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Ring Opening of Nonactivated 2-(1-Aminoalkyl) Aziridines: Unusual Regio- and Stereoselective C-2 and C-3 Cleavage

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We have studied the ring opening of nonactivated amino aziridines **1** by water under acidic conditions. Depending on the acid used, amino aziridines are cleaved at C-3 or C-2 with high regioselectivity, and total stereoselectivity, affording chiral 2,3-diaminoalkan-1-ols **3** or 1,3-diaminoalkan-2-ols **4** in high yield.

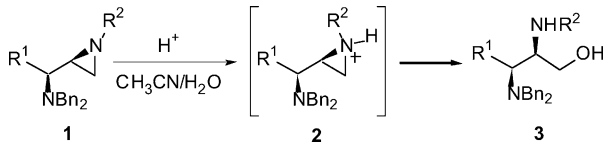
Introduction

Chiral aziridines are useful synthetic intermediates for the synthesis of biologically important compounds because of their ability to undergo nucleophilic ring opening reactions.[1] Hence, control of the regio- and stereoselectivity of the ring opening is essential for this purpose. Over the past few years a great number of ring opening reactions of aziridines have been reported.[1c,2] However, in these reactions, nonactivated aziridine[2j] has been scarcely used in comparison with activated aziridines.

Moreover, to the best of our knowledge, there are very few examples in the literature in which the regioselectivity of the ring opening of a determined activated aziridine with the same nucleophile is different depending on the reaction conditions.[3]

In addition, water has been used as the nucleophile in stereocontrolled ring opening reactions of nonactivated aziridines to a limited extent,[4] despite this process being potentially able to furnish the synthetically important chiral 1,2-amino alcohols.[5]

SCHEME 1. C-3 Ring Opening of Amino Aziridines 1



Recently, we reported the synthesis of nonactivated enantiopure amino aziridines **1** (Scheme 1) by reduction of α-amino ketimines derived from 1-aminoalkyl chloromethyl ketones.[6] The ring opening of these aziridines with heteronucleophiles was able to provide differently functionalized diamino compounds. Herein, we report the ring opening of amino aziridines by water with total regio- and stereoselectivity at C-2 and C-3, obtaining chiral 2,3-diaminoalkan-1-ols **3** and 1,3-diaminoalkan-2-ols **4**.

Results and Discussion

Ring opening reactions of amino aziridines **1** with water were carried out in acidic conditions to activate the aziridine ring. First, we tested the use of protic acids in this process. Thus, treatment of **1** with 1 equiv of *p*-toluenesulfonic acid (TsOH) in a 7/1 CH_3CN/H_2O mixture afforded 2,3-diaminoalkan-1-ols **3** with high yield, as shown in Table 1.

The reaction proceeded very smoothly at room temperature (24 h are required), while when a refluxing temperature was used the reaction was completed in only 0.5−1 h. These more drastic conditions did not affect the

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(1) (a) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599. (b) Pearson, W. H.; Lian, B. W.; Bergmeier, S. C. In *Comprehensive Heterocyclic Chemistry II*; Padwa, A., Ed.; Pergamon: Oxford, UK, 1996; Vol. 1A, pp 1−60. (c) McCoull, W.; Davis, F. A. *Synthesis* **2000**, 1347.

