# Stereoselective Syntheses of Epothilones A and B via Nitrile Oxide Cycloadditions

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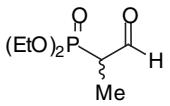
**Supporting Information**

## General Methods

All reactions were performed using oven dried glassware under an atmosphere of dry nitrogen unless otherwise specified. Tetrahydrofuran, diethyl ether, toluene, acetonitrile, and methylene chloride were purified by distillation and dried by passage over activated alumina under an argon atmosphere ($H_2O$ content < 30 ppm, Karl-Fischer titration). Triethylamine, diispropylamine, and pyridine were distilled from KOH and 2-propanol was distilled from sodium. Methanesulfonyl chloride and trifluoromethylsulfonic anhydride were distilled from phosphorous pentoxide. Triethylchlorosilane (TESCl), $Et_2N^iPr$ (Hünig's base), and *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) were distilled prior to use. Butyl lithium (n-BuLi) was titrated with recrystallized (toluene), dried diphenylacetic acid prior to use. All other commercial reagents were used without further purification. Chromatographic purification of products (flash chromatography) was performed on E. Merck Silica Gel 60 (230-400 mesh) using a forced flow of eluant at 0.5-1.0 bar . Concentration under reduced pressure was performed by rotary evaporation at 40 °C at the appropriate pressure. Purified compounds were further dried for 12-48 h under high vaccum (0.05 torr). NMR spectra were recorded on a Varian Mercury 300 operating at 300 MHz and 75 MHz for $^1H$ and $^{13}C$

acquisitions respectively, and are referenced to the internal solvent signals. Data are reported as follows: (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constants(s) in Hz). IR spectra were recorded on a Perkin Elemer Spectrum RXI FT-IR spectrophotometer. Optical rotations were measure on a Jasco DIP-1000 polarimeter operating at the sodium D line with a 100 mm path length cell, and are reported as follows: $[\alpha]^T$, concentration (g/100 ml), and solvent. Thin layer chromatography was performed using Merck Silica Gel 60 $F^{254}$ plates and visualized by fluorescence quenching under UV light. In addition, TLC plates were stained using ceric ammonium molybdate or potassium permanganate stain.

Chemical names were generated with Autonom 2.0 (Beilstein Informationssysteme GmbH) and modified where appropriate.




**16**

**(1-Methyl-2-oxo-ethyl)-phosphonic acid diethyl ester (16)**[1]. To a solution of BuLi (2.47 M in hexanes, 21.2 ml, 52.5 ml, 1.05 equiv) in 35 ml THF at –60 °C was added diethylmethylphosphonate (7.5 ml, 0.050 mol, 1.0 equiv) in 15 ml THF to give an off-white precipitate. After 5 min, MeI (3.27 ml, 52.5 mmol, 1.05 equiv) in 15 ml THF was added via cannula and the reaction allowed to warm to 23 °C to give a clear, colorless solution. After recooling to –60 °C, BuLi (2.47 M, 21.2 ml, 52.5 mmol) was added, and after 15 min, DMF (4.26 ml, 55.0 mmol, 1.10 equiv) in 15 ml THF was added via cannula. The reaction was slowly warmed to 23 °C to give a clear solution which was quenched by the addition of 2 *N* HCl (100 ml). To the resulting mixture was added 2 ml of aq. $Na_2S_2O_3$ and the aqueous layer extracted with $CH_2Cl_2$ (2 x 100 ml). The combined organic solutions were washed with brine (200 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by vacuum transfer with heating afforded **16** (7.89 g, 81 %) as a pale oil.

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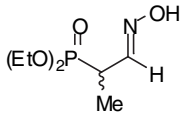
[1] This procedure has been previously reported. It is repeated here for convenience, see: Aboujaoude, E. E.; Collignon, N. *Syn. Comm.* **1983***,* 634.

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 9.70 (dd, 1H, *J* = 0.7, 1.7), 4.70 (d hept, 2H, *J* = 8.0, 6.0), 3.00 (dqd, 1H, *J* = 28.0 , 7.0, 1.7), 1.30 (dd, 3H, *J* = 18.0, 7.0), 1.30 (d, 12 H, *J* = 6.0).



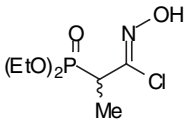

**17**

**(2-Hydroxyimino-1-methyl-ethyl)-phosphonic acid diethyl ester (39).** To **16** (3.90 g, 20.0 mmol, 1.00 equiv) in 95% EtOH (50 ml) at rt was added $NH_2OH$•HCl (2.78 g, 40.0 mmol, 2.00 equiv) in $H_2O$ (20 ml). The clear solution was stirred 10 h before being poured into $H_2O$ (50 ml) and extracted with $CH_2Cl_2$ (3 x 50 ml). The combined organic solutions were washed with brine (100 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatrography (EtOAc) provided **17** (3.84 g, 92% yield) as a slightly yellow oil.

**$^1$H NMR** (300 MHz, $CDCl_3$): δ 9.9-8.9 (brs, 1 H), 7.37 (*t*, 0.7 H, *J* = 4.7), 6.61 (*dd*, 0.3 H, *J* = 32.2, 3.1) 4.13-4.03 (m, 4 H), 3.94-3.76 (m, 0.3 H), 2.86 (dt, 0.7 H, *J* = 23.2, 3.1), 1.41-0.88 (m, 9 H)

**$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 148.1, 147.5, 63.1, 62.9, 34.4, 28.7, 16.9, 16.5, 12.5, 12.2

**IR** (thin film): 3250, 2984, 2938, 2939, 1645, 1453, 1210, 1025, 962, 795.



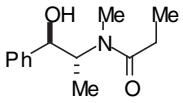

**18**

**(2-Chloro-2-hydroxyimino-1-methyl-ethyl)-phosphonic acid diethyl ester (18).** To **17** (1.26 g, 6.00 mmol, 1.00 equiv) in 60 ml $CH_2Cl_2$ at –78 °C was added *tert*-BuOCl (683 µl, 6.00 mmol, 1.0 0eq) dropwise to give a deep blue solution which was stirred 1 h at –78 °C before warming to rt over 1.5 h to give a clear, colorless solution.

This solution could be used directly for the hydroxyl directed nitrile oxide cycloaddition or concentrated under reduced pressure and purified by flash chromatography (EtOAc) to provide the pure, but unstable, hydroximinoyl chloride **18** (1.26 g, 86% yield) as a clear, colorless oil.

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 4.21-4.10 (m, 4 H), 3.19-3.09 (m, 1 H), 1.77 (brs, 1 H), 1.48 (dd, 3 H, *J* = 17.4, 7.2), 1.38-1.13 (m, 6 H)

**IR** (thin film): 3186, 3063, 2987, 2909, 1630, 1455, 1222, 1165, 1054, 1023, 984, 797

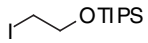



**32**

**(*R,R*)-*N*-(2-Hydroxy-1-methyl-2-phenylethyl)-*N*-methylpropionamide (32).**[2] To (1*R*,2*R*)-(-)-pseudoephedrine (25.0 g, 151 mmol, 1.00 equiv) in 270 ml $CH_2Cl_2$ at 23 °C was added $NEt_3$ (23.1 ml, 0.170 mol, 1.10 equiv), and propionic anhydride (28.8 ml, 160 mmol, 1.07 equiv) in 1 ml portions over 5 min. After 20 min, the reaction solution was washed with sat. aq. $NaHCO_3$ (200 ml), 1 *N* HCl (2 x 200 ml), brine (200 ml), and dried over $Na_2SO_4$. Concentration gave a white solid which was dried under vacuum for 3 h. This solid was dissolved in 140 ml boiling toluene and placed in a water bath at 80 °C and allowed to slowly cool to 23 °C. Further cooling at -20 °C overnight followed by filtration and drying afforded pure **32** (29.2 g, 88%) as white crystals.

**MP:** 114-115 °C

**$^1$H NMR** ($C_6D_6$, 300 MHz) δ 6.95-7,45 (m, 5 H), 4,83 (brs, 1 H), 4.51 (t, 1 H, *J* = 7.2), 4.2-4.0 (m, 2 H), 3.75-3.60 (m, 1 H), 2.77 (s, 3 H), 2.40 (m, 2 H), 2.06 (s, 3 H), 1.73 (m, 2 H), 1.22 (t, 3 H, *J* = 7.3), 0.9-1.1 (m, 6 H), 0.53 (d, 3 H, *J* = 6.7)




**33**

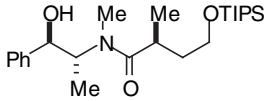
**2-Iodo-1-[(triisopropylsilyl)oxy]ethanol (33)**[2]**.** To a solution of 2-iodoethanol (24.8 g, 144 mmol, 1.00 equiv) in 70 ml DMF at 0 °C was added imidazole (12.8 g, 189 mmol, 1.30 equiv) followed by dropwise addition of TIPSCl (40.4 ml, 189 mmol, 1.30 equiv). After 2 h, the product separates from the DMF to give a heterogeneous mixture. The product was separated

[2] Myers, A. G.; Yang, B. H.; Chen, H.; McKinstry, l.; Kopecky, D. J.; Gleason, J. l. *J. Am. Chem. Soc.* **1997**, *119*, 6496.

and purified by passage through a small plug of silica gel (pentane) to afford **33** (49.4 g, 99% yield).

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 3.89 (t, 2 H, *J* = 7.2), 3.21 (t, 2H, *J* = 7.2), 1.03-1.13 (m, 21H)

**IR** (thin film) 2942, 2857, 1123, 1094, 1068, 999, 717, 682, 659

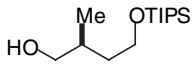



**34**

**(1*R*,2*R*)-*N*-(2-Hydroxy-1-methyl-2-phenyl-ethyl)-*N*,2-dimethyl-4-[(triisopropylsilyl)oxy]butanamide (34).** To a suspension of flame dried LiCl (23 g, 0.64 mol, 6.0 equiv) in 200 ml THF at 0 °C was added $^{i}Pr_2NH$ (32.1 ml, 229 mmol, 3.00 equiv) followed by BuLi (2.58 M in hexanes, 82.5 ml, 213 mmol, 2.80 equiv). The yellow slurry was stirred 15 min at 0 °C, 20 min at 23 °C, and then cooled to -78 °C. Amide **32** (24.7 g, 107 mmol, 1.40 equiv) in 350 ml THF was added via cannula and stirred 45 min. After warming to 0 °C for 15 min, 23 °C for 15 min, and recooling to -78 °C, 2-iodo-1-[(triisopropylsilyl)oxy]ethanol (**33**) (25.0 g, 76.2 mmol, 1.00 equiv) was added neat and the reaction mixture warmed to 0 °C for 18 h. The reaction was quenched by the addition of sat. aq. $NH_4Cl$ (200 ml) and extracted with EtOAc (2 x 300 ml). The combined organic solutions were washed with brine (400 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (4:1 hexanes/EtOAc) gave **34** (29.9 g, 93% yield) as a thick oil.[2]

**$^1$H NMR** ($CDCl_3$, 300 MHz) (7:1 rotamer ratio, * denotes minor rotamer peak), δ 7.31 (d, 2 H, *J* = 7.4), 7.25* (d, 2 H, *J* = 7.4), 7.03-7.22 (m, 3 H), 4.55 (t, 1 H, *J* = 7.3), 4.14-4.38 (m, 1H), 3.97-4.07* (m, 1 H), 3.78* (t, 2 H, *J* = 5.8), 3.43-3.61 (m, 2 H), 2.80-2.92 (m, 1 H), 2.79* (s, 3 H), 2.47 (s, 3 H), 1.90-2.02 (m, 1 H), 1.43-1.57 (m, 1 H), 0.97-1.17 (m, 27 H), 0.63 (d, 3 H, *J* = 7.66)

**IR** (thin film) 2942, 2866, 1621, 1463, 1105, 701, 680, 658




**35**

**(2*S*)-Methyl-4-(triisopropyl-silanyloxy)-butan-1-ol (35).** To a solution of $^{i}Pr_2NH$ (60.5 ml, 433 mmol, 4.20 equiv) in 300 ml THF at 0 °C was added BuLi (2.46 M in hexanes, 167 ml, 412 mmol, 4.00 equiv) and the yellow solution warmed to 23 °C for 10 min before recooling to 0 °C. Ammonia-borane complex (90%, 15.0 g, 433 mmol, 4.2 equiv) was added as a solid in portions to give a white slurry which was stirred at 23 °C for 1 h. Amide **34** (43.4 g, 103 mmol, 1.00 equiv) in 300 ml THF was added to the reaction mixture at 0 °C and warmed to 23 °C for 2 h. The mixture was recooled to 0 °C and carefully quenched with 650 ml 2 N HCl and extracted with $Et_2O$ (3 x 500 ml). The combined organic solutions were washed with 1.5 M HCl (500 ml) and brine (500 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (4:1 hexanes/EtOAc) provided **35** (26.4 g, 99%) as a colorless oil.

**Optical Rotation:** $[\alpha]_D^{29}$ (c 1.785, $CHCl_3$) = –6.8

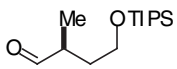
**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 3.86-3.80 (m, 1 H), 3.76-3.69 (m, 1 H), 3.55-3.48 (m, 1 H), 3.44-3.37 (m, 1 H), 3.16 (dd, 1 H, *J* = 7.6, 5.1), 1.87-1.77 (m, 1 H), 1.63-1.53 (m, 2 H), 1.17-1.03 (m, 21 H), 0.91 (d, 3 H, *J* = 6.6)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 68.3, 62.1, 37.8, 34.7, 17.9, 17.5, 11.9

**IR** (thin film) 3354, 2943, 2867, 1463, 1384, 1101, 1071, 1043, 1012, 997, 830, 737, 680, 658

**EI-MS:** 243.2 (M-H)

**Anal. Calc'd** for ($C_{14}H_{32}O_2Si$) C, 64.55%; H, 12.38%; found C, 64.71%; H, 12.08%




**(2*S*)-Methyl-4-(triisopropyl-silanyloxy)-butyraldehyde**. Prior to use, NMO (15.5 g, 132 mmol, 1.50 equiv) was dried by azeotropic distallation with toluene and further dried under vacuum for 2 h. The dry NMO was dissolved in 450 ml $CH_2Cl_2$ and 4Å molecular sieves (22 g) and alcohol **35** (23.0 g,

88.8 mmol) were added. The mixture stirred was stirred 20 min at 23 °C before tetrapropylammonium perruthenate (TPAP) (1.0 g, 3.0 mol %) was added in portions as a solid to give a red suspension. After 1.5 h, the reaction mixture was diluted with 1.2 l pentane, filtered over a short column of silica gel, and the product eluted with 2:1 pentane/ether (1 l) to provide the aldehyde (20.1 g, 88 %) as a slightly colored oil.

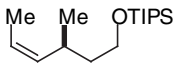
**Optical Rotation:** $[\alpha]_D^{23}$ (c 1.225, $CHCl_3$) = +16.9

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 9.66 (s, 1 H), 3.82-3.68 (m, 2 H), 2.58-2.51 (m, 1 H), 2.03-1.92 (m, 1 H), 1.67-1.57 (m, 1 H), 1.11 (d, 3 H), 1.05-0.99 (m, 21 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 205.0, 60.5, 43.4, 33.8, 17.9, 13.1, 11.8

**IR** (thin film) 2941, 2866, 2713, 1729, 1460, 1382, 1248, 1105, 882

**Anal. Calc'd** for ($C_{14}H_{30}O_2Si$) C, 65.06%; H 11.70%; found C, 64.89%; H, 11.56%




**36**

**Triisopropyl-(3*S*-methyl-hex-(4*Z*)-enyloxy)-silane (36).** A suspension of ethyl triphenylphosphonium iodide (55.0 g, 131 mmol. 1.80 equiv) in 600 ml THF was cooled to 0 °C and $NaNH_2$ (4.25 g, 109 mmol, 1.50 equiv) added as a solid in portions over 5 min. After 30 min, the cooling bath was removed, the reaction warmed to 23 °C for 6 h to give a dark red slurry. This mixture was cooled to –20 °C and the aldehyde (18.7 g, 72.8 mmol, 1.00 equiv) was added in 200 ml THF via cannula. After 30 min at this temperature, the reaction was allowed to warm to 23 °C and stirred for 10 h. The reaction was quenched by addition of MeOH (5 ml) and the resulting pale yellow mixture stirred 20 min before dilution with pentane (1 l). Filtration through a short column of silica gel and elution with 2:1 pentane/$Et_2O$ (1.2 l) provided a white sludge. Dilution with pentane (400 ml) and filtration followed by washing with additional pentane (300 ml) gave olefin **36** (18.5 g, 95%) as a pale liquid. 93:7 *cis:trans* ratio as measured by $^1$H NMR (*cis* methyne, 2.64 ppm; *trans* methyne, 2.23 ppm)..

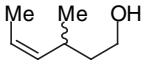
**Optical Rotation:** $[\alpha]_D^{29}$ (c 0.675, $CHCl_3$) = +5.9

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.42-5.34 (m, 1 H), 5.19-5.11 (m, 1 H), 3.71-3.59 (m, 2 H), 2.70-2.64 (m, 1 H), 1.61 (d, 3 H, *J* = 6.7), 1.63-1.59 (m, 1 H), 1.56-1.47 (m, 1 H), 1.12-0.99 (m, 21 H), 0.96 (d, 2 H, *J* = 6.7)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 136.7, 122.6, 61.5, 40.5, 27.7, 21.1, 20.9, 18.0, 12.9, 12.0

**IR** (thin film) 2943, 2867, 1462, 1831, 1104, 1012, 995, 882

**HRMS** (FAB) calc'd for $(C_{13}H_{27}OSi)^+$ [M-$^i$Pr], 227.1831; found, 227.1834

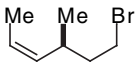



**(+/-)-3-Methyl-hex-4-en-ol**. To a solution of 3-methyl-butyrolactone (2.00 g, 20.0 mmol) in 150 ml $CH_2Cl_2$ at -78 °C was added DIBAL-H (1.0 M in $CH_2Cl_2$, 30 ml, 30 mmol, 1.5 equiv) dropwise over 15 min. After 4 h, the reaction was quenched with MeOH (2 ml), poured onto sat. aq. sodium potassium tartrate (120 ml), and stirred 10 h at rt. The mixture was extracted with $CH_2Cl_2$ (2 x 100 ml). The combined organic solutions were washed with brine (100 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure to afford the lactol.

To a suspension of $NaNH_2$ (1.95 g, 50.0 mmol, 2.50 equiv) in 200 ml THF at 0 °C was added ethyltriphenylphosphonium iodide (23.4 g, 56 mmol, 2.80 equiv) in portions over 10 min. The off-white mixture was warmed to 23 °C and stirred 3 h to give a red slurry. After cooling to 0 °C, the lactol was added in 30 ml THF over 3 min. The reaction was stirred 5 h at 23 °C before quenching with MeOH (5 ml). The mixture was filtered over celite, the filter cake washed with $Et_2O$, and the filtrate concentrated under reduced pressure. The residue was diluted with $Et_2O$ (200 ml), washed with brine (100 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (4:1 hexanes/EtOAc) gave 3-methyl-hex-4-en-ol (1.47 g, 68%) as a clear liquid.

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.4 (dt, 1 H, *J* = 9.0, 6.0), 5.15 (t, 1 H, *J* = 9.0), 3.60 (t, 2 H, *J* = 6.9), 2.53-2.62 (m, 1 H), 1.60 (d, 3 H, *J* = 6.0), 1.42-1.49 (m, 2 H), 1.25 (br s, 1 H, OH), 0.95 (d, 3 H, *J* = 7.5)

Other spectral characteristics were identical to those previously reported.[3]




**59**

**6-Bromo-(4*S*)-methyl-hex-(2*Z*)-ene (37).** To a solution of $PPh_3$ (10.4 g, 39.6 mmol, 1.20 equiv) in 100 ml $CH_2Cl_2$ at 0 °C was added $Br_2$ (2.04 ml, 29.6 mmol, 1.20 equiv) and the mixture stirred 25 min to give a yellow slurry to which $ZnBr_2$ (370 mg, 1.65 mmol, 0.05 equiv) was added. After an additional 20 min at 0 °C, silyl ether **36** (8.94 g, 33.0 mmol, 1.00 equiv) in 60 ml $CH_2Cl_2$ was added via cannula and the solution gradually became clear and colorless upon stirring for 2 h at rt. The reaction solution was washed with $H_2O$ (2 x 90 ml) and brine (90 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure (5 °C) to give a white solid which was washed with pentane (250 ml). This solution was concentrated under reduced pressure and the resulting liquid purified by short path vacuum distillation to afford bromide **37** (5.08 g, 88%) as a clear, volatile liquid.

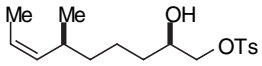
**Optical Rotation:** $[\alpha]_D^{25}$ (c 1.095, pentane) = + 48.1

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.52-5.42 (m, 1 H), 5.12-5.03 (m, 1 H), 3.44-3.27 (m, 2 H), 2.74-2.69 (m, 1 H), 1.93-1.81 (m, 1 H), 1.78-1.67 (m, 1 H), 1.64 (d, 3 H, *J* = 6.9), 0.97 (d, 3 H, *J* = 7.1)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 134.9, 124.2, 40.2, 32.2, 30.0, 20.7, 13.1

**IR** (thin film) 3004, 2958, 2873, 1449, 1257, 1213, 1048, 957, 724, 650

**HRMS** (FAB) calc'd for $(C_7H_{13}Br)^+$, 176.0201; found, 176.0203




**40**

**(2*R*, 6*S*)–Toluene-4-sulfonic acid 2-hydroxy-6-methyl-non-(7*Z*)-enyl ester (40).** To flame dried Mg (turnings, 2.4 g, 0.010 mol, 9.0 equiv) in a 100 ml round bottom flask equipped with a reflux condenser and a stir bar was added 8 ml $Et_2O$. To this suspension was added 1,2-dibromoethane (50 µl) without stirring and heated gently with a heat gun. An additional portion of 1,2-dibromoethane (50 µl) was added and heated gently until vigorous reaction had

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[3] Reitz, A. B,; Nortey, S. O.; Maryanoff, B. E.; Liotta, D.; Monaham, R. *J. Org. Chem.* **1987,** *52,* 4191.

begun, at which point magnetic stirring was started. When the exotherm had subsided, bromide **37** (2.50 g, 12.8 mmol, 1.00 equiv) in 8 ml $Et_2O$ was added slowly until the vigorous reaction had begun. An additional portion of $Et_2O$ (8 ml) was added, followed by dropwise addition of the remaining bromide solution. The resulting mixture was warmed to reflux for 2 h, cooled to rt, and diluted with $Et_2O$ (20 ml) to give a 0.3 M solution of the Grignard reagent.

