Supporting Information

New Strategy for the Construction of Epoxy-bridged Tetrahydropyran Frameworks from Trioxane Precursors. Application to a Concise Synthesis of a Riesling Acetal

Martín J. Riveira, Agustina La-Venia, Mirta P. Mischne*

Instituto de Química Rosario. Facultad de Ciencias Bioquímicas y Farmacéuticas,

Universidad Nacional de Rosario, Suipacha 531, S2002LRK Rosario, Argentina.

mischne@iquir-conicet.gov.ar

Table of Contents

GENERAL INFORMATION

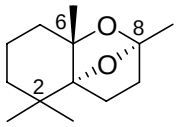
Chemical reagents were purchased from commercial suppliers and were used without further purification unless otherwise noted. Solvents were analytical grade or were purified by standard procedures prior to use. Toluene was distilled from Na under an atmosphere of dry N_2. Yields were calculated for material judged homogenous by thin layer chromatography and nuclear magnetic resonance (NMR). All reactions were monitored by thin layer chromatography (TLC) performed on silica gel 60 F_{254} pre-coated aluminum sheets, visualized by a 254 nm UV lamp, and stained with an ethanolic solution of 4-anisaldehyde. Glassware for reactions was oven dried at 125 °C and cooled under a dry atmosphere prior to use. Column flash chromatography was performed using silica gel 60 (230 – 400 mesh). Melting points were taken on an electrothermal melting point apparatus and are uncorrected. Nuclear magnetic resonance spectra were acquired at 300 MHz for ^{1}H and 75 MHz for ^{13}C using $CDCl_3$ as solvent. Chemical shifts for proton nuclear magnetic resonance (^{1}H NMR) spectra are reported in parts per million relative to the signal of tetramethylsilane at 0 ppm (internal standard) and coupling constants (*J*) are reported in hertz (Hz). Chemical shifts for carbon nuclear magnetic resonance (^{13}C NMR) spectra are reported in parts per million relative to the center line of the $CDCl_3$ triplet at 76.9 ppm. IR spectra were obtained using an FT-IR spectrometer and only partial spectral data are listed. High resolution mass spectra were performed on a mass spectrometer.

EXPERIMENTAL SECTION AND SPECTROSCOPIC DATA

General procedure for hydrogenation (Table 1).

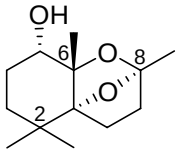
To a solution of 1 mmol of trioxane **5** in EtOAc (50 ml, 20 mM), was added PtO_2 (wt % according to Table 1) and the resulting suspension was degassed three times (three vacuum/hydrogen cycles to remove air). The suspension was vigorously stirred under a hydrogen atmosphere (balloon, ca.1atm) at room temperature for the time indicated in Table 1, filtered through celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with hexanes/EtOAc as eluent to obtain the desired reduced product (**6**).

2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undecane (6a)



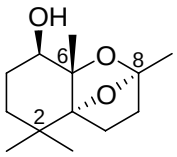
Colorless oil. Yield: 80%. IR (film): ν = 2920, 1450, 1390, 1180, 920 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.96-1.43 (m, 8H), 1.54 (s, 3H), 1.37 (s, 3H), 1.36 (dt, J = 12.9, 2.9 Hz, 1H), 1.32-1.25 (m, 1H), 1.08 (s, 3H), 0.96 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 107.5, 92.1, 81.6, 39.2, 37.9, 37.5, 34.4, 26.1, 25.1, 24.0, 23.0, 19.8, 19.7. HRMS: *m/z* calcd for $C_{13}H_{22}O_2$ (M^+) 210.1619, found 210.1618.

***syn*-2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undecan-5-ol (6b).**



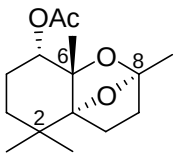
Colorless oil. Yield: 85%. IR (film): ν = 3555, 2944, 1476, 1396, 1024 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.52 (bs, 1H), 3.04 (bs, 1H), 2.05 (td, J = 13.7, 3.5 Hz, 1H), 1.98-1.60 (m, 6H), 1.61 (s, 3H), 1.35 (s, 3H), 1.12 (dt, J = 13.6, 3.4 Hz, 1H), 1.10 (s, 3H), 0.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 107.9, 93.6, 81.3, 72.9, 36.7, 33.6, 30.4, 25.8, 25.6, 25.5, 24.1, 22.6, 18.9. HRMS: *m/z* calcd for $C_{13}H_{23}O_3$ ($M + H^+$) 227.1642, found 227.1643.

***anti*-2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undecan-5-ol (6c).**



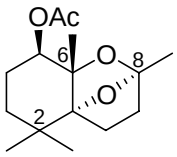
Colorless crystals. Yield: 90%. Mp: 57.0-58.0 °C. IR (film): ν = 3448, 2939, 1457, 1388, 1010 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.85 (dd, J = 12.3, 4.2 Hz, 1H), 2.01-1.60 (m, 6H), 1.54 (s, 3H), 1.44 (td, J = 12.8, 3.1 Hz, 1H), 1.37 (dt, J = 12.8, 3.1 Hz, 1H), 1.32 (s, 3H), 1.07 (s, 3H), 0.95 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 108.3, 93.5, 85.4, 76.6, 37.2, 36.1, 34.3, 26.8, 25.8, 25.7, 24.0, 19.7, 15.1. HRMS: *m/z* calcd for $C_{13}H_{23}O_3$ (M + H$^+$) 227.1642, found 227.1645.

***syn*-2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undec-5-yl Acetate (6d).**



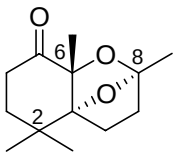
Colorless crystals. Yield: 70%. Mp: 89.5-90.0 °C. IR (KBr): ν = 2984, 1730, 1392, 1256 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.82 (t, J = 3 Hz, 1H), 2.12 (s, 3H), 2.05-1.60 (m, 7H), 1.51 (s, 3H), 1.39 (s, 3H), 1.36 (dt, J = 13.4, 3.3 Hz, 1H), 1.12 (s, 3H), 0.99 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.4, 107.5, 91.9, 79.7, 73.4, 37.1, 33.6, 31.1, 25.8, 25.4, 23.8, 23.7, 23.2, 21.5, 18.9. HRMS: *m/z* calcd for $C_{15}H_{25}O_4$ (M + H$^+$) 269.1747, found 269.1755.

***anti*-2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undec-5-yl Acetate (6e).**



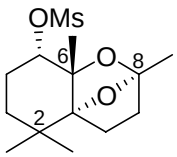
Colorless oil. Yield: 75%. IR (film): ν = 2940, 1743, 1389, 1242, 1014 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.00 (dd, J = 12.4, 4.2 Hz, 1H), 2.06 (s, 3H), 2.01-1.59 (m, 6H), 1.54 (s, 3H), 1.48-1.40 (m, 1H), 1.38 (s, 3H), 1.35-1.31 (m, 1H), 1.08 (s, 3H), 0.97 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.4, 108.4, 93.7, 83.3, 78.7, 37.2, 35.6, 34.1, 25.6, 25.4, 24.7, 23.8, 21.3, 19.4, 16.2. HRMS: *m/z* calcd for $C_{15}H_{25}O_4$ (M + H$^+$) 269.1747, found 269.1750.

2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undecan-5-one (6f).



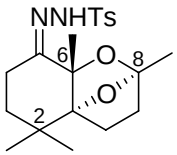
Colorless crystals. Yield: 80%. Mp: 95.5-96.0 °C (Hexane). IR (KBr): ν = 2968, 2943, 1726, 1011, 937 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.62 (td, J = 14.7, 5.7 Hz, 1H), 2.35 (ddd, J = 14.7, 4.0, 3.0 Hz, 1H), 2.09 (td, J = 14.7, 4.0 Hz, 1H), 2.01-1.60 (m, 5H), 1.55 (s, 3H), 1.43 (s, 3H), 1.19 (s, 3H), 1.14 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 210.4, 107.8, 95.4, 85.4, 37.3, 36.2, 35.1, 33.8, 25.1, 24.1, 22.8, 20.0, 18.6. HRMS: *m/z* calcd. for $C_{13}H_{21}O_3$ (M + H$^+$) 225.1485, found 225.1487.

syn-**2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undec-5-yl Mesylate (7).**



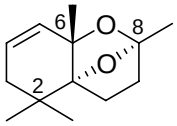
Methanesulfonyl chloride (0.08 ml, 1.03 mmol) was added dropwise to a stirring solution of alcohol **6b** (0.116 g, 0.51 mmol) and DMAP (0.013g, 0.106 mmol) in pyridine (8.5 ml, 0.06 M). After 18 hours, the reaction was quenched with water (15 ml) and transferred to a separatory funnel with ether (50 ml). The phases were separated and the aqueous phase extracted with ether (2 × 50 ml). The combined organic phases were washed with HCl (5% P/V, 2 × 50 ml), brine (2 × 50 ml) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to obtain a colorless solid, the title compound, that did not require further purification (0.147 g, 0.48 mmol, isolated yield 95 %). Colorless crystals**.** Mp: 148.5-149.0 °C. IR (KBr): ν = 2972, 1332, 1172, 1016 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.38 (t, J = 2.8 Hz, 1H), 3.01 (s, 3H), 2.11 (td, J = 14.3, 3.5, 1H), 2.03-1.66 (m, 6H), 1.59 (s, 3H), 1.39 (s, 3H), 1.19 (dt, J = 14.0, 3.0 Hz, 1H), 1.12 (s, 3H), 0.99 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 108.3, 91.8, 82.7, 79.1, 38.4, 37.3, 33.5, 30.4, 25.6, 25.4, 25.3, 23.7, 23.1, 18.6. HRMS: *m/z* calcd for $C_{14}H_{25}O_5S$ (M + H$^+$) 305.1423, found 305.1424.

2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undecan-5-one Tosylhydrazone (8).



