Total Synthesis of Archaeal 72-Membered Macrocyclic Tetraether Lipids

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Total synthesis of archaeal 72-membered macrocyclic tetraether lipids **3a** and **3b** is reported. The synthesis was principally composed of preparation of the functionalized half-sized diether compounds **11** and **15** first followed by appropriate dimerization through Julia coupling and final macrocyclization of the crucial dialdehydes **23** and **31** by McMurry coupling. This strategy appeared to be advantageous for the stereoselective synthesis of both natural 72-membered tetraether lipids **3a** and **3b** using common synthetic intermediates. In addition, this approach was so designed that its synthetic flexibility would allow construction of unnatural structural variants for physicochemical studies. Also described are the results of differential scanning calorimetric analysis of the synthesized lipids **3a** and **3b**. Both **3a** and **3b** showed almost the same phase behavior with the broad endothermic phase transition at −53 °C. The enthalpy of the phase transition, ΔH, was estimated to be 1.8 and 1.9 kcal/mol for **3a** and **3b**, respectively. The physicochemical as well as polymorphismic properties of **3a** and **3b** turned out to be indistinguishable despite of their regioisomeric structures. The physical structure of the phases in terms of the chemical structure is also discussed.

Introduction

Archaea (archaebacteria) have currently been attracting wide attention due to their evolutionary diversity from eubacteria and eukaryotes.[1] Among the major interests in archaea are unique chemical structures of the membrane core lipids. Archaeal membrane lipids are structurally unique in that the glycerol core is linked to the isoprenoid chains with ethereal bonding as shown in structure of **1**, in contrast to the ester linkages with fatty acids in eubacterial and eukaryotic membrane lipids.[2] These unusual lipids have attracted attention in connection with their physicochemical properties. Several modeling and synthetic studies have been reported in order to investigate the stability, fluidity, and permeability of the archaeal membrane lipids.[3] The most striking features of archaeal membrane lipids are found in the presence of macrocyclic structures as large as 36- and 72-membered rings (**2** and **3ab**) as shown in Figure 1. Concerning to the stereochemistry of these macrocyclic archaeal lipids, Heathcock and co-workers were successful in showing the absolute stereochemistry of the biphytane of the archaeal tetraether lipid by a synthetic approach.[4] In addition, Arigoni *et al*. reported recently that the 72-membered lipids exist as a mixture of regioisomers in terms of the glycerol arrangements such as **3a** and **3b** in several methanogenic and thermophilic archaebacteria such as *Methanobacterium thermoautotrophicum*, *Thermoplasma*, and *Sulfolobus*.[5]

The physical nature of a membrane composed of these macrocyclic lipids is quite intriguing.[3] The 72-membered lipids are considered to form a unimolecular membrane structure, in contrast to the ubiquitous bilayer assembly, or to constitute a trans-membrane orientation.[6] Recently,

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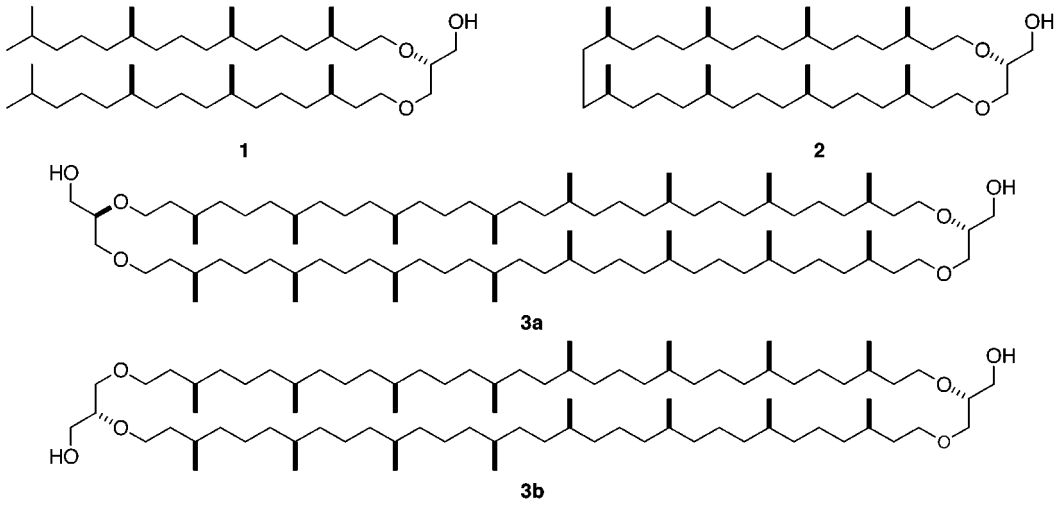

Figure 1. Typical structures of archaeal membrane lipids **1**, **2**, and **3ab**.

we reported the syntheses of the macrocyclic 36-membered lipid found in *Methanococcus jannaschii* and of the desmethylated analogues of 72-membered lipids.[7] Our continuing efforts have now yielded the first total synthesis of archaeal 72-membered macrocyclic tetraether lipids, and we wish to report here the full details of the synthesis.

Results and Discussion

The basic synthetic plan was similar to the preparation of the desmethylated 72-membered lipids.[7e] Thus, the synthesis was principally composed of preparation of the functionalized half-sized diether compounds **11** and **15** first followed by appropriate dimerization through Julia coupling[8] and final macrocyclization of the crucial dialdehydes **23** and **31** by McMurry coupling.[9] This strategy appeared to be advantageous for the stereoselective synthesis of both natural 72-membered tetraether lipids **3a** and **3b** using common synthetic intermediates.

The synthesis started with the bifuctionalized C_{20} isoprenoid unit **4**[7d] as shown in Scheme 1. The mono-TBS ether **4** was oxidized under Swern conditions to give aldehyde **11** (83%), which was subjected to acetal formation with *sn*-1-*O*-benzylglycerol **6**[10] in the presence of *p*-toluenesulfonic acid and $MgSO_4$, followed by deprotection of the TBS group with TBAF, to give the acetal product **7** in 93% yield as a diastereomeric mixture in a ratio of 7:3. After protection of the resulting hydroxyl group with a MPM group, the acetal derivative **8** was treated with DIBAL-H to give a mixture of positionally isomeric monoalkylated benzylglycerol derivatives, which were easily separable by silica gel column chromatography to afford *sn*-2-*O*-alkylated benzylglycerol **9** and *sn*-3-*O*-alkylated benzylglycerol **10** in 50 and 44% yields, respectively.[11] The *sn*-2-*O*-alkylated glycerol **9** was further alkylated *via* its sodium alkoxide with the mesylate derivative[7d] of **4** to afford 2,3-*O*-disubstituted *sn*-1-*O*-benzylglycerol **11** in 86% yield. Subsequent deprotection of the TBS group with TBAF afforded half-sized diether compound **12**. The half-sized lipid **12** was converted into two appropriate coupling precursors, sulfone **13** and aldehyde **14**, which were then coupled together by Julia coupling to lead to a precursor of McMurry coupling. Thus, mesylation of **12** under the usual conditions and subsequent treatment with thiophenol, followed by *m*-CPBA afford the sulfone **13** in 88% yield. The other coupling partner in the Julia method, the aldehyde **14**, was prepared from **12** by Swern oxidation in 96% yield. The *sn*-3-*O*-alkylated glycerol **15** was also manipulated in the same manner as the synthesis of **14** from **11** to give aldehyde **17** in 86% yield (two steps). It should be emphasized here that the key intermediates **13**, **14**, and **17** were prepared from a common precursor.

As shown in Scheme 2, the lithium carbanion prepared from the sulfone **13** with butyllithium was treated with the aldehyde **14** in THF at −25 °C to successfully furnish *β*-hydroxy sulfone **18**.[8] After acetylation to **19**, a reductive elimination reaction of **19** was carried out with an excess amount of SmI_2 in THF and HMPA,[12] which proceeded smoothly to give olefin **20** in an excellent yield (88%) as a mixture of the geometrical isomers. The isomeric ratio was estimated as 85:15 (*E*/*Z*) by ^{13}C NMR. Catalytic hydrogenation of the resulting double bond of **20** with Pd/C leading to **21** was somewhat troublesome. Epimerization of the chiral centers neighboring the double bond was observed. This may be due to a minute amount of residual sulfurous impurity from the prior reaction, because the epimerization ratio varied from time to time. Thus, to secure the stereochemically defined hydrogenation, the olefin **20** was subjected to diimide reduction with potassium azodicarboxylate and

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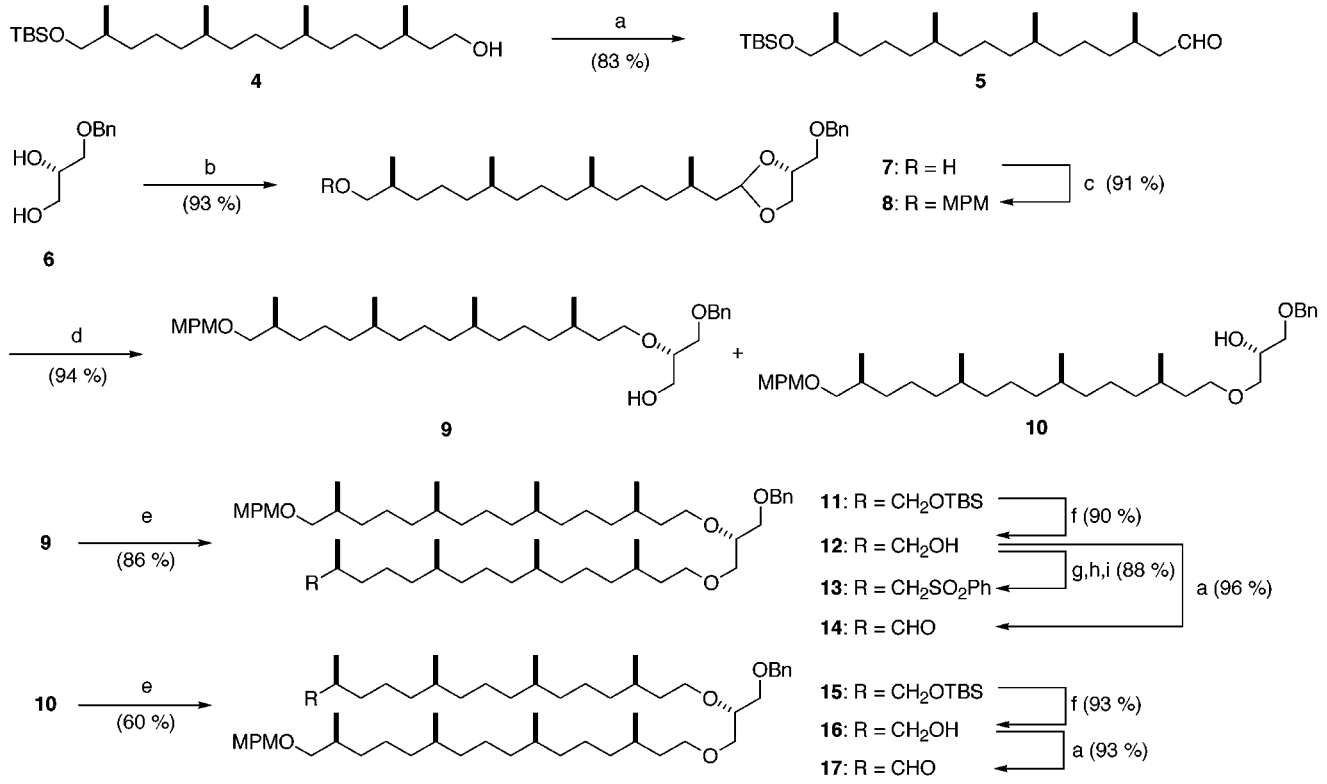
Scheme 1[a]



