STEREOSELECTIVE SYNTHESIS OF OPTICALLY ACTIVE DIETHANOLAMINES UTILIZING DIASTEREOSELECTIVE REACTION OF 1,3-OXAZOLIDINES WITH GRIGNARD REAGENTS

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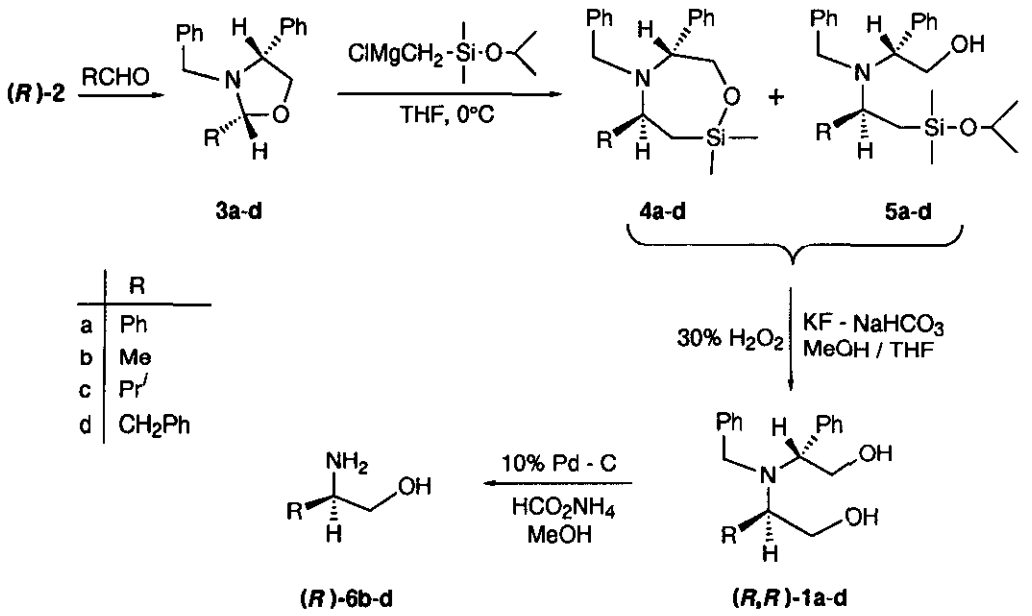
Abstract — The highly diastereoselective addition of isopropoxydimethylsilylmethylmagnesium chloride to *N*-benzyl-1,3-oxazolidines derived from (*R*)-phenylglycinol, followed by oxidation of adducts with hydrogen peroxide in the presence of potassium fluoride, provided the 1-substituted (1*R*,1'*R*)-*N*-benzyl-1'-phenyl-2,2'-dihydroxydiethylamines (**1a-d**).

Chiral 1,3-oxazolidines, readily synthesized by condensing (*S*)- or (*R*)-*N*-alkyl-2-hydroxyethanolamines such as (*S*)-*N*-alkylvalinol or (*R*)-*N*-alkylphenylglycinol with carbaldehydes,[1] react with various organometallic reagents in a high diastereoselective manner, ultimately providing a route for generating chiral amines in high chemical and optical yields.[2] We have already reported asymmetric syntheses of the indolizine alkaloid, (+)-monomorine I,[3] and chiral auxiliaries, (*R*,*R*)-2,5-bis(aryl)pyrrolidines,[4] by the application of this type of reaction. As part of a program aimed at expanding the synthetic utility of this reaction, we have accomplished the asymmetric synthesis of 1-substituted

(1*R*,1'*R*)-*N*-benzyl-1'-phenyl-2,2'-dihydroxydiethylamines (**1a–d**), which were useful as chiral auxiliaries for the stereoselective syntheses.[5]



