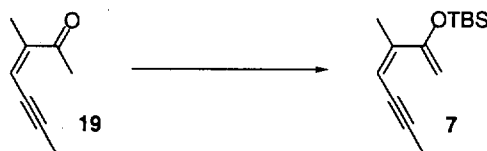


General Procedures. All non-aqueous reactions were carried out under nitrogen atmosphere in oven-dried (120°C) glassware. Tetrahydrofuran (THF) and diethyl ether (Et₂O) were distilled immediately prior to use from sodium metal/benzophenone ketyl. Methylene chloride (CH₂Cl₂, EM Science) and benzene (EM Science) were distilled from calcium hydride prior to use. Methanol (MeOH, EM Science) was distilled from magnesium methoxide. Dimethyl sulfoxide (DMSO) and N, N-dimethylformide (DMF) were distilled from calcium hydride and stored over 4Å molecular sieves. Triethylamine (Et₃N, EM Science), 2,6-lutidine (Acros) and pyridine (py., EM Science) were distilled from calcium hydride immediately prior to use. The molarities indicated for organolithium reagents were established by titration with 2,6-di-tert-butyl-4-methylphenol and 1,10-phenanthroline as indicator. Dibutylboron triflate was purchased from Fluka and used as received. All other commercially obtained reagents were used as received. Rochelle's salt solution refers to 2M aqueous sodium potassium tartrate.

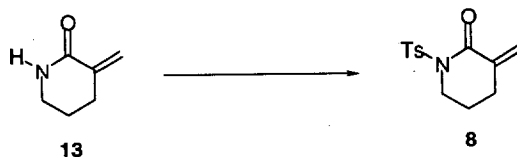


Diene 7. In a 250 mL round bottom flask was added THF (130 mL) and 2.0M sodium(bis(trimethylsilyl)amide) (NaHMDS) in THF (14.7 mL, 29.4 mmol). The solution was cooled to -78°C and then ketone **19** (3.27 g, 26.8 mmol) in THF (10 mL) was added over 30 min via syringe pump. After addition was complete, the solution was stirred for an additional 10 min and then TBSOTf (7.4 mL, 32.1 mmol) was added dropwise. The reaction was stirred for 30 min and quenched with pH 7 buffer (20 mL) at -78°C. After warming to ambient temperature, the aqueous layer was extracted with ether (3 X 150 mL), washed with brine, and the combined

organics were dried over Na_2SO_4 . ^1H NMR analysis of the crude reaction mixture indicated that no olefin isomerization had occurred during the reaction. On smaller scale, rapid purification by passing through a silica gel plug with hexane as eluent could minimize isomerization. However, in this particular run, purification gave 5.22 g (82%) of diene **7** as a slightly yellow oil as a 2:1 (*Z/E*) ratio by ^1H NMR. $R_f = 0.71$ (1:5-EtOAc:hexanes); IR (thin film) 2957, 2930, 2858, 2223, 1579, 1251 cm^{-1} ; HRMS (FAB) Calcd for $\text{C}_{14}\text{H}_{25}\text{OSi}$ [$\text{M}+\text{H}$]: 237.1675. Found: 237.1656.

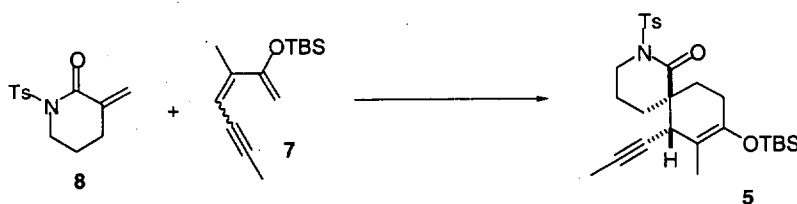
(*Z*)-isomer: ^1H NMR (300 MHz, CDCl_3) δ 5.41-5.36 (m, 1H), 4.88 (d, $J = 1.2$ Hz, 1H), 4.46 (d, $J = 0.9$ Hz, 1H), 1.95 (app dd, $J = 0.9$ Hz, 2.4 Hz, 3H), 1.84 (app d, $J = 0.6$ Hz, 3H), 0.93 (s, 9H), 0.17 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 155.3, 143.5, 107.2, 95.3, 90.3, 78.3, 25.7, 21.4, 18.3, 4.6, -4.6.

