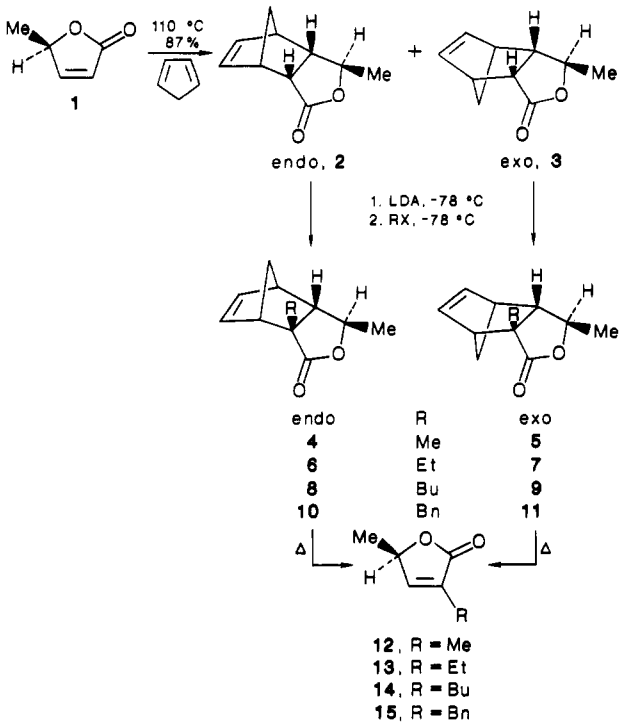
Scheme I



^{13}C NMR 180.20, 136.83, 136.20, 79.54, 60.52, 52.34, 49.86, 48.99, 44.88, 28.78, 22.16, 10.58. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.98; H, 8.83.

(−)-(1*S*,2*R*,5*R*,6*S*,7*R*)-2-Butyl-5-methyl-4-oxatricyclo-[5.2.1.0^{2,6}]dec-8-en-3-one (8): yield 83%; bp 120 °C (0.02 Torr); $[\alpha]^{20}_D$ −50.9° ($CHCl_3$, *c* 3.66); IR (neat) 1750, 1565 cm^{-1}; MS, *m/e* (relative intensity) 221 (M + 1, 0.9), 155 (89.7), 91 (18.7), 66 (100.0), 65 (23.5), 43 (26.7), 41 (27.2); ^{1}H NMR 0.72–2.18 (11 H, complex absorption), 1.35 (3 H, d, *J* = 6.66 Hz), 2.35 (1 H, dd, *J* = 4.00 Hz, *J′* = 2.66 Hz), 2.83 (1 H, m), 3.05 (1 H, m), 3.95 (1 H, dq, *J* = 6.66 Hz, *J′* = 2.66 Hz), 6.27 (2 H, complex absorption); ^{13}C NMR 179.64, 137.18, 135.04, 77.61, 59.86, 52.14, 51.54, 49.43, 46.26, 36.88, 28.38, 22.76, 22.09, 13.51. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.66; H, 9.21.

(+)-(1*R*,2*R*,5*R*,6*S*,7*S*)-2-Butyl-5-methyl-4-oxatricyclo-[5.2.1.0^{2,6}]dec-8-en-3-one (9): yield 86%; bp 120 ° C (0.02 Torr); $[\alpha]^{20}_D$ +4.5° ($CHCl_3$, *c* 4.40); IR (neat) 1750, 1565 cm^{-1}; MS, *m/e* (relative intensity) 221 (M + 1, 0.9), 155 (100.0), 91 (21.1), 77 (19.1), 67 (18.7), 66 (97.1), 65 (25.8), 43 (31.3), 41 (26.8); ^{1}H NMR 0.70–1.97 (12 H, complex absorption), 1.40 (3 H, d, *J* = 6.66 Hz), 2.85 (1 H, m), 2.97 (1 H, m), 4.22 (1 H, dq, *J* = 6.66 Hz, *J′* = 2.66 Hz), 6.22 (2 H, complex absorption); ^{13}C NMR 180.38, 136.81, 136.28, 79.59, 59.77, 52.65, 50.09, 49.04, 44.80, 35.86, 28.49, 22.84, 22.22, 13.60. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.54; H, 9.22.

(−)-(1*S*,2*R*,5*R*,6*S*,7*R*)-2-Benzyl-5-methyl-4-oxatricyclo-[5.2.1.0^{2,6}]dec-8-en-3-one (10): yield 100% mp 122–124 °C; $[\alpha]^{20}_D$ −6.8° ($CHCl_3$, *c* 2.65); IR ($CHCl_3$) 1750, 1605, 1580 cm^{-1}; MS, *m/e* (relative intensity) 254 (M, 0.8), 107 (58.5), 92 (100.0), 91 (51.0), 85 (45.8), 83 (72.2), 79 (85.7), 77 (74.6), 65 (35.2), 51 (33.0), 50 (18.3), 48 (18.0), 47 (33.5); ^{1}H NMR 0.32 (3 H, d, *J* = 6.66 Hz), 1.73 (2 H, complex absorption), 2.36 (1 H, dd, *J* = 4.00 Hz, *J′* = 2.66 Hz), 2.65 (1 H, d, *J* = 13.30 Hz), 3.00 (2 H, complex absorption), 3.58 (1 H, d, *J* = 13.30 Hz), 3.80 (1 H, dq, *J* = 6.66 Hz, *J′* = 2.66 Hz), 6.30 (2 H, complex absorption), 6.97–7.53 (5 H, complex absorption); ^{13}C NMR 179.80, 137.55, 137.03, 135.71, 129.92, 128.53, 126.90, 78.17, 62.50, 52.16, 50.48, 49.69, 46.58, 42.84, 20.66. Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.53; H, 7.50.

