Supporting Information

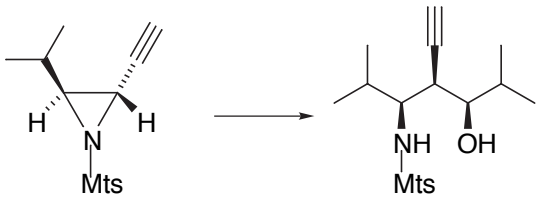
Umpolung of Chiral 2-Ethynylaziridines: Indium(I)-mediated Stereoselective Synthesis of Nonracemic 1,3-Amino Alcohols Bearing Three Chiral Centers, Catalyzed by Palladium(0)

Hiroaki Ohno, Hisao Hamaguchi, and Tetsuaki Tanaka*

Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka 565-0871, Japan

General Methods. Melting points are uncorrected. Nominal (LRMS) and exact mass (HRMS) spectra were recorded on a JEOL JMS-01SG-2 or JMS-HX/HX 110A mass spectrometer. ^{1}H NMR spectra were recorded in $CDCl_3$. Chemical shifts are reported in parts per million downfield from internal Me_4Si (s = singlet, d = doublet, dd = double doublet, ddd = doublet of double doublet, t = triplet, m = multiplet). Optical rotations were measured in $CHCl_3$ with a JASCO DIP-360 digital polarimeter. For flash chromatography, silica gel 60 H (silica gel for thin-layer chromatography, Merck) or silica gel 60 (finer than 230 mesh, Merck) was employed. InI is available from the Aldrich, which was crushed before use.

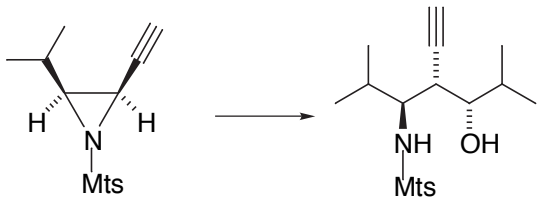
The requisite 2-ethynylaziridines were synthesized according to our procedure, see: Ohno, H.; Toda, A.; Takemoto, Y.; Fujii, N.; Ibuka, T. *J. Chem. Soc., Perkin Trans. 1*, **1999**, 2949.



3a **6a**

General Procedure for Synthesis of 2-Ethynyl-1,3-amino Alcohols from 2-Ethynylaziridines. Synthesis of (3*R*,4*R*,5*S*)-4-Ethynyl-2,6-dimethyl-5-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-heptan-3-ol (6a). To a stirred solution of the aziridine **3a** (58.3 mg, 0.2 mmol) in a mixed solvent of THF (0.8 mL) and HMPA (0.2 mL) were added H_2O (4 μL, 0.2 mmol), isobutyraldehyde (27 μL, 0.3 mmol), InI (62.8 mg, 2.6 mmol) and $Pd(PPh_3)_4$ (11.6 mg, 5 mol%, 0.01 mmol) successively at room temperature. The mixture was stirred for 4 h at this temperature and quenched with 1N HCl (1 mL). The whole was extracted with Et_2O and the extract was washed with water and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with hexane–EtOAc (4:1) gave the title compound **6a** (30.7 mg, 42% yield). Colorless oil; $[\alpha]^{23}_D$ –31.4 (*c* 1.13, $CHCl_3$); IR (KBr) cm^{-1}: 3525 (OH), 3305 ($NHSO_2$), 2114 (C≡C), 1328 ($NHSO_2$). ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.70 (d, *J*

= 6.8 Hz, 3H, CMe), 0.85 (d, *J* = 6.8 Hz, 3H, CMe), 0.89 (d, *J* = 6.8 Hz, 6H, 2×CMe), 1.59-1.71 (m, 1H, Me_2CH), 1.78-1.91 (m, 1H, Me_2CH), 2.20 (d, *J* = 4.3 Hz, 1H, OH), 2.25 (d, *J* = 1.6 Hz, 1H, C≡CH), 2.26 (s, 3H, PhMe), 2.62 (s, 6H, 2×PhMe), 2.72-2.78 (m, 1H, 4-H), 3.01-3.07 (m, 1H, 3-H), 3.23 (ddd, *J* = 9.2, 6.8, 2.4 Hz, 1H, 5-H), 4.98 (d, *J* = 9.2 Hz, 1H, NH), 6.94 (s, 2H, Ph). ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ 15.6, 19.2, 19.3, 19.6, 21.0, 23.1, 30.4, 33.3, 39.1, 59.1, 74.8, 76.0, 81.2, 131.8, 135.7, 138.0, 141.7. MS (FAB) *m/z* (%) 366 (MH^+, 100). HRMS (FAB) Calcd $C_{20}H_{32}NO_3S$ (MH^+): 366.2103. Found: 366.2113.



7a **8a**

Synthesis of (3*S*,4*S*,5*S*)-4-Ethynyl-2,6-dimethyl-5-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-heptan-3-ol (8a). By a procedure identical with that described for the synthesis of the 1,3-amino alcohol **6a** from **3a**, the aziridine **7a** (87.4 mg, 0.3 mmol) was converted into the title compound **8a** (64.7 mg, 59% yield). Colorless crystals; mp 66 °C (hexane–Et_2O); $[\alpha]^{27}_D$ –35.1 (*c* 1.45, $CHCl_3$); IR (KBr) cm^{-1}: 3537 (OH), 3302 ($NHSO_2$), 2116 (C≡C), 1313 ($NHSO_2$). ^{1}H-NMR (270 MHz, $CDCl_3$) *δ*: 0.46 (d, *J* = 6.8 Hz, 3H, CMe), 0.82 (d, *J* = 6.8 Hz, 3H, CMe), 0.86 (d, *J* = 6.8 Hz, 3H, CMe), 1.02 (d, *J* = 6.5 Hz, 3H, CMe), 1.87-2.01 (m, 1H, Me_2CH), 2.09 (d, *J* = 2.4 Hz, 1H, C≡CH), 2.28-2.35 (m, 1H, Me_2CH), 2.29 (s, 3H, PhMe), 2.55 (d, *J* = 9.5 Hz, 1H, OH), 2.64 (s, 6H, 2× PhMe), 3.04-3.07 (m, 1H, 4-H), 3.34-3.40 (m, 1H, 3-H), 3.48 (ddd, *J* = 10.3, 10.0, 3.0 Hz, 5-H), 4.73 (dd, *J* = 10.3, 4.1 Hz, NH), 6.94 (s, 2H, Ph). ^{13}C-NMR (67.8 MHz, $CDCl_3$) *δ*: 15.8, 19.1, 19.8, 20.3, 21.0, 23.3, 29.7, 32.0, 40.5, 59.2, 73.1, 74.0, 80.8, 131.8, 135.3, 138.1, 142.0. MS (EI) *m/z* (%) 367 (M+2, 0.2), 254 (100). *Anal*. Calcd for $C_{20}H_{31}NO_3S$: C, 65.72; H, 8.55; N, 3.83. Found: C, 65.44; H, 8.70; N, 3.61.