Archaebacterial Isoprenoids. Synthesis of 2,3-Di-*O*-phytanyl-*sn*-glycerol and Its 1,2-Isomer

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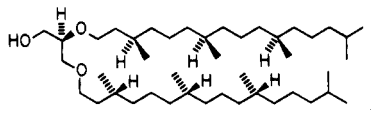
2,3-Di-*O*-phytanyl-*sn*-glycerol (1), the major ether-lipid component of most archaebacterial membranes, and its 1,2-isomer (2) were synthesized in good overall yields from 3-*O*-benzyl-*sn*-glycerol (3). The 1-position of 3 was blocked selectively with *tert*-butyldiphenylsilyl chloride and the C2 hydroxyl, alkylated with (3*R*,-*S*,7*R*,11*R*)-phytanyl triflate (6). Removal of benzyl or *tert*-butyldiphenylsilyl protecting groups, alkylation with (3*R*,*S*,7*R*,11*R*)-phytanyl triflate, and removal of the remaining blocking group gave the 2,3- and 1,2-ethers, respectively. The C3 carbons in the phytanyl diastereomers were resolved in the ^{13}C NMR spectra of 1 and 2. Resonances for 1 were assigned by comparison with a spectrum of authentic 2,3-di-*O*-(3′*R*,7′*R*,11′*R*)-phytanyl-*sn*-glycerol isolated from *Methanobacterium thermoautotrophicum* ΔH.

Archaebacteria are unique life forms that diverged from other organisms before even the simplest present day prokaryotes had evolved. Among the many features that distinguish archaebacteria from eubacteria and eukaryotes are the unusual structures of archaebacterial membrane lipids. The hydrocarbon region of the membranes in these primitive organisms is constructed from isoprenoid alcohols joined to glycerol through ether linkages instead of the normal straight-chain fatty acid glycerol ester structures.[1] The basic structural unit is a phytanyl glyceryl diether, 2,3-di-*O*-[(*R*,*R*,*R*)-3′,7′,11′,15′-tetramethylhexadecyl]-*sn*-glycerol (1). A few modifications in the isoprenoid chain,



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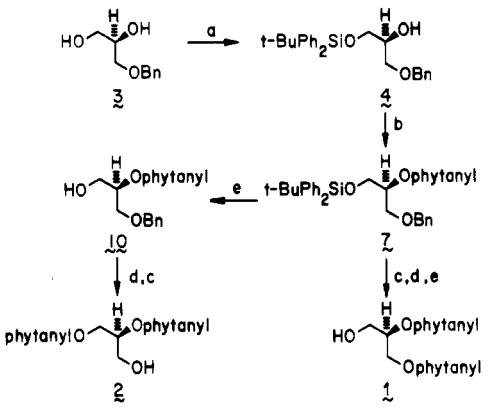
including a novel 4–4′ linkage of phytanyl units, which presumably are important for imparting rigidity to the membrane, are also known.[1,2] The absolute configuration of the three chiral centers in the phytane chain is *R*,[3] the same as the corresponding centers in natural phytol and phytanol from nonarchaebacterial sources.

In conjunction with a study of the biosynthesis of these unusual ether-linked lipids, we needed a reliable synthesis of 1. The published procedure required 10 steps to convert readily obtainable 3-*O*-benzyl-*sn*-glycerol (3) to 1 in an overall yield of approximately 10% and used a considerable excess of phytanyl bromide in the etherification step.[4] We shortened the synthesis to five steps and increased the overall yield to 61%. The new procedure also introduces the phytanyl side chain in an efficient manner compatible with the synthesis of labeled material.

Results and Discussion

The synthesis of 2,3-di-*O*-phytanyl-*sn*-glycerol (1) and its 1,2-isomer (2) is outlined in Scheme I. The C1 hydroxyl of 3-*O*-benzyl-*sn*-glycerol (3), readily obtained from D-mannitol,[5] was selectively blocked with *tert*-butyldiphenylsilyl chloride according to the procedure of Hanessian and Lavallee.[6] Several attempts to convert

Scheme I. Synthesis of 2,3-Di-*O*-(3′*R*,*S*,7*R*,11′*R*)-phytanyl-*sn*-glycerol (1) and 1,2-Di-*O*-(3′*R*,*S*,7′*R*,11′*R*)-phytanyl-*sn*-glycerol (2)[a]



[a] Key: (a) *t*-$BuPh_2SiCl$, imidazole; (b) NaH, phytanyl triflate; (c) H_2, $Pd/BaSO_4$; (d) KH, phytanyl triflate; (e) *n*-Bu_4NF.

differentially blocked glycerol 4 to phytanyl ether 7 by a Williamson synthesis using phytanyl bromide or phytanyl iodide gave disappointing results. The halides underwent elimination in preference to displacement, and a reasonable conversion of 4 to 7 required large excesses of the phytanyl halide and base.

