Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Diastereotopic group selectivity and chemoselectivity of alkylidene carbene reactions on 8-oxabicyclo[3.2.1]oct-6-ene ring systems

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Supplementary Electronic Information

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General Experimental

Unless otherwise stated, all reactions were run under an argon atmosphere using dry solvents, and commercially available reagents were used as supplied. ^{n}BuLi was purchased as either 2.5 M or 1.6 M solutions in hexanes, and the solutions were titrated with menthol in the presence of 1-(biphenyl-4-yl)-3-phenyl-2-azapropene ("BLUE"). ^{t}BuOOH was prepared as a 3.3 M solution in toluene using a known literature procedure.[5] THF, Et_2O, CH_2Cl_2 and toluene were dried by passing through activated alumina columns. Iodoalkene **10**,[1] ketones **9a**[2] and **9b**[3] and aminoaziridine **15**[4] were prepared according to literature procedures. Analytical TLC was carried out on Merck 60 F245 aluminium backed silica plates. Short wave UV (245 nm) or vanillin solution were used to visualise components.

Flash chromatography was carried out using Merck silica gel 60.

^{1}H spectra were obtained on a Bruker AVIII 300 Spectrometer and a Bruker AVIII 400 Spectrometer at 300 and 400 MHz, respectively. ^{13}C spectra were obtained on a Bruker AVIII 400 Spectrometer and Bruker AV 400 Spectrometer at 100 MHz. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are reported in Hz and refer to $^{3}J_{H\text{-}H}$ unless otherwise stated. ^{1}H NMR are referenced to residual $CHCl_3$ at 7.26 ppm, and ^{13}C NMR to $CDCl_3$ at 77.2 ppm. nOe spectra were obtained on a Bruker AV 400 Spectrometer.

FTIR spectra were obtained as neat compounds using a Perkin Elmer Spectrum 100 FT-IR Spectrometer.

Mass spectra were recorded on a LCT spectrometer utilising electrospray ionisation (ES) (recorded in the positive mode) with a methanol mobile phase, or electron impact ionisation (EI), and are reported as (*m*/*z* (%)). HRMS were recorded on a LCT spectrometer using lock mass incorporated into the mobile phase.

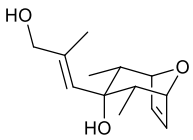
Melting points were determined using open glass capillaries on a Gallenkamp melting point apparatus and are uncorrected.

X-ray crystallography

Suitable crystals of **22** were selected and a dataset was measured by the EPSRC UK National Crystallography Service[6] on a Bruker KappaCCD diffractometer at the window of a Bruker FR591 rotating anode. The data collection was driven by COLLECT[7] and processed by DENZO[8] and an absorption correction was applied using SADABS[9] The structure was solved in SHELXS-97,[10] and was refined by a full-matrix least-squares procedure on F^2 in SHELXL-97.[5] All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms were added at calculated positions and refined by use of a riding model with isotropic displacement parameters based on the equivalent isotropic displacement parameter (U_{eq}) of the parent atom. Figures were produced using OLEX2.[11]

Experimental procedures and analytical data

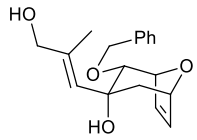
3-*exo*-((*E*)-3-Hydroxy-2-methylprop-1-en-1-yl)-2,4-*endo*,*endo*-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-ol (11a).



11a

To a solution of **10**[1c] (468 mg, 1.50 mmol) in THF (8 mL) at -78 °C, was added ^{n}BuLi (2.09 M in hexanes, 0.720 mL, 1.50 mmol) dropwise over 15 min. The reaction was stirred at -78 °C for 30 min before a solution of **9a**[2] (152 mg, 1.00 mmol) in THF (2 mL) was added. The reaction was allowed to warm to room temperature and was stirred at room temperature for 16 h before being quenched with NH_4Cl (15 mL of a saturated aqueous solution) and extracted with Et_2O (3 x 15 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was dissolved in THF (20 mL) and TBAF (1 M in THF, 1.20 mL, 1.20 mmol) was added. The reaction was stirred at room temperature for 16 h before being washed with H_2O (10 mL) and extracted with Et_2O (2 x 10 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 70:30→50:50) to afford **11a** (186 mg, 83%) as a white solid. m.p. 124-126 °C; R_f 0.20 (hexane/EtOAc 50:50); υ_{max} neat/cm^{-1} 3537, 3326, 2915, 1373, 1241, 1061, 1046, 930, 675; δ_H (400 MHz, $CDCl_3$) 0.86 (d, 6H, *J* 7.3 Hz, C*H*$_3$CH), 1.85 (d, 3H, *J* 0.7 Hz, =CC*H*$_3$), 1.90 (s, 1H, O*H*), 2.18 (qd, 2H, *J* 7.3, 3.5 Hz, CH$_3$C*H*), 3.92 (s, 2H, =CC*H*$_2$), 4.51 (d, 2H, *J* 3.5 Hz, =CHC*H*OCH), 5.02 (s, 1H, C=C*H*), 6.55 (s, 2H, =C*H*CHOCH); δ_C (100 MHz, $CDCl_3$) 11.2 (2 x CH_3, *C*H$_3$CH), 14.7 (CH_3, =C*C*H$_3$), 42.7 (2 x CH, CH$_3$*C*H), 69.9 (CH_2, =C*C*H$_2$), 78.1 (C, *C*OH), 82.7 (2 x CH, =CH*C*HOCH), 130.8 (CH, C=*C*H), 135.9 (2 x CH, =*C*HCHOCH), 136.4 (C, *C*=CH); *m/z* HRMS (ES) calcd for $C_{13}H_{20}NaO_3^+$ 247.1310, found 247.1307; (ES) 233 (11%), 247 ([M+Na]$^+$, 100).

(±)-(1*S*,2*R*,3*R*,5*S*)-2-Benzyloxy-3-((*E*)-3-hydroxy-2-methylprop-1-en-1-yl)-8-oxabicyclo[3.2.1]oct-6-en-3-ol (11b).

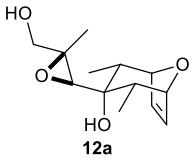


11b

To a solution of **10**[1c] (2.04 g, 6.53 mmol) in THF (43 mL) at -78 °C was added ^{n}BuLi (1.41 M in hexanes, 4.63 mL, 6.53 mmol) dropwise over 15 min. The resulting mixture was stirred at -78 °C for 30 min before a solution of **9b**[3] (1.00 g, 4.35 mmol) in THF (9 mL) was added. The reaction was allowed to warm to room temperature and was stirred at room temperature for 24 h before being quenched with NH_4Cl (30 mL of a saturated aqueous solution) and extracted with Et_2O (3 x 25 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was dissolved in THF (43 mL) and TBAF (1 M in THF, 5.20 mL, 5.20 mmol) was added. The reaction was stirred at room temperature for 18 h before being washed with H_2O (25 mL) and extracted with Et_2O (3 x 25 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 40:60) to afford **11b** (858 mg, 62%) as a yellow solid. m.p. 52-54 °C; R_f 0.14 (hexane/EtOAc 40:60); υ_{max} neat/cm^{-1} 3443, 2940, 2873, 1454, 1314, 1053, 884, 731, 696; δ_H (400 MHz, $CDCl_3$) 1.79 (d, 3H, ^4J 1.2 Hz, =CC*H*$_3$), 1.90 (dd, 1H, ^2J 14.6 Hz, *J* 0.9 Hz, =CHCHC*H*$_{2eq}$), 2.03 (dd, 1H, ^2J 14.6 Hz, *J* 4.5 Hz, =CHCHC*H*$_{2ax}$), 3.00 (s, 1H, O*H*), 3.76 (d, 1H, *J* 4.4 Hz, =CHCHC*H*), 3.87 (d, 2H, ^4J 0.8 Hz, =CC*H*$_2$), 4.62 (d, 1H, ^2J 12.0 Hz, C*H*$_2$O), 4.64-4.68 (m, 2H, =CHC*H*CH, C*H*$_2$O), 4.74 (br d, 1H, *J* 4.5 Hz, =CHC*H*CH$_2$), 5.35 (m, 1H, C=C*H*), 6.26 (dd, 1H, *J* 6.2, 1.7 Hz, =C*H*CHCH), 6.32 (dd, 1H, *J* 6.1, 1.7 Hz, =C*H*CHCH$_2$), 7.25-7.40 (m, 5H, *H*$_{Ar}$); δ_C (100 MHz, $CDCl_3$) 14.6 (CH_3, =C*C*H$_3$), 38.3 (CH_2, =CHCH*C*H$_2$), 69.2 (CH_2, =C*C*H$_2$), 72.8 (CH_2, *C*H$_2$O), 73.4 (C, *C*OH), 78.2 (CH, =CH*C*HCH), 78.8 (CH, =CH*C*HCH$_2$), 78.8 (CH, =CHCH*C*H), 128.3 (3 x CH, *C*H$_{Ar}$), 128.6 (2 x CH, *C*H$_{Ar}$), 130.9 (CH, =*C*HCHCH), 134.3 (CH, C=*C*H), 135.8 (CH, =*C*HCHCH$_2$),

136.2 (C, *C*=CH), 137.8 (C, *C*CH_{Ar}); *m/z* HRMS (ES) calcd for $C_{18}H_{22}NaO_4^+$ 325.1416, found 325.1411; (ES) 325 ($[M+Na]^+$, 100%).

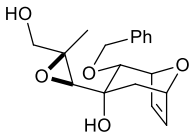
(±)-(1*R*,2*S*,3*S*,4*R*,5*S*)-3-(3-Hydroxymethyl-3-methyloxiran-2-yl)-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-ol (12a).



12a

To a solution of **11a** (50 mg, 0.220 mmol) and $VO(acac)_2$ (1.20 mg, 4.4 µmol) in CH_2Cl_2 (3 mL) at room temperature, was added ^tBuOOH[5] (3.3 M in toluene, 0.200 mL, 0.670 mmol) dropwise over 10 min. The reaction was stirred for 6 h at room temperature. Upon complete conversion, the reaction was purified by column chromatography (hexane/EtOAc 50:50) to afford **12a** (53mg, 100%) as a white solid. m.p. 94-96 °C; R_f 0.15 (hexane/EtOAc 50:50); υ_{max} neat/cm^{-1} 3394, 2958, 2928, 2873, 1450, 1344, 1078, 1051, 933, 833, 670; δ_H (400 MHz, $CDCl_3$) 0.89 (d, 3H, *J* 7.3 Hz, C*H*$_3$CH), 1.00 (d, 3H, *J* 7.3 Hz, C*H*$_3$CH), 1.48 (s, 3H, C*H*$_3$CO), 1.76 (s, 1H, O*H*), 1.92 (br s, 1H, O*H*), 2.15 (qd, 1H, *J* 7.3, 3.7 Hz, CH_3C*H*), 2.30 (qd, 1H, *J* 7.3, 3.6 Hz, CH_3C*H*), 2.76 (s, 1H, C*H*OC), 3.48-3.58 (m, 2H, OCC*H*$_2$), 4.46 (dd, 1H, *J* 3.6, 1.7 Hz, =CHC*H*OCH), 4.49 (dd, 1H, *J* 3.6, 1.7 Hz, =CHC*H*OCH), 6.43 (dd, 1H, *J* 6.1, 1.7 Hz, =C*H*), 6.47 (dd, 1H, *J* 6.1, 1.7 Hz, =C*H*); δ_C (100 MHz, $CDCl_3$) 11.4 (CH_3, *C*H_3CH), 11.5 (CH_3, *C*H_3CH), 15.3 (CH_3, *C*H_3CO), 38.2 (CH, CH_3*C*H), 42.7 (CH, CH_3*C*H), 60.1 (C, *C*OCH), 66.2 (CH_2, *C*H_2CO), 66.8 (CH, CO*C*H), 73.4 (C, *C*OH), 82.6 (CH, =CH*C*HOCH), 82.7 (CH, =CH*C*HOCH), 134.7 (CH, =*C*H), 134.9 (CH, =*C*H); *m/z* HRMS (ES) calcd for $C_{13}H_{20}NaO_4^+$ 263.1259, found 263.1268; (ES) 263 ($[M+Na]^+$, 100%).

(±)-(1*S*,2*R*,3*S*,5*S*)-2-Benzyloxy-3-((2*R*,3*R*)-3-hydroxymethyl-3-methyloxiran-2-yl)-8-oxabicyclo[3.2.1]oct-6-en-3-ol (12b).

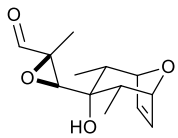


12b

To a solution of **11b** (621 mg, 2.06 mmol) and $VO(acac)_2$ (26.4 mg, 0.10 mmol) in CH_2Cl_2 (30 mL) at room temperature was added ^tBuOOH[5] (3.3 M in toluene, 1.87 mL, 6.18 mmol) dropwise over 10 min. The reaction was stirred for 6 h at room temperature. Upon complete conversion the reaction was partially concentrated and purified by column chromatography (petrol/EtOAc 40:60) to afford **12b** (446 mg, 68%, 9:1 d.r.) as a clear, pale yellow oil. Analytically pure **12b** can be isolated in 49% yield from the crude reaction mixture as a white solid. Analytical data for **12b**. m.p. 109-112 °C; R_f 0.26 (petrol/EtOAc 40:60); υ_{max} neat/cm^{-1} 3476, 3405, 2945, 2929, 1457, 1052, 982, 882, 741, 720, 682; δ_H (400 MHz, $CDCl_3$) 1.49 (s, 3H, C*H*$_3$CO), 1.69 (d, 1H, ^2J 14.4 Hz, =CHCHC*H*$_{2eq}$), 1.97 (dd, 1H, ^2J 14.4 Hz, J 4.5 Hz, =CHCHC*H*$_{2ax}$), 2.81 (s, 1H, C*H*OC), 2.92 (br s, 1H, O*H*), 3.58 (ABq, 2H, ^2J 12.3 Hz, C*H*$_2$CO), 3.75 (d, 1H, J 4.4 Hz, =CHCHC*H*), 4.63 (dd, 1H, J 4.4, 1.6 Hz, =CHC*H*CH), 4.69 (d, 1H, ^2J 11.7 Hz, C*H*$_2$O), 4.74 (br d, 1H, J 4.5 Hz, =CHC*H*CH$_2$), 4.81 (d, 1H, ^2J 11.7 Hz, C*H*$_2$O), 6.25 (dd, 1H, J 6.1, 1.6 Hz, =C*H*CHCH), 6.30 (dd, 1H, J 6.1, 1.6 Hz, =C*H*CHCH$_2$), 7.28-7.50 (m, 5H, *H*$_{Ar}$); δ_C (100 MHz, $CDCl_3$) 14.1 (CH$_3$, *C*H$_3$CO), 33.8 (CH$_2$, =CHCH*C*H$_2$), 60.7 (C, CHO*C*), 65.7 (CH$_2$, *C*H$_2$CO), 66.0 (CH, *C*HOC), 70.0 (C, *C*OH), 73.0 (CH$_2$, C*H*$_2$O), 78.2 (2 x CH, =CH*C*HCH$_2$, =CH*C*HCH), 79.3 (CH, =CHCH*C*H), 128.3 (3 x CH, *C*H$_{Ar}$), 128.7 (2 x CH, *C*H$_{Ar}$), 131.1 (CH, =*C*HCHCH), 135.2 (CH, =*C*HCHCH$_2$), 137.9 (C, *C*CH$_{Ar}$); *m*/*z* HRMS (ES) calcd for $C_{18}H_{22}NaO_5^+$ 341.1365, found 341.1370; (ES) 341 ([M+Na]$^+$, 100%), 342 ([M+Na+H]$^+$, 17). Peaks in ^{1}H NMR in 9:1 mixture assignable to minor isomer: 1.46 (s, 3H, C*H*$_3$CO), 1.85 (d, ^2J 14.5 Hz, =CHCHC*H*$_{2eq}$), 2.13 (dd, 1H, ^2J 14.5 Hz, J 4.2 Hz, =CHCHC*H*$_{2ax}$), 2.90 (s, 1H, C*H*OC), 3.50-3.63 (m, 2H, C*H*$_2$CO), 3.78 (d, 1H, J 4.3 Hz, =CHCHC*H*), 4.68-4.75 (m, 3H,

=CHC*H*CH, C*H*$_2$O), 4.81 (br d, 1H, *J* 4.4 Hz, =CHC*H*CH$_2$), 6.30 (dd, 1H, *J* 6.1, 1.6 Hz, =C*H*CHCH), 6.35 (dd, 1H, *J* 6.1, 1.6 Hz, =C*H*CHCH$_2$), 7.31-7.44 (m, 5H, *H*$_{Ar}$).

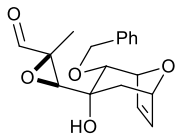
(±)-3-((1*R*,2*S*,3*S*,4*R*,5*S*)-3-Hydroxy-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-2-methyloxirane-2-carbaldehyde (13a).



13a

To a solution of **12a** (833 mg, 3.47 mmol) in CH_2Cl_2 (43 mL) at room temperature, was added $NaHCO_3$ (2.92 g, 34.7 mmol). The resulting solution was stirred for 30 min before being cooled to 0 °C. DMP (2.21 g, 5.21 mmol) was added to the reaction, and the mixture was warmed to room temperature and stirred for 2.5 h. Upon completion, ice cold $NaHCO_3$ (20 mL of a saturated aqueous solution) was added, followed by $Na_2S_2O_3$ (20 mL of a saturated aqueous solution), and the reaction mixture extracted with CH_2Cl_2 (3 x 25 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 75:25) to afford **13a** (741 mg, 90%) as a white solid. m.p. 83-85 °C; R_f 0.58 (hexane/EtOAc 50:50); υ_{max} neat/cm^{-1} 3571, 2967, 2826, 1725, 1086, 1048, 935, 837, 741; δ_H (400 MHz, $CDCl_3$) 0.88 (d, 3H, *J* 7.3 Hz, C*H*$_3$CH), 1.05 (d, 3H, *J* 7.3 Hz, C*H*$_3$CH), 1.63 (s, 3H, C*H*$_3$CO), 1.75 (s, 1H, O*H*), 2.13 (qd, 1H, *J* 7.3, 3.6 Hz, CH$_3$C*H*), 2.39 (qd, 1H, *J* 7.3, 3.6 Hz, CH$_3$C*H*), 2.75 (s, 1H, C*H*OC), 4.51 (dd, 2H, *J* 3.6, 1.5 Hz, =CHC*H*OCH), 6.49 (app. qd, 2H, *J* 6.1, 1.5 Hz, =C*H*), 8.81 (s, 1H, C*H*O); δ_C (100 MHz, $CDCl_3$) 10.9 (CH$_3$, *C*H$_3$CO), 11.4 (2 x CH$_3$, *C*H$_3$CH), 38.4 (CH, CH$_3$*C*H), 42.6 (CH, CH$_3$*C*H), 61.4 (C, CO*C*H), 66.1 (CH, *C*HOC), 73.9 (C, *C*OH), 82.4 (CH, =CH*C*HOCH), 82.5 (CH, =CH*C*HOCH), 134.9 (CH, =*C*H), 135.3 (CH, =*C*H), 200.1 (CH, *C*HO); *m/z* HRMS (ES) calcd for $C_{13}H_{18}NaO_4^+$ 261.1103, found 261.1109; (ES) 261 ([M+Na]$^+$, 6%), 293 ([M+Na+MeOH]$^+$, 100).

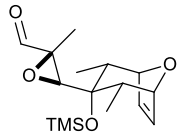
(±)-(2*S*,3*R*)-3-((1*S*,2*R*,3*S*,5*S*)-2-Benzyloxy-3-hydroxy-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-2-methyloxirane-2-carbaldehyde (13b).



13b

To a solution of **12b** (389 mg, 1.22 mmol) in CH_2Cl_2 (12 mL) at room temperature was added $NaHCO_3$ (823 mg, 9.80 mmol). The resulting suspension was stirred at room temperature for 30 min before being cooled to 0 °C. DMP (623 mg, 1.47 mmol) was added, the reaction was warmed to room temperature and stirred for 7 h before additional DMP (311 mg, 0.740 mmol) was added and the reaction stirred for a further 3 h. Additional DMP (311 mg, 0.740 mmol) was added and the reaction stirred for 12 h. Upon completion, the reaction was quenched with cold $NaHCO_3$ (6.1 mL of a saturated aqueous solution), followed by NaS_2O_3 (6.1 mL of a saturated aqueous solution) and the reaction mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 70:30) to afford **13b** (284 mg, 74%) as a white solid. m.p. 95-97 °C; R_f 0.33 (petrol/EtOAc 70:30); υ_{max} neat/cm^{-1} 3537, 2967, 2939, 1723, 1100, 1049, 887, 732, 695; δ_H (400 MHz, $CDCl_3$) 1.62 (s, 3H, CH_3CO), 1.67 (d, 1H, ^2J 14.4 Hz, =CHCHCH_{2eq}), 1.90 (ddd, 1H, ^2J 14.4 Hz, J 4.5 Hz, ^4J 1.6 Hz, =CHCHCH_{2ax}), 2.81 (s, 1H, C*H*OC), 3.02 (d, 1H, ^4J 1.6 Hz, O*H*), 3.82 (d, 1H, J 4.4 Hz, =CHCHC*H*), 4.66 (dd, 1H, J 4.4, 1.7 Hz, =CHC*H*CH), 4.71-4.76 (m, 2H, =CHC*H*CH_2, CH_2O), 4.84 (d, 1H, ^2J 11.7 Hz, CH_2O), 6.24 (dd, 1H, J 6.1, 1.7 Hz, =C*H*CHCH), 6.29 (dd, 1H, J 6.1, 1.7 Hz, =C*H*CHCH_2), 7.29-7.47 (m, 5H, H_{Ar}), 8.82 (s, 1H, C*H*O); δ_C (100 MHz, $CDCl_3$) 9.7 (CH_3, *C*H_3CO), 33.4 (CH_2, =CHCH*C*H_2), 61.8 (C, CHO*C*), 65.7 (CH, *C*HOC), 70.2 (C, *C*OH), 73.0 (CH_2, *C*H_2O), 78.0 (2 x CH, =CHC*H*CH, =CHC*H*CH_2), 78.6 (CH, =CHCH*C*H), 128.3 (2 x CH, *C*H_{Ar}), 128.5 (CH, *C*H_{Ar}), 128.8 (2 x CH, *C*H_{Ar}), 130.8 (CH, =*C*HCHCH), 135.3 (CH, =*C*HCHCH_2), 137.5 (C, *C*CH_{Ar}), 199.5 (CH, *C*HO); *m*/*z* HRMS (ES) calcd for $C_{18}H_{20}NaO_5^+$ 339.1208, found 339.1220; (ES) 339 ($[M+Na]^+$, 60%), 371 ($[M+Na+MeOH]^+$, 100).

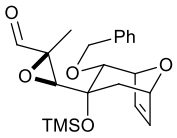
(±)-(2*S*,3*S*)-3-((1*R*,2*S*,3*S*,4*R*,5*S*)-2,4-Dimethyl-3-trimethylsilyloxy-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-2-methyloxirane-2-carbaldehyde (14a).



14a

To a solution of **13a** (30 mg, 0.130 mmol) and Et_3N (49 mg, 0.070 mL, 0.480 mmol) in CH_2Cl_2 (1.2 mL) at 0 °C was added TMSOTf (73 mg, 0.060 mL, 0.320 mmol) dropwise over 10 min. The reaction was stirred at room temperature for 4 h before being quenched with $NaHCO_3$ (1 mL of a saturated aqueous solution) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 90:10) to afford **14a** (33 mg, 82%) as a white solid. m.p. 58-60 °C; R_f 0.41 (petrol/EtOAc 90:10); υ_{max} neat/cm^{-1} 2963, 2935, 1731, 1250, 1088, 718; δ_H (400 MHz, $CDCl_3$) 0.17 (s, 9H, Si(C*H*$_3$)$_3$), 0.85 (d, 3H, *J* 7.2 Hz, C*H*$_3$CH), 0.89 (d, 3H, *J* 7.0 Hz, C*H*$_3$CH), 1.64 (s, 3H, C*H*$_3$CO), 1.94-2.06 (m, 2H, CH$_3$C*H*), 3.09 (s, 1H, COC*H*), 4.37 (dd, 1H, *J* 3.7, 1.4 Hz, =CHC*H*O), 4.43 (dd, 1H, *J* 3.9, 1.3 Hz, =CHC*H*O), 6.18-6.23 (m, 2H, =C*H*), 8.74 (s, 1H, C*H*O); δ_C (100 MHz, $CDCl_3$) 2.6 (3 x CH_3, Si(*C*H$_3$)$_3$), 10.0 (CH_3, *C*H$_3$CO), 12.8 (CH_3, *C*H$_3$CH), 13.3 (CH_3, *C*H$_3$CH), 37.8 (CH, CH$_3$*C*H), 40.7 (CH, CH$_3$*C*H), 62.0 (C, *C*OCH), 66.2 (CH, *C*HCO), 78.7 (C, *C*OSi), 82.5 (CH, =CH*C*HO), 82.6 (CH, =CH*C*HO), 132.6 (CH, =*C*H), 133.6 (CH, =*C*H), 199.7 (CH, *C*HO); *m/z* HRMS (ES) calcd for $C_{16}H_{26}NaO_4Si^+$ 333.1498, found 333.1507; (ES) 333 ([M+Na]$^+$, 12%), 365 ([M+Na+MeOH]$^+$, 100).

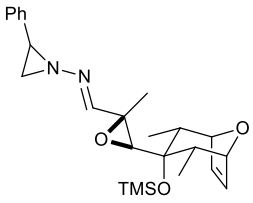
Preparation of (2*S*,3*S*)-3-((1*S*,2*R*,3*S*,5*S*)-2-Benzyloxy-3-trimethylsilyloxy-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-2-methyloxirane-2-carbaldehyde (14b).



14b

To a solution of **13b** (204 mg, 0.650 mmol) and Et_3N (263 mg, 0.360 mL, 2.60 mmol) in CH_2Cl_2 (6.5 mL) at 0 °C was added TMSOTf (376 mg, 0.310 mL, 1.69 mmol) dropwise over 10 min. The reaction was stirred at room temperature for 4 h before being quenched with $NaHCO_3$ (1 mL of a saturated aqueous solution) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organics were dried over $MgSO_4$, filtered and dried *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 90:10) to afford **14b** (201 mg, 80%) as a white solid. m.p. 107-109 °C; R_f 0.21 (petrol/EtOAc 70:30); υ_{max} neat/cm^{-1} 2956, 2910, 2868, 2848, 1725, 1238, 1104, 907, 836, 690; δ_H (400 MHz, $CDCl_3$) 0.13 (s, 9H, Si(C*H*$_3$)$_3$), 1.49 (s, 3H, C*H*$_3$CO), 1.63 (dd, 1H, ^2J 14.5 Hz, *J* 1.0 Hz, =CHCHC*H*$_{2eq}$), 1.91 (dd, 1H, ^2J 14.5 Hz, *J* 4.4 Hz, =CHCHC*H*$_{2ax}$), 2.88 (s, 1H, C*H*OC), 3.61 (d, 1H, *J* 4.0 Hz, =CHCHC*H*), 4.62-4.72 (m, 4H, =CHC*H*CH, =CHC*H*CH$_2$, C*H*$_2$O), 6.19 (dd, 1H, *J* 6.1, 1.7 Hz, =C*H*CHCH), 6.26 (dd, 1H, *J* 6.1, 1.7 Hz, =C*H*CHCH$_2$), 7.28-7.41 (m, 5H, *H*$_{Ar}$), 8.65 (s, 1H, C*H*O); δ_C (100 MHz, $CDCl_3$) 3.4 (3 x CH_3, Si(*C*H$_3$)$_3$), 10.0 (CH_3, *C*H$_3$CO), 36.9 (CH_2, =CHCHC*H*$_2$), 61.3 (C, CHO*C*), 66.5 (CH, *C*HOC), 71.9 (CH_2, *C*H$_2$O), 75.1 (C, *C*OH), 77.5 (CH, =CHC*H*CH), 78.1 (CH, =CHC*H*CH$_2$), 79.1 (CH, =CHCHC*H*), 128.5 (CH, *C*H$_{Ar}$), 128.6 (2 x CH, *C*H$_{Ar}$), 128.8 (2 x CH, *C*H$_{Ar}$), 131.9 (CH, =*C*HCHCH$_2$), 134.5 (CH, =*C*HCHCH), 137.7 (C, *C*CH$_{Ar}$), 199.4 (CH, *C*HO); *m*/*z* HRMS (ES) calcd for $C_{22}H_{32}NaO_6Si^+$ ([M+Na+MeOH]$^+$) 443.1866, found 443.1871; (ES) 411 ([M+Na]$^+$, 25%), 443 ([M+Na+MeOH]$^+$, 100).

(±)-(*E*)-*N*-(((2*R*,3*S*)-3-((1*R*,2*S*,3*S*,4*R*,5*S*)-2,4-Dimethyl-3-trimethylsilyloxy-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-2-methyloxiran-2-yl)methylene)-2-phenylaziridin-1-amine (16a).

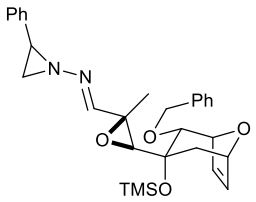


16a

To a solution of **14a** (547 mg, 1.78 mmol) in CH_2Cl_2 (25 mL) at 0 °C was added $NaHCO_3$ (1.5 g, 17.8 mmol) and **15**[4] (690 mg, 3.56 mmol). The reaction was stirred at 0 °C for 2 h, then washed with H_2O (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 90:10) to afford **16a** (548 mg, 73%, d.r. 1:1) as a bright yellow oil. R_f 0.41 (petrol/EtOAc 90:10); υ_{max} neat/cm^{-1} 2955, 1456, 1250, 1086, 834; δ_H (400 MHz, $CDCl_3$) 0.14 (2 x s, 9H, (C*H*$_3$)$_3$Si), 0.84-0.90 (m, 6H, C*H*$_3$CH, Isomer A+B), 1.67 (s, 3H, C*H*$_3$CO, Isomer A+B), 1.99-2.13 (m, 2H, CH$_3$C*H*, Isomer A+B), 2.38 (dd, 1H, *J* 4.8 Hz, ^2J 0.9 Hz, C*H*$_2$N, Isomer A+B), 2.41 (dd, 0.5H, *J* 7.8 Hz, ^2J 0.9 Hz, C*H*$_2$N, Isomer A), 2.51 (dd, 0.5H, *J* 7.8 Hz, ^2J 0.9 Hz, C*H*$_2$N, Isomer B), 2.97 (2 x s, 1H, C*H*OC, Isomer A+B), 3.01 (dd, 0.5H, *J* 7.7, 4.8 Hz, C*H*N, Isomer A), 3.04 (dd, 0.5H, *J* 7.8, 4.8 Hz, C*H*N, Isomer B), 4.36-4.38 (m, 1H, =CHC*H*OCH, Isomer A+B), 4.42 (dd, 1H, *J* 3.8, 0.9 Hz, =CHC*H*OCH, Isomer A+B), 6.17-6.22 (m, 2H, =C*H*, Isomer A+B), 7.22-7.36 (m, 6H, C*H*=N, *H*$_{Ar}$, Isomer A+B); δ_C (100 MHz, $CDCl_3$) 2.5 (3 x CH_3, Si(CH_3)$_3$), 12.9 (CH_3, *C*H$_3$CH, Isomer A+B), 13.2 (CH_3, *C*H$_3$CH, Isomer A+B), 13.5 (CH_3, *C*H$_3$CO, Isomer A+B), 38.0 (CH, CH$_3$*C*H, Isomer A+B), 40.6 (0.5 x CH_2, *C*H$_2$N, Isomer B), 40.7 (CH, CH$_3$*C*H, Isomer A+B), 41.1 (0.5 x CH_2, *C*H$_2$N, Isomer A), 44.0 (0.5 x CH, *C*HN, Isomer B), 44.8 (0.5 x CH, *C*HN, Isomer A), 58.7 (C, CHO*C*, Isomer A+B), 69.7 (0.5 x CH, *C*HOC, Isomer A), 69.8 (0.5 x CH, *C*HOC, Isomer B), 78.7 (C, *C*OSi, Isomer A+B), 82.7 (2 x CH, =CH*C*HOCH, Isomer A+B), 126.6 (2 x CH, *C*H$_{Ar}$, Isomer A+B), 127.6 (CH, *C*H$_{Ar}$, Isomer A+B), 128.7 (2 x CH, *C*H$_{Ar}$, Isomer A+B), 132.6 (CH, =*C*H, Isomer A+B), 133.6 (CH, =*C*H, Isomer A+B), 138.3 (0.5 x C,

CCH_{Ar}, Isomer A), 138.4 (0.5 x C, *C*CH_{Ar}, Isomer B), 163.9 (0.5 x CH, *C*H=N, Isomer A), 164.2 (0.5 x CH, *C*H=N, Isomer B); *m/z* HRMS (ES) calcd for $C_{24}H_{34}N_2NaO_3Si^+$ 449.2236, found 449.2244; (ES) 449 ($[M+Na]^+$, 100%).

(±)-*N*-(((2*R*,3*S*)-3-((1*S*,2*R*,3*S*,5*S*)-2-Benzyloxy-3-trimethylsilyloxy-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-2-methyloxiran-2-yl)methylene)-2-phenylaziridin-1-amine and (±)-*N*-(((2*R*,3*S*)-3-((1*S*,2*R*,3*S*,5*S*)-2-Benzyloxy-3-trimethylsilyloxy-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-2-methyloxiran-2-yl)methylene)-2-phenylaziridin-1-amine (16b).

