Convergent and Stereospecific Synthesis of Skipped Polyenes and Polyunsaturated Fatty Acids

Todd K. Macklin and Glenn C. Micalizio*

The Scripps Research Institute, 130 Scipps Way, Jupiter, FL 33458

E-mail: micalizio@scripps.edu

SUPPORTING INFORMATION:

General. All reactions were conducted in flame-dried glassware under an argon atmosphere with dry solvents, unless otherwise noted. Dry diethyl ether (Et_2O), tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), *N*,*N*-dimethylformamide (DMF) and toluene (PhMe) were obtained by passing HPLC grade solvents through activated alumina columns. Anhydrous solutions of acetonitrile (MeCN) and benzene (PhH) were freshly distilled from calcium hydride and sodium / benzophenone respectively. Chlorotitanium triisopropoxide was obtained as a 1M solution in hexanes from Aldrich and used as purchased. *n*-Butyllithium solution was purchased from Aldrich and titrated monthly against *N*-benzylbenzamide. *c*-C_5H_9MgCl was purchased from Aldrich and titrated monthly using 1,10-phenatholine / *s*-butanol. [$Pd(PPh_3)_4$] was purchased from Strem. Reactions were monitored by thin-layer chromatography (TLC) carried out on 250 µm E. Merck silica gel plates (60F-254) and visualized using *p*-anisaldehyde[1] or phosphomolybdic acid stain with heat as a developing agent. Silica gel for flash column chromatography was purchased from Silicycle (P60, particle size 40-63 µm). ^1H and ^{13}C NMR data were recorded at 400 and 100 MHz using a Bruker AM-400 instrument with chemical shifts relative to residual $CHCl_3$ (7.24 and 77.16 ppm). Infrared spectra were recorded on a PerkinElmer SpectrumOne FT-IR instrument. Low resolution mass spectrometry were performed on a Shimadzu QP2010S (RTX-5 column) GCMS using EI and Varian 500-MS IT LCMS (ESI) using soft negative ionization. HRMS data (TOF ionization) were obtained by the University of Florida Mass Spectrometry lab, usually as ($M + H^+$) or ($M + Na^+$) ions. Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials, unless otherwise stated and all compounds purified by chromatography were sufficiently pure for use in further experiments, unless indicated otherwise. Relative stereochemistry was defined using the *R**/*S** convention proposed by IUPAC. Brine refers to a saturated aqueous solution of NaCl.

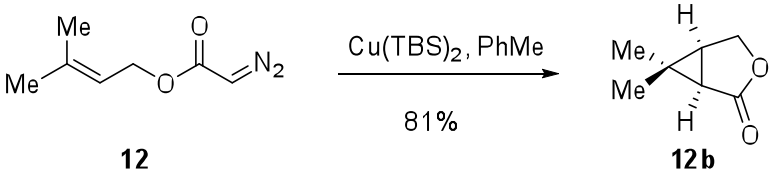
General Procedure A: Corey-Myers Diazoacetic Ester Cyclopropanation[2]

To a dry, argon flushed 3-neck RBF fitted with a condenser and drip funnel containing $Cu(TBS)_2$[3] (0.05 mmol) in PhMe (25 mL) at 120 °C is added diazoacetic ester (1 mmol, prepared as described by Corey from allylic alcohols and glyoxylic acid chloride tosylhydrazone[2]) in

[1] See http://www.ux1.eiu.edu/~cfthb/research/handbook/TLCstains.htm for the recipe.
[2] Corey; E. J.; Myers, A. G. *Tetrahedron Lett.* **1984**, *25*, 3559 – 3562.
[3] Sacconi, L.; Ciampolini, M. *J. Chem. Soc.* **1964**, 274 – 280.

PhMe (10 mL) from the drip funnel (1 drop / 8-10 seconds) until the addition is complete and the reaction is stirred for an additional 30 min. The reaction is cooled, concentrated, and purified by flash column chromatography (EtOAc or Et_2O in hexanes) to yield pure bicyclic lactone.

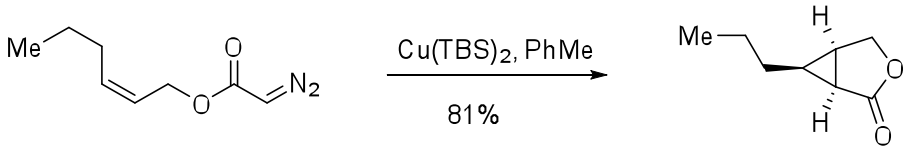
(1*R,5*S**)-6,6-Dimethyl-3-oxabicyclo[3.1.0]hexan-2-one (12b)**



12 **12b**

The titled compound was prepared according to Procedure A using the following quantities of reagents: 3,3-Dimethylallyl 2-diazoacetate (**12**) (2.0 g, 12.98 mmol) in PhMe (130 mL) and $Cu(TBS)_2$ (270 mg, 0.65 mmol) in PhMe (325 mL). After column chromatography (50% Et_2O in hexanes) **12b** was isolated as a colourless oil (1.32 g, 81%). Spectroscopic data was in full accordance to that found in the literature.[4]

(1*S,5*R**,6*S**)-6-Propyl-3-oxabicyclo[3.1.0]hexan-2-one (13b)**

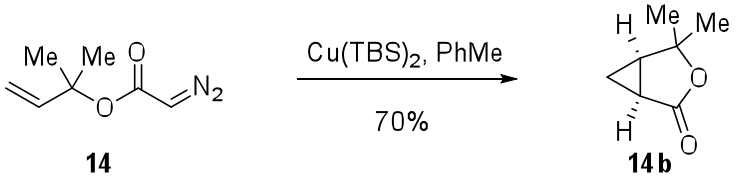


13 **13b**

The titled compound was prepared according to Procedure A using the following quantities of reagents: (*Z*)-Hex-2-enyl 2-diazoacetate (**13**) (2.0 g, 11.9 mmol) in PhMe (120 mL) and $Cu(TBS)_2$ (250 mg, 0.60 mmol) in PhMe (300 mL). After column chromatography (30% EtOAc in hexanes) **13b** was isolated as a colourless oil (1.35 g, 81%). Spectroscopic data was in full accordance to that found in the literature for the non-racemic compound.[5]

[4] Hirao, T.; Harano, Y.; Yamana, Y.; Hamada, Y, Nagata, S.; Agawa, T. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1341 – 1347.
[5] Doyle, M. P.; Patterson, C. S.; Zhou, Q.-L.; Nishiyama, H. *Chem. Comm.* **1997**, *2*, 211 – 212.

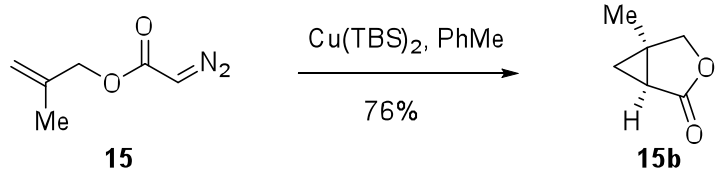
(1*S,5*R**)-4,4-Dimethyl-3-oxabicyclo[3.1.0]hexan-2-one (14b)**



14 **14b**

The titled compound was prepared according to Procedure A using the following quantities of reagents: 1,1-Dimethylallyl 2-diazoacetate (**14**) (1.5 g, 9.74 mmol) in PhMe (100 mL) and $Cu(TBS)_2$ (203 mg, 0.49 mmol) in PhMe (250 mL). After column chromatography (50% Et_2O in hexanes) **14b** was isolated as a colourless oil that slowly solidified at RT (850 mg, 70%). Spectroscopic data was in full accordance to that found in the literature.[4]

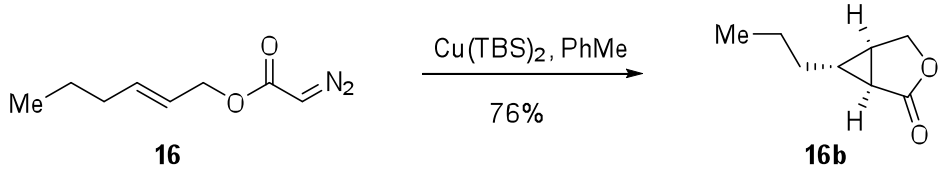
(1*S,5*R**)-5-Methyl-3-oxabicyclo[3.1.0]hexan-2-one (15b)**



15 **15b**

The titled compound was prepared according to Procedure A using the following quantities of reagents: 2-Methylallyl 2-diazoacetate (**15**) (2.0 g, 14.27 mmol) in PhMe (150 mL) and $Cu(TBS)_2$ (300 mg, 0.71 mmol) in PhMe (350 mL). After column chromatography (30% EtOAc in hexanes) **15b** was isolated as a colourless oil (1.22 g, 76%). Spectroscopic data was in full accordance to that found in the literature.[6]

(1*R,5*S**,6*S**)-6-Propyl-3-oxabicyclo[3.1.0]hexan-2-one (16b)**

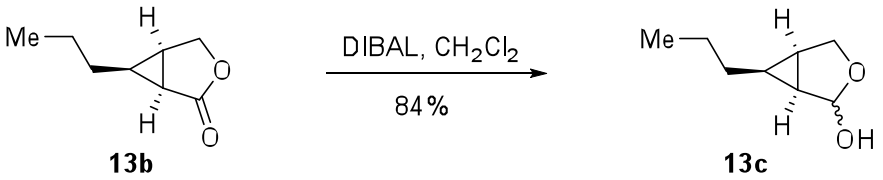


16 **16b**

[6] Hirao, T.; Harano, Y.; Yamana, Y.; Hamada, Y, Nagata, S.; Agawa, T. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1341 – 1347.

The titled compound was prepared according to Procedure A using the following quantities of reagents: (*E*)-Hex-2-enyl 2-diazoacetate (**16**) (2.0 g, 11.9 mmol) in PhMe (120 mL) and $Cu(TBS)_2$ (250 mg, 0.60 mmol) in PhMe (300 mL). After column chromatography (30% EtOAc in hexanes) **16b** was isolated as a colourless oil (1.28 g, 76%). Spectroscopic data was in full accordance to that found in the literature for the non-racemic compound.[7]

(1*S,5*R**,6*S**)-6-Propyl-3-oxabicyclo[3.1.0]hexan-2-ol (13c)**

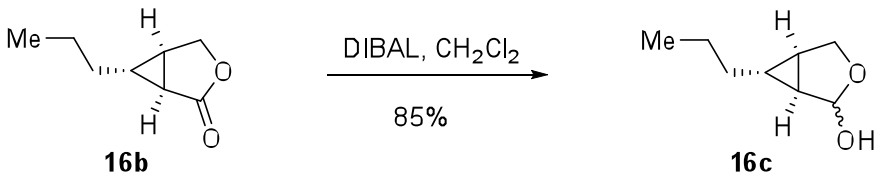


13b **13c**

To a RBF containing 6-propyl-3-oxabicyclo[3.1.0]hexan-2-one (**13b**) (420 mg, 3.0 mmol) in CH_2Cl_2 (6 mL) at -78 ^oC was added DIBAL (4.5 mL, 4.5 mmol, 1.0 M in hexanes) dropwise by syringe. After 1 h, MeOH (2 mL) and saturated aqueous sodium potassium tartrate (5 mL) were added and the reaction was allowed to warm and stir overnight. The phases were separated and the aqueous phase extracted with CH_2Cl_2, organic extracts combined, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (30% EtOAc in hexanes) to yield pure **13c** (358 mg, 84%) as a light yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 5.20 (bs, 1H), 4.15 (dd, *J* = 3.3, 8.5, 1H), 3.75 (d, *J* = 8.5, 1H), 3.02 (bd, *J* = 25.1, 1H), 1.72 – 1.69 (m, 2H), 1.39 – 1.26 (m, 4H), 0.90 (t, *J* = 7.1, 3H), 0.92 – 0.86 (m, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 98.0, 66.8, 27.4, 23.7, 23.5, 19.8, 19.5, 14.1 ppm; IR (thin film, NaCl) 3390, 2958, 2927, 2873, 1682, 1463, 1307, 1074, 1016, 989, 904 cm^{-1}; LRMS (EI) calcd for $C_8H_{14}O_2$ 142.2 (M^+, *m/z*), observed 142.1 (M^+), 28 (100%).

[7] Doyle, M. P.; Austin, R. E.; Bailey, A. S.; Dwyer, M. P.; Dyatkin, A. B.; Kalinin, A. V.; Kwan, M. M. Y.; Liras, S.; Oalmann, C. J.; Pieters, R. J.; Protopopova, M. N.; Raab, C. E.; Roos, G. H. P.; Zhou, Q.-L.; Martin, S. F. *J. Am. Chem. Soc.* **1995**, *117*, 5763 – 5775.

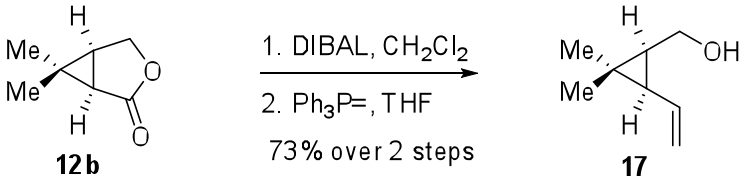
(1*S,5*R**,6*R**)-6-Propyl-3-oxabicyclo[3.1.0]hexan-2-ol (16c)**



16b **16c**

To a RBF containing 6-propyl-3-oxabicyclo[3.1.0]hexan-2-one (**16b**) (500 mg, 3.6 mmol) in CH_2Cl_2 (7 mL) at -78 ^oC was added DIBAL (5.4 mL, 5.4 mmol, 1.0 M in hexanes) dropwise by syringe. After 1 h, MeOH (2 mL) and saturated aqueous sodium potassium tartrate (5 mL) were added and the reaction was allowed to warm and stir overnight. The phases were separated and the aqueous phase extracted with CH_2Cl_2, organic extracts combined, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (50% EtOAc in hexanes) to yield pure **16c** (431 mg, 85%) as a light yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 5.24 (d, *J* = 4.2, 1H), 3.96 (dt, *J* = 1.5, 8.0, 1H), 3.77 (dd, *J* = 0.4, 8.1, 1H), 2.89 (d, *J* = 4.4, 1H), 1.43 (dd, *J* = 1.6, 3.6, 2H), 1.39 – 1.33 (m, 3H), 1.22 – 1.17 (m, 2H), 0.88 (t, *J* = 7.3, 3H), 0.58 – 0.52 (m, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 98.5, 68.0, 33.0, 22.3, 22.2, 20.4, 13.9 ppm; IR (thin film, NaCl) 3391, 2958, 2926, 2873, 1698, 1464, 1294, 1063, 1008, 896 cm^{-1}; LRMS (EI) calcd for $C_8H_{14}O_2$ 142.2 (M^+, *m/z*), observed 141.9 (M^+), 28 (100%).

((1*R,3*S**)-2,2-dimethyl-3-vinylcyclopropyl)methanol (17)**

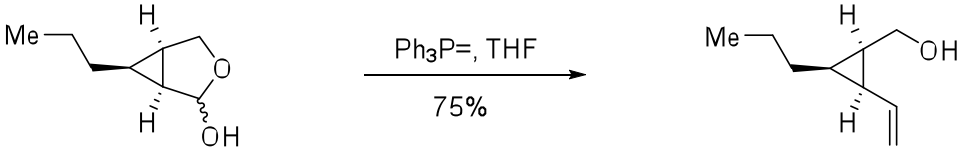


12b **17**

To a RBF containing 6,6-dimethyl-3-oxabicyclo[3.1.0]hexan-2-one (**12b**) (500 mg, 3.96 mmol) in CH_2Cl_2 (10 mL) at -78 ^oC was added DIBAL (6.0 mL, 6.0 mmol, 1.0 M in hexanes) dropwise by syringe. After 1 h, MeOH (3 mL) and saturated aqueous sodium potassium tartrate (5 mL) were added, the bath was removed and then solution was stirred for 2 hours. The phases were separated and the aqueous phase extracted with CH_2Cl_2, organic extracts combined, filtered

through $MgSO_4$, concentrated *in vacuo* to afford the crude lactol that was used directly in the following reaction. To a RBF containing methyltriphenylphosphonium bromide (2.12 g, 6.0 mmol) in THF (15 mL) at 0 °C was added *n*-BuLi (2.2 mL, 5.8 mmol, 2.5 M in hexanes). The bath was removed and the orange mixture stirred for 30 min. After recooling to 0 °C, the crude lactol in THF (2 mL) was added by cannula and the bath removed. The solution was then stirred for an additional 3 h. Saturated aqueous NH_4Cl was added and the reaction diluted with Et_2O, layers separated, aqueous phase extracted with Et_2O, organic extracts combined, filtered through $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (40% Et_2O in hexanes) to yield pure **17** (365 mg, 73%) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.58 (dt, *J* = 10.2, 16.9, 1H), 5.17 (ddd, *J* = 0.6, 2.1, 16.9, 1H), 5.02 (ddd, *J* = 0.6, 2.1, 10.3, 1H), 3.68 (ddd, *J* = 7.9, 11.6, 28.2, 2H), 1.48 (bs, 1H), 1.40 (t, *J* = 9.3, 1H), 1.14 – 1.08 (m, 1H), 1.09 (s, 3H), 1.07 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.0, 116.3, 60.3, 32.5, 31.6, 28.9, 22.1, 15.6 ppm; IR (thin film, NaCl) 3347, 2946, 1632, 1454, 1376, 1019, 988, 896 cm^{-1}; LRMS (EI) calcd for $C_8H_{14}O$ 126.2 (M^+, *m/z*), observed 126.1 (M^+), 95 (100%).

((1*S,2*S**,3*R**)-2-Propyl-3-vinylcyclopropyl)methanol (18)**

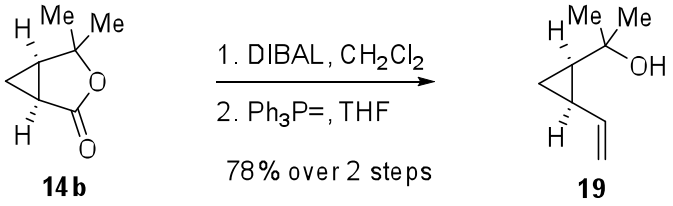


13c **18**

To a RBF containing methyltriphenylphosphonium bromide (3.98g, 11.2 mmol) in THF (80 mL) at RT was added NaHMDS (9.7 mL, 9.7 mmol, 1.0 M in THF) dropwise by syringe and the bright yellow mixture was stirred for 90 min before the addition of 6-propyl-3-oxabicyclo[3.1.0]hexan-2-ol (**13c**) (1.043 g, 7.4 mmol) in THF (12 mL) by cannula. After 2 h the mixture was diluted with CH_2Cl_2 (75 mL), filtered through silica, and concentrated *in vacuo*. The residue was purified by flash column chromatography (30% EtOAc in hexanes) to yield pure **18** (772 mg, 75%) as a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (dt, *J* = 10.2, 16.9, 1H), 5.26 – 5.22 (m, 1H), 5.06 (dd, *J* = 2.0, 10.3, 1H), 3.79 (dd, *J* = 7.3, 11.5, 1H), 3.68 (dd, *J* =

8.6, 11.5, 1H), 1.68 (dd, J = 9.0, 18.4, 1H), 1.43 – 1.32 (m, 5H), 1.29 – 1.24 (m, 1H), 1.17 – 1.11 (m, 1H), 0.90 (t, J = 6.9, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.1, 116.7, 59.9, 26.3, 24.3, 23.2, 23.0, 22.5, 14.2; IR (thin film, NaCl) 3351, 2958, 2931, 2872, 1633, 1465, 1021, 897 cm^{-1}; LRMS (EI) calcd for $C_9H_{16}O$ 140.2 (M^+, *m/z*), observed 140.1 (M^+), 55 (100%).

2-((1*S,2*S**)-2-vinylcyclopropyl)propan-2-ol (19)**

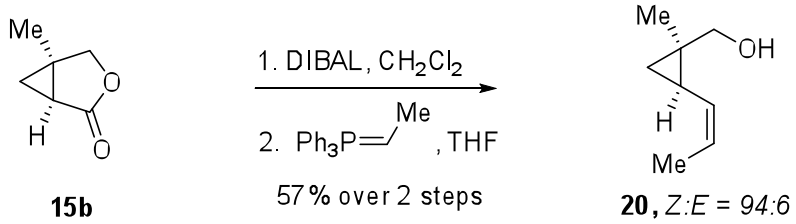


14b **19**

To a RBF containing 4,4-dimethyl-3-oxabicyclo[3.1.0]hexan-2-one (**14b**) (745 mg, 5.91 mmol) in CH_2Cl_2 (15 mL) at -78 ^{o}C was added DIBAL (8.9 mL, 8.87 mmol, 1.0 M in hexanes) dropwise by syringe. After 1 h, MeOH (4 mL) and saturated aqueous sodium potassium tartrate (6 mL) are added and the bath removed. The solution is then stirred for an additional 2 hours. The phases were separated and the aqueous phase extracted with CH_2Cl_2, organic extracts combined, filtered through $MgSO_4$, concentrated *in vacuo* to afford the crude lactol that was used directly in the following reaction. To a RBF containing methyltriphenylphosphonium bromide (5.28 g, 14.8 mmol) in THF (25 mL) at 0 ^{o}C is added *n*-BuLi (5.67 mL, 14.2 mmol, 2.5 M in hexanes) and the bath was removed and the orange mixture stirred for 30 min. After recooling to 0 ^{o}C, the crude lactol in THF (3 mL) was added by cannula and the bath removed. The solution was then stirred for an additional 3 h. Saturated aqueous NH_4Cl was added and the reaction diluted with Et_2O, layers separated, aqueous phase extracted with Et_2O, organic extracts combined, filtered through $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (40% Et_2O in hexanes) to yield pure **19** (580 mg, 78%) as a colourless oil. Spectroscopic data was in full accordance to that found in the literature.[8]

[8] Apparu, M.; Barrelle, M. *Tetrahedron* **1978**, *34*, 1691 – 1679.

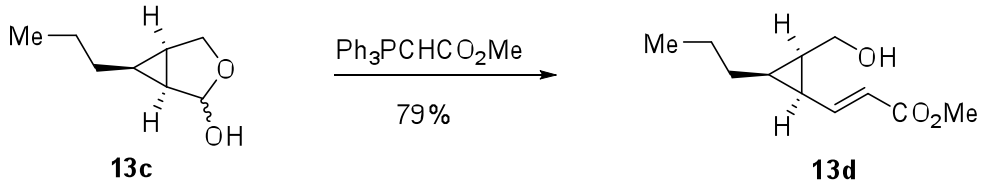
((1*R,2*R**)-1-Methyl-2-((*Z*)-prop-1-enyl)cyclopropyl)methanol (20)**



15b **20**, *Z:E* = *94:6*

To a RBF containing 5-methyl-3-oxabicyclo[3.1.0]hexan-2-one (**15b**) (366 mg, 3.27 mmol) in CH_2Cl_2 (6 mL) at -78 ^oC was added DIBAL (4.9 mL, 4.9 mmol, 1.0 M in hexanes) dropwise by syringe. After 1 h, MeOH (3 mL) and saturated aqueous sodium potassium tartrate (5 mL) are added and the reaction was allowed to warm and stir for 2 hours. The phases were separated and the aqueous phase extracted with CH_2Cl_2, organic extracts combined, filtered through $MgSO_4$, concentrated *in vacuo* to afford the crude lactol that was used directly in the following reaction. To a RBF containing ethyltriphenylphosphonium bromide (1.32 g, 3.95 mmol) in THF (5 mL) at -78 ^oC is added NaHMDS (3.9 mL, 3.95 mmol, 1.0 M in THF) and the bath was removed and the orange mixture stirred for 30 min. After recooling to -78 ^oC, the crude lactol in THF (2 mL) was added by canula and the bath removed allowing stirring for 3 h. Saturated aqueous NH_4Cl was added and the reaction diluted with EtOAc, layers separated, aqueous phase extracted with EtOAc, organic extracts combined, filtered through $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (40% Et_2O in hexanes) to yield **20** (235 mg, 57%, *Z:E* = 94:6) as a colourless oil; ^1H NMR (400 MHz, $CDCl_3$) δ ^1H NMR (400 MHz, $CDCl_3$) δ 5.52 (dqd, *J* = 1.2, 6.8, 10.7, 1H), 5.14 (ddq, *J* = 1.7, 9.2, 10.8, 1H), 3.61 (dd, *J* = 6.6, 11.5, 1H), 3.40 (d, *J* = 11.6, 1H), 1.71 (dd, *J* = 1.7, 6.8, 3H), 1.46 (td, *J* = 5.7, 8.6, 1H), 1.35 (bs, 1H), 1.19 (s, 3H), 0.78 (dd, *J* = 4.6, 8.2, 1H), 0.50 (t, *J* = 5.0, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 129.8, 126.0, 68.2, 25.5, 22.4, 22.4, 20.7, 13.4 ppm; IR (thin film, NaCl) 3366, 2952, 2868, 1672, 1445, 1385, 1035, 1020 cm^{-1}; LRMS (EI) calcd for $C_8H_{14}O$ 126.2 (M^+, *m/z*), observed 126.1 (M^+), 67 (100%).

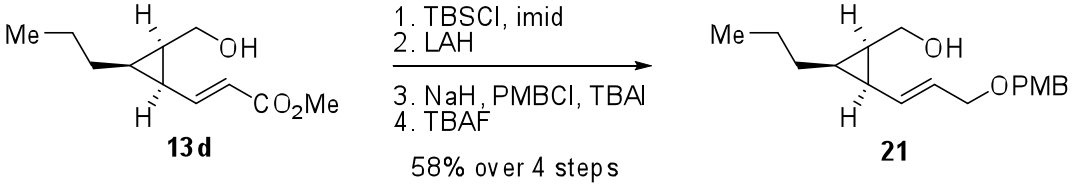
(*E*)-Methyl 3-((1*S,2*R**,3*R**)-2-(hydroxymethyl)-3-propylcyclopropyl)acrylate (13d)**



13c **13d**

A RBF containing an enantiomeric mixture of 6-propyl-3-oxabicyclo[3.1.0]hexan-2-ol **(13c)** (500 mg, 3.52 mmol) and methyl (triphenylphoranylidene) acetate (1.53 g, 4.58 mmol) in benzene (18 mL) was heated to 90 ^{o}C for 6h. The concentrated residue was purified by flash column chromatography (40% EtOAc in hexanes) to yield pure **13d** (550 mg, 79%) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.76 (dd, *J* = 11.2, 15.3, 1H), 5.95 (d, *J* = 15.3, 1H), 3.81 (dd, *J* = 7.3, 11.6, 1H), 3.70 (dd, *J* = 8.2, 11.6, 1H), 3.65 (s, 3H), 2.17 (s, 1H), 1.75 (dt, *J* = 8.4, 11.1, 1H), 1.60 – 1.51 (m, 1H), 1.51 – 1.37 (m, 2H), 1.38 – 1.27 (m, 3H), 0.86 (t, *J* = 7.2, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 147.3, 121.5, 59.0, 51.5, 27.2, 26.3, 25.3, 23.1, 22.6, 14.0 ppm; IR (thin film, NaCl) 3418, 2957, 2872, 1716, 1699, 1639, 1436, 1266, 1148, 1025 cm^{-1}; LRMS (EI) calcd for $C_{11}H_{18}O_3$ 198.2 (M^+, *m/z*), observed 198.1 (M^+), 81 (100%).

