Asymmetric Synthesis of Acyclic Amines Through Zr- and Hf-Catalyzed Enantioselective Alkylzinc Reagents to Imines

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SUPPORTING INFORMATION

Materials and Reagents

Infrared (IR) spectra were recorded on a Perkin Elmer 781 spectrophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a Varian Unity 300 (300 MHz) or Varian GN-400 (400 MHz). Chemical shifts are reported with the solvent resonance as the internal standard ($CHCl_3$: δ 7.26). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity 300 (75 MHz) or Varian GN-400 (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm with the solvent as the internal reference $CDCl_3$: δ 77.0 ppm. Enantiomeric ratios were determined by chiral HPLC. Analytical liquid chromatography (HPLC) was performed on a Shimadzu chromatograph with a Chiralcel OD (4.6 x 250 mm) chiral column by Chiral Technologies. Optical rotations were measured on a Rudolph Research Analytical Autopol IV polarimeter.

All reactions were conducted in oven- (135 °C) and flame-dried glassware under an inert atmosphere of dry argon or nitrogen. Diethylzinc, dimethylzinc (2.0 M in toluene), Zr(O*i*-Pr)$_4$ •HO*i*-Pr (99.9%), *o*-anisidine, and all commercially available aldehydes were purchased from Aldrich and used without further purification except the following: hydrocinnamaldehyde and heptaldehyde were distilled from $CaCl_2$ and valeraldehyde was distilled under inert atmosphere. 4-(3-oxo-propyl)benzoic acid methyl ester,[1] 6-oxohexanoic acid isopropyl ester,[2] 5-oxopentanoic acid methoxymethylamide, 6-oxohexanoic acid methoxymethylamide,[3] 2-*tert*-butyldiphenylsiloxyacetaldehyde,[4] and 4-*tert*-butyldimethylsiloxybutyraldehyde[5] were prepared according to literature procedures. Di(4-methylpentyl)zinc and dioctylzinc were prepared via a B-Zn exchange according to literature precedence.[6] Boc-valine, Boc-phenylalanine, EDC (1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride) and HOBt (*N*-hydroxybenzotriazole) were purchased from Advanced Chemtech and used without further purification. Toluene was distilled from Na/benzophenone ketyl. Dichloromethane, triethylamine, and butylamine were distilled from CaH_2.

General procedure for multi-component Zr-catalyzed addition of dialkylzinc reagents to imines. The ligand and Zr(O*i*-Pr)$_4$•HO*i*-Pr were weighed into a flame-dried, round-bottomed flask inside a N_2 atmosphere glovebox. The contents were dissolved in toluene and the colorless solution was allowed to stir for 5 min at 22 °C. *o*-Anisidine was added to the vessel immediately followed by the addition of aldehyde. The flask was capped with a septum, sealed with PTFE tape, removed from the glovebox and allowed to stir for an additional 40 min at 22 °C. The reaction vessel was placed in an ice bath and allowed to cool to 0 °C. Dialkylzinc was added through syringe under positive pressure of N_2 and the reaction mixture was allowed to stir. The solution was quenched with saturated NH_4Cl and poured into a separatory funnel containing Et_2O. In some instances a precipitate of ligand and Zr salts formed and was removed by filtration. The mixture was washed three times with Et_2O and the combined organics were washed with brine, dried over $MgSO_4$, and concentrated. The products could be further purified by silica gel chromatography. Optical purity was determined by chiral HPLC (Chiralcel OD).

