Regiochemical Control in the Metal-Catalyzed Transposition of Allylic Silyl Ethers

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Supporting Information

Materials and Methods

All compounds were purchased from Aldrich and used without purification unless otherwise indicated. $\text{RuCp}(\text{CH}_3\text{CN})_3\text{PF}_6$ was purchased from Strem Chemicals, Inc. Acetone was distilled from MgSO_4 . Dichloromethane was distilled from CaH_2 . Flash chromatography was performed using silica gel 60 Å (32-63 mesh) from Sorbent Technologies. Reactions were monitored by thin layer chromatography (TLC) using 0.25 mm E. Merck precoated silica gel 60 (particle size 0.040 – 0.063 mm). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer. Chemical shifts are reported in parts per million (ppm) values relative to the internal standard tetramethyl silane (TMS). Multiplicities were reported as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), multiplet (m), broad (b). The reported NMR data is for the major isomer. High resolution mass spectra (ESI) were provided by the University of Wisconsin-Madison mass spectrometry facility.

General procedure for Alder-ene reaction: A solution of TBS-protected 4-propene-2-ol (50 mg, 0.25 mmol) in 2 mL dry acetone was added 4,4,5,5-tetramethyl-2-(prop-1-ynyl)-1,3,2-dioxaborolane¹ (42 mg, 0.25 mmol) and the solution degassed by bubbling N₂ for 10 min. RuCp(CH₃CN)₃PF₆ (10 mg, 0.023 mmol) was added and the reaction stirred at room temperature until no further conversion of alkene is detected by TLC (1–2h). After this time, the solvent is evaporated and the residue purified by silica gel chromatography (Hex:Et₂O, 20:1), giving ~5 mg of recovered alkene and 66 mg (72%) **1e** as a colorless oil.

1e: ¹H NMR (300 MHz, CDCl₃) δ 5.51 (m, 2H), 5.14 (s, 1H), 4.26 (m, 1H), 3.11 (abq, *J*_{ab} = 14.8 Hz, 1H), 3.07 (abq, *J*_{ab} = 14.8 Hz, 1H), 1.82 (d, 1.3 Hz, 3H), 1.25 (s, 12H), 1.19 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 161.37, 136.20, 127.37, 82.82, 69.56, 39.30, 26.49, 26.15, 25.05, 24.84, 18.54, -4.28, -4.52; **HRMS** (ESI) calcd for C₂₀H₃₉BO₃Si [M+Na]⁺: 389.2659, found 389.2666.

5a: ¹H NMR (300 MHz, CDCl₃) δ 5.46 (m, 2H), 5.15 (s, 1H), 4.04 (m, 1H), 3.10 (d, *J* = 5.8 Hz, 2H), 1.82 (d, *J* = 1.1 Hz, 3H), 1.46 (m, 2H), 1.26 (m, 6H), 1.25 (s, 12H), 0.88 (bs, 12H), 0.03 (s, 3H), 0.01 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 161.33, 135.25, 128.36, 82.80, 73.89, 45.31, 39.36, 38.70, 32.04, 26.16, 25.06, 22.88, 21.27, 18.50, 14.25, -3.96, -4.54; **HRMS** (ESI) calcd for C₂₄H₄₇BO₃Si [M+Na]⁺: 445.3285, found 445.3273.

5b: ¹H NMR (300 MHz, CDCl₃) δ 5.63 (dt, *J* = 15.4, 6.7 Hz, 1H), 5.51 (dd, *J* = 15.4, 9.6 Hz, 1H), 5.15 (d, *J* = 1.4 Hz, 1H), 4.54 (abq, *J*_{ab} = 13.3 Hz, 2H), 4.29 (bq, *J* = 6.0 Hz, 1H), 3.41 (abx, *J*_{ab} = 9.7 Hz, *J*_{ax} = 7.4 Hz, 1H), 3.39 (abx, *J*_{ab} = 9.7 Hz, *J*_{bx} = 4.5 Hz, 1H), 3.13 (d, *J* = 6.8 Hz, 2H), 1.82 (d, *J* = 1.3 Hz, 3H), 1.24 (s, 12H), 0.89 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 161.09, 138.83, 131.77, 130.1, 128.47, 127.72, 127.60, 82.82, 75.55, 73.50, 72.87, 39.46, 26.49, 29.11, 25.04,

¹ Brown, H. C.; Bhat, N. G.; Srebnik, M. *Tetrahedron Lett.* **1988**, 29, 2631.

18.53, -4.30, -4.49; **HRMS** (ESI) calcd for $C_{27}H_{45}BO_4Si$ $[M+Na]^+$: 495.3078, found 495.3072.

