

8.8 Hz, 1 H, W2), 7.31 (s, 1 H, 1b), 7.15 (d,  $J = 8.6$  Hz, 1 H, 1f), 7.06 (d,  $J = 8.7$  Hz, 1 H, 1e), 6.93 (d,  $J = 8.3$  Hz, 2 H, 2b and 2f), 6.85 (d,  $J = 8.2$  Hz, 1 H, W1), 6.70 (t,  $J = 2.1$  Hz, 1 H, 3d), 6.61 (s, 1 H, 3b), 6.60 (d,  $J = 8.5$  Hz, 2 H, 2c and 2e), 6.22 (s, 1 H, 3f), 5.31 (d,  $J = 7$  Hz, 1 H, X3), 5.18 (d,  $J = 8.2$  Hz, 1 H, X1), 4.63 (ddd,  $J = 10.0, 8.8, 5.2$  Hz, 1 H, X2), 4.01 (m, 2 H,  $-\text{OCH}_2\text{CH}_3$ ), 3.76 (s, 3 H,  $\text{OCH}_3$ ), 3.74 (s, 3 H,  $\text{OCH}_3$ ), 2.84 (dd,  $J = 13.6, 10.0$  Hz, 1 H, Z2), 2.55 (dd,  $J = 13.6, 5.2$  Hz, 1 H, Z2'), 1.37 (s, 9 H, Boc), 1.08 (t,  $J = 7.0$  Hz,  $\text{CH}_2\text{CH}_3$ ).  $^{13}\text{C}$  NMR (DMSO- $d_6$ , 50 MHz):  $\delta$  169.69, 169.51, 168.89, 160.60, 159.05, 155.72, 154.32, 149.90, 142.75, 140.84, 131.80, 129.90, 127.48, 121.31, 120.28, 114.97, 112.96, 108.56, 103.51, 102.69, 78.37, 61.31, 55.84, 55.72, 55.49, 53.44, 36.81, 28.13, 13.81. IR (KBr):  $\nu_{\text{max}}$  3500–3200, 3000, 1740, 1695, 1670, 1630, 1620, 1590, 1520, 1375, 1275, 1142, 1130, 1060, 1040, 870, 845, 690  $\text{cm}^{-1}$ . MS (EI):  $m/e$  549 (fragment ion,  $\text{M}^+ - \text{Boc}$ ).

Anal. Calcd for  $\text{C}_{34}\text{H}_{39}\text{N}_3\text{O}_{10}$ : C, 62.85; H, 6.05; N, 6.47. Found: C, 62.80; H, 6.00; N, 6.49.

**Acknowledgment.** We thank Dr. Rama Rao for his keen interest and encouragement. We also thank Dr. J.

A. R. P. Sharma for helping us to draw the ball and stick representation of 2.

**Registry No.** 1, 61036-62-2; 2, 143145-51-1; 3, 99-10-5; 4, 2150-44-9; 5, 19520-74-2; 6, 129866-90-6; 7, 143145-52-2; 8, 143145-53-3; 9, 143145-54-4; 10, 143145-55-5; 11, 143145-56-6; 12, 143145-57-7; 13, 143145-58-8; 14, 143145-58-8; 15, 143145-60-2; 16, 143145-61-3; 17, 143145-62-4; 18, 143145-63-5; 19, 143145-64-6; 20, 143145-65-7; 21, 143234-79-1; 22, 143145-66-8; 23, 143145-67-9; 24, 143145-68-0; 25, 143171-01-1; 26, 143145-69-1; 27, 143145-70-4; 28, 143171-02-2; Z-D-Tyr-OH, 20989-17-7; 4-MeOC<sub>6</sub>H<sub>4</sub>CHO, 123-11-5; HS(CH<sub>2</sub>)<sub>3</sub>SH, 109-80-8; Me<sub>3</sub>SiCH<sub>2</sub>CH<sub>2</sub>OH, 2916-68-9; (R)-H<sub>2</sub>NCH(Ph)CH<sub>2</sub>OH, 56613-80-0; (S)-H<sub>2</sub>NCH(Ph)CH<sub>2</sub>OH, 64205-12-5.

**Supplementary Material Available:**  $^1\text{H}$  NMR spectra of 4–9 and 12 and both  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of 10, 14, 17, 18, 22, 25, and 2 (21 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

## Aluminoxy Acetals from $\alpha$ -Amino Esters: Chirality Transfer via Sequential Addition of Hydride and C-Nucleophiles. 2-Amino Alcohols and Sphingosines<sup>†</sup>

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The reaction of  $\alpha$ -imino esters (O'Donnell's Schiff bases) with aluminum hydrides to produce acetal-like intermediates and subsequent reaction with carbon nucleophiles has been studied. Treatment of optically pure imine-protected amino esters with  $\text{iBu}_2\text{AlH}$  or  $\text{iBu}_2\text{AlH} \cdot \text{Bu}_3\text{Al}$ , followed by  $\text{RMgX}$  or  $\text{RLi}$  provided *threo*-2-amino alcohols in high yield (73–85%) and excellent “syn” stereoselectivity (8:1 to >20:1, *threo* or *like* product preferred). Use of nonpolar solvents ( $\text{CH}_2\text{Cl}_2$ –hexane) provided the highest stereoselectivities. Use of the less-reactive  $\text{iBu}_2\text{AlH} \cdot \text{Bu}_3\text{Al}$  complex lowered the amount of undesired primary alcohol products observed. Thermally labile aluminoxy acetal intermediates were observed by  $^1\text{H}$  NMR and were trapped with *N*-(trimethylsilyl)imidazole to produce relatively stable monosilyl acetals (mixed acetals). Alanine-derived Schiff bases 2a–e showed a correlation between the steric bulk of the ester and *threo* selectivity. The presence of THF reduced this correlation, suggesting the C-nucleophile addition involves a Lewis acid-assisted  $\text{S}_{\text{N}}2$ -like displacement of the aluminoxy acetal or displacement of a tight-ion pair. In addition to the synthesis of optically pure aryethanolamines 6a–d from representative amino acids, *threo*-sphingosines 8a–d were synthesized from L-serine-derived Schiff base 4b, and 1-deoxy-*threo*-sphingosines 9a–d were synthesized from L-alanine in a similar fashion. Experimental details are provided.

### Introduction

As part of our program for the development of methods for the synthesis of complex carbohydrates, we became interested in the synthesis of sphingosines (Scheme I). Sphingosines<sup>2</sup> and their derivatives (cf. ceramides, cerebrosides, glycosphingolipids, gangliosides, and their lyso derivatives)<sup>3</sup> are known to play diverse roles in many biological systems. Glycosphingolipids influence cell metabolism in vertebrates, as well as in lower organisms (fungi).<sup>7c</sup> Galactosyl ceramide has recently been shown to be a receptor for HIV binding in cells lacking the CD4 receptor.<sup>4e</sup> Analogs of glycosphingolipids have been the

subject of much interest as inhibitors of influenza-induced sialidase activity, as well as endoglycoceramidase inhib-

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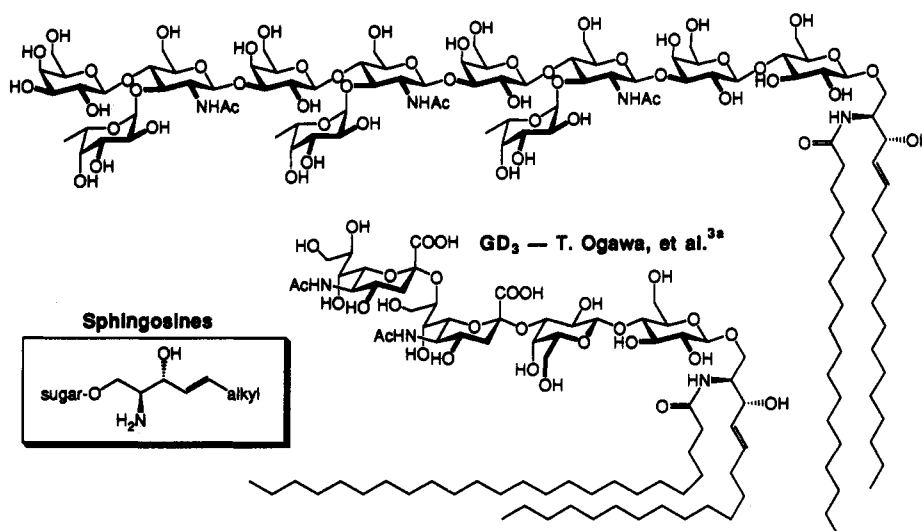
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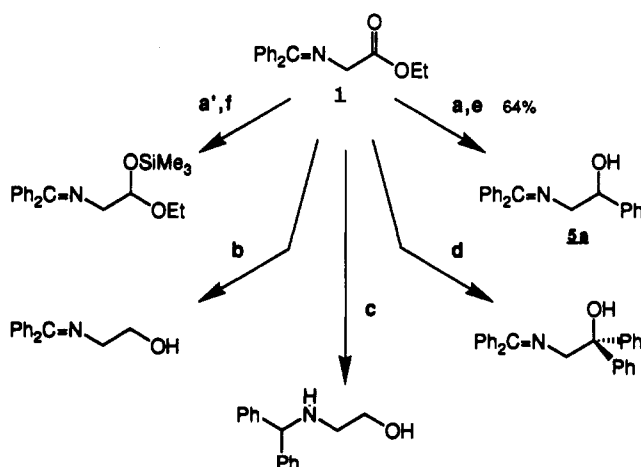
<sup>†</sup> This paper is dedicated to Professor Gilbert J. Stork on the occasion of his 70th birthday.

<sup>‡</sup> University of Arizona Undergraduate Biology Research Program participant, funded in part by a grant from the Howard Hughes Medical Institute.

Scheme I  
Antigen Le<sub>x</sub> — Nicolaou, et al.<sup>3b</sup>



Scheme II<sup>a</sup>



<sup>a</sup> (a) 2 iBu<sub>2</sub>AlH/CH<sub>2</sub>Cl<sub>2</sub>/-78 °C; (a') iBu<sub>2</sub>AlH-iBu<sub>2</sub>Al/CH<sub>2</sub>Cl<sub>2</sub>/-78 °C; (b) 2.5 iBu<sub>2</sub>AlH/CH<sub>2</sub>Cl<sub>2</sub>/0 °C/4 h; (c) 5 iBu<sub>2</sub>AlH/CH<sub>2</sub>Cl<sub>2</sub>/rt/16 h; (d) 3PhMgBr/Et<sub>2</sub>O/rt/1 h; (e) 3PhMgBr/Et<sub>2</sub>O/-78 °C → rt; (f) TMS-imidazole.

itors.<sup>4a</sup> Perhaps most importantly, sphingosines and their derivatives have been shown to influence the transfer of

information between developing vertebrate cells.<sup>4</sup>

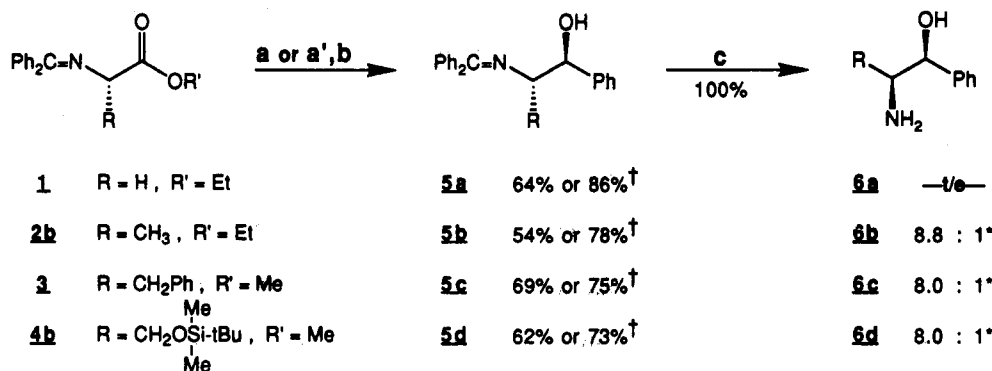
While several methods for the synthesis of optically pure sphingosines have been utilized,<sup>7</sup> one of the most straightforward approaches is based on the use of L-serine as a source of chirality. In this approach, suitably protected L-serine esters are converted to their corresponding  $\alpha$ -amino aldehyde and reacted with various carbon nucleophiles. While optically active  $\alpha$ -amino aldehydes derived from their corresponding  $\alpha$ -amino acids are potentially useful in a number of synthetic contexts,<sup>8</sup> these

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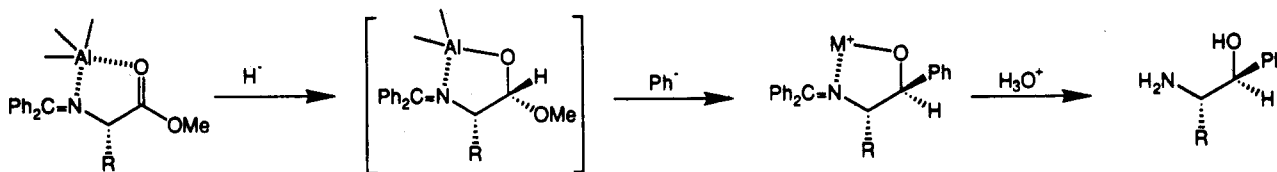
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Scheme III<sup>a</sup>

<sup>a</sup> (a) 2 equiv of  $\text{iBu}_2\text{AlH}/\text{CH}_2\text{Cl}_2/-78^\circ\text{C}$ ; (a') 1 equiv of  $\text{iBu}_2\text{AlH}-\text{Al}(\text{iBu})_3/\text{CH}_2\text{Cl}_2/-78^\circ\text{C}$ ; (b) 3 equiv of  $\text{PhMgBr}/\text{Et}_2\text{O}/-78^\circ\text{C} \rightarrow 0^\circ\text{C}$ ; (c)  $\text{H}_3\text{O}^+$ . <sup>†</sup>Yield using method a'. \**threo/erythro* ratio by NMR.

