Ruthenium-Catalyzed Enyne Cycloisomerizations. Effect of Allylic Silyl Ether on Regioselectivity

Barry M. Trost, Jean-Philippe Surivet and F.Dean Toste

*Department of Chemistry, Stanford University,
Stanford, California, 94305*

Supplementary Material

General Techniques. Reactions were carried out in clean, dry glassware under inert atmosphere using high quality solvents. Anhydrous solutions of reaction mixtures were transferred *via* an oven-dried syringe or cannula. Dichloromethane (CH₂Cl₂), toluene, acetonitrile and diethyl ether (Et₂O) were obtained by passing through commercially available alumina columns. Anhydrous tetrahydrofuran (THF) was obtained by distillation from sodium benzophenone ketyl. Anhydrous acetone was obtained by distillation from freshly activated Drierite). Triethylamine, diisopropylamine, pyridine were distilled from calcium hydride prior to use. Yields refer to chromatographically and spectroscopically homogenous materials. Reagents were purchased at the highest commercial quality and used without further purification. Reactions were monitored by thin layer chromatography separations carried out on 0.2-mm E. Merck silica gel plates (60 F254) using UV light as a visualizing agent and phosphomolybdic acid, *p*-anisaldehyde, or potassium permanganate solutions and heat as developing agents. Flash chromatographies were performed with E. Merck silica gel (0.040-0.063 mm grade). Melting points were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected. ¹H and ¹³C nuclear magnetic resonance (NMR) were recorded on Varian Gemini-300 (300 and 75MHz respectively) or a Varian Unity Inova 500 (500 and 125MHz respectively). Chemical shifts are reported in delta (δ) units, in parts per million ppm) relative to the singlet at 7.24 ppm for chloroform-*d*. Splitting pattern are designated as s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet; and br, broad. Coupling constants (*J*) are reported in Hertz (Hz). Infrared (IR) data were recorded in sodium plates on PerkinElmer Paragon 500 FT-IR spectrometer. Absorbance frequencies are reported in reciprocal centimeters (cm⁻¹). Optical rotation data were obtained with a Jasco DIP-360 digital polarimeter at the sodium D line (589 nm) in the solvent and concentration indicated. High resolution mass spectral (HRMS) data were obtained from Mass Spectrometry Resource, School of Pharmacy, University of California-San Francisco, on a Kratos MS9 spectrometer. Elemental analyses (Anal.) were performed by M-H-W Laboratories of Phoenix, AZ.

(*E*)-4,4-(Bismethoxycarbonyl)-1-(*tert*-butyldimethylsilyl)-oct-7-yn-1-ol (6)

To a degassed solution of (η^3 -C₃H₅PdCl)₂ (0.035g, 0.095mmol), triphenylphosphine (0.201g, 0.76mmol) and cesium carbonate (1.37g, 4.22mmol) in THF (15mL), were added alkyne **5** (0.85g, 5mmol) and methyl carbonate **4** (1 g, 3.84mmol). The reaction mixture was heated at 60°C for 2h, and then partitioned between Et₂O (20mL) and 1N NaHSO₄ (20mL). The aqueous layer was extracted with Et₂O (2 x 20mL). The combined organic layers were dried over magnesium sulfate (MgSO₄), and concentrated *in vacuo*. The residue was chromatographed eluting with 6:1 petroleum ether : diethyl ether to afford enyne **6** (0.840g, 2.36mmol) as a colorless oil. I.R. (neat): 3291, 2955, 1740, 1437, 1208, 837 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ : 5.69 (dt, *J* = 4.9, 15.1Hz, 1H), 5.44 (ttd, *J* = 1.6, 7.0, 15.1Hz, 1H), 4.09 (d, *J* = 5.0Hz, 2H), 3.72 (s, 6H), 2.79 (d, *J* = 7.0Hz, 2H), 2.77 (d, *J* = 2.5Hz, 2H), 2.00 (t, *J* = 2.5Hz, 1H), 0.88 (s, 9H), 0.03 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ : 170.1 (2), 134.7, 122.9, 78.7, 71.4, 63.2, 56.9, 52.7 (2), 34.8, 25.8 (3), 22.5, 18.3, -5.2 (2). Anal. Calc'd for C₉H₁₃NO₄: C, 60.98; H, 8.52; Found: C, 60.79, H, 8.44.

1-[(*E*)-4-(*tert*-Butyldimethylsilyloxy)-but-2-enyl]-(4-methylbenzenesulfonyl)-amino]-prop-2-yne (8a**)**

To a degassed solution of (η^3 -C₃H₅PdCl)₂ (0.094g, 0.257mmol), triphenylphosphine (0.540g, 2.05mmol), cesium carbonate (3.7g, 11.39mmol) and alkyne **7a** (2.6g, 12.4mmol) in THF (20mL), were added methyl carbonate **4** (2.7g, 10.3mmol). The reaction mixture was heated at 60°C for 1h, and then partitioned between Et₂O (100mL) and 1N NaHSO₄ (100mL). The aqueous layer was extracted with Et₂O (2 x 100mL). The combined organic layers were dried over MgSO₄, and concentrated *in vacuo*. The residue was chromatographed eluting with 6:1 petroleum ether : diethyl ether to afford **8a** (3.37g, 8.56mmol) as a colorless oil. I.R. (neat): 3275, 2929, 2119, 1598, 1350, 1163 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ : 7.75 (d, *J* = 8.3Hz, 2H), 7.31 (d, *J* = 8.3Hz, 2H), 5.81 (td, *J* = 4.4, 15.1Hz, 1H), 5.61 (td, *J* = 6.8, 15.1Hz, 1H), 4.16 (d, *J* = 4.4Hz, 2H), 4.10 (d, *J* = 2.4Hz, 2H), 3.85 (d, *J* = 6.8Hz, 2H), 2.44 (s, 3H), 2.01 (t, *J* = 2.4Hz, 1H), 0.91 (s, 9H), 0.07 (s, 6H). ¹³C NMR (125 MHz, CDCl₃) δ : 143.4, 135.9, 135.3, 129.4 (2), 127.7 (2), 122.9, 76.4, 73.6, 62.7, 47.8, 35.6, 25.8 (3), 21.5, 18.3, -5.2 (2). Anal. Calc'd for C₂₀H₃₁NO₃SSi: C, 61.03; H, 7.94; N, 3.55; S, 8.14; Found: C, 60.77; H, 7.92; N, 3.42; S, 8.26.

