Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

Concise, Enantioselective, and Versatile Synthesis of (−)-Englerin A Based on a Platinum-Catalyzed [4C+3C] Cycloaddition of Allenedienes

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Contents

General Procedures

All the reactions were conducted in dry solvents under argon atmosphere unless otherwise stated. Dry solvents were freshly distilled under argon from an appropriate drying agent before use. Gold complexes and $PtCl_2$ were purchased from Aldrich. Compounds **9**,[1] (S,S)-**Ru1**,[2] (R,R,R)-**Au1**[3] and L-Shi catalyst[4] are known and were synthesized according to the reported procedures. All other reagents used were bought from Aldrich, Alfa Aesar, TCI or Acros and used without further purification. The abbreviation "rt" refers to reactions carried out approximately at 23 °C. Reaction mixtures were stirred using Teflon-coated magnetic stirring bars. Reaction temperatures were maintained using Thermowatch-controlled silicone oil baths. Thin-layer chromatography (TLC) was performed on silica gel plates and components were visualized by observation under UV light, and/or by treating the plates with *p*-anisaldehyde or cerium nitrate solutions, followed by heating. Flash chromatography was carried out on silica gel (40-63 µm) unless otherwise stated. Dryings were performed with anhydrous Na_2SO_4. Concentration refers to the removal of volatile solvents via distillation using a Büchi rotary evaporator followed by residual solvent removal under high vacuum. NMR spectra were recorded in $CDCl_3$, at 300 MHz (Varian), 400 MHz (Varian) or 500 MHz (Bruker and Varian). Chemical shifts were reported in parts per million (δ) using the residual solvent signals (Methanol-d_4: δ_H 3.31, δ_C 49.00; $CDCl_3$: δ_H 7.26, δ_C 77.16) as the internal standards for the 1H and 13C NMR spectra and coupling constants (*J*) in Hz. Carbon types and structure assignments were determined from DEPT-NMR and two-dimensional experiments (HMQC and HMBC, COSY 1D-nOe and NOESY). NMR spectra were analyzed using MestreNova© NMR data processing software (www.mestrelab.com). The following abbreviations are used to indicate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; dd, double doublet; ddd, doublet of doublet of doublets; td, triple doublet; dt, doublet of triplets; ddt, doublet of doublet of triplets; dtd, doublet of triplet of doublets; m, multiplet; br, broad. Mass spectra (ESI-MS) were acquired using IT-MS Bruker AmaZon SL at CIQUS and also using chemical ionization (CI) electron impact (EI), or electrospray ionization (ESI) at the CACTUS facility of the University of Santiago de Compostela. The reactions were monitored by TLC. Enantioselectivities were determined in an Agilent GC system 6890N with Chiraldex G-TA 30m x 0.25mm analytical columns. Optical rotations were measured by used a Jasco P-2000 polarimeter.

Full Reference 3, main manuscript:

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[1] B. M. Trost, C. Jonasson, M. Wuchrer, *J. Am. Chem. Soc*. **2001**, *123***,** 1273.
[2] K-J. Haack, S. Hashiguchi, A. Fujii, T. Ikariya, R. Noyori, *Angew. Chem. Int. Ed.* **1997**, *36*, 285.
[3] I. Alonso, B. Trillo, F. López, S. Montserrat, G. Ujaque, L. Castedo, A. Lledós, J. L. Mascareñas, *J. Am. Chem. Soc.* **2009**, *131*, 13020.
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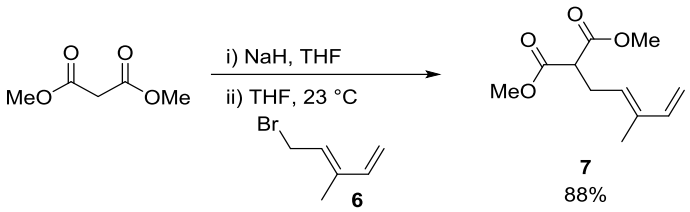
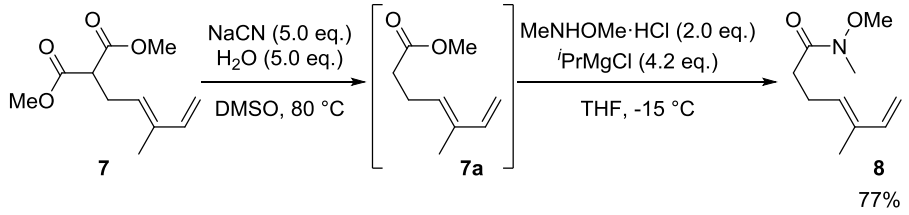
Synthesis of (-)-englerin A

Dimethyl (*E*)-2-(3-methylpenta-2,4-dien-1-yl)malonate (**7**):



A solution of dimethyl malonate (35.1 mL, 306.0 mmol, 3.0 eq.) in THF (60 mL) was added to an ice-cooled suspension of NaH (4.89 g, 60% in mineral oil, 122 mmol, 1.2 eq.) in THF (450 mL). After stirring at 23 °C for 1 h, a solution of dienyl bromide **6**[5] (16.4 g, 102.0 mmol, 1.0 eq.) was added at 0 °C. The reaction mixture was allowed to stir for 3 h at 23 °C, poured into water and extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and concentrated, and the resulting crude product was purified by flash chromatography (SiO_2, 5 to 20% EtOAc/hexanes) to give the diester **7** as a colorless oil (19.1 g, 88% yield). $\mathbf{R_f}$ = 0.49 (30% Et_2O/hexanes). **^{1}H NMR** (300 MHz $CDCl_3$) δ 6.33 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.39 (t, *J* = 7.5 Hz, 1H), 5.13 (d, *J* = 17.4 Hz, 1H), 4.98 (d, *J* = 10.7 Hz, 1H), 3.73 (s, 6H), 3.43 (t, *J* = 7.6 Hz, 1H), 2.75 (t, *J* = 7.5 Hz, 2H), 1.77 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.34 (CO), 140.92 (CH), 136.79 (C), 127.21 (CH), 112.00 (CH_2), 52.54 (CH_3), 51.53 (CH), 27.72 (CH_2), 11.69 (CH_3). **LRMS** (*m/z*, ESI): 235.09 $[M+Na]^+$, 185.05, 138.98, 105.04. **HRMS-ESI** Calculated for $C_{11}H_{16}NaO_4$ $[M+Na]^+$: 235.0941, found 235.0936.

(*E*)-*N*-Methoxy-*N*,5-dimethylhepta-4,6-dienamide (**8**):



A solution of **7** (15.0 g, 70.7 mmol, 1.0 eq.), NaCN (17.3 g, 353 mmol, 5.0 eq.), and water (6.37 mL, 353 mmol, 5.0 eq.) in DMSO (707 mL) was stirred for 48 h at 80 °C. When the reaction was complete water (700 mL) was added, and the resulting mixture was extracted with pentane (3 x 250 mL). The combined pentane fractions were washed with water and dried over Na_2SO_4, filtered and concentrated in vacuo to give ester **7a** as a colorless oil (8.83 g, 81%) which was used without purification in the next step.

MeNHOMe·HCl (11.13 g, 114 mmol, 2.0 eq.), followed by ^{i}PrMgCl (2.0 M in THF, 120 mL, 240 mmol, 4.2 eq.) were added to a solution of the crude product **7a** (8.80 g, 57.1 mmol, 1.0 eq.) in THF (500 mL) at −15 °C The resulting mixture was warmed to 0 °C and stirred for 3 h before NH_4Cl (sat.) (50 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (3× 100 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash

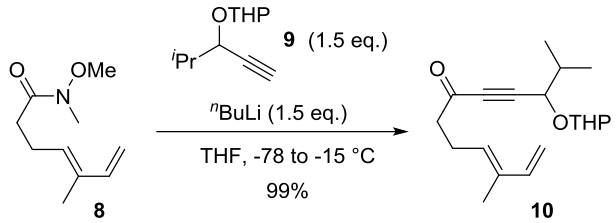
[5] Compound **6** is commercially available, and can also be obtained quantitatively by the protocol described in: S. Yildizhan, S. Schulz, *Synlett* **2011**, *19*, 2831.

chromatography (SiO_2, 20 to 60% EtOAc/hexanes) to give the Weinreb amide **8** as a pale yellow oil (9.93 g, 95%).

Compound **7a**:[6] $\mathbf{R_f}$ = 0.58 (30% Et_2O/hexanes). **^{1}H NMR** (300 MHz $CDCl_3$) δ 6.36 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.46 (t, *J* = 6.9 Hz, 1H), 5.12 (d, *J* = 17.4 Hz, 1H), 4.95 (d, *J* = 10.7 Hz, 1H), 3.65 (s, 3H), 2.51 – 2.29 (m, 4H), 1.76 (s, 3H).). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.8 (C), 141.8 (CH), 135.8 (C), 131.3 (CH), 111.6 (CH_2), 51.9 (CH_3), 34.3 (CH_2), 24.3 (CH_2), 11.9 (CH_3).

Compound **8**: $\mathbf{R_f}$ = 0.60 (50% EtOAc/hexanes). **^{1}H NMR** (300 MHz $CDCl_3$) δ 6.36 (dd, *J* = 17.3, 10.5 Hz, 1H), 5.50 (t, *J* = 6.3 Hz, 1H), 5.10 (d, *J* = 17.3 Hz, 1H), 4.94 (d, *J* = 10.7 Hz, 1H), 3.67 (s, 3H), 3.18 (s, 3H), 2.53 – 2.44 (m, 4H), 1.77 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.09 (C), 141.47 (CH), 135.08 (C), 131.49 (CH), 111.15(CH_2), 61.24 (CH_3), 32.20 (CH_3), 31.66 (CH_2), 23.32 (CH_2), 11.57 (CH_3). **LRMS** (*m/z*, ESI): 184.13 $[M+H]^+$, 159.12, 145.10. **HRMS-ESI** Calculated for $C_{10}H_{18}NO_2$ $[M+H]^+$: 184.1332, found 184.1340.

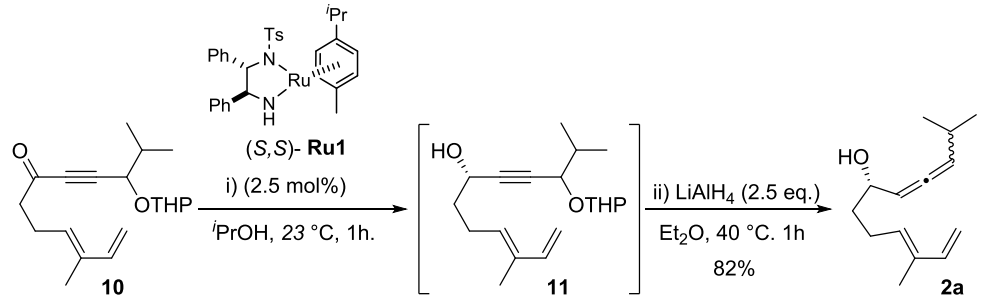
(*E*)-2,10-Dimethyl-3-((tetrahydro-2H-pyran-2-yl)oxy)dodeca-9,11-dien-4-yn-6-one (**10**):



^{n}BuLi (13.5 ml, 2.5M in hexanes, 33.7 mmol, 1.5 eq.) was slowly added (0.2 mL/min) to a solution of propargyl ether **9** (6.15 g, 33.7 mmol 1.5 eq.) in THF (225 mL) at −78 °C. The reaction was stirred 30 min at −78 °C and a solution of the Weinreb amide **8** (4.12 g, 22.5 mmol, 1.0 eq.) in THF (25 mL) was added. The solution was warmed to −15 °C. After 1 h, consumption of starting material was observed by TLC, NH_4Cl (sat.) was added and the resulting mixture was diluted with EtOAc and water. The aqueous layer was separated and extracted with EtOAc (3× 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of the crude material by flash chromatography (SiO_2, 1 to 20% EtOAc/hexanes) affords the diene-ynone **10** as a 1:1 mixture of diastereomers (6.78 g, 99% yield, pale yellow oil).[7] $\mathbf{R_f}$ = 0.46 and 0.51 (30% Et_2O/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.29 (dd, *J* = 17.4, 10.6 Hz, 1H), 5.39 (t, *J* = 7.4 Hz, 1H), 5.07 (d, *J* = 17.4 Hz, 1H), 4.91 (d, *J* = 10.8 Hz, 1.5H), 4.75 – 4.64 (m, 0.5H), 4.32 (d, *J* = 6.1 Hz, 0.5H), 4.13 (d, *J* = 5.9 Hz, 0.5H), 3.96 (td, *J* = 10.6, 9.8, 0.5H), 3.74 (td, *J* = 10.1, 9.0, 0.5H), 3.56 – 3.44 (m, 1H), 2.61 (t, *J* = 7.4 Hz, 2H), 2.46 (q, *J* = 7.4 Hz, 2H), 2.08 – 1.88 (m, 1H), 1.87 – 1.75 (m, 1H), 1.71 (s, 3H), 1.68 – 1.57 (m, 2H), 1.57 – 1.45 (m, 3H), 1.07 – 0.91 (m, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 186.74 (C), 186.57(C), 141.10 (CH), 141.05 (CH), 135.40 (C), 135.32 (C), 130.07 (CH), 129.90 (CH), 111.44 (CH_2), 111.35 (CH_2), 99.22 (CH), 95.65 (CH), 91.71 (C), 90.55 (C), 84.88 (C), 84.07 (C), 72.86 (CH), 69.91 (CH), 62.16 (CH_2), 62.00 (CH_2), 45.23 (CH_2), 45.17 (CH_2), 33.03 (CH), 30.33 (CH_2), 30.30 (CH_2), 25.43 (CH_2), 22.80 (CH_2), 19.09 (CH_2), 18.76 (CH_2), 18.60 (CH_3), 18.28 (CH_3), 18.18 (CH_3), 17.71 (CH_3), 11.68 (CH_3). **LRMS-CI** (*m/z*, *I*): 305 ($[M+H]^+$, 18), 221 (25), 203 (75), 161 (63), 85 (100). **HRMS-CI** Calculated for $C_{19}H_{29}O_3$ $[M+H]^+$: 305.2117, found 305.2109.

[6] Compound **7a** has been previously reported, see: P. Andersson, J. Bäckvall, *J. Org. Chem*. **1991**, *56*, 5349.
[7] Compound **10** was obtained and used in the next step as a mixture of diastereomers.

(6*S*,*E*)-2,10-Dimethyldodeca-3,4,9,11-tetraen-6-ol (**2a**):



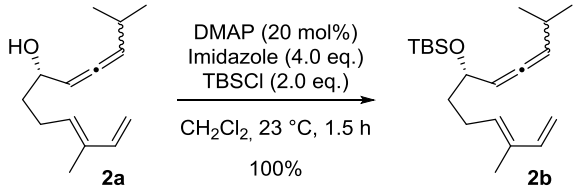
A solution of diene-ynone **10** (4.7 g, 15.44 mmol, 1.0 eq.) in ^{i}PrOH (25 mL) was added to a solution of (S,S)-**Ru1** (231 mg, 0.386 mmol, 2.5 mol%) in ^{i}PrOH (125 mL) at 23 °C. After stirring the mixture for 1 h, the volatiles were concentrated in vacuo, redissolved in ether and filtered over a Florisil® pad to give propargylic alcohol **11** as a colorless oil (4.73 g, quant.), which was subsequently used in the next step without further purification. A solution of crude product **11** (4.73 g, 15.44 mmol, 1.0 eq.) in Et_2O (125 mL) was added at 23 °C to a suspension of $LiAlH_4$ (1.45 g, 38.6 mmol, 2.5 eq.) in Et_2O (25 mL). The mixture was warmed to 40 °C and, after 2 h, the reaction was cooled in an ice bath and cold water was added, stirred for 1 h, filtered over silica and concentrated in vacuo. Purification of the crude residue by flash chromatography (SiO_2, 5 to 20% EtOAc/hexanes) afforded the allenediene **2a** as a mixture of diastereomers (2.61 g, 82% yield, colorless oil).[8]

Compound **11**:[8] $\mathbf{R_f}$ = 0.39 (30% Et_2O/hexanes. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.34 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.47 (t, *J* = 7.5 Hz, 1H), 5.08 (d, *J* = 17.4 Hz, 1H), 4.99 – 4.88 (m, 2H), 4.39 (t, *J* = 5.4 Hz, 1H), 4.21 (d, *J* = 6.2 Hz, 1H), 3.78 (ddd, *J* = 11.5, 9.0, 3.2 Hz, 1H), 3.56 – 3.46 (m, 1H), 2.43 (s, 1H), 2.30 (q, *J* = 7.7, 7.0 Hz, 2H), 2.05 – 1.82 (m, 1H), 1.82 – 1.70 (m, 7H), 1.63 – 1.47 (m, 4H), 1.02 (d, *J* = 3.0 Hz, 3H), 1.00 (d, *J* = 3.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 141.41 (CH), 134.96 (C), 131.67 (CH), 110.99 (CH_2), 95.18 (CH), 87.23 (C), 82.75 (C), 70.28 (CH), 62.05 (CH_2), 61.96 (CH), 37.59 (CH_2), 33.22 (CH), 30.51 (CH_2), 25.59 (CH_2), 24.11 (CH_2), 19.19 (CH_2), 18.76 (CH_3), 18.27 (CH_3), 11.73 (CH3). **LRMS-CI** (*m/z*, *I*): 307 ([M+H]$^+$, 25), 204 (78), 177 (81), 135 (96), 121 (98), 86 (100).

Compound **2a**: $\mathbf{R_f}$ = 0.57 (20% EtOAc/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.36 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.49 (t, *J* = 7.4 Hz, 1H), 5.39 – 5.20 (m, 2H), 5.07 (d, *J* = 17.3 Hz, 1H), 4.92 (d, *J* = 10.7 Hz, 1H), 4.20 – 4.03 (m, 1H), 2.39 – 2.18 (m, 3H), 1.90 – 1.80 (m, 1H), 1.74 (s, 3H), 1.63 (td, *J* = 7.7, 6.1 Hz, 2H), 1.03 (d, *J* = 3.0 Hz, 3H), 1.00 (d, *J* = 3.0 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 200.87 (C), 200.55 (C), 141.54 (CH), 134.55 (C), 132.38 (CH), 110.72 (CH_2), 102.14 (CH), 101.65 (CH), 96.92 (CH), 69.85 (CH), 69.28 (CH), 37.22 (CH_2), 27.99 (CH), 24.42 (CH_2), 24.32 (CH_2), 22.55 (CH_3), 11.73 (CH_3). **LRMS** (*m/z*, ESI): 207.17 [M+H]$^+$, 189.16, 145.10. **HRMS-ESI** Calculated for $C_{14}H_{23}O$ [M+H]$^+$: 207.1743, found 207.1738.

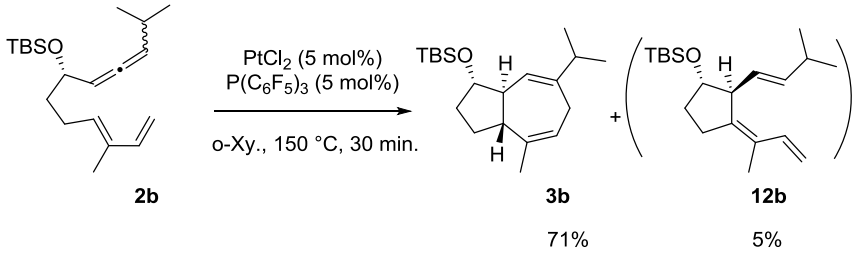
[8] Compounds **11** and **2a** were obtained and used in the next step as a mixture of diastereomers.

***tert*-Butyl(((6*S*,*E*)-2,10-dimethyldodeca-3,4,9,11-tetraen-6-yl)oxy)dimethylsilane** (**2b**):



A solution of allenediene **2a** (2.43 g, 11.78 mmol, 1.0 eq.) in CH_2Cl_2 (20 mL) was added to a solution of imidazole (3.21 g, 47.1 mmol, 4.0 eq.), DMAP (288 mg, 2.35 mmol, 20 mol%) and TBSCl (3.55 g, 23.55 mmol, 2.0 eq.) in CH_2Cl_2 (60 mL). The resulting reaction mixture was stirred for 1.5 h at 23 °C, water (10 mL) was added and the resulting mixture was extracted with CH_2Cl_2. The combined extracts were washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, 5% Et_2O/hexanes with 0.5% Et_3N) to give allenediene **2b** as a mixture of diastereomers (3.78 g, quant., colorless oil).[9] $\mathbf{R_f}$ = 0.83 (20% Et_2O/hexanes). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.38 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.51 (t, *J* = 7.4 Hz, 1H), 5.24 – 5.13 (m, 2H), 5.09 (d, *J* = 17.3 Hz, 1H), 4.93 (d, *J* = 10.6 Hz, 1H), 4.21 – 4.09 (m, 1H), 2.39 – 2.11 (m, 3H), 1.75 (s, 3H), 1.70 – 1.57 (m, 2H), 1.03 (t, *J* = 6.6 Hz, 6H), 0.91 (s, 9H), 0.08 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 201.39 (C), 201.09 (C), 141.72 (CH), 141.69 (CH), 134.26 (C), 133.00 (CH), 132.91 (CH), 110.50 (CH_2), 100.24 (CH), 99.69 (CH), 96.97 (CH), 72.26 (CH), 71.32 (CH), 38.71 (CH_2), 38.54 (CH_2), 28.40 (CH), 28.05 (CH), 26.05 (CH_3), 24.54 (CH_2), 24.36 (CH_2), 22.91 (CH_3), 22.86 (CH_3), 22.73 (CH_3), 22.62 (CH_3), 18.35 (C), 11.78 (CH_3), -4.00 (CH_3), -4.69 (CH_3). **LRMS-CI:** (*m/z*, *I*): 321 ($[M+H]^+$, 43), 305 (94), 263 (95), 239 (92), 189 (90), 81 (100). **LRMS** (*m/z*, ESI): 321.26 $[M+H]^+$, 189.16, 133.10, 105.06. **HRMS-ESI** Calculated for $C_{20}H_{37}OSi$ $[M+H]^+$: 321.2614, found 321.2686.

***tert*-Butyl(((1*S*,3a*R*,8a*S*)-7-Isopropyl-4-methyl-1,2,3,3a,6,8a-hexahydroazulen-1-yl)oxy)dimethylsilane** (**3b**):



A solution of allenediene **2b** (2.0 g, 6.24 mmol, 1.0 eq.) in o-xylene (10 mL) was added to a suspension of $PtCl_2$ (83.0 mg, 0.312 mmol, 5 mol%) and tris(pentafluorophenyl)phosphine (166 mg, 0.312 mmol, 5 mol%) in o-xylene (52 ml) which was previously heated at 150 °C. The mixture was stirred for 30 min and, after completion of the reaction (the progress of the process was monitored by TLC), allowed to cool down to 23 °C and filtered through a pad of Florisil®, eluting with Et_2O. The filtrate was concentrated in vacuo and purified by flash chromatography (SiO_2 15-40 µm, 0.1 to 5% Et_2O/hexanes) to afford the cycloadduct **3b** (1.42 g, 71% yield, colorless oil) and the triene **12b** (100 mg, 5% yield, yellow oil).

[9] Compound **2b** was obtained and used in the next step as a mixture of diastereomers.

Compound **3b**: R_f = 0.41 (1% Et_2O/hexanes). $[\alpha]_D^{20.1}$= -24.39 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.50 (d, *J* = 4.8 Hz, 1H), 5.36 (ddt, *J* = 7.6, 3.9, 1.9 Hz, 1H), 3.97 (td, *J* = 8.7, 6.0 Hz, 1H), 2.94 (d, *J* = 17.2 Hz, 1H), 2.52 – 2.42 (m, 2H), 2.22 – 2.09 (m, 2H), 1.94 (dtd, *J* = 12.9, 8.8, 7.2 Hz, 1H), 1.87 – 1.79 (m, 1H), 1.62 (s, 3H), 1.61 – 1.56 (m, 1H), 1.56 – 1.46 (m, 1H), 0.98 (d, *J* = 6.7 Hz, 6H), 0.90 (s, 9H), 0.074 (s, 3H), 0.068 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.45 (C), 139.14 (C), 123.39 (CH), 120.86 (CH), 79.26 (CH), 50.56 (CH), 44.02 (CH), 36.36 (CH), 32.40 (CH_2), 29.85 (CH_2), 27.79 (CH_2), 26.11 (CH_3), 23.10 (CH_3), 21.56 (CH_3), 21.30 (CH_3), 18.38 (C), -4.21 (CH_3), -4.35 (CH_3). **LRMS-EI** (*m/z*, *I*): 307 (M^+, 6), 263 (100), 187 (39), 145 (75), 75 (98). **HRMS-EI** Calculated for $C_{20}H_{36}OSi$ $[M]^+$: 320.2535, found 320.2541. GC analysis on Chiraldex G-TA 30m x 0.25mm showed a 99.1% enantiomeric excess. The relative stereochemistry of the **3b** was determined by nOe experiments (Figure 1).

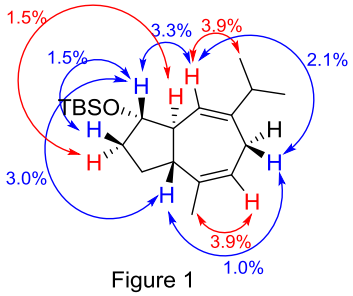
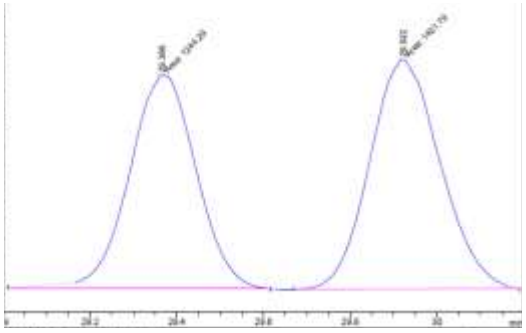


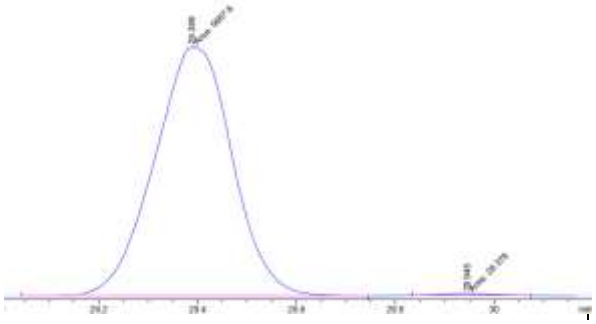
Figure 1

Racemic sample: [10]



Peak #	RT [min]	Type	Width [min]	Area	Area %
1	29.366	MM	0.179	1244.288	47.024
2	29.922	MM	0.188	1401.792	52.976

Asymmetric sample



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	29.388	MM	0.1827	5987.60156	546.17566	99.56142
2	29.945	MM	0.1383	26.37597	3.17790	0.43858

Compound **12b**: R_f = 0.50 (1% Et_2O/hexanes). $[\alpha]_D^{21.5}$= +76.66 (*c* 0.97, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.66 (dd, *J* = 17.3, 10.8 Hz, 1H), 5.33 (dd, *J* = 15.1, 6.9 Hz, 1H), 5.19 (dd, *J* = 15.5, 6.9 Hz, 1H), 5.03 (d, *J* = 17.9 Hz, 1H), 4.87 (d, *J* = 10.8 Hz, 1H), 3.98 (q, *J* = 3.7 Hz, 1H), 3.19 (d, *J*

[10] The racemic sample of compound **3b** was prepared by treatment of the diene-ynone **10** with $LiAlH_4$ (2.5 eq.) to afford the racemic allenediene **2a** (81% yield), which was subsequently protected with TBSCl and submitted to the cycloaddition process to yield **3b**, as described above for the asymmetric version.

= 7.1 Hz, 1H), 2.53 (dt, *J* = 17.0, 8.3 Hz, 1H), 2.40 – 2.27 (m, 1H), 2.27 – 2.19 (m, 1H), 1.85 – 1.80 (m, 1H), 1.77 (s, 3H), 1.64 – 1.59 (m, 1H), 0.95 (s, 3H), 0.94 (s, 3H), 0.86 (s, 9H), 0.04 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.56 (C), 138.44 (CH), 137.22 (CH), 127.56 (CH), 126.77 (C), 109.71 (CH_2), 79.75 (CH), 54.74 (CH), 32.60 (CH_2), 31.06 (CH), 28.84 (CH_2), 25.89 (CH_3), 22.57 (CH_3), 18.17 (C), 14.45 (CH_3), -4.56 (CH_3), -4.59 (CH_3). **LRMS** (*m/z*, ESI): 321.26 $[M+H]^+$, 261.18, 247.16, 133.10, 105.07. **HRMS-ESI** Calculated for $C_{20}H_{37}OSi$ $[M+H]^+$: 321.2608, found 321.2609. The relative stereochemistry of the **12b** was determined by nOe experiments (Figure 2).

