Asymmetric Synthesis of Allyl- and α -Allenylamines from Chiral Imines and Alkynes *via* (η^2 -Imine)Ti(O-*i*-Pr)₂ Complexes.

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General: ¹H and ¹³C NMR spectra were taken on a Varian Gemini-300 spectrometer at 300 and 75 MHz, respectively. CDCl₃ was used as the solvent. Chemical shifts are reported in parts per million (δ value) from Me₄Si (δ 0 ppm for ¹H NMR) or based on the central peak of the solvent (CDCl₃) (δ 77.0 ppm for ¹³C NMR) as an internal standard. Signal patterns are indicated as br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are given in hertz. Infrared (IR) spectra were recorded on a JASCO A-100 FT-IR spectrometer and are reported in wave numbers (cm⁻¹). Ti(O-*i*-Pr)₄ was distilled and stored under argon atmosphere. Isopropylmagnesium chloride was prepared in Et₂O as a 1.20~1.60 M solution from 2-chloropropane and magnesium turnings by the conventional procedure, titrated and stored under argon atmosphere. The molar concentration of a freshly prepared Grignard reagent was determined by a standard acid/base titration with Methyl Orange as an indicator. All reactions sensitive to moisture and/or oxygen were carried out under argon. Dry solvents (Et₂O, THF, hexane and CH₂Cl₂) were purchased from Kanto Chemicals. (*R*)-*O*-Methyl phenylglycinol was prepared from (*R*)-phenylglycinol¹ by treatment with KH and MeI.² Imines were prepared by stirring an aldehyde and an amine in THF in the presence of anhydrous MgSO₄ followed by filtering, concentration of the resulting residue, and dried under reduced pressure. The resulting imines were directly used without purification.

(*R*)-(Deuteriophenylmethyl)-[(*R*)-2-methoxy-1-phenylethyl]amine: To a solution of (*R*)-benzylidene-(2-methoxy-1-phenylethyl)amine (**3a**) (120 mg, 0.50 mmol) and Ti(O-*i*-Pr)₄ (0.22 mL, 0.75 mmol) in ether (4 mL) was added dropwise *i*-PrMgCl (1.16 mL, 1.29 M in ether, 1.50 mmol) at -40 °C. After being stirred for 2.5 h at -35 °C, the mixture was allowed to warm to 0 °C and stirred for 30 min. After addition of D₂O (0.2 mL), the mixture was stirred for 15 min. NaF (1 g) and Celite (1 g) were added. The resulting mixture was filtered through a pad of Celite, concentrated under reduced pressure, and chromatographed on silica gel to afford the titled compound (104 mg) in 86% yield. The deuterium incorporation and diastereomeric ratio were determined by 300 MHz ¹H NMR analysis.

^1H NMR δ 2.05 (br, 1H, NH), 3.31 (s, 3H, -OMe), 3.42~3.45 (m, 2H, -CH₂OMe), 3.68 (s, 1H, PhCHDNH-), 3.95 (dd, J = 4.8, 7.8 Hz, 1H, -CH(Ph)CH₂OMe), 7.22~7.44 (m, 10H, Ph); ^{13}C NMR δ 51.0 (t, J = 20.5 Hz), 58.8, 61.9, 77.8, 126.7, 127.4, 127.6, 128.1, 128.2, 128.3, 140.3, 140.4; IR(neat) 3331, 3083, 3060, 3025, 2886, 2085, 1950, 1879, 1810, 1603, 1452, 1353, 1103, 970, 701; $[\alpha]_{\text{D}}^{26}$ -77.6 (c 1.11, CHCl₃).

Typical Procedure for Synthesizing Allylamines 6 and 7.

(R)-[(R)-2-Methoxy-1-phenylethyl]-[(E)-1-phenyl-3-(trimethylsilyl)prop-2-enyl]amine (6a) (entry 1 in Table 1): To a solution of imine **3a** (120 mg, 0.50 mmol) and Ti(*O-i*-Pr)₄ (0.22 mL, 0.75 mmol) in ether (4 mL) was added dropwise *i*-PrMgCl (1.16 mL, 1.29 M in ether, 1.50 mmol) at -40 °C. After being stirred for 2.5 h at -35 °C, the mixture was allowed to warm to 0 °C and stirred for 30 min. After being cooled to -35 °C, trimethylsilylacetylene (0.14 mL, 1.0 mmol) was added and the resulting mixture was stirred for 3 h at -35 °C. After addition of saturated aqueous NaHCO₃ (0.15 mL), the mixture was stirred for 15 min. NaF (1 g) and Celite (1 g) were added. The resulting mixture was filtered through a pad of Celite, concentrated under reduced pressure, and chromatographed on silica gel to afford **6a** (137 mg) in 81% yield. ^1H NMR δ 0.10 (s, 9H, -Si(CH₃)₃), 2.17 (br, 1H, -NH-), 3.35 (s, 3H, -OMe), 3.46 and 3.51 (dd, J = 4.2, 9.6 Hz and J = 8.1, 9.6 Hz, each 1H, CH₂OMe), 3.98 (d, J = 7.2 Hz, 1H, PhCH(NH)), 4.06 (dd, J = 4.5, 8.1 Hz, 1H, CH(Ph)CH₂OMe), 5.68 (dd, J = 0.9, 18.6 Hz, 1H, CH=CH-TMS), 5.98 (dd, J = 7.5, 18.6 Hz, 1H, CH=CH-TMS), 7.19~7.38 (m, 10H, Ph); ^{13}C NMR δ -1.0, 58.6, 59.1, 64.0, 77.7, 126.7, 127.0, 127.2, 127.7, 128.2, 128.3, 131.8, 140.7, 143.1, 146.5; IR (neat) 3324, 3061, 3027, 2953, 2890, 1942, 1601, 1453, 1247, 1195, 1108, 1028, 990, 837, 757, 699; $[\alpha]_{\text{D}}^{28}$ -57.1 (c 1.05, CHCl₃); Anal. Calcd. for C₂₁H₂₉NOSi: C, 74.28; H, 8.61; N, 4.13. Found: C, 74.47; H, 8.29; N, 4.24.

