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Total Selective Synthesis of Enantiopure O^1-Acyl-3-aminoalkane-1,2-diols by Ring Opening of Aminoepoxides with Carboxylic Acids

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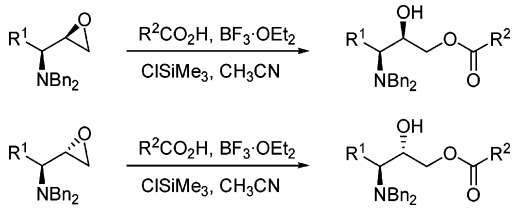

Synthesis of (2*R*,3*S*)- or (2*S*,3*S*)-O^1-acyl-3-aminoalkane-1,2-diols by ring opening of enantiopure (2*R*,1′*S*)- or (2*S*,1′*S*)-2-(1-aminoalkyl)epoxides **1** or **2**, with carboxylic acids in the presence of $BF_3{\cdot}Et_2O$ and chlorotrimethylsilane, is described. The conversion takes place with total selectivity and in good yield. In addition, (2*R*,3*S*)-*O*,*O*-diacyl-3-aminoalkane-1,2-diols **3** were also prepared from reaction of (2*R*,1′*S*)-2-(1-aminoalkyl)epoxides **1** with carboxylic acids under the same reaction conditions and without chlorotrimethylsilane. Mechanisms to explain both transformations are proposed.

Introduction

3-Amino-1,2-alkanediols have proved to be valuable building blocks for the synthesis of various biologically active molecules such as protease inhibitors,[1] glycosphingolipides,[2] or polyhydroxylated nitrogen heterocycles.[3]

A common structural feature of most of these compounds is the absolute *S* configuration of the carbon bonded to the amine function, as in natural α-amino acids, with the absolute configuration of the secondary carbon bearing the hydroxy group *R* or *S*. Accordingly, a general and efficient method to prepare the diastereoisomers (2*R*,3*S*)- or (2*S*,3*S*)-3-aminoalkane-1,2-diols would be desirable.

Despite the efforts devoted to the synthesis of enantiopure 3-amino-1,2-alkanediols,[4] there are no broad scope methodologies for preparing such compounds. Especially, the methods to obtain efficiently both monoprotected syn and anti (2*R*,3*S*)- or (2*S*,3*S*)-3-aminoalkane-1,2-diols in an enantiopure manner are scarce.

Previously, we reported an efficient synthesis of enantiopure (2*R*,1′*S*)- or (2*S*,1′*S*)-2-(1-aminoalkyl)epoxides by total stereoselective reduction with $LiAlH_4$ of the easily available, from natural α-amino acids, α-amino-α′-chloroketones[5] or by highly stereoselective addition of in situ generated iodomethyllithium (from diiodomethane and methyllithium) to α-amino aldehydes.[6]

According to these results, we now report a new and easy methodology to prepare both syn and anti diastereoisomers (2*R*,3*S*)- and (2*S*,3*S*)-O^1-acyl-3-aminoalkane-

(1) Kempf, D.; Sham, H. *Curr. Pharm. Des.* **1996**, *2*, 225−246.
(2) Peterson, M. A.; Polt, R. *J. Org. Chem.* **1993**, *58*, 4309−4314 and references cited therein.
(3) For some syntheses, see: (a) Overhand, M.; Hecht, S. M. *J. Org. Chem.* **1994**, *59*, 4721−4722. (b) Veith, U.; Schwardt, O.; Jäger, V. *Synlett* **1996**, 1181−1183. (c) Zanardi, F.; Battistini, L.; Nespi, M.; Rassu, G.; Spanu, P.; Cornia, M.; Casiraghi, G. *Tetrahedron: Asymmetry* **1996**, *7*, 1169−1180. (d) Hümmer, W.; Dubois, E.; Gracza, T.; Jäger, V. *Synthesis* **1997**, 634−642. (e) Du Bois, J.; Tomooka, C. S.; Hong, J.; Carreira, E. M. *J. Am. Chem. Soc.* **1997**, *119*, 3179−3180.
(4) (a) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599−619. (b) Bunnage, M. E.; Chernega, A. N.; Davies, S. G.; Goodwin, C. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2373. (c) Pastó, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron: Asymmetry* **1995**, *6*, 2329−2342. (d) Pastó, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron: Asymmetry* **1996**, *7*, 243−262 and references cited therein. (e) Meunier, N.; Veith, U.; Jäger, V. *J. Chem. Soc., Chem. Commun.* **1996**, 331−332. (f) Rayner, C. *Synlett* **1997**, 11−21. (g) Bloch, R. *Chem. Rev.* **1998**, *98*, 1407−1438 and references cited therein. (h) Hutin, P.; Larcheveque, M. *Tetrahedron Lett.* **2000**, *41*, 2369−2372. (i) Righi, G.; Chionne, A.; Bonini, C. *Eur. J. Org. Chem.* **2000**, 3127−3131. (j) Righi, G.; Ronconi, S.; Bonini, C. *Eur. J. Org. Chem.* **2002**, 1573−1577. (k) Bickley, J. F.; Roberts, S. M.; Runhui, Y.; Skidmore, J.; Smith, C. B. *Tetrahedron* **2003**, *59*, 5731−5736.
(5) Barluenga, J.; Baragaña, B.; Alonso, A.; Concellón, J. M. *J. Chem. Soc., Chem. Commun.* **1994**, 969−970.
(6) Barluenga, J.; Baragaña, B.; Concellón, J. M. *J. Org. Chem.* **1995**, *60*, 6696−6699.

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SCHEME 1. Ring Opening of (2*R*,1′*S*)-2-(1-Dibenzylaminoethyl)epoxide 1 with H_2O

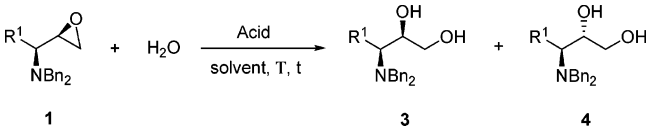


TABLE 1. Ring Opening of (2*R*,1′*S*)-2-(1-Dibenzylaminoethyl)epoxide 1 with H_2O

entry	epoxide	R^1	acid	solvent	*T* (°C)	time (min)	**3**/**4**[a]	yield (%)[b]
1	**1a**	Me	$BF_3{\cdot}Et_2O$	toluene	80	30	3:1	76
2	**1a**	Me	$BF_3{\cdot}Et_2O$	toluene	25	120	1:3.6	74
3	**1a**	Me	*p*-TsOH	CH_3CN	80	30	3:2	79
4	**1c**	Bn	*p*-TsOH	CH_3CN	80	30	1:1	82
5	**2c**	Bn	*p*-TsOH	CH_3CN	80	30	1:1	84

[a] Relation determined by ^1H NMR analysis of the crude products. [b] Isolated yield after column chromatography based on the starting aminoepoxide **1**.

