Highly Diastereoselective Synthesis of *Threo* or *Erythro* Aminoalkyl Epoxides from α-Amino Acids

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α-Chloro-α'-(dibenzylamino) methylketones **3** are synthesized in enantiomerically pure form starting from α-amino acids. Reduction of amino ketones **3** and further epoxidation affords *threo* aminoalkyl epoxides **6** with diastereoisomeric excess ranging between 94% and 98%. The synthesis of *erythro* amino epoxides **9** is also described by reaction of α-amino aldehydes **7** with *in situ* generated (halomethyl)lithium. Amino epoxides **9** were obtained with a diastereoisomeric excess ranging between 91% and 98%.

Introduction

α-Amino epoxides are highly useful intermediates in the synthesis of amino sugars,[1] polyoxygenated α-amino acids,[2] or hydroxyethylene dipeptide isosteres,[3] which are used in the synthesis of protease inhibitors[4] and other pharmacologically important compounds.[5]

On the other hand, α-amino epoxides and peptidyl epoxides can be used as chiral building blocks for further chemical transformations, yielding products of predetermined stereo- and regiochemistry, because of the well known versatility of the epoxide moiety in organic synthesis.[6]

There are four general methodologies to stereoselectively prepare α-amino epoxides:[7] The direct epoxidation of α-amino aldehydes by sulfonium ylides,[8] the epoxidation of allylamines,[5,9] the reductive amination of keto epoxides,[4a] and the stereoselective reduction of chloromethyl ketones.[10] In all these cases, only one of the diastereoisomers (*erythro* or *threo*) is available. In general, the diastereoisomeric excess (de) is less than 90% and the yields moderate (about 50%).

Recently, we have reported a direct method to obtain, without racemization, halogenated α-hydroxy ketones[11] by reaction of *O*-protected natural ethyl lactates with *in situ* generated mono- or bis(halomethyl)lithium, along with the preparation of the chloromethyl ketone derived from L-alanine and its further transformation into the corresponding amino epoxide. In the present paper we report an improvement and generalization of the synthesis of the *erythro* and *threo* isomers of *N*-protected α-amino epoxides starting from *N*-protected α-amino aldehydes or α-amino ketones, respectively. These processes take place with high diastereoselectivity (de ≥ 90%) and full retention of the sterochemistry at the α-carbon of the starting α-amino aldehyde or α-amino ketone. We also describe the generalization of the synthesis of α-amino-α'-chloro methyl ketones.[12]

Results and Discussion

Treatment of ethyl *N,N*-dibenzylated α-amino carboxylates **1** with (chloromethyl)lithium generated *in situ* at −78 °C gave, after hydrolysis, the corresponding chlorinated amino ketone **3** in high yields (see Experimental Section and Scheme 1).

Compounds **1** were preparated by esterification of the corresponding α-amino acids with ethanol[13] and further treatment with benzyl bromide in the presence of diisopropylethylamine (60% yield). When the reaction was carried out with the corresponding benzyl ester (tribenzylated amino acid), the yield of **3** was lower and the amino ketone appeared contaminated by small amounts of impurities which complicated its purification. Using the ethyl esters **1** the isolation of the pure ketones **3** required only removal of the solvents (purity >95%,

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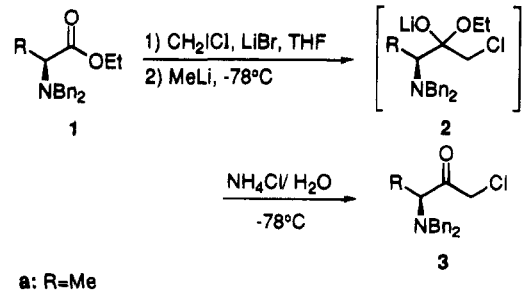
Scheme 1