(2) (a) Wu, J.; Hou, X.-L.; Dai, L.-X. *J. Org. Chem.* **2000**, *65*, 1344. (b) Kim, B. M.; Bae, S. J.; So, S. M.; Yoo, H. T.; Chang, S. K.; Lee, J. H.; Kang, J. *Org. Lett.* **2001**, *3*, 2349. (c) Vicario, J. L.; Badía, D.; Carrillo, L. *J. Org. Chem.* **2001**, *66*, 5801. (d) Sabitha, G.; Babu, R. S.; Rajkumar, M.; Reddy, C. S.; Yadav, J. S. *Tetrahedron Lett.* **2001**, *42*, 3955. (e) Paul, B. J.; Hobbs, E.; Buccino, P.; Hudlicky, T. *Tetrahedron Lett.* **2001**, *42*, 6433. (f) Mao, H.; Joly, G. J.; Peeters, K.; Hoornaert, G. J.; Compernolle, F. *Tetrahedron* **2001**, *57*, 6955. (g) Xiong, C.; Wang, W.; Cai, C.; Hruby, V. J. *J. Org. Chem.* **2002**, *67*, 1399. (h) Aggarwal, V. K.; Alonso, E.; Ferrara, M.; Spey, S. E. *J. Org. Chem.* **2002**, *67*, 2335. (i) Yadav, J. S.; Reddy, B. V. S.; Sadashiv, K.; Harikishan, K. *Tetrahedron Lett.* **2002**, *43*, 2099. (j) Anand, R. V.; Pandey, G.; Singh, V. K. *Tetrahedron Lett.* **2002**, *43*, 3975.

(3) Only the ring opening of activated 2,3-aziridino alcohols by different hydride and methyl-transfer reagents led to regio- and stereoselective C-2 and C-3 cleavage, depending on the chelate effect of the reagent: (a) Tanner, D.; He, H. M.; Somfai, P. *Tetrahedron* **1992**, *48*, 6069. (b) Tanner, D.; He, H. M. *Tetrahedron* **1992**, *48*, 6079. (c) Tanner, D.; Gautun, O. R. *Tetrahedron* **1995**, *51*, 8279.

(4) (a) Davis, F. A.; Zhou, P. *Tetrahedron Lett.* **1994**, *35*, 7525. (b) Katagiri, T.; Takahashi, M.; Fujimura, Y.; Ihara, H.; Uneyama, K. *J. Org. Chem.* **1999**, *64*, 7323.

(5) The 1,2-amino alcohol moiety is a common structural component in naturally occurring and synthethic molecules, as well as being used as a chiral auxiliary: (a) Bergmeier, S. C. *Tetrahedron* **2000**, *56*, 2561. (b) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835.

(6) Concellón, J. M.; Bernad, P. L.; Riego, E.; García-Granda, S.; Forcén-Acebal, A. *J. Org. Chem.* **2001**, *66*, 2764. A later alternative synthesis of *N*,*N*-dibenzylamino aziridines: Reetz, M. T.; Lee, W. K. *Org. Lett.* **2001**, *3*, 3119.

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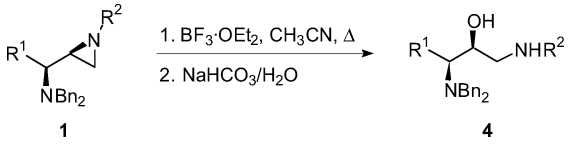
TABLE 1. C-3 Ring Opening of Amino Aziridines 1

entry	product[a]	R^1	R^2	conditions	yield (%)[b]
1	**3a**	Me	Bn	80 °C, 1 h	72[c]
2	**3a**	Me	Bn	20 °C, 24 h	90[d]
3	**3b**	Me	Pr	80 °C, 1 h	76[c]
4	**3b**	Me	Pr	20 °C, 24 h	92[d]
5	**3c**	*i*-Bu	Bn	80 °C, 0.5 h	78
6	**3c**[e]	*i*-Bu	Bn	80 °C, 0.5 h	
7	**3d**	*i*-Bu	allyl	80 °C, 0.5 h	75
8	**3e**	Bn	Bn	80 °C, 0.5 h	74

[a] Unless otherwise noted, TsOH was used as protic acid. [b] Isolated yield after column chromatography based on the starting amino aziridine **1**. [c] This product was isolated together with the corresponding regioisomer **4** (see text). Regioselectivity was determined by 300-MHz ^{1}H and ^{13}C NMR analysis of the crude products **3**. [d] Isolated yield of the crude product based on the starting amino aziridine **1**. [e] Concentrated H_2SO_4 was used as protic acid.

