minor product from MCPBA epoxidation of **1**, and compound **7a** (65 mg, 32%): mp 255–257 °C; IR (CH_2Cl_2) 3550, 2940, 1760, 1720, 1180, 1080 cm^{-1}; mass spectrum (NICI, ammonia reagent gas), calcd for $C_{29}H_{38}O_{12}$ *m/e* 578.2363, found 578.2359; ^1H NMR δ 0.76 (3 H, s, 14-H), 1.28 (3 H, d, J = 6.3 Hz, 14′-H), 1.33 (3 H, s, 12′-H), 1.60 (3 H, s, 16-H), 2.19 (1 H, ddd, $J_{3\beta,4}$ = 4.7 Hz, $J_{2,3\beta}$ = 4.8 Hz, J_{gem} = 15.3 Hz, 3β-H), 2.39 (1 H, dd, $J_{3\alpha,4}$ = 8.3 Hz, J_{gem} = 15.3 Hz, 3α-H), 2.73 and 3.13 (1 H each, AB, J = 4.0 Hz, 13-H), 3.07 (1 H, d, J = 5.3 Hz, 10-H), 3.40 (1 H, m, 4′-H), 3.44 (1 H, s, 2′-H), 3.52 (1 H, d, J = 5.3 Hz, 11-H), 3.73 (1 H, dd, $J_{6',7}$ = $J_{6,13'}$ = 4.3 Hz, 6′-H), 3.78 (1 H, m, 7′-H), 3.84 (2 H, m, 5′-H), 3.92 (1 H, d, J = 4.8 Hz, 2-H), 4.30 and 4.42 (1 H each, AB, J = 12.4 Hz, 15-H), 4.39 (1 H, m, 13′-H), 5.46 (1 H, ddd, $J_{8',10'}$ = 1.5 Hz, $J_{8',9'}$ = 7.9 Hz, $J_{7',8'}$ = 8.3 Hz, 8′-H), 5.75 (1 H, dd, J = 8.3 and 4.7 Hz, 4-H), 5.99 (1 H, dd, J = 1.5 and 11.4 Hz, 10′-H), 6.19 (1 H, dd, J = 7.9 and 11.4 Hz, 9′-H); ^{13}C NMR δ 7.5 (C14), 11.5 (C12′), 15.6 (C14′), 17.3 (C7), 22.2 (C16), 26.3 (C8), 34.6 (C3), 43.4 (C6), 47.8 (C13), 49.0 (C5), 52.7 (C2′ or C9), 57.4 (C2′ or C9), 57.7 (C10), 63.6 (C15), 64.8 (C3′), 65.9 (C12), 67.4 (C11), 72.6 (C5′), 74.7 (C13′), 75.2 (C4 or C7′ or C8′), 76.2 (C4 or C7′ or C8′), 76.5 (C4 or C7′ or C8′), 78.2 (C2 or C4′), 78.6 (C2 or C4′), 81.9 (C6′), 121.9 (C10′), 147.5 (C9′), 167.4 (C1′ and C11′). Diacetate **7b**: mass spectrum (NICI, ammonia reagent gas), calcd for $C_{33}H_{42}O_{14}$ *m/e* 662.2575, found 662.2565; ^1H NMR δ 0.78 (3 H, s, 14-H), 1.26 (3 H, d, J = 6.4 Hz, 14′-H), 1.33 (3 H, s, 12′-H), 1.65 (3 H, s, 16-H), 2.17 (1 H, ddd, $J_{3\beta,4}$ = 4.6 Hz, $J_{2,3\beta}$ = 4.7 Hz, J_{gem} = 15.4 Hz, 3β-H), 2.38 (1 H, dd, $J_{3\alpha,4}$ = 8.3 Hz, J_{gem} = 15.4 Hz, 3α-H), 2.73 and 3.15 (1 H each, AB, J = 4.0 Hz, 13-H), 3.07 (1 H, d, J = 5.3 Hz, 10-H), 3.42 (1 H, s, 2′-H), 3.53 (1 H, d, J = 5.3 Hz, 11-H), 3.71 (1 H, dd, J = 5.0 and 10.3 Hz, 5′β-H), 3.90 (2 H, m, 6′-H, 5′α-H), 3.91 (1 H, d, J = 4.7 Hz, 2-H), 4.30 and 4.44 (1 H each, AB, J = 12.3 Hz, 15-H), 4.35 (1 H, dd, J = 7.6 and 5.0 Hz, 4′-H), 4.79 (1 H, dd, J = 3.3 and 9.9 Hz, 7′-H), 5.50 (1 H, dd, J = 8.0 and 9.9 Hz, 8′-H), 5.72 (1 H, dd, J = 4.6 and 8.3 Hz, 4-H), 6.05 (2 H, m, 9′-H and 10′-H).

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1,4- and 1,5-Stereoselection by Sequential Aldol Addition to α,β-Unsaturated Aldehydes Followed by Claisen Rearrangement. Application to Total Synthesis of the Vitamin E Side Chain and the Archaebacterial C_{40} Diol[1]

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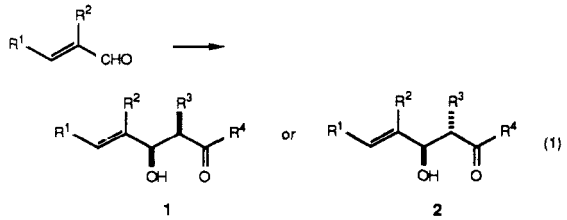
A synthetic strategy has been developed wherein the high 1,2-stereoselection obtainable from aldol reaction of an α,β-unsaturated aldehyde is parlayed by a subsequent Claisen rearrangement into 1,4- or 1,5-stereoselection. For example, diol monoethers **26** and **31**, obtained in three steps from aldol **11**, are subjected to Claisen rearrangement to obtain amides **40** and **41** or ester **42**. The diastereomeric diol monoethers **29** and **32** are similarly converted into the diastereomeric amides **43** and **44**. The use of this strategy for 1,5-stereoselection is illustrated. Esters **52** and **53** can be converted via the *E* enolates into unsaturated acids **56** and **57**. The same acids are obtainable from the diastereomeric esters **54** and **55**, by conducting the Ireland–Claisen rearrangement with the *Z* enolates. The diastereomeric unsaturated acids **58** and **59** arise via the *Z* enolates of esters **52** and **53** or the *E* enolates of esters **54** and **55**. The 1,4-stereoselection strategy is illustrated with a synthesis of hydrocarbon **45**. This stereorational synthesis establishes the relative stereochemistry of the C_{30} diol from Messel shale kerogen. The 1,5-stereoselection strategy is demonstrated with a synthesis of (±)-**67**, the vitamin E side-chain alcohol. This synthetic protocol is further illustrated with a total synthesis of the archaebacterial C_{40} diol (**69**) and one of its diastereomers (**70**). The latter syntheses provide the final information to fully define the structure of compound **112**, an archaebacterial membrane substance that is a 72-membered ring tetraether with 18 stereocenters.

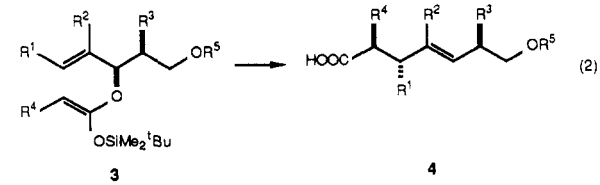
Introduction

Under certain conditions, the addition of preformed enolates to aldehydes gives α-substituted-β-hydroxy carbonyl compounds with high diastereoselectivity.[2] If an α,β-unsaturated aldehyde is employed as the educt, one may prepare either syn or anti aldols (**1** or **2**, eq 1). Since aldols **1** and **2** are also allylic alcohols, the possibility exists of parlaying the high 1,2 stereoselectivity of the aldol reaction into either 1,4 or 1,5 stereoselectivity by using the Claisen rearrangement. For example, as shown in eq 2,



(1)

1 **2**



(2)

3 **4**

the *Z* ester enolate **3**, derived from syn aldol **1**, should be transformable into **4**, in which new 1,4 and 1,5 stereorelationships exist. By controlling the relative stereochemistry in the aldol (e.g., **1** or **2**) and the geometry of the enolate double bond,[3] a great deal of synthetic versatility

(1) Part 42 in the series Acyclic Stereoselection. For part 41, see: Mori, I.; Bartlett, P. A.; Heathcock, C. H. *J. Am. Chem. Soc.*, submitted for publication.

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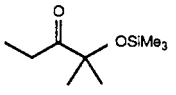
Table I. Preparation of Aldols 10–15

ketone	aldehyde	product	yield, %	stereochemical homogeneity
5	7	10	80	>98:2
5	8	11	97	>98:2
5	9	12	99	>98:2
6	7	13	88	86:14[a]
6	8	14	80	90:10[a]
6	9	15	88	>98:2

[a] The minor isomer in these cases was the syn diastereomer.

is possible. In this paper, we report in full our investigation of this strategy for stereoselective synthesis.[4]

Preparation of Claisen Rearrangement Substrates: Racemic Series. Initial investigations were carried out with the α-(trimethylsilyl)oxy ketone **5**[5] and 2,6-di-*tert*-butyl)-4-methylphenyl propionate (BHT propionate, **6**),[6] which give the *Z* and *E* lithium enolates, respectively, upon deprotonation by lithium diisopropylamide (LDA). The aldehydes utilized were acrolein (**7**), crotonaldehyde (**8**), and methacrolein (**9**). Aldol reactions were carried out under the conditions reported previously.[5,6] In this manner, aldols **10–15** were prepared; yields and stereochemical data are summarized in Table I. Each of the three aldehydes gives a single stereoisomeric aldol (syn) with ketone **5**. With ester **6**, methacrolein also gives only a single aldol product (anti), but acrolein and crotonaldehyde give anti/syn mixtures of about 9:1. In the case of acrolein, the initially formed mixture may be enriched by recrystallization, and in the case of crotonaldehyde, the two diastereomeric aldols are separable by chromatography.



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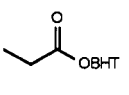

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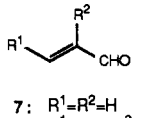
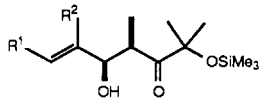
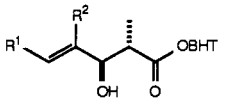


7: R^1=R^2=H
8: R^1=Me, R^2=H
9: R^1=H, R^2=Me



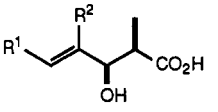
10: R^1=R^2=H
11: R^1=Me, R^2=H
12: R^1=H, R^2=Me



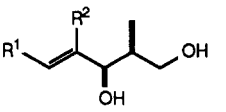
13: R^1=R^2=H
14: R^1=Me, R^2=H
15: R^1=H, R^2=Me

Aldols **10–12** are cleaved with periodic acid in tetrahydrofuran[7] to provide β-hydroxy acids **16–18**, which are reduced by lithium aluminum hydride in refluxing tetrahydrofuran to afford diols **19–21**. The BHT aldols **13–15** are reduced similarly to obtain the diastereomeric diols **22–24**.

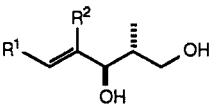
Diols **19–24** react with *tert*-butyldimethylsilyl chloride in the presence of 4-(dimethylamino)pyridine (DMAP) and triethylamine to afford the monoethers **25–30**; yields for this monoprotection are generally about 65%. The crotonaldehyde-derived diols **20** and **23** were also transformed into the triphenylmethyl (trityl) ethers **31** and **32**.



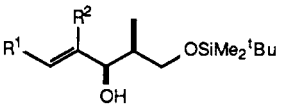
16: R^1=R^2=H
17: R^1=Me, R^2=H
18: R^1=H, R^2=Me



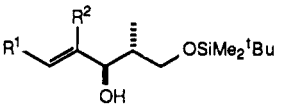
19: R^1=R^2=H
20: R^1=Me, R^2=H
21: R^1=H, R^2=Me



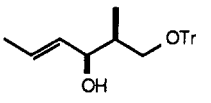
22: R^1=R^2=H
23: R^1=Me, R^2=H
24: R^1=H, R^2=Me



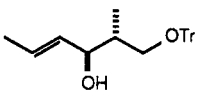
25: R^1=R^2=H
26: R^1=Me, R^2=H
27: R^1=H, R^2=Me



28: R^1=R^2=H
29: R^1=Me, R^2=H
30: R^1=H, R^2=Me



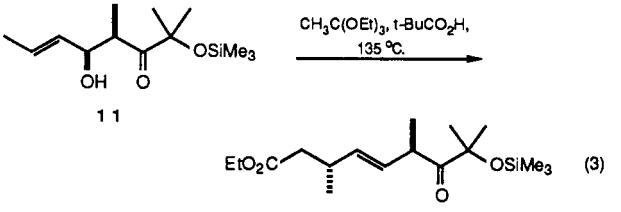
31



32

Preparation of Claisen Rearrangement Substrates: Scalemic[8] Series. The Evans oxazolidone protocol[9] was used to prepare the 2*S*,3*R* and 2*R*,3*S* β-hydroxy acids **35** and **38**, as shown in Scheme I. These scalemic synthons were transformed by the routes already described into scalemic versions of diol **19** and ether **25**.

1,4-Stereoselection by the Aldol–Claisen Strategy. We first examined the Claisen rearrangement of aldol **11** under the Johnson–Faulkner orthoacetate conditions.[10] Although the rearranged keto ester **39** was obtained by this method in 40% yield (eq 3), not surprisingly, the major



11

39

products seemed to derive from β elimination. Even lower yields of the rearrangement product were obtained with the Eschenmoser amide acetal variant,[11] retroaldolization being the principal competing process in this case. Better success was realized with allylic alcohols **26** and **31** (eq 4). With trityl ether **31** the orthoacetate conditions gave the desired rearrangement product (**42**) in 60% yield, but this product was still accompanied by substantial amounts of byproducts resulting from dehydration. However, the Eschenmoser conditions converted alcohol **31** into amide **41** in nearly quantitative yield; a similar high yield was obtained in the conversion of silyl ether **26** to amide **40**.

(4) Preliminary communications on portions of this work have appeared: (a) Heathcock, C. H.; Jarvi, E. T. *Tetrahedron Lett.* **1982**, *23*, 2825. (b) Heathcock, C. H.; Finkelstein, B. L. *J. Chem. Soc., Chem. Commun.* **1983**, 919. (c) Heathcock, C. H.; Jarvi, E. T.; Rosen, T. *Tetrahedron Lett.* **1984**, *25*, 243. (d) Heathcock, C. H.; Finkelstein, B. L.; Aoki, T.; Poulter, C. D. *Science (Washington, D.C.)* **1985**, *229*, 862. (e) Heathcock, C. H.; Radel, P. A. *J. Org. Chem.* **1986**, *51*, 4322.

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(7) Ireland, R. E.; Newbould, J. *J. Org. Chem.* **1963**, *28*, 23.

(8) The term **scalemic** has been suggested by Professor James Brewster, Purdue University, to describe an unequal mixture of enantiomers (personal communication). According to Brewster's suggestion, scalemic and racemic are the macroscopic analogues of chiral and achiral, adjectives that are best reserved for single objects such as molecules.

(9) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127.

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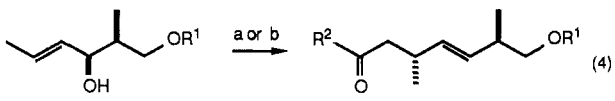
(11) Felix, D.; Gschwend-Steen, K.; Wick, A. E.; Eschenmoser, A. *Helv. Chim. Acta* **1969**, *52*, 1030.



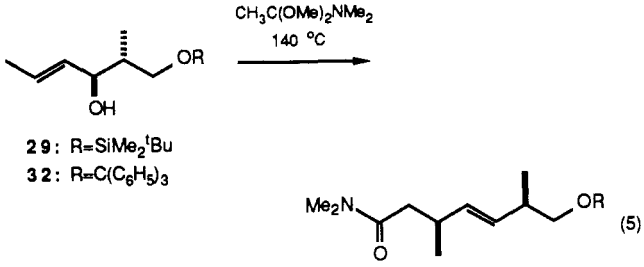
26: R^1=$SiMe_2{}^tBu$
31: R^1=$C(C_6H_5)_3$

40: R^1=$SiMe_2{}^tBu$, R^2=NMe_2
41: R^1=$C(C_6H_5)_3$, R^2=NMe_2
42: R^1=$C(C_6H_5)_3$, R^2=OEt

(4)

a. $CH_3C(OEt)_3$, t-$BuCO_2H$, 135 °C. b. $CH_3C(OMe)_2NMe_2$, 140 °C.

Allylic alcohols **29** and **32** were subjected to the Eschenmoser–Claisen rearrangement to obtain unsaturated amides **43** and **44** in 92–98% yield (eq 5).



29: R=$SiMe_2{}^tBu$
32: R=$C(C_6H_5)_3$

43: R=$SiMe_2{}^tBu$
44: R=$C(C_6H_5)_3$

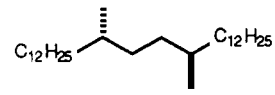
(5)

Determination of the stereoselectivity of the foregoing Claisen rearrangements was not straightforward. The ^{13}C NMR spectrum of silyl ether **40**, measured at 62.89 MHz, showed the expected number of signals, but several were accompanied by small upfield shoulders. Resolution at this frequency was inadequate for accurate analysis of the diastereomer ratio. The observation that the ^{13}C NMR resonances of the minor isomer are almost coincident with those of the major isomer suggests that the minor product also has an *E* double bond (i.e., is **43**), since there is normally a large gauche shift for the allylic carbons in cis and trans isomeric alkenes.[12]

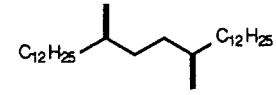
After experimenting with a number of columns and conditions, we were successful in resolving the isomers of the trityl ethers by high performance liquid chromatography (HPLC) with a Pirkle type I-A column;[13] the analysis showed the diastereomer ratio of the product resulting from ether **31** to be 90:10. Similar analysis of the product from **32** showed it to be a 95:5 mixture of diastereomers. ^{13}C NMR spectra of mixtures of amides **40** and **43** and careful HPLC analysis showed that the minor isomer in each case does have the *E* double bond. Thus, Claisen rearrangement of alcohol **26** affords amides **40** and **43** in a ratio of 90:10 and rearrangement of **29** provides the same two isomers in a ratio of 5:95. Suitable control experiments showed that these product ratios are time-independent and therefore not the result of equilibration.

The stereochemistry of these Claisen rearrangements may be discussed in light of Scheme II for an intermediate derived from the syn isomers **26** and **31**. Chair transition state A and boat transition state B lead to the observed major products **40–42**, which have an *E* double bond and the 3*R**,6*R** configuration at the two stereocenters; of these, transition state A is clearly the more probable. Chair transition state C and boat transition state D would lead to isomeric products having a *Z* double bond and the 3*S**,6*R** configuration at the two stereocenters. There is no suprafacial transition state that will convert the syn derivative to the 3*S**,6*R** derivatives **43** and **44**. Since antarafacial Claisen rearrangement is unlikely, we conclude that the minor isomers in all of these rearrangements must arise by a heterolytic, nonconcerted mechanism.

Application in Synthesis: Stereochemistry of the C_{30} Diol from Messel Shale Kerogen. To demonstrate the utility of the foregoing strategy for 1,4-stereoselection in synthesis, we set about to prepare hydrocarbon **45**, one



45



46

isomer of a hydrocarbon prepared by Albrecht and coworkers from the diethers of 13,16-dimethyloctacosane-1,28-diol, isolated from Messel shale kerogen.[14] As shown in Scheme III, the double bond in unsaturated amide **40** was reduced with diimide, generated by the air oxidation of hydrazine hydrate with cupric acetate catalysis, to provide **47**. Several attempts to accomplish this reduction by catalytic methods resulted in loss of stereochemical homogeneity, presumably because of double-bond isomerization. For example, hydrogenation over Adams catalyst (reduced PtO_2), Rh/Al_2O_3, and Ir/C gave **47** and its diastereomer in ratios of 5.5:1, 3.5:1, and 6:1, respectively. After removal of the *tert*-butyldimethylsilyl protecting group, alcohol **48** was oxidized by the Praikh method[15] to give the aldehyde, which was condensed with undecylidenetriphenylphosphorane[16] to obtain **49**, mainly as the *Z* stereoisomer. Amide **49** was reduced by lithium in ammonia with added *tert*-butyl alcohol to give, after workup, aldehyde **50** in 45% yield.[17] The synthesis of **45** was completed by condensation of **50** with decylidenetriphenylphosphorane[18] to give the *Z*,*Z* diene **51**, which was hydrogenated over Ir/C. The comparison of the synthetic **45** with an authentic sample of naturally derived hydrocarbon was performed in Strasbourg by Albrecht and Chappe; details of this comparison, which establish that the Messel shale C_{30} diol has the relative stereochemistry of **46**, have been described elsewhere.[2b]

1,5-Stereoselection by the Aldol–Claisen Strategy. Initial experiments with the Johnson–Faulkner and Eschenmoser variants of the Claisen rearrangement using propionate or propionamide derivatives (e.g., eq 2, R^4 = methyl) were not promising. Furthermore, these variants do not offer the possibility to control the enol geometry. We therefore turned our attention to the Ireland enolate–Claisen rearrangement.[3] Acylation of the acrolein and methacrolein-derived diol monoethers **25**, **27**, **28**, and **30** is carried out by treatment with propionyl chloride and pyridine in methylene chloride; esters **52–55** were thus prepared. As is shown in Scheme IV, esters **52** and **53** give the 2,6-syn products **56** and **57** if the rearrangement is carried out by way of the *E* enolate,[19] whereas the 2,6-anti

(12) For (*E*)- and (*Z*)-2,5-dimethyl-3-hexene the ^{13}C NMR resonances for C-1, C-2, and C-3 are (*E*) 23.24, 31.64, 134.91; (*Z*) 23.76, 27.20, 135.45. de Haan, J. W.; van de Ven, L. J. M. *Org. Magn. Reson.* **1973**, *5*, 147.

(13) Pirkle, W. H.; House, D. W. *J. Chromatogr.* **1980**, *192*, 143.

(14) (a) Chappe, B.; Michaelis, W.; Albrecht, P. *Advances in Organic Geochemistry* **1979**; Douglas, A. G., Maxwell, J. R., Eds.; Pergamon: Oxford, 1980; p 265. (b) Chappe, B.; Michaelis, W.; Albrecht, P.; Ourisson, G. *Naturwissenschaften* **1979**, *66*, 522. (c) Chappe, B.; Albrecht, P.; Michaelis, W. *Science (Washington, D.C.)* **1982**, *217*, 65.

(15) Praikh, H. K.; von E. Doering, W. *J. Am. Chem. Soc.* **1967**, *89*, 5055.

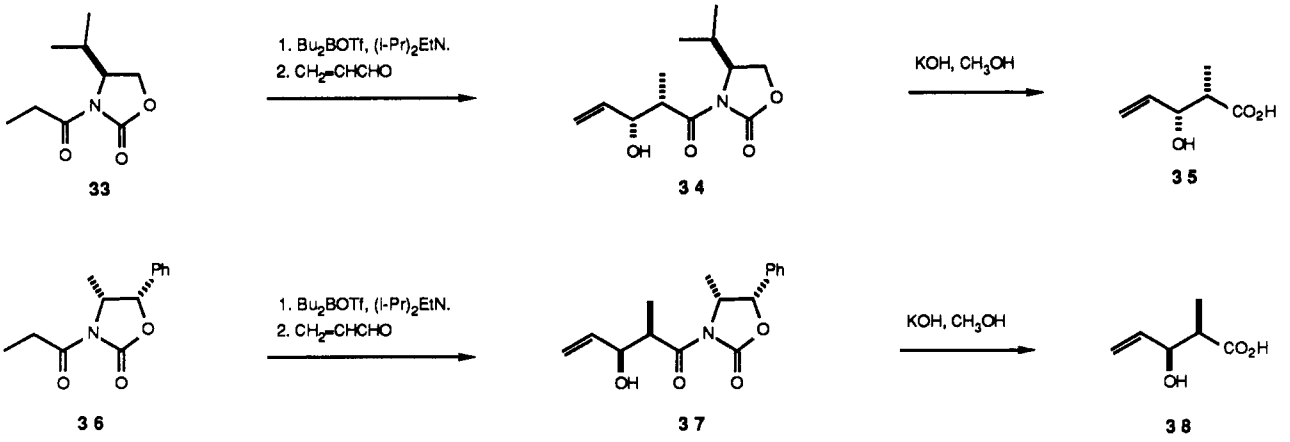
(16) Starratt, A. N. *Chem. Phys. Lipids* **1976**, *16*, 215.

(17) For a previous application of this procedure for conversion of an amide to an aldehyde, see: Birch, A. J.; Craig, J. C.; Slaytor, M. *Aust. J. Chem.* **1955**, *8*, 512.

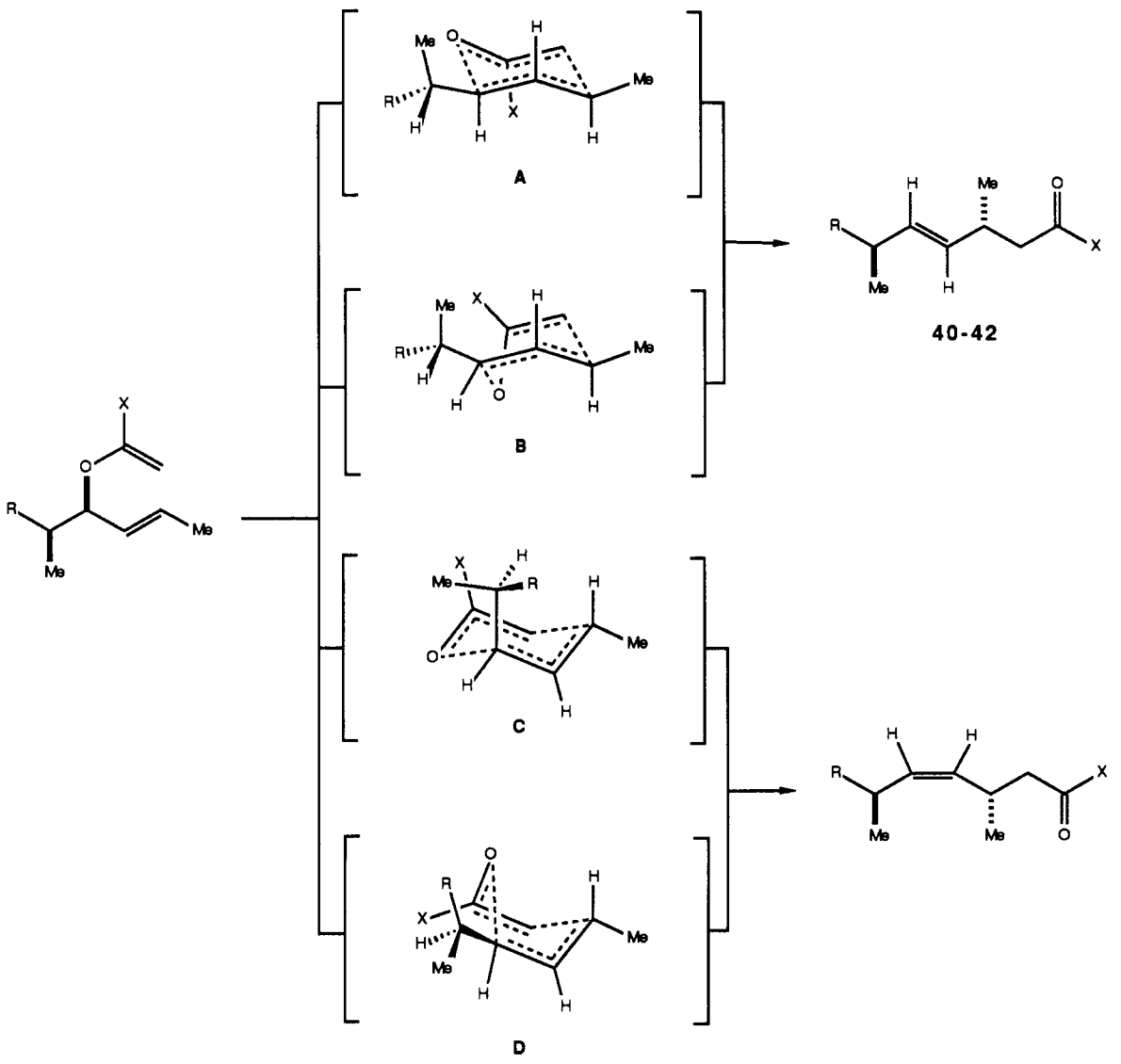
(18) Chasin, D. G.; Perkins, E. G. *Chem. Phys. Lipids* **1971**, *6*, 8.