In a separate reaction flask, (*R*)-tosyl-glycidol **39** ( 2.92 g, 12.8 mmol, 1.00 equiv) in 80 ml $Et_2O$ was cooled to –78 °C and $Li_2CuCl_4$ (0.1 M in THF, 10 ml, 1 mmol, 0.1 equiv) added to give an orange suspension. The solution of Grignard reagent prepared above (0.30 M in $Et_2O$, 43 ml, 13 mmol, 1.0 equiv) was added via syringe and the mixture stirred 2 h at –78 °. The reaction was quenched with sat. aq. $NH_4Cl$ and the resulting mixture warmed to rt and stirred 20 min to give two clear layers. The aqueous phase was extracted with $Et_2O$ (2 x 60 ml) and the combined organic solutions washed with brine (70 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (3:1 hex/EtOAc) to give tosylate **40** (1.72 g, 43% yield).

**Optical Rotation:** $[\alpha]_D^{26}$ (c 0.806, $CHCl_3$) = –12.1

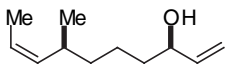
**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 7.80 (d, 2 H, *J* = 8.1), 7.35 (d, 2 H, *J* = 8.1), 5.41-5.29 (m, 1 H), 5.14-5.06 (m, 1 H), 4.02 (dd, 1 H, *J* = 9.7, 2.8), 3.88 (dd, 1 H, *J* = 6.9, 9.7), 3.90-3.81 (m, 1 H), 2.45 (s, 3 H), 2.44-2.37 (m, 1 H), 2.06 (brs, 1 H, OH), 1.57 (dd, 3 H, *J* = 6.9, 1.5), 1.46-1.10 (m, 6 H), 0.90 (d, 3 H, *J* = 6.5)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 145.3, 137.1, 133.1, 130.2, 128.2, 122.8, 74.1, 69.6, 37.3, 32.9, 31.2, 23.2, 21.7, 21.1, 13.0

**IR** (thin film) 3535, 3005, 2926, 2867, 1598, 1454, 1360, 1181, 1177, 1097, 967, 832, 814, 668

**HRMS** (MALDI) calc'd for $(C_{17}H_{26}O_4SNa)^+$, 349.1449; found, 349.1438

**Anal. Calc'd** for ($C_{17}H_{26}O_4S$) C, 62.55%; H 8.03%; found C, 62.70%; H, 8.11%




**24**

**(7*S*)-Methyl-deca-1,(8*Z*)-dien-(3*R*)-ol (24).** To a suspension of trimethylsulfonium triflate (6.28 g, 27.8 mmol, 5.00 equiv) in 150 ml $Et_2O$ at –40 °C was added BuLi (2.5 M in hexanes,

10.9 ml, 27.2 mmol, 4.90 equiv) and the reaction stirred 10 min. Tosylate **40** (1.81 g, 5.60 mmol, 1.00 equiv) in 50 ml $Et_2O$ was added via cannula and the reaction warmed to –18 °C. The white slurry was stirred 12 h at this temperature, quenched by the addition of MeOH (1 ml), and stirred 10 min at rt. The mixture was filtered over a bed of Celite and the product eluted with 6:1 hexanes/EtOAc (400 ml). Purification by flash chromatography (6:1 hexanes/EtOAc) provided **24** (810 mg, 85%) as a clear liquid.

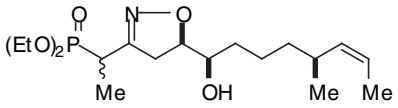
**Optical Rotation:** $[\alpha]_D^{28}$ (c 1.167, $CHCl_3$) = –10.0

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.86 (ddt, 1 H, *J* = 16.7, 10.4, 6.3), 5.43-5.31 (m, 1 H), 5.26-5.08 (m, 3H), 4.17-4.03 (m, 1 H), 2.51-2.42 (m, 1 H), 1.59 (dd, 3 H, *J* = 6.7, 0.9), 1.57-1.21 (m, 6 H), 0.92 (d, 3 H, *J* = 6.6)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 141.0, 136.8, 122.1, 114.3, 73.0, 37..1, 36.9, 31.0, 23.0, 20.8, 12.8

**IR** (thin film) 3355, 2928, 2863, 1453, 992, 922, 722

**HRMS** (FAB) calc'd for ($C_{11}H_{18}$, M-$H_2O$), 150.1409; found, 150.1410




**23**

**(1*R*, 5*S*)-{1-[5-(Hydroxy-5-methyl-oct-(6*Z*)-enyl)-4,(5*R*)-dihydroisoxazol-3-yl]-ethyl}-phosphonic acid diethyl ester (44)**. To a solution of allylic alcohol **24** (1.12 g, 6.66 mmol, 1.00 equiv) and $^i$PrOH (1.72, 22.0 mmol, 3.30 equiv) in 250 ml $CH_2Cl_2$ at 0 °C was added EtMgBr (3.0 M in $Et_2O$, 6.9 ml, 20 mmol, 3.0 equiv) to give a cloudy suspension. Upon stirring 20 min at 0 °C, a clear solution is formed to which hydroximinoyl chloride **18** (1.79 g, 7.33 mmol, 1.10 equiv) was added in 30 ml $CH_2Cl_2$ and the slighly colored solution allowed to warm to rt. After 18 h, the reaction was quenched by the addition of sat. aq. $NH_4Cl$ (100 ml) and extracted with EtOAc (3 x 90 ml). The combined organic solutions were washed with brine (150 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (1:1 hexanes/EtOAc – 100% EtOAc) afforded isoxazoline **23** (1.94 g, 76% yield) and recovered allylic alcohol **424**(0.33 g, 24%) as clear oils.

**Optical Rotation:** $[\alpha]_D^{27}$ (c 0.840, $CHCl_3$) = –69.8

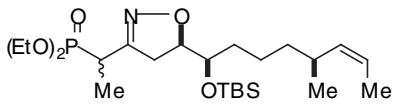
**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.40-5.30 (m, 1 H), 5.17-5.10 (m, 1 H), 4.53-4.44 (m, 1 H), 4.19-4.09 (m, 4 H), 3.51-3.43 (m, 1 H), 3.24-2.86 (m, 3 H), 1.59 (dd, 3 H, *J* = 6.5, 1.5), 1.55-1.20 (m, 6 H), 1.47 (d, 1.5 H [0.5 $CH_3$], *J* = 7.1), 1.42 (d, 1.5 H [0.5 $CH_3$], *J* = 7.1), 1.33 (t, 6 H, *J* = 7.1), 0.92 (d, 3 H, *J* = 6.5) (includes both diastereomers)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 157.3, 137.2, 122.6, 83.4, 73.2, 73.1, 62.7 (t, *J* = 7.5), 38.1, 37.5, 35.6, 33.2, 31.4, 31.2, 23.5, 21.1, 16.5, 16. 4, 13.5, 13.0, 12.3 (includes both diastereomers)

**IR** (thin layer) 3407, 2986, 2934, 2866, 1465, 1251, 1022, 966, 800

**HRMS** (MALDI) calc'd for $(C_{18}H_{34}NO_5PNa)^+$, 398.2072; found, 398.2072

**Anal. Calc'd** for ($C_{18}H_{34}NO_5P$) C, 57.58%; H, 9.13%; N, 3.73; found C, 57.32%; H, 9.17%; N, 3.71%




**43**

**(1-{(5*R*)-[(1*R*)-(*tert*-Butyl-dimethyl-silanyloxy)-(5*S*)-methyl-oct-(6*Z*)-enyl]-4,(5*R*)-dihydroisoxazol-3-yl}-ethyl)-phosphonic acid diethyl ester (43).** To **23**(2.90 g, 7.67 mmol, 1.00 equiv) in 70 ml $CH_2Cl_2$ at 0° C was added $Et_2N^iPr$ (2.66 ml, 15.3 mmol, 2.00 equiv) followed by dropwise addition of TBSOTf (3.12 ml, 15.3 mmol, 2.00 equiv). After 25 min at 0° C, the reaction was quenched by careful addition of saturated, aqueous $NaHCO_3$ (30 ml) and stirred 10 min at rt. The aqueous phase was extracted with $CH_2Cl_2$ (3 x 50 ml) and the combined organic solutions were washed with brine (100 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (2:1 hexanes/EtOAc) afforded silyl ether **43** (3.25 g, 90% yield) as a clear, colorless oil.

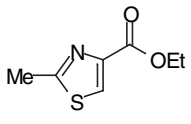
**Optical Rotation:** $[\alpha]_D^{25}$ (c 1.650, $CHCl_3$) = –36.8

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.40-5.32 (m, 1 H), 5.11 (tt, 1 H, *J* = 9.9, 0.8), 4.60-4.51 (m, 1 H), 4.16-4.11 (m, 4 H), 3.72-3.67 (m, 1 H), 3.18-2.93 (m, 3 H), 2.47-2.41 (m, 1 H), 1.59 (dd, 3H, *J* = 6.8, 1.7), 1.47 (d, 1.5 H [0.5 $CH_3$], *J* = 7.3), 1.42 (d, 1.5 H [0.5 $CH_3$], *J* = 7.3), 1.49-1.23 (m, 6 H), 1.33 (t, 6 H, *J* = 7.1), 0.91 (d, 3 H, *J* = 6.5), 0.88 (s, 9 H), 0.08 (s, 3 H), 0.05 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 156.1, 136.9, 122.3, 122.3, 83.0, 72.8, 62.6 (t, *J* = 7.5), 37.6, 36.6, 36.5, 33.1, 31.6, 21.3, 25.8, 23.6,21.1, 18.1, 16.5, 16.4, 13.0, 12.4, 12.3, -4.3, -4.7 (includes both diastereomers)

**IR** (thin film) 2930, 2857, 1462, 1390, 1255, 1100, 1054, 1024, 965, 837, 777

**HRMS** (FAB) calc'd for $(C_{24}H_{48}NO_5PSiH)^+$, 490.3118; found, 490.3115

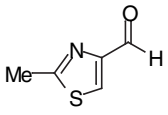



**Ethyl 4-methyl-thiazol-2-carboxylic acid ester.**[4] To a solution of thioacetamide (15.4 g, 205 mmol, 1.03 equiv) in 110 ml EtOH was added ethyl bromopyruvate (90%, 43.3 g, 0.200 mol, 1.00 equiv) in portions over 10 min. After a short induction period, the reaction warms up and a bright yellow solution forms which is stirred 12 h at 23 °C. The reaction was poured onto 2.5 *N* HCl (150 ml), stirred 30 min, and washed with $Et_2O$ (3 x 75 ml). The aqueous solution was cautiously neutralized with excess, solid $NaHCO_3$ and extracted with $CH_2Cl_2$ (3 x 100 ml). The $CH_2Cl_2$ solutions were washed with brine, dried over $Na_2SO_4$, and concentrated under reduced pressure to give a yellow solid. Purification by flash chromatography (2:1 hexanes/EtOAc) followed by recrystallization from pentane/$Et_2O$ (8:1) gave ethyl 4-methyl-thiazol-2-carboxylic acid (31.1 g, 91%) as white needles.

**MP:** 58 °C

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 8.04 (s, 1H), 4.42 (q, 2 H, *J* = 7.1), 2.77 (s, 3 H), 1.40 (t, 3 H, *J* = 7.1)

**Anal. Calc'd** for ($C_7H_9NO_2S$) C, 49.10%; H, 5.30%; N, 8.18%; found C, 49.23%; H, 5.49%; N, 8.11%




**44**

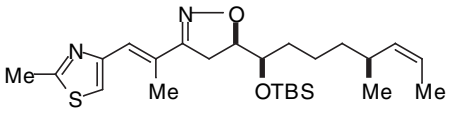
[4] Jones, E. R. H.; Robinson, F. A.; Strachan, M. N. *J. Am. Chem. Soc.* **1946**, *58*, 87.

**4-Methyl-thiazole-2-carboxaldehyde (44).**[5] To a solution of ethyl 4-methyl-thiazol-2-carboxylic acid ester (20.0 g, 117 mmol, 1.00 equiv) in 1.1 l $CH_2Cl_2$ from a freshly opened bottle at –78° C was added DIBAL-H (1.00 M in $CH_2Cl_2$, 176 mmol, 1.50 equiv) via an addition funnel over 1 h. After the addition was completed, the clear solution was stirred at –78 °C for 2 h and the progress of the reaction monitored by $^1$H NMR. An additional portion of DIBAL-H (1.00 M in $CH_2Cl_2$, 75.0 ml, 75.0 mmol) was added over 30 min and the clear solution stirred 3 h. The reaction was quenched by cautious addition of MeOH (5 ml) at -78 °C and poured onto a saturated aqueous solution of sodium potassium tartrate (700 ml). The biphasic mixture was rapidly stirred overnight whereupon two clear, colorless layers formed. The aqueous layer was withdrawn and extracted with $CH_2Cl_2$ (2 x 400 ml). The combined organic solutions were washed with brine (500 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure to give **44** (13.9 g, 94 % yield) as a yellow powder. As necessary, this product was recrystallized from pentane/$Et_2O$.

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 10.00 (s, 1H), 8.05 (s, 1H) 7.33 (s, 1H), 2.81 (s, 3H)

**IR** (thin film) 3073, 1698, 1435, 1338, 1132

**Anal. Calc'd** for ($C_5H_5NOS$) C, 47.23%; H, 3.96%; N, 11.01%; found C, 47.43%; H, 4.17%; N, 10.98%




**45**

**(5*R*)-[(1*R*)-(*tert*-Butyl-dimethyl-silanyloxy)-(5*S*)-methyl-oct-(6*Z*)-enyl]-3-[1-methyl-2-(2-methyl-thiazol-4-yl)-vinyl]-4,(5*R*)-dihydro-isoxazole (45).** To phosphonate **43** (3.23 g, 6.61 mmol, 1.00 equiv) in 40 ml THF at -78 °C was added freshly prepared LHMDS (0.50 M in THF, 24 ml, 12 mmol, 1.8 equiv) to give a yellow solution. After 20 min at this temperature, aldehyde **44** (1.85 g, 14.5 mmol, 2.00 equiv) in 15 ml THF was added and the reaction stirred 1 h at -78 °C and then warmed slowly to rt. After 4 h at this temperature, the reaction was quenched by the addition of sat. aq. $NEt_3$ (50 ml). The mixture was extracted with EtOAc (3 x

[5] Baganz, H.; Rüger, J. *Chem. Ber.* **1968**, *101*, 3872.

70 ml) and the combined organic solutions washed with brine (100 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (7:1 hexanes/EtOAc) afforded *trans*-olefin **45** (2.60 g, 85% yield) and the *cis*-isomer (265 mg, 9% yield).

**Optical Rotation:** $[\alpha]_D^{23}$ (c 1.370, $CHCl_3$) = –78.8

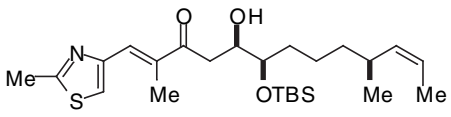
**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 7.15 (s, 1 H), 6.71 (s, 1H), 5.39-5.32 (m, 1 H), 5.13-5.05 (m, 1 H), 4.67 (ddd, 1 H, *J* = 10.3, 8.4, 5.3), 3.75-3.70 (m, 1 H), 3.17-3.02 (m, 2H), 2.72 (s, 3H), 2.51-2.28 (m, 1H), 2.35 (s, 3H), 1.59 (dd, 3H, *J* = 6.8, 1.9), 1.45-1.25 (m, 6H), 0.91 (d, 3H, *J* = 6.5), 0.87 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 165.0, 160.0, 152.0, 129.9, 125.8, 122.3, 122.2, 118.0, 83.6, 72.8, 37.3, 34.8, 31.4, 25.6, 23.4, 20.9, 18.9, 17.9, 14.8, 12.8, -4.6, -4.8

**IR** (thin film) 3377, 2927, 2855, 1594, 1462, 1368, 1225, 1102, 836, 776

**HRMS** (FAB) calc'd for $(C_{25}H_{42}N_2O_2SSiH)^+$, 463.2814; found, 463.2812

**Anal. Calc'd** for ($C_{25}H_{42}N_2O_2SSi$) C, 64.89%; H, 9.15%; N, 6.05; found C, 64.88%; H, 9.37; N, 5.99




**46**

**(6*R*)-(*tert*-Butyl-dimethyl-silanyloxy)-(5*R*)-hydroxy-2,(10*S*)-dimethyl-1-(2-methyl-thiazol-4-yl)-trideca-(1*E*,11*Z*)-dien-3-one (46).** To isoxazoline **67** (154 mg, 0.334 mmol, 1.00 equiv) in 12 ml degassed THF at 0 °C was added $SmI_2$ (0.1 M in THF, 12 ml, 1.2 mmol, 3.6 equiv) slowly, maintaining a dark blue-green color throughout the reaction. After the addition was complete, additional $SmI_2$ (1 ml) was added to the dark blue solution was stirred 20 min at 0 °C. After quenching the reaction with $O_2$ to give a bright yellow solution, $H_2O$ (8 ml) and $B(OH)_3$ (0.3 g) were added and the mixture was stirred 30 min at rt. Following the addition of $Et_2O$ (10 ml) and careful separation of the layers to avoid an emulsion, the aqueous phase was extracted with $Et_2O$ (3 x 15 ml). The combined organic solutions were washed with brine (30

ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (6:1 hexanes/EtOAc) afforded ketone **46** (114 mg, 73%) as a colorless oil.

**Optical Rotation:** $[\alpha]_D^{25}$ (c 0.924, $CHCl_3$) = +35.6

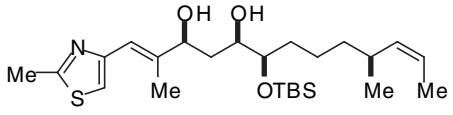
**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 7.53 (s, 1 H), 7.36 (s, 1 H), 5.41-5.35 (m, 1 H), 5.14 (tt, 1 H, *J* = 9.5, 1.7), 4.13-4.08 (m, 1 H), 3.72-3.67 (m, 1 H), 3.03 (dd, 1 H, *J* = 16.8, 4.0), 2.91 (dd, 1 H, *J* = 16.8, 8.4), 2.86 (d, 1 H, *J* = 5.6, OH), 2.76 (s, 3 H), 2.64-2.50 (m, 1 H), 2.25 (s, 3 H), 1.60 (dd, 3 H, *J* = 6.8, 1.9), 1.44-1.18 (m, 6 H), 0.93 (d, 3 H, *J* = 6.9), 0.89 (s, 9 H), 0.8 (s, 3 H), 0.5 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 202.3, 165.5, 151.8, 137.4, 137.1, 131.6, 122.3, 121.8, 74.3, 70.1, 39.9, 37.7, 37.3, 32.7, 31.3, 25.9, 23.7, 21.1, 19.3, 18.1, 13.3, -4.3, -4.4

**IR** (thin film) 3497, 2946, 2928, 2854, 1654. 1626. 1460, 1255, 1182, 1081, 836

**HRMS** (MALDI) calc'd for $(C_{25}H_{43}NO_3SSiNa)^+$, 488.2631; found, 488.2604

**Anal. Calc'd** for ($C_{25}H_{43}NO_3SSi$) C, 64.47%; H, 9.30%; N, 3.01; found C, 64.42%; H, 9.44; N, 3.15




**49**

**(6*R*)-(*tert*-Butyl-dimethyl-silanyloxy)-2,(10*S*)-dimethyl-1-(2-methyl-thiazol-4-yl)-trideca-(1*E*,11*Z*)-diene-(3*S*,5*R*)-diol (49).** A solution of $BEt_3$ (1.0 M in THF, 0.040 ,l, 0.40 mmol, 1.1 equiv) in 3.5 ml THF and 1.0 ml MeOH at rt was stirred for 20 min before being cooled to –78 °C. Ketone **46** (171 mg, 0.369 mmol, 1.00 equiv) in 3.0 ml THF was added via cannula and stirred 1 h at –78 °C before $NaBH_4$ (0.100 g, 2.70 mmol, 6.75 equiv) was added as a solid in two portions. After 4 h and 6 h at –78 °C, additional $NaBH_4$ (50 mg) was added and after 7 h the reaction was quenched by addition of sat. aq. $NH_4Cl$ (10 ml). The mixture was extracted with EtOAc (3 x 15 ml), and the combined organic solutions were washed with brine (30 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (3:2 hexanes/EtOAc) provided diol **49** (157 mg, 91% yield) as a clear, colorless oil.

**Optical Rotation:** $[\alpha]_D^{23}$ (c 1.453, $CHCl_3$) = + 3.2

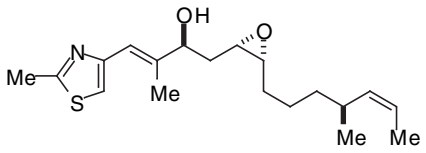
**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 6.95 (s, 1 H), 6.59 (s, 1 H), 5.43-5.26 (m, 1 H), 5.16-5.07 (m, 1 H), 4.41 (t, 1 H, *J* = 6.0), 3.81-3.74 (m, 1 H), 3.64 (d, 1 H, *J* = 6.4, OH), 3.55-3.48 (m, 1 H), 2.86 (d, 1 H, *J* = 5.0, OH), 2.71 (s, 1 H), 2.50-2.39 (m, 1 H), 2.05 (s, 3 H), 1.72-1.67 (m, 1 H), 1.65-1.56 (m, 2 H), 1.59 (dd, 3 H, *J* = 6.8, 1.9), 1.43-1.15 (m, 5 H), 0.92 (d, 3 H, *J* = 6.9), 0.90 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.5, 153.0, 141.8, 137.0, 122.4, 118.7, 115.6, 78.1, 75.4, 74.2, 38.3, 37.7, 33.2, 31.2, 25.9, 23.1, 21.2, 19.2, 18.1, 14.4, 13.0, -4.2, -4.5

**IR** (thin film) 3350, 2954, 2879, 2850, 1510, 1439, 1256, 1086, 836

**HRMS** (MALDI) calc'd for $(C_{25}H_{45}NO_3SSiNa)^+$, 490.2787; found, 490.2778

**Anal. Calc'd** for ($C_{25}H_{43}NO_3SSi$) C, 64.19%; H, 9.70%; N, 2.99%; found C, 64.26%; H, 9.68; N, 2.85%




**25**

**3-Methyl-1-[(2*S*,3*R*)-3-((4*S*)-methyl-hept-(5*E*)-enyl)-oxiranyl]-4-(2-methyl-thiazol-4-yl)-but-(3*Z*)-en-(2*S*)-ol (21).** To diol **49** (101 mg, 0.216 mmol, 1.00 equiv) in 5 ml $CH_2Cl_2$ at 0 °C was added $NEt_3$ (123 µl, 0.864 mmol, 4.00 equiv) followed by $SOCl_2$ (0.50 M in $CH_2Cl_2$, 0.65 ml, 0.33 mmol, 1.5 equiv). The resulting yellow solution was stirred 20 min at 0 °C, quenched with $H_2O$ (5 ml), and extracted with $CH_2Cl_2$ (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure to give a yellow-brown oil which was used without further purification.