((1*R,2*S**,3*R**)--2-((*E*)-3-(4-Methoxybenzyloxy)prop-1-enyl)-3-propylcyclopropyl)methanol (21)**

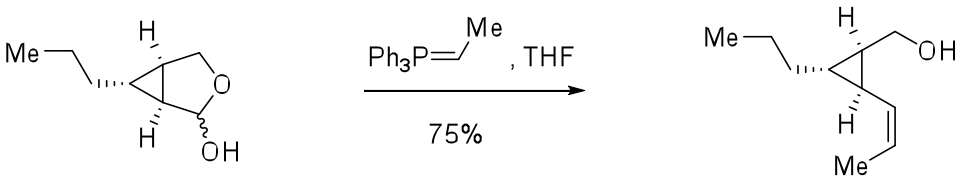


13d **21**

A RBF containing (*E*)-methyl 3-(2-(hydroxymethyl)-3-propylcyclopropyl)acrylate **13d** (450 mg, 2.27 mmol), TBSCl (376 mg, 2.5 mmol), imidazole (170 mg, 2.5 mmol) in DMF (11 mL) is stirred at RT for 20 h. The reaction was then diluted with water (60 mL) and extracted twice with Et_2O, organic extracts combined, washed with brine, filtered through $MgSO_4$, and concentrated *in vacuo* to afford the crude product that was then dissolved in THF (11 mL), cooled to 0 ^{o}C, and treated by syringe with LAH (2.3 mL, 2.3 mmol, 1 M in THF). The mixture

was allowed to warm to RT and stirred for 1 h, recooled to 0 ^{o}C, and quenched slowly with saturated aqueous sodium potassium tartrate (10 mL). After rapid stirring for 1 h at RT, the layers are separated and the aqueous layer is extracted twice with Et_2O, organic extracts combined, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (20% EtOAc in hexanes) to yield pure product (220 mg) and impure fractions (405 mg) which contained a small amount of over reduction product. This pure product (220 mg, 0.77 mmol) was mixed in a RBF with PMBCl (147 μL, 1.1 mmol), TBAI (28 mg, 0.08 mmol) in DMF (5 mL) and NaH (62 mg, 1.54 mmol, 60% in mineral oil) was added in one portion at RT. After 20 h of stirring, the mixture was quenched with saturated aqueous NH_4Cl (5 mL) and diluted with water (20 mL), extracted twice with Et_2O, organic extracts combined, washed with brine, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (10% EtOAc in hexanes) to yield the product. This product was then dissolved in THF (5 mL) and treated by syringe at RT with TBAF (950 μL, 0.95 mmol, 1 M in THF, dried by stirring in Na_2SO_4 for 30 min), and stirred for 4 h. The reaction was then quenched with solid $CaCO_3$ (~50 mg) and saturated aqueous NH_4Cl (5 mL), layers separated, aqueous layer extracted twice with Et_2O, organic extracts combined, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (20 to 40% EtOAc in hexanes) to yield pure **21** (160 mg, 58% over 4 steps) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.18 (m, 2H), 6.89 – 6.80 (m, 2H), 5.80 (dt, J = 6.3, 15.2, 1H), 5.52 (ddt, J = 1.2, 10.0, 15.2, 1H), 4.41 (s, 2H), 3.94 (dt, J = 1.1, 6.4, 2H), 3.78 (s, 3H), 3.74 (dd, J = 3.8, 11.2, 1H), 3.66 (dd, J = 8.3, 11.6, 1H), 1.68 (dd, J = 8.8, 18.5, 1H), 1.44 (bs, 1H), 1.42 – 1.28 (m, 5H), 1.20 – 1.09 (m, 1H), 0.94 – 0.84 (m, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.5, 130.6, 130.0, 129.6, 128.8, 114.0, 71.6, 70.7, 59.7, 55.4, 26.3, 24.2, 23.2, 22.4, 21.6, 14.2 ppm; IR (thin film, NaCl) 3418, 2956, 2859, 1614, 1514, 1463, 1302, 1248, 1173, 1035, 820 cm^{-1}; HRMS (GC-CI) calcd for $C_{18}H_{27}O_3$, 291.1963 $(M + H)^+$ *m/z*; observed, 291.1962 $(M + H)^+$ *m/z*.

((1*S,2*R**,3*R**)-2-((*Z*)-Prop-1-enyl)-3-propylcyclopropyl)methanol (22)**



13c **22,** *Z:E* = 95:5

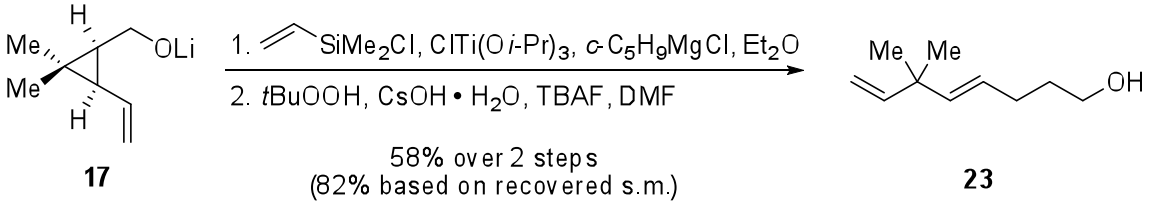
To a RBF containing ethyltriphenylphosphonium bromide (1.2 g, 3.21 mmol) in THF (5 mL) at -78 ^{o}C was added NaHMDS (3.21 mL, 3.21 mmol, 1.0 M in THF) The bath was removed and the orange mixture was stirred for 30 min. After recooling to -78 ^{o}C, 6-propyl-3-oxabicyclo[3.1.0]hexan-2-ol **(13c)** (300 mg, 2.14 mmol) in THF (2 mL) was added by cannula. The bath was removed and the solution was stirred for 3 h. Saturated aqueous NH_4Cl was added and the reaction was diluted with EtOAc, layers separated, aqueous phase extracted with EtOAc, organic extracts combined, filtered through $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (35% Et_2O in hexanes) to yield **22** (270 mg, 75%, *Z:E* = 95:5) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.49 (dqd, *J* = 1.1, 6.8, 10.7, 1H), 5.13 (ddq, *J* = 1.7, 9.4, 11.0, 1H), 3.75 (dd, *J* = 6.3, 11.6, 1H), 3.43 (dd, *J* = 9.0, 11.6, 1H), 1.70 (dd, *J* = 1.7, 6.8, 3H), 1.45 – 1.23 (m, 6H), 1.12 (tdd, *J* = 5.1, 6.3, 8.8, 1H), 0.88 (t, *J* = 7.1, 3H), 0.70 (dq, *J* = 5.0, 6.5, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 129.0, 125.4, 63.6, 35.7, 28.4, 26.6, 21.5, 14.0, 13.3 ppm; IR (thin film, NaCl) 3351, 2957, 2919, 2873, 1651, 1464, 1408, 1033 724 cm^{-1}; LRMS (EI) calcd for $C_{10}H_{18}O$ 154.2 (M^+, *m/z*), observed 154.1 (M^+), 81 (100%).

General Procedure B: Coupling of Vinylsilane with Vinylcyclopropanes

To a RBF containing $ClTi(O\textit{i}\text{-}Pr)_3$ (3 mmol, 1.0 M in hexanes) and chlorodimethylvinylsilane (3 mmol) in Et_2O (0.1 M) at -78 ^{o}C is added *c*-C_5H_9MgCl (6 mmol) by syringe and the mixture is warmed to -50 ^{o}C and stirred for 1 h becoming deep brown in colour. In a separate RBF containing vinylcyclopropane (1 mmol) in THF (~0.2 M) at -78 ^{o}C is added *n*-BuLi (1.2 mmol) by syringe and the mixture was warmed to 0 ^{o}C over 20 min and then added by cannula to the titanium complex that had been re-cooled to -70 ^{o}C. The mixture is then slowly warmed to RT over 2–3 h and treated with 1N HCl (~5 mL / mmol vinylcyclopropane) with rapid stirring.

After 10 min the now colourless mixture is further diluted with EtOAc and then filtered through a pad of silica rinsing with additional EtOAc. After concentration *in vacuo*, the non-polar product fractions were separated from the unreacted vinylcyclopropane by flash column chromatography (15% EtOAc in hexanes followed by flushing with EtOAc) and used directly in the following Tamao oxidation. To a cooled (0 °C) solution of *t*BuOOH (30 mmol, 70% in H_2O) in DMF (0.2 M) is added CsOH • H_2O (25 mmol). After the mixture is warmed to RT, a solution of crude isopropoxysilane / silanol in THF (~0.5 M) was added. After 10 min, TBAF (10 mmol, 1.0 M in THF) is added, the mixture is heated to 70 °C, and stirred at that temperature for 6 h. The mixture is then cooled to RT, and saturated aqueous $Na_2S_2O_3$ was slowly added with rapid stirring. The mixture is then further diluted with water and extracted twice with Et_2O. The organic extracts are then combined and filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (EtOAc or Et_2O in hexanes) to yield pure 1,4-dienyl alcohol. Alternatively the crude product could be oxidized by stirring with KF (8 mmol), $KHCO_3$ (4 mmol), and H_2O_2 (5 mmol, 30%) in MeOH / THF (0.1 M, 50:50) for 1-2 days. This reaction is then quenched by the slow addition of saturated aqueous $Na_2S_2O_3$, diltuted with E_2O and water, layers separated, aqueous extracted with Et_2O, organic extracts combined and filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (EtOAc or Et_2O in hexanes).

(*E*)-6,6-Dimethylocta-4,7-dien-1-ol (23)

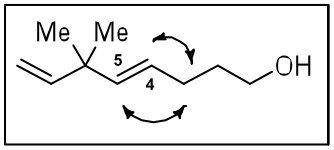


17 **23**

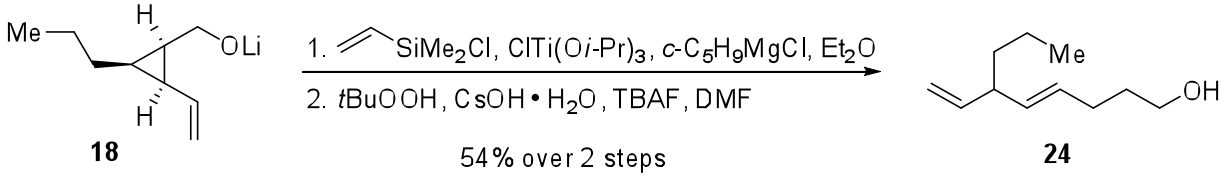
The titled compound was prepared according to Procedure B using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (3.0 mL, 3.0 mmol), chlorodimethylvinylsilane (310 μL, 2.25 mmol), *c*-C_5H_9MgCl (3.0 mL, 6.0 mmol, 2.0 M in Et_2O) in Et_2O (7.5 mL), and 2,2-dimethyl-3-vinylcyclopropyl)methanol **17** (95 mg, 0.75 mmol), *n*-BuLi (360 μL, 0.9 mmol, 2.5 M in

hexanes) in THF (2 mL). Unreacted vinylcyclopropane was recovered (28 mg). Oxidation: alkyl silane in THF (2 mL), *t*BuOOH (3.2 mL, 22.5 mmol), CsOH • H_2O (3.3 g, 18.8 mmol), TBAF (7.5 mL, 7.5 mmol) in DMF (5 mL). After workup, flash column chromatography (40% Et_2O in hexanes) to yield **23** (67 mg, 58%, >20:1 *E:Z*, 82% brsm) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (dd, *J* = 10.6, 17.4, 1H), 5.43 (dt, *J* = 1.0, 15.6, 1H), 5.33 (dt, *J* = 6.5, 15.6, 1H), 4.94 – 4.84 (m, 2H), 3.61 (t, *J* = 6.5, 2H), 2.06 (td, *J* = 1.0, 7.4, 2H), 1.60 (td, *J* = 6.7, 13.8, 2H), 1.05 (s, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.7, 139.6, 126.1, 110.5, 62.7, 39.2, 32.6, 29.2, 27.3 ppm; IR (thin film, NaCl) 3352, 2961, 2869, 1470, 1360, 1059, 911 cm^{-1}; HRMS (GC-CI) calcd for $C_{10}H_{19}O$, 155.1436 $(M + H)^+$ *m/z*; observed, 155.1429 $(M + H)^+$ *m/z*.

Alkene geometry at C4-C5 was assigned by nOe:



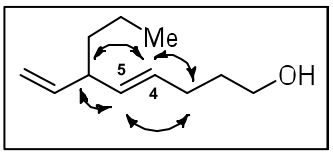
(*E*)-6-Vinylnon-4-en-1-ol (24)



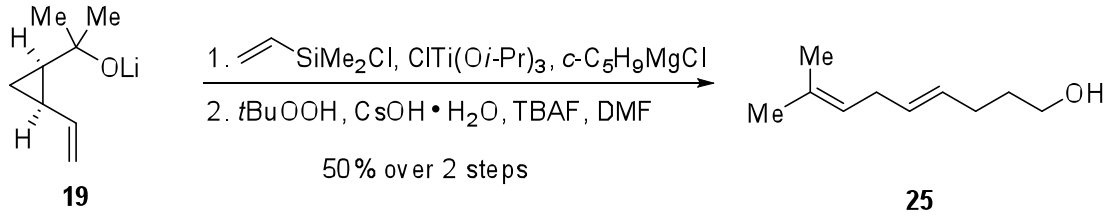
The titled compound was prepared according to Procedure B using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (2.14 mL, 2.14 mmol), chlorodimethylvinylsilane (295 μL, 2.14 mmol), *c*-C_5H_9MgCl (2.1 mL, 4.28 mmol, 2.01 M in Et_2O) in Et_2O (7 mL), and (2-propyl-3-vinylcyclopropyl)methanol **18** (100 mg, 0.71 mmol), *n*-BuLi (240 μL, 0.86 mmol, 2.5 M in hexanes) in THF (3 mL). Oxidation: alkyl silane in DMF (2 mL), *t*BuOOH (3.0 mL, 21 mmol), CsOH • H_2O (2.5 g, 14.2 mmol), TBAF (7.0 mL, 7.0 mmol) in DMF (5 mL). After workup, flash column chromatography (15% EtOAc in hexanes) yielded **24** (65 mg, 54%, >20:1 *E:Z*) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72 – 5.64 (m, 1H), 5.44 – 5.29 (m, 2H), 4.97 – 4.94 (m, 1H), 4.93 – 4.91 (m, 1H), 3.63 (t, *J* = 6.5, 3H), 2.65 – 2.61 (m, 1H), 2.08 (dd, *J* = 6.9, 13.9, 2H), 1.66 – 1.59 (m, 2H), 1.34 – 1.17 (m, 5H), 0.86 (t, *J* = 7.1, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.4, 133.9, 129.6, 113.6, 62.8, 46.7, 37.2, 32.6, 29.2, 26.2, 20.5, 14.2 ppm; IR

(thin film, NaCl) 3351, 2957, 2930, 2872, 1635, 1464, 1270, 1126, 1059, 911, 771 cm^{-1}; HRMS (GC-CI) calcd for $C_{11}H_{21}O$, 169.1592 $(M + H)^+$ *m/z*; observed, 169.1592 $(M + H)^+$ *m/z*.

Alkene geometry at C4-C5 was assigned by nOe:



(*E*)-8-Methylnona-4,7-dien-1-ol (25)

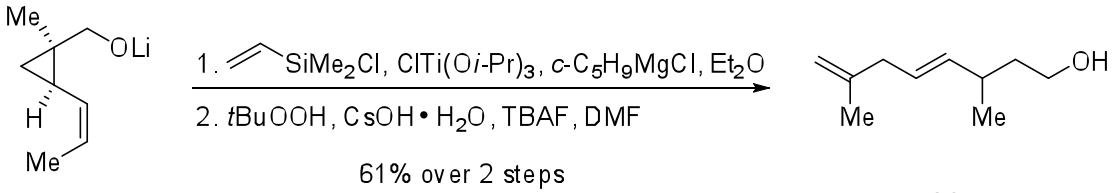


19 **25**

The titled compound was prepared according to Procedure B using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (1.9 mL, 1.9 mmol), chlorodimethylvinylsilane (262 μL, 1.9 mmol), *c*-C_5H_9MgCl (1.9 mL, 3.8 mmol, 2.0 M in Et_2O) in Et_2O (7 mL), and 2-(2-vinylcyclopropyl)propan-2-ol **19** (80 mg, 0.63 mmol), *n*-BuLi (300 μL, 0.76 mmol, 2.5 M in hexanes) in THF (2 mL). Oxidation: alkyl silane, KF (290 mg, 5.07 mmol), $KHCO_3$ (260 mg, 2.54 mmol), H_2O_2 (360 μL, 3.17 mmol) in MeOH/THF (6 mL, 50:50) for 48 h. After workup, flash column chromatography (40% Et_2O in hexanes) to yield pure **25** (49 mg, 50%, >20:1 *E:Z*) as a colourless oil; ^1H NMR (400 MHz, $CDCl_3$) δ ^1H NMR (400 MHz, $CDCl_3$) δ 5.43 (dq, *J* = 1.8, 1.3 Hz, 2H), 5.13 (tdt, *J* = 7.2, 2.8, 1.4 Hz, 1H), 3.66 (d, *J* = 6.4 Hz, 2H), 2.68 (dd, *J* = 2.1, 1.1 Hz, 2H), 2.13 – 2.04 (m, 2H), 1.71 (d, *J* = 1.1 Hz, 3H), 1.68 – 1.60 (m, 2H), 1.61 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 132.4, 129.7, 129.6, 122.5, 62.8, 32.5, 31.4, 30.5, 29.0, 17.8 ppm; IR (thin film, NaCl) 3338, 2927, 2875, 1448, 1376, 1055, 966 cm^{-1}; LRMS (EI) calcd for $C_{11}H_{18}O$ 154.2 (M^+, *m/z*), observed 154.1 (M^+), 67 (100%).

Alkene geometry at C4-C5 was assigned by analogy to other examples (see **23**, **24**, **26** and **27**).

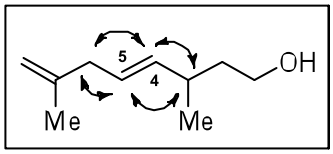
(*E*)-3,7-Dimethylocta-4,7-dien-1-ol (26)



20 **26**

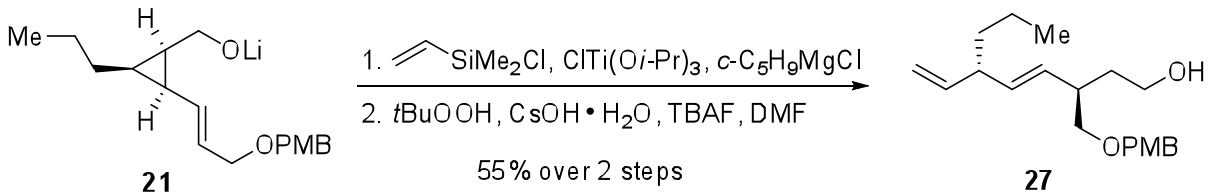
The titled compound was prepared according to Procedure B using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (3.0 mL, 3.0 mmol), chlorodimethylvinylsilane (310 μL, 2.25 mmol), *c*-C_5H_9MgCl (3.0 mL, 6.0 mmol, 2.0 M in Et_2O) in Et_2O (7.5 mL), and methyl-2-((*Z*)-prop-1-enyl)cyclopropyl)methanol **20** (95 mg, 0.75 mmol), *n*-BuLi (360 μL, 0.9 mmol, 2.5 M in hexanes) in THF (2 mL). Oxidation: alkyl silane in THF (2 mL), *t*BuOOH (3.2 mL, 22.5 mmol), $CsOH \bullet H_2O$ (3.3 g, 18.8 mmol), TBAF (7.5 mL, 7.5 mmol) in DMF (5 mL). After workup, flash column chromatography (40% Et_2O in hexanes) to yield **26** (70 mg, 61%, >20:1 *E:Z*) as a colourless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 5.46 – 5.25 (m, 2H), 4.67 (d, *J* = 11.5, 2H), 3.67 – 3.56 (m, 2H), 2.65 (d, *J* = 6.6, 2H), 2.25 (dt, *J* = 7.2, 14.3, 1H), 1.67 (s, 3H), 1.58 – 1.48 (m, 2H), 0.98 (d, *J* = 6.8, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 137.8, 126.8, 110.5, 61.5, 41.3, 39.9, 34.0, 22.5, 21.3 ppm; IR (thin film, NaCl) 3334, 2961, 2929, 1651, 1455, 1373, 1128, 1050 971, 888 cm^{-1}; HRMS (GC-CI) calcd for $C_{10}H_{19}O$, 155.1436 $(M + H)^+$ *m/z*; observed, 155.1438 $(M + H)^+$ *m/z*.

Alkene geometry at C4-C5 was assigned by nOe:



For Compound **26**: The 1,4-diene product isolated was contaminated with a minor product of unknown structure. If this minor product is the Z-alkene isomer, selectivity for this process can be calculated to be = ≥ 10:1 (based on integration in the 1H NMR spectrum).

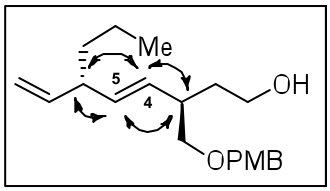
(3*R,6*S**,*E*)-3-((4-Methoxybenzyloxy)methyl)-6-vinylnon-4-en-1-ol (27)**



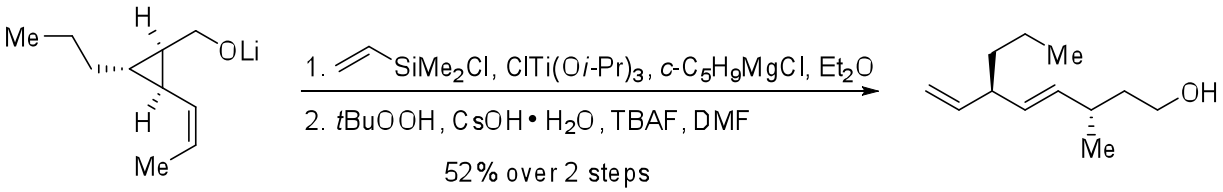
21 **27**

The titled compound was prepared according to Procedure B using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (630 μL, 0.63 mmol), chlorodimethylvinylsilane (310 μL, 0.63 mmol), *c*-C_5H_9MgCl (630 μL, 1.26 mmol, 2.0 M in Et_2O) in Et_2O (3 mL), and an enantiomeric mixture of 2,2-dimethyl-3-vinylcyclopropyl)methanol **21** (60 mg, 0.21 mmol), *n*-BuLi (100 μL, 0.25 mmol, 2.5 M in hexanes) in THF (1 mL). Oxidation: alkyl silane in THF (2 mL), *t*BuOOH (0.9 mL, 6.3 mmol), $CsOH \bullet H_2O$ (930 mg, 5.3 mmol), TBAF (2.1 mL, 2.1 mmol) in DMF (2 mL). After workup, flash column chromatography (30 to 40% EtOAc in hexanes) to yield pure **27** (37 mg, 55%, >20:1 *E:Z*, >20:1 dr) as a colourless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 3H), 6.89 – 6.81 (m, 2H), 5.67 (ddd, *J* = 7.3, 10.6, 16.9, 1H), 5.37 (dd, *J* = 7.4, 15.7, 1H), 5.26 (dd, *J* = 8.5, 15.8, 1H), 5.00 – 4.94 (m, 1H), 4.93 (d, *J* = 1.1, 1H), 4.42 (s, 2H), 3.78 (s, 3H), 3.69 – 3.64 (m, 1H), 3.62 – 3.56 (m, 1H), 3.40 (dd, *J* = 5.2, 9.2, 1H), 3.32 (dd, *J* = 7.6, 9.2, 1H), 2.63 (dd, *J* = 7.1, 14.1, 1H), 2.51 – 2.37 (m, 1H), 2.10 (s, 1H), 1.74 (ddt, *J* = 5.8, 7.5, 13.4, 1H), 1.65 – 1.53 (m, 2H), 1.37 – 1.22 (m, 5H), 0.86 (t, *J* = 7.1, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 142.1, 134.7, 130.9, 130.4, 129.5, 114.0, 113.9, 74.3, 73.0, 61.5, 55.5, 46.7, 40.9, 37.2, 36.0, 20.5, 14.2 ppm; IR (thin film, NaCl) 3380, 2956, 2930, 2871, 1608, 1513, 1250, 1103, 1025 cm^{-1}; HRMS (GC-CI) calcd for $C_{20}H_{31}O_3$, 319.2273 $(M + H)^+$ *m/z*; observed, 319.2265 $(M + H)^+$ *m/z*.

Alkene geometry at C4-C5 was assigned by nOe:



(3*S,6*R**,*E*)-3-Methyl-6-vinylnon-4-en-1-ol (28)**



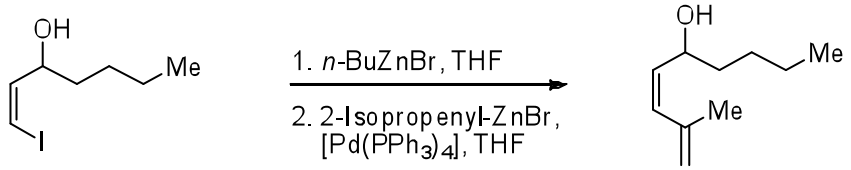
22 **28**

The titled compound was prepared according to Procedure B using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (1.56 mL, 1.56 mmol), chlorodimethylvinylsilane (215 μL, 1.56 mmol), *c*-C_5H_9MgCl (1.56 mL, 3.12 mmol, 2.0 M in Et_2O) in Et_2O (5 mL), and 2-((*Z*)-prop-1-enyl)-3-propylcyclopropyl)methanol **22** (80 mg, 0.52 mmol), *n*-BuLi (230 μL, 0.63 mmol, 2.5 M in

hexanes) in THF (2 mL). Oxidation: alkyl silane in THF (2 mL), *t*BuOOH (2.2 mL, 15.6 mmol), CsOH • H_2O (2.3 g, 13 mmol), TBAF (5.2 mL, 5.2 mmol) in DMF (5 mL). After workup, flash column chromatography (15% EtOAc in hexanes) to yield pure **28** (49 mg, 52%, >20:1 *E:Z*, >20:1 dr) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.68 (ddd, *J* = 7.24, 10.4, 25.2, 1H), 5.32 – 5.23 (m, 2H), 4.97 – 4.94 (m, 1H), 4.92 – 4.91 (m, 1H), 3.67 – 3.58 (m, 2H), 2.64 – 2.59 (m, 1H), 2.28 – 2.21 (m, 1H), 1.61 – 1.46 (m, 2H), 1.34 – 1.23 (m, 4H), 0.98 (d, *J* = 6.8, 3H), 0.86 (t, *J* = 7.1, 4H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.4, 135.8, 132.1, 113.6, 61.7, 46.6, 40.1, 37.3, 34.2, 21.4, 20.5, 14.2 ppm; IR (thin film, NaCl) 3338, 2958, 2928, 2872, 1457, 1128, 1052, 971, 911, 772 cm^{-1}; HRMS (GC-CI) calcd for $C_{12}H_{23}O$, 183.1749 $(M + H)^+$ *m/z*; observed, 183.1752 $(M + H)^+$ *m/z*.