Scheme IV



methods often suffer from configurational instability (enolization) under a variety of reaction conditions.<sup>9</sup> In addition, stereoselectivities in these reactions are often modest at best.<sup>6n,7a-g,11</sup>

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Newman<sup>7a</sup> was the first to attempt the stereoselective addition of carbon nucleophiles to a protected serine aldehyde derivative. Since then, there have been a number of syntheses based on this approach. The most notable and widely used example is that developed by Garner<sup>7c-e</sup> which uses a BOC-protected oxazolidine to protect both the hydroxyl and amino functionality. Garner's method is attractive in that it avoids the racemization problems typically associated with this type of reaction. Another widely applicable approach to the protection of  $\alpha$ -amino aldehydes which avoids the problem of enolization has been used by Rapoport, and it employs the 9-phenyl-fluorenyl blocking group for the amine.<sup>10,11</sup>

It is clear that new diastereoselective methods for the synthesis of  $\beta$ -amino alcohols from  $\alpha$ -amino acid derivatives which are more configurationally stable than  $\alpha$ -amino aldehydes would be useful. Studies performed in our laboratory have revealed that sequential treatment of O'Donnell's Schiff base esters<sup>16</sup> with  $\text{iBu}_2\text{AlH}$  or

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$i\text{Bu}_3\text{Al}\cdot i\text{Bu}_2\text{AlH}$  and  $\text{PhMgBr}$  provide the corresponding  $\alpha$ -amino alcohols in excellent chemical and stereochemical yield. Stereoselectivities were at least 8:1 in favor of the *threo* (*syn* or *like*) isomer when either  $i\text{Bu}_2\text{AlH}$  or  $i\text{Bu}_3\text{Al}\cdot i\text{Bu}_2\text{AlH}$  were used as hydride source. Chemical yields were markedly superior for the  $i\text{Bu}_3\text{Al}\cdot i\text{Bu}_2\text{AlH}/\text{PhMgBr}$  case. Stereoselectivities increased to greater than 15:1 were observed when alkyllithium reagents in hexane were substituted for the Grignard reagents. Since both hydride and Grignard or alkyllithium reagents were added to the reaction mixture at  $-78^\circ\text{C}$ , the racemization problems associated with isolating the intermediate  $\alpha$ -amino aldehyde have been avoided. Evidence obtained in this laboratory suggests that the  $\alpha$ -amino aldehyde resulting from DIBAL reduction of the ester is *not* the reactive species. Instead, the thermally labile aluminoy acetal<sup>24h</sup>

generated by delivery of one hydride to the chelating imino ester is shown to be the reactive intermediate. This conclusion is supported by a study of the directing ability of bulky ester groups, as well as the low-temperature stability and trapping of the intermediate aluminoy acetals. Details of these experiments as well as the application of this methodology in the stereoselective synthesis of *threo*-sphingosines are presented.

***threo*-1-Arylethanolamines.** Preliminary experiments were performed with the commercially available Schiff base 1 to determine the reactivity of the imine moiety toward aluminum hydrides and Grignard reagents (Scheme II). The hindered imine bond proved to be remarkably stable toward  $i\text{Bu}_2\text{AlH}$  in  $\text{CH}_2\text{Cl}_2$  at  $-78^\circ\text{C}$  and totally inert toward  $\text{PhMgBr}$  in  $\text{Et}_2\text{O}$ . At higher temperatures (e.g. rt)  $i\text{Bu}_2\text{AlH}$  reduced the  $\text{Ph}_2\text{C}=\text{N}$  group to  $\text{Ph}_2\text{CH}-\text{NH}$ , but only after the ester was completely reduced to the primary alcohol. In the absence of added  $\text{PhMgBr}$ , reduction to the aluminoy acetal<sup>18</sup> was extremely slow, as indicated by the reaction with TMS-imidazole to provide the monosilyl acetal. Even after 30 h at  $-78^\circ\text{C}$ , reduction of the chelating ester 1 was not complete in the absence of  $\text{RLi}$  or  $\text{RMgX}$ . Treatment of 1 with 2 equiv of  $i\text{Bu}_2\text{AlH}$  in  $\text{CH}_2\text{Cl}_2$  at  $-78^\circ\text{C}$  for 1 h, followed by 3 equiv of  $\text{PhMgBr}$  in  $\text{Et}_2\text{O}$ , and warming to rt afforded the crystalline secondary alcohol 5a in 64% yield after aqueous workup. Thus, sequential addition of  $\text{H}^-$  followed by  $\text{Ph}^-$  to chelating Schiff base esters was shown to be plausible.

The diastereoselectivity of the reaction with  $i\text{Bu}_2\text{AlH}$  and  $\text{PhMgBr}$  was examined using the Schiff base esters derived from L-alanine, 2b, L-phenylalanine, 3, and L-serine, 4b (Scheme III). It was possible to isolate either the protected  $\beta$ -amino alcohols 5a-d by quenching the reaction with  $\text{NaHCO}_3$  or the known phenylethanolamines<sup>19</sup> 6a-d by an acidic workup. In each case the reaction was found to be highly *threo* selective (Scheme III), the two byproducts consisting of the *erythro* isomer, and the primary alcohol from overreduction. The sense of the stereocontrol may be predicted by invoking the cyclic Cram chelate model<sup>20</sup> for initial hydride delivery to the ester, followed by subsequent inversion of the resulting aluminoy acetal by the incoming nucleophile (Scheme IV). The solvent dependence of the reaction supports this mechanistic interpretation (*vide infra*).

**Solvent Effects and Mechanistic Implications.** Two equivalents of  $i\text{Bu}_2\text{AlH}$  were required for complete conversion of the Schiff base esters; use of lesser amounts resulted in recovery of unreacted starting material.<sup>21</sup> Unfortunately, use of 2 equiv of  $i\text{Bu}_2\text{AlH}$  resulted in the formation of significant amounts of overreduced primary alcohols. We reasoned that the additional  $\text{H}^-$  from the second equivalent of DIBAL was competing with  $\text{Ph}^-$  for the electrophilic aluminoy acetal (aldehyde) in the alkylation step. The simplest solution to the overreduction problem proved to be the use of a 1:1 mixture of  $i\text{Bu}_2\text{AlH}$  and  $i\text{Bu}_3\text{Al}$ ,<sup>22</sup> which resulted in a 20–30% increase in yield of the desired product with a corresponding decrease in the amount of undesired primary imino alcohol. This reagent is stable for months in neat form or as a solution

(20) (a) Cram, D. J.; Kopecky, K. R. *J. Am. Chem. Soc.* 1959, 81, 1224. (b) Duhamel, P.; Duhamel, L.; Gralak, J. *Tetrahedron Lett.* 1972, 2329. (c) Still, W. C.; McDonald, J. H. *Tetrahedron Lett.* 1980, 1031. (d) Keck, G. E.; Boden, E. P. *Tetrahedron Lett.* 1984, 25, 265, 1879, 1883. (e) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* 1984, 23, 556. (f) Frye, S. V.; Eliel, E. L.; Cloux, R. *J. Am. Chem. Soc.* 1987, 109, 1862. (g) Nichols, M. A.; McPhail, A. T.; Arnett, E. M. *J. Am. Chem. Soc.* 1991, 113, 6222. As was pointed out by a very astute referee, probably the first conscious recognition of chelation control in the reduction of  $\alpha$ -amino ketones was by Sorm et al. who reduced derivatives of dehydrochloramphenicol using Al-catalyzed Meerwein-Ponndorf-Verley reaction conditions. These reactions displayed either  $\alpha$ - or  $\beta$ -chelation control, depending on the protecting groups: (h) Sicher, J.; Svoboda, M.; Hrdá, M.; Rudinger, J.; Sorm, F. *Collect. Czech. Chem. Commun.* 1953, 18, 487–499.

(21) Similar bidentate ligands are known to form planar, five-membered cyclic complexes of either 1:1 or 2:1 stoichiometry with aluminum alkyls. Examples of both 5-coordinate aluminum alkyls have been characterized by X-ray analysis, cf.: (a) van Vliet, M. R. P.; Buysingh, P.; van Koten, G.; Vrieze, K.; Kojic-Prodic, B.; Spek, A. L. *Organometallics* 1985, 4, 1701. (b) van Vliet, M. R. P.; van Koten, G.; de Keijser, M. S.; Vrieze, K. *Organometallics* 1987, 6, 1652. (c) Sierra, M. L.; de Mel, V. S. V.; Oliver, J. P. *Organometallics* 1989, 8, 2486, as well as 4-coordinate aluminum alkyls. Cf.: (d) van Vliet, M. R. P.; van Koten, G.; Rottevel, M. A.; Schrap, M.; Vrieze, K.; Kojic-Prodic, B.; Spek, A. L.; Duisenberg, A. J. M. *Organometallics* 1986, 5, 1389. (e) van der Steen, F. H.; van Mier, G. P. M.; Spek, A. L.; Kroon, J.; van Koten, G. *J. Am. Chem. Soc.* 1991, 113, 5742. (f) Amirkalili, S.; Hitchcock, P. B.; Smith, J. D.; Stamper, J. G. *J. Chem. Soc., Dalton Trans.* 1980, 2493. (g) Power, M. B.; Bott, S. G.; Atwood, J. L.; Barron, A. R. *J. Am. Chem. Soc.* 1990, 112, 3446. Such complexes have been invoked as important intermediates for carbonyl addition reactions: (h) Neumann, H. M.; Laemmle, J.; Ashby, E. C. *J. Am. Chem. Soc.* 1973, 95, 2597. (i) Ashby, E. C.; Laemmle, J. T. *Chem. Rev.* 1975, 75, 521. (j) Ashby, E. C.; Laemmle, J. T. *J. Org. Chem.* 1975, 40, 1469. (k) Ashby, E. C.; Smith, R. S. *J. Organomet. Chem.* 1982, 225, 71. (l) Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* 1985, 107, 4573. (m) Maruoka, K.; Itoh, T.; Sakurai, M.; Nanoshita, K.; Yamamoto, H. *J. Am. Chem. Soc.* 1988, 110, 3588. (n) Kai, Y.; Yasuoka, N.; Kasai, N.; Kakudo, M. *Bull. Chem. Soc. Jpn.* 1972, 45, 3403.

(22) Replacement of the second  $\text{H}^-$  equivalent with a bridging ligand such as  $\text{Cl}^-$  or  $\text{PhO}^-$  also suppressed the overreduction.<sup>21b</sup>  $\text{Et}_2\text{AlCl}\cdot i\text{Bu}_2\text{AlH}$  was formed by mixing equimolar amounts of DIBAL and  $\text{Et}_2\text{AlCl}$ , and  $i\text{Bu}_2\text{AlOPh}\cdot i\text{Bu}_2\text{AlH}$  was formed by adding phenol to DIBAL, but these reagents were not stable enough for prolonged storage at room temperature.

(23) (a) Pasynkiewicz, S.; Sliwa, E. *J. Organomet. Chem.* 1965, 3, 121. (b) Eisch, J. J.; Rhee, S. G. *J. Organomet. Chem.* 1974, 42, C73. (c) Vestin, R.; Vestin, U.; Kowalewski, J. *Acta Chem. Scand.* A 1985, 39, 767. (d) Smith, M. B. *J. Organomet. Chem.* 1970, 22, 273. (e) Yamamoto, O.; Hayamizu, K.; Yanagisawa, M. *J. Organomet. Chem.* 1974, 73, 17.