(19) In describing the stereochemistry of ester enolates, the convention of Evans is followed, wherein the metal-associated oxygen of the enolate is the stereochemical determinant, regardless of the nature of the metal. See: Evans, D. A. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3.

Scheme I



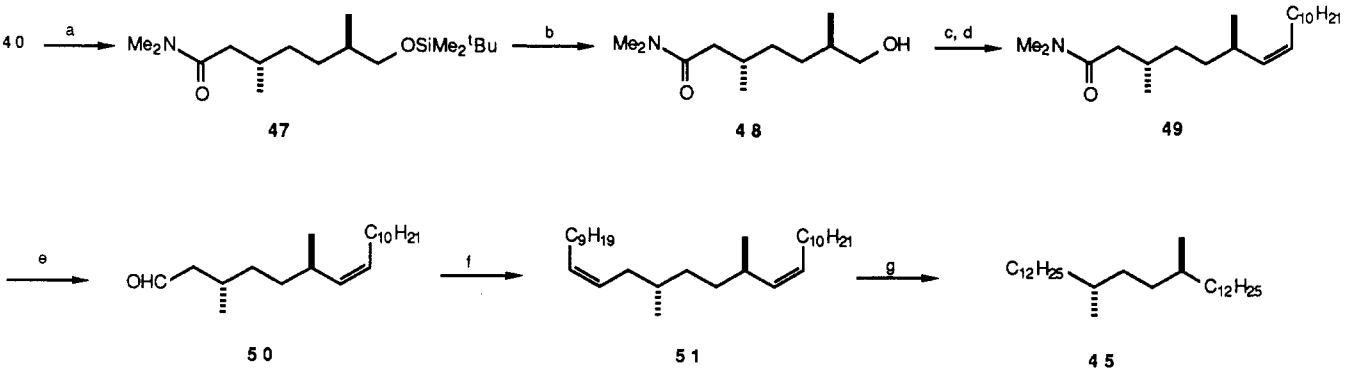
Scheme II



products **58** and **59** are produced if the rearrangement involves the intermediate *Z* enolate. With the diastereomeric esters **54** and **55** just the opposite is true; products **58** and **59** result from the *E* enolate Claisen rearrangement and **56** and **57** are produced from the *Z* enolate intermediate. Although we have prepared each of the four compounds **56–59**, only six of the eight possible transformations summarized in Scheme IV were actually carried out. The yields obtained are summarized in Table II.

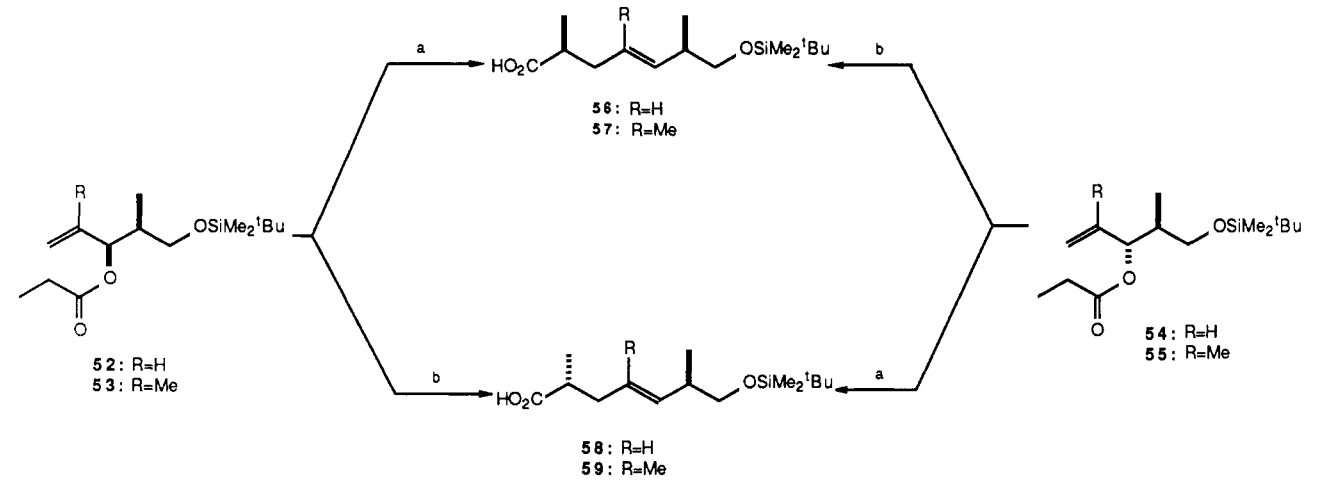
We found diastereomers **56** and **58** to be very difficult to distinguish by using the ^{13}C NMR spectrometers available to us when the rearrangements in Scheme IV were studied (62.89–75.47 MHz). We were also unsuccessful in finding derivatives of **56** and **58** that could be resolved by analytical HPLC. That the rearrangements carried out with racemic substrates gave products of greater than 90% diastereomeric purity could be demonstrated by ^{13}C NMR spectra of mixtures of (±)-**56** and

Scheme III[a]



[a] (a) NH_2NH_2–H_2O, $Cu(OAc)_2$; (b) $(n\text{-}Bu)_4N^+F^-$, THF; (c) $C_5H_5NSO_3$, DMSO, CH_2Cl_2; (d) $C_{10}H_{21}CH{=}PPh_3$; (e) Li, NH_3, *t*-BuOH; (f) $C_9H_{19}CH{=}PPh_3$; (g) H_2, Ir/C, EtOH.

Scheme IV[a]



[a] (a) *E* enolate conditions: i, LDA, THF, −78 °C; ii, *t*-$BuMe_2SiCl$, HMPA; iii, 0 °C; (b) *Z* enolate conditions: i, LDA, THF, HMPA, −78 °C; ii, *t*-$BuMe_2SiCl$; iii, 0 °C.

Table II. Claisen Rearrangements of Esters 52–55 (Scheme IV)

ester	enolate	product	yield, %	Claisen stereoselectivity
(*S**,*S**)-**52**	*E*	(±)-**56**	48	>90:10[a]
(*R*,*R*)-**52**	*E*	(+)-**56**	80	95.5:4.5[b]
(*S*,*S*)-**52**	*E*	(−)-**56**	86	95.5:4.5[b]
(*S*,*S*)-**52**	*Z*	(+)-**58**	80	94.5:5.5[b]
(*S**,*R**)-**54**	*E*	(±)-**58**	84	>90:10[a]
(*S**,*R**)-**54**	*Z*	(±)-**56**	58	>90:10[a]
(*S**,*R**)-**53**	*E*	(±)-**57**	65	>90:10[a]
(*S**,*S**)-**55**	*E*	(±)-**59**	63	>90:10[a]

[a] Ratio estimated by ^{13}C NMR spectroscopy; see text. [b] Ratio determined by ^{19}F NMR spectroscopy on a derived Mosher ester; see text.

(±)-**58**. However, the resolution at these frequencies was not sufficient to assign a more precise value for the stereochemical purity.

With the scalemic esters (*S*,*S*)-**52** and (*R*,*R*)-**52**, however, we were able to make use of an interesting method to arrive at an exact value of the stereochemical purity of products (+)-**56**, (−)-**56**, and (+)-**58**. The method is illustrated in Scheme V for (−)-**56**, obtained by rearrangement of the *E* enolate of (*R*,*R*)-**52**. Saturation of the double bond (H_2 over Adams' catalyst) gives (−)-**60**, which is methylated to obtain ester (−)-**63**. Desilylation, followed by acylation of the resulting primary alcohol with Mosher's acid chloride, (*R*)-2-methyl-2-phenyl-3,3,3-trifluoropropionyl chloride,[20] provides the diester **64**. Examination of this material by ^{19}F NMR spectroscopy showed two singlets in a ratio of 98.5:1.5. This ratio, then, corresponds to the stereoselectivity of the aldol addition leading from *N*-propionyloxazolidone **33** to aldol **34** (Scheme I). Reduction of (−)-**60** affords primary alcohol (+)-**61**, which is similarly converted into the Mosher ester **62**. ^{19}F NMR analysis of this material shows two singlets in the ratio of 94:6, corresponding to the ratio of *R* and *S* configuration at C-2 in (−)-**56**. From these independent determinations of the stereochemical homogeneity at the two stereocenters, we can easily compute the stereoselectivity (*X*) of the Claisen rearrangement:

$$0.985X + 0.015(1 - X) = 0.94$$

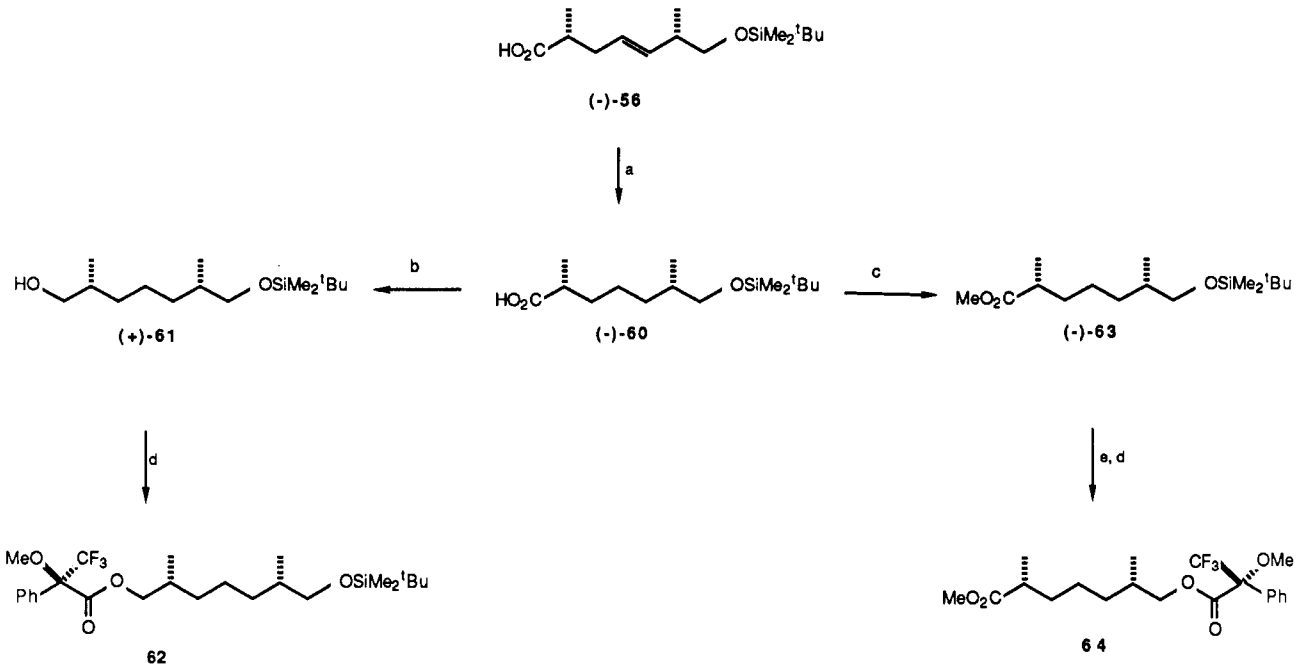
$$X = 0.955$$

Similar exercises were carried out with (+)-**56** and (+)-**58** to derive the Claisen stereoselectivities shown in Table II.

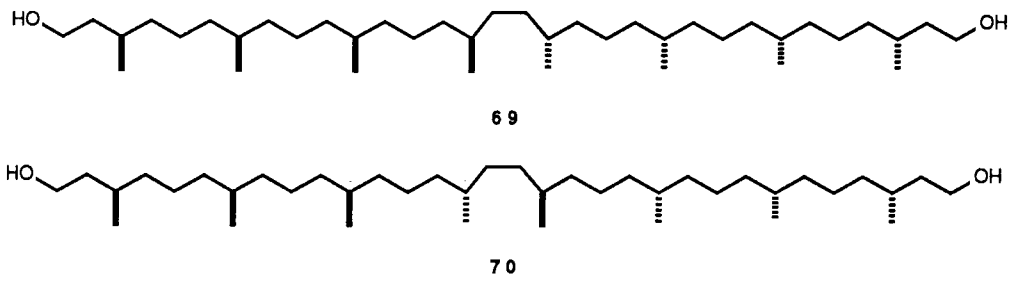
Application in Synthesis: Synthesis of the Vitamin E Side-Chain Alcohol. As a first demonstration of the value of the aldol-Claisen sequence for 1,5-stereoselection, we carried out a synthesis of the racemic alcohol **67** (Scheme VI), the scalemic version of which has been converted into vitamin E.[21] Tosylate (±)-**65**, obtained in

(20) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

Scheme V[a]



[a] (a) H_2, PtO_2, EtOAc; (b) $LiAlH_4$, ether; (c) CH_2N_2, ether; (d) (*S*)-2-methyl-2-phenyl-3,3,3-trifluoropripionyl chloride, DMAP, CH_2Cl_2; (e) $(n\text{-Bu})_4N^+F^-$, THF.

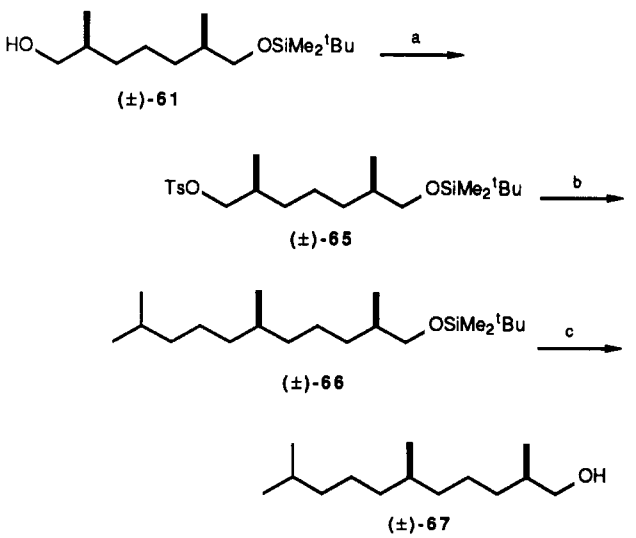


the normal manner from (±)-**61**, was coupled with (3-methylbutyl)magnesium bromide by Kochi's conditions[22] to obtain ether (±)-**66**. Standard deprotection of the latter substance provided (±)-**67**, identical by ^{13}C NMR spectroscopy with a sample supplied us by Dr. Noal Cohen of Hoffman La Roche.

Application in Synthesis: Synthesis of the Archaebacterial C_{40} Diol and a Stereoisomer. As a further application of the strategy being developed, we turned our attention to the "archaebacterial C_{40} diol".[23] Although the gross structure of this substance had been established as **68**, the stereochemistry was not known. As shown in Scheme VII, the C_{40} diol structure may be visualized as arising from four C_{10} units, E–H, each having two stereocenters with a 1,5 relationship. We have shown that the aldol-Claisen sequence can provide C_9 units of the sort required, with any desired stereochemistry. In principle, then, we could synthesize each one of the 132 stereoisomers of structure **68**, compare them with the naturally derived material, and thereby determine the stereochemistry of the natural product.

Several considerations led us to prepare two of these isomers, **69** and **70**. First, because of the primitive nature

Scheme VI[a]

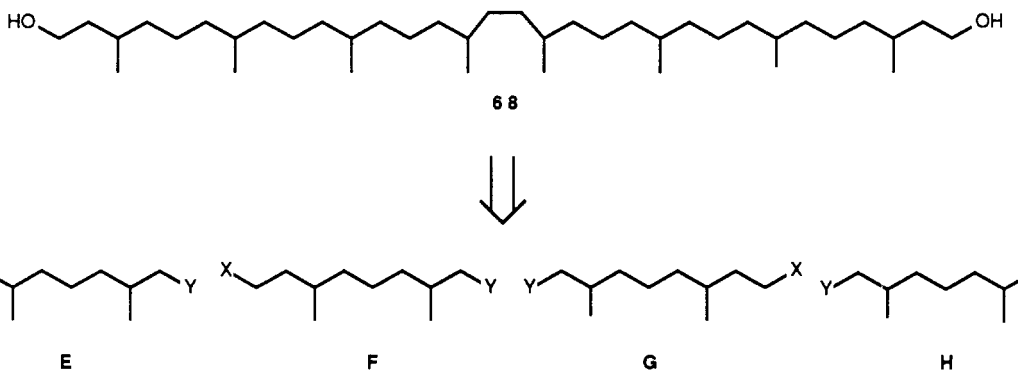


[a] (a) *p*-TsCl, C_5H_5N, CH_2Cl_2; (b) $Me_2CHCH_2CH_2MgBr$, Li_2CuCl_4, THF; (c) $(n\text{-Bu})_4N^+F^-$, THF.

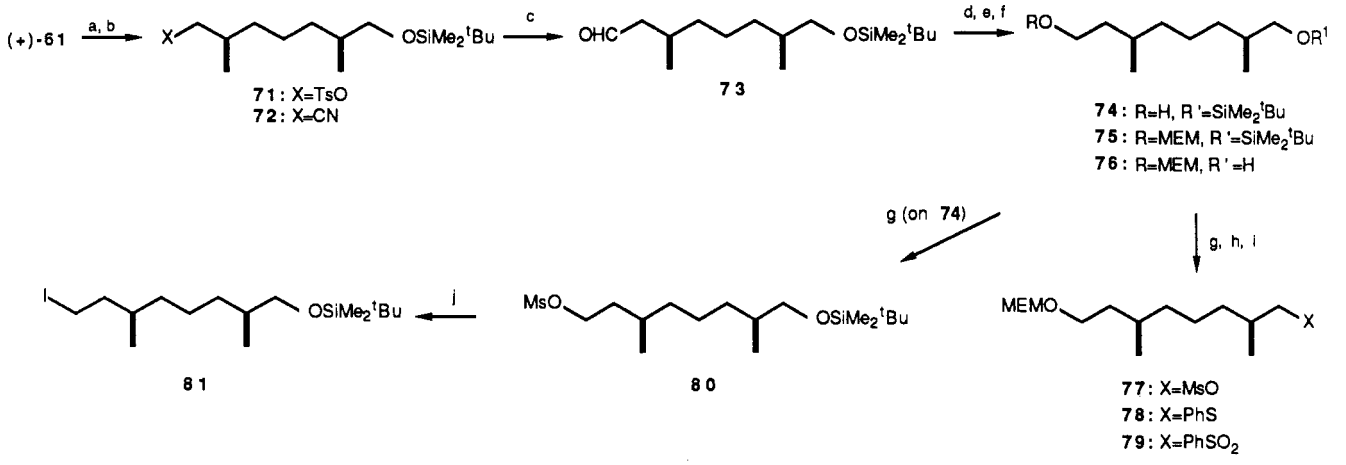
of the organisms giving rise to the C_{40} diol, it is likely that each of the similar stereocenters is created by a single enzyme, probably one in which a trisubstituted double bond is saturated. Thus, it is probable that the stereocenters at C-3, C-7, C-11, C-22, C-26, and C-30 all have the same absolute configuration. Furthermore, it is likely that

(21) (a) Cohen, N.; Eichel, W. F.; Lopresti, R. J.; Neukom, C.; Saucy, G. *J. Org. Chem.* **1976**, *41*, 3505. (b) Cohan, N.; Scott, C. G.; Neukom, C.; Lopresti, R. J.; Weber, G.; Saucy, G. *Helv. Chim. Acta* **1981**, *64*, 1158.
(22) Tamura, M.; Kochi, J. *Synthesis* **1971**, 303.
(23) For a background discussion of this portion of the project, see the introductory paragraphs of ref 4d.

Scheme VII

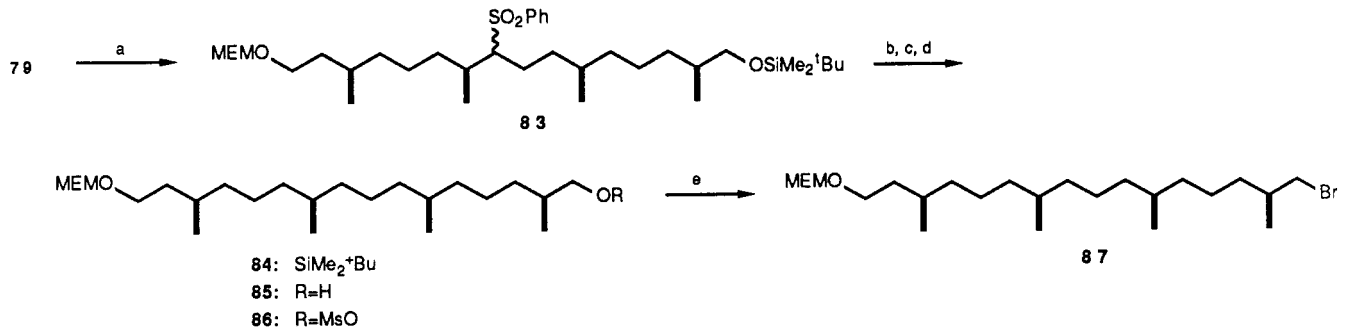


Scheme VIII[a]



[a] (a) *p*-TsCl, C_5H_5N, CH_2Cl_2; (b) KCN, 18-crown-6, CH_3CN; (c) Dibal, pentane; (d) $LiAlH_4$, ether; (e) $CH_3OCH_2CH_2OCH_2Cl$, DMAP, $(i\text{-Pr})_2NEt$, CH_2Cl_2; (f) HF, H_2O, CH_3CN; (g) CH_3SO_2Cl, C_5H_5N, CH_2Cl_2; (h) PhSLi, THF, 25 °C; (i) *m*-CPBA, CH_2Cl_2; (j) $(n\text{-Bu})_4N^+I^-$, THF.

Scheme IX[a]



[a] (a) i, 2 equiv of *n*-buLi, THF, ii, 81, HMPA; (b) Li, THF, HMPA, *t*-BuOH, Na_2HPO_4; (c) HF, CH_3CN; (d) CH_3SO_2Cl, C_5H_5N, CH_2Cl_2; (e) $(n\text{-Bu})_4N^+Br^-$, THF.

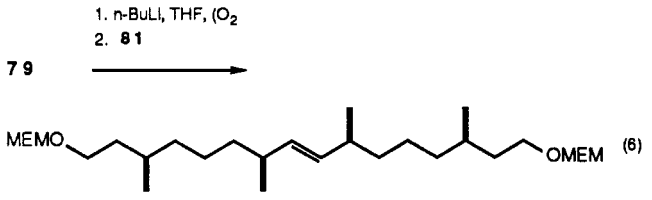
these centers have the *R* absolute configuration, since Kates has shown that the related C_{20} alcohol dihydrophytol, obtained from the archaebacterium *Halobacterium cutirubrum* has the 3*R*,7*R*,11*R* configuration.[24] However, stereocenters C-15 and C-18 are another matter. The biosynthesis of the C_{40} diol has not yet been elucidated. It is possible that the C-16, C-17 bond is formed before the C-15 and C-18 stereochemistry is created. In such a case, one would probably except these centers to be formed by the same biosynthetic step utilized for creation of the other stereocenters; isomer **69** would then correspond to the C_{40} diol. If the C-16,C-17 is formed after double-bond reduction has occurred, by activation of one of the terminal methyl groups of dihydrophytol, one could imagine that the C_{40} diol might be either **69** or **70**. Thus, these two structures are, on biosynthetic grounds, the most likely candidates. But there is another reason to prepare these two isomers. Our plan was to compare our synthetic material with a naturally derived sample by ^{13}C NMR spectroscopy. We believed that, of the many isomers of gross structure **68**, compounds **69** and **70** would have the most similar ^{13}C NMR spectra. Like diol **69**, **70** has C_2 symmetry and can show a maximum of 20 ^{13}C NMR resonances. In addition, the stereochemical differences in these two isomers occur only at C-15 and C-18, far away from the functional ends of the chain. By having *both* isomers in hand, we could demonstrate that our method

(24) Kates, M.; Joo, C. N.; Palameta, B.; Shier, T. *Biochemistry* **1967**, *6*, 3329.

of comparison can distinguish between such stereoisomers.

Our first target was diol **69**. The basic synthetic plan was to convert the diol monoether (+)-**61** into a 10-carbon unit, couple two of these units to give a 20-carbon block, and dimerize the latter substance to obtain **69**. Conversion of (+)-**61** to suitably protected and functionalized homologated versions is summarized in Scheme VIII. Tosylation of (+)-**61** affords **71**, which is homologated by Liotta's method,[25] using potassium cyanide and 18-crown-6 in acetonitrile. Reduction of nitrile **72** with diisobutylaluminum hydride affords aldehyde **73**. The carbonyl group is further reduced with lithium aluminum hydride and the resulting primary alcohol **74** is protected as the (2-methoxyethoxy)methyl (MEM) ether (**75**).[26] Removal of the *tert*-butyldimethylsilyl ether gives alcohol **76**, which is transformed into mesylate **77**. Displacement of the mesylate with lithium thiophenoxide affords sulfide **78**, which is oxidized by *m*-chloroperoxybenzoic acid (MCPBA) to obtain sulfone **79**. Mesylation of **74** affords **80**, which is transformed by tetra-*n*-butylammonium iodide in refluxing THF into iodide **81**.

Initial attempts to couple sulfone **79** and iodide **81** produced a surprising result. Treatment of the sulfone with 1.5 equiv of *n*-butyllithium at −20 °C in THF that had not been thoroughly degassed, followed by cooling to −78 °C, addition of iodide **81**, and warming to room temperature, gave none of the expected alkylation product. Instead, alkene **82** was produced in 45% yield (eq 6). A



82

brief investigation of this unusual reaction showed that oxygen is involved and that alkene formation may be suppressed by carrying out the alkylation in rigorously degassed THF.[27] Oxidative coupling of two sulfone anions, mediated by oxygen, could give a bis sulfone. Compounds of this kind are known to undergo reductive elimination with reagents such as sodium amalgam.[28] In the current case, the sulfone anion itself could be the reducing agent (which, in principle, could make the overall reaction catalytic in oxygen).

