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Regio- and Stereoselective C-2 and C-3 Cleavage of 2-(1-Aminoalkyl)aziridines with Alcohols, Carboxylic Acids, and Sodium Iodide

José M. Concellón,* Estela Riego, and José Ramón Suárez

Departamento de Química Orgánica e Inorgánica, Facultad de Química, Universidad de Oviedo, Julián Clavería, 8, 33071 Oviedo, Spain

jmcg@sauron.quimica.uniovi.es

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Ring opening of nonactivated aziridines **1** using several nucleophiles, such as alcohols, carboxylic acids, and sodium iodide, is described. Depending on the nucleophile used, aziridines **1** are cleaved at C-3 or C-2 with total regio- and stereoselectivity, affording chiral 2-alkoxy-1,3-diamines **2** with alcohols, or *O*-acylated-1-hydroxy-2,3-diamines **6** with carboxylic acids in moderate or high yield. In the case of the aziridines derived from phenylalanine, treatment with NaI afford *trans*-4-phenylbut-3-en-1,2-diamines **9**, generating the alkene with total diastereoselectivity. Mechanisms have been proposed to explain these reactions.

Introduction

The ability of aziridines to undergo highly regio- and stereoselective ring-opening reactions gives them great value in organic synthesis.[1] For this reason, a large number of ring-opening reactions of chiral, activated aziridines have been reported.[1c,2] However, to the best of our knowledge, there are a very few examples in the literature concerning the ring opening of nonactivated aziridines.[3]

Recently, we described the synthesis of enantiopure 2-(1-aminoalkyl)aziridines[4] and the ring opening of these nonactivated amino aziridines[5] by water with total regio- and stereoselectivity at C-2 and C-3, obtaining chiral 1,3-diaminoalkan-2-ols and 2,3-diaminoalkan-1-ols, respectively.

Herein, we report a generalization of the ring opening of chiral, nonactivated amino aziridines **1** with other nucleophiles, such as alcohols, carboxylic acids, and sodium iodide.

Results and Discussion

Reaction of 1 with Alcohols. Ring-opening reactions of amino aziridines **1** with different alcohols were carried out in the presence of $BF_3{\cdot}OEt_2$, to activate the aziridine ring.[6] Thus, a solution of nonactivated amino aziridines **1** in the corresponding alcohol was treated with 1 equiv of $BF_3{\cdot}OEt_2$, and heated at reflux for 2 h. The hydrolysis of the reaction mixture led to 2-alkoxy-1,3-diamines **2** in high yields (Scheme 1, Table 1).

The ring-opening reaction of amino aziridines **1** was highly regio- and stereoselective (no others isomers of **2** were detected by ^1H and ^{13}C NMR spectra). In this reaction, the aziridine undergoes an unusual ring opening at C-2, with retention of the configuration at this center.

To establish unambiguously this regio- and stereochemistry, compound **2c** was debenzylated, by reaction with HCO_2H in the presence of Pd/C, and treated with triphosgene, affording the corresponding tetrahydropyrimidin-2-one **3c** (Scheme 2). The ^1H NMR coupling constant between C*H*Bn and C*H*OMe ($J = 7.4$ Hz),[7] and a NOESY experiment on compound **3c** show a cis relative

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(6) $BF_3{\cdot}OEt_2$ is commonly used in Lewis acid-catalyzed ring openings of aziridines. See: (a) Reference 1c. (b) Reference 2g. (c) Bodenan, J.; Chanet-Ray, J.; Vessiere, R. *Synthesis* **1992**, 288. (d) Dauban, P.; Dodd, R. H. *J. Org. Chem.* **1997**, *62*, 4277. (e) Cantrill, A. A.; Osborn, H. M. I.; Sweeney, J. *Tetrahedron* **1998**, *54*, 2181.

(7) The coupling constant of C*H*Bn and C*H*OMe was established by irradiation of signals of ^1H NMR of **3c**. Irradiations at 3.16 and 3.46 (CH_2Ph) transformed the m at 3.75−3.69 (C*H*Bn) into a dd with $J = 7.3$, 5.0 Hz and 7.5, 4.6 Hz, respectively. Irradiation at 3.75−3.69 (C*H*Bn) transformed the t at 3.16 and 3.46 into a d with $J = 4.9$ and 5.0 Hz (CH_2Ph), respectively.

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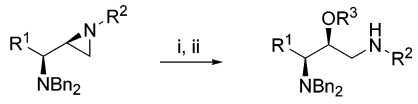
SCHEME 1. C-2 Ring Opening of Amino 1 with Alcohols[a]



1 **2**

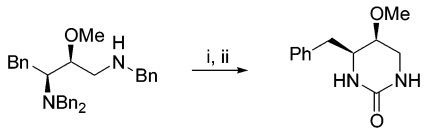
[a] Reagents and conditions: (i) $BF_3{\cdot}OEt_2$, R^3OH, Δ; (ii) $NaHCO_3$, H_2O.