Scheme 2

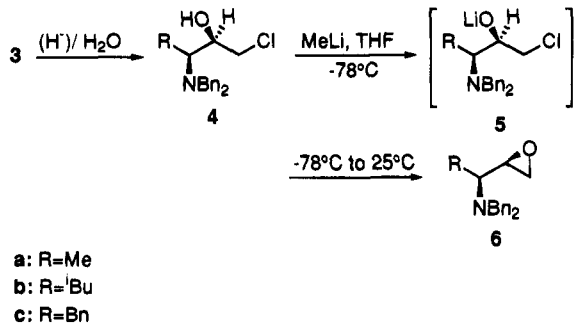


Table 1. Synthesis of *Threo* Amino Epoxides 6

product	R	conditions	yield (%) 4a[a]	6a[b]	de[c]
6a	Me	$NaBH_4$, −20 °C	76	81[d]	76
6a	Me	$LiAlH_4$, −78 °C	88	81[d]	90
6a	Me	$LiAlH_4$, −100 °C	78	81[d]	94
6b	iBu	$NaBH_4$, −20 °C	75	75	90
6b	iBu	$LiAlH_4$, −100 °C	82	75	98
6c	Bn	$NaBH_4$, −20 °C	70	82	90
6c	Bn	$LiAlH_4$, −100 °C	80	82[d]	96

[a] Isolated yield based on the starting ketone **3**. [b] Isolated yield based on the crude starting alcohol **4**. [c] Diastereoisomeric excess determinated by 300 MHz ^1H NMR analysis of the crude products **6**. [d] ee > 99% HPLC (Chiracel OD-H; UV detector 215 nm; 0.8 mL/min; 50:1 hexane/2-propanol; t_R: **6a**, 14.51 min, **6c**, 15.24 min).[15]

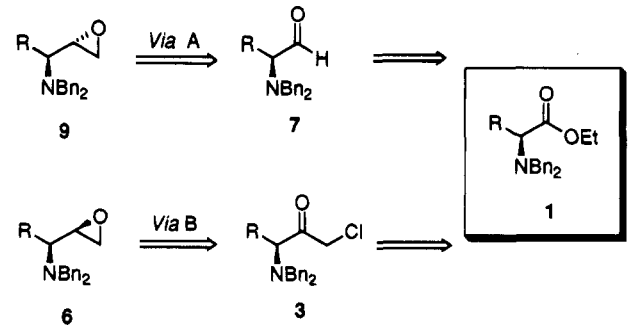
300 MHz ^1H NMR spectroscopy). (Chloromethyl)lithium was generated *in situ* by treatment of chloroiodomethane with methyllithium. The synthesis of the amino ketones **3** proceeds via intermediate **2** which is stable under the reaction conditions due to the presence of the electronegative chlorine and nitrogen substituents.[14]

The enantiomeric purity of α-amino ketones **3** was determinated by chiral HPLC (Chiracel OD-H) analysis. The enantiomeric excess (ee) values turned out to be >99% showing that essentially no racemization occurs in the synthesis of ketones **3**.[15]

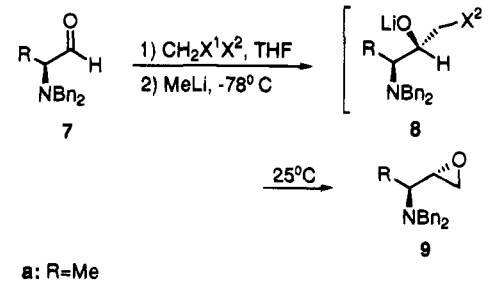
Scheme 2 outlines our synthetic preparation of *threo* amino epoxides **6**. Reduction of amino ketones **3** with $NaBH_4$ or $LiAlH_4$ at different temperatures afforded the alcohol **4**, which upon treatment with methyllithium gave the amino oxirane **6**. Yields and diastereoisomeric excess are summarized in Table 1.

The diastereoselectivity of the reduction was improved at lower temperatures and when $LiAlH_4$ was employed instead of $NaBH_4$. Thus, when the reduction was carried out with $LiAlH_4$ at −100 °C, the diastereoisomeric excess (de) was higher than 90% (300 MHz ^1H NMR spectroscopy). We also tested the racemization of compound **6a** and **6c** (chiral HPLC analysis), being the ee > 99%.[15]

Scheme 3



Scheme 4



A retrosynthetic analysis (Scheme 3) suggested that the other amino epoxide diastereoisomer could be obtained from amino aldehydes **7**[16] and (chloromethyl)lithium, assuming that the formation of **6** or **9** comes from the sequential addition of two different nucleophiles, hydride and (chloromethyl)lithium, to the ester function of **1**. Thus, depending on the order of addition, both diastereoisomers *erythro* (*via* **A**) and the *threo* (*via* **B**) could be prepared. In fact, treatment of amino aldehyde **7** with (halomethyl)lithium gave the corresponding alcoholate **8**. When the reaction mixture was allowed to warm to room temperature the amino epoxide **9** was obtained, as shown in Scheme 4.