A satisfactory solution was found by the replacement of halogen by the highly reactive triflate leaving group.[7] Treatment of alcohol 4 with a modest excess of phytanyl triflate (6) and sodium hydride at room temperature resulted in a smooth conversion to ether 7. Removal of the benzyl moiety, etherification of the hydroxyl at C3 with phytanyl triflate, and removal of the *tert*-butyldiphenylsilyl group gave 2,3-diether 1. Its 1,2-isomer, 2, was also obtained from 7 in three steps by simply reversing the order in which the blocking groups were removed.

Natural 2,3-di-*O*-(3′*R*,7′*R*,11′*R*)-phytanyl-*sn*-glycerol isolated from *Methanobacterium thermoautotrophicum* ΔH according to the procedure of Bligh and Dyer[8] had $[\alpha]_D$ +7.8°, in agreement with the rotation reported for the diether obtained from other archaebacterial sources.[9] Our synthetic diether prepared with (3*R*,S,7*R*,11*R*)-phytanol

(1) Kates, M. In "Ether Lipids: Chemistry and Biology"; Snyder, F., Ed.; Academic Press: New York, 1972; pp 351–398.
(2) Heathcock, C. H.; Finkelstein, B. L.; Aoki, T.; Poulter, C. D. *Science (Washington, D.C.)* **1985**, *229*, 862–864.
(3) Kates, M.; Joo, C. N.; Palameta, B.; Shier, T. *Biochemistry* **1967**, *6*, 3329–3338.
(4) Kates, M.; Palameta, B.; Yengoyan, L. S. *Biochemistry* **1965**, *4*, 1595–1599.
(5) Golding, B. T.; Ioannou, P. V. *Synthesis* **1977**, 423–424.
(6) Hanessian, S.; Lavallee, P. *Can. J. Chem.* **1975**, *53*, 2975–2977.
(7) Beard, C. D.; Baum, K.; Grakauskas, V. *J. Org. Chem.* **1973**, *38*, 3673–3677.
(8) Bligh, E. G.; Dyer, W. J. *Can. J. Biochem. Physiol.* **1959**, *37*, 911–917.
(9) Kates, M.; Yengoyan, L. S.; Sastry, P. S. *Biochim. Biophys. Acta* **1965**, *98*, 252–268.

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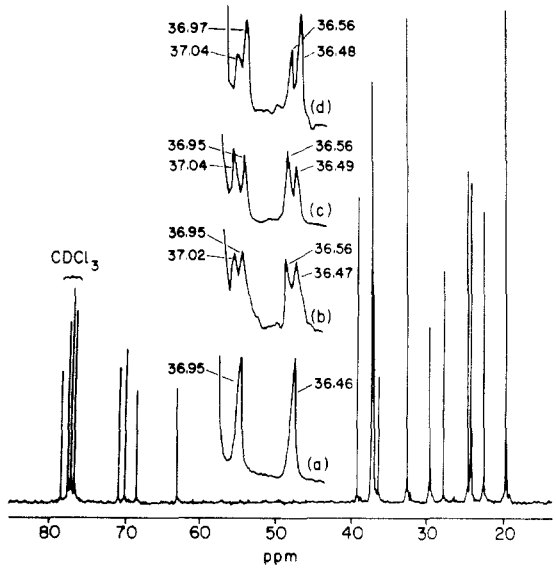

Figure 1. 75.4-MHz ^{13}C NMR spectrum of natural diether 1 from *M. thermoautotrophicum* ΔH, 20 mg in 0.3 mL of $CDCl_3$. Insets are expansions of the region between ca. 36 and 37 ppm: (a) natural 1; (b) synthetic 1; (c) synthetic 2; (d) 20 mg of synthetic 1 and 10 mg of natural 1.

obtained by catalytic hydrogenation of (7*R*,11*R*)-phytol had a slightly lower rotation $[\alpha]_D$ +7.1°. The unnatural 1,2-isomer had $[\alpha]_D$ −7.0°.

