SUPPORTING INFORMATION

Total Syntheses of Amphidinolide X and Y

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General. All reactions were carried out under Ar. The solvents used were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O (Mg-anthracene), CH_2Cl_2 (P_4O_{10}), MeCN, Et_3N, pyridine, DMF (CaH_2), MeOH (Mg), hexane, cyclohexane, toluene, benzene (Na/K). Flash chromatography: Merck silica gel 60 (230-400 mesh). NMR: Spectra were recorded on a DPX 300, AV 400, or DMX 600 spectrometer (Bruker) in the solvents indicated; chemical shifts (δ) are given in ppm relative to residual solvent peaks, coupling constants (J) in Hz. IR: Nicolet FT-7199 spectrometer, wavenumbers in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), (ESI) Finnigan MAT 95, accurate mass determination: Finnigan MAT 95, Bruker APEX III FT-ICR-MS (7 T magnet). Melting points: Büchi melting point apparatus (uncorrected). Elemental analyses: H. Kolbe, Mülheim/Ruhr. All commercially available compounds (Lancaster, Fluka, Aldrich) were used as received unless stated otherwise.

Preparation of the Common Tetrahydrofuran Segment

Compounds **10, 11, 12, 13** were prepared according to literature procedures.[1]

[(2*S*,3*S*)-3-(2-{[*tert*-Butyl(diphenyl)silyl]oxy}ethyl)oxiran-2-yl]methanol (14). L(+)-Diethyl tartrate (L(+)-DET, 312 mg, 1.5 mmol) and Ti(O-*i*-Pr)$_4$ (359 mg, 1.3 mmol) were added to a suspension of powdered 4Å molecular sieves (100 mg/mmol) in CH_2Cl_2 (32 mL) at –20 °C. The mixture was stirred for 30 min at that temperature before a solution of anhydrous *t*-BuOOH in decane (5 M, 5.0 mL, 25.0 mmol) was added dropwise. After stirring for another 30 min at –20 °C, a solution of allylic alcohol **13** (4.3 g, 12.5 mmol) in CH_2Cl_2 (24 mL) was added slowly via syringe and the resulting mixture was stirred for 18 h at –20 °C. For work-up, the reaction was quenched with a solution of citric acid (2.0 g) and $FeSO_4$ (6.6 g) in water (20 mL) at 0 °C. The organic layer was separated and the aqueous layer was extracted three times with *tert*-butyl methyl ether. The combined organic layers were treated with 30% NaOH saturated with NaCl (50 mL) and stirred vigorously for 30 min at 0 °C. The organic layer was separated and the aqueous layer was again repeatedly extracted with *tert*-butyl methyl ether. The combined organic phases were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography of the residue (hexanes/ethyl acetate, 5/1) provided epoxide **14** as a colorless oil (4.4 g, 97%). The enantiomeric excess (ee = 83%) was determined by HPLC by comparison with the racemate (250 mm Chiralcel OD-H, Ø 4.6 mm, n-heptane/2-propanol = 90/10, 0.5 mL/min, 3.2 MPa, 298 K, UV, 220 nm). $[\alpha]_D^{20} = -16.7$ (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.66 (4H, m), 7.46-7.37 (6H, m), 3.91 (1H, ddd, *J* = 12.5, 5.1, 2.5 Hz), 3.83 (1H, t, *J* = 6.4 Hz), 3.81 (1H, t, *J* = 5.7 Hz), 3.62 (1H, ddd, *J* = 12.5, 6.9, 4.5 Hz), 3.13 (1H, dt, *J* = 5.7, 2.3 Hz), 2.98 (1H, dt, *J* = 4.5, 2.5 Hz), 1.82 (2H, q, *J* = 6.0 Hz), 1.74 (1H, t, *J* = 6.3 Hz), 1.07 (9H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.7, 133.7, 129.8, 127.8, 61.8, 60.9, 58.7, 53.9, 35.0, 27.0, 19.3. IR: 3433, 3071, 2957, 2930, 2857, 1472, 1428, 1111, 823, 739, 703 cm^{-1}. MS (EI) *m/z* (rel. intensity): 299 ([M-^{t}Bu]$^+$, <0.2), 269 (32), 225 (9), 199 (100). HRMS (ESI): *calcd.* for ($C_{21}H_{28}O_3Si$+Na): 379.1705, *found* 379.1701 (M+Na). Anal. *calcd.* for $C_{21}H_{28}O_3Si$: C 70.74, H 7.92, *found* C 70.67, H 8.04.

***tert*-Butyl{2-[(2*S*,3*S*)-3-ethynyloxiran-2-yl]ethoxy}diphenylsilane (15).** Oxalyl chloride (2.3 mL, 25.9 mmol) was added dropwise to a solution of DMSO (2.8 mL, 38.9 mmol) in CH_2Cl_2 (30 mL) at –78 °C. A solution of the epoxy alcohol **14** (4.6 g, 13.0 mmol) in CH_2Cl_2 (30 mL) was then introduced and the mixture was stirred for 1 h at –78 °C before it was treated with Et_3N (7.2 mL, 51.9 mmol) and allowed to warm to ambient temperature. After stirring for an additional hour, the reaction was quenched with brine (60 mL) and the organic layer was successively washed with sat. $NaHCO_3$ (aq.), water, and brine. The organic layer

[1] Narco, K.; Baltas, M.; Gorrichon, L. *Tetrahedron* **1999**, *55*, 14013.

was dried over Na_2SO_4, filtered and concentrated to give the crude aldehyde (4.6 g), which was used without further purification.

Dry K_2CO_3 (3.6 g, 26.0 mmol) was added to a solution of the aldehyde in MeOH (200 mL), followed by the slow addition of dimethyl-1-diazo-2-oxopropyl phosphonate (3.0 g, 15.6 mmol)[2] at 0 °C. The mixture was stirred for 6 h at that temperature before it was brought to ambient temperature and stirred for additional 2 h. For work up, the mixture was diluted with *tert*-butyl methyl ether (100 mL) and quenched with aq. sat. $NaHCO_3$ (150 mL). The aqueous layer was repeatedly extracted with *tert*-butyl methyl ether and the combined organic layers were dried over Na_2SO_4, filtered, and evaporated. Flash chromatography (hexanes/ethyl acetate, 20/1) of the residue gave acetylene **15** as a colorless oil (3.0 g, 67% over both steps). $[\alpha]_D^{20}$ = +1.1 (c = 1.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.66 (4H, m), 7.46-7.37 (6H, m), 3.82-3.78 (2H, m), 3.30 (1H, dt, *J* = 5.7, 2.1 Hz), 3.19 (1H, t, *J* = 1.8 Hz), 2.33 (1H, d, *J* = 2.6 Hz), 1.83-1.76 (2H, m), 1.07 (9H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.7, 133.6, 129.9, 127.9, 80.7, 72.0, 60.5, 58.4, 45.3, 35.0, 27.0, 19.3. IR: 3288, 3071, 2957, 2931, 2858, 2126, 1472, 1428, 1112, 823, 703 cm^{-1}. MS (EI) *m/z* (rel. intensity): 293 ([M-^{t}Bu]$^+$, 53), 263 (68), 249 (22), 237 (10), 225 (30), 221 (100). HRMS (CI): *calcd.* for ($C_{22}H_{26}O_2Si$+H): 351.1780, *found* 351.1779 (MH^+). Anal. *calcd.* for $C_{22}H_{26}O_2Si$: C 75.38, H 7.48, *found* C 75.48, H 7.39.

***tert*-Butyl(diphenyl){2-[(2*S*,3*S*)-3-prop-1-ynyloxiran-2-yl]ethoxy}silane (16).** Solid LiHMDS (1.8 g, 10.8 mmol) was added in portions over 5 min to a solution of compound **15** (3.15 g, 9.0 mmol) in THF (230 mL) at −78 °C. The resulting mixture was stirred for 1 h at −78 °C before it was treated with MeOTf (1.2 mL, 10.8 mmol) and allowed to reach −20 °C over 1 h. The reaction was quenched at that temperature with sat. $NaHCO_3$ (aq.) and poured into a mixture of *tert*-butyl methyl ether and aq. sat. $NaHCO_3$. The aqueous layer was repeatedly extracted with *tert*-butyl methyl ether, the combined organic layers were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 20/1) to give product **16** as a colorless oil (3.1 g, 95%). $[\alpha]_D^{20}$ = –2.0 (c = 1.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.66 (4H, m), 7.46-7.37 (6H, m), 3.81-3.78 (2H, m), 3.23 (1H, dt, *J* = 5.7, 2.2 Hz), 3.15-3.14 (1H, m), 1.86 (3H, d, *J* = 1.7 Hz), 1.79-1.75 (2H, m), 1.07 (9H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.7, 133.7, 129.8, 127.8, 80.5, 76.2, 60.6, 58.5, 45.2, 35.1, 27.0, 19.3, 3.8. IR: 3071, 2957, 2930, 2857, 2244, 1472, 1428, 1112, 823, 702 cm^{-1}. MS (EI) *m/z* (rel. intensity): 307 ([M-^{t}Bu]$^+$, 100). HRMS (CI): *calcd.* for ($C_{23}H_{28}O_2Si$+H): 365.1937, *found* 365.1938 (MH^+). Anal. *calcd.* for $C_{23}H_{28}O_2Si$: C 75.78, H 7.74, *found* C 75.69, H 7.62.

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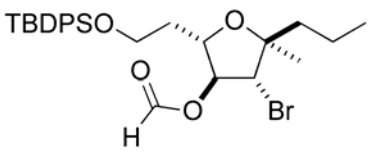
[2] (a) Ohira, S. *Synth. Commun*. **1989**, *19*, 561. (b) Müller, S.; Liepold, B.; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, 521.

(3*S*,4*R*)-1-{[*tert*-Butyl(diphenyl)silyl]oxy}-6-methylnona-4,5-dien-3-ol (17) and Isomer 18. A solution of $Fe(acac)_3$ (120 mg, 0.34 mmol) in toluene (30 mL) was added to a solution of propargyl epoxide **16** (2.5 g, 6.9 mmol) in toluene (280 mL) at −5 °C. The resulting mixture was stirred for 5 min at −5 °C before a solution of propylmagnesium chloride in Et_2O (2 M, 4.5 mL, 8.9 mmol) was added via syringe over a period of 10 min, causing a color change from bright red to black during the addition. After stirring for 5 min at −5 °C, the reaction was quenched with aq. sat. NH_4Cl (150 mL) and diluted with *tert*-butyl methyl ether. The aqueous layer was repeatedly extracted with *tert*-butyl methyl ether, the combined organic layers were dried over Na_2SO_4, filtered and concentrated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 25/1) to give an inseparable *syn/anti* = 8:1 mixture of allenols **17** and **18** as a pale yellow oil (1.7 g, 62%). $[\alpha]_D^{20}$ = −10.8 (c = 1.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (4H, m), 7.46-7.37 (6H, m), 5.19 (1H, o, *J* = 2.8 Hz), 4.43-4.40 (1H, m), 3.91 (1H, dt, *J* = 10.4, 5.7 Hz), 3.84 (1H, dt, *J* = 10.4, 6.0 Hz), 2.70 (1H, bs), 1.96-1.91 (2H, m), 1.81 (2H, q, *J* = 5.9 Hz), 1.67 (3H, d, *J* = 2.8 Hz), 1.44 (2H, h, *J* = 7.4 Hz), 1.06 (9H, s), 0.91 (3H, t, *J* = 7.3 Hz). (Minor isomer **18**: 0.90 (t, *J* = 7.3 Hz)). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 135.7, 133.5, 129.9, 127.9, 102.8, 94.9, 69.3, 62.4, 39.4, 36.3, 27.0, 20.9, 19.3, 19.2, 13.9. IR: 3435, 3071, 2958, 2931, 2858, 1964, 1472, 1428, 1112, 823, 702 cm^{-1}. MS (EI) *m/z* (rel. intensity): 351 ([M-^{t}Bu]$^+$, 5), 333 (10), 229 (12), 211 (9), 199 (100). HRMS (ESI): *calcd.* for ($C_{26}H_{36}O_2Si$+Na): 431.2382, *found* 431.2385 (M+Na). Anal. *calcd.* for $C_{26}H_{36}O_2Si$: C 76.42, H 8.88, *found* C 76.26, H 8.98.

***tert*-Butyl {2-[(2*S*,5*R*)-5-methyl-5-propyl-2,5-dihydrofuran-2-yl]ethoxy}diphenyl silane (19) and Isomer *epi*-19.** $AgNO_3$ (750 mg, 4.4 mmol) and $CaCO_3$ (800 mg, 8.0 mmol) were added to a solution of the allenols **17** and **18** (1.6 g, 4.0 mmol) in acetone/water (4/1, 110 mL). The reaction mixture was stirred for 15 h in the dark before it was diluted with water (30 mL). The acetone was removed under reduced pressure, the remaining aqueous phase was repeatedly extracted with *tert*-butyl methyl ether, and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. Flash chromatography of the residue (hexanes/ethyl acetate, 30/1) provided an inseparable mixture of dihydrofurans **19** and *epi*-**19** as a colorless oil (1.5 g, 90%, d.r. = 8:1, NMR). $[\alpha]_D^{20}$ = +30.5 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, C_6D_6) δ 7.82-7.78 (4H, m), 7.24-7.22 (6H, m), 5.52 (1H, dd, *J* = 6.0, 1.3 Hz), 5.40 (1H, dd, *J* = 6.0, 2.4 Hz), 5.03-4.99 (1H, m), 3.97-3.85 (2H, m), 1.92-1.77 (2H, m), 1.57-1.22 (5H, m), 1.23 (3H, s), 1.18 (9H, s), 0.87 (3H, t, *J* = 7.2 Hz). (minor diastereomer *epi*-**19**: 5.37 (dd, *J* = 6.0, 2.3 Hz)). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.1, 136.0, 134.50, 134.0, 129.9, 129.5, 83.1, 82.0, 61.7, 44.2, 40.1, 27.2, 26.6, 19.5, 18.4, 14.9. IR: 3071, 2959, 2931, 2858, 1472, 1428, 1112, 823, 702 cm^{-1}. MS (EI) *m/z* (rel. intensity): 408 ([M$^+$], 0.7), 351 (31), 199 (82), 183 (19), 154 (22) 135 (100). HRMS (ESI): *calcd.* for ($C_{26}H_{36}O_2Si$+Na): 431.2382, *found* 431.2380 (M+Na). Anal. *calcd.* for $C_{26}H_{36}O_2Si$: C 76.42, H 8.88, *found* C 76.28, H 8.94.

(2*S*,3*S*,4*R*,5*R*)-4-Bromo-2-(2-{[*tert*-butyl(diphenyl)silyl]oxy}ethyl)-5-methyl-5-propyl-tetrahydrofuran-3-yl formate (20) and its isomer *epi*-20. NBS (1.9 g, 10.4 mmol) was added in portions to a solution of dihydrofurans **19** and *epi*-**19** (1.45 g, 3.7 mmol) in DMF/water (15/1, 38 mL) at –5 °C. After stirring for 6 h in the dark at –5 °C, the reaction was diluted with water (100 mL), the aqueous phase was repeatedly extracted with pentane, the combined organic layers were dried over Na_2SO_4, filtered and concentrated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 50/1). The diastereoisomers generated in the iron catalyzed allenol formation were separated at this stage yielding the (19*R*)-configured[§] bromoformate **20** (1.1 g, 58%) and the diastereomeric (19*S*)-bromoformate *epi*-**20** (140 mg, 7%) as pale yellow oils. Analytical and spectroscopic data of (19*R*)-**20**: $[\alpha]_D^{20}$ = –1.3 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (1H, s), 7.69-7.65 (4H, m), 7.44-7.35 (6H, m), 5.44 (1H, dt, *J* = 4.5, 0.8 Hz), 4.14 (1H, dt, *J* = 9.4, 4.8 Hz), 4.09 (1H, d, *J* = 4.5 Hz), 3.85-3.75 (2H, m), 2.09-2.01 (1H, m), 1.90 (1H, ddt, *J* = 14.0, 9.0, 5.2 Hz), 1.73-1.32 (5H, m), 1.36 (3H, s), 1.05 (9H, s), 0.94 (3H, t, *J* = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 135.7, 133.9, 129.7, 127.8, 84.3, 83.8, 77.3, 60.6, 59.1, 42.4, 37.7, 27.0, 23.2, 19.4, 17.6, 14.6. IR: 3071, 2959, 2931, 2858, 1733, 1472, 1428, 1159, 1112, 823, 702 cm^{-1}. MS (EI) *m/z* (rel. intensity): 477 and 475 ([M-^{t}Bu]$^+$, 7), 431 (45) and 429 (43), 349 (68), 255 (98), 227 (37), 199 (96), 183 (31), 151 (100). HRMS (ESI): *calcd.* for ($C_{27}H_{37}BrO_4Si$+Na): 555.1542, *found* 555.1545 (M+Na). Anal. *calcd.* for $C_{27}H_{37}BrO_4Si$: C 60.78, H 6.99, Br 14.98, Si 5.26, *found* C 60.83, H 6.85, Br 14.87, Si 5.30.

(2*S*,3*S*,4*R*,5*S*)-4-bromo-2-(2-((*tert*-butyl(diphenyl)silyl)oxy)ethyl)-5-methyl-5-propyltetrahydrofuran-3-yl formate (*epi*-20). 

$[\alpha]_D^{20}$ = –5.5 (c = 1.07, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (1H, s), 7.68-7.65 (4H, m), 7.44-7.35 (6H, m), 5.45 (1H, dt, *J* = 6.4, 0.8 Hz), 4.13 (1H, d, *J* = 6.3 Hz), 4.04 (1H, ddd, *J* = 9.0, 6.5, 4.0 Hz), 3.84-3.73 (2H, m), 2.05-1.96 (1H, m), 1.84 (1H, ddt, *J* = 13.9, 9.1, 5.1 Hz), 1.70-1.35 (5H, m), 1.34 (3H, s), 1.04 (9H, s), 0.95 (3H, t, *J* = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 135.7, 133.9, 129.7, 127.7, 83.5, 83.3, 76.4, 60.4, 56.9, 41.5, 37.6, 27.0, 25.7, 19.4, 17.3, 14.6. IR: 3071, 2959, 2932, 2858, 1735, 1472, 1428, 1162, 1112, 823, 703 cm^{-1}. MS (EI) *m/z* (rel. intensity): 477 and 475 ([M-^{t}Bu]$^+$, 13), 431 (46) and 429 (46), 349 (65), 255 (99), 227 (38), 199 (100). HRMS (ESI): *calcd.* for ($C_{27}H_{37}BrO_4Si$+Na): 555.1542, *found* 555.1546 (M+Na).

(2*S*,3*R*,5*R*)-2-(2-{[*tert*-Butyl(diphenyl)silyl]oxy}ethyl)-5-methyl-5-propyltetrahydrofuran-3-ol (22). $(TMS)_3SiH$ (850 µL, 2.76 mmol) and AIBN (30 mg, 0.18 mmol) were added to a solution of bromoformate (19*R*)-**20** (980 mg, 1.84 mmol) in toluene (90 mL) and the resulting mixture was stirred at 80 °C for 4 h. The solution was allowed to reach ambient temperature before the solvent was evaporated. The residue was dissolved in MeOH (100

[§] Amphidinolide X numbering

mL). Aq. sat. $NaHCO_3$ (ca. 12 mL) was added dropwise and the reaction mixture was stirred for 2 h before it was diluted with water (25 mL). A standard extractive work up with *tert*-butyl methyl ether followed by flash chromatography (hexanes/ethyl acetate, 8/1) of the crude product provided the title compound as a colorless oil (705 mg, 90%). $[\alpha]_D^{20}$ = –18.1 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (4H, m), 7.47-7.38 (6H, m), 4.05 (1H, q, *J* = 7.5 Hz), 3.84 (2H, dd, *J* = 7.1, 4.1 Hz), 3.79 (1H, ddd, *J* = 8.2, 7.1, 4.7 Hz), 3.52 (1H, bs), 2.24 (1H, dd, *J* = 12.4, 8.1 Hz), 1.90-1.73 (3H, m), 1.48-1.33 (4H, m), 1.31 (3H, s), 1.07 (9H, s), 0.92 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.7, 133.1, 130.0, 128.0, 82.8, 81.8, 76.6, 62.3, 45.4, 44.9, 36.8, 27.6, 27.0, 19.2, 17.9, 14.8. IR: 3438, 3071, 2959, 2932, 1613, 1513, 1428, 1249, 1111, 1087, 1038, 822, 703 cm^{-1}. MS (EI) *m/z* (rel. intensity): 369 ([M-^{t}Bu]$^+$, 9), 351 (100). HRMS (ESI): *calcd.* for ($C_{26}H_{38}O_3Si$+Na): 449.2488, *found* 449.2493 (M+Na). Anal. *calcd.* for $C_{26}H_{38}O_3Si$: C 73.19, H 8.98, *found* C 72.98, H 9.06.

***tert*-Butyl(2-{(2*S*,3*R*,5*R*)-3-[(4-methoxybenzyl)oxy]-5-methyl-5-propyltetrahydro-furan-2-yl}ethoxy)diphenylsilane (23).** *p*-Methoxybenzyl trichloroacetimidate (800 mg, 2.81 mmol) and PPTS (29 mg, 0.12 mmol) were added over 5 min to a solution of compound **22** (200 mg, 0.47 mmol) in CH_2Cl_2/cyclohexane (1/2, 6.0 mL) at 0 °C. The reaction mixture was stirred at ambient temperature for 48 h before it was filtered through a pad of Celite. The filtrate was evaporated and the residue was purified by flash chromatography (hexanes/ethyl acetate, 40/1) to give the title compound as a colorless oil (196 mg, 76%). $[\alpha]_D^{20}$ = –19.9 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (4H, m), 7.43-7.34 (6H, m), 7.21 (2H, d, *J* = 8.6 Hz), 6.85 (2H, d, *J* = 8.6 Hz), 4.41 (1H, d, *J* = 11.4 Hz), 4.37 (1H, d, *J* = 11.4 Hz), 4.11 (1H, dt, *J* = 7.2, 5.0 Hz), 3.80 (3H, s), 3.81-3.76 (3H, m), 1.94 (1H, dd, *J* = 13.1, 7.3 Hz), 1.88-1.74 (3H, m), 1.46-1.27 (4H, m), 1.28 (3H, s), 1.05 (9H, s), 0.90 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 135.8, 134.2, 130.7, 129.6, 129.2, 127.7, 114.0, 84.2, 82.8, 79.6, 71.3, 61.3, 55.4, 45.5, 42.7, 37.9, 27.0, 26.4, 19.3, 18.0, 14.8. IR: 3070, 2958, 2931, 1613, 1428, 1112, 1086, 1038, 702 cm^{-1}. MS (EI) *m/z* (rel. intensity): 489 ([M-^{t}Bu]$^+$, 0.3), 351 (6), 199 (4), 121 (100). HRMS (ESI): *calcd.* for ($C_{34}H_{46}O_4Si$+Na): 569.3063, *found* 569.3064 (M+Na). Anal. *calcd.* for $C_{34}H_{46}O_4Si$: C 74.68, H 8.48, *found* C 74.53, H 8.42.

2-{(2*S*,3*R*,5*R*)-3-[(4-Methoxybenzyl)oxy]-5-methyl-5-propyltetrahydrofuran-2-yl}-ethanol (24). A solution of TBAF in THF (1 M, 990 μL, 0.99 mmol) was added dropwise to a solution of compound **23** (180 mg, 0.33 mmol) in THF (9.5 mL). After stirring for 3 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and diluted with *tert*-butyl methyl ether and water. The aqueous layer was extracted with *tert*-butyl methyl ether and the combined organic phases were dried over Na_2SO_4, filtered and evaporated. Flash chromatography (hexanes/ethyl acetate, 2/1) of the residue provided the title alcohol as a colorless oil (98 mg, 97%). $[\alpha]_D^{20}$ = –37.1 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (2H, d, *J* = 8.7 Hz), 6.88 (2H, d, *J* = 8.7 Hz), 4.47 (1H, d, *J* = 11.3 Hz), 4.38 (1H, d, *J* = 11.3 Hz), 4.06 (1H, ddd, *J* = 8.0, 5.7, 4.7 Hz), 3.80 (3H, s), 3.80-3.74 (3H, m), 2.49 (1H, bs), 2.04 (1H, dd, *J* = 12.9, 7.6 Hz), 1.90-1.71 (2H, m), 1.77 (1H, dd, *J* = 12.9, 5.1 Hz), 1.50-1.28 (3H, m), 1.30 (3H, s), 0.91

(3H, t, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 130.2, 129.4, 114.1, 83.7, 83.5, 82.3, 71.7, 61.6, 55.4, 45.3, 42.6, 36.3, 26.5, 18.0, 14.7. IR: 3444, 2959, 2933, 1613, 1514, 1249, 1173, 1084, 1036, 821 cm^{-1}. MS (EI) *m/z* (rel. intensity): 308 ([M$^+$], 6), 137 (7), 121 (100). HRMS (ESI): *calcd.* for ($C_{18}H_{28}O_4$+Na): 331.1885, *found* 331.1884 (M+Na).

(2*R*,4*R*,5*S*)-5-(2-Iodoethyl)-4-[(4-methoxybenzyl)oxy]-2-methyl-2-propyltetrahydrofuran (25). PPh_3 (98 mg, 0.38 mmol) and imidazole (31 mg, 0.50 mmol) were added to a solution of compound **24** (77 mg, 0.25 mmol) in Et_2O/MeCN (3/1, 2.6 mL). After stirring for 5 min, a solution of iodine (95 mg, 0.38 mmol) in Et_2O/MeCN (3/1, 0.65 mL) was added dropwise and the resulting mixture was stirred for 2 h. The reaction was quenched with sat. aq. NH_4Cl (3 mL), diluted with *tert*-butyl methyl ether and water, the aqueous layer was repeatedly extracted with *tert*-butyl methyl ether, the combined organic layers were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 25/1) to give iodide **25** as a colorless oil (96 mg, 92%). $[\alpha]_D^{20}$ = –34.7 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* = 8.7 Hz), 6.89 (2H, d, *J* = 8.7 Hz), 4.46 (1H, d, *J* = 11.4 Hz), 4.39 (1H, d, *J* = 11.4 Hz), 3.95 (1H, dt, *J* = 8.3, 4.6 Hz), 3.81 (3H, s), 3.73 (1H, dt, *J* = 7.5, 4.6 Hz), 3.26-3.15 (2H, m), 2.16-1.94 (3H, m), 1.79 (1H, dd, *J* = 13.1, 4.2 Hz), 1.47-1.26 (4H, m), 1.29 (3H, s), 0.91 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 130.4, 129.3, 114.1, 83.3, 83.2, 82.2, 71.5, 55.5, 45.4, 42.7, 39.4, 26.5, 18.0, 14.8, 1.9. IR: 2958, 2932, 2870, 1613, 1513, 1249, 1173, 1037, 821 cm^{-1}. MS (EI) *m/z* (rel. intensity): 418 ([M$^+$], 7), 375 (5), 233 (4), 137 (4), 121 (100). HRMS (ESI): *calcd.* for ($C_{18}H_{27}IO_3$+Na): 441.0903, *found* 441.0899 (M+Na). Anal. *calcd.* for $C_{18}H_{27}IO_3$: C 51.68, H 6.51, *found* C 51.64, H 6.43.

Building Blocks A and C

(2*S*,3*R*)-3-Methyl-1-(2-methyl-1,3-dioxolan-2-yl)pent-4-yn-2-ol (30). PPh_3 (50 mg, 0.20 mmol) was added to a solution of $Pd(OAc)_2$ (45 mg, 0.20 mmol) in THF (40 mL) at –78°C and the mixture was stirred until a clear solution had formed. Mesylate **29** (855 mg, 5.77 mmol) was then added followed by aldehyde **28** (500 mg, 3.84 mmol).[3] A solution of Et_2Zn in hexane (1 M, 11.5 mL, 11.5 mmol) was added dropwise over 10 min at –78°C. After stirring at that temperature for 10 min, the solution was stirred for 16 h at –20°C. For work up, an aq. sat. solution of $NaHCO_3$ was slowly added (gas evolution!) and the product was extracted with *tert*-butyl methyl ether. The combined organic phases were washed with water, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ EtOAc, 4:1 + 2% Et_3N) to afford a 4.5:1 mixture of the *anti*-configured alcohol **30** and its *syn*-configured isomer **31** (460 mg, 65 %). These isomers can be

[3] Langer, P.; Freifeld, I. *Synlett* **2001**, 523-525.

separated by flash chromatography (hexanes/EtOAc, 10:1 + 2% Et_3N → hexanes/EtOAc, 4:1 + 2% Et_3N). The enantiomeric excess of *anti*-**30** (ee = 94%) was determined by HPLC by comparison of both enantiomers (250 mm Chiralpak AD, *n*-heptane/2-propanol = 99/1, 0.5 mL/min, 0.7 mPa, RI, E = 32). Analytical and spectroscopic data of *anti*-**30**: $[\alpha]_D^{20}$ = +2.1° (c = 1.1, MeOH). ^{1}H NMR (400 MHz, C_6D_6) δ 4.00-3.95 (1H, m), 3.40-3.26 (5H, m), 2.59-2.53 (1H, m), 2.02 (1H, dd, *J* = 9.6, 14.5 Hz), 1.95 (1H, dd, *J* = 2.3, 14.5 Hz), 1.86 (1H, d, *J* = 2.5 Hz), 1.31 (3H, d, *J* = 7.0 Hz), 1.21 (3H, s). ^{13}C NMR (100 MHz, C_6D_6) δ 110.4, 86.0, 70.5, 70.1, 64.6, 64.2, 42.3, 32.8, 24.2, 16.1. IR: 3515, 3290, 2983, 2887, 2112, 1379, 1257, 1220, 1156, 1109, 1042, 983, 949, 822 cm^{-1}. MS (EI) *m/z* (rel. intensity): 169 ([M-CH_3]$^+$, 4), 87 (100), 43 (46). HRMS (ESI): *calcd.* for ($C_{10}H_{16}O_3$+Na): 207.0997, *found* 207.0997 (M+Na). Anal. *calcd.* for $C_{10}H_{16}O_3$: C 65.19, H 8.75, *found* C 65.08, H 8.71.

2-{(2*S*,3*R*)-2-[(4-Methoxybenzyl)oxy]-3-methylpent-4-ynyl}-2-methyl-1,3-dioxolane (32). NaH (391 mg, 16.3 mmol) was added to a solution of alcohol **30** (1.00 g, 5.43 mmol) in DMF (54 mL) at 0°C. The mixture was stirred for 1 h at that temperature before *p*-methoxybenzyl chloride (1.58 mL, 10.9 mmol) was added followed by tetra-*n*-butylammonium iodide (199 mg, 0.543 mmol). The mixture was stirred for 1 h at 0°C and for 16 h at room temperature. For work up, the reaction was carefully quenched with brine (H_2 evolution!) and the mixture was repeatedly extracted with *tert*-butyl methyl ether. The combined organic phases were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 10:1 + 2 % Et_3N → hexanes/EtOAc, 4:1 + 2 % Et_3N) to afford protected alcohol **32** as a colorless syrup (1.55 g, 94 %). $[\alpha]_D^{20}$ = –5.4° (c = 0.85, MeOH). ^{1}H NMR (400 MHz, C_6D_6) δ 7.23 (2H, d, *J* = 8.7 Hz), 6.78 (2H, d, *J* = 8.7 Hz), 4.37 (1H, d, *J* = 11.2 Hz), 4.29 (1H, d, *J* = 11.2 Hz), 3.78-3.74 (1H, m), 3.63-3.53 (4H, m), 2.90-2.86 (1H, m), 2.29 (1H, dd, *J* = 3.5, 14.6 Hz), 2.07 (1H, dd, *J* = 7.2, 14.6 Hz), 1.89 (3H, d, *J* = 2.5 Hz), 1.46 (3H, s). ^{13}C NMR (100 MHz, C_6D_6) δ 159.7, 131.1, 129.5, 114.0, 109.6, 86.5, 78.0, 71.2, 70.2, 64.5, 64.4, 54.8, 40.2, 29.9, 25.0, 15.3. IR: 3289, 2982, 2882, 2111, 1613, 1514, 1249, 1052, 821 cm^{-1}. MS (EI) *m/z* (rel. intensity): 304 ([M$^+$], 1), 121 (100), 115 (19), 87 (23), 43 (13). HRMS (ESI): *calcd.* for ($C_{18}H_{24}O_4$+Na): 327.1572, *found* 327.1578 (M+Na). Anal. *calcd.* for $C_{18}H_{24}O_4$: C 71.03, H 7.95, *found* C 70.89, H 7.86.

