Probing the Lewis Acid Catalyzed Intramolecular Diels-Alder Cyclizations of Allylic Alkoxy-Substituted (*Z*)-1,3-Dienes

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Supporting Information

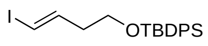
General Methods: All reaction solvents were purified before use. Tetrahydrofuran, dichloromethane, and toluene were purified by passing through a solvent column composed of activated A-1 alumina. Unless indicated, all chemicals were used as purchased without further purification.

Physical Properties and Spectroscopic Measurements: Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon-13 (^{13}C) NMR spectra were recorded on a Varian Inova-500 spectrometer at 500 MHz and 126 MHz respectively. The proton signal of residual, non-deuterated solvent (δ 7.26 ppm for $CHCl_3$) was used as an internal reference for ^{1}H spectra. For ^{13}C spectra, chemical shifts are reported relative to the δ 77.23 ppm resonance of $CDCl_3$. Coupling constants are reported in Hz. Infrared (IR) spectra were recorded as thin films on a Perkin-Elmer Spectrum 1000 FTIR. Mass spectra were recorded on a ZVG 70-250-S spectrometer manufactured by Micromass Corp. (Manchester UK).

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F_{254} glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with *p*-anisaldehyde solution (*p*-anisaldehyde in ethanolic sulfuric acid). Column chromatography was performed using Kieselgel 60 (230-400 mesh) silica gel. The amount of silica gel used for purification was 50-100 : 1 weight ratio of silica gel : crude product.

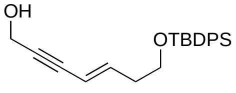
HPLC purifications were performed using an HPLC system composed of two Rainin HPXL pumps connected to various Dynamax® axial compression columns packed with Rainin 60 Å irregular silica gel. Samples were loaded into the system with a 2 mL Rheodyne 7125 injector and were detected using a Rainin Dynamax® UV-C detector. Integration of the various signals was performed using the reprocessing program within the Dynamax® HPLC Method Manager.

Experimental



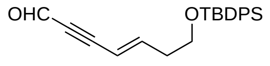
8

(1*E*)-4-(*tert*-butyl-diphenyl-silanyloxy)-1-iodo-but-1-ene (8). To a stirred solution of TBDPS-protected homopropargyl alcohol **7** (5.28 g, 17.1 mmol) in CH_2Cl_2 (60 mL) under N_2 was added $Cp_2Zr(H)Cl$ (5.58 g, 20.6 mmol). The solution was stirred for 25 min at ambient temperature, after which I_2 (5.43 g, 21.4 mmol) was added in one portion, and the resulting solution was stirred for 30 min. After this time, a 20% $Na_2S_2O_3$ (aq) solution (80 mL) was added and the mixture stirred for 1 h. The layers were then separated and the aqueous layer extracted with CH_2Cl_2 (2 x 50 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated. Purification of the crude product by chromatography on SiO_2 (15 % ethyl acetate/hexanes) gave 6.43 g (86%) of **8** as a clear oil: ^{1}H NMR ($CDCl_3$, 500 MHz) d 7.68-7.66 (m, 4 H), 7.45-7.39 (m, 6 H), 6.55 (dt, *J* = 14.7, 7.3 Hz, 1 H), 6.08 (dt, *J* = 14.7, 1.2 Hz, 1 H), 3.71 (t, *J* = 6.3 Hz, 2 H), 2.30 (m, 2 H), 1.07 (s, 9 H) ; ^{13}C NMR ($CDCl_3$, 125 MHz) d 143.3, 135.6, 133.6, 129.6, 127.7, 67.0, 62.3, 39.1, 26.8, 19.2; IR (neat) 3070, 3049, 2957, 2930, 2857, 1607, 1589, 1471, 1427, 1111, 950, 823, 738, 701, 613 cm^{-1}; HRMS (CI, NH_3) for $C_{20}H_{26}IOSi$ $[M+H]^+$ calcd. 437.0798, found 437.0790.



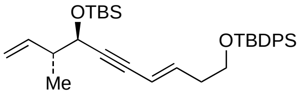
9

(4*E*)-7-(*tert*-butyl-diphenyl-silanyloxy)-hept-4-en-2-yn-1-ol (9). A mixture of **8** (6.9 g, 15.8 mmol) and propargyl alcohol (1.16 g, 20.6 mmol) in freshly distilled triethylamine (150 mL) was degassed by bubbling through argon for 20 min. $Pd(PPh_3)_2Cl_2$ (667 mg, 0.95 mmol) and CuI (450 mg, 2.37 mmol) were added and the resulting mixture stirred for 3 h. The reaction was poured into a saturated $NaHCO_3$ (aq) solution (100 mL), which was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by chromatography on SiO_2 (20 % ethyl acetate/hexanes) gave 4.76 g (83%) of **9** as a clear yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) d 7.68-7.66 (m, 4 H), 7.45-7.37 (m, 6 H), 6.18 (dt, *J* = 15.9, 7.3 Hz, 1 H), 5.56 (dt, *J* = 15.9, 1.9 Hz, 1 H), 4.38 (d, *J* = 3.7 Hz, 2 H), 3.71 (t, *J* = 6.6 Hz, 2 H), 2.36 (m, 2 H), 1.71 (t, *J* = 5.86, 1 H), 1.06 (s, 9 H); ^{13}C NMR ($CDCl_3$, 125 MHz) d 141.9, 135.5, 133.7, 129.6, 127.6, 110.7, 85.9, 84.4, 62.8, 51.2, 36.3, 26.8, 19.1; IR (neat) 3390, 3071, 2930, 2858, 1471, 1427, 1260, 1111, 1018, 957, 799, 702 cm^{-1}; HRMS (ES) for $C_{23}H_{28}O_2SiNa$ $[M+Na]^+$ calcd. 387.1756, found 387.1758.