Alkene geometry at C4-C5 was assigned by analogy to other examples (see assignments for compounds **23**, **24**, **26**, and **27**).

(*Z*)-2-Methylnona-1,3-dien-5-ol (29)



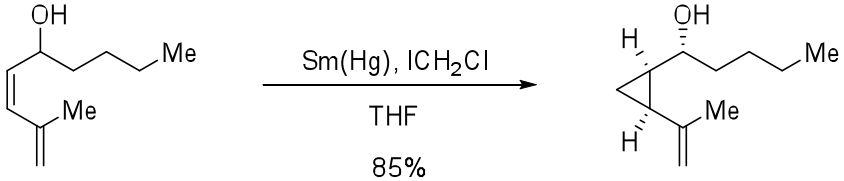
29

To a solution of *n*-butylzinc bromide [prepared from *n*-BuLi (9.17 mL, 22.9 mmol, 2.5 M in hexanes) and zinc bromide (22.9 mL, 22.9 mmol, 1 M in THF) in THF (10 mL)], a solution of (*Z*)-1-iodohept-1-en-3-ol[9] (5.0 g, 20.8 mmol) in THF (10 mL) was added dropwise at 0 °C. After 20 min at this temperature, the reaction mixture was cannulated into a solution of isopropenylzinc bromide [prepared from isopropenylmagnesium bromide (84 mL, 42 mmol, 0.5 M in THF) and zinc bromide (42 mL, 42 mmol, 1 M in THF)]. $[Pd(PPh_3)_4]$ (1.2 g, 1.02 mmol) was added in one portion and the mixture was warmed and heat to 70 °C for 1 h. The reaction was cooled and quenched by addition of saturated aqueous NH_4Cl, diluted with water and Et_2O, layers separated, aqueous phase extracted with Et_2O, organic extracts combined, washed with brine, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column

[9] I. Marek; C. Meyer; J.-F. Normant, *Org. Synth.* **1997**, *74*, 194 – 204.

chromatography (25 to 30 % Et_2O in hexanes) to yield **29** (3.1 g, 97%) as a light yellow oil of adequate purity for characterization and use in the following step; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (d, *J* = 11.8 Hz, 1H), 5.39 (dd, *J* = 11.8, 9.2 Hz, 1H), 5.02 – 4.93 (m, 1H), 4.87 (s, 1H), 4.60 (dt, *J* = 8.2, 6.4 Hz, 1H), 1.86 (s, 3H), 1.75 (s, 1H), 1.64 – 1.53 (m, 1H), 1.45 (ddt, *J* = 9.8, 6.7, 5.6 Hz, 1H), 1.39 – 1.24 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.3, 133.8, 132.5, 116.5, 68.0, 37.6, 27.7, 23.2, 22.8, 14.1 ppm; IR (thin film, NaCl) 3421, 2958, 2933, 2872, 1458, 1378, 1121, 1055 cm^{-1}; LRMS (EI) calcd for $C_{11}H_{18}O$ 154.2 (M^+, *m/z*), observed 154.1 (M^+), 97 (100%).

(*R)-1-((1*R**,2*S**)-2-(prop-1-en-2-yl)cyclopropyl)pentan-1-ol (30)**

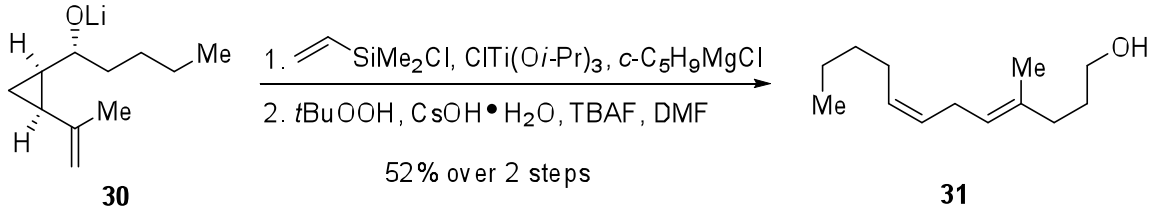


29 **30**

To a suspension of samarium powder (10 g, 97.25 mmol) and $HgCl_2$ (3.6 g, 19.45 mmol) dispensed in a glovebox in THF (260 mL) was added (*Z*)-2-methylnona-1,3-dien-5-ol (2.05 g, 19.45 mmol). To the vigorously stirred mixture, ICH_2Cl (4.8 mL, 97.25 mmol) was added dropwise at -50 °C. The reaction mixture was gradually allowed to warm to RT over a period of 2 h. It was then poured into cold saturated aqueous K_2CO_3 solution (200 mL) overlaid with diethyl ether (200 mL). After stirring for 20 min, the resulting mixture was filtered through Celite and the removed solids were thoroughly washed with Et_2O. The layers were separated, aqueous layer extracted with Et_2O, organic extracts combined, washed with brine, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (30% Et_2O in hexanes) to yield pure **30** (1.9 g, 85%, >99 de) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.88 – 4.75 (m, 1H), 4.63 (s, 1H), 3.17 – 3.03 (m, 1H), 1.80 (s, 3H), 1.55 – 1.38 (m, 4H), 1.36 – 1.23 (m, 4H), 1.10 (ddd, *J* = 17.5, 8.7, 5.8 Hz, 1H), 0.87 (t, *J* = 7.2 Hz, 1H), 0.79 – 0.69 (m, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.7, 110.9, 71.3, 37. 8, 28.0, 25.3, 24.5, 23.2, 22.8, 14.2, 7.2 ppm; IR (thin film, NaCl) 3352, 2957, 2932, 2859, 1646, 1455, 1377, 1035,

986, 885 cm^{-1}; HRMS (GC-CI) calcd for $C_{11}H_{21}O$, 169.1592 $(M + H)^+$ *m/z*; observed, 169.1590 $(M + H)^+$ *m/z*.

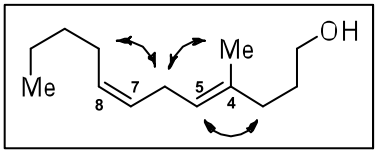
(4*E*,7*Z*)-4-Methyldodeca-4,7-dien-1-ol (31)



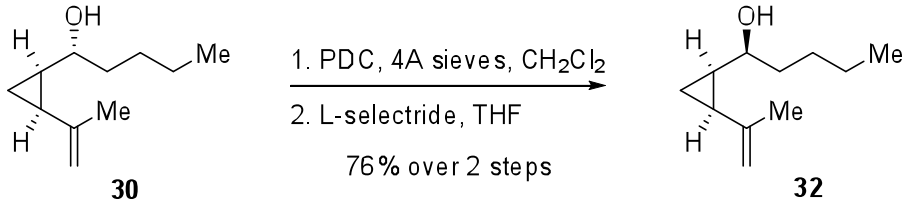
30 **31**

The titled compound was prepared according to Procedure B using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (1.78 mL, 1.78 mmol), chlorodimethylvinylsilane (246 μL, 1.78 mmol), *c*-C_5H_9MgCl (1.78 mL, 3.56 mmol, 2.0 M in Et_2O) in Et_2O (6 mL), and 2-(prop-1-en-2-yl)cyclopropyl)pentan-1-ol **30** (100 mg, 0.59 mmol), *n*-BuLi (286 μL, 0.71 mmol, 2.5 M in hexanes) in THF (2 mL). Oxidation: crude alkyl silane in THF (2 mL), *t*BuOOH (2.55 mL, 17.8 mmol), $CsOH \bullet H_2O$ (2.63 g, 14.9 mmol), TBAF (6 mL, 6 mmol) in DMF (6 mL). After workup, flash column chromatography (20% EtOAc in hexanes) yielded pure **31** (60.5 mg, 52%, >20:1 *E:Z*, >20:1 dr) as a colourless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 5.43 – 5.26 (m, 2H), 5.21 – 5.12 (m, 1H), 3.63 (t, *J* = 6.5 Hz, 2H), 2.73 (dd, *J* = 7.1, 6.5 Hz, 2H), 2.06 (q, *J* = 7.5 Hz, 4H), 1.73 – 1.66 (m, 2H), 1.64 (s, 3H), 1.37 – 1.29 (m, 5H), 0.94 – 0.86 (m, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.1, 130.1, 128.2, 123.5, 63.0, 36.1, 32.0, 30.9, 27.1, 26.4, 22.5, 16.0, 14.1 ppm; IR (thin film, NaCl) 3399, 2956, 2933, 2872, 1458, 1377, 1252, 1047 979 cm^{-1}; LRMS (EI) calcd for $C_{13}H_{24}O$ 196.2 (M^+, *m/z*), observed 196.1 (M^+), 28 (100%).

Alkene geometry at C4-C5 and C7-C8 was assigned by nOe:



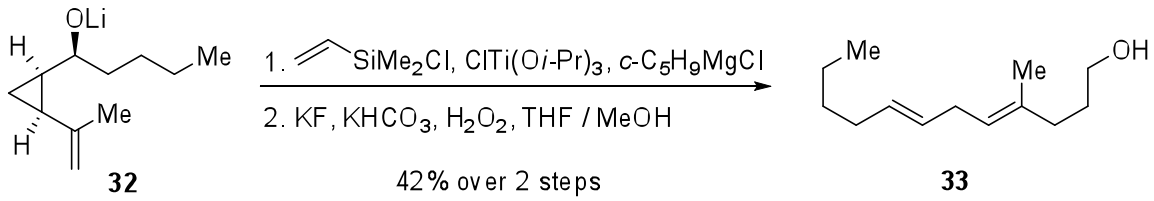
(*S)-1-((1*R**,2*S**)-2-(prop-1-en-2-yl)cyclopropyl)pentan-1-ol (32)**



30 **32**

To a vigorously stirred mixture of **30** (700 mg, 4.15 mmol) and 4Å powdered molecular sieves (3 g) in CH_2Cl_2 (40 mL) was added PDC (3.1 g, 8.3 mmol). After 15 h at RT, the reaction mixture was filtered through Florisil and washed with CH_2Cl_2. Concentration *in vacuo* yielded the cyclopropyl ketone (630 mg, 91%) as a colourless oil that was of sufficient purity for the following step. To this crude ketone (600 mg, 3.61 mmol) in THF (20 mL) at -78 ^oC was added L-selectride (5.4 mL, 5.4 mmol, 1M in THF) and the reaction was stirred for 30 min. The reaction was quenched with MeOH and diluted with water and Et_2O, layers separated, aqueous layer extracted with Et_2O, organic extracts combined, washed with brine, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (5 to 10 % EtOAc in hexanes) to yield pure **32** (460 mg, 76%) as a colourless oil along with pure **30** (70 mg, 12%); ^1H NMR (400 MHz, $CDCl_3$) δ 4.92 – 4.84 (m, 1H), 4.65 (s, 1H), 3.11 (dt, *J* = 12.2, 4.4 Hz, 1H), 1.97 – 1.87 (m, 3H), 1.63 – 1.55 (m, 2H), 1.53 – 1.26 (m, 5H), 1.12 (ddd, *J* = 18.2, 8.9, 5.7 Hz, 1H), 0.91 (t, *J* = 7.1 Hz, 3H), 0.83 – 0.73 (m, 1H), 0.52 (dd, *J* = 11.5, 5.6 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.9, 110.7, 71.9, 37.4, 28.1, 25.6, 24.7, 23.0, 22.2, 14.2, 7.8 ppm; IR (thin film, NaCl) 3368, 2957, 2931, 2860, 1647, 1455, 1037, 884 cm^{-1}; HRMS (GC-CI) calcd for $C_{11}H_{21}O$, 169.1592 $(M + H)^+$ *m/z*; observed, 169.1597 $(M + H)^+$ *m/z*.

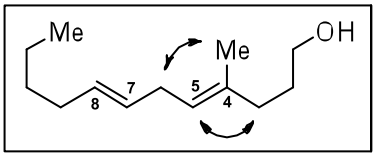
(4*E*,7*E*)-4-Methyldodeca-4,7-dien-1-ol (33)



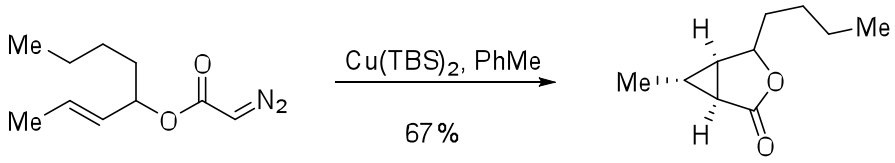
32 **33**

The titled compound was prepared according to Procedure B using the following quantities of reagents: ClTi(O*i*-Pr)$_3$ (1.78 mL, 1.78 mmol), chlorodimethylvinylsilane (246 μL, 1.78 mmol), *c*-C_5H_9MgCl (1.78 mL, 3.56 mmol, 2.0 M in Et_2O) in Et_2O (6 mL), and 2-(prop-1-en-2-yl)cyclopropyl)pentan-1-ol **32** (100 mg, 0.59 mmol), *n*-BuLi (300 μL, 0.71 mmol, 2.4 M in hexanes) in THF (2 mL). Oxidation: alkyl silane, KF (202 mg, 3.56 mmol), $KHCO_3$ (190 mg, 1.78 mmol), H_2O_2 (680 μL, 5.94 mmol) in MeOH / THF (10 mL, 50:50) for 32 h. After workup, flash column chromatography (20% Et_2O in hexanes) yielded pure **33** (49 mg, 42%, >20:1 *E:Z*, >20:1 dr) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.47 – 5.29 (m, 2H), 5.22 – 5.14 (m, 1H), 3.64 (dd, *J* = 8.5, 4.3 Hz, 2H), 2.73 – 2.64 (m, 2H), 2.13 – 2.06 (m, 2H), 1.98 (dd, *J* = 12.6, 7.0 Hz, 2H), 1.76 – 1.63 (m, 2H), 1.57 (s, 3H), 1.35 – 1.26 (m, 5H), 0.88 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.4, 130.7, 128.5, 123.2, 63.0, 36.1, 32.4, 31.9, 31.3, 30.9, 22.4, 16.0, 14.1 ppm; IR (thin film, NaCl) 3356, 2956, 2926, 2857, 1455, 1363, 1059, 966 cm^{-1}; LRMS (EI) calcd for $C_{13}H_{24}O$ 196.2 (M^+, *m/z*), observed 196.1 (M^+), 28 (100%).

Alkene geometry at C4-C5 and C7-C8 was assigned by nOe:

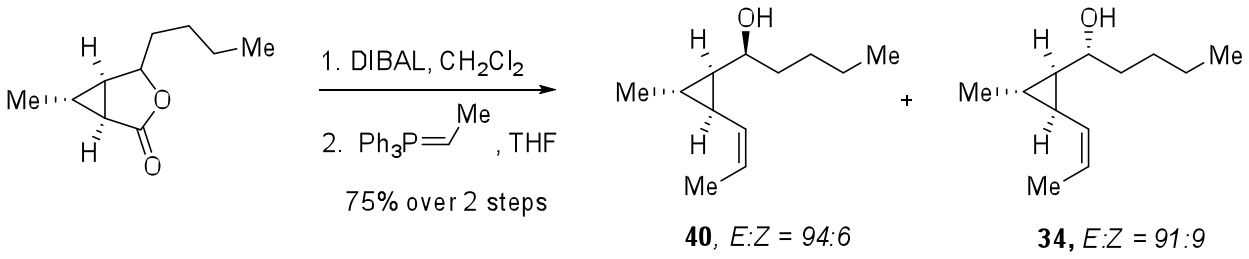


(1*R,5*S**,6*S**)-4-Butyl-6-methyl-3-oxabicyclo[3.1.0]hexan-2-one**



The titled compound was prepared according to Procedure A using the following quantities of reagents: (*E*)-oct-2-en-4-yl 2-diazoacetate (2.8 g, 14.27 mmol) in PhMe (140 mL) and $Cu(TBS)_2$ (300 mg, 0.71 mmol) in PhMe (350 mL) yielded after column chromatography (30% Et_2O in hexanes) the product (1.6 g, 67%, 3:1 dr) as a colourless oil of inseparable diastereomers that were used directly in the following reduction / olefination step.

(*S)-1-((1*R**,2*S**,3*S**)-2-Methyl-3-((*Z*)-prop-1-enyl)cyclopropyl)pentan-1-ol (40) and (*R**)-1-((1*R**,2*S**,3*S**)-2-methyl-3-((*Z*)-prop-1-enyl)cyclopropyl)pentan-1-ol (34)**



To a RBF containing a 4-butyl-6-methyl-3-oxabicyclo[3.1.0]hexan-2-one (1.3 g, 7.73 mmol) in CH_2Cl_2 (40 mL) at -78 ^oC was added DIBAL (11.6 mL, 11.6 mmol, 1.0 M in hexanes) dropwise by syringe. After 1 h, MeOH (5 mL) and saturated aqueous sodium potassium tartrate (20 mL) were added and the reaction was allowed to warm and stir for 2 hours. The phases were separated and the aqueous phase extracted with CH_2Cl_2, organic extracts combined, filtered through $MgSO_4$, concentrated *in vacuo* to afford the crude lactol that was used directly in the following reaction. To a RBF containing ethyltriphenylphosphonium bromide (6.6 g, 17.8 mmol) in THF (20 mL) at -78 ^oC was added NaHMDS (17.8 mL, 17.8 mmol, 1.0 M in THF). The bath was removed and the orange mixture stirred for 30 min. After recooling to -78 ^oC, the crude lactol in THF (5 mL) was added by cannula. The bath was removed and the solution was stirred for 3 h. Saturated aqueous NH_4Cl was added and the reaction diluted with Et_2O, layers separated, aqueous phase extracted with Et_2O, organic extracts combined, filtered through $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (40% Et_2O in hexanes) to yield **40** (1.05 g, 75%, *Z:E* = 94:6) as a colourless oil and **34** (190 mg, 14%, *Z:E* = 91:9) as a colourless oil; **40**: ^1H NMR (400 MHz, $CDCl_3$) δ 5.56 (dqd, *J* = 10.7, 6.8, 1.1 Hz, 1H), 5.25 – 5.16 (m, 1H), 3.32 – 3.08 (m, 1H), 1.75 (dd, *J* = 6.8, 1.7 Hz, 3H), 1.68 (d, *J* = 1.9 Hz, 1H), 1.65 – 1.51 (m, 2H), 1.45 – 1.30 (m, 5H), 1.11 (d, *J* = 6.0 Hz, 3H), 0.91 (dd, *J* = 8.4, 5.9 Hz, 3H), 0.89 – 0.83 (m, 1H), 0.76 (dd, *J* = 11.0, 5.1 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 129.5, 125.7, 73.4, 37.1, 34.8, 28.0, 23.0, 22.2, 21.5, 18.3, 14.2, 13.4 ppm; IR (thin film, NaCl) 3419, 2954, 2928, 2861, 1650, 1447, 1409, 1379, 1005, 727 cm^{-1}; LRMS (EI) calcd for $C_{12}H_{22}O$ 182.3 (M^+, *m/z*), observed 182.2 (M^+), 82 (100%). **34**: ^1H NMR (400 MHz, $CDCl_3$) δ 5.46 (dqd, *J* = 10.7, 6.8, 1.1 Hz, 1H), 5.03 (ddq, *J* = 10.9, 9.3, 1.7 Hz, 1H), 3.22 (dt, *J* = 8.9, 6.0

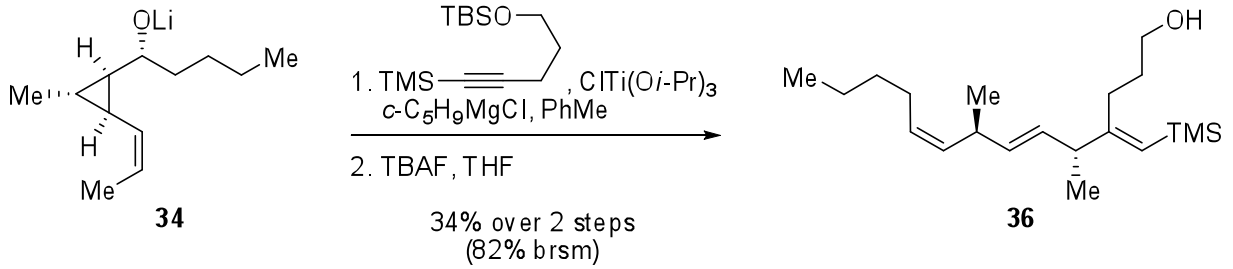
Hz, 1H), 1.68 (dd, J = 6.8, 1.7 Hz, 3H), 1.53 – 1.45 (m, 3H), 1.45 – 1.39 (m, 2H), 1.36 – 1.23 (m, 4H), 1.13 (d, J = 5.7 Hz, 3H), 0.90 – 0.86 (m, 3H), 0.86 – 0.79 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 129.5, 124.8, 72.8, 37.0, 34.0, 27.6, 23.3, 22.9, 20.4, 18.7, 14.1, 13.2 ppm; IR (thin film, NaCl) 3357, 2955, 2929, 2861, 1651, 1458, 1408, 1379, 1001, 728 cm^{-1}; LRMS (EI) calcd for $C_{12}H_{22}O$ 182.3 (M^+, *m/z*), observed 182.1 (M^+), 82 (100%).

General Procedure C: Synthesis of Synthetic Fatty Acids by Coupling Alkynes with Vinylcyclopropane Carbinols

To a RBF containing alkyne (2 mmol) and $ClTi(O\textit{i}\text{-}Pr)_3$ (2 – 2.5 mmol, 1.0 M in hexanes) in PhMe (0.1 M) at -78 °C is added *c*-C_5H_9MgCl (4 – 5 mmol) by syringe and the mixture is warmed to -30 °C and stirred for 1 h (becoming deep brown in colour). In a separate RBF containing a vinylcyclopropane carbinol (1 mmol) in Et_2O (< 0.3 M) at -78 °C is added *n*-BuLi (1.2 mmol) by syringe and the mixture is warmed to 0 °C over 20 min and then added by cannula to the titanium complex that had been re-cooled to -78 °C. The mixture is then slowly warmed to RT over 3 h and treated with 1N HCl (~5 mL / mmol vinylcyclopropane) with rapid stirring. After 10 min the now colourless mixture is further diluted with EtOAc and then filtered through a pad of silica rinsing with additional EtOAc. After concentration *in vacuo*, the non-polar product fractions are separated from the unreacted vinylcyclopropane by flash column chromatography (0 to 5% Et_2O in hexanes followed by flushing with EtOAc) and used directly in the following reaction. To this crude product in a plastic vial dissolved in MeCN / CH_2Cl_2 (5 mL, 1:1) at 0 °C is added HF • pyridine by plastic syringe in 1 mL / 5 min increments. When the reaction is complete (indicated by TLC), the reaction mixture is poured slowly into a plastic beaker containing stirred saturated aqueous $NaHCO_3$ (100 mL) at 0 °C, then diluted with Et_2O. The layers are separated, the aqueous phase extracted with Et_2O, organic extracts combined and filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (10 – 15% EtOAc in hexanes). The resultant alcohol which could contain small amounts of reduction side products was used directly in the following oxidation. The purified skipped polyene alcohol (ie 0.5 mmol) in DMF (3 mL) is added PDC (2.0 mmol) and two drops of water at RT and the reaction is stirred for 12 h. The reaction mixture is then poured into brine (15 mL) and extracted three times with Et_2O, extracts combined, washed with brine, filtered through

$MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (20% EtOAc in hexanes) to yield the pure product.

(4*E*,6*E*,9*Z*)-5,8-dimethyl-4-((trimethylsilyl)methylene)tetradeca-6,9-dien-1-ol (36)



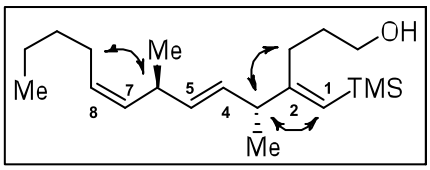
The titled compound was prepared according to Procedure C using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (1.5 mL, 1.5 mmol), *tert*-butyldimethyl(5-(trimethylsilyl)pent-4-ynyloxy)silane[10] (325 mg, 1.2 mmol), *c*-C_5H_9MgCl (1.6 mL, 3.0 mmol, 1.9 M in Et_2O) in PhMe (6 mL), and (*S*)-1-(2-methyl-3-((Z)-prop-1-enyl)cyclopropyl)pentan-1-ol **34** (110 mg, 0.6 mmol), *n*-BuLi (270 μL, 0.66 mmol, 2.5 M in hexanes) in Et_2O (2 mL). Unreacted vinylcyclopropane **34** was recovered (66 mg) and the oily product fractions were dissolved in THF (2 mL), treated with TBAF (2.76 mL, 2.4 mmol) at 0 ^oC and stirred to 20 ^oC over 3 h. The reaction was quenched with solid $CaCO_3$ (~50 mg) and saturated aqueous $NaHCO_3$, diltured with Et_2O, layers separated, aqueous phase extracted with Et_2O, organic extracts combined, washed with brine, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (10 – 15% EtOAc in hexanes) to yield pure **36** (64 mg, 34% over 2 steps, 82% brsm) as a colourless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 5.40 – 5.10 (m, 5H), 3.66 – 3.61 (m, 2H), 3.56 (dt, *J* = 8.8, 4.8 Hz, 1H), 3.12 (dd, *J* = 15.6, 6.6 Hz, 1H), 2.80 (pent, *J* = 6.9 Hz, 1H), 2.22 – 2.16 (m, 2H), 2.07 – 1.99 (m, 2H), 1.67 (ddd, *J* = 9.2, 8.1, 4.1 Hz, 2H), 1.34 – 1.22 (m, 6H), 1.08 (d, *J* = 6.9 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.90 (dd, *J* = 4.2, 2.9 Hz, 3H), 0.10 (s, 9H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.7, 134.2, 133.8, 132.9, 128.8, 122.2, 63.4, 43.9, 34.7, 32.8, 32.1, 31.9,

[10] Page, P. C. B.; Rosenthal, S. *Tetrahedron* **1990**, *46*, 2573 – 2586.

