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, $-OCH_2CH_3$), 3.76 (s, 3 H, $OCH_3$), 3.74 (s, 3 H, $OCH_3$), 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, $CH_2CH_3$). $^{13}C$ 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): $\nu_{max}$ 3500–3200, 3000, 1740, 1695, 1670, 1630, 1620, 1590, 1520, 1375, 1275, 1142, 1130, 1060, 1040, 870, 845, 690 cm$^{-1}$. MS (EI): $m/e$ 549 (fragment ion, $M^+$ – Boc).

Anal. Calcd for $C_{34}H_{39}N_3O_{10}$: C, 62.85; H, 6.05; N, 6.47. Found: C, 62.80; H, 6.00; N, 6.49.

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**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-$MeOC_6H_4CHO$, 123-11-5; $HS(CH_2)_3SH$, 109-80-8; $Me_3SiCH_2CH_2OH$, 2916-68-9; (*R*)-$H_2NCH(Ph)CH_2OH$, 56613-80-0; (*S*)-$H_2NCH(Ph)CH_2OH$, 64205-12-5.

**Supplementary Material Available:** $^1H$ NMR spectra of **4–9** and **12** and both $^1H$ and $^{13}C$ 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 α-Amino Esters: Chirality Transfer via Sequential Addition of Hydride and C-Nucleophiles. 2-Amino Alcohols and Sphingosines†

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The reaction of α-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 $iBu_2AlH$ or $iBu_2AlH$-$Bu_3Al$, followed by RMgX or 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 ($CH_2Cl_2$–hexane) provided the highest stereoselectivities. Use of the less-reactive $iBu_2AlH$·$iBu_3Al$ complex lowered the amount of undesired primary alcohol products observed. Thermally labile aluminoxy acetal intermediates were observed by $^1H$ 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 $S_N2$-like displacement of the aluminoxy acetal or displacement of a tight-ion pair. In addition to the synthesis of optically pure arylethanolamines **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[2] and their derivatives (cf. ceramides, cerebrosides, glycosphinolipids, gangliosides, and their *lyso* derivatives)[3] are known to play diverse roles in many biological systems. Glycosphingolipids influence cell metabolism in vertebrates, as well as in lower organisms (fungi).[7c] Galactosyl ceramide has recently been shown to be a receptor for HIV binding in cells lacking the CD4 receptor.[4e] Analogs of glycosphingolipids have been the subject of much interest as inhibitors of influenza-induced sialidase activity, as well as endoglycoceramidase inhib-

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

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

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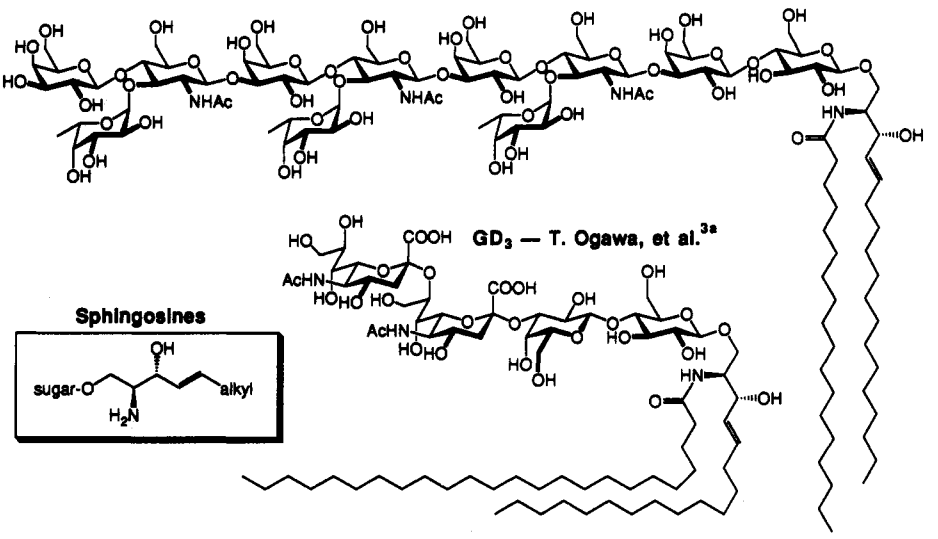
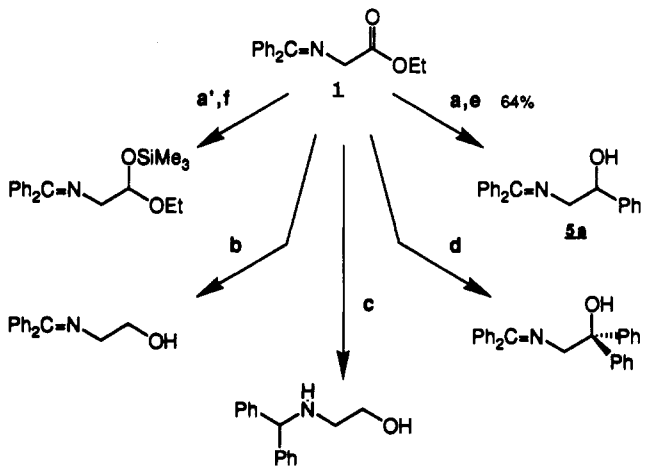
0022-3263/92/1957-5469$03.00/0 

**Scheme I**




**Scheme II**[a]




[a] (a) 2 $iBu_2AlH/CH_2Cl_2/-78$ °C; (a') $iBu_2AlH{\cdot}iBu_2Al/CH_2Cl_2/-78$ °C; (b) 2.5 $iBu_2AlH/CH_2Cl_2/0$ °C/4 h; (c) 5 $iBu_2AlH/CH_2Cl_2/rt/16$ h; (d) $3PhMgBr/Et_2O/rt/1$ h; (e) $3PhMgBr/Et_2O/-78$ °C → rt; (f) TMS-imidazole.

itors.[4a] Perhaps most importantly, sphingosines and their derivatives have been shown to influence the transfer of information between developing vertebrate cells.[4]

While several methods for the synthesis of optically pure sphingosines have been utilized,[7] 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 α-amino aldehyde and reacted with various carbon nucleophiles. While optically active α-amino aldehydes derived from their corresponding α-amino acids are potentially useful in a number of synthetic contexts,[8] these

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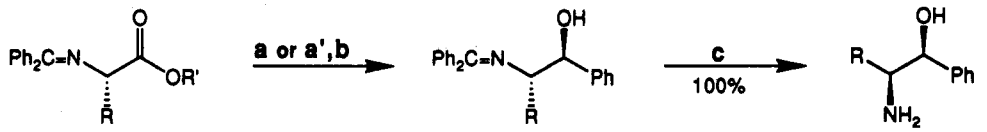
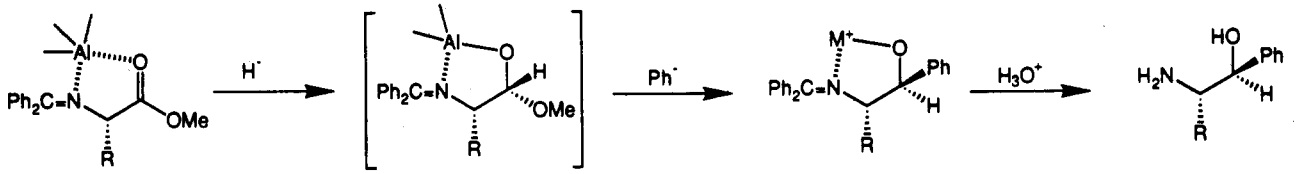
**Scheme III**[a]




| | | | | | |
|---|---|---|---|---|---|
| 1 | R = H, R' = Et | 5a | 64% or 86%[†] | 6a | —t/e— |
| 2b | R = $CH_3$, R' = Et | 5b | 54% or 78%[†] | 6b | 8.8 : 1* |
| 3 | R = $CH_2Ph$, R' = Me | 5c | 69% or 75%[†] | 6c | 8.0 : 1* |
| 4b | R = $CH_2OSi(Me)_2$-tBu, R' = Me | 5d | 62% or 73%[†] | 6d | 8.0 : 1* |

[a] (a) 2 equiv of $iBu_2AlH/CH_2Cl_2/-78$ °C; (a') 1 equiv of $iBu_2AlH{\cdot}AliBu_3/CH_2Cl_2/-78$ °C; (b) 3 equiv of PhMgBr/$Et_2O/-78$ °C → 0 °C; (c) $H_3O^+$. [†] Yield using method a'. *threo/erythro ratio by NMR.