The starting 1,3-oxazolidines (**3a–d**) were readily prepared by the condensation of (*R*)-*N*-benzylphenylglycinol [(*R*)-**2**][6] with several carbaldehyde (benzaldehyde,[1b] acetaldehyde,[1b] isobutyraldehyde and phenylacetaldehyde) in high yields. However, these products were confirmed to consist of thermodynamic mixture,[7] depending on the asymmetric center at the 2-position of the 1,3-oxazolidine ring; the minor compound amounted to 10% as judged from the ^{1}H-nmr(270 MHz) spectra. The reaction of **3a–d** with an excess amount of isopropoxydimethylsilylmethylmagnesium chloride[8] in tetrahydrofuran at 0°C furnished the cyclized products (**4a–d**) together with ring-opened products (**5a–d**) in a ratio of 2:1-7:1 with very high diastereomeric excesses. Indeed, the ^{1}H-nmr(270Mz) spectra of the crude products did not indicate the presence of any diastereoisomers, and the major products (**4a–d**) could be isolated in 41–68% yields by column

chromatography from the crude products. Since, however the minor products (**5a–d**) were too labile to purify completely by column chromatography on silica gel, the mixture of **4a–d** and **5a–d** was used for the subsequent reaction without purification. Oxidative cleavage of the carbon-silicon bond of the crude mixture of **4a–d** and **5a–d**, according to the procedure described by Tamao,[9] provided the essentially single oxidized products (**1a–d**) in 53–87% yields from **3a–d**, as evidenced by the ^{1}H-nmr(270MHz) spectra of the crude product mixture. The stereochemistry of the newly formed chiral center in **1a–d** was elucidated as followed. The configuration of **1a** has to be *R,R* because it possesses an optical rotation, while the compound with the *S,R* configuration, being a meso compound, would have been optically inactive. On the other hand, since this reasoning cannot be used for elucidation of the configuration of the other products, **1b–d** were submitted to reductive cleavage of the benzyl groups under 10% Pd/C–ammonium formate conditions, so affording known optically active ethanolamines (**6b–d**), whose configurations were confirmed to be *R* by the comparison with the reported specific rotation.[10] Consequently, the stereochemistry of **1a–d** was determined. Thus, we achieved a simple and novel synthesis of (1*R*,1'*R*)–diethanol–amines (**1a–d**) by employing the diastereoselective reaction of chiral 1,3–oxazolidines with Grignard reagent as a key reaction.

EXPERIMENTAL

General Procedures Melting points were measured with a Yanagimoto Micro Melting Point apparatus and uncollected. Ir spectra were recorded on a 215 Hitachi Grating ir spectrophotometer. ^{1}H–Nmr spectra were obtained on a JEOL PMX 270 instrument, and chemical shifts are reported in ppm on the δ–scale from internal Me_4Si. Mass spectra were measured with a JEOL JMS D–300 spectrometer by using the chemical ionization(CI)

(isobutane) methods. Optical rotations were taken with a JASCO-DIP-370 polarimeter at room temperature.

General Procedure for the Reaction of (*R*)-2 with Carbaldehydes. An carbaldehyde (isobutyraldehyde or phenylacetaldehyde, 12 mmol) were added to a solution of (*R*)-**2** (2.27 g, 10 mmol)[6] in benzene (50 ml), and the mixture was refluxed for 2 h using a Dean-Stark trap. After cooling, the mixture was concentrated under reduced pressure to give the oily residue, which was purified by distillation to give the *N*-benzyl-1,3-oxazolidines (**3c** or **3d**).

***(2R,4R)*-*N*-Benzyl-2-isopropyl-4-phenyl-1,3-oxazolidine (3c):** Colorless oil; yield 86%; bp 160°C (0.6 mmHg). ^{1}H-Nmr analysis of the crude product indicated a 94:6 ratio of diastereoisomers, which were inseparable by column chromatography. $[\alpha]_D$ −76.8° (*c*=0.95, $CHCl_3$). Ms *m/z*: CI, 282(M^++1); EI, 238 [M^+−$CH(CH_3)_2$]. *Anal.* Calcd for $C_{10}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.40; H, 8.32; N, 4.95. For the (2*R*,4*R*)-isomer (major product); ^{1}H-Nmr ($CDCl_3$) δ: 0.93(d, *J*=6.7 Hz,3H, CH_3), 0.95(d, *J*=6.7 Hz, 3H, CH_3), 1.52[m, 1H, $CH(CH_3)_2$], 3.56(d, *J*=14.0 Hz, 1H, $PhCH_2$), 3.64(dd, *J*=7.3, 8.5 Hz, 1H, CH_2O), 3.85(d, *J*=14.0 Hz, 1H, $PhCH_2$), 3.92(dd, *J*=6.7, 8.5 Hz, 1H, CH_2O), 4.13(dd, *J*=6.7, 7.3 Hz, 1H, PhCH), 4.22(d, *J*=2.4 Hz, 1H, NCHO), 7.13-7.52(m, 10H, aromatic H).

