SUPPORTING INFORMATION FOR

The first enantioselective synthesis of Palinurin

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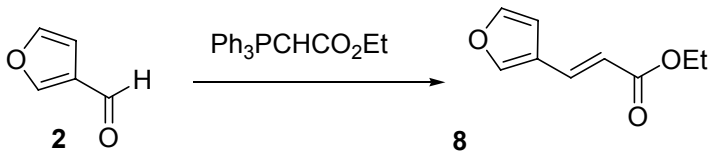
Experimental Procedures

General: Melting points were obtained in open capillary tubes and are not corrected. ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ at 400 and 100 MHz, respectively. All reactions were monitored by thin layer chromatography that was performed on precoated sheets of silica gel 60, and flash column chromatography was done with silica gel 60 (230-400 mesh) of Merck. Eluting solvents are indicated in the text.

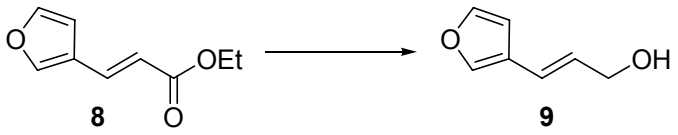
Compound 8



To a solution of aldehyde **2** (10.1 g, 104.7 mmol) in THF (280 mL) was added Ph_3PCHCO_2Et (40.2 g, 115.3 mmol) and the mixture refluxed for 2 h and allowed to reach room temperature. The solvent was removed and the residue was purified by column chromatography on silica gel using 30% EtOAc /Hexane as eluent, to afford ester **8** (17.3g, 99%) as a white solid; m.p. = 38-40 ºC, Rf = 0.6 (50% EtOAc /Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.58 (1H, s, CH); 7.50 (1H, d, *J*= 15,8 Hz, CH); 7.36 (1H, s, CH-2); 6.52 (1H, s, CH); 6.10 (1H, d, *J*= 15.8 Hz, CH); 4.18 (2H, q, *J*= 7.1 Hz, CH_2-OEt); 1.25 (3H, t, *J*= 7.1 Hz, CH_3-OEt).
^{13}C-NMR ($CDCl_3$, δ): 166.8 (C=O); 144.3 (CH); 114.3 (CH); 134.4 (CH); 122.5 (C); 117.9 (CH); 107.3 (CH); 60.2 (CH_2-OEt); 14.2 (CH_3-OEt).
IR (film): ν = 1710, 1610 cm^{-1}
MS (EI$^+$) [m/z, (%)]: 166.06 ([M]$^+$, 67); 121.03 ([M-OEt]$^+$, 100); 93.03 (30); 64.99 (28).
HRMS (EI$^+$): Calcd. For $C_9H_{10}O_3$ 166.0630 , found 166.0632.

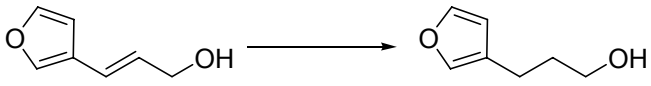
Compound 9



To a solution of ester **8** (17.3 g, 104 mmol) in Et_2O (61 mL) at 0ºC was added portionwise $LiAlH_4$ (11.9 g, 313 mmol). At the end of the addition the cooling bath was removed and the mixture stirred at room temperature for 1 h. The reaction was quenched with drops of H_2O at 0ºC and stirred for 30 mn. Na_2SO_4 was added and the solids removed by filtration. The filtrate was concentrated under reduced pressure affording virtually pure allylic alcohol **9** (12.3 g, 95%) as a yellowish liquid; Rf = 0,31 (50% EtOAc /Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.40 (1H, s, CH); 7.35 (1H, s, CH); 6.51 (1H, s, CH); 6.46 (1H, d, *J*= 15.9 Hz, CH); 6.09 (1H, td, *J*= 13.8 Hz, *J*= 5.9 Hz, CH); 4.25 (2H, d, *J*= 5.9 Hz, CH_2).
^{13}C-NMR ($CDCl_3$, δ): 143.6 (CH); 140.5 (CH); 128.1 (CH); 123.6 (C); 121.2 (CH); 107.5 (CH); 63.6 (CH_2).
IR (film): ν = 3365 (br) cm^{-1}
MS (EI^+) [m/z, (%)]: 124.13 ($[M]^+$, 4); 123.12 ($[M-1]^+$,9); 97.10 (22); 83.07 (26); 81.06 (36); 71.05 (32); 69.03 (68); 68.96 ($[M-C_3H_3O]^+$, 100).
HRMS (EI^+): Calcd. For $C_7H_8O_2$ 123.0810, found 123.0802.

Compound 10



9 **10**

A suspension of allylic alcohol **9** (4.1 g, 33 mmol) and Pd/C (10%) (0.32 g, 0.3 mmol) in MeOH (30 mL) was vigorously stirred under H_2 atmosphere for 7 h. At the end of the reaction (TLC), the mixture was filtered through celite and the filtrate was concentrated under reduced pressure affording virtually pure alcohol **10** (4.1 g, 98%) as a colorless oil, Rf = 0,31 (50% EtOAc /Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.34 (1H, s, CH); 7.23 (1H, s, CH); 6.27 (1H, s, CH); 3.68 (2H, t, *J*= 6.3 Hz, CH_2); 2.51 (2H, t, *J*= 7.7 Hz, CH_2); 1.82 (2H, q, *J*= 7.1 Hz, CH_2); 1.57 (1H, br s, -OH).
^{13}C-NMR ($CDCl_3$, δ): 142.8 (CH); 138.9 (CH); 124.4 (C); 110.9 (CH); 62.3 (CH_2); 32.8 (CH_2); 21.0 (CH_2).
IR (film): ν = 3350 (br) cm^{-1}
MS (EI^+) [m/z, (%)]:126.07 ($[M]^+$, 20); 125.06 ($[M-1]^+$,100); 113.06 (36); 112.05 (20); 111.05 (21); 109.7 ($[M-OH]^+$, 15); 97.06 (20); 95.05 ($[M-CH_3O]^+$, 20); 82.03 (28); 81.02 ($[M-C_2H_5O]^+$, 39); 79.04 (25); 67.02 ($[M-C_3H_7O]^+$, 31).
HRMS (EI^+): Calcd. For $C_7H_9O_2$ 125.0603, found 125.0607.

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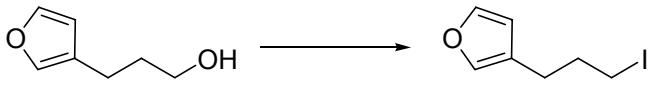
Compound 11

11 is a known compound (Mihelcic, J.; Moeller, K. D. *Journal of the American Chemical Society*, 2004, **126**, 9106.)

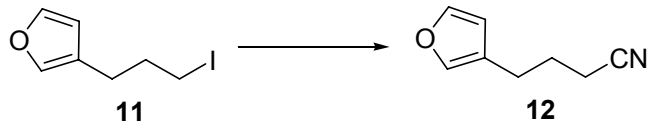


10 **11**

To a solution of alcohol **10** (0.87 g, 6.9 mmol) in THF (50 mL) were added PPh_3 (2.16 g, 8.25 mmol) and imidazole (1.4 g, 20.6 mmol) and the mixture was stirred at room temperature till complete dissolution of the reagents. It was then cooled to -20ºC and I_2 (2.26 g, 8.9 mmol) was added . After stirring at this temperature for 15 mn, the cooling bath was removed and the mixture stirred at room temperature for 30 mn. The reaction was quenched at 0ºC with an aqueous saturated solution of $NaHCO_3$ (49 mL), and the resulting white precipitate was removed by filtration. The aqueous phase was extracted with *tert*-butylmethylether (TBME) (3 x 50 mL) and the combined organic phases were washed with 10% aqueous solution of Na_2SO_3 (150 mL) and H_2O (150 mL), dried over Na_2SO_3, filtered and the solvent evaporated to give a residue which was chromatographed on silica gel using dichloromethane as eluent, affording iodide **11** (1.3 g, 80%) as a yellow oil; Rf = 0,80 (50% EtOAc /Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.35 (1H, t, *J*= 1.5 Hz, CH); 7.25 (1H, s, CH); 6.26 (1H, s, CH); 3.18 (2H, t, *J*= 6.7 Hz, CH_2); 2.54 (2H, t, *J*= 7.2 Hz, CH_2); 1.08 (2H, q, *J*= 6.9 Hz, CH_2)
^{13}C-NMR ($CDCl_3$, δ): 143.0 (CH); 139.3 (CH); 123.0 (C); 110.8 (CH); 33.4 (CH_2); 25.3 (CH_2); 6.3 (CH_2).
MS(FAB$^+$) [m/z, (%)]: 235.98 ([M]$^+$, 36); 221.11 (37); 219.17 (26); 217.16 (21); 207.11 (34); 205.17 (28); 203.17 (27); 202.17 (20); 193.17 (29); 191.18 (40); 181.18 (28); 177.22 (36); 169.12 (35); 167.20 (40); 165.22 (65); 163.25 (54); 161.24 (47); 159.23 (52); 155.22(64); 154.20 (100); 151.33 (43); 151.17 (50); 151.07 (54).
HRMS (EI$^+$): Calcd. For C_7H_9OI 235.9698, found 235.9759.

Compound 12



11 **12**

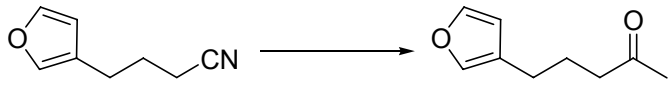
To a solution of iodide **11** (1.1 g, 4.6 mmol) in DMSO (12 mL) was added NaCN (324 mg, 6.5 mmol) and the mixture was stirred at 90ºC for 1 h and allowed to reach room temperature. H_2O (50 mL) was added and the product extracted with TBME (3 x 50 mL). The combined organic phases were dried, filtered and evaporated to afford

virtually pure nitrile **12** (625 mg, 99%) as a colorless liquid; Rf = 0,70 (50% EtOAc /Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.37 (1H, t, *J*= 1.7 Hz, CH); 7.26 (1H, dd, *J*= 1.6 Hz, *J*= 0.9 Hz, CH); 6.25 (1H, s, CH-2); 2.60 (2H, t, *J*= 7.3 Hz, CH_2); 2.33 (2H, t, *J*= 7.1 Hz, CH_2); 1.91 (2H, q, *J*= 7.3 Hz, CH_2)
^{13}C-NMR ($CDCl_3$, δ): 134.3 (CH); 139.4 (CH); 122.5 (C); 119.4 (C); 110.5 (CH); 25.7 (CH_2); 23.5 (CH_2); 16.4 (CH_2)
IR (film): ν= 2258 cm^{-1}
MS (EI^+) [m/z, (%)]:135.07 ($[M]^+$, 29); 95.05 ($[M-C_2H_2N]^+$, 5); 82.04 (30); 81.03 ($[M-C_3H_4N]^+$, 100).
HRMS (EI^+): Calcd. For C_8H_9NO 135.0684, found 135.0685.

Compound 3

3 is a known compound (W. H. Miles, C. J. Berreth, P. M. Smiley, *Tetrahedron Lett.* 1993, **34**, 5221)

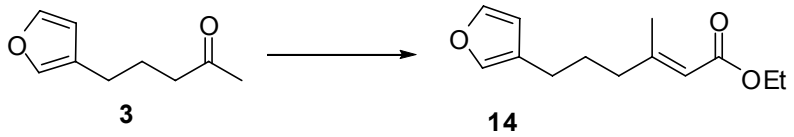


12 **3**

To a solution of nitrile **12** (3.58 g, 25.8 mmol) in Et_2O (60 mL) at 0ºC was added MeLi (51.6 mL of a 1.5M solution in Et_2O, 77.46 mmol) and the mixture was stirred for 30 mn. The reaction was quenched by adding an aqueous saturated solution of NH_4Cl and the product extracted with EtOAc (3 x 50 mL). The combined organic phases were washed with an aqueous saturated solution of $NaHCO_3$ (100 mL), dried, filtered and evaporated to give a residue which was chromatographed on silica gel using 5% EtOAc /Hexane as eluent, affording ketone **3** (3.92 g, 80%) as a colorless liquid; Rf = 0,65 (50% EtOAc/Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.32 (1H, s, CH); 7.18 (1H, s, CH); 6.23 (1H, s, CH); 2.40 (4H, c, *J*= 7.1 Hz, CH_2-3, CH_2); 2.09 (3H, s, CH_3); 1.80 (2H, q, *J*= 7.4 Hz, CH_2).
^{13}C-NMR ($CDCl_3$, δ): 208.6 (C=O); 142.8 (CH); 138.9 (CH); 124.2 (C); 110.8 (CH); 42.8 (CH_2); 29.9 (CH_3); 23.9 (CH_2); 23.8 (CH_2).
IR (film): ν= 1720 cm^{-1}
MS (EI^+) [m/z, (%)]: 152.08 ($[M]^+$, 6); 134.07 ($[M-H_2O]^+$,12); 94.04 ($[M-C_3H_6O]^+$, 100).
HRMS (EI^+): Calcd. For $C_9H_{12}O_2$ 152.0837, found 152.0832.

Compound 14

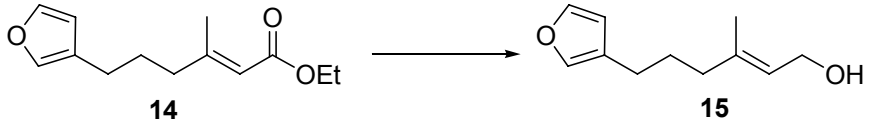


3 **14**

To a mixture of NaH (2.8 g, 70.8 mmol) in THF (70 mL) at 0ºC was added $(EtO)_2P(O)CH_2CO_2Et$ (16.5 mL, 82.9 mmol). The cooling bath was then removed and the mixture stirred at room temperature for 18 h. A solution of ketone **3** (1.8 g, 11.8 mmol) in THF (10 mL) was added and stirring was continued at room temperature for 24 h. The reaction was quenched with an aqueous saturated solution of NH_4Cl and the product extracted with EtOAc (3 x 100 mL). The combined organic phases were dried, filtered and evaporated to give a residue which was chromatographed on silica gel using 10% EtOAc/Hexane as eluent, affording ester **14** (2.6 g, 99%) as a colorless liquid; Rf = 0,73 (100% AcOEt).

^{1}H-NMR ($CDCl_3$, δ): 7.34 (1H, s, CH); 7.20 (1H, s, CH); 6.24 (1H, s, CH); 5.65 (1H, s, CH); 4.13 (2H, q, *J*= 6.9 Hz, CH_2-OEt); 2.44 (2H, td, *J*= 20.0 Hz, *J*= 7.6 Hz, CH_2); 2.14 (5H, m, CH_3 and CH_2); 1,72 (2H, q, *J*= 7.5 Hz, CH_2); 1.26 (3H, t, *J*= 7.2 Hz, CH_3-OEt)
^{13}C-NMR ($CDCl_3$, δ): 166.8 (C=O); 159.5 (C); 142.8 (CH); 138.9 (CH); 124.4 (C); 115.8 (CH); 110.8 (CH); 59.5 (CH_2-OEt); 40.3 (CH_2); 27.6 (CH_2); 24.2 (CH_2); 18.7 (CH_3); 14.3 (CH_3-OEt)
IR (film): ν= 1709 cm^{-1}
MS (FAB^+) [m/z, (%)]: 223.16 ($[M+1]^+$,44); 222.14 ($[M]^+$,25); 221.15 (39); 219.18 (22); 217.16 (22); 215.13 (24); 209.14 (30); 207.15 (34); 203.17 (25); 202.16 (26); 193.16 (100); 192.15 (34); 191.17 (50); 177.21 (63); 163.24 (67); 155.23 (43); 154.21 (66); 151.36 (51); 151.16 (59).
HRMS (FAB^+): Calcd. For $C_{13}H_{19}O_3$ 223.1334, found 223.1340.

Compound 15

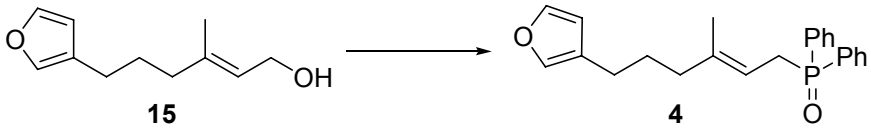


14 **15**

To a solution of ester **14** (684 mg, 3.1 mmol) in dichloromethane (20 mL) at -78ºC was added Dibal (7.7 mL of a 1.0 M solution in hexane, 7.7 mmol) and the mixture was stirred at this temperature for 30 mn. TBME (4 mL) and H_2O (0.5 mL) were added and the cooling bath was removed and stirring continued until formation of a white gel. H_2O (0.5 mL) and an aqueous 4.0 M solution of NaOH (0.5 mL) were added and the stirring continued until formation of a white precipitate. Na_2SO_4 was added and the salts were filtered under reduced pressure affording virtually pure allylic alcohol **15** (589 mg, 99%) as a colorless liquid; Rf = 0,65 (50% EtOAc/Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.33 (1H, s, CH); 7.20 (1H, s, CH); 6.25 (1H, s, CH); 5.41 (1H, qt, *J*= 1.2 Hz, *J*= 6.9 Hz, CH); 4.15 (2H, d, *J*= 6.9 Hz, CH_2); 2.39 (2H, t, *J*= 7.6 Hz, CH_2); 2.05 (2H, t, *J*= 7.7 Hz, CH_2); 1.69 (2H, t, *J*= 7.5 Hz, CH_2); 1.66 (3H, s, CH_3).
^{13}C-NMR ($CDCl_3$, δ): 142.8 (CH); 139.5 (C); 138.8 (CH); 124.9 (C); 123.6 (CH); 110.9 (CH); 59.4 (CH_2); 39.0 (CH_2); 27.9 (CH_2); 24.3 (CH_2); 16.2 (CH_3).
IR (film): ν= 3333 (br) cm^{-1}
MS (EI^+) [m/z, (%)]: 180.11 ($[M]^+$, 4); 95.03 (30); 94.02 ($[M-C_5H_{10}O]^+$, 91); 82.00 ($[M-C_6H_{12}O]^+$, 100); 71.00 (24).
HRMS (EI^+): Calcd. For $C_{11}H_{16}O_2$ 180.1150, found 180.1145.

Compound 4



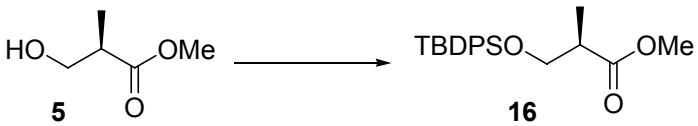
To a cooled (-20ºC) solution of allylic alcohol **15** (390 mg, 1.75 mmol) in Et_2O (2.5 mL) was added dropwise PBr_3 (85 µL, 0.87 mmol). The mixture was stirred for 2 h, quenched with H_2O (10 mL) and extracted with Et_2O (3 x 10 mL). The combined organic phases were washed with aqueous saturated solutions of $NaHCO_3$ (2 X10 mL) and NaCl (10 mL). Drying and solvent evaporation afforded the corresponding allylic bromide (429 mg, 89%) as an unstable colorless oil; Rf = 0,75 (50% EtOAc/Hexane). This allylic bromide will be used in the next step without further purification.
A solution of PPh_2H (250 µL; 1,44 mmol) in THF (6 mL) was cooled to 0ºC and *n*-BuLi (576 mL of a 2.5 M solution in hexane, 1.44 mmol) was added. The bright red solution was stirred for 30 mn and cooled to -78ºC before adding a solution of the previously obtained allylic bromide (191 mg; 0,79 mmol) in THF (4 mL). The mixture was stirred at this temperature for 1 h, allowed to reach 0ºC before adding a solution of 5% H_2O_2 (8 mL). Stirring was continued for 30 mn and the product extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were dried, filtered and evaporated to give a residue which was chromatographed on silica gel using 50% EtOAc/Hexane as eluent, affording phosphine oxide **4** (268 mg, 93%) as a white solid; m.p. = 67-69 ºC, Rf = 0,12 (50% EtOAc/Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.69 (4H, m, CH_o-Ph); 7.48 (6H, m, $CH_{p,m}$-Ph); 7.31 (1H, s, CH-5 furyl); 7.15 (1H, s, CH-2 furyl); 7.10 (1H, s, CH-2 furyl); 6.21 (1H, s, CH-4 furyl); 6.18 (1H, s, CH-4 furyl); 5.25 (1H, c, *J*= 6.5 Hz, CH-2); 3.09 (2H, dd, *J*= 14.7 Hz, *J*= 7.6 Hz, CH_2-1); 3.02 (2H, dd, *J*= 14.69 Hz, *J*= 7.63 Hz, CH_2-1); 2.29 (2H, t, *J*= 7.63 Hz, CH_2-6); 2.22 (2H, t, *J*= 7.6 Hz, CH_2-6); 1.97 (2H, m, CH_2-4); 1.87 (2H, t, *J*= 7.9 Hz, CH_2-4); 1.65 (2H, d, *J*= 3.4 Hz, CH_2-5); 1.52 (2H, q, *J*= 7.6 Hz, CH_2-5); 1.44 (3H, s, CH_3-3)

^{13}C-NMR ($CDCl_3$, δ): 142.6 (CH-5 furyl); 140.8 (C-3); 138.8 (CH-2 furyl); 134.0 (C-Ph); 122.4 (C-Ph); 131.7 (CH_p-Ph); 131.7 (CH_p-Ph); 131.1 (CH_o-Ph); 131.0 (CH_o-Ph); 128.5 (CH_m-Ph); 128.4 (CH_m-Ph); 124.8 (C-3 furyl); 112.7 (CH-2 furyl); 110.9 (CH-4 furyl); 39.1 (CH_2-4); 31.1 y 30.4 (CH_2-1); 27.8 (CH_2-5); 23.9 (CH_2-6);16.2 (CH_3-3).
IR (film): ν= 1190 (br) cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 366.10 ($[M+2]^+$, 26); 365.10 ($[M+1]^+$, 100); 202.08 (34); 201.08 (45).
HRMS (FAB$^+$): Calcd. For $C_{23}H_{26}O_2P$ 365.1670, found 365.1672.

Compound 16

16 is a known compound (J.M. Clough; H. Dube; B. J. Martin; G. Pattenden; K. S. Reddy; I. R. Waldron, *Organic & Biomolecular Chemistry* 2006, **4**, 2906)

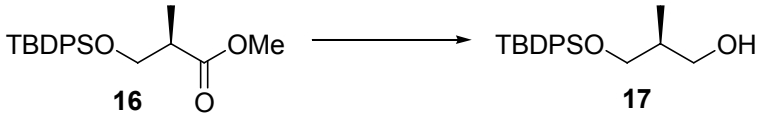


To a solution of alcohol **5** (0,96 g; 8,12 mmol) in DMF (30 mL), were added imidazole (1,1 g; 16,24 mmol), DMAP (catalytic) and TBDPSCl (2,3 mL; 8,94 mmol). The mixture was srirred at room temperature for 12 h, quenched with water and the product extracted with TBME (3 x 50 mL). The combined organic phases were washed with brine (2 x 75 mL), dried and rotatory evaporated to give a residue which was chromatographed on silica gel using 3% EtOAc/Hexane as eluent, affording **16** (3.2 g, 99%) as a colorless liquid, Rf: 0,30 (10% EtOAc/Hexane); $[\alpha]_D^{20}$= -18.3 (C=1.6 , $CHCl_3$)

^{1}H-NMR ($CDCl_3$, δ): 7.65 (4H, dd, *J*= 7.7 Hz, *J*= 1.7 Hz, CH_o-Ph); 7.38 (6H, m, $CH_{p,m}$-Ph); 3.82 (1H, dd, *J*= 9.7 Hz, *J*= 6.9 Hz, CH-3); 3.72 (1H, dd, *J*= 9.8 Hz, *J*= 5.9 Hz, CH-3); 3.68 (3H, s, -OCH_3); 2.71 (1H, sex., *J*= 6.8 Hz, CH-2); 1,15 (3H, d, *J*= 7.1 Hz, CH_3-2); 1.02 (9H, s, CH_3-*tert*-BuSi).
^{13}C-NMR ($CDCl_3$, δ): 175.4 (C=O); 135.6 (CH_o-Ph); 133.5 (C-Ph); 129.6 (CH_p-Ph); 127.6 (CH_m-Ph); 65.9 (CH_2-3); 51.5 (CH_3O); 42.4 (CH-2); 26.7 (CH_3-*tert*-BuSi); 19.2 (C-Si); 13.5 (CH_3-2).
IR (film): ν= 1741 cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 357.16 ($[M+1]^+$, 5); 300.08 (25); 299.31 ($[M-$ *tert*-Bu$]^+$, 100); 279.11 (48); 213.10 (26).
HRMS (FAB$^+$): Calcd. For $C_{21}H_{29}O_3Si$ 357.1886, found 357.1897.