The small difference in the rotations of natural and synthetic 1 reflects the presence of C3′ stereoisomers.[4] Although retention times on thin-layer chromatography and ^1H NMR, IR, and mass spectra for natural and synthetic 2,3-diether are identical, the ^{13}C spectrum of synthetic 1 shows an additional peak for each of the C2′ carbons in the phytanyl moieties because of the presence of C3 diastereomers. The ^{13}C spectrum of natural 1 is shown in Figure 1. Resonances for C2′ in the central and terminal phytanyl residues are assigned to peaks at 36.46 and 36.95 ppm, respectively. The single peaks for these two carbons are readily discernable in the expansion shown in inset a. Inset b is from the same region of synthetic diether 1. In addition to the two peaks shown in a, two addition resonances appear at 36.56 and 37.02 ppm. A similar four-line pattern is seen for 1,2-diether 2. The new resonances in synthetic 1 slightly downfield from those for the natural all-*R* stereoisomer clearly result from the (3*S*,7*R*,11*R*)-phytanyl diastereomer. As illustrated in inset d, a mixture of natural and synthetic 1 shows a large increase in the intensity of the higher field resonances for both C2′ carbons. The integrated intensities of the diastereomeric C2′ peaks are almost equal, indicating little or no asymmetric induction from the chiral centers of C7 and C11 during hydrogenation of phytol.

Experimental Section

General Methods. All solvents used were reagent grade and distilled. Tetrahydrofuran was heated at reflux over sodium with benzophenone as an indicator until the blue color of benzophenone ketyl persisted. Methylene chloride was distilled from phosphorus pentoxide, and pyridine, from calcium hydride. Baker silica gel (230–400 mesh) was used for flash chromatography.[10] Analytical thin-layer chromatography utilized 0.25-mm Merck 50 GF_{254} silica gel plates. Compounds were visualized by spraying with vanillin–sulfuric acid (1:134, w/w) and heating on a hot plate.

IR spectra were recorded on a Perkin-Elmer Model 299 infrared spectrophotomer. ^1H, ^{13}C, and ^{19}F NMR spectra were obtained with acetone-d_6 or chloroform-*d* solutions on Varian EM-390 or SC-300 spectrometers using tetramethylsilane (^1H and ^{13}C) or fluorotrichloromethane (^{19}F) as internal standards. Electron impact and chemical ionization mass spectra were recorded on a Varian MAT 1125 mass spectrometer. Optical rotations were measured on a Perkin-Elmer 141 digital polarimeter using a 1-dm cell.

3-*O*-Benzyl-*sn*-glycerol (3). Following the procedure of Debost and co-workers,[11] D-mannitol (Sigma) was converted to the 1,2,5,6-di-*O*-isopropylidene derivative. Cleavage of the 3,4-diol moiety and reduction of the resulting aldehyde with sodium borohydride according to LeCocq and Ballou[12] followed by benzylation and deprotection[5] yielded 3-*O*-benzyl-*sn*-glycerol in an overall yield of 58%: $[\alpha]^{26}_D$ +6.30° (neat); bp 140–142 °C (0.7 mm) [lit.[5] bp 134 °C (0.6 mm)].

1-*O*-(*tert*-Butyldiphenylsilyl)-3-*O*-benzyl-*sn*-glycerol (4). Unsymmetrically blocked glycerol 4 was prepared from 3 by a procedure similar to that reported by Hanassian and Lavallee.[6] A solution of benzyl ether 3 (2.00 g, 11 mmol), *tert*-butyldiphenylsilyl chloride (3.01 g, 11 mmol), and imidazole (1.50 g, 22 mmol) in 3.6 mL of dry dimethylformamide was allowed to stand at room temperature for 3 h. Ether was added, and the organic phase was extracted three times with water. The ethereal solution was dried over magnesium sulfate, and solvent was removed at reduced pressure. The residue was purified by flash chromatography by elution with ethyl acetate–hexane (3:17, v/v) to yield 4.44 g (96%) of a colorless oil: $[\alpha]^{23}_D$ −1.1° (neat); IR (neat) 3575, 3460, 3070, 3050, 3030, 2935, 2855, 1588, 1494, 1470, 1460, 1453, 1426, 1389, 1360, 1110, 823, 739, 700 cm^{-1}; ^1H NMR (acetone-d_6) 1.08 (9, s, t-Bu CH_3), 3.32–4.22 (5, m, H at C1, C2, and C3), 4.52 (2, s, benzylic CH_2), 7.29 (5, br s, aromatic protons), 7.40 (6, m, silyl phenyl protons), 7.73 ppm (4, m, silyl phenyl protons); mass spectrum (EI) *m/z* 181 (M − $SiPh_2$-*t*-Bu), 91 (CH_2Ph). Anal. Calcd for $C_{26}H_{32}SiO_3$: C, 74.24; H, 7.67. Found: C, 74.03; H, 7.39.