SCHEME 2. C-2 Ring Opening of Amino Aziridines 1



1 **4**

yield of the reaction or the purity of products. Only compounds **3a** and **3b** (Table 1, entries 1 and 3) were isolated together with a small amount (8%, 300-MHz ^{1}H NMR spectroscopy) of the product corresponding to a ring opening at C-2 with retention of the configuration, as explained later. When the reaction took place at room temperature, the regioselectivity improved in a ratio of 19/1.

In the case of aziridines with R^1 = ^{i}Bu, Bn (Table 1, entries 5−7), no regioisomers or byproducts were observed by NMR analysis (300 MHz) of the crude reaction of 2,3-diaminoalkan-1-ols **3** at reflux temperature.

Nevertheless, when the reaction was carried out with sulfuric acid under the previous conditions, the starting amino aziridines were recovered together with unidentified byproducts.

The acid-promoted ring opening reaction of amino aziridines **1** in the presence of water could take place through highly reactive aziridinium salts **2** (Scheme 1), which suffer an attack by water at the less hindered position.

In addition, the effect of Lewis acids on the ring opening reaction of amino aziridines **1** was examined. To do this, BF_3·OEt_2 was chosen, since it is commonly used in Lewis acid-catalyzed ring openings of aziridine[1c,2g,7]

Thus, a solution of amino aziridines **1** in dry acetonitrile was treated with 1 equiv of BF_3·OEt_2, and heated for 1 h. The hydrolysis of the reaction mixture led to 1,3-diaminoalkan-2-ols **4** in high yields (Scheme 2, Table 2).

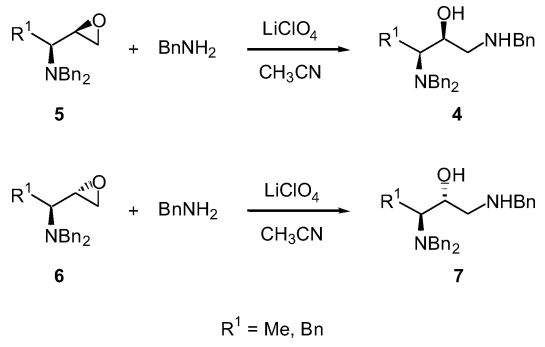
Once more, excepting compounds **4** with R^1 = Me (Table 2, entries 1 and 2), which were isolated together with the regioisomers **3a**,**b** in a 7/1 ratio in the best examples (conversion = 72%),[8] the ring opening reaction

TABLE 2. C-2 Ring Opening of Amino Aziridines 1

entry	product	R^1	R^2	yield (%)[a]
1	**4a**	Me	Bn	40[b]
2	**4b**	Me	Pr	38[b]
3	**4c**	*i*-Bu	Bn	81
4	**4d**	*i*-Bu	allyl	78
5	**4e**	Bn	Bn	75
6	**4f**	TBSO−CH_2	Bn	76

[a] Isolated yield after column chromatography based on the starting amino aziridine **1**. [b] This product was isolated together with the corresponding regioisomer **3** in a 7/1 ratio, and the starting amino aziridine **1**. Regioselectivity was determined by 300-MHz ^{1}H and ^{13}C NMR analysis of the crude products **4**.

SCHEME 3. Ring Opening of Amino Epoxides 5 and 6



of amino aziridines **1** was totally regio- and stereoselective, as shown by the ^{1}H and ^{13}C NMR spectra of **4**. However, unlike the previous reaction, the aziridine suffers an unusual ring opening at C-2, with retention of the configuration at this center.

The assignment of this unexpected regio- and stereochemistry was made after carrying out the ring opening reaction of epoxides **5** and **6**[9] with benzylamine (Scheme 3). Under these conditions, the epoxide ring is opened at the less substituted oxirane carbon, and consequently, the stereochemistry of the C-2 in the epoxide and in the product has not changed.[10] By comparison of data for the products from epoxides and the corresponding compounds **4** (from **1**), we can affirm that the diamino alcohols derived from **5** and **4** are the same. Likewise, the ring opening of amino aziridines **1** with TsOH must have taken place on C-3.