Compound 17

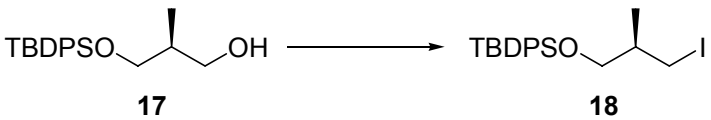
17 is a known compound (J.M. Clough; H. Dube; B. J. Martin; G. Pattenden; K. S. Reddy; I. R. Waldron, *Organic & Biomolecular Chemistry* 2006, **4**, 2906)



To a solution of ester **16** (1,6 g; 4,55 mmol) in CH_2Cl_2 (30 mL) at -78ºC, was added Dibal (9.1 mL of a 1.0 M solution in hexane, 9.1 mmol) and the mixture stirred for 2 h. TBME (8,5 mL) and H_2O (1,3 mL) were added and the mixture allowed to reach room temperature, stirring vigorously until formation of a white gel. H_2O (1,3 mL) and a 4,0 M solution of NaOH (1,3 mL) were added and stirring continued until formation of a white precipitate. Na_2SO_4 was added and the solids removed by filtration. After solvent evaporation the residue was chromatographed on silica gel using 10% EtOAc/Hexane as eluent, affording alcohol **17** (1.6 g, 99%) as a colorless liquid, Rf = 0,15 (10% EtOAc/Hexane); $[\alpha]_D^{20}$= -8.0 (C=0.6 , $CHCl_3$)

^{1}H-NMR ($CDCl_3$, δ): 7.67 (4H, dd, *J*= 7.8 Hz, *J*= 1.6 Hz, CH_o-Ph); 7.41 (6H, m, $CH_{p,m}$-Ph); 3.72 (1H, dd, *J*= 10.0 Hz, *J*= 4.4 Hz, CH-3); 3.67 (2H, s.a., CH_2-1); 3.59 (1H, dd, *J*= 10.0 Hz, *J*= 7.6 Hz, CH-3); 2.49 (1H, s.a., -OH); 1.99 (1H, sex., *J*= 6.4 Hz, CH-2); 1.05 (9H, s, CH_3-*tert*-Bu); 0.82 (3H, d, *J*= 6,9 Hz, CH_3-2).
^{13}C-NMR ($CDCl_3$, δ): 135.6 (CH_o-Ph); 133.2 (C-Ph); 129.8 (CH_m-Ph); 127.8 (CH_p-Ph); 68.7 (CH_2-3); 67.7 (CH_2-1); 37.3 (CH-2); 26.8 (CH_3-*tert*-Bu); 19.1 (C-Si); 13.1 (CH_3-2).
IR (film): ν= 3364 (br) cm^{-1}
MS (FAB$^+$) [m/z, (%)]:329.11 ([M+1]$^+$, 43); 311.11 ([M-OH]$^+$, 21); 271.05 ([M-*terc*-Bu]$^+$, 38); 199.10 (100); 197.12 (30); 193.12 (26).
HRMS (FAB$^+$): Calcd. For $C_{20}H_{29}O_2Si$ 329.1937, found 329.1935.

Compound 18

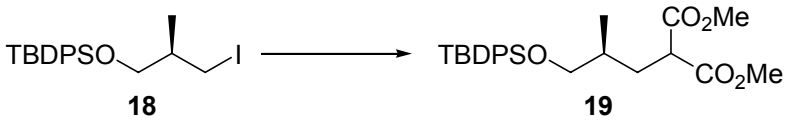


To a solution of alcohol **17** (2,5 g; 7,69 mmol) in THF (33 mL) were added PPh_3 (2,4 g; 9,28 mmol) and imidazole (1,6 g; 23,07 mmol) and the mixture was stirred at room temperature till complete disolution of the reagents. It was then cooled to -20ºC and I_2 (2,2 g; 8,46 mmol) was added . After stirring at this temperature for 15 mn, the cooling bath was removed and the mixture stirred at room temperature for 30 mn. The reaction was quenched at 0ºC with an aqueous saturated solution of $NaHCO_3$ (50 mL), and the resulting white precipitate was removed by filtration. The aqueous phase was extracted

with *tert*-butylmethylether (TBME) (3 x 50 mL) and the combined organic phases were washed with 10% aqueous solution of Na_2SO_3 (100 mL) and H_2O (100 mL), dried over Na_2SO_3, filtered and the solvent evaporated to give a residue which was chromatographed on silica gel using 10% EtOAc/Hexane as eluent, affording iodide **18** (3 g, 90%) as a yellow liquid; Rf = 0.85 (50% EtOAc /Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.68 (4H, m, CH_o-Ph); 7.43 (6H, m, $CH_{p,m}$-Ph); 3.60 (1H, dd, *J*= 10.1 Hz, *J*= 4.9 Hz, CH-1); 3.48 (1H, dd, *J*= 10.0 Hz, *J*= 6.9 Hz, CH-1); 3.41 (1H, dd, *J*= 9.5 Hz, *J*= 5.1 Hz, CH-3); 3.34 (1H, dd, *J*= 9.5 Hz, *J*= 5.8 Hz, CH-3); 1.74 (1H ,sex., *J*= 5.9 Hz, CH-2); 1.08 (9H, s, CH_3-*tert*-BuSi); 0.98 (3H, d, *J*= 6.7 Hz, CH_3-2).
^{13}C-NMR ($CDCl_3$, δ): 135.6 (CH_o-Ph); 133.6 (C-Ph); 129.7 (CH_m-Ph); 127.7 (CH_p-Ph); 67.3 (CH_2-1); 37.5 (CH-2); 26.8 (CH_3-*tert*-BuSi); 19.3 (C-Si); 17,31 (CH_2-3); 13.5 (CH_3-2).
MS (FAB$^+$) [m/z, (%)]: 439.05 ([M+1]$^+$, 3); 380.97 ([M-*tert*-Bu]$^+$, 41); 308.91 (100); 246.92 (34); 199.09 (26); 197.11 (38).
HRMS (FAB$^+$): Calcd. For $C_{20}H_{28}OSiI$ 439.0954, found 439.0967.

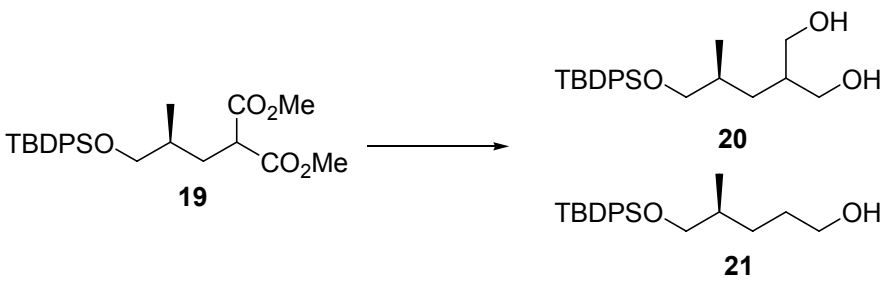
Compound 19



To a solution of NaH (0,55 g; 13,6 mmol) in DMF (1,5 mL) and THF (10 mL) was added dimethyl malonate (1,6 mL; 13,6 mmol) and the resulting white foam was stirred for 15 mn. Iodide **18** (3 g; 6,9 mmol) in THF (20 mL) was added and the mixture stirred for 18 h and allowed to reach room temperature. EtOAc (100 mL) was added and the mixture washed with brine (2 x 100 mL) and H_2O (2 x 100 mL), dried and rotatory evaporated to give a residue which was chromatographed on silica gel using 6% EtOAc/Hexane as eluent, affording diester **19** (2.8 g, 91%) as a colorless oil, Rf = 0,50 (30% EtOAc/Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.64 (4H, dd, *J*= 7.8 Hz, *J*= 1.5 Hz, CH_o-Ph); 7.39 (6H, m, $CH_{p,m}$-Ph); 3.71 (6H, s,-OCH_3); 3.52 (1H, t, *J*= 7.7 Hz, CH-2); 3.49 (2H, d, *J*= 5.7 Hz, CH_2-5); 2.11 (1H, m, CH-3); 1.76 (1H, m, CH-3); 1.67 (1H, m, CH-4); 1.05 (9H, s, CH_3-*tert*-BuSi); 0,92 (3H, d, *J*= 6.5 Hz, CH_3-4).
^{13}C-NMR ($CDCl_3$, δ): 170.1 (C=O); 170.0 (C=O); 135.6 (CH_o-Ph); 133.7 (C-Ph); 129.6 (CH_m-Ph); 127.6 (CH_p-Ph); 68.4 (CH_2-5); 52.4 (CH_3O); 49.7 (CH-2); 33.7 (CH-4); 32.6 (CH_2-3); 26.8 (CH_3-*tert*-BuSi); 19.3 (C-Si); 16.6 (CH_3-4).
IR (film): ν= 1737 cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 443.33 ([M+1]$^+$, 8); 386.23 (29); 385.22 ([M-*tert*-Bu]$^+$, 100); 365.24 (36); 213.17 (40).
HRMS (FAB$^+$): Calcd. For $C_{25}H_{35}O_5Si$ 443.2254, found 443.2254.

Compounds 20 and 21



To a solution of diester **19** (2,6 g; 5,77 mmol) in DMSO (120 mL), was added NaCl (1,2 g; 20,2 mmol) and H_2O (415,5 mL) and the mixture heated at 160ºC while stirring, for 4 h. It was then allowed to reach room temperature. EtOAc (100 mL) was added and the mixture washed with brine (2 x 100 mL) and H_2O (2 x 100 mL). The organic phase was dried, filtered and rotatory evaporated. The residue was dissolved in Et_2O (44 mL) in a round bottom flask fitted with a reflux condenser and ice-cooled. $LiAlH_4$ (0,64 g; 16,95 mmol) was added portionwise. At the end of the addition, the cooling bath was removed and the mixture stirred at room temperature for 30 mn then recooled. H_2O was added dropwise until complete destruction of excess $LiAlH_4$ and the mixture stirred for 30 mn before adding Na_2SO_4.The solids were removed by filtration and the filtrate concentrated to afford a residue which was chromatographed on silica gel using 10% EtOAc/Hexane as eluent, affording diol **20** (300 mg, 16%) as a colorless liquid, Rf = 0,15 (50% EtOAc/Hexane) and alcohol **21** (1,47 g, 73%) as colorless liquid, Rf = 0,60 (50% EtOAc/Hexane)

Diol **20**.

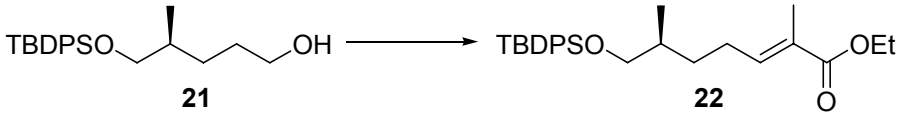
^{1}H-NMR ($CDCl_3$, δ):): 7.64 (4H, d, *J*= 6.8 Hz, CH_o-Ph); 7.39 (6H, m, $CH_{p,m}$-Ph); 3.75 (2H, dt, *J*= 10.8 Hz, *J*= 3.5 Hz, CH_2-1); 3.59 (2H, m, CH_2-1); 3.47 (2H, d, *J*= 5.7 Hz, CH_2-5); 1.92 (1H, s, -OH); 1.81 (1H, s, -OH); 1.69 (1H, sex., *J*= 6.6 Hz, CH-4); 1.35 (1H, q, *J*= 6.8 Hz, CH-2); 1.05 (9H, s, CH_3-*tert*-BuSi); 0.98 (2H, dd, *J*= 13.9 Hz, *J*= 6.8 Hz, CH_2-3); 0.92 (3H, d, *J*= 6.8 Hz, CH_3-4).
^{13}C-NMR ($CDCl_3$, δ): 135.6 (CH_0-Ph); 133.9 (C-Ph); 129.6 (CH_m-Ph); 127.6 (CH_p-Ph); 68.9 (CH_2-5); 67.3 (CH_2-1); 66.5 (CH_2-1); 39.4 (CH-2); 33.3 (CH-4); 31.2 (CH_2-3); 26.7 (CH_3-*tert*-BuSi); 19.3 (C-Si); 17.2 (CH_3-4).
IR (film): ν= 3353 (br) cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 387.23 ($[M+1]^+$, 14); 199.11 (100); 197.13 (52).
HRMS (FAB$^+$): Calcd. For $C_{23}H_{35}O_3Si$ 387.2355, found 387.2351.

Alcohol **21**.

^{1}H-NMR ($CDCl_3$, δ): 7.66 (4H, dd, *J*= 7.9 Hz, *J*= 1.6 Hz, CH_o-Ph); 7.39 (6H, m, $CH_{p,m}$-Ph); 3.59 (2H, t, *J*= 6.7 Hz, CH_2-1); 3.51 (1H, dd, *J*= 9.9 Hz, *J*= 5.9 Hz, CH-5); 3.46 (1H, dd, *J*= 9.86 Hz, *J*= 6.20 Hz, CH-5); 1.66 (1H, sex., *J*= 6.4 Hz, CH-4); 1.61-

1.39 (4H, m, -OH, CH_2-2, CH-3); 1.16 (1H, m, CH-3); 1.05 (9H, s, CH_3-*tert*-BuSi); 0.92 (3H, d, *J*= 6.7 Hz, CH_3-4).
^{13}C-NMR ($CDCl_3$, δ): 135.6 (CH_o-Ph); 134.0 (C-Ph); 129.5 (CH_m-Ph); 127.6 (CH_p-Ph); 68.8 (CH_2-5); 63.3 (CH_2-1); 35.5 (CH-4); 30.2 (CH_2-2); 29.2 (CH_2-3); 26.9 (CH_3-*tert*-BuSi); 19.3 (C-Si); 16.8 (CH_3-4).
IR (film): ν= 3363 (br) cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 357.15 ($[M+1]^+$, 14); 299.07 ($[M\text{-}tert\text{-}Bu]^+$, 14); 199.09 (100); 197.11 (42).
HRMS (FAB$^+$): Calcd. For $C_{22}H_{33}O_2Si$ 357.2250, found 357.2264.

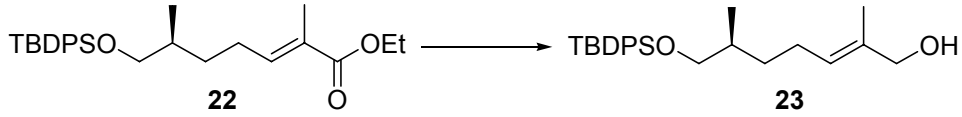
Compound 22



To a solution of alcohol **21** (566 mg; 1,6 mmol) in CH_2Cl_2 (12 mL) were added 4Å molecular sieves (362 mg), 4-methylmorpholine N-oxide (NMO, 373 mg, 3,2 mmol) and a catalytic amount of TPAP. The mixture was stirred at room temperature for 3 h, filtered through celite and the solvent rotatory evaporated to give a residue which was dissolved in THF (100 mL). $Ph_3PCCH_3CO_2Et$ (575 mg; 1,6 mmol) was added and the mixture refluxed for 18 h, allowed to reach room temperature and the solvent removed. The residue which was chromatographed on silica gel using 5% EtOAc/Hexane as eluent, affording diol **22** (696 mg, 60%) as a colorless oil, Rf = 0,45 (10% EtOAc/Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.65 (4H, d, *J*= 7.6 Hz, CH_o-Ph); 7.39 (6H, m, $CH_{p,m}$-Ph); 6.73 (1H, t, *J*= 7.2 Hz, CH-3); 4.18 (2H, c, *J*= 7.0 Hz, CH_2-OEt); 3.48 (2H, dd, *J*= 5.4 Hz, *J*= 3.9 Hz, CH_2-7); 2.14 (1H, q, *J*= 7.4 Hz, CH-6); 1.64 (3H, s, CH_3-2); 1.27 (5H, m, CH_3-OEt, CH_2-5); 1.04 (9H, s, CH_3-*tert*-BuSi); 0.93 (3H, d, *J*= 6.5 Hz, CH_3-6).
^{13}C-NMR ($CDCl_3$, δ): 168.3 (C=O); 142.4 (CH-3); 135.6 (CH_o-Ph); 134.0 (C-Ph); 129.6(CH_p-Ph); 127.7 (C-2); 127.6 (CH_m-Ph); 68.5 (CH_2-7); 60.3 (CH_2-OEt); 35.4 (CH-6); 32.0 (CH_2-5); 26.9 (CH_3-*tert*-BuSi); 26.2 (CH_2-4), 19.3 (C-Si); 16.7 (CH_3-6); 14.3 (CH_3-OEt); 12.3 (CH_3-2).
IR (film): ν= 1709 cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 381.16 ($[M\text{-}tert\text{-}Bu]^+$, 94); 199.08 ($[M\text{-}C_{15}H_{27}O_2]^+$, 100).
HRMS (FAB$^+$): Calcd. For $C_{23}H_{29}O_3Si$ 381.1886, found 381.1894.

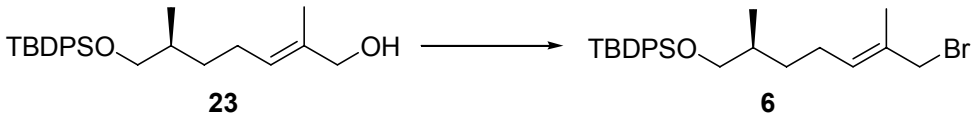
Compound 23



To a solution of ester **22** (0,83 g; 1,89 mmol) in CH_2Cl_2 (12 mL) at -78ºC was added Dibal (5.7 mL of a 1.0 M solution in hexane, 5.7 mmol) and the mixture was stirred at this temperature for 30 mn. TBME (2.6 mL) and H_2O (0.4 mL) were added and the cooling bath was removed and stirring continued until formation of a white gel. H_2O (0.4 mL) and an aqueous 4.0 M solution of NaOH (0.4 mL) were added and the stirring continued until formation of a white precipitate. Na_2SO_4 was added and the salts were filtered under reduced pressure to give a residue which was chromatographed on silica gel using 8% EtOAc/Hexane as eluent, affording allylic alcohol **23** (0,72 g, 96%) as a colorless liquid, Rf = 0,60 (30% EtOAc/Hexane); $[\alpha]_D^{20}$=-1.0 (C=3.4 , $CHCl_3$).

^{1}H-NMR ($CDCl_3$, δ): 7.66 (4H, dd, *J*= 7.8 Hz, *J*= 1.5 Hz, CH_o-Ph); 7.39 (6H, m, $CH_{p,m}$-Ph); 5.37 (1H, t, *J*= 7.0 Hz, CH-3); 3.98 (2H, s, CH_2-1); 3.52 (1H, dd, *J*= 9.8 Hz, *J*= 5.6 Hz, CH-7); 3.46 (1H, dd, *J*= 9.9 Hz, *J*= 6.1 Hz, CH-7); 2.02 (2H, sept., *J*= 7.9 Hz, CH_2-4); 1.67 (1H, m, CH-5); 1.64 (3H, s, CH_3-2); 1.51 (1H, m, CH-5); 1.37(1H, s.a., -OH); 1,18 (1H, m, CH-5); 1.05 (9H, s, CH_3-*tert*-BuSi); 0.94 (3H, d, *J*= 6.7 Hz, CH_3-6).
^{13}C-NMR ($CDCl_3$, δ): 135.6 (CH_o-Ph); 134.6 (C-2); 134.1 (C-Ph); 129.5(CH_p-Ph); 127.6 (CH_m-Ph); 126.6 (CH-3); 69.5 (CH_2-7); 68.7 (CH_2-1); 35.4 (CH-6); 32.9 (CH_2-5); 26.9 (CH_3-*tert*-BuSi); 25.3 (CH_2-4), 19.3 (C-Si); 16.8 (CH_3-6); 13.3 (CH_3-2).
IR (film): ν= 3333 (br) cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 321.12 ([M-*tert*-Bu-OH]$^+$, 4); 199.08 ([M-$C_{13}H_{26}O$]$^+$, 100).
HRMS (FAB$^+$): Calcd. For $C_{21}H_{25}OSi$ 321.1675, found 321.1664.

Compound 6

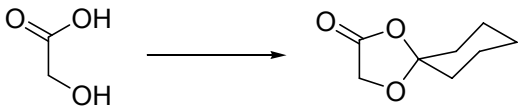


To a solution of allylic alcohol **23** (0,52 g; 1,31 mmol) in CH_2Cl_2 (12,5 mL) at 0ºC, were added CBr_4 (0,52 g; 1,57 mmol) and PPh_3 (450 mg; 2,09 mmol) and the mixture stirred for 1 h. Hexane (40 mL) was added and the resulting white precipitate was removed by filtration through celite. The filtrate was concentrated till formation of the same white precipitate which was again removed by filtration through celite. The solvent was removed affording virtually pure allylic bromide **6** (0,6 g, 99%) as a colorless liquid, Rf = 0,70 (30% EtOAc/Hexane).

^{1}H-NMR ($CDCl_3$, δ): 7.66 (4H, dd, *J*= 7.8 Hz, *J*= 1.6 Hz, CH_o-Ph); 7.40 (6H, m, $CH_{p,m}$-Ph); 5.57 (1H, t, *J*= 7.1 Hz, CH-3); 3.96 (2H, s, CH_2-1); 3.51 (1H, dd, *J*= 9.8 Hz, *J*= 5.8 Hz , CH-7); 3.46 (1H, dd, *J*= 9.8 Hz, *J*= 5.9 Hz, CH-7); 2.01 (2H, sex., *J*= 6.3 Hz, CH_2-4); 1.73 (3H, s, CH_3-2); 1.65 (1H, sex., *J*= 6.4 Hz, CH-5); 1.53 (1H, m, CH-5); 1.19 (1H, m, CH-6); 1.06 (9H, s, CH_3-*tert*-BuSi); 0.93 (3H, d, *J*= 6.7 Hz, CH_3-6).
^{13}C-NMR ($CDCl_3$, δ): 135.6 (CH_o-Ph); 134.0 (C-Ph); 131.8 (CH-3); 129.5 (CH_p-Ph); 127.6 (CH_m-Ph); 68.6 (CH_2-7); 41.9 (CH_2-1); 35.3 (CH-6); 32.5 (CH_2-4); 26.9 (CH_3-*tert*-BuSi); 25.8 (CH_2-5), 19.3 (C-Si); 16.8 (CH_3-6); 14.6 (CH_3-2).
MS (FAB^+) [m/z, (%)]: 459.06 ($[M+1]^+$, 8); 401.23 ($[M\text{-}tert\text{-BuSi}]^+$, 50).
HRMS (FAB^+): Calcd. For $C_{25}H_{36}BrOSi$ 459.1719, found 459.1523.

Compound 25

25 is a known compound (S. Hanessian, A. Tehim, P. Chen, *J. Org. Chem.* 1993, **58**, 7768)



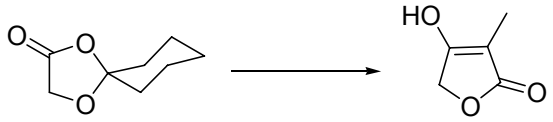
24 **25**

To a solution of acid **24** (15,4 g; 202,3 mmol) in Et_2O (500 mL) at 0ºC was added $BF_3{\cdot}OEt_2$ (38,5 mL; 303,5 mmol) and freshly distilled cyclohexanone (21 mL; 202,3 mmol). The mixture was stirred at this temperature for 1 h, the cooling bath was removed and stirring was continued at room temperature for 2 days. An aqueous solution of 10% AcNa (1000 mL) was added and the mixture stirred for 20 mn and extracted with TBME (3 x 750 mL). The combined organic phases were dried and rotatory evaporated to give a residue which was chromatographed on silica gel using 1% EtOAc/Hexane as eluent, affording **25** (23.1 g, 73%) as a white solid ; m.p. = 38-40 ºC, Rf = 0.6 (50% EtOAc /Hexane).