1-[(*E*)-4-(*tert*-Butyldimethylsilyloxy)-but-2-enyl]-(4-methylbenzenesulfonyl)-amino]-but-3-yne (8b**)**

To a degassed solution of (η^3 -C₃H₅PdCl)₂ (0.050g, 0.137mmol), triphenylphosphine (0.300g, 1.14mmol), cesium carbonate (2.3g, 7.08mmol) and alkyne **7b** (1.7g, 7.61mmol) in THF (20mL), were added methyl carbonate **4** (1.6g, 6.1mmol). The reaction mixture was heated at 60°C for 1h, and then partitioned between Et₂O (40mL) and 1N NaHSO₄ (40mL). The aqueous layer was extracted with Et₂O (2 x 40mL). The combined organic layers were dried over MgSO₄, and concentrated *in vacuo*. The residue was chromatographed eluting with 10:1 petroleum ether : diethyl ether to afford **8b** (2.47g, 6.05mmol) as a colorless oil. I.R. (neat) : 3291, 2928, 2121, 1599, 1471, 1342, 1160 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ : 7.68 (d, *J* = 8.0Hz, 2H), 7.28 (d, *J* = 8.0Hz, 2H), 5.68 (td, *J* = 4.1, 15.4Hz, 1H), 5.47 (td, *J* = 7.8, 15.4Hz, 1H), 4.10 (br d, *J* = 1.7Hz, 2H), 3.85 (d, *J* = 6.6Hz, 1H), 3.27 (t, *J* = 7.3Hz, 2H), 2.44 (m, 2H), 2.43 (s, 3H), 1.96 (t, *J* = 1.7Hz, 1H), 0.86 (s, 9H), 0.02 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ : 143.2, 136.8, 134.5, 129.7 (2), 127.0 (2), 123.8, 80.9, 70.0, 62.6, 50.0, 45.6, 25.8 (3), 21.4, 19.3, 18.2, -

5.3 (2). Anal. Calc'd for $C_{21}H_{33}NO_3SSi$: C, 61.87; H, 8.16; S, 7.86; N, 3.43; Found: C, 61.86; H, 7.96; N, 3.54; S, 7.96.

Methyl 4-[(*E*)-4-(*tert*-Butyldimethylsilyloxy)-but-2-enyl]-(4-methylbenzenesulfonyl)-amino]-but-2-ynoate (9a**)**

To a cold ($-78^{\circ}C$) solution of alkyne **8a** (1g, 2.54mmol) in THF (12ml) was added *n*-BuLi (1.6N, 1.8 ml, 2.88mmol). The solution was stirred for 1h at $-78^{\circ}C$, and methyl chloroformate (1mL) was added dropwise. The reaction was allowed to warm up over 1h, and water (10mL) was added. The aqueous phase was extracted with Et₂O (4 x 20mL). The combined ethereal extracts were washed with brine (20mL) and dried over MgSO₄. The residue was chromatographed eluting with 6:1 petroleum ether : diethyl ether to afford **9a** (0.912g, 2.02mmol) as a colorless oil. I.R. (neat): 2955, 2240, 1719, 1352, 1255, 1164, 837 cm^{-1} . ¹H NMR (500 MHz, CDCl₃): δ 7.74 (d, *J* = 8.3Hz, 2H), 7.33 (d, *J* = 8.3Hz, 2H), 5.82 (dt, *J* = 4.2, 15.3Hz, 1H), 5.62 (dt, *J* = 6.9, 15.1Hz, 1H), 4.21 (s, 2H), 4.17 (d, *J* = 4.2Hz, 2H), 3.83 (d, *J* = 6.9Hz, 2H), 3.71 (s, 3H), 2.44 (s, 3H), 0.90 (s, 9H), 0.6 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ 152.9, 143.9, 135.9, 135.2, 129.6 (2), 127.6 (2), 122.3, 80.4, 76.8, 62.6, 52.6, 48.3, 35.5, 25.8 (3), 21.5, 18.3, -5.2 (2). Anal. Calc'd for $C_9H_{13}NO_4$: C, 58.50; H, 7.36; N, 3.10; Found: C, 58.38; H, 7.31; N, 3.06.

Methyl 5-[(*E*)-4-(*tert*-Butyldimethylsilyloxy)-but-2-enyl]-(4-methylbenzenesulfonyl)-amino]-pent-2-ynoate (9b**)** was obtained using the same protocol used for the preparation of **9a**. The crude mixture was chromatographed eluting with 5 : 1 petroleum ether : diethyl ether to afford **9b** in 75% yield as a colorless oil. I.R. (neat): 2954, 2242, 1716, 1435, 1341, 1257 cm^{-1} . ¹H NMR (300 MHz, CDCl₃): δ 7.68 (d, *J* = 8.3Hz, 2H), 7.29 (d, *J* = 8.3Hz, 2H), 5.79 (td, *J* = 4.4, 15.1Hz, 1H), 5.47 (td, *J* = 6.6, 15.1Hz, 1H), 4.10 (dd, *J* = 1.2, 4.4Hz, 2H), 3.84 (d, *J* = 6.6Hz, 2H), 3.28 (t, *J* = 7.8Hz, 2H), 2.61 (t, *J* = 7.8Hz, 2H), 2.41 (s, 3H), 0.86 (s, 9H), 0.01 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 153.7, 143.5, 136.4, 134.9, 129.7 (2), 127.0 (2), 123.5, 85.8, 74.1, 62.5, 52.6, 50.3, 44.7, 25.8 (3), 21.4, 19.7, 18.2, -5.3 (2). Anal. Calc'd for $C_{23}H_{35}NO_5SSi$: C, 59.32; H, 7.57; S, 6.88; N, 3.00; Found: C, 59.09; H, 7.67; N, 3.06; S, 6.67.

1-[(*E*)-4-(*tert*-Butyldimethylsilyloxy)-but-2-enyl]-(4-methylbenzenesulfonyl)-amino]-3-trimethylsilyl-prop-2-yne (10**)**

To a cold ($-78^{\circ}C$) solution of alkyne **8a** (0.904g, 2.3mmol) in THF (12mL) was added *n*-BuLi (1.6N, 1.8 ml, 2.88mmol). The solution was stirred for 20 min. at $-78^{\circ}C$, and trimethylsilyl chloride (1mL) was added dropwise. The reaction was allowed to warm up over 1h, and water (10mL) was added. The aqueous phase was extracted with Et₂O (4 x 20mL). The combined ethereal extracts were washed with brine (20mL) and dried over MgSO₄. The residue was chromatographed eluting with 6:1 petroleum ether : diethyl ether to afford **10** (0.660g, 1.41mmol) as a colorless oil. I.R. (neat): 2956, 2178, 1646, 147, 1251 cm^{-1} . ¹H NMR (300 MHz, CDCl₃): δ 7.71 (d, *J* = 8.3Hz, 2H), 7.27 (d, *J* = 8.3Hz, 2H), 5.77 (td, *J* = 4.6, 15.3Hz, 1H), 5.59 (td, *J* = 6.6, 15.9Hz, 1H), 4.14 (m, 2H), 4.07 (s, 2H), 3.80 (d, *J* = 6.5Hz, 2H), 2.40 (s, 3H), 0.88 (s, 9H), 0.04 (s, 6H), -0.02 (s, 9H). ¹³C NMR (75 MHz,

CDCl₃): δ 143.2, 136.0, 135.2, 129.4 (2), 127.7 (2), 123.0, 97.7, 90.8, 62.8, 47.6, 36.6, 25.8 (3), 21.4, 18.3, -0.45 (3), -5.3 (2). Anal. Calc'd for C₂₃H₃₉NO₅SSi: C, 59.30; H, 8.44; N, 3.00; S, 6.88; Found: C, 59.12; H, 8.60; N, 2.91; S, 7.12.