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

entry	product	R^1	R^2	R^3	yield (%)[a]
1	**2a**	Me	Bn	*i*-Pr	78
2	**2b**	*i*-Bu	Bn	Me	80
3	**2c**	Bn	Bn	Me	83
4	**2d**	Bn	Bn	*i*-Pr	88
5	**2e**	Bn	Cy	Me	85

[a] Isolated yield after column chromatography based on the starting amino aziridine **1**.

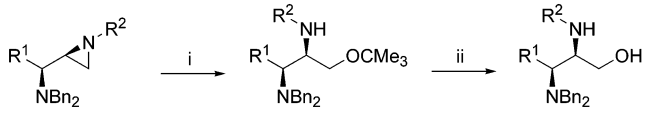
SCHEME 2. Preparation of Tetrahydropyrimidin-2-one 3c[a]



2c **3c**

[a] Reagents and conditions: (i) Pd/C, HCO_2H, MeOH, Δ; (ii) $(Cl_3CO)_2CO$, CH_2Cl_2, 0 °C.

SCHEME 3. Reaction of Aziridine 1 with *tert*-Butyl Alcohol[a]



1 **5** **4**

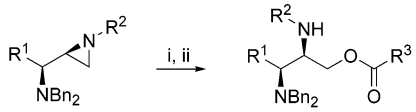
R^1 = *i*-Bu, R^2 = allyl

[a] Reagents and conditions: (i) $BF_3{\cdot}OEt_2$, *t*-BuOH, Δ; (ii) $BF_3{\cdot}OEt_2$ and then $NaHCO_3/H_2O$.

configuration between these hydrogens. This regio- and stereochemistry are in accordance with those observed in the reaction of aziridines **1** with H_2O in the presence of $BF_3{\cdot}OEt_2$.[5]

Reaction of *tert*-butyl alcohol with the amino aziridine **1** with R^1 = *i*-Bu, R^2 = allyl at reflux temperature for 1.5 h afforded a mixture of the 2,3-diaminoalkan-1-ol **4**[5] (55%) and 1-*tert*-butoxy-2,3-diamine **5** (28%). A longer reaction time (15 h) gave the 2,3-diaminoalkan-1-ol **4** as the only one product (73%). These results could be explained by assuming that *tert*-butyl alcohol opens the aziridine ring at C-3 instead of C-2, due to steric hindrance, affording the 1-*tert*-butoxy-2,3-diamine **5**. Under the reaction conditions, compound **5** would be *O*-deprotected by $BF_3{\cdot}OEt_2$, giving 2,3-diaminoalkan-1-ol (Scheme 3). To support this mechanism, compound **5** (R^1 = *i*-Bu, R^2 = allyl) was obtained by reaction of **1** with *tert*-butyl alcohol for 1.5 h at reflux temperature. After purification by column chromatography, **5** was treated with $BF_3{\cdot}OEt_2$ at 0 °C in CH_2Cl_2 for 2 h,[8] affording the corresponding product **4**.

SCHEME 4. C-3 Ring Opening of Amino Aziridines 1 with Carboxylic Acids[a]



1 **6**

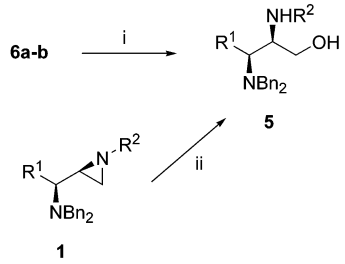
[a] Reagents and conditions: (i) $BF_3{\cdot}OEt_2$, R^3CO_2H, CH_3CN, Δ; (ii) $NaHCO_3/H_2O$.

TABLE 2. C-3 Ring Opening of Amino Aziridines 1 with Carboxylic Acids

entry	product	R^1	R^2	R^3	yield (%)[a]
1	**6a**	Bn	Bn	Me	63
2	**6b**	*i*-Bu	Bn	Me	69
3	**6c**	Bn	Bn	HC=CHPh	58
4	**6d**	*i*-Bu	allyl	Me	57

[a] Isolated yield after column chromatography based on the starting amino aziridine **1**.

SCHEME 5. Reduction of 6a and 6b[a]



[a] Reagents and conditions: (i) $LiAlH_4$, THF, 0 °C; (ii) H_2O/TsOH.

The reaction of amino aziridines **1** was also carried out with alcohols in the presence of *p*-toluenesulfonic acid in 7/1 CH_3CN/ROH, to open the aziridine ring at C-3.[9] However, no reaction of aziridine **1** with ROH was observed.

Reaction of 1 with Carboxylic Acids. The reaction was also performed in the presence of $BF_3{\cdot}OEt_2$ to activate the aziridine ring. Thus, treatment of amino aziridines **1** with different carboxylic acids in refluxing acetonitrile for 2 h afforded *O*-acylated 2,3-diaminoalkan-1-ols **6** in good yields (Scheme 4 and Table 2).