(+)-(1*R*,2*R*,5*R*,6*S*,7*S*)-2-Benzyl-5-methyl-4-oxatricyclo-[5.2.1.0^{2,6}]dec-8-en-3-one (11): yield 96%; mp 88–90 °C; $[\alpha]^{20}_D$ +61.6° ($CHCl_3$, *c* 1.92); IR ($CHCl_3$) 1750, 1605, 1580 cm^{-1}; MS, *m/e* (relative intensity) 254 (M, 3.6), 189 (100.0), 143 (58.7), 129 (17.9), 128 (27.6), 115 (39.8), 91 (77.5), 85 (69.2), 83 (94.0), 77 (19.4), 66 (94.5), 65 (34.9), 51 (19.0), 48 (26.5), 47 (48.3); ^{1}H NMR 0.37 (3 H, d, *J* = 6.66 Hz), 1.41–1.80 (3 H, complex absorption), 2.22 (1 H, d, *J* = 13.33 Hz), 2.85 (1 H, br s), 3.07 (1 H, m), 3.40 (1 H, d, *J* = 13.33 Hz), 4.03 (1 H, dq, *J* = 6.66 Hz, *J′* = 2.66 Hz), 6.35 (2 H, complex absorption), 6.90–7.45 (5 H, complex absorption); ^{13}C NMR 180.22, 138.03, 137.30, 136.50, 129.78, 128.30, 126.66, 79.98, 62.77, 50.66, 50.04, 49.03, 44.92, 41.28, 20.31. Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.15; H, 7.06.

General Procedure for the Pyrolysis of Adducts 4–11. Specific conditions of temperature, time, and solvent used in each case are listed in Table I, as well as yields and optical rotations of the resulting butenolides. A typical experiment was run as follows: A solution of the adduct (2 mmol) in a solvent (60 mL) was heated in a sealed tube. The solvent was distilled and the residue chromatographed on silica gel (hexane–ether) to afford the butenolides.

(−)-(*R*)-3,5-Dimethyl-2(5*H*)-furanone (12): bp 120 °C (16 Torr) [lit.[11] bp 100–103 °C (45 Torr)]; IR (neat) 1750, 1665 cm^{-1}; ^{1}H NMR 1.40 (3 H, d, *J* = 7.21 Hz), 1.92 (3 H, t, *J* = 1.60 Hz), 4.98 (1 H, q, *J* = 7.21 Hz), 7.01 (1 H, q, *J* = 1.60 Hz); ^{13}C NMR 173.89, 149.84, 128.92, 77.01, 18.55, 9.94.

(−)-(*R*)-3-Ethyl-5-methyl-2(5*H*)-furanone (13): bp 130 °C (13 Torr) [lit.[5] bp 59–62 °C (0.57 Torr)]; IR (neat) 1750, 1650 cm^{-1}; ^{1}H NMR 1.16 (3 H, t, *J* = 7.20 Hz), 1.40 (3 H, d, *J* = 7.21 Hz), 2.30 (2 H, q, *J* = 7.20 Hz), 5.0 (1 H, q, *J* = 7.21 Hz), 7.01 (1 H, m); ^{13}C NMR 173.36, 148.33, 135.16, 77.17, 18.77, 18.24, 11.41.

(−)-(*R*)-3-Butyl-5-methyl-2(5*H*)-furanone (14): bp 90 °C (0.1 Torr) [lit.[12] $[\alpha]^{20}_D$ +11.7° ($CHCl_3$, *c* 0.16) for the (+)-*S* enantiomer; no bp given]; IR (neat) 1750, 1650 cm^{-1}; ^{1}H NMR 0.92 (3 H, m), 1.05–1.73 (4 H, complex absorption), 2.23 (2 H, complex absorption), 1.39 (3 H, d, *J* = 7.21 Hz), 4.96 (1 H, q, *J* = 7.21 Hz), 6.96 (1 H, m); ^{13}C NMR 173.63, 148.90, 133.93, 77.19, 29.33, 24.63, 22.02, 18.94, 13.46.

(−)-(*R*)-3-Benzyl-5-methyl-2(5*H*)-furanone (15): bp 120 °C (0.02 Torr); IR (neat) 1750, 1600, 1655 cm^{-1}; ^{1}H NMR 1.37 (3 H, d, *J* = 7.21 Hz), 3.57 (2 H, m), 4.97 (1 H, q, *J* = 7.21 Hz), 6.82 (1 H, m), 7.22 (5 H, complex absorption); ^{13}C NMR 173.02, 150.30, 137.24, 133.43, 128.56, 128.39, 126.42, 77.35, 31.33, 18.31. Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.61; H, 6.68.