**Scheme IV**




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

Newman[7a] 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[7e-g] 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 α-amino aldehydes which avoids the problem of enolization has been used by Rapoport, and it employs the 9-phenylfluorenyl blocking group for the amine.[10,11]

It is clear that new diastereoselective methods for the synthesis of β-amino alcohols from α-amino acid derivatives which are more configurationally stable than α-amino aldehydes would be useful. Studies performed in our laboratory have revealed that sequential treatment of O'Donnell's Schiff base esters[16] with $iBu_2AlH$ or

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(19) (a) 1-Phenyl-2-aminoethanol: Pouchert, C. J. *Aldrich Handbook of NMR Spectra*; Aldrich Chemical Co.: Milwaukee, WI, 1983; Vol. 1, 1079A. (b) (1*S*,2*S*)-(+)-2-Amino-1-phenyl-1-propanol: Baudet, M.; Gelbcke, M. *Anal. Lett.* **1979**, *12B*, 325. The (1*R*,2*R*)-(−)-isomer is available from Aldrich Chemical Co. as the HCl salt. (c) (1*S*,2*S*)-(+)-2-Amino-1,3-diphenyl-1-propanol: Marcot, B.; Rabaron, A.; Viel, C.; Bellec, C.; Deswarte, S.; Maitte, P. *Can. J. Chem.* **1981**, *59*, 1224. (d) Identical with (1*S*,2*S*)-(+)-2-amino-1-phenyl-1,3-propanediol from Aldrich Chemical Co.

$iBu_3Al{\cdot}iBu_2AlH$ and PhMgBr provide the corresponding α-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 $iBu_2AlH$ or $iBu_3Al{\cdot}iBu_2AlH$ were used as hydride source. Chemical yields were markedly superior for the $iBu_3Al{\cdot}iBu_2AlH$/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 °C, the racemization problems associated with isolating the intermediate α-amino aldehyde have been avoided. Evidence obtained in this laboratory suggests that the α-amino aldehyde resulting from DIBAL reduction of the ester is *not* the reactive species. Instead, the thermally labile aluminoxy acetal[24h] 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 aluminoxy 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 $iBu_2AlH$ in $CH_2Cl_2$ at −78 °C and totally inert toward PhMgBr in $Et_2O$. At higher temperatures (e.g. rt) $iBu_2AlH$ reduced the $Ph_2C{=}N$ group to $Ph_2CH{-}NH$, but only after the ester was completely reduced to the primary alcohol. In the absence of added PhMgBr, reduction to the aluminoxy acetal[18] was extremely slow, as indicated by the reaction with TMS-imidazole to provide the monosilyl acetal. Even after 30 h at −78 °C, reduction of the chelating ester **1** was not complete in the absence of RLi or RMgX. Treatment of **1** with 2 equiv of $iBu_2AlH$ in $CH_2Cl_2$ at −78 °C for 1 h, followed by 3 equiv of PhMgBr in $Et_2O$, and warming to rt afforded the crystalline secondary alcohol **5a** in 64% yield after aqueous workup. Thus, sequential addition of $H^-$ followed by $Ph^-$ to chelating Schiff base esters was shown to be plausible.

The diastereoselectivity of the reaction with $iBu_2AlH$ and 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 β-amino alcohols **5a–d** by quenching the reaction with $NaHCO_3$ or the known phenylethanolamines[19] **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[20] for initial hydride delivery to the ester, followed by subsequent inversion of the resulting aluminoxy 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 $iBu_2AlH$ were required for complete conversion of the Schiff base esters; use of lesser amounts resulted in recovery of unreacted starting material.[21] Unfortunately, use of 2 equiv of $iBu_2AlH$ resulted in the formation of significant amounts of overreduced primary alcohols. We reasoned that the additional $H^-$ from the second equivalent of DIBAL was competing with $Ph^-$ for the electrophilic aluminoxy acetal (aldehyde) in the alkylation step. The simplest solution to the overreduction problem proved to be the use of a 1:1 mixture of $iBu_2AlH$ and $iBu_3Al$,[22] 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 α-amino ketones was by Sorm et al. who reduced derivatives of dehydrochloramphenicol using Al-catalyzed Meerwein–Pondorf–Verley reaction conditions. These reactions displayed either α- or β-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.; Rotteveel, 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.; Sakuria, 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.

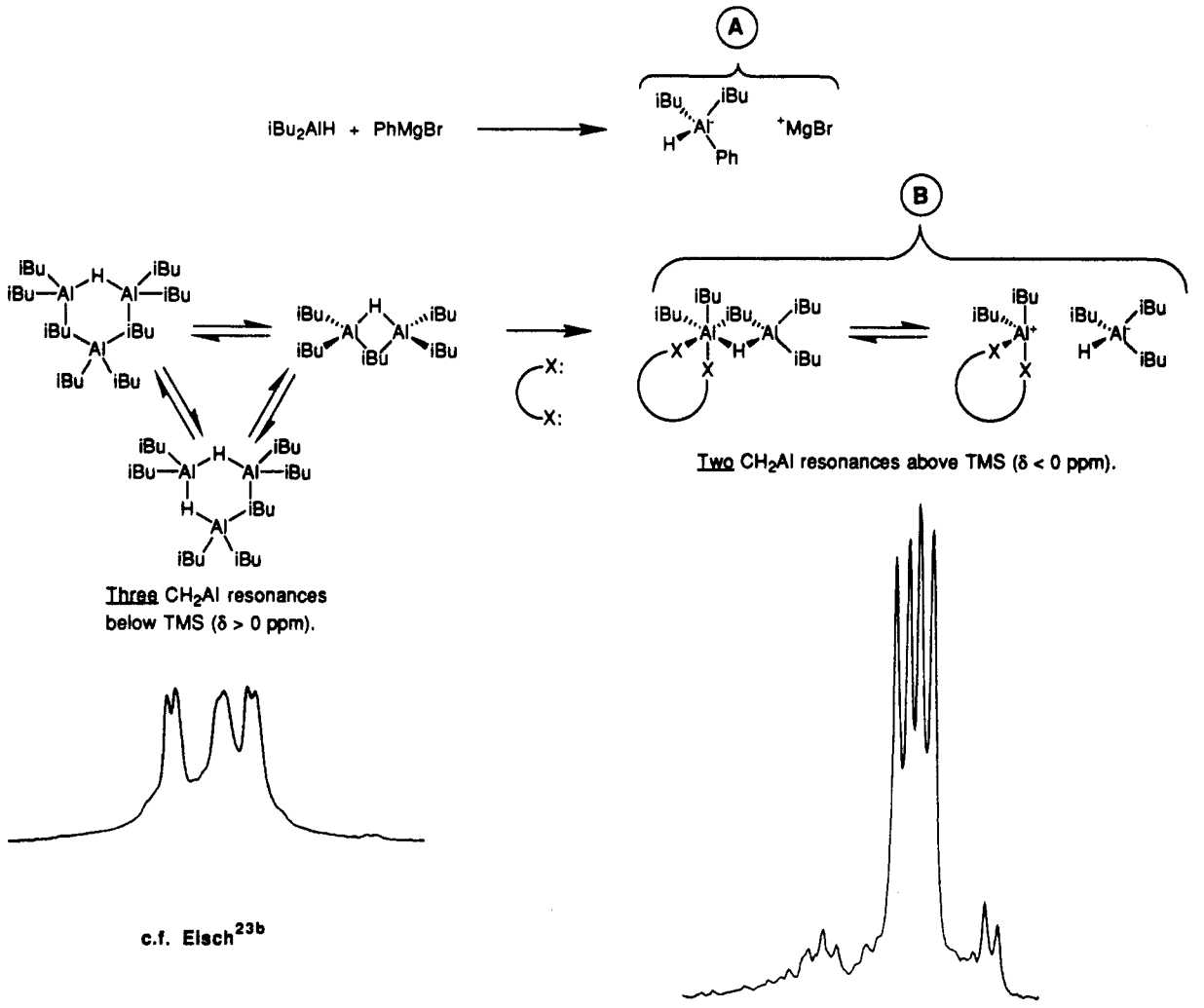
(22) Replacement of the second $H^-$ equivalent with a *bridging ligand* such as $Cl^-$ or $PhO^-$ also supressed the overreduction.[21l,m] $Et_2AlCl{\cdot}iBu_2AlH$ was formed by mixing equimolar amounts of DIBAL and $Et_2AlCl$, and $iBu_2AlOPh{\cdot}iBu_2AlH$ was formed by adding phenol to DIBAL, but 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 ($S_N1$ vs $S_N2$) 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.; Elliot, 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.; Elliot, 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 $S_N2$-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 β-amino alcohols. Normally, $J_{anti} < J_{syn}$: (a) Seebach, D.; Beck, A. K.; Mukhopadhlyay, 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.

