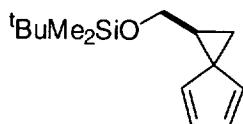


General Procedures: All reactions were performed using oven dried glassware under an atmosphere of dry nitrogen. Tetrahydrofuran, diethyl ether, and methylene chloride were purified by passing over activated alumina under an argon atmosphere. All reagents were purchased from Aldrich or Fluka and used without further purification with the following exceptions: Tributyltinhydride was distilled at reduced pressure (<1 torr). Triethylamine was distilled from KOH. Dimethylformamide was stored over 4Å molecular sieves prior to use. Diisopropylamine was distilled from KOH. Benzyl alcohol was stored over 4Å molecular sieves prior to use. Propane-1,3-diol was distilled at reduced pressure (<1 torr) from K₂CO₃. Carbon tetrachloride was passed over silica gel, distilled under dry N₂, then sparged with Ar for 30 min with sonication before use. Chromatographic purification of products was performed on Fluka Silica Gel 60 using a forced flow of EtOAc/hexanes eluant (unless noted otherwise) at 0.1-0.15 bar.¹ NMR spectra were recorded on a Varian Mercury 300 operating at 300 MHz and 75 MHz for ¹H and ¹³C, respectively, and are referenced to the internal solvent signals. Some ¹H-NMR signals were broadened due to carbamate rotamers and are indicated with the prefix "b" (i.e. "bd" indicates a broadened doublet). IR spectra were recorded on a Perkin Elmer Spectrum RXI FT-IR spectrometer. Optical rotations were measured on a Jasco DIP-1000 polarimeter operating at the sodium D line. Thin layer chromatography was performed using Merck Silica Gel 60 F₂₅₄ TLC plates and visualized by fluorescence quenching under UV light. In addition, all TLC plates were stained using either ceric ammonium molybdate or anisaldehyde stain. Combustion analyses were performed by the Mikroelementaranalysesches Laboratorium at the ETH in Zürich.



Silyl ether 7. A solution of alcohol **6** (59.7g, 0.489 mol) and Et₃N (82 mL, 0.59 mol) in 500 ml DMF was cooled to 0°C and TBSCl (81.0g, 0.537 mol) in 300 mL DMF was added over a period of 15 min. A white precipitate was formed rapidly. The reaction was allowed to warm to room temperature and was stirred for an additional 30 min. The mixture was then poured onto 2L of ice water and extracted with 3 x 300 mL pentane. The combined extracts were dried over Na₂SO₄ and concentrated *in vacuo* to give 115g of **7** as a colorless oil that was used without further purification.

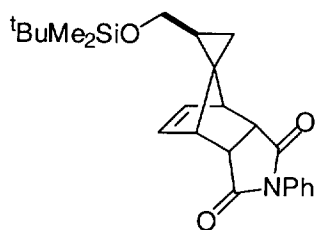
¹H-NMR (CDCl₃, 300 MHz) δ 6.54 (d, 1H, J=5.2), 6.49 (d, 1H, J=5.0), 6.29 (d, 1H, J=5.2), 6.09 (d, 1H, J=5.0), 3.89 (dd, 1H, J=11.0, 5.4), 3.75 (dd, 1H, J=11.0, 6.8), 2.30-2.35 (m, 1H), 1.81 (dd, 1H, J=8.6, 4.1), 1.74 (dd, 1H, J=7.3, 4.1), 0.89 (s, 9H), 0.06 (s, 6H)

¹³C-NMR (CDCl₃, 75 MHz) δ 139.3, 134.9, 130.2, 128.4, 64.2, 41.8, 29.5, 25.9, 18.3, 17.4, -5.2

IR (thin film) ν 2956, 2930, 2858, 1472, 1256, 1111, 1089, 1006

MS (CI) calcd for C₁₄H₂₄OSi 236.1596 found 236.1590.

¹ Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.



Diels-Alder adduct 8. To a solution of **7** (116g, 0.491 mol) in 500 ml dichloromethane was added a solution of N-phenylmaleimide (83g, 0.48 mol) in 500 ml dichloromethane at 0°C over a period of 30 min. The resulting yellow mixture was then filtered and concentrated *in vacuo*. The residue was recrystallized twice from 800 ml cyclohexane to afford 70g of white powder. The mother liquor was concentrated *in vacuo* and the residue dissolved in 500 ml of chlorobenzene. After stirring at reflux for 24 hours the solvent was removed *in vacuo* and the residue was recrystallized from cyclohexane again. This cycle was repeated three times to yield an additional 72g of microcrystalline solid for a combined yield of 142g of **8** (74%).