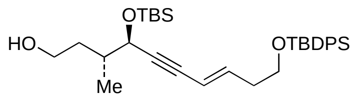
10

(4*E*)-7-(*tert*-butyl-diphenyl-silanyloxy)-hept-4-en-2-ynal (10). To a solution of propargyl alcohol **9** (3.07 g, 8.42 mmol) in CH_2Cl_2 (180 mL) was added MnO_2 (14.6 g, 168 mmol) and the resulting suspension was stirred for 12 h, after which it was filtered through a pad of Celite and concentrated. Purification of the crude product by chromatography on SiO_2 (10 % ethyl acetate/hexanes) gave 2.44 g (80%) of **10** as a clear yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) d 9.32 (d, *J* = 1.2 Hz, 1 H), 7.67-7.64 (m, 4 H), 7.45-7.39 (m, 6 H), 6.62 (dt, *J* = 15.9, 7.1 Hz, 1 H), 5.75 (d, *J* = 16.2, 1.2 Hz, 1 H), 3.79 (t, *J* = 6.1 Hz, 2 H), 2.46 (m, 2 H), 1.06 (s, 9 H); ^{13}C NMR ($CDCl_3$, 125 MHz) d 176.7, 150.7, 135.5, 133.3, 129.7, 127.7, 109.1, 94.3, 87.8, 62.1, 36.7, 26.7, 19.1; IR (neat) 3071, 3049, 2957, 2931, 2858, 2183, 1660, 1621, 1472, 1368, 1169, 1111, 961, 737, 702, 613 cm^{-1}; HRMS (ES) for $C_{24}H_{30}O_3SiNa$ $[M+MeOH+Na]^+$ calcd. 417.1862, found 417.1854.



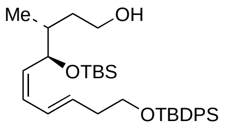
11

(3*E*)-(7*R*,8*R*)-(tert-butyl-dimethyl-silanyloxy)-1-(*tert*-butyl-dimethyl-silanyloxy)-8-methyl-deca-3,9-dien-5-yne (11). To a mixture of 4 Å molecular sieves (400 mg) in toluene (10 mL) was added diisopropyl-(*S*,*S*)-tartrate-(*E*)-crotylboronate (12.3 mL of a 0.6 M solution in toluene, 7.36 mmol). The resulting mixture was cooled to –78 °C, and a solution of **10** (2.23g, 6.14 mmol) in toluene (7 mL) was added dropwise. This mixture was stirred for 4 h, after which a 2N NaOH (aq) solution (7 mL) was added. After being allowed to warm to room temperature, the mixture was filtered through a pad of Celite and extracted with ether (3 x 20 mL). The combined ether layers were dried over K_2CO_3 and concentrated. The residue was dissolved in a EtOAc/hexanes (9:1) mixture and filtered through a plug of silica gel. Concentration of the filtrate yielded a yellow oil. (A portion of this oil was purified by HPLC and subjected to Mosher ester analysis which determined the enantiomeric purity of the homoallylic alcohol to be 73% ee) The residue was redissolved in a 2:1 mixture of CH_2Cl_2/DMF (10 mL). To this mixture was added TBS-Cl (1.02 g, 6.75 mmol), imidazole (460 mg, 6.75 mmol) and a few crystals of DMAP. After being stirred for 12 h, the reaction mixture was poured into water (25 mL) and extracted with hexane (3 x 15 mL). The combined hexane extracts were washed with brine, dried over Na_2SO_4, and concentrated to yield a crude yellow oil. Purification of the crude product by chromatography on SiO_2 (20% CH_2Cl_2/hexanes) gave 2.41 g (70%) of **11** as a clear oil: $[a]^{24}_{D}$ = -23.8 (*c* = 1.04 in $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) d 7.68-7.65 (m, 4 H), 7.43-7.36 (m, 6 H), 6.11 (dt, *J* = 16.2, 6.9 Hz, 1 H), 5.84 (ddd, *J* = 17.6, 10.6, 6.7 Hz, 1 H), 5.54 (dd, *J* = 16.1, 1.8 Hz, 1 H), 5.06 (m, 2 H), 4.33 (dd, *J* = 5.7, 1.8 Hz, 1 H), 3.69 (t, *J* = 6.6 Hz, 2 H), 2.41 (q, *J* = 6.6 Hz, 1 H), 2.35 (qd, *J* = 6.6, 1.1 Hz, 2 H), 1.10 (d, *J* = 6.59, 3 H), 1.05 (s, 9 H), 0.95 (s, 9 H), 0.13 (s, 3 H), 0.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) d 140.8, 140.2, 135.6, 133.7, 129.6, 127.6, 115.0, 111.2, 88.3, 83.8, 67.5, 62.9, 44.9, 36.3, 26.8, 25.8, 19.2, 18.2, 15.1, -4.4, -5.1; IR (neat) 3071, 2957, 2930, 2893, 2857, 1472, 1427, 1252, 1111, 837, 777, 701 cm^{-1}; HRMS (ES) for $C_{33}H_{48}O_2Si_2Na$ $[M+Na]^+$ calcd. 555.3091, found 555.3080.