(R)-[(R)-2-Methoxy-1-phenylethyl]-[(Z)-3-iodo-1-phenyl-3-(trimethylsilyl)prop-2-enyl]amine (7a) (eq 1): After the reaction of **3a** with a Ti(*O-i*-Pr)₄/*i*-PrMgCl reagent according to the aforementioned procedure for preparation of **6b**, to the resulting mixture containing the corresponding imine-titanium complex was added a solution of iodine (254 mg, 1.0 mmol) in THF (3 mL) at -35 °C. After being stirred for 1 hour, saturated aqueous NaHCO₃ (0.15 mL) was added. The following workup as mentioned above afforded **7a**. ^1H NMR δ 0.24 (s, 9H, Si(CH₃)₃), 2.27 (br, 1H, NH), 3.38 (s, 3H, OMe), 3.46~3.53 (m, 2H, CH₂OMe), 4.06 (dd, J = 4.8, 8.1 Hz, 1H, CH(Ph)CH₂OMe), 4.59 (d, J = 8.1 Hz, 1H, PhCH(NH)), 6.21 (d, J = 8.1 Hz, CH=CI(TMS)), 7.22~7.46 (m, 10H, Ph); ^{13}C NMR δ -1.2, 58.6, 59.2, 65.8, 77.5, 114.3, 126.8, 127.0, 127.3, 128.0, 128.2, 128.3, 140.4, 141.4, 148.7; IR

(neat) 3433, 3320, 3061, 3027, 2955, 2886, 1601, 1453, 1354, 1249, 1194, 1100, 1028, 841, 755, 699: $[\alpha]_D^{29}$ –33.4 (c 1.02, CHCl_3); Anal. Calcd. for $\text{C}_{21}\text{H}_{28}\text{INOSi}$: C, 54.19; H, 6.06; N, 27.27. Found: C, 53.9; H, 6.03; N, 2.93.

(R)-[(R)-2-Methoxy-1-phenylethyl]-[(E)-1-phenylnon-2-enyl]amine (6b) (entry 2 in Table 1): ^1H NMR δ 0.91 (t, J = 6.9 Hz, 3H, CH_3), 1.20~1.45 (m, 8H, CH_2), 2.00~2.18 (m, 3H, NH and $\text{CH}=\text{CHCH}_2$), 3.36 (s, 3H, OMe), 3.47~3.52 (m, 2H, CH_2OMe), 3.92~3.96 (m, 1H, $\text{PhCH}(\text{NH})$), 4.15 (dd, J = 6.0, 6.9 Hz, 1H, $\text{CH}(\text{Ph})\text{CH}_2\text{OMe}$), 5.41~5.47 (m, 2H, $\text{CH}=\text{CH}$), 7.18~7.42 (m, 10H, Ph); ^{13}C NMR δ 14.2, 22.8, 29.0, 29.6, 31.8, 32.4, 58.7, 59.0, 60.9, 77.8, 126.6, 126.9, 127.2, 127.7, 128.1, 128.3, 131.1, 133.1, 140.8, 144.0; IR (neat) 3321, 3061, 3026, 2926, 1947, 1879, 1663, 1602, 1453, 1379, 1194, 1110, 969, 758, 699: $[\alpha]_D^{29}$ –40.2 (c 1.05, CHCl_3); Anal. Calcd. for $\text{C}_{24}\text{H}_{33}\text{NO}$: C, 82.00; H, 9.46; N, 3.98. Found: C, 81.84; H, 9.58; N, 4.10.

(R)-[(E)-1,3-Diphenylprop-2-enyl]-[(R)-2-methoxy-1-phenylethyl]amine (6c) (entry 3 in Table 1): ^1H NMR δ 2.19 (br, 1H, NH), 3.34 (s, 3H, OMe), 3.44~3.54 (m, 2H, CH_2OMe), 4.14~4.21 (m, 2H, $\text{PhCH}(\text{NH})$ and $\text{CH}(\text{Ph})\text{CH}_2\text{OMe}$), 6.21 (dd, J = 8.4, 15.9 Hz, 1H, $\text{CH}=\text{CHPh}$), 6.38 (d, J = 15.9 Hz, 1H, $\text{CH}=\text{CHPh}$), 7.18~7.45 (m, 15H, Ph); ^{13}C NMR δ 58.7, 59.2, 61.1, 77.7, 126.3, 126.9, 127.3, 128.2, 128.3, 128.4, 131.3, 131.4, 136.8, 140.6, 143.2; IR (neat) 3321, 3060, 3925, 2925, 2887, 1600, 1492, 1453, 1353, 1306, 1194, 1028, 967, 910, 746, 700: $[\alpha]_D^{29}$ –80.4 (c 0.89, CHCl_3); Anal. Calcd. for $\text{C}_{24}\text{H}_{25}\text{NO}$: C, 83.93; H, 7.34; N, 4.08. Found: C, 83.91; H, 7.71; N, 4.38.