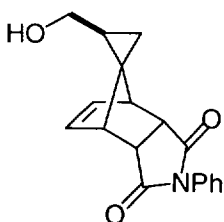
MP 156-157 °C

¹H-NMR (CDCl₃, 300 MHz) δ 0 7.36-7.46 (m, 3H), 7.14 (d, 2H, J =7.2), 6.32 (s, 2H), 3.59 (dd, 1H, J=10.8, 6.7), 3.56 (s, 2H), 3.45 (dd, 1H, J=10.8, 7.0), 3.14 (s, 1H), 2.89 (s, 1H), 1.26-1.29 (m, 1H), 0.88 (s, 9H), 0.69 (dd, 1H, J =8.7, 5.5), 0.43 (t, 1H, J=5.5), 0.04 (s, 6H)

¹³C-NMR (CDCl₃, 75 MHz) δ 176.6, 134.8, 133.8, 131.8, 129.0, 128.5, 126.6, 64.0, 52.2, 51.0, 46.7, 46.0, 45.6, 25.9, 21.7, 18.3, 11.8, -5.27, -5.32

IR (thin film) ν 2954, 2929, 2857, 1710, 1494, 1472, 1379, 1255, 1182, 1082

MS (CI) calcd for C₂₄H₃₁NO₃Si 409.2073 found 409.2144



Alcohol 10. To a solution of **8** (10.6g) in 30 ml THF at 23 °C was added 150 ml 48% HF / acetonitrile / water (5:95:1.5 v/v/v) and the reaction stirred one hour. Saturated NaHCO₃ was then added portionwise until bubbling ceased and pH was approximately neutral (by pH paper). The reaction was extracted 5 x 100 ml dichloromethane and the combined extracts washed 1 x 300 ml saturated aqueous NaCl and dried over Na₂SO₄. Solvent removal *in vacuo* afforded analytically pure **10** in quantitative yield as a colorless solid.

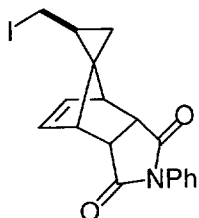
MP 159-160 °C

¹H-NMR (CDCl₃, 300 MHz) δ 0 7.5-7.3 (m, 3H), 7.15 (m, 2H), 6.41 (m, 2H), 3.62 (m, 1H), 3.54 (s, 2H), 3.35 (dd, 1H, J = 11, 8), 3.13 (s, 1H), 2.91 (s, 1H), 1.36 (m, 1H), 0.76 (dd, 1H, J = 8, 5), 0.44 (dd, 1H, J = 5, 5)

¹³C-NMR (CDCl₃, 75 MHz) δ 11.85, 21.40, 45.19, 45.70, 46.28, 50.70, 52.33, 63.86, 126.36, 128.43, 128.87, 131.51, 134.22, 135.35, 176.10, 176.19

IR (thin film) ν 3461, 2992, 2876, 1707, 1497, 1380, 1285, 1183, 1032, 913, 723

Elemental Analysis calc'd for $C_{18}H_{17}O_3N_1$: C, 73.20%, H, 5.80%, N, 4.74%; found C, 73.09%, H, 5.86%, N, 4.74%



Iodide 11. To a solution of **10** (14.5g, 49.1 mmol), triphenylphosphine (19.2g, 73.2 mmol), and imidazole (5.12g, 75.2 mmol) in 450 ml dichloromethane cooled with an ice/salt bath was added I_2 (18.8g, 74.1 mmol) in one portion. The reaction became opaque orange-brown over 10 min then was warmed to room temperature and stirred an additional 15 min. The reaction was then treated with 50 ml of saturated aqueous Na_2SO_3 and stirred until colorless. The organic layer was washed 1 x 200 ml 10% $CuSO_4$, 2 x 200 ml water, 1 x 200 ml saturated $NaCl$ and dried over Na_2SO_4 . Partial solvent removal *in vacuo* afforded a viscous solution which was subjected to silica gel chromatography (1:1 hexanes/EtOAc) to give **11** as a colorless solid. 18.5g (93%)

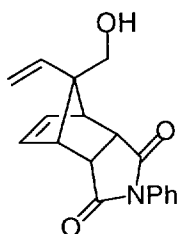
MP 148-149 °C (dec.)

1H -NMR ($CDCl_3$, 300 MHz) δ 7.46-7.36 (m, 3H), 7.15 (m, 2H), 6.38 (m, 2H), 3.54 (d, 2H, $J = 1$), 3.14 (m, 3H), 2.92 (s, 1H), 1.60 (m, 1H), 0.95 (dd, 1H, $J = 8, 5$), 0.42 (dd, 1H, $J = 5, 5$)

^{13}C -NMR ($CDCl_3$, 75 MHz) δ 7.31, 17.28, 23.51, 45.26, 45.35, 45.72, 50.66, 57.36, 126.37, 128.44, 128.88, 131.53, 133.79, 135.00, 175.90, 175.95

IR (thin film) ν 2989, 1772, 1710, 1598, 1499, 1455, 1378, 1285, 1182, 912, 874, 724

Elemental Analysis calc'd for $C_{18}H_{16}O_2N_1I$: C, 53.35%, H, 3.98%, N, 3.46%; found C, 53.53%, H, 4.07%, N, 3.49%



Alcohol 12. A solution of iodide **11** (30.2g, 74.5 mmol) in 700 ml benzene was vigorously aerated for 30 min with dry air passing through a fritted glass dispersion tube. While aeration continued, Bu_3SnH (50.0g, 172 mmol, diluted to 100 ml with benzene) was added dropwise *via* pressure equalizing addition funnel over a period of 2 h. Aeration was stopped when **11** was consumed (as indicated by TLC). The orange reaction was then stirred an additional 15h during which time some white precipitate formed. With stirring, 750 ml hexanes was added and the resulting copious white precipitate was collected by filtration to give 15.8g of **12**. The filtrate was concentrated and the residue was purified by silica gel chromatography (4:1 EtOAc/hexanes) to give an additional 3.15g of **12** for a combined yield of 19.0g (86%).