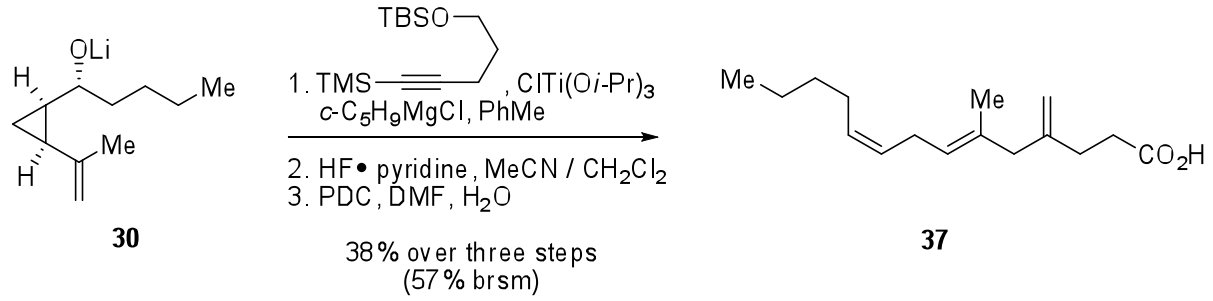
27.2, 22.5, 21.5, 20.0, 14.1, 0.6 ppm; IR (thin film, NaCl) 2959, 2928, 2859, 1713, 1442, 1249, 894 cm-1; LRMS (EI) calcd for $C_{28}H_{38}OSi$ 322.6 (M^+, *m/z*), observed 307.5 $(M - CH_3)^+$.

The stereochemical assignment for skipped triene **36** was made based on the following analysis:

1) alkene geometry at C1-C2 was assigned by nOe (see below),
2) alkene geometry at C7-C8 was assigned by nOe (see below),
3) alkene geometry at C4-C5 was assigned based on analogy to previous examples (see assignments for compounds **23**, **24**, **26**, and **27**),
4) relative stereochemistry at C3 was assigned based on the combination of the model established for the stereospecific coupling and syn carbometallation.



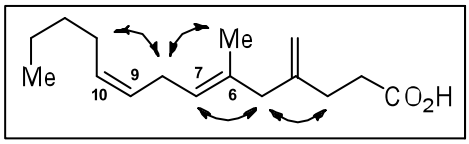
(6*E*,9*Z*)-6-Methyl-4-methylenetetradeca-6,9-dienoic acid (37)



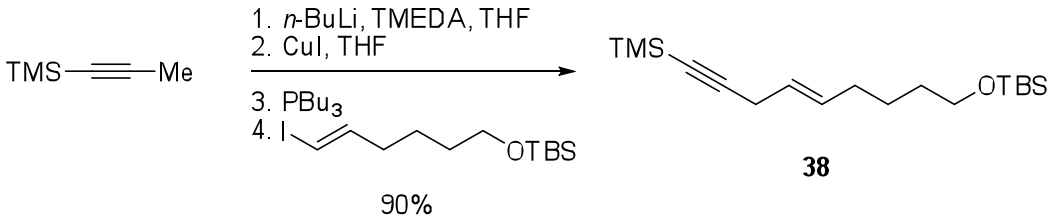
The titled compound was prepared according to Procedure C using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (1.2 mL, 1.2 mmol), *tert*-butyldimethyl(5-(trimethylsilyl)pent-4-ynyloxy)silane[8] (325 mg, 1.2 mmol), *c*-C_5H_9MgCl (1.26 mL, 2.4 mmol, 1.9 M in Et_2O) in PhMe (6 mL), and 2-(prop-1-en-2-yl)cyclopropyl)pentan-1-ol (**34,** 100 mg, 0.6 mmol), *n*-BuLi (270 μL, 0.66 mmol, 2.5 M in hexanes) in Et_2O (2 mL). Unreacted vinylcyclopropane **30** was recovered (34 mg). Desilylation: HF • pyridine (2 mL, 70%) in MeCN / CH_2Cl_2 (5 mL, 1:1). Oxidation: crude alcohol (75 mg, 0.32 mmol), PDC (482 mg, 1.28 mmol) in DMF (2 mL) and water (1 drop) yielded **37** (63 mg, 38% over 3 steps, 57% brsm) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43 – 5.29 (m, 2H), 5.26 (t, *J* = 7.1 Hz, 1H), 4.80 (d, *J* = 8.1 Hz, 2H), 2.78 (s, 2H), 2.74 (t, *J* = 7.0 Hz, 2H), 2.53 (t, *J* = 7.6 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.04 (q, *J* = 6.5 Hz, 2H), 1.64 (d, *J* = 1.2 Hz, 3H), 1.38 – 1.28 (m, 3H), 0.93 – 0.88 (m, 3H) ppm; ^{13}C NMR (126

MHz, $CDCl_3$) δ 179.5, 145.2, 132.7, 130.3, 128.1, 125.8, 110.8, 39.2, 32.6, 32.0, 30.5, 27.1, 26.5, 23.4, 22.5, 14.1 ppm; IR (thin film, NaCl) 2959, 2928, 2859, 1713, 1442, 1249, 894 cm^{-1}; LRMS (ESI) calcd for $C_{16}H_{25}O_2$ 250.4 (M^+, *m/z*), observed 249.8 $(M - H)^+$.

Alkene geometry at C6-C7 and C9-C10 was assigned by nOe:



(*E*)-*tert*-Butyldimethyl-(9-(trimethylsilyl)non-5-en-8-ynyloxy)silane (38)

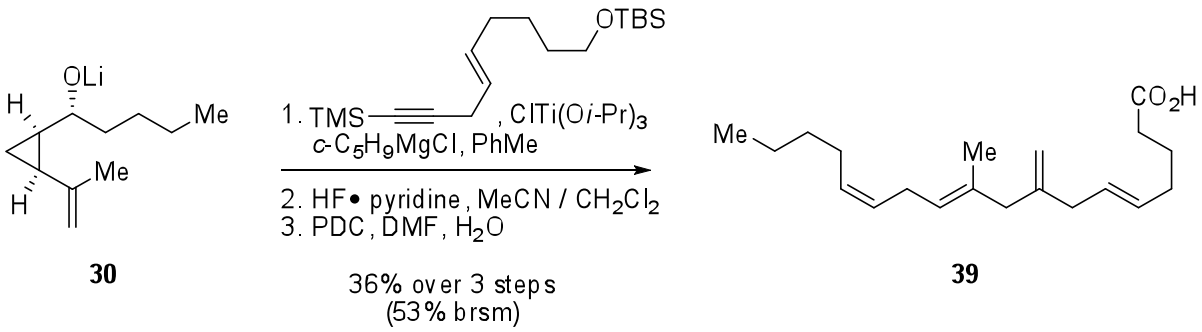


To a RBF containing 1-trimethylsilyl-1-propyne (1.97 mL, 13.2 mmol) and TMEDA (2.12 mL, 14.1 mmol) in THF (20 mL) at -78 °C was added *n*-BuLi (5.7 mL, 14.1 mmol, 2.5 M in hexanes). This transparent yellow reaction was then allowed to warm to 0 °C, stirred for 45 min, then transfer by cannula to a mixture of CuI (2.86 g, 15.0 mmol) in THF (10 mL) at -78 °C. After stirring for an additional 30 min PBu_3 (3.26 mL, 13.2 mmol) was added and the reaction was allowed to warm slowly to –20 °C over 20 min. (*E*)-*tert*-Butyldimethyl(9-(trimethylsilyl)non-5-en-8-ynyloxy)silane[11] (3.0 g, 8.82 mmol) was then added by syringe and the dark brown mixture was left to warm slowly to RT over night. The reaction was quenched by addition of saturated aqueous NH_4Cl, diluted with water and Et_2O, layers separated, aqueous phase extracted with Et_2O, organic extracts combined, washed with brine, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography (1 to 3 % Et_2O in hexanes) to yield pure **38** (2.56 g, 90%) as a light yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 5.67 (dtt, *J* = 15.2, 6.8, 1.7 Hz, 1H), 5.39 (dtt, *J* = 15.2, 5.5, 1.4 Hz, 1H), 3.60 (t, *J* = 6.4 Hz, 2H), 2.95 (ddd, *J* = 5.5, 2.9, 1.3 Hz, 2H), 2.04 (ddd, *J* = 8.2, 7.3, 1.3 Hz, 2H), 1.56 – 1.49 (m, 2H), 1.45 – 1.39 (m, 2H), 0.89 (s, 9H), 0.16 (s, 9H), 0.05 (s, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 132.4, 123.9, 104.9, 86.3, 63.2, 32.5, 32.2, 26.1, 25.6, 23.2, 18.5, 0.3, -5.1 ppm; IR (thin film, NaCl)

[11] Piers, E.; Coish, P. D. G. *Synthesis* 2001, *2*, 251–261.

2955, 1608, 1456, 1247, 1058, 836 cm^{-1}; LRMS (EI) calcd for $C_{28}H_{38}OSi$ 324.6 (M^+, *m/z*), observed 309.1 $(M - CH_3)^+$, 147 (100%).

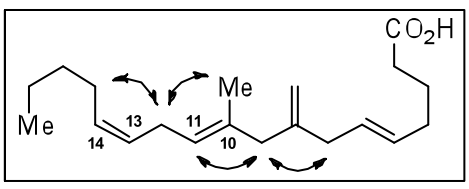
(5*E*,10*E*,13*Z*)-10-Methyl-8-methyleneoctadeca-5,10,13-trienoic acid (39)



30 36% over 3 steps (53% brsm) **39**

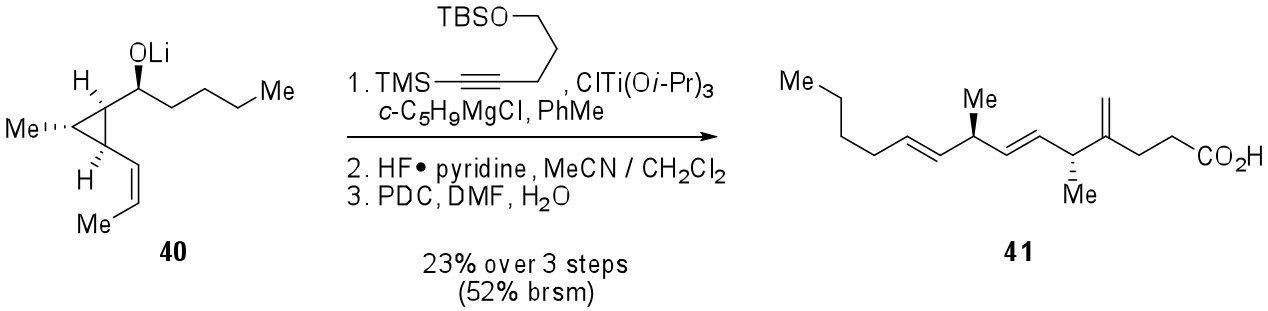
The titled compound was prepared according to Procedure C using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (1.5 mL, 1.5 mmol), (*E*)-*tert*-butyldimethyl(9-(trimethylsilyl)non-5-en-8-ynyloxy)silane (**38**, 390 mg, 1.2 mmol), *c*-C_5H_9MgCl (1.6 mL, 3.0 mmol, 1.9 M in Et_2O) in PhMe (6 mL), and (*R*)-1-(2-methyl-3-((*Z*)-prop-1-enyl)cyclopropyl)pentan-1-ol **30** (110 mg, 0.6 mmol), *n*-BuLi (270 μL, 0.66 mmol, 2.5 M in hexanes) in Et_2O (2 mL). Unreacted vinylcyclopropane **30** was recovered (31 mg). Desilylation: HF • pyridine (3 mL, 70%) in MeCN / CH_2Cl_2 (4 mL, 1:1). Oxidation: crude alcohol (84 mg, 0.29 mmol), PDC (435 mg, 1.16 mmol) in DMF (2 mL) and water (1 drop) yielded **39** (65 mg, 36% over 3 steps, 53% brsm) as a colourless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 5.52 – 5.27 (m, 4H), 5.24 (t, *J* = 7.2 Hz, 1H), 4.76 (d, *J* = 5.7 Hz, 2H), 2.76 – 2.68 (m, 4H), 2.65 (d, *J* = 5.2 Hz, 2H), 2.37 – 2.32 (m, 2H), 2.11 – 1.98 (m, 4H), 1.73 (dd, *J* = 14.8, 7.4 Hz, 2H), 1.64 (d, *J* = 1.2 Hz, 3H), 1.35 – 1.30 (m, 4H), 0.93 – 0.88 (m, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.5, 146.2, 133.07, 131.1, 130.1, 129.1, 128.3, 125.5, 110.8, 45.0, 39.3, 38.8, 32.0, 31.9, 27.1, 26.6, 24.7, 23.6, 22.5, 14.1 ppm; IR (thin film, NaCl) 2957, 2927, 1709, 1436, 1247, 970, 894, 838 cm^{-1}; LRMS (ESI) calcd for $C_{20}H_{31}O_2$ 304.5 (M^+, *m/z*), observed 303.9 $(M - H)^+$.

Alkene geometry at C10-C11 and C13-C14 was assigned by nOe:



For Compound **39**: The 1,4-diene product isolated was contaminated with a minor product of unknown structure. If this minor product is an olefin isomer, selectivity for this process can be calculated to be = 20:1 (based on integration in the 1H NMR spectrum).

(6*E*,9*E*)-5,8-Dimethyl-4-methylenetetradeca-6,9-dienoic acid (41)



The titled compound was prepared according to Procedure C using the following quantities of reagents: $ClTi(O\textit{i}\text{-}Pr)_3$ (1.2 mL, 1.2 mmol), *tert*-butyldimethyl(5-(trimethylsilyl)pent-4-ynyloxy)silane[8] (325 mg, 1.2 mmol), *c*-C_5H_9MgCl (1.26 mL, 2.4 mmol, 1.9 M in Et_2O) in PhMe (6 mL), and (*R*)-1-(2-methyl-3-((Z)-prop-1-enyl)cyclopropyl)pentan-1-ol **40** (110 mg, 0.6 mmol), *n*-BuLi (270 μL, 0.66 mmol, 2.5 M in hexanes) in Et_2O (2 mL). Unreacted vinylcyclopropane **40** was recovered (60 mg). Desilylation: HF • pyridine (3 mL, 70%) in MeCN / CH_2Cl_2 (4 mL, 1:1). Oxidation: crude alcohol (48 mg, 0.18 mmol), PDC (271 mg, 0.72 mmol) in DMF (2 mL) and water (1 drop) yielded pure **41** (39 mg, 23% over 3 steps, 52% brsm) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 – 5.22 (m, 4H), 4.84 (s, 1H), 4.74 (d, J = 1.0 Hz, 1H), 2.83 – 2.71 (m, 2H), 2.55 – 2.47 (m, 2H), 2.37 – 2.29 (m, 2H), 1.99 (dd, J = 12.0, 7.1 Hz, 2H), 1.35 – 1.26 (m, 4H), 1.12 (d, J = 6.9 Hz, 3H), 1.04 (d, J = 6.9 Hz, 3H), 0.89 (t, J = 7.1 Hz, 3H). ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.4, 151.8, 134.7, 134.6, 132.3, 129.1, 108.5, 42.9, 39.3, 32.8, 32.4, 31.9, 29.0, 22.3, 20.8, 19.4, 14.1 ppm; IR (thin film, NaCl) 2961, 2927, 2872, 1712, 1455, 1295, 970, 895 cm^{-1}; LRMS (ESI) calcd for $C_{17}H_{27}O_2$ 264.4 (M^+, *m/z*), observed 263.8 $(M - H)^+$.

The stereochemical assignment for the polyunsaturated fatty acid **41** was made by analogy to previous examples (i.e. **36**).

Figure S1: H^1 (400 MHz, $CDCl_3$) and C^{13} CPD (100 MHz, $CDCl_3$) of **13c**

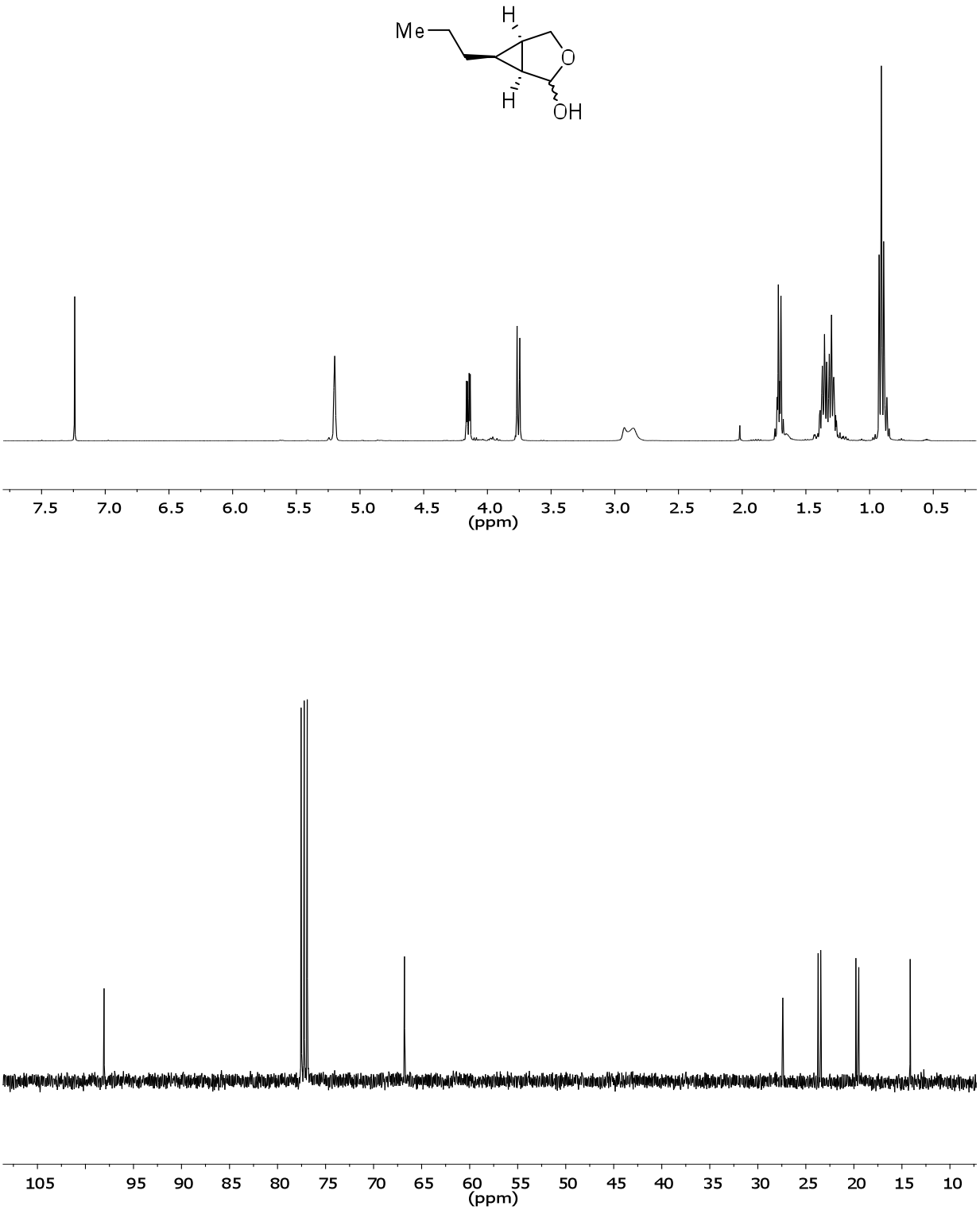
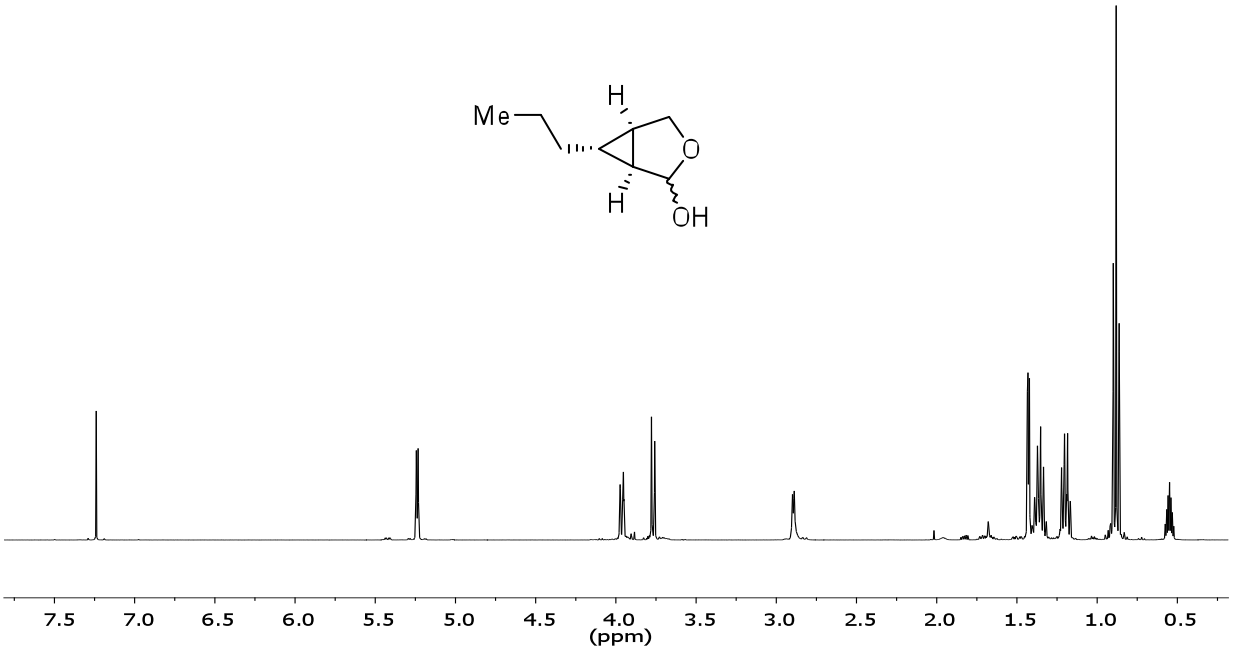