^{1}H-RMN ($CDCl_3$, δ): 4,32 (2H, s, CH_2-2); 1,82 (2H, m, $CH_{ec.}$-2', $CH_{ec.}$-6'); 1,78-1,61 (6H, m, $CH_{ax.}$-2', $CH_{ax.}$-6', CH_2-3', CH_2-5'); 1,45 (2H, m, CH_2-4').
^{13}C-RMN ($CDCl_3$, δ): 171.5 (C=O); 113.5 (C-1'); 63.3 (CH_2-2); 35.3 (CH_2-6', CH_2-2'); 24.4 (CH_2-4'); 23.0 ((CH_2-5', CH_2-3').
IR (film): ν= 1710 cm^{-1}
MS (EI^+) [m/z, (%)]: 156.08 ($[M]^+$, 23); 113.02 ($[M\text{-}C_2H_3O]^+$, 56); 98.07 ($[M\text{-}C_2H_2O_2]^+$, 100); 70.04 (23).
HRMS (EI^+): Calcd. For $C_8H_{12}O_3$ 156.0786, found 156.0789.

Compound 26

26 is a known compound (R. Ramage, G. J. Griffiths, F. E. Shut, J. N. Sweeney, *J. Chem. Soc. Perkin Trans 1*. 1984, **7**, 1539)



25 **26**

To a solution of diisopropylamine (9,2 mL; 65,6 mmol) in THF (66 mL) at -78ºC was added dropwise *n*-BuLi (25 mL of a 2.5 M solution in hexane, 62.5 mmol) and the mixture was stirred at this temperature for 25 mn. Methyl propionate (6 mL; 62,5 mmol) in THF (62,5 mL) was then added and stirring was continued for 25 mn. Compound **25** (3,9 mg; 25 mmol) in THF (62,5 mL) was added to the mixture at -78ºC. The cooling bath was removed and the mixture stirred at room temperature overnight. The organic solvent was removed under vacuum, Et_2O (10 mL) and H_2O (10 mL) were added and the mixture acidified to pH=1 with HCl. The aqueous phase was saturated with NaCl and extracted with 10% MeOH/CH_2Cl_2 (15 x 100 mL). The combined organic phases were dried and rotatory evaporated to give a solid residue which was washed several times with Et_2O affording **26** (1,46 g, 51%).as a white solid ; m.p. = 180-182 ºC, Rf = 0.05 (50% EtOAc /Hexane).

^{1}H-NMR (DMSO, δ): 4.55 (2H, t, *J*= 1.2 Hz, CH_2-5); 1.57 (3H, q, *J*= 1.2 Hz, CH_3-3)
^{13}C-NMR (DMSO, δ): 175.2 (C-4); 172.9 (C-2); 94.4 (C-3); 66.5 (CH_2-5); 5.9 (CH_3-3).
IR (film): ν= 3345 (br), 1762, 1678 cm^{-1}
MS (EI$^+$) [m/z, (%)]: 114.03 ([M]$^+$, 100).
HRMS (EI$^+$): Calcd. For $C_5H_6O_3$ 114.0317, found 114.0305.

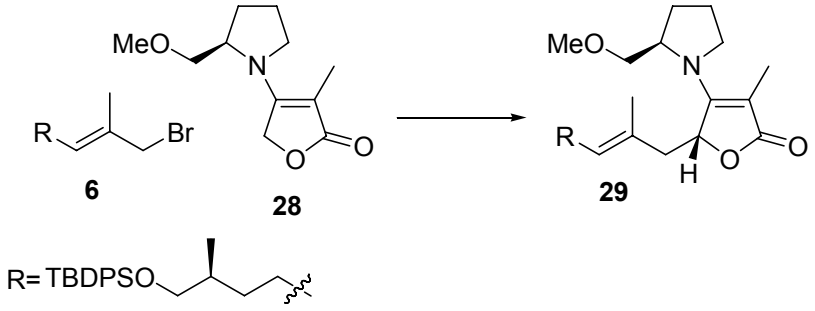
Compound 28

26 **28**

To a solution of **26** (332 mg; 2,9 mmol) in C_6H_6 (8 mL) was added (*R*)-2-methoxymethylpyrrolidine (0,36 mL; 2,9 mmol) and a catalytic amount of p-TsOH. The reaction flask was fitted with a Dean-Stark and the mixture heated at 130ºC for 24 h. The solvent was then removed under vacuum and the residue was chromatographed on silica gel using 20% EtOAc/Hexane as eluent, affording **28** (493 mg, 80%) as a yellow oil, Rf: 0,25 (100% EtOAc).

^{1}H-NMR ($CDCl_3$, δ): 4.68 (1H, d, *J*=14.6 Hz, CH-5); 4.53 (1H, d, *J*= 14.5 Hz, CH-5); 3.98 (1H, m, CH-2'); 3.57 (1H, q, *J*= 5.3 Hz, CH_2-5'); 3.43 (1H, q, *J*= 8.5 Hz, CH-5'); 3.33 (1H, m, CH-1''); 3.30 (3H, s, -OCH_3); 3.25 (1H, dd, *J*= 6.7 Hz, *J*= 9.4 Hz ,CH-1''); 1.95 (4H, m, CH_2-3',CH_2-4'); 1.92 (3H, s, CH_3-3).
^{13}C-NMR ($CDCl_3$, δ): 177.2 (C=O); 160.3 (C-4); 88.9 (C-3); 77.5 (CH_2-1''); 66.7 (CH_2-5); 59.3 (CH-2'); 58.8 (-OCH_3); 48.7 (CH_2-5'); 28.1 (CH_2-3'); 23.0 (CH_2-4'); 9.0 (CH_3-3).
IR (film): ν= 1731, 1621 cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 213.22 ($[M+1]^+$,100); 212.22 ($[M]^+$,18); 166.27 (23).
HRMS (FAB$^+$): Calcd. For $C_{11}H_{18}NO_3$ 212.1287, found 212.1287

Compound 29



To a solution of diisopropylamine (110 µL; 0,78 mmol) in THF (2 mL) and HMPA (272 µL) at -78ºC was added dropwise *n*-BuLi (314 µL of a 2.5 M solution in hexane, 0.78 mmol) and the mixture was stirred at this temperature for 25 mn. Compound **28** (61 mg; 0,32 mmol) in THF (2 mL) was added and the mixture stirred for 1 h, before adding bromide **6** (96 mg; 0,21 mmol) in THF (2 mL). Stirring was continued overnight at -78ºC. The reaction was quenched with aqueous saturated solution of NH_4Cl (10 mL) and the product extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were dried and rotatory evaporated to give a residue which was chromatographed on silica gel using 15% EtOAc/Hexane as eluent, affording **29** (90 mg, 75%) as a yellowish oil, Rf = 0.40 (50% EtOAc /Hexane); $[\alpha]_D^{20}$= -13.1 (C=1.0 , $CHCl_3$)

^{1}H-NMR ($CDCl_3$, δ): 7.65 (4H, m, CH_o-Ph); 7.37 (6H, m, $CH_{p,m}$-Ph); 5.20 (1H, s, CH-3'''); 4.79 (1H, d, *J*= 4.7 Hz, CH-5); 4.73 (1H, d, *J*= 4.7 Hz, CH-5); 4.16 (1H, m, CH-2'); 3.62-3.14 (6H, m, CH_2-7'', CH_2-1'', CH_2-5'); 3.32 (3H, s, -OCH_3); 3.31 (3H, s, -OCH_3); 2.65 (1H, d, *J*= 13.9 Hz, CH-1'''); 2.51 (1H, d, *J*= 13.9 Hz, CH-1'''); 2.17-1.82 (6H, m, CH_2-4''', CH_2-3', CH_2-4'); 1.90 (3H, s, CH_3-3); 1.88 (3H, s, CH_3-3); 1.66 (3H, s, CH_3-2'''); 1.65 (3H, s, CH_3-2'''); 1.67-1.58 (1H, m, CH-6'''); 1.54-1.40 (1H, m, CH-5'''); 1.22- 1.08 (1H, m, CH-5'''); 1.04 (9H, s, CH_3-*tert*-BuSi); 0.91 (3H, d, *J*= 6,8 Hz, CH_3-6''').
^{13}C-NMR ($CDCl_3$, δ): 175.8 (C=O); 163.0 and 162.2 (C-4); 135.3 (CH_o-Ph); 134.0 (C-Ph); 129.6 and 129.6 (C-2'''); 129.3 (CH_p-Ph); 128.9 and 128.5 (CH-3'''); 127.3 (CH_m-Ph); 90.5 and 89.1 (C-3); 76.8 and 77.8 (CH-5); 74.3 and 72.8 (CH_2-1''); 68.5 (CH_2-

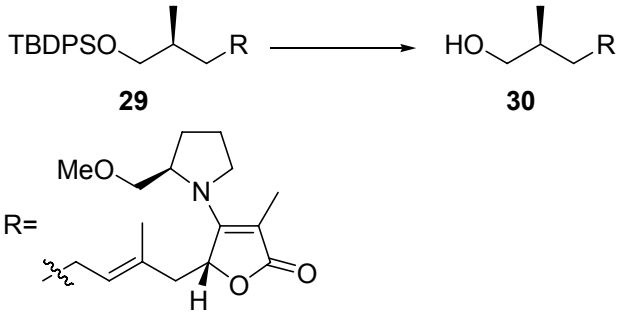
7’’’); 59.2 and 59.1 (-OCH_3); 58.4 (CH-2’); 48.9 (CH_2-5’); 44.0 and 42.2 (CH_2-1’’’); 35.2 (CH-6’’’); 32.7 (CH_2-5’’’); 28.1 and 27.6 (CH_2-3’); 26.6 (CH_3-*tert*-BuSi); 25.3 and 25.2 (CH_2-4’’’); 23.3 (CH_2-4’); 19.0 (C-Si); 16.5 and 16.4 (CH_3-6’’’); 9.2 and 9.1 (CH_3-3).

IR (film): ν= 1736, 1619 cm^{-1}

MS (FAB^+) [m/z, (%)]: 590.28 ($[M+1]^+$, 16); 533.21 (32); 532.21 (79); 513.25 (38); 512.24 (100).

HRMS (FAB^+): Calcd. For $C_{36}H_{52}NO_4Si$ 590.3666, found 590.3676.

Compound 30



To a solution of **29** (85 mg; 0.15 mmol) in THF (2 mL) was added TBAF (150 µL of 1.0 M in THF, 0.15 mmol) and the mixture stirred for 3 h. H_2O (5 mL) was added and the product extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phases were dried and rotatory evaporated to give a residue which was chromatographed on silica gel using 30% EtOAc/Hexane as eluent, affording alcohol **30** (51 mg, 89%) as a yellowish oil, Rf = 0.12 (50% EtOAc /Hexane).

^{1}H-NMR ($CDCl_3$, δ): 5.20 (1H, s, CH-3’’’); 4.83 (1H, d, *J*= 4,8 Hz, CH-5); 4.76 (1H, d, *J*= 4.8 Hz, CH-5); 4.25-4.05 (1H, m, CH-2’); 3.69-3.11 (6H, m, CH_2-7’’, CH_2-1’’, CH_2-5’); 3.31 (3H, s, -OCH_3); 2.65 (1H, d, *J*= 14.9 Hz, CH-1’’’); 2.55 (1H, d, *J*= 14.9 Hz, CH-1’’’); 2.22-1.77 (6H, m, CH_2-4’’’, CH_2-3’, CH_2-4’); 1.88 (3H, s, CH_3-3); 1.85 (3H, s, CH_3-3); 1.65 (3H, s, CH_3-2’’’); 1.63 (3H, s, CH_3-2’’’); 1.60-1.38 (1H, m, CH-6’’’, CH-5’’’); 1.12 (1H, m, CH-5’’’); 0.88 (3H, dd, *J*= 6.5 Hz, *J*= 1,7 Hz, CH_3-6’’’).

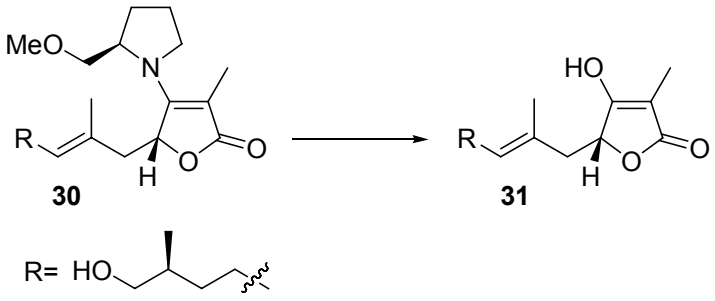
^{13}C-NMR ($CDCl_3$, δ): 176.3 and 176.2 (C=O); 163.2 and 162.5 (C-4); 129.7 and 129.3 (C-2’’’); 129.5 and 129.1 (CH-3’’’); 89.4 and 89.1 (C-3); 76.5 (CH-5); 74.5 and 72.5 (CH_2-1’’); 68.1 (CH_2-7’’’); 59.4 and 59.3 (-OCH_3); 58.6 and 58.3 (CH-2’); 49.3 and 49.2 (CH_2-5’); 43.6 and 42.7 (CH_2-1’’’); 35.0 and 34.8 (CH-6’’’); 32.7 (CH_2-5’’’); 28.3 and 27.8 (CH_2-3’); 25.3 and 25.1 (CH_2-4’’’); 23.5 and 22.3 (CH_2-4’); 16.7 and 16.4 (CH_3-6’’’); 9.4 and 9.2 (CH_3-3).

IR (film): ν= 3376 (br), 1736, 1619 cm^{-1}

MS (FAB^+) [m/z, (%)]: 352.23 ($[M+1]^+$, 13).

HRMS (FAB^+): Calcd. For $C_{20}H_{34}NO_4$ 352.2488, found 352.2377.

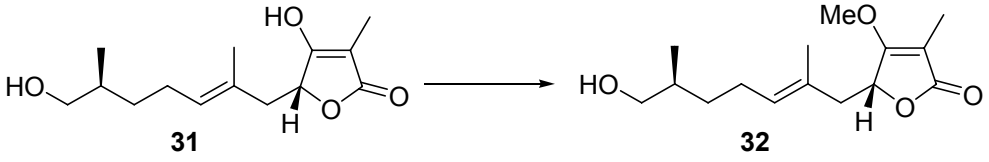
Compound 31



To a solution of alcohol **30** (103 mg; 0,29 mmol) in THF (10 mL) was added 10% HCl (3 mL) and the mixture heated at 50ºC for 48 h, before adding H_2O (15 mL) and extracting with CH_2Cl_2 (3x 10 mL). The combined organic phases were dried and rotatory evaporated to give a residue which was chromatographed on silica gel using 40% EtOAc/Hexane as eluent, affording diol **31** (36 mg, 90%) as a colorless oil, Rf = 0.10 (100% EtOAc).

^{1}H-NMR ($CDCl_3$, δ): 5.24 (1H, t, *J*= 7.3 Hz, CH-3'); 4.76 (1H, brs., CH-5); 3.42 (2H, dd, *J*= 6.4 Hz, *J*= 3.3 Hz, CH-7'); 2.62 (1H, dd, *J*= 14.5 Hz, *J*= 3.2 Hz, CH-1'); 2.27 (1H, dd, *J*= 14.3 Hz, *J*= 7.1 Hz, CH-1´); 2.08-1.88 (2H, m, CH_2-4'); 1.67 (3H, s, CH_3-3); 1.58 (1H, m, CH-6'); 1.55 (3H, s, CH_3-2'); 1.44 (1H, m, CH-5'); 1.14 (1H, m, CH-5'); 0.87 (3H, d, *J*= 6.7 Hz, CH_3-6').
^{13}C-NMR ($CDCl_3$, δ): 177.2 (C-4); 175.9 (C=O); 129.3 (C-2'); 129.2 (CH-3'); 97.0 (C-3); 78.1 (CH-5); 68.7 (CH_2-7'); 41.8 (CH_2-1'); 34.9 (CH-6'); 33.0 (CH_2-5'); 25.4 (CH_2-4'); 17.1 (CH_3-2'); 16.7 (CH_3-6'); 6.3 (CH_3-3).
IR (film): ν= 3331 (br), 1756, 1672 cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 256.23 ($[M+1]^+$, 67); 255.10 ($[M]^+$, 22); 155.25 (33); 154.25 (100).
HRMS (FAB$^+$): Calcd. For $C_{14}H_{22}O_4$ 254.1518, found 254.1608.

Compound 32



To a solution of diol **31** (38 mg; 0,15 mmol) in THF (1 mL) at 0ºC was first added MeOH (6,1 µL; 0,15 mmol) then PPh_3 (39 mg; 0,15 mmol) and DIAD (30 µL; 0,15 mmol). The resulting mixture was stirred at 0ºC for 16 h. The solvent was then removed under vacuum and the residue was chromatographed on silica gel using 20%

EtOAc/Hexane as eluent, affording **32** (36 mg, 90%) as a yellow liquid, Rf = 0,40 (100% EtOAc); $[\alpha]_D^{20}$= 29.3 (C=0.85 , $CHCl_3$)

^{1}H-NMR ($CDCl_3$, δ): 5.23 (1H, q, *J*= 6.6 Hz, CH-3'); 4.65 (1H, d, *J*= 7.8 Hz, CH-5); 4.07 (3H, s, -OCH_3); 3.42 (2H, m, CH-7'); 2.55 (1H, d, *J*= 14.5 Hz, CH-1'); 2.15 (1H, dd, *J*= 14.4 Hz, *J*= 7.4 Hz, CH-1´); 2.07-1.90 (2H, m, CH_2-4'); 1.94 (3H, s, CH_3-3); 1.63 (3H, s, CH_3-2'); 1.61 (1H, m, CH-6'); 1.44 (1H, m, CH-5'); 1.14 (1H, m, CH-5'); 0.90 (3H, m, CH_3-6').

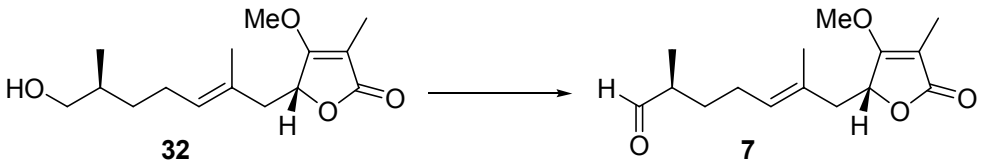
^{13}C-NMR ($CDCl_3$, δ): 175.1 (C-4); 173.3 (C=O); 129.5 (CH-3'); 129.1 (C-2'); 97.6 (C-3); 76.9 (CH-5); 68.2 (CH_2-7'); 58.6 (CH_3-O); 41.7 (CH_2-1'); 35.1 (CH-6'); 32.9 (CH_2-5'); 25.3 (CH_2-4'); 16.8 (CH_3-2'); 16.4 (CH_3-6'); 8.3 (CH_3-3).

IR (film): ν= 3357 (br), 1757, 1672 cm^{-1}

MS (FAB$^+$): 269.17 ($[M+1]^+$, 100); 268.15 ($[M]^+$, 22); 207.13 (25); 185.20 (32); 155.25 (23); 154.25 (63).

HRMS (FAB$^+$): Calcd. For $C_{15}H_{25}O_4$ 269.1753, found 269.1757.

Compound 7



To a solution of oxalyl chloride (0,61 mL of a 2. M solution in CH_2Cl_2, 1,22 mmol) in CH_2Cl_2 (0,5 mL) at -78ºC was added dropwise a solution of DMSO (0,61 mL; 2,44 mmol) in CH_2Cl_2 (0,9 mL) and the mixture stirred for 20 mn before adding alcohol **32** (163 mg; 0,61 mmol) in CH_2Cl_2 (0,87 mL). After stirring for 20 mn, Et_3N (0,61 mL) was added, the cooling bath was removed and the mixture stirred at room temperature for 30 mn. H_2O (20 mL) was added and the product extracted with EtOAc (3 x 20 mL). The combined organic phases were dried and rotatory evaporated to afford virtually pure aldehyde **7** (161 mg, 99%) as a colorless liquid, Rf = 0,65 (100% EtOAc).

^{1}H-NMR ($CDCl_3$, δ): 9.60 (1H, s, CHO); 5.23 (1H, q, *J*= 7.1 Hz, CH-3'); 4.65 (1H, d, *J*= 7.9 Hz, CH-5); 4.08 (3H, s, -OCH_3); 2.55 (1H, d, *J*= 15.5 Hz, CH-6'); 2.33 (1H, m, CH-1'); 2.15 (1H, dd, *J*= 14.9 Hz, *J*= 7.9 Hz, CH-1'); 2.05 (2H, q, *J*= 7.3 Hz, CH_2-4'); 1.96 (3H, s, CH_3-3); 1.75 (1H, m, CH-5'); 1.64 (3H, s, CH_3-2'); 1.58 (1H, m, CH-6'); 1.39 (1H, m, CH-5');1.08 (3H, d, *J*= 7,1 Hz, CH_3-6').

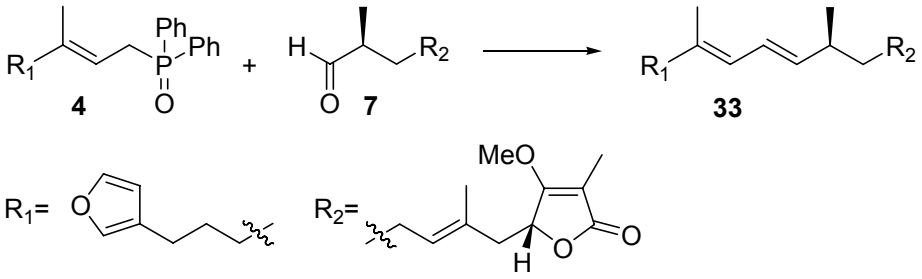
^{13}C-NMR ($CDCl_3$, δ): 205.0 (C=O); 174.8 (C-4); 173.1 (C=O); 130.6 (C-2'); 127.8 (CH-3'); 97.7 (C-3); 76.8 (CH-5); 58.7 (-OCH_3); 45.7 (CH-6'); 41.7 (CH_2-1'); 30.2 (CH-5'); 32.9 (CH_2-5'); 25.3 (CH_2-4'); 16.7 (CH_3-2'); 13.0 (CH_3-6'); 8.4 (CH_3-3).

IR (film): ν= 1757, 1738, 1672 cm^{-1}

MS (FAB$^+$) [m/z, (%)]: 267.17 ($[M+1]^+$, 27); 266.15 ($[M]^+$, 7); 251.17 (32); 155.25 (43); 154.25 (100).

HRMS (FAB$^+$): Calcd. For $C_{15}H_{22}O_4$ 266.1518, found 266.1458.

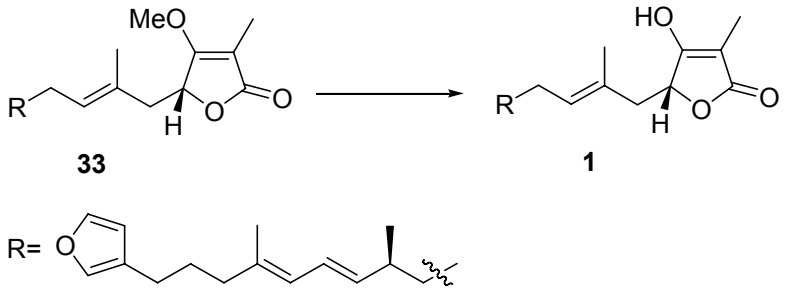
Compound 33



To phosphine oxide **4** (4 mL of a 0,086 M solution in THF, 0.35 mmol) at -78ºC was added *n*-BuLi (111 μL of a 2.5 M solution in hexane, 0.28 mmol) and the resulting deep red solution was stirred for 1 h before adding aldehyde **7** (37 mg; 0,14 mmol) in THF (3 mL). After stirring for 30 mn the mixture was allowed to reach room temperature overnight. The mixture was quenched with an aqueous saturated solution of NH_4Cl (5 mL) and extracted with con EtOAc (3 x 10 mL). The organic phases were washed with brine (20 mL), dried and rotatory evaporated to give a residue which was chromatographed on silica gel using 5% EtOAc/Hexane as eluent, affording compound **33** [57 mg, 40%, E;E / E;Z (8/1)] as a colorless oil, Rf = 0.30 (30% EtOAc/Hexane).

