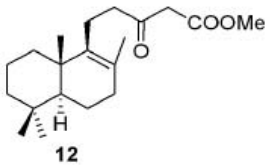



**11**




**11**

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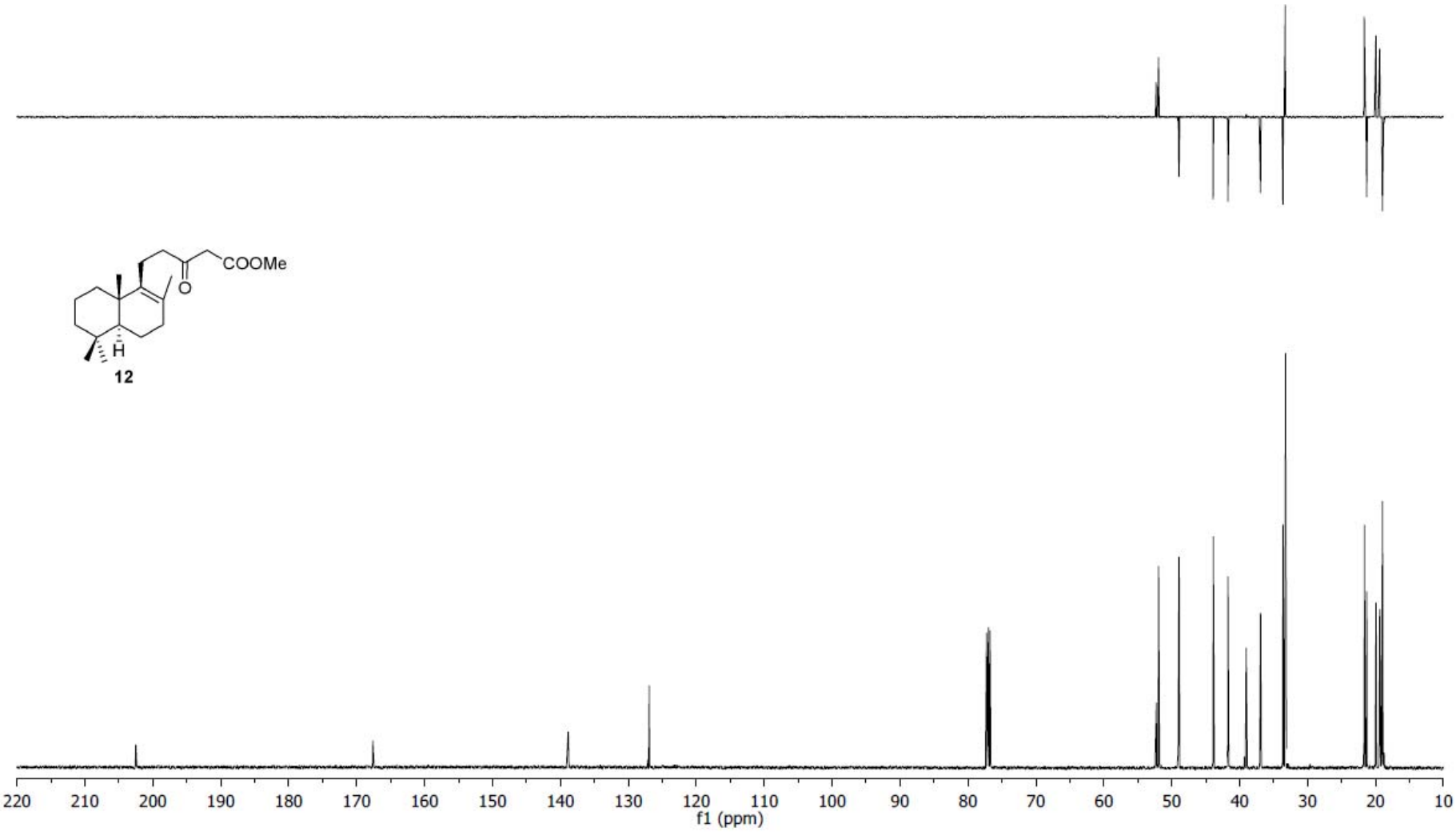

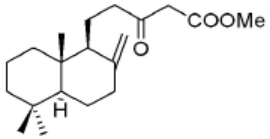


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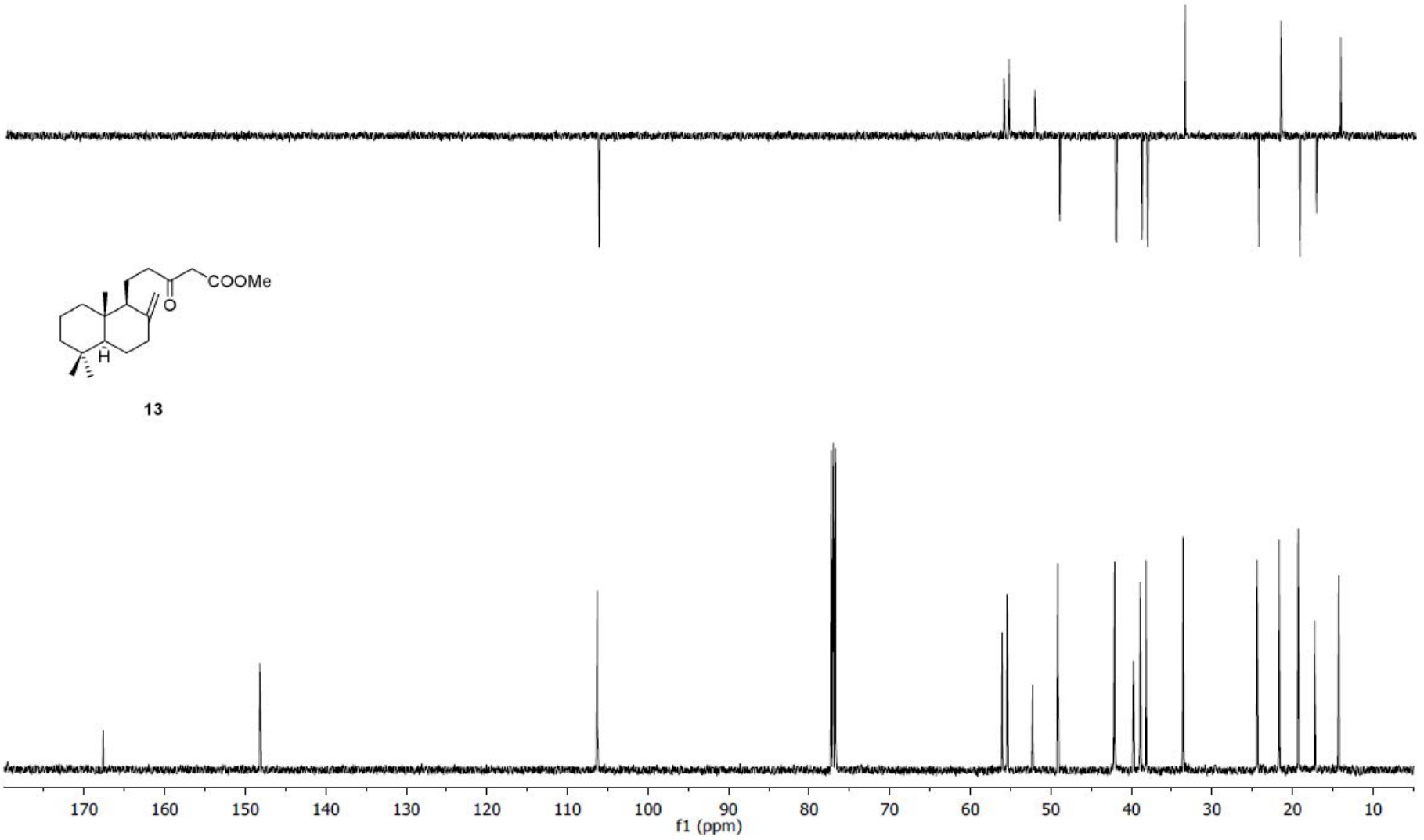


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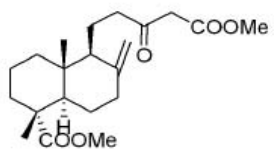


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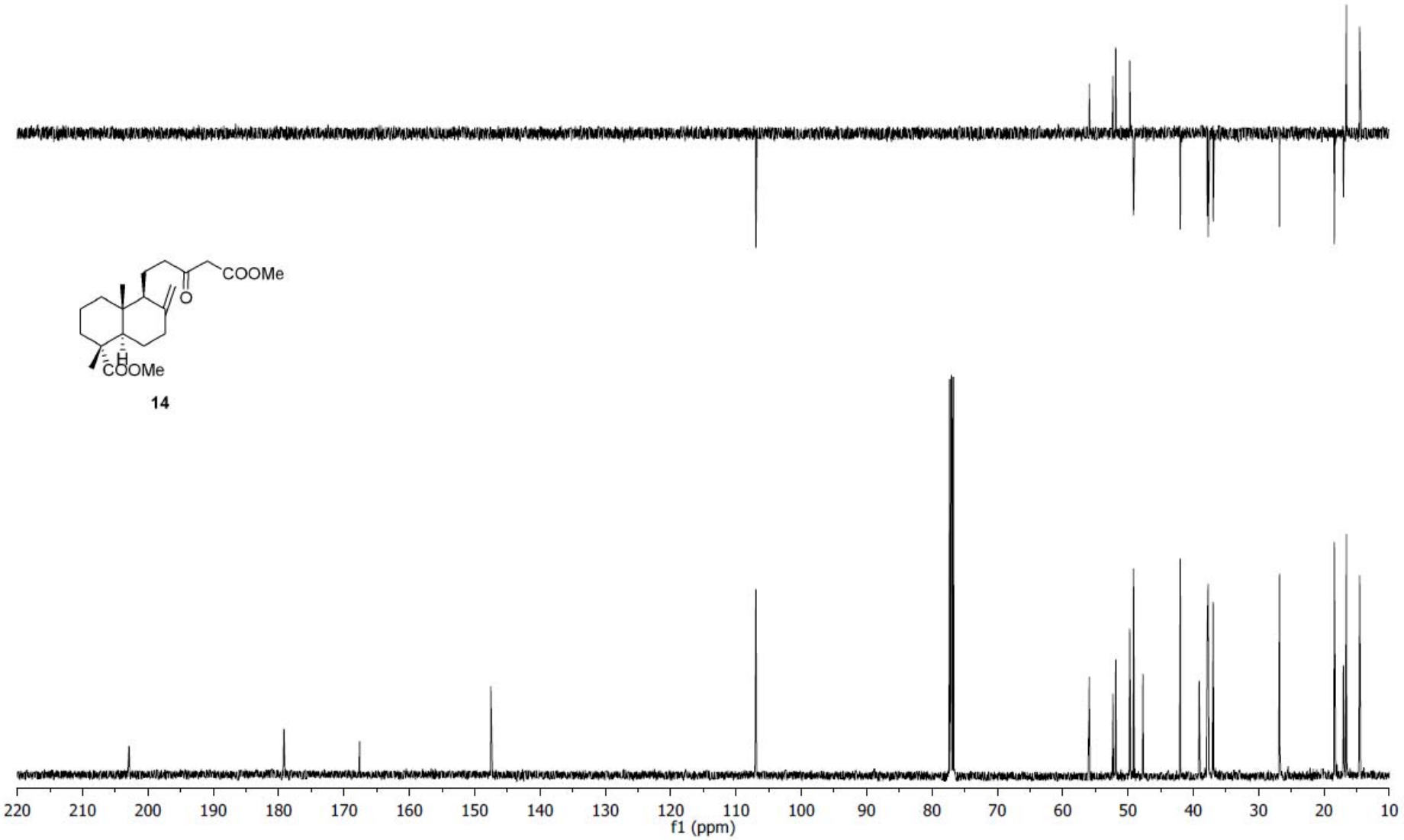


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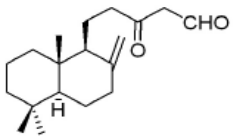


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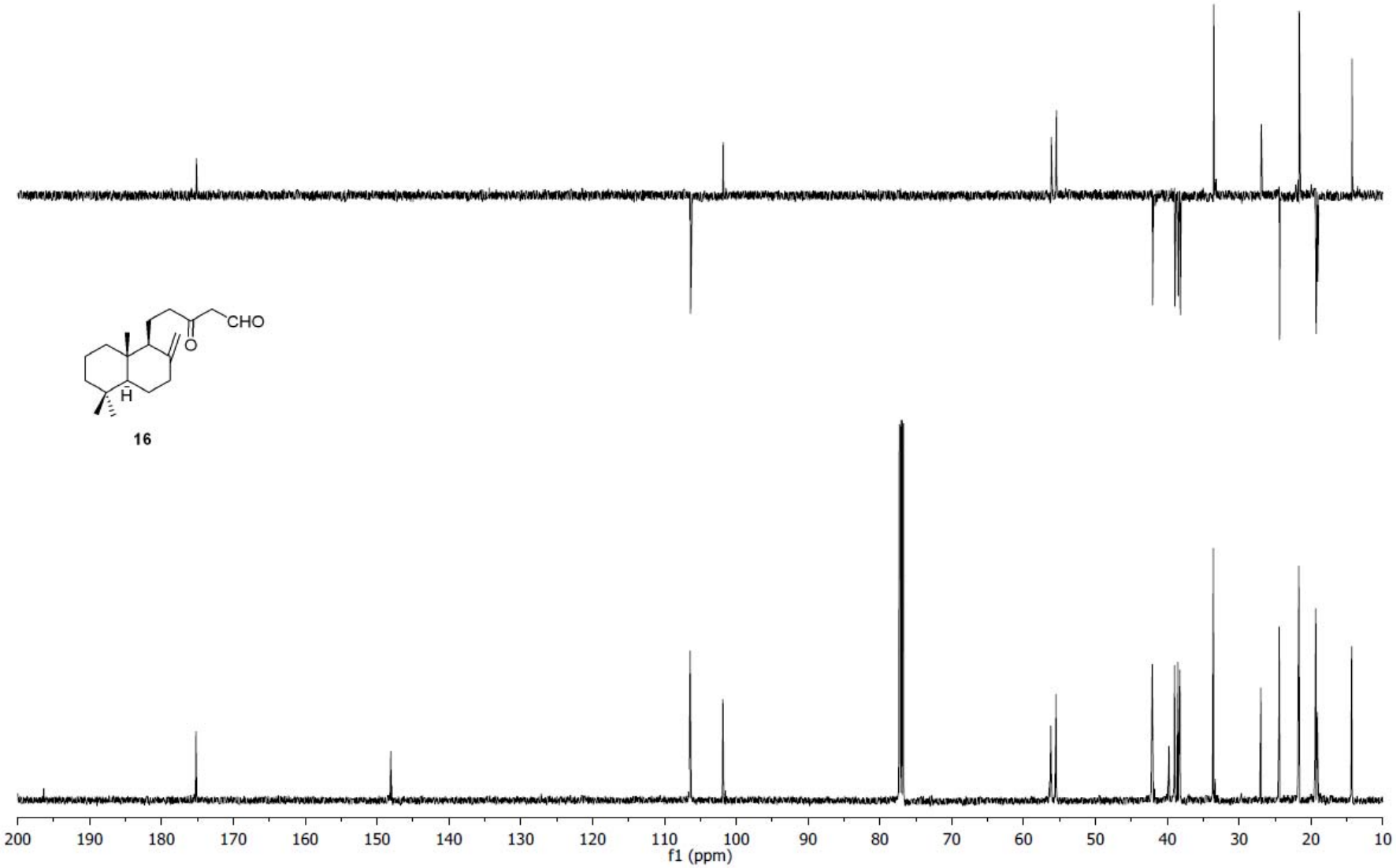


