CHEMISTRY
A EUROPEAN JOURNAL

Supporting Information

Total Synthesis of Berkelic Acid

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General: All reactions were carried out under Ar in flame-dried glassware. The solvents used were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O (Mg/anthracene), CH_2Cl_2, Et_3N, hexane, pentane, toluene (Na/K), DMF (Desmodur 15, dibutyl tin dilaurat). Flash Chromatography (FC): Merck silica gel 60 (230-400 mesh), CombiFlash, Companion (Teledyne Isco). NMR: Spectra were recorded on a Bruker DPX 300, AV 400 or AV 600 spectrometer in the solvents indicated; chemical shifts were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: $\delta_C \equiv 77.0$ ppm; residual $CHCl_3$ in $CDCl_3$: $\delta_H \equiv 7.24$ ppm; CD_2Cl_2 $\delta_C \equiv 53.8$ ppm; residual CH_2Cl_2 in CD_2Cl_2: $\delta_H \equiv 5.32$ ppm; C_6D_6: $\delta_C \equiv 128.0$ ppm; residual C_6H_6 in C_6D_6: $\delta_H \equiv 7.15$ ppm; $[D]_8$-toluene: $\delta_C \equiv 137.9$ ppm; residual toluene in $[D]_6$-toluene: $\delta_H \equiv 2.09$ ppm; $[D]_4$-methanol: $\delta_C \equiv$ 49.0 ppm; residual methanol in $[D]_4$-methanol: $\delta_H \equiv 3.30$ ppm). *Where indicated, the signal assignments are unambiguous; the numbering scheme is arbitrary as shown in the inserts*. The assignments are based upon 1D and 2D spectra recorded using the following pulse sequences from Bruker standard pulse program library: DEPT; COSY (*cosygpqf* and *cosydqtp*); HSQC (*inviedetgs; hsqcedetgp; hsqcedetgpsisp*) optimized for ^1J(C,H) = 145 Hz; HMBC (*hmbcgplpndgf*) for correlations via ^nJ(C,H); HSQC-TOCSY (*invietgsml*) using an MLEV17 mixing time of 120 ms. IR: Spectrum 1 (Bruker) spectrometer, wavenumbers ($\tilde{\nu}$) in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: ESQ 3000 (Bruker), accurate mass determinations: Finnigan MAT 95 or Bruker APEX III FT-MS (7 T magnet). Melting points: Büchi melting point apparatus B-540 (corrected). Elemental analyses: H. Kolbe, Mülheim/Ruhr. All commercially available compounds (Fluka, Lancaster, Aldrich) were used as received.

Building Blocks

(*R*)-(+)-2-Pentyloxirane: *m*CPBA (> 70 %, 43.3 g, 176 mmol) was added in portions over 30 min to a solution of 1-heptene (14.4 g, 147 mmol) in CH_2Cl_2 (300 mL) at 0 °C. After stirring for 14 h at ambient temperature, the mixture was filtered through a plug of Celite®, which was washed with CH_2Cl_2 (3 x 100 mL). The combined filtrates were washed with aq. sat. $Na_2S_2O_3$ (2x 150 mL), aq. sat. $NaHCO_3$ (2 x 150 mL) and brine (150 mL), dried (Na_2SO_4), and concentrated. Distillation of the residue gave *rac*-2-pentyloxirane as a colorless liquid (12.9 g, 76 %).

Water (710 µL, 39.4 mmol, 0.55 equiv.) was added dropwise at 0 °C to a mixture of *rac*-2-pentyloxirane (9.31 g, 71.4 mmol), (*R*,*R*)-(–)-*N*,*N´*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamino cobalt(II) (215 mg, 0.356 mmol, 0.5 mol%) and acetic acid (82 µL, 1.43 mmol, 2 mol%) and the mixture was allowed to warm to ambient temperature. After 13 h, inspection of an aliquot by ^{1}H NMR indicated ≈ 54 % conversion of the substrate. Na_2SO_4 (1 g) was introduced, the insoluble materials were filtered off, and the remainder purified by distillation to provide (*R*)-(+)-2-pentyloxirane (4.48 g, 48 %). The enantiomeric excess (*ee* > 99 %) was determined by GC in comparison with the racemate [column: 28 m BGB-177, 0.6 bar H_2, $T_{injector}$ = 220 °C, T-program: 50 °C → 220 °C (1 °C min^{-1}); FID; t_R(*R*) = 14.00 min, t_R(*S*) = 14.39 min]; b.p. = 35-37 °C (10-12 Torr); $[\alpha]_D^{25}$ = + 9.9 (*c* = 1.03 in $CHCl_3$), (ref [1]: $[\alpha]_D^{25}$ = + 9.6 (*c* = 1 in $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 2.93-2.85 (m, 1H), 2.72 (dd, *J* = 5.1 , 4.0 Hz, 1H), 2.44 (dd, *J* = 5.1, 2.5 Hz, 1H), 1.57-1.21 (m, 8H), 0.94-0.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 52.3, 47.0, 32.4, 31.6, 25.6, 22.5, 13.9; IR (film): ṽ = 2959, 2926, 2860, 1466, 1259, 916, 829 cm^{-1}; MS (EI): *m*/*z* (%): 113 (<1) [M^+ - H], 85 (12), 71 (100); HRMS (CI) calcd for $C_7H_{15}O$ [M^+ + H]: 115.1123; found: 115.1122.

5-Bromoresorcinol: A solution of BBr_3 (27.5 mL, 290.8 mmol) in CH_2Cl_2 (200 mL) was added dropwise over 3.5 h to a suspension of 1-bromo-3,5-dimethoxybenzene **13** (28.7 g, 132.2 mmol) in CH_2Cl_2 (130 mL) at –78 °C. The mixture was allowed to warm to ambient temperature and was stirred for 63 h until TLC control indicated the completed deprotection. The reaction was quenched by the slow addition of water (200 mL) at –78 °C (the generated HBr was neutralized by bubbling through an aq. sat. $NaHCO_3$ trap). After the gas evolution had ceased, the mixture was warmed to ambient temperature. Brine (50 mL) was added and the mixture extracted with ethyl acetate (5 x 300 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated to give a viscous oil that solidified after 2 h under high vacuum. A suspension of this solid material in hexane (300 mL) was heated under reflux until a clear solution was formed (ca. 15 min). After reaching room temperature, the mixture was further cooled to –5 °C using a salt/ice bath and the white solid collected by filtration. After washing with ice-cold hexane (2 x 30 mL), the product was dried in air for 30 min and under high vacuum for 3 h giving the title compound as a white powder (23.8 g, 95 %). m.p. = 90-

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[1] P. Gupta, S. V. Naidu, P. Kumar, *Tetrahedron Lett*. **2004**, *45*, 849-851.

91 °C (hexane) (ref [2]: 85-86 °C); ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 8.61 (s, 2H), 6.53 (d, J = 2.1 Hz, 2H), 6.33 (t, J = 2.1 Hz, 1H); ^{13}C NMR (100 MHz, [D$_6$]acetone): δ = 160.3, 123.0, 111.9, 102.7; IR (film): $\tilde{\nu}$ = 3596, 3237 (br), 1595, 1470, 1296, 1197, 1148, 989, 826 cm^{-1}; MS (EI): *m/z* (%): 188 (100) [M^+], 109 (24), 81 (38), 69 (29); HRMS (EI) calcd for $C_6H_5BrO_2$ [M^+]: 187.9473; found: 187.9472. The reported data are consistent with those previously reported.[2]

3,5-Bis(benzyloxy)bromobenzene (14): Benzyl bromide (25.8 mL, 217 mmol) was added to a suspension of 5-bromoresorcinol (20.0 g, 106 mmol) and K_2CO_3 (58.5 g, 423 mmol) in DMF (220 mL) and the mixture was stirred at ambient temperature for 13 h. The mixture was poured into water (800 mL) and the resulting suspension stirred for 30 min. The product was collected by filtration and washed thoroughly with water (3 x 250 mL) before drying in air for 1 h. The solid was dissolved in *tert*-butyl methyl ether, the solution was dried (Na_2SO_4), filtered and evaporated, and the residue purified by crystallization from hexane to give the title compound as a white crystalline solid (3 crops, 35.6 g, 91 %). m.p. = 66-67 °C (hexane) (ref [3]: 59-61 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67-7.28 (m, 10H), 6.78 (d, J = 2.0 Hz, 2H), 6.55 (t, J = 2.0 Hz, 1H), 5.01 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4, 130.3, 128.6, 128.2, 122.9, 111.0, 101.4, 70.3; IR (film): $\tilde{\nu}$ = 3088, 3065, 3035, 2930, 2872, 1602, 1560, 1435, 1380, 1150, 1054 cm^{-1}; MS (EI): *m/z* (%): 368 (6) [M^+], 181 (7), 91 (100); HRMS (EI) calcd for $C_{20}H_{17}BrO_2$ [M^+]: 368.0412; found: 368.0415. The reported data are consistent with those previously reported.[3]

(*R*)-(−)-1-[3,5-Bis(benzyloxy)phenyl]heptan-2-ol (15): A mixture of compound **14** (4.59 g, 12.4 mmol) and dibromoethane (23 µL) in THF (36 mL) was added over 2 h to a refluxing suspension of activated magnesium turnings (154 mg, 6.34 mmol) and dibromoethane (12 µL) in THF (7.6 mL). After the addition was completed, the mixture was heated under reflux for 1.5 h before being cooled to –50 °C. (*R*)-(+)-2-Pentyloxirane (625 mg, 5.47 mmol) was introduced followed by CuCl(cod)[4] (241 mg, 1.16 mmol) and the resulting mixture allowed to warm to ambient temperature overnight. For work-

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[2] G. C. Dol, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Eur. J. Org. Chem*. **1998**, 359-364.

[3] F. Effenberger, M. Koch, W. Streicher, *Chem. Ber*. **1991**, *124*, 163-173.

[4] Freshly recrystallised CuI can also be used and gives comparable yields (23.0 mmol scale, 76 %).

up, the reaction was quenched with aq. sat. NH_4Cl, the mixture was concentrated to a small volume and extracted with *tert*-butyl methyl ether (3 x 60 mL). The combined organic phases were washed with brine (2 x 60 mL), dried (Na_2SO_4), and evaporated. After purification of the residue by flash chromatography (hexanes/ethyl acetate, 12:1), the title compound was isolated as a white solid (3.63 g, 74 %). On larger scale, the product was isolated in 62 % yield (9.09 g). The enantiomeric excess (*ee* > 99 %) was determined by HPLC in comparison with the racemate [250 mm Chiralcel AD, ∅ 4.6 mm, *n*-heptane/2-propanol = 95:5, 0.8 mL min^{-1}, 2.1 MPa, 298 K, UV, 220 nm; t_R(minor) = 28.80 min, t_R(major) = 35.75 min]. m.p. = 65-66 °C (ref [5]: 65.8-66.5 °C); $[\alpha]_D^{20} = -3.8$ (*c* = 1.01 in EtOH) (ref [5]: $[\alpha]_D^{20} = -3.03$ (*c* = 1.17 in EtOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48-7.28 (m, 10H), 6.52 (t, *J* = 2.3 Hz, 1H), 6.48 (d, *J* = 2.3 Hz, 2H), 5.03 (s, 4H), 3.84-3.74 (m, 1H), 2.77 (dd, *J* = 13.6, 4.0 Hz, 1H), 2.57 (dd, *J* = 13.5, 8.5 Hz, 1H), 1.60-1.20 (m, 8H), 0.91 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.1, 141.0, 136.9, 128.6, 128.0, 127.5, 108.6, 100.2, 72.5, 70.0, 44.4, 36.8, 31.8, 25.4, 22.6, 14.1; IR (film): $\tilde{\nu}$ = 3400 (br), 3066, 3030, 2955, 2927, 2856, 1608, 1593, 1498, 1451, 1376, 1292, 1155, 1045, 820, 736, 711 cm^{-1}; MS (EI): *m*/*z* (%): 404 (<1) [M^+], 181 (5), 91 (100); HRMS (ESI^+) calcd for $C_{27}H_{32}NaO_3$ [M^+ + Na]: 427.2244; found: 427.2241. The reported data are consistent with those previously reported.[5] The enantiomer was prepared analogously.

((*R*)-(+)-1-(3,5-Dihydroxyphenyl)heptan-2-ol (16): Pd/C (10 % *w*/*w*, 450 mg) was added to a solution of compound **15** (9.03 g, 22.3 mmol) in acetic acid (4.5 mL) and MeOH (225 mL) and the resulting suspension stirred under a hydrogen atmosphere (1 atm) for 41 h. For work-up, the mixture was filtered through a pad of Celite®, eluting with MeOH (250 mL), and the combined filtrates were evaporated to provide the title compound as an off-white solid (5.03 g, quant.). m.p. = 134-135 °C (ref [5]: 141.2-142.3 °C); $[\alpha]_D^{20} = +3.2$ (*c* = 2.20 in EtOH) (ref [5]: $[\alpha]_D^{21} = +4.3$ (*c* = 2.21 in EtOH)); ^{1}H NMR (400 MHz, [D_6]acetone): δ = 8.62 (br s, 2H; ArO*H*), 6.22 (d, *J* = 2.3 Hz, 2H), 6.19 (t, *J* = 2.1 Hz, 1H), 3.79-3.67 (m, 1H), 3.46-3.21 (br s, 1H; O*H*), 2.55 (d, *J* = 6.5 Hz, 2H), 1.59-1.16 (m, 8H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, [D_6]acetone): δ = 159.1, 142.7, 108.7, 101.2, 72.7, 45.3, 37.7, 32.7, 26.2, 23.3, 14.3; IR (film): $\tilde{\nu}$ = 3260 (br), 2952, 2930, 2861, 2516, 2429, 1597, 1485, 1467, 1326, 1162, 1149, 824 cm^{-1}; MS (EI): *m*/*z* (%): 224 (10) [M^+], 124 (100); HRMS (ESI^+) calcd for $C_{13}H_{20}NaO_3$ [M^+ + Na]: 247.1310; found: 247.1307. The reported data are consistent with those previously reported.[5] The

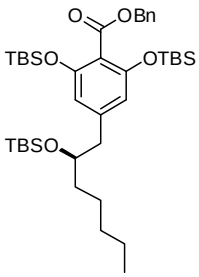
[5] T. Rödel, H. Gerlach, *Liebigs Ann. Chem*. **1997**, 213-216.

enantiomer was prepared analogously from (*S*)-(+)-1-[3,5-bis(benzyloxy)phenyl]heptan-2-ol (12.9 mmol scale, 98 %).

(*R*)-(−)-Benzyl (2,6-dihydroxy)-4-(2-hydroxyheptyl)benzoate (17): Compound **16** (4.1 g, 18.3 mmol) was dried under high vacuum for 12 h prior to use. Glycerin (13.5 g) and $KHCO_3$ (11.9 g, 118.8 mmol) were dried under vacuum at 60 °C for 12 h prior to use. The compounds were then mixed in a 500 mL Schlenk-tube under argon and homogenized. Argon was replaced by $CO_{2(g)}$ and the tube purged with CO_2 for several minutes before being placed in a preheated oil-bath at 150 °C and stirred vigorously under a stream of CO_2 for 10 h. Stirring *must* be maintained throughout the reaction (reaction monitoring by TLC is difficult and potentially misleading). The mixture was allowed to reach room temperature before being further cooled to 0 °C whereupon a brown solid was obtained. Ethyl acetate (60 mL) was added followed by HCl (2 M, 150 mL), causing complete dissolution of the material (caution: effervescence). The layers were separated and the aqueous phase extracted with ethyl acetate (5 x 100 mL), dried (Na_2SO_4), filtered and concentrated to provide the crude carboxylic acid as a viscous brown oil.

NEt_3 (2.55 mL, 18.3 mmol) was added dropwise to a solution of the crude product in DMF (20 mL). Benzyl bromide (2.2 mL, 18.3 mmol) was slowly introduced and the resulting mixture stirred for 3 h before being diluted with EtOAc (60 mL) and successively washed with aq. NH_4Cl (10 % *w*/*w*, 60 mL) and $NaHCO_3$ (5 % *w*/*w*, 50 mL). The organic phase was dried (Na_2SO_4), filtered and evaporated, and the residue purified by flash chromatography (hexanes/ethyl acetate 1:4) to give the title compound (3.88 g, 59 %, 87 % brsm) as an off-white solid. m.p. = 74-76 °C; $[\alpha]_D^{20} = -28.2$ (*c* = 0.8 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.90-9.10 (br s, O*H*), 7.45-7.35 (m, 5H), 6.34 (s, 2H), 5.49 (s, 2H), 3.86-3.78 (m, 1H), 2.70 (dd, *J* = 13.4, 4.3 Hz, 1H), 2.56 (dd, *J* = 13.4, 8.3 Hz, 1H), 1.60-1.21 (m, 8H+O*H*), 0.91-0.85 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.3, 168.9, 148.8, 129.0, 128.7, 128.4, 108.9, 71.7, 67.8, 44.0, 36.6, 31.4, 25.0, 22.3, 13.7; IR (film): $\tilde{\nu}$ = 3411, 3349, 2927, 1731, 1644, 1572, 1474, 1464, 1456, 1402, 1358 cm^{-1}; MS (EI): *m*/*z* (%): 358 (9) [M^+], 258 (4), 91 (100); HRMS (ESI$^+$) calcd for $C_{21}H_{26}NaO_5$ [M^+ + Na]: 381.1672; found:381.1672. The enantiomer was prepared analogously from ((*S*)-(–)-1-(3,5-dihydroxyphenyl)heptan-2-ol (11.6 mmol scale, 74 %).

(*R*)-(−)-Benzyl 2-(*tert*-butyldimethylsilyloxy)-4-(2-(*tert*-butyl-dimethylsilyl-oxy)-heptyl)-6-hydroxy-benzoate: TBSCl (3.53 g, 23.4 mmol) was added to a solution of compound **17** (2.1 g, 5.86 mmol) and



imidazole (2.39 g, 35.2 mmol) in CH_2Cl_2 (60 mL) at 0 °C and the mixture was stirred for 30 min at 0 °C and at room temperature for 3.5 h. The resulting suspension was filtered and the solid washed with CH_2Cl_2 (2 x 50 mL). The combined filtrates were concentrated and the remaining yellow oil purified by flash chromatography (hexanes/ethyl acetate, 100:1→80:1) to give the title compound as a colorless oil (3.59 g, 89 %). $[\alpha]_D^{20} = -9.1$ (*c* = 1.2 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42-7.38 (m, 2H), 7.36-7.27 (m, 3H), 6.26 (s, 2H), 5.27 (app. d, *J* = 12.5 Hz, 1H), 5.21 (app. d, *J* = 12.4 Hz, 1H), 3.81-3.73 (m, 1H), 2.64 (dd, *J* = 13.2, 5.4 Hz, 1H), 2.56 (dd, *J* = 13.2, 7.1 Hz, 1H), 1.42-1-18 (m, 8H), 0.92 (s, 18H), 0.89-0.83 (m, 12H), 0.88 (s, 6H), 0.17 (s, 6H), 0.16 (s, 6H), 0.03 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.7, 153.3, 141.9, 128.5, 128.4, 128.1, 117.2, 113.5, 73.6, 66.9, 44.2, 36.2, 31.9, 25.9, 25.6, 25.0, 22.7, 18.1, 18.0, 14.0, -4.3, -4.4, -4.6, -4.7; IR (film): $\tilde{\nu}$ = 2951, 2929, 2858, 1735, 1606, 1571, 1462, 1428, 1252, 1086, 826, 774 cm^{-1}; MS (EI): *m*/*z* (%): 643 (42) [M^+ - *t*Bu], 599 (5), 553 (6), 512 (41), 511 (100), 495 (23), 467 (12), 215 (12), 91 (89), 73 (72); HRMS (ESI$^+$) calcd for $C_{39}H_{68}NaO_5Si_3$ [M^+ + Na]: 723.4267; found: 723.4264. The enantiomer was prepared analogously (5.58 mmol scale, 88 %).

(*R*)-(−)-Benzyl 2-(*tert*-butyldimethylsilyloxy)-4-(2-(*tert*-butyldimethylsilyloxy)heptyl)-6-hydroxy-benzoate (18): A solution of the tris-TBS ether described above (3.50 g, 4.99 mmol) and K_2CO_3 (697 mg, 5.04 mmol) in MeOH (28 mL) was stirred at 45 °C for 40 min until TLC indicated the complete consumption of the substrate.[6] Thereafter, aq. sat. NH_4Cl (10 mL) was added and the mixture concentrated to a small volume. The product was extracted with *tert*-butyl methyl ether (3 x 100 mL), the combined organic layers were dried (Na_2SO_4), filtered and evaporated. Flash chromatography of the residue (hexanes/ethyl acetate, 20:1) gave the desired mono-deprotected phenol **18** (2.12 g, 72 %) and a second fraction consisting of the bis-deprotected phenol (445 mg, 19 %). Analytical and spectral data of **18**: $[\alpha]_D^{20} = -12.3$ (*c* = 1.5 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$):

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[6] Prolonged reaction times led to increased amounts of double deprotection. Whereas the starting material and the mono-deprotected product are inseparable by flash chromatography, the bis-deprotected compound can be readily removed.

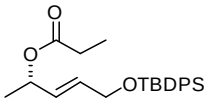
δ = 11.36 (s, 1H; O*H*), 7.44-7.40 (m, 2H), 7.38-7.30 (m, 3H), 6.41 (d, *J* = 1.5 Hz, 1H), 6.17 (d, *J* = 1.6 Hz, 1H), 5.40 (app. d, *J* = 12.2 Hz, 1H), 5.36 (app. d, *J*= 12.2 Hz, 1H), 3.85-3.77 (m, 1H), 2.64 (dd, *J* = 13.1, 5.9 Hz, 1H), 2.57 (dd, *J* = 13.1, 6.8 Hz, 1H), 1.41-1.16 (m, 8H), 0.91 (s, 9H), 0.89-0.86 (m, 12H), 0.14 (s, 3H), 0.13 (s, 3H), 0.01 (s, 3H), -0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 163.1, 156.8, 147.4, 135.6, 128.7, 128.5, 128.3, 112.9, 111.2, 103.8, 73.2, 66.8, 44.4, 36.8, 31.9, 25.9, 25.8, 25.0, 22.6, 18.4, 18.1, 14.0, -4.0, -4.1, -4.6, -4.7; IR (film): $\tilde{\nu}$ = 2951, 2929, 2857, 1654, 1618, 1567, 1426, 1388, 1251, 1204, 1089, 832, 773 cm^{-1}; MS (EI): *m*/*z* (%): 529 (34) [M^+ - *t*Bu], 421 (39), 397 (76), 305 (11), 249 (15), 215 (11), 91 (100), 73 (42); HRMS (ESI$^+$) calcd for $C_{33}H_{54}NaO_5Si_2$ [M^+ + Na]: 609.3402; found: 609.3406. The enantiomer was prepared analogously (2.40 mmol scale, 80 %).

Iodide 19: NIS (1.21 mg, 5.37 mmol) was added to a solution of phenol **18** (2.1 g, 3.58 mmol) in CH_2Cl_2 (30 mL) at 0 °C and the resulting mixture stirred at room temperature for 14 h giving an orange suspension. Aq. sat. $Na_2S_2O_3$ (30 mL) was added and the mixture stirred until a colorless organic layer was obtained (2-3 min). The phases were separated and the aqueous layer extracted with *tert*-butyl methyl ether (3 x 40 mL), the combined extracts were dried (Na_2SO_4), filtered and evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate, 100:1→30:1) gave the title compound as a colorless oil (2.16 g, 85 %). $[\alpha]_D^{20} = -28.1$ (*c* = 1.1 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.40 (s, 1H), 7.42-7.31 (m, 5H), 6.34 (s, 1H), 5.40 (d, *J* = 12.2 Hz, 1H), 5.38 (d, *J* = 12.2 Hz, 1H), 4.10-4.01 (m, 1H), 2.89-2.81 (m, 2H), 1.50-1.20 (m, 8H), 0.90 (s, 9H), 0.90-0.84 (m, 3H), 0.86 (s, 9H), 0.24 (s, 3H), 0.13 (s, 3H), -0.00 (s, 3H), -0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7, 161.6, 156.8, 149.8, 128.8, 128.6, 128.5, 115.1, 83.3, 71.4, 67.3, 49.0, 37.3, 32.0, 26.0, 25.7, 25.0, 22.7, 18.6, 18.1, 14.0, -4.0, -4.1, -4.3, -4.7; IR (film): $\tilde{\nu}$ = 2953, 2929, 2857, 1651, 1598, 1536, 1395, 1359, 1249, 1195, 1095, 1048, 832, 807, 773 cm^{-1}; MS (EI): *m*/*z* (%): 655 (81) [M^+ - *t*Bu], 547 (27), 471 (100), 396 (20), 353 (12), 280 (11), 215 (28), 159 (6), 91 (95), 73 (48). The enantiomer was prepared analogously (1.70 mmol scale, 91 %).