To the unpurified cyclic sulfite (0.216 mmol, 1.00 equiv) in 6 ml THF at rt was added $Bu_4NF•3H_2O$ (273 mg, 0.864 mmol, 4.00 equiv) as a solid. The dark yellow solution was heated to reflux for 6 h, cooled to rt, diluted with $H_2O$ (6 ml), and extracted with $Et_2O$ (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and

concentrated under reduced pressure. Purification by flash chromatography (1:1 hexanes/EtOAc) provided epoxide **21** (58 mg, 80% yield for two steps).

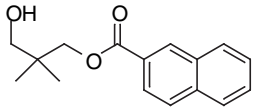
**Optical Rotation:** $[\alpha]_D^{28}$ (c 0.704, $CHCl_3$) = –11.4

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 6.95 (s, 1 H), 6.14 (s, 1 H), 5.44-5.28 (m, 1 H), 5.18-5.09 (m, 1 H), 4.44-3.35 (m, 1 H), 3.17 (ddd, 1 H, *J* = 4.1, 8.1, 4.1), 2.99-2.92 (m, 1 H), 2.71 (s, 3 H), 2.52-2.40 (m, 1 H), 2.20 (d, 1 H, *J* = 3.7, OH), 2.06 (s, 3 H), 1.93 (ddd, 1 H, *J* = 14.3, 8.4, 4.1), 1.70 (ddd, 1 H, *J* = 14.3, 7.8, 4.1), 1.60 (dd, 3 H, *J* = 6.9, 1.6), 1.58-1.09 (m, 6 H), 0.93 (d, 3 H, *J* = 6.5)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 152.7, 141.8, 136.9, 122.5, 118.9, 115.8, 110.0, 75.4, 57.1, 54.3, 37.3, 33.5, 31.3, 28.2, 24.4, 21.1, 19.2, 14.5, 13.0

**IR** (thin film) 3392, 2958, 2924, 2859, 1508, 1450, 1374, 1187, 1053, 967, 723

**HRMS** (MALDI) calc'd for $(C_{19}H_{29}NO_2SSiNa)^+$, 358.1817; found, 358.1807




**Naphthalene-2-carboxylic acid 3-hydroxy-2,2-dimethyl-propyl ester.** To neopentyl glycol (13.1 g, 0.126 mol, 8.00 equiv) in 75 ml $CH_2Cl_2$ at 0 °C was added $NEt_3$ (4.46 ml, 31.4 mmol, 2.00 equiv) followed by dropwise addition of 2-naphthoylchloride (3.00 g, 15.7 mmol, 1.00 equiv). When addition was complete, DMAP (0.1 g, 0.8 mmol, 0.05 equiv) was added and the slurry warmed slowly to rt to give a clear solution which was stirred 20 h at rt. The reaction was diluted with hexanes (150 ml) and washed with $H_2O$ (2 x 100 ml) and brine (100 ml) and dried over $Na_2SO_4$. Concentration gave a white solid which was recrystallized (hexanes) to give the mono-ester (3.56 g, 88% yield) as a white, crystalline solid.

**MP:** 71 °C

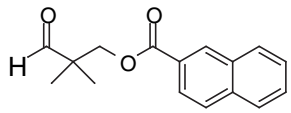
**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 8.56 (s, 1 H), 8.06 (dd, 1 H, *J* = 8.4, 1.7), 7.97 (d, 1 H, *J* = 7.8), 7.89 (d, 2 H, *J* = 8.4), 7.62-7.51 (m, 2 H), 4.26 (s, 2 H), 3.43 (s, 2 H), 1.06 (s, 6 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 167.4, 135.6, 132.5, 131.2, 129.4, 128.4, 128.3, 127.8, 127.2, 126.8, 125.2, 69.9, 68.3, 36.9, 21.7

**IR** (thin film) 3436, 3061, 2963, 2875, 1716, 1473, 1372, 1284, 1230, 1197, 1098, 778, 762

**EI-MS:** 258.1 $(M)^+$

**Anal. Calc'd** for ($C_{16}H_{18}O_3$) C, 74.40%; H, 7.02; found C, 74.20%; H, 7.14%



**57g**

**Naphthalene-2-carboxylic acid 2,2-dimethyl-3-oxo-propyl ester (57g)**. To the mono-ester (17.1 g, 67.0 mmol, 1.00 equiv) in 500 ml $CH_2Cl_2$ at rt was added NMO (9.41 g, 80.4 mmol, 1.20 equiv) and 4 Å molecular sieves (20 g). The mixture was stirred 1 h at rt before tetrapropyl ammonium perruthenate (TPAP) (0.70 g, 2.0 mmol, 0.03 equiv) was added in portions over 20 min. The resulting dark red slurry was stirred 30 min at rt, diluted with pentane (300 ml), filtered over a plug of silica and the product eluted with 1:1 pentane/$Et_2O$ (800 ml). Concentrate under reduced pressure gave a thick oil which was purified by flash chromatography (5:1 hexanes/EtOAc) to give the aldehyde **57g** (12.8 g, 75% yield) as a white solid.

**MP:** 51 °C

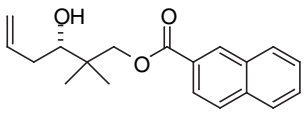
**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 9.69 (s, 1 H), 8.55 (s, 1 H), 8.00 (dd, 1 H, *J* = 8.4, 1.7), 7.95 (d, 1 H, *J* = 8.1), 7.87 (d, 2 H, *J* = 8.1), 7.62-7.51 (m, 2 H), 4.43 (s, 2 H), 3.43 (s, 2 H), 1.25 (s, 6 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 203.5, 166.4, 135.6, 132.5, 131.2, 129.4, 128.4, 128.3, 127.8, 126.9, 126.7, 125.1, 68.5, 46.7, 19.0

**IR** (thin film) 3061, 2973, 2713, 1720, 1471, 1368, 1284, 1228, 1196, 1130, 1097, 984, 779, 763

**EI-MS:** 256.1 $(M)^+$

**Anal. Calc'd** for ($C_{16}H_{16}O_3$) C, 74.98%; H, 6.29%; found C, 74.85%; H, 6.45%



**58g**

**Naphthalene-2-carboxylic acid (3*S*)-hydroxy-2,2-dimethyl-hex-5-enyl ester (58g).** To a suspension of $TiF_4$ (0.25 g, 2.0 mmol, 5.0 mol %) in 10 ml $CH_3CN$ was added (*S*)-BINOL (1.15 g, 4.00 mmol, 10.0 mol %) and the mixture stirred 15 min before the solvent was removed under reduced pressure. After 10 min at 1.0 torr, the residue was dissolved in 10 ml $CH_2Cl_2$ and cooled to 0 °C. To this solution was added allyltrimethylsilane (12.7 ml, 80.0 mmol, 2.00 equiv) and stirred 1 h to give a dark precipitate to which aldehyde **57g** (10.3 g, 40.0 mmol, 1.00 equiv) was added neat in two portion to give a dark red-orange solution. This solution was allowed to stir 5 days at 0 °C at which time analysis by $^1$H NMR showed the reaction to be complete . The reaction mixture was diluted with 2:1 pentane:ether (500 ml), filtered over silica gel and eluted with 2:1 pentane:$Et_2O$ (500 ml). Following rotary evaporation, the resulting residue was treated with 5:95:1.5 HF:MeCN:$H_2O$ (80 ml) for 0.5 h, dissolved in $Et_2O$ (200 ml), washed with 2 *N* NaOH (2 x 50 ml), brine (100 ml), dried over $Na_2SO_4$, and concentrated to give a yellow oil (11.65 g, 98% yield). Purification by crystallization from hexanes provided **58g** (8.30 g, 72% yield) as a white solid in 92% ee. (Determined by chiral HPLC analysis (Chiradex OD), 98:2 hexanes/iPrOH.

**Optical Rotation:** $[\alpha]_D^{25}$ (c 0.950, $CHCl_3$) = +11.9

**MP:** 46.5 °C

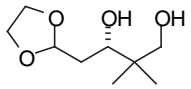
**$^1$H NMR** (300 MHz, $CDCl_3$) d 8.61 (s, 1H), 8.06 (dd, *J* = 8.7, 1.6, 1 H), 7.97 (d, *J* = 7.78, 1 H), 7.92 (d, *J* = 8.7, 1 H), 7.60-7.53 (m, 2 H), 5.97-5.83 (m, 1 H), 5.19 (d, *J* = 8.6, 1 H), 5.14 (s, 1 H), 4.48 (d, *J* = 10.9, 1 H), 4.13 (d, J = 10.9, 1 H), 3.59 (td, *J* = 8.4, 3.4, 1 H), 2.45-2.39 (m, 1 H), 2.20 (d, *J* = 3.4, 1 H), 2.17-2.12 (m, 1 H), 1.10 (s, 3H), 1.07 (s, 3H)

**$^{13}$C NMR** (75 MHz, $CDCl_3$): 167.0, 136.1, 135.6, 132.5, 131.1, 129.4, 128.3, 128.2, 127.8, 127.5, 126.7, 125.2, 118.0, 74.1, 71.2, 38.7, 36.2, 21.8, 19.4

**IR** (KBr) 3493, 3068, 2971, 2892, 1683, 1475, 1373, 1274, 1230, 1198, 905, 776

**EI-MS**: 298.1 $(M)^+$

**Anal**. **Calc'd.** for ($C_{19}H_{22}O_3$) C, 76.48%; H, 7.43%; found, C, 76.64%; H, 7.26%




**60**

**4-[1,3]Dioxolan-2-yl-2,2-dimethyl-butane-1,(3*S*)-diol (60).** Into a solution of **58g** (2.50 g, 8.38 mmol, 1.00 equiv) in 10:1 $CH_2Cl_2$/MeOH (80 ml) at –78 °C was bubbled a stream of $O_3$ in $O_2$ until TLC analysis indicated complete consumption of the starting mateiral. The reaction was purged with $O_2$ for 20 min before $Me_2S$ (5 ml) was added and the reaction warmed slowly to rt and stirred 6 h. The solution was concentrated under reduced pressure and dissolved in $C_6H_6$ (40 ml). Ethylene glycol (4 ml) and CSA (20 mg) were added and the mixture heated to reflux for 3 h. After cooling to rt, $NEt_3$ (1 ml) was added and solution concentrated under reduced pressure.

Unpurified acetal **59** (8.36 mmol, 1.0 0eq) was dissolved in THF (60 ml) and cooled to 0° C before $LiAlH_4$ (0.440 g, 11.5 mmol, 1.40 equiv) was added in portions. After 2 h at 0 °C, the reaction was quenched by cautious addition of EtOAc (3 ml) and $Na_2SO_4 \bullet 10H_2O$ (10 g) was added and the mixture stirred 1 h at rt. Following filtration and concentration under reduced pressure, the product was purified by flash chromatography (1:3 hexanes/EtOAc) to provide diol **60** (1.15 g, 73% yield) as a thick oil.

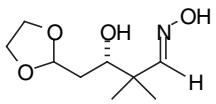
**Optical Rotation:** $[\alpha]_D^{25}$ (c 1.440, $CHCl_3$) = –10.9

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.06 (dd, 1 H, *J* = 5.6, 3.1), 4.07-3.80 (m, 5 H), 3.56-3.42 (m, 3 H, 1 OH), 3.18-3.09 (m, 1 H, OH), 1.96 (ddd, 1 H, *J* = 14.6, 3.1, 1.3), 1.77 (ddd, 1 H, *J* = 14.6, 10.6, 5.6), 0.90 (s, 3 H), 0.89 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 104.2, 75.3, 72.1, 65.1, 64.8, 38.0, 35.2, 22.4, 18.7

**IR** (thin film) 3412, 2957, 2881, 1474, 1412, 1137, 1076, 1037, 946, 880, 824

**Anal. Calc'd** for ($C_9H_{18}O_4$) C, 56.82%; H, 9.54%; found C, 56.61%; H, 9.61%



**62**

**4-[1,3]Dioxolan-2-yl-(3*S*)-hydroxy-2,2-dimethyl-butyraldehyde oxime (62).** To diol **60** (735 mg, 3.93 mmol, 1.00 equiv) in 35 ml $CH_2Cl_2$ at 0 °C was added TEMPO (13 mg, 0.080 mmol, 2.0 mol %) and KBr (47 mg, 0.39 mmol, 0.10 equiv). The mixture was vigourously stirred and NaOCl (approx. 1.5 M in $H_2O$, 4.0 ml, 5.9 mmol, 1.5 equiv) in 25 ml pH 8.6 buffer (0.5 M $NaHCO_3$/0.05 M $Na_2CO_3$) was added in portions. Additional NaOCl solution was added in portions until the reaction maintained a dark color and TLC analysis indicated the complete consumption of the starting material. The reaction was quenched by addition of MeOH (1 ml) and the aqueous phase extracted with $CH_2Cl_2$ (3 x 30 ml). The combined organic solutions were washed with brine (60 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure to provide aldehyde **61** which was used without further purification.

To the unpurified aldehyde (3.93 mmol, 1.00 equiv) in 30 ml EtOH was added $NH_2OH$•HCl (409 mg, 5.90 mmol, 1.50 equiv) in pyridine (4 ml). The resulting clear solution was stirred 2 h at rt, concentrated under reduced pressure, and azeotroped with cyclohexane (3 x 5 ml). To the resulting oil was added $H_2O$ (10 ml) and the mixture extracted with EtOAc (3 x 15 ml). The combined organic solutions were washed with brine (40 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (1:1 hexanes/EtOAc) afforded oxime **62** (663 mg, 84% yield for two steps) as a slightly yellow oil.

**Optical Rotation:** $[\alpha]_D^{31}$ (c 1.195, $CHCl_3$) = –8.3

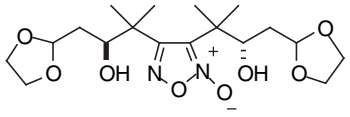
**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 8.65 (brs, 1 H, OH), 7.40 (s, 1 H), 5.04 (t, 1 H, *J* = 4.6), 4.02-3.75 (m, 5 H), 3.31 (brs, 1 H, OH), 1.89 (ddd, 1 H, *J* = 14.3, 4.1, 1.6), 1.72 (ddd, 1 H, *J* = 14.3, 10.6, 4.6), 1.09 (s, 3 H), 1.08 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 157.2, 103.7, 73.2, 65.0, 64.7, 41.0, 35.2, 22.1, 21.2

**IR** (thin film) 3392, 2972, 2892, 1413, 1301, 1215, 1136, 1081, 1035, 944, 827

**EI-MS:** 184.2 ($MH^+$–$H_2O$)

**Anal. Calc'd** for ($C_9H_{17}NO_4$) C, 53.19%; H, 8.43; found C, 53.04%; N, 6.89%; H, 8.40%; N, 6.93%



**63**

**3,4-Bis-(3-[1,3]dioxolan-2-yl-(2*S*)-hydroxy-1,1-dimethyl-propyl)-furazan-2-ol; compund with hydroxylamine (63)**. To oxime **62** (645 mg, 3.22 mmol, 1.00 equiv) in 32 ml $CH_2Cl_2$ at –78 °C was added $^t$BuOCl (365 µl, 3.22 mmol, 1.00 equiv) dropwise over 10 min. The reaction becomes quickly blue and was stirred 1.5 h at –78 °C before $NEt_3$ (550 µl, 3.86 mmol, 1.20 equiv) was added. The blue solution became instantly colorless and turned yellow-green upon warming to rt. Concentration under reduced pressure produced a white solid which was suspended in $Et_2O$, filtered over a bed of Celite, and the filtrate concentrated to give nitrile oxide **52** (618 mg, 97% yield) as a clear oil which was used without further purification. [**IR** (thin film) 2285]

The unpurified nitrile oxide (618 mg, 3.12 mmol, 1.00 equiv) in 4.0 ml $C_6H_6$ was heated to reflux for 16 h, cooled to rt, and concentrated under reduced pressure. Purification by flash chromatography (3:2 – 2:3 hexanes/EtOAc) provided the dimer **63** (404 mg, 67% yield) as a clear, colorless oil.

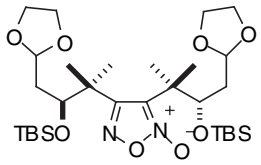
**Optical Rotation:** $[\alpha]_D^{23}$ (c 0.790, $CHCl_3$) = –28.1

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.07-5.02 (m, 2 H), 4.42-4.37 (m, 2 H), 4.04-3.81 (m, 8 H), 2.13 (ddd, 1 H, *J* = 14.0, 10.3, 2.5), 1.87-1.64 (m, 3 H), 1.46 (s, 3 H), 1.40 (s, 3 H), 1.32 (s, 3 H), 1.20 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 158.3, 103.7, 103.2, 101.5, 82.1, 71.4, 68.2, 65.0, 64.9, 57.8, 43.4, 40.9, 35.6, 34.2, 26.9, 24.3, 23.1, 22.7

**IR** (thin film) 3456, 2974, 2890, 11746, 1550, 1392, 1212, 1138, 1072, 1032, 947

**HRMS** (MALDI) calc'd for ($C_{18}H_{30}N_2O_7Na$, $MNa^+$–[O]), 409.1951; found, 409.1942




**51**

**(2*S*,2'*S*)-*3*,4-Bis-(2-(*tert*-butyl-dimethyl-silanyloxy)-3-[1,3]dioxolan-2-yl-2-hydroxy-1,1-dimethyl-propyl)-furazan-2-ol; compund with hydroxylamine (64).** To dimer **63** (331 mg, 0.819 mmol, 1.00 equiv) in 10 ml $CH_2Cl_2$ at 0 °C was added $Et_2N^iPr$ (1.12 ml, 6.56 mmol, 8.00 equiv). After stirring 10 min, TBSOTf (1.13 ml, 4.92 mmol, 6.00 equiv) was added dropwise and the reaction allowed to warm to rt and stirred 2 h. The reaction was quenched by addition of ph 8.6 buffer (phosphate, 10 ml) and extracted with $CH_2Cl_2$ (2 x 20 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (8:1 hexanes/EtOAc) afforded a major product (282 mg, 55% yield) and a minor product (154 mg, 29% yield), both of which showed spectral analysis consistent with the expected product.

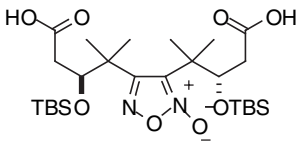
**Optical Rotation:** $[\alpha]_D^{28}$ (c 1.036, $CHCl_3$) = –9.21

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.00 (dd, 1 H, *J* = 7.2, 3.1), 4.89-4.82 (m, 2 H), 4.52 (dd, 1 H, *J* = 9.0, 2.2), 3.96-3.72 (m, 8 H), 1.94-1.73 (m, 2 H), 1.62-1.42 (m, 2 H), 1.47 (s, 3 H), 1.45 (s, 3 H), 1.44 (s, 3 H), 1.42 (s, 3 H), 0.91 (s, 9 H), 0.87 (s, 9 H), 0.10 (s, 6 H), 0.06 (s, 3 H), -0.06 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 162.7, 122.7, 102.4, 102.1, 72.0, 68.3, 64.7 (4 C's), 44.1, 42.1, 38.9, 38.3, 26.1 (6 C's), 22.2, 20.2, 18.4, 18.3, -3.6, -4.0, -4.3, -4.5

**IR** (thin film) 2955, 2930, 2886, 2857, 1729, 1552, 1472, 1257, 1139, 1096, 1039, 862, 837, 776

**HRMS** (MALDI) calc'd for $(C_{30}H_{58}N_2O_7Si_2Na, MNa\text{-}O)^+$, 637.3680; found, 637.3656



**51**

**(*2S,2'S*)-*3*-(*tert*-Butyl-dimethyl-silanyloxy)-4-{4-[2-(*tert*-butyl-dimethyl-silanyloxy)-3 -3-carboxy-1,1-dimethyl-propyl]-2-hydroxy-furazan-3-yl}-4-methyl-pentanoic acid; compound with hydroxylamine (76).** To silyl ether **64** (55.0 mg, 0.0873 mmol, 1.00 equiv) in 5 ml acetone was added $FeCl_3$•$SiO_2$ (1.28 g, 23.0 mass equiv) and the yellow mixture stirred at rt. After 8 h, the reaction was filtered over silica gel, eluted with $CH_2Cl_2$, concentrated under reduced pressure, and redissolved in 6 ml acetone and treated with an additional portion of $FeCl_3$•$SiO_2$ (500 mg). After stirring 12 h at rt, the reaction mixture was again filtered over silica was and the product eluted with $CH_2Cl_2$. Analysis by $^1$H NMR showed clean formation of the dialdehyde which was used without further purification.

To the unpurified dialdehyde (34.1 mg, 0.0629 mmol, 1.00 equiv) in 6 ml *tert*-BuOH and 1.5 ml 2-methyl-2-butene at 0 °C was added $NaClO_2$ (85.3 mg, 0.943 mmol, 15.0 equiv) in pH 3.8 buffer (1.0 M, phosphate). After 1.5 h, pH 2 buffer (1.0 M, phosphate) was added (until reaction pH ~2) and the mixture extracted with EtOAc (5 x 8 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure to provide diacid **51** (quant. yield) as a white foam.