**Scheme V**

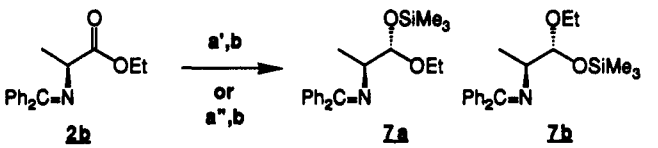



in hexanes. $iBu_2AlH$-$iBu_3Al$ in hexanes is the reagent (method a′, Scheme II) now routinely used in the reduction/alkylation chemistry.

Whereas $iBu_2AlH$ is known to be trimeric in noncoordinating solvents, the addition of $iBu_3Al$ provides an equilibrium mixture of interconverting 2:1 trimer, 1:2 trimer, and 1:1 dimer[23] (Scheme V). The $AlCH_2$ resonances for this mixture in $CD_2Cl_2$ at −47 °C appear at +0.1589, +0.0815, and +0.0410 ppm as doublets in the $^1H$ NMR. This mixture undergoes a profound and immediate change upon addition of 1 equiv of Schiff base **2a**, shifting to a pair of 7-Hz doublets at −0.2117 and −0.2374 ppm.[38] This result suggests that the 1:1 dimer may form a complex with the bidentate Schiff base prior to reduction/alkylation. This interpretation is consistent with the increasing carbanionic character of the unsymmetrical "ate complex" **B** as the bidentate ligand supplies more electron density to the aluminum metal via σ-donation. The aluminoxy acetal forms much more slowly (72 h) at −78 °C in the absence of added PhMgBr because "ate complex" **B** is much less reactive than the discrete "ate complex" **A**. Complexes such as **A** are known to be powerful reducing agents.[17]

Mechanistic studies reveal two important points concerning the reaction sequence: (1) although $iBu_2AlH$ or $iBu_3Al$-$iBu_2AlH$ alone will stereoselectively deliver hydride to the ester in $CH_2Cl_2$ or $PhCH_3$ at −78 °C very slowly, *the ate complex formed upon addition of RMgX or RLi is the kinetically active reducing agent*,[17] and (2) the subsequent alkylation step is extremely solvent dependent, and is *best characterized as a Lewis acid-assisted $S_N2$ process (tight ion-pair displacement)*.

**Scheme VI**[a]




| Conditions | Ratio 7a : 7b |
|---|---|
| a' | 6.5 : 1 |
| a" | 2 : 1 |

[a] (a′) $iBu_2AlH$-$AliBu_3/CH_2Cl_2$/−78 °C/72 h; (a″) $iBu_2AlH$-$PhLi/CH_2Cl_2$-$Et_2O$/−78 °C/2 h; (b) TMS-imidazole/−78 °C → 0 °C.

To gain additional insight on the mechanism of this reaction, the intermediate aluminoxy acetal[26] derived from **2b** was trapped with (trimethylsilyl)imidazole to provide the somewhat labile monosilyl acetal **7a** (Scheme VI). In the absence of a nucleophile such as PhMgBr (c.f. "ate complex" **B** in Scheme V), reduction occurred very slowly,

(26) Racemic monosilyl acetals have been synthesized via $Rh^I$-catalyzed hydrosilation of esters: (a) Ojima, I.; Kumagai, M.; Nagai, Y. *J. Organomet. Chem.* **1976**, *111*, 43. They have also been generated in the reaction of esters with organometallics in the presence of $Me_3SiCl$: (b) Reetz, M. T.; Heimbach, H.; Schwellnus, K. *Tetrahedron Lett.* **1984**, *25*, 511. (c) Cooke, M. P. *J. Org. Chem.* **1986**, *51*, 951. Chiral, optically active monosilyl-acetals such as **7a** and **7b** have synthetic uses as electrophiles, as well. A study of this aspect is underway and will be the subject of a forthcoming communication.

but cleanly at −78 °C to afford a 6.5:1 mixture[27] of **7a** and **7b** after 72 h. Presumably, hydride reduction of imino ester **2b** proceeds through a cyclic Cram chelate to yield **7a** as the major product, although definative proof of the configurations of **7a** or **7b** does not exist. If the reaction mixture is warmed to −23 °C for only 1 h and trapped with TMS-imidazole at −78 °C as before, complete reduction is observed and a 1:3 mixture of **7a** and **7b** is recovered. This suggests that equilibration of the initally formed "*syn*" aluminoxy acetal to the more stable "*anti*" form occurs at higher temperatures. This equilibration process can be compared to the "anomerization"[35] of carbohydrate derivatives via ion-pair mechanisms.

If a discrete aluminum "ate complex" was generated from $iBu_2AlH{\cdot}iBu_3Al$ and PhLi (cf. "ate complex" A in Scheme IV) and used to accomplish the reduction,[17] a 2:1 mixture of the two isomeric monosilyl acetals **7a** and **7b** was formed *in 2 h* at −78 °C. Clearly, the more reactive aluminate hydride donor was not as selective in the ester reduction as the more Lewis acidic 1:1 DIBAL–TRIBAL mixture. Very similar conditions (2 equiv of $iBu_2AlH$/3 equiv of PhLi) also provided much poorer selectivity (nearly 2:1) in the alkylation reaction **2b** → **5b**. Thus, we feel confident in stating that the initial hydride transfer step is stereochemically significant.