Aldehyde 20: Substrate **19** (1.40 g, 1.96 mmol) was dried by azeotropic distillation with toluene (10 mL) and then under high vacuum for 2 h prior to use. It was dissolved in Et_2O (22 mL) and the solution cooled to –100 °C before MeLi (1.6 M in Et_2O, 1.6 mL, 2.55 mmol) was added over 2 min. After stirring for 20 min at –100 °C, *t*BuLi (2.2 M in pentane, 2.2 mL, 4.9 mmol) was added dropwise

and the resulting yellow solution stirred for 20 min before dry DMF (1.5 mL, 19.6 mmol) was introduced. The suspension was allowed to warm to –35 °C over 2 h before being recooled to –55 °C. Freshly distilled acetyl chloride (1.4 mL, 19.6 mmol) was added dropwise and the mixture was brought to –25 °C over 2 h. The reaction was quenched at –25 °C with vigorous stirring upon slow addition of pH 7-buffer (5 mL). After reaching ambient temperature, the mixture was diluted with brine (10 mL), extracted with EtOAc (5 x 25 mL), the combined organic phases were dried (Na_2SO_4), filtered and evaporated, and the residue purified by flash chromatography (hexanes/ethyl acetate, 20:1 → 6:1) to give the title compound as a pale yellow oil (970 mg, 75 %). $[\alpha]_D^{20} = -22.9$ (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.10 (s, 1H), 7.44-7.32 (m, 5H), 6.16 (s, 1H), 5.30 (s, 2H), 3.91-3.80 (m, 1H), 3.11 (dd, *J* = 13.0, 4.8 Hz, 1H), 2.98 (dd, *J* = 13.0, 7.8 Hz, 1H), 1.97 (s, 3H), 1.51-1.2 (m, 8H), 0.94 (s, 9H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.82 (s, 9H), 0.26 (s, 3H), 0.24 (s, 3H), -0.07 (s, 3H), -0.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.0, 168.6, 163.9, 157.5, 151.9, 147.1, 135.5, 128.7, 128.6, 128.4, 121.1, 120.6, 119.4, 73.2, 67.1, 40.9, 37.7, 32.0, 25.9, 25.4, 24.6, 22.6, 20.2, 18.1, 18.0, 14.0, -4.1, -4.4, -4.8, -4.9; IR (film): $\tilde{\nu}$ = 2931, 2901, 2857, 1767, 1586, 1470, 1390, 1365, 1205, 1179, 1149, 1110, 1021, 980 cm^{-1}; MS (EI): *m/z* (%): 599 (26) [M^+ - *t*Bu], 557 (19), 491 (5), 449 (100), 425 (10), 349 (4), 215 (23), 91 (41), 73 (30); HRMS (ESI$^+$) calcd for $C_{36}H_{56}NaO_7Si_2$ [M^+ + Na]: 679.3456; found: 679.3449. The enantiomer was prepared analogously (0.70 mmol scale, 87 %).

(*S,E*)-(−)-5-(*tert*-Butyldiphenylsilyloxy)pent-3-en-2-yl propionate (*ent*-23): A solution of freshly distilled propionyl chloride (5.7 mL, 66 mmol) in CH_2Cl_2 (15 mL) was added dropwise to a solution of alcohol **22** (11.2 g, 33.0 mmol)[7] and pyridine (13.5 mL, 167 mmol) in CH_2Cl_2 (60 mL) at -20 °C and the mixture stirred for 45 min until TLC control indicated complete conversion. For work-up, aq. sat. NH_4Cl (40 mL) was added and the product was extracted with *tert*-butyl methyl ether (600 mL in several portions). The combined organic phases were washed with aq. sat. NH_4Cl (2x 200 mL) and brine (100 mL), dried (Na_2SO_4), and evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate, 10:1) provided the title compound as a colorless oil (12.8 g, 98 %). The enantiomeric excess (*ee* = 98 %) was determined by HPLC in comparison with the racemate [250 mm Chiralcel OD-H, Ø 4.6 mm, *n*-heptane/2-propanol = 99:1, 0.5 mL min^{-1}, 2.1 MPa, 298 K, UV, 220 nm; t_R (major) = 8.27 min, t_R (minor) = 8.62 min]. $[\alpha]_D^{20} = -35.0$ (*c* =

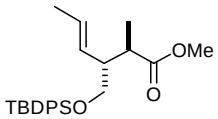


[7] Y. Ichikawa, K. Tsuboi, M. Isobe, *J. Chem. Soc. Perkin Trans. 1* **1994**, 2791-2796.

1.03 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71-7.64 (m 4H), 7.48-7.34 (m, 6H), 5.83-5-71 (m, 2H), 5.45-5.33 (m, 1H), 4.26-4.15 (m, 2H), 2.42. (q, J = 7.6 Hz, 2H), 1.30 (d, J = 6.6 Hz, 3H), 1.15 (t, J = 7.6 Hz, 3H), 1.07 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7, 135.5, 133.6, 130.7, 129.6, 129.4, 127.6, 70.2, 63.5, 27.9, 26.8, 20.3, 19.2, 9.1; IR (film): $\tilde{\nu}$ = 3071, 2932, 2891, 2858, 1733, 1472, 1462, 1427, 1185, 1110, 1037, 964, 822, 739 cm^{-1}; MS (EI): *m*/*z* (%): 339 (2) [M^+ - *t*Bu], 255 (100), 199 (69), 183 (9), 135 (6), 57 (11); HRMS (ESI$^+$) calcd for $C_{24}H_{32}NaO_3Si$ [M^+ + Na]: 419.2013; found: 419.2014; elemental analysis calcd (%) for $C_{24}H_{32}O_3Si$ (396.6): C 72.68, H 8.13; found: C 72.49, H 8.06.

Compound 23: DIAD (1.30 mL, 6.75 mmol) was added dropwise to a solution of alcohol **22** (2.0 g, 5.87 mmol), propionic acid (505 µL, 6.75 mmol) and PPh_3 (1.77 g, 6.75 mmol) in toluene (16 mL) at 0 °C. The reaction was stirred at 0 °C for 1 h and room temperature for 2 h. EtOAc (20 ml) was added and the mixture washed with HCl (1 M, 20 mL) and brine (20 mL), dried (Na_2SO_4), filtered and evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate, 20:1→10:1) gave the title compound as a colorless oil (1.18 g, 59 %). The spectroscopic data were identical to those reported above. The enantiomeric excess (93 % *ee*) was determined by HPLC of the corresponding alcohol.

(2*R*,3*R*,*E*)-Methyl 3-((*tert*-butyldiphenylsilyloxy)methyl)-2-methylhex-4-enoate (*ent*-24): *n*BuLi (1.6

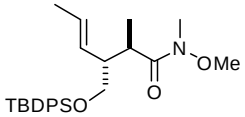


M in hexane, 9.5 mL, 15.1 mmol) was added over 6 min to a colorless solution of hexamethyldisilazane (3.2 mL, 15.3 mmol) in hexane (30 mL) at –78 °C and the reaction stirred for 30 min, giving a white suspension. The cooling-bath was removed, the mixture warmed to room temperature and stirring continued for 1 h giving a colorless solution. The mixture was then concentrated and the resulting white LiHMDS powder dried under high vacuum for 30 min. The freshly prepared LiHMDS was dissolved in toluene (70 mL) and NEt_3 (21.2 mL, 151 mmol) added before the resulting colorless solution was cooled to –78 °C. A solution of compound *ent*-**23** (2.0 g, 5.0 mmol) in toluene (5 mL) was added dropwise and the resulting mixture stirred at –78 °C for 2 h before warming to room temperature over 14.5 h and stirring for a further 30 min. For work up, the mixture was cooled to 0 °C before the reaction was *carefully* quenched with H_2O (20 mL) under vigorous stirring, followed by addition of HCl (1 M, 20 mL). The mixture was transferred to an Erlenmeyer flask and further HCl (1 M) added until pH = 1 was reached, whereupon

the layers were separated and the aqueous phase extracted with EtOAc (3 x 75 mL). The combined organic layers were dried (Na_2SO_4) filtered and evaporated to provide the crude carboxylic acid as a yellow oil.

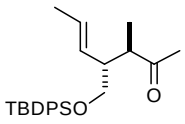
$TMSCHN_2$ (2 M in Et_2O, 7.3 mL, 14.6 mmol) was added over 5 min via a dropping funnel to a solution of the crude acid in MeOH (17 mL, technical grade) at 0 °C. The mixture was stirred at 0 °C for 15 min and room temperature for 1 h. Excess $TMSCHN_2$ was destroyed by the addition of 10 drops of acetic acid (until gas evolution had ceased) and the mixture was adsorbed onto silica and purified by flash chromatography (hexanes/ethyl acetate, 60:1→20:1) to provide the title compound as a colorless oil (1.88 g, 77 %). The diastereomeric ratio (2*R*:2*S* = 96:4) was determined by HPLC [column: 50 mm Zorbax XDB, ∅ 1.8 mm, MeOH/H_2O = 80:20, 1.0 mL min^{-1}, 15.7 MPa, 308 K, UV, 220 nm; t_R (minor) = 16.55 min, t_R (major) = 17.57 min]. ***Anti*-isomer (2*R*, major):** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70-7.62 (m, 4H), 7.47-7.33 (m, 6H), 5.47 (dq, *J* = 15.6, 6.3 Hz, 1H), 5.24 (ddq, *J* = 15.1, 9.0, 1.5 Hz, 1H), 3.69-3.50 (m, 2H), 3.62 (s, 3H), 2.80 (pent, *J* = 7.1 Hz, 1H), 2.69-2.55 (m, 1H), 1.65 (dd, *J* = 6.4, 1.5 Hz, 3H), 1.09-1.01 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.7, 135.6, 133.7, 133.7, 129.6, 128.6, 128.4, 127.6, 65.4, 51.4, 47.5, 39.8, 26.8, 19.3, 18.1, 13.3; IR (film): $\tilde{\nu}$ = 3073, 2931, 2857, 1736, 1472, 1459, 1428, 1192, 1105, 1047, 967, 822, 739 cm^{-1}; MS (EI): *m*/*z* (%): 379 (5) [M^+ - CH_3O], 353 (100) [M^+ - *t*Bu], 213 (98), 183 (22), 135 (12); HRMS (ESI^+) calcd for $C_{25}H_{34}NaO_3Si$ [M^+ + Na]: 433.2169; found: 433.2165; elemental analysis calcd (%) for $C_{25}H_{34}O_3Si$ (410.6): C 73.13, H 8.35; found: C 73.06, H 8.30. ***Syn*-isomer (2*S*, minor):** characteristic signals: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.79 (pent, *J* = 6.9 Hz, 1H), 2.45-2.32 (m, 1H), 1.12 (d, *J* = 7.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.6, 129.6, 127.8, 64.9, 51.2, 48.5, 40.3, 18.0, 14.8. The enantiomer **24** was prepared analogously (4.09 mmol scale, 81 %).

(2*R*,3*R*,*E*)-(+)-3-((*tert*-Butyldiphenylsilyloxy)methyl)-*N*-methoxy-*N*,2-dimethylhex-4-enamide: *N*,*O*-Dimethylhydroxylamine hydrochloride (641 mg, 6.58 mmol) was dried under high vacuum for 1 h prior to use. Compound *ent*-**24** (1.8 g, 4.38 mmol) and THF (28 mL) were introduced and the mixture was cooled to –25 °C. *i*PrMgCl (2 M in THF, 6.6 mL, 13.2 mmol) was added dropwise and the mixture stirred for 1 h at -25 °C before warming to room temperature over 30 min. For work-up, aq. sat. NH_4Cl and brine were added (10 mL each) and the product extracted with ethyl acetate (3 x 15 mL). The combined organic phases were



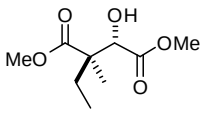
dried (Na_2SO_4) and evaporated and the diastereomers of the product separated by flash chromatography (hexanes/ethyl acetate, 30:1 → 4:1) to give the title compound as a colorless syrup (1.52 g, 79 %). $[\alpha]_D^{20}$ = + 24.2 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71-7.60 (m, 4H), 7.47-7.31 (m, 6H), 5.49 (dq, *J* = 15.2, 6.2 Hz, 1H), 5.36 (ddd, *J* = 15.3, 9.1, 1.4 Hz, 1H), 3.68-3.58 (m, 5H), 3.25-3.06 (br s, 4H); 2.65-2.52 (m, 1H), 1.67 (dd, *J* = 5.2, 1.4 Hz, 3H), 1.10-1.00 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.5 (br), 135.7, 135.6, 133.9, 133.8, 129.9, 129.5, 129.5, 127.8, 127.5, 127.5, 65.9, 61.3, 47.4, 35.3, 32.3 (br), 26.9, 19.3, 18.1, 14.8; IR (film): $\tilde{\nu}$ = 2961, 2932, 2857, 1660, 1472, 1461, 1427, 1383, 1176, 1105, 997, 823, 739 cm^{-1}; MS (EI): *m/z* (%): 424 (<1) [M^+ - CH_3], 382 (100) [M^+ - *t*Bu], 379 (9), 213 (12), 135 (21); HRMS (ESI$^+$) calcd for $C_{26}H_{37}NNaO_3Si$ [M^+ + Na]: 462.2435; found: 462.2433; elemental analysis calcd (%) for $C_{26}H_{37}NO_3Si$ (439.7): C 71.03, H 8.48; found: C 70.88, H 8.43. The enantiomer was prepared analogously from **24** (2.44 mmol scale, 95 %).

(3*R*,4*R*,*E*)-(+)-4-((*tert*-Butyldiphenylsilyloxy)methyl)-3-methylhept-5-en-2-one (*ent*-25): MeMgBr (3 M in Et_2O, 3.4 mL, 10.24 mmol) was added over 10 min to a solution of the Weinreb-amide described above (1.5 g, 3.41 mmol) in THF (15 mL) at –20 °C and the mixture warmed to 0 °C over 2.5 h to complete the conversion. The reaction was quenched by the careful addition of aq. sat. NH_4Cl (10 mL) and extracted with *tert*-butyl methyl ether (3 x 10 mL). The combined organic phases were dried (Na_2SO_4) and evaporated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 6:1) to provide the title compound as a colorless oil (1.24 g, 92 %). $[\alpha]_D^{20}$ = + 1.2 (*c* = 1.3 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68-7.60 (m, 4H), 7.46-7.34 (m, 6H), 5.42 (dqd, *J* = 15.3, 6.4, 0.6 Hz, 1H), 5.15 (ddq, *J* = 15.2, 9.1, 1.6 Hz, 1H), 3.61 (dd, *J* = 10.2, 5.4 Hz, 1H), 3.54 (dd, *J* = 10.1, 7.3 Hz, 1H), 2.84 (pent, *J* = 6.9 Hz, 1H), 2.66-2.56 (m, 1H), 2.11 (s, 3H), 1.61 (dd, *J* = 6.4, 1.6 Hz, 3H), 1.06 (s, 9H), 0.96 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.2, 135.6, 135.6, 133.6, 133.6, 129.7, 128.4, 128.2, 127.7, 65.6, 47.3, 46.9, 28.7, 26.9, 19.3, 18.1, 12.2; IR (film): $\tilde{\nu}$ = 2961, 2932, 2857, 1660, 1472, 1461, 1427, 1383, 1176, 1105, 997, 823, 739 cm^{-1}; MS (EI): *m/z* (%): 337 (69) [M^+ - *t*Bu], 265 (9), 253 (15), 199 (100), 183 (29), 139 (31), 123 (11); HRMS (ESI$^+$) calcd for $C_{25}H_{34}NaO_2Si$ [M^+ + Na]: 417.2220; found: 417.2221; elemental analysis calcd (%) for $C_{25}H_{34}O_2Si$ (394.6): C 76.09, H 8.68; found: C 76.15, H 8.73. The enantiomer **25** was prepared analogously (1.82 mmol scale, 92 %).



Diester *ent*-27: A solution of dimethyl L-malate *ent*-**26** (4.03 g, 24.9 mmol) in THF (5.0 mL) was added over 3 min to a freshly prepared solution of LDA [*n*BuLi (1.6 M in hexane, 34 mL, 54 mmol), diisopropylamine (7.8 mL, 55 mmol) in THF (95 mL)] at –71 °C internal temperature. After 1 h, MeI (4.2 mL, 68 mmol) was introduced and the mixture stirred for 18 h at that temperature. For work-up, acetic acid (5.2 mL) in Et_2O (8.0 mL) was added, the mixture was diluted with Et_2O (400 mL), and the organic phase washed with water (50 mL), aq. sat. $NaHCO_3$ (50 mL), and brine (50 mL), dried (Na_2SO_4), and evaporated. Purification of the residue by flash chromatography (pentane/Et_2O, 2:1 → 1:1) provided the title compound (2.20 g, 50 %) as a colorless oil. The diastereoselectivity (*anti*:*syn* = 91:9) was determined by ^{1}H NMR. **Major isomer (*anti*, 3*R*):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.27 (dd, *J* = 6.4, 3.7 Hz, 1H), 3.80 (s, 3H), 3.68 (s, 3H), 3.15 (d, *J* = 6.6 Hz, 1H; O*H*), 3.03 (qd, *J* = 7.2, 3.7 Hz, 1H), 1.30 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7, 173.4, 72.4, 52.7, 52.0, 43.1, 13.1; **minor isomer (*syn*, 3*S*):** characteristic signals: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.62 (dd, *J* = 5.4, 3.6 Hz, 1H), 3.81 (s, 3H), 3.73 (s, 3H), 2.93 (qd, *J* = 7.2, 3.7 Hz, 1H), 1.16 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 71.4, 52.8, 52.2, 42.9; IR (film): $\tilde{\nu}$ = 3496 (br), 2987, 2956, 1729, 1453, 1437, 1202, 1138, 1101, 1067, 1005 cm^{-1}; MS (EI): *m*/*z* (%): 145 (6) [M^+ - OMe], 117 (100), 85 (88), 57 (61); HRMS (CI) calcd for $C_7H_{13}O_5$ [M^+ + H]: 177.0763; found: 177.0762. The reported data are consistent with those previously reported.[8] The enantiomer **27** was prepared analogously from dimethyl D-malate **26** (38.0 mmol scale, 50 %).

Compound *ent*-28: A solution of compound *ent*-**27** (3.30 g, 18.7 mmol) in THF (3.0 mL) was added



over 8 min to a freshly prepared solution of LDA [*n*BuLi (1.6 M in hexane, 23.9 mL, 38.3 mmol), diisopropylamine (6.3 mL, 45.0 mmol) in THF (50 mL)] at -74 °C internal temperature. After 135 min, EtI (4.0 mL, 50.5 mmol) was introduced and stirring continued at –78 °C for 5.5 h before the mixture was warmed to 4 °C over the course of 13 h. For work-up, acetic acid (4.8 mL) in Et_2O (5.0 mL) was added giving a pale-yellow slurry. The mixture was diluted with Et_2O (300 mL) and H_2O (50 mL), the aqueous layer was extracted with Et_2O (2 × 100 mL), and the combined organic phases were successively washed with aq. sat. $Na_2S_2O_3$ (150 mL), aq. sat. $NaHCO_3$ (150 mL), and brine (150 mL), dried (Na_2SO_4), and concentrated. Purification of the

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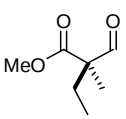
[8] D. Wasmuth, D. Arigoni, D. Seebach, *Helv. Chim. Acta* **1982**, *65*, 344-352.

residue by flash chromatography (pentane/Et_2O, 2:1→1:1) provided the title compound (2.18 g, 57 %) as a colorless oil. The diastereoselectivity (*anti*:*syn* = 95:5) was determined by ^1H NMR. **Major isomer (*anti,* 3*R*):** ^1H NMR (400 MHz, $CDCl_3$): δ = 4.28 (d, *J* = 8.1 Hz, 1H), 3.78 (s, 3H), 3.72 (s, 3H), 3.35 (d, *J* = 8.1 Hz, 1H, O*H*), 1.84 (dq, *J* = 14.3, 7.3 Hz, 1H), 1.59 (dq, *J* = 14.2, 7.4 Hz, 1H), 1.14 (s, 3H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 173.3, 75.7, 52.4, 52.1, 50.6, 28.3, 16.7, 8.7; IR (film): $\tilde{\nu}$ = 3508 (br), 2955, 2881, 1729, 1453, 1436, 1386, 1232, 1157, 1133, 1091, 980 cm^{-1}; MS (EI): *m/z* (%): 173 (3) [M^+ - OMe], 145 (80) [M^+ - CO_2Me], 127 (23), 113 (78), 101 (67), 85 (29), 59 (75), 43 (100); HRMS (CI) calcd for $C_9H_{17}O_5$ [M^+ + H]: 205.1076; found: 205.1075; **minor isomer (*syn,* 3*S*)** characteristic signals: ^1H NMR (400 MHz, $CDCl_3$): δ = 4.46 (d, *J* = 5.8 Hz, 1H), 1.04 (s, 3H). The reported data are consistent with those previously reported.[8] The enantiomer **28** was prepared analogously from substrate **27** (18.7 mmol scale, 60 %).

Compound *ent*-29: A mixture comprising diester *ent*-**28** (393 mg, 1.92 mmol) and KOH (238 mg, 4.2 mmol) in MeOH/water (9:1, 3.8 mL) was stirred for 3 h until TLC control indicated the completed consumption of the substrate. For work-up, water (30 mL) and Et_2O (30 mL) were added and the mixture was acidified to pH = 1 with aq. HCl (2 M). The aqueous phase was extracted with Et_2O (3 x 20 mL) and the combined organic phases were dried (Na_2SO_4) and evaporated to provide the title compound as a colorless oil (361 mg, 99 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 4.38 (s, 1H), 3.73 (s, 3H), 1.86 (dq, *J* = 14.3, 7.3 Hz, 1H), 1.69 (dq, *J* = 14.2, 7.3 Hz, 1H), 1.21 (s, 3H), 0.87 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.3, 176.0, 74.9, 52.3, 50.8, 28.4, 16.8, 8.7; IR (film): $\tilde{\nu}$ = 3460 (br), 2977, 2881, 1714, 1459, 1436, 1386, 1335, 1238, 1158, 1134, 1086 cm^{-1}; MS (EI): *m/z* (%): 159 (11) [M^+ - OMe], 145 (62), 128 (17), 116 (65), 113 (100), 101 (62), 59 (85); HRMS (ESI^+) calcd for $C_8H_{14}NaO_5$ [M^+ + Na]: 213.0733; found: 213.0733. The enantiomer **29** was prepared analogously starting from compound **28** (3.42 mmol scale, 94 %).

Aldehyde *ent*-30: A solution of acid *ent*-**29** (250 mg, 1.31 mmol) and Et_3N (92 µL, 0.66 mmol) was

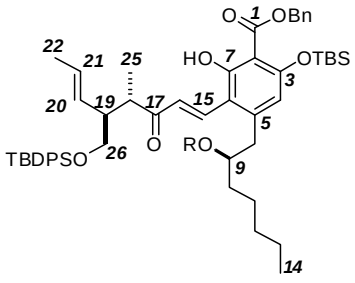


subjected to electrolysis for 2.5 h under permanent stirring and water cooling [Laboratory Power Supply PS-2403-D (*Voltcraft*); Electrodes: Platinum, 2 x 2 cm^2 surface area, 0.5 cm distance apart, Voltage 24 V], after which time the current dropped from 0.38 mA to 0.07 mA. The yellow mixture was concentrated and the residue purified by flash

chromatography (hexanes/ethyl acetate, 4:1), giving the title aldehyde as a colorless oil (111 mg, 59 %). $[\alpha]_D^{20} = -3.4$ (*c* = 1.84 in $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.70 (s, 1H), 3.75 (s, 3H), 1.94 (dq, *J* = 14.3, 7.4 Hz, 1H), 1.77 (dq, *J* = 14.3, 7.4 Hz, 1H), 1.28 (s, 3H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.7, 172.7, 58.1, 52.3, 27.4, 16.2, 8.6; IR (film): $\tilde{\nu}$ = 2974, 2881, 2840, 1744, 1721, 1459, 1435, 1245, 1149, 1132 cm^{-1}; MS (GC-EI): *m*/*z* (%): 116 (49), 113 (19), 101 (100), 84 (42), 73 (24), 69 (64), 59 (50); HRMS (CI) calcd for $C_7H_{13}O_3$ [M^+ + H]: 145.0865; found: 145.0865. The enantiomer **30** was prepared analogously starting from acid **29** (1.31 mmol scale, 55 %).

Completion of the Total Synthesis

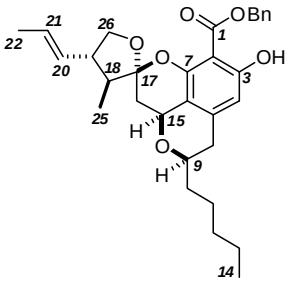
Compound 31: LDA (0.5 M in THF, 1.67 mL, 0.84 mmol) was added to a solution of methyl ketone **25** (322 mg, 0.82 mmol) in THF (5.2 mL) at –78 °C. The mixture was stirred for 15 min before a solution of aldehyde **20** (480 mg, 0.73 mmol) in THF (8.5 mL + 0.5 mL wash) was added dropwise over 7 min. The resulting yellow solution was stirred at –78 °C for 20 min before warming slowly to room temperature over 1.5 h. The reaction was cooled to 0 °C and aq. sat. NH_4Cl (5 mL) introduced. The layers were separated and the aqueous phase extracted with ethyl acetate (5 x 5 mL). The combined extracts were dried (Na_2SO_4), filtered and evaporated. Flash chromatography of the residue (hexanes/ethyl acetate, gradient 30:1) gave the title compound as a colorless oil (471 mg, 65 %). $[\alpha]_D^{20} = -32.7$ (*c* = 1.2 in CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 12.55 (s, 1H; 7-O*H*), 7.68 (d, *J* =



15.8 Hz, 1H; H15), 7.68-7.62 (m, 4H; TBDPS), 7.43-7.30 (m, 6H; TBDPS), 7.33 (d, *J* = 15.8 Hz, 1H; H16), 6.28 (s, 1H; H4), 5.45 (app. d, *J* = 12.4 Hz, 1H; PhC*H*$_2$O), 5.43 (dqd, *J* = 15.3, 6.4, 0.6 Hz, 1H; H21), 5.40 (app. d, *J* = 12.4 Hz, 1H; PhC*H*$_2$O), 5.24 (ddq, *J* = 15.3, 9.0, 1.6 Hz, 1H; H20), 3.88-3.81 (m, 1H; H9), 3.61 (AB part of ABX, *J* = 10, 3.7 Hz, 1H; H26a), 3.60 (AB part of ABX, *J* = 10, 4.8 Hz, 1H; H26b), 3.07, (m, 1H; H18), 2.87 (dd, *J* = 13,4, 7.4 Hz, 1H; H8a), 2.78 (dd, *J* = 13.4, 6.9 Hz, 1H; H8b), 2.73-2.67 (m, 1H; H19), 1.62 (dd, *J* = 6.4, 1.6 Hz, 3H; H22), 1.45-1.18 (m, 8H; H10-H13), 1.03 (s, 9H; TBDPS), 1.00 (d, *J* = 7.0 Hz, 3H; H25), 0.92 (s, 9H, 3-TBS), 0.86 (m, 3H; H14), 0.81 (s, 9H; 9-TBS), 0.18 (s, 3H; 3-TBS), 0.17 (s, 3H; 3-TBS), -0.05 (s, 3H; 9-TBS), -0.17 (s, 3H; 9-TBS); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 203.6 (C17), 171.9 (C1), 164.5 (C7), 157.9 (C3), 149.0 (C5), 135.9 (TBDPS), 135.9 (TBDPS), 135.9 (Ph) 134.9 (C15), 134.1 (TBDPS), 134.0 (TBDPS),

129.8 (TBDPS), 129.8 (TBDPS), 129.3 (C20), 129.0 (Ph), 128.8 (Ph), 128.7 (Ph), 128.2 (C21), 128.2 (C16), 127.9 (TBDPS), 127.7 (TBDPS), 115.8 (C6), 115.2 (C4), 104.2 (C2), 73.4 (C9), 67.4 (Ph*C*H_2), 65.8 (C26), 47.4 (C19), 45.8 (C18), 42.7 (C8), 37.8 (C10), 32.3 (C12), 26.9 (TBDPS), 25.9 (9-TBS), 25.8 (3-TBS), 25.2 (C11), 23.0 (C13), 19.5 (TBDPS), 18.7 (3-TBS), 18.2 (C22), 18.1 (9-TBS), 14.2 (C14), 12.8 (C25), -3.7 (3-TBS), -3.9 (3-TBS), -4.7 (9-TBS), -4.8 (9-TBS); IR (film): $\tilde{\nu}$ = 2952, 2926, 2857, 1682, 1654, 15885, 1543, 1439, 1411, 1373, 1358, 1254, 1197, 1173, 1105, 1053, 775 cm^{-1}; HRMS (ESI^+) calcd for $C_{59}H_{87}O_7Si_3$ [M^+]: 991.5754; found: 991.5758. The enantiomer *ent*-**31** was prepared analogously (0.29 mmol scale, 65 %).