Ethyl (R,E)-4-[(R)-2-methoxy-1-phenylethylamino]-4-phenylbut-2-enoate (6d) (entry 4 in Table 1): ^1H NMR δ 1.32 (t, J = 7.2 Hz, 3H, CH_2CH_3), 2.33 (br, 1H, $-\text{NH}-$), 3.37 (s, 3H, OMe), 3.46~3.53 (m, 2H, CH_2OMe), 4.07 (dd, J = 5.7, 6.9 Hz, 1H, $\text{CH}(\text{Ph})\text{CH}_2\text{OMe}$), 4.19 (d, J = 7.8 Hz, 1H, $\text{PhCH}(\text{NH})$), 4.23 (q, J = 7.2 Hz, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 5.93 (dd, J = 1.2, 15.6 Hz, 1H, $\text{CH}=\text{CHCO}_2\text{Et}$), 6.97 (dd, J = 7.8, 15.6 Hz, 1H, $\text{CH}=\text{CHCO}_2\text{Et}$), 7.23~7.42 (m, 10H, Ph); ^{13}C NMR δ 14.3, 58.8, 59.5, 59.8, 60.4, 77.5, 121.8, 127.0, 127.3, 127.4, 127.5, 128.4, 128.4, 140.1, 141.1, 148.5, 166.1; IR (neat) 3320, 3061, 3028, 2981, 2928, 2886, 2250, 1718, 1649, 1602, 1493, 1453, 1368, 1268, 1167, 1110, 1029, 983, 911, 760, 700: $[\alpha]_D^{26}$ –38.7 (c 1.07, CHCl_3); Anal. Calcd. for $\text{C}_{21}\text{H}_{25}\text{NO}_3$: C, 74.31; H, 7.42; N, 4.13. Found: C, 74.13; H, 7.22; N, 4.17.

(R)-[(R)-2-Methoxy-1-phenylethyl]-[(E)-1-phenyl-3-(p-toluenesulfonyl)prop-2-enyl]amine (6e) (entry 5 in Table 1): ^1H NMR δ 2.30 (br, 1H, $-\text{NH}-$), 2.46 (s, 3H, CH_3Ar), 3.32 (s, 3H, $-\text{OMe}$), 3.36~3.56 (m, 2H, CH_2OMe), 3.93 (t, $J = 6.3$ Hz, 1H, $\text{CH}(\text{Ph})\text{CH}_2\text{OMe}$), 4.22 (d, $J = 7.2$ Hz, 1H, $\text{PhCH}(\text{NH})$), 6.46 (dd, $J = 1.2, 15.2$ Hz, 1H, $\text{CH}=\text{CHSO}_2\text{Tol}$), 6.96 (dd, $J = 7.2, 15.2$ Hz, 1H, $\text{CH}=\text{CHTs}$), 7.18~7.80 (m, 14H, Ph); ^{13}C NMR δ 21.7, 58.8, 59.2, 59.6, 77.4, 127.0, 127.4, 127.5, 127.6, 127.7, 128.4, 128.5, 129.8, 131.3, 131.4, 137.5, 139.6, 144.2, 145.7; IR (neat) 3321, 3029, 2925, 2254, 1598, 1493, 1453, 1319, 1146, 1083, 971, 912, 814, 733, 701, 663; $[\alpha]_{\text{D}}^{27} -34.2$ (c 0.84, CHCl_3); Anal. Calcd. for $\text{C}_{25}\text{H}_{27}\text{NO}_3\text{S}$: C, 71.2; H, 6.46; N, 3.32. Found: C, 71.1; H, 6.78; N, 2.85.

(R)-[(E)-1-(2-iodophenyl)-3-(trimethylsilyl)prop-2-enyl]-[(R)-2-methoxy-1-phenylethyl]amine (6f) (entry 6 in Table 1): ^1H NMR δ 0.07 (s, 9H, SiMe_3), 2.04 (br, 1H, NH), 3.37 (s, 3H, OMe), 3.46~3.58 (m, 2H, CH_2OMe), 4.00 (dd, $J = 5.1, 7.2$ Hz, 1H, $\text{NHCH}(\text{Ph})$), 4.43 (d, $J = 6.6$ Hz, 1H, ArCH), 5.80 (dd, $J = 0.9, 18.3$ Hz, 1H, $\text{CH}=\text{CHTMS}$), 6.00 (dd, $J = 6.6, 18.3$ Hz, 1H, $\text{CH}=\text{CHTMS}$), 6.88 (ddd, $J = 2.1, 7.2, 7.8$ Hz, 1H, Ar), 7.18~7.38 (m, 7H, Ph and Ar), 7.76 (dd $J = 0.9, 7.8$ Hz, 1H Ar); ^{13}C NMR δ -1.4, 58.8, 59.6, 68.0, 77.2, 100.2, 127.4, 128.1, 128.3, 128.4, 128.6, 128.7, 131.8, 139.6, 140.8, 145.2, 145.8; IR(neat) 3425, 3335, 3060, 2953, 2091, 1610, 1457, 1247, 1194, 1114, 1011, 837, 755, 700cm^{-1} ; $[\alpha]_{\text{D}}^{26} -44.3$ (c 1.07, CHCl_3); Anal. Calcd. for $\text{C}_{21}\text{H}_{28}\text{INOSi}$: C, 54.19; H, 6.06; N, 3.01. Found: C, 54.33; H, 6.01; N, 3.31.