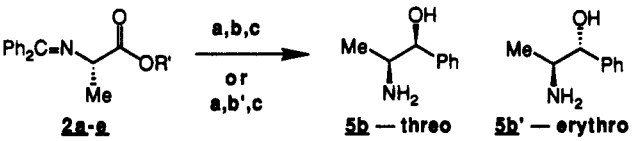
That the intermediate aluminoxy acetal is long lived at −78 °C and is indeed stable enough to be trapped with TMS-imidazole is not surprising in light of the examples of similar chelated tetrahedral intermediates that have been previously generated.[12-15,26] For example, the long-standing problem of controlling the addition of metal alkyls to esters to provide ketones has been solved by stabilizing the intermediate tetrahedral structure by chelation. There are numerous methods for reducing the resultant ketones stereoselectively to provide the corresponding secondary alcohol.[12] Rapoport has demonstrated that the classical direct conversion of a free carboxylate to a ketone via alkyllithium addition can be effected with the proper choice of N-protection and by modification of the reaction conditions (use of RLi–RMgX mixtures).[13] Mukaiyama[14a,b] and Weinreb[14c] inter alia[14d] have used chelation to stabilize the intermediate metaloxy acetals derived from the addition of an organometallic to thiopyridyl esters and *N*-methoxy-*N*-methylamides, respectively.

Meyers,[15a] Comins,[15b] and Burke,[15c] inter alia,[15d-f] have used chelation to stablize intermediate metaloxy acetals in order to affect sequential, stereoselective delivery of a hydride and/or organometallic reagents to provide secondary and tertiary alcohols directly from the carboxylic acid derivative. Mechanistically, this process has generally been viewed as a two-step process involving the elimination of alkoxide from the metaloxy acetal to produce a transient ketone or aldehyde,[8p,15b,c] followed by addition of the second nucleophile, although Meyers' scheme suggests a displacement reaction.[15a] Ibuka, Fujii, and Yamamoto[8p] observed a highly (15:1) *threo*-selective reaction when t-Boc-protected methylalaninate was treated sequentially with DIBAL and $H_2C{=}CHMgCl$ (but *not* when treated with $H_2C{=}CHMgBr$). These authors presumed that an aluminum-chelated t-Boc-amino aldehyde (cyclic Cram transition state[20]) was the intermediate responsible for the observed *threo* selectivity. Kiyooka[24h] has invoked racemic aluminoxy-acetals as long-lived intermediates, but has not presented any stereochemical data.

There are two plausible mechanistic extremes for the conversion of the aluminoxy acetal intermediate to the observed *threo*-alcohol:[24] (1) an $S_N1$-like mechanism involving *elimination* of an alkoxy group to generate an aldehyde intermediate which would suffer Cram-controlled addition by the Grignard, and (2) an $S_N2$-like mechanism involving a *displacement* of the alkoxy group with inversion. In the presence of aluminum alkyls, one can imagine that a pathway intermediate between these $S_N1$ and $S_N2$ extremes is possible, e.g. a Lewis acid-assisted displacement.[24c] Alternatively, one might wish to envision the intermediate pathway as a displacement of a tight ion-pair. If the $S_N1$-like mechanism is operative, then the identity of the alkoxy group of the aluminoxy acetal should *not* affect the stereoselectivity of the alkylation reaction.

A series of alanine Schiff base esters **2a–e** were studied to determine the effect of increasing the steric bulk of the ester on the stereoselectivity of the $iBu_2AlH{\cdot}iBu_3Al$/PhMgBr reaction (Scheme VII). The reaction mixtures were hydrolyzed directly to the phenylpropanolamines **5b** with 1 N HCl, washed with $Et_2O$, converted to the free bases, and analyzed by 250-MHz $^1H$ NMR without any further purification. When $Et_2O$ was used as a cosolvent, there was a correlation between the bulk of the ester and the observed *threo* selectivity. As the bulk of the ester increased from Me (**2a**) to t-Bu (**2e**), the *threo* selectivity increased from 7.6:1 to 11:1. This provides evidence that the alkoxy group plays a role in the alkylation step of the reaction. If the intermediate in this reaction were an aldehyde, either free or aluminum-chelated,[8o-q] one would expect the same stereoselectivity, regardless of the bulk

**Scheme VII**[a]




**2a-e** **5b** — threo **5b'** — erythro

| Ester | | In $Et_2O$ | In $Et_2O$/THF |
|---|---|---|---|
| **2a** | R' = Me | 7.6 : 1 | 2.7 : 1 |
| **2b** | R' = Et | 8.8 : 1 | 2.6 : 1 |
| **2c** | R' = $CH_2Ph$ | 6.3 : 1 | 2.6 : 1 |
| **2d** | R' = $CHPh_2$ | 10.7 : 1 | 3.2 : 1 |
| **2e** | R' = tBu | 11.0 : 1 | 3.8 : 1 |

[a] (a) 1 equiv of $iBu_2AlH{\cdot}iBu_3Al/CH_2Cl_2/-78$ °C; (b) 3 equiv of PhMgBr/$Et_2O/-78$ °C → 0 °C; (b') 3 equiv of PhMgBr/$Et_2O$–THF (1:1)/−78 °C → 0 °C; (c) $H_3O^+$.

(27) Monosilyl acetal **7a** was isolated by flash chromatography on $SiO_2$ with 10% EtOAc/hexanes. (The corresponding mixed acetal derived from alanine *methyl* ester was *not* stable to $SiO_2$ chromatoraphy.) $^1H$ NMR (250 MHz, $CDCl_3$): δ 7.65–7.10 (m, 10 H), 4.82 (d, *J* = 6.3 Hz, 1 H), 3.80–3.60 (m, 1 H), 3.50–3.30 (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). $[\alpha]_D$ = +31.4 (*c* = 4.4, $CHCl_3$). NOE studies were inconclusive. Monosilyl acetal **7b** could *not* be isolated in pure form, but was observed as mixtures with **7a**.

(28) Observed mp 87–89 °C for **13** (lit. mp 86–87 °C[7e] and 88.0–88.5 °C[7h]). We were unable to dissolve enough of the amino diol **13** in either wet or dry $CHCl_3$ to observe a reliable optical rotation.[7e] Observed $[\alpha]_D$ = +8.2° (*c* = 2.3/$CHCl_3$) for **14** (lit. $[\alpha]_D$ 8.43° ($CHCl_3$)[7b] and 8.78° (*c* = 1.2, $CHCl_3$)[7n]]. See the Experimental Section for $^1H$ and $^{13}C$ NMR data and MS data for **13** and **14**.

(29) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(30) (a) Szabó, L. Z.; Li, Y.; Polt, R. *Tetrahedron Lett.* **1991**, *32*, 585. (b) Polt, R.; Szabó, L. Z.; Treiberg, J.; Li, Y.; Hruby, V. J., submitted to *J. Am. Chem. Soc.* (c) Szabó, L.; Polt, R., manuscript in preparation. (d) Polt, R.; Peterson, M. A., manuscript in preparation.

(31) Peterson, M. A.; Polt, R. *Synth. Commun.* **1992**, *22*, 477.

(32) Perrin, D. D.; Armarego, W. L. *Purification of Laboratory Chemicals*; Plenum Press: New York, 1988.

(33) Attached proton test: Patt, S.; Shoolery, J. N. *J. Magn. Reson.* **1982**, *46*, 535.

(34) Zweifel, G.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 2753.

(35) Lemieux, R. U. *Adv. Carbohydr. Res.* **1954**, *9*, 1.