Even in thoroughly degassed THF, alkylation of the monoanion of sulfone **79** is sluggish. However, the dianion, produced by treatment of **79** with 2 equiv of *n*-butyllithium, reacts with iodide **81** in a mixture of THF and HMPA to give sulfone **83** in 65–85% yield (Scheme IX). Considerable difficulty was experienced in desulfonylation of **83**. After exploring a number of methods, we found that best yields are obtained with a method developed by Danheiser and Bronson, wherein the reduction is accomplished by lithium wire in a mixture of THF and HMPA, with *tert*-butyl alcohol added as a proton source.[29] We modified the Danheiser–Bronson procedure by adding a buffer (Na_2HPO_4) and carried out the reaction in a sonicator bath. Under these conditions, the reduction of **83** is quite reproducible and the yield of alcohol **85**, although not spectacular, is reasonable (45–50%). Mesylate **86** is displaced with tetra-*n*-butylammonium bromide in THF to obtain bromide **87**.

The final bond construction was achieved by oxidation of the Grignard reagent derived from bromide **87** with silver nitrate (eq 7). The best yield we were able to obtain in this oxidative dimerization was 30%, probably because of the very small scale (0.2–0.3 mmol) on which the reaction was carried out. The principal side reaction (30–40%) was simple reduction to the C_{20} ether **89**; about 10% of an alcohol resulting from oxidation of the Grignard reagent was also formed. Removal of the MEM protecting group, which was accomplished by HBr in aqueous methanol,[30] gives the C_{40} diol **69**; similar treatment of ether **89** provides dihydrophytol (**90**).

For the synthesis of isomer **70** we must have stereochemically different C_{10} units. Synthesis of the first began with diol monoether (−)-**61** and is summarized in Scheme X. The free hydroxyl of (−)-**61** is protected as the MEM ether **91**, and the silyl group is then removed to obtain **92**. The derived tosylate **93** is homologated by the Liotta method to give nitrile **94**, which is reduced with diisobutylaluminum hydride to aldehyde **95**. Reduction of the carbonyl group affords alcohol **96**, which is protected as the *tert*-butyldiphenylsilyl ether **97**.[31] Removal of the MEM protecting group again proved troublesome. In this case, the problem was solved by the use of trimethylsilyl iodide, generated in situ from trimethylsilyl chloride and sodium iodide.[32] The resulting alcohol, **98**, is converted into mesylate **99**, which is transformed into iodide **100** by the standard method.

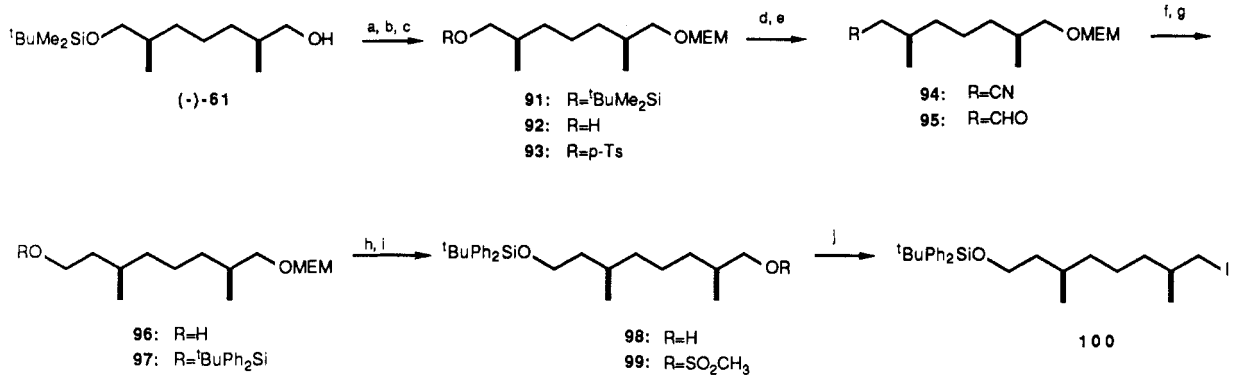
The other essential building block for the synthesis of **70** was prepared from unsaturated acid **58**, as shown in Scheme XI. Saturation of the double bond is accomplished by catalytic hydrogenation over Adams' catalyst. The resulting acid **101** is reduced with lithium aluminum hydride to obtain alcohol **102**, which is converted by the standard method into mesylate **103**. The derived iodide **104** is alkylated with lithiomethyl phenyl sulfone in a mixture of the THF and HMPA to obtain **105**.

As shown in Scheme XII, sulfone **105** and iodide **100** were united to obtain **106**,[33] which was desulfonylated by treatment with sodium amalgam in buffered methanol. The *tert*-butyldimethylsilyl ether may be hydrolyzed by treatment with 0.67% HCl in ethanol at 0 °C; alcohol **108** is obtained in 87% yield. The conditions for this selective hydrolysis are crucial; use of only slightly more concentrated acid, higher reaction temperature, or prolonged reaction time leads to the diol, which is essentially useless for further transformations. Construction of the C_{20} unit is completed by transformation of mesylate **109** into bromide **110**.

As shown in eq 8, coupling was accomplished by oxidation of the Grignard reagent derived from bromide **110** with silver ion; diether **111** is produced in about 40% yield. Once again, the major byproducts are the ether of dihydrophytol and the primary alcohol resulting from oxidation of the Grignard reagent. Synthesis of C_{40} diol

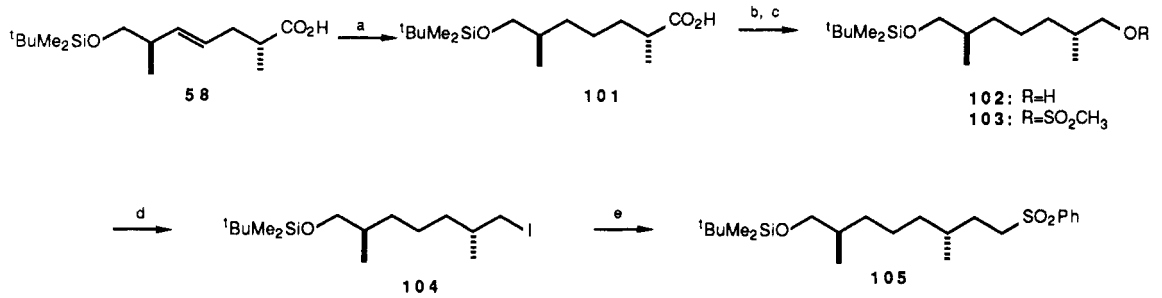
(25) Cook, F. L.; Bowers, C. W.; Liotta, C. L. *J. Org. Chem.* **1974**, *39*, 3416.
(26) Corey, E. J.; Gras, J.-L.; Ulrich, P. *Tetrahedron Lett.* **1974**, 809.
(27) R. L. Danheiser and his co-workers have discovered the same reaction in another system; personal communication.
(28) De Lucchi, O.; Lucchini, V.; Pasquato, L.; Modena, G. *J. Org. Chem.* **1984**, *49*, 596.
(29) R. L. Danheiser, private communication.
(30) A number of other methods that have been reported to be effective for the removal of this often recalcitrant protecting group were examined and found to be less satisfactory than HBr and methanol.
(31) Hanessian, S.; Lavalle, P. *Can. J. Chem.* **1975**, *53*, 2975.
(32) Rigby, J. H.; Wilson, J. Z. *Tetrahedron Lett.* **1984**, *25*, 1429.
(33) Alkylation of a sulfone anion by an isobutyl-type iodide is not straightforward, and the correct reaction conditions for this transformation were found only after extensive development. For a complete description, see: Radel, P. A. Ph.D. Dissertation, University of California, Berkeley, 1986, Chapter 5.

Scheme X[a]

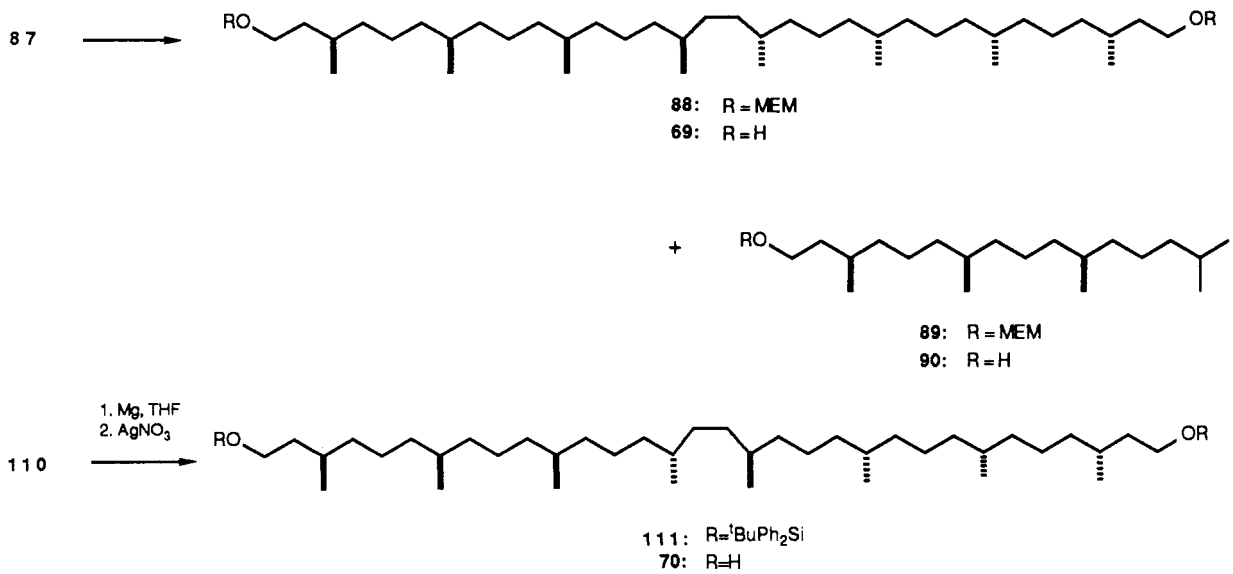


[a] (a) $CH_3OCH_2CH_2OCH_2Cl$, $(i\text{-}Pr)_2NEt$, DMAP, CH_2Cl_2; (b) HF, CH_3CN; (c) *p*-TsCl, C_5H_5N, DMAP, CH_2Cl_2; (d) KCN, 18-crown-6, CH_3CN; (e) Dibal, hexane; (f) $LiAlH_4$, THF; (g) *t*-$BuPh_2SiCl$, Et_3N, DMAP, CH_2Cl_2; (h) Me_3SiCl, NaI; (i) CH_3SO_2Cl, C_5H_6, CH_2Cl_2; (j) $(n\text{-}Bu)_4N^+I^-$, THF.

Scheme XI[a]



[a] (a) H_2, PtO_2, EtOH; (b) $LiAlH_4$, THF; (c) CH_3SO_2Cl, C_5H_5N, CH_2Cl_2; (d) $(n\text{-}BuLi)_4N^+I^-$, THF; (e) $PhSO_2CH_2Li$, THF, HMPA.

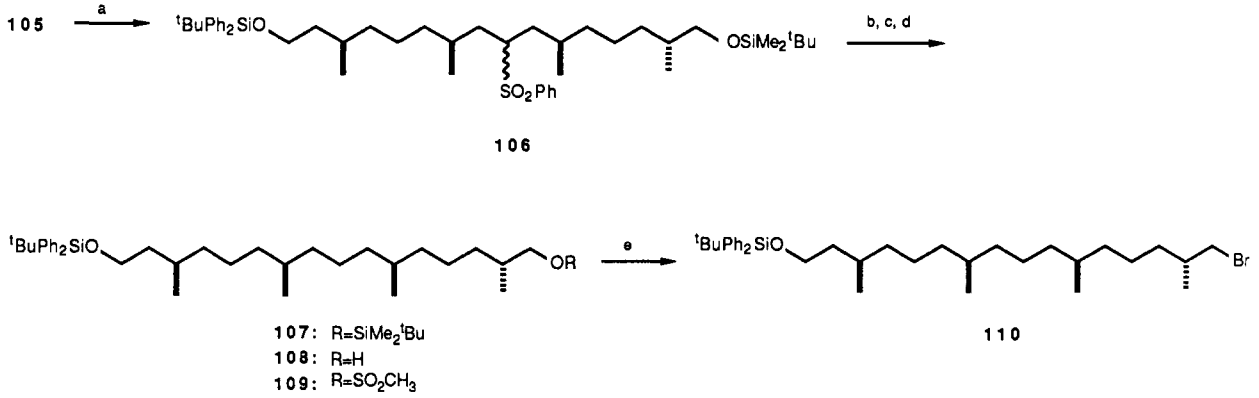


isomer **70** is completed by removal of the *tert*-butyldiphenylsilyl groups; HCl in aqueous THF is employed for this purpose.

Stereochemistry of the Archaebacterial C_{40} Diol. Isomers **69** and **70** were compared with a sample of the naturally derived archaebacterial C_{40} diol by high-field ^{13}C NMR. At 125.76 MHz, using a Bruker WP-500 spectrometer, the spectra of **69** and the natural material were indistinguishable, except for the presence of small signals attributable to minor isomers in the synthetic specimen. Because the C_{10} building block used in the synthesis of **69** was a mixture of stereoisomers (an enantiomeric ratio of 99.3:0.7 in the oxazolidone alkylation and a diastereomeric ratio of 95.5:4.5 in the Claisen rearrangement), the synthetic **69** should be a mixture of diastereomers in the ratio 73.5:9.4:9.4:2.2:2.2, assuming no stereochemical recognition in any of the coupling steps. The major isomer has C_2 symmetry and shows only 20 ^{13}C NMR resonances, whereas the minor isomers lack this symmetry and could show up to 40 resonances.

On the other hand, the spectrum of **70** is clearly different from that of **69** in the chemical shifts of several resonances. The chemical shifts, along with tentative carbon assignments, are presented in Table III. As shown in the table, six resonances differ by at least 0.05 ppm, an amount easily distinguishable at the frequency used. The largest dif-

Scheme XII[a]



[a] (a) i, *n*-BuLi, THF; ii, **110**, HMPA; (b) Na/Hg, MeOH, Na_2HPO_4; (c) 0.67% HCl, THF, 0 °C; (d) CH_3SO_2Cl, C_5H_5N, CH_2Cl_2; (e) $(n\text{-}Bu)_4N^+Br^-$, THF.

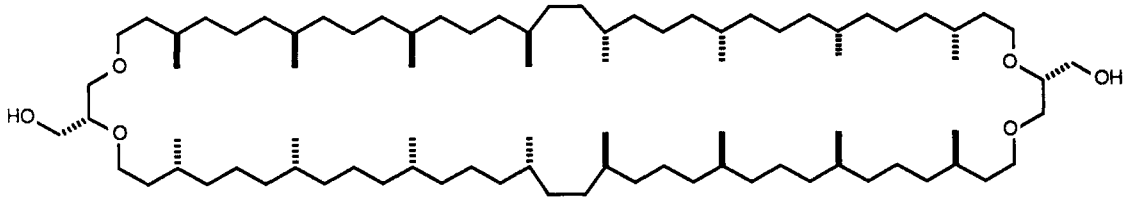


Table III. ^{13}C NMR Chemical Shifts for Diols 69 and 70

C	diol **69**	diol **70**	difference
1	61.268	61.280	−0.01
2	39.944	39.993	−0.05
3	29.494	29.548	−0.05
4	37.403	37.365	0.04
5	24.356	24.377	−0.02
6	37.396	37.392	0.00
7	32.789	32.792	−0.01
8	37.416	37.459	−0.04
9	24.452	24.486	−0.02
10	37.315	37.325	−0.01
11	32.796	32.816	−0.02
12	37.509	37.500	0.01
13	24.473	24.486	0.01
14	37.560	37.500	0.06
15	33.045	33.054	−0.01
16	34.297	34.433	−0.14
C-3 Me	19.680	19.688	−0.01
C-7 Me	19.777	19.775	0.00
C-11 Me	19.797	19.737	0.06
C-15 Me	19.748	19.688	0.06

ferences are found in the resonances of C-14, C-16, and the methyl groups at C-11 and C-15.

Thus, the present syntheses establish the relative stereochemistry of the archaebacterial C_{40} diol to be as in **69**. The synthetic material is found to be dextrorotatory, as is the naturally derived diol. Thus, structure **69** also represents the absolute configuration of the compound. Since the absolute configuration of the glycerol stereocenters has been previously established,[34] the full stereostructure of the archaebacterial lipid is shown to be **112**.

Experimental Section

General. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Ether and tetrahydrofuran (THF) were distilled from sodium/benzophenone immediately prior to use. Methylene chloride was distilled from phosphorus pentoxide. Hexane was distilled at atmospheric pressure. Ethanol and methanol were distilled from magnesium metal. Triethylamine (TEA), pyridine, hexamethylphosphoric triamide (HMPA), diisopropylamine, and diisopropylethylamine were distilled from calcium hydride. *tert*-Butyldimethylsilyl chloride was distilled at reduced pressure. All reactions were conducted under a nitrogen atmosphere unless otherwise indicated. Boiling points and melting points (Pyrex capillary) are uncorrected. All ^1H NMR spectra were recorded with $CDCl_3$ as solvent unless otherwise noted. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Significant ^1H NMR data are tabulated in order: multiplicity (s, singlet; d, doublet; t, triplet, q, quartet; m, multiplet), number of protons, coupling constant(s) in hertz. ^{13}C NMR spectra were measured at 62.89 MHz, 75.47 MHz, or 125 MHz. Minor diastereomers are indicated in parentheses. ^{19}F NMR spectra were measured at 235 MHz. Mass spectra data are tabulated as m/z (intensity expressed as percent of total ion current). Optical rotations were recorded with chloroform as solvent. Flash chromatography refers to the procedure of Still.[35] Elemental analyses were performed by the Microanalytical Laboratory, operated by the College of Chemistry, University of California, Berkeley, CA.

General Procedure for Aldol Reactions with Ketone 5: (4*R,5*R**)-5-Hydroxy-2,4,6-trimethyl-2-[(trimethylsilyl)oxy]-6-hepten-3-one (12).** To a stirring solution of 42 mL (30.26 g, 0.30 mol) of diisopropylamine in 300 mL of dry THF at 0 °C, under a nitrogen atmosphere, was added 166 mL (0.27 mol) of a 1.63 M solution of *n*-butyllithium in hexane. This solution was cooled further to −78 °C and then stirred as 48.28 g (0.256 mol) of 2-methyl-2-[(trimethylsilyl)oxy]-3-pentanone (**5**)[5] was added over a period of 10 min. The resulting solution was stirred for 25 min and 29.3 mL (24.53 g, 0.35 mol) of methacrolein was added all at once, followed by 450 mL of saturated aqueous NH_4Cl. After being warmed to room temperature, the mixture was partitioned between 150 mL of ether and 100 mL of water. The layers were separated and the aqueous layer was washed with three 200-mL portions of ether. The combined ether fractions were washed once with 1% aqueous HCl, dried ($MgSO_4$), and filtered. The filtrate was concentrated on a rotary evaporator to give 66.11 g (100%) of pure **12**. NMR and TLC showed no impurities to be present

(34) Kushwaha, S. C.; Kates, M.; Sprott, G. D.; Smith, I. C. P. *Biochim. Biophys. Acta* **1981**, *664*, 156.

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

and no further purification was attempted. IR (film): 3600–3300 (br), 2970 (s), 2870 (m), 1710 (s), 1450 (m), 1375 (m), 1250 (s) cm^{-1}. ^1H NMR: δ 0.19 (s, 9), 1.04 (d, 3, J = 7), 1.38 (s, 6), 1.73 (s, 3), 3.1 (br s, 1), 3.61 (m, 1), 4.36 (d, 1, J = 3), 4.98 (s, 1), 5.15 (s, 1). Anal. Calcd for $C_{13}H_{26}O_3Si$: C, 60.43; H, 10.14. Found: C, 60.80; H, 10.31.

(4*R,5*S**)-5-Hydroxy-2,4-dimethyl-2-[(trimethylsilyl)oxy]-6-hepten-3-one (10).** This compound was prepared from acrolein by the foregoing procedure in 72% yield on a 10.6-mmol scale. IR (film): 3450, 2970, 1710 cm^{-1}. ^1H NMR: δ 0.22 (s, 9), 1.12 (d, 3, J = 7), 1.38 (s, 3), 1.39 (s, 3), 3.08 (d, 1, J = 2), 3.47 (dq, 1, J = 4, 7), 4.37 (m, 1), 5.17 (dt, 1, J = 2, 11), 5.29 (dt, 1, J = 2, 17), 5.79 (ddd, 1, J = 4, 11, 17). ^{13}C NMR: δ 2.1, 11.5, 27.0, 27.4, 44.0, 72.8, 115.2, 138.2, 218.3. Anal. Calcd for $C_{12}H_{24}O_3Si$: C, 58.97; H, 9.90. Found: C, 58.98; H, 10.17.

(*E*,4*R,5*S**)-5-Hydroxy-2,4-dimethyl-2-[(trimethylsilyl)oxy]-6-octen-3-one (11).** This compound was prepared from crotonaldehyde by the foregoing procedure in 97% yield on a 48.6-mmol scale. IR (film) 3550, 1710 cm^{-1}. ^1H NMR: δ 0.20 (s, 9), 1.10 (d, 3, J = 8), 1.37 (s, 3), 1.38 (s, 3), 1.73 (d, 3, J = 8), 3.42 (dq, 1, J = 8, 3), 4.28 (m, 1), 5.43 (dd, 1, J = 17, 7), 5.68 (dq, 1, J = 17, 8). ^{13}C NMR: δ 2.0, 12.0, 17.2, 26.8, 27.2, 44.4, 72.9, 80.3, 126.7, 131.5, 217.8. Anal. Calcd for $C_{13}H_{26}O_3Si$: C, 60.40; H, 10.16. Found: C, 60.38; H, 10.17.

General Procedure for Aldol Reactions with Ester 6: 2′,6′-Di-*tert*-butyl-4-methylphenyl (2*S,3*R**)-3-Hydroxy-2,4-dimethyl-4-pentenoate (15).** To 30.3 mL of 1.51 M *n*-butyllithium (45.7 mmol) in hexane and 42 mL of THF was added 7.00 mL (50.0 mmol) of diisopropylamine. The LDA solution was cooled to −78 °C and 11.49 g (41.6 mmol) of BHT propionate[6] in 9 mL of THF was added. A precipitate was observed within a few minutes. After 30 min more at −78 °C, 6.0 mL (72.7 mmol) of freshly distilled methacrolein ($CaSO_4$) was added over a 2-min period. After 20 min more at −78 °C, 15 mL of saturated NH_4Cl was added all at once. The product was isolated by ether extraction, giving 14.36 g of crude product. Pentane crystallization gave 11.3 g of crystalline **15** and 3.0 g of oil which was chromatographed to give 1.40 g of **15**, one isomer by ^{13}C NMR. Thus, 12.7 g (88%) of **15** was obtained by a combination of chromatography and crystallization. Recrystallization from hexane gave analytically pure **15**, mp 70–71 °C. IR (KBr): 3440, 1705 cm^{-1}. ^1H NMR: δ 1.33 (s, 9), 1.34 (s, 9), 1.79 (s, 3), 2.32 (s, 3), 2.86 (quintet, 1, J = 7), 4.30 (d, 1, J = 7), 5.01 (d, 2, J = 6), 7.14 (m, 2). ^{13}C NMR: δ 13.4, 16.2, 21.3, 31.3, 31.4, 35.0, 43.6, 77.7, 114.9, 126.8, 127.1, 134.6, 141.67, 141.73, 143.3, 145.7, 176.4 (229 mg/0.77 mL). Anal. Calcd for $C_{22}H_{34}O_3$: C, 76.26; H, 9.86. Found: C, 76.19; H, 10.02.

2′,6′-Di-*tert*-butyl-4-methylphenyl (2*S,3*S**)-3-Hydroxy-2-methyl-4-pentenoate (13).** This compound was prepared from acrolein by the foregoing procedure on a 1.46-mmol scale. The crude aldol was obtained in 88% yield as a 6:1 mixture of diastereomers. Crystallization from hexane gave a solid, mp 63–65 °C, shown by ^{13}C NMR spectroscopy to be a 20:1 mixture. IR (film): 3500, 2900, 1720 cm^{-1}. ^1H NMR: δ 1.32 (s, 9), 1.33 (s, 9), 1.46 (d, 3, J = 7.5), 2.32 (s, 3), 2.85 (quintet, 1, J = 7), 3.71 (d, 1, J = 3), 4.36 (m, 1), 5.25 (m, 1), 5.36 (m, 1), 5.92 (ddd, 1, J = 7, 10, 17), 7.13 (m, 2). ^{13}C NMR (taken with 6:1 mixture, minor isomer peaks shown in parentheses): δ 12.8 (10.0), 21.2, 31.2, 31.3, 34.9, 35.0, 45.8 (45.1), 73.8 (71.6), 117.1 (115.9), 126.7, 126.9, 134.4 (134.0), 137.3, 141.6, 145.6, 175.3. Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.87; H, 9.69. Found: C, 75.66; H, 9.61.

2′,6′-Di-*tert*-butyl-4-methylphenyl (*E*,2*S,3*S**)-3-Hydroxy-2-methyl-4-hexenoate (14).** This compound was prepared by the foregoing procedure from crotonaldehyde on a 7.23-mmol scale in 81% yield. The crude product, mp 78–79 °C, was shown by ^{13}C NMR to be a 9:1 mixture of diastereomers. IR (film): 3550, 1725 cm^{-1}. ^1H NMR: δ 1.32 (s, 9), 1.33 (s, 9), 1.43 (d, 3, J = 7), 1.73 (dd, 3, J = 6, 1), 2.32 (s, 3), 2.83 (m, 1), 4.30 (m, 1), 5.52 (dd, 1, J = 17, 7), 5.79 (dq, 1, J = 17, 6), 7.12 (s, 3). ^{13}C NMR: δ (10.3), 13.1, 17.5, 21.3, 31.5, 35.2, 46.3, (72.0), 74.0, 126.9, 127.1, 128.9, 130.9, 134.5, 142.0, 145.9, 175.6. Anal. Calcd for $C_{22}H_{34}O_3$: C, 76.24; H, 9.91. Found: C, 76.06; H, 10.21.

General Procedure for Periodic Acid Cleavage of Aldols 10–12: (2*R,3*S**)-3-Hydroxy-2-methyl-4-pentenoic Acid (16).** To 5.00 g (20.5 mmol) of aldol **10** in 5 mL of THF was added at 0 °C 5.61 g (24.6 mmol) of H_5IO_6 in 70 mL of THF (distilled). After 10 min, the cooling bath was removed. Stirring was continued for 1 h and 20 min. Ether (100 mL) was added and the mixture was filtered. The filter paper was rinsed with 100 mL of ether. The combined filtrates were stirred for 10 min with a slurry of 25 g of $NaHSO_3$ in 30 mL of water. The initial brown color went to light yellow. Layers were separated and the slurry was extracted with 100 mL more of ether. Upon evaporation, the combined organic layers yielded 2.88 g (100%) of **16** as an oil. This was used as such in an $LiAlH_4$ reduction. IR (film): 3500–2500, 1780–1680 cm^{-1}. ^1H NMR: δ 1.15 (d, 3, J = 7), 2.68 (dq, 1, J = 4, 7), 4.42 (m, 1), 5.05–5.30 (m, 2), 5.70 (ddd, 1, J = 2, 11, 7).