Typical Procedure for Synthesizing α -Allenylamines 9.

(R)-[(R)-2-Methoxy-1-phenylethyl]-[(1-phenylbuta-2,3-dienyl)amine (9aa) (entry 1 in Table 2): To a solution of **3a** (120 mg, 0.50 mmol) and $\text{Ti}(\text{O}-i\text{-Pr})_4$ (0.22 mL, 0.75 mmol) in ether (4 mL) was added dropwise $i\text{-PrMgCl}$ (1.16 mL, 1.29 M in ether, 1.50 mmol) at -40°C . After being stirred for 2.5 h at -35°C , the mixture was allowed to warm to 0°C and stirred for 30 min. After being cooled to -35°C , propargyl bromide (**8a**) (68 μL , 0.90 mmol) was added. After being stirred for 2 h at this temperature, saturated aqueous NaHCO_3 (0.15 mL) was added and the resulting mixture was stirred for 15 min at room temperature. NaF (1 g) and Celite (1 g) was added. The resulting mixture was filtered through a pad of Celite, concentrated under reduced pressure, and chromatographed on silica

gel to afford **9aa** (103 mg) in 74% yield. ^1H NMR δ 2.24 (br, 1H, $-\text{NH}-$), 3.36 (s, 3H, $-\text{OMe}$), 3.47~3.51 (m, 2H, $-\text{CH}_2\text{OMe}$), 4.09 (d, $J = 8.4$ Hz, 1H, $\text{CH}(\text{Ph})\text{NH}-$), 4.25 (dd, $J = 6.0, 7.2$ Hz, 1H, $-\text{NHCH}(\text{Ph})\text{CH}_2\text{OMe}$), 4.76 and 4.81 (2ddd, $J = 1.2, 6.3, 10.5$ Hz and $J = 1.5, 6.6, 9.3$ Hz, each 1H, $\text{CH}=\text{C}=\text{CH}_2$), 5.20 (dt, $J = 8.7, 6.6$ Hz, 1H, $\text{CH}=\text{C}=\text{CH}_2$), 7.20~7.43 (m, 10H, Ph); ^{13}C NMR δ 58.4, 58.8, 59.5, 76.0, 77.7, 92.5, 126.8, 126.9, 127.3, 127.8, 128.2, 128.3, 140.4, 143.3, 208.0; IR (neat) 3322, 3060, 3027, 2983, 2917, 2887, 2853, 2824, 1951, 1601, 1453, 1352, 1194, 1097, 1027, 844, 759, 699; $[\alpha]_{\text{D}}^{27} -55.0$ (c 1.01, CHCl_3); Anal. Calcd. for $\text{C}_{19}\text{H}_{21}\text{NO}$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.97; H, 7.80; N, 5.10.

(R)-[(R)-2-Methoxy-1-(2-iodophenyl)-ethyl]-(1-phenylbuta-2,3-dienyl)amine (9ba) (entry 2 in Table 2): ^1H NMR δ 2.28 (br, 1H, NH), 3.38 (s, 3H, OMe), 3.49~3.56 (m, 2H, CH_2OMe), 4.14 (dd, $J = 5.4, 7.2$ Hz, 1H, $\text{NHCH}(\text{Ph})$), 4.47 (dt, $J = 7.5, 1.8$ Hz, 1H, $\text{ArCH}(\text{NH})$), 4.78~4.84 (m, 2H, $\text{CH}=\text{C}=\text{CH}_2$), 5.25 (dt, $J = 7.2, 6.6$ Hz, $\text{CH}=\text{C}=\text{CH}_2$), 6.88 (dt, $J = 1.8, 7.5$ Hz, 1H, Ar), 7.18~7.46 (m, 7H, Ar), 7.74 (dd, $J = 1.2, 8.1$ Hz, 1H, Ar); ^{13}C NMR δ 58.8, 59.9, 62.3, 77.20, 77.24, 92.8, 127.2, 127.5, 128.2, 128.3 (2C), 128.5, 128.7, 139.6, 140.4, 145.6, 208.2; IR(neat) 3441, 3324, 3060, 2925, 2103, 1952, 1653, 1457, 1351, 1194, 1115, 845, 755, 700cm^{-1} ; $[\alpha]_{\text{D}}^{27} -49.4$ (c 1.05, CHCl_3); Anal. Calcd. for $\text{C}_{19}\text{H}_{20}\text{INO}$: C, 56.31; H, 4.97; N, 3.46. Found: C, 56.06; H, 5.04; N, 3.06.