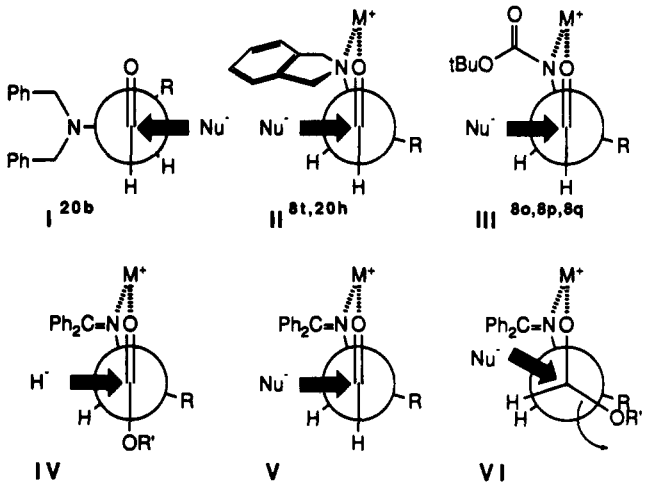



Figure 1.

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 aluminoxy 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 aluminoxy 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-α-amino aldehydes[20b,g] showed that steric interference with the chelating-ability of the nitrogen lone pair (e.g. by *N,N*-dibenzyl substitution[8t]) 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.[20e] 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.[8t] Several groups[8o-q] 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.[20] It is unclear whether Rapoport's 9-phenylfluorenyl-protected α-amino aldehydes[10] 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 α-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**

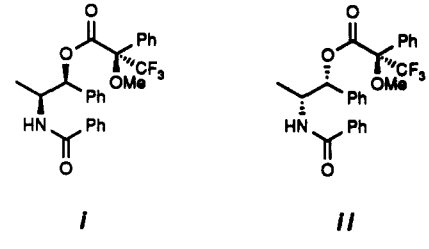

Figure 2.

($S_N1$-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 aluminoxy 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 aluminoxy 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** ↔ **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. Garners's t-Boc-protected cyclic aldehyde[7e]), facile loss of optical activity in α-amino aldehyde derivatives is a general problem, especially under the basic conditions encountered during nucleophilic additions to aldehydes.[8r,9-11] 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.[36] Similarly, known sphingosine triacetate **14** (vide infra) showed an optical rotation of 93–97%[28] of the expected value.[7b,n] Carbohydrate-bearing glycosphingolipids

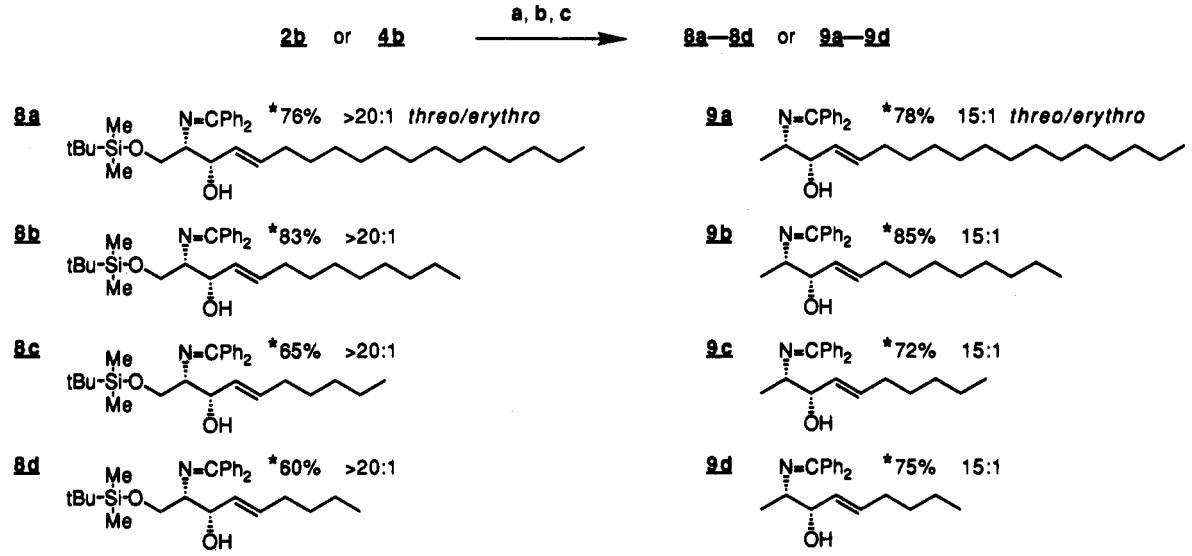
(36) The Mosher ester[37] i was prepared from synthetic amino alcohol **6b** and compared with the diastereomeric Mosher ester ii prepared from the commercially available[19b] enantiomer of **6b**, (1*R*,2*R*)-(−)-norpseudoephedrine hydrochloride using $^1H$ NMR (250 MHz). No trace of ii could be detected 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 μmol) was added 1 g of $CD_2Cl_2$ (ampoule), and spectra were obtained at several temperatures. The changes observed in the spectra were reversible.[23b] 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 μmol) 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**[a]



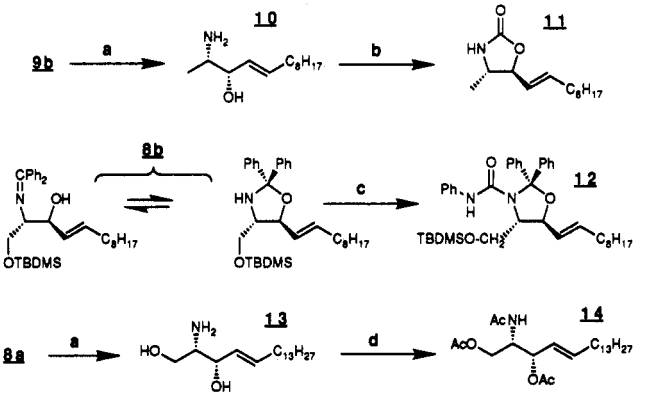

[a] (a) $iBu_2AlH{\cdot}iBu_3Al/CH_2/Cl_2/-78$ °C; (b) RLi/hexane/−78 °C → 0 °C; (c) $NaHCO_3$. * Isolated yields. *Threo/erythro* ratios were determined on the crude reaction mixtures by 250-MHz $^1H$ NMR.

prepared[30d] from sphingosines **8a–d** showed no evidence of diastereoisomerism.[39]

**Synthetic Applications: Sphingosines.** *threo*-Sphingosines, their 1-*O*-glycosyl derivatives (psychosines), and ceramide derivatives are of interest as PKC inhibitors,[6] and neuro-protective agents.[6h] Toward these ends, we have synthesized a series of *threo*-sphingosines of various chain lengths. Reaction of the protected serine **4b** with $iBu_2AlH{\cdot}iBu_3Al$ in $CH_2Cl_2$ at −78 °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-deoxysphingosine" derivatives **9a–d** in a similar fashion. The stereochemical outcome of these reactions run in $CH_2Cl_2$/hexanes was superb, and $SiO_2$ flash chromatography[29] provided the diastereomerically pure Schiff bases in the yields indicated. Subsequent glycosylation showed that the sphingosines were enantiomerically pure as well.[30c,39]

The diastereomeric ratios were determined by 250-MHz $^1H$ 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**[a]

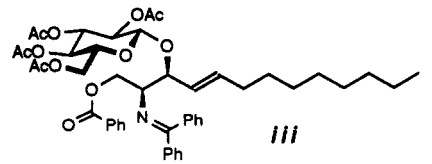



[a] (a) 1 N HCl; (b) O=C(imidazole)$_2$; (c) PhN=C=O; (d) $Ac_2O$.