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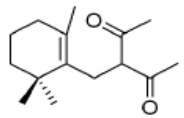

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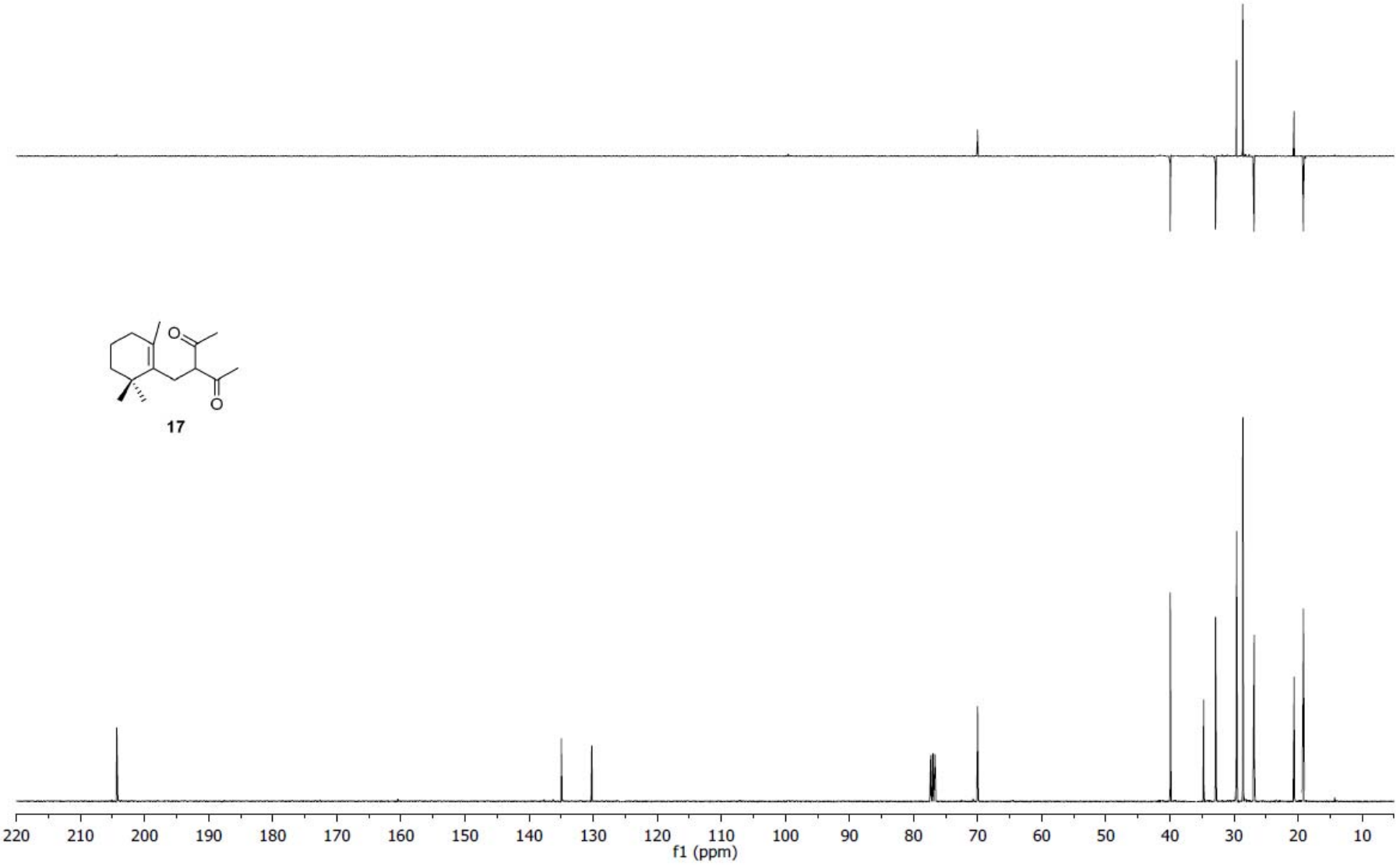


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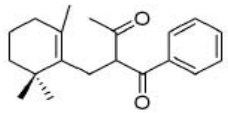

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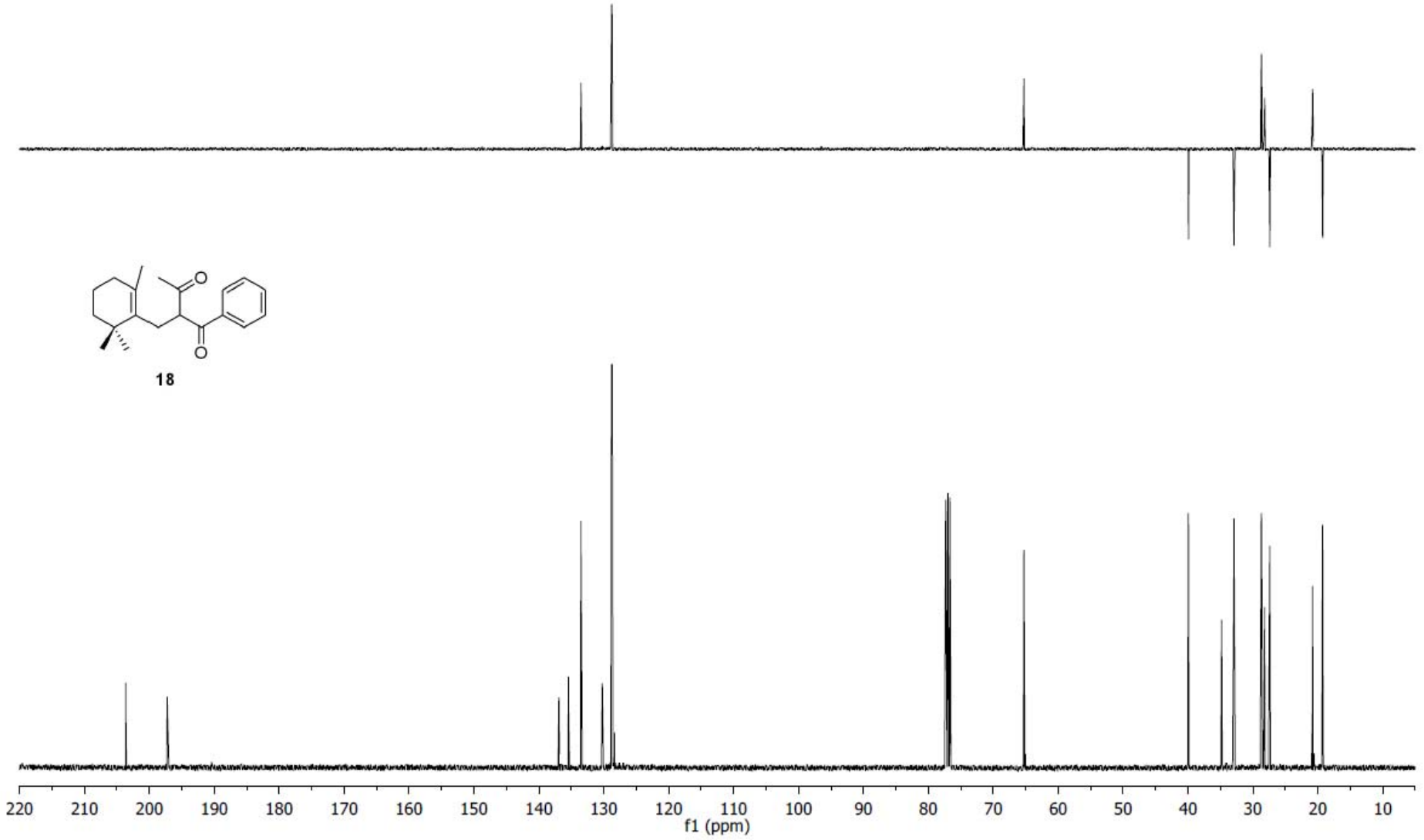