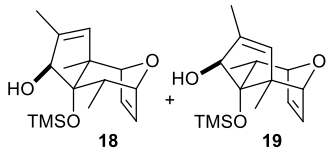


16b

To a solution of **14b** (250 mg, 0.640 mmol) in CH_2Cl_2 (9 mL) at 0 °C was added $NaHCO_3$ (521 mg, 6.20 mmol) followed by **15**[4] (239 mg, 1.23 mmol). The reaction was stirred at 0 °C for 2 h before being washed with H_2O (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 90:10) to afford **16b** (285 mg, 88%, 1:1 d.r.) as a yellow oil. Analytically pure samples of the diastereoisomers **16b** and **16b'** were obtained through column chromatography (hexane/EtOAc 90:10). Analytical data for **16b** (Absolute stereochemistry on aziridine arbitrarily assigned). R_f 0.14 (petrol/EtOAc 90:10); υ_{max} neat/cm^{-1} 3060, 3031, 2960, 2917, 2870, 1637, 1494, 1243, 1144, 1101, 899, 835, 694; δ_H (400 MHz, $CDCl_3$) 0.11 (s, 9H, $Si(CH_3)_3$), 1.55 (s, 3H, C*H*$_3$CO), 1.65 (d, 1H, ^2J 14.5 Hz, =CHCHC*H*$_{2eq}$), 1.99 (dd, 1H, ^2J 14.5 Hz, *J* 4.5 Hz, =CHCHC*H*$_{2ax}$), 2.36 (d, 1H, *J* 4.9 Hz, C*H*$_2$N), 2.41 (d, 1H, *J* 7.5 Hz, C*H*$_2$N), 2.80 (s, 1H, C*H*OC), 3.05 (dd, 1H, *J* 7.5, 4.9 Hz, C*H*N), 3.62 (d, 1H, *J* 4.0 Hz, =CHCHC*H*), 4.62 (dd, 1H, *J* 4.0, 1.7 Hz, =CHC*H*CH), 4.66 (s, 2H, C*H*$_2$O), 4.68 (br d, 1H, *J* 4.5 Hz, =CHC*H*CH_2), 6.18 (dd, 1H, *J* 6.1, 1.6 Hz, =C*H*$CHCH_2$), 6.24 (dd, 1H, *J* 6.1, 1.7 Hz, =C*H*CHCH), 7.23-7.37 (m, 11H, *H*$_{Ar}$, C*H*=N); δ_C (100 MHz, $CDCl_3$) 3.4 (3 x CH_3, $Si(CH_3)_3$), 13.4 (CH_3, *C*H_3CO), 37.1 (CH_2, =CHCHC*H*$_2$), 40.9 (CH_2, *C*H_2N), 44.0 (CH, *C*HN), 58.2 (C, CHO*C*), 69.8 (CH, *C*HOC), 72.1 (CH_2, *C*H_2O),

75.2 (C, *C*OSi), 77.8 (CH, =CH*C*HCH), 78.2 (CH, =CH*C*HCH$_2$), 79.5 (CH, =CHCH*C*H), 126.6 (2 x CH, *C*H$_{Ar}$), 127.6 (CH, *C*H$_{Ar}$), 128.3 (CH, *C*H$_{Ar}$), 128.5 (2 x CH, *C*H$_{Ar}$), 128.6 (2 x CH, *C*H$_{Ar}$), 128.7 (2 x CH, *C*H$_{Ar}$), 131.9 (CH, =*C*HCHCH), 134.5 (CH, =*C*HCHCH$_2$), 137.9 (C, CH$_2$*C*CH$_{Ar}$), 138.5 (C, CH*C*CH$_{Ar}$), 163.5 (CH, *C*H=N); *m*/*z* HRMS (ES) calcd for $C_{29}H_{36}N_2NaO_4Si^+$ 527.2342, found 527.2355; (ES) 527 ([M+Na]$^+$, 100%). Analytical data for **16b'** (Absolute stereochemistry on aziridine arbitrarily assigned). R_f 0.08 (petrol/EtOAc 90:10); υ_{max} neat/cm^{-1} 3032, 2952, 1636, 1455, 1244, 1146, 1100, 900, 835, 750, 694; δ_H (400 MHz, $CDCl_3$) 0.11 (s, 9H, Si(CH$_3$)$_3$), 1.55 (s, 3H, C*H*$_3$CO), 1.65 (d, 1H, ^2J 14.5 Hz, =CHCHC*H*$_{2eq}$), 1.99 (dd, 1H, ^2J 14.5 Hz, *J* 4.3 Hz, =CHCHC*H*$_{2ax}$), 2.37 (d, 1H, *J* 4.9 Hz, C*H*$_2$N), 2.46 (d, 1H, *J* 7.7 Hz, C*H*$_2$N), 2.81 (s, 1H, C*H*OC), 3.01 (dd, 1H, *J* 7.7, 4.9 Hz, C*H*N), 3.62 (d, 1H, *J* 3.9 Hz, =CHCHC*H*), 4.62 (dd, 1H, *J* 3.9, 1.3 Hz, =CHC*H*CH), 4.66 (d, 2H, ^2J 2.9 Hz, C*H*$_2$O), 4.68 (br d, 1H, *J* 4.3 Hz, =CHC*H*CH$_2$), 6.18 (dd, 1H, *J* 6.1, 1.3 Hz, =CHCHCH$_2$), 6.24 (dd, 1H, *J* 6.1, 1.5 Hz, =CHCHCH), 7.22-7.38 (m, 11H, *H*$_{Ar}$, C*H*=N); δ_C (100 MHz, $CDCl_3$) 3.4 (3 x CH$_3$, Si(*C*H$_3$)$_3$), 13.4 (CH$_3$, *C*H$_3$CO), 37.1 (CH$_2$, =CHCH*C*H$_2$), 40.5 (CH$_2$, *C*H$_2$N), 44.6 (CH, *C*HN), 58.2 (C, CHO*C*), 69.8 (CH, *C*HOC), 72.1 (CH$_2$, *C*H$_2$O), 75.2 (C, *C*OSi), 77.8 (CH, =CH*C*HCH), 78.2 (CH, =CH*C*HCH$_2$), 79.5 (CH, =CHCH*C*H), 126.6 (2 x CH, *C*H$_{Ar}$), 127.6 (CH, *C*H$_{Ar}$), 128.3 (CH, *C*H$_{Ar}$), 128.5 (2 x CH, *C*H$_{Ar}$), 128.6 (2 x CH, *C*H$_{Ar}$), 128.7 (2 x CH, *C*H$_{Ar}$), 131.9 (CH, =*C*HCHCH), 134.5 (CH, =*C*HCHCH$_2$), 138.0 (C, CH$_2$*C*CH$_{Ar}$), 138.4 (C, CH*C*CH$_{Ar}$), 163.6 (CH, *C*H=N); *m*/*z* HRMS (ES) calcd for $C_{29}H_{36}N_2NaO_4Si^+$ 527.2342, found 527.2349; (ES) 395 ([M+Na-(N$_2$CH$_2$CHPh)]$^+$, 3%), 527 ([M+Na]$^+$, 100).

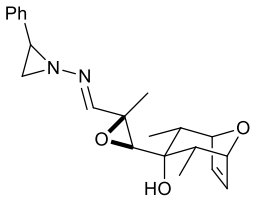
(±)-(1*S*,3a*S*,4*S*,7*R*,8*S*,8a*S*)-2,3a,8-Trimethyl-8a-trimethylsilyloxy-1,3a,4,7,8,8a-hexahydro-4,7-epoxyazulen-1-ol (18) and (±)-(1*S*,3a*R*,4*R*,7*S*,8*R*,8a*R*)-2,3a,8-Trimethyl-8a-trimethylsilyloxy-1,3a,4,7,8,8a-hexahydro-4,7-epoxyazulen-1-ol (19).



A solution of **16a** (190 mg, 0.450 mmol) in toluene (90 mL) was heated at reflux for 3 h. After this time the toluene was evaporated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 90:10) to afford **19** (27 mg, 21%) as a pale yellow solid followed by **18** (57 mg, 43%) as a pale yellow solid. Analytical data for **19**. m.p. 140-142 °C; R_f 0.40 (hexane/EtOAc 80:20); υ_{max} neat/cm^{-1} 3404, 2962, 2961, 2907, 2887, 1445, 1245, 909, 834, 730; δ_H (400 MHz, $CDCl_3$) 0.11 (s, 9H, Si(C*H*$_3$)$_3$), 0.85 (d, 3H, *J* 7.3 Hz, C*H*$_3$CH), 0.91 (s, 3H, C*H*$_3$C), 1.25 (br s, 1H, O*H*), 1.74 (qd, 1H, *J* 7.3, 3.6 Hz, CH$_3$C*H*), 1.80 (d, 3H, ^4J 1.5 Hz, =CC*H*$_3$), 3.60 (br s, 1H, C*H*OH), 4.33-4.42 (m, 2H, =CHC*H*OC), 5.59 (m, 1H, C=C*H*), 6.20 (dd, 1H, *J* 6.1, 1.6 Hz, =C*H*CHCH), 6.25 (dd, 1H, *J* 6.1, 1.6 Hz, =C*H*CHC); δ_C (100 MHz, $CDCl_3$) 3.1 (3 x CH_3, Si(*C*H$_3$)$_3$), 12.5 (CH_3, *C*H$_3$CH), 15.6 (CH_3, =C*C*H$_3$), 23.9 (CH_3 *C*H$_3$C), 38.3 (CH, CH$_3$*C*H), 51.4 (C, *C*CHO), 82.8 (CH, =CH*C*HC), 83.8 (CH, CH*C*HCH), 83.9 (C, *C*OSi), 84.0 (CH, *C*HOH), 132.3 (CH, =*C*HCHCH), 133.2 (CH, =*C*HCHC), 138.0 (CH, C=*C*H), 138.7 (C, *C*=CH); *m/z* HRMS (ES) calcd for $C_{16}H_{26}NaO_3Si$ 317.1549, found 317.1545; (ES) 317 ([M+Na]$^+$, 100%). Analytical data for **18**. m.p. 117-119 °C; R_f 0.53 (hexane/EtOAc 80:20); υ_{max} neat/cm^{-1} 3403, 2963, 2931, 2908, 2888, 1246, 1050, 891, 834; δ_H (400 MHz, $CDCl_3$) 0.14 (s, 9H, Si(C*H*$_3$)$_3$), 0.78 (s, 3H, C*H*$_3$C), 0.90 (d, 3H, *J* 7.1 Hz, C*H*$_3$CH), 1.25 (br s, 1H, O*H*), 1.70 (t, 3H, ^4J 1.3 Hz, =CC*H*$_3$), 2.19 (qd, 1H, *J* 7.1, 4.0 Hz, CH$_3$C*H*), 4.27 (d, 1H, *J* 1.0 Hz, =CHC*H*C), 4.35 (dd, 1H, *J* 4.0, 1.1 Hz, =CHC*H*CH), 4.54 (br s, 1H, C*H*OH), 5.47 (m, 1H, C=C*H*), 6.17-6.21 (m, 2H, =C*H*); δ_C (100 MHz, $CDCl_3$) 2.4 (3 x CH_3, Si(*C*H$_3$)$_3$), 13.8 (CH_3, =C*C*H$_3$), 13.9 (CH, *C*H$_3$CH), 20.6 (CH_3, *C*H$_3$C), 34.1 (CH, CH$_3$*C*H), 49.0 (C, *C*CHO), 82.4 (CH, =CH*C*HCH), 83.9 (CH, =CH*C*HC), 86.6 (CH,

*C*HOH), 87.7 (C, *C*OSi), 132.2 (CH, =*C*H), 132.6 (CH, =*C*H), 134.1 (CH, C=*C*H), 137.6 (C, *C*=CH); *m/z* HRMS (ES) calcd for $C_{16}H_{26}NaO_3Si^+$ 317.1549, found 317.1552; (ES) 317 ($[M+Na]^+$, 100%).

(±)-(1*R*,2*S*,3*S*,4*R*,5*S*)-2,4-Dimethyl-3-((2*R*,3*R*)-3-methyl-3-((2-phenylaziridin-1-yl)imino)methyl)oxiran-2-yl)-8-oxabicyclo[3.2.1]oct-6-en-3-ol (20a).

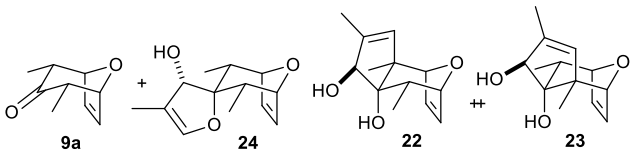


20a

To a solution of **16a** (50 mg, 0.120 mmol) in THF (2.4 mL) at room temperature was added TBAF (1 M in THF, 0.140 mL, 0.140 mmol) in one portion. The reaction was stirred at room temperature for 16 h before being washed with H_2O (5 mL) and extracted with Et_2O (3 x 5 mL). The combined organics were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (petrol/EtOAc 70:30, deactivated with 0.1% Et_3N) to afford **402** (40 mg, 93%, d.r. 1:1) as a bright yellow oil. R_f 0.40 (hexane/EtOAc 70:30); υ_{max} neat/cm^{-1} 3570, 2934, 1456, 1079, 1051, 932, 725, 697, 664; δ_H (400 MHz, $CDCl_3$) 0.90 (2 x d, 3H, *J* 7.3 Hz, C*H*$_3$CH, Isomer A+B), 1.02 (2 x d, 3H, *J* 7.3 Hz, C*H*$_3$CH, Isomer A+B), 1.67 (2 x s, 3H, C*H*$_3$CO, Isomer A+B), 1.74 (s, 1H, O*H*, Isomer A+B), 2.15 (qd, 1H, *J* 7.3, 3.7 Hz, CH$_3$C*H*, Isomer A+B), 2.31 (qd, 1H, *J* 7.0, 3.2 Hz, CH$_3$C*H*, Isomer A+B), 2.36 (dt, 1H, *J* 4.7 Hz, ^2J 0.5 Hz, C*H*$_2$N, Isomer A+B), 2.42 (dd, 0.5H, *J* 7.7 Hz, ^2J 0.5 Hz, C*H*$_2$N, Isomer B), 2.48 (dd, 0.5H, *J* 7.7 Hz, ^2J 0.5 Hz, C*H*$_2$N, Isomer A), 2.63 (2 x s, 1H, C*H*OC, Isomer A+B), 3.01 (dd, 0.5H, *J* 7.7, 4.7 Hz, C*H*N, Isomer A), 3.07 (dd, 0.5H, *J* 7.7, 4.7 Hz, C*H*N, Isomer B), 4.48 (dd, 1H, *J* 3.2, 1.4 Hz, =CHC*H*OCH, Isomer A+B), 4.49-4.51 (m, 1H, =CHC*H*OCH, Isomer A+B), 6.45 (dd, 1H, *J* 6.1, 1.4 Hz, =C*H*, Isomer A+B), 6.48 (dd, 1H, *J* 6.1, 1.4 Hz, =C*H*, Isomer A+B), 7.21-7.34 (m, 5H, *H*$_{Ar}$), 7.38 (2 x s, 1H, C*H*=N, Isomer A+B); δ_C (100 MHz, $CDCl_3$) 11.4 (CH$_3$, *C*H$_3$CH, Isomer A+B), 14.4 (CH$_3$, *C*H$_3$CO, Isomer A+B), 38.3 (CH, CH$_3$*C*H, Isomer A+B), 40.5 (0.5 x CH$_2$, *C*H$_2$N, Isomer A), 41.0 (0.5 x CH$_2$, *C*H$_2$N, Isomer B), 42.6 (CH, CH$_3$*C*H, Isomer A+B), 43.9

(0.5 x CH, *C*HN, Isomer B), 44.5 (0.5 x CH, *C*HN, Isomer A), 58.2 (C, CHO*C*, Isomer A+B), 69.5 (CH, *C*HOC, Isomer A+B), 73.7 (C, *C*OH, Isomer A+B), 82.5 (2 x CH, =CH*C*HOCH, Isomer A+B), 126.5 (2 x CH, *C*H_{Ar}, Isomer A+B), 127.5 (CH, *C*H_{Ar}, Isomer A+B), 128.6 (2 x CH, *C*H_{Ar}, Isomer A+B), 134.8 (CH, =*C*H, Isomer A+B), 135.0 (CH, =*C*H, Isomer A+B), 138.3 (0.5 x C, *C*CH_{Ar}, Isomer A), 138.4 (0.5 x C, *C*CH_{Ar}, Isomer B), 163.5 (CH, *C*H=N, Isomer A+B); *m/z* HRMS (ES) calcd for $C_{21}H_{26}N_2NaO_3^+$ 377.1847, found 377.1844; (ES) 377 ($[M+Na]^+$, 100%), 378 ($[M+Na+H]^+$, 17).

(±)-(1*S*,3a*S*,4*S*,7*R*,8*S*,8a*S*)-2,3a,8-Trimethyl-1,3a,4,7,8,8a-hexahydro-4,7-epoxyazulene-1,8a-diol (22) and (±)-(1*S*,3a*R*,4*R*,7*S*,8*R*,8a*R*)-2,3a,8-Trimethyl-1,3a,4,7,8,8a-hexahydro-4,7-epoxyazulene-1,8a-diol (23).



A solution of **20a** (154 mg, 0.440 mmol) in toluene (88 mL) was heated at reflux for 6 h. After this time the toluene was evaporated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 70:30→50:50) to afford **23** (28 mg, 30%) as a pale yellow solid followed by **22** (11 mg, 12%) as a pale yellow crystal. Analytical data for **23**. m.p. 109-112 °C; R_f 0.28 (hexane/EtOAc 1:1); υ_{max} neat/cm^{-1} 3334, 2963, 2932, 2890, 1722, 1446, 1352, 1192, 1052, 952, 907, 654; δ_H (400 MHz, $CDCl_3$) 0.90 (d, 3H, *J* 7.4 Hz, C*H*$_3$CH), 0.96 (s, 3H, C*H*$_3$C), 1.82-1.88 (m, 4H, CH_3C*H*, =CC*H*$_3$), 2.58 (s, 1H, O*H*), 3.66 (s, 1H, C*H*OH), 4.42-4.47 (m, 2H, =CHC*H*O), 5.65 (q, 1H, ^{4}*J* 1.5 Hz, C=C*H*), 6.43 (app. qd, 2H, *J* 6.2, 1.6 Hz, =C*H*); δ_C (100 MHz, $CDCl_3$) 11.2 (CH_3, *C*H_3CH), 15.7 (CH_3, =C*C*H_3), 22.4 (CH_3, *C*H_3C), 38.5 (CH, CH_3*C*H), 51.5 (C, *C*CHOH), 78.1 (C, *C*OH), 82.5 (CH, =CH*C*HC), 83.6 (CH, =CH*C*HCH), 84.0 (CH, *C*HOH), 132.9 (CH, =*C*HCHCH), 134.5 (CH, =*C*HCHC), 137.5 (C, *C*=CH), 138.6 (CH, C=*C*H); *m/z* HRMS (ES) calcd for $C_{13}H_{18}NaO_3^+$ 245.1154, found 245.1149; (ES) 245 ($[M+Na]^+$, 100%). Analytical data for **22**. m.p. 187-190 °C; R_f 0.15 (hexane/EtOAc 1:1); υ_{max} neat/cm^{-1} 3516,

3401, 2927, 2871, 1721, 1447, 1285, 1041, 1029, 954, 734, 560; δ_H (400 MHz, $CDCl_3$) 0.86 (s, 3H, C*H*$_3$C), 0.99 (d, 3H, *J* 7.3 Hz, C*H*$_3$CH), 1.73 (t, 3H, ^4J 1.5 Hz, =CC*H*$_3$), 2.39 (qd, 1H, *J* 7.2, 3.6 Hz, CH$_3$C*H*), 4.37 (d, 1H, *J* 1.2 Hz, =CHC*H*C), 4.43 (dd, 1H, *J* 4.0, 1.2 Hz, =CHC*H*CH), 4.57 (br s, 1H, C*H*OH), 5.45-5.48 (m, 1H, C=C*H*), 6.44-6.48 (m, 2H, =C*H*); δ_C (100 MHz, $CDCl_3$) 12.9 (CH$_3$, *C*H$_3$CH), 13.8 (CH$_3$, =C*C*H$_3$), 19.3 (CH$_3$, *C*H$_3$C), 33.9 (CH, CH$_3$*C*H), 48.7 (C, *C*CHOH), 82.3 (CH, =CH*C*HCH), 83.7 (CH, =CH*C*HC), 84.8 (C, *C*OH), 86.3 (CH, *C*HOH), 132.6 (CH, C=*C*H), 134.0 (CH, =*C*HCHCH), 134.8 (CH, =*C*HCHC), 138.4 (C, *C*=CH); *m/z* HRMS (ES) calcd for $C_{13}H_{18}NaO_3^+$ 245.1154, found 245.1159; (ES) 245 ($[M+Na]^+$, 100%). Peaks in ^{1}H NMR assignable to **24**: 6.16 (s, 1H, CH$_3$C=C*H*). Peaks in ^{1}H NMR assignable to **9b**: 2.80 (qd, 2H, *J* 7.0, 4.9 Hz, C*H*CH$_3$).

2,4-*endo*,*endo*-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (9a).

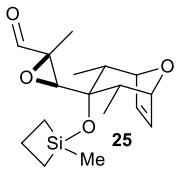

9a

From **20a** *with LiHMDS*: To a solution of **20a** (184.0 mg, 0.52 mmol) in toluene (104 mL) at room temperature was added LiHMDS (1 M in THF, 0.57 mL, 0.57 mmol). The resulting solution was stirred at room temperature for 15 min before being heated at reflux for 3 h. After cooling to room temperature, NH_4Cl (10 mL of a saturated aqueous solution) was added and the reaction was extracted with CH_2Cl_2 (3 x 10 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 90:10) to afford **9a** (17 mg, 22%) as a yellow oil. δ_H (400 MHz, $CDCl_3$) 0.95 (d, 6H, *J* 7.0 Hz, C*H*$_3$), 2.79 (qd, 2H, *J* 7.0, 4.6 Hz, CH$_3$C*H*), 4.83 (d, 2H, *J* 4.6 Hz, C*H*OCH), 6.32 (s, 2H, =C*H*); δ_C (100 MHz, $CDCl_3$) 10.3 (2 x CH$_3$, *C*H$_3$), 50.6 (2 x CH, CH$_3$*C*H), 82.9 (2 x CH, =CH*C*HOCH), 133.7 (2 x CH, =*C*H), 206.1 (C, *C*=O); *m/z* (EI) 55 (5%), 67 (14), 68 (7), 81 (100), 95 (43), 96 (47), 109 (5), 137 ($[M-O]^+$, 27), 152 (M^+, 38), 153 ($[M+H]^+$, 5). Analytical data in agreement with literature values.[2]

From **20a** *with PhB(OH)$_2$*: A solution of **20a** (168 mg, 0.48 mmol) and PhB(OH)$_2$ (59 mg, 0.48 mmol) in toluene (96 mL) was heated at reflux for 3 h with a Dean-Stark apparatus attached. The reaction was cooled to room temperature, 2,2-dimethyl-1,3-diol (50mg, 0.48 mmol) added and the reaction stirred at room temperature for 30 min before the solvent was evaporated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 90:10) to afford **9a** (38 mg, 52%) as a yellow oil. Analytical data as above.

From **26**: A solution of **26** (26.7 mg, 0.06 mmol) in toluene (12 mL) was heated at reflux for 3 h. After cooling to room temperature the solvent was evaporated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 90:10) to afford **9a** (3 mg, 35%) as a yellow oil. Analytical data as above.

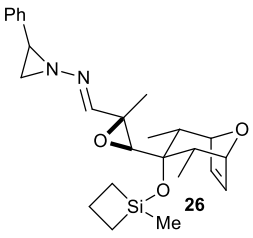
(±)-(2*S*,3*S*)-3-((1*R*,2*S*,3*S*,4*R*,5*S*)-2,4-Dimethyl-3-((1-methylsiletan-1-yl)oxy)-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-2-methyloxirane-2-carbaldehyde (25).



To a solution of **13a** (50 mg, 0.210 mmol) in THF (1.2 mL) at 0 °C was added KHMDS (0.5 M in toluene, 1.26 mL, 0.630 mmol) dropwise over 5 min. 1-Chloro-1-methylsilacyclobutane (76 mg, 0.080 mL, 0.630 mmol) was added immediately and the reaction stirred at room temperature for 30 min. The reaction was quenched with $NaHCO_3$ (2 mL of a saturated aqueous solution) and extracted with EtOAc (3 x 5 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (petrol/EtOAc 90:10) to afford **25** (38 mg, 56%) as a clear colourless oil. R_f 0.26 (petrol/EtOAc 90:10); υ_{max} neat/cm^{-1} 2968, 2933, 1731, 1251, 1076; δ_H (400 MHz, $CDCl_3$) 0.30 (s, 3H, SiC*H*$_3$), 0.89 (2 x d, 6H, *J* 7.0 Hz, C*H*$_3$CH), 1.21-1.27 (m, 3H, SiC*H*$_2$), 1.33-1.51 (m, 2H, SiC*H*$_2$, SiCH$_2$C*H*$_2$), 1.64 (s, 3H, C*H*$_3$CCO), 1.91-2.08 (m, 3H, CH$_3$C*H*, SiCH$_2$C*H*$_2$), 3.18 (s, 1H, C*H*OC), 4.40 (dd, 1H, *J* 3.5, 1.0 Hz, =CHC*H*OCH), 4.45 (dd, 1H, *J* 3.7, 1.0 Hz, =CHC*H*OCH), 6.23 (app. qd, 2H, *J* 6.3,

1.0 Hz, =C*H*), 8.74 (s, 1H, C*H*O); δ_C (100 MHz, $CDCl_3$) 0.09 (CH_3, Si*C*H_3), 10.0 (CH_3, *C*H_3CCHO), 12.5 (CH_3, *C*H_3CH), 12.9 (CH_2, SiCH_2*C*H_2), 13.0 (CH_3, *C*H_3CH), 21.4 (CH_2, Si*C*H_2), 22.2 (CH_2, Si*C*H_2), 37.5 (CH, CH_3*C*H), 40.7 (CH, CH_3*C*H), 61.9 (C, CH*C*O), 66.2 (CH, *C*HOC), 79.4 (C, *C*OSi), 82.4 (2 x CH, =CH*C*HOCH), 132.7 (CH, =*C*H), 133.6 (CH, =*C*H), 199.7 (CH, *C*HO); *m/z* HRMS (ES) calcd for $C_{17}H_{26}NaO_4Si^+$ 345.1498, found 345.1500; (ES) 345 ($[M+Na]^+$, 8%), 377 ($[M+Na+MeOH]^+$, 100).

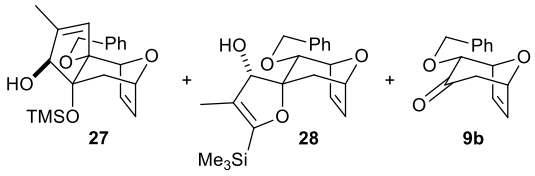
(±)-(*E*)-*N*-(((2*R*,3*S*)-3-((1*R*,2*S*,3*S*,4*R*,5*S*)-2,4-Dimethyl-3-((1-methylsiletan-1-yl)oxy)-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-2-methyloxiran-2-yl)methylene)-2-phenylaziridin-1-amine (26).



To a solution of **25** (38 mg, 0.120 mmol) in CH_2Cl_2 (2 mL) at 0 °C was added $NaHCO_3$ (101 mg, 1.20 mmol) and **15**[4] (47 mg, 0.240 mmol). The reaction was stirred at 0 °C for 2 h, then washed with H_2O (2 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 90:10) to afford **26** (27 mg, 50%, d.r. 1:1) as yellow oil. R_f 0.41 (petrol/EtOAc 90:10); υ_{max} neat/cm^{-1} 2964, 2932, 1457, 1122, 1083, 916, 720, 696; δ_H (400 MHz, $CDCl_3$) 0.27 (2 x s, 3H, SiC*H*$_3$, Isomer A+B), 0.87 (2 x d, 3H, *J* 6.9 Hz, C*H*$_3$CH, Isomer A+B), 0.91 (2 x d, 3H, *J* 7.1 Hz, C*H*$_3$CH, Isomer A+B), 1.13-1.37 (m, 5H, SiC*H*$_2$, SiCH$_2$C*H*$_2$, Isomer A+B), 1.68 (s, 3H, C*H*$_3$CO), 1.89-1.99 (m, 1H, SiCH$_2$C*H*$_2$, Isomer A+B), 2.07-2.14 (m, 2H, CH$_3$C*H*), 2.39 (dd, 1H, *J* 4.9 Hz, ^{2}*J* 0.6 Hz, C*H*$_2$N, Isomer A+B), 2.42 (dd, 0.5H, *J* 7.8 Hz, ^{2}*J* 0.7 Hz, C*H*$_2$N, Isomer A), 2.50 (dd, 0.5H, *J* 7.8 Hz, ^{2}*J* 0.6 Hz, C*H*$_2$N, Isomer B), 3.02 (dd, 0.5H, *J* 7.8, 4.9 Hz, C*H*N, Isomer B), 3.08-3.13 (m, 1.5H, C*H*OC, Isomer A+B, C*H*N, Isomer A), 4.38-4.42 (m, 1H, =CHC*H*O, Isomer A+B), 4.45 (dd, 1H, *J* 3.8, 1.1 Hz, =CHC*H*O, Isomer A+B), 6.19-6.25 (m, 2H, =C*H*, Isomer A+B), 7.23-7.35 (m, 5H, *H*$_{Ar}$); δ_C (100 MHz, $CDCl_3$) 0.1 (CH_3, Si*C*H_3, Isomer A+B), 12.6 (CH_3, *C*H_3CH, Isomer

A+B), 12.9 (CH_2, $SiCH_2CH_2$, Isomer A+B), 13.0 (CH_3, CH_3CH, Isomer A+B), 13.5 (CH_3, CH_3CO, Isomer A+B), 21.4 (CH_2, $SiCH_2$, Isomer A+B), 22.0 (CH_2, $SiCH_2$, Isomer A+B), 37.6 (CH, CH_3CH, Isomer A+B), 40.6 (CH, CH_3CH, Isomer A+B), 41.2 (0.5 x CH_2, CH_2N, Isomer B), 42.0 (0.5 x CH_2, CH_2N, Isomer A), 44.0 (0.5 x CH, CHN, Isomer A), 44.7 (0.5 x CH, CHN, Isomer B), 58.7 (C, CHOC, Isomer A+B), 69.6 (0.5 x CH, CHOC, Isomer A), 69.7 (0.5 x CH, CHOC, Isomer B), 79.4 (C, COSi, Isomer A+B), 82.5 (2 x CH, =CHCHO, Isomer A+B), 126.5 (2 x CH, CH_{Ar}, Isomer A+B), 127.6 (CH, CH_{Ar}, Isomer A+B), 128.6 (2 x CH, CH_{Ar}, Isomer A+B), 132.7 (CH, =CH, Isomer A+B), 133.5 (CH, =CH, Isomer A+B), 138.3 (0.5 x C, CCH_{Ar}, Isomer A), 138.4 (0.5 x C, CCH_{Ar}, Isomer B), 163.8 (0.5 x CH, CH=N, Isomer A), 164.1 (0.5 x CH, CH=N, Isomer B); *m/z* HRMS (ES) calcd for $C_{25}H_{34}N_2NaO_3Si^+$ 461.2236, found 461.2239; (ES) 461 ($[M+Na]^+$, 100%).

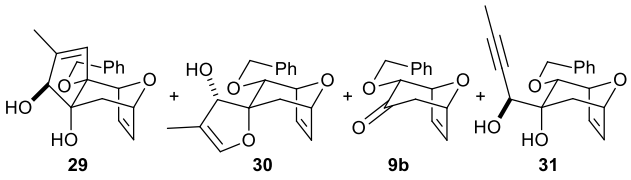
(±)-(1*S*,3a*R*,4*S*,7*S*,8a*R*)-3a-(benzyloxy)-2-methyl-8a-((trimethylsilyl)oxy)-1,3a,4,7,8,8a-hexahydro-4,7-epoxyazulen-1-ol 27



A solution of **16b** (55 mg, 0.110 mmol) in toluene (22 mL) was heated to reflux for 3 h. After cooling to room temperature the toluene was evaporated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 85:15) to afford **27**, **28** and **9b** as a 2.4:1:1.2 mixture by ^{1}H NMR (79% combined, from which **27** was isolated in 41% yield). Analytical data for **27**. m.p. 94-97 °C; R_f 0.32 (petrol/EtOAc 75:25); υ_{max} neat/cm^{-1} 3487, 3423, 3028, 2940, 1246, 1131, 1111, 1091, 1066, 907, 834, 743; δ_H (400 MHz, $CDCl_3$) 0.09 (s, 9H, $Si(CH_3)_3$), 1.56 (dd, 1H, ^2J 14.1 Hz, J 1.3 Hz, =CHCHCH_{2eq}), 1.87 (s, 3H, =CCH_3), 2.05 (d, 1H, J 7.5 Hz, O*H*), 2.21 (dd, 1H, ^2J 14.1 Hz, J 5.2 Hz, =CHCHCH_{2ax}), 4.42 (d, 1H, ^2J 11.6 Hz, CH_2O), 4.47 (d, 1H, J 7.5 Hz, =CC*H*OH), 4.50-4.55 (m, 2H, =CHC*H*C, CH_2O), 4.73 (br d, 1H, J 5.2 Hz, =CHC*H*CH_2), 5.51-5.61 (m, 1H, C=C*H*), 6.21 (dd, 1H, J 6.0, 1.5 Hz, =C*H*$CHCH_2$), 6.31 (dd, 1H, J 6.0 , 1.7

Hz, =C*H*CHC), 7.19-7.42 (m, 5H, H_{Ar}); δ_C (100 MHz, $CDCl_3$) 2.7 (3 x CH_3, Si(CH_3)$_3$), 14.3 (CH_3, =CCH_3), 33.5 (CH_2, =CHCHCH_2), 66.5 (CH_2, CH_2O), 77.8 (CH, =CHCHCH$_2$), 81.1 (CH, =CHCHC), 83.7 (C, =CHCHC), 84.2 (C, COSi), 86.2 (CH, CHOH), 127.3 (3 x CH, CH_{Ar}), 128.1 (CH, C=CH), 128.4 (2 x CH, CH_{Ar}), 131.7 (CH, =CHCHC), 133.7 (CH, =CHCHCH$_2$), 140.1 (C, CCH$_{Ar}$), 146.9 (C, C=CH); *m/z* HRMS (ES) calcd for $C_{21}H_{28}NaO_4Si^+$ 395.1655, found 395.1654; (ES) 395 ($[M+Na]^+$, 100%. Peaks in ^{1}H NMR of mixture assignable to **9b**: 2.38 (d, 1H, ^2J 15.2 Hz, =CHCHCH_{2eq}), 2.76 (dd, 1H, ^2J 15.4 Hz, J 4.9 Hz, =CHCHCH_{2ax}), 4.13 (d, 1H, J 5.0 Hz, CHOCH$_2$). Peaks in ^{1}H NMR of mixture assignable to **28**: 4.07 (d, 1H, ^2J 11.7 Hz, CHOH), 4.25 (d, 1H, J 3.8 Hz, =CHCHCH).

(±)-(1*S*,2*R*,2'*R*,3'*S*,5*S*)-2-Benzyloxy-4'-methyl-3'*H*-8-oxaspiro[bicyclo[3.2.1]oct[6]ene-3,2'-furan]-3'-ol (30) and (±)-(1*S*,2*R*,3*R*,5*S*)-2-Benzyloxy-3-((*S*)-1-hydroxybut-2-yn-1-yl)-8-oxabicyclo[3.2.1]oct-6-en-3-ol (31) and (±)-(1*S*,3a*R*,4*S*,7*S*,8a*R*)-3a-Benzyloxy-2-methyl-1,3a,4,7,8,8a-hexahydro-4,7-epoxyazulene-1,8a-diol (29) and (±)-(1*S*,2*R*,5*S*)-2-Benzyloxy-8-oxabicyclo[3.2.1]oct-6-en-3-one (9b).