The reaction was carried out using (chloro-, (bromo-, or (iodomethyl)lithium, being generated by treatment of chloroiodomethane, dibromomethane, or diiodomethane with methyllithium, respectively.

Analysis of Table 2 reveals that the higher diastereoselectivity was obtained using (iodomethyl)lithium (de = 91−98%), being similar in the case of (chloromethyl)-lithium and (bromomethyl)lithium (Table 2) (300 MHz ^1H NMR spectroscopy).

The high proclivity of the *N*-protected aldehyde derived from phenylalanine to racemize has been carefully documented.[17] Under these reaction conditions, the amino oxirane **9c** was synthetized with no detectable racemization (chiral HPLC analysis indicated that less than 1% of the opposite enantiomer was present in the amino epoxide, ee > 98%).[15] Further analysis of the amino

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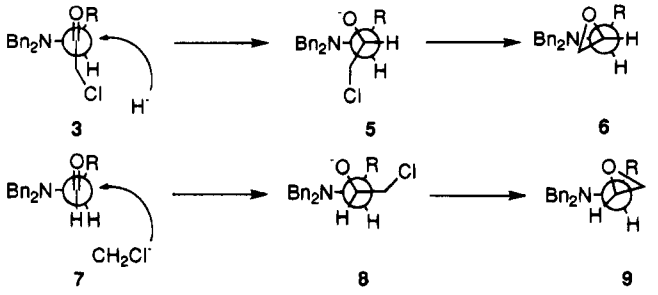
Table 2. Synthesis of *Erythro* Epoxides 9

product	R	X^1	X^2	yield (%)[a]	de[b]
9a	Me	I	Cl	72[c]	91
9a	Me	Br	Br	85	93
9a	Me	I	I	78[c]	98
9b	^{i}Bu	I	Cl	70	72
9b	^{i}Bu	Br	Br	80	80
9b	^{i}Bu	I	I	80	91
9c	Bn	I	Cl	71	80
9c	Bn	Br	Br	81	81
9c	Bn	I	I	81[c]	92

[a] Isolated yield based on the starting aldehyde **7**. [b] Diastereoisomeric excess determined by 300 MHz ^{1}H NMR analysis of the crude products **9**. [c] ee > 99% HPLC (Chiracel OD-H; UV detector: **9a**, 220 nm, **9c**, 215 nm; 0.8 mL/min; 50:1 hexane/2-propanol; t_R: **9a**, 13.58 min, **9c**, 17.33 min).[15]

Scheme 5



aldehyde by chiral HPLC showed that this minor epimerization occurred at the amino aldehyde preparation step.[15]

The stereochemistry of amino epoxides **6** and **9** were established unambiguously by comparison with the *erythro* amino epoxide **9a** obtained by treatment of the amino aldehyde **7a** with methylsulfonium ylide, previously described.[8a] The NMR data of diastereoisomer **9** indicated that it is identical to the product obtained with the ylide.

Thus, the addition of (halomethyl)lithium to **7** and the hydride to **3** takes place under nonchelation control which can be explained assuming that the energetically more favored transition state has the larger substituent (dibenzylamine) *anti* to the attack of the (halomethyl)lithium or hydride (Scheme 5). These results are in agreement with the previously report for the addition of other organolithium compounds to dibenzylated amino aldehydes[13] or for the reduction of α-amino ketones.[18]

In conclusion, the results reported represent a general method for the preparation of *erythro* or *threo* amino epoxides with high yield and stereoselectivity (de > 90%) from easily available starting materials. Moreover, the experimental procedure is simple so this method constitutes a convenient synthesis of the important chiral building blocks amino epoxides **6** and **9**.