2-{(2*S*,3*R*)-2-[(4-Methoxybenzyl)oxy]-3-methylhex-4-ynyl}-2-methyl-1,3-dioxolane (33). LiHMDS (2.00 g, 11.9 mmol) was added to a solution of alkyne **32** (1.21 g, 3.98 mmol) in THF (40 mL) at –78°C. The reaction was stirred for 1 h at that temperature and for 30 min at –20°C. The mixture was cooled to –78°C before MeI (1.24 mL, 19.9 mmol) was introduced, and stirring was continued for 16 h at –20°C → 5°C. An aq. sat. solution of NH_4Cl was added, the aqueous layer was extracted with *tert*-butyl methyl ether, the combined organic phases were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 15:1 + 2 % Et_3N) to afford alkyne **33** as a colorless syrup (1.20 g, 95 %). $[\alpha]_D^{20}$ = –12.1° (c = 1.0, MeOH). ^{1}H NMR (400 MHz, C_6D_6) δ 7.25 (2H, d, *J* = 8.6 Hz), 6.78 (2H, d, *J* = 8.6 Hz), 4.41 (1H, d, *J* = 11.1 Hz), 4.36 (1H, d, *J* = 11.1 Hz), 3.82-

3.78 (1H, m), 3.64-3.54 (4H, m), 3.31 (3H, s), 2.96-2.93 (1H, m), 2.36 (1H, dd, *J* = 3.0, 14.5 Hz), 2.11 (1H, dd, *J* = 7.3, 14.5 Hz), 1.55 (3H, d, *J* = 2.4 Hz), 1.50 (3H, s), 1.24 (3H, d, J= 7.0 Hz). ^{13}C NMR (100 MHz, C_6D_6) δ 159.6, 131.5, 129.5, 113.9, 109.8, 81.6, 78.5, 77.1, 71.1, 64.4, 64.3, 54.7, 40.2, 30.1, 25.0, 15.6, 3.4. IR: 3306, 2980, 2881, 1613, 1514, 1249, 1052, 822 cm^{-1}. MS (EI) *m/z* (rel. intensity): 318 ([M$^+$], 0.4), 121 (100), 87 (15). HRMS (ESI): *calcd.* for ($C_{19}H_{26}O_4$+Na): 341.1729, *found* 341.1726 (M+Na). Anal. *calcd.* for $C_{19}H_{26}O_4$: C 71.67, H 8.23, *found* C 71.48, H 8.20.

2-{(2*S*,3*R*,4*E*)-5-Iodo-2-[(4-methoxybenzyl)oxy]-3-methylhex-4-enyl}-2-methyl-1,3-dioxolane (34). A solution of alkyne **33** (294 mg, 0.923 mmol) in benzene (18 mL) was added to Cp_2ZrHCl (595 mg, 2.31 mmol) under Ar. The mixture was stirred for 4 h at 50°C and then cooled to ambient temperature. The mixture was diluted with CH_2Cl_2 (10 mL), cooled to –15°C and treated with a saturated solution of I_2 in CH_2Cl_2 until the purple color persisted. At that point, a sat. aq. solution of $Na_2S_2O_3$ was immediately added. A standard extractive work up followed by flash chromatography of the crude product (hexanes/EtOAc, 20:1 + 2 % Et_3N → hexanes/EtOAc, 6:1 + 2 % Et_3N) afforded vinyl iodide **34** as a colorless syrup (251 mg, 61 %). $[\alpha]_D^{20}$ = +19.0° (c = 1.0, MeOH). ^{1}H NMR (400 MHz, C_6D_6) δ 7.27 (2H, d, *J* = 8.6 Hz), 6.80 (2H, d, *J* = 8.6 Hz), 6.43 (1H, dd, *J* = 1.4, 9.9 Hz), 4.50 (1H, d, *J* = 11.2 Hz), 4.32 (1H, d, *J* = 11.2 Hz), 3.52-3.33 (4H, m), 3.32 (3H, s), 2.72-2.67 (1H, m), 2.24 (3H, d, *J* = 1.4 Hz), 1.97 (1H, dd, *J* = 4.9, 14.8 Hz), 1.86 (1H, dd, *J* = 5.6, 14.8 Hz), 1.30 (3H, s), 0.95 (3H, d, *J* = 6.9 Hz). ^{13}C NMR (100 MHz, C_6D_6) δ 159.7, 143.7, 131.5, 129.7, 114.1, 109.4, 94.6, 78.4, 71.3, 64.6, 64.4, 54.8, 41.1, 40.2, 28.3, 24.9, 16.7. IR: 2958, 2877, 1612, 1514, 1248, 1038, 821 cm^{-1}. MS (EI) *m/z* (rel. intensity): 431 ([M-CH_3]$^+$, 0.2), 121 (100), 87 (18). HRMS (ESI): *calcd.* for ($C_{19}H_{27}O_4I$+Na): 469.0852, *found* 469.0849 (M+Na).

(2*S*,3*R*,4*E*)-5-Iodo-3-methyl-1-(2-methyl-1,3-dioxolan-2-yl)hex-4-en-2-ol (39). An aq. phosphate buffer solution (pH 7, 3 mL) was added to a solution of alcohol **34** (287 mg, 0.643 mmol) in CH_2Cl_2 (10 mL). DDQ (584 mg, 2.57 mmol) was then introduced at 0°C and the mixture was stirred for 2 h at ambient temperature. H_2O was added, the mixture was extracted with CH_2Cl_2, the combined organic phases were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 15:1 + 1 % Et_3N → hexanes/EtOAc, 4:1 + 1 % Et_3N) to afford alcohol **39** as a colorless syrup (187 mg, 89 %). $[\alpha]_D^{20}$ = +32.0° (c = 1.0, MeOH). ^{1}H NMR (400 MHz, C_6D_6) δ 6.50 (1H, qd, *J* = 1.5, 9.9 Hz), 3.77 (1H, dd, *J* = 3.7, 10.3 Hz), 3.45 (1H, s), 3.39-3.32 (4H, m), 2.24-2.18 (1H, m), 2.16 (3H, d, *J* = 1.5 Hz), 1.75 (1H, dd, *J* = 10.3, 14.5 Hz), 1.58 (1H, dd, *J* = 1.6, 14.5 Hz), 1.14 (3H, s), 1.01 (3H, d, *J* = 6.9 Hz). ^{13}C NMR (100 MHz, C_6D_6) δ 143.4, 110.4, 94.0, 70.9, 64.6, 64.1, 43.3, 41.8, 27.9, 24.2, 16.9. IR: 3520, 2979, 2882, 1634 ,1378, 1040 cm^{-1}. MS (EI) *m/z* (rel. intensity): 311 ([M-CH_3]$^+$, 2), 131 (16), 87 (100), 43 (35). HRMS (ESI): *calcd.* for ($C_{11}H_{19}O_3I$+Na): 349.0277, *found* 349.0274 (M+Na). Anal. *calcd.* for $C_{11}H_{19}O_3I$: C 40.51, H 5.87, *found* C 40.63, H 5.95.

Methyl (2*E*,4*S*)-4-methyl-6-[(triisopropylsilyl)oxy]hex-2-enoate (36). DBU (573 μL, 3.83 mmol) and methyl diethylphosphonoacetate (804 μL, 4.38 mmol) were added to a suspension of flame dried LiCl (186 mg, 4.38 mmol) in CH_3CN (36 mL). Aldehyde **35** (943 mg, 3.65 mmol)[4] in CH_3CN (36 mL) was added and the mixture was stirred for 16 h at ambient temperature. A standard extractive work up followed by flash chromatography of the crude product (hexanes/EtOAc, 15:1) furnished ester **36** as a colorless syrup (1.08 g, 94 %). $[\alpha]_D^{20}$ = +39.5° (c = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.90 (1H, dd, *J* = 7.8, 15.7 Hz), 5.79 (1H, dd, *J* = 1.1, 15.7 Hz), 3.72 (3H, s), 3.68 (1H, td, *J* = 1.8, 6.3 Hz), 2.60-2.51 (1H, m), 1.64-1.53 (2H, m), 1.09-1.00 (24 H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 154.8, 119.4, 61.1, 51.5, 39.1, 33.2, 19.4, 18.1, 12.1. IR: 2944, 2867, 1729, 1657, 1463, 1107, 883, 681 cm^{-1}. MS (EI) *m/z* (rel. intensity): 299 ($[M\text{-}CH_3]^+$, < 0.07), 271 ($[M\text{-}^iPr]^+$, 100), 145 (25), 133 (13), 117 (14), 109 (17), 89 (10), 81 (29), 75 (17). HRMS (ESI): *calcd.* for ($C_{17}H_{34}O_3Si$+Na): 337.2175, *found* 337.2177 (M+Na). Anal. *calcd.* for $C_{17}H_{34}O_3Si$: C 64.92, H 10.90, *found* C 64.99, H 10.93.

Methyl (2*E*,4*S*)-6-hydroxy-4-methylhex-2-enoate (37). A solution of compound **36** (400 mg, 1.27 mmol) in CH_3CN (13 mL) was placed in a plastic bottle. Excess HF·pyridine (1.00 mL) was added and the mixture was stirred for 90 min at ambient temperature. For work up, aq. sat. $NaHCO_3$ was introduced and the mixture was extracted with *tert*-butyl methyl ether. The combined organic phases were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (pentanes/ *tert*-butyl methyl ether, 1:1) to afford the title alcohol **37** as a colorless syrup (202 mg, 100 %). $[\alpha]_D^{20}$ = +45.0° (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (1H, dd, *J* = 8.0, 15.7 Hz), 5.77 (1H, dd, *J* = 1.2, 15.7 Hz), 3.68 (3H, s), 3.62-3.56 (2H, m), 2.51-2.44 (1H, m), 2.17 (1H, s), 1.59 (2H, q, *J* = 6.7 Hz), 1.04 (3H, d, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 154.3, 119.6, 60.4, 51.5, 38.6, 33.2, 19.4. IR: 3430, 2955, 1725, 1656, 1436, 1275. MS (EI) *m/z* (rel. intensity): 158 ($[M^+]$, 10), 127 (71), 81 (100), 55 (64), 41 (75). HRMS (ESI): *calcd.* for ($C_8H_{14}O_3$): 158.0943, *found* 158.0944 (M). Anal. *calcd.* for $C_8H_{14}O_3$: C 60.74, H 8.92, *found* C 60.83, H 9.06.

(3*S*,4*E*)-6-Methoxy-3-methyl-6-oxohex-4-enoic acid (38). Oxalyl chloride (150 μL, 1.72 mmol) was added to a solution of DMSO (184 μL, 2.58 mmol) in CH_2Cl_2 (7 mL) at –78°C. A solution of alcohol **37** (136 mg, 0.86 mmol) in CH_2Cl_2 (7 mL) was added and the mixture was stirred for 1 h at –78°C. Et_3N (483 μL, 3.44 mmol) was then introduced and the mixture was stirred for 1 h at ambient temperature. The reaction was quenched with brine, the aqueous layer was extracted with *tert*-butyl methyl ether, the combined organic phases were evaporated, and the residue was re-dissolved in *tert*-butyl methyl ether. The organic solution was washed with H_2O, dried over Na_2SO_4, filtered and evaporated to give the crude aldehyde which was used without any further purification.

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[4] Bode, J. W.; Carreira, E. M. *J. Org. Chem*. **2001**, *66*, 6410.

2-Methylbut-2-ene (2.00 mL) and NaH_2PO_4 (306 mg, 2.58 mmol) in H_2O (3.4 mL) were added to a solution of this aldehyde (134 mg, 0.86 mmol) in *t*-BuOH (15 mL) at ambient temperature. $NaClO_2$ (231 mg, 2.58 mmol) was introduced and the mixture was stirred for 2 h. The solvent was evaporated and the residue was dissolved in EtOAc. H_2O was added, the mixture was acidified with 2 M HCl until pH 5 was reached, and the resulting mixture was repeatedly extracted EtOAc. The combined organic phases were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 1:1 → EtOAc) to afford carboxylic acid **38** as a colorless syrup (136 mg, 92 % over 2 steps). $[\alpha]_D^{20}$ = +24.8° (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (1H, dd, *J* = 7.2, 15.8 Hz), 5.85 (1H, dd, *J* = 1.4, 15.8 Hz), 3.73 (3H, s), 2.90-2.83 (1H, m), 2.48 (1H, dd, *J* = 7.0, 15.8 Hz), 2.39 (1H, dd, *J* = 7.3, 15.8 Hz), 1.15 (3H, d, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 167.1, 151.8, 120.4, 51.7, 40.0, 32.8, 19.2. IR: 3100, 2967, 2674, 1723, 1657, 1278. MS (EI) *m/z* (rel. intensity): 172 ([M^+], 2), 154 (44), 140 (50), 122 (100), 95 (59), 94 (56), 71 (58), 67 (58), 41 (58). HRMS (ESI): *calcd.* for ($C_8H_{12}O_4$+Na): 195.0633, *found* 195.0634 (M+Na). Anal. *calcd.* for $C_8H_{12}O_4$: C 55.81, H 7.02, *found* C 55.74, 7.12.

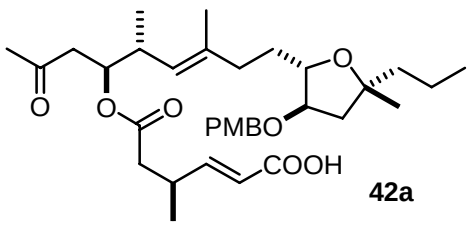
Total Synthesis of Amphidinolide X

Ester 40. Et_3N (180 μL, 1.29 mmol) was added to a solution of carboxylic acid **38** (74 mg, 0.432 mmol) in toluene (4 mL). 2,4,6-Trichlorobenzoyl chloride (68 μL, 0.432 mmol) was introduced and the resulting mixture was stirred for 1h at ambient temperature. A solution of alcohol **39** (128 mg, 0.392 mmol) and DMAP (48 mg, 0.392 mmol) in toluene (4 mL) was added and the reaction mixture was allowed to stir for 1h. Evaporation of the solvent followed by flash chromatography of the residue (hexanes/EtOAc, 4:1 + 1 % Et_3N) provided ester **40** as a colorless syrup (200 mg, 96 %). $[\alpha]_D^{20}$ = +17.4° (c = 1.0, MeOH). ^{1}H NMR (400 MHz, C_6D_6) δ 6.96 (1H, dd, *J* = 7.1, 15.7 Hz), 6.21 (1H, dd, *J* = 1.5, 9.9 Hz), 5.83 (1H, dd, *J* = 1.4, 15.7 Hz), 5.26-5.22 (1H, m), 3.59-3.45 (4H, m), 3.43 (3H, s), 2.69-2.62 (1H, m), 2.50-2.44 (1H, m), 2.18 (3H, d, 1.5 Hz), 2.09 (1H, dd, *J* = 7.0, 15.5 Hz), 2.00 (1H, dd, *J* = 7.2, 15.5 Hz), 1.93 (1H, dd, *J* = 7.9, 14.8 Hz), 1.72 (1H, dd, *J* = 3.2, 14.8 Hz), 1.24 (3H, s), 0.83 (3H, d, *J* = 6.8 Hz), 0.79 (3H, d, *J* = 6.9 Hz). ^{13}C NMR (100 MHz, C_6D_6) δ 170.9, 166.6, 152.3, 142.1, 120.5, 109.0, 95.7, 72.5, 64.6, 64.5, 51.0, 41.3, 40.5, 40.1, 33.1, 28.0, 24.4, 19.0, 16.3. IR: 2968, 1727, 1657, 1273, 1173, 1041, 987. MS (EI) *m/z* (rel. intensity): 480 ([M^+], 0.03), 87 (100), 43 (15). HRMS (ESI): *calcd.* for ($C_{19}H_{29}O_6I$+Na): 503.0907, *found* 503.0907 (M+Na).

Compound 41. A solution of *tert*-BuLi in pentane (1.7 M, 438 μL, 0.744 mmol) was added to a mixture of Et_2O (577 μL) and THF (577 μL) at –78°C before a solution of alkyl iodide **25** (52 mg, 0.124 mmol) in THF (3.47 mL) was added dropwise (additional 577 μL of THF were used to rinse the flask). The mixture was stirred for 5 min at –78°C before 9-MeO-9-BBN (126 μL, 0.744 mmol) was introduced causing an immediate color change from yellow to

colorless. The mixture was stirred for 15 min at –78°C and for 1 h at ambient temperature. An aq. solution of K_3PO_4 (3 M, 248 μL, 0.744 mmol) was added followed by a solution of the vinyl iodide **40** (60 mg, 0.124 mmol) in DMF (3.47 mL) (additional 577 μL of DMF were used to rinse the flask). A solution of (dppf)$PdCl_2$ (4.5 mg, 0.0062 mmol) and $AsPh_3$ (3.8 mg, 0.012 mmol) in DMF (500 μL) was then added and the mixture was stirred for 2 h at ambient temperature. The mixture was diluted with hexanes/EtOAc (4:1 + 1 % Et_3N) before it was filtered through a pad of silica (hexanes/EtOAc, 4:1 + 1 % Et_3N was used to rinse the silica pad). The combined filtrates were successively washed with sat. aq. $NaHCO_3$, sat. aq. NH_4Cl and brine, the organic phase was dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 15:1 + 1 % Et_3N → hexanes/EtOAc, 6:1 + 1 % Et_3N) to afford compound **41** as a colorless syrup (59 mg, 74 %). $[\alpha]_D^{20} = -13.5°$ (c = 1.0, MeOH). ^{1}H NMR (400 MHz, C_6D_6) δ 7.25 (2H, d, *J* = 8.7 Hz), 7.02 (1H, dd, *J* = 7.1, 15.8 Hz), 6.84 (2H, d, *J* = 8.7 Hz), 5.86 (1H, dd, *J* = 1.4, 15.8 Hz), 5.45-5.41 (1H, m), 5.27 (1H, d, *J* = 9.4 Hz), 4.36 (1H, d, *J* = 11.5 Hz), 4.29 (1H, d, *J* = 11.5 Hz), 4.14 (1H, td, *J* = 5.0, 7.4 Hz), 3.70-3.49 (5H, m), 3.42 (3H, s), 3.34 (3H, s), 2.75-2.67 (2H, m), 2.33-2.23 (1H, m), 2.23-2.16 (2H, m), 2.12-2.03 (2H, m), 1.90 (1H, dd, *J* = 2.4, 14.9 Hz), 1.82-1.70 (4H, m), 1.65 (3H, d, *J* = 1.1 Hz), 1.51-1.33 (4H, m), 1.38 (3H, s), 1.34 (3H, s), 1.00 (3H, d, *J* = 6.8 Hz), 0.90 (3H, t, *J* = 7.2 Hz), 0.86 (3H, d, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, C_6D_6) δ 171.0, 166.6, 159.8, 152.5, 137.0, 131.2, 129.4, 126.0, 120.4, 114.2, 109.3, 84.5, 82.4, 82.2, 73.5, 71.5, 64.61, 64.58, 54.9, 51.0, 45.7, 43.2, 41.0, 40.8, 37.4, 36.5, 33.9, 33.2, 26.4, 24.6, 19.0, 18.2, 16.9, 16.6, 14.9. IR: 2960, 2870, 1727, 1514, 1249, 1172, 1036. MS (EI) *m/z* (rel. intensity): 644 ([M^+], 0.4), 140 (39), 122 (11), 121 (100), 87 (68). HRMS (ESI): ***calcd.*** for ($C_{37}H_{56}O_9$+Na): 667.3822, *found* 667.3819 (M+Na).

Compound 42a. Dry LiI was added to a solution of ester **41** (33 mg, 0.051 mmol) in pyridine (2 mL) and the resulting mixture was stirred for 30 h at 125°C. The mixture was cooled to 0°C before it was diluted with CH_2Cl_2 (10 mL) and washed with HCl (2 M, 12 mL). The aqueous phase was repeatedly extracted with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4, filtered and evaporated, and the residue was rapidly passed through silica (hexanes/EtOAc, 1:1 + 1 % HOAc). The crude acid **42** thus formed was used in the next step without further purification.



42a

H_2O (1 mL) was added to a solution of crude **42** in HOAc (1 mL) and the resulting mixture was stirred for 15 min at 65°C. After cooling to ambient temperature, the mixture was diluted with EtOAc and H_2O, and the aqueous phase was repeatedly extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 4:1 + 1 % HOAc) to afford carboxylic acid **42a** as a colorless syrup (16 mg, 53 % over 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* = 8.7 Hz), 6.99 (1H, dd, *J* =

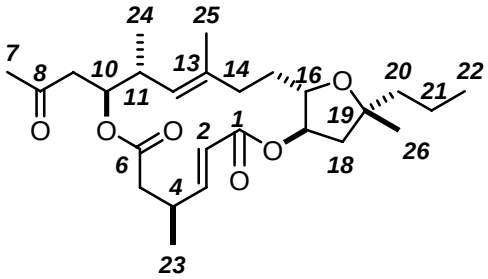
7.1, 15.7 Hz), 6.88 (2H, d, *J* = 8.7 Hz), 5.80 (1H, dd, *J* = 1.3, 15.7 Hz), 5.25-5.22 (1H, m), 4.99 (1H, d, *J* = 8.6 Hz), 4.47 (1H, d, *J* = 11.4 Hz), 4.38 (1H, d, *J* = 11.4 Hz), 3.92 (1H, dt, *J* = 6.9, 5.2 Hz), , 3.80 (3H, s), 3.74 (1H, dt, *J* = 7.1, 4.8 Hz), 2.87-2.79 (1H, m), 2.72-2.62 (1H, m), 2.62 (1H, dd, *J* = 7.6, 16.6 Hz), 2.53 (1H, dd, *J* = 5.3, 16.6 Hz), 2.36 (2H, dd, *J* = 1.2, 7.0 Hz), 2.13-1.96 (3H, m), 2.11 (3H, s), 1.78 (1H, dd, *J* = 4.2, 13.0 Hz), 1.63-1.42 (4H, m), 1.59 (3H, d, *J* = 1.1 Hz), 1.38-1.26 (2H, m), 1.31 (3H, s), 1.12 (3H, d, *J* = 6.8 Hz), 0.92 (3H, d, *J* = 5.5 Hz), 0.91 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.9, 171.2, 169.8, 159.4, 154.1, 137.4, 130.5, 129.4, 124.9, 120.1, 114.0, 83.6, 83.2, 81.9, 73.8, 71.4, 55.4, 45.6, 45.2, 42.6, 40.8, 35.9, 35.6, 33.3, 33.0, 30.4, 26.3, 19.0, 18.0, 17.1, 16.5, 14.8. IR: 2961, 1723, 1699, 1514, 1248, 1171, 1036. MS (EI) *m/z* (rel. intensity): 428 (3), 140 (22), 122 (12), 121 (100), 43 (14). HRMS (ESI): *calcd.* for ($C_{34}H_{50}O_8$+Na): 609.3403, *found* 609.3407 (M+Na).

Seco-Acid 43. An aqueous phosphate buffer solution (pH 7, 1 mL) was added to a solution of acid **42a** (15 mg, 0.026 mmol) in CH_2Cl_2 (1 mL). DDQ (23 mg, 0.102 mmol) was introduced at 0°C and the mixture was stirred for 5 h at ambient temperature. H_2O was added and the mixture was repeatedly extracted with CH_2Cl_2, the combined organic phases were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 4:1 + 1 % HOAc → hexanes/EtOAc, 2:1 + 1 % HOAc) to afford carboxylic acid **43** as a colorless syrup (10 mg, 84 %). $[\alpha]_D^{20}$ = –19.5° (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (1H, dd, *J* = 7.5, 15.7 Hz), 5.80 (1H, dd, *J* = 1.2, 15.7 Hz), 5.26-5.20 (1H, m), 5.02 (1H, d, *J* = 9.6 Hz), 4.04 (1H, td, *J* = 5.1, 7.4 Hz), 3.80-3.75 (1H, m), 2.88-2.77 (1H, m), 2.70-2.50 (3H, m), 2.43-2.31 (2H, m), 2.17-2.03 (4H, m), 2.12 (3H, s), 1.75-1.25 (7H, m), 1.59 (3H, d, *J* = 1.2 Hz), 1.33 (3H, s), 1.12 (3H, d, *J* = 6.8 Hz), 0.92 (3H, d, *J* = 6.2 Hz), 0.91 (3H, t, *J* = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.0, 169.4, 154.9, 137.1, 125.2, 120.3, 83.7, 83.0, 73.8, 46.2, 45.8, 45.5, 41.1, 36.0, 35.7, 33.5, 32.3, 30.4, 26.9, 19.3, 18.0, 17.5, 16.4, 14.7. IR: 3427, 2964, 1718, 1656, 1451, 1379, 1264, 1162, 1081, 988. MS (EI) *m/z* (rel. intensity): 466 ([M^+], 1), 308 (14), 156 (67), 107 (26), 95 (33), 84 (31), 71 (40), 55 (25), 43 (100). HRMS (ESI): *calcd.* for ($C_{26}H_{42}O_7$+Na): 489.2828, *found* 489.2827 (M+Na).

Amphidinolide X (1). Et_3N (11 µL, 0.081 mmol) and 2,4,6-trichlorobenzoyl chloride (3.8 µL, 0.024 mmol) were added to a solution of hydroxy acid **43** (7.5 mg, 0.016 mmol) in THF (2 mL). The mixture was stirred for 1h at room temperature before most of the THF was removed under a flow of Ar. The residue was diluted with toluene (5 mL) and the resulting solution was added over 2 h via syringe pump to a solution of DMAP (39 mg, 0.322 mmol) in toluene (20 mL) at ambient temperature. Once the addition was complete, the mixture was stirred for an additional 2h. For work up, the solvent was evaporated and the remaining syrup was purified by flash chromatography (hexanes/EtOAc, 10:1 → 6:1) to afford amphidinolide X **1** as a colorless syrup (4.5 mg, 62 %). $[\alpha]_D^{17}$ = –25.6° (c = 1.0, $CHCl_3$) [lit.[2]: $[\alpha]_D^{17}$ = –12° (c = 1.0, $CHCl_3$)]. ^{1}H NMR: *see Table 1*. ^{13}C NMR: *see Table 2*. IR: 2963, 1721, 1451, 1262, 1185, 1079 cm^{-1}.

For copies of pertinent NMR spectra of this series, see the Supporting Information to: Lepage, O.; Kattnig, E.; Fürstner, A. J. Am. Chem. Soc. ***2004****, 126, 15970.*

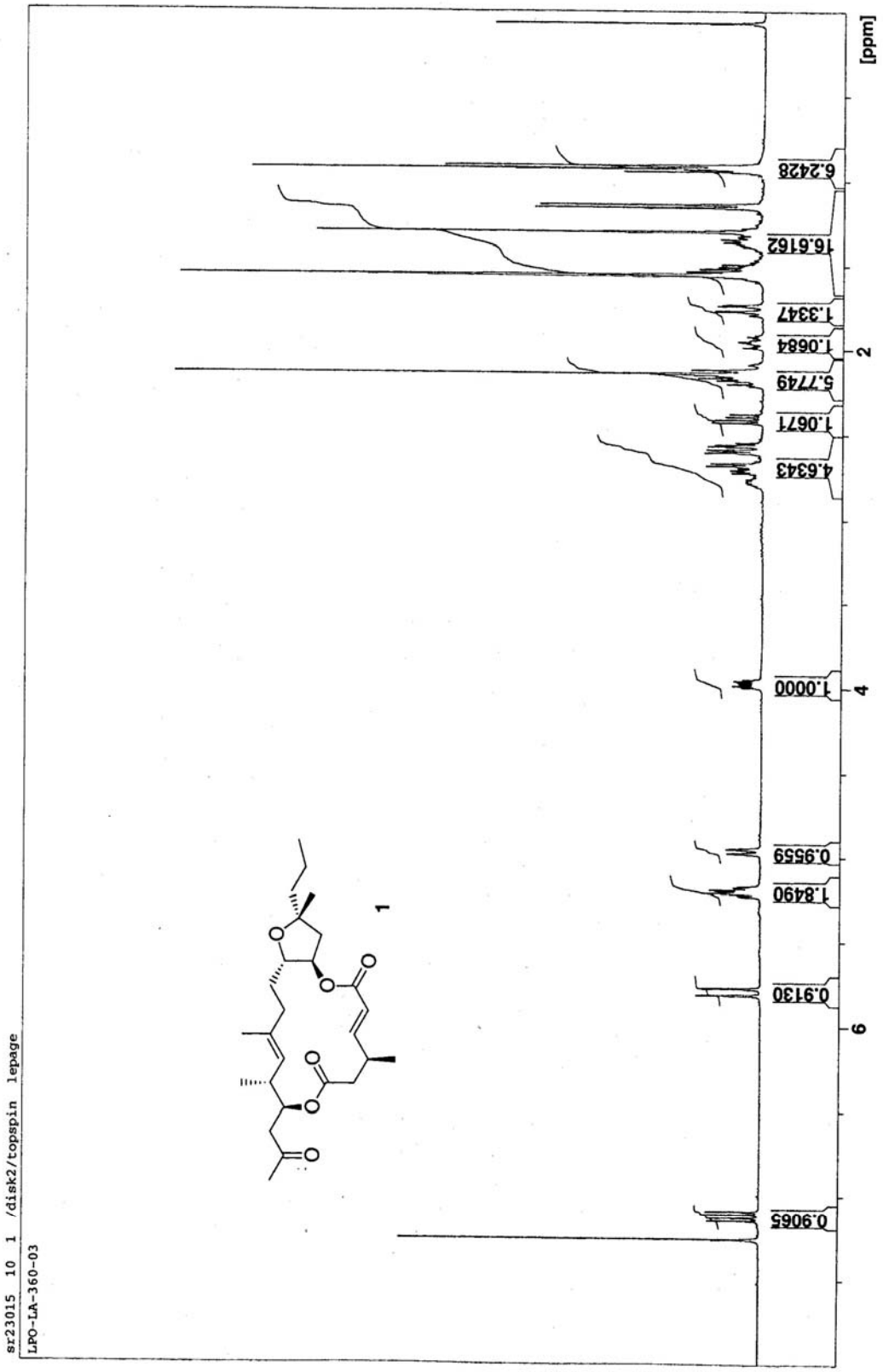
Table 1: Comparison of the ^{1}H NMR spectrum of authentic **1** with that of the synthetic sample (600 MHz, $CDCl_3$). Numbering scheme as shown in the insert.



