Palladium-Catalyzed Asymmetric Synthesis of Axially Chiral (Allenylmethyl)silanes and Chirality Transfer to Stereogenic Carbon Centers in S_E' Reactions

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Supporting Information

Experimental Section

General. All anaerobic and/or moisture sensitive manipulations were carried out with standard Schlenk techniques under predried nitrogen or with glovebox techniques under prepurified argon. NMR spectra were recorded on a JEOL JNM LA500 spectrometer (¹H, 500 MHz; ¹³C, 125 MHz). ¹H and ¹³C chemical shifts are reported in ppm downfield of internal tetramethylsilane. Optical rotations were measured on a JASCO DIP-370 polarimeter. (3-Bromopenta-2,4-dienyl)trimethylsilane (**1**),¹ [PdCl(π -allyl)]₂,² dpbp,³ ^tBuCH(OMe)₂ (**4z**),⁴ Pd(dba)₂,⁵ and (*R*)-segphos⁶ were prepared according to the reported methods. All the other chemicals were obtained from commercial sources.

Palladium-Catalyzed Synthesis of (Allenylmethyl)silanes (3a-c). Non-asymmetric synthesis of the (allenylmethyl)silanes **3a-c** was conducted according to a reported procedure.⁷ The reaction conditions and results are described in Table 1. A typical procedure is given for the preparation of dimethyl 2-methyl-2-[5-(trimethylsilyl)penta-2,3-dienyl]propane-1,3-dioate (**3a**): A mixture of [PdCl(π -allyl)]₂ (1.6 mg, 8.7 μ mol/Pd), dpbp (4.9 mg, 9.4 μ mol), and **1** (104 mg, 474 μ mol) was dissolved in THF (5 mL) and the solution was added to Na[CMe(COOMe)₂] (**2a**, 80.5 mg, 479 μ mol) by cannula transfer under nitrogen. The mixture was stirred at 23 °C for 12 h, then filtered through a short pad of SiO₂ to remove precipitated inorganic salts. The silica gel pad was washed with small amount of Et₂O three times and the combined solution was evaporated to dryness under reduced pressure. The yellow residue was chromatographed on silica gel (hexane/Et₂O = 4/1) to give the (allenylmethyl)silane (122 mg, 91% yield; **3a**) as colorless oil. The characterization data of the allenic products are listed below.

Asymmetric synthesis of the (allenylmethyl)silanes (*R*)-**3a** and (*R*)-**3b** was performed according to a reported method⁸ with slight modifications. The reaction conditions and the results are described in Table 1. A typical procedure is given for the preparation of (*R*)-**3a**: A mixture of Pd(dba)₂ (130 mg, 226 μ mol), (*R*)-segphos (155 mg, 254 μ mol), and **2a** (460 mg, 2.74 mmol) was dissolved in THF (15 mL). After stirring the solution at 40 °C for 15 min, to this was added **1** (500 mg, 2.28 mmol) by means of syringe. The mixture was stirred at 40 °C for 24 h, then filtered through a short pad of SiO₂ to remove precipitated inorganic salts. The silica gel pad was washed with a small amount of Et₂O three times and the combined solution was evaporated to dryness under reduced pressure. The yellow residue was chromatographed on silica gel (hexane/Et₂O = 4/1) to give **3a** (367 mg, 57% yield) as colorless oil.

The enantiopurity of (*R*)-**3a** and (*R*)-**3b** was determined to be 79 and 87% ee, respectively, by HPLC analysis with a chiral stationary phase column (**3a**, Daicel Chiralpak AD, hexane/*i*PrOH = 100/1, 0.5 mL/min; **3b**, Daicel Chiralcel OG, hexane/*i*PrOH = 98/2, 0.2 mL/min). The absolute configurations of both **3a** and **3b** were deduced to be (*R*) by the Lowe-Brewster rule⁹ from the signs of optical rotation (**3a**, $[\alpha]^{20}_D = -60$ (*c* 0.99, CHCl₃); **3b**, $[\alpha]^{20}_D = -60$ (*c* 1.01, CHCl₃)).