(*E*)-isomer: ^1H NMR (300 MHz, CDCl_3) δ 6.00-5.95 (m, 1H), 4.53 (d, $J = 1.2$ Hz, 1H), 4.35 (br s, 1H), 2.04 (d, $J = 2.4$ Hz, 3H), 2.00 (br s, 3H), δ 0.96 (s, 9H), 0.17 (s, 6H).



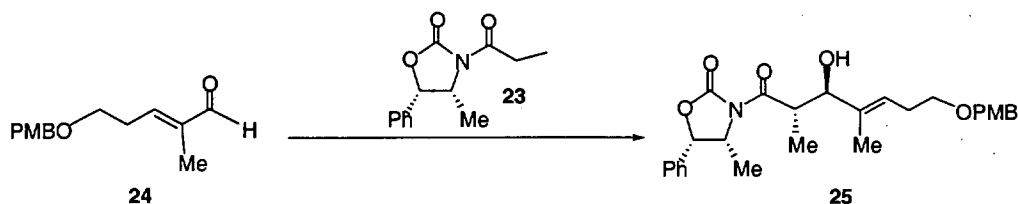
Dienophile 8. Lactam **13** (0.504 g, 5.44 mmol) was dissolved in THF (60 mL) in a 100 mL round bottom flask. The solution was cooled to -78 $^{\circ}\text{C}$ (CO_2 /acetone) and 1.0 M sodium(bis(trimethylsilyl)amide) (NaHMDS) in THF (5.98 mL, 5.98 mmol) was added dropwise via syringe. After 10 min, *p*-toluenesulfonyl chloride (TsCl) (1.14 g, 5.98 mmol) was added in one portion and the resulting solution was stirred for 30 min. The reaction was warmed to ambient temperature (23 $^{\circ}\text{C}$) and quenched with sat. aqueous sodium bicarbonate, washed with water, brine, and concentrated under reduced pressure. Flash column chromatography on silica gel (50-60% $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) afforded 1.37 g (95%) of dienophile **8** as a colorless, crystalline solid. Large scale purification was performed by recrystallization from ethyl acetate: m.p. =

119.5-120.5 °C (ether); R_f = 0.12 (1:4-EtOAc:hexanes); ^1H NMR (300 MHz, CDCl_3) 7.93 (d, J = 8.4 Hz, 2H), 7.32 (dd, J = 0.3, 9.0 Hz, 2H), 6.26 (app q, J = 1.5 Hz, 1H), 5.42 (app q, J = 1.8 Hz, 1H) 4.01 (t, J = 5.8 Hz, 2H), 2.56 (tt, J = 1.80, 6.30 Hz, 2H), 2.43 (s, 3H), 2.01-1.92 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 163.6, 144.6, 136.9, 136.2, 129.3, 128.5, 125.8, 47.3, 29.1, 23.2, 21.6. HRMS (FAB) Calcd for $\text{C}_{13}\text{H}_{16}\text{NO}_3\text{S}[\text{M}+\text{H}]$:266.0851. Found 266.0862. Anal Calcd for $\text{C}_{13}\text{H}_{14}\text{NO}_3\text{S}$: C, 58.85; H, 5.70. Found: C, 58.61; H, 5.72.