12

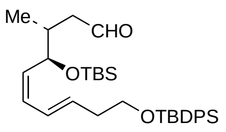
(7*E*)-(3*R*,4*R*)-4-(*tert*-butyl-dimethyl-silanyloxy)-10-(*tert*-butyl-diphenyl-silanyloxy)-3-methyl-dec-7-en-5-yn-1-ol (12). To a solution of **11** (2.39 g, 4.49 mmol) in dry THF (32 mL) at 0 °C was added dropwise a solution of 9-BBN (9.87 mL, 4.94 mmol) in THF. The cooling bath was removed and the solution stirred at ambient temperature for 3 h, after which time the solution was cooled again to 0 °C. H_2O_2 (5 mL of a 30% aqueous solution) and NaOH (5 mL of a 3N aqueous solution) were added and the mixture stirred for 3 h. The layers were separated and the aqueous layer extracted with Et_2O (3 x 5 mL) and the combined extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by chromatography on SiO_2 (20% ethyl acetate/hexanes) gave 2.20 g (90%) of **12** as a clear oil: $[a]^{24}_{D}$ = -68.9 (*c* = 1.05 in $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) d 7.66-7.64 (m, 4 H), 7.44-7.36 (m, 6 H), 6.11 (dt, *J* = 15.9, 7.3 Hz, 1 H), 5.53 (dq, *J* = 15.9, 1.7 Hz, 1 H), 4.37 (dd, *J* = 4.9, 1.7 Hz, 1 H), 3.75 (dt, *J* = 10.7, 6.4 Hz, 1 H), 3.69 (t, *J* = 6.6 Hz, 3 H), 3.66 (m, 1 H), 2.34 (qd, *J* = 6.6, 1.5 Hz, 2 H), 1.89 (m, 2 H), 1.57 (m, 1 H), 1.04 (s, 9 H), 1.01 (d, *J* = 6.8 Hz, 3 H), 0.91 (s, 9 H), 0.14 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) d 141.1, 135.8, 133.9, 129.8, 127.8, 111.4, 88.6, 84.1, 67.9, 63.1, 60.9, 37.5, 36.5, 35.4, 27.0, 26.0, 19.4, 18.4, 15.7, -4.2, -4.9; IR (neat) 3149, 3072, 3050, 2956, 2931, 2887, 2857, 1728, 1472, 1428, 1255, 1111, 837, 702, 613 cm^{-1}; HRMS (ES) for $C_{33}H_{50}O_3Si_2Na$ $[M+Na]^+$ calcd. 573.3196, found 573.3192.



13

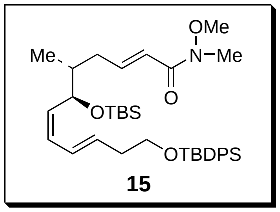
(5*Z*,6*E*)-(3*R*,4*R*)-4-(*tert*-butyl-dimethyl-silanyloxy)-10-(*tert*-butyl-diphenyl-silanyloxy)-3-methyl-deca-5,7-dien-1-ol (13). N_2 was bubbled through a suspension of