(3*R*,*S*,7*R*,11*R*)-3,7,11,15-Tetramethylhexadecan-1-ol [(3*R*,*S*,7*R*,11*R*)-Phytanol, 5]. Phytanol 5 was obtained from *R,R*-phytol (Accurate Chemical and Scientific Corp.) by catalytic hydrogenation according to published procedures.[9]

(3*R*,*S*,7*R*,11*R*)-3,7,11,15-Tetramethylhexadecan-1-yl Triflate [(3*R*,*S*,7*R*,11*R*)-Phytanyl Triflate, 6]. A solution of 129 mg (0.43 mmol) of phytanol (5)[9] in 1 mL of methylene chloride was slowly added to 155 mg (0.55 mmol) of triflic anhydride and 43.5 mg (0.55 mmol) of pyridine in 2 mL of methylene chloride. The mixture was allowed to stir for 1 h at room temperature; water was added. Layers were separated, and the aqueous layer was extracted with methylene chloride. The combined organic layers were washed with saturated sodium chloride and dried over a mixture of anhydrous sodium carbonate and magnesium sulfate (1:1, v/v). Solvent was removed at reduced pressure to give 191 mg of a light brown viscous oil: IR (neat) 2959, 2870, 2830, 1462, 1418, 1380, 1365, 1250, 1211, 1150, 1035, 935 cm^{-1}; ^1H NMR ($CDCl_3$) 0.83–0.90 (15, CH_3s), 1.20 (24, br s, CH_2 and CH), and 4.55 ppm (2, t, J = 6.0 Hz, protons at C1); ^{19}F NMR ($CDCl_3$) 75.3 ppm (s, CF_3). According to its NMR spectrum, this material was approximately 90% pure and was used without purification.

1-*O*-(*tert*-Butyldiphenylsilyl)-2-*O*-[(3′*R*,*S*,7′*R*,11′*R*)-3′,7′,11′,17′-tetramethylhexadec-1-yl]-3-*O*-benzyl-*sn*-glycerol [1-*O*-(*tert*-Butyldiphenylsilyl)-2-*O*-(3′*R*,*S*,7′*R*,11′*R*)-phytanyl-3-*O*-benzyl-*sn*-glycerol, 7]. A solution of 388 mg (1.3 mmol) of triflate 6 in 12 mL of dry tetrahydrofuran was added to a suspension of 420 mg (1.0 mmol) of 4 and 31 mg (1.3 mmol) of sodium hydride in 12 mL of tetrahydrofuran. The mixture was allowed to stir at room temperature for 3 h before water was added. The resulting mixture was extracted with ether, the ether extract was dried over magnesium sulfate, and solvent was removed at reduced pressure. The residue was purified by flash chromatography by elution with ethyl acetate–hexane (3:97, v/v) to yield 597 mg (85%) of a colorless oil: $[\alpha]^{23}_D$ −4.3° (*c* 5.1, $CHCl_3$); IR (neat) 3070, 3050, 3030, 2955, 2930, 2860, 1589, 1462, 1428, 1377, 1110, 820, 736, 699 cm^{-1}; ^1H NMR ($CDCl_3$) 0.83–0.90 (15, phytanyl CH_3s), 1.06 (9, s, *t*-Bu CH_3s), 1.20 (24, br s, phytanyl

(10) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

(11) Debost, J.-L.; Gelas, J.; Horton, D. *J. Org. Chem.* **1983**, *48*, 1381–1382.

(12) LeCocq, J.; Ballou, C. E. *Biochemistry* **1964**, *3*, 976–980.