1,2-diols in enantiopure form by a selective opening of the oxirane ring of (2*R*,1′*S*)- and (2*S*,1′*S*)-2-(1-aminoalkyl)epoxides with different carboxylic acids in the presence of $BF_3{\cdot}OEt_2$ and chlorotrimethylsilane. In addition, (2*R*,3*S*)-*O,O*-diacyl-3-aminoalkane-1,2-diols were also obtained by ring opening of (2*R*,1′*S*)-2-(1-aminoalkyl)epoxides with carboxylic acids in the absence of chlorotrimethylsilane under the same reaction conditions. Reaction mechanisms have been proposed to justify the formation of these products.

Results and Discussion

A conceptually simple approach to (2*R*,3*S*)- or (2*S*,3*S*)-3-aminoalkane-1,2-diols would involve the ring opening of (2*R*,1′*S*)- or (2*S*,1′*S*)-2-(1-aminoalkyl)epoxides with H_2O. Consequently, initial attempts to obtain (2*R*,3*S*)-3-aminoalkane-1,2-diols **3** were performed by treating a solution of (2*R*,1′*S*)-2-(1-dibenzylaminoethyl)epoxide **1a** in toluene with H_2O in the presence of $BF_3{\cdot}Et_2O$ at 80 °C or at room temperature. In both cases, a mixture of the diastereoisomers (2*R*,3*S*)- and (2*S*,3*S*)-3-aminobutane-1,2-diol (3:1 and 1:3.6, respectively) was obtained (Scheme 1, Table 1, entries 1 and 2). Different reaction conditions were tested to improve this low stereoselectivity. So, a solution of aminoepoxides **1a** and **1c** in acetonitrile was allowed to react with H_2O in the presence of *p*-toluenesulfonic acid (*p*-TsOH) at reflux temperature; however, a 3:2 and 1:1 mixture of the same diastereoisomersof (2*R*,3*S*)- and (2*S*,3*S*)-3-aminoalkane-1,2-diols was again obtained. The same reaction conditions applied to the anti aminoepoxide **2c** also produced a 1:1 mixture of diastereoisomers (Scheme 1, Table 1).

Synthesis of Enantiopure Aminodiesters 5. As a consequence of the previous results, another alternative method to obtain (2*R*,3*S*)- or (2*S*,3*S*)-3-aminoalkane-1,2-diols was examined. This is the reaction of the corresponding aminoepoxides **1** or **2** with carboxylic acids and further deprotection. So, treatment of **1** with a solution of 3 equiv of acetic or cynnamic acid in acetonitrile in the presence of $BF_3{\cdot}Et_2O$ at reflux temperature for 6 h gave the corresponding aminodiester **5** in high yield (Scheme 2, Table 2). The presence of $BF_3{\cdot}Et_2O$ is essential[7] to carry out the epoxide ring opening; in the absence of $BF_3{\cdot}Et_2O$, unreacted epoxide **1b** was fully recovered after treatment of a solution of **1b** in acetonitrile with acetic acid during 6 h at reflux temperature.

SCHEME 2. Synthesis of Aminodiesters 5

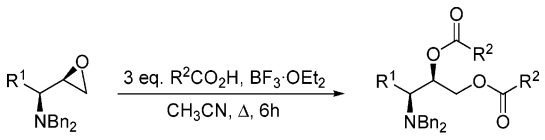
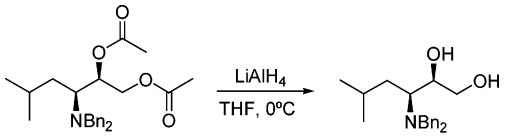


TABLE 2. Synthesis of Aminodiesters 5

entry	**5**	R^1	R^2	yield (%)[a]
1	**5a**	*i*-Bu	Me	78
2	**5b**	Bn	Me	74
3	**5c**	Bn	PhCH=CH	70

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

SCHEME 3. Reduction of 5a



When the aminoepoxide **1c** was treated with a lower amount of acetic acid (1 equiv instead of 3), a 1:1 mixture of the diester **5** and the 4-phenyl-3-aminobutane-1,2-diol, produced by the ring opening of **1c** with H_2O during the final hydrolysis of the reaction, was isolated.[8] This result indicates that the esterification reaction of the alkoxide group generated after the ring opening of the epoxide is faster than the oxirane ring opening.

The ring-opening reaction of aminoepoxides **1** with carboxylic acids was totally selective, as shown by the ^1H NMR (300 MHz) and ^{13}C NMR spectra of the crude reaction mixtures, in which no isomers were observed. Other products such as those derived from the epoxide ring opening by nitrile were not observed, indicating that the reaction of nitrile is slower than that with carboxylic acids.

The structure of compounds **5**, as depicted in Scheme 2, was further conformed after reduction of compound **5a** with $LiAlH_4$ (Scheme 3). The ^1H and ^{13}C NMR spectral data of the obtained aminodiols **3b** were identical to the same materials prepared by a different method.[9]

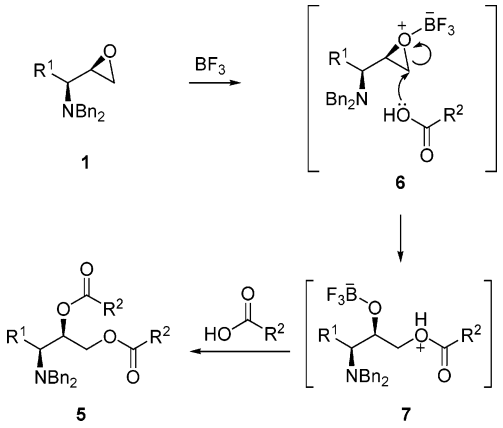
To explain the regio- and stereochemistry of the reaction of **1** with carboxylic acids, we propose the mechanism outlined in Scheme 4. After coordination of the oxirane oxygen with the Lewis acid, a ring opening

(7) To see a recent paper describing the ring opening of aminoepoxides with nitriles to obtain (2*R*,3*S*)- and (2*S*,3*S*)-1,3-diaminoalkane-2-ols, see: Concellón, J. M.; Suarez, J. R.; del Solar, V. *J. Org. Chem.* **2005**, *70*, 7447−7450.