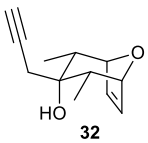


To a solution of **16b** (241 mg, 0.480 mmol) in THF (10 mL) at room temperature was added TBAF (1 M in THF, 0.580 mL, 0.580 mmol). The reaction was stirred at room temperature for 3 h before being quenched with H_2O (10 mL) and extracted with Et_2O (3 x 10 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 80:20, deactivated with 0.1% Et_3N) to afford **20b** as an impure mixture of diastereoisomers. A solution of crude **20b** in toluene (74 mL) was heated to reflux for 3 h. After cooling to room temperature the toluene was evaporated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 75:25→50:50) to afford **9b** (13 mg, 11%) as a clear oil followed by **30** (28 mg, 20%) as an

off-white solid followed by **31** (8.5 mg, 6%) as a clear oil followed by **29** (27 mg, 18%) as an off-white solid. Analytical data for **30**. m.p. 109-111 °C; R_f 0.31 (petrol/EtOAc 75:25); υ_{max} neat/cm^{-1} 3442, 2937, 1675, 1675, 1454, 1048, 982, 732, 696; δ_H (400 MHz, $CDCl_3$) 1.66 (d, 1H, *J* 11.9 Hz, O*H*), 1.66 (br s, 3H, =CCH_3), 1.74 (dd, 1H, ^2J 14.2 Hz, *J* 1.1 Hz, =CHCHCH_{2eq}), 1.95 (dd, 1H, ^2J 14.2 Hz, *J* 3.9 Hz, =CHCHCH_{2ax}), 4.08 (d, 1H, *J* 11.9 Hz, C*H*OH), 4.27 (d, 1H, *J* 3.9 Hz, =CHCHC*H*), 4.63 (d, 1H, ^2J 11.8 Hz, CH_2O), 4.72-4.77 (m, 3H, =CHC*H*CH, =CHC*H*CH_2, CH_2O), 6.13 (s, 1H, C=C*H*), 6.24 (dd, 1H, *J* 6.1, 1.7 Hz, =C*H*CHCH), 6.36 (dd, 1H, *J* 6.1, 1.7 Hz, =C*H*CHCH_2), 7.30-7.36 (m, 5H, H_{Ar}); δ_C (100 MHz, $CDCl_3$) 8.8 (CH_3, =C*C*H_3), 39.8 (CH_2, =CHCH*C*H_2), 72.0 (CH_2, CH_2O), 75.8 (CH, =CHCH*C*H), 77.1 (CH, =CH*C*HCH_2), 78.6 (CH, =CH*C*HCH), 86.9 (CH, *C*HOH), 87.2 (C, *C*O), 111.9 (C, *C*=CH), 128.1 (2 x CH, *C*H_{Ar}), 128.3 (CH, *C*H_{Ar}), 128.8 (2 x CH, *C*H_{Ar}), 131.7 (CH, =*C*HCHCH_2), 134.7 (CH, =*C*HCHCH), 138.1 (C, *C*CH_{Ar}), 142.9 (CH, C=*C*H); *m*/*z* HRMS (ES) calcd for $C_{18}H_{20}NaO_4^+$ 323.1259, found 323.1267; (ES) 323 ($[M+Na]^+$, 100%). Analytical data for **31**. R_f 0.22 (petrol/EtOAc 50:50); υ_{max} neat/cm^{-1} 3416, 2922, 2868, 1719, 1050, 1454, 1050, 727, 697; δ_H (400 MHz, $CDCl_3$) 1.70 (d, 1H, ^2J 14.5 Hz, =CHCHCH_{2eq}), 1.86 (d, 3H, ^4J 2.1 Hz, ≡CCH_3), 2.26 (dd, 1H, ^2J 14.5 Hz, *J* 4.6 Hz, =CHCHCH_{2ax}), 3.92 (d, 1H, *J* 4.5 Hz, =CHCHC*H*), 4.14 (q, 1H, ^4J 2.1 Hz, C*H*OH), 4.62-4.73 (m, 3H, =CHC*H*CH, CH_2O), 4.82 (d, 1H, *J* 4.6 Hz, =CHC*H*CH_2), 6.25 (dd, 1H, *J* 6.1, 1.6 Hz, =C*H*CHCH), 6.31 (dd, 1H, *J* 6.1, 1.6 Hz, =C*H*CHCH_2), 7.34-7.38 (m, 5H, H_{Ar}); δ_C (100 MHz, $CDCl_3$) 4.0 (CH_3, ≡C*C*H_3), 31.4 (CH_2, =CHCHCH_2), 70.0 (CH, *C*HOH), 73.0 (CH_2, *C*H_2O), 74.6 (CH, =CHCH*C*H), 75.2 (C, *C*OH), 76.6 (C, ≡*C*CH_3), 77.0 (CH, =CH*C*HCH), 78.7 (CH, =CH*C*HCH_2), 84.0 (C, *C*≡CCH_3), 128.3 (2 x CH, *C*H_{Ar}), 128.5 (CH, *C*H_{Ar}), 128.8 (2 x CH, *C*H_{Ar}), 130.6 (CH, =*C*HCHCH), 136.1 (CH, =*C*HCHCH_2), 137.5 (C, *C*CH_{Ar}); *m*/*z* HRMS (ES) calcd for $C_{18}H_{20}NaO_4^+$ 323.1259, found 323.1258; (ES) 323 ($[M+Na]^+$, 100%). Analytical data for **29**. m.p. 93-95 °C; R_f 0.16 (petrol/EtOAc 50:50); υ_{max}

neat/cm^{-1} 3508, 3370, 3035, 2937, 2875, 2851, 1316, 1051, 882, 737, 696; δ_H (400 MHz, $CDCl_3$) 1.55 (dd, 1H, ^2J 14.7 Hz, J 1.2 Hz, =CHCHCH_{2eq}), 1.86 (t, 3H, ^4J 1.3 Hz, =CCH_3), 2.10 (dd, 1H, ^2J 14.7 Hz, J 4.4 Hz, =CHCHCH_{2ax}), 4.43 (d, 1H, ^2J 11.2 Hz, CH_2O), 4.49 (d, 1H, ^2J 11.2 Hz, CH_2O), 4.54 (br s, 1H, C*H*OH), 4.69 (d, 1H, J 1.6 Hz, =CHC*H*C), 4.76 (d, 1H, J 4.4 Hz, =CHC*H*CH_2), 5.64-5.69 (m, 1H, C=C*H*), 6.25 (dd, 1H, J 6.1, 1.6 Hz, =C*H*CHCH_2), 6.31 (dd, 1H, J 6.1, 1.6 Hz, =C*H*CHC), 7.24-7.38 (m, 5H, H_{Ar}); δ_C (100 MHz, $CDCl_3$) 14.3 (CH_3, =C*C*H_3), 31.3 (CH_2, =CHCH*C*H_2), 66.4 (CH_2, *C*H_2O), 78.1 (CH, =CH*C*HCH_2), 79.5 (CH, =CH*C*HC), 81.7 (C, *C*OH), 81.9 (C, =CHCH*C*), 86.4 (CH, *C*HOH), 125.3 (CH, C=*C*H), 127.6 (2 x CH, *C*H_{Ar}), 127.9 (CH, *C*H_{Ar}), 128.7 (2 x CH, *C*H_{Ar}), 130.7 (CH, =*C*HCHCH_2), 135.1 (CH, =*C*HCHC), 138.7 (C, *C*CH_{Ar}), 149.7 (C, *C*=CH); *m*/*z* HRMS (ES) calcd for $C_{18}H_{20}NaO_4^+$ 323.1259, found 323.1244; (ES) 323 ([M+Na]$^+$, 100%). Analytical data for **9b.** δ_H (400 MHz, $CDCl_3$) 2.38 (d, 1H, ^2J 15.4 Hz, =CHCHCH_{2eq}), 2.76 (dd, 1H, ^2J 15.4 Hz, J 4.9 Hz, =CHCHCH_{2ax}), 4.13 (d, 1H, J 5.0 Hz, C*H*OCH_2), 4.64 (d, 1H, ^2J 12.1 Hz, CH_2O), 4.91 (dd, 1H, J 5.0, 1.6 Hz, =CHC*H*CH), 4.96-5.01 (m, 2H, =CHC*H*CH_2, CH_2O), 6.30 (dd, 1H, J 6.0, 1.6 Hz, =C*H*CHCH_2), 6.34 (dd, 1H, J 6.0, 1.7 Hz, =C*H*CHCH), 7.28-7.39 (m, 5H, H_{Ar}). δ_C (100 MHz, $CDCl_3$) 46.2 (CH_2, =CHCH*C*H_2), 73.7 (CH_2, *C*H_2O), 78.6 (CH, =CH*C*HCH_2), 80.0 (CH, =CH*C*HCH), 84.4 (CH, *C*HOCH_2), 128.1 (2 x CH, *C*H_{Ar}), 128.2 (CH, *C*H_{Ar}), 128.7 (2 x CH, *C*H_{Ar}), 132.0 (CH, =*C*HCHCH_2), 134.8 (CH, =*C*HCHCH), 137.8 (C, *C*CH_{Ar}), 205.1 (C, *C*=O). *m*/*z* (EI) 91 ([Bn]$^+$, 100%), 139 ([M-Bn]$^+$, 10), 158 (11), 201 (11), 230 ([M]$^+$, 9). Analytical data in agreement with literature values.[3]

3-*exo*-(Prop-2-yn-1-yl)-2,4-*endo*,*endo*-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-ol (32).

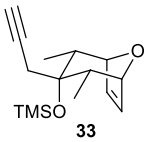


32

To a suspension of Mg (314 mg, 13.1 mmol) and $HgCl_2$ (54 mg, 0.200 mmol) in Et_2O (10 mL) at room temperature was added propargyl bromide (80% in toluene, 1.50 mL, 13.1 mmol) at a rate to maintain a gentle reflux. The resulting solution was cooled to 0 °C and a solution of **9a** (1.00 g, 6.57 mmol) in Et_2O (6 mL) was

added in one portion. The reaction was allowed to warm to room temperature over 2 h before being stirred at room temperature for 24 h. The reaction was quenched with NH_4Cl (15 mL of a saturated aqueous solution) and extracted with Et_2O (3 x 10 mL). The combined organics were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane:EtOAc 75:25) to afford **32** (958 mg, 76%) as a white solid. Analytical data in agreement with literature values.[12]

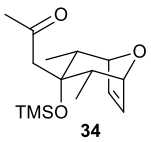
((2,4-*endo*,*endo*-Dimethyl-3-*exo*-(prop-2-yn-1-yl)-8-oxabicyclo[3.2.1]oct-6-en-3-yl)oxy)trimethylsilane (33).



33

To a solution of **32** (732 mg, 3.80 mmol) and Et_3N (1.56 g, 2.10 mL, 15.2 mmol) in CH_2Cl_2 (38 mL) at 0 °C was added TMSOTf (2.20 g, 1.79 mL, 9.90 mmol) dropwise over 10 mins. The reaction was stirred at room temperature for 5 h. The reaction was quenched with $NaHCO_3$ (20 mL of a saturated aqueous solution), and extracted with CH_2Cl_2 (3 x 15 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane:EtOAc 95:5) to afford **33** (907 mg, 90%) as a white solid. Analytical data in agreement with literature values.[12]

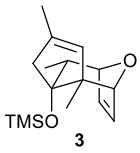
1-(2,4-*endo*,*endo*-Dimethyl-3-*exo*-((trimethylsilyl)oxy)-8-oxabicyclo[3.2.1]oct-6-en-3-yl)propan-2-one (34).



34

To a solution of **33** (200 mg, 0.750 mmol) and H_2O (30 µl, 1.50 mmol) in acetone (6 mL) at room temperature was added PPTS (283 mg, 1.13 mmol) and $Hg(OAc)_2$ (72 mg, 0.230 mmol). The reaction was stirred at room temperature for 24 h. The reaction was diluted with Et_2O, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane:EtOAc 90:10) to afford **34** (145 mg, 69%) as a colourless oil. Analytical data in agreement with literature values.[12]

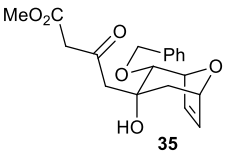
(±)-Trimethyl(((3a*R*,4*R*,7*S*,8*R*,8a*R*)-2,3a,8-trimethyl-1,3a,4,7,8,8a-hexahydro-4,7-epoxyazulen-8a-yl)oxy)silane (3).



3

To a solution of (diazomethyl)trimethylsilane (2 M in hexanes, 0.140 mL, 0.270 mmol) in THF (6.9 mL) at -78 °C was added ^{n}BuLi (2.14 M in hexanes, 0.130 mL, 0.290 mmol) dropwise. The reaction was stirred at -78 °C for 30 min before a solution of **34** (50 mg, 0.180 mmol) in THF (2.1 mL) was added dropwise. The resulting mixture was stirred at -78 °C for 1 h, then stirred at room temperature for 3 h, before being quenched with H_2O (5 mL). The aqueous layer was extracted with Et_2O (3 x 5 mL) and the combined organics dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 98:2) to afford **3** (32 mg, 64%) as a clear, colourless oil. υ_{max} neat/cm^{-1} 2960, 2922, 1248, 1093, 901; δ_H (400 MHz, $CDCl_3$) 0.08 (s, 9H, Si(C*H*$_3$)$_3$), 0.78 (s, 3H, C*H*$_3$C), 0.81 (d, 3H, *J* 7.3 Hz, C*H*$_3$CH), 1.67 (s, 3H, =CC*H*$_3$), 1.90 (qd, 1H, *J* 7.3, 3.4 Hz, CH$_3$C*H*), 1.98 (d, 1H, ^{2}*J* 14.8 Hz, =CC*H*$_2$), 2.40 (d, 1H, ^{2}*J* 14.8 Hz, =CC*H*$_2$), 4.33 (dd, 1H, *J* 3.4, 1.6 Hz, =CHC*H*CH), 4.36 (d, 1H, *J* 1.4 Hz, =CHC*H*C), 5.37 (s, 1H, C=C*H*), 6.15 (dd, 1H, *J* 6.2, 1.6 Hz, =C*H*CHC), 6.20 (dd, 1H, *J* 6.2, 1.4 Hz, =C*H*CHCH); δ_C (100 MHz, $CDCl_3$) 2.5 (3 x CH$_3$, Si,(*C*H$_3$)$_3$), 12.3 (CH$_3$, *C*H$_3$CH), 17.7 (CH$_3$, =C*C*H$_3$), 19.9 (CH$_3$, *C*H$_3$C), 40.0 (CH, CH$_3$*C*H), 49.1 (CH$_2$, =C*C*H$_2$), 52.0 (C, *C*CHO), 82.6 (CH, =CH*C*HCH), 83.7 (CH, =CH*C*HC), 84.5 (C, *C*OSi), 132.1 (CH, =*C*HCHC), 132.7 (CH, =*C*HCHCH), 133.4 (CH, C=*C*H), 136.0 (C, *C*=CH). Analytical data in agreement with literature values.[12]

(±)-Methyl 4-((1*S*,2*R*,3*R*,5*S*)-2-(benzyloxy)-3-hydroxy-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-3-oxobutanoate (35).

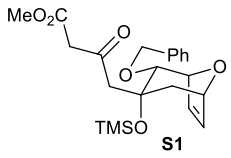


35

To a solution of diisopropylamine (1.76 g, 2.44 mL, 17.4 mmol) in THF (18 mL) at 0 °C was added ^{n}BuLi (1.60 M in hexanes, 10.9 mL, 17.4

mmol) dropwise. The resulting solution was stirred at 0 °C for 30 min before methyl acetoacetate (1.01 g, 0.940 mL, 8.70 mmol) was added dropwise. The reaction was stirred for 1 h at 0 °C before a solution of **9b** (500 mg, 2.17 mmol) in THF (4 mL) was added in one portion. The reaction was stirred at room temperature for 20 h before being quenched with HCl (20 mL of a 1 M aqueous solution) and extracted with Et_2O (3 x 15 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 70:30→60:40) to afford **35** (547 mg, 70%) as a bright yellow oil. R_f 0.09 (hexane/EtOAc 75:25); υ_{max} neat/cm^{-1} 3535, 2951, 1742, 1704, 1322, 1052, 726, 699; ^{1}H NMR indicates that **35** exists in ~6:1 keto:enol ratio. The data reported is of the major keto tautomer with identifiable enol peaks following: δ_H (400 MHz, $CDCl_3$) 1.80 (d, 1H, ^2J 14.4 Hz, =CHCHCH_{2eq}), 2.04 (ddd, 1H, ^2J 14.4 Hz, J 4.4 Hz, ^4J 1.2 Hz, =CHCHCH_{2ax}), 2.41 (d, 1H, ^2J 13.3 Hz, CH_2C=O), 2.73 (d, 1H, ^2J 13.3 Hz, CH_2C=O), 3.46 (d, 1H, ^2J 15.9 Hz, C$H_2$$CO_2$Me), 3.54 (d, 1H, ^2J 15.9 Hz, C$H_2$$CO_2$Me), 3.66 (d, 1H, J 4.2 Hz, =CHCHC*H*), 3.68 (s, 3H, OCH_3), 4.61 (d, 1H, ^2J 11.6 Hz, CH_2O), 4.66-4.70 (m, 2H, =CHC*H*CH, CH_2O), 4.74 (d, 1H, J 4.4 Hz, =CHC*H*CH_2), 6.26 (dd, 1H, J 6.1, 1.7 Hz, =C*H*CHCH), 6.33 (dd, 1H, J 6.1, 1.7 Hz, =C*H*$CHCH_2$), 7.36 (m, 5H, H_{Ar}); Enol Peaks: 4.98 (s, 1H, C*H*=COH), 12.07 (s, 1H, CH=CO*H*); δ_C (100 MHz, $CDCl_3$) 37.8 (CH_2, =CHCH*C*H_2), 51.0 (CH_2, *C*$H_2$$CO_2$Me), 52.4 ($CH_3$, O*C*$H_3$), 56.1 ($CH_2$, *C*$H_2$C=O), 72.8 ($CH_2$, C$H_2$O), 77.3 (CH, =CH*C*HCH), 77.5 (C, *C*OH), 77.9 (CH, =CHCH*C*H), 78.6 (CH, =CH*C*HCH_2), 128.3 (2 x CH, *C*H_{Ar}), 128.6 (CH, *C*H_{Ar}), 128.9 (2 x CH, *C*H_{Ar}), 131.0 (CH, =*C*H), 136.3 (CH, =*C*H), 137.6 (C, *C*CH_{Ar}), 168.0 (C, *C*O_2Me), 201.7 (C, *C*=O); Enol Peaks: 92.3 (CH, *C*H=COH); *m/z* HRMS (ES) calcd for $C_{19}H_{22}NaO_6^+$ 369.1314, found 369.1330; (ES) 253 ($[M-Bn]^+$, 47%), 369 ($[M+Na]^+$, 100%).

(±)-Methyl 4-((1*S*,2*R*,3*R*,5*S*)-2-Benzyloxy-3-trimethylsilyloxy-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-3-oxobutanoate (S1).

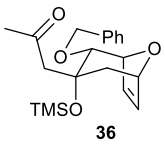


S1

To a solution of **35** (393 mg, 1.10 mmol) and Et_3N (445 mg, 0.610 mL, 4.40 mmol) in CH_2Cl_2 (11 mL) at 0 °C was added TMSOTf (636 mg, 0.520 mL, 2.86 mmol) dropwise. The reaction was stirred at room temperature for 5 h before being quenched with $NaHCO_3$ (10 mL of a saturated aqueous solution) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organics were dried over $MgSO_4$, filtered and dried *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 85:15) to afford **S1** (421 mg, 92%) as a bright yellow oil. R_f 0.11 (petrol/EtOAc 90:10); υ_{max} neat/cm^{-1} 2952, 1747, 1718, 1650, 1626, 1242, 1077, 834, 750, 726, 698; ^{1}H NMR indicates that **S1** exists in ~3:1 keto:enol ratio. The data reported is of the major keto tautomer with identifiable enol peaks following: δ_H (400 MHz, $CDCl_3$) 0.04 (s, 9H, Si(C*H*)$_3$), 1.80 (dd, 1H, ^2J 14.0 Hz, J 1.1 Hz, =CHCHC*H*$_{2eq}$), 2.09 (dd, 1H, ^2J 14.0 Hz, J 4.2 Hz, =CHCHC*H*$_{2ax}$), 2.56 (d, 1H, ^2J 15.9 Hz, C*H*$_2$C=O), 2.77 (d, 1H, ^2J 15.9 Hz, C*H*$_2$C=O), 3.31 (d, 1H, ^2J 15.7 Hz, C*H*$_2$CO$_2$Me), 3.36 (d, 1H, ^2J 15.7 Hz, C*H*$_2$CO$_2$Me), 3.68 (d, 1H, J 3.8 Hz, =CHCHC*H*), 3.71 (s, 3H, OC*H*$_3$), 4.57 (d, 1H, ^2J 11.7 Hz, C*H*$_2$O), 4.62 (dd, 1H, J 3.8, 1.4 Hz, =CHC*H*CH), 4.66-4.70 (m, 2H, =CHC*H*CH$_2$, C*H*$_2$O), 6.17 (app. qd, 2H, J 6.2, 1.4 Hz, =C*H*CHCH$_2$, =C*H*CHCH), 7.31-7.38 (m, 5H, *H*$_{Ar}$); Enol peaks: 1.65 (dd, 1H, ^2J 14.1 Hz, J 1.1 Hz, =CHCHC*H*$_{2eq}$), 2.18 (dd, 1H, ^2J 14.1 Hz, J 4.2 Hz, =CHCHC*H*$_{2ax}$), 2.31 (d, 1H, ^2J 13.2 Hz, C*H*$_2$C=O), 2.46 (d, 1H, ^2J 13.2 Hz, C*H*$_2$C=O), 4.93 (s, 1H, C*H*=COH), 12.08 (s, 1H, CH=O*H*); δ_C (100 MHz, $CDCl_3$) 3.1 (3 x CH_3, Si(*C*H$_3$)$_3$), 39.6 (CH_2, =CHCH*C*H$_2$), 50.8 (CH_2, *C*H$_2$CO$_2$Me), 52.4 (CH_3, O*C*H$_3$), 54.0 (CH_2, *C*H$_2$C=O), 72.4 (CH_2, *C*H$_2$O), 75.6 (C, *C*OSi), 77.4 (CH, =CH*C*HCH), 78.6 (CH, =CH*C*HCH$_2$), 78.7 (CH, =CHCH*C*H), 128.3 (CH, *C*H$_{Ar}$), 128.7 (2 x CH, *C*H$_{Ar}$), 128.9 (2 x CH, *C*H$_{Ar}$), 131.6 (CH, =*C*HCHCH$_2$), 134.7 (CH, =*C*HCHCH), 138.0 (C, *C*CH$_{Ar}$), 167.6 (C, *C*O$_2$CH$_3$), 200.3 (C,

C=O); Enol Peaks: 39.2 (CH_2, =CHCH*C*H_2), 47.6 (CH_2, *C*H_2C=O), 51.3 (CH_3, O*C*H_3), 92.6 (CH, *C*H=COH), 172.9 (C, *C*O_2Me), 174.8 (CH=*C*OH); *m*/*z* HRMS (ES) calcd for $C_{22}H_{30}NaO_6Si^+$ 441.1709, found 441.1723; (ES) 441 ($[M+Na]^+$, 100%).

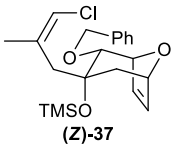
(±)-1-((1*S*,2*R*,3*R*,5*S*)-2-Benzyloxy-3-trimethylsilyloxy-8-oxabicyclo[3.2.1]oct-6-en-3-yl)propan-2-one (36).



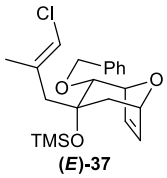
36

To a solution of **S1** (53 mg, 0.130 mmol) and H_2O (0.05 mL, 0.520 mmol) in DMSO (0.34 mL) was added NaCl (15 mg, 0.250 mmol). The mixture was heated to reflux for 3 h before being allowed to cool to room temperature. The reaction was purified by column chromatography (hexane/EtOAc 90:10) to afford **36** (33 mg, 70%) as a clear colourless oil. R_f 0.31 (petrol/EtOAc 90:10); υ_{max} neat/cm^{-1} 2951, 1703, 1354, 1243, 1102, 834, 750, 725, 698; δ_H (400 MHz, $CDCl_3$) 0.04 (s, 9H, Si(C*H*$_3$)$_3$), 1.79 (dd, 1H, ^2J 14.0 Hz, *J* 1.2 Hz, =CHCHC*H*$_{2eq}$), 2.04 (s, 3H, C*H*$_3$C=O), 2.09 (dd, 1H, ^2J 14.0 Hz, *J* 4.2 Hz, =CHCHC*H*$_{2ax}$), 2.45 (d, 1H, ^2J 15.3 Hz, C*H*$_2$C=O), 2.69 (d, 1H, ^2J 15.3 Hz, C*H*$_2$C=O), 3.68 (d, 1H, *J* 3.8 Hz, =CHCHC*H*), 4.58 (d, 1H, ^2J 11.7 Hz, C*H*$_2$O), 4.62 (dd, 1H, *J* 3.8, 1.6 Hz, =CHC*H*CH), 4.65-4.71 (m, 2H, =CHC*H*CH$_2$, C*H*$_2$O), 6.16 (dd, 1H, *J* 6.2, 1.5 Hz, =C*H*CHCH$_2$), 6.19 (dd, 1H, *J* 6.2, 1.6 Hz, =C*H*CHCH), 7.28-7.39 (m, 5H, *H*$_{Ar}$); δ_C (100 MHz, $CDCl_3$) 3.1 (3 x CH_3, Si(*C*H$_3$)$_3$), 32.4 (CH_3, *C*H$_3$C=O), 39.7 (CH_2, =CHCHC*H*$_2$), 54.7 (CH_2, C*H*$_2$C=O), 72.5 (CH_2, C*H*$_2$O), 75.6 (C, *C*OSi), 77.5 (CH, =CH*C*HCH), 78.7 (CH, =CH*C*HCH$_2$), 78.8 (CH, =CHCH*C*H), 128.3 (CH, *C*H$_{Ar}$), 128.7 (2 x CH, *C*H$_{Ar}$), 128.9 (2 x CH, *C*H$_{Ar}$), 131.7 (CH, =*C*HCHCH), 134.7 (CH, =*C*HCHCH$_2$), 138.1 (C, *C*CH$_{Ar}$), 206.5 (C, *C*=O); *m*/*z* HRMS (ES) calcd for $C_{20}H_{28}NaO_4Si^+$ 383.1655, found 383.1660; (ES) 383 ($[M+Na]^+$, 100%).

(*Z*)-(±)-(((1*S*,2*R*,3*S*,5*S*)-2-Benzyloxy-3-(3-chloro-2-methylallyl)-8-oxabicyclo[3.2.1]oct-6-en-3-yl)oxy)trimethylsilane ((*Z*)-37) and (*E*)-(±)-(((1*S*,2*R*,3*S*,5*S*)-2-Benzyloxy-3-(3-chloro-2-methylallyl)-8-oxabicyclo[3.2.1]oct-6-en-3-yl)oxy)trimethylsilane ((*E*)-37).



(*Z*)-37

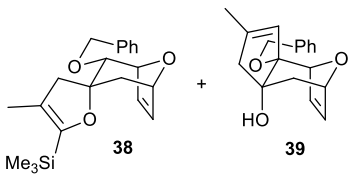


(*E*)-37

To a solution of diisopropylamine (87 mg, 0.120 mL, 0.860 mmol) in THF (2.5 mL) at 0 °C was added ^{n}BuLi (1.42 M in hexanes, 0.610 mL, 0.860 mmol) dropwise. The reaction was stirred for 45 min before being cooled to -78 °C. (Chloromethyl)triphenylphosphonium chloride (297 mg, 0.860 mmol) was added portion-wise and the suspension stirred at -78 °C for 30 min. A solution of **36** (142 mg, 0.390 mmol) in THF (2.5 mL) was added over 5 min and the reaction was allowed to warm to room temperature. After stirring for 16 h at room temperature the reaction was quenched with NH_4Cl (10 mL of a saturated aqueous solution) and extracted with EtOAc (3 x 10 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 98:2) to afford **(*Z*)-37** followed by **(*E*)-37** (122 mg, 80% *E*:*Z* 1:1) as clear, colourless oils. Analytical data for **(*Z*)-37**. R_f 0.16 (petrol/EtOAc 99:1); υ_{max} neat/cm^{-1} 2952, 1243, 1097, 833, 750, 724, 697; δ_H (400 MHz, $CDCl_3$) 0.05 (s, 9H, $Si(CH_3)_3$), 1.60 (dd, 1H, ^2J 14.2 Hz, J 1.1 Hz, =CHCHCH_{2eq}), 1.79 (d, 3H, ^4J 1.4 Hz, =CCH_3), 2.00 (dd, 1H, ^2J 14.2 Hz, J 4.3 Hz, =CHCHCH_{2ax}), 2.47 (d, 1H, ^2J 13.7 Hz, =CCH_2), 2.60 (d, 1H, ^2J 13.6 Hz, =CCH_2), 3.63 (d, 1H, J 3.8 Hz, =CHCHC*H*), 4.63 (dd, 1H, J 3.8, 1.6 Hz, =CHC*H*CH), 4.65-4.69 (m, 2H, =CHC*H*CH_2, CH_2O), 4.71 (d, 1H, ^2J 11.6 Hz, CH_2O), 5.92 (br s, 1H, =C*H*Cl), 6.16 (dd, 1H, J 6.2, 1.5 Hz, =C*H*CHCH), 6.19 (dd, 1H, J 6.2, 1.6 Hz, =C*H*CHCH_2), 7.28-7.43 (m, 5H, H_{Ar}); δ_C (100 MHz, $CDCl_3$) 3.5 (3 x CH_3, $Si(CH_3)_3$), 23.2 (CH_3, =C*C*H_3), 38.6 (CH_2, =CHCH*C*H_2), 44.5 (CH_2, =C*C*H_2), 72.5 (CH_2, *C*H_2O), 77.2 (C, *C*OSi), 77.4 (CH, =CH*C*HCH$_2$), 78.8 (CH, =CH*C*HCH), 80.9 (CH, =CHCH*C*H), 115.1 (CH, =*C*HCl), 128.2 (CH, *C*H_{Ar}), 128.7 (2 x CH, *C*H_{Ar}), 128.8 (2 x CH, *C*H_{Ar}), 131.6 (CH,

=*C*HCHCH$_2$), 134.6 (CH, =*C*HCHCH), 135.9 (C, *C*=CHCl), 138.2 (C, *C*CH$_{Ar}$); *m*/*z* HRMS (ES) calcd for $C_{21}H_{29}{}^{35}Cl\ NaO_3Si^+$ 415.1472, found 415.1479; (ES) 415 ([M(^{35}Cl)+Na]$^+$, 100%), 417 ([M(^{37}Cl)+Na]$^+$, 38%). Analytical data for **(*E*)-37**. R_f 0.20 (petrol/EtOAc 99:1); υ_{max} neat/cm^{-1} 2951, 1244, 1100, 1077, 834, 750, 725, 698; δ_H (400 MHz, $CDCl_3$) 0.04 (s, 9H, Si(C*H*$_3$)$_3$), 1.59 (dd, 1H, ^2J 14.1 Hz, *J* 1.2 Hz, =CHCHC*H*$_{2eq}$), 1.79 (d, 3H, ^4J 1.2 Hz, =CC*H*$_3$), 1.93 (dd, 1H, ^2J 14.1 Hz, *J* 4.2 Hz, =CHCHC*H*$_{2ax}$), 2.17 (d, 1H, ^2J 14.2 Hz, =CC*H*$_2$), 2.37 (d, 1H, ^2J 14.2 Hz, =CC*H*$_2$), 3.52 (d, 1H, 3.9 Hz, =CHCHC*H*), 4.61 (d, 1H, ^2J 11.7 Hz, C*H*$_2$O), 4.64-4.71 (m, 3H, =CHC*H*CH, =CHC*H*CH$_2$, C*H*$_2$O), 5.70 (d, 1H, ^4J 1.1 Hz, =C*H*Cl), 6.16 (dd, 1H, *J* 6.1, 1.6 Hz, =C*H*CHCH), 6.19 (dd, 1H, *J* 6.1, 1.7 Hz, =C*H*CHCH$_2$), 7.30-7.37 (m, 5H, *H*$_{Ar}$); δ_C (100 MHz, $CDCl_3$) 3.4 (3 x CH_3, Si(*C*H$_3$)$_3$), 19.0 (CH_3, =C*C*H$_3$), 39.3 (CH_2, =CHCHC*H*$_2$), 49.8 (CH_2, =C*C*H$_2$), 72.7 (CH_2, *C*H$_2$O), 77.1 (C, *C*OSi), 77.4 (CH, =CH*C*HCH), 78.8 (CH, =CH*C*HCH$_2$), 79.3 (CH, =CHCH*C*H), 116.2 (CH, =*C*HCl), 128.4 (CH, *C*H$_{Ar}$), 128.7 (2 x CH, *C*H$_{Ar}$), 128.9 (2 x CH, *C*H$_{Ar}$), 131.6 (CH, =*C*HCHCH$_2$), 134.5 (CH, =*C*HCHCH), 135.1 (C, *C*=CHCl), 138.0 (C, *C*CH$_{Ar}$); *m*/*z* HRMS (ES) calcd for $C_{21}H_{29}{}^{35}ClNaO_3Si^+$ 415.1472, found 415.1485; (ES) 415 ([M(^{35}Cl)+Na]$^+$, 100%), 417 ([M(^{37}Cl)+Na]$^+$, 20%).

(±)-((1*S*,2*R*,2'*S*,5*S*)-2-Benzyloxy-4'-methyl-3'*H*-8-oxaspiro[bicyclo[3.2.1]oct[6]ene-3,2'-furan]-5'-yl)trimethylsilane (38) and (±)-(3a*R*,4*S*,7*S*,8a*S*)-3a-Benzyloxy-2-methyl-1,3a,4,7,8,8a-hexahydro-4,7-epoxyazulen-8a-ol (39).



*Starting from ketone **36***. To a solution of (diazomethyl)trimethylsilane (2 M in hexanes, 0.110 mL, 0.210 mmol) in THF (5.4 mL) at -78 °C was added ^{n}BuLi (1.60 M in hexanes, 0.140 mL, 0.220 mmol) dropwise. The reaction was stirred at -78 °C for 30 min before a solution of **36** (50 mg, 0.140 mmol) in THF (1.6 mL) was added dropwise over 10 min. The resulting mixture was stirred at -78 °C for 1 h, then stirred at room temperature for

3 h, before being quenched with H_2O (5 mL). The aqueous layer was extracted with Et_2O (3 x 5 mL) and the combined organics dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude reaction mixture was dissolved in THF (1.4 mL) and TBAF (1 M in THF, 0.170 mL, 0.170 mmol) added. The reaction was stirred for 18 h at room temperature before being washed with H_2O (2 mL) and extracted with Et_2O (3 x 5 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 98:2→90:10) to afford **38** (22 mg, 45%) as a clear, colourless oil followed by **39** (6 mg, 15%) as a clear, colourless oil.

*From vinyl chloride **37**.* To a mixture of **(*Z*)-** and **(*E*)-37** (36mg, 0.090 mmol) in THF (0.7 mL) at room temperature was added NaHMDS (2 M in THF, 0.180 mL, 0.360 mmol) dropwise. The reaction was stirred at room temperature for 18 h. The reaction was quenched with NH_4Cl (2 mL of a saturated aqueous solution) before H_2O (2 mL) and EtOAc (5 mL) were added and the layers separated. The aqueous layer was washed with EtOAc (2 x 5 mL) and CH_2Cl_2 (1 x 5 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude reaction mixture was dissolved in THF (1.8 mL) and TBAF (1 M in THF, 0.110 mL, 0.110 mmol) added. The reaction was stirred for 18 h at room temperature before being washed with H_2O (2 mL) and extracted with Et_2O (3 x 5 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc 98:2→90:10) to afford **38** (8 mg, 25%) as a clear, colourless oil followed by **39** (7 mg, 29%) as a clear, colourless oil.