CH_2s and CHs), 3.27–3.87 (7, m, phytanyl C1 and glycerol C1, C2, and C3 protons), 4.51 (2, s, benzylic CH_2), 7.27 (5, s benzyl aromatic protons), 7.37 (6, m, silyl phenyl protons), 7.64 ppm (4, m, silyl phenyl protons); mass spectrum (EI) m/z 643 (M – *t*-Bu), 239 (M – $SiPh_2$-*t*-Bu), 91 (CH_2Ph). Anal. Calcd for $C_{46}H_{72}SiO_3$: C, 78.79; H, 10.35. Found: C, 79.03; H, 10.21.

1-*O*-(*tert*-Butyldiphenylsilyl)-2-*O*-[(3′*R*,*S*,7′*R*,11′*R*)-3,7,11,15-tetramethylhexadec-1-yl]-*sn*-glycerol [1-*O*-(*tert*-Butyldiphenylsilyl)-2-*O*-(3′*R*,*S*,7′*R*,11′*R*)-phytanyl-*sn*-glycerol, 8]. A suspension of 565 mg (0.81 mmol) of **7** and 350 mg of 5% palladium on barium sulfate was shaken for 12 h at room temperature under 15 psi of hydrogen. The suspension was filtered, solvent was removed at reduced pressure, and the residue was purified by flash chromatography upon elution with ethyl acetate–hexane (1:9, v/v) to afford 442 mg (90%) of a colorless oil: $[\alpha]^{23}_D$ –9.8° (*c* 5.2, $CHCl_3$); IR (neat) 3452, 3070, 3046, 2957, 2930, 2860, 1590, 1463, 1428, 1378, 1362, 1111, 820, 737, 702 cm^{-1}; ^1H NMR ($CDCl_3$) 0.82–0.90 (15, phytanyl CH_3s) 1.06 (9, s, *t*-Bu CH_3s), 1.20 (24 m, phytanyl CH_2s and CHs), 2.04 (1, br s, hydroxyl proton), 3.17–3.60 (7, m, phytanyl C1 and glycerol C1, C2, and C3 protons), 7.40 (6, m, silyl phenyl protons), 7.65 ppm (4, m, silyl phenyl protons); mass spectrum (EI) m/z 553 (M – *t*-Bu). Anal. Calcd for $C_{39}H_{66}SiO_3$: C, 76.65; H, 10.89. Found: C, 76.61; H, 10.63.

1-*O*-(*tert*-Butyldiphenylsilyl)-2,3-di-*O*-[(3′*R*,*S*,7′*R*,11′*R*)-3′,7′,11′,15′-tetramethylhexadec-1-yl]-*sn*-glycerol [1-*O*-(*tert*-Butyldiphenylsilyl)-2,3-di-*O*-(3′*R*,*S*,7′*R*,11′*R*)-phytanyl-*sn*-glycerol, 9]. A solution of 108 mg (0.36 mmol) of triflate **6** in 2 mL of tetrahydrofuran was added to a suspension of 100 mg (0.16 mmol) of **8** and 14.0 mg (0.34 mmol) of potassium hydride in 2.5 mL of tetrahydrofuran. The suspension was allowed to stir at room temperature for 3 h before water was added, and the resulting mixture was extracted with ether. The combined extracts were dried over magnesium sulfate, and solvent was removed at reduced pressure. The residue was purified by flash chromatography upon elution with ethyl acetate–hexane (3:97, v/v) to yield 124 mg (85%) of a colorless oil: $[\alpha]^{23}_D$ –0.76° (*c* 3.5, $CHCl_3$); IR (neat) 3070, 3060, 2985, 2930, 2861, 1590, 1463, 1428, 1377, 1364, 1113, 824, 739, 703 cm^{-1}; ^1H NMR ($CDCl_3$) 0.84–0.90 (30, phytanyl CH_3s), 1.05 (9, s, *t*-Bu CH_3s), 1.21 (48, br s, phytanyl CH_2s and CHs), 3.24–3.83 (9, m, phytanyl C1 and glyceryl C1, C2, and C3 protons), 7.37 (6, m, silyl phenyl protons), 7.67 ppm (4, m, silyl phenyl protons); mass spectrum (FAB, glycerol matrix, Xe at 7 kV) m/z 834 (M – *t*-Bu + H), 814 (M – Ph + H). Anal. Calcd for $C_{59}H_{106}SiO_3$: C, 79.48; H, 11.98. Found: C, 79.79; H, 11.82.