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Registry No. **2**, 111533-91-6; **3**, 111613-19-5; **4**, 115093-25-9; **5**, 115181-93-6; **6**, 115183-48-7; **7**, 115093-26-0; **8**, 115183-49-8; **9**, 115093-27-1; **10**, 115093-28-2; **11**, 115181-94-7; **12**, 59417-65-1; **13**, 115093-29-3; **14**, 115093-30-6; **15**, 115093-31-7; ethyl bromide, 74-96-4; butyl bromide, 109-65-9; benzyl bromide, 100-39-0.

Supplementary Material Available: Data from NOE experiments and from molecular mechanics calculations (2 pages). Ordering information is given on any current masthead page.

(11) Kawata, T.; Inayama, S.; Sata, K. *Chem. Pharm. Bull.* **1980**, *28*, 277.

(12) Bernardi, A.; Beretta, M. G.; Colombo, L; Gennari, C.; Poli, G.; Scolastico, C. *J. Org. Chem.* **1985**, *50*, 4442.

A Stereodivergent Synthesis of D-*erythro*-Sphingosine and D-*threo*-Sphingosine from L-Serine

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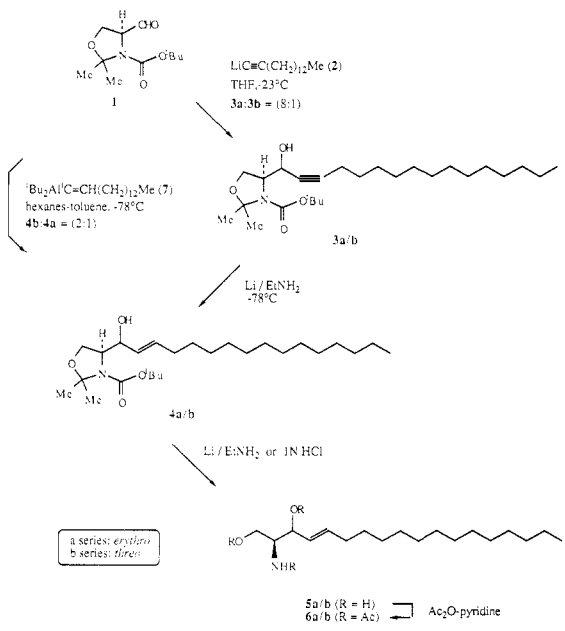
The sphingosine bases are a group of long-chain amino alcohols incorporated into the structures of various glycosphingolipids.[1] These compounds are important mem-

Scheme I

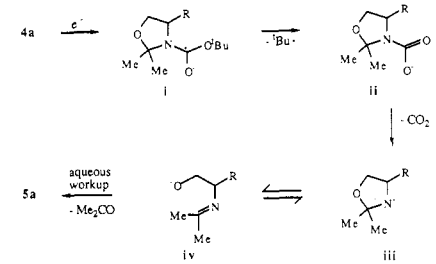


brane components and at least in some cases appear to function as receptors for a variety of chemical stimuli.[2] Thus there has been a great deal of interest in glycosphingolipids resulting in renewed efforts to devise more efficient syntheses of them and their constituent sphingosine bases.

Conceptually, the simplest strategy for sphingosine synthesis is still the one first set down by Newman some 15 years ago, wherein a long-chain carbon nucleophile is added to a protected serine-derived aldehyde to afford sphingosine derivatives directly.[3] However, this approach has generally been marred by either poor diastereoselectivity during the addition reaction or low overall yields.[4] In this paper we describe a concise solution to these problems that allows the stereocontrolled synthesis of D-*erythro*-sphingosine (**5a**) and D-*threo*-sphingosine (**5b**) in just 5 steps from commercial *N*-BOC-L-serine. The procedure for the erythro series has the added virtue of not requiring any chromatographic separations along the way, making it amenable to large-scale production of **5a** and related sphingosine bases (Scheme I).

Our synthesis actually began with the known oxazolidine aldehyde 1, available in >60% yield from *N*-BOC-L-serine in just 3 steps and which we have previously shown to be at least 95% enantiomerically pure.[5] The addition of lithium 1-pentadecyne (**2**)[6] to the aldehyde **1** proceeded with very good erythro stereoselectivity to give an 8:1 mixture of propargylic alcohols **3a** and **3b**. If so desired, pure **3a** could be isolated in 74% yield after flash chromatography. This stereochemical result was anticipated on the basis of our experience with other anionic additions to **1** under nonchelating conditions[7] and was subsequently confirmed by the conversion of **3a** to D-*erythro*-sphingosine (**5a**).

Whereas treatment of **3a** with excess lithium in liquid ammonia at −33 °C resulted in incomplete reduction of the triple bond (perhaps due to the insolubility of **3a**), the application of Benkeser's reduction conditions using lithium in ethylamine at −78 °C led to clean formation of the protected sphingosine derivative **4a**.[8] From a practical standpoint, it was not even necessary to isolate **3a** before its subsequent reduction. Thus, the addition reaction mixture could be added directly to a cold $Li/EtNH_2$ solution to give crude **4a** in nearly quantitative yield from **1** after extractive workup. Surprisingly, material at this stage was always found to be contaminated with a small amount of D-*erythro*-sphingosine (**5a**), which apparently resulted from fragmentation of the *N*-BOC oxazolidine system under the strongly reducing reaction conditions.[9] Further purification of **4a** at this stage could be achieved via flash chromatography, if desired. Deprotection of **4a** with hot aqueous HCl afforded the desired product **5a** in 65% overall yield (from **1**) after basic extractive workup and trituration of the crude material with cold pentane. On the other hand, exposure of **3a** to longer reduction times resulted in complete conversion of **4a** to **5a** directly via the novel fragmentation reaction described above. Both procedures afforded homogeneous **5a** in 65–68% overall yield from **1** after extractive workup, trituration of the crude material with cold pentane, and (with the direct procedure) final recrystallization from hexanes–EtOAc.