(8) The 4-phenyl-3-aminobutane-1,2-diol was obtained as a 1:1 mixture of diastereoisomers according to the described results of the ring opening of aminoepoxide **1c** with H_2O.

(9) 3-Aminoalkane-1,2-diols can be obtained by successive reaction of (2*R*,1′*S*)- or (2*S*,1′*S*)-2-(1-aminoalkyl)epoxides with ketones in the presence of $BF_3{\cdot}Et_2O$ and further treatment with HCl: Concellón, J. M.; Suárez, J. R.; García-Granda, S.; Díaz, M. R. *Org. Lett.* **2005**, *7*, 247−250.

SCHEME 4. Proposed Mechanism



SCHEME 5. Synthesis of (2*R*,3*S*)-*O*^{1}-Acyl-3-aminoalkane-1,2-diols 8

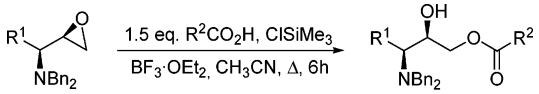


TABLE 3. Synthesis of (2*R*,3*S*)-*O*^{1}-Acyl-3-aminoalkane-1,2-diols 8

entry	8	R^1	R^2	yield (%)[a]
1	**8a**	Me	$CH_3(CH_2)_4$	70
2	**8b**	Me	PhCH=CH	73
3	**8c**	*i*-Bu	Me	63
4	**8d**	*i*-Bu	$CH_3(CH_2)_4$	69
5	**8e**	Bn	Me	71
6	**8f**	Bn	CH_3CH_2CH=CH	64

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

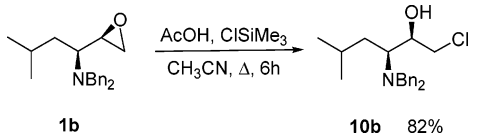
at C-3 by nucleophilic attack of the carboxylic acid would occur. The alcoholate function in intermediate **7** would react with a second equivalent of carboxylic acid to afford the diester **5**. Therefore, no change in the absolute configuration of both stereogenic centers takes place during the reaction.

Synthesis of Enantiopure Aminoesters 8 and 9. Interestingly, when the ring opening of aminoepoxides **1** was carried out with 1.5 equiv of carboxylic acid and in the presence of 1.5 equiv of chlorotrimethylsilane (with $BF_3{\cdot}Et_2O$ at reflux of acetonitrile), (2*R*,3*S*)-*O*^{1}-acyl-3-aminoalkane-1,2-diols **8** were obtained in good yield and with total selectivity (Scheme 5, Table 3).

In the absence of $BF_3{\cdot}Et_2O$, no ring opening of **1** by the carboxylic acids took place and the oxirane ring eventually was opened by a chloride anion generated from chlorotrimethylsilane; so, treatment of **1b** with acetic acid in the presence of chlorotrimethylsilane (without $BF_3{\cdot}Et_2O$) afforded (2*R*,3*S*)-3-amino-1-chloro-6-methylhexan-2-ol **10b** as a single diastereoisomer. This transformation could be explained by taking into account that, after coordination of $ClSiMe_3$ with the oxiranic oxygen of compounds **1**, chloride anions would be generated and could open the oxirane ring by attacking at C-3, affording the corresponding chlorohydrine (Scheme 6).

To investigate the scope of the ring opening by carboxylic acids in the presence of $ClSiMe_3$, we have submitted the other diastereoisomers, (2*S*,3*S*)-2-(1-aminoalkyl)-

SCHEME 6. Synthesis of Chlorohydrine 10b



SCHEME 7. Synthesis of (2*S*,3*S*)-*O*^{1}-Acyl-3-aminoalkane-1,2-diols 9

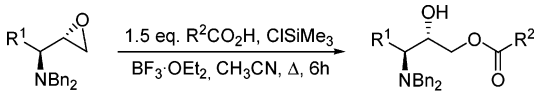
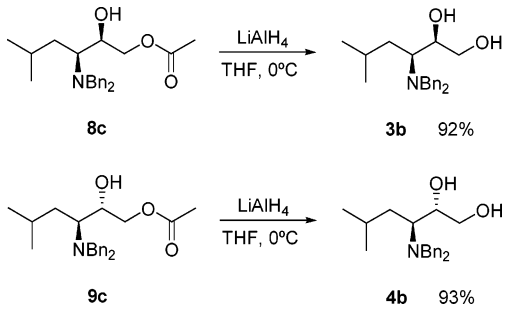


TABLE 4. Synthesis of (2*S*,3*S*)-*O*^{1}-Acyl-3-aminoalkane-1,2-diols 9

entry	9	R^1	R^2	de (%)[a]	yield (%)[b]
1	**9a**	Me	CH_3CH_2CH=CH	>98 (>98)	72
2	**9b**	Me	$CH_3(CH_2)_4$	>98 (>98)	71
3	**9c**	*i*-Bu	Me	92 (91)	66
4	**9d**	*i*-Bu	$CH_3(CH_2)_4$	89 (91)	63
5	**9e**	Bn	Me	90 (92)	61
6	**4f**	Bn	CH_3CH_2CH=CH	91 (92)	60

[a] Diastereoisomeric excess determined by ^{1}H NMR analysis of the crude products **9**; de of the starting aminoepoxides **2** is given in parentheses. [b] Isolated yield after column chromatography based on the starting aminoepoxide **2**.