Zn (12.0 g, 18.3 mmol) in H_2O (60 mL) for 30 min. $Cu(OAc)_2 \bullet 2H_20$ (1.13 g, 6.24 mmol) was added and the mixture stirred for another 30 min. $AgNO_3$ (1.24 g, 7.34 mmol) was added, resulting in a slight exotherm, and the resulting mixture was stirred for 1 h. The solid was then filtered and washed with H_2O (2 x 25 mL), MeOH (2 x 25 mL), acetone (2 x 25 mL), and Et_2O (2 x 25 mL). The solid was suspended in a 1:1 mixture of H_2O:MeOH (30 mL). A solution of acetylene **12** (2.02 g, 3.67 mmol) in MeOH (10 mL) was added to the suspension. The resulting mixture was stirred for 40 h, after which time it was filtered through a pad of Celite. The filter cake was washed with Et_2O (3 x 50 mL) and the layers separated. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated to give 1.60 g (79%) of **13** as a clear oil: ^1H NMR ($CDCl_3$, 500 MHz) d 7.68-7.65 (m, 4 H), 7.44-7.36 (m, 6 H), 6.25 (m, 1 H), 5.95 (t, *J* = 11.2 Hz, 1 H), 5.69 (dt, *J* = 15.1, 7.1 Hz, 1 H), 5.33 (m, 1 H), 4.37 (m, 1 H), 3.71 (t, *J* = 6.6 Hz, 3 H), 3.61-3.56 (m, 1 H), 2.41 (m, 1 H), 2.36 (q, *J* = 6.8 Hz, 2 H), 2.12 (m , 1 H), 1.90-1.85 (m, 1 H), 1.75-1.68 (m, 2 H), 1.04 (s, 9 H), 0.91 (d, *J* = 4.2 Hz, 3 H), 0.88 (s, 9 H), 0.05 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) d 135.6, 133.9, 132.9, 131.8, 129.6, 128.6, 127.6, 127.0, 73.0, 63.5, 60.3, 37.4, 36.3, 34.6, 26.8, 25.8, 19.2, 18.1, 15.9, -4.2, -4.9; IR (neat) 3365, 3071, 3024, 2956, 2930, 2857, 1471, 1428, 1255, 1111, 836, 775, 702, 613 cm^{-1}; HRMS (ES) for $C_{33}H_{52}O_3Si_2Na$ $[M+Na]^+$ calcd. 575.3353, found 575.3351.



14

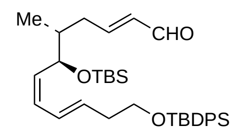
(5*Z*,6*E*)-(3*R*,4*R*)-4-(*tert*-butyl-dimethyl-silanyloxy)-10-(*tert*-butyl-diphenyl-silanyloxy)-3-methyl-deca-5,7-dienal (14). To a solution of **13** (310 mg, 0.561 mmol) and pyridine (23 µL, 0.281 mmol) in CH_2Cl_2 (2.5 mL) at 0 °C was added Dess-Martin periodinane (356 mg, 0.841 mmol). The mixture was stirred for 10 min, after which a saturated solution of H_2O in CH_2Cl_2 (1.5 mL) was added dropwise. The mixture was warmed to room temperature and stirred for 90 min. The reaction was poured into a saturated $NaHCO_3$ (aq) solution (10 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were washed with a 20% $Na_2S_2O_3$ (aq) solution (2 x 5 mL), brine, dried over Na_2SO_4, and concentrated yielding 309 mg (99%) of **14** as a clear oil: $[a]^{24}_{D}$ = -2.7 (*c* = 1.01 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) d 9.75 (broad s, 1 H), 7.72-7.68 (m, 4 H), 7.47-7.37 (m, 6 H), 6.32-6.22 (m, 1 H), 6.02 (t, *J* = 11.4 Hz, 1 H), 5.74 (dt, *J* = 14.7, 7.3 Hz, 1 H), 5.24 (broad t, *J* = 9.9 Hz, 1 H), 4.34 (broad t, *J* = 7.7 Hz, 1 H), 3.74 (app t., *J* = 6.4 Hz, 2 H), 2.61 (dd, *J* = 16.1, 5.1 Hz, 1 H), 2.39 (m, 2 H), 2.25 (m, 1 H), 2.15 (dt, *J* = 13.2, 6.6 Hz, 1 H), 1.07 (s, 9 H), 0.94 (d, *J* = 6.7 Hz, 3 H), 0.89 (s, 9 H), 0.47 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) d 202.8, 135.8, 134.1, 133.6, 131.4, 129.8, 128.5, 127.8, 127.2, 72.7, 63.7, 47.1, 36.4, 36.1, 27.1, 26.1, 19.4, 18.3, 16.6, -3.9, -4.7; IR (neat) 3071, 3049, 3024, 2956, 2930, 2891, 2857, 2712, 1726, 1471, 1428, 1389, 1252, 1111, 950, 836, 776, 702, 613 cm^{-1}; HRMS (ES) for $C_{33}H_{50}O_3Si_2Na$ $[M+Na]^+$ calcd. 573.3196, found 576.3209.



15

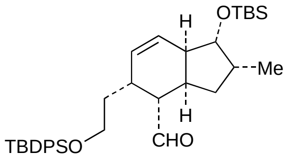
(2*E*,7*Z*,9*E*)-(5*R*,6*R*)-6-(*tert*-butyl-dimethyl-silanyloxy)-12-(*tert*-butyl-diphenyl-silanyloxy)-5-methyl-dodeca-2,7,9-trienoic acid methoxy-methyl-amide (15). To a suspension of NaH (19 mg, 0.75 mmol) in THF (5 mL) at 0 °C was added diethyl (N-methoxy-N-methylcarbamoylmethyl)phosphonate (142 mg, 0.572 mmol) dropwise over 10 min. The resulting mixture was allowed to warm to room temperature and stirred for 1 h. A solution of **14** (210 mg, 0.381 mmol) in THF (1 mL) was added over 10 min. The solution was stirred for 1 h, after which it was quenched with a saturated solution (aq) of NH_4Cl (5 mL). The layers were separated and the aqueous layer extracted with Et_2O (2 x 4 mL). The combined organic extracts were washed with a saturated solution (aq) of $NaHCO_3$, washed with brine, dried over Na_2SO_4, and concentrated. Purification of the crude product by chromatography on SiO_2 (20% ethyl acetate/hexanes) gave 210 mg (87%) of **15** as a clear oil: ^{1}H NMR ($CDCl_3$, 500 MHz) d 7.68-7.65 (m, 4 H), 7.44-7.36 (m, 6 H), 6.97 (ddd, *J* = 15.1, 8.3, 6.6 Hz, 1 H), 6.40 (app.