Once more, ^1H and ^{13}C NMR spectra showed the presence of only one isomer, indicating that the regioselectivity of the reaction was total.

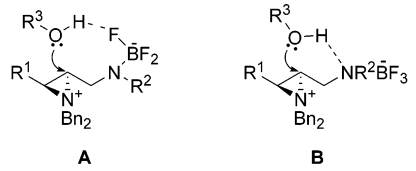
The structure of compounds **6**, as depicted in Scheme 4, was established after reduction of compounds **6a** and **6b** with $LiAlH_4$ (Scheme 5).

By comparison of ^1H and ^{13}C NMR spectra of the reduction products from **6a** and **6b** with the corresponding 2,3-diaminoalkan-1-ols **4** obtained from reaction of **1** with H_2O in the presence of *p*-toluenesulfonic acid,[5] we confirmed that both diamino alcohols are the same.

Mechanism. To explain the different regio- and stereochemistry of the reaction of **1** with alcohols and

(8) The reaction of **5** with $TiCl_4$ at 0 °C in CH_2Cl_2 also affords the alcohol **4**.

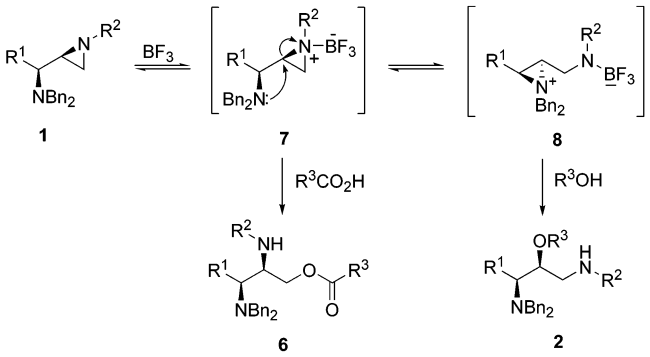
(9) In those conditions, treatment of **1** with H_2O afforded 2,3-diaminoalkan-1-ols. See: Reference 5.



A **B**

FIGURE 1. Attack on the aziridinium salt **8** at C-2.

SCHEME 6. Proposed Mechanism for Transformation of 1 into 2 and 6



carboxylic acids, we propose the mechanism depicted in Scheme 6. After coordination of the aziridine nitrogen to the Lewis acid, an intramolecular ring opening at C-2 by nucleophilic attack of the dibenzylamino group, with subsequent inversion of configuration, would afford the aziridinium salt **8**.[10] Alcohols would react through **8** to afford 2-alkoxy-1,3-diamines **2**, with subsequent second inversion of the configuration at C-2. In the case of *tert*-butyl alcohol the reaction takes place through **7** instead **8**, due to steric hindrance. In the presence of carboxylic acids, the prevalence of **8** may be diminished via protonation of the dibenzylamino group, reducing its ability to open the aziridine to form **8**, and consequently carboxylic acid would react through **7**.

The total regioselectivity observed in the ring opening of intermediate aziridinium salt **8** with different alcohols could be explained by formation of a hydrogen bond between alcohol and a fluorine atom in **8**, as shown in structure **A** in Figure 1, or alternatively between alcohol and the nitrogen (**B** in Figure 1). Thus, the C-2 would be the carbon most accessible to the oxygen atom of the alcohol, and the reaction would take place through this carbon.

Reaction of 1 with Sodium Iodide. The use of NaI as nucleophile in the ring-opening reaction of amino aziridine **1**, in the presence of $BF_3{\cdot}OEt_2$, led to a complex mixture of products when R^1 = Me, *i*-Bu. However, with R^1 = Bn, the treatment of a solution of amino aziridines and $BF_3{\cdot}OEt_2$ in acetonitrile with NaI at reflux temperature for 12 h gave 4-phenylbut-3-en-1,2-diamines **9a** and **9b** (Scheme 7). In this process the double bond was generated with total diastereoselectivity (^{1}H NMR, 300 MHz).

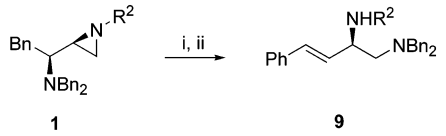
The *E*-stereochemistry of the double bond was established on the basis of the ^{1}H NMR coupling constants between the olefinic protons of compounds **9a** and **9b**. The values of J = 15.8 and 15.9 Hz (**9a** and **9b**, respectively) are in agreement with a trans relationship.