SCHEME 8. Reduction of 8c and 9c



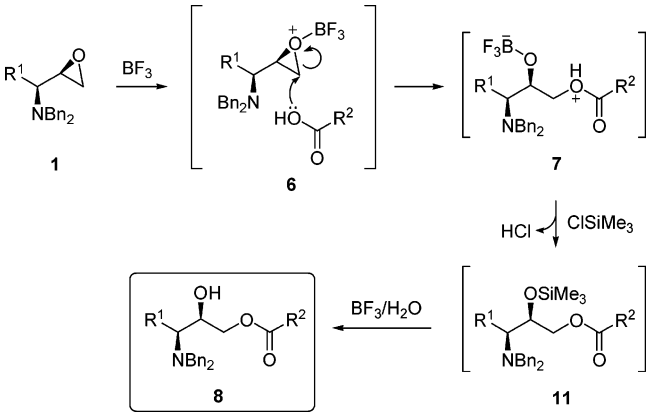
epoxides **2**, to the same reaction conditions, obtaining the corresponding (2*S*,3*S*)-*O*^{1}-acyl-3-aminoalkane-1,2-diols **9** in good yield and with total or very high selectivity (Scheme 7, Table 4).

The selectivity of the reactions was determined by ^{1}H NMR spectroscopy (300 MHz) of the crude mixture of products, showing the presence of a single diastereoisomer **8** (from aminoepoxide **1**) and a mixture of diastereoisomers **9** (from **2**) in the same relationship as that of the starting aminoepoxides **2**. The synthesis of aminodiesters **9** with the same diastereoisomeric excess (de) as that of the starting aminoepoxides **2**[5] was an indirect support of the total selectivity of the ring-opening reaction. After purification of compounds **9** by column chromatography, the major diastereoisomer was isolated as a single stereoisomer.

The absolute configuration of aminoesters **8** and **9** was established after reduction of **8c** and **9c** with $LiAlH_4$ and comparison of the spectroscopic data of the obtained **3b** and **4b** with that recorded from the same diols (Scheme 8).[8]

The regiochemistry of the ester group in compounds **8** and **9** was determined by comparison of the ^{1}H and ^{13}C

SCHEME 9. Proposed Mechanism



NMR data of diester **5a** with the corresponding monoester **8c**. The signals of the methine *CH*−OAc group in the ^{13}C and ^1H NMR spectra of **5a** were shifted upfield in the monoacylated derivative **8c** (from 72.7 and 5.25 to 62.0 and 3.10 ppm, respectively), which indicates that the unprotected hydroxyl function in **8c** is attached to this carbon. Opposite to that, the signals of the methylene CH_2−OAc group in compound **5a** display shifts similar to those of **8c**. This regiochemistry has also been confirmed by the HMBC 2D-NMR experiment performed on **8b**, which showed correlation between the methylene hydrogens of the CH_2OCOCH=CHPh and the carbonyl carbon (CH_2OCOCH=CHPh) and no interaction between the hydrogens of C*H*OH and the carbonyl carbon. Consequently, the acylated hydroxy group of **8b** would be the primary alcohol function, and hence, all these data can support the assigned structures for compounds **8** and **9**.

The reaction seems to be general, and as is shown in Tables 3 and 4, the opening of the oxirane ring can be performed by using aliphatic saturated or unsaturated carboxylic acids with aminoepoxides derived from alanine, phenylalanine, or leucine.

It is noteworthy that the selective monoprotection of diols is difficult to achieve.[10]

The formation of compounds **8** or **9** can be explained by assuming that, after reaction with BF_3, the oxirane ring is opened at C-3 by the carboxylic acid with total selectivity. The alcoholate intermediate **7** would be silylated by chlorotrimethylsilane affording an aminodiol, **11**, with both oxygen atoms protected. The silylated oxygen moiety would be deprotected by the BF_3 during the final hydrolysis to afford the final product **8** (Scheme 9).

Conclusions

We have described an easy synthesis of (2*R*,3*S*)- or (2*S*,3*S*)-O^1-acyl-3-aminoalkane-1,2-diols in high yield and with total or very high stereoselectivity by a selective opening of the oxirane ring of (2*R*,1′*S*)- and (2*S*,1′*S*)-2-(1-aminoalkyl)epoxides with different carboxylic acids in the presence of BF_3·OEt_2 and chlorotrimethylsilane. When the reaction was carried out in the absence of chlorotrimethylsilane, (2*R*,3*S*)- or (2*S*,3*S*)-*O*,*O*-diacyl-3-aminoalkane-1,2-diols were obtained, without epimerization, in high yield. Mechanisms to explain both transformations are proposed.

Experimental Section

General Procedure for the Synthesis of 5. To a stirred solution of the corresponding aminoepoxide **1** (0.2 mmol) in acetonitrile (2 mL) were added BF_3·OEt_2 (0.025 mL, 0.2 mmol) and the corresponding carboxylic acid (3 equiv) at room temperature. After stirring at 80 °C 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 over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Flash column chromatography on silica gel (hexane/EtOAc 20:1) provided pure compounds **5**. Yields are given in Table 1.

(2*R*,3*S*)-*O*,*O*-Diacetyl-3-dibenzylamino-5-methylhexane-1,2-diol (5a): colorless oil; $[\alpha]^{25}_D = -14.3$ (*c* 1.05, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.36−7.26 (m, 10 H), 5.27−5.22 (m, 1 H), 4.29 (dd, J = 11.7, 7.3 Hz, 1 H), 4.12 (dd, J = 6.8, 4.1 Hz, 1 H), 3.91 (d, J = 13.3 Hz, 2 H), 3.44 (d, J = 13.3 Hz, 2 H), 2.92−2.85 (m, 1 H), 2.12 (s, 3 H), 1.93 (s, 3 H), 1.74−1.63 (m, 1 H), 1.53−1.45 (m, 1 H), 1.40−1.29 (m, 1 H), 0.87 (d, J = 6.6 Hz, 3 H), 0.84 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6 (C), 170.2 (C), 139.9 (2 × C), 129.0 (4 × CH), 128.2 (4 × CH), 126.9 (2 × CH), 72.7 (CH), 64.8 (CH_2), 55.0 (2 × CH_2), 54.5 (CH), 33.3 (CH_2), 24.5 (CH), 23.4 (CH_3), 22.1 (CH_3), 21.0 (CH_3), 20.7 (CH_3); MS (70 eV, EI) *m/z* (%) 411 (M^+, <1), 282 (10), 266 (100), 181 (19), 91 (98), 65 (8); HRMS (70 eV) calcd for $C_{25}H_{33}NO_4$ (M^+) 411.2404, found 411.2411; IR (neat) 3027, 2959, 1741, 1493, 1454 cm^{-1}; R_f = 0.60 (hexane/EtOAc 10:1). Anal. Calcd for $C_{25}H_{33}NO_4$: C, 72.96; H, 8.08; N, 3.40. Found: C, 73.08; H, 8.15; N, 3.32.

