

Highly 2,3-*trans* Stereoselective Allylations of 2,3-O-Isopropylidene Protected Pyrrolidines: Circumventing the N-acyliminium ion Chemistry? **Pedro de Armas, Fernando García-Tellado, Jose Juan Marrero-Tellado**

### Supporting Information

#### General experimental procedure:

**Synthesis of 2:** To solution of **1** (100mg, 0.23mmol) was added and Allyltrimethylsilane (0.14 ml, 0.92 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 ml) in a dry flask nitrogen atmosphere. The mixture was cooled to -78<sup>0</sup>C and BF<sub>3</sub>.Et<sub>2</sub>O (0.06 ml, 0.47 mmol) was slowly added. After 5 min, the cooling bath was removed, and the mixture was stirred for 50 min. The organic phase was washed once with water, dried over MgSO<sub>4</sub>, concentrated and percolated through a pad of silica gel to give **2** as an oily residue (52 mg, 52%). The <sup>1</sup>H NMR spectrum of the oily residue showed signals for just one diastereoisomer. An aliquot was further purified by flash chromatography (EtOAc/n-hexane 15/85).

Selected physical data for **2** (acetate): [ $\alpha$ ]<sub>D</sub><sup>25</sup> = + 15<sup>0</sup> (c= 0.3 CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>, 65 °C)  $\delta$  = 0.0 (s, 3H; MeSi), 0.05 (s, 3H; MeSi), 0.93 (s, 9H; t-BuSi), 1.8 (s, 3H; AcO), 2.66 (m, 2H; CH<sub>2</sub>-CH=CH<sub>2</sub>), 3.4 (dd, J = 11 and 5.5 Hz, 2H; H-5), 4.02 (app q, J=5.5 Hz; C4-H), 4.09 (app dd, J = 5 and 4.5 Hz, 1H; C-2), 5.1-5.01 (m, 3H; CH<sub>2</sub>=CH-, C3-H), 5.18 (d, J = 12.5 Hz, 1H; CH<sub>2</sub>OBn), 5.23 (d, J = 12.5, 1H; CH<sub>2</sub>OBn), 5.8 (m, 1H; -CH=CH<sub>2</sub>), 7.12 (t, J = 7.5 Hz, 1H; Ar), 7.18 (t, J = 7.5 Hz, 2H; Ar), 7.34 (d, J = 7.5 Hz, 2H; Ar); <sup>13</sup>C NMR (100 MHz, C<sub>6</sub>D<sub>6</sub>, 65 °C):  $\delta$  = -5.5 x 2C, 17.7, 19.9, 25.2 x 3C, 34.0, 51.6, 58.1, 66.7, 70.1, 73.1, 116.0, 127.4, 127.9, 128.2, 135.2, 137.2, 154.5, 168.6; IR (chloroform) :  $\nu$  = 3026, 2956, 2360, 2341, 1741, 1695, 1418, 1357 cm<sup>-1</sup>; HMRS calcd for C<sub>20</sub>H<sub>30</sub>NO<sub>5</sub>Si [(M<sup>+</sup>-CH<sub>2</sub>CH=CH<sub>2</sub>)] 392.516, found 392.250.

The configuration assigned at C-1 was unambiguously determined from <sup>1</sup>H-<sup>1</sup>H decoupling experiments to show a <sup>3</sup>J (H-2, H-3) ≈ 0 Hz, confirming a 2,3-*trans* relationship and a NOESY experiment showed nOes between H-3 and allylic protons and H-4, and between H-2 and H<sub>α</sub>-5.

**Synthesis of 4:** To solution of **3** (206mg, 0.63mmol) was added and allyltrimethylsilane (0.8 ml, 0.5 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (7 ml) in a dry flask nitrogen atmosphere. The mixture was cooled to -78<sup>0</sup>C and BF<sub>3</sub>.Et<sub>2</sub>O (0.06 ml, 0.47 mmol) was slowly added. After 5 min, the cooling bath was removed, and the mixture was stirred for 50 min. The organic phase was washed once with water, dried over MgSO<sub>4</sub>, concentrated and percolated through a pad of silica gel to give **4** as an oily residue (135 mg, 62%). The <sup>1</sup>H NMR spectrum of the oily residue showed signals for just one diastereoisomer. An aliquot was further purified by flash chromatography (EtOAc/n-hexane 70/30).