(*E*,2*R,3*S**)-3-Hydroxy-2-methyl-4-hexenoic Acid (17).** Aldol **11** was cleaved according to the foregoing procedure on a 48.6-mmol scale to obtain β-hydroxy acid **17**. IR (film) 3400, 1710 cm^{-1}. ^1H NMR: δ 1.10 (d, 3, J = 8), 1.70 (d, 3, J = 8), 4.37 (m, 1), 5.50 (dd, J = 17, 7), 5.75 (dq, J = 17, 8).

(2*R,3*R**)-3-Hydroxy-2,4-dimethyl-4-pentenoic Acid (18).** Aldol **12** was cleaved according to the foregoing procedure on a 15.4-mmol scale to obtain β-hydroxy acid **18**. IR (film): 3700–3200 (br), 3050–2800 (br), 1725 (s), 1460 (m), 1215 (br) cm^{-1}. ^1H NMR: δ 1.33 (d, 3, J = 7), 1.61 (s, 3), 2.56 (m, 1), 4.29 (d, 1, J = 4), 4.77 (s, 1), 4.89 (s, 1).

General Procedure for $LiAlH_4$ Reduction of β-Hydroxy Acids 16–18. (*E*,2*S,3*S**)-2-Methyl-4-hexene-1,3-diol (20).** The crude acid **17** was dissolved in 75 mL of THF and added to a solution of 2.84 g (75.0 mmol) of $LiAlH_4$ in 75 mL of THF over a 15-min period. The reaction mixture was heated at reflux for 2.5 h, cooled to 0 °C, and quenched by the addition of 2.8 mL of water, 2.8 mL of 15% aqueous NaOH, and 8.5 mL of water. The aluminum salts were removed by filtration and washed with 100 mL of ethyl acetate. The organic layer was separated and dried ($MgSO_4$) and the solvent was removed with a rotary evaporator. The residue was purified by flash chromatography (125 g of silica gel, 60% ether/hexane as eluant) to obtain 3.37 g (25.9 mmol, 53% overall from aldol **11**) of **20** as a colorless oil. IR (film): 3350 cm^{-1}. ^1H NMR: δ 0.91 (d, 3, J = 8), 1.57 (d, 3, J = 6), 3.48 (br s, 2), 5.41 (dd, J = 15, 6), 5.64 (dd, J = 15, 6). Anal. Calcd for $C_7H_{14}O_2$: C, 64.56; H, 10.86. Found: C, 64.62; H, 10.85.

(2*S,3*S**)-2-Methyl-4-pentene-1,3-diol (19).** Crude **16** (2.88 g, 22 mmol) was reduced in the foregoing manner to obtain diol **19** in 82% overall yield from aldol **10**: IR (film) 3500–3200 cm^{-1}. ^1H NMR: δ 0.85 (d, 3, J = 7), 1.90 (m, 1), 3.7–3.9 (m, 2), 4.40 (m, 1), 5.25–5.50 (m, 2), 6.00 (ddd, 1, J = 4, 11, 17).

(2*S*,3*S*)-2-Methyl-4-pentene-1,3-diol (19). Reduction of scalemic acid **38** provided diol **19**, 95% on a 2.95-mmol scale: $[\alpha]_D$ −27.9° (*c* 0.027, CH_2Cl_2); the ^1H NMR spectrum was identical with that of the racemic diol. ^{13}C NMR: δ 11.63, 40.01, 66.28, 78.02, 115.94, 138.79. Anal. Calcd for $C_6H_{12}O_2$: C, 62.04; H, 10.41. Found: C, 61.83; H, 10.44.

(2*S,3*R**)-2,4-Dimethyl-4-pentene-1,3-diol (21).** β-Hydroxy acid **18** was reduced by the foregoing procedure to obtain diol **21** in 74% overall yield from aldol **12**: IR (film) 3350 cm^{-1}. ^1H NMR: δ 0.75 (d, 3, J = 7), 1.70 (s, 3), 1.7–1.8 (m, 1), 2.40 (br s, 1), 3.60–3.70 (m, 2), 4.17 (m, 1), 4.90 (d, 2, J = 11).

General Procedure for $LiAlH_4$ Reduction of β-Hydroxy Esters 13–15: (2*R,3*S**)-2-Methyl-4-pentene-1,3-diol (22).** To a stirring solution of 15.7 g (0.41 mol) of $LiAlH_4$ in 750 mL of THF (mechanical stirrer) was added 47.98 g (0.144 mol) of **13** (6:1 mixture of diastereomers) in 100 mL of THF. The mixture was refluxed for 4 h and 50 mL of ethyl acetate was added. After the conventional Fieser and Fieser workup, the solids were removed by filtration and washed with 500 mL of ether. Evaporation of the combined filtrates gave 50 g of crude product. This material was percolated through silica gel, eluting first with hexane (BHT collected) and then with ether (**22** collected). The ether fractions yielded 14.0 g (83%) of **22** as a 6:1 mixture of diastereomers. This material contained minor impurities and was used as such. IR (film): 3200–3450 cm^{-1}. ^1H NMR (minor isomer in parentheses): δ 0.86 (d, 3, J = 7), 1.82 (m, 1), 2.89 (br, 2), 3.59–3.80 (m, 2), 4.05 (t, 1, J = 7), 5.16–5.32 (m, 2), 5.87 (ddd, 1, J = 7, 10, 17). ^{13}C NMR: δ 13.0 (10.8), 39.9 (39.7), 66.2 (65.2), 77.5 (74.6), 115.5 (114.9), 139.4 (138.5).

(*E*,2*R,3*S**)-2-Methyl-4-hexene-1,3-diol (23).** A similar reduction of β-hydroxy ester **14** (1.81-mmol scale) provided diol **23** (colorless oil, 73%). IR (film): 3325 cm^{-1}. ^1H NMR: δ 0.81

(d, 3, J = 7), 1.72 (dd, 3, J = 6, 1), 3.64 (m, 2), 3.95 (m, 1), 5.48 (dd, 1, J = 17, 7), 5.67 (dq, 1, J = 17, 6). Mass spectrum: m/z (relative intensity) 130 (0.13), 115 (0.34), 112 (1.87), 97 (2.29), 94 (0.68), 71 (31.42). HRMS calcd for $C_7H_{14}O_2$: 130.0994, found 130.0990.

(2*R,3*R**)-2,4-Dimethyl-4-pentene-1,3-diol (24).** Reduction of β-hydroxy ester **15** by the foregoing procedure on a 32.2-mmol scale afforded diol **24** (colorless oil, 75%). IR: 3350 cm^{-1}. ^1H NMR: δ 0.75 (d, 3, J = 7), 1.71 (s, 3), 1.81 (m, 1), 3.60–3.70 (m, 2), 3.91 (m, 1), 4.60–4.67 (m, 1), 4.88 (d, 2, J = 11, or two s). ^{13}C NMR: δ 13.3, 16.4, 36.6, 66.9, 81.6, 112.8, 145.5.

General Procedure for Preparation of Diol Monoethers 25–30: (*E*,2*S,3*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-hexen-3-ol (26).** To a solution of 1.113 g (8.55 mmol) of diol **20** and 0.42 (3.42 mmol) of 4-(dimethylamino)pyridine (DMAP) in 13 mL of CH_2Cl_2 was added 1.42 g (9.41 mmol) of *tert*-butyldimethylsilyl chloride. After 5 min 1.31 mL (9.50 g, 9.41 mmol) of triethylamine was added dropwise over a 5-min period. After 5 h 100 mL of ether was added. The organic phase was washed with cold 5% HCl (2 × 15 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (60 g of silica gel, 8% ether in hexanes as eluant) to give 1.45 g (5.93 mmol, 69%) of **26** as a colorless oil. IR (film): 3450 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.90 (s, 9), 1.72 (d, 3, J = 6), 3.66 (m, 2), 4.18 (m, 1), 5.54 (dd, 1, J = 15, 5), 5.68 (dq, J = 15, 6). ^{13}C NMR: δ −5.7, 11.2, 17.5, 18.0, 25.7, 40.3, 66.7, 67.3, 126.2, 132.0. Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 63.86; H, 11.57. Found: C, 63.77; H, 11.36.

The following monoethers were prepared from the corresponding diols by essentially the foregoing procedure.

(2*S,3*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-penten-3-ol (25).** IR (film): 3500 cm^{-1}. ^1H NMR: δ 0.07 (s, 6), 0.86 (d, 3, J = 7), 0.90 (s, 9), 1.94 (m, 1), 3.33 (d, 1, J = 5), 3.64–3.74 (m, 2), 4.27 (m, 1), 5.18 (dd, 1, J = 1, 11), 5.29 (dd, 1, J = 1, 17), 5.88 (ddd, 1, J = 5, 11, 17). Anal. Calcd for $C_{12}H_{26}O_2Si$: C, 62.49; H, 11.37. Found: C, 62.37; H, 11.15.

(2*R*,3*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-penten-3-ol (25). Scalemic diol **19** gave **25**, $[\alpha]_D$ +11.8° (*c* 0.77). The IR and NMR spectra were identical with those of the racemic monoether. Anal. Calcd for $C_{12}H_{26}O_2Si$: C, 62.54; H, 11.37. Found: C, 62.46; H, 11.37.

(2*S*,3*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-penten-3-ol (25). Similar treatment of the 2*S*,3*S* diol provided monoether **25**, $[\alpha]_D$ −13.65° (*c* 0.107, CH_2Cl_2). The IR and ^1H NMR spectra were identical with those of the 2*S**,3*S** and 2*R*,3*R* isomers. ^{13}C NMR: δ −5.68, 11.05, 18.07, 25.78, 39.44, 67.12, 75.56, 114.91, 138.54. Anal. Calcd for $C_{12}H_{26}O_2Si$: C, 62.55; H, 11.37. Found: C, 62.42; H, 11.26.

(2*S,3*R**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2,4-dimethyl-4-penten-3-ol (27).** IR (film): 3420 cm^{-1}. ^1H NMR: δ 0.03 (s, 6), 0.82 (d, 3, J = 7), 0.87 (s, 9), 1.65 (s, 3), 1.79 (m, 1), 2.98 (d, 1, J = 3), 3.66 (m, 2), 4.19 (m, 1), 4.85 (s, 1), 4.98 (s, 1). ^{13}C NMR: δ −5.7, 9.6, 18.1, 19.3, 25.8, 37.1, 67.5, 76.6, 110.3, 345.5.

(2*R,3*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-penten-3-ol (28).** This compound was prepared as an intermediate in the preparation of propionate **54**.

(*E*,2*R,3*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-hexen-3-ol (29).** IR (film): 3450 cm^{-1}. ^1H NMR: δ 0.07 (s, 6), 0.90 (s, 9), 1.72 (d, 3, J = 6), 3.66 (m, 2), 4.18 (m, 1), 5.54 (dd, 1, J = 15, 5), 5.68 (dq, 1, J = 15, 6). ^{13}C NMR: δ −5.7, 11.2, 17.5, 26.7, 40.3, 66.7, 75.0, 126.2, 132.0. Anal. Calcd for $C_{13}H_{18}O_2Si$: C, 63.86; H, 11.57. Found: C, 63.77; H, 11.36.

(2*R,3*R**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2,4-dimethyl-4-penten-3-ol (30).** The usual conditions (1–2% DMAP) gave only mixtures and an incomplete reaction. A mixture of 1.0 g (7.7 mmol) of **24**, 1.27 g (8.4 mmol) of *tert*-butyldimethylsilyl chloride, 1.17 mL (8.4 mmol) of Et_3N, 280 mg (2.3 mmol) of DMAP, and 7 mL of CH_2Cl_2 was stirred at room temperature for 105 min. Normal workup gave 1.90 g (100%) of **30** as an oil. ^1H NMR: δ 0.04 (s, 6), 0.80 (d, 3, J = 7), 0.90 (s, 9), 1.75 (s, 3), 1.90 (m, 1), 3.60–4.05 (m, 3), 4.90 (m, 2).

General Procedure for the Preparation of Trityl Ethers 31 and 32. (*E*,2*S,3*S**)-2-Methyl-1-(triphenylmethoxy)-4-hexen-3-ol (31).** To a solution of 247 mg (1.90 mmol) of **20** in 4 mL of CH_2Cl_2 at 0 °C was added 0.40 mL (0.29 g, 2.85 mmol) of triethylamine followed by 582 mg (2.09 mmol) of triphenylmethyl chloride (added in four portions). After addition of 5 mg of DMAP, the reaction mixture was allowed to warm to room temperature. After 2.5 h, the reaction mixture (now heterogeneous) was taken up in 25 mL of CH_2Cl_2 and the organic layer washed with cold 5% HCl (10 mL). After drying (Na_2SO_4), the solvent was removed with a rotary evaporator and the remaining viscous oil was purified by flash chromatography (40 g of silica gel, 5% ether in hexanes eluant) to obtain 535.3 mg (1.44 mmol, 76%) of **31** as a very viscous oil. IR (film): 3425, 1600 cm^{-1}. ^1H NMR: δ 0.93 (d, 3, J = 7), 1.64 (d, 3, J = 6), 2.01 (m, 1), 3.10 (m, 2), 4.26 (dd, 1, J = 6, 4), 5.27 (dd, 1, J = 17, 6), 5.60 (dq, 1, J = 17, 6). An analytical sample was prepared by bulb-to-bulb distillation (oven temperature 140 °C, 0.05 Torr). Anal. Calcd for $C_{26}H_{28}O_2$: C, 83.92; H, 7.59. Found: C, 83.77; H, 7.58.

(*E*,2*R,3*S**)-2-Methyl-1-(triphenylmethoxy)-4-hexen-3-ol (32).** Diol **23** was treated similarly to obtain ether **32** as a viscous oil (74% on a 0.48-mmol scale). IR (film): 3450, 1605 cm^{-1}. ^1H NMR: δ 0.86 (d, 3, J = 7), 1.64 (d, 3, J = 6), 3.47 (m, 2), 3.96 (m, 1), 5.38 (dd, 1, J = 17, 7), 5.60 (dq, 1, J = 17, 7), 7.20–7.45 (m, 15). Anal. Calcd for $C_{26}H_{28}O_2$: C, 83.82; H, 7.59. Found: C, 83.89; H, 7.61.

(2′*S*,3′*R*,4*S*)-3-(3′-Hydroxy-2′-methyl-1′-oxo-4′-pentenyl)-4-(methylethyl)-2-oxazolidone (34). To a solution of 25.0 g (135 mmol) of **33**[9] in 275 mL of CH_2Cl_2 at 0 °C was added 45.5 g (166 mmol) of di-*n*-butylboron triflate and 30.6 mL (22.7 g, 175 mmol) of diisopropylethylamine. After 45 min at 0 °C the solution was cooled to −78 °C and 13.5 mL (11.3 g, 202 mmol) of freshly distilled acrolein was added over 2 min. After 30 min at −78 °C the reaction mixture was allowed to warm to room temperature and kept at this temperature for 90 min. The mixture was poured into 300 mL of pH 7 buffer and 400 mL of ether was added. The layers were separated and the aqueous layer was extracted with ether (2 × 300 mL). The combined organic layers were washed with brine (200 mL) and the solvent was removed with a rotary evaporator. The residue was dissolved in 400 mL of methanol and cooled to 0 °C and 135 mL of 30% H_2O_2 was added dropwise over a 30-min period. After 60 min at 0 °C, 400 mL of water was added and the methanol was removed with a rotary evaporator. The aqueous layer was extracted with ether (3 × 300 mL). The combined organic layers were washed with cold 5% HCl (50 mL), saturated aqueous $NaHCO_3$ (100 mL), and brine (100 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator to obtain 32.5 g (135 mmol, 100%) of **34** as a viscous colorless oil. This material contained a small amount of imide **33**, but it was used in subsequent steps without further purification. An analytical sample was obtained by flash chromatography (45% ether in hexanes as eluant). IR (film): 3500, 1775, 1685 cm^{-1}. ^1H NMR: δ 0.88 (d, 3, J = 7), 0.93 (d, 3, J = 7), 1.22 (d, 3, J = 6), 2.37 (m, 1), 3.87 (m, 1), 4.27 (m, 2), 4.50 (m, 2), 5.21 (dd, 1, J = 11, 1), 5.35 (dd, 1, J = 17, 1), 5.86 (m, 1). ^{13}C NMR: δ 11.2, 14.5, 17.7, 28.2, 42.3, 58.1, 63.2, 72.2, 115.8, 137.3, 153.5, 176.5. $[\alpha]_D$ +88.0° (*c* 1.02). Anal. Calcd for $C_{12}H_{19}NO_4$: C, 59.72; H, 7.95; N, 5.81. Found: C, 59.52; H, 7.85; N, 5.68.

(2*S*,3*R*)-3-Hydroxy-2-methyl-4-pentenoic Acid (35) and (2*R*,3*R*)-2-Methyl-4-pentene-1,3-diol (19). To a solution of 11.74 g (48.73 mmol) of **34** in 100 mL of methanol at 0 °C was added 100 mL of 2 N KOH over 10 min. After 45 min at 0 °C the methanol was removed with a rotary evaporator. The aqueous phase was washed with CH_2Cl_2 (3 × 40 mL) and acidified to pH 2 with 2 N HCl at 0 °C. Solid Na_2SO_4 was added to the aqueous solution, and it was extracted with ethyl acetate (4 × 50 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator to give crude acid **35**. IR (film): 3400, 1710 cm^{-1}. ^1H NMR: δ 1.20 (d, 3, J = 7), 2.70 (dq, 1, J = 7, 4), 4.48 (m, 1), 5.24 (dd, 1, J = 11, 1), 5.34 (dd, 1, J = 17, 1), 5.87 (m, 1).

A solution of the foregoing crude acid in 100 mL of ether was added dropwise to a stirring (mechanical) slurry of 2.73 g (73 mmol) of $LiAlH_4$ in 250 mL of ether. After 12 h, 2.7 mL of water, 2.7 mL of 15% aqueous NaOH and 8.2 mL of water were added, and the mixture was refluxed for 1 h, dried ($MgSO_4$), and filtered. The aluminum salts were extracted with 150 mL of THF and the combined organic layers were concentrated with a rotary evaporator. The residue was purified by flash chromatography (100 g of silica gel, 60% ether in hexanes as eluant) to give 3.05 g (2.63 mmol, 54%) of **19** as a colorless oil. IR (film): 3350 cm^{-1}. ^1H NMR: δ 0.88 (d, 3, J = 7), 1.98 (dq, J = 7, 4), 3.69 (m, 2), 4.33

(m, 1), 5.22 (dd, 1, J = 9, 1), 5.30 (dd, 1, J = 18, 1), 5.93 (m, 1). $[\alpha]_D$ +22.5° (c 1.00). Anal. Calcd for $C_6H_{12}O_2$: C, 62.04; H, 10.41. Found: C, 61.83; H, 10.44.

(2′*R*,3′*S*,4*R*,5*S*)-3-(3′-Hydroxy-2′-methyl-1′-oxo-5′-pentenyl)-4-methyl-5-phenyl-2-oxazolidone (37). A 25-mL round-bottomed flask was charged with 0.499 g of imide **36** (2.14 mmol) in 5 mL of CH_2Cl_2 and cooled to 0 °C. Di-*n*-butylboron triflate (0.677 g, 2.99 mmol, 1.4 equiv) was added dropwise to the solution, followed by 0.331 g of diisopropylethylamine (2.57 mmol, 1.2 equiv). The yellow solution was stirred at 0 °C for 45 min to ensure complete enolization. After cooling to −78 °C, 0.302 g of acrolein (5.39 mmol, 2.52 equiv) in 1 mL of CH_2Cl_2 was added slowly with a syringe pump over a 1-h period. An additional 0.100 g of acrolein (1.79 mmol, 0.84 equiv) was added rapidly. After 10 min, the reaction mixture was allowed to warm to room temperature for a 1.5-h period. Reaction was quenched by addition of pH 7 phosphate buffer followed by 4.0 mL of 30% aqueous hydrogen peroxide solution at 0 °C. After 1 h, the reaction mixture was extracted three times with CH_2Cl_2. The organic layers were dried and concentrated to a yellow oil. Chromatography on 30 g of silica gel, eluting with a gradient system of ether/hexane (1:9 to 1:1), yielded 0.492 g of aldol **37** (80%) and 10% of imide **36**. IR (film): 3540, 3060, 3025, 2970, 2930, 2560, 1770, 1680, 1340, 1240, 1190 cm^{-1}. $[\alpha]_D$ +77.8° (c 0.095, CH_2Cl_2). ^{1}H NMR: δ 0.89 (d, 3, J = 7), 1.23 (d, 3, J = 7), 3.14 (br s, 1), 3.90 (m, 1), 4.50 (m, 1), 4.80 (m, 1), 5.27 (m, 2), 5.69 (d, 1, J = 7), 5.88 (m, 1), 7.34 (m, 5). ^{13}C NMR: δ 10.7, 14.2, 42.5, 54.7, 72.6, 78.8, 115.9, 125.4, 128.5, 128.6, 132.9, 137.4, 152.6, 175.9. Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.61; N, 4.84. Found: C, 66.25; H, 6.64; N, 4.73.

(2*R*,3*S*)-3-Hydroxy-2-methyl-4-pentenoic Acid (38). A 10-mL flask was charged with 0.485 g (1.68 mmol) of aldol **37** in 3 mL of methanol and cooled to 0 °C. Aqueous KOH (3.36 mL, 6.71 mmol, 4 equiv, 2 N) was added slowly and the mixture was stirred for a 45-min period. After removal of methanol at 0 °C (reduced pressure), the reaction mixture was extracted twice with ether. The aqueous layer was neutralized while cold to the methyl orange endpoint (aqueous HCl). The aqueous solution was extracted with two portions of ether, which were combined, dried ($MgSO_4$), and concentrated to obtain a residue. This material was chromatographed on 16 g of silica gel with 1:1 ether/hexane to obtain 0.168 g of hydroxy acid **38** (77%). IR (film): 3300, 2950, 1705, 1450, 1400, 1260, 1100, 1020 cm^{-1}. $[\alpha]_D$ −2.01° (c 0.200, CH_2Cl_2). ^{1}H NMR: δ 1.20 (d, 3, J = 8), 2.69 (m, 1), 3.50 (q, 1, J = 7), 4.48 (m, 1), 5.30 (m, 2), 5.86 (m, 1), 7.00 (br s, 2). ^{13}C NMR: δ 10.81, 44.35, 73.03, 116.79, 136.74, 180.31.

Ethyl (*E*,3*R,6*R**)-3,6,8-Trimethyl-8-[(trimethylsilyl)oxy]-7-oxo-4-nonenoate (39).** To a solution of 203.4 mg (0.79 mmol) of aldol **11** in 1.5 mL of triethyl orthoacetate was added one drop of pivalic acid. The reaction mixture was heated at 135 °C for 1.5 h while removing ethanol by distillation. After cooling, the mixture was mixed with 25 mL of ether and the organic layer was washed with saturated $NaHCO_3$ (10 mL) and brine (10 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (5 g of silica gel, 5% ether in hexanes as eluant) to obtain 102.8 mg (40%) of **39** as a colorless oil. IR (film): 1735, 1720 cm^{-1}. ^{1}H NMR: δ 0.15 (s, 9), 1.00 (d, 3, J = 7), 1.10 (d, 3, J = 7), 1.23 (t, 3, J = 7), 1.31 (s, 6), 2.24 (m, 2), 3.92 (dq, 1, J = 8, 3), 4.10 (q, 2, J = 7), 5.45 (m, 2). ^{13}C NMR: δ 2.2, 14.1, 15.4, 17.9, 19.9, 33.5, 41.6, 42.6, 60.0, 65.7, 80.2, 129.4, 135.1, 172.1, 215.4. Anal. Calcd for $C_{17}H_{32}O_4Si$: C, 62.14; H, 9.84. Found: C, 61.81; H, 9.61.

(*E*,3*R,6*R**)-7-[(*tert*-Butyldimethylsilyl)oxy]-3,6-dimethyl-4-heptenoic Acid, Dimethylamide (40).** To a solution of 1.45 g (5.93 mmol) of **26** in 10 mL of *o*-xylene was added 1.59 g (12 mmol) of (1,1-dimethoxyethyl)dimethylamine. The solution was heated at 140 °C for 1.5 h while removing methanol by distillation. After cooling, the solvent was removed with a rotary evaporator and a vacuum pump (0.1 Torr) to give a yellow oil. This oil was purified by passage through a plug of silica gel (40% ether in hexanes as eluant) to give 1.78 g (96%) of **40** as a colorless oil. IR (film): 1645 cm^{-1}. ^{1}H NMR: δ 0.01 (s, 6), 0.87 (s, 9), 0.93 (d, 3, J = 7), 1.02 (d, 3, J = 7), 2.92 (s, 3), 2.98 (s, 3), 3.37 (m, 2), 5.37 (m, 2). ^{13}C NMR: δ −5.7, 16.4, 17.9, 19.8, 25.5, 33.3, 37.1, 38.9, 40.1, 67.7, (131.0), 131.2, 134.1, 171.5. Anal. Calcd for $C_{17}H_{35}NO_2Si$: C, 65.10; H, 11.27; N, 4.47. Found: C, 64.89; H, 11.09; N, 4.39.

(*E*,3*R,6*R**)-3,6-Dimethyl-7-(triphenylmethoxy)-4-heptenoic Acid, Dimethylamide (41).** The foregoing procedure was applied to ether **31** on a 0.5-mmol scale to obtain **41** as a colorless, viscous oil (82%). IR (film): 1630 cm^{-1}. ^{1}H NMR: δ 0.98 (d, 3, J = 7), 1.06 (d, 3, J = 7), 2.91 (s, 3), 2.94 (s, 3), 5.38 (d, 1, J = 9), 5.42 (d, 1, J = 9), 7.40 (m, 15). ^{13}C NMR: δ 17.2, 20.1, 33.6, 35.1, 37.2, 37.3, 40.3, 68.0, 85.9, 126.6, 127.4, 128.5, 131.7, 134.2, 144.2, 171.8. HPLC analysis (1.2% isopropyl alcohol in hexanes as eluant, 0.8 mL/min) showed this material to be a 9:1 mixture (major compound, t_R 43.6 min; minor compound, t_R 40.0 min). Anal. Calcd for $C_{30}H_{35}NO_2$: C, 81.58; H, 8.00: N, 3.17. Found: C, 81.29; H, 7.96; N, 3.11.

Ethyl (*E*,3*R,6*R**)-3,6-Dimethyl-7-(triphenylmethoxy)-4-heptenoate (42).** To a solution of 198.2 mg (0.53 mmol) of **31** in 1.5 mL of triethyl orthoacetate was added one drop of pivalic acid. The reaction mixture was heated at 135 °C for 1.5 h while removing ethanol by distillation. After cooling, the reaction mixture was taken up in 25 mL of ether and the organic layer was washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (10 g of silica gel, 3% ether in hexanes as eluant) to obtain 143.2 mg (0.32 mmol, 61%) of **42** as a colorless viscous oil. IR (film): 1725, 1600 cm^{-1}. ^{1}H NMR: δ 0.98 (d, 3, J = 8), 1.05 (d, 3, J = 7), 1.23 (t, 3, J = 8), 2.97 (m, 2), 4.05 (q, 2, J = 8), 5.38 (m, 2), 7.40 (m, 15). ^{13}C NMR: δ 17.3, 20.3, 33.8, 37.3, 42.0, 60.0, 68.1, 86.0, 126.7, 127.6, 128.6, 132.4, 133.6, 144.3, 172.5. Anal. Calcd for $C_{30}H_{34}O_3$: C, 81.40; H, 7.76. Found: C, 81.19; H, 7.71.