(2*R*,3*S*)-*O*,*O*-Diacetyl-3-dibenzylamino-4-phenylbutane-1,2-diol (5b): colorless oil; $[\alpha]^{25}_D = -8.7$ (*c* 1.60, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.13 (m, 15 H), 5.11−5.06 (m, 1 H), 4.31 (dd, J = 11.6, 7.3 Hz, 1 H), 4.12 (d, J = 13.3 Hz, 2 H), 4.04 (dd, J = 11.6, 4.4 Hz, 1 H), 3.53 (d, J = 13.3 Hz, 2 H), 3.22−3.10 (m, 2 H), 2.74 (dd, J = 12.7, 8.9 Hz, 1 H), 2.18 (s, 3 H), 1.85 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (C), 169.1 (C), 139.5 (2 × C), 138.8 (C), 129.1 (2 × CH), 128.9 (4 × CH), 128.5 (2 × CH), 128.2 (4 × CH), 127.0 (2 × CH), 126.2 (CH), 72.3 (CH), 64.4 (CH_2), 59.3 (CH), 55.3 (2 × CH_2), 30.6 (CH_2), 21.1 (CH_3), 20.6 (CH_3); MS (70 eV, EI) *m/z* (%) 445 (M^+, 5), 354 (100), 300 (88), 294 (47), 181 (28); HRMS (70 eV) calcd for $C_{28}H_{31}NO_4$ (M^+) 445.2253, found 445.2210; IR (neat) 3062, 3028, 2962, 1742, 1494, 1454 cm^{-1}; R_f = 0.53 (hexane/EtOAc 10:1). Anal. Calcd for $C_{28}H_{31}NO_4$: C, 75.48; H, 7.01; N, 3.14. Found: C, 75.60; H, 6.95; N, 3.21.

(2*R*,3*S*)-*O*,*O*-Dicinamoyl-3-dibenzylamino-4-phenylbutane-1,2-diol (5c): colorless oil; $[\alpha]^{25}_D = -10.9$ (*c* 2.10, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 15.9 Hz, 1 H), 7.56−7.23 (m, 26 H), 6.55 (d, J = 15.9 Hz, 1 H), 6.22 (d, J = 15.9 Hz, 1 H), 5.42−5.35 (m, 1 H), 4.59 (dd, J = 11.5, 7.4 Hz, 1 H), 4.30−4.16 (m, 3 H), 3.62 (d, J = 13.3 Hz, 2 H), 3.32−3.23 (m, 2 H), 2.85 (dd, J = 14.1, 10.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2 (C), 165.8 (C), 145.6 (CH), 144.6 (CH), 139.6 (2 × C), 139.0 (C), 134.3 (C), 134.0 (C), 130.4 (CH), 130.1 (CH), 129.3, 128.9, 128.7, 128.6, 128.5, 128.3, 128.1, 127.9 (20 × CH), 127.1 (2 × CH), 126.2 (CH), 117.7 (CH), 117.5 (CH), 72.2 (CH), 64.5 (CH_2), 59.6 (CH), 55.6 (2 × CH_2), 30.8 (CH_2); MS (70 eV, EI) *m/z* (%) 530 ($M^+ - C_7H_7$, 5), 300 (31), 181 (54), 170 (50), 131 (100), 119 (40); HRMS (70 eV) calcd for $C_{35}H_{32}NO_4$ ($M^+ - C_7H_7$) 530.2331, found 530.2355; IR (neat) 3062, 3028, 2956, 1714, 1634, 1495, 1451 cm^{-1}; R_f = 0.65 (hexane/EtOAc 10:1). Anal. Calcd for $C_{42}H_{39}NO_4$: C, 81.13; H, 6.32; N, 2.25. Found: C, 81.26; H, 6.41; N, 2.16.

(10) Previous transformations of the *N*-Boc aminoepoxide derived from leucine into (2*S*,3*S*)-O^1-acetyl-3-amino-4-methylpentane-1,2-diol have been described: Ohmoto, K.; Okuma, M.; Yamamoto, T.; Kijima, H.; Sekioka, T.; Kitagawa, K.; Yamamoto, S.; Tanaka, K.; Kawabata, K.; Sakata, A.; Imawaka, H.; Nakai, H.; Toda, M. *Bioorg. Med. Chem.* **2001**, *9*, 1307−1323.

General Procedure for the Synthesis of Compounds 8 and 9. To a stirred solution of the corresponding amino-epoxide **1** or **2** (0.2 mmol) in acetonitrile (2 mL) were added $BF_3{\cdot}OEt_2$ (0.025 mL, 0.2 mmol), $ClSiMe_3$ (0.03 mL, 0.22 mmol), and the corresponding carboxylic acid (1.5 equiv) at room temperature. After stirring at 80 °C 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 over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Flash column chromatography on silica gel (hexane/EtOAc 20:1) provided pure compounds **8** and **9**. Yields are given in Tables 3 and 4.

(2*R*,3*S*)-*O*^{1}-Hexanoyl-3-dibenzylaminobutane-1,2-diol (8a): colorless oil; $[\alpha]^{25}_D = -22.2$ (*c* 1.11, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.40−7.27 (m, 10 H), 5.23−5.15 (m, 1 H), 3.93 (d, J = 13.6 Hz, 2 H), 3.78 (dd, J = 11.8, 7.2 Hz, 1 H), 3.57 (dd, J = 8.2, 3.6 Hz, 1 H), 3.38 (d, J = 13.6 Hz, 2 H), 3.11 (dd, J = 5.4, 1.3 Hz, 1 H), 2.39 (apparent q, J = 6.9 Hz, 2 H), 1.73−1.63 (m, 2 H), 1.39−1.29 (m, 4 H), 1.12 (d, J = 6.9 Hz, 3 H), 0.98−0.92 (m 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.1 (C), 139.6 (2 × C), 128.8 (4 × CH), 128.2 (4 × CH), 127.0 (2 × CH), 75.8 (CH), 54.6 (2 × CH_2), 53.6 (CH), 45.3 (CH_2), 34.4 (CH_2), 31.2 (CH_2), 24.6 (CH_2), 22.3 (CH_2), 13.9 (CH_3), 9.1 (CH_3); IR (neat) 3454, 2956, 2902, 1737, 1494, 1454 cm^{-1}; R_f = 0.42 (hexane/EtOAc 10:1). Anal. Calcd for $C_{24}H_{33}NO_3$: C, 75.16; H, 8.67; N, 3.65. Found: C, 75.29; H, 8.76; N, 6.57.