Experimental Section

General. Analytical TLC was conducted in precoated silica gel 60 F-254 on aluminum sheets; compounds were visualized with UV light or iodine. Optical rotations were measured in chloroform. ^{1}H NMR spectra were recorded at 300 or 200 MHz. ^{13}C NMR spectra were recorded at 75 or 50 MHz. Chemical shifts are reported in ppm relative to TMS in $CDCl_3$. Only the most significant IR absortions and the molecular ions and/or base peaks in MS are given. The enantiomeric purity was determined by chiral HPLC analysis using a Chiracel OD-H (0.46 × 25 cm, Diacel) column.

Amino acids, all of the natural L (*S*) configuration, benzyl bromide, *N,N*-diisopropylethylamine, diiodomethane, chloroiodomethane, dibromomethane, methyllithium, lithium bromide, $NaBH_4$, and $LiAlH_4$ were purchased from Aldrich and were used without further purification. Ethyl α-amino esters were obtained by esterification with ethanol.[11] *N,N*-Dibenzylamino esters were obtined by refluxing, in $CHCl_3$, the corresponding amino ester with benzyl bromide in presence of *N,N*-diisopropylethylamine during 5 h. All the reactions were conducted in oven-dried glasswere under dry nitrogen. All solvents were purified before use. THF was distilled from sodium benzophenone ketyl; methanol was distilled from magnesium turnings.

(*N,N*-Dibenzylamino)-1-chloro Ketones 3. To a −78 °C stirred solution of the corresponding protected α-amino ester **1** (10 mmol), chloroiodomethane (1.31 mL; 18 mmol), and LiBr (0.8g; 10 mmol) in dry THF (40 mL) was added methyllithium (12 mL of 1.5 M solution in diethyl ether; 18 mmol) dropwise over 5 min. After stirring at −78 °C for 30 min, the mixture was treated with a saturated aqueous solution of NH_4Cl (5 mL) and extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude ketones **3** were reduced without further purification. The crude product was chromatographed on silica gel (10:1 hexane/ethyl acetate) to provide pure ketones **3** in order to determinate the enantiomeric excess or the optical rotation.

(*S*)-3-(Dibenzylamino)-1-chlorobutan-2-one (3a) (87% yield): R_f 0.52 (5:1 hexane−EtOAc); $[\alpha]^{25}_D$ −116.5° (*c* 4.2, $CHCl_3$); ^{1}H NMR δ 1.13 (d, *J* = 6.7 Hz, 3 H), 3.32 (d, *J* = 13.5 Hz, 2 H), 3.40 (q, *J* = 6.7 Hz, 1 H), 3.59 (d, *J* = 13.5 Hz, 2 H), 4.13 (d, *J* = 16.1 Hz, 1 H), 4.49 (d, *J* = 16.1 Hz, 1 H), 7.15−7.27 (m, 10 H); ^{13}C NMR δ 6.3, 47.8, 54.5, 61.0, 127.4, 128.5, 128.6, 138.3, 203.0; IR (KBr) 1736 cm^{-1}; MS, *m/z* 266 (M^+ − Cl, <1), 265 (M^+ − HCl, <1), 224 (M^+ − $COCH_2Cl$, M^+ − C_6H_5, 37), 91 (100). Anal. Calcd for $C_{18}H_{20}ClNO$: C, 71.63; H, 6.68; N, 4.64. Found: C, 71.55; H, 6.70; N, 4.67. Chiral HPLC analysis ee >99% (UV detector 215 nm, 0.8 mL/min, 30:1 hexane/ethanol, t_R 14.15 min).[15]