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.26 (dd, 1 H, *J* = 6.2, 4.1), 4.87-4.83 (m, 1 H), 2.51-2.42 (m, 2 H), 2.37-2.28 (m, 2 H), 1.57 (s, 3 H), 1.51 (s, 3 H), 1.48 (s, 3 H), 1.46 (s, 3 H), 0.91 (s, 9 H), 0.86 (s, 9 H), 0.13 (s, 3 H), 0.09 (s, 3 H), 0.08 (s, 3 H), -0.07 (s, 3 H)

**IR** (KBr) 3414, 2856, 2938, 2858, 1713, 1554, 1473, 1390, 1362, 1258, 1097, 837, 770

**EI-MS:** 573.1 $(M-H)^+$

This compound was best characterized as its dimethylester: To diacid **51** (12 mg, 0.0021 mmol) in 1 ml MeOH was added $TMSCHN_2$ (2.0 M in hexanes) until a yellow color persists. Concentration under reduced pressure and purification by flash chromatography (9:1 hexanes/EtOAc) afforded the dimethylester as a clear, colorless oil.

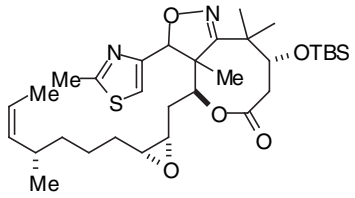
**Optical Rotation:** $[\alpha]_D^{23}$ (c 0.575, $CHCl_3$) = +3.4

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 5.21 (t, 1 H, *J* = 5.3), 4.82 (t, 1 H, *J* = 5.3), 3.63 (s, 3 H), 3.62 (s, 3 H), 2.41 (t, 4 H, *J* = 5.3), 1.53 (s, 3 H), 1.49 (s, 3 H), 1.47 (s, 3 H), 1.45 (s, 3 H), 0.89 (s, 9 H), 0.84 (s, 9 H), 0.10 (s, 3 H), 0.03 (s, 3 H), 0.01 (s, 3 H), -0.05 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 172.8, 172.1, 162.6, 122.3, 72.5, 69.6, 51.8, 44.0, 42.1, 39.7, 39.2, 25.9 (6 C's), 25.8, 25.6, 22.9. 21.7, 20.1, 18.1, -4.3, -4.6, -4.8, -4.9

**IR** (thin film) 2954, 2929, 2858, 1740, 1553, 1462, 1438, 1361, 1293, 1257, 1177, 1092, 836, 777

**HRMS** (MALDI) calc'd for ($C_{28}H_{54}N_2O_7Si_2Na$, MNa-O)$^+$, 609.3367; found, 609.3352




**66**

**(8*S*)-(*tert*-Butyl-dimethyl-silanyloxy)-3a,9,9-trimethyl-4-[(2*S*,3*R*)-((4*S*)-methyl-hept-(5*Z*)-enyl)-oxiranylmethyl]-3-(2-methyl-thiazol-4-yl)-3a,4,8,9-tetrahydro-3H,7H-2,5-dioxa-1-aza-cyclopentacylcoacten-6-one (66).** Diacid **51** (12.4 mg, 0.0217 mmol, 0.50 equiv) and epoxide **21** (14.5 mg, 0.0433, 1.00 equiv) were combined in 3.0 ml $CH_3CN$ and treated with BOP (42.0 mg, 0.0952 mmol, 2.20 equiv) followed by DMAP (31.6 mg, 0.260 mmol, 6.00 equiv). The reaction was stirred 40 h at rt, diluted with $H_2O$ (5 ml) and $CH_2Cl_2$ (10 ml), and extracted with $CH_2Cl_2$ (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (8:1 – 1:1 hexanes/EtOAc) provided diester **65** (7.0 mg, 27% yield) and recovered **25**(7.9 mg, 55 %).

**IR** (thin film) 2928, 2853, 1734, 1558, 1458, 1458, 1255, 1179, 1091, 836, 777

**MALDI-TOF MS:** 1209.7 $(MH)^+$

Diester **65** (7.0 mg, 0.0056 mmol, 1.0 equiv) in 40 ml degassed benzene was heated to 150° C in a sealed tube. After 36 h at this temperature, the reaction was cooled to rt,

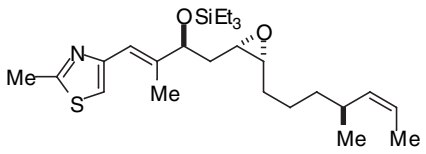
concentrated under reduced pressure, and purified by flash chromatography to afford the uncyclized nitrile oxide (1.1 mg, 16%) and cycloadduct **66** (3.1 mg, 44% yield).

**$^1$H NMR** ($CDCl_3$, 500 MHz) δ 6.84 (s, 1 H), 5.52 (dd, 1 H, *J* = 11.7, 2.9), 5.44-5.37 (m, 2 H), 4.65 (brs, 1 H), 4.31-4.06 (bm, 1 H), 2.97-2.85 (m, 2 H), 2.72 (s, 3 H), 2.59-2.48 (m, 1 H), 1.88-1.81 (m, 1 H), 1.68-1.63 (m, 1 H), 1.61 (dd, 3 H, *J* = 6.8, 1.8), 1.50-1.40 (m, 4 H), 1.37-1.1.15 (m, 2 H), 1.28 (s, 3 H), 1.25 (s, 3 H), 1.10 (s, 3 H), 0.96 (d, 3 H, *J* = 6.5), 0.91 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 170.0, 166.5, 149.3, 136.8, 122.6, 122.6, 117.2, 91.1, 78.9, 76.7, 57.2, 53.5, 41.3, 37.3, 36.9, 36.8, 29.7, 28.7, 28.2, 25.8, 24.5, 21.1, 19.2, 18.0, 16.3, 13.0, -4.35, -4.87

**IR** (thin film) 2958, 2928, 2856, 1751, 1461, 1284, 1259, 1086, 864, 837

**HRMS** (MALDI) calc'd for $(C_{23}H_{52}N_2O_5SSiNa)^+$, 627.3264; found, 627.3260




**2-Methyl-4-[2-methyl-4-[(2*S*, 3*R*)-*3*-((4*S*)-methyl-(*Z*)-hept-5-enyl)-oxiranyl]-(3*S*)-(triethyl-silanyloxy)-but-(1*E*)-enyl]-thiazole.** To epoxide **21** (72.0 mg, 0.215 mmol, 1.00 equiv) in 3.0 ml $CH_2Cl_2$ at 0 °C was added $NEt_3$ (185 µl, 1.30 mmol, 6.00 equiv) followed by TESCl (95 µl, 0.90 mmoL, 4.0 equiv) and DMAP (1 mg). The clear, colorless solution was stirred 15 h at rt before the reaction was quenched with sat. aq. $NaHCO_3$ (5 ml) and extracted with $CH_2Cl_2$ (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (10:1 hexanes/EtOAc) provided the TES-ether (75.6 mg, 79% yield) as a clear colorless oil.

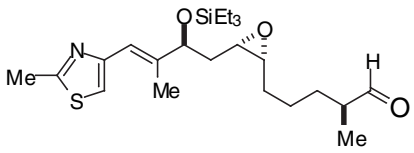
**Optical Rotation:** $[\alpha]_D^{29}$ (c 1.300, $CHCl_3$) = –7.7

**$^1$H NMR** ($CDCl_3$, 300 MHz) δ 6.94 (s, 1 H), 6.53 (s, 1 H), 5.45-5.28 (m, 1 H), 5.18-5.09 (m, 1 H), 4.36 (dd, 1 H, *J* = 8.4, 4.1), 3.08 (ddd, 1 H, *J* = 4.3, 8.7, 4.3), 2.94-2.90 (m, 1 H), 2.71 (s, 3 H), 2.51-2.39 (m, 1 H), 2.03 (s, 3 H), 1.86 (ddd, 1 H, *J* = 14.0, 8.7, 4.3), 1.62 (ddd, 1 H, *J* = 14.0, 7.8, 4.3), 1.60 (dd, 3 H, *J* = 6.9, 1.6), 1.51-1.18 (m, 6 H), 0.94 (d, 3 H, *J* = 6.5), 0.95 (t, 9 H, *J* = 7.8), 0.63 (q, 6 H, *J* = 7.8)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.5, 153.0, 142.3, 136.9, 122.5, 118.8, 115.4, 76.2, 57.4, 54.5, 37.3, 35.4, 31.3, 24.4, 21.1, 19.2, 17.9, 14.0, 6.9, 4.8

**IR** (thin film) 2955, 2913, 2879, 1506, 1458, 1240, 1182, 1079, 1005, 962

**HRMS** (MALDI) calc'd for $(C_{25}H_{43}NO_2SSiNa)^+$, 472.2681; found, 472.2676




**70**

**(2*S*)-Methyl-5-{(2*S*,3*R*)-[3-methyl-4-(2-methyl-thiazol-4-yl)-(2*S*)-(triethyl-silanyloxy)-but-(3*E*)-enyl]-oxiranyl}-pentanal (70).** To the olefin (72 mg, 0.16 mmol, 1.0 equiv) in 4:4:1 $^t$BuOH/THF/$H_2O$ (3.6 ml) at 0 °C was added NMO (23 mg, 0.19 mmol, 1.2 equiv) followed by $OsO_4$ (4% w/w in $H_2O$, 0.04 ml, 0.006 mmol, 0.04 equiv). The yellow solution was warmed to rt, stirred 18 h, and quenched by the addition of sodium bisulfite (10 mg). The reaction was diluted with $H_2O$ (5 ml) and extracted with EtOAc (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure to give a slightly yellow oil which was used without further purification.

To the unpurified diol (0.16 mmol, 1.0 equiv) in 5.0 ml EtOAc at 0 °C was added $Pb(OAc)_4$ (approx. 90%, 107 mg, 0.240 mmol, 1.50 equiv) in two portions. The reaction becomes bright yellow and a precipitate formed rapidly. After 15 min, the reaction was diluted with EtOAc (5 ml), filtered over a small plug of silica gel, and eluted with $Et_2O$ (50 ml). Concentration under reduced pressure and purification by flash chromatography (6:1 – 4:1 hexanes/EtOAc) provided aldehyde **70** (52.3 mg, 76% for two steps) and recovered olefin (4.4 mg).

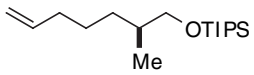
**Optical Rotation:** $[\alpha]_D^{25}$ (c 0.625, $CHCl_3$) = –4.8

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 9.63 (d, 1 H, *J* = 1.6), 6.94 (s, 1 H), 6.53 (s, 1 H), 4.36 (dd, 1 H, *J* = 9.0, 4.1), 3.10 (ddd, 1 H, *J* = 4.4, 7.8, 4.4), 2.95-2.93 (m, 1 H), 2.71 (s, 3 H), 2.34 (dq, 1 H, *J* = 11.5, 1.6), 2.03 (s, 3 H), 1.86 (ddd, 1 H, *J* = 14.0, 9.0, 4.4), 1.78-1.71 (m, 1 H), 1.61 (ddd, 1 H, *J* = 14.0, 7.5, 4.4), 1.61-1.37 (m, 6 H), 1.11 (d, 3 H, *J* = 6.8), 0.95 (t, 9 H, *J* = 7.8), 0.62 (q, 6 H, *J* = 7.8)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 205.2, 164.9, 153.3, 142.4, 119.1, 115.6, 76.2, 57.1, 54.6, 46.4, 35.5, 30.3, 28.2, 24.2, 19.2, 14.0, 13.3, 6.9, 4.8

**IR** (thin film) 2955, 2879, 1725, 1460, 1236, 1182, 1078, 1008

**HRMS** (MALDI) calc'd for $(C_{23}H_{39}NO_3SSiNa)^+$, 460.2318; found, 460.2319




**Triisopropyl-((2*S*)-methyl-hept-6-enyloxy)-silane.** To the alcohol (6.5 g, 0.050 mol, 1.0 equiv) in DMF (20 ml) at 0 °C was added imidazole (7.37 g, 0.110 mol, 2.20 equiv) followed by TIPSCl (11.7 ml, 55.0 mmol, 1.10 equiv). The cloudy mixture was stirred 10 h at rt, poured onto $H_2O$ (30 ml), and extracted with pentane (3 x 50 ml). The combined organic solutions were washed with brine (70 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by vacuum distillation (0.5 torr, 108-110 °C) afforded the silyl ether (12.6 g, 88% yield).

**Optical Rotation:** $[\alpha]_D^{29}$ (c 1.202 , $CHCl_3$) = –2.0

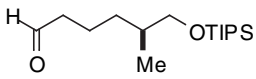
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 5.82 (ddt, 1 H, *J* = 17.1, 10.2, 6.8), 5.03-4.91 (m, 2 H), 3.53 (dd, 1 H, *J* = 9.3, 5.9), 3.45 (dd, 1 H, *J* = 9.3, 6.5). 2.08-1.98 (m, 2 H), 1.67-2.01 (m, 4 H), 1.15-0.99 (m, 22 H), 0.89 (d, 3 H, *J* = 6.6)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 139.1, 114.2, 68.6, 35.9, 34.2, 32.7, 26.4, 18.1, 17.7, 12.3

**IR** (thin film) 2943, 2867, 1463, 1388, 1102, 1069, 996, 910, 882

**EI-MS:** 284.4 ($M^+$)

**Anal. calc'd** for ($C_{17}H_{36}OSi$) C, 71.76%; H, 12.84%; found, C, 71.56%; H, 12.84%




**73**

**(5*S*)-Methyl-6-(triisopropyl-silanyloxy)-hexanal (73)**. Into a solution of the olefin (4.90 g, 17.1 mmol, 1.00 equiv) in 150 ml $CH_2Cl_2$ at –78 °C was bubbled a stream of $O_3$ in $O_2$ until the solution became blue and this color maintained for 2 min. The reaction was purged with $O_2$ for 20 min before $PPh_3$ (4.40 g, 16.7 mmol, 0.950 equiv) was added as a solid and the resulting mixture warmed slowly to rt and stirred 4 h. Concentration under reduced pressure gave a white precipitate which was suspended in pentane (75 ml) and filtered over a pad of Celite, eluding with additional pentane. Concentration under reduced pressure and filtration were repeated, and the resulting oil was purified by flash chromatography (20:1 hexanes/EtOAc) to give **73** (4.09 g, 83% yield).

**Optical Rotation:** $[\alpha]_D^{29}$ (c 1.635, $CHCl_3$) = –3.5

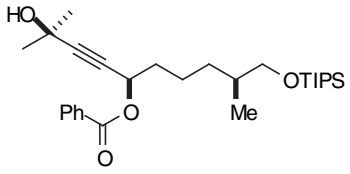
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 9.77 (t, 1 H, *J* = 1.9), 3.51 (d, 1 H, *J* = 6.2), 3.50 (d, 1 H, *J* = 6.2), 2.41 (dt, 2 H, *J* = 7.5, 1.9), 1.80-1.49 (m, 4 H), 1.19-0.99 (m, 22 H), 0.90 (d, 3 H, *J* = 6.5)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 203.0, 68.4, 44.2, 35.9, 32.8, 19.7, 18.0, 16.6, 12.0

**IR** (thin film). 2944, 2866, 2715, 1729, 1463, 1389, 1256, 1101, 1068, 914, 882

**EI-MS**: 243.2 (M-$^i$Pr)

**Anal. calc'd** for ($C_{16}H_{34}O_2Si$) C, 67.07%; H, 11.96%; found, C, 66.99%; H, 11.77%




**75**

**Benzoic acid 4-hydroxy-4-methyl-(1*R*)-[(4*S*)-methyl-5-(triisopropyl-silanyloxy)-pentyl]-pent-2-ynyl ester (75).** A mixture of $Zn(OTf)_2$ (9.45 g, 26.0 mmol, 2.00 equiv) and (+)-*N*-methyl-ephedrine (4.90 g, 27.3 mmol, 2.10 equiv) under $N_2$ were suspended in 22 ml toluene and $NEt_3$ (3.88 ml, 27.3 mmol, 2.10 equiv) added in one portion. The resulting slurry

was stirred 2 h at rt before 3-methylbutyn-3-ol (2.67 ml, 27.3 mmol, 2.10 equiv) was added neat and the reaction stirred 20 min before **73** (3.74 g, 13.0 mmol, 1.00 equiv) in 27 ml of toluene was added over 8 h with the assistance of a syringe pump. Following complete addition, the mixture was stirred an additional 18 h at rt and quenched by the addition of saturated, aqueous $NH_4Cl$ (50 ml). After stirring for 30 min, the mixture was diluted with $H_2O$ (200 ml) and $Et_2O$ (100 ml). The aqueous phase was extracted with $Et_2O$ (3 x 100 ml) and the combined organic solutions were washed with brine (250 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure to give a crude oil which was used without further purification.

Comparision of the crude $^{13}C$ NMR against that of a sample of pure, diastereomerically mixture material (prepared by addition of the corresponding lithium acetylide to **73**) revealed that the addition had occurred in >20:1 dr.

To the unpurified propargylic diol (13.0 mmol, 1.00 equiv) in 90 ml $CH_2Cl_2$ at 0 °C was added $NEt_3$ (2.40 ml, 16.9 mmol, 1.30 equiv), BzCl (1.97 ml, 16.9 mmol, 1.30 equiv), and DMAP (158 mg, 1.30 mmol, 0.10 equiv). After 1 h at rt, the reaction was diluted with sat. aq. $NH_4Cl$ (50 ml) and $H_2O$ (50 ml), and the aqueous phase extracted with $CH_2Cl_2$ (3 x 80 ml). The combined organic solutions were washed with brine (100 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (7:1 hexanes/EtOAc) provided **75** (4.44 g, 72% yield for two steps) as a clear, colorless oil.

**Optical Rotation:** $[\alpha]_D^{23}$ (c 1.235, $CHCl_3$) = +12.3

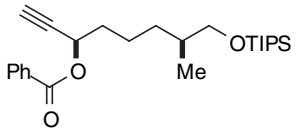
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 8.08 (m, 2 H), 7.58 (tt, 1 H, *J* = 6.3, 1.3), 7.47-7.26 (m, 2 H), 5.64 (t, 1 H, *J* = 6.5), 3.53 (dd, 1 H, *J* = 9.5, 5.9), 3.48 (dd, 1 H, *J* = 9.5, 6.2), 1.91-1.84 (m, 2 H), 1.69-1.42 (m, 4 H), 1.51 (s, 6 H), 1.19-0.98 (m, 22 H), 0.90 (d, 3 H, *J* = 6.5)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 165.6, 133.1, 130.0, 129.8, 128.4, 90.2, 79.2, 68.4, 65.1, 64.4, 35.9, 35.2, 32.6, 31.3, 32.6, 18.1, 16.7, 12.0

**IR** (thin film).3430, 2943, 2866, 1724, 1462, 1267, 1106, 1069, 1026, 951, 882.

**HRMS** (MALDI) calc'd for $(C_{28}H_{46}O_4SiNa)^+$, 497.3063; found, 497.3058

**Anal. calc'd** for ($C_{28}H_{46}O_4Si$) C, 70.84%; H, 9.77%; found, C, 70.81%; H, 9.86%




**76**

**Benzoic acid (1*R*)-[(4*S*)-methyl-5-(triisopropyl-silanyloxy)-pentyl]-prop-2-ynyl ester (76)**. To **75** (2.11 g, 4.45 mmol, 1.00 equiv) in 15 ml toluene at rt was added $K_2CO_3$ (615 mg, 4.45 mmol, 1.00 equiv) and 18-crown-6 (353 mg, 1.34 mmol, 0.300 equiv) and the mixture heated to reflux under $N_2$. After 26 h at this temperature, the reaction was cooled to rt, diluted with $Et_2O$ (30 ml) and $H_2O$ (25 ml), and the aqueous phase extracted with $Et_2O$ (3 x 20 ml). The combined organic solutions were washed with brine (70 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (15:1 hexanes/EtOAc) provided **76** (1.58 g, 85% yield) as a colorless oil.

**Optical Rotation:** $[\alpha]_D^{28}$ (c 1.195, $CHCl_3$) = +17.1

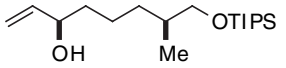
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 8.09-8.05 (m, 2 H), 7.58 (tt, 1 H, *J* = 6.3, 1.3), 7.48-7.42 (m, 2 H), 5.60 (dt, 1 H, *J* = 6.5, 2.2), 3.76-3.46 (m, 2 H), 3.48 (d, 1 H, *J* = 2.2), 1.96-1.87 (m, 2 H), 1.70-1.25 (m, 4 H), 1.22-1.09 (m, 1 H), 1.11-0.98 (m, 21 H), 0.91 (d, 3 H, *J* = 6.5)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 165.5, 133.2, 129.9, 128.4, 81.3, 73.6, 68.4, 64.,4, 35.8, 35.0, 32.7, 22.5, 18.1, 16.7, 12.0

**IR** (thin film) 3311, 2944, 2866, 1726, 1463, 1265, 1106, 1069, 1026, 882

**EI-MS:** 416.2 (M+)

**Anal. calc'd** for ($C_{25}H_{40}O_3Si$) C, 72.06%; H, 9.68%; found, C, 72.05%; H, 9.58%




**77**

**(7*S*)-Methyl-8-(triisopropyl-silanyloxy)-oct-1-en-(3*R*)-ol (77).** To **76** (3.03 g, 7.28 mmol, 1.00 equiv) in 60 ml $Et_2O$ at 0 °C was added $LiAlH_4$ (1.38 g, 36.4 mmol, 5.00 equiv) in portions over 30 min. After warming to rt, the mixture was stirred 5 h before cooling to 0 °C and carefully quenching the reaction with EtOAc (3 ml). Following addition of $Na_2SO_4$•$10H_2O$ (10 g) to the grey slurry and stirring 2 h at rt, the resulting white, grainy powder was filtered and washed with EtOAc (250 ml). The combined organic solutions were concentrated under

reduced pressure and purified by flash chromatography (7:1 hexanes/EtOAc) to provide **77** (2.20 g, 93% yield) as a clear, colorless oil.