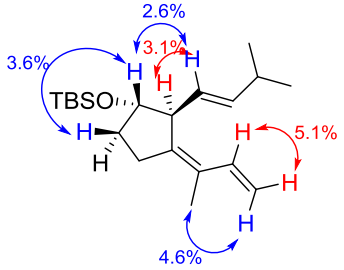
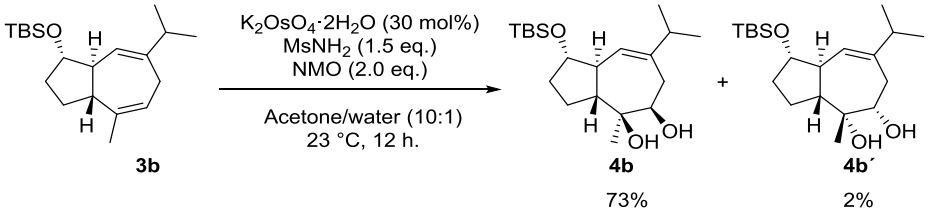


Figure 2

(1*S*,3a*R*,4*S*,5*R*,8a*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-7-isopropyl-4-methyl-1,2,3,3a,4,5,6,8a-octahydroazulene-4,5-diol (**4b**):



A solution of cycloadduct **3b** (564 mg, 1.76 mmol, 1.0 eq.) and *N*-methylmorpholine *N*-oxide (412 mg, 3.52 mmol, 2.0 eq.) in acetone (5 mL) was added to a solution of K_2OsO_4 (194 mg, 0.528 mmol, 30 mol%) and methanesulfonamide (251 mg, 2.64 mmol, 1.5 eq.) in acetone (35 mL) and water (4 mL) at 23 °C. The mixture was stirred for 12 h before Na_2SO_3 (sat.) (20 mL) was added, and the resulting mixture was stirred for additional 30 min. The volatile materials were concentrated in vacuo and the aqueous layer was extracted with EtOAc (3× 50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of the crude residue by flash chromatography (SiO_2, 10 to 50% EtOAc/hexanes) afforded the diol **4b** (455 mg, 73% yield, colorless foam) and its isomer **4b´** (12 mg, 2% yield, pale brown foam).[11]

Compound **4b**: $\mathbf{R_f}$ = 0.46 (50% EtOAc/hexanes). $[\alpha]_D^{21.2}$ = +52.79 (*c* 0.99, $CHCl_3$). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.63 (dt, *J* = 2.8, 1.3 Hz, 1H), 3.84 (td, *J* = 8.3, 6.5 Hz, 1H), 3.58 (t, *J* = 7.8 Hz, 1H), 2.48 (ddd, *J* = 16.0, 8.5, 1.6 Hz, 1H), 2.28 (s, 1H), 2.25 (d, *J* = 1.5 Hz, 1H), 2.23 – 2.18 (m, 1H), 2.02 – 1.94 (m, 1H), 1.93 – 1.77 (m, 3H), 1.68 (ddd, *J* = 12.2, 8.2, 4.1 Hz, 1H), 1.59 (s, 1H), 1.52 – 1.45 (m, 1H), 1.23 (s, 3H), 1.01 (d, *J* = 4.8 Hz, 3H), 0.99 (d, *J* = 4.7 Hz, 3H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.15 (C), 126.58 (CH), 79.81 (CH), 76.40 (C), 75.29 (CH), 48.83 (CH), 45.60 (CH), 37.28 (CH), 33.68 (CH_2), 33.19 (CH_2), 26.18 (CH_3), 22.11

[11] Other frequently used dihydroxylation conditions were less efficient and selective. For instance, treatment of **3b** with OsO_4 (30 mol%) in THF/Acetone/H_2O (6:6:1) and NMO (1 eq.) at 23 °C, provided **4b** in 35% yield, together with **4b´** in 10% yield.

(CH_2), 21.78 (CH_3), 21.61 (CH_3), 19.24 (CH_3), 18.42 (C), -4.02 (CH_3), -4.29 (CH_3). **LRMS** (*m/z*, ESI): 377.24 $[M+Na]^+$, 319.24, 245.07, 187.15. **HRMS-ESI** Calculated for $C_{20}H_{38}NaO_3Si$ $[M+Na]^+$: 377.2482, found 377.2484. The relative stereochemistry of the **4b** was determined by nOe experiments (Figure 3).

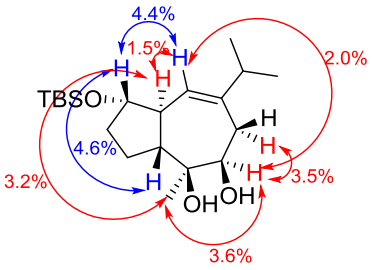


Figure 3

Compound **4b´**: $\mathbf{R_f}$ = 0.52 (50% EtOAc/hexanes). $[\alpha]_D^{21.3}$= -31.25 (*c* 0.94, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.58 (d, *J* = 3.4 Hz, 1H), 3.89 – 3.74 (m, 1H), 3.32 (t, *J* = 8.6 Hz, 1H), 2.71 (dd, *J* = 15.0, 10.0 Hz, 1H), 2.47 – 2.33 (m, 1H), 2.32 (s, 1H), 2.20 (dt, *J* = 13.2, 6.6 Hz, 1H), 2.11 (t, *J* = 3.3 Hz, 1H), 1.98 – 1.75 (m, 2H), 1.67 (s, 1H), 1.64 – 1.57 (m, 2H), 1.50 – 1.42 (m, 1H), 1.20 (s, 3H), 1.00 (d, *J* = 1.4 Hz, 3H), 0.98 (s, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.65 (C), 126.79 (CH), 79.68 (CH), 75.35 (CH), 74.80 (C), 48.18 (CH), 46.31 (CH), 36.67 (CH), 34.39 (CH_2), 32.63 (CH_2), 26.02 (CH_3), 25.76 (CH_3), 22.08 (CH_2), 21.48 (CH_3), 21.09 (CH_3), 18.26 (C), -4.18 (CH_3), -4.44 (CH_3). **LRMS** (*m/z*, ESI): 377.24 $[M+Na]^+$, 3190.24, 205.16, 158.09. **HRMS-ESI** Calculated for $C_{20}H_{38}NaO_3Si$ $[M+Na]^+$: 377.2482, found 377.2481. The relative stereochemistry of the **4b´** was determined by nOe experiments (Figure 4).

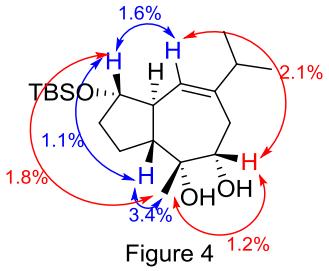
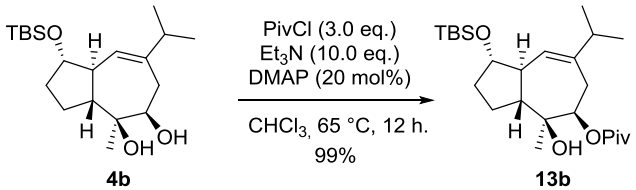


Figure 4

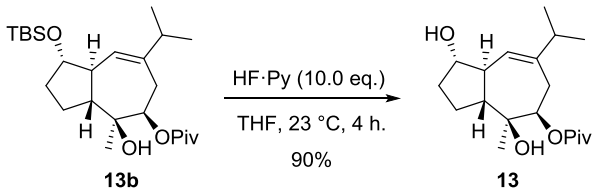
(1*S*,3a*R*,4*S*,5*R*,8a*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-4-hydroxy-7-isopropyl-4-methyl-1,2,3,3a,4,5,6,8a-octahydroazulen-5-yl pivalate (**13b**):



Et_3N (5.0 mL, 35.8 mmol, 10.0 eq.), pivaloyl chloride (1.32 mL, 10.74 mmol, 3.0 eq.) and DMAP (88 mg, 0.72 mmol, 20 mol%) were successively added to a solution of diol **4b** (1.27 g, 3.58 mmol, 1.0 eq.) in $CHCl_3$ (120 mL) at 0 °C. The resulting mixture was warmed to 65 °C and stirred for 12 h. After completion of the reaction, the mixture allowed to cool down to 23 °C and it was directly absorbed in silica, concentrated in vacuo and purified by flash chromatography (SiO_2, 2.5 to 30% EtOAc/hexanes with 5% CH_2Cl_2) to afford **13b** (1.56 g, 99% yield, pale brown oil). $\mathbf{R_f}$ = 0.60 (50% EtOAc/hexanes). $[\alpha]_D^{19.2}$ = +18.07 (*c* 1.12, $CHCl_3$). **^{1}H NMR**

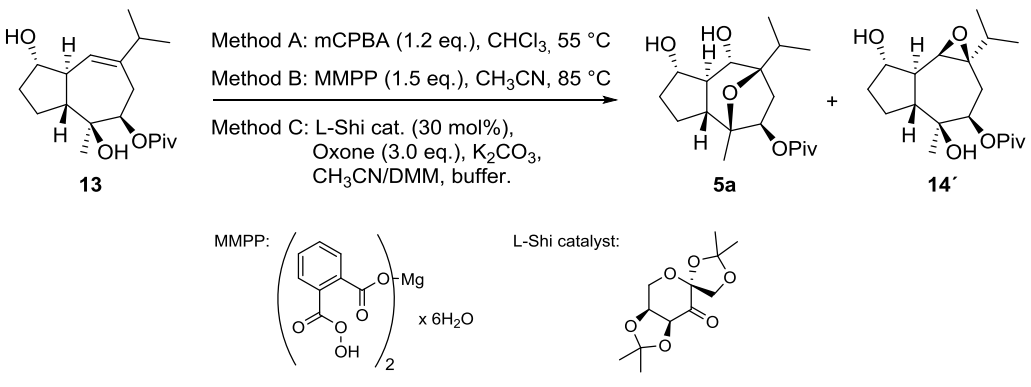
(500 MHz, $CDCl_3$) δ 5.54 (d, *J* = 2.2 Hz, 1H), 4.72 (dd, *J* = 9.3, 1.2 Hz, 1H), 3.80 (q, *J* = 7.6 Hz, 1H), 2.63 (ddd, *J* = 17.4, 9.2, 1.7 Hz, 1H), 2.10 (p, *J* = 7.7, 7.1 Hz, 1H), 2.05 – 1.97 (m, 3H), 1.91 – 1.73 (m, 2H), 1.74 – 1.61 (m, 1H), 1.53 – 1.42 (m, 1H), 1.27 – 1.23 (m, 1H), 1.22 (s, 3H), 1.21 (s, 9H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.68 (CO), 143.32 (C), 124.68 (CH), 79.66 (CH), 77.74 (CH), 75.75 (C), 48.91 (CH), 45.79 (CH), 39.20 (C), 37.02 (CH), 33.65 (CH_2), 30.84 (CH_2), 27.42 (CH_3), 27.14 (CH_3), 26.01 (CH_3), 22.00 (CH_2), 21.49 (CH_3), 19.84 (CH_3), 18.24 (C), -4.20 (CH_3), -4.45 (CH_3). **LRMS** (*m/z*, ESI): 461.30 $[M+Na]^+$, 347.22, 319.24, 187.14. **HRMS-ESI** Calculated for $C_{25}H_{46}NaO_4Si$ $[M+Na]^+$: 461.3058, found 461.3059.

(1*S*,3a*R*,4*S*,5*R*,8a*S*)-1,4-Dihydroxy-7-isopropyl-4-methyl-1,2,3,3a,4,5,6,8a-octahydroazulen-5-yl pivalate (**13**):



HF·Py (2.78 mL, ~70% in pyridine, 21.65 mmol, 10.0 eq.) was added dropwise to a solution of the silyl ether **13b** (950 mg, 2.165 mmol, 1.0 eq.) in THF (10 mL) in a falcon type tube (50 mL). The mixture was stirred for 4 h at 23 °C. After completion of the reaction, the mixture was cooled at 0 °C and Na_2CO_3 (sat.) (20 mL) was added. The aqueous layer was separated and extracted with EtOAc (3× 30 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of the crude residue by flash chromatography (SiO_2, 20 to 50% EtOAc/hexanes with 10% CH_2Cl_2) afforded the alcohol **13** as a white foam (630 mg, 90% yield). $\mathbf{R}_f$ = 0.48 (50% EtOAc/hexanes). $[\alpha]_D^{19.9}$ = -1.29 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.59 (s, 1H), 4.73 (dd, *J* = 9.0, 1.2 Hz, 1H), 3.92 (q, *J* = 7.2 Hz, 1H), 2.61 (ddd, *J* = 16.4, 9.0, 1.6 Hz, 1H), 2.11 (p, *J* = 6.8 Hz, 1H), 2.07 – 2.01 (m, 3H), 1.99 – 1.87 (m, 3H), 1.87 – 1.76 (m, 1H), 1.73 (dt, *J* = 13.6, 6.7 Hz, 1H), 1.52 (ddt, *J* = 12.5, 9.3, 7.2 Hz, 1H), 1.22 (s, 3H), 1.20 (s, 9H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.87 (CO), 144.20 (C), 124.58 (CH), 79.67 (CH), 77.60 (CH), 75.73 (C), 49.21 (CH), 47.14 (CH), 39.32 (C), 37.21 (CH), 33.80 (CH_2), 30.65 (CH_2), 27.52 (CH_3), 22.61 (CH_2), 21.52 (CH_3), 21.42 (CH_3), 19.93 (CH_3). **LRMS** (*m/z*, ESI): 347.22 $[M+Na]^+$, 236.07, 205.16, 187.15. **HRMS-ESI** Calculated for $C_{19}H_{32}NaO_4$ $[M+Na]^+$: 347.2193, found 347.2198.

(1*S*,3a*R*,4*S*,5*R*,7*R*,8*S*,8a*S*)-1,8-Dihydroxy-7-isopropyl-4-methyldecahydro-4,7-epoxyazulen-5-yl pivalate (**5a**):



Method A (Table 2, entry 4): *m*CPBA (85 mg, 0.370 mmol, 1.2 eq.) was added to a solution of alcohol **13** (100 mg, 0.308 mmol, 1.0 eq.) in $CHCl_3$ (10 mL) at 23 °C and warmed to 55 °C for 5 h. After completion of the reaction, the mixture was allowed to cool to 23 °C and $NaHCO_3$ (sat.) (10 mL) was added. The aqueous layer was separated and extracted with CH_2Cl_2 (3× 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo to give a crude residue which was purified by flash chromatography (SiO_2 15-40 µm, 10 to 70% EtOAc/hexanes with 10% CH_2Cl_2) to give the oxatryciclic compound **5a** (52 mg, 50% yield, white foam) and the epoxide **14´** (52 mg, 50% yield, amorphous solid).

Method B (Table 2, entry 5): MMPP (2.05 g, 4.13 mmol, 1.5 eq.) was added to a solution of alcohol **13** (894 mg, 2.76 mmol, 1.0 eq.) in CH_3CN (92 mL). The suspension was stirred for 4 h at 85 °C, cooled down to 23 °C, filtered and concentrated in vacuo. The white solid residue was dissolved in EtOAc, and the resulting organic phase was washed with Na_2SO_3 (10%), $NaHCO_3$ (sat.), and water, dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of the crude was carried out as for Method A, to give **5a** (470 mg, 50% yield) and **14´** (468 mg, 50% yield).

Method C (Table 2, entry 7): Alcohol **13** (440 mg, 1.36 mmol, 1.0 eq.) was dissolved in CH_3CN (6.5 mL) and dimethoxymethane (DMM) (13 mL). Then, a Borax buffer solution [20 mL, 0.05 M solution of $Na_2B_4O_7{\cdot}10H_2O$ in 4×10^{-4} M aqueous Na_2(EDTA)], $(^nBu)_4NHSO_4$ (0.015 g, 0.04 mmol), and L-Shi catalyst (105 mg, 0.407 mmol, 30 mol%) were subsequently added. A solution of Oxone® (2.5 g, 4.07 mmol, 3.0 eq) in aqueous Na_2(EDTA) (12 mL, 4×10^{-4} M) and a solution of K_2CO_3 (1.31 g, 9.49 mmol, 7.0 eq.) in water (12 mL) were added dropwise separately over a period of 1.5 h. The mixture was stirred at 23 °C for 12 h, diluted with water (50 mL), and extracted with EtOAc (4 × 50 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The crude was redissolved in CH_3CN (20 mL) and warmed at 85 °C for 2 h. Then, the reaction mixture was cooled down to 23 °C, absorbed in silica, and evaporated under vacuo. Purification of the crude residue was carried out as for Method A, to give **5a** (328 mg, 71% yield) and **14´** (73 mg, 16% yield).

Compound **5a**: $\mathbf{R_f}$ = 0.28 (50% EtOAc/hexanes). $[\alpha]_D^{18.8}$ = -2.69 (*c* 0.93, $CHCl_3$). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.02 (dd, *J* = 7.8, 2.8 Hz, 1H), 4.07 (td, *J* = 8.9, 5.7 Hz, 1H), 3.69 (d, *J* = 9.1 Hz, 1H), 2.51 (dd, *J* = 14.5, 7.8 Hz, 1H), 2.47 (brs, 2H), 2.18 – 2.06 (m, 1H), 1.97 (hept, *J* = 7.0 Hz, 1H), 1.67 – 1.58 (m, 2H), 1.57 – 1.47 (m, 2H), 1.47 – 1.40 (m, 1H), 1.39 – 1.30 (m, 1H), 1.21 (s, 9H), 1.13 (s, 3H), 1.04 (d, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.20 (CO), 86.09 (C), 84.39 (C), 77.07 (CH), 74.91 (CH), 74.49 (CH), 51.43 (CH), 48.22 (CH), 39.04 (CH_2), 38.99 (C), 32.23 (CH_2), 31.54 (CH), 27.27 (CH_3), 23.54 (CH_2), 18.46 (CH_3), 18.16 (CH_3), 17.17 (CH_3). **LRMS** (*m/z*, ESI): 341.23 $[M+H]^+$, 239.16, 221.15, 203.14. **HRMS-ESI** Calculated for $C_{19}H_{33}O_5$ $[M+H]^+$: 41.2323, found 341.2320. The relative stereochemistry of the **5a** was determined by nOe experiments (Figure 5).

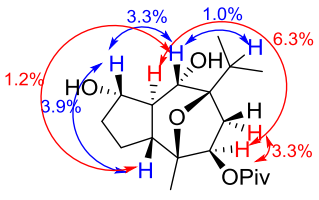


Figure 5

Compound **14´**: $\mathbf{R_f}$ = 0.39 (50% EtOAc/hexanes). $[\alpha]_D^{21.6}$= +37.11 (*c* 1.01, $CHCl_3$). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.60 (dd, *J* = 10.6, 1.3 Hz, 1H), 4.15 (q, *J* = 6.5 Hz, 1H), 3.11 (d, *J* = 1.0 Hz, 1H), 2.30 (dd, *J* = 15.6, 10.6 Hz, 1H), 2.05 (dt, *J* = 11.5, 8.6 Hz, 1H), 1.93 – 1.85 (m, 3H), 1.80 – 1.71 (m, 2H), 1.64 (dd, *J* = 15.6, 1.4 Hz, 1H), 1.57 (ddd, *J* = 12.5, 8.6, 6.3 Hz, 1H), 1.48 (p, *J* = 6.9 Hz, 1H), 1.24 (s, 9H), 1.11 (s, 3H), 0.96 (d, *J* = 5.3 Hz, 3H), 0.95 (d, *J* = 5.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.46 (CO), 77.02 (CH), 76.75 (CH), 74.68 (C), 65.70 (C), 61.82 (CH), 48.91 (CH), 40.67 (CH), 39.30 (C), 37.52 (CH), 34.76 (CH_2), 28.61 (CH_2), 27.46 (CH_3), 22.76 (CH_2), 20.24 (CH_3), 18.10 (CH_3), 17.28 (CH_3). **LRMS** (*m/z*, ESI): 363.21 $[M+Na]^+$, 277.11, 236. **HRMS-ESI** Calculated for $C_{19}H_{32}NaO_5$ $[M+Na]^+$: 363.2142, found 363.2151. The relative stereochemistry of the **14´** was determined by nOe experiments (Figure 6).

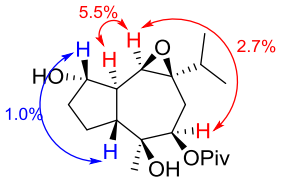
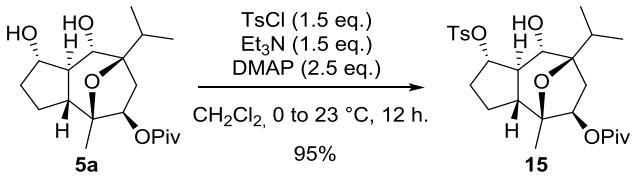


Figure 6

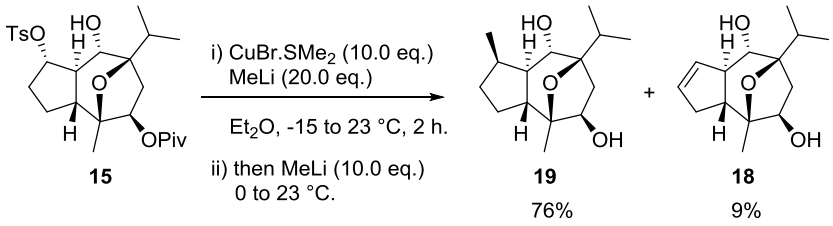
(1*S*,3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-8-Hydroxy-7-isopropyl-4-methyl-1-(tosyloxy)decahydro-4,7-epoxy-azulen-5-yl pivalate (**15**):



p-Toluenesulfonyl chloride (248 mg, 1.30 mmol, 1.5 eq.) and Et_3N (181 µL, 1.30 mmol, 1.5 eq.) were added to a solution of the diol **5a** (295 mg, 0.866 mmol, 1.0 eq.) in CH_2Cl_2 (4 mL). The mixture was cooled in an ice-water bath and DMAP (2.65 mg, 2.17 mmol, 2.5 eq.) was added. After 10 min the ice bath was removed and stirring was continued at 23 °C for additional 12 h. The mixture was poured into $NaHSO_4$ (30% aq.) and the organic phase was separated and washed with water and brine, dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of the crude residue by flash chromatography (SiO_2, 5 to 30% EtOAc/hexanes with 5% CH_2Cl_2) afforded **15** (407 mg, 95% yield, white foam).

$\mathbf{R_f}$ = 0.61 (50% EtOAc/hexanes). $[\alpha]_D^{20.2}$= -24.41 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.98 (dd, *J* = 7.9, 2.8 Hz, 1H), 4.73 (td, *J* = 9.1, 5.7 Hz, 1H), 3.68 (d, *J* = 9.4 Hz, 1H), 2.78 (brs, 1H), 2.50 (dd, *J* = 14.6, 7.9 Hz, 1H), 2.44 (s, 3H), 2.06 – 1.90 (m, 2H), 1.74 – 1.61 (m, 3H), 1.61 – 1.53 (m, 1H), 1.51 – 1.41 (m, 1H), 1.38 (td, *J* = 12.8, 6.1 Hz, 1H), 1.19 (s, 9H), 1.10 (s, 3H), 1.03 (d, *J* = 7.0 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.99 (CO), 145.27 (C), 133.33 (C), 130.04 (CH), 127.94 (CH), 86.08 (C), 84.13 (CH), 83.85 (C), 74.54 (CH), 72.85 (CH), 50.31 (CH), 48.02 (CH), 38.92 (C), 38.86 (CH_2), 31.42 (CH), 29.61 (CH_2), 27.23 (CH_3), 23.31 (CH_2), 21.78 (CH_3), 18.43 (CH_3), 18.02 (CH_3), 16.99 (CH_3). **LRMS** (*m/z*, ESI): 495.24 $[M+H]^+$, 477.23, 375.16, 323.21. **HRMS-ESI** Calculated for $C_{26}H_{39}O_7S$ $[M+H]^+$: 495.2411, found 495.2410.

(1*R*,3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-7-Isopropyl-1,4-dimethyldecahydro-4,7-epoxyazulene-5,8-diol (19):[12]



MeLi (2.0 mL, 1.6 M, 3.24 mmol, 20.0 eq.) was added dropwise to a stirred suspension of CuBr·SMe_2 (332 mg, 1.62 mmol, 10.0 eq.) in Et_2O (3.0 mL) at −15 °C. After being stirred for 30 min, a solution of the tosylate **15** (80.0 mg, 0.162 mmoles, 1.0 eq.) in Et_2O (3.0 mL) was added dropwise. The resultant suspension was stirred at 23 °C for 2 h, cooled down to 0 °C and MeLi (1.0 mL, 1.6 M, 1.62 mmol, 10.0 eq.) was added dropwise. The resulting mixture was stirred for an additional hour, cooled in an ice-water bath and water (2 mL) was added, followed by NH_4Cl (sat.). Extraction with EtOAc (3× 20 mL) provided an organic phase which was dried over Na_2SO_4, filtered, concentrated in vacuo and purified by flash chromatography (SiO_2 15-40 µm, 20 to 50% EtOAc/hexanes with 10% CH_2Cl_2) to afford the diol **19** (31.3 mg, 76% yield, white solid) and the alkene **18** (3.5 mg, 9% yield, white solid).

Compound **19**: $\mathbf{R_f}$ = 0.39 (50% EtOAc/hexanes). $[\alpha]_D^{19.2}$= -53.71 (*c* 1.0, $CHCl_3$). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.93 (dd, *J* = 7.6, 2.5 Hz, 1H), 3.63 (d, *J* = 10.2 Hz, 1H), 2.46 (dd, *J* = 14.5, 7.6 Hz, 1H), 2.30 (ddd, *J* = 15.5, 7.1, 2.7 Hz, 1H), 2.05 – 1.92 (m, 2H), 1.72 – 1.64 (m, 1H), 1.62 – 1.54 (m, 2H), 1.25 (brs, 2H), 1.23 (s, 3H), 1.23 – 1.16 (m, 2H), 1.13 – 1.06 (m, 1H), 1.06 (d, *J* = 6.9 Hz, 6H), 0.89 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 85.62 (C), 85.26 (C), 73.43 (CH), 70.97 (CH), 47.96 (CH), 47.86 (CH), 41.93 (CH_2), 32.13 (CH), 31.53 (CH_2), 30.61 (CH), 25.94 (CH_2), 19.39 (CH_3), 18.38 (CH_3), 17.57 (CH_3), 17.09 (CH_3). **LRMS** (*m/z*, ESI): 277.12 $[M+Na]^+$, 237.18, 201.16. **HRMS-ESI** Calculated for $C_{15}H_{26}NaO_3$ $[M+Na]^+$: 277.1774, found 277.1772. The relative stereochemistry of the compound **19** was determined by nOe experiments (Figure 7).

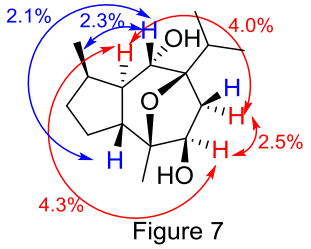


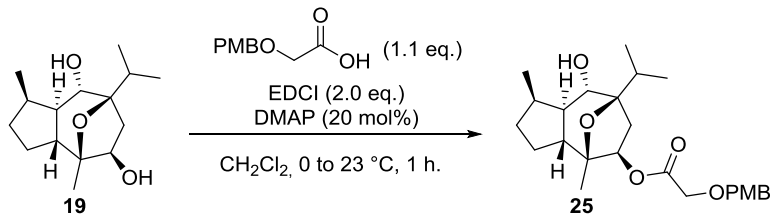
Figure 7

Compound **18**: $\mathbf{R_f}$ = 0.36 (50% EtOAc/hexanes). $[\alpha]_D^{22.3}$= -144.26 (*c* 0.64, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.10 (dt, *J* = 5.9, 1.3 Hz, 1H), 5.84 (ddd, *J* = 5.9, 4.4, 2.9 Hz, 1H), 4.20 – 4.02 (m, 1H), 3.61 (dd, *J* = 10.6, 3.6 Hz, 1H), 2.53 (dd, *J* = 14.6, 7.4 Hz, 1H), 2.23 (dddd, *J* = 14.2, 6.1, 3.1, 0.7 Hz, 1H), 2.17 – 2.03 (m, 1H), 1.99 (p, *J* = 7.0 Hz, 1H), 1.95 – 1.77 (m, 1H), 1.74 (dd, *J* = 12.3, 6.1 Hz, 1H), 1.64 (dd, *J* = 14.6, 2.6 Hz, 1H), 1.58 (brs, 1H), 1.50 – 1.39 (m, 1H), 1.25 (s, 3H), 1.06 (dd, *J* = 6.9, 1.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) 132.72 (CH), 131.96 (CH), 86.54 (C), 84.52 (C), 74.28 (CH), 72.64 (CH), 55.01 (CH), 49.37 (CH), 42.10 (CH_2), 32.49 (CH_2), 31.84 (CH), 18.76

[12] Compound **19** has been previously reported, see: a) H. Kusama, A. Tazawa, K. Ishida, N. Iwasawa, *Chem. Asian J.* **2016**, *11*, 64; b) J. Wang, S. G. Chen, B. F. Sun, G. Q. Lin, Y. J. Shang, *Chem. Eur. J.* **2013**, *19*, 2539.

(CH_3), 18.41 (CH_3), 17.40 (CH_3). **LRMS** (*m/z*, ESI): 239.23 $[M+H]^+$, 221.15, 141.02. **LRMS** (*m/z*, ESI): 261.14 $[M+Na]^+$, 221.15, 161.03. **HRMS-ESI** Calculated for $C_{14}H_{22}NaO_3$ $[M+Na]^+$: 261.1461, found 261.1449.