[a]Reagents: (a) Swern oxidation; (b) (1) compound **5**, *p*-TsOH, $MgSO_4/CH_2Cl_2$, (2) TBAF/THF; (c) NaH, MPMCl/DMF; (d) DIBAH/toluene; (e) NaH, mesylate of **4**/DMSO; (f) TBAF/THF; (g) MsCl, Et_3N/CH_2Cl_2; (h) PhSH, K_2CO_3/DMF; (i) *m*-CPBA/CH_2Cl_2

acetic acid to give **21** in an excellent yield without epimerization. Deprotection of the MPM groups with DDQ in $CH_2Cl_2-H_2O$ was performed to afford diol **22** in 90% yield. The key precursor dialdehyde for McMurry coupling **23** was then prepared from **22** by subsequent oxidation under Swern conditions in 96% yield.

The crucial 72-membered ring formation reaction was performed with the dialdehyde **23** with the aid of a low-valent titanium coupling known as McMurry coupling.[9] The intramolecular coupling of **23** was carried out under high dilution conditions for a prolonged time. The reaction proceeded quite smoothly to yield macrocyclic tetraether **24** in 59% yield as a single isomer of the double bond as was observed in the case of the 36-membered ring formation.[7d] Usually, the yield of this coupling reaction ranged from 50 to 65%. Finally, reduction of the double bond of **24** by diimide reduction again, followed by deprotection of the benzyl group by catalytic hydrogenation over Pd−C, afforded the 72-membered tetraether core lipid **3a** in 62% yield (two steps). The EI-MS spectrum of the product **3a**, *m*/*z* 1301 (M^+) and 1283 ($M^+ - H_2O$), firmly supported the structure.

The synthesis of the positional isomer **3b** started from the sulfone **13** and the aldehyde **17**, and similar manipulations as described above gave the regioisomeric dialdehyde **31** as shown in Scheme 3. A McMurry coupling of the dialdehyde **31** also went smoothly to afford in 66% yield the cyclized product **32** as a single isomer. Reduction and deprotection gave the regioisomeric **3b** in 70%, *m*/*z*: 1301 (M^+), 1283 ($M^+ - H_2O$).

The synthesized 72-membered lipids **3a** and **3b** were in good agreement with the natural 72-membered lipid mixture in all spectral properties including IR, mass, and ^1H and ^{13}C NMR spectra as well as optical rotations. This means that both regioisomeric 72-membered lipids **3a** and **3b** were not distinguishable in usual spectroscopic means. Furthermore, especially in ^{13}C NMR spectra, both **3a** and **3b** showed the same symmetrical spectral pattern, thereby clearly indicating that no epimerization at the α-positions of carbonyl groups or double bonds occurred during the synthesis.

As was mentioned above briefly, the membranes of archaeal tetraether lipids of methanogens and themoacidophiles essentially consist of bipolar monolayer structures in which each lipid molecule spans the entire thickness of the membrane. These structures would be related to the membrane stability at the high growth temperatures of these archaea.[6] The organized structures of these tetraether lipids are intriguing in terms of physiological conditions. Several publications dealt with the structure and polymorphism of a variety of tetraether lipid mixtures extracted from thermoacidophilic archaea as studied by X-ray scattering as well as differential scanning calorimetry.[13] While the nature and characteristic of the lipids comprising a single bipolar macrocyclic isomer is interesting for various aspects, it has been beyond current research due to the lack of availability of such single compounds. The first total synthesis described above has now allowed us to pursue a new area of research, and we describe here our

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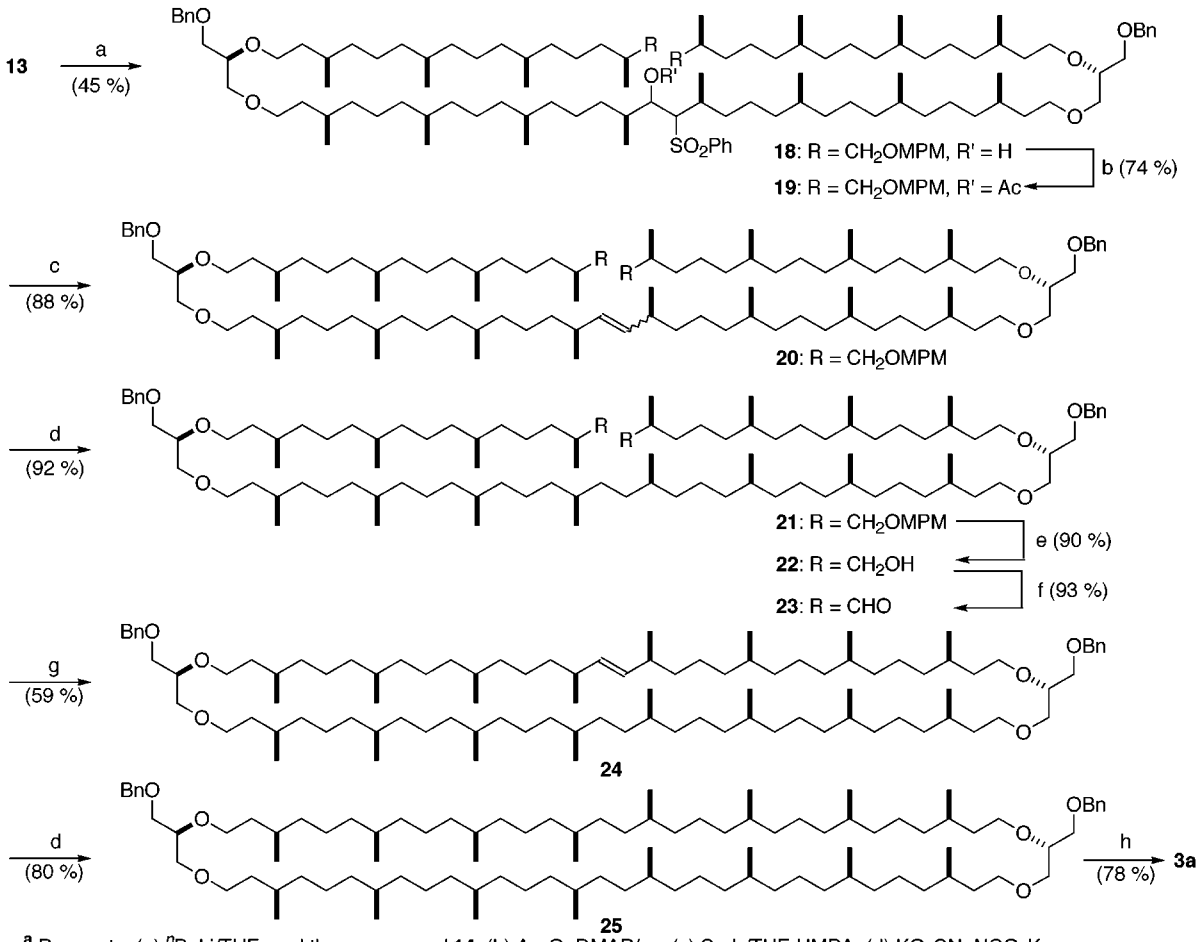
Scheme 2[a]



[a] Reagents: (a) ^{n}BuLi/THF, and then compound **14**; (b) Ac_2O, DMAP/py; (c) SmI_2/THF-HMPA; (d) $KO_2CN{=}NCO_2K$, AcOH/MeOH-EtOAc; (e) DDQ/CH_2Cl_2-H_2O; (f) Swern oxidation; (g) $TiCl_3$, Zn-Cu/DME; (h) H_2, Pd-C/EtOAc

preliminary results of the differential scanning calorimetric analysis of the chemically pure synthetic tetraether lipids **3a** and **3b**.

Differential scanning calorimetric thermograms of the synthesized **3a** and **3b** in the absence of water are depicted in Figure 2. The lipids were immiscible with water. While the peaks were small and broadened, both compounds clearly showed the existence of endothermic phase transition at low temperature. The enthalpy, ΔH, the corresponding entropy variation, ΔS, and the transition temperatures, T_c, are collected in Table 1. The facts that both **3a** and **3b** indicated almost the same phase behavior as shown in Figure 2 and Table 1 suggest that the physicochemical as well as polymorphismic properties of **3a** and **3b** are indistinguishable despite of their regioisomeric structures.

It was reported that a mixture of tetraether lipids, in which each biphytanyl chain contains 0 to 4 cyclopentane rings, shows a lamellar phase ($L_{\beta'}$) in the temperature range from −19 to 19 °C under dry conditions and the lamellar structure melts above 19 °C by the X-ray scattering method.[13b] In addition, it is known that the phase transition temperature is shifted toward lower temperature as the number of cyclopentane rings in the tetraether structure decreases.[13] Calorimetric measurements on **3a** and **3b** indicated the presence of phase transitions at low temperature, such as −53 °C, which might be characteristic of the melting transition in the absence of water. Although we do not have a rationale for the detailed polymorphism of **3a** and **3b** at the present time, it seems most likely that the hydrocarbon chains of both **3a** and **3b** are stiff and parallel as in a lamellar structure below the transition temperature and the ordered structures collapse above the phase transition.