Dimethyl 2-methyl-2-[5-(trimethylsilyl)penta-2,3-dienyl]propane-1,3-dioate (3a): ¹H NMR (500 MHz, CDCl₃): δ 0.01 (s, 9H), 1.25 (ddd, *J* = 13.8, 8.5, and 2.3 Hz, 1H), 1.28 (ddd, *J* = 13.8, 8.8, and 2.6 Hz, 1H), 1.43 (s, 3H), 2.52 (ddd, *J* = 13.9, 7.8, and 2.2 Hz, 1H), 2.55 (ddd, *J* = 13.9, 7.8, and 2.4 Hz, 1H), 3.710 (s, 3H), 3.711 (s, 3H), 4.87-4.92 (m, 1H), 5.01-5.07 (m, 1H). ¹³C{¹H} NMR (125 MHz, CDCl₃): δ -1.94, 17.88, 19.76, 36.28, 52.48, 52.53, 53.93, 84.41, 87.24, 172.31, 172.40, 206.37. Anal. Calcd for C₁₄H₂₄O₄Si: C, 59.12; H, 8.50. Found: C, 59.01; H, 8.54.

Diethyl 2-acetylamino-2-[5-(trimethylsilyl)penta-2,3-dienyl]propane-1,3-dioate (3b): ¹H NMR (CDCl₃): δ 0.01 (s, 9H), 1.25-1.27 (m, 8H), 2.04 (s, 3H), 2.97 (ddd, *J* = 14.4, 8.1, and 2.2 Hz, 1H), 3.02 (ddd, *J* = 14.4, 7.1, and 2.2 Hz, 1H), 4.19-4.29 (m, 4H), 4.78-4.84 (m, 1H), 5.00-5.06 (m, 1H), 6.78 (br, 1H). ¹³C{¹H} NMR (CDCl₃): δ -1.95, 14.01, 14.02, 17.80, 23.03, 32.99, 62.52, 62.54, 66.50, 83.22, 87.48, 167.65, 167.76, 168.84, 206.41. Anal. Calcd for C₁₇H₂₉O₅NSi: C, 57.44; H, 8.22; N, 3.94. Found: C, 57.31; H, 8.09; N, 4.00.

Di-*tert*-butyl *N*-[5-(trimethylsilyl)penta-2,3-dienyl]imino-dicarboxylate (3c): ¹H NMR (500 MHz, CDCl₃): δ 0.01 (s, 9H), 1.28 (ddd, *J* = 13.9, 8.3, and 2.4 Hz, 1H), 1.32 (ddd, *J* = 13.9, 8.8, and 2.7 Hz, 1H), 1.49 (s, 18H), 4.10 (ddd, *J* = 14.9, 6.3, and 2.4 Hz, 1H), 4.15 (ddd, *J* = 14.9, 5.4, and 2.7 Hz, 1H), 5.08-5.17 (m, 2H). ¹³C{¹H} NMR (125 MHz, CDCl₃): δ -1.93, 17.89, 28.11, 45.61, 82.14, 87.45, 89.28, 152.26, 204.42. Anal. Calcd for C₁₈H₃₃O₄NSi: C, 60.81; H, 9.36; N, 3.94. Found: C, 60.69; H, 9.35; N, 3.88.

TiCl₄-Promoted S_E' Reaction of (Allenylmethyl)silanes with Acetals/Aldehyde. The reaction conditions and results are summarized in Table 2. A typical procedure is given for the preparation of (*E*)-dimethyl 2-[3-(1-methoxy-2-phenylethyl)penta-2,4-dienyl]-2-methylpropane-1,3-dioate (**5ax**): Under a nitrogen atmosphere, a solution of PhCH₂CH(OMe)₂ (189 mg, 1.14 mmol) and TiCl₄ (1.0 M CH₂Cl₂ solution, 1.1 mL, 1.1 mmol) in CH₂Cl₂ (5 mL) was cooled to -78 °C and to this was added (allenylmethyl)silane (*R*)-**3a** (202 mg, 710 μmol; 79% ee) by means of syringe. The solution was stirred at this temperature until total consumption of **3a** (ca. 8 h, checked by TLC). The reaction mixture was quenched with water and extracted with ether twice. The combined organic solution was washed with saturated NaCl solution, and dried over anhydrous MgSO₄. After removal of the solvent, the crude material was chromatographed on silica gel (hexane/Et₂O = 4/1) to give the conjugated diene (219 mg, 89% yield; **5ax**) as colorless oil. The characterization data of the 1,3-dienyl products are listed below.