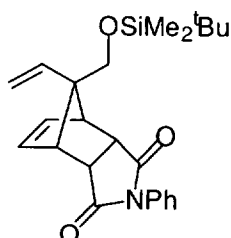
MP 172-173 °C

¹H-NMR (CDCl₃, 300 MHz) δ 0 7.38-7.46 (m, 3H), 7.14 (dd, 2H, J= 7, 1), 6.19 (dd, 2H, J= 2, 2), 5.72 (dd, 1H, J= 18, 11), 5.27 (dd, 1H, J= 11, 0.8), 5.06 (dd, 1H, J= 18, 0.8), 3.57 (m, 4H), 3.43 (s, 2H)

¹³C-NMR (CDCl₃, 75 MHz) δ 44.20, 48.54, 62.66, 73.42, 118.67, 126.31, 128.45, 128.88, 131.52, 133.69, 137.72, 176.22

IR (thin film) ν 3456, 2979, 1772, 1706, 1469, 1381, 1185, 727, 691, 622

Elemental Analysis calc'd for C₁₈H₁₇O₃N₁: C, 73.20%, H, 5.80%, N, 4.74%; found C, 73.09%, H, 5.86%, N, 4.74%



Silyl ether 13. To a solution of alcohol **12** (6.0g, 20 mmol), triethylamine (5.0ml, 36 mmol), and DMAP (0.24g, 2.0 mmol), in 100 ml DMF cooled with an ice/water bath was added Me₂BuSiCl (3.97g, 26 mmol). The reaction was allowed to warm to 23 °C and was stirred 5 h before quenching with 100 ml water and extracting the aqueous layer 3 x 200 ml pentane. The combined organic layers were washed 1 x 200 mL water, 1 x 200 ml 1N HCl, 1 x 200 ml saturated NaHCO₃, 1 x 200 ml saturated aqueous NaCl then dried over Na₂SO₄. Solvent removal *in vacuo* gave **13** as an orange oil that was purified by silica gel chromatography (4:1 hexanes/EtOAc) to give pure **13** as a colorless solid. 7.66g (92%)

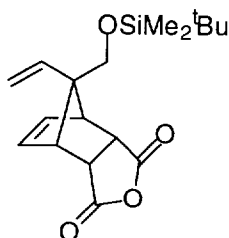
MP 100-101 °C

¹H-NMR (CDCl₃, 300 MHz) δ 0 7.45-7.37 (m, 3H), 7.14 (dd, 2H, J= 7, 1.5), 6.17 (dd, 2H, J= 2, 2), 5.76 (dd, 1H, J= 18, 11), 5.10 (dd, 1H, J= 11, 0.8), 4.93 (dd, 1H, J= 18, 0.8), 3.57 (m, 4H), 3.41 (s, 2H), 0.90 (s, 9H), 0.01 (s, 6H)

¹³C-NMR (CDCl₃, 75 MHz) δ -5.71, 18.02, 25.43, 44.47, 48.66, 64.33, 72.92, 116.64, 126.35, 128.35, 128.84, 131.66, 133.63, 138.65, 176.48

IR (thin film) ν 2928, 2856, 1713, 1497, 1472, 1378, 1256, 1183, 1094, 839, 775, 726

Elemental Analysis calc'd for C₂₄H₃₁O₃N₁Si: C, 70.38%, H, 7.63%, N, 3.42%; found C, 70.44%, H, 7.66%, N, 3.48%



Anhydride 14. To a solution of imide **13** (3.49g, 8.52 mmol) in 100 ml THF at 23 °C was added LiOH (1M, 25 ml, 25 mmol) dropwise. The reaction was stirred for 5 min then

quenched by dropwise addition of NaHSO_4 (1M, 25 ml, 25 mmol). The mixture was diluted with 100 ml saturated aqueous NaCl , extracted 3 x 100 mL dichloromethane, and the combined organic layers dried over NaSO_4 . Solvent removal *in vacuo* yielded a colorless solid that was dissolved in 700 ml toluene at 23 °C. After 2 h the reaction was poured on to 1L of ice cold 1M HCl and shaken vigorously. The organic layer was then washed 1 x 500 ml saturated NaCl and dried over Na_2SO_4 . Solvent removal *in vacuo* afforded pure **14** as a colorless solid. 2.71g (95%) An analytical sample was obtained by recrystallization from hexanes.