Compound 32: Freshly distilled acetyl chloride (0.66 mL, 9.38 mmol) was added dropwise to a solution of MeOH (0.38 mL, 9.38 mmol) in CH_2Cl_2 (4 mL) at 0 °C. After stirring at 0 °C for 15 min a solution of compound **31** (465 mg, 0.47 mmol) in CH_2Cl_2 (7 mL) was slowly introduced. The resulting yellow solution was stirred at 0 °C for 30 min and for a further 16 h at ambient temperature. The solvent was evaporated and the residue purified by flash chromatography (hexanes/ethyl acetate, 60:1 → 40:1) to give the title compound as a colorless oil (218 mg, 92 %). $[\alpha]_D^{20}$ = –128.1 (*c* = 0.8 in CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 11.41 (s, 1H; 3-OH), 7.44-7.31 (m, 5H, Ph), 6.29 (s, 1H; H4),



5.41 (app. d, *J* = 12.2, 1H; PhC*H*$_2$O), 5.32 (app. d, *J* = 12.2 Hz, 1H; PhC*H*$_2$O), 5.24 (dq, *J* = 15.1, 6.4 Hz, 1H; H21), 5.13 (ddq, *J* = 15.1, 8.5, 1.6 Hz, 1H; H20), 4.68 (dd, *J* = 12.4, 5.4 Hz, 1H; H15), 3.95 (app. t, *J* = 8.5 Hz, 1H; H26a), 3.81-3.75 (m, 1H; H9), 3.51 (app. t, *J* = 8.5 Hz, 1H; H26b), 2.75 (ddm, *J* = 17.5, 4.1 Hz, 1H; H8eq), 2.56 (ddm, *J* = 17.5, 11.0 Hz, 1H; H8ax), 2.46-2.39 (m, 1H; H19), 2.09 (dd, *J* = 12.1, 5.4 Hz, 1H; H16eq), 1.87 (app. t, *J* = 12.3 Hz, 1H; H16ax), 1.69 (dq, *J* = 11.1, 6.7 Hz, 1H; H18), 1.64 (dd, *J* = 6.4, 1.5 Hz, 3H; H22), 1.64-1.25 (m, 8H; H10-13), 0.91-0.88 (m, 3H; H14), 0.80 (d, *J* = 6.7 Hz, 3H; H25); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 171.6 (C1), 162.5 (C3), 152.5 (C7), 142.0 (C5), 136.1 (Ph), 130.5 (C20), 129.1. 128.9, 128.8 (Ph), 127.9 (C21), 113.2 (C6), 109.7 (C17), 108.5 (C4), 100.2 (C2), 75.2 (C9), 72.5 (C26), 68.3 (C15), 67.4 (CH_2Ph), 49.3 (C18), 47.4 (C19), 36.6 (C10), 34.8 (C8), 34.4 (C16), 32.2 (C12), 25.4 (C11), 23.0 (C13), 18.0 (C22), 14.2 (C14), 10.8 (C25); IR (film): $\tilde{\nu}$ = 2931, 2855, 1737, 1711, 1653, 1607, 1583, 1455, 1428, 1391, 1344, 1299, 1237, 1205 1171, 1090, 1004, 965, 910, 838 cm^{-1}; MS (EI): *m*/*z* (%): 506 (14) [M^+], 416 (26), 415 (100), 397 (45), 369 (38), 311 (7), 262 (12), 234 (53), 91 (51); HRMS (ESI^+) calcd for $C_{31}H_{38}NaO_6$ [M^+ + Na]: 529.2560;

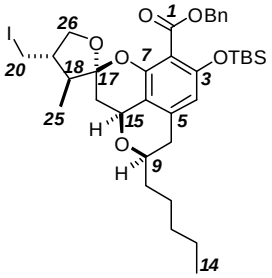
found: 529.2560. The enantiomer *ent*-**32** was prepared analogously from *ent*-**31** (70.5 µmol scale, 95 %).

Compound 33: Imidazole (27 mg, 0.39 mmol) and *tert*-butyldimethylsilyl chloride (45 mg, 0.30 mmol) were sequentially added to a solution of compound **32** (100 mg, 0.20 mmol) in CH_2Cl_2 (1.2 mL). The resulting pale yellow suspension was stirred for 2.5 h before being diluted with CH_2Cl_2 (1.2 mL), cooled to 0 °C and quenched with aq. sat. NH_4Cl (2.5 mL). The layers were separated and the aqueous phase extracted with CH_2Cl_2 (3 x 2.5 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated. Flash chromatography of the residue (hexanes:ethyl acetate, 30:1) gave compound **33** as a colorless oil (122 mg, 98 %). $[\alpha]_D^{20}$ = –110.2 (*c* = 1.0 in CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 7.42-7.39 (m, 2H; Ph), 7.36-7.29 (m, 3H; Ph), 6.17 (s, 1H, H4), 5.48 (dq, *J* = 15.0, 6.5 Hz, 1H; H21), 5.30 (app. d, *J* = 12.3 Hz, 1H; PhC*H*$_2$O), 5.20 (app. d, *J* = 12.3 Hz, 1H; PhC*H*$_2$O), 5.20 (ddq, *J* = 15.1, 8.7, 1.6 Hz, 1H; H20), 4.71 (ddm, *J* = 12.3, 5.3 Hz, 1H; H15), 3.96 (app. t, *J* = 8.6 Hz, 1H; H26a), 3.82-3.78 (m, 1H; H9), 3.52 (app. t, *J* = 8.6 Hz, 1H; H26b), 2.72 (ddm, *J* = 16.9, 3.9 Hz, 1H; H8eq), 2.53 (ddm, *J* = 16.9, 11.1 Hz, 1H; H8ax), 2.53-2.48 (m, 1H; H19), 2.09 (dd, *J* = 12.3, 5.3 Hz, 1H; H16eq), 1.87 (t, *J* = 12.3 Hz, 1H; H16ax), 1.71 (dq, *J* = 11.2, 6.7 Hz, 1H; H18), 1.68 (dd, *J* = 6.4, 1.5 Hz, 3H; H22), 1.65-1.25 (m, 8H; H10-13), 0.94 (s, TBS; 9H), 0.90 (m, 3H; H14), 0.81 (d, *J* = 6.7 Hz, 3H; H25), 0.19 (s, 3H; TBS), 0.18 (s, 3H; TBS); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 166.0 (C1), 152.5 (C3), 149.1 (C7), 136.4 (Ph), 136.1 (C5), 130.5 (C20), 128.8 (Ph), 128.7 (Ph), 128.4 (Ph), 128.2 (C21), 115.1 (C6), 112.5 (C2), 111.0 (C4), 109.3 (C17), 75.6 (C9), 72.3 (C26), 68.3 (C15), 66.9 (Ph*C*H$_2$), 49.3 (C18), 47.8 (C19), 36.6 (C10), 35.0 (C16), 34.3 (C8), 32.2 (C12), 25.6 (TBS), 25.4 (C11), 23.0 (C13), 18.3 (TBS), 18.1 (C22), 14.2 (C14), 10.9 (C25), -4.3 (TBS), -4.4 (TBS); IR (film): $\tilde{\nu}$ = 2931, 2855, 1737, 1711, 1653, 1607, 1583, 1455, 1428, 1391, 1344, 1299, 1237, 1205 1171, 1090, 1004, 965, 910, 838 cm^{-1}; MS (EI): *m*/*z* (%): 563 (32) [M^+ - *t*Bu], 511 (14), 471 (11), 425 (100), 375 (20), 335 (23), 277 (7), 167 (35), 91 (78), 73 (13); HRMS (ESI$^+$) calcd for $C_{37}H_{52}NaO_6Si$ [M^+ + Na]: 643.3425; found: 643.3432. The enantiomer *ent*-**33** was prepared analogously from *ent*-**32** (7.3 µmol scale, 92 %).

Compound 34: OsO_4 (2.5 % in *t*BuOH, 81 µL, 8.1 µmol) and *N*-methylmorpholine-*N*-oxide (21 mg, 177.2 µmol) were sequentially added to a solution of compound **33** (100 mg, 161.1 µmol) in acetone (2.8 mL). The resulting yellow mixture was stirred for 2 h before the dropwise addition of aq. sat. $Na_2S_2O_3$ and brine (1:1, 4 mL). The layers were separated and the aqueous phase extracted with EtOAc (5 x 2 mL). The combined extracts were dried (Na_2SO_4), filtered and concentrated. The resulting yellow oil (114 mg) was dissolved in CH_2Cl_2 (2 mL) and $Pb(OAc)_4$ (75 mg, 169.1 µmol) in CH_2Cl_2 (0.75 mL) added dropwise. The off-white suspension was stirred for 20 min before the reaction was quenched at 0 °C with aq. sat. $NaHCO_3$ (2 mL). The resulting suspension was filtered through a Celite® plug that was rinsed with EtOAc (5 x 3 mL). The combined filtrates were washed with brine (5 mL), dried (Na_2SO_4), filtered and evaporated. A solution of the residue in THF (1.8 mL) was added to a solution of $NaBH_4$ (18 mg, 483.2 µmol) in H_2O (0.63 mL) at 0 °C and the resulting mixture was stirred at ambient temperature for 20 min before the dropwise addition of brine (0.5 mL) and sat. aq. NH_4Cl (0.5 mL). The aqueous phase was extracted with EtOAc (3 x 1 mL) and the combined extracts were dried (Na_2SO_4), filtered and concentrated. Purification of the crude product by flash chromatography (hexanes/ethyl acetate 8:1 $\rightarrow$ 4:1) gave the title compound as a colorless oil (79 mg, 80 %); $[\alpha]_D^{20}$ = –107.1 (*c* = 0.9 in CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 7.47-7.41 (m, 2H; Ph), 7.37-7.29 (m, 3H; Ph), 6.18 (s, 1H, H4), 5.32 (app. d, *J* = 12.1 Hz, 1H; PhC*H*$_2$O), 5.17 (app. d, *J* = 12.1 Hz, 1H; PhC*H*$_2$O), 4.70 (ddm, *J* = 12.3, 5.3 Hz, 1H; H15), 3.92 (app. t, *J* = 8.6 Hz, 1H; H26a), 3.82-3.78 (m, 1H; H9), 3.66 (app. t, *J* = 8.6 Hz, 1H; H26b), 3.64 (dd, *J* = 10.7, 4.5 Hz, 1H; H20a), 3.49 (dd, *J* = 10.7, 6.6 Hz, 1H; H20b), (2.73 (ddm, *J* = 16.9, 4.0 Hz, 1H; H8eq), 2.53 (ddm, *J* = 16.9, 11.0 Hz, 1H; H8ax), 2.08 (dd, *J* = 12.3, 5.4 Hz, 1H; H16eq), 1.96-1.90 (m, 1H; H19), 1.87 (t, *J* = 12.3 Hz, 1H; H16ax), 1.78 (dq, *J* = 10.5, 6.8 Hz, 1H; H18), 1.68-1.20 (m, 9H; H10-13, OH), 0.94 (s, TBS; 9H), 0.89 (m, 3H; H14), 0.86 (d, *J* = 6.7 Hz, 3H; H25), 0.20 (s, 3H; TBS), 0.18 (s, 3H; TBS); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 166.0 (C1), 152.5 (C3), 149.0 (C7), 136.6 (Ph), 136.2 (C5), 129.2 (2 x Ph), 128.8 (2 x Ph), 128.4 (Ph), 115.0 (C6), 112.7 (C2), 111.0 (C4), 109.7 (C17), 75.6 (C9), 70.0 (C26), 68.3 (C15), 66.8 (Ph*C*H$_2$), 63.3 (C20), 45.8 (C19), 45.0 (C18), 36.6 (C10), 34.5 (C16), 34.4 (C8), 32.2 (C12), 25.6 (TBS), 25.4 (C11), 23.0 (C13), 18.3 (TBS), 14.2 (C14), 12.0 (C25), -4.3 (TBS), -4.4 (TBS); IR (film): $\tilde{\nu}$ = 3250-3600, 2930, 2859, 1732, 1613, 1586, 1429, 1374, 1274, 1204, 1177, 1092, 1005,

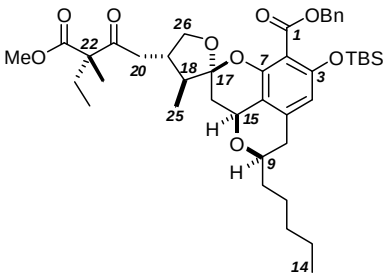
838 cm^{-1}; MS (EI): *m*/*z* (%): 553 (23) [M^+ - *t*Bu], 501 (18), 461 (8), 425 (85), 375 (28), 335 (100), 277 (6), 249 (6), 157 (25), 91 (64), 73 (11); HRMS (ESI^+) calcd for $C_{35}H_{50}NaO_7Si$ [M^+ + Na]: 633.3218; found: 633.3225. The enantiomer *ent*-**34** was prepared analogously (33.8 µmol scale, 97 %).

Compound 35: A solution of freshly sublimed iodine (66 mg, 262.0 µmol) in CH_2Cl_2 (1 mL) was added



dropwise to a solution of compound **34** (80 mg, 131.0 µmol), PPh_3 (53 mg, 262 µmol) and imidazole (27 mg, 393 µmol) in CH_2Cl_2 (1 mL). The mixture was stirred for 3 h before being washed with aq. sat. $Na_2S_2O_3$ (3 x 1mL), dried (Na_2SO_4), filtered and evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate, 10:1) afforded iodide **35** as a colorless oil (94 mg, 94 %); $[\alpha]_D^{20}$ = –74.9 (*c* = 1.08 in CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 7.46-7.42 (m, 2H; Ph), 7.39-7.30 (m, 3H; Ph), 6.19 (s, 1H, H4), 5.28 (app. d, *J* = 11.9 Hz, 1H; PhCH_2O), 5.21 (app. d, *J* = 11.9 Hz, 1H; PhCH_2O), 4.70 (ddm, *J* = 12.2, 5.3 Hz, 1H; H15), 3.95 (app. t, *J* = 8.5 Hz, 1H; H26a), 3.81-3.77 (m, 1H; H9), 3.55 (dd, *J* = 8.5, 7.8 Hz, 1H; H26b), 3.27 (dd, *J* = 10.0, 3.8 Hz, 1H; H20a), 3.08 (dd, *J* = 10.0, 8.0 Hz, 1H; H20b), 2.73 (ddm, *J* = 17.1, 3.9 Hz, 1H; H8eq), 2.53 (ddm, *J* = 17.1, 11.1 Hz, 1H; H8ax), 2.10 (dd, *J* = 12.3, 5.3 Hz, 1H; H16eq), 1.92-1.87 (m, 1H; H19), 1.83 (t, *J* = 12.3 Hz, 1H; H16ax), 1.69 (dq, *J* = 10.3, 6.8 Hz, 1H; H18), 1.63-1.20 (m, 8H; H10-13), 0.95 (s, TBS; 9H), 0.90 (m, 3H; H14), 0.80 (d, *J* = 6.7 Hz, 3H; H25), 0.20 (s, 3H; TBS), 0.19 (s, 3H; TBS); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 165.9 (C1), 152.5 (C3), 148.8 (C7), 136.5 (Ph), 136.2 (C5), 129.4 (2 x Ph), 128.9 (2 x Ph), 128.6 (Ph), 115.0 (C6), 112.6 (C2), 111.2 (C4), 110.1 (C17), 75.6 (C9), 73.5 (C26), 68.1 (C15), 66.9 (PhCH_2), 45.6 (C18), 44.9 (C19), 36.6 (C10), 34.7 (C16), 34.3 (C8), 32.2 (C12), 25.6 (TBS), 25.4 (C11), 23.0 (C13), 18.3 (TBS), 14.2 (C14), 11.3 (C25), 9.1 (C20), -4.3 (TBS), -4.4 (TBS); IR (film): $\tilde{\nu}$ = 2951, 2929, 2859, 1732, 1614, 1585, 1484, 1456, 1428, 1373, 1273, 1202, 1175, 1095, 1020, 998, 838 cm^{-1}; MS (EI): *m*/*z* (%): 663 (24) [M^+ - *t*Bu], 611 (8), 571 (10), 537 (4), 320 (15), 485 (4), 425 (100), 375 (16), 335 (22), 267 (20), 141 (6), 918 (78), 73 (12); HRMS (ESI^+) calcd for $C_{35}H_{49}NaO_6Si$ [M^+ + Na]: 743.2235; found: 743.2233. The enantiomer *ent*-**35** was prepared analogously from *ent*-**34** (32.7 µmol scale, 93 %).

Compound 36: Iodide **35** (50 mg, 69.4 µmol) was dried by azeotropic distillation with toluene (0.5 mL) and then under high vacuum. A stock solution of **30** (40 mg, 278 µmol) in Et_2O (1.1 mL) was stirred over MS 4 Å for 10 min. *t*BuLi (2.2 M in pentane, 76 µL, 166.5 µmol) was added dropwise over



1 min to a solution of **35** in Et_2O (1.9 mL) at –105 °C giving a yellow solution. After 4 min the solution of aldehyde **30** was introduced and the mixture stirred for 10 min at –105 °C before the dropwise addition of brine (1 mL) with vigorous stirring. The mixture was warmed to room temperature and the layers were separated, the aqueous phase was extracted with ethyl acetate (5 x 5 mL), the combined organic phases were dried (Na_2SO_4), filtered, and concentrated, and the residue purified by flash chromatography (hexanes/ethyl acetate, 6:1 → 4:1) to give the corresponding alcohol as a mixture of diastereomers (39.4 mg). This mixture was used directly in the next step.

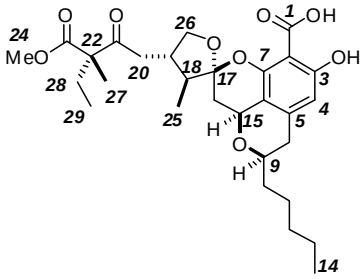
Dess–Martin periodinane (68 mg, 160 µmol) was added to a suspension of the crude alcohol (39.4 mg) and K_2CO_3 (44 mg, 320 µmol) in CH_2Cl_2 (2.0 mL) at 0 °C. After stirring for 30 min, the reaction was quenched with aq. sat. $Na_2S_2O_3$ (2 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 3 mL), the combined organic layers were dried (Na_2SO_4), filtered and concentrated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 6:1) to give the title compound as a colorless oil (29 mg, 74 %); $[\alpha]_D^{20}$ = –58.1 (*c* = 0.5 in CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 7.44-7.40 (m, 2H; Ph), 7.39-7.28 (m, 3H; Ph), 6.17 (s, 1H, H4), 5.25 (AB, *J* = 12.1 Hz, 1H; PhC*H*$_2$O), 5.23 (AB, *J* = 12.1 Hz, 1H; PhC*H*$_2$O), 4.71 (dd, *J* = 12.1, 5.2 Hz, 1H; H15), 4.22 (dd, *J* = 8.6, 8.4 Hz, 1H; H26a), 3.81-3.77 (m, 1H; H9), 3.71 (s, 3H; OMe), 3.39 (dd, *J* = 8.6, 7.5 Hz, 1H; H26b), 2.73 (A part of ABC system, *J* = 10.0, 3.8 Hz, 1H; H20a), 2.72 (ddm, *J* = 17.0, 3.5 Hz, 1H; H8a), 2.53 (ddm, *J* = 17.0, 11.1 Hz, 1H; H8b), 2.41-2.31 (B and C parts of ABC system, 2H; H19, H20b), 2.06 (dd, *J* = 12.1, 5.3 Hz, 1H; H16eq), 1.95 (dq, *J* = 14.0, 7.5, 1H; H28a), 1.87 (dd, *J* = 12.2, 12.1 Hz, 1H; H16ax), 1.82 (dq, *J* = 14.0, 7.5, 1H; H28b), 1.66-1.42 (m, 4H; H18, H10, H11a), 1.41-1.20 (m, 5H; H11b-13), 1.32 (s, 3H; H27), 0.94 (s, TBS; 9H), 0.92-0.87 (m, 3H; H14), 0.84 (t, *J* = 7.5 Hz, 3H; H29), 0.84 (d, *J* = 6.7 Hz, 3H; H25), 0.19 (s, 3H; TBS), 0.17 (s, 3H; TBS); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 207.0 (C21), 173.7 (C23), 166.0 (C1), 152.5 (C3), 149.0 (C7), 136.3 (Ph), 136.1 (C5), 129.1 (2 x Ph), 128.8 (2 x Ph), 128.4 (Ph), 115.0 (C6), 112.6 (C2), 111.0 (C4), 108.9 (C17), 75.6 (C9), 73.0 (C26), 68.3 (C15), 67.1 (Ph*C*H$_2$), 60.0 (C22), 52.6 (C24), 48.5 (C18), 42.1 (C20), 39.2 (C19), 36.6 (C10), 34.9 (C8), 34.3 (C16), 32.2 (C12), 28.2 (C28), 25.6 (TBS), 25.4 (C11), 23.0 (C13), 18.6 (C27), 18.3 (TBS), 14.2 (C14), 11.5 (C25), 8.8 (C29), -4.3 (TBS), -4.4 (TBS); IR (film): $\tilde{\nu}$ = 2951, 2929, 2855, 2329, 1733, 1714, 1613, 1585, 1484, 1453, 1428, 1271, 1259, 1201, 1175, 1095,

1003, 837 cm^{-1}; MS (EI): *m/z* (%): 679 (27) [M^+ - *t*Bu], 627 (10), 587 (5), 483 (14), 425 (97), 375 (36), 335 (100), 283 (16), 183 (17), 123 (8), 91 (77), 73 (13); HRMS (ESI$^+$) calcd for $C_{42}H_{60}NaO_9Si$ [M^+ + Na]: 759.3899; found: 759.3901. The enantiomer *ent*-**36** was prepared analogously from *ent*-**34** (13.5 µmol scale, 97 %).