***N*-[(2-Hydroxyphenyl)methyl]-L-valyl-*N*-butyl-L-phenylalaninamide** (**1a**) was synthesized as described previously[5b] to yield a white solid; melting point =174 °C. IR (CH_2Cl_2): 3672 (w), 3420 (m), 3314 (m), 3087 (m), 2987 (m), 2980 (m), 2936 (m), 2867 (m), 2313 m), 1665 (s), 1590 (m), 1495 (s), 1388 (m), 1092 (m), 846 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31-7.25 (5H, m), 7.16 (1H, ddd, *J* = 7.6, 6.8, 1.6 Hz), 7.07 (1H, d, *J* = 8.4 Hz), 6.82 (1H, d, *J* = 7.6 Hz), 6.68 (1H, ddd, *J* = 7.2, 7.2, 1.2 Hz), 6.64 (1H, ddd, *J* = 7.2, 7.2, 1.2 Hz), 6.25 (1H, dd, *J* = 5.6, 4.8 Hz), 4.85 (1H, dt, *J* = 15.6, 8.0 Hz), 3.73 (1H, d, *J* = 13.6 Hz), 3.33 (1H, d, *J* = 14.0 Hz), 3.23 (1H, m), 3.11-3.04 (4H, m), 2.72 (1H, s), 1.70 (1H, dq, *J* = 13.6, 6.8 Hz), 1.41-1.32 (2H, m), 1.29-1.20 (2H, m), 0.90-0.86 (6H, m), 0.83 (3H, d, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.0, 170.6, 157.5, 136.6, 129.1, 128.9, 128.7, 128.6, 127.0, 122.3, 119.1, 116.3, 67.0, 54.5, 50.6, 39.4, 38.8, 31.6, 31.4, 20.1, 19.7, 19.0, 13.8; Anal. calcd for $C_{25}H_{35}N_3O_3$: C, 70.56; H, 8.29; N, 9.87. Found: C, 70.49; H, 8.23; N, 9.91. Optical Rotation: $[\alpha]^{25}_D$ -31.3 (c 10.4, $CHCl_3$).

***N*-[(2-Hydroxy-5-methoxyphenyl)methyl]-L-valyl-*N*-butyl-L-phenylalaninamide (1b)** was synthesized according to the procedure described for 1a to yield a white solid; melting point = 149 °C. IR (CH_2Cl_2): 3692 (m), 3427 (m), 3320 (m), 2987 (s), 2968 (s), 2924 (s), 2873 (s), 1671 (s), 1615, (w), 1508 (s), 1476 (s), 1224 (m), 1149 (s), 1048 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34-7.25 (5H, m), 6.78-6.71 (3H, m), 6.41 (1H, d, *J* = 2.4 Hz), 5.76 (1H, br), 4.73 (1H, dt, *J* = 8.0, 7.6 Hz), 3.74 (1H, d, *J* = 15.2 Hz), 3.73 (3H, s), 3.39 (1H, d, *J* = 13.6 Hz), 3.18 (1H, dq, *J* = 21.0, 7.2 Hz), 3.14-3.04 (3H, m), 2.76 (1H, d, *J* = 6.4 Hz), 2.20 (1H, br), 1.82 (1H, dq, *J* =13.2, 6.8 Hz), 1.33 (2H, m), 1.25 (2H, m), 0.90 (6H, dd, *J* = 13.6, 6.8 Hz), 0.86 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.8, 170.2, 152.4, 151.1, 136.4, 129.1, 128.7, 127.0, 123.3, 116.8, 114.7, 113.6, 67.3, 55.8, 54.6, 50.9, 39.4, 38.9, 31.7, 31.4, 20.0, 19.6, 18.8, 13.8; Anal. calcd for $C_{26}H_{37}N_3O_4$: C, 68.54; H, 8.19; N, 9.22. Found: C, 68.49; H, 7.98; N, 9.07. Optical Rotation: $[\alpha]^{25}_D$ -23.5 (c 3.0, $CHCl_3$).

***N*-[(3,5-Di-tertbutyl-2-hydroxyphenyl)methyl]-L-valyl-*N*-butyl-L-phenylalaninamide (1c)** was synthesized according to the procedure described for **1a** to yield a white solid; melting point = 145 ^{o}C. IR (neat, thin film): 3448 (s), 3281 (s), 2961 (m), 1636 (s), 1558 (m), 1457 (w), 1237 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.37 (1H, br s), 7.35-7.23 (7H, m), 6.73 (1H, d, *J* = 2.4 Hz), 6.45 (1H, br s), 5.58 (1H, br s), 4.71 (1H, dd, *J* = 8.0, 8.0 Hz), 3.78 (1H, d, *J* = 13.6 Hz), 3.46 (1H, d, *J* = 13.6 Hz), 3.22-3.04 (4H, m), 2.74 (1H, d, *J* = 6.4 Hz), 2.27 (1H, br s), 1.89-1.80 (2H, m), 1.63 (1H, br s), 1.42 (9H, s), 1.33-1.16 (4H, m), 1.29 (9H, s), 0.96 (3H, d, *J* = 6.8 Hz), 0.09 (1H, d, *J* = 6.8 Hz), 0.85 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.2, 170.6, 154.4, 140.8, 136.8, 136.2, 129.3, 128.9, 127.3, 123.7, 123.3, 122.0, 67.4, 54.7, 51.7, 39.4, 39.2, 35.0, 34.3, 31.8, 31.7, 31.5, 29.8, 20.0, 19.8, 18.9, 13.7. Anal. calcd for $C_{33}H_{51}N_3O_3$: C, 73.70; H 9.56; N, 7.81. Found: C, 73.69; H, 9.60; N, 7.64. Optical Rotation $[\alpha]^{25}_{D}$ -9.0 (c 1.0, CH_2Cl_2).