1-[[*(Z)*-4-(*tert*-Butyldimethylsilyloxy)-but-2-enyl]-(4-methylbenzenesulfonyl)-amino]-prop-2-yne (12 a**)**

To an ice cooled solution of alcohol **11** (0.430g, 2.11mmol) in THF (12mL) was added triphenylphosphine (0.666g, 2.54mmol), tosylamine **7a** (0.532g, 2.54mmol) and diisopropyl azodicarboxylate (0.5mL, 2.54mmol). The reaction mixture was stirred at room temperature for 2h. The volatiles were removed under vacuum. The residue was directly purified by chromatography eluting with 5:1 petroleum ether : diethyl ether to yield alkyne **12a** (0.648g, 1.57mmol) as a colorless oil. I.R. (neat): 3274, 2929, 1350, 1162 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 7.75 (d, *J* = 8.3Hz, 2H), 7.31 (d, *J* = 8.3Hz, 2H), 5.79 (ddt, *J* = 1, 5.8, 11.2Hz, 1H), 5.40 (td, *J* = 7.3, 11.2Hz, 1H), 4.26 (br d, *J* = 5.8Hz, 2H), 4.10 (d, *J* = 2.4Hz, 2H), 3.90 (d, *J* = 7.3Hz, 2H), 2.45 (s, 3H), 2.02 (t, *J* = 2.4Hz, 1H), 0.89 (s, 9H), 0.06 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ 143.5, 135.8, 135.4, 129.4 (2), 127.7 (2), 123.8, 76.4, 73.6, 59.0, 43.2, 35.7, 25.8 (3), 21.5, 18.2, -5.2 (2). Anal. Calc'd for C₂₀H₃₁NO₃SSi: C, 61.02; H, 7.93; N, 3.55; Found: C, 61.35; H, 7.52; N, 3.69.

Methyl 4-[[*(Z)*-4-(*tert*-butyldimethylsilyloxy)-but-2-enyl]-(4-methylbenzenesulfonyl)-amino]-but-2-ynoate (13**)**

To a cold (-78°C) solution of alkyne **12a** (0.340g, 0.863mmol) in THF (5 mL) was added *n*-BuLi (1.6N, 0.7mL, 1.12mmol). The solution was stirred for 1h at -78°C, and methyl chloroformate (0.5mL) was added dropwise. The reaction was allowed to warm up over 1h, and water (10mL) was added. The aqueous phase was extracted with Et₂O (4 x 20mL). The combined ethereal extracts were washed with brine (20mL) and dried over MgSO₄. The residue was chromatographed eluting with 5:1 petroleum ether : ether to give alkynoate **13** (0.346g, 0.766mmol) as a colorless oil. I.R. (neat): 3029, 2955, 2240, 1720, 1256, 1164 cm⁻¹.

¹H NMR (500 MHz, CDCl₃) δ : 7.73 (d, *J* = 8.3Hz, 2H), 7.32 (d, *J* = 8.3Hz, 2H), 5.80 (ttd, *J* = 1.5, 6.1, 11Hz, 1H), 5.37 (ttd, *J* = 1.5, 7.3, 11Hz, 1H), 4.23 (dd, *J* = 1.7, 6.1Hz, 2H), 4.20 (s, 2H), 3.88 (d, *J* = 7.1Hz, 2H), 3.69 (s, 3H), 2.43 (s, 3H), 0.87 (s, 9H), 0.04 (s, 6H). ¹³C NMR (125 MHz, CDCl₃) δ : 152.7, 143.9, 135.9, 135.1, 129.6 (2), 127.5, 123.3, 80.4, 76.8, 58.8, 52.5, 43.6, 35.7, 25.7 (3), 21.4, 18.1, -5.4 (2).

HRMS : Calc'd for C₂₁H₃₀NO₅SSi : [M⁺-CH₃] 436.1613; Found : 436.1610.

1-[[*(Z)*-4-(*tert*-Butyldimethylsilyloxy)-but-2-enyl]-(4-methylbenzenesulfonyl)-amino]-but-3-yne (12b**)**

To an ice cooled solution of alcohol **11** (0.86g, 4.22mmol) in THF (25 mL) was added triphenylphosphine (1.33g, 5.07mmol), tosylamine **7b** (1.2g, 5.0mmol) and diisopropyl azodicarboxylate (1.0mL, 5.1 mmol). The reaction mixture was stirred at room temperature for 2h. The volatiles were removed under vacuum. The residue was directly purified by chromatography eluting with 3:1 petroleum ether : ether to yield alkyne **12b** (1.005g, 2.46mmol) as a colorless oil. I.R. (neat): 3310, 2929, 1345, 1160, 1092 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.72

(d, $J = 8.3\text{Hz}$, 2H), 7.32 (d, $J = 8.3\text{Hz}$, 2H), 5.69 (ttd, $J = 1.5$, 6.1, 11.2Hz, 1H), 5.33 (ttd, $J = 1.8$, 7.0, 11.2Hz, 1H), 4.21 (dd, $J = 1.8$, 6.1Hz, 1H), 3.96 (d, $J = 7.0\text{Hz}$, 1H), 3.30 (d, $J = 7.5\text{Hz}$, 1H), 3.29 (d, $J = 7.5\text{Hz}$, 1H), 2.50 (dd, $J = 2.7$, 7.8Hz, 1H), 2.49 (dd, $J = 2.7$, 7.8Hz, 1H), 2.45 (s, 3H), 1.99 (t, $J = 2.7\text{Hz}$, 1H), 0.89 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ 143.3, 136.7, 133.6, 129.7 (2), 127.1 (2), 125.1, 80.9, 70.1, 59.1, 46.1, 45.4, 25.8 (3), 21.5, 19.5, 18.2, -5.2 (2). Anal. Calc'd for $\text{C}_{21}\text{H}_{33}\text{NO}_3\text{SSi}$: C, 61.87; H, 8.15; S, 7.86; N, 3.43; Found: C, 61.79; H, 8.33; S, 7.97; N, 3.66.

Ethyl (4S)-4-hydroxy-pent-2-enoate (**16**)

To a solution of silyl ether **15** (4g), in CH_2Cl_2 (50 ml) was added water (10mL) and trifluoroacetic acid (20 ml). The reaction was stirred at room temperature for 15 min., and the volatiles were removed under reduced pressure. The residue was chromatographed eluting with 1 : 1 diethyl ether : petroleum ether to give α,β -unsaturated ester **16** (2.05 g, 14.2mmol) as a clear oil. $[\alpha]_{\text{D}} = 23.4$ (c 2.1, CHCl_3). I.R. (neat): 3433, 2980, 1718, 1657, 1272 cm^{-1} . ^1H NMR (500 MHz, CDCl_3) δ : 6.97 (dd, $J = 4.7$, 15.6Hz, 1H), 6.04 (dd, $J = 1.7$, 15.6Hz, 1H), 4.51 (ddq, $J = 1.7$, 4.7, 6.6Hz, 1H), 4.22 (q, $J = 7.0\text{Hz}$, 2H), 1.88 (d, 1H), 1.36 (d, $J = 6.6\text{Hz}$, 2H), 1.31 (t, $J = 7.0\text{Hz}$, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ : 166.5, 150.8, 119.6, 67.2, 60.4, 22.7, 14.2.