(2*R*,3*S*)-*O*^{1}-(3-Phenylpropenoyl)-3-dibenzylaminobutane-1,2-diol (8b): colorless oil; $[\alpha]^{25}_D = -12.3$ (*c* 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 16.0 Hz, 1 H), 7.55−7.28 (m, 15 H), 6.39 (d, J = 16.0 Hz, 1 H), 4.42 (dd, J = 11.8, 2.3 Hz, 1 H), 4.11 (dd, J = 11.8, 5.4 Hz, 1 H), 3.90 (d, J = 13.1 Hz, 2 H), 3.86−3.81 (m, 1 H), 3.40 (d, J = 13.1 Hz, 2 H), 2.92−2.83 (m, 1 H), 1.17 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7 (C), 144.8 (CH), 138.4 (2 × C), 134.3 (C), 130.1 (CH), 128.9 (4 × CH), 128.7 (2 × CH), 128.5 (4 × CH), 128.0 (2 × CH), 127.2 (2 × CH), 117.7 (CH), 69.5 (CH), 65.6 (CH_2), 54.2 (CH), 53.1 (2 × CH_2), 8.2 (CH_3); IR (neat) 3403, 3028, 2968, 1712, 1638, 1496, 1451 cm^{-1}; R_f = 0.44 (hexane/EtOAc 10:1). Anal. Calcd for $C_{27}H_{29}NO_3$: C, 78.04; H, 7.03; N, 3.37. Found: C, 78.18; H, 7.15; N, 3.29.

(2*R*,3*S*)-*O*^{1}-Acetyl-3-dibenzylamino-5-methylhexane-1,2-diol (8c): colorless oil; $[\alpha]^{25}_D = -17.1$ (*c* 1.47, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.27 (m, 10 H), 4.55 (dd, J = 11.6, 6.2 Hz, 1 H), 4.41 (dd, J = 11.6, 6.2 Hz, 1 H), 4.12 (d, J = 13.5 Hz, 2 H), 3.62 (d, J = 13.5 Hz, 2 H), 3.10 (apparent t, J = 6.2 Hz, 1 H), 2.13 (s, 3 H), 1.91−1.82 (m, 1 H), 1.73−1.62 (m, 2 H), 1.24−1.25 (m, 1 H), 0.88 (d, J = 6.6 Hz, 3 H), 0.79 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (C), 139.5 (2 × C), 129.1 (4 × CH), 128.1 (4 × CH), 127.0 (2 × CH), 62.0 (CH), 61.7 (CH_2), 59.7 (CH), 55.5 (2 × CH_2), 44.3 (CH_2), 24.8 (CH), 23.1 (CH_3), 21.0 (2 × CH_3); MS (70 eV, EI) *m/z* (%) 351 ($M^+ - H_2O$, <1), 300 (10), 282 (100), 266 (54), 148 (8); HRMS (70 eV) calcd for $C_{23}H_{29}NO_2$ ($M^+ - H_2O$) 351.2198, found 351.2166; IR (neat) 3365, 2957, 1745, 1455, 1369 cm^{-1}; R_f = 0.40 (hexane/EtOAc 10:1). Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.89; H, 8.31; N, 3.68.

(2*R*,3*S*)-*O*^{1}-Hexanoyl-3-dibenzylamino-5-methylhexane-1,2-diol (8d): colorless oil; $[\alpha]^{25}_D = -3.6$ (*c* 1.57, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.45−7.23 (m, 10 H), 4.57 (dd, J = 11.5, 5.9 Hz, 1 H), 4.42 (dd, J = 11.3, 5.9 Hz, 1 H), 4.15 (d, J = 13.6 Hz, 2 H), 3.62 (d, J = 13.6 Hz, 2 H), 3.09 (dd, J = 5.9, 5.1 Hz, 1 H), 2.39 (apparent t, J = 7.2 Hz, 2 H), 1.86−1.59 (m, 4 H), 1.40−1.19 (m, 6 H), 0.90 (apparent t, J = 6.5 Hz, 6 H), 0.80 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.5 (C), 139.5 (2 × C), 129.1 (4 × CH), 128.1 (4 × CH), 127.0 (2 × CH), 62.0 (CH), 61.5 (CH_2), 59.8 (CH), 55.5 (2 × CH_2), 44.3 (CH_2), 34.3 (CH_2), 31.2 (CH_2), 24.8 (CH), 24.6 (CH_2), 23.1 (CH_3), 22.2 (CH_2), 20.9 (CH_3), 13.8 (CH_3); MS (70 eV, EI) *m/z* (%) 407 ($M^+ - H_2O$, <1), 338 (67), 267 (44), 181 (100), 148 (8); HRMS (70 eV) calcd for $C_{27}H_{37}NO_2$ ($M^+ - H_2O$) 407.2824, found 407.2813; IR (neat) 3364, 2959, 1740, 1494, 1455 cm^{-1}; R_f = 0.41 (hexane/EtOAc 10:1). Anal. Calcd for $C_{27}H_{39}NO_3$: C, 76.20; H, 9.24; N, 3.29. Found: C, 76.38; H, 9.14; N, 3.36.

(2*R*,3*S*)-*O*^{1}-Acetyl-3-dibenzylamino-4-phenylbutane-1,2-diol (8e): colorless oil; $[\alpha]^{25}_D = +21.1$ (*c* 1.90, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.22 (m, 15 H), 4.51 (dd, J = 11.6, 7.9 Hz, 1 H), 4.27 (d, J = 13.5 Hz, 2 H), 3.94−3.87 (m, 1 H), 3.50 (d, J = 13.5 Hz, 2 H), 3.24−3.14 (m, 4 H), 1.86 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3 (C), 139.3 (2 × C), 138.8 (C), 129.1 (2 × CH), 128.7 (4 × CH), 128.4 (2 × CH), 128.3 (4 × CH), 127.2 (2 × CH), 126.4 (CH), 67.1 (CH_2), 61.1 (CH), 60.4 (CH), 55.8 (2 × CH_2), 30.9 (CH_2), 20.6 (CH_3); MS (70 eV, EI) *m/z* (%) 385 ($M^+ - H_2O$, 3), 330 (100), 300 (46), 270 (14), 181 (8); HRMS (70 eV) calcd for $C_{26}H_{27}NO_2$ ($M^+ - H_2O$) 385.2042, found 385.2071; IR (neat): 3434, 3027, 2932, 1743, 1495, 1454 cm^{-1}; R_f = 0.46 (hexane/EtOAc 10:1). Anal. Calcd for $C_{26}H_{29}NO_3$: C, 77.39; H, 7.24; N, 3.47. Found: C, 77.53; H, 7.46; N, 3.32.