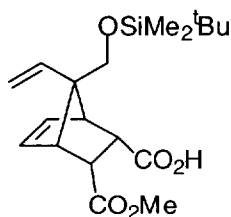
MP 98-99 °C

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ 6.23 (dd, 2H, J = 2, 2), 5.72 (dd, 1H, J = 17, 11), 5.12 (d, 1H, J = 11), 4.89 (d, 1H, J = 17), 3.72 (d, 2H, J = 2), 3.50 (s, 2H), 3.40 (m, 2H), 0.91 (s, 9H), 0.04 (s, 6H)

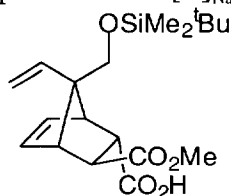
$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz) δ -5.77, 17.95, 25.55, 45.87, 46.88, 49.11, 49.45, 64.42, 67.72, 73.58, 115.88, 117.15, 134.22, 134.65, 137.61, 139.70, 171.14, 178.00

IR (thin film) ν 3081, 2955, 2929, 2857, 1782, 1717, 1472, 1416, 1254, 1092, 914, 838, 776, 735, 671

Elemental Analysis calc'd for $\text{C}_{18}\text{H}_{26}\text{O}_4\text{Si}$: C, 64.64%, H, 7.73%, N, 0.00%; found C, 64.49%, H, 7.73%, N, 0.03%



Cis-Acid ester 15. To a suspension of anhydride **14** (2.54g, 7.61 mmol) in 25 ml CCl_4 and 25 ml toluene cooled with an ice/water bath was added methanol (0.90 ml, 22 mmol) followed by quinine (2.71g, 8.35 mmol). The heterogeneous white mixture became homogeneous over two hours and was then diluted with 200 ml EtOAc and washed 2 x 200 ml 1N HCl , 1 x 200 ml brine and dried over Na_2SO_4 . Solvent removal *in vacuo* gave quantitative return of acid-ester **15** as a colorless oil that was used without further purification. $[\alpha]_{\text{Na}} -2.13$ ($c = 0.825$, CDCl_3)



Trans acid-ester 16. To a solution of lithium diisopropylamide (20.0 ml 1.6M BuLi /hexane + 4.6 ml diisopropylamine, 32 mmol) in 50 ml Et_2O cooled with an ice/water bath was added acid-ester **15** (2.25g, 6.15 mmol) dropwise as a solution in 20 ml Et_2O over 15 min. The reaction gradually turned yellow and, after 30 min, was poured onto 150 ml ice-cold 1N NaHSO_4 then extracted 2 x 200 ml EtOAc . The combined organic layers were washed 1 x 200 ml water, 1 x 200 ml brine then dried over Na_2SO_4 . Solvent removal *in vacuo* gave acid-ester **16** as a yellow oil that was purified by silica gel

chromatography (30:1 CH₂Cl₂/HOAc) to give 1.64g (73%) of pure **16** as a colorless oil that crystallized on standing.

MP 99-100 °C

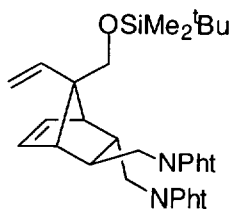
Optical rotation: $[\alpha]_{\text{Na}} +7.20$ (c = 0.957, CDCl₃)

¹H-NMR (CDCl₃, 300 MHz) δ 6.27 (m, 1H), 5.98 (m, 1H), 5.70-5.80 (dd, 1H, *J*=17.7, 10.9), 5.05 (dd, 1H, *J*=10.9, 1.4), 4.90 (dd, 1H, *J*=17.7, 1.4), 3.72 (s, 3H), 3.62 (m, 1H), 3.51 (d, 1H, *J*=10.6), 3.34 (d, 1H, *J*=10.6), 3.26 (s, 2H), 2.76 (d, 1H, *J*=5.0), 0.85 (s, 9H), -0.02 (s, 3H), -0.03 (s, 3H)

¹³C-NMR (CDCl₃, 75 MHz) δ 179.84, 173.67, 140.38, 138.27, 133.40, 115.91, 69.09, 64.56, 52.25, 50.00, 49.58, 47.87, 45.50, 25.83, 18.26, -5.47, -5.69

IR (thin film) ν 3077, 2953, 2856, 1737, 1732, 1708, 1471, 1435, 1417, 1314, 1257, 1229, 1198, 1093, 1070, 1005, 912, 838, 775

Elemental Analysis calc'd for C₁₉H₃₀O₅Si: C, 62.26%, H, 8.25%, N, 0.00%; found C, 62.29%, H, 8.16%, N, 0.00%



Bisphthalimide 17. To a solution of acid ester **16** (0.974g, 2.66 mmol) in 30 ml Et₂O cooled with an ice bath was added LAH (0.306g, 8.06 mmol) portionwise over 10 minutes. Some gas evolution was noted. The reaction was allowed to warm to room temperature and after 1.5hr it was cooled again with an ice bath and sequentially treated with 0.3 ml water (gas evolution!), 0.3 ml 15% NaOH, and 0.9 ml water. The resulting grey slurry was warmed to room temperature and stirred (~5min) until it turned white and it was filtered through celite. The filter cake was pulverized and rinsed 10 x 20 ml CH₂Cl₂. The colorless filtrate was evaporated *in vacuo* to yield 0.701g (81%) of the corresponding diol as a single compound by ¹H-NMR.