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 –OCH–HCN– resonances. This is *not* consistant with the empirical rules for stereochemical assignment,[25] 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 –OCH–HCN– resonances of **12** was also inconsistant 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.[28] 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 β-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*) aluminoxy acetals, and (3) high degree of *threo* stereoselectivity. That the aluminoxy acetals are indeed the reactive intermediates involved in this chemistry is implicated by their long life and stability at −78 °C, their isolation as trapped monosilyl acetals, and the stereochemical effects of the ester moieties. The glycosylation

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



iii

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-(1→3)-(2*S*,3*S*,4*E*)-1-*O*-benzoyl-2-[*N*-(diphenylmethylene)amino]-4-tridecen-3-ol (iii).** $^1H$ NMR ($CDCl_3$): δ 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 $^{13}C$ NMR ($CDCl_3$): δ 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 ($BzOCH_2$), 63.62 (=NCH), 62.00 ($AcOCH_2$-6), 32.24, 31.72, 29.30, 29.19, 29.10, 28.95, 22.51 ($CH_2$'s), 20.63, 20.43, 19.63 ($H_3C$=O's), 13.99 ($CH_3$). $[\alpha]_D$ = −12.5° ($c$ = 0.80, $CHCl_3$).

of the Schiff base-protected sphingosines to provide psychosines and ceramides will be the subject of a forthcoming paper.[30d]

## 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[32] and freshly distilled prior to use. For flash chromatography,[29] 400–230-mesh silica gel 60 (E. Merck No. 9385) was employed. All compounds described were >95% pure by $^1H$ and $^{13}C$ NMR, and purity was confirmed by elemental analysis in several representative cases. The $^1H$ and $^{13}C$ NMR spectra were obtained on a Bruker WM-250 spectrometer at 250 and 62.9 MHz, respectively. Chemical shifts are reported in δ vs $Me_4Si$ in $^1H$ spectra and vs $CDCl_3$ in $^{13}C$ 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 $CH_2Cl_2$ (100 mL) and stirred overnight under argon.[16] The reaction was poured into 1% $NaHCO_3$, washed (2 × saturated $NaHCO_3$), and dried ($K_2CO_3$), 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. $^1H$ NMR ($CDCl_3$): δ 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). $^{13}C$ NMR APT[33] ($CDCl_3$): δ 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 ($OCH_3$), 51.86 (=NCH), 19.00 ($CH_3$). $[\alpha]_D$ = −105.4° ($c$ = 3.25, $CHCl_3$). IR (KBr): 1748.7, 1629.0, 1448.2, 1448.0, 1368.2, 1281.4, 1196.3, 1071.6, 712.0 $cm^{-1}$.

**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. $^1H$ NMR ($CDCl_3$): δ 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). $^{13}C$ NMR ($CDCl_3$): δ 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 ($OCH_2CH_3$), 60.33 (=NCH), 18.87 ($OCH_2CH_3$), 13.90 ($CH_3$). IR (KBr): 1736.3, 1624.8, 1449.5, 1375.9, 1285.0, 1196.9, 1127.6, 787.1, 704.2. $[\alpha]_D$ = −90.0° ($c$ = 2, $CHCl_3$).

**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[30] (4.5 g, 12.8 mmol) in 50 mL of $CH_2Cl_2$ and stirred for 28 h at rt under argon.[16] The mixture was then washed (0.1% $NaHCO_3$, 2 × saturated $NaHCO_3$) and dried over $K_2CO_3$. 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%). $^1H$ NMR ($CDCl_3$): δ 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). $^{13}C$ NMR ($CDCl_3$): δ 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 ($OCH_2Ph$), 60.53 (=NCH), 19.01 ($CH_3$). IR (neat): 1919.2, 1736.9, 1619.3, 1490.1, 1448.9, 1178.6 $cm^{-1}$. $[\alpha]_D$ = −65.7° ($c$ = 1.3, $CHCl_3$).

**Benzhydryl *N*-(Diphenylmethylene)-L-alaninate (2d).** A solution of L-alanine benzhydryl ester hydrotosylate[31] 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. $^1H$ NMR ($CDCl_3$): δ 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). $^{13}C$ NMR ($CDCl_3$): δ 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 ($OCHPh_2$), 60.64 (=NCH), 18.61 ($CH_3$). IR (KBr): 3060.3, 2931.0, 2355.1, 1736.9, 1625.2, 1495.9, 1448.9, 1372.5, 1178.6, 1119.9 $cm^{-1}$. $[\alpha]_D$ = −46.5° ($c$ = 2.2, $CHCl_3$).

**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. $^1H$ NMR ($CDCl_3$): δ 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). $^{13}C$ NMR ($CDCl_3$): δ 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 ($OCH_3$), 39.63 ($CH_2Ph$). IR (KBr): 1743.3, 1625.9, 1445.9, 1286.0, 1200.7, 1169.0, 694.3 $cm^{-1}$. $[\alpha]_D$ = −285.7° ($c$ = 2.3, $CHCl_3$).

**Methyl *N*-(Diphenylmethylene)-L-serinate (4a).** Reaction as in **2a**. Recyrstallization (EtOAc/hexanes) yielded **4a** as 5.18 g of white crystals (18.3 mmol, 89%), mp 87–89 °C. $^1H$ NMR ($CDCl_3$): δ 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). $^1H$ NMR (benzene-$d_6$): δ 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). $^{13}C$ NMR ($CDCl_3$): δ 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: $OCH_2$, NCH, and $OCH_3$ 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 $cm^{-1}$. MS (EI): 283 ($M^+$), 224 (M − $CO_2Me$), 206 (M − $H_2O$ − $CO_2Me$, 100). Anal. Calcd for $C_{17}H_{17}NO_3$: C (72.07), H (6.05), N (4.94). Found: C (71.78), H (5.94), N (4.96). $[\alpha]_D$ = −136.14° ($c$ = 8.5, $CHCl_3$).

**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% $NaHCO_3$ (2 × 15 mL), and dried ($MgSO_4$), 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. $^1H$ NMR ($CDCl_3$): δ 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). $^{13}C$ NMR ($CDCl_3$): δ 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 ($SiOCH_2$), 64.43 (=NCH), 51.63 ($OCH_3$), 25.61 (C-$CH_3$), 18.02 (quaternary, SiC), −5.51, −5.62 ($SiCH_3$). IR (neat): 1725.2, 1625.1, 1285.6, 1125.3, 1074.6, 829.9, 779.2, 686.4 $cm^{-1}$. MS (70 eV): 397 ($M^+$), 382 (M − $CH_3$), 340 (M − tBu, 100). $[\alpha]_D$ = −95.1° ($c$ = 3.6, $CHCl_3$).

**Synthesis of Norpseudoephedrines: Method A** (2 equiv of DIBAL). The Schiff base esters (1.0 mmol) were dissolved in 10 mL of dry $CH_2Cl_2$ 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 $Et_2O$) 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 $NaHCO_3$. An additional 20 mL of $CH_2Cl_2$ was used in several portions to ensure complete transfer. These exact proportions of $CH_2Cl_2$:$NaHCO_3$ are recommended to avoid the formation of intractable emulsions. The aqueous layer was extracted with two additional 20-mL portions of $CH_2Cl_2$, and the combined organic layers were dried ($K_2CO_3$), filtered through Celite, and evaporated under reduced pressure. The products were purified via flash chromatography except for **5a** which was recrystallized directly from $CH_2Cl_2$ or THF.