Analytical data for **38**. R_f 0.13 (petrol/EtOAc 98:2); υ_{max} neat/cm^{-1} 2951, 2911, 1309, 1246, 1050, 837, 696; δ_H (400 MHz, $CDCl_3$) 0.08 (s, 9H, Si(CH_3)$_3$), 1.60 (s, 3H, =CCH_3), 1.79 (dd, 1H, ^2J 14.1 Hz, J 1.5 Hz, =CHCHCH_{2eq}), 1.85 (dd, 1H, ^2J 14.1 Hz, J 3.6 Hz, =CHCHCH_{2ax}), 2.23 (dd, 1H, ^2J 15.9 Hz, ^4J 0.9 Hz, =CCH_2), 2.44 (dd, 1H, ^2J 15.9 Hz, ^4J 1.0 Hz, =CCH_2), 3.55 (d, 1H, J 3.7 Hz, =CHCHCH), 4.52 (d, 1H, ^2J 12.2 Hz, CH_2O), 4.64-4.70 (m, 3H,

=CHC*H*CH, =CHC*H*CH_2, C*H_2*O), 6.13 (dd, 1H, *J* 6.1, 1.4 Hz, =C*H*CHCH_2), 6.20 (dd, 1H, *J* 6.1, 1.4 Hz, =C*H*CHCH), 7.19-7.33 (m, 5H, *H_{Ar}*); δ_C (100 MHz, $CDCl_3$) -1.3 (3 x CH_3, Si(*C*H_3)$_3$), 12.2 (CH_3, =C*C*H_3), 41.6 (CH_2, =CHCH*C*H_2), 51.7 (CH_2, =C*C*H_2), 72.5 (CH_2, *C*H_2O), 78.6 (CH, =CH*C*HCH), 79.1 (CH, =CH*C*HCH_2), 83.3 (CH, =CHCH*C*H), 84.5 (C, *C*OCSi), 117.6 (C, *C*=CSi), 127.4 (2 x CH, *C*H_{Ar}), 127.6 (CH, *C*H_{Ar}), 128.4 (2 x CH, *C*H_{Ar}), 131.3 (CH, =*C*HCHCH), 133.7 (CH, =*C*HCHCH_2), 139.3 (C, *C*CH_{Ar}), 153.8 (C, C=*C*Si); *m*/*z* HRMS (ES) calcd for $C_{21}H_{28}NaO_3Si^+$ 379.1705, found 379.1717; (ES) 379 ([M+Na]$^+$, 100%), 380 ([M+Na+H]$^+$, 46). Analytical data for **39**. R_f 0.10 (petrol/EtOAc 90:10); υ_{max} neat/cm^{-1} 3537, 2918, 1441, 1086, 1051, 886, 727, 697; δ_H (400 MHz, $CDCl_3$) 1.76 (dd, 1H, ^2J 14.2 Hz, *J* 4.1 Hz, =CHCHC*H*$_{2ax}$), 1.85 (br s, 3H, =CC*H*$_3$), 1.95 (dd, 1H, ^2J 14.2 Hz, *J* 1.1 Hz, =CHCHC*H*$_{2eq}$), 2.19 (d, 1H, ^2J 16.2 Hz, =CC*H*$_2$), 2.54 (d, 1H, ^2J 16.2 Hz, =CC*H*$_2$), 3.08 (s, 1H, O*H*), 4.49 (ABq, 2H, ^2J 11.4 Hz, C*H*$_2$O), 4.67 (dt, 1H, *J* 4.1, 1.1 Hz, =CHC*H*CH_2), 4.73 (s, 1H, =CHC*H*C), 5.56 (m, 1H, =C*H*), 6.29-6.33 (m, 2H, =C*H*CHCH_2, =C*H*CHCH), 7.27-7.36 (m, 5H, *H_{Ar}*); δ_C (100 MHz, $CDCl_3$) 18.0 (CH_3, =C*C*H_3), 39.6 (CH_2, =CHCH*C*H_2), 54.7 (CH_2, =C*C*H_2), 65.9 (CH_2, *C*H_2O), 78.1 (CH, =CH*C*HCH_2), 78.1 (C, =CHCH*C*), 79.9 (CH, =CH*C*HC), 85.2 (C, *C*OH), 125.7 (CH, C=*C*H), 127.5 (2 x CH, *C*H_{Ar}), 127.7 (CH, *C*H_{Ar}), 128.6 (2 x CH, *C*H_{Ar}), 131.9 (CH, =*C*HCHCH_2), 134.5 (CH, =*C*HCHC), 139.3 (C, *C*CH_{Ar}), 147.8 (C, *C*=CH); *m*/*z* HRMS (ES) calcd for $C_{18}H_{20}NaO_3^+$ 307.1310, found 307.1295; (ES) 307 ([M+Na]$^+$, 100%).

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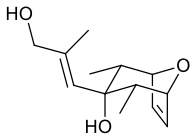
NMR Spectra



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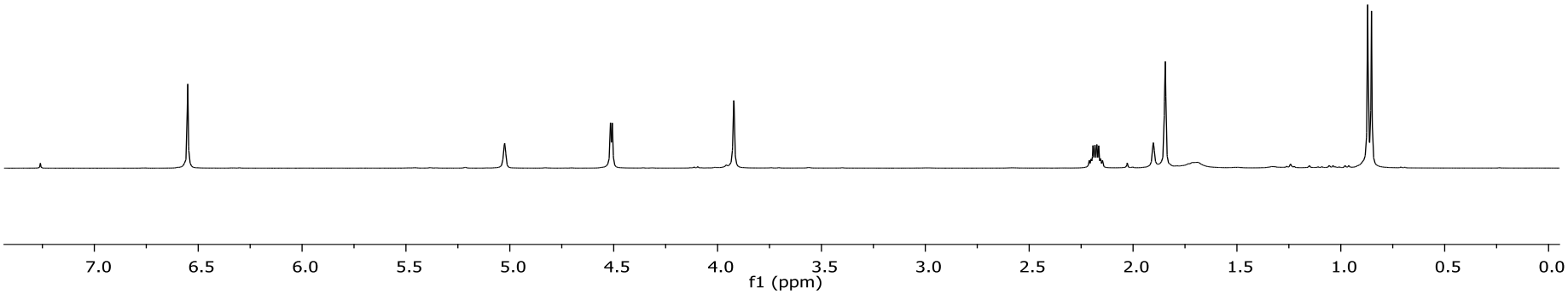

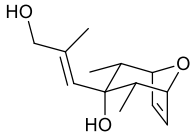

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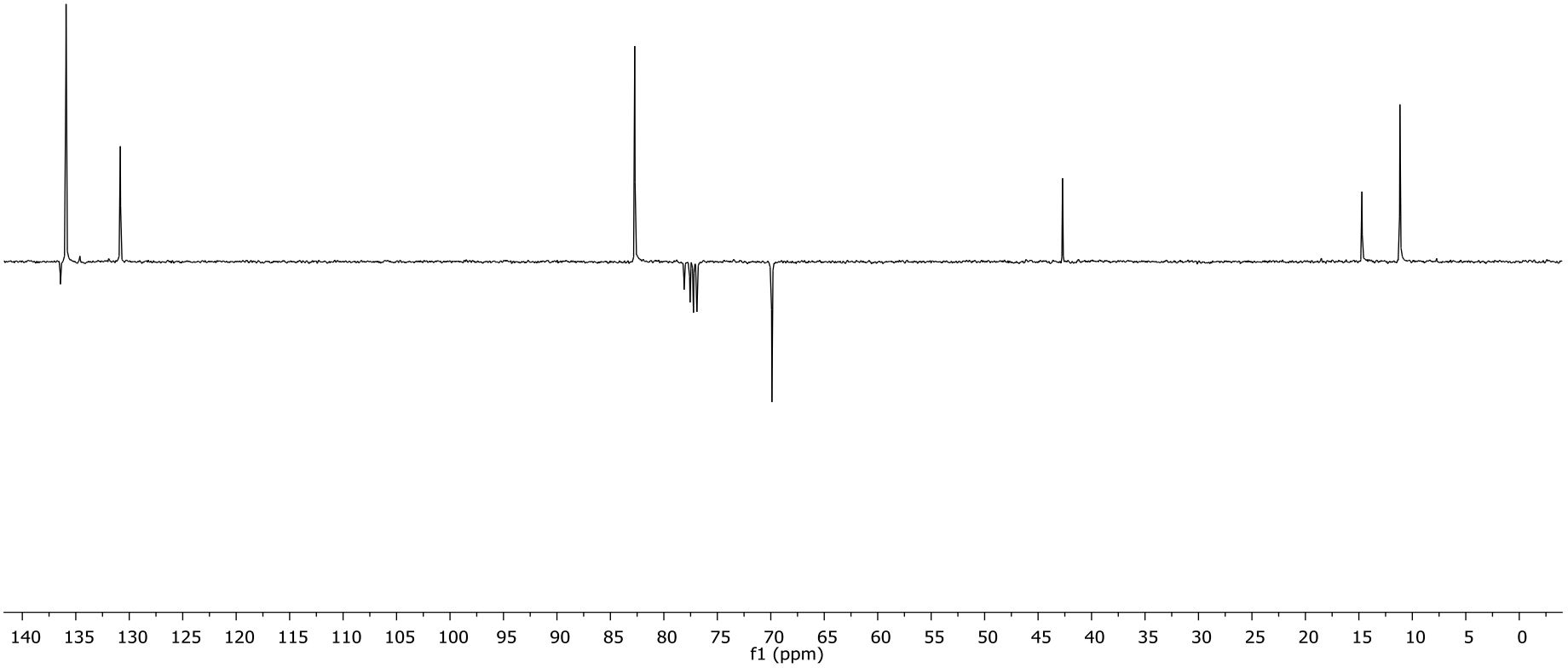

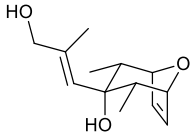

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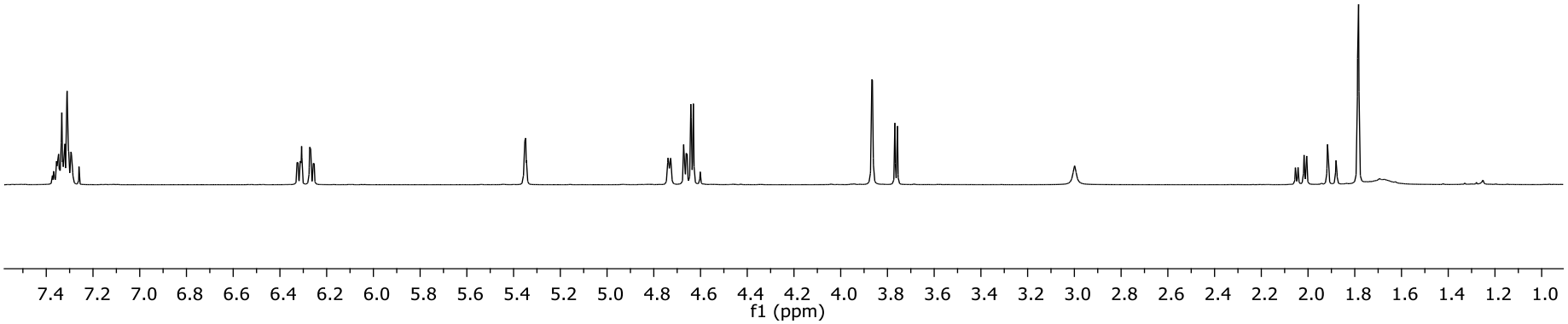

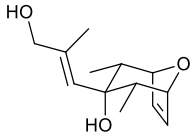

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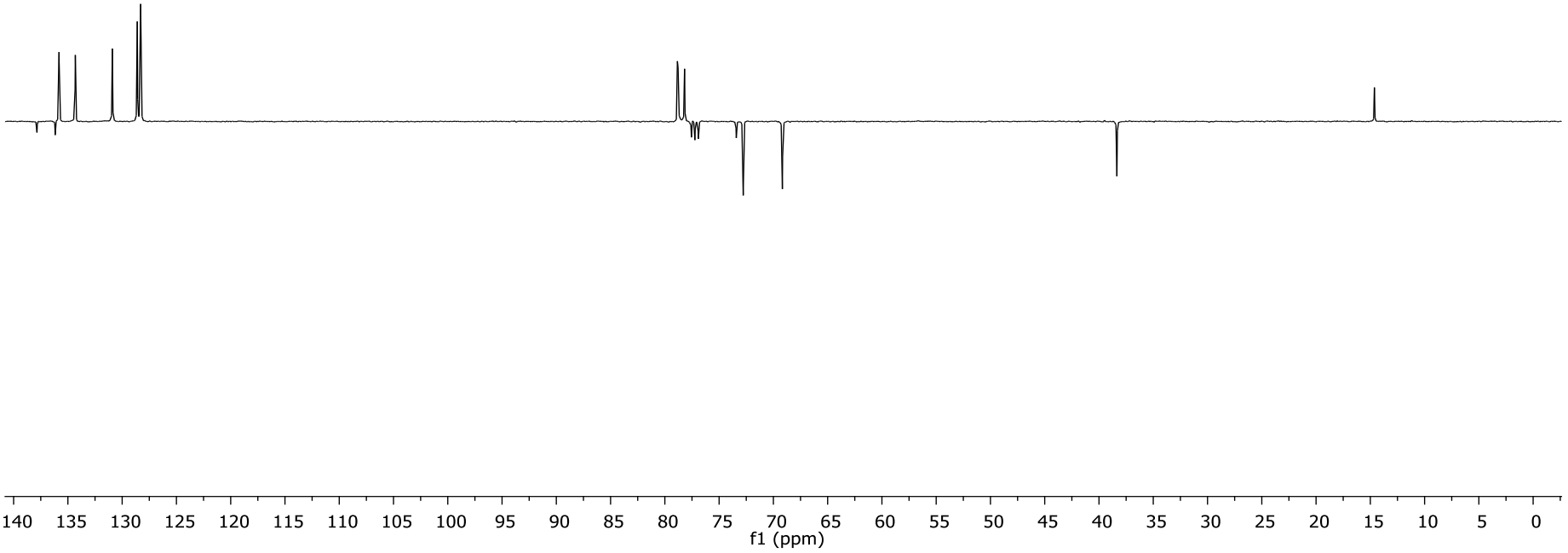

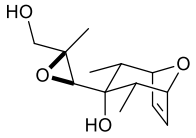

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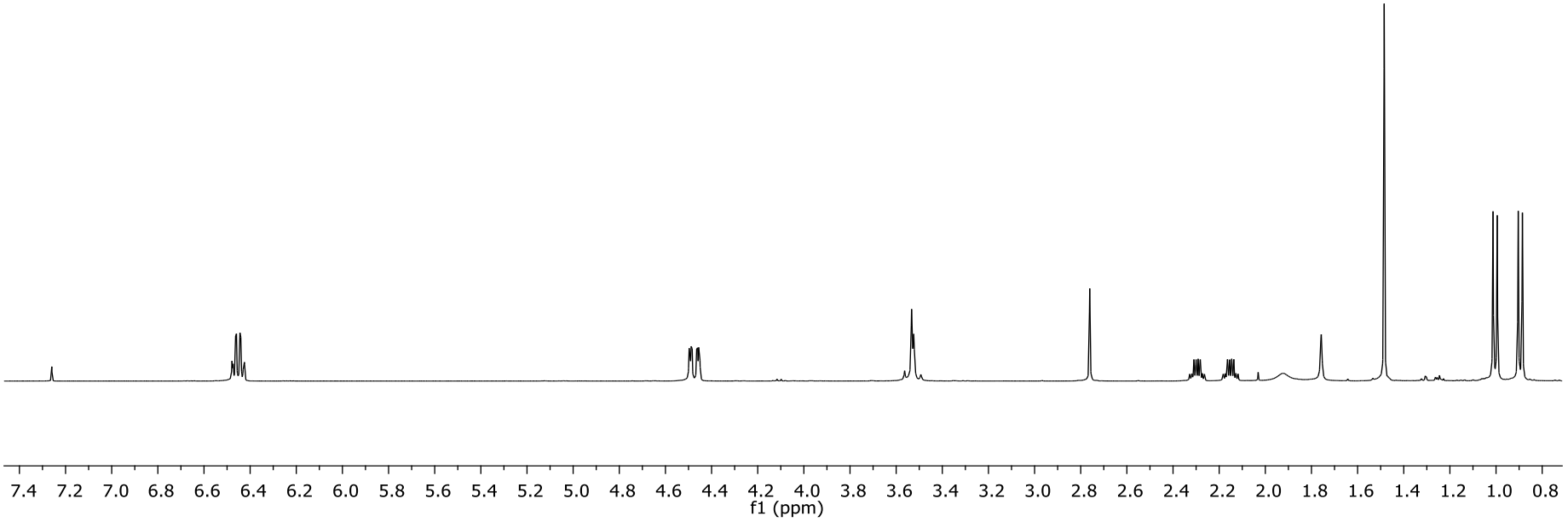

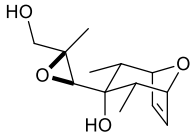

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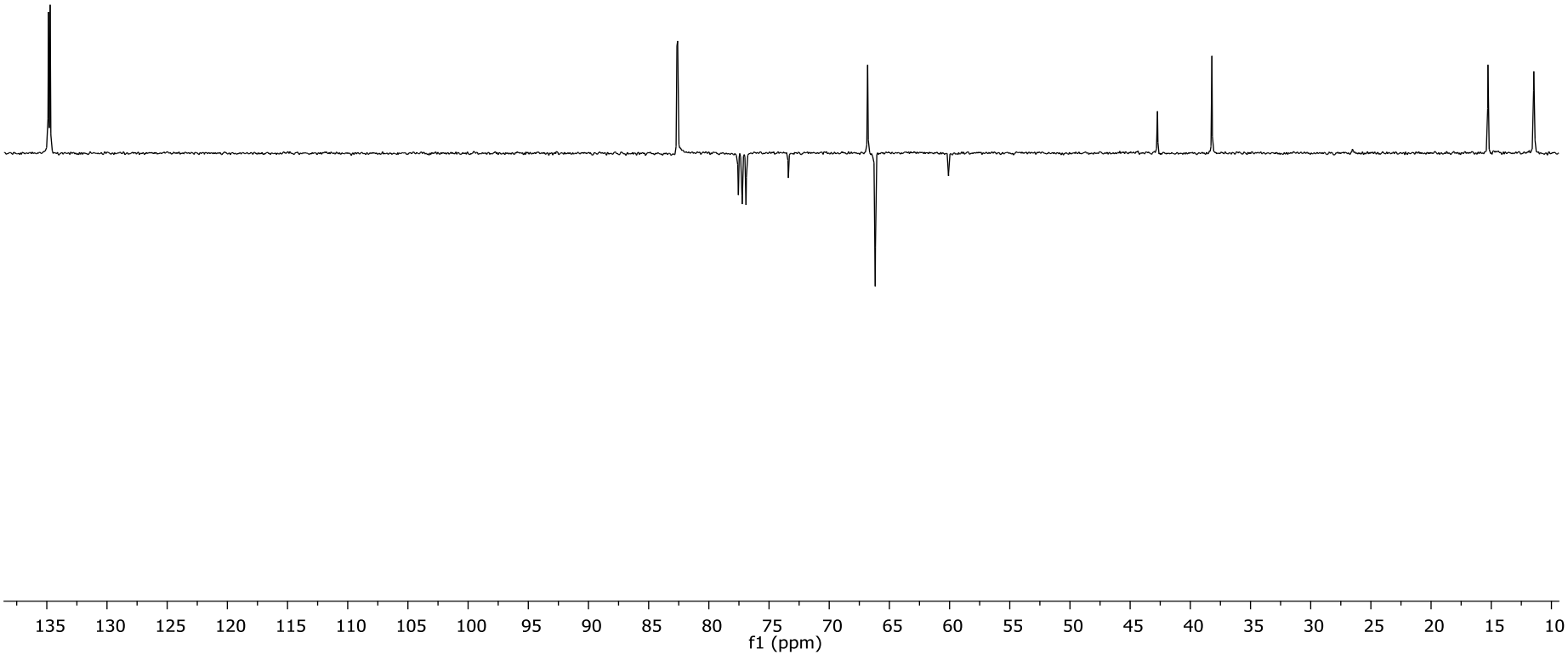

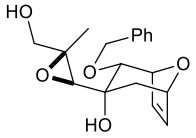

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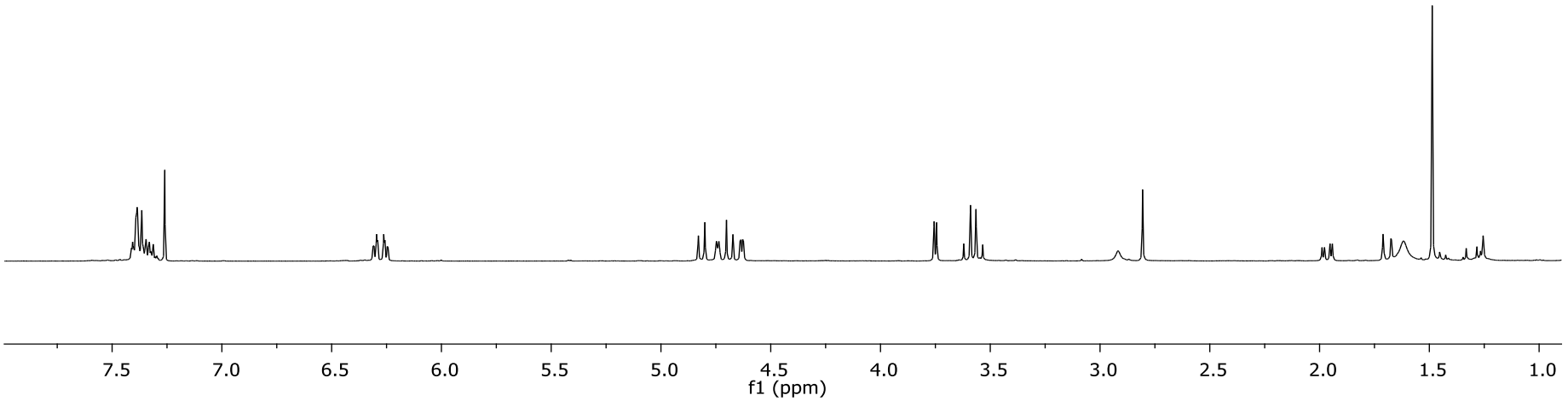
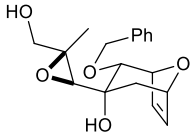
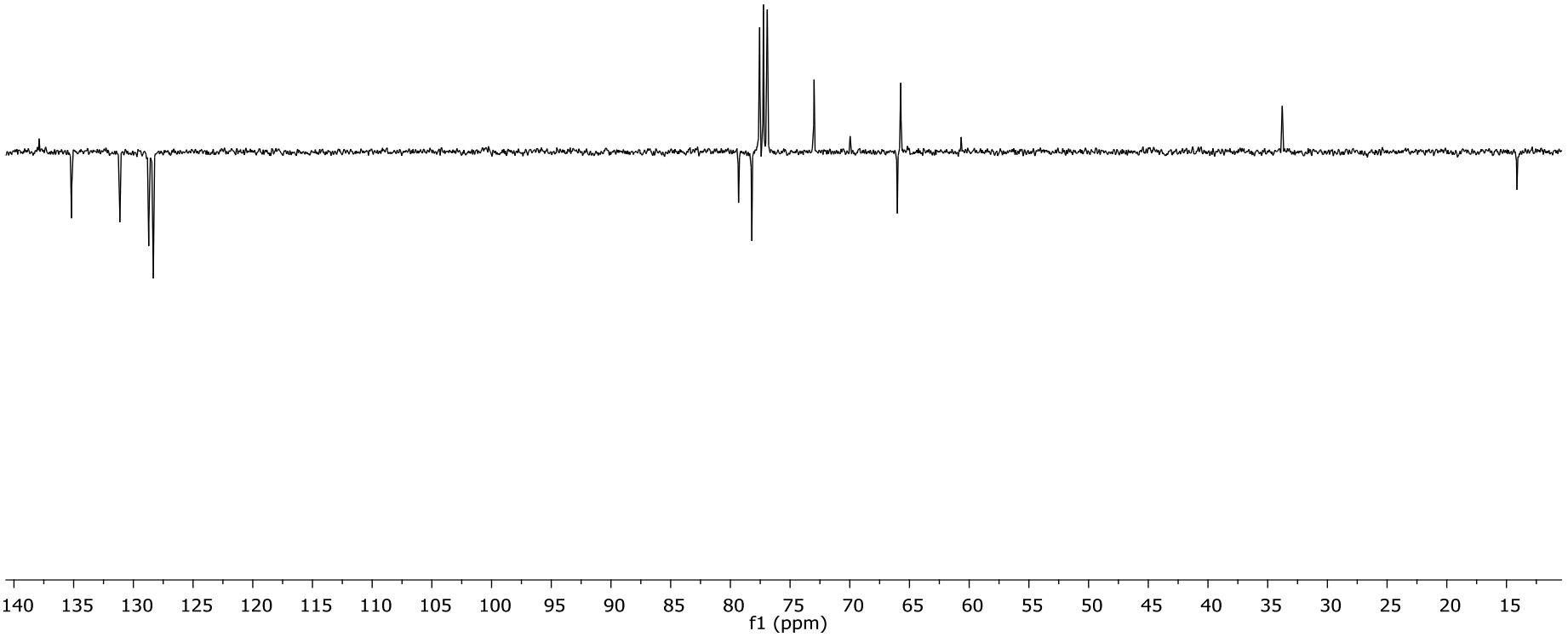
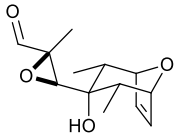
400 MHz, $CDCl_3$