(*E*,3*S,6*R**)-7-[(*tert*-Butyldimethylsilyl)oxy]-3,6-dimethyl-4-heptenoic Acid, Dimethylamide (43).** The foregoing procedure was applied to **29** on a 2.04-mmol scale to obtain amide **43** as a colorless oil (98%). IR (film): 1645 cm^{-1}. ^{1}H NMR: δ 0.01 (s, 6), 0.87 (s, 9), 0.93 (d, 3, J = 7), 1.02 (d, 3, J = 7), 2.92 (s, 3), 2.98 (s, 3), 3.37 (m, 2), 5.37 (m, 2). ^{13}C NMR: δ −5.7, 16.4, 17.9, 19.8, 25.5, 33.3, 37.1, 38.9, 40.1, 67.7, (131.0), 131.2, 134.1, 171.5. Anal. Calcd for $C_{17}H_{35}NO_2Si$: C, 65.10; H, 11.27; N, 4.47. Found: C, 64.89; H, 11.09; N, 4.39.

(*E*,3*S,6*R**)-3,6-Dimethyl-7-(triphenylmethoxy)-4-heptenoic Acid, Dimethylamide (44).** The foregoing procedure was applied to **32** on a 0.264-mmol scale to obtain amide **44** as a colorless, viscous oil (92%). IR (film): 1640 cm^{-1}. ^{1}H NMR: δ 1.05 (d, 3, J = 7), 1.09 (d, 3, J = 7), 2.90 (s, 3), 2.92 (s, 3), 5.46 (m, 2), 7.20–7.45 (m, 15). ^{13}C NMR: δ 17.2, 20.1, 33.5, 35.2, 37.2, 37.3, 40.3, 68.1, 85.9, 126.7, 127.5, 128.6, (131.6), 131.6, 131.7, 134.3, 144.2, 171.9; HPLC analysis (1.2% isopropyl alcohol in hexanes as eluant, 0.8 mL/min) showed this to be a 19:1 mixture (major compound, t_R 40.1 min; minor compound, t_R 43.6 min). Anal. Calcd for $C_{30}H_{35}NO_2$: C, 81.58; H, 8.00; N, 3.17. Found: 81.39; H, 7.90; N, 3.15.

(3*S,6*R**)-7-[(*tert*-Butyldimethylsilyl)oxy]-3,6-dimethylheptanoic Acid, Dimethylamide (47).** To a solution of 1.170 g (3.73 mmol) of compound **40** in 20 mL of absolute ethanol was added 4.5 mL (4.6 g, 93 mmol) of hydrazine and 0.1 g of copper(II) acetate hydrate. Air was bubbled through the reaction mixture with a fritted glass filter stick. After 24, 48, and 72 h additional 4.5-mL portions of hydrazine hydrate and 20-mL portions of absolute ethanol were added. After a total reaction time of 4 days the reaction mixture was filtered through a pad of Celite and the ethanol was removed with a rotary evaporator. The residue was dissolved in 75 mL of ethyl acetate and washed with cold 5% HCl (2 × 15 mL) and brine (15 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (25 g of silica gel with 45% ether in hexanes as eluant) to give 0.949 g (81%) of **47** as a colorless oil. IR (film): 1645 cm^{-1}. ^{1}H NMR: δ 0.03 (s, 6), 0.86 (d, 3, J = 7), 0.89 (s, 9), 0.94 (d, 3, J = 6), 2.93 (s, 3), 3.00 (s, 3), 3.40 (m, 2). ^{13}C NMR: δ −5.5, (16.4), 16.7, 18.1, (19.6), 19.8, 25.8, 30.3, 30.5, (34.2), 34.3, 35.2, (35.6), 35.8, 37.3, 40.3, (40.5), 67.9, (68.2), 172.5. Anal. Calcd for $C_{17}H_{37}NO_2Si$: C, 64.68; H, 11.84; N, 4.44. Found: C, 64.61; H, 11.89; N, 4.37.

(3*S,6*R**)-7-Hydroxy-3,6-dimethylheptanoic Acid, Dimethylamide (48).** To a solution of 0.949 g (3.01 mmol) of **47** in 10 mL of THF was added 6 mL (3.30 mmol) of a 0.55 M solution of tetra-*n*-butylammonium fluoride in THF. After 24 h, 75 mL of ethyl acetate was added. The organic layer was washed with water (10 mL) and brine (10 mL) and dried ($MgSO_4$). The solvent

was removed with a rotary evaporator and the residue was purified by passage through a plug of Florisil with ether as eluant. This procedure gave 0.591 g (2.81 mmol, 93%) of **48** as a colorless oil. IR (film): 3450, 1640 cm^{-1}. ^1H NMR: δ 0.91 (d, 3, J = 7), 0.95 (d, 3, J = 7), 2.95 (s, 3), 3.02 (s, 3), 3.46 (m, 2). ^{13}C NMR: δ 16.7, 19.9, 30.1, 30.2, 33.9, 35.2, 35.6, 37.4, 40.2, 67.5, 172.7. Anal. Calcd for $C_{11}H_{23}NO_2$: C, 65.61; H, 11.54; N, 6.96. Found: C, 65.26; H, 11.25; N, 6.80.

(3*S,6*R**)-3,6-Dimethyl-7-octadecenoic Acid, Dimethylamide (49).** Into a 25-mL round-bottomed flask were placed 379.6 mg (1.80 mmol) of **48**, 1.0 mL (0.373 g, 0.72 mmol) of triethylamine, and a stirring bar. The flask was fitted with a 50-mL dropping funnel containing 0.86 g (5.4 mmol) of SO_3-pyridine complex. The flask was cooled to 10 °C and 6 mL of 3:1 DMSO/CH_2Cl_2 was added to the dropping funnel. The contents of the dropping funnel were stirred quickly and added in one portion to the flask. After 45 min at 10 °C, 5 mL of water was added to the reaction mixture. Ethyl acetate (50 mL) was added and the layers were separated. The organic layer was washed with cold 5% HCl (2 × 10 mL), water (10 mL), and brine (10 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (15 g of silica gel, 80% ether in hexanes as eluant) to give 264.3 mg (73%) of aldehyde as a colorless oil. IR (film): 1720, 1635 cm^{-1}. ^1H NMR: δ 0.96 (d, 3, J = 6), 1.10 (d, 3, J = 7), 2.95 (s, 3), 3.01 (s, 3), 9.62 (t, 1, J = 0.5). ^{13}C NMR: δ 13.3, 19.7, 27.9, 30.1, 34.0, 35.2, 37.3, 40.1, 46.2, 172.1, 205.0.

A mixture of 0.47 g (2.00 mmol) of 1-bromoundecane and 0.58 g (2.10 mmol) of triphenylphosphine was heated at 85 °C for 48 h. After cooling to 0 °C, 4 mL of ether and 1.33 mL (2.0 mmol) of a 1.5 M solution of n-butyllithium in hexanes were added. After 4 h at room temperature 4 mL of THF was added to make the reaction mixture homogeneous. After cooling to −20 °C, 171.9 mg (0.86 mmol) of the foregoing aldehyde in 2 mL of ether was added dropwise. After 1 h at −20 °C the reaction mixture was allowed to warm slowly to room temperature. After 8 h, 5 mL of saturated aqueous NH_4Cl and 15 mL of ether were added. The layers were separated and the aqueous layer was extracted with ether. The combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (16 g of silica gel, 30% ether in hexanes as eluant) to give 226.6 mg (78%) of **49** as a colorless oil. IR (film): 1640 cm^{-1}. ^1H NMR: δ 0.88 (t, 3, J = 7), 0.92 (d, 6, J = 7), 1.26 (br s, 20), 2.95 (s, 3), 3.00 (s, 3), 5.09 (dd, 1, J = 8, 8), 5.28 (dt, 1, J = 8, 6). Mass spectrum: m/z (relative intensity) 337 (0.77), 322 (0.43), 87 (3.58). Anal. Calcd for $C_{22}H_{43}NO$: C, 78.25; H, 12.86; N, 4.15. Found: C, 78.16; H, 12.69; N, 3.98.

(13*S,16*R**)-13,16-Dimethyl-10,17-octaeicosadiene (51).** To 25 mL of anhydrous ammonia (distilled from sodium) was added 60 mg (8.6 mmol) of lithium. The blue solution was cooled to −78 °C. One drop of *tert*-butyl alcohol was added. Amide **49** (48.8 mg, 0.145 mmol) in 2.5 mL of THF was added dropwise. The reaction mixture was allowed to warm to −33 °C, at which temperature it was maintained for 3.5 h. Solid NH_4Cl (0.1 g) was added cautiously and the ammonia was allowed to evaporate. To the residue were added 10 mL of water and 25 mL of ether. The layers were separated and the aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with cold 5% HCl (10 mL) and brine (10 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (1.6 g of silica gel, 1% ether in hexane as eluant) to give 19.4 mg (45%) of aldehyde **50** as a colorless oil. IR (film): 1735 cm^{-1}. ^1H NMR: δ 0.88 (t, 3, J = 7), 0.93 (d, 3, J = 7), 0.95 (d, 3, J = 7), 1.26 (br s, 20), 5.09 (dd, 1, J = 8, 8), 5.28 (dt, 1, J = 8, 6), 9.74 (t, 1, J = 2).

Decyltriphenylphosphonium bromide (72.1 mg, 0.15 mmol) was placed in a 10-mL, round-bottomed flask and 1 mL of ether was added. To this mixture was added 0.085 mL (0.13 mmol) of a 1.5 M solution of n-butyllithium in hexanes. After 3.5 h the red solution was cooled to −20 °C and 18.7 mg (0.0635 mmol) of aldehyde **50** in 2 mL of ether was added. The reaction mixture was allowed to warm slowly to room temperature over 8 h and was then taken up in 10 mL of hexanes and filtered through a plug of Celite. The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (1 g of silica gel with hexanes as eluant) to give 12.3 mg (0.0294 mmol, 46%) of **51** as a colorless oil. IR (film): 1455 cm^{-1}. ^1H NMR: δ 0.89 (m, 12), 1.26 (br s, 34), 5.30 (m, 4). Anal. Calcd for $C_{30}H_{58}$: C, 86.04; H, 13.96. Found: C, 86.12; H, 13.92.

(13*S,16*R**)-13,16-Dimethyloctaeicosane (45).** To a solution of 12.3 mg (0.029 mmol) of diene **51** in 1.5 mL of ethyl acetate was added 10 mg of 5% iridium on carbon. The reaction mixture was placed under an atmosphere of hydrogen. Uptake of hydrogen ceased after 5 h, whereupon the catalyst was removed by filtration and the filtrate evaporated to provide 12.3 mg (99%) of **45** as a white solid, mp 38–41.5 °C. IR (film): 1450 cm^{-1}. ^1H NMR: δ 0.84 (d, 6, J = 7), 0.88 (d, 6, J = 7), 1.25 (br s, 48). Anal. Calcd for $C_{30}H_{62}$: C, 85.19; H, 14.81. Found: C, 85.56; H, 14.48.

General Procedure for the Preparation of Esters 52 and 53: (2*S,3*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-penten-3-yl Propanoate (52).** A mixture of 2.65 g (11 mmol) of **25**, 1.20 mL (15 mmol) of pyridine, 1.30 mL (15 mmol) of propionyl chloride, and 35 mL of CH_2Cl_2 was stirred (room temperature). After 2 h saturated $NaHCO_3$ (2 mL) was added and the mixture was extracted with 120 mL of CH_2Cl_2. The CH_2Cl_2 layer was washed with dilute HCl and evaporated, giving 3.8 g of crude product. This material was chromatographed on a short plug of silica gel, eluting with 20% ether–hexane, to obtain 3.3 g (100%) of oily **52**. IR (film): 1740 cm^{-1}. ^1H NMR: δ 0.02 (s, 6), 0.88 (s, 9), 0.91 (d, 3, J = 7), 1.15 (t, 3, J = 7), 1.86 (quintet, 1, J = 5), 2.35 (q, 2, J = 7), 3.44 (dd, 1, J = 6, 10), 3.53 (dd, 1, J = 6, 10), 5.13–5.38 (m, 3), 5.78 (ddd, 1, J = 6, 10, 18). ^{13}C NMR: δ −5.53, 9.20, 11.67, 18.23, 25.84, 27.80, 39.76, 64.47, 74.83, 116.47, 135.46, 173.45. Anal. Calcd for $C_{15}H_{30}O_3Si$: C, 62.88; H, 10.55. Found: C, 62.88; H, 10.46.

The (+)-2*S*,3*S* and (−)-2*R*,3*R* isomers were prepared in a similar manner from the corresponding scalemic alcohols: $[\alpha]_D$ +0.33° (*c* 0.108, CH_2Cl_2); $[\alpha]_D$ −0.77° (*c* 1.17, $CHCl_3$). The IR and NMR spectra of the scalemic esters were identical with those observed for the racemic material; both isomers gave satisfactory elemental analyses.

(2*S,3*R**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2,4-dimethyl-4-penten-3-yl Propanoate (53).** The foregoing general procedure was employed to convert alcohol **27** into ester **53**, 96% on a 15.6-mmol scale. IR (film): 1720 cm^{-1}. ^1H NMR: δ 0.02 (s, 6), 0.98 (s, 9), 1.15 (t, 3, J = 8), 1.72 (s, 3), 1.94 (m, 1), 2.35 (q, 2, J = 8), 3.41 (dd, 1, J = 4, 8), 3.47 (dd, 1, J = 6, 10), 4.87 (d, 2, J = 9), 5.22 (d, 1, J = 5). Anal. Calcd for $C_{16}H_{32}O_3Si$: C, 63.95; H, 10.73; Found: C, 63.86; H, 10.79.

(2*S,3*R**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-penten-3-yl Propanoate (54).** The foregoing procedures were employed to transform diol **22** (6:1 mixture with **19**) into ester **54** (R_f 0.64, 20% ether–hexane), 92% on a 0.16-mol scale. IR (film): 1740 cm^{-1}. ^1H NMR: δ 0.0 (s, 6), 0.89 (s, 9), 1.15 (t, 3, J = 7.6), 1.94 (quintet, 1, J = 6), 2.33 (q, 2, J = 7.6), 3.51 (m, 2), 5.18–5.30 (m, 3), 5.76 (ddd, 1, J = 7, 11, 17). ^{13}C NMR: δ −5.5, 9.0, 12.4, 18.2, 25.8, 27.8, 29.5, 64.4, 75.6, 117.4, 134.7, 173.1. Anal. Calcd for $C_{15}H_{30}O_3Si$: C, 62.88; H, 10.55. Found: C, 62.93; H, 10.44.

(2*S,3*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2,4-dimethyl-4-penten-3-yl Propanoate (55).** The general procedure was employed to convert alcohol **30** into ester **55**, 93% on a 4-mmol scale. IR: 1740 cm^{-1} (neat). ^1H NMR: δ 0.1 (s, 6), 0.86 (d, 3, J = 6), 0.88 (s, 9), 1.13 (t, 3, J = 7), 1.68 (s, 3), 1.95 (m, 1), 2.31 (q, 2, J = 7), 3.46 (dd, 1, J = 10, 6.5), 3.60 (dd, 1, J = 4, 10), 4.95 (m, 2), 5.04 (d, 1, J = 8). Anal. Calcd for $C_{16}H_{32}O_3Si$: C, 63.95; H, 10.73. Found: C, 63.89; H, 10.59.

General Procedure for Claisen Rearrangement of Esters 52–55. Method A: (*E*,2*S*,6*R*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-4-heptenoic Acid (56). A 50-mL round-bottomed flask, equipped with a rubber septum inlet and reflux condenser, was charged with 0.72 mL of diisopropylamine (0.510 g, 3.04 mmol, 1.20 equiv) and 1.6 mL of hexane and cooled to −78 °C. A solution of n-butyllithium in hexane (3.19 mL, 1.45 M, 4.62 mmol, 1.1 equiv) was added, and the reaction mixture was warmed to 0 °C for a 10-min period. After the solution was recooled to −78 °C, 7.00 mL of THF was added, and 1.20 g of ester **52** (4.20 mmol) was added slowly over an 8-min period. The solution was stirred at −78 °C for a 25-min period and a solution of 0.694 g of *tert*-butyldimethylsilyl chloride (4.62 mmol, 1.1 equiv) in 3.0 mL of HMPA was added over 5-min. Stirring was main-

tained at −78 °C for another 30 min, after which the cooling bath was removed and the reaction mixture was allowed to warm for 20 min. The yellow solution was heated at reflux for 2 h, cooled, and extracted with 20 mL of cold 5% aqueous HCl and 100 mL of pentane. The aqueous layer was reextracted with 75 mL of pentane and the combined pentane layers were washed four times with 20 mL-portions of water, dried, and concentrated to an oil. This material was dissolved in 20 mL of THF and cooled to 0 °C. An aqueous solution of K_2CO_3 (20 mL, 1 M) was added, and stirring was maintained at 0 °C for a 2-h period. The ethereal solvent was removed under reduced pressure and the aqueous mixture was cooled to 10 °C, acidified with concentrated HCl to the methyl orange endpoint, and extracted with four 200-mL aliquots of ether. The combined ethereal layers were dried and concentrated to 1.485 g of a crude product, acid **56**. ^1H and ^{13}C NMR spectroscopy showed 85% completion. A sample was dissolved in aqueous K_2CO_3 and extracted with ether. The aqueous layer was then acidified and extracted with four aliquots of ether to provide an analytical sample in 80% yield. IR (film): 3050 (br), 1710, cm^{-1}; $[\alpha]_D$ +10.98° (*c* 0.090, CH_2Cl_2). ^1H NMR: δ 0.02 (s, 6), 0.93 (d, 13, *J* = 7), 1.10 (d, 30, *J* = 7), 2.46 to 2.05 (complex m, 4), 3.40 (m, 2), 5.36 (m, 2). ^{13}C NMR: δ −5.36, 16.11, 16.69, 18.31, 25.91, 36.47, 39.33, 39.65, 68.13, 126.26, 135.83, 182.46. Elemental analysis was performed on the methyl ester of **56**, which was obtained upon treating the acid with diazomethane. Anal. Calcd for $C_{16}H_{32}SiO_3$: C, 63.95; H, 10.73. Found: C, 63.87; H, 10.99.

(*E*,2*R*,6*S*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-4-heptenoic Acid (56). This stereoisomer was prepared by the foregoing procedure in 86% yield on a 16.6-mmol scale: $[\alpha]_D$ −8.8° (*c* 0.69). An analytical sample was obtained by flash chromatography (30% ether in hexanes as eluant). Anal. Calcd for $C_{15}H_{30}O_3Si$: C, 62.88; H, 10.55. Found: C, 62.89; H, 10.37. The IR and NMR spectra were identical with those of the *E*,2*S*,6*R* enantiomer.

(*E*,2*S,6*R**)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,4,6-trimethyl-4-heptenoic Acid (57).** Similar treatment of ester **53** afforded **57** (65% on a 7-mmol scale). ^1H NMR: δ 0.05 (s, 6), 0.90 (s, 9), 0.90 (m, 6), 1.60 (s, 3), 2.00–2.65 (m, 3), 3.35 (m, 2), 5.00 (d, 1, *J* = 9). ^{13}C NMR: δ −5.3, 16.0, 17.3, 18.3, 25.9, 35.5, 43.5, 67.8, 130.5, 132.1, 182.9.

(*E*,2*R,6*R**)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-4-heptenoic Acid (58).** The foregoing general procedure was used to transform a 6:1 mixture of esters **54** and **52** into a similar mixture of **58** and **56** (84% on an 8.3-mmol scale). IR (film): 3000 (br), 1705 cm^{-1}. ^1H NMR: δ 0.03 (s, 6), 0.88 (s, 9), 0.95 (3 H, d, *J* = 7), 1.15 (3 H, d, *J* = 7), 2.13–2.50 (m, 4), 3.36 (1 H, dd, *J* = 7, 10), 3.46 (1 H, dd, *J* = 6, 10), 5.40 (1 H, d, *J* = 4), 5.40 (1 H, t, *J* = 5). ^{13}C NMR: δ −5.4, −3.9, 16.1, 16.7, 18.3, 25.9, 36.5, 39.4, 39.6, 68.1, 126.2, 135.8, 182.6. Anal. Calcd for $C_{15}H_{30}O_3Si$: C, 62.88; H, 10.55. Found: C, 62.54; H, 10.42.

(*E*,2*R,6*R**)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,4,6-trimethyl-4-heptenoic Acid (59).** Ester **55** was converted by the foregoing procedure into **59** (63% on a 2.1-mmol scale). IR: 3600–2500, 1705 cm^{-1} (film). ^1H NMR: δ 0.0 (s, 6), 0.88 (s, 9), 0.90 (d, 6, *J* = 7), 1.12 (d, 3, *J* = 7), 1.62 (s, 3), 2.03 (dd, 1, *J* = 8, 13), 2.38 (dd, 1, *J* = 7, 13), 2.49–2.63 (m, 2), 3.33 (dd, 1, *J* = 7, 10), 3.41 (dd, 1, *J* = 6, 10), 4.96 (d, 1, *J* = 9). ^{13}C NMR: δ −5.4, 15.9, 16.2, 17.2, 18.3, 25.9, 35.5, 43.8, 67.9, 130.8, 132.0.

General Procedure for Claisen Rearrangement of Esters 52–55. Method B: (*E*,2*R*,6*R*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-4-heptenoic Acid (58). A 15-mL round-bottomed flask was charged with diisopropylamine (0.254 g, 0.36 mL, 2.52 mmol, 1.2 equiv) and 0.40 mL of hexane and cooled to −78 °C. A solution of *n*-butyllithium (1.57 mL, 2.36 mmol, 1.49 M, 1.1 equiv) in hexane was added and the clear solution was warmed to 0 °C for a 10-min period. The solvent was removed under nitrogen, tetrahydrofuran (2.69 mL) and HMPA (0.81 mL) were added, and the resulting solution was cooled to −78 °C. Ester **52** (0.600 g, 2.10 mmol) was added over a 3-min period. Stirring was maintained at −78 °C for 15 min. A solution of *tert*-butyldimethylsilyl chloride (0.347 g, 2.36 mmol, 1.1 equiv) in 0.60 mL of THF was added slowly and the solution was stirred for 15 min. The cooling bath was then removed and the reaction mixture was allowed to warm over 20 min to room temperature. The solution was heated at reflux for 2 h, cooled to room temperature, diluted with pentane, and extracted with 1% aqueous HCl. After two washes with water, the pentane layer was dried over $MgSO_4$ and concentrated to a colorless oil. This oil was dissolved in 10 mL of THF and 10 mL of 1 M aqueous K_2CO_3 was added at 0 °C. After being stirred at room temperature for 45 min, the mixture was concentrated under reduced pressure to remove the THF. The aqueous layer was extracted twice with pentane, saturated with Na_2SO_4, and acidified to the methyl orange endpoint with concentrated HCl at 10 °C. The aqueous mixture was extracted with four 45-mL portions of ether. The combined ethereal layers were dried over $MgSO_4$ and concentrated to a light yellow oil (0.589 g, 98% crude yield). The crude product was generally used in further reactions without purification. A small sample was purified by chromatography to give 80% of pure acid for spectral analysis. IR (film): 3000 (br), 1705 cm^{-1}. $[\alpha]_D$: +0.82° (*c*, 0.095, CH_2Cl_2). ^1H NMR: δ 0.00 (s, 6), 0.86 (s, 9), 0.92 (d, 3, *J* = 7), 1.13 (d, 3, *J* = 7), 2.44–2.25 (m, 4), 3.38 (m, 2), 5.37 (m, 2). ^{13}C NMR: δ −5.32, 16.19, 16.70, 18.35, 25.92, 36.49, 39.39, 39.56, 68.11, 126.20, 135.91, 182.43. Elemental analysis was performed on the methyl ester, which was obtained by treating acid **58** with diazomethane. Anal. Calcd for $C_{16}H_{32}O_3Si$: C, 63.89; H, 10.82. Found: C, 63.97; H, 10.66.

The foregoing procedure was employed to prepare the *E*,2*S**,6*R** isomer of acid **56** (6:1 mixture with **58**) from the 6:1 mixture of **54** and **52**, the *E*,2*S**,6*R** isomer of **57** from **55**, and the *E*,2*R**,6*R** isomer of **59** from **53**. In each case, the IR and NMR spectra were identical with those of the compounds prepared by method A.

(2*R*,6*S*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethylheptanoic Acid (60). A mixture of 4.228 g (14.76 mmol) of **56** and 51 mg of PtO_2 in 45 mL of ethyl acetate was placed under a hydrogen atmosphere. After 3 h hydrogen uptake ceased. The reaction mixture was filtered and the solvent was removed with a rotary evaporator to obtain 4.215 g (14.61 mmol, 99%) of **60** as a pale yellow oil. This material was used without further purification. IR (film): 3200, 1710 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.87 (d, 3, *J* = 7), 0.90 (s, 9), 1.03–1.78 (m, 3), 1.19 (d, 3, *J* = 7), 2.48 (m, 1), 3.40 (m, 2). ^{13}C NMR: δ −5.3, 16.1, 16.9, 18.3, 24.5, 25.9, 33.0, 33.8, 35.5, 39.4, 68.3, 183.4. $[\alpha]_D$ −11.8° (*c* 0.65). An analytical sample was obtained by passage through a plug of silica gel (30% ether in hexanes as eluant). Anal. Calcd for $C_{15}H_{32}O_3Si$: C, 62.45; H, 11.18. Found: C, 62.29; H, 11.01.

Methyl (2*R*,6*S*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethylheptanoate (63). To a solution of 470.2 mg (1.63 mmol) of **60** in 2 mL of ether was added excess ethereal diazomethane. The excess diazomethane was decomposed with $MgSO_4$. The reaction mixture was filtered and the solvent was removed with a rotary evaporator. The residue was purified by flash chromatography (3% ether in hexanes as eluant) to give 410.4 mg (1.36 mmol, 83%) of **63** as a colorless oil. IR (film): 1740 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.86 (d, 3, *J* = 7), 0.90 (s, 9), 1.02–1.78 (m, 3), 1.15 (d, 3, *J* = 7), 2.48 (m, 2), 3.40 (m, 2), 3.68 (s, 3). ^{13}C NMR: δ −5.5, 16.5, 17.0, 18.1, 24.5, 25.8, 32.9, 34.0, 35.5, 39.3, 51.2, 177.0. $[\alpha]_D$ −11.7° (*c* 1.03). Anal. Calcd for $C_{16}H_{34}O_3Si$: C, 63.52; H, 11.33. Found: C, 63.70; H, 11.24.