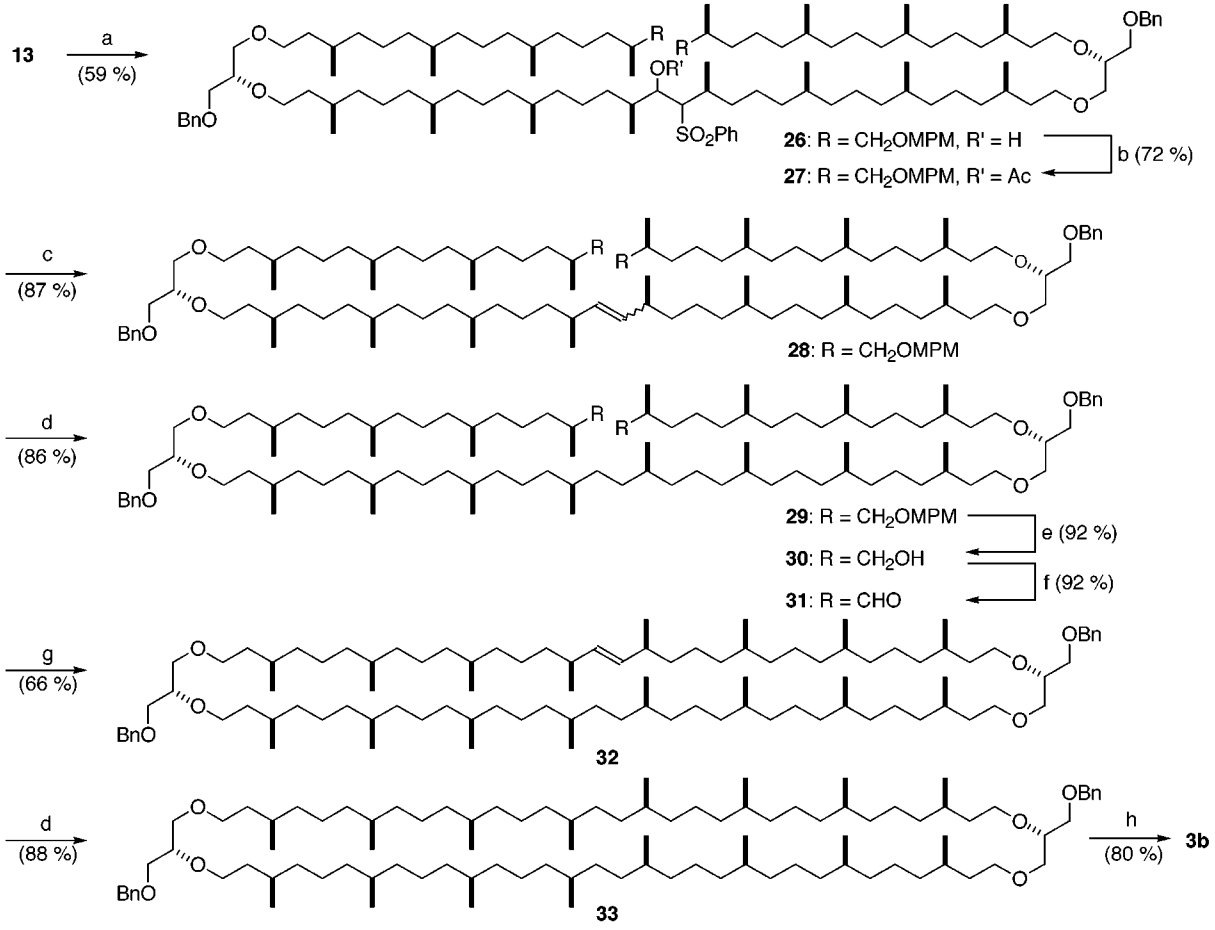
In summary, we have accomplished the first total synthesis of the 72-membered macrocyclic tetraether lipids using McMurry coupling. These results may stimulate investigations to gain more insight into the characteristics of the thermophilic archaeal macrocyclic diether lipids. Also described are the preliminary results of calorimetric analysis of the synthesized tetraether lipids **3a** and **3b**. Further characterizations composed of these lipids are currently in progress and will be reported in due course.

Experimental Section

General Information. All reactions, except for catalytic hydrogenation reactions, were carried out in an inert (Ar or N_2) atmosphere. Column chromatography was carried out with Kieselgel 60 (70−230 mesh or 230−400 mesh, Merck). THF and DME were distilled from sodium/benzophenone ketyl prior to use. Pyridine and triethylamine were distilled from potassium hydroxide. DMF was distilled from $CaSO_4$, and benzene, DMSO, CH_2Cl_2, HMPA, and toluene were distilled from calcium hydride.

(3*R*,7*R*,11*S*,15*S*)-16-[(*tert*-Butyldimethylsilyl)oxy]-3,7,11,15-tetramethylhexadecanal (5). To a stirred solution of oxalyl chloride (2.69 g, 21.2 mmol) in CH_2Cl_2 (90 mL) was slowly added DMSO (4.0 mL, 56.6 mmol) at −78 °C. The

Scheme 3[a]



[a] Reagents: (a) ^{n}BuLi/THF, and then compound **17**; (b) Ac_2O, DMAP/py; (c) SmI_2/THF-HMPA; (d) $KO_2CN{=}NCO_2K$, AcOH/MeOH-EtOAc; (e) DDQ/CH_2Cl_2-H_2O; (f) Swern oxidation; (g) $TiCl_3$, Zn-Cu/DME; (h) H_2, Pd-C/EtOAc

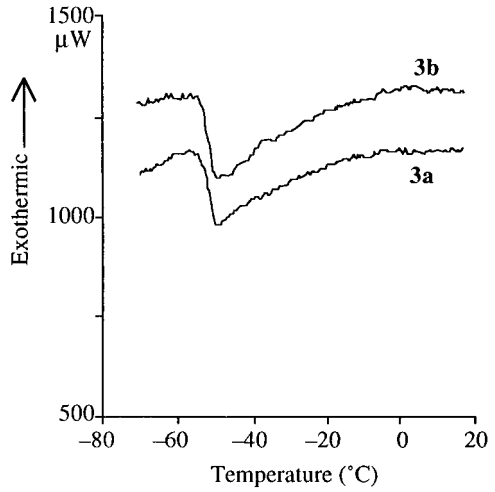


Figure 2. Differential scanning calorimetric thermograms of the synthesized lipids **3a** and **3b** performed at a scan rate of 2 °C/min on warming.

Table 1. Phase Transitions of the Lipids 3a and 3b[a]

lipid	T_c (°C)	ΔH (kcal mol^{-1})	ΔS (cal mol^{-1} deg^{-1})
3a	−53.4	1.8	8.4
3b	−53.5	1.9	8.6

[a] Thermograms were scanned at the temperature range from −80 to 40 °C at a scanning rate of 2 °C/min. The enthalpy, ΔH, the corresponding entropy variation, ΔS, and the transition temperatures, T_c, are given for **3a** and **3b**.

mixture was stirred for 45 min. A solution of **4** (6.07 g, 14.2 mmol) in CH_2Cl_2 (26 mL) was added dropwise over 5 min. The mixture was stirred for 30 min and warmed to −60 °C, and stirring was continued for 1.5 h. Then, Et_3N (9.8 mL, 70.7 mmol) was added dropwise over 5 min. The mixture was gradually warmed to room temperature, and a saturated aqueous NH_4Cl solution was added. The mixture was extracted three times with EtOAc. The combined organic phase was washed with saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was chromatographed over silica gel with hexane−EtOAc (50:1) to give aldehyde **5** (5.02 g, 83%) as an oil: $[\alpha]^{27}_D$ +4.45 (*c* 1.22, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.07 (s, 6H), 0.83−0.90 (m, 18H), 0.98 (d, J = 5.1 Hz, 3H), 1.00−1.43 (m, 20H), 1.58 (m, 1H), 2.05 (m, 1H), 2.23 (ddd, J = 2.7, 7.8, 16.1 Hz, 1H), 2.40 (ddd, J = 1.7, 5.4, 15.6 Hz, 1H), 3.35 (dd, J = 6.6, 9.8 Hz, 1H), 3.45 (dd, J = 5.9, 9.8 Hz, 1H), 9.76 (dd, J = 1.7, 2.7 Hz, 1H); ^{13}C NMR (75 MHz) δ −5.30, 16.79, 18.35, 19.70, 19.75, 20.01, 24.42, 24.48, 25.95, 28.18, 32.73, 33.48, 35.74, 37.05, 37.23, 37.33, 51.05, 68.41, 203.22; IR (neat) 775, 837, 1095, 1252, 1730, 2856, 2927, 2954 cm^{-1}. Anal. Calcd for $C_{26}H_{54}O_2Si$: C, 73.17; H, 12.75. Found: C, 73.13; H, 12.93.

(4*R*)-4-[(Benzyloxy)methyl]-2-[(2*R*,6*R*,10*S*,14*S*)-15-hydroxy-2,6,10,14-tetramethylpentadecanyl]-1,3-dioxolane (7). A mixture of **5** (4.90 g, 11.5 mmol), 1-*O*-benzyl-*sn*-glycerol **6** (2.40 g, 13.3 mmol), *p*-toluenesulfonic acid (146 mg, 0.84 mmol), and $MgSO_4$ (1.40 g, 11.7 mmol) in CH_2Cl_2 (40 mL) was stirred for 12 h at room temperature. The mixture was filtered, EtOAc and saturated aqueous $NaHCO_3$ were added to the filtrate, and the organic phase was separated. The aqueous phase was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na_2-

SO_4), filtered, and concentrated to dryness. The residue was dissolved in THF (40 mL), and a solution of TBAF (17.4 mL, 1 M in THF, 17.4 mmol) was added. The mixture was stirred for 3.5 h at room temperature. After concentration, the residue was chromatographed over silica gel with hexane−EtOAc (7:1) to give oily **7** as a 7:3 mixture of diastereomers (5.09 g, 93%): ^{1}H NMR (300 MHz) δ 0.80−0.95 (m, 12H), 0.97−1.74 (m, 25H), 3.38−3.59 (m, 4H), 3.64 (dd, J = 6.8, 8.0 Hz, 0.3H), 3.79 (dd, J = 5.4, 8.3 Hz, 0.7H), 3.90 (dd, J = 6.8, 8.3 Hz, 0.7H), 4.12 (dd, J = 6.6, 8.3 Hz, 0.3H), 4.18−4.33 (m, 1H), 4.57 (s, 0.6H), 4.58 (s, 1.4H), 4.94 (t, J = 4.9 Hz, 0.7H), 5.03 (dd, J = 4.4, 5.9 Hz, 0.3H), 7.22−7.35 (m, 5H); ^{13}C NMR (75 MHz) δ 16.60, 19.72, 19.85, 19.93, 24.12, 24.34, 29.21, 32.68, 33.43, 35.72, 37.18, 37.25, 37.28, 37.57, 37.67, 40.98, 41.11, 67.34, 67.37, 68.25, 68.31, 70.45, 71.03, 73.41, 74.30, 74.57, 103.73, 104.28, 127.61, 127.67, 127.69, 128.35, 137.87; IR (neat) 698, 735, 982, 1030, 1103, 1128, 1377, 1456, 2860, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{30}H_{52}O_4$: C, 75.58; H, 10.99. Found: C, 75.78; H, 11.29.