Berkelic acid benzyl ester (**36a)**: *n*Bu_4NF (1.0 M in THF, 35.6 µL, 35.6 µmol) was added to a colorless solution of compound **36** (25 mg, 33.9 µmol) in THF (0.5 mL). The reaction was stirred for 40 min before being diluted with EtOAc (1 mL) and washed sequentially with H_2O (0.5 mL) and brine (0.5 mL). The organic phase was dried (Na_2SO_4), filtered, and concentrated to a pale yellow oil. Purification by flash chromatography (hexanes/ethyl acetate, 6:1→4:1) through a short plug of silica gave berkelic acid benzyl ester (20 mg, 95 %) as a colorless oil. $[\alpha]_D^{20}$ = –46.0 (*c* = 0.2 in CH_2Cl_2); ^{1}H NMR (600 MHz, CD_3OD): δ = 7.49-7.43 (m, 2H; Ph), 7.39-7.28 (m, 3H; Ph), 6.26 (s, 1H, H4), 5.41 (app. d, *J* = 11.8 Hz, 1H; PhC*H*$_2$O), 5.31 (app. d, *J* = 11.8 Hz, 1H; PhC*H*$_2$O), 4.68 (dd, *J* = 12.3, 5.3 Hz, 1H; H15), 4.15 (app. t, *J* = 8.4 Hz, 1H; H26a), 3.81-3.76 (m, 1H; H9), 3.74 (s, 3H; OMe), 3.36 (app. t, *J* = 8.3 Hz, 1H; H26b), 2.78 (dm, *J* = 17.5 Hz, 1H; H8a), 2.64 (dd, *J* = 17.8, 3.4 Hz, 1H; H20a), 2.53 (ddm, *J* = 17.5, 11.1 Hz, 1H; H8b), 2.45 (dd, *J* = 17.8, 10.2, 1H, H20b), 2.41-2.34 (m, 1H, H19), 2.05 (dd, *J* = 12.1, 5.4 Hz, 1H; H16eq), 1.97 (dq, *J* = 13.9, 7.5, 1H; H28a), 1.84 (dq, *J* = 13.9, 7.5, 1H; H28b), 1.81 (dd, *J* = 12.3, 12.2 Hz, 1H; H16ax), 1.68-1.44 (m, 4H; H18, H10, H11a), 1.43-1.20 (m, 5H; H11b-13), 1.34 (s, 3H; H27), 0.91 (m, 3H; H14), 0.86 (t, *J* = 7.5 Hz, 3H; H29), 0.71 (d, *J* = 6.7 Hz, 3H; H25); ^{13}C NMR (150 MHz, CD_3OD): δ = 208.8 (C21), 174.8 (C23), 171.9.0 (C1), 162.5 (C3), 153.0 (C7), 142.0 (C5), 137.0 (Ph), 130.7 (2 x Ph), 129.7 (2 x Ph), 129.6 (Ph), 113.9 (C6), 110.2 (C17), 109.1 (C4), 102.1 (C2), 76.5 (C9), 73.7 (C26), 69.6 (C15), 68.4 (Ph*C*H$_2$), 61.0 (C22), 52.9 (C24), 49.1 (C18), 42.5 (C20), 39.8 (C19), 37.4 (C10), 35.4 (C8), 34.9 (C16), 33.0 (C12), 29.0 (C28), 26.2 (C11), 23.7 (C13), 19.1 (C27), 14.4 (C14), 11.5 (C25), 9.1 (C29); IR (film): $\tilde{\nu}$ = 2951, 2925, 2854, 1742, 1712, 1654, 1607, 1583, 1456, 1300, 1247, 1206, 1172, 1088, 1007, 803 cm^{-1}; MS (EI): *m/z* (%): 622 (15) [M^+], 532 (32), 531 (100) [M^+ - $PhCH_2$], 438 (7), 409 (11), 369 (57), 331 (7), 262 (10), 234 (45), 183 (22), 91 (66); HRMS (ESI$^+$) calcd for $C_{36}H_{46}NaO_9Si$ [M^+ + Na]: 645.3034; found: 645.3035. ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 11.45 (s, 1H; OH), 7.50-7.42 (m, 2H; Ph), 7.37-7.29 (m, 3H; Ph), 6.28 (s, 1H, H4), 5.40 (app. d, *J* = 11.8 Hz, 1H; PhC*H*$_2$O), 5.32 (app. d, *J* = 11.8 Hz, 1H; PhC*H*$_2$O), 4.67 (dd, *J* =

12.3, 5.5 Hz, 1H; H15), 4.18 (app. t, *J* = 8.4 Hz, 1H; H26a), 3.81-3.76 (m, 1H; H9), 3.72 (s, 3H; OMe), 3.34 (dd, *J* = 8.4, 7.8 Hz, 1H; H26b), 2.76 (ddm, *J* = 17.5, 4.1 Hz, 1H; H8a), 2.57 (m, 1H; H20a), 2.55 (ddm, *J* = 17.5, 11.0 Hz, 1H; H8b), 2.41-2.34 (m, 1H, H19), 2.35 (m, 1H H20b), 2.05 (dd, *J* = 12.2, 5.5 Hz, 1H; H16eq), 1.96 (dq, *J* = 14.0, 7.5, 1H; H28a), 1.85 (dd, *J* = 12.3, 12.2 Hz, 1H; H16ax), 1.81 (dq, *J* = 14.0, 7.5, 1H; H28b), 1.62-1.42 (m, 4H; H18, H10, H11a), 1.41-1.20 (m, 5H; H11b-13), 1.31 (s, 3H; H27), 0.89 (m, 3H; H14), 0.85 (t, *J* = 7.5 Hz, 3H; H29), 0.72 (d, *J* = 6.8 Hz, 3H; H25); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 207.1 (C21), 173.6 (C23), 171.5.0 (C1), 162.6 (C3), 152.4 (C7), 142.0 (C5), 135.9 (Ph), 129.8 (2 x Ph), 128.9 (2 x Ph), 128.7 (Ph), 113.1 (C6), 109.2 (C17), 108.5 (C4), 100.2 (C2), 75.2 (C9), 72.9 (C26), 68.4 (C15), 67.6 (Ph*C*H_2), 60.0 (C22), 52.6 (C24), 48.4 (C18), 41.9 (C20), 38.7 (C19), 36.6 (C10), 34.8 (C8), 34.1 (C16), 32.2 (C12), 28.2 (C28), 25.4 (C11), 23.0 (C13), 18.7 (C27), 14.2 (C14), 11.2 (C25), 8.8 (C29). The enantiomer was prepared analogously (13.0 µmol scale, 77 %).

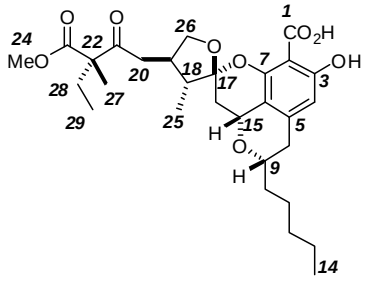
(–)-Berkelic acid ((–)1): $Pd(OH)_2$ (2 mg) was added to a solution of ester **36a** (6.2 mg, 10 µmol) in



EtOAc (0.8 mL). The resulting black suspension was purged with H_2 and vigorously stirred under a static H_2 atmosphere for 1 h whereupon TLC indicated complete consumption of the ester. The mixture was rapidly filtered through a pad of silica (10 micron, ca. 1 cm), eluting with distilled and degassed Et_2O (2 mL, approximately 4 column volumes). Evaporation of the filtrates gave the title compound as a white solid (4.7 mg, 88 %). $[\alpha]_D^{20}$ = –68.0 (*c* = 0.1 in MeOH); $[\alpha]_D^{20}$ = –71.4 (*c* = 0.05 in MeOH). ^{1}H NMR (600 MHz, CD_3OD): δ = 6.27 (s, 1H; H4), 4.72 (dd, *J* = 12.4, 5.3, 1H; H15), 4.30 (app. t, *J* = 8.5 Hz, 1H; H26a), 3.84-3.78 (m, 1H; H9), 3.73 (s, 3H; 24-MeO), 3.50 (dd, *J* = 8.5, 8.4 Hz, 1H; H26b), 2.88 (dd, *J* = 17.8, 3.4 Hz, 1H; H20a), 2.79 (ddm, *J* = 17.3, 3.4, 1H; H8a), 2.70-2.62 (m, 1H; H19), 2.54 (ddm, *J* = 17.3, 11.1, 1H; H8b), 2.53 (dd, *J* = 17.8, 10.2, 1H; H20b), 2.14 (dd, *J* = 12.2, 5.3 Hz, 1H; H16eq), 1.98-1.80 (m, 3H; H28, H18), 1.91 (app. t, *J* = 12.2 Hz, 1H; H16ax), 1.65-1.49 (m, 3H; H10, H11a), 1.47-1.23 (m, 5H; H11b, H12, H13), 1.32 (s, 3H; H27), 1.08 (d, *J* = 6.7 Hz, 3H; H25), 0.92 (m, 3H; H14), 0.83 (t, *J* = 7.5 Hz, 3H; H29); ^{13}C NMR (150 MHz, CD_3OD): δ = 208.8 (C21), 174.8 (C23), 173.7 (C1), 163.4 (C3), 153.1 (C7), 142.2 (C5), 113.7 (C6), 110.7 (C17), 109.3 (C4), 101.2 (C2), 76.6 (C9), 74.1 (C26), 69.5 (C15), 61.0 (C22), 52.9 (24-MeO), approx 49.2 (C18-hidden by solvent signal), 42.6 (C20), 40.5 (C19), 37.4 (C10), 35.4 (C8), 35.0 (C16), 33.0 (C12), 28.9 (C28), 26.2 (C11), 23.7 (C13), 18.9 (C27), 14.4 (C14), 11.9 (C25), 9.0 (C29);

IR (film): $\tilde{\nu}$ = 3230, 2931, 2858, 1744, 1710, 1693, 1632, 1584, 1456, 1435, 1386, 1347, 1308, 1244, 1204, 1173, 1070, 1002, 984, 883, 806 cm^{-1}; HRMS (ESI^-) calcd for $C_{29}H_{39}O_9$ [M^+]: 531.2560; found: 531.2598.IR (film): $\tilde{\nu}$ = 3230, 2931, 2858, 1744, 1710, 1693, 1632, 1584, 1456, 1435, 1386, 1347, 1308, 1244, 1204, 1173, 1070, 1002, 984, 883, 806 cm^{-1}; HRMS (ESI^-) calcd for $C_{29}H_{39}O_9$ [M^-]: 531.2600; found: 531.2596. Non-natural **(+)-berkelic acid ((+)-1)** was prepared analogously (10.0 µmol scale, 87 %).

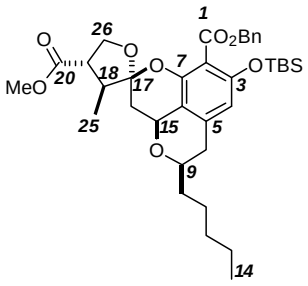
C22(*S*)-Diastereomer of (+)-berkelic acid: This compound was prepared by following the same route



using iodide *ent*-**35** and aldehyde **30**. It showed the following spectral properties: ^{1}H NMR (600 MHz, CD_3OD): δ = 6.28 (s, 1H; H4), 4.73 (ddm, *J* = 12.4, 5.3, 1H; H15), 4.30 (app. t, *J* = 8.5 Hz, 1H; H26a), 3.83-3.78 (m, 1H; H9), 3.72 (s, 3H; 24-MeO), 3.49 (dd, *J* = 8.5, 8.4 Hz, 1H; H26b), 2.92 (dd, *J* = 17.9, 3.4 Hz, 1H; H20a), 2.80 (ddm, *J* = 17.4, 3.8, 1H; H8a), 2.71-2.63 (m, 1H; H19), 2.55 (ddm, *J* = 17.3, 11.0, 1H; H8b), 2.50 (dd, *J* = 17.9, 10.3 1H; H20b), 2.14 (dd, *J* = 12.2, 5.3 Hz, 1H; H16eq), 1.98-1.80 (m, 3H; H28, H18), 1.91 (app. t, *J* = 12.2 Hz, 1H; H16ax), 1.65-1.49 (m, 3H; H10, H11a), 1.47-1.23 (m, 5H; H11b, H12, H13), 1.33 (s, 3H; H27), 1.08 (d, *J* = 6.7 Hz, 3H; H25), 0.92 (m, 3H; H14), 0.82 (t, *J* = 7.5 Hz, 3H; H29); ^{13}C NMR (150 MHz, CD_3OD): δ = 208.8 (C21), 174.8 (C23), 173.7 (C1), 163.4 (C3), 153.1 (C7), 142.2 (C5), 113.7 (C6), 110.7 (C17), 109.3 (C4), 101.2 (C2), 76.6 (C9), 74.1 (C26), 69.5 (C15), 61.0 (C22), 52.9 (24-MeO), approx. 49.2 (C18-hidden by solvent signal), 42.6 (C20), 40.4 (C19), 37.4 (C10), 35.4 (C8), 35.0 (C16), 33.0 (C12), 28.8 (C28), 26.2 (C11), 23.7 (C13), 18.8 (C27), 14.4 (C14), 11.9 (C25), 8.9 (C29); IR (film): $\tilde{\nu}$ = 3230, 2931, 2858, 1744, 1710, 1693, 1632, 1584, 1456, 1435, 1386, 1347, 1308, 1244, 1204, 1173, 1070, 1002, 984, 883, 806 cm^{-1}; HRMS (ESI^-) calcd for $C_{29}H_{39}O_9$ [M^+]: 531.2560; found: 531.2598.

Analogue

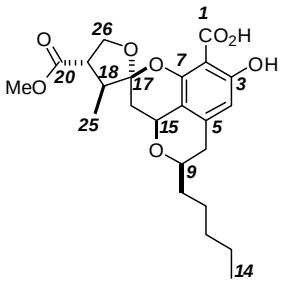
Compound 37: OsO_4 (2.5 % in *t*BuOH, 4 µL, 0.4 µmol) and *N*-methylmorpholine-*N*-oxide (1 mg, 8.9



µmol) were sequentially added to a solution of compound **32** (5.0 mg, 8.1 µmol) in acetone (0.15 mL). The resulting yellow solution was stirred for 2 h before the dropwise addition of aq. sat. $Na_2S_2O_3$ and brine (1:1, 0.1 mL). The layers were separated and the aqueous phase extracted with EtOAc

(5 x 0.3 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated. A solution of $Pb(OAc)_4$ (3.7 mg, 169.1 µmol) in CH_2Cl_2 (0.15 mL) was added dropwise to a solution of the crude diol in CH_2Cl_2 (0.15 mL) and the resulting off-white suspension was stirred for 20 min. The reaction was quenched with aq. sat. $NaHCO_3$ (0.2 mL) at 0 °C and the resulting suspension filtered through a Celite® plug that was carefully rinsed with EtOAc (5 x 0.3 mL). The combined filtrates were washed with brine (0.2 mL), dried (Na_2SO_4), filtered and evaporated, and the residue dissolved in *t*BuOH (40 µL), H_2O (20 µL) and *trans*-2-butene (34 µL, 324 µmol). $NaClO_2$ (80 %, 3.7 mg, 32.4 µmol) and NaH_2PO_4 (4 mg, 32.4 µmol) were added and the mixture stirred for 2.5 h. After evaporation of all volatile materials, the residue was dissolved in MeOH (30 µL). $TMSCHN_2$ (12 µL, 24.3 µmol) was added at 0 °C and the mixture stirred for 20 min before the reaction was quenched by dropwise addition of HOAc. Evaporation of all volatile materials followed by purification of the residue by flash chromatography furnished ester **37** as a colorless oil (5.0 mg, 96 %). $[\alpha]_D^{20}$ = –56.3 (*c* = 0.5 in CH_2Cl_2); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 7.43-7.30 (m, 5H; Ph), 6.19 (s 1H, H4), 5.31 (app. d, *J* = 12.0 Hz, 1H, PhC*H*$_2$O), 5.18 (app. d, *J* = 12.0 Hz, 1H, PhC*H*$_2$O) 4.72 (ddt, *J* = 12.2, 5.4, < 1 Hz, 1H; H15), 3.98-3.92 (m, 2H; H26), 3.82-3.76 (m, 1H; H9), 3.71 (s, 3H, MeO28), 2.73 (dd, *J* = 17.0, 3.9 Hz, 1H; H8a), 2.65 (ddd, *J* = 10.6, 9.2, 7.6 Hz, 1H, H19), 2.53 (dd, *J* = 17.1, 11.1 Hz, 1H, H8b), 2.23 (dq, *J* = 10.7, 6.7 Hz, 1H, H18), 2.13 (dd, *J* = 12.3, 5.4 Hz, 1H, H16eq), 1.87 (t, *J* = 12.3 Hz, 1H, H16ax), 1.64-1.57 (m, 1H, H10a), 1.54-1.26 (m, 7H; H10b-H13), 0.95 (s, 9H, OTBS), 0.92 (d, *J* = 6.7 Hz, 3H; H25), 0.92-0.88 (m, 3H; H14), 0.20 (s, 3H, OTBS), 0.18 (s, 3H, OTBS);^{13}C NMR (150 MHz, CD_2Cl_2): δ = 173.8 (C20), 165.8 (C1), 152.5 (C3), 148.6 (C7), 136.4 (Ph), 136.2 (C5), 129.2 (Ph), 128.8 (Ph), 128.7 (Ph), 114.9 (C6), 112.6 (C2), 111.3 (C4), 109.4 (C17), 75.6 (C9), 68.8 (C26), 68.2 (C15), 66.9 (C30), 52.3 (C21), 48.6 (C19), 47.3 (C18), 36.6 (C10), 34.3 (C8), 34.0 (C16), 32.2 (C12), 25.6 (OTBS), 25.4 (C11), 23.0 (C13), 18.3 (OTBS), 14.2 (C14), 12.1 (C25), -4.3 (OTBS), -4.4 (OTBS); IR (film): $\tilde{\nu}$ = 2954, 2930, 2857, 1732, 1614, 1585, 1429, 1260, 1202, 1172, 1092, 1004, 835, 781 cm^{-1}; MS (EI): *m*/*z* (%): 581 (27) [M^+ - *t*Bu], 529 (10), 489 (15), 425 (100), 375 (17), 335 (23), 277 (13), 185 (25), 91 (85), 73 (13); HRMS (ESI$^-$) calcd for $C_{36}H_{50}NaO_8$ [M^+ + Na]: 661.3167; found: 661.3166.

Compound 38: *n*Bu_4NF (1 M in THF, 16 µL, 16.4 µmol) was added to a solution of compound **37** (10 mg, 15.7 µmol) in THF (500 µL). The reaction was stirred for 40 min before being diluted with EtOAc (500 µL) and washed sequentially with H_2O (200 µL) and brine (200 µL). The organic phase was dried



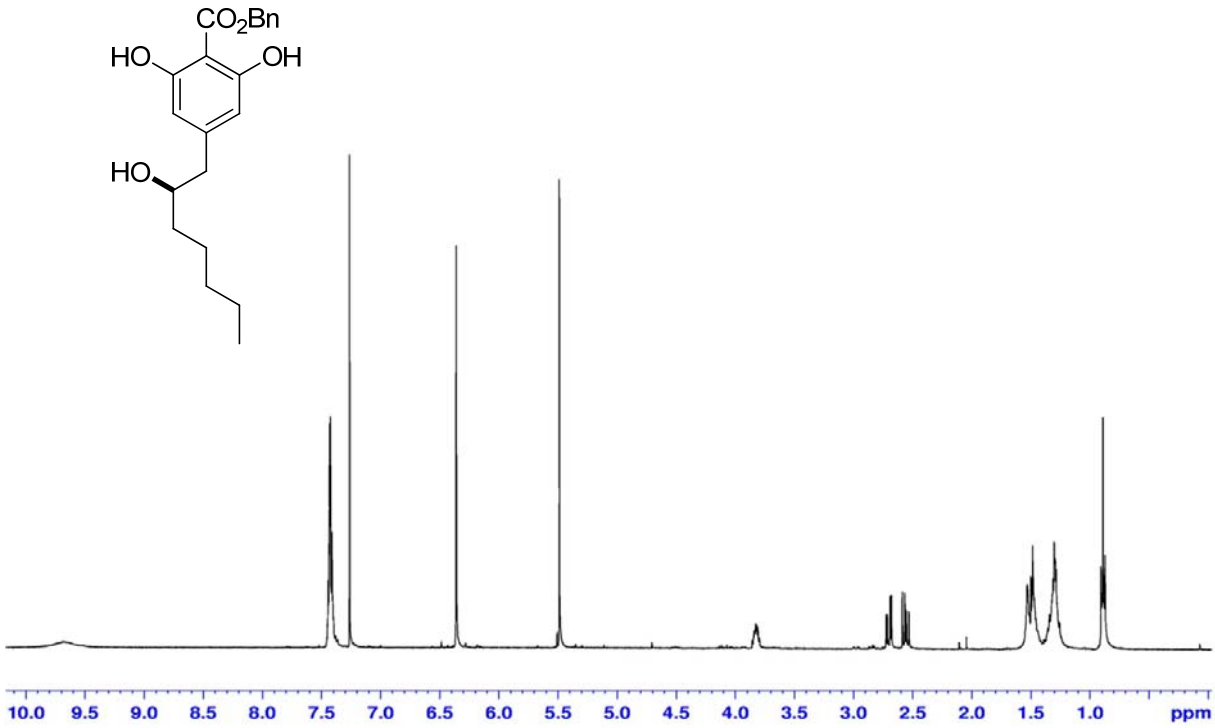
(Na_2SO_4), filtered, and concentrated to a pale yellow oil (7 mg). This crude product was dissolved in EtOAc (0.4 mL) and $Pd(OH)_2$ (1 mg) was added. The resulting black suspension was purged with H_2 and vigorously stirred under a static H_2 atmosphere for 1 h. The reaction was rapidly filtered through a pad of silica (10 micron, ca. 1 cm), eluting with distilled and degassed Et_2O (2 mL, approximately 4 column volumes). Evaporation of the combined filtrates gave the title compound as a white solid (7 mg, 85 %); ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 11.77 (s, 1H; OH), 10.09 (s br, 1H; CO_2H), 6.44 (s, 1H, H4), 4.77 (dd, *J* = 12.2, 5.4, 1H; H15), 4.32 (app. t, *J* = 9,3 Hz, 1H; H26a), 4.20 (dd, *J* = 9.3, 7.9 Hz, 1H, H26b), 3.83 (m, 1H; H9), 3.75 (s, 3H, MeO21), 3.10 (ddd, *J* = 11.0, 9.5, 7.9 Hz, 1H; H19), 2.82 (ddt, *J* = 17.7, 4.1, <1 Hz, 1H, H8a); 2.60 (ddt, *J* = 17.7, 11.0, <1.0 Hz, 1H; H8b), 2.57 (dq, *J* = 11.0, 6.9 Hz, 1H; H18), 2.31 (dd, *J* = 12.5, 5.4 Hz, 1H; H16 eq), 2.08 (app. t, *J* = 12.4 Hz, 1H; H16ax), 1.64-1.26 (m, 8H; H10-H13), 1.22 (d, *J* = 6.9 Hz, 3H; H25), 0.90 (m, 3H; H14); ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 172.7 (C20), 170.8 (C1), 162.7 (C3), 149.9 (C7), 143.0 (C5), 113.1 (C17), 112.7 (C6), 110.8 (C4), 98.8 (C2), 75.5 (C9), 69.8 (C26), 67.5 (C15), 52.8 (C21), 48.9 (C19), 47.4 (C18), 36.5 (C10), 34.6 (C8), 34.0 (C16), 32.1 (C12), 25.3 (C11), 23.0 (C13), 14.2 (C14), 12.8 (C25).

Crystal data for 11:[9] $C_{23}H_{31}IO_6$, *M* = 530.38 g mol^{-1}, colorless, crystal dimensions 0.11 x 0.07 x 0.03 mm, orthorhombic $P2_12_12_1$, at 100 K *a* = 9.046(4), *b* = 15.684(7), *c* = 32.313(13) Å, *V* = 4584(3) Å^3, *Z* = 8, ρ = 1.537 Mg m^{-3}, μ = 11.275 mm^{-1}, Cu-Kα (λ = 1.54178 Å). $2\Theta_{max}$ = 55.37°, 52608 total reflections, 5778 unique (R_{int} = 0.47), R_1 = 0.093, wR_2 = 0.261, highest peak 0.9 e Å^3.

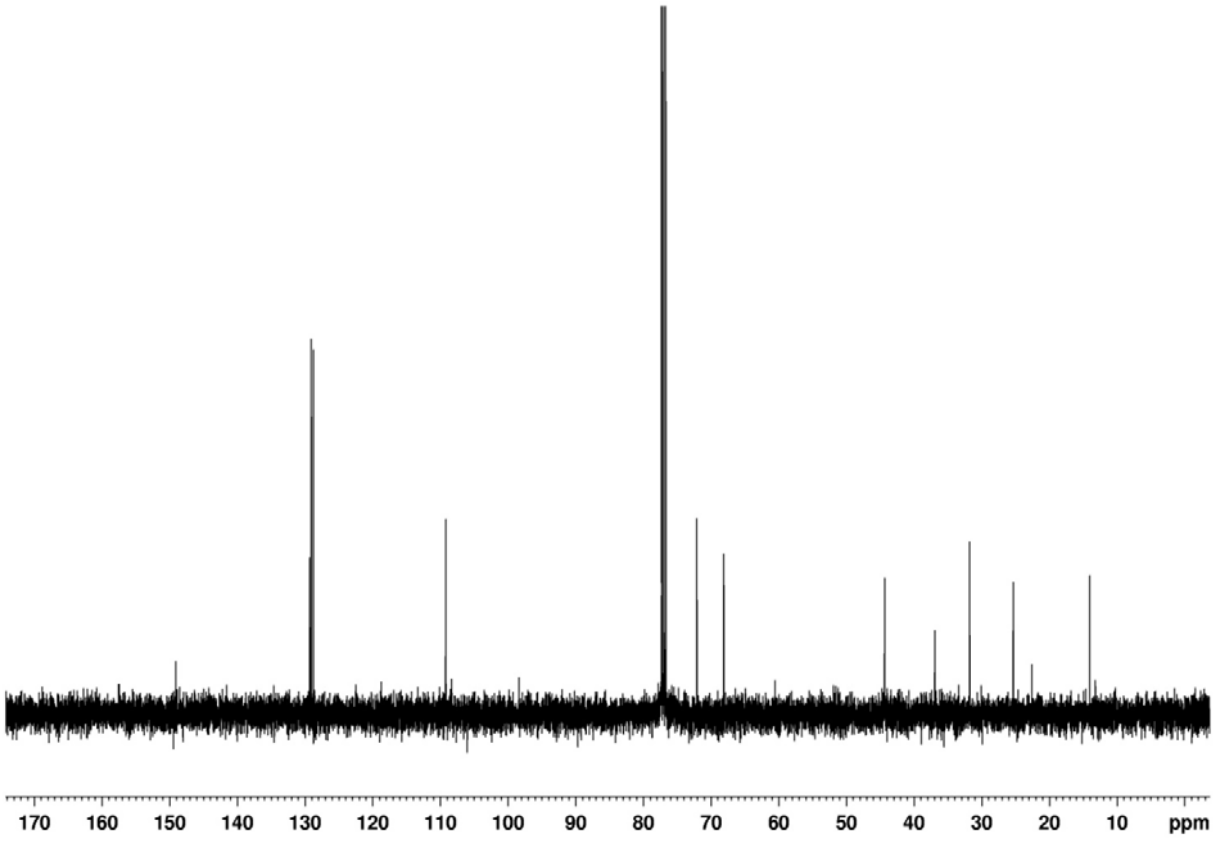
The X-ray diffraction data were collected using a Bruker AXS X8 Proteum diffractometer; data were integrated using SAINT, followed by direct methods for structure solution (SHELXS-97, Sheldrick, 1997) and full matrix least-squares based on FP^{2P} (SHELXL-97, Sheldrick, 1997). Data have been deposited with the Cambridge Crystallographic Data Centre and can be obtained free of charge from The Cambridge Crystallographic Data Center via ww.ccdc.cam.uk/data_request/cif, quoting the reference number CCDC 693829.

[9] Figure 2 in our original communication erroneously displayed compound **5** rather than iodide **11** as stated in the legend. Although the structure of the iodide was contained in the Supporting Information and had been deposited at the Cambridge Crystallographic Data Centre (CCDC 693829), we present it here again to avoid any doubts or ambiguities.