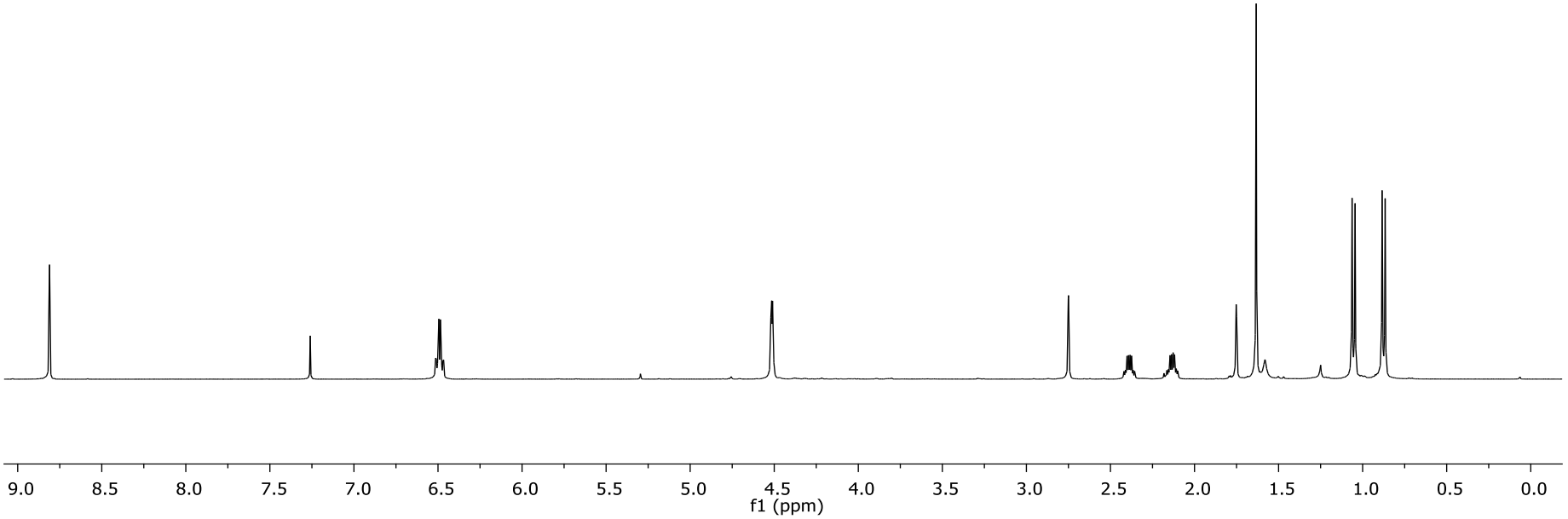


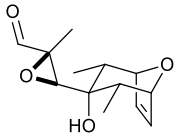
12b
100 MHz, $CDCl_3$



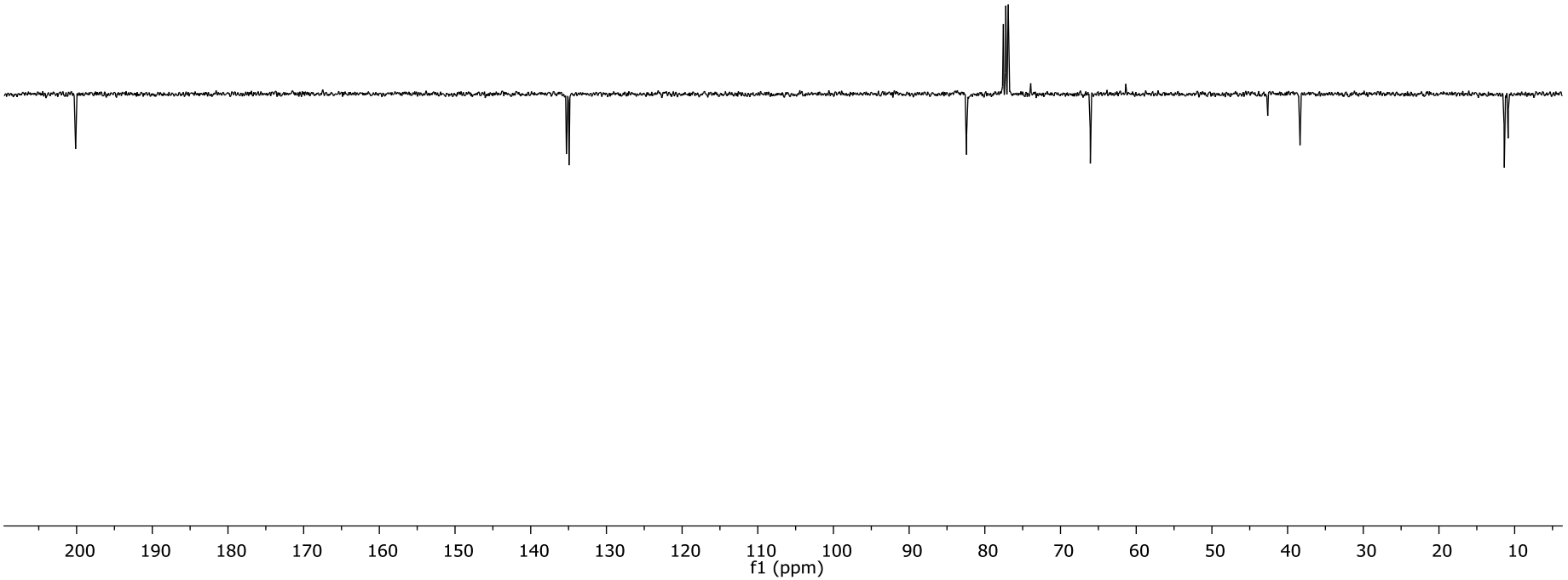


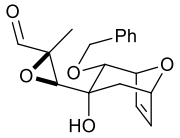
13a
400 MHz, $CDCl_3$



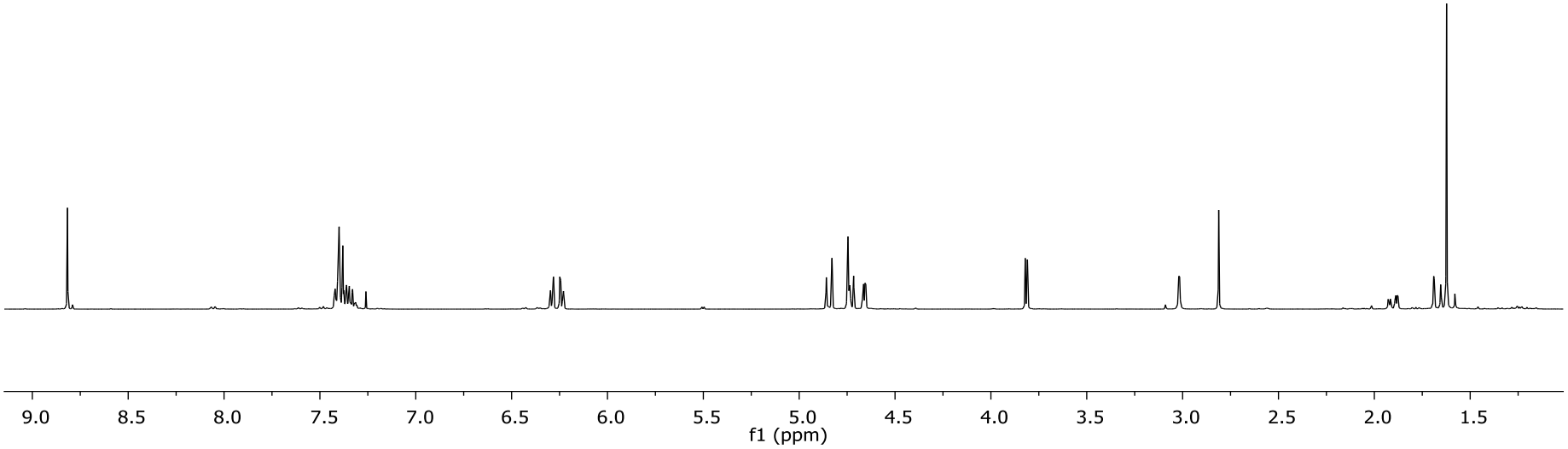


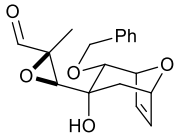
13a
100 MHz, $CDCl_3$



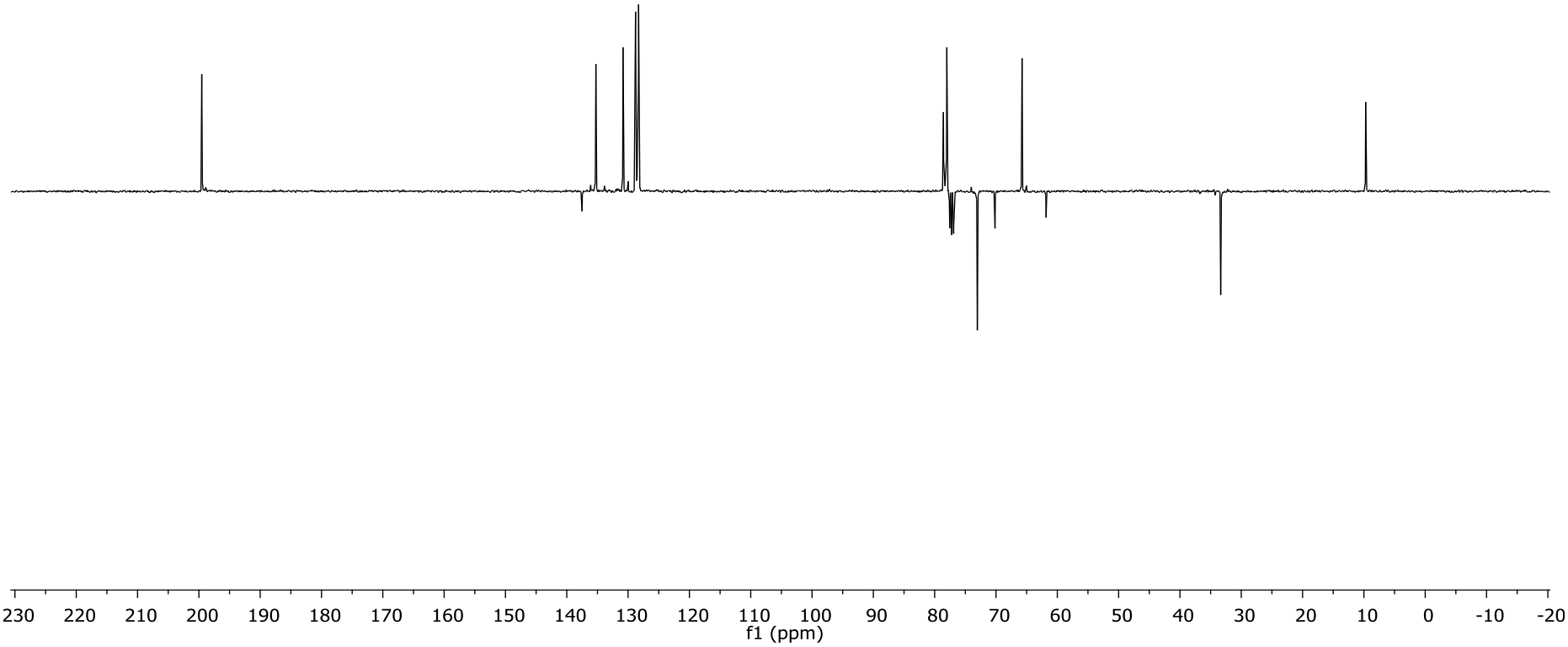


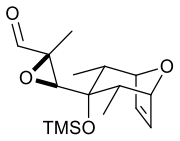
13b
400 MHz, $CDCl_3$



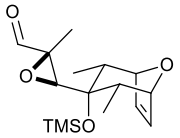


13b
100 MHz, $CDCl_3$



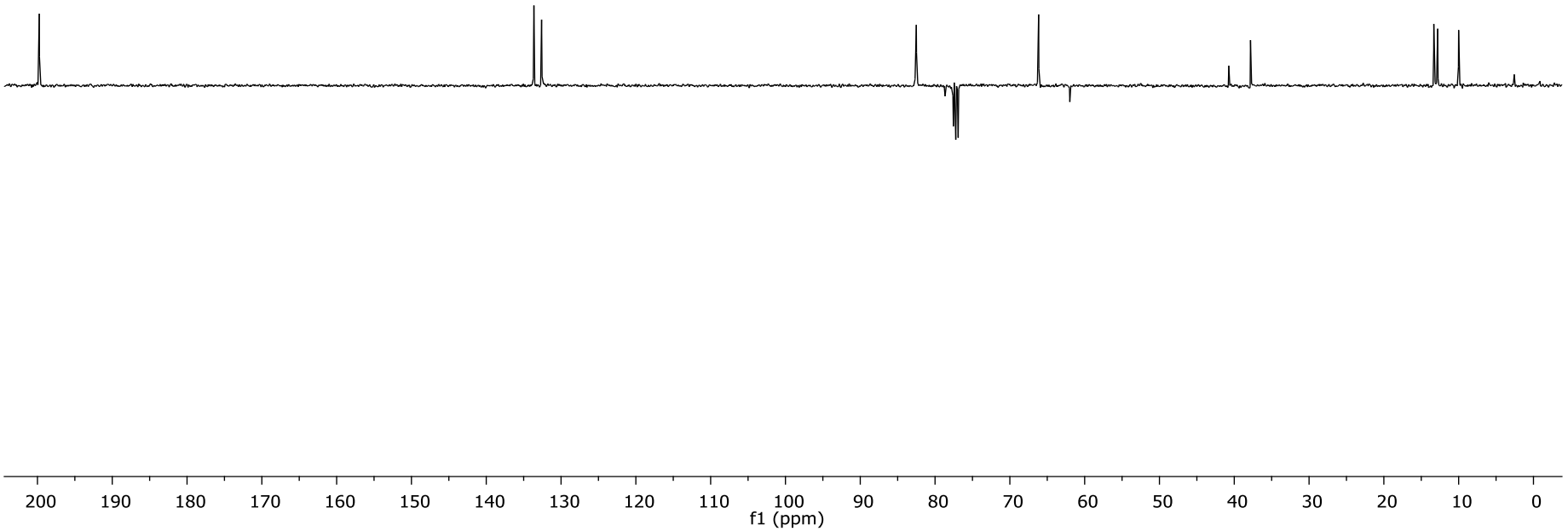


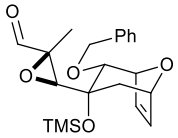
14a
400 MHz, $CDCl_3$



14a

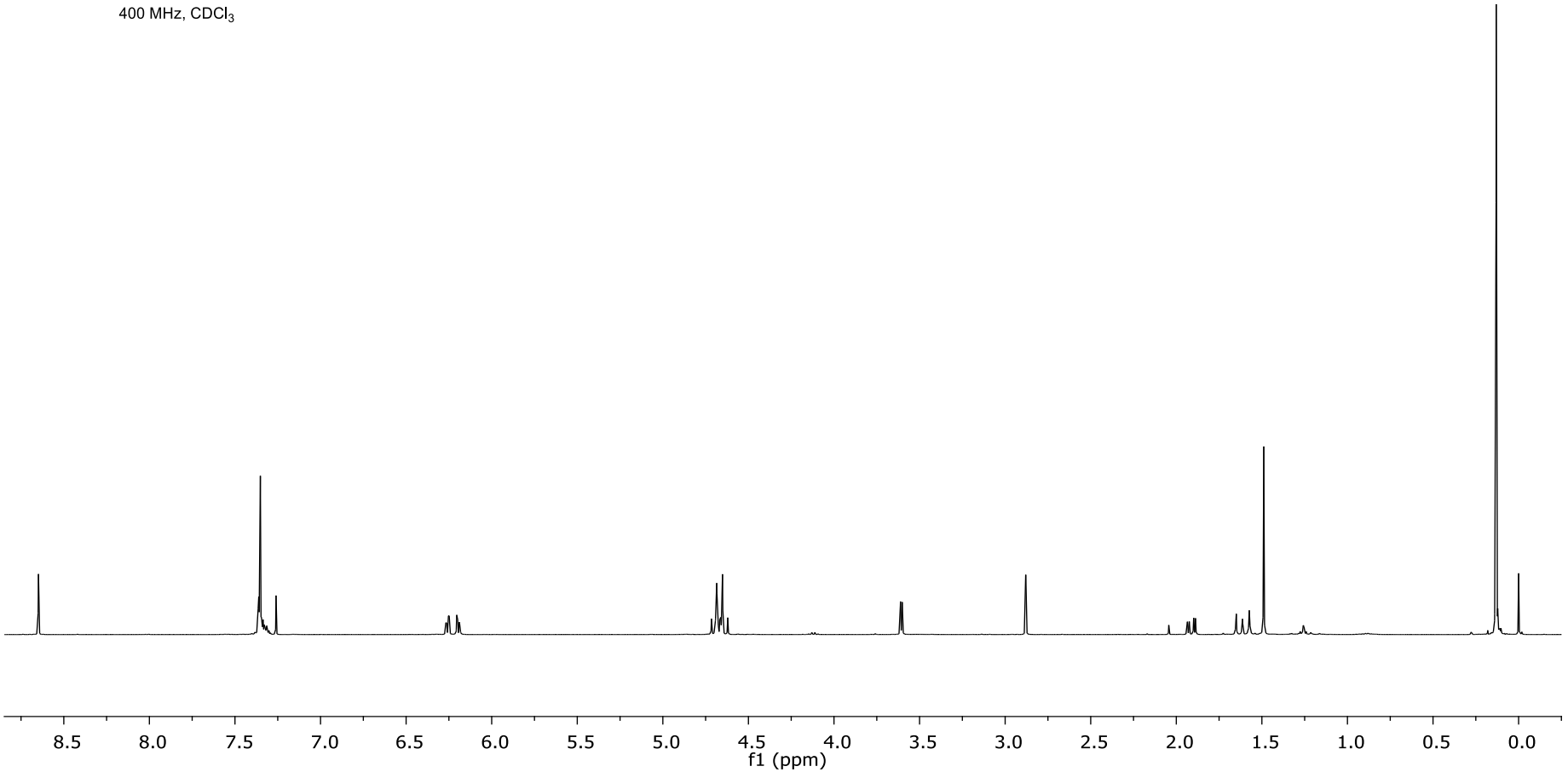
100 MHz, $CDCl_3$

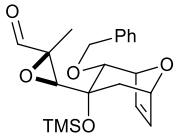




14b

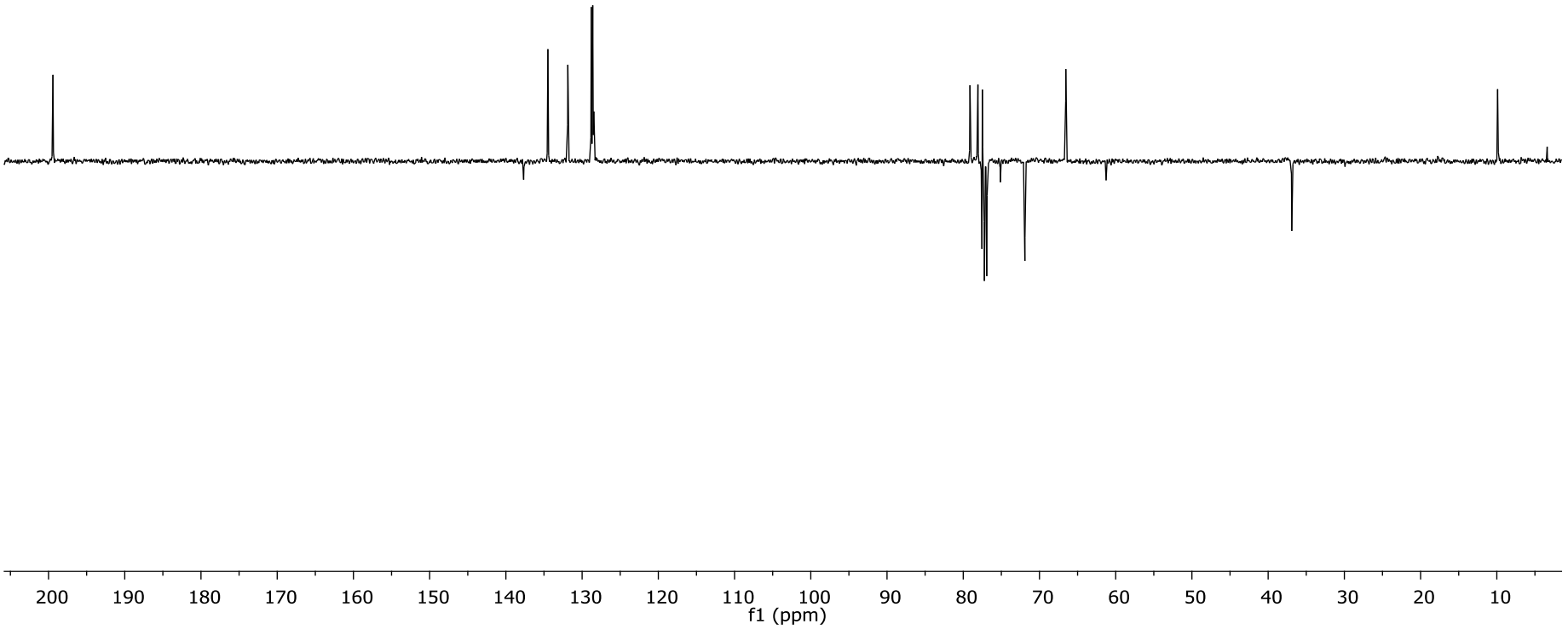
400 MHz, $CDCl_3$

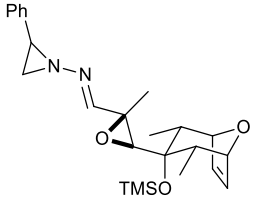




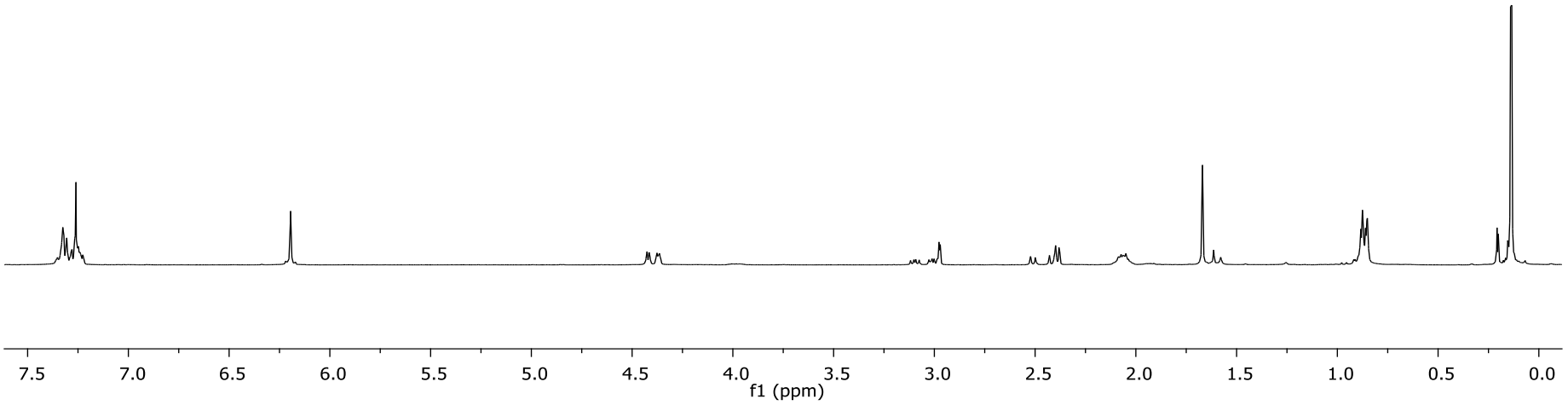
14b

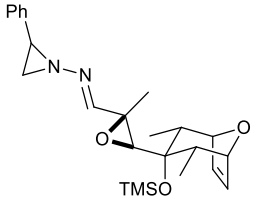
100 MHz, $CDCl_3$



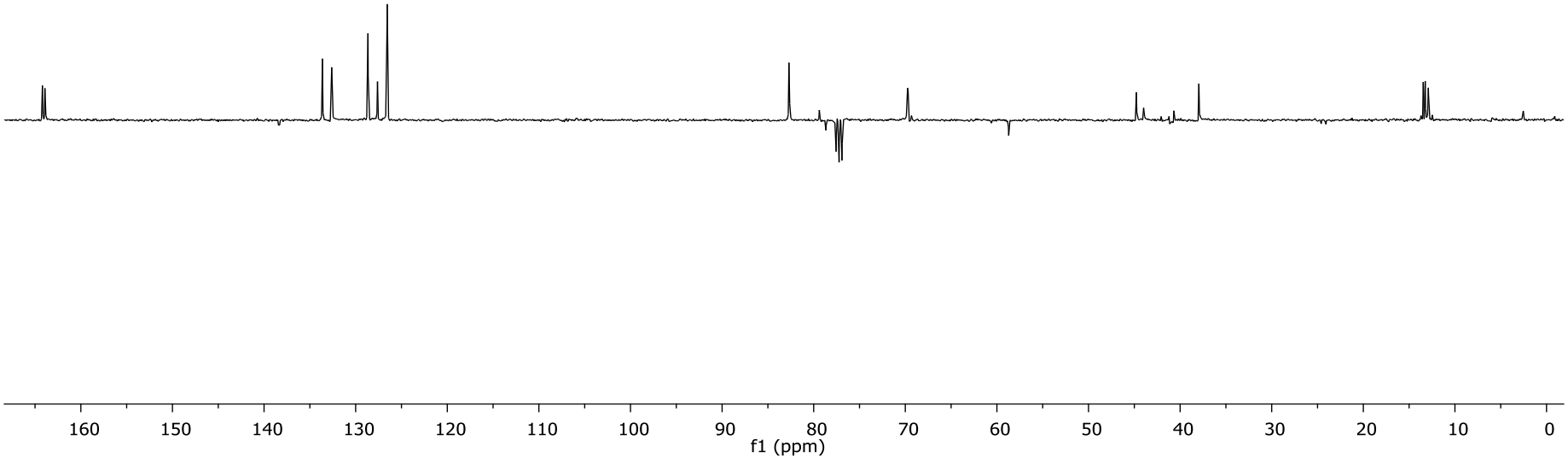


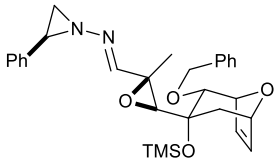
16a
400 MHz, $CDCl_3$



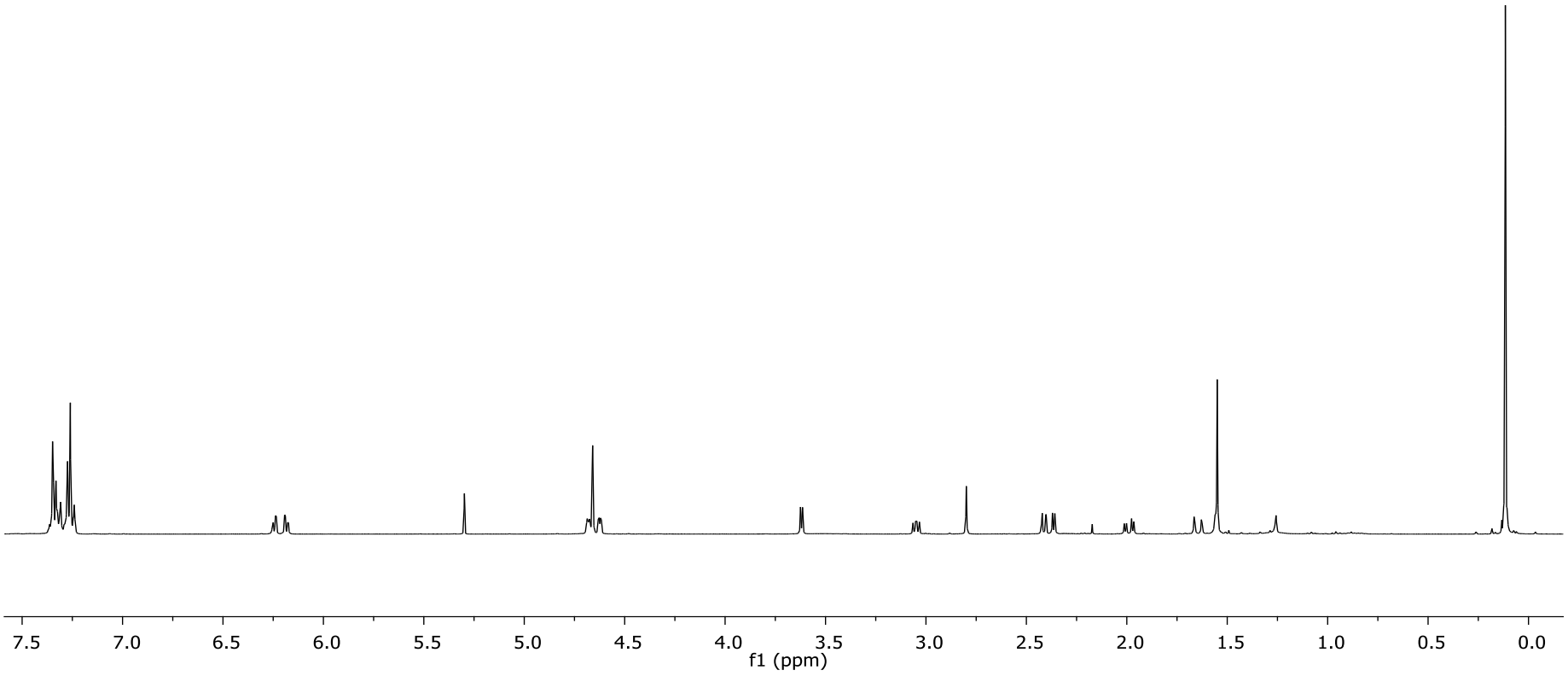


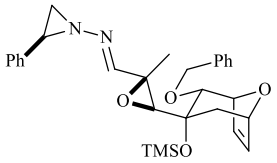
16a
100 MHz, $CDCl_3$



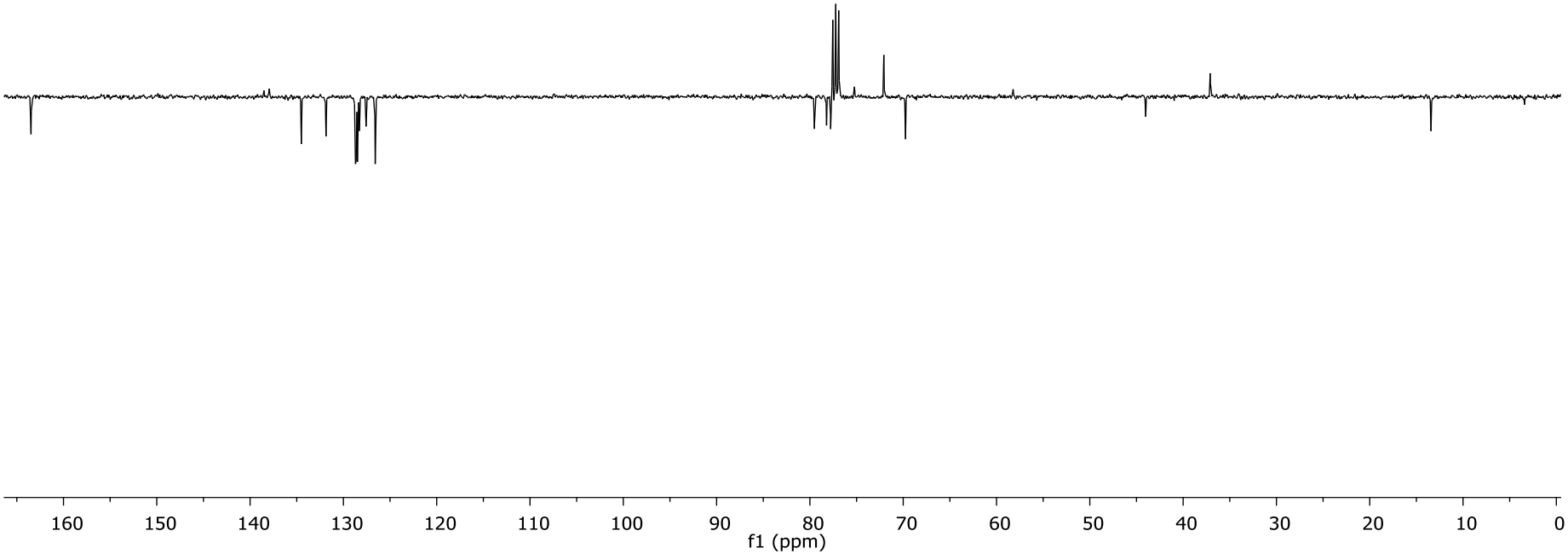


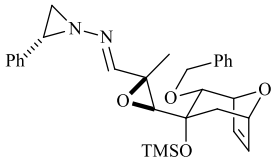
16b
400 MHz, $CDCl_3$



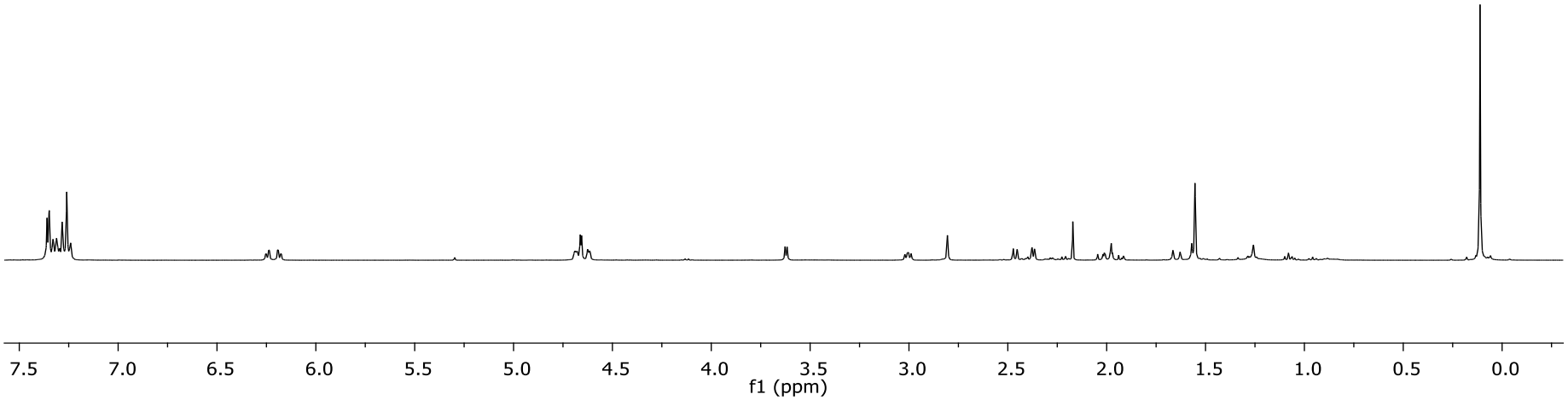


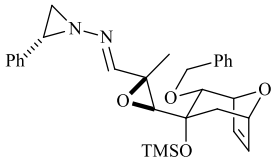
16b
100 MHz, $CDCl_3$



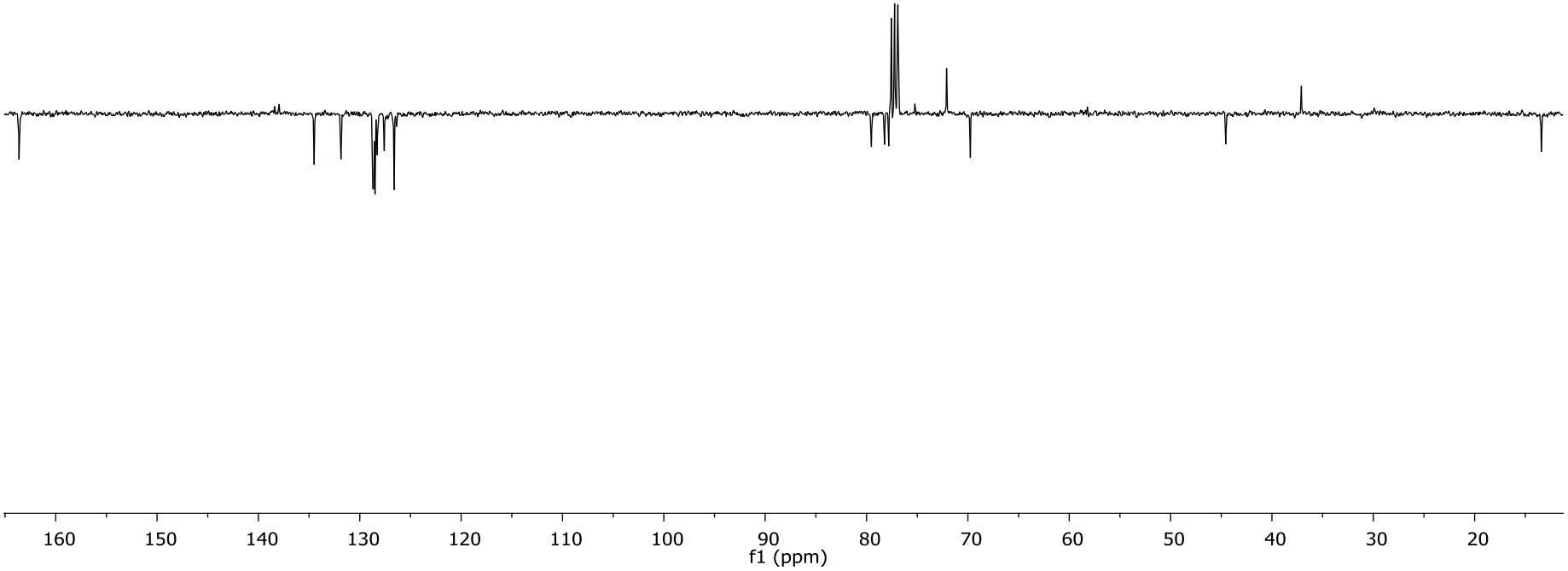


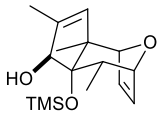
16b'
400 MHz, $CDCl_3$



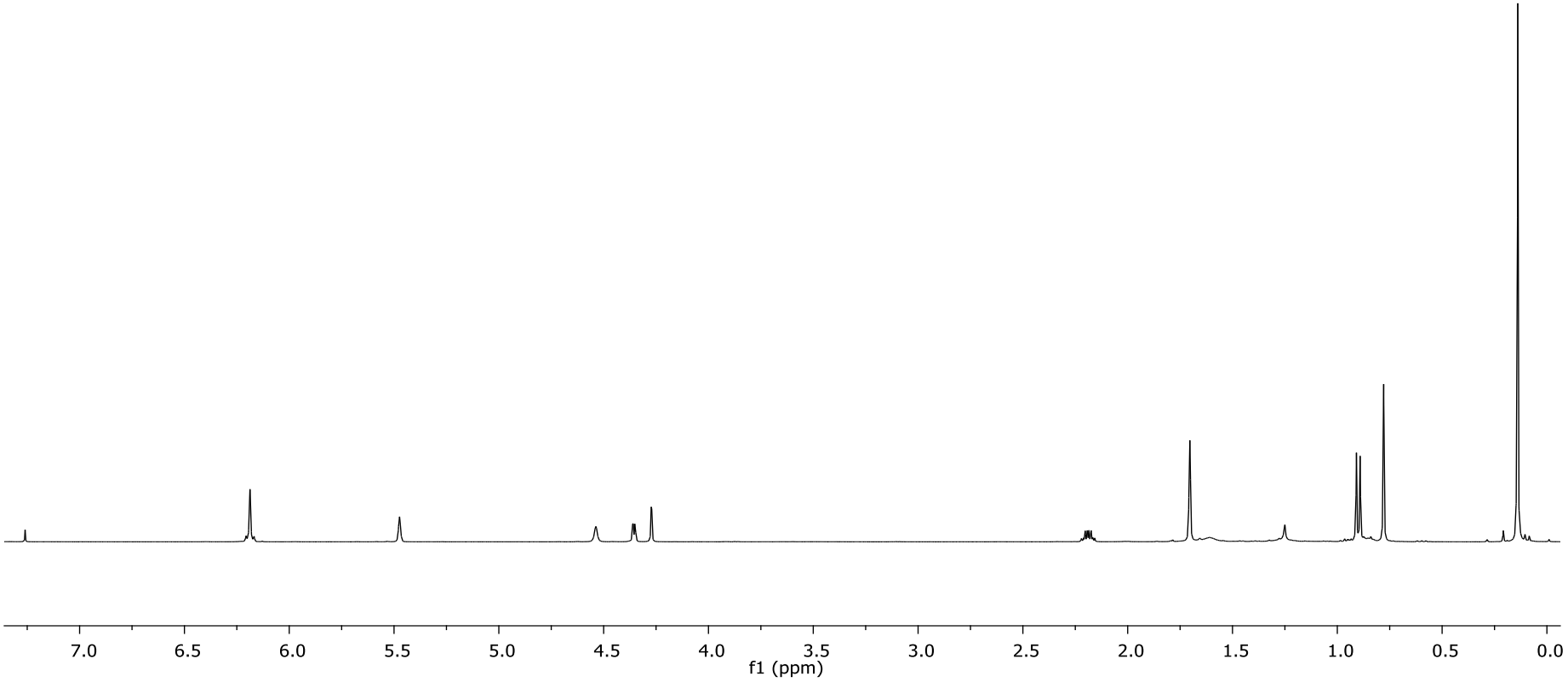


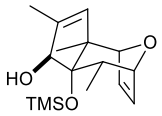
16b'
100 MHz, $CDCl_3$