Experimental procedure for preparation of tosylamines **17a** and **17b**

Table 1

16 (g, mmol)	Tosylamines (g, mmol)	PPh_3 (g, mmol)	DIAD (ml, mmol)
0.5; 3.46	7a ; 1.07, 5.2	1.35, 5.14	1, 5.1
0.576, 4	7b ; 1, 4.47	1.35, 5.14	1, 5.1

To an ice cooled solution of alcohol **16** (see Table 1) in THF (0.2M) was added triphenylphosphine (see Table 1), tosylamine (see Table 1) and diisopropyl azodicarboxylate (see Table 1). The reaction mixture was stirred at room temperature for 2h. The volatiles were removed under vacuum. The residue was directly purified by chromatography eluting with 3 : 2 petroleum ether : diethyl ether 3:2 then 1:1 v/v) to yield impure alkyne (see Table 2) as a colorless oil.

Experimental procedure for preparation of silyl ether **19a** and **19b**

Table 2

Alkyne (g)	DIBAL-H (mL)	Alcohol (g, mmol)	DMAP (g, mmol)	TBDMS-Cl (g, mmol)	Products (g, mmol)
17a ; 1	8	18a ,0.5, 1.7	0.42, 3.43	0.26, 1.7	19a ; 0.592, 1.45
17b , 1.2	10	18b , 0.74, 2.4	0.6, 4.91	0.36, 2.4	19b ; 0.898, 2.12

To a cold (-78°C) solution of impure alkyne (see Table 2) in Et₂O (30 ml), was added DIBAL-H (1M, see Table 2). The reaction was stirred at -78°C until completion (between 20 and 30 min.). Water (one tenth of the DIBAL-H volume introduced) and Et₂O (30mL) were added. The reaction mixture was stirred one hour at room temperature and the heterogeneous mixture was filtered over Celite (Et₂O). The filtrate was evaporated to dryness. The residue was chromatographed (Pet.Eth. : Et₂O 1:3 v/v) to yield the corresponding alcohol (see Table 2). The latter substance was taken up in CH₂Cl₂ (0.4M). 4-DMAP (see Table 2), and *t*-butyldimethylsilyl chloride (see Table 2) were added. The reaction was stirred at room temperature until completion (around 1h). After concentration *in vacuo*, the residue was directly chromatographed eluting with 9 : 1 petroleum ether : diethyl ether to afford the corresponding product (see Table 2) as a colorless oil.

1-[[*(4R)*-(*E*)-4-(*tert*-Butyldimethylsilyloxy)-4-methyl-but-2-enyl]-(*4*-methylbenzenesulfonyl)-amino]-prop-2-yne (19a**)**

[α]_D = 28.4 (c 2.37, CHCl₃). I.R. (neat): 3277, 2955, 1337, 1156 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.81 (d, *J* = 8.3Hz, 2H), 7.29 (d, *J* = 8.3Hz, 2H), 5.66 (dt, 4.1, 15.6Hz, 1H), 5.61 (dd, *J* = 4.4, 15.6Hz, 1H), 4.58 (m, 1H), 4.13 (dd, *J* = 2.4, 18.3Hz, 1H), 4.13 (m overlapped, 2H), 3.90 (dd, *J* = 2.5, 18.3Hz, 1H), 2.43 (s, 3H), 2.15 (t, *J* = 2.5Hz, 1H), 1.31 (d, *J* = 6.8Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ 143.1, 137.7, 132.2, 129.3 (2), 128.4, 127.4 (2), 80.2, 72.2, 62.9, 54.1, 32.3, 25.8 (3), 21.5, 18.3, 17.8, -5.3 (2). Anal. Calc'd for C₂₁H₃₃NO₃SSi: C, 61.87; H, 8.15; S, 7.86; N, 3.43; Found: C, 61.70; H, 7.95; N, 3.45; S, 7.69.

1-[[*(4R)*-(*E*)-4-(*tert*-Butyldimethylsilyloxy)-but-2-enyl]-(*4*-methylbenzenesulfonyl)-amino]-but-3-yne (19b**)**

[α]_D = 50.7 (c 1.91, CHCl₃). I.R. (neat) : 3310, 2929, 1341, 1154 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.73 (d, *J* = 8.3Hz, 2H), 7.29 (d, *J* = 8.3Hz, 2H), 5.60 (ddt, *J* = 1.7, 4.4, 15.6Hz, 1H), 5.45 (ddt, *J* = 1, 4.8, 15.6Hz, 1H), 4.54 (m, 1H), 4.09 (m, 1H), 3.26 (ddd, *J* = 5.6, 10.5, 15.1Hz, 1H), 3.18 (ddd, *J* = 5.6, 10.0, 15.1Hz, 1H), 2.64 (dddd, *J* = 2.7, 5.6, 10.2, 15.9Hz, 1H), 2.53 (dddd, *J* = 2.4, 5.6, 0.2, 15.9Hz, 1H), 2.01 (t, *J* = 2.4Hz, 1H), 1.23 (d, *J* = 6.8Hz,

3H), 0.88 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ 143.1, 137.6, 132.0, 129.6 (2), 128.5, 127.1 (2), 81.1, 70.0, 62.8, 53.9, 42.5, 25.8 (3), 21.7, 21.4, 18.3, 18.1, -5.3 (2). Anal. Calc'd for $\text{C}_{22}\text{H}_{35}\text{NO}_3\text{SSi}$: C, 62.66; H, 8.36; N, 3.32; S, 7.60; Found: C, 62.76; H, 8.26; N, 3.35; S, 7.67.