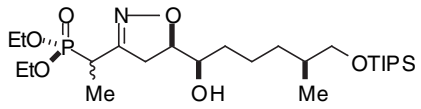
**Optical Rotation:** $[\alpha]_D^{29}$ (c 1.078, $CHCl_3$) = –5.4

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 5.87 (ddd, 1 H, *J* = 17.1, 10.2, 6.2), 2.25-1.08 (m, 2 H), 4.14-4.06 (m, 1 H), 3.52 (dd, 1 H, *J* = 9.7, 6.0), 3.46 (dd, 1 H, *J* = 9.7, 6.2), 1.74-1.35 (m, 4 H), 1.35-1.23 (m, 1 H), 1.14-0.97 (m, 21 H), 0.90 (d, 3 H, *J* = 6.5)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 141.3, 114.6, 73.3, 68.6, 37.4, 36.0, 33.1, 22.8, 18.1, 16.7, 12.0

**EI-MS:** 269.1 (M-$^i$Pr)

**Anal. calc'd** for ($C_{18}H_{38}O_2Si$) C, 68.73%; H, 12.17%; found, C, 68.73%; H, 12.06%.




**78**

**(1-{5-[(1*R*)-Hydroxy-(5*S*)-methyl-6-(triisopropyl-silanyloxy)-hexy]-4,(5*R*)-dihydro-isoxazol-3-yl}-ethyl)-phosphonic acid deithyl ester (78)**. To **77** (1.10 g, 3.40 mmol, 1.00 equiv) and $^i$PrOH (858 _l, 1 1.2 mmol, 3.30 equiv) in 100 ml $CH_2Cl_2$ at 0° C was added EtMgBr (3.0 M in $Et_2O$, 0.010 mol, 3.0 equiv). After 20 min at 0 °C, **18** (1.08 g, 4.42 mmol, 1.30 equiv) in 18 ml $CH_2Cl_2$ was added in portions over 20 min. After 3 h at 0° C, the reaction was allowed to warm to rt and stirred 36 h before being quenched with sat. aq. $NH_4Cl$ (70 ml) and the aqueous phase extracted with EtOAc (3 x 80 ml). The combined organic solutions were washed with brine (150 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (7:1 -> 2:1 -> 1:3 hexanes/EtOAc) afforded **78** (1.01 g, 56 % yield) and recovered **77** (0.43 g, 38 % yield).

**Optical Rotation:** $[\alpha]_D^{27}$ (c 1.074, $CHCl_3$) = –35.1

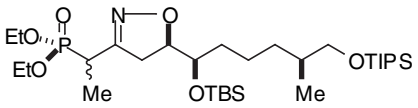
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 4.52-4.44 (m, 1 H), 4.19-4.10 (m, 4 H), 3.55-3.43 (m, 3 H), 3.25-2.87 (m, 3 H), 1.86-1.68 (brs, 1 H), 1.70-1.25 (m, 5 H), 1.48 (d, 1.5 H (0.5 C*H*$_3$ of two diast.), *J* = 7.5), 1.42 (d, (0.5 C*H*$_3$ of two diast.), *J* = 7.2), 1.33 (t, 6 H, *J* = 7.1), 1.12-0.98 (m, 21 H), 0.90 (d, 3 H, 6.8) (includes both diastereomers)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 157.2, 157.1, 157.1, 83.4, 83.3, 73.1, 73.0, 62.8, 62.7, 38.0, 38.0, 36.0, 33.8, 33.7, 33.2, 31.4, 23.2, 18.0, 16.7, 16.5, 16.4, 12.4, 12.3, 12.3, 12.2, 12.0 (includes both diastereomers)

**IR** (thin film).3401, 2942, 2866, 1462, 1251, 1220, 1098, 1066, 1023, 966, 883

**HRMS** (MALDI) calc'd for $(C_{25}H_{52}NO_6PSiNa)^+$, 544.3199; found, 544.3192

**Anal. calc'd** for ($C_{25}H_{52}NO_6PSi$) C, 57.55%; H, 10.05%; N, 2.68; found, C, 57.29%; H, 10.25%; N, 2.68%




**79**

**(1-{5-[(1*R*)-(*tert*-Butyl-dimethyl-silanyloxy)-(5*S*)-methyl-6-(triisopropyl-silanyloxy)-hexy]-4,(5*R*)-dihydro-isoxazol-3-yl}-ethyl)-phosphonic acid diethyl ester (139)**. To **78** (1.15 g, 2.16 mmol, 1.00 equiv) in 22 ml $CH_2Cl_2$ at 0° C was added $Et_2N^iPr$ (753 _l, 4.32 mmol, 2.00 equiv) followed by dropwise addition of TBSOTf (991 _l, 4.32 mmol, 2.00 equiv). After 25 min at 0° C, the reaction was quenched by careful addition of saturated, aqueous $NaHCO_3$ (15 ml) and stirred 10 min at rt. The aqueous phase was extracted with $CH_2Cl_2$ (3 x 20 ml) and the combined organic solutions were washed with brine (50 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (3:1 hexanes/EtOAc) afforded **79** (1.19 g, 87% yield) as a clear, colorless oil.

**Optical Rotation:** $[\alpha]_D^{27}$ (c 1.360, $CHCl_3$) = –26.5

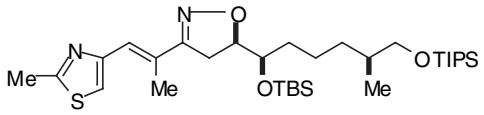
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 4.62-4.51 (m, 1 H), 4.16 (t, 2 H, *J* = 7.2), 4.11 (t, 2 H, *J* = 7.2), 3.76-3.67 (m, 1 H), 3.52 (dd, 1 H, *J* = 9.3, 5.7), 3.43 (dd, 1 H, *J* = 9.34, 6.5), 3.20-2.86 (m, 3 H), 1.64-1.52 (m, 1 H), 1.48 (d, 1.5 H (0.5 C*H*$_3$ of two diast.), *J* = 7.2), 1.42 (d, 1.5 H (0.5 C*H*$_3$ of two diast.), *J* = 7.4), 1.52-1.38 (m, 4 H), 1.33 (t, 6 H, *J* = 7.2), 1.35-1.19 (m, 2 H), 1.11-0.98 (m, 21 H), 0.89 (d, 3 H, *J* = 6.5), 0.88 (s, 9 H), 0.09 (s, 3 H), 0.06 (s, 3 H) (includes both diastereomers)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 156.3, 156.2, 156.1, 83.0, 72.8. 68.6. 65.4 (q, *J* = 7.3), 36.7, 36.6, 36.0, 33.4, 33.2, 31.9, 31.3, 25.8, 23.1, 18.1, 16.7, 16.5, 16.4, 12.3, 12.2, 12.0, 4.4, 4.6 (includes both diastereomers)

**IR** (thin film) 3339, 2943, 2865, 1558, 1463, 1255, 1099, 1056, 1023, 967, 882, 837

**HRMS** (MALDI) calc'd for $(C_{31}H_{66}NO_6PSi_2Na)^+$, 658.4064; found, 658.4055

**Anal. calc'd** for ($C_{31}H_{66}NO_6PSi_2$) C, 58.54%; H, 10.46%; N, 2.20%; found, C, 58.26%; H, 10.36%; N, 2.19%




**140**

**5-[(1*R*)-(*tert*-Butyl-dimethyl-silanyloxy)-(5*S*)-methyl-6-(triisopropyl-silanyloxy)-hexyl]-3-[1-methyl-(2*E*)-(2-methyl-thiazol-4-yl)-vinyl]-4,(5*R*)-dihydro-isoxazole (80).** To 7**9** (1.18 g, 1.86 mmol, 1.00 equiv) in 18 ml $CH_3CN$ at rt was added LiCl (95 mg, 2.23 mmol, 1.20 equiv) followed by DBU (286 _l, 1.86 mmol, 1.00 equiv) and the mixture stirred 20 min at rt. To the resulting yellow slurry, **44** (381 mg, 3.00 mmol, 1.60 equiv) was added as a solid. After 0.5 h and 1 h, addition portions of DBU (100 _l) were added before the reaction was quenched with $H_2O$ (10 ml) and brine (15 ml). This solution was extracted with $CH_2Cl_2$ (3 x 40 ml) and the combined organic solutions washed with brine (50 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography afforded **80** (910 mg, 80% yield, 6:1 *trans:cis*) as a slightly yellow oil.

**Optical Rotation:** $[\alpha]_D^{26}$ (c 1.314, $CHCl_3$) = –61.4

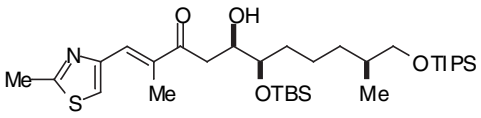
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.16 (s, 1 H), 6.73 (s, 1 H), 4.67 (ddd, 1 H, *J* = 10.0, 5.6, 4.4), 3.80-3.68 (m, 1 H), 3.52 (dd, 1 H, *J* = 9.3, 5.9), 3.43 (dd, 1 H, *J* = 9.3, 6.2), 3.13-1.07 (m, 2 H), 2.73 (s, 3 H), 2.36 (s, 3H), 1.65-1.37 (m, 5 H), 1.37-1.20 (m, 2 H), 1.13-0.98 (m, 21 H), 0.89 (d, 3 H, *J* = 6.5), 0.88 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.9, 159.9, 152.1, 129.9, 125.8, 117.9, 83.9, 73.1, 68.6, 36.0, 35.2, 33.3, 32.1, 25.8, 23.1, 23.0, 19.1, 18.1, 16.7, 15.2, 11.9, -4.4, -4.5

**IR** (thin film) 2944, 2865, 1462, 1255, 1102, 882, 836

**HRMS** (MALDI) calc'd for $(C_{32}H_{60}N_2O_3SSiNa)^+$, 631.3761; found, 631.3763

**Anal. calc'd** for ($C_{32}H_{60}N_2O_3SSi$) C, 63.10%; H, 9.93%; N, 4.60%; found, C, 63.03%; H, 9.81%; N, 4.53%




**81**

**(6*R*)-(*tert*-Butyl-dimethyl-silanyloxy)-(5*R*)-hydroxy-2,(10*S*)-dimethyl-1-(2-methyl-thiazol-4-yl)-11-(triisopropyl-silanyloxy)-undec-(1*E*)-en-3-one (81)**. To **80** (0.190 g, 0.312 mmol, 1.00 equiv) in 10.0 ml degassed THF at 0 °C was added $SmI_2$ (0.10 M in THF, 10 ml, 10 mmol, 3.0 equiv) dropwise at such a rate as to maintain a dark blue-green color. To the resulting dark blue reaction was added additional $SmI_2$ (1 ml) and the reaction stirred 15 min at 0 °C before the remaining $SmI_2$ was quenched with $O_2$ to give a yellow solution. The solution was warmed to rt, diluted with $H_2O$ (7 ml) and treated with $B(OH)_3$ (0.1 g). After stirring 30 min at rt, the mixture was extracted with $Et_2O$ (3 x 40 ml), and the combined organic solutions were washed with brine (80 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (7:1 hexanes/EtOAc) afforded **81** (146 mg, 76% yield, *trans* only) as a clear, colorless oil.

**Optical Rotation:** $[\alpha]_D^{27}$ (c 1.038, $CHCl_3$) = +19.9

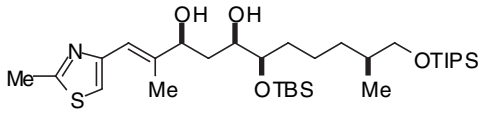
**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 7.53 (s, 1 H), 7.35 (s, 1 H), 4.16-4.07 (m, 1 H), 3.74-3.68 (m, 1 H), 3.54 (dd, 1 H, *J* = 9.7, 5.9), 3.44 (dd, 1 H, *J* = 9.7, 6.5), 3.04 (dd, 1 H, *J* = 16.9, 3.8), 2.91 (dd, 1 H, *J* = 16.9, 8.4), 2.87 (d, 1 H, OH, *J* = 5.6), 2.76 (s, 3 H), 2.25 (s, 3 H), 1.74-1.22 (m, 7 H), 1.15-0.99 (m, 21 H), 0.90 (d, 3 H, *J* = 6.5), 0.90 (s, 9 H), 0.08 (s, 3 H), 0.06 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) $\delta$ 202.3, 165.5, 151.8, 137.4, 131.6, 121.8, 74.3, 70.1, 68.6, 39.9, 36.1, 33.4, 32.9, 25.9, 23.1, 23.2, 19.2, 18.1, 16.7, 13.2, 12.0, -4.3, -4.4

**IR** (thin film) 3469, 2944, 2865, 1559, 1462, 1388, 1256, 1096, 1070, 882, 836

**HRMS** (MALDI) calc'd for $(C_{32}H_{61}NO_4SSiNa)^+$, 634.3758; found, 634.3753

**Anal. calc'd** for ($C_{32}H_{61}NO_4SSi$) C, 62.79%; H, 10.04%; N, 2.29%; found, C, 62.99%; H, 9.84%; N, 2.26%.




**82**

**(6*R*)-(*tert*-Butyl-dimethyl-silanyloxy)-2,(10*S*)-dimethyl-1-(2-methyl-thiazol-4-yl)-11-(triisopropyl-silanyloxy)-undec-(1*E*)-en-(3*S*,5*R*)-diol (82).** To $BEt_3$ (1.0 M in THF, 640 _l, 0.64 mmol, 1.1 equiv) in 4.0 ml THF at rt was added MeOH (1.1 ml) and the clear solution stirred 0.5 h before being cooled to –78 °C. Ketone **81** (355 mg, 0.579 mmol, 1.00 equiv) in 3.0 ml THF was added via cannula and the reaction stirred 1 h at –78° C before $NaBH_4$ (110 mg, 2.90 mmol, 5.00 equiv) was added as a solid in two portions. After 3 and 5 h, additional portions of $NaBH_4$ (50 mg) were added and after 6 h the reaction was quenched by the cautious addition of sat. aq. $NH_4Cl$ (5 ml) at –78 °C. After warming to rt, the aqueous phase was extracted with EtOAc (3 x 15 ml) and the combined organic solutions were washed with brine (30 ml) and dried over $Na_2SO_4$. Concentration under reduced pressure gave an oil which was azeotroped with MeOH (4 x 5 ml) and purified by flash chromatography (3:2 hexanes/EtOAc) to give **82** (322 mg, 90% yield) as a clear, colorless oil.

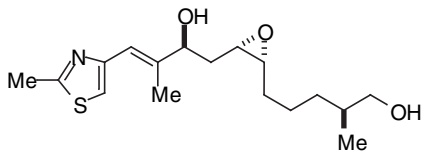
**Optical Rotation:** $[\alpha]_D^{24}$ (c 1.325, $CHCl_3$) = +0.5

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.96 (s, 1 H), 6.60 (s, 1 H), 4.42 (t, 1 H, *J* = 6.2), 3.83-3.68 (m, 1 H), 3.65-3.60 (m, 1 H, OH), 3.58-3.41 (m, 2 H), 2.90-2.81 (brs, 1 H, OH), 2.73 (s, 3 H), 2.05 (s, 3 H), 1.73-1.49 (m, 3 H), 1.48-1.22 (m, 2 H), 1.12-0.98 (m, 21 H), 0.91 (s, 9 H), 0.90 (d, 3 H, *J* = 6.5), 0.09 (s, 3 H), 0.08 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.5, 153.0, 142.0, 118.4, 115.5, 78.0, 75.3, 74.3, 68.6, 37.8, 36.0, 33.5, 33.1, 25.9, 22.9, 21.0, 19.1 18.1, 16.7, 14.4, 12.0, –4.3,-4.5

**IR** (thin film).3338, 2945, 2865, 1509, 1462, 1388, 1363, 1256, 1094, 882, 836.

**HRMS** (MALDI) calc'd for $(C_{32}H_{63}NO_4SSi_2Na)^+$, 636.3914; found, 636.3907




**84**

**1-[(*2S*,3*R*)-(5-Hydroxy-(4*S*)-methyl-pentyl)-oxiranyl]-3-methyl-4-(2-methyl-thiazol-4-yl)-but-(3*E*)-en-(2*S*)-ol (84).** To **82** (301 mg, 0.491 mmol, 1.00 equiv) in 5 ml $CH_2Cl_2$ at 0 °C was added $NEt_3$ (284 _l, 2.00 mmol, 4.00 equiv) followed by $SOCl_2$ (0.75 M in $CH_2Cl_2$, 1.0 ml, 0.75 mmol, 1.5 equiv). The resulting yellow solution was stirred 20 min at 0 °C, quenched with $H_2O$ (5 ml), and extracted with $CH_2Cl_2$ (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure to give a yellow-brown oil which was used without further purification.

To the unpurified cyclic sulfite (0.49 mmol, 1.0 equiv) in 12 ml THF at rt was added $Bu_4NF•3H_2O$ (789 mg, 2.5 mmol, 5.0 equiv) as a solid. The dark yellow solution was heated to reflux for 2 h, cooled to rt, diluted with $H_2O$ (10 ml), and extracted with EtOAc (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (4:1 hexanes/EtOAc) provided **84** (122 mg, 77% yield for two steps) as a clear, colorless oil.

**Optical Rotation:** $[\alpha]_D^{29}$ (c 1.248, $CHCl_3$) = –11.3

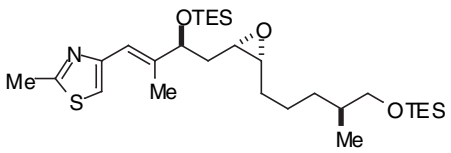
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.97 (s, 1 H), 6.62 (s, 1 H), 4.42 (dd, 1 H, *J* = 8.7, 4.4), 3.51 (dd, 1 H, *J* = 10.3, 6.2), 3.45 (dd, 1 H, *J* = 10.3, 6.2), 3.17 (ddd, 1 H, *J* = 4.4, 7.8, 4.4), 3.00-2.94 (m, 1 H), 2.72 (s, 3 H), 2.05 (s, 3 H), 1.93 (ddd, 1 H, *J* = 14.0, 9.0, 4.1), 1.78 (ddd, 1 H, *J* = 14.0, 7.8, 4.1), 1.78-1.41 (m, 7 H), 0.93 (d, 3 H, *J* = 6.5)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.9, 152.6, 142.0, 118.8, 115.7, 75.2, 68.1, 57.2, 54.5, 35.7, 33.5, 32.9, 28.2, 24.0, 19.1, 16.5, 14.5

**IR** (thin film).3369, 2925, 2870, 1726, 1508, 1452, 1384, 1273, 1190, 1038

**HRMS** (MALDI) calc'd for $(C_{17}H_{29}NO_4SNa)^+$, 348.1609; found, 348.1603

**Anal. calc'd** for ($C_{17}H_{29}NO_4S•H_2O$) C, 59.45%; H, 8.51%; N, 4.08%; found, C, 59.64%; H, 8.32%; N, 3.82%




**85**

**2-Methyl-4-[2-methyl-4-{(2*S*,3*R*)-[(4*S*)-methyl-5-(triethyl-silanyloxy)-pentyl]-oxiranyl}-(3*S*)-(triethyl-silanyloxy)-but-(1*E*)-enyl]-thiazole (85).** To **84** (170 mg, 0.523 mmol, 1.00 equiv) in 5.0 mmol $CH_2Cl_2$ at 0 °C was added $NEt_3$ (592 _l, 4.16 mmol, 8.00 equiv) followed by TESCl (276 _l, 2.62 mmoL, 5.00 equiv) and DMAP (2 mg). The clear, colorless solution was stirred 3 h at 0° C and 4.5 h at rt before the reaction was quenched with sat. aq. $NaHCO_3$ (5 ml) and extracted with $CH_2Cl_2$ (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatrography (10:1 hexanes/EtOAc) provided **85** (214 mg, 75% yield) as a clear colorless oil.

**Optical Rotation:** $[\alpha]_D^{26}$ (c 1.155, $CHCl_3$) = –7.4

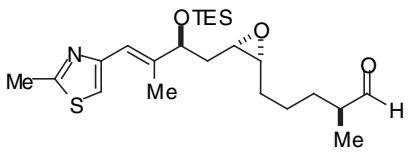
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.94 (s, 1 H), 6.54 (s, 1 H), 4.36 (dd, 1 H, *J* = 9.0, 4.1), 3.44 (dd, 1 H, *J* = 9.7, 6.2), 3.34 (dd, 1 H, *J* = 9.7, 6.8), 3.09 (ddd, 1 H, *J* = 4.4, 7.8, 4.4), 2.97-2.92 (m, 1 H), 2.72 (s, 3 H), 2.02 (s, 3 H), 1.87 (ddd, 1 H, *J* = 14.0, 9.0, 4.4), 1.66-1.33 (m, 7 H), 1.17-1.03 (m, 1 H), 0.95 (t, 18 H, *J* = 7.5), 0.88 (d, 3 H, *J* = 6.5), 0.66-0.55 (m, 12 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.5, 152.9, 142.3, 118.7, 115.3, 76.2, 68.1, 57.3, 54.5, 35.9, 35.4, 33.2, 28.5, 24.1, 19.2, 16.6, 14.0, 6.9, 6.8, 4.8, 4.4

**IR** (thin film).2954, 2876, 1458, 1239, 1088, 1006, 877

**HRMS** (MALDI) calc'd for $(C_{29}H_{55}NO_3SSi_2Na)^+$, 576.3339; found, 576.3338

**Anal. calc'd** for ($C_{29}H_{55}NO_3SSi_2$) C, 62.87%; H, 10.01%; N, 2.53%; found, C, 63.05%; H, 9.95%; N, 2.55%




**70**

**(2*S*)-Methyl-5-{(*2S,3R*)-[3-methyl-4-(2-methyl-thiazol-4-yl)-2-(triethyl-silanyloxy)-but-(3*E*)-enyl]-oxiranyl}-pentanal (70).** Silyl ether **85** (0.120 g, 0.217 mmol, 1.00 equiv) in 10:2:1 THF:AcOH:$H_2O$ (3.0 ml) was warmed to 30 °C for 3.5 h before cooling to rt and careful quenching with sat. aq. $NaHCO_3$ (10 ml). The mixture was extracted with $CH_2Cl_2$ (3 x 10 ml) and the combined organic solutions washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure.

To the unpurified alcohol in 3.0 ml $CH_2Cl_2$ at rt was added NMO (47 mg, 0.40 mmol, 1.5 equiv) and 4 Å molecular sieves (350 mg) and the slurry stirred 0.5 h at rt before TPAP (5.0 mg, 0.013 mmol, 0.050 equiv) was added as a solid. After 20 min, the reaction mixture was diluted with pentane (5 ml) and filtered over a small plug of silica gel, eluting with $Et_2O$ (50 ml). Purification by flash chromatrography (5:1 hexanes/EtOAc) provided **70** (101 mg, 81% yield for two steps) as a clear, colorless oil.