To a solution of the diol (1.22g, 3.76 mmol), prepared as described above, in 60 ml THF at room temperature was added PPh₃ (2.47g, 9.42 mmol) and phthalimide (1.12g, 7.61 mmol) followed by diethylazodicarboxylate (1.5 ml, 9.5 mmol) dropwise over 5 min. The yellow reaction was stirred for 30 min then it was diluted with 300 ml EtOAc and washed 1 x 100 ml 10% Na₂SO₃, and 2 x 100 ml 10% K₂CO₃. The combined aqueous washes were back extracted 1 x 50 ml EtOAc and the combined organic layers were then washed 1 x 100 ml brine and dried over Na₂SO₄. Rotary evaporation gave a viscous yellow oil that was purified by silica gel chromatography (gradient 5:1 → 2:1 hexane/EtOAc) to yield 1.92g (88%) **17** as a colorless foam.

MP 140-142 °C

Optical rotation: $[\alpha]_{\text{Na}} -46.9$ (c = 0.925, CDCl₃)

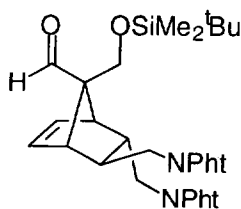
¹H-NMR (CDCl₃, 300 MHz) δ 7.73-7.79 (m, 2H), 7.58-7.67 (m, 6H), 6.30 (dd, 1H, *J*=5.6, 3.4), 6.15 (dd, 1H, *J*=5.6, 2.8), 5.79 (dd, 1H, *J*=17.7, 10.9), 5.01 (dd, 1H, *J*=10.9, 1.6), 4.85 (dd, 1H, *J*=17.7, 1.6), 4.06-4.16 (m, 2H), 3.85 (dd, 1H, *J*=14.0, 6.2), 3.63 (d, 1H,

$J=10.9$), 3.36 (dd, 1H, $J=13.7$, 9.0), 3.22 (dd, 1H, $J=13.4$, 5.3), 2.85 (s, 1H), 2.72 (m, 1H), 2.65 (s, 1H), 1.72 (m, 1H), 0.84 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H)

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz) δ 168.66, 168.07, 142.99, 138.42, 134.31, 133.76, 133.68, 132.84, 132.19, 131.96, 123.60, 123.19, 123.08, 114.80, 68.49, 64.74, 49.69, 49.47, 44.69, 41.58, 41.26, 40.52, 25.85, 18.18, -5.33, -5.49

IR (thin film) ν 2928, 2884, 2854, 1772, 1715, 1467, 1435, 1397, 1347, 1302, 1255, 1188, 1093, 1070, 1002, 912, 837, 777, 713

Elemental Analysis calc'd for $\text{C}_{34}\text{H}_{38}\text{O}_5\text{N}_2\text{Si}$: C, 70.07%, H, 6.57%, N, 4.81%; found C, 69.88%, H, 6.68%, N, 4.63%



Aldehyde 18. To a vigorously stirring mixture of NMO (0.79g, 6.7 mmol), $(\text{DHQD})_2\text{PHAL}$ (0.11g, 0.13 mmol), and OsO_4 (0.45 ml, 4% in water, 0.07 mmol) in 15 ml water and 5 ml THF was added diene **17** (1.36g, 2.33 mmol) dropwise as a solution in 5 ml THF. The reaction was stirred at 23 °C for 23 h then 5 ml sat. aq. Na_2SO_3 was added and the reaction was stirred 1 h. It was then extracted 3 x 50 ml CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4 . Concentration *in vacuo* gave an oil which was purified by silica gel chromatography (1:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) to give 1.31g (98%) of a 6:5 mixture of two diastereomeric diols.

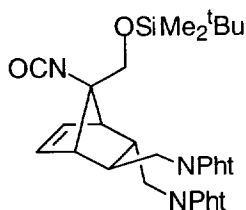
To a solution of diol (1.03g, 1.67 mmol), prepared as described above, in 30 ml THF and 20 ml water was added K_2CO_3 (0.42g, 3.0 mmol) followed by NaIO_4 (1.06g, 4.95 mmol, in 2 ml water). The mixture stirred for 1h during which time some white precipitate formed then it was extracted 3 x 100 ml EtOAc and the combined organics were washed 1 x 100 ml 10% Na_2SO_3 , 1 x 100 ml brine and dried over Na_2SO_4 . Concentration *in vacuo* followed by purification by silica gel chromatography (1:1 hexane/EtOAc) gave 0.900g (92%) aldehyde **18** as a colorless foam.