The stereochemistry in the ring opening reaction of amino aziridines **1** in the presence of BF_3·OEt_2 could be explained with a double inversion at C-2 in the aziridine ring. For this matter, an anchimeric assistance of the dibenzylamino group in amino aziridines is proposed, and the reaction could take place through aziridinium salt **9** (Scheme 4).[11]

In this way, after the coordination of the aziridine nitrogen to the Lewis acid, an intramolecular ring opening reaction at C-2, with the consequent inversion

(7) (a) Bodenan, J.; Chanet-Ray, J.; Vessiere, R. *Synthesis* **1992**, 288. (b) Dauban, P.; Dodd, R. H. *J. Org. Chem.* **1997**, *62*, 4277. (c) Cantrill, A. A.; Osborn, H. M. I.; Sweeney, J. *Tetrahedron* **1998**, *54*, 2181.

(8) Longer reaction times or the use of 1.5 equiv of BF_3·OEt_2 led to a 3/1 mixture of regioisomers.

(9) Barluenga, J.; Baragaña, B.; Concellón, J. M. *J. Org. Chem.* **1995**, *60*, 6696.

(10) Unpublished results, except for the ring opening of **6** (R^1 = Bn): Concellón, J. M.; Cuervo, H.; Fernández-Fano, R. *Tetrahedron* **2001**, *57*, 8983.

(11) Previously, other *N*,*N*-dibenzylated aziridinium salts were proposed as intermediates in reactions of 2,3-epoxyamines: (a) Liu, Q.; Marchington, A. P.; Boden, N.; Rayner, C. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 511. (b) Liu, Q.; Marchington, A. P.; Rayner, C. M. *Tetrahedron* **1997**, *53*, 15729.

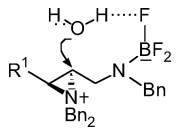
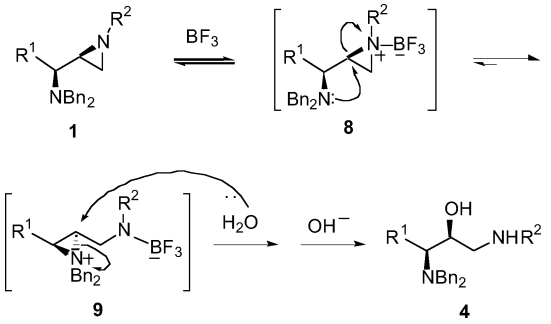


FIGURE 1. Attack to the aziridinium salt **9** at C-2.

SCHEME 4. Proposed Mechanism for Transformation of 1 into 4



of its configuration, would occur by means of the nucleophilic attack of the dibenzylamino group, affording aziridinium salt **9**. Then, water from the hydrolysis process would attack the intermediate compound **9** at C-2, which would suffer the second inversion of configuration, yielding 1,3-diaminoalkan-2-ols **4**.

However, the aziridinium salts **9** with R^1 = Me, and the corresponding intermediate **8**, could be in an equilibrium, although displaced in favor of **9**, wherefore compounds **3a**,**b** were also obtained after hydrolysis.

The total regioselectivity observed in the ring opening of intermediate aziridinium salt **9** with water could be explained by means of formation of a hydrogen bond between water and a fluorine atom of the BF_3 moiety in **9**, as shown in Figure 1. Thus, C-2 would be the carbon most accessible to the oxygen atom of water, and the reaction would take place through this carbon.

In conclusion, we have achieved the ring opening of amino aziridines **1** with different regioselectivity, and in totally stereoselective form, obtaining chiral 2,3-diaminoalkan-1-ols or 1,3-diaminoalkan-2-ols in high yield. At present, we are studying ring opening reactions of amino aziridines **1** with other nucleophiles.

Experimental Section

General Procedure for the Synthesis of 2,3-Diaminoalkan-1-ols 3. A solution of the corresponding amino aziridine **1** (0.2 mmol) and TsOH (0.04 g, 0.2 mmol) in acetonitrile/H_2O (1/0.13 mL) was stirred at reflux temperature for 0.5 h. Then, the reaction was hydrolyzed with an aqueous saturated solution of sodium bicarbonate (5 mL) and extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. Flash column chromatography (silica gel, dichloromethane:MeOH:NH_3 90:1:1) provided pure compound **3**. Yields are given in Table 1.