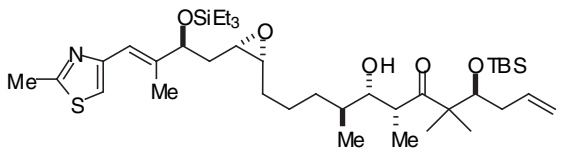
**Optical Rotation:** $[\alpha]_D^{25}$ (c 0.625, $CHCl_3$) = –4.8

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 9.63 (d, 1 H, *J* = 1.6), 6.94 (s, 1 H), 6.53 (s, 1 H), 4.36 (dd, 1 H, *J* = 9.0, 4.1), 3.10 (ddd, 1 H, *J* = 4.4, 7.8, 4.4), 2.95-2.93 (m, 1 H), 2.71 (s, 3 H), 2.34 (dq, 1 H, *J* = 11.5, 1.6), 2.03 (s, 3 H), 1.86 (ddd, 1 H, *J* = 14.0, 9.0, 4.4), 1.78-1.71 (m, 1 H), 1.61 (ddd, 1 H, *J* = 14.0, 7.5, 4.4), 1.61-1.37 (m, 6 H), 1.11 (d, 3 H, *J* = 6.8), 0.95 (t, 9 H, *J* = 7.8), 0.62 (q, 6 H, J= 7.8)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 205.2, 164.9, 153.3, 142.4, 119.1, 115.6, 76.2, 57.1, 54.6, 46.4, 35.5, 30.3, 28.2, 24.2, 19.2, 14.0, 13.3, 6.9, 4.8

**IR** (thin film) 2955, 2879, 1725, 1460, 1236, 1182, 1078, 1008

**HRMS** (MALDI) calc'd for $(C_{23}H_{39}NO_3SSiNa)^+$, 460.2318; found, 461.2319




**71**

**(4*S*)-(*tert*-Butyl-dimethyl-silanyloxy)-(8*R*)-hydroxy-5,5-(7*R*,9*S*)-tetramethyl-12-{(2*R*,3*S*)-3-methyl-4-(2-methyl-thiazole-4-yl)-(2*S*)-(triethyl-silanyloxy)-but-(3*E*)-enyl]-oxirnayl}-dodec-1-en-6-one (71).** To **68** (98.0 mg, 0.336 mmol, 1.50 equiv) in 3.0 _l THF at –78 °C was added freshly prepared LDA (0.5 M in THF, 672 _l, 0.336 mmol, 1.50 equiv) and the reaction stirred 15 min at this temperature, warmed to –40 °C for 20 min, and recooled to –78 °C. Aldehyde **70** (96.0 mg, 0.224 mmol, 1.00 equiv) in 2.0 _l THF was added via cannula and stirred 1 h at –78 °C. The reaction was quenched at –78 °C by addition of sat. aq. $NH_4Cl$ (5 ml) and extracted with $Et_2O$ (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatrography (6:1 hexanes/EtOAc) provided **71** (139 mg, 86% yield) as a clear, colorless oil.

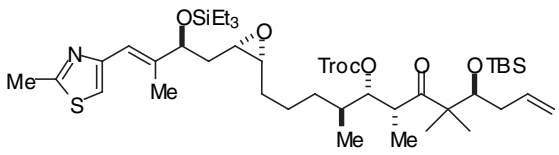
**Optical Rotation:** $[\alpha]_D^{26}$ (c 1.875, $CHCl_3$) = –19.6

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.93 (s, 1 H), 6.52 (s, 1 H), 5.85-5.71 (m, 1 H), 5.04-4.98 (m, 2 H), 4.35 (dd, 1 H, *J* = 9.0, 4.0), 3.92 (dd, 1 H, *J* = 6.5, 4.4), 3.52 (s, 1 H, OH), 3.32 (d, 1 H, *J* = 9.0), 3.25 (q, 1 H, *J* = 7.0), 3.09 (ddd, 1 H, *J* = 4.4, 7.8, 4.4), 2.98-2.91 (m, 1 H), 2.70 (s, 3 H), 2.24-2.04 (m, 2H), 2.01 (s, 3 H), 1.89 (ddd, 1 H, *J* = 14.0, 9.0, 4.4), 1.89-1.76 (m, 1 H), 1.68-1.28 (m, 6 H), 1.60 (ddd, 1 H, *J* = 14.0, 7.5, 4.0), 1.18 (s, 3 H), 1.12 (s, 1 H), 1.03 (d, 3 H, 6.9), 0.94 (t, 9 H, *J* = 7.5), 0.89 (s, 9 H), 0.83 (d, 3 H, *J* = 6.9) , 0.61 (q, 6 H, *J* = 7.5), 0.07 (s, 3 H), 0.06 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 222.5, 164.5, 153.0, 142.3, 136.3, 118.8, 116.7, 115.4, 76.5, 76.1, 74.9, 57.4, 54.6, 54.4, 41.1, 40.0, 35.6, 35.3, 32.8, 28.6, 26.1, 23.9, 23.4, 19.4, 19.2, 18.2, 15.3, 14.0, 9.7, 6.9, 4.8, -3.5, -4.0

**IR** (thin film) 3369, 2955, 2877, 1680, 1461, 1388, 1255, 1079, 1002. 837

**HRMS** (MALDI) calc'd for $(C_{39}H_{71}NO_5SSi_2Na)^+$, 744.4489; found, 744.4489




**Carbonic acid (5*S*)-(*tert*-butyl-dimethyl-silanyloxy)-(2*S*),4,4-trimethyl-(1*S*)- ((1*S*)-methyl-4-{(*2S*,3*R*)-[3-methyl-4-(2-methyl-thiazol-4-yl)-(2*S*)-(triethyl-silanyloxy)-but –(3*E*)-enyl]-oxiranyl}-butyl)-3-oxo-oct-7-enyl ester 2,2,2-trichloro-ethyl ester.** To **71** (102 mg, 0.141 mmol, 1.00 equiv) in 4.0 ml $CH_2Cl_2$ at 0 °C was added pyridine (0.23 ml, 0.82 mmol, 20 equiv) followed by dropwise addition of TrocCl (0.114 _l, 0.845 mmol, 6.00 equiv). After 2 h, $H_2O$ (5 ml) and $CH_2Cl_2$ (5 ml) were added and the aqueous layer extracted with $CH_2Cl_2$ (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatrography (7:1 hexanes/EtOAc) provided the Troc ester (115 mg, 91% yield) as a clear colorless oil.

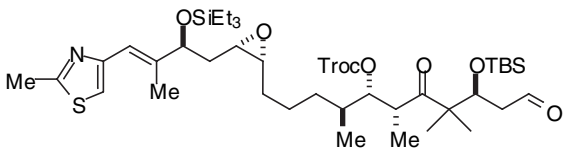
**Optical Rotation:** $[\alpha]_D^{21}$ (c 1.110, $CHCl_3$) = –30.2

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.93 (s, 1 H), 6.52 (s, 1 H), 5.77 (ddt, 1 H, *J* = 17.0, 10.0, 7.1), 5.02-4.98 (m, 2 H), 4.85 (d, 1 H, *J* = 11.8), 4.85 (d, 1 H, *J* = 11.8), 4.83 (dd, 1 H, *J* = 12.1, 7.4), 4.69 (d, 1 H, *J* = 11.8), 4.34 (dd, 1 H, *J* = 9.0, 4.1), 4.14 (d, 1 H, *J* = 7.8), 3.76 (dd, 1 H, *J* = 6.5, 4.1), 3.49-3.40 (m, 1 H), 3.08 (ddd, 1 H, *J* = 4.4, 7.8, 4.4), 2.94-2.88 (m, 1 H), 2.70 (s, 3 H), 2.28-2.17 (m, 1 H), 2.06-1.94 (m, 1 H), 2.01 (s, 3 H), 1.83 (ddd, 1 H, *J* = 14.0, 9.0, 4.4), 1.76-1.65 (m, 1 H), 1.63-1.14 (m, 7 H), 1.57 (ddd, 1 H, *J* = 14.0, 7.5, 4.0), 1.30 (s, 3 H), 1.07 (d, 3 H, *J* = 6.5), 1.04 (s, 3 H), 0.94 (t, 9 H, *J* = 7.8), 0.89 (s, 9 H), 0.61 (q, 6 H, *J* = 7.8), 0.06 (s, 3 H), 0.06 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) _ 215.7, 164.2, 154.3, 152.9, 142.2, 136.5, 118.8, 116.6, 115.4, 94.8, 82.9, 78.0, 76.3, 76.1, 57.1, 54.5, 54.0, 42.3, 39.5, 35.3, 35.0, 31.4, 28.5, 26.1, 24.0 (two C's), 20.0, 19..2, 18.2, 16.1, 14.0. 11.6, 6.9, 4.8, -3.6, -3.9

**IR** (thin film) 2955, 2879, 1759, 1698, 1462, 1384, 1250, 1081, 992, 927, 837

**HRMS** (ESI) calc'd for $(C_{42}H_{72}Cl_3NO_7SSi_2Na)^+$, 918.3531; found, 918.3649




**86**

**Carbonic acid (5*S*)-(*tert*-butyl-dimethyl-silanyloxy)-(2*R*),4,4-trimethyl-(1*S*)- ((1*R*)-methyl-4-{(*2S*, 3*R)*-[3-methyl-4-(2-methyl-thiazol-4-yl)-(2*S*)-(triethyl-silanyloxy)-but –(3*E*)-enyl]-oxiranyl}-butyl)-3,7-dioxo-heptyl ester 2,2,2-trichloro-ethyl ester (86)**. To the Troc ester (113 mg, 0.126 mmol, 1.00 equiv) in 4:4:1 tBuOH:THF:$H_2O$ (3.4 ml) at 0 °C was added NMO (17.6 mg, 0.151 mmol, 1.20 equiv) followed by $OsO_4$ (4 wt % in $H_2O$, 40 _l, 0.006 mmol, 0.04 equiv). The yellow solution was warmed to rt, stirred 18 h, and quenched by the addition of sodium bisulfite (10 mg). The reaction was diluted with $H_2O$ (5 ml) and extracted with EtOAc (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure to give a slightly yellow oil which was used without further purification.

To the crude diol (0.126 mmol, 1.00 equiv) in 3.0 ml EtOAc at 0 °C was added $Pb(OAc)_4$ (approx. 90%, 93 mg, 0.19 mmol, 1.5 equiv) in two portions. The reaction became bright yellow and a precipitate formed rapidly. After 8 min, the reaction was diluted with EtOAc (5 ml), filtered over a small plug of silica gel, and eluted with $Et_2O$ (50 ml). Concentration under reduced pressure and purification by flash chromatography (4:1 hexanes/EtOAc) provided **86** (98.0 mg, 86% for two steps).

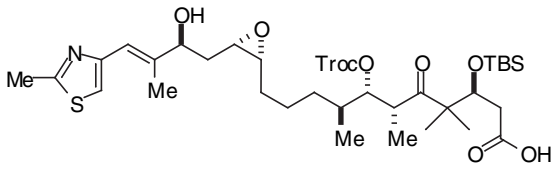
**Optical Rotation:** $[\alpha]_D^{22}$ (c 1.012, $CHCl_3$) = –32.4

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 9.74 (t, 1 H, *J* = 1.0), 6.93 (s, 3 H), 6.52 (s, 1 H), 4.84 (d, 1 H, *J* = 11.8), 4.75 (dd, 1 H, *J* = 7.7, 4.1), 4.68 (d, 1 H, *J* = 11.8), 4.36-4.32 (m, 2 H), 3.49-3.40 (m, 1 H), 3.08 (ddd, 1 H, *J* = 4.4, 7.8, 4.4), 2.96-2.88 (m, 1 H), 2.70 (s, 3 H), 2.65 (dd, 1 H, *J* = 17.7, 4.1), 2.40 (ddd, 1 H, *J* = 17.7, 5.3, 1.0), 2.01 (s, 3 H), 1.83 (ddd, 1 H, *J* = 14.0, 9.0, 4.4), 1.84-1.64 (m, 2 H), 1.62-1.15 (m, 6 H), 1.34 (s, 1 H), 1.06 (d, 3 H, *J* = 6.9), 1.03 (s, 3 H), 0.96 (d, 3 H, *J* = 6.9(, 0.94 (t, 9 H, *J* = 7.8), 0.61 (q, 6 H, *J* = 7.8), 0.11 (s, 3 H), 0.02 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 215.5, 200.5, 164.5.,154.2, 142.2, 118.8, 115.4, 94.7, 82.3, 76.6, 76.1, 72.2, 57.1, 54.5, 53.4, 49.4, 42.2, 35.3, 34.9, 31.6, 28.5, 25.9, 23.9, 23.0, 20.0, 19.2, 18.1, 16.0, 14.0, 11.2, 6.9, 6.8, 4.8, 4.7, -4.4, -4.5

**IR** (thin film).2956, 2845, 1758, 1726, 1699, 1463, 1385, 1251, 1082, 1003, 837, 776, 731

**HRMS** (ESI) calc'd for $(C_{41}H_{70}C_{13}NNaO_8SSi_2H)^+$ 898.3504, found 898.3479, calc'd for $(MNa)^+$, 920.3324; found, 920.3311; calc'd for $(MK)^+$, 936.3063, found 936.3077




**87**

**(3*S*)-(*tert*-Butyl-dimethyl-silanyloxy)-11-{(*2S*,3*R*)-[(2*S*)-hydroxy-3-methyl-4-(2-methyl-thiazol-4-yl)-but-(3*E*)-enyl]-oxiranyl}-4,4,(6*S*),(8*R*)-tetramethyl-5-oxo-(7*S*)-(2,2,2-trichloro-ethoxycarbonyloxy)-undecanoic acid (87).** To **86** (94.6 mg, 0.105 mmol, 1.00 equiv) in 4.0 ml THF at 0 °C was added diluted HF•pyr (0.4 ml of a solution prepared by adding 1.0 ml commerical HF•pyr to 4.0 ml pyr at –20° C with vigourous stirring). The reaction was warmed to rt and stirred 1.5 h before EtOAc (10 ml) was added and this solution carefully neutralized by addition to a cold (-10 °C) solution of sat. aq. $NaHCO_3$ (5 ml). The aqueous phase was extracted with EtOAc (3 x 10 ml), and the combined organic solutions washed with brine (20 ml) and dried over $Na_2SO_4$. Concentration under reduced pressure followed by azetropic removal of pyridine (3 x 5 ml cyclohexane) provided the alcohol (82.8 mg, 100% crude yield) which was used without further purification.

To the unpurified alcohol (82.8 mg, 0.104 mmol, 1.00 equiv) in 4.0 ml *tert*-BuOH and 1.3 ml 2-methyl-2-butene at 0 °C was added $NaClO_2$ (90.4 mg, 1.04 mmol, 10.0 equiv) in 700 _l pH 3.6 buffer (Citric acid-$Na_2HPO_4$). The reaction was stirred at 0 °C for 1.5 h, acidified with pH 2 buffer (phosphate), and extracted with EtOAc (4 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (1:1 hexanes/EtOAc) gave **87** (63.2 mg, 76% yield for two steps) as a white foam.

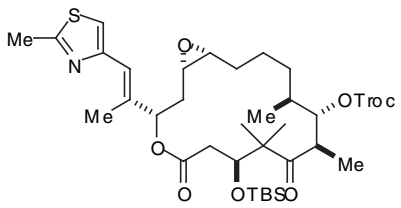
**Optical Rotation:** $[\alpha]_D^{21}$ (c 1.575, $CHCl_3$) = –39.7

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.96 (s, 1 H), 6.68 (s, 1 H), 4.88 (d, 1 H, *J* = 11.8), 4.78 (dd, 1 H, *J* = 7.8, 3.4), 4.68 (d, 1 H, *J* = 11.8), 3.50-3.39 (m, 1 H), 3.44 (dd, 1 H, *J* = 6.9, 3.6), 3.15-3.07 (m, 1 H), 3.03-2.99 (m, 1 H), 2.69 (s, 3 H), 2.60 (dd, 1 H, *J* = 17.1 2.8), 2.27 (dd, 1 H, *J* = 17.1, 6.9), 2.01 (s, 3 H), 1.90 (dd, 1 H, *J* = 6.9, 1.6), 1.89-1.68 (m, 2 H), 1.64-1.19 (m, 6 H), 1.22 (s, 3 H), 1.11 (s, 3 H), 1.08 (d, 3 H, *J* = 6.9), 0.99 (d, 3 H, *J* = 6.9), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 215.1, 175.9, 165.3, 154.2, 152.2, 142.3, 118.4, 115.5, 94.7, 81.7, 76.6, 75.0, 73.8, 67.2, 54.8, 54.3, 41.2, 39.9, 34.8, 33.6, 31.8, 28.1, 26.0, 23.4, 22.9, 19.0, 18.8, 18.2, 15.8, 14.9, 11.4, -4.3, -4.7

**IR** (thin film) 3393, 2931, 2858, 1757, 1702, 1463, 1385, 1252, 1088, 1061, 925, 836, 777, 732

**HRMS** (ESI) calc'd for $(C_{35}H_{57}NO_9SSiNa)^+$, 800.2589, found 800.2564, calc'd for $(MNa)^+$, 822.2408; found, 822.2399




**88**

**Carbonic acid (7*S*)-(*tert*-butyl-dimethyl-silanyloxy)-8,8, (10*R*,12*S*)-tetramethyl-(3*S*)-[1-methyl-(2*E*)-(2-methyl-thiazol-4-yl)-vinyl]-5,9-dioxo-4,17-dioxa-bicyclo[14.1.0]heptadec-(11*S*)-yl ester 2,2,2-trichloro-ethyl ester (88).** To **87** (60.7 mg, 0.0758 mmol, 1.00 equiv) in 5.0 ml THF at 0 °C was added $NEt_3$ (65 _l, 0.455 mmol, 6.00 equiv) followed by 2,4,6-trichlorobenzoylchloride (59.2 _l, 0.379 mmol, 5.00 equiv). The clear solution was stirred 0.5 h at 0 °C, warmed to rt, and diluted with 10 ml toluene. This solution was added, with the aid of a syringe pump, to a solution of DMAP (72.4 mg, 0.758 mmol, 10.0 equiv) in 28 ml toluene over 3 h to give a cloudy mixture. This slurry was filtered over a plug of silica gel and the product eluted with 1:1 hexanes/EtOAc (200 ml). Concentration under reduced pressure and

purification by flash chromatography (4:1 hexanes/EtOAc) provided **88** (43.1 mg, 74% yield) as an off-white gum.

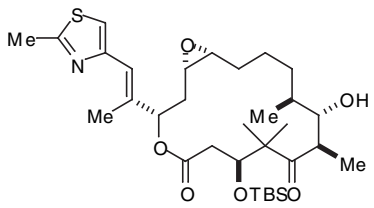
**Optical Rotation:** $[\alpha]_D^{30}$ (c 1.075, $CDCl_3$) = +3.9

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.99 (s, 1 H), 6.56 (s, 1 H), 5.24-5.18 (m, 2 H), 4.87 (d, 1 H, *J* = 11.8), 4.74 (d, 1 H, *J* = 11.8), 4.02 (d, 1 H, *J* = 10.6), 3.32-3.20 (m, 1 H), 3.05-2.97 (m, 1 H), 2.87-2.81 (m, 2 H), 2.71 (s, 3 H), 2.63 (dd, 1 H, *J* = 16.2, 10.6), 2.29-2.22 (m, 1 H), 2.10 (s, 3 H), 1.91-1.22 (m, 9 H), 1.21 (s, 3 H), 1.19 (s, 3 H), 1.10 (d, 3 H, *J* = 6.5), 1.01 (d, 3 H, *J* = 6.8), 0.86 (s, 9 H), .16 (s, 3 H), -0.07 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 212.2, 171.0, 164.9, 154.6, 152.2, 137.2, 120.8, 116.9, 94.8, 86.5, 77.2, 76.7, 57.9, 55.4, 53.3, 46.0, 38.7, 35.2, 33.1, 30.9, 29.7, 26.7, 26.2, 25.5, 25.1, 23.8, 19.3, 19.1, 18.7, 16.3, 14.4, -3.3, -5.9

**IR** (thin film) 2931, 2854, 1761, 1699, 1462, 1384, 1247, 1158, 1096, 1067, 929, 827, 777, 732

**HRMS** (MALDI) calc'd for $(C_{35}H_{54}Cl_3NO_8SSiH)^+$, 782.2483; found, 782.2483




**89**

**(7*S*)-(*tert*-Butyl-dimethyl-silanyloxy)-(11*S*)-hydroxy-8,8,(10*R*,12*S*)-tetramethyl-(3*S*)-[1-methyl-(2*E*)-(2-methyl-thiazol-4-yl)-vinyl]-4,17-dioxa-bicyclo[14.1.0]heptadecane-5,9-dione (89).** To **88** (42.2 mg, 0.0538 mmol, 1.00 equiv) in 4.5 ml MeOH at rt was added $NH_4Cl$ (342 mg, 6.45 mmol, 120 equiv) followed by Zn (dust, 343 mg, 5.34 mmol, 100 equiv). After 5 min at rt, the mixture was filtered over a plug of celite and the filter pad washed with EtOAc (60 ml). Concentration under reduced pressure and purification by flash chromatography provided **89** (26.3 mg, 82% yield) as a white gum. The remaining material (7.9 mg) was identified as the dichloroethoxycarbonate product (**90**).

