Supplementary Material for:

Highly Enantioselective Syntheses of *anti* Homoaldol Products by (–)-Sparteine Mediated Lithiation/Transmetalation/Substitution of Allylic Amines

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Experimental

General. All glassware used in lithiation reactions was either flame dried or oven dried, and cooled under a nitrogen atmosphere. Solvents and reagents were used as received, unless noted. Toluene and dichloromethane were freshly distilled from CaH_2 under N_2 prior to use. Methyl *t*-butyl ether (MTBE) and tetrahydrofuran (THF) were distilled from Na/benzophenone under N_2. DMF was distilled over Linde type 4A molecular sieves. *n*-BuLi in hexane was used at a concentration determined by titration with *N*-pivaloyl-*o*-toluidine.[1] (–)-Sparteine was distilled under N_2 from CaH_2 prior to first use.

Analytical thin layer chromatography was carried out on Merck silica gel plates with QF-254 indicator. The products were revealed with UV light or exposure to ceric ammonium molybdate (CAM). Flash chromatography was performed with 230-400 mesh silica gel (Merck) and petroleum ether and ethyl acetate as obtained directly from the bottles. Preparative HPLC was perfomed with a Dynamax 60A column coupled to a Rainin HPX pump system attached to a Rheodyne 7125 Syringe Loading Sample Injector and a Knauer UV detector (254 nm). Analytical chiral stationary phase HPLC was performed on a Rainin HPLX pump system coupled to a Rainin Dynamax Model UV-C Absorbance Detector. Either a 5 μm Rexchrom Reversible, covalent Pirkle (*S*, *S*)-Whelk-O column (Regis Chemical Co., Morton Grove, IL 60053-9975, 25 cm x 4.6 mm i.d.) or a ChiralPak AD column (Daicel Chemical Industries, Ltd., 25 cm x 4.6 mm i.d.) with isopropanol/hexane mobil phase was used to affect enantiomeric separations.

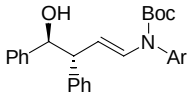
^1H and ^{13}C NMR spectra were obtained at the University of Illinois VOICE NMR Laboratory on either a Varian Unity 400 (400 MHz ^1H; 100 MHz ^{13}C) or a Varian Unity 500 (500 MHz ^1H; 126 MHz ^{13}C). Chemical shifts (δ) are reported in ppm relative to the solvent (acetone-d_6: 2.05 ppm, ^1H; 29.22, 205.7 ppm, ^{13}C; or chloroform-*d*: 7.26 ppm, ^1H; 77.23 ppm, ^{13}C). Peak multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), and br (broad). Coupling constants (*J*) are reported in hertz (Hz). Mass spectrometric data was acquired at the University of Illinois Mass Spectrometry Laboratory by electron ionization (EI) or fast atom bombardment (FAB)

[1] Suffert, J. *J. Org. Chem.* **1989**, *54*, 510.

technique. The purity of compounds was determined to be > 95 % by ^{13}C NMR when HRMS was used to determine elemental composition. Elemental analyses were carried out by the University of Illinois Microanalytical Service Laboratory. Melting points were acquired on a Thomas-Hoover melting point apparatus and are uncorrected. Optical rotations were obtained on a Perkin Elmer-341 digital polarimeter and are reported as $[\alpha]^{T}_{D}$ = ° (*c*, solvent) where T = temperature, and concentration, *c* = g/100mL.

Diastereomeric purity was determined by ^{1}H NMR integration or gas chromatographic analysis.

"Standard workup" refers to dilution with ether, addition of 2 M HCl, separation of phases, extraction of the aqueous layer with ether (3x), combination of the organic phases, drying with $MgSO_4$ and concentration by rotary evaporation.

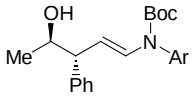


3

Representative Lithiation/Transmetalation/Substitution of *N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-phenyl-(*E*)-2-propene-1-amine (1): Preparation of (3*R*, 4*S*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3,4-diphenyl-4-hydroxy-(*E*)-1-butene-1-amine (3)

To a precooled (-78 °C) solution of (–)-sparteine (0.36 mL, 1.56 mmol) and *n*-BuLi (0.96 mL, 1.34 mmol) in toluene (10 mL) under N_2 was added precooled **1** (379 mg, 1.11 mmol) in toluene (5 mL, reaction concentration = 0.074 M) and the reaction mixture immediately turned bright yellow. After stirring the reaction mixture for 45 minutes, Et_2AlCl (0.74 mL, 1.34 mmol, 1.8 M solution in toluene) was added dropwise, whereupon the color of the reaction mixture faded to light yellow. After stirring for 45 minutes, PhCHO (0.23 mL, 2.23 mmol) was added dropwise. The mixture was stirred at –78 °C for 2 hr, and then quenched with MeOH (1 mL). Standard workup afforded the crude product as a yellow oil, which was purified by column chromatography (80:20 petroleum ether:EtOAc) to give the product as a white solid (402 mg, 85 %): m.p. = 51-54 °C. Careful separation of *E* and *Z* isomers was achieved by preparative HPLC with a solvent system of 90:10 petroleum ether:EtOAc. The enantiomeric ratio of **3** was

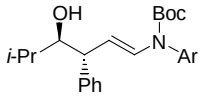
determined directly to be 97:3 by CSP-HPLC (ChiralPak AD column, 10 % *i*-PrOH/hexane, 0.7 mL/min). The major enantiomer (3*R*, 4*S*) had a retention time of 27.56 minutes while the retention time of the minor enantiomer (3*S*, 4*R*) was 22.61 minutes. ^{1}H NMR (acetone-d_6, 500 MHz) δ 1.33 (s, 9H, C(CH$_3$)$_3$), 3.58 (m, 1H, PhCHCH=CHN–), 3.84 (s, 3H, OCH$_3$), 4.10 (d, 1H, *J* = 4.0 Hz, OH), 4.81 (dd, 1H, *J* = 6.0, 4.0 Hz, CH–OH), 4.87 (dd, 1H, *J* = 14.3, 9.4 Hz, CH=CHN-), 7.10 (m, 15H, CH=CHN–, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 27.2, 54.7, 55.1, 77.0, 80.0, 109.9, 114.0, 125.7, 126.4, 126.6, 127.2, 127.7, 128.3, 129.6, 131.4, 131.7, 143.0, 144.0, 152.1, 158.6. Anal. Calcd for $C_{28}H_{31}NO_4$: C, 75.48 %; H, 7.01 %; N, 3.14 % Found: C, 75.46 %; H, 6.96 %; N, 2.87 %.