2-Methoxy-N-((S)-1-(3-((S)-1-(2-methoxyphenylamino)propyl)phenyl)propyl)phenylamine (4) was synthesized according to the general procedure with 2 equiv of *o*-anisidine (**3**) to yield a colorless oil. IR (neat, thin film): 3421 (w), 2961 (m), 2930 (m), 1602 (m), 1511 (s), 1456 (m), 1425 (w), 1338 (w), 1220 (m), 1023 (m), 734 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32-7.20 (2H, m), 6.78-6.59 (3H, m), 4.70 (1H, br s), 4.21 (1H, br s), 3.80 (3H, s), 1.95-1.80 (2H, m), 0.99-0.92 (3H, t, *J* = 7.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.8, 144.3, 137.7, 128.9, 125.4, 124.9, 121.3, 116.3, 111.4, 109.4, 60.0, 55.6, 31.8, 11.0; Anal. calcd for $C_{26}H_{32}N_2O_2$: C, 77.19; H, 7.97; N, 6.92; Found: C, 77.25; H, 8.01; N, 6.55. Optical Rotation: $[\alpha]^{25}_{D}$ +1.1 (c 1. 09, CH_2Cl_2).

2-Phenoxy-N-((S)-1-(3-((S)-1-(2-phenoxyphenylamino)propyl)phenyl)propyl)phenylamine (5) was synthesized according to the general procedure with 2 equiv of *o*-anisidine (**3**) to yield a colorless oil. IR (neat, thin film): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3427 (w), 2955 (m), 1607 (m), 1513 (s), 1432(w), 1331 (m), 1216 (s), 741 (s): ^{1}H NMR ($CDCl_3$, 400 MHz): δ7.35-6.97 (4H, m), 7.26-6.97 (14H, m), 6.85-6.77 (4H, m), 6.57 (2H, dt, *J* = 7.6, 1.2 Hz), 6.36 (2H, dd, *J* = 8.0, 1.6 Hz), 4.57 (2H, d, *J* = 5.6 Hz), 4.9 (2H, q, *J* = 6.8 Hz), 1.81-1.68 (4H, m), 0.84 (6H, t, *J* = 7.2 Hz): ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.95, 144.16, 142.96, 139.89, 129.85, 128.95, 125.24, 125.02, 124.99, 122.83, 119.51, 117.5, 116.7, 112.9; Anal calcd for $C_{36}H_{36}N_2O_2$**:** C, 81.79; H, 6.86; N, 5.30 Found: C, 81.49; H, 7.11; N, 5.18. Optical rotation $[\alpha]^{25}_{D}$ +109.5 (c 0.633, CH_2Cl_2).

2-(Methylthio)-N-((S)-1-(3-((S)-1-(2-(methylthio)phenylamino)propyl)phenyl)propyl) phenylamine (6) was synthesized according to the general procedure with 2 equiv of *o*-anisidine (**3**) to yield a colorless oil. IR (neat , thin film): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37 (1H, dd, *J* = 7.6, 0.8 Hz), 7.27-7.23 (3H, m), 7.16 (2H, dd, *J* = 7.2, 1.6 Hz), 6.91 (2H, dt, *J* = 8.0, 0.8 Hz), 6.56 (2H, t, *J*= 7.2 Hz), 6.25 (2H, d, *J* = 8.0 Hz), 5.42 (2H, br s), 4.22 (1H, t, *J* = 6.6 Hz), 2.36 (6H, s), 1.90-1.82 (4H, m), 0.97 (6H, t, *J* = 7.6 Hz): ^{13}C NMR ($CDCl_3$, 100 MHz): δ147.7, 144.1, 134.2, 129.5, 129.0, 125.1, 125.0, 119.7, 116.9, 111.6, 59.9, 31.8, 18.5,

10.9; Anal calcd for $C_{26}H_{32}N_2S_2$: C, 71.51; H, 7.39; N, 6.42; Found: C, 71.59; H, 7.76; N, 6.23. Optical rotation $[\alpha]^{25}_D$ +208.3.0 (c 1.64, CH_2Cl_2).