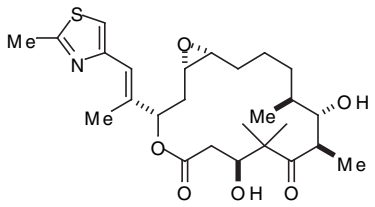
**Optical Rotation:** $[\alpha]_D^{22}$ (c 0.6250, $CH_2Cl_2$) = –32.6

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.00 (s, 1 H), 6.56 (s, 1 H), 5.23 (d, 1 H, *J* = 10.6), 4.06 (d, 1 H, *J* = 9.3), 3.93-3.90 (m, 1 H), 3.07-2.98 (m, 1 H), 2.89-2.79 (m, 2 H), 2.71 (s, 3 H), 2.69 (dd, 1 H, *J* = 10.7), 2.29-2.21 (m, 1 H), 2.10 (s, 3 H), 1.86-1.68 (m, 4 H), 1.64-1.23 (m, 5 H), 1.20 (s, 3 H), 1.17 (s, 3 H), 1.14 (d, 3 H, *J* = 6.5), 1.03 (d, 3 H, *J* = 7.2), 0.85 (s, 9 H), 0.15 (s, 3 H), -0.05 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 216.5, 171.0, 164.9, 152.1, 137.3, 120.5, 117.0, 77.2, 74.4, 58.0, 55.7, 53.4, 44.6, 39.1, 37.6, 32.9, 29.7, 27.1, 26.1, 25.5, 24.9, 23.2, 19.2, 18.7, 18.1, 15.1, 14.8, -3.5, -5.7

**IR** (thin film) 3393, 2930, 2854, 1742, 1696, 1462, 1388, 1256, 1158, 1096, 1068, 979, 837, 776

**HRMS** (MALDI) calc'd for $(C_{32}H_{53}NO_6SSiNa)^+$, 630.3261; found, 630.3272




**1a**

**Epothilone A (1a).** **89** (9.1 mg, 0.015 mmol, 1.0 equiv) was dissolved in 1.5 ml HF•pyr (3:1 pyr:[commerical HF•pyr]) and warmed to 35-40 °C under Ar. After 3 days, an additional portion of HF•pyr solution (0.3 ml) was added and heating continued for 4 days (7 days in total). The reaction was cooled to room temperature, diluted with EtOAc (7 ml) and added cautiously to a stirring solution of $NaHCO_3$ (10 ml of a 10% aqeous solution) at 0 °C. The aqueous phase was washed with EtOAc (4 x 10 ml) and the combined organic solutions were washed with brine (20 ml) and dried over $Na_2SO_4$. Concentration under reduced pressure and azetropic removal (3 x 5 ml cyclohexane) of residual pyridine gave a slighly yellow oil which was judged 40% conversion by $^1$H NMR analysis (remainder starting material). Purification by column chromatography (1:1 hexanes/EtOAc) afforded recovered **1a** (3.2 mg) and synthetic epothilone A (2.6 mg, 38% yield) identical in all respects to that previously reported.

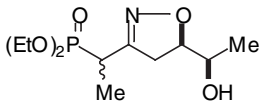
**Optical Rotation:** $[\_]_D^{22}$ (c. 0.02, MeOH) = –44

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.71 (s, 1 H), 6.47 (s, 1 H), 5.46 (dd, 1 H, *J* = 8.3, 2.5), 4.23-4.00 (m, 1 H), 3.81-3.69 (m, 1 H), 3.54 (d, 1 H, OH, *J* = 6.9), 3.03(dq, 1 H, *J* = 6.8, 6.7), 2.77 (ddd, 1 H, *J* = 7.9, 4.4, 4.4), 2.68-2.59 (m, 1 H), 2.40 (dd, 1 H, *J* = 14.4, 10.8), 2.22 (s, 3 H), 2.20 (dd, 1 H, *J* = 14.4, 3.2), 2.07 (s, 3 H), 1.87 (ddd, 1 H, *J* = 15.1, 5.0, 2.7), 1.81-1.74 (m, 1 H), 1.70-1.64 (m, 2 H), 1.52-1.48 (m, 1 H), 1.41-1.14 (m, 5 H), 1.06 (d, 3 H, *J* = 6.9), 1.03 (s, 3 H), 0.97 (s, 3 H), 0.95 (s, 3 H, *J* = 6.9)

**$^{13}$C NMR** ($C_6D_6$, 125 MHz) δ 291.0, 120.2, 164.8, 153.1, 137.5, 120.0, 116.7, 76.7, 75.2, 73.6, 57.2, 54.2, 52.9, 43.9, 39.2, 36.3, 31.7, 30.4, 27.4, 24.0, 21.1, 20.7, 18.8, 17.4, 15.7, 14.7

**IR** (thin film) 3357, 2923, 2853, 1740, 1465

**HRMS** (MALDI) calc'd for $(C_{26}H_{40}NO_6SNa)^+$, 416.2396; found, 416.2393




**20**

**{1-[5-((1*R*)-Hydroxy-ethyl)-4,(5*R*)-dihydro-isoxazol-3-yl]-ethyl}-phosphonic acid diethyl ester (106).** To (*R*)-3-buten-2-ol (0.55 ml, 6.5 mmol, 1.3 equiv) and $^i$PrOH (1.26 ml, 16.5 mmol, 3.30 equiv) in 200 ml $CH_2Cl_2$ at 0 °C was added EtMgBr (3.0 M in $Et_2O$, 5.0 ml, 15 mmol, 3.0 equiv) and the mixture stirred 0.5 h before **18** (1.22 g, 5.00 mmol, 1.00 equiv) in 25 ml $CH_2Cl_2$ was added in one portion. The slightly yellow solution was allowed to warm slowly to rt and stirred 36 h, at which time it was quenched by the addition of sat. aq. $NH_4Cl$ (150 ml) and $H_2O$ (50 ml). The aqueous layer was extracted with EtOAc (3 x 100 ml) and the combined organic solutions were washed with brine (300 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Flash chromatography (15% acetone in EtOAc) afforded (1.09 g, 79% yield) **20** as a clear, colorless oil.

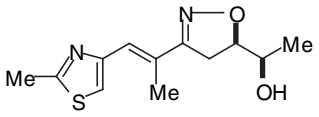
**Optical Rotation:** $[\alpha]_D^{24}$ (c 1.254, $CHCl_3$) = -72.0

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 4.46-4.37 (m, 1H), 4.20-4.03 (m, 4H), 3.73-3.63 (m, 1H), 3.24-3.06 (m, 2H), 3.03-2.83 (m, 1H), 1.50-1.40 (m, 3H), 1.36-1.30 (m, 3H), 1.21 (dd, 3H, *J* = 6.2, 2.8)

**$^{13}$C NMR** (75 MHz, $CDCl_3$, * denotes minor diastereomeric peak) δ 156.9*, 156.8, 84.4, 84.3*, 69.2*, 69.1, 62.7* (d, *J* = 7.3), 62.6 (d, *J* = 7.3), 38.0*, 37.8, 32.3* (d, *J* = 140.4), 32.2 (d, *J* =140.4), 18.8*, 18.6, 16.5*, 16.4, 12.3* (d, *J* = 6.1), 12.2 (d, *J* = 4.9)

**IR** (thin film) 3402, 2982, 2939,, 1458, 1393, 1249, 1219, 1054, 1021, 967, 895

**Anal. Calc'd** for $C_{11}H_{22}NO_5P$: C, 47.31; H, 7.94; N, 5.02. Found: C, 47.61; H, 7.84; N, 5.06.




**91**

**1-{3-[1-Methyl-(2*E*)-(2-methyl-thiazol-4-yl)-vinyl]-4,(5*R*)-dihydro-isoxazol-5-yl) –ethan-(2*R*)-ol (91).** To (511 mg, 2.16 mmol, 1.00 equiv) in 25 ml $CH_3CN$ was added LiCl (127 mg, 2.60 mmol, 1.20 equiv) followed by DBU (332 _l, 2.16 mmol, 1.00 equiv) and the yellow, slightly cloudy mixture was stirred 15 min at rt before **44** (475 mg, 3.75 mmol, 1.50 equiv) was added as a solid in two portions. After 1 h an additional portion of DBU (100 _l) was added and the mixture stirred 1.5 h before $H_2O$ (10 ml) and brine (15 ml) were added and the resulting solution extracted with EtOAc (3 x 30 ml). The combined organic solutions were washed with brine (50 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatrography (3:2 EtOAc/hexanes) provided **91** (405 mg, 93% yield, 8:1 *trans:cis*) as a clear, colorless oil.

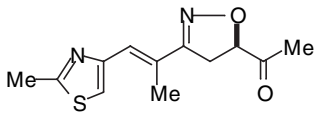
**Optical Rotation:** $[\alpha]_D^{27}$ (c 1.046, $CHCl_3$) = –109.1

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.17 (s, 1 H), 6.72 (s, 1 H), 4.53 (ddd, 1 H, *J* = 10.5, 7.5, 5.6), 3.80-3.70 (m, 1 H), 3.23 (dd, 1 H, *J* = 16.2, 10.5), 3.02 (dd, 1 H, *J* = 16.2, 7.5), 2.73 (s, 3 H), 2.37 (s, 3 H), 2.20-2.18 (m, 1 H), 1.26 (d, 3H, *J* = 6.2). (*trans* olefin isomer only)

**$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 165.2, 160.5, 151.9, 129.5, 126.4, 118.4, 85.4, 69.3, 36.4, 19.2, 18.9, 15.0. (*trans* olefin isomer only)

**IR** (thin film) 3400, 2969, 2926, 1440, 1371, 1181, 1135, 938, 911

**HRMS** (MALDI) calc'd for $(C_{12}H_{16}N_2O_2SNa)^+$, 275.0830; found: 275.0827



**92**

**1-{3-[1-Methyl-(2*E*)-(2-methyl-thiazol-4-yl)-vinyl]-4,(5*R*)-dihydro-isoxazol-5-yl) –ethanone (92).** To **91** (1.25 g, 5.00 mmol, 1.00 equiv) in 50 ml $CH_2Cl_2$ at rt was added NMO (878 mg, 7.50 mmol, 1.50 equiv) and 4 Å molecular sieves (4 g). The mixture was stirred 0.5 h at rt before TPAP (90 mg, 0.25 mmol, 0.05 equiv) was added as a solid in two portions to give a green mixture. After 10 min, the reaction had become dark red and after 20 min the mixture was diluted with pentane (50 ml) and filtered over a plug of silica gel, eluting with 3:1 $Et_2O/CH_2Cl_2$ (200 ml). Purification by flash chromatography (2:1 hexanes/EtOAc) provided **92** (1.05 g, 86% yield) as a white powder. Recrystallization ($Et_2O$) provided material free of any *cis* olefin isomer.

**Optical Rotation:** $[\alpha]_D^{22}$ (c 1.040, $CHCl_3$) = –233.5

**MP**: 94 °C

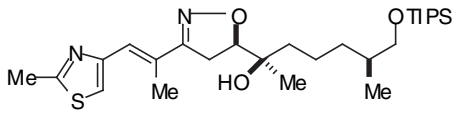
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.17 (s, 1 H), 6.72 (s, 1 H), 4.98 (dd, 1H, *J* = 11.5, 6.5), 3.49 (dd, 1 H, *J* = 16.5, 6.2), 3.35 (dd, 1 H, *J* = 16.5, 11.5), 2.73 (s, 3H), 2.39 (s, 3 H), 2.33 (s, 3 H)

**$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 207.4, 165.2, 160.1, 151.8, 128.8, 127.1, 118.9, 85.0, 36.5, 26.3, 19.2, 15.1

**IR** (KBr) 3419, 1720, 1617, 1507, 1361, 1300, 1182, 1128, 936, 901, 754, 630

**EI-MS**: 501.9 (13.1, $[2M+H]^+$), 500.8 (53.0, [2M]), 251.0 (100.0, $[M+H]^+$)

**Anal. calc'd** for $C_{12}H_{14}N_2O_2S$: C, 57.58%; H, 5.64%; N, 11.19%; found, C 57.62%; H, 5.75%; N, 11.05%



**94**

**(6*S*)-Methyl-2-{3-[1-methyl-(2*E*)-(1-methyl-2-(2-methyl-thiazol-4-yl)-vinyl]-4,(5*S*)-dihydro-isoxazol-5-yl}-7-triispropylsilanyloxy-heptan-(2*R*)-ol (94).** To **92** (201 mg, 0.801 mmol, 1.00 equiv) in 15 ml THF at –78 °C was added the precooled (–78 °C) Grignard reagent

**93** (1.2 mmol, 1.5 equiv) via cannula. The initially clear, colorless solution becomes cloudy and the resulting slurry was stirred 30 min at –78 °C. The reaction was quenched with sat. aq. $NH_4Cl$ (15 ml), warmed to rt, and extracted with $Et_2O$ (3 x 20 ml). The combined organic solutions were washed with brine (40 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (5:2 hexanes/EtOAc) provided **94** (327 mg, 81% yield) as a clear, colorless oil and as a single diastereomer by $^1H$ and $^{13}C$ NMR analysis.

**Optical Rotation:** $[\alpha]_D^{24}$ (c 1.375, $CHCl_3$) = –68.1

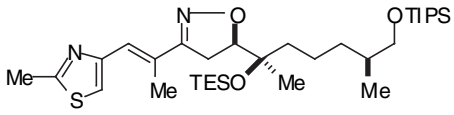
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.16 (s, 1H), 6.74 (s, 1H), 4.57 (dd, 1H, *J* = 9.3, 10.8), 3.53 (dd, 1 H, *J* = 5.9, 9.65), 3.47 (dd, 1 H, *J* = 6.5, 9.65), 3.25 (dd, 1H, *J* = 9.3, 16.2), 3.12 (dd, 1 H, *J* = 10.8, 16.2), 2.73 (s, 3 H), 2.36 (s, 3 H), 1.73 (s, 1 H, OH), 1.70-1.30 (m, 7 H), 1.16-1.05 (m, 3 H), 1.05 (d, 18 H, *J* = 3.4), 1.12 (s, 3H), 0.91 (d, 3 H, *J* = 6.9)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 165.1, 160.8, 152.0, 129.6, 126.3, 118.2, 87.2, 73.1, 68.6, 39.6, 36.0, 34.8, 33.7, 21.5, 21.2, 19.2, 18.1, 16.8, 14.9, 12.0

**IR** (thin film) 3393, 2942, 2865, 1462, 1371, 1099, 1068, 1099, 1068, 916, 882, 774

**HRMS** (MALDI) calc'd for $(C_{33}H_{63}NO_4SSi_2Na)^+$, 531.3053; found, 531.3050

**Anal. calc'd** for $C_{27}H_{48}N_2O_3SiS$: C, 63.73%; H, 9.51%; N, 5.51%; found, C 63.84%; H, 9.49%; N, 5.38%




**95**

**5-[1,(5*S*)-Dimethyl-(1*R*)-(triethyl-silanyloxy)-6-(triisopropyl-silanyloxy)-hexyl]-3-[1-methyl-(2*E*)-(2-methyl-thiazol-4-yl)-vinyl]-4,(5*S*)-dihydro-isoxazole (95).** To **94** (0.640 g, 1.27 mmol, 1.00 equiv) in 12 ml $CH_2Cl_2$ at 0 °C was added Hünig's base (648 _l, 3.81 mmol, 3.00 equiv) followed by dropwise addition of TESOTf (604 _l, 3.18 mmol, 2.50 equiv). After 15 min, the reaction was quenched with sat. aq. $NaHCO_3$ (10 ml) and extracted with $CH_2Cl_2$ (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (10:1 hexanes/EtOAc) provided **95** (781 mg, 98% yield) as a clear, colorless oil.

**Optical Rotation:** $[\alpha]_D^{29}$ (c 1.730, $CHCl_3$) = –81.6

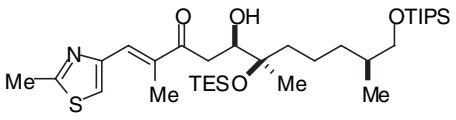
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.16 (s, 1 H), 6.72 (s, 1 H), 4.56 (dd, 1 H, *J* = 8.4, 11.2), 3.55-3.41 (m, 2 H), 3.21 (dd, 1 H, *J* = 8.4, 16.5), 3.08 (dd, 1 H, *J* = 11.2, 16.5), 2.74 (s, 1 H), 2.36 (s, 1 H), 1.73-1.53 (m, 2H), 1.51-1.30 (m, 5H), 1.19 (s, 3H), 1.12-1.01 (m, 3 H), 1.05 (d, 18 H, *J* = 3.4), 0.90 (d, 3 H, *J* = 6.9), 0.92 (t, 9 H, *J* = 7.8), 0.58 (q, 6 H, *J* = 7.8)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.9, 159.8, 152.2, 130.1, 125.5, 117.8, 87.4, 76.4, 68.6, 38.7, 35.9, 34.9, 33.8, 24.0, 21.5, 19.2, 18.1, 16.7, 15.0, 12.0, 7.1, 6.8

**IR** (thin film) 2946, 2871, 1462, 1373, 1097, 1014, 916, 882

**HRMS** (MALDI) calc'd for $(C_{33}H_{62}N_2O_3Si_2SNa)^+$, 645.3917; found, 645.3915

**Anal. calc'd** calc'd for ($C_{33}H_{62}N_2O_3Si_2S$) C, 63,61%; H, 10,03%; N, 4.50%; found, C, 63.74%; H, 10.04%; N, 4.61%




**96**

**(5*R*)-Hydroxy-2,6,(10*S*)-trimethyl-1-(2-methyl-thiazol-4-yl)-(6*R*)-(triethyl-silanyloxy)-11-(triisopropyl-silanyloxy)-undec-(1*E*)-en-3-one (96).** To **95** (171 mg, 0.275 mmol, 1.00 equiv) in 12 ml degassed THF at 0 °C was added $SmI_2$ (0.10 M in THF, 8.0 ml, 0.80 mmol, 2.9 equiv) slowly, maintaining a dark blue-green color throughout the reaction period. After the addition was complete, additional $SmI_2$ (1.0 ml) was added and the dark blue solution was stirred 20 min at 0 °C before the reaction was quenched with $O_2$, To the resulting bright yellow solution was added $H_2O$ (8 ml) and $B(OH)_3$ (0.25 g) and the mixture stirred 30 min at rt. Following addition of $Et_2O$ (10 ml) and careful separation of the layers to avoid an emulsion, the aqueous phase was extracted with $Et_2O$ (3 x 15 ml). The combined organic solutions were washed with brine (30 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatrography (8:1 hexanes/EA) provided **96** (127 mg, 75%) as a clear, colorless oil.

**Optical Rotation:** $[\alpha]_D^{22}$ (c 1.080, $CHCl_3$) = +20.7

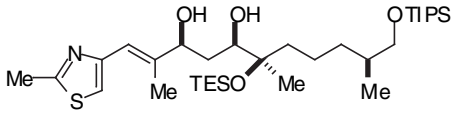
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.53 (s, 1 H), 7.35 (s, 1 H), 4.03-3.98 (m, 1 H), 3.56-3.51 (m, 1 H), 3.48-3.42 (m, 1 H), 3.04-2.80 (m, 2 H), 2.76 (s, 3 H), 2.25 (s, 3 H), 1.72-1.59 (m, 2 H), 1.53 (t, 1 H, *J* = 1.1, OH), 1.49-1.29 (m, 5 H), 1.24 (s, 3 H), 1.05 (d, 18 H, *J* = 5.3) 1.05 (sept, 3 H, *J* = 5.3), 0.95 (t, 9 H, *J* = 7.8), 0.90 (d, 3 H, *J* = 6.9), 0.61 (q, 6 H, *J* = 7.8)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 202.4, 165.4, 151.8, 137.6, 131.5, 121.5, 76.6, 73.7, 68.6, 39.0, 36.1, 33.9, 33.8, 24.0, 21.3, 19.3, 18.1, 16.8, 13.4, 12.0, 7.2, 6.9

**IR** (thin film) 2946, 2863, 1658, 1460, 1095, 1070, 1012, 883

**HRMS** (MALDI) calc'd for $(C_{33}H_{63}NO_4SSi_2Na)^+$, 648.3914; found, 648.3904

**Anal. calc'd** for $(C_{33}H_{63}NO_4SSi_2)$ C, 63.31%; H, 10.14%; N, 2.24%; found, C, 63.43%; H, 10.00%; N, 2.30%




**97**

**2,6,(10*S*)-Trimethyl-1-(2-methyl-thiazol-4-yl)-(6*R*)-(triethyl-silanyloxy)-11-(triisopropyl-silanyloxy)-undec-(1*E*)-en-(3*S*,5*R*)-diol (97).** A solution of $BEt_3$ (1.0 M in THF, 440 _l, 0.440 mmol, 1.10 equiv) in 3.5 ml THF and 1.0 ml MeOH at rt was stirred for 20 min before being cooled to –78 °C. Ketone **96** (249 mg, 0.400 mmol, 1.00 equiv) in 3.0 ml THF was added via cannula and stirred 1 h at –78 °C before $NaBH_4$ (100 mg, 2.70 mmol, 6.75 equiv) was added as a solid in two portions. After 4 h, 6 h, and 9 h at –78 °C, additional $NaBH_4$ was added (50 mg) and after 10.5 h the reaction was quenched by addition of sat. aq. $NH_4Cl$ (10 ml). The mixture was extracted with EtOAc (3 x 15 ml), and the combined organic solutions were washed with brine (30 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (3:2 hexanes/EtOAc) provided **97** (221 mg, 88% yield) as a clear, colorless oil.

**Optical Rotation:** $[\alpha]_D^{27}$ (c 0.922, $CHCl_3$) = +8.2

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.94 (s ,1 H), 6.60 (s, 1 H), 4.38-4.36 (m 1 H), 3.97 (d, 1 H, *J* = 4.4), 3.77-3.71 (m, 1 H), 3.52-3.42 (m, 2 H), 2.81 (d, 1 H, *J* = 4.4), 2.71 (s, 3 H), 2.05 (s, 3 H),

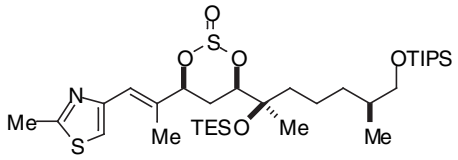
1.76-1.50 (m, 4 H), 1.53 (t, 2.0, OH), 1.48-1.12 (m, 5 H), 1.17 (s, 3 H), 1.05 (d, 18 H, *J* = 5.3), 1.05 (sept, 3 H, *J* = 5.3), 0.96 (t, 9 H, *J* = 7.8), 0.89 (d, 3 H, *J* = 7.8), 0.62 (q, 6 H, J= 7.8)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.5, 153.1, 141.9, 118,6, 115.5, 78.1, 77.2, 76.6, 68.6, 39.8, 36.1, 36.0, 33.8, 23.1, 21.2, 19.2, 18.1, 16.7, 14.5, 12.0, 7.13, 6.8

**IR** (thin film). 3369 (br), 2946, 2871, 1461, 1381, 1240, 1157, 1096, 1012, 882.

**HRMS** (MALDI) calc'd for $(C_{33}H_{65}NO_4SSi_2Na)^+$, 650.4071; found, 650.4063

**Anal. calc'd** for ($C_{33}H_{65}NO_4SSi_2$) C, 63.10%; H, 10.43%; N, 2.23%; found, C, 63.32%; H, 10.30%; N, 2.17%




**4-(2-{6-[1,(5*S*)-Dimethyl-(1*R*)-(triethyl-silanyloxy)-6-(triisopropyl-silanyloxy)-hexyl]-2-oxo-2l4-[(1*R*),3,2]dioxathian-4-yl}-(*E*)-propenyl)-2-methyl-thiazole.** To **97** (95.0 mg, 0.151 mmol, 1.00 equiv) in 2.5 ml $Et_2O$ at –78 °C was added pyridine (0.036 µl, 0.451 mmol, 3.20 equiv, d 0.978) followed by $SOCl_2$ (1.0 M in $CH_2Cl_2$, 210 _l, 0.21 mmol, 1.5 equiv). After 15 min at –78 °C, the reaction was quenched by addition of sat. aq. $NaHCO_3$ (2 ml), the mixture warmed to rt and diluted with $H_2O$ (2 ml) and $Et_2O$ (8 ml). The aqueous phase was extracted with $Et_2O$ (3 x 10 ml) and the combined organic solutions washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure.