(R)-[(R)-2-Methoxy-1-(1-naphthyl)-ethyl]-(1-phenylbuta-2,3-dienyl)amine (9ca) (entry 3 in Table 2): ^1H NMR δ 2.14 (br, 1H, NH), 3.39 (s, 3H, OMe), 3.52~3.58 (m, 2H, CH_2OMe), 4.37 (dd, $J = 4.8, 5.4$ Hz, $\text{NHCH}(\text{Ph})$), 4.78~4.93 (m, 3H, (1-naphthyl) CH - and $\text{CH}=\text{C}=\text{CH}_2$), 5.43 (dt, $J = 8.4, 6.3$ Hz, 1H, $\text{CH}=\text{C}=\text{CH}_2$), 7.30~7.87 (m, 12H, Ph and 1-naphthyl); ^{13}C NMR δ 54.7, 58.8, 59.8, 76.5, 77.4, 93.0, 123.8, 123.9, 125.4, 125.7, 127.7, 127.8, 128.3, 128.5, 128.7, 131.1, 134.0, 139.3, 140.6, 208.6; IR(neat) 3441, 3325, 3060, 2099, 1952, 1653, 1598, 1453, 1395, 1194, 1096, 969, 909, 845, 778, 701cm^{-1} ; $[\alpha]_{\text{D}}^{27} -33.9$ (c 1.05, CHCl_3); Anal. Calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}$: C, 83.85; H, 7.04; N, 4.25. Found: C, 83.69; H, 6.97; N, 4.15.

(R)-[(R)-2-Methoxy-1-(2-naphthyl)-ethyl]-(1-phenylbuta-2,3-dienyl)amine (9da) (entry 4 in Table 2): ^1H NMR

δ 2.05 (br, 1H, NH), 3.40 (s, 3H, OMe), 3.52~3.58 (m, 2H, CH₂OMe), 4.25~4.35 (m, 2H, NHCH(Ph) and (2-naphthyl)CH(NH)), 4.78~4.91 (m, 2H, CH=C=CH₂), 5.31 (dt, J = 8.1, 6.6 Hz, 1H, CH=C=CH₂), 7.24~7.86 (m, 12H, Ph and 2-naphthyl); ¹³C NMR δ 58.5, 58.7, 59.6, 76.2, 77.7, 92.8, 125.2, 125.7, 125.9, 126.0, 127.5, 127.6, 128.02 (2C), 128.04, 128.5, 132.1, 133.5, 140.7, 141.1, 208.6; IR(neat) 3441, 3324, 3059, 2926, 2096, 1952, 1631, 1601, 1453, 1354, 1194, 1095, 969, 909, 846, 816, 734, 701cm⁻¹; [α]_D²⁷ -39.1 (c 1.08, CHCl₃); Anal. Calcd. for C₂₃H₂₃NO: C, 83.85; H, 7.04; N, 4.25. Found: C, 83.77; H, 7.06; N, 4.19.

(R)-[(R)-2-Methoxy-1-(4-*tert*-butyldimethylsiloxyphenyl)-ethyl]-(1-phenylbuta-2,3-dienyl)amine (9ea)

(entry 5 in Table 2): ¹H NMR δ 0.187 and 0.190 (2s, 6H, SiMe₂*t*Bu), 0.98 (s, 9H, SiMe₂*t*Bu), 1.96 (br, 1H, -NH-), 3.36 (s, 3H, OMe), 3.46~3.53 (m, 2H, CH₂OMe), 4.04(d, J = 8.1Hz, 1H, PhCHNH), 4.23 (dd, J =5.1, 8.1Hz, 1H, NHCH(Ph)), 4.75 and 4.80 (2dd, J = 7.2, 10.5 Hz and J = 5.7, 10.5 Hz, each 1H, CH=C=CH₂), 5.18 (dt, J = 8.1, 6.9 Hz, 1H, CH=C=CH₂), 6.77 (d, J = 8.1 Hz, 2H, Ar), 7.21~7.44 (m, 7H, Ar); ¹³C NMR δ -4.6, 18.1, 25.6, 57.9, 58.7, 59.5, 75.9, 77.7, 92.9, 119.8, 127.5, 127.7, 128.0 (C2), 128.4, 136.4, 140.8, 154.7, 208.5; IR(neat) 3432, 3031, 2929, 1952, 1607, 1507, 1472, 1362, 1253, 1093, 913, 838, 781, 701cm⁻¹; [α]_D²⁷ -34.0 (c 1.01, CHCl₃); Anal. Calcd. for C₂₅H₃₅NO₂Si: C, 73.30; H, 8.61; N, 3.42. Found: C, 73.46; H, 8.72; N, 3.42.