The enantiopurity of the products (see Table 2) were determined by HPLC analysis with a chiral stationary phase column Daicel Chiralcel OD-H (**5ax**, hexane/*i*PrOH = 100/1, 0.2 mL/min; **5ay**, double columns connected in series, hexane/*i*PrOH = 500/1, 0.5 mL/min; **5bx**, hexane/*i*PrOH = 98/2, 0.5 mL/min; **5by**, hexane/*i*PrOH = 500/1, 0.5 mL/min).

The absolute configurations of both **5ay** and **5by** were determined as follows. The diene **5** was treated with a mixture of K₂CO₃/NaIO₄/KMnO₄ (6 equiv/16 equiv/2.3 equiv) in *t*BuOH/H₂O

(1/2 v/v) for 12 h. By this treatment, both **5ay** and **5by** were converted into t BuCH(OMe)COOH. The crude carboxylic acid was treated with etherial CH_2N_2 , and then the obtained methyl ester was purified by vacuum transfer. The absolute configuration of the ester from both **5ay** and **5by**, t BuCH(OMe)COOMe, was determined to be (*S*) by comparison of retention time on the chiral HPLC with that of an authentic sample (*S*)- t BuCH(OMe)COOMe, which was prepared from commercially available (*S*)- t BuCH(OH)COOH (Aldrich). The methyl ester t BuCH(OMe)COOMe was too volatile to be purified in a small scale, and thus determination of the absolute configuration by the signs of optical rotation was given up.

(*E*)-Dimethyl 2-[3-(1-methoxy-2-phenylethyl)penta-2,4-dienyl]-2-methylpropane-1,3-dioate (5ax**):** ^1H NMR (CDCl_3): δ 1.33 (s, 3H), 2.75 (dd, J = 14.9 and 8.1 Hz, 1H), 2.78 (dd, J = 14.9 and 7.8 Hz, 1H), 2.84 (dd, J = 14.2 and 7.3 Hz, 1H), 2.88 (dd, J = 14.2 and 5.4 Hz, 1H), 3.17 (s, 3H), 3.69 (s, 3H), 3.70 (s, 3H), 4.02 (dd, J = 7.3 and 5.4 Hz, 1H), 5.23 (d, J = 11.5 Hz, 1H), 5.40 (dd, J = 8.1 and 7.8 Hz, 1H), 5.46 (d, J = 17.8 Hz, 1H), 6.57 (dd, J = 17.8 and 11.5 Hz, 1H), 7.17-7.19 (m, 3H), 7.25-7.28 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 19.81, 33.36, 42.13, 52.55, 52.56, 53.71, 56.34, 84.46, 116.19, 124.53, 126.06, 128.11, 129.16, 130.89, 138.89, 139.22, 172.19, 172.25. Anal. Calcd for $\text{C}_{20}\text{H}_{26}\text{O}_5$: C, 69.34; H, 7.56. Found: C, 69.45; H, 7.64.

(*E*)-Dimethyl 2-[3-(1-methoxy-2,2-dimethylpropyl)penta-2,4-dienyl]-2-methylpropane-1,3-dioate (5ay**):** ^1H NMR (CDCl_3): δ 0.85 (s, 9H), 1.44 (s, 3H), 2.81 (dd, J = 14.8 and 7.6 Hz, 1H), 2.90 (dd, J = 14.8 and 8.2 Hz, 1H), 3.16 (s, 3H), 3.56 (s, 1H), 3.72 (s, 6H), 5.16 (d, J = 11.5 Hz, 1H), 5.29 (d, J = 17.7 Hz, 1H), 5.42 (dd, J = 8.2 and 7.6 Hz, 1H), 6.61 (dd, J = 17.7 and 11.5 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 20.08, 26.76, 33.72, 35.66, 52.58 (2C), 53.89, 56.71, 88.79, 115.72, 125.07, 133.94, 138.10, 172.37, 172.39. Anal. Calcd for $\text{C}_{17}\text{H}_{28}\text{O}_5$: C, 65.36; H, 9.03. Found: C, 65.07; H, 9.01.