(*S*)-3-(Dibenzylamino)-1-chloro-5-methylhexan-2-one (3b) (90% yield): R_f 0.53 (10:1 hexane−EtOAc); $[\alpha]^{25}_D$ −82.5° (*c* 0.88, $CHCl_3$); ^{1}H NMR δ 0.89 (d, *J* = 6.4 Hz, 3 H), 0.98 (d, *J* = 6.4 Hz, 3 H), 1.45−1.63 (m, 2 H), 1.86−1.97 (m, 1 H), 3.49−3.56 (m, 1 H), 3.54 (d, *J* = 13.7 Hz, 2 H), 3.78 (d, *J* = 13.7 Hz, 2 H), 4.16 (d, *J* = 15.4 Hz, 1 H), 4.52 (d, *J* = 15.4 Hz, 1 H), 7.36−7.42 (m, 10 H); ^{13}C NMR δ 22.0, 23.2, 25.3, 30.9, 47.5, 54.2, 62.2, 127.2, 128.3, 128.7, 138.6, 201.5; IR (KBr) 1730 cm^{-1}; MS, *m/z* 344 (M^+ + 1, <1), 286 (M^+ − C_4H_9, <1), 266 (M^+ − $COCH_2Cl$, M^+ − C_6H_5, 58), 91 (100).

(*S*)-3-(Dibenzylamino)-1-chloro-4-phenylbutan-2-one (3c) (85% yield): R_f 0.40 (10:1 hexane−ether); $[\alpha]^{25}_D$ −45.4° (*c* 0.39, $CHCl_3$); ^{1}H NMR δ 3.09 (dd, *J* = 3.8, 13.3 Hz, 1 H), 3.34 (dd, *J* = 9.5, 13.3 Hz, 1 H), 3.66 (d, *J* = 13.7 Hz, 2 H), 3.77 (dd, *J* = 3.8, 9.5 Hz, 1 H), 3.92 (d, *J* = 16.1 Hz, 1 H), 3.94 (d, *J* = 13.7 Hz, 2 H), 4.59 (d, *J* = 16.1 Hz, 1 H), 7.26−7.47 (m, 15 H); ^{13}C NMR δ 28.7, 47.8, 54.5, 66.6, 126.1, 127.4, 128.4, 128.5, 128.8, 129.4, 138.3, 138.5, 200.5; IR (KBr) 1737 cm^{-1}; MS, *m/z* 376 (M^+ − 1, <1), 342 (M^+ − Cl, <1), 300 (M^+ − $COCH_2Cl$, M^+ − C_6H_5, 46), 91 (100).

(*N,N*-Dibenzylamino)-1-chloro Alcohols 4. Method A. To a −20 °C stirred solution of the corresponding ketone **3** (3 mmol) in dry methanol (10 mL) was added $NaBH_4$ (0.22 g, 6 mmol). After stirring for 4 h at −20 °C, the reaction was quenched with H_2O and extracted with ether (3 × 20 mL). The combined organic phase was dried (Na_2SO_4), and the solvents were removed to give amino alcohols **4**.

Method B. To a −100 °C stirred solution of the corresponding ketone **3** (3 mmol) in dry THF (15 mL) was added $LiAlH_4$ (0.9 mL of 1 M solution in THF, 0.9 mmol). After stirring for 6 h at −100 °C the reaction was carefully quenched with water, and the mixture was filtered through Celite and extracted with dichloromethane (3 × 20 mL). Drying (Na_2SO_4), filtering, and evaporating provided the corresponding amino alcohol **4**.

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The crude amino alcohol **4** was epoxidized without further purification. The crude product was chromatographed over silica gel (5:1 hexane/ethyl acetate) to provide the pure amino alcohol **4** to measure the optical rotation.

(2*R*,3*S*)-3-(Dibenzylamino)-1-chlorobutan-2-ol (4a): R_f 0.35 (10:1 hexane–EtOAc); $[\alpha]^{25}_D$ +35.9° (*c* 0.92, $CHCl_3$); ^1H NMR δ 1.10 (d, *J* = 6.7 Hz, 3 H), 2.81–2.95 (m, 1 H), 3.38 (d, *J* = 13.4 Hz, 2 H), 3.42–4.48 (m, 1 H), 3.67–3.77 (m, 2 H), 3.85 (d, *J* = 13.4 Hz, 2 H), 4.53 (br, 1 H), 7.28–7.39 (m, 10 H); ^{13}C NMR δ 7.7, 46.7, 52.9, 55.1, 70.7, 126.8, 128.0, 128.5, 138.1; IR (KBr) 3432–3235 (br) cm^{-1}; MS, *m*/*z* 300 (M^+ – 3, <1), 267 (M^+ – HCl, <1), 224 (M^+ – $CHOHCH_2Cl$, 1), 91 (100). Anal. Calcd for $C_{18}H_{22}ClNO$: C, 71.16; H, 7.30; N, 4.61. Found: C, 71.00; H, 7.33; N, 4.60.