**Method B** (1:1 DIBAL–TRIBAL). The Schiff base esters (1.0 mmol) were dissolved in 10 mL of dry $CH_2Cl_2$ 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 $Et_2O$). 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. $^1$H NMR ($CDCl_3$): 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). $^{13}$C NMR APT[33] ($CDCl_3$): 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 ($CH_2N$=), 55.00 ($CH_2NH$). (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$^{-1}$. MS (70 eV): 301 ($M^+$), 283 (M − $H_2O$), 194 (M − PhCHOH), 91 ($C_7H_7$, 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). $^1$H NMR ($CDCl_3$): 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). $^{13}$C NMR APT[33] ($CDCl_3$): 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 ($CH_3$). IR (neat): 1726.4, 1490.0, 1450.8, 1235.9, 749.7, 698.9, 630.4 cm$^{-1}$. $[\alpha]_D$ = +198.9° ($c$ = 1, $CHCl_3$).

**(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). $^1$H NMR ($CDCl_3$): 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). $^{13}$C NMR ($CDCl_3$): 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 ($CH_2Ph$), 37.05 ($CH_2Ph$). (Note: oxazolidine–imine tautomerism.) IR (neat): 1601.0, 1495.2, 1451.3, 1222.0, 1028.7, 953.7, 743.8, 701.0 cm$^{-1}$. $[\alpha]_D$ = +68.4° ($c$ = 2.4, $CHCl_3$).

**(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). $^1$H NMR ($CDCl_3$) 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). $^{13}$C NMR APT[33] ($CDCl_3$): 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 ($CH_2OSi$), 25.75 (C-$CH_3$), 18.10 (quaternary, SiC), −5.5 ($SiCH_3$). 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$^{-1}$. $[\alpha]_D$ = +101.9° ($c$ = 7.7, $CHCl_3$).

**(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 $CH_2Cl_2$ (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 $CH_2Cl_2$ (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 $NaHCO_3$. The aqueous layer was washed with three 20-mL portions of $CH_2Cl_2$, and the combined organic layers were then dried ($K_2CO_3$) and evaporated under reduced pressure. The product was purified via flash chromatography[29] to yield 252 mg of an inseparable (6.5:1) mixture of **7a** and **7b** (0.71 mmol, 71%). $^1$H NMR ($CDCl_3$): 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). $^{13}$C NMR APT[33] ($CDCl_3$) **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 ($CH_2O$), 59.15 (CHN), 17.59, 15.28 ($CH_3$), 0.59 ($SiCH_3$). 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$^{-1}$. $[\alpha]_D$ = +31.43° ($c$ = 4.4, $CHCl_3$). High-resolution MS (CI-isobutane): M + 1 = 356.2035 ($C_{21}H_{30}NSiO_2$ = 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/$Et_2O$) 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 $CH_2Cl_2$ (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 $CH_2Cl_2$ (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 $NaHCO_3$. The aqueous layer was washed with three 20-mL portions of $CH_2Cl_2$, and the combined organic layers were then dried ($K_2CO_3$) and evaporated under reduced pressure. Analysis of the crude $^{13}$C NMR revealed the two possible diastereomeric products were formed in a 2:1 ratio. **7b**. $^{13}$C NMR APT[33] ($CDCl_3$): 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 ($CH_2O$), 62.56 (CHN), 17.45, 15.01 ($CH_3$), −0.52 ($SiCH_3$).

**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[31] (prepared by I–Li exchange from the corresponding (*E*)-iodoalkenes)[34] were substituted for the PhMgBr/$Et_2O$. The reactions were worked up as before.

**Cleavage of Schiff Base Protecting Groups.** This was accomplished essentially as described by O'Donnell.[16] 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 $CH_2Cl_2$ 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 $CH_2Cl_2$. The combined organic layers were dried ($K_2CO_3$), 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). $^1$H NMR ($CDCl_3$): 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). $^{13}$C NMR APT[33] ($CDCl_3$): 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 ($OCH_2$), 59.41 (CNH), 32.21, 31.90, 29.66, 29.60, 29.45, 29.34, 29.08 ($CH_2$), 25.78 ($SiCCH_3$), 22.66 (quaternary, SiC), 14.10 ($CH_3$), −5.49, −5.54 ($SiCH_3$). 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$^{-1}$. $[\alpha]_D$ = +46.7° ($c$ = 0.9, $CHCl_3$).

**(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[7e,7h] mp 86–87 °C and 88.0–88.5 °C). $^1$H NMR ($CDCl_3$): 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)**[7e] from **13**. $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR APT[33] ($CDCl_3$): δ 170.54, 169.96, 169.75 (OC=O), 137.17, 123.99 (HC=CH), 72.94 (OCH), 62.97 ($CH_2O$), 50.72 (CNH), 32.15, 31.79, 29.54, 29.45, 29.30, 29.21, 29.00, 28.68 ($CH_2$), 23.10 (OAc), 22.57 ($CH_2$), 20.95, 20.63 (OAc), 13.98 ($CH_3$). IR (neat): 1747.1, 1653.8, 1540.3, 1456.8, 1371.1, 1231.8, 1045.4, 968.5 cm$^{-1}$. $[\alpha]_D$ = +8.2° ($c$ = 2.2, $CHCl_3$) [lit. values[7b,7n] +8.43°; +8.78° ($c$ = 1.2, $CHCl_3$)].

**(2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-1-*O*-(*tert*-butyldimethylsilyl)-4-tridecene-1,3-diol (8b)** (oil, 15% EtoAc/petroleum ether, 65% method B). $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR APT[33] ($CDCl_3$): δ 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 ($CH_2O$), 59.35 (NCH), 32.16, 31.81, 29.36, 29.21, 29.03 ($CH_2$), 25.74 ($CH_3$, tBu), 22.62, 18.13 ($CH_2$), 14.07 ($CH_3$), -5.52, -5.57 ($SiCH_3$). 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$^{-1}$. $[\alpha]_D$ = +41.9° ($c$ = 2.8, $CHCl_3$). **(2*S*,3*S*,4*E*)-2-Amino-4-tridecene-1,3-diol** from **8b**. Waxy solid. $^1$H NMR ($CDCl_3$): δ 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); $^{13}$C NMR APT ($CDCl_3$): δ 134.05, 129.46 (HC=CH), 73.08 (OCH), 63.56 ($CH_2O$), 56.61 (CHN), 32.33, 31.83, 29.39, 29.24, 29.16, 22.60 ($CH_2$), 14.04 ($CH_3$). IR (neat): 3600–3200, 2925.0, 1458.3, 1379.9, 1253.9, 1028.0, 968.7, 853.3 cm$^{-1}$. $[\alpha]_D$ = -4.0° ($c$ = 0.63, $CHCl_3$). MS (CI-isobutane): 230 (M + 1), 212 (M + 1 - $H_2O$). HRMS (CI-isobutane): M + 1 = 230.2129 (calcd for $C_{13}H_{28}NO_2$ (M + 1) 230.2120).

**(2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-1-*O*-(*tert*-butyldimethylsilyl)-4-decene-1,3-diol (8c)** (oil, 10% EtoAc/petroleum ether, 40% method A, 60% method B). $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR ($CDCl_3$): δ 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$^{-1}$. $[\alpha]_D$ = +51.3° ($c$ = 0.9, $CHCl_3$), **(2*S*,3*S*,4*E*)-2-Amino-4-decene-1,3-diol** from **8c**. Waxy solid. $^1$H NMR ($CDCl_3$): δ 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); $^{13}$C NMR ($CDCl_3$): δ 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$^{-1}$. $[\alpha]_D$ = -2.10° ($c$ = 1.1, $CHCl_3$). MS (CI-isobutane): 188 (M + 1), 170 (M + 1 - $H_2O$). HRMS (CI - isobutane): M + 1 = 188.1672 (calcd for $C_{10}H_{22}NO_2$ (M + 1) 188.1651).