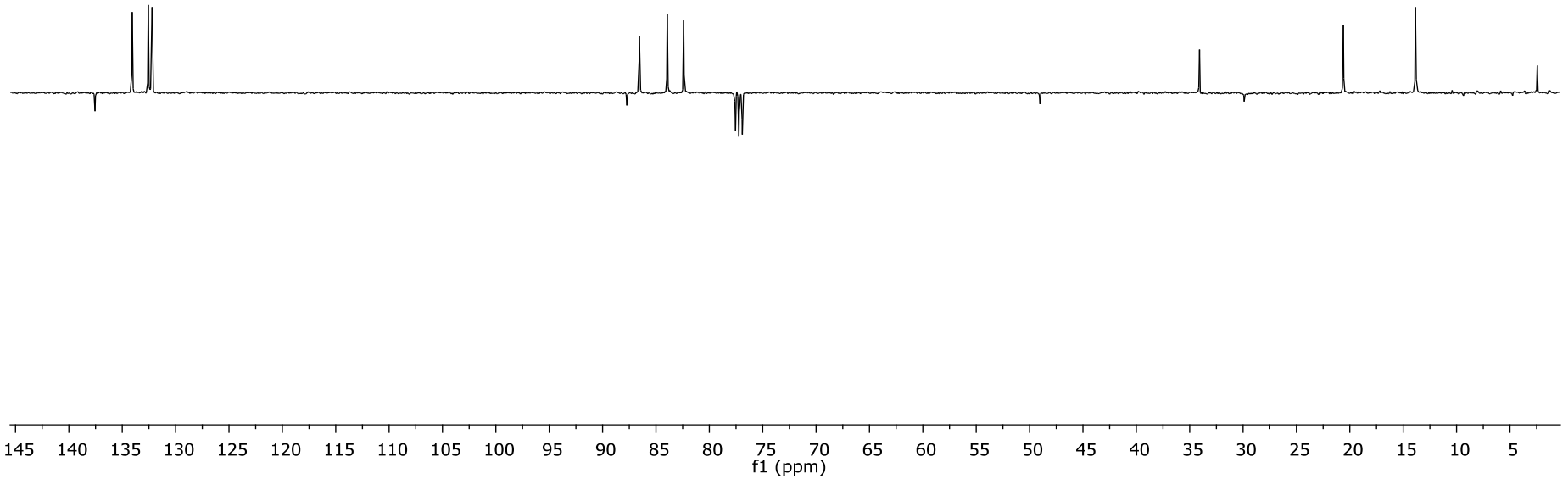
18
400 MHz, $CDCl_3$

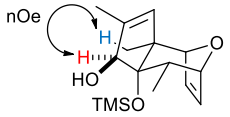




18

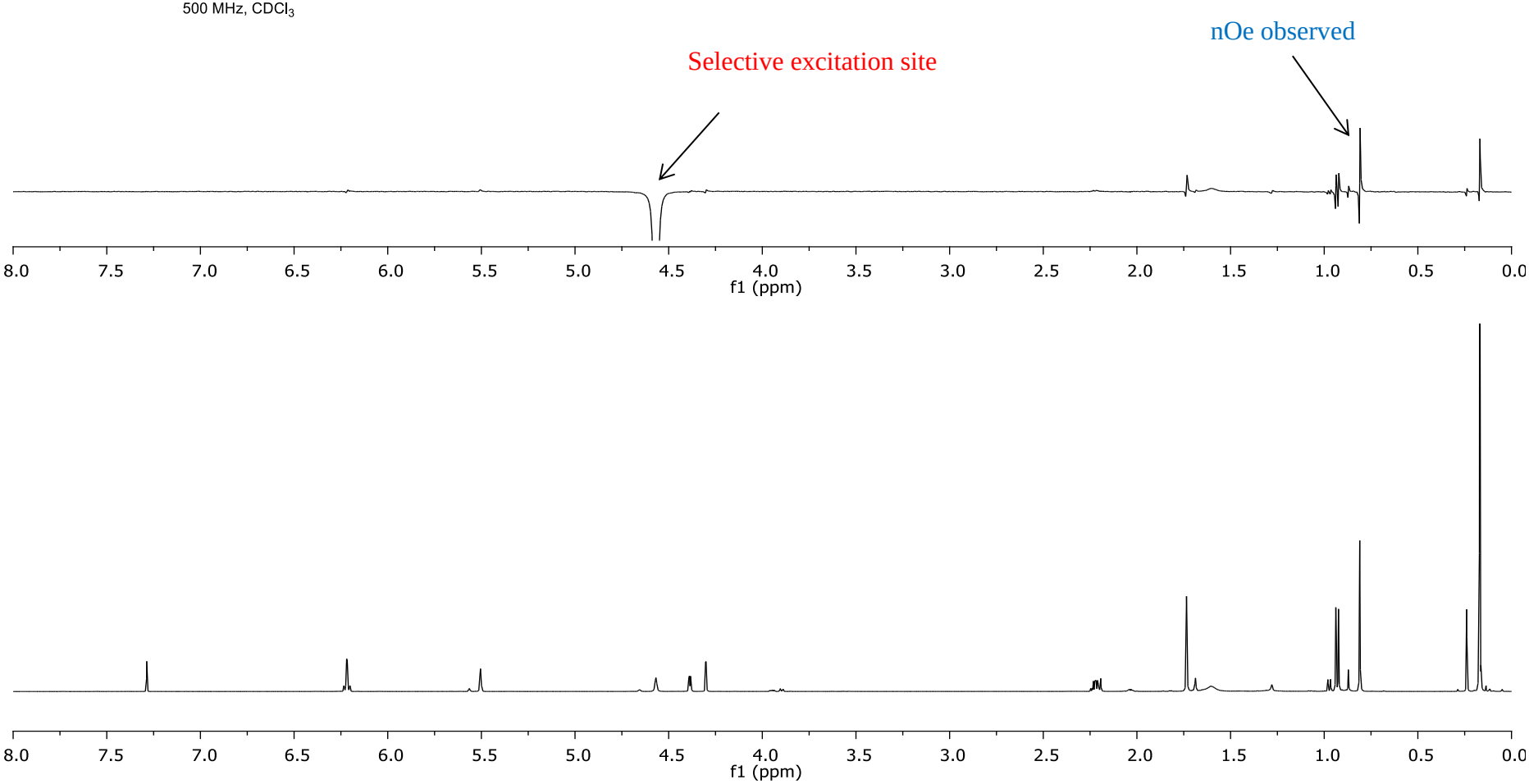
100 MHz, $CDCl_3$

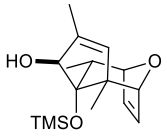




18

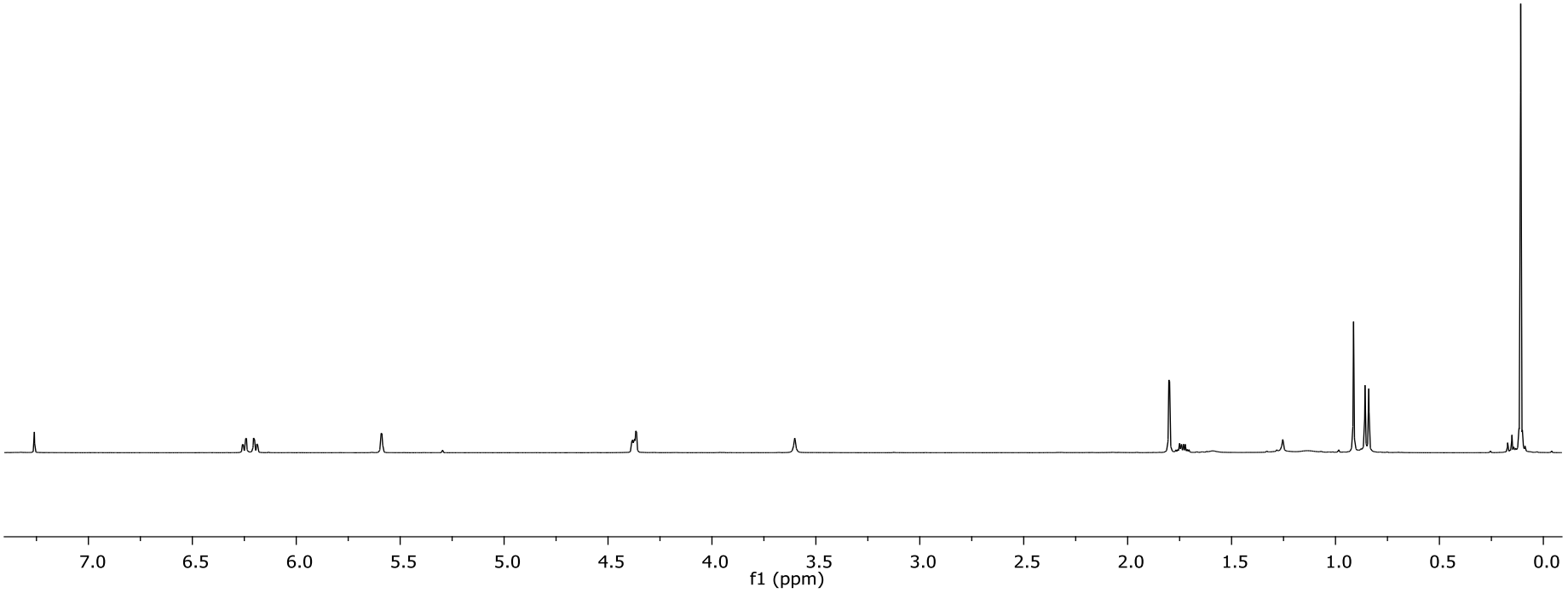
500 MHz, $CDCl_3$

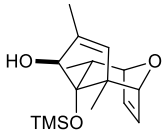




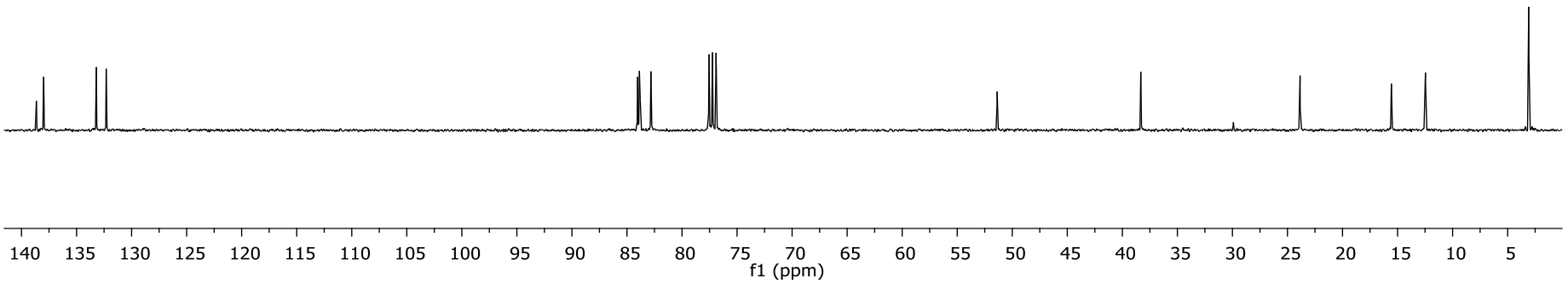
19

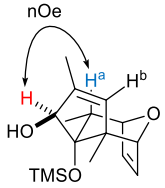
400 MHz, $CDCl_3$





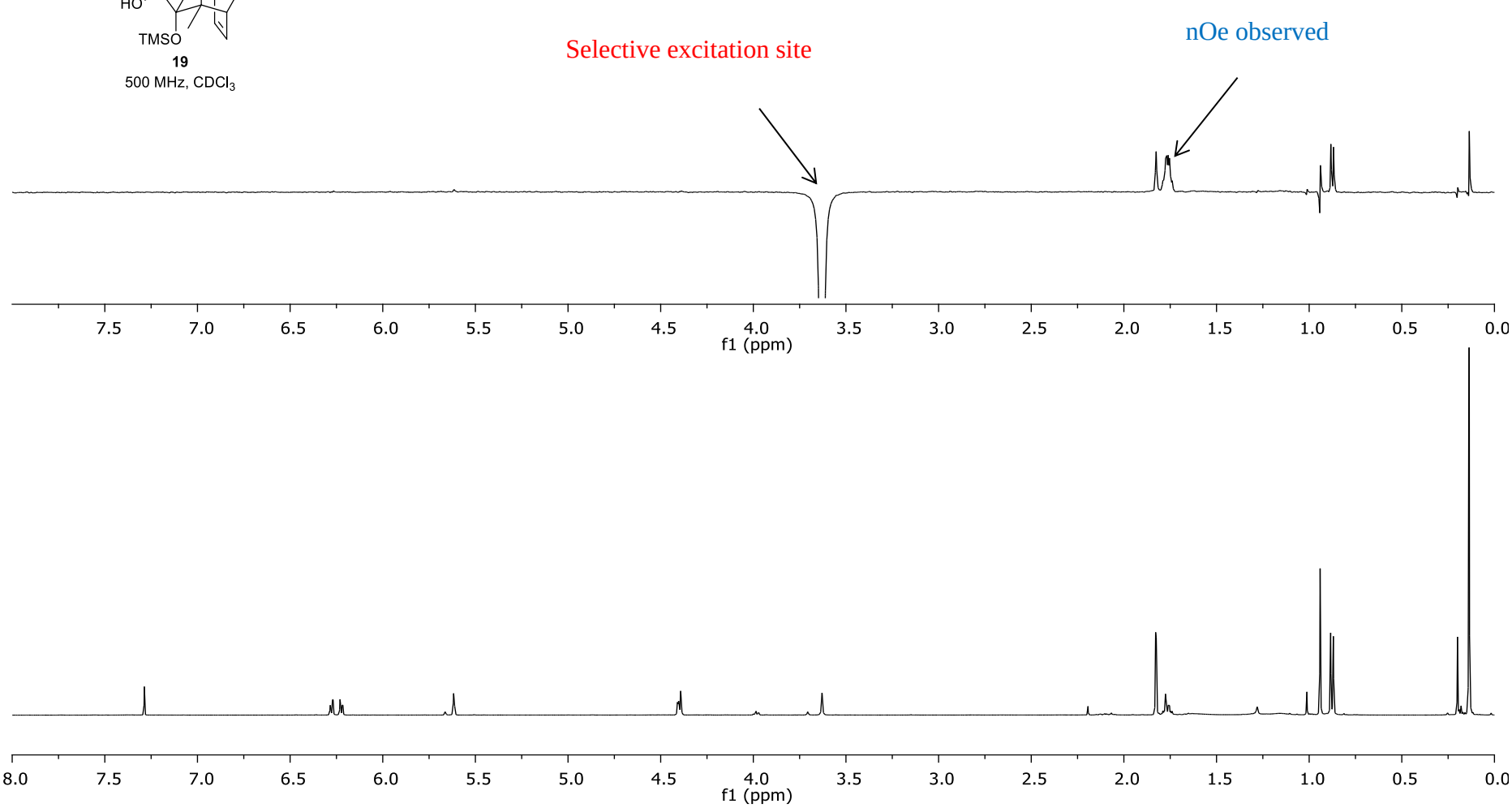
19
100 MHz, $CDCl_3$

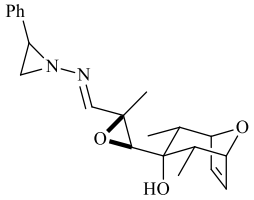




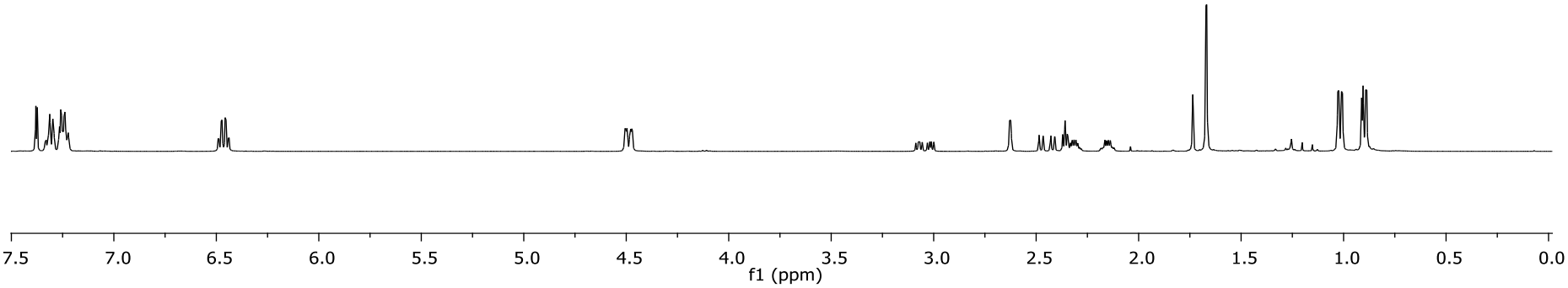
19

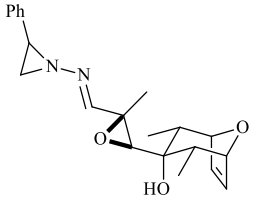
500 MHz, $CDCl_3$



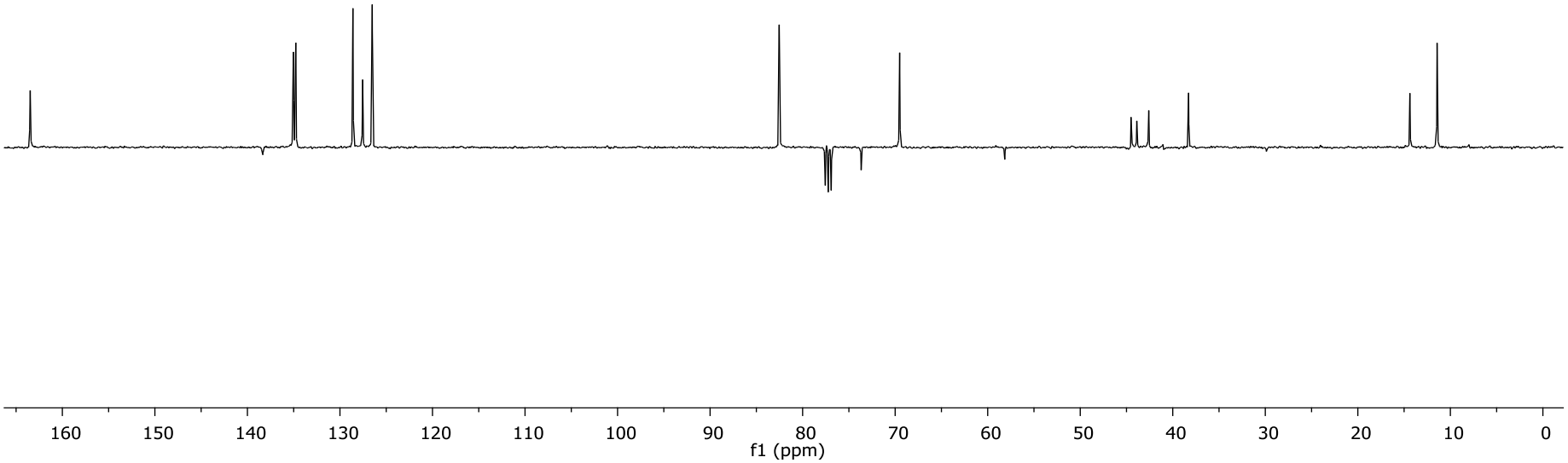


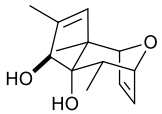
20a
400 MHz, $CDCl_3$



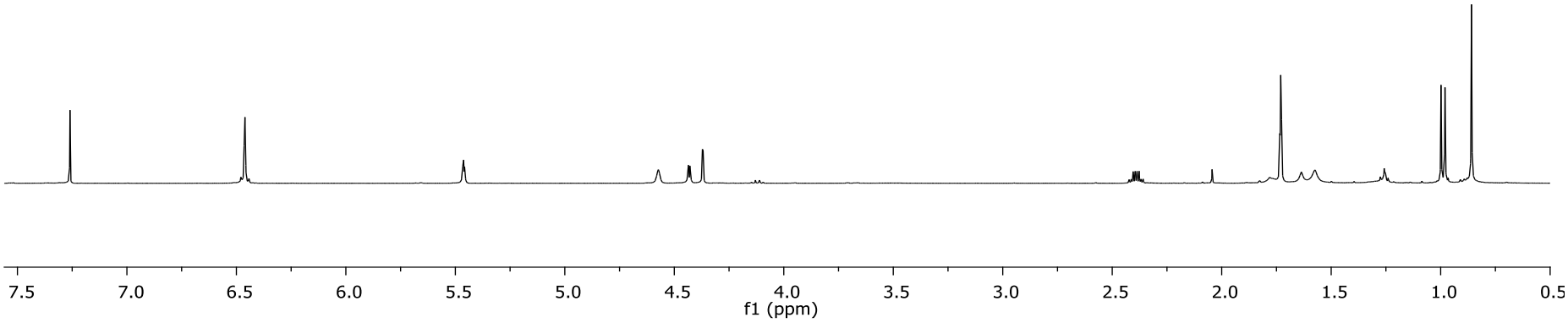


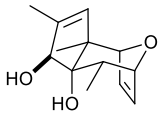
20a
100 MHz, $CDCl_3$



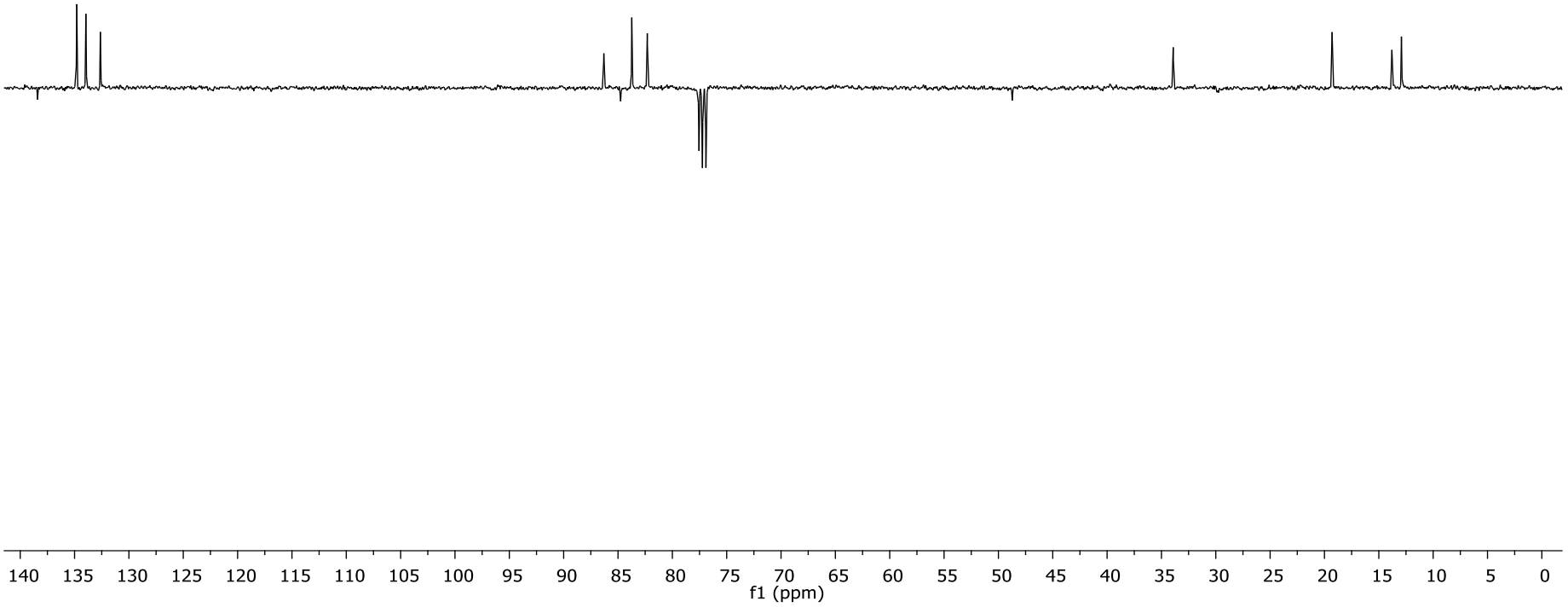


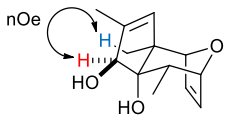
22
400 MHz, $CDCl_3$



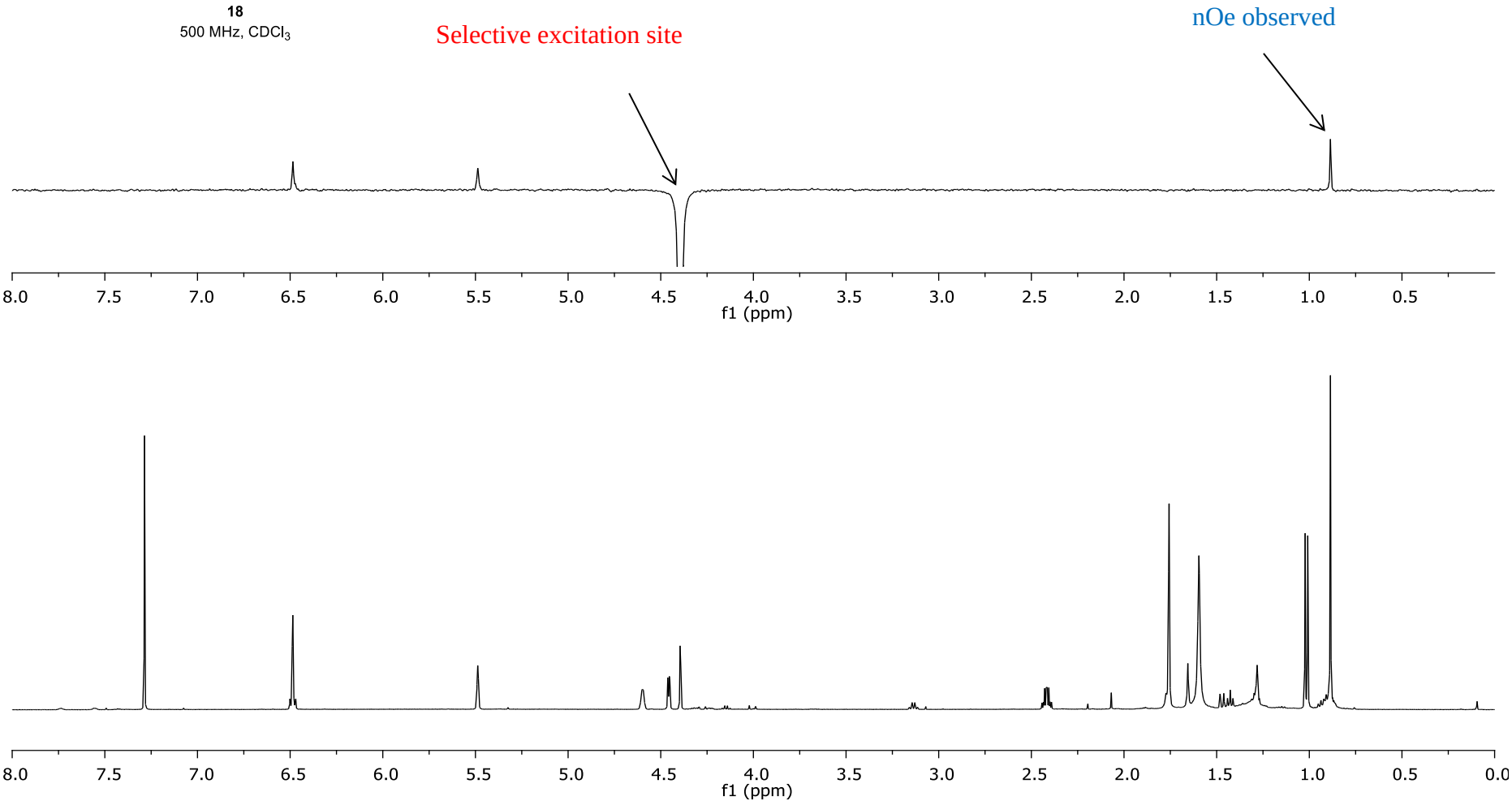


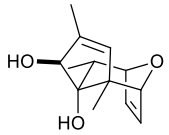
22
100 MHz, $CDCl_3$



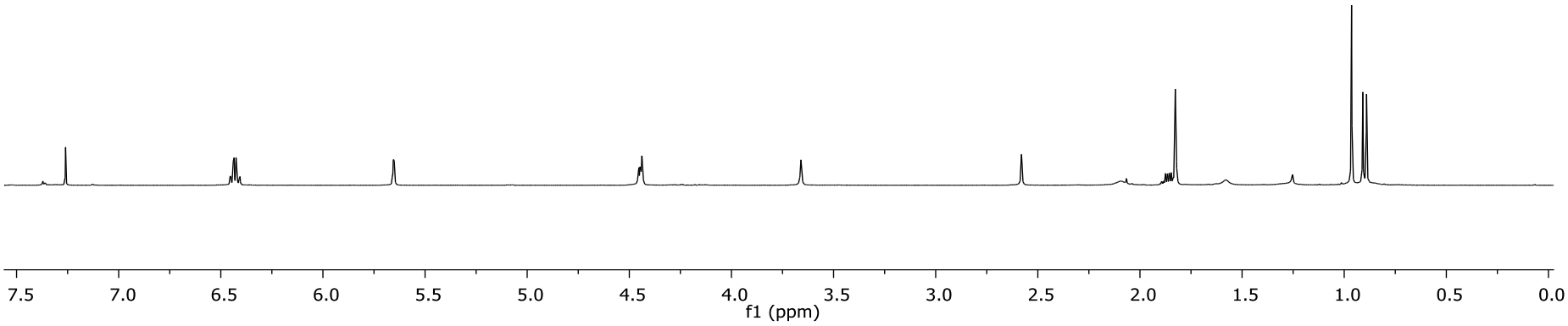


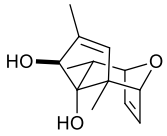
18
500 MHz, $CDCl_3$





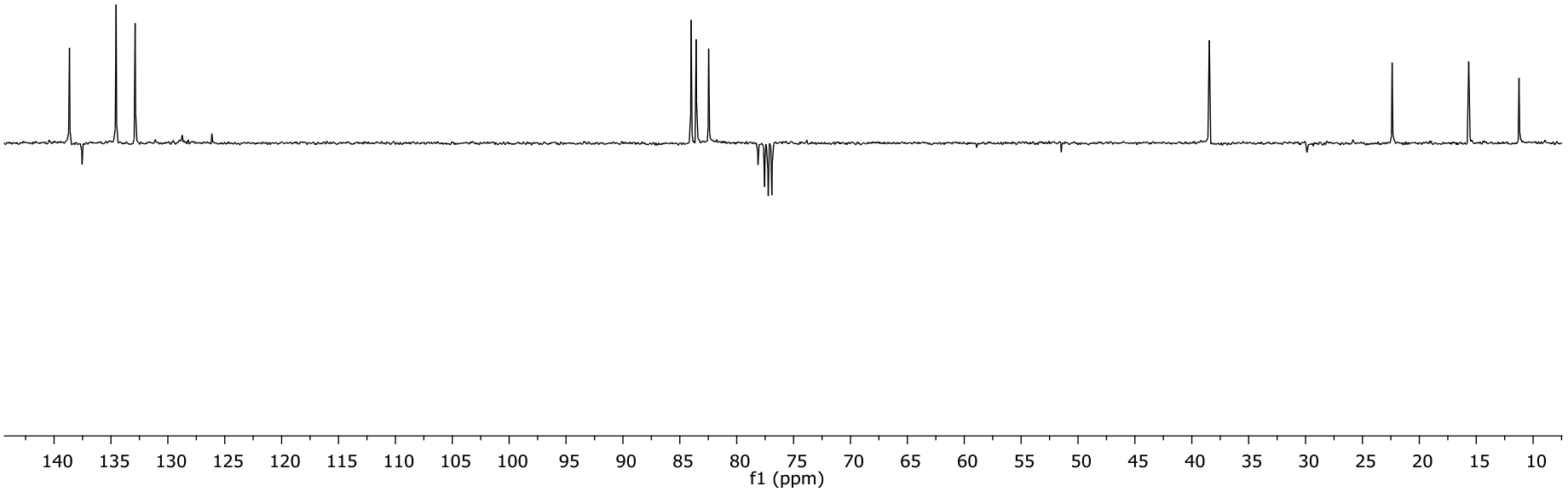
23
400 MHz, $CDCl_3$

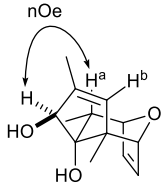




23

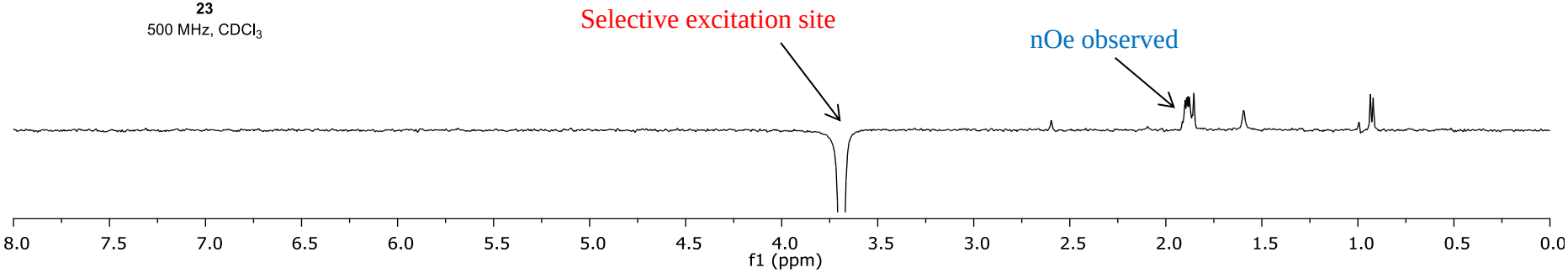
100 MHz, $CDCl_3$

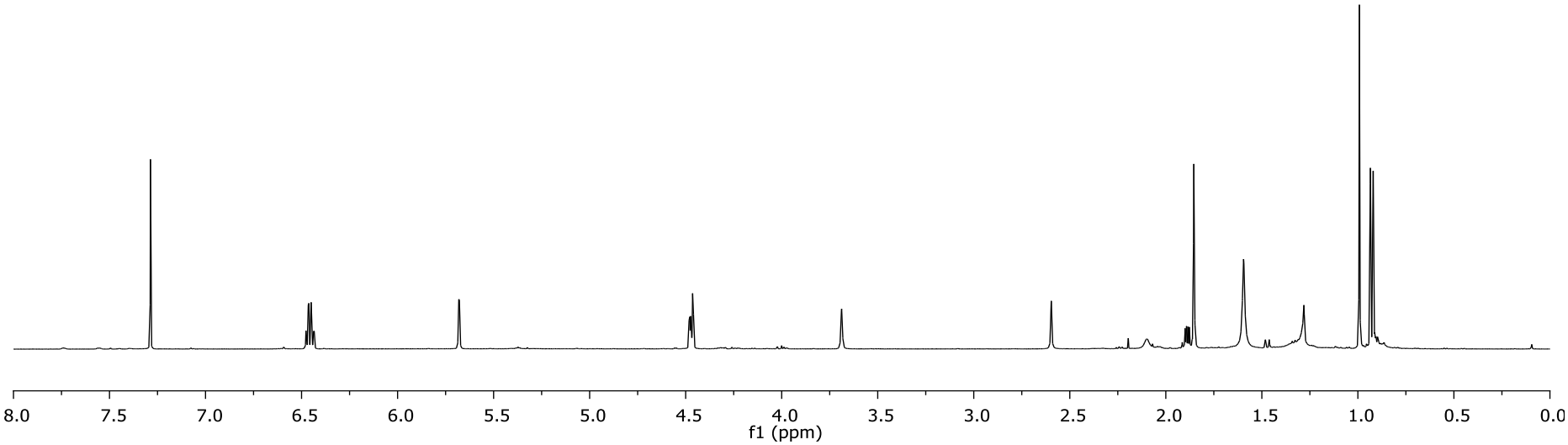




23

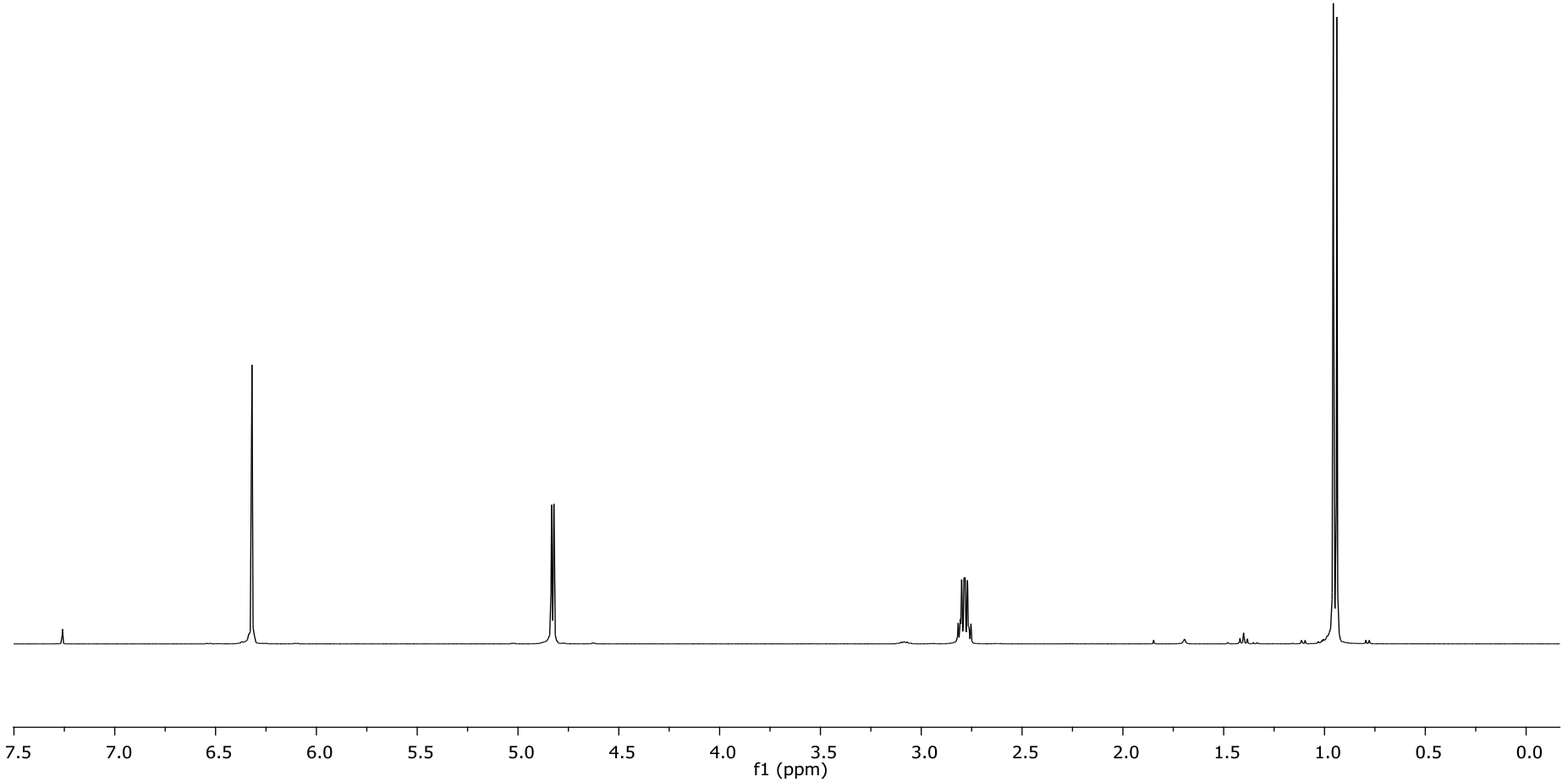
500 MHz, $CDCl_3$





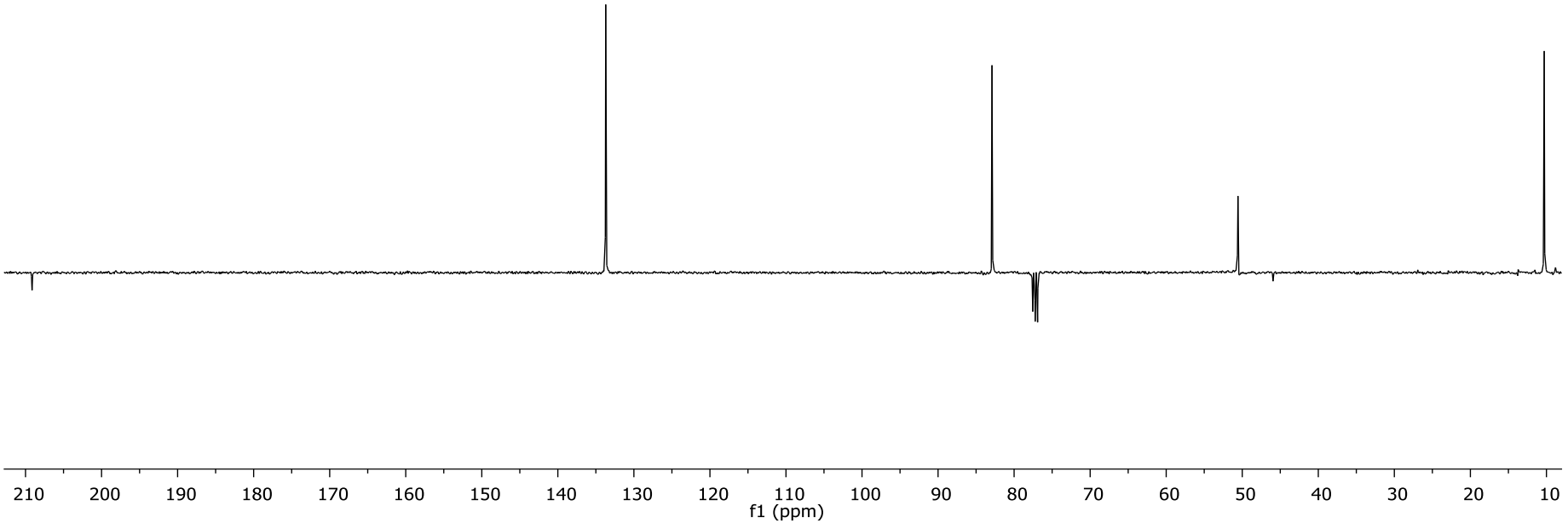
9a

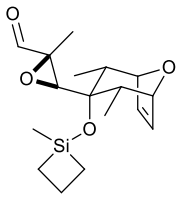
400 MHz, $CDCl_3$



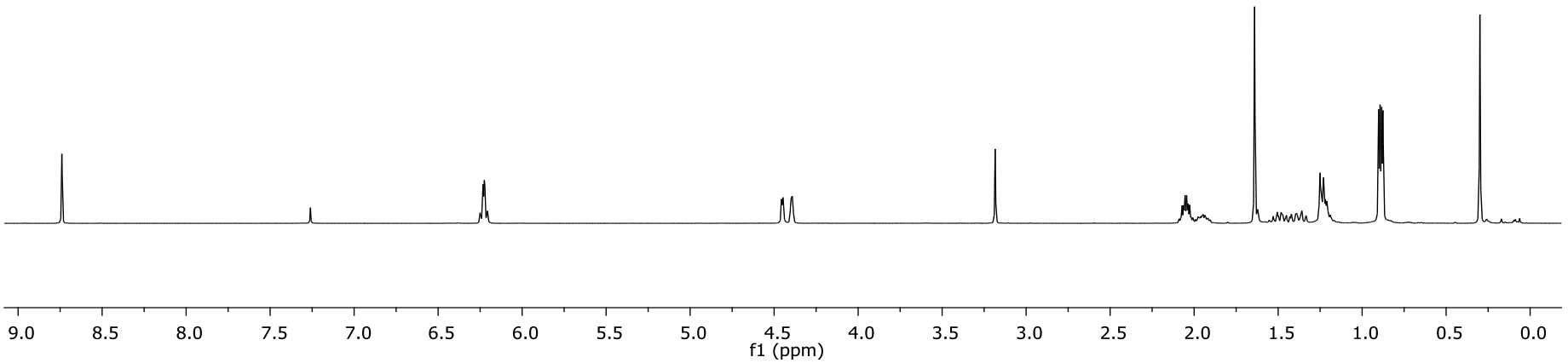