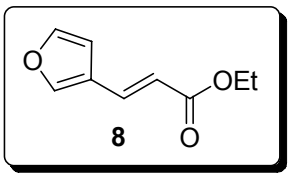
^{1}H-NMR ($CDCl_3$, δ): 7.33 (1H, s, CH-5 furyl); 7.19 (1H, s, CH-2 furyl); 6.25 (1H, s, CH-4 furyl); 6.18 (1H, dd, *J*= 15.0 Hz, *J*= 10.9 Hz, CH-8‘); 5.78 (1H, d, *J*= 11.1 Hz, CH-9’); 5.42 (1H, dq, *J*= 7.8 Hz, *J*= 2.8 Hz, CH-7’); 5.22 (1H, t, *J*= 6.7 Hz, CH-3’); 4.64 (1H, d, *J*= 6.7 Hz, CH-5); 4.07 (3H, s, CH_3-4); 2.53 (1H, d, *J*= 14.4 Hz ,CH-1’); 2.39 (2H, t, *J*= 7.5 Hz, CH-13’); 2.15 (2H, m, CH-1’, CH-6’); 2.06 (2H, t, *J*= 7.5 Hz, C-11’); 1.96 (3H, s CH_3-3); 1.66 (8H, m, CH_3-10’, CH_3-2’, CH_2-4’); 1.28 (4H, m, CH_2-12’, CH_2-5’); 0.99 (3H, d, *J*= 6.4 Hz, CH_3-6’).
^{13}C-NMR ($CDCl_3$, δ): 174.9 (C-4); 173.3 (C=O); 142.6 (CH-5 furyl); 138.9 (CH-2 furyl); 138.1 (CH-7’); 136.1 (C-10’); 129.3 (C-2’); 129.2 (CH-3’); 126.0 (CH-9’); 125.1 (CH-8’); 125.0 (C-3 furyl); 111.0 (CH-4 furyl); 97.5 (C-3); 77.1 (CH-5); 58.6 (CH_3-O); 41.9 (CH_2-1’); 39.3 (CH_2-11’); 36.9 (CH_2-5’); 36.6 (CH-6’); 28.1 (CH_2-12’); 25.9 (CH_2-4’); 24.4 (CH_2-13’); 20.8 (CH_3-6’); 16.8 (CH_3-10’);16.5 (CH_3-2’); 8.4 (CH_3-3).
IR (film): ν= 1752, 1665 cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 414.29 (20); 413.29 ($[M+1]^+$, 67); 412.27 ($[M]^+$, 32); 411.27 (20); 285.23 (27); 209.20 (37); 203.23 (29); 195.21 (22); 189.23 (33); 183.24 (22); 178.23 (29); 175.27 (45); 173.28 (31); 169.25 (20); 167.26 (20); 165.26 (37); 163.29 (20); 161.30 (33); 159.30 (34); 155.28 (20); 154.27 (100); 151.44 (22).
HRMS (FAB$^+$): Calcd. For $C_{26}H_{37}O_4$ 413.2692, found 413.2694.

Compound 1



To a solution of triene **33** (23 mg; 56 μmol) in HMPA (200 μL) was added *n*-C_3H_7SLi (224 μL of a 0.5 M solution in HMPA, 0.11 mmol) and the mixture was stirred at room temperature for 2 h; 10% HCl (2 mL) was added and the product extracted with CH_2Cl_2 (3 x 5 mL). The combined organic phases were dried and rotatory evaporated to give a residue which was chromatographed on silica gel using 15% EtOAc/Hexane as eluent, affording palinurin **1** (20 mg, 90%) as a colorless oil, Rf = 0.25 (100% EtOAc); $[\alpha]_D^{20}$= 28.8 (C=0.12 , $CHCl_3$).

^{1}H-NMR ($CDCl_3$, δ): 7.33 (1H, d, *J*= 1.4 Hz, CH-5 furilo); 7.19 (1H, s, CH-2 furilo); 6.25 (1H, s, CH-4 furilo); 6.18 (1H, dd, *J*= 14.9 Hz, *J*= 10,9 Hz, CH-8‘); 5.78 (1H, d, *J*= 10.4 Hz, CH-9’); 5.42 (1H, dd, *J*= 15.2 Hz, *J*= 7.9, CH-7’); 5.28 (1H, t, *J*= 6.8 Hz, CH-3’); 4.74 (1H, c, *J*= 3.7 Hz, CH-5); 2.59 (1H, dd, *J*= 14.3 Hz, *J*= 3.7 Hz, CH-1’); 2.38 (2H, t, *J*= 7.6 Hz, CH_2-13’); 2.25 (1H, dd, *J*= 14.1 Hz, *J*= 7.9 Hz, CH-1’); 2.15 (1H, m, CH-6’); 2.05 (2H, t, *J*= 7.6 Hz, CH_2-11’); 1.97 (2H, q, *J*= 7.2 Hz, CH_2-4’); 1.72 (3H, s, CH_3-10’); 1.70 (3H, s, CH_3-2’); 1.66 (3H, s, CH_3-3); 1.30 (4H, m, CH_2-12’, CH_2-5’); 0.99 (3H, d, *J*= 6.8 Hz, CH_3-6’).
^{13}C-NMR ($CDCl_3$, δ): 177.1 (C-4); 176.4 (C=O); 142.6 (CH-5 furyl); 138.9 (CH-2 furyl); 138.0 (CH-7’); 136.2 (C-10’); 129.8 (CH-2’); 129.3 (C-3’); 125.9 (CH-9’); 125.1 (CH-8’); 124.9 (CH-3 furyl); 111.0 (CH-4 furyl); 96.4 (C-3); 77.6 (CH-5); 41.9 (CH_2-1’); 39.3 (CH_2-11’); 36.9 (CH_2-5’); 36.7 (CH-6’); 28.2 (CH_2-12’); 26.0 (CH_2-4’); 24.4 (CH_2-13’); 20.8 (CH_3-6’); 16.6 (CH_3-10’);16.5 (CH_3-2’); 5.9 (CH_3-3).
IR (film): ν= 3423 (br), 1755, 1673 cm^{-1}
MS (FAB$^+$) [m/z, (%)]: 399.20 ($[M+1]^+$, 63); 398.13 ($[M]^+$, 72); 356.08 (18); 355.07 (73); 341.02 (37); 326.97 (54); 283.07 (35); 282.05 (31); 281.14 (65); 267.01 (44); 251.05 (19).
HRMS (FAB$^+$): Calcd. For $C_{25}H_{35}O_4$ 399.2535, found 399.2534.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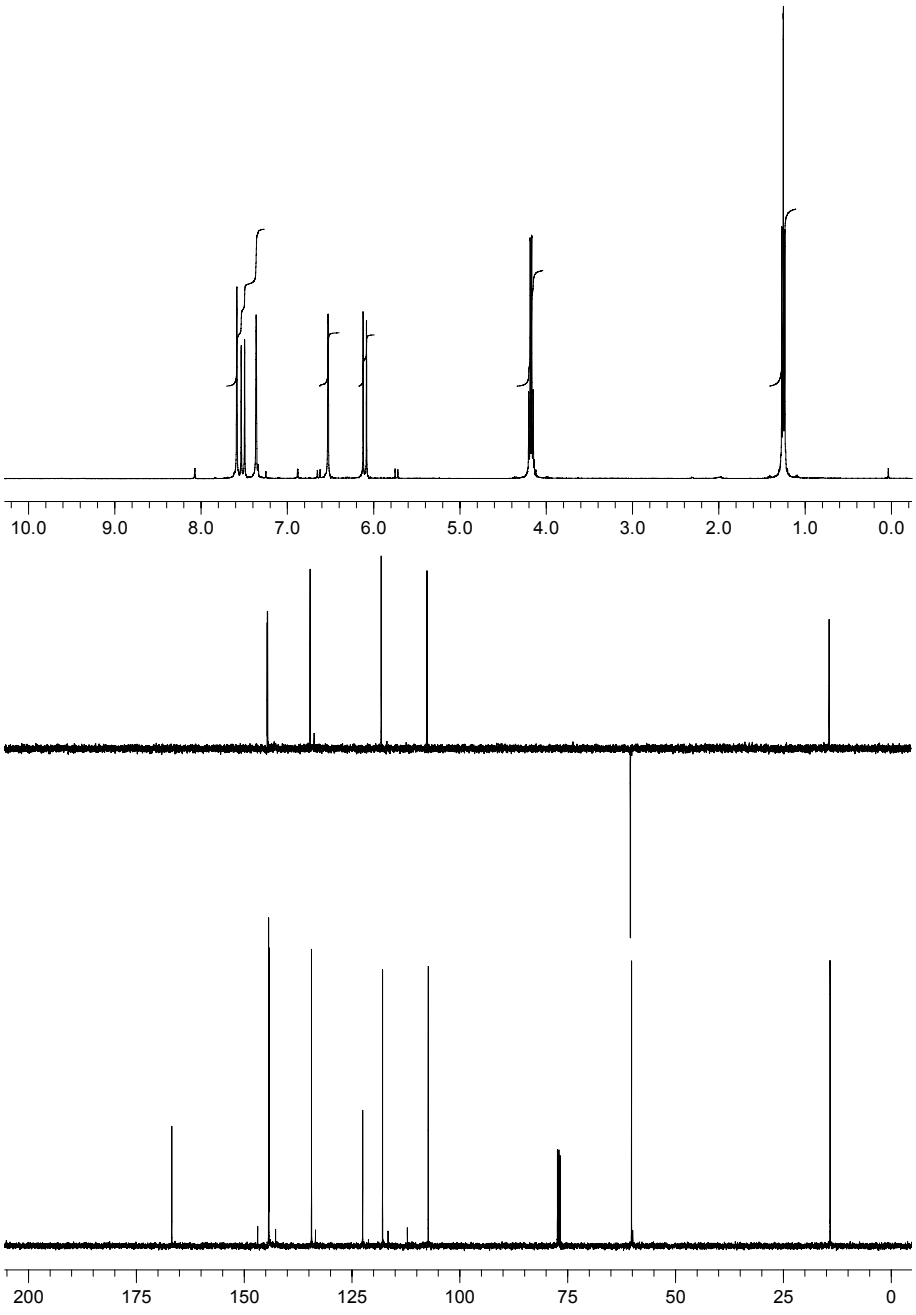
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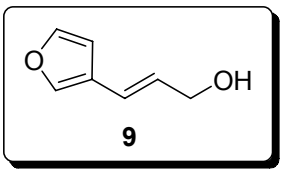

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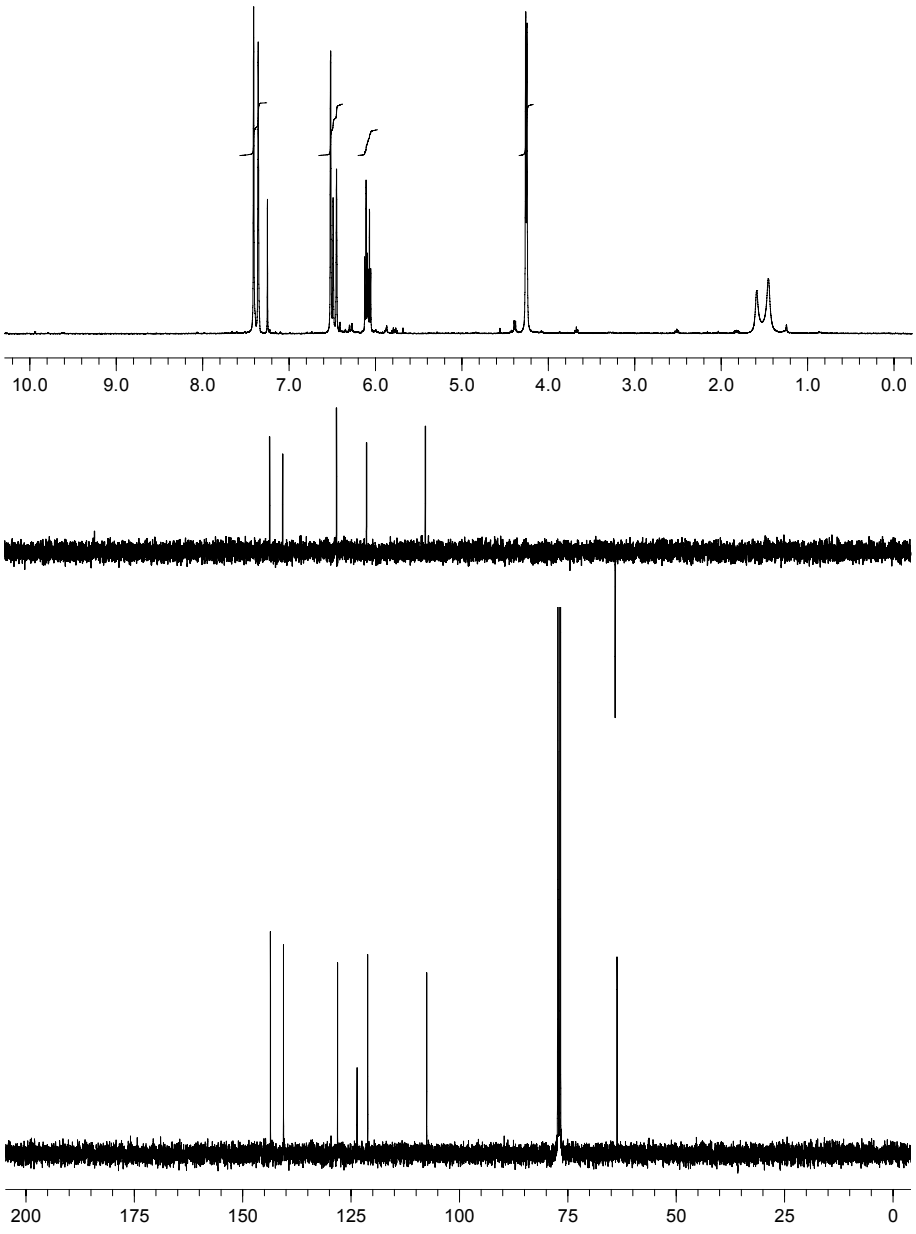

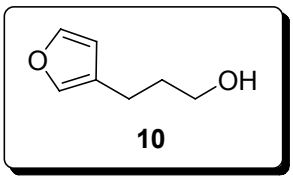

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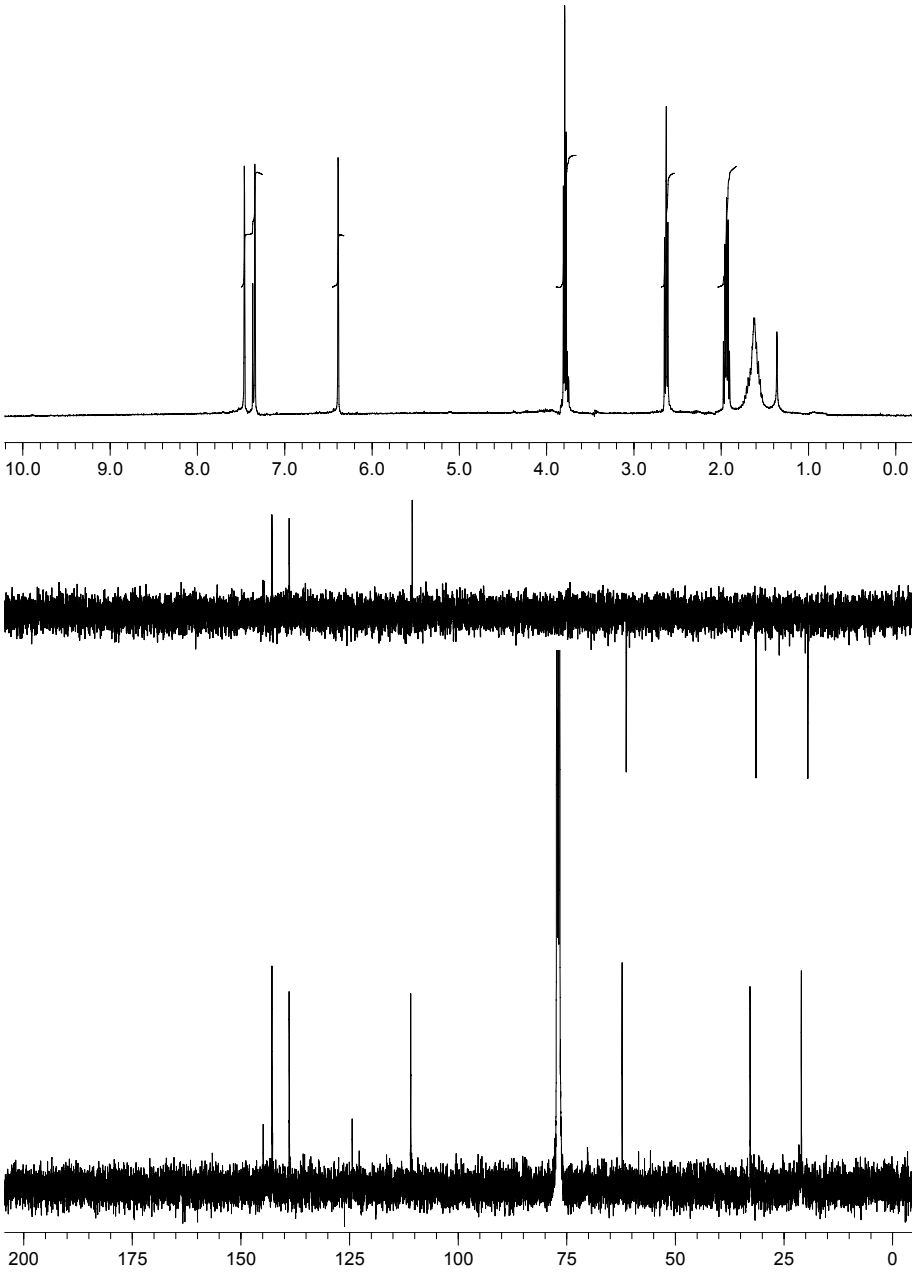

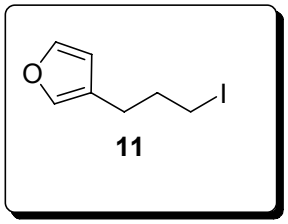

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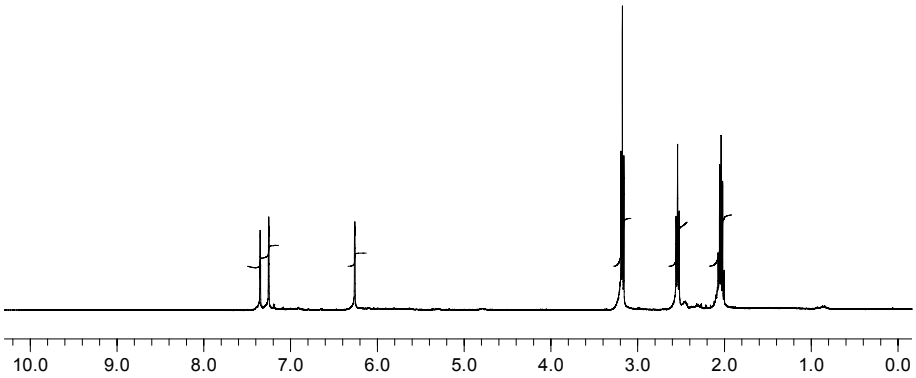

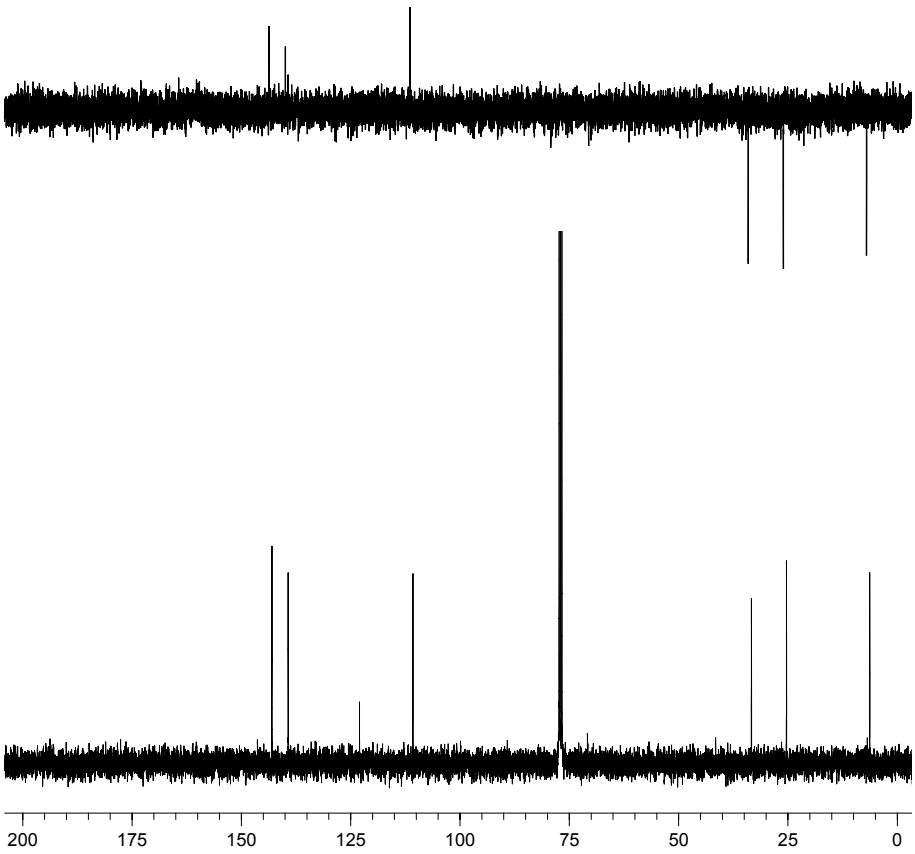

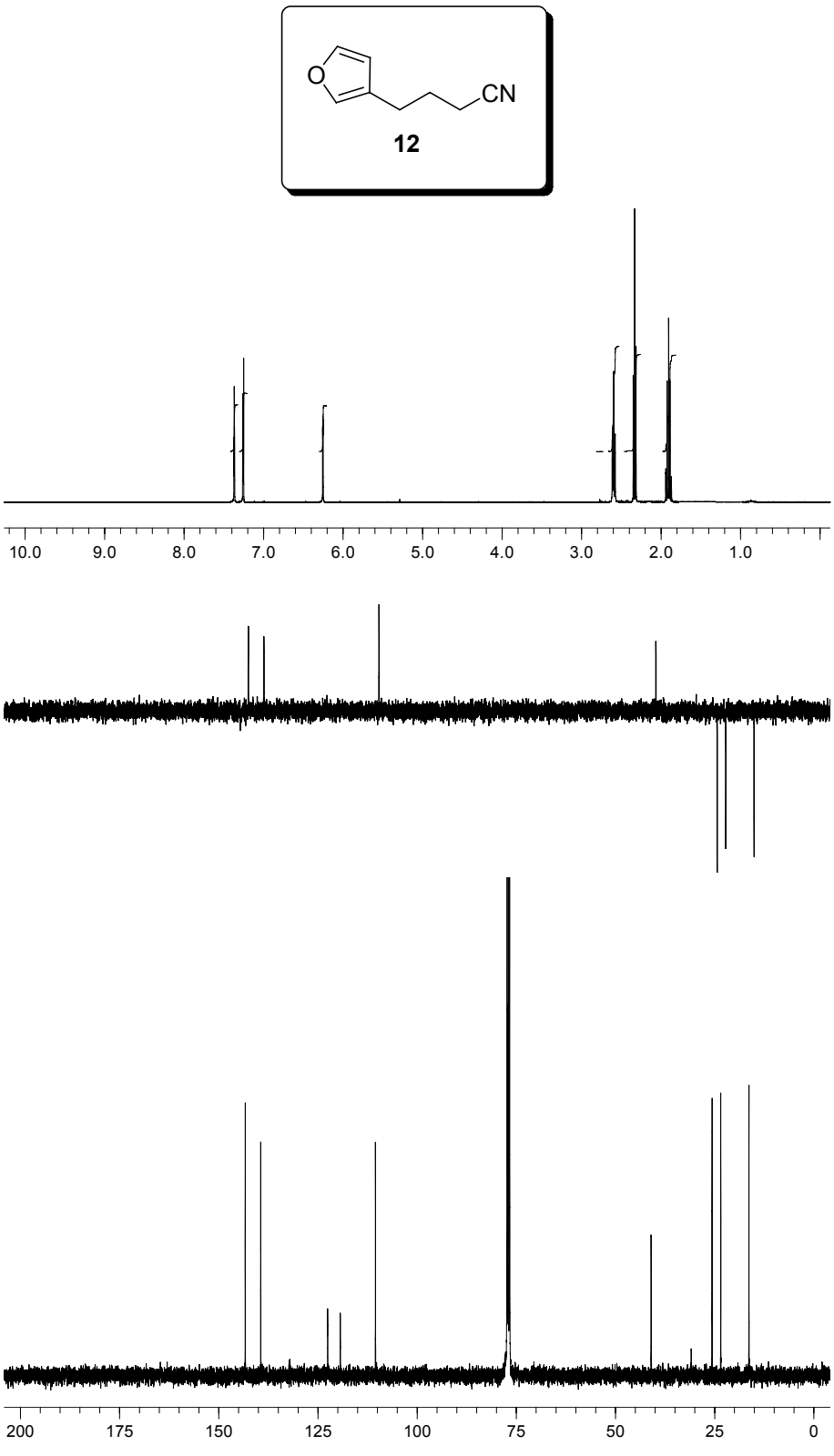
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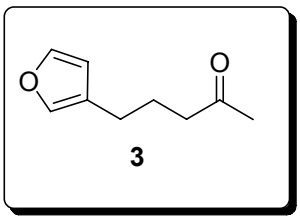