4

(3*R*, 4*R*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-phenyl-4-hydroxy-(*E*)-1-pentene-1-amine (4)

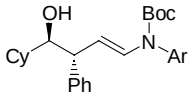
4 was obtained using acetaldehyde as the electrophile following a procedure similar to that reported for the preparation of **3**. The crude product was purified by column chromatography (80:20 petroleum ether:EtOAc) to afford **4** as a colorless oil in 66 % yield. The enantiomeric ratio of **4** was determined directly to be 92:8 by CSP-HPLC (ChiralPak AD column, 2.5 % i-PrOH/hexane, 1.0 mL/min). The major enantiomer (3*R*, 4*R*) had a retention time of 22.19 minutes while the retention time of the minor enantiomer (3*S*, 4*S*) was 35.28 minutes. ^{1}H NMR (acetone-d_6, 400 MHz) δ 0.97 (d, 3H, *J* = 6.3 Hz, CH$_3$), 1.36 (s, 9H, C(CH$_3$)$_3$), 3.18 (dd, 1H, *J* = 9.3, 7.1 Hz, PhCH), 3.42 (br-s, 1H, OH), 3.81 (s, 3H, OCH$_3$), 3.85 (t, 1H, *J* = 6.1 Hz, CH–OH), 4.80 (dd, 1H, *J* = 14.2, 9.0 Hz, CH=CHN–), 6.96-7.27 (m, 10 H, CH=CHN–, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 21.6, 27.7, 55.0, 55.4, 70.5, 80.4, 111.1, 114.4, 126.2, 128.3, 128.4, 129.9, 131.7, 132.1, 144.1, 152.5, 158.9. HRMS-FAB (M+1) Calcd for $C_{23}H_{30}NO_4$: 384.2175 Found, 384.2177.



5

(3*R*, 4*R*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-phenyl-4-hydroxy-5,5-dimethyl-(*E*)-1-pentene-1-amine (5)

5 was obtained using isobutyraldehyde as the electrophile following a procedure similar to that reported for the preparation of **3**. The crude product was purified by column chromatography (80:20 petroleum ether:EtOAc) to afford **5** as a colorless oil in 61 % yield. The enantiomeric ratio of **5** was determined directly to be 95:5 by CSP-HPLC (ChiralPak AD column, 2.5 % i-PrOH/hexane, 1.0 mL/min). The major enantiomer (3*R*, 4*R*) had a retention time of 9.03 minutes while the retention time of the minor enantiomer (3*S*, 4*S*) was 13.12 minutes. ^{1}H NMR (acetone-d_6, 400 MHz) δ 0.86 (d, 3H, J = 6.8 Hz, CH_3), 0.90 (d, 3H, J = 6.6 Hz, CH_3), 1.36 (s, 9H, $C(CH_3)_3$), 1.45 (m, 1H, C<u>H</u>$(CH_3)_2$), 3.26 (d, 1H, J = 4.9 Hz, OH), 3.43 (m, 2H, C<u>H</u>–OH, PhC<u>H</u>), 3.82 (s, 3H, OCH_3), 4.80 (dd, 1H, J = 14.2, 8.8 Hz, C<u>H</u>=CHN–), 6.96-7.27 (m, 10 H, CH=C<u>H</u>N–, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 15.7, 19.9, 27.6, 30.5, 51.1, 55.0, 78.8, 80.4, 111.4, 114.4, 126.1, 128.2, 128.5, 129.9, 131.5, 132.1, 144.4, 152.5, 158.9. Anal. Calcd for $C_{25}H_{33}NO_4$: C, 72.96 %; H, 8.08 %; N, 3.40 % Found: C, 73.16 %; H, 8.18 %; N, 3.20 %.

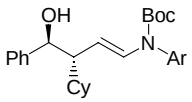


6

(3*R*, 4*R*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-phenyl-4-hydroxy-4-cyclohexyl-(*E*)-1-butene-1-amine (6)

6 was obtained using cyclohexanecarboxaldehyde as the electrophile following a procedure similar to that reported for the preparation of **3**. The crude product was purified by column chromatography (80:20 petroleum ether:EtOAc) to afford **6** as a colorless oil in 66 % yield. The enantiomeric ratio of **6** was determined directly to be 98:2 by CSP-HPLC (ChiralPak AD column, 2.5 % i-PrOH/hexane, 1.0 mL/min). The major enantiomer (3*R*, 4*R*) had a retention time of 12.31 minutes while the retention time

of the minor enantiomer (3*S*, 4*S*) was 19.87 minutes. ^{1}H NMR (acetone-d_6, 400 MHz) δ 0.80-1.86 (m, 11 H, CyH), 1.35 (s, 9H, C(CH_3)$_3$), 3.21 (d, 1H, *J* = 4.9 Hz, OH), 3.43 (m, 1H, PhCH), 3.47 (q, 1H, *J* = 6.8 Hz, C<u>H</u>–OH), 3.83 (s, 3H, OCH_3), 4.79 (dd, 1H, *J* = 14.2, 8.8 Hz, C<u>H</u>=CHN–), 6.87-7.43 (m, 10 H, CH=C<u>H</u>N–, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 26.2, 26.57, 26.62, 26.64, 27.65, 30.3, 40.5, 50.3, 55.0, 78.3, 80.4, 111.4, 114.4, 126.1, 128.2, 128.5, 129.9, 131.5, 132.2, 144.6, 152.5, 158.9. HRMS-FAB (M+1) Calcd for $C_{28}H_{38}NO_4$: 452.2801 Found, 452.2799.

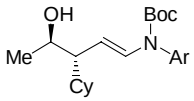


7

Representative Lithiation of *N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-cyclohexyl-(*E*)-2-propene-1-amine (2): Preparation of (3*S*, 4*S*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-cyclohexyl-4-hydroxy-4-phenyl-(*E*)-1-butene-1-amine (7)