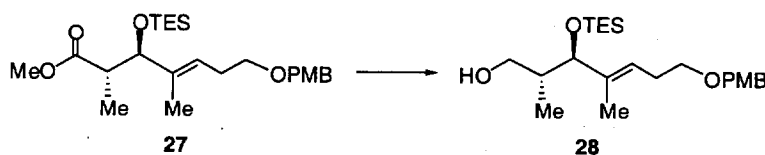
Spirocycle 5. In a 250 mL round bottom flask, dienophile **8** (3.29 g, 12.4 mmol) was dried azeotropically with benzene and then diluted in 147 mL CH_2Cl_2 . The resulting solution was cooled to -78°C , 1.8 M Et_2AlCl in toluene (6.89 mL, 12.4 mmol) was added dropwise, and the solution was stirred for 20 min. Diene **7** (3.08 g, 13.0 mmol) was then added dropwise and the reaction was maintained at -30°C for 3 h. The reaction was quenched at -78°C with sat. NaHCO_3 (45 mL) and warmed to ambient temperature. The aqueous layer was extracted with CH_2Cl_2 (3X50 mL), washed with brine, and the organics were dried over Na_2SO_4 . After concentrating under reduced pressure, the crude product was purified by silica gel chromatography (1:4-EtOAc:hexanes) to give 4.28 g (67%) spirocycle **5** as a light yellow solid. Recrystallization from ether gave colorless, clear crystals which were suitable for x-ray analysis. M.p. = $136.5\text{--}137.5^\circ\text{C}$ (ether); R_f = 0.37 (1:5-EtOAc:hexanes); IR (KBr pellet) 2955, 2930, 2857, 1686, 1354, 1262, 1170, 1102 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.89 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 4.13-4.03 (m, 1H), 3.80-3.70 (m, 1H), 3.67 (br s, 1H), 2.42 (s, 3H), 2.10-

1.70 (m, 8H), 1.67 (d, $J = 2.4$ Hz, 3H), 1.62 (app q, $J = 1.5$ Hz, 3H), 0.92 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 174.9, 144.1, 141.5, 136.2, 129.0, 128.3, 109.5, 79.2, 77.3, 47.3, 47.1, 40.2, 30.0, 26.3, 25.7, 25.6, 21.5, 20.5, 18.0, 14.5, 3.3, -3.95, -4.0; HRMS (FAB) Calcd for $\text{C}_{27}\text{H}_{40}\text{NO}_4\text{SSi}$ [$\text{M}+\text{H}$]: 502.2447. Found: 502.2425; Anal Calcd for $\text{C}_{27}\text{H}_{39}\text{NO}_4\text{SSi}$: C, 64.63; H, 7.83; N, 2.79. Found: C, 64.54; H, 8.02; N, 2.80. Note: To prevent desilylation, this silyl enol ether was best stored in base washed glassware and NMR spectra were recorded in buffered chloroform (containing 0.1% d^5 -pyridine).



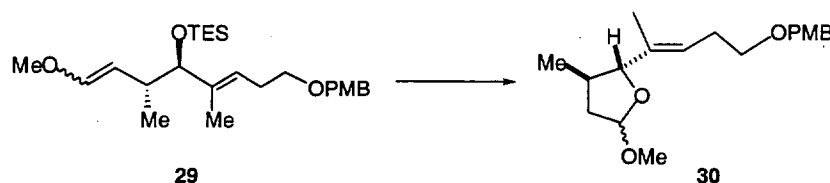
Anti-Aldol Product 25. To a cooled (0°C) solution of imide **23** (4.88 g, 21.0 mmol) in 63 mL of Et_2O was added Bu_2BOTf (42 mL, 42 mmol) followed by diisopropylethylamine (4.19 mL, 24.0 mmol). The resulting yellow slurry was stirred for 45 min then cooled to -78°C . Over a 30 min period was added a -78°C solution of aldehyde **24** (6.12 g, 26 mmol) in 30 mL Et_2O . The solution was stirred for 6 h and then diluted with Et_2O (30 mL). The reaction was quenched at -78°C with 1M tartaric acid (60 mL), warmed to 22°C , and then stirred for 2 h. The reaction mixture was partitioned between Et_2O and H_2O . The aqueous layer was extracted with Et_2O (2 X 50 mL), and the combined organic layers were washed with saturated NaHCO_3 (2 X 50 mL). The combined organic layers were then cooled to 0°C and a 3:1 MeOH/ 30 % H_2O_2 solution (60 mL) was added. After 30 min at 22°C , the solution was washed with saturated NaHCO_3 (40 mL), brine (40 mL) and dried (Mg_2SO_4). Concentration of the organic layer provided a yellow oil. Analysis of the crude 300 MHz ^1H NMR showed a mixture of three aldol products in a ratio of $\sim 5:1:0.5$. Purification by flash chromatography on SiO_2 eluting with hexanes: EtOAc (7:3)