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ 9.60 (s, 1H), 7.79-7.83 (m, 2H), 7.62-7.72 (m, 6H), 6.43 (dd, 1H, $J=3.4$, 5.6), 6.31 (dd, 1H, $J=2.8$, 5.6), 4.15 (d, 1H, $J=10.9$), 3.93-4.06 (m, 2H), 3.84 (dd, 1H, $J=14.0$, 6.8), 3.23-3.41 (m, 2H), 3.11 (s, 1H), 2.97 (s, 1H), 2.65-2.69 (m, 1H), 1.73-1.80 (m, 1H), 0.85 (s, 9H), 0.07 (s, 3H), 0.04 (s, 3H)

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz) δ 206.27, 168.56, 167.99, 138.58, 133.94, 133.86, 132.03, 131.83, 123.32, 123.18, 76.16, 62.20, 47.74, 47.04, 44.26, 41.10, 40.37, 39.95, 26.90, 25.70, 18.06, -5.57, -5.77

IR (thin film) ν 2928, 2855, 1770, 1715, 1467, 1397, 1257, 1087, 838, 778, 713

HRMS(MALDI) calc'd for $(\text{C}_{33}\text{H}_{36}\text{O}_6\text{N}_2\text{SiNa})^+$, 607.2240; found, 607.2236



Isocyanate 19. To a solution of aldehyde **18** (0.431g, 0.737 mmol) in 20 ml ^tBuOH and 0.2 ml DMSO was added dropwise a solution of NaClO₂ (0.343g, 3.79 mmol) and KH₂PO₄ (1.01g, 7.45 mmol) in 4 ml water. The resulting yellow reaction was stirred until colorless (~1h) then it was further acidified with 1N NaHSO₄ (7.5 ml, 7.5 mmol) and extracted 3 x 100 ml EtOAc. The combined organic layers were then washed 1 x 100 ml water, 1 x 100 ml brine and dried over Na₂SO₄. Concentration *in vacuo* gave a colorless solid (0.58g, >100%) that was purified by silica gel chromatography (1:1 hexane/EtOAc with 5% HOAc) to give 0.418g (94%) of the corresponding carboxylic acid. In practice, the crude material was found to contain ~5% of the acid chloride and thus was carried on to subsequent steps unpurified.

To a solution of crude carboxylic acid (0.214g, 0.356 mmol), prepared as described above, in 10 ml CH₂Cl₂ was added (COCl)₂ (0.037 ml, 0.42 mmol) dropwise followed by one drop of DMF (~0.005 ml). Gas evolution was noted and the reaction was stirred for 1.5h then concentrated *in vacuo* to give a yellow solid residue. The residue was dissolved in 4 ml dry DMSO and NaN₃ (0.056g, 0.86 mmol) was added. The solution was stirred for 1.5h then it was diluted with 10 ml water and extracted 3 x 10 ml EtOAc. The combined organics were washed 5 x 10 ml water, 1 x 10 ml brine then dried over Na₂SO₄. Concentration *in vacuo* gave a yellow oily residue that was redissolved in 15 ml benzene and heated to reflux for 2h. (Completion of the reaction was determined by FTIR as evidenced by the disappearance of the N₃ absorbance and appearance of the NCO absorbance.) Evaporation of solvent *in vacuo* yielded a yellow solid that was purified by silica gel chromatography (3:2 hexane/EtOAc) to give 0.144g (67%, 4 steps) of isocyanate **19** as a white solid.

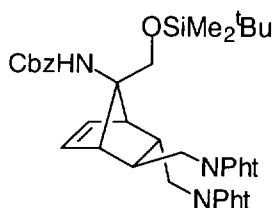
Optical rotation: [α]_{N_a} -33.0 (c = 1.08, CDCl₃)

¹H-NMR (CDCl₃, 300 MHz) δ 7.78-7.81 (m, 2H), 7.59-7.77 (m, 6H), 6.44 (dd, 1H, J=3.1, 5.6), 6.31 (dd, 1H, J=3.2, 5.6), 4.21 (d, 1H, J=10.9), 3.75-3.98 (m, 3H), 3.33 (dd, 1H, J=13.7, 9.0), 3.20 (dd, 1H, J=13.7, 5.6), 2.83 (s, 1H), 2.73 (s, 1H), 2.52-2.57 (m, 1H), 1.68-1.75 (m, 1H), 0.87 (s, 9H), 0.11 (s, 3H), 0.072 (s, 3H)

¹³C-NMR (CDCl₃, 75 MHz) δ 168.54, 167.91, 137.64, 133.98, 133.87, 132.56, 131.99, 131.78, 125.54, 123.34, 123.19, 83.47, 64.82, 52.22, 51.33, 42.72, 41.23, 39.70, 39.65, 25.76, 18.13, -5.36, -5.52

IR (thin film) ν 2928, 2855, 2249, 1771, 1715, 1467, 1435, 1396, 1348, 1085, 838, 779, 724

Elemental Analysis calc'd for C₃₃H₃₅N₃O₆Si: C, 66.31%, H, 5.90%, N, 7.03%; found C, 66.06%, H, 6.03%, N, 7.02%



Cbz Amine 20. Isocyanate **19** (0.503g, 0.841 mmol) was dissolved in 5 ml THF and added via cannula to a solution of BnOLi (0.102g BnOH + 0.6 mL 1.6M BuLi) in 20 mL THF at 0 °C. The reaction was poured onto 20 mL ice cold 1N NaHSO₄ and extracted 2 x 20 mL EtOAc. The combined organic layers were washed 1 x 20 mL sat. NaHCO₃ and 1 x 20 mL sat. NaCl then dried over Na₂SO₄. Removal of solvent *in vacuo* gave a colorless resin that was purified by silica gel chromatography (grad. 3:1 → 1:1 hexanes/EtOAc) to give **20** as 0.450g (76%) of colorless foam.