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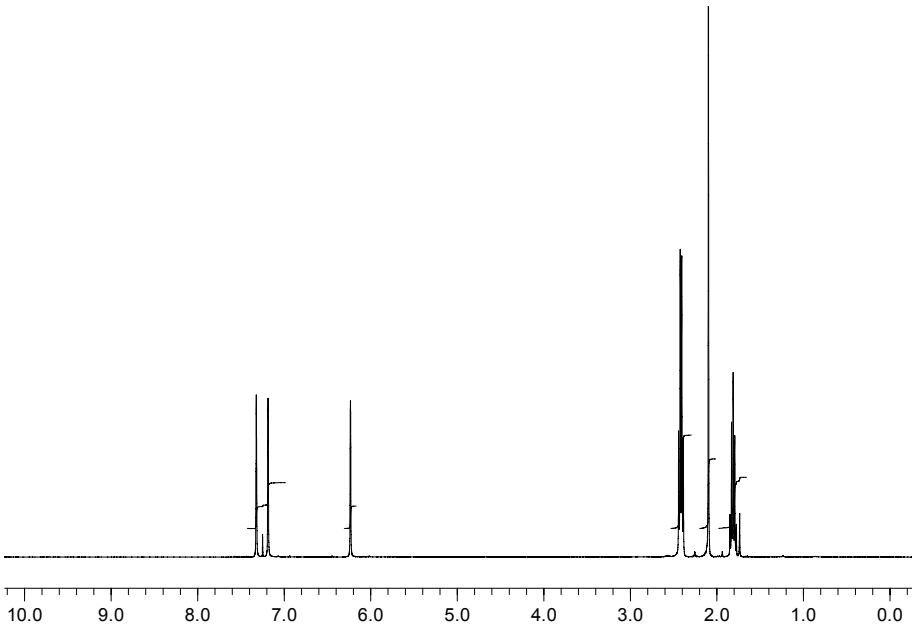

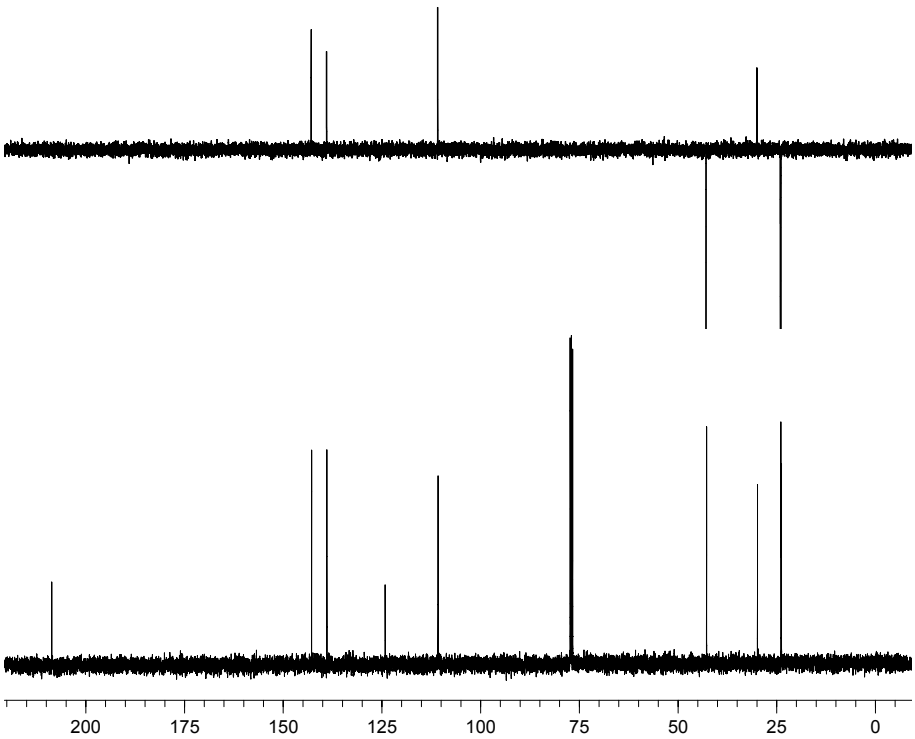

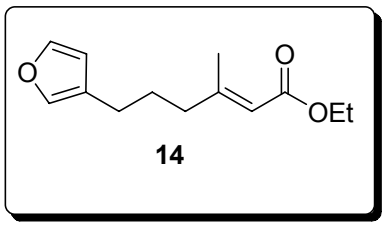

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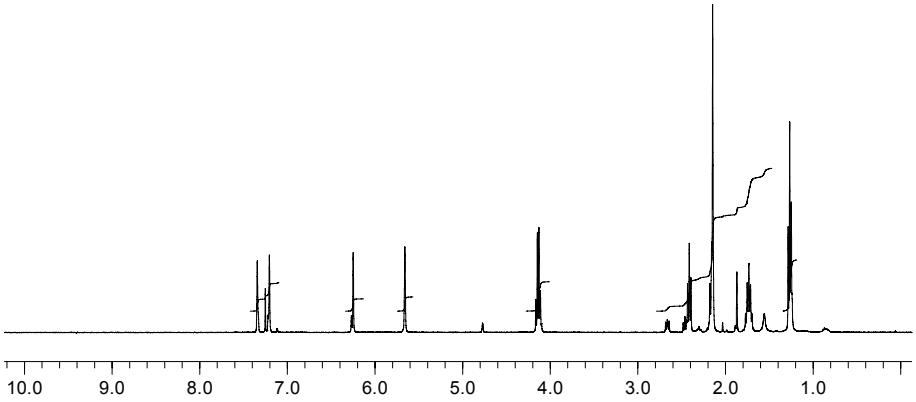

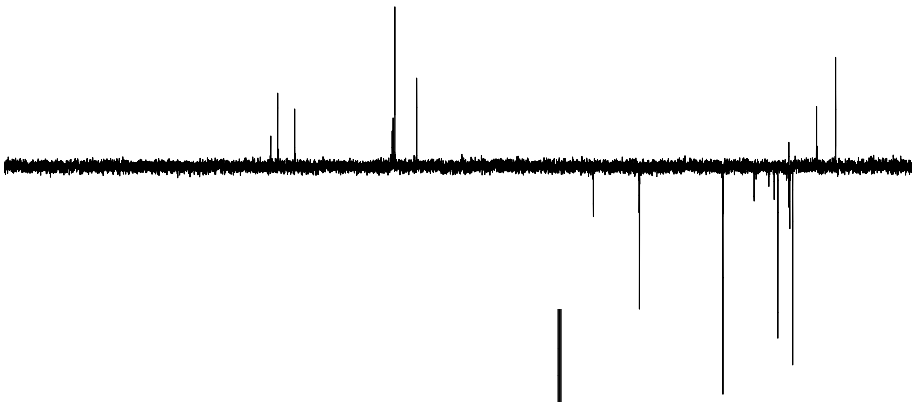

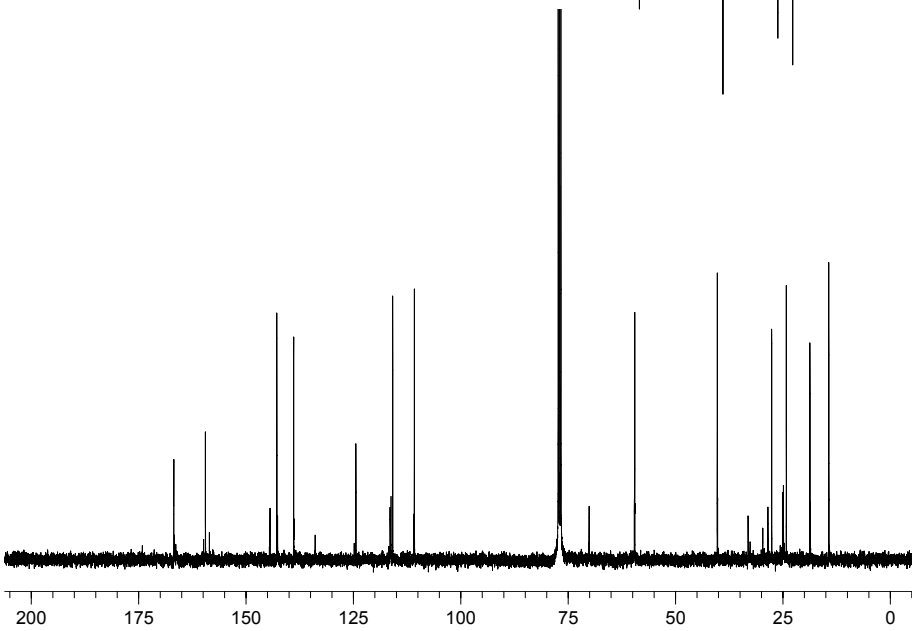

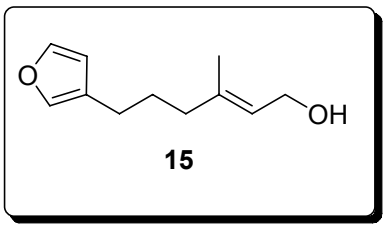

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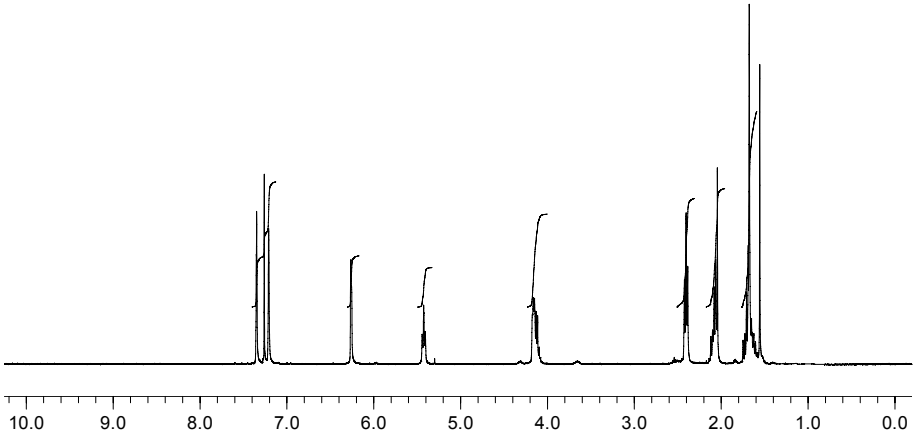