[1-(4-Diethoxymethylphenyl)propyl]-(2-methoxyphenyl)amine (7) was synthesized according to the general procedure with 2 equiv of *o*-anisidine (**3**) to yield a colorless oil. IR (neat, thin film): 3444 (w), 2972 (m), 2930 (m), 2873 (m), 1702 (w), 1602 (s), 1512 (s), 1455(s), 1344 (m), 1222 (s), 1112 (m), 1052 (s), 1029 (w), 736 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.42 (2H, d, *J* = 8.4 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 6.76 (1H, dd, *J* = 8.0, 1.6 Hz), 6.69 (1H, dt, *J* = 7.6, 1.2), 6.56 (1H, dt, *J* = 7.6, 1.2 Hz), 6.35 (1H, dd, *J* = 8.0, 1.6 Hz), 5.48 (1H, s), 4.23 (1H, t, *J* = 6.4 Hz), 3.89 (3H, s), 3.65-3.52 (4H, m), 1.93-1.80 (2H, m), 1.24 (6H, t, *J* = 7.2 Hz), 0.98 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.7, 144.5, 137.7, 137.6, 126.9, 126.5, 121.25, 116.25, 110.9, 109.4, 101.8, 61.2, 59.5, 55.6, 31.8, 15.3, 11.0; Anal. calcd for $C_{21}H_{29}NO_3$: C, 73.44; H, 8.51; N, 4.08; Found: C, 73.72; H, 8.35; N, 3.99. Optical Rotation: $[\alpha]^{25}_D$ +12.0 (c 1.50, CH_2Cl_2).

4-[3-(2-Methoxyphenylamino)pentyl]benzoic acid methyl ester (8) was synthesized according to the general procedure to yield a tan solid; melting point = 75 °C. IR (neat, thin film): 3414 (w), 2924 (s), 2848 (w), 1720 (s), 1595 (m), 1513 (m), 1451 (m), 1278 (s), 1193 (w), 1111 (w) 1029 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.94 (2H, d, *J* = 8.4 Hz), 7.23 (2H, d, *J* = 8.4 Hz), 6.83 (1H, dt, *J* = 7.2, 0.8 Hz), 6.78 (1H, d, *J* = 8.0 Hz), 6.62 (1H, dt, *J* = 7.6, 1.6Hz), 6.51 (1H, d, *J* = 8.4 Hz), 4.07 (1H, br s), 3.91 (3H, s), 3.85 (3H, br s), 3.35-3.29 (1H, m), 2.84-2.7 (2H, m), 1.94-1.78 (2H, m), 1.67-1.52 (2H, m), 0.93 (3H, t, *J* = 7.6); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.3, 148.08, 146.83, 138.01, 129.83, 128.6, 121.44, 115.84, 110.14, 109.74, 55.58, 53.41, 5210, 36.04, 32.58, 29.85, 27.66, 10.25; Anal. calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28. Found: C, 73.56; H, 7.81; N, 4.5. Optical Rotation: $[\alpha]^{25}_D$ +5.3 (c 1.50, CH_2Cl_2).

(2*S*)-2-[(2-Methoxyphenyl)amino]-1-butanol (9 after desilylation) was synthesized according to the general procedure to yield a colorless oil. Deprotection of the silyl ether with TBAF followed by purification on silica gel afforded the desired amino alcohol as colorless oil. IR (neat, thin film): 3421 (br), 3069 (m), 3043 (m), 2974 (s), 2955 (s), 2880 (s), 2848 (s), 1596 (s), 1514 (s), 1464 (s), 1432 (s), 1344 (s), 1036 (s), 922 (s), 740 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 6.86 (1H, ddd, *J* = 7.6, 7.2, 1.6 Hz), 6.79 (1H, dd, *J* = 7.6, 1.2 Hz), 6.70 (1H, d, *J* = 7.6 Hz), 6.69 (1H, ddd, *J* = 7.6, 7.2, 1.6 Hz), 4.12 (1H, br), 3.86 (3H, s), 3.76 (1H, dd, *J* = 11.2, 3.6 Hz), 3.55 (1H, dd, *J* = 11.2, 6.0 Hz), 3.44-3.41 (1H, m), 2.05 (1H, br), 1.67-1.53 (2H, m), 0.97 (3H, t, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.9, 137.5, 121.1, 116.7, 110.8, 109.6, 64.3, 56.6, 55.5, 25.1, 10.7; Anal. calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found: C, 67.41; H, 8.69; N, 7.00. Optical Rotation: $[\alpha]^{25}_D$ -5.7 (c 0.96, $CHCl_3$).