(24) Mechanistic divergence ( $\text{S}_{\text{N}}1$  vs  $\text{S}_{\text{N}}2$ ) in the Lewis acid-catalyzed reaction of acetals with various nucleophiles has been noted: (a) Hosomi, A.; Ando, M.; Sakurai, H. *Chem. Lett.* 1986, 365. (b) Denmark, S. E.; Willson, T. M. *J. Am. Chem. Soc.* 1989, 111, 3475. (c) Mori, I.; Ishihara, K.; Flippin, L. A.; Nozaki, K.; Yamamoto, H.; Bartlett, P. A.; Heathcock, C. H. *J. Org. Chem.* 1990, 55, 6107. (d) Silverman, R.; Edington, C.; Elliott, J. D.; Johnson, W. S. *J. Org. Chem.* 1987, 52, 180. (e) Choi, V. M. F.; Elliott, J. D.; Johnson, W. S. *Tetrahedron Lett.* 1984, 25, 591. (f) Bartlett, P. A.; Johnson, W. S.; Elliott, J. D. *J. Am. Chem. Soc.* 1983, 105, 2088. (g) Burgess, L. E.; Meyers, A. I. *J. Am. Chem. Soc.* 1991, 113, 9858. (h) Kiyooka, S.; Shirouchi, M. *J. Org. Chem.* 1992, 57, 1. For kinetic data and arguments which support the notion of an  $\text{S}_{\text{N}}2$ -like process, see: (i) Aymes, T. L.; Jencks, W. P. *J. Am. Chem. Soc.* 1989, 111, 7888. (j) Aymes, T. L.; Jencks, W. P. *J. Am. Chem. Soc.* 1989, 111, 7900.

(25) Vicinal coupling constants of cyclic carbamates have been used to assign the configuration of  $\beta$ -amino alcohols. Normally,  $J_{\text{anti}} < J_{\text{syn}}$ : (a) Seebach, D.; Beck, A. K.; Mukhopadhyay, T.; Thomas, E. *Helv. Chem. Acta* 1982, 65, 1101. (b) Kobayashi, S.; Isobe, T.; Ohono, W. *Tetrahedron Lett.* 1983, 24, 5079. But, these vicinal coupling values may be ambiguous, or even reversed when the substituents on the oxazolidinone ring are large: (c) Kano, S.; Yokomatsu, T.; Iwasawa, H.; Shibuya, S. *Chem. Lett.* 1987, 1531. Also see: refs 6n, 8k, 8l, and 8p.





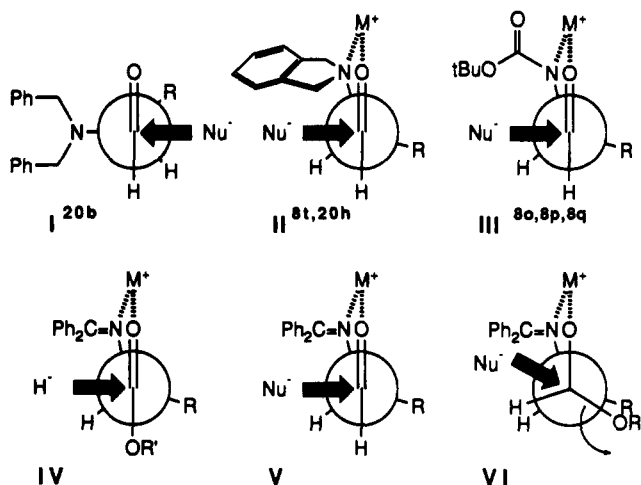


Figure 1.

of the ester moiety. When THF, a more polarizing solvent, was used as a cosolvent, the *threo* selectivity dropped, and remained relatively constant at 3:1 for the various esters. One plausible interpretation of this result is that the chelate ring of the initial complex is opened by THF, providing a greater percentage of the minor aluminoxyl acetal. Another interpretation is that the increased polarity of the THF medium increases the rate of alkoxide elimination (solvent-separated ion-pair formation), favoring the  $S_N1$ -like pathway. In either case, these results imply that the initial reduction step to form the chiral aluminoxyl acetal center is stereochemically significant in the reduction/alkylation sequence, at least in the less polar solvents used in this study (e.g.  $CH_2Cl_2$ ,  $Et_2O$ , toluene, and hexane).

It is useful to compare the proposed transition states for our imine-chelated electrophiles with other closely related reactions (Figure 1). Duhamel's pioneering work with racemic  $N,N$ -dialkyl- $\alpha$ -amino aldehydes<sup>20b,g</sup> showed that steric interference with the chelating-ability of the nitrogen lone pair (e.g. by  $N,N$ -dibenzyl substitution<sup>8t</sup>) led to a Felkin-Ahn-type transition state I and *erythro* or *like* products, but that smaller groups (e.g.  $N,N$ -dimethyl substitution) permitted chelation control.<sup>20e</sup> This was unfortunate, since one would like to have removable protection for nitrogen. Reetz showed that one could "tie back" the benzyl groups to favor the chelated transition state II and that this benzylic protection could be removed subsequent to the reaction.<sup>8t</sup> Several groups<sup>8o-q</sup> have now demonstrated that acyl-protected amines can provide the anionic chelated transition state III once the N-H proton has been removed to generate an imine-like nitrogen. This explains why such a trivial modification of the reaction conditions (e.g.  $H_2C=CHMgCl$  vs  $H_2C=CHMgBr$ ) can alter the course of the reaction so dramatically—the relative rate of deprotonation vs addition becomes extremely important, since deprotonation generates a chelating substrate from a substrate which normally undergoes Felkin-Ahn addition.<sup>20</sup> It is unclear whether Rapoport's 9-phenylfluorenyl-protected  $\alpha$ -amino aldehydes<sup>10</sup> undergo deprotonation in all cases prior to nucleophilic addition or not. The problem with these approaches is that they require high temperatures ( $-20$  to  $0$  °C) to promote N-deprotonation, which is not conducive for the formation of stable chelates, and promotes deprotonation of the  $\alpha$ -carbon (racemization) at the same time. The use of O'Donnell's Schiff base esters permits the chelation controlled addition of hydride (transition state IV) without the use of high temperatures. Although a portion of the desired *threo* product may arise from transition state V

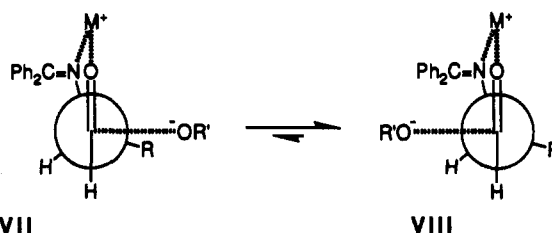


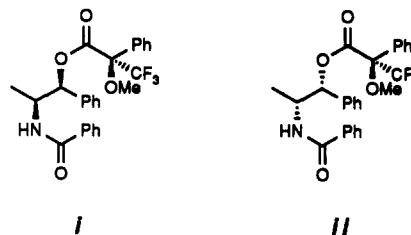
Figure 2.

( $S_N1$ -like pathway), we feel that some of the product arises from transition state VI ( $S_N2$ -like pathway).

It is impossible to either confirm or deny the possibility that the aluminoxyl acetals can exist as tight ion-pairs VII or VIII (Figure 2) based on the available data. Indeed, the decrease in diastereoselectivity observed with coordinating solvents may be due to increased "leakage" between the two structures VII and VIII, rather than a change from the  $S_N2$ -like to an  $S_N1$ -like mechanism. Eclipsing interactions between the R group and the R'O group should favor structure VIII if equilibration between the two ion-pairs were observed. The parallel increase in stereoselectivity with steric bulk of the ester presented in Scheme VII suggests that configurational equilibration (inversion) of the aluminoxyl acetal via ion-pair rearrangement is not a major pathway at low temperatures and in the absence of THF, since one would expect the equilibrium VII  $\leftrightarrow$  VIII to shift to the right as the steric bulk of the R'O group increases and result in decreased stereoselectivity.

**Racemization Studies.** Although some Boc-protected amino aldehyde derivatives show resistance to racemization (cf. Garner's t-Boc-protected cyclic aldehyde<sup>7a</sup>), facile loss of optical activity in  $\alpha$ -amino aldehyde derivatives is a general problem, especially under the basic conditions encountered during nucleophilic additions to aldehydes.<sup>8r,9-11</sup> Comparison of the optical rotations of synthetic products 6b-d to authentic material showed less than 3% racemization. This result was confirmed by an analysis of Mosher amides derived from 6b and its enantiomer.<sup>36</sup> Similarly, known sphingosine triacetate 14 (vide infra) showed an optical rotation of 93–97%<sup>28</sup> of the expected value.<sup>7b,n</sup> Carbohydrate-bearing glycosphingolipids

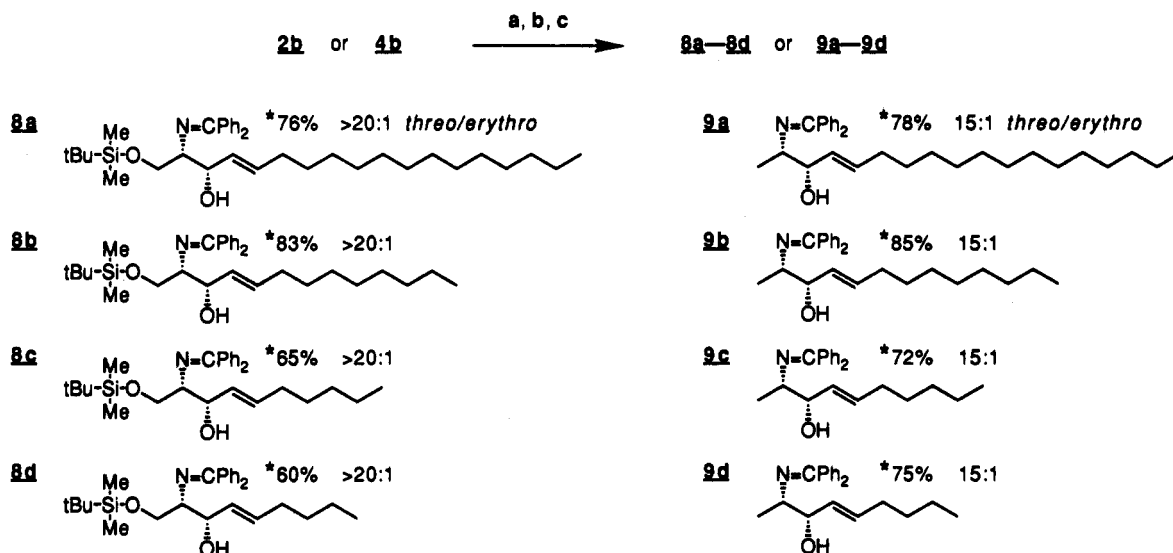
(36) The Mosher ester<sup>37</sup> i was prepared from synthetic amino alcohol 6b and compared with the diastereomeric Mosher ester ii prepared from the commercially available<sup>19b</sup> enantiomer of 6b, (1R,2R)-(-)-norpseudoephedrine hydrochloride using  $^1H$  NMR (250 MHz). No trace of ii could be detected in i. Authentic mixtures of i and ii were measured to check this method.



(37) (a) Hassner, A.; Alexanian, V. *Tetrahedron Lett.* 1978, 4475–8.  
(b) Garner, P.; Park, J. M. *J. Org. Chem.* 1987, 52, 2361–4.

(38) The  $^1H$  NMR experiments were performed at 500 MHz. To a septum-sealed 5-mm NMR tube containing 7.0 mg of a 1:1 (w/w) mixture of  $iBu_2AlH$  and  $iBu_3Al$  (21  $\mu$ mol) was added 1 g of  $CD_2Cl_2$  (ampoule), and spectra were obtained at several temperatures. The changes observed in the spectra were reversible.<sup>23b</sup> After the DIBAL/TRIBAL spectra were obtained, the sample was removed and frozen in liquid  $N_2$ . After freezing, 5.5 mg of Schiff base 2a (21  $\mu$ mol) in 1 g of  $CD_2Cl_2$  was added via syringe, and the sample was quickly re-inserted into the NMR probe. As the sample thawed, the spectra in Scheme V were obtained.