Ethyl (4*R*,5*S*) 5-hydroxy-4-methyl-hex-2-enoate (21)

To a solution of silyl ether **20** (4.0g, 13.9mmol) in CH_2Cl_2 (30mL) was added water (5 mL) and trifluoroacetic acid (20 ml). The solution was stirred at room temperature for 15 min. The volatiles were removed under reduced pressure and the residue was purified by chromatography eluting with 1 : 1 petroleum ether : diethyl ether to afford alcohol **21** (2.04g, 11.86mmol) as an oil. $[\alpha]_{\text{D}} = 29.7$ (c 1.17, CH_2Cl_2). I.R. (neat): 3444, 2976, 1718, 1651 cm^{-1} . ^1H NMR (500 MHz, CDCl_3) : δ 6.94 (dd, $J = 8.3, 15.6\text{Hz}$, 1H), 5.89 (dd, $J = 1.2, 15.6\text{Hz}$, 1H), 4.20 (q, $J = 7.0\text{Hz}$, 2H), 3.75 (app pent, $J = 6.0\text{Hz}$, 1H), 2.36 (m, 1H), 2.09 (br s, 1H), 1.30 (t, $J = 7.0\text{Hz}$, 3H), 1.20 (d, $J = 6.3\text{Hz}$, 3H), 1.09 (d, $J = 6.8\text{Hz}$, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 166.5, 150.3, 122.22, 70.7, 60.3, 44.0, 20.5, 15.3, 14.2. Anal. Calc'd for $\text{C}_9\text{H}_{16}\text{O}_3$: C, 62.76; H, 9.36; Found: C, 62.54; H, 9.24.

(2*S*,3*R*)6-(*tert*-Butyldimethylsilyloxy)-3-methyl-hex-4-en-2-ol (22)

To a solution of alcohol **21** (2.04g, 11.4mmol) in CH_2Cl_2 (25mL) were added successively pyridinium *p*-toluenesulfonate (0.251g, 1mmol) and dihydropyran (2.7mL, 30mmol). The solution was stirred at room temperature for 8h. The solution was concentrated under reduced pressure and the residue directly chromatographed (P.Eth. : Et_2O 3:1 v/v) to afford a colorless oil. The latter material was taken up in Et_2O (60 ml). To the cold (-78°C) solution was then added DIBAL-H (1M, 30mL, 30mmol). The solution was stirred for 30 min. at -78°C and water (3mL) and technical Et_2O (30mL) were added. The solution was stirred for 1h at room temperature. The heterogeneous solution was filtered over Celite (Et_2O) and the filtrate concentrated *in vacuo*. The residue was purified by chromatography (petroleum ether : diethyl ether 1:2 v/v) to afford 2.1g of a colorless oil. This material was dissolved in CH_2Cl_2 (25 ml). Triethylamine (3.3mL, 23.6mmol), 4-DMAP (0.250g, 2.04mmol) and *t*-butyldimethylsilyl chloride (1.8g, 12mmol) were added. The solution was stirred at room temperature for 3h. Water (20mL) was then added, and the aqueous phase was extracted with CH_2Cl_2 (3 x 20mL). The combined organic layers were washed with brine (30mL) and dried over MgSO_4 . After evaporation to dryness, the residue was purified by chromatography (petroleum ether : diethyl ether 10:1 v/v) to afford 2.936g of a colorless oil. To a solution of the latter (2.8g, 8.5mmol) in Et_2O (80mL) was added $\text{MgBr}_2 \cdot \text{OEt}_2$ (6.6g, 25.5mmol). The suspension was stirred at room temperature for 2h, and then was filtrated on a pad of silica gel (Et_2O). To the filtrate was added water (100 ml). The aqueous phase was extracted with Et_2O (2 x 50mL). The combined ethereal layers were dried over MgSO_4 and concentrated *in vacuo*. The residue was chromatographed eluting with 2 : 1 petroleum ether : diethyl ether to afford first the remaining starting material (0.7 g) and then the alcohol **22** (1.3g, 5.31mmol) as a colorless oil. $[\alpha]_{\text{D}} = 15.6$ (c 1.23, CHCl_3). I.R. (neat) : 3419, 2958, 1255, 1095 cm^{-1} . ^1H NMR (500 MHz, CDCl_3) δ : 5.63 (td, $J = 4.8, 15.6\text{Hz}$, 1H), 5.52 (dd, $J = 7.8, 15.6\text{Hz}$, 1H), 4.14 (d, $J = 4.8\text{Hz}$, 2H), 3.53 (pent, $J = 6.4\text{Hz}$, 1H), 2.11 (hex, $J = 6.8\text{Hz}$, 1H), 1.13 (d, $J = 6.4\text{Hz}$, 3H), 0.98 (d, $J = 6.8\text{Hz}$, 3H), 0.88 (s, 9H), 0.04 (s,

6H). ^{13}C NMR (125 MHz, CDCl_3) δ : 132.3, 131.3, 70.9, 63.6, 44.4, 25.8 (3), 19.9, 18.3, 6.1, -5.1 (2). HRMS : Calc'd for $\text{C}_{13}\text{H}_{27}\text{OSi}$: $[\text{M}^+ - \text{OH}]$ 227.1831; Found : 227.1842

1-[[**(2R,5R)-(E)-5-(tert-Butyldimethylsilyloxy)-1,2-dimethyl-pent-3-enyl**]-**(4-methylbenzenesulfonyl)-amino**]-prop-2-yne (**23**)

To an ice cooled solution of alcohol **22** (0.63g, 2.57mmol) in THF (13mL) was added triphenylphosphine (1.35g, 5.15mmol), tosylamine **7a** (1.07g, 5.15mmol) and diisopropyl azodicarboxylate (1.0mL, 5.1mmol). The reaction mixture was stirred at room temperature for 8h. The volatiles were removed under vacuum. The residue was directly purified by chromatography eluting with 3 : 1 petroleum ether : diethyl ether to yield alkyne **23** (0.180g, 0.424mmol) as a colorless oil. $[\alpha]_{\text{D}} = 5.2$ (c 1.26, CHCl_3). I.R. (neat) : 3310, 2930, 1340, 1156 cm^{-1} . ^1H NMR (500 MHz, CDCl_3) δ : 7.76 (d, $J = 8.3\text{Hz}$, 2H), 7.25 (d, $J = 8.3\text{Hz}$, 2H), 5.57 (td, $J = 4.9, 15.1\text{Hz}$, 1H), 5.42 (dd, $J = 8.5, 15.1\text{Hz}$, 1H), 4.10 (d, $J = 4.9\text{Hz}$, 2H), 4.08 (dd partially overlapped, $J = 2.4, 18.5\text{Hz}$, 1H), 3.92 (dd, $J = 2.4, 18.5\text{Hz}$, 1H), 3.67 (dq, $J = 6.8, 9.5\text{Hz}$, 1H), 2.40 (s, 3H), 2.36 (m overlapped, 1H), 2.12 (t, $J = 2.4\text{Hz}$, 1H), 1.00 (d, $J = 6.8\text{Hz}$, 3H), 0.98 (d, $J = 6.8\text{Hz}$, 3H), 0.88 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3) δ : 143.1, 137.7, 132.5, 130.5, 129.3 (2), 127.4 (2), 79.7, 72.3, 63.5, 58.3, 41.7, 31.9, 25.9 (2), 21.4, 18.6, 18.3, 16.6, -5.1 (2). HRMS : Calc'd for $\text{C}_{19}\text{H}_{28}\text{NO}_3\text{SSi}$: $[\text{M}^+ - \text{C}_4\text{H}_9]$ 378.1559; Found : 378.1545.