If desired, this material could be purified by flash chromatography (8:1 hexanes/EtOAc) to give the pure cyclic sulfite (81.4 mg, 80% yield) as a single stereoisomer. In practice, the crude material was used directly in the next step.

**Optical Rotation:** $[\alpha]_D^{22}$ (c 1.548, $CHCl_3$) = –4.5

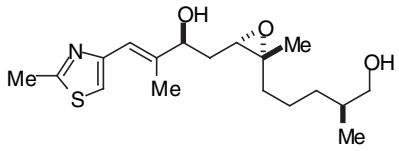
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.01 (s, 1 H), 6.57 (s, 1 H), 5.43 (d, 1 H, *J* = 11.8), 4.80 (d, 1 H, *J* = 11.8), 3.52-3.44 (m, 2 H), 2.72 (s, 3 H), 2.28 (q, 1 H, *J* = 13.9), 2.11 (s, 3 H), 1.83 (d, 1 H, *J* = 13.9), 1.69-1.50 (m, 2 H), 1.50- 1.18 (m, 5 H), 1.25 (s, 1 H), 1.05 (d, 18 H, *J* = 7.8), 1.05 (sept, 3 H, *J* = 7.8), 0.95 (t, 9 H, *J* = 7.8), 0.90 (d, 3 H, *J* = 6.5), 0.60 (q, 6 H, *J* = 7.8)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.9, 152.1, 136.4, 121.3, 117.0, 76.1, 73.2, 72.6, 68.5, 38.9, 35.8, 33.7, 30.2, 23.9, 21.1, 19.2, 18.1, 16.6, 14.5, 12.0, 7.1, 6.9

**IR** (thin film).2953, 2871, 1462, 1377, 1186, 1099, 1014, 882

**MALDI-TOF MS**: 674.1 $(MH)^+$

**HRMS** (MALDI) calc'd for $(M\text{-}SO_2)^+$, 610.4145; found, 610.4250; calc'd for $(MNa\text{-}SO_2)$, 632.3965, found 632.4067




**98**

**1-[3-(5-Hydroxy-(4*S*)-methyl-pentyl)-(2*S*,3*R*)-methyl-oxiranyl]-3-methyl-4-(2-methyl-thiazol-4-yl)-but-(3*E*)-en-(2*S*)-ol (98).** To the cyclic sulfite (78.0 mg, 0.116 mmol, 1.0 equiv) in 5.0 ml THF was added TBAF•$3H_2O$ (168 mg, 0.531 mmol, 5.0 equiv) and the yellow solution warmed to 65° C. After 2 h, the reaction was cooled to rt, diluted with $H_2O$ (10 ml), and extracted with EtOAc (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatrography (2:1 – 3:1 EtOAc/hexanes) provided **98** (30.2 mg, 77% yield) as a clear colorless oil.

**Optical Rotation:** $[\alpha]_D^{23}$ (c 1.405, $CHCl_3$) = –16.4

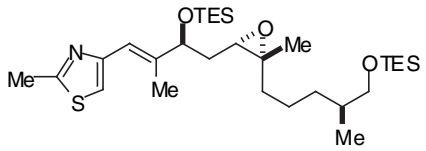
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.93 (s, 1 H), 6.60 (s, 1 H), 4.35 (dd, 1 H, *J* = 8.5, 4.0), 3.48-3.41 (m, 2 H), 2.98 (dd, 1 H, *J* = 7.8, 4.1), 2.68 (s, 3 H), 2.01 (s, 3 H), 1.94 (ddd, 1 H, *J* = 14.3, 8.5, 4.0), 1.68 (ddd, 1 H, *J* = 14.3, 7.8, 4.1), 1.64-1.31 (m, 7H), 1.28 (s, 3 H), 0.90 (d, 3 H, *J* = 6.5)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.8, 152.6, 142.2, 118.7, 115.6, 75.1, 68.0, 61.9, 61.1, 35.7, 34.1, 33.3, 33.1, 22.8, 22.2, 19.1, 16.6, 14.6

**IR** (thin film). 3369, 2927, 2871, 1448, 1379, 1190, 1048, 879, 854

**HRMS** (MALDI) calc'd for $(C_{18}H_{29}NO_3SNa)^+$, 362.1766; found, 362.1759

**Anal. calc'd** for ($C_{18}H_{29}NO_3S$) C, 63.68%; H, 8.61%; N, 4.13%; found, C, 63.71%; H, 8.48%; N, 3.93%




**99**

**2-Methyl-4-[2-methyl-4-{3-methyl-(2*S*,3*R*)-[(4*S*)-methyl-5-(triethyl-silanyloxy)-pentyl]-oxiranyl}-(3*S*)-(triethyl-silanyloxy)-but-(1*E*)-enyl]-thiazole (99).** To **98** (54 mg, 0.16 mmol, 1.0 equiv) in 2.5 ml $CH_2Cl_2$ at 0 °C was added $NEt_3$ (182 _l, 1.28 mmol, 8.00 equiv) followed by TESCl (84.3 _l, 0.800 mmoL, 5.00 equiv) and DMAP (2 mg). The clear, colorless solution was allowed to warm slowly to rt and stirred 12 h before the reaction was quenched with sat. aq. $NaHCO_3$ (5 ml) and extracted with $CH_2Cl_2$ (3 x 10 ml). The combined organic solutions were washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatrography (15:1 hexanes/EtOAc) provided **99** (71.1 mg, 79% yield) as a clear colorless oil.

**Optical Rotation:** $[\alpha]_D^{27}$ (c 0.956, $CHCl_3$) = –6.2

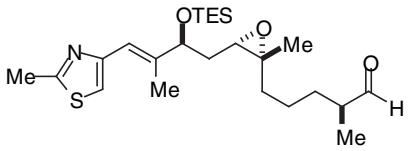
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.93 (s, 1 H), 5.53 (s, 1 H), 4.34 (dd, 1 H, *J* = 9.3, 4.2), 3.46-3.32 (m, 2 H), 2.89 (dd, 1 H, *J* = 7.5, 4.4), 2.71 (s, 3 H), 2.02 (s, 3 H), 1.90 (ddd, 1 H, *J* = 14.0, 9.3, 4.4), 1.60 (ddd, 1 H, *J* = 14.0, 7.5, 4.2), 1.61-1.31 (m, 7 H), 1.28 (s, 3 H), 0.95 (t, 18 H, *J* = 7.8), 0.87 (d, 3 H, *J* = 6.5), 0.66-0.54 (m, 12 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 164.4, 153.0, 142.3, 118.7, 115.3, 76.2, 68.1, 62.1, 61.0, 36.1, 35.9, 33.5, 22.9, 22.4, 19.2, 16.6, 14.0, 6.9, 6.8, 4.8, 4.4

**IR** (thin film). 2954, 2913, 2879, 1460, 1414, 1377, 1240, 1087, 1008, 883

**HRMS** (MALDI) calc'd for $(C_{30}H_{57}NO_3SSi_2Na)^+$, 590.3495; found, 590.3495

**Anal. calc'd** for ($C_{30}H_{57}NO_3SSi_2$) C, 63.44%; H, 10.11%; N, 2.47%; found, C, 63.45%; H, 10.13%; N, 2.62%




**69**

**(2*S*)-Methyl-5-{2-methyl-(2*S*,3*R*)-[3-methyl-4-(2-methyl-thiazol-4-yl)-(2*S*)-(triethyl-silanyloxy)-but-(3*E*)-enyl]-oxiranyl}-pentanal (69).** Silyl ether **99** (56.7 mg, 0.100 mmol, 1.0 equiv) in 10:2:1 THF:AcOH:$H_2O$ (4.0 ml) was warmed to 40 °C for 3.5 h before being cooled to rt and carefully quenched with sat. aq. $NaHCO_3$ (10 ml). The mixture was extracted with $CH_2Cl_2$ (3 x 10 ml) and the combined organic solutions washed with brine (20 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure.

To the unpurified alcohol in 2.0 ml $CH_2Cl_2$ at rt was added NMO (18 mg, 0.15 mmol, 1.5 equiv) and 4 Å molecular sieves (200 mg) and the slurry stirred 0.5 h at rt before TPAP (4 mg, 0.01 mmol, 0.1 equiv) was added as a solid. After 30 min, the reaction mixture was diluted with pentane (5 ml) and filtered over a small plug of silica gel, eluting with $Et_2O$ (40 ml). Purification by flash chromatrography (7:1 – 5:1 hexanes/EtOAc) provided **69** (28.8 mg, 64% yield) as a clear colorless oil.

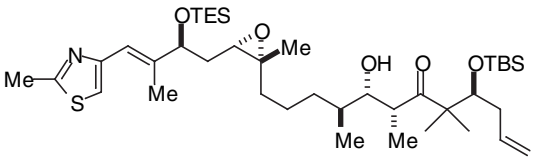
**Optical Rotation:** $[\alpha]_D^{27}$ (c 1.32, $CHCl_3$) = –8.3

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 9.61 (d, 1 H, *J* = 1.9), 6.93 (s, 1 H), 6.52 (s, 1 H), 4.33 (dd, 1 H, *J* = 9.0, 3.7), 2.89 (dd, 1 H, *J* = 7.5, 4.5), 2.70 (s, 3 H), 2.37-2.30 (m, 1 H), 2.02 (s, 3 H), 1.89 (ddd, 1 H, *J* = 14.0, 9.0, 4.5), 1.73-1.67 (m, 1 H), 1.49 (ddd, 1 H, *J* = 14.0, 7.5,3.7), 1.52-1.32 (m, 5 H), 1.27 (s, 3 H), 1.09 (d, 3 H, *J* = 7.1), 0.94 (t, 9 H, *J* = 7.8), 0.61 (q, 6 H, *J* = 7.8)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 204.9, 164.5, 152.9, 142.2, 118.8, 115.4, 76.1, 62.0, 60.7, 46.3, 36.0, 33.0, 30.6, 22.9, 22.2, 19.2, 14.0, 13.3, 6.9, 4.7

**IR** (thin film).2955, 2879, 1725, 1458, 1377, 1240, 1182, 1075, 1008, 879

**HRMS** (MALDI) calc'd for $(C_{24}H_{41}NO_3SSiNa)^+$, 474.2474; found, 474.2468




**100**

**(4*S*)-(*tert*-Butyl-dimethyl-silanyloxy)-(8*R*)-hydroxy-5,5-(7*R*,9*S*)-tetramethyl-12-{(2*R*,3*S*)-methyl-3-methyl-4-(2-methyl-thiazole-4-yl)-(2*S*)-(triethyl-silanyloxy)-but-(3*E*)-enyl]-oxirnayl}-dodec-1-en-6-one (100).** To **68** (24 mg, 0.083 mmol, 1.5 equiv) in 750 µl THF at –78 °C was added freshly prepared LDA (0.50 M in THF, 0.17 _l, 83 _mol, 1.5 equiv) and the reaction stirred 15 min at this temperature, warmed to –40 °C for 20 min, and recooled to –78 °C. Aldehyde **69** (24.2 mg, 0.0560 mmol, 1.00 equiv) in 800 _l THF was added via cannula and stirred 1 h at –78 °C. After warming to –40 °C, the reaction was quenched by addition of sat. aq. $NH_4Cl$ (4 ml) and extracted with $Et_2O$ (3 x 8 ml). The combined organic solutions were washed with brine (15 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatrography (6:1 hexanes/EtOAc) provided **100** (32.5 mg, 83% yield) as a clear colorless oil.

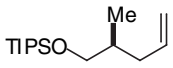
**Optical Rotation:** $[\alpha]_D^{26}$ (c 1.505, $CHCl_3$) = –17.9

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.93 (s, 1 H), 6.52 (s, 1 H), 5.83-5.74 (m, 1 H), 5.04-4.98 (m, 2 H), 4.34 (dd, 1 H, *J* = 9.0, 4.0), 3.92 (dd, 1 H, *J* = 6.2, 4.3), 3.51 (s, 1 H, OH), 3.30 (d, 1 H, *J* = 9.7), 3.25 (q, 1 H, *J* = 7.0), 2.89 (dd, 1 H, *J* = 7.5, 4.4), 2.71 (s, 3 H), 2.22-2.06 (m, 2 H), 2.01 (s, 3 H), 1.90 (ddd, 1 H, *J* = 14.0, 9.0, 4.4), 1.81-1.68 (m, 1 H), 1.60 (ddd, 1 H, *J* = 14.0, 7.5, 4.0), 1.58-1.42 (m, 4 H), 1.40-1.29 (m, 1 H), 1.28 (s, 3 H), 1.18 (s, 3 H), 1.12 (s, 3 H), 1.03 (d, 3 H, *J* = 7.0), 0.95 (t, 9 H, *J* = 7.8), 0.90 (s, 9 H), 0.83 (d, 3 H, *J* = 6.8), 0.62 (q, 6 H, *J* = 7.8), 0.07 (s, 3 H), 0.06 (s, 3 H)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 222.5, 164.4, 153.0, 142.3, 136.3, 118.8, 116.8, 115.3, 76.5, 76.1, 75.0, 62.2, 54.4, 41.1, 39.6, 36.0, 35.6, 33.4, 33.1, 26.1, 23.4, 22.7, 22.3, 19.4, 19/2. 18.2, 15.3, 14.1, 9.7, 6.9, 4.8, -3.5, -4.0

**IR** (thin film) 3492, 2956, 2931, 2877, 1727, 1687, 1462, 1379, 1255, 1079, 1002, 938, 912, 837

**HRMS** (MALDI) calc'd for $(C_{40}H_{73}NO_5SSi_2Na)^+$, 758.4646; found, 758.4635




**Triisopropyl-((2*S*)-methyl-pent-4-enyloxy)-silane.** To the corresponding alcohol (5.0 g, 50 mmol, 1.0 equiv) in DMF (20 ml) at 0 °C was added imidazole (7.37 g, 110 mmol, 2.20 equiv) followed by TIPSCl (11.7 ml, 55.0 mmol, 1.10 equiv). The cloudy mixture was stirred 4 h at rt, poured onto $H_2O$ (30 ml), and extracted with pentane (3 x 50 ml). The combined organic solutions were washed with brine (70 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by vacuum distillation (0.5 torr, 75-82 °C) afforded the silyl ether (12.4 g, 97% yield).

**Optical Rotation:** $[\alpha]_D^{29}$ (c 1.202, $CHCl_3$) = –2.0

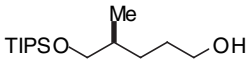
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 5.81 (ddt, 1 H, *J* = 17.1, 10.0, 6.9), 5.04-4.97 (m, 2 H), 3.56-3.47 (m, 2 H), 2.28-2.19 (m, 1 H), 1.92-1.83 (m, 1 H), 1.75-1.64 (m, 1 H), 1.12-0.96 (m, 21 H), 0.89 (d, 3 H, *J* = 6.9)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 137.7, 115.8, 68.2, 37.7, 36.1, 18.0, 17.7, 16.4, 12.0

**IR** (thin film) 2944, 2867, 1462, 1383, 1104, 1070, 994, 911, 882

**EI-MS**: 255.3 (M-H)

**Anal. calc'd** for ($C_{15}H_{32}OSi$) C, 70.24%; H, 12.57%; found, C, 70,26%; H, 12.39%.




**(4*S*)-Methyl-5-(triisopropyl-silanyloxy)-pentan-1-ol.** To the olefin (2.56 g, 10.0 mmol, 1.00 equiv) in 80 ml THF at rt was added 9-BBN (0.5 M in THF, 40 mmol, 2.0 equiv) over 20 min. The clear colorless solution was stirred 6 h at rt and cooled to 0 °C, whereupon 2 N NaOH (20 ml) and $H_2O_2$ (20 ml) were added and the mixture stirred for 1 h at 0 °C and 10 h at rt. Following extraction with $Et_2O$ (2 x 100 ml), the combined organic solutions were washed with brine (100 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification

by flash chromatography (10:1 hexanes/EtOAc) provided the product (2.61 g, 96% yield) as a clear, colorless oil.

**Optical Rotation:** $[\alpha]_D^{29}$ (c 1.224, $CHCl_3$) = –1.0

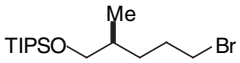
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 3.64 (t, 2 H, *J* = 6.5), 3.54 (dd, 1 H, *J* = 9.7, 6.2), 3.49 (dd, 1 H, *J* = 9.7, 6.2), 1.71-1.40 (m, 4 H), 1.21-1.0 (m, 22 H), 0.91 (d, 3 H, *J* = 6.8)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 68.5, 63.2, 35.8, 30.2, 29.2, 18.0, 16.8, 12.0

**IR** (thin film) 3339, 2943, 2867, 1463, 1102, 1066, 882

**EI-MS:** 229.3 (M-$^i$Pr)

**Anal. calc'd** for ($C_{15}H_{34}O_2Si$) C, 65.63%; H, 12.48%; found, C, 65.83%; H, 12.32%




**(5-Bromo-(2*S*)-methyl-pentyloxy)-triisopropyl-silane.** To $PPh_3$ (2.69 g, 10.2 mmol, 1.10 equiv) in 90 ml $CH_2Cl_2$ at 0 °C was added $Br_2$ (0.480 ml, 9.31 mmol, 1.00 equiv) dropwise. After 20 min, imidazole (0.630 g, 9.31 mmol, 1.00 equiv) was added at 0 °C, followed by the alcohol (2.55 g, 9.31 mmol, 1.00 equiv) in 10 ml $CH_2Cl_2$. After 20 min at this temperature, the reaction was quenched with $H_2O$ (20 ml) and extracted with $CH_2Cl_2$ (3 x 50 ml). The combined organic solutions were washed with brine (80 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (hexanes) provided the bromide (2.99 g, 96% yield) as a clear, colorless oil.

**Optical Rotation:** $[\alpha]_D^{29}$ (c 1.425, $CHCl_3$) = –2.8

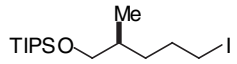
**$^1$H NMR** (300 MHz, $CDCl_3$) δ 3.51 (dd, 2 H, *J* = 5.9, 1.0), 3.41 (dt, 2 H, *J* = 6.9, 1.4), 2.01-1.79 (m, 2 H), 1.70-1.52 (m, 2 H), 1.29-1.18 (m, 1 H), 1.16-1.07 (m, 21 H), 0.91 (d, 3 H, *J* = 6.5)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 68.5, 35.5, 34.2, 32.0, 30.6, 18.1, 16.7, 12.0

**IR** (thin film) 2943, 2866, 1462, 1102, 882

**EI-MS:** 337.2 (M)

**Anal. calc'd** for ($C_{15}H_{33}BrOSi$) C, 53.40%; H, 9.86%; found, C, 53.61%; H, 9.72%




**(5-Iodo-(2*S*)-methyl-pentyloxy)-triisopropyl-silane.** To $PPh_3$ (2.02 g, 7.70 mmol, 1.10 equiv) in 60 ml $CH_2Cl_2$ at 0 °C was added $I_2$ (1.78 g, 7.00 mmol, 1.0 equiv) dropwise. After 20 min, imidazole (476 mg, 7.00 mmol, 1.00 equiv) was added at 0 °C, followed by the alcohol (1.93 g, 7.00 mmol, 1.00 equiv) in 10 ml $CH_2Cl_2$. After 15 min at this temperature, the reaction was quenched with $H_2O$ (20 ml) and extracted with $CH_2Cl_2$ (3 x 50 ml). The combined organic solutions were washed with brine (80 ml), dried over $Na_2SO_4$, and concentrated under reduced pressure. Purification by flash chromatography (100% hexanes) provided the iodide (2.13 g, 80% yield) as a clear, colorless oil.

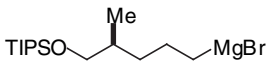
**Optical Rotation:** $[\alpha]_D^{23}$ (c 1.228, $CHCl_3$) = –2.3

**$^1$H NMR** (300 MHz, $CDCl_3$) δ 3.55-3.45 (m, 2 H), 3.21-3.14 (m, 2 H), 1.98-1.74 (m, 2 H), 1.70-1.49 (m, 2 H), 1.26-1.00 (m, 22 H), 0.90 (d, 3 H, *J* = 6.8)

**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ 68.4, 35.3, 34.3, 31.4, 18.1, 16.7, 12.0, 7.4

**IR** (thin film) 2943, 2866, 1462, 1104, 1068, 882, 681

**EI-MS:** (M-H) 383.1




**93**

**4*S*)-Methyl-5-(triisopropyl-silanyloxy)-pentanyl magnesium bromide (93). Method A**. To flame dried Mg (turnings, 1.92 g, 80.0 mmol, 10.0 equiv) in a 100-ml round bottom flask equipped with a reflux condenser and a stir bar was added 6 ml THF. To this suspension was added 1,2-dibromoethane (40 µl) without stirring and heated gently with a heat gun. An additional portion of 1,2-dibromoethane (40 µl) was added and heated gently until vigorous reaction had begun, at which point magnetic stirring was started. When the exotherm had subsided, the bromide (2.69 g, 8.00 mmol, 1.0 equiv) in 2.0 ml THF was added slowly until the vigorous reaction had begun, followed by dropwise addition of the remaining bromide solution. The resulting mixture was stirred 40 min at rt and diluted with THF (12 ml) to give a 0.4 M solution of **93**.

**Method B.** To the iodide (1.57 g, 2.00 mmol, 1.00 equiv) in 10 ml $Et_2O$ at –78 °C was added *tert*-BuLi (1.7 M in pentane, 2.5 ml, 4.2 mmol, 2.1 equiv). The clear, colorless solution was stirred 15 min at this temperature before $MgBr_2$ (1.0 M in 3:1 $Et_2O/C_6H_6$, 2.4 ml, 2.4 mmol, 1.2 equiv) was added. The mixture was stirred until all solids had dissolved, followed by an additional 20 min of stirring at –78 °C to provide a 0.16 M solution of **93.**