provided alcohol **25** (5.12 g, 68%) as a viscous, colorless oil. On standing at 22°C, the aldol adduct **25** crystalized as colorless needle-like crystals: $R_f = 0.19$ (7:3-hexane:ethyl acetate); $[\alpha]_D^{23} +18.5^\circ$ (c 1.22, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 0.88 (d, $J=6.6$ Hz, 3H), 1.04 (m, $J=2.1, 6.6$ Hz, 3H), 1.67 (d, $J=1.2$ Hz, 3H), 2.34 (q, $J=6.6$ Hz, 3H), 3.43 (t, $J=6.6$ Hz, 2H), 3.78 (s, 3H), 4.11 (m, 2H), 4.41 (s, 2H), 4.76 (m, $J=6.6$ Hz, 1H), 5.45 (dq, $J=7.2, 1.2$ Hz, 1H), 5.64 (d, $J=7.2$ Hz, 1H), 6.85 (dt, $J=8.7, 2.1$ Hz, 2H), 7.20-7.40 (m, 7H); ^{13}C NMR (75 MHz, CDCl_3) δ 11.0, 14.3, 14.8, 28.4, 40.6, 55.2, 69.2, 72.5, 77.2, 78.9, 81.1, 113.7, 125.5, 125.6, 128.7, 129.1, 130.5, 133.3, 136.3, 153.4, 159.1, 176; IR (thin film) 3489, 2929, 1783, 1696, 1509 cm^{-1} ; HRMS (FAB) Calcd for $\text{C}_{27}\text{H}_{33}\text{NO}_6$ $[M+\text{Na}]$: 490.2206. Found: 490.2227; Anal. Calcd for $\text{C}_{27}\text{H}_{33}\text{NO}_6$: C, 69.36; H, 7.11; N, 2.99; Found: C, 69.30; H, 7.17; N, 2.92.



Alcohol 28. To a cooled (-78°C) solution of ester **27** (6.57 g, 15.05 mmol) in CH_2Cl_2 (150 mL) was added 1M solution of DIBAL-H in CH_2Cl_2 (33.11 mmol, 33.11 mL) slowly. The reaction was stirred at -78°C for 30 min, then quenched with 1M tartaric acid (34 mL) at -78°C slowly and warmed to 22°C . The reaction mixture was separated and the organic phase was washed with H_2O (2 X 50 mL). The aqueous phase was extracted with Et_2O (3 X 30 mL). The combined organic layers were washed with saturated NaHCO_3 solution (50 mL), brine (50 mL), dried over MgSO_4 , and concentrated *in vacuo*. Purification by flash chromatography on SiO_2 eluting with hexanes: EtOAc (9:1 \rightarrow 4:1, gradient elution) gave alcohol **28** as a colorless oil (5.74 g, 93%); $R_f = 0.45$ (7:3-hexane:ethyl acetate); $[\alpha]_D^{23} +3.16^\circ$ (c 3.99, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 0.62 (q, $J=7.8$ Hz, 6H), 0.75 (d, $J=6.9$ Hz, 3H), 0.96 (t, $J=7.8$ Hz, 9H), 1.62 (s,