(R)-[(R)-2-Methoxy-1-(2,4,6-trimethylphenyl)-ethyl]-(1-phenylbuta-2,3-dienyl)amine (9fa) (entry 6 in Table 2): ¹H NMR δ 2.19 (s, 6H, 2,6-Ar(Me)₂), 2.22 (s, 3H, 4-MeAr), 2.48 (br, 1H, NH), 3.38 (s, 3H, OMe), 3.46~3.58 (m, 2H, CH₂OMe), 4.18 (t, J = 6.6 Hz, 1H, NHCH(Ph)), 4.57 (dt, J = 2.7, 6.9 Hz, (mesityl)CHNH), 4.69~4.83 (m, 2H, CH=C=CH₂), 5.31 (dt, J = 6.9, 6.6 Hz, CH=C=CH₂), 6.76 (a, 2H, Ar), 7.20~7.38 (m, 5H, Ph); ¹³C NMR δ 20.5, 20.6, 54.1, 58.8, 60.2, 76.3, 77.6, 91.7, 127.5, 128.0, 128.3, 130.0, 136.1(x2), 136.5, 141.1, 208.2; IR(neat) 3419, 2923, 1952, 1610, 1453, 1375, 1194, 1093, 1027, 970, 849, 760, 701cm⁻¹ [α]_D²⁷ -86.2 (c 1.02, CHCl₃); Anal. Calcd. for C₂₂H₂₇NO: C, 82.20; H, 8.47; N, 4.36. Found: C, 82.58; H, 8.17; N, 4.21.

(S)-(2-Hexyl-1-phenyl-buta-2,3-dienyl)-[(R)-2-methoxy-1-phenylethyl]amine (9ab) (entry 7 in Table 2): ¹H NMR δ 0.85 (t, J = 6.9 Hz, 3H, CH₃), 1.10~1.40 (m, 8H, (CH₂)₄), 1.53~1.66 (m, 1H, C=C=C(R)CH₂), 1.72~1.88 (m,

1H, C=C=C(R)CH₂), 2.36 (br, 1H, NH), 3.56 (s, 3H, OMe), 3.41~3.54 (m, 2H, CH₂OMe), 4.00 (s, 1H, PhCH(NH)), 4.12 (dd, *J* = 4.5, 8.4 Hz, 1H, -CH(Ph)CH₂OMe), 4.87~4.93 (m, 2H, C=C=CH₂), 7.10~7.44 (m, 10H, Ph); ¹³C NMR δ 14.2, 22.7, 27.4, 27.9, 29.0, 31.7, 58.8, 59.7, 61.0, 77.7, 77.9, 104.6, 126.7, 127.1, 127.2, 127.6, 128.0, 128.2, 140.6, 142.7, 205.5; IR (neat) 3331, 3061, 3026, 2926, 1953, 1601, 1453, 1379, 1194, 1107, 970, 843, 759, 700; [α]_D²⁶ -6.2 (*c* 1.07, CHCl₃); Anal. Calcd. for C₂₅H₃₃NO: C, 82.6; H, 9.15; N, 3.85. Found: C, 82.3; H, 9.09; N, 3.54.

(S)-(1,2-Diphenyl-buta-2,3-dienyl)-[(R)-2-methoxy-1-phenylethyl]amine (9ac) (entry 8 in Table 2): ¹H NMR δ 3.27 (s, 3H, -OMe), 3.45 and 3.53 (2dd, *J* = 4.2, 9.6 Hz, and *J* = 9.3, 9.6 Hz, each 1H, CH₂OMe), 4.20 (dd, *J* = 4.2, 9.0 Hz, 1H, CH(Ph)CH₂OMe), 4.55 (s, 1H, PhCH(NH)-), 5.30 (d, *J* = 12.0 Hz, 1H, =C=CH₂), 5.39 (d, *J* = 12.0 Hz, 1H, =C=CH₂), 7.10~7.59 (m, 15H, Ph); ¹³C NMR δ 58.6, 58.7, 60.0, 77.8, 80.5, 107.4, 126.6, 126.7, 126.9, 127.3, 127.5, 128.0, 128.2, 128.2, 128.3, 135.3, 140.6, 142.8, 208.1; IR (neat) 3328, 3060, 3027, 2925, 1939, 1599, 1494, 1452, 1351, 1194, 1108, 971, 852, 761, 698; [α]_D²⁸ +15.2 (*c* 0.75, CHCl₃); Anal. Calcd. for C₂₅H₂₅NO: C, 84.47; H, 7.09; N, 3.94. Found: C, 84.74; H, 7.13; N, 4.15.

(R)-[(R)-2-Methoxy-1-phenylethyl]-(1-phenyldeca-2,3-dienyl)amine (9ad) (entry 9 in Table 2): The following data were recorded using a mixture of two diastereomeric isomers. ¹H NMR δ 0.85 and 0.91 (2t, each *J* = 6.9 Hz, 3H, CH₃), 1.20~1.45 (m, 8H, (CH₂)₄), 1.92~2.11 (m, 2H, CH=C=CH-CH₂), 2.22 (br, 1H, NH), 3.36 (s, 3H, OMe), 3.46~3.51 (m, 2H, CH₂OMe), 4.01~4.07 (m, 1H, PhCH(NH)), 4.22~4.31 (m, 1H, CH(Ph)CH₂OMe), 5.09~5.25 (m, 2H, CH=C=CH), 7.18~7.44 (m, 10H, Ph); ¹³C NMR δ 14.16 and 14.22, 22.6 and 22.7, 28.7 and 28.9, 29.0 and 29.1, 29.59 and 29.60, 31.7 and 31.8, 58.66 and 58.70, 58.8 and 58.9, 59.4 and 59.5, 77.7 and 77.8, 92.4, 93.2 and 93.3, 126.7, 126.8, 127.2 and 127.3, 127.7, 127.8, 128.1, 128.1, 128.2, 128.2, 140.5, 140.6, 143.8, 203.4 and 203.6; IR (neat) 3322, 3061, 3027, 2926, 1958, 1602, 1453, 1379, 1194, 1099, 1027, 970, 758, 700; Anal. Calcd. for C₂₅H₃₃NO: C, 82.60; H, 9.15; N, 3.85. Found: C, 82.7; H, 9.50; N, 3.81.