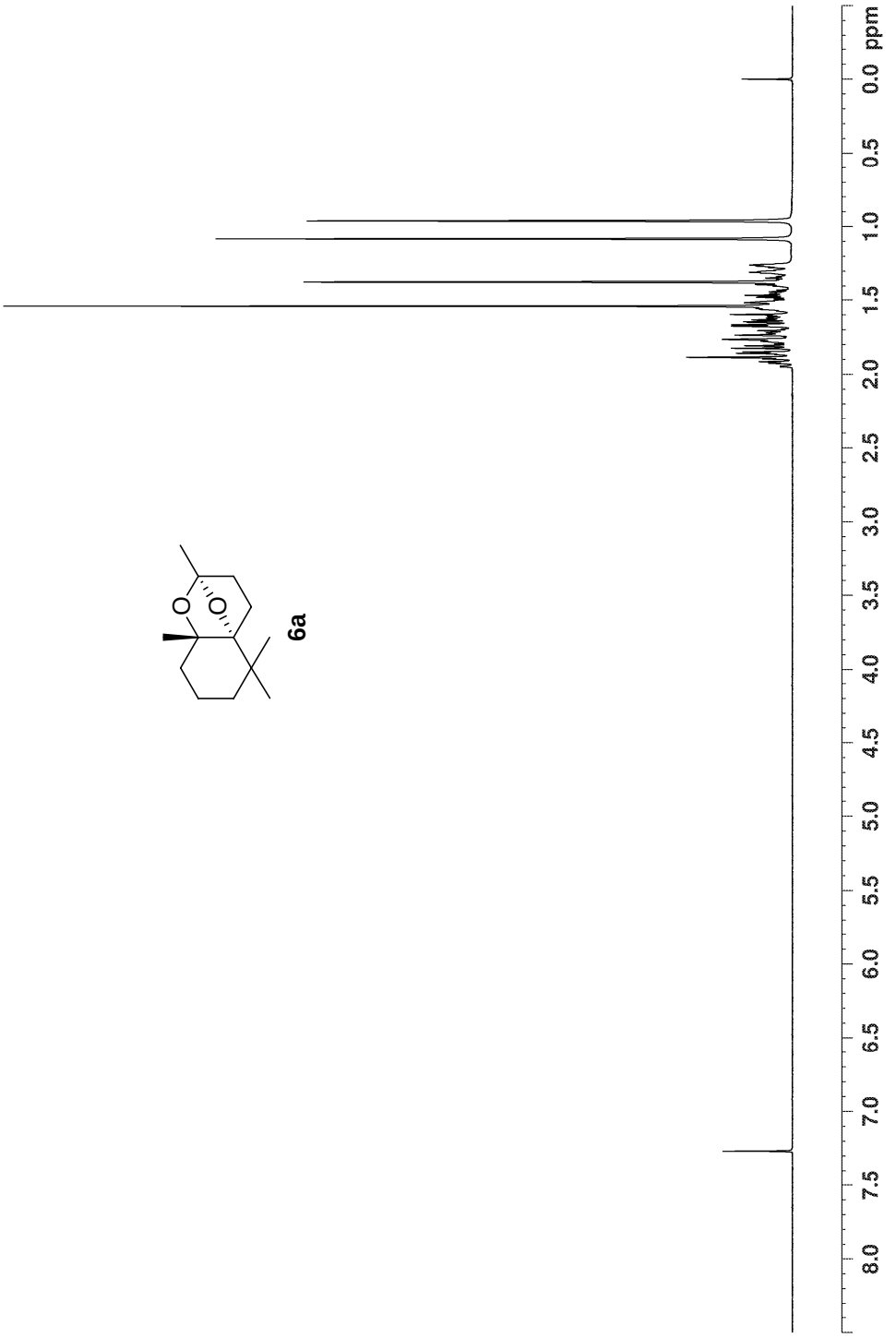
Colorless glass. IR (KBr): ν = 3200, 2978, 1476, 1448, 1351, 1169 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 10.48 (sb, 1H), 7.79 (m, 2H), 7.28 (m, 2H), 2.42 (s, 3H), 2.39-2.19 (m, 2H), 1.91-1.60 (m, 5H), 1.46 (s, 3H), 1.37 (ddd, *J* = 13.3, 4.5, 3.1 Hz, 1H), 1.33 (s, 3H), 1.05 (s, 3H), 1.01 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 156.0, 143.3, 136.2, 129.2 x 2, 127.4 × 2, 108.2, 94.7, 85.9, 37.0, 35.4, 33.7, 29.4, 25.6, 23.6, 22.5, 21.4, 19.5, 18.2. HRMS: *m/z* calcd for $C_{20}H_{29}N_2O_4S$ (M + H^+) 393.1848, found 393.1854.

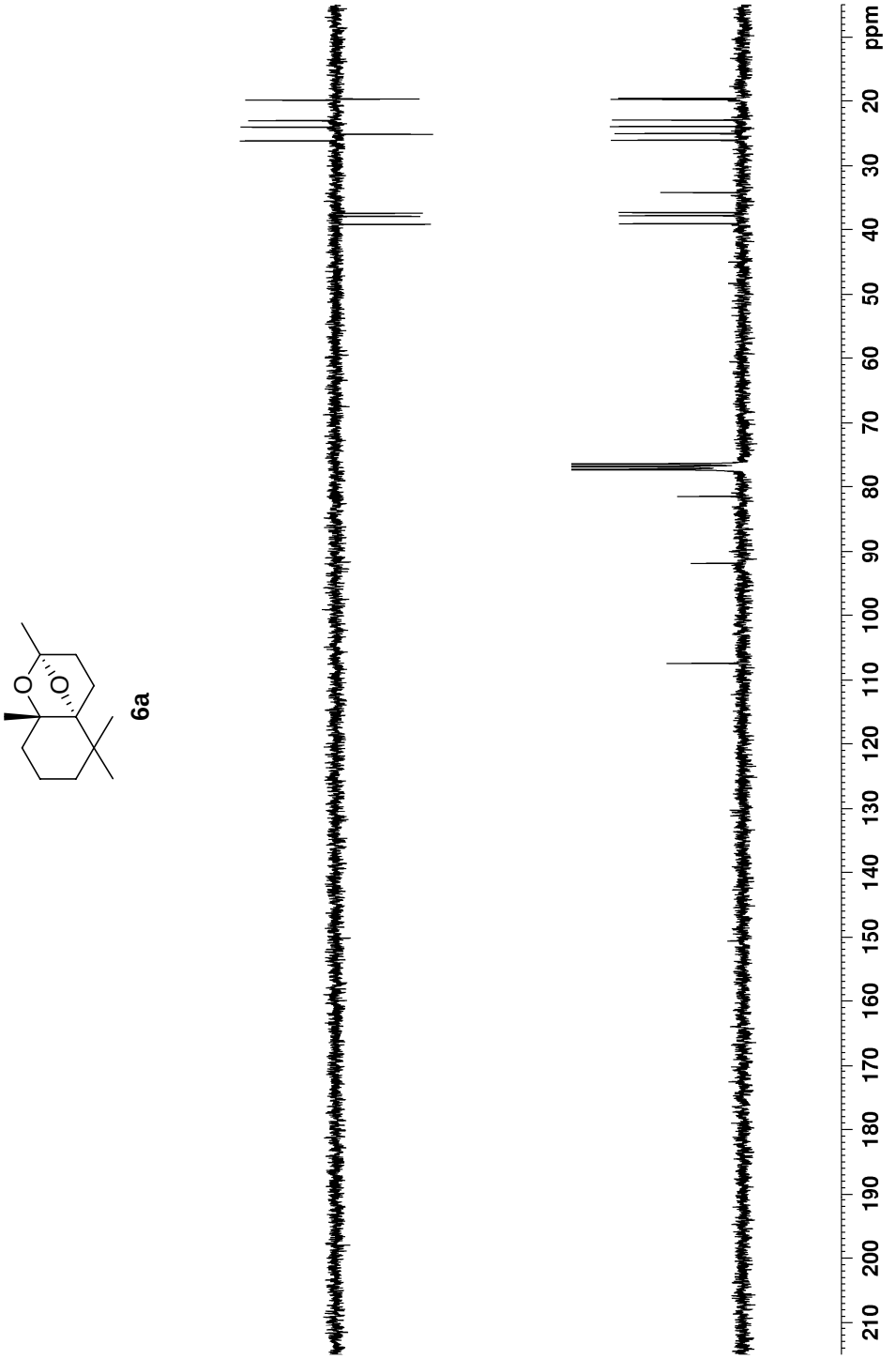
2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undec-4-ene (3).