3H), 1.81-1.94 (m, 1H), 2.37 (q, $J=6.9$ Hz, 2H), 3.24 (s, 1H), 3.49 (t, $J=6.9$ Hz, 2H), 3.64 (d, $J=5.4$ Hz, 2H), 3.83 (s, 3H), 3.87 (d, $J=8.4$ Hz, 1H), 4.46 (s, 2H), 5.40 (t, $J=6.9$ Hz, 1H), 6.88 (dt, $J=6.9$, 3 Hz, 2H), 7.28 (dt, $J=6.9$, 3 Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 4.7, 6.7, 11.3, 14.1, 28.2, 38.1, 55.2, 67.5, 69.3, 72.5, 85.3, 113.7, 124.1, 129.1, 130.5, 137.6, 159.1; IR (thin film) 3466, 2957, 1612, 1509, 1092 cm^{-1} ; HRMS (FAB) Calcd for $\text{C}_{23}\text{H}_{40}\text{O}_4\text{Si}[\text{M}+\text{Na}]$: 431.2594. Found: 431.2589; Anal. Calcd for $\text{C}_{23}\text{H}_{40}\text{O}_4\text{Si}$: C, 67.60; H, 9.86; Found: C, 67.51; H, 9.89.

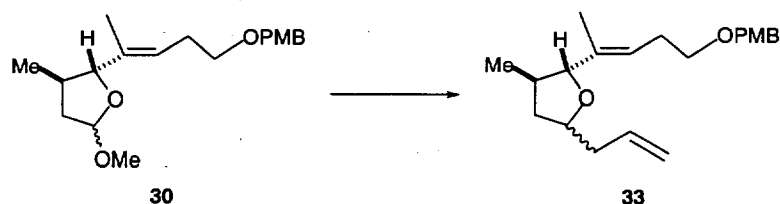


Methoxy Furanose 30. To a solution of methoxy olefin **29** (846 mg, 1.95 mmol) in CH_3OH (20 mL) was added $p\text{-TsOH}$ (37.08 mg, 0.19 mmol) in 1 mL CH_3OH at 0°C . The ice bath was removed and the reaction mixture was stirred at 22°C for 30 min. The reaction was quenched carefully by pouring it into aqueous NaHCO_3 (40 mL). The pH was adjusted to neutral by the addition of solid NaHCO_3 , and the mixture was extracted with CH_2Cl_2 (3 X 45 mL). The combined organic layers were washed with brine (40 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by flash chromatography on SiO_2 eluting with hexanes:EtOAc (9:1) yielded 583 mg (86%) of furanose **30** as a colorless oil and as a mixture (1.5:1) of diastereomers: $R_f = 0.35$ (4:1-hexane:ethyl acetate); IR (thin film) 2953, 1612, 1512, 1454, 1249 cm^{-1} ; MS (FAB) Calcd for $\text{C}_{19}\text{H}_{28}\text{O}_4[\text{M}+\text{Na}]$: 343. Found: 343.

Major isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.97 (d, $J=6.6$ Hz, 3H), 1.67 (d, $J=1.2$ Hz, 3H), 1.61-1.71 (m, 1H), 2.09 (dd, $J=6.6$, 12.6 Hz, 1H), 2.19-2.31 (m, 1H), 2.42 (q, $J=6.9$ Hz, 2H), 3.39 (s, 3H), 3.50 (dt, $J=1.2$, 6.9 Hz, 2H), 3.83 (s, 3H), 3.85 (d, $J=8.7$ Hz, 1H), 4.48 (s, 2H), 4.94 (d, $J=4.8$ Hz, 1H), 5.45 (dt, $J=6.8$, 1.2 Hz, 1H), 6.90 (dt, $J=8.7$, 3 Hz, 2H), 7.28 (dt, $J=8.7$, 3 Hz,

2H); ^{13}C NMR (75 MHz, CDCl_3) δ 10.8, 15.7, 28.7, 34.1, 41.7, 54.5, 55.3, 69.4, 72.5, 93.6, 104.3, 113.7, 125.0, 129.2, 130.6, 135.5, 159.1.