TABLE 3. Reaction of 1 with Sodium Iodide

entry	product	R^2	yield (%)[a]
1	**9a**	Bn	67
2	**9b**	Cy	60

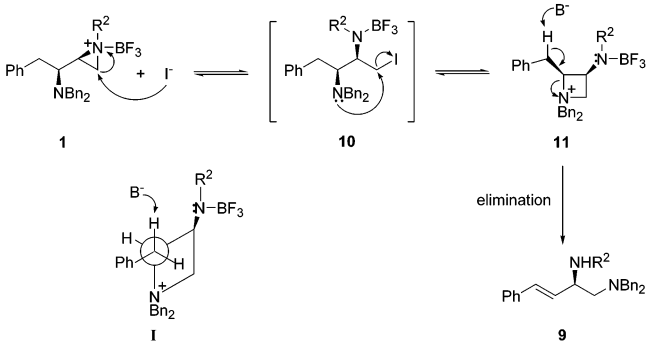
[a] Isolated yield after column chromatography based on the starting amino aziridine **1**.

SCHEME 7. Reaction of 1 with Sodium Iodide[a]



[a] Reagents and conditions: (i) $BF_3{\cdot}OEt_2$, NaI, CH_3CN, Δ; (ii) $NaHCO_3/H_2O$.

SCHEME 8. Proposed Mechanism for Transformation of 1 into 9



Mechanism. The behavior of the amino aziridines **1** with R^1 = Bn when iodide is used, could be explained by assuming that the iodide attacks the aziridine ring at C-3, affording a diamino iodide compound **10**. This intermediate could experience two equilibrated ring-closure process to produce the starting compound **1** or the azetidinium salt **11**, being in equilibrium both species. But, when R^1 = Bn, the intermediate **11** could undergo a spontaneous *β*-elimination, with concurrent ring opening, yielding diamine **9**.

To explain the stereochemistry of the double bond, we tentatively propose an anti elimination by assuming a transition state generated from intermediate **I**, as depicted in Scheme 8.

In conclusion, we have achieved the ring opening of nonactivated amino aziridines **1** with different nucleophiles, such as alcohols, carboxylic acids, and iodide. These transformations were carried out with total regio- and stereoselectivity, obtaining chiral 2-alkoxy-1,3-diamines **2**, *O*-acylated 2,3-diaminoalkan-1-ols **6**, and 4-phenylbut-3-en-1,2-diamines **9** in high yields. The prepared compounds **2**, **6**, and **9** bear two differently substituted amine groups.

Experimental Section

General Procedure of Synthesis of 2-Alkoxy-1,3-diamines 2. To a stirred solution of the corresponding amino aziridine **1** (0.2 mmol) in the corresponding alcohol (1 mL) was

(10) Previously, other *N*,*N*-dibenzylated aziridinium salts are 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.

added $BF_3{\cdot}OEt_2$ (0.025 mL, 0.2 mmol) at room temperature. After stirring at reflux temperature for 2 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 (hexane/EtAcO 3:1) provided pure compounds **2**. (Yields are given in Table 1.)

(2*S*,3*S*)-*N*^{1},*N*^{3},*N*^{3}-Tribenzyl-2-isopropoxybutan-1,3-diamine (2a): $[\alpha]^{25}_D$ −20.7 (*c* 1.45, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.23 (m, 15 H), 3.86 (AB syst, J = 13.4 Hz, 4 H), 3.84−3.60 (m, 2 H), 3.60 (AB syst, J = 13.1 Hz, 2 H), 2.79−2.71 (m, 3 H), 1.19 (d, J = 6.6 Hz, 3 H), 1.17 (d, J = 6.0 Hz, 3 H), 1.16 (d, J = 6.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8 (2 × C), 140.4 (C), 129.0, 128.2, 128.0, 127.9, 126.6 (15 × CH), 73.1 (CH), 68.8 (CH), 61.1 (CH), 55.1 (2 × CH_2), 53.6 (CH_2), 46.2 (CH_2), 23.6 (CH_3), 22.1 (CH_3), 18.2 (CH_3); MS (70 eV, EI) *m*/*z* (%) 416 (M^+, <1), 297 (100), 254 (26), 181 (25), 162 (25); HRMS (70 eV) calcd for $C_{28}H_{36}N_2O$ 416.2828, found 416.2848; IR (neat) 3313, 2970, 2928, 1748, 1494, 1454 cm^{-1}; R_f = 0.38 (hexane/EtOAc 1:1). Anal. Calcd for $C_{28}H_{36}N_2O$: C, 80.73; H, 8.71; N, 6.72. Found: C, 80.76; H, 8.73; N, 6.70.

(2*S*,3*S*)-*N*^{1},*N*^{3},*N*^{3}-Tribenzyl-2-methoxy-5-methylhexan-1,3-diamine (2b): $[\alpha]^{25}_D$ −6.2 (*c* 0.72, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.22 (m, 15 H), 3.82 (AB syst, J = 13.4 Hz, 4 H), 3.70 (AB syst, J = 13.4 Hz, 2 H), 3.54−3.50 (m, 1 H), 3.33 (s, 3 H), 2.95−2.76 (m, 3 H), 1.80 (br s, 1 H), 1.60−1.42 (m, 3 H), 0.93 (d, J = 6.0 Hz, 3 H), 0.91 (d, J = 6.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.6 (C), 140.5 (2 × C), 128.9, 128.8, 128.2, 128.1, 128.0, 126.7 (15 × CH), 80.3 (CH), 58.7 (CH), 57.5 (CH_3), 55.2 (2 × CH_2), 53.7 (CH_2), 45.8 (CH_2), 40.3 (CH_2), 24.6 (CH), 23.3 (CH_3), 22.5 (CH_3); MS (70 eV, EI) *m*/*z* (%) 430 (M^+, 2), 339 (24), 266 (48), 181 (46), 132 (39), 91 (100); HRMS (70 eV) calcd for $C_{29}H_{38}N_2O$ 430.2984, found 430.3007; IR (neat) 3320, 3084, 3062, 3027, 2821, 1603, 1494, 1454 cm^{-1}; R_f = 0.28 (hexane/EtOAc 3:1).