(2*R*,3*S*)-3-(Dibenzylamino)-1-chloro-5-methylhexan-2-ol (4b): R_f 0.33 (5:1 hexane–ether); $[\alpha]^{25}_D$ +2.0 (*c* 0.9, $CHCl_3$); ^1H NMR δ 0.94 (d, *J* = 6.2 Hz, 3 H), 0.97 (d, *J* = 6.2 Hz, 3 H), 1.26–1.36 (m, 1 H), 1.58–1.75 (m, 2 H), 2.74–2.81 (m, 1 H), 3.45 (d, *J* = 13.3 Hz, 2 H), 3.51 (dd, *J* = 6.0, 11.6 Hz, 1 H), 3.63 (dd, *J* = 2.6, 11.6 Hz, 1 H), 3.71 (ddd, *J* = 2.6, 6.0, 8.1 Hz, 1 H), 3.89 (d, *J* = 13.3 Hz, 2 H), 4.26 (br, 1 H), 7.25–7.35 (m, 10 H); ^{13}C NMR δ 22.6, 23.3, 25.8, 35.1, 48.2, 54.1, 57.5, 71.7, 127.1, 128.3, 128.8, 138.9; IR (KBr) 3500–3130 (br) cm^{-1}; MS, *m*/*z* 347 (M^+ + 2, <1), 346 (M^+ + 1, <1), 345 (M^+, <1), 344 (M^+ –1, 2), 266 (M^+ – $CHOHCH_2Cl$, 30), 91 (100).

(2*R*,3*S*)-3-(Dibenzylamino)-1-chloro-4-phenylbutan-2-ol (4c): R_f 0.36 (10:1 hexanes–EtOAc); $[\alpha]^{25}_D$ +7.7° (*c* 1.04, $CHCl_3$); ^1H NMR δ 2.88 (dd, *J* = 7.6, 12.7 Hz, 1 H), 3.04–3.26 (m, 2 H), 3.37–3.49 (m, 2 H), 3.49 (d, *J* = 13.0 Hz, 2 H), 3.76–3.83 (m, 1 H), 4.08 (d, *J* = 13.0 Hz, 2 H), 7.30–7.42 (m, 15 H); ^{13}C NMR δ 31.0, 48.7, 54.2, 61.0, 71.0, 126.1, 127.0, 128.2, 128.4, 128.7, 128.9, 138.6, 139.2; IR (KBr) 3500–3300 (br) cm^{-1}; MS, *m*/*z* 381 (M^+ + 2, <1), 380 (M^+ + 1, <1), 379 (M^+, <1), 378 (M^+ –1, <1), 344 (M^+ –Cl, >1), 91 (100).

Amino Epoxides 6. To a −78 °C stirred solution of the corresponding amino alcohol **4** (2.5 mmol) in THF (10 mL) was added methyllithium (2.5 mL of 1.5 M solution in diethyl ether; 3.75 mmol). After stirring at 25 °C for 2 h the reaction was treated with a saturated aqueous solution of NH_4Cl (3 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude epoxides **6** were examined by ^1H NMR to give the diastereoisomeric excess reported in Table 2. Column flash chromatography over silica gel (15:1 hexane–ethyl acetate) provided pure *threo* amino epoxides **6**.