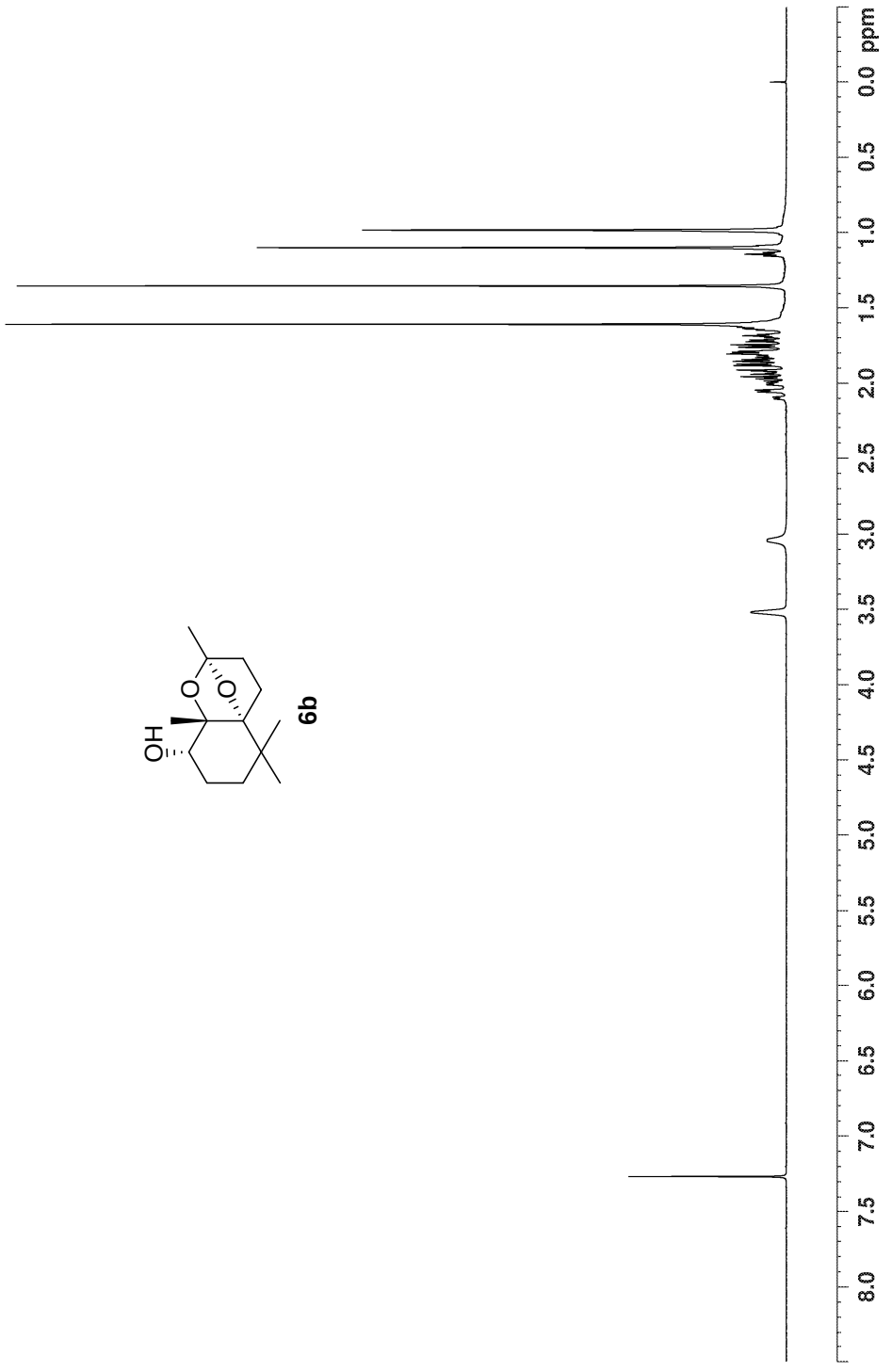


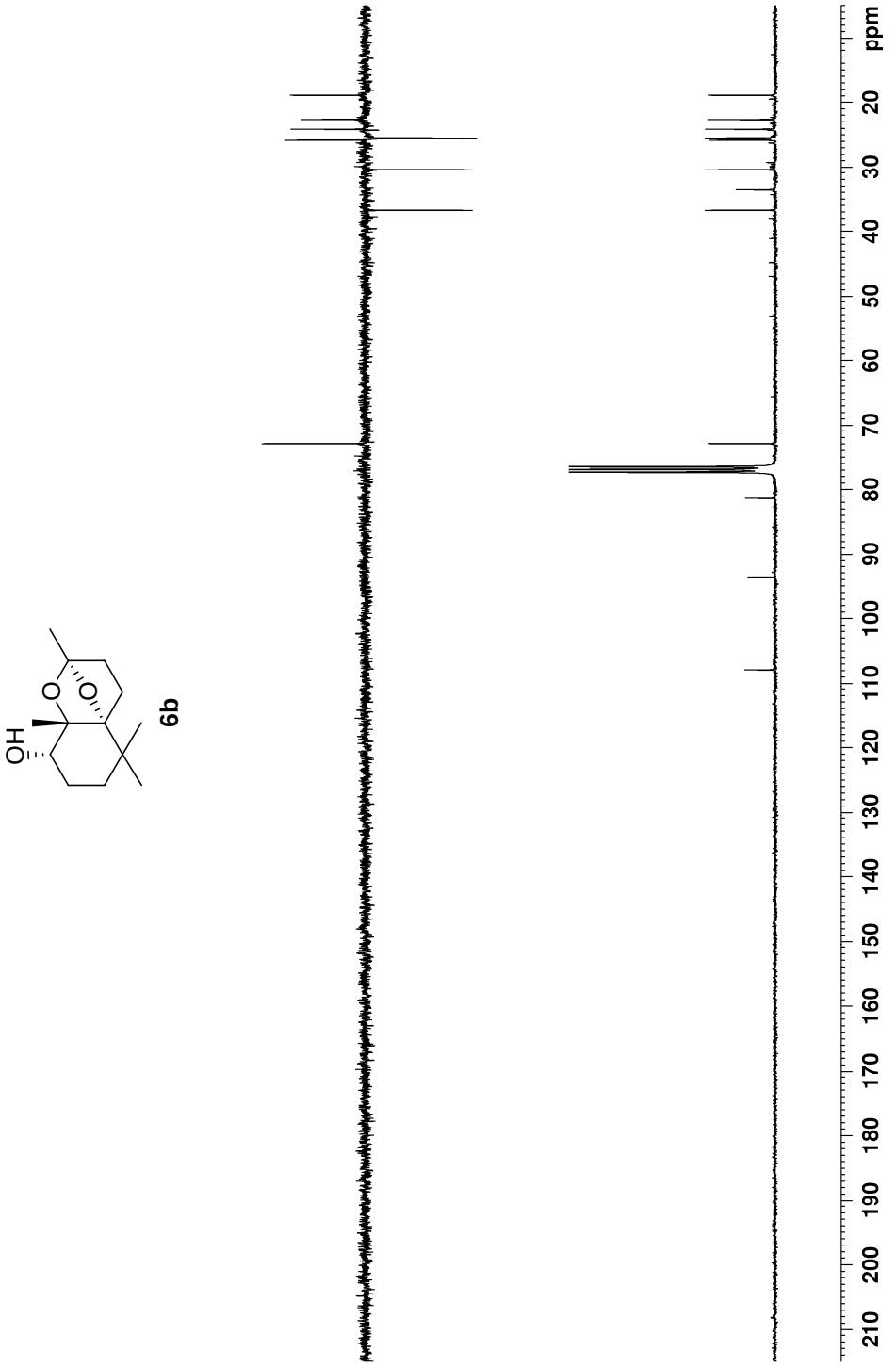
Colorless oil. IR (film): ν = 3020, 2972, 2939, 1473, 1394, 1165, 1055 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.52 (ddd, *J* = 10.2, 5.5, 2.2 Hz, 1H), 5.36 (dd, *J* = 10.2, 2.9 Hz, 1H), 2.28 (dt, *J* = 17.6, 2.2 Hz, 1H), 2.00-1.69 (m, 5H), 1.52 (s, 3H), 1.37 (s, 3H), 1.13 (s, 3H), 0.97 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 131.1, 123.6, 106.7, 91.5, 79.2, 37.6, 37.3, 33.1, 25.2, 24.15, 24.12, 23.9, 19.4.