Minor isomer: ^1H NMR (300 MHz, CDCl_3) δ 1.02 (d, $J=6.9$ Hz, 3H), 1.49-1.58 (m, 1H), 1.64 (d, $J=1.2$ Hz, 3H), 1.90-2.08 (m, 1H), 2.34-2.45 (m, 1H), 2.42 (q, $J=6.9$ Hz, 2H), 3.40 (s, 3H), 3.50 (dt, $J=1.2, 6.9$ Hz, 2H), 3.84 (s, 3H), 3.93 (d, $J=8.7$ Hz, 1H), 4.48 (s, 2H), 5.06 (dd, $J=3.0, 5.4$ Hz, 1H), 5.50 (dt, $J=6.8, 1.2$ Hz, 1H), 6.90 (dt, $J=8.7, 3$ Hz, 2H), 7.28 (dt, $J=8.7, 3$ Hz, 2H).

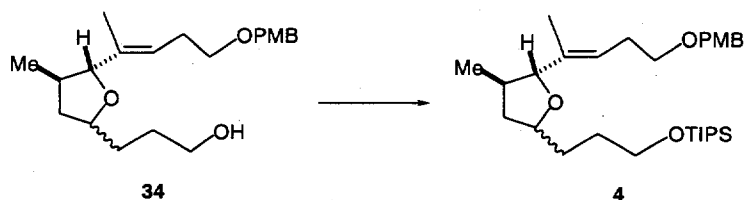


Trisubstituted Tetrahydrofuran 33. To a cooled (0°C) solution of methoxy furanose **30** (171.9 mg, 0.537 mmol) and allyltrimethyl silane (256 μl , 1.61 mmol) in 5 mL CH_2Cl_2 was added $\text{BF}_3\cdot\text{OEt}_2$ (74.7 μl , 0.591 mmol) dropwise. After stirring for 3 h, the reaction was quenched at 0°C by addition of saturated NaHCO_3 (2 mL) and then warmed to ambient temperature. The layers were separated and the aqueous layer was extracted with Et_2O (3 X 10 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO_4 , and concentrated *in vacuo*. Purification of the yellow oil by flash chromatography on SiO_2 eluting with hexanes: EtOAc (9:1) gave 168 mg (95%) of inseparable diastereomeric tetrahydrofurans **33** (4:1; $\alpha:\beta$) as a colorless oil: $R_f = 0.26$ (9:1-hexane:ethyl acetate); IR (thin film) 3075, 2957, 1612, 1512, 1037 cm^{-1} ; HRMS (FAB) Calcd for $\text{C}_{21}\text{H}_{30}\text{O}_3[\text{M}+\text{Na}]$: 353.2093. Found: 353.2077.

Major isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.97 (d, $J=6.9$ Hz, 3H), 1.67 (s, 3H), 1.60-1.73 (m, 1H), 1.81-1.89 (m, 1H), 1.96-2.44 (m, 4H), 2.40 (q, $J=7.5$ Hz, 2H), 3.48 (dt, $J=1.2, 7.5$ Hz, 2H), 3.69 (d, $J=8.1$ Hz, 1H), 3.83 (s, 3H), 4.02-4.14 (m, 1H), 4.47 (s, 2H), 5.06-5.14 (m, 2H), 5.46 (t, $J=6.9$ Hz, 1H), 5.77-5.93 (m, 1H), 6.90 (dt, $J=8.7, 3$ Hz, 2H), 7.29 (dt, $J=8.7, 3$ Hz, 2H); ^{13}C

NMR (75 MHz, CDCl₃) δ 11.3, 16.9, 28.5, 35.9, 39.0, 40.8, 55.2, 69.5, 72.5, 77.0, 92.3, 113.7, 116.7, 123.9, 129.2, 130.6, 134.9, 135.7, 159.1.