5c: 1H NMR (300 MHz, $CDCl_3$) δ 7.24 (m, 2H), 7.15 (m, 3H), 5.52 (m, 2H), 5.43 (s, 1H), 4.08 (q, $J = 5.9$ Hz, 1H), 3.85 (d, $J = 1.2$ Hz, 2H), 3.21 (s, 3H), 3.11 (d, $J = 5.4$ Hz, 2H), 2.61 (m, 2H), 1.77 (m, 2H), 1.24 (s, 12H), 0.88 (s, 9H), 0.02 (s, 3H), 0.0 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.36, 142.75, 134.82, 128.72, 128.58, 128.49, 125.82, 83.06, 76.41, 73.23, 58.41, 40.38, 34.92, 31.88, 26.15, 25.04, 18.47, -3.89, -4.52; **HRMS** (ESI) calcd for $C_{28}H_{47}BO_4Si$ $[M+Na]^+$: 509.3234, found 509.3244.

5d: 1H NMR (300 MHz, $CDCl_3$) δ 5.88 (ddd, $J = 17.3$, 10.7, 4.7 Hz, 1H), 5.49 (m, 2H), 5.25 (bd, $J = 17.3$ Hz, 1H), 5.14 (bs, 1H), 5.10 (dt, $J = 10.7$, 1.7 Hz, 1H), 4.72 (bs, 2H), 4.31 (m, 1H), 3.71 (m, 1H), 3.53 (m, 1H), 3.10 (d, $J = 5.5$ Hz, 2H), 2.24 (m, 2H), 1.95 (m, 4H), 1.81 (bs, 3H), 1.24 (s, 12H), 0.87 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.15, 144.66, 139.11, 134.40, 129.25, 114.79, 108.85, 82.82, 78.79, 75.65, 71.04, 44.96, 40.85, 39.34, 26.56, 25.07, 18.42, -3.88, -4.53; **HRMS** (ESI) calcd for $C_{28}H_{49}BO_4Si$ $[M+Na]^+$: 511.3391, found 511.3374.

General procedure for allylic [1,3]-transposition: To a flame-dried vile under N_2 atmosphere was added **5a** (51 mg, 0.12 mmol) in ~2 mL solvent (CH_2Cl_2 or Et_2O). Re_2O_7 (3 mg, 0.006 mmol) was added under N_2 atmosphere (glove bag). The reaction was stirred at room temperature and monitored by TLC. After 2 h, the solvent is removed and the residue purified by silica gel chromatography (Hex:EtOAc, 5:1–2:1). The cyclic boronic acids obtained could be identified by crude 1H NMR, however, quality spectra were obtained only after further derivitization.

General procedure for Suzuki coupling: A solution of **6a** (~20 mg, ~0.1 mmol) and (Z)-ethyl 3-iodoacrylate (28 mg, 0.12 mmol) in 1 mL THF/H₂O (3:1) was degassed by bubbling N₂ through the solution for 10 min. Pd(PPh₃)₄ (6 mg, 0.005 mmol) was added and the reaction stirred 5 min. TIOEt (45 mg, 0.18 mmol) was then added giving immediate precipitation of yellow salts. After 1h the reaction was diluted with ether and filtered through a silica plug. The organic layer was washed with brine and dried over MgSO₄. The solvent was removed in vacuo and the residue purified by silica gel chromatography.

4: ¹H NMR (300 MHz, CDCl₃) δ 7.36 (d, *J* = 11.8 Hz, 1H), 6.88 (t, *J* = 11.8 Hz, 1H), 5.70 (dq, *J* = 15.3, 6.4, 1.0 Hz, 1H), 5.60 (d, *J* = 11.8 Hz, 1H), 5.51 (ddq, *J* = 15.3, 6.7, 1.4 Hz, 1H), 4.22 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.62 (dd, *J* = 13.2, 8.3 Hz, 1H), 2.33 (dd, *J* = 13.2, 5.2 Hz, 1H), 1.96 (s, 3H), 1.70 (d, *J* = 6.3 Hz, 3H), 1.56 (bs, 1H), 1.29 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.95, 146.08, 140.16, 133.41, 127.43, 124.88, 116.07, 71.54, 60.04, 40.53, 25.68, 17.85, 14.53; HRMS (ESI) calcd for C₁₃H₂₀O₃ [M+Na]⁺: 247.1310, found 247.1300.

7a: ¹H NMR (300 MHz, CDCl₃) δ 7.36 (d, *J* = 11.8 Hz, 1H), 6.88 (t, *J* = 11.8 Hz, 1H), 5.68 (dt, *J* = 15.8, 6.7 Hz, 1H), 5.59 (d, *J* = 11.8 Hz, 1H), 5.48 (dd, *J* = 15.8, 6.6 Hz, 1H), 4.22 (m, 1H), 4.18 (q, *J* = 7.0 Hz, 2H), 2.61 (dd, *J* = 13.3, 8.1 Hz, 1H), 2.35 (dd, *J* = 13.3, 5.3 Hz, 1H), 2.00 (m, 2H), 1.96 (s, 3H), 1.40-1.24 (m, 6H), 1.29 (t, *J* = 7.0 Hz, 3H), 0.88 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.93, 146.08, 140.18, 132.81, 132.00, 124.85, 116.03, 71.59, 60.01, 40.60, 32.32, 31.57, 28.91, 25.68, 22.70, 14.51, 14.21; HRMS (ESI) calcd for C₁₇H₂₈O₃ [M+Na]⁺: 303.1936, found 303.1951.