9a

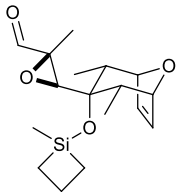
100 MHz, $CDCl_3$



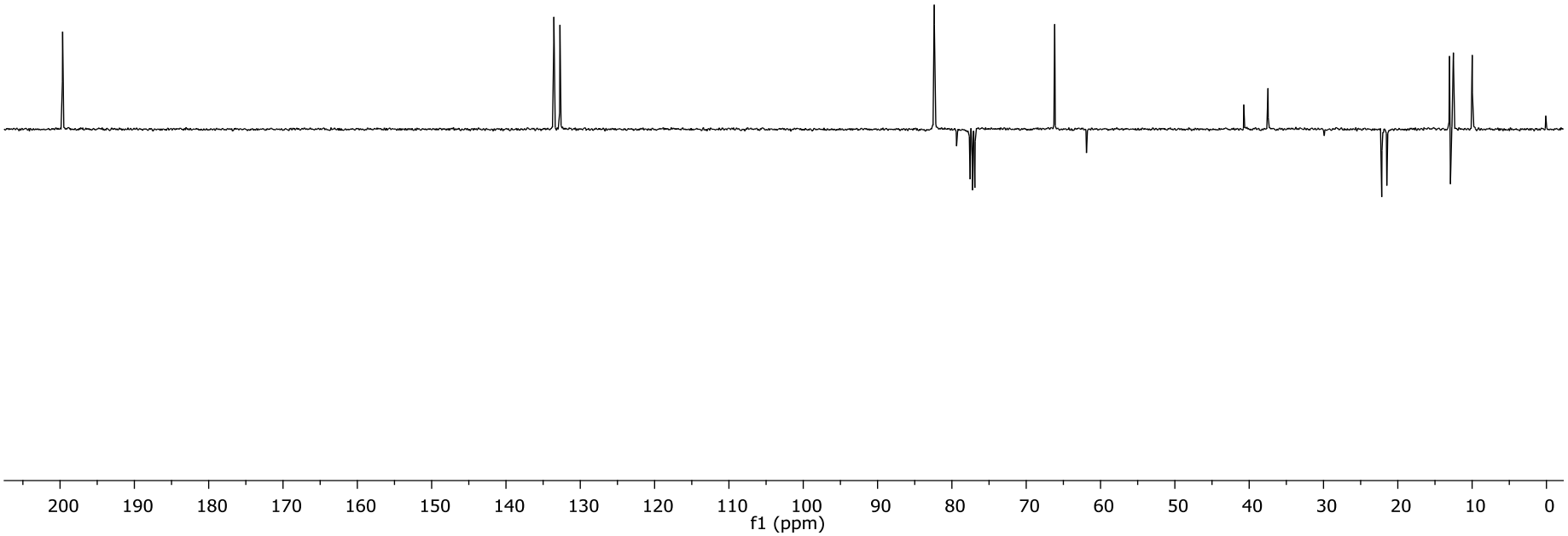


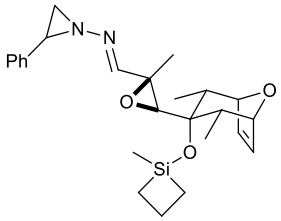
25
400 MHz, $CDCl_3$



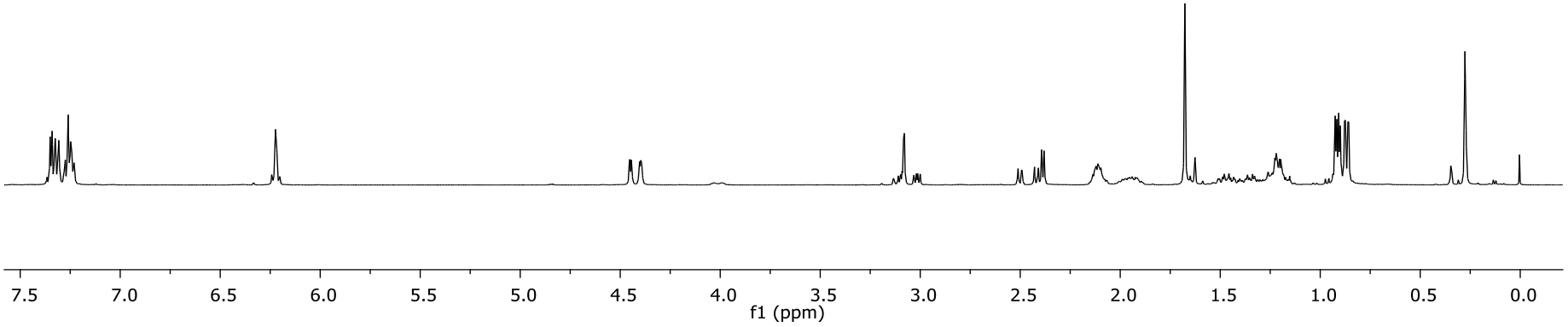


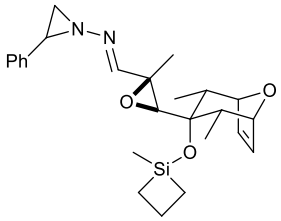
25
100 MHz, $CDCl_3$



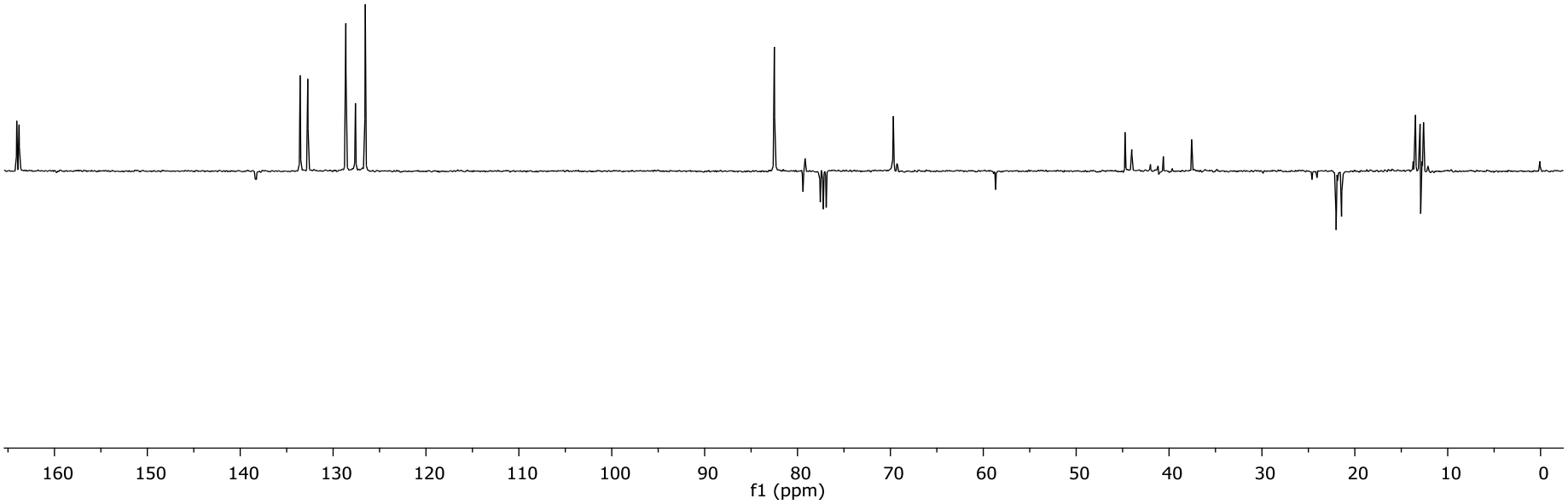


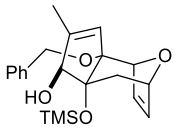
26
400 MHz, $CDCl_3$





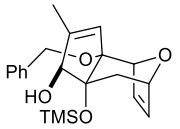
26
100 MHz, $CDCl_3$





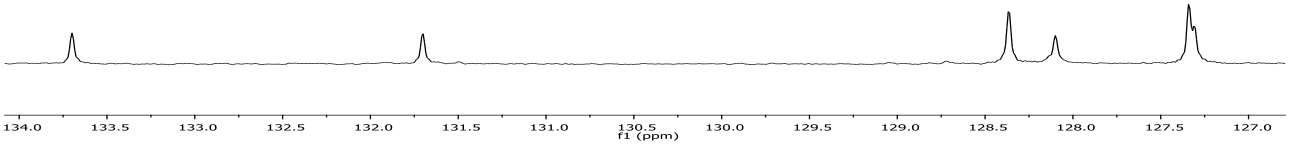
27

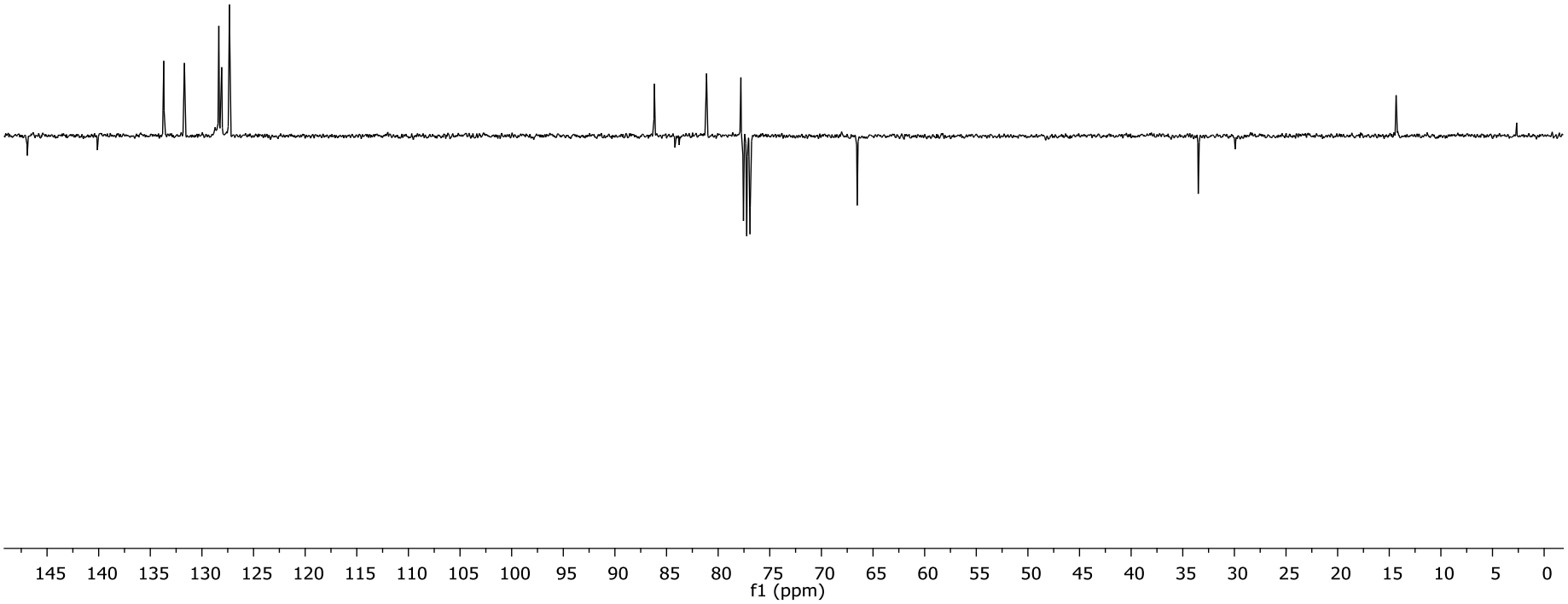
400 MHz, $CDCl_3$

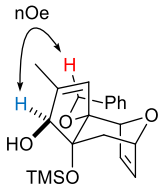


27

100 MHz, $CDCl_3$

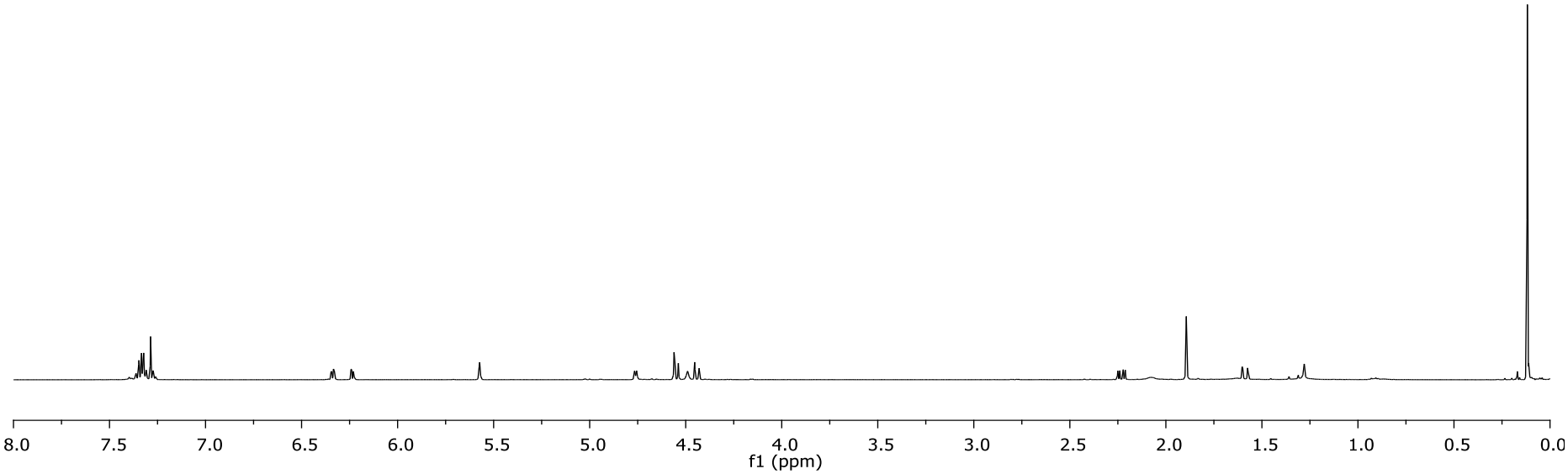


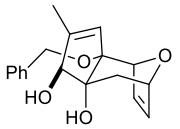




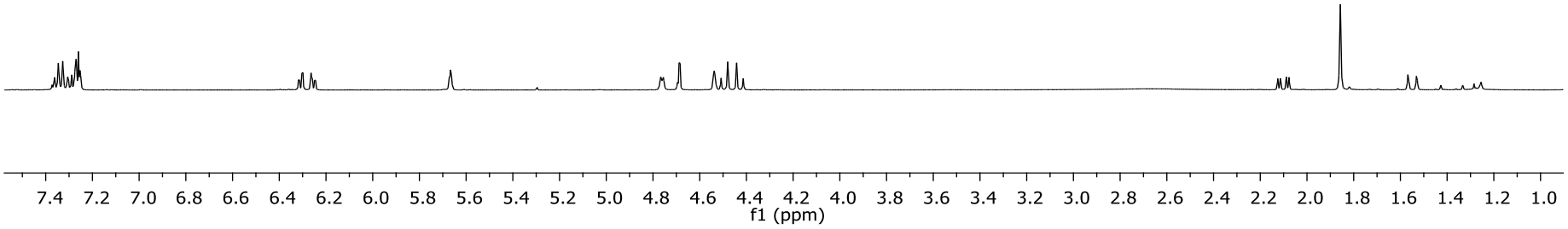
27

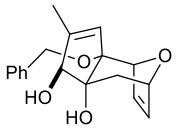
400 MHz, $CDCl_3$



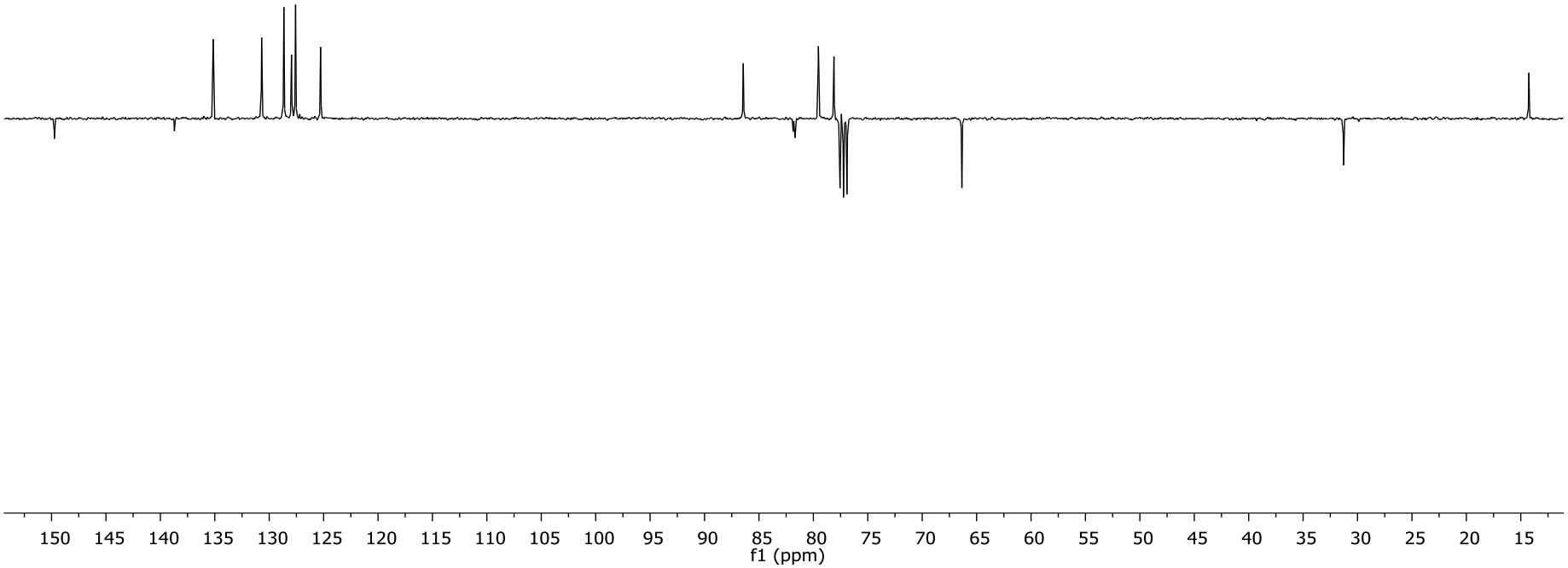


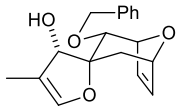
29
400 MHz, $CDCl_3$



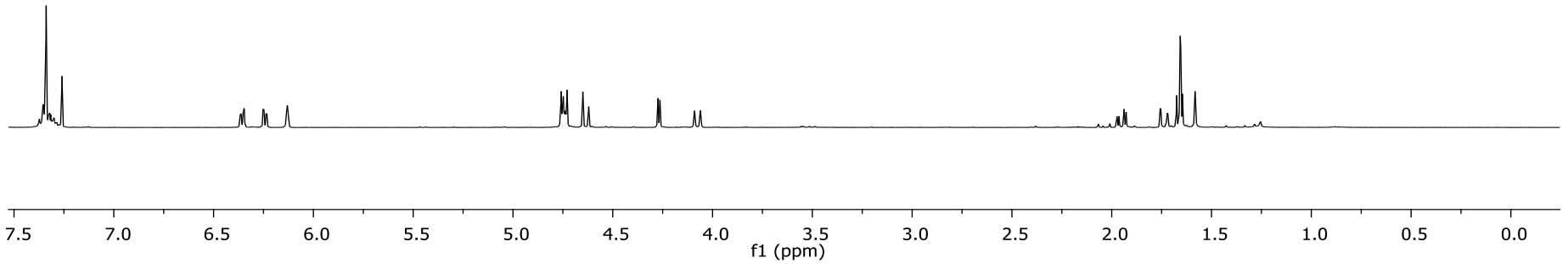


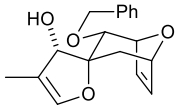
29
100 MHz, $CDCl_3$





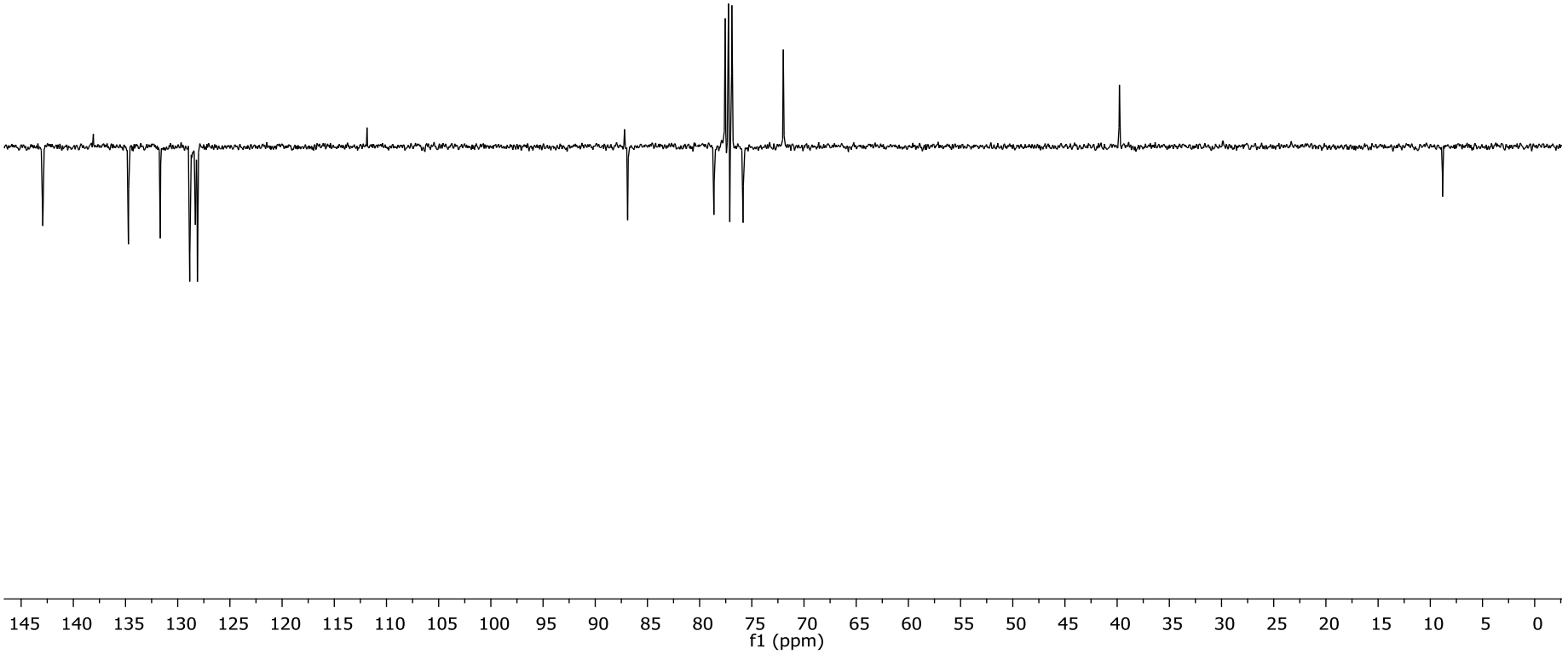
30
400 MHz, $CDCl_3$

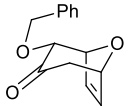




30

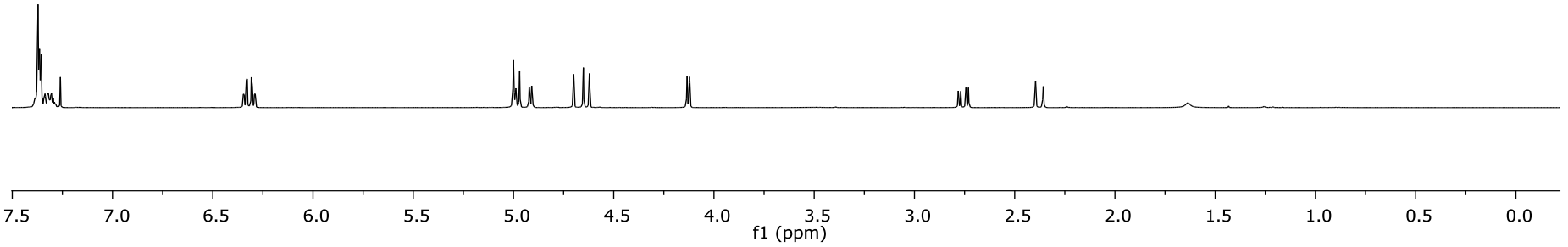
100 MHz, $CDCl_3$

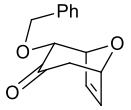




9b

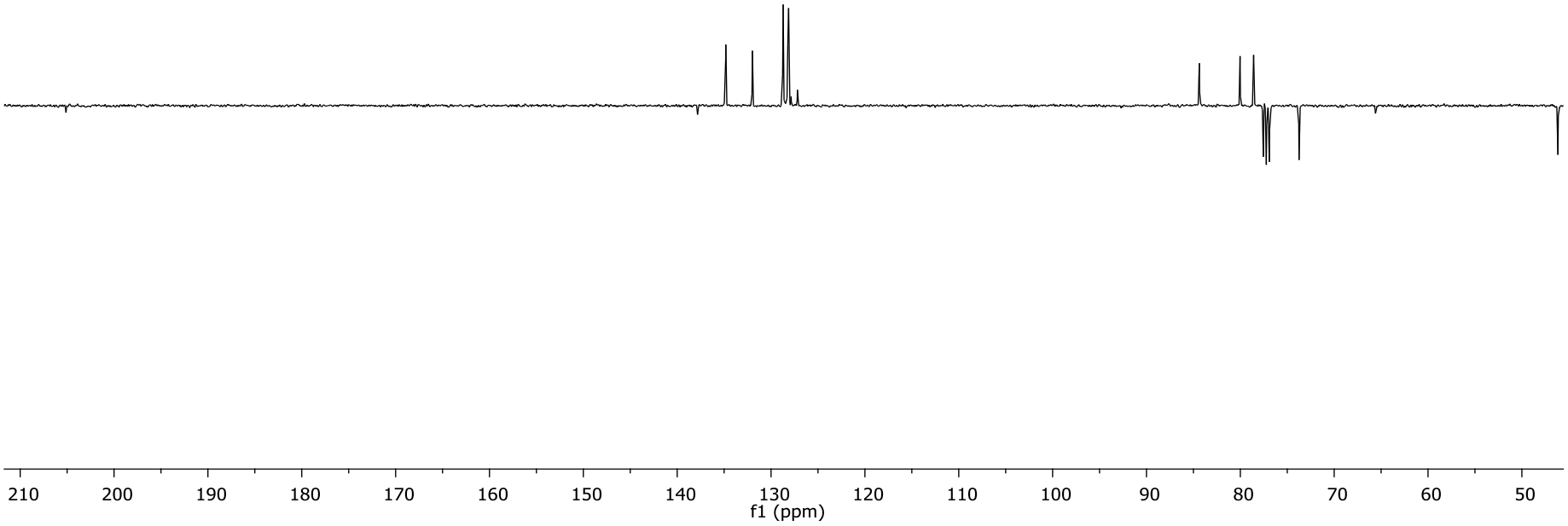
400 MHz, $CDCl_3$

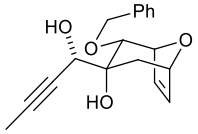




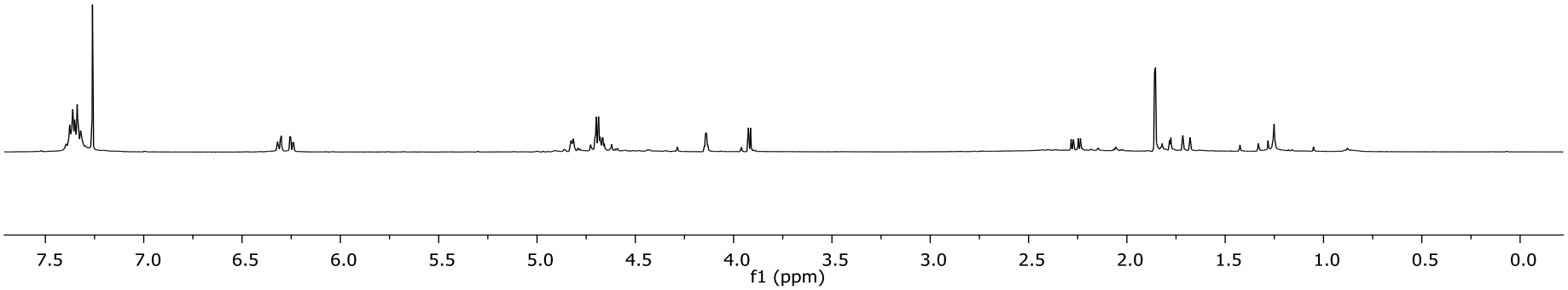
9b

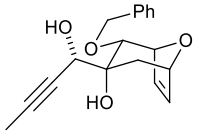
100 MHz, $CDCl_3$



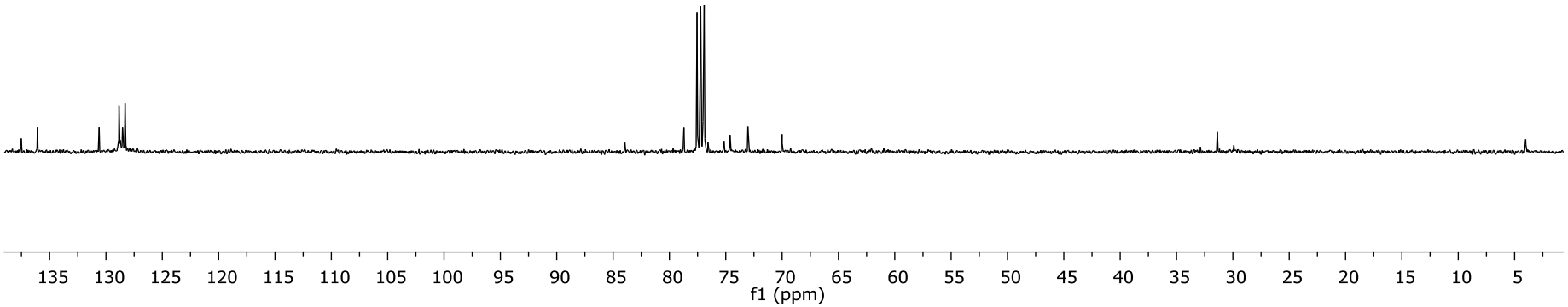


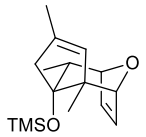
31
400 MHz, $CDCl_3$