(2*R*,6*S*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-1-heptanol (61). To a solution of 0.95 g (25 mmol) of $LiAlH_4$ in 50 mL of ether at 0 °C was added dropwise a solution of 4.215 g (14.61 mmol) of **60** in 75 mL of ether. The reaction mixture was allowed to warm to room temperature. After 3 h, 0.95 mL of water, 0.95 mL of 15% aqueous NaOH, and 2.85 mL of water were added. The reaction mixture was dried ($MgSO_4$) and filtered, and the solvent was removed with a rotary evaporator to obtain 3.932 g (98%) of **61** as a colorless oil. IR (film): 3375 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.87 (d, 3, *J* = 6.6), 0.90 (s, 9), 0.93 (d, 3, *J* = 6.7), 1.02–1.44 (m, 6), 1.62 (m, 2), 3.44 (m, 4). ^{13}C NMR: δ 5.4, (16.5), 16.6, (16.64), 16.7, 18.3, 24.2, 29.9, 33.4, 35.7, 68.2, 68.3, (68.4). $[\alpha]_D$ +3.1° (*c* 1.76). An analytical sample was obtained by passage through a plug of silica gel (20% ether in hexanes as eluant). Anal. Calcd for $C_{15}H_{34}O_2Si$: C, 65.63; H, 12.48. Found: C, 65.62; H, 12.35.

General Procedure for the Synthesis of MTPA Esters. To a 0.2 M solution of alcohol in CH_2Cl_2 was added 2.5 equiv of DMAP, followed by 2.0 equiv of a 0.4 M solution of either (*R*)- or (*S*)-2-methoxy-2-phenyl-3,3,3-trifluoropropionyl chloride (2 equiv). After 12 h, ether was added and the organic layer was

washed with cold 5% HCl and saturated aqueous $NaHCO_3$ and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue purified by flash chromatography.

Methyl (2*R*,6*S*,2′*R*)-2,6-Dimethyl-7-(2′-methoxy-2′-phenyl-3′,3′,3′-trifluoropropanoxy)heptanoate (64). To a solution of 57.3 mg (0.910 mmol) of **63** in 1 mL of THF was added 0.58 mL (0.29 mmol) of a 0.5 M solution of tetra-*n*-butylammonium fluoride in THF. After 16 h, 25 mL of ether and 5 mL of water were added. The layers were separated and the organic layer was washed with 10 mL of 5% HCl and dried (Na_2SO_4). The solvent was removed with a rotary evaporator. The residue was purified by passage through a plug of silica gel (20% ether in hexanes as eluant) to give 31.2 mg (0.17 mmol, 87%) of the desilylated material as a colorless oil. Following the general ester formation procedure, 23.5 mg (0.12 mmol) of the desilylated compound gave 26.3 mg (0.065 mmol, 52%) of **64** as a colorless oil (10% ether in hexanes as chromatography solvent). IR (film): 1745, 1735 cm^{-1}. ^1H NMR: δ 0.92 (d, 3, J = 6.7), 1.14 (d, 3, J = 7), 1.18–1.70 (m, 6), 1.84 (m, 1), 2.43 (m, 1), 3.55 (d, 3, J = 1.2), 3.67 (s, 3), 4.15 (m, 2), 7.41 (m, 3), 7.52 (m, 2). Anal. Calcd for $C_{20}H_{27}F_3O_5$: C, 59.40; H, 6.73. Found: C, 59.14; H, 6.73.

(2*R*,2′*R*,6′*S*)-7′-[(*tert*-Butyldimethylsilyl)oxy]-2′,6′-dimethyl-1′-heptyl 2-Methoxy-2-phenyl-3,3,3-trifluoropropanoate (62). Following the general procedure 11.4 mg (0.042 mmol) of **61** gave 18.4 mg (93%) of **62** (4% ether in hexanes as chromatography solvent) as a colorless oil. IR (film): 1750 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.86 (d, 3, J = 6.7), 0.90 (s, 9), 0.92 (d, 3, J = 6.8), 0.97–1.46 (m, 6), 1.57 (m, 1), 1.90 (m, 1), 3.35 (dd, 1, J = 9.8, 6.7), 4.25 (dd, 1, J = 11.9, 5.6), 7.40 (m, 3), 7.53 (m, 2). Anal. Calcd for $C_{25}H_{41}F_3O_4Si$: C, 61.20; H, 8.42. Found: C, 60.74; H, 8.41.

Application of this procedure to the racemic alcohol gave 68% yield of a mixture of **62** and its diastereomer as a colorless oil. The spectra of this mixture were identical with those of compound **62**, except for an additional peak at δ 4.17 (d, 2, J = 6.1) in the ^1H NMR spectrum.

(2*S,6*R**)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-1-heptyl *p*-Toluenesulfonate (65).** A mixture of 1.184 g (4.3 mmol) of alcohol **61**, 822 mg (4.3 mmol) of *p*-toluenesulfonyl chloride, 0.38 mL (4.7 mmol) of pyridine, and 5 mL of CH_2Cl_2 was stirred at room temperature for 22 h. Workup with ether and 5% HCl gave 1.70 g of crude tosylate, which was chromatographed (silica gel, 5% ether–hexane) to obtain 1.65 g (93%) of **65** and 50 mg of recovered **61**. IR: (neat) 1460, 1360 cm^{-1}. ^1H NMR: δ 0.05 (s, 6), 0.89–0.90 (m, 6), 0.90 (s, 9), 1.0–1.7 (m, 6), 2.45 (s, 3), 3.35 (d, 2, J = 7), 3.90 (d, 2, J = 7), 7.40 (m, 2), 7.80 (m, 2). Anal. Calcd for $C_{22}H_{40}O_4SiS$: C, 61.64; H, 9.40. Found: C, 61.84; H, 9.30.

(2*R,6*R**)-1-[(*tert*-Butyldimethylsilyl)oxy]-2,6,10-trimethylundecane (66).** To 0.957 g (2.23 mmol) of **65** in 1.6 mL of THF at −78 °C was added 4.90 mL (4.3 mmol) of 0.88 M THF solution of isoamylmagnesium bromide. To this solution was added 0.16 mL of 0.1 M Li_2CuCl_4 in THF. After 20 min at −78 °C, the mixture was stirred at 0 °C for 1 h and at room temperature for 30 h. The reaction solution was partitioned between 70 mL of hexane and 1 M H_2SO_4. Evaporation of the organic layer gave 850 mg of residue, which was chromatographed (5% ether–hexane) to obtain 620 mg of **66** (85%) and 71 mg of **65**. ^1H NMR: δ 0.04 (s, 6), 0.83–0.90 (m, 12), 0.90 (s, 9), 1.0–1.6 (m, 15), 3.35–3.55 (m, 2). Mass spectrum: m/z 328 (parent), 313, 271.

(2*R,6*R**)-2,6,10-Trimethylundecan-1-ol (67).** A mixture of 590 mg (1.8 mmol) of **66**, 1 mL of THF, and 3.6 mL of 1.0 M tetra-*n*-butylammonium fluoride (in THF) was stirred at room temperature for 24 h. Water (40 mL) was added and the mixture was extracted twice with 40 mL of 5% ether–hexane. Evaporation of solvents gave 550 mg of crude alcohol **67**. Chromatography (hexane followed by 10% ether–hexane; silica gel) gave 300 mg (78%) of **67** (R_f 0.22, 20% ether–hexane). IR: (neat) 3300 cm^{-1}. ^1H NMR: δ 0.80–0.88 (m, 12), 1.03–1.65 (m, 15), 2.7 (br s, 1), 3.33 (dd, 1, J = 5, 9), 3.46 (dd, 1, J = 5, 9). ^{13}C NMR: δ 16.60, 19.68, 22.57, 22.66, 24.37, 24.75, 27.93, 32.71, 33.46, 35.72, 37.21, 37.33, 39.31, 68.22. A 1:1 mixture of this material and an authentic sample of scalemic alcohol **67** provided by Cohen showed exact coincidence of all peaks. Anal. Calcd for $C_{14}H_{30}O$: C, 78.43; H, 14.10. Found: C, 78.09; H, 13.89. Mass spectrum: m/z 213, 196, 181.

(2*R*,6*S*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-1-heptyl *p*-Toluenesulfonate (71). To a solution of 3.932 g (14.32 mmol) of **61** and 3.5 mL (3.4 g, 43 mmol) of pyridine in 35 mL of CH_2Cl_2 at 0 °C was added 3.50 g (18.4 mmol) of *p*-toluenesulfonyl chloride. The reaction mixture was allowed to warm to room temperature. After 48 h, 100 mL of ether was added and the organic layer was washed with cold 5% HCl (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and brine (50 mL). The solvent was removed with a rotary evaporator to obtain 5.892 g (96%) of **71** as a colorless oil. IR (film): 1600, 1370 cm^{-1}. ^1H NMR: δ 0.03 (s, 9), 0.83 (d, 3, J = 6.7), 0.88 (d, 3, J = 6.5), 0.89 (s, 9), 0.98–1.41 (m, 6), 1.57 (m, 1), 1.79 (m, 1), 2.46 (s, 3), 3.33 (dd, 1, J = 9.8, 6.4), 3.41 (dd, 1, J = 9.8, 6.0), 3.79 (dd, 1, J = 9.3, 6.4), 3.89 (dd, 1, J = 9.3, 5.8), 7.35 (d, 2, J = 8.1), 7.80 (d, 2, J = 8.3). $[\alpha]_D$ −3.2° (c 0.66). An analytical sample was obtained by flash chromatography (5% ether in hexanes as eluant). Anal. Calcd for $C_{22}H_{40}O_4SSi$: C, 61.64; H, 9.40. Found: C, 61.84; H, 9.30.

(3*R*,7*S*)-8-[(*tert*-Butyldimethylsilyl)oxy]-3,7-dimethyloctanenitrile (72). To a solution of 5.892 g (13.74 mmol) of **71** and 468.8 mg (1.77 mmol) of 18-crown-6 in 16 mL of acetonitrile was added 2.01 g (30.9 mmol) of KCN. The heterogeneous mixture was stirred vigorously and heated at reflux for 36 h. After cooling, 100 mL of ether was added and the mixture was filtered through a pad of Celite. The organic layer was washed with water (25 mL) and brine (25 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue purified by flash chromatography (100 g of silica gel, 4% ether in hexanes as eluant) to obtain 3.50 g (90%) of **72** as a colorless oil. IR (film): 2250 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.88 (d, 3, J = 6.7), 0.90 (s, 9), 1.08 (d, 3, J = 6.7), 1.23–1.44 (m, 6), 1.60 (m, 1), 1.88 (m, 1), 2.23 (dd, 1, J = 17, 6.7), 2.34 (dd, 1, J = 17, 5.7), 3.38 (dd, 1, J = 9.8, 6.2), 3.44 (dd, 1, J = 9.8, 6.1). $[\alpha]_D$ −7.5° (c 3.37). Anal. Calcd for $C_{16}H_{33}NOSi$: C, 67.78; H, 11.73; N, 4.94. Found: C, 67.82; H, 11.62; N, 4.86.

(3*R*,7*S*)-8-[(*tert*-Butyldimethylsilyl)oxy]-3,7-dimethyloctanal (73). To a solution of 2.626 g (9.26 mmol) of **72** in 18.5 mL of hexanes at −78 °C was added (11.3 mL, 11.1 mmol) of a 0.98 M solution of diisobutylaluminum hydride in pentane over a period of 30 min. After an additional 2 h at −78 °C, the reaction mixture was allowed to warm to 0 °C and was maintained at that temperature for 30 min. The reaction mixture was quenched by the addition of 10 mL of cold 5% HCl and 100 mL of ether was added. The layers were separated, and the organic layer was washed with cold 5% HCl (40 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (35 g of silica gel, 3% ether in hexanes as eluant) to obtain 2.179 g (7.60 mmol; 82%) of **73** as a colorless oil. IR (film): 1735 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.88 (d, 3, J = 6.7), 0.90 (s, 9), 0.97 (d, 3, J = 6.6), 1.04–1.47 (m, 6), 1.60 (m, 1), 2.06 (m, 1), 2.23 (ddd, 1, J = 16, 7.8, 2.6), 2.4 (ddd, 1, J = 16, 6.7, 2.0), 3.36 (dd, 1, J = 9, 6.4), 3.44 (dd, 1, J = 9, 6), 9.76 (dd, 1, J = 2.6, 2). $[\alpha]_D$ +4.4° (c 2.18). Anal. Calcd for $C_{16}H_{34}O_2Si$: C, 67.07; H, 11.96. Found: C, 67.23; H, 11.98.

(3*R*,7*S*)-8-[(*tert*-Butyldimethylsilyl)oxy]-3,7-dimethyl-1-octanol (74). To a solution of 0.80 g (21 mmol) of $LiAlH_4$ in 20 mL of ether at 0 °C was added 5.49 g (19.2 mmol) of **73** in 80 mL of ether over a period of 10 min. After 4 h at room temperature 0.8 mL of water, 0.8 mL of 15% aqueous NaOH, and 2.4 mL of water were added. The solution was dried ($MgSO_4$) and filtered. The solvent was removed with a rotary evaporator to give 5.31 g (96%) of **74** as a colorless oil. This material was used without further purification. IR (film): 3350 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.87 (d, 3, J = 7.4), 0.90 (s, 9), 0.93 (d, 3, J = 6.3), 1.00–1.45 (m, 6), 1.45–1.76 (m, 2), 3.35 (dd, 1, J = 9.4, 6.6), 3.45 (dd, 1, J = 9.4, 7.8), 3.69 (m, 2). ^{13}C NMR: δ −5.4, (16.6), 16.7, 18.3, 19.6, 24.2, 25.9, 29.4, 33.37, 35.7, (37.36), 37.4, 39.8, (39.9), 60.8, 68.3. $[\alpha]_D$ 0° (c 1.05). An analytical sample was obtained by flash chromatography (20% ether in hexanes as eluant). Anal. Calcd for $C_{16}H_{36}O_2Si$: C, 66.60; H, 12.58. Found: C, 66.53; H, 12.28.

(2*S*,6*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-8-[(2′-methoxyethoxy)methoxy]octane (75). To a solution of 1.681 g (5.82 mmol) of **74**, 50 mg (0.41 mmol) of DMAP, and 6.08 mL (4.51 g, 34.9 mmol) of diisopropylethylamine in 18 mL of CH_2Cl_2 at 0 °C was added 2.00 mL (2.18 g, 17.5 mmol) of (2-methoxyethoxy)methyl chloride. The reaction mixture was allowed to warm to room temperature. After 16 h, 100 mL of ether

was added. The organic layer was washed with cold 5% HCl (2 × 30 mL), saturated aqueous $NaHCO_3$ (30 mL), and dried (Na_2SO_4). The solvent was removed with a rotary evaporator. The residue was purified by flash chromatography (100 g of silica gel, 12% ether in hexanes as eluant) to give 1.927 g (88%) of **75** as a colorless oil. IR (film): 1260 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.87 (d, 3, J = 6.5), 0.90 (m, 12), 0.98–1.46 (m, 6), 1.48–1.72 (m, 2), 3.35 (dd, 1, J = 9.7, 6.6), 3.41 (s, 3), 3.44 (dd, 1, J = 9.7, 5.9), 3.58 (m, 4), 3.70 (m, 2), 4.72 (s, 2). ^{13}C NMR: δ −5.4, 16.7, 18.3, 19.5, 24.2, 25.9, 29.8, 33.4, 35.7, 36.7, 37.4, 58.9, 66.1, 68.3, 71.8, 95.4. $[\alpha]_D$ −1.1° (c 3.10). Anal. Calcd for $C_{20}H_{44}O_4Si$: C, 63.78; H, 11.77. Found: C, 63.66; H, 11.80.

(2*S*,6*R*)-2,6-Dimethyl-8-[(2′-methoxyethoxy)methoxy]-1-octanol (76). To a solution of 1.927 g (5.12 mmol) of **75** in 2 mL of acetonitrile at 0 °C was added 0.6 mL of 40% aqueous HF. After 60 min, 25 mL of saturated aqueous $NaHCO_3$ and 75 mL of ether were added. The layers were separated, the organic layer was washed with brine (20 mL) and dried ($MgSO_4$). The solvent was removed with a rotary evaporator. The residue was purified by passage through a plug of silica gel (50% ether in hexanes as eluant) to give 1.296 g (96%) of **76** as a colorless oil. IR (film): 3450 cm^{-1}. ^1H NMR: δ 0.89 (d, 3, J = 6.6), 0.92 (d, 3, J = 6.8), 1.03–1.72 (m, 6), 3.41 (s, 3), 3.46 (m, 2), 3.56 (m, 4), 3.70 (m, 2), 4.72 (s, 2). ^{13}C NMR: δ (16.4), 16.5, 19.4, 24.1, 29.6, 33.3, 35.5, 36.4, (37.1), 37.2, 58.8, 66.0, 66.5, 67.9, 71.6, 95.3. $[\alpha]_D$ −3.8° (c 2.68). Anal. Calcd for $C_{14}H_{30}O_2$: C, 64.09; H, 11.52. Found: C, 63.98; H, 11.40.

(2*S*,6*R*)-2,6-Dimethyl-8-[(2′-methoxyethoxy)methoxy]-1-octyl Methanesulfonate (77). To a solution of 1.296 g (4.94 mmol) of **76** and 40 mL (3.9 g, 49 mmol) of pyridine in 50 mL of CH_2Cl_2 at 0 °C was added 1.15 mL (1.7 g, 14.8 mmol) of methanesulfonyl chloride. The reaction mixture was allowed to warm to room temperature. After 12 h, 200 mL of ether was added. The organic layer was washed with cold 5% HCl (50 mL), saturated aqueous $NaHCO_3$ (25 mL), and brine (25 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator. The residue was purified by flash chromatography (40 g of silica gel, 45% ether in hexanes as eluant) to give 1.681 g (100%) of **77** as a colorless oil. IR (film): 1360, 1325 cm^{-1}. ^1H NMR: δ 0.89 (d, 3, J = 6.5), 0.99 (d, 3, J = 6.7), 1.05–1.71 (m, 7), 1.90 (m, 1), 3.00 (s, 3), 3.40 (s, 3), 3.57 (m, 4), 3.68 (m, 2), 4.00 (dd, 1, J = 9.5, 6.6), 4.09 (dd, 1, J = 9.5, 5.8), 4.71 (s, 2). $[\alpha]_D$ +1.2° (c 1.45). Anal. Calcd for $C_{15}H_{32}O_6S$: C, 52.91; H, 9.47. Found: C, 52.93; H, 9.26.

(2*S*,6*R*)-2,6-Dimethyl-8-[(2′-methoxyethoxy)methoxy]-1-(phenylthio)octane (78). To a solution of 0.60 mL (0.70 g, 6.4 mmol) of thiophenol in 2 mL of THF at −20 °C was added 4.27 mL (6.4 mmol) of a 1.5 M solution of n-butyllithium in hexanes. To this solution was added a solution of 869.7 mg (2.55 mmol) of **77** in 10 mL of THF. The cooling bath was removed and the reaction mixture was allowed to stand at room temperature for 12 h. Saturated aqueous NH_4Cl (10 mL) and ether (30 mL) were added to the reaction mixture. The aqueous layer was extracted with ether (10 mL). The combined organic layers were washed with 5% aqueous NaOH (2 × 10 mL) and brine (10 mL) and were dried ($MgSO_4$). The solvent was removed with a rotary evaporator. The residue was purified by flash chromatography (20 g of silica gel, 15% ether in hexanes as eluant) to obtain 794.7 mg (88%) of **78** as a colorles oil. IR (film): 1590, 1485 cm^{-1}. ^1H NMR: δ 0.88 (d, 3, J = 6.5), 1.02 (d, 3, J = 6.7), 1.06–1.81 (m, 10), 2.74 (dd, 1, J = 12.5, 7.5), 2.95 (dd, 1, J = 12.5, 5.8), 3.40 (s, 3), 3.58 (m, 4), 3.69 (m, 2), 4.71 (s, 2), 7.18 (m, 1), 7.30 (m, 4). $[\alpha]_D$ +0.77° (c 2.73). Anal. Calcd for $C_{20}H_{34}O_3S$: C; 67.75; H, 9.67. Found: C, 67.49; H, 9.55.

(2*S*,6*R*)-2,6-Dimethyl-8-[(2′-methoxyethoxy)methoxy]-1-(phenylsulfonyl)octane (79). To a solution of 794.7 mg (2.24 mmol) of **78** in 50 mL of CH_2Cl_2 at 0 °C was added 1.14 g (5.62 mmol) of 85% m-chloroperoxybenzoic acid (m-CPBA). The ice bath was removed and the reaction mixture was allowed to stand at room temperature for 12 h. The excess m-CPBA was reduced with 1 mL of dimethyl sulfide. After 20 min, the volatiles were removed with a rotary evaporator. The residue was dissolved in 100 mL of ether. The organic layer was washed with saturated aqueous $NaHCO_3$ (15 mL) and brine (15 mL) and was dried (Na_2SO_4). The solvent was removed with a rotary evaporator. The residue was purified by flash chromatography (15 g of silica gel, 45% ether in hexanes as eluant) to give 838.9 mg (97%) of **79** as a viscous colorless oil. IR ($CHCl_3$): 1445, 1305, 1145 cm^{-1}. ^1H NMR: δ 0.85 (d, 3, J = 6.5), 1.07 (d, 3, J = 5.8), 1.13–1.63 (m, 9), 2.11 (m, 1), 2.92 (dd, 1, J = 14, 7.7), 3.08 (dd, 1, J = 14, 4.6), 3.40 (s, 3), 3.57 (m, 4), 3.69 (m, 2), 4.71 (m, 2), 7.60 (m, 3), 7.92 (m, 2). Mass spectrum: m/z (relative intensity) 386 (0.01), 355 (0.07), 327 (1.27), 3.11 (0.39), 297 (1.49), 281 (1.37), 279 (1.58), 59 (3.38). $[\alpha]_D$ +1.8° (c 2.03). HRMS: calcd for $C_{19}H_{31}O_4S$ (M − 31) 355.1943, found 355.1949.

(3*R*,7*S*)-8-[(*tert*-Butyldimethylsilyl)oxy]-3,7-dimethyl-1-octyl Methanesulfonate (80). To a solution of 1.138 g (3.94 mmol) of **74** and 3.2 mL (3.1 g, 40 mmol) of pyridine in 20 mL of CH_2Cl_2 at 0 °C was added 0.92 mL (1.36 g, 11.8 mmol) of methanesulfonyl chloride. The ice bath was removed and the reaction mixture was allowed to stand at room temperature for 12 h. The reaction mixture was diluted with 50 mL of ether. The organic layer was washed with cold 5% HCl (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator. The residue was purified by flash chromatography (40 g of silica gel, 12% ether in hexanes as eluant) to obtain 1.235 g (85%) of **80** as a colorless oil. IR (film): 1360 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.87 (d, 3, J = 6.7), 0.90 (s, 9) 0.93 (d, 3, J = 6.5), 1.01–1.69 (m, 9), 1.82 (m, 1), 3.01 (s, 3), 3.36 (dd, 1, J = 9.8, 6.4), 3.45 (dd, 1, J = 9.8, 6.0) 4.30 (m, 2). $[\alpha]_D$ −1.4° (c 1.66). Anal. Calcd for $C_{17}H_{38}O_4SSi$: C, 55.69; H, 10.45. Found: C, 56.01; H, 10.35.

(3*R*,7*S*)-8-[(*tert*-Butyldimethylsilyl)oxy]-3,7-dimethyl-1-iodooctane (81). To a solution of 593.8 mg (1.62 mmol) of mesylate **80** in 10 mL of THF was added 3.5 g (9.7 mmol) of tetra-n-butylammonium iodide. The reaction mixture was heated at reflux for 2 h. (At this temperature the reaction mixture was homogeneous.) It was transferred to a separatory funnel with 10 mL of THF (including solids) and 75 mL of ether was added. The organic layer was washed with water (20 mL), 0.5 M $Na_2S_2O_3$ (20 mL), and brine (20 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator. The residue was purified by flash chromatography (15 g of silica gel, 0.5% ether in hexanes as eluant) to obtain 564.9 mg (88%) of **81** as a colorless oil. IR (film): 1465 cm^{-1}. ^1H NMR: δ 0.05 (s, 6), 0.87 (d, 3, J = 6.7), 0.88 (d, 3, J = 6.5), 0.90 (s, 9), 0.97–1.70 (m, 9), 1.91 (m, 1), 3.21 (m, 2), 3.36 (dd, 1, J = 9.6, 6.5), 3.45 (dd, 1, J = 9.6, 5.9). $[\alpha]_D$ −7.4° (c 0.90). Mass spectrum: m/z (relative intensity) 397 (0.01), 383 (0.02), 341 (2.36), 213 (2.35), 83 (6.29). HRMS: calcd for $C_{16}H_{34}IOSi$ (M − 1) 397.1423, found 397.1414.

(*E*,3*R*,7*S*,10*S*,14*R*)-3,7,10,14-Tetramethyl-1,16-bis[(2′-methoxyethoxy)methoxy]-8-hexadecene (82). To a solution of 52.4 mg (0.136 mmol) of **79** in 0.5 mL of THF at −20 °C was added dropwise 0.14 mL (6.21 mmol) of a 1.5 M solution of n-butyllithium in hexanes. After 45 min the reaction mixture was cooled to −78 °C and 54.8 mg (0.138 mmol) of **81** in 0.9 mL of THF was added. The reaction mixture was maintained at −78 °C for 1 h and allowed to warm to room temperature slowly. After 12 h 2 mL of saturated aqueous NH_4Cl was added. The reaction mixture was diluted with 25 mL of ether. The organic layer was washed with brine (10 mL) and dried ($MgSO_4$). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (5 g of silica gel, 30% ether in hexanes as eluant) to obtain 14.8 mg (45%) of **82** as a colorless oil. In addition, 46.2 mg (84%) of **81** and 11 mg (21%) of **79** were recovered. IR ($CHCl_3$): 2850 cm^{-1}. ^1H NMR: δ 0.88 (d, 6, J = 6.4), 0.94 (d, 6, J = 6.7), 1.03–1.79 (m, 18), 2.04 (m, 2), 3.41 (s, 6), 3.57 (m, 8), 3.69 (m, 4), 4.72 (s, 4), 5.20 (m, 2). ^{13}C NMR: δ 19.5, 21.1, 24.6, 29.7, 36.7, 36.8, 37.1, 37.4, 59.0, 66.2, 66.6, 71.8, 95.4, 134.5. Anal. Calcd for $C_{28}H_{56}O_6$: C, 68.81; H, 11.55. Found: C, 68.92; H, 11.45.