7b: ¹H NMR (300 MHz, CDCl₃) δ 7.39 (d, *J* = 11.6 Hz, 1H), 7.33 (m, 5H), 6.87 (t, *J* = 11.6 Hz, 1H), 5.82 (m, 2H), 5.60 (d, *J* = 11.6 Hz, 1H), 4.52 (s, 2H), 4.32 (m, 1H), 4.17 (q, *J* = 7.3 Hz,

2H), 4.03 (bd, $J = 4.3$ Hz, 2H), 2.63 (dd, $J = 13.2, 8.4$ Hz, 1H), 2.37 (dd, $J = 13.2, 4.9$ Hz, 1H), 1.97 (s, 3H), 1.29 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.90, 145.59, 139.97, 138.44, 134.82, 128.62, 127.93, 127.86, 125.14, 116.35, 72.59, 70.76, 70.19, 60.07, 40.35, 25.61, 14.53; **HRMS** (ESI) calcd for $\text{C}_{20}\text{H}_{26}\text{O}_4$ $[\text{M}+\text{Na}]^+$: 353.1729, found 353.1742.

7c: ^1H NMR (300 MHz, CDCl_3) δ 7.51 (d, $J = 11.8$ Hz, 1H), 7.28 (m, 2H), 7.18 (m, 3H), 6.85 (t, $J = 11.8$ Hz, 1H), 5.73 (d, $J = 11.8$ Hz, 1H), 5.73 (dt, $J = 15.5, 6.9$ Hz, 1H), 5.51 (dd, $J = 15.5, 6.7$ Hz, 1H), 4.19 (q, $J = 7.0$ Hz, 2H), 4.19 (m, 1H), 4.03 (abq, $J = 12.0$ Hz, 1H), 3.96 (abq, $J = 12.0$ Hz, 1H), 3.37 (s, 3H), 2.81 (d, $J = 3.3$ Hz, 1H), 2.69 (m, 2H), 2.51 (m, 2H), 2.35 (m, 2H), 1.30 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.50, 144.24, 141.92, 139.02, 133.00, 131.27, 128.62, 128.50, 126.07, 118.84, 77.83, 72.05, 60.25, 58.45, 37.48, 35.69, 34.17, 14.48; **HRMS** (ESI) calcd for $\text{C}_{21}\text{H}_{28}\text{O}_4$ $[\text{M}+\text{Na}]^+$: 367.1885, found 367.1894.

7e: ^1H NMR (300 MHz, CDCl_3) δ 7.40 (d, $J = 11.7$ Hz, 1H), 7.32 (m, 5H), 6.91 (t, $J = 11.7$ Hz, 1H), 6.62 (d, $J = 16.0$ Hz, 1H), 6.22 (dd, $J = 16.0, 6.5$ Hz, 1H), 5.61 (d, $J = 11.7$ Hz, 1H), 4.48 (m, 1H), 4.17 (q, $J = 7.0$ Hz, 2H), 2.73 (dd, $J = 13.5, 8.4$ Hz, 1H), 2.45 (dd, $J = 13.5, 5.4$ Hz, 1H), 2.00 (s, 3H), 1.29 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.91, 145.53, 139.72, 136.71, 131.51, 130.65, 128.81, 127.96, 126.71, 125.19, 116.38, 71.43, 60.07, 40.60, 25.72, 14.52; **HRMS** (ESI) calcd for $\text{C}_{18}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{Na}]^+$: 309.1467, found 309.1478.

7f: ^1H NMR (300 MHz, CDCl_3) δ 7.54 (d, $J = 11.8$ Hz, 1H), 7.31 (m, 5H), 6.90 (t, $J = 11.8$ Hz, 1H), 6.63 (d, $J = 15.8$ Hz, 1H), 6.23 (dd, $J = 15.8, 6.2$ Hz, 1H), 5.73 (d, $J = 11.8$ Hz, 1H), 4.43 (m, 1H), 4.19 (q, $J = 7.0$ Hz, 2H), 4.07 (abq, $J = 12.5$ Hz, 1H), 4.01 (abq, $J = 12.5$ Hz, 1H), 3.39 (s, 3H), 2.67 (abx, $J_{\text{ab}} = 13.8, J_{\text{ax}} = 4.2$ Hz, 1H), 2.60 (abx, $J_{\text{ab}} = 13.8, J_{\text{bx}} = 8.3$ Hz, 1H), 1.30 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.50, 143.83, 138.81, 1136.88, 131.82, 130.29, 128.75, 127.82, 126.69, 126.40, 119.18, 77.91, 72.04, 60.27, 58.50, 37.56, 14.47; **HRMS** (ESI) calcd for $\text{C}_{19}\text{H}_{24}\text{O}_4$ $[\text{M}+\text{Na}]^+$: 339.1572, found 339.1559.

Mosher's ester for
homoallylic alcohol
leading to **5c**

Mosher's ester for rac-**7c**

84:16 dr
Mosher's ester for
homoallylic alcohol
leading to **5e**

50:50 dr
Mosher's ester for **7e**