Minor isomer: ¹H NMR (300 MHz, CDCl₃) δ 0.97 (d, J =6.9 Hz, 3H), 1.65 (s, 3H), 1.60-1.73 (m, 1H), 1.81-1.89 (m, 1H), 1.96-2.44 (m, 4H), 2.40 (q, J =7.5 Hz, 2H), 3.48 (dt, J =1.2, 7.5 Hz, 2H), 3.78 (d, J =9.0 Hz, 1H), 3.83 (s, 3H), 4.02-4.14 (m, 1H), 4.47 (s, 2H), 5.06-5.14 (m, 2H), 5.42 (t, J =6.9 Hz, 1H), 5.77-5.93 (m, 1H), 6.90 (dt, J =8.7, 3 Hz, 2H), 7.29 (dt, J =8.7, 3 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 11.1, 16.1, 28.5, 37.8, 40.6, 40.9, 55.2, 69.5, 72.5, 78.5, 91.5, 113.7, 116.7, 123.9, 129.2, 130.6, 135.1, 135.7, 159.1.



TIPS Ether 4. To a cold (-78°C) solution of alcohol **34** (33.8 mg, 0.1 mmol) in dry CH₂Cl₂ (1 mL) was added freshly distilled 2,6-lutidine (34 μ L, 0.29 mmol) followed by TIPSOTf (28.7 μ L, 0.11 mmol). The reaction mixture was stirred at -78°C for 40 min and then quenched by addition of saturated NaHCO₃ solution (1 mL). The layers were separated and the aqueous phase was extracted with Et₂O (2 X 5 mL). The combined organic layers were washed with H₂O (2 mL) and brine (2 mL), dried over MgSO₄, and concentrated in vacuo. Purification by flash chromatography on SiO₂ eluting with hexanes:EtOAc (9:1) furnished a mixture (4:1; α : β) of silyl ethers **4** (48 mg, 99%) as a colorless oil: R_f = 0.33 (9:1-hexane:ethyl acetate); IR (thin film) 2938, 1505, 1098, 1033 cm⁻¹; HRMS (FAB) Calcd for C₃₀H₅₂O₄Si[M+H]⁺: 505.3713. Found 505.3700.

Major isomer: ¹H NMR (300 MHz, CDCl₃) δ 0.97 (d, J =6.6 Hz, 3H), 1.08 (s, 21H), 1.64 (s, 3H), 1.50-1.85 (m, 6H), 1.96-2.12 (m, 1H), 2.40 (q, J =7.5 Hz, 2H), 3.48 (dt, J =1.2, 7.5 Hz, 2H), 3.69

(d, $J=8.4$ Hz, 1H), 3.73 (t, $J=6.0$ Hz, 2H), 3.83 (s, 3H), 3.96-4.07 (m, 1H), 4.47 (s, 2H), 5.45 (t, $J=7.2$ Hz, 1H), 6.90 (dt, $J=8.7$, 3 Hz, 2H), 7.29 (dt, $J=8.7$, 3 Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 11.3, 12.0, 17.1, 18.0, 28.5, 29.4, 32.7, 36.0, 39.8, 55.2, 63.4, 69.5, 72.5, 77.6, 92.2, 113.7, 123.7, 129.2, 130.6, 135.9, 159.1.

Minor isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.98 (d, $J=6.3$ Hz, 3H), 1.08 (s, 21H), 1.64 (s, 3H), 1.50-1.85 (m, 6H), 2.12-2.24 (m, 1H), 2.40 (q, $J=7.5$ Hz, 2H), 3.48 (dt, $J=1.2$, 7.5 Hz, 2H), 3.80 (d, $J=9.6$ Hz, 1H), 3.73 (t, $J=6.0$ Hz, 2H), 3.83 (s, 3H), 3.96-4.07 (m, 1H), 4.47 (s, 2H), 5.41 (t, $J=7.2$ Hz, 1H), 6.90 (dt, $J=8.7$, 3 Hz, 2H), 7.29 (dt, $J=8.7$, 3 Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 11.2, 12.4, 16.2, 17.7, 28.5, 29.5, 32.7, 37.8, 41.5, 55.2, 63.4, 69.5, 72.5, 79.3, 91.3, 113.7, 123.7, 129.2, 130.6, 135.9, 159.1.