To a precooled (-78 °C) solution of (–)-sparteine (0.35 mL, 1.51 mmol) and *n*-BuLi (0.93 mL, 1.29 mmol) in toluene (10 mL) under N_2 was added precooled **2** (373 mg, 1.08 mmol) in toluene (5 mL, reaction concentration = 0.072 M) and the reaction mixture turned bright yellow within 15 seconds. After stirring the reaction mixture for 1 hr, Et_2AlCl (0.72 mL, 1.29 mmol, 1.8 M solution in toluene) was added dropwise, whereupon the color of the reaction mixture faded to light yellow. After transmetalation for 45 minutes, PhCHO (0.22 mL, 2.16 mmol) was added dropwise. The mixture was stirred at –78 °C for 2 hr, and then quenched with MeOH (1 mL). Standard workup afforded the crude product as a yellow oil, which was purified by column chromatography (80:20 petroleum ether:EtOAc) to give **7** as a colorless oil (383 mg, 82 %). The enantiomeric ratio of **7** was determined directly to be 94:6 by CSP-HPLC ((*S*, *S*)-Whelk-O column, 20 % *i*-PrOH/hexane, 1.0 mL/min). The major enantiomer (3*S*, 4*S*) had a retention time of 7.42 minutes while the retention time of the minor enantiomer (3*R*, 4*R*) was 6.34 minutes. ^{1}H NMR (acetone-d_6, 500 MHz) δ 0.81-1.94 (m, 12H, CyH, CyC<u>H</u>), 1.32 (s, 9H, C(CH_3)$_3$), 3.80 (s, 3H, OCH_3), 3.83 (m, 1H, PhC<u>H</u>), 4.34 (dd, 1H, *J*

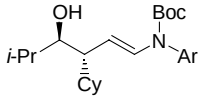
= 14.2, 10.3 Hz, CH=CHN–), 4.81 (m, 1H, OH), 6.67 (d, 1H, *J* = 14.6 Hz, CH=CHN–), 7.00-7.25 (m, 9H, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 27.2, 27.3, 28.2, 29.4, 30.3, 31.4, 38.4, 54.6, 55.1, 73.0, 79.8, 108.7, 113.9, 126.2, 126.3, 127.4, 129.6, 131.2, 132.0, 145.4, 152.0, 158.5. HRMS-FAB (M+1) Calcd for $C_{28}H_{38}NO_4$: 452.2801 Found, 452.2803.



8

(3*S*, 4*R*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-cyclohexyl-4-hydroxy-(*E*)-1-pentene-1-amine (8)

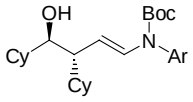
8 was obtained using acetaldehyde as the electrophile following a procedure similar to that reported for the preparation of **7**. The crude product was purified by column chromatography (80:20 petroleum ether:EtOAc) to afford **8** as a colorless oil in 72 % yield. The enantiomeric ratio of **8** was determined directly to be 93:7 by CSP-HPLC (ChiralPak AD column, 10 % i-PrOH/hexane, 0.7 mL/min). The major enantiomer (3*S*, 4*R*) had a retention time of 7.60 minutes while the retention time of the minor enantiomer (3*R*, 4*S*) was 8.40 minutes. ^{1}H NMR (acetone-d_6, 500 MHz) δ 0.85-1.62 (m, 11H, CyH), 1.03 (d, 3H, *J* = 6.2 Hz, CH_3), 1.36 (s, 9H, $C(CH_3)_3$), 1.80 (m, 1H, CyCH), 3.04 (d, 1H, *J* = 4.4 Hz, OH), 3.81 (s, 3H, OCH_3), 3.87 (m, 1H, CHOH), 4.33 (dd, 1H, *J* = 14.3, 10.2 Hz, CH=CHN–), 6.97 (m, 3H, ArH, CH=CHN–), 7.09 (d, 2H, *J* = 9.0 Hz, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 21.8, 26.2, 26.4, 27.3, 27.3, 30.7, 31.3, 38.3, 54.0, 54.6, 65.7, 79.8, 109.3, 114.0, 129.5, 131.0, 132.1, 152.2, 158.4. Anal. Calcd for $C_{23}H_{35}NO_4$: C, 70.92 %; H, 9.06 %; N, 3.60 % Found: C, 70.76 %; H, 9.01 %; N, 3.60 %.



9

(3*S*, 4*R*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-cyclohexyl-4-hydroxy-5,5-dimethyl-(*E*)-1-pentene-1-amine (9)

9 was obtained using isobutyraldehyde as the electrophile following a procedure similar to that reported for the preparation of **7**. The crude product was purified by column chromatography (80:20 petroleum ether:EtOAc) to afford **9** as a colorless oil in 81 % yield. The enantiomeric ratio of **9** was determined directly to be 94:6 by CSP-HPLC (ChiralPak AD column, 5 % i-PrOH/hexane, 0.7 mL/min). The major enantiomer (3*S*, 4*R*) had a retention time of 7.40 minutes while the retention time of the minor enantiomer (3*R*, 4*S*) was 8.03 minutes. ^{1}H NMR (acetone-d_6, 500 MHz) δ 0.82 (d, 3H, *J* = 6.6 Hz, CH_3), 0.86-1.67 (m, 11H, CyH), 0.90 (d, 3H, *J* = 6.6 Hz, CH_3), 1.36 (s, 9H, $C(CH_3)_3$), 1.83 (m, 2H, CyC<u>H</u>, $(CH_3)_2C\underline{H}$), 3.08 (d, 1H, *J* = 5.7 Hz, OH), 3.22 (m, 1H, C<u>H</u>OH), 3.81 (s, 3H, OCH_3), 4.37 (dd, 1H, *J* = 14.5, 10.4 Hz, C<u>H</u>=CHN–), 6.96 (d, 2H, *J* = 9.0 Hz, ArH), 7.00 (d, 1H, *J* = 14.5 Hz, CH=C<u>H</u>N–), 7.08 (d, 2H, *J* = 9.0 Hz, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 19.2, 19.9, 26.3, 26.4, 26.6, 28.1, 31.1, 31.45, 31.54, 37.8, 49.3, 55.4, 74.8, 80.4, 110.5, 114.6, 129.7, 129.9, 131.9, 152.3, 158.2. Anal. Calcd for $C_{25}H_{39}NO_4$: C, 71.81 %; H, 9.41 %; N, 3.35 % Found: C, 71.60 %; H, 9.10 %; N, 3.54 %.

