Supplementary Material:

Total Synthesis of (-)-Laulimalide

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All the moisture sensitive reactions were carried out under nitorgen atmosphere. Anhydrous solvents were obtained as follows: THF, distilled from sodium and benzophenone; dichloromethane, distillation from P_2O_5; pyridine, toluene and benzene, distillation from CaH_2. All other solvents were HPLC grade. Column chromatography was performed with Whatman 240-400 mesh silica gel under low pressure of 5-10 psi. Thin-layer chromatography (TLC) was carried out with E. Merck silica gel 60-F-254 plates. ^1H and ^{13}C NMR spectra were recorded on Bruker AM 400, Avance 400 and Avance 500 spectrometers.

TBS ether 6. To a solution of lactone **5** (146 mg, 0.561 mmol) in CH_2Cl_2 (3 mL) at -78 °C was added DIBAL (1.0 M in hexane; 0.67 mL, 0.67 mmol). The mixture was stirred at -78 °C for 30 min and then quenched with 10% Roche's

salt solution. The resulting mixture was warmed to 23 °C and stirred for 1 h. The layers were separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was dissolved in EtOH (3 mL). CSA (6 mg) was added. The resulting mixture was stirred at 23 °C for 30 min. The mixture was quenched with Et_3N (2 drops) and concentrated. The residue was purified by silica gel chromatography (5% EtOAc/hexane) to afford the ethyl acetal (a colorless oil, 134 mg, 82%) as a colorless oil. $[\alpha]_D^{23}$-23 (*c* 1.12, $CHCl_3$); IR(thin film): 2954, 2925, 1453, 1272, 1103 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.40-7.12 (m, 5H), 6.00 (m, 1H), 5.73 (m, 1H), 4.96 (s, 1H), 4.51 (s, 2H), 4.03 (m, 1H), 3.83 (m, 1H), 3.50 (m, 1H), 3.37 (dd, *J* = 8.9, 5.8 Hz, 1H), 3.27 (dd, *J* = 9.0, 6.8 Hz, 1H), 2.13 (m, 1H), 1.97-1.93 (m, 2H), 1.72-1.64 (m, 2H), 1.23 (dt, *J* = 7.1, 1.6 Hz, 3H), 0.99 (d, *J* = 6.7 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 138.6, 129.1, 128.2, 127.5, 127.3, 125.5, 94.4, 76.1, 72.9, 63.7, 63.0, 39.4, 31.3, 29.7, 16.5, 15.2. MS(ESI): 313 (M^+ + Na), 181.

To a mixture of the above ethyl acetal (7.58 g, 26.1 mmol) and vinyloxy-*tert*-butyldimethylsilane (6.33 g, 39.2 mmol) in CH_2Cl_2 (50 mL) was added Montmorillonite K-10 (7.6 g) with ice cooling. After stirring at 23 °C for 30 min, the mixture was filtered through Celite and concentrated. The residue was dissolved in MeOH (50 mL). $NaBH_4$ (1.5 g, 39.7 mmol) was slowly added at 0 °C. After stirring for 30 min at 0 °C, the mixture was quenched by saturated aqueous NH_4Cl. The mixture was extracted with 30% EtOAc/hexane. The

combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel chromatography (20% EtOAc/hexane) to afford the alcohol (a colorless oil, 4.11 g, 54%) as a single isomer. IR(thin film): 3417, 2928, 2872, 1092, 1071 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.36-7.29 (m, 5H), 5.84 (m, 1H), 5.67 (dd, J = 10.3, 1.7 Hz, 1H), 4.53 (s, 2H), 4.40 (brd, J = 8.3 Hz, 1H), 3.99-3.78 (m, 3H), 3.36 (dd, J = 9.1, 6.2 Hz, 1H), 3.27 (dd, J = 9.1, 6.4 Hz, 1H), 2.70 (brs, 1H), 2.12-2.05 (m, 2H), 1.96-1.86 (m, 2H), 1.79 (m, 1H), 1.68 (m, 1H), 1.23 (m, 1H), 0.99 (d, J = 6.7 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 139.1, 129.7, 128.7, 128.0, 127.8, 124.6, 76.6, 73.4, 71.3, 66.0, 61.2, 39.5, 36.3, 31.3, 30.2, 17.4. MS(ESI): 290 (M^+ + H), 181.

To a solution of the above alcohol (5.05 g, 17.4 mmol) in DMF (20 mL) was added imidazole (1.78 g, 26.2 mmol) followed by TBSCl (3.15 g, 20.9 mmol). The resulting suspension was stirred at 23 °C for 3 h. 20% EtOAc/hexane and water were added. The layers were separated and the aqueous layer was extracted with 20% EtOAc/hexane. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel chromatography (2% EtOAc/hexane) to afford the TBS ether **6** as a colorless oil (5.29 g, 75%). IR(thin film): 2929, 2856, 1471, 1361, 1254, 1097 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.37-7.29 (m, 5H), 5.83 (m, 1H), 5.73 (dd, J = 10.3, 1.6 Hz, 1H), 4.54 (s, 2H), 4.36 (m, 1H), 3.83-3.73 (m, 3H), 3.41 (dd, J = 9.1, 5.7 Hz, 1H), 3.31 (dd, J = 9.1, 6.7 Hz, 1H), 2.13 (m, 1H), 2.02-1.97 (m, 2H), 1.86 (m, 1H), 1.75-1.68 (m, 2H), 1.26 (m, 1H), 1.01 (d, J = 6.7

Hz, 3H), 0.93 (s, 9H), 0.10 (s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 139.4, 130.4, 128.7, 127.9, 127.8, 124.4, 76.7, 73.2, 69.8, 65.3, 60.3, 40.0, 37.3, 31.9, 30.1, 26.4, 18.8, 17.3, -4.9. MS(ESI): 405 (M^+ + H), 299, 181.

Iodide 7. To a stirred solution of lithium (225 mg, 32.1 mmol) in liquid ammonia (50 mL) was added a solution of TBS ether **6** in THF (5 mL). The resulting mixture was stirred for 10 min. Solid NH_4Cl was added until the blue color disappeared. The mixture was warmed to 23°C. Water and CH_2Cl_2 was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel chromatography (15% EtOAc/hexane) to afford the alcohol as a colorless oil (3.86 g, 95%). IR(thin film): 3419, 2929, 2858, 1471, 1255, 1096 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.81 (brd, J = 10.2 Hz, 1H), 5.72 (brd, J = 10.2 Hz, 1H), 4.38 (brs, 1H), 3.78-3.72 (m, 3H), 3.52 (m, 1H), 3.44 (m, 1H), 2.50 (brs, 1H), 1.99-1.97 (m, 2H), 1.90-1.85 (m, 2H), 1.71 (m, 1H), 1.64 (m, 1H), 1.34 (m, 1H), 1.20 (m, 1H), 0.95 (d, J = 6.7 Hz, 3H), 0.93 (s, 9H), 0.07 (s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 129.9, 124.3, 70.3, 68.9, 66.6, 60.0, 40.5, 37.4, 33.8, 32.0, 26.3, 18.7, 17.9, -5.0. MS(ESI): 515 (M^+ + H), 297, 181.

To a suspension of the above alcohol (3.86 g, 12.3 mmol), PPh_3 (6.475 g, 24.6 mmol) and imidazole (2.51 g, 36.9 mmol) in 2:1 Et_2O- CH_3CN (30 mL) at 0 °C was slowly added I_2 (6.22g, 24.5 mmol). After 30 min, 10% $Na_2S_2O_3$ and

EtOAc was added. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel chromatography (5% EtOAc/hexane) to afford the iodide **7** as a colorless oil (5.03 g, 96%). IR(thin film): 2927, 2856, 1254, 1095 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.83 (m, 1H), 5.72 (dd, J = 10.1, 1.7 Hz, 1H), 4.36 (brd, J = 7.0 Hz, 1H), 3.79-3.73 (m, 3H), 3.32 (dd, J = 9.5, 4.6 Hz, 1H), 3.31 (dd, J = 9.5, 6.1 Hz, 1H), 1.99-1.96 (m, 2H), 1.84-1.81 (m, 2H), 1.70-1.66 (m, 2H), 1.29 (m, 1H), 1.02 (d, J = 6.7 Hz, 3H), 0.91 (s, 9H), 0.09 (s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 130.3, 124.2, 69.7, 65.5, 60.2, 42.9, 37.3, 31.4, 30.9, 26.4, 20.5, 18.8, 18.3, -4.9. MS(ESI): 447 (M^+ + Na), 332, 301.

Lactone 9. To a suspension of NaH (585 mg, 60% dispersion in mineral oil, 14.6 mmol) in DMF (40 mL) at 0 °C was added a solution of lactone **8** (5.24 g, 13.9 mmol) in DMF (5 mL). After 15 min, a solution of iodide **7** (5.03 g, 11.8 mmol) in DMF (5 mL) was added dropwise. The mixture was warmed to 23 °C and heated at 60 °C for 12 h. The mixture was then cooled to 23 °C. 25% EtOAc/hexane and water was added. The layers were separated and the aqueous layer was extracted with 25% EtOAc/hexane. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel chromatography (10% EtOAc/hexane) to afford the lactone **9** (a colorless oil, 7.04 g, 89%) as a mixture of isomers (4.2 : 1, by 500 MHz ^{1}H

NMR). Major isomer: IR(thin film): 2928, 1769, 1513, 1309 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 7.4 Hz, 2H), 7.71 (t, J = 7.4 Hz, 1H), 7.58 (t, J = 8.2 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 6.92 (d, J = 8.6 Hz, 2H), 5.77-5.71 (m, 1H), 5.66 (d, J = 10.1 Hz, 1H), 4.84 (m, 1H), 4.49 (dd, J = 24.3, 11.5 Hz, 2H), 4.28 (brs, 1H), 3.83 (s, 3H), 3.73-3.54 (m, 5H), 2.94 (dd, J = 15.1, 7.2 Hz, 1H), 2.68 (dd, J = 15.1, 8.4 Hz, 1H), 2.12-2.04 (m, 2H), 1.90-1.76 (m, 4H), 1.70-1.62 (m, 2H), 1.27 (m, 1H), 0.91 (s, 9H), 0.87 (d, J = 6.5 Hz, 3H), 0.07 (s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 159.8, 135.0, 134.6, 131.9, 131.4, 130.1, 130.1, 129.2, 129.1, 124.4, 114.3, 76.4, 73.3, 72.4, 71.3, 69.9, 64.4, 60.2, 55.8, 41.6, 40.0, 37.2, 31.8, 28.6, 26.4, 26.0, 23.1, 21.2, 18.8, 14.5, -4.9.

Alcohol 11. To a solution of lactone **9** (6.51 g, 9.68 mmol) in THF (50 mL) at 0 °C was added Red-Al (3.9 mL, 19.4 mmol; 65% w/w) dropwise. After 10 min, the reaction was quenched with 10% Roche's salt solution. The mixture was stirred at 23 °C for 2 h and then was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to give the crude diol **10** which was used for the next reaction without further purification.

To a solution of the above diol **10** in CH_2Cl_2 (50 mL) was added sequentially Et_3N (5.4 mL, 38.7 mmol), DMAP (237 mg, 1.94 mmol) and benzoyl chloride (3.4 mL, 29 mmol). After stirring at 23 °C for 12 h, the mixture was washed with saturated aqueous $NaHCO_3$, 1 M $NaHSO_4$, brine, dried

over anhydrous Na_2SO_4 and concentrated. The crude dibenzoate was used for the next reaction immediately.

To a solution of the above dibenzoate in MeOH (50 mL) at -20 °C was added Na_2HPO_4 (8.2 g, 58 mmol) followed by sodium amalgam (6% w/w, 37.1 g). The suspension was stirred vigorously for 2 h and then was allowed to warm to 23 °C and stirred for 1 h. After this period, The mixture was quenched with saturated aqueous NH_4Cl. The mixture was decanted. Water and 25% EtOAc/hexane were added and the layers were separated. The aqueous layer was extracted with 25% EtOAc/hexane. The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated. The residue was chromatographed over silica gel (10% EtOAc/hexane) to furnish the alcohol **11** as a colorless oil (3.61 g, 72%). $[\alpha]_D^{23}$-27 (c 0.33, $CHCl_3$); IR(thin film): 3498, 2927, 2856, 1514, 1250 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 5.82 (m, 1H), 5.67 (dd, *J* = 10.3, 1.6 Hz, 1H), 4.90 (s, 1H), 4.86 (s, 1H), 4.52 (s, 2H), 4.35 (m, 1H), 3.96 (m, 1H), 3.83 (s, 3H), 3.79-3.72 (m, 3H), 3.50 (dd, *J* = 7.6, 3.4 Hz, 1H), 3.38 (dd, *J* = 7.6, 7.2 Hz, 1H), 2.40 (brs, 1H), 2.18 (d, *J* = 6.7 Hz, 2H), 2.05 (dd, *J* = 13.3, 5.6 Hz, 1H), 1.95-1.83 (m, 5H), 1.72-1.60 (m, 2H), 1.16 (m, 1H), 0.91 (s, 9H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.05 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.7, 144.7, 130.5, 130.4, 129.8, 124.5, 115.0, 114.2, 74.4, 73.5, 69.9, 68.6, 65.1, 60.3, 55.7, 45.0, 43.4, 40.3, 37.2, 32.0, 27.1, 26.4, -4.9. MS(ESI): 519 (M^+ + H), 483, 399.