**(2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-1-*O*-(*tert*-butyldimethylsilyl)-4-nonene-1,3-diol (8d)** (oil, 5% EtoAc/petroleum ether, 60% method B). $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR APT[33] ($CDCl_3$): δ 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 ($CH_2O$), 31.18, 31.13 ($CH_2$), 25.70 ($CH_3$, tBu), 22.05 ($CH_2$), 18.11 (quaternary, tBu), 13.79 ($CH_3$), -5.56, -5.62 ($SiCH_3$). IR (neat): 2928.4, 1449.9, 1254.1, 1121.1, 969.3, 837.2, 777.1, 750.2, 701.7, 631.1 cm$^{-1}$. $[\alpha]_D$ = +55.5° ($c$ = 3.2, $CHCl_3$). **(2*S*,3*S*,4*E*)-2-Amino-4-nonene-1,3-diol** from **8d**, mp 68–71 °C. $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR APT[33] ($CDCl_3$): δ 133.74, 129.71 (HC=CH), 73.54 (OCH), 64.25 ($CH_2O$), 56.33 (CNH), 31.87, 31.20, 22.11 ($CH_2$), 13.81 ($CH_3$). 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$^{-1}$. $[\alpha]_D$ = -5.2° ($c$ = 0.9, $CHCl_3$). MS (CI-isobutane): 174 (M + 1), 156 (M + 1 - $H_2O$). HRMS (CI-isobutane): M + 1 = 174.1492 (calcd for $C_9H_{20}NO_2$ (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.

**(2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-4-octadecen-3-ol (9a)** (oil, 10% EtoA/petroleum ether, 78% method B). $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR APT[33] ($CDCl_3$): δ 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 ($CH_2$), 15.77 (1-$CH_3$), 14.06 (18-$CH_3$). 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$^{-1}$. $[\alpha]_D$ = +75.8° ($c$ = 2.7, $CHCl_3$). **(2*S*,3*S*,4*E*)-2-Amino-4-octadecen-3-ol** from **9a**, mp 67–70 °C. $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR APT[33] ($CDCl_3$): δ 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 ($CH_2$), 20.18, 14.03 ($CH_3$). 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$^{-1}$. Anal. Calcd for $C_{18}H_{37}NO$: C (76.32), H (13.07), N (4.95). Found: C (74.83), H (13.31), N (5.26). $[\alpha]_D$ = +9.7° ($c$ = 1.1, $CHCl_3$).

**(2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-4-tridecen-3-ol (9b)** (oil, 10% EtoAc/petroleum ether, 71% method B). $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR APT[33] ($CDCl_3$): δ 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 ($CH_2$), 15.78 ($CH_3$), 14.10 ($CH_3$). 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$^{-1}$. $[\alpha]_D$ = +79.5° ($c$ = 2.8, $CHCl_3$). **(2*S*,3*S*,4*E*)-2-Amino-4-tridecen-3-ol (10)** from **9b**. Waxy solid. $^1$H NMR ($CDCl_3$): δ 5.72 (dt, $J$ = 6.7, 15.4 Hz, 1 H), 5.41 (dt, $J$ = 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). $^{13}$C NMR APT[33] ($CDCl_3$): δ 133.81, 130.34 (HC=CH), 77.32 (OCH), 51.33 (CNH), 32.27, 31.80, 29.36, 29.18, 29.12, 22.60 ($CH_2$), 20.20 (1-$CH_3$), 14.04 (13-$CH_3$). IR (neat): 3500–3100, 2924.5, 1559.0, 1457.3, 1377.2, 968.8 cm$^{-1}$. $[\alpha]_D$ = +7.36° ($c$ = 0.4, $CHCl_3$). MS (CI-isobutane): 214 (M + 1), 196 (M + 1 - $H_2O$). HRMS (CI-isobutane): M + 1 = 214.2166 (calcd for $C_{13}H_{28}NO$ (M +1) 214.2171).

**(2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-4-decen-3-ol (9c)** (oil, 10% EtoAc/hexanes, 45% method A, 72% method B). $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR ($CDCl_3$): δ 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 $cm^{-1}$. $[\alpha]_D$ = +84.3° ($c$ = 3, $CHCl_3$). **(2*S*,3*S*,4*E*)-2-Amino-4-decen-3-ol** from **9c**. Waxy solid. $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR ($CDCl_3$): δ 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, $cm^{-1}$. $[\alpha]_D$ = +4.6° ($c$ = 0.9, $CHCl_3$). MS (CI-isobutane): 172 (M + 1), 154 (M + 1 − $H_2O$). HRMS (CI-isobutane): M + 1 = 172.1680 (calcd for $C_{10}H_{22}NO$ (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). $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR ($CDCl_3$): δ 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 $cm^{-1}$. $[\alpha]_D$ = +64.6° ($c$ = 1.2, $CHCl_3$). **(2*S*,3*S*,4*E*)-2-Amino-4-nonen-3-ol** from **9d**. Oil. $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR APT[33] ($CDCl_3$): δ 133.61, 130.46 (HC=CH), 77.33 (OCH), 51.30 (CNH), 31.92, 31.24, 22.10 ($CH_2$), 20.08 (1-$CH_3$), 13.81 (9-$CH_3$). IR (neat): 3500–3000, 2926.4, 1582.7, 1453.8, 1378.3, 1141.1, 1093.4, 1037.5, 970.0, 865.8, 730.1 $cm^{-1}$. $[\alpha]_D$ = +10.9° ($c$ = 3.4, $CHCl_3$). MS (CI-isobutane): 158 (M + 1), 140 (M + 1 − $H_2O$). HRMS (CI-isobutane): M + 1 = 158.1544 (calcd for $C_9H_{20}NO$ (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 $Et_2O$, washed (3 × 1 N HCl, 1 × saturated $NaHCO_3$), and dried ($K_2CO_3$), and the solvent was removed under reduced pressure to provide crude material. Chromatography[29] (50% EtOAc/hexanes) provided 93 mg of pure product (70%, 0.39 mmol) as an oil. $^1$H NMR ($CDCl_3$): δ 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). $^{13}$C NMR APT[33] ($CDCl_3$): δ 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 ($CH_2$), 19.22 (4-$CH_3$), 14.06 ($CH_3$). $[\alpha]_D$ = −29.9° ($c$ = 1.6, $CHCl_3$).

**(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 PhN=C=O (1.8 mmol, 2.2 equiv) and stirred at rt overnight. Pyridine and unreacted phenyl isocyanate were removed under reduced pressure, and chromatography[29] (20% EtOAc/petroleum ether) provided 409 mg of the pure product (78% yield, 0.65 mmol) as an oil. $^1$H NMR ($CDCl_3$): δ 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); $^{13}$C NMR APT[33] ($CDCl_3$): δ 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 ($CH_2O$), 32.19, 31.74, 29.30, 29.08, 28.69 ($CH_2$), 25.80 ($SiCCH_3$), 22.54 ($SiCCH_3$), 14.01 ($CH_3$), −5.40 ($SiCH_3$). IR (neat): 1673.6, 1596.9, 1528.7, 1441.9, 1332.1, 1249.5, 1102.7, 836.9, 751.6, 700.1 $cm^{-1}$. $[\alpha]_D$ = −14.1° ($c$ = 1.2, $CHCl_3$).

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**Supplementary Material Available:** $^1$H NMR (250 MHz) and $^{13}$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.

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# An Efficient, Regiocontrolled Synthesis of 5-Aryl-2-carbethoxypyrroles from 3-Aryl-3-chloropropeniminium Salts[1]

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A variety of 3-aryl-3-chloropropeniminium salts react with α-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[2] 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.

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