(4*R*)-4-[(Benzyloxy)methyl]-2-[(2*R*,6*R*,10*S*,14*S*)-15-[(4-methoxybenzyl)oxy]-2,6,10,14-tetramethylpentadecanyl]-1,3-dioxolane (8). To prewashed NaH (630 mg, 6.55 mmol) was added a solution of acetal **7** (4.99 g, 10.5 mmol) in DMF (30 mL). The mixture was stirred for 30 min at room temperature, and 4-methoxybenzyl chloride (2.85 mL, 20.9 mmol) was added. After 15 min of stirring at room temperature, the mixture was warmed to 40 °C, and stirring was continued at the same temperature for 3 h. After the solution was cooled to 0 °C, hexane and water were added to the mixture. The layers were separated, and the aqueous layer was extracted four times with hexane. The organic phase was washed with saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was chromatographed over silica gel with hexane−EtOAc (100:1−20:1) to give oily **8** (5.67 g, 91%): ^{1}H NMR (300 MHz) δ 0.80−0.95 (m, 12H), 0.97−1.78 (m, 24H), 3.20 (dd, J = 6.8, 9.0 Hz, 1H), 3.30 (dd, J = 5.9, 9.0 Hz, 1H), 3.44 (dd, J = 5.9, 9.8 Hz, 0.7H), 3.49 (dd, J = 4.9, 10.0 Hz, 0.3H), 3.55 (dd, J = 5.6, 9.8 Hz, 0.7H), 3.58 (dd, J = 5.4, 10.0 Hz, 0.3H), 3.63 (dd, J = 7.1, 8.3 Hz, 0.3H), 3.78 (dd, J = 5.3, 8.0 Hz, 0.7H), 3.80 (s, 3H), 3.89 (dd, J = 7.1, 8.0, 0.7H), 4.12 (dd, J = 6.9, 8.3 Hz, 0.3H), 4.18−4.32 (m, 1H), 4.43 (s, 2H), 4.57 (s, 0.6H), 4.58 (s, 1.4H), 4.94 (t, J = 5.1 Hz, 0.7H), 5.03 (dd, J = 4.4, 5.6 Hz, 0.3H), 6.87 (dt, J = 8.8, 2.2 Hz, 2H), 7.22−7.35 (m, 7H); ^{13}C NMR (75 MHz) δ 17.27, 19.80, 19.94, 20.02, 24.23, 24.40, 24.50, 29.32, 32.82, 33.49, 34.06, 37.31, 37.36, 37.41, 37.66, 37.77, 41.10, 41.21, 55.29, 67.45, 67.48, 70.55, 71.14, 72.63, 73.52, 74.40, 74.66, 75.79, 103.82, 104.37, 113.72, 127.72, 127.76, 127.80, 128.45, 128.51, 129.14, 130.96, 137.98, 159.04; IR (neat) 698, 737, 820, 978, 1038, 1097, 1173, 1248, 1302, 1362, 1377, 1464, 1514, 1587, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{38}H_{60}O_5$: C, 76.47; H, 10.13. Found: C, 76.50; H, 10.37.

1-*O*-Benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol (9) and 1-*O*-Benzyl-3-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol (10). A solution of DIBAH (23.4 mL, 1 M in toluene, 23.4 mmol) was added to a solution of **8** (5.64 g, 9.42 mmol) in toluene (20 mL) at −78 °C. The mixture was stirred for 20 min at the same temperature and then at 0 °C for 26 h. The reaction was quenched by addition of saturated aqueous NH_4Cl. After 10 min, ether and 2 N HCl were added. The etherial layer was separated, and the aqueous phase was extracted three times with ether. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was purified by flash chromatography over silica gel with hexane−EtOAc (5:1) to give less mobile product **9** (2.81 g, 50%) and more mobile product **10** (2.47 g, 44%). **9**: $[\alpha]^{27}_D$ −3.71 (*c* 1.38, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.95 (m, 12H), 0.97−1.83 (m, 24H), 2.19 (br, 1H), 3.20 (dd, J = 6.8, 9.0 Hz, 1H), 3.30 (dd, J = 6.1, 9.0 Hz, 1H), 3.45−3.76 (m, 7H), 3.78 (s, 3H), 4.42 (s, 2H), 4.55 (s, 2H), 6.87 (dt, J = 8.8, 2.2 Hz, 2H), 7.22−7.35 (m, 7H); ^{13}C NMR (75 MHz) δ 17.19, 19.65, 19.73, 24.31, 24.42, 29.78, 32.73, 32.75, 33.41, 33.98, 37.03, 37.28, 37.30, 37.34, 37.45, 55.18, 62.80, 68.64, 69.98, 72.55, 73.46, 75.71, 78.49, 113.66, 127.58, 127.64, 128.35, 129.03, 130.90, 138.00, 158.99; IR (neat) 698, 735, 820, 1039, 1095, 1173, 1248, 1302, 1363, 1377, 1462, 1514, 1612, 2858, 2925, 2951, 3452 cm^{-1}. Anal. Calcd for $C_{38}H_{62}O_5$: C, 76.21; H, 10.43. Found: C, 76.28; H, 10.58. **10**: $[\alpha]^{27}_D$ +1.49 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.95 (m, 12H), 0.97−1.81 (m, 24H), 2.50 (br, 1H), 3.20 (dd, J = 6.8, 9.0 Hz, 1H), 3.29 (dd, J = 5.9, 9.0 Hz, 1H), 3.43−3.59 (m, 6H), 3.80 (s, 3H), 3.99 (m, 1H), 4.43 (s, 2H), 4.56 (s, 2H), 6.87 (dt, J = 8.8, 2.2 Hz, 2H), 7.22−7.35 (m, 7H); ^{13}C NMR (75 MHz) δ 17.21, 19.69, 19.76, 24.34, 24.46, 29.88, 32.78, 32.80, 33.44, 34.01, 36.55, 37.32, 37.34, 37.36, 37.39, 37.48, 55.25, 69.52, 69.98, 71.38, 71.79, 72.58, 73.43, 113.68, 127.71, 128.41, 129.10, 130.91, 138.00, 159.00; IR (neat) 698, 735, 820, 1038, 1097, 1111, 1173, 1248, 1302, 1362, 1377, 1456, 1514, 1612, 2858, 2925, 2951, 3452 cm^{-1}. Anal. Calcd for $C_{38}H_{62}O_5$: C, 76.21; H, 10.43. Found: C, 76.23; H, 10.72.

1-*O*-Benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-3-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(*tert*-butyldimethylsilyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol (11). To prewashed NaH (171 mg, 7.13 mmol) was added a solution of **9** (2.13 g, 3.56 mmol) in DMSO (18 mL). The mixture was stirred for 1 h at room temperature, and a solution of the mesylate[7d] of **4** (1.78 g, 3.52 mmol) in DMSO (13 mL) was added. The mixture was stirred for 5 h at room temperature. After the solution was cooled to 0 °C, EtOAc and water were added to the mixture. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic phase was washed with saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was chromatographed over silica gel with hexane−EtOAc (20:1) to give **11** (3.05 g, 86%) as an oil: $[\alpha]^{26}_D$ +2.60 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.03 (s, 6H), 0.80−0.95 (m, 33H), 0.97−1.81 (m, 48H), 3.20 (dd, J = 6.8, 9.0 Hz, 1H), 3.30 (dd, J = 6.1, 9.0 Hz, 1H), 3.35 (dd, J = 6.6, 9.8 Hz, 1H), 3.41−3.65 (m, 10H), 3.79 (s, 3H), 4.43 (s, 2H), 4.55 (s, 2H), 6.87 (dt, J = 8.8, 2.2 Hz, 2H), 7.22−7.35 (m, 7H); ^{13}C NMR (75 MHz) δ −5.37, 16.79, 17.20, 18.32, 19.66, 19.69, 19.73, 24.34, 24.45, 25.93, 29.81, 29.90, 32.74, 32.77, 32.80, 33.44, 33.51, 34.02, 35.75, 36.64, 37.10, 37.32, 37.39, 37.51, 55.20, 68.39, 68.86, 69.95, 70.35, 70.80, 72.58, 73.33, 75.74, 77.96, 113.68, 127.44, 127.53, 128.26, 129.04, 130.95, 138.44, 159.02; IR (neat) 696, 735, 775, 837, 1099, 1248, 1362, 1377, 1462, 1514, 1612, 2856, 2927, 2952 cm^{-1}. Anal. Calcd for $C_{64}H_{116}O_6Si$: C, 76.13; H, 11.58. Found: C, 76.28; H, 11.88.

1-*O*-Benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-3-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-hydroxy-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol (12). A solution of TBAF (4.45 mL, 1 M in THF, 4.45 mmol) was added to a solution of **11** (2.99 g, 2.97 mmol) in THF (20 mL). The mixture was stirred for 10 h at room temperature and concentrated *in vacuo*. The residue was chromatographed over silica gel with hexane−EtOAc (8:1) to give **12** (2.39 g, 90%) as an oil: $[\alpha]^{24}_D$ +0.84 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.95 (m, 24H), 0.97−1.80 (m, 49H), 3.19 (dd, J = 6.8, 9.0 Hz, 1H), 3.30 (dd, J = 6.1, 9.0 Hz, 1H), 3.37−3.65 (m, 11H), 3.80 (s, 3H), 4.43 (s, 2H), 4.55 (s, 2H), 6.87 (dt, J = 8.8, 2.2 Hz, 2H), 7.22−7.35 (m, 7H); ^{13}C NMR (75 MHz) δ 16.64, 17.21, 19.68, 19.71, 19.76, 24.36, 24.39, 24.43, 24.48, 29.82, 29.90, 32.75, 32.79, 32.82, 33.45, 33.48, 34.03, 35.78, 36.63, 37.10, 37.31, 37.36, 37.40, 37.52, 37.54, 55.24, 68.34, 68.88, 69.97, 70.33, 70.80, 72.80, 73.35, 75.76, 77.95, 113.69, 127.48, 127.57, 128.29, 129.08, 130.94, 138.43, 159.02; IR (neat) 698, 735, 820, 1039, 1099, 1111, 1248, 1377, 1462, 1514, 1612, 2858, 2925, 2951, 3465 cm^{-1}. Anal. Calcd for $C_{58}H_{102}O_6$: C, 77.80; H, 11.48. Found: C, 77.78; H, 11.58.