2,3-Di-*O*-[(3′*R*,*S*,7′*R*,11′*R*)-3′,7′,11′,15′-tetramethylhexadec-1-yl]-*sn*-glycerol [2,3-Di-*O*-(3′*R*,*S*,7′*R*,11′*R*)-phytanyl-*sn*-glycerol, 1]. A 0.28-mL portion of 1 M tetra-*n*-butylammonium fluoride in tetrahydrofuran (Aldrich) was added to 123 mg (0.138 mmol) of **9** in tetrahydrofuran. The mixture was allowed to stir for 30 min before water was added. The resulting mixture was extracted with ether, the combined extracts were dried over magnesium sulfate, and solvent was removed at reduced pressure. The residue was purified by flash chromatography upon elution with ethanol–hexane (1:19, v/v) to yield 87 mg (97%) of a colorless oil: $[\alpha]^{23}_D$ +7.1° (*c* 1.2, $CHCl_3$); IR (neat) 3450, 2955, 2927, 2870, 1461, 1376, 1366, 1115, 1048 cm^{-1}; ^1H NMR ($CDCl_3$) 0.83–0.90 (30, phytanyl CH_3s), 1.22 and 1.27 (48, br s, phytanyl CH_2s and CHs), 2.09 (1, br s, hydroxyl proton), 3.39–3.87 ppm (9, m, phytanyl C1 and glyceryl C1, C2, and C3 protons); ^{13}C NMR ($CDCl_3$) 19.45, 19.52, 19.59, 22.45, 22.55, 24.20, 24.32, 24.64, 27.82, 29.69, 29.73, 32.65, 36.48, 36.56, 36.97, 37.04, 37.17, 37.28, 37.33, 39.25, 63.06, 68.62, 70.13, 70.93, 71.00, 78.30 ppm; mass spectrum (EI) m/z 652 (M), (CI, methane) m/z 653 (M + H). Anal. Calcd for $C_{43}H_{88}O_3$: C, 79.07; H, 13.58. Found: C, 78.83; H, 13.37.

2-*O*-[(3′*R*,*S*,7′*R*,11′*R*)-3′,7′,11′,15′-Tetramethylhexadec-1-yl]-3-*O*-benzyl-*sn*-glycerol [2-*O*-(3′*R*,*S*,7′*R*,11′*R*)-Phytanyl-3-*O*-benzyl-*sn*-glycerol, 10]. The *tert*-butyldiphenylsilyl protecting group in **7** (266 mg, 0.38 mmol) was removed as described for the conversion of **9** to **1**. Flash chromatography using ethyl acetate–hexane (1:4, v/v) gave 158 mg (87%) of a colorless oil: $[\alpha]^{23}_D$ +8.3° (*c* 5.2, $CHCl_3$); IR (neat) 3440, 3090, 3062, 3030, 2955, 2928, 2890, 1462, 1454, 1377, 1366, 1208, 1096, 1049, 1031, 736, 700 cm^{-1}; ^1H NMR ($CDCl_3$) 0.83–0.91 (15, phytanyl CH_3s), 1.20 (24, br s, phytanyl CH_2s and CHs), 2.03 (1, br s, hydroxyl proton), 3.33–3.83 (7, m, phytanyl C1 and glyceryl C1, C2, and C3 protons), 4.50 (2, s, benzylic CH_2), 7.28 ppm (5, s, aromatic protons); mass spectrum (EI) m/z 462 (M), 91 (CH_2Ph). Anal. Calcd for $C_{30}H_{54}O_3$: C, 77.87; H, 11.76. Found: C, 77.83; H, 11.45.

1,2-Di-*O*-[(3′*R*,*S*,7′*R*,11′*R*)-3′,7′,11′,15′-tetramethylhexadec-1-yl]-3-*O*-benzyl-*sn*-glycerol [1,2-Di-*O*-(3′*R*,*S*,7′*R*,11′*R*)-phytanyl-3-*O*-benzyl-*sn*-glycerol, 11]. Alcohol **8** (39 mg, 0.084 mmol) was converted to ether **11** upon treatment with 6.8 mg (0.17 mmol) of potassium hydride and 51 mg (0.17 mmol) of triflate **6** by the procedure used for preparation of **9**. Flash chromatography using ethyl acetate–hexane (1:19, v/v) gave 54 mg (85%) of a colorless oil: $[\alpha]^{23}_D$ –0.4° (*c* 3.5, $CHCl_3$); IR (neat) 3085, 3065, 3030, 2955, 2928, 2870, 1462, 1376, 1365, 1117, 731, 698 cm^{-1}; ^1H NMR ($CDCl_3$) 0.83–0.90 (30, phytanyl CH_3s), 1.20 (48, br s, phytanyl CH_2s and CHs), 3.23–3.70 (9, m, phytanyl C1 and glyceryl C1, C2, and C3 protons), 4.50 (2, s, benzylic CH_2), 7.26 ppm (5, s, aromatic protons); mass spectrum (EI) m/z 651 (M – CH_2Ph), 444 (M – $C_{20}H_{42}O$), 297 ($C_{20}H_{41}O$), 91 (CH_2Ph). Anal. Calcd for $C_{50}H_{94}O_3$; C, 80.79; H, 12.75. Found: C, 80.56; H, 12.93.