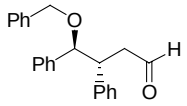


10

(3*S*, 4*R*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-cyclohexyl-4-hydroxy-5-cyclohexyl-(*E*)-1-butene-1-amine (10)

10 was obtained using cyclohexanecarboxaldehyde as the electrophile following a procedure similar to that reported for the preparation of **7**. The crude product was purified by column chromatography (80:20 petroleum ether:EtOAc) to afford **10** as a colorless oil in 84 % yield. The enantiomeric ratio of **10** was determined directly to be 95:5 by CSP-HPLC (ChiralPak AD column, 2.5 % i-PrOH/hexane, 1.0 mL/min). The major enantiomer (3*S*, 4*R*) had a retention time of 8.92 minutes while the retention time of the minor enantiomer (3*R*, 4*S*) was 11.11 minutes. ^{1}H NMR (acetone-d_6, 400 MHz) δ 0.74-2.13 (m, 23 H, CyH, Cy–C<u>H</u>CH=CHN–), 1.38 (s, 9H, $C(C\underline{H}_3)_3$), 3.03 (d, 1H, *J* =

5.7 Hz, OH), 3.30 (m, 1H, C<u>H</u>–OH), 3.82 (s, 3H, OCH_3), 4.39 (dd, 1H, *J* = 14.4, 10.3 Hz, C<u>H</u>=CHN–), 6.94-7.11 (m, 5 H, CH=C<u>H</u>N–, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 26.2, 26.3, 26.36, 26.40, 26.58, 26.64, 26.76, 26.79, 27.7, 31.4, 31.6, 38.3, 41.2, 49.3, 55.0, 74.3, 80.2, 110.3, 114.3, 129.8, 131.0, 132.6, 152.6, 158.7. HRMS-FAB (M+1) Calcd for $C_{28}H_{44}NO_4$: 458.3270 Found, 458.3268.



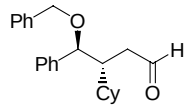
11

Representative *O*-Protection and Hydrolysis of Homoaldol Precursors: Preparation of (3*R*, 4*S*)-3,4-diphenyl-4-benzoxy-butan-1-al (11)

To a stirred solution of **3** (90 mg, 0.202 mmol) in DMF (3 mL, 0.070 M) under N_2 at 0 °C was added NaH (34 mg, 0.839 mmol, 60 % dispersion in mineral oil). The light yellow solution was stirred for 30 minutes, whereupon benzyl bromide (0.10 mL, 0.839 mmol) was added. The mixture was warmed to rt, stirred for 2 hr, and then quenched with MeOH (1 mL). The solution was diluted with ether and poured into H_2O. The layers were separated and the aqueous layer was extracted with ether (3 x 25 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to provide the crude *O*-protected enecarbamate product as a yellow oil. ^{1}H NMR (acetone-d_6, 400 MHz) δ 1.34 (s, 9H, $C(CH_3)_3$), 3.67 (t, 1H, *J* = 8.3 Hz, PhC<u>H</u>CH=C–), 3.85 (s, 3H, OCH_3), 4.27 (AB, 2H, *J* = 12.2 Hz; ν_a = 4.36 ppm; ν_b = 4.18 ppm, PhC<u>H</u>$_2$), 4.56 (d, 1H, *J* = 5.4 Hz, PhC<u>H</u>OCH_2–), 4.95 (dd, 1H, *J* = 14.2, 8.5 Hz, C<u>H</u>=CHN–), 6.99-7.41 (m, 20H, ArH, CH=C<u>H</u>N–). The crude product was used in the next step without further purification.

The crude *O*-protected enecarbamate was dissolved in $CHCl_3$ (5 mL). HCl (6 M, 4 mL) was added and the reaction mixture was stirred for 2 hr. The solution was poured into 10 % $NaHCO_3$ (50 mL), and the organic layer was removed. The aqueous layer was washed with CH_2Cl_2 (3 x 25 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to provide the crude product as a yellow oil. The crude product was purified by column chromatography (85:15 petroleum ether:EtOAc) to give the pure **11** as a colorless oil (39 mg, 59 % over two steps). $[\alpha]^{20}_D$ = -16.6 (*c* = 4.13

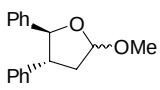
in $CHCl_3$) for a sample with *anti*:*syn* = 81:19. ^{1}H NMR (acetone-d_6, 400 MHz) δ 2.81 (m, 1H, C$\underline{H}_2$CHO), 3.13 (m, 1H, C$\underline{H}_2$CHO), 3.68 (q, 1H, *J* = 6.6 Hz, PhC$\underline{H}$CH$_2$), 4.33 (AB, 2H, *J* = 11.5 Hz; ν_a = 4.37 ppm; ν_b = 4.28 ppm, PhC$\underline{H}_2$), 4.58 (d, 1H, *J* = 8.54 Hz, PhC$\underline{H}$OCH$_2$), 7.09-7.34 (m, 15H, ArH), 9.69 (t, 1H, *J* = 2.2 Hz, C$\underline{H}$O). ^{13}C NMR (acetone-d_6, 100 MHz) δ 46.8, 48.1, 70.6, 85.5, 126.7, 127.6, 127.75, 127.78, 127.9, 128.2, 128.3, 128.4, 128.8, 138.6, 140.3, 141.3, 201.0. HRMS-FAB (M+1) Calcd for $C_{23}H_{23}O_2$: 331.1698 Found, 331.1698.



12

(3*R*, 4*S*)-3-cyclohexyl-4-benzoxy-4-phenyl-butan-1-al (12)

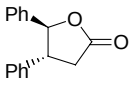
12 was obtained using **7** as the substrate following a procedure similar to that reported for the preparation of **11**. The crude product was purified by column chromatography (85:15 petroleum ether:EtOAc) to afford **12** as a colorless oil in 64 % yield (over two steps). $[\alpha]^{20}_D$ = -38.9 (*c* = 2.64 in $CHCl_3$). Crude *O*-protected enecarbamate: ^{1}H NMR (acetone-d_6, 400 MHz) δ 0.75-1.66 (m, 11H, CyH), 1.33 (s, 9H, C(CH$_3$)$_3$), 2.05 (m, 1H, CyC$\underline{H}$), 3.85 (s, 3H, OCH$_3$), 4.27 (AB, 2H, *J* = 12.2 Hz; ν_a = 4.37 ppm; ν_b = 4.18 ppm, PhC$\underline{H}_2$), 4.38 (dd, 1H, *J* = 14.4, 10.5 Hz, C$\underline{H}$=CHN–), 4.52 (d, 1H, *J* = 4.9 Hz, PhC$\underline{H}$O–), 7.21-7.40 (m, 15H, ArH, CH=C$\underline{H}$N–). Aldehyde **12**: ^{1}H NMR (acetone-d_6, 400 MHz) δ 0.91-1.70 (m, 11H, CyH), 2.32 (m, 1H, Cy–C$\underline{H}$), 2.44 (m, 1H, C$\underline{H}_2$CHO), 4.23 (AB, 2H, *J* = 11.7 Hz; ν_a = 4.32 ppm; ν_b = 4.23 ppm, PhC$\underline{H}_2$), 4.21 (d, 1H, *J* = 8.30 Hz, PhC$\underline{H}$OCH$_2$), 7.24-7.42 (m, 10H, ArH), 9.70 (dd, 1H, *J* = 2.9, 1.5 Hz, C$\underline{H}$O). ^{13}C NMR (acetone-d_6, 100 MHz) δ 26.4, 26.5, 26.7, 28.3, 31.7, 38.4, 42.2, 46.6, 70.4, 83.1, 127.6, 127.7, 128.0, 128.1, 128.4, 128.7, 138.6, 141.3, 201.7. HRMS-FAB (M-1) Calcd for $C_{23}H_{27}O_2$: 335.2011 Found, 335.2008.