Aldehyde 2. To a stirred solution of the alcohol **11** (3.64 g, 7.02 mmol) in CH_2Cl_2 (10 mL) was added *i*Pr_2NEt (7.5 mL, 42.1 mmol) followed by MOMCl (2.7 mL, 35.1 mmol). After stirring at 23 °C for 3 h, The mixture was washed with 1 M $NaHSO_4$, brine, dried over anhydrous Na_2SO_4 and evaporated. The residue was dissolved in CH_2Cl_2 (10 mL). pH 7 buffer (0.5 mL) and DDQ (1.9 g, 8.42 mmol) was sequentially added. The green suspension was stirred at 23 °C for 2 h. The resulting orange suspension was then washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue was chromatographed over silica gel (15% EtOAc/hexane) to give the alcohol as a colorless oil (2.5 g, 81%). $[\alpha]_D^{23}$-18 (c 0.38, $CHCl_3$); IR(thin film): 3458, 2952, 2928, 2857, 1462, 1251 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.78 (m, 1H), 5.67 (d, *J* = 10.4 Hz, 1H), 4.83 (s, 1H), 4.81 (s, 1H), 4.69 (dd, *J* = 12.8, 5.9 Hz, 2H), 4.30 (d, *J* = 7.6 Hz, 1H), 3.75-3.58 (m, 5H), 3.47 (m, 1H), 3.40 (s, 3H), 3.07 (dd, *J* = 8.6, 4.1 Hz, 1H), 2.26 (dd, *J* = 14.4, 7.0 Hz, 1H), 2.13 (dd, *J* = 14.4, 6.4 Hz, 1H), 2.02-1.78 (m, 6H), 1.69-1.55 (m, 2H), 1.09 (m, 1H), 0.95 (s, 9H), 0.86 (d, *J* = 6.3 Hz, 3H), 0.04 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 144.0, 129.8, 124.0, 113.5, 96.6, 79.8, 69.4, 65.2, 64.4, 59.8, 55.5, 44.8, 42.6, 37.8, 36.7, 31.5, 26.6, 25.9, 19.1, 18.2, -5.4. MS(ESI): 443 (M^+ + H), 363, 279.

To a stirred solution of DMSO (0.98 mL, 13.8 mmol) in CH_2Cl_2 (20 mL) at -78 °C was added oxalyl chloride (0.72 mL, 8.27 mmol) dropwise. After 2 minutes, the above alcohol (2.38 g, 5.51 mmol) in CH_2Cl_2 (5 mL) was added

dropwise. The mixture was stirred at -78 °C for 30 min. After this period, iPr$_2$NEt (4.9 mL, 27.6 mmol) was added dropwise. The resulting mixture was stirred at -78 °C for an additional 2 min and warmed to 23 °C. The mixture was washed with cold 1 M aqueous $NaHSO_4$, brine, dried over anhydrous Na_2SO_4 and evaporated. The residue was chromatographed over silica gel (10% EtOAc/hexane) to afford aldehyde **2** as a colorless oil (2.02 g, 85%) which was used for next reaction immediately. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.63 (d, J = 1.2 Hz, 1H), 5.78 (m, 1H), 5.69 (d, J = 10.6 Hz, 1H), 4.91 (s, 1H), 4.88 (s, 1H), 4.69 (dd, J = 12.8, 7.0 Hz, 2H), 4.31 (brd, J = 7.6 Hz, 1H), 4.06 (m, 1H), 3.75-3.58 (m, 3H), 3.38 (s, 3H), 2.41-2.30 (m, 2H), 2.02-1.81 (m, 6H), 1.69-1.55 (m, 2H), 1.09 (m, 1H), 0.88 (s, 9H), 0.86 (d, J = 6.3 Hz, 3H), 0.05 (s, 6H).

Alcohol 15. To a solution of dibromide **12** (225 mg, 0.80 mmol) in THF (2 mL) at -78 °C was added nBuLi (1 mL, 1.6 mmol; 1.6 M in hexane). The resulting dark red solution was stirred at -78 °C for 1 h, then warmed to 23 °C for 1 h. The mixture was cooled to -78 °C, then a solution of aldehyde **13** (108 mg, 0.31 mmol) in THF (2 mL) was added dropwise. The mixture was stirred at -78 °C for 1 h and then was quenched by saturated aqueous NH_4Cl. The mixture was extracted with EtOAc. The organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was chromatographed over silica gel (30% EtOAc/hexane) to furnish the alkynyl alcohol (a colorless oil,

92.3 mg, 64%) as a mixture of isomers (*anti* : *syn* = 1.8 : 1, by 400 MHz ^{1}H-NMR).

To a solution of the above alcohol (786 mg, 1.67 mmol) in wet CH_2Cl_2 (6 mL) was added Dess-Martin periodiane (1 g, 2.36 mmol). After 10 min, The mixture was diluted with ether and washed with a mixture (1:1) of 10% aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$ (15 mL), followed by brine. The aqueous layer was extracted with ether. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. Silica gel chromatography (20% EtOAc/hexane) provided the ketone as a pale yellow oil (632 mg, 81%). $[\alpha]_D^{23}$-82 (c 0.22, $CHCl_3$); IR(thin film): 2933, 2837, 2213, 1679, 1514, 1306 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.3 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.45 (d, *J* = 1.5 Hz 1H), 4.67 (d, *J* = 5.7 Hz, 1H), 4.64 (d, *J* = 11.5 Hz, 1H), 4.32 (d, *J* = 11.5 Hz, 1H), 4.26 (m, 1H), 4.12 (m, 1H), 4.02 (dd, *J* = 8.4, 4.3 Hz, 1H), 3.80 (s, 3H), 3.17-3.13 (m, 2H), 2.32 (d, *J* = 17.0 Hz, 1H), 2.21-2.04 (m, 3H), 1.71 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.2, 159.6, 138.7, 133.9, 129.9, 129.7, 129.4, 128.7, 128.1, 119.4, 113.9, 94.7, 81.8, 81.6, 72.4, 63.9, 62.9, 55.3, 51.8, 34.5, 25.2, 22.9. MS(ESI): 491 (M^+ + Na), 443, 411, 181.

To a solution of the above ketone (1.46 g, 3.13 mmol) in THF (10 mL) at -78 °C was added L-Selectride (4.7 mL, 4.7 mmol; 1.0 M in THF) dropwise. The mixture was stirred at -78 °C for 30 min and then was quenched by saturated aqueous NH_4Cl. The mixture was extracted with EtOAc. The combined organic

layers were washed with brine and dried over Na_2SO_4 and evaporated. The residue was chromatographed over silica gel (40% EtOAc/hexane) to furnish the alcohol **15** as a colorless oil (1.27 g, 87%) as a single isomer. $[\alpha]_D^{23}$-54 (c 0.26, $CHCl_3$); IR(thin film): 3469, 2928, 2637, 1612, 1513, 1446, 1304, 1248 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.64 (t, *J* = 6.9 Hz, 1H), 7.56 (t, *J* = 7.1 Hz, 2H), 7.24 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.39 (s, 1H), 4.64 (d, *J* = 11.1 Hz, 1H), 4.51 (d, *J* = 11.1 Hz, 1H), 4.42 (t, *J* = 4.9 Hz, 1H), 4.32 (t, *J* = 4.9 Hz, 1H), 4.20 (d, *J* = 15.9 Hz, 1H), 4.08 (d, *J* = 15.9 Hz, 1H), 3.79 (s, 3H), 3.64 (m, 1H), 3.19-3.05 (m, 2H), 2.62 (d, *J* = 4.4 Hz, 1H), 2.16 (brs, 2H); 2.15-1.90 (m, 2H), 1.69 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.5, 138.9, 133.7, 130.2, 129.8, 129.6, 129.3, 128.0, 119.4, 113.9, 85.4, 82.9, 78.9, 73.1, 64.5, 64.2, 63.3, 55.3, 52.2, 35.6, 24.2, 22.9. MS(ESI): 493 (M^+ + Na), 351, 181.

Acetal 16. To a solution of alcohol **15** (1.27 g, 2.7 mmol) in THF (6 mL) at -40 °C was added Red-Al (1.3 mL, 4.3 mmol; 65% w/w) dropwise. The mixture was warmed to -20 °C and stirred for 1 h and then was quenched by 10% Roche's salt solution. The mixture was stirred at 23 °C for 2 h and then was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was chromatographed over silica gel (40% EtOAc/hexane) to furnish the allylic alcohol as a colorless oil (1.03 g, 81%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J*

= 7.3 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.9 Hz, 2H), 7.21 (dd, J = 6.7, 1.9 Hz, 2H), 6.87 (dd, J = 6.7, 1.9 Hz, 1H), 5.83 (ddd, J = 15.7, 5.2, 0.7 Hz, 1H), 5.73 (ddd, J = 15.7, 5.9, 1.0 Hz, 1H), 5.43 (s, 1H), 4.49 (dd, J = 16.3, 11.1 Hz, 2H), 4.18 (brs, 2H), 4.07 (m, 1H), 4.00 (m, 1H), 3.52 (ddd, J = 10.3, 5.4, 1.6 Hz, 1H), 3.19-3.11(m, 2H), 2.48 (brs, 1H), 2.05-1.95 (m, 2H), 1.90 (m, 1H), 1.88 (d, J = 14.5 Hz, 1H), 1.72 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.9, 139.4, 134.1, 133.8, 133.5, 131.7, 130.1, 129.7, 128.4, 120.1, 114.4, 79.6, 73.7, 73.5, 73.0, 66.0, 55.7, 52.6, 36.0, 24.2, 23.4. MS(ESI): 495 (M^+ + Na), 353, 181.

To a solution of the above alcohol (354 mg, 0.79 mmol) in CH_2Cl_2 (10 mL) was added trifluoroacetic acid (0.3 mL). After stirring at 23 °C for 1 h, the mixture was quenched by saturated aqueous $NaHCO_3$. The layers were separated and aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was dissolved in CH_2Cl_2 (10 mL), *p*-methoxybenzylidene dimethylacetal (204 mg, 1.12 mmol) and CSA (5 mg) were sequentially added. The mixture was stirred at 23 °C for 30 min and then was quenched by Et_3N (2 drops). The mixture was concentrated. The residue was purified by silica gel chromatography (40% EtOAc/hexane) to afford the acetal **16** (a colorless oil, 250 mg, 71%) as a mixture of isomers (4.3 : 1, by ^{13}C NMR). Major isomer: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.1 Hz, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.59 (t, J = 8.0 Hz, 2H), 7.37 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 5.96 (dd, J = 15.5, 5.1 Hz, 1H), 5.86 (s, 1H), 5.80 (ddd, J = 15.5, 7.6, 1.3 Hz, 1H), 5.44 (s, 1H), 4.20-4.18 (m, 3H), 4.07 (m, 1H),

3.83 (m, 1H), 3.80 (s, 3H), 3.39 (m, 1H), 3.20 (m, 1H), 2.12-2.02 (m, 3H), 1.92 (d, J = 16.8 Hz, 1H), 1.71 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 160.9, 139.4, 136.8, 134.3, 131.6, 130.0, 129.8, 128.4, 128.4, 126.3, 120.1, 114.2, 103.7, 83.7, 79.4, 73.3, 66.1, 55.7, 53.7, 36.0, 25.7, 23.3. MS(ESI): 493 (M^+ + Na), 335, 317, 181.