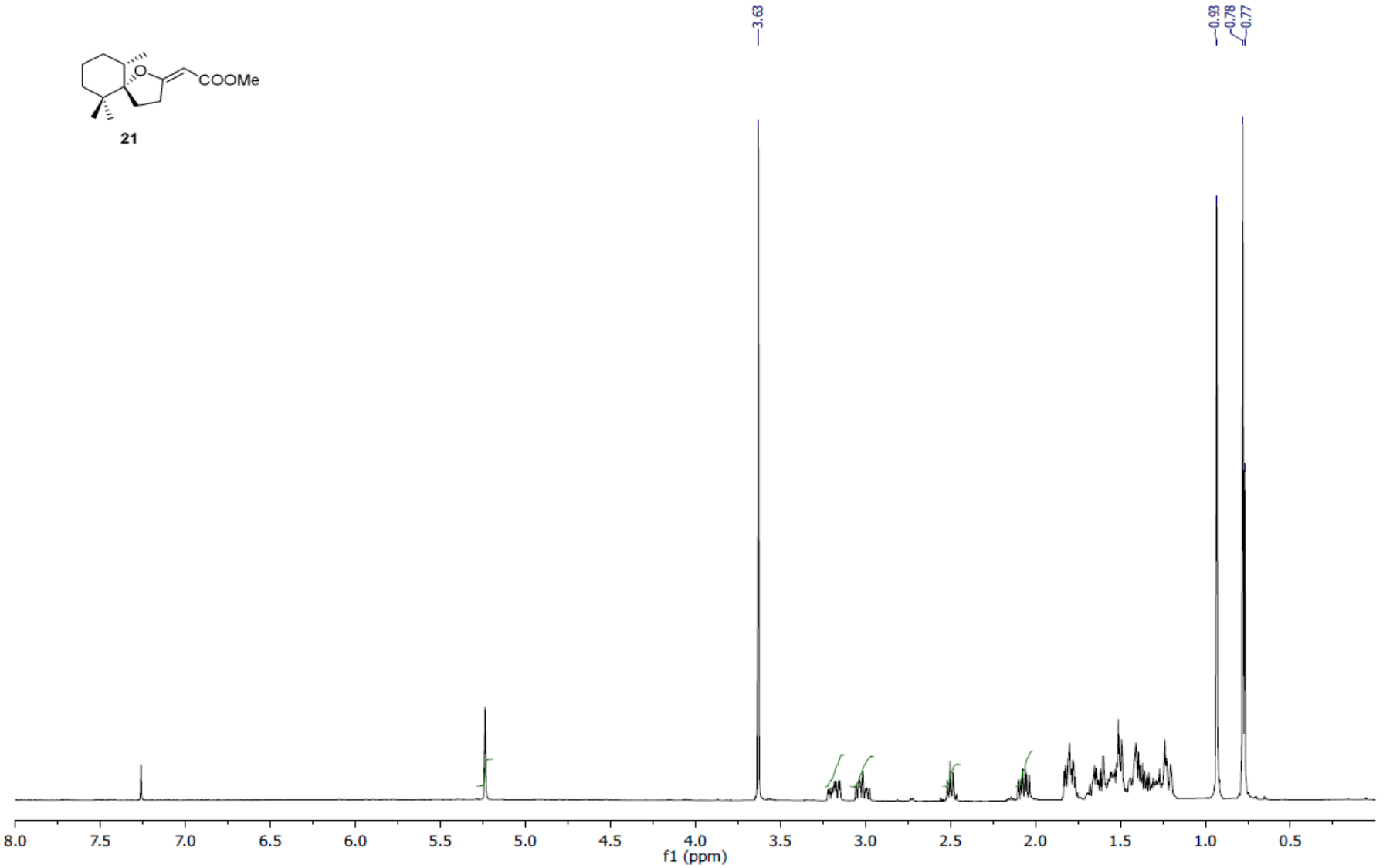

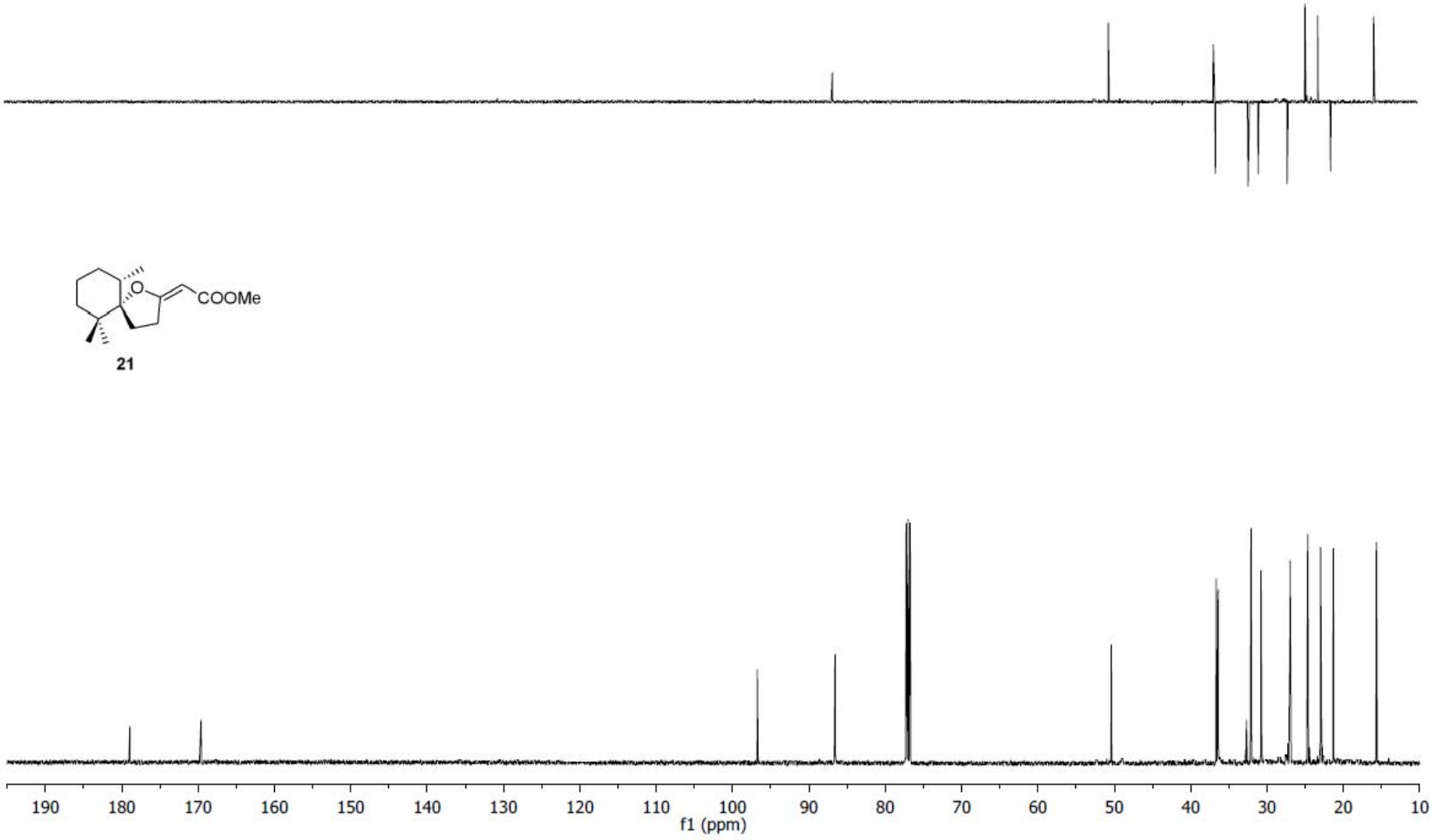


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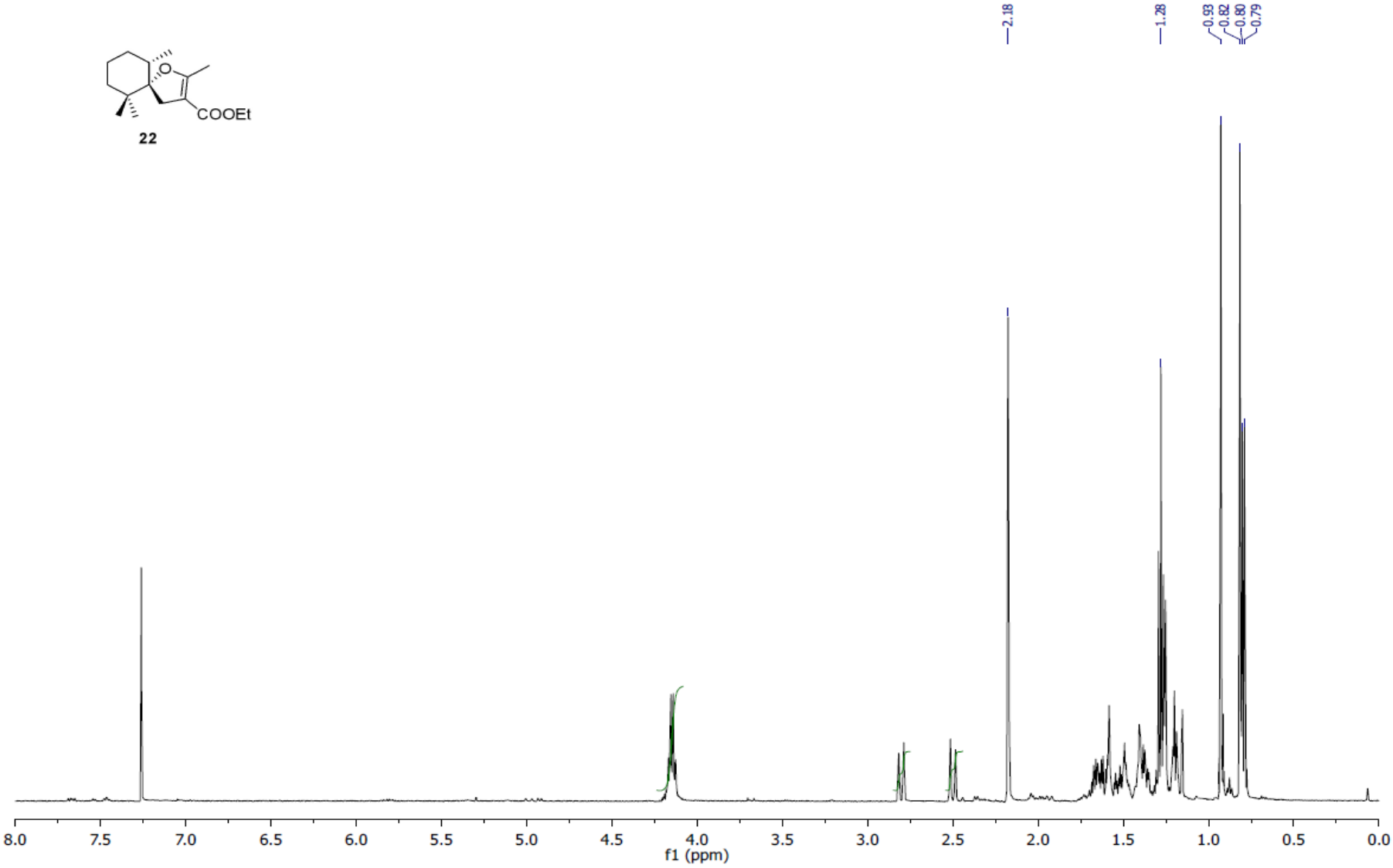