***N*-[(1*S*)-1-Ethylheptyl]-2-methoxy-phenylamine (Table 1 entries 1 and 2)** was synthesized according to the general procedure to yield a colorless oil. IR (neat, thin film): 3427 (m), 3062 (m), 3043 (m), 2949 (s), 2861 (s), 1608 (s), 1514 (s), 1464 (s), 1338 (s), 1243 (s), 1218 (s), 1180 (s), 1105 (s), 1029 (s), 897 (w), 784 (w), 734 (s) cm^{-1}; ^1H NMR ($CDCl_3$,

400 MHz): δ 6.85 (1H, dd, *J* = 8.0, 7.6 Hz), 6.76 (1H, d, *J* = 7.6 Hz), 6.60 (1H, dd, *J* = 8.0, 7.6 Hz), 6.58 (1H, d, *J* = 7.6 Hz), 4.06 (1H, d, *J* = 5.2 Hz), 3.84 (3H, s), 3.27 (1H, q, *J* = 6.0 Hz), 1.64-1.57 (1H, m), 1.56-1.44 (3H, m), 1.42-1.27 (8H, m), 0.92 (3H, t, *J* = 7.4 Hz), 0.88 (3H, dd, *J* = 7.2, 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.4, 138.0, 121.1, 115.2, 109.7, 109.4, 55.5, 53.9, 34.5, 31.9, 29.6, 27.3, 26.1, 22.8, 14.2, 10.2; Anal. calcd for $C_{16}H_{27}NO$: C, 77.06; H, 10.91; N, 5.62. Found: C, 76.82; H, 10.71; N, 5.48. Optical Rotation: $[\alpha]^{25}_D$ -1.84 (c 1.0, $CHCl_3$).

***N*-[(1*S*)-1-Ethyl-3-methylbutyl]-2-methoxy-phenylamine (Table 1 entries 3 and 4)** was synthesized according to the general procedure to yield the desired product as a colorless oil. IR (neat, thin film): 3427 (m), 3075 (m), 3043 (m), 2968 (s), 2886 (s), 2855 (s), 1602 (s), 1540 (s), 1464 (s), 1438 (s), 1363 (s), 1243 (s), 1180 (s), 1111 (s), 1029 (s), 771 (m), 740 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.85 (1H, tt, *J* = 7.6, 1.2 Hz), 6.76 (1H, dd, *J* = 8.2, 1.2 Hz), 6.60 (1H, dt, *J* = 8.0, 1.2 Hz), 6.59 (1H, dd, *J* = 8.0, 1.2 Hz), 4.02 (1H, br), 3.84 (3H, s), 3.36 (1H, br), 1.76 (1H, ddq, *J* = 14.4, 6.8, 6.4 Hz), 1.64-1.31 (4H, m), 0.95 (3H, d, *J* = 6.8 Hz), 0.91 (3H, t, *J* = 7.6 Hz), 0.88 (3H, d, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.4, 137.9, 121.0, 115.1, 109.6, 109.4, 55.4, 51.6, 44.2, 27.6, 25.1, 23.3, 22.8, 10.0; Anal. calcd for $C_{14}H_{23}NO$: C, 75.97; H, 10.47; N, 6.33. Found: C, 76.24; H, 10.31; N, 6.34. Optical Rotation: $[\alpha]^{25}_D$ +13.5 (c 0.42, $CHCl_3$).

***N*-[(1*S*,4*Z*)-1-Ethyl-4-decenyl]-2-methoxy-phenylamine (Table 1 entries 5 and 6)** was synthesized according to the general procedure using to yield the desired product as a colorless oil. IR (neat, thin film): 3421 (m), 3081 (m), 3050 (m), 3012 (s), 2949 (s), 2918 (s), 2880 (s), 1684 (m), 1602 (s), 1514 (s), 1464 (s), 1438 (s), 1357 (m), 1237 (s), 1162 (s), 1048 (s), 734 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.84 (1H, ddd, *J* = 8.0, 7.6, 1.6 Hz), 6.77 (1H, dd, *J* = 8.0, 1.6 Hz), 6.60 (1H, ddd, *J* = 8.0, 7.6, 1.6 Hz), 6.58 (1H, dd, *J* = 7.6, 1.6 Hz), 5.39-5.34 (2H, m), 4.07 (1H, br), 3.84 (3H, s), 3.29 (1H, br), 2.15-2.08 (2H, m), 1.98 (2H, dt, *J* = 7.6, 6.0 Hz), 1.65-1.49 (4H, m), 1.34-1.22 (6H, m), 0.93 (3H, t, *J* = 7.6 Hz), 0.87 (3H, t, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.5, 137.9, 130.3, 129.0, 121.1, 115.3, 109.8, 109.4, 55.5, 53.7, 34.5, 31.6, 29.5, 27.4, 27.3, 23.9, 22.7, 14.2, 10.2; Anal. calcd for $C_{19}H_{31}NO$: C, 78.84; H, 10.79; N, 4.84. Found: C, 78.82; H, 10.78; N, 4.64. Optical Rotation: $[\alpha]^{25}_D$ +1.17 (c 0.73, $CHCl_3$).