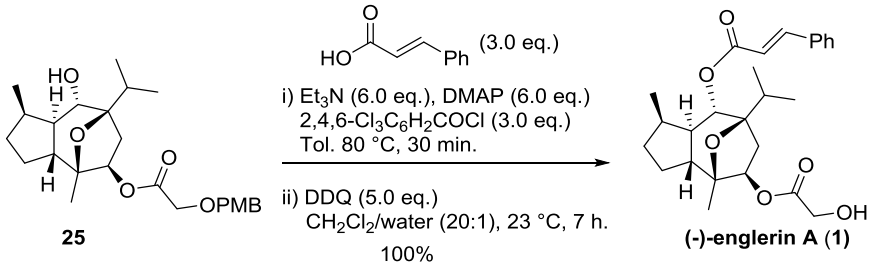
(1*R*,3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-8-hydroxy-7-isopropyl-1,4-dimethyldecahydro-4,7-epoxyazulen-5-yl 2-((4-methoxybenzyl)oxy)acetate (**25**): [13]



EDCI (31.7 mg, 0.165 mmol, 2.0 eq.) was added to a solution of the diol **19** (21.0 mg, 0.083 mmol, 1.0 eq.), 2-(4-methoxybenzyloxy)acetic acid (17.8 mg, 0.091 mmol, 1.1 eq.) and DMAP (2.0 mg, 0.017 mmol, 20 mol%) in CH_2Cl_2 (1.0 mL) at 0 °C. After stirring at 23 °C for 1 h, water (2.0 mL) was added, and the mixture was partitioned between EtOAc (30 mL) and water (5 mL). The organic layer was washed with NH_4Cl (sat.) (5 mL), water (5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4, filtered, concentrated in vacuo. The resulting crude residue was purified by flash chromatography (SiO_2, 5 to 30% EtOAc/hexanes) to afford **25** (28.9 mg, 83% yield) as a colorless oil.

R_f = 0.61 (50% EtOAc/hexanes). $[\alpha]_D^{23.1}$= -30.31 (*c* 0.92, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.2 Hz, 2H), 6.88 (d, *J* = 8.3 Hz, 2H), 5.12 (dd, *J* = 7.9, 2.9 Hz, 1H), 4.57 (s, 2H), 4.08 (s, 2H), 3.80 (s, 3H), 3.65 (d, *J* = 10.1 Hz, 1H), 2.46 (dd, *J* = 14.5, 7.9 Hz, 1H), 2.38 – 2.25 (m, 1H), 2.10 – 1.88 (m, 2H), 1.77 – 1.60 (m, 2H), 1.57 (dd, *J* = 12.7, 7.1 Hz, 1H), 1.37 (brs, 1H), 1.32 (dt, *J* = 10.2, 3.1 Hz, 1H), 1.27 – 1.18 (m, 2H), 1.16 (s, 3H), 1.05 (dd, *J* = 6.9, 2.8 Hz, 6H), 0.89 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.33 (CO), 159.63 (C), 129.88 (CH), 129.29 (C), 114.03 (CH), 86.05 (C), 84.52 (C), 75.81 (CH), 73.12 (CH_2), 70.75 (CH), 66.95 (CH_2), 55.42 (CH_3), 48.10 (CH), 48.04 (CH), 38.70 (CH_2), 32.25 (CH), 31.42 (CH_2), 30.65 (CH), 25.65 (CH_2), 19.17 (CH_3), 18.41 (CH_3), 17.53 (CH_3), 16.99 (CH_3). **LRMS** (*m/z*, ESI): 455.24 $[M+Na]^+$, 403.22, 373.25, 219.05. **HRMS-ESI** Calculated for $C_{25}H_{36}NaO_6$ $[M+Na]^+$: 455.2404, found 455.2403.

(-)-englerin A (**1**):



2,4,6-trichlorobenzoyl chloride (30 µL, 0.194 mmol, 3.0 eq.) was added to a solution of (*E*)-cinnamic acid (28.8 mg, 0.194 mmol, 3.0 eq.) and Et_3N (54 µL, 0.388 mmol, 6.0 eq.) in toluene (0.5 mL) at 0 °C and the resulting mixture was stirred at 23 °C for 2 h. Then, a solution of

[13] Compound **25** has been previously reported, see: T. Hanari, N. Shimada, Y. Kurosaki, N. Thrimurtulu, H. Nambu, M. Anada, S. Hashimoto, *Chem. Eur. J.* **2015**, *21*, 11671.

compound **25** (28.0 mg, 0.065 mmol, 1.0 eq.) in toluene (0.5 mL) was added followed by addition of DMAP (47.4 mg, 0.388 mmol) and the mixture was stirred at 80 °C for 30 min. After completion of the reaction, $NaHCO_3$ (sat.) was added, and the mixture was partitioned between EtOAc (30 mL) and water (5 mL). The organic layer was washed with NH_4Cl (sat.) (5 mL), water (5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The resulting crude mixture was purified by flash chromatography (SiO_2, 5 to 20% EtOAc/hexanes) to afford the corresponding diester **26** (36.4 mg, 100%) as a colorless oil. $\mathbf{R_f}$ = 0.40 (20% EtOAc/hexanes). $[\alpha]_D^{24.4}$= -40.62 (*c* 0.81, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.53 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.43 – 7.34 (m, 3H), 7.31 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.39 (d, *J* = 15.9 Hz, 1H), 5.20 (dd, *J* = 7.9, 3.0 Hz, 1H), 5.13 (d, *J* = 10.2 Hz, 1H), 4.59 (s, 2H), 4.10 (s, 2H), 3.81 (s, 3H), 2.67 (dd, *J* = 14.5, 7.9 Hz, 1H), 2.14 (h, *J* = 7.1 Hz, 1H), 2.02 – 1.93 (m, 1H), 1.89 (p, *J* = 7.1 Hz, 1H), 1.83 – 1.67 (m, 3H), 1.58 – 1.51 (m, 1H), 1.35 – 1.23 (m, 2H), 1.21 (s, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.95 (dd, *J* = 9.4, 7.1 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.21 (CO), 165.56 (CO), 159.49 (C), 145.10 (CH), 134.24 (C), 130.35 (CH), 129.71 (CH), 129.07 (C), 128.86 (CH), 128.08 (CH), 117.97 (CH), 113.86 (CH), 85.43 (C), 84.49 (C), 75.52 (CH), 72.98 (CH_2), 71.19 (CH), 66.78 (CH_2), 55.25 (CH_3), 47.49 (CH), 46.89 (CH), 39.92 (CH_2), 32.95 (CH), 31.16 (CH), 30.92 (CH_2), 24.55 (CH_2), 19.02 (CH_3), 18.18 (CH_3), 17.44 (CH_3), 16.87 (CH_3). **LRMS** (*m/z*, ESI): 585.28 $[M+Na]^+$, 437.23, 389.20, 219.06. **HRMS-ESI** Calculated for $C_{34}H_{42}NaO_7$ $[M+Na]^+$: 585.2823, found 585.2815.

DDQ (40.7 mg, 0.179 mmol, 5.0 eq.) was added to a solution of diester **26** (20.2 mg, 0.036 mmol, 1.0 eq.) in CH_2Cl_2 (0.38 mL) and water (19 µL) at 0 °C, and the mixture was stirred at 23 °C for 7 h. After completion of the reaction, $NaHCO_3$ (sat.) (2 mL) was added and the mixture was partitioned between EtOAc (40 mL) and water (5 mL). The organic layer was washed with $NaHCO_3$ (sat.) (5 mL), water (5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The resulting crude residue was purified by flash chromatography (SiO_2, 10 to 20% EtOAc/hexanes) to afford (-)-englerin A (15.9 mg, 100%) as a white amorphous solid.

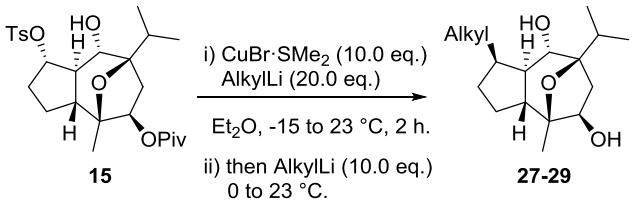
$\mathbf{R_f}$ = 0.36 (20% EtOAc/hexanes). $[\alpha]_D^{18.6}$= -47.86 (*c* 0.21, MeOH). **^{1}H NMR** (500 MHz, CD_3OD) δ 7.69 (d, *J* = 16.0 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.43 – 7.37 (m, 3H), 6.51 (d, *J* = 16.0 Hz, 1H), 5.26 (dd, *J* = 8.0, 3.0 Hz, 1H), 5.12 (d, *J* = 10.1 Hz, 1H), 4.15 (s, 2H), 2.70 (dd, *J* = 14.5, 8.0 Hz, 1H), 2.13 (h, *J* = 7.0 Hz, 1H), 2.03 – 1.95 (m, 1H), 1.91 – 1.81 (m, 2H), 1.79 – 1.72 (m, 2H), 1.70 – 1.65 (m, 1H), 1.35 – 1.24 (m, 3H), 1.19 (s, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 7.1 Hz, 3H), 0.93 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, CD_3OD) δ 173.96 (CO), 167.31 (CO), 146.78 (CH), 135.65 (C), 131.64 (CH), 130.06 (CH), 129.33 (CH), 118.79 (CH), 86.67 (C), 86.05 (C), 76.63 (CH), 72.45 (CH), 61.03 (CH_2), 48.91 (CH), 48.01 (CH), 40.71 (CH_2), 34.09 (CH), 32.46 (CH), 32.00 (CH_2), 25.52 (CH_2), 19.24 (CH_3), 18.58 (CH_3), 17.74 (CH_3), 17.24 (CH_3). **LRMS** (m/z, ESI): 465.22 $[M+Na]^+$, 443.23 $[M+H]^+$, 425.23, 219.16. **HRMS-ESI** Calculated for $C_{26}H_{34}NaO_6$ $[M+Na]^+$: 465.2248, found 465.2246.

NMR (Methanol-d_4, 500 MHz) data for natural and synthetic (-)-englerin A

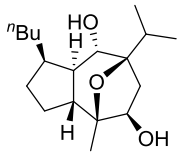
δ_H (m, *J* (Hz), xH)			δ_C		
Natural	Synthetic	Δ	Natural	Synthetic	Δ
7.68 (d, 16.0, 1H)	7.69 (d, 16.0, 1H)	0.01	173.94	173.96	0.02
7.61 (m, 2H)	7.61 (m, 2H)	0.00	167.26	167.31	0.05
7.40 (brdd, 3.5, 3.0, 3H)	7.41 (m, 3H)	0.01	146.75	146.78	0.03
6.50 (d, 16.0, 1H)	6.51 (d, 16.0, 1H)	0.01	135.62	135.65	0.03
5.23 (dd, 8.0, 2.5, 1H)	5.26 (dd, 8.0, 3.0, 1H)	0.03	131.64	131.64	0.00
5.10 (d, 10.0, 1H)	5.12 (d, 10.1, 1H)	0.02	130.06	130.06	0.00
4.14 (brs, 2H)	4.15 (s, 2H)	0.01	129.33	129.33	0.00
2.67 (dd, 14.0, 8.0, 1H)	2.70 (dd, 14.5, 8.0, 1H)	0.03	118.80	118.79	-0.01
2.12 (m, 1H)	2.13 (m, 1H)	0.01	86.44	86.67	0.23
1.98 (m, 1H)	2.00 (m, 1H)	0.02	86.01	86.05	0.04
1.86 (dd, 14.0, 2.5, 1H)	1.86 (m, 2H)	0.00	76.61	76.63	0.02
1.86 (m, 1H)	-	-	72.43	72.45	0.02
1.73 (m, 1H)	1.75 (m, 2H)	0.02	61.03	61.03	0.00
1.71 (m, 1H)	-	-	48.89	48.91	0.02
1.63 (m, 1H)	1.68 (m, 1H)	0.05	47.99	48.01	0.02
1.30 (m, 2H)	1.30 (m, 2H)	0.00	40.69	40.71	0.02
1.18 (s, 3H)	1.19 (s, 3H)	0.01	34.04	34.09	0.05
1.00 (d, 7.0, 3H)	1.01 (d, 6.8, 3H)	0.01	32.43	32.46	0.03
0.95 (d, 7.0, 3H)	0.96 (d, 7.1, 3H)	0.01	31.99	32.00	0.01
0.92 (d, 7.0, 3H)	0.93 (d, 7.1, 3H)	0.01	25.52	25.52	0.00
			19.25	19.24	-0.01
			18.59	18.58	-0.01
			17.77	17.74	-0.03
			17.27	17.24	-0.03

Synthesis of (-)-englerin A analogues

S_N2 substitutions with cuprates $(Alkyl)_2CuLi{\cdot}SMe_2$ (27-29):[14]



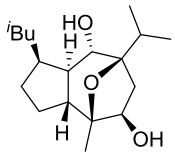
(1*R*,3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-1-butyl-7-isopropyl-4-methyldecahydro-4,7-epoxyazulene-5,8-diol (27):



27

39% yield (unoptimized). $\mathbf{R_f}$ = 0.37 (20% EtOAc/hexanes). $[\alpha]_D^{22.3}$= -22.30 (*c* 0.91, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.92 (dd, *J* = 7.6, 2.5 Hz, 1H), 3.67 (d, *J* = 10.2 Hz, 1H), 2.45 (dd, *J* = 14.5, 7.6 Hz, 1H), 2.15 – 2.03 (m, 1H), 1.98 (dt, *J* = 13.8, 6.9 Hz, 1H), 1.92 – 1.79 (m, 1H), 1.73 – 1.63 (m, 1H), 1.63 – 1.58 (m, 1H), 1.58 – 1.49 (m, 2H), 1.49 – 1.39 (m, 3H), 1.39 – 1.24 (m, 6H), 1.21 (s, 3H), 1.06 (d, *J* = 6.9 Hz, 6H), 1.02 – 0.94 (m, 1H), 0.89 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 85.65 (C), 85.27 (C), 73.36 (CH), 70.85 (CH), 48.76 (CH), 48.05 (CH), 41.90 (CH_2), 36.45 (CH), 32.12 (CH), 30.67 (CH_2), 30.17 (CH_2), 28.84 (CH_2), 26.11 (CH_2), 23.15 (CH_2), 19.39 (CH_3), 18.39 (CH_3), 17.57 (CH_3), 14.33 (CH_3). **LRMS** (*m/z*, ESI): 319.22 $[M+Na]^+$, 290.15, 282.27, 261.22, 243.21. **HRMS-ESI** Calculated for $C_{18}H_{32}NaO_3$ $[M+Na]^+$: 319.2244, found 219.2237.

(1*R*,3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-1-isobutyl-7-isopropyl-4-methyldecahydro-4,7-epoxyazulene-5,8-diol (28):

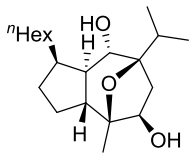


28

41% yield (unoptimized). $\mathbf{R_f}$ = 0.41 (50% EtOAc/hexanes). $[\alpha]_D^{21.6}$= -58.21 (*c* 0.99, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.92 (t, *J* = 5.9 Hz, 1H), 3.65 (d, *J* = 10.2 Hz, 1H), 2.44 (dd, *J* = 14.5, 7.6 Hz, 1H), 2.22 (dtt, *J* = 11.4, 7.6, 3.4 Hz, 1H), 1.98 (hept, *J* = 7.0 Hz, 1H), 1.91 – 1.78 (m, 1H), 1.72 – 1.62 (m, 1H), 1.65 – 1.47 (m, 3H), 1.44 (d, *J* = 6.9 Hz, 1H), 1.38 – 1.23 (m, 3H), 1.21 (s, 3H), 1.21 – 1.12 (m, 1H), 1.10 (d, *J* = 10.5 Hz, 1H), 1.06 (d, *J* = 6.8 Hz, 6H), 1.03 – 0.97 (m, 1H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 85.64 (C), 85.25 (C), 73.34 (CH), 70.74 (CH), 48.78 (CH), 47.96 (CH), 41.91 (CH_2), 40.10 (CH_2), 33.70 (CH), 32.20 (CH), 28.70 (CH_2), 26.12 (CH_2), 25.60 (CH), 24.36 (CH_3), 21.67 (CH_3), 19.39 (CH_3), 18.39 (CH_3), 17.58 (CH_3). **LRMS** (*m/z*, ESI): 319.22 $[M+Na]^+$, 261.22, 243.21. **HRMS-ESI** Calculated for $C_{18}H_{32}NaO_3$ $[M+Na]^+$: 319.2244, found 319.2245.

[14] Prepared following the same procedure previously used for the preparation of the **19**, but using the corresponding cuprate obtained from the desired alkyllithium and $CuBr{\cdot}SMe_2$.

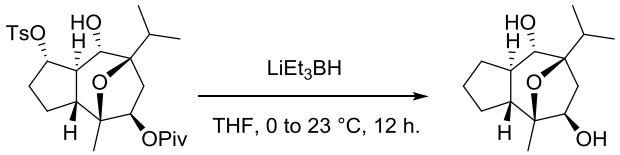
(1*R*,3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-1-hexyl-7-isopropyl-4-methyldecahydro-4,7-epoxyazulene-5,8-diol (29):



29

35% yield (unoptimized). $\mathbf{R_f}$ = 0.49 (50% EtOAc/hexanes). $[\alpha]_D^{24.4}$= -73.86 (*c* 0.49, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.92 (d, *J* = 5.9 Hz, 1H), 3.67 (d, *J* = 10.2 Hz, 1H), 2.45 (dd, *J* = 14.5, 7.6 Hz, 1H), 2.15 – 2.01 (m, 1H), 1.98 (p, *J* = 6.9 Hz, 1H), 1.92 – 1.79 (m, 1H), 1.71 – 1.62 (m, 1H), 1.61 – 1.49 (m, 3H), 1.48 – 1.41 (m, 1H), 1.41 – 1.22 (m, 11H), 1.22 (s, 3H), 1.18 – 1.10 (m, 1H), 1.06 (d, *J* = 6.9 Hz, 6H), 1.03 – 0.91 (m, 1H), 0.88 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 85.64 (C), 85.27 (C), 73.37 (CH), 70.85 (CH), 48.77 (CH), 48.04 (CH), 41.90 (CH_2), 36.48 (CH), 32.11 (CH), 32.08 (CH_2), 31.02 (CH_2), 29.79 (CH_2), 28.85 (CH_2), 27.91 (CH_2), 26.11 (CH_2), 22.82 (CH_2), 19.39 (CH_3), 18.39 (CH_3), 17.56 (CH_3), 14.24 (CH_3). **LRMS** (*m/z*, ESI): 347.28 $[M+Na]^+$, 307.26, 289.25, 282.28. **HRMS-ESI** Calculated for $C_{20}H_{36}NaO_3$ $[M+Na]^+$: 347.2557, found 347.2557.

(3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-7-isopropyl-4-methyldecahydro-4,7-epoxyazulene-5,8-diol (**30**):

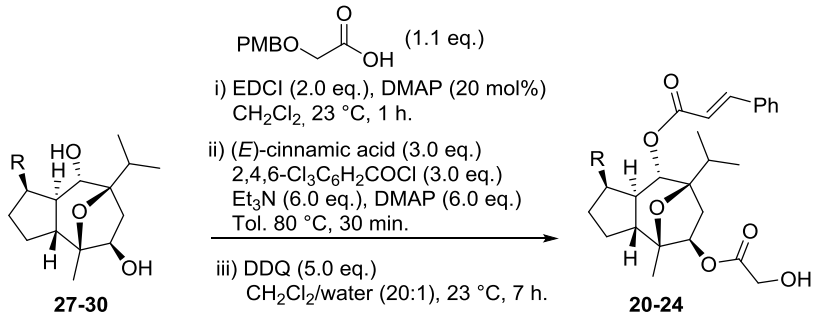


15 **30**

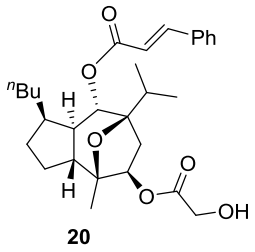
A solution of $LiEt_3BH$ (1.0M in THF, 849 µL, 0.849 mmol, 7.0 eq.) was added dropwise to a solution of **15** (60.0 mg, 0.121 mmol, 1.0 eq.) in THF (750 µL) at 0 °C. The mixture was stirred at 23 °C for 12 h. After completion of the reaction, water (2 mL) was added and the volatile materials were concentrated in vacuo. The aqueous layer was extracted with CH_2Cl_2 (3× 10 mL) and the organic phase was dried over anhydrous Na_2SO_4, filtered, concentrated in vacuo to give a crude residue which was purified by flash chromatography (SiO_2, 10 to 60% EtOAc/hexanes with 10% CH_2Cl_2) to afford the corresponding diol **30** (16.9 mg, 58% yield).

$\mathbf{R_f}$ = 0.26 (50% EtOAc/hexanes). $[\alpha]_D^{23.4}$= -35.77 (*c* 0.84 $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.92 (td, *J* = 7.4, 2.5 Hz, 1H), 3.53 – 3.43 (m, 1H), 2.47 (dd, *J* = 14.5, 7.5 Hz, 1H), 2.03 – 1.90 (m, 2H), 1.79 – 1.62 (m, 3H), 1.63 – 1.57 (m, 1H), 1.41 – 1.33 (m, 3H), 1.26(dd, *J* = 6.1, 3.2 Hz, 1H), 1.22 (s, 3H), 1.19 – 1.09 (m, 2H), 1.06 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 85.76 (C), 85.17 (C), 75.17 (CH), 73.53 (CH), 52.56 (CH), 45.51 (CH), 42.24 (CH_2), 31.80 (CH), 28.12 (CH_2), 25.55 (CH_2), 21.70 (CH_2), 19.25 (CH_3), 18.32 (CH_3), 17.42 (CH_3). **LRMS** (*m/z*, ESI): 263.16 $[M+Na]^+$, 223.17, 221.16, 203.15. **HRMS-ESI** Calculated for $C_{14}H_{24}NaO_3$ $[M+Na]^+$: 263.1623, found 263.1617.

Esterification of diols 27-30:[15]

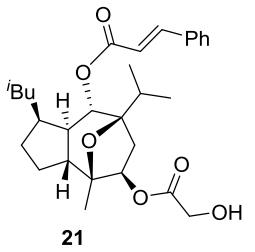


(1*R*,3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-1-butyl-5-(2-hydroxyacetoxy)-7-isopropyl-4-methyldecahydro-4,7-epoxyazulen-8-yl cinnamate (20):


20

52% yield, 3 steps from **27** (unoptimized) $\mathbf{R_f}$ = 0.38 (20% EtOAc/hexanes). $[\alpha]_D^{19.6}$= -62.82 (*c* 1.0 $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 16.0 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.45 – 7.34 (m, 3H), 6.39 (d, *J* = 16.0 Hz, 1H), 5.26 – 5.13 (m, 2H), 4.19 (d, *J* = 5.4 Hz, 2H), 2.68 (dd, *J* = 14.5, 7.9 Hz, 1H), 2.37 (t, *J* = 5.5 Hz, 1H), 1.89 (p, *J* = 6.9 Hz, 2H), 1.86 – 1.75 (m, 2H), 1.76 – 1.62 (m, 3H), 1.61 – 1.52 (m, 2H), 1.51 – 1.36 (m, 1H), 1.37 – 1.25 (m, 4H), 1.19 (s, 3H), 1.16 – 1.03 (m, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 7.1 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.22 (CO), 165.56 (CO), 145.15 (CH), 134.45 (C), 130.53 (CH), 129.05 (CH), 128.26 (CH), 118.19 (CH), 85.74 (C), 84.71 (C), 76.62 (CH), 71.15 (CH), 60.80 (CH_2), 48.48 (CH), 47.40 (CH), 40.02 (CH_2), 37.02 (CH), 33.15 (CH), 29.93 (CH_2), 29.47 (CH_2), 27.88 (CH_2), 24.91 (CH_2), 22.88 (CH_2), 19.10 (CH_3), 18.36 (CH_3), 17.62 (CH_3), 14.29 (CH_3). **LRMS** (*m/z*, ESI): 507.27 $[M+Na]^+$, 485.29 $[M+H]^+$,337.24, 261.22. **HRMS-ESI** Calculated for $C_{29}H_{40}NaO_6$ $[M+Na]^+$: 507.2717, found 507.2718.

(1*R*,3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-1-isobutyl-5-(2-hydroxyacetoxy)-7-isopropyl-4-methyldecahydro-4,7-epoxyazulen-8-yl cinnamate (21):

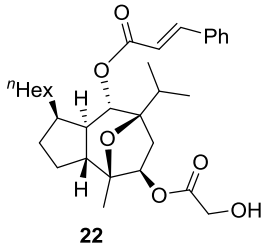

21

41% yield, 3 steps from **28** (unoptimized) $\mathbf{R_f}$ = 0.30 (20% EtOAc/hexanes). $[\alpha]_D^{19.9}$= -63.94 (*c* 0.93 $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 16.0 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.45 – 7.33 (m, 3H), 6.39 (d, *J* = 16.0 Hz, 1H), 5.22 (dd, *J* = 7.9, 3.0 Hz, 1H), 5.19 (d, *J* = 10.2 Hz, 1H), 4.20 (d, *J* = 5.4 Hz, 2H), 2.67 (dd, *J* = 14.5, 7.9 Hz, 1H), 2.36 (t, *J* = 5.5 Hz, 1H), 2.08 – 1.95 (m, 1H), 1.89 (p, *J* = 7.0 Hz, 1H), 1.84 – 1.68 (m, 4H), 1.63 – 1.53 (m, 1H), 1.52 – 1.33 (m, 3H), 1.32 – 1.23 (m, 3H), 1.19 (s, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 2H), 0.77 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.22 (CO), 165.46 (CO), 145.10 (CH), 134.47 (C), 130.52 (CH), 129.04 (CH), 128.27 (CH), 118.17 (CH), 85.73 (C), 84.76 (C), 76.63 (CH), 71.08 (CH), 60.80 (CH_2), 48.51 (CH), 47.49 (CH), 40.06 (CH_2), 38.88 (CH_2), 34.69 (CH), 33.24 (CH), 28.28 (CH_2), 25.83 (CH), 24.82 (CH_2), 24.46 (CH_3), 21.34 (CH_3), 19.10 (CH_3), 18.36 (CH_3), 17.63 (CH_3).

[15] Obtained following the previously described procedures for the preparation of the (-)-englerin A from **19**, but using the corresponding diol **27-30**, instead of **19** as starting material.

LRMS (*m/z*, ESI): 507.27 $[M+Na]^+$, 485.29 $[M+H]^+$, 372.26, 350.25. **HRMS-ESI** Calculated for $C_{29}H_{41}O_6$ $[M+H]^+$: 485.2898, found 485.2890.

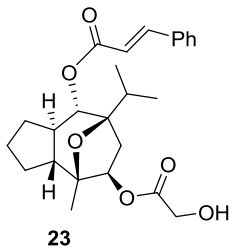
(1*R*,3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-1-hexyl-5-(2-hydroxyacetoxy)-7-isopropyl-4-methyldecahydro-4,7-epoxyazulen-8-yl cinnamate (22):



22

58% yield, 3 steps from **29** (unoptimized) $\mathbf{R_f}$ = 0.36 (50% EtOAc/hexanes). $[\alpha]_D^{22.2}$= -96.25 (*c* 0.80 $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 16.0 Hz, 1H), 7.59 – 7.47 (m, 2H), 7.48 – 7.32 (m, 3H), 6.39 (d, *J* = 16.0 Hz, 1H), 5.25 – 5.14 (m, 2H), 4.19 (d, *J* = 5.3 Hz, 2H), 2.67 (dd, *J* = 14.5, 7.9 Hz, 1H), 2.35 (t, *J* = 5.5 Hz, 1H), 1.89 (p, *J* = 6.9 Hz, 2H), 1.86 – 1.77 (m, 1H), 1.79 – 1.59 (m, 4H), 1.56 (brs, 2H), 1.50 – 1.38 (m, 1H), 1.37 – 1.20 (m, 8H), 1.19 (s, 3H), 1.15 – 1.05 (m, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 7.1 Hz, 3H), 0.88 – 0.83 (m, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.22 (CO), 165.57 (CO), 145.17 (CH), 134.45 (C), 130.53 (CH), 129.05 (CH), 128.26 (CH), 118.18 (CH), 85.75 (C), 84.71 (C), 76.62 (CH), 71.15 (CH), 60.79 (CH_2), 48.48 (CH), 47.39 (CH), 40.01 (CH_2), 37.01 (CH), 33.15 (CH), 32.01 (CH_2), 29.71 (CH_2), 29.48 (CH_2), 27.88 (CH_2), 27.61 (CH_2), 24.92 (CH_2), 22.82 (CH_2), 19.09 (CH_3), 18.36 (CH_3), 17.62 (CH_3), 14.26 (CH_3). **LRMS** (*m/z*, ESI): 536.31 $[M+Na]^+$, 513.32 $[M+H]^+$, 437.31, 381.30, 365.27. **HRMS-ESI** Calculated for $C_{31}H_{45}O_6$ $[M+H]^+$: 513.3211, found 513.3216.