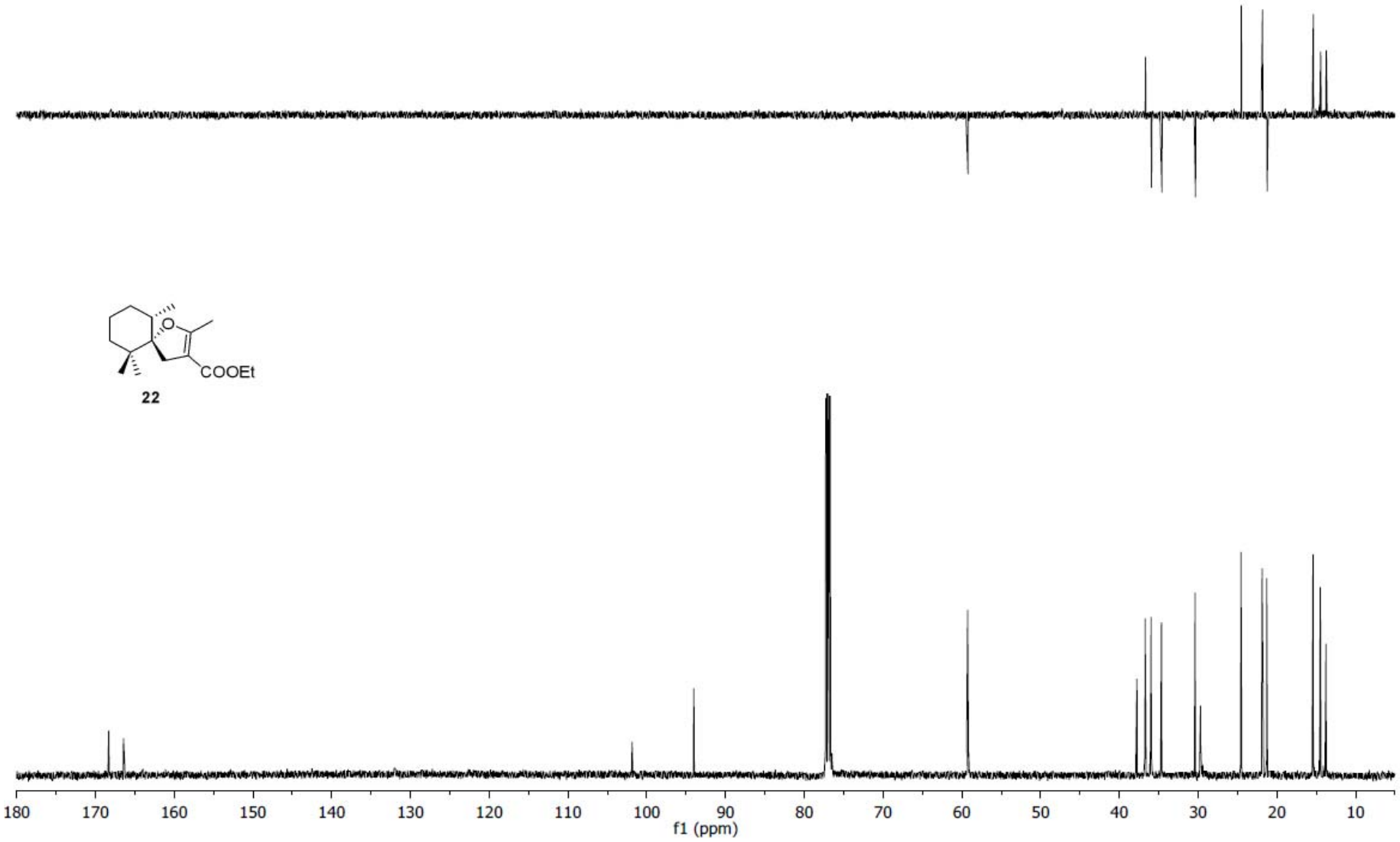

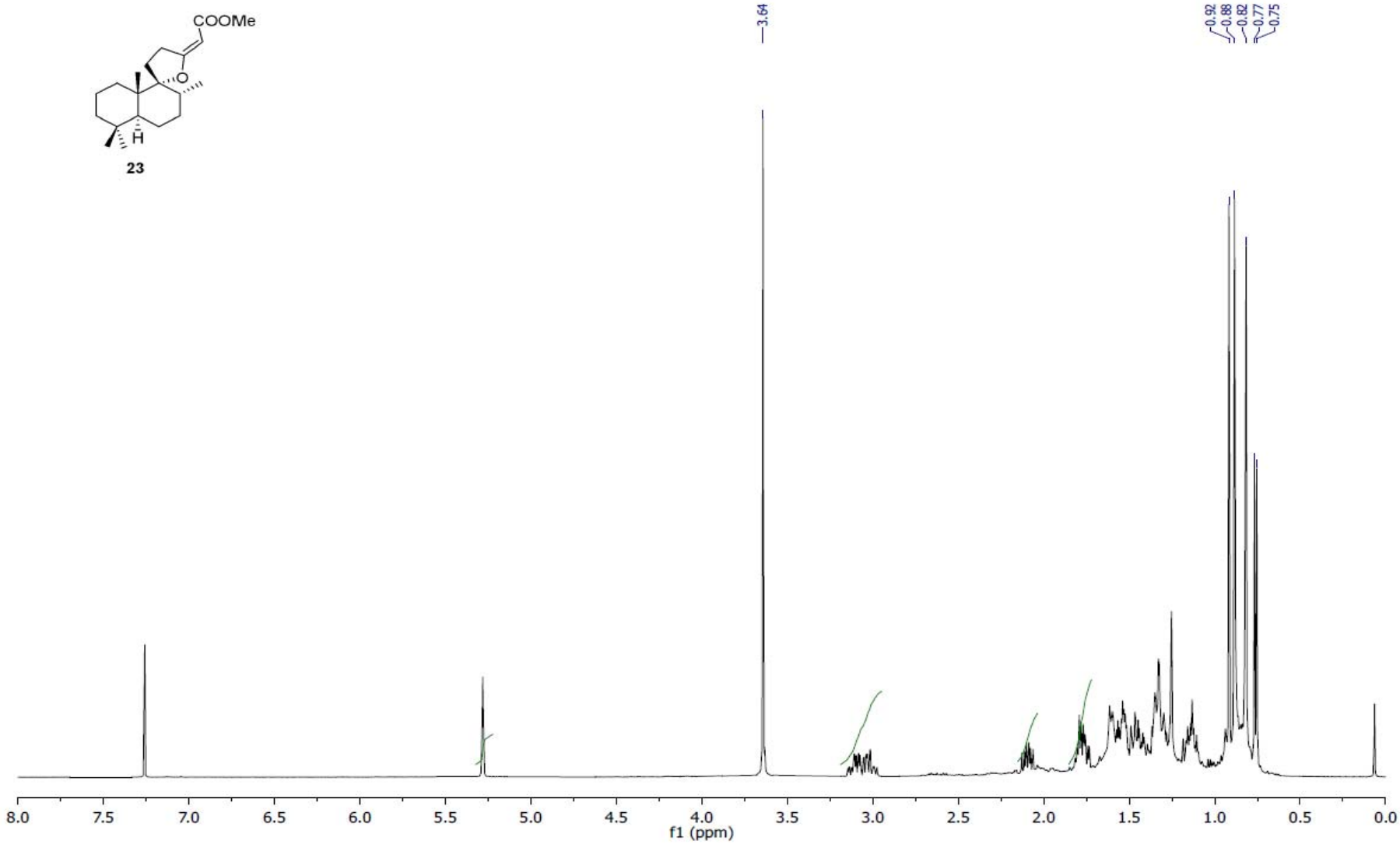

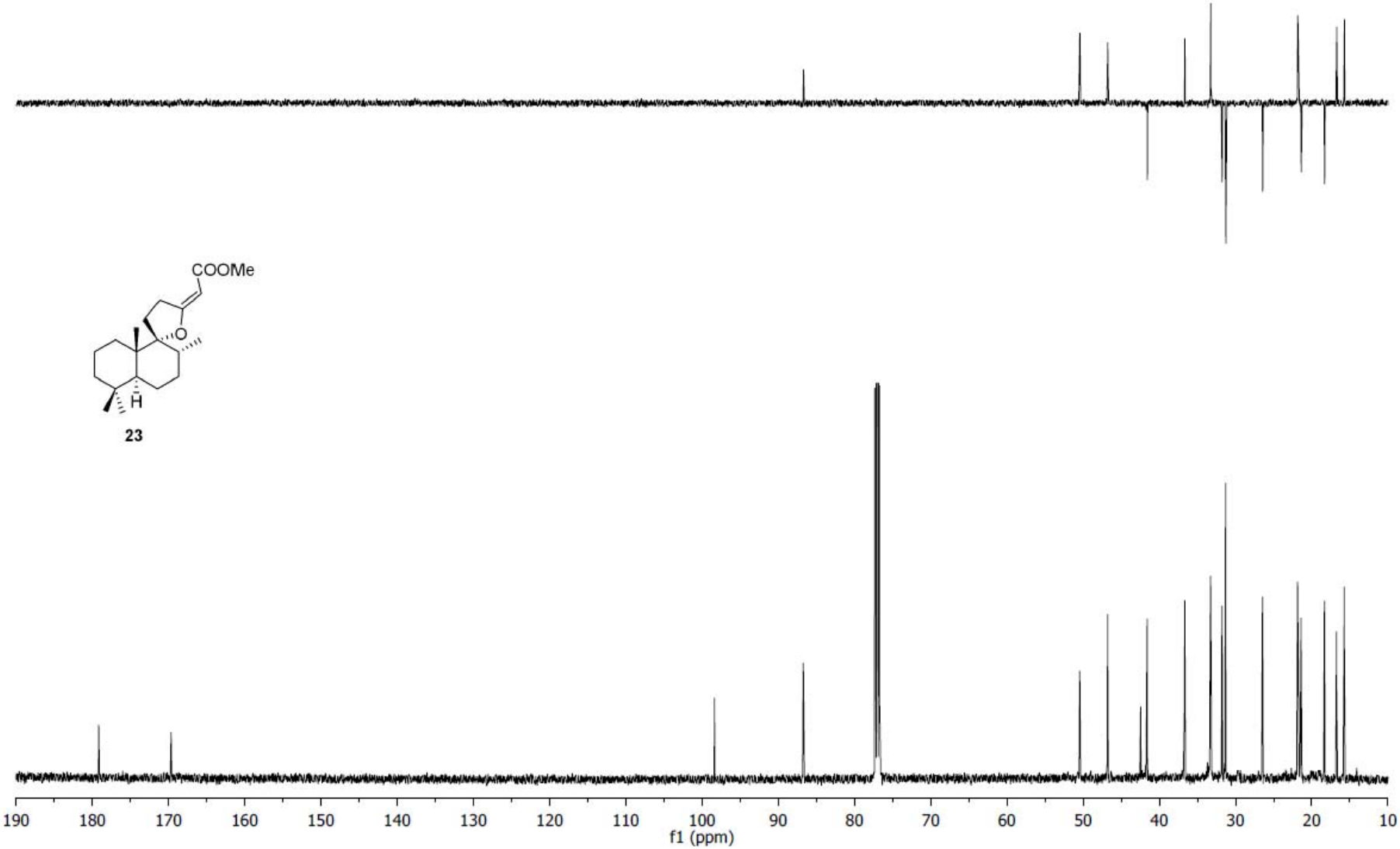


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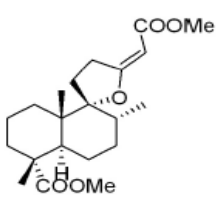


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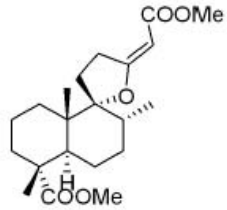


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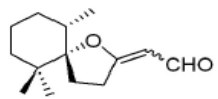
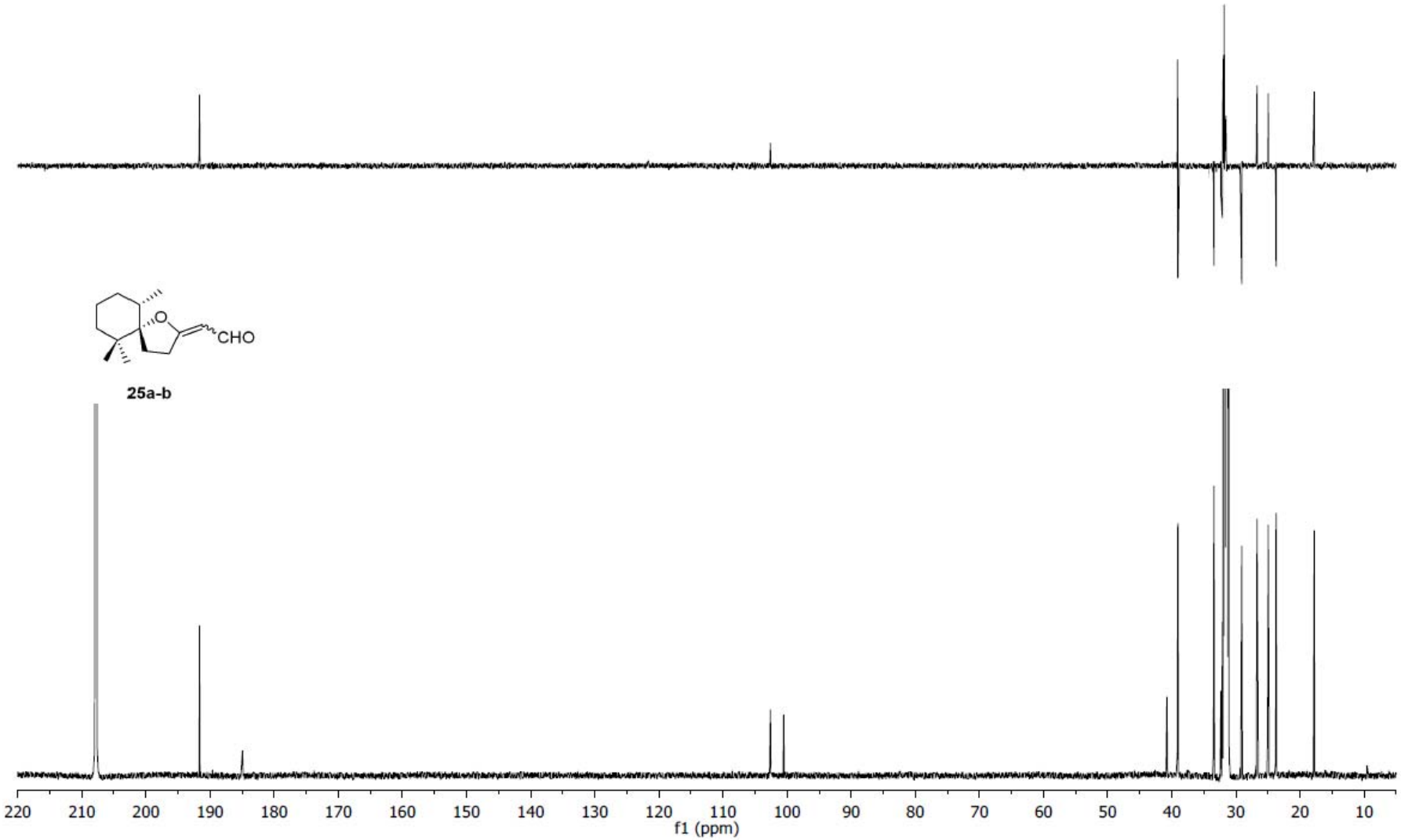
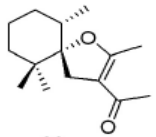