(2*S*,3*S*)-*N*^{1},*N*^{3},*N*^{3}-Tribenzyl-2-methoxy-4-phenylbutan-1,3-diamine (2c): $[\alpha]^{25}_D$ +7.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.19 (m, 20 H), 3.90 (AB syst, J = 13.4 Hz, 4 H), 3.70−3.52 (m, 3 H), 3.29 (s, 3 H), 3.05−2.81 (m, 5 H), 1.78 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5, 139.3 (4 × C), 129.4, 129.0, 128.2, 128.1, 127.9, 126.6, 125.8 (20 × CH), 84.0 (CH), 59.0 (CH), 58.2 (CH_3), 55.2 (2 × CH_2), 53.3 (CH_2), 46.0 (CH_2), 37.9 (CH_2); IR (neat) 3314, 3084, 3061, 3027, 2826, 1602, 1495, 1454 cm^{-1}; R_f = 0.49 (hexane/EtOAc 1:1). Anal. Calcd for $C_{32}H_{36}N_2O$: C, 82.72; H, 7.81; N, 6.03. Found: C, 82.90; H, 7.84; N, 6.01.

(2*S*,3*S*)-*N*^{1},*N*^{3},*N*^{3}-*T*ribenzyl-2-isopropoxy-4-phenylbutan-1,3-diamine (2d): $[\alpha]^{25}_D$ −1.4 (*c* 0.23, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.10 (m, 20 H), 3.93 (AB syst, J = 13.4 Hz, 4 H), 3.90−3.85 (m, 1 H), 3.68 (AB syst, J = 14.7 Hz, 2 H), 3.44−3.37 (m, 1 H), 3.04−2.85 (m, 5 H), 1.78 (br s, 1 H), 1.08 (d, J = 6.0 Hz, 3 H), 0.92 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.7 (2 × C), 140.5 (C), 139.9 (C), 129.4, 129.1, 128.2, 128.1, 128.0, 127.9, 126.7, 126.6, 125.6 (20 × CH), 79.2 (CH), 70.1 (CH), 59.3 (CH), 55.4 (2 × CH_2), 53.6 (CH_2), 45.3 (CH_2), 38.6 (CH_2), 22.7 (CH_3), 22.1 (CH_3); IR (neat) 3331, 3085, 3062, 3027, 1602, 1495 cm^{-1}; R_f = 0.49 (hexane/EtOAc 1:1). Anal. Calcd for $C_{34}H_{40}N_2O$: C, 82.88; H, 8.18; N, 5.69. Found: C, 82.90; H, 8.20; N, 5.71.

(2*S*,3*S*)-*N*^{1}-Cyclohexyl-*N*^{3},*N*^{3}-dibenzyl-2-methoxy-4-phenylbutan-1,3-diamine (2e): $[\alpha]^{25}_D$ +7.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.23 (m, 15 H), 3.85 (AB syst, J = 13.3 Hz, 4 H), 3.66−3.64 (m, 1 H), 3.28 (s, 3 H), 3.00−2.70 (m, 5 H), 2.07−1.98 (m, 1 H), 1.78−1.65 (m, 5 H), 1.32−0.98 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5 (2 × C), 139.1 (C), 129.4, 129.1, 128.0, 126.6, 125.9 (15 × CH), 83.7 (CH), 59.2 (CH), 58.0 (CH_3), 56.2 (CH), 55.1 (2 × CH_2), 43.4 (CH_2), 37.8 (CH_2), 33.4 (2 × CH_2), 26.0 (CH_2), 24.9 (CH_2), 24.8 (CH_2); MS (70 eV, EI) *m*/*z* (%) 456 (M^+, <1), 345 (51), 344 (100), 91 (81); HRMS (70 eV) calcd for $C_{31}H_{40}N_2O$ 456.3135, found 456.3136; IR (neat) 3308, 3027, 2926, 2852, 1609, 1494, 1098 cm^{-1}; R_f = 0.41 (hexane/EtOAc 1:1).