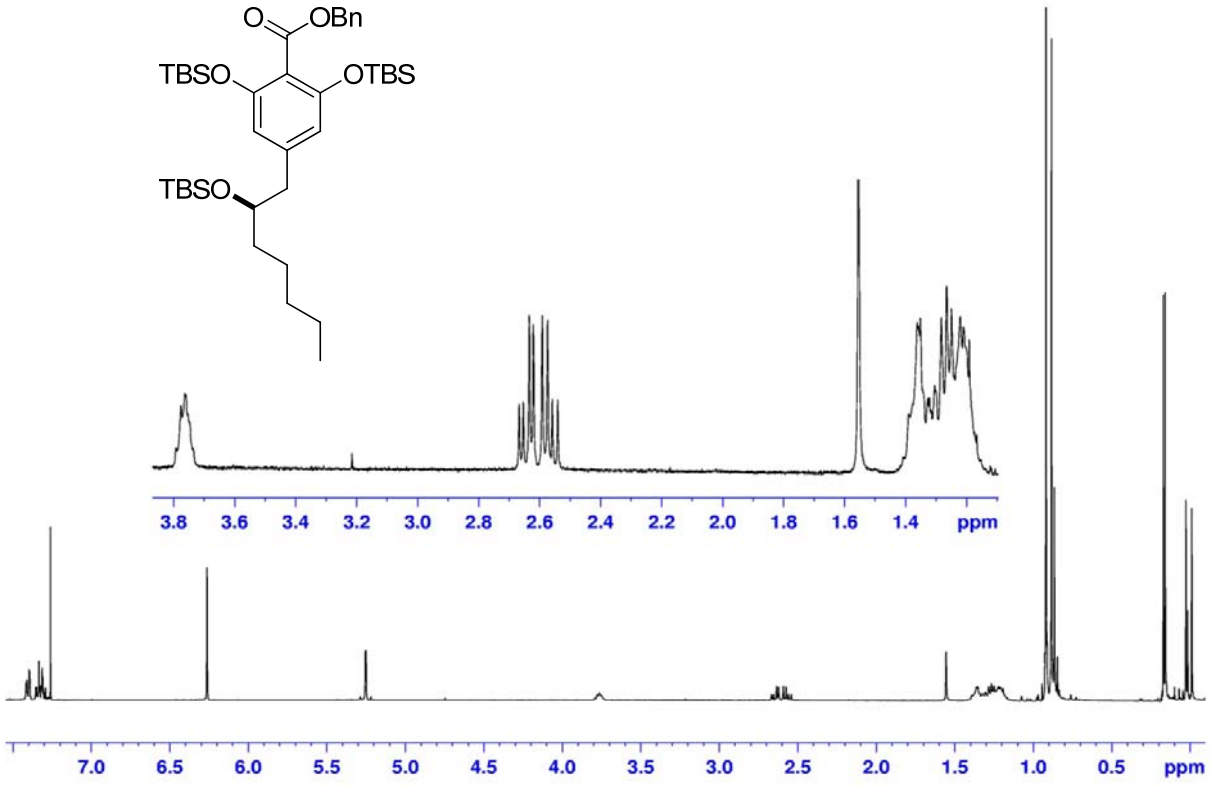
Compound 17: ^{1}H NMR ($CDCl_3$, 400 MHz)



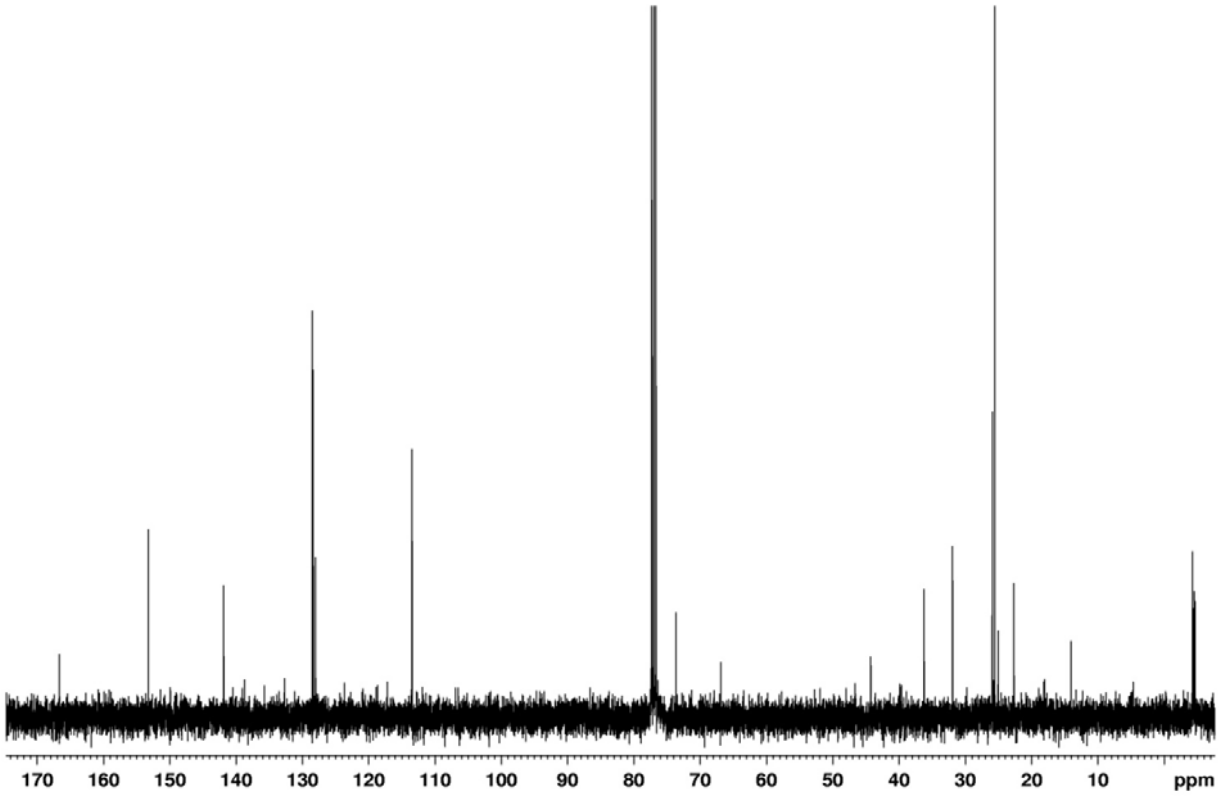
^{13}C NMR ($CDCl_3$, 100 MHz)



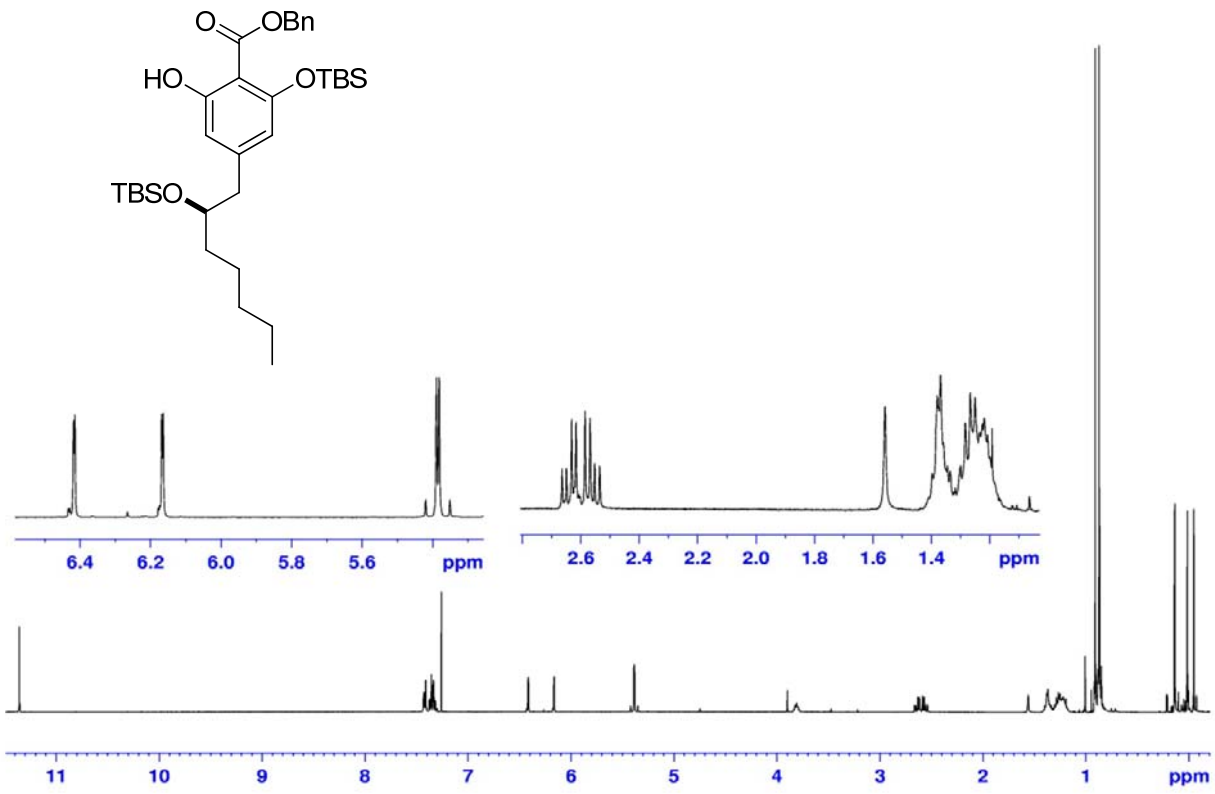
^{1}H NMR ($CDCl_3$, 400 MHz)



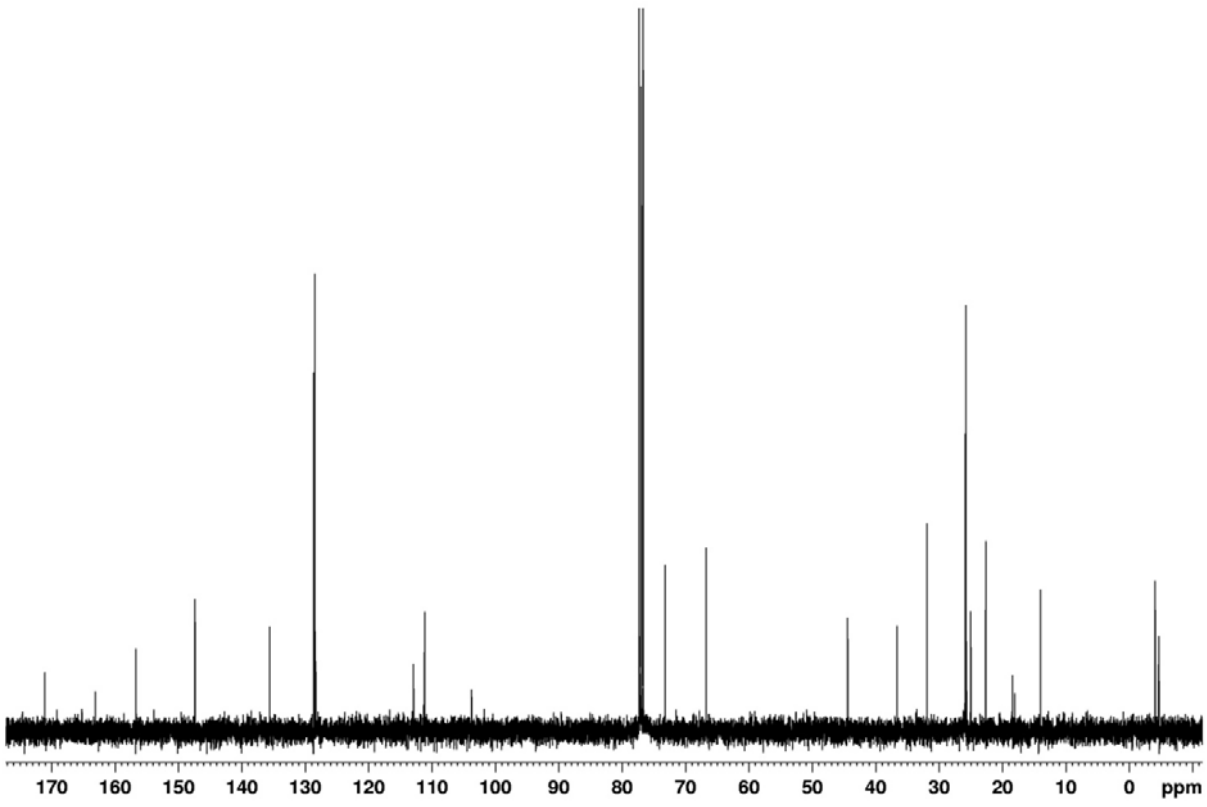
^{13}C NMR ($CDCl_3$, 100 MHz)



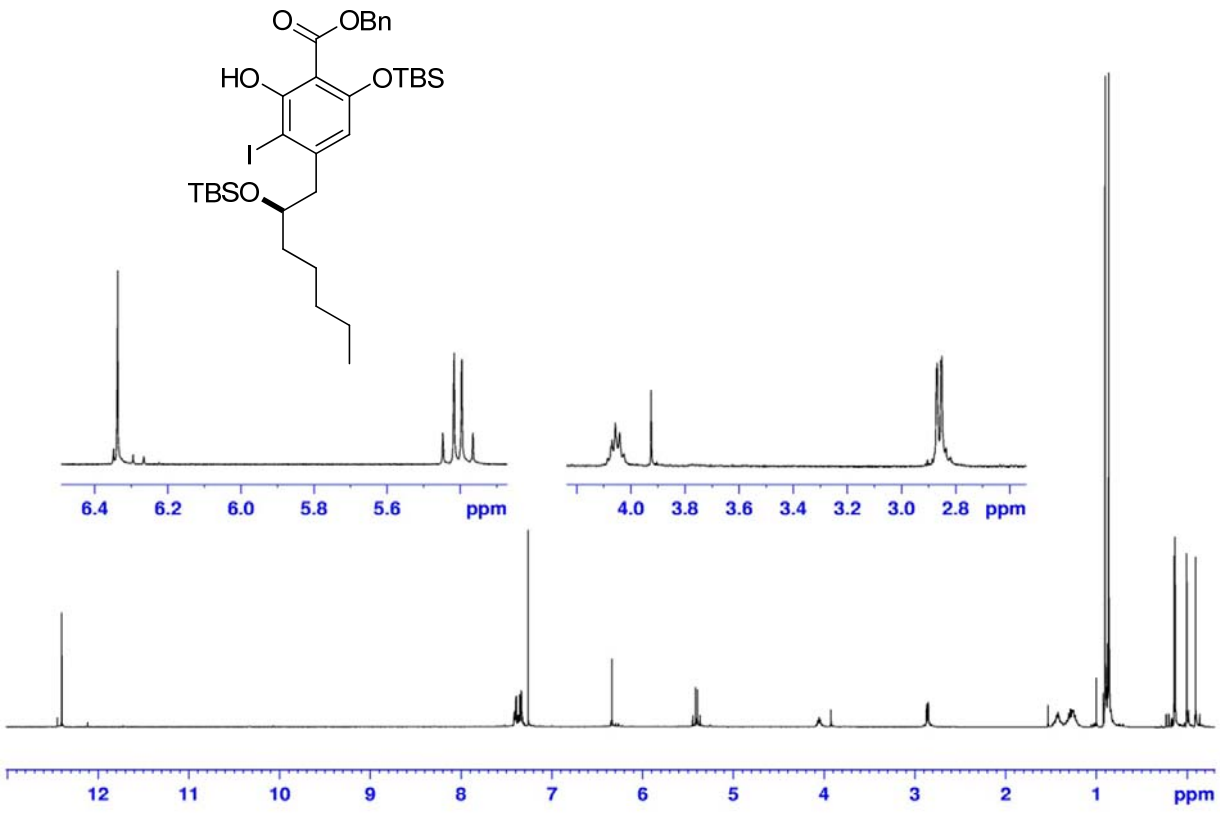
Compound 18: ^{1}H NMR ($CDCl_3$, 400 MHz)



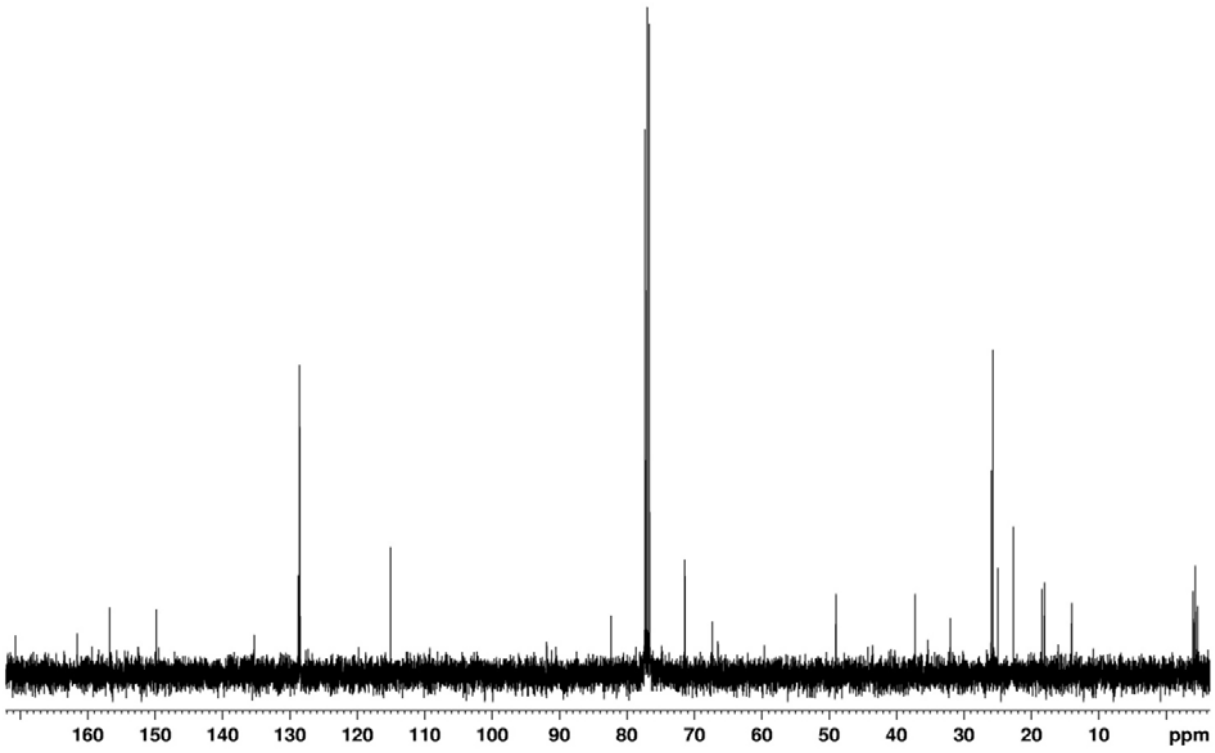
^{13}C NMR ($CDCl_3$, 100 MHz)



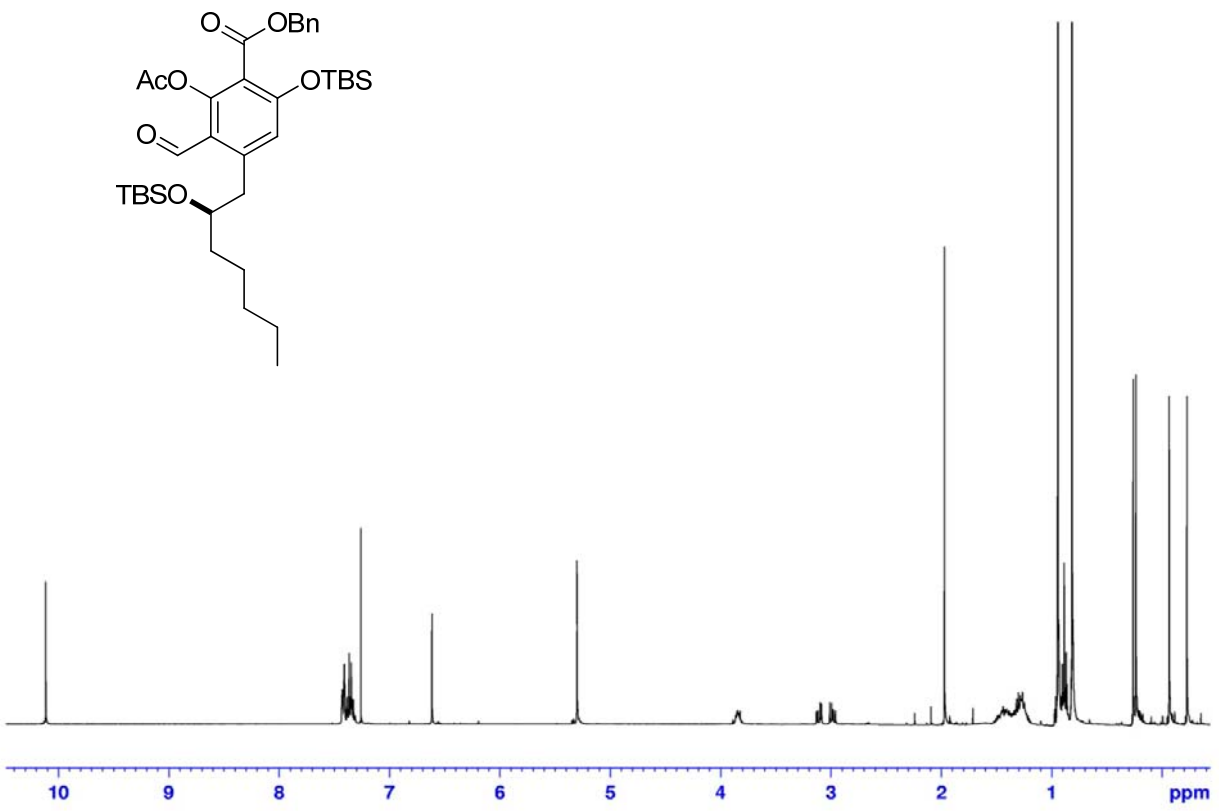
Compound 19: ^{1}H NMR ($CDCl_3$, 400 MHz)



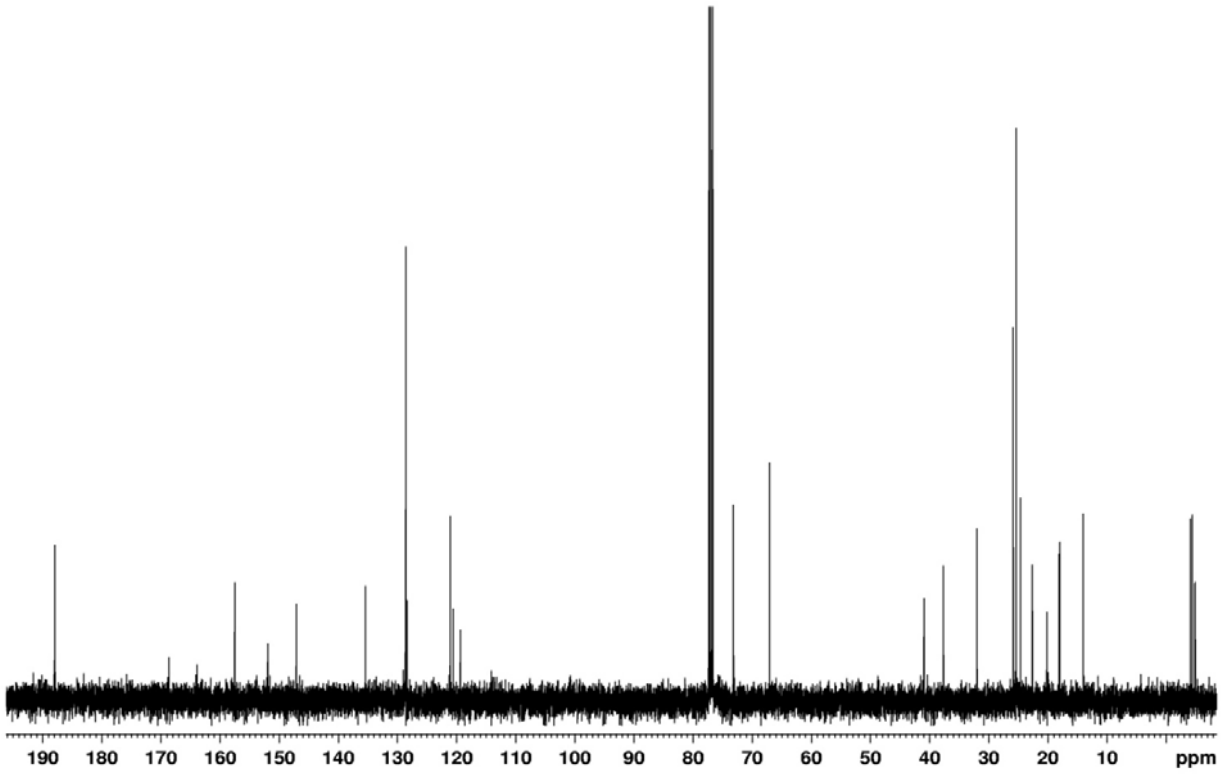
^{13}C NMR ($CDCl_3$, 100 MHz)