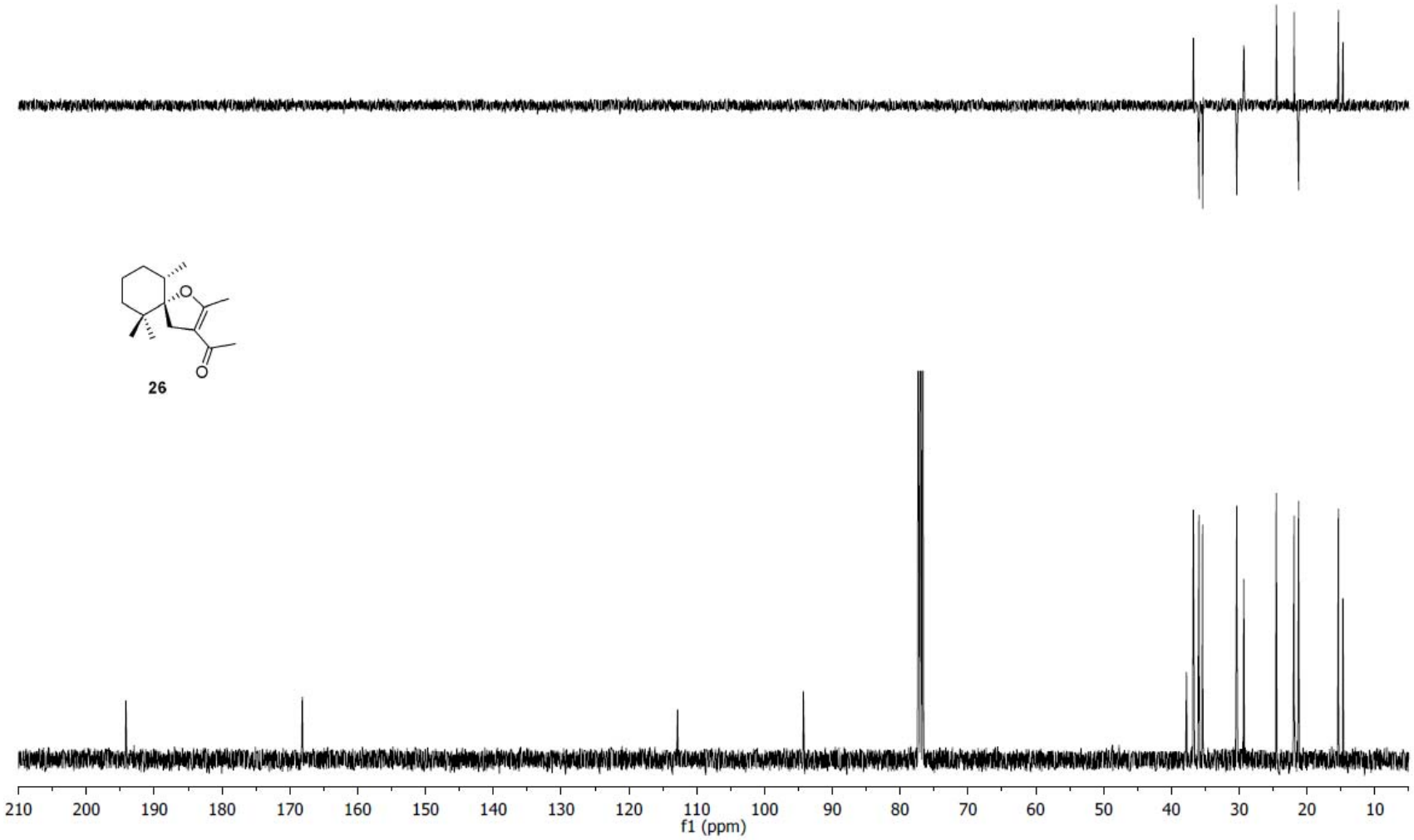

**25a-b**

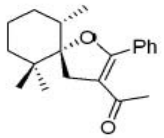



**25a-b**

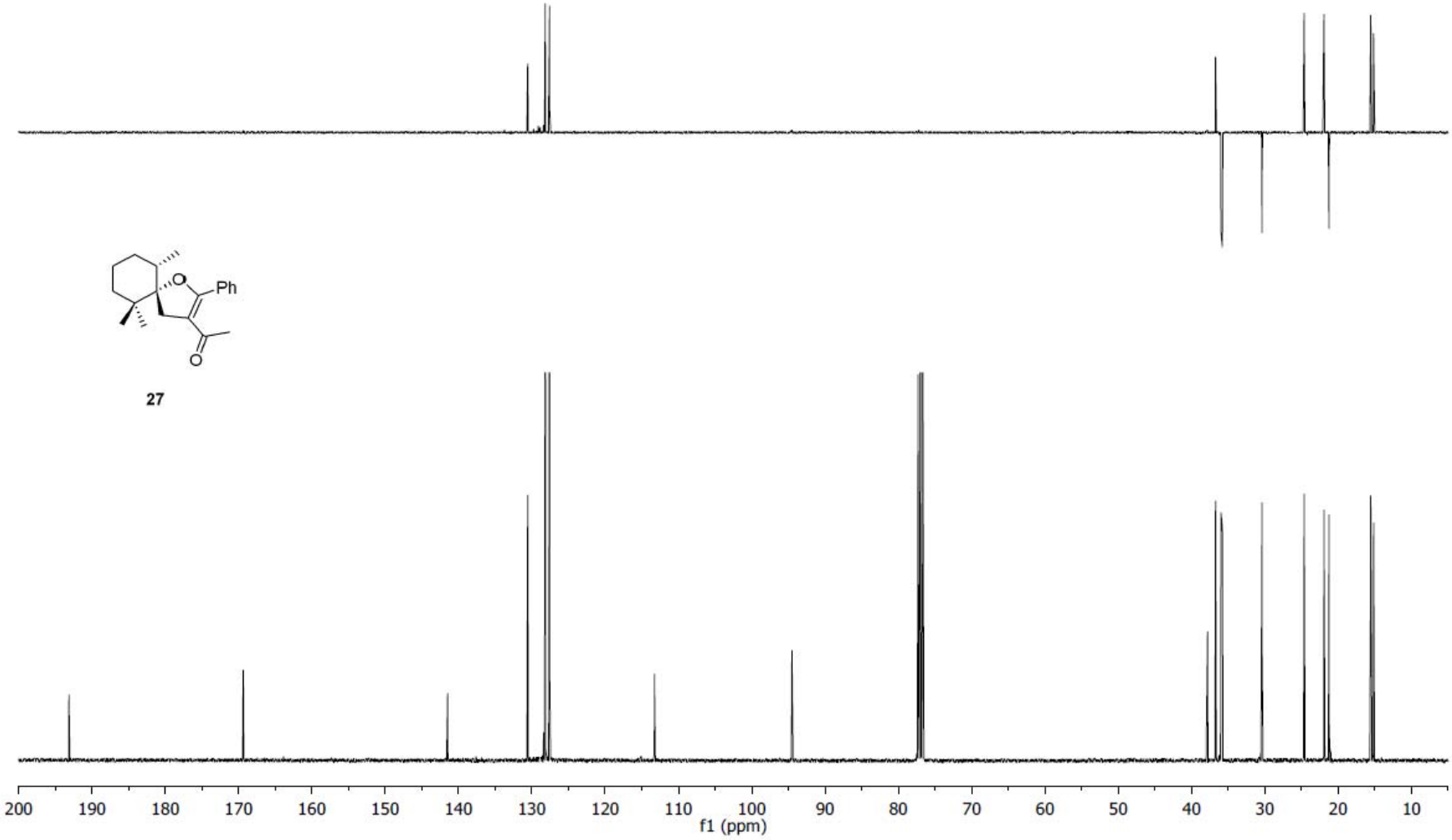


**26**

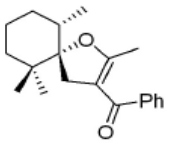





27




27

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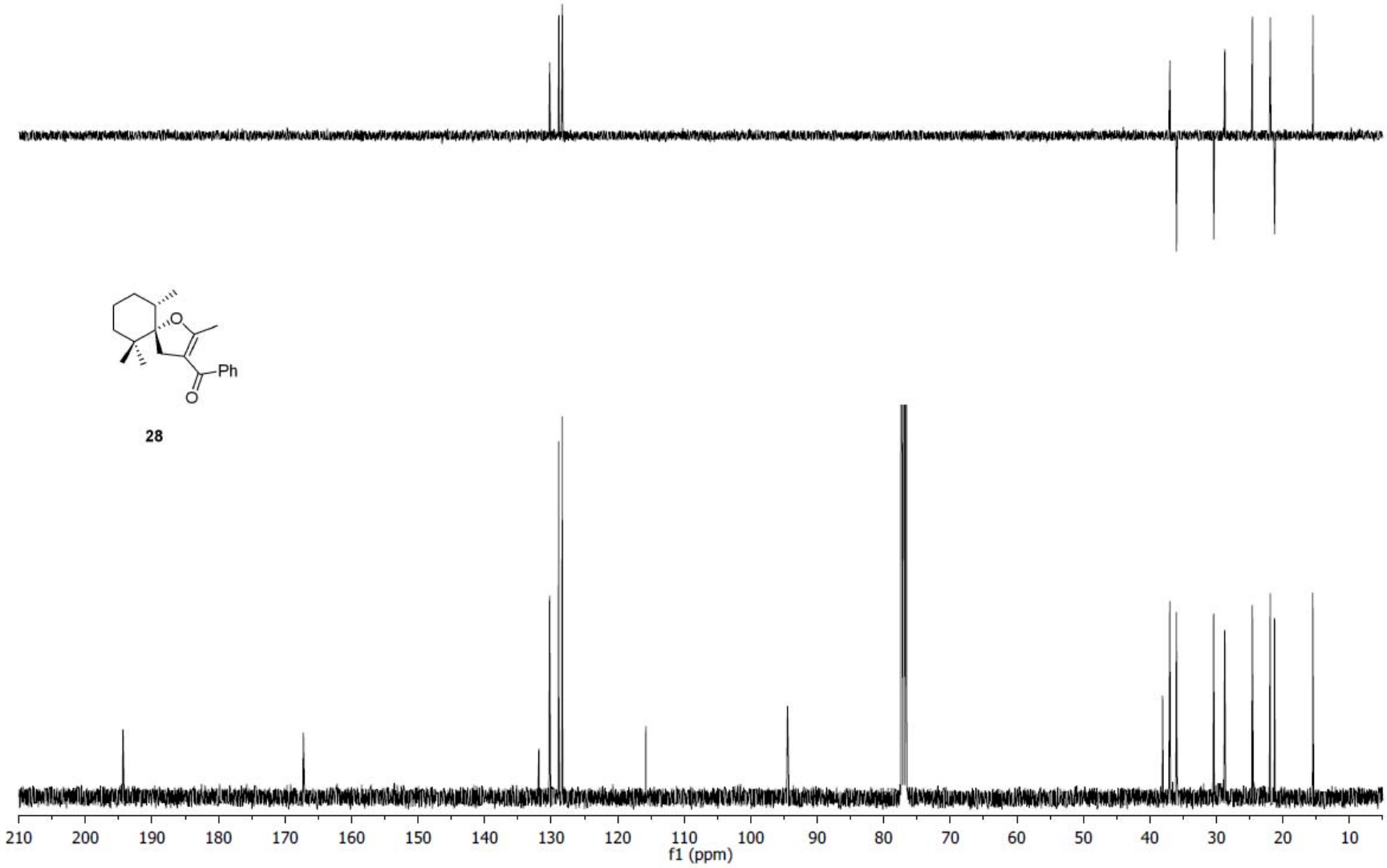


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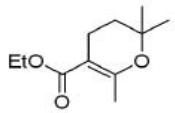
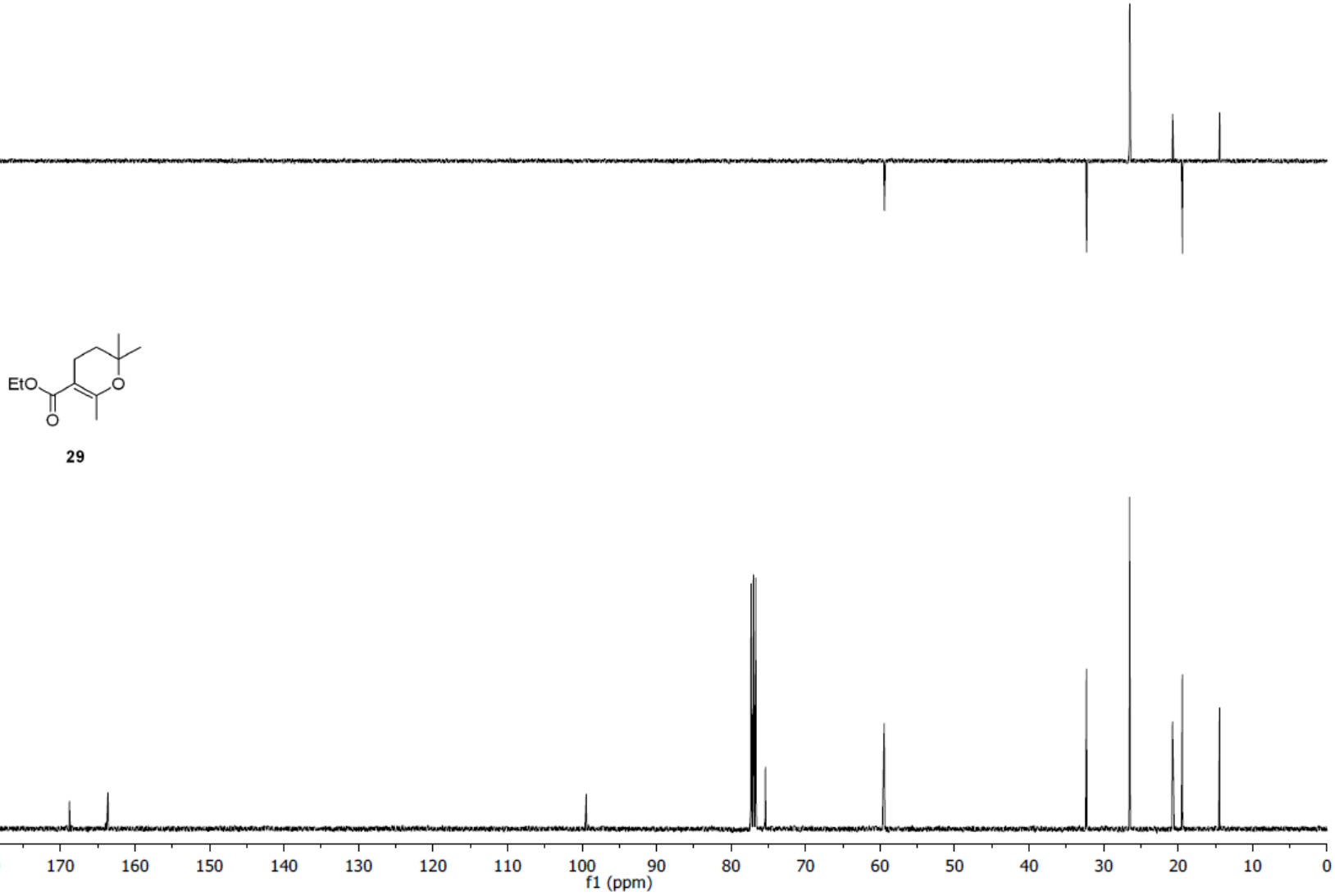
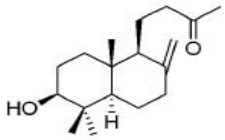