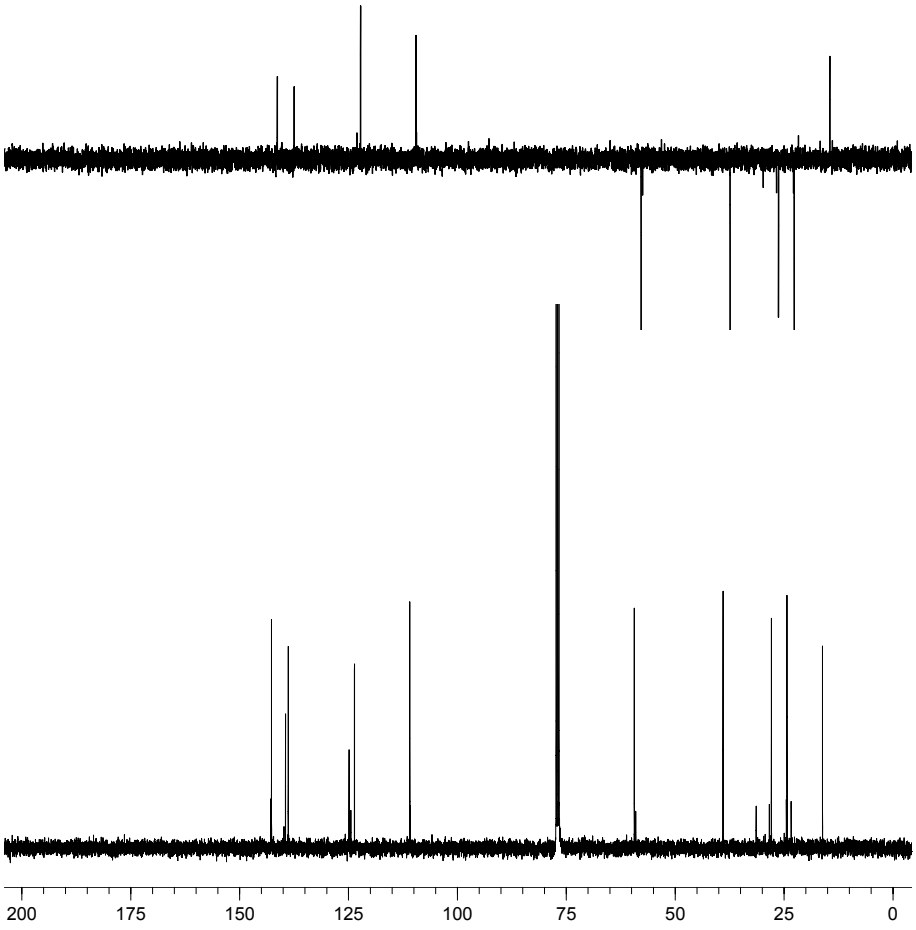

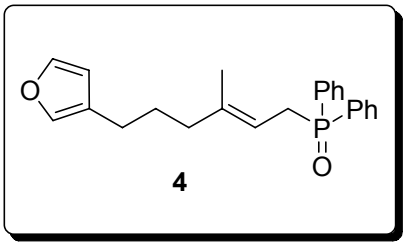
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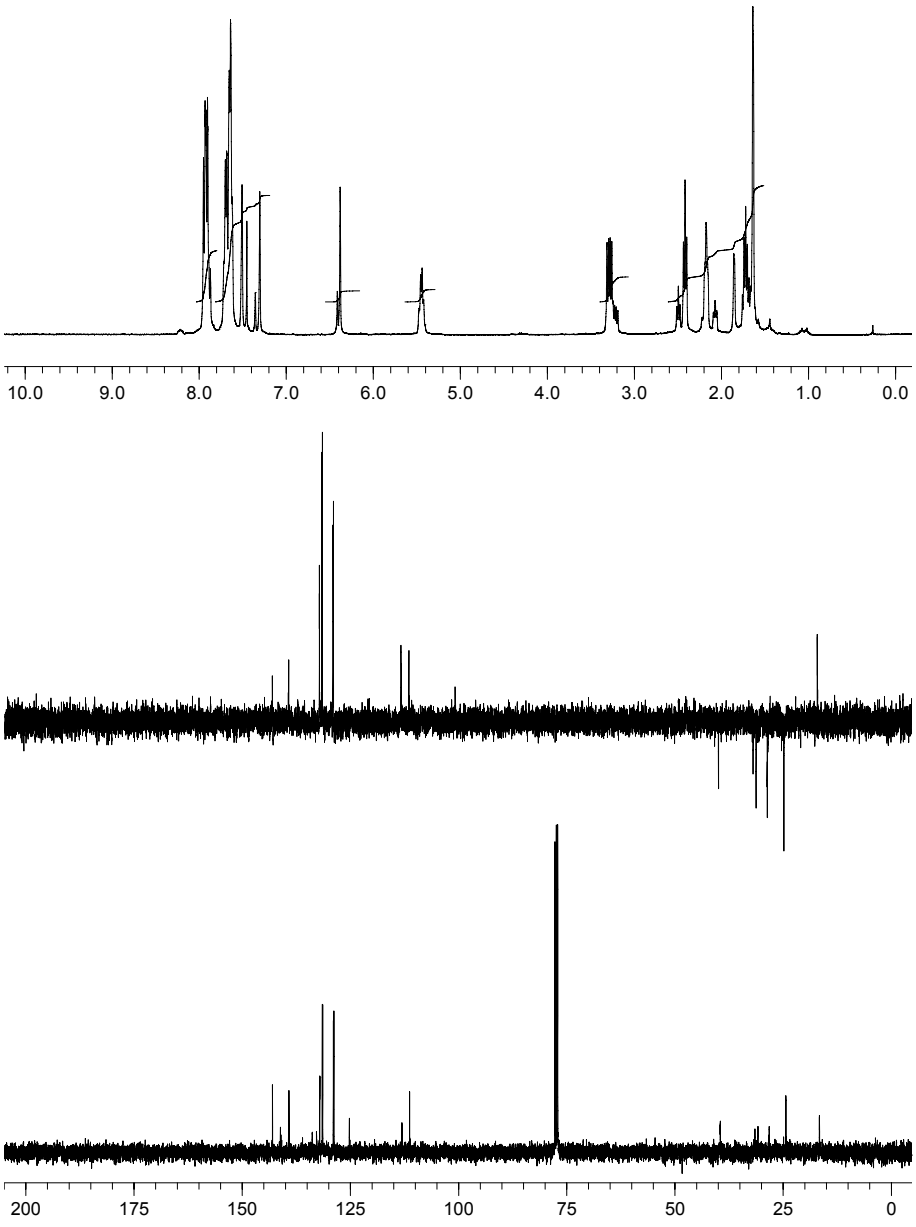
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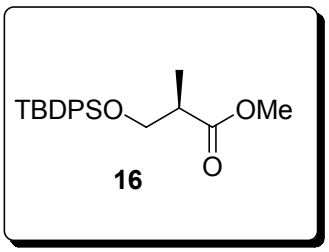
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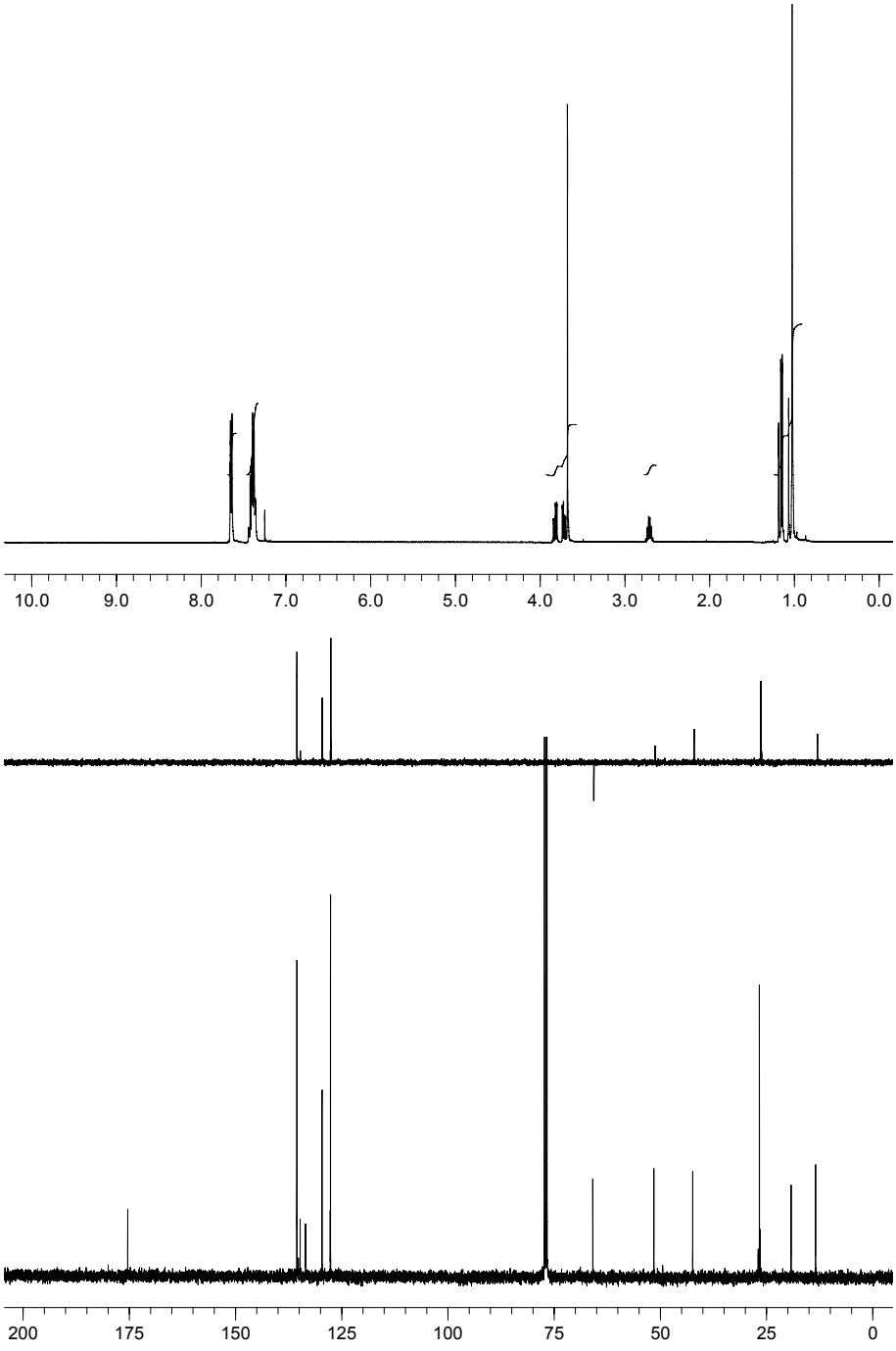
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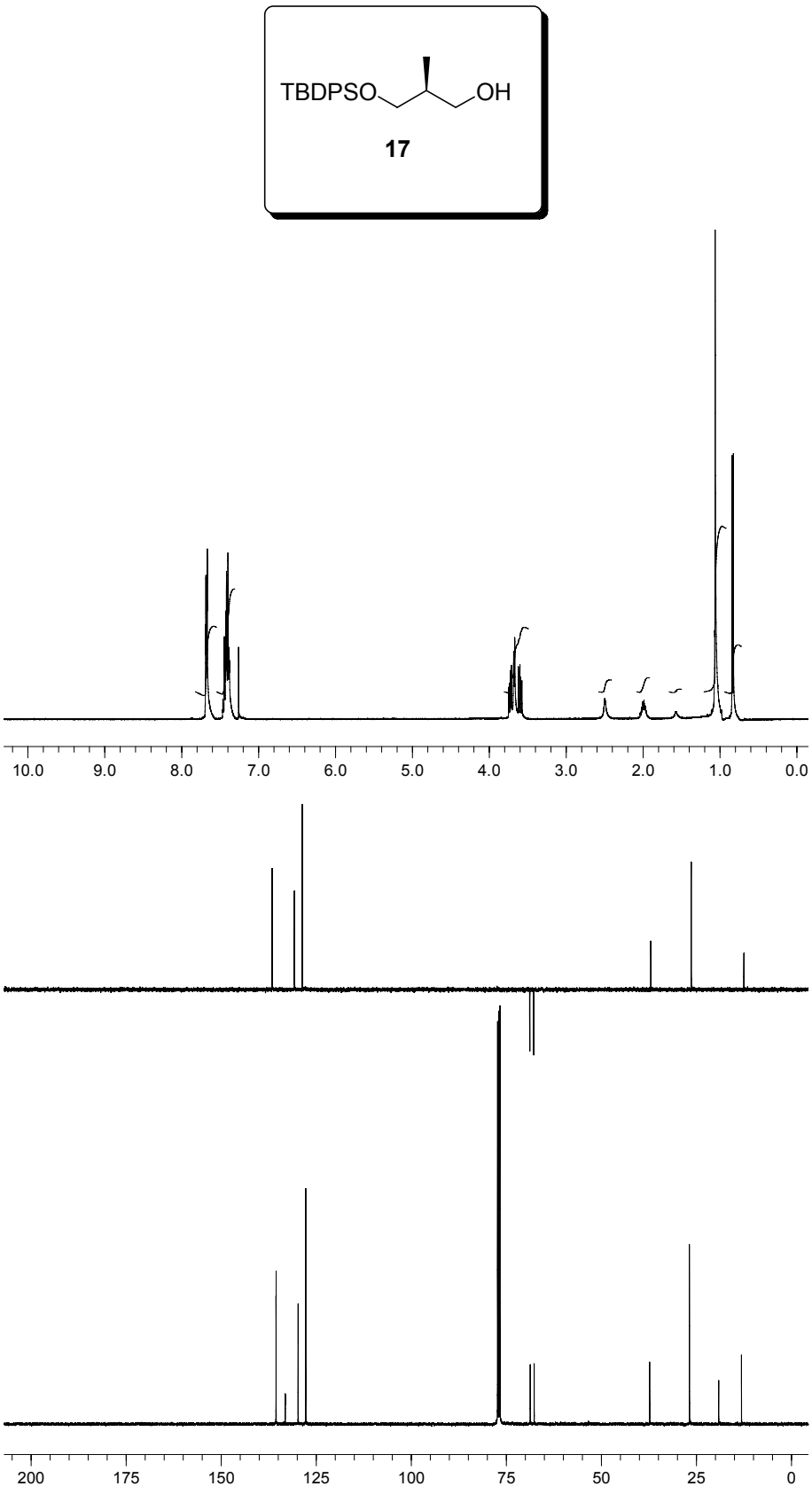
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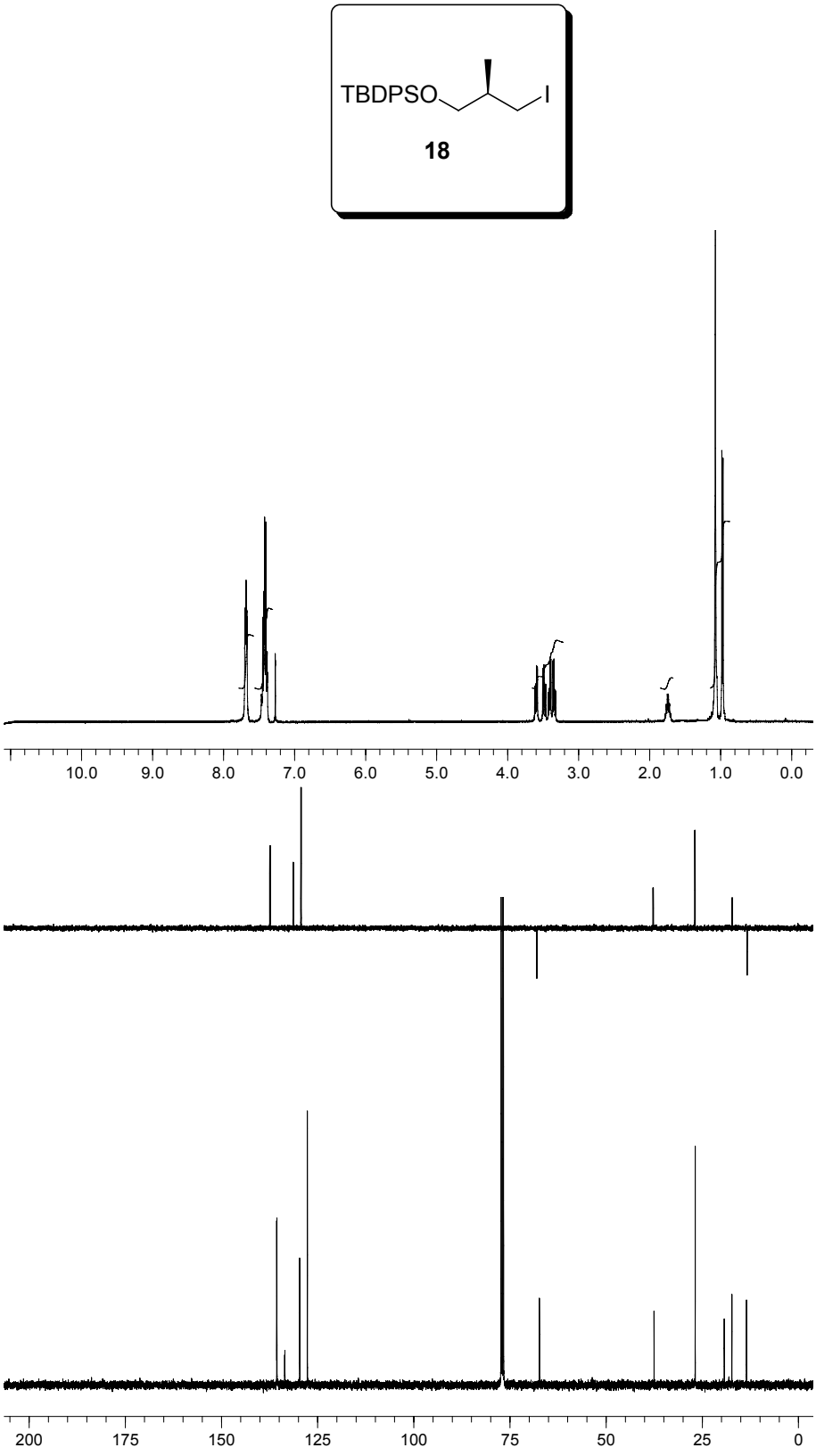
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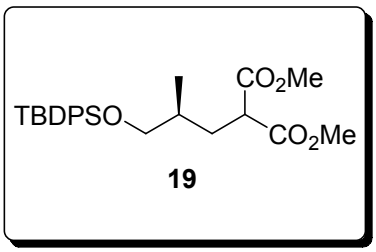
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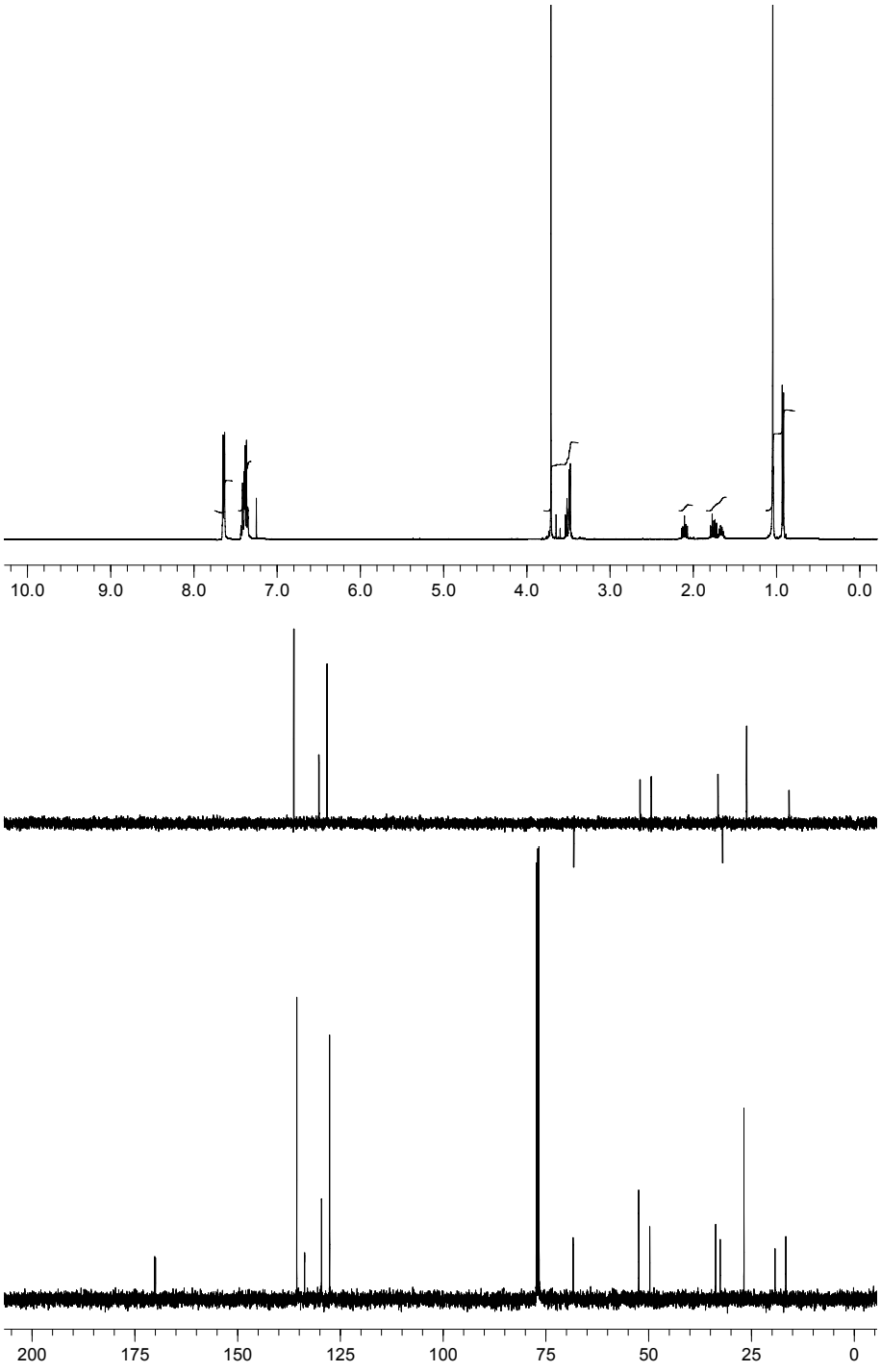
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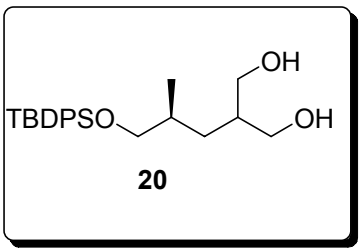
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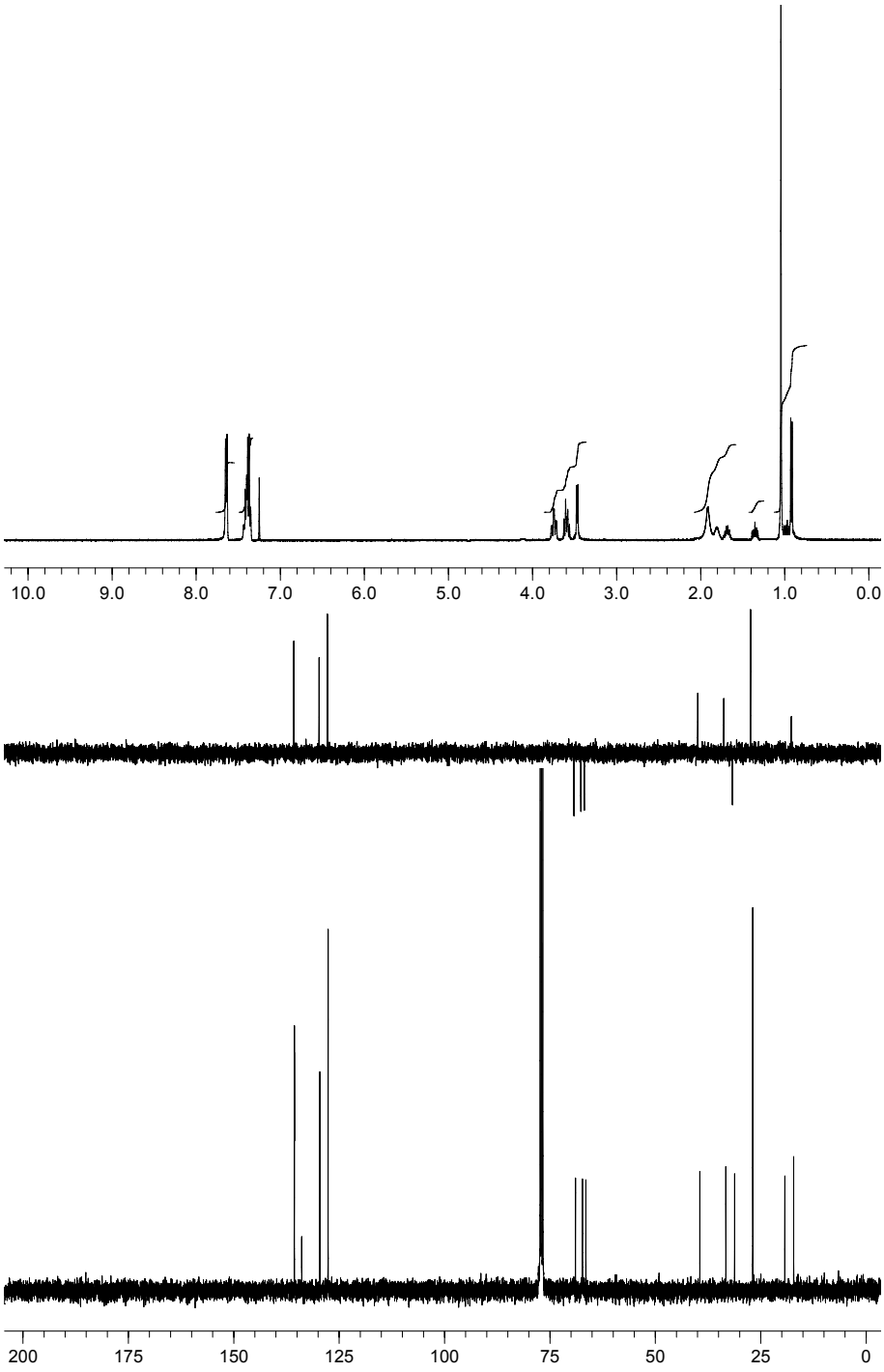
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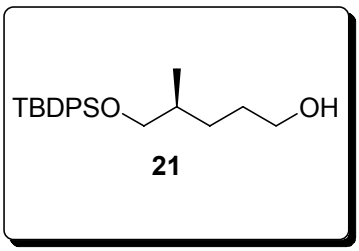
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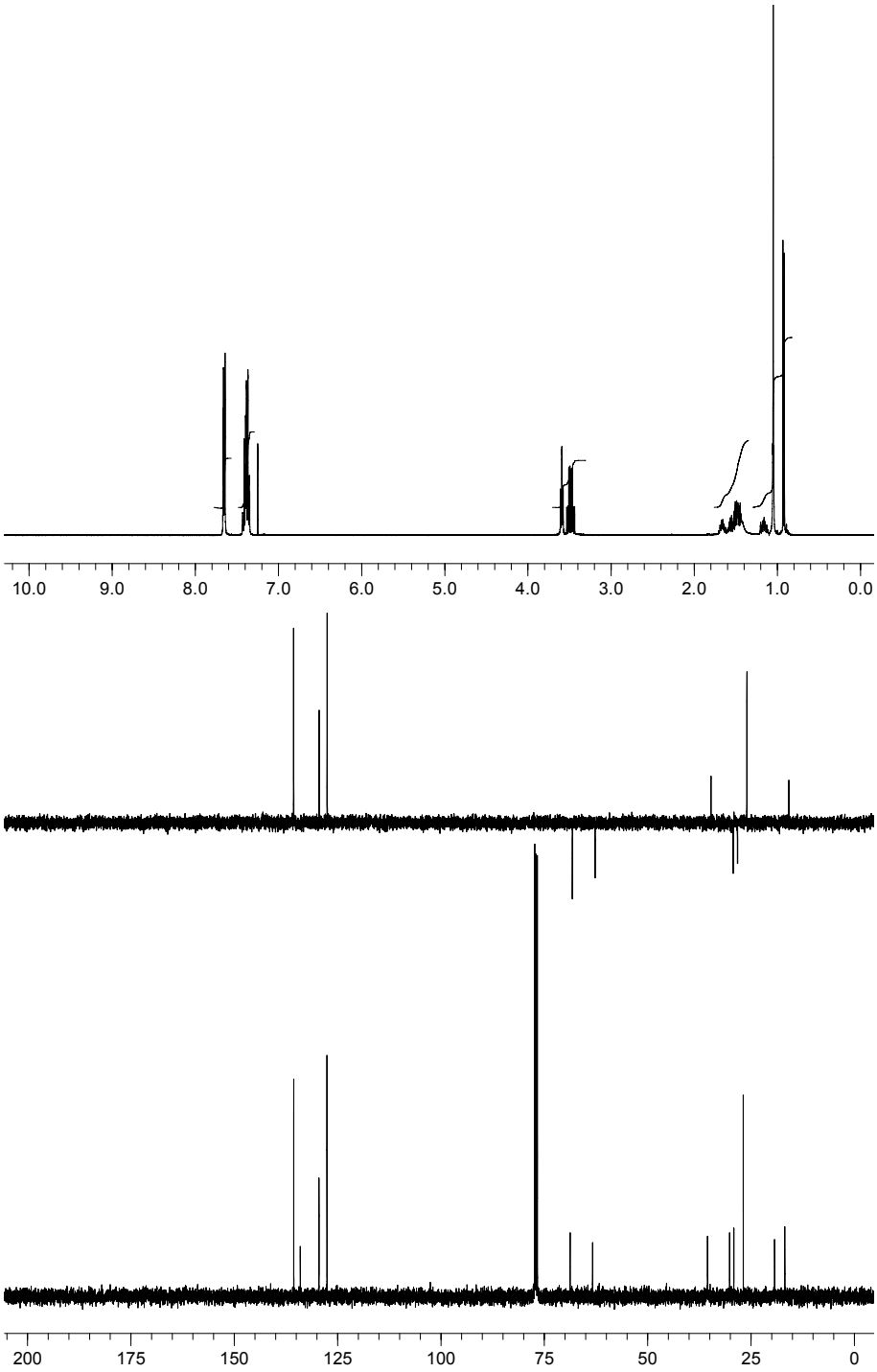
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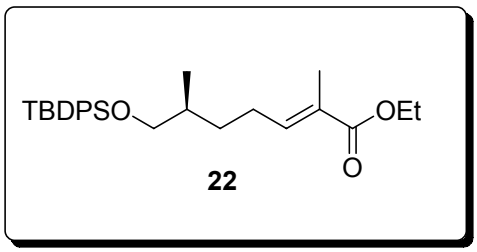
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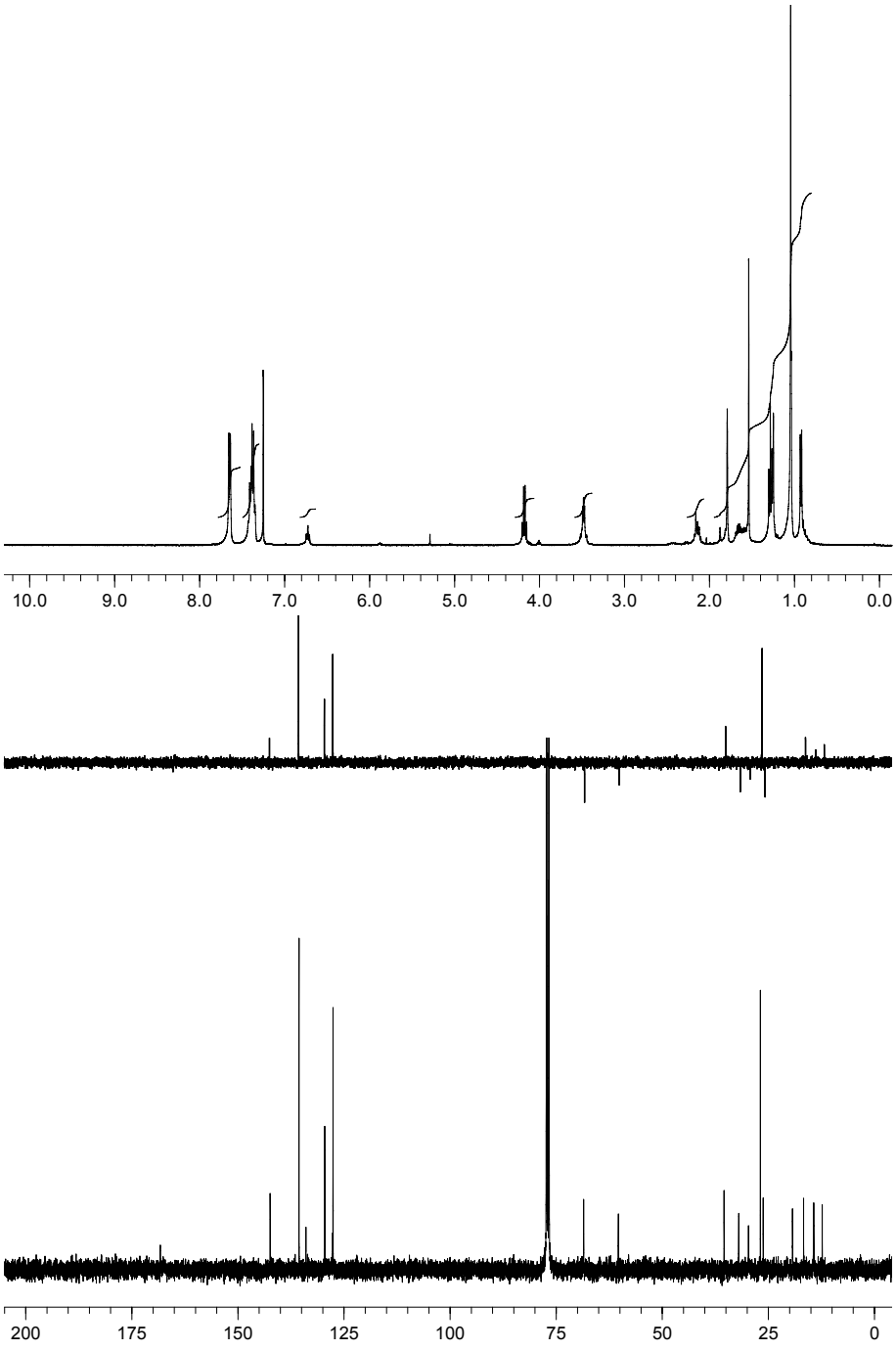
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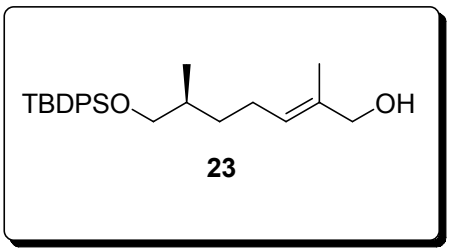
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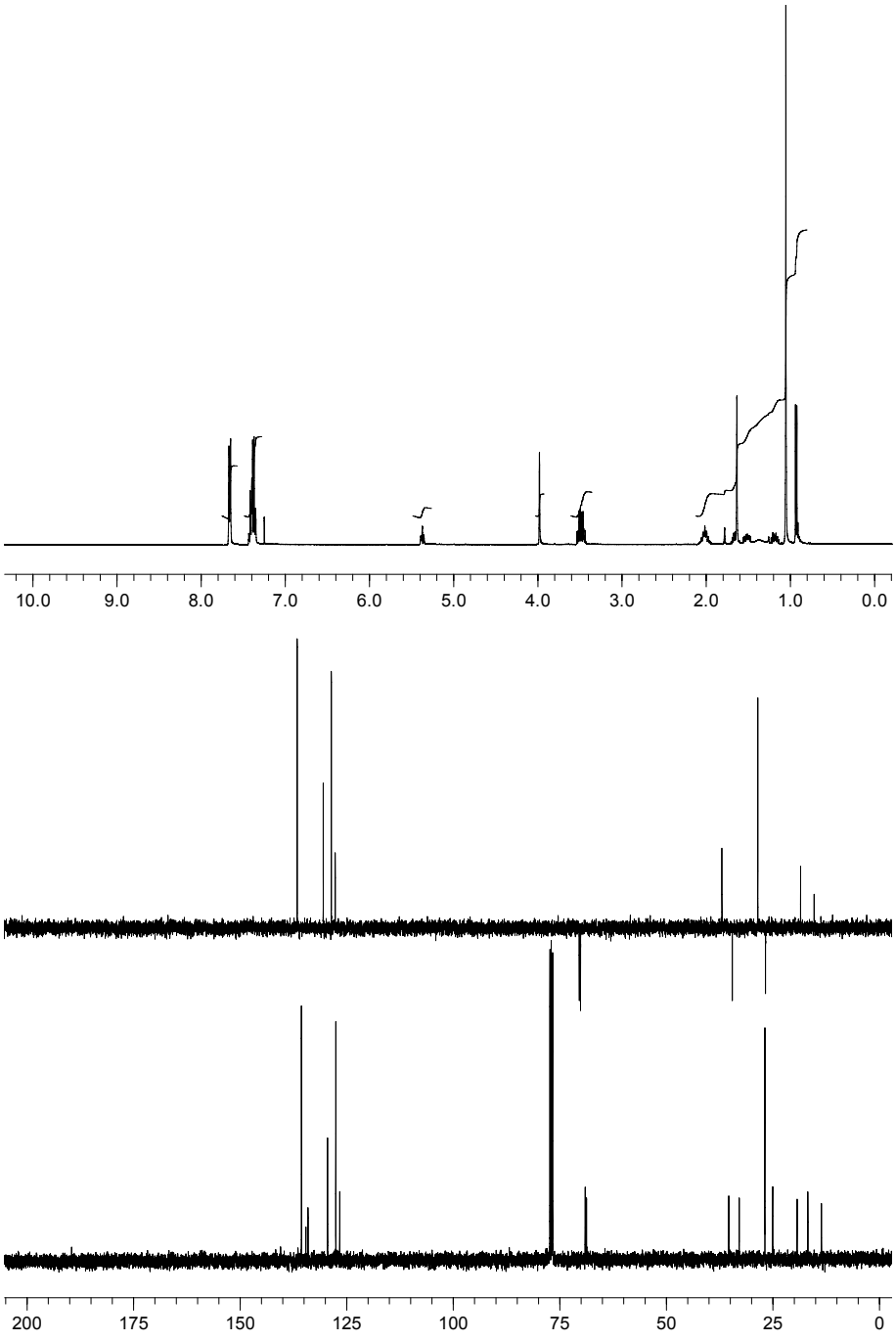
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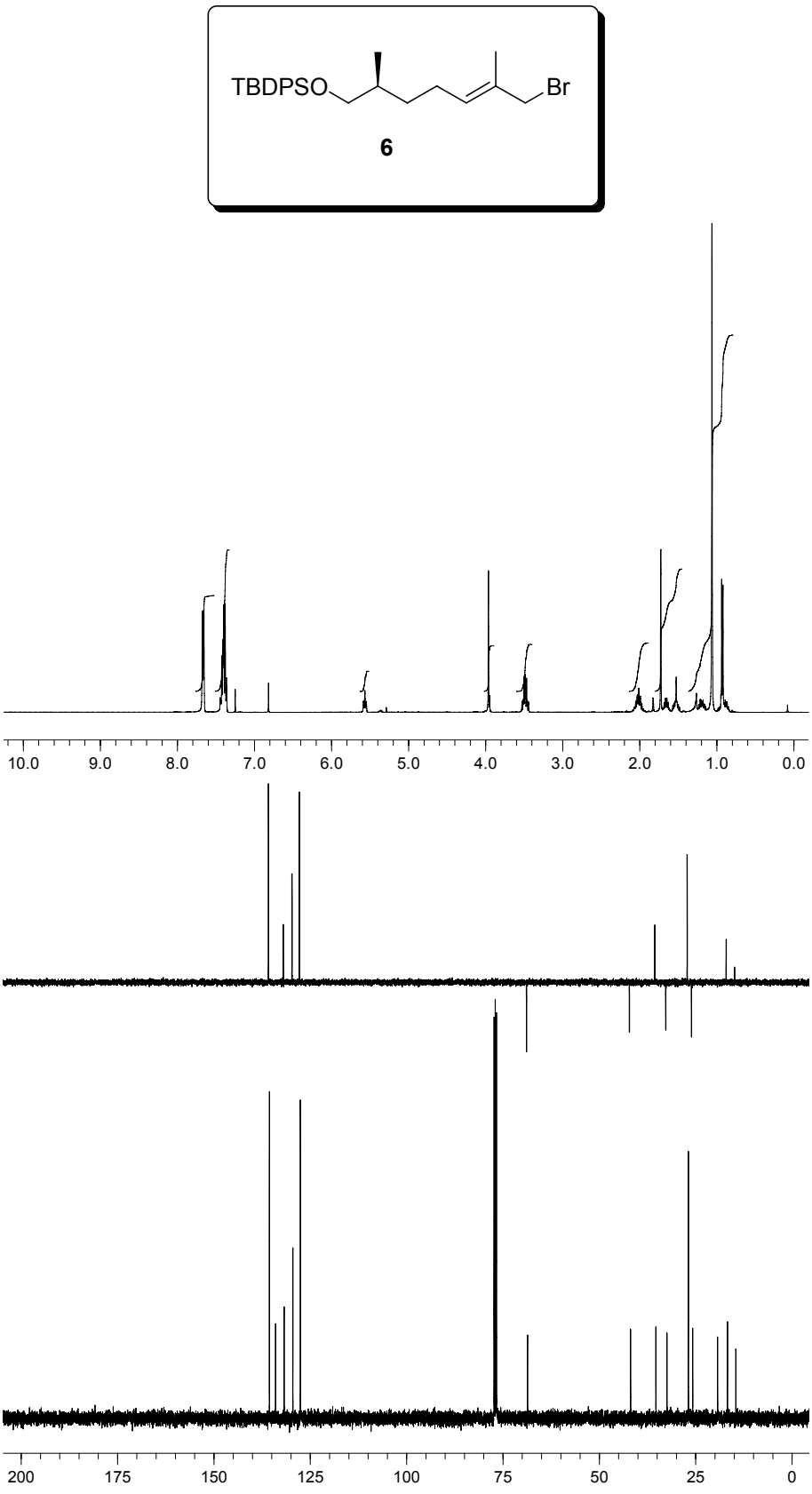
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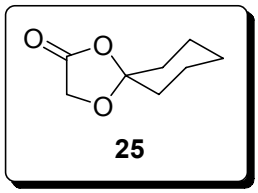