Figure S2: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **16c**



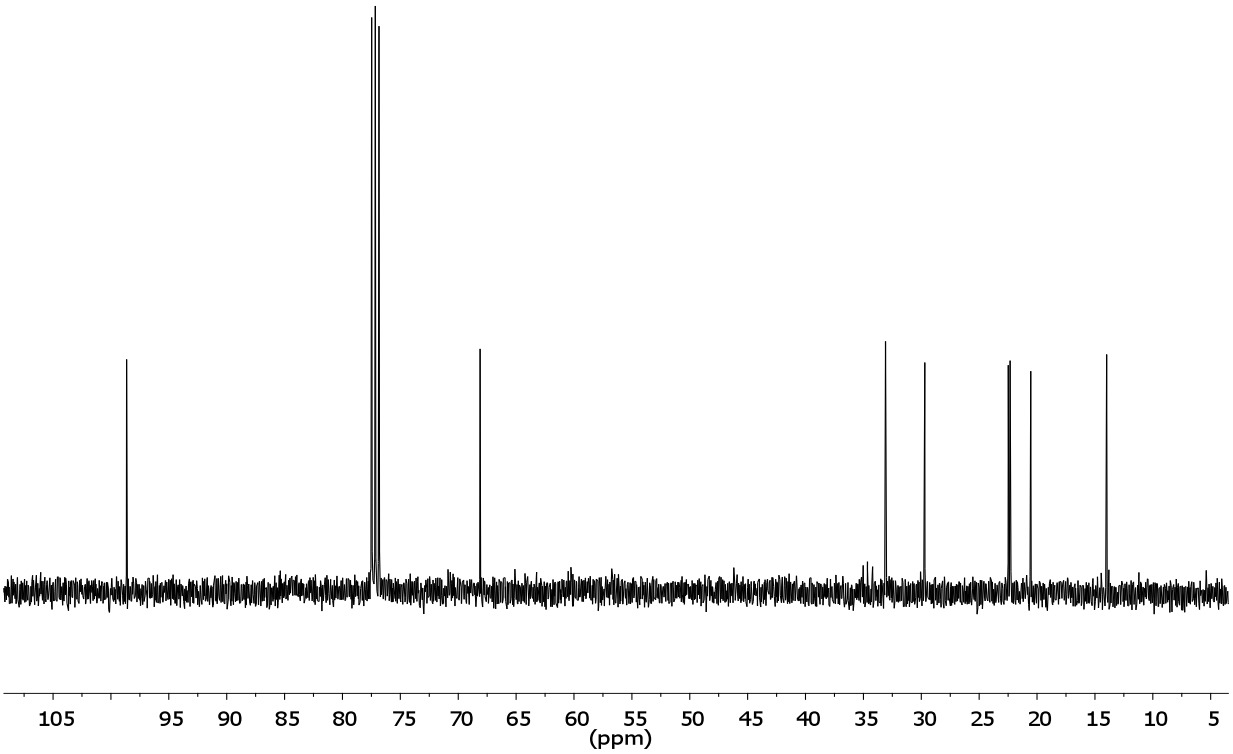


Figure S3: H^1 (400 MHz, $CDCl_3$) and C^{13}APT (100 MHz, $CDCl_3$) of **17**

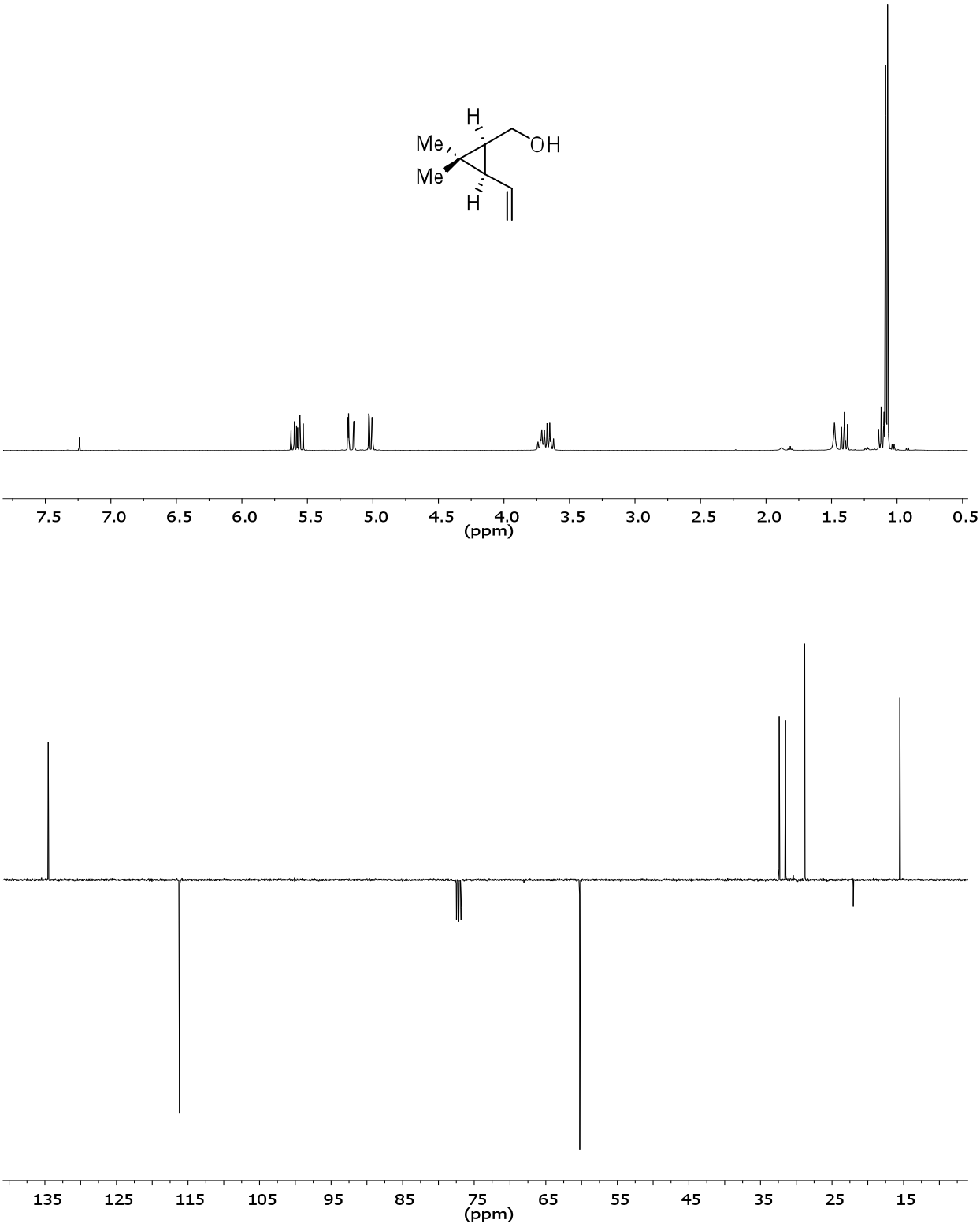


Figure S4: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **18**

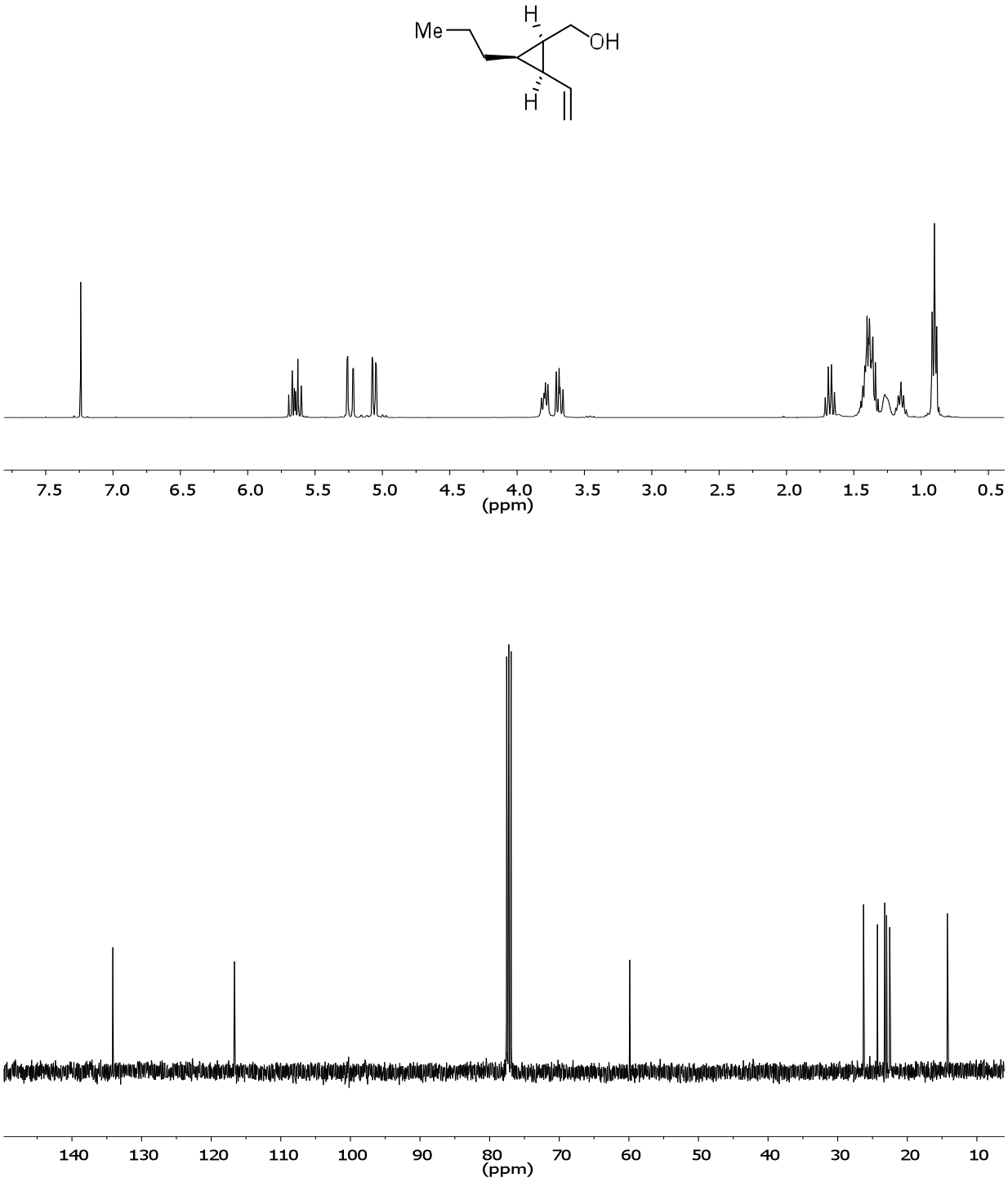


Figure S5: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **20** (*Z:E = 94:6*)

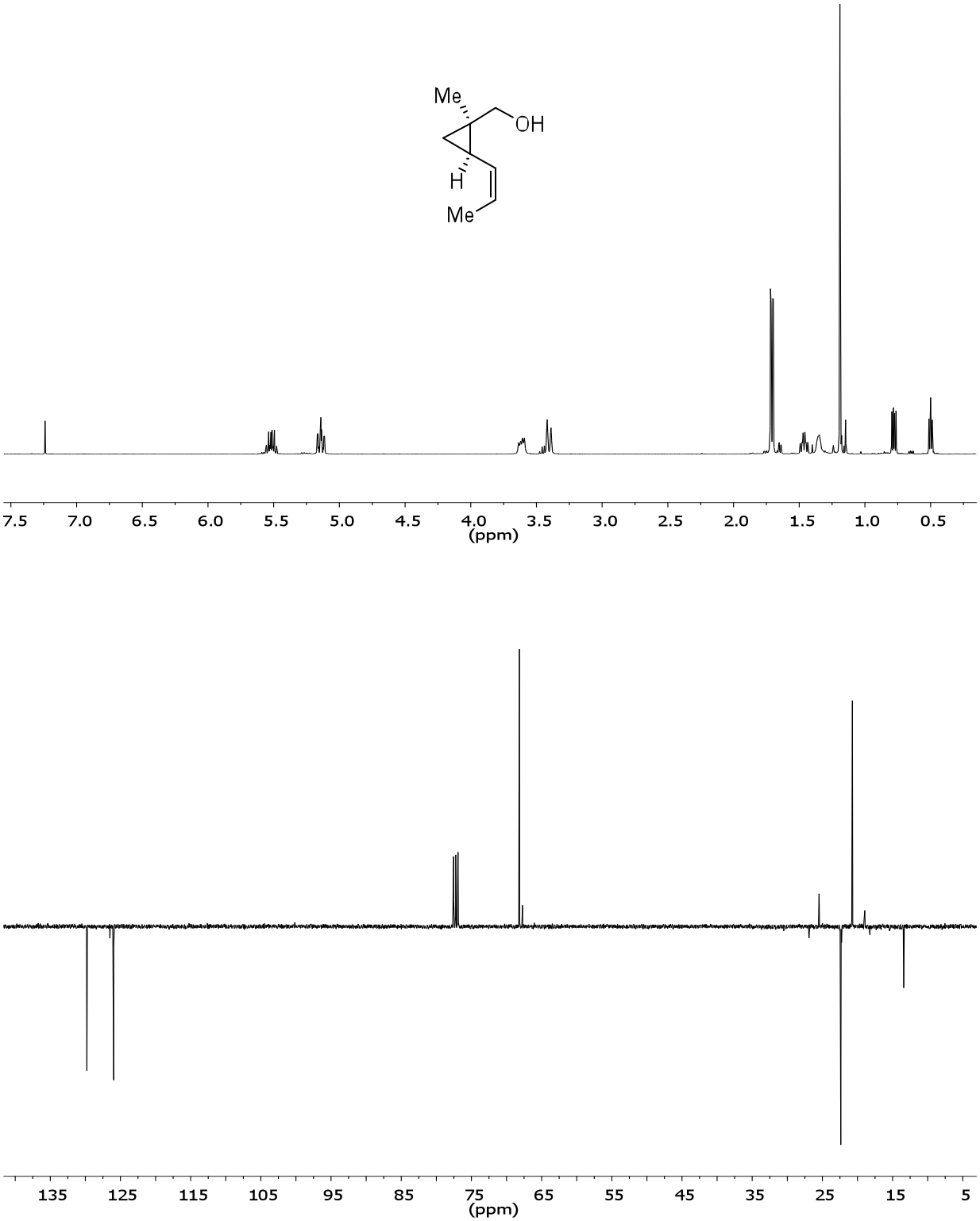


Figure S6: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **13d**

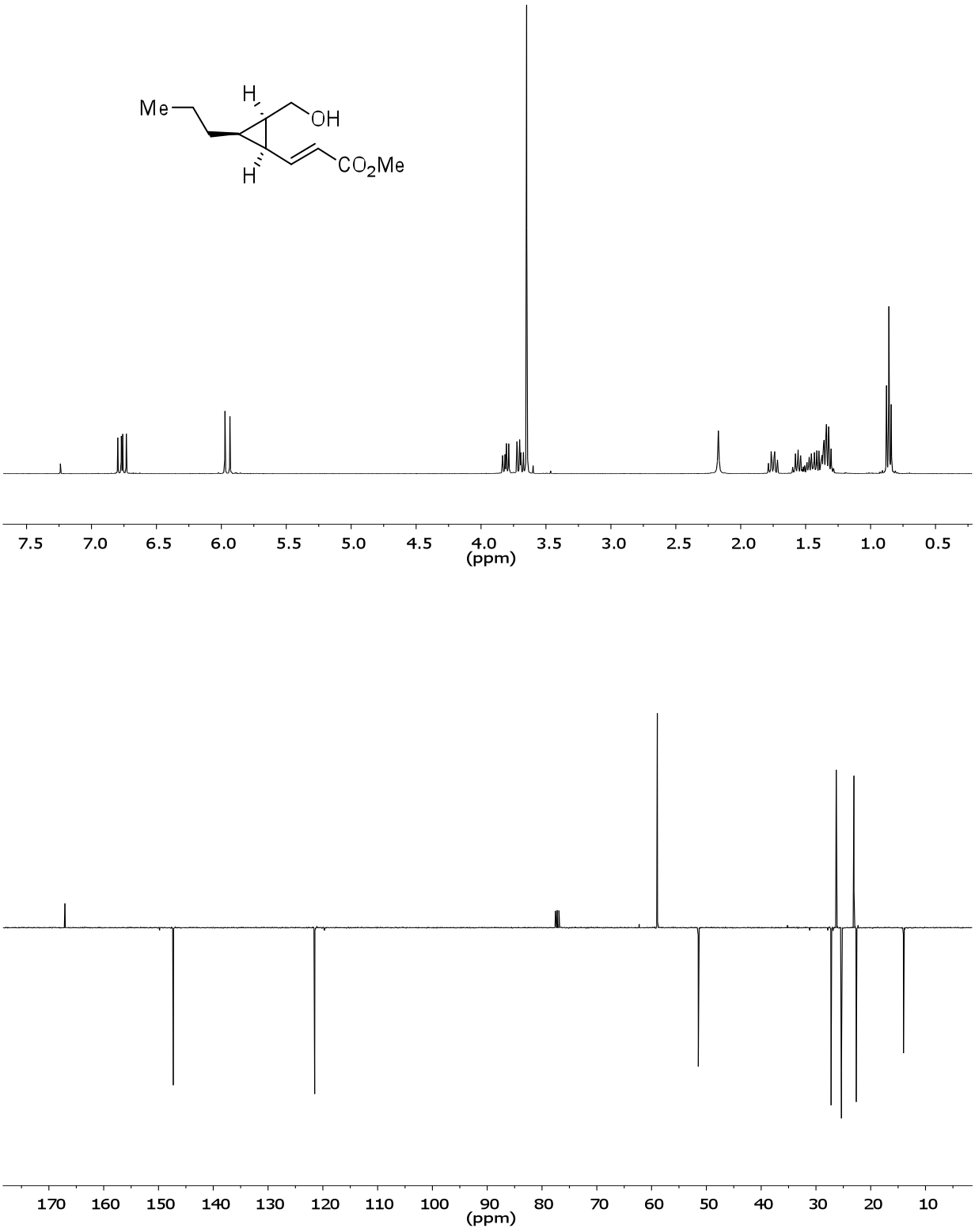


Figure S7: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **21**

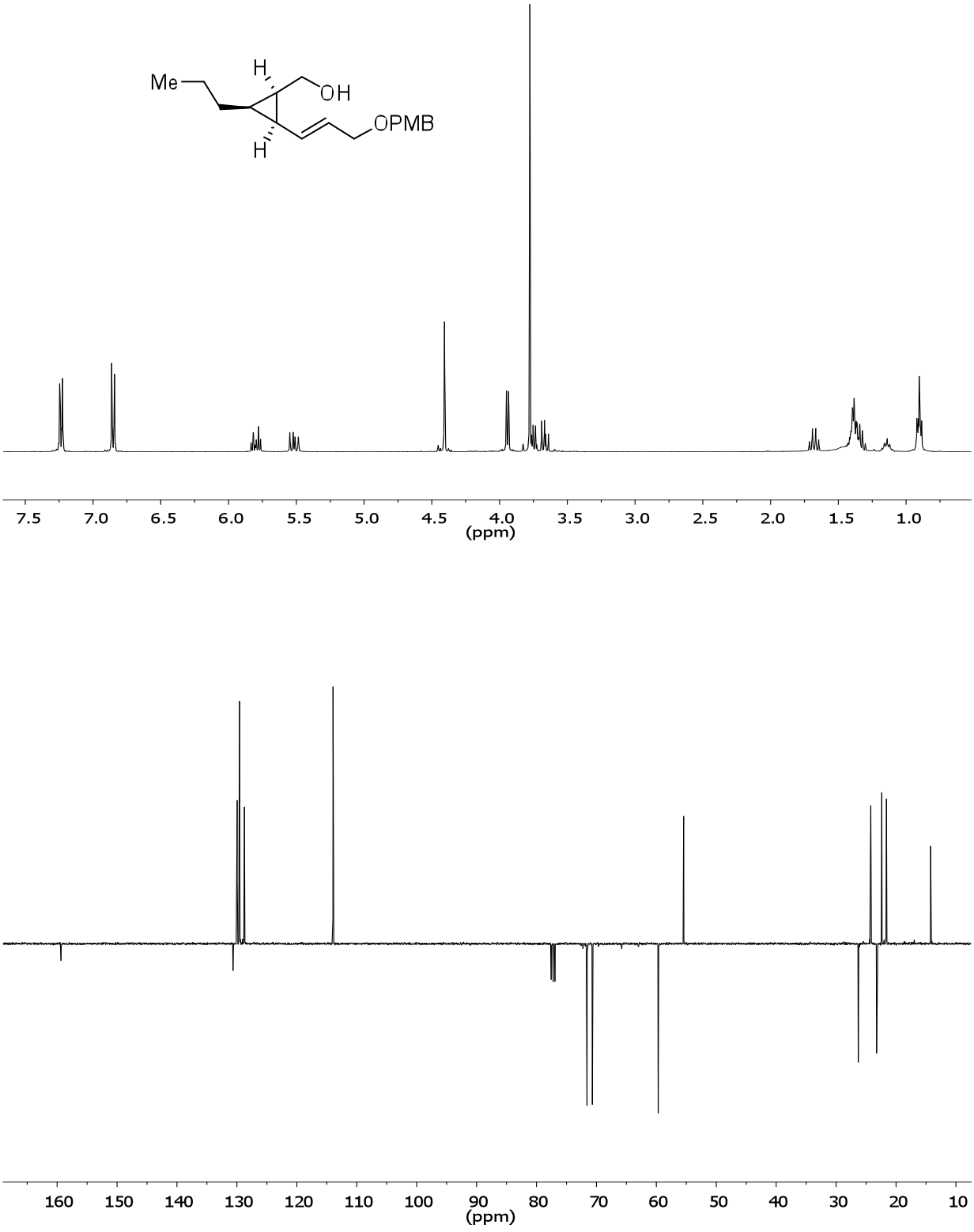


Figure S8: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **22** (*Z:E = 95:5*)