(1*R*)-[1′(*S*)-(Dibenzylamino)ethyl]oxirane (6a): R_f 0.50 (10:1 hexane–ether); $[\alpha]^{25}_D$ +4.2° (*c* 0.47, $CHCl_3$); ^1H NMR δ 1.12 (d, *J* = 7.0 Hz, 3 H), 2.56 (dd, *J* = 2.9, 5.1 Hz, 1 H), 2.74 (dd, *J* = 4.1, 5.1 Hz, 1 H), 2.86 (m, 1 H), 3.16 (ddd, *J* = 2.9, 4.1, 6.7 Hz, 1 H), 3.74 (d, *J* = 13.8 Hz, 2 H), 3.88 (d, *J* = 13.8 Hz, 2 H), 7.23–7.50 (m, 10 H); ^{13}C NMR δ 11.1, 43.8, 53.7, 54.2, 54.4, 126.7, 128.1, 128.5, 140.1; IR (KBr) 3028 cm^{-1}; MS, *m*/*z* 267 (M^+, 2), 224 (M^+ – C_2H_3O, 39), 91 (100); HRMS calcd for $C_{18}H_{21}NO$ 267.1623, found 267.1630. Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.64; H, 7.93; N, 5.25.

(1*R*)-[1′(*S*)-(Dibenzylamino)-3-methylbutyl]oxirane (6b): R_f 0.46 (10:1 hexane–ether); $[\alpha]^{25}_D$ −19.2° (*c* 0.53, $CHCl_3$); ^1H NMR δ 0.65 (d, *J* = 6.4, 3 H), 0.91 (d, *J* = 6.4, 3 H), 1.15 (ddd, *J* = 5.2, 8.6, 13.8, 1 H), 1.65 (ddd, *J* = 5.1, 9.0, 13.8, 1H), 1.84–1.95 (m, 1 H), 2.45 (dd, *J* = 2.6, 5.2, 1 H), 2.49–2.57 (m, 1 H), 2.76 (dd, *J* = 4.3, 5.2, 1 H), 3.16–3.21 (m, 1 H), 3.84 (2d, *J* = 13.3, 2 H), 3.95 (2d, *J* = 13.3, 2 H), 7.27–7.50 (m, 10 H); ^{13}C NMR δ 21.7, 23.4, 24.2, 38.0, 43.8, 52.4, 54.2, 56.9, 126.7, 128.0, 128.9, 140.2 ; IR (KBr) 3030 cm^{-1}; MS, *m*/*z* 309 (M^+, 2), 266 (M^+ – C_2H_3O, 28), 91 (100); HRMS calcd for $C_{21}H_{27}NO$ 309.2093, found 309.2088.

(1*R*)-[1′(*S*)-(Dibenzylamino)-2-phenylethyl]oxirane (6c): R_f 0.38 (15:1 hexane–ethyl acetate); $[\alpha]^{25}_D$ −4.7° (*c* 0.60, $CHCl_3$); ^1H NMR δ 2.25 (dd, *J* = 2.5, 5.1 Hz, 1 H), 2.64 (dd, *J* = 4.1, 5.1 Hz, 1 H), 2.76–2.86 (m, 2 H), 2.97–3.10 (m,1 H), 3.20 (ddd, *J* = 2.5, 4.1, 6.7 Hz, 1 H), 3.87 (d, *J* = 14.0 Hz, 2 H), 3.94 (d, *J* = 14.0 Hz, 2 H), 7.05–7.35 (m, 15 H); ^{13}C NMR δ 34.8, 44.2, 51.9, 54.1, 61.1, 125.9, 126.6, 127.9, 128.0, 128.5, 129.1, 139.0, 139.7; IR (KBr) 3028 cm^{-1}; MS, *m*/*z* 344 (M^+ + 1, <1), 343 (M^+, <1), 342 (M^+ −1, <1), 91 (100).

Amino Epoxides 9. To a −78 °C stirred solution of α-amino aldehyde **7** (2.5 mmol) and the corresponding dihalomethane (5 mmol) in dry THF (10 mL) was added methyllithium (3.3 mL of 1.5 M solution in diethyl ether, 5 mmol) dropwise. After stirring at-78 °C for 30 min, the mixture was allowed to warm to room temperature. Stirring was continued for 2 h at room temperature and then, the reaction was hydrolyzed with saturated aqueous NH_4Cl (4 mL) and extracted with ether (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and the solvents were removed in vacuo. The crude epoxides **9** were examined by ^1H NMR to give the diasteromeric excess reported in Table 2. Column flash chromatography over silica gel (15:1 hexane–ethyl acetate) provided pure *erythro* amino epoxides **9**.