1-*O*-Benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-3-*O*-[(3*R*,7*R*,11*S*,15*S*)-3,7,11,15-tetramethyl-16-(phenylsulfonyl)-hexadecanyl]-*sn*-glycerol (13). To a solution of **12** (1.56 g, 1.74 mmol) and triethylamine (0.361 mL, 2.61 mmol) in CH_2Cl_2 (5 mL) was added methanesulfonyl chloride (0.162 mL, 2.09 mmol) at 0 °C, and the mixture was stirred for 1.5 h at the same temperature. EtOAc and water were added, and the

organic phase was separated. The aqueous phase was extracted three times with EtOAc. The combined organic phase was washed with saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The resulting residue was dissolved in DMF (10 mL), K_2CO_3 (337 mg, 2.44 mmol) and thiophenol (0.282 mL, 2.76 mmol) were added, and the resulting mixture was stirred for 30 h at room temperature. Water and hexane were added, and the organic phase was separated. The aqueous phase was extracted five times with hexane. The combined organic phase was successively washed with 2 N HCl, saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was dissolved in CH_2Cl_2 (19 mL), and 3-chloroperbenzoic acid (1.16 g, 6.75 mmol) was added at 0 °C. The mixture was stirred for 7 h at 0 °C. A saturated aqueous Na_2SO_3 solution was added, and the mixture was stirred for 30 min. The mixture was extracted with EtOAc, and the layers were separated. The aqueous phase was extracted three times with EtOAc. The combined organic phase was successively washed with 10% aqueous NaOH, saturated aqueous Na_2SO_3, and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was chromatographed over silica gel with hexane−EtOAc (10:1) to give phenyl sulfone **13** (1.56 g, 88%) as an oil: $[\alpha]^{21}_D$ +5.22 (*c* 0.58, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.97 (m, 24H), 0.97−1.82 (m, 47H), 2.07 (m, 1H), 2.92 (dd, J = 8.1, 14.1 Hz, 1H), 3.08 (dd, J = 4.4, 14.1 Hz, 1H), 3.20 (dd, J = 6.8, 9.0 Hz, 1H), 3.30 (dd, J = 5.9, 9.0 Hz, 1H), 3.80 (s, 3H), 4.43 (s, 2H), 4.55 (s, 2H), 6.87 (dt, J = 8.8, 2.2 Hz, 2H), 7.22−7.35 (m, 7H), 7.56 (m, 2H), 7.64 (m, 1H), 7.91 (m, 2H); ^{13}C NMR (75 MHz) δ 17.31, 19.73, 19.77, 19.80, 19.85, 20.04, 23.88, 24.45, 24.53, 24.56, 28.68, 29.78, 29.99, 32.76, 32.87, 32.91, 34.11, 36.72, 36.90, 37.16, 37.19, 37.42, 37.48, 37.62, 55.34, 62.66, 68.97, 70.06, 70.40, 70.87, 72.68, 73.44, 75.84, 78.04, 113.77, 127.58, 127.66, 127.94, 128.38, 129.17, 129.32, 133.56, 138.52, 159.10; IR (neat) 600, 690, 737, 822, 1038, 1088, 1099, 1111, 1149, 1248, 1306, 1378, 1462, 1514, 1612, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{64}H_{106}O_7S$: C, 75.39; H, 10.48. Found: C, 75.27; H, 10.68.

1-*O*-Benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-3-*O*-[(3*R*,7*R*,11*S*,15*S*)-15-formyl-3,7,11,15-tetramethylpentadecanyl]-*sn*-glycerol (14). To a stirred solution of oxalyl chloride (216 mg, 1.70 mmol) in CH_2Cl_2 (11 mL) was added DMSO (0.24 mL, 3.38 mmol) at −78 °C. The mixture was stirred for 1 h. A solution of **12** (764 mg, 0.853 mmol) in CH_2Cl_2 (8 mL) was added dropwise over 5 min. The mixture was stirred for 15 min at −78 °C and then for 1.5 h at −60 °C. Then, Et_3N (0.78 mL, 5.63 mmol) was added dropwise over 5 min. The mixture was warmed gradually to room temperature, and saturated aqueous NH_4Cl was added. The mixture was extracted three times with EtOAc. The combined organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was chromatographed over silica gel with hexane−EtOAc (9:1) to give aldehyde **14** (733 mg, 96%) as an oil: $[\alpha]^{24}_D$ +6.85 (*c* 0.957, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.95 (m, 24H), 0.97−1.80 (m, 48H), 2.33 (ddd, J = 2.0, 6.6, 13.2 Hz, 1H), 3.20 (dd, J = 6.8, 9.0 Hz, 1H), 3.30 (dd, J = 6.0, 9.0 Hz, 1H), 3.41−3.65 (m, 9H), 3.80 (s, 3H), 4.43 (s, 2H), 4.55 (s, 2H), 6.87 (dt, J = 8.8, 2.2 Hz, 2H), 7.22−7.35 (m, 7H), 9.61 (d, J = 2.0 Hz, 1H); ^{13}C NMR (75 MHz) δ 13.35, 17.21, 19.64, 19.67, 19.71, 19.75, 24.35, 24.39, 24.44, 24.46, 29.81, 29.89, 30.87, 32.64, 32.78, 32.80, 33.44, 34.02, 36.63, 36.99, 37.09, 37.32, 37.36, 37.39, 37.51, 46.33, 55.22, 68.87, 69.95, 70.32, 70.79, 72.58, 73.34, 75.74, 77.95, 113.68, 127.47, 127.55, 128.28, 129.06, 130.93, 138.43, 159.01, 205.33; IR (neat) 698, 735, 820, 1039, 1099, 1111, 1248, 1377, 1462, 1514, 1612, 1728, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{58}H_{100}O_6$: C, 77.97; H, 11.28. Found: C, 78.27; H, 11.58.

1-*O*-Benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(*tert*-butyldimethylsilyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-3-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol (15). Compound **10** (915 mg, 1.53 mmol) was treated in the same manner as described for the preparation of **11** to give **15** (911 mg, 60%) as an oil: $[\alpha]^{22}_D$ +1.90 (*c* 0.935, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.04 (s, 6H), 0.80−0.95 (m, 33H), 0.97−1.81 (m, 48H), 3.20 (dd, J = 6.6, 9.0 Hz, 1H), 3.30 (dd, J = 5.9, 9.0 Hz, 1H), 3.35 (dd, J = 6.6, 9.5 Hz, 1H), 3.40−3.65 (m, 10H), 3.80 (s, 3H), 4.43 (s, 2H), 4.55 (s, 2H), 6.87 (dt, J = 8.8, 2.2 Hz, 2H), 7.22−7.35 (m, 7H); ^{13}C NMR (75 MHz) δ −5.36, 16.80, 17.21, 18.35, 19.67, 19.71, 19.75, 24.35, 24.47, 25.96, 29.77, 29.88, 32.75, 32.78, 32.81, 33.44, 33.50, 34.01, 35.75, 36.62, 37.09, 37.32, 37.39, 37.51, 55.22, 68.41, 68.87, 69.95, 70.29, 70.76, 72.58, 73.33, 75.73, 77.92, 113.67, 127.48, 127.56, 128.28, 129.07, 130.91, 138.41, 158.99; IR (neat) 696, 735, 775, 837, 1099, 1248, 1362, 1377, 1462, 1514, 1612, 2856, 2927, 2952 cm^{-1}. Anal. Calcd for $C_{64}H_{116}O_6Si$: C, 76.13; H, 11.58. Found: C, 75.93; H, 11.82.

1-*O*-Benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-hydroxy-3,7,11,15-tetramethylhexadecanyl]-3-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol (16). Compound **15** (859 mg, 0.85 mmol) was treated in the same manner as described for the preparation of **12** to give **16** (706 mg, 93%) as an oil: $[\alpha]^{25}_D$ +0.05 (*c* 0.717, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.95 (m, 24H), 0.97−1.80 (m, 49H), 3.20 (dd, J = 6.8, 8.8 Hz, 1H), 3.30 (dd, J = 6.1, 8.8 Hz, 1H), 3.40 (dd, J = 6.6, 10.2 Hz, 1H), 3.43−3.64 (m, 10H), 3.80 (s, 3H), 4.43 (s, 2H), 4.55 (s, 2H), 6.87 (dt, J = 8.8, 2.2 Hz, 2H), 7.22−7.35 (m, 7H); ^{13}C NMR (75 MHz) δ 16.62, 17.20, 19.66, 19.70, 19.75, 24.34, 24.38, 24.40, 24.45, 29.79, 29.87, 32.73, 32.77, 32.80, 33.43, 33.46, 33.99, 35.75, 36.60, 37.06, 37.23, 37.28, 37.34, 37.50, 55.21, 68.33, 68.86, 69.95, 70.27, 70.75, 72.57, 73.32, 75.73, 77.91, 113.66, 127.48, 127.56, 128.27, 129.07, 130.88, 138.38, 158.99; IR (neat) 698, 735, 820, 1039, 1099, 1111, 1248, 1377, 1462, 1514, 1612, 2858, 2925, 2951, 3473 cm^{-1}. Anal. Calcd for $C_{58}H_{102}O_6$: C, 77.80; H, 11.48. Found: C, 77.77; H, 11.72.

1-*O*-Benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-15-formyl-3,7,11,15-tetramethylpentadecanyl]-3-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol (17). Compound **16** (546 mg, 0.611 mmol) was treated in the same manner as described for **14** to give aldehyde **17** (603 mg, 93%) as an oil: $[\alpha]^{23}_D$ +7.20 (*c* 0.840, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.95 (m, 24H), 0.97−1.80 (m, 48H), 2.33 (ddd, J = 2.0, 6.6, 13.2 Hz, 1H), 3.20 (dd, J = 6.8, 9.0 Hz, 1H), 3.30 (dd, J = 5.9, 9.0 Hz, 1H), 3.41−3.65 (m, 9H), 3.80 (s, 3H), 4.43 (s, 2H), 4.55 (s, 2H), 6.87 (dt, J = 8.8, 2.2 Hz, 2H), 7.22−7.35 (m, 7H), 9.61 (d, J = 2.0 Hz, 1H); ^{13}C NMR (75 MHz) δ 13.34, 17.20, 19.63, 19.66, 19.70, 19.73, 24.34, 24.39, 24.43, 24.45, 29.81, 29.89, 30.86, 32.63, 32.76, 32.78, 33.43, 34.00, 36.62, 36.98, 37.09, 37.37, 37.45, 37.50, 46.32, 55.21, 68.86, 69.95, 70.32, 70.77, 72.58, 73.33, 75.73, 77.94, 113.68, 127.46, 127.54, 128.27, 129.06, 130.92, 138.42, 159.00, 205.34; IR (neat) 698, 735, 820, 1039, 1101, 1111, 1248, 1377, 1462, 1514, 1612, 1728, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{58}H_{100}O_6$: C, 77.97; H, 11.28. Found: C, 78.11; H, 11.38.