(*E*)-Dimethyl 2-[3-(1-hydroxy-2-phenylethyl)penta-2,4-dienyl]-2-methylpropane-1,3-dioate (5az**):** ^1H NMR (CDCl_3): δ 1.36 (s, 3H), 1.71 (br, 1H), 2.71 (dd, J = 13.9 and 8.7 Hz, 1H), 2.75 (dd, J = 14.8 and 7.7 Hz, 1H), 2.81 (dd, J = 14.8 and 8.1 Hz, 1H), 3.00 (dd, J = 13.9 and 3.8 Hz, 1H), 3.70 (s, 3H), 3.71 (s, 3H), 4.62 (dd, J = 8.7 and 3.8 Hz, 1H), 5.26 (dt, J = 11.5 and 1.2 Hz, 1H), 5.41 (d, J = 17.8 Hz, 1H), 5.59 (dd, J = 8.1 and 7.7 Hz, 1H), 6.61 (ddt, J = 17.8, 11.5, and 1.2 Hz, 1H), 7.21-7.24 (m, 3H), 7.29-7.32 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 19.87, 33.27, 43.48, 52.57, 52.60, 53.79, 73.11, 115.75, 123.07, 126.51, 128.47, 129.34, 130.98, 138.63, 142.01, 172.25, 172.31. Anal. Calcd for $\text{C}_{19}\text{H}_{24}\text{O}_5$: C, 68.66; H, 7.28. Found: C, 68.61; H, 7.33.

(*E*)-Diethyl 2-acetylmino-2-[3-(1-methoxy-2-phenylethyl)penta-2,4-dienyl]propane-1,3-dioate (5bx**):** ^1H NMR (CDCl_3): δ 1.24 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.2 Hz, 3H), 1.97 (s, 3H), 2.81 (dd, J = 14.2 and 7.8 Hz, 1H), 2.86 (dd, J = 14.2 and 4.9 Hz, 1H), 3.15 (s, 3H), 3.24 (d, J = 8.1 Hz, 2H), 4.05 (dd, J = 7.8 and 4.9 Hz, 1H), 4.10-4.27 (m, 4H), 5.20 (d, J = 11.5 Hz, 1H), 5.33 (t, J = 8.1 Hz, 1H), 5.44 (d, J = 17.8 Hz, 1H), 6.55 (dd, J = 17.8 and 11.5 Hz, 1H), 6.66 (br, 1H), 7.18-7.22 (m, 3H), 7.26-7.29 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 13.94, 13.95, 22.98, 30.36, 42.31, 56.40, 62.61, 62.64, 66.11, 83.72, 115.87, 122.81, 126.12, 128.12, 129.13, 130.92, 139.15, 139.90, 167.54, 167.56, 169.03. Anal. Calcd for $\text{C}_{23}\text{H}_{31}\text{O}_6\text{N}$: C, 66.17; H, 7.48; N, 3.35. Found: C, 65.90; H, 7.50; N, 3.27.

(E)-Diethyl 2-acetylamino-2-[3-(1-methoxy-2,2-dimethylpropyl)penta-2,4-dienyl]propane-1,3-dioate (5by): ^1H NMR (CDCl_3): δ 0.84 (s, 9H), 1.26 (t, $J = 7.3$ Hz, 6H), 2.01 (s, 3H), 3.14 (s, 3H), 3.28 (dd, $J = 15.1$ and 7.8 Hz, 1H), 3.37 (dd, $J = 15.1$ and 8.3 Hz, 1H), 3.59 (s, 1H), 4.19-4.28 (m, 4H), 5.14 (d, $J = 11.5$ Hz, 1H), 5.29 (d, $J = 17.6$ Hz, 1H), 5.31 (dd, $J = 8.3$ and 7.8 Hz, 1H), 6.61 (dd, $J = 17.6$ and 11.5 Hz, 1H), 6.75 (br, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 13.97 (2C), 23.03, 26.69, 30.61, 35.57, 56.70, 62.64, 62.66, 66.23, 88.14, 115.56, 123.47, 133.82, 138.93, 167.73, 167.75, 169.05. Anal. Calcd for $\text{C}_{20}\text{H}_{33}\text{O}_6\text{N}$: C, 62.64; H, 8.67; N, 3.65. Found: C, 62.43; H, 8.95; N, 3.37.

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