(−)-(2*R*,3*S*)-2-Benzylamino-3-(dibenzylamino)butan-1-ol (3a): R_f 0.16 (ethyl acetate); $[\alpha]^{20}_D$ −43.0 (*c* 1.08, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.24 (m, 15 H), 3.84 (AB syst., J = 13.2 Hz, 2 H), 3.83 (AB syst., J = 13.2 Hz, 2 × 2 H), 3.79−3.70 (m, 1 H), 2.98 (dd, J = 12.5, 6.8 Hz, 1 H), 2.78 (dd, J = 12.5, 4.8 Hz, 1 H), 2.66−2.59 (m, 1 H), 1.20 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1 (C), 139.1 (2 C), 128.9 (4 CH), 128.3 (4 CH), 128.2 (2 CH), 127.9 (2 CH), 127.0 (2 CH), 126.9 (CH), 65.6 (CH), 64.1 (CH), 54.3 (2 CH_2), 54.2 (CH_2), 46.3 (CH_2), 20.0 (CH_3); IR (neat) 3396, 3321, 1102; HRMS calcd for $C_{25}H_{30}N_2O$ 374.2358, found 374.2331.

(−)-(2*R*,3*S*)-3-Dibenzylamino-2-(propylamino)butan-1-ol (3b): R_f 0.12 (CH_2Cl_2/MeOH/NH_3 90/1/1); $[\alpha]^{25}_D$ −30.0 (*c* 0.96, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.22 (m, 10 H), 3.81 (AB syst., J = 13.2 Hz, 2 × 2 H), 3.77−3.71 (m, 1 H), 2.92 (dd, J = 12.5, 6.8 Hz, 1 H), 2.72 (dd, J = 12.5, 5.1 Hz, 1 H), 2.61−2.53 (m, 3 H), 1.60−1.48 (m, 2 H), 1.18 (d, J = 6.3 Hz, 3 H), 0.98 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3 (2 C), 128.9 (4 CH), 128.2 (4 CH), 127.0 (2 CH), 66.0 (CH), 63.8 (CH), 54.4 (2 CH_2), 52.0 (CH_2), 47.0 (CH_2), 23.0 (CH_2), 20.1 (CH_3), 11.7 (CH_3); IR (neat) 3396, 3314, 1106.

(−)-(2*R*,3*S*)-2-Benzylamino-3-dibenzylamino-5-methylhexan-1-ol (3c): R_f 0.30 (hexane/ethyl acetate 1/1); $[\alpha]^{20}_D$ −29.6 (*c* 1.21, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.24 (m, 15 H), 3.84 (AB syst., J = 13.4 Hz, 2 H), 3.82 (AB syst., J = 13.1 Hz, 2 × 2 H), 3.63−3.58 (m, 1 H), 2.98 (dd, J = 12.5, 6.6 Hz, 1 H), 2.74 (dd, J = 12.5, 4.6 Hz, 1 H), 2.65−2.58 (m, 1 H), 1.97−1.83 (m, 1 H), 1.26−1.22 (m, 2 H), 0.94 (d, J = 6.6 Hz, 3 H), 0.92 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1 (C), 139.1 (2 C), 129.0 (4 CH), 128.4 (2 CH), 128.3 (4 CH), 128.0 (2 CH), 127.1 (2 CH), 127.0 (CH), 67.2 (CH), 63.1 (CH), 54.4 (2 CH_2), 54.2 (CH_2), 46.3 (CH_2), 43.7 (CH_2), 24.8 (CH), 24.0 (CH_3), 21.4 (CH_3); IR (neat) 3414, 3333, 1102. Anal. Calcd for $C_{28}H_{36}N_2O$: C, 80.73; H, 8.71; N, 6.72. Found: C, 80.56; H, 8.73; N, 6.70.