1,2-Di-*O*-[(3′*R*,*S*,7′*R*,11′*R*)-3′,7′,11′,15′-tetramethylhexadec-1-yl]-*sn*-glycerol [1,2-Di-*O*-(3′*R*,*S*,7′*R*,11′*R*)-phytanyl-*sn*-glycerol, 2]. The benzyl group in **11** (33 mg, 0.44 mmol) was removed by hydrogenolysis as previously described for conversion of **7** to **8**. Flash chromatography using ethyl acetate–hexane (3:17, v/v) gave 27 mg (94%) of a colorless oil: $[\alpha]^{23}_D$ –7.0° (*c* 2.7, $CHCl_3$); IR (neat) 3450, 2955, 2930, 2870, 1462, 1377, 1367, 1112, 1048 cm^{-1}; ^1H NMR ($CDCl_3$) 0.83–0.90 (30, phytanyl CH_3s), 1.21 (48, br s, phytanyl CH_2s and CHs), 2.14 (1, br s, hydroxyl proton), 3.27–3.91 ppm (9, m, phytanyl C1 and glyceryl C1, C2, and C3 protons); ^{13}C NMR ($CDCl_3$) 19.45, 19.52, 19.59, 22.46, 22.56, 24.21, 24.33, 24.65, 27.83, 29.69, 29.76, 36.48, 36.68, 36.56, 36.95, 37.05, 37.22, 37.29, 37.38, 39.26, 63.09, 68.63, 70.13, 71.00, 78.31 ppm; mass spectrum (CI, methane) m/z 653 ($M + H^+$). Anal. Calcd for $C_{43}H_{88}O_3$: C, 79.07; H, 13.58. Found: C, 79.18; H, 13.79.

Isolation of 1 from *M. thermoautotrophicum* ΔH. Following the procedure of Bligh and Dyer,[7] 63 mg of natural **1** was isolated from 36.2 g of freeze-dried cells, $[\alpha]^{23}_D$ +7.8° (*c* 6.3, $CHCl_3$) [lit $[\alpha]^{21}_D$ +7.8 (*c* 1.96, $CHCl_3$)].[8] The chromatographic mobility under several conditions, IR spectrum, and ^1H NMR spectrum are identical with synthetic **1**. Differences in their ^{13}C NMR spectra are discussed in the results section.

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Registry No. **1** (isomer 1), 23315-10-8; **1** (isomer 2), 99341-12-5; **1** (isomer 3), 99341-13-6; **1** (isomer 4), 99341-14-7; **2** (isomer 1), 99341-19-2; **2** (isomer 2), 99341-20-5; **2** (isomer 3), 99341-21-6; **2** (isomer 4), 99341-22-7; **3**, 56552-80-8; **4**, 99298-07-4; **5** (isomer 1), 18654-63-2; **5** (isomer 2), 99211-81-1; **6** (isomer 1), 99298-08-5; **6** (isomer 2), 99341-06-7; **7** (isomer 1), 99298-09-6; **7** (isomer 2), 99341-07-8; **8** (isomer 1), 99298-10-9; **8** (isomer 2), 99341-08-9; **9** (isomer 1), 99298-11-0; **9** (isomer 2), 99341-09-0; **9** (isomer 3), 99341-10-3; **9** (isomer 4), 99341-11-4; **10** (isomer 1), 99298-12-1; **10** (isomer 2), 99341-15-8; **11** (isomer 1), 95188-80-0; **11** (isomer 2), 99341-16-9; **11** (isomer 3), 99341-17-0; **11** (isomer 4), 99341-18-1.