**29**

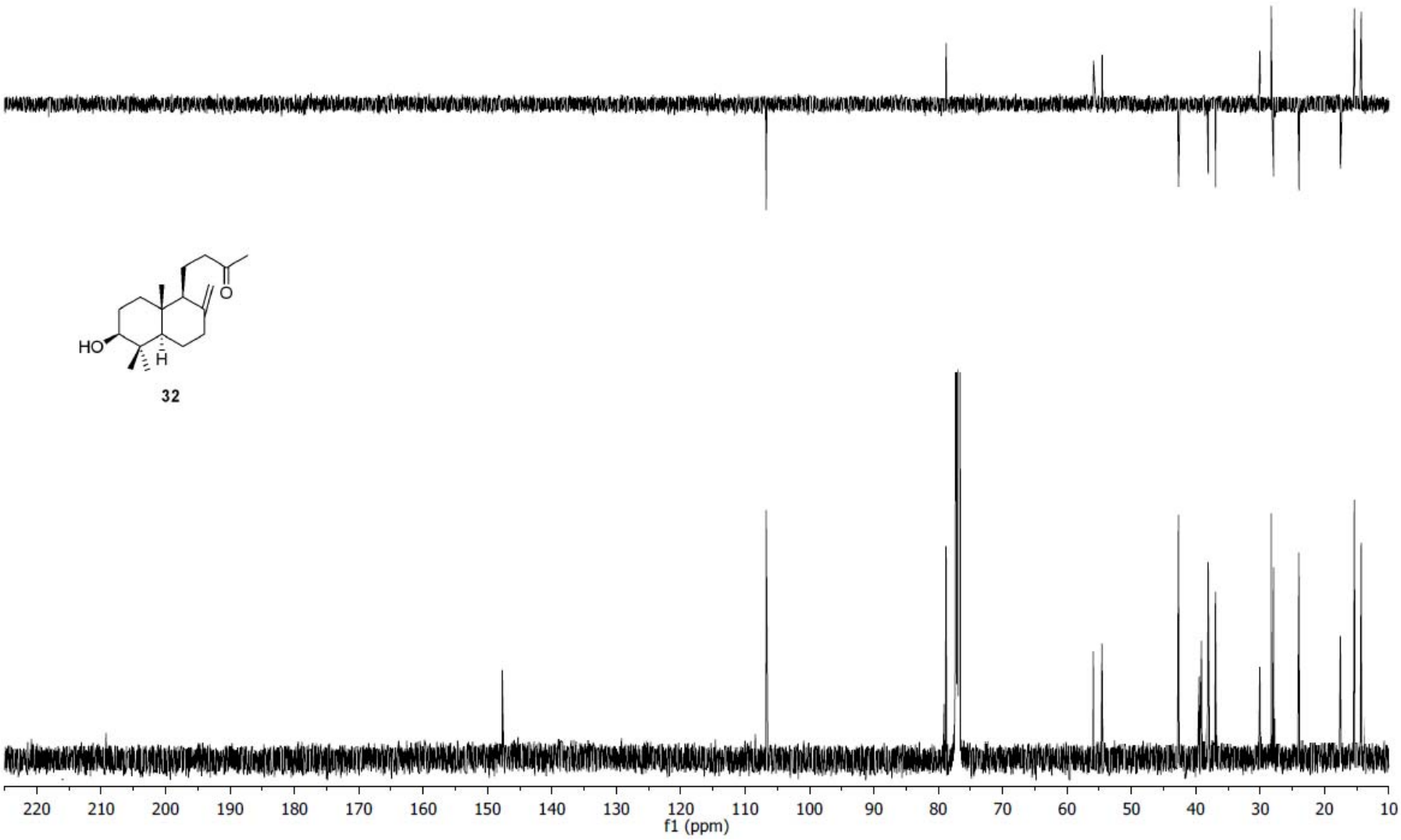



**29**

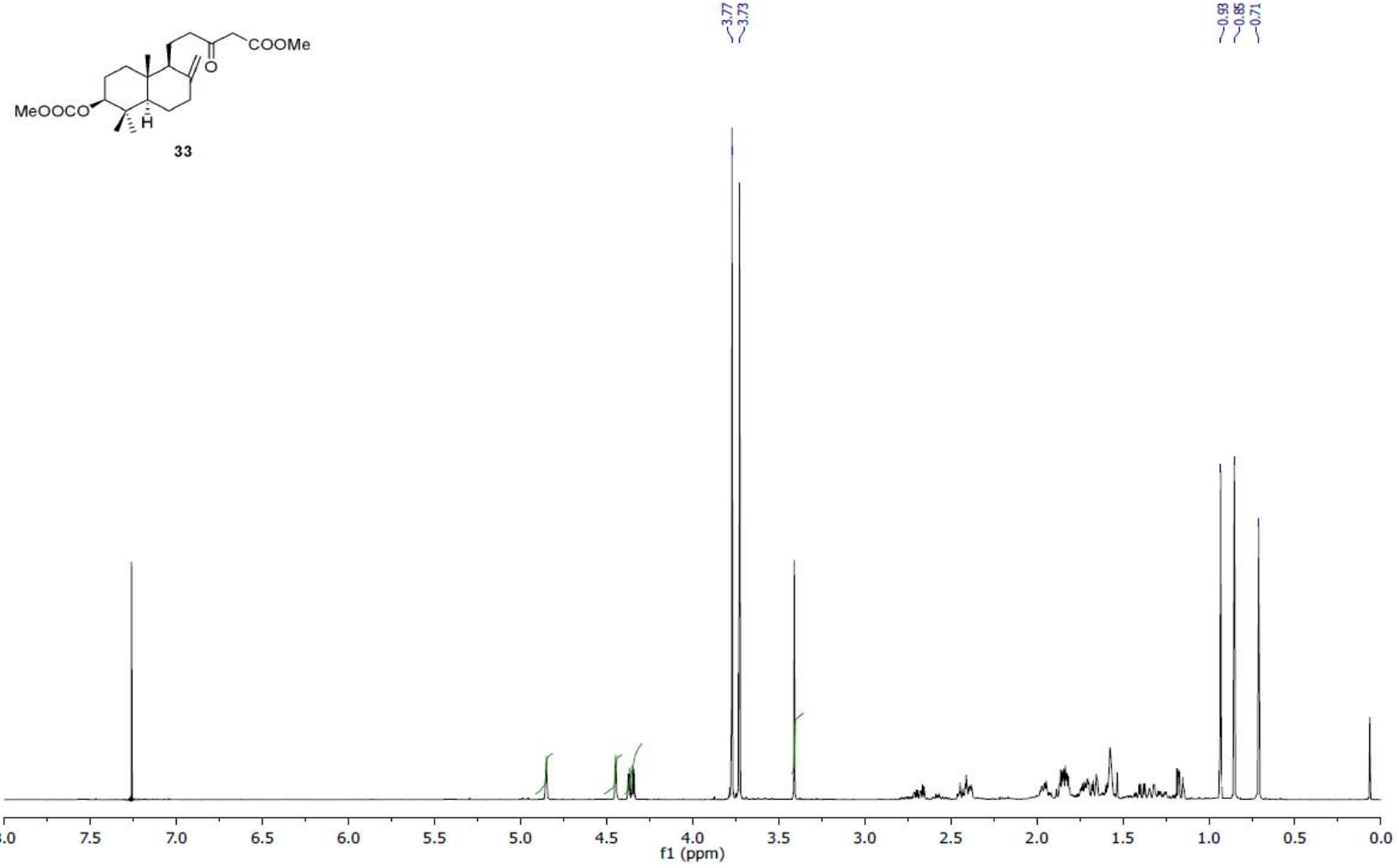

HO
H
O

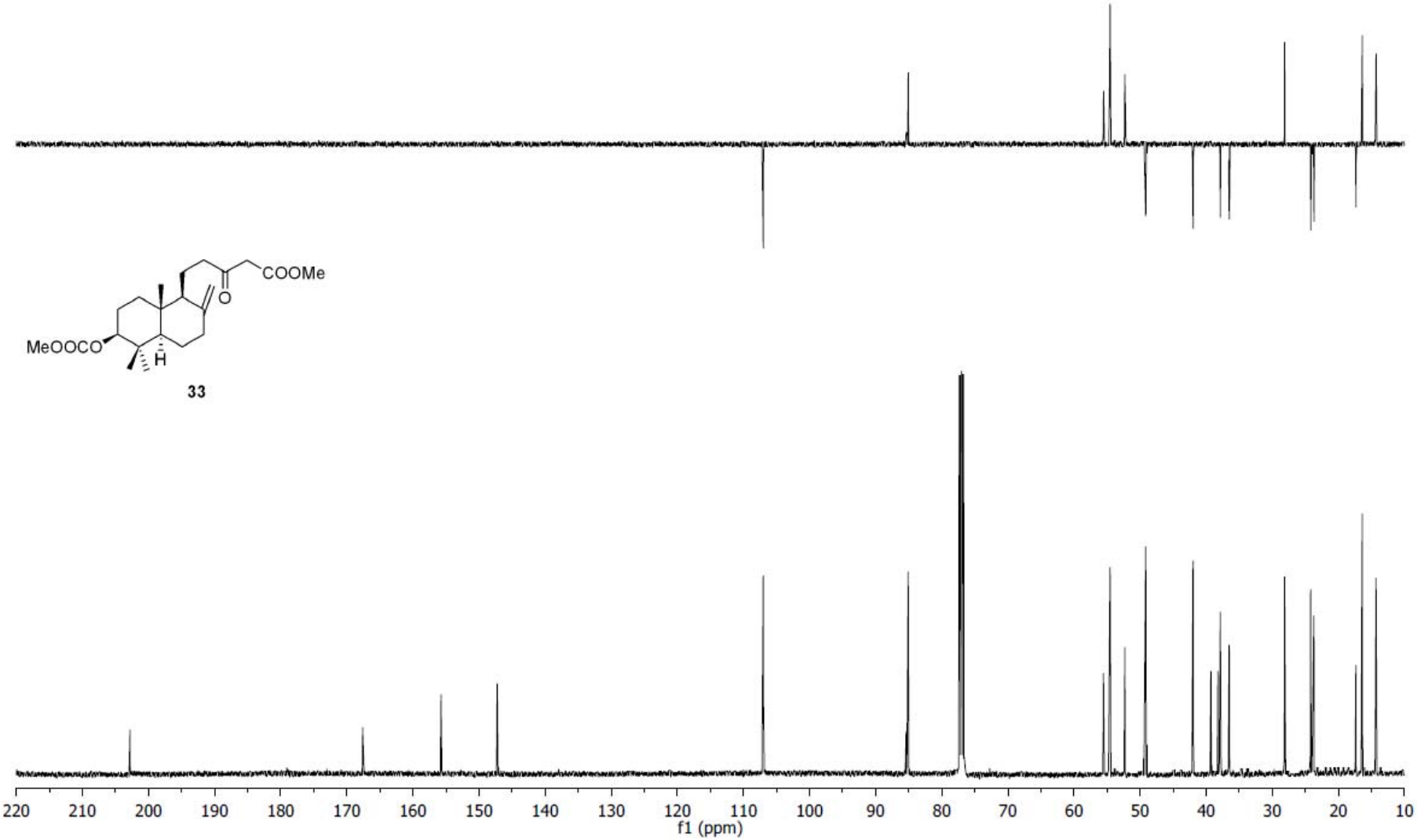
32

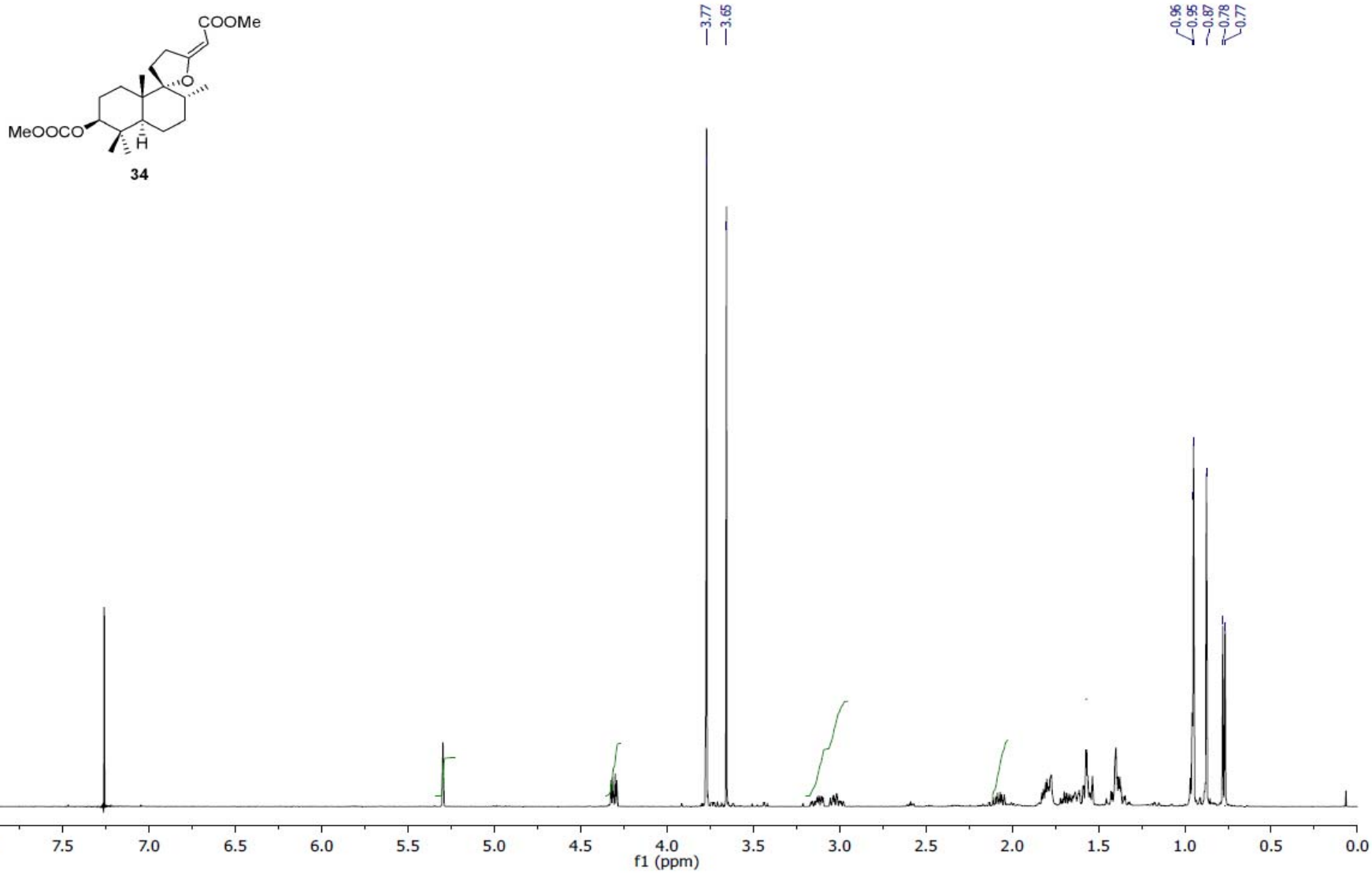

2.10
0.99
0.77
0.69
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

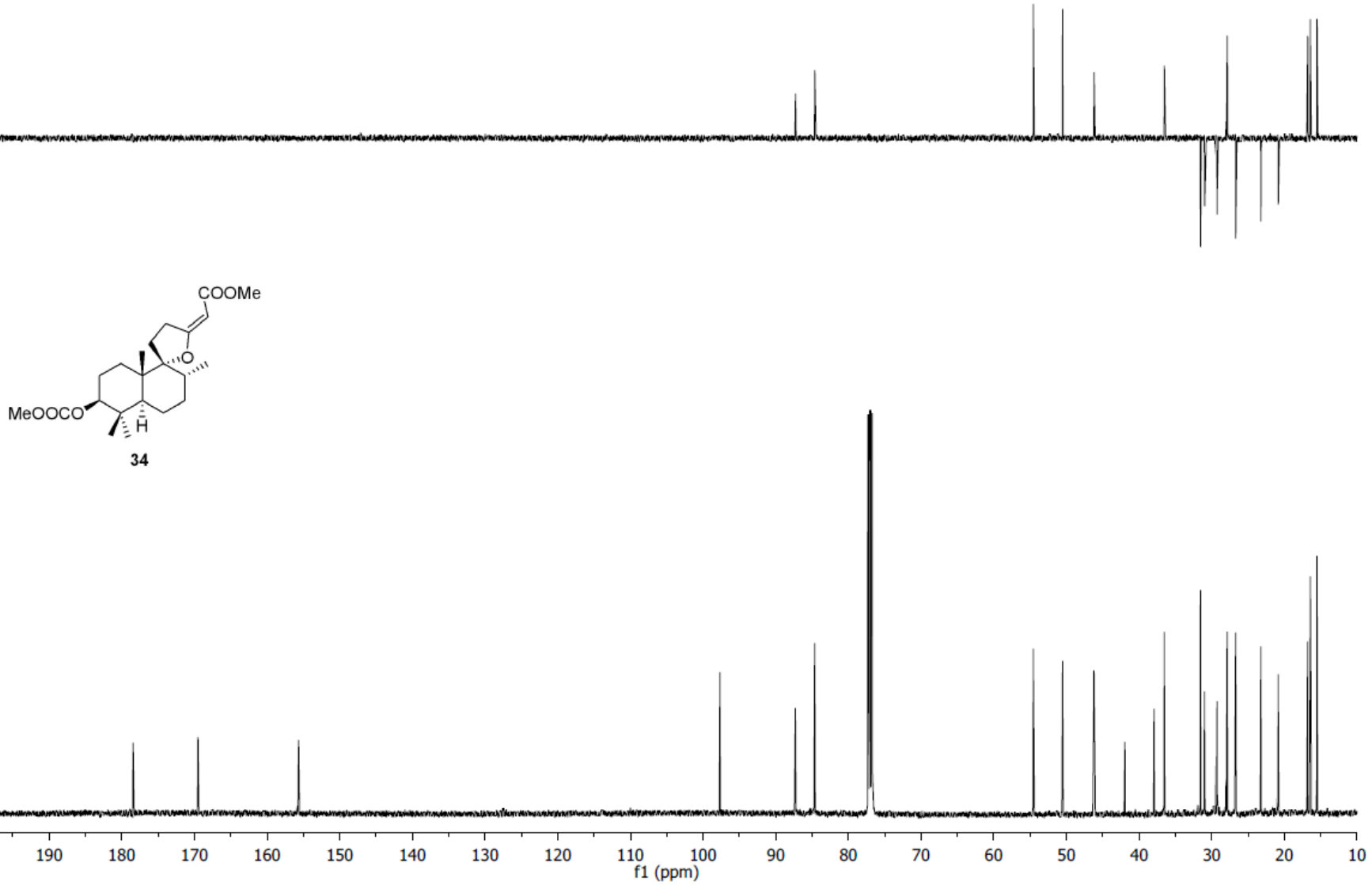



**32**

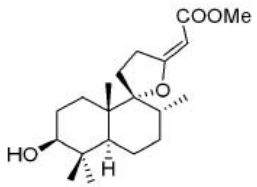




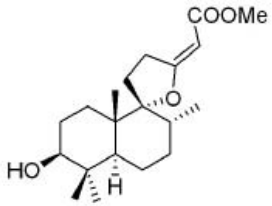

COOMe
MeOOCO
H
34
3.77
3.65
0.96
0.95
0.87
0.78
0.77
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