13

Representative Hydrolysis of Homoaldol Precursors: Preparation of 2-Methoxy-(4*R*, 5*S*)-diphenyltetrahydrofuran (13)

To a stirred solution of **3** (170 mg, 0.382 mmol) in MeOH (5 mL, 0.076 M) at r.t. was added methanesulfonic acid (25 μL, 0.380 mmol). The reaction was allowed to stir overnight and was then poured into a mixture of KOH (25 mL) and brine (25 mL). The white, cloudy solution was extracted with ether (3 x 25 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to give a light yellow oil. The oil was purified by column chromatography (80:20 petroleum ether:EtOAc) to give two diastereomers of **13** (45 %, 42 mg). The less retained diastereomer was obtained as a clear oil and was characterized spectroscopically: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.03-2.11, 2.79-2.86 (m, 2H, CH_2), 3.18 (q, 1H, *J* = 9.6 Hz, CHC<u>H</u>CH_2), 3.42 (s, 3H, CH_3), 4.91 (d, 1H, *J* = 9.5 Hz, C<u>H</u>CHCH_2), 5.31 (dd, 1H, *J* = 5.4, 2.7 Hz, C<u>H</u>OMe), 7.18-7.31 (m, 10H, ArH). ^{13}C NMR (acetone-d_6, 126 MHz) δ 42.5, 53.8, 54.5, 85.9, 105.0, 126.5, 126.7, 126.8, 127.8, 128.2, 128.7, 140.6, 141.0. The more retained diastereomer was obtained as a white solid and was also characterized: m.p. = 95-97 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.29-2.45 (m, 2H, CH_2), 3.43 (m, 1H, CHC<u>H</u>CH_2), 3.46 (s, 3H, CH_3), 4.95 (d, 1H, *J* = 9.8 Hz, C<u>H</u>CHCH_2), 5.18 (d, 1H, *J* = 4.8 Hz, C<u>H</u>OMe), 7.18-7.30 (m, 10H, ArH). ^{13}C NMR (acetone-d_6, 126 MHz) δ 42.1, 52.4, 54.2, 89.0, 104.9, 126.8, 127.0, 127.6, 128.0, 128.3, 128.7, 139.8, 142.4. HRMS-EI (M+) Calcd for $C_{17}H_{18}O_2$: 254.1307 Found, 254.1303.

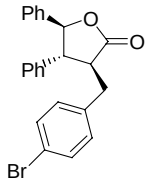


14

Representative Oxidation of Methanolysis Products: Preparation of (4*R*, 5*S*)-Diphenylbutyrolactone (14)

To a stirring solution of **13** (38 mg, 0.150 mmol) in CH_2Cl_2 (10 mL, 0.015 M) was added *m*-CPBA (78 mg, 0.45 mmol) and BF_3•OEt_2 (5.5 μL, 0.045 mmol). The cloudy reaction mixture was allowed to stir overnight and was then poured into $NaHSO_3$ (aq.) (50 mL). The organic layer was removed and the aqueous layer washed with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with $NaHCO_3$ (aq.),

dried over $MgSO_4$, filtered and concentrated to afford the crude light yellow oil. The oil was purified by column chromatography (90:10 petroleum ether:EtOAc) to give the white solid **14** in 83 % (30 mg) yield: m.p. = 105-107 °C. $[\alpha]^{20}_D$ = +102.4 (*c* = 3.86 in $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.01 (dd, 2H, *J* = 10.7, 4.5 Hz, CH_2), 3.77 (q, 1H, *J* = 9.1 Hz, C<u>H</u>CH_2), 3.51 (d, 1H, *J* = 9.5 Hz, O–CH), 7.24-7.37 (m, 10H, ArH). ^{13}C NMR (acetone-d_6, 126 MHz) δ 37.0, 50.4, 86.7, 126.3, 127.3, 127.6, 128.3, 128.4, 128.6, 138.0, 138.1, 174.3. HRMS-EI (M+) Calcd for $C_{16}H_{14}O_2$: 238.0993 Found, 238.0988.

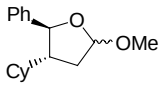


15

(3*S*, 4*R*, 5*S*)-3-(*p*-Bromobenzyl)-4,5-diphenylbutyrolactone (15)

To a stirred solution of potassium bis(trimethylsilyl) amide (KHMDS, 0.13 mL, 0.180 mmol) in THF (2 mL, 0.09 M) at –78 °C under N_2 was added a solution of **14** (23 mg, 0.097 mmol) in THF (3 mL, 0.032 M). The mixture was allowed to stir for 1 hr, whereupon *p*-bromobenzyl bromide (36 mg, 0.144 mmol) in THF (3 mL, 0.072 M) was added. The resulting solution was stirred for 2 hr and NH_4Cl (aq., 1 mL) was added. The solvent was removed *in vacuo* and the residue was taken up into ether and poured over 25 mL H_2O. The organic layers were combined and dried over $MgSO_4$, filtered, and concentrated to afford the crude light yellow oil. The oil was purified by column chromatography (90:10 petroleum ether:EtOAc) to give the white solid **15** in 12 % (6 mg) yield: m.p. = 122-124 °C. Crystals suitable for X-ray analysis were grown by vapor diffusion from ether/pentane. The enantiomeric ratio of **15** was determined directly to be 88:12 by CSP-HPLC ((*S*, *S*)-Whelk-O column, 2 % *i*-PrOH/hexane, 1.5 mL/min). The major enantiomer (3*S*, 4*R*, 5*S*) had a retention time of 51.0 minutes while the retention time of the minor enantiomer (3*R*, 4*S*, 5*R*) was 32.1 minutes. The supernatant was enriched in the minor enantiomer (e.r. = 80:20). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.94 (dd, 1H, *J* = 5.8, 9.0 Hz, C<u>H</u>C<u>H</u>CH_2), 3.13 (m, 2H, CH_2), 3.58 (m, 1H, C<u>H</u>CH_2), 6.27 (d, 1H, *J* = 9.6 Hz, O–CH), 6.94-7.34 (m, 10H, ArH). ^{13}C NMR (acetone-d_6, 126 MHz) δ 33.4, 49.2, 56.3, 85.2, 120.0, 126.5, 127.6, 128.5, 128.6, 128.8, 128.9, 131.3, 131.8, 136.9,

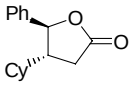
137.6, 137.9, 175.9. HRMS-EI (M+) Calcd for $C_{23}H_{19}O_2Br$: 406.0568 Found, 406.0566.