(−)-(2*R*,3*S*)-2-Allylamino-3-dibenzylamino-5-methylhexan-1-ol (3d): R_f 0.12 (hexane/ethyl acetate 1/1); $[\alpha]^{20}_D$ −15.8 (*c* 1.08, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.22 (m, 10 H), 5.96 (ddt, J = 17.1, 10.2, 5.7 Hz, 1 H), 5.26 (dd, J = 17.1, 1.7 Hz, 1 H), 5.18 (dd, J = 10.2, 1.4 Hz, 1 H), 3.83 (AB syst., J = 13.2 Hz, 2 × 2 H), 3.65−3.59 (m, 1 H), 3.28−3.25 (m, 2 H), 2.96 (dd, J = 12.7, 7.0 Hz, 1 H), 2.71 (dd, J = 12.7, 4.4 Hz, 1 H), 2.63−2.56 (m, 1 H), 1.96−1.82 (m, 1 H), 1.25 (t, J = 6.6 Hz, 2 H), 0.93 (d, J = 6.6 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1 (2 C), 136.7 (CH), 128.9 (4 CH), 128.3 (4 CH), 127.0 (2 CH), 115.8 (CH_2), 67.3 (CH), 63.0 (CH), 54.4 (2 CH_2), 52.6 (CH_2), 46.4 (CH_2), 43.7 (CH_2), 24.7 (CH), 24.0 (CH_3), 21.4 (CH_3); IR (neat) 3414, 3331, 1644, 1103; HRMS calcd for $C_{24}H_{34}N_2O$ 366.2671, found 366.2673.

(−)-(2*R*,3*S*)-2-Benzylamino-3-dibenzylamino-4-phenylbutan-1-ol (3e): R_f 0.24 (hexane/ethyl acetate 1/1); $[\alpha]^{20}_D$ −0.5 (*c* 0.64, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.22 (m, 20 H), 3.90−3.83 (m, 1 H), 3.84 (AB syst., J = 13.2 Hz, 2 × 2 H), 3.82 (AB syst., J = 13.1 Hz, 2 H), 3.07−2.96 (m, 2 H), 2.86 (dd, J = 12.5, 4.8 Hz, 1 H), 2.79−2.73 (m, 1 H), 2.60 (dd, J = 14.0, 8.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.9 (C), 139.0 (3 C), 129.2 (2 CH), 129.0 (4 CH), 128.3 (6 CH), 128.1 (2 CH), 128.0 (2 CH), 127.0 (3 CH), 126.0 (CH), 70.7 (CH), 61.8 (CH), 54.4 (2 CH_2), 54.1 (CH_2), 46.3 (CH_2), 40.8 (CH_2); IR (neat) 3404, 3333, 1128; HRMS calcd for $C_{31}H_{34}N_2O$ 450.2671, found 450.3138.

General Procedure for the Synthesis of 1,3-Diaminoalkan-2-ols 4. To a stirred solution of the corresponding amino aziridine **1** (0.2 mmol) in dry acetonitrile (1 mL) under nitrogen atmosphere was added BF_3·OEt_2 (0.025 mL, 0.2 mmol) at room temperature. After being stirred at reflux temperature for 1 h, an aqueous saturated solution of sodium bicarbonate (5 mL) was added and the mixture was stirred at room temperature for 5 min. Then, the aqueous phase was extracted with diethyl ether (3 × 5 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. Flash column chromatography over silica gel (dichloromethane:MeOH:NH_3 90:1:1) provided pure compounds **4**. Yields are given in Table 2.