Alcohol 3. To a solution of acetal **16** (92 mg, 0.20 mmol) in CH_2Cl_2 (10 mL) at -78 °C was added DIBAL (0.6 mL, 0.6 mmol; 1.0 M in hexane) dropwise. The mixture was stirred at -78 °C for 30 min and then was quenched by 10% Roche's salt solution. The mixture was stirred at 23 °C for 2 h. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel chromatography (40% EtOAc/hexane) to afford the alcohol **3** (a colorless oil, 68 mg, 74%) as a single regio isomer. $[\alpha]_D^{23}$-26 (c 0.97, $CHCl_3$); IR(thin film): 3498, 2930, 2837, 1612, 1446, 1303, 1249 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 7.2 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.9 Hz, 2H), 7.20 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.85 (dd, J = 15.8, 4.9 Hz, 1H), 5.56 (dd, J = 15.8, 6.6 Hz, 1H), 5.45 (s, 1H), 4.55 (d, J = 11.3 Hz, 1H), 4.24 (d, J = 11.3 Hz, 1H), 4.26 (s, 2H), 4.07 (m, 1H), 3.80 (s, 3H), 3.58-3.57 (m, 2H), 3.33 (m, 1H), 3.14 (m, 1H), 2.74 (brs, 1H), 2.06-2.04 (m, 2H), 1.94-1.89 (m, 2H), 1.74 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.7, 139.5, 137.6, 134.1,

131.6, 130.1, 130.0, 129.7, 128.5, 126.8, 120.2, 114.3, 82.8, 73.2, 72.1, 70.4, 66.1, 55.7, 53.4, 36.0, 26.3, 23.4. MS(ESI): 495 (M^+ + Na), 338, 181.

Alcohol 17. To a solution of the alcohol **3** (296 mg, 0.63 mmol) in THF (6 mL) at -78 °C was added *n*BuLi (0.82 mL, 1.31 mmol; 1.6 M in hexane). The resulting orange suspension was stirred for 15 min. A solution of aldehyde **2** (90 mg, 0.205 mmol) was added dropwise. The resulting mixture was warmed to -40 °C and stirred for 2 h before quenching with saturated aqueous NH_4Cl. The mixture was diluted with EtOAc and the layers were separated. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and evaporated. The residue was chromatographed over silica gel (30% EtOAc/hexane) to furnish the hydroxy sulfone as a colorless oil (104 mg).

To a solution of the above hydroxysulfone in CH_2Cl_2 (3 mL) was sequentially added Et_3N (0.1 mL, 0.684 mmol), DMAP (5 mg) and Ac_2O (55 μL, 0.58 mmol). The resulting mixture was stirred at 23°C for 3 h. The mixture was washed with saturated aqueous $NaHCO_3$, 1 M $NaHSO_4$, and brine. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated to afford the diacetate as a colorless oil which was used for next reaction without further purification.

To a solution of the above diacetate in MeOH (3 mL) at -20 °C was added Na_2HPO_4 (64 mg, 0.45 mmol), followed by sodium amalgam (5% w/w, 750 mg).

The resulting suspension was vigorously stirred at -20 °C for 2 h. The mixture was warmed to 23 °C and stirred for 30 min. After this period, the mixture was quenched with saturated NH_4Cl. The mixture was decanted. Water and 25% EtOAc/hexane was added. The layers were separated. The aqueous layer was extracted with 25% EtOAc/hexane. The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated. The residue was chromatographed over silica gel (10 % EtOAc/hexane) to furnish the *E*-isomer **17** (52 mg, 34%) along with *Z*-isomer (16 mg, 10%). *E*-isomer **17**: $[\alpha]_d^{23}$-56 (*c* 0.54, $CHCl_3$); IR(thin film): 3503, 2926, 2855, 1513, 1035 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 5.82 (dd, *J* = 15.9, 5.1 Hz, 1H), 5.78(m, 1H), 5.69-5.59 (m, 3H), 5.43 (s, 1H), 5.32 (dd, *J* = 15.4, 8.1 Hz, 1H), 4.83 (s, 1H), 4.79 (s, 1H), 4.66 (d, *J* = 6.6 Hz, 1H), 4.55 (d, *J* = 11.4 Hz, 1H), 4.47 (d, *J* = 6.6 Hz, 1H), 4.30 (m, 1H), 4.26 (d, *J* = 11.4 Hz, 1H), 4.19 (s, 2H), 4.11-4.06 (m, 2H), 3.79 (s, 3H), 3.75-3.64 (m, 4H), 3.56 (m, 1H), 3.32 (s, 3H), 2.70 (brs, 1H), 2.29 (m, 2H), 2.17-1.80 (m, 10H), 1.71 (s, 3H), 1.68-1.60 (m, 2H), 1.13 (m, 1H), 0.88 (s, 9H), 0.86 (d, *J* = 6.3 Hz, 3H), 0.04 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.2, 144.2, 136.1, 132.6, 131.2, 130.0, 129.9, 129.8, 129.5, 127.2, 124.0, 119.7, 113.7, 113.3, 93.5, 82.0, 75.5, 73.0, 72.9, 69.9, 69.4, 65.6, 64.6, 59.8, 55.3, 55.2, 44.7, 42.8, 42.0, 36.7, 35.6, 35.5, 31.5, 26.5, 25.9, 22.9, 19.1, 18.3, -5.4. MS(ESI): 777 (M^+ + Na), 693, 383, 181. *Z*-isomer: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.5 Hz, 2H), 6.87 (m, 2H), 5.82 (dd, *J* = 15.9, 5.1 Hz, 1H), 5.78(m, 1H), 5.69-5.59 (m, 3H), 5.43 (s, 1H), 5.34 (t, *J* = 9.4 Hz, 1H), 4.86 (s,

1H), 4.80 (s, 1H), 4.64 (d, J = 6.8 Hz, 1H), 4.54 (d, J = 11.4 Hz, 1H), 4.45 (d, J = 6.8 Hz, 1H), 4.29 (m, 1H), 4.27 (d, J = 11.4 Hz, 1H), 4.19 (s, 2H), 4.08 (m, 1H), 3.80 (s, 3H), 3.79-3.50 (m, 4H), 3.43 (m, 1H), 3.31 (s, 3H), 2.67 (brs, 1H), 2.29 (m, 2H), 2.17-1.80 (m, 10H), 1.72 (s, 3H), 1.68-1.60 (m, 2H), 1.08 (m, 1H), 0.88 (s, 9H), 0.84 (d, J = 6.3 Hz, 3H), 0.05 (s, 6H).

Phosphonate 18. To a mixture of Alcohol **17** (26 mg, 0.035 mmol) and bis-(ß,ß,ß-trifluoroethyl)phosphonoacetic acid (24.2 mg, 0.08 mmol) in THF (3 mL) was added sequentially iPr$_2$NEt (28 µL, 0.16 mmol) and 2, 4, 6-trichlorobenzoyl chloride (19 µL, 0.10 mmol). The resulting mixture was stirred at 23 °C for 30 min. After this period, the mixture was concentrated and the residue was dissolved in benzene (3 mL). DMAP (27 mg, 0.24 mmol) was added. The resulting white suspension was stirred at 23°C for 30 min. The mixture was diluted with EtOAc and washed with saturated $NaHCO_3$, 1M $NaHSO_4$ and brine. The aqueous was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated. The residue was dissolve in AcOH-THF-H_2O (3:1:1) (2 mL). The resulting mixture was stirred at 23°C for 3 h. The mixture was poured into water and extracted with 50% EtOAc/hexane (3 X 10 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 and evaporated. The residue was chromatographed over silica gel (40% EtOAc/hexane) to furnish the phosphonate **18** (32 mg, 100%) as a colorless oil. $[\alpha]_d^{23}$-88 (c 0.08, $CHCl_3$); IR(thin film): 3500, 2927, 1739, 1299, 1265, 1174,

1070 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.84 (dd, *J* = 15.7, 5.3 Hz, 1H), 5.80 (m, 1H), 5.66 (m, 1H), 5.62 (dd, *J* = 15.7, 7.5 Hz, 1H), 5.48 (dd, *J* = 15.4, 7.8 Hz, 1H), 5.45 (s, 1H), 5.33 (dd, *J* = 15.4, 7.6 Hz, 1H), 4.99 (m, 1H), 4.81 (s, 1H), 4.78 (s, 1H), 4.58 (d, *J* = 6.8 Hz, 1H), 4.54 (d, *J* = 11.6 Hz, 1H), 4.43-4.37 (m, 6H), 4.24 (d, *J* = 11.6 Hz, 1H), 4.18 (s, 2H), 4.08-4.05 (m, 2H), 3.86-3.75 (m, 4H), 3.31 (s, 3H), 3.78 (s, 3H), 3.14 (dd, *J* = 20.7, 3.4 Hz, 1H), 2.42 (m, 1H), 2.34-2.26 (m, 3H), 2.17-1.85 (m, 10H), 1.71 (s, 3H), 1.71-1.60 (m, 2H), 1.09 (m, 1H), 0.88 (d, *J* = 5.8 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 164.3, 159.3, 144.0, 136.3, 133.9, 131.2, 129.8, 129.6, 129.3, 127.7, 126.2, 124.2, 119.7, 113.8, 93.5, 78.3, 76.7, 73.1, 70.8, 70.1, 65.6, 62.6, 60.6, 55.3, 55.2, 44.7, 42.2, 41.8, 35.8, 35.6, 34.5, 33.1, 31.0, 29.7, 26.7, 22.9, 19.3.

Macrolactone 19 and 20. To a solution of the above phosphonate **18** (30 mg, 0.035 mmol) in wet CH_2Cl_2 (2.5 mL) was added Dess-Martin periodiane (40 mg, 0.094 mmol). After 10 min, the resulting white suspension was subjected to direct silica gel chromatography (25% EtOAc/hexane) to furnish the aldehyde (25.2 mg, 79%) as a colorless oil.

To a solution of 18-crown-6 (53 mg, 0.2 mmol) in toluene (27 mL) was added anhydrous K_2CO_3 (27.6 mg, 0.2 mmol). The resulting suspension was stirred at 23°C for 3 h. The suspension was cooled to -20 °C and a solution of the above aldehyde in toluene (5 mL) was added dropwise. The mixture was stirred

at -20 °C for 30 min and then at 0°C for 2.5 h. The mixture was diluted with EtOAc, washed with water and brine, and the combined aqueous phase was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated. Silica gel chromatography of the residue (10% EtOAc/hexane) afforded the *Z*-isomer **20** (5.2 mg) and *E*-isomer **19** (10 mg) (combined yield 84%). *Z*-isomer **20**: $[\alpha]_d^{23}$-120 (c 0.38, $CHCl_3$); IR(thin film): 2924, 2852, 1719, 1513, 1248 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.34 (m, 1H), 5.89 (d, *J* = 11.6 Hz, 1H), 5.83 (dd, *J* = 15.8, 5.5 Hz, 1H), 5.84 (m, 1H), 5.70 (d, *J* = 10.6 Hz, 1H), 5.62-5.53 (m, 2H), 5.43 (s, 1H), 5.40 (m, 1H), 5.06 (m, 1H), 4.82 (s, 1H), 4.76 (s, 1H), 4.64 (d, *J* = 6.8 Hz, 1H), 4.58 (d, *J* = 11.8 Hz, 1H), 4.46 (d, *J* = 6.8 Hz, 1H), 4.30 (d, *J* = 11.8 Hz, 1H), 4.19 (s, 2H), 4.15-4.06 (m, 3H), 3.86 (m, 1H), 3.80 (s, 3H), 3.61 (m, 1H), 3.31 (s, 3H), 2.44-1.81 (m, 12H), 1.70 (s, 3H), 1.50 (m, 1H), 1.21 (m, 1H), 1.14 (m, 1H), 0.84 (d, *J* = 6.8 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.7, 159.4, 147.5, 144.8, 135.9, 133.3, 131.7, 130.6, 129.6, 129.0, 126.9, 125.1, 121.9, 120.1, 114.1, 94.0, 79.7, 74.9, 74.2, 73.7, 72.0, 70.6, 67.6, 66.0, 55.7, 44.9, 43.1, 42.3, 36.1, 34.5, 33.3, 31.6, 28.7, 23.3, 20.2. MS(ESI): 685 (M^+ + Na), 601, 583. *E*-isomer **19**: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 6.90 (m, 2H), 6.87 (d, *J* = 8.6 Hz, 1H), 5.86 (d, *J* = 17.0 Hz, 1H), 5.89-5.83 (m, 2H), 5.71-5.58 (m, 3H), 5.49 (dd, *J* = 15.5, 7.1 Hz, 1H), 5.45 (s, 1H), 5.14 (m, 1H), 4.84 (s, 1H), 4.77 (s, 1H), 4.65 (d, *J* = 6.8 Hz, 1H), 4.61 (d, *J* = 12.0 Hz, 1H), 4.47 (d, *J* = 6.8 Hz, 1H), 4.37 (m, 1H), 4.35 (d, *J*

= 12.0 Hz, 1H), 4.21 (brs, 1H), 4.15 (m, 1H), 4.10 (m, 1H), 3.89 (t, J = 6.2 Hz, 1H), 3.82 (s, 3H), 3.70 (m, 1H), 3.30 (s, 3H), 2.56 (m, 1H), 2.36-2.16 (m, 5H), 2.04 (d, J = 14.9 Hz, 1H), 1.95-1.77 (m, 6H), 1.73 (s, 3H), 1.55 (t, J = 12.9 Hz, 1H), 1.07 (dd, J = 12.9, 10.5 Hz, 1H), 0.89 (m, 1H), 0.80 (d, J = 5.7 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.6, 159.5, 146.5, 145.0, 135.9, 135.0, 131.7, 130.7, 129.7, 129.2, 127.9, 127.0, 126.1, 123.4, 120.1, 114.1, 94.4, 79.8, 74.9, 74.5, 73.7, 72.0, 70.5, 66.0, 65.3, 55.7, 45.0, 43.9, 41.8, 36.9, 36.1, 32.7, 26.2, 23.3, 18.6. MS(ESI): 685 (M^+ + Na), 601, 583.