(3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-5-(2-hydroxyacetoxy)-7-isopropyl-4-methyldecahydro-4,7-epoxyazulen-8-yl cinnamate (23):[16]

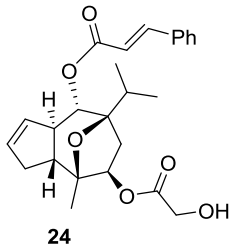


23

18% yield, 3 steps from **30** (unoptimized) $\mathbf{R_f}$ = 0.22 (20% EtOAc/hexanes). $[\alpha]_D^{24.0}$= -33.06 (*c* 0.37 $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.58 – 7.45 (m, 2H), 7.45 – 7.32 (m, 3H), 6.40 (d, *J* = 16.0 Hz, 1H), 5.19 (dd, *J* = 7.8, 3.0 Hz, 1H), 4.98 (d, *J* = 9.0 Hz, 1H), 4.20 (d, *J* = 5.3 Hz, 2H), 2.67 (dd, *J* = 14.5, 7.8 Hz, 1H), 2.35 (t, *J* = 5.5 Hz, 1H), 1.92 (p, *J* = 6.9 Hz, 1H), 1.86 – 1.77 (m, 2H), 1.77 – 1.59 (m, 3H), 1.52 (dd, *J* = 12.3, 6.5 Hz, 1H), 1.47 – 1.34 (m, 2H), 1.31 – 1.25 (m, 1H), 1.20 (s, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.21 (CO), 166.08 (CO), 145.35 (CH), 134.42 (C), 130.57 (CH), 129.06 (CH), 128.27 (CH), 118.04 (CH), 85.57 (C), 84.67 (C), 76.70 (CH), 74.97 (CH), 60.80 (CH_2), 52.42 (CH), 44.43 (CH), 40.58 (CH_2), 32.99 (CH), 28.64 (CH_2), 25.14 (CH_2), 21.41 (CH_2), 18.93 (CH_3), 18.39 (CH_3), 17.43 (CH_3). **LRMS** (*m/z*, ESI): 451.21 $[M+Na]^+$, 429.23 $[M+H]^+$, 381.29, 353.26, 282.28. **HRMS-ESI** Calculated for $C_{25}H_{32}NaO_6$ $[M+Na]^+$: 451.2091, found 451.2085.

[16] Compound **23** is known in its racemic form, see: L. Dong, X. Jiao, X. Liu, C. Tian, *J. Asian Nat. Prod. Res*., **2014**, *16*, 629.

(3a*R*,4*S*,5*R*,7*R*,8*S*,8a*R*)-5-(2-hydroxyacetoxy)-7-isopropyl-4-methyl-3,3a,4,5,6,7,8,8a-octahydro-4,7-epoxyazulen-8-yl cinnamate (24):[17]

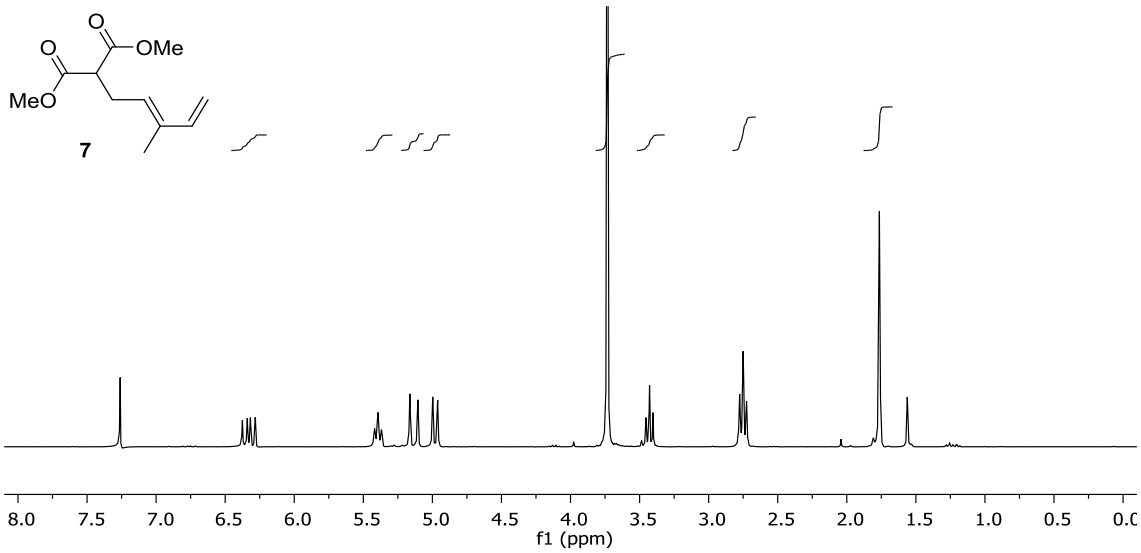


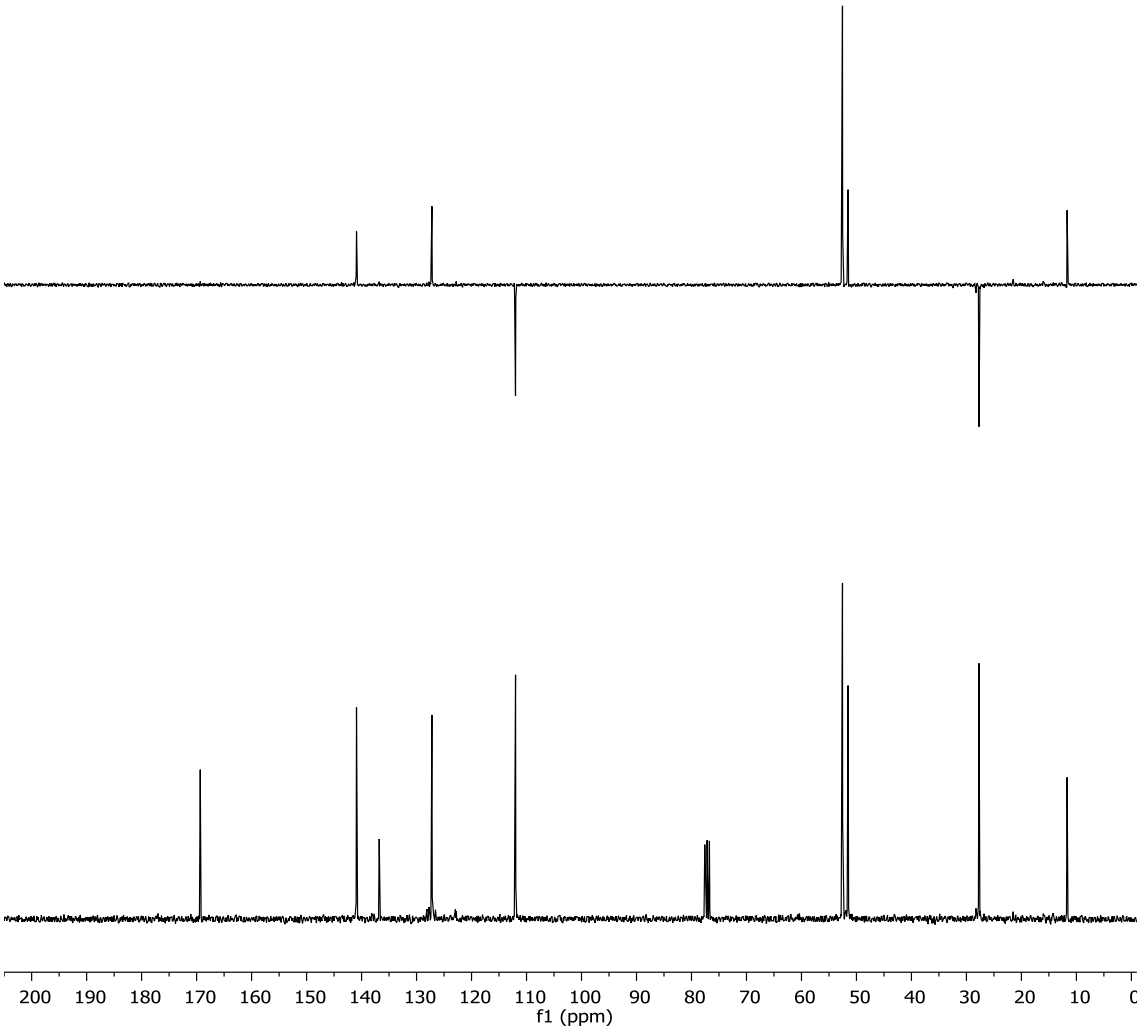
24

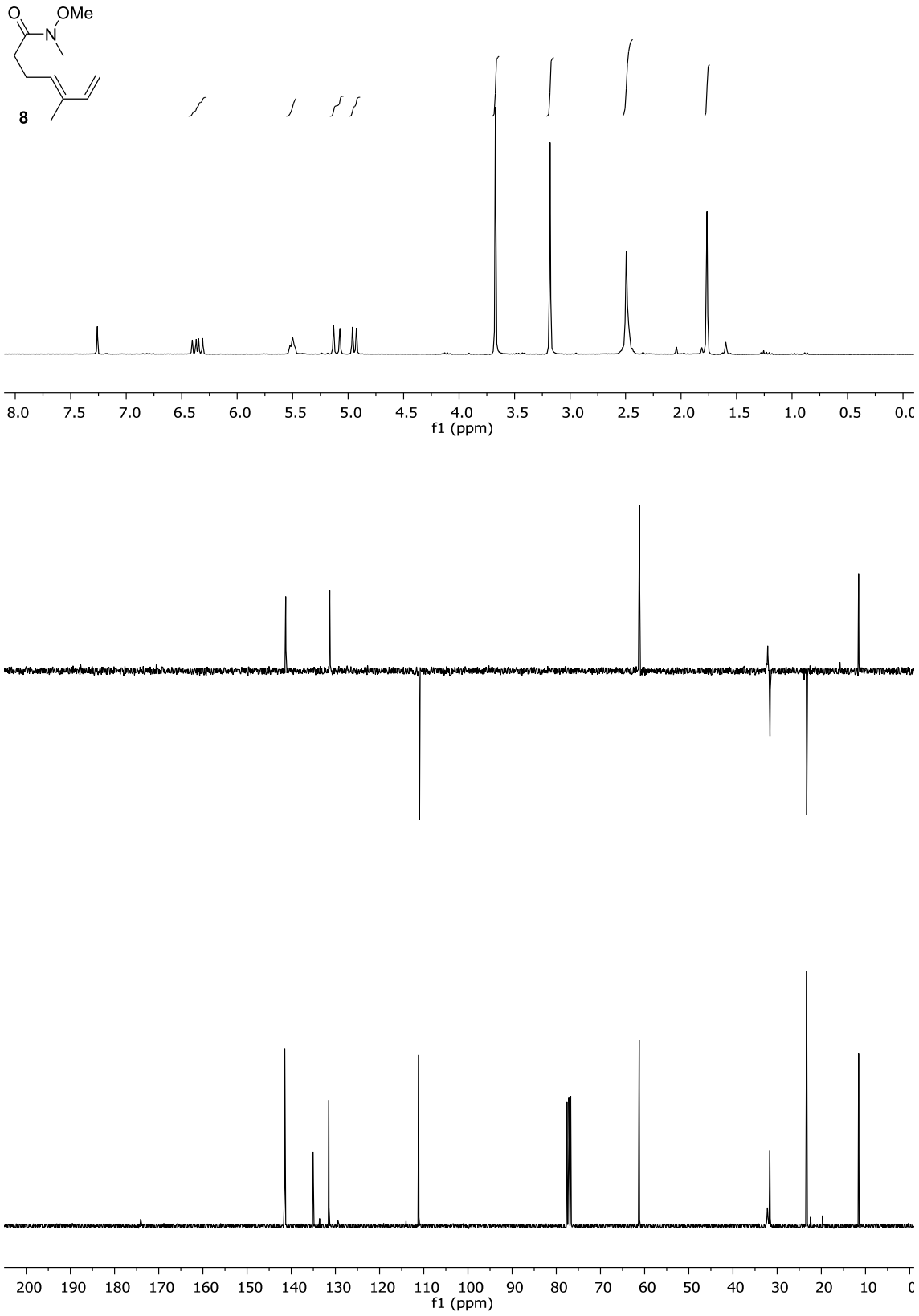
57% yield, (unoptimized). $\mathbf{R_f}$ = 0.30 (20% EtOAc/hexanes). $[\alpha]_D^{22.3}$= -60.60 (*c* 0.64 $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 16.0 Hz, 1H), 7.60 – 7.45 (m, 2H), 7.49 – 7.33 (m, 3H), 6.42 (d, *J* = 16.0 Hz, 1H), 5.97 (dd, *J* = 6.0, 1.8 Hz, 1H), 5.85 – 5.78 (m, 1H), 5.35 (dd, *J* = 7.7, 2.9 Hz, 1H), 5.04 (d, *J* = 10.3 Hz, 1H), 4.21 (brs, 2H), 2.73 (dd, *J* = 14.6, 7.7 Hz, 1H), 2.47 – 2.22 (m, 3H), 2.01 – 1.83 (m, 4H), 1.23 (s, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 7.1 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.19 (C), 166.17 (C), 145.58 (C), 134.38 (C), 133.17 (CH), 131.36 (CH), 130.65 (CH), 129.09 (CH), 128.31 (CH), 117.94 (CH), 86.27 (C), 83.96 (C), 77.15 (CH), 72.98 (CH), 60.80 (CH_2), 54.87 (CH), 48.20 (CH), 40.51 (CH_2), 32.98 (CH), 32.06 (CH_2), 18.49 (CH_3), 18.43 (CH_3), 17.38 (CH_3). **LRMS** (*m/z*, ESI): 449.19 $[M+Na]^+$, 427.21 $[M+H]^+$, 413.31, 351.19, 338.34. **HRMS-ESI** Calculated for $C_{25}H_{30}NaO_6$ $[M+Na]^+$: 449.1935, found 449.1933.

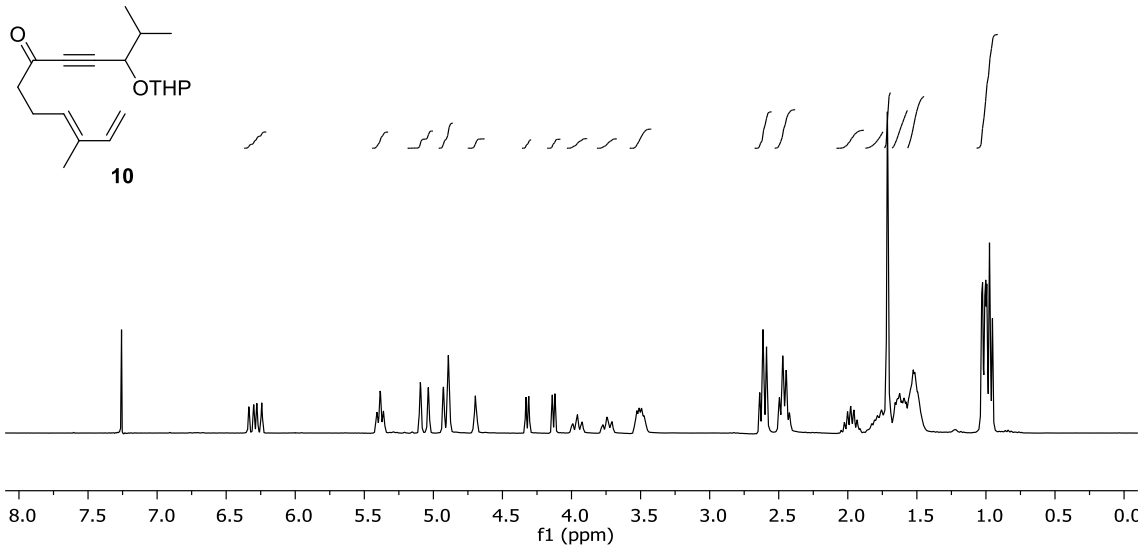
[17] Obtained following the previously described method for the preparation of the (-)-englerin A from **19**, but using **18** as starting material.