d, 1 H), 6.29-6.25 (m, 1 H), 5.99-5.96 (app. t, 1 H), 5.69 (dt, *J* = 14.9, 7.3 Hz, 1 H), 5.27-5.23 (app. t, 1 H), 4.30 (dd, *J* = 8.79, 6.34 Hz, 1 H), 3.71 (t, *J* = 6.59 Hz, 2 H), 3.68 (s, 3 H), 3.24 (s, 3 H), 2.56-2.51 (m, 1 H), 2.39-2.35 (aq, 2 H), 2.06-1.99 (m, 1 H), 1.74-1.69 (m, 1 H), 1.04 (s, 9 H), 0.88 (s, 9 H), 0.84 (d, *J* = 6.8 Hz, 3 H), 0.03 (s, 3 H), -0.01 (s, 3 H); ^{13}C NMR (CDCl$_3$, 125 MHz) d 147.3, 135.8, 134.1, 133.2, 131.7, 129.8, 127.9, 127.8, 127.5, 120.1, 72.7, 63.8, 61.9, 40.2, 36.5, 35.6, 27.1, 26.1, 26.0, 19.4, 18.4, 15.7, -3.8, -4.6; IR (neat) 3071, 2956, 2930, 2894, 2857, 1666, 1636, 1471, 1462, 1428, 1379, 1252, 1111, 836, 776, 729, 702 cm^{-1}; HRMS (ES) for $C_{37}H_{57}NO_4Si_2Na$ [M+Na]$^+$ calcd. 658.3724, found 658.3718.



1

(2*E*,7*Z*,9*E*)-(5*R*,6*R*)-6-(*tert*-butyl-dimethyl-silanyloxy)-12-(*tert*-butyl-diphenyl-silanyloxy)-5-methyl-dodeca-2,7,9-trienal (1). A solution of **15** (28 mg, 0.44 mmol) in THF (0.5 mL) was cooled to -78 °C under N$_2$. A 1.0 M solution if DIBAl-H in hexanes (131 µL, 131 µmol) was added dropwise over 5 min. After being stirred for 90 min at -78 °C, this solution was poured into a mixture of 1 M L-tartaric acid solution (aq) (0.6 mL) and hexanes (0.4 mL) and stirred for 1 h. The mixture was then extracted with Et$_2$O (3 x 2 mL) and the combined organic extracts were washed with a saturated solution (aq) of NaHCO$_3$, washed with brine, and dried over MgSO$_4$, and concentrated. Purification of the crude product by chromatography on SiO$_2$ (15% ethyl acetate/hexanes) gave 19 mg (74%) of **1** as a clear oil: [a]$^{24}_{D}$ = -1.5 (*c* = 2.96 in CHCl$_3$); ^{1}H NMR (CDCl$_3$, 500 MHz) d 9.52 (d, *J* = 8.1 Hz, 1 H), 7.71-7.68 (m, 4 H), 7.46-7.37 (m, 6 H), 6.85 (ddd, *J* = 15.1, 8.1, 6.6 Hz, 1 H), 6.31-6.26 (m, 1 H), 6.13 (broad dd, *J* = 15.6, 8.1 Hz, 1 H), 6.02 (t, *J* = 11.2 Hz, 1 H), 5.74 (dt, *J* = 15.1, 7.1 Hz, 1 H), 5.28 (app. t, *J* = 9.3 Hz, 1 H), 4.34 (dd, *J* = 8.8, 6.4 Hz, 1 H), 3.74 (t, *J* = 6.4 Hz, 2 H), 2.67-2.62 (m, 1 H), 2.39 (q, *J* = 6.6 Hz, 2 H), 2.15 (m, 1 H), 1.07 (s, 9 H), 0.90 (s, 9 H), 0.88 (d, *J* = 7.1 Hz, 3 H), 0.53 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (CDCl$_3$, 125 MHz) d 193.9, 158.5, 135.5, 134.1, 133.8, 133.4, 131.3, 129.6, 129.3, 127.6, 126.9, 72.5, 63.4, 39.8, 36.2, 35.6, 26.8, 25.8, 19.1, 18.1, 15.7, -4.0, -4.9; IR (neat) 2930, 2857, 1694, 1472, 1428, 1256, 1111, 836, 776, 738, 701, 668 cm^{-1}; HRMS (ES) for $C_{35}H_{52}O_3Si_2Na$ $[M+Na]^+$ calcd. 599.3353, found 599.3347.