Position	Natural 1, δ (multiplicity, *J* in Hz)	Synthetic 1, δ (multiplicity, *J* in Hz)	Δδ
2	5.79 (d, *15.8*)	5.79 (d, *15.8*)	±0
3	7.12 (dd, *7.2, 15.8*)	7.12 (dd, *7.2, 15.8*)	±0
4	2.79 (m)	2.78 (m)	-0.01
5	2.58 (dd, *3.7, 13.4*)	2.58 (dd, *3.6, 13.4*)	±0
	2.41 (dd, *6.3, 13.4*)	2.41 (dd, *6.4, 13.4*)	±0
7	2.14 (s)	2.14 (s)	±0
9	2.69 (dd, *6.0, 16.5*)	2.69 (dd, *6.0, 16.5*)	±0
	2.57 (dd, *8.2, 16.5*)	2.58 (dd, *7.2, 16.5*)	+0.01
10	5.21 (m)	5.20 (m)	-0.01
11	2.69 (m)	2.69 (m)	±0
12	4.95 (d, *10.3*)	4.96 (d, *10.3*)	+0.01
14	2.18 (m)	2.17 (m)	-0.01
	2.11 (br. t, *9.4*)	2.12 (m)	+0.01
15	1.95 (tt, *2.9, 13.4*)	1.95 (tt, *3.2, 13.5*)	±0
	1.54 (m)	1.54 (m)	±0
16	3.97 (dt, *11.1, 3.6*)	3.97 (dt, *11.3, 3.6*)	±0
17	5.19 (m)	5.21 (m)	+0.02
18	2.16 (m)	2.18 (m)	+0.02
	1.75 (dd, *2.4, 13.8*)	1.75 (dd, *2.5, 13.9*)	±0
20	1.50 (m)	1.51 (m)	+0.01
21	1.34 (m)	1.35 (m)	+0.01
22	0.92 (t, *7.4*)	0.93 (t, *7.3*)	+0.01
23	1.14 (d, *6.8*)	1.15 (d, *6.9*)	+0.01
24	0.92 (d, *6.8*)	0.93 (d, *6.9*)	+0.01
25	1.55 (s)	1.55 (s)	±0
26	1.30 (s)	1.30 (s)	±0

Table 2: Comparison of the ^{13}C NMR spectrum of authentic **1** with that of the synthetic sample (150 MHz, $CDCl_3$). Numbering scheme as shown in the insert to Table 1.

Position	Natural 1	Synthetic 1	Δδ
1	165.7	165.8	+0.1
2	120.2	120.4	+0.2
3	153.2	153.2	±0.0
4	33.1	33.2	+0.1
5	41.4	41.6	+0.2
6	170.7	170.8	+0.1
7	30.4	30.5	+0.1
8	205.5	205.4	-0.1
9	47.1	47.3	+0.2
10	74.2	74.4	+0.2
11	35.5	35.7	+0.2
12	126.0	126.1	+0.1
13	135.5	135.6	+0.1
14	35.3	35.5	+0.2
15	30.4	30.5	+0.1
16	80.5	80.6	+0.1
17	78.4	78.6	+0.2
18	43.5	43.7	+0.2
19	82.9	83.0	+0.1
20	44.2	44.4	+0.2
21	17.8	17.9	+0.1
22	14.6	14.7	+0.1
23	17.5	17.7	+0.2
24	18.1	18.2	+0.1
25	15.4	15.5	+0.1
26	24.5	24.7	+0.2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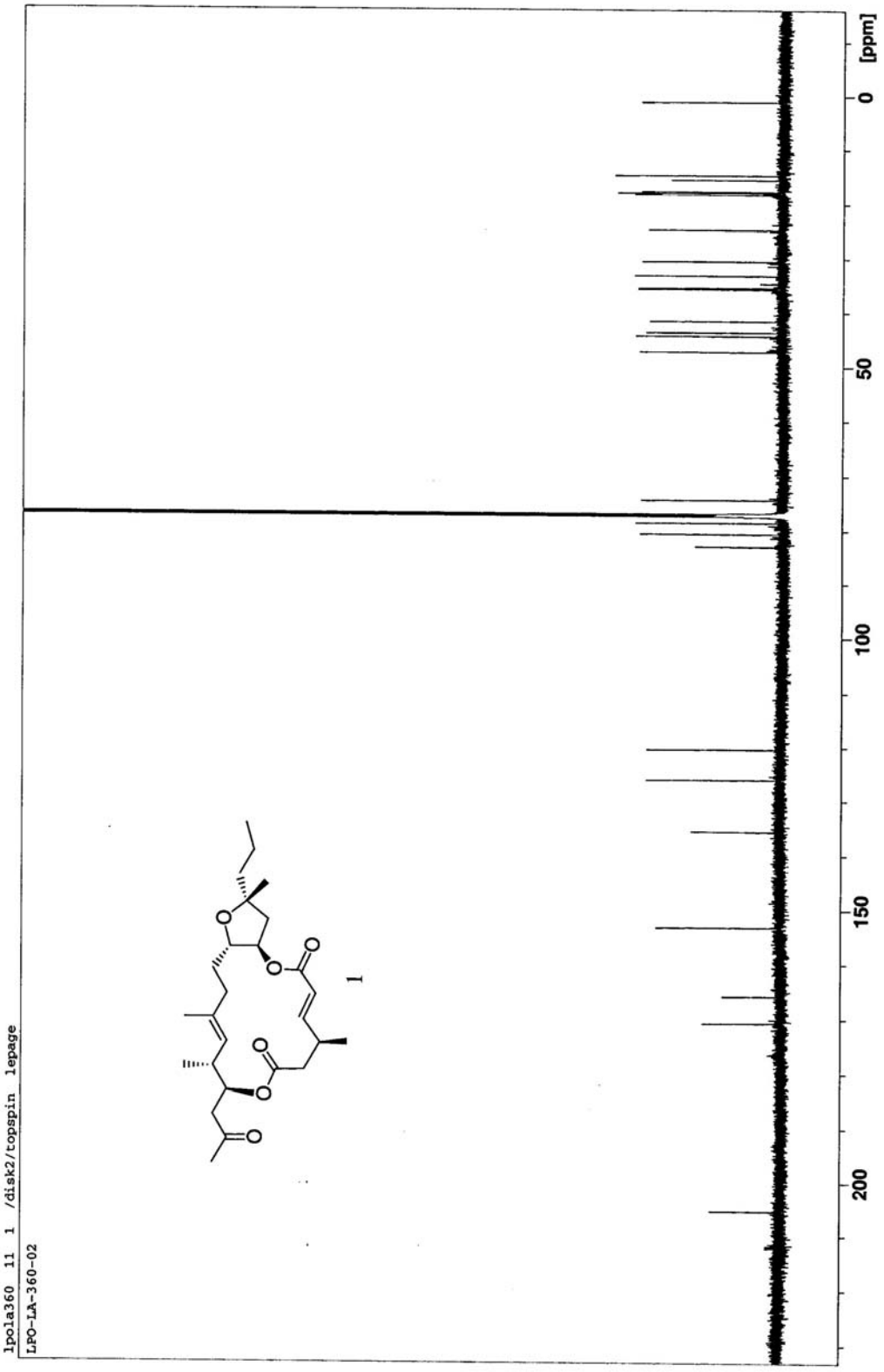
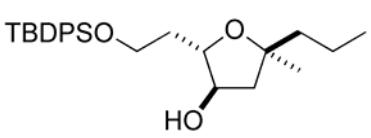
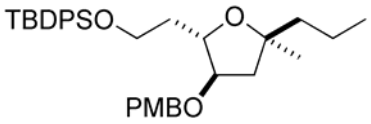
1


lpola360 11 1 /disk2/topspin lepage
LPO-LA-360-02
1
200
150
100
50
0 [ppm]

19-epi-Amphidinolide X

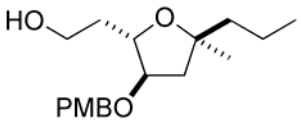
(2*S*,3*R*,5*S*)-2-(2-((*tert*-Butyl(diphenyl)silyl)oxy)ethyl)-5-methyl-5-propyltetrahydrofuran-3-ol (*epi*-22). 

$(TMS)_3SiH$ (91 μL, 0,297 mmol) and AIBN (3.2 mg, 0.020 mmol) were added to a solution of bromoformate *epi*-**20** (105 mg, 0.197 mmol) in toluene (10 mL) and the resulting mixture was stirred at 80 °C for 4 h. The solution was allowed to reach ambient temperature before the solvent was evaporated. The residue was dissolved in MeOH (10 mL). Aq. sat. $NaHCO_3$ (1 mL) was added dropwise and the reaction mixture was stirred for 2 h before it was diluted with water (2 mL). A standard extractive work up with *tert*-butyl methyl ether followed by flash chromatography (hexanes/ethyl acetate, 8/1) of the crude product provided the title compound as a colorless oil (73 mg, 87%). $[\alpha]_D^{20}$ = –13.4 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.66 (4H, m), 7.47-7.38 (6H, m), 4.12 (1H, q, *J* = 7.8 Hz), 3.84-3.81 (2H, m), 3.73 (1H, ddd, *J* = 4.4, 7.5, 8.4 Hz), 3.68 (1H, bs), 2.11 (1H, dd, *J* = 12.5, 7.7 Hz), 1.92-1.73 (3H, m), 1.65-1.30 (4H, m), 1.21 (3H, s), 1.07 (9H, s), 0.94 (3H, t, *J* = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.7, 132.9, 130.1, 128.0, 83.5, 81.6, 76.2, 62.4, 45.1, 44.9, 37.1, 28.2, 26.9, 19.2, 17.9, 14.8. IR: 3435, 3071, 2959, 2932, 1589, 1472, 1428, 1112, 1086, , 738, 702 cm^{-1}. MS (EI) *m/z* (rel. intensity): 369 ([M-^{t}Bu]$^+$, 10), 351 (100). HRMS (ESI): *calcd.* for ($C_{26}H_{38}O_3Si$+Na): 449.2488, *found* 449.2491 (M+Na).

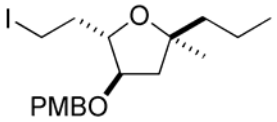
***tert*-Butyl(2-((2*S*,3*R*,5*S*)-3-((4-methoxybenzyl)oxy)-5-methyl-5-propyltetrahydrofuran-2-yl)ethoxy)diphenylsilane (*epi*-23).** 

p-Methoxybenzyl trichloroacetimidate (232 mg, 0.820 mmol) and PPTS (10 mg, 0.041 mmol) were added over 5 min to a solution of alcohol *epi*-**22** (70 mg, 0.164 mmol) in CH_2Cl_2/cyclohexane (1/2, 1.8 mL) at 0 °C. The reaction mixture was stirred at ambient temperature for 48 h before it was filtered through a pad of Celite. The filtrate was evaporated and the residue was purified by flash chromatography (hexanes/ethyl acetate, 40/1) to give the title compound as a colorless oil (48 mg, 54%). $[\alpha]_D^{20}$ = –17.9 (c = 0.97, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (4H, m), 7.43-7.34 (6H, m), 7.20 (2H, d, *J* = 8.7 Hz), 6.85 (2H, d, *J* = 8.7 Hz), 4.41 (1H, d, *J* = 11.4 Hz), 4.36 (1H, d, *J* = 11.4 Hz), 4.02 (1H, dt, *J* = 7.3, 5.3 Hz), 3.80 (3H, s), 3.84-3.75 (3H, m), 1.88 (1H, d, *J* = 6.1 Hz), 1.91-1.76 (3H, m), 1.67-1.23 (4H, m), 1.15 (3H, s), 1.05 (9H, s), 0.91 (3H, t, *J* = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 135.8, 134.2, 130.7, 129.6, 129.2, 127.7, 113.9, 84.0, 82.5, 79.5, 71.4, 61.2, 55.4, 43.6, 43.1, 38.1, 27.7, 22.8, 19.4, 18.0, 14.8. IR: 2958, 2932, 1613, 1428, 1111, 1084, 1037, 702 cm^{-1}. MS (EI) *m/z* (rel. intensity): 489 ([M-^{t}Bu]$^+$, 0.3), 351 (5), 199 (4), 121 (100). HRMS (CI): *calcd.* for ($C_{34}H_{46}O_4Si$+H): 547.3241, *found* 547.3244

2-{(2*S*,3*R*,5*S*)-3-((4-methoxybenzyl)oxy)-5-methyl-5-propyltetrahydrofuran-2-yl)ethanol (*epi*-24) A solution of TBAF in THF (1 M, 192 µL, 0.192 mmol) was added dropwise to a solution of compound *epi*-**23** (35 mg, 64.0 µmol) in THF (185 µL). After stirring for 3 h, the reaction was quenched with sat. aq. NH_4Cl (500 µL) and diluted with *tert*-butyl methyl ether (1.0 mL). The aqueous layer was extracted with *tert*-butyl methyl ether and the combined organic phases were dried over Na_2SO_4, filtered and evaporated. Flash chromatography (hexanes/ethyl acetate, 2/1) of the residue provided alcohol *epi*-**24** as a colorless oil (19 mg, 96%). $[\alpha]_D^{20}$ = –43.5 (c = 0.97, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (2H, d, *J* = 8.6 Hz), 6.88 (2H, d, *J* = 8.6 Hz), 4.48 (1H, d, *J* = 11.2 Hz), 4.39 (1H, d, *J* = 11.2 Hz), 3.96 (1H, ddd, *J* = 7.6, 6.6, 4.7 Hz), 3.85 (1H, dd, *J* = 13.7, 6.5), 3.81 (3H, s), 3.76-3.73 (2H, m), 2.94 (1H, bs), 1.99 (1H, dd, *J* = 12.6, 7.4 Hz), 1.92-1.26 (8H, m), 1.20 (3H, s), 0.93 (3H, t, *J* = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 129.5, 130.1, 114.1, 83.3, 83.1, 82.6, 71.9, 61.6, 55.4, 43.8, 42.9, 36.4, 27.7, 17.9, 14.7. IR: 3444, 2959, 2933, 1613, 1514, 1249, 1173, 1084, 1036, 821 cm^{-1}. MS (EI) *m/z* (rel. intensity): 308 (M^+, 7), 137 (8), 121 (100). HRMS (EI): *calcd.* for ($C_{18}H_{28}O_4$): 308.1988, *found* 308.1987 (M^+).

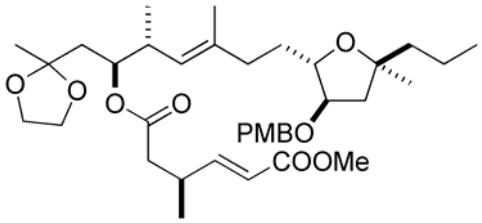


(2*S*,4*R*,5*S*)-5-(2-iodoethyl)-4-((4-methoxybenzyl)oxy)-2-methyl-2-propyltetrahydrofuran (*epi*-25). PPh_3 (24 mg, 92 µmol) and imidazole (8 mg, 123 µmol) were added to a solution of alcohol *epi*-**24** (19 mg, 61 µmol) in Et_2O/MeCN (3/1, 640 µL). After stirring for 5 min, a solution of iodine (24 mg, 92 µmol) in Et_2O/MeCN (3/1, 160 µL) was added dropwise and the resulting mixture was stirred for 2 h. The reaction was quenched with sat. aq. NH_4Cl (500 µL) and diluted with *tert*-butyl methyl ether (750 µL). The aqueous layer was repeatedly extracted with *tert*-butyl methyl ether, the combined organic layers were dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetate, 25/1) to give *epi*-**25** as a colorless oil (23 mg, 89%). $[\alpha]_D^{20}$ = –32.1 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (2H, d, *J* = 8.6 Hz), 6.89 (2H, d, *J* = 8.6 Hz), 4.47 (1H, d, *J* = 11.4 Hz), 4.38 (1H, d, *J* = 11.4 Hz), 3.85 (1H, ddd, *J* = 8.0, 5.9, 4.1 Hz), 3.81 (3H, s), 3.77 (1H, dd, *J* = 12.8, 5.9 Hz), 3.27-3.15 (2H, m), 2.19-1.86 (3H, m), 1.90 (1H, dd, *J* = 6.4, 3.6 Hz), 1.67-1.26 (4H, m), 1.17 (3H, s), 0.92 (3H, t, *J* = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 130.3, 129.3, 114.0, 82.9, 82.8, 82.2, 71.6, 55.5, 43.6, 43.2, 39.4, 27.7, 18.0, 14.8, 2.0. IR: 2958, 2932, 2870, 1613, 1513, 1249, 1173, 1037, 821 cm^{-1}. MS (EI) *m/z* (rel. intensity): 418 (M^+, 8), 375 (6), 233 (5), 137 (4), 121 (100). HRMS (ESI): *calcd.* for ($C_{18}H_{27}IO_3$+Na): 441.0903, *found* 441.0903 (M+Na).

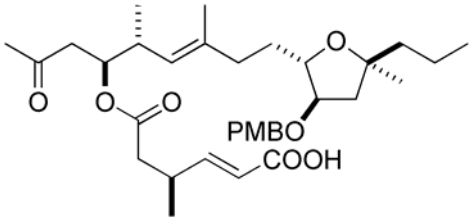


Compound 44. A solution of *tert*-BuLi in pentane (1.7 M, 177 µL, 0.301 mmol) was added to a mixture of Et_2O (233 µL) and THF (233 µL) at –78°C before a solution of alkyl iodide *epi*-**25** (21 mg, 50.2 µmol) in THF (1.4 mL) was added dropwise (additional 233 µL of THF were used to rinse the flask). The mixture was stirred for 5 min at –78°C before 9-MeO-9-BBN (51 µL, 0.301 mmol) was introduced causing an immediate color change from yellow to colorless.

The mixture was stirred for 15 min at −78°C and for 1 h at ambient temperature. An aq. solution of K_3PO_4 (3 M, 100 µL, 0.301 mmol) was added, followed by a solution of vinyl iodide **40** (24 mg, 50.2 µmol) in DMF (1.4 mL) (additional 230 µL of DMF were used to rinse the flask). A solution of (dppf)$PdCl_2$ (1.8 mg, 2.5 µmol) and $AsPh_3$ (1.5 mg, 5.0 µmol) in DMF (200 µL) was then added and the mixture was stirred for 2 h at ambient temperature. The mixture was diluted with hexanes/EtOAc (4/1 + 1 % Et_3N) before it was filtered through a pad of silica (hexanes/EtOAc, 4/1 + 1 % Et_3N was used to rinse the pad). The combined filtrates were successively washed with sat. aq. $NaHCO_3$, sat. aq. NH_4Cl and brine, the organic phase was dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 15/1 + 1 % Et_3N to hexanes/EtOAc, 6/1 + 1 % Et_3N) to afford compound **44** as a colorless oil (14 mg, 43 %). $[\alpha]_D^{20}$ = −10.9 (c = 1.0, MeOH). ^{1}H NMR (400 MHz, C_6D_6) δ 7.24 (2H, d, *J* = 8.6 Hz), 7.02 (1H, dd, *J* = 7.1, 15.7 Hz), 6.83 (2H, d, *J* = 8.7 Hz), 5.86 (1H, dd, *J* = 1.3, 15.7 Hz), 5.43 (1H, ddd, *J* = 8.3, 4.3, 2.5 Hz), 5.27 (1H, d, *J* = 9.4 Hz), 4.37 (1H, d, *J* = 11.5 Hz), 4.28 (1H, d, *J* = 11.5 Hz), 4.06 (1H, dt, *J* = 7.6, 5.2 Hz), 3.73 (1H, dt, *J* = 7.3, 5.3 Hz), 3.68-3.49 (4H, m), 3.42 (3H, s), 3.34 (3H, s), 2.78-2.66 (2H, m), 2.37-2.29 (1H, m), 2.25-2.16 (2H, m), 2.12-2.03 (2H, m), 1.89 (1H, dd, *J* = 2.4, 15.0 Hz), 1.87-1.71 (4H, m), 1.65 (3H, d, *J* = 1.1 Hz), 1.51-1.33 (4H, m), 1.34 (3H, s), 1.20 (3H, s), 1.00 (3H, d, *J* = 6.9 Hz), 0.93 (3H, t, *J* = 7.2 Hz), 0.86 (3H, d, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, C_6D_6) δ 171.0, 166.6, 159.8, 152.5, 137.0, 131.2, 129.4, 126.0, 120.4, 114.2, 109.3, 84.2, 82.3, 82.1, 73.5, 71.7, 64.62, 64.59, 54.9, 51.0, 43.8, 40.9, 40.8, 37.4, 36.5, 34.1, 33.2, 27.8, 24.6, 19.0, 18.2, 16.9, 16.6, 15.0 (one overlapping signal).



Compound 45a. Dry LiI was added to a solution of ester **44** (13 mg, 20 µmol) in pyridine (780 µL) and the resulting mixture was stirred for 30 h at 125°C. The mixture was then cooled to 0°C before it was diluted with CH_2Cl_2 (3.9 mL) and washed with HCl (2 M, 4 mL). The aqueous phase was repeatedly extracted with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4, filtered and evaporated. The residue was rapidly passed through silica (hexanes/EtOAc, 1/1 + 1 % HOAc) and the crude acid **45** thus formed was used in the next step without further purification.



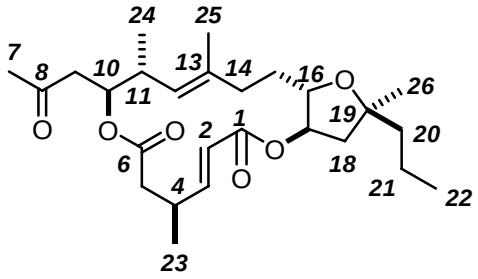
H_2O (400 µL) was added to a solution of crude acid **45** in HOAc (400 µL) and the resulting mixture was stirred for 15 min at 65°C. After cooling to ambient temperature, the mixture was diluted with EtOAc and H_2O, and the aqueous phase was repeatedly extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 4/1 + 1 % HOAc) to afford carboxylic acid **45a** as a colorless oil (6.5 mg, 57 % over 2 steps). $[\alpha]_D^{20}$ = −15.7 (c = 1.0,

$CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* = 8.6Hz), 7.00 (1H, dd, *J* = 15.7, 7.0 Hz), 6.88 (2H, d, *J* = 8.6 Hz), 5.79 (1H, d, *J* = 15.8 Hz), 5.25-5.20 (1H, m), 5.02 (1H, d, *J* = 9.5 Hz), 4.49 (1H, d, *J* = 11.4 Hz), 4.39 (1H, d, *J* = 11.4 Hz), 3.92-3.76 (2H, m), 3.81 (3H, s), 2.85-2.79 (1H, m), 2.70-2.59 (1H, m), 2.62 (1H, dd, *J* = 16.4, 7.5 Hz), 2.52 (1H, dd, *J* = 16.7, 5.6 Hz), 2.47-2.34 (2H, m), 2.16-1.86 (4H, m), 2.11 (3H, s), 1.72-1.51 (4H, m), 1.56 (3H, d, *J* = 0.9 Hz), 1.42-1.24 (2H, m), 1.24 (3H, s), 1.12 (3H, d, *J* = 6.9 Hz), 0.94-0.91 (6H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.0, 171.2, 169.8, 159.4, 153.7, 137.3, 130.4, 129.4, 124.8, 120.2, 114.0, 83.1, 82.8, 82.1, 73.9, 71.7, 55.4, 47.0, 43.4, 43.2, 41.1, 36.0, 35.6, 33.3, 32.9, 30.5, 27.3, 19.0, 17.9, 17.4, 16.4, 14.8.

19-*epi*-Amphidinolide X (47). An aqueous phosphate buffer solution (pH 7, 330 µL) was added to a solution of acid **45a** (5 mg, 8.5 µmol) in CH_2Cl_2 (330 µL). DDQ (8 mg, 34 µmol) was introduced at 0°C and the mixture was stirred for 15 h at ambient temperature. H_2O was added and the mixture was repeatedly extracted with CH_2Cl_2, the combined organic phases were dried over Na_2SO_4, filtered and evaporated. The residue was dissolved in hexanes/ethyl acetate, 4/1 + 1% acetic acid and filtered through a pad of silica (hexanes/ethyl acetate, 4/1 + 1% acetic acid was used to rinse the pad) to give crude seco-acid **46** as pale yellow oil which was used without any further purification in the final macrolactonisation.

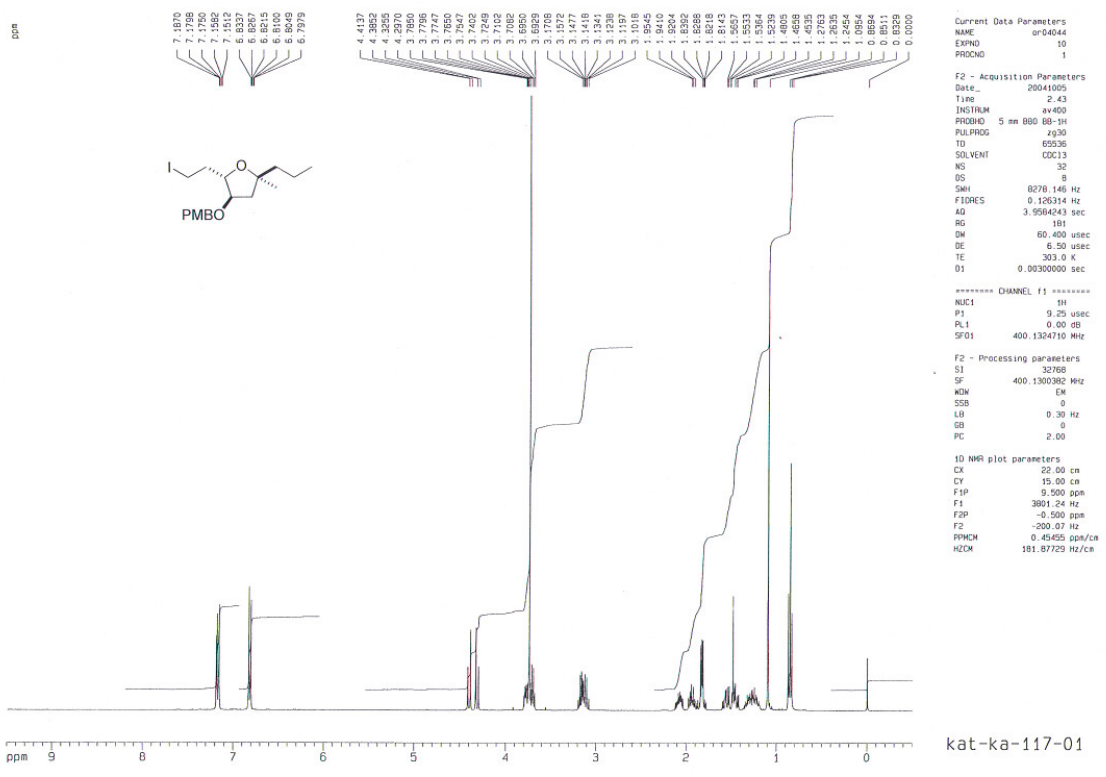
Et_3N (4.5 µL, 32 µmol) and 2,4,6-trichlorobenzoyl chloride (2.0 µL, 13 µmol) were added to a solution of crude seco-acid **46** in THF (860 µL). The mixture was stirred for 1 h at room temperature before most of the THF was removed under a flow of Ar. The residue was diluted with toluene (2.2 mL) and the resulting solution was added via syringe pump over 2 h to a solution of DMAP (16 mg, 130 µmol) in toluene (8.6 mL) at ambient temperature. Once the addition was complete, the mixture was stirred for an additional 2 h. For work up, the solvent was evaporated and the remaining syrup was purified by flash chromatography (hexanes/EtOAc, 10:1) to afford 19-amphidinolide X **47** as a colorless oil (1.5 mg, 39% over 2 steps). $[\alpha]_D^{17}$ = –17° (c = 0.15, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz) and ^{13}C NMR ($CDCl_3$, 150 MHz) see Table 3.

Table 3: ^{1}H NMR ($CDCl_3$, 600 MHz) and ^{13}C NMR ($CDCl_3$, 150 MHz) of 19-*epi*-amphidinolide X (**47**).