(1*S*)-[1′(*S*)-(Dibenzylamino)ethyl]oxirane[8a] (9a): R_f 0.51 (10:1 hexane–ethyl acetate); $[\alpha]^{25}_D$ +9.3° (*c* 0.68, $CHCl_3$); ^1H NMR δ 1.09 (d, *J* = 7.0 Hz, 3 H), 2.46 (dd, *J* = 2.9, 4.8 Hz, 1 H), 2.72 (dd, *J* = 4.1, 4.8 Hz, 1 H), 2.78–2.91 (m, 1 H), 3.11–3.17 (m, 1 H), 3.65 (d, *J* = 14.0 Hz, 2 H), 3.87 (d, *J* = 14.0 Hz, 2 H), 7.22–7.45 (m, 10 H); ^{13}C NMR δ 8.7, 44.5, 53.5, 54.0, 55.1, 126.6, 128.0, 128.2, 139.9; IR (KBr) 3066 cm^{-1}; MS, *m*/*z* 267 (M^+, 2), 224 (M^+ – C_2H_3O, 8), 91 (100); HRMS calcd for $C_{18}H_{21}NO$ 267.1623, found 267.1629.

(1*S*)-[1′(*S*)-(Dibenzylamino)-3-methylbutyl]oxirane (9b): R_f 0.60 (10:1 hexane–ethyl acetate); $[\alpha]^{25}_D$ −14.1° (*c* 0.32, $CHCl_3$); ^1H NMR δ 0.69 (d, *J* = 6.5, 3 H), 0.88 (d, *J* = 6.5, 3 H), 1.25 (ddd, *J* = 5.7, 8.0, 14.0, 1 H), 1.58–1.71 (m, 1H), 1.80–1.96 (m, 1 H), 2.43–2.53 (m, 1 H), 2.57 (dd, *J* = 2.9, 5.1, 1 H), 2.83 (dd, *J* = 4.1, 5.1, 1 H), 3.04–3.11 (m, 1 H), 3.67 (2d, *J* = 13.8, 2 H), 3.87 (2d, *J* = 13.8, 2 H), 7.24–7.42 (m, 10 H); ^{13}C NMR δ 22.1, 23.3, 24.3, 36.9, 46.0, 51.9, 54.2, 56.4, 126.9, 128.1, 128.6, 140.0 ; IR (KBr) 3028 cm^{-1}; MS, *m*/*z* 309 (M^+, 2), 266 (M^+ – C_2H_3O, 28), 91 (100); HRMS calcd for $C_{21}H_{27}NO$ 309.2093, found 309.2106. Anal. Calcd for $C_{21}H_{27}NO$: C, 81.51; H, 8.79; N,4.53. Found: C, 81.30; H, 8.65; N, 4.55.

(1*S*)-[1′(*S*)-(Dibenzylamino)-2-phenylethyl]oxirane[8a] (9c): R_f 0.36 (15:1 hexane–ethyl acetate); $[\alpha]^{25}_D$ +6.5° (*c* 0.80, $CHCl_3$); ^1H NMR δ 2.59 (dd, *J* = 2.8, 4.9 Hz, 1 H), 2.85 (dd, *J* = 4.1, 4.9 Hz, 1 H), 2.87–2.95 (m, 2 H), 3.05–3.13 (m,1 H), 3.21–3.25 (m, 1 H), 3.81 (d, *J* = 13.7 Hz, 2 H), 3.93 (d, *J* = 13.7 Hz, 2 H), 7.16–7.39 (m, 15 H); ^{13}C NMR δ 33.6, 45.9, 51.9, 54.0, 60.1, 125.9, 126.7, 128.0, 128.1, 128.3, 129.4, 139.3, 139.4; IR (KBr) 3051 cm^{-1}; MS, *m*/*z* 344 (M^+ + 1, <1), 343 (M^+, <1), 342 (M^+ −1, <1), 91 (100); HRMS calcd for $C_{24}H_{25}NO$ 343.1936, found 343.1934.

Supporting Information Available: Copies of the ^1H and ^{13}C NMR spectra for all compounds (24 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from ACS; see any current masthead page for ordering information.

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