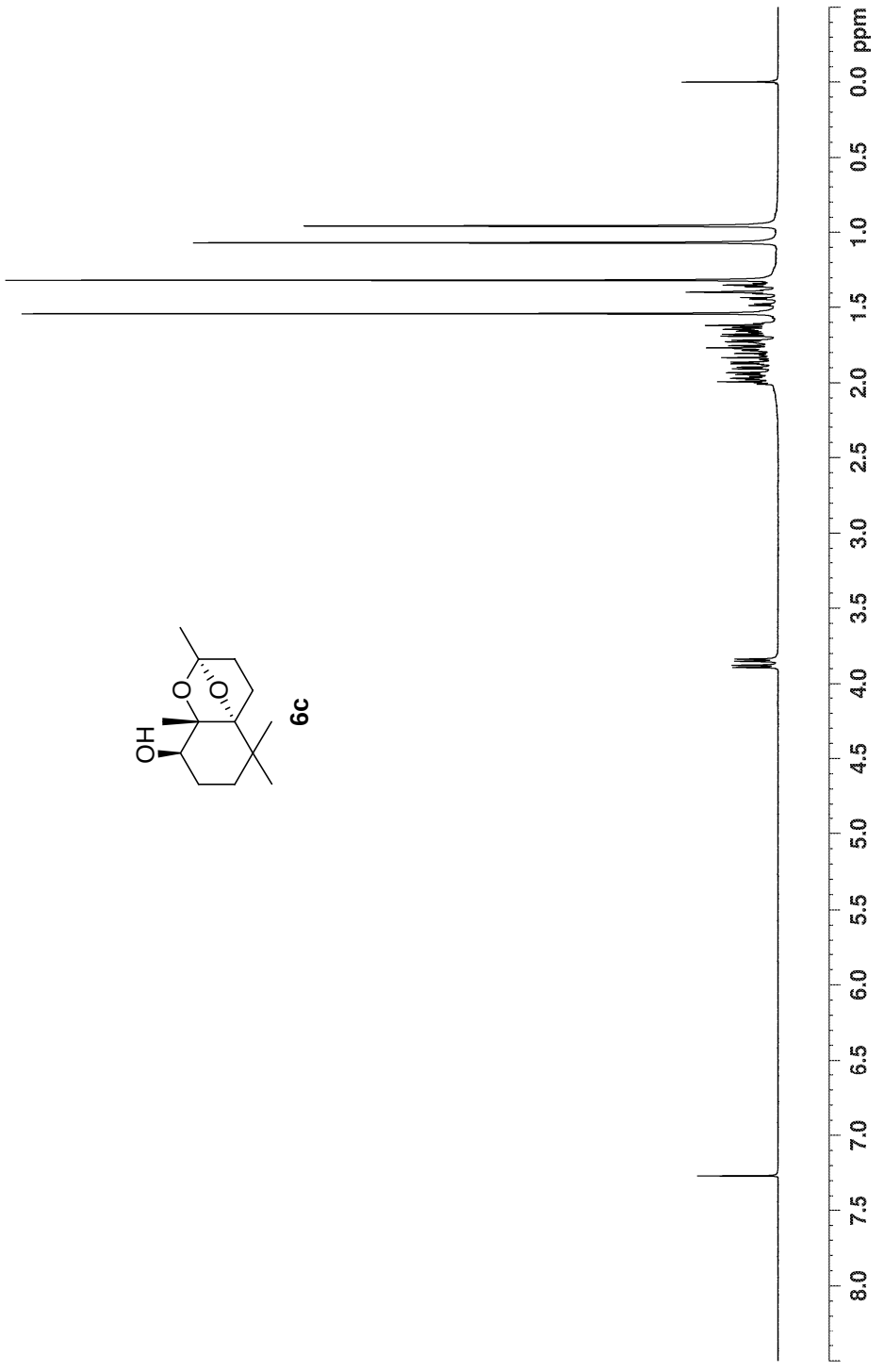
NMR SPECTRA

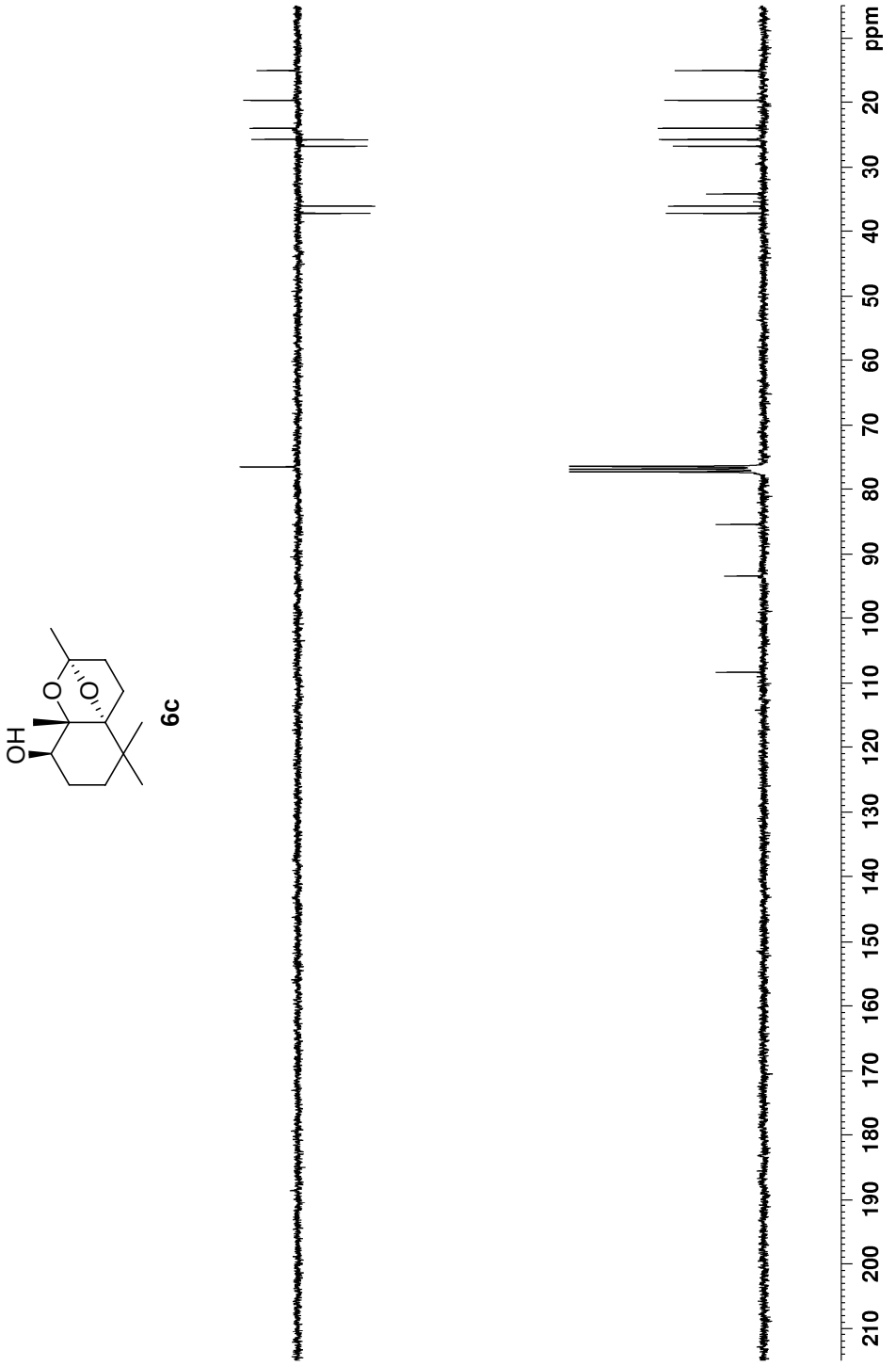


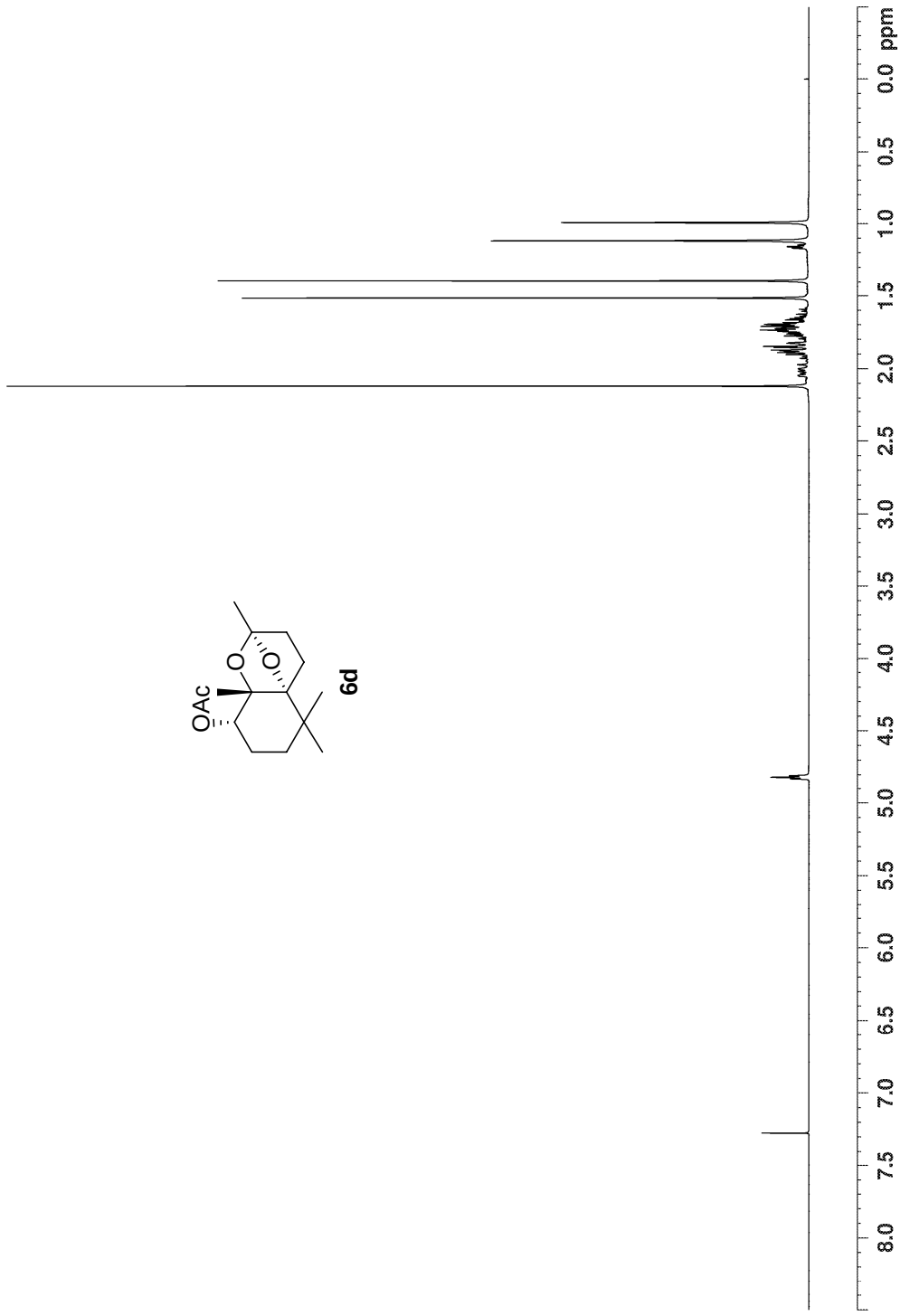

6a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

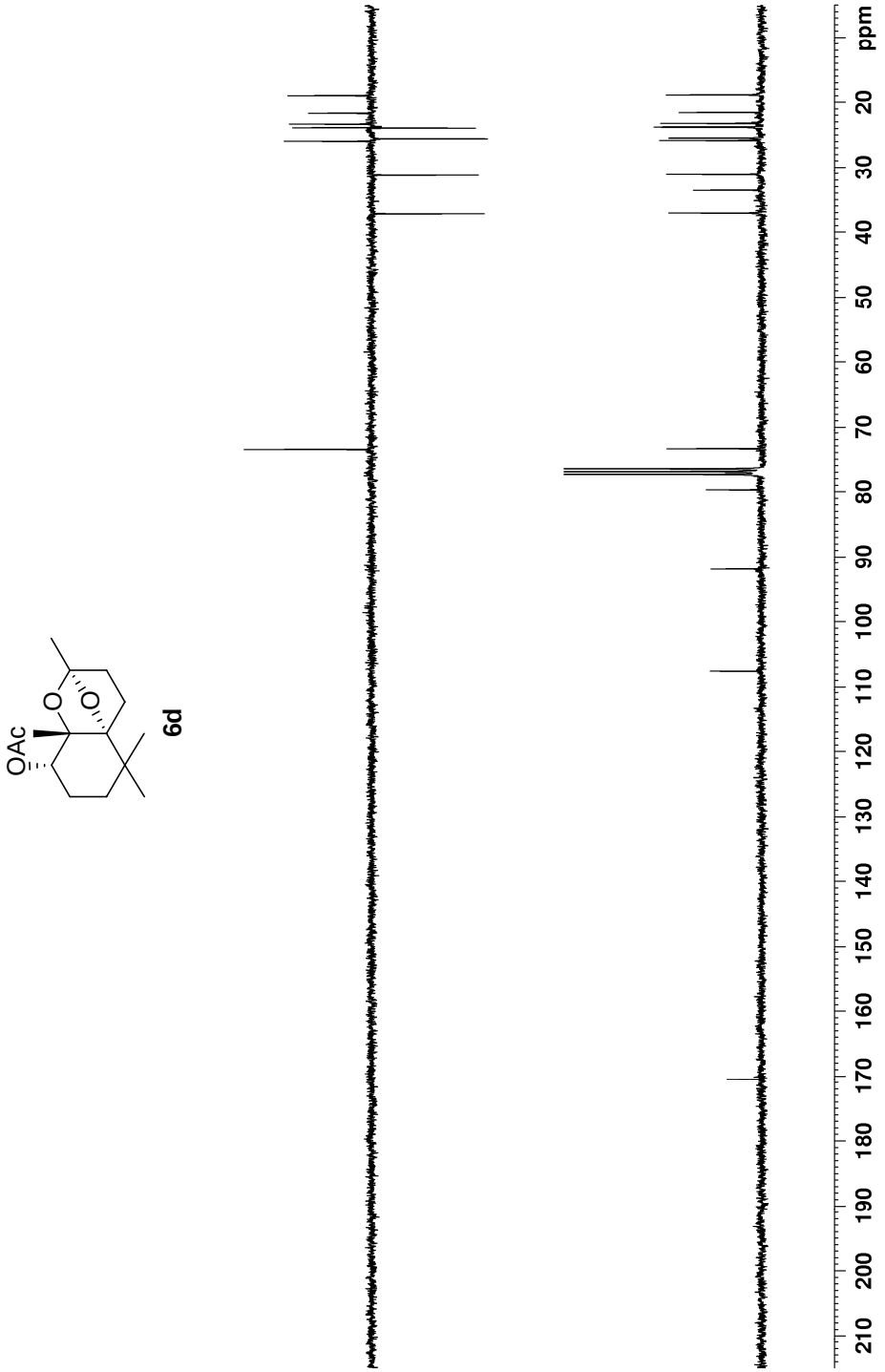

OH
O
O
6b
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

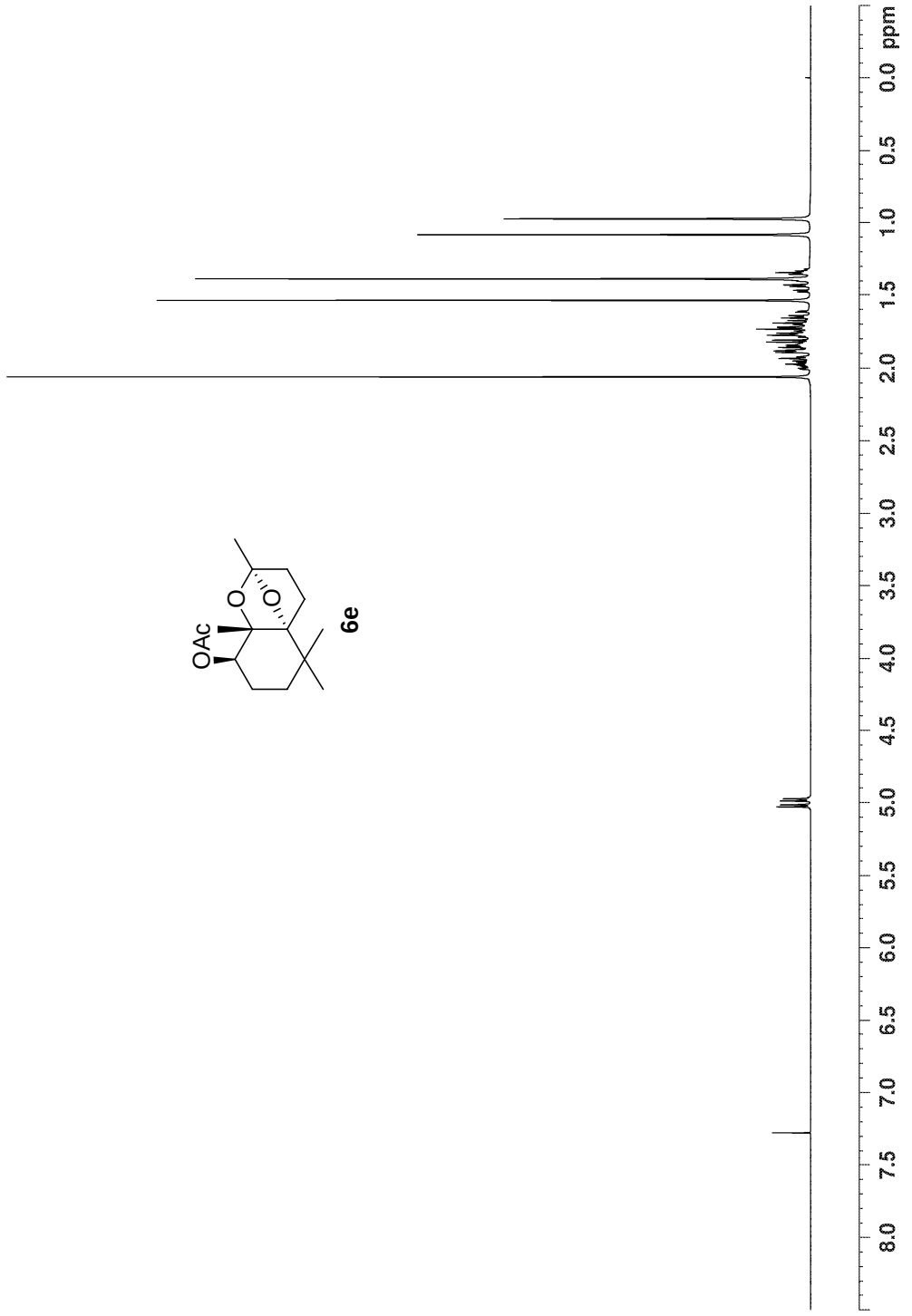

OH
O
O