19-*epi*-Amphidinolide X (**47**)

position	^{1}H NMR δ (multiplicity, *J* in Hz)	^{13}C NMR (δ)
1		165.7
2	5.79 (dd, *1.3, 15.8*)	120.4
3	7.11 (dd, *7.5*, *15.8*)	153.2
4	2.77 (m)	33.2
5	2.58 (dd, *3.5*, *13.1*) 2.41 (dd, *6.5*, *13.4*)	41.7
7	2.15 (s)	170.8
9	2.69 (dd, *16.2*, *5.8*) 2.58 (dd, *16.5*, *7.1*)	30.4
10	5.21 (m)	205.3
11	2.69 (m)	47.2
12	4.96 (d, *10.2*)	74.4
14	2.19 (m) 2.11 (m)	35.7
15	1.97 (tt, *3.2*, *13.3*) 1.55 (m)	126.0
16	3.93 (dt, *10.5*, *4.2*)	135.6
17	5.21 (m)	35.4
18	2.11 (m) 1.90 (dd, *3.4*, *13.7*)	30.9
20	1.61 (m)	80.7
21	1.32 (m)	78.8
22	0.92 (t, *7.3*)	41.9
23	1.15 (d, *6.9*)	82.9
24	0.92 (d, *6.8*)	44.2
25	1.55 (s)	18.0
26	1.25 (s)	14.9



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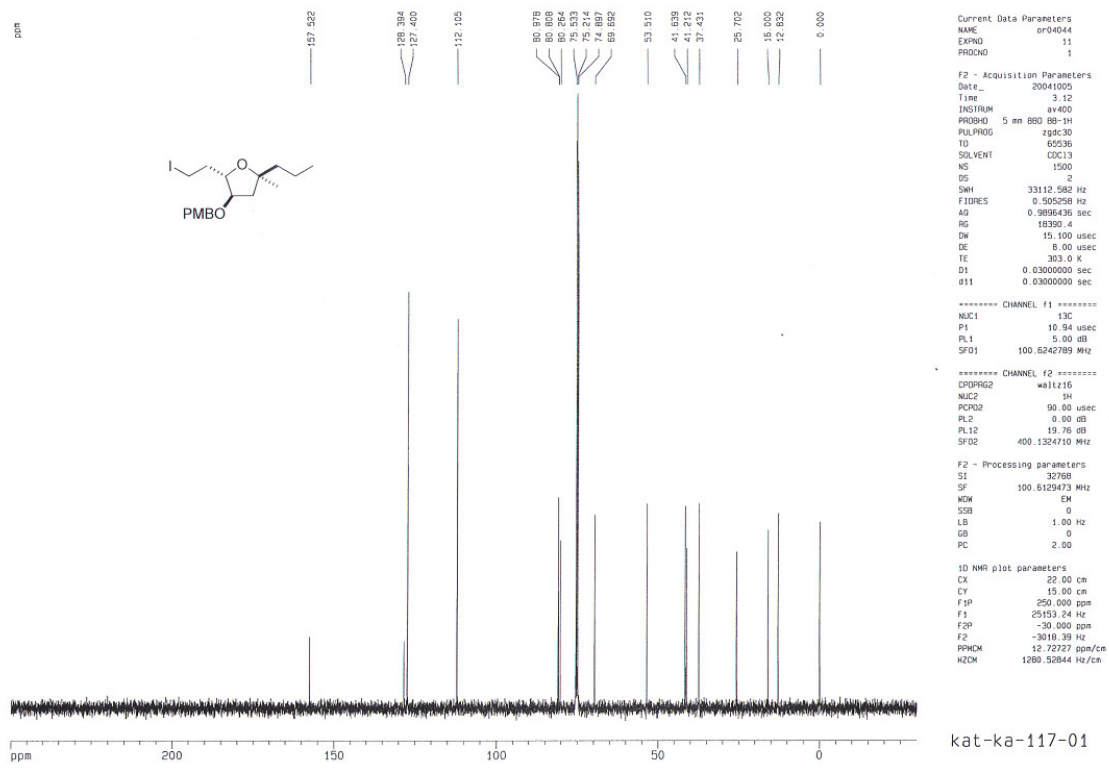

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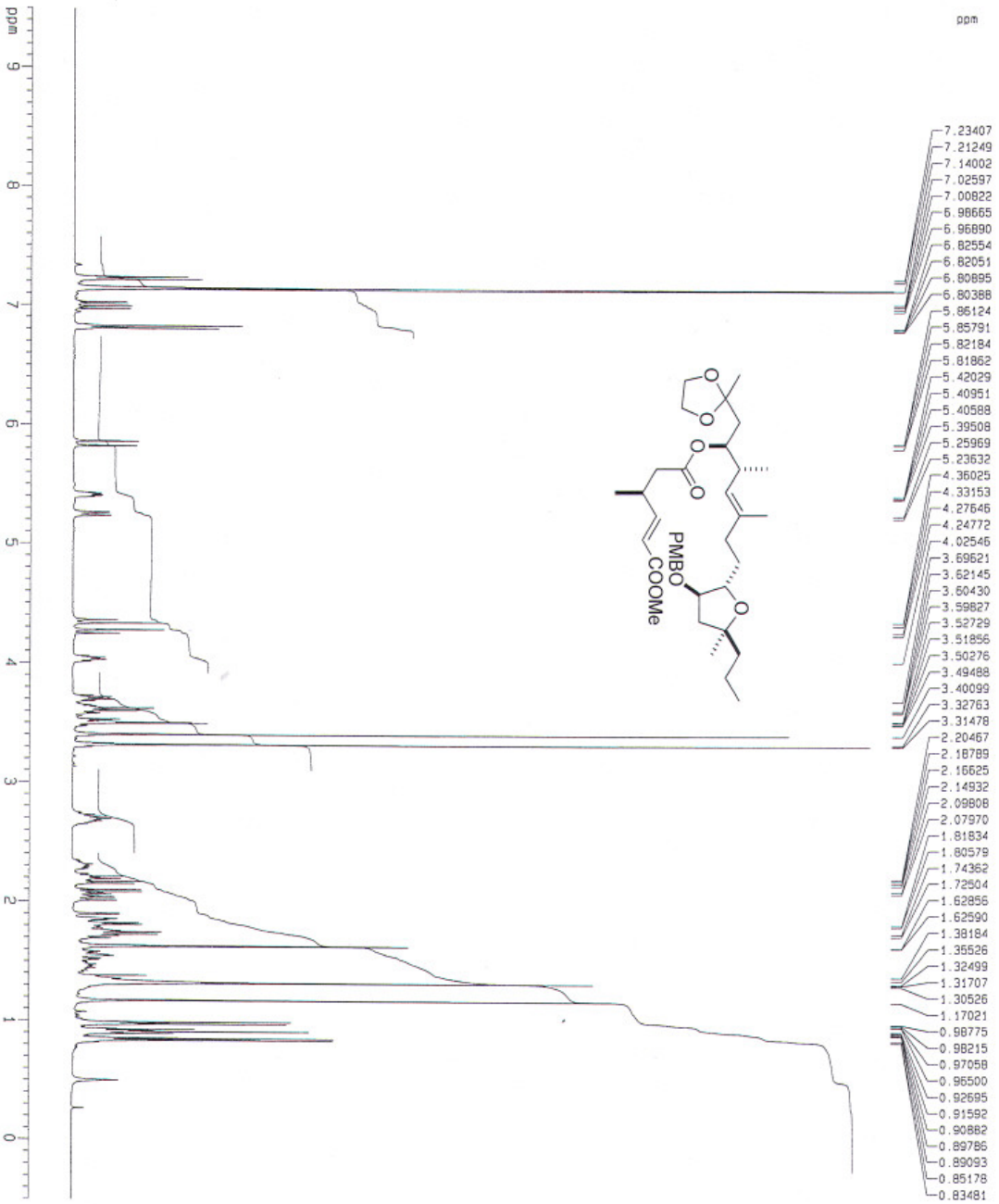


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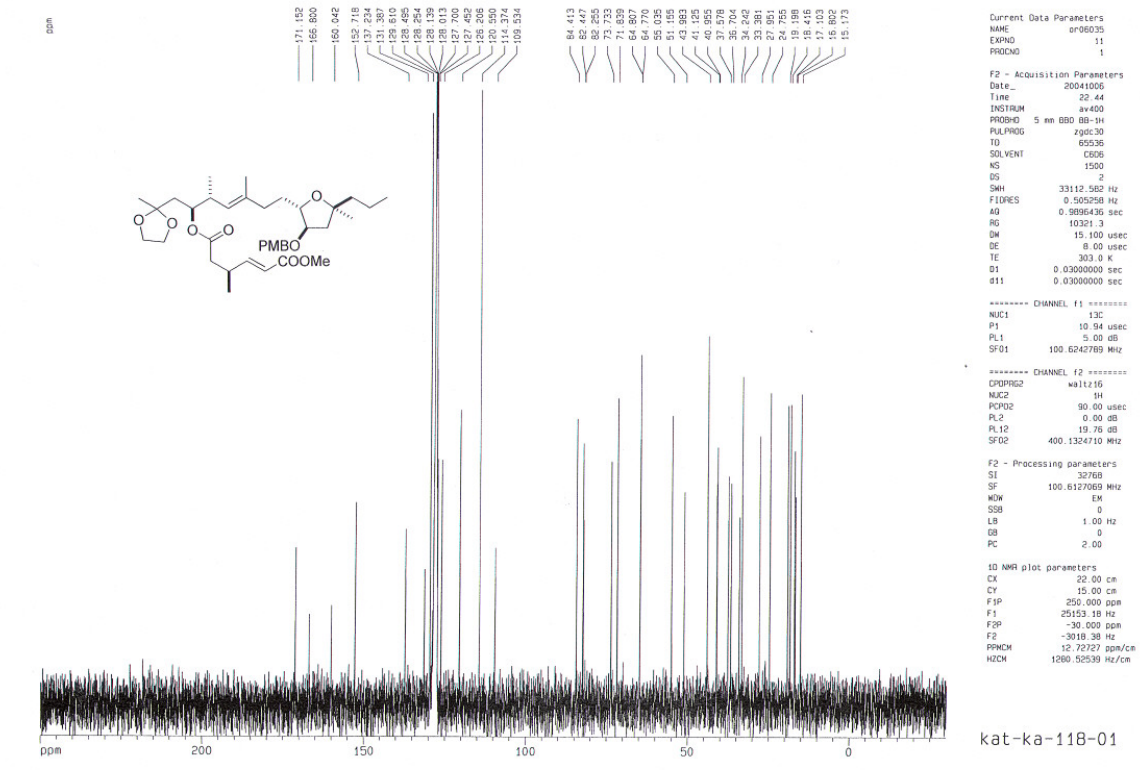
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43.135
40.955
37.578
36.704
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33.381
27.951
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NUC2 1H
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PL2 0.00 dB
PL12 19.76 dB
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SF 100.6127069 MHz
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SSB 0
LB 1.00 Hz
GB 0
PC 2.00
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CY 15.00 cm
F1P 250.000 ppm
F1 25153.18 Hz
F2P -30.000 ppm
F2 -3018.38 Hz
PPMCM 12.72727 ppm/cm
HZCM 1280.52539 Hz/cm
kat-ka-118-01
ppm
200
150
100
50
0

Amphidinolide Y: Preparation of the Building Blocks

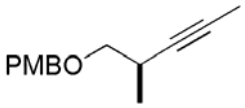
Methyl (2*S*)-3-((4-methoxybenzyl)oxy)-2-methylpropanoate (49). *p*-Methoxybenzyl trichloroacetimidate (23.4 g, 83 mmol) and PPTS (1.5 g, 5.9 mmol) were added to a solution of (2*S*)-methyl 3-hydroxy-2-methylpropionate **48** (7.0 g, 59 mmol) in CH_2Cl_2 (120 mL). After stirring for 17 h at ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (80 mL) and quenched with aq. sat. $NaHCO_3$ (40 mL). The organic layer was successively washed with aq. sat. $NaHCO_3$, water, and brine, before it was dried over Na_2SO_4 and filtered. The solvent was evaporated and the residue purified by flash chromatography (hexanes/ethyl acetate, 25/1) to provide product **49** as a colorless oil (11.8 g, 84%). $[\alpha]_D^{20}$ = +8.7 (c = 1.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (2H, d, *J* = 8.7 Hz), 6.87 (2H, d, *J* = 8.7 Hz), 4.45 (2H, s), 3.80 (3H, s), 3.69 (3H, s), 3.63 (1H, dd, *J* = 9.2, 7.2 Hz), 3.46 (1H, dd, *J* = 9.2, 6.0 Hz), 2.77 (1H, h, *J* = 7.1 Hz), 1.17 (3H, d, *J* = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 159.4, 130.5, 129.3, 113.9, 72.9, 71.8, 55.4, 51.8, 40.4, 14.2. IR: 1739, 1612, 1586, 1514, 1248, 1091 cm^{-1}. MS (EI) *m/z* (rel. intensity): 238 (M^+, 12), 137 (100). HRMS (ESIpos): *calcd.* for ($C_{13}H_{18}O_4$+Na): 261.1097, *found* 261.1097 (M+Na).

(2*S*)-3-((4-Methoxybenzyl)oxy)-2-methylpropanal (50). A solution of DIBAL-H in hexanes (1 M, 67 mL, 67 mmol) was added dropwise over 15 min to a solution of ester **49** (14.3 g, 60 mmol) in CH_2Cl_2 (430 mL) at −78°C. After stirring for 2 h at that temperature, the reaction was quenched by pouring the cold solution into an aq. potassium-sodium tartrate solution (1 M, 500 mL). The resulting mixture was stirred vigorously at ambient temperature until phase separation occurred. The aqueous phase was repeatedly extracted with *tert*-butyl methyl ether, the combined organic layers were dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetate, 60/1) to provide aldehyde **50** (9.8 g, 78%) as a colorless oil. $[\alpha]_D^{20}$ = +14.8 (c = 1.85, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (1H, d, *J* = 1.6 Hz), 7.16 (2H, d, *J* = 8.7 Hz), 6.81 (2H, d, *J* = 8.7 Hz), 3.73 (3H, s), 3,58 (2H, dd, *J* = 9.4, 6.7 Hz), 3.53 (2H, *J* = dd, 9.4, 5.3 Hz), 2.61-2.53 (1H, m), 1.05 (3H, d, *J* = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 159.5, 130.1, 129.4, 114.0, 73.1, 70.0, 55.4, 46.9, 10.9. IR: 2724, 1724, 1612, 1586, 1514, 1248, 1095 cm^{-1}. MS (EI) *m/z* (rel. intensity): 208 (M^+, 11), 137 (76), 121 (100). HRMS (EI(DE)): *calcd.* for $C_{12}H_{16}O_3$: 208.1099, *found* 208.1100 (M).

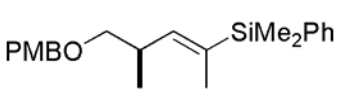
1-((((2*R*)-4,4-Dibromo-2-methylbut-3-enyl)oxy)methyl)-4-methoxybenzene. PPh_3 (33 g, 125 mmol) was added in portions to a stirred solution of CBr_4 (21 g, 63 mmol) in CH_2Cl_2 (270 mL) at 0°C. After the mixture had been stirred for 1h at 0°C, the brown suspension was cooled to −78°C and a solution of aldehyde **50** (8.7 g, 42 mmol) in CH_2Cl_2 (80mL) was added dropwise over 30 min. After stirring had been continued for an additional hour at −78°C, the reaction was quenched

by pouring the cold solution into vigorously stirred hexanes (700 mL). The precipitates were filtered off, the filtrate was evaporated and the residue purified by flash chromatography (hexanes/ethyl acetate, 60/1) to give the title compound as a colorless oil (13.6 g, 90%). $[\alpha]_D^{20}$ = –7.3 (c = 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* = 8.6 Hz), 6.89 (2H, d, *J* = 8.6 Hz), 6.30 (1H, d, *J* = 9.1 Hz), 4.48-4.41 (2H, m), 3.81 (3H, s), 3.39-3.31 (2H, m), 2.82-2.72 (1H, m), 1.05 (3H, d, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 141.4, 130.5, 129.3, 114.0, 88.9, 72.9, 72.8, 55.4, 38.9, 16.0. IR: 1612, 1586, 1514, 1248, 1095 cm^{-1}. MS (EI) *m/z* (rel. intensity): 366, 364, and 362 (M^+, 2, 4, 2), 136 (16), 121 (100). HRMS (EI(DE)): *calcd.* for $C_{13}H_{16}Br_2O_2$: 361.9517, *found* 361.9522 (M).

1-Methoxy-4-((((2*R*)-2-methylpent-3-ynyl)oxy)methyl)benzene (52).[5] A solution of *n*-BuLi in hexanes (1.65 M, 46 mL) was added dropwise over 15 min to a solution of 1-((((2*R*)-4,4-dibromo-2-methylbut-3-enyl)oxy)methyl)-4-methoxybenzene (13.2 g, 36 mmol) in THF (300 mL) at –78°C. The temperature was then allowed to raise to –20°C and stirring was continued for 1 h at this temperature. The reaction was again cooled to –78°C before MeI (6.8 mL, 109 mmol) was added dropwise over 5 min. The mixture was allowed to reach ambient temperature and was stirred for 15 h before the reaction was quenched with aq. sat. NH_4Cl (80 mL). The aqueous layer was repeatedly extracted with *tert*-butyl methyl ether, the combined organic phases were dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetate, 60/1) to provide product **52** as a colorless oil (7.2 g, 91%). $[\alpha]_D^{20}$ = +2.2 (c = 0.95, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (2H, d, *J* = 8.6 Hz), 6.88 (2H, d, *J* = 8.6 Hz), 4.50 (1H, d, *J* = 11.8 Hz), 4.47 (1H, d, *J* = 11.8 Hz), 3.81 (3H, s), 3.46 (1H, dd, *J* = 9.1, 6.1 Hz), 3.29 (1H, dd, *J* = 9.1, 7.5 Hz), 2.72-2.62 (1H, m), 1.77 (3H, d, *J* = 2.4 Hz), 1.16 (3H, d, *J* = 6.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 130.7, 129.4, 113.9, 81.4, 76.6, 74.3, 72.8, 55.4, 26.9, 18.3, 3.7. IR: 1612, 1586, 1513, 1248, 1092 cm^{-1}. MS (EI) *m/z* (rel. intensity): 218 (M^+, 2), 203 (9), 176 (19), 135 (10), 121 (100). HRMS (EI(DE)): *calcd.* for $C_{14}H_{18}O_2$: 218.1307, *found* 218.1310 (M).



((1*E*,3*R*)-4-((4-Methoxybenzyl)oxy)-1,3-dimethylbut-1-enyl)(dimethyl)phenyl-silane (55). A solution of freshly prepared $LiSiMe_2Ph$ in THF (0.36 M, 157 mL, 56 mmol)[6] was added to CuCN (2.5 g, 28 mmol) at 0°C. After stirring for 30 min at this temperature, the dark red solution was cooled to –78°C before a solution of alkyne **52** (4.1 g, 19 mmol) in THF (20 mL) was added dropwise over 5 min. The reaction mixture was stirred for 30 min at –78°C before it was allowed to reach 0°C and stirred for another 15 min at this temperature. After quenching with aq. sat. NH_4Cl (40 mL), the organic layer was successively washed with water and brine,

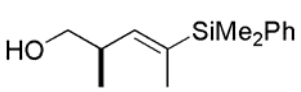


[5] The enantiomer is described in: Organ, M. G.; Wang, J. *J. Org. Chem.* **2003**, *68*, 5568.

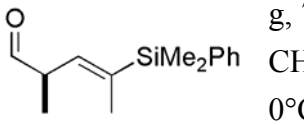
[6] Fleming, I.; Newton, T. W.; Roessler, F. *J. Chem. Soc. Perkin Trans. 1* **1981**, 2527.

dried over Na_2SO_4 and filtered. The solvent was evaporated and the residue purified by flash chromatography (hexanes/ethyl acetate, 25/1) to provide vinylsilane **55** as a colorless oil (6.1 g, 92 %). $[\alpha]_D^{20}$ = –12.8 (c = 1.45, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.48 (2H, m), 7.35-7.31 (3H, m), 7.24 (2H, d, *J* = 8.7 Hz), 6.87 (2H, d, *J* = 8.7 Hz), 6.62 (1H, dd, *J* = 8,8, 1,7 Hz), 4.44 (2H, s), 3.81 (3H, s), 3.33 (1H, dd, *J* = 9.1, 6.4 Hz), 3.27 (1H, dd, *J* = 9.1, 7.2 Hz), 2.99-2.88 (1H, m), 1.69 (3H, d, *J* = 1.7 Hz), 1.00 (3H, d, *J* = 6.7 Hz), 0.32 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 144.2, 138.9, 134.5, 134.1, 131.0, 129.2, 128.9, 127.8, 113.9, 74.9, 72.7, 55.4, 33.4, 17.5, 15.1, -3.2, -3.2. IR: 2957, 1427, 1247, 1110 cm^{-1}. MS (EI) *m/z* (rel. intensity): 354 (M^+, 1), 202 (12), 161 (6), 135 (22), 121 (100). HRMS (ESIpos): *calcd.* for ($C_{22}H_{30}O_2SiNa$): 377.1907, *found* 377.1909 (M+Na). Anal. *calcd.* for $C_{22}H_{30}O_2Si$: C 74.53, H 8.53, *found* C 74.42, H 8.50.

(2*R*,3*E*)-4-(Dimethyl(phenyl)silyl)-2-methylpent-3-en-1-ol (56). DDQ (4.6 g, 20 mmol) was added in portions to a solution of vinylsilane **55** (6.0 g, 16.8 mmol) in CH_2Cl_2/pH 7 buffer (10/1, 140 mL) at 0°C. The mixture was then allowed to reach ambient temperature and stirring was continued for 1 h. After the reaction had been quenched with aq. sat. $NaHCO_3$ (40 mL), the aqueous phase was repeatedly extracted with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4, filtered and evaporated to give an inseparable mixture of crude alcohol **56** and *p*-methoxybenzaldehyde. A solution of this residue in MeOH (125 mL) at 0°C was reacted with $NaBH_4$ (0.70, 18.5 mmol) to reduce the aldehyde by-product. After the mixture had been stirred for 1 h at ambient temperature, the reaction was quenched with aq. sat. NH_4Cl (50 mL). MeOH was removed under reduced pressure and the residue diluted with water and *tert*-butyl methyl ether. The aqueous layer was repeatedly extracted with *tert*-butyl methyl ether, the combined organic phases were dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetate, 10/1) to provide pure alcohol **56** as a colorless oil (3.6 g, 92%). $[\alpha]_D^{20}$ = +20.9 (c = 1.19, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.48 (2H, m), 7.36-7.33 (3H, m), 5.57 (1H, dq, *J* = 9.1, 1.7 Hz), 3.51 (1H, dd, *J* = 10.4, 6.1 Hz), 3.40 (1H, dd, *J* = 10.4 7.8 Hz), 2.91-2.80 (1H, m), 1.72 (3H, d, *J* = 1.7 Hz), 1.38 (1H, bs), 0.97 (3H, d, *J* = 6.7 Hz), 0.34 (6H, d, *J* = 0.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 138.5, 137.0, 134.0, 129.0, 127.9, 67.7, 35.8, 16.7, 15.4, -3.3. IR: 3341, 3068, 1618, 1428, 1248 cm^{-1}. MS (EI) *m/z* (rel. intensity): 219 ([M-Me]$^+$, 27), 203 (6), 177 (26), 157 (20), 135 (100). HRMS (ESIpos): *calcd.* for ($C_{14}H_{22}OSiNa$): 257.1332, *found* 257.1334 (M+Na). Anal. *calcd.* for $C_{14}H_{22}OSi$: C 71.73, H 9.46, *found* C 71.87, H 9.54.



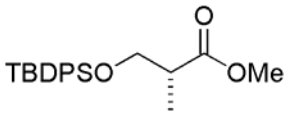
(2*R*,3*E*)-4-(Dimethyl(phenyl)silyl)-2-methylpent-3-enal (57). Dess-Martin periodinane (3.3 g, 7.7 mmol)[7] was added to a solution of alcohol **56** (1.2 g, 5.1 mmol) in CH_2Cl_2 (125 mL) at 0°C. After the mixture had been stirred for 4 h at 0°C, the reaction was quenched with aq. sat. $NaHCO_3$/$Na_2S_2O_3$ (1/1, 45



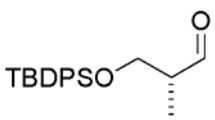
[7] Boeckman, R. K., Jr.; Shao, P.; Mullins, J. J. *Org. Synth.* **2000**, *77*, 141.

mL), and stirring was continued for 10 min at 0°C. The organic layer was successively washed with aq. sat. $NaHCO_3$, water, and brine, before it was dried over Na_2SO_4 and filtered. The filtrate was concentrated to a volume of ca. 10 mL before it was rapidly filtered through a short pad of silica. Concentration of the filtrate provided the sensitive aldehyde **57** as a colorless oil (1.1 g, 92%). $[\alpha]_D^{20}$ = –140.8 (c = 1.13, $CHCl_3$). ^{1}H NMR (400 MHz, C_6D_6) δ 9.25 (1H, d *J* = 1.6 Hz), 7.48-7.45 (2H, m), 7.24-7.19 (3H, m), 5.60 (1H, dq, *J* = 8.5, 1,7 Hz), 3.13-3.05 (1H, m), 1.55 (3H, d, *J* = 1.7 Hz), 0.93 (3H, d, *J* = 6.9 Hz), 0.27 (6H, s). ^{13}C NMR (100 MHz, C_6D_6) δ 199.1, 140.4, 137.9, 136.8, 134.3, 129.5, 128.2, 46.9, 15.7, 13.7, -3.5, -3.5. IR: 2808, 2710, 1723, 1610, 1428, 1249 cm^{-1}. MS (EI) *m/z* (rel. intensity): 232 (M^+, 2), 217 (16), 177 (5), 155 (15), 135 (100). HRMS (EI(FE)): *calcd.* for ($C_{14}H_{20}OSi$): 232.1283, *found* 232.1279 (M). Anal. *calcd.* for $C_{14}H_{20}OSi$: C 72.36, H 8.67, *found* C 72.30, H 8.62.

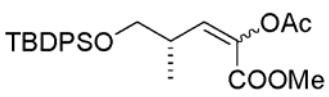
Methyl (2*R*)-3-((*tert*-butyl(diphenyl)silyl)oxy)-2-methylpropanoate (58). TBDPSCl (23.8 g, 87 mmol) was added to a solution of (2*R*)-methyl 3-hydroxy-2-methylpropionate *ent*-**48** (8.5 g, 72 mmol), imidazole (7.4 g, 108 mmol), and DMAP (0.4 g, 3.6 mmol) in CH_2Cl_2 (240 mL). After stirring for 16 h at ambient temperature, the reaction mixture was quenched with water, and the organic layer was successively washed with water and brine before it was dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetate, 60/1) to provide ester **58** as a colorless oil (23.1 g, 90%). $[\alpha]_D^{20}$ = –17.8 (c = 1.16, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.64 (4H, m), 7.45-7.36 (6H, m), 3.83 (1H, dd, *J* = 9.8, 6.9 Hz), 3.72 (1H, dd, *J* = 9.8, 5.8 Hz), 3.69 (3H, s), 2.72 (1H, h, *J* = 7.0 Hz), 1.16 (3H, d, *J* = 7.0 Hz), 1.03 (9H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 135.7, 133.7, 129.8, 127.8, 66.1, 51.7, 42.6, 26.9, 19.4, 13.6. IR: 3071, 2932, 1742, 1472, 1428, 1199, 1112 cm^{-1}. MS (EI) *m/z* (rel. intensity): 325 ($[M\text{-}OMe]^+$, 4), 299 (100). HRMS (ESIpos): *calcd.* for ($C_{21}H_{28}O_3Si$+Na): 379.1700, *found* 379.1698 (M+Na).



(2*R*)-3-((*tert*-Butyl(diphenyl)silyl)oxy)-2-methylpropanal (59). A solution of DIBAL-H in hexanes (1 M, 69 mL, 69 mmol) was added dropwise over 15 min to a solution of ester **58** (21.8 g, 61 mmol) in hexanes (430 mL) at –78°C. After stirring for 2 h at –78°C, the reaction was quenched by pouring the cold solution into an aq. potassium-sodium tartrate solution (1 M, 550 ml). The resulting mixture was vigorously stirred at ambient temperature until phase separation occurred. The aqueous layer was repeatedly extracted with *tert*-butyl methyl ether, the combined organic layers were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 60/1) to provide aldehyde **59** as a colorless oil (15.7 g, 79%). $[\alpha]_D^{20}$ = –21.5 (c = 1.44, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (1H, d, *J* = 1.6 Hz), 7.66-7.64 (4H, m), 7.46-7.37 (6H, m), 3.90 (1H, dd, *J* = 10.3 5.1 Hz), 3.85 (1H, dd, *J* = 10.3, 6.3 Hz), 2.61-2.53 (1H, m), 1.10 (3H, d, *J* = 7.0 Hz), 1.05 (9H, s).). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.5, 135.7, 133.4, 130.0, 127.9, 64.3, 49. 0, 26.9, 19.4, 10.5. IR: 3071, 2932, 2714, 1737, 1472, 1428, 1112 cm^{-1}. MS (EI) *m/z* (rel. intensity): 269 (83), 239 (82), 199

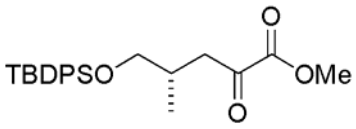


(25), 191 (70), 183 (100). HRMS (ESIpos): *calcd.* for ($C_{20}H_{26}O_2Si$+Na): 349.1594, *found* 349.1593 (M+Na).

Methyl (2*E*,4*S*)-2-(acetyloxy)-5-((*tert*-butyl(diphenyl)silyl)oxy)-4-methylpent-2-enoate (61). 

LiHMDS (6.8 g, 40 mmol) was added to a solution of methyl 2-(acetyloxy)-2-(dimethoxyphosphoryl)acetate **60** (9.7 g, 40 mmol)[8] in THF (145 mL) at −78°C. After stirring for 30 min at that temperature, a solution of aldehyde **59** (11.0 g, 34 mmol) in THF (25 mL) was added dropwise over 10 min. Stirring was continued for 1 h at −78°C before the mixture was allowed to reach ambient temperature and stirred for additional 2 h. The reaction was then quenched with water and the aqueous phase was repeatedly extracted with *tert*-butyl methyl ether. The combined organic layers were dried over Na_2SO_4, filtered, and evaporated, and the residue was purified by flash chromatography to give methyl enoate **61** as a colorless oil (13.5 g, 91%, *E*/*Z* = 6/1). $[\alpha]_D^{20}$ = +22.0 (c = 1.46, $CHCl_3$). *E*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.63 (4H, m), 7.44-7-35 (6H, m), 5.85 (1H, d, *J* = 10.1 Hz), 3.75 (3H, s), 3.63-3.48 (3H, m), 2.19 (3H, s), 1.10 (3H, d, *J* = 6.6 Hz), 1.04 (9H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 162.5, 137.3, 136.8, 135.7, 133.7, 129.8, 127.8, 68.0, 52.2, 34.3, 27.0, 20.6, 19.4, 17.1. IR: 3071, 2932, 1762, 1733, 1662, 1472, 1428, 1229, 1112 cm^{-1}. MS (EI) *m/z* (rel. intensity): 409 ([M-OMe]$^+$, 3), 383 (100). HRMS (ESIpos): *calcd.* for ($C_{25}H_{32}O_5Si$+Na): 463.1911, *found* 463.1907 (M+Na). Anal. *calcd.* for $C_{25}H_{32}O_5Si$: C 68.15, H 7.32, *found* C 67.96, H 7.28.

Z-isomer: ^{1}H NMR (400 MHz, $CDCl_3$, characteristic signals only): δ 6.46 (1H, d, *J* = 10.0 Hz), 3.77 (3H, s), 2.20 (3H, s), 1.05 (9H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 162.5, 137.3, 136.8, 135.8, 134.3, 129.8, 127.8, 67.3, 52.5, 34.3, 27.0, 20.5, 19.4, 17.1.

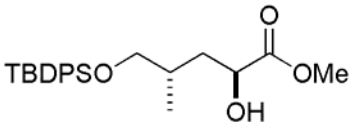
Methyl (4*S*)-5-((*tert*-butyl(diphenyl)silyl)oxy)-4-methyl-2-oxopentanoate (62). 

NaOMe (1.5 g, 28 mmol) was added to a solution of compound **61** (10.2 g, 23 mmol) in MeOH (230 mL) at −40°C. After the mixture had been stirred for 6 h at this temperature, the reaction was quenched with aq. sat. NH_4Cl (40 mL) and the resulting mixture was allowed to reach ambient temperature. MeOH was removed under reduced pressure and the aqueous phase was repeatedly extracted with *tert*-butyl methyl ether. The combined organic layers were dried over Na_2SO_4, filtered, and evaporated, and the residue was purified by flash chromatography (hexanes/ethyl acatate, 30/1) to provide ketoester **62** as a colorless oil (7.9 g, 86%). $[\alpha]_D^{20}$ = −10.1 (c = 1.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.63 (4H, m), 7.45-7.36 (6H, m), 3.84 (3H, s), 3.57 (1H, dd, *J* = 10.0, 5.1 Hz), 3.46 (1H, dd, *J* = 10.0, 7.0 Hz), 3.08 (1H, dd, *J* = 17.1, 5.8 Hz), 2.67, (1H, dd, *J* = 17.1, 7.6 Hz), 2.42-2.30 (1H, m), 1.05 (9H, s), 0.94 (3H, d, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 161.7, 135.7,

[8] (a) Nakamura, E. *Tetrahedron Lett*. **1981**, *22*, 663. (b) Schmidt, U.; Langner, J.; Kirschbaum, B.; Braun, C. *Synthesis* **1994**, 11, 1138.

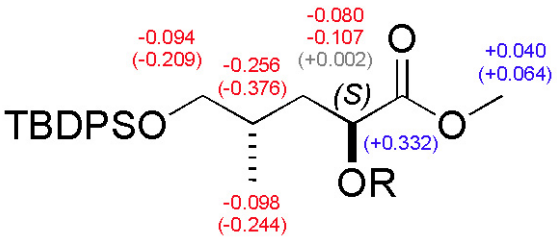
133.7, 129.8, 127.8, 68.3, 53.0, 43.4, 32.1, 27.0, 19.4, 16.8. IR: 3071, 2932, 1754, 1731, 1472, 1428, 1263, 1112 cm^{-1}. MS (EI) *m/z* (rel. intensity): 341 (53), 313 (20), 281 (6), 235 (15), 213 (100). HRMS (ESIpos): *calcd.* for ($C_{23}H_{30}O_4Si$+Na): 421.1806, *found* 421.1803 (M+Na). Anal. *calcd.* for $C_{23}H_{30}O_4Si$: C 69.24, H 7.51, *found* C 69.26, H 7.46.

Methyl (2*S*,4*S*)-5-((*tert*-butyl(diphenyl)silyl)oxy)-2-hydroxy-4-methylpentanoate (63).