(2*R*,3*S*)-*O*^{1}-Penta-2-enoyl-3-dibenzylamino-4-phenylbutane-1,2-diol (8f): colorless oil; $[\alpha]^{25}_D = +14.5$ (*c* 1.30, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.24 (m, 15 H), 5.56−5.37 (m, 2 H), 4.55 (dd, J = 11.6, 7.9 Hz, 1 H), 4.27 (d, J = 13.5 Hz, 2 H), 3.95−3.85 (m, 1 H), 3.50 (d, J = 13.5 Hz, 2 H), 3.22−3.08 (m, 4 H), 2.82 (apparent d, J = 5.8 Hz, 1 H), 2.22−2.12 (m, 1 H), 1.67 (dd, J = 6.0, 1.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (C), 138.4 (2 × C), 137.9 (C), 128.4 (2 × CH), 128.1 (4 × CH), 127.7 (2 × CH), 127.4 (4 × CH), 127.1 (CH), 126.2 (2 × CH), 125.4 (CH), 121.4 (CH), 66.2 (CH_2), 60.2 (CH), 59.5 (CH), 54.9 (2 × CH_2), 36.6 (CH_2), 30.0 (CH_2), 16.9 (CH_3); MS (70 eV, EI) *m/z* (%) 333 ($M^+ - C_7H_7$, 2), 225 (60), 224 (100), 181 (22), 91 (97); HRMS (70 eV) calcd for $C_{19}H_{43}N_2S$ ($M^+ - C_7H_7$) 321.2359, found 321.2351; IR (neat) 3449, 3027, 2936, 1740, 1602, 1495, 1454 cm^{-1}; R_f = 0.47 (hexane/EtOAc 10:1).

(2*S*,3*S*)-*O*^{1}-Penta-2-enoyl-3-dibenzylaminobutane-1,2-diol (9a): colorless oil; $[\alpha]^{25}_D = +33.3$ (*c* 2.76, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.41−7.24 (m, 11 H), 5.55−5.51 (m, 1 H), 4.66−4.58 (m, 1 H), 4.17−4.12 (m, 2 H), 3.77 (d, J = 13.6 Hz, 2 H), 3.44 (d, J = 13.6 Hz, 2 H), 3.11−2.97 (m, 1 H), 2.90−2.86 (m, 2 H), 1.71 (d, J = 5.0 Hz, 3 H), 1.28 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.8 (C), 139.1 (2 × C), 129.4 (CH), 128.8 (4 × CH), 128.3 (4 × CH), 127.1 (2 × CH), 122.4 (CH), 66.0 (CH_2), 61.5 (CH), 54.7 (CH), 54.1 (2 × CH_2), 37.5 (CH_2), 17.9 (CH_3), 9.7 (CH_3); MS (70 eV, EI) *m/z* (%) 350 ($M^+ - OH$, 2), 322 (11), 255 (13), 224 (100), 181 (11); HRMS (70 eV) calcd for $C_{23}H_{28}NO_2$ ($M^+ - OH$) 350.2120, found 350.2126; IR (neat) 3456, 3029, 2969, 1740, 1494, 1453 cm^{-1}; R_f = 0.39 (hexane/EtOAc 10:1). Anal. Calcd for $C_{23}H_{29}NO_3$: C, 75.17; H, 7.95; N, 3.81. Found: C, 75.32; H, 8.09; N, 3.78.

(2*S*,3*S*)-*O*^{1}-Hexanoyl-3-dibenzylaminobutane-1,2-diol (9b): colorless oil; $[\alpha]^{25}_D = +35.3$ (*c* 2.04, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.35−7.27 (m, 10 H), 4.63−4.50 (m, 1 H), 4.18−4.13 (m, 2 H), 3.64 (d, J = 13.6 Hz, 2 H), 3.44 (d, J = 13.6 Hz, 2 H), 3.08−2.96 (m, 1 H), 2.16 (apparent t, J = 6.9 Hz, 1 H), 1.63−1.53 (m, 2 H), 1.49−1.27 (m, 8 H), 0.91 (t, J = 4.9 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.4 (C), 139.2 (2 × C), 128.8 (4 × CH), 128.7 (4 × CH), 127.0 (2 × CH), 66.6 (CH_2), 61.6 (CH), 54.7 (CH), 54.1 (2 × CH_2), 33.9 (CH_2), 31.1 (CH_2), 24.3 (CH_2), 22.2 (CH_2), 13.9 (CH_3), 9.7 (CH_3); MS (70 eV, EI) *m/z* (%) 366 ($M^+ - OH$, <1), 339 (13), 338 (45), 225 (12), 224 (100); HRMS (70 eV) calcd for $C_{24}H_{32}NO_2$ ($M^+ - OH$) 366.2433, found 366.2433; IR (neat) 3453, 2957, 2902, 1739, 1495, 1454 cm^{-1}; R_f = 0.44 (hexane/EtOAc 10:1). Anal. Calcd for $C_{24}H_{33}NO_3$: C, 75.16; H, 8.67; N, 3.65. Found: C, 75.33; H, 8.74; N, 6.59.

(2*S*,3*S*)-*O*^{1}-Acetyl-3-dibenzylamino-5-methylhexane-1,2-diol (9c): colorless oil; $[\alpha]^{25}_D = +11.1$ (*c* 0.85, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.41−7.28 (m, 10 H), 4.52−4.49 (m, 2 H), 4.28−4.23 (m, 1 H), 3.78 (AB system, J = 13.9, 6.0 Hz, 4 H), 3.06 (apparent q, J = 5.9 Hz, 1 H), 2.14 (s, 3 H), 1.82−1.62 (m, 2 H), 1.53−1.43 (m, 1 H), 0.91 (d, J = 2.3 Hz, 3 H), 0.88 (d, J = 2.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7

(C), 139.3 (2 × C), 128.8 (4 × CH), 128.2 (4 × CH), 127.1 (2 × CH), 61.6 (CH_2), 60.4 (CH), 60.2 (CH), 54.8 (2 × CH), 45.5 (CH_2), 25.0 (CH), 23.2 (CH_3), 21.1 (CH_3), 21.0 (CH_3); MS (70 eV, EI) *m/z* (%) 352 (M^+ − OH, <1), 282 (92), 269 (70), 266 (100); HRMS (70 eV) calcd for $C_{23}H_{30}NO_2$ (M^+ − OH) 352.2277, found 352.2270; IR (neat) 3364, 2958, 1743, 1454, 1368 cm^{-1}; R_f = 0.42 (hexane/EtOAc 10:1). Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.92; H, 8.35; N, 3.65.