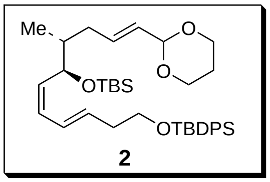
16

Lewis acid catalyzed IMDA Reaction of 1 (16). A solution of **1** (51 mg, 89 µmol) in CH_2Cl_2 (3 mL) was cooled to -78 °C under an atmosphere of argon. A 1.0 M solution of methyl aluminum dichloride in hexanes (Aldrich) (54 µL, 54 µmol) was added dropwise over 10 min, giving a yellow solution. The solution was placed in a -25 °C bath and stirred for two hours, after which it was quenched with a saturated solution of Rochelle's salt (aq) (5 mL). The resulting mixture was extracted with Et_2O (2 x 20 mL), and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated. Purification of the crude product by chromatography on SiO_2 (5% ethyl acetate/hexanes) gave 34 mg (66%) of a 65:35 mixture of **16** to **17** + **18.** Cycloadduct **16** was isolated by HPLC purification through silica gel (3% ethyl acetate/hexanes): ^{1}H NMR ($CDCl_3$, 500 MHz) d 9.77 (d, *J* = 2.7 Hz, 1 H), 7.67-7.65 (m, 4 H), 7.45-7.37 (m, 6 H), 5.73-5.64 (m, 2 H), 3.76-3.73 (m, 3 H), 2.81-2.75 (m, 2 H), 2.49-2.47 (m, 1 H), 2.43-2.41 (m, 1 H), 1.95-1.88 (m, 1 H), 1.83-1.77 (m, 1 H), 1.71-1.64 (m, 2 H), 1.44 (ddd, *J* = 12.7, 7.8, 4.6 Hz, 1 H), 1.06 (s, 9 H), 0.92 (d, *J* = 6.8 Hz, 3 H), 0.90 (s, 9 H), 0.57 (s, 3 H), 0.47 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) d 204.5, 135.8, 134.0, 130.9, 130.1, 129.9, 127.9, 81.2, 62.0, 54.6, 45.2, 37.3, 36.1, 33.8, 29.3, 27.1, 25.2, 19.7, 18.7, 14.5, -0.05, -4.2, -4.5; IR (neat) 3071, 3049, 3017, 2955, 1930, 2894, 2857, 1721, 1472, 1428, 1252, 1111, 835, 775, 702, 613 cm^{-1}; HRMS (ES) for $C_{35}H_{52}O_3Si_2Na$ $[M+Na]^+$ calcd. 599.3353, found 599.3345.

The structures of cycloadducts **17** and **18** were identified based upon partial ^{1}H NMR data from the isomeric mixture that matched data from the epimerization experiments of cycloadducts **21** and **22**. Partial data is listed below:

17: ^{1}H NMR ($CDCl_3$, 500 MHz) d 9.68 (d, *J* = 2.7 Hz, 1 H), 5.86 (d, *J* = 9.9 Hz, 1 H), 5.68 (dq, *J* = 12.5, 4.0 Hz, 1 H), 0.65 (s, 1 H), 0.58 (s, 1 H).

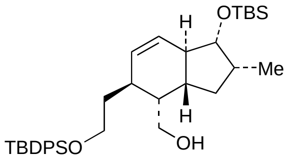
18: ^{1}H NMR ($CDCl_3$, 500 MHz) d 9.69 (d, *J* = 2.2 Hz, 1 H), 5.79 (d, *J* = 9.9 Hz, 1 H), 5.68 (dq, *J* = 12.8, 4.4 Hz, 1 H), 0.01 (s, 6 H).