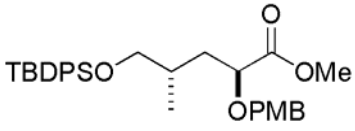


Ketoester **62** (7.5 g, 18.8 mmol) was solubilized under Ar in an autoclave (200 mL) in degassed MeOH (94 mL). $[Et_2NH_2][Ru_2Cl_5((S)\text{-binap})_2]$ (400 mg, 0.24 mmol)[9] and a stock solution of HCl in MeOH (14 mM, 1.3 mL, 18 µmol) were added. The autoclave was purged four times with hydrogen before the mixture was hydrogenated for 2.5 h under 20 bar hydrogen pressure at ambient temperature. The reaction mixture was filtered through a pad of Celite (rinsed with hexanes/ethyl acetate, 4/1), the combined filtrates were evaporated and the residue was purified by flash chromatography (hexanes/ethyl acetate, 10/1) to provide hydroxyester **63** as a colorless oil (dr ≥ 23/1, 6.9 g, 92%). $[\alpha]_D^{20}$ = –6.0 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.67 (4H, m), 7.46-7.37 (6H, m), 4.28 (1H, dd, *J* = 9.2, 1.3 Hz), 3.78 (3H, s), 3.54-3.52 (2H, m), 3.04 (1H, s), 2.07-1.96 (1H, m), 1.78 (1H, ddd, *J* = 14.0, 10.0, 4.7 Hz), 1.64 (1H, ddd, *J* = 13.9, 8.9, 3.3 Hz), 1.07 (9H, s), 0.98 (3H, d, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1 135.7, 133.7, 129.7, 127.8 69.3, 69.2, 52.6 38.8, 32.8 27.0, 19.4, 16.4. IR: 3496, 3071, 2931, 1738, 1472, 1428, 1218, 1112, 1086 cm^{-1}. MS (EI) *m/z* (rel. intensity): 311 (1), 283 (7), 265 (100). HRMS (ESIpos): *calcd.* for ($C_{23}H_{32}O_4Si$+Na): 423.1962, *found* 423.1958 (M+Na). Anal. *calcd.* for $C_{23}H_{32}O_4Si$: C 68.96, H 8.05, *found* C 68.91, H 7.94; *minor diastereomer*: ^{1}H NMR (400 MHz, $CDCl_3$, characteristic signal): δ 3.79 (3H, s).

Analysis of the Mosher esters derived from compound 63: $\Delta\delta^{SR}$ values in ppm from ^{1}H (and ^{13}C) NMR spectra of the MTPA esters.



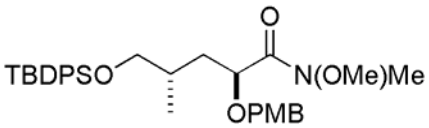
Methyl (2*S*,4*S*)-5-((*tert*-butyl(diphenyl)silyl)oxy)-2-((4-methoxybenzyl)oxy)-4-methylpentanoate (64).



$BF_3{\cdot}OEt_2$ (6.9 µL, 55 µmol) was added dropwise to a solution of hydroxyester **63** (8.8 g, 21.8 mmol) and *p*-methoxybenzyl trichloroacetimidate (8.6 g, 32.8 mmol) in

[9] King, S. A.; Keller, J. *Org. Synth.* **2005**, *81*, 178.

CH_2Cl_2/C_6H_{12} (1/2, 70 mL) at 0°C, causing the immediate formation of a white precipitate. After stirring for 1 h at 0°C, the reaction mixture was filtered through a pad of Celite, the filtrate was evaporated and the residue purified by flash chromatography (hexanes/ethyl acetate, 30/1) to give product **64** as a colorless oil (9.6 g, 84%). $[\alpha]_D^{20}$ = –33.6 (c = 1.04, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (4H, m), 7.44-7.34 (6H, m), 7.24 (2H, d, *J* = 8.7 Hz), 6.86 (2H, d, *J* = 8.7 Hz), 4.61 (1H, d, *J* = 11.3 Hz), 4.30 (1H, d, *J* = 11.3 Hz), 3.99 (1H, dd, *J* = 9.7, 3.7 Hz), 3.80 (3H, s), 3.73 (3H, s), 3.52 (1H, dd, *J* = 9.9, 5.4 Hz), 3.45 (1H, dd, *J* = 9.9, 5.9 Hz), 1.97-1.87 (2H, m), 1.55-1.48 (1H, m), 1.04 (9H, s), 0.86 (3H, d, *J* = 6.6 Hz).). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 159.5, 135.8, 134.0, 129.9, 129.7, 129.7, 127.7, 113.9, 76.1, 72.0, 69.1, 55.4, 52.0, 36.7, 32.3, 27.0, 19.5, 16.2. IR: 3071, 2932, 1751, 1737, 1613, 1514, 1471, 1428, 1249, 1201, 1112 cm^{-1}. MS (EI) *m/z* (rel. intensity): 463 ([M-^{t}Bu]$^+$, 0.4), 213 (2), 199 (4), 183 (2), 121 (100). HRMS (ESIpos): *calcd.* for ($C_{31}H_{40}O_5Si$+Na): 543.2537, *found* 543.2537 (M+Na). Anal. *calcd.* for $C_{31}H_{40}O_5Si$: C 71.50, H 7.74, *found* C 71.44, H 7.65; *minor diastereomer*: ^{1}H NMR (400 MHz, $CDCl_3$, characteristic signal) δ 0.97 (1H, d, *J* = 6.6 Hz).

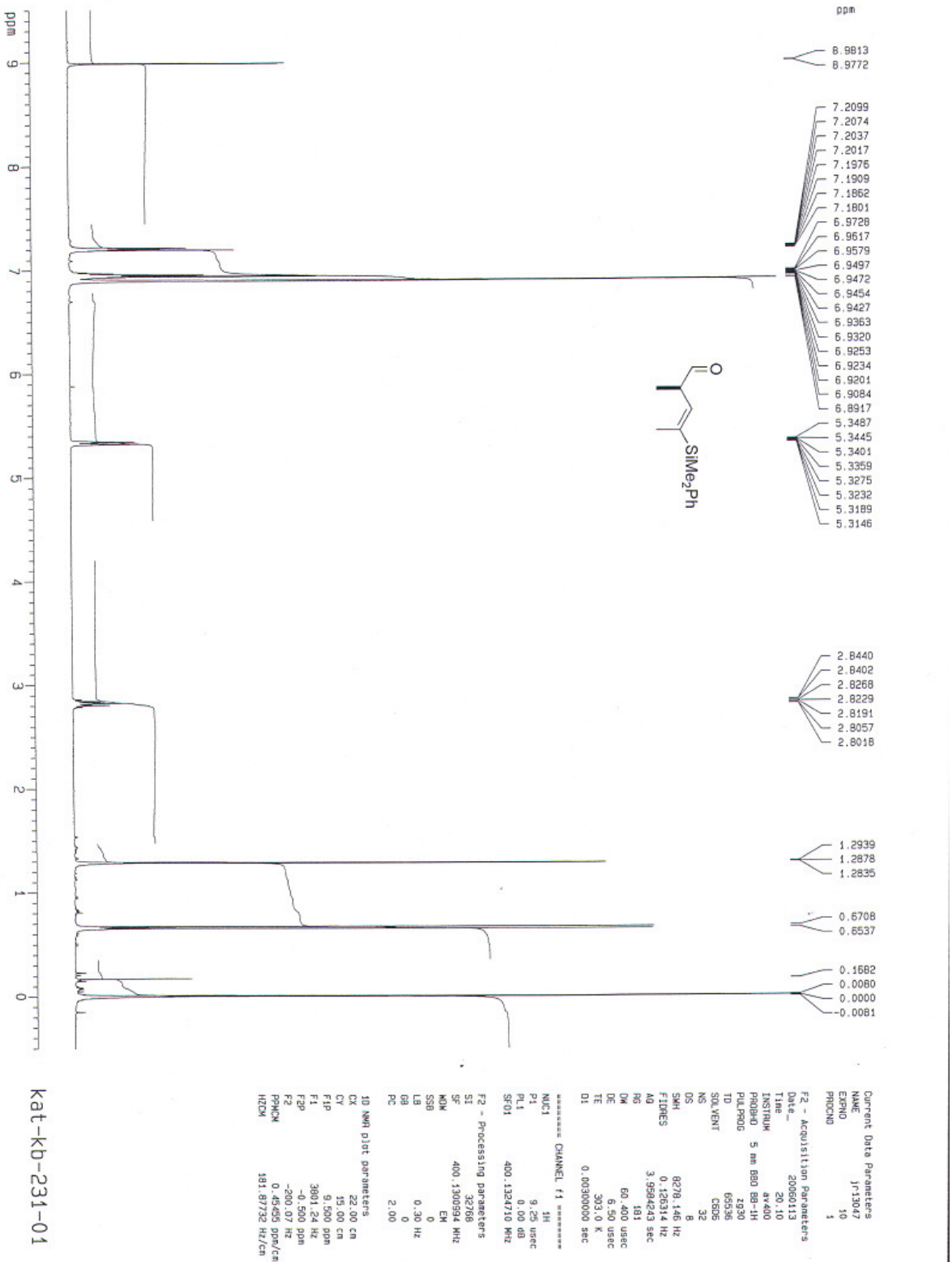
(2*S*,4*S*)-5-((*tert*-butyl(diphenyl)silyl)oxy)-*N*-methoxy-2-((4-methoxybenzyl)oxy)-*N*,4-dimethylpentanamide (65). 

LiOH (0.94 g, 40.6 mmol) was added to a solution of ester **64** (8.1 g, 15.6 mmol) in MeOH/THF/water (4/1/1, 155 mL). After the mixture had been stirred for 24 h at ambient temperature, the reaction was quenched with aq. HCl (2 M, 35 mL) and the aqueous layer was repeatedly extracted with *tert*-butyl methyl ether. The combined organic phases were dried over Na_2SO_4, filtered, and evaporated, and the resulting crude acid was used in the next step without further purification.

The crude acid was dissolved in CH_2Cl_2 (100 mL), and the resulting mixture was cooled to 0°C before Et$N(i$Pr$)_2$ (3.3 mL, 18.7 mmol), N,O-dimethylhydroxylamin-hydrochloride (1.8 g, 18.7 mmol), DCC (3.4 g, 16.4 mmol), and DMAP (95 mg, 0.78 mmol) were added successively. The mixture was stirred for 2 h at 0°C and for another 14 h at ambient temperature. The precipitates formed were filtered off before the reaction was quenched with water. The aqueous phase was repeatedly extracted with *tert*-butyl methyl ether, the combined organic layers were dried over Na_2SO_4, filtered, and evaporated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 4/1) to give amide **65** as a colorless oil (7.4 g, 86% over 2 steps). $[\alpha]_D^{20}$ = –37.9 (c = 1.09, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.64 (4H, m), 7.44-7.35 (6H, m), 7.26 (2H, d, *J* = 8.7 Hz), 6.86 (2H, d, *J* = 8.7 Hz), 4.62 (1H, d, *J* = 11.5 Hz), 4.32-4.29 (1H, m), 4.27 (1H, d, *J* =11.5 Hz), 3.80 (3H, s), 3.59-3.55 (1H, m), 3.57 (3H, s), 3.46 (1H, dd, *J* = 9.8, 6.2 Hz), 3.20 (3H, s), 2.03-1.95 (1H, m), 1.90 (1H, ddd, *J* = 13.9, 10.0, 4.0 Hz), 1.45, (1H, ddd, *J* = 13.9, 9.8, 3.0 Hz), 1.05 (9H, s), 0.89 (3H, d, *J* = 6.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 159.4, 135.7, 134.0, 130.1, 129.8, 129.6, 127.7, 113.8, 73.4, 71.1, 69.3, 61.3, 55.4, 35.9, 32.6, 32.4, 27.0, 19.4, 16.1. IR: 3070, 2932, 1677, 1612, 1513, 1389, 1428, 1112, 999 cm^{-1}. MS (EI) *m/z* (rel. intensity): 492 ([M-^{t}Bu]$^+$, 2), 413

(5), 275 (14), 199 (9), 121 (100). HRMS (ESIpos): *calcd.* for ($C_{32}H_{43}O_5Si$+Na): 572.2803, *found* 572.2800 (M+Na). Anal. *calcd.* for $C_{32}H_{43}O_5Si$: C 69.91, H 7.88, N 2.55, *found* C 69.79, H 7.69, N 2.45.

(3*S*,5*S*)-6-((*tert*-butyl(diphenyl)silyl)oxy)-3-((4-methoxybenzyl)oxy)-5-methyl-hexan-2-one (66). A solution of MeMgBr in Et_2O (3 M, 11.8 mL, 35.4 mmol) was added dropwise over 10 min to a solution of amide **65** (6.5 g, 11.8 mmol) in THF (45 mL) at 0°C. After the mixture had been stirred for 1 h at 0°C, the reaction was carefully quenched with aq. sat. NH_4Cl (15 mL) and the aqueous phase was repeatedly extracted with *tert*-butyl methyl ether. The combined organic layers were dried over Na_2SO_4, filtered, and evaporated, and the residue purified by flash chromatography to provide methylketone **66** as a colorless oil (5.4 g, 91%). $[\alpha]_D^{20}$ = –36.2 (c = 1.42, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.63 (4H, m), 7.44-7.34 (6H, m), 7.22 (2H, d, *J* = 8.7 Hz), 6.86 (2H, d, *J* = 8.7 Hz), 4.49, (1H, d, *J* = 11.3 Hz), 4.29 (1H, d, *J* = 11.3 Hz), 3.81-3.78 (1H, m), 3.81 (3H, s), 3.52 (1H, dd, *J* = 9.9, 5.8 Hz), 3.47 (1H, dd, *J* = 9.9, 5.9 Hz), 2.15 (3H, s), 1.99-1.88 (1H, m), 1.81 (1H, ddd, *J* = 13.9, 10.0, 4.2 Hz), 1.33 (1H, ddd, *J* = 13.9, 9.5, 3.7 Hz), 1.05 (9H, s), 0.87 (3H, d *J* = 6.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.2, 159.5, 135.8, 134.0, 129.9, 129.8, 129.7, 127.7, 114.0, 83.2, 72.3, 69.1, 55.4, 35.8, 32.3, 27.0, 25.2, 19.5, 16.3. IR: 3071, 2932, 1714, 1612, 1514, 1471, 1428, 1249, 1112 cm^{-1}. MS (EI) *m/z* (rel. intensity): 447 ([M-^{t}Bu]$^+$, 0.1), 199 (6), 121 (100). HRMS (ESIpos): *calcd.* for ($C_{31}H_{40}O_4Si$+Na): 527.2588, *found* 527.2587 (M+Na).). Anal. *calcd.* for $C_{31}H_{40}O_4Si$: C 73.77, H 7.99, *found* C 73.62, H 7.86.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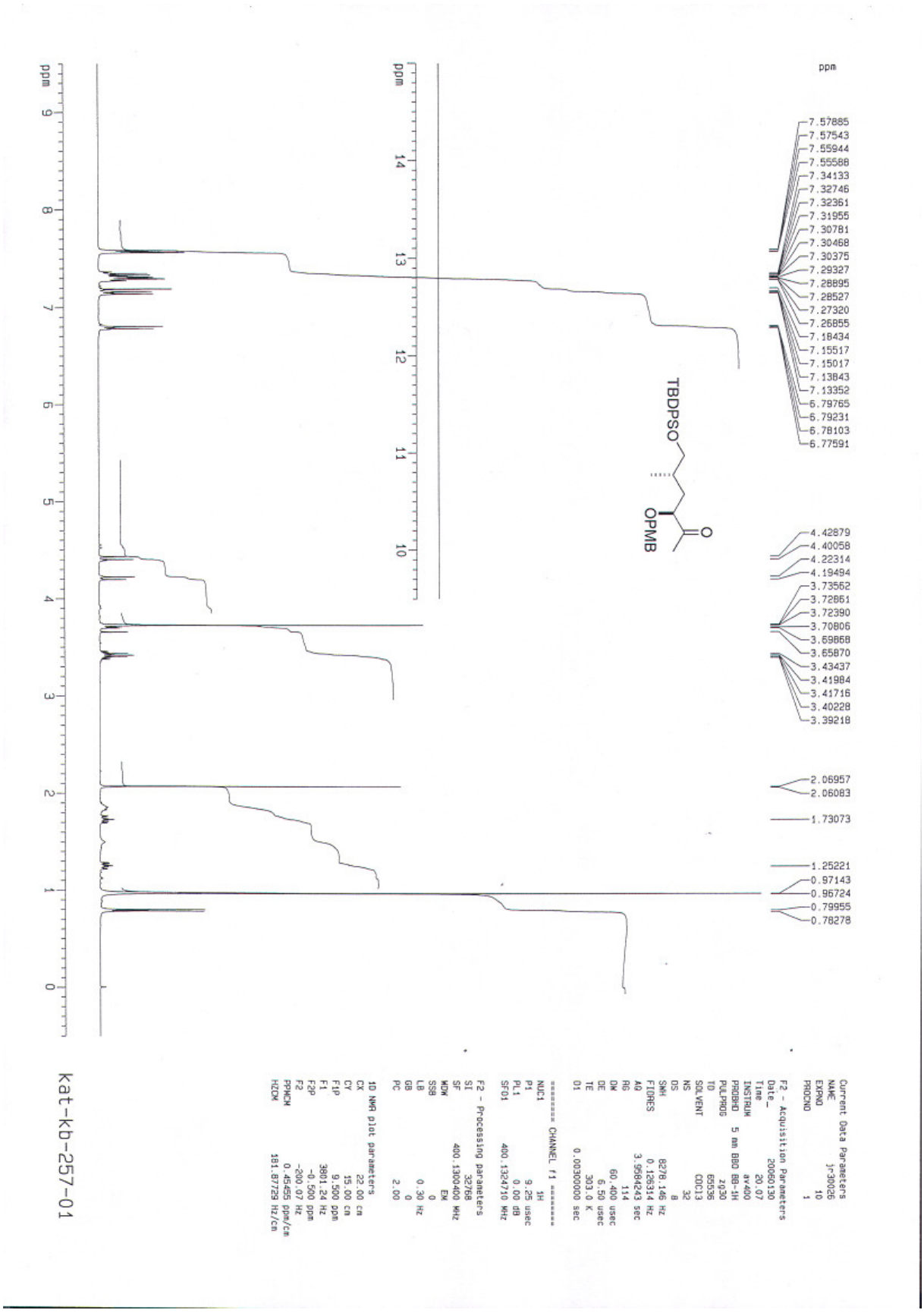
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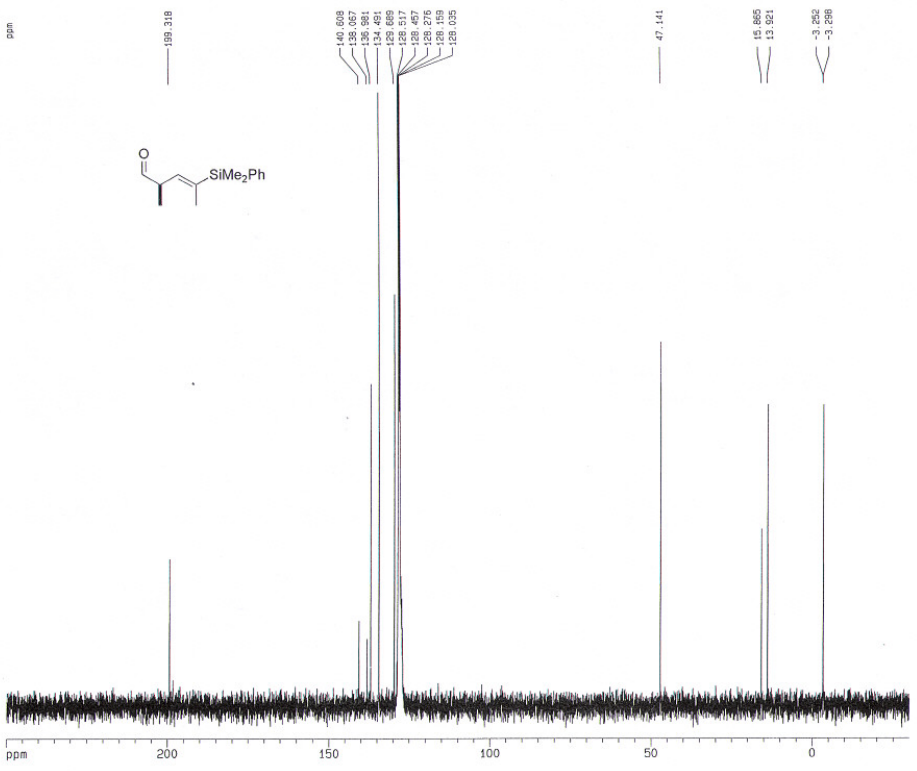

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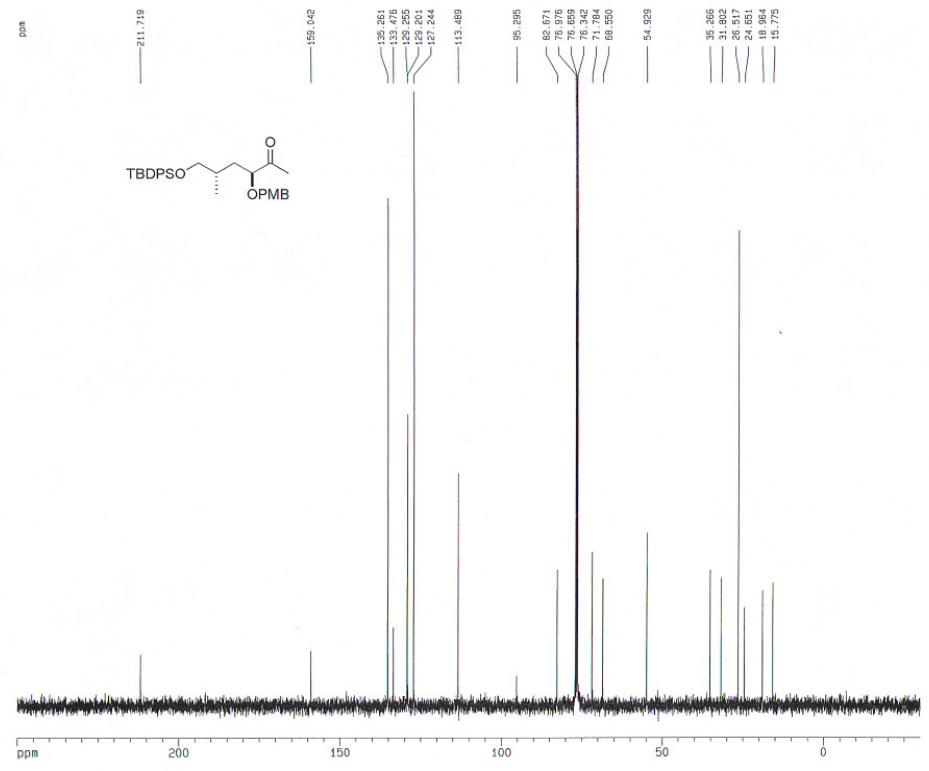

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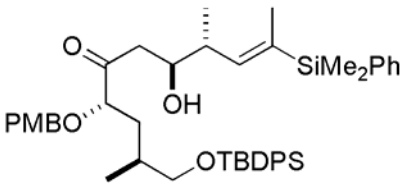
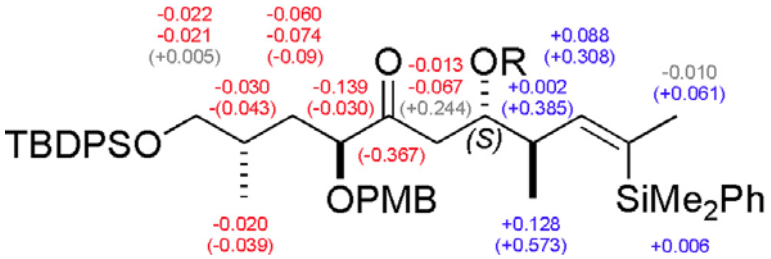
HZCM 1280.52661 Hz/cm

Amphidinolide Y: Elaboration of the Western Domain

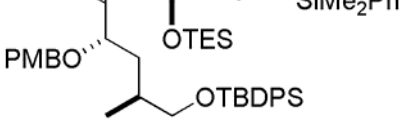
Aldol products 68 and 69. A solution of ketone **66** (2.22 g, 4.40 mmol) in toluene (6.5 mL) was added dropwise to a solution of Et_2BOTf (0.93 g, 4.26 mmol) and $EtN(iPr)_2$ (0.75 mL, 4.33 mmol) in toluene (13 mL) at −78°C. The resulting mixture was stirred for 90 min at that temperature (formation of white precipitates) before it was cooled to −90°C. A solution of aldehyde **57** (0.85 g, 3.67 mmol) in toluene (6.5 mL) was then added dropwise over 30 min, and stirring was continued for 90 min once the addition was complete. The reaction was quenched with MeOH/pH 7 buffer (1/1, 10 mL), the mixture was allowed to reach 0°C and treated dropwise with MeOH/30% H_2O_2 (2/1, 6.5 mL). Stirring was continued for 30 min at 0°C before the mixture was partitioned between water (15mL) and *tert*-butyl methyl ether (10 mL). The aqueous phase was repeatedly extracted with *tert*-butyl methyl ether, the combined organic layers were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/ethyl acetates, 15/1 to 10/1) to give an inseparable mixture of the aldol products **68** and **69** as a colorless oil (2.27 g, 84%, d.r. = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (4H, m), 7.48-7.28 (11H, m), 7.20 (2H, d, *J* = 8.6 Hz), 6.84 (2H, d, *J* = 8.6 Hz), 5.75 (1H, dd, *J* = 9.3, 1.7 Hz), 4.50 (1H, d, *J* = 11.1 Hz), 4.26 (1H, d, *J* = 11.1 Hz), 3.97-3.93 (1H, m), 3.83-3.77 (1H, m), 3.79 (3H, s), 3.51 (1H, dd, *J* = 9.9, 5.7 Hz), 3.45 (1H, dd, *J* = 9.9, 6.1 Hz), 2.75-2.51 (3H, m), 1.96-1.88 (1H, m), 1.80-1.73 (1H, m), 1.68 (3H, d, *J* = 1.6 Hz), 1.56 (1H, bs), 1.36-1.29 (1H, m), 1.04 (9H, s), 1.01 (3H, d, *J* = 6.8 Hz), 0.86 (3H, d, *J* = 6.7 Hz), 0.33 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.0, 159.6, 142.3, 138.6, 136.5, 135.8, 134.0, 134.0, 129.8, 129.7, 129.6, 129.0, 127.9, 127.7, 114.0, 83.0, 72.3, 71.2, 69.0, 55.4, 41.6, 38.2, 35.8, 32.4, 27.0, 19.5, 16.7, 16.3, 15.4, -3.2. IR: 3519, 3069, 2931, 1711, 1613, 1514, 1471, 1428, 1249, 1111 cm^{-1}. MS (ESIpos) *m/z*: 775 ($[M+K]^+$), 759 ($[M+Na]^+$). HRMS (ESIpos): *calcd.* for ($C_{45}H_{60}O_5Si_2$+Na): 759.3871, *found* 759.3872 (M+Na). Anal. *calcd.* for $C_{45}H_{60}O_5Si_2$: C 73.32, H 8.20, *found* C 73.18, H 8.16; characteristic signals of the minor diastereoisomer **69**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61-5.57 (1H, m), 0.31 (3H, d, *J* = 1.4 Hz).



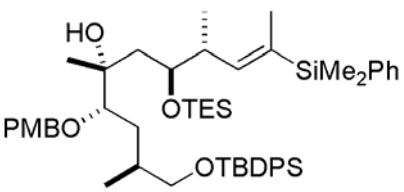
Analysis of the Mosher esters derived from aldol 68: $\Delta\delta^{SR}$ values in ppm from ^{1}H (and ^{13}C) NMR spectra of MTPA esters.



Compounds 70 and 71. TESCl (0.85 mL, 5.05 mmol) was added dropwise to a solution of alcohols **68** and **69** (2.48 g, 3.36 mmol) and imidazole (0.46 g, 6.72 mmol) in CH_2Cl_2 (35 mL) at 0°C. After stirring for 30 min at 0°C and additional 30 min at ambient temperature, the reaction was quenched with water. The organic layer was successively washed with water and brine, dried over Na_2SO_4, filtered and evapoated. The residue was purified by flash chromatography (hexanes/ethyl acetates, 25/1) to give products **70** and **71** as a colorless oil (2.59 g, 91%, d.r. = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.62 (4H, m), 7.48-7.27 (11H, m), 7.21 (2H, d, *J* = 8.7 Hz), 6.84 (2H, d, *J* = 8.7 Hz), 5.68 (1H, dd, *J* = 9.1, 1.7 Hz), 4.52 (1H, d, *J* = 11.0 Hz), 4.27-4.22 (1H, m), 4.18 (1H, d, *J* = 11.0 Hz), 3.79 (3H, s), 3.79-3.74 (1H, m), 3.51 (1H, dd, *J* = 9.8, 5.3 Hz), 3.41 (1H, dd, *J* = 9.8, 6.3 Hz), 2.85 (1H, dd, *J* = 17.7, 7.4 Hz), 2.79-2.59 (1H, m), 2.36 (1H, dd, *J* = 17.7, 4.7 Hz), 1.95-1.86 (1H, m), 1.77-1.64 (1H, m), 1.65 (3H, d, *J* = 1.7 Hz), 1.35-1.25 (1H, m), 1.03 (9H, s), 0.98 (3H, d, *J* = 6.9 Hz), 0.93 (9H, t, *J* = 7.8 Hz), 0.86 (3H, d, *J* = 6.6 Hz), 0.59 (6H, q, *J* = 7.8 Hz), 0.29 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.6, 159.5, 143.0, 135.8, 135.2, 134.0, 129.9, 129.8, 129.7, 128.9, 127.8, 127.7, 114.0, 83.3, 72.1, 70.7, 69.1, 55.4, 41.9, 38.3, 35.8, 32.5, 27.0, 19.5, 16.3, 16.0, 15.3, 7.1, 5.3, –3.2, –3.3 (2 overlapping signals). IR: 3069, 2933, 1716, 1613, 1514, 1462, 1428, 1249, 1111 cm^{-1}. MS (ESIpos) *m/z*: 889 ([M+K]$^+$), 873 ([M+Na]$^+$). HRMS (ESIpos): *calcd.* for ($C_{51}H_{74}O_5Si_3$+Na): 873.4736, *found* 873.4739 (M+Na). Anal. *calcd.* for $C_{51}H_{74}O_5Si_3$: C 71.95, H 8.76, *found* C 72.08, H 8.73; characteristic signals of the minor diastereomer **71**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72-5.69 (1H, m), 1.67 (3H, d, *J* = 1.5 Hz), 0.30 (3H, s).