(2*S*,6*R*,10*S*,14*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-16-[(2′-methoxyethoxy)methoxy]-9-(phenylsulfonyl)-2,6,10,14-tetramethylhexadecane (83). To a solution of 497.0 mg (1.29 mmol) of **79** in 7 mL of degassed THF under an argon atmosphere at −78 °C was added 1.71 mL (2.57 mmol) of a 1.5 M solution of n-butyllithium in hexanes. After 1 h at −78 °C the reaction mixture was allowed to warm to −20 °C for 30 min. After cooling to −78 °C, 616.7 mg (1.55 mmol) of **81** in 5.5 mL of degassed THF was added followed by 1.25 mL of HMPA. The reaction mixture was maintained at −78 °C for 1 h and then allowed to warm slowly to room temperature. After 12 h, 4 mL of saturated aqueous NH_4Cl and 50 mL of ether were added. The organic layer was

washed with water (4 × 10 mL) and brine (10 mL) and dried ($MgSO_4$). The solvent was removed with a rotary evaporator and the residue purified by flash chromatography (65 g of silica gel, a gradient of 30–60% ether in hexanes as eluant) to obtain 548.8 mg (65%) of **83** as a colorless, viscous oil. In addition, 39.8 mg (8%) of **79** was recovered. IR (film): 1460, 1445, 1300, 1145 cm^{-1}. Major isomer ^1H NMR: δ 0.05 (s, 6), 0.78 (d, 3, J = 6.3), 0.84 (d, 3, J = 6.4), 0.86 (d, 3, J = 6.6), 0.90 (s, 9), 1.03 (d, 3, J = 6.8), 1.01–1.92 (m, 21), 2.23 (m, 1), 2.84 (m, 1), 3.35 (dd, 1, J = 9.8, 6.6), 3.40 (s, 3), 3.44 (dd, 1, J = 9.8, 6.0), 3.57 (m, 4), 3.70 (m, 2), 4.72 (s, 2), 7.60 (m, 3), 7.89 (m, 2). Mass spectrum (chemical ionization): m/z (relative intensity) 656 (0.01), 655 (0.01), 641 (0.02), 625 (0.04), 613 (0.01), 599 (1.25), 581 (0.66), 567 (0.39), 549 (1.02). Anal. Calcd for $C_{36}H_{68}O_6SSi$: C, 65.81; H, 10.43. Found: C, 65.47; H, 10.42.

(2*S*,6*S*,10*R*,14*R*)-2,6,10,14-Tetramethyl-16-[(2′-methoxyethoxy)methoxy]-1-hexadecanol (85). To a solution of 500.7 mg (0.762 mmol) of **83** in 10 mL of THF and 2 mL of HMPA in a 50-mL pear-shaped flask under an argon atmosphere were added 0.5 g of Na_2HPO_4, 0.1 mL of *tert*-butyl alcohol, and 30 mg (4.3 mmol) of lithium wire. The lithium wire was cut into four pieces and washed first with methanol and then with pentane prior to its addition. The reaction mixture was placed in a sonicator bath at 0 °C and was sonicated for 2 h. Solid NH_4Cl (0.5 g) and 50 mL of ether were added. The organic layer was washed with water (25 mL), 5% HCl (25 mL), and water (3 × 25 mL) and dried ($MgSO_4$). The solvent was removed with a rotary evaporator to give crude **84**. IR ($CHCl_3$): 1250 cm, 1190 cm^{-1}. ^1H NMR: δ 0.04 (s, 6), 0.84 (d, 3, J = 6), 0.86, 0.98 (m, 9), 0.96 (s, 9), 1.01–1.65 (m, 24), 3.41 (s, 3), 3.46 (m, 2), 3.56 (m, 4), 3.70 (m, 2), 4.72 (s, 2). Mass spectrum (CI): m/z (relative intensity) 515 (0.02), 501 (0.08), 485 (0.07), 441 (4.73), 89 (34.24).

Crude **84** was dissolved in 5 mL of acetonitrile. The solution was cooled to 0 °C and 8 drops of 40% aqueous HF was added. The reaction mixture was allowed to warm to room temperature. After 1 h, 2 mL of saturated aqueous $NaHCO_3$ and 25 mL of ether were added. The layers were separated and the organic layer was washed with water (2 × 10 mL). The solvent was removed with a rotary evaporator and the residue was dissolved in 25 mL of ether and washed with water (10 mL) and dried ($MgSO_4$). The solvent was again removed and the residue was purified by flash chromatography (15 g of silica gel, 40% ether in hexanes as eluant) to obtain 132.8 mg (43%) of **85** as a colorless oil. IR ($CHCl_3$): 3625 cm^{-1}. ^1H NMR: δ 0.85 (d, 3, J = 6.4), 0.86 (d, 3, J = 6.4), 0.89 (d, 3, J = 6.5), 0.93 (d, 3, J = 6.4), 1.03–1.50 (m, 2), 1.50–1.75 (m, 4), 3.41 (s, 3), 3.42 (dd, 1, J = 10.3, 6.5), 3.53 (dd, 1, J = 10.3, 5.7), 3.58 (m, 4), 3.71 (m, 2), 4.73 (s, 2). ^{13}C NMR: δ 16.6, 19.6, 19.7, 19.8, 24.37, 24.42, 29.9, 32.76, 32.78, 33.5, 35.8, 36.7, 37.3, 37.4, 37.5, 59.0, 66.2, 66.7, 68.4, 71.8, 95.5. $[\alpha]_D$ −2.8° (c 1.08). Anal. Calcd for $C_{24}H_{50}O_4$: C, 71.59; H, 12.52. Found: C, 71.82; H, 12.19.

(2*S*,6*S*,10*R*,14*R*)-2,6,10,14-Tetramethyl-16-[(2′-methoxyethoxy)methoxy]-1-hexadecyl Methanesulfonate (86). To a solution of 150.1 mg (0.373 mmol) of **85** and 0.3 mL (0.3 g, 3.7 mmol) of pyridine in 2 mL of CH_2Cl_2 at 0 °C was added 0.1 mL (0.14 g, 1.2 mmol) of methanesulfonyl chloride. The reaction mixture was allowed to warm to room temperature. After 3 h, 25 mL of ether was added. The organic layer was washed with saturated aqueous $NaHCO_3$ (2 × 10 mL), 5% HCl (10 mL), and brine (10 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (5 g of silica gel, 40% ether in hexanes) to obtain 170.8 mg (95%) of **86** as a colorless oil. IR ($CHCl_3$): 1365 cm^{-1}. ^1H NMR: δ 0.85 (d, 3, J = 6.4), 0.86 (d, 3, J = 6.4), 0.89 (d, 3, J = 6.5), 0.99 (d, 3, J = 6.7), 1.02–1.71 (m, 23), 1.90 (m, 1), 3.02 (s, 3), 3.41 (s, 3), 3.59 (m, 4), 3.71 (m, 2), 4.02 (dd, 1, J = 9.4, 6.7), 4.11 (dd, 1, J = 9.4, 5.7), 4.73 (s, 2). ^{13}C NMR: δ 16.5, 19.6, 19.67, 19.72, 24.1, 24.3, 24.4, 29.8, 32.7, 32.8, 33.0, 33.04, 36.7, 37.06, 37.15, 37.17, 37.3, 37.4, 66.2, 66.6, 71.8, 74.6, 95.4. $[\alpha]_D$ +1.7° (c 1.43). Anal. Calcd for $C_{25}H_{52}O_6S$: C, 62.46; H, 10.90. Found: C, 62.57; H, 10.85.

(2*S*,6*S*,10*R*,14*R*)-1-Bromo-2,6,10,14-tetramethyl-16-[(2′-methoxyethoxy)methoxy]hexadecane (87). To a solution of 170.8 mg (0.355 mmol) of **86** in 3.5 mL of THF was added 0.72 mg (2.2 mmol) of tetra-*n*-butylammonium bromide. The reaction mixture was heated at reflux for 2 h. After cooling, 50 mL of ether was added. The organic layer was washed with water (15 mL) and 0.5 M $Na_2S_2O_3$ (15 mL) and dried ($MgSO_4$). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (4 g of silica gel, 10% ether in hexanes as eluant) to obtain 158.0 mg (0.339 mmol, 96%) of **87** as a colorless oil. IR ($CHCl_3$): 1465 cm^{-1}. ^1H NMR: δ 0.85 (d, 3, J = 6.4), 0.86 (d, 3, J = 6.4), 0.90 (d, 3, J = 6.5), 1.02 (d, 3, J = 6.6), 1.03–1.70 (m, 23), 1.80 (m, 1), 3.33 (dd, 1, J = 9.7, 6.1), 3.41 (s, 3), 3.42 (dd, 1, J = 9.7, 5.1), 3.58 (m, 4), 3.71 (m, 2), 4.73 (s, 2). Mass spectrum: m/z (relative intensity) 466 (0.46), 464 (0.44), 435 (0.30), 43.3 (0.29), 391 (0.77), 389 (0.98), 59 (6.08). HRMS: calcd for $C_{24}H_{49}{}^{81}BrO_3$ 466.2845, found 466.2856.

(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-Octamethyl-1,32-bis[(2′-methoxyethoxy)methoxy]duotricontane (88). To 101.7 mg (0.218 mmol) of **87** under an argon atmosphere was added 20.2 mg (0.83 mmol) of magnesium turnings. After the addition of 0.5 mL of THF, 0.02 mL (43 mg, 0.22 mmol) of dibromoethane was added. The solution was heated at reflux for 2 h. After 6 h at room temperature 141 mg (0.83 mmol) of $AgNO_3$ and 2 mL of THF were added. After 12 h, 2 mL of saturated aqueous NH_4Cl was added and the reaction mixture was diluted with 30 mL of ether. The organic layer was washed with 5% HCl (10 mL) and water (10 mL) and dried ($MgSO_4$). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (6.5 g of silica gel, gradient 10–50% ether in hexanes as eluant) to obtain 24.9 mg (30%) of **88**, 34.9 mg (41%) of **89**, and 17.3 mg (20%) of **85** as colorless oils.

Compound **88**. ^1H NMR: δ 0.85 (d, 18, J = 6.3), 0.90 (d, 6, J = 6.4), 1.02–1.48 (m, 48), 1.58 (m, 4), 3.41 (s, 6), 3.58 (m, 8), 3.70 (m, 4), 4.73 (s, 4). ^{13}C NMR: δ 19.60, 19.66, 19.73, 19.76, 24.4, 24.5, 29.8, 32.8, 33.0, 34.3, 36.7, 37.3, 37.4, 37.6, 59.0, 66.3, 66.6, 71.8, 95.5. Mass spectrum (CI): m/z (relative intensity) 770 (0.01), 695 (0.05), 618 (1.57). HRMS: calcd for $C_{45}H_{91}O_4$ (M − 75) 695.6921, found 695.6938.

Compound **89**. ^1H NMR: δ 0.85 (d, 9, J = 5.9), 0.89 (d, 6, J = 6.3), 1.03–1.75 (m, 24), 3.41 (s, 3), 3.58 (m, 4), 3.70 (m, 2), 4.72 (s, 2). ^{13}C NMR: δ 19.6, 19.7, 22.6, 22.7, 24.3, 24.4, 24.8, 28.0, 29.8, 32.8, 36.7, 37.27, 37.31, 37.36, 37.43, 39.3, 59.0, 66.2, 66.6, 71.8, 95.4. Mass spectrum (CI): m/z (relative intensity) 387 (0.14), 89 (59.96). $[\alpha]_D$ +1.9° (c 1.66). Anal. Calcd for $C_{24}H_{50}O_3$: C, 74.55; H, 13.03. Found: C, 74.19; H, 12.85.

(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-Octamethylduotricontane-1,32-diol (69). To a solution of 17.8 mg (0.0231 mmol) of **88** in 0.2 mL of methanol was added 0.3 mL of 48% aqueous HBr. After 8 h, 25 mL of ether was added. The layers were separated. The organic layer was washed with saturated $NaHCO_3$ (10 mL) and brine (10 mL) and dried ($MgSO_4$). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (2.5 g silica gel, 1:2 ether/hexane as eluant) to obtain 6.5 mg of **69** as a colorless oil. IR ($CHCl_3$): 3630 cm^{-1}. ^1H NMR: δ 0.85 (d, 18, J = 6.6), 1.03–1.70 (m, 52), 3.70 (m, 4). ^{13}C NMR: δ 19.69, 19.76, 19.78, 19.80, 24.37, 24.47, 24.49, 29.51, 32.80, 33.06, 34.31, 37.31, 37.38, 37.41, 37.49, 37.55, 39.95, 61.27. Mass spectrum: m/z (relative intensity) 594 (0.98), 576 (0.34), 558 (0.34), 57 (3.16). $[\alpha]_D$ +1.9° (c 0.97). HRMS: calcd for $C_{40}H_{82}O_2$ 594.6315, found 594.6315.

(3*R*,7*R*,11*R*)-3,7,11,15-Tetramethyl-1-hexadecanol (Dihydrophytol) (90). To a solution of **89** in 0.2 mL of 1:1 methanol/water was added 0.2 mL of 0.48% aqueous HBr. The reaction mixture was heated at 35 °C for 24 h. After cooling 25 mL of ether was added. The organic layer was washed with saturated $NaHCO_3$ (10 mL) and brine (10 mL) and dried ($MgSO_4$). The solvent was removed with a rotary evaporator and the residue was purified by flash chromatography (0.5 g of silica gel, 1:5 ether/hexane as eluant) to obtain 3.7 mg (77%) of **90** as a colorless oil. IR ($CHCl_3$): 3650 cm^{-1}. ^1H NMR: δ 0.85 (d, 6, J = 6.6), 0.87 (d, 6, J = 6.6), 0.90 (d, 3, J = 6.6), 0.95–1.70 (m, 24), 3.69 (m, 2). ^{13}C NMR: δ 19.68, 19.76, 19.79, 22.63, 22.73, 24.37, 24.46, 24.80, 27.98, 29.52, 32.79, 32.80, 37.28, 37.31, 37.38, 37.44, 37.49, 39.36, 39.96, 61.28. Mass spectrum: m/z (relative intensity) 297 (0.09), 280 (0.18), 57 (10.38). $[\alpha]_D$ +1.9° (c 0.84). The acetate of this material coeluted with the less volatile of the two isomers produced by the hydrogenation and acetylation of phytol.

(2*S*,6*R*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-1-[(2′-methoxyethoxy)methoxy]heptane (91). A 15-mL round-bottomed flask was charged with alcohol **61** (0.485 g, 1.77 mmol), diisopropylethylamine (0.820 g, 6.36 mmol, 3.0 equiv),

DMAP (0.013 g, 0.10 mmol, 0.05 equiv) and 5 mL of CH_2Cl_2 and cooled to 0 °C, and (methoxyethoxy)methyl chloride (0.61 mL, 0.661 g, 5.30 mmol, 2.5 equiv) was added. After 15 h, 40 mL of ether was added and the mixture was extracted successively with two 10-mL aliquots of dilute $NaHCO_3$, a 10-mL aliquot of 1% HCl, and two 10-mL aliquots of water. The ether layer was dried over $MgSO_4$ and concentrated to an oil. Chromatography on 12 g of silica gel with 1:9 ether/hexane gave 0.447 g (70%) of ether **91**. $[\alpha]_D$ +1.54° (*c* 0.080, CH_2Cl_2). ^1H NMR: δ 0.02 (s, 6), 0.90–0.80 (complex m, 15), 1.4–1.0 (complex m, 6), 1.55 (m, 1), 1.68 (m, 1), 3.31 (m, 4), 3.36 (s, 3), 3.56 (complex m, 4), 4.68 (s, 1). ^{13}C NMR: δ −5.39, 16.73, 17.09, 18.30, 25.90, 33.39, 33.87, 35.68, 58.96, 66.57, 68.31, 71.76, 73.33, 95.56. Anal. Calcd for $C_{19}H_{42}O_4Si$: C, 62.93; H, 11.67. Found: C, 63.30; H, 11.44.

(2*S*,6*R*)-2,6-Dimethyl-1-[(2′-methoxyethoxy)methoxy]-heptan-7-ol (92). A 15-mL round-bottomed flask was charged with silyl ether **91** (0.447 g, 1.24 mmol) and 5 mL of acetonitrile. After the solution was cooled to 0 °C, 8 drops of concentrated hydrofluoric acid was added and the solution was stirred for a 45-min period. The reaction mixture was diluted with 90 mL of ether and washed successively with 30 mL of water, 20 mL of saturated $NaHCO_3$, and 20 mL of brine. The ether layer was dried and concentrated to 0.353 g of an oil. Chromatography on 10 g of silica gel with 3:7 ether/hexane gave 0.267 g (87%) of alcohol **92**. IR (film): 3450 cm^{-1}. $[\alpha]_D$ +6.17° (*c* 0.079, CH_2Cl_2). ^1H NMR: δ 0.874 (d, 3, *J* = 7), 0.878 (d, 3, *J* = 7), 1.8 to 1.0 (complex m, 8), 3.32 (m, 2), 3.36 (s, 3), 3.41 (m, 2), 3.56 (complex m, 4), 4.70 (s, 2). ^{13}C NMR: δ 16.59, 17.12, 24.14, 33.35, 33.68, 33.79, 36.43, 58.92, 66.61, 68.09, 71.68, 73.23, 95.5. Anal. Calcd for $C_{13}H_{28}O_4$: C, 62.87; H, 11.36. Found: C, 62.69; H, 11.29.

(2*S*,6*R*)-2,6-Dimethyl-1-[(2′-methoxyethoxy)methoxy]-7-heptyl *p*-Toluenesulfonate (93). A 15-mL round-bottomed flask was charged with alcohol **92** (0.663 g, 2.67 mmol), DMAP (0.017 g, 0.14 mmol, 0.05 equiv), pyridine (1.13 mL, 1.10 g, 13.9 mmol, 5 equiv), and 5 mL of CH_2Cl_2 and cooled to 0 °C. A solution of *p*-toluenesulfonyl chloride (1.60 g, 8.01 mmol, 3 equiv) in 1 mL of CH_2Cl_2 was added and the reaction mixture was kept at room temperature overnight. The next morning, the solution was diluted with 100 mL of ether and washed successively with 15-mL aliquots of water, 5% HCl, saturated $NaHCO_3$, and brine. The ether layer was dried, concentrated, and purified by chromatography on 40 g of silica gel with a gradient solvent system (2:8 ether/hexane to 1:1 ether/hexane) to give 0.948 g (88%) of tosylate **93**. $[\alpha]_D$ −2.27° (*c* 0.070, CH_2Cl_2). ^1H NMR: δ 0.87 (d, 6, *J* = 7), 1.40–1.00 (complex m, 6), 1.85–1.60 (complex m, 2), 2.45 (s, 3), 3.34 (m, 2), 3.39 (s, 3), 3.63 (complex m, 4), 3.83 (m, 2), 4.70 (s, 2), 7.34 (d, 2, *J* = 7), 7.78 (d, 2, *J* = 7). ^{13}C NMR: δ 16.30, 16.89, 21.45, 23.74, 32.61, 32.74, 33.14, 33.43, 58.84, 66.50, 71.63, 73.04, 74.85, 95.44, 127.69, 129.65, 132.95, 144.47. Anal. Calcd for $C_{20}H_{34}O_6S$: C, 59.68; H, 8.51; S, 7.97. Found: C, 59.29; H, 8.46; S, 7.77.

(3*R*,7*S*)-3,7-Dimethyl-8-[(2′-methoxyethoxy)methoxy]octanenitrile (94). A 25-mL round-bottomed flask was charged with tosylate **93** (0.948 g, 2.36 mmol), anhydrous KCN (1.53 g, 20.4 mmol, 10 equiv), 18-crown-6 (0.044 g, 0.16 mmol, 0.07 equiv), and 8 mL of distilled acetonitrile. The slurry was heated at reflux for 40 h. Water (60 mL) and ether (200 mL) were added and the ether layer was separated. The organic phase was washed extensively with water, dried, and concentrated to an oil. Chromatography on 40 g of silica gel with 1:5 ether/hexane gave 0.547 g (90%) of nitrile **94**. IR (film): 2400, 1520 cm^{-1}. $[\alpha]_D$ −3.43° (*c* 0.055, CH_2Cl_2). ^1H NMR: δ 0.92 (d, 3, *J* = 7), 1.07 (d, 3, *J* = 7), 1.42 to 1.10 (complex m, 6), 1.95–1.80 (complex m, 2), 2.28 (t, 2, *J* = 6), 3.36 (m, 2), 3.39 (s, 3), 3.60 (complex m, 4), 4.71 (s, 2). ^{13}C NMR: δ 16.88, 19.32, 24.02, 24.24, 30.25, 33.13, 33.30, 35.92, 58.84, 66.50, 72.98, 95.43, 118.71. Anal. Calcd for $C_{14}H_{27}O_3N$: C, 65.38; H, 10.51; N, 5.45. Found: C, 65.36; H, 10.45; N, 5.39.

(3*R*,7*S*)-3,7-Dimethyl-8-[(2′-methoxyethoxy)methoxy]octan-1-ol (96). A 100-mL round-bottomed flask was charged with nitrile **94** (0.547 g, 2.13 mmol) and 21 mL of hexane and cooled to −70 °C. A solution of diisobutylaluminum hydride (2.55 mL, 1 M, 2.55 mmol, 1.2 equiv) in hexane was added and the clear solution was stirred at −78 °C for 30 min and at room temperature for 4 h. Saturated NH_4Cl (21 mL) was added and the solution was stirred for 20 min. An 8.0-mL aliquot of cold 5% H_2SO_4 was added and the reaction mixture was extracted immediately with two 100-mL portions of ether. The ether fractions were combined, washed with brine, and concentrated to give 0.612 g (100%) of aldehyde **95**.

This oil, carried on without further purification, was added as a solution in 3 mL of THF to a 25-mL round-bottomed flask that had been charged with 4.30 mL of a 1 M solution of $LiAlH_4$ in THF (0.163 g, 4.30 mmol, 2 molar equiv) and 8 mL of THF. The reaction mixture was stirred for 2 h at room temperature. The excess hydride was destroyed by successive addition of 0.16 mL of water, 0.16 mL of 15% NaOH, and 0.48 mL of water. The slurry was filtered and the filter cake rinsed well with 100 mL of ether. The solids were heated at reflux in 30 mL of THF for 1 h, filtered once again, and rinsed well with ether. The filtrates were combined, dried, and concentrated to 0.598 g of an oil. Chromatography on 20 g of silica gel with 3:7 ether/hexane gave 0.428 g (77%) of alcohol **96**. IR (film): 3450, 2950, 2900, 1470, 1390, 1120, 1060 cm^{-1}. $[\alpha]_D$ +1.98° (*c* 0.054, CH_2Cl_2). ^1H NMR: δ 0.89 (d, 3, *J* = 7), 0.91 (d, 3, *J* = 7), 1.80–1.00 (complex m, 11), 3.36 (m, 2), 3.39 (s, 3), 3.60 (complex m, 4), 3.67 (m, 2), 4.71 (s, 2). ^{13}C NMR: δ 16.97, 19.53, 24.11, 29.37, 33.29, 33.67, 37.27, 39.76, 58.91, 60.95, 66.53, 71.69, 73.25, 95.49.

(3*R*,7*S*)-1-[(*tert*-Butyldiphenylsilyl)oxy]-3,7-dimethyl-8-[(2′-methoxyethoxy)methoxy]octane (97). A 10-mL round-bottomed flask was charged with alcohol **96** (1.075 g, 4.10 mmol), DMAP (0.025 g, 0.21 mmol, 0.05 eq), triethylamine (1.37 mL, 1.04 g, 10.25 mmol, 2.5 equiv), and CH_2Cl_2 (5.0 mL) and cooled to 0 °C. A solution of *tert*-butyldiphenylsilyl chloride (1.74 g, 6.15 mmol, 1.5 equiv) in CH_2Cl_2 (5.0 mL) was added and stirring was continued for 4 h. The reaction mixture was diluted with ether, washed successively with cold 5% HCl, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting oil was dissolved in CH_2Cl_2 (10.0 mL) and cooled to 0 °C. (Trimethylsilyl)imidazole (0.80 g, 5.7 mmol, 1.4 equiv) was added and the solution was stirred for 2 h. The mixture was diluted with ether and water and extracted, and the organic layer was separated, dried over $MgSO_4$, and concentrated. The resulting colorless oil was purified by chromatography on silica gel (80 g, 1:9 ether/hexanes as eluant) to obtain 1.96 g of ether **97** (96%). $[\alpha]_D$ −0.68° (*c* 0.071, CH_2Cl_2). ^1H NMR: δ 0.81 (d, 3, 6.5), 0.91 (d, 3, 7), 1.05 (s, 9), 1.35 (m, 7), 1.60 (m, 3), 3.31 (m, 2), 3.39 (s, 3), 3.56 (m, 2), 3.68 (m, 4), 4.71 (s, 2), 7.38 (m, 6), 7.67 (m, 4). ^{13}C NMR: δ 17.14, 19.18, 19.72, 24.25, 26.53, 26.85, 29.35, 33.41, 33.81, 37.33, 39.58, 58.99, 62.19, 66.60, 71.77, 73.39, 95.58, 127.54, 129.45, 134.77, 135.54. Anal. Calcd for $C_{30}H_{48}SiO_4$: C, 71.95; H, 9.66. Found: C, 71.88; H, 9.49.

(2*S*,6*R*)-8-[(*tert*-Butyldiphenylsilyl)oxy]-2,6-dimethyloctan-1-ol (98). A 50-mL round-bottomed flask was charged with ether **97** (1.045 g, 2.09 mmol), 21 mL of distilled acetonitrile, and 2 mL of CH_2Cl_2 and cooled to −30 °C. A slurry of anhydrous NaI (1.57 g, 10.5 mmol, 5 equiv) in 10.5 mL of acetonitrile was added, followed immediately by 1.33 mL of freshly distilled trimethylsilyl chloride (1.14 g, 10.5 mmol, 5 equiv). After being stirred at −30 °C for a 20-min period, the reaction was quenched by addition of 21 mL of saturated $NaHCO_3$ and removed from the cooling bath. The mixture was extracted well with ether. The organic layer was washed successively with two aliquots of water, aqueous $Na_2S_2O_3$, and brine. The solution was dried, concentrated to an oil, and purified by chromatography on 40 g of silica gel with 1:9 ether/hexane to give 0.618 g (75%) of alcohol **98**. IR (film): 3350 cm^{-1}. $[\alpha]_D$ −4.20° (*c* 0.015, CH_2Cl_2). ^1H NMR: δ 0.81 (d, 3, *J* = 6.3), 0.91 (d, 3, *J* = 6.7), 1.04 (s, 9), 1.35 (m, 4), 1.59 (m, 3), 3.40 (m, 2), 3.69 (m, 2), 7.38 (m, 6), 7.66 (m, 4). ^{13}C NMR: δ 16.64, 19.22, 19.77, 24.31, 26.89, 29.42, 33.41, 35.80, 37.36, 39.63, 62.26, 68.37, 127.55, 129.47, 134.22, 135.57. Anal. Calcd for $C_{26}H_{40}O_2Si$: C, 75.67; H, 9.77. Found: C, 75.31; H, 9.80.

(2*S*,6*R*)-8-[(*tert*-Butyldiphenylsilyl)oxy]-2,6-dimethyl-1-octyl Methanesulfonate (99). A 10-mL round-bottomed flask was charged with alcohol **98** (0.102 g, 0.248 mmol), triethylamine (0.10 mL, 0.075 g, 0.743 mmol, 3 equiv), and 0.5 mL of methylene chloride and the solution was cooled to 0 °C. Methanesulfonyl chloride (0.04 mL, 0.057 g, 0.496 mmol, 2 equiv) was added, the reaction mixture was removed from the cooling bath, and stirring was continued at room temperature overnight. The next morning, the mixture was diluted with ether, washed successively with cold 5% HCl, saturated $NaHCO_3$, and brine, dried, concentrated to an oil, and purified by chromatography on 4 g of silica gel with

1:9 ether/hexane to give 0.99 g (82%) of mesylate **99** as a colorless oil. $[\alpha]_D$ +2.32° (*c* 0.090, CH_2Cl_2). ^1H NMR: δ 0.83 (d, 3, *J* = 6.4), 0.98 (d, 3, *J* = 6.7), 1.06 (s, 9), 1.46–1.12 (complex m, 7), 1.61 (m, 2), 1.85 (m, 1), 2.99 (s, 3), 3.70 (t, 2, *J* = 7), 4.02 (m, 2), 7.39 (m, 6), 7.68 (m, 4). ^{13}C NMR: δ 16.46, 19.17, 19.65, 23.97, 26.84, 29.26, 32.94, 32.98, 37.04, 37.14, 39.49, 62.08, 74.59, 127.54, 129.42, 134.03, 135.51. Anal. Calcd for $C_{27}H_{42}O_4SSi$: C, 66.08; H, 8.63. Found: C, 66.41; H, 8.65.