Selected physical data for **4** (tert-Butyl dimethyl ether): [ $\alpha$ ]<sub>D</sub><sup>25</sup> = + 16.13<sup>0</sup> (c= 0.2 CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  = 0.03 (s, 3H; MeSi), 0.04 (s, 3H; MeSi), 0.82 (s, 9H; t-BuSi), 2.54 (m, 2H; CH<sub>2</sub>-CH=CH<sub>2</sub>), 2.78 (dd, J = 10.3 and 13.5 Hz.; 2H CH<sub>2</sub>-Ph), 3.81 (m, 1H; C2-H), 4.07 (s, 1H, C3-H), 4.49 (m, 1H; C5-H), 4.91 (dd, J = 3.5 Hz, J = 6.1 Hz, 1H; C4-H), 5.05 (m, 2H; CH=CH<sub>2</sub>), 5.14 (d, J = 11.7 Hz, 2H; OCH<sub>2</sub>Ph), 5.96, (m, 2H; CH=CH<sub>2</sub>), 7.19 (12H; Ar), 7.35 (8H; Ar), 7.92 (s, 1H, CHO); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = -4.32, -3.89, 18.38, 26.2 x 3C, 37.23, 60.9, 65.9, 67.65, 76.0.9,

78.26, 118.47, 118.56, 126.99, 128.41, 128.62, 128.98, 129.11, 129.65, 134.89, 138.58, 156.41, 159.95, 160.02; IR (chloroform) :  $\nu = 2925, 2885, 1725, 1690, 1105 \text{ cm}^{-1}$ ; HMRS calcd for  $\text{C}_{26}\text{H}_{34}\text{NO}_5\text{Si} [(M^+-\text{CH}_2\text{CH}=\text{CH}_2)]$  468.2206, found 468.2244.

The configuration assigned at C-1 was unambiguously determined from  $^1\text{H}$ - $^1\text{H}$  decoupling experiments to show a  $^3J$  (H-2, H-3)  $\approx 0$  Hz, confirming a 2,3-trans relationship and a NOESY experiment showed nOes between H-2 and allylic protons and H-4, and H-5.

**Synthesis of 6:** To solution of **5** (121mg, 0.22mmol) was added and allyltrimethylsilane (0.14 ml, 0.9 mmol) in  $\text{CH}_2\text{Cl}_2$  (6 ml) in a dry flask nitrogen atmosphere. The mixture was cooled to  $-78^\circ\text{C}$  and  $\text{BF}_3\cdot\text{Et}_2\text{O}$  (0.06 ml, 0.47 mmol) was slowly added. After 5 min, the cooling bath was removed, and the mixture was stirred for 50 min. The organic phase was washed once with water, dried over  $\text{MgSO}_4$ , concentrated and percolated through a pad of silica gel to give **6** as an oily residue (70 mg, 60%). The  $^1\text{H}$  NMR spectrum of the oily residue showed signals for just one diastereoisomer. An aliquot was further purified by flash chromatography (EtOAc/n-hexane 70/30).

Selected physical data for **6** (acetate):  $[\alpha]_{\text{D}}^{25} = +6.25^0$  ( $c = 0.6, \text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6, 65^\circ\text{C}$ )  $\delta = 0.043$  (s, 3H; MeSi), 0.083 (s, 3H; MeSi), 0.96 (s, 9H; t-BuSi), 0.97 (s, 9H; t-BuSi), 1.77 (s, 3H, AcO), 2.52 (m, 2H; CH<sub>2</sub>-CH=CH<sub>2</sub>), 3.76 (m, 2H CH<sub>2</sub>-OTBDMS), 4.29 (m, 1H; C2-H), 4.37 (dd,  $J = 3 \text{ Hz}, J = 4 \text{ Hz}$ , 1H, C4-H), 4.56 (m, 1H; C5-H), 4.6 (m, 1H; C2-H), 5.1 (d,  $J = 12.5 \text{ Hz}$ , 2H; OCH<sub>2</sub>Ph), 5.24-5.20 (m, 3H; C3-H, CH=CH<sub>2</sub>), 5.89, (m, 1H; CH=CH<sub>2</sub>), 7.11 (t,  $J = 7.5$ , 1H; Ar), 7.18 (t,  $J = 7.5$ , 2H; Ar), 7.31 (d,  $J = 7.5$ , 2H; Ar);  $^{13}\text{C}$  NMR (100 MHz,  $\text{C}_6\text{D}_6, 65^\circ\text{C}$ ):  $\delta = -5.55 \times 2\text{C}, -5.21 \times 2\text{C}, 17.6 \times 2\text{C}, 19.76, 25.42 \times 6\text{C}, 36.0, 38.2, 61.68, 64.09, 66.23, 66.94, 76.6, 80.51, 117.33, 127.7, 128.0, 128.2, 128.4, 134.4, 136.7, 159.7, 169.1$ ; IR (chloroform) :  $\nu = 3010, 2949, 2858, 1733, 1696, 1411, 1352, 1226 \text{ cm}^{-1}$ ; HMRS calcd for  $\text{C}_{30}\text{H}_{51}\text{NO}_6\text{Si}_2 [(M^+)]$  577.9190, found 577.9390.