Compound 72 and Isomers. A solution of MeMgBr in Et_2O (1 M, 6.0 mL, 6.0 mmol) was added dropwise over 10 min to a solution of ketones **70** and and **71** (2.57 g, 3.02 mmol) in Et_2O (30 mL) at –78°C. After stirring for 45 min at –78°C, the reaction was quenched with aq. sat. NH_4Cl (10 mL) and the mixture was allowed to reach ambient temperature. The organic phase was successively washed with water and brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetates, 25/1) to give an inseparable mixture of **72** together with two other diastereoisomers as a colorless oil (2.51 g, 96%, d.r. = 15:2.6:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.64 (4H, m), 7.49-7.25 (11H, m), 7.22 (2H, d,

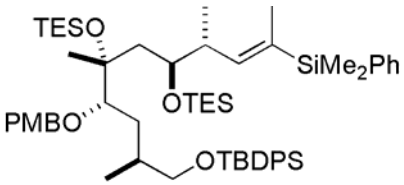


J = 8.7 Hz), 6.80 (2H, d, *J* = 8.7 Hz), 5.49 (1H, dd, *J* = 8.6, 1.7 Hz), 4.72 (1H, d, *J* = 11.0 Hz), 4.54 (1H, d, *J* = 11.0 Hz), 4.11-4.02 (1H, m), 3.77 (3H, s), 3.55 (1H, dd, *J* = 9.7, 5.5 Hz), 3.41 (1H, dd, *J* = 9.7, 7.2 Hz), 3.33-3.30 (1H, m), 2.87-2.79 (1H, m), 1.98-1-89 (1H, m), 1.79 (1H, dd, *J* = 14.4, 10.5 Hz), 1.71 (3H, d, *J* = 1.7 Hz), 1.59-1.11 (4H, m), 1.09 (3H, s), 1.05 (9H, s), 1.01-0.97 (12H, m), 0.86 (3H, d, *J* = 6.6 Hz), 0.69 (6H, q, *J* = 7.8 Hz), 0.27 (6H, d, *J* = 5.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 143.5, 138.4, 135.8, 135.6, 134.2, 133.9, 131.7, 129.6, 129.4, 129.0, 127.8, 127.7, 113.8, 84.8, 75.9, 74.6, 73.3, 69.9, 55.4, 41.5, 39.3, 36.4, 34.3, 33.1, 22.9, 19.5, 16.6, 15.5, 13.4, 7.1, 5.6, –3.3, –3.4. IR: 3504, 3069, 2934, 1613, 1514, 1428, 1248, 1112 cm^{-1}. MS (EI) *m/z* (rel. intensity): 395 (9), 347 (2), 273 (13), 213 (8), 135 (13), 121 (100). HRMS (ESIpos): *calcd.* for ($C_{52}H_{78}O_5Si_3$+Na): 889.5049, *found* 889.5051 (M+Na). Anal. *calcd.* for $C_{52}H_{78}O_5Si_3$: C 72.00, H 9.06, *found* C 71.86, H 8.97.

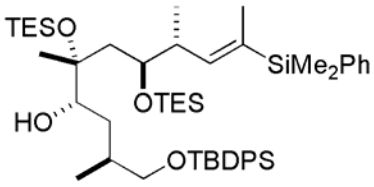
minor diastereoisomer, (dr = 15/**2.6**/1): ^{1}H NMR (400 MHz, $CDCl_3$, characteristic signals): δ 5.92 (1H, dd, *J* = 8.5, 1.7 Hz), 3.77 (3H, s), 0.32 (6H, s).

minor diastereoisomer, (dr = 15/2.6/**1**): ^{1}H NMR (400 MHz, $CDCl_3$, characteristic signals) δ 5.88 (1H, dd, *J* = 8.7, 1.8 Hz), 3.79 (3H, s), 0.31 (6H, s).

Compound 75. TESOTf (0.97 mL, 4.27 mmol) was added dropwise to a solution of alcohol **72** (and the inseparable isomers) (2.47 g, 2.85 mmol) and 2,6-lutidine (0.66 mL, 5.69 mmol) in CH_2Cl_2 (30 mL) at –78°C. After stirring for 30 min at that temperature and for an additional hour at 0°C, the reaction was quenched with water. The organic phase was successively washed with water and brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetates, 60/1) to give protected alcohol **75** as a colorless oil (2.58 g, 92%, d.r. = 15:2.6:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.65 (4H, m), 7.50-7.29 (11H, m), 7.23 (2H, d, *J* = 8.7 Hz), 6.82 (2H, d, *J* = 8.7 Hz), 5.75 (1H, dd, *J* = 9.0, 1.6 Hz), 4.77 (1H, d, *J* = 10.8 Hz), 4.47 (1H, d, *J* = 10.8 Hz), 4.04-4.01 (1H, m), 3.79 (3H, s), 3.61 (1H, dd, *J* = 10.1, 1.3 Hz), 3.53 (1H, dd, *J* = 9.7, 5.8 Hz), 3.45 (1H, dd, *J* = 9.7, 6.5 Hz), 2.82-2.74 (1H, m) 1.97-1.92 (2H, m), 1.73-1.64 (1H, m), 1.68 (3H, d, *J* = 1.6 Hz), 1.40-1.09 (2H, m), 1.23 (3H, s), 1.05 (9H, s), 0.99-0.86 (24H, m), 0.69-0.55 (12H, m), 0.30 (6H, d, *J* = 1.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 143.9, 138.8, 135.8, 134.2, 134.1, 134.0, 132.1, 129.6, 129.0, 128.9, 127.8, 127.7, 113.7, 82.4, 78.3, 73.5, 71.9, 70.1, 55.4, 42.3, 39.6, 34.5, 33.2, 27.0, 25.6, 19.5, 16.9, 15.4, 15.2, 7.6, 7.4, 7.3, 5.7, –3.1, –3.4. IR: 3069, 2955, 1614, 1514, 1428, 1247, 1112 cm^{-1}. MS (EI) *m/z* (rel. intensity): 655 (2), 519 (4), 347 (58), 189 (5), 135 (18), 121 (100). HRMS (ESIpos): *calcd.* for ($C_{58}H_{92}O_5Si_4$+Na): 1003.5914, *found* 1003.5916 (M+Na). Anal. *calcd.* for $C_{58}H_{92}O_5Si_4$: C 70.96, H 9.45, *found* C 70.87, H 9.41; characteristic signals of the minor diastereoisomers (overlapping): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96-5.93 (1H, m), 3.80 (3H, s), 1.65 (3H, d, *J* = 1.7 Hz), 1.27 (3H, s), 0.31 (6H, s).

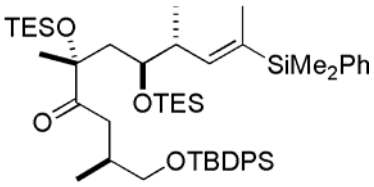


Compound 75a. DDQ (0.89 g, 3.91 mmol) was added in portions to a solution of compound



75 (2.56 g, 2.61 mmol) in CH_2Cl_2/pH 7 buffer (1/1, 50 mL) at 0°C. The reaction mixture was stirred for 5 h at 0°C before it was quenched with aq. sat. $NaHCO_3$ (15 mL) and partitioned between CH_2Cl_2 (75 mL) and water (30 mL). The organic layer was successively washed with water and brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetates, 100/1) to give alcohol **75a** as a colorless oil (2.06 g, 92%, d.r. = 15:2.6:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (4H, m), 7.50-7.30 (11H, m), 5.63 (1H, dd, *J* = 8.8, 1.7 Hz), 4.10 (1H, dd, *J* = 8.6, 3.3 Hz), 3.61-3.48 (3H, m), 3.26 (1H, dd, *J* = 4.1, 1.4 Hz), 2.90-2.79 (1H, m), 2.00-1.92 (1H, m), 1.86 (1H, dd, *J* = 14.8, 9.8 Hz), 1.71 (3H, d, *J* = 1.7 Hz), 1.46-1.24 (3H, m), 1.14 (3H, s), 1.06 (9H, s), 1.01-0.83 (24H, m), 0.73-0.53 (12H, m), 0.33 (6H, d, *J* = 6.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 138.6, 135.8, 135.2, 134.3, 134.0, 129.5, 129.0, 127.8, 127.7, 77.4, 73.4, 71.3, 70.2, 42.1, 39.6, 34.4, 32.9, 27.0, 24.2, 19.5, 16.6, 15.6, 13.9, 7.5, 7.2, 7.1, 5.5, –3.2, –3.6. IR: 3510, 2957, 1613, 1428, 1247, 1112 cm^{-1}. MS (ESIpos) *m/z*: 883 ([M+Na]$^+$). Anal. *calcd.* for $C_{50}H_{84}O_4Si_4$: C 69.70, H 9.83, *found* C 69.78, H 9.81; characteristic signals of the minor diastereoisomers (overlapping): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 (1H, dd, *J* = 8.4, 1.7 Hz), 3.15 (1H, m), 1.67 (3H, d, *J* = 1.7 Hz), 1.18 (3H, s), 0.32 (6H, d, *J* = 5.8 Hz).

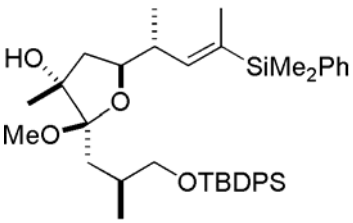
Compound 76. Dess-Martin periodinane (1.51 g, 3.57 mmol) was added to a solution of



alcohol **75a** (2.05 g, 2.38 mmol) and pyridine (0.96 mL, 11.9 mmol) in CH_2Cl_2 (40 mL) at 0°C. After stirring for 30 min at 0°C and for additional 4 h at ambient temperature, the reaction was quenched with aq. sat. $NaHCO_3$/$Na_2S_2O_3$ (1/1, 15 mL), and stirring was continued for 10 min. The organic phase was then successively washed with aq. sat. $NaHCO_3$, water, and brine, before it was dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography to give ketone **76** as a colorless oil (1.91 g, 93%, d.r. = 15:2.6:1). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.68-7.64 (4H, m), 7.49-7.29 (11H, m), 5.67 (1H, dd, *J* = 8.8, 1.7 Hz), 3.90-3.86 (1H, m), 3.51 (2H, d, *J* = 5.6 Hz), 2.89-2.73 (1H, m), 2.82 (1H, dd, *J* = 17.4, 4.5 Hz), 2.36 (1H, dd, *J* = 17.4, 8.8 Hz), 2.30-2.23 (1H, m), 1.93 (1H, dd, *J* = 14.1, 8.4 Hz), 1.68 (3H, d, *J* = 1.7 Hz), 1.57 (1H, dd, *J* = 14.1, 3.1 Hz), 1.32 (3H, s), 1.05 (9H, s), 1.00-0.83 (24H, m), 0.71-0.53 (12H, m), 0.31 (6H, d, *J* = 3.3 Hz). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 212.4, 144.0, 139.2, 136.1, 135.2, 134.5, 134.5, 130.1, 129.3, 128.2, 128.1, 81.5, 71.5, 69.1, 44.4, 41.2, 39.4, 32.0, 27.3, 27.2, 19.7, 17.3, 15.6, 14.8, 7.7, 7.5, 7.4, 5.8, –3.0, –3.3. IR: 2956, 1719, 1615, 1428, 1246, 1112 cm^{-1}. MS (EI) *m/z* (rel. intensity): 801 ([M-^{t}Bu]$^+$, 0.6), 655 (14), 523 (7), 441 (7), 391 (6), 347 (100). HRMS (ESIpos): *calcd.* for ($C_{50}H_{82}O_4Si_4$+Na): 881.5182, *found* 881.5180 (M+Na). Anal. *calcd.* for $C_{50}H_{82}O_4Si_4$: C 69.87, H 9.62, *found* C 69.75, H 9.55; characteristic signals of the minor

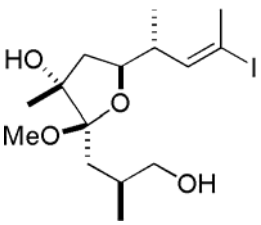
diastereoisomers (overlapping): ^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.88 (1H, d, *J* = 9.0, 1.7 Hz), 3.73-3.69 (1H, m), 1.66 (3H, d, *J* = 1.7 Hz), 1.37 (3H, s), 0.30 (6H, s).

Compound 77. CSA (98 mg, 0.42 mmol) was added to a solution of ketone **76** (1.45 g, 1.69 mmol) in MeOH/THF (5/1, 21 mL) at 0°C. The reaction was stirred for 6 h at 0°C before it was quenched with water (5 mL). The resulting mixture was repeatedly extracted with *tert*-butyl methyl ether, the combined organic layers were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/ethyl acetate, 40/1 + 1% NEt_3) to give the diastereomerically pure compound **77** (440 mg) as well as a separate fraction containing all other diastereomers (266 mg, together 65%).



This fraction containing the other diastereomers was dissolved in MeOH (3.5 mL) and a catalytic amount of PPTS (4.2 mg, 16.7 μmol) was added. The mixture was stirred for 1 h before it was filtered through a pad of silica and the filtrate was evaporated. The residue was again subjected to flash chromatography to give a second crop of compound **77** (105 mg) Overall yield of **77**: 50%. $[\alpha]_D^{20}$ = –24.5 (c = 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.72-7.69 (4H, m), 7.56-7.32 (11H, m), 5.82 (1H, dd, *J* = 9.0, 1.7 Hz), 4.04 (1H, q, *J* = 7.9 Hz), 3.49 (1H, dd, *J* = 9.7, 5,5 Hz), 3.44 (1H, dd, *J* = 9.7, 7.7 Hz), 3.19 (3H, s), 2.72-2.63 (1H, m), 2.38 (1H, bs), 2.13-2.02 (1H, m), 2.01 (1H, dd, *J* = 15.2, 3.0 Hz), 1.90 (2H, d, *J* = 8.0 Hz), 1.73 (1H, dd, *J* = 15.2, 8.1 Hz), 1.68 (3H, d, *J* = 1.7 Hz), 1.40 (3H, s), 1.07 (9H, s), 0.96 (3H, d, *J* = 6.7 Hz), 0.91 (3H, d, *J* = 6.8 Hz), 0.34 (6H, d, *J* = 8.1 Hz). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 145.5, 139.5, 136.2, 134.6, 134.1, 133.5, 130.2, 129.3, 128.2, 128.2, 110.3, 82.6, 81.8, 71.0, 49.0, 44.6, 39.5, 33.3, 31.7, 27.2, 23.1, 19.6, 18.1, 16.8, 15.2, -2.8, -3.2. IR: 3458, 2958, 1620, 1428, 1247, 1112 cm^{-1}. MS (EI) *m/z* (rel. intensity):): 587 ([M-^{t}Bu]$^+$, 2), 555 (28), 441 (20), 423 (28), 371 (14), 339 (10), 293 (32), 213 (25), 199 (31), 185 (46), 135 (100). HRMS (ESIpos): *calcd.* for ($C_{39}H_{56}O_4Si_2$+Na): 667.3609, *found* 667.3606 (M+Na). Anal. *calcd.* for $C_{39}H_{56}O_4Si_2$: C 72.62, H 8.75, *found* C 72.68, H 8.71.

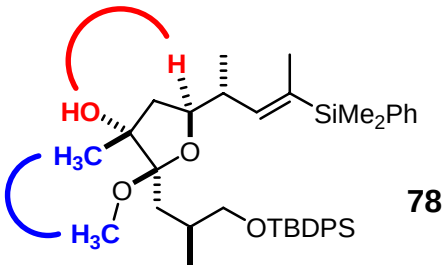
Compound 78. NIS (1.03 g, 4.57 mmol) was added in portions to a solution of vinylsilane **77** (590 mg, 0.92 mmol) in CH_3CN (11.4 mL) and the resulting mixture was stirred in the dark for 5 h at 0°C before it was filtered through a pad of basic alumina. Hexanes/ethyl acetate (10/1) was used to rinse the alumina pad and the combined filtrates were evaporated. The residue was used without further purification in the next step.



The residue was solubilized in THF (10 mL), cooled to 0°C, and treated with a solution of TBAF in THF (1 M, 2.75 mL, 2.75 mmol). After stirring for 90 min at 0°C, the reaction was quenched with water (3 mL) and the aqueous phase was repeatedly extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered and evaporated, and the residue was purified by flash chromatography (hexanes, ethyl acetate, 2/1 + 1% NEt_3) to

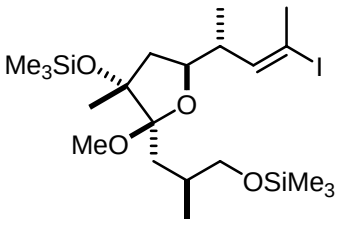
give diol **78** as a colorless oil (262 mg, 72% over 2 steps). $[\alpha]_D^{20}$ = +5.8 (c = 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.09 (1H, dd, *J* = 9.7, 1.5 Hz), 3.94 (1H, ddd, *J* = 9.8, 7.8, 6.3 Hz), 3.60-3.54 (1H, m), 3.34-3.23 (2H, m), 3.22 (3H, s), 2.47-2.39 (2H, m), 2.39 (3H, d, *J* = 1.5 Hz), 2.05-1.95 (1H, m), 1.91 (1H, dd, *J* = 15.5, 4.4 Hz), 1.89-1.80 (2H, m), 1.75 (1H, dd, *J* = 15.5, 5.3 Hz), 1.38 (3H, s), 0.92 (3H, d, *J* = 6.9 Hz), 0.89 (3H, d, *J* = 6.9 Hz). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 145.2, 110.6, 93.9, 82.3, 81.4, 70.0, 49.0, 44.6, 42.4, 34.3, 30.6, 28.3, 22.9, 18.9, 16.8. IR: 3347, 2958, 1638, 1066, 1019 cm^{-1}. MS (EI) *m/z* (rel. intensity): 367 ([M-OMe]$^+$, 1), 325 (3), 265 (5), 208 (13), 203 (2), 171 (100). HRMS (ESIpos): *calcd.* for ($C_{15}H_{27}IO_4$+Na): 421.0846, *found* 421.0844 (M+Na).

Characteristic and strong *NOE*'s observed in compound **78**

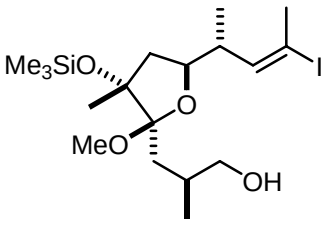


78

Compounds 78a,b. TMSCl (410 µL, 3.20 mmol) was added dropwise to a solution of diol **78** (255 mg, 0.640 mmol) and imidazole (305 mg, 4.48 mmol) in CH_2Cl_2 (6.4 mL) at 0°C. The reaction mixture was stirred for 30 min at 0°C and for 3 h at ambient temperature before it was quenched with water (2 mL). The organic phase was successively washed with water and brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes, ethyl acetate, 10/1 + 1% NEt_3) to give diprotected alcohol **78a** (288 mg, 83%) and a second fraction containing the monoprotected alcohol **78b** (32 mg, 11%) as colorless oils each. Compound **78a**: $[\alpha]_D^{20}$ = –7.7 (c = 1.10, CH_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.00 (1H, dd, *J* = 9.8, 1.5 Hz), 3.82, (1H, ddd, *J* = 10.2, 7.7, 5.8 Hz), 3.43 (1H, dd, *J* = 9.6, 5.1 Hz), 3.21 (1H, dd, *J* = 9.6, 7.5 Hz), 3.06 (3H, s), 2.34-2.29 (1H, m), 2.29 (3H, d, *J* = 1.5 Hz), 1.84-1.76 (2H, m), 1.68 (1H, dd, *J* = 12.5, 10.2 Hz), 1.60 (1H, dd, *J* = 14.8, 4.8 Hz), 1.39 (1H, dd, *J* = 14.8 7.4 Hz), 1.27 (3H, s), 0.84 (3H, d, *J* = 6.8 Hz), 0.80 (3H, d, *J* = 6.9 Hz), 0.05 (9H, s), 0.00 (9H, s). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 145.4, 111.3, 93.7, 85.5, 81.5, 69.3, 48.6, 44.1, 42.3, 32.8, 32.0, 28.3, 22.6, 17.6, 16.9, 2.5, -0.2. IR: 2957, 2875, 1638, 1250, 1143, 1019 cm^{-1}. MS (EI) *m/z* (rel. intensity): 542 (M$^+$, < 0.6), 347 (21), 329 (13), 303 (8), 277 (31), 257 (8), 225 (14), 208 (66), 143 (100) HRMS (ESIpos): *calcd.* for ($C_{21}H_{43}IO_4Si_2$+Na): 565.1637, *found*



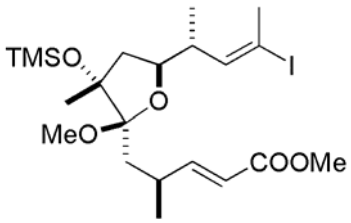
78a



78b

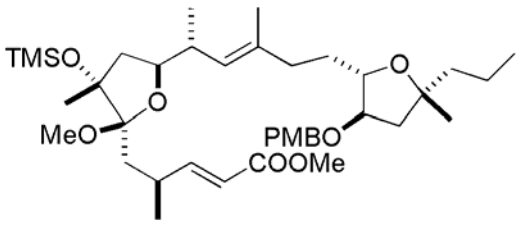
565.1638 (M+Na). Compound **78b**: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.99 (1H, dd, *J* = 9.8, 1.5 Hz), 3.90 (1H, ddd, *J* = 10.4, 7.7, 5.6 Hz), 3.38-3.33 (1H), 3.23-3.17 (1H, m), 3.10 (3H, s), 2.72 (1H, bs), 2.40-2.32 (1H, m), 2.30 (3H, d, *J* = 1.5 Hz), 1.96-1.88 (1H, m), 1.84 (1H, dd, *J* = 12.5, 5.6 Hz), 1.71 (1H, dd, *J* = 12.5, 10.4 Hz), 1.67 (1H, dd, *J* = 15.1, 6.7 Hz), 1.52 (1H, dd, *J* = 15.1, 4.4 Hz), 1.26 (3H, s), 0.83 (3H, d, *J* = 6.9 Hz), 0.82 (3H, d, *J* = 6.9 Hz), 0.07 (9H, s). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 144.8, 110.8, 94.2, 86.1, 82.4, 70.2, 48.6, 43.4, 42.0, 34.8, 32.3, 28.3, 22.3, 18.8, 16.8, 2.4.

Compound 81. DMSO (196 µL, 2.76 mmol) was added dropwise to a solution of oxalyl chloride (121 µL, 1.38 mmol) in CH_2Cl_2 (2.3 mL) at −78°C. After stirring for 10 min at this temperature, a solution of compound **78a** (250 mg, 0.461 mmol) in CH_2Cl_2 (2.3 mL) was added dropwise and stirring was continued for 1 h at that temperature. The reaction mixture was subsequently treated with NEt_3 (770 µL, 5.53 mmol) and stirred for 15 min at −78°C before it was allowed to reach 0°C. Stirring was continued for another 15 min at 0°C before the reaction was quenched with brine (1.0 mL) and diluted with CH_2Cl_2 (5 mL). The organic phase was washed twice with brine, dried over Na_2SO_4, filtered and evaporated to give crude aldehyde **80** as a pale yellow oil, which was used without further purification in the next step.

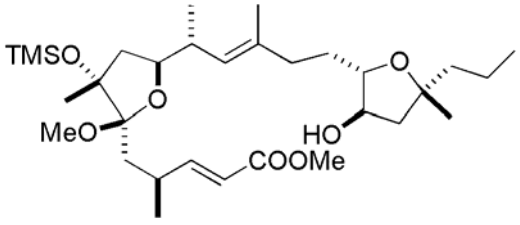


LiHMDS (116 mg, 0.692 mmol) was added to a solution of methyl diethylphosphonoacetate (145 mg, 0.692 mmol) in THF (2.1 mL) at −78°C. After stirring for 30 min at that temperature, a solution of crude aldehyde **80** in THF (2.5 mL) was added dropwise over 10 min. Stirring was continued for 1 h at −78°C and for another 30 min at 0°C before the reaction was quenched with water (1 mL) and the mixture was diluted with *tert*-butyl methyl ether (5 mL). The organic layer was successively washed with water and brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetate, 40/1 + 1% NEt_3) to provide ester **81** (190 mg, 76% over 2 steps) as a colorless oil. $[\alpha]_D^{20}$ = +0.4 (c = 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.98 (1H, dd, *J* = 15.8, 7.3 Hz), 6.07 (1H, dd, *J* = 9.7, 1.5 Hz), 5.75 (1H, dd, *J* = 15.8, 1.3 Hz), 3.92 (1H, ddd, *J* = 10.4, 7.3, 5.6 Hz), 3.69 (3H, s), 3.16 (3H, s), 2.70-2.60 (1H, m), 2.46-2.39 (1H, m), 2.38 (3H, d, *J* = 1.5 Hz), 1.89 (1H, dd, *J* = 12.6, 5.6 Hz), 1.84 (1H, dd, *J* = 14.9, 6.3 Hz), 1.79-1.73 (2H, m), 1.34 (3H, s), 1.08 (3H, d, *J* = 6.9 Hz), 0.90 (3H, d, *J* = 6.9 Hz), 0.15 (9H, s). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 167.8, 156.9, 145.1, 118.7, 110.7, 93.8, 85.6, 81.7, 51.7, 48.7, 43.9, 41.9, 35.9, 32.7, 28.3, 22.6, 20.4, 16.9, 2.5. IR: 2960, 2875, 1725, 1251 cm^{-1}. MS (EI) *m/z* (rel. intensity): 524 (M^+, 0.7), 493 (5), 397 (3), 329 (62), 297 (11), 259 (50), 239 (9), 208 (64), 143 (100) HRMS (ESIpos): *calcd.* for ($C_{21}H_{37}IO_5Si$+Na): 547.1347, *found* 547.1350 (M+Na).

Compound 82. A solution of *tert*-BuLi in pentane (2.1 M, 320 μL, 0.674 mmol) was added to a mixture of Et_2O (140 μL) and THF (140 μL) at −78°C before a solution of alkyl iodide **25** (47 mg, 0.112 mmol) in THF (920 μL) was added dropwise. After the mixture has been stirred for 5 min at −78°C, 9-MeO-9-BBN (93 μL, 0.674 mmol) was added dropwise causing an immediate color change from bright yellow to colorless. The reaction mixture was stirred for 5 min at −78°C before it was allowed to reach ambient temperature. Stirring was continued for another 1 h at this temperature (formation of white precipitates were observed). Aq. K_3PO_4 (3M, 225 μL, 0.674 mmol) and a solution of vinyl iodide **81** (61 mg, 0.112 mmol) in DMF (920 μL) were then successively added, followed by a solution of $AsPh_3$ (3.4 mg, 11.2 μmol) and Pd(dppf)Cl_2 (4.1 mg, 5.6 μmol) in DMF (180 μL). The reaction mixture was stirred for 90 min at ambient temperature before it was diluted with hexanes/ethyl acetate (10/1, 2.5 mL) and filtered through a pad of basic alumina (hexanes/ethyl acetate, 10/1 was used to rinse the pad). The combined filtrates were successively washed with aq. sat. $NaHCO_3$, water, and brine, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetate, 20/1 + 1% NEt_3) to give compound **82** (61 mg, 79%) as a colorless oil. $[\alpha]_D^{20}$ = –35.4 (c = 1.03, CH_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.25 (2H, d, *J* = 8.7 Hz), 6.98 (1H, dd, *J* = 15.8, 7.3 Hz), 6.86 (2H, d, *J* = 8.7 Hz), 5.74 (1H, dd, *J* = 15.8, 1.3 Hz), 5.05 (1H, dd, *J* = 9.3, 1.1 Hz), 4.43 (1H, d, *J* = 11.2 Hz), 4.36 (1H, d, *J* = 11.2 Hz), 3.97-3.85 (2H, m), 3.79 (3H, s), 3.76-3.72 (1H, m), 3.68 (3H, s), 3.15 (3H, s), 2.69-2.60 (1H, m), 2.51-2.36 (1H, m), 2.12-1.94 (2H, m), 1.97 (1H, dd, *J* = 13.1, 7.3 Hz), 1.87 (1H, dd, *J* = 12.5, 5.5 Hz), 1.84-1.71 (4H, m), 1.64-1.29 (6H, m), 1.61 (3H, d, *J*= 1.1 Hz), 1.34 (3H, s), 1.26 (3H, s), 1.08 (3H, d, *J* = 6.9 Hz), 0.91 (3H, t, *J* = 7.1 Hz), 0.85 (3H, d, *J* = 6.8 Hz), 0.15 (9H, s). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 167.8, 159.7, 157.1, 135.1, 131.3, 129.7, 128.5, 118.6, 114.2, 110.5, 85.7, 84.7, 82.9, 82.6, 82.5, 71.7, 55.8, 51.6, 48.7, 45.9, 43.6, 43.1, 38.6, 36.4, 36.0, 34.0, 32.7, 26.5, 22.8, 20.3, 18.4, 17.4, 16.7, 15.0, 2.5. IR: 2958, 2872, 1725, 1655, 1613, 1514, 1251 cm^{-1}. MS (EI) *m/z* (rel. intensity): 657 ([M-OMe]$^+$, 1), 567 (1), 535 (4), 329 (36), 297 (11), 259 (5), 239 (9), 207 (6), 143 (57), 121 (100). HRMS (ESIpos): *calcd.* for ($C_{39}H_{64}IO_8Si$+Na): 711.4263, *found* 711.4265 (M+Na).

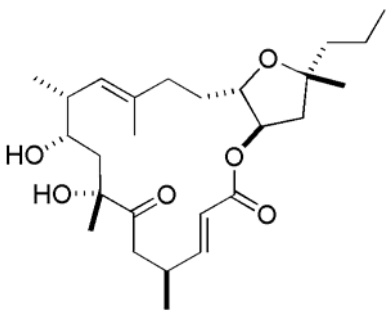


Compound 83. DDQ (16 mg, 69.7 μmol) was added in portions to a vigorously stirred solution of compound **82** (24 mg, 34.8 μmol) in CH_2Cl_2/pH 7 buffer (1/1, 3.6 mL) at 0°C. The mixture was stirred 1 h at 0°C and for 6 h at ambient temperature. During this time more DDQ (24 mg, 104 μmol) was added in portions to achieve complete conversion. The reaction was then quenched with water (2.5 mL) and diluted with CH_2Cl_2 (3 mL). The aqueous phase was



repeatedly extracted with CH_2Cl_2, the combined organic layer were washed with aq. sat. $Na_2S_2O_3$, dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetate, 15/1 + 1% NEt_3 → 6/1 + 1% NEt_3) to give compound **83** (10 mg, 51%) as a colorless oil. $[\alpha]_D^{20}$ = –29.3 (c = 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.00 (1H, dd, *J* = 15.8, 7.2 Hz), 5.74 (1H, dd, *J* = 15.8, 1.2 Hz), 5.09 (1H, dd, *J* = 9.2, 1.1 Hz), 4.07-4.01 (1H, m), 3.90 (1H, ddd, *J* = 10.2, 8.2, 5.6 Hz), 3.73-3.68 (1H, m), 3.68 (3H, s), 3.14 (3H, s), 2.68-2.61 (1H, m), 2.43 (1H, d, *J* = 3.9 Hz), 2.39-2.33 (1H, m), 2.18-2.05 (2H, m), 2.02 (1H, dd, *J* = 13.0, 7.3 Hz), 1.94 (1H, dd, *J* = 12.6, 5.6 Hz), 1.84-1.72 (3H, m), 1.68-1.52 (3H, m), 1.6 (3H, d, *J* = 1.2 Hz), 1.45-1.29 (4H, m), 1.34 (3H, s), 1.26 (3H, s), 1.07 (3H, d, *J* = 6.9 Hz), 0.90 (3H, t, *J* = 7.1 Hz), 0.82 (3H, d, *J* = 6.8 Hz), 0.15 (9H, s). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 168.0, 157.3, 134.7, 129.2, 118.5, 110.7, 85.7, 84.8, 82.8, 82.6, 76.7, 51.7, 48.6, 46.0, 45.7, 44.2, 39.5, 36.3, 35.8, 32.7, 32.3, 27.1, 22.7, 20.4, 18.4, 17.4, 16.4, 15.0, 2.8. IR: 3429, 2958, 2872, 1725, 1654, 1251 cm^{-1}. MS (EI) *m/z* (rel. intensity): 537 ([M-OMe]$^+$, 2), 446 (8), 329 (59), 297 (17), 259 (11), 252 (11), 239 (13), 207 (9), 179 (8), 143 (100). HRMS (ESIpos): *calcd.* for ($C_{31}H_{56}IO_7Si$+Na): 591.3687, *found* 591.3685 (M+Na).