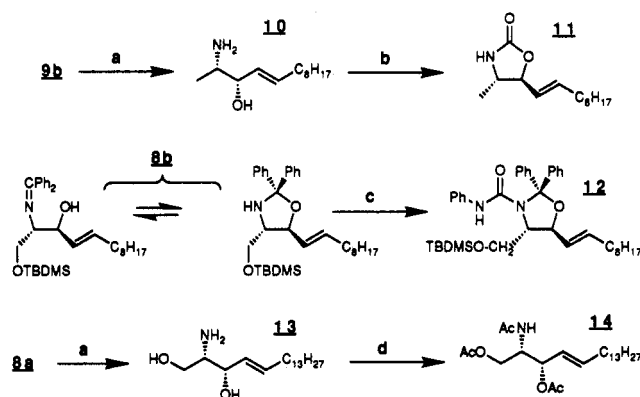
Scheme VIII<sup>a</sup>

<sup>a</sup> (a)  $i\text{Bu}_2\text{AlH} \cdot i\text{Bu}_3\text{Al} / \text{CH}_2\text{Cl}_2 / -78^\circ\text{C}$ ; (b)  $\text{RLi} / \text{hexane} / -78^\circ\text{C} \rightarrow 0^\circ\text{C}$ ; (c)  $\text{NaHCO}_3$ . \* Isolated yields. Threo/erythro ratios were determined on the crude reaction mixtures by 250-MHz  $^1\text{H}$  NMR.

prepared<sup>30d</sup> from sphingosines 8a–d showed no evidence of diastereoisomerism.<sup>39</sup>

**Synthetic Applications: Sphingosines.** *threo*-Sphingosines, their 1-*O*-glycosyl derivatives (psychosines), and ceramide derivatives are of interest as PKC inhibitors,<sup>6</sup> and neuro-protective agents.<sup>6h</sup> Toward these ends, we have synthesized a series of *threo*-sphingosines of various chain lengths. Reaction of the protected serine 4b with  $i\text{Bu}_2\text{AlH} \cdot i\text{Bu}_3\text{Al}$  in  $\text{CH}_2\text{Cl}_2$  at  $-78^\circ\text{C}$ , followed by addition of a (*E*)-1-lithioalkene furnished a series of *threo*-sphingosine derivatives 8a–d (Scheme VIII). Reaction with the alanine derivative 2b provided the “1-deoxy-sphingosine” derivatives 9a–d in a similar fashion. The stereochemical outcome of these reactions run in  $\text{CH}_2\text{Cl}_2$ /hexanes was superb, and  $\text{SiO}_2$  flash chromatography<sup>28</sup> provided the diastereomerically pure Schiff bases in the yields indicated. Subsequent glycosylation showed that the sphingosines were enantiomerically pure as well.<sup>30c,39</sup>

The diastereomeric ratios were determined by 250-MHz  $^1\text{H}$  NMR spectroscopy of the crude reaction mixtures. The configuration of 9b was examined by hydrolysis of the N- and O-protection with acid (Scheme IX), followed by

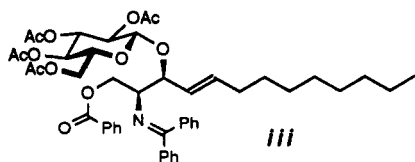
Scheme IX<sup>a</sup>

<sup>a</sup> (a) 1 N HCl; (b)  $\text{O}=\text{C}(\text{imidazole})_2$ ; (c)  $\text{PhN}=\text{C}=\text{O}$ ; (d)  $\text{Ac}_2\text{O}$ .

treatment of the resulting alcohol 10 with carbonyldiimidazole to furnish the oxazolidinone 11, which displayed a vicinal coupling constant of 7.6 Hz for the  $-\text{OCH}-\text{HCN}-$  resonances. This is *not* consistent with the empirical rules for stereochemical assignment,<sup>25</sup> assuming that the configuration of 9b and 10 is indeed *threo*. Reaction of 8b with phenyl isocyanate provided the oxazolidine 12. The vicinal coupling constant for the  $-\text{OCH}-\text{HCN}-$  resonances of 12 was also inconsistent with a *threo* assignment for 8b ( $J = 7.7$  Hz). In light of this apparent discrepancy, Schiff base 8a was hydrolyzed to the amino diol 13, which was acylated to provide the triacetate 14 which was identical in every respect with the known compound.<sup>28</sup> Thus the *threo* assignment implicated by the norpseudoephedrine syntheses was confirmed unambiguously for sphingosines 8a–d and 9a–d.

In conclusion, we have developed a convenient one-pot, *threo*-selective synthesis of  $\beta$ -amino alcohols and sphingosines. The key features of this method are (1) availability and easy preparation of the crystalline Schiff base esters, (2) intermediacy of the nonenolizable (*nonracemizing*) aluminoyl acetals, and (3) high degree of *threo* stereoselectivity. That the aluminoyl acetals are indeed the reactive intermediates involved in this chemistry is implicated by their long life and stability at  $-78^\circ\text{C}$ , their isolation as trapped monosilyl acetals, and the stereochemical effects of the ester moieties. The glycosylation

(39) Glycosylated *threo*-sphingosines<sup>30d</sup> (e.g. iii) show no evidence of diastereoisomerism, indicating that significant racemization of the original chiral center has not occurred.



*O*-(2,3,4,6-Tetra-*O*-acetyl- $\beta$ -D-glucopyranosyl)-(1 $\rightarrow$ 3)-(2*S*,3*S*,4*E*)-1-*O*-benzoyl-2-[*N*-(diphenylmethylene)amino]-4-tridecen-3-ol (iii).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  8.00–7.90 (m, 2 H), 7.60–7.50 (m, 4 H), 7.40–7.10 (m, 9 H), 5.77 (dt,  $J = 6.6, 15.4$  Hz, 1 H), 5.54 (dd,  $J = 8.7, 15.4$  Hz, 1 H), 5.17–5.03 (m, 3 H), 4.49 (d,  $J = 7.4$  Hz, 1 H), 4.40–4.21 (m, 4 H), 4.15–3.99 (m, 2 H), 3.61–3.56 (m, 1 H), 2.10–2.00 (m, 2 H), 2.09 (s, 3 H), 2.01 (s, 3 H), 1.94 (s, 3 H), 1.38 (s, 3 H), 1.25–1.15 (m, 12 H), 0.86 (t,  $J = 7$  Hz, 3 H). ATP  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  170.49, 170.22, 170.07, 169.28, 169.22, 165.98 (C=O's, C=N), 139.96, 136.26 (quaternary, aromatic), 135.90, 132.76 (HC=CH), 130.05 (quaternary, aromatic), 129.87, 129.45, 128.76, 128.32, 128.13, 127.75, 127.34 (aromatic), 100.06 (OCHO), 84.68 (OCH, allylic), 73.03 (AcOCH-3), 71.50 (OCH-5), 70.91 (AcOCH-2), 68.26 (AcOCH-4), 65.52 (BzOCH<sub>2</sub>), 63.62 (=NCH), 62.00 (AcOCH<sub>2</sub>-6), 32.24, 31.72, 29.30, 29.19, 29.10, 28.95, 22.51 ( $\text{CH}_2$ 's), 20.63, 20.43, 19.63 ( $\text{CH}_3\text{C}=\text{O}$ 's), 13.99 ( $\text{CH}_3$ ).  $[\alpha]_D = -12.5^\circ$  ( $c = 0.80, \text{CHCl}_3$ ).



of the Schiff base-protected sphingosines to provide psychosines and ceramides will be the subject of a forthcoming paper.<sup>30d</sup>

## Experimental Section

**General Methods.** All air- and moisture-sensitive reactions were performed under an argon atmosphere in flame-dried reaction flasks using standard schlenk methodology. All solvents were dried over standard drying agents<sup>32</sup> and freshly distilled prior to use. For flash chromatography,<sup>29</sup> 400–230-mesh silica gel 60 (E. Merck No. 9385) was employed. All compounds described were >95% pure by <sup>1</sup>H and <sup>13</sup>C NMR, and purity was confirmed by elemental analysis in several representative cases. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were obtained on a Bruker WM-250 spectrometer at 250 and 62.9 MHz, respectively. Chemical shifts are reported in  $\delta$  vs Me<sub>4</sub>Si in <sup>1</sup>H spectra and vs CDCl<sub>3</sub> in <sup>13</sup>C spectra. All melting points were measured on a Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer 1600 Series FT IR. Optical rotations were measured on a Randolph Research, AutoPol III polarimeter using the Na D line. Elemental analyses were performed by Desert Analytics, Tucson, AZ. Nominal and exact mass were obtained on a JEOL JMS-01SG-2 mass spectrometer.

**Schiff Base Esters: Methyl *N*-(diphenylmethylene)-L-alaninate (2a).** Diphenylketimine (7.0 g, 39 mmol) was added to a stirred solution of L-alanine methyl ester hydrochloride (4.33 g, 31.1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) and stirred overnight under argon.<sup>16</sup> The reaction was poured into 1% NaHCO<sub>3</sub>, washed (2  $\times$  saturated NaHCO<sub>3</sub>), and dried (K<sub>2</sub>CO<sub>3</sub>), and the solvent was removed under reduced pressure to provide crude product. Chromatography (40% EtOAc/hexanes) yielded 6.62 g of a white solid (25 mmol, 80%), mp 69–72 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.70–7.50 (m, 2 H), 7.50–7.10 (m, 8 H), 4.18 (q,  $J$  = 6.7 Hz, 1 H), 3.71 (s, 3 H), 1.42 (d,  $J$  = 6.7 Hz, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>):  $\delta$  173.13 (O=CO), 169.48 (C=N), 139.22, 135.96 (quaternary, aromatic), 130.11, 128.55, 128.46, 128.40, 127.84, 127.43 (CH, aromatic), 60.36 (OCH<sub>3</sub>), 51.86 (=NCH), 19.00 (CH<sub>3</sub>). [ $\alpha$ ]<sub>D</sub> = –105.4° ( $c$  = 3.25, CHCl<sub>3</sub>). IR (KBr): 1748.7, 1629.0, 1448.2, 1448.0, 1368.2, 1281.4, 1196.3, 1071.6, 712.0 cm<sup>–1</sup>.

**Ethyl *N*-(Diphenylmethylene)-L-alaninate (2b).** Reaction as in 2a. Recrystallization (10% EtOAc/hexanes) provided pure product as a white solid (12.97 g, 46.2 mmol, 85%), mp 52–53 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.80–7.10 (m, 10 H), 4.16 (m, 3 H), 1.42 (d,  $J$  = 6.7 Hz, 3 H), 1.25 (t,  $J$  = 7 Hz, 3 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  172.46 (O=CO), 169.25 (C=N), 139.20, 136.00 (quaternary, aromatic), 129.96, 128.44, 128.30, 127.73, 127.35 (aromatic), 60.45 (OCH<sub>2</sub>CH<sub>3</sub>), 60.33 (=NCH), 18.87 (OCH<sub>2</sub>CH<sub>3</sub>), 13.90 (CH<sub>3</sub>). IR (KBr): 1736.3, 1624.8, 1449.5, 1375.9, 1285.0, 1196.9, 1127.6, 787.1, 704.2. [ $\alpha$ ]<sub>D</sub> = –90.0° ( $c$  = 2, CHCl<sub>3</sub>).

**Benzyl *N*-(Diphenylmethylene)-L-alaninate (2c).** Diphenylketimine (1.98 g, 10.9 mmol) was added to a stirred solution of L-alanine benzyl ester hydrotosylate<sup>30</sup> (4.5 g, 12.8 mmol) in 50 mL of CH<sub>2</sub>Cl<sub>2</sub> and stirred for 28 h at rt under argon.<sup>16</sup> The mixture was then washed (0.1% NaHCO<sub>3</sub>, 2  $\times$  saturated NaHCO<sub>3</sub>) and dried over K<sub>2</sub>CO<sub>3</sub>. The solvent was removed under reduced pressure and the resulting oil chromatographed (10% EtOAc/petroleum ether) to provide pure product as a colorless oil (3.0 g, 8.7 mmol, 80%). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.70–7.60 (m, 2 H), 7.4–7.25 (m, 11 H), 7.20–7.10 (m, 2 H), 5.19 (d,  $J$  = 12.5 Hz, 1 H), 5.12 (d,  $J$  = 12.5 Hz, 1 H), 4.21 (q,  $J$  = 6.7 Hz, 1 H), 1.45 (d,  $J$  = 6.7 Hz, 3 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  172.49 (O=CO), 169.78 (C=N), 139.32, 136.08, 135.88 (quaternary, aromatic), 130.20, 128.64, 128.48, 128.34, 127.95, 127.81 (aromatic), 66.27 (OCH<sub>2</sub>Ph), 60.53 (=NCH), 19.01 (CH<sub>3</sub>). IR (neat): 1919.2, 1736.9, 1619.3, 1490.1, 1448.9, 1178.6 cm<sup>–1</sup>. [ $\alpha$ ]<sub>D</sub> = –65.7° ( $c$  = 1.3, CHCl<sub>3</sub>).

**Benzhydryl *N*-(Diphenylmethylene)-L-alaninate (2d).** A solution of L-alanine benzhydryl ester hydrotosylate<sup>31</sup> was reacted as in 2a. Chromatography (20% EtOAc/petroleum ether) provided pure product as a white solid in 81% yield (2.1 g, 5.3 mmol), mp 82–85 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.70–7.60 (m, 2 H), 7.40 (m, 16 H), 7.20–7.10 (m, 2 H), 6.89 (s, 1 H), 4.25 (q,  $J$  = 6.7 Hz, 1 H), 1.48 (d,  $J$  = 6.7 Hz, 3 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  171.14 (O=CO), 169.52 (C=N), 139.85, 135.82 (quaternary, aromatic), 130.05, 128.45, 128.27, 128.11, 127.74, 127.59, 127.44, 127.27, 126.88, 126.56 (aromatic), 76.64 (OCHPh<sub>2</sub>), 60.64 (=NCH), 18.61 (CH<sub>3</sub>). IR

(KBr): 3060.3, 2931.0, 2355.1, 1736.9, 1625.2, 1495.9, 1448.9, 1372.5, 1178.6, 1119.9 cm<sup>–1</sup>. [ $\alpha$ ]<sub>D</sub> = –46.5° ( $c$  = 2.2, CHCl<sub>3</sub>).