***(2R,4R)*-*N*,2-Dibenzyl-4-phenyl-1,3-oxazolidine (3d):** Colorless oil; yield 68%; bp 198°C (0.5 mmHg). ^{1}H-Nmr analysis of the crude product indicated a 90:10 ratio of diastereoisomers, which were inseparable by column chromatography. $[\alpha]_D$ −30.3° (*c*=1.16, $CHCl_3$). Ms *m/z*: CI, 330 (M^++1); EI, 238(M^+−$PhCH_2$). *Anal.* Calcd for $C_{23}H_{23}NO$: C, 83.85; H, 7.04; N, 4.25. Found: C, 83.55; H, 6.96; N, 4.25. For the (2*R*,4*R*)-isomer (major product); ^{1}H-nmr ($CDCl_3$)δ: 2.67(m, 2H, $PhCH_2CH$), 3.60(dd, *J*=7.9, 8.5 Hz, 1H, CH_2O), 3.59(d, *J*=13.4 Hz, 1H, $PhCH_2N$), 3.91(d, *J*=13.4 Hz, 1H, $PhCH_2N$), 3.93(dd, *J*=6.7, 8.5 Hz, 1H, CH_2O), 4.08(dd, *J*=6.7, 7.9 Hz,

1H, PhCH), 4.60(dd, *J*= 4.2, 6.1 Hz, 1H, NCHO), 7.13–7.41(m, 15H, aromatic H).

Reaction of (2*R*,4*R*)–3a–d with $ClMgCH_2SiMe_2OCH(Me)_2$. To a stirred solution of Grignard reagent, prepared from chloromethyldimethylisopropoxysilane (13.34 g, 80 mmol) and Mg (2.14 g, 88 mmol), in THF (100 ml) was added dropwise at 0°C a solution of oxazolidine (**3a–d**)(20 mmol) in THF (20 ml) under nitrogen over a 30 min period. After the reaction mixture had been stirred at room temperature for 24 h, it was quenched with small amount of water and filtered through a little Celite. The filtrate was dried over Na_2SO_4 and concentrated to give the residue which was subjected to column chromatography on silica gel with hexane–ether (10:1) as eluent. The first fraction gave the cyclized products (**4a–d**), and the second fraction gave the ring-opened products (**5a–5d**).

(4*R*,6*R*)–*N*–Benzyl–1,1–dimethyl–4,6–diphenyl–1,2,5–siloxazaperhydroepine (4a): Colorless plates; yield, 41%; mp 138–140°C(hexane–MeOH). $[\alpha]_D$ −110.0° (*c*= 1.17, $CHCl_3$). Ms *m/z*: CI, 388(M^++1); EI, 387(M^+), 296(M^+–$PhCH_2$). ^{1}H–Nmr ($CDCl_3$)δ: 0.19[s, 3H, $Si(CH_3)_2$], 0.36[s, 3H, $Si(CH_3)_2$], 1.23(dd, *J*=2.4, 14.6 Hz, 1H, CH_2Si), 1.70(dd, *J*=12.2, 14.6 Hz, 1H, CH_2Si), 3.73(d, *J*=13.4 Hz, 1H, $PhCH_2$), 3.82(dd, *J*=3.0, 3.6 Hz, 1H, PhCH), 3.88(d, *J*=13.4 Hz, 1H, $PhCH_2$), 4.21(dd, *J*=3.6, 12.8 Hz, 1H, CH_2O), 4.40(dd, *J*=2.4, 12.2 Hz, 1H, $CHCH_2Si$), 4.46(dd, *J*=3.0, 12.8 Hz, 1H, CH_2O), 7.11–7.58(m, 15H, aromatic H). *Anal*. Calcd for $C_{25}H_{29}NOSi$: C, 77.47; H, 7.54; N, 3.61. Found: C, 77.72; H, 7.51; N, 3.65.