4,4-Dimethyl-9-trimethylsilyl-non-2-en-8-yn-1-ol

To a solution of ester **28bⁱ** (3.9g, 16.2mmol) in Et_2O (100mL) cooled at -78°C , was added DIBAL-H (1M, 50mL, 50mmol). The resulting solution was stirred for 20 min. and water (5mL) was added. The solution was stirred for 1h at room temperature. The resulting mixture was filtered through Celite and thoroughly washed with Ether. The filtrate was then concentrated *in vacuo* to afford crude alcohol. To a solution oxalyl chloride (2mL, 22.9mmol) in CH_2Cl_2 (50mL) was added at -78°C a solution of DMSO (3mL, 42.2mmol) in CH_2Cl_2 (10mL). After 10 min., a solution of alcohol (crude, previously prepared), in CH_2Cl_2 (15mL) was added. The resulting mixture was stirred at -78°C for 20 min. and triethylamine (10mL, 70mmol) was added slowly over 30 min. The solution was then gradually warmed up to room temperature and stirred then for 1h. A saturated solution of NaHCO_3 (30mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 x 50mL). The combined organic layers were then dried over magnesium sulfate and concentrated *in vacuo*. The crude aldehyde was then dried azeotropically with toluene. The crude material was taken up in toluene (100mL) and carboethoxymethylene triphenylphosphorane (7g, 20mmol) was added. The mixture was refluxed for 1h and then evaporated to dryness. The residue was taken up in 3 : 1 petroleum ether : diethyl ether (100mL). The suspension was then filtered over a pad of silica gel, and the pad thoroughly washed (3 : 1 petroleum ether : diethyl ether). The filtrate was then concentrated under reduced pressure, and the resulting residue (**28b**) was diluted with Et_2O (60mL). The solution was cooled to -78°C , and

DIBAL-H (1M, 32mL, 32mmol) was added. The resulting solution was stirred for 20 min. and water (3.2mL) was added. The solution was stirred for 1h. at room temperature. The resulting mixture was filtered through Celite and thoroughly washed with Et₂O. The filtrate was then concentrated *in vacuo*. The residue was chromatographed eluting 1 : 1 petroleum ether : diethyl ether to afford allylic alcohol (2.52g, 11.0mmol) as a colorless oil. I.R. (neat) : 3333, 2958, 2174, 1249 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ : 5.63 (d, *J* = 15.7Hz, 1H), 5.55 (td, *J* = 5.6, 15.7Hz, 1H), 4.13 (d, *J* = 5.6Hz, 2H), 2.18 (t, *J* = 7.1Hz, 2H), 1.45 (m, 2H), 1.37 (m, 2H), 1.01 (s, 6H), 0.16 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ 142.5, 125.1, 107.5, 84.3, 64.0, 42.0, 35.5, 27.0, 24.0, 20.4, 0.15.

HRMS : Calc'd for C₁₃H₂₃OSi : [M⁺-CH₃] 223.1518; Found : 223.1511.

1-*tert*-Butyldimethylsilyloxy-4,4-dimethyl-non-2-en-8-yne (30b)

To a solution of allylic alcohol (0.750g, 3.34mmol) in CH₂Cl₂ (7mL) was added at room temperature 4-DMAP (0.614 g, 5.0mmol) and *t*-butyldimethylsilyl chloride (0.510 g, 3.37mmol). The solution was stirred for 1h. and then concentrated under reduced pressure. The residue was directly purified over silica gel eluting with 10 : 1 petroleum ether : diethyl ether to afford silyl ether (1.04 g). The latter material was dissolved in MeOH (14 mL) and potassium carbonate (0.4 g) was added. The mixture was stirred overnight at room temperature. The volatiles were removed under reduced pressure, and the residue was filtered through a pad of silica gel eluting with 10 : 1 petroleum ether : diethyl ether to afford alkyne **30b** (0.760g, 2.70mmol) as a colorless oil. I.R. (neat): 3314, 2956, 2956, 2119, 1472, 1254, 1105 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) : δ 5.57 (d, *J* = 15.6Hz, 1H), 5.55 (td, *J* = 5.4, 15.6Hz, 1H), 4.13 (d, *J* = 5.4Hz, 2H), 2.18 (td, *J* = 2.7, 6.1Hz, 2H), 1.95 (t, *J* = 2.7Hz, 1H), 1.46 (m, 2H), 1.39(m, 2H), 1.01 (s, 6H), 0.92 (s, 9H), 0.08 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ 140.3, 125.5, 84.6, 68.1, 64.3, 42.0, 35.3, 27.0, 25.9, 23.8, 19.0, 18.4, -5.0. Calc'd for C₁₉H₂₈NO₃SSi : [M⁺-C₄H₉] 223.1518; Found : 223.1502.

(*E*)-1-*tert*-Butyl-dimethylsilyloxy-4,4-dimethyl-oct-2-en-7-yne (30a)

Starting from alkenoate **28a** (0.520g, 2.0mmol) and performing the same sequence, alkyne **30a** (0.334g, 1.25mmol) was recovered as a colorless oil. I.R. (neat) : 3314, 2957, 2120, 1472, 1104 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ : 5.2 (d, *J* = 15.7Hz, 1H), 5.42 (td, *J* = 4.6, 15.7Hz, 1H), 4.14 (d, *J* = 4.6Hz, 2H), 2.07 (m, 2H), 1.91 (t, *J* = 2.7Hz, 1H), 1.57 (m, 2H), 0.99 (s, 6H), 0.90 (s, 9H), 0.06 (s, 6H). ¹³C NMR (125 MHz, CDCl₃) δ : 139.1, 126.3, 85.2, 67.7, 64.1, 41.7, 35.5, 26.7 (2), 25.9 (3), 18.4, 14.0, -5.0 (2). Anal. Calc'd for C₁₆H₃₀O₃Si : C, 72.11; H, 11.34; Found: C, 72.36; H, 11.30.

Methyl 9-(*tert*-butyldimethylsilyloxy)-6,6-dimethyl-non-7-en-2-ynoate 31

To a cold (-78°C) solution of alkyne **30a** (0.230g, 0.87mmol) in THF (12ml) was added *n*-BuLi (1.6N, 0.7ml, 1.12mmol). The solution was stirred for 1h at -78°C, and methyl chloroformate (0.5mL) was added dropwise. The reaction was allowed to warm up over 1h, and water (10mL) was added. The aqueous phase was extracted with Et₂O (4 x 20mL). The combined ethereal extracts were washed with brine (20mL) and dried over MgSO₄. The residue was chromatographed eluting with 9 : 1 petroleum ether : diethyl ether to afford **31** (0.211 g, 0.65 mmol) as a colorless oil. I.R. (neat): 2956, 1718, 2239, 1254 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ : 5.52 (d, *J* = 15.6Hz, 1H), 5.47 (td, *J* = 4.9, 15.6Hz, 1H), 4.18 (m, 2H), 3.76 (s, 3H), 2.23 (dd, *J* = 8.1, 8.3Hz, 2H), 1.64 (m, 2H), 1.01 (s, 6H), 0.92 (s, 9H), 0.06 (s, 6H). ¹³C NMR (125 MHz, CDCl₃) δ : 154.2, 138.5, 126.9, 90.4, 72.5, 64.0, 52.5, 40.3, 35.5, 26.7 (2), 25.9 (3), 18.4, 14.4, -5.0 (2). Anal. Calc'd for C₁₄H₂₃O₃Si [M⁺-C₄H₉]: 268.1494; Found: 268.1448