**Methyl *N*-(Diphenylmethylene)-L-phenylalaninate (3).** Reaction as in 2a. Recrystallization (5% EtOAc/hexanes) provided pure product 3 (5.7 g, 16.6 mmol, 76%), mp 55–57 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.60–7.00 (m, 13 H), 6.68 (d,  $J$  = 6 Hz, 2 H), 4.26 (dd,  $J$  = 4.3, 9.2 Hz, 1 H), 3.72 (s, 3 H), 3.28 (dd,  $J$  = 4.3, 13.2, 1 H), 3.17 (dd,  $J$  = 9.3, 13.2 Hz, 1 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  172.17 (O=CO), 170.76 (C=N), 139.20, 137.74, 135.88 (quaternary, aromatic), 130.15, 129.70, 128.62, 128.18, 128.01, 127.85, 127.44, 126.17 (aromatic), 67.10 (=NCH), 52.07 (OCH<sub>3</sub>), 39.63 (CH<sub>2</sub>Ph). IR (KBr): 1743.3, 1625.9, 1445.9, 1286.0, 1200.7, 1169.0, 694.3 cm<sup>–1</sup>. [ $\alpha$ ]<sub>D</sub> = –285.7° ( $c$  = 2.3, CHCl<sub>3</sub>).

**Methyl *N*-(Diphenylmethylene)-L-serinate (4a).** Reaction as in 2a. Recrystallization (EtOAc/hexanes) yielded 4a as 5.18 g of white crystals (18.3 mmol, 89%), mp 87–89 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.70–7.20 (m, 10 H), 4.25 (t,  $J$  = 5.1 Hz, 0.3 H), 4.00–3.93 (m, 2.6 H), 3.76 (s, 2 H), 3.72 (s, 1 H), 3.14–3.10 (broad s, 0.7 H), 2.57 (dd,  $J$  = 5.8, 7.7 Hz, 0.3 H). <sup>1</sup>H NMR (benzene-*d*<sub>6</sub>):  $\delta$  8.00–7.85 (m, 2 H), 7.80–7.70 (m, 2 H), 7.30–7.00 (m, 6 H), 4.44 (t,  $J$  = 5.3 Hz, 0.3 H), 4.20–4.10 (broad s, 0.5 H), 3.90–3.70 (m, 2 H), 4.50 (d,  $J$  = 6 Hz, 0.8 H), 3.33 (s, 0.7 H), 3.24 (s, 2 H), 2.60–2.50 (broad s, 0.3 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  172.57 (O=CO), 142.78, 142.54 (quaternary, aromatic), 130.60, 128.78, 128.53, 128.13, 127.98, 127.78, 127.60, 126.51, 125.57 (CH aromatic), 101.07 (OCN), 67.29, 66.46, 64.15, 59.56, 52.41, 52.12. (Note: OCH<sub>2</sub>, NCH, and OCH<sub>3</sub> resonances appear twice due to imine-oxazolidine tautomerism.) IR (KBr): 3500–3300, 1736.4, 1446.6, 1338.5, 1228.4, 750.9, 703.7, 630.6 cm<sup>–1</sup>. MS (EI): 283 (M<sup>+</sup>), 224 (M – CO<sub>2</sub>Me), 206 (M – H<sub>2</sub>O – CO<sub>2</sub>Me, 100). Anal. Calcd for C<sub>17</sub>H<sub>17</sub>NO<sub>3</sub>: C (71.78), H (5.94), N (4.96). [ $\alpha$ ]<sub>D</sub> = –136.14° ( $c$  = 8.5, CHCl<sub>3</sub>).

**Methyl *O*-(*tert*-Butyldimethylsilyl)-*N*-(diphenylmethylene)-L-serinate (4b).** To a stirred solution of methyl *N*-(diphenylmethylene)-L-serinate (4a) (3.20 g, 11.3 mmol) in dry DMF (10 mL) were added imidazole (1.97 g, 28.9 mmol) and chloro-*tert*-butyldimethylsilane (2.76 g, 18.3 mmol). The mixture was stirred under argon for 24 h. The reaction mixture was poured into diethyl ether, washed with 1% NaHCO<sub>3</sub> (2  $\times$  15 mL), and dried (MgSO<sub>4</sub>), and the solvent was removed under reduced pressure. Recrystallization (5% EtOAc/hexanes) yielded 4.10 g of white crystals (10.3 mmol, 92%), mp 57–59 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.7–7.2 (m, 10 H), 4.30 (dd,  $J$  = 5.4, 7.6 Hz, 1 H), 4.11 (dd,  $J$  = 5.4, 9.8 Hz, 1 H), 3.92 (dd,  $J$  = 7.6, 9.8 Hz, 1 H), 3.68 (s, 3 H), 0.82 (s, 9 H), 0.00 (s, 3 H), –0.023 (s, 3 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  171.28 (O=CO), 170.75 (C=N), 139.25, 135.94 (quaternary, aromatic), 130.08, 128.64, 128.41, 128.86, 128.17, 127.91 (aromatic), 67.48 (SiOCH<sub>2</sub>), 64.43 (=NCH), 51.63 (OCH<sub>3</sub>), 25.61 (C-CH<sub>3</sub>), 18.02 (quaternary, SiC), –5.51, –5.62 (SiCH<sub>3</sub>). IR (neat): 1725.2, 1625.1, 1285.6, 1125.3, 1074.6, 829.9, 779.2, 686.4 cm<sup>–1</sup>. MS (70 eV): 397 (M<sup>+</sup>), 382 (M – CH<sub>3</sub>), 340 (M – tBu, 100). [ $\alpha$ ]<sub>D</sub> = –95.1° ( $c$  = 3.6, CHCl<sub>3</sub>).

**Synthesis of Norpseudoeophedrine: Method A** (2 equiv of DIBAL). The Schiff base esters (1.0 mmol) were dissolved in 10 mL of dry CH<sub>2</sub>Cl<sub>2</sub> and cooled to –78 °C under an argon atmosphere. Two equivalents of diisobutylaluminum hydride (DIBAL) was then added (4.0 mL 0.5 M DIBAL in hexanes) over 90 min via syringe pump. The reactions were stirred an additional 15 min before 3 equiv of PhMgBr (1.0 mL 3.0 M PhMgBr in Et<sub>2</sub>O) was added in one portion. The pale yellow solutions were stirred an additional 15 min at –78 °C and then warmed to room temperature. After the mixture was stirred at room temperature for 3 h, the reaction was quenched by pouring into 15 mL of saturated NaHCO<sub>3</sub>. An additional 20 mL of CH<sub>2</sub>Cl<sub>2</sub> was used in several portions to ensure complete transfer. These exact proportions of CH<sub>2</sub>Cl<sub>2</sub>:NaHCO<sub>3</sub> are recommended to avoid the formation of intractable emulsions. The aqueous layer was extracted with two additional 20-mL portions of CH<sub>2</sub>Cl<sub>2</sub>, and the combined organic layers were dried (K<sub>2</sub>CO<sub>3</sub>), filtered through Celite, and evaporated under reduced pressure. The products were purified via flash chromatography except for 5a which was recrystallized directly from CH<sub>2</sub>Cl<sub>2</sub> or THF.

**Method B** (1:1 DIBAL–TRIBAL). The Schiff base esters (1.0 mmol) were dissolved in 10 mL of dry CH<sub>2</sub>Cl<sub>2</sub> and cooled to –78 °C under an argon atmosphere. One equivalent of DIBAL–TRIBAL (1:1) was added (2.0 mL of 0.5 M solution in hexanes)

over 15 min via syringe pump. After addition was complete, 3 equiv of PhMgBr was added in one portion (1.0 mL of 3 M solution in Et<sub>2</sub>O). The reactions were allowed to stir for 1 h at -78 °C followed by 1 h at rt and worked up as for method A above. (Solvent systems used for chromatography and yields for the two methods are listed in parentheses.)

***N*-(Diphenylmethylene)-1-phenylethanolamine (5a)** (white solid, 64% method A, 86% method B), mp 148–151 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.7–7.6 (m, 2 H), 7.5–7.2 (m, 11 H), 7.1–7.0 (m, 2 H), 4.96 (dd, *J* = 3.8, 8.4 Hz, 1 H), 3.72 (s, 1 H), 3.62 (dd, *J* = 3.8, 14.4 Hz, 1 H), 3.47 (dd, *J* = 8.5, 14.4 Hz, 1 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>): 169.89 (N=C), 142.13 (quaternary, aromatic), 139.17, 136.49 (quaternary, aromatic), 130.31, 128.55, 128.39, 128.23, 128.08, 127.49, 127.40, 126.07, 125.85, (CH, aromatic), 101.02 (NCO), 79.00 (CHO), 73.71 (CHOH), 61.36 (CH<sub>2</sub>N=), 55.00 (CH<sub>2</sub>NH). (Note: oxazolidine-imine tautomerism.) IR (KBr): 3500–3100, 1617.9, 1490.2, 1444.5, 1316.7, 1093.8, 1060.4, 1026.6, 689.0, 542.3, 461.3 cm<sup>-1</sup>. MS (70 eV): 301 (M<sup>+</sup>), 283 (M - H<sub>2</sub>O), 194 (M - PhCHOH), 91 (C<sub>7</sub>H<sub>7</sub>, 100).

**(1*S*,2*S*)-2-[*N*-(Diphenylmethylene)amino]-1-phenylpropan-1-ol (5b)** (oil, 15% EtOAc/petroleum ether, 54% method A, 78% method B). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.9–7.75 (m, 2 H), 7.7–7.55 (m, 2 H), 7.4–7.1 (m, 11 H), 4.42 (d, *J* = 8.5, Hz 1 H), 3.11 (dq, *J* = 6.4, 8.5 Hz, 1 H), 2.58–2.36 (broad s, 1 H), 1.22 (d, *J* = 6.4 Hz, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>): 145.50, 139.71 (quaternary, aromatic), 128.26, 128.21, 128.09, 127.65, 127.44, 127.15, 126.71, 126.30, 125.38 (CH, aromatic), 99.91 (OCN), 88.57 (OCH), 62.99 (=NCH), 15.58 (CH<sub>3</sub>). IR (neat): 1726.4, 1490.0, 1450.8, 1235.9, 749.7, 698.9, 630.4 cm<sup>-1</sup>. [α]<sub>D</sub> = +198.9° (*c* = 1, CHCl<sub>3</sub>).

**(1*S*,2*S*)-2-[*N*-(Diphenylmethylene)amino]-1,3-diphenylpropan-1-ol (5c)** (oil, 10% EtOAc/petroleum ether, 69% method A, 75% method B). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.8–7.0 (m, 20 H), 5.88 (d, *J* = 7 Hz, 0.5 H), 4.86–4.81 (broad s, 0.25 H), 4.58 (d, *J* = 8.2 Hz, 0.75 H), 3.9–3.8 (broad s, 0.25 H), 3.63–3.56 (dt, *J* = 2.8, 6.9 Hz, 0.3 H), 3.48–3.40 (m, 0.75 H), 3.0 (d, *J* = 7 Hz, 0.5 H), 2.87 (dd, *J* = 4.2, 14.4 Hz, 0.75 H), 2.72 (dd, *J* = 8.8, 14.4 Hz, 0.75 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 169.36 (N=C), 145.17, 145.09, 143.03, 139.71, 138.82, 138.47, 138.03 (quaternary, aromatic), 135.80, 129.89, 129.74, 129.65, 128.70, 128.10, 128.03, 127.92, 127.80, 127.48, 127.34, 127.27, 127.03, 126.98, 126.77, 126.66, 125.99, 125.95, 125.77, 125.68, 125.43 (aromatic), 99.78 (OCN), 85.63 (PhCHO), 75.64 (PhCHOH), 69.70 (=NCH), 67.82 (CHNH), 39.99 (CH<sub>2</sub>Ph), 37.05 (CH<sub>2</sub>Ph). (Note: oxazolidine-imine tautomerism.) IR (neat): 1601.0, 1495.2, 1451.3, 1222.0, 1028.7, 953.7, 743.8, 701.0 cm<sup>-1</sup>. [α]<sub>D</sub> = +68.4° (*c* = 2.4, CHCl<sub>3</sub>).

**(1*S*,2*S*)-2-[*N*-(Diphenylmethylene)amino]-3-*O*-(*tert*-butyldimethylsilyl)-1-phenylpropane-1,3-diol (5d)** (oil, 10% EtOAc/petroleum ether, 62% method A, 73% method B). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.9–7.75 (m, 2 H), 7.65–7.50 (m, 2 H), 7.45–7.15 (m, 11 H), 4.96 (d, *J* = 8.4 Hz, 1 H), 3.89 (dd, *J* = 3.2, 10.8 Hz, 1 H), 3.67 (dd, *J* = 1.6, 10.8 Hz, 1 H), 3.4–3.25 (broad s, 1 H), 3.20–3.14 (m, 1 H), 0.88 (s, 9 H), 0.11 (s, 3 H), 0.07 (s, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>): δ 145.58, 145.34, 140.46 (quaternary, aromatic), 128.32, 128.11, 128.06, 127.55, 127.49, 127.26, 126.85, 126.64, 125.71 (CH, aromatic), 100.09 (OCN), 81.86 (OCH), 68.33 (NCH), 59.13 (CH<sub>2</sub>OSi), 25.75 (C-CH<sub>3</sub>), 18.10 (quaternary, SiC), -5.5 (SiCH<sub>3</sub>). IR (neat): 1662.2, 1600.5, 1490.4, 1450.0, 1253.7, 1089.6, 1065.1, 837.2, 777.6, 750.4, 699.2 cm<sup>-1</sup>. [α]<sub>D</sub> = +101.9° (*c* = 7.7, CHCl<sub>3</sub>).