(2*S*,3*S*)-*N*^{2}-Allyl-*N*^{3},*N*^{3}-dibenzyl-1-tert-butoxy-5-methylhexan-2,3-diamine (5): $[\alpha]^{25}_D$ −11.3 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.21 (m, 10 H), 6.02−5.92 (m, 1 H), 5.27−5.13 (m, 2 H), 3.82 (AB syst, J = 13.4 Hz, 4 H), 3.81−3.71 (m, 1 H), 3.32−3.26 (m, 2 H), 3.04−2.88 (m, 2 H), 2.79−2.77 (m, 1 H), 1.91−1.76 (m, 1 H), 1.71 (br s, 1 H), 1.31−1.20 (m, 2 H), 1.09 (s, 9 H), 0.80 (d, J = 6.6 Hz, 3 H), 0.77 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.1 (2 × C), 137.1, 129.4, 129.0, 128.0, 126.6 (11 × CH), 115.5 (CH_2), 73.1 (C), 71.3 (CH), 58.8 (CH), 55.9 (2 × CH_2), 52.4 (CH_2), 45.2 (CH_2), 41.7 (CH_2), 28.8 (3 × CH_3), 24.3 (CH), 23.1 (CH_3), 22.5 (CH_3); MS (70 eV, EI) *m*/*z* (%) 422 (M^+, 2), 352 (72), 296 (44), 279 (52), 91 (100), 57 (51); HRMS (70 eV) calcd for $C_{28}H_{42}N_2O$ 422.3292, found 422.3278; IR (neat) 3063, 3027, 2956, 2868, 2454, 1364, 1193 cm^{-1}; R_f = 0.30 (hexane/EtOAc 1:1).

Preparation of (4*S*,5*S*)-4-Benzyl-5-methoxymethyltetrahydropyrimidin-2-one (3c). A solution of the diamine **2c** (0.3 g, 0.66 mmol) in 30 mL of MeOH/HCO_2H 5% (28.5:1.5), in the presence of Pd/C (0.3 g), was heated 2 h at reflux. Then, the mixture was filtered through Celite and concentrated. The residue was solved in CH_2Cl_2 (10 mL) and washed with a saturated solution of K_2CO_3 (2 × 10 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated.

The obtained debenzylated diamine (0.1 g, 0.52 mmol) was treated with a solution of triphosgene (0.17 g, 0.57 mmol) and NEt_3 (0.10 mL, 1.14 mmol) in CH_2Cl_2 (2 mL) at 0 °C for 12 h. Then, a saturated solution of NH_4Cl (4 mL) was added to quench the reaction. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, and the solvent was removed in vacuo. The product was purified by column chromatography (silica gel, EtOAc) yielding pure compound **3c** (90 mg, 0.41 mmol, 62%): $[\alpha]^{25}_D$ −7.9 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.10 (m, 5 H), 5.13 (br s, 1 H), 5.06 (br s, 1 H), 3.75−3.69 (m, 1 H), 3.46 (t, J = 7.7 Hz, 1 H), 3.41−3.37 (m, 1 H), 3.36 (s, 3 H), 3.16 (t, J = 7.7 Hz, 1 H), 2.80 (2 × dd, J = 6.3, 4.8 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4 (C), 137.1 (C), 129.4 (2 × CH), 128.4 (2 × CH), 126.6 (CH), 84.5 (CH), 58.7 (CH_3), 55.8 (CH), 43.0 (CH_2), 36.3 (CH_2); R_f = 0.10 (EtOAc). Anal. Calcd for $C_{12}H_{16}N_2O_2$: C, 65.43; H, 7.32; N, 12.72. Found: C, 65.48; H, 7.35; N, 12.71.

General Procedure for the Synthesis of *O*-Acylated 2,3-Diaminoalkan-1-ols 6. To a stirred solution of the corresponding amino aziridine **1** (0.2 mmol) in acetonitrile (1 mL) were added $BF_3{\cdot}OEt_2$ (0.025 mL, 0.2 mmol) and the corresponding carboxylic acid (0.6 mmol) at room temperature. After stirring at reflux temperature for 2 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 (hexane/EtOAc 3:1) provided pure compounds **6**. Yields are given in Table 2.

(2*R*,3*S*)-2-(Benzylamino)-3-(dibenzylamino)-4-phenylbutyl acetate (6a): $[\alpha]^{25}_D$ +4.70 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.10 (m, 20 H), 5.46−5.40 (m, 1 H), 3.79 (AB syst, J = 13.4 Hz, 4 H), 3.66 (AB syst, J = 13.4 Hz, 2 H), 3.11−3.01 (m, 3 H), 2.90−2.69 (m, 2 H), 1.96 (s, 3 H), 1.85 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2 (C), 140.2, 140.0, 137.7 (4 × C), 129.3, 129.1, 128.2, 128.1, 128.0, 126.9, 126.8, 126.3 (20 × CH), 75.0 (CH), 59.3 (CH), 55.2 (2 × CH_2), 53.5 (CH_2), 45.1 (CH_2), 38.7 (CH_2), 21.1 (CH_3); MS (70 eV, EI) *m*/*z* (%) 492 (M^+, <1), 401 (9), 373 (85), 91 (100); HRMS (70 eV) calcd for $C_{33}H_{36}N_2O_2$ 492.2777, found 492.2712; IR (neat) 3323, 3062, 3027, 2924, 2846, 1736, 1495, 1454, 1369, 1237 cm^{-1}; R_f = 0.25 (hexane/EtOAc 3:1). Anal. Calcd for $C_{33}H_{36}N_2O_2$: C, 80.45; H, 7.37; N, 5.69. Found: C, 80.49; H, 7.40; N, 5.67.