(Z)-1-tert-Butyldimethylsilyloxy-4-(prop-2-ynyloxy)-but-2-ene 25

To an ice cooled suspension of sodium hydride (95%, 0.760g, 30mmol) in THF (20mL) was added *cis* 1,4-but-2-ene-diol (1.76g, 20mmol) in THF (10mL). The suspension was stirred for 20 min. at room temperature. The suspension was cooled down (0°C) and tetrabutyl ammonium iodide (0.1g, cat.) and propargyl bromide (80% in toluene, 2.4mL, 22mmol) were added. The solution was then stirred for 2h at room temperature. Acetic acid (2mL) was added and the volatiles were removed *in vacuo*. The residue was directly chromatographed (Pet.Eth. : Et₂O 9:1 then 2:1) to afford ether **24** (0.730g, 5.78 mmol).

The latter substance was taken up in CH₂Cl₂ (15mL). 4-DMAP (1.06g, 8.67mmol) and *t*-butyldimethylsilyl chloride (0.880g, 5.85mmol) were added. The reaction mixture was stirred for 2h at room temperature. After evaporation to dryness, the residue was directly purified by chromatography eluting with 20 : 1 petroleum ether : diethyl ether to afford alkyne **25** (1.32g, 5.49 mmol). I.R. (neat): 3310, 2930, 1471, 1084 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ : 5.76 (ttd, *J* = 1.4, 5.8, 11.2Hz, 1H), 5.59 (ttd, *J* = 1.7, 6.6, 11.2Hz, 1H), 4.29 (dd, *J* = 1.7, 5.8Hz, 1H), 4.17 (dd partially overlapped, *J* = 1.4, 6.6Hz, 1H), 4.16 (d, *J* = 2.5Hz, 2H), 2.45 (t, *J* = 2.5Hz, 1H), 0.92 (s, 9H), 0.09 (s, 6H). ¹³C NMR (125 MHz, CDCl₃) δ : 133.7, 125.8, 79.6, 74.4, 65.1, 59.4, 57.0, 25.9 (3), 18.3, -5.2 (2). Anal. Calc'd for C₁₃H₂₄O₂Si : C, 64.94; H, 10.06; Found: C, 65.12; H, 9.96.

Methyl (Z)-4-[4-(tert-butyldimethylsilyloxy)-but-2-enyloxy]-but-2-ynoate (26)

To a cold (-78°C) solution of alkyne **25** (0.860g, 3.55mmol) in THF (20mL) was added *n*-BuLi (1.6N, 2.4 mL, 3.84mmol). The solution was stirred for 1h at -78°C, and methyl chloroformate (0.6 ml) was added dropwise. The reaction was allowed to warm up over 1h, and water (10mL) was added. The aqueous phase was extracted with Et₂O (4 x 20mL). The combined ethereal extracts were washed with brine (20mL) and dried over MgSO₄. The residue was chromatographed eluting with 9 : 1 petroleum ether : diethyl ether to afford first alkyne **25** (0.129g, 0.536mmol) and then alkynoate **26** (0.680g, 2.27mmol) as a colorless oil I.R. (neat) : 2955, 2238, 1722, 1254, 1087 cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ : 5.77 (ttd, *J* = 1.4, 6.1, 11.2Hz, 1H), 5.57 (ttd, *J* = 1.8, 6.6, 11.2Hz, 1H), 4.28 (s, 2H), 4.27 (tdd partially overlapped, *J* = 0.9, 1.8, 6.6Hz, 1H), 4.17 (tdd, *J* = 0.7, 1.4, 6.1Hz, 1H), 3.8 (s, 3H), 0.91

(s, 9H), 0.09 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3) δ : 153.4, 134.2, 125.2, 83.5, 77.7, 65.6, 59.4, 56.7, 52.7, 25.8 (3), 18.2, -5.2 (2). Anal. Calc'd for $\text{C}_{15}\text{H}_{26}\text{O}_4\text{Si}$: C, 60.36; H, 8.78; Found: C, 60.22; H, 8.60

(1S)-4-[[*(E)*-4-(*tert*-Butyldimethylsilyloxy)-1-methyl-but-2-enyl]-(4-methylbenzenesulfonyl)-amino]-but-2-ynoic acid methyl ester **51**

To a cold (-78°C) solution of alkyne **19a** (0.30g, 0.70mmol) in THF (5mL) was added *n*-BuLi (1.6N, 0.6mL, 0.9mmol). The solution was stirred for 1h at -78°C , and methyl chloroformate (0.5mL) was added dropwise. The reaction was allowed to warm up over 1h, and water (10mL) was added. The aqueous phase was extracted with Et_2O (4 x 20mL). The combined ethereal extracts were washed with brine (20mL) and dried over MgSO_4 . After evaporation to dryness, the residue was chromatographed eluting with 3 : 1 petroleum ether : diethyl ether 3:1 to give alkynoate **51** (0.282g, 0.60mmol) as a colorless oil. $[\alpha]_{\text{D}}^{25} = 18.4$ (c 1.21, CHCl_3). I.R. (neat): 2954, 2241, 1719 cm^{-1} . ^{1}H NMR (500 MHz, CDCl_3): δ 7.79 (d, $J = 8.3\text{Hz}$, 2H), 7.29 (d, $J = 8.3\text{Hz}$, 2H), 5.64 (ttd, 1.5, 4.4, 15.6Hz, 1H), 5.53 (ddt, $J = 1.5$, 4.4, 15.6Hz, 1H), 4.55 (m, 1H), 4.24 (d, $J = 19.0\text{Hz}$, 1H), 4.11 (td, $J = 1.4$, 4.4Hz, 2H), 3.98 (d, $J = 19.0\text{Hz}$, 1H), 3.74 (s, 3H), 2.41 (s, 3H), 1.24 (d, $J = 7.1\text{Hz}$, 3H), 0.86 (s, 9H), 0.22 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3) δ : 153.3, 143.5, 137.3, 132.8, 129.6 (2), 127.9, 127.4 (2), 84.0, 75.5, 62.8, 53.8, 52.6, 32.1, 25.8 (3), 21.5, 18.3, 17.5, -5.3 (2). Anal. Calc'd for $\text{C}_{23}\text{H}_{35}\text{NO}_5\text{Si}$: C, 59.32; H, 7.57; N, 3.06; S, 6.88; Found C, 59.47; H, 7.36; N, 3.07; S, 6.69. HRMS : Calc'd for $\text{C}_{23}\text{H}_{35}\text{NO}_5\text{Si}:[\text{M}^+]$ 465.2005; Found : 465.1997