Isomerization of *E*-macrolactone 19. A solution of macrolactone **19** (4.8 mg, 7.3 x 10^{-3} mmol) in Et_2O (3 mL) was irridated under UV for 50 min in a Rayonet photochemical reactor. After this period, the mixture was concentrated. The residue was purified by silica gel chromatography (10% EtOAc/Hexanes) to furnish *Z*-macrolactone **20** (1.6 mg, 33%) along with *E*-macrolactone **19** (1.6 mg, 33%).

Laulimalide 1. A mixture of macrolactone **20** (15.6 mg, 0.024 mmol) and PPTS (81 mg, 0.32 mmol) in *tert*-butyl alcohol (1 mL) was heated at 83 °C for 8 h. The mixture was cooled to 23 °C and poured into water. The resulting mixture was extracted with 25% EtOAc/hexane (3 x 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and evaporated. The residue was chromatographed over silica gel eluting with 20% EtOAc/hexane

to furnish the allylic alcohol as a colorless oil (6.5 mg, 45%). $[\alpha]_d^{23}$-125 (*c* 0.14, $CHCl_3$); IR(thin film): 3500, 2924, 1718, 1513, 1249 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.31 (m, 1H), 5.91(d, *J* = 11.6 Hz, 1H), 5.84 (dd, *J* = 15.6, 6.2 Hz, 1H), 5.83 (m, 1H), 5.70 (d, *J* = 10.6 Hz, 1H), 5.63-5.58 (m, 3H), 5.43 (s, 1H), 5.06 (m, 1H), 4.84 (s, 2H), 4.59 (d, *J* = 11.8 Hz, 1H), 4.31 (d, *J* = 11.8 Hz, 1H), 4.19 (s, 2H), 4.15-4.06 (m, 3H), 3.85 (m, 1H), 3.80 (s, 3H), 3.55 (m, 1H), 2.33-1.76 (m, 12H), 1.65 (s, 3H), 1.60-1.58 (m, 2H), 1.28-1.21 (m, 2H), 1.12 (m, 1H), 0.79 (d, *J* = 6.8 Hz, 3H). MS(ESI): 641 (M^+ + Na), 601, 583, 463.

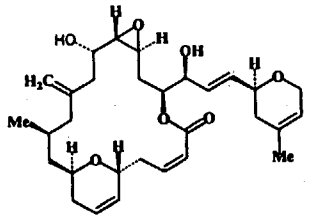
To a suspension of powdered 4 Å molecular sieves (50 mg) in CH_2Cl_2 (1 mL) at -20 °C were sequentially added diethyl D-tartrate (16.4 mg, 0.08 mmol) and $Ti(O\textit{i}Pr)_4$ (20 μl, 0.067 mmol). The resulting mixture was stirred for 15 min at -20 °C, and then *tert*-butyl hydroperoxide (20 μl, 0.13 mmol; 6.7 M in *n*-decane) was added dropwise. The mixture was stirred for 15 min and then a solution of the above alcohol (6.5 mg, 0.011 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The resulting mixture was stirred for 1 h at -20 °C. After this period, a mixture of 4 *N* NaOH (1 mL) and brine (1 mL) was added and the resulting mixture was stirred at 0 °C for 1 h. The layers were separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated to give a residue which was used for next reaction immediately. An analytical sample was isolated by silica gel chromatography (20% EtOAc/hexanes). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J*

= 8.6 Hz, 2H), 6.86 (dd, *J* = 6.8, 2.0 Hz, 2H), 6.42 (dt, *J* = 11.3, 3.6 Hz, 1H), 5.91-5.81(m, 3H), 5.68 (d, *J* = 10.2 Hz, 1H), 5.59 (ddd, J = 15.8, 6.9, 1.1 Hz, 1H), 5.43 (s, 1H), 5.21 (dd, *J* = 10.4, 5.1 Hz, 1H), 4.84 (s, 1H), 4.83 (s, 1H), 4.59 (d, *J* = 11.7 Hz, 1H), 4.32 (d, *J* = 11.7 Hz, 1H), 4.30 (m, 1H), 4.19 (s, 2H), 4.09-4.03 (m, 3H), 3.87 (t, *J* = 6.0 Hz, 1H), 3.80 (s, 3H), 3.75 (m, 1H), 3.04 (m, 1H), 2.87 (t, *J* = 2.5 Hz, 1H), 2.40-1.74 (m, 12H), 1.59 (s, 3H), 1.45-1.30 (m, 3H), 0.82 (d, *J* = 6.3 Hz, 3H).

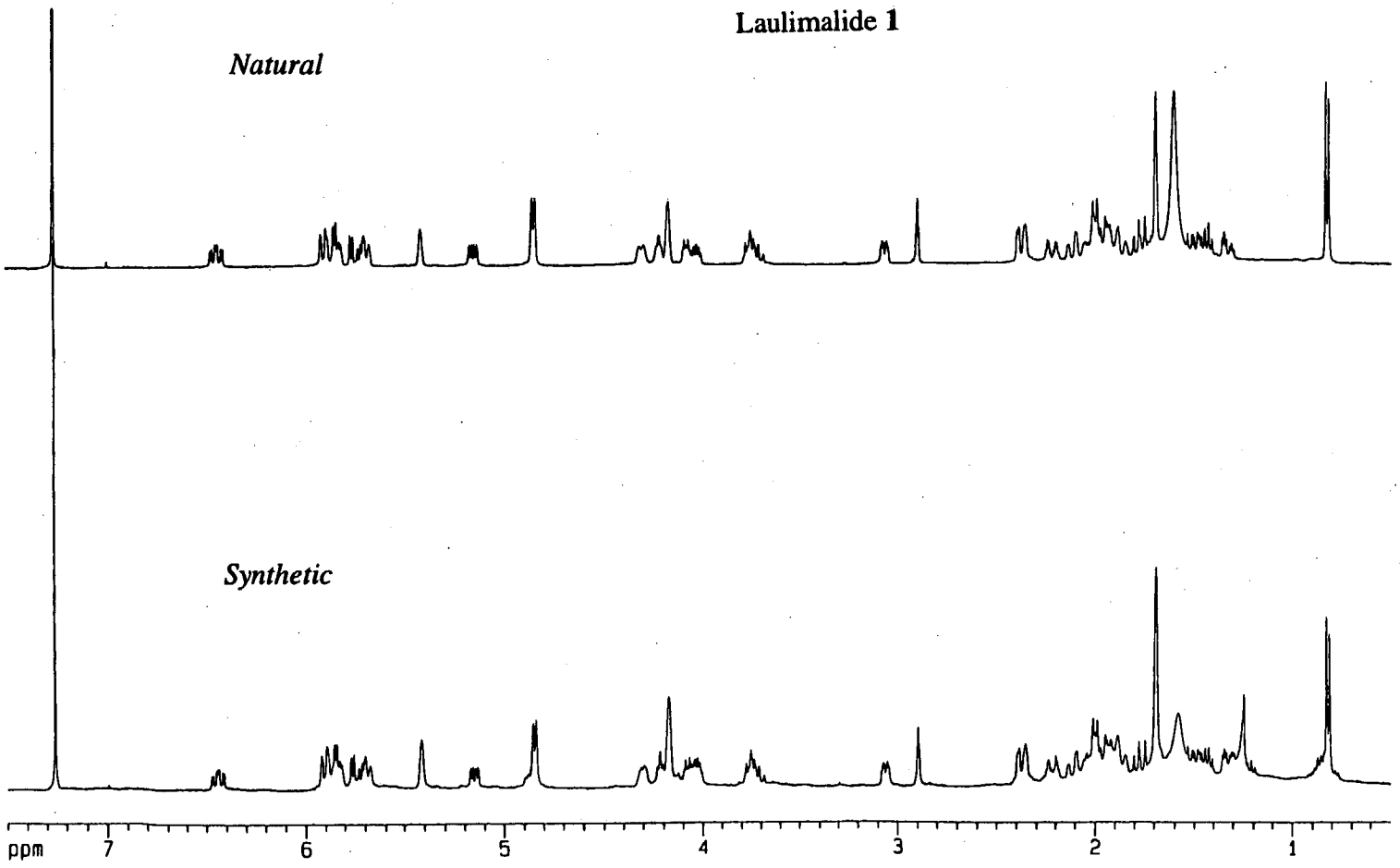
To a suspension of the above epoxide in CH_2Cl_2 (1 mL) and pH 7 buffer (50 μl) was added DDQ (8 mg, 0.0352 mmol). The green mixture was stirred at 23 °C for 2 h. The resulting orange suspension was then washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated. The residue was chromatographed over silica gel eluting with 25% EtOAc/hexane to give laulimalide **1** as a colorless oil (2.6 mg, 48%). $[\alpha]_D^{23}$-196 (c 0.23, $CHCl_3$); IR(thin film): 3427, 2923, 1716, 1644, 1167 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.45 (m, 1H), 5.91 (d, *J* = 10.3 Hz, 1H), 5.84 (ddd, *J* = 16.2, 5.3, 0.9 Hz, 1H), 5.83 (m, 1H), 5.74 (ddd, *J* = 16.2, 6.2, 0.9 Hz, 1H), 5.69 (brd, *J* = 10.1 Hz, 1H), 5.42 (s, 1H), 5.16 (ddd, *J* = 11.2, 5.2, 1.6 Hz, 1H), 4.86 (s, 1H), 4.85 (s, 1H), 4.31 (brd, *J* = 9.1 Hz, 1H), 4.22 (m, 1H), 4.17 (brs, 2H), 4.07 (m, 1H), 4.03 (m, 1H), 3.76 (m, 1H), 3.72 (m, 1H), 3.08 (m, 1H), 2.90 (t, *J* = 2.6 Hz, 1H), 2.38 (m, 1H), 2.36 (m, 1H), 2.22 (m, 1H), 2.12 (brd, *J* = 15.7 Hz, 1H), 2.02-1.72 (m, 6H), 1.69 (s, 3H), 1.49 (m, 1H), 1.45 (m ,1H), 1.33 (m, 1H), 0.82 (d, *J* = 6.3 Hz, 3H); ^{13}C-

NMR (125 MHz, $CDCl_3$) δ 166.5, 150.7, 145.3, 134.3, 131.6, 129.1, 128.9, 125.6, 120.9, 120.1, 113.0, 73.9, 73.5, 73.4, 72.7, 68.3, 67.0, 66.1, 61.1, 52.5, 46.0, 43.8, 37.5, 36.0, 34.2, 33.8, 32.1, 29.9, 23.3, 21.2. MS(ESI): 515 (M^+ + H), 497, 479, 181.