(2*R*,3*S*)-2-(Benzylamino)-3-(dibenzylamino)-4-methylhexyl acetate (6b): $[\alpha]^{25}_D$ +1.30 (*c* 1.3, $CHCl_3$); ^{1}H NMR (300

MHz, $CDCl_3$) δ 7.42−7.23 (m, 15 H), 5.39−5.36 (m, 1 H), 3.78 (AB syst, J = 13.4 Hz, 4 H), 3.71 (AB syst, J = 13.4 Hz, 2 H), 2.94−2.83 (m, 2 H), 2.68 (dd, J = 11.4, 6.2 Hz, 1 H), 2.11 (s, 3 H), 1.83 (br s, 1 H), 1.74−1.68 (m, 1 H), 1.39−1.33 (m, 2 H), 0.93 (d, J = 8.9 Hz, 3 H), 0.90 (d, J = 6.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (C), 140.3, 140.1, (3 × C), 129.0, 128.2, 128.1, 127.9, 126.8, 126.7 (15 × CH), 72.6 (CH), 59.7 (CH), 55.1 (2 × CH_2), 53.7 (CH_2), 45.2 (CH_2), 41.2 (CH_2), 24.3 (CH), 23.3 (CH_3), 22.0 (CH_3), 21.3 (CH_3); IR (neat) 3323, 3062, 3027, 2924, 2846, 1736, 1495, 1454, 1369, 1237 cm^{-1}; R_f = 0.25 (hexane/EtOAc 3:1). Anal. Calcd for $C_{30}H_{38}N_2O_2$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.55; H, 8.39; N, 6.13.

(2*R*,3*S*)-2-(Benzylamino)-3-(dibenzylamino)-4-phenylbutyl 3-phenylpropionate (6c): $[\alpha]^{25}_D$ +16.3 (*c* 3.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J = 15.9 Hz, 1 H), 7.47−7.10 (m, 25 H), 6.38 (d, J = 15.9 Hz, 1 H), 5.61−5.55 (m, 1 H), 3.83 (AB syst, J = 13.4 Hz, 4 H), 3.66 (AB syst, J = 13.4 Hz, 2 H), 3.20−3.07 (m, 2 H), 2.96−2.74 (m, 3 H), 1.82 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1 (C), 145.0 (CH), 140.3, 140.1, 137.7, 134.1 (5 × C), 130.2, 129.3, 129.1, 128.7, 128.2, 128.1, 128.0, 127.9, 126.9, 126.7, 126.2 (25 × CH), 117.8 (CH), 75.2 (CH), 59.3 (CH), 55.4 (2 × CH_2), 53.5 (CH_2), 45.1 (CH_2), 38.7 (CH_2); MS (70 eV, EI) *m*/*z* (%) 580 (M^+, <1), 330 (13), 300 (91), 238 (39), 131 (80), 91 (100); HRMS (70 eV) calcd for $C_{40}H_{40}N_2O_2$ 580.2090, found 580.3088; IR (neat) 3421, 3027, 2924, 2342, 1707, 1636, 1495, 1452 cm^{-1}; R_f = 0.28 (hexane/EtOAc 3:1).

(2*R*,3*S*)-2-(Allylamino)-3-(dibenzylamino)-5-methylhexyl acetate (6d): $[\alpha]^{25}_D$ +4.0 (*c* 1.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.23 (m, 10 H), 5.89−5.78 (m, 1 H), 5.33−5.27 (m, 1 H), 5.18−5.08 (m, 2 H), 3.76 (AB syst, J = 13.4 Hz, 4 H), 3.15−3.01 (m, 2 H), 2.91−2.84 (m, 1 H), 2.75 (dd, J = 12.0, 7.7 Hz, 1 H), 2.60 (dd, J = 12.2, 6.7 Hz, 1 H), 2.09 (s, 3 H), 1.75 (br s, 1 H), 1.71−1.62 (m, 1 H), 1.45−1.28 (m, 2 H), 0.89 (d, J = 6.6 Hz, 3 H), 0.87 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (C), 140.0 (2 × C), 136.8 (CH), 129.0, 128.1, 126.9 (10 × CH), 115.6 (CH_2), 72.5 (CH), 59.7 (CH), 55.0 (2 × CH_2), 52.0 (CH_2), 45.3 (CH_2), 41.3 (CH_2), 24.3 (CH), 23.4 (CH_3), 21.9 (CH_3), 21.3 (CH_3); MS (70 eV, EI) *m*/*z* (%) 408 (M^+, <1), 338 (100), 321 (76), 296 (74), 236 (36); HRMS (70 eV) calcd for $C_{26}H_{36}N_2O_2$ 408.2777, found 408.2773; IR (neat) 3325, 3028, 2957, 2930, 1733, 1454, 1368, 1240 cm^{-1}; R_f = 0.23 (hexane/EtOAc 3:1).