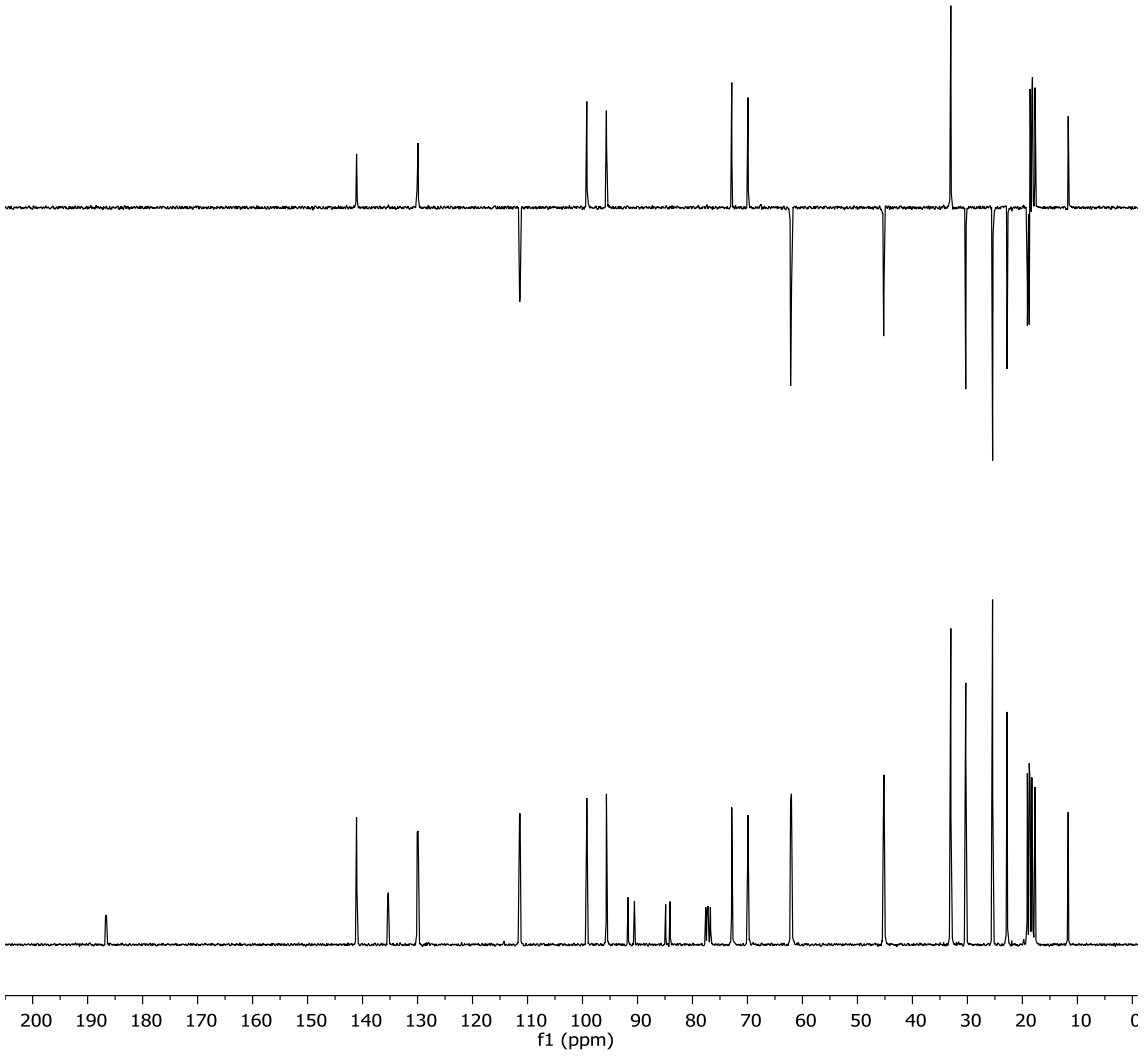
NMR Spectra

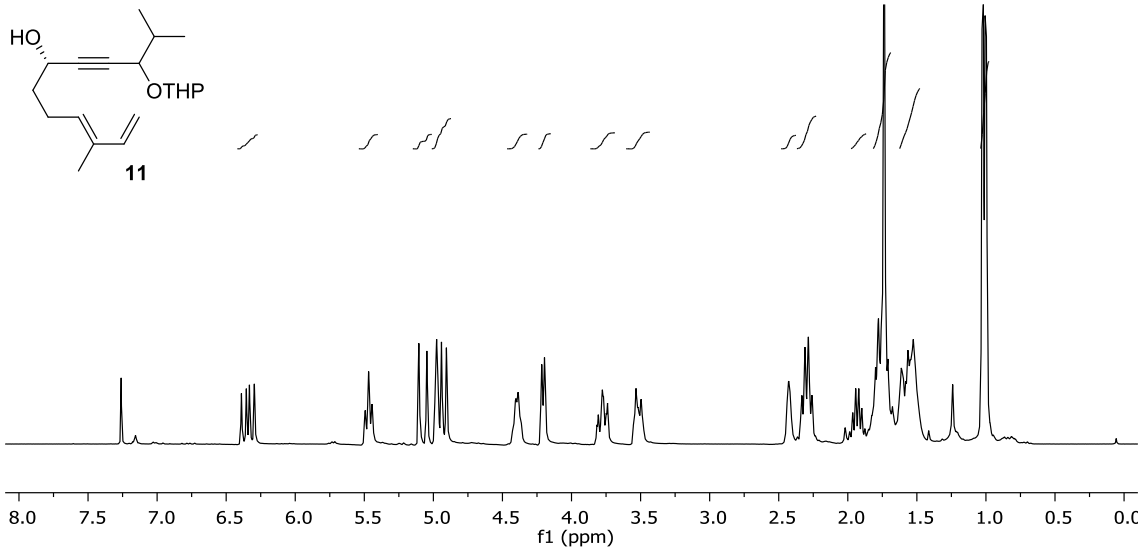

O
OMe
O
MeO
7
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

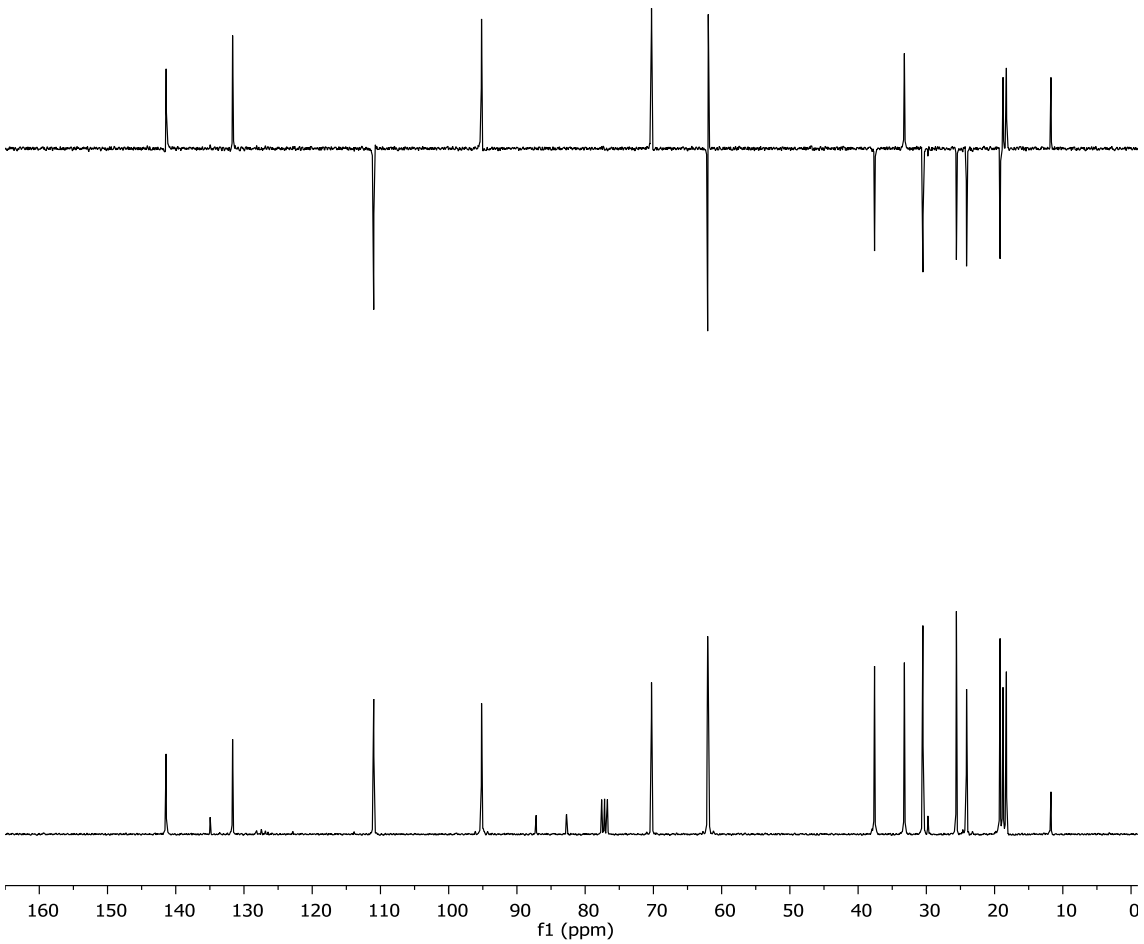

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

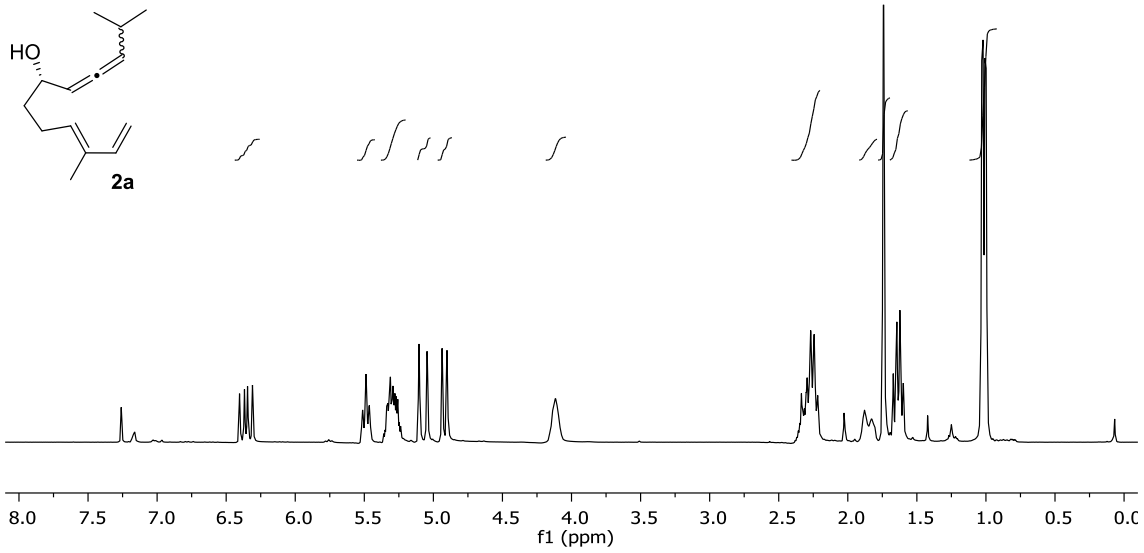

O
OMe
N
8
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

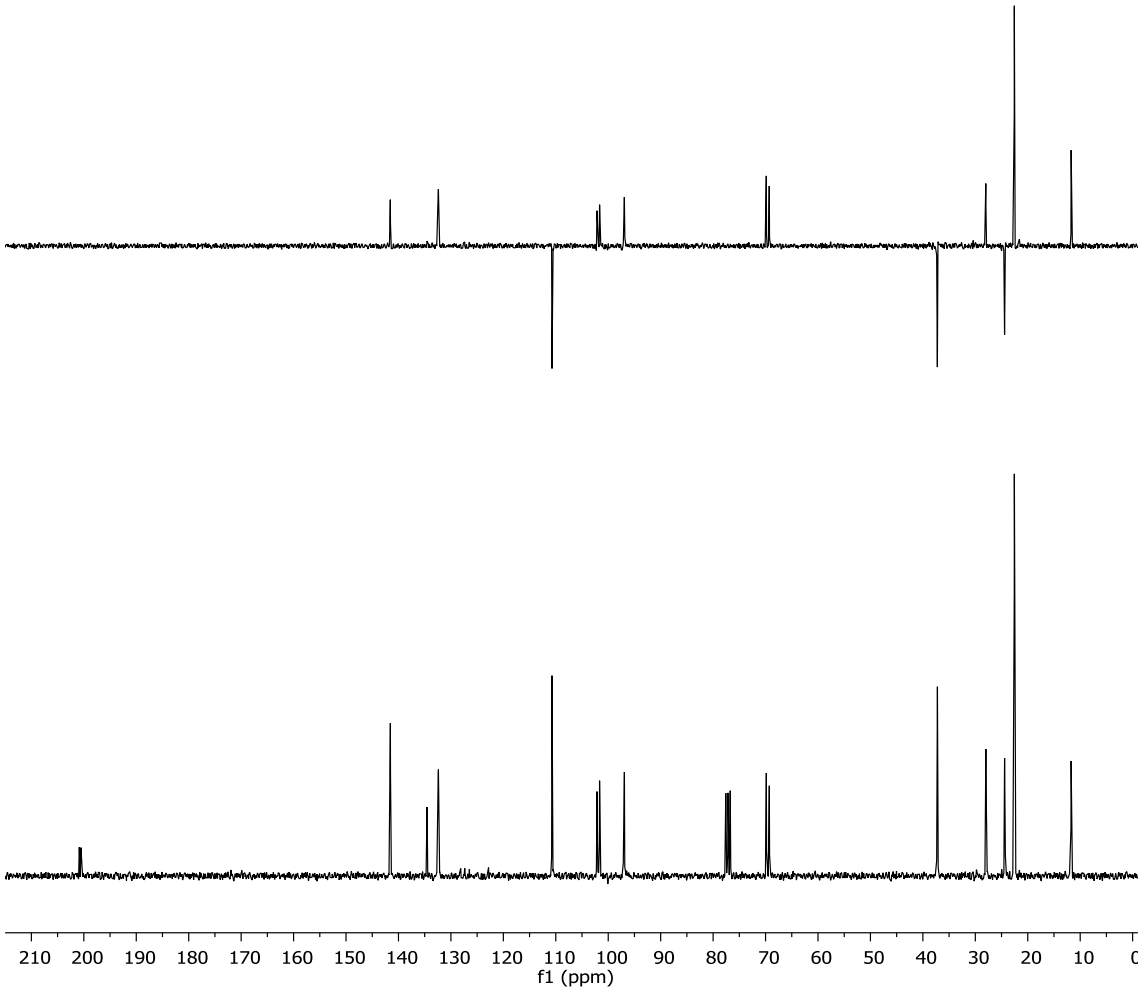

O
OTHP
10
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

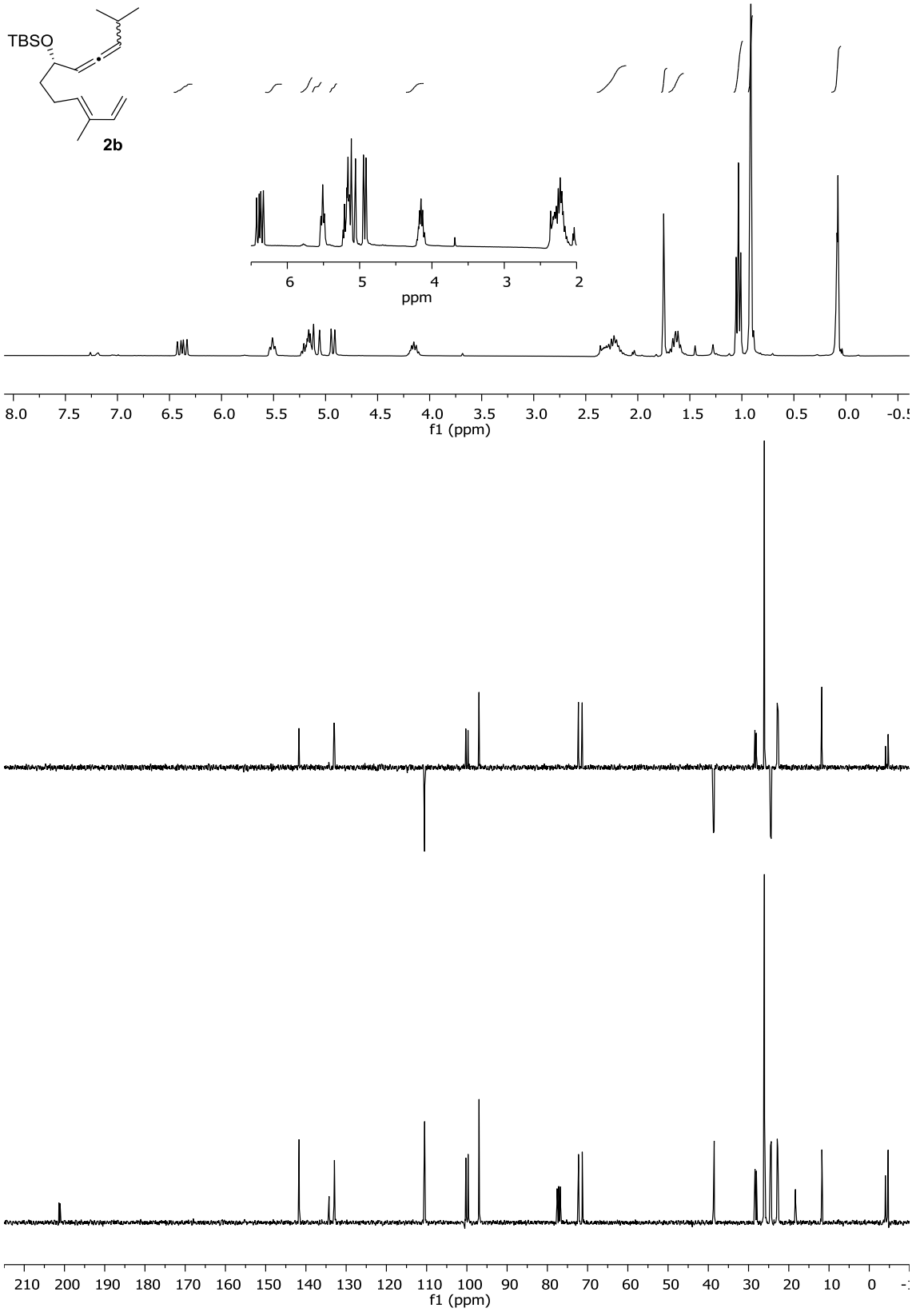

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

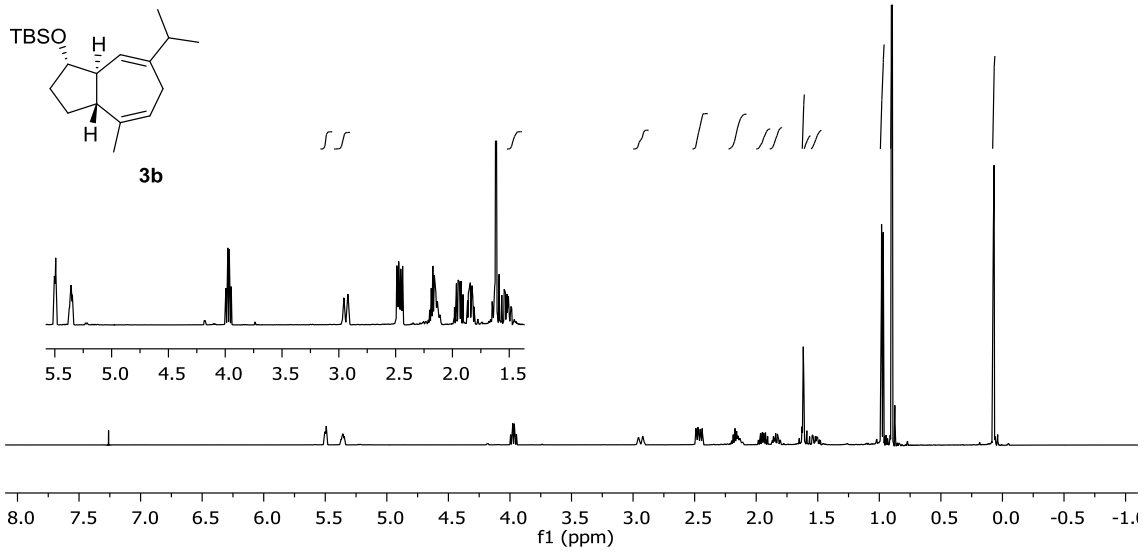

HO
OTHP
11
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

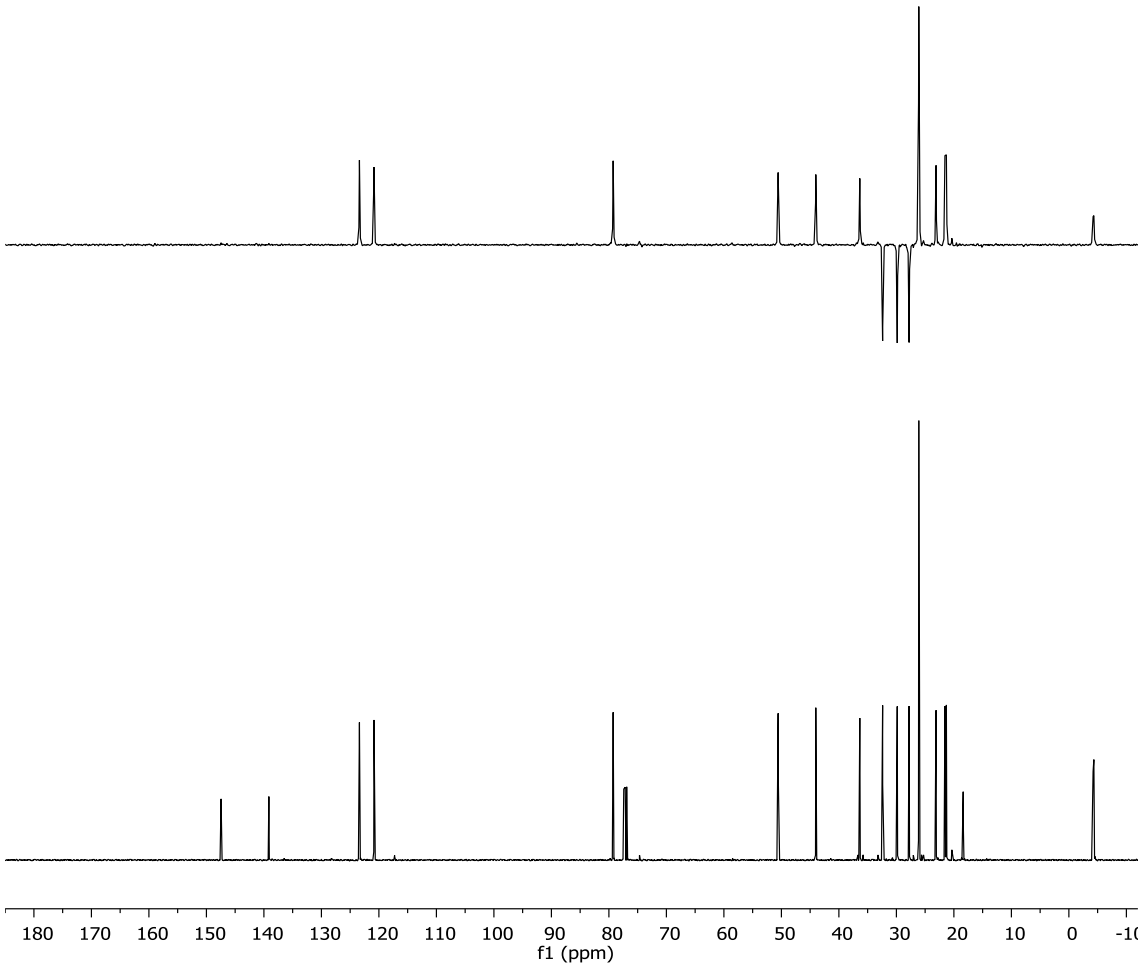

160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

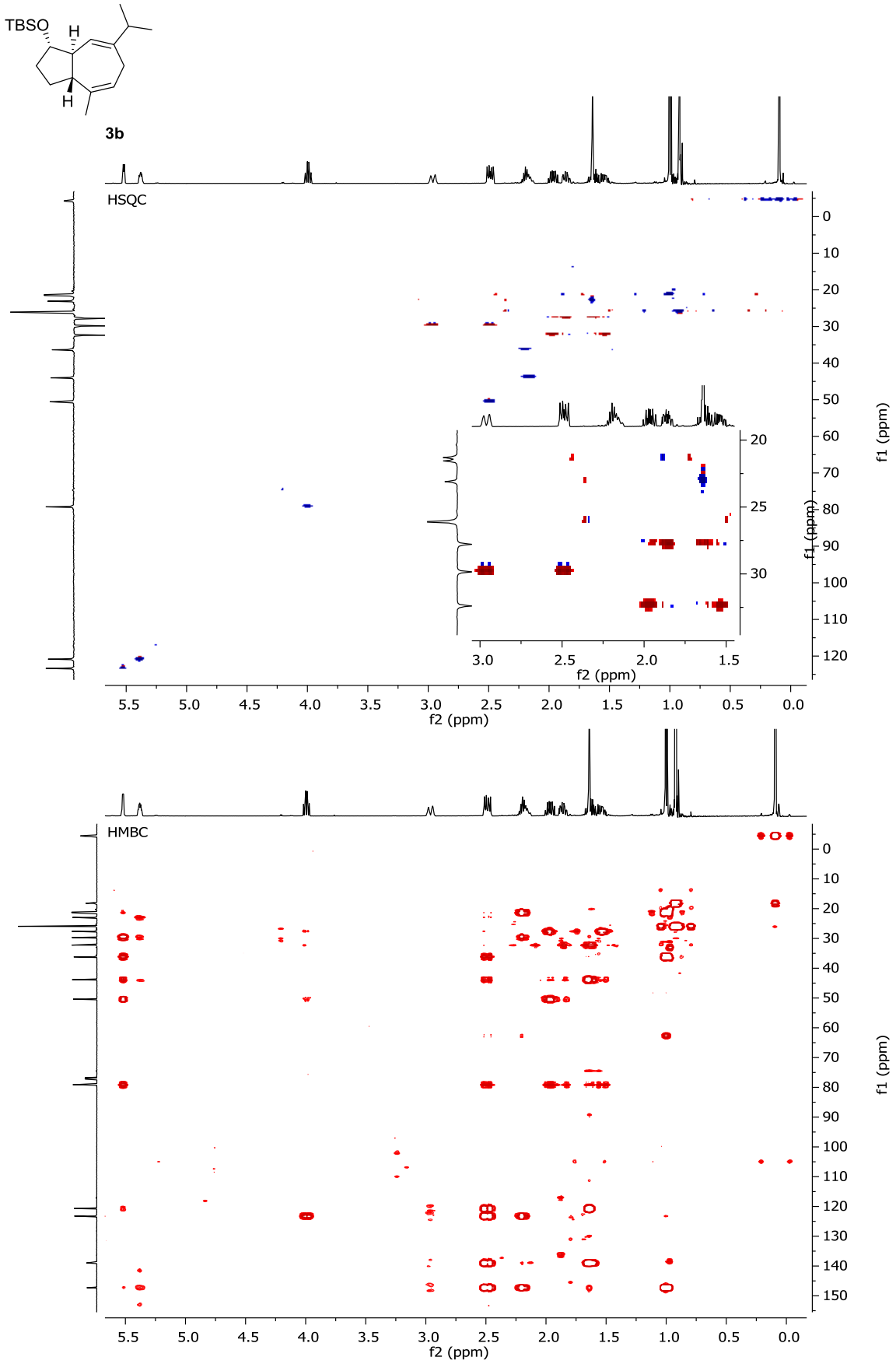

HO
2a
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

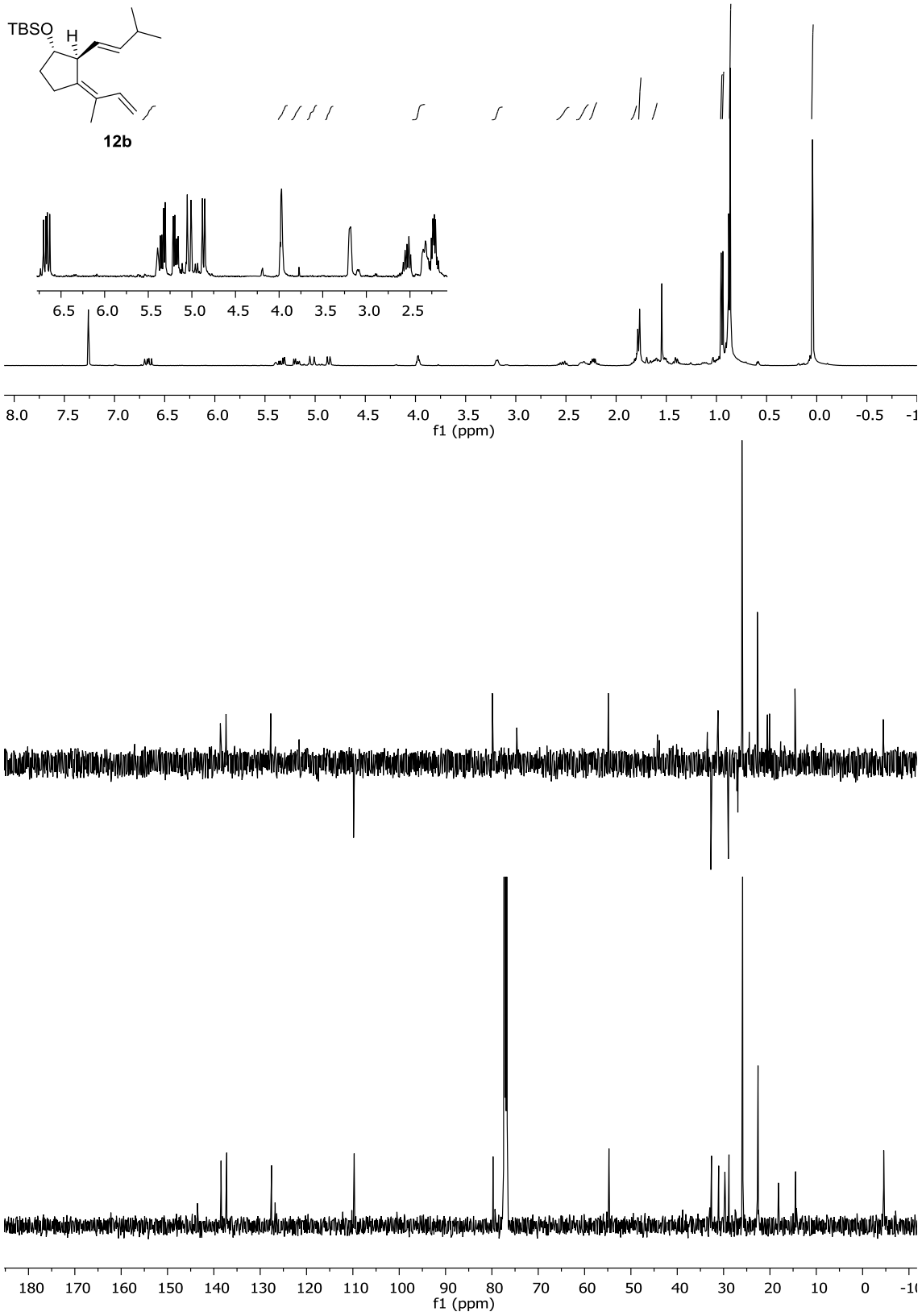

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

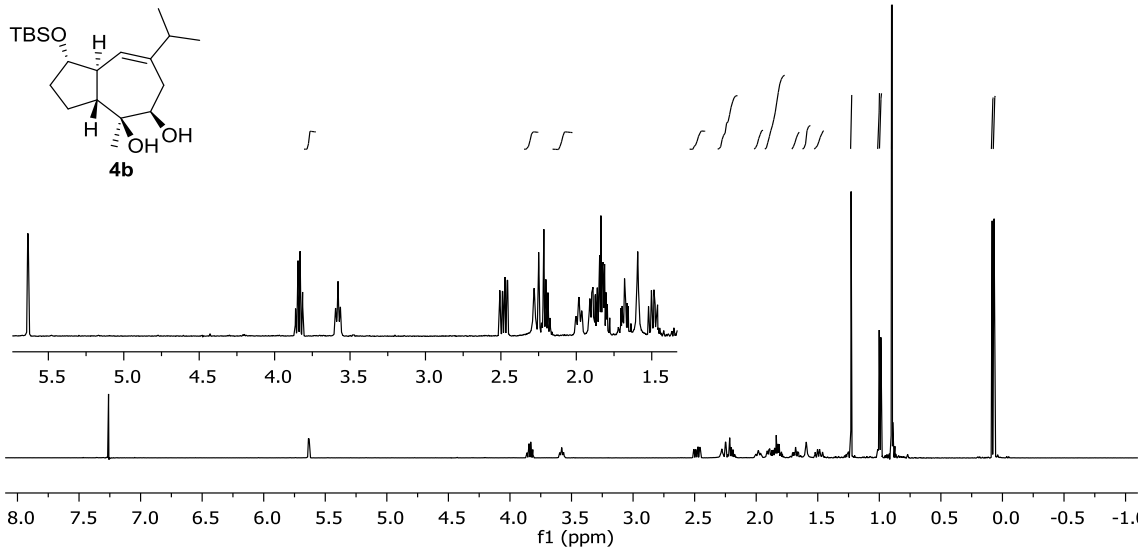

TBSO
2b
6
5
4
3
2
ppm
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

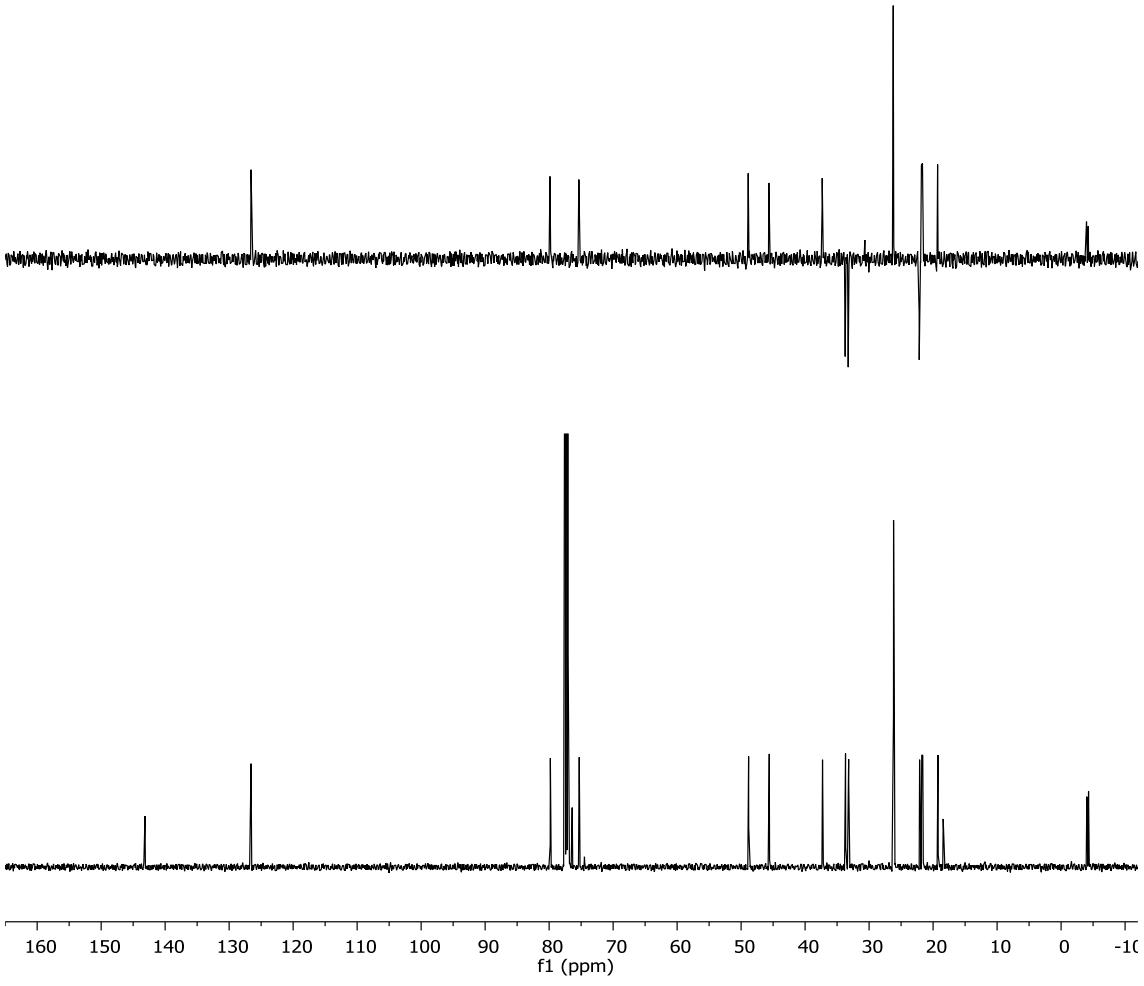

TBSO
H
H
3b
5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

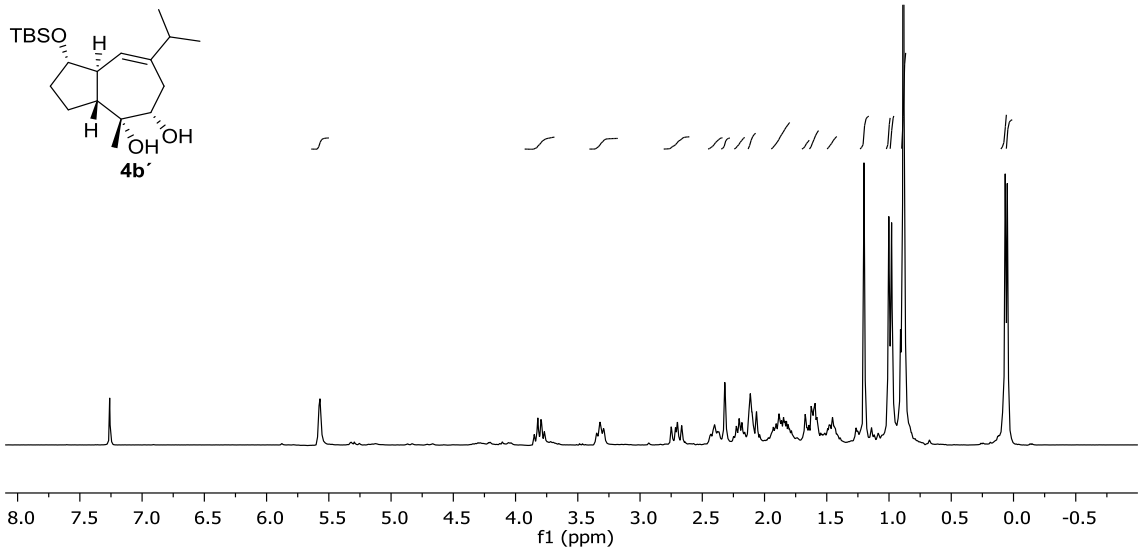

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

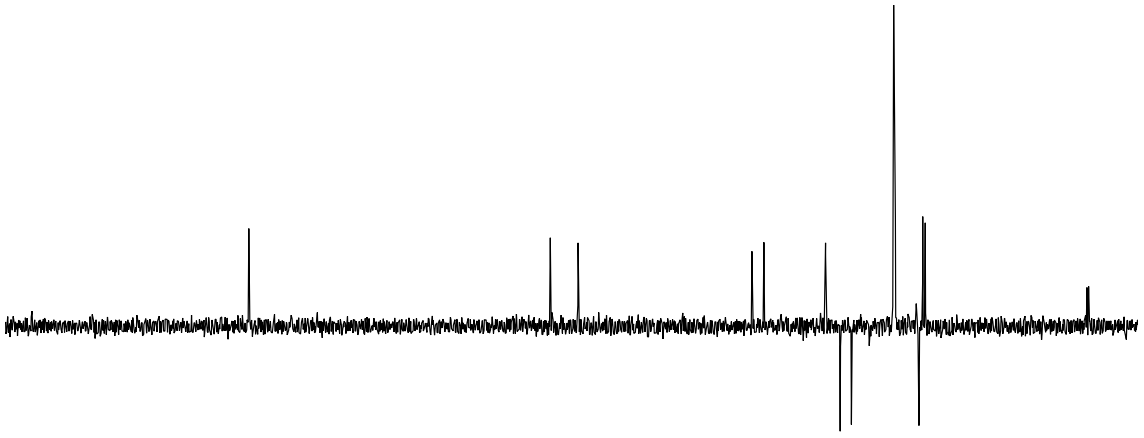

TBSO
H
H
3b
HSQC
f2 (ppm)
f1 (ppm)
HMBC
f2 (ppm)
f1 (ppm)