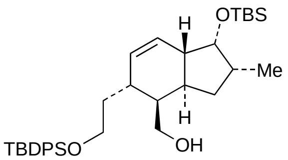
2

Acetal (2). To a solution of **1** (142 mg, 0.246 mmol) in THF (0.5 mL) was added propanediol (187 mg, 2.46 mmol), 2-methoxy-1, 3-dioxane (127 µL, 0.98 mmol) and a crystal of TsOH•H_2O. The resulting solution was stirred for 3 h, after which 10 mL of a 50% saturated solution of $NaHCO_3$ (aq) was added. This mixture was extracted with hexanes (4 x 5 mL). The organic extracts were combined, washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by chromatography on SiO_2 (5% ethyl acetate/hexanes) gave 129 mg (83%) of **2** as a clear oil. ^{1}H NMR ($CDCl_3$, 500 MHz) d 7.69-7.67 (m, 4 H), 7.45-7.37 (m, 6 H), 6.28 (dd, *J* = 15.1, 11.2 Hz, 1 H), 5.96 (t, *J* = 11.2 Hz, 1 H), 5.88 (dt, *J* = 15.1, 7.3 Hz, 1 H), 5.68 (dt, *J* = 14.9, 7.1 Hz, 1 H), 5.52 (dd, *J* = 15.6, 5.1 Hz, 1 H), 5.24 (app. t, 1 H), 4.94 (d, *J* = 5.1 Hz, 1 H), 4.26 (dd, *J* = 9.0, 6.6 Hz, 1 H), 4.15 (dd, *J* = 10.7, 4.9 Hz, 2 H), 3.83 (td, *J* = 12.2, 2.4 Hz, 2 H), 3.71 (t, *J* = 6.6 Hz, 2 H), 2.16-2.05 (m, 1 H), 1.82-1.76 (m, 1 H), 1.63 (m, 1 H), 1.35 (dt, *J* = 13.9, 1.2 Hz, 2 H), 1.27 (broad s, 1 H), 1.06 (s, 9 H), 0.87 (s, 9 H), 0.82 (d, *J* = 6.8 Hz, 3 H), 0.02 (s, 3 H), -0.02 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) d 135.9, 134.7, 134.1, 132.8, 131.9, 129.8, 129.2, 128.1, 127.9, 127.7, 101.5, 72.9, 67.1, 63.9, 40.3, 36.5, 35.4, 27.1, 26.1, 25.9, 19.5, 18.4, 15.5, -3.8, -4.6; IR (neat) 3072, 2957, 2930, 2856, 1652, 1471, 1428, 1378, 1257, 1143, 1111, 1086, 702 cm^{-1}; HRMS (ES) for $C_{38}H_{58}O_4Si_2Na$ [M+Na]$^+$ calcd. 657.3771, found 657.3777.

Lewis Acid Catalyzed IMDA Reaction of 2 (Mixture 19). A solution of acetal **2** (46 mg, 73 µmol) in CH_2Cl_2 (2.4 mL) was cooled to –78 °C under an atmosphere of argon. A 1.0 M solution of dimethyl aluminum chloride in CH_2Cl_2 (Aldrich) (44 µL, 44 µmol) was added dropwise over 10 min. This solution was immediately placed in a –20 °C bath and stirred for 45 min, after which it was quenched with a saturated solution of Rochelle's salt (aq) (5 mL). The resulting mixture was extracted with Et_2O (2 x 20 mL), and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated. Partial purification of the crude products on SiO_2 (10% ether/hexanes) gave 27 mg (58%) of the mixture of cycloadducts **19** as a clear oil.



20a
(from cycloadduct **21**)

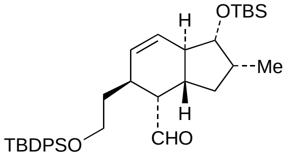


20b
(from cycloadduct **22**)

Deprotection and Reduction of Cycloadducts 19 (20). A solution of cycloadduct mixture **19** (24 mg, 38 µmol) in CH_2Cl_2 (0.7 mL) under N_2 was cooled to –78 °C. A 1.5 M solution of dimethyl boron bromide in CH_2Cl_2 (150 µL, 226 µmol) was added dropwise over 5 min. After being stirred for 2.5 h at –78 °C, the solution was warmed to –45 °C bath for 1 h, followed by 0 °C for two additional hours. The solution was then poured into a vigorously stirred mixture of THF (6 mL) and a saturated $NaHCO_3$ (aq) solution (3 mL) and stirred for 10 min. This mixture was extracted with EtOAc (3 x 5 mL). The combined organic extracts were washed with a saturated NH_4Cl (aq) solution (5 mL), washed with brine, dried over $MgSO_4$ and concentrated to give 20 mg (92%) of a mixture of 4 aldehydes by ^{1}H NMR. This mixture was dissolved in a 2:1 mixture of MeOH/THF (0.3 mL) and the resulting solution cooled to 0 °C. A spatula tip of $NaBH_4$ was added and the solution stirred for 30 min, after which it was poured into a saturated NH_4Cl (aq) solution (5 mL). This mixture was extracted with EtOAc (3 x 3 mL) and the combined organic extracts washed with brine, dried over Na_2SO_4 and concentrated giving 20 mg of the crude cycloadduct alcohol mixture. This mixture was purified first by preparative TLC (15% EtOAc/hexanes) and then by HPLC (15%

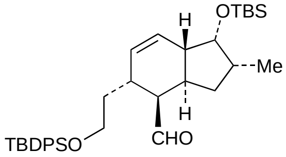
EtOAc/hexanes) to give pure samples of the two major cycloadduct diastereomers: 3.2 mg of the alcohol **20a** (corresponding to cycloadduct **21**): ^{1}H NMR ($CDCl_3$, 500 MHz) d 7.68-7.68 (m, 4 H), 7.43-7.26 (m, 6 H), 5.83 (app. d, *J* = 9.8 Hz, 1 H), 5.51 (dt, *J* = 9.8, 3.6 Hz, 1 H), 3.79-3.73 (m, 3 H), 3.66 (t, *J* = 9.3 Hz 1 H), 3.45 (app. t, *J* = 9.5 Hz, 1 H), 2.45-2.42 (m, 1 H), 2.22-2.13 (m, 1 H), 1.91-1.86 (m, 1 H), 1.81 (dt, *J* = 12.2, 7.1 Hz, 1 H), 1.76-1.73 (m, 1 H), 1.69-1.62 (m, 1 H), 1.54-1.48 (m, 2 H), 1.25-1.18 (m, 2 H), 1.04 (s, 9 H), 0.92-0.90 (m, doublet under singlet, 12 H), 0.06 (s, 3 H), 0.05 (s, 3 H);