3,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-16-Hydroxy-3,7,11,15,18,22,26,30-octamethyl-17-(phenylsulfonyl)dotriacontane-1,32-diyl]bis{1-*O*-benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol} (18). A solution of butyllithium (0.59 mL, 1.47 M in hexane, 0.867 mmol) was added dropwise to a stirred solution of **13** (807 mg, 0.792 mmol) in THF (7 mL) over 5 min at −78 °C. After 15 min at −78 °C, the mixture was warmed to 0 °C, stirred for 15 min, and then recooled to −25 °C. A solution of **14** (700 mg, 0.784 mmol) in THF (7 mL) was added. After 1 h at −25 °C, saturated aqueous NH_4Cl was added. The mixture was extracted three times with ether. The combined organic phase was washed with saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was purified by flash chromatography over silica gel with hexane−ether (4:1) to give oily **18** (739 mg, 45%) as a mixture of diastereomers: ^{1}H NMR (300 MHz) δ 0.74−0.97 (m, 48H), 0.97−1.82 (m, 95H), 2.00−2.40 (m, 1H), 3.05−3.77 (m, 19.7H), 3.20 (dd, J = 6.8, 9.0 Hz, 2H), 3.30 (dd, J = 6.1, 9.0 Hz, 2H), 3.80 (s, 6H), 4.10 (m, 0.3H), 4.43 (s, 4H), 4.55 (s, 4H), 6.87 (dt, J = 8.8, 2.2 Hz, 4H), 7.22−7.35 (m, 14H), 7.56 (m, 2H), 7.64 (m, 1H), 7.91 (m, 2H); ^{13}C NMR (75 MHz) δ 17.22, 19.68, 19.71, 19.76, 24.36, 24.48, 29.84, 29.93, 32.79, 32.82, 33.46, 34.03, 36.66, 37.11, 37.34, 37.41, 37.54, 55.24, 68.89, 69.98, 70.35, 70.81, 72.59, 73.36, 75.76,

77.97, 113.70, 127.48, 127.57, 128.28, 129.02, 129.07, 130.96, 138.45, 159.04; IR (neat) 696, 733, 820, 1039, 1099, 1111, 1248, 1302, 1377, 1462, 1514, 1612, 2856, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{122}H_{206}O_{13}S$: C, 76.60; H, 10.85. Found: C, 76.51; H, 11.08.

3,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-16-Acetoxy-3,7,11,15,18,22,26,30-octamethyl-17-(phenylsulfonyl)dotriacontane-1,32-diyl]bis{1-*O*-benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol} (19). A mixture of **18** (728 mg, 0.380 mmol), acetic anhydride (0.50 mL, 5.3 mmol), DMAP (64 mg, 0.53 mmol), and pyridine (5 mL) was stirred for 13 h at room temperature. EtOAc and water were added. The organic phase was separated, and the aqueous phase was extracted three times with EtOAc. The combined organic phase was successively washed with 2 N HCl, saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was chromatographed over silica gel with hexane−EtOAc (8:1) to give *β*-acetoxy sulfone **19** (562 mg, 74%) as an oil: ^{1}H NMR (300 MHz) δ 0.72−0.97 (m, 48H), 0.97−1.80 (m, 95H), 2.04 (s 1.1H), 2.07 (s, 0.9H), 2.09−2.35 (m, 1H), 2.10 (s, 0.7H), 2.14 (s, 0.3H), 3.14 (m, 0.35H), 3.20 (dd, J = 6.8, 9.0 Hz, 2H), 3.30 (dd, J = 6.1, 9.0 Hz, 2H), 3.35−3.67 (m, 18.65H), 3.80 (s, 6H), 4.43 (s, 4H), 4.58 (s, 4H), 4.95−5.06 (m, 0.33H), 5.18−5.21 (m, 0.67H), 6.87 (dt, J = 8.8, 2.2 Hz, 4H), 7.22−7.35 (m, 14H), 7.56 (m, 2H), 7.64 (m, 1H), 7.92 (m, 2H); ^{13}C NMR (75 MHz) δ 17.22, 19.70, 19.76, 24.36, 24.47, 29.82, 29.92, 32.78, 32.82, 33.45, 34.02, 36.65, 37.11, 37.33, 37.40, 37.55, 55.24, 68.88, 69.98, 70.33, 70.78, 72.59, 73.35, 75.75, 77.95, 113.69, 127.48, 127.56, 128.29, 128.83, 129.07, 130.94, 138.44, 159.02; IR (neat) 696, 735, 820, 1038, 1101, 1111, 1248, 1306, 1377, 1462, 1514, 1612, 1747, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{124}H_{208}O_{14}S$: C, 76.18; H, 10.72. Found: C, 75.97; H, 10.85.

3,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-Octamethyldotriacont-16-ene-1,32-diyl]bis{1-*O*-benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol} (20). To a stirred solution of SmI_2 in THF (0.1 M, 30.3 mL, 3.03 mmol) was slowly added HMPA (1.52 mL, 8.69 mmol) at room temperature. After 35 min, a solution of **19** (546 mg, 0.279 mmol) in THF (9 mL) was added and the mixture was stirred for 1.5 h at room temperature. Ether and 2 N HCl were added. The mixture was extracted three times with ether. The combined organic phase was successively washed with 2 N HCl, saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was chromatographed over silica gel with hexane to hexane−EtOAc (200:1 to 10:1) to afford oily **20** (432 mg, 88%) as a mixture of geometrical isomers (E/Z = 85:15): ^{1}H NMR (300 MHz) δ 0.80−0.97 (m, 48H), 0.97−1.80 (m, 94H), 2.02 (m, 1.7H), 2.38 (m, 0.3H), 3.20 (dd, J = 6.8, 9.0 Hz, 2H), 3.30 (dd, J = 6.1, 9.0 Hz, 2H), 3.41−3.65 (m, 18H), 3.80 (s, 6H), 4.43 (s, 4H), 4.55 (s, 4H), 5.02 (dd, J = 1.8, 7.2 Hz, 0.3H), 5.18 (dd, J = 2.2, 4.7 Hz, 1.7H), 6.87 (dt, J = 8.8, 2.2 Hz, 4H), 7.22−7.35 (m, 14H); ^{13}C NMR (75 MHz) δ 17.20, 19.69, 19.73, 21.15, 24.34, 24.46, 24.48, 24.71, 29.81, 29.90, 31.20, 32.74, 32.77, 32.80, 33.44, 34.01, 36.63, 36.67, 37.09, 37.32, 37.39, 37.53, 55.22, 68.87, 69.96, 70.33, 70.77, 72.58, 73.33, 75.74, 77.94, 113.68, 127.45, 127.54, 128.27, 129.06, 130.93, 133.57, 134.55, 138.42, 159.00; IR (neat) 696, 735, 820, 1039, 1101, 1111, 1248, 1377, 1462, 1514, 1612, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{116}H_{200}O_{10}$: C, 79.39; H, 11.49. Found: C, 79.69; H, 11.78.

3,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-Octamethyldotriacontane-1,32-diyl]bis{1-*O*-benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol} (21). Potassium azodicarboxylate (3.89 g, 24.0 mmol) was added to a solution of **20** (421 mg, 0.240 mmol) in methanol (5 mL) and EtOAc (10 mL). A solution of acetic acid (2.76 mL, 48.0 mmol) in methanol (2 mL) and EtOAc (4 mL) was added dropwise over 30 min at room temperature. The suspension was stirred until the bright yellow color disappeared. Hexane and water were added, and the mixture was extracted three times with hexane. The combined organic phase was washed with water, dried (Na_2SO_4), filtered, and concentrated to dryness. This procedure was repeated until olefinic signals disappeared from the ^{1}H NMR. The obtained crude product was chromatographed over silica gel with hexane−EtOAc (20:1) to give 21 (389 mg, 92%) as an oil: $[\alpha]^{23}_D$ +2.84 (*c* 0.895, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.95 (m, 48H), 0.97−1.80 (m, 100H), 3.19 (dd, J = 6.8, 9.0 Hz, 2H), 3.30 (dd, J = 5.9,9.0 Hz, 2H), 3.41−3.65 (m, 18H), 3.80 (s, 6H), 4.43 (s, 4H), 4.55 (s, 4H), 6.87 (dt, J = 8.8, 2.2 Hz, 4H), 7.22−7.35 (m, 14H); ^{13}C NMR (75 MHz) δ 17.21, 19.67, 19.71, 19.75, 24.36, 24.48, 29.81, 29.89, 32.78, 32.81, 33.05, 33.44, 34.01, 34.31, 36.62, 37.09, 37.33, 37.39, 37.52, 37.57, 55.23, 68.87, 69.96, 70.31, 70.77, 72.58, 73.33, 75.74, 77.93, 113.68, 127.48, 127.57, 128.28, 129.08, 130.91, 138.42, 159.00; IR (neat) 696, 735, 820, 1039, 1101, 1111, 1248, 1377, 1462, 1514, 1612, 2856, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{116}H_{202}O_{10}$: C, 79.30; H, 11.59. Found: C, 79.17; H, 11.67.

3,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-Octamethyldotriacontane-1,32-diyl]bis{1-*O*-benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-hydroxy-3,7,11,15-tetramethylhexadecanyl]-*sn*-glycerol} (22). To a stirred solution of **21** (344 mg, 0.196 mmol) in CH_2Cl_2 (7.2 mL) and H_2O (0.4 mL) was added 2,3-dichloro-5,6-dicyanobenzoquinone (145 mg, 0.637 mmol) at room temperature. The mixture was stirred for 30 min. EtOAc and water were added, the organic phase was separated, and the aqueous phase was extracted four times with EtOAc. The combined organic phase was washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was chromatographed over silica gel with hexane−EtOAc (5:1) to give **22** (266 mg, 90%) as an oil: $[\alpha]^{23}_D$ −0.04 (*c* 0.680, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.94 (m, 48H), 0.97−1.72 (m, 100H), 3.37−3.64 (m, 22H), 4.55 (s, 4H), 7.22−7.35 (m, 10H); ^{13}C NMR (75 MHz) δ 16.64, 19.71, 19.76, 24.35, 24.39, 24.42, 24.48, 29.81, 29.89, 32.74, 32.81, 33.05, 33.47, 34.31, 35.77, 36.62, 37.08, 37.22, 37.36, 37.42, 37.53, 37.56, 68.36, 68.88, 69.96, 70.30, 70.77, 73.34, 77.93, 127.48, 127.57, 128.28, 138.41; IR (neat) 696, 733, 1113, 1377, 1462, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{100}H_{186}O_8$: C, 79.20; H, 12.36. Found: C, 79.50; H, 12.37.