The ring-opened products **(5a):** Colorless oil; yield 25%. Ms *m/z*: CI, 448 (M^++1); EI, 416(M^+–CH_2OH). ^{1}H–Nmr ($CDCl_3$)δ: −0.33[s, 3H, $Si(CH_3)_2$], −0.35[s, 3H, $Si(CH_3)_2$], 0.98[d, *J*=6.1 Hz, 3H, $OCH(CH_3)_2$], 0.99[d, *J*=6.1 Hz, 3H, $OCH(CH_3)_2$], 1.22(dd, *J*=4.9, 14.5 Hz, 1H, CH_2Si), 1.28(dd, *J*= 10.5, 14.5 Hz, 1H, CH_2Si), 2.10(br s, 1H, OH), 3.43(d, *J*=15.6 Hz, 1H, $PhCH_2$), 3.51(dd, *J*= 11.3, 6.1 Hz, 1H, CH_2OH), 3.70(dd, *J*=11.3, 7.3 Hz,

1H, CH_2OH), 3.75[septet, J=6.1 Hz, 1H, $OC\underline{H}(CH_3)_2$], 3.89(dd, J=6.1, 7.3 Hz, 1H, PhCH), 4.09(dd, J=4.9, 10.4 Hz, 1H, $C\underline{H}CH_2Si$), 4.20(d, J=15.6 Hz, 1H, $PhCH_2$), 7.12–7.41(m, 15H, aromatic H), which was not stable enough to obtain a satisfactory microanalysis.

(4*R*,6*R*)-*N*-Benzyl-1,1,6-trimethyl-4-phenyl-1,2,5-siloxazaperhydroepine (4b): Colorless oil; yield 43%; bp 90-93°C(0.5 mmHg). $[\alpha]_D$ −41.8° (c=1.02, $CHCl_3$). Ms m/z: CI, 326(M^++1); EI, 325(M^+), 310(M^+-CH_3). ^{1}H-Nmr($CDCl_3$)δ: 0.12[s, 3H, $Si(CH_3)_2$], 0.24[s, 3H, $Si(CH_3)_2$], 0.88(dd, J=3.6, 15.2 Hz, 1H, CH_2Si), 1.12(dd, J=10.3, 15.2 Hz, 1H, CH_2Si), 1.27 (d, J=6.1 Hz, 3H, CH_3), 3.34(m, 1H, $C\underline{H}CH_3$), 3.70(d, J=14.0 Hz, 1H, $PhCH_2$), 3.92(d, J=14.0 Hz, 1H, $PhCH_2$), 3.98(dd, J=3.0, 5.4 Hz, 1H, PhCH), 4.14(dd, J=5.4, 12.8 Hz, 1H, CH_2O), 4.30 (dd, J=3.0, 12.8 Hz, 1H, CH_2O), 7.16–7.47(m, 10H, aromatic H). HIms m/z: Calcd for $C_{20}H_{27}NOSi$: (M^+) 325.1860. Found: 325.1860.

The ring-opened products **(5b):** Colorless oil; yield 28%. Ms m/z: CI, 386 (M^++1); EI, 354(M^+-CH_2OH). ^{1}H-Nmr ($CDCl_3$)δ: 0.05[s, 3H, $Si(CH_3)_2$], 0.07 [s, 3H, $Si(CH_3)_2$], 0.69(d, J=6.1 Hz, CH_3), 0.91(dd, J=8.3, 15.1 Hz, 1H, CH_2Si), 0.96(dd, J=5.8, 15.1 Hz, 1H, CH_2Si), 1.12[d, J=6.1 Hz, 3H, $OCH(C\underline{H}_3)_2$], 1.14[d, J=6.1 Hz, 3H, $OCH(C\underline{H}_3)_2$], 3.06(br s, 1H, OH), 3.29(m, 1H, $C\underline{H}CH_2Si$), 3.46(m, 1H, PhCH), 3.50(d, J=14.0 Hz, 1H, $PhCH_2$), 3.89–4.03(m, 4H), 7.16–7.43(m, 10H, aromatic H), which was not stable enough to obtain a satisfactory microanalysis.