16

2-Methoxy-(4*R*, 5*S*)-4-cyclohexyl-5-phenyl-tetrahydrofuran (16)

16 was obtained using **7** as the substrate following a procedure similar to that reported for the preparation of **13**. The crude product was purified by column chromatography (85:15 petroleum ether:EtOAc) to afford colorless oil **16** as a equal mixture of two diastereomers in 73 % yield. The less retained diastereomer was obtained as a clear oil and was characterized spectroscopically: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.71-1.84 (m, 11H, CyH), 1.95-2.04 (m, 2H, CH_2), 2.33-2.41 (m, 1H, CyC<u>H</u>), 3.39 (s, 3H, CH_3), 4.74 (d, 1H, *J* = 8.9 Hz, PhC<u>H</u>), 5.16 (dd, 1H, *J* = 5.6, 2.7 Hz, C<u>H</u>OMe), 7.23-7.38 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.4, 26.5, 26.7, 30.6, 32.8, 37.0, 39.6, 52.4, 55.4, 82.8, 105.2, 127.6, 128.0, 128.6, 141.8. The more retained diastereomer was obtained as a colorless oil and was also characterized: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.69-1.74 (m, 11H, CyH), 1.81-1.89 (m, 1H, CyC<u>H</u>), 2.15 (dd, 1H, *J* = 12.5, 6.6 Hz, CH_2), 2.34 (m, 1H, CH_2), 3.39 (s, 3H, CH_3), 4.70 (d, 1H, *J* = 9.0 Hz, PhC<u>H</u>), 5.01 (d, 1H, *J* = 4.9 Hz, C<u>H</u>OMe), 7.25-7.41 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.5, 26.6, 30.8, 32.8, 38.0, 40.2, 50.9, 54.9, 86.9, 105.1, 127.7, 128.1, 128.6, 143.4. HRMS-EI (M+) Calcd for $C_{17}H_{24}O_2$: 260.1776 Found, 260.1777.

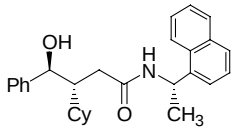


17

(4*R*, 5*S*)-4-Cyclohexyl-5-phenyl-butyrolactone (17)

17 was obtained using **16** as the substrate following a procedure similar to that reported for the preparation of **14**. The crude product was purified by column chromatography (85:15 petroleum ether:EtOAc) to afford colorless oil **17** in 79 % yield. $[\alpha]^{20}_D$ = +23.4° (*c* = 5.95 in $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.85-1.81 (m, 11H,

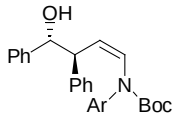
CyH), 2.40 (m, 1H, CyC<u>H</u>), 2.42-2.49, 2.68-2.73 (m, 2H, CH_2), 5.25 (d, *J* = 6.6 Hz, PhC<u>H</u>), 7.31-7.41 (m, 5H, ArH). ^{13}C NMR (acetone-d_6, 126 MHz) δ 26.2, 26.3, 26.4, 29.9, 31.5, 32.4, 40.1, 49.5, 84.8, 126.5, 128.8, 129.0, 139.7, 176.8. HRMS-EI (M+) Calcd for $C_{16}H_{20}O_2$: 244.1463 Found, 244.1467.



18

(3*R*, 4*S*, 1'*S*)-3-Cyclohexyl-4-hydroxy-*N*-(1-naphthalen-1-yl-ethyl)-4-phenyl-butyramide (18)

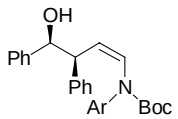
To (*S*)-(–)-1-(1-naphthyl)-ethylamine (55 μL, 0.342 mmol) in CH_2Cl_2 (1.5 mL) under N_2 was added Me_3Al (0.17 mL, 0.342 mmol, 2 M solution in toluene). The mixture was stirred for 30 minutes and a solution of **17** in CH_2Cl_2 (2 mL) was added dropwise. The reaction was warmed to 40 °C, stirred for 2 days, cooled to rt, and 2 M HCl (~ 4 mL) was slowly added. The organic layer was removed and the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give the crude product as a yellow oil. The crude product was purified by column chromatography to provide the white solid **18** as a single diastereomer (61 mg, 41 %): m.p. = 120-124 °C. Crystals suitable for X-ray crystallography were grown by recrystallization from hexane/MeOH. ^{1}H NMR (acetone-d_6, 400 MHz) δ 0.91-1.98 (m, 12H, CyH, CyC<u>H</u>), 1.64 (d, 3H, *J* = 6.9 Hz, CH_3), 2.20 (dd, 1H, *J* = 15.8, 3.4 Hz, CH_2), 2.42 (dd, 1H, *J* = 15.9, 6.0 Hz, CH_2), 4.85 (m, 1H, PhC<u>H</u>), 5.90 (qn, 1H, *J* = 7.3 Hz, C<u>H</u>CH_3), 6.16 (d, 1H, *J* = 7.7 Hz, OH), 7.21-7.58 (m, 10H, ArH), 7.81 (d, 1H, *J* = 7.9 Hz, ArH), 7.89 (d, 1H, *J* = 7.5 Hz, NH), 8.09 (d, 1H, *J* = 8.4 Hz, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 20.7, 26.2, 26.4, 26.6, 27.7, 29.9, 30.6, 31.3, 34.0, 37.1, 45.7, 48.8, 73.5, 122.8, 123.4, 125.5, 126.9, 127.1, 128.5, 128.7, 129.1, 131.2, 134.2, 138.0, 144.9, 173.5. HRMS-FAB (M+1) Calcd for $C_{28}H_{34}NO_2$: 416.2590 Found, 416.2591.