6b
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

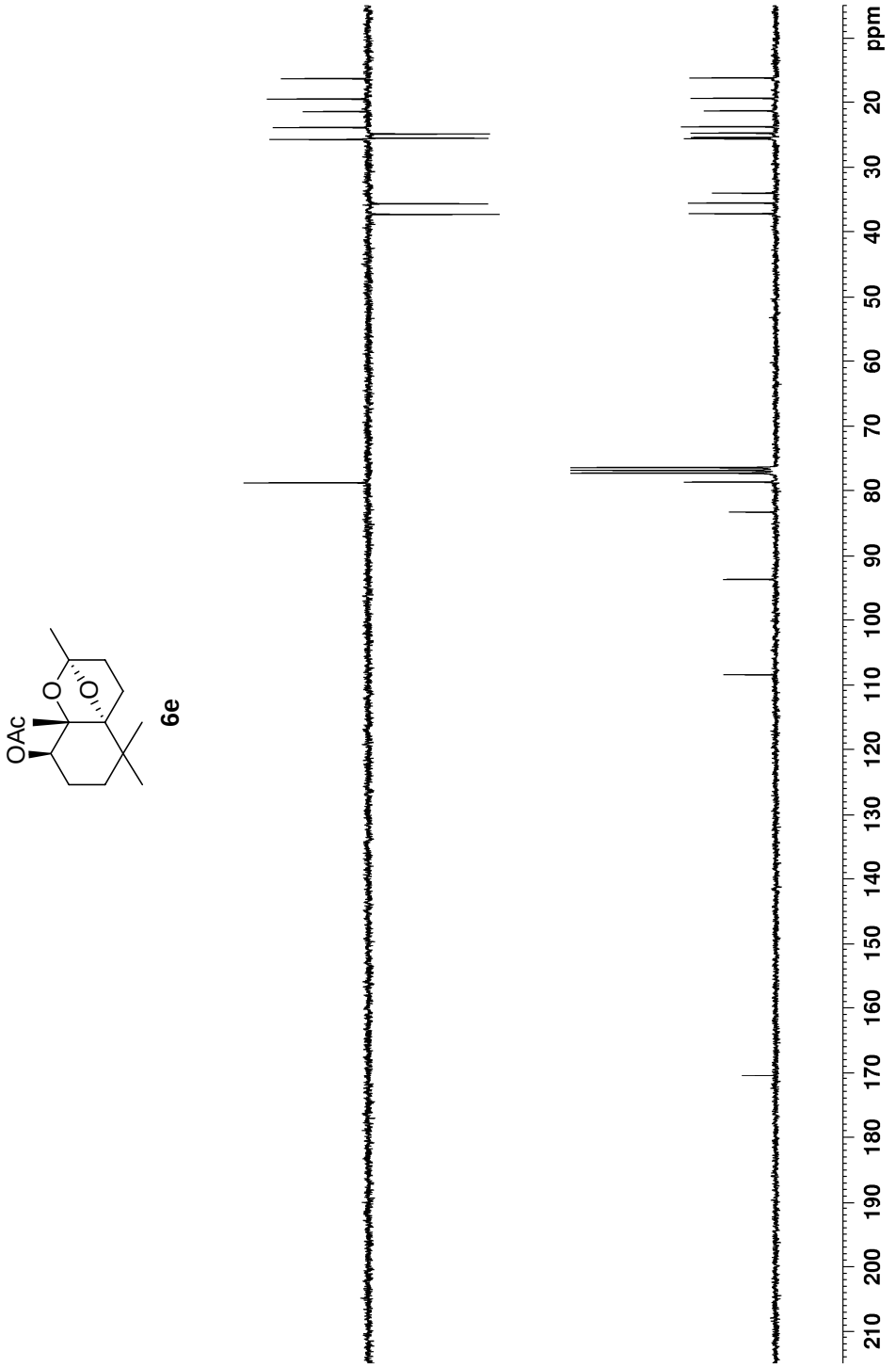

OH
O
O
6c
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

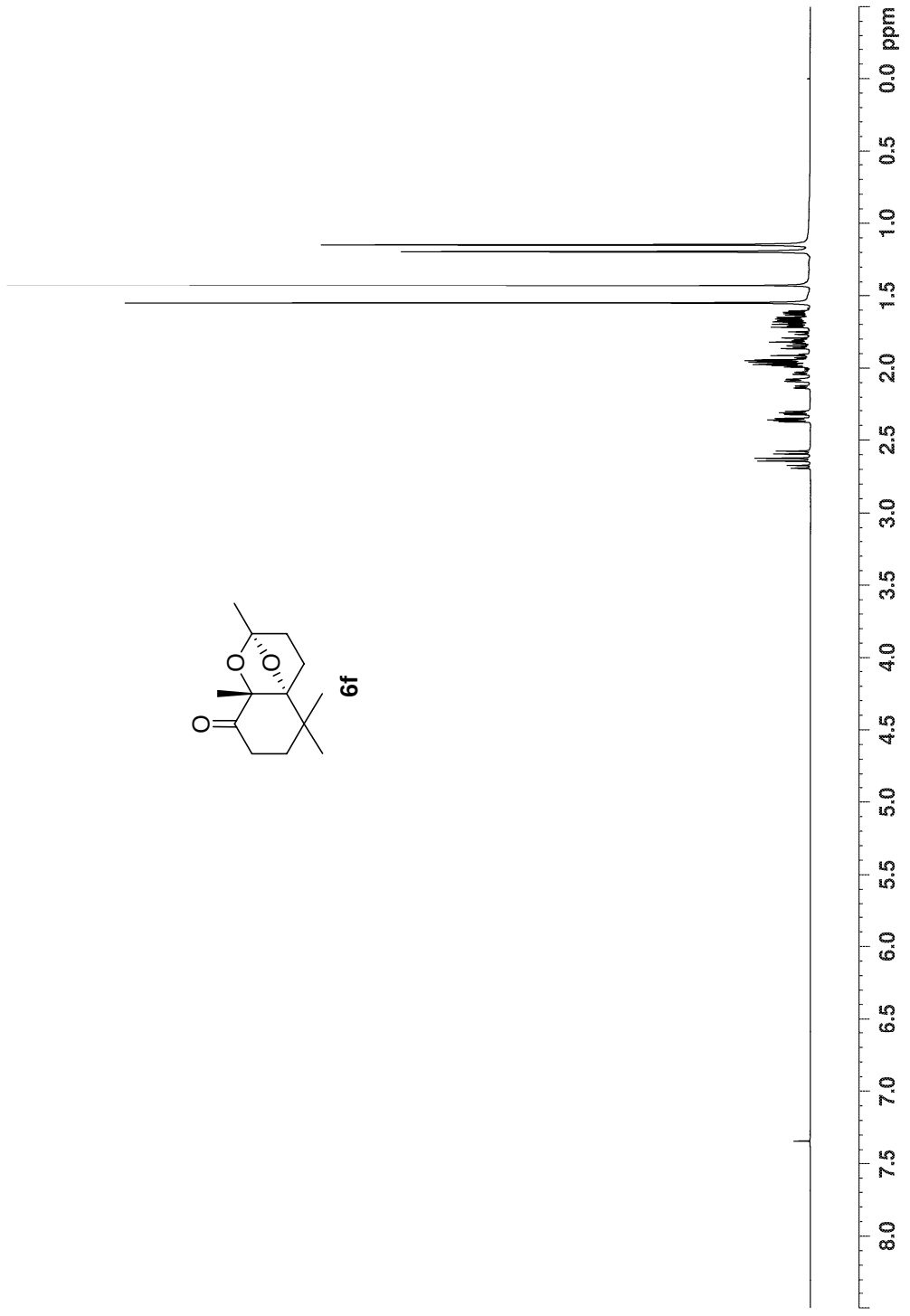

OH
O
O
6c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

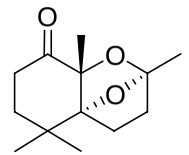

OAc
O
O
6d