(2*S*,6*R*)-8-[(*tert*-Butyldiphenylsilyl)oxy]-2,6-dimethyl-1-iodooctane (100). A 10-mL round-bottomed flask was charged with mesylate **99** (0.101 g, 0.21 mmol), tetra-*n*-butylammonium iodide (0.380 g, 1.03 mmol, 5 equiv), and 1 mL of THF. The mixture, shielded from light, was heated at reflux. After a 5-h period had passed, the mixture was cooled to room temperature, diluted with ether and water, extracted with water, and separated. The aqueous layer was rewashed with ether. The combined organic layers were washed with repeated aliquots of saturated $NaHCO_3$ and saturated $Na_2S_2O_3$, until no solids remained in suspension. The solution was then washed with brine, dried over $MgSO_4$, concentrated to an oil, and purified by chromatography on 4 g of silica gel with 1:19 ether/hexane to give iodide **100** (97%). $[\alpha]_D$ +0.35° (*c* 0.040, CH_2Cl_2). ^1H NMR: δ 0.84 (d, 3, *J* = 6.4), 0.98 (d, 3, *J* = 7), 1.07 (s, 9), 1.40–1.00 (m, 8), 1.59 (m, 2), 3.20 (m, 2), 3.71 (m, 2), 7.40 (m, 6), 7.69 (m, 4). ^{13}C NMR: δ 17.98, 19.19, 19.71, 20.67, 24.23, 26.87, 29.23, 34.69, 36.63, 36.97, 39.55, 62.11, 127.55, 129.48, 134.06, 135.54. Anal. Calcd for $C_{26}H_{39}IOSi$: C, 59.76; H, 7.52. Found: C, 60.11; H, 7.62.

(2*R*,6*R*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethylheptanoic Acid (101). A 15-mL round-bottomed flask was charged with acid **58** (0.105 g, 0.37 mmol), PtO_2 (0.015 g), and 7 mL of ethanol. The reaction mixture was stirred for 3 h under a hydrogen atmosphere at room temperature, diluted with ether, filtered through a Supercel pad, dried, and concentrated to a colorless oil (0.098 g, 93%). IR (film): 3300–2800 (br), 1700 cm^{-1}. $[\alpha]_D$ −4.01° (*c* 0.087, CH_2Cl_2). ^1H NMR: δ 0.04 (s, 6), 0.86 (m, 12), 1.13 (d, 3, *J* = 7), 1.39–1.06 (m, 6), 1.57 (m, 1), 2.41 (m, 1), 3.36 (m, 2). ^{13}C NMR: δ −5.38, 16.62, 17.78, 18.33, 24.51, 25.93, 33.77, 35.52, 39.32, 68.26, 183.04.

(2*R*,6*R*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-1-heptanol (102). A 15-mL round-bottomed flask was charged with $LiAlH_4$ (0.064 g, 1.68 mmol, 3.8 equiv) and 5 mL of THF. A solution of acid **101** (0.127 g, 0.441 mmol) in 2 mL of THF was added dropwise and the mixture was stirred for 3 h at room temperature. Excess hydride was destroyed by addition of Na_2SO_4 decahydrate (0.22 g, 0.672 mmol, 1.52 equiv). The resultant slurry was diluted with THF, filtered, and rinsed well. The solids were heated at reflux for a 1-h period in a fresh portion of THF, filtered, and rinsed well with THF. The combined filtrates were dried over $MgSO_4$ and concentrated to a colorless oil (0.104 g, 99%). IR (film): 3325 cm^{-1}. $[\alpha]_D$ +6.69° (*c* 0.065, CH_2Cl_2). ^1H NMR: δ 0.002 (s, 6), 0.86 (m, 15), 1.60–1.00 (m, 9), 3.40 (m, 4). ^{13}C NMR: δ −5.37, 16.53, 16.66, 18.35, 24.31, 25.94, 33.39, 35.71, 68.36, 68.42. Anal. Calcd for $C_{15}H_{34}OSi$: C, 65.63; H, 12.48. Found: C, 65.59; H, 12.56.

(2*R*,6*R*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-1-heptyl Methanesulfonate (103). A 15-mL round-bottomed flask was charged with alcohol **102** (0.575 g, 2.11 mmol), triethylamine (0.641 g, 6.34 mmol, 3 equiv), and 2 mL of CH_2Cl_2. After cooling the solution to 0 °C, distilled methanesulfonyl chloride (0.484 g, 4.22 mmol, 2 equiv) was added. After being stirred overnight at room temperature, the reaction mixture was diluted with 180 mL of ether and extracted well with water. The layers were separated and the aqueous layer was reextracted with 50 mL of ether. The ether layers were combined, washed successively with 1% HCl, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated to a yellow oil. The oil was purified by chromatography on 20 g of silica gel with 1:9 ether/hexane to yield 0.551 g (78%) of mesylate **103**. $[\alpha]_D$ +2.32° (*c* 0.090, CH_2Cl_2). ^1H NMR: δ 0.02 (s, 6), 0.83 (d, 3, *J* = 7), 0.86 (s, 3), 0.95 (d, 3, *J* = 7), 1.39–1.00 (m, 6), 1.53 (m, 1), 1.83 (m, 1), 2.97 (s, 3), 3.36 (m, 2), 4.02 (m, 2). ^{13}C NMR: δ −5.46, 16.27, 16.53, 18.23, 25.56, 25.84, 32.88, 33.08, 33.50, 37.04, 68.19, 74.63. Anal. Calcd for $C_{16}H_{36}O_4SiS$: C, 54.50; H, 10.29. Found: C, 54.13; H, 10.63.

(2*R*,6*R*)-7-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-1-iodoheptane (104). A 15-mL round-bottomed flask was charged with mesylate **103** (0.551 g, 1.57 mmol), anhydrous tetra-*n*-butylammonium iodide (2.90 g, 7.87 mmol, 5 equiv), and 7 mL of THF. The reaction mixture was heated at reflux in the absence of light for a 5-h period and then was diluted with 200 mL of ether. The ether solution was washed successively with water, saturated $Na_2S_2O_3$, and brine. The pale yellow solution was then dried over $MgSO_4$, concentrated to an oil, and purified by chromatography on 20 g of silica gel with 1:19 ether/hexane to yield 0.535 g (89%) of iodide **104**. $[\alpha]_D$ +0.19° (*c* 0.083, CH_2Cl_2). ^1H NMR: δ 0.02 (s, 6), 0.85 (d, 3, *J* = 7), 0.87 (s, 9), 0.95 (d, 3, *J* = 7), 1.70 to 1.01 (m, 8), 3.17 (m, 2), 3.38 (m, 2). ^{13}C NMR: δ −5.35, 16.69, 17.84, 18.30, 20.55, 24.24, 25.94, 33.08, 34.65, 35.57, 36.67, 68.23. Anal. Calcd for $C_{15}H_{33}IOSi$: C, 46.87, H, 8.65. Found: C, 46.76; H, 8.76.

(3*R*,7*R*)-8-[(*tert*-Butyldimethylsilyl)oxy]-3,7-dimethyl-1-octyl Phenyl Sulfone (105). A 10-mL round-bottomed flask was charged with methyl phenyl sulfone (0.162 g, 1.04 mmol, 2 equiv) and 2.5 mL of THF and cooled to −78 °C. A hexane solution of *n*-butyllithium (0.675 mL, 1.54 M, 1.04 mmol, 2 equiv) was added and the slurry was stirred at −78 °C for 30 min. The pale yellow solution was warmed to −30 °C, 2.35 mL of HMPA was added, and the temperature was maintained at −30 °C for another 30 min. The mixture was warmed to −25 °C and removed from the cooling bath and a precooled (−25 °C) solution of iodide **104** (0.169 g, 0.44 mmol) in 0.3 mL of THF was rapidly added. The next morning, the reaction was quenched with 1 mL of saturated aqueous NH_4Cl, diluted with 50 mL of ether, and extracted with 10 mL of water. The layers were separated, the aqueous layer was reextracted with 50 mL of ether, and each ether solution was washed with 6 aliquots of water. The ether solutions were combined, dried, concentrated to an oil, and purified by chromatography on 6 g of silica gel with 1:9 ether/hexane to give 0.131 (74%) of sulfone **105**. $[\alpha]_D$ −0.91° (*c* 0.018, CH_2Cl_2). ^1H NMR: δ 0.02 (s, 6), 0.80 (d, 3, *J* = 7), 0.81 (d, 3, *J* = 7), 0.89 (s, 9), 1.60 to 0.89 (m, 10), 3.04 (m, 2), 3.33 (m, 2), 7.55 (m, 3), 7.88 (m, 2). ^{13}C NMR: δ −5.36, 16.59, 18.33, 19.08, 24.10, 25.93, 29.21, 31.87, 33.19, 36.60, 54.43, 68.32, 128.00, 129.23, 133.58, 139.15. Anal. Calcd for $C_{22}H_{40}O_3SSi$: C, 64.03; H, 9.77. Found: C 64.32; H, 9.86.

(2*R*,6*R*,8*R,10*S*,14*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-16-[(*tert*-butyldiphenylsilyl)oxy]-2,6,10,14-tetramethyl-8-hexadecyl Phenyl Sulfone (106).** A 2.5-mL Wheaton flask was charged with sulfone **105** (0.117 g, 0.284 mmol, 1.5 equiv) and cooled to −78 °C. A hexane solution of *n*-butyllithium (0.184 mL, 1.54 M, 0.284 mmol, 1.5 equiv) was added, and the yellow solution was stirred for a 30-min period at −78 °C. The reaction mixture was then warmed to −30 °C, 0.16 mL of HMPA was added, and stirring was continued for a 2-h period at −30 °C. The reaction flask was removed from the cooling bath and a solution of iodide **100** (0.099 g, 0.189 mmol) in 0.15 mL of THF was added rapidly. The next morning, the reaction was quenched by addition of saturated NH_4Cl. The reaction mixture was diluted with ether and water and extracted well. The aqueous layer was reextracted with ether. The combined ether layers were washed six times with water, dried over $MgSO_4$, and purified by chromatography on 8 g of silica gel with a gradient solvent system of hexane to 1:1 ether/hexane to give 0.092 g (66%) of sulfone **106**. ^1H NMR: δ 0.02 (s, 6), 0.77 (d, 3, *J* = 6.5), 0.78 (d, 3, *J* = 6.5), 0.82 (d, 6, *J* = 6.6), 0.88 (s, 9), 1.02 (s, 9), 2.00 to 1.05 (m, 24), 3.02 (m, 1), 3.34 (m, 2), 3.65 (m, 2), 7.37 (m, 6), 7.60 (m, 4), 7.65 (m, 3), 7.86 (m, 2). ^{13}C NMR: δ −5.35, 14.11, 15.25, 16.64, 16.75, 18.32, 18.86, 18.95, 19.18, 19.25, 19.60, 19.68, 19.85, 19.89, 23.84, 23.88, 24.06, 24.13, 24.20, 25.94, 26.85, 29.33, 29.39, 29.66, 30.36, 30.41, 30.44, 30.45, 30.62, 33.32, 35.66. Anal. Calcd for $C_{48}H_{78}O_4SSi_2$: C, 71.50; H, 9.73. Found: C, 71.90; H, 9.76.

(2*R*,6*S*,10*R*,14*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-16-[(*tert*-butyldiphenylsilyl)oxy]-2,6,10,14-tetramethylhexadecane (107). A 10-mL round-bottomed flask was charged with sulfone **106** (0.167 g, 0.207 mmol), disodium hydrogen phosphate (0.300 g, 7.04 mmol, 34 equiv), 6% sodium mercury amalgam (1.5 g, 6.72 mmol, 32.5 equiv), and 1.3 mL of methanol. After stirring for 2 h, the slurry was triturated with 5 mL of ethyl acetate, and the supernatant solvent was decanted. This process was repeated with ten more aliquots of ethyl acetate. The combined organic layers were washed successively with water, saturated NH_4Cl, and brine, dried over $MgSO_4$, and concentrated to an oil. This oil was purified by chromatography on 4 g of silica

gel with a gradient of hexane to 1:1 ether/hexane to give 0.118 g (86%) of diether **107**. $[\alpha]_D$ −0.692° (*c* 0.013, CH_2Cl_2). ^1H NMR: δ 0.03 (s, 6), 0.80 (d, 3, *J* = 7), 0.83 (d, 3, *J* = 7), 0.86 (d, 3, *J* = 7), 0.87 (d, 3, *J* = 7), 0.89 (s, 9), 1.04 (s, 9), 1.45 to 1.11 (complex m, 21), 1.60 (m, 2), 2.00 (m, 1), 3.39 (m, 2), 3.67 (m, 2), 7.38 (m, 6), 7.66 (m, 4). ^{13}C NMR: δ −5.35, 16.76, 18.37, 19.21, 19.67, 19.74, 19.81, 24.42, 24.52, 25.99, 26.89, 29.41, 29.71, 32.76, 32.83, 33.49, 35.77, 37.34, 37.43, 37.52, 39.66, 62.25, 68.50, 127.56, 129.47, 135.57, 137.73. Anal. Calcd for $C_{42}H_{74}Si_2O_2$: C, 75.61; H, 11.18. Found: C, 75.35; H, 11.27.

(2*R*,6*S*,10*R*,14*R*)-16-[(*tert*-Butyldiphenylsilyl)oxy]-2,6,10,14-tetramethyl-1-hexadecanol (108). A 5-mL round-bottomed flask was charged with diether **107** (0.100 g, 0.15 mmol) and 0.4 mL of THF. The solution was cooled to 0 °C and 0.4 mL of a precooled solution of 1% HCl in ethanol was added. After a 1-h period, another 0.3 mL of the acid solution was added. After 1 h the solution was diluted with ether, washed successively with aliquots of saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated to an oil. Chromatography of the crude product on 4 g of silica gel, using a gradient of hexane to 1:1 ether/hexane gave 0.072 g (87%) of alcohol **108**. IR (film): 3350 (br) cm^{-1}. $[\alpha]_D$ +2.24° (*c* 0.021, CH_2Cl_2). ^1H NMR: δ 0.80 (d, 3, *J* = 7), 0.84 (d, 3, *J* = 7), 0.85 (d, 3, *J* = 7), 0.92 (d, 3, *J* = 7), 1.05 (s, 9), 1.45 to 1.18 (complex m, 21), 1.62 (m, 2), 1.80 (m, 1), 3.46 (m, 2), 3.70–3.69 (dt, 2, *J* = 7, 7), 7.38 (m, 6), 7.66 (m, 4). ^{13}C NMR: δ 16.53, 19.17, 19.66, 19.77, 24.36, 24.37, 24.47, 26.85, 29.37, 32.73, 32.79, 33.41, 35.73, 37.25, 37.28, 37.39, 37.48, 39.61, 62.82, 68.43, 127.54, 129.45, 134.13, 135.55. Anal. Calcd for $C_{36}H_{60}SiO_2$: C, 78.20; H, 10.94. Found: C, 78.20; H, 10.77.

(2*R*,6*S*,10*R*,14*R*)-16-[(*tert*-Butyldiphenylsilyl)oxy]-2,6,10,14-tetramethyl-1-hexadecyl Methanesulfonate (109). A 5-mL round-bottomed flask was charged with alcohol **108** (0.060 g, 0.109 mmol), pyridine (0.08 mL, 0.5 mmol, 5 equiv), and 0.6 mL of CH_2Cl_2. The solution was cooled to 0 °C, methanesulfonyl chloride (0.04 mL, 0.2 mmol, 2 equiv) was added, the reaction mixture was removed from the bath, and stirring was continued for 2 h. The solution was diluted with a 20:1 pentane/ether mixture, washed successively with aliquots of cold 1% HCl, saturated $NaHCO_3$, and brine, dried, and concentrated to an oil. This material was purified by chromatography on 3 g of silica gel with 1:9 ether/hexane to yield 0.060 g (89%) of mesylate **109**. $[\alpha]_D$ −0.133° (*c* 0.015, CH_2Cl_2). ^1H NMR: δ 0.87 (complex m, 9), 1.00 (d, 3), 1.06 (s, 9), 1.44 to 1.05 (complex m, 21), 1.75 to 1.65 (complex m, 2), 1.98 to 1.81 (complex m, 1), 3.01 (s, 3), 3.70 (m, 2), 3.95 (m, 2), 7.37 (m, 6), 7.68 (m, 4). ^{13}C NMR: δ 16.37, 19.15, 19.59, 19.75, 24.06, 24.34, 24.43, 26.82, 29.32, 32.66, 32.75, 32.97, 37.00, 37.11, 37.24, 37.25, 37.39, 39.57, 62.17, 74.67, 127.50, 129.42, 134.06, 135.49. HRMS (FAB): calcd for $C_{37}H_{63}PO_4SiS$ (M + H) 631.6496, found 631.4206.

(2*R*,6*S*,10*R*,14*R*)-16-[(*tert*-Butyldiphenylsilyl)oxy]-2,6,10,14-tetramethyl-1-bromohexadecane (110). A 10-mL round-bottomed flask was charged with mesylate **109** (0.070 g, 0.11 mmol), anhydrous tetra-*n*-butylammonium bromide (0.178 g, 0.55 mmol, 5 equiv), and 1 mL of THF. The solution was heated at reflux for 2 h, cooled to room temperature, and diluted with ether and saturated $NaHCO_3$ solution. The organic phase was separated, washed with Na_2SO_3 and brine, dried over $MgSO_4$, and concentrated to an oil. Chromatography on 4.0 g of silica gel with hexane yielded 0.70 g (99%) of bromide **110**. $[\alpha]_D$ +0.35° (*c* 0.023, CH_2Cl_2). ^1H NMR: δ 0.83 (d, 3, *J* = 7), 0.85 (d, 3, *J* = 7), 0.87 (d, 3, *J* = 7), 1.02 (d, 3, *J* = 7), 1.06 (s, 9), 1.50 to 1.08 (complex m, 21), 1.60 (m, 2), 2.03 (m, 1), 3.34 (m, 2), 3.70 (dt, 2, *J* = 7), 7.41 (m, 6), 7.78 (m, 4). ^{13}C NMR: δ 18.79, 19.21, 19.73, 19.81, 24.32, 24.41, 24.47, 26.89, 29.40, 32.70, 32.81, 35.21, 37.04, 37.32, 37.42, 39.65, 41.58, 62.24, 127.55, 129.46, 134.15, 135.56. HRMS: calcd for $C_{31}H_{50}SiOBr$ (M − *t*-Bu) 559.2876, found 559.2756.

(3*R*,7*R*,11*S*,15*R*,18*R*,22*S*,26*R*,30*R*)-1,32-Bis[(*tert*-butyldiphenylsilyl)oxy]-3,7,11,15,18,22,26,30-octamethyldotricontane (111). A 0.5-mL Wheaton flask was charged with bromide **110** (0.070 g, 0.114 mmol) and in a drybox freshly scored magnesium turnings (0.040 g, 1.59 mmol, 1.4 equiv) were added. Ether (0.15 mL) was added and the resulting mixture was stirred and heated at reflux for a 5.5-h period. The mixture was then cooled and transferred to a drybox. Anhydrous $AgNO_3$ (0.038 g, 0.228 mmol, 2 equiv) was added and the reaction vessel was shielded from light and stirred overnight at room temperature. The next morning, saturated NH_4Cl and ether were added and the mixture was extracted and separated. The ether layer was washed with water until the pH of the water layer was neutral, dried over $MgSO_4$, and concentrated to an oil. Preparative thick layer chromatography (silica gel) with 1:99 ether/hexane gave 0.024 g (40%) of coupled product **111**. ^1H NMR: δ 0.80 (d, 6, *J* = 6.6), 0.84 (d, 18, *J* = 6.5), 1.04 (s, 18), 1.26 (m, 48), 1.56 (m, 4), 3.69 (m, 4), 7.38 (m, 12), 7.66 (m, 8). ^{13}C NMR: δ 19.21, 19.68, 19.74, 19.80, 24.40, 24.51, 26.88, 29.41, 32.62, 32.63, 34.44, 37.33, 37.40, 37.44, 37.54, 39.66, 62.26, 127.56, 129.47, 134.19, 135.58. $[\alpha]_D$ −2.41° (*c* 0.019, CH_2Cl_2). HRMS: calcd for $C_{68}H_{109}O_2Si_2$ (M − 57) 1013.7936, found 1013.7577.

(3*R*,7*R*,11*S*,15*R*,18*R*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-Octamethylduotricontane-1,32-diol (70). A 5-mL round-bottomed flask was charged with diether **111** (0.027 g, 0.252 mmol), 0.2 mL of THF, and 0.2 mL of ethanol and cooled to 0 °C. Concentrated HCl (0.1 mL) was added and the solution was stirred overnight at room temperature. The mixture was diluted with ether, washed with $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated to an oil. Chromatography on 1 g of silica gel with a gradient solvent system of 1:9 ether/hexane to pure ether gave 0.012 g (78%) of diol **70**. IR (film): 3340 cm^{-1}. $[\alpha]_D$ +1.77° (*c* 0.010, CH_2Cl_2). ^1H NMR: δ 0.80 (d, 18, *J* = 6.5), 0.87 (d, 6, *J* = 7), 1.44 to 0.95 (m, 50), 1.59 (m, 4), 3.65 (m, 4). ^{13}C NMR: δ 19.688, 19.737, 19.775, 24.377, 24.486, 29.548, 32.792, 32.813, 33.054, 34.433, 37.325, 37.365, 37.392, 37.459, 37.500, 39.993, 61.279. HRMS: calcd for $C_{40}H_{82}O_2$ 594.6523, found 594.6312.

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Registry No. **5**, 72507-50-7; **6**, 72959-50-3; **7**, 107-02-8; **8**, 123-73-9; **9**, 78-85-3; (±)-**10**, 83651-41-6; (±)-**11**, 113564-08-2; (±)-**12**, 100806-39-1; (±)-**13**, 83651-51-8; (±)-(2*R**,3*S**)-**13**, 83651-52-9; (±)-**14**, 113489-74-0; (±)-(2*R**,3*S**)-**14**, 113489-73-9; (±)-**15**, 100806-15-3; (±)-**16**, 83651-42-7; (±)-**17**, 113564-09-3; (±)-**18**, 100896-12-6; (±)-**19**, 83651-43-8; (2*S*,3*S*)-**19**, 113564-18-4; (2*R*,3*R*)-**19**, 99529-24-5; (±)-**20**, 113489-75-1; (±)-**21**, 102745-52-8; (±)-**22**, 83651-53-0; (±)-**23**, 113489-76-2; (±)-**24**, 113564-10-6; (±)-**25**, 83651-44-9; (2*R*,3*R*)-**25**, 99529-25-6; (2*S*,3*S*)-**25**, 113564-07-1; (±)-**26**, 113489-77-3; (±)-**27**, 113489-78-4; (±)-**28**, 113564-11-7; (±)-**29**, 113489-79-5; (±)-**30**, 113489-80-8; (±)-**31**, 113489-81-9; (±)-**32**, 113489-82-0; **33**, 77877-19-1; **34**, 113489-83-1; **35**, 99529-23-4; **36**, 77877-20-4; **37**, 113489-84-2; **38**, 113564-12-8; (±)-**39**, 113489-85-3; (±)-**40**, 113489-86-4; (±)-**41**, 113489-87-5; (±)-**42**, 113507-07-6; (±)-**43**, 113489-88-6; (±)-**44**, 113489-89-7; **45**, 87964-96-3; (±)-**46**, 113489-90-0; (±)-**47**, 113489-91-1; (±)-**48**, 113489-92-2; (±)-**48** (aldehyde), 113490-22-5; (±)-**49**, 113489-93-3; (±)-**50**, 113489-94-4; (±)-**51**, 113489-95-5; (±)-**52**, 83651-45-0; (2*S*,3*S*)-**52**, 104486-22-8; (2*R*,3*R*)-**52**, 99529-26-7; (±)-**53**, 113489-96-6; (±)-**54**, 113564-13-9; (±)-**55**, 113489-97-7; (±)-**56**, 113564-20-8; (*E*,2*S*,6*R*)-**56**, 113564-14-0; (*E*,2*R*,6*S*)-**56**, 113564-21-9; (*E*,2*S*,6*R*)-**56** (methyl ester), 113490-23-6; (±)-**57**, 113489-98-8; (±)-**58**, 113564-19-5; (*E*,2*R*,6*R*)-**58**, 113564-15-1; (*E*,2*R*,6*R*)-**58** (methyl ester), 113490-24-7; (±)-**59**, 113489-99-9; (−)-**60**, 99529-28-9; (±)-**61**, 83651-48-3; (+)-**61**, 99529-29-0; (−)-**61**, 92934-89-9; **62**, 113490-00-9; (2*R*,2′*S*,6′*R*)-**62**, 113565-39-2; (−)-**63**, 113490-01-0; **63** (desilyl deriv), 113490-21-4; **64**, 113490-02-1; (±)-**65**, 83651-49-4; (±)-**66**, 83651-50-7; (±)-**67**, 63568-64-9; **69**, 99529-30-3; **70**, 104486-21-7; **71**, 92934-94-6; **72**, 99474-33-6; **73**, 99474-34-7; **74**, 99474-35-8; **75**, 99474-36-9; **76**, 99474-37-0; **77**, 99474-38-1; **78**, 99474-39-2; **79**, 99474-40-5; **80**, 99474-41-6; **81**, 99474-42-7; **82**, 113490-03-2; **83**, 113490-04-3; **84**, 113490-05-4; **85**, 99474-43-8; **86**, 99474-44-9; **87**, 99474-45-0; **88**, 99474-46-1; **89**, 113490-06-5; **90**, 18654-63-2; **90** (acetate), 113564-22-0; **91**, 113490-07-6; **92**, 113490-08-7; **93**, 113490-09-8; **94**, 113490-10-1; **95**, 113490-11-2; **96**, 113490-12-3; **97**, 113490-13-4; **98**, 113490-14-5; **99**, 113507-08-7; **100**, 104423-51-0; **101**, 113564-16-2; **102**, 113564-17-3; **103**, 113490-15-6; **104**, 113490-16-7; **105**, 104423-52-1; **106**, 104423-53-2; **107**, 113490-17-8; **108**, 113490-18-9; **109**, 113490-19-0; **110**, 104423-50-9; **111**, 113490-20-3; **112**, 99529-31-4; $C_{11}H_{23}Br$, 693-67-4; $C_{10}H_{21}PPh_3^+Br^-$, 32339-43-8; (*R*)-2-methoxy-2-phenyl-3,3,3-trifluoropropionyl chloride, 39637-99-5; (*S*)-2-methoxy-2-phenyl-3,3,3-trifluoropropionyl chloride, 20445-33-4.