Proton standard parameters, BBI probe



Laulimalide **1**



Current Data Parameters

NAME	N928
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

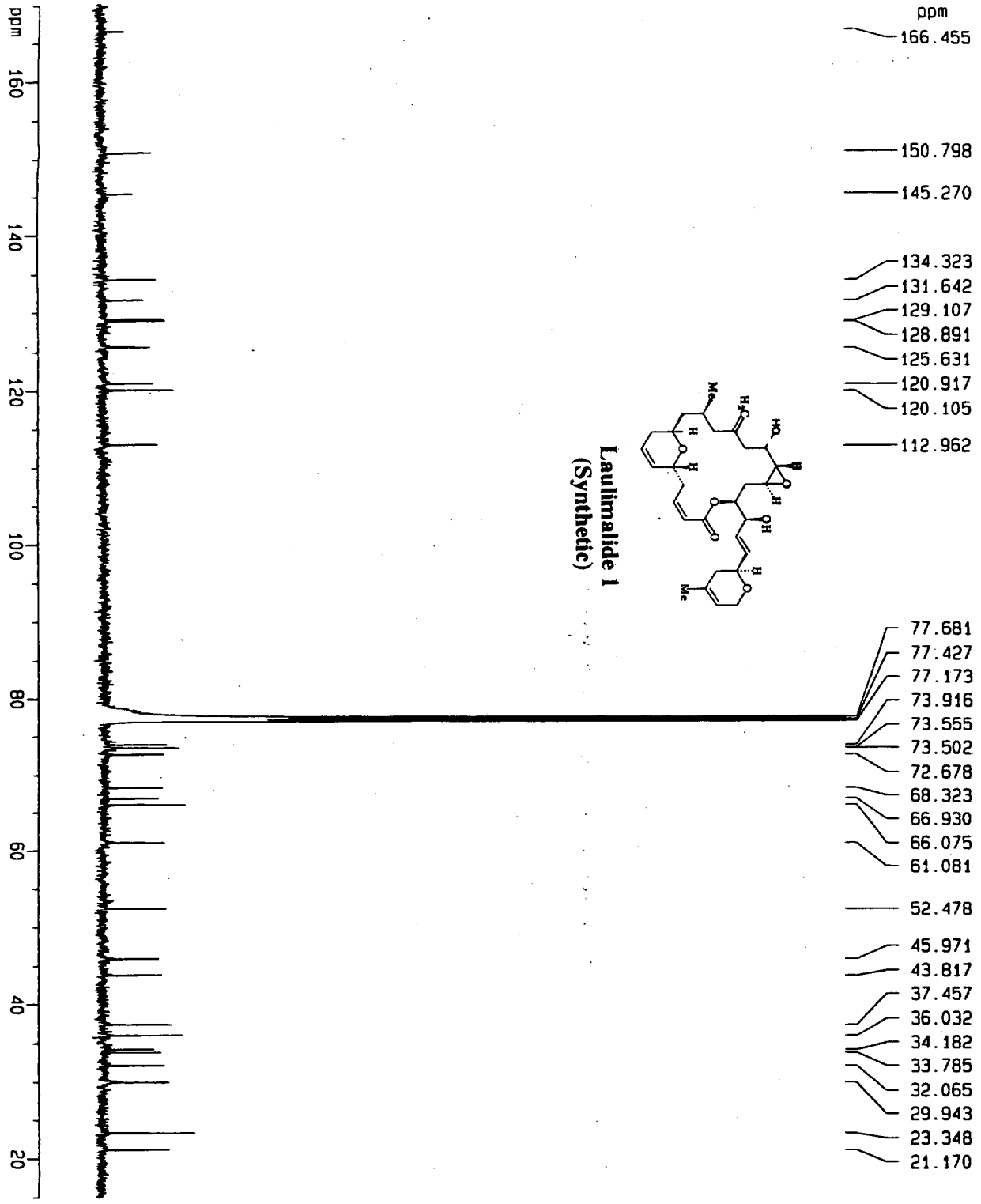
Date_	20000923
Time	19.11
INSTRUM	spect
PROBHD	5 mm BBI 1H-B
PULPROG	zg
TD	16384
SOLVENT	CDCl3
NS	16
DS	2
SWH	4789.272 Hz
FIDRES	0.292314 Hz
AQ	1.7105396 sec
RG	128
DW	104.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
P1	4.00 usec
SFO1	400.1342000 MHz
NUC1	1H
PL1	0.00 dB

F2 - Processing parameters

SI	8192
SF	400.1320090 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
F1P	7.500 ppm
F1	3000.99 Hz
F2P	0.500 ppm
F2	200.07 Hz
PPMCM	0.35000 ppm/cm
HZCM	140.04620 Hz/cm

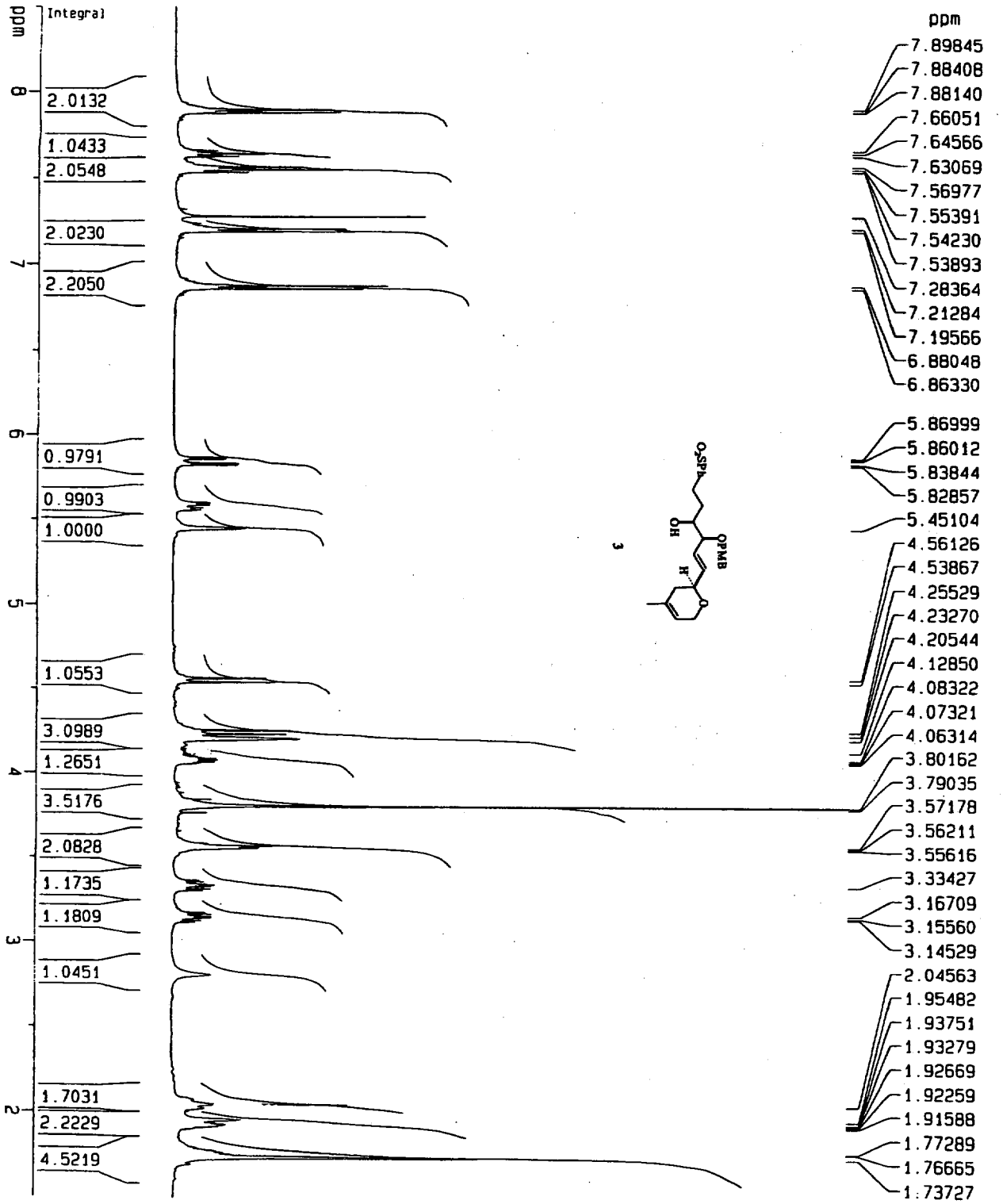



```
Current Data Parameters
NAME                  N922
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_              20000921
Time                 12.15
INSTRUM              spect
PROBHD     5 mm BBO BB-1
PULPROG              zgpg
TD                   32768
SOLVENT              CDCl3
NS                    8656
DS                       2
SWH              30303.031 Hz
FIDRES               0.924775 Hz
AQ                0.5407220 sec
RG                    13004
DW                 16.500 usec
DE                  6.00 usec
TE                  300.0 K
d11              0.03000000 sec
d12              0.00002000 sec
PL13                22.00 dB
D1               2.00000000 sec
CPDPRG2                waltz16
PCPD2                80.00 usec
SFO2           500.1320000 MHz
NUC2                       1H
PL2                  3.00 dB
PL12                22.00 dB
P1                   3.80 usec
SFO1           125.7715724 MHz
NUC1                      13C
PL1                  3.00 dB

F2 - Processing parameters
SI                       32768
SF             125.7577390 MHz
WDW                         EM
SSB                          0
LB                    3.00 Hz
GB                           0
PC                        1.40

1D NMR plot parameters
CX                      20.00 cm
F1P                   170.000 ppm
F1                  21378.81 Hz
F2P                   15.000 ppm
F2                  1886.37 Hz
PPMCM                7.75000 ppm/cm
HZCM               974.62244 Hz/cm
```



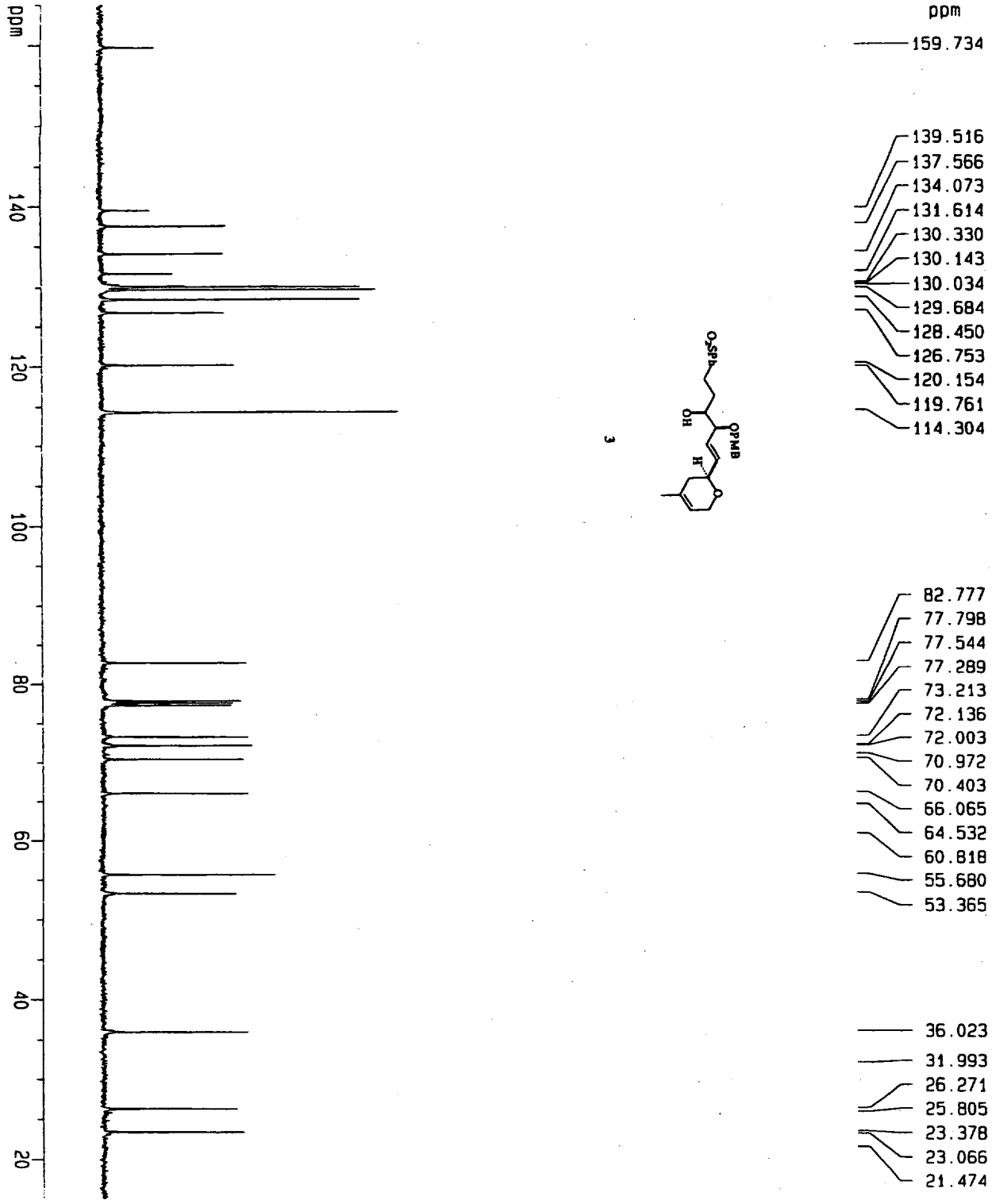
Proton standard parameters, BBO probe

```
Current Data Parameters
NAME                  3
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_              20000627
Time                  17.48
INSTRUM               spect
PROBHD     5 mm BBO BB-1
PULPROG               zg
TD                 32768
SOLVENT           CDCl3
NS                    8
DS                    2
SWH             6009.615 Hz
FIDRES          0.183399 Hz
AQ              2.7263477 sec
RG                 25.4
DW                 83.200 usec
DE                  6.00 usec
TE                300.0 K
D1                1.00000000 sec
P1                   5.00 usec
SFO1           500.1327507 MHz
NUC1                  1H
PL1                3.00 dB

F2 - Processing parameters
SI                 16384
SF             500.1300000 MHz
WDW                   EM
SSB                   0
LB                 0.20 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX                20.00 cm
F1P                8.500 ppm
F1              4251.10 Hz
F2P                1.500 ppm
F2               750.20 Hz
PPMCM          0.35000 ppm/cm
HZCM           175.04550 Hz/cm
```