(R)-(1,4-Diphenylbuta-2,3-dienyl)-[(R)-2-methoxy-1-phenylethyl]amine (9ae) (entry 10 in Table 2): ¹H NMR δ 2.36 (br, 1H, -NH-), 3.33 and 3.42 (s, 3H, -OMe), 3.48~3.57 (m, 2H, -CH₂OMe), 4.23 and 4.26 (d, *J* = 9.0 Hz, 1H, PhCH(NH)-), 4.28~4.40 (m, 1H, -CH(Ph)CH₂OMe), 5.63 (m, 1H, -CH=C=CHPh), 6.25~6.33 (m, 1H, -CH=C=CHPh), 7.20~7.60 (m, 15H, Ph); ¹³C

NMR δ 58.7 and 58.8, 58.8 and 59.0, 59.6 and 59.8, 77.6 and 77.8, 95.6 and 95.7, 97.3 and 97.5, 126.6, 126.8, 126.8, 126.9, 127.0, 127.3, 127.4, 127.6, 127.8, 128.2, 128.3, 128.4, 131.4, 134.2 and 134.5, 140.2 and 140.3, 204.6 and 204.7; IR (neat) 3322, 3061, 3028, 2925, 1945, 1599, 1494, 1453, 1381, 1352, 1194, 1098, 1027, 970, 912, 880, 821, 759, 699; Anal. Calcd. for $C_{25}H_{25}NO$: C, 84.47; H, 7.09; N, 3.94. Found: C, 84.71; H, 6.93; N, 4.15.

(R)-1-Phenylpropylamine: A solution of **6a** (1.59 g, 3.42 mmol) in dry DMF (18 mL) was treated with TBAF (3.42 mL, 1 M in THF, 3.42 mmol). After 8 h the reaction mixture was quenched with H_2O , extracted with ether, dried over $MgSO_4$, and then concentrated under reduced pressure to afford a crude mixture. Purification by silica gel chromatography gave propargylamine **10** (729 mg) in 80% yield. 1H NMR δ 2.32 (br, 1H, -NH-), 2.55 (d, $J = 1.8$ Hz, 1H, -C $\equiv$ CH), 3.39 (s, 3H, -OMe), 3.47~3.53 (m, 2H, -CH₂OMe), 4.32 (br s, 1H, PhCH(NH)-), 4.49 (dd, $J = 6.0$, 7.8 Hz, 1H, -NHCH(Ph)-), 7.25~7.60 (m, 10H, Ph); ^{13}C NMR δ 50.8, 58.6, 60.1, 73.7, 77.5, 83.4, 127.3, 127.5, 127.7, 127.8, 128.3, 128.5, 139.5, 140.0; IR(neat) 3289, 3030, 2887, 1602, 1453, 1353, 1273, 1194, 1096, 965, 760, 699 cm^{-1} ; $[\alpha]_D^{27} -114.3$ (c 1.01, $CHCl_3$).

A solution of **10** (587 mg, 2.20 mmol) in dry MeOH was added $Pd(OH)_2/C$ (50 mg) and then treated with H_2 gas. After 20 min the reaction mixture was filtered to remove $Pd(OH)_2/C$ and then concentrated to afford a crude which was subjected directly to the next reaction.. To a solution of the corresponding amine (593 mg, 1.50 mmol) in dry CH_2Cl_2 (7.5 mL) was added dropwise boron tribromide (7.5 mL, 1 M in CH_2Cl_2 7.5 mmol) at $-78^\circ C$ under Ar atmosphere. After being stirred for 1 h at $-78^\circ C$, the solution was warmed to $-20^\circ C$ and then stirring for an additional 4h at this temperature. The reaction was quenched with sat. $NaHCO_3$ aq. (10 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude mixture of the corresponding alcohol (280 mg, 1.10 mmol) which was subjected directly to the next reaction. To a solution of the demethylated product in MeOH (5.5 mL) was added 40% aqueous $MeNH_2$ (0.85 mL, 11 mmol) and H_5IO_6 (742 mg, 3.3 mmol) dissolved in H_2O (2.8 mL). After the mixture was stirred over 17h, 10% aqueous $NaOH$ (3.7 mL) was added, MeOH was removed under reduced pressure, the organic phase was extracted with ether, and dried over $MgSO_4$. Concentration of the extracts afforded a crude product. Silica gel chromatography afforded 1-phenylpropylamine (**11**) (116 mg) in 39% overall yield (3 steps)³: 1H NMR δ 0.87 (t, $J = 7.5$ Hz, 3H, -CH₂CH₃), 1.58(br, 2H, -NH₂), 1.72 (dq, $J = 6.6$, 7.5 Hz, 2H, -CH₂CH₃), 3.80 (t, $J = 6.6$ Hz, 1H, PhCH(NH₂)-), 7.20~7.37 (m, 5H, Ph); ^{13}C NMR δ 10.9, 32.4, 57.8, 126.4, 126.8, 128.4, 146.4; $[\alpha]_D^{28} +14.9$ (c 0.29, benzene). Reported optical rotation for (*S*)-1-phenylpropylamine: $[\alpha]_D^{22} -16.1$ (c 2.43, benzene).⁴