**(1*S*,2*S*)-2-[*N*-(Diphenylmethylene)amino]-1-ethoxy-1-siloxypropane (7a).** Method C. To a stirred solution of ethyl *N*-(diphenylmethylene)-L-alaninate (2b) (283 mg, 1.0 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (4 mL) at -78 °C was added 2.4 mL of 0.5 M DIBAL-TRIBAL (1:1) in hexanes (1.2 mmol, 1.2 equiv) over 15 min. The resulting yellow solution was allowed to stir 72 h at -78 °C. TMS-imidazole (426 mg, 3 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) was then added. The reaction was stirred for 2 h at -78 °C followed by an additional hour at rt. The yellow color persisted during the entire period at -78 °C but was discharged as the reaction mixture came to rt. The clear solution was quenched by pouring onto 15 mL of saturated NaHCO<sub>3</sub>. The aqueous layer was washed with three 20-mL portions of CH<sub>2</sub>Cl<sub>2</sub>, and the combined organic layers were then dried (K<sub>2</sub>CO<sub>3</sub>) and evaporated under reduced pressure. The product was purified via flash chromatography<sup>29</sup> to yield 252 mg of an inseparable (6.5:1) mixture of 7a and 7b (0.71 mmol,

71%). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.65–7.10 (m, 10 H), 4.82 (d, *J* = 6.4 Hz, 1 H), 3.8–3.6 (m, 1 H), 3.5–3.3 (m, 2 H), 1.14 (t, *J* = 7 Hz, 3 H), 1.12 (d, *J* = 6.4 Hz, 3 H), 0.15 (s, 6 H), 0.09 (s, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>): 7a: δ 167.22 (imine), 140.19, 137.02 (quaternary aromatics), 129.61, 129.55, 128.31, 128.23, 128.15, 128.04, 127.96, 127.84, 127.76, 127.34 (CH, aromatic), 101.41 (SiOCHO), 62.92 (CH<sub>2</sub>O), 59.15 (CHN), 17.59, 15.28 (CH<sub>3</sub>), 0.59 (SiCH<sub>3</sub>). IR (neat): 1627.1, 1599.1, 1578.9, 1490.1, 1446.0, 1372.7, 1313.9, 1287.6, 1250.4, 1152.9, 1119.1, 1058.9, 1029.0, 952.9, 883.9, 840.3, 695.5, 647.9 cm<sup>-1</sup>. [α]<sub>D</sub> = +31.43° (*c* = 4.4, CHCl<sub>3</sub>). High-resolution MS (CI-isobutane): M + 1 = 356.2035 (C<sub>21</sub>H<sub>30</sub>NSiO<sub>2</sub> = 356.2046).

**(1*S*,2*S*)-2-[*N*-(Diphenylmethylene)amino]-1-ethoxy-1-siloxypropane and (1*R*,2*S*)-2-[*N*-(Diphenylmethylene)amino]-1-ethoxy-1-siloxypropane (2:1 7a-7b Mixture).** Method D (1:1:1 DIBAL-TRIBAL-PhLi). 1:1 DIBAL-TRIBAL (5 mL of 0.5 M in hexanes) was added to a flame-dried reaction vessel and chilled to -78 °C. PhLi (1.4 mL of 1.8 M in 7:3 cyclohexane/Et<sub>2</sub>O) was added while stirring at -78 °C. The mixture was stirred for 1 h at -78 °C and then was allowed to warm to rt prior to use.

To a stirred solution of ethyl *N*-(diphenylmethylene)-L-alaninate, 2b (140 mg, 0.5 mmol), in dry CH<sub>2</sub>Cl<sub>2</sub> (2 mL) at -78 °C was added 1.4 mL of 0.4 M DIBAL-TRIBAL-PhLi (1:1:1) in hexanes (0.56 mmol, 1.1 equiv) over 15 min. The resulting solution was allowed to stir for 1 h at -78 °C. TMS-imidazole (213 mg, 1.5 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) was then added. The reaction was stirred for an additional hour at -78 °C followed by 1 h at rt. The reaction was quenched by pouring into 15 mL of saturated NaHCO<sub>3</sub>. The aqueous layer was washed with three 20-mL portions of CH<sub>2</sub>Cl<sub>2</sub>, and the combined organic layers were then dried (K<sub>2</sub>CO<sub>3</sub>) and evaporated under reduced pressure. Analysis of the crude <sup>13</sup>C NMR revealed the two possible diastereomeric products were formed in a 2:1 ratio. 7b. <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>): δ 166.95 (imine), 139.81, 136.69 (quaternary aromatics), 129.61, 129.55, 128.31, 128.23, 128.15, 128.04, 127.96, 127.84, 127.76, 127.34 (CH, aromatic), 101.32 (SiOCHO), 67.68 (CH<sub>2</sub>O), 62.56 (CHN), 17.45, 15.01 (CH<sub>3</sub>), -0.52 (SiCH<sub>3</sub>).

**Protected Sphingosine Schiff Bases.** The protected sphingosine derivatives 8a–d and 9a–d were synthesized from 4b and 2b using method A/method B as above, with the exception that (*E*)-lithioalkenes in hexane solution<sup>31</sup> (prepared by I-Li exchange from the corresponding (*E*)-iodoalkenes)<sup>34</sup> were substituted for the PhMgBr/Et<sub>2</sub>O. The reactions were worked up as before.

**Cleavage of Schiff Base Protecting Groups.** This was accomplished essentially as described by O'Donnell.<sup>16</sup> The Schiff base-protected amino alcohols were dissolved in 1–3 mL of THF and 1–3 mL of 3% HCl. The solution was stirred at rt until TLC indicated that hydrolysis of the Schiff base was complete (usually 1–3 h). The reaction mixture was transferred to a separatory funnel and the aqueous layer washed with several volumes of CH<sub>2</sub>Cl<sub>2</sub> to remove benzophenone. The aqueous layer was then made basic by addition of 2 N NaOH, and the product was extracted with several volumes of CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried (K<sub>2</sub>CO<sub>3</sub>), and solvent was removed under reduced pressure. Isolated amino alcohols were obtained in approximately quantitative yield.

**(2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-1-*O*-(*tert*-butyldimethylsilyl)-4-octadecene-1,3-diol (8a)** (oil, 5% EtOAc/petroleum ether, 78% method B). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.70–7.60 (m, 2 H), 7.50–7.40 (m, 2 H), 7.30–7.10 (m, 6 H), 5.64 (dt, *J* = 6.7, 15.2 Hz, 1 H), 5.24 (dd, *J* = 8.4, 15.2 Hz, 1 H), 4.28 (t, *J* = 8.4 Hz, 1 H), 3.84 (dd, *J* = 3.0, 10.6 Hz, 1 H), 3.60 (dd, *J* = 1.7, 10.6 Hz, 1 H), 3.10–3.00 (broad s, 1 H), 2.90–2.80 (m, 1 H), 2.10–1.90 (m, 2 H), 1.30–1.10 (broad s, 22 H), 0.90–0.80 (m, 12 H), 0.02 (s, 3 H), 0.00 (s, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>): 145.55, 145.17 (quaternary aromatic), 134.99, 129.31 (HC=CH), 128.05, 127.84, 127.37, 127.08, 126.67, 125.72 (aromatic), 99.46 (OCN), 80.82 (OCH), 65.21 (OCH<sub>2</sub>), 59.41 (CNH), 32.21, 31.90, 29.66, 29.60, 29.45, 29.34, 29.08 (CH<sub>2</sub>), 25.78 (SiCCH<sub>3</sub>), 22.66 (quaternary, SiC), 14.10 (CH<sub>3</sub>), -5.49, -5.54 (SiCH<sub>3</sub>). IR (neat): 2925.5, 1463.5, 1450.1, 1254.1, 1122.4, 968.4, 837.4, 770.0, 750.4, 701.7, 631.3, 532.2 cm<sup>-1</sup>. [α]<sub>D</sub> = +46.7° (*c* = 0.9, CHCl<sub>3</sub>). **(2*S*,3*S*,4*E*)-2-Amino-4-octadecene-1,3-diol (*D*-threo-sphingosine) (13)** from 8a, mp 87–89 °C (lit. values<sup>7a,7b</sup> mp 86–87 °C and 88.0–88.5 °C). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 5.75 (dt, *J* = 7, 15.1

Hz, 1 H), 5.46 (dd,  $J = 6.2$ , 15.1 Hz, 1 H), 3.99 (t,  $J = 5.6$  Hz, 1 H), 3.71–3.65 (m, 1 H), 3.57–3.50 (m, 1 H), 2.79–2.75 (m, 1 H), 2.06–2.00 (m, 2 H), 1.80–1.50 (broad s, 4 H), 1.25 (broad s, 22 H), 0.88 (t,  $J = 6.4$  Hz, 3 H). **D-threo-sphingosine triacetate (14)**<sup>76</sup> from 13. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  5.77 (dt,  $J = 6.6$ , 14.2 Hz, 1 H), 5.64 (d,  $J = 9.7$  Hz, 1 H), 5.40 (m, 2 H), 4.43–4.37 (m, 1 H), 4.08 (dd,  $J = 2$ , 5.5 Hz, 2 H), 2.08–1.98 (m, 11 H, contains three singlets at 2.08, 2.07, 2.00), 1.25 (broad s, 22 H), 0.88 (t,  $J = 6.6$  Hz, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>):  $\delta$  170.54, 169.96, 169.75 (OC=O), 137.17, 123.99 (HC=CH), 72.94 (OCH), 62.97 (CH<sub>2</sub>O), 50.72 (CNH), 32.15, 31.79, 29.54, 29.45, 29.30, 29.21, 29.00, 28.68 (CH<sub>2</sub>), 23.10 (OAc), 22.57 (CH<sub>2</sub>), 20.95, 20.63 (OAc), 13.98 (CH<sub>3</sub>). IR (neat): 1747.1, 1653.8, 1540.3, 1456.8, 1371.1, 1231.8, 1045.4, 968.5 cm<sup>-1</sup>. [ $\alpha$ ]<sub>D</sub> = +8.2° ( $c = 2.2$ , CHCl<sub>3</sub>) [lit. values<sup>7b,7n</sup> +8.43°; +8.78° ( $c = 1.2$ , CHCl<sub>3</sub>)].

**(2S,3S,4E)-2-[N-(Diphenylmethylene)amino]-1-O-(tert-butylidimethylsilyl)-4-tridecene-1,3-diol (8b)** (oil, 15% EtOAc/petroleum ether, 65% method B). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.80–7.70 (m, 2 H), 7.50–7.40 (m, 2 H), 7.30–7.10 (m, 6 H), 5.66 (dt,  $J = 6.7$ , 15.2 Hz, 1 H), 5.24 (dd,  $J = 8.4$ , 15.2 Hz, 1 H), 4.29 (t,  $J = 8.3$  Hz, 1 H), 3.84 (dd,  $J = 3.3$ , 10.6 Hz, 1 H), 3.60 (dd,  $J = 2.1$ , 10.6 Hz, 1 H), 3.20–3.00 (broad s, 1 H), 2.95–2.85 (m, 1 H), 2.10–1.90 (m, 2 H), 1.40–1.15 (broad s, 12 H), 0.90–0.75 (m, 12 H), 0.02 (s, 3 H), 0.00 (s, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>):  $\delta$  145.49, 145.13 (quaternary, aromatic), 134.90, 129.31 (HC=CH), 127.99, 127.81, 127.34, 127.05, 126.64, 125.67 (aromatic), 99.44 (quaternary, OCN), 80.79 (OCH), 65.17 (CH<sub>2</sub>O), 59.35 (NCH), 32.16, 31.81, 29.36, 29.21, 29.03 (CH<sub>2</sub>), 25.74 (CH<sub>3</sub>, tBu), 22.62, 18.13 (CH<sub>3</sub>), 14.07 (CH<sub>3</sub>), -5.52, -5.57 (SiCH<sub>3</sub>). IR (neat): 2926.8, 1465.8, 1450.7, 1254.1, 1121.7, 1065.8, 1009.9, 968.2, 837.4, 778.0, 750.6, 701.1, 631.4 cm<sup>-1</sup>. [ $\alpha$ ]<sub>D</sub> = +41.9° ( $c = 2.8$ , CHCl<sub>3</sub>).