(4*R*,6*R*)-*N*-Benzyl-1,1-dimethyl-4-phenyl-6-isopropyl-1,2,5-siloxaza-perhydroepine (4c): Colorless oil; Yield 64%; bp 210–214°C (0.5 mmHg). $[\alpha]_D$ −10.7° (c=1.07, $CHCl_3$). Ms m/z: CI, 354(M^++1); EI, 310[$M^+-CH(CH_3)_2$]. ^{1}H-Nmr ($CDCl_3$)δ: 0.16[s, 3H, $Si(CH_3)_2$], 0.30[s, 3H, $Si(CH_3)_2$], 0.80[d, J=6.7 Hz, 3H, $CH(C\underline{H}_3)_2$], 0.85[d, J=6.7 Hz, 3H, $CH(C\underline{H}_3)_2$], 1.06(m, 2H, CH_2Si), 1.78 [m, 1H, $C\underline{H}(CH_3)_2$], 2.71(m, 1H, $C\underline{H}CH_2Si$), 3.81(d, J=13.4 Hz, 1H, $PhCH_2$), 3.88(dd, J= 3.0, 5.4 Hz, 1H, PhCH), 3.98(d, J=13.4 Hz, 1H, $PhCH_2$), 4.15 (dd, J=5.4, 12.8 Hz, 1H,

CH_2O), 4.32(dd, *J*=3.0, 12.8 Hz, 1H, CH_2O), 7.14–7.45(m, 10H, aromatic H). *Anal.* Calcd for $C_{22}H_{31}NOSi$: C, 74.74; H, 8.84; N, 3.96. Found: C, 74.87; H, 8.97; N, 3.96.

The ring-opened products **(5c)**: Colorless oil; yield 15%. Ms *m/z*: CI, 414 (M^++1); EI, 382(M^+–CH_2OH). ^{1}H–Nmr ($CDCl_3$)δ: 0.11[s, 3H, $Si(CH_3)_2$], 0.14 [s, 3H, $Si(CH_3)_2$], 0.64(dd, *J*=6.1, 15.3 Hz, 1H, CH_2Si), 0.67[d, *J*=7.3 Hz, 3H, $CH(CH_3)_2$], 0.72[d, *J*=7.3 Hz, 3H, $CH(CH_3)_2$], 0.92(dd, *J*=6.7, 15.3 Hz, 1H, CH_2Si), 1.23[d, *J*=6.1 Hz, 6H, $OCH(CH_3)_2$], 1.40[m, 1H, $CH(CH_3)_2$], 2.99(br s, 1H, OH), 3.09(m, 1H, $CHCH_2Si$), 3.57(dd, *J*=5.2, 2.4 Hz, 1H, PhCH), 3.72(d, *J*=14.7 Hz, 1H, $PhCH_2$), 3.90(dd, *J*=8.9, 5.2 Hz, 1H, CH_2OH), 3.98(d, *J*=14.7 Hz, 1H, $PhCH_2$), 3.99(dd, *J*=8.9, 2.4 Hz, 1H, CH_2OH), 4.00[septet, *J*= 6.1 Hz, 1H, $OCH(CH_3)_2$], 7.23–7.52(m, 10H, aromatic H), which was not stable enough to obtain a satisfactory microanalysis.

(4*R*,6*R*)–*N*,6–Dibenzyl–1,1–dimethyl–4–phenyl–1,2,5–siloxazaperhydroepine (4d): Colorless needless; yield 68%; mp 78–80°C(hexane). $[\alpha]_D$ –9.6° (*c*=0.73, $CHCl_3$). Ms *m/z*: CI, 402(M^++1); EI, 310(M^+–$PhCH_2$). ^{1}H–Nmr($CDCl_3$) δ: 0.00[s, 3H, $Si(CH_3)_2$], 0.24[s, 3H, $Si(CH_3)_2$], 0.83(dd, *J*=3.0, 15.2 Hz, 1H, CH_2Si), 1.07(dd, *J*=10.3, 15.2 Hz, 1H, CH_2Si), 2.70(dd, *J*=8.5, 13.4 Hz, 1H, $PhCH_2CH$), 3.14(dd, *J*=5.4, 13.4 Hz, 1H, $PhCH_2CH$), 3.40(m, 1H, $PhCH_2CH$), 3.81(d, *J*=13.4 Hz, 1H, $PhCH_2$), 3.91(dd, *J*=2.4, 5.4 Hz, 1H, PhCH), 4.40(d, *J*=13.4 Hz, 1H, $PhCH_2$), 4.34(dd, *J*=2.4, 12.8 Hz, 1H, CH_2O), 4.45(dd, *J*=5.4, 12.8 Hz, 1H, CH_2O), 6.95–7.36(m, 15H, aromatic H). *Anal.* Calcd for $C_{26}H_{31}NOSi$: C, 77.76; H, 7.78; N, 3.49. Found: C, 77.94; H, 7.82; N, 3.46.