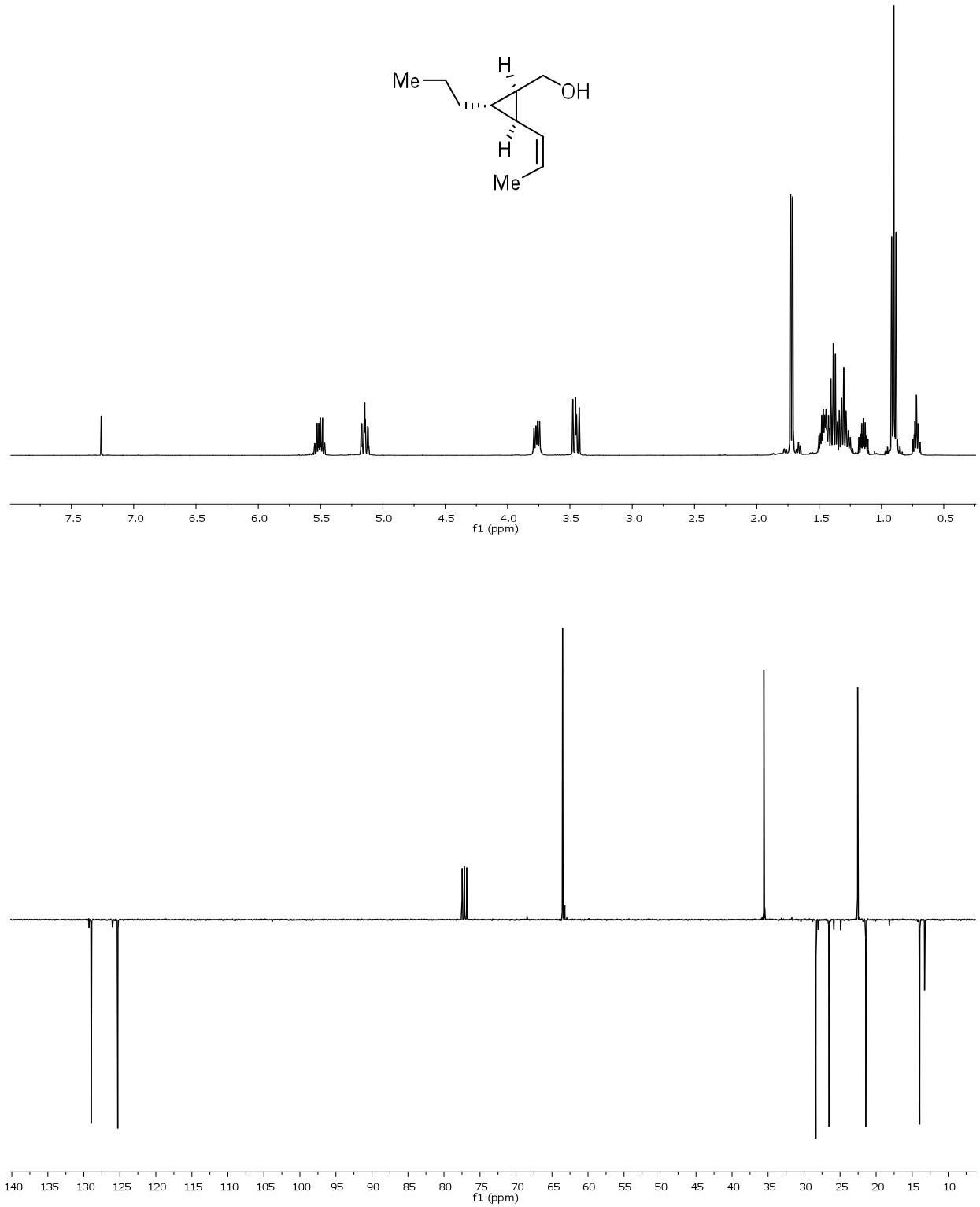


Figure S9: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **23**

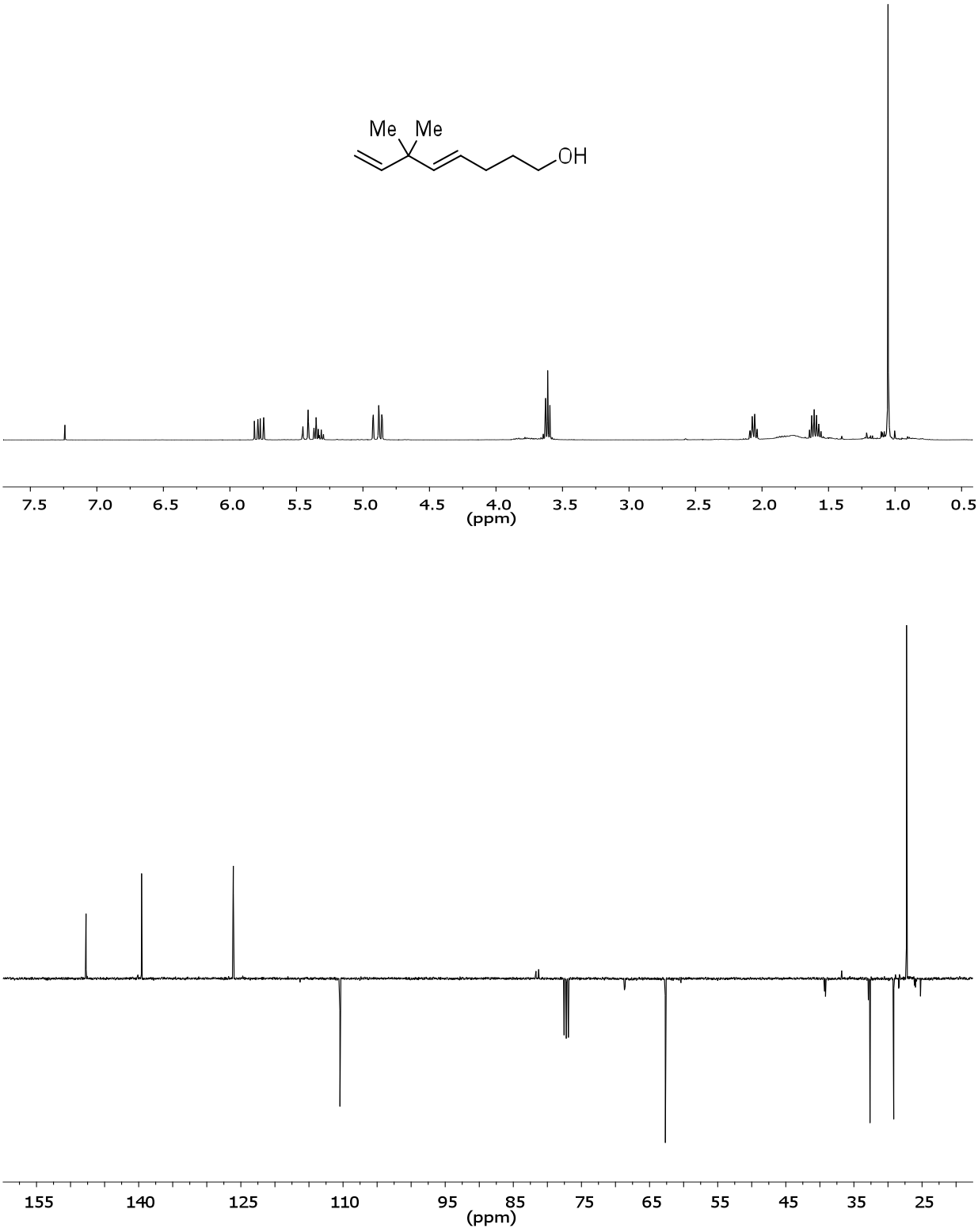


Figure S10: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **24**

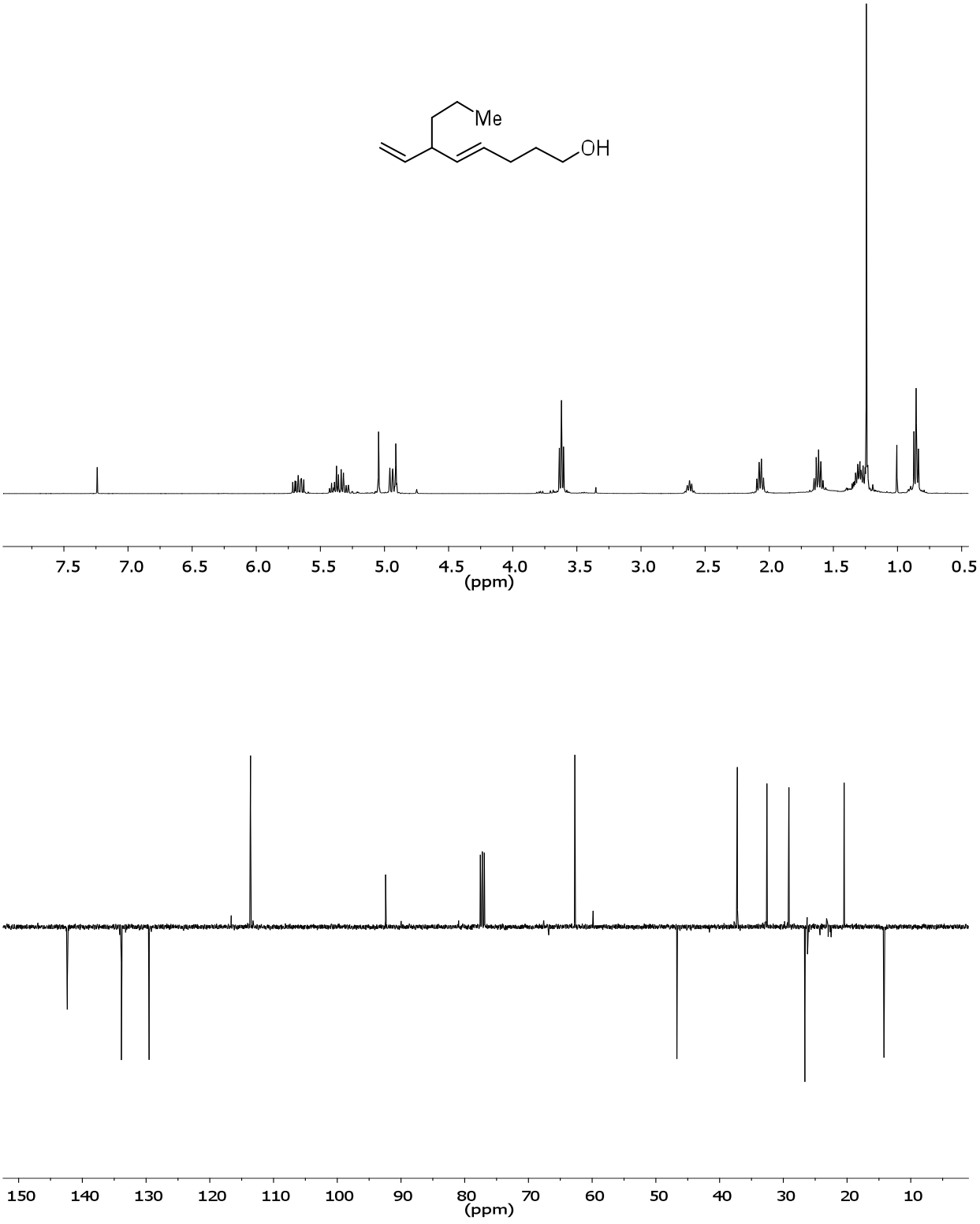


Figure S11: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **25**

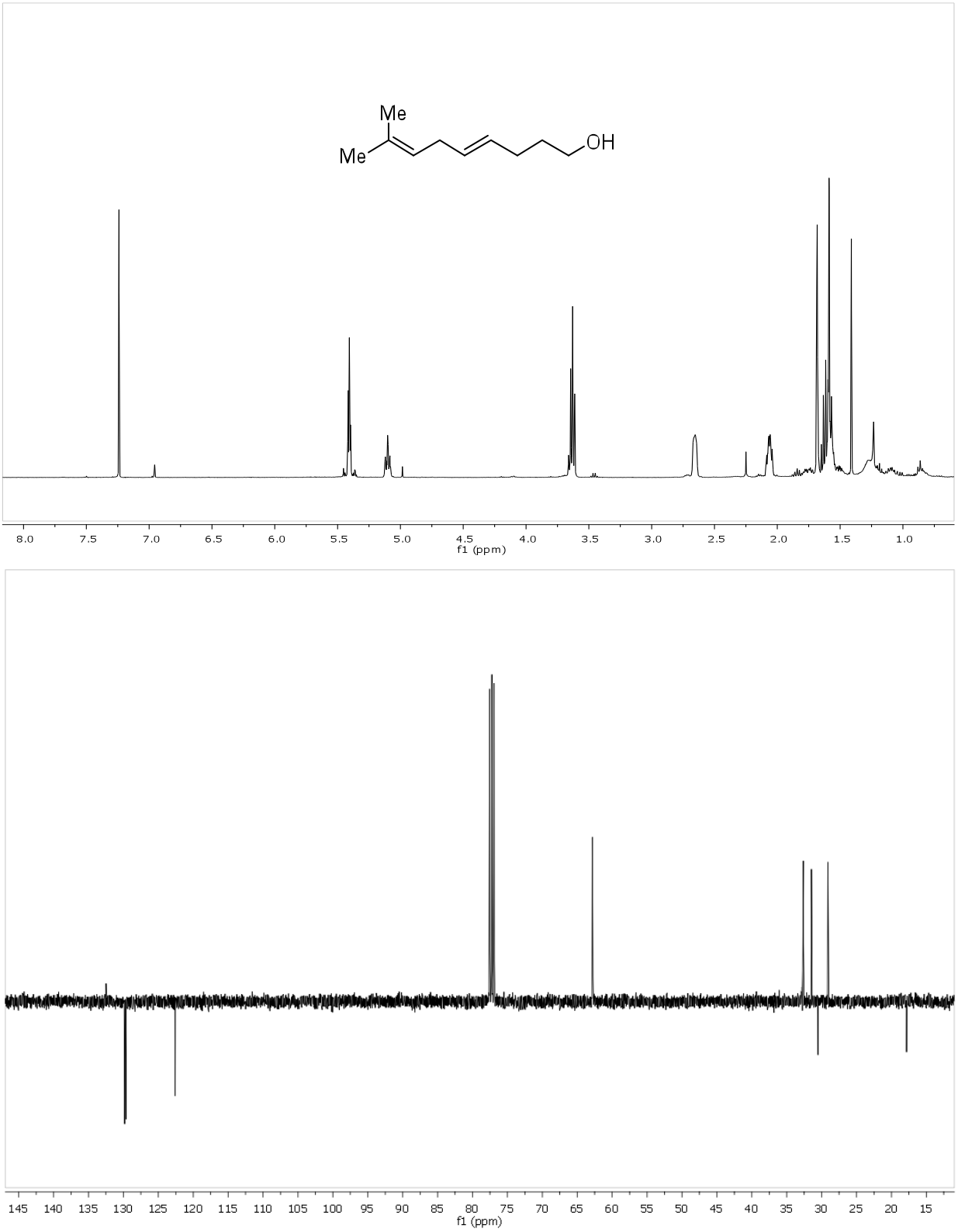


Figure S12: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **26**

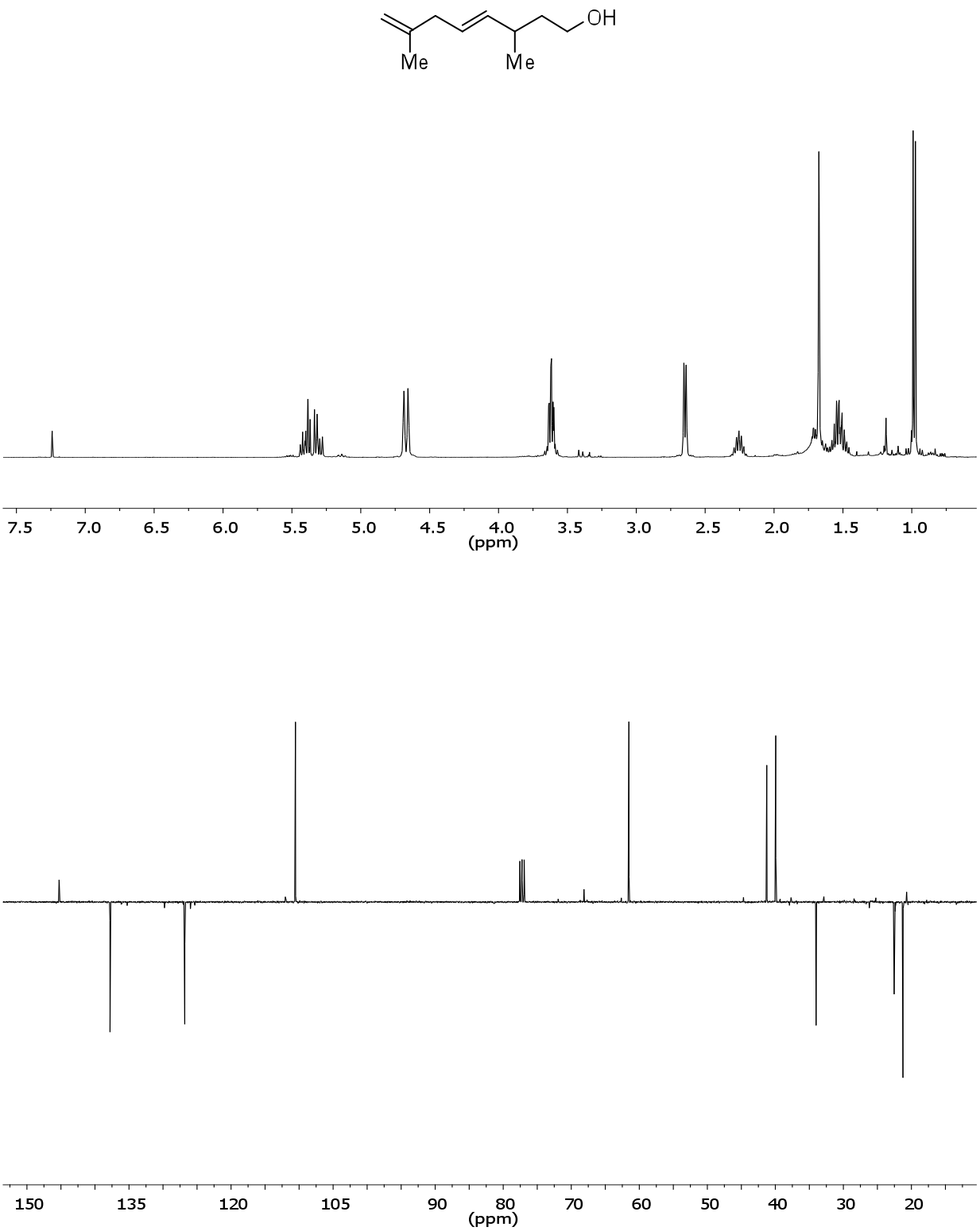


Figure S13: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **27**

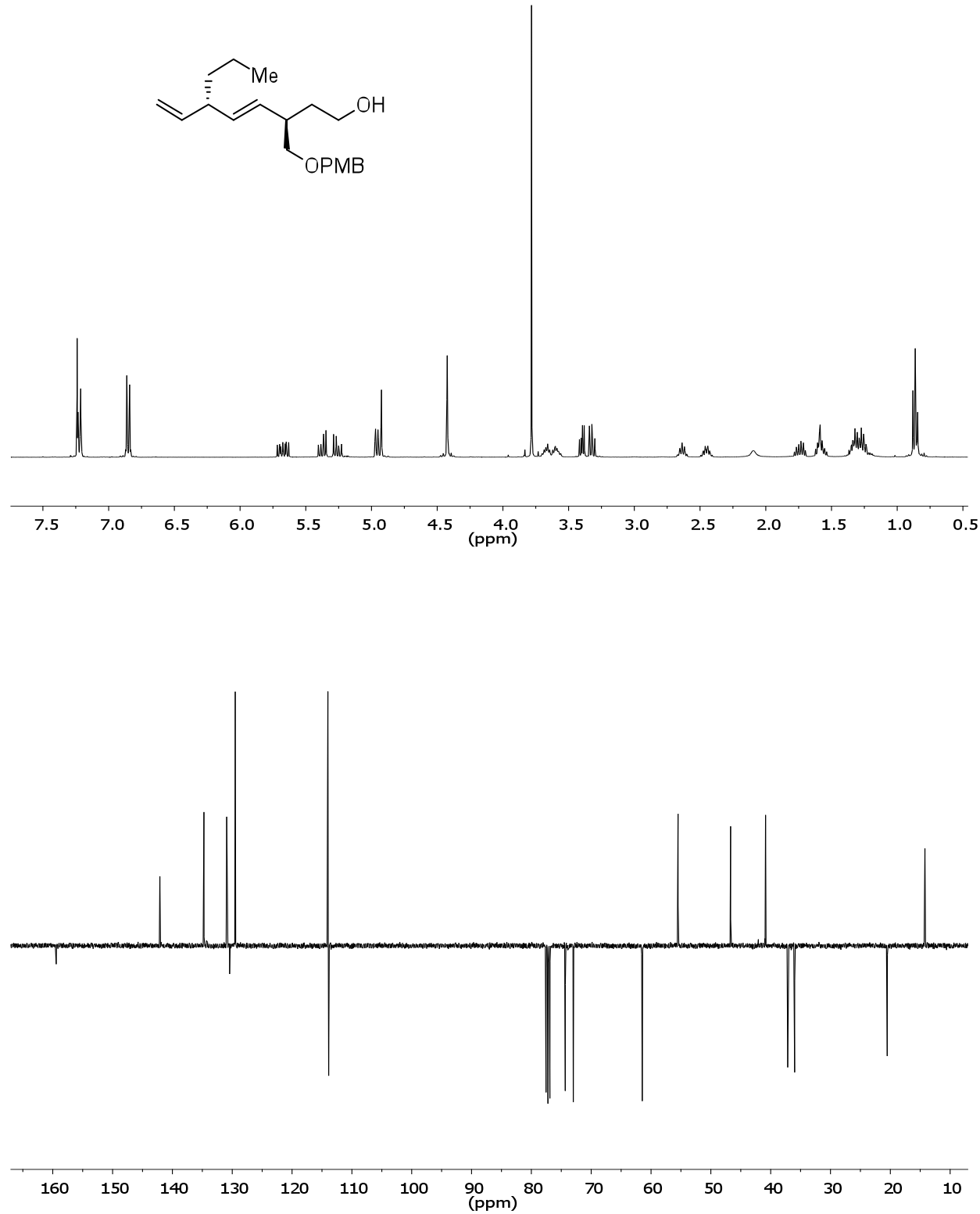


Figure S14: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **28**

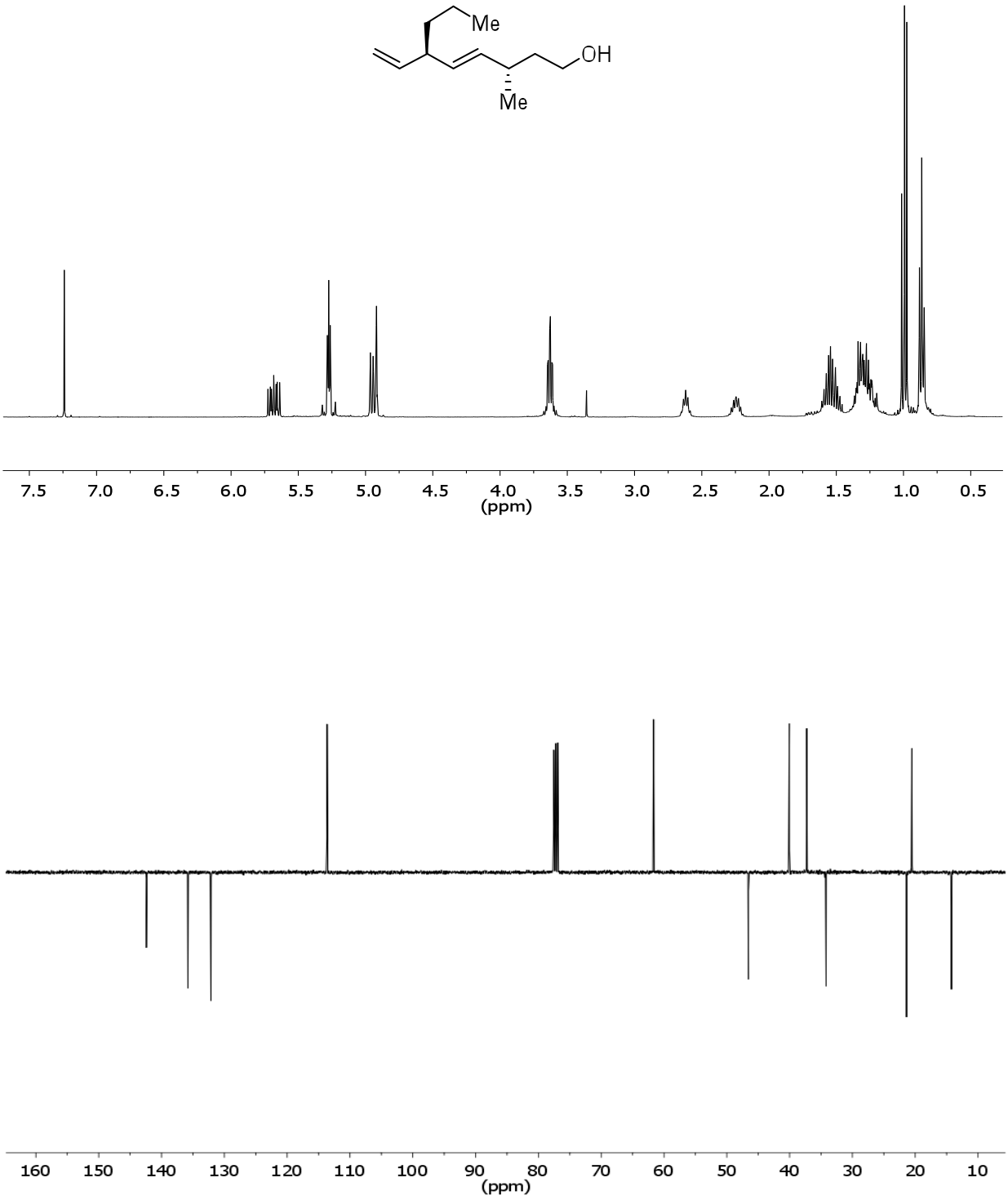
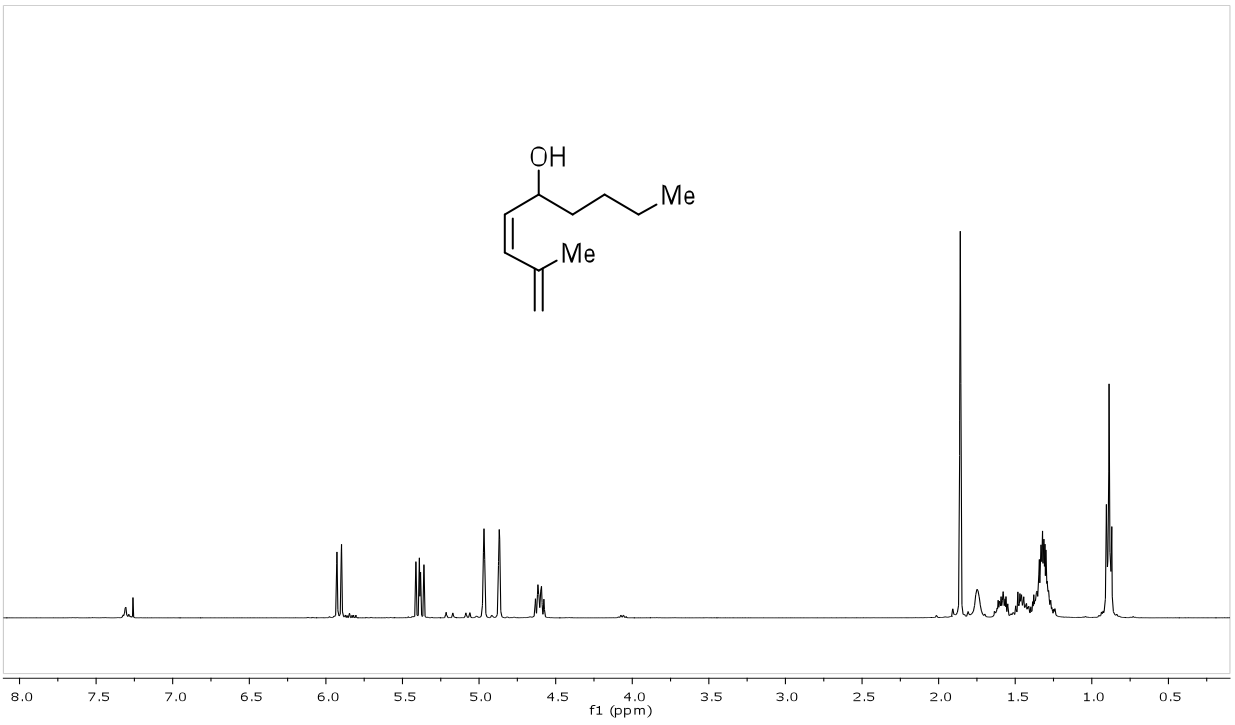


Figure S15: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **29**



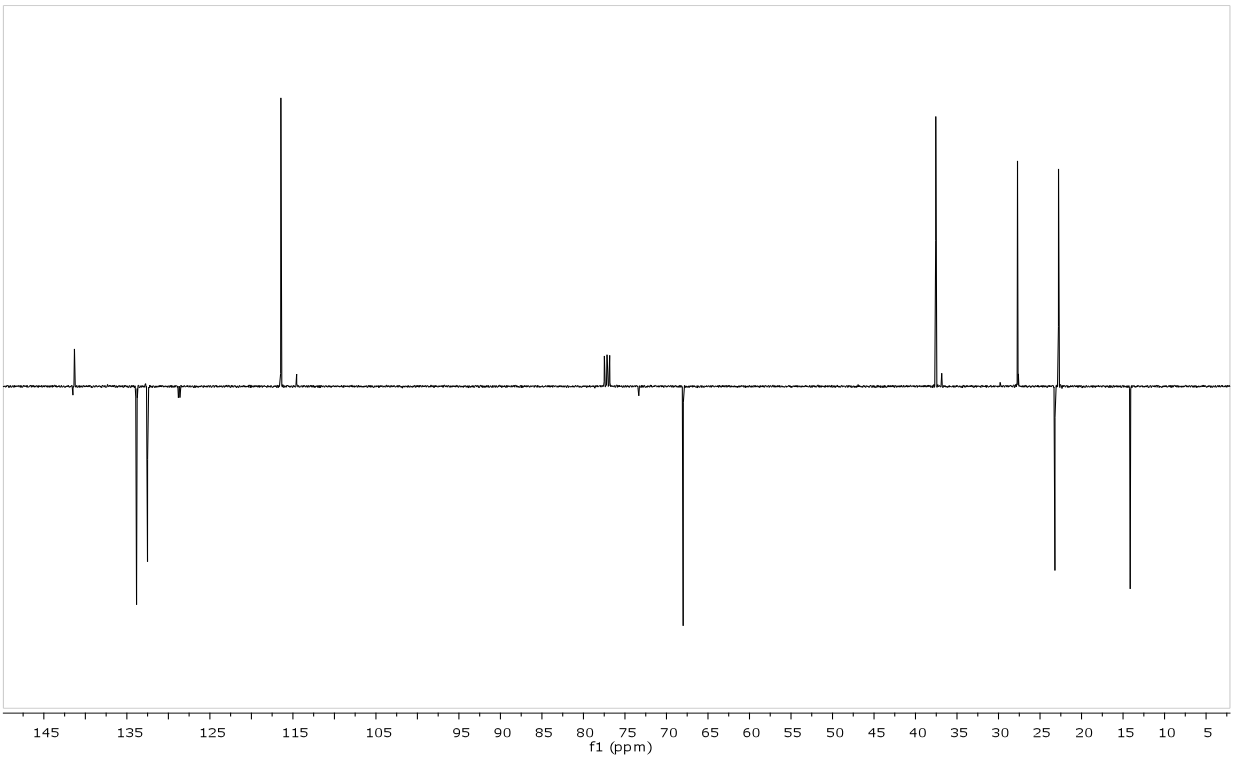
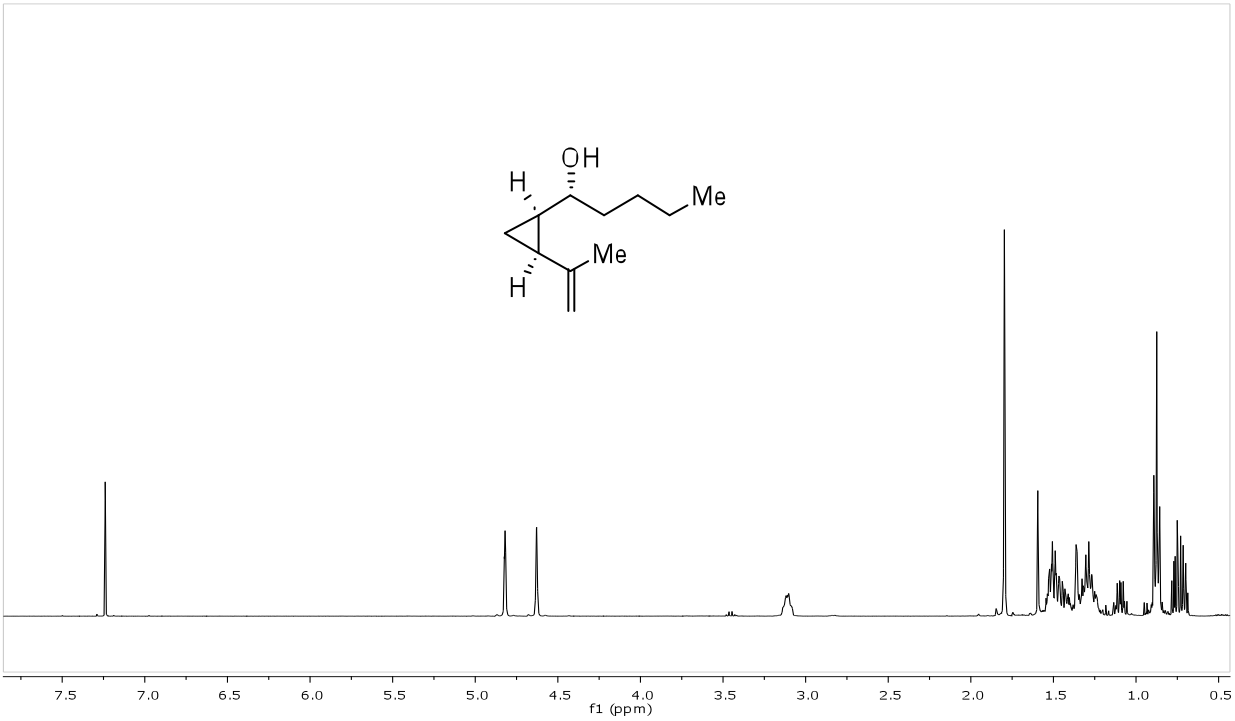