22

(3*S*, 4*R*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3,4-diphenyl-4-hydroxy-(*Z*)-1-butene-1-amine (22)

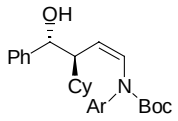
22 was obtained using TiCl(O*i*-Pr)$_3$ as transmetalating agent following a procedure similar to that reported for the preparation of **3**. All experimental observations are as reported for the preparation of **3**, except the reaction mixture turns black upon addition of TiCl(O*i*-Pr)$_3$. **Note**: Care should be taken to add at least 1.1 eq. of TiCl(O*i*-Pr)$_3$, as *anti*:*syn* ratios of the product may be low if a deficient amount of transmetalating reagent is used. The crude product was purified by column chromatography (80:20 petroleum ether:EtOAc) to afford **4** as a colorless oil in 52 % yield with *anti*:*syn* = 86:14. Following is the NMR data for the major *anti* diastereomer. The NMR data for the *syn* diastereomer is reported for **23**. The enantiomeric ratio of the major *anti* diastereomer of **22** was determined directly to be 98:2 by CSP-HPLC (ChiralPak AD column, 10 % i-PrOH/hexane, 0.7 mL/min). The major enantiomer (3*S*, 4*R*) had a retention time of 18.56 minutes while the retention time of the minor enantiomer (3*R*, 4*S*) was 17.40 minutes. The enantiomeric ratio of the minor *syn* diastereomer of **22** was determined directly to be > 99:1 by CSP-HPLC (ChiralPak AD column, 10 % i-PrOH/hexane, 0.7 mL/min). The major enantiomer had a retention time of 20.42 minutes while the minor enantiomer was not detected. ^{1}H NMR (acetone- d_6, 400 MHz) δ 1.33 (s, 9H, C(CH$_3$)$_3$), 3.30 (m, 1H, PhC<u>H</u>CH=CHN–), 3.83 (s, 3H, OCH$_3$), 4.03 (d, 1H, *J* = 4.4 Hz, OH), 4.69 (dd, 1H, *J* = 6.3, 4.2 Hz, PhC<u>H</u>OH), 5.30 (dd, 1H, *J* = 10.5, 1.2 Hz, <u>H</u>C=CHN–), 6.50 (d, 1H, 9.0 Hz, HC=C<u>H</u>N–), 6.78-7.21 (m, 14H, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 27.2, 49.6, 54.7, 76.6, 80.0, 113.7, 116.8, 125.6, 126.5, 126.6, 127.1, 127.2, 127.4, 128.5, 128.8, 134.6, 140.9, 143.6, 152.8, 157.8. HRMS-FAB (M+1) Calcd for $C_{28}H_{32}NO_4$: 446.2331 Found, 446.2335.



23

***N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3,4-*syn*-diphenyl-4-hydroxy-(*Z*)-1-butene-1-amine (23)**

23 was obtained using Ti(O*i*-Pr)$_4$ as transmetalating agent and MTBE as solvent following a procedure similar to that reported for the preparation of **3**. The crude product was purified by column chromatography (80:20 petroleum ether:EtOAc) to afford **23** as a colorless oil in 63 % yield. Compound **23** is spectroscopically identical to **22**, except that the ratio *anti*:*syn* = 46:54. The enantiomeric ratio of the major *syn* diastereomer of **23** was determined directly to be 95:5 by CSP-HPLC (ChiralPak AD column, 10 % i-PrOH/hexane, 0.7 mL/min). The major enantiomer (unassigned) had a retention time of 21.19 minutes while the retention time of the minor enantiomer (unassigned) was 26.29 minutes. The enantiomeric ratio of the minor *anti* diastereomer of **23** was determined directly to be 83:17 by CSP-HPLC (ChiralPak AD column, 10 % i-PrOH/hexane, 0.7 mL/min). The major enantiomer (3*S*, 4*R*) had a retention time of 19.23 minutes while the minor enantiomer (3*R*, 4*S*) had a retention time of 17.97 minutes. The NMR data for the *anti* diastereomer is reported for **22**. Following is the NMR data for the major *syn* diastereomer. ^{1}H NMR (acetone- d_6, 400 MHz) δ 1.34 (s, 9H, C(CH$_3$)$_3$), 3.28 (m, 1H, PhCHCH=CHN–), 3.80 (s, 3H, OCH$_3$), 4.19 (d, 1H, J = 3.9 Hz, OH), 4.64 (t, 1H, J = 5.0 Hz, PhCHOH), 5.44 (t, 1H, J = 9.9 Hz, HC=CHN–), 6.62 (d, 1H, 9.3 Hz, HC=CHN–), 6.78-7.21 (m, 14H, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 27.2, 50.0, 54.8, 77.3, 80.1, 113.5, 116.8, 125.7, 126.45, 126.49, 127.2, 127.3, 127.4, 128.3, 128.8, 134.2, 141.8, 143.8, 152.9, 157.8.

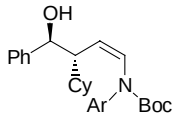


24

(3*R*, 4*R*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-cyclohexyl-4-hydroxy-4-phenyl-(*Z*)-1-butene-1-amine (24)

24 was obtained using TiCl(O*i*-Pr)$_3$ as transmetalating agent following a procedure similar to that reported for the preparation of **7**. All experimental observations are as reported for the preparation of **7**, except the reaction mixture turns black upon addition of TiCl(O*i*-Pr)$_3$. The crude product was purified by column chromatography

(80:20 petroleum ether:EtOAc) to afford **24** as a colorless oil in 38 % yield. The enantiomeric ratio of **24** was determined directly to be 94:6 by CSP-HPLC ((*S, S*)-Whelk-O column, 30 % i-PrOH/hexane, 1.0 mL/min). The major enantiomer (3*R*, 4*R*) had a retention time of 6.41 minutes while the retention time of the minor enantiomer (3*S*, 4*S*) was 9.08 minutes. ^{1}H NMR (acetone- d_6, 400 MHz) δ 0.82-1.73 (m, 11H, CyH), 1.39 (s, 9H, $C(CH_3)_3$), 1.93 (m, 1H, CyC<u>H</u>), 3.80 (s, 3H, OCH_3), 3.78 (m, 1H, PhC<u>H</u>), 4.59 (d, 1H, *J* = 5.4 Hz, OH), 5.07 (dd, 1H, *J* = 11.0, 9.3 Hz, C<u>H</u>=CHN–), 6.65 (d, 1H, *J* = 9.3 Hz, CH=C<u>H</u>N–), 6.74-7.23 (m, 9H, ArH). ^{13}C NMR (acetone-d_6, 100 MHz) δ 26.4, 26.5, 26.6, 27.5, 31.5, 39.4, 48.7, 54.9, 73.2, 80.0, 113.6, 126.6, 126.7, 127.6, 128.6, 129.9, 134.6, 145.2, 153.2, 157.7. HRMS-FAB (M+1) $C_{28}H_{38}NO_4$: 452.2801 Found, 452.2800.