3,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-Octamethyldotriacontane-1,32-diyl]bis{1-*O*-benzyl-2-*O*-[(3*R*,7*R*,11*S*,15*S*)-15-formyl-3,7,11,15-tetramethylpentadecanyl]-*sn*-glycerol} (23). To a stirred solution of oxalyl chloride (51 mg, 0.40 mmol) in CH_2Cl_2 (7 mL) was added DMSO (92 μL, 1.3 mmol) at −78 °C. After 1 h, a solution of **22** (122 mg, 0.081 mmol) in CH_2Cl_2 (6 mL) was added dropwise over 5 min. The mixture was stirred for 10 min at −78 °C and then for 1.5 h at −60 °C. Then, Et_3N (0.22 mL, 1.6 mmol) was added dropwise over 5 min. The mixture was gradually warmed to room temperature, and saturated aqueous NH_4Cl was added. The mixture was extracted three times with EtOAc. The combined organic phase was washed with saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was chromatographed over silica gel with hexane−EtOAc (20:1) to give **23** (114 mg, 93%) as an oil: $[\alpha]^{25}_D$ +7.81 (*c* 0.650, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.90 (m, 42H), 0.97−1.74 (m, 104H), 2.33 (ddd, J = 2.0, 6.6, 13.2, 2H), 3.37−3.64 (m, 18H), 4.55 (s, 4H), 7.22−7.35 (m, 10H), 9.61 (d, J = 2.0, 2H); ^{13}C NMR (75 MHz) δ 13.35, 19.64, 19.67, 19.71, 19.74, 24.34, 24.40, 24.43, 24.48, 29.80, 29.87, 30.85, 32.64, 32.79, 33.04, 34.30, 36.62, 36.98, 37.08, 37.16, 37.32, 37.36, 37.41, 37.52, 37.55, 46.33, 68.86, 69.94, 70.29, 70.76, 73.32, 77.92, 127.47, 127.56, 128.27, 138.40, 205.37; IR (neat) 665, 698, 735, 1115, 1377, 1462, 1730, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{100}H_{182}O_8$: C, 79.41; H, 12.13. Found: C, 79.45; H, 12.26.

(2*S*,7*R*,11*R*,15*S*,19*S*,22*S*,26*S*,30*R*,34*R*,39*S*,43*R*,47*R*,51*S*,55*S*,58*S*,62*S*,66*R*,70*R*)-2,39-Bis[(benzyloxy)methyl]-7,11,15,19,22,26,30,34,43,47,51,55,58,62,66,70-hexadecamethyl-1,4,37,40-tetraoxacyclodoheptacont-56-ene (24). Powdered $TiCl_3$ (0.3 g, 1.95 mmol) and Zn−Cu couple (0.3 g, 4.45 mmol) were placed in a Schlenk tube. DME (45 mL) was added, and the mixture was refluxed for 2 h. A solution of dialdehyde **23** (101 mg, 0.068 mmol) in DME (5 mL) was added to the refluxing slurry *via* a motor-driven syringe pump over

a 45 h period. After an additional 18 h reflux period, the reaction mixture was cooled to room temperature and 20% aqueous K_2CO_3 solution (30 mL) was added. The resulting mixture was stirred for 4 h. The organic phase was separated, and the aqueous phase was extracted 10 times with ether. The combined organic extract was washed with saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was chromatographed over silica gel with hexane−EtOAc (20:1) to give **24** (58 mg, 59%) as an oil: $[\alpha]^{26}_D$ +7.08 (c 1.273, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.97 (m, 48H), 0.97−1.68 (m, 98H), 2.02 (m, 2H), 3.43−3.65 (m, 18H), 4.55 (s, 4H), 5.16 (dd, J = 2.2, 4.6, 2H), 7.22−7.35 (m, 10H); ^{13}C NMR (75 MHz) δ 19.74, 19.77, 19.80, 19.82, 21.33, 24.39 24.45, 24.50, 24.78, 29.76, 29.83, 32.77, 32.80, 32.82, 33.05, 34.29, 36.62, 36.83, 37.09, 37.35, 37.39, 37.45, 37.51, 37.59, 37.63, 68.81, 69.89, 70.30, 70.96, 73.35, 77.94, 127.49, 127.58, 128.30, 134.65, 138.41; IR (neat) 696, 733, 1115, 1377, 1458, 2858, 2925, 2951 cm^{-1}; EI-MS m/z 1479 (M^+), 1387, 1282, 91. Anal. Calcd for $C_{100}H_{182}O_6$: C, 81.13; H, 12.39. Found: C, 81.30; H, 12.50.

(2*S*,7*R*,11*R*,15*S*,19*S*,22*S*,26*S*,30*R*,34*R*,39*S*,43*R*,47*R*,51*S*,55*S*,58*S*,62*S*,66*R*,70*R*)-2,39-Bis[(benzyloxy)methyl]-7,11,15,19,22,26,30,34,43,47,51,55,58,62,66,70-hexadecamethyl-1,4,37,40-tetraoxacyclodoheptacontane (25). Compound **24** (96 mg, 0.064 mmol) was treated in the same manner as described for the preparation of **21** to give **25** (77 mg, 80%) as an oil: $[\alpha]^{25}_D$ +1.61 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.92 (m, 48H), 0.97−1.68 (m, 104H), 3.43−3.65 (m, 18H), 4.55 (s, 4H), 7.22−7.35 (m, 10H); ^{13}C NMR (75 MHz) δ 19.76, 19.80, 19.82, 24.38, 24.46, 29.74, 29.84, 32.80, 32.82, 33.05, 34.30, 36.62, 37.05, 37.37, 37.46, 37.51, 68.79, 69.89, 70.31, 70.97, 73.35, 77.94, 127.49, 127.58, 128.30, 138.41; IR (neat) 696, 733, 1115, 1377, 1462, 2858, 2925, 2951 cm^{-1}; EI-MS m/z 1481 (M^+), 1389 ($M^+ - CH_2Ph$), 1284, 91. Anal. Calcd for $C_{100}H_{184}O_6$: C, 81.01; H, 12.51. Found: C, 80.75; H, 12.69.

(2*S*,7*R*,11*R*,15*S*,19*S*,22*S*,26*S*,30*R*,34*R*,39*S*,43*R*,47*R*,51*S*,55*S*,58*S*,62*S*,66*R*,70*R*)-2,39-Bis(hydroxymethyl)-7,11,15,19,22,26,30,34,43,47,51,55,58,62,66,70-hexadecamethyl-1,4,37,40-tetraoxacyclodoheptacontane (3a). A mixture of **25** (73 mg, 0.049 mmol) and 10% Pd−C (22 mg) in EtOAc (15 mL) was stirred for 3.5 h under an atmospheric pressure of hydrogen at 40 °C. The mixture was filtered, and the filtrate was concentrated to dryness. The residue was chromatographed over silica gel with hexanes−EtOAc (5:1) to give **3a** (50 mg, 78%) as an oil: $[\alpha]^{25}_D$ +8.68 (*c* 1.68, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.92 (m, 48H), 0.97−1.68 (m, 104H), 2.21 (br, 2H), 3.42−3.74 (m, 18H); ^{13}C NMR (75 MHz) δ 19.74, 19.80, 19.82, 24.34, 24.43, 29.75, 29.86, 32.75, 33.02, 34.26, 36.53, 37.01, 37.33, 37.48, 63.03, 68.56, 70.05, 71.02, 78.32; IR (neat) 1051, 1117, 1377, 1462, 2858, 2925, 2951, 3452 cm^{-1}; EI-MS m/z 1301 (M^+), 1283 ($M^+ - H_2O$), 1271, 650. Anal. Calcd for $C_{86}H_{172}O_6$: C, 79.32; H, 13.31. Found: C, 79.04; H, 13.60.

2,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-16-Hydroxy-3,7,11,15,18,22,26,30-octamethyl-17-(phenylsulfonyl)dotriacontane-1,32-diyl]-2′,3-bis-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]bis(1-*O*-benzyl-*sn*-glycerol) (26). Sulfone **13** (700 mg, 0.686 mmol) and aldehyde **17** (559 mg, 0.625 mmol) were treated in the same manner as described for the preparation of **18** to give β-hydroxy sulfone **26** (700 mg, 59%) as an oil: ^{1}H NMR (300 MHz) δ 0.74−0.97 (m, 48H), 0.97−1.82 (m, 95H), 2.00−2.40 (m, 1H), 3.05−3.77 (m, 19.7H), 3.20 (dd, J = 6.8, 9.0 Hz, 2H), 3.30 (dd, J = 5.9, 9.0 Hz, 2H), 3.78 (s, 6H), 4.10 (m, 0.3H), 4.43 (s, 4H), 4.55 (s, 4H), 6.87 (dt, J = 8.8, 2.2 Hz, 4H), 7.22−7.35 (m, 14H), 7.56 (m, 2H), 7.64 (m, 1H), 7.91 (m, 2H); ^{13}C NMR (75 MHz) δ 17.20, 19.66, 19.69, 19.74, 24.34, 24.44, 29.79, 29.87, 32.75, 32.79, 33.43, 33.99, 36.61, 37.07, 37.30, 37.36, 37.51, 55.20, 68.85, 69.94, 70.29, 70.75, 72.56, 73.32, 75.72, 77.91, 113.65, 127.45, 127.54, 128.27, 128.32, 129.00, 129.06, 129.20, 138.40, 158.99; IR (neat) 696, 733, 820, 1039, 1099, 1111, 1248, 1302, 1377, 1462, 1514, 1612, 2856, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{122}H_{206}O_{13}S$: C, 76.60; H, 10.85. Found: C, 76.54; H, 11.04.