The 400-MHz ^1H NMR spectrum of our synthetic material was identical with that of an authentic sample of D-*erythro*-sphingosine. Further confirmation of our

(1) (a) Kennedy, J. F.; White, C. A. *Bioactive Carbohydrates*; Wiley: New York, 1983; Chapter 10. (b) Shapiro, D. "Chemistry of Sphingolipids"; *Chemistry of Natural Products*; Lederer, E., Ed.; Hermann: Paris, 1969.

(2) Cf. Kanfer, J. N. In *Handbook of Lipid Research*; Hanahan, D. J., Ed.; Plenum: New York, 1983; Vol. 3, pp 437–471. But see the cautionary notes presented in the concluding section as well.

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(4) For some other enantioselective approaches to the sphingosines, see: (a) Ito, Y.; Sawamura, M.; Hayashi, T. *Tetrahedron Lett.* **1988**, *29*, 239. (b) Findeis, M. A.; Whitesides, G. M. *J. Org. Chem.* **1987**, *52*, 2838. (c) Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *Tetrahedron* **1986**, *42*, 917. (d) Schmidt, R. R.; Zimmermann, P. *Tetrahedron Lett.* **1986**, *27*, 481. (e) Julina, R.; Herzig, T.; Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1986**, *69*, 368. (f) Kiso, M.; Nakamura, A.; Nakamura,J. *J. Carbohydr. Chem.* **1986**, *5*, 335. (g) Roush, W. R.; Adam, M. A. *J. Org. Chem.* **1985**, *50*, 3752. (h) Obayashi, M.; Schlosser, M. *Chem. Lett.* **1985**, 1715. (i) Koike, K.; Nakahara, Y.; Ogawa, T. *Glycoconjugate J.* **1984**, *1*, 107. (j) Bernet, B.; Vasella, A. *Tetrahedron Lett.* **1983**, *24*, 5491. (k) Schmidt, R. R.; Klaeger, R. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 210. (l) Shoyama, Y.; Okabe, H.; Kishimoto, Y.; Costello, C. *J. Lipid Res.* **1978**, *19*, 250. (m) Reist, E. J.; Christie, P. H. *J. Org. Chem.* **1970**, *35*, 4127. (n) For a review of earlier syntheses, see ref 1.

(5) Garner, P.; Park, J. M. *J. Org. Chem.* **1987**, *52*, 2361.

(6) 1-Pentadecyne was prepared in 80% yield by the alkylation of sodium acetylide with 1-bromotridecane in 3:1 tetrahydrofuran–hexamethylphosphoric triamide at ambient temperature. Except for the use of these solvents and a higher reaction temperature, the procedure was identical with one reported for the preparation of 1-hexyne: Campbell, K. N.; Campbell, B. K. In *Organic Syntheses*; Rabjohn, N., Ed.; Wiley: New York, 1963; Collect. Vol. 4, pp 117–120.

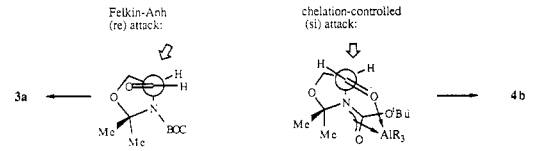
(7) (a) Garner, P.; Ramakanth, S. *J. Org. Chem.* **1986**, *51*, 2609. (b) Garner, P.; Park, J. M. *J. Org. Chem.* **1988**, *53*, 2979 and unpublished results. (c) See also ref 3a.

(8) Benkeser, R. A.; Schroll, G.; Sauve, D. M. *J. Am. Chem. Soc.* **1955**, *77*, 3378.

(9) The reductive cleavage of structurally similar proline peptide bonds by lithium in methylamine had previously been observed: Patchornik, A.; Wilchek, M.; Sarid, S. *J. Am. Chem. Soc.* **1964**, *86*, 1457 and references cited therein. However, the amide radical anion corresponding to our presumed intermediate i would of course be incapable of subsequent fragmentation as shown.

structural assignments as well as the optical purity of synthetic **5a** came after its conversion to the known crystalline triacetate **6a** and comparison of its physical properties with those reported in the literature. *The described procedure affords* D-*erythro-sphingosine* (***5a***) *in 40% overall yield from* L-*serine without the need for any chromatographic separation and represents the most efficient synthesis of this substance yet reported.*

In order to compare our results with related approaches to sphingosine, the addition of Newman's *trans*-vinylalane reagent **7** (from DIBAL + 1-pentadecyne)[10] to **1** was also investigated. Much to our surprise and in contrast to the acetylide addition described above, this reaction was found to be moderately threo-selective, resulting in the formation of a 2:1 mixture of the diastereomeric 2° allylic alcohols **4b** and **4a**. These compounds could be isolated at this stage in >80% yield by flash chromatography if desired. Stereochemical assignments for **4b** rest on its correlation with the known D-*threo*-sphingosine (**5b**) and its corresponding triacetate **6b**. This reversal in the diastereofacial selectivity during the addition may reflect some sort of chelation-control in the transition state[11] and is consistent with our observations on other Lewis acid catalyzed additions to **1** as well.[7a] As expected, hydrolytic deprotection of **4b**/**4a** with 1 N HCl afforded a 2:1 mixture of D-*threo*-sphingosine (**5b**) and D-*erythro*-sphingosine (**5a**) in >60% combined yield from **1**.