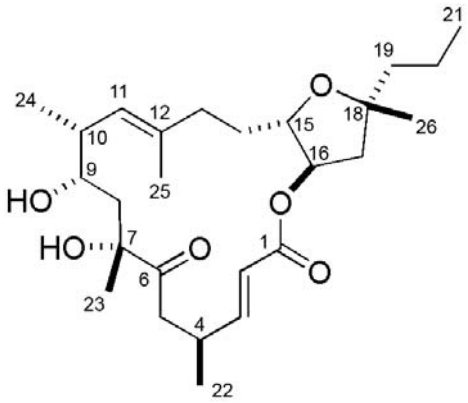
Amphidinolide Y (2). A solution of LiOH (11.4 mg, 47.5 μmol) in MeOH (360 μL) was added to a solution of methylester **83** (9 mg, 15.8 μmol) in THF/water (1/1, 180 μL). After stirring for 17 h at ambient temperature, the mixture was cooled to 0°C and diluted with *tert*-butyl methyl ether (2 mL) before being quenched with aq. sat. NH_4Cl (300 μL). The aqueous solution was *rapidly* extracted with *tert*-butyl methyl ether (several times). The combined organic phases were dried over Na_2SO_4 and filtered. NEt_3 (6.6 μL, 47.5 μmol) were added before the filtrate was evaporated. The corresponding triethylamonium salt **84** of the *seco*-acid was immediately used in the next step without further purification.



2,4,6-Trichlorobenzoyl chloride (3.7 μL, 23.7 μmol) was added to a solution of compound **84** and NEt_3 (11 μL, 79.0 μmol). The reaction mixture was stirred for 1 h at ambient temperature before it was filtered through a short pad of Celite which was prewashed with copious amounts of dry THF. The patch was rinsed with excess THF before most of the solvent was removed under a flow of Argon. The residue was diluted with toluene (4.5 mL) and the resulting solution was added dropwise over 2 h (via syringe pump) to a solution of DMAP (38.6 mg, 316 μmol) in toluene (20.3 mL) at ambient temperature. After complete addition stirring was continued for 2 h. The reaction mixture was neutralized with aq. sat. $NaHCO_3$ (3 mL) and the organic layer washed twice with brine before it was dried over Na_2SO_4 and evaporated. The residue was filtered through a pad of silica (hexanes/ethyl acetate, 10/1 + 1% NEt_3) to remove the DMAP and the crude macrocycle **85** was used in the next step without further purification.

The crude compound **85** was dissolved in HOAc/MeOH/H_2O (4/1/1, 240 µL) and the resulting solution was stirred for 4 h at ambient temperature. The reaction was diluted with *tert*-butyl methyl ether (500 µL) and quenched with aq. sat. $NaHCO_3$. The aqueous layer was repeatedly extracted with *tert*-butyl methyl ether, the combined organic phases were dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography (hexanes/ethyl acetate, 4/1) to give amphidinolide Y (**2**) as a colorless oil (4 mg, 56% over 3 steps). $[\alpha]_D^{17}$ = –28.0° (c = 1.00, $CHCl_3$) [lit.: $[\alpha]_D^{17}$ = –33° (c = 1.00, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$, 400 MHz) see Table 4. ^{13}C NMR ($CDCl_3$, 100 MHz) see Table 5.

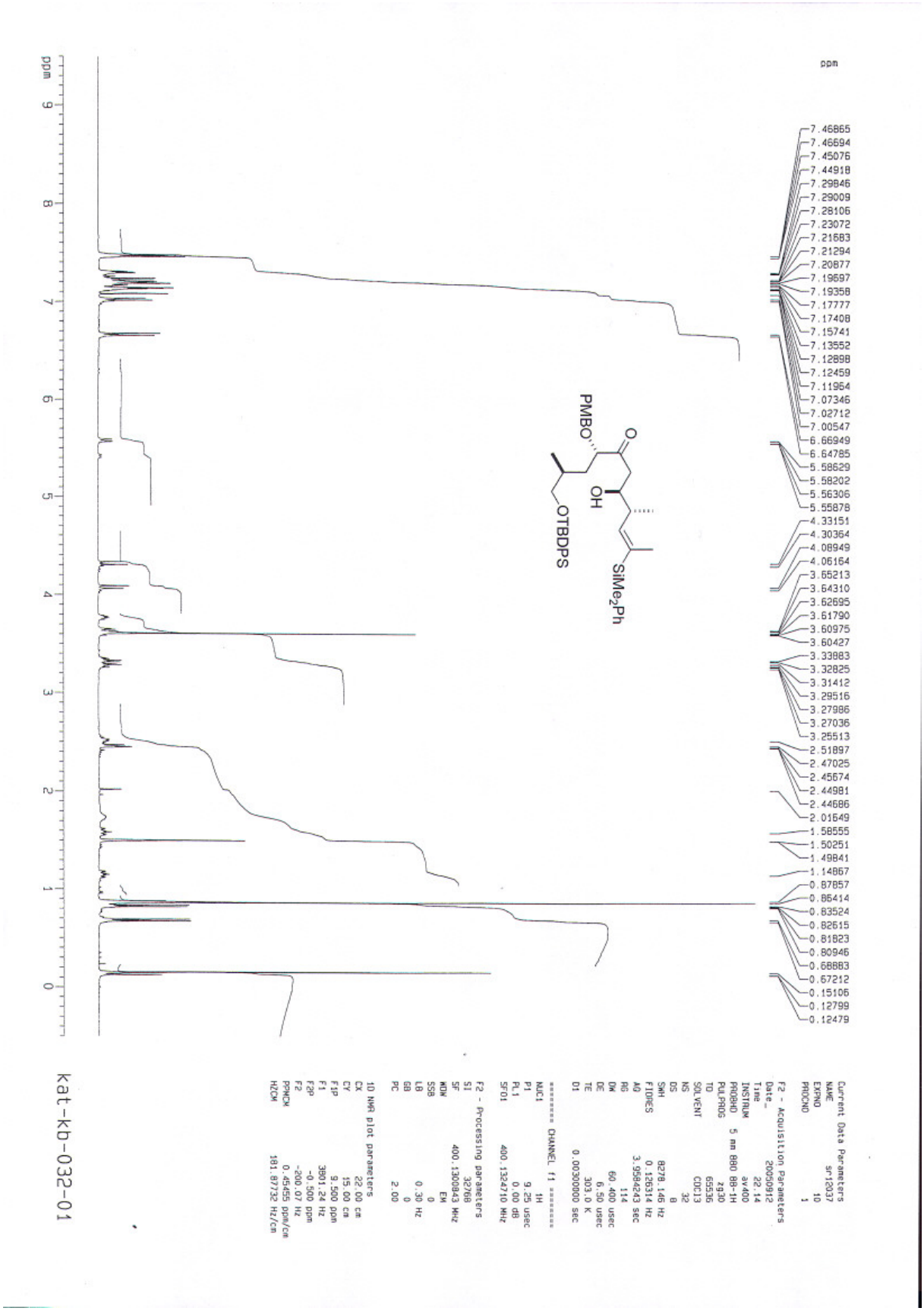
Table 4: Comparison of the ^{1}H NMR spectrum of natural ($CDCl_3$, 600 MHz) and synthetic amphidinolide Y (**2**) ($CDCl_3$, 400 MHz).

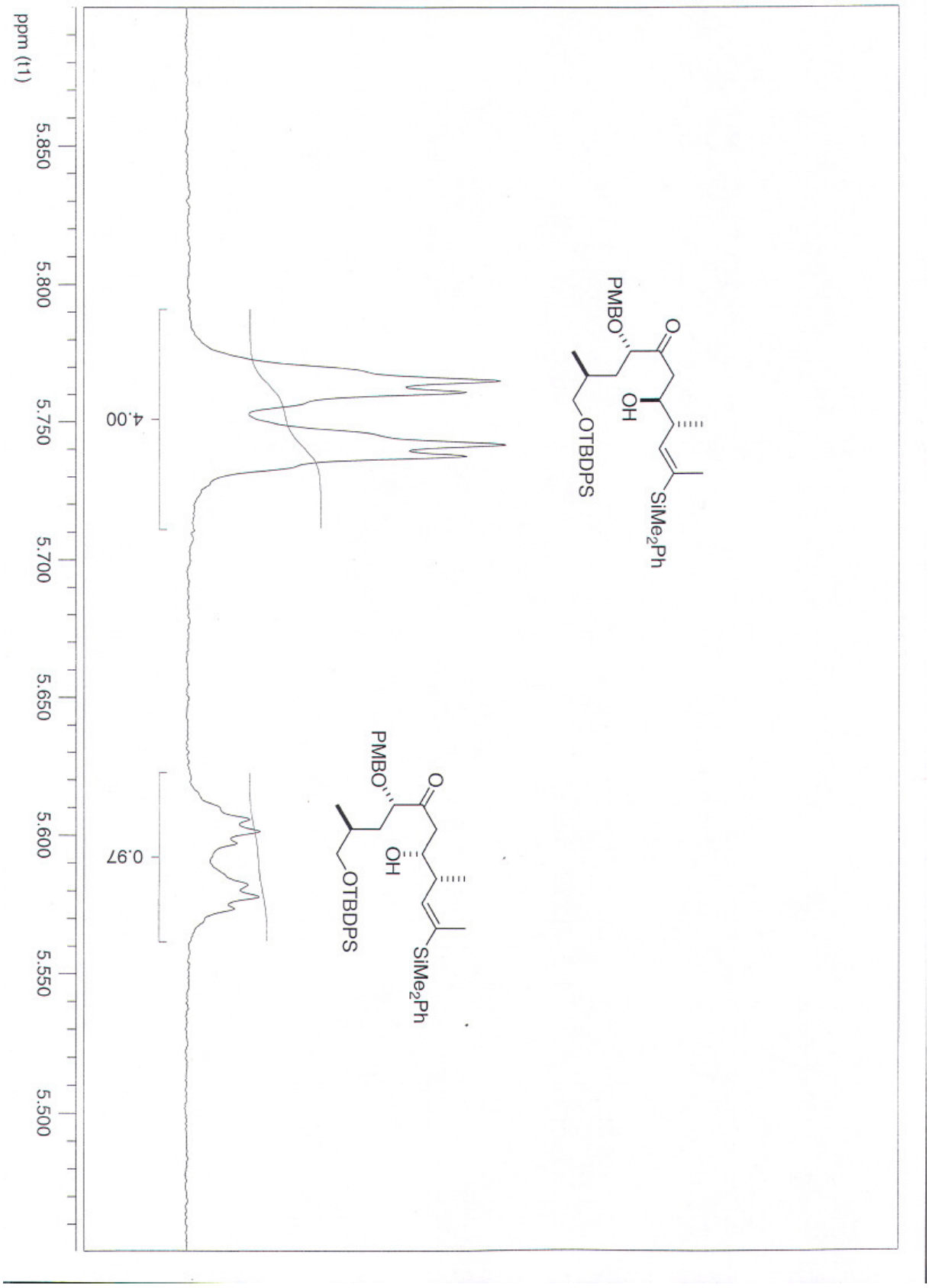


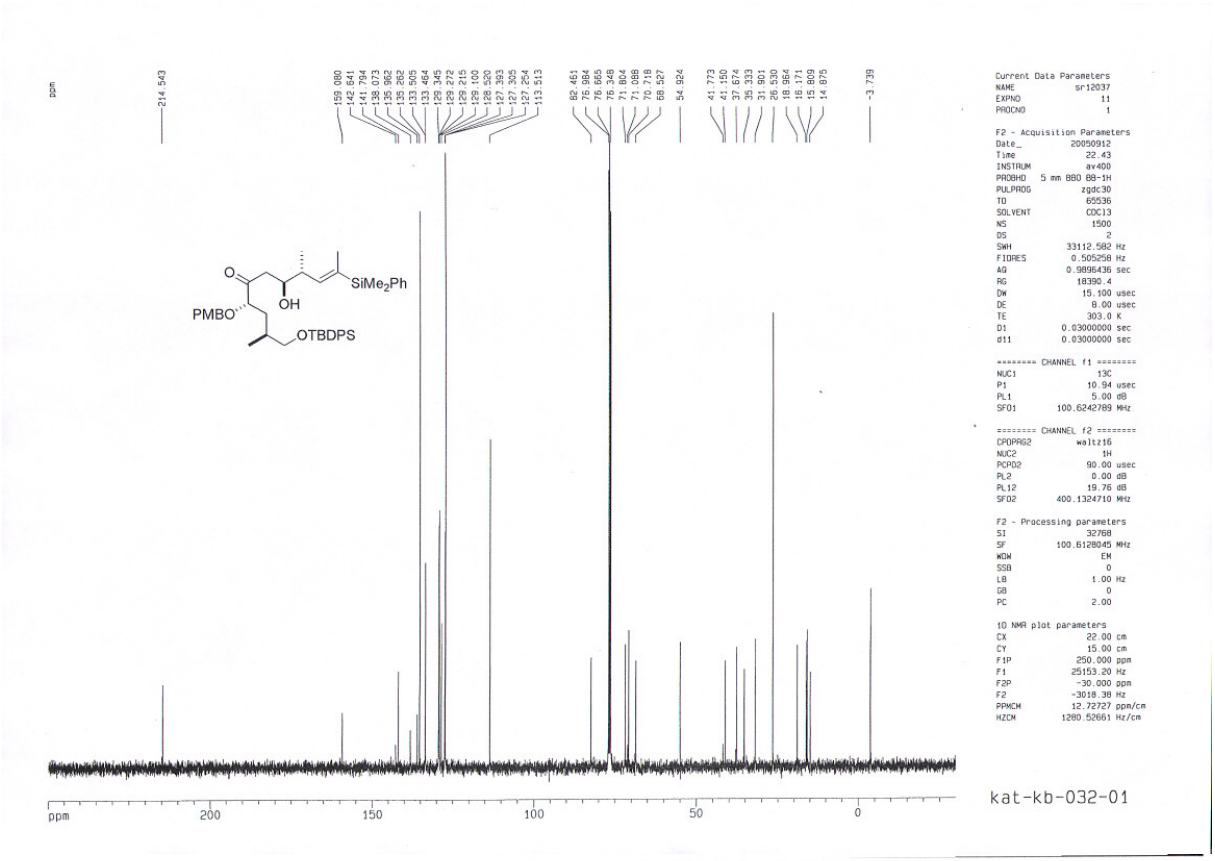
position	natural 2 δ (multiplicity, *J* in Hz)	synthetic 2 δ (multiplicity, *J* in Hz)	Δδ
2	5.78 (d, 15.6)	5.78 (d, 15.7)	0
3	6.59 (dd, 15.6, 9.5)	6.60 (dd, 15.7, 9.4)	0.01
4	3.06 (m)	3.06 (m)	0
5a	2.94 (dd, 17.8, 11.5)	2.94 (dd, 17.6, 11.4)	0
5b	2.38 (dd, 17.8, 2.1)	2.37 (dd, 17.6, 2.2)	-0.01
8a	1.97 (d, 14.5)	1.97 (d, 14.3)	0
8b	1.76 (dd, 14.5, 9.0)	1.76 (dd, 14.3, 9.0)	0
9	3.11 (t, 9.0)	3.11 (t, 9.0)	
10	2.25 (m)	2.26 (m)	0.01
11	4.86 (m)	4.87 (m)	0.01
13	2.13 (m)	2.13 (m)	0
14a	1.86 (m)	1.85 (m)	-0.01
14b	1.48 (m)	1.48 (m)	0
15	3.92 (dt, 11.0, 4.1)	3.92 (dt, 7.0, 4.1)	0
16	4.87 (m)	4.87 (m)	0
17a	2.10 (dd, 14.3, 7.4)	2.11 (dd, 13.8, 7.4)	0.01
17b	1.76 (dd, 14.3, 2.4)	1.77 (dd, 14.2, 2.5)	0.01
19	1.47 (m)	1.48 (m)	0.01
20	1.32 (m)	1.31 (m)	-0.01
21	0.91 (t, 7.0)	0.91 (t, 7.2)	0
22	1.10 (d, 6.7)	1.10 (d, 6.8)	0
23	1.35 (s)	1.36 (s)	0.01
24	0.87 (d, 6.5)	0.87 (d, 6.7)	0
25	1.70 (brs)	1.70 (brs)	0
26	1.23 (s)	1.24 (s)	0.01

Table 5: Comparison of the ^{13}C NMR spectrum of natural ($CDCl_3$, 150 MHz) and synthetic ($CDCl_3$, 150 MHz) amphidinolide Y; numbering scheme as shown in the insert in Table 4.

position	natural Y (δ)	synthetic Y (δ)	Δδ
1	165.81	165.93	0.12
2	120.05	120.17	0.12
3	153.56	153.72	0.16
4	32.07	32.24	0.17
5	42.60	42.74	0.12
6	211.09	211.23	0.14
7	77.26	77.38	0.12
8	44.94	45.08	0.14
9	71.01	71.14	0.13
10	39.23	39.38	0.15
11	128.61	128.74	0.13
12	138.21	138.37	0.16
13	34.74	34.90	0.16
14	33.97	34.08	0.11
15	79.99	80.11	0.12
16	78.67	78.82	0.15
17	42.67	42.81	0.14
18	82.96	83.09	0.13
19	44.85	45.00	0.15
20	17.82	17.99	0.17
21	14.55	14.73	0.18
22	19.89	20.07	0.18
23	26.58	26.75	0.17
24	16.84	17.00	0.16
25	17.51	17.66	0.15
26	25.74	25.91	0.17


PMBO
OH
OTBDPS
SiMe2Ph
O
ppm
7.46865
7.46694
7.45076
7.44918
7.29846
7.29009
7.28106
7.23072
7.21683
7.21294
7.20877
7.19697
7.19358
7.17777
7.17408
7.15741
7.13552
7.12898
7.12459
7.11964
7.07346
7.02712
7.00547
6.66949
6.64785
5.58629
5.58202
5.56306
5.55878
4.33151
4.30364
4.08949
4.06164
3.65213
3.64310
3.62695
3.61790
3.60975
3.60427
3.33883
3.32825
3.31412
3.29516
3.27986
3.27036
3.25513
2.51897
2.47025
2.45674
2.44981
2.44686
2.01549
1.58555
1.50251
1.49841
1.14867
0.87857
0.86414
0.83524
0.82615
0.81823
0.80946
0.68883
0.67212
0.15106
0.12799
0.12479
Current Data Parameters
NAME sr12037
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20050912
Time 22.14
INSTRUM av400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 8
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 114
DW 60.400 usec
DE 6.50 usec
TE 303.0 K
D1 0.00300000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 9.25 usec
PL1 0.00 dB
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300043 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 9.500 ppm
F1 3801.24 Hz
F2P -0.500 ppm
F2 -200.07 Hz
PPMCM 0.45455 ppm/cm
HZCM 181.87732 Hz/cm
ppm
9
8
7
6
5
4
3
2
1
0
kat-kb-032-01


PMBO
OH
OTBDPS
SiMe2Ph
PMBO
OH
OTBDPS
SiMe2Ph
4.00
0.97
ppm (t1)
5.850
5.800
5.750
5.700
5.650
5.600
5.550
5.500



Current Data Parameters
NAME sr12037
EXPNO 11
PROCNO 1

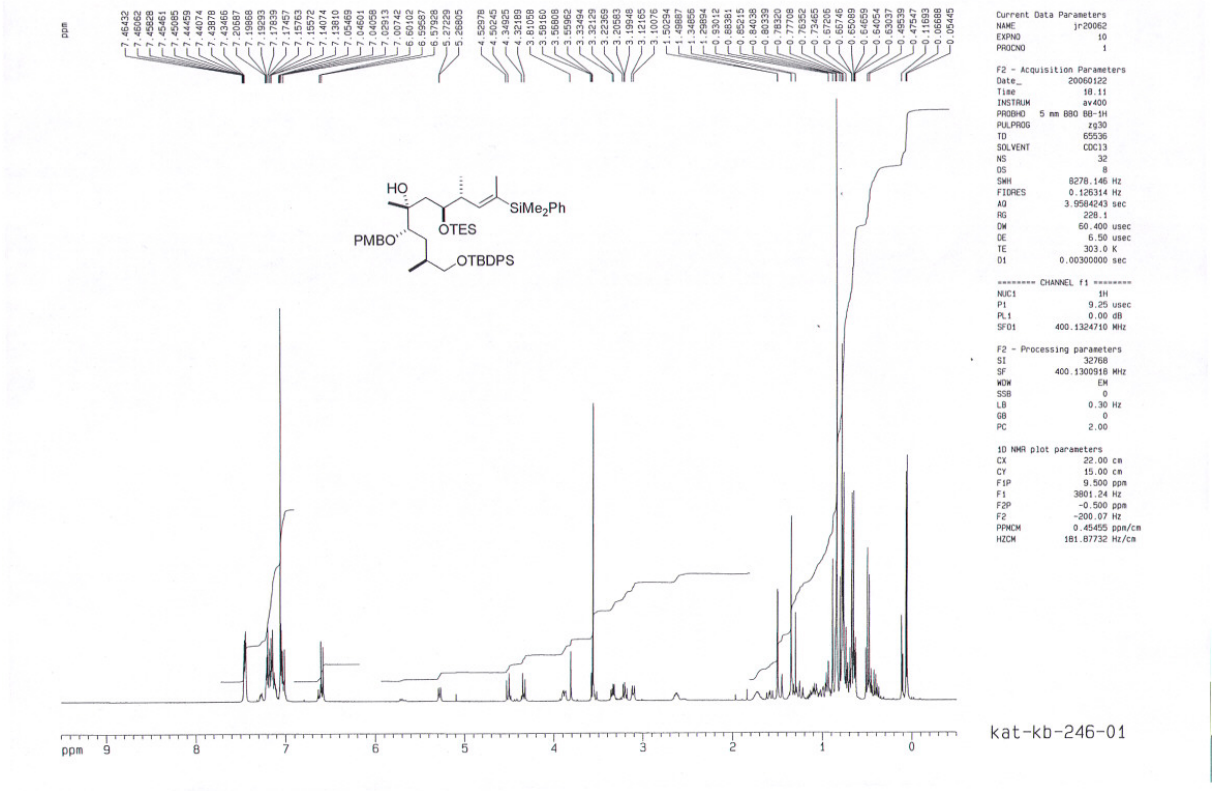
F2 - Acquisition Parameters
Date_ 20050912
Time 22.43
INSTRUM av400
PROBHD 5 mm BBO BB-1H
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 1500
DS 2
SWH 33112.582 Hz
FIDRES 0.505258 Hz
AQ 0.9896436 sec
RG 18390.4
DW 15.100 usec
DE 6.00 usec
TE 303.0 K
D1 0.03000000 sec
d11 0.03000000 sec

======== CHANNEL f1 ========
NUC1 13C
P1 10.94 usec
PL1 5.00 dB
SFO1 100.6242789 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 0.00 dB
PL12 19.76 dB
SFO2 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 100.6128045 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 250.000 ppm
F1 25153.20 Hz
F2P -30.000 ppm
F2 -3018.38 Hz
PPMCM 12.72727 ppm/cm
HZCM 1280.52661 Hz/cm



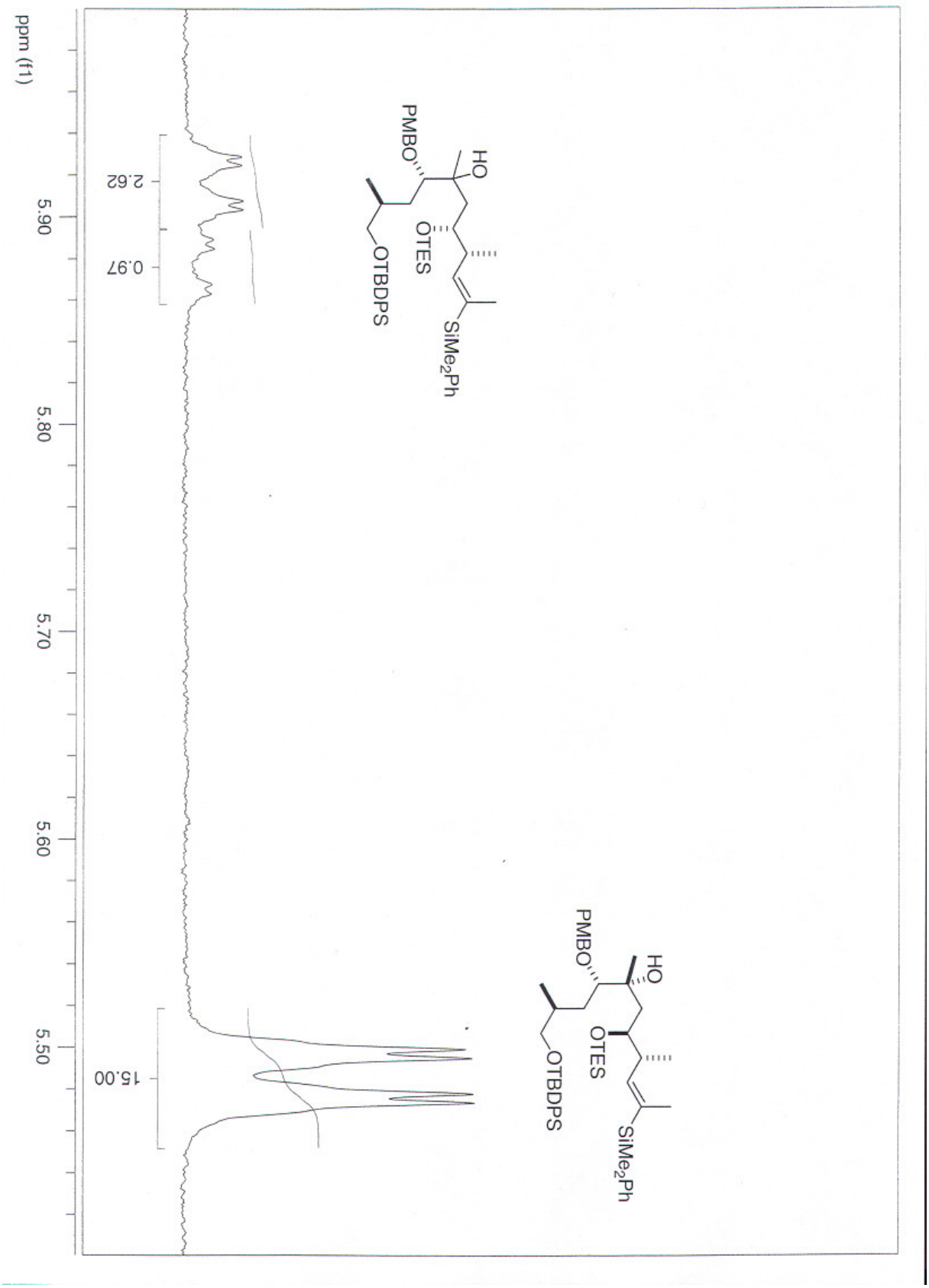
Current Data Parameters
NAME jr20062
EXPNO 10
PROCNO 1

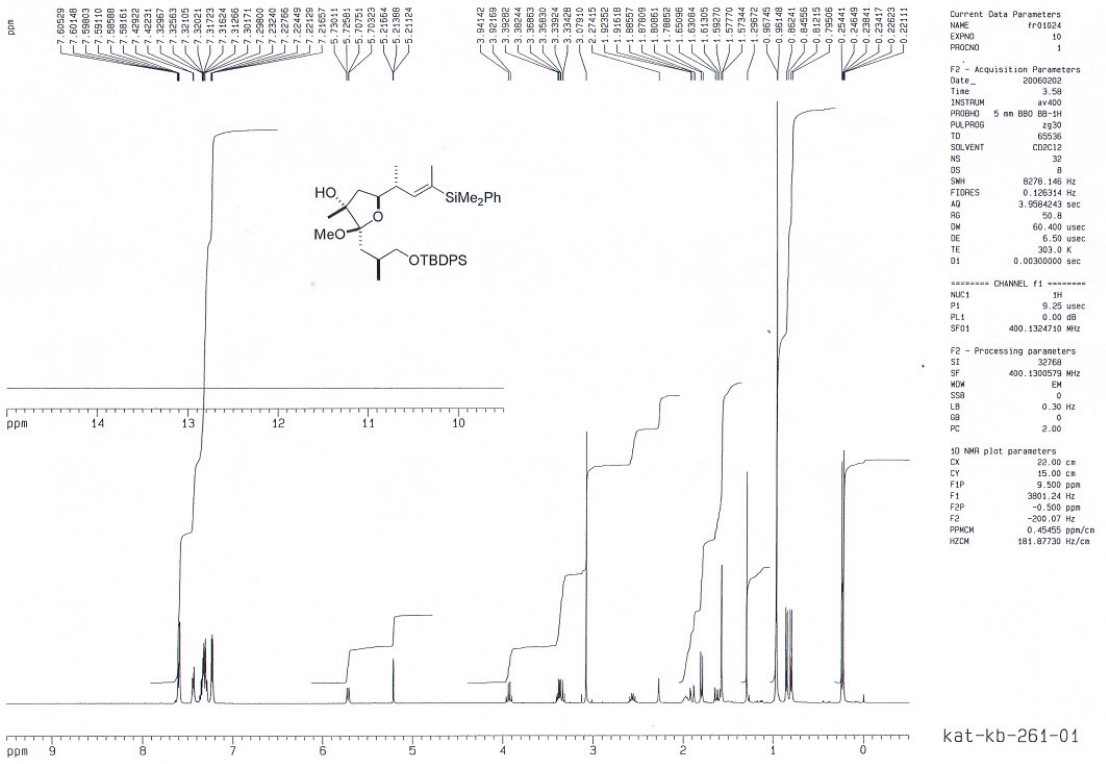
F2 - Acquisition Parameters
Date_ 20060122
Time 18.11
INSTRUM av400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 8
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 228.1
DW 60.400 usec
DE 6.50 usec
TE 303.0 K
D1 0.00300000 sec

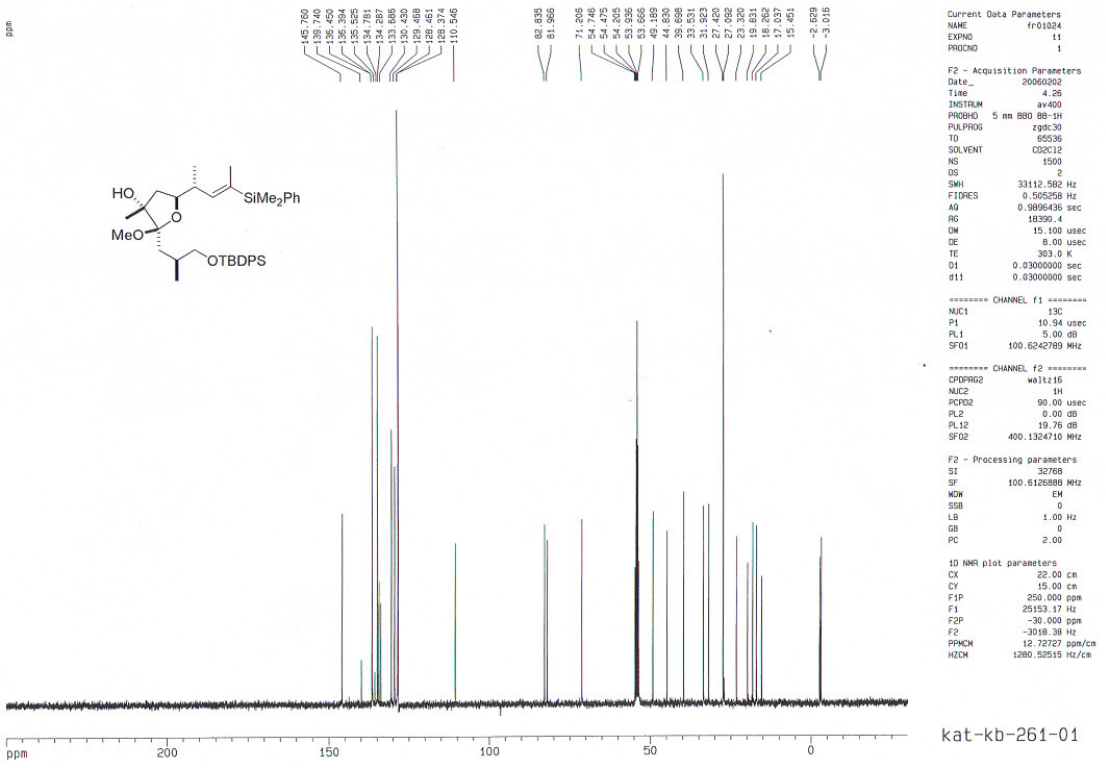
======== CHANNEL f1 ========
NUC1 1H
P1 9.25 usec
PL1 0.00 dB
SFO1 400.1324710 MHz