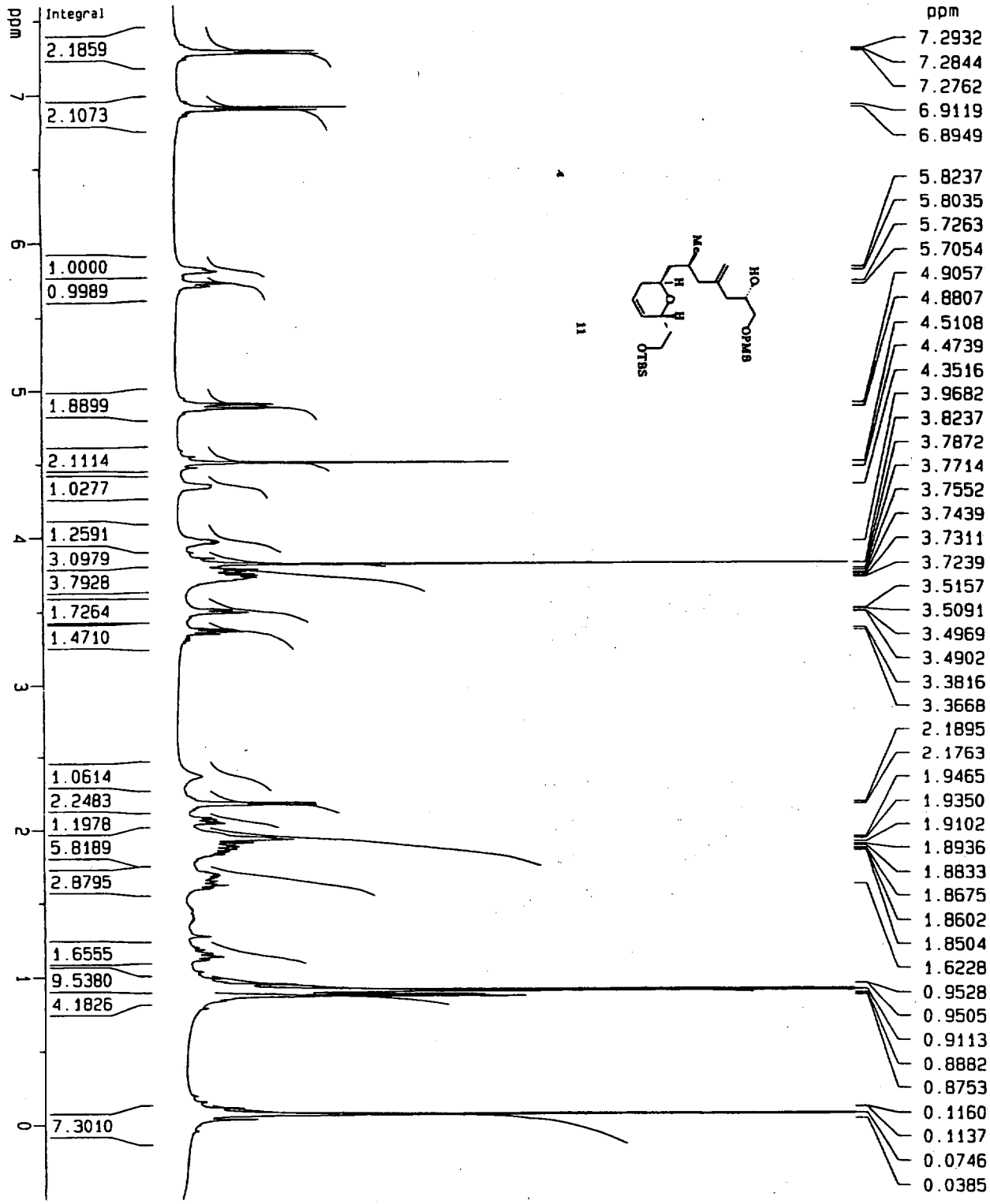
Carbon-13 standard parameters, BBO probe

```
Current Data Parameters
NAME                  3
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20000627
Time              17.52
INSTRUM            spect
PROBHD  5 mm BBO BB-1
PULPROG           zgpg
TD                32768
SOLVENT           CDCl3
NS                   86
DS                    2
SWH           30303.031 Hz
FIDRES        0.924775 Hz
AQ            0.5407220 sec
RG                 8192
DW               16.500 usec
DE                6.00 usec
TE              300.0 K
D11           0.03000000 sec
D12           0.00002000 sec
PL13             22.00 dB
D1            2.00000000 sec
CPDPRG2             waltz16
PCPD2              80.00 usec
SFO2          500.1320000 MHz
NUC2                   1H
PL2               3.00 dB
PL12             22.00 dB
P1                3.00 usec
SFO1          125.7715724 MHz
NUC1                  13C
PL1               0.00 dB

F2 - Processing parameters
SI                   32768
SF            125.7577390 MHz
WDW                     EM
SSB                      0
LB                3.00 Hz
GB                       0
PC                1.40

1D NMR plot parameters
CX                20.00 cm
F1P              165.000 ppm
F1             20750.03 Hz
F2P              15.000 ppm
F2              1886.37 Hz
PPMCM          7.50000 ppm/cm
HZCM          943.18292 Hz/cm
```



Proton standard parameters, BBO probe

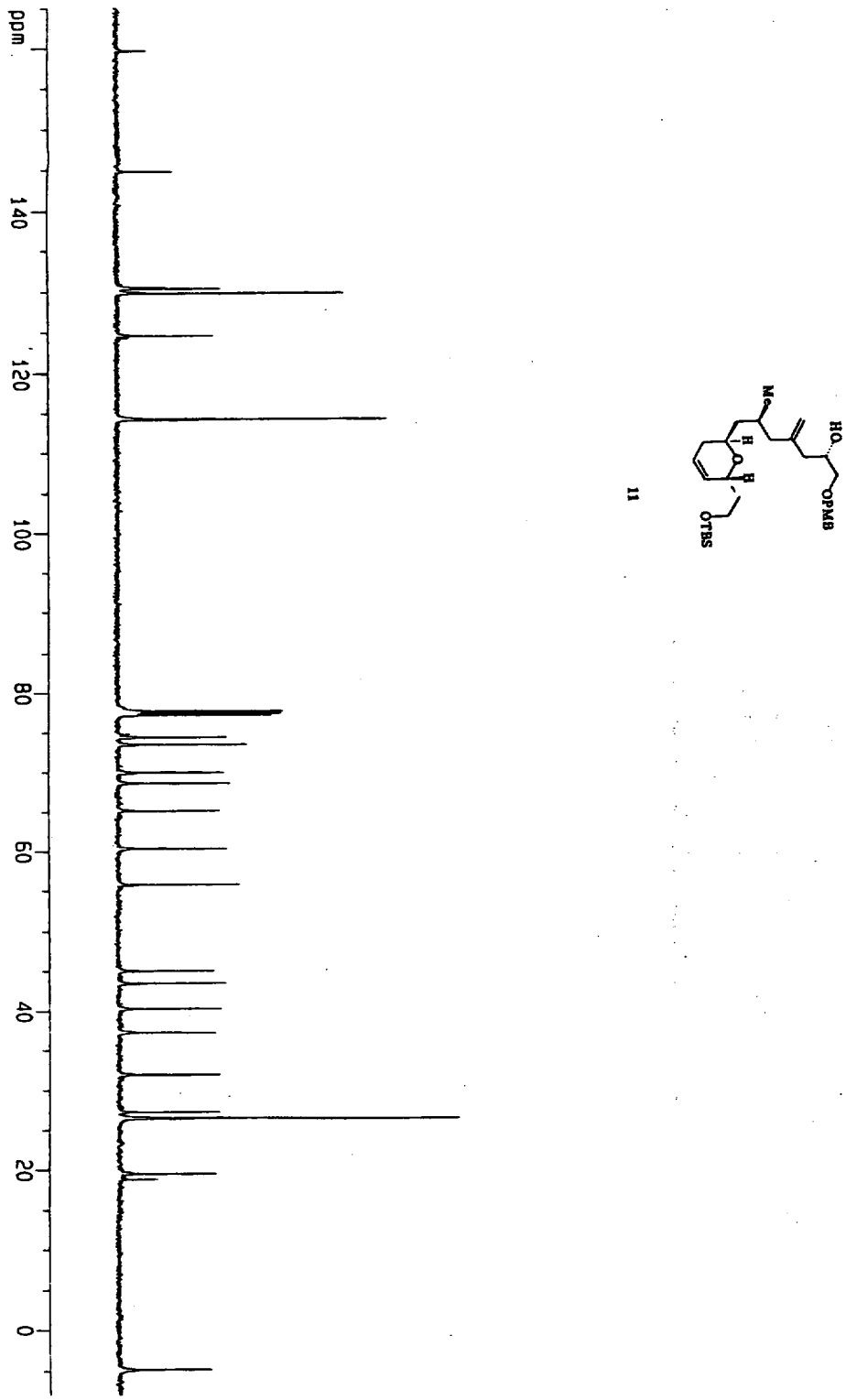
```
Current Data Parameters
NAME                  L100
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_              20000326
Time                 17.14
INSTRUM              spect
PROBHD  5 mm BBO BB-1H
PULPROG                 zg
TD                   32768
SOLVENT              CDCl3
NS                       8
DS                       2
SWH                6009.615 Hz
FIDRES             0.183399 Hz
AQ                 2.7263477 sec
RG                      20.2
DW                   83.200 usec
DE                    6.00 usec
TE                   300.0 K
D1                1.00000000 sec
P1                    5.50 usec
SFO1           500.1327507 MHz
NUC1                     1H
PL1                   0.00 dB

F2 - Processing parameters
SI                      16384
SF             500.1300000 MHz
WDW                        EM
SSB                         0
LB                       0.20 Hz
GB                          0
PC                       1.00

1D NMR plot parameters
CX                      20.00 cm
F1P                   7.600 ppm
F1                 3800.99 Hz
F2P                  -0.500 ppm
F2                 -250.07 Hz
PPMCM              0.40500 ppm/cm
HZCM              202.55266 Hz/cm
```