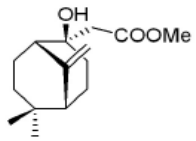

**34**




35




35

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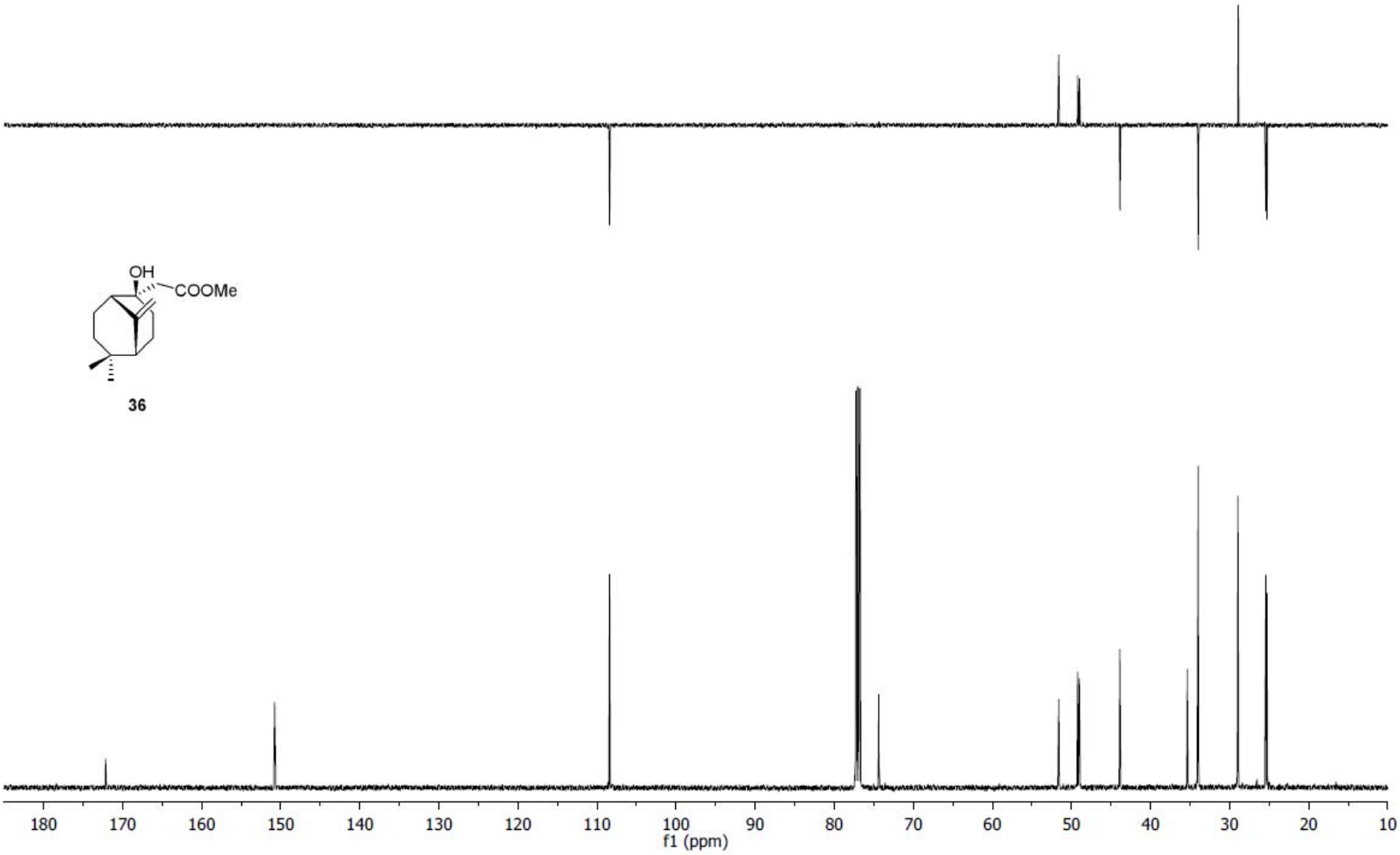
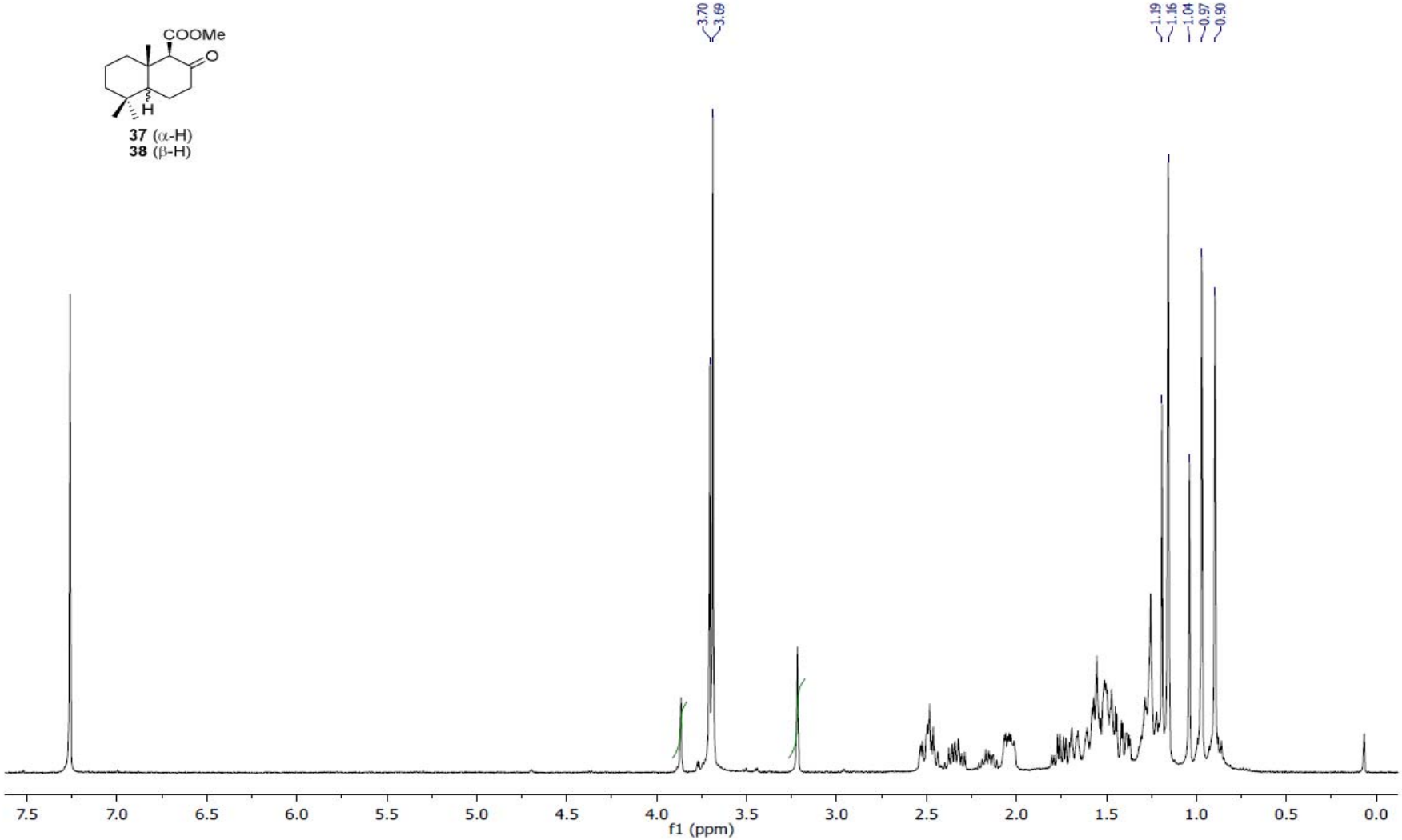
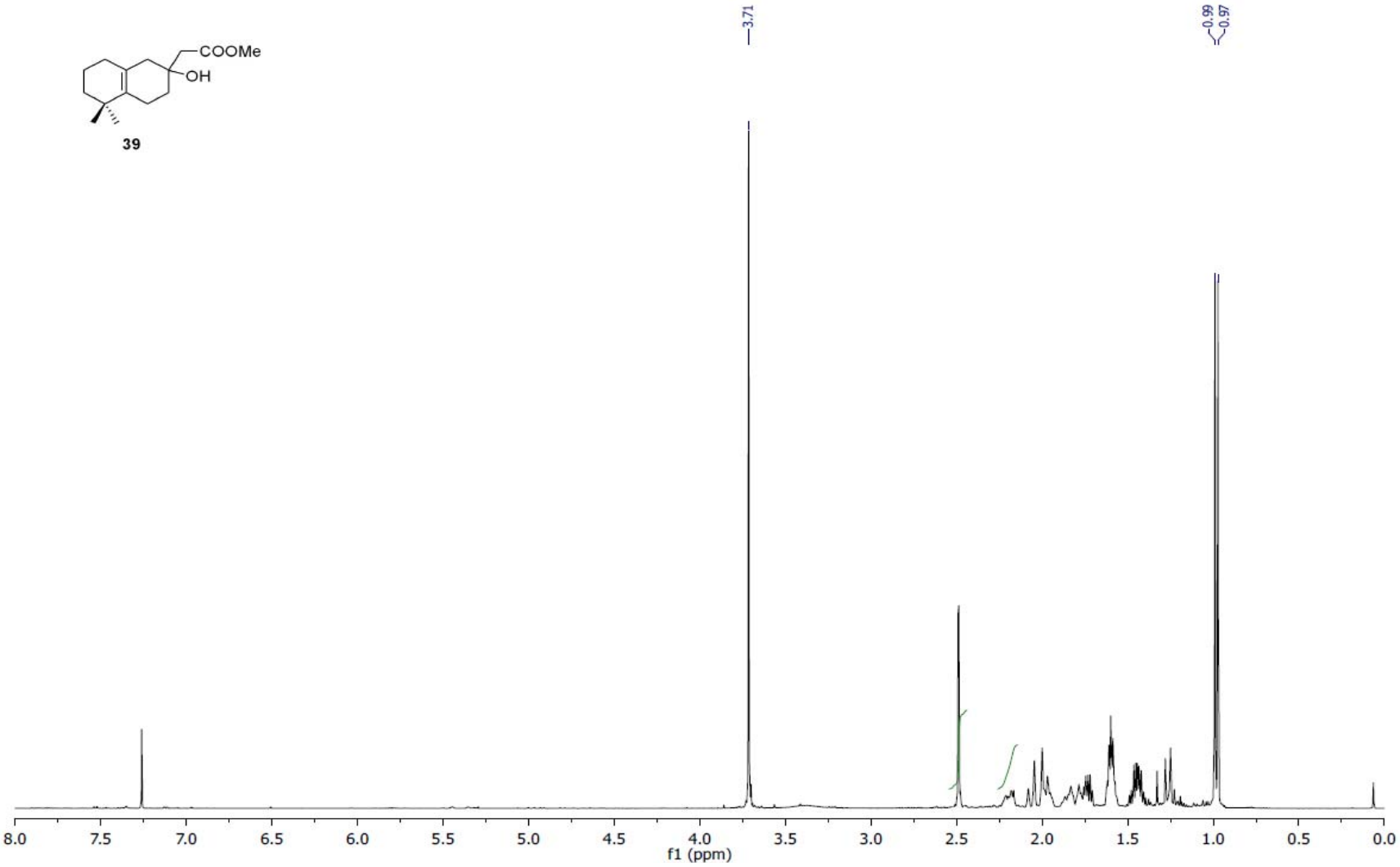
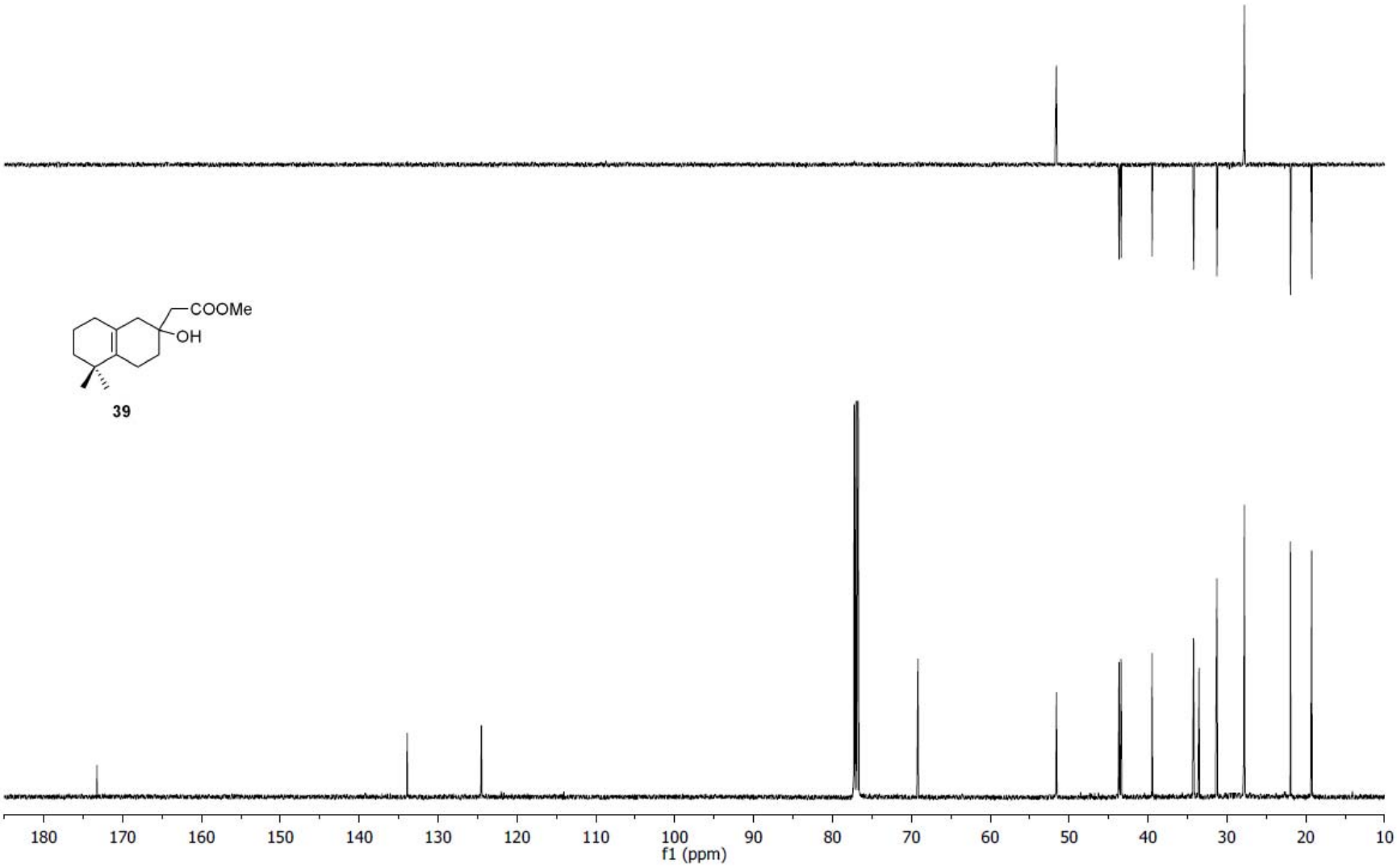