(+)-(2*S*,3*S*)-1-Benzylamino-3-(dibenzylamino)butan-2-ol (4a): R_f = 0.40 (dichloromethane/MeOH/ NH_3 90/5/1); $[\alpha]^{25}_D$ +18.7 (*c* 0.58, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.24 (m, 15 H), 3.78 (AB syst., J = 13.1 Hz, 2 H), 3.71−3.66 (m, 1 H), 3.62 (AB syst., J = 13.4, 2 × 2 H), 2.84−2.76 (m, 2 H), 2.46 (dd, J = 11.8, 7.3 Hz, 1 H), 1.04 (d, J = 6.6 Hz, 3 H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2 (C), 138.8 (2 C), 128.9 (4 CH), 128.3 (4 CH), 128.1 (2 CH), 127.9 (2 CH), 127.1 (2 CH), 126.6 (CH), 70.4 (CH), 56.0 (CH), 53.9 (CH_2), 53.2 (2 CH_2), 52.0 (CH_2), 8.1 (CH_3); IR (neat) 3387, 3336, 1145. Anal. Calcd for $C_{25}H_{30}N_2O$: C, 80.17; H, 8.07; N, 7.48. Found: C, 80.30; H, 8.12; N, 7.49.

(+)-(2*S*,3*S*)-3-Dibenzylamino-1-(propylamino)butan-2-ol (4b): R_f 0.25 (dichloromethane/MeOH/ NH_3 90/5/1); $[\alpha]^{25}_D$ +30.1 (*c* 0.45, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.22 (m, 10 H), 3.68 (td, J = 7.5, 2.1 Hz, 1 H), 3.58 (AB syst., J = 13.2 Hz, 2 × 2 H), 2.72−2.57 (m, 2 H), 2.56−2.48 (m, 2 H), 2.39 (dd, J = 11.7, 8.3 Hz, 1 H), 1.56−1.39 (m, 2 H), 1.04 (d, J = 6.8 Hz, 3 H), 0.88 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8 (2 C), 128.9 (4 CH), 128.4 (4 CH), 127.1 (2 CH), 70.3 (CH), 56.2 (CH), 53.2 (2 CH_2), 53.0 (CH_2), 51.9 (CH_2), 23.0 (CH_2), 11.6 (CH_3), 8.2 (CH_3); IR (neat) 3380, 3330, 1144; HRMS calcd for $C_{21}H_{30}N_2O$ 326.2358, found 326.2369.

(+)-(2*S*,3*S*)-1-Benzylamino-3-dibenzylamino-4-methylhexan-2-ol (4c): R_f 0.22 (hexane/ethyl acetate 1/1); $[\alpha]^{25}_D$ +2.6 (*c* 0.71, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.23 (m, 15 H), 3.78 (AB syst., J = 13.1 Hz, 2 H), 3.71 (td, J = 7.4, 2.7 Hz, 1 H), 3.62 (AB syst., J = 13.4 Hz, 2 × 2 H), 2.74 (dd, J = 11.7, 2.7 Hz, 1 H), 2.73−2.66 (m, 1 H), 2.56 (dd, J = 11.7, 7.4 Hz, 1 H), 1.73−1.54 (m, 2 H), 1.35−1.26 (m, 1 H), 0.95 (d, J = 6.3 Hz, 3 H), 0.94 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.7 (C), 139.4 (2 C), 128.9 (4 CH), 128.3 (4 CH), 128.2 (2 CH), 128.1 (2 CH), 127.0 (2 CH), 126.8 (CH), 70.5 (CH), 58.3 (CH), 54.0 (2 CH_2), 53.7 (CH_2), 52.4 (CH_2), 35.1 (CH_2), 26.0 (CH), 23.3 (CH_3), 22.7 (CH_3); IR (neat) 3388, 3330, 1144; HRMS calcd for $C_{28}H_{36}N_2O$ 416.2828, found 416.2792.