and 5.0 mg of the alcohol **20b** (corresponding to cycloadduct **22**): ^{1}H NMR ($CDCl_3$, 500 MHz) d 7.68-7.67 (m, 4 H), 7.43-7.38 (m, 6 H), 5.74 (app. d, *J* = 10.0 Hz, 1 H), 5.53 (dt, *J* = 10.0, 3.2 Hz, 1 H), 4.01 (t, *J* = 3.9 Hz, 1 H), 3.79-3.70 (m, 3 H), 3.47-3.43 (m, 1 H), 2.45-2.42 (m, 1 H), 2.36-2.29 (m, 1 H), 2.12-2.07 (m, 1 H), 1.87-1.84 (m, 1 H), 1.83-1.79 (m, 3 H), 1.75 (broad d, *J* = 12.2 Hz, 1 H), 1.72-1.65 (m, 1 H), 1.62-1.54 (m, 1 H), 1.05 (s, 9 H), 0.95 (d, *J* = 7.3 Hz, 3 H), 0.85 (m, 9 H), 0.02 (broad s, 6 H);



21

Spectroscopic data for ***trans*-fused cycloadduct 21**: $[a]^{24}_{D}$ = -8.6 (*c* = 0.36 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) d 9.76 (d, *J* = 2.4 Hz, 1 H), 7.66-7.62 (m, 4 H), 7.44-7.36 (m, 6 H), 5.90 (broad d, *J* = 9.8 Hz, 1 H), 5.59 (dt, *J* = 10.0, 3.2 Hz, 1 H), 3.71 (t, *J* = 6.4 Hz, 2 H), 3.66 (under 3.71, 1 H), 2.82-2.81 (m, 1 H), 2.48-2.44 (m, 1 H), 2.26-2.19 (m, 1 H), 2.05-1.96 (m, 2 H), 1.69-1.61 (m, 2 H), 1.56-1.53 (m, 1 H), 1.35 (ddd, *J* = 12.5, 12.5, 7.3 Hz, 1 H), 1.04 (s, 9 H), 0.90 (m, 12 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) d 204.6, 135.8, 131.0, 129.9, 128.4, 127.9, 125.8, 76.8, 62.1, 51.5, 45.8, 35.1, 34.7, 32.9, 29.7, 26.8, 25.9, 19.4, 18.5, 17.2, 1.3, -4.3, -4.4; IR (neat) 3072, 3050, 3020, 2957, 2930, 2858, 1723, 1472, 1428, 1388, 1361, 12 51, 1112, 876, 837, 702 cm^{-1}; HRMS (ES) for $C_{35}H_{52}O_3Si_2Na$ [M+Na]$^+$ calcd. 599.3353, found 599.3340.



22

Spectroscopic data for ***trans*-fused cycloadduct 22**: $[a]^{24}_{D}$ = -10.9 (*c* = 0.35 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) d 9.79 (d, *J* = 1.9 Hz, 1 H), 7.66-7.63 (m, 4 H), 7.43-7.37 (m, 6 H), 5.79 (broad d, *J* = 10.0 Hz, 1 H), 5.60 (dt, *J* = 10.0, 3.7 Hz, 1 H), 4.03 (t, *J* = 3.9 Hz, 1 H), 3.71 (t, *J* = 7.1 Hz, 2 H), 2.82-2.77 (m, 1 H), 2.56-2.54 (m, 1 H), 2.47-2.40 (m, 1 H), 2.18-2.13 (m, 1 H), 2.06-2.03 (m, 1 H), 1.95 (q, *J* = 12.4 Hz, 1 H), 1.74-1.67 (m, 1 H), 1.62-1.57 (m, 1 H), 1.25 (m, 1 H), 1.04 (s, 9 H), 0.95 (d, *J* = 7.3 Hz, 3 H), 0.85 (m, 9 H), 0.02 (broad s, 6 H); ^{13}C NMR ($CDCl_3$, 125 MHz) d 205.6, 136.8, 134.0, 131.7, 129.9, 128.2, 127.9, 128.2, 127.9, 75.3, 62.2, 51.2, 47.2, 38.6, 37.9, 35.3, 32.9, 27.1, 26.2, 19.4, 18.5, 16.6, -3.8, -3.9; IR (neat) 3071, 3049, 3020, 2956, 2858, 1722, 1472, 1428, 1252, 1111, 877, 702 cm^{-1}; HRMS (ES) for $C_{35}H_{52}O_3Si_2Na$ $[M+Na]^+$ calcd. 599.3353, found 599.3367.