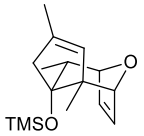
31
100 MHz, $CDCl_3$





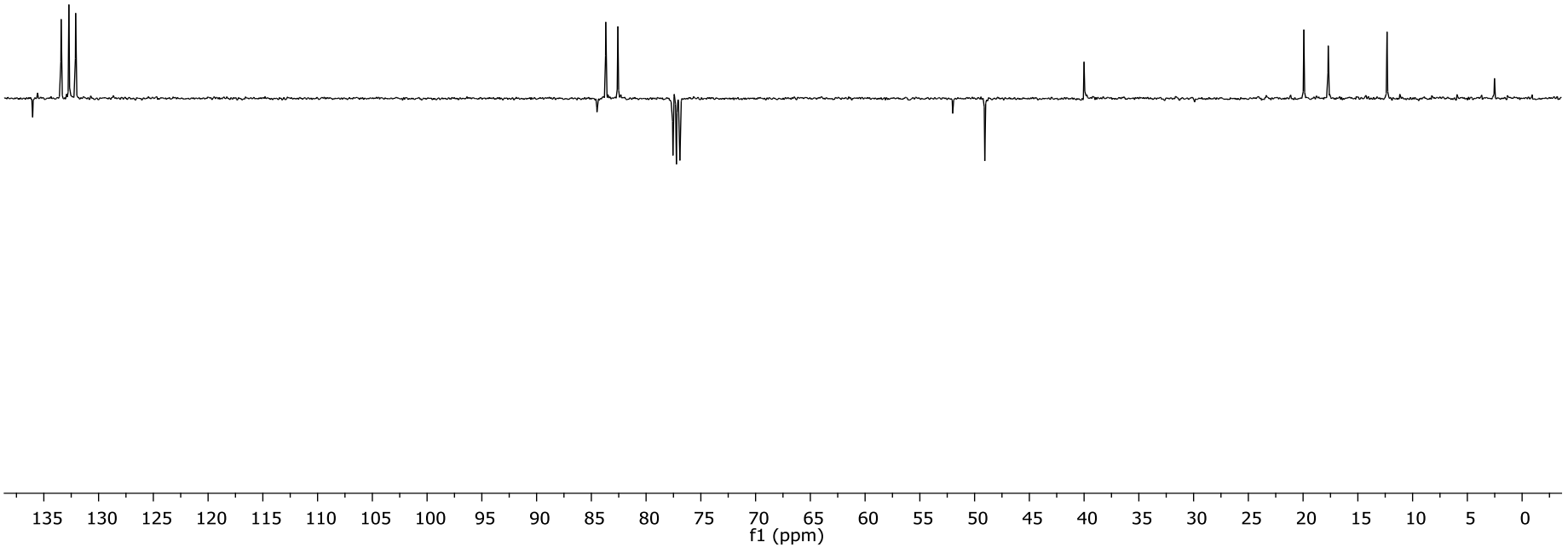
3

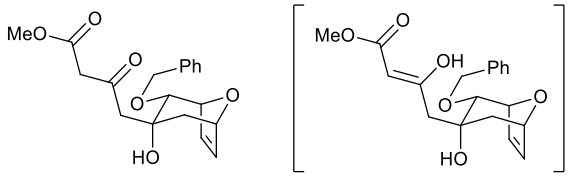
400 MHz, $CDCl_3$



3

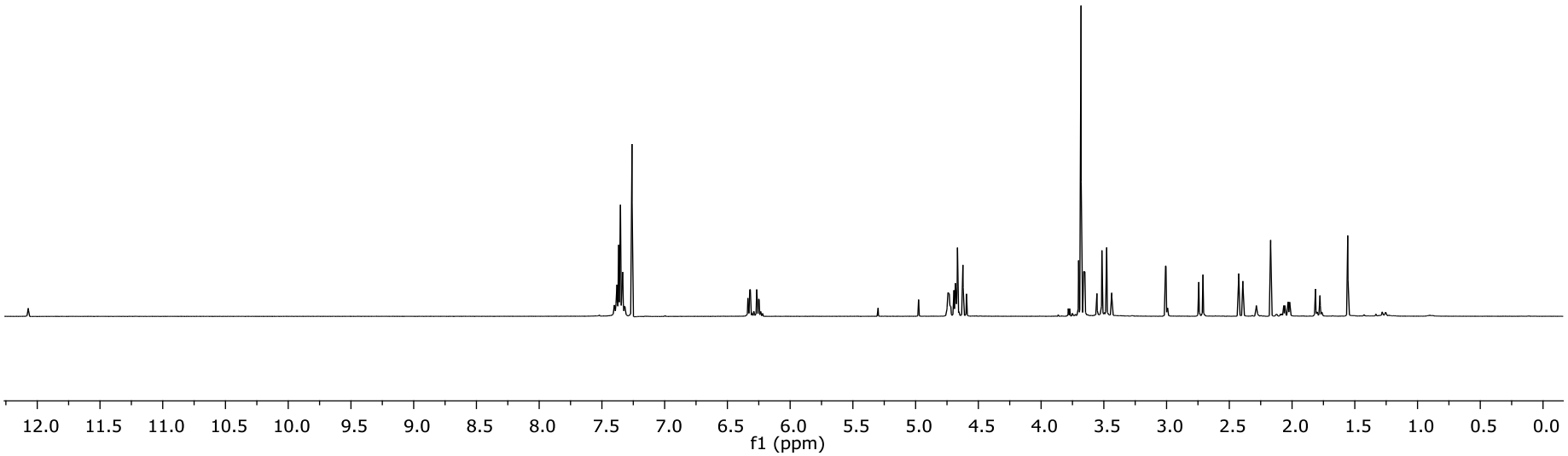
100 MHz, $CDCl_3$

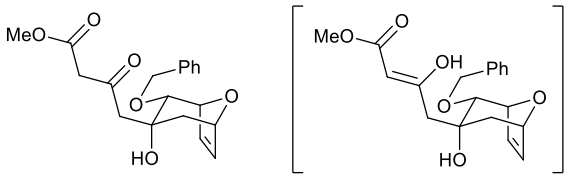




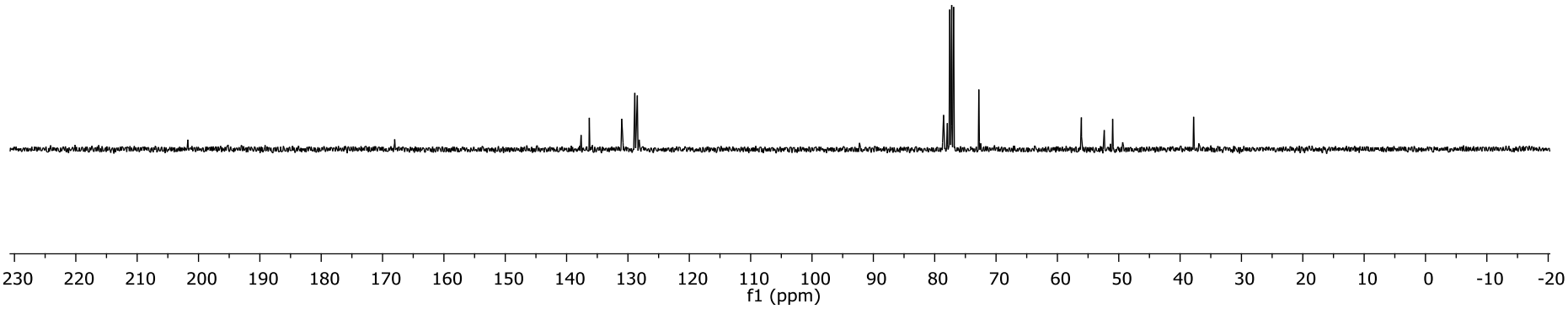
35

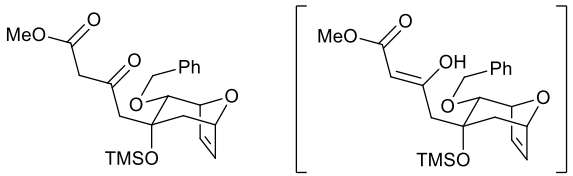
400 MHz, $CDCl_3$





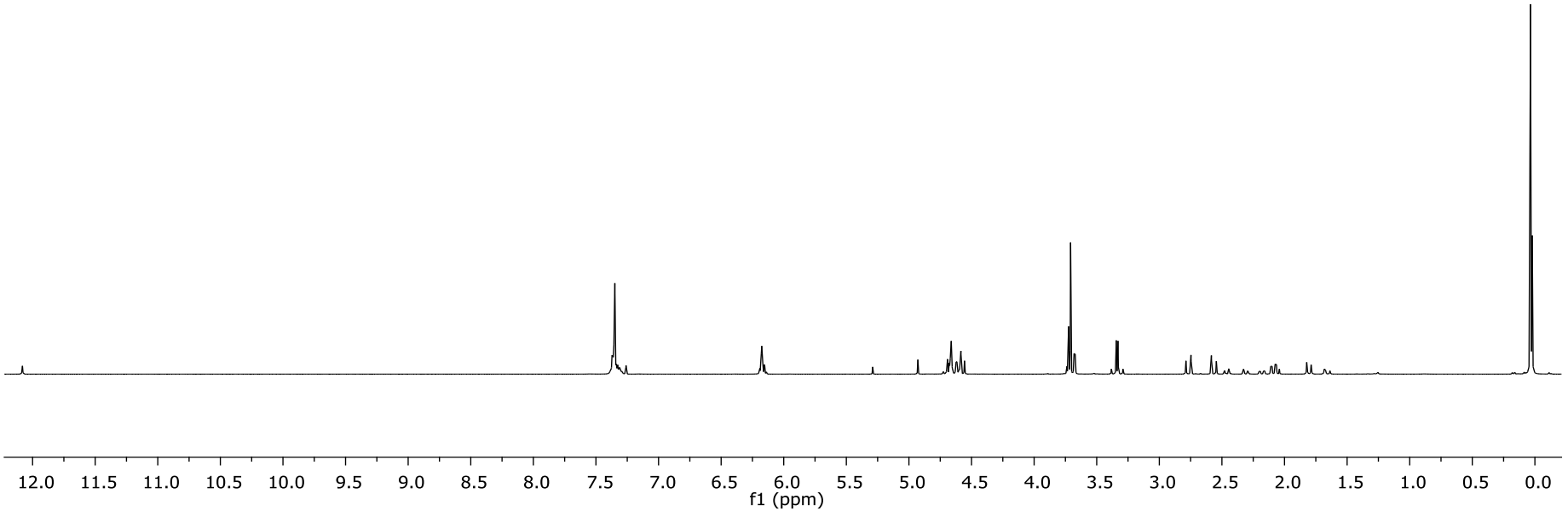
35
100 MHz, $CDCl_3$

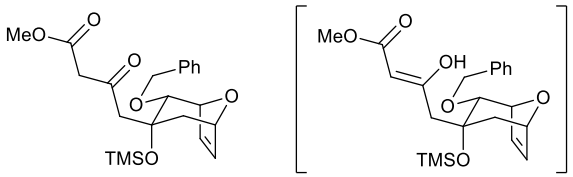




S1

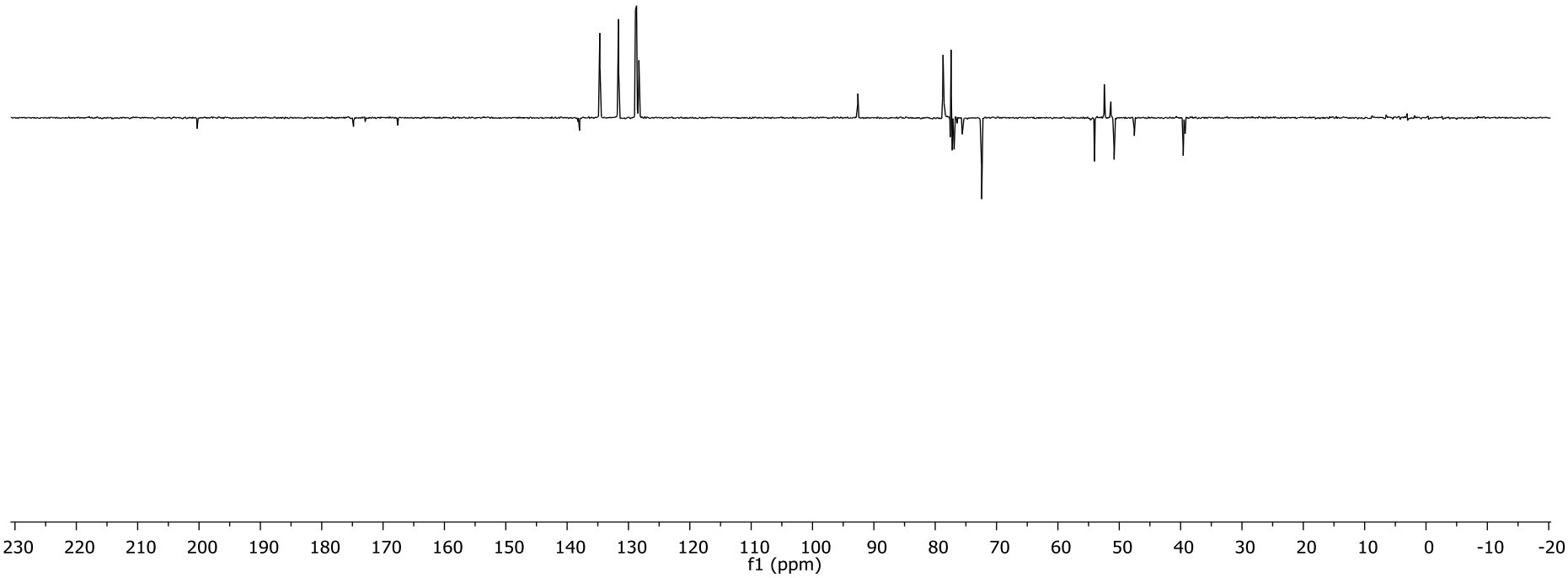
400 MHz, $CDCl_3$

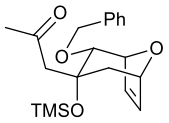




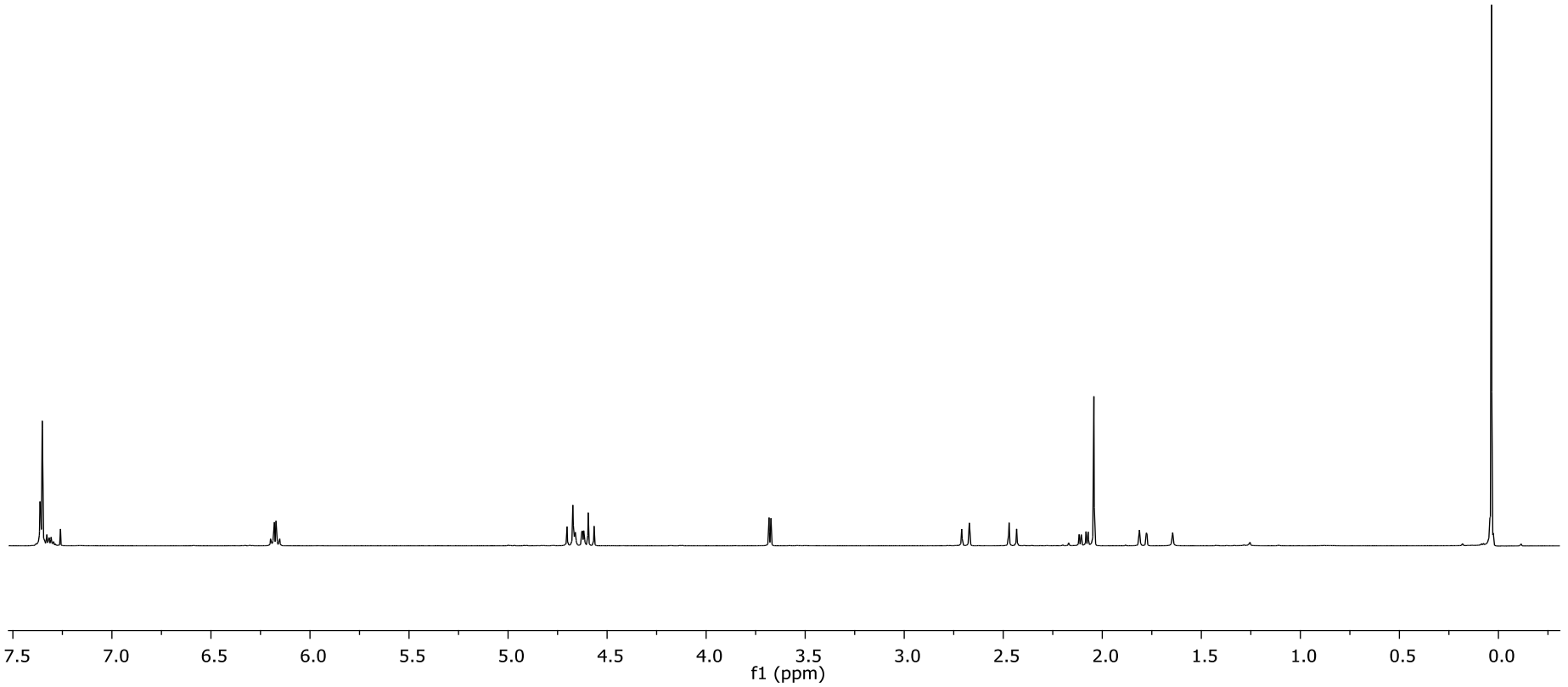
S1

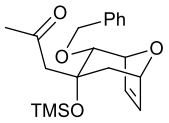
100 MHz, $CDCl_3$





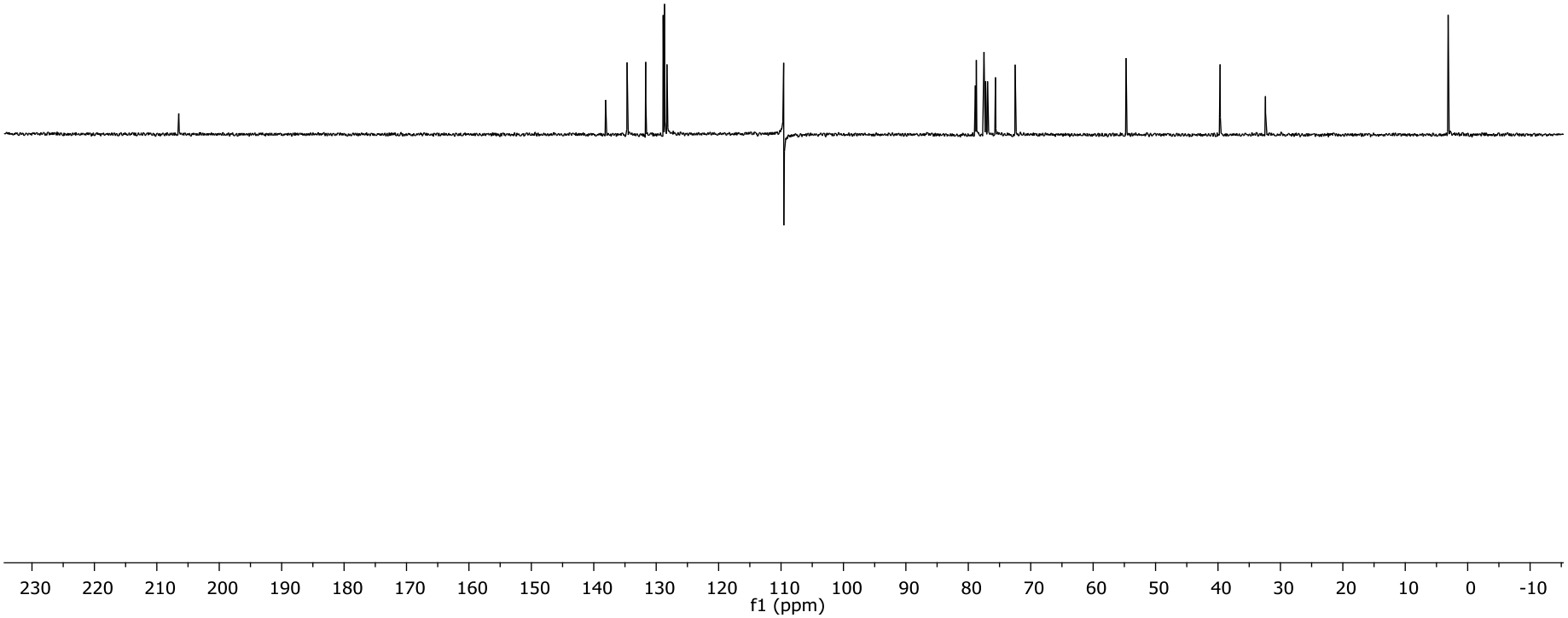
36
400 MHz, $CDCl_3$

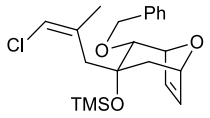




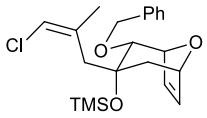
36

100 MHz, $CDCl_3$

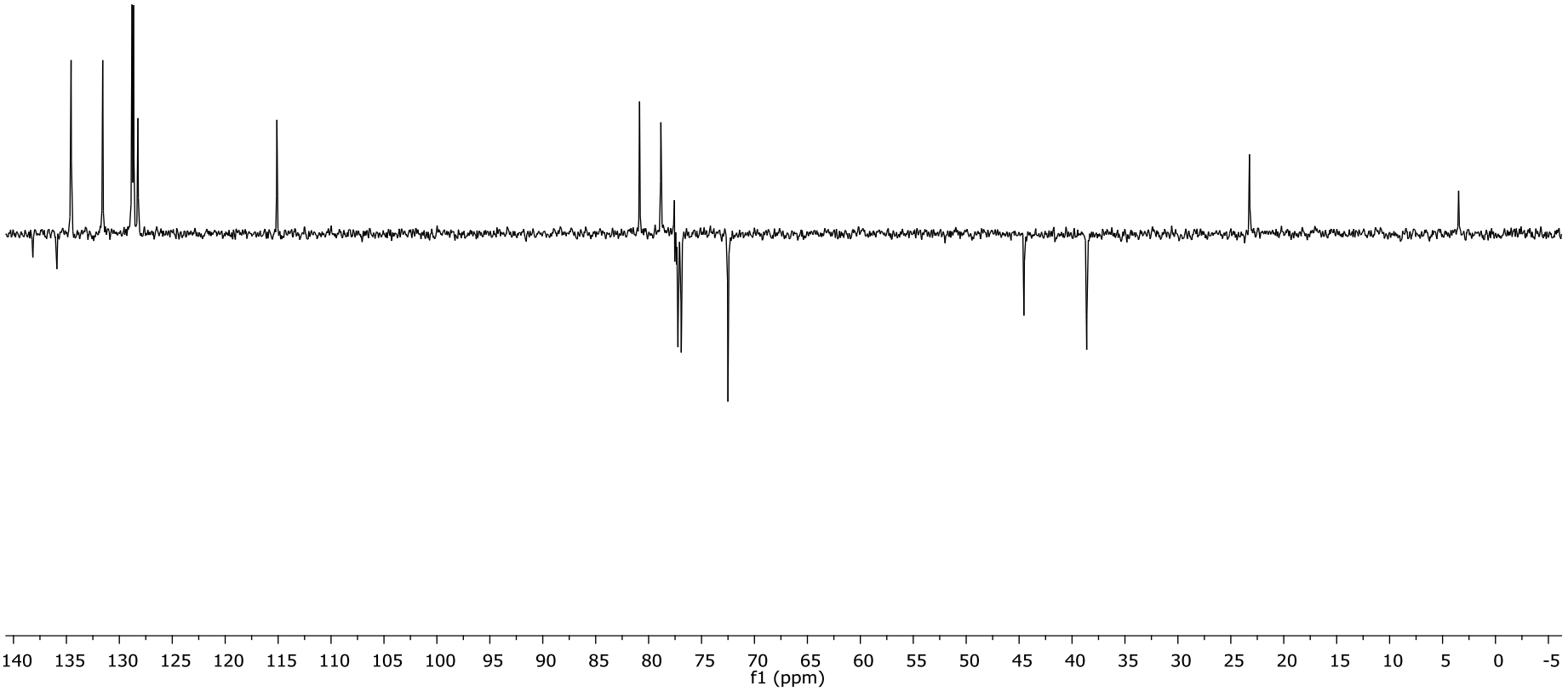


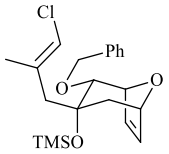


(*Z*)-37
400 MHz, $CDCl_3$

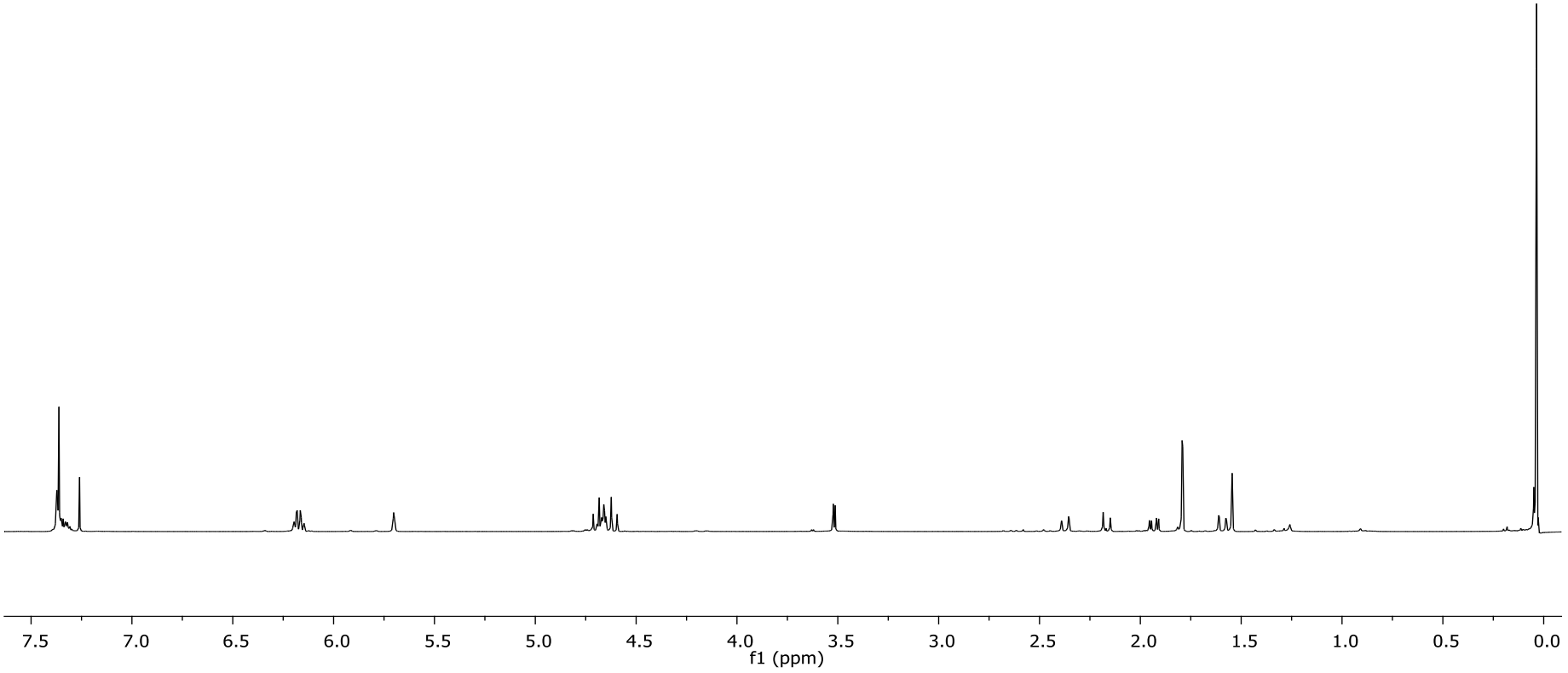


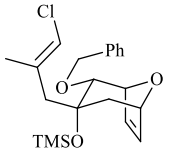
(*Z*)-37
100 MHz, $CDCl_3$



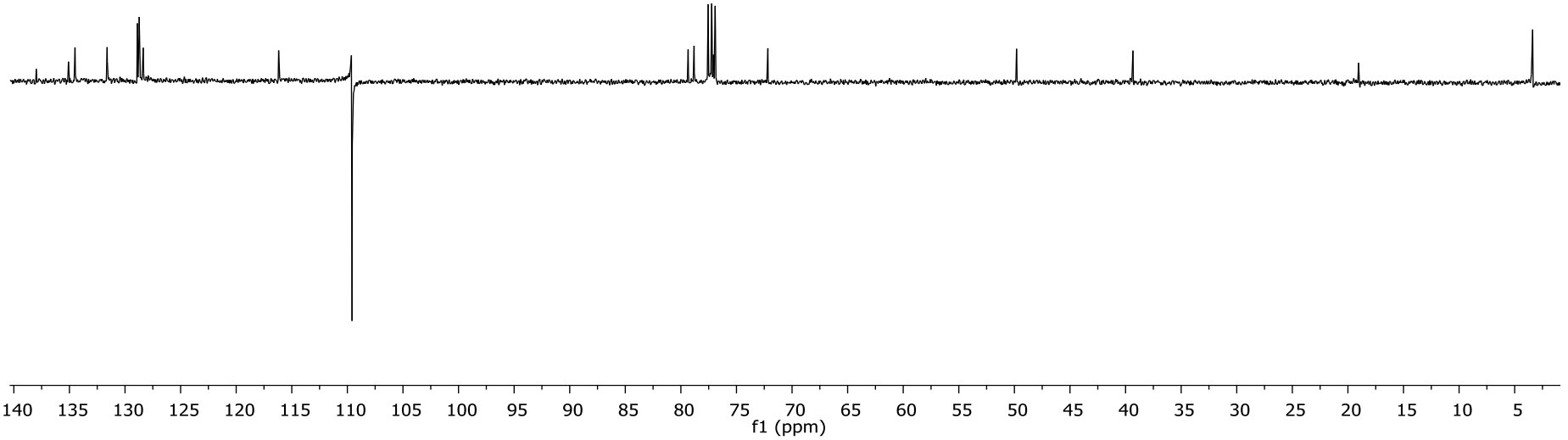


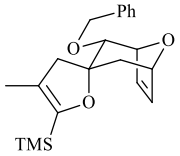
(*E*)-37
400 MHz, $CDCl_3$





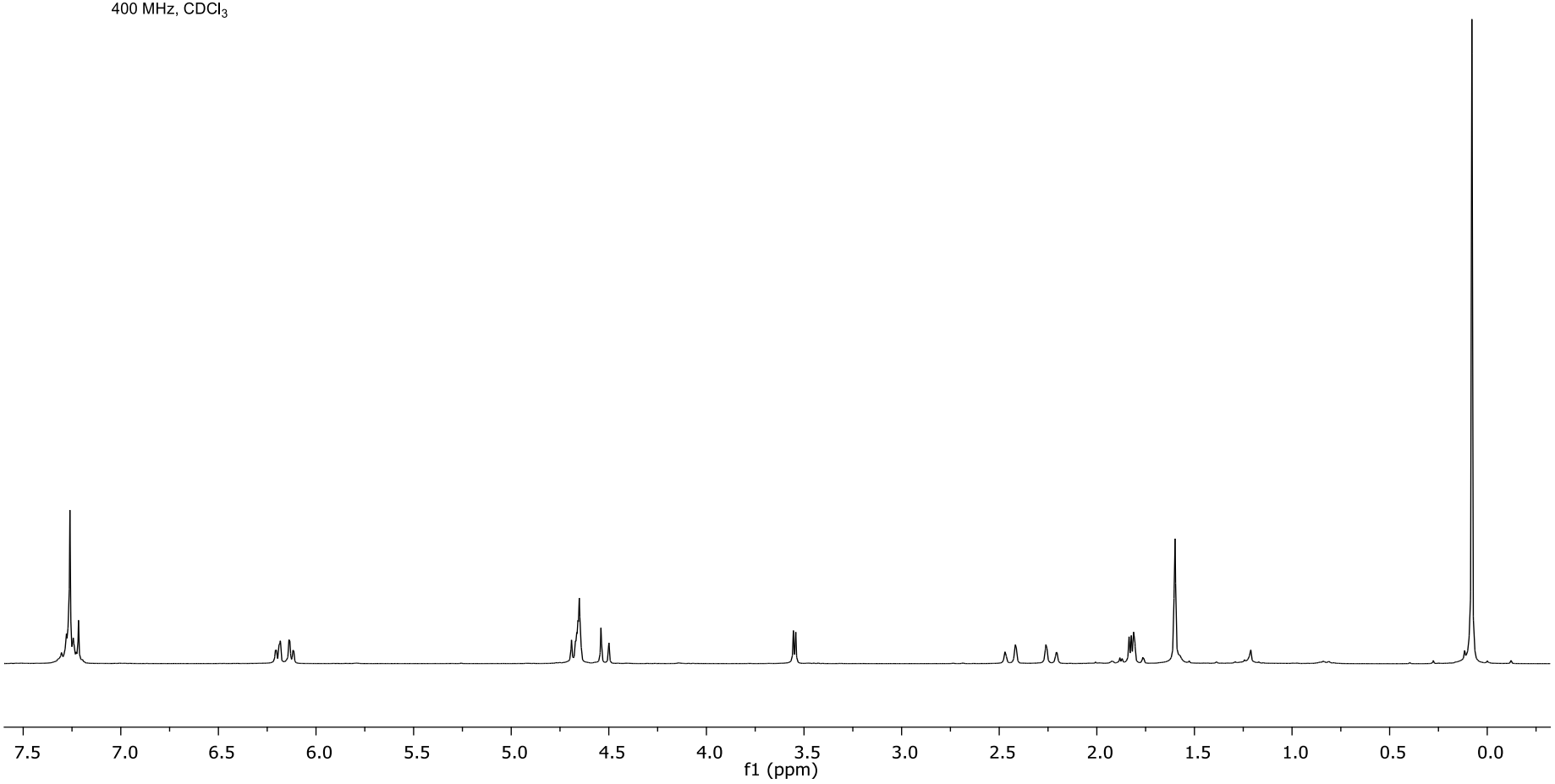
(*E*)-37
100 MHz, $CDCl_3$

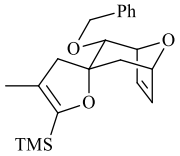




38

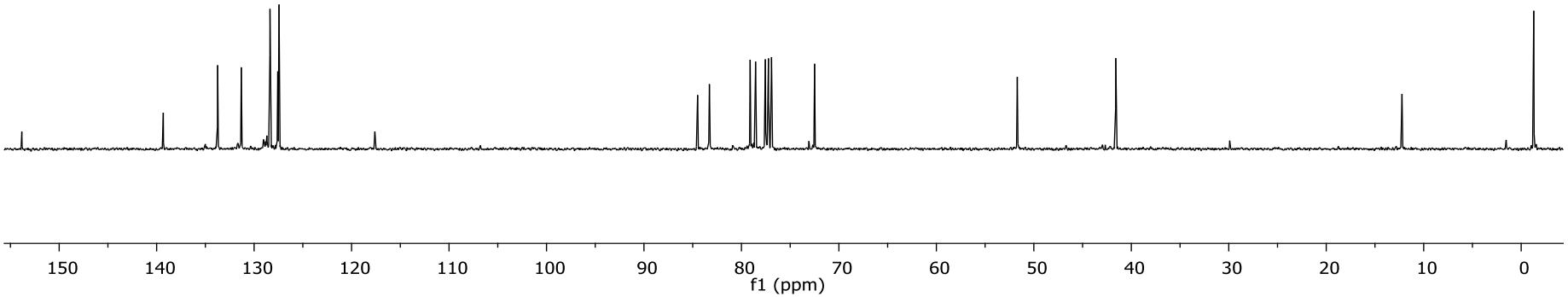
400 MHz, $CDCl_3$

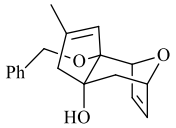




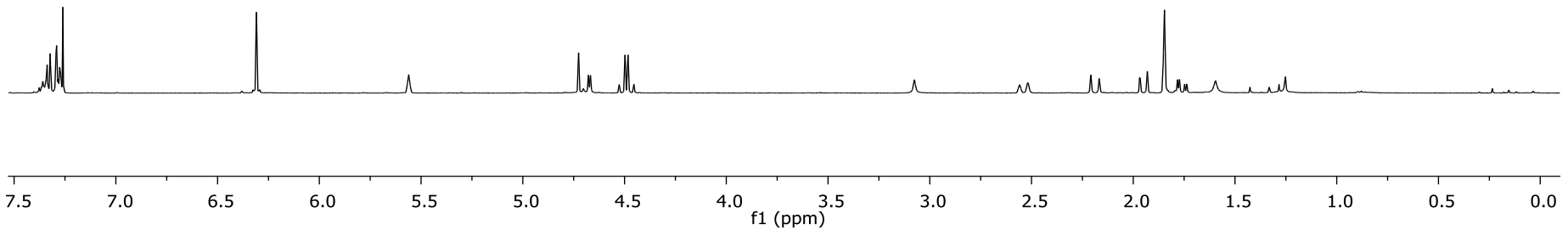
38

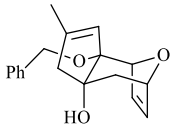
100 MHz, $CDCl_3$





39
400 MHz, $CDCl_3$





39
100 MHz, $CDCl_3$