(R)-1-Phenylbuta-2,3-dienylamine (13): To a solution of amine **9aa** (450 mg, 1.61 mmol) in dry CH_2Cl_2 (8 mL) was added dropwise boron tribromide in CH_2Cl_2 (1 M, 4.8 mL, 4.8 mmol) at -78°C under Ar atmosphere. After being stirred for 1 h at -78°C , the solution was warmed to -20°C and then stirred for an additional 4 h at this temperature. The reaction was quenched with sat. NaHCO_3 aq. (10 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine, dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure to give a crude mixture of the corresponding alcohol (130 mg, 0.89 mmol) which was subjected directly to the next reaction. To a solution of the demethylated product in MeOH (4.5 mL) was added 40 % aqueous MeNH_2 (0.69 mL, 8.9 mmol) and H_5IO_6 (607 mg, 2.67 mmol) dissolved in H_2O (2.2 mL). After the mixture was stirred over 17 h, 10% aqueous NaOH (3 mL) was added, MeOH was removed under reduced pressure, the organic phase was extracted with ether, and dried over MgSO_4 . Concentration of the extracts afforded a crude product. Silica gel chromatography afforded **12** (105 mg) in 45% overall yield (2 steps)³: ^1H NMR δ 1.65 (br, 2H, NH_2), 4.54~4.59 (m, 1H, $\text{PhCH}(\text{NH}_2)$), 4.90 and 4.91 (2d, $J = 6.6$ Hz and $J = 6.3$ Hz, each 1H, $\text{CH}=\text{C}=\text{CH}_2$), 5.41 (dt, $J = 5.7, 6.6$ Hz, 1H, $\text{CH}=\text{C}=\text{CH}_2$), 7.23~7.40 (m, 5H, Ph); ^{13}C NMR δ 54.3, 77.9, 96.4, 126.4, 127.1, 128.4, 144.5, 206.6; IR (neat) 3366, 3297, 3060, 3027, 2966, 2925, 2860, 1954, 1675, 1492, 1363, 1261, 1113, 1075, 1027, 849, 762, 700; $[\alpha]_{\text{D}}^{27} +65.4$ (c 1.08, CHCl_3).

A solution of **12** (65 mg, 0.447 mmol) in dry MeOH was added $\text{Pd(OH)}_2/\text{C}$ (10 mg) and then treated with H_2 gas. After 20 min the reaction mixture was filtered to remove $\text{Pd(OH)}_2/\text{C}$ and then concentrated to afford a crude mixture of **13**. The residue was purified by column chromatography on silica gel to afford **13** (49 mg, 73%): ^1H NMR δ 0.90 (t, $J = 7.2$ Hz, 3H, CH_2CH_3), 1.20~1.70 (m, 6H, $\text{CH}_2\text{CH}_2\text{CH}_3$ and NH_2), 3.89 (t, $J = 6.6$ Hz, 1H, $\text{PhCH}(\text{NH}_2)$), 7.20~7.36 (m, 5H, Ph); ^{13}C NMR δ 13.9, 19.6, 41.8, 56.0, 126.4, 126.9, 128.5, 146.6; $[\alpha]_{\text{D}}^{26} +22.4$ (c 0.32, solvent). Reported optical rotation for (S)-1-phenylbutylamine: $[\alpha]_{\text{D}}^{25} -22.2$ (c 5.1, CHCl_3).⁵

References

1. Prepared by LiAlH_4 reduction of 2-phenylglycine: To a suspension of LiAlH_4 (12.55 g, 330 mmol) in THF (400 mL) was added portionwise *D*-2-phenylglycine (25.0 g, 165 mmol) at 0°C . After being refluxed for 7 h, the reaction was quenched by sequential addition of THF (60.0 mL), water (30.0 mL), 15% NaOH aq. (15.0 mL) and water (90.0 mL). The resulting mixture was filtered through a pad of Celite, concentrated under reduced pressure to provide a crude *D*-2-phenylglycinol which was subjected directly to the next reaction (*O*-methylation). For other reaction conditions, see: McKennon, M. J.; Meyers, A. I. *J. Org. Chem.* **1993**, 58, 3568.
2. Smith, III, A. B.; Yager, K. M.; Philips, B. W.; Taylor, C. M. *Org. Synth.* **1997**, 75, 19.
3. For the procedure of demethylation and following oxidative cleavage were reported, see: Yanada, R.; Negoro, N.; Okaniwa, M.; Ibuka, T. *Tetrahedron* **1999**, 55, 13947.
4. Kawakami, T., Ohtake H., Arakawa, H., Okachi, T., Imada Y., Murahashi, S. *Bull. Chem. Soc. Jpn.* **2000**, 73, 2423.
5. Yamamoto, Y.; Shimoda, H.; Oda, J.; Inouye, Y. *Bull. Chem. Soc. Jpn.* **1976**, 49, 3247.