The ring-opened products **(5d)**: Colorless oil; yield 10%. Ms *m/z*: CI, 462 (M^++1); EI, 402[M^+–$OCH(CH_3)_2$]. ^{1}H–Nmr ($CDCl_3$)δ: -0.19[s, 3H, $Si(CH_3)_2$], -0.01[s, 3H, $Si(CH_3)_2$], 0.60(dd, *J*=5.2, 15.0 Hz, 1H, CH_2Si), 1.08(dd, *J*= 7.9, 15.0 Hz, 1H, CH_2Si), 1.20[d, *J*=6.1 Hz, 3H, $OCH(CH_3)_2$], 1.22[d, *J*= 6.1 Hz, 3H, $OCH(CH_3)_2$], 2.30(dd, *J*=13.4, 8.5 Hz, $PhCH_2CH$), 2.44(dd, *J*=

13.4, 5.2 Hz, $PhC\underline{H}_2CH$), 3.46(m, 2H, $C\underline{H}CH_2Si$ and OH), 3.64(d, J=14.3 Hz, 1H, $PhCH_2$), 3.91–4.03(m, 3H), 4.09(d, J=14.3 Hz, 1H, $PhCH_2$), 7.10–7.45(m, 15H, aromatic H), which was not stable enough to obtain a satisfactory microanalysis.

Oxidation of Crude Mixture of 4a–d and 5a–d with Hydrogen peroxide. To a stirred solution of crude mixture of **4a–d** and **5a–d** obtained from **3a–d** (10 mmol) with Grignard reagent (40 mmol) in methanol (100 ml) and tetrahydrofuran (100 ml) was added at room temperature potassium fluoride (3.48 g, 60 mmol), sodium bicarbonate (3.36 g, 40 mmol) and 30% hydrogen peroxide (240 ml, 1.9 mol)) in one portion. After reaction mixture had been stirred at room temperature for 48 h, an excess amount of sodium thiosulfate was added in one portion, and the mixture was stirred for 2 h at the same temperature. The mixture was then filtered through a little Celite, and the filtrate was concentrated to leave the residue, which was dissolved in 50% K_2CO_3 solution (100 ml) and extracted with ether (50 ml x 3). The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated to give the oily residue, which was subjected to column chromatography on silica gel with hexane–AcOEt (1:1) to give the diethanolamines (**1a–d**).

(1*R*,1'*R*)–*N*-Benzyl–1,1'–diphenyl–2,2'–dihydroxydiethylamine (1a): Colorless plates; yield 86%; mp 137.5–139°C(AcOEt). $[\alpha]_D$ −165.6° (c= 1.01, $CHCl_3$). Ms m/z: CI, 348(M^++1); EI, 316(M^+–CH_2OH). ^{1}H–Nmr ($CDCl_3$)δ: 2.39(brs, 2H, OH), 3.47(d, J=15.2 Hz, 1H, $PhCH_2$), 3.71(dd, J=4.2, 10.3 Hz, 2H, 2x$C\underline{H}_2OH$), 4.04(dd, J=9.1, 10.3 Hz, 2H, 2x$C\underline{H}_2OH$), 4.07(dd, J=4.2, 9.1 Hz, 2H, 2xPhCH), 4.12(d, J=15.2 Hz, 1H, $PhCH_2$), 7.04–7.46(m, 15H, aromatic H). *Anal.* Calcd for $C_{23}H_{25}NO_2$: C, 79.50; H, 7.25; N, 4.03. Found: C, 79.59; H, 7.30; N, 4.01. Ir($CHCl_3$): 3600(OH)cm^{-1}.