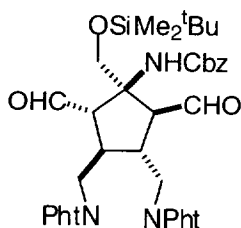
Optical rotation: $[\alpha]_{\text{Na}} -27.1$ (c = 0.700, CDCl₃)

¹H-NMR (CDCl₃, 300 MHz) δ 7.82 (m, 2H), 7.59-7.77 (m, 6H), 7.35 (m, 5H), 6.31 (dd, 1H, *J*=5.7, 3.1), 6.21 (dd, 1H, *J*=5.7, 3.1), 5.04 (bs, 1H), 5.00 (d, 1H, *J*=12.5), 4.91 (d, 1H, *J*=12.5), 4.18-4.03 (m, 3H), 3.81 (dd, 1H, *J*=14, 6.2), 3.35 (dd, 1H, *J*=13.7, 9.7), 3.23-3.15 (m, 2H), 2.85 (s, 1H), 2.65 (m, 1H), 1.75 (m, 1H), 0.87 (s, 9H), 0.12 (s, 3H), -0.01 (s, 3H)

¹³C-NMR (CDCl₃, 75 MHz) δ 168.58, 167.91, 154.94, 136.65, 136.23, 133.86, 133.73, 132.40, 132.13, 131.92, 128.47, 128.06, 127.98, 123.27, 123.16, 78.20, 66.18, 61.86, 50.79, 48.90, 42.61, 41.38, 40.41, 39.89, 25.85, 18.18, -5.46, -5.57

IR (thin film) ν 3369, 2945, 2929, 2846, 1771, 1716, 1468, 1435, 1397, 1347, 1251, 1069, 834

Elemental Analysis calc'd for C₄₀H₄₃O₇N₃Si: C, 68.06%, H, 6.14%, N, 5.95%; found C, 67.93%, H, 6.38%, N, 5.94%



Dialdehyde 22. Into a solution of **20** (0.447g, 0.634 mmol) in 10 ml CH₂Cl₂ cooled to -78°C was bubbled a dilute stream of O₃ in O₂ until the solution became blue. It was then flushed with N₂ and PPh₃ (0.201g, 0.766 mmol) was added and the reaction was warmed to 23 °C. After 30 min, K₂CO₃ (0.3g, 2 mmol) was added to the solution and it was stirred an addition 2h. The reaction was then filtered through celite and concentrated *in vacuo* to give a pale yellow oil that was purified by silica gel chromatography (3:2 hexane/EtOAc) to give 0.410g (88%) of pure **22** as a colorless foam.

Optical rotation: $[\alpha]_{\text{Na}} +19.9$ (c = 0.600, CDCl₃)

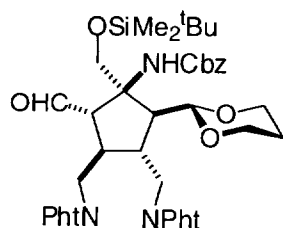
¹H-NMR (CDCl₃, 300 MHz) δ 9.76 (s, 1H), 9.64 (d, 1H, *J*=1.2), 7.85 (m, 4H), 7.75 (m, 4H), 7.36 (m, 3H), 7.20 (m, 2H), 5.54 (bs, 1H), 4.91 (d, 1H, *J*=12.2), 4.84 (d, 1H,

$J=12.2$), 4.08-4.15 (bm, 2H), 3.85-3.95 (m, 2H), 3.64-3.72 (m, 2H), 3.47 (d, 1H, $J=8.4$), 2.88 (bm, 1H), 2.62 (d, 1H, $J=11.2$), 2.58 (bm, 1H), 0.76 (s, 9H), -0.05 (s, 3H), -0.07 (s, 3H)

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz) δ 200.63, 199.72, 168.96, 168.9, 154.98, 134.20, 134.02, 131.98, 131.90, 128.52, 128.21, 123.57, 123.44, 67.98, 66.75, 64.76, 60.24, 58.35, 41.02, 39.32, 38.51, 38.38, 25.60, 17.97, -5.83, -5.80

IR (thin film) ν 3369, 2929, 2856, 1712, 1506, 1467, 1433, 1391, 1352, 1251, 1084, 913, 839, 779, 723

Elemental Analysis calc'd for $\text{C}_{40}\text{H}_{43}\text{N}_3\text{O}_9\text{Si}$: C, 65.11%, H, 5.87%, N, 5.69%; found C, 64.88%, H, 5.98%, N, 5.44%



Mono-acetal 23. To a vigorously stirring solution of distilled 1,3-propanediol (0.2 mL) in 5 mL dry ether was added dialdehyde **22** (0.101g, 0.137 mmol) and PPTS (0.097g, 0.380 mmol). After 1.5h the reaction was treated with 0.1g NaHCO_3 and filtered through celite. The filtrate was concentrated *in vacuo* and the residue purified by silica gel chromatography (grad. 2:1 \rightarrow 1:1 hexanes/EtOAc) to give 0.015g (15%) of starting dialdehyde **22** and 0.055g (59% based on unrecovered **22**) of **23** as a colorless foam.