***N*-[(1*S*)-1-Cyclopropylpropyl]-2-methoxy-phenylamine (Table 1 entries 6 and 7)** was synthesized according to the general procedure using to yield a colorless oil. IR (neat, thin film): 3440 (s), 3069 (s), 2999 (s), 2987 (s), 2930 (s), 2873 (s), 2842 (s), 1608 (s), 1520 (s), 1457 (s), 1445 (s), 1350 (s), 1256 (s), 1180 (s), 1054 (s), 752 (s) cm-1; ^{1}H NMR (CDCl3, 400 MHz): δ 6.85 (1H, ddd, *J* = 8.0, 7.6, 1.2 Hz), 6.77 (1H, dd, *J* = 7.6, 1.2 Hz), 6.63 (1H, ddd, *J* = 8.0, 7.6, 1.2 Hz), 6.58 (1H, dd, *J* = 8.0, 1.2 Hz), 4.22 (1H, br), 3.86 (3H, s), 2.81 (1H, q, *J* = 6.4 Hz), 1.69 (2H, ddt, *J* = 7.6, 7.2, 6.0 Hz), 1.01 (3H, t, *J* = 7.2 Hz), 0.96 (1H, ddt, *J* = 8.0, 7.6, 2.8 Hz), 0.57-0.43 (2H, m), 0.30-0.28 (2H, m); ^{13}C NMR (CDCl3, 100 MHz): δ 146.3, 138.1, 121.0, 115.5, 110.0, 109.4, 57.9, 55.4, 28.4, 16.1, 10.4, 3.6, 2.3; Anal. calcd for $C_{13}H_{19}NO$: C,

76.06; H, 9.33; N, 6.82. Found: C, 76.09; H, 9.11; N, 6.82. Optical Rotation: $[\alpha]^{25}_{D}$ -30.8 (c 1.0, $CHCl_3$).

***N*-[(2-Hydroxyphenyl)methylene]-L-valyl-*N*-butyl-L-phenylalaninamide** (**13**) was synthesized as described previously[5a] to yield a white solid; melting point = 161 °C. IR (neat, thin film): 3415 (m), 2968 (m), 2930 (s), 2930 (s), 2867 (m), 2307 (w), 1665 (s), 1610 (s), 1508 (s), 1420 (s), 1394 (w), 1149 (s), 1123 (s), 1010 (s), 891 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.25 (1H, s), 7.42-7.37 (1H, m), 7.32-7.29 (3H, m), 7.26-7.21 (3H, m), 7.04 (1H, d, *J* = 8.4 Hz), 6.94 (1H, t, *J* = 7.6 Hz), 6.57 (1H, br s), 5.92 (1H, br s), 4.57 (1H, q, *J* = 8.0 Hz), 3.63 (1H, d, *J* = 4.4 Hz), 3.21-3.12 (1H, m), 3.14-3.02 (3H, m), 2.38-2.31 (1H, m), 1.36-1.29 (2H, m), 1.22-1.16 (2H, m), 0.84 (3H, t, *J* = 7.2 Hz), 0.79 (3H, d, *J* = 7.2 Hz), 0.65 (3H, d, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.1, 170.0, 167.8, 160.5, 136.5, 133.2, 132.0, 129.1, 128.7, 126.9, 119.1, 118.2, 117.1, 79.2, 54.8, 39.3, 37.9, 32.1, 31.4, 20.0, 19.6, 16.7, 13.8; Anal. calcd for $C_{25}H_{33}N_3O_3$: C, 70.89; H, 7.85; N, 9.92. Found: C, 70.73; H, 7.81; N, 9.92. Optical Rotation: $[\alpha]^{25}_{D}$ +15.6 (c 6.3, $CHCl_3$).

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