It is noteworthy that stereocontrol in the opposite sense could be achieved during these organometallic additions to the oxazolidine aldehyde **1** by varying the reagent type so as to either preclude or favor (apparent) chelation-control. Furthermore, the observed fragmentation of the *N*-BOC oxazolidine moiety at −78 °C by lithium in ethylamine extends the utility of this system to situations where the usual acidic deprotection conditions are to be avoided. The described solution to the sphingosine problem thus provides another example of how aldehyde **1** can be used for the stereocontrolled assembly of vicinal amino alcohols and suggests that such control may be a general attribute of this readily available, chiral synthon. Further work dealing with this issue and the application of our results to other synthetic targets will be forthcoming.

Experimental Section

TLC analysis was performed on Merck silica gel 60 F-254 plates and visualized by charring with (A) 5% anisaldehyde in 95:5:1 EtOH–HOAc–H_2SO_4 or (B) 0.3% ninhydrin in (97:3) *n*-BuOH–AcOH. Melting points are uncorrected. Optical rotations were determined with a Perkin-Elmer Model 241 polarimeter and are the average of at least four measurements. Combustion analyses were performed on TLC homogeneous or recrystallized samples by Galbraith Labs, Inc.

1,1-Dimethylethyl [*R*-(*R,*S**)]-2,2-Dimethyl-4-(1-hydroxy-2-hexadecynyl)-3-oxazolidinecarboxylate (3a).** To a −23 °C solution of 1-pentadecyne (3.490 g, 16.75 mmol) in dry THF (150 mL) was added 2.3 M *n*-BuLi (6.20 mL, 14.3 mmol) under N_2 atmosphere. The resulting suspension of lithium acetylide **2** was stirred at this temperature for 30 min when a −23 °C solution of aldehyde **1** (2.820 g, 12.31 mmol) in dry THF (75 mL) was added via cannula using positive N_2 pressure. The colorless solution was stirred at −23 °C for 1.5 h when the TLC in 4:1 hexanes–EtOAc showed the clean formation of two products, $R_{f_{major}}$ 0.43 (char A) and $R_{f_{minor}}$ 0.39, at the expense of starting material, R_f 0.33. Analysis of the ^{1}H NMR spectrum of this crude product after extractive workup indicated an 8:1 mixture of **3a** and **3b**. At this point pure **3a** could be obtained in 74% yield as a colorless oil after flash chromatography on silica gel, eluting with 9:1 hexanes–EtOAc: $[\alpha]_D$ −39.7° (*c* 1.41, $CHCl_3$); IR (neat) 3440, 2220, 1700 cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6, 60 °C) δ 4.70 (m, H), 4.20–3.65 (m, 3 H), 2.06 (pseudo t, 2 H), 1.70 (br s, 3 H), 1.48 (br s, 3 H), 1.38 (s, 9 H), 1.30 (br s, 22 H), 0.91 (pseudo t, 3 H), 0.45 (br s, H, exchanged with D_2O). Anal. Calcd for $C_{26}H_{47}NO_4$: C, 71.35; H, 10.82; N, 3.20. Found: C, 71.01; H, 10.85; N, 3.30. For purposes of comparison, a sample of pure **3b** was also obtained via careful chromatography: $[\alpha]_D$ −31.7° (*c* 0.88, $CHCl_3$); IR (neat) 3450, 2230, 1700 cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6, 60 °C) δ 4.82 (br s, 1 H), 4.17 (dd, *J* = 9.5, 1.7 Hz, 1 H), 4.13 (br s, 1 H), 3.82 (dd, *J* = 9.1, 6.2 Hz, 1 H), 2.06 (td, *J* = 6.2, 1.0 Hz, 2 H), 1.67 (br s, 3 H), 1.45 (br s, 3 H), 1.36 (s, 9 H), 1.30 (br s, 22 H), 0.91 (t, *J* = 6.3 Hz, 3 H), 0.47 (br s, H, exchanged with D_2O); HRMS (FAB, glycerol matrix), *m*/*z* 438.3583 (calcd for $C_{26}H_{48}NO_4$ (M + H$^+$), 438.3505).