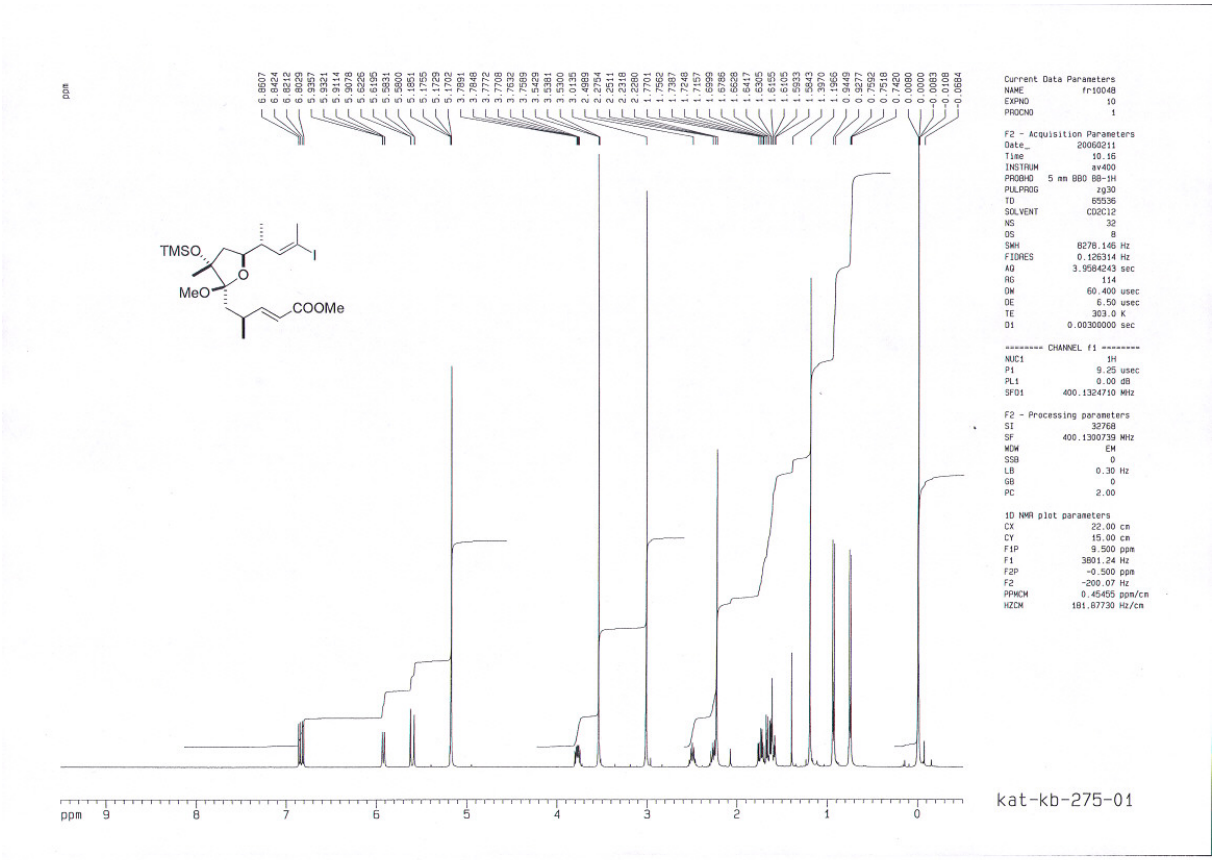
F2 - Processing parameters
SI 32768
SF 400.1300918 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00

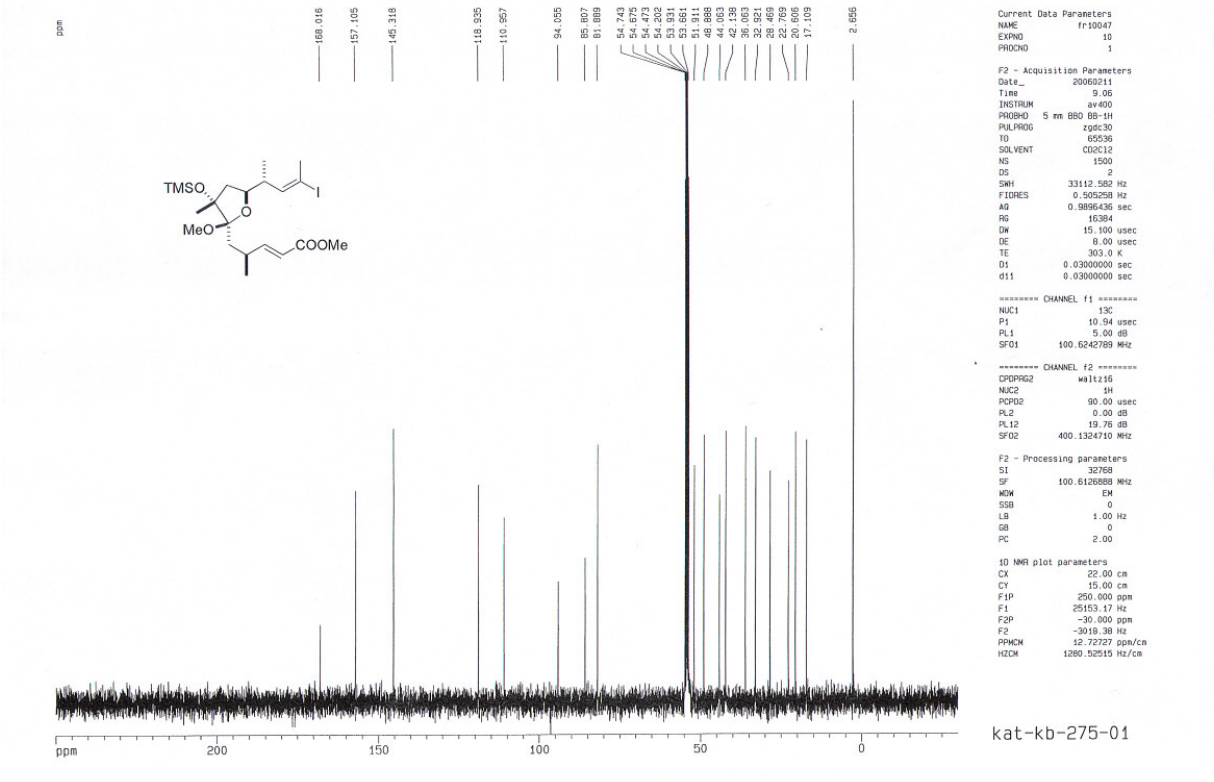
1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 9.500 ppm
F1 3801.24 Hz
F2P -0.500 ppm
F2 -200.07 Hz
PPMCM 0.45455 ppm/cm
HZCM 181.87732 Hz/cm

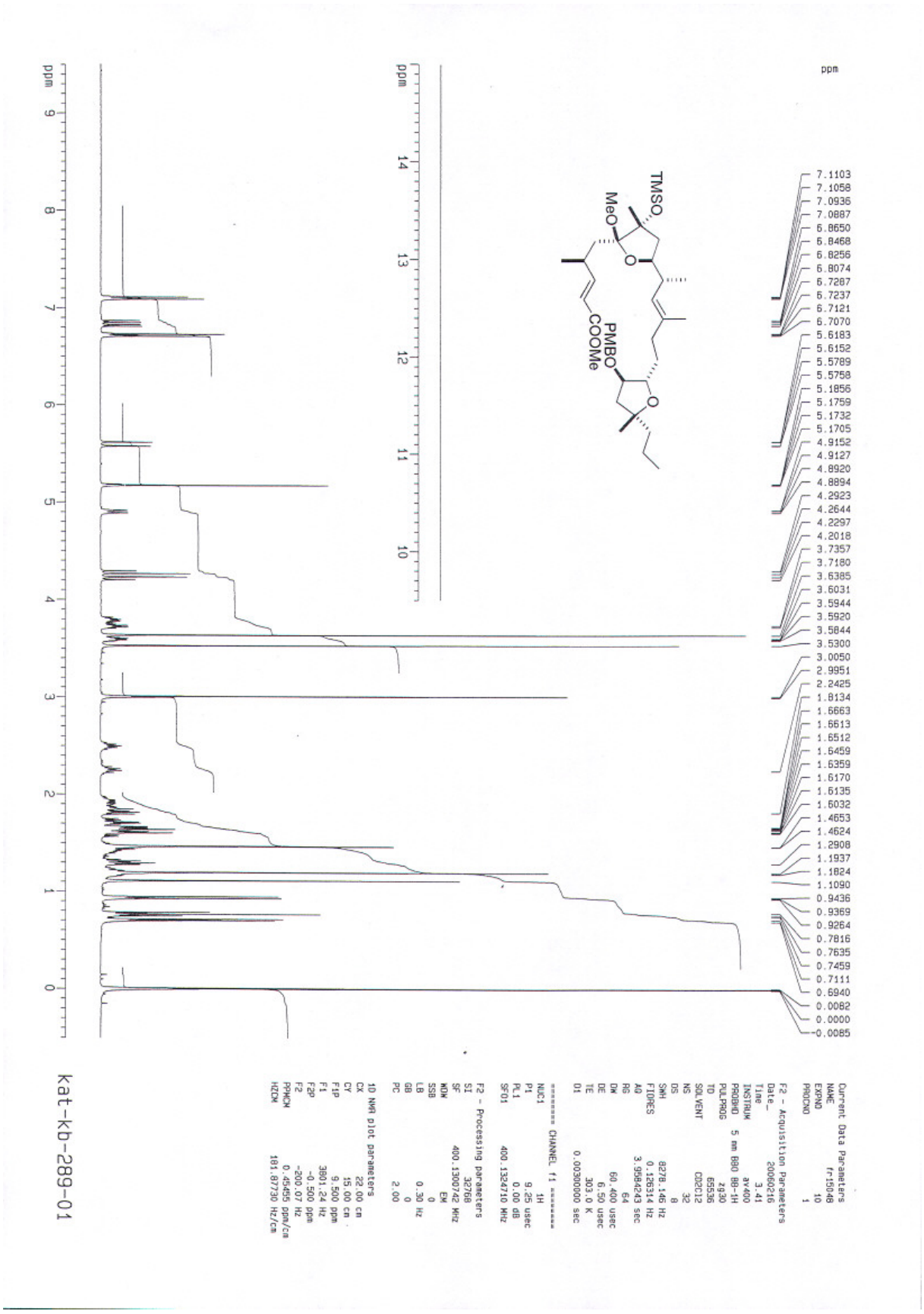

ppm (f1)
5.90
5.80
5.70
5.60
5.50
2.62
0.97
15.00
PMBO
HO
OTES
OTBDPS
SiMe2Ph
PMBO
HO
OTES
OTBDPS
SiMe2Ph

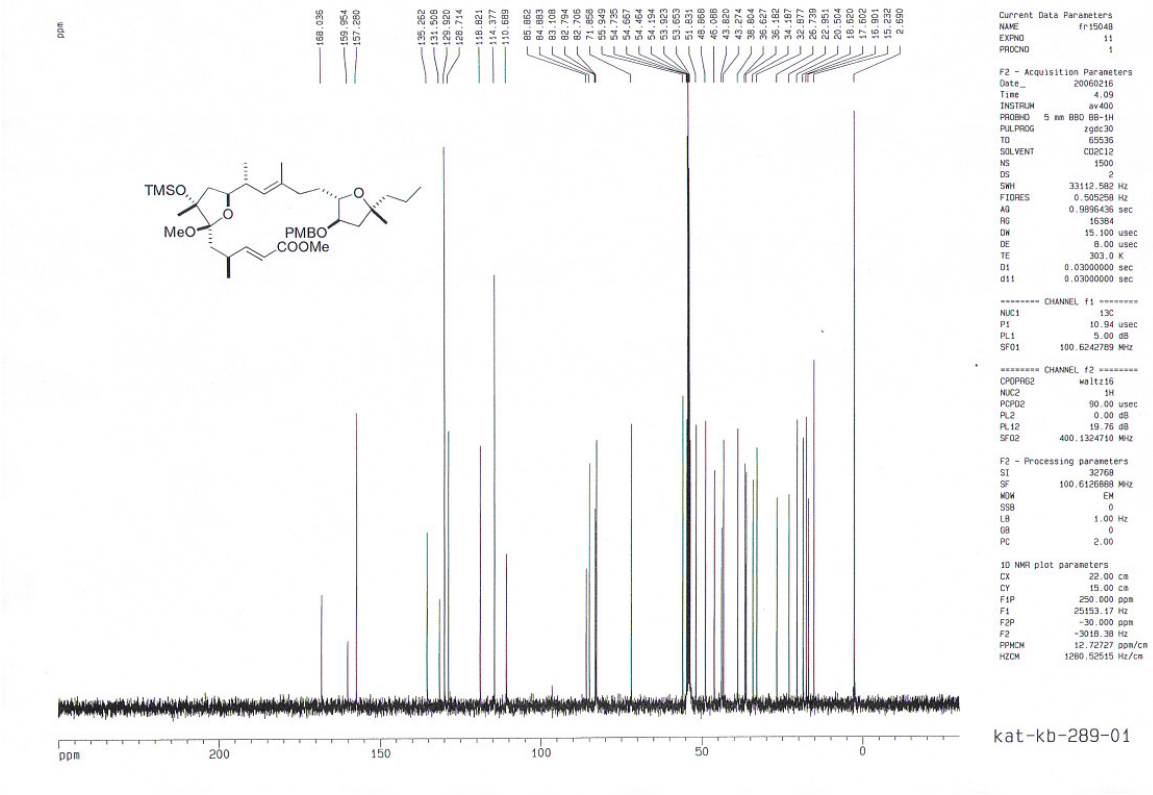

HO
MeO
O
SiMe2Ph
OTBDPS
kat-kb-261-01


HO
MeO
O
SiMe2Ph
OTBDPS
kat-kb-261-01


TMSO
MeO
COOMe
kat-kb-275-01


TMSO
MeO
COOMe
kat-kb-275-01


TMSO
MeO
PMBO
COOMe
ppm
7.1103
7.1058
7.0936
7.0887
6.8650
6.8468
6.8256
6.8074
6.7287
6.7237
6.7121
6.7070
5.6183
5.6152
5.5789
5.5758
5.1856
5.1759
5.1732
5.1705
4.9152
4.9127
4.8920
4.8894
4.2923
4.2644
4.2297
4.2018
3.7357
3.7180
3.6385
3.6031
3.5944
3.5920
3.5844
3.5300
3.0050
2.9951
2.2425
1.8134
1.6663
1.6613
1.6512
1.6459
1.6359
1.6170
1.6135
1.6032
1.4653
1.4624
1.2908
1.1937
1.1824
1.1090
0.9436
0.9369
0.9264
0.7816
0.7635
0.7459
0.7111
0.6940
0.0082
0.0000
-0.0085
Current Data Parameters
NAME
EXPNO
PROCNO
F2 - Acquisition Parameters
Date_
Time
INSTRUM
PROBHD 5 mm BBO BB-1H
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
======== CHANNEL f1 ========
NUC1
P1
PL1
SF01
F2 - Processing parameters
SI
SF
WDW
SSB
LB
GB
PC
1D NMR plot parameters
CX
CY
F1P
F1
F2P
F2
PPMCM
HZCM
kat-kb-289-01

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Current Data Parameters
NAME                 fr15048
EXPNO                     11
PROCNO                     1

F2 - Acquisition Parameters
Date_              20060216
Time                   4.09
INSTRUM                av400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT              CD2C12
NS                     1500
DS                        2
SWH              33112.582 Hz
FIDRES           0.505258 Hz
AQ               0.9896436 sec
RG                    16384
DW                 15.100 usec
DE                  8.00 usec
TE                  303.0 K
D1              0.03000000 sec
d11             0.03000000 sec

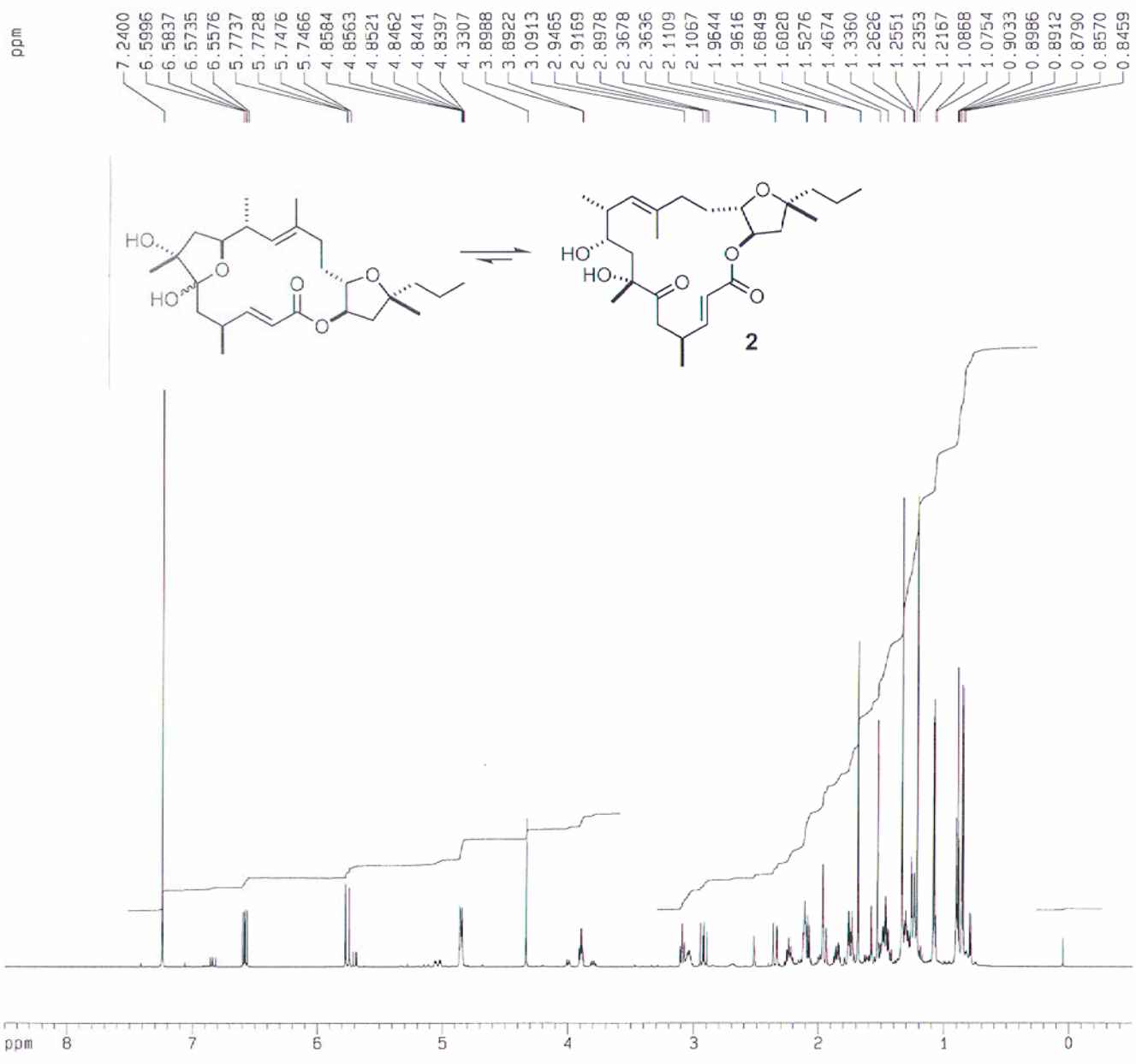
======== CHANNEL f1 ========
NUC1                    13C
P1                   10.94 usec
PL1                   5.00 dB
SF01          100.6242789 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                90.00 usec
PL2                   0.00 dB
PL12                 19.76 dB
SF02          400.1324710 MHz

F2 - Processing parameters
SI                      32768
SF            100.6126880 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       2.00

1D NMR plot parameters
CX                     22.00 cm
CY                     15.00 cm
F1P                  250.000 ppm
F1                  25153.17 Hz
F2P                  -30.000 ppm
F2                  -3018.38 Hz
PPMCM               12.72727 ppm/cm
HZCM             1280.52515 Hz/cm
```

HG09 292




```
Current Data Parameters
NAME                  kat32301
EXPNO                       10
PROCNO                       1
OU                           u
USER                      bara

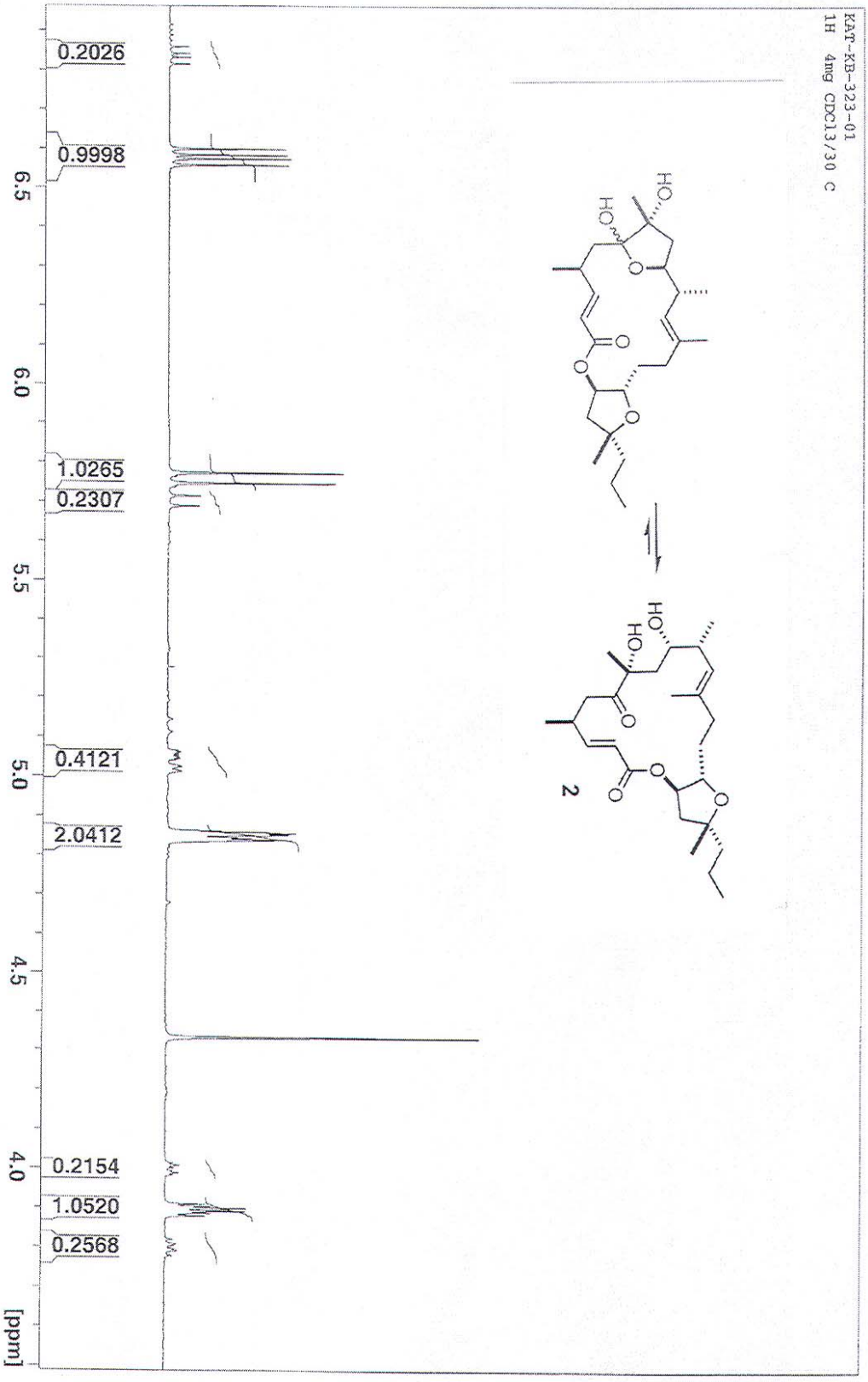
F2 - Acquisition Parameters
Date_                  20060515
Time                      11.44
INSTRUM                  dmx600
PROBHD    5 mm TXI 13C Z
PULPROG                    zg30
TD                        65536
SOLVENT                   CDCl3
NS                          128
DS                            2
SWH                   12019.230 Hz
FIDRES                0.183399 Hz
AQ                    2.7263477 sec
RG                          512
DW                     41.600 usec
DE                      4.50 usec
TE                        303.0 K
D1                    1.00000000 sec

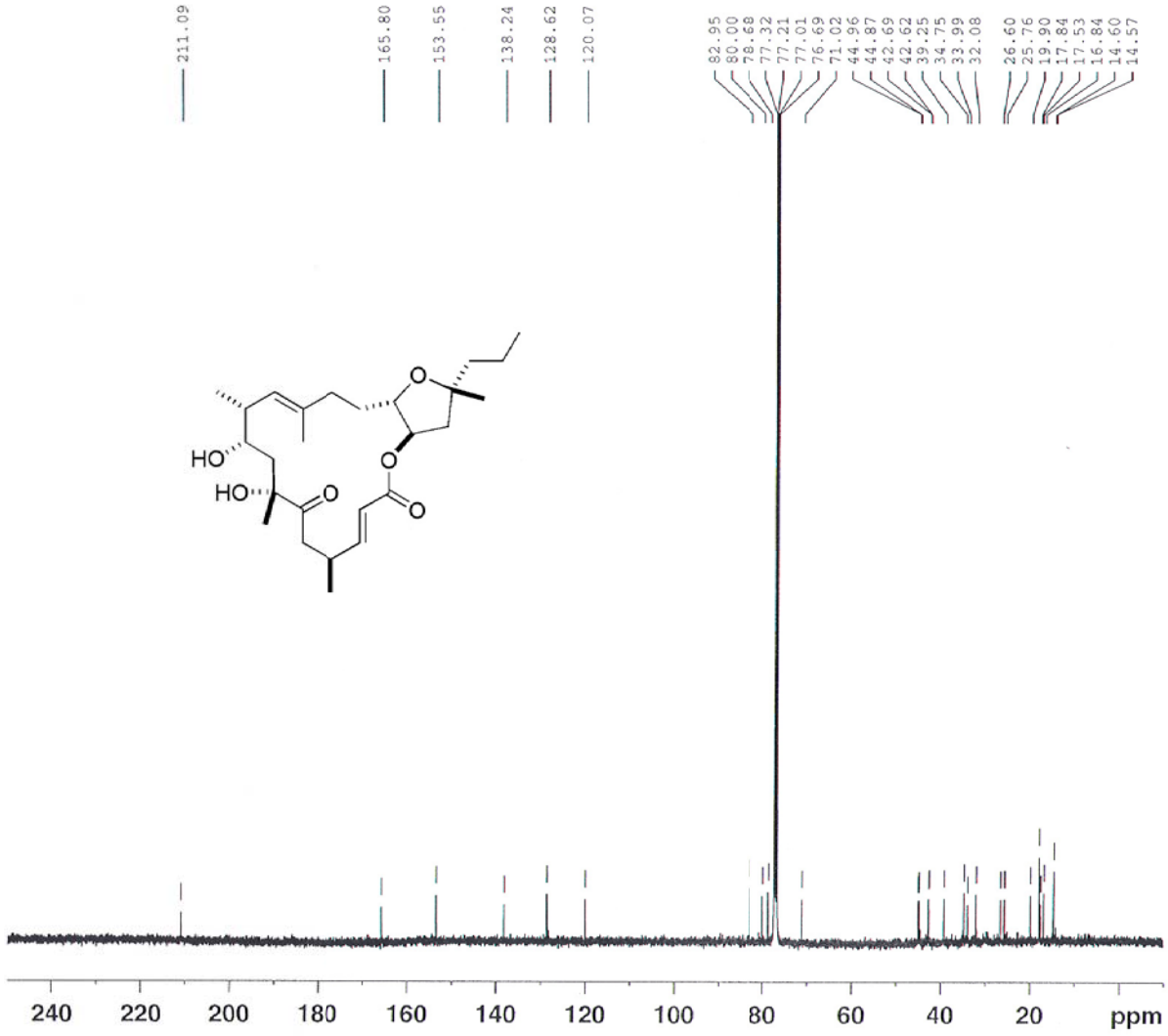
======== CHANNEL f1 ========
NUC1                         1H
P1                      10.20 usec
PL1                      0.00 dB
SFO1                600.2242403 MHz

F2 - Processing parameters
SI                        65536
SF                600.2200246 MHz
SR                       24.60 Hz
WDW                         no
SSB                          0
LB                       0.00 Hz
GB                           0
PC                        1.00

1D NMR plot parameters
CX                       20.00 cm
CY                       13.00 cm
F1P                      8.500 ppm
F1                     5101.87 Hz
F2P                     -0.500 ppm
F2                     -300.11 Hz
PPMCM                 0.45000 ppm/cm
HZCM                270.09900 Hz/cm
```

KAT-KB-323-01
1H 4mg CDCl3/30 C


kat32301 10 1 /disk2/topspin kattnig
KAT-KB-323-01
1H 4mg CDCl3/30 C
0.2026
0.9998
1.0265
0.2307
0.4121
2.0412
0.2154
1.0520
0.2568
6.5
6.0
5.5
5.0
4.5
4.0
[ppm]
HO
HO
O
O
O
O
HO
HO
O
O
O
O
2




```
Current Data Parameters
NAME                  KAT32301
EXPNO                        2
PROCNO                       1
DU              /opt/topspin
USER                     wiswo

F2 - Acquisition Parameters
Date_                 20060320
Time                      8.17
INSTRUM                  spect
PROBHD   5 mm BBI 1H-BB
PULPROG                  zgdc
TD                       65536
SOLVENT                  CDCl3
NS                      210190
DS                           4
SWH                 31250.000 Hz
FIDRES              0.476837 Hz
AQ                  1.0486259 sec
RG                     18390.4
DW                    16.000 usec
DE                     7.50 usec
TE                     300.0 K
O1                  12576.60 Hz
O2                   1600.52 Hz
d11                0.03000000 sec
D1                 0.01000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       13C
P1                        2.50 usec
PL1                      -2.00 dB
SFO1              100.6253456 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  80.00 usec
PL12                   22.00 dB
PL2                     0.00 dB
SFO2              400.1316005 MHz

F2 - Processing parameters
SI                       32768
SF                100.6127678 MHz
WDW                         EM
SSB                          0
LB                      0.80 Hz
GB                           0
PC                        1.40
SR                      -1.16 Hz
HZpPT                0.953674 Hz
```

KAT-KB-323-01