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


OAc
O
O
6d
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

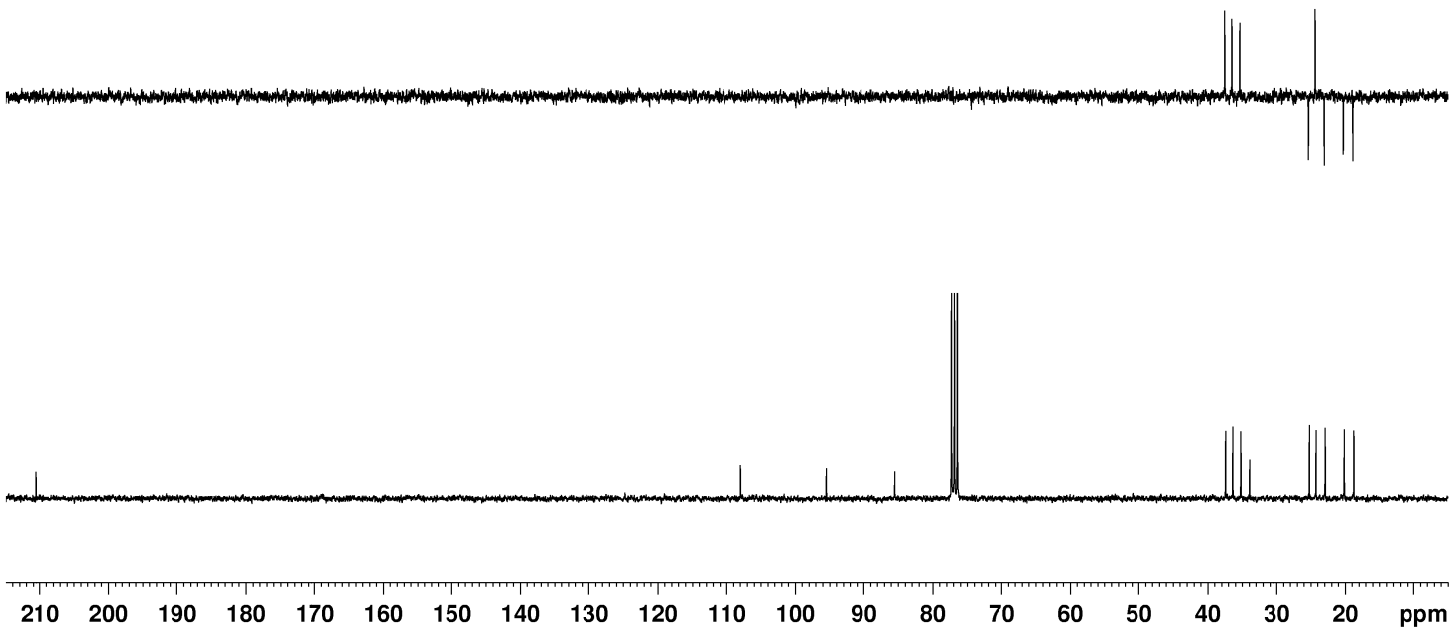

OAc
O
O
6e
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

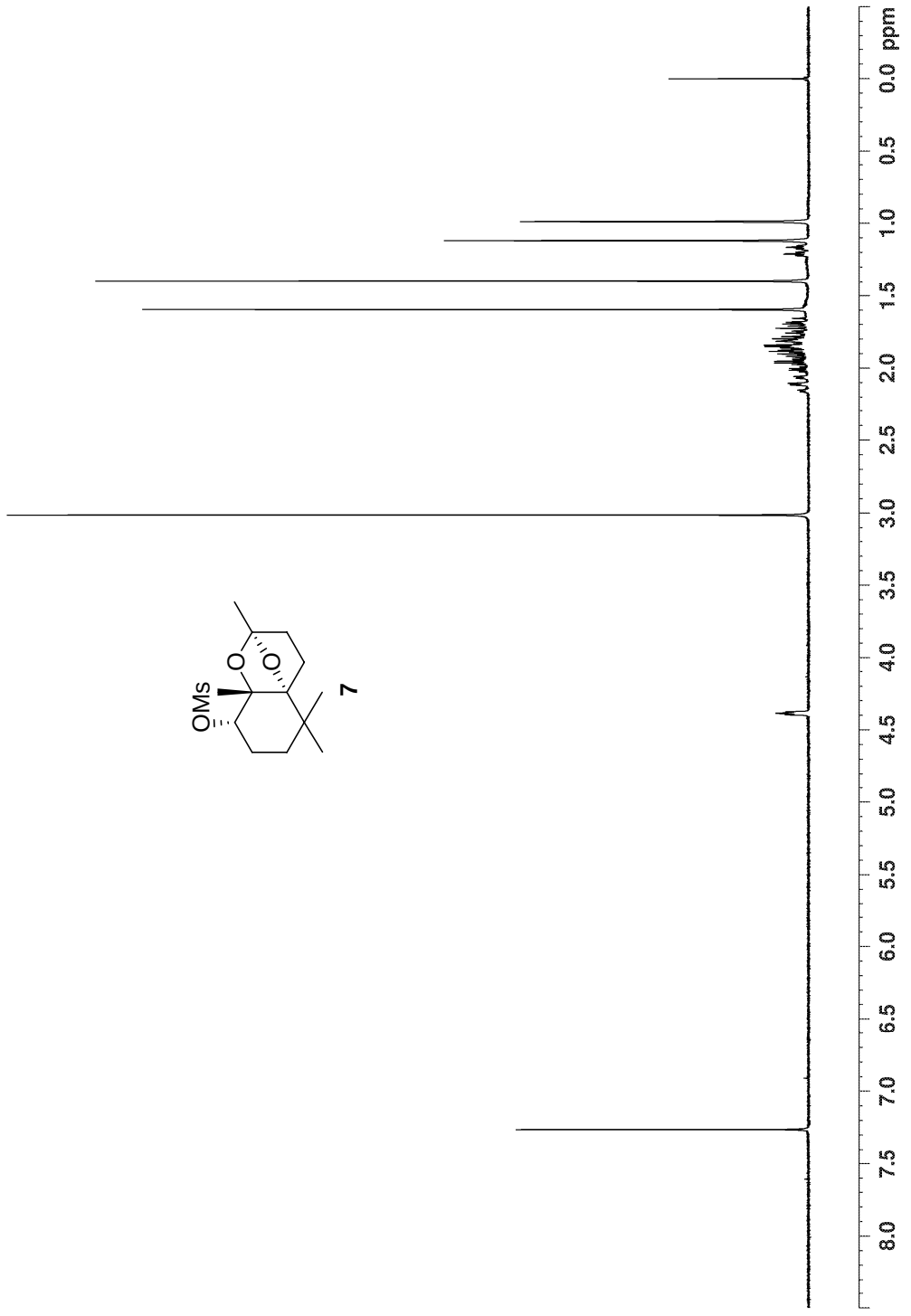

OAc
O
O
6e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

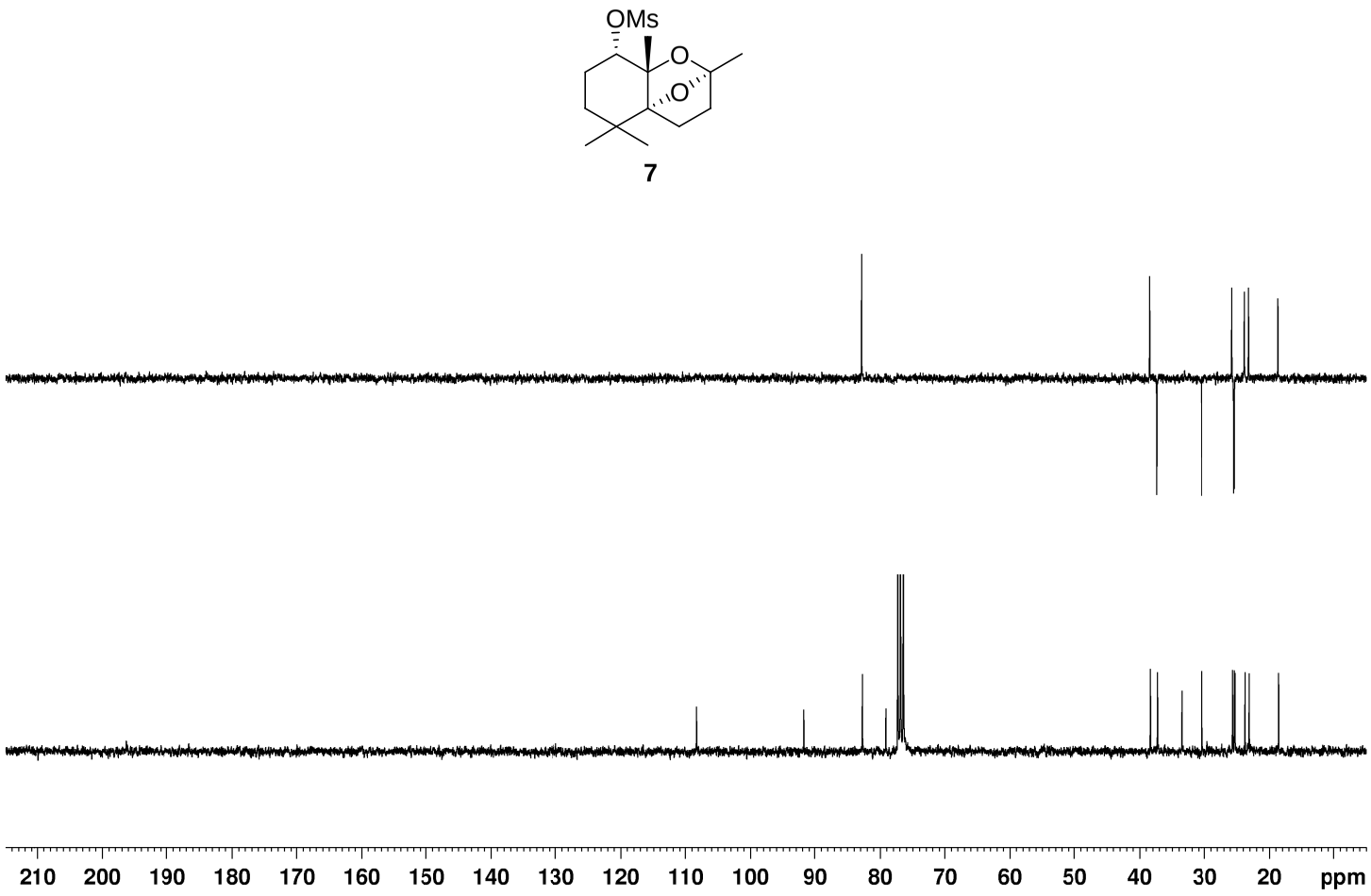