**(2S,3S,4E)-2-Amino-4-tridecene-1,3-diol from 8b**. Waxy solid. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  5.75 (dt,  $J = 6.9$ , 15.4 Hz, 1 H), 5.4 (dd,  $J = 6.7$ , 15.4 Hz, 1 H), 4.04 (t,  $J = 6.1$  Hz, 1 H), 3.70 (dd,  $J = 3.4$ , 11 Hz, 1 H), 3.56 (dd,  $J = 6.2$ , 11 Hz, 1 H), 3.15–2.90 (broad s, 4 H), 2.90–2.80 (m, 1 H), 2.15–2.00 (m, 2 H), 1.50–1.20 (m, 12 H), 0.90 (t,  $J = 7$  Hz, 3 H); <sup>13</sup>C NMR APT (CDCl<sub>3</sub>):  $\delta$  134.05, 129.46 (HC=CH), 73.08 (OCH), 63.56 (CH<sub>2</sub>O), 56.61 (CHN), 32.33, 31.83, 29.39, 29.24, 29.16, 22.60 (CH<sub>2</sub>), 14.04 (CH<sub>3</sub>). IR (neat): 3600–3200, 2925.0, 1458.3, 1379.9, 1253.9, 1028.0, 968.7, 853.3 cm<sup>-1</sup>. [ $\alpha$ ]<sub>D</sub> = -4.0° ( $c = 0.63$ , CHCl<sub>3</sub>). MS (CI-isobutane): 230 (M + 1), 212 (M + 1 - H<sub>2</sub>O). HRMS (CI-isobutane): M + 1 = 230.2129 (calcd for C<sub>13</sub>H<sub>28</sub>NO<sub>2</sub> (M + 1) 230.2120).

**(2S,3S,4E)-2-[N-(Diphenylmethylene)amino]-1-O-(tert-butylidimethylsilyl)-4-decene-1,3-diol (8c)** (oil, 10% EtOAc/petroleum ether, 40% method A, 60% method B). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.90–7.80 (m, 2 H), 7.80–7.70 (m, 2 H), 7.65–7.20 (m, 6 H), 5.74 (dt,  $J = 6.7$ , 15.2 Hz, 1 H), 5.32 (ddt,  $J = 1.3$ , 8.4, 15.2 Hz, 1 H), 4.36 (t,  $J = 8.2$  Hz, 1 H), 3.91 (dd,  $J = 3.0$ , 10.7 Hz, 1 H), 3.68 (dd,  $J = 1.6$ , 10.7 Hz, 1 H), 3.21–3.10 (broad s, 1 H), 3.00–2.90 (m, 1 H), 2.15–2.00 (m, 2 H), 1.50–1.20 (m, 6 H), 0.90–0.80 (broad s, 12 H), 0.09 (s, 3 H), 0.08 (s, 3 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  145.52, 135.08, 130.02, 129.23, 128.05, 127.84, 127.41, 127.08, 126.66, 125.70, 99.41, 80.82, 65.16, 59.36, 32.16, 31.27, 28.72, 25.89, 25.75, 22.45, 14.01, -5.57. IR (neat): 2928.9, 1448.5, 1251.7, 1089.1, 960.8, 832.4, 781.1, 695.5 cm<sup>-1</sup>. [ $\alpha$ ]<sub>D</sub> = +51.3° ( $c = 0.9$ , CHCl<sub>3</sub>).

**(2S,3S,4E)-2-Amino-4-decene-1,3-diol from 8c**. Waxy solid. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  5.76 (dt,  $J = 6.7$ , 15.4 Hz, 1 H), 5.46 (dd,  $J = 6.7$ , 15.4 Hz, 1 H), 3.98 (t,  $J = 6.0$  Hz, 1 H), 3.69 (dd,  $J = 4.3$ , 10.7 Hz, 1 H), 3.54 (dd,  $J = 6.2$ , 10.7 Hz, 1 H), 2.82–2.76 (m, 1 H), 2.15–2.00 (m, 2 H), 2.10–1.75 (broad s, 4 H), 1.44–1.20 (m, 6 H), 0.88 (t,  $J = 7$  Hz, 3 H); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  133.8, 129.8, 73.4, 64.0, 56.4, 32.2, 31.4, 28.8, 22.4, 13.9. IR (neat): 3500–3100, 2924.5, 1559.0, 1457.3, 1377.2, 968.8 cm<sup>-1</sup>. [ $\alpha$ ]<sub>D</sub> = -2.10° ( $c = 1.1$ , CHCl<sub>3</sub>). MS (CI-isobutane): 188 (M + 1), 170 (M + 1 - H<sub>2</sub>O). HRMS (CI-isobutane): M + 1 = 188.1672 (calcd for C<sub>10</sub>H<sub>22</sub>NO<sub>2</sub> (M + 1) 188.1651).

**(2S,3S,4E)-2-[N-(Diphenylmethylene)amino]-1-O-(tert-butylidimethylsilyl)-4-nonene-1,3-diol (8d)** (oil, 5% EtOAc/petroleum ether, 60% method B). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.75–7.65 (m, 2 H), 7.50–7.40 (m, 2 H), 7.30–7.10 (m, 6 H), 5.67 (dt,  $J = 6.8$ , 15.3 Hz, 1 H), 5.25 (ddt,  $J = 1.3$ , 7.1, 15.3 Hz, 1 H), 4.30 (t,  $J = 8.3$  Hz, 1 H), 3.85 (dd,  $J = 3.3$ , 10.6 Hz, 1 H), 3.6 (dd,  $J = 2.1$ , 10.6 Hz, 1 H), 3.12–3.00 (broad s, 1 H), 2.94–2.89 (m, 1 H), 2.03–2.00 (m, 2 H), 1.40–1.20 (m, 4 H), 0.90–0.80 (m, 12 H), 0.03 (s, 3 H), 0.02 (s, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>):  $\delta$  145.47, 145.12

(quaternary, aromatic), 134.89, 129.21 (HC=CH), 128.15, 127.97, 127.92, 127.78, 127.33, 127.03, 126.61, 125.65 (CH, aromatics), 99.39 (OCN), 80.77 (OCH), 65.13 (NCH), 59.34 (CH<sub>2</sub>O), 31.18, 31.13 (CH<sub>2</sub>), 25.70 (CH<sub>3</sub>, tBu), 22.05 (CH<sub>2</sub>), 18.11 (quaternary, tBu), 13.79 (CH<sub>3</sub>), -5.56, -5.62 (SiCH<sub>3</sub>). IR (neat): 2928.4, 1449.9, 1254.1, 1121.1, 969.3, 837.2, 777.1, 750.2, 701.7, 631.1 cm<sup>-1</sup>. [ $\alpha$ ]<sub>D</sub> = +55.5° ( $c = 3.2$ , CHCl<sub>3</sub>). **(2S,3S,4E)-2-Amino-4-nonene-1,3-diol from 8d**, mp 68–71 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  5.75 (ddt,  $J = 1$ , 6.8, 15.4 Hz, 1 H), 5.46 (ddt,  $J = 1.3$ , 6.8, 15.4 Hz, 1 H), 4.00 (t,  $J = 6.0$  Hz, 1 H), 3.68 (dd,  $J = 4.3$ , 10.8 Hz, 1 H), 3.54 (dd,  $J = 6.2$ , 10.8 Hz, 1 H), 2.90–2.80 (m, 1 H), 2.34–2.15 (broad s, 4 H), 2.15–2.0 (m, 2 H), 1.45–1.20 (m, 4 H), 0.90 (t,  $J = 7$  Hz, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>):  $\delta$  133.74, 129.71 (HC=CH), 73.54 (OCH), 64.25 (CH<sub>2</sub>O), 56.33 (CNH), 31.87, 31.20, 22.11 (CH<sub>2</sub>), 13.81 (CH<sub>3</sub>). IR (KBr): 3600–3000, 2925.7, 1583.5, 1456.8, 1378.7, 1053.9, 1023.9, 969.5, 860.1, 583.1, 487.4 cm<sup>-1</sup>. [ $\alpha$ ]<sub>D</sub> = -5.2° ( $c = 0.9$ , CHCl<sub>3</sub>). MS (CI-isobutane): 174 (M + 1), 156 (M + 1 - H<sub>2</sub>O). HRMS (CI-isobutane): M + 1 = 174.1492 (calcd for C<sub>9</sub>H<sub>20</sub>NO<sub>2</sub> (M + 1) 174.1494). Anal. Calcd: C, 62.43; H, 10.98; N, 8.09. Found: C, 62.38; H, 11.17; N, 8.07.

**(2S,3S,4E)-2-[N-(Diphenylmethylene)amino]-4-octadecen-3-ol (9a)** (oil, 10% EtOAc/petroleum ether, 78% method B). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.75–7.65 (m, 2 H), 7.60–7.50 (m, 2 H), 7.30–7.10 (m, 6 H), 5.71 (dt,  $J = 6.9$ , 15.2 Hz, 1 H), 5.28 (dd,  $J = 8.2$ , 15.3 Hz, 1 H), 3.83 (t,  $J = 8.3$  Hz, 1 H), 2.94 (dq,  $J = 6.4$ , 8.3 Hz, 1 H), 2.40–2.20 (broad s, 1 H), 2.03–1.96 (m, 2 H), 1.25 (broad s, 22 H), 1.18 (d,  $J = 6.4$  Hz, 3 H), 0.88 (t,  $J = 6.6$  Hz, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>):  $\delta$  145.80, 145.31 (quaternary, aromatic), 134.91, 129.93 (HC=CH), 128.69, 128.30, 128.08, 127.83, 127.61, 127.27, 126.92, 126.21, 125.36 (aromatic), 99.22 (OCN), 87.28 (OCH), 59.52 (CNH), 32.18, 31.85, 29.60, 29.40, 29.30, 29.02, 22.61 (CH<sub>2</sub>), 15.77 (1-CH<sub>3</sub>), 14.06 (18-CH<sub>3</sub>). IR (neat): 2923.9, 2852.9, 1489.1, 1450.2, 1378.1, 1232.6, 1067.3, 1029.3, 966.8, 749.2, 702.0 cm<sup>-1</sup>. [ $\alpha$ ]<sub>D</sub> = +75.8° ( $c = 2.7$ , CHCl<sub>3</sub>). **(2S,3S,4E)-2-Amino-4-octadecen-3-ol from 9a**, mp 67–70 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  5.72 (dd,  $J = 6.7$ , 15.4 Hz, 1 H), 5.40 (dd,  $J = 7.3$ , 15.4 Hz, 1 H), 3.67 (t,  $J = 7.3$  Hz, 1 H), 2.81–2.7 (m, 1 H), 2.7–2.5 (broad s, 3 H), 2.10–2.00 (m, 2 H), 1.26 (broad s, 22 H), 1.06 (d,  $J = 6.5$  Hz, 3 H), 0.88 (t,  $J = 7$  Hz, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>):  $\delta$  133.69, 130.44 (HC=CH), 77.36 (OCH), 51.33 (CNH), 32.28, 31.84, 29.59, 29.41, 29.28, 29.13, 22.60 (CH<sub>2</sub>), 20.18, 14.03 (CH<sub>3</sub>). IR (KBr): 3500–3300, 3344.4, 3277.8, 2922.2, 2855.6, 1466.7, 1450.0, 1372.2, 1094.4, 1038.9, 961.1 cm<sup>-1</sup>. Anal. Calcd for C<sub>18</sub>H<sub>37</sub>NO: C (76.32), H (13.07), N (4.95). Found: C (74.83), H (13.31), N (5.26). [ $\alpha$ ]<sub>D</sub> = +9.7° ( $c = 1.1$ , CHCl<sub>3</sub>).

**(2S,3S,4E)-2-[N-(Diphenylmethylene)amino]-4-tridecen-3-ol (9b)** (oil, 10% EtOAc/petroleum ether, 71% method B). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.75–7.65 (m, 2 H), 7.60–7.50 (m, 2 H), 7.4–7.2 (m, 6 H), 5.71 (dt,  $J = 6.9$ , 15.2 Hz, 1 H), 5.31 (ddt,  $J = 1.3$ , 8.3, 15.2 Hz, 1 H), 3.83 (t,  $J = 8.3$  Hz, 1 H), 3.00–2.90 (m, 1 H), 2.50–2.30 (broad s, 1 H), 2.10–1.90 (m, 2 H), 1.40–1.20 (m, 12 H), 1.18 (d,  $J = 6.4$  Hz, 3 H), 0.88 (t,  $J = 7$  Hz, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>):  $\delta$  145.78, 145.31 (quaternary, aromatic), 135.00 (HC=), 133.17 (aromatic), 129.96 (=CH), 128.67, 128.34, 128.11, 127.97, 127.84, 127.70, 127.61, 127.29, 126.95, 126.23, 125.37 (aromatic), 99.23 (NCO), 87.29 (OCH), 59.53 (NCH), 32.18, 31.80, 29.33, 29.19, 29.04, 28.98, 22.60 (CH<sub>2</sub>), 15.78 (CH<sub>3</sub>), 14.10 (CH<sub>3</sub>). IR (neat): 3297.9, 2925.7, 1489.6, 1450.6, 1378.3, 1232.6, 1067.5, 1029.7, 967.7, 750.2, 702.8, 630.4 cm<sup>-1</sup>. [ $\alpha$ ]<sub>D</sub> = +79.5° ( $c = 2.8$ , CHCl<sub>3</sub>).