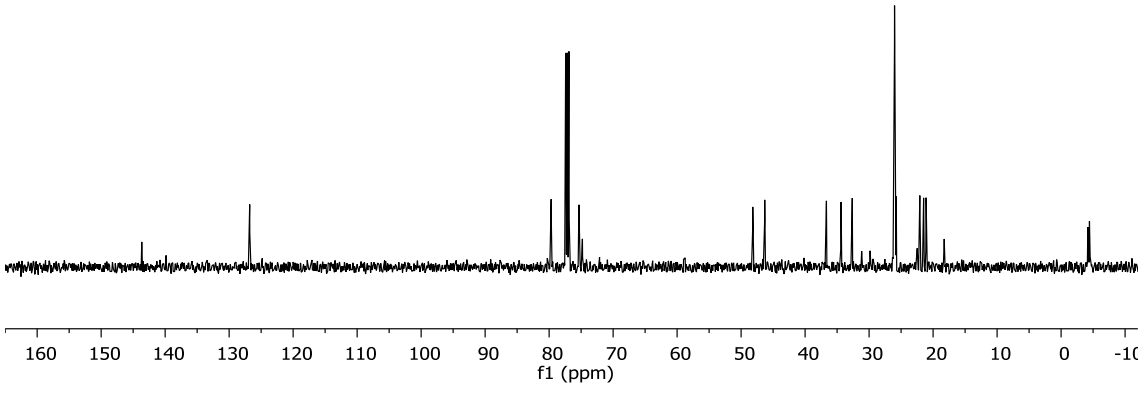

TBSO
H
12b
6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

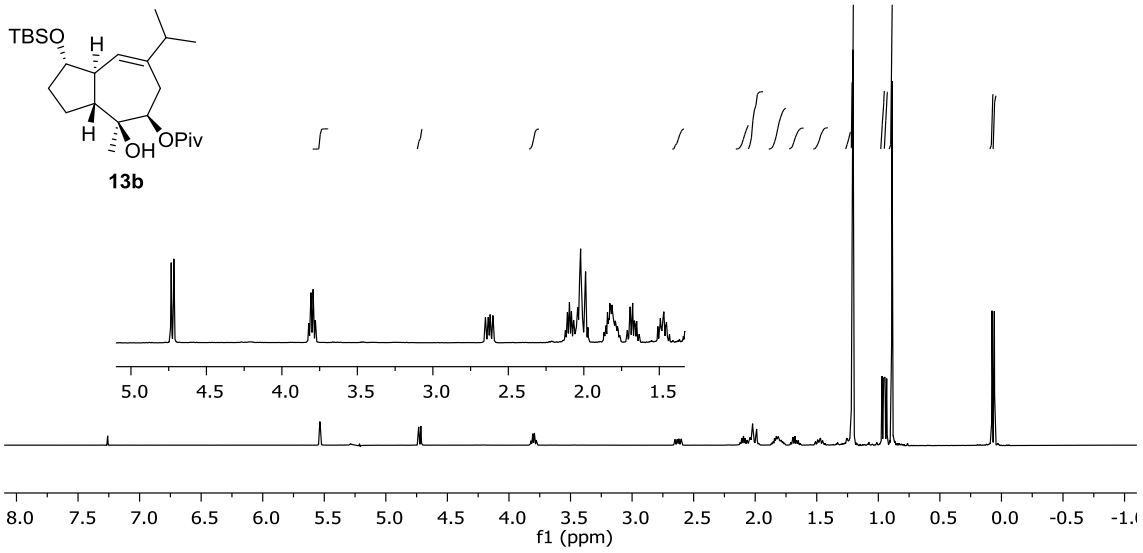

TBSO
H
H
OH
OH
4b
5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

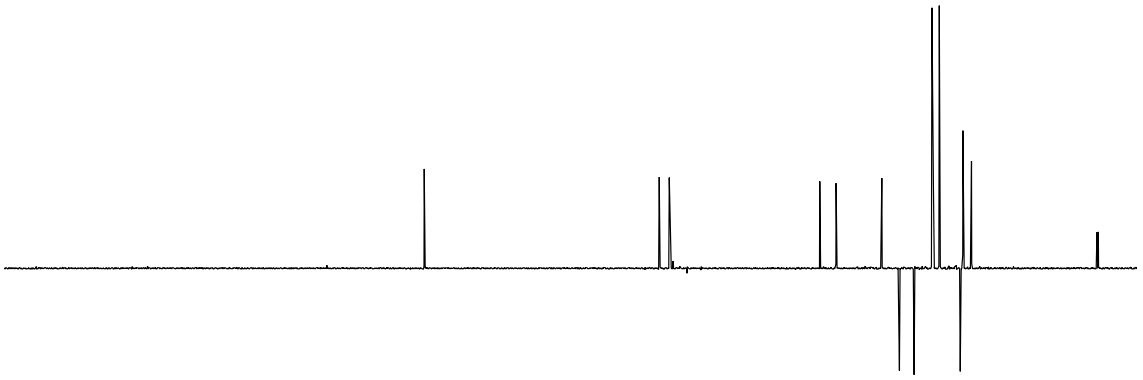

160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

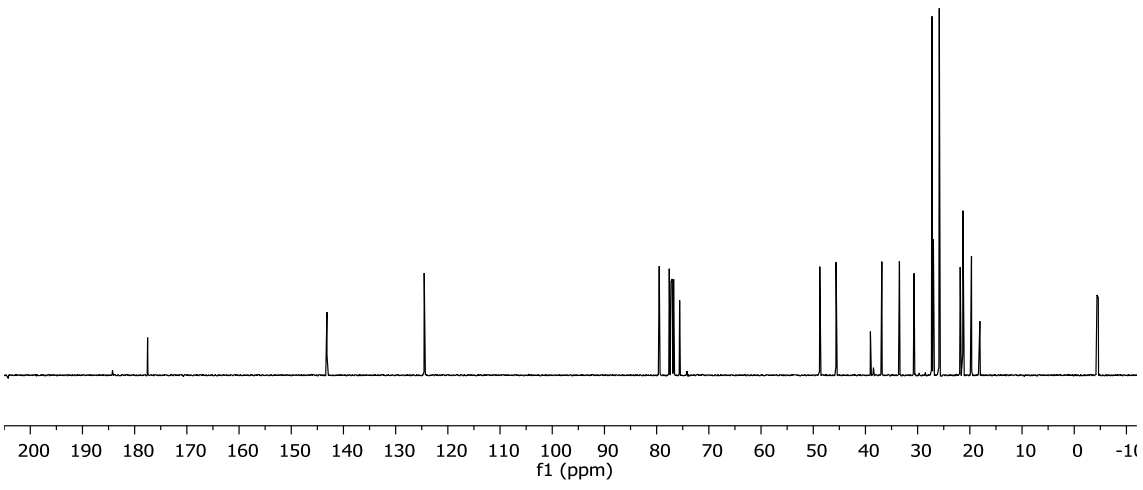

TBSO
H
H
OH
OH
4b´
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

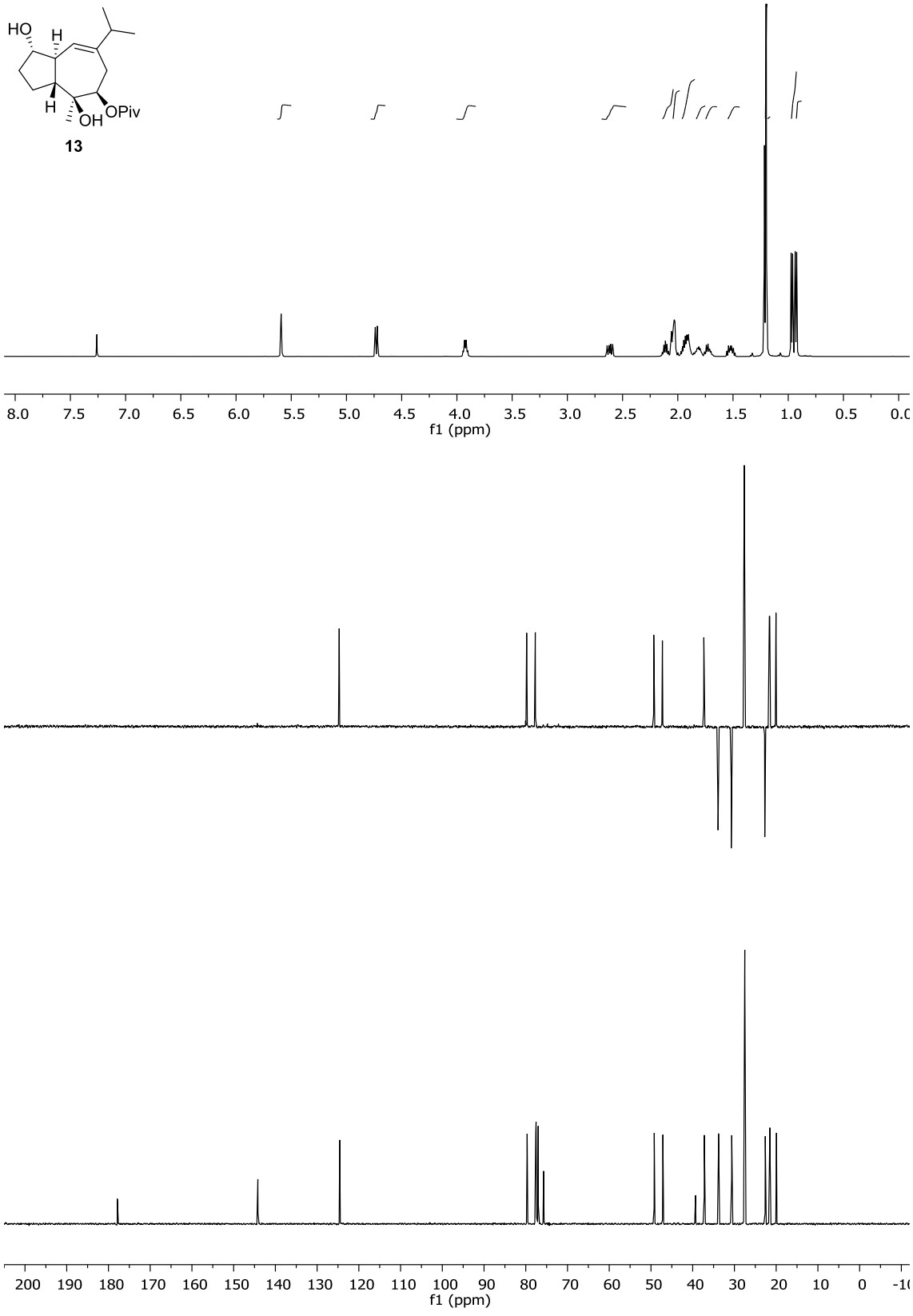


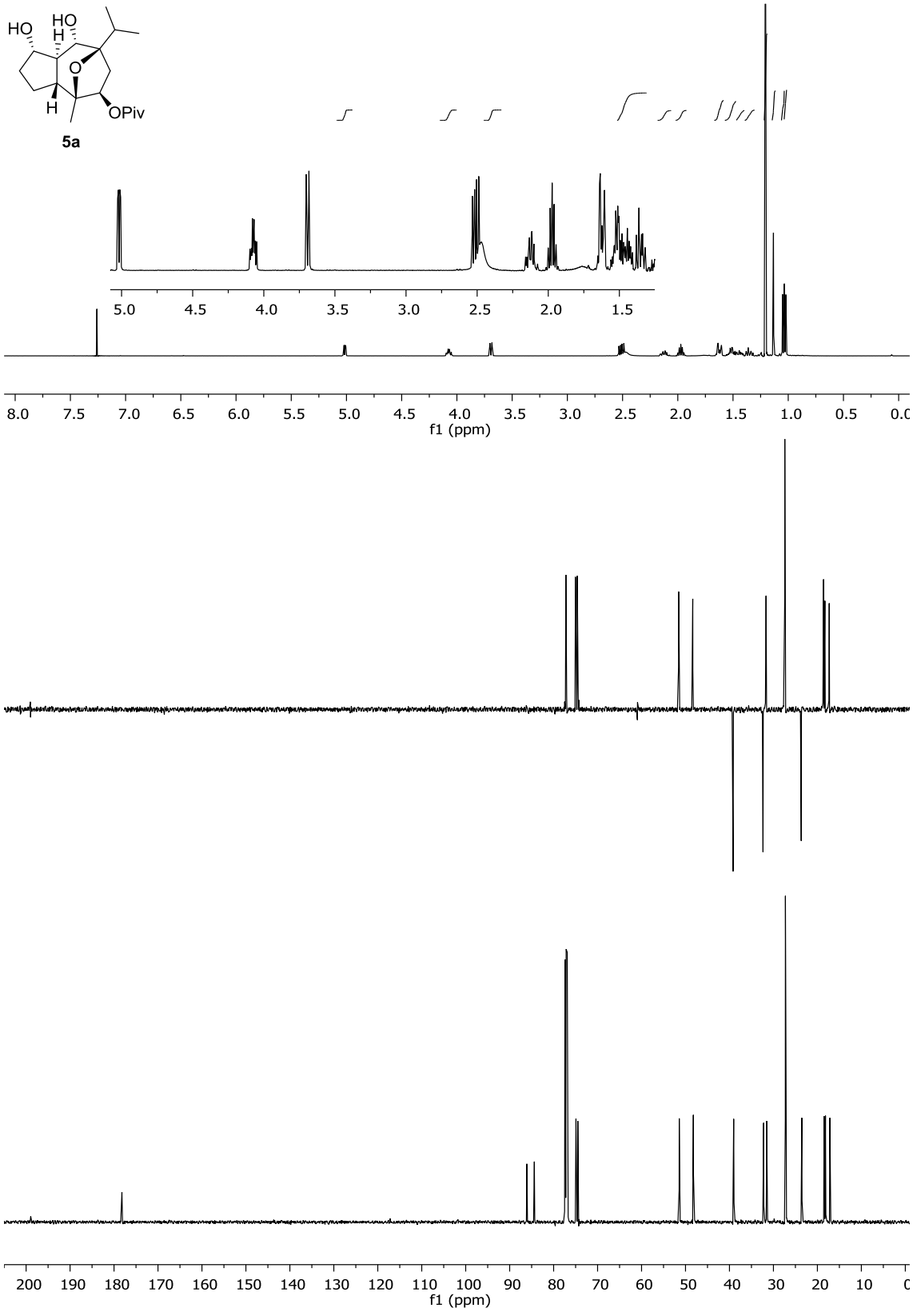

160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

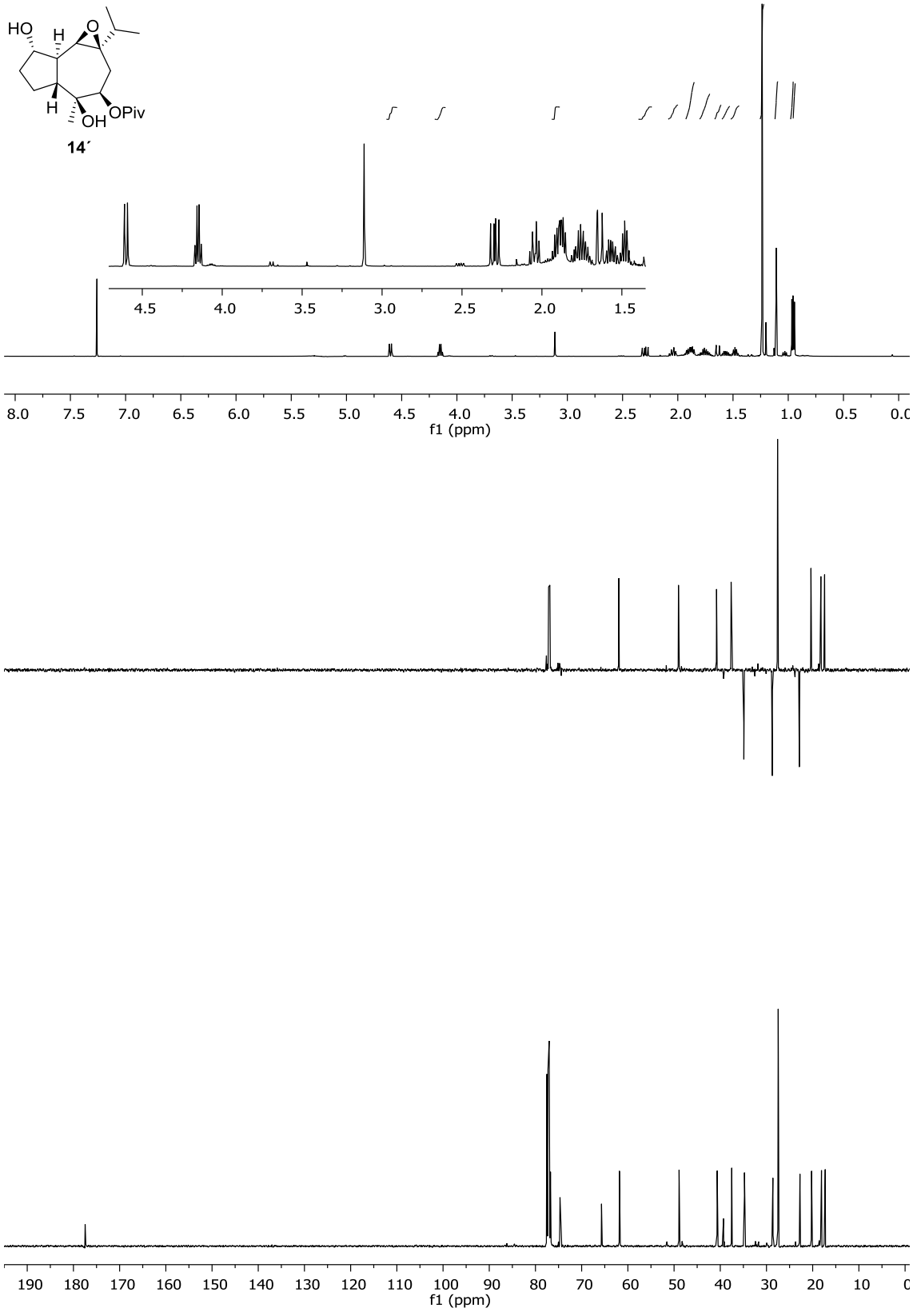

TBSO
H
H
OH
OPiv
13b
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

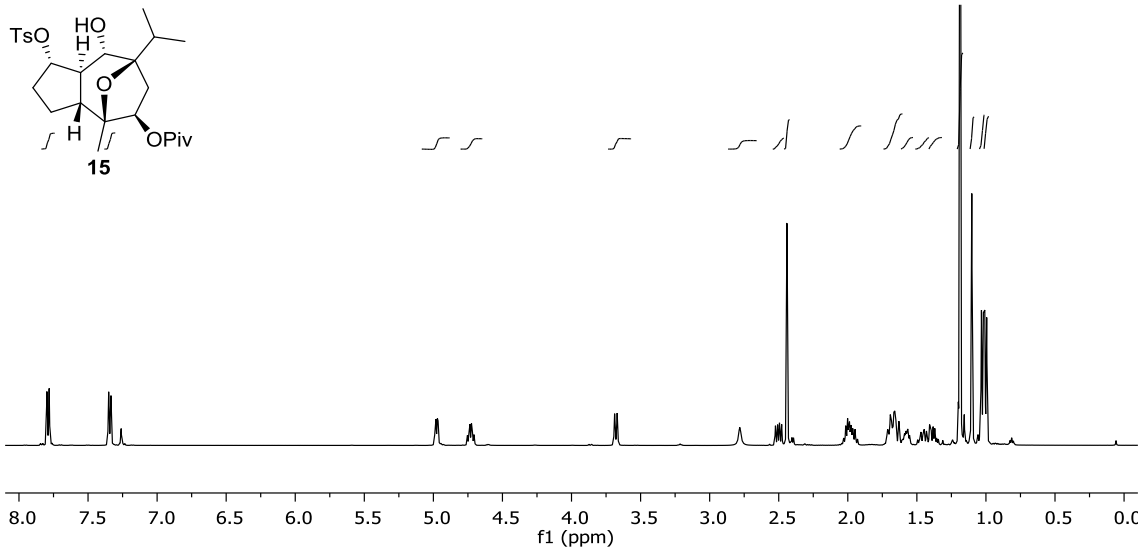


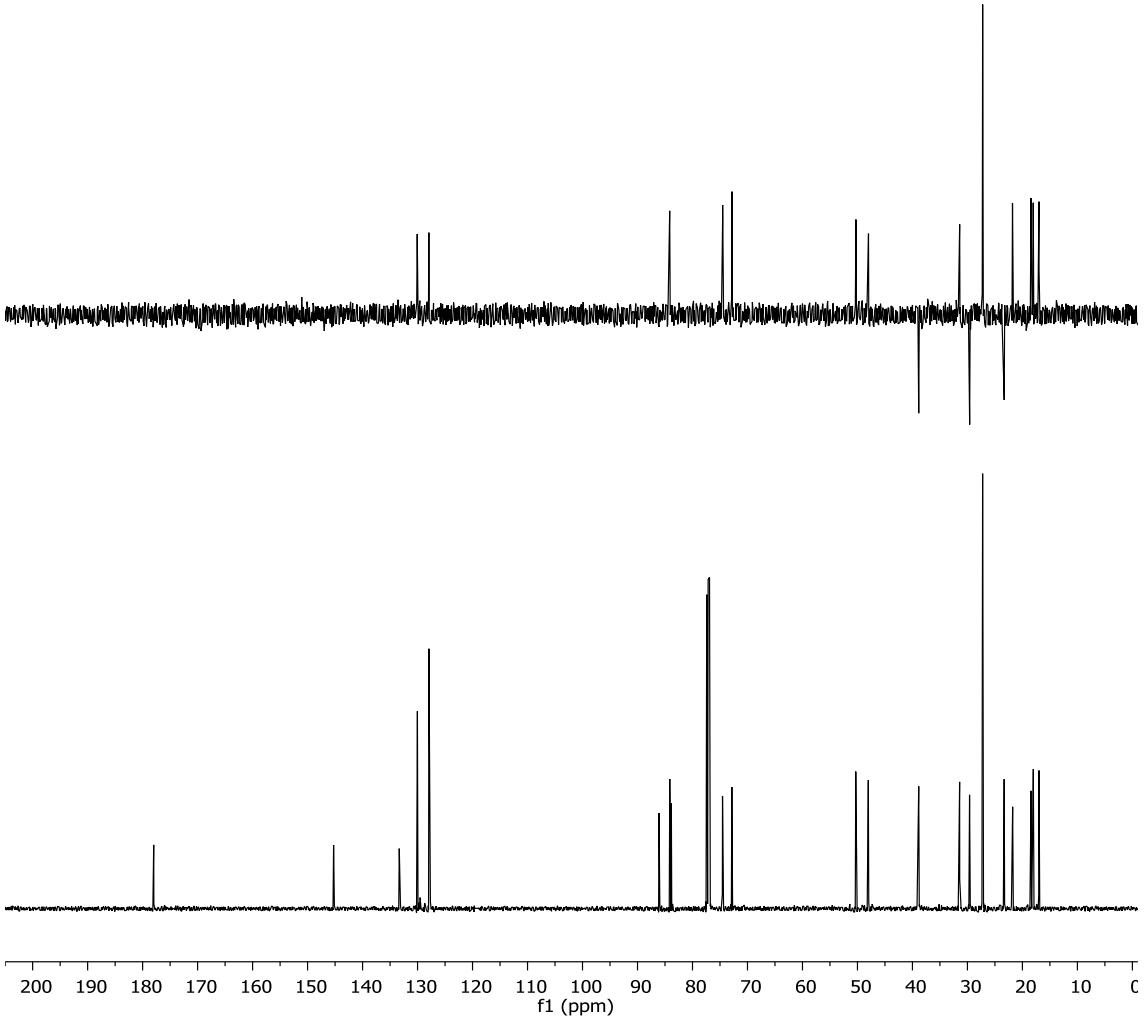

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

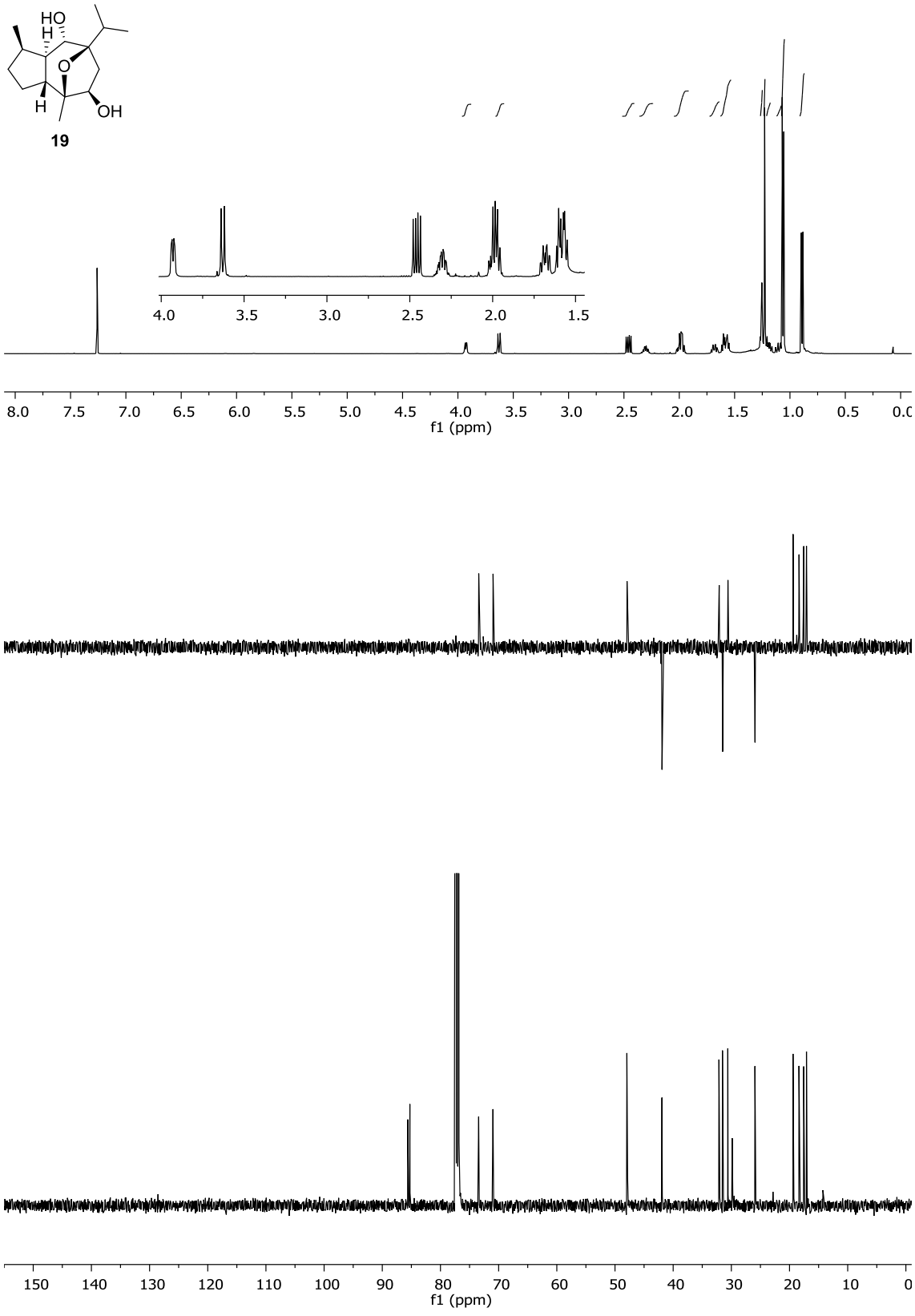

HO
H
H
OH
OPiv
13
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

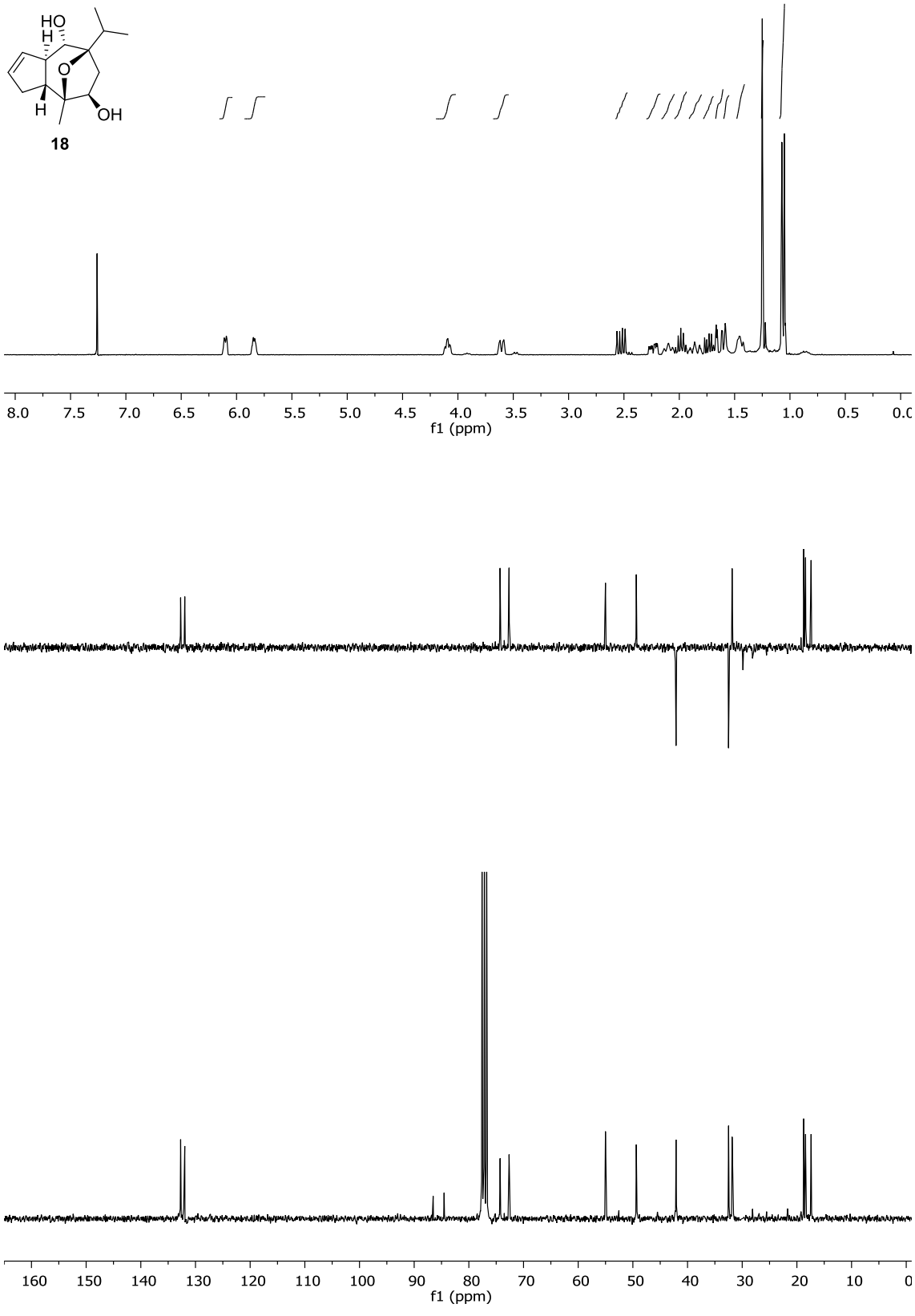

HO
HO
H
O
H
OPiv
5a
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

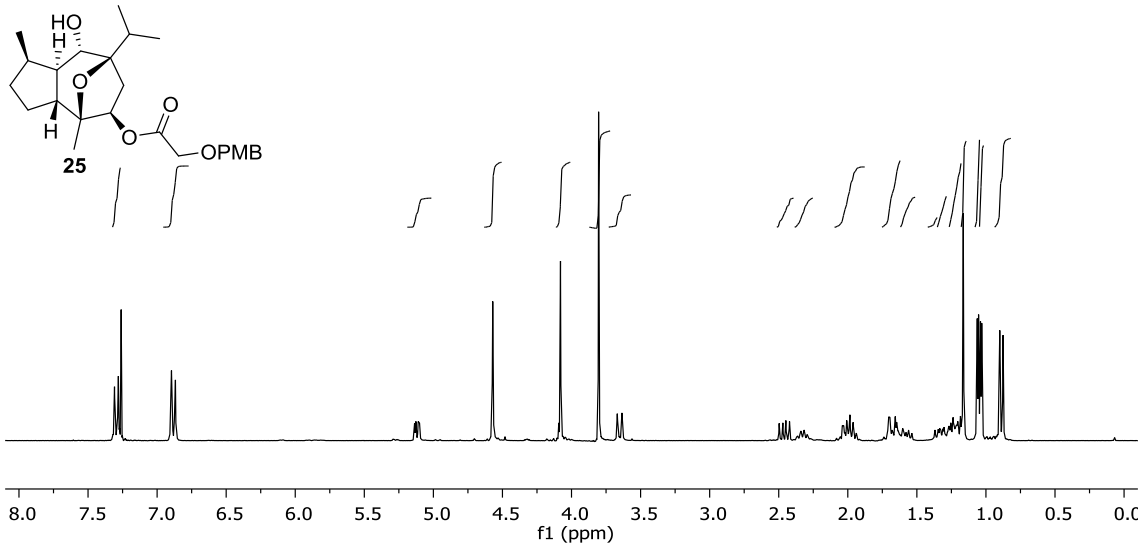

HO
H
O
H
OH
OPiv
14´
4.5
4.0
3.5
3.0
2.5
2.0
1.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