Carbon-13 standard parameters, BBO probe

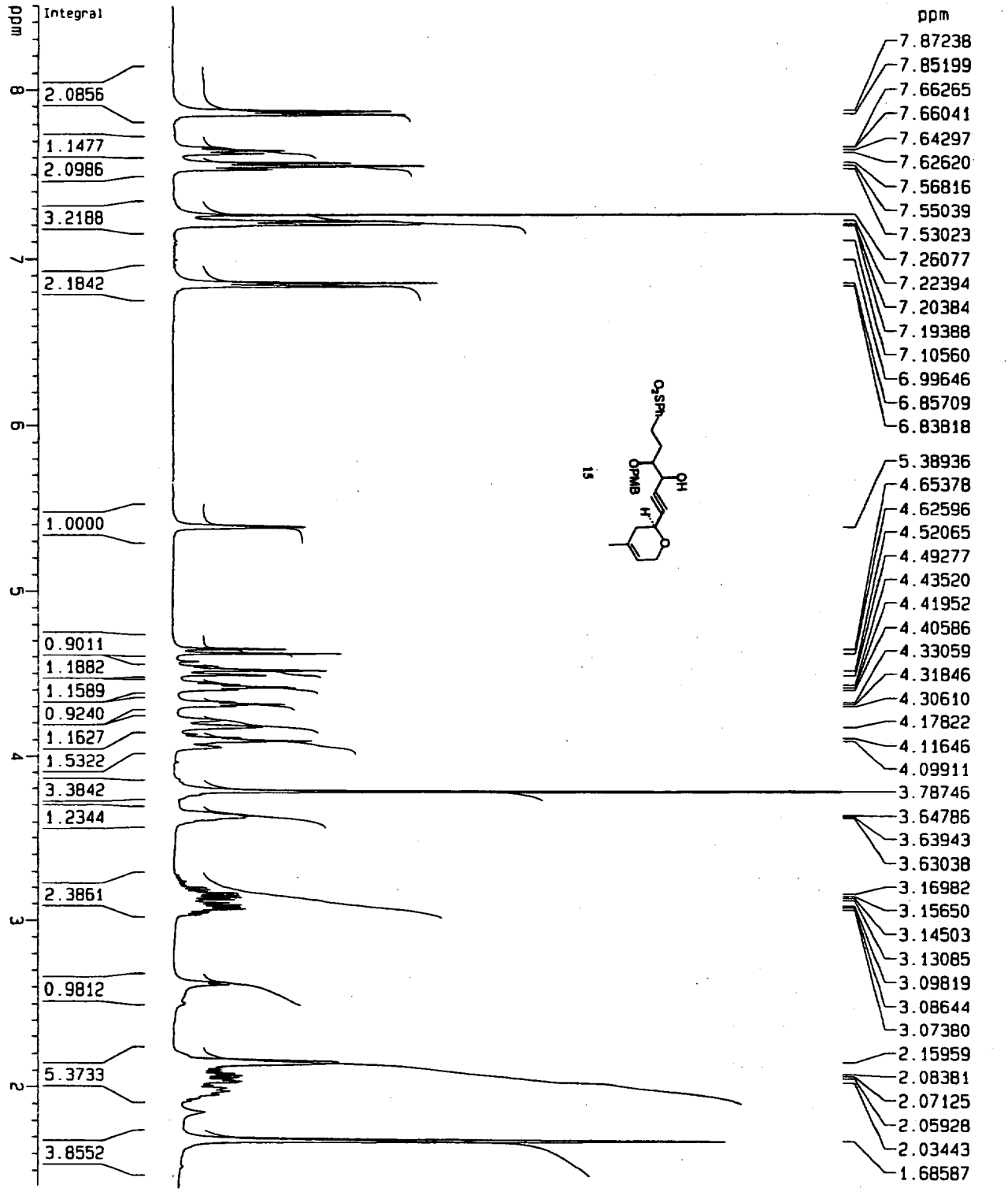



```
Current Data Parameters
NAME                  L100
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_              20000326
Time                 17.23
INSTRUM              spect
PROBHD  5 mm BBO BB-1H
PULPROG              zpg9
TD                  32768
SOLVENT              CDCl3
NS                     256
DS                       2
SWH              30303.031 Hz
FIDRES           0.924775 Hz
AQ               0.5407220 sec
RG                    8192
DW                 16.500 usec
DE                  6.00 usec
TE                 300.0 K
d11              0.03000000 sec
d12              0.00002000 sec
PL13                17.20 dB
D1               2.00000000 sec
CPDPRG2               waltz16
PCPD2                80.00 usec
SFO2          500.1320000 MHz
NUC2                     1H
PL2                 0.00 dB
PL12                17.20 dB
P1                  3.00 usec
SFO1          125.7715724 MHz
NUC1                    13C
PL1                 0.00 dB

F2 - Processing parameters
SI                     32768
SF            125.7577390 MHz
WDW                       EM
SSB                        0
LB                   3.00 Hz
GB                         0
PC                      1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                165.000 ppm
F1               20750.03 Hz
F2P                 -8.000 ppm
F2               -1006.06 Hz
PPMCM              8.65000 ppm/cm
HZCM          1087.80457 Hz/cm
```



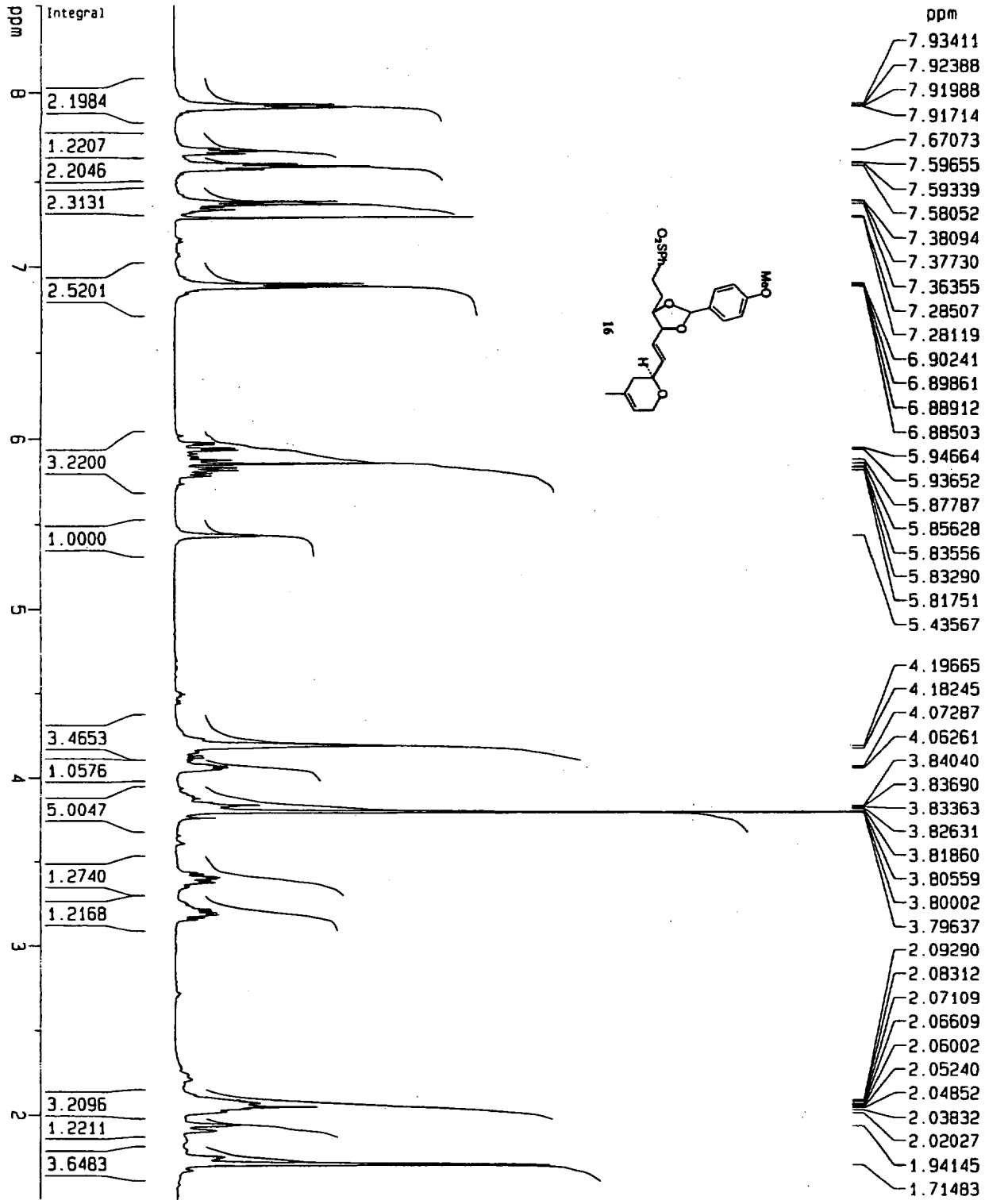
Proton standard parameters, BBI probe

Current Data Parameters
NAME M156
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20000624
Time 17.39
INSTRUM spect
PROBHD 5 mm BBI 1H-B
PULPROG zg
TD 16384
SOLVENT CDCl3
NS 8
DS 2
SWH 4789.272 Hz
FIDRES 0.292314 Hz
AQ 1.7105396 sec
RG 16
DW 104.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
P1 4.00 usec
SFO1 400.1342000 MHz
NUC1 1H
PL1 0.00 dB

F2 - Processing parameters
SI 8192
SF 400.1320090 MHz
MDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 8.500 ppm
F1 3401.12 Hz
F2P 1.400 ppm
F2 560.18 Hz
PPMCM 0.35500 ppm/cm
HZCM 142.04686 Hz/cm