N-(4-Methylbenzenesulfonyl)-34-(2-hydroxyethyl)-4-methoxycarbonyl-methylenepyrrolidine (67**)** To a solution of silyl enol ether **34** (0.120g, 0.265 mmol) in CH_2Cl_2 (5mL) was added water (0.1mL) and trifluoroacetic acid (2mL). The reaction was stirred at room temperature for 15 min. and the volatiles were removed under reduced pressure. The residue was purified by chromatography (eluting with 1:3 diethyl ether petroleum ether to afford the corresponding aldehyde (0.088g, 0.260mmol) as a clear oil. I.R. (neat): 2846, 1188, 1658, 1164 cm^{-1} . ^{1}H NMR (500 MHz, CDCl_3): δ 9.74 (s, 1H), 7.72 (d, $J = 8.3\text{Hz}$, 2H), 7.34 (d, $J = 8.3\text{Hz}$, 2H), 5.70 (s, 1H), 5.30 (d, $J = 18.3\text{Hz}$, 1H), 4.21 (dd, $J = 2.4$, 18.3Hz, 1H), 3.69 (s, 3H), 3.48 (dd, $J = 7.4$, 9.5Hz, 1H), 3.27 (m, 1H), 2.94 (m, 1H), 2.75 (dd, $J = 4.6$, 18.8Hz, 1H), 2.71 (dd, $J = 7.8$, 18.8Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 198.7, 165.7, 160.2, 143.9, 131.9, 129.7 (2), 127.8 (2), 113.3, 52.1, 51.8, 51.4, 46.6, 38.0, 21.4. To a solution of this aldehyde (0.072g, 0.213mmol) in MeOH (5mL) was added NaBH_4 (0.016g, 0.426mmol). The solution was stirred at room temperature for 30 min. and water (2mL) was added. The mixture was then concentrated *in vacuo*. The residue was diluted with water (3mL) and extracted with CH_2Cl_2 (3 x 10mL). The combined organic layers were dried over MgSO_4 and concentrated under reduced pressure. The residue was chromatographed eluting with 9:1 diethyl ether : petroleum ether to afford alcohol **67** (0.065 g, 0.191mmol) as a colorless oil. I.R. (film): 3540, 2951, 1713, 1667, 1345, 1162 cm^{-1} . ^{1}H NMR (300 MHz, CDCl_3) δ : 7.74 (d, $J = 8.3\text{Hz}$, 2H), 7.34 (d, $J = 8.3\text{Hz}$, 2H), 5.7 (br d, $J = 2.4\text{Hz}$, 1H), 4.30 (dd, $J = 2.7$, 18.3Hz, 1H), 4.20 (dt, $J = 2.5$, 18.3Hz, 1H), 3.69 (m, 5H), 3.50 (m, 1H)

2.98 (m, 2H), 2.43 (s, 3H), 2.00 (s, 1H), 1.86 (m, 1H), 1.62 (tq, $J = 5.6, 8.8\text{Hz}$, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 166.1, 161.6, 143.9, 131.7, 129.7 (2), 127.8 (2), 112.7, 60.0, 52.3, 51.9, 51.3, 41.4, 34.8, 21.4. Anal. Calc'd for $\text{C}_{16}\text{H}_{21}\text{NO}_5\text{S}$: C, 56.62; H, 6.24; N, 4.13; S, 9.45; Found: C, 56.91; H, 6.14; N, 4.17; S, 9.49.

Methyl-[5-(4-methylbenzenesulfonyl)-hexahydro-furo[2,3-*c*]pyrrol-6a-yl]-acetate (68)

I.R. (neat) : 2953, 1736, 1345, 1165 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 7.65 (d, $J = 8.3\text{Hz}$, 2H), 7.31 (d, $J = 8.3\text{Hz}$, 2H), 3.82 (d, $J = 5.2\text{Hz}$, 1H), 3.81 (d, $J = 5.4\text{Hz}$, 1H), 3.60 (s, 3H), 3.43 (d, $J = 10.8\text{Hz}$, 1H), 3.18 (dd, $J = 7.9, 9.8\text{Hz}$, 1H), 3.10 (d, $J = 10.8\text{Hz}$, 1H), 3.05 (dd, $J = 3.8, 9.8\text{Hz}$, 1H), 2.68 (hept, $J = 3.9\text{Hz}$, 1H), 2.58 (d, $J = 15.2\text{Hz}$, 1H), 2.54 (d, $J = 15.2\text{Hz}$, 1H), 2.41 (s, 3H), 2.10 (qd, $J = 8.1, 11.5\text{Hz}$, 1H), 1.75 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ 170.3, 143.7, 131.7, 129.6 (2), 128.0 (2), 89.5, 68.3, 58.2, 53.5, 51.7, 46.6, 41.8, 32.5, 21.5. Anal. Calc'd for $\text{C}_{16}\text{H}_{21}\text{NO}_5\text{S}$: C, 56.62; H, 6.24; N, 4.13; S, 9.45; Found: C, 56.84; H, 6.32; N, 4.27; S, 9.33.

N-(4-Methylbenzenesulfonyl)-3-[2-(2-Oxo-dihydro-furan-3-ylidene)-ethyl]-4-methoxy-

carbonylmethylenepyrrolidine (69). To a solution of aldehyde (0.083g, 0.246mmol) in CH_2Cl_2 (3 ml) was added 2-triphenylphosphoranylide- γ -butyrolactone (0.170g, 0.492mmol). The reaction mixture was stirred at room temperature for 90 min. The crude mixture was concentrated *in vacuo* and the residue was purified on silica gel eluting with 4 : 1 ethyl acetate : petroleum ether to afford lactone **69** (0.092g, 0.227mmol) as a white solid. m.p.: 91–92°C. I.R. (neat) : 2951, 1754, 1714, 1670, 1436, 1346, 1163 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 7.69 (d, $J = 8.3\text{Hz}$, 2H), 7.33 (d, $J = 8.3\text{Hz}$, 2H), 6.58 (m, 1H), 5.75 (br s, 1H), 4.39 (m, 3H), 4.11 (dd, $J = 2.5, 8.1\text{Hz}$, 1H), 3.60 (s, 3H), 3.18 (dd, $J = 6.6, 9.5\text{Hz}$, 1H), 3.04 (dd, $J = 4.9, 9.5\text{Hz}$, 1H), 2.92 (m, 2H), 2.82 (m, 1H), 2.41 (s, 3H), 2.40 (m partially overlapped, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ 170.5, 165.7, 159.8, 144.0, 135.2, 131.6, 129.8 (2), 128.6, 127.8 (2), 113.6, 65.5, 52.2, 51.4, 51.1, 43.4, 33.2, 25.1, 21.4. HRMS: Calc'd for $\text{C}_{19}\text{H}_{20}\text{NO}_5\text{S}$ [$\text{M}^+ - \text{CH}_3\text{O}$]: 374.1062; Found: 374.1024.

References

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