O
O
O
6f
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

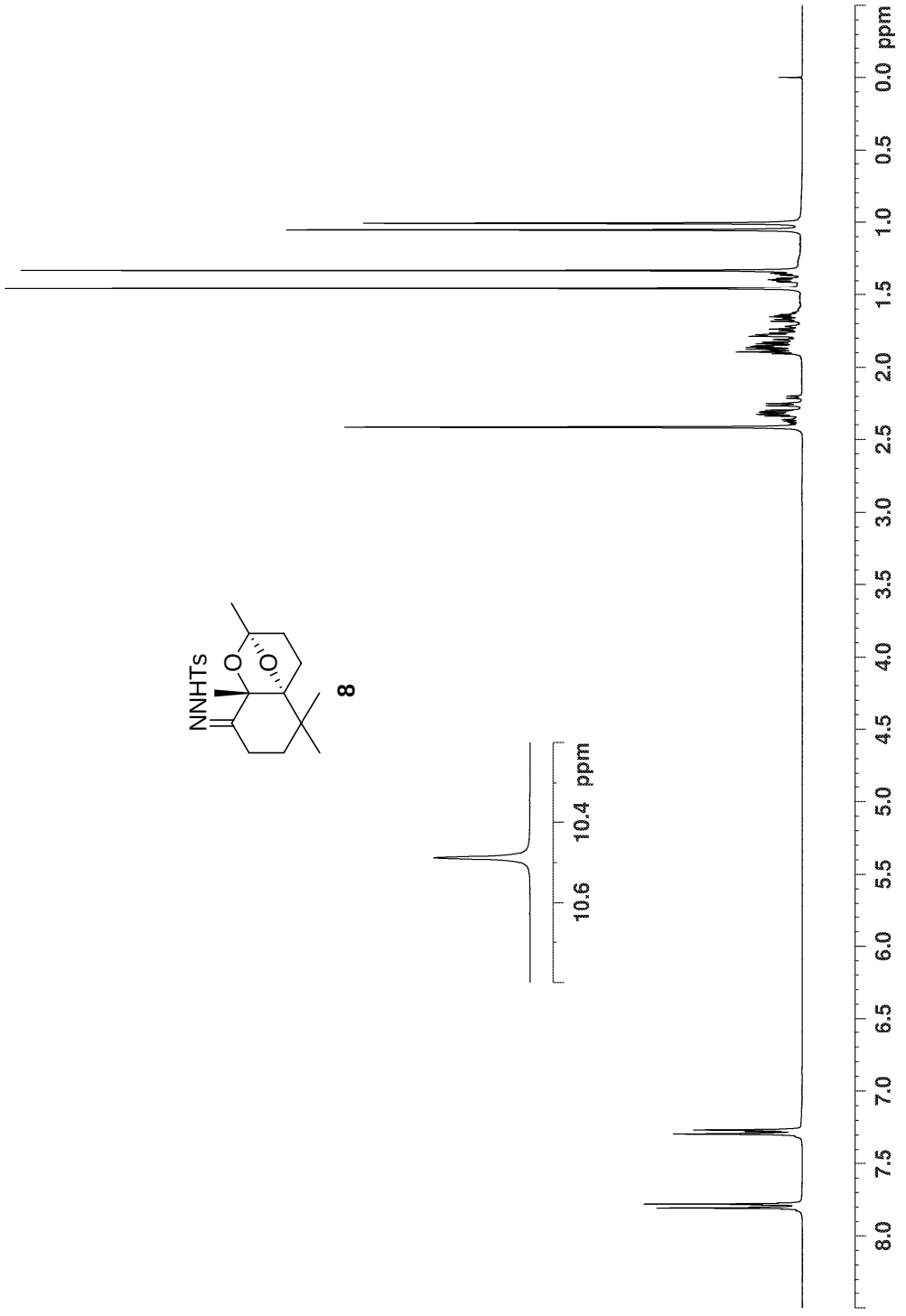

O
O
O

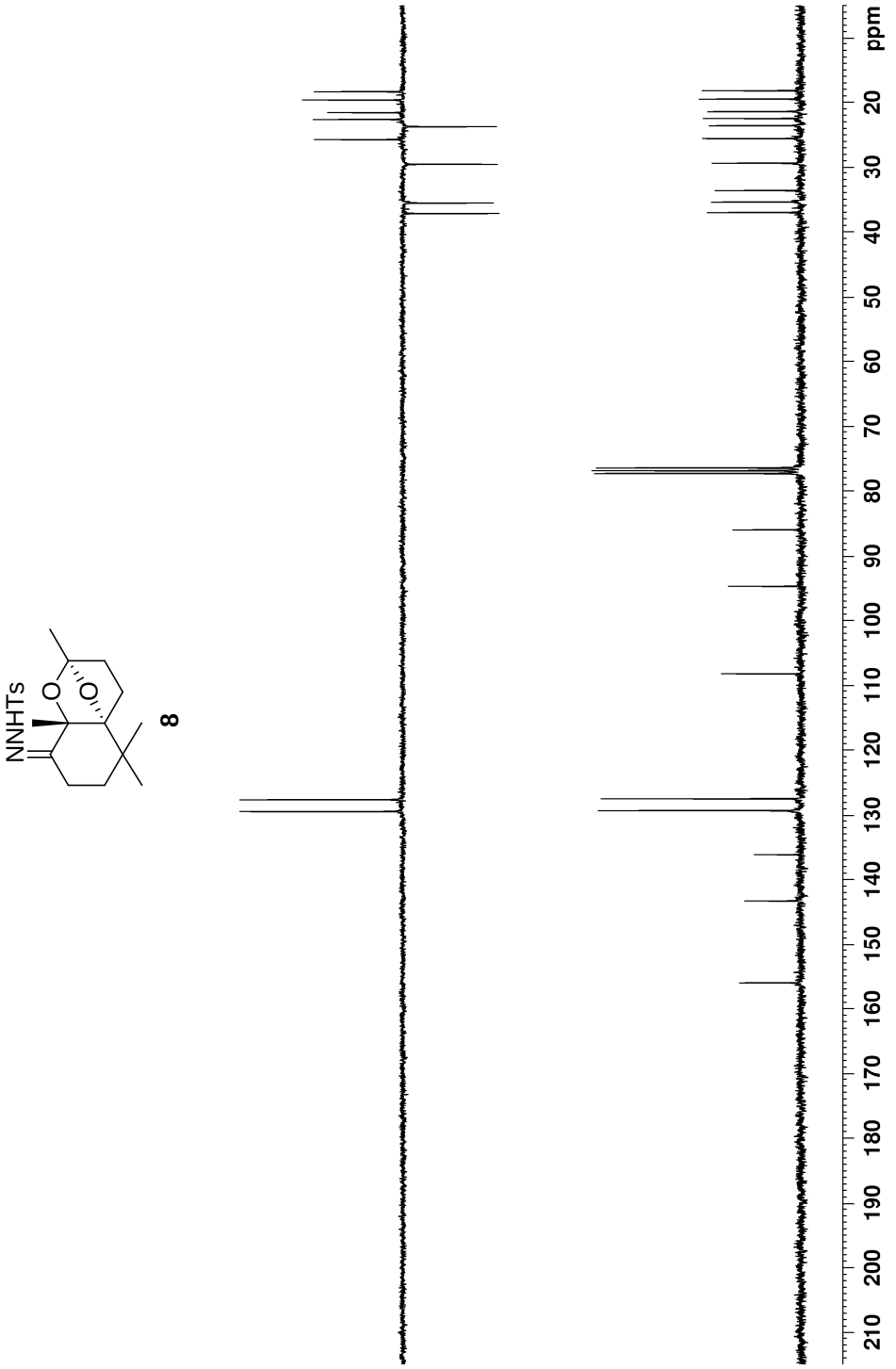
6f

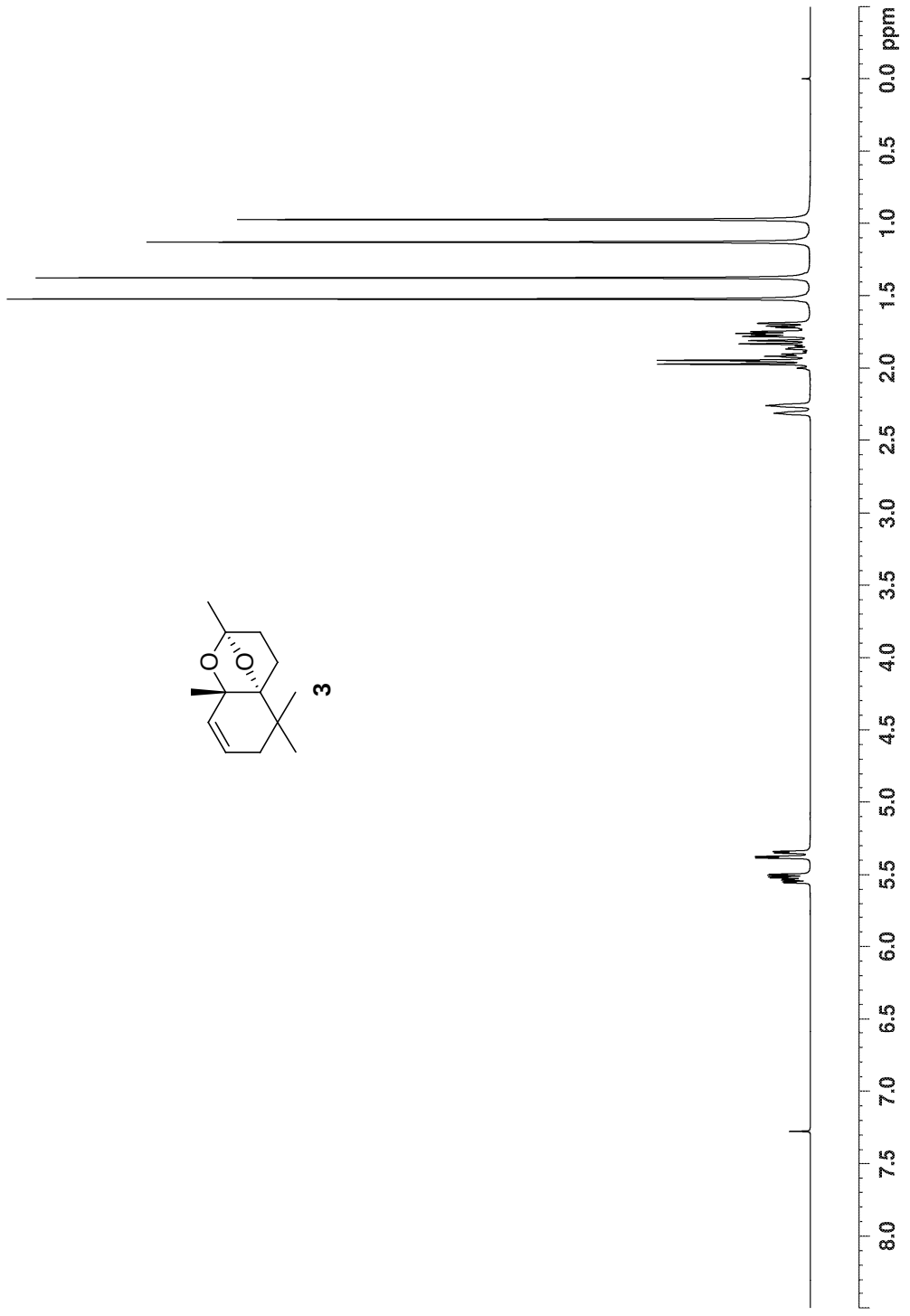

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

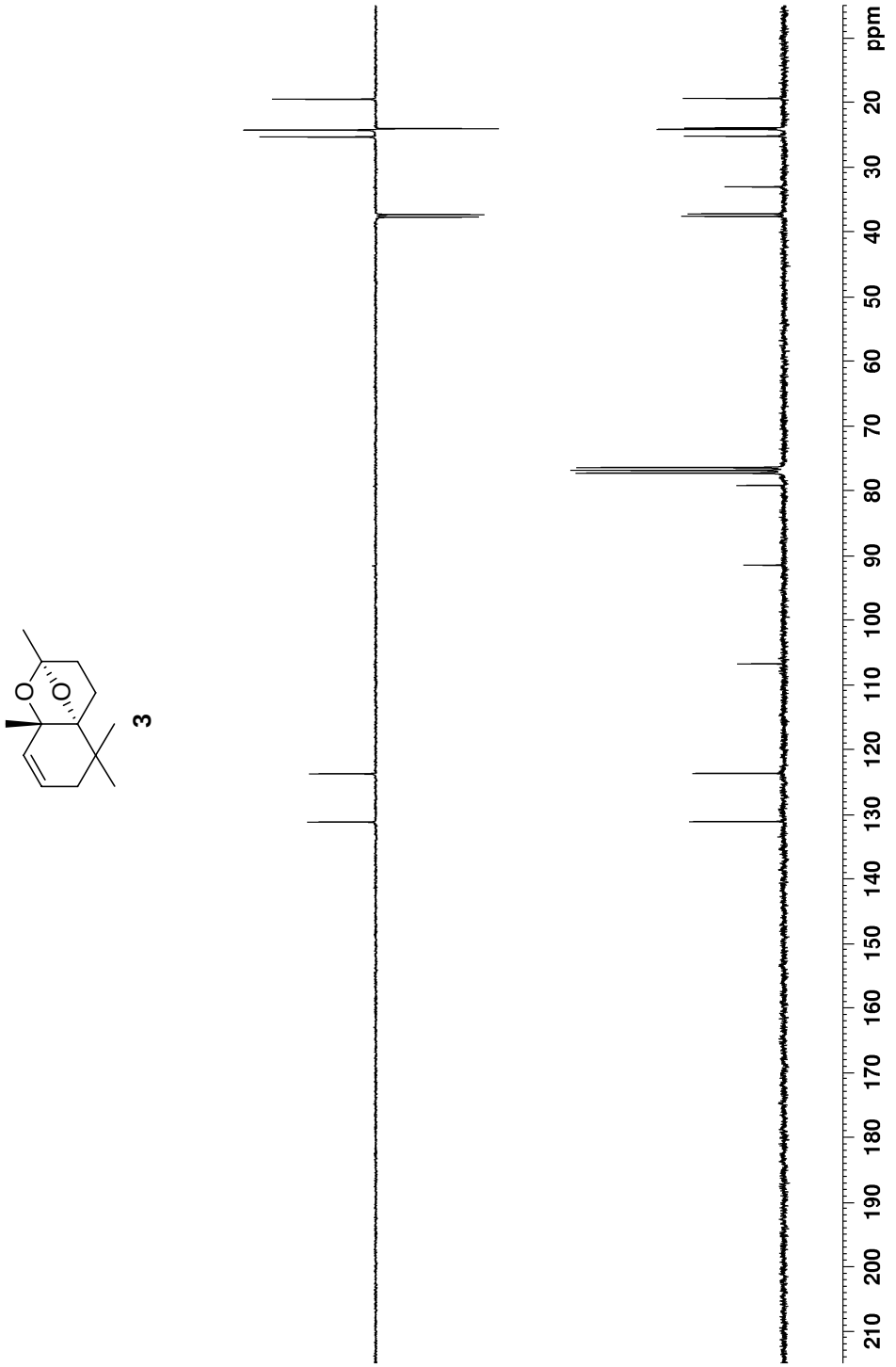

OMs
O
O
7
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


OMs
O
O
7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


NNHTs
O
O
8
10.6
10.4 ppm
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 ppm


NNHTs
O
O
8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


3
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
ppm


O
O
3
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210