1,1-Dimethylethyl [*R*-[*R,*S**-(*E*)]]-2,2-Dimethyl-4-(1-hydroxy-2-hexadecenyl)-3-oxazolidinecarboxylate (4a).** A 105-mL portion of the −23 °C addition reaction mixture described above was added directly to a −78 °C blue solution of Li^0 (0.451 g, 0.0650 mol) in $EtNH_2$ (75 mL) via cannula using positive N_2 pressure. After stirring at −78 °C for 1 h, the TLC in (4:1) hexanes–EtOAc showed the clean formation of alkene **4a**, R_f 0.37 (char A), at the expense of starting alkyne **3a**, R_f 0.41. Some sphingosine formation was also noted even at this point (see text). The reaction was quenched at −78 °C with 8.8 g of solid NH_4Cl, and the ethylamine was allowed to evaporate at room temperature overnight followed by residual solvent removal on a rotory evaporator. The resulting white solid was partitioned between 300 mL of H_2O and 2 × 300 mL of Et_2O. The combined Et_2O layers were washed with brine (300 mL), dried with Na_2SO_4, filtered and concentrated to give 2.660 g of a waxy solid. If desired, pure **4a** could be obtained as a colorless oil after flash chromatography on silica gel, eluting with 12:1 hexanes–EtOAc: $[\alpha]_D$ −28° (*c* 0.65, $CHCl_3$); IR (neat) 3400, 1700 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6, 60 °C) δ 5.79 (dt, *J* = 15.3, 6.6 Hz, 1 H), 5.55 (dd, *J* = 15.3, 5.3 Hz, 1 H), 4.30 (br s, 1 H), 3.97 (br s, 1 H), 3.79 (br s, 1 H), 3.66 (dd, *J* = 8.8, 6.8 Hz, 1 H), 2.03 (q, *J* = 7.1 Hz, 1 H), 1.64 (br s, 3 H), 1.45 (br s, 3 H), 1.39 (br s, 9 H), 1.31 (br s, 22 H), 0.90 (t, *J* = 6.6 Hz, 3 H), 0.43 (br s, H, exchanged with D_2O). Anal. Calcd for $C_{26}H_{49}NO_4$: C, 71.02; H, 11.23; N, 3.19. Found: C, 70.69; H, 11.38; N, 3.29.

(2*S*,3*R*,4*E*)-2-Amino-1,3-dihydroxy-4-octadecene (D-*erythro*-Sphingosine) (5a). Method A. Crude **4a** was dissolved in 1 N HCl (100 mL) and THF (100 mL) and heated at 70 °C with stirring for 18 h under N_2 when the TLC in 4:1:1 *n*-BuOH–H_2O–HOAc showed clean formation of product **5a**, R_f 0.62 (char B), at the expense of starting material (and intermediate *N*-BOC sphingosine) at the solvent front. The amber reaction mixture was cooled to ambient temperature and the THF was evaporated at 25 °C on the rotory evaporator. The resulting acidic solution was extracted with 4 × 200 mL of 1:1 hexanes–Et_2O to remove the neutral byproducts and then basified to pH 10 with cold 1 N NaOH (105 mL—a white precipitate formed) and extracted with 3 × 300 mL of CH_2Cl_2. The combined extracts were divided into three portions and washed with brine (150 mL), treated with decolorizing carbon, dried with Na_2SO_4, filtered, and concentrated in vacuo to give 1.405 g of crude product. This material was triturated with cold pentane (10 mL) to give 1.117 g of a TLC and NMR homogeneous solid, mp 72–75 °C, in 65% yield overall from **1**. Recrystallization from 1:1 hexanes–EtOAc afforded 0.774 g of pure **5a** as a white solid: mp 72–75 °C (shr at 70 °C) [lit.[3e] mp 72–75 °C]; $[\alpha]_D$ −0.58° (*c* 1.67, $CHCl_3$) [lit.[3e] −1.3° (*c* 3.5, $CHCl_3$)]; IR (KBr) 3300, 1579 cm^{-1}; ^{1}H NMR (400 MHz, 1.9 mg/0.5 mL $CDCl_3$, room temperature) δ 5.75 (dt, *J* = 15.4, 7.5 Hz, 1 H), 5.46 (dd, *J* = 15.5, 6.9 Hz, 1 H), 4.04 (t, *J* = 6.2 Hz, 1

(10) Newman, H. *Tetrahedron Lett.* **1971**, 4571. For a more detailed look at the hydroalumination process, see: Negishi, E.; Takahashi, T.; Baba, S. *Org. Synth.* **1987**, *66*, 60 and references cited therein.

(11) While it may be premature for us to comment on the mechanistic details of this alane addition (i.e. whether it is bimolecular or termolecular), there is some X-ray crystallographic evidence for pentacoordinated aluminum: Cf. Robinson, G. H.; Sangokoya, S. A. *J. Am. Chem. Soc.* **1988**, *110*, 1494 and references cited therein.

H), 3.67 (dd, J = 10.9, 4.5 Hz, 1 H), 3.60 (dd, J = 10.7, 5.9 Hz, 1 H), 2.87 (q, J = 5.1 Hz, 1 H), 2.04 (q, J = 7.0 Hz, 2 H), 1.95 (br s, 4 H, exchanged with D_2O), 1.24 (br s, 22 H), 0.86 (t, J = 6.7 Hz, 3 H). This NMR spectrum matched one obtained for a sample of naturally derived material (Sigma Chem. Co.): HRMS (FAB, glycerol matrix), m/z 300.2927 (calcd for $C_{18}H_{38}NO_2$ (M + H^+), 300.2902).