ent-24

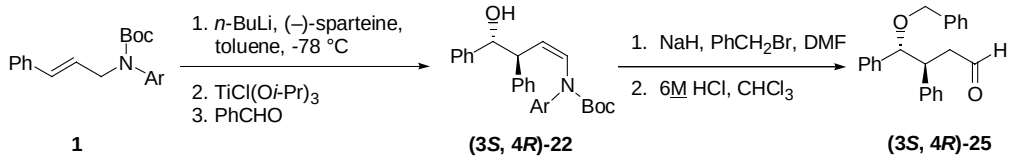
(3*S*, 4*S*)-*N*-(*t*-Butoxycarbonyl)-*N*-(4-methoxyphenyl)-3-cyclohexyl-4-hydroxy-4-phenyl-(*Z*)-1-butene-1-amine (ent-24)

ent-24 was obtained using Ti(O*i*-Pr)$_4$ as transmetalating agent and MTBE as solvent following a procedure similar to that reported for the preparation of **7**. The crude product was purified by column chromatography (80:20 petroleum ether:EtOAc) to afford **ent-24** as a colorless oil in 69 % yield. The enantiomeric ratio of **ent-24** was determined directly to be 86:14 by CSP-HPLC ((*S, S*)-Whelk-O column, 30 % i-PrOH/hexane, 1.0 mL/min). The major enantiomer (3*S*, 4*S*) had a retention time of 8.40 minutes while the retention time of the minor enantiomer (3*R*, 4*R*) was 6.22 minutes. Compound **ent-24** is spectroscopically identical to **24**.

Determination of Absolute Configuration of Products Obtained by Transmetalation with TiCl(O*i*-Pr)$_3$ or Ti(O*i*-Pr)$_4$ and Subsequent Reaction with PhCHO (Table 2).

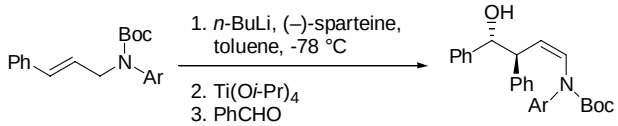
Products **22-24** were *O*-protected with NaH/benzylbromide and hydrolyzed to the corresponding aldehydes **25-27**, as reported for the preparation of **11** and **12**.

Comparison of optical rotations was made with (3*R*, 4*S*)-**11** $[\alpha]^{20}_{D}$ = -16.6 (*c* = 4.13 in $CHCl_3$) and (3*R*, 4*S*)-**12** $[\alpha]^{20}_{D}$ = -38.9 (*c* = 2.64 in $CHCl_3$) for a sample with *anti*:*syn* = 81:19. The absolute configurations of **11** and **12** were determined by X-ray crystal analysis of derivatives **15** and **18**, respectively.



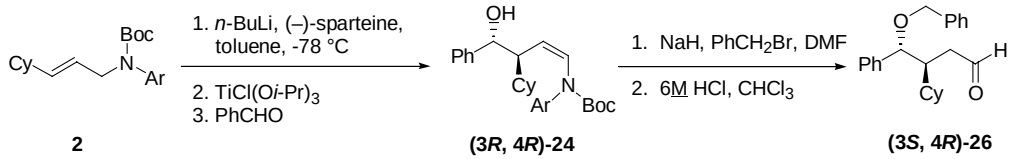
1 **(3*S*, 4*R*)-22** **(3*S*, 4*R*)-25**

Compound **25**, obtained after lithiation, TiCl(O*i*-Pr)$_3$ transmetalation, reaction with PhCHO, *O*-protection, and hydrolysis of **1,** was spectroscopically identical to **11**. The *O*-protection of **22** must be carried out below 0 °C (not warmed to rt) to prevent cleavage of **22** to provide **1**. For **11**, $[\alpha]^{20}_{D}$ = -16.6 (*c* = 4.13 in $CHCl_3$). For **25**, $[\alpha]^{20}_{D}$ = +14.0 (*c* = 2.23 in $CHCl_3$), indicating the opposite absolute configuration for **25**, or (3*S*, 4*R*).



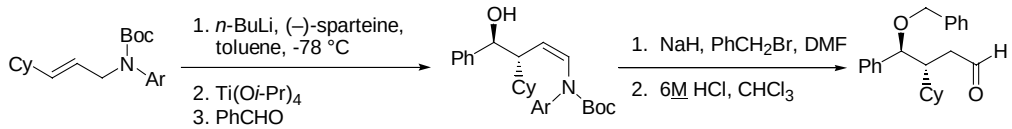
1 ***anti*-(3*S*, 4*R*)-23**

The absolute configuration of the major enantiomer of the *anti* diastereomer of **23** was determined by comparison of the chiral HPLC trace of **23** with (3*S*, 4*R*)-**22**. The major enantiomer of the *anti* diastereomer of **23** (major enantiomer retention time = 19.23 minutes; minor enantiomer = 17.97 minutes) is the same as that reported for **22** (major enantiomer retention time = 18.56 minutes; minor enantiomer = 17.40 minutes), indicating the major enantiomer of the *anti* diastereomer of **23** to have the (3*S*, 4*R*) configuration. The absolute configurations of the enantiomers of the *syn* diastereomer remain unassigned.



2 **(3*R*, 4*R*)-24** **(3*S*, 4*R*)-26**

Compound **26**, obtained after lithiation, TiCl(O*i*-Pr)$_3$ transmetalation, reaction with PhCHO, *O*-protection, and hydrolysis of **2,** was spectroscopically identical to **12**. For **12**, $[\alpha]^{20}_D$ = -38.9 (*c* = 2.64 in $CHCl_3$). For **26**, $[\alpha]^{20}_D$ = +55.9 (*c* = 0.98 in $CHCl_3$), indicating the opposite absolute configuration for **26**, or (3*S*, 4*R*).



2 **(3*S*, 4*S*)-24** **(3*R*, 4*S*)-27**

Compound **27**, obtained by lithiation, Ti(O*i*-Pr)$_4$ transmetalation, reaction with PhCHO, *O*-protection, and hydrolysis of **2,** was spectroscopically identical to **12**. For **12**, $[\alpha]^{20}_D$ = -38.9 (*c* = 2.64 in $CHCl_3$). For **27**, $[\alpha]^{20}_D$ = -40.0 (*c* = 2.31 in $CHCl_3$), indicating the same absolute configuration for **27**, or (3*R*, 4*S*).