**(2S,3S,4E)-2-Amino-4-tridecen-3-ol (10) from 9b**. Waxy solid. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  5.72 (dt,  $J = 6.7$ , 15.4 Hz, 1 H), 5.41 (dd,  $J = 7.0$ , 15.4 Hz, 1 H), 3.65 (t,  $J = 7.0$  Hz, 1 H), 2.90–2.70 (m, 1 H), 2.30–2.15 (broad s, 3 H), 2.10–2.00 (m, 2 H), 1.40–1.20 (m, 12 H), 1.10 (d,  $J = 6.5$  Hz, 3 H), 0.88 (t,  $J = 7$  Hz, 3 H). <sup>13</sup>C NMR APT<sup>33</sup> (CDCl<sub>3</sub>):  $\delta$  133.81, 130.34 (HC=CH), 77.32 (OCH), 51.33 (CNH), 32.27, 31.80, 29.36, 29.18, 29.12, 22.60 (CH<sub>2</sub>), 20.20 (1-CH<sub>3</sub>), 14.04 (13-CH<sub>3</sub>). IR (neat): 3500–3100, 2924.5, 1559.0, 1457.3, 1377.2, 968.8 cm<sup>-1</sup>. [ $\alpha$ ]<sub>D</sub> = +7.36° ( $c = 0.4$ , CHCl<sub>3</sub>). MS (CI-isobutane): 214 (M + 1), 196 (M + 1 - H<sub>2</sub>O). HRMS (CI-isobutane): M + 1 = 214.2166 (calcd for C<sub>13</sub>H<sub>28</sub>NO (M + 1) 214.2171).

**(2S,3S,4E)-2-[N-(Diphenylmethylene)amino]-4-decen-3-ol (9c)** (oil, 10% EtOAc/hexanes, 45% method A, 72% method B). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.75–7.65 (m, 2 H), 7.60–7.50 (m, 2 H), 7.40–7.10 (m, 6 H), 5.71 (dt,  $J = 6.8$ , 15.2 Hz, 1 H), 5.30 (ddt,  $J = 1.3$ , 8.2, 15.2 Hz, 1 H), 3.83 (t,  $J = 8.2$  Hz, 1 H), 3.00–2.90 (m, 1 H), 2.50–2.30 (broad s, 1 H), 2.10–1.90 (m, 2 H), 1.50–1.20 (m,

6 H), 1.18 (d,  $J = 6.4$  Hz, 3 H), 0.87 (t,  $J = 7$  Hz, 3 H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  145.81, 135.61, 128.28, 128.20, 127.93, 127.37, 127.02, 126.29, 125.42, 99.29, 87.38, 59.59, 32.21, 31.33, 28.71, 22.45, 15.84, 14.01. IR (neat): 2926.2, 1450.4, 1232.9, 957.3, 750.0, 702.8, 630.2  $\text{cm}^{-1}$ .  $[\alpha]_D = +84.3^\circ$  ( $c = 3$ ,  $\text{CHCl}_3$ ). (2*S*,3*S*,4*E*)-2-Amino-4-decen-3-ol from 9c. Waxy solid.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  5.72 (dt,  $J = 7.0$ , 15.4 Hz, 1 H), 5.41 (ddt,  $J = 1.2$ , 7.0, 15.4 Hz, 1 H), 3.20 (t,  $J = 7.0$  Hz, 1 H), 2.79–2.73 (m, 1 H), 2.03–2.00 (m, 2 H), 2.00–1.77 (broad s, 3 H), 1.44–1.20 (m, 6 H), 1.08 (d,  $J = 6.3$  Hz, 3 H), 0.88 (t,  $J = 6.8$  Hz, 3 H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  133.9, 130.3, 77.4, 51.3, 32.2, 31.3, 28.7, 22.5, 20.5, 13.9. IR (neat): 3600–3200, 2925.4, 1581.5, 1456.1, 1378.0, 1094.1, 1037.5, 971.5,  $\text{cm}^{-1}$ .  $[\alpha]_D = +4.6^\circ$  ( $c = 0.9$ ,  $\text{CHCl}_3$ ). MS (CI-isobutane):  $M + 1 = 172$  (M + 1), 154 (M + 1 –  $\text{H}_2\text{O}$ ). HRMS (CI-isobutane):  $M + 1 = 172.1680$  (calcd for  $\text{C}_{10}\text{H}_{22}\text{NO}$  (M + 1) 172.1701).

(2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-4-nonen-3-ol (9d) (oil, 10% EtOAc/petroleum ether, 73% method B).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  7.90–7.80 (m, 2 H), 7.80–7.60 (m, 2 H), 7.60–7.20 (m, 6 H), 5.71 (dt,  $J = 6.8$ , 15.3 Hz, 1 H), 5.30 (dd,  $J = 8.3$ , 15.3 Hz, 1 H), 3.80 (t,  $J = 8.3$  Hz, 1 H), 3.00–2.90 (m, 1 H), 2.50–2.20 (broad s, 1 H), 2.10–1.90 (m, 2 H), 1.40–1.20 (m, 4 H), 1.18 (d,  $J = 6.3$  Hz, 3 H), 0.87 (t,  $J = 7$  Hz, 3 H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  135.19, 130.05, 128.64, 128.22, 127.93, 127.05, 126.31, 125.43, 99.25 (OCN), 87.41 (OCH), 59.59 (CNH), 31.95, 31.21, 22.18, 15.86, 13.90. IR (neat): 2957.8, 2926.2, 1726.8, 1662.3, 1450.0, 1276.5, 1067.7, 1029.1, 968.0, 749.8, 702.4, 630.0  $\text{cm}^{-1}$ .  $[\alpha]_D = +64.6^\circ$  ( $c = 1.2$ ,  $\text{CHCl}_3$ ). (2*S*,3*S*,4*E*)-2-Amino-4-nonen-3-ol from 9d. Oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  5.73 (ddt,  $J = 0.8$ , 6.7, 15.3 Hz, 1 H), 5.41 (ddt,  $J = 1.4$ , 7.0, 15.3 Hz, 1 H), 3.64 (t,  $J = 6.7$  Hz, 1 H), 2.82–2.72 (m, 1 H), 2.10–2.03 (m, 5 H), 1.40–1.33 (m, 4 H), 1.21 (d,  $J = 6.5$  Hz, 3 H), 0.90 (t,  $J = 7$  Hz, 3 H).  $^{13}\text{C}$  NMR APT<sup>33</sup> ( $\text{CDCl}_3$ ):  $\delta$  133.61, 130.46 (HC=CH), 77.33 (OCH), 51.30 (CNH), 31.92, 31.24, 22.10 ( $\text{CH}_2$ ), 20.08 (1- $\text{CH}_3$ ), 13.81 (9- $\text{CH}_3$ ). IR (neat): 3500–3000, 2926.4, 1582.7, 1453.8, 1378.3, 1141.1, 1093.4, 1037.5, 970.0, 865.8, 730.1  $\text{cm}^{-1}$ .  $[\alpha]_D = +10.9^\circ$  ( $c = 3.4$ ,  $\text{CHCl}_3$ ). MS (CI-isobutane):  $M + 1 = 158$  (M + 1), 140 (M + 1 –  $\text{H}_2\text{O}$ ). HRMS (CI-isobutane):  $M + 1 = 158.1544$  (calcd for  $\text{C}_9\text{H}_{20}\text{NO}$  (M + 1) 158.1545).

(4*S*,5*S*)-5-((*E*)-Dec-1-en-1-yl)-4-methyl-2-oxazolidinone (11). To a flame-dried reaction flask was added amino alcohol 10 (119 mg, 0.56 mmol), carbonyldiimidazole (118 mg, 0.73 mmol), and 2 mL of freshly distilled THF. The resulting solution was stirred for 2 h at rt. The THF was evaporated, the resulting residue was dissolved in  $\text{Et}_2\text{O}$ , washed ( $3 \times 1$  N HCl,  $1 \times$  saturated  $\text{NaHCO}_3$ ), and dried ( $\text{K}_2\text{CO}_3$ ), and the solvent was removed under reduced pressure to provide crude material. Chromatography<sup>29</sup> (50% EtOAc/hexanes) provided 93 mg of pure product (70%, 0.39 mmol) as an oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  6.20 (broad s, 1 H), 5.85 (dd,  $J = 6.8$ , 15.4 Hz, 1 H), 5.50 (ddt,  $J = 7.9$ , 15.4, 1.4 Hz, 1 H), 4.43 (apparent t,  $J = 7.6$  Hz, 1 H), 3.70–3.50 (m, 1 H),

2.10–2.00 (m, 2 H), 1.25 (broad s, 12 H), 0.88 (t,  $J = 6.6$  Hz, 3 H).  $^{13}\text{C}$  NMR APT<sup>33</sup> ( $\text{CDCl}_3$ ):  $\delta$  159.31 (C=O), 137.75, 125.31 (HC=CH), 85.21 (OCH), 54.27 (CNH), 32.10, 31.80, 29.33, 29.17, 29.04, 28.63, 22.60 ( $\text{CH}_2$ ), 19.22 (4- $\text{CH}_3$ ), 14.06 ( $\text{CH}_3$ ).  $[\alpha]_D = -29.9^\circ$  ( $c = 1.6$ ,  $\text{CHCl}_3$ ).

(4*S*,5*S*)-2,2-Diphenyl-5-((*E*)-dec-1-en-1-yl)-4-((*tert*-butyldimethylsiloxy)methyl)-*N*-(phenylcarbamoyl)oxazolidine (12). (2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-1-*O*-(*tert*-butyldimethylsilyl)-4-tridecene-1,3-diol (8b) (421 mg, 0.83 mmol) in dry pyridine (2 mL) was treated with  $\text{PhN}=\text{C}=\text{O}$  (1.8 mmol, 2.2 equiv) and stirred at rt overnight. Pyridine and unreacted phenyl isocyanate were removed under reduced pressure, and chromatography<sup>29</sup> (20% EtOAc/petroleum ether) provided 409 mg of the pure product (78% yield, 0.65 mmol) as an oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  7.70–7.60 (m, 2 H), 7.50–7.20 (m, 9 H), 7.20–7.10 (m, 2 H), 6.90–6.80 (m, 2 H), 6.43 (broad s, 1 H), 5.83 (dt,  $J = 6.4$ , 15.4 Hz, 1 H), 5.66 (dd,  $J = 7.1$ , 15.4 Hz, 1 H), 4.25 (apparent t,  $J = 7.7$  Hz, 1 H), 4.18–4.12 (m, 1 H), 3.92 (dd,  $J = 3.9$ , 10.5 Hz, 1 H), 3.84 (dd,  $J = 4.7$ , 10.5 Hz, 1 H), 2.10–2.0 (m, 2 H), 1.40–1.20 (broad s, 12 H), 0.90–0.80 (m, 12 H), 0.01 (s, 3 H), 0.00 (s, 3 H);  $^{13}\text{C}$  NMR APT<sup>33</sup> ( $\text{CDCl}_3$ ):  $\delta$  152.69 (C=O), 141.70, 140.58, 138.37 (quaternary, aromatic), 136.63, 128.52 (HC=CH), 128.46, 128.37, 128.23, 128.12, 126.70, 122.76, 119.49 (aromatic), 98.08 (OCN), 79.12 (OCH), 64.65 (HC-N), 62.65 ( $\text{CH}_2\text{O}$ ), 32.19, 31.74, 29.30, 29.08, 28.69 ( $\text{CH}_2$ ), 25.80 ( $\text{SiCCH}_3$ ), 22.54 ( $\text{SiCCH}_3$ ), 14.01 ( $\text{CH}_3$ ), –5.40 ( $\text{SiCH}_3$ ). IR (neat): 1673.6, 1596.9, 1528.7, 1441.9, 1332.1, 1249.5, 1102.7, 836.9, 751.6, 700.1  $\text{cm}^{-1}$ .  $[\alpha]_D = -14.1^\circ$  ( $c = 1.2$ ,  $\text{CHCl}_3$ ).

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**Supplementary Material Available:**  $^1\text{H}$  NMR (250 MHz) and  $^{13}\text{C}$  NMR (62.5 MHz) spectra of compounds 2a–14 and amino alcohols (sphingosines) derived from the hydrolysis of compounds 8a–d and 9a–d (59 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

## An Efficient, Regiocontrolled Synthesis of 5-Aryl-2-carbethoxypyrroles from 3-Aryl-3-chloropropeniminium Salts<sup>1</sup>

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A variety of 3-aryl-3-chloropropeniminium salts react with  $\alpha$ -amino acid esters under basic conditions to produce 2-carbethoxy-5-arylpyrroles in a regioselective manner. The overall process represents a short, efficient, and convergent synthesis of 2,5-disubstituted pyrroles, and azomethine ylides or azapentadienyl anions may be involved as intermediates.

We have recently reported<sup>2</sup> a short, convergent and regiocontrolled synthesis of 4-aryl-2-carbethoxypyrroles from

the condensation of 2-arylvinamidinium salts (1) with either glycine ethyl ester or sarcosine ethyl ester.