Method B. The remaining acetylide addition reaction mixture described above (120 mL) was added directly to a −78 °C blue solution of Li^0 (0.482 g, 0.0695 mol) in $EtNH_2$ (75 mL) via cannula using positive N_2 pressure. After stirring at −78 °C for 4 h the TLC in 4:1:1 n-BuOH–H_2O–HOAc showed the complete formation of sphingosine **5a** at the expense of starting alkyne **3a** and the intermediate alkene **4a**. The reaction was allowed to warm to ambient temperature overnight and then quenched with 8.8 g of solid NH_4Cl. The remaining ethylamine and solvent were removed on a rotory evaporator and the resulting white solid was partitioned between 300 mL of H_2O and 2 × 300 mL of Et_2O. The combined Et_2O layers were washed with brine (300 mL), dried with Na_2SO_4, filtered, and concentrated to give crude **5a** as a waxy solid (2.4364 g). Trituration of this crude material with cold pentane (10 mL) left 1.450 g of an off-white solid which was recrystallized from 1:1 hexanes–EtOAc to give 1.339 g of **5a** as a TLC and NMR homogeneous white solid in 68% overall yield, mp 68–70 °C. This product was spectroscopically indistinguishable from the synthetic **5a** prepared by hydrolysis of **4a**. Further recrystallization from 1:1 hexanes–EtOAc afforded 0.865 g of **5a**: mp 72–75 °C (shr at 70°); $[\alpha]_D$ −0.78° (c 2.02, $CHCl_3$).

D-*threo*-Sphingosine (5b) and D-*erythro*-Sphingosine (5a) via Alane Addition. A solution of 1-pentadecyne (1.00 g, 4.82 mmol) in dry hexanes (6.5 mL–distilled from Na^0) was treated with a solution of 1.5 M DIBAL in toluene (3.25 mL, 4.88 mmol) and the mixture heated at 60 °C for 2 h under N_2. At this time, the TLC in hexanes showed the disappearance of starting alkyne at R_f 0.66 (char A) and the clean formation of (presumed) alane-derived 1-pentadecene at R_f 0.92. The vinylalane solution was cooled to −78 °C (a suspension formed) and to it was added a −78 °C solution of aldehyde 1 (0.850 g, 3.71 mmol) in dry toluene (3.3 mL–distilled from Na^0) via cannula over 5 min. The resulting suspension was stirred for 2 h during which time the mixture was allowed to warm to −60 °C, whereupon a colorless solution formed. The TLC in 3:1 hexanes–EtOAc showed the clean formation of two products, $R_{f_{major}}$ 0.44 (char B) and $R_{f_{minor}}$ 0.47, at the expense of starting material at R_f 0.42. The mixture was poured into ice–water (80 mL), acidified to pH 1 with 1 N HCl (15 mL), and extracted with 3 × 150 mL of Et_2O. The combined extracts were washed with brine (80 mL), dried with $MgSO_4$, filtered, and concentrated to give 1.855 g of crude product as a colorless oil which was shown by NMR analysis to contain a 2:1 mixture of diastereomers **4b** and **4a**. An enriched sample (**4b**:**4a** = 7:1) was obtained separately by careful flash chromatography of the crude mixture on silica gel, eluting with 12:1 hexanes–EtOAc: $[\alpha]_D$ −39° (c 0.25, $CHCl_3$); IR (neat) 3470, 1700, 1670 cm^{-1}; ^1H NMR data for **4b** (400 MHz, C_6D_6, 60 °C) δ 5.70 (dt, J = 15.6, 6.8 Hz, 1 H), 5.52 (dd, J = 15.5, 7.1 Hz, 1 H), 4.40 (t, J = 7.2 Hz, 1 H), 3.95 (pseudo t, J = 6.3 Hz, 1 H), 3.89 (br d, J = 9.1 Hz, 1 H), 3.67 (dd, J = 6.4, 4.9 Hz, 1 H), 1.99 (q, J = 6.8 Hz, 2 H), 1.65 (br s, 3 H), 1.46 (br s, 3 H), 1.39 (br s, 9 H), 1.31 (br s, 22 H), 0.91 (t, J = 6.9 Hz, 3 H), 0.55 (br s, H, exchanged with D_2O); HRMS (FAB, glycerol matrix), m/z 440.3732 (calcd for $C_{26}H_{50}NO_4$ (M + H^+), 440.3740).

The crude 2:1 mixture of **4b** and **4a** described above was combined with 1 N HCl (80 mL) and THF (80 mL) and heated at 70–80 °C with stirring for 16 h under N_2 when the TLC in 3:1 hexanes–EtOAc no longer showed any starting material at R_f 0.46. After cooling and removal of the THF with a rotary evaporator, the reaction mixture was extracted with 3 × 150 mL of 1:1 Et_2O–hexanes to remove any neutral byproducts, basified to pH 10 with 1 N NaOH (85 mL), and then extracted with 3 × 200 mL of CH_2Cl_2. The combined extracts were dried with Na_2SO_4, filtered, and concentrated in vacuo to give 770 mg (69% yield) of a pale yellow waxy solid. This material was shown to consist of a 2:1 mixture of **5b** and **5a** by ^1H NMR analysis. A sample of analytically pure **5b** was prepared by deprotection of chromatographically enriched **4b** (vide supra) followed by two recrystallizations from hexanes–CH_2Cl_2: mp 86–87 °C [lit.[4g] mp 88.0–88.5 °C]; $[\alpha]_D$ −2.65° (c 1.13, $CHCl_3$); IR (KBr) 3350, 1590 cm^{-1}; ^1H NMR (400 MHz, 1.9 mg/0.5 mL $CDCl_3$, room temperature) δ 5.72 (dt, J = 15.5, 6.5 Hz, 1 H), 5.44 (dd, J = 15.6, 6.8 Hz, 1 H), 3.97 (t, J = 6.0 Hz, 1 H), 3.66 (dd, J = 10.8, 4.5 Hz, 1 H), 3.53 (dd, J = 10.7, 6.43 Hz, 1 H), 2.77 (q, J = 4.7 Hz, 1 H), 2.03 (q, J = 6.9 Hz, 2 H), 1.96 (br s, 4 H, exchanged with D_2O), 1.24 (br s, 22 H), 0.86 (t, J = 6.7 Hz, 3 H); HRMS (FAB, glycerol matrix), m/z 300.2895 (calcd for $C_{18}H_{38}NO_2$ (M + H^+), 300.2902).