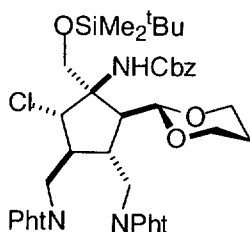
Optical rotation: $[\alpha]_{\text{Na}} +20.3$ ($c = 1.65$, CDCl_3)

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz) δ 9.68 (s, 1H), 7.84-7.80 (m, 4H), 7.70-7.77 (m, 4H), 7.24-7.30 (m, 5H), 6.06 (bs, 1H), 5.12 (d, 1H, $J=14.3$), 4.95 (d, 1H, $J=14.3$), 4.66 (d, 1H, $J=2.5$), 4.27 (bd, 1H, $J=10.3$), 3.99 (dd, 1H, $J=14, 6.2$), 3.89 (m, 2H), 3.77 (m, 2H), 3.65 (d, 1H, $J=10.3$), 3.37-3.55 (bm, 3H), 3.08 (d, 1H, $J=8.1$), 2.55-2.70 (bm, 2H), 2.13 (dd, 1H, $J=6.8, 2.2$), 1.61-1.82 (bm, 1H), 1.07 (bd, 1H, $J=12.1$), 0.86 (s, 9H), -0.28 (s, 6H)

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz) δ 199.84, 168.71, 155.00, 133.83, 133.71, 132.27, 132.03, 128.44, 128.20, 127.99, 123.28, 123.10, 100.74, 67.91, 66.75, 66.70, 66.23, 62.40, 60.92, 48.73, 40.38, 40.22, 39.33, 39.25, 25.61, 18.00, -5.76, -5.81

IR (thin film) ν 3365, 2930, 2856, 1772, 1715, 1512, 1468, 1435, 1397, 1362, 1251, 1086, 1002, 913, 875, 838

HRMS(MALDI) calc'd for $(\text{C}_{43}\text{H}_{49}\text{N}_3\text{O}_{10}\text{SiNa})^+$, 818.3085; found, 818.3089



Axinellamine core 25. To a solution of **23** (0.060g, 0.075 mmol) in 2 mL ^tBuOH at 23 °C was added KMnO₄ (0.016g, 0.10 mmol) dissolved in 1.5 mL pH=7 buffer (1.25 M phosphate). After 45 min the reaction was poured onto 10 mL ice cold 1 N NaHSO₄ and extracted 2 x 5 mL EtOAc. The combined organic layers were dried over Na₂SO₄. Solvent removal *in vacuo* gave 0.064g (quant.) of crude carboxylic acid **24**.

A solution of **24** (0.021g, 0.0259 mmol), thiopyridine-*N*-oxide (0.0044g, 0.035 mmol), and DMAP (0.001g, 0.008 mmol) in 1.0 mL CCl₄ in a sealed tube was subjected to 4 cycles of freeze-pump-thaw then transferred then EDC (0.010g, 0.052 mmol) was added and the bright yellow reaction stirred at 23 °C until it became colorless (~12 h). The reaction was directly purified by silica gel chromatography (grad. 2:1 → 1:1 hexanes/EtOAc) to give 0.016g (76%) of **25** as a colorless resin.

Optical rotation: $[\alpha]_{\text{Na}} +30.4$ ($c = 0.650$, CDCl₃)

¹H-NMR (CDCl₃, 300 MHz, an inseparable contaminant was present, <5%, and is believed to be the minor diastereomeric chloride) δ 7.84 (m, 4H), 7.77 (m, 4H), 7.05-7.25 (m, 5H), 5.64 (bs, 1H), 5.10 (d, 1H, $J=12.1$), 4.97 (bd, 1H, $J=12.1$), 4.73 (d, 1H, $J=1.6$), 4.41 (d, 1H, $J=6.2$), 4.18 (dd, 1H, $J=5.0, 8.7$), 3.95-3.65 (m, 5H), 3.45-3.15 (bm, 4H), 2.82 (m, 1H), 2.74 (m, 1H), 2.56 (dd, 1H, $J=6.5, 1.6$), 1.60-1.80 (m, 2H), 0.87 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H)

¹³C-NMR (CDCl₃, 75 MHz) δ 168.63, 168.17, 155.05, 133.76, 133.44, 132.53, 132.08, 128.42, 127.99, 123.26, 122.86, 100.08, 66.96, 66.59, 66.47, 66.41, 64.92, 51.67, 48.58, 42.11, 41.38, 38.84, 26.03, 25.35, 18.46, -5.49, -5.59

IR (thin film) ν 3360, 2929, 1772, 1715, 1506, 1468, 1396, 1359, 1251, 1115, 913, 838

HRMS(MALDI) calc'd for (C₄₂H₄₈ClO₉N₃SiNa)⁺, 824.2746; found, 824.2727