Reduction of 6a and 6b. To a stirred solution of the corresponding *O*-acylated 1-hydroxy-2,3-diamine **6** (0.2 mmol) in THF (2 mL) was added $LiAlH_4$ (0.2 mL, 0.2 mmol, 1 M in THF) at 0 °C. After stirring at this temperature for 12 h, the reaction was quenched with an aqueous saturated solution of NH_4Cl (5 mL). Then, the mixture was filtered through Celite, and the layers were separated. 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. The products were purified by flash column chromatography over silica gel (hexane/EtOAc 3:1) yielding pure diamino alcohols **4**.[5]

General Procedure for the Synthesis of 4-Phenylbut-3-en-1,2-diamines 9. To a stirred solution of the corresponding amino aziridine **1** (0.2 mmol) in acetonitrile (1 mL) were added BF_3·OEt_2 (0.025 mL, 0.2 mmol) and NaI (0.09 g, 0.6 mmol) at room temperature. After stirring at reflux temperature for 12 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 (hexane/EtOAc 5:1) provided pure compounds **9**. Yields are given in Table 3.

(2*R*)-(*E*)-*N*^{1},*N*^{1},*N*^{2}-Tribenzyl-4-phenylbut-3-en-1,2-diamine (9a): $[\alpha]^{25}_D$ +3.8 (*c* 0.98, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.24 (m, 20 H), 6.55 (d, J = 15.9 Hz, 1 H), 6.01 (dd, J = 15.9, 8.2 Hz, 1 H), 3.71 (AB syst, J = 13.4 Hz, 2 H), 3.60 (AB syst, J = 13.4 Hz, 4 H), 3.39 (ddd, J = 10.0, 8.2, 4.0 Hz, 1 H), 2.76 (dd, J = 12.5, 10.0 Hz,1 H), 2.50 (dd, J = 12.5, 4.0 Hz, 1 H), 2.42 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5 (C), 139.0 (2 × C), 136.9 (C), 131.9, 131.4, 128.8, 128.4, 128.3, 128.2, 128.1, 127.3, 127.0, 126.7, 126.2 (22 × CH), 59.3 (CH_2), 58.7 (2 × CH_2), 58.0 (CH), 51.3 (CH_2); MS (70 eV, EI) *m*/*z* (%) 432 (M^+, 2), 341 (49), 300 (61), 223 (100); HRMS (70 eV) calcd for $C_{31}H_{32}N_2$ 432.2565, found 432.2515; IR (neat) 3308, 3084, 3061, 3026, 1651, 1601, 1494, 1454 cm^{-1}; R_f = 0.28 (hexane/EtOAc 3:1). Anal. Calcd for $C_{31}H_{32}N_2$: C, 86.07; H, 7.44; N, 6.47. Found: C, 86.10; H, 7.44; N, 6.47.

(2*R*)-(*E*)-*N*^{1},*N*^{1},-Dibenzyl-*N*^{2}-cyclohexyl-4-phenylbut-3-en-1,2-diamine (9b): $[\alpha]^{25}_D$ +6.1 (*c* 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.23 (m, 15 H), 6.45 (d, J = 15.8 Hz, 1 H), 5.98 (dd, J = 15.8, 8.0 Hz, 1 H), 3.62 (AB syst, J = 13.5 Hz, 4 H), 2.72−2.64 (m, 1 H), 2.48−2.36 (m, 2 H), 1.98−1.83 (m, 1 H), 1.70−1.60 (m, 3 H), 1.30−0.88 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0 (2 × C), 137.0 (C), 132.9, 130.7, 128.9, 128.4, 128.2, 127.2, 127.0, 126.2 (17 × CH), 59.6 (CH_2), 58.6 (2 × CH_2), 56.3 (CH), 54.5 (CH), 34.9 (CH_2), 33.2 (CH_2), 26.1 (CH_2), 25.2 (CH_2), 25.1 (CH_2); IR (neat) 3309, 3026, 2926, 2851, 2342, 1752, 1494, 1450 cm^{-1}; R_f = 0.14 (hexane/EtOAc 3:1). Anal. Calcd for $C_{30}H_{36}N_2$: C, 84.86; H, 8.55; N, 6.60. Found: C, 84.83; H, 8.57; N, 6.62.

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Supporting Information Available: General methods and ^{1}H and ^{13}C NMR spectra of compounds **2**, **3c**, **5**, **6**, and **9**. This material is available free of charge via Internet at http://pubs.acs.org.

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