(+)-(2*S*,3*S*)-1-Allylamino-3-dibenzylamino-4-methylhexan-2-ol (4d): R_f 0.32 (dichloromethane/ MeOH/NH_3 90/5/1); $[\alpha]^{25}_D$ +13.7 (*c* 0.74, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.22 (m, 10 H), 5.89 (ddt, J = 17.4, 10.2, 6.0 Hz, 1 H), 5.15 (dd, J = 17.4, 1.7 Hz, 1 H), 5.07 (dd, J = 10.2, 1.7 Hz, 1 H), 3.68 (AB syst., J = 13.4 Hz, 2 × 2 H), 3.67 (td, J = 8.2, 2.6 Hz, 1H), 3.23−3.20 (m, 2 H), 2.68 (dd, J = 11.7, 2.6 Hz, 1 H), 2.63−2.57 (m, 1 H), 2.46 (dd, J = 11.7, 8.2 Hz, 1 H), 1.72−1.54 (m, 2 H), 1.33−1.24 (m, 1 H), 0.94 (d, J = 6.3 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3 (2 C), 136.6 (CH), 128.9 (4 CH), 128.3 (4 CH), 127.0 (2 CH), 115.6 (CH_2), 70.6 (CH), 58.6 (CH), 53.9 (2 CH_2), 52.6 (CH_2), 52.3 (CH_2), 35.2 (CH_2), 26.1 (CH), 23.3 (CH_3), 22.8 (CH_3); IR (neat) 3388, 3321, 1643, 1145. Anal. Calcd for $C_{24}H_{34}N_2O$: C, 78.64; H, 9.35; N, 7.64. Found: C, 78.80; H, 9.38; N, 7.59.

(+)-(2*S*,3*S*)-1-benzylamino-3-dibenzylamino-4-phenylbutan-2-ol (4e): R_f 0.21 (hexane/ethyl acetate 1/1); $[\alpha]^{25}_D$ +13.2 (*c* 0.78, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.29 (m, 20 H), 3.72 (AB syst., J = 13.4 Hz, 2 × 2 H), 3.70−3.65 (m, 1 H), 3.62 (AB syst., J = 13.1 Hz, 2 H), 3.12 (dd, J = 13.7, 5.1 Hz, 1 H), 3.01−2.93 (m, 1 H), 2.79 (dd, J = 13.7, 7.7 Hz, 1 H), 2.54 (dd, J = 12.0, 2.1 Hz, 1 H), 2.43 (dd, J = 12.0, 7.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1 (C), 139.4 (2 C), 139.1 (C), 129.2 (2 CH), 129.0 (4 CH), 128.4 (2 CH), 128.3 (2 CH), 128.2 (4 CH), 128.1 (2 CH), 127.1 (2 CH), 127.0 (CH), 126.0 (CH), 69.6 (CH), 61.7 (CH), 54.4 (2 CH_2), 53.5 (CH_2), 52.3 (CH_2), 31.5 (CH_2); IR (neat) 3300, 1133. Anal. Calcd for $C_{31}H_{34}N_2O$: C, 82.63; H, 7.61; N, 6.22. Found: C, 82.49; H, 7.67; N, 6.24.

(+)-(2*S*,3*S*)-1-Benzylamino-3-dibenzylamino-4-(*tert*-butyldimethylsilanyloxy)butan-2-ol (4f): R_f 0.43 (dichloromethane/MeOH/NH_3 90/5/1); $[\alpha]^{25}_D$ +25.8 (*c* 0.63, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.26 (m, 15 H), 3.87−3.80 (m, 3 H), 3.83 (AB syst., J = 13.2 Hz, 2 × 2 H), 3.74 (AB syst., J = 13.1 Hz, 2 H), 2.88−2.82 (m, 1 H), 2.76 (dd, J = 12.0, 2.6 Hz, 1 H), 2.48 (dd, J = 12.0, 7.1 Hz, 1 H), 0.95 (s, *9* H), 0.11 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.4 (C), 139.3 (2 C), 129.1 (4 CH), 128.3 (4 CH), 128.2 (2 CH), 128.0 (2 CH), 127.0 (2 CH), 126.6 (CH), 67.0 (CH), 61.2 (CH), 59.5 (CH_2), 54.6 (2 CH_2), 53.8 (CH_2), 52.1 (CH_2), 25.8 (3 CH_3), 18.0 (C), −5.6 (CH_3), −5.8 (CH_3); IR (neat) 3422, 3330, 1091; HRMS calcd for $C_{31}H_{44}N_2O_2Si$ 504.3172, found 504.31858.

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Supporting Information Available: Spectroscopy data for compounds **7** and copies of ^{13}C NMR spectra for compounds **3**, **4**, and **7a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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