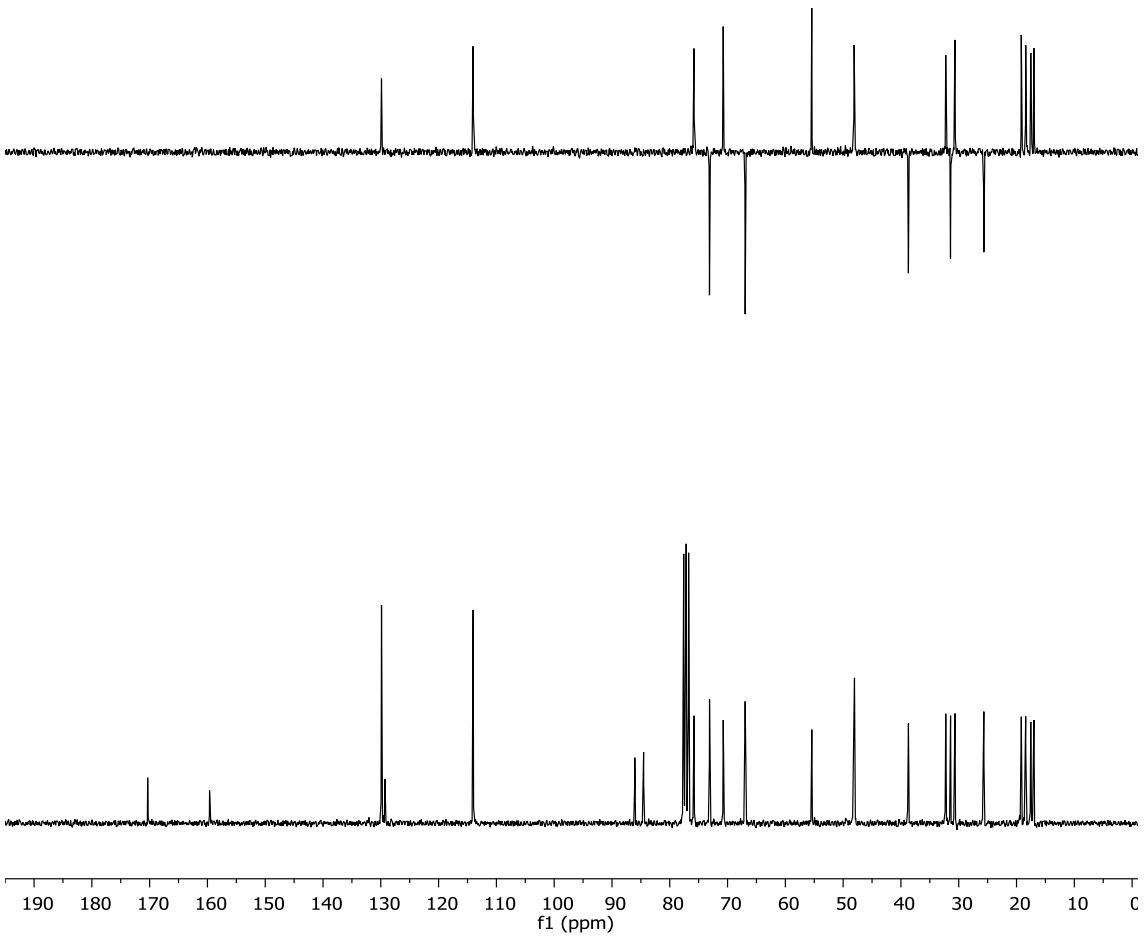

TsO
HO
H
O
H
OPiv
15
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

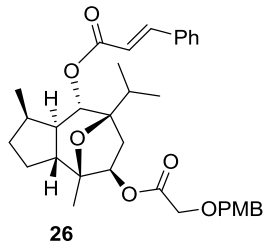

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


HO
H
O
H
OH
19
4.0
3.5
3.0
2.5
2.0
1.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

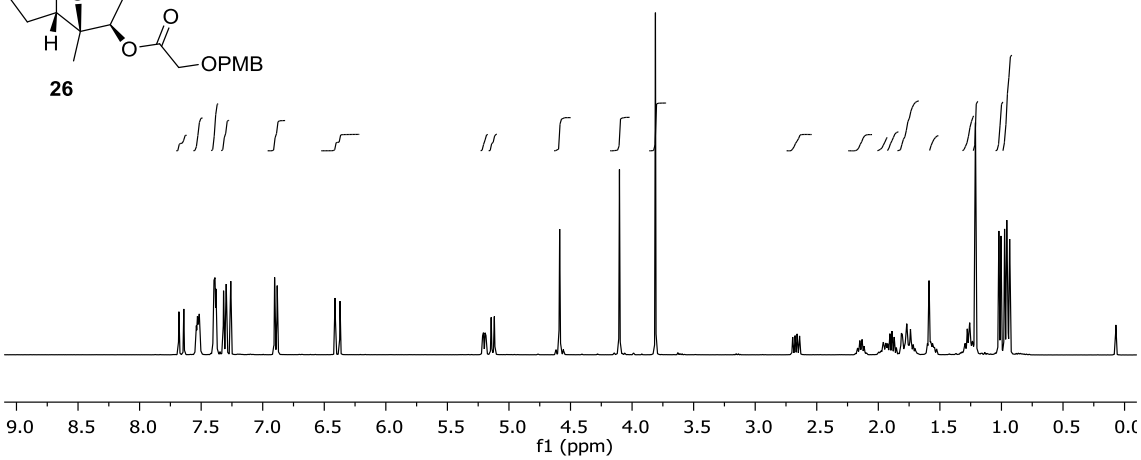

HO
H
O
H
OH
18
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

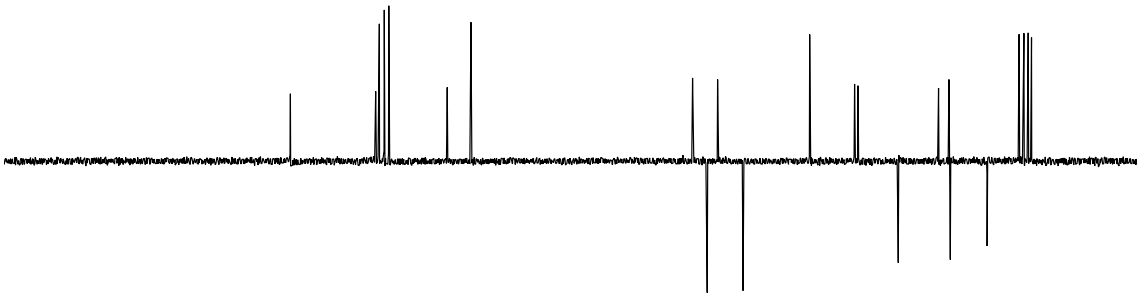

HO
H
O
O
H
O
OPMB
25
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

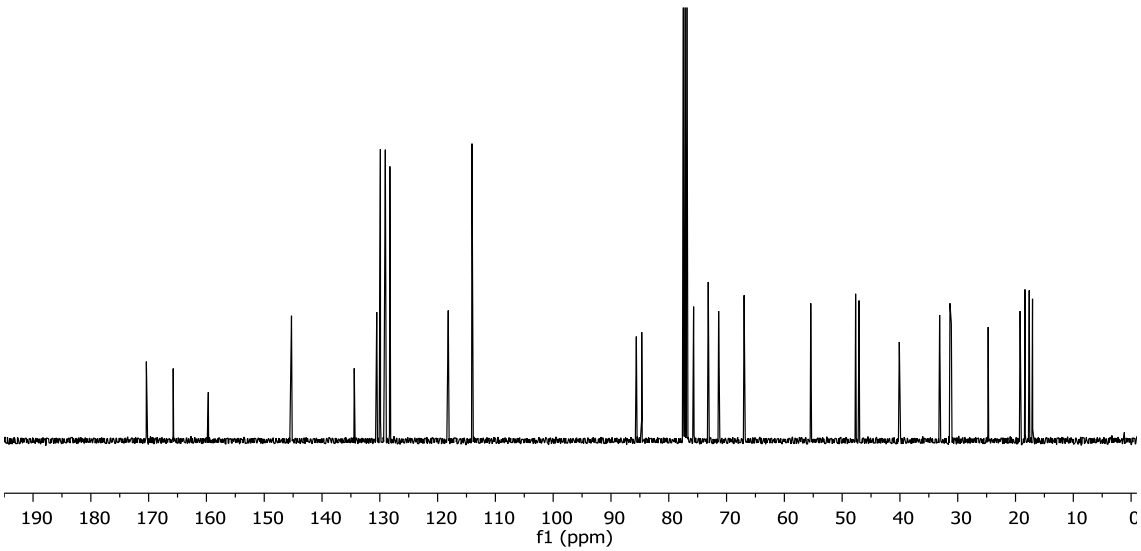

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

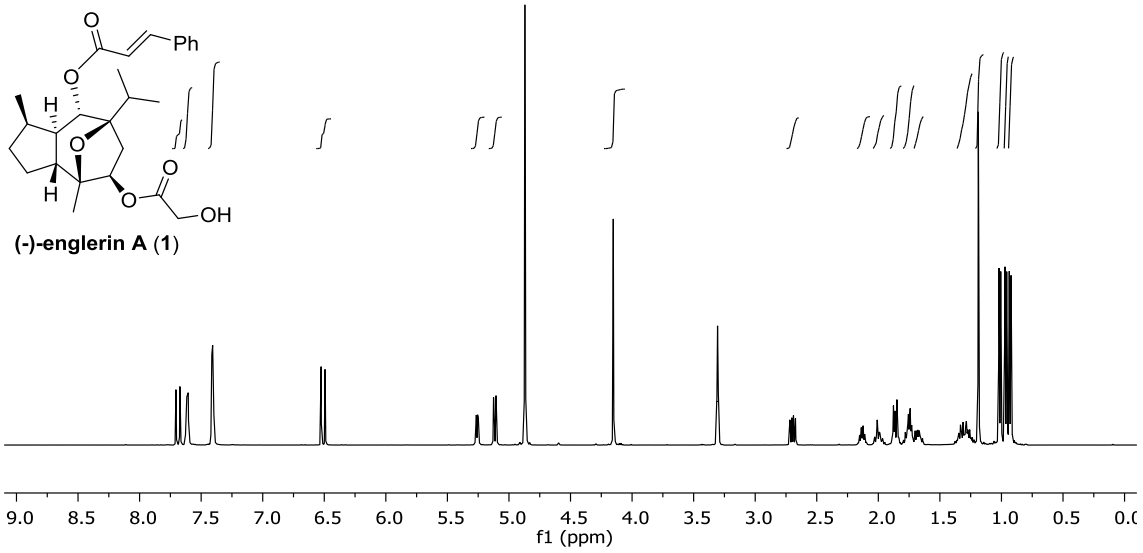

O
Ph
O
H
O
H
O
O
OPMB

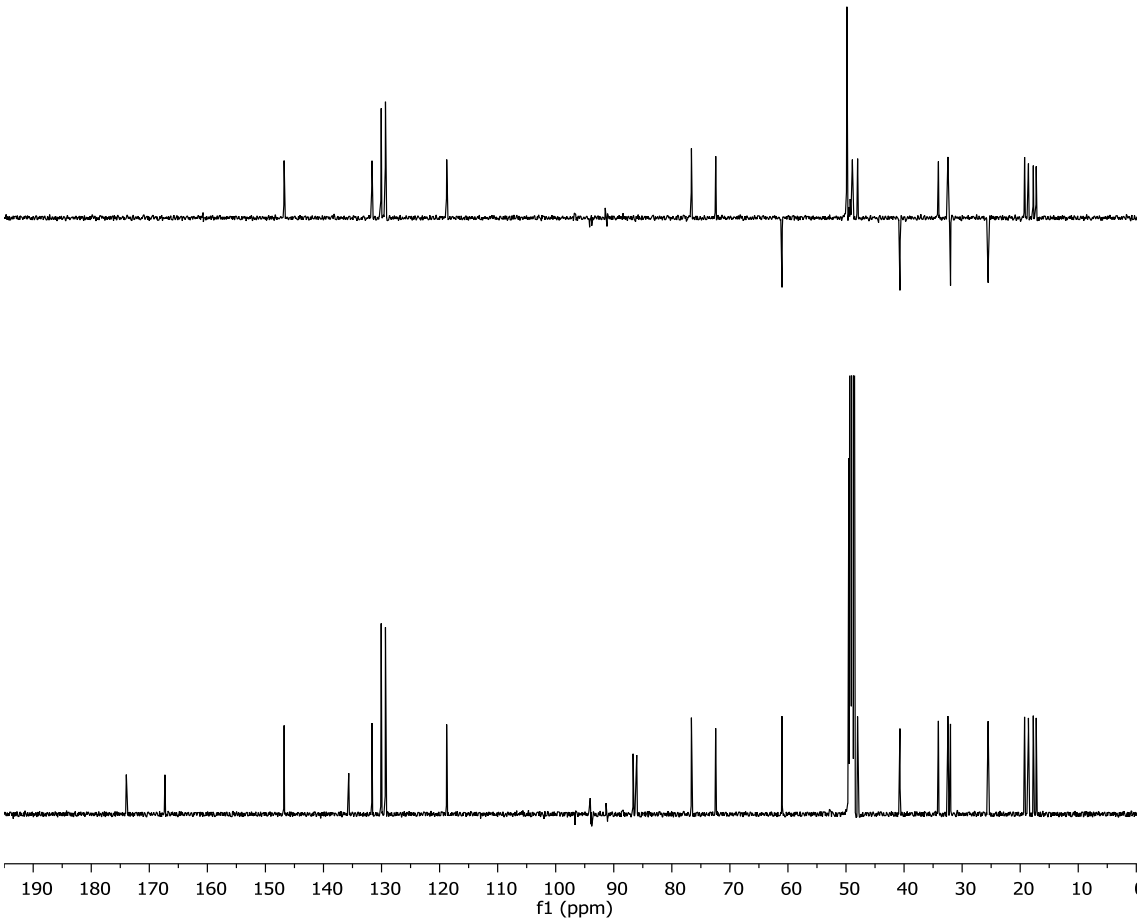
26

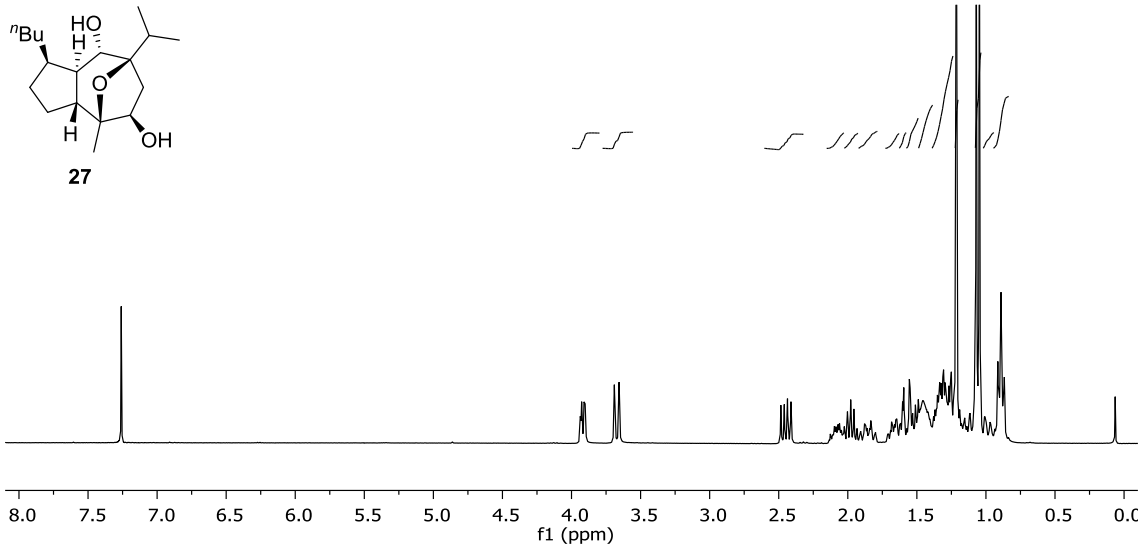

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

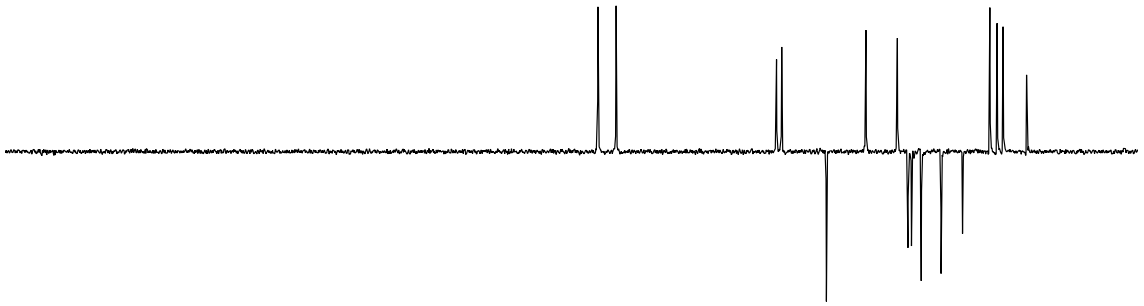


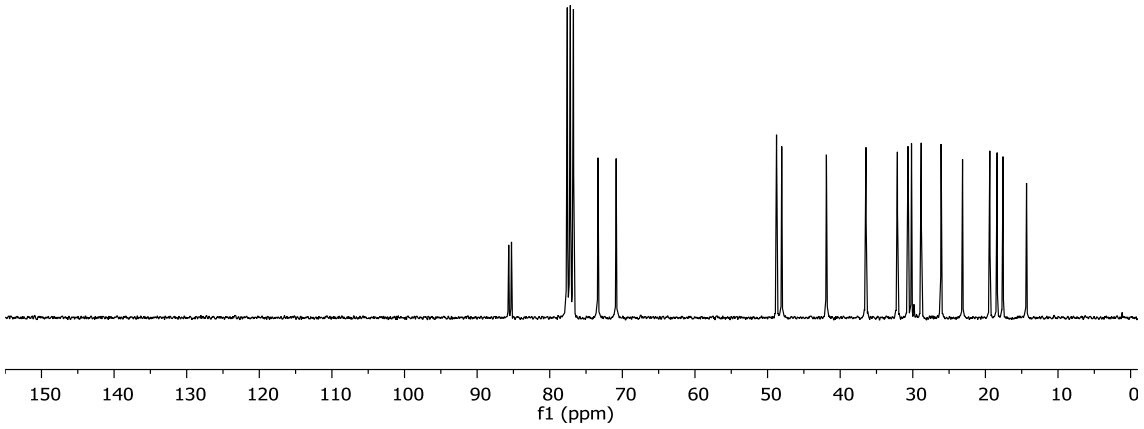

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

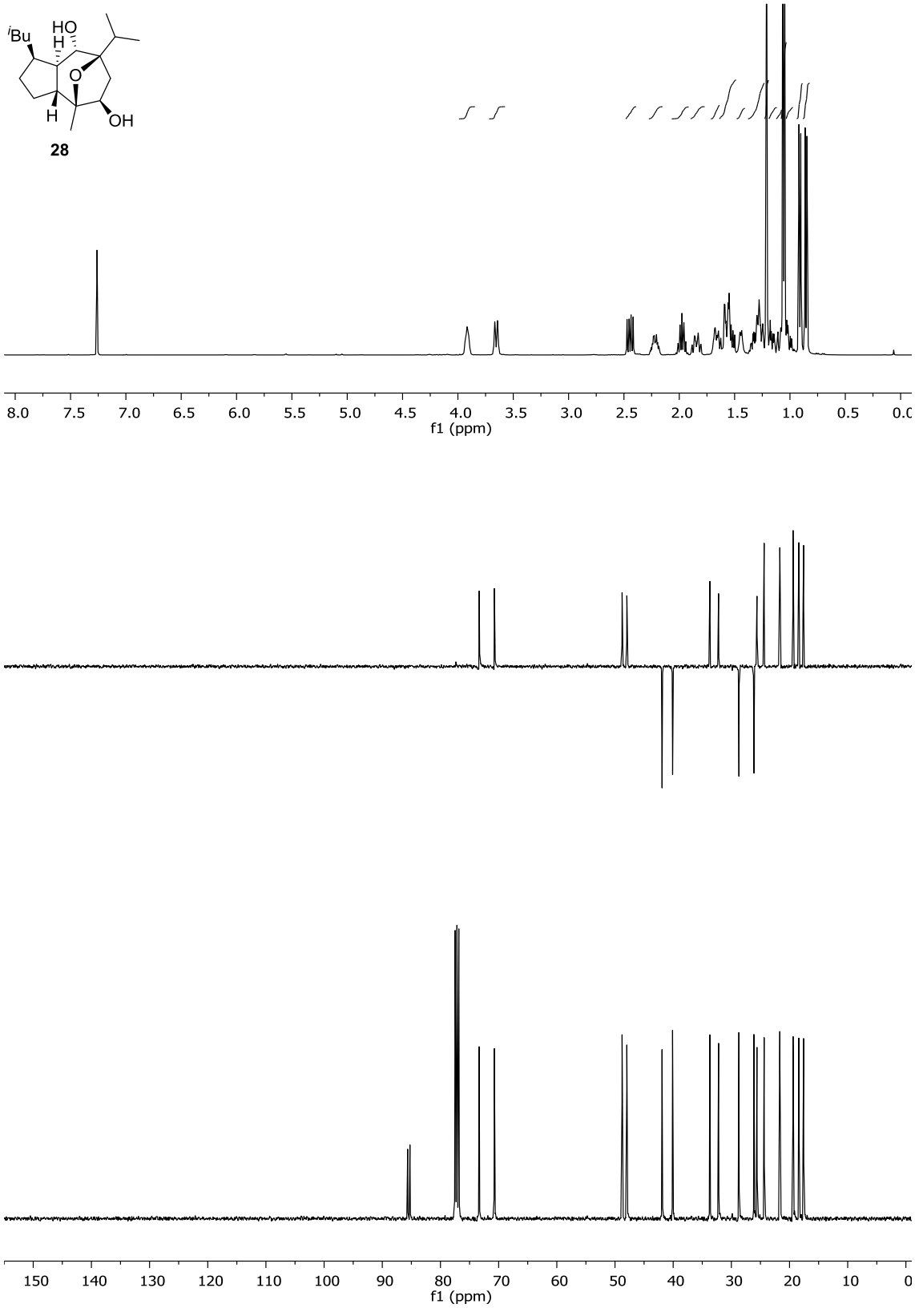

O
Ph
O
H
O
H
O
O
OH
(-)-englerin A (1)
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