(1*R*,1'*R*)–*N*-Benzyl–1–phenyl–1'–methyl–2,2'–dihydroxydiethylamine (1b):

Colorless plates; yield 87%; mp 140-141°C(CH_2Cl_2-hexane). $[\alpha]_D$ −216.3° (*c*=1.03, $CHCl_3$). Ms *m/z*: CI, 286(M^++1); EI, 254(M^+−CH_2OH). ^{1}H-Nmr($CDCl_3$) δ: 0.53(d, *J*=6.1 Hz, 3H, CH_3), 2.08(br s, 2H, OH), 3.41(m, 1H, C<u>H</u>CH_3), 3.39–3.48(m, 2H, C<u>H</u>$_2$OH), 3.61(d, *J*=14.6 Hz, 1H, Ph<u>CH</u>$_2$), 3.61(dd, *J*=5.5, 10.9 Hz, 1H, PhCHC<u>H</u>$_2$), 3.84(dd, *J*=5.5, 10.9 Hz, 1H, PhC<u>H</u>CH_2), 3.87(d, *J*=1 4.6 Hz, 1H, Ph<u>CH</u>$_2$), 4.09(t, *J*=10.9 Hz, 1H, PhCHC<u>H</u>$_2$), 7.23–7.48(m, 10H, aromatic H). *Anal*. Calcd for $C_{18}H_{23}NO_2$: C, 75.75; H, 8.12; N, 4.91. Found: C, 75.60; H, 8.19; N, 4.84. Ir($CHCl_3$): 3450(OH)cm^{-1}.

(1*R*,1'*R*)-*N*-Benzyl-1-phenyl-1'-isopropyl-2,2'-dihydroxydiethylamine (1c): Colorless plates; yield 53%; mp 89–90°C(CH_2Cl_2-hexane). $[\alpha]_D$ −133.9° (*c*=1.05, $CHCl_3$). Ms *m/z*: CI, 314(M^++1); EI, 282(M^+−CH_2OH). ^{1}H-Nmr($CDCl_3$) δ: 0.63[d, *J*=6.7 Hz, 3H, $CH(C\underline{H}_3)_2$], 0.76[d, *J*=6.7 Hz, 3H, $CH(C\underline{H}_3)_2$], 1.47[m, 1H, C<u>H</u>$(CH_3)_2$], 2.84(m, 1H, NC<u>H</u>CH), 3.08(br s, 2H, OH), 3.58(dd, *J*=10.3, 14.0 Hz, 1H, C<u>H</u>$_2$OH), 3.60(dd, *J*=3.6, 14.0 Hz, 1H, C<u>H</u>$_2$OH), 3.67 (dd, *J*=4.2, 10.9 Hz, 1H, PhCHC<u>H</u>$_2$), 3.84(d, *J*=14.0 Hz, 1H, Ph<u>CH</u>$_2$), 3.99 (dd, *J*=4.2, 9.7 Hz, 1H, PhC<u>H</u>CH_2), 4.08(dd, *J*=9.7, 10.9 Hz, 1H, PhCHC<u>H</u>$_2$), 4.21(d, *J*=14.0 Hz, 1H, Ph<u>CH</u>$_2$), 7.25–7.46(m, 10H, aromatic H). *Anal*. Calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68; N, 4.47. Found: C, 76.55; H, 8.78; N, 4.41. Ir($CHCl_3$): 3400(OH)cm^{-1}.

(1*R*,1'*R*)-*N*,1'-Dibenzyl-1-phenyl-2,2'-dihydroxydiethylamine (1d): Colorless oil; yield 70%; bp 247–250°C (0.5 mmHg). $[\alpha]_D$ −22.9° (*c*=1.11, $CHCl_3$). Ms *m/z*: CI, 362(M^++1); EI, 330(M^+−CH_2OH). ^{1}H-Nmr($CDCl_3$)δ: 2.21 (dd, *J*=6.1, 12.8 Hz, 1H, PhC<u>H</u>$_2$CH), 2.24(dd, *J*=12.8, 14.6 Hz, 1H, PhC<u>H</u>$_2$CH), 2.88(br s, 2H, OH), 3.35(m, 1H, PhCH$_2$C<u>H</u>), 3.47(dd, *J*=4.2, 11.6 Hz, 1H, C<u>H</u>$_2$OH), 3.49(dd, *J*=6.7, 11.6 Hz, 1H, C<u>H</u>$_2$OH), 3.65(dd, *J*=4.8, 10.9 Hz, 1H, PhCHC<u>H</u>$_2$), 3.76(d, *J*=14.0 Hz, 1H, Ph<u>CH</u>$_2$), 3.98(dd, *J*=4.8, 10.3 Hz, 1H, PhC<u>H</u>CH_2), 4.12(dd, *J*=10.3, 10.9 Hz, 1H, PhCHC<u>H</u>$_2$), 6.87–7.65(m, 15H, aromatic H). *Anal*. Calcd for $C_{24}H_{27}NO_2$: C, 79.74; H, 7.53; N, 3.88. Found: C, 79.48; H, 7.52; N, 3.90. Ir($CHCl_3$): 3450(OH)cm^{-1}.