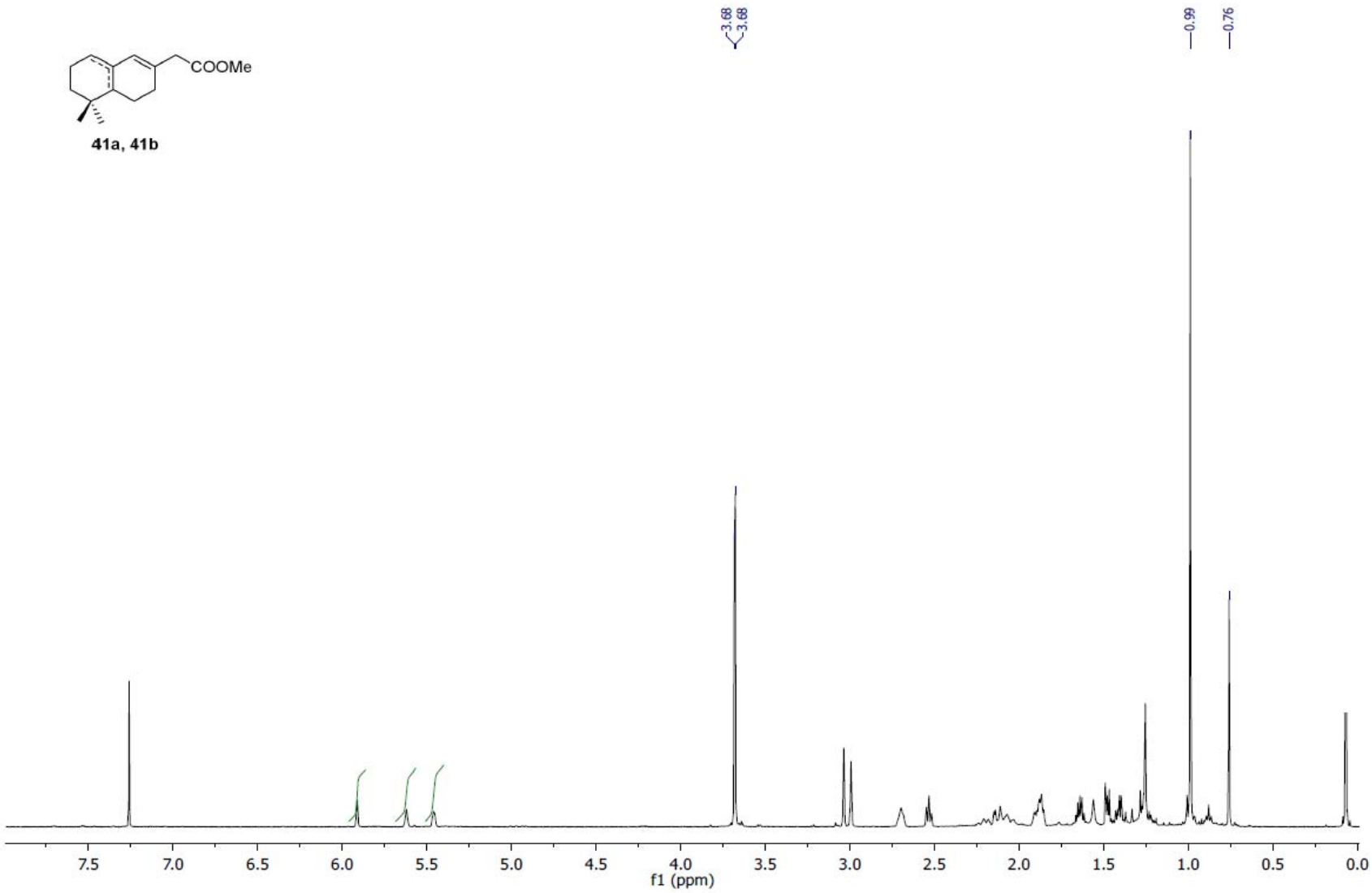

**36**

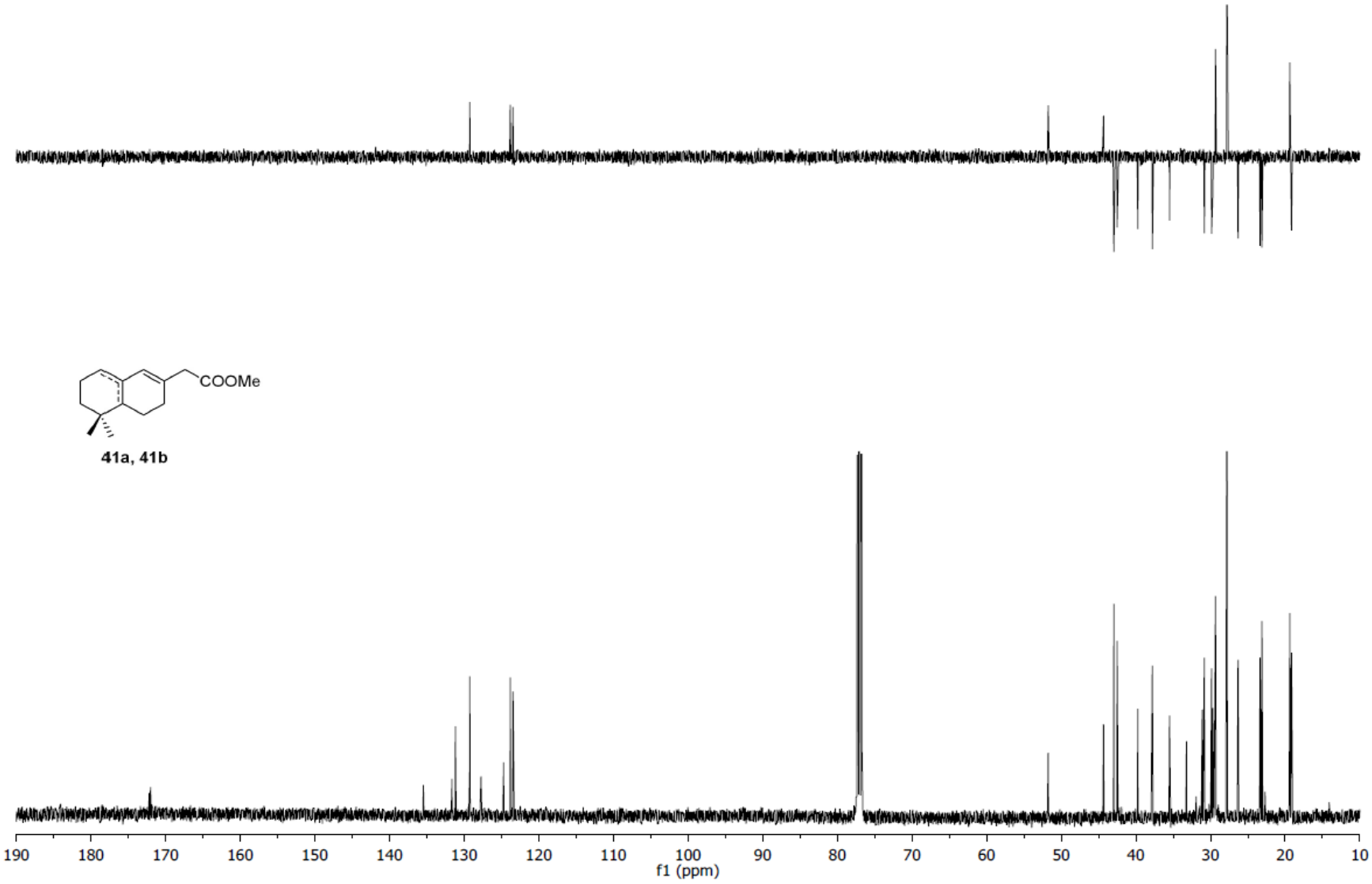


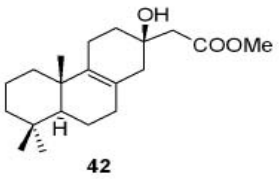




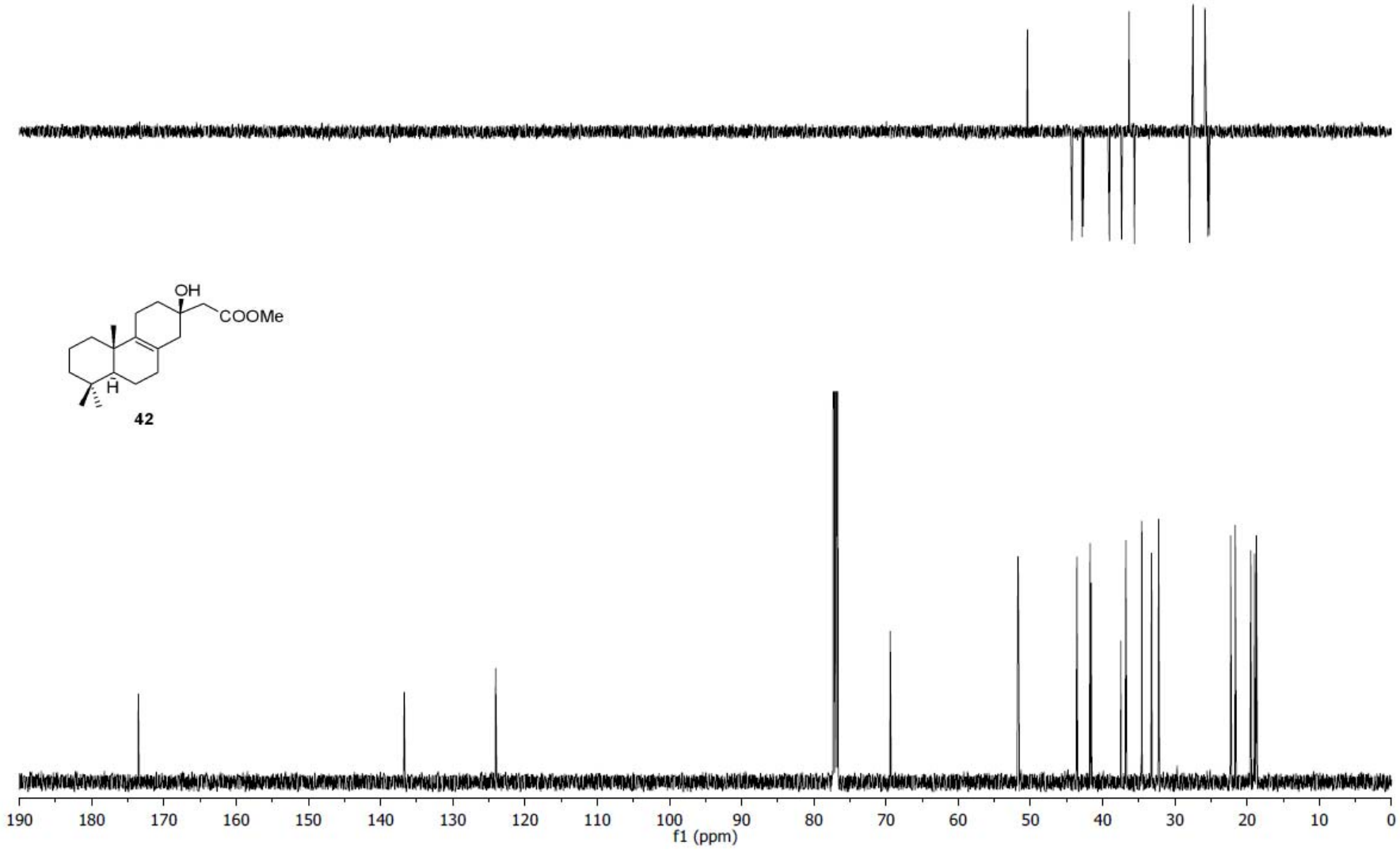

**39**








**42**


OH
COOMe
H
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190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)