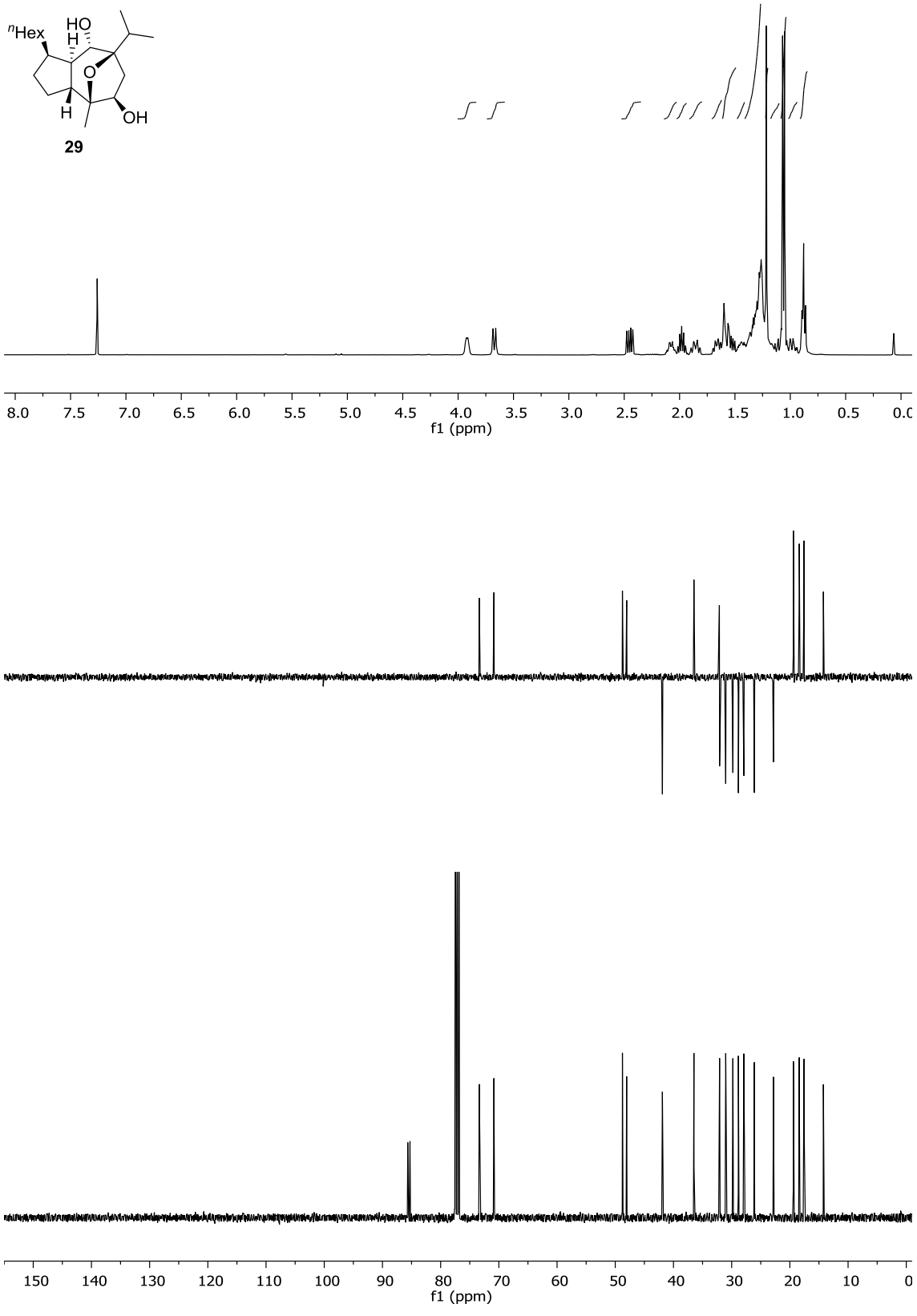

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

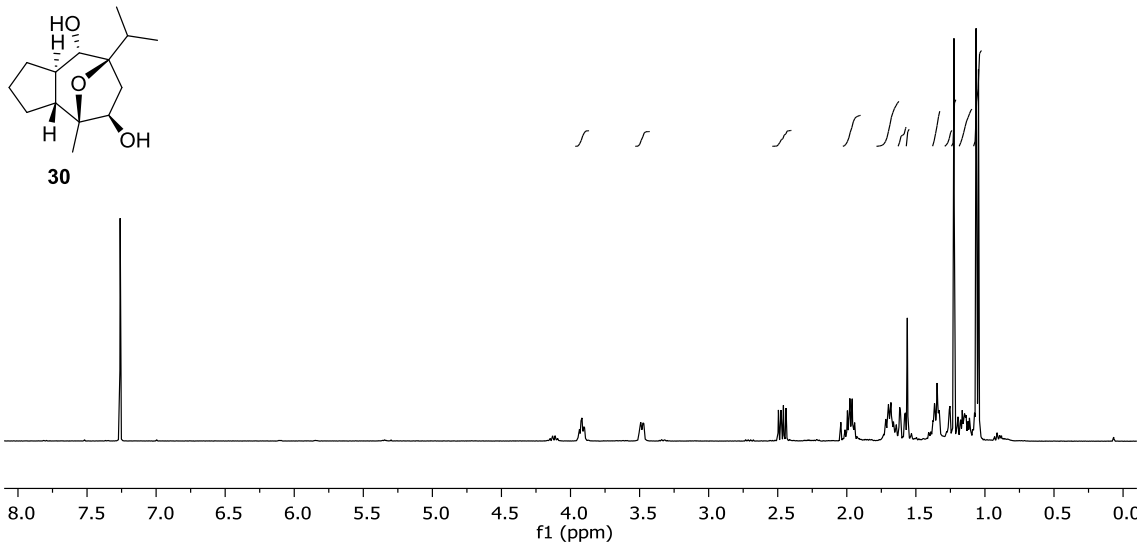

nBu
HO
H
O
H
OH
27
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

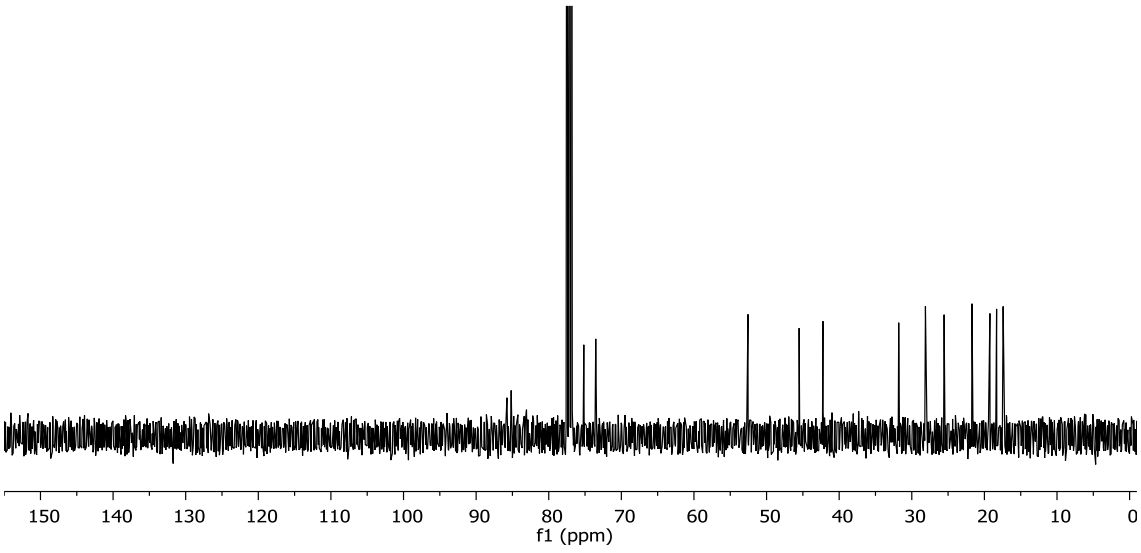


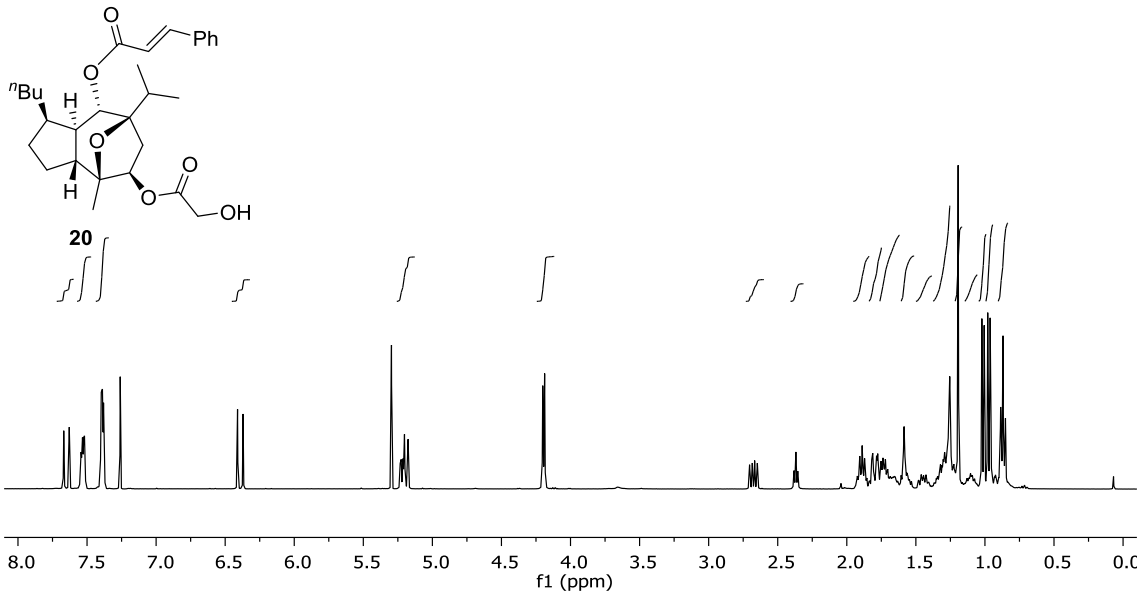

150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

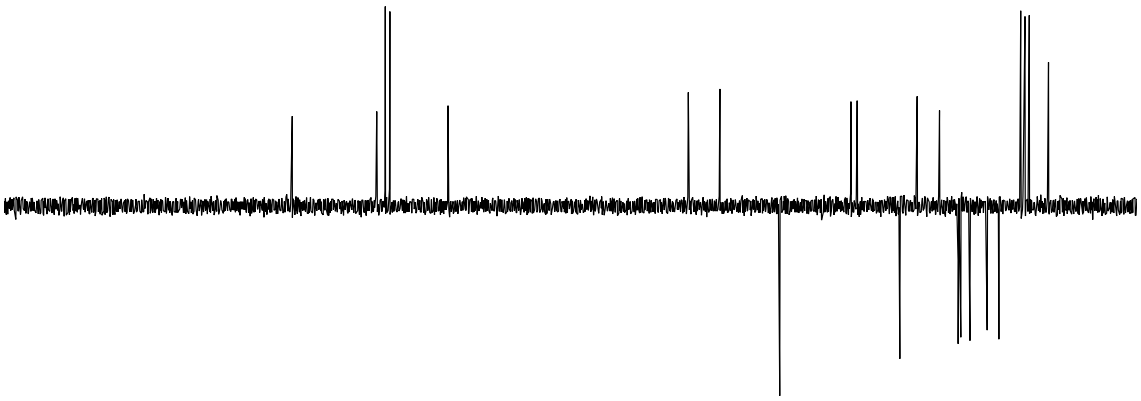

iBu
HO
H
O
H
OH
28
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

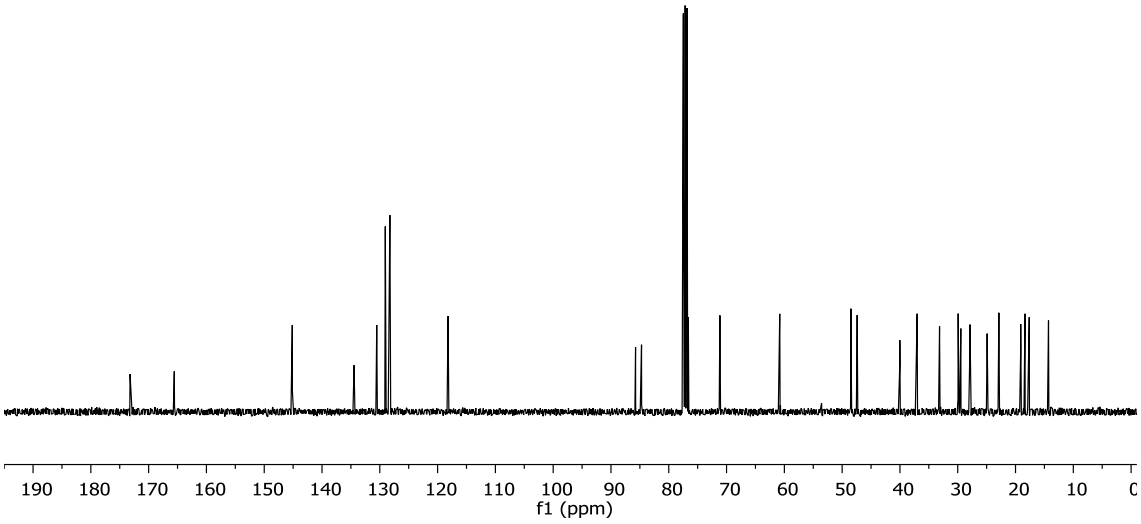

nHex
HO
H
O
H
OH
29
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

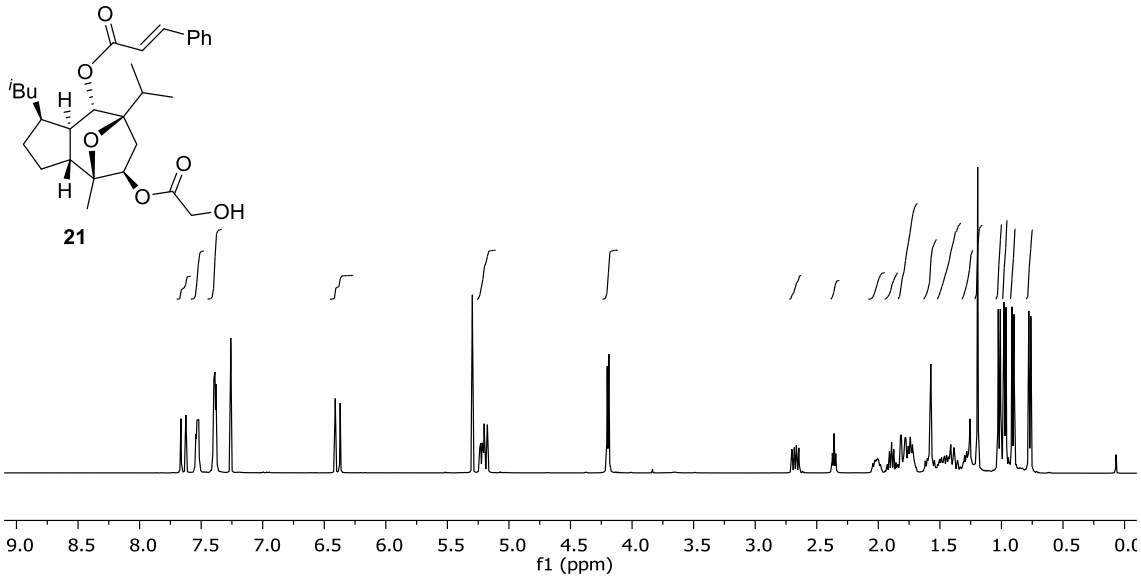

HO
H
O
H
OH
30
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

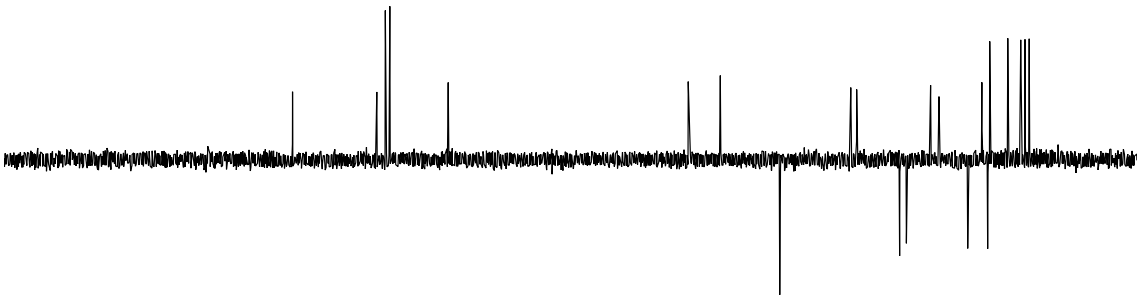

150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

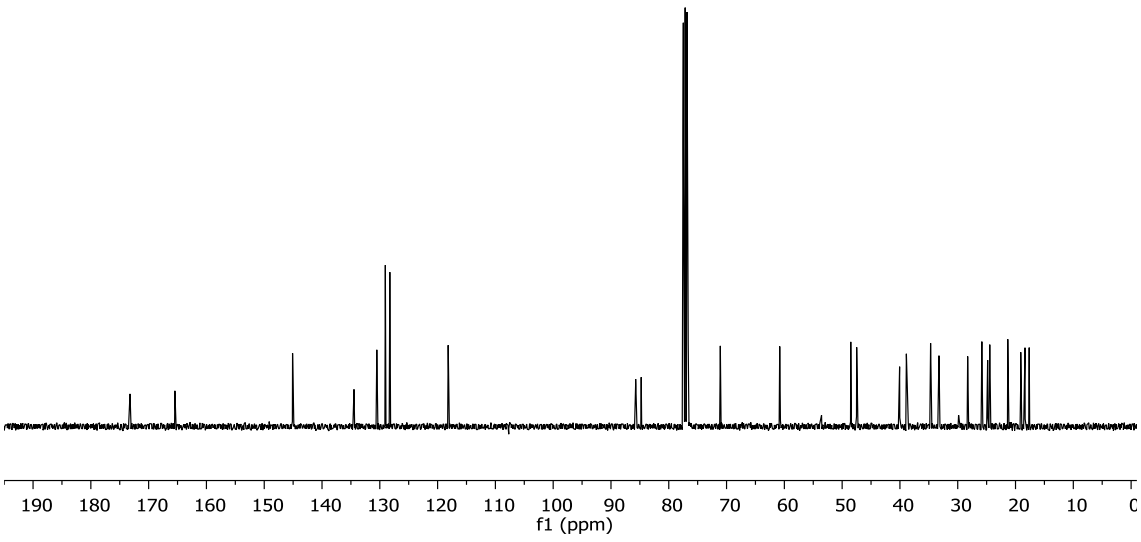

O
Ph
O
nBu
H
O
H
O
O
OH
20
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

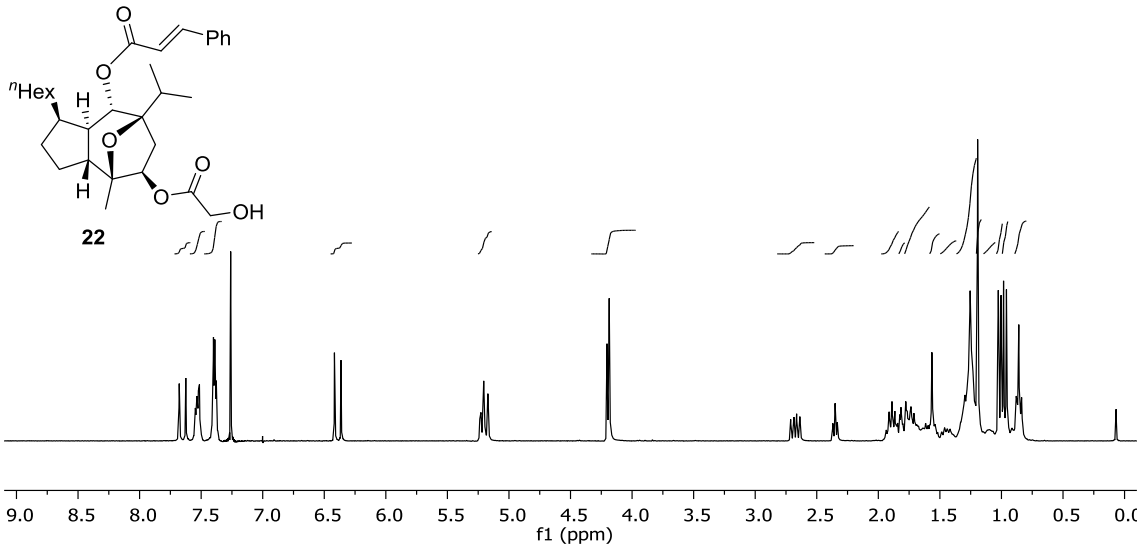


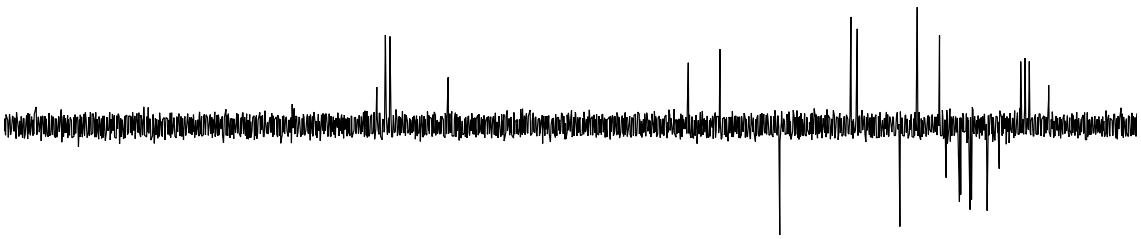

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

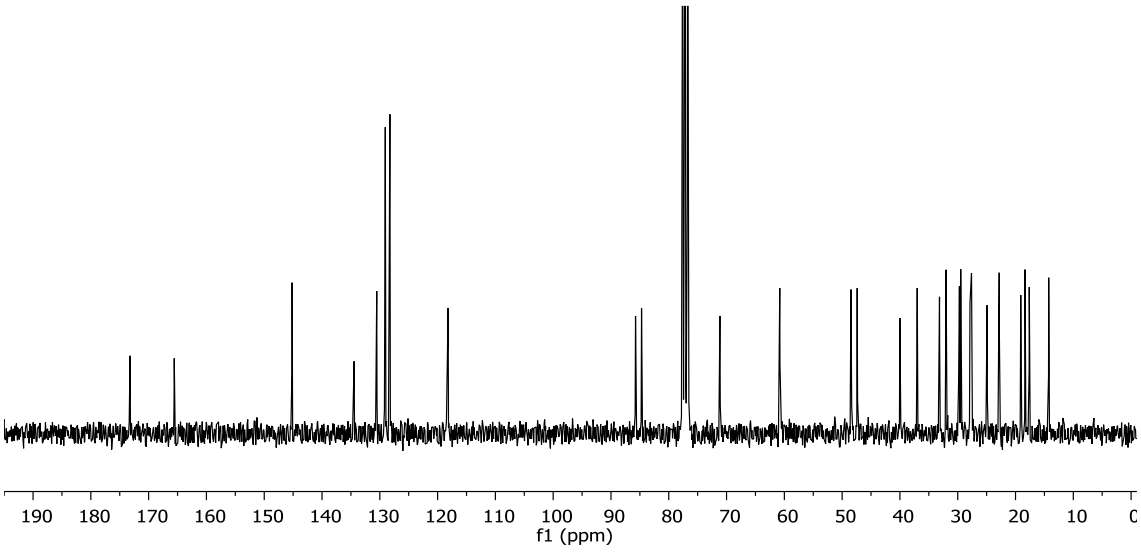

O
Ph
O
iBu
H
O
H
O
O
OH
21
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

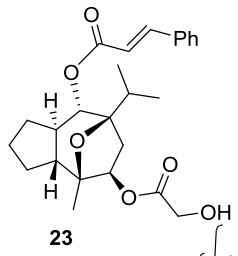



190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

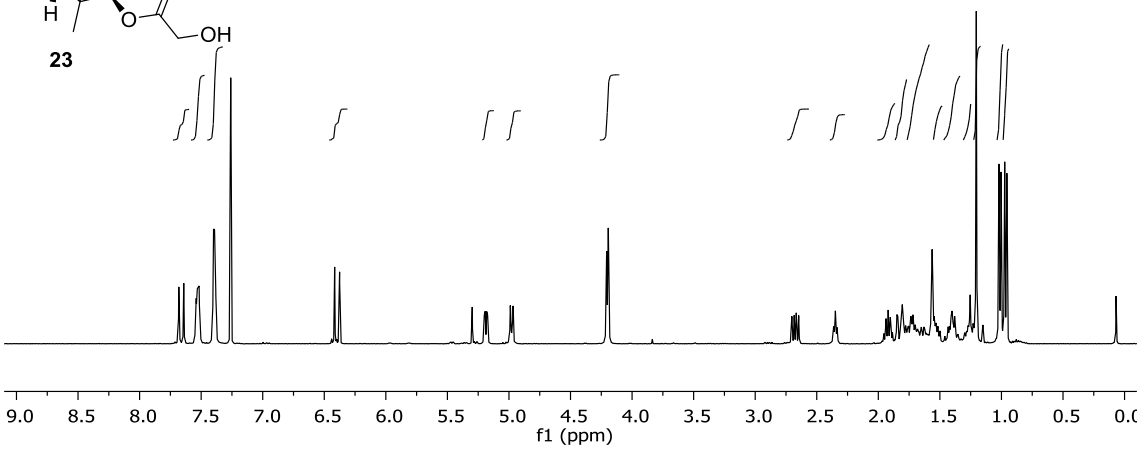

O
Ph
O
nHex
H
O
H
O
O
OH
22
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

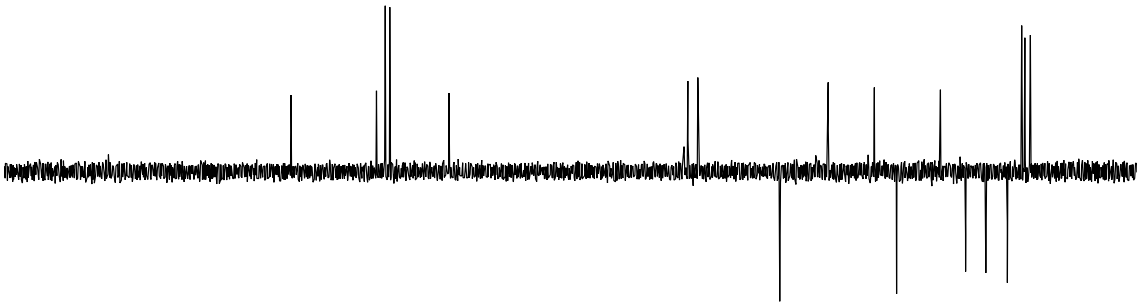


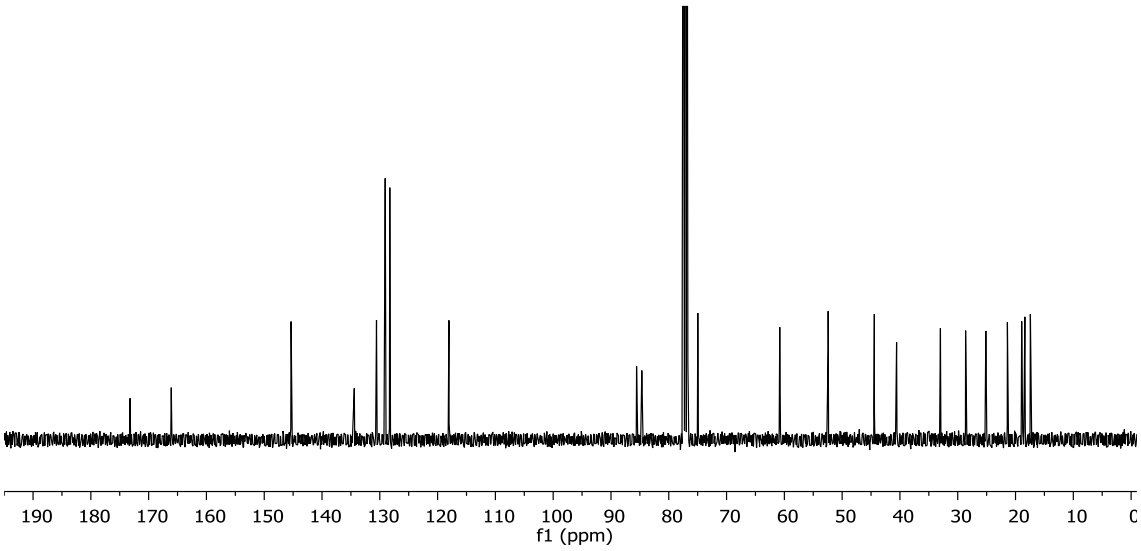

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

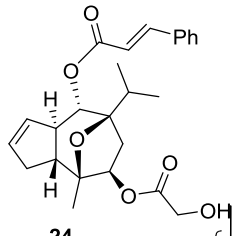

O
Ph
O
H
O
H
O
O
OH

23

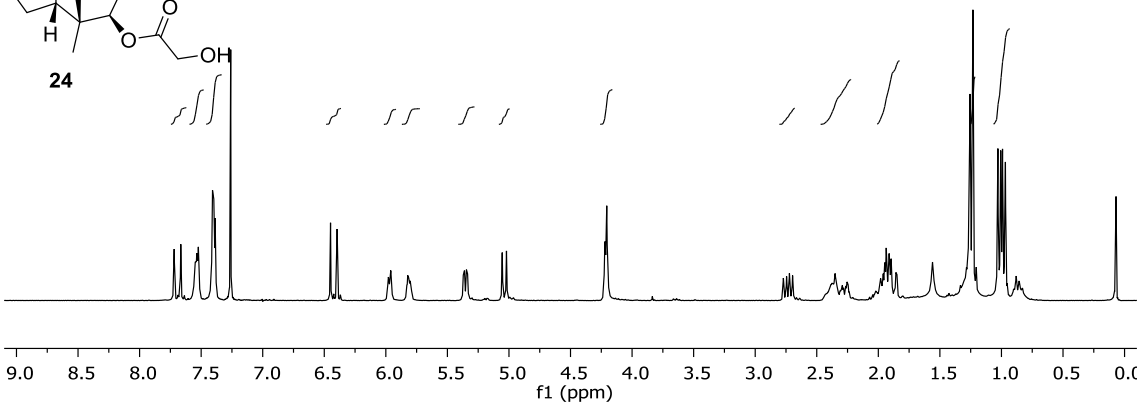

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

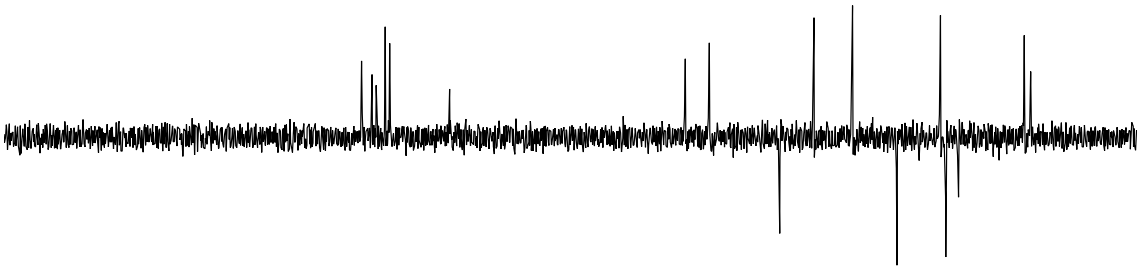


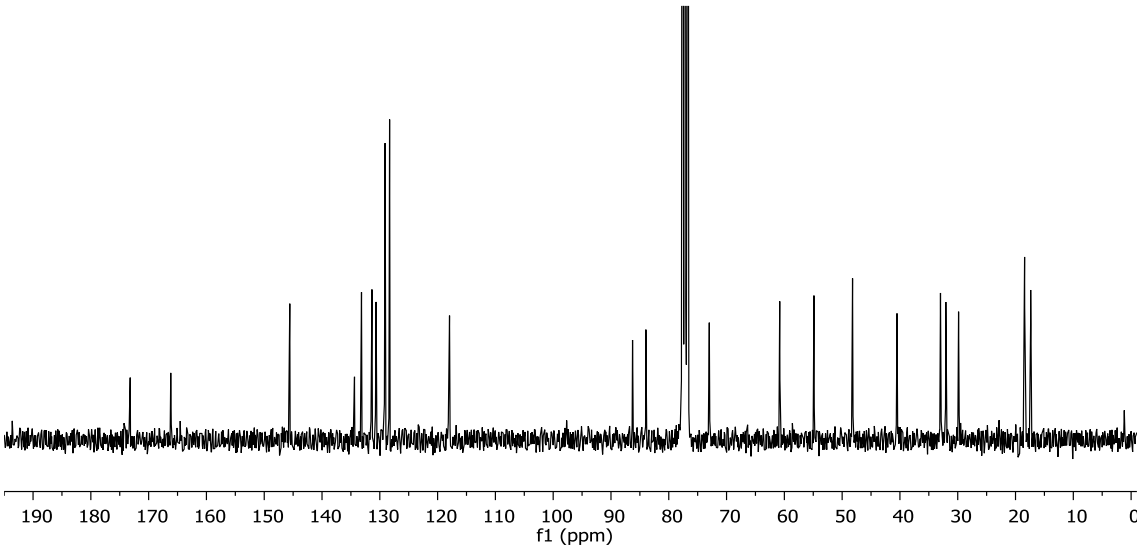

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O
Ph
O
H
O
H
O
O
OH

24


9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)




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