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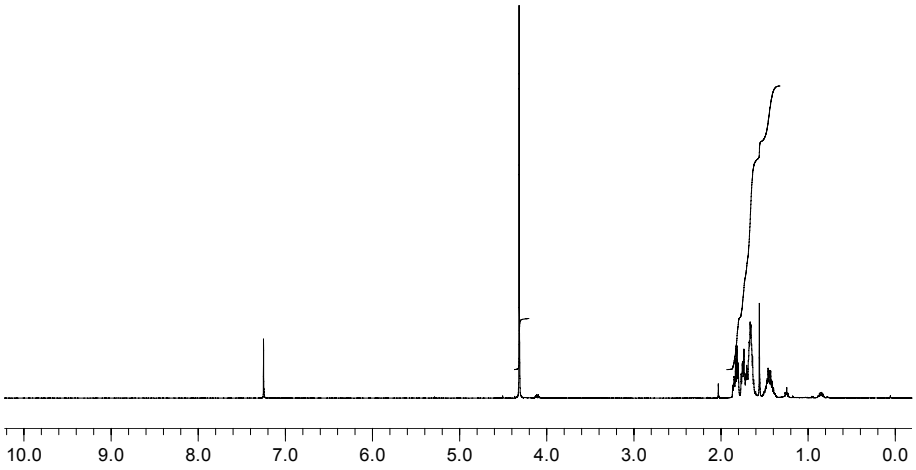

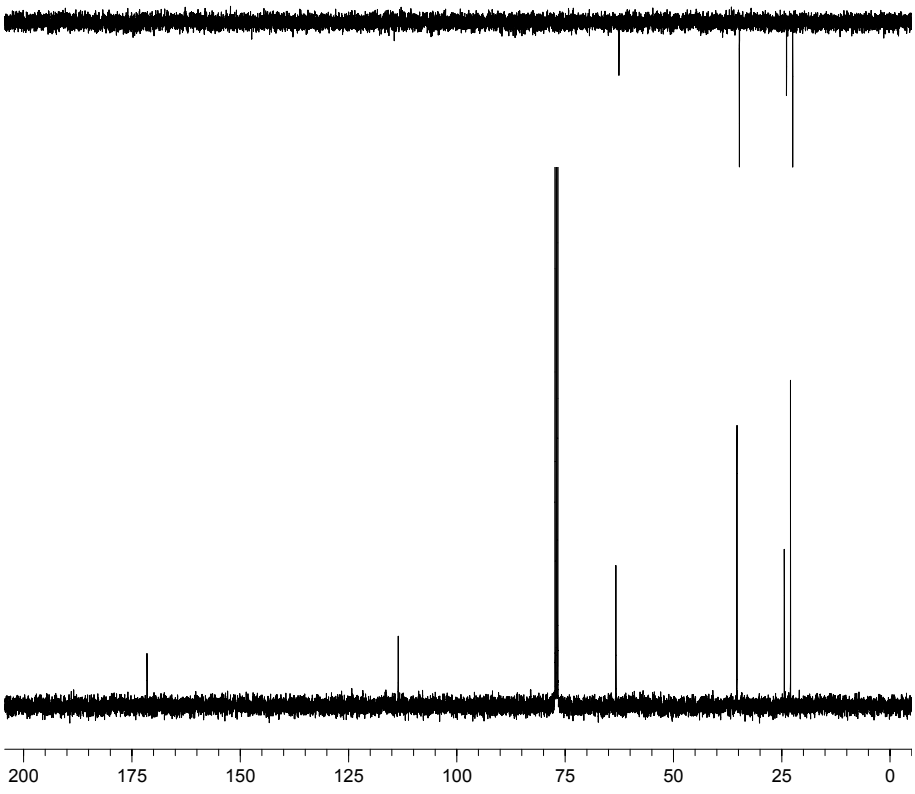

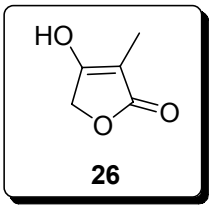

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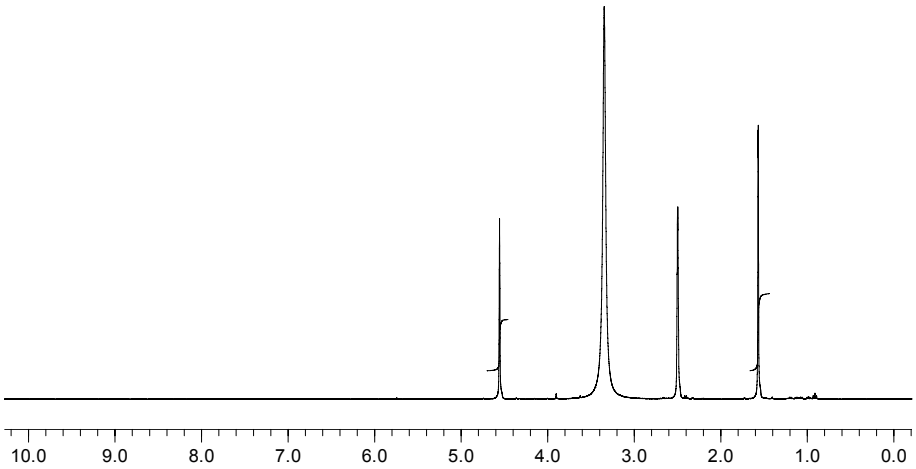