2,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-16-Acetoxy-3,7,11,15,18,22,26,30-octamethyl-17-(phenylsulfonyl)dotriacontane-1,32-diyl]-2′,3-bis-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]bis(1-*O*-benzyl-*sn*-glycerol) (27). Compound **26** (681 mg, 0.356 mmol) was treated in the same manner as described for the preparation of **19** to give β-acetoxy sulfone **27** (503 mg, 72%) as an oil: ^{1}H NMR (300 MHz) δ 0.72−0.97 (m, 48H), 0.97−1.80 (m, 95H), 2.04 (s, 1.1H), 2.07 (s, 0.9H), 2.09−2.35 (m, 1H), 2.11 (s, 0.7H), 2.15 (s, 0.3H), 3.14 (m, 0.35H), 3.20 (dd, J = 6.8, 9.0 Hz, 2H), 3.30 (dd, J = 6.1, 9.0 Hz, 2H), 3.36−3.67 (m, 1.65H), 3.79 (s, 6H), 4.43 (s, 4H), 4.55 (s, 4H), 4.95−5.06 (m, 0.33H), 5.18−5.21 (m, 0.67H), 6.87 (dt, J = 8.8, 2.2 Hz, 4H), 7.22−7.35 (m, 14H), 7.56 (m, 2H), 7.64 (m, 1H), 7.93 (m, 2H); ^{13}C NMR (75 MHz) δ 17.22, 19.68, 19.71, 19.76, 24.35, 24.46, 29.81, 29.89, 32.77, 32.81, 33.44, 34.01, 36.62, 37.09, 37.32, 37.38, 37.40, 37.53, 55.21, 68.87, 69.95, 70.30, 70.76, 72.58, 73.33, 75.73, 77.93, 113.67, 127.48, 127.56, 128.28, 128.83, 129.07, 129.12, 130.91, 138.42, 159.00; IR (neat) 696, 735, 820, 1038, 1099, 1111, 1248, 1306, 1377, 1462, 1514, 1612, 1747, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{124}H_{208}O_{14}S$: C, 76.18; H, 10.72. Found: C, 76.28; H, 10.91.

2,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-Octamethyldotriacont-16-ene-1,32-diyl]-2′,3-bis-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]bis(1-*O*-benzyl-*sn*-glycerol) (28). Compound **27** (493 mg, 0.252 mmol) was treated in the same manner as described for the preparation of **20** to give oily **28** (385 mg, 87%) as a mixture of geometrical isomers (E/Z = 85:15): ^{1}H NMR (300 MHz) δ 0.80−0.97 (m, 48H), 0.97−1.80 (m, 94H), 2.02 (m, 1.7H), 2.38 (m, 0.3H), 3.20 (dd, J = 6.8, 9.0 Hz, 2H), 3.30 (dd, J = 6.1, 9.0 Hz, 2H), 3.41−3.65 (m, 18H), 3.80 (s, 6H), 4.43 (s, 4H), 4.55 (s, 4H), 5.02 (dd, J = 1.8, 7.2 Hz, 0.3H), 5.18 (dd, J = 2.2, 4.7 Hz, 1.7H), 6.87 (dt, J = 8.8, 2.2 Hz, 4H), 7.22−7.35 (m, 14H); ^{13}C NMR (75 MHz) δ 17.21, 19.70, 19.75, 21.17, 24.35, 24.47, 24.50, 24.72, 29.81, 29.89, 31.57, 32.75, 32.78, 32.81, 33.44, 34.01, 36.63, 36.70, 37.09, 37.25, 37.39, 37.53, 55.21, 68.87, 69.95, 70.31, 70.77, 72.58, 73.33, 75.74, 77.94, 113.68, 127.47, 127.55, 128.27, 129.06, 130.91, 133.57, 134.56, 138.42, 159.00; IR (neat) 696, 735, 820, 1039, 1101, 1111, 1248, 1377, 1462, 1514, 1612, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{116}H_{200}O_{10}$: C, 79.39; H, 11.49. Found: C, 79.33; H, 11.79.

2,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-Octamethyldotriacontane-1,32-diyl]-2′,3-bis-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-[(4-methoxybenzyl)oxy]-3,7,11,15-tetramethylhexadecanyl]bis(1-*O*-benzyl-*sn*-glycerol) (29). Compound **28** (377 mg, 0.215 mmol) was treated in the same manner as described for the preparation of **21** to give **29** (324 mg, 86%) as an oil: $[\alpha]^{23}_D$ +3.63 (*c* 0.420, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.95 (m, 48H), 0.97−1.80 (m, 100H), 3.19 (dd, J = 6.8, 9.0 Hz, 2H), 3.30 (dd, J = 6.1, 9.0 Hz, 2H), 3.41−3.65 (m, 18H), 3.80 (s, 6H), 4.43 (s, 4H), 4.55 (s, 4H), 6.87 (dt, J = 8.8, 2.2 Hz, 4H), 7.22−7.35 (m, 14H); ^{13}C NMR (75 MHz) δ 17.21, 19.68, 19.71, 19.76, 24.35, 24.48, 29.80, 29.88, 32.78, 32.81, 33.05, 33.44, 34.01, 34.31, 36.62, 37.09, 37.32, 37.38, 37.41, 37.52, 37.56, 55.22, 68.87, 69.95, 70.29, 70.76, 72.58, 73.33, 75.73, 77.92, 113.67, 127.48, 127.56, 128.28, 129.08, 130.91, 138.41, 158.99; IR (neat) 696, 733, 820, 1039, 1099, 1111, 1248, 1377, 1462, 1514, 1612, 2856, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{116}H_{202}O_{10}$: C, 79.30; H, 11.59. Found: C, 79.05; H, 11.70.

2,3′-*O*-(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-Octamethyldotriacontane-1,32-diyl]-2′,3-bis-*O*-[(3*R*,7*R*,11*S*,15*S*)-16-hydroxy-3,7,11,15-tetramethylhexadecanyl]bis(1-*O*-benzyl-*sn*-glycerol) (30). Compound **29** (288 mg, 0.164 mmol) was treated in the same manner as described for the preparation of **22** to give diol **30** (228 mg, 92%) as an oil: $[\alpha]^{23}_D$ +0.54 (*c* 0.580, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.80−0.94 (m, 48H), 0.97−1.72 (m, 100H), 3.37−3.64 (m, 22H), 4.55 (s, 4H), 7.22−7.35 (m, 10H); ^{13}C NMR (75 MHz) δ 16.63, 19.70, 19.76, 24.34, 24.39, 24.47, 29.79, 29.86, 32.73, 32.79, 33.03, 33.46, 34.30, 35.75, 36.60, 37.06, 37.28, 37.34, 37.41, 37.50, 37.55, 68.33, 68.86, 69.94, 70.26, 70.75, 73.32, 77.91, 127.47, 127.56, 128.27, 138.37; IR (neat) 696, 733, 1113,

1377, 1462, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{100}H_{186}O_8$: C, 79.20; H, 12.36. Found: C, 79.14; H, 12.60.

2,3′-*O*-[(3*R*,7*R*,11*S*,15*S*,18*S*,22*S*,26*R*,30*R*)-3,7,11,15,18,22,26,30-octamethyldotriacontane-1,32-diyl]-2′,3-bis-*O*-[(3*R*,7*R*,11*S*,15*S*)-15-formyl-3,7,11,15-tetramethylpentadecanyl]bis(1-*O*-benzyl-*sn*-glycerol) (31). Compound **30** (196 mg, 0.129 mmol) was treated in the same manner as described for the preparation of **23** to give dialdehyde **31** (179 mg, 92%) as an oil: $[\alpha]^{23}_D$ +9.05 (*c* 0.775, $CHCl_3$); ^1H NMR (300 MHz) δ 0.80−0.90 (m, 42H), 0.97−1.74 (m, 104H), 2.33 (ddd, J = 2.0, 6.6, 13.2 Hz, 2H), 3.37−3.64 (m, 18H), 4.55 (s, 4H), 7.22−7.35 (m, 10H), 9.61 (d, J = 2.0 Hz, 2H); ^{13}C NMR (75 MHz) δ 13.35, 19.65, 19.67, 19.71, 19.75, 24.35, 24.39, 24.44, 24.48, 29.79, 29.87, 30.85, 32.64, 32.79, 33.04, 34.30, 36.62, 36.98, 37.08, 37.16, 37.32, 37.36, 37.41, 37.50, 37.55, 46.33, 68.86, 69.94, 70.28, 70.76, 73.32, 77.92, 127.47, 127.55, 128.27, 138.40, 205.35; IR (neat) 698, 735, 1115, 1377, 1462, 1728, 2858, 2925, 2951 cm^{-1}. Anal. Calcd for $C_{100}H_{182}O_8$: C, 79.41; H, 12.13. Found: C, 79.19; H, 12.32.

(2*S*,7*R*,11*R*,15*S*,19*S*,22*S*,26*S*,30*R*,34*R*,38*S*,43*R*,47*R*,51*S*,55*S*,58*S*,62*S*,66*R*,70*R*)-2,38-Bis[(benzyloxy)methyl]-7,11,15,19,22,26,30,34,43,47,51,55,58,62,66,70-hexadecamethyl-1,4,37,40-tetraoxacyclodoheptacont-20-ene (32). Compound **31** (147 mg, 0.097 mmol) was treated in the same manner as described for the preparation of **24** to give cyclic compound **32** (94 mg, 66%) as an oil: $[\alpha]^{24}_D$ +7.06 (*c* 1.03, $CHCl_3$); ^1H NMR (300 MHz) δ 0.80−0.97 (m, 48H), 0.97−1.68 (m, 98H), 2.02 (m, 2H), 3.43−3.65 (m, 18H), 4.55 (s, 4H), 5.16 (dd, J = 2.2, 4.6 Hz, 2H), 7.22−7.35 (m, 10H); ^{13}C NMR (75 MHz) δ 19.75, 19.80, 19.82, 21.33, 24.39 24.45, 24.78, 29.74, 29.84, 32.77, 32.80, 32.82, 33.05, 34.29, 36.64, 36.83, 37.09, 37.36, 37.39, 37.44, 37.50, 37.60, 68.78, 69.89, 70.32, 70.97, 73.35, 77.95, 127.48, 127.57, 128.29, 134.65, 138.42; IR (neat) 696, 733, 1115, 1377, 1462, 2858, 2925, 2951 cm^{-1}; EI-MS *m*/*z* 1479 (M^+), 1387, 1282, 91. Anal. Calcd for $C_{100}H_{182}O_6$: C, 81.13; H, 12.39. Found: C, 80.94; H, 12.69.

(2*S*,7*R*,11*R*,15*S*,19*S*,22*S*,26*S*,30*R*,34*R*,38*S*,43*R*,47*R*,51*S*,55*S*,58*S*,62*S*,66*R*,70*R*)-2,38-Bis[(benzyloxy)methyl]-7,11,15,19,22,26,30,34,43,47,51,55,58,62,66,70-hexadecamethyl-1,4,37,40-tetraoxacyclodoheptacontane (33). Compound **32** (90 mg, 0.061 mmol) was treated in the same manner as described for the preparation of **25** to give **33** (80 mg, 88%) as an oil: $[\alpha]^{24}_D$ +1.92 (c 2.46, $CHCl_3$); ^1H NMR (300 MHz) δ 0.80−0.92 (m, 48H), 0.97−1.68 (m, 104H), 3.43−3.65 (m, 18H), 4.55 (s, 4H), 7.22−7.35 (m, 10H); ^{13}C NMR (75 MHz) δ 19.76, 19.80, 19.82, 24.38, 24.46, 29.75, 29.84, 32.78, 32.80, 33.05, 34.30, 36.64, 37.07, 37.37