(2*S*,3*S*)-*O*¹-Hexanoyl-3-dibenzylamino-5-methylhexane-1,2-diol (9d): colorless oil; $[\alpha]^{25}_D$ = +1.3 (*c* 1.50, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−7.07 (m, 10 H), 4.50 (apparent d, *J* = 5.4 Hz, 1 H), 4.17−4.09 (m, 2 H), 3.84 (d, *J* = 13.7 Hz, 2 H), 3.70 (d, *J* = 13.7 Hz, 2 H), 3.56 (dd, *J* = 17.5, 13.3 Hz, 1 H), 3.05 (apparent q, *J* = 5.6 Hz, 1 H), 2.40−2.33 (m, 3 H), 1.80−1.47 (m, 3 H), 1.41−1.31 (m, 4 H), 0.94 (t, *J* = 6.9 Hz, 3 H), 0.89 (d, *J* = 4.1 Hz, 3 H), 0.87 (d, *J* = 4.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1 (C), 139.3 (2 × C), 128.8 (4 × CH), 128.2 (4 × CH), 127.1 (2 × CH), 61.3 (CH_2), 60.5 (CH), 60.2 (CH), 54.8 (2 × CH_2), 45.4 (CH_2), 34.4 (CH_2), 31.3 (CH_2), 24.9 (CH), 24.6 (CH_2), 23.2 (CH_3), 22.3 (CH_2), 20.9 (CH_3), 13.9 (CH_3); MS (70 eV, EI) *m/z* (%) 354 (M^+− C_5H_{11}, <1), 339 (24), 266 (73), 147 (34), 144 (23), 105 (100); HRMS (70 eV) calcd for $C_{22}H_{28}NO_3$ (M^+ − C_5H_{11}) 354.2069, found 354.2077; IR (neat) 3363, 2957, 1738, 1494, 1454 cm^{-1}; R_f = 0.43 (hexane/EtOAc 10:1). Anal. Calcd for $C_{27}H_{39}NO_3$: C, 76.20; H, 9.24; N, 3.29. Found: C, 76.43; H, 9.16; N, 3.34.

(2*S*,3*S*)-*O*¹-Acetyl-3-dibenzylamino-4-phenylbutane-1,2-diol (9e): colorless oil; $[\alpha]^{25}_D$ = −11.2 (*c* 0.87, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.31−7.12 (m, 15 H), 4.61 (dd, *J* = 12.1, 3.5 Hz, 1 H), 4.48 (dd, *J* = 11.4, 6.9 Hz, 1 H), 4.36−4.29 (m, 1 H), 3.75 (AB system, *J* = 13.6 Hz, 4 H), 3.60−3.51 (m, 1 H), 3.19−3.13 (m, 1 H), 2.70 (dd, *J* = 14.3, 9.1 Hz, 1 H), 2.10 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (C), 139.1 (2 × C), 138.1 (C), 129.3 (2 × CH), 128.8 (4 × CH), 128.4 (2 × CH), 128.3 (4 × CH), 127.1 (2 × CH), 126.7 (CH), 62.0 (CH), 61.2 (CH_2), 59.5 (CH), 54.7 (2 × CH_2), 42.8 (CH_2), 21.0 (CH_3); MS (70 eV, EI) *m/z* (%) 403 (M^+, <1), 386 (15), 330 (29), 282 (100); HRMS (70 eV) calcd for $C_{26}H_{29}NO_3$ (M^+) 403.2147, found 403.2161; IR (neat) 3430, 3062, 3028, 1741, 1495, 1454 cm^{-1}; R_f = 0.48 (hexane/EtOAc 10:1). Anal. Calcd for $C_{26}H_{29}NO_3$: C, 77.39; H, 7.24; N, 3.47. Found: C, 77.50; H, 7.39; N, 3.35.

(2*S*,3*S*)-*O*¹-Penta-2-enoyl-3-dibenzylamino-4-phenylbutane-1,2-diol (9f): colorless oil. $[\alpha]^{25}_D$ = −5.8 (*c* 1.80, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.39−7.21 (m, 16 H), 5.68−5.60 (m, 1 H), 4.72−4.51 (m, 2 H), 4.30−4.11 (m, 2 H), 3.62 (AB system, *J* = 13.7 Hz, 4 H), 3.59−3.52 (m, 1 H), 3.20−3.02 (m, 2 H), 2.67 (dd, *J* = 14.1, 9.3 Hz, 1 H), 1.72 (d, *J* = 4.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9 (C), 139.0 (2 × C), 138.1 (C), 129.2 (2 × CH), 128.8 (4 × CH), 128.4 (2 × CH), 128.3 (5 × CH), 127.1 (2 × CH), 126.7 (CH), 122.4 (CH), 61.9 (CH_2), 61.3 (CH), 59.5 (CH), 54.7 (2 × CH_2), 42.7 (CH_2), 38.2 (CH_2), 17.9 (CH_3); MS (70 eV, EI) *m/z* (%) 425 (M^+ − H_2O, 1), 370 (21), 339 (26), 338 (81), 323 (27), 322 (100); HRMS (70 eV) calcd for $C_{29}H_{31}NO_2$ (M^+ − H_2O) 425.2355, found 425.2354; IR (neat)3414, 3063, 2960, 1737, 1495, 1454 cm^{-1}; R_f = 0.50 (hexane/EtOAc 10:1). Anal. Calcd for $C_{29}H_{33}NO_3$: C, 78.52; H, 7.50; N, 3.16. Found: C, 78−72; H, 7.36; N, 3.02.

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Supporting Information Available: ^{13}C NMR spectra of compounds **5**, **8**, and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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