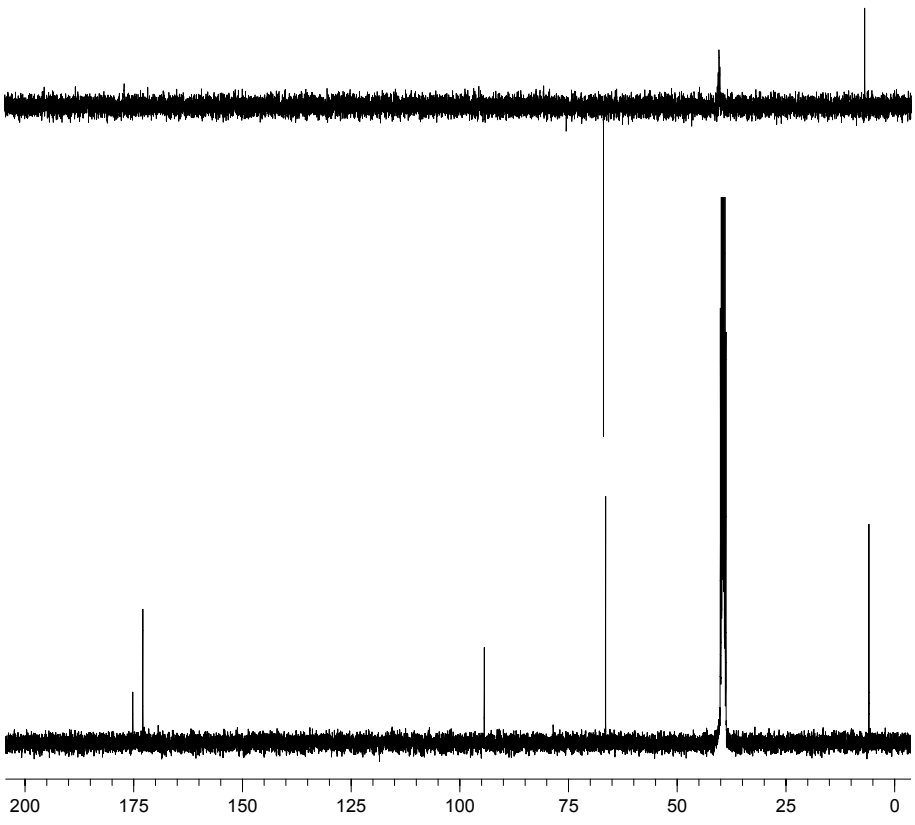

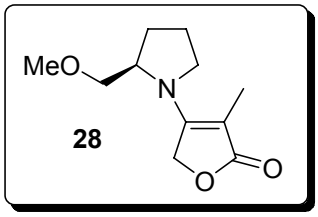
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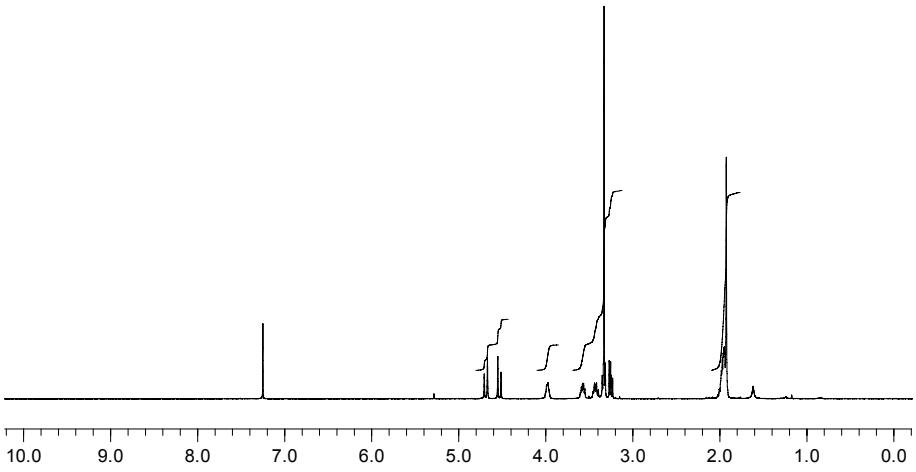
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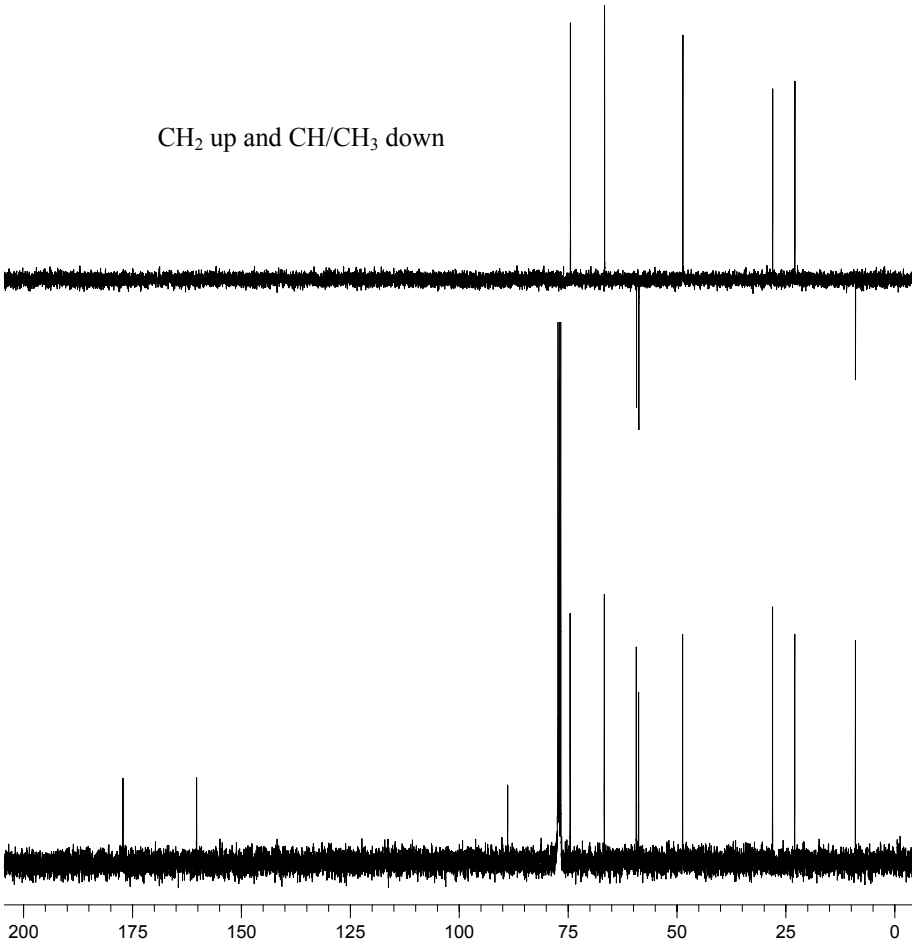
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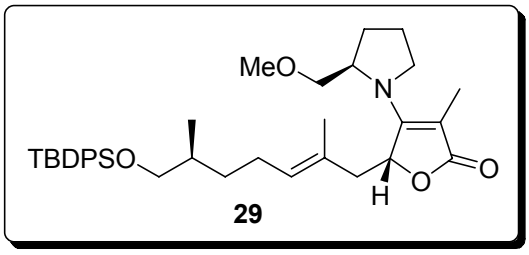
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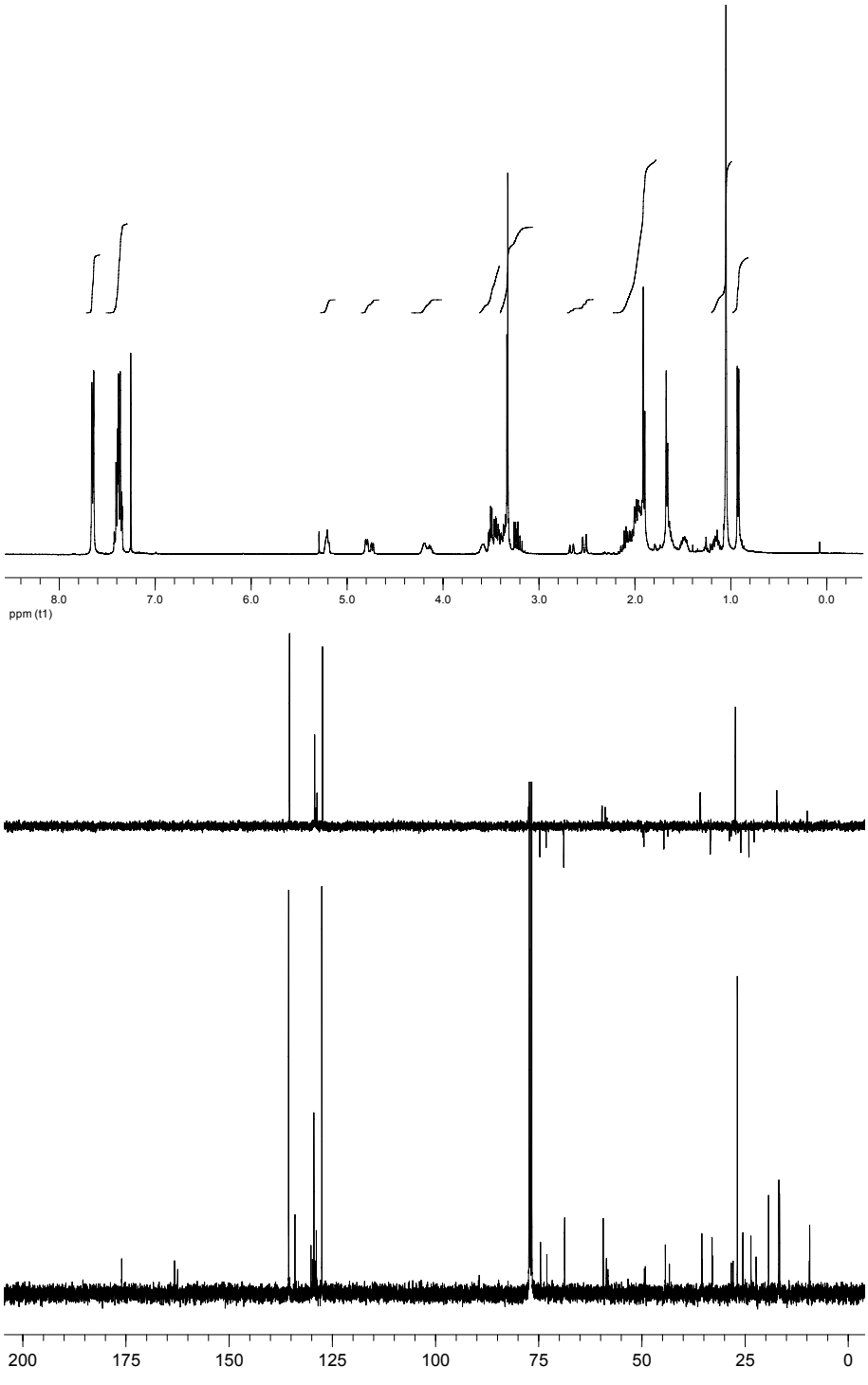
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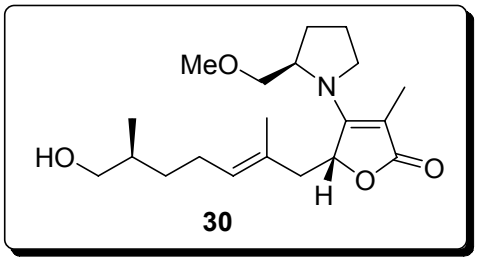
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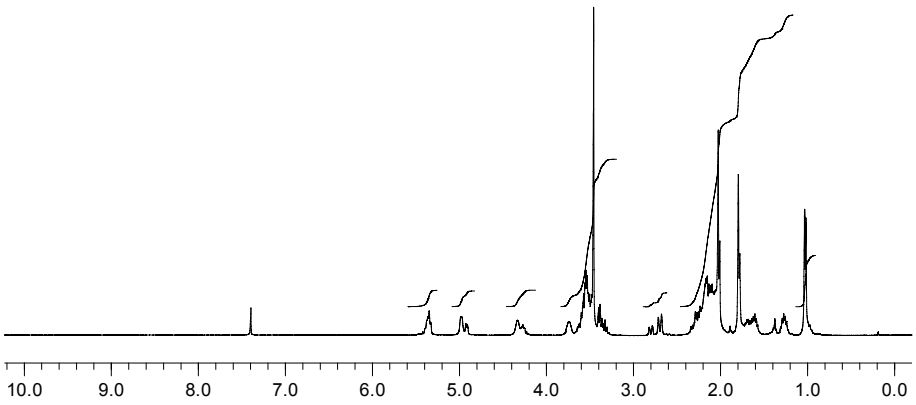
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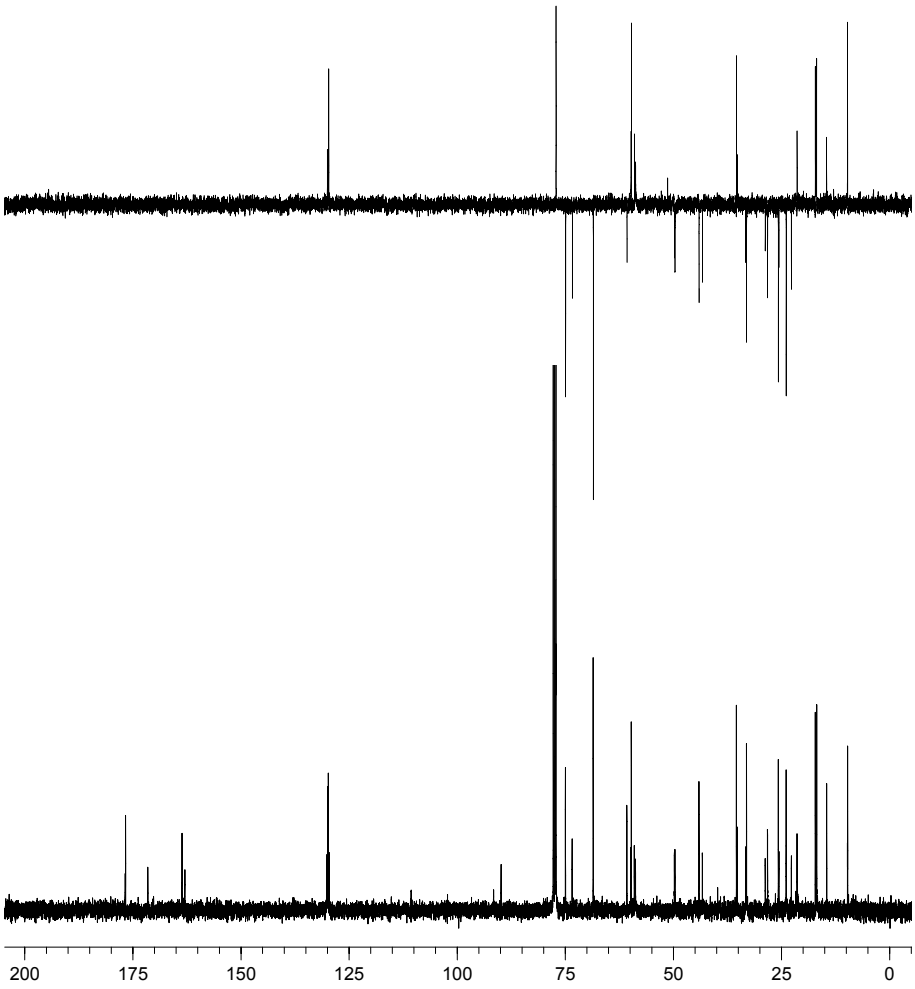
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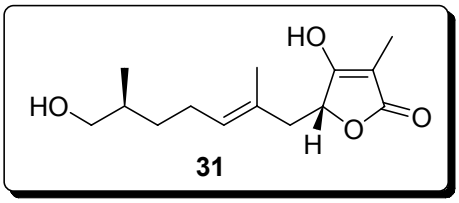
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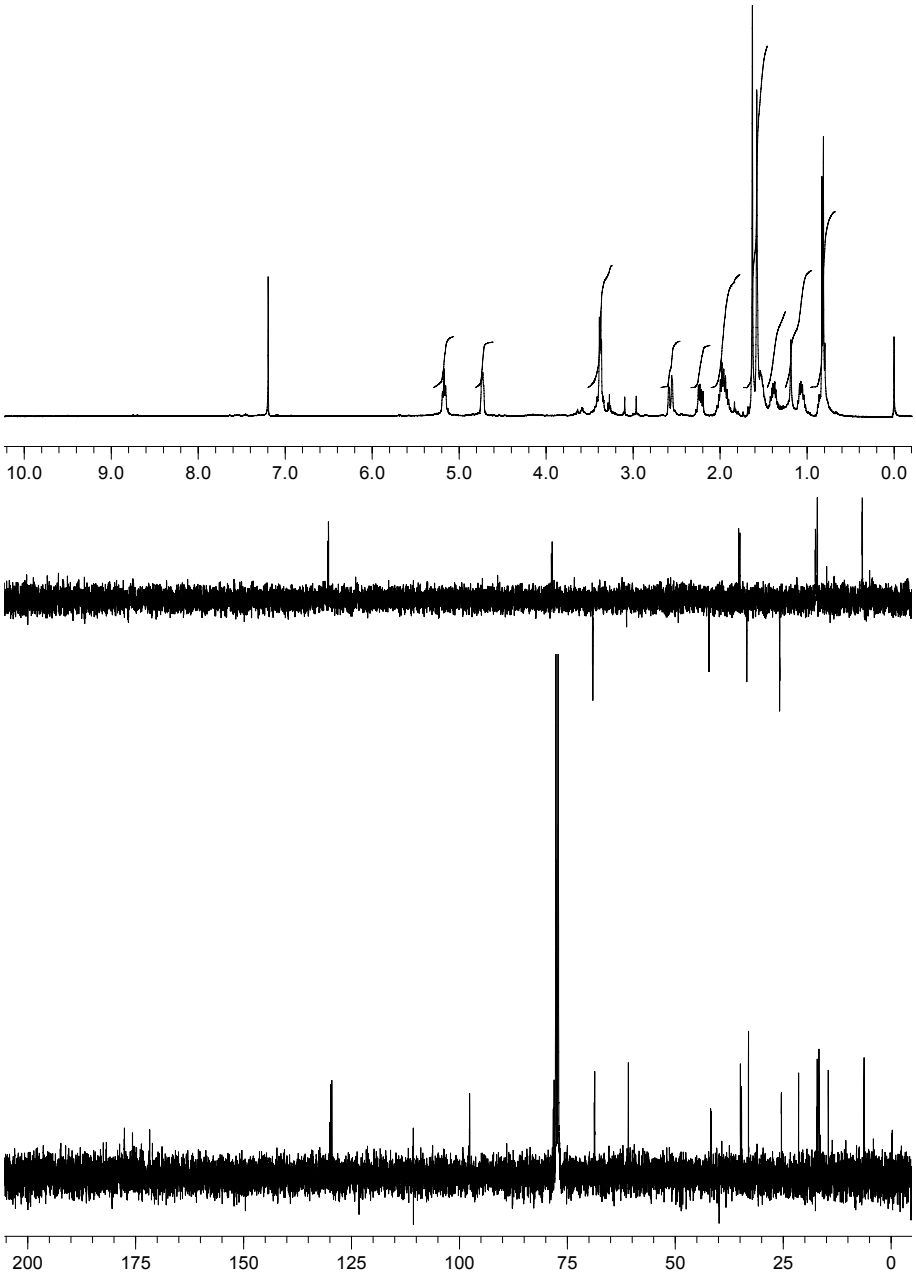
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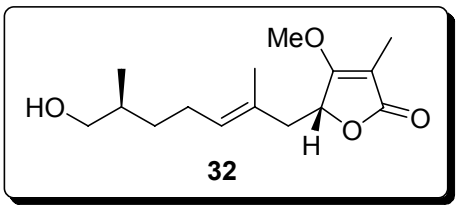
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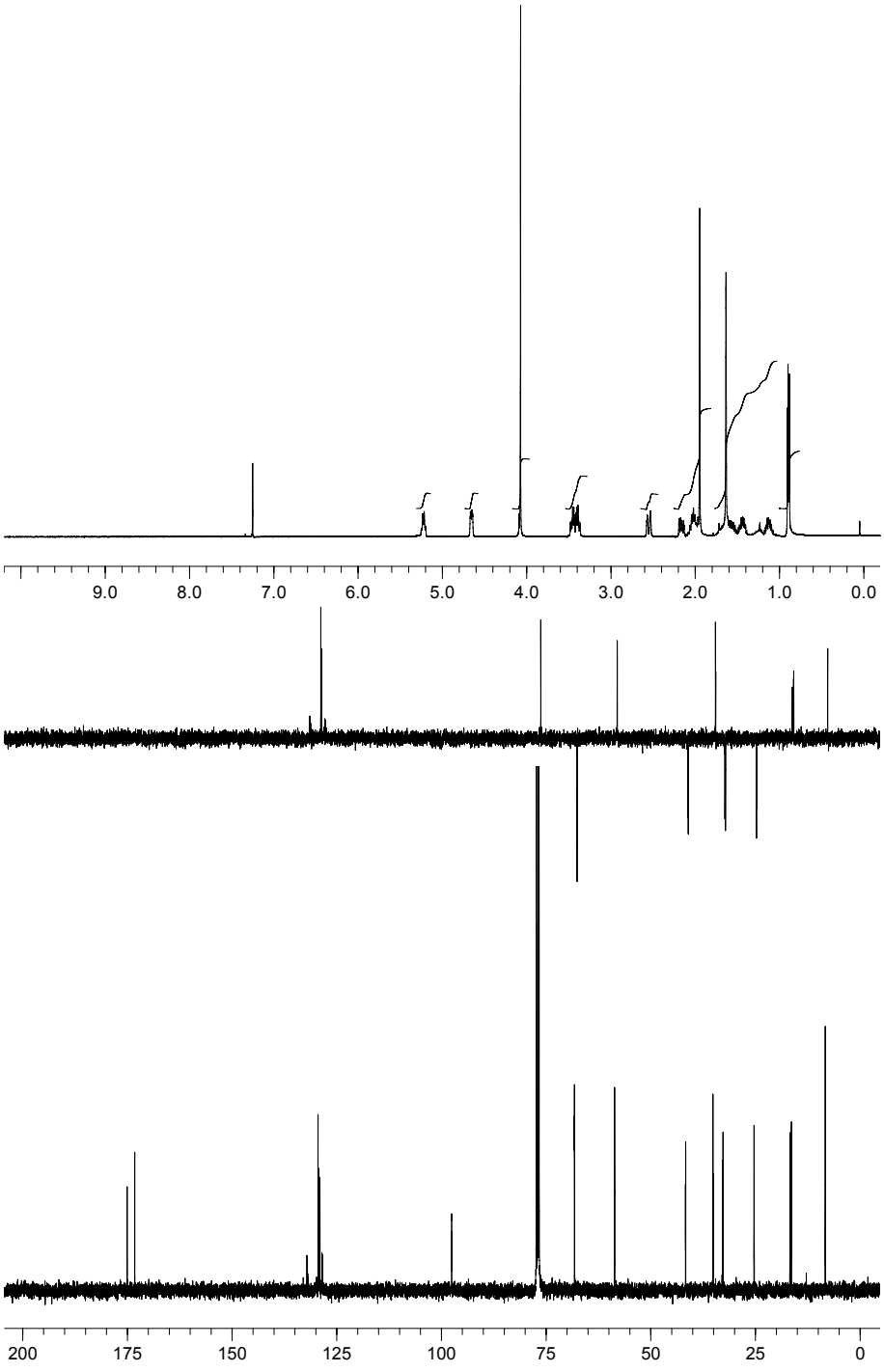
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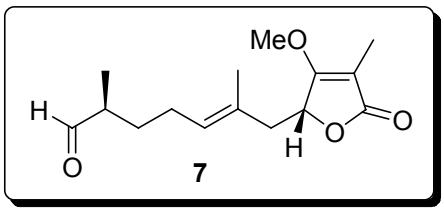
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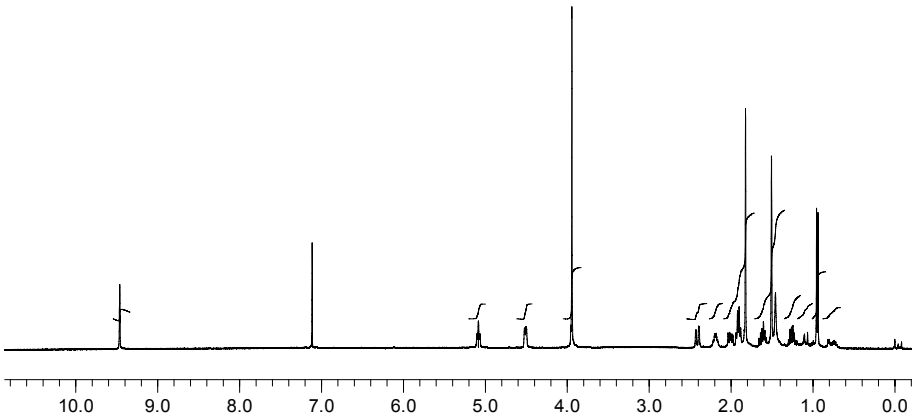
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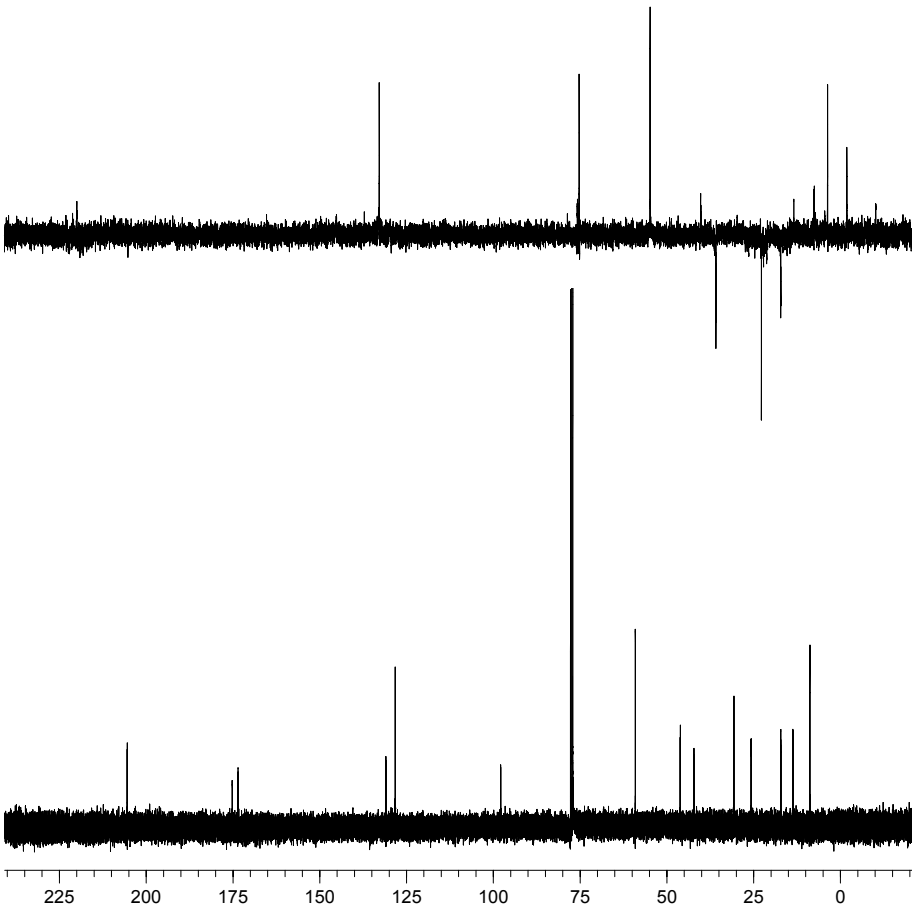
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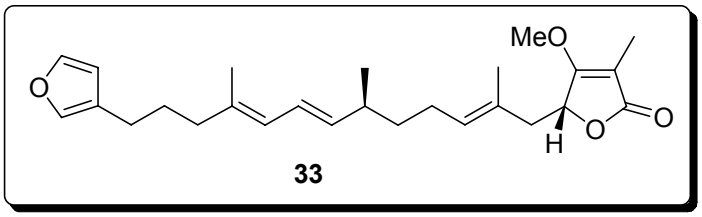
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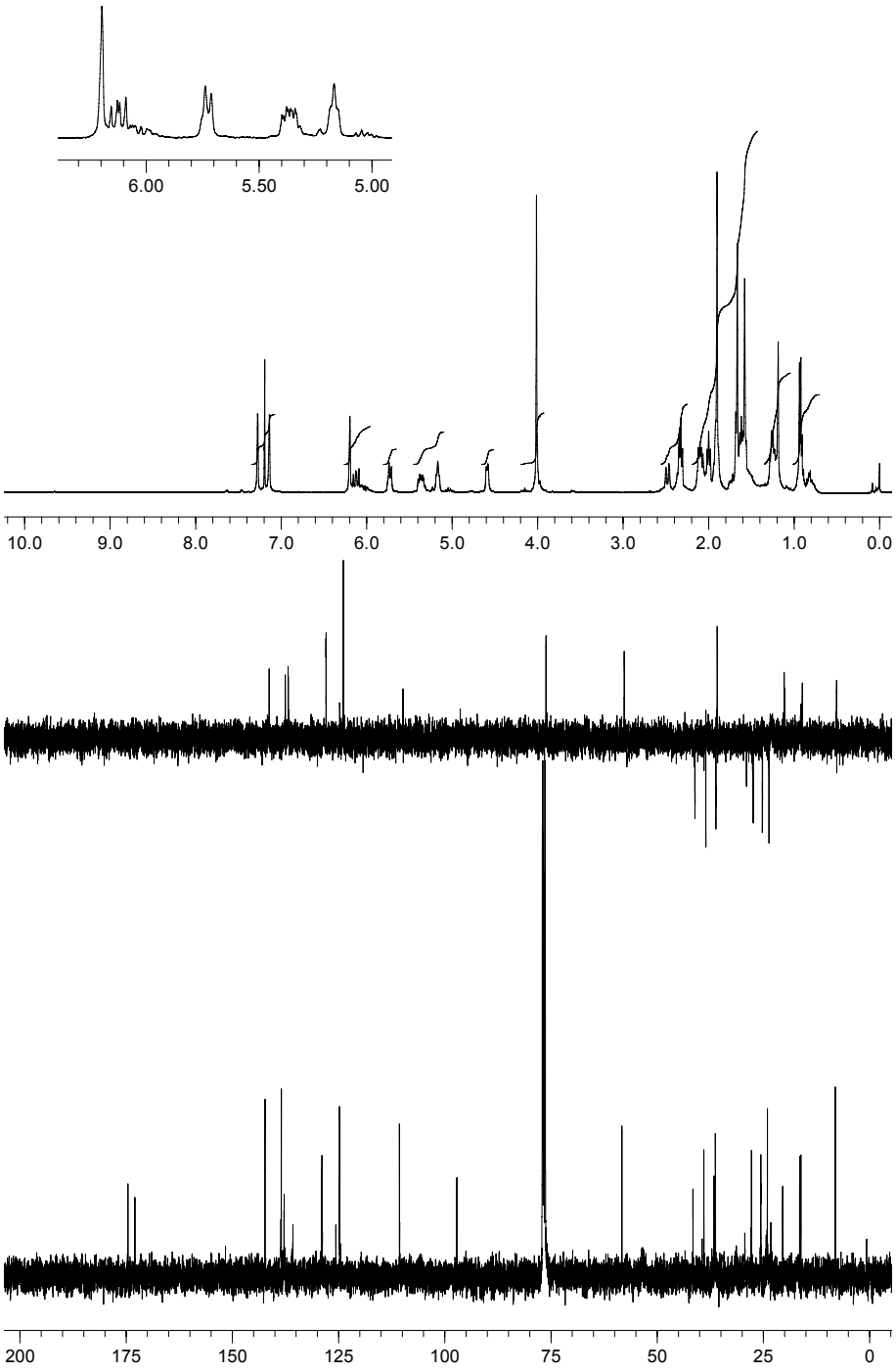
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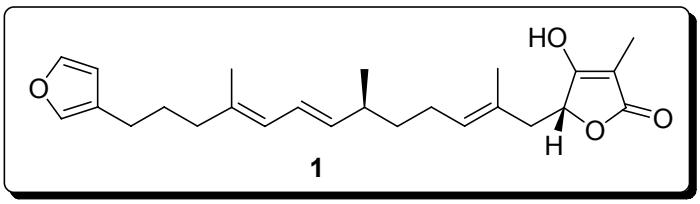
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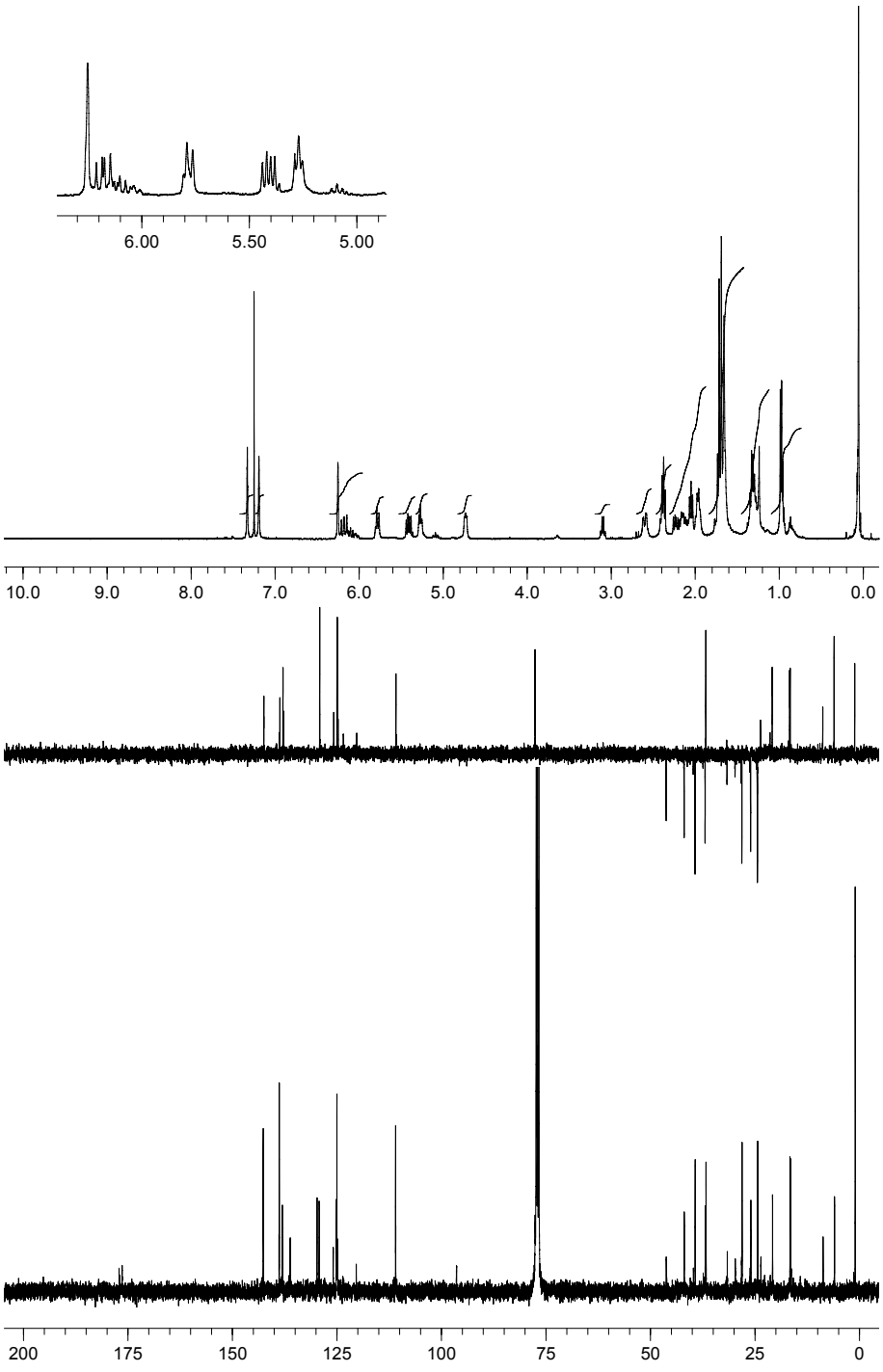
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