***N,O,O*-Triacetyl-D-*erythro*-sphingosine (6a) and *N,O,O*-Triacetyl-D-*threo*-sphingosine (6b).** In each case a 0.08 M solution of synthetic sphingosine (**5a** or **5b**) was treated with an equal volume of acetic anhydride and pyridine and then stirred at ambient temperature for 2 h. The volatiles were removed in vacuo, leaving the respective triacetates as a white solids in essentially quantitative yield. Triacetate **6a** was purified by recrystallization from hexanes–CH_2Cl_2: R_f 0.41 in 1:1 EtOAc–hexanes (developed 3 times); mp 102.5–103.5 °C [lit.[3c] mp 103.5–104.5 °C, lit.[4a] mp 103 °C, lit.[4b,e] mp 101–102 °C]; $[\alpha]_D$ −13.0° (c 1.08, $CHCl_3$) [lit.[3c] −12.9° ($CHCl_3$), lit.[4a] −12.2° (c 1, $CHCl_3$), lit.[4b] −13.3° (c 1.4, $CHCl_3$), lit.[4e] −12.8° (c 1, $CHCl_3$)]; IR (KBr) 3293, 1741, 1657, 1555 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, room temperature) δ 5.77 (dt, J = 15.3, 6.8 Hz, 1 H), 5.61 (d, J = 9.2 Hz, 1 H), 5.37 (dd, J = 15.4, 7.4 Hz, 1 H), 5.26 (pseudo t, J = 6.5 Hz, 1 H), 4.40 (m, 1 H), 4.28 (dd, J = 11.5, 6.1 Hz, 1 H), 4.03 (dd, J = 11.5, 3.4 Hz, 1 H), 2.06–1.96 (m, 11 H, contains three singlets at 2.15, 2.05, and 1.96), 1.25 (br s, 22 H), 0.86 (t, J = 6.7 Hz, 3 H). Anal. Calcd for $C_{24}H_{43}NO_5$: C, 67.73; H, 10.18; N, 3.29. Found: C, 67.36; H, 10.18; N, 3.18. **6b** was purified by selectively crystallizing out **6a** from a hexanes–CH_2Cl_2 solution as described above followed by evaporation of the filtrate: R_f 0.35 in 1:1 EtOAc–hexanes (developed 3 times); mp 42–44 °C [lit.[3c] mp 43–43.5 °C (from CH_2Cl_2–light petroleum ether)]; $[\alpha]_D$ +7.02° (c 2.05, $CHCl_3$) [lit.[3c] +8.43° ($CHCl_3$), lit.[4a] +8.78° (c 1.2, $CHCl_3$)]; IR (KBr) 3290, 1745, 1650, 1550 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, room temperature) δ 5.75 (dt, J = 13.9, 7.0 Hz, 1 H), 5.62 (d, J = 9.2 Hz, 1 H), 5.38 (m, 2 H), 4.38 (m, 1 H), 4.06 (m, 2 H), 2.06–1.96 (m, 11 H, contains three singlets at 2.06, 2.05, and 1.98), 1.25 (br s, 22 H), 0.86 (t, J = 6.8 Hz, 3 H). Anal. Calcd for $C_{24}H_{43}NO_5$: C, 67.73; H, 10.18; N, 3.29. Found: C, 67.73; H, 10.18; N, 3.29.

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Note Added in Proof: After submission of this manuscript, we became aware of two other sphingosine syntheses based on stereocontrolled additions to the oxazolidine aldehyde 1: Herold, P. *Helv. Chim. Acta* **1988**, *71*, 354. Nimkar, S.; Menaldino, D.; Merrill, A. H.; Liotta, D. *Tetrahedron Lett.* **1988**, *29*, 3037.

Registry No. 1, 102308-32-7; 2, 105563-08-4; **3a**, 115464-01-2; **3b**, 115464-02-3; **4a**, 115464-03-4; **4b**, 115464-04-5; **5a**, 123-78-4; **5b**, 25695-95-8; **6a**, 2482-37-3; **6b**, 78779-96-1; 7, 41765-25-7; Br-$(CH_2)_{12}$Me, 765-09-3; NaC≡CH, 1066-26-8; HC≡C$(CH_2)_{12}$Me, 765-13-9.

Potassium Fluoride Catalyzed Fluorodesulfonylations of Aryl Sulfonyl Fluorides

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Although the conversion of aryl sulfonyl chlorides or bromides to the corresponding aryl halide proceeds in good yield upon the action of light[1] or metallic catalysts,[2,3]