Figure S16: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **30**



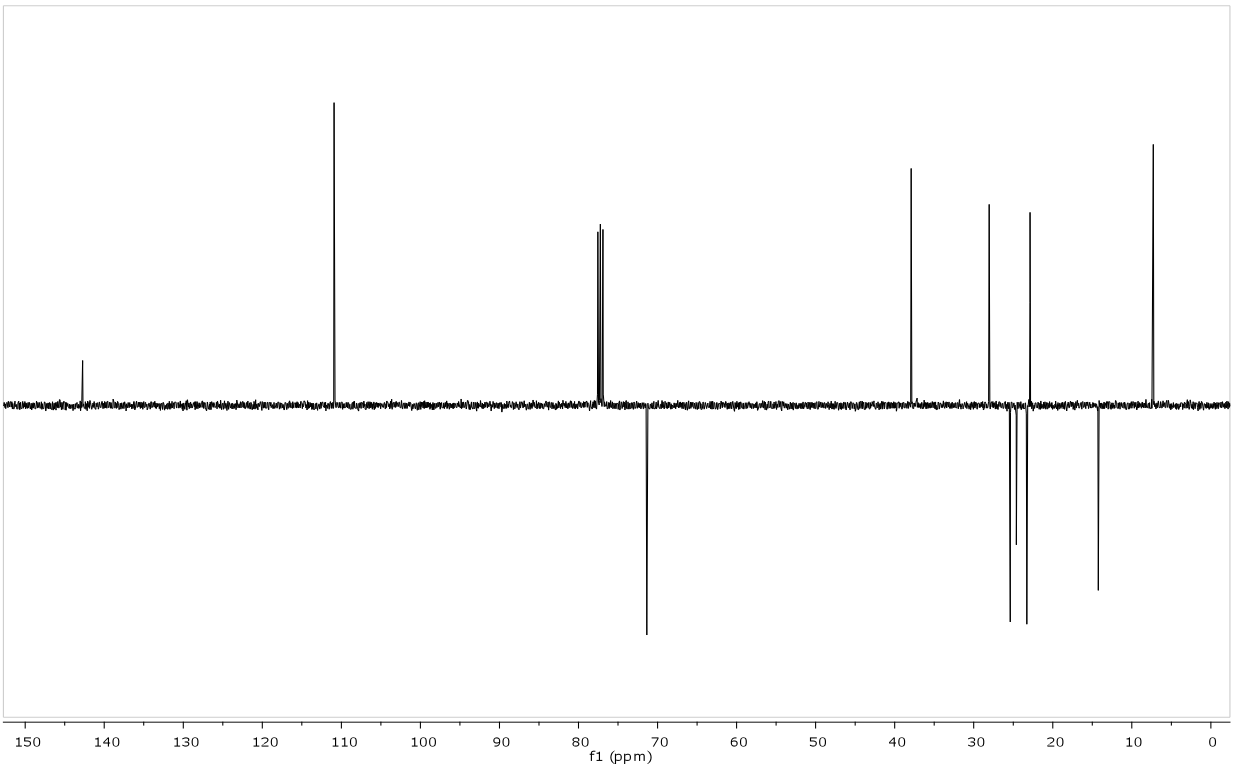
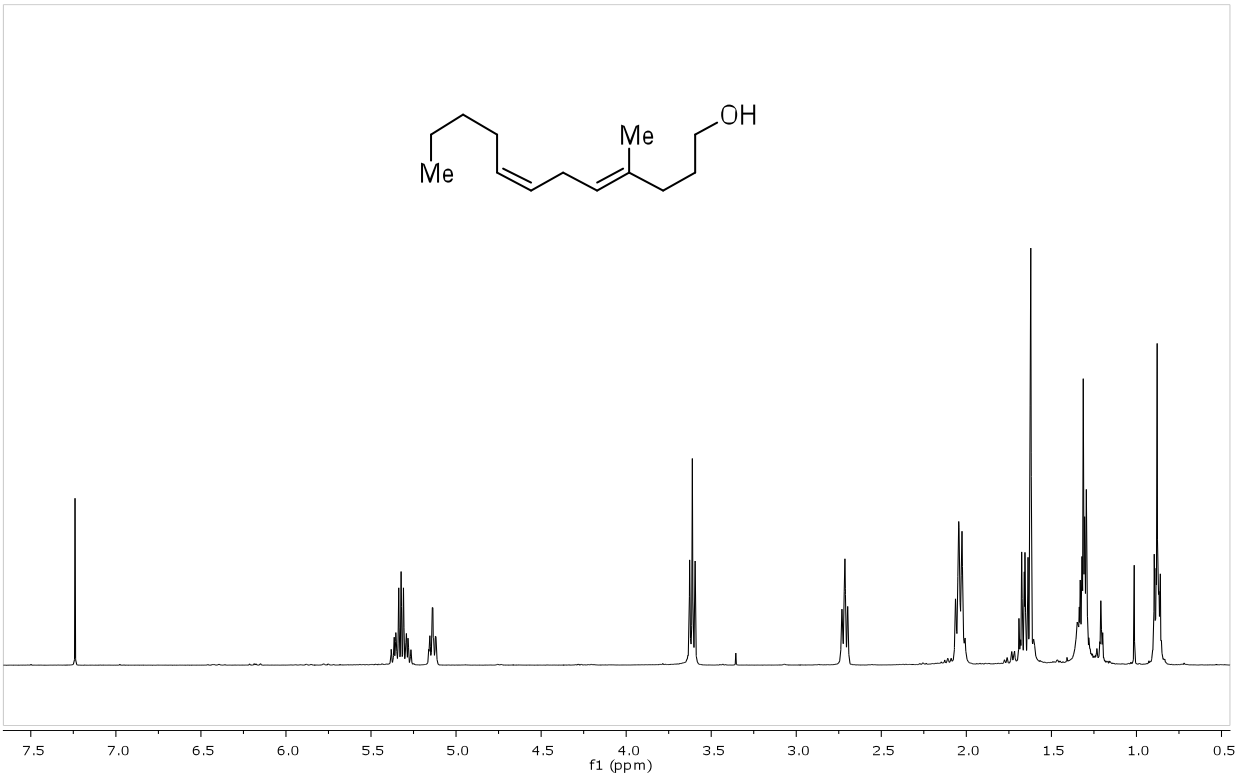


Figure S17: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **31**



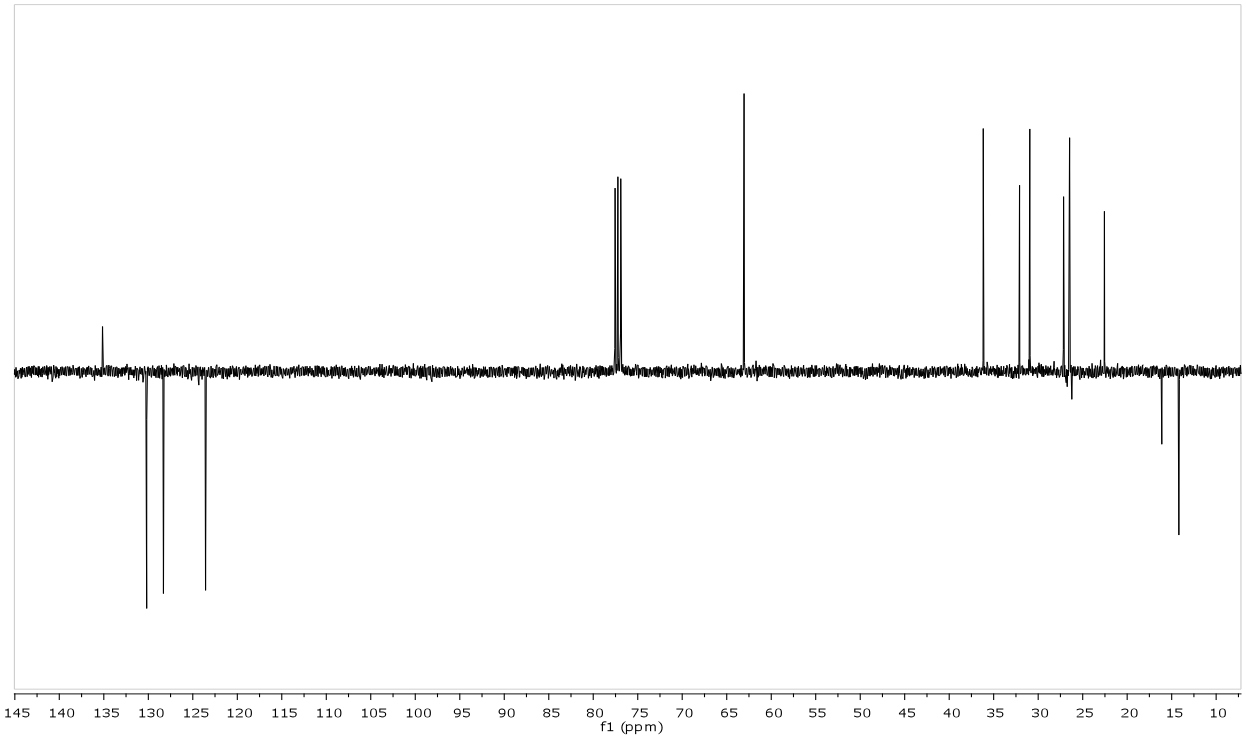


Figure S18: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **32**

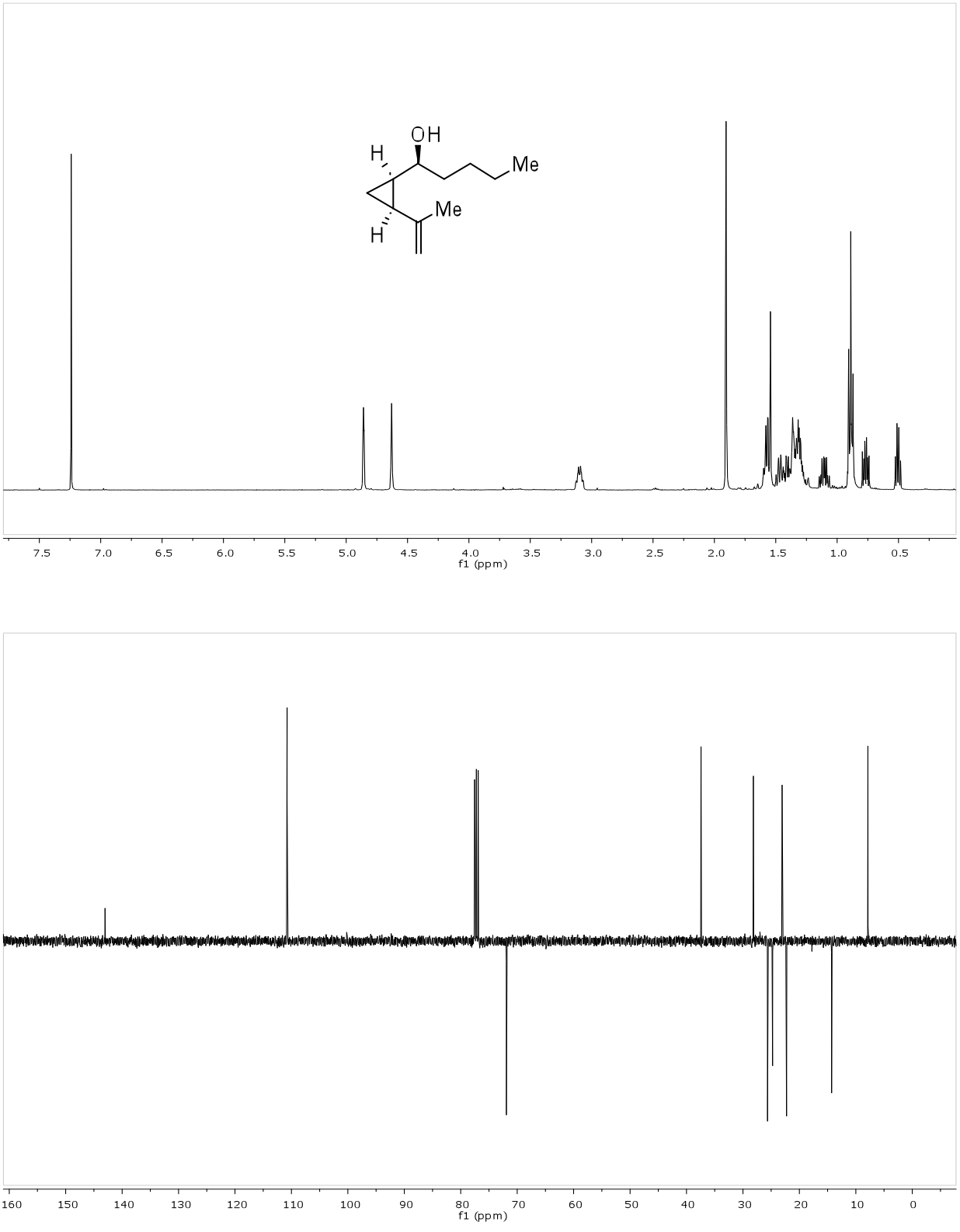
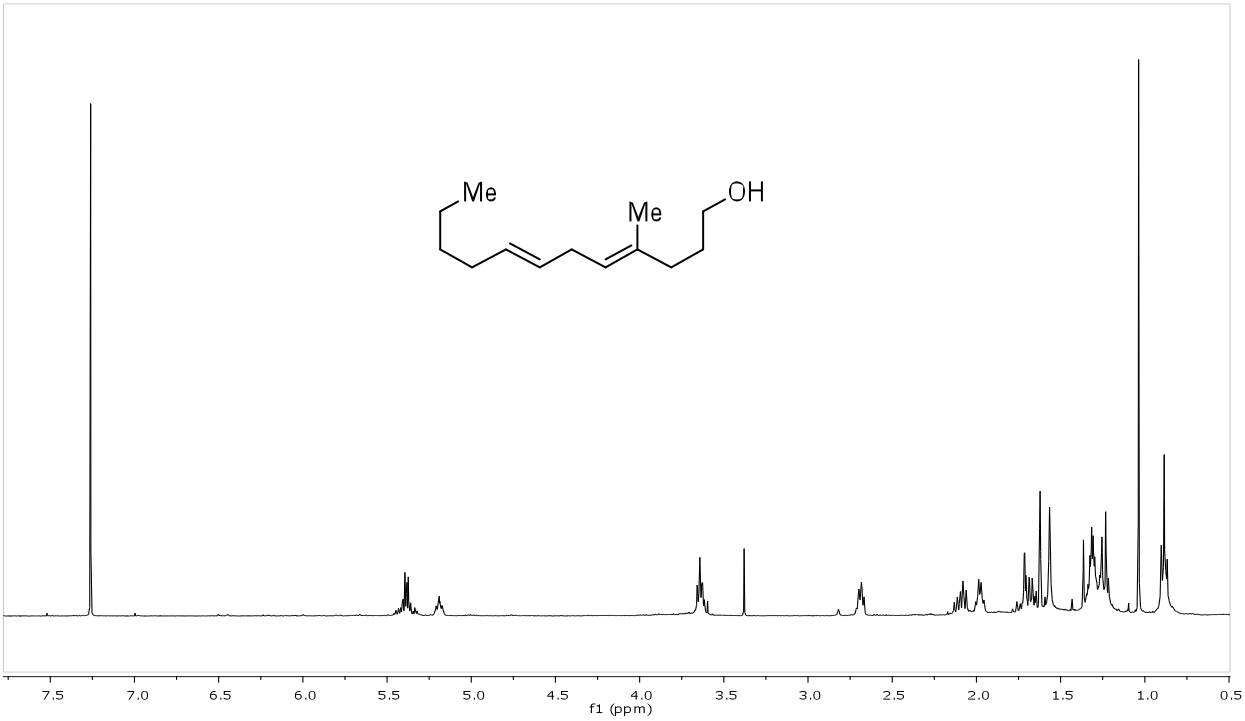


Figure S19: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **33**



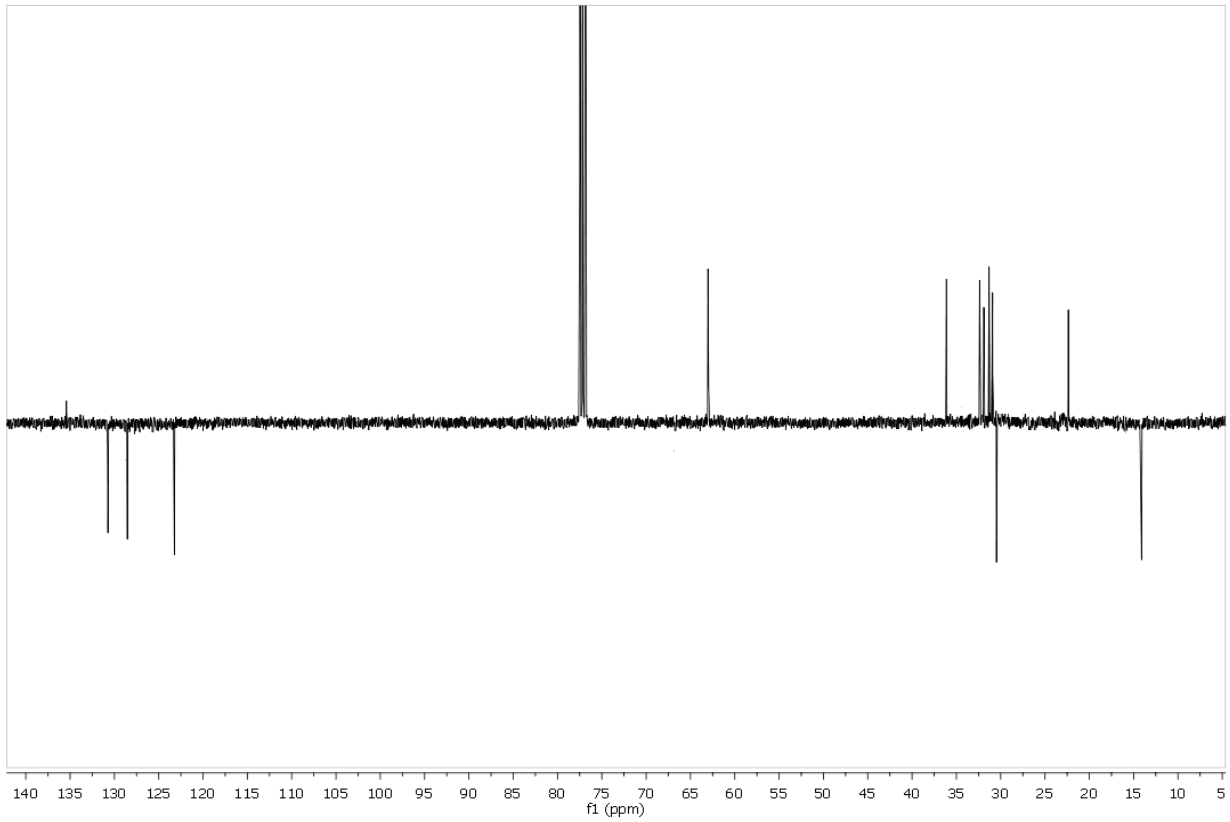
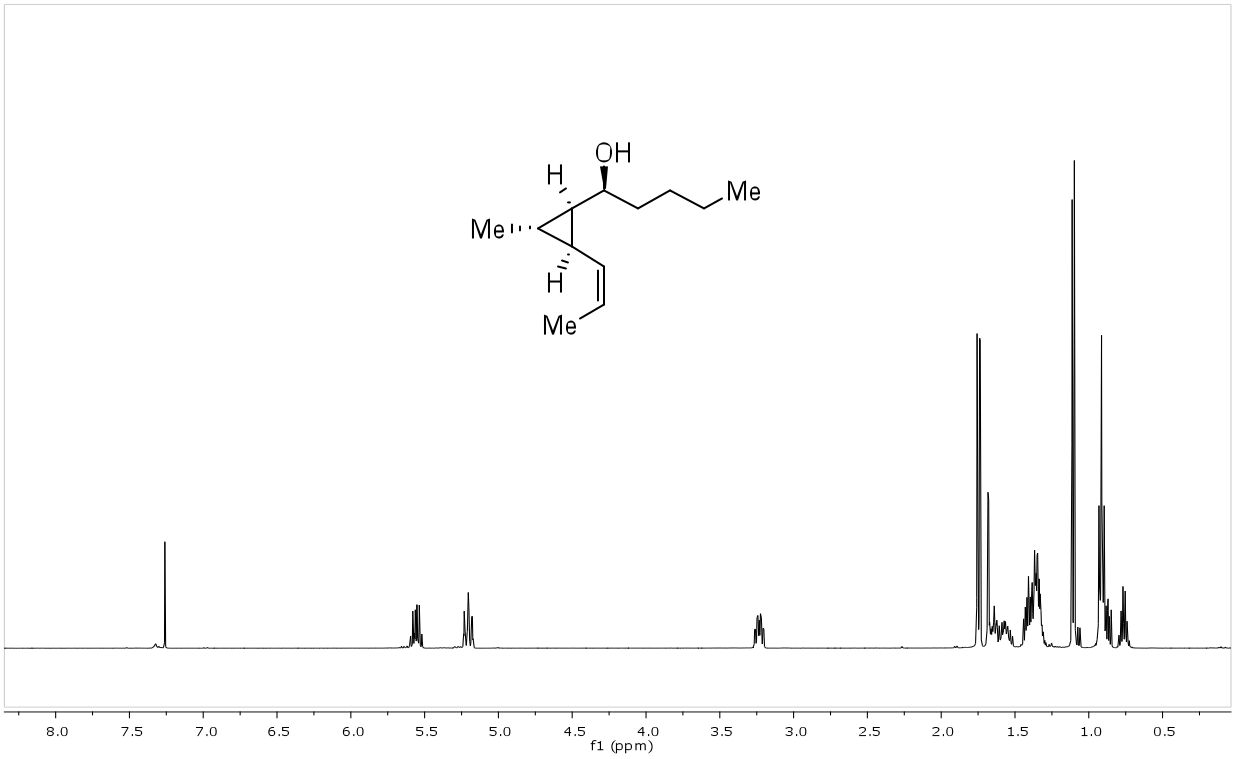


Figure S20: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **40** (*Z:E = 94:6*)



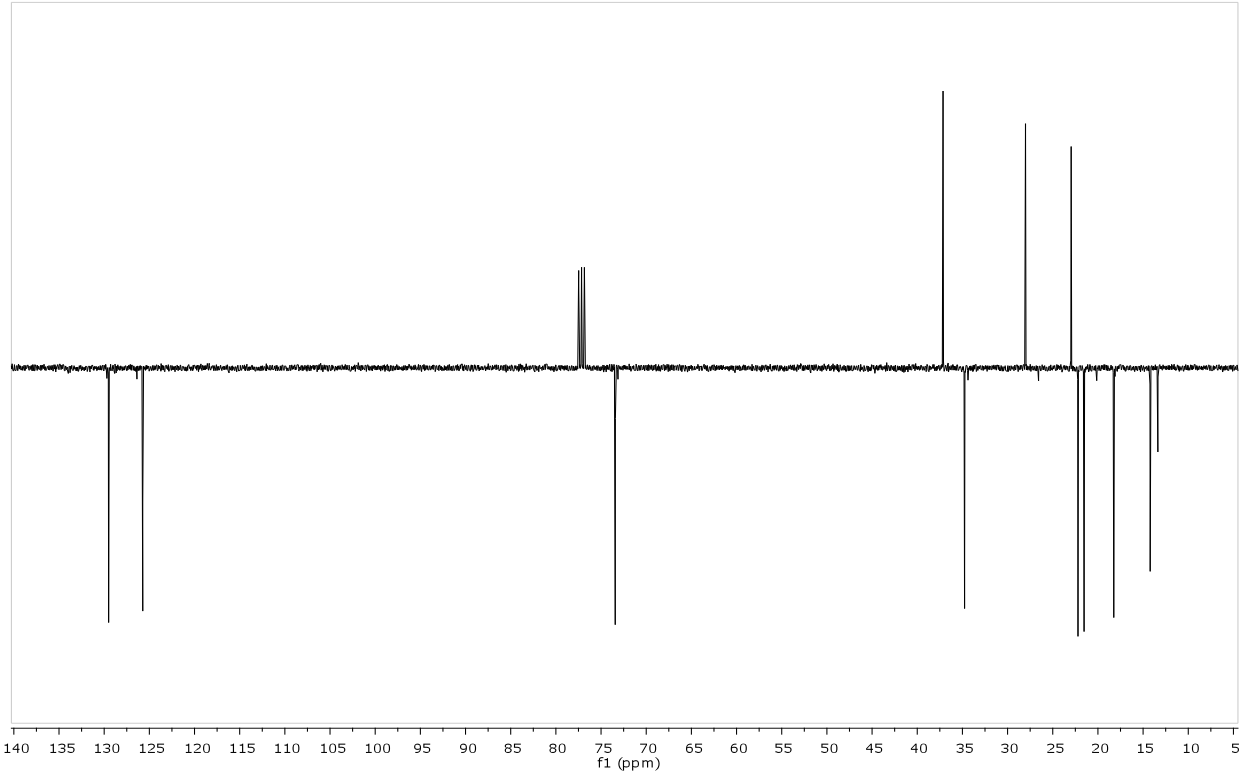
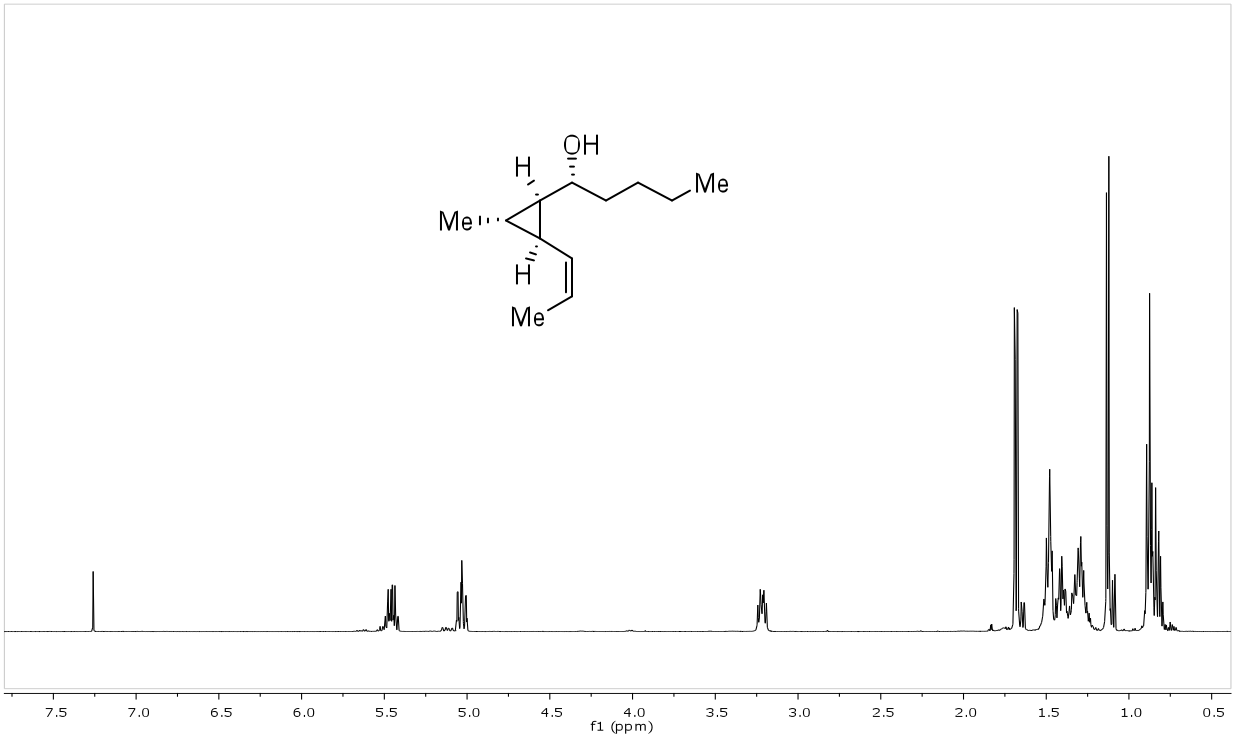