Reductive Cleavage of 1b–d with 10% Pd/C-ammonium formate. A mixture of **1b–d** (15 mmol), ammonium formate (4.73 g, 75 mmol) and 10% palladium on carbon (0.5 g – 2 g) in methanol (40 ml) was refluxed for 2 h. After the catalyst was filtered through Celite, a solution of saturated HCl in ethanol (5 ml) was added dropwise to this filtrate and concentrated. The resulting residue was dissolved in CH_2Cl_2 (40 ml) and the precipitate was filtered off. After evaporation of the solvent, the residue was dissolved in 5% aqueous HCl (20 ml) and the aqueous solution was washed with ether. The aqueous phase was basified with 50% NaOH solution, and extracted with CH_2Cl_2 (20 ml x 4). The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated to give the oily residue, which was purified by distillation to give the (*R*)-ethanolamines (**6b-d**) in 53–80% yields. The spectroscopic data of the synthetic (*R*)-**6b–d** including the specific optical rotation were identical with authentic specimen, which were purchased from Aldrich.

(*R*)-2-Amino-1-propanol (Alaninol) (6b): Colorless oil; yield 71%; bp 71–73°C (11 mmHg). ^{1}H-Nmr($CDCl_3$)δ: 1.06(d, *J*=6.7 Hz, 3H, CH_3), 2.08(s, 3H, OH and NH_2), 3.03(m, 1H, NCH), 3.24(dd, *J*=7.9, 10.4 Hz, 1H, CH_2OH), 3.54(dd, *J*=4.3, 10.4 Hz, 1H, CH_2OH). $[\alpha]_D$ −20.1° (*c*=1.23, $CHCl_3$).

(*R*)-2-Amino-3-methyl-1-butanol (Valinol) (6c): Colorless oil; yield 53%; bp 80–81°C (8 mmHg). ^{1}H-Nmr($CDCl_3$)δ: 0.92[d, *J*=6.7 Hz, 3H, $CH(CH_3)_2$], 0.94[d, *J*=6.7 Hz, 3H, $CH(CH_3)_2$], 1.56[m, 1H, $CH(CH_3)_2$], 1.88(s, 3H, OH and NH_2), 2.57(ddd, *J*=4.3, 6.7, 8.5 Hz, 1H, NCH), 3.29(dd, *J*=8.5, 10.4 Hz, 1H, CH_2OH), 3.65(dd, *J*=4.3, 10.4 Hz, 1H, CH_2OH). HCl salt; colorless plates. $[\alpha]_D$ −14.3° (*c*=1.11, EtOH).

(*R*)-2-Amino-3-phenyl-1-propanol (Phenylalaninol) (6d): Colorless plates; yield 80%; bp 120–122°C (4 mmHg), mp 95°C(ether). ^{1}H-Nmr($CDCl_3$)δ: 1.78 (s, 3H, OH and NH_2), 2.54(dd, *J*=8.0, 13.4 Hz, 1H, CH_2Ph), 2.80(dd, *J*=4.9, 13.4 Hz, 1H, CH_2Ph), 3.14(m, 1H, NCH), 3.39(dd, *J*=7.3, 10.4 Hz, 1H,

CH_2OH), 3.65(dd, J=3.7, 10.4 Hz, 1H, CH_2OH), 7.17–7.36(m, 5H, aromatic H). $[\alpha]_D$ +23.2° (c=1.13, EtOH).

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