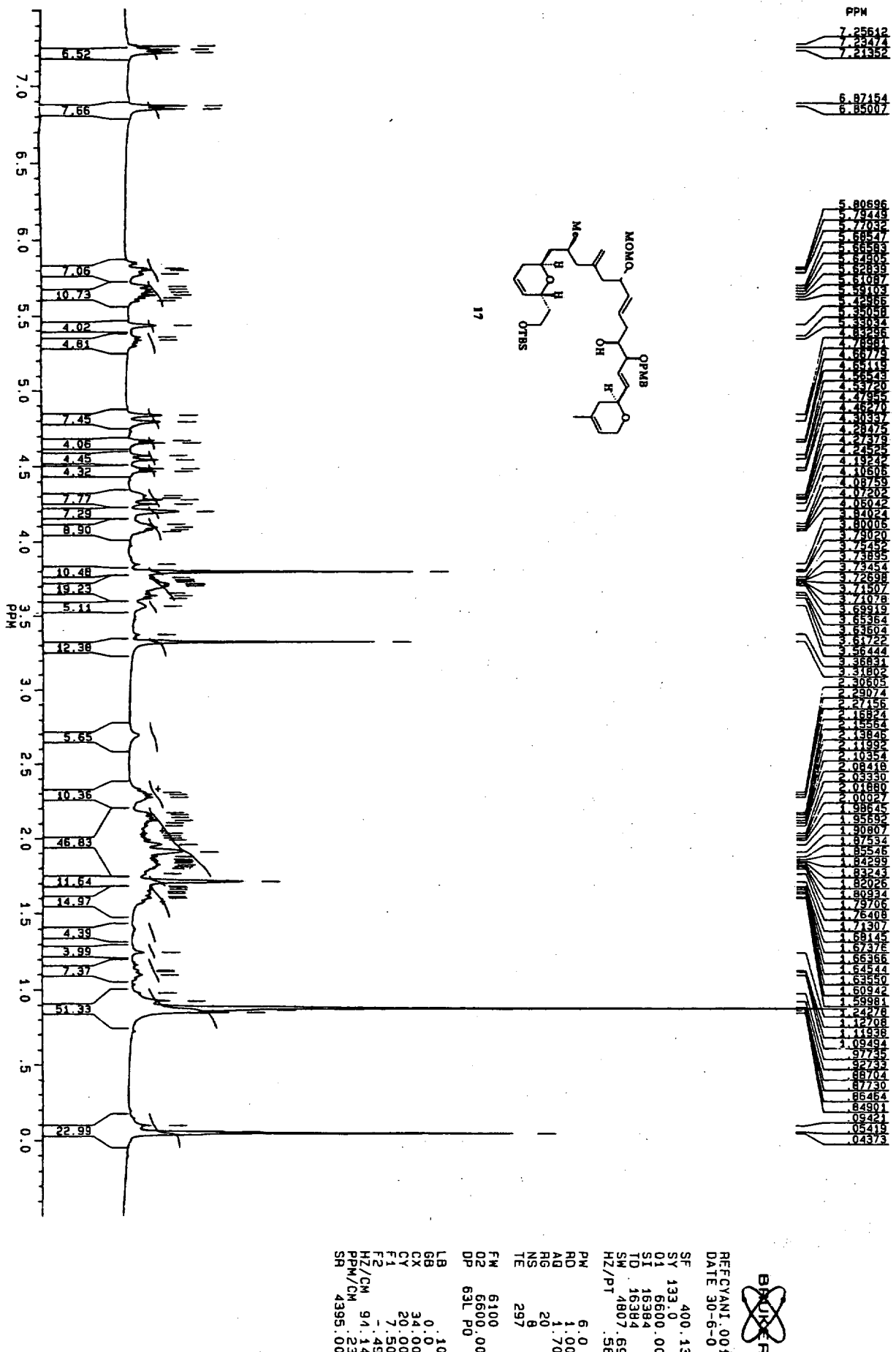
Proton standard parameters, BBO probe

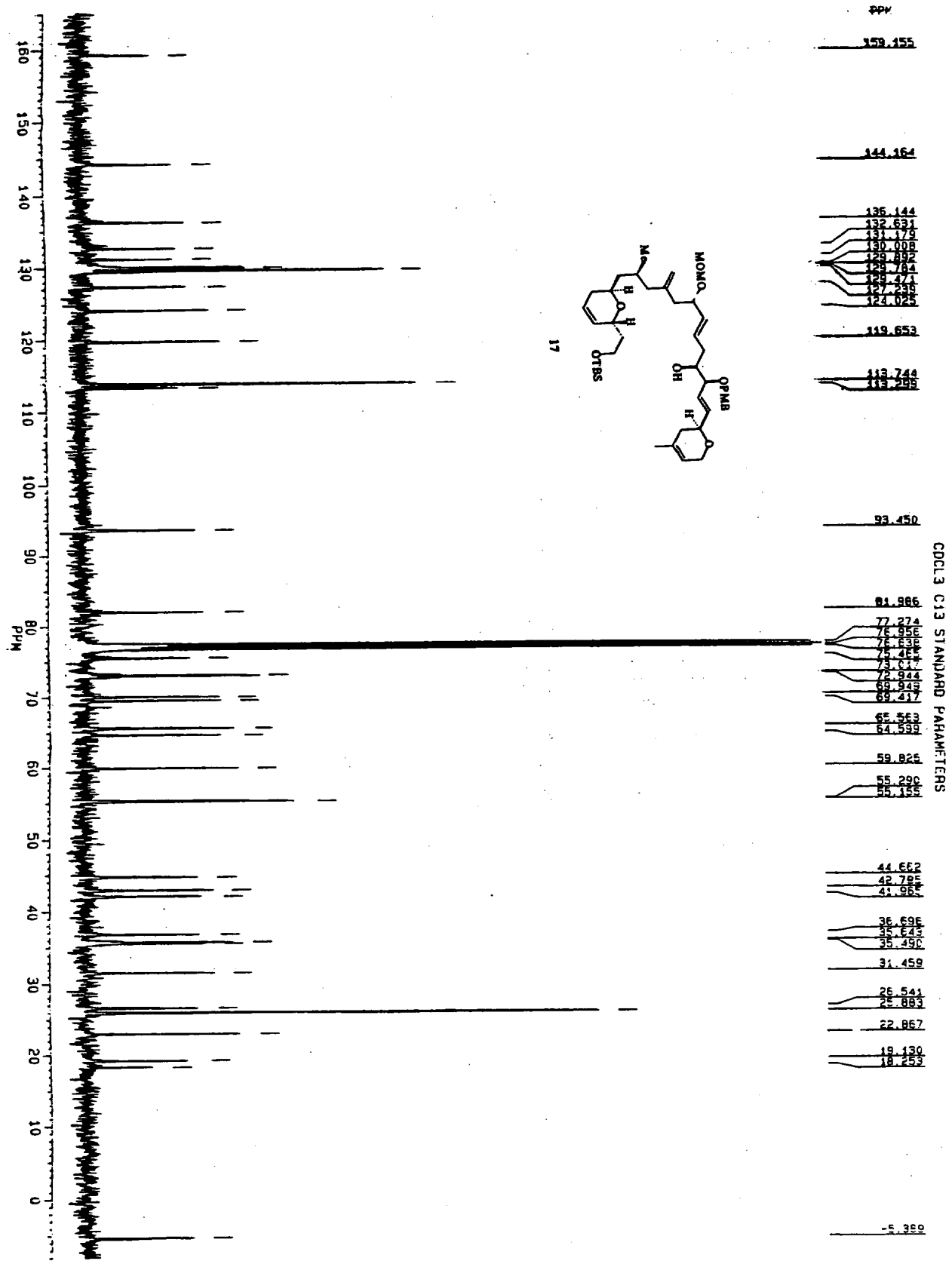
Current Data Parameters
NAME N400
EXPNO 1
PROCNO 1

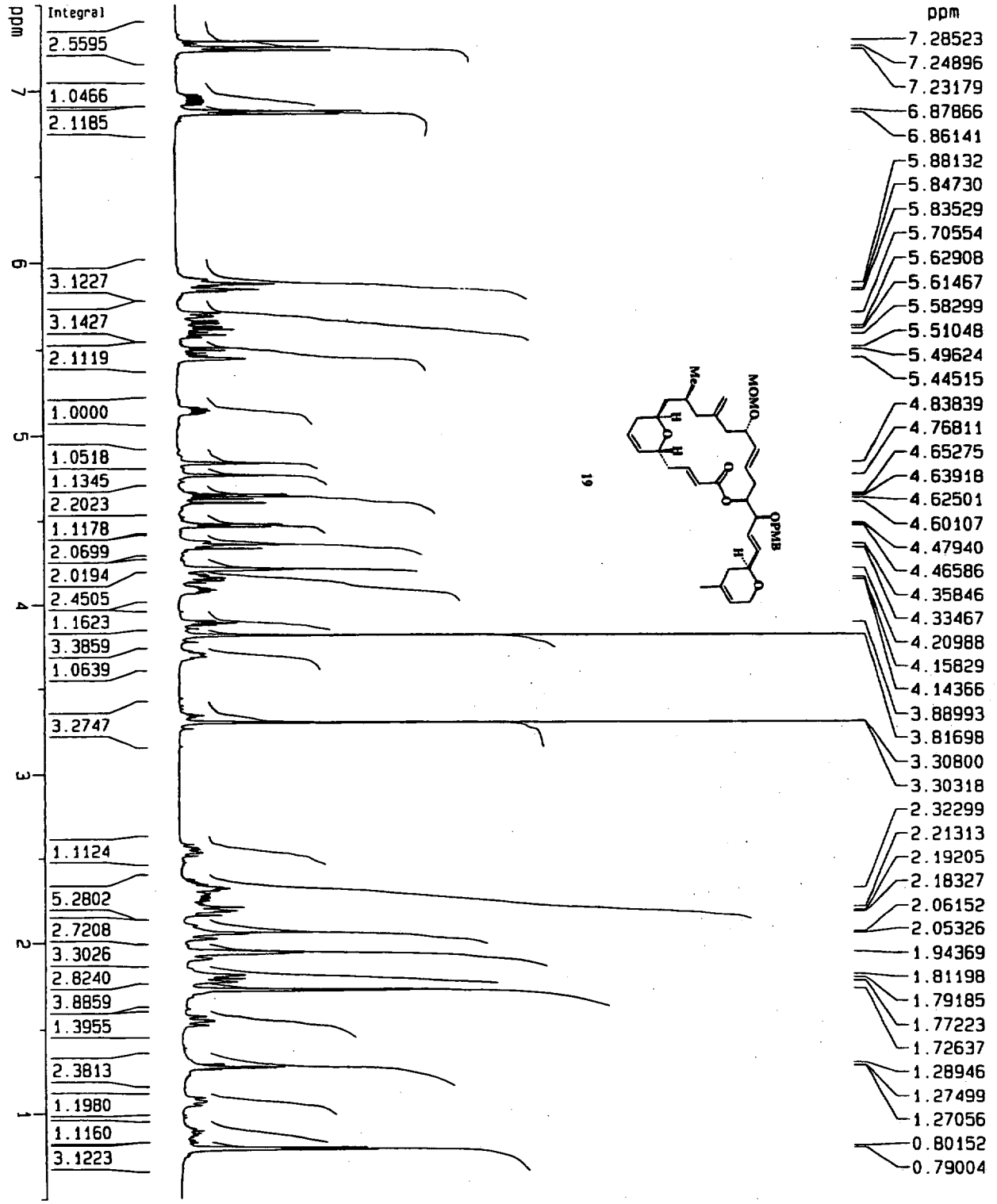
F2 - Acquisition Parameters
Date_ 20000626
Time 19.27
INSTRUM spect
PROBHD 5 mm BBO BB-1
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 6009.615 Hz
FIDRES 0.183399 Hz
AQ 2.7263477 sec
RG 32
DW 83.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
P1 5.00 usec
SFO1 500.1327507 MHz
NUC1 1H
PL1 3.00 dB

F2 - Processing parameters
SI 16384
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 8.500 ppm
F1 4251.10 Hz
F2P 1.500 ppm
F2 750.20 Hz
PPMCM 0.35000 ppm/cm
HZCM 175.04550 Hz/cm







Proton standard parameters, BBO probe

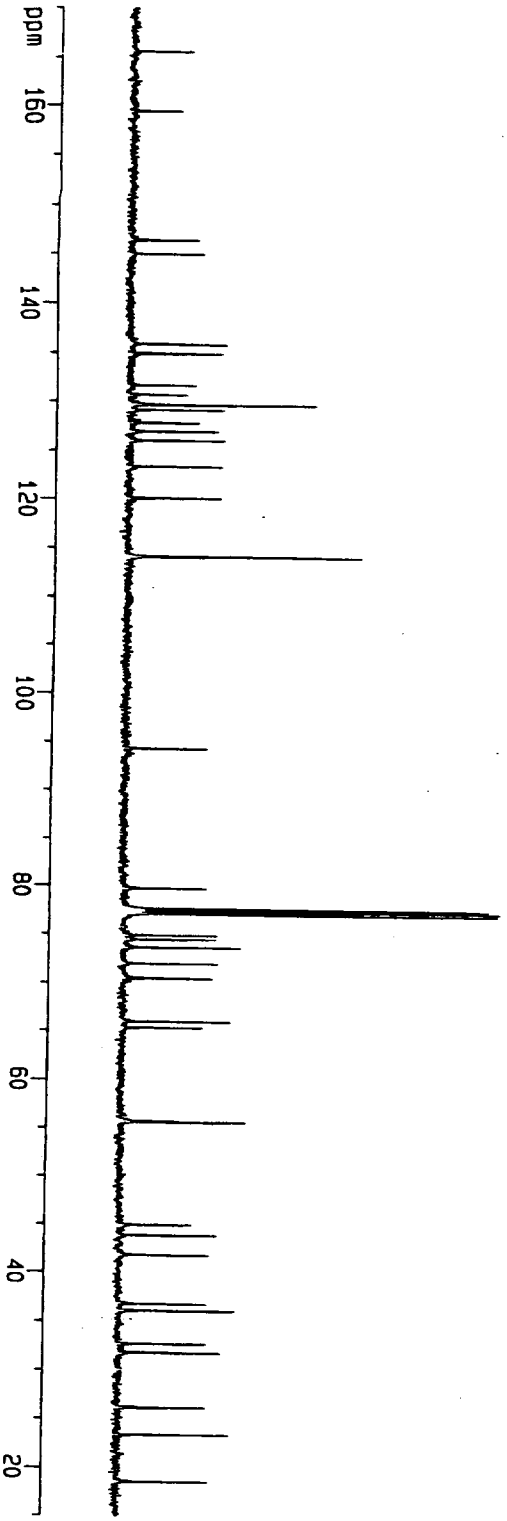
Current Data Parameters
NAME M703
EXPNO 3
PROCNO 1

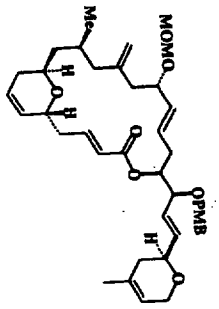
F2 - Acquisition Parameters
Date_ 20000703
Time 15.00
INSTRUM spect
PROBHD 5 mm BBO BB-1
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 6009.615 Hz
FIDRES 0.183399 Hz
AQ 2.7263477 sec
RG 64
DW 83.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
P1 5.00 usec
SFO1 500.1327507 MHz
NUC1 1H
PL1 3.00 dB

F2 - Processing parameters
SI 16384
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 7.500 ppm
F1 3750.98 Hz
F2P 0.500 ppm
F2 250.07 Hz
PPMCM 0.35000 ppm/cm
HZCM 175.04550 Hz/cm

Carbon-13 standard parameters, BBO probe





19

ppm
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145.029
135.869
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130.708
129.711
129.151
127.853
126.980
126.078
123.369
120.110
114.100
94.353
79.801
77.705
77.451
77.197
74.880
74.487
73.659
71.982
70.483
66.005
65.333
55.705
55.652
44.992
43.892
41.827
36.878
36.138
32.674
31.793
30.103
26.177
23.348
18.604

Current Data Parameters
NAME M703
EXPNO 4
PROCNO 1

F2 - Acquisition Parameters
Date_ 20000703
Time 15.09
INSTRUM spect
PROBHD 5 mm BBO BB-1
PULPROG zgpg
TD 32768
SOLVENT CDCl3
NS 240
DS 2
SWH 30303.031 Hz
FIDRES 0.924775 Hz
AQ 0.5407220 sec
RG 8192
DW 16.500 usec
DE 6.00 usec
TE 300.0 K
D11 0.03000000 sec
D12 0.00002000 sec
PL13 22.00 dB
D1 2.00000000 sec
CPDPRG2 waltz16
PCPD2 80.00 usec
SFO2 500.1320000 MHz
NUC2 1H
PL2 3.00 dB
PL12 22.00 dB
P1 3.00 usec
SFO1 125.7715724 MHz
NUC1 13C
PL1 0.00 dB

F2 - Processing parameters
SI 32768
SF 125.7577390 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
F1P 170.000 ppm
F1 21378.81 Hz
F2P 15.000 ppm
F2 1886.37 Hz
PPMCM 7.75000 ppm/cm
HZCM 974.62244 Hz/cm