Figure S21: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **34** (*Z:E = 91:9*)



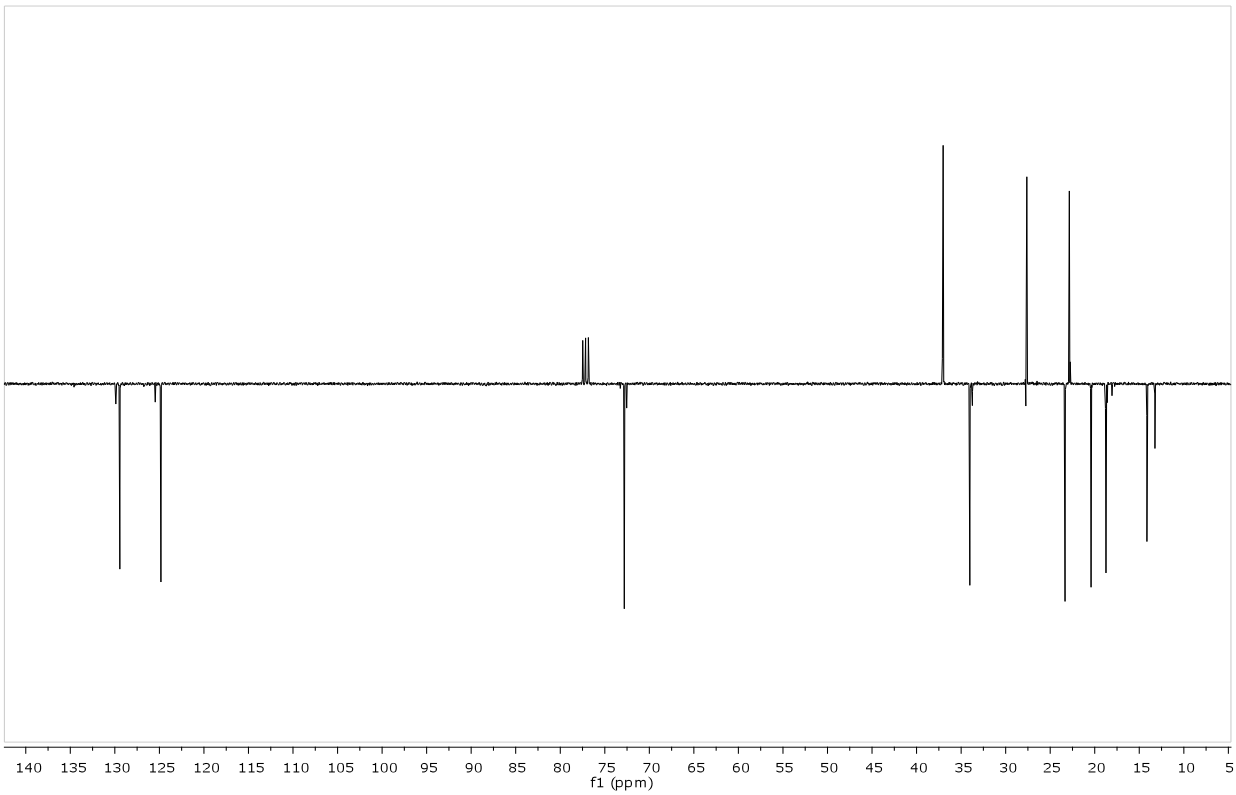


Figure S22: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **36**

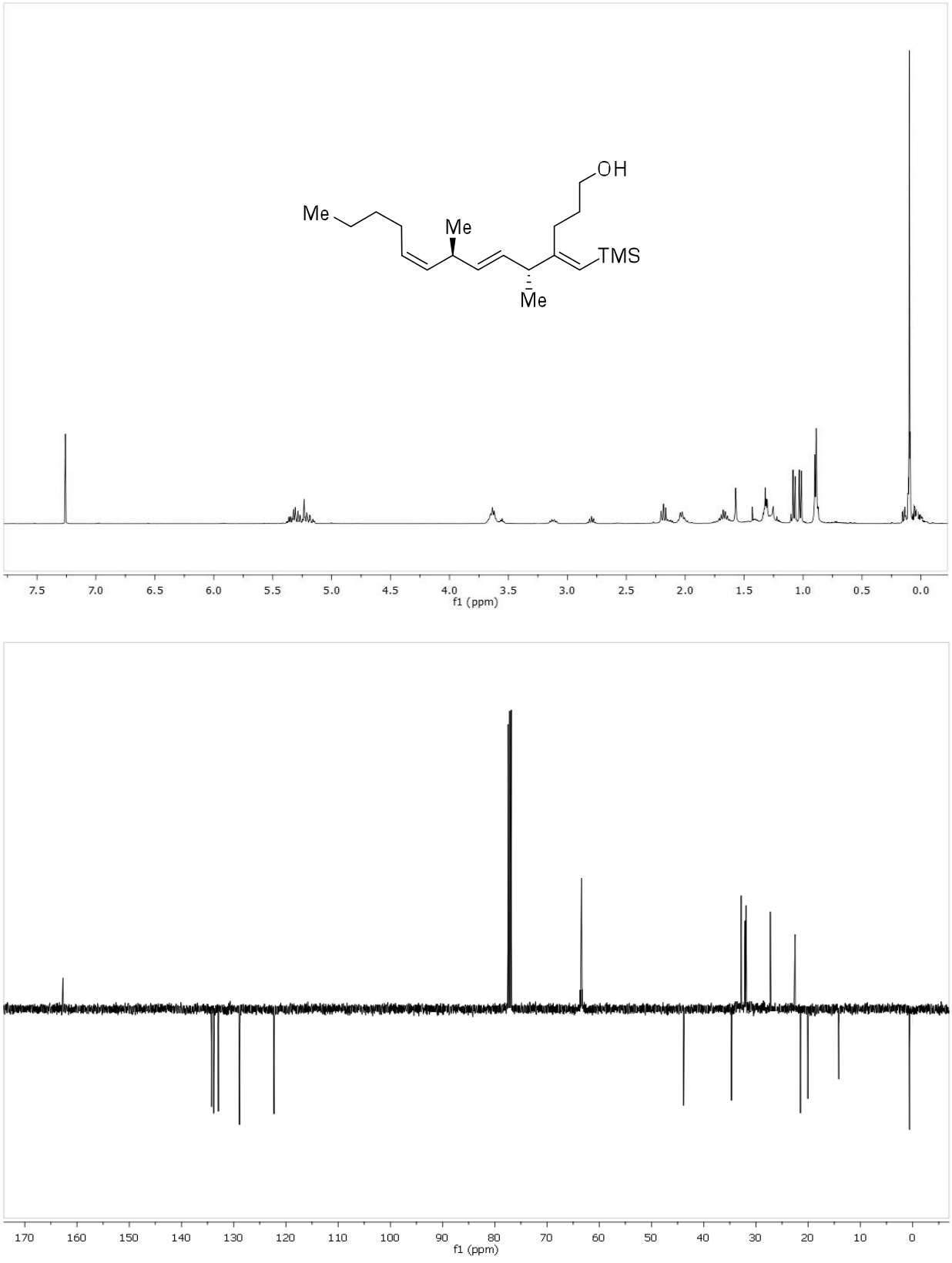
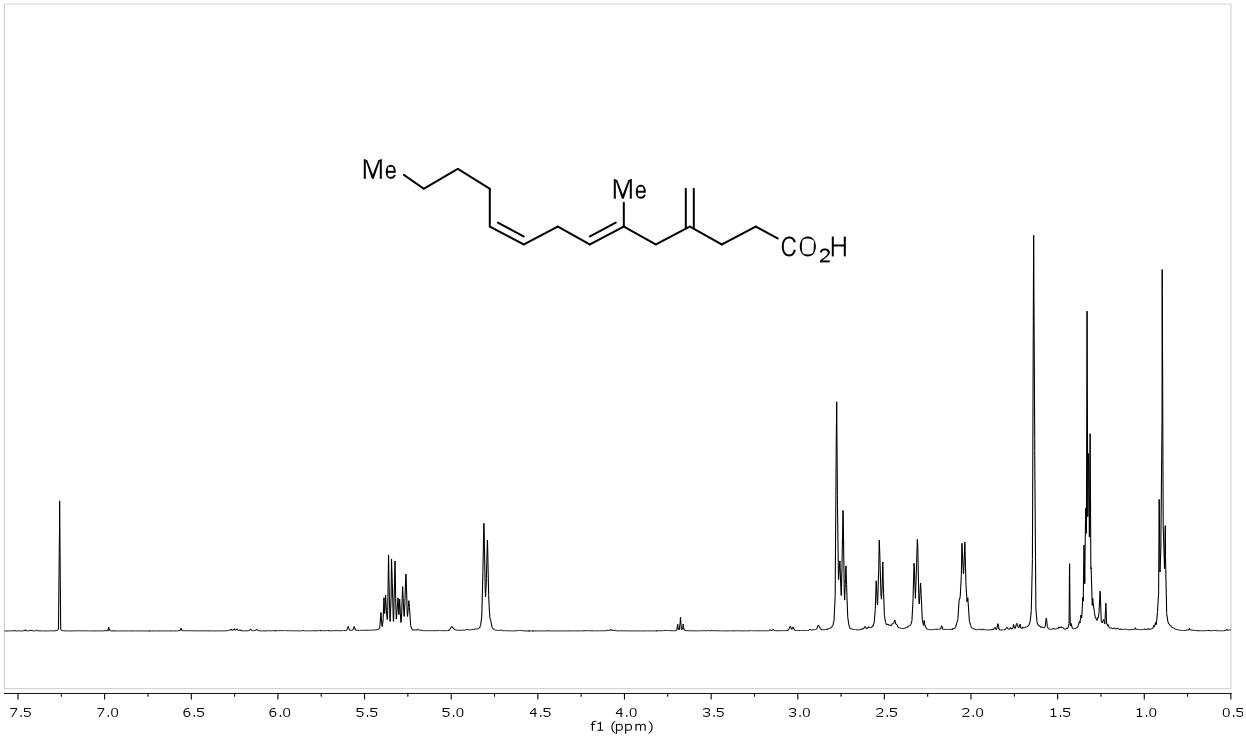


Figure S23: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **37**



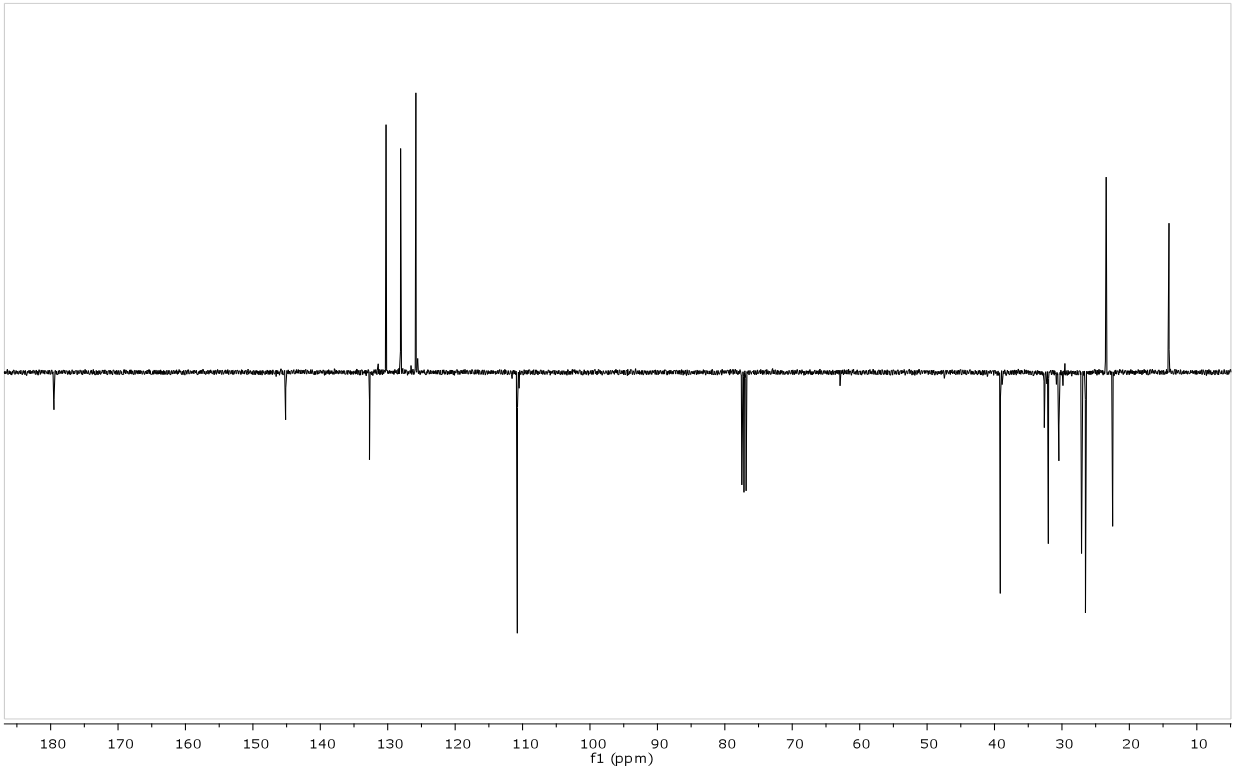
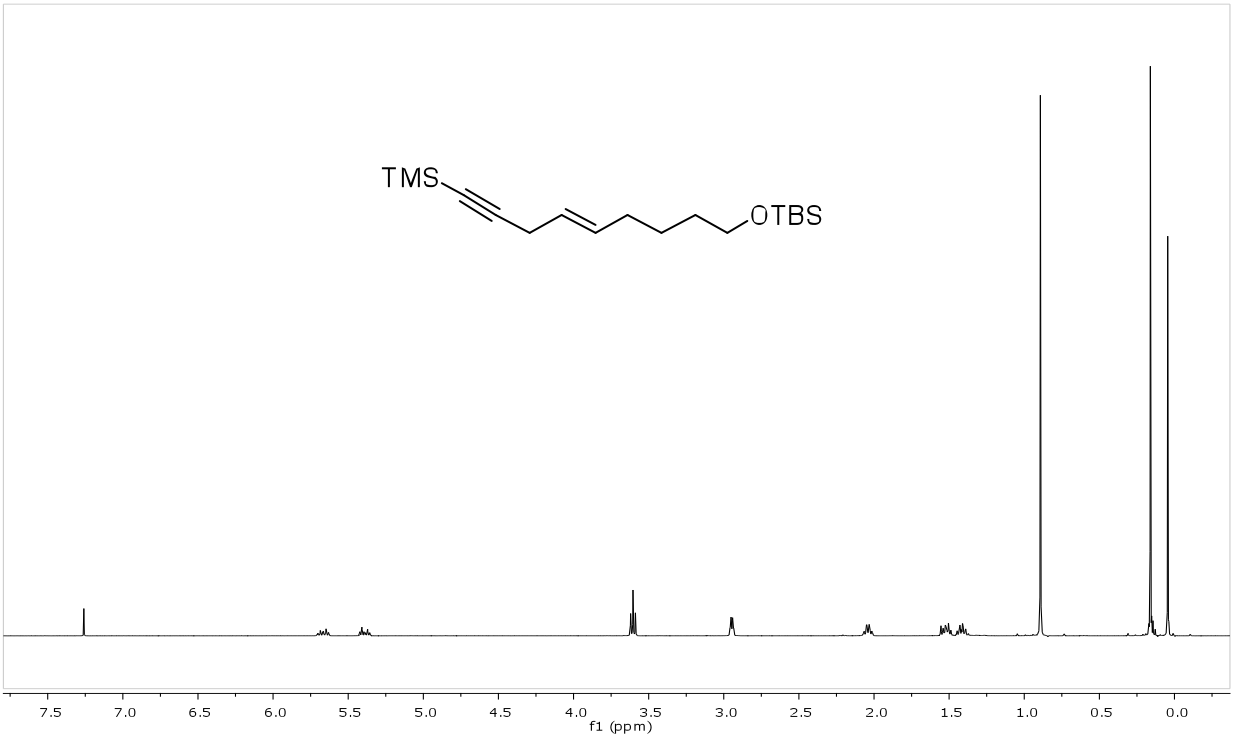


Figure S24: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **38**



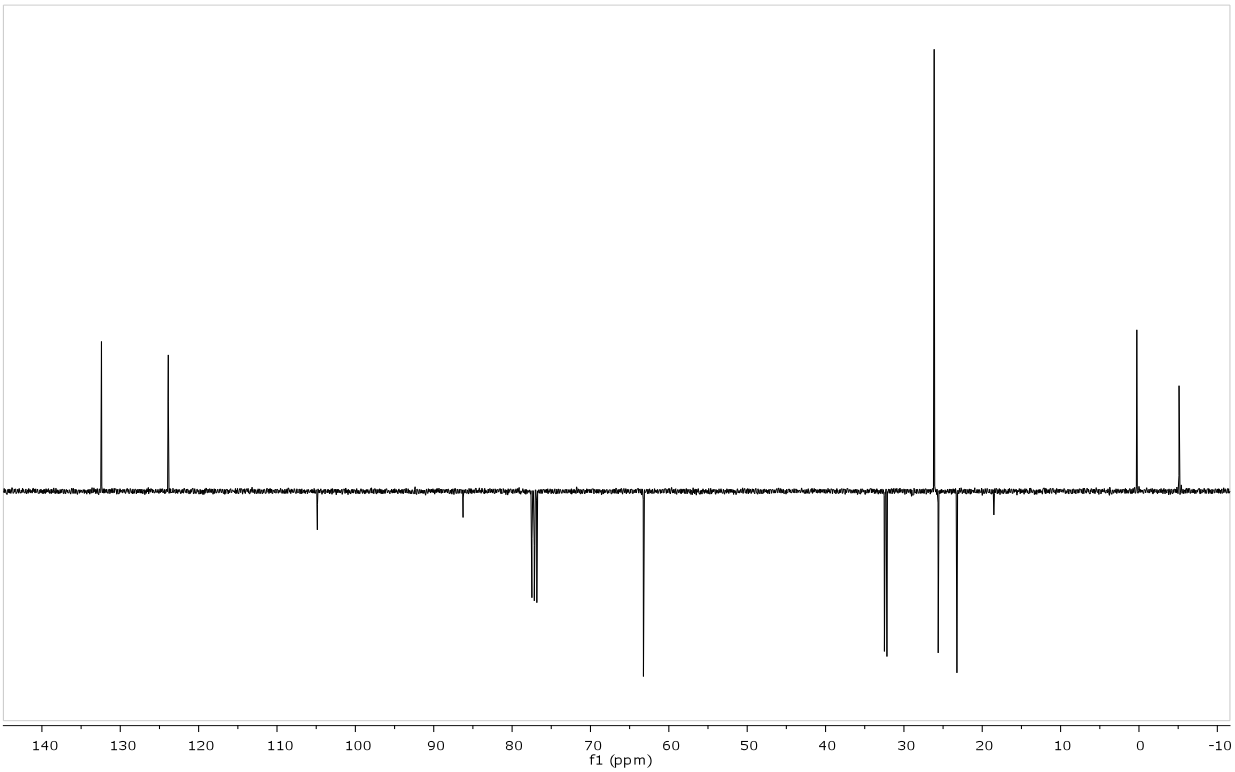
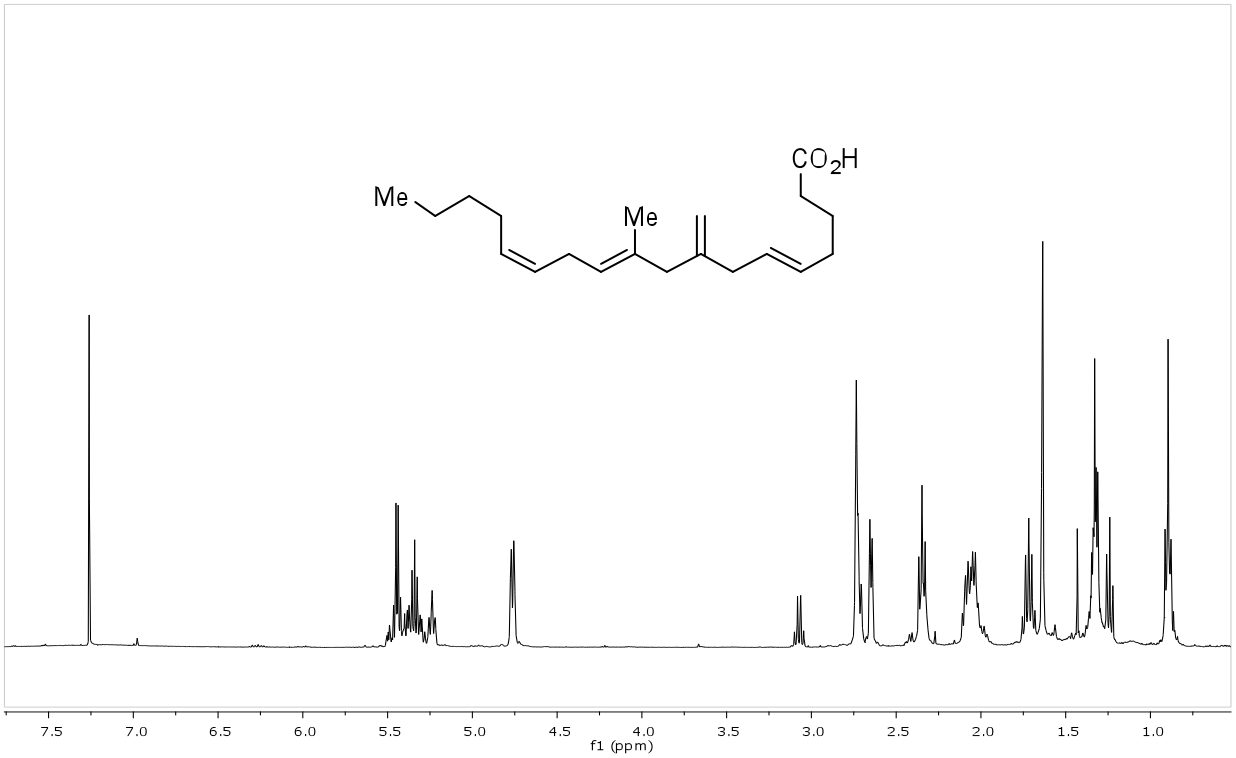


Figure S25: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **39**



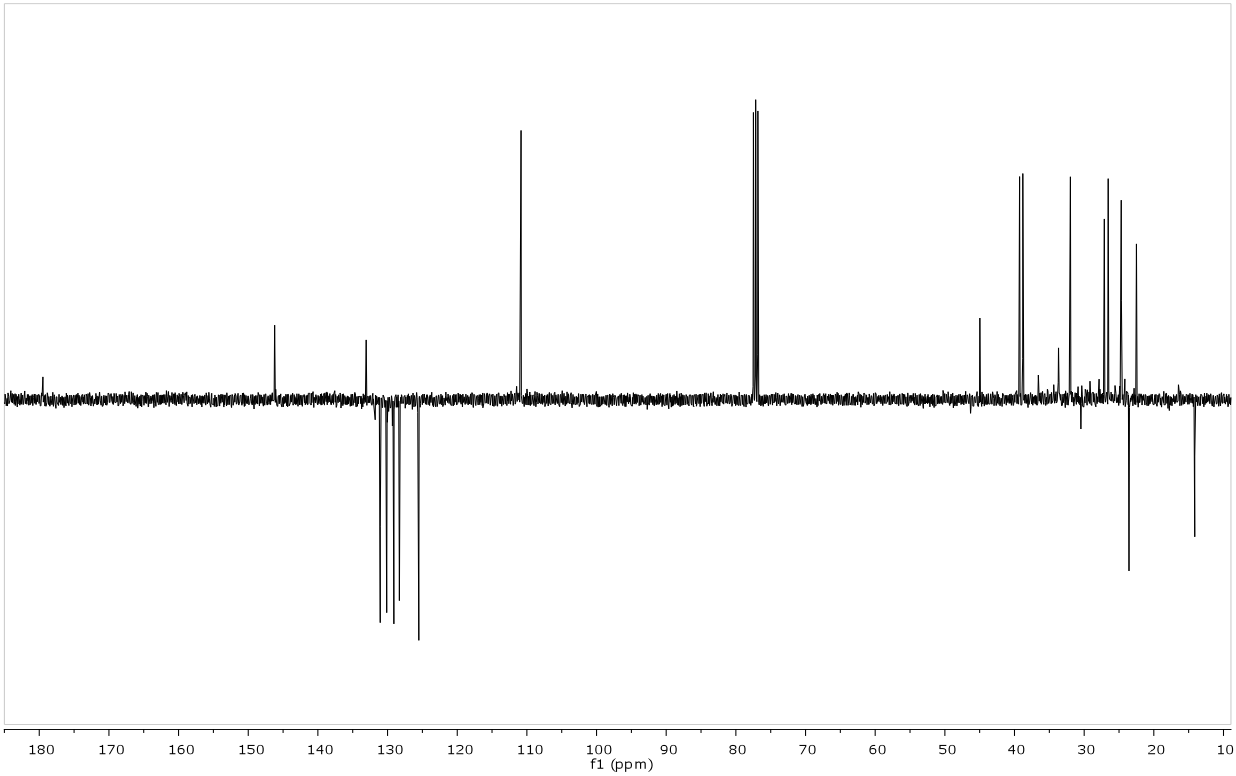


Figure S26: H^1 (400 MHz, $CDCl_3$) and $C^{13}CPT$ (100 MHz, $CDCl_3$) of **41**