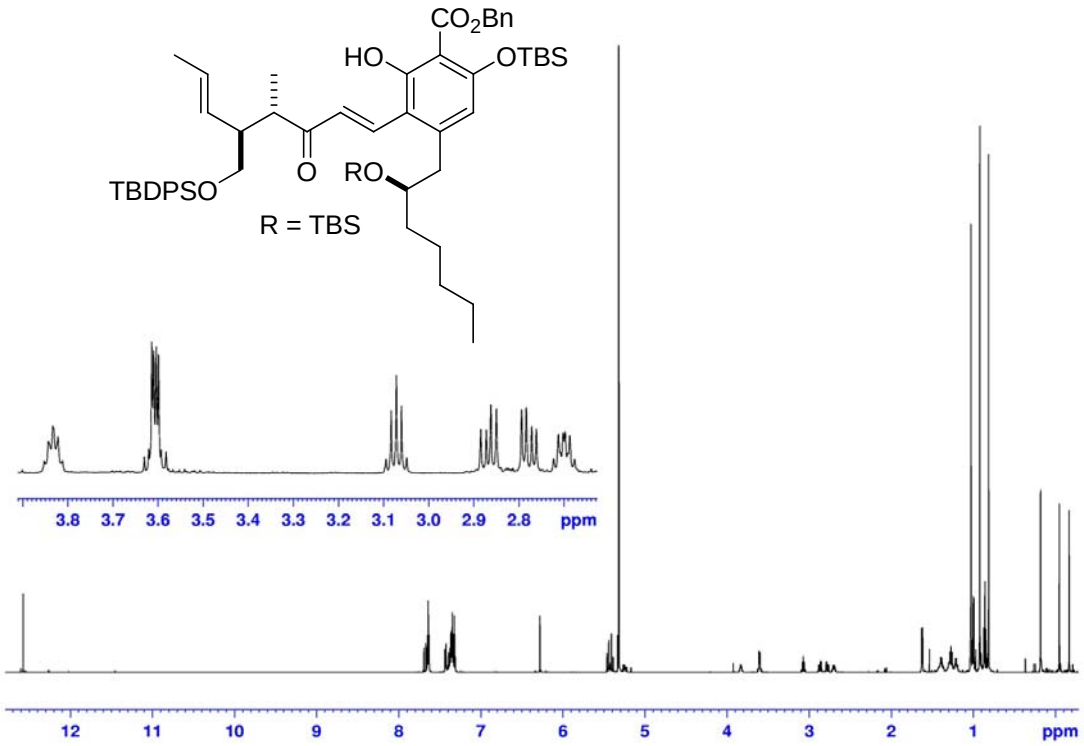
Compound 20: ^{1}H NMR ($CDCl_3$, 400 MHz)



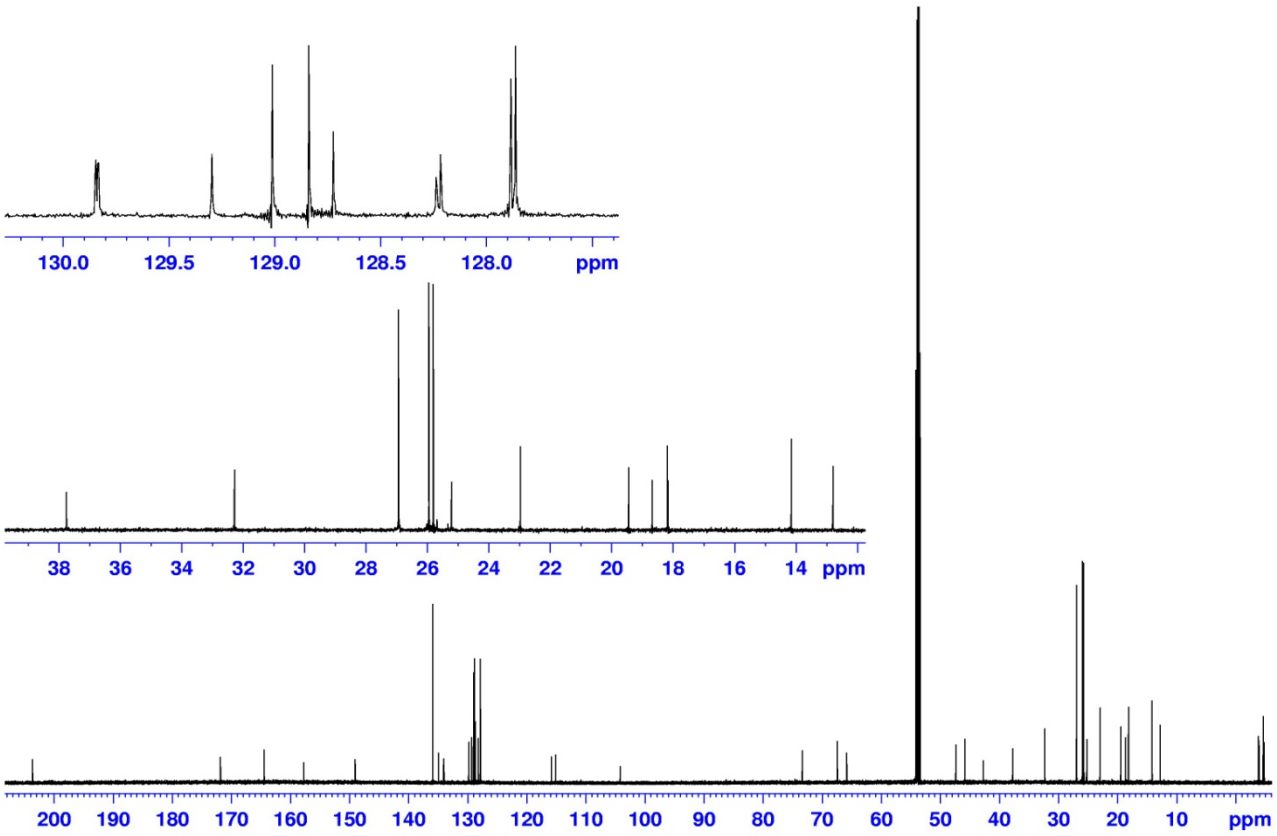
^{13}C NMR ($CDCl_3$, 100 MHz)



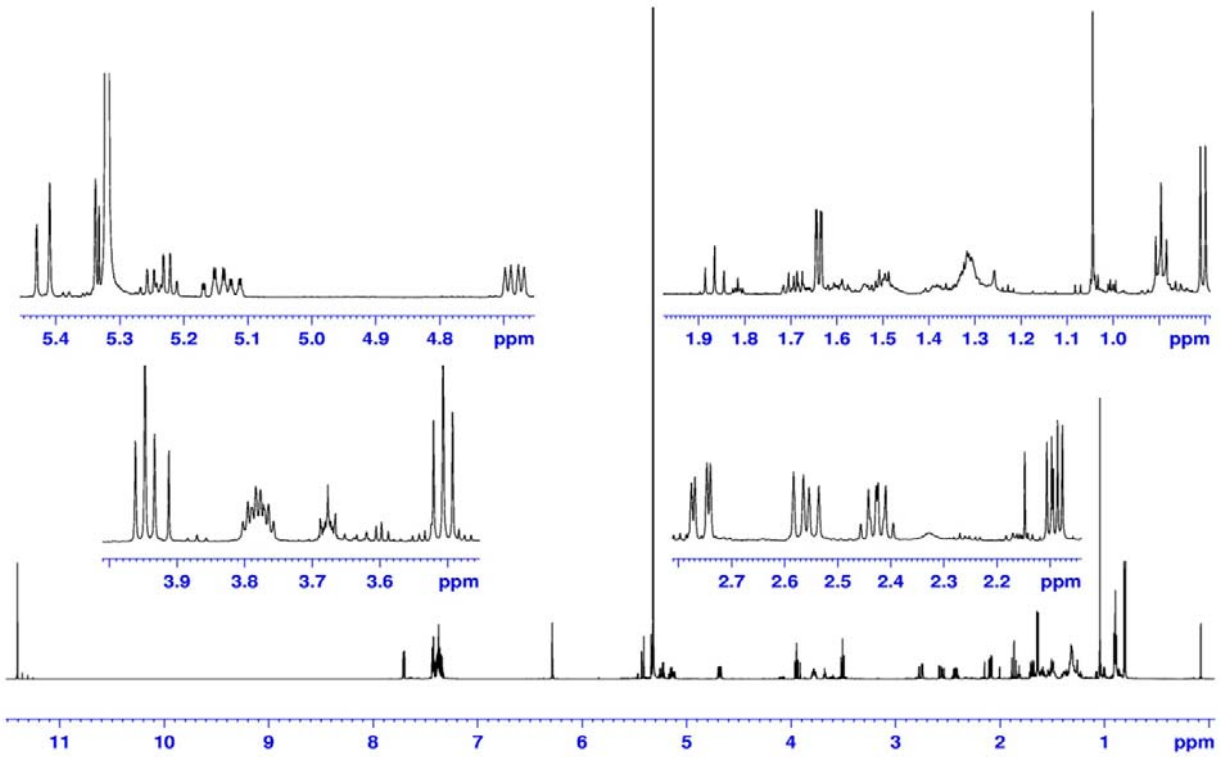
Compound 31: ^{1}H NMR (CD_2Cl_2, 600 MHz)



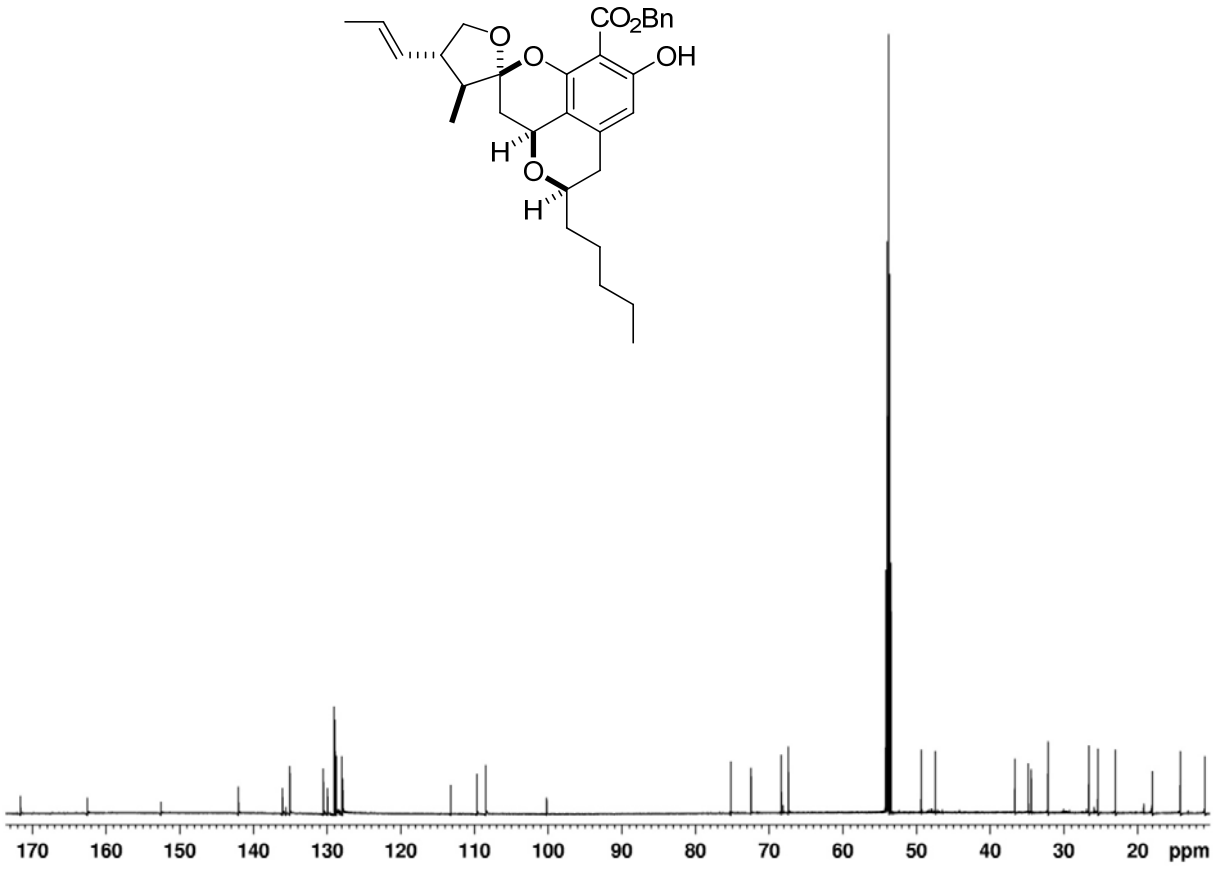
^{13}C NMR (CD_2Cl_2, 150 MHz)



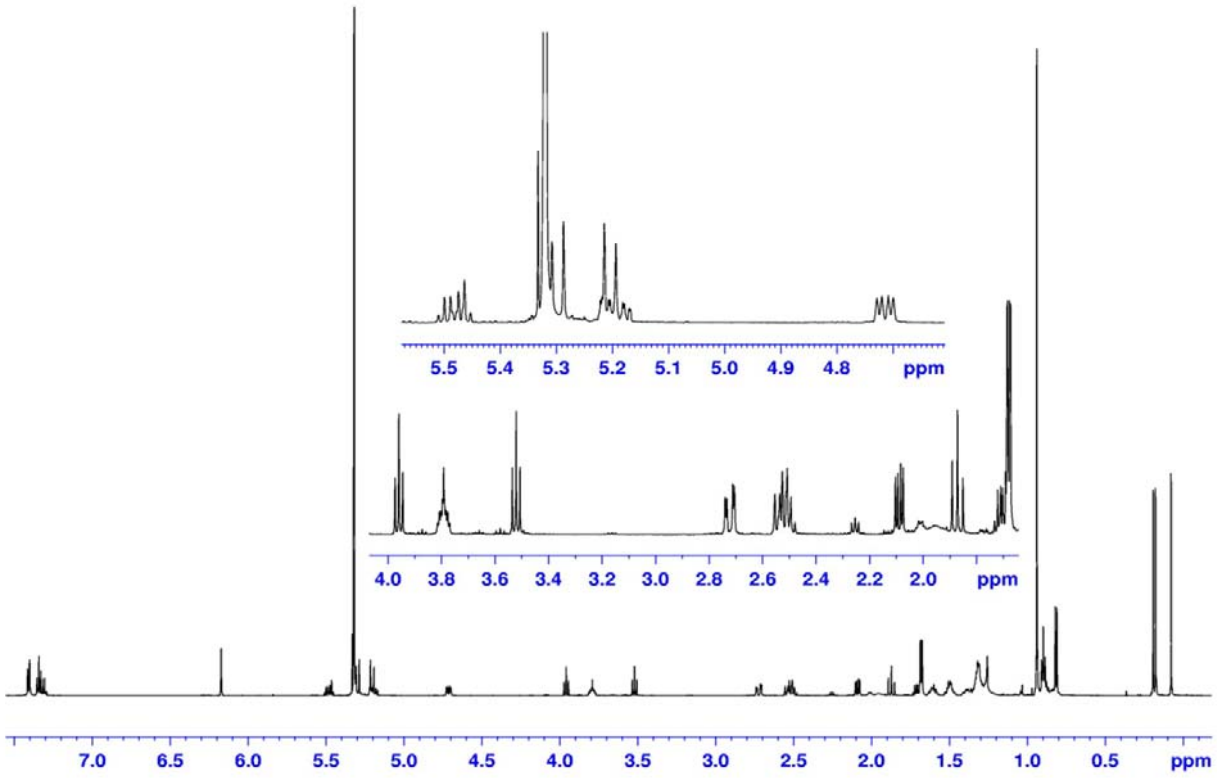
Compound 32: ^{1}H NMR (CD_2Cl_2, 600 MHz)



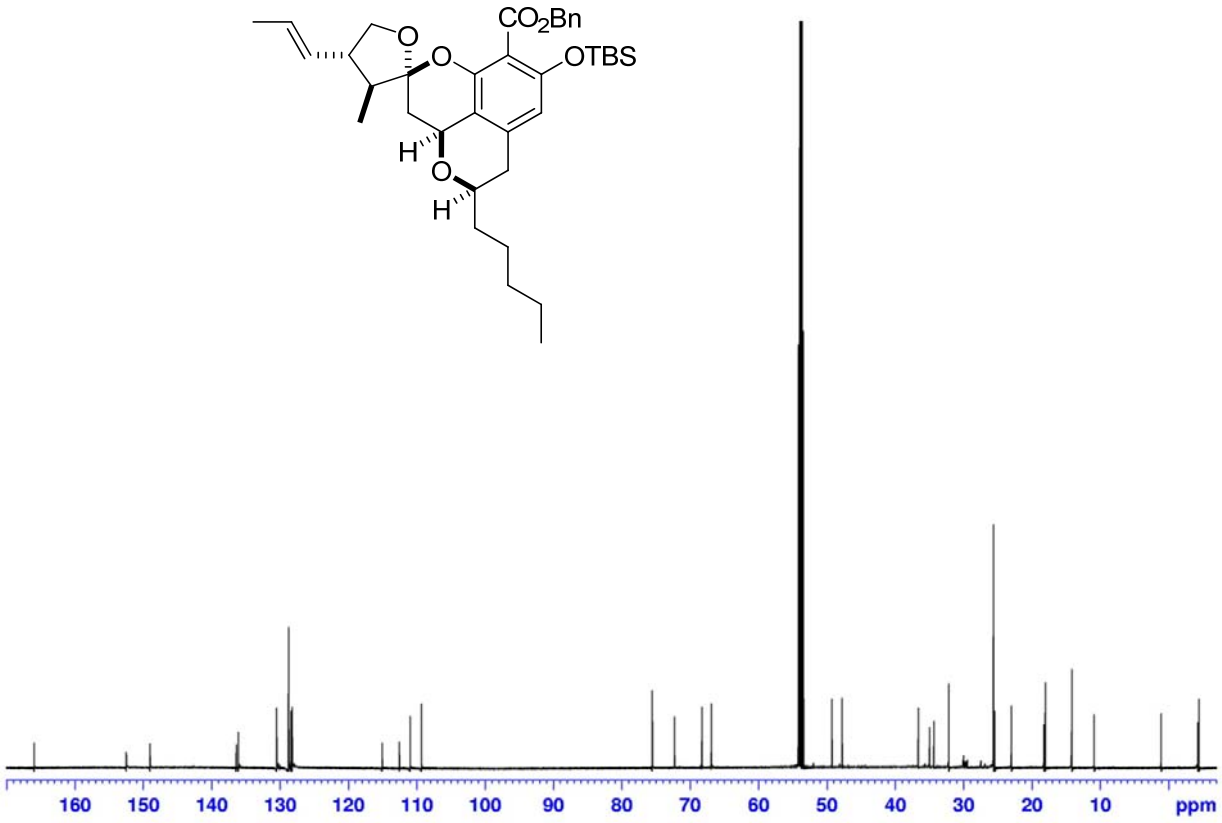
^{13}C NMR (CD_2Cl_2, 150 MHz)



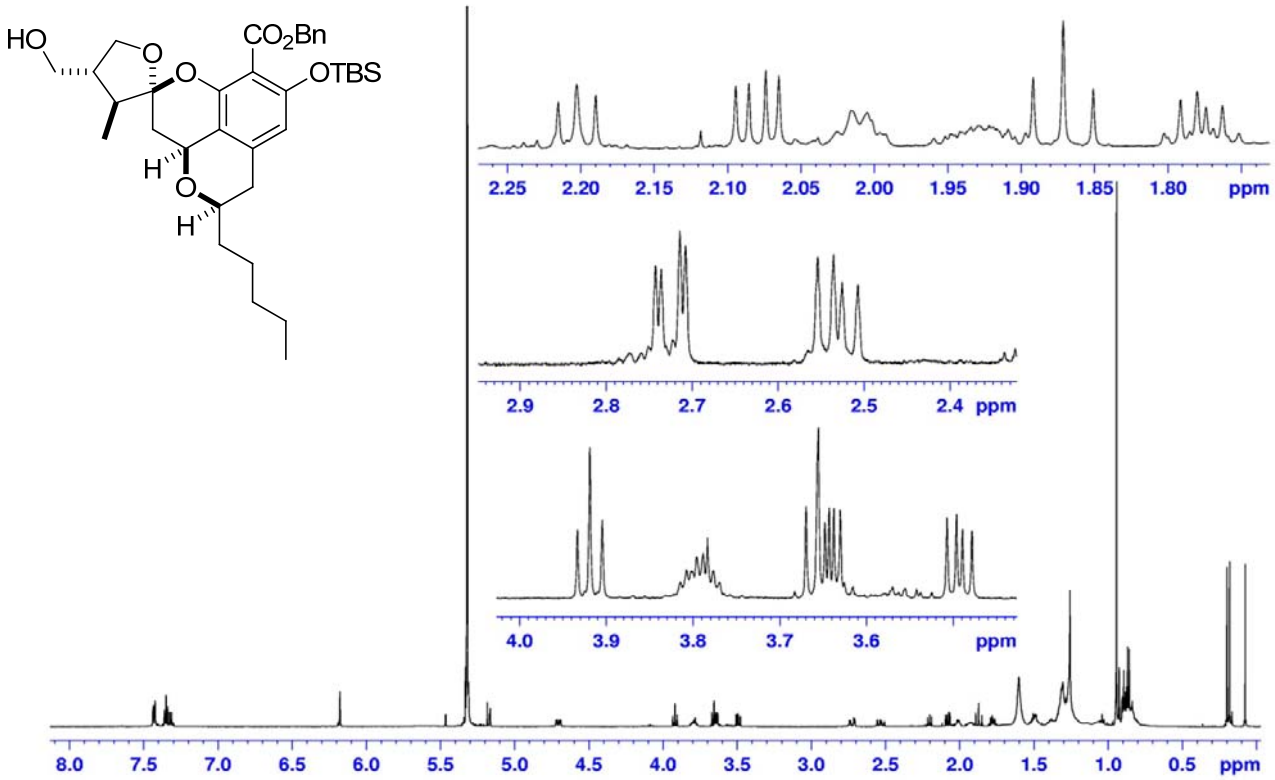
Compound 33: ^{1}H NMR (CD_2Cl_2, 600 MHz)



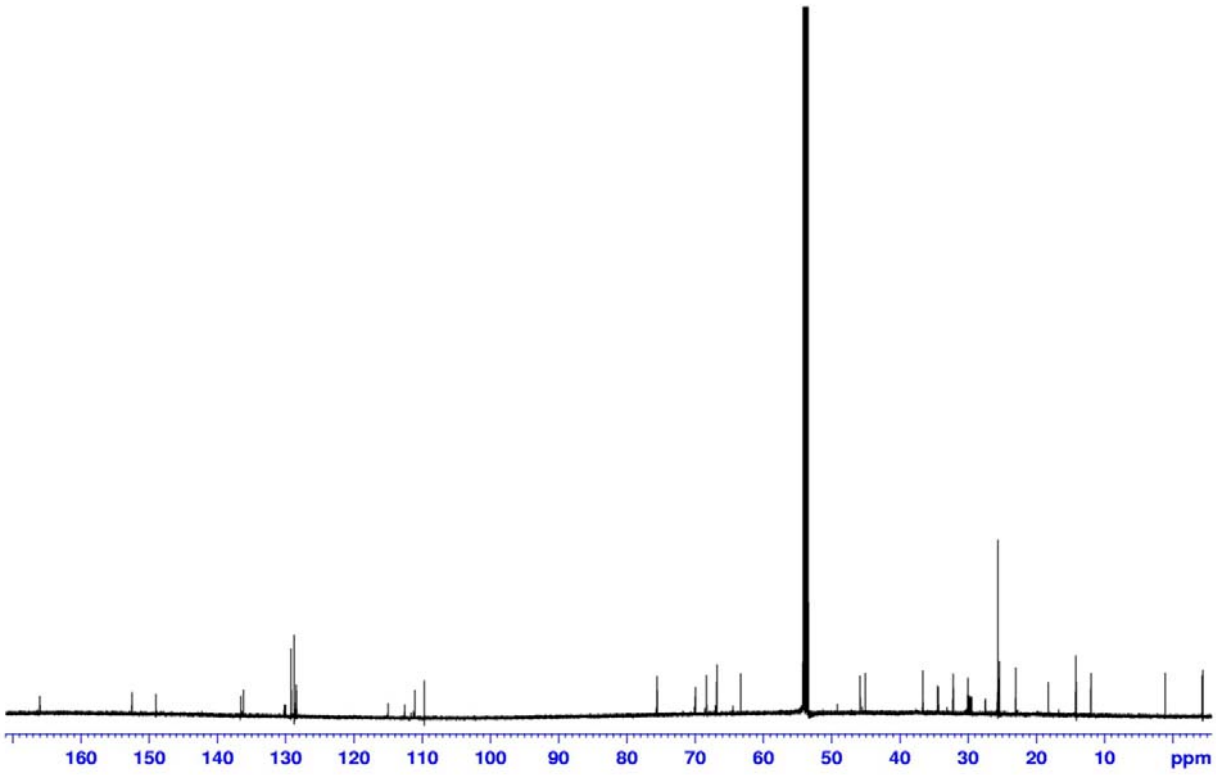
^{13}C NMR (CD_2Cl_2, 150 MHz)



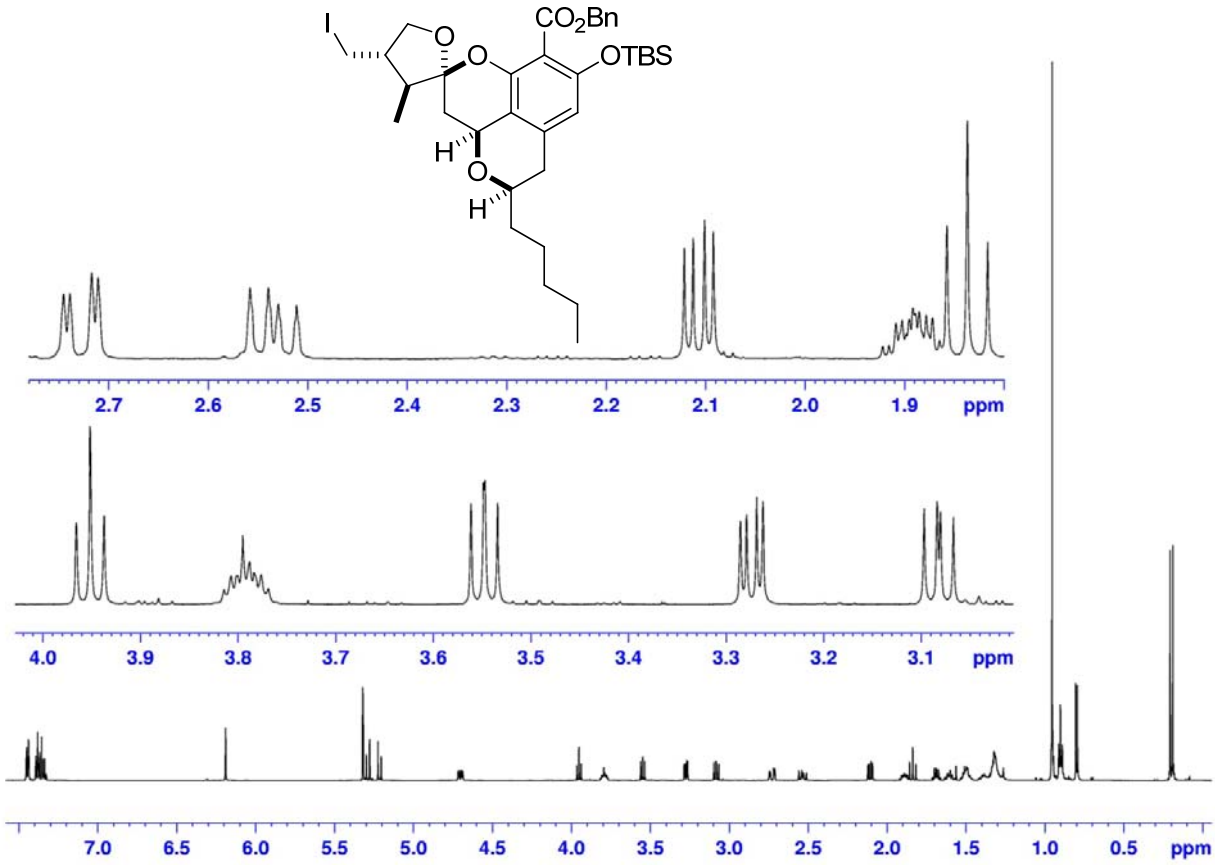
Compound 34: ^{1}H NMR (CD_2Cl_2, 600 MHz)



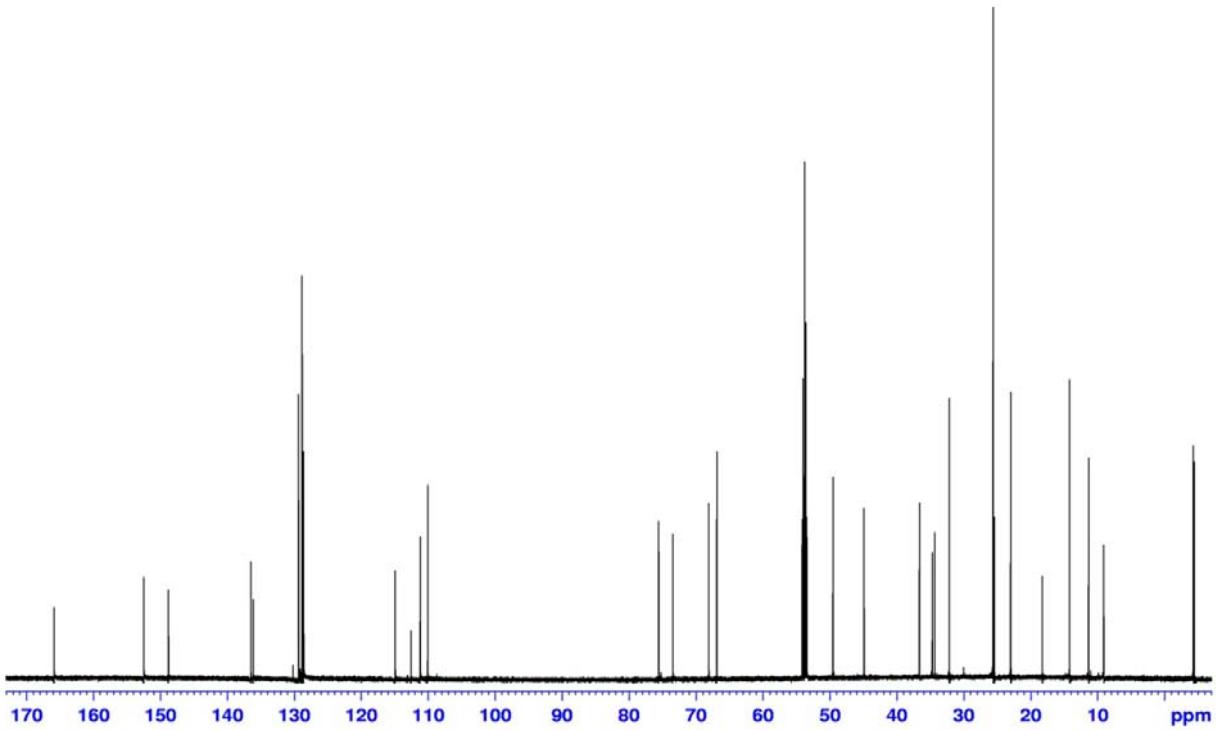
^{13}C NMR (CD_2Cl_2, 150 MHz)



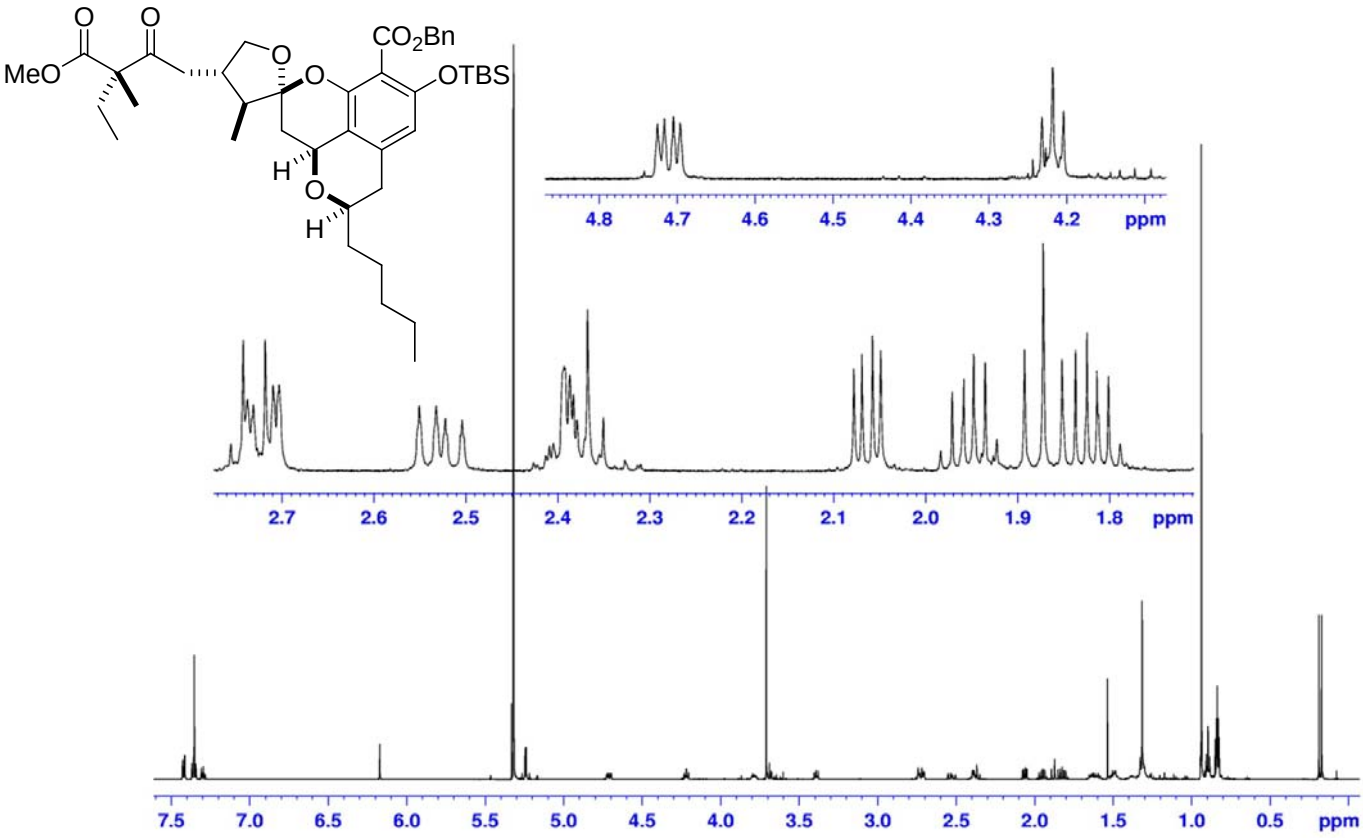
Compound 35: ^{1}H NMR (CD_2Cl_2, 600 MHz)



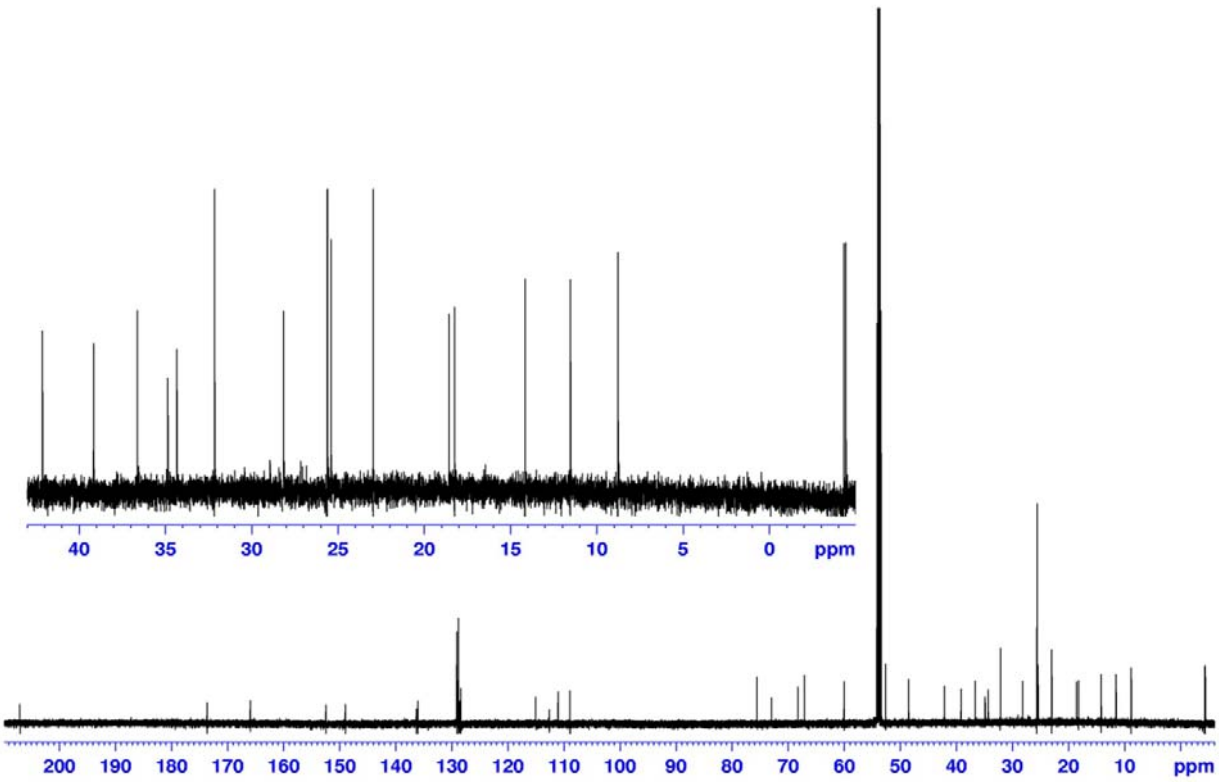
^{13}C NMR (CD_2Cl_2, 150 MHz)



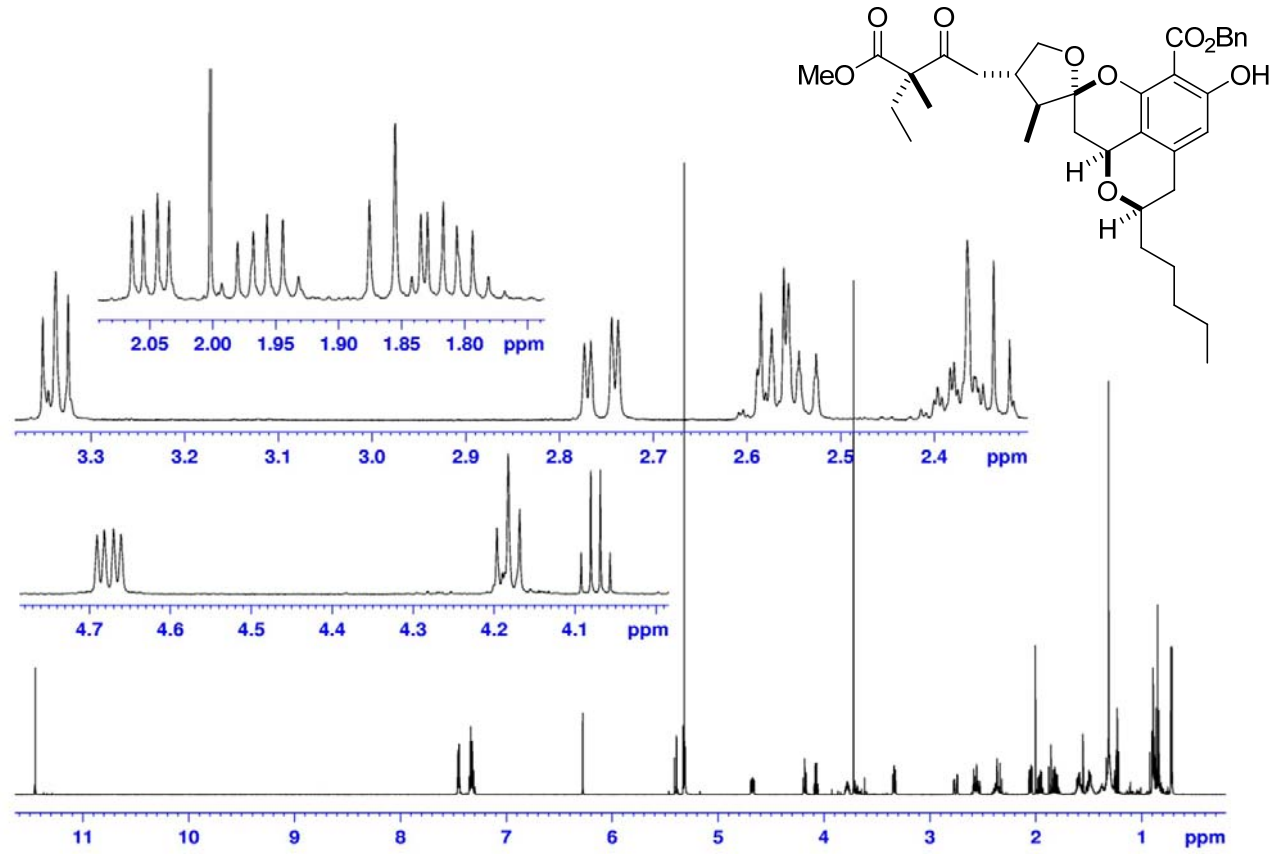
Compound 36: ^{1}H NMR (CD_2Cl_2, 600 MHz)



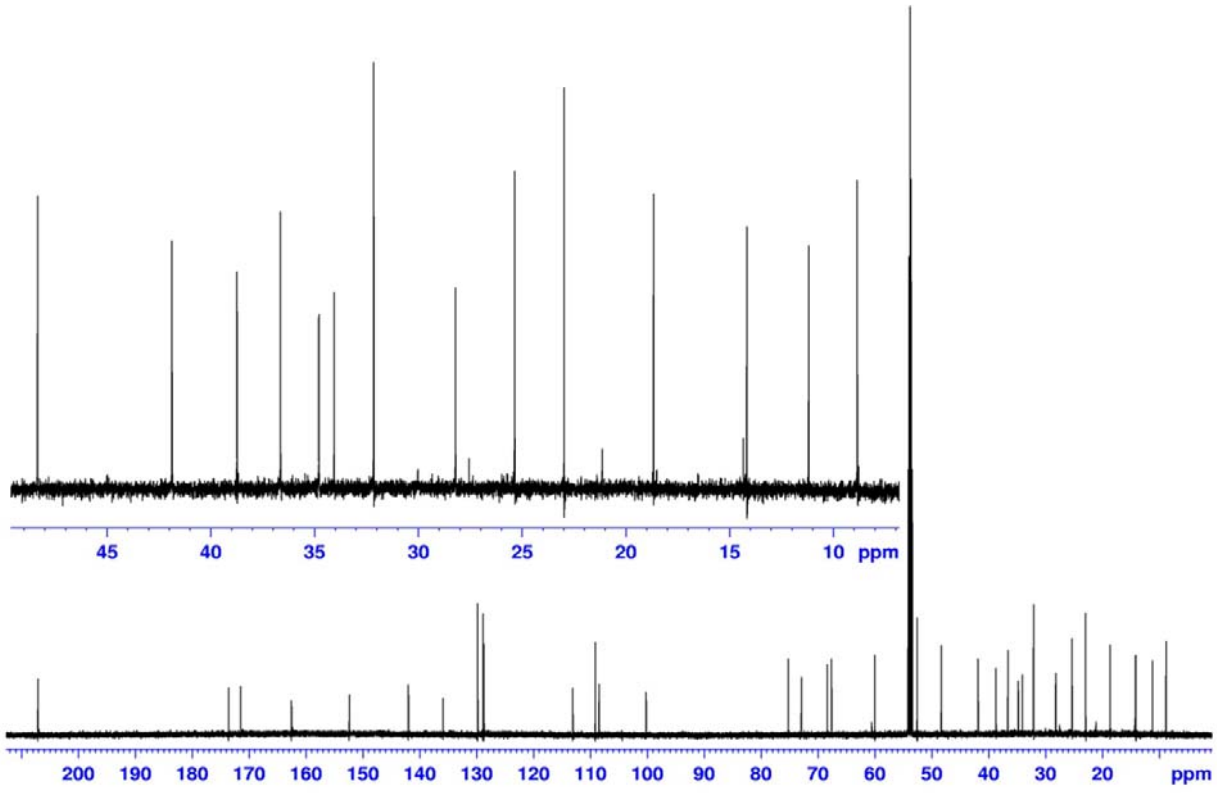
^{13}C NMR (CD_2Cl_2, 150 MHz)



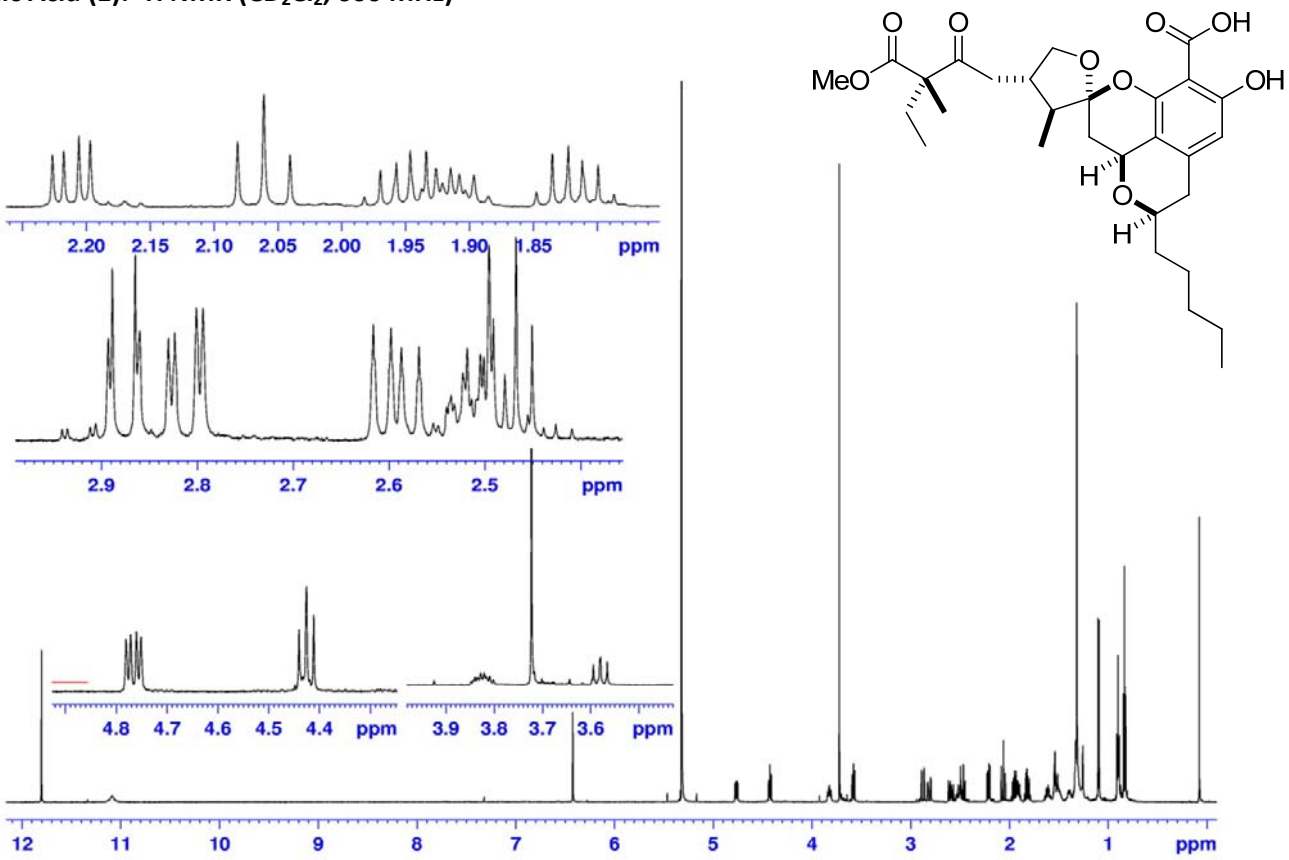
Berkelic Acid Benzyl Ester: ^{1}H NMR (CD_2Cl_2, 600 MHz)



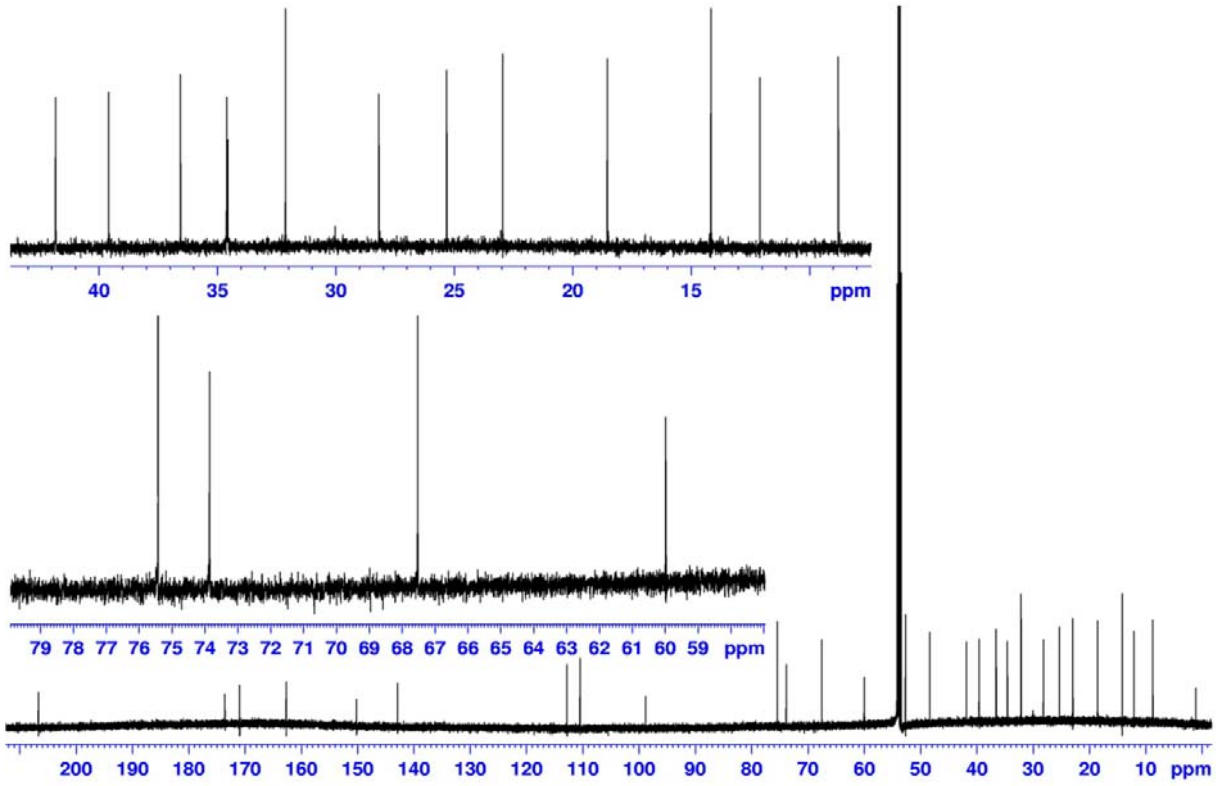
^{13}C NMR (CD_2Cl_2, 150 MHz)



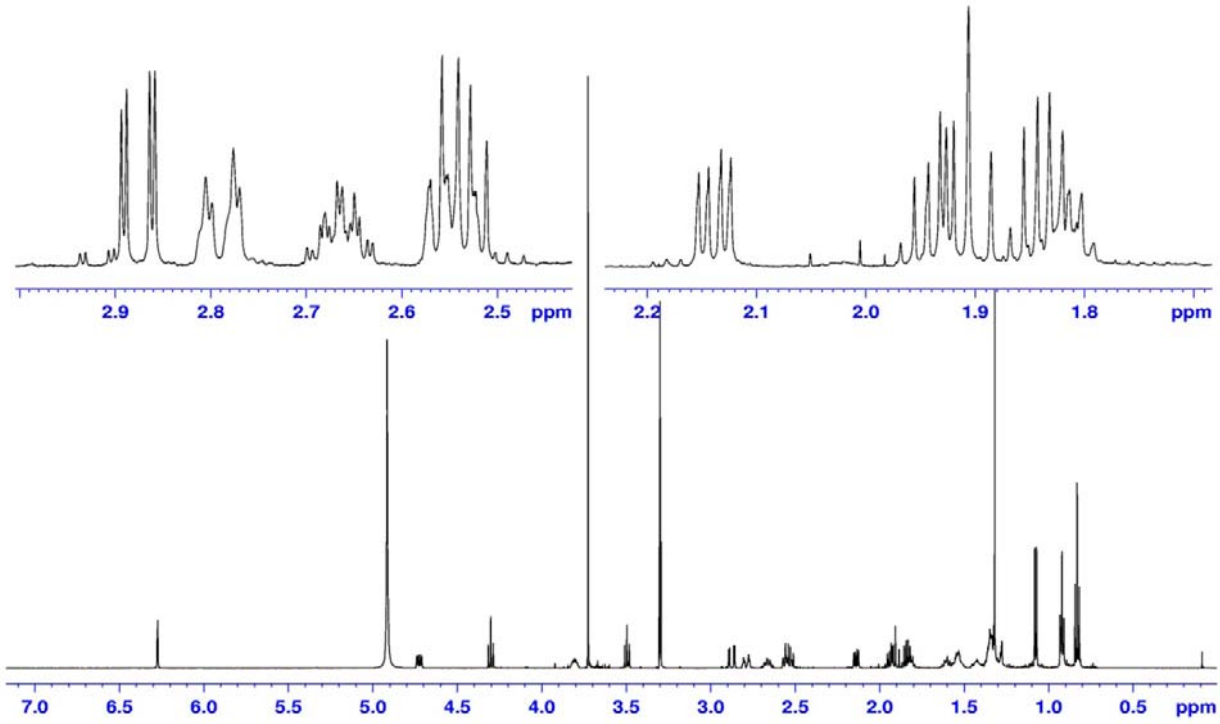
Berkelic Acid (1): ^{1}H NMR (CD_2Cl_2, 600 MHz)



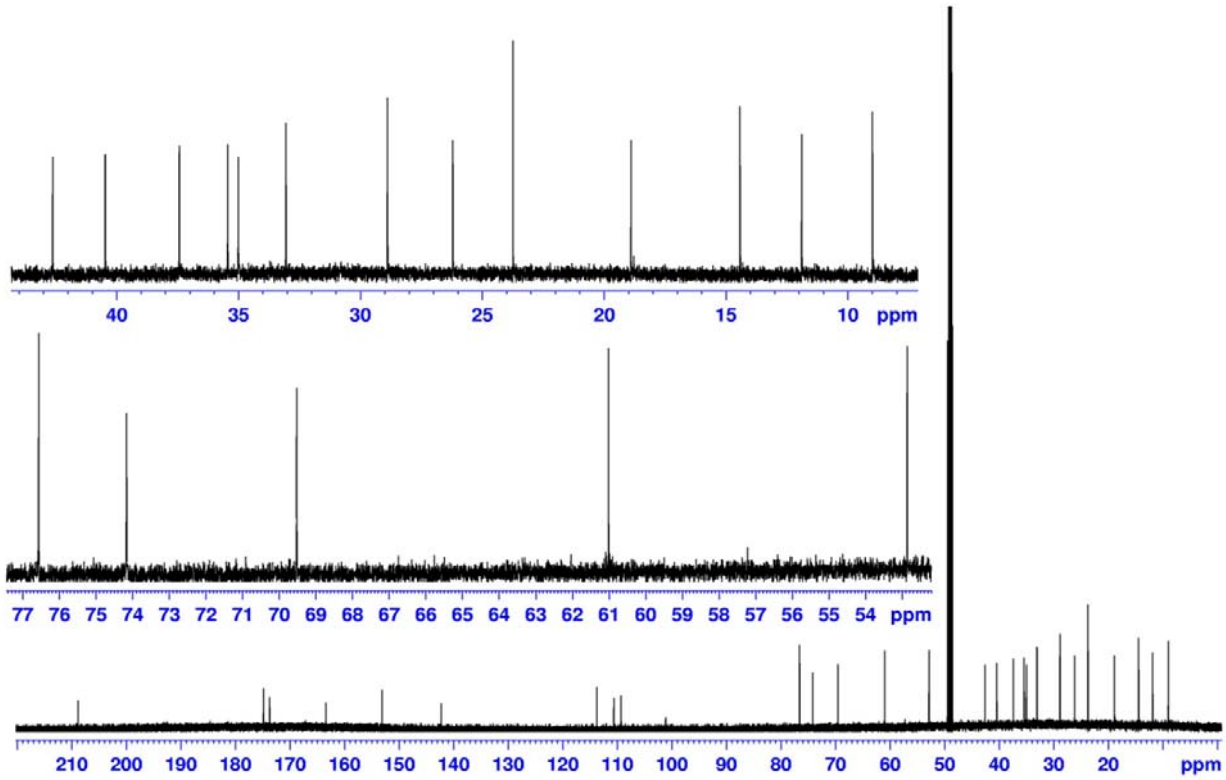
^{13}C NMR (CD_2Cl_2, 150 MHz)



Berkelic Acid (1): ^{1}H NMR (CD_3OD, 600 MHz)

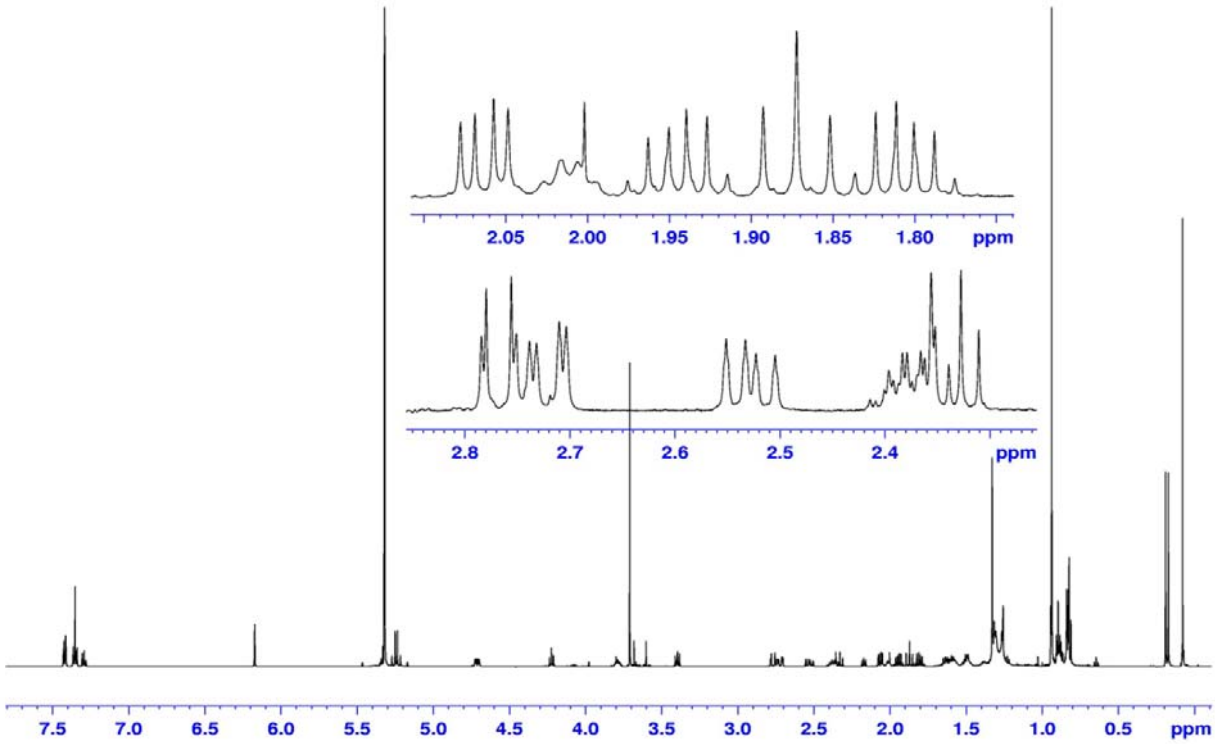


^{13}C NMR (CD_3OD, 150 MHz)

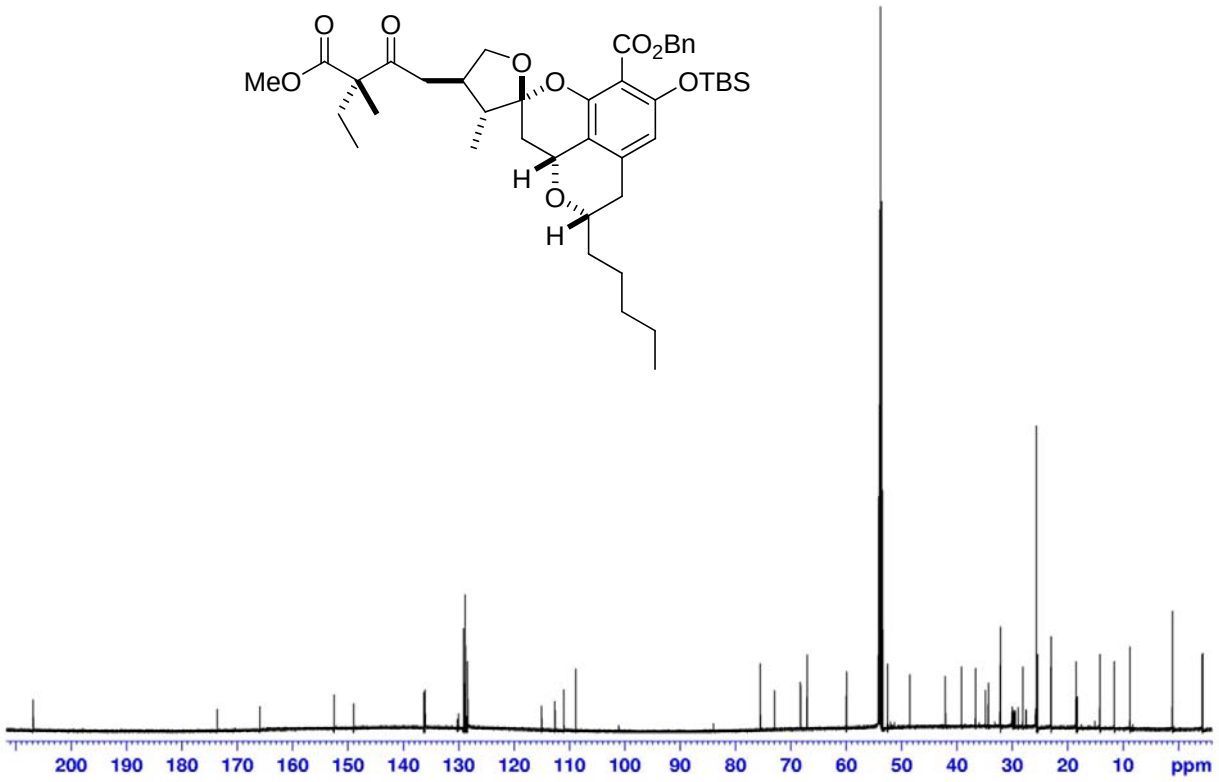


***Ent*-(+)-Series**

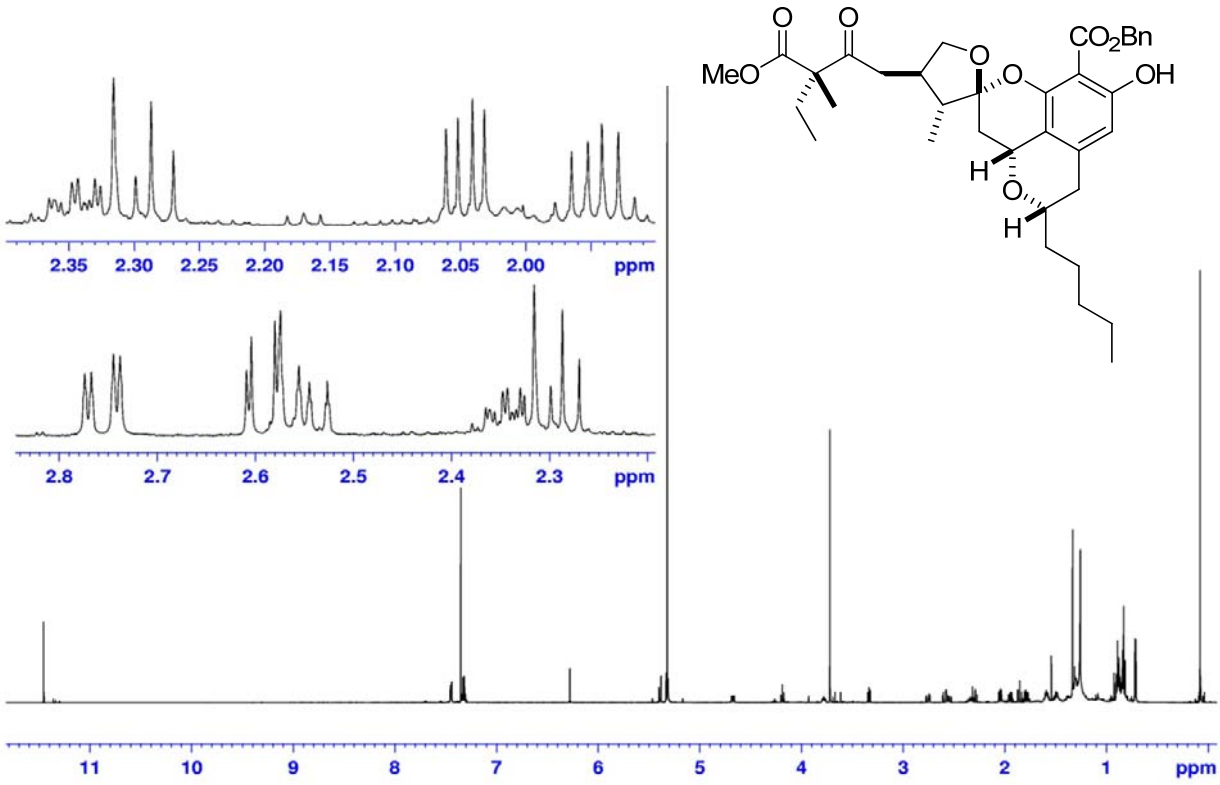
^{1}H NMR (CD_2Cl_2, 600 MHz)



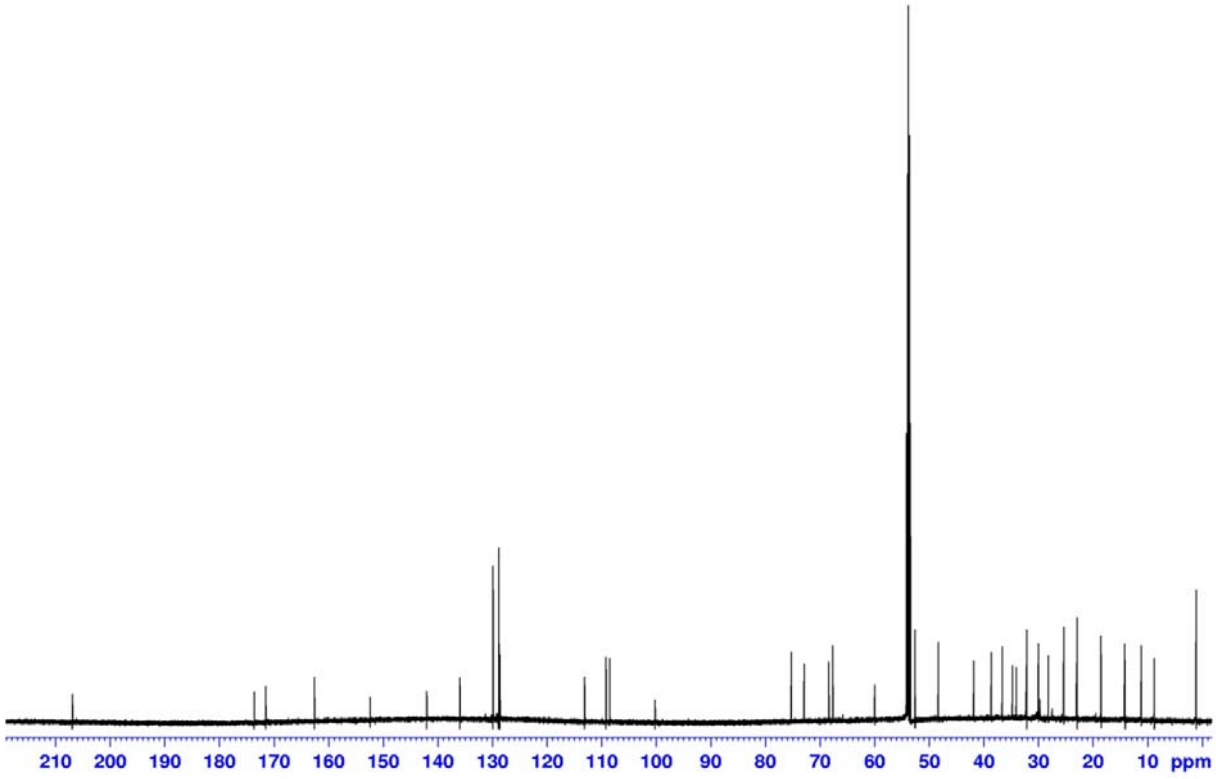
^{13}C NMR (CD_2Cl_2, 150 MHz)



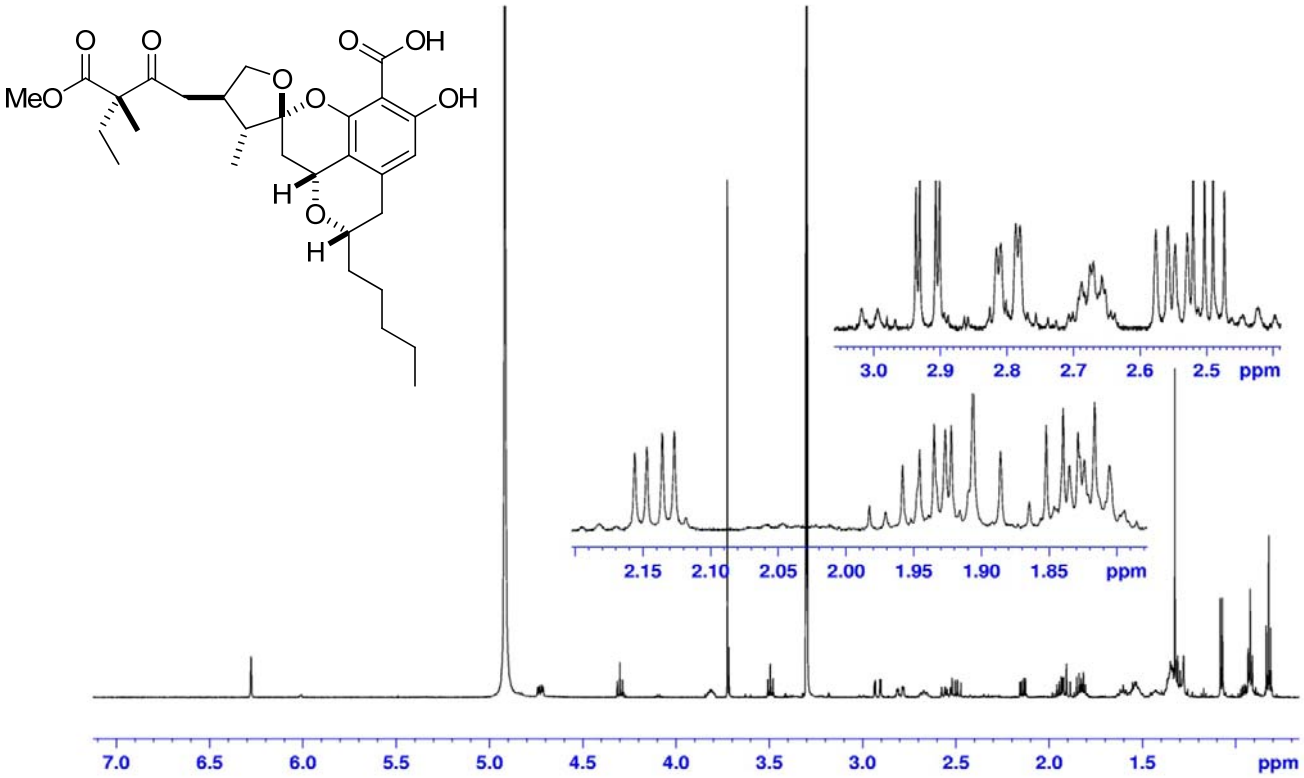
C22(*S*)-Diastereomer of (+)-Berkelic acid benzyl ester: ^{1}H NMR (CD_2Cl_2, 600 MHz)



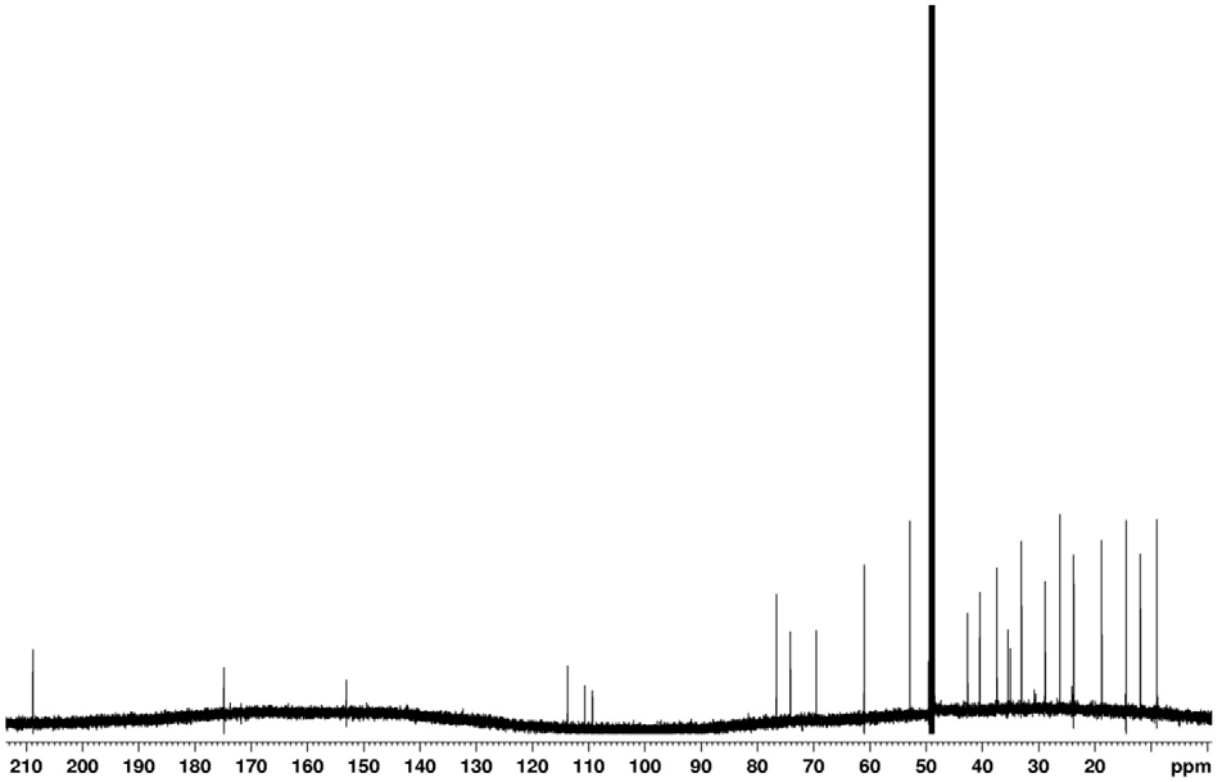
^{13}C NMR (CD_2Cl_2, 150 MHz)



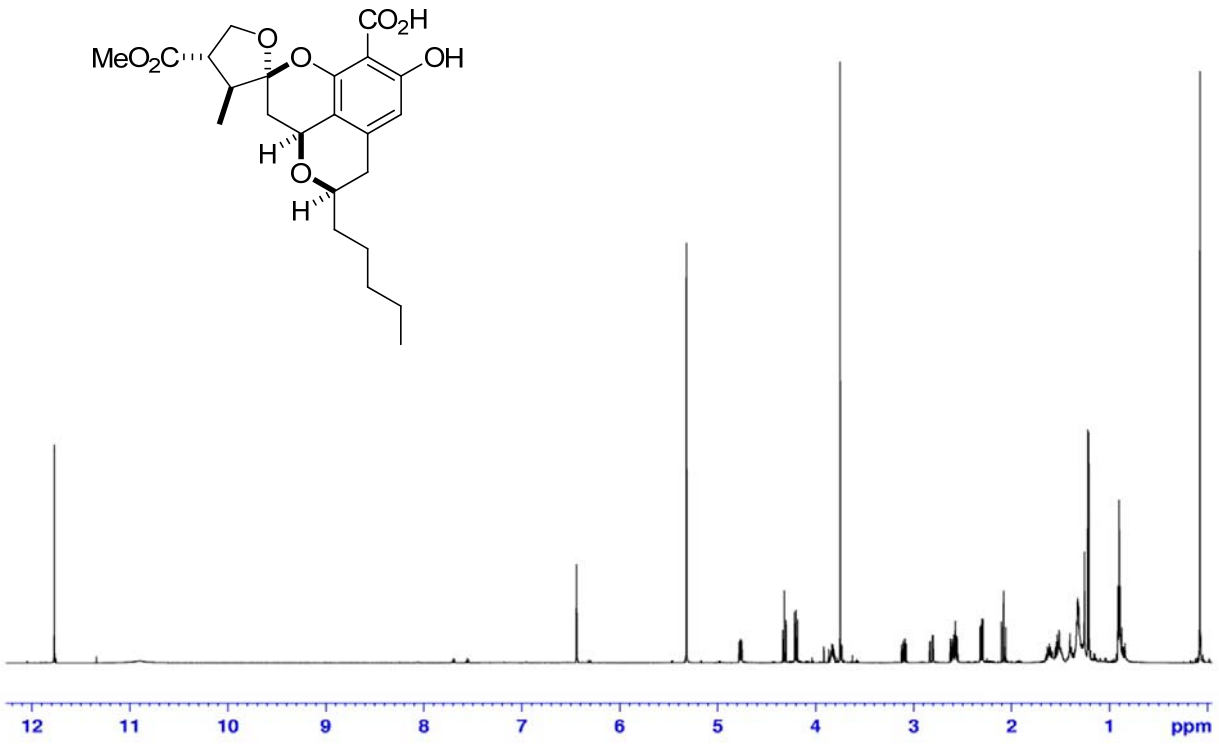
C22(*S*)-Diastereomer of (+)-Berkelic acid: ^{1}H NMR (CD_3OD, 600 MHz)



^{13}C NMR (CD_3OD, 150 MHz)



Compound 38: ^{1}H NMR (CD_2Cl_2, 600 MHz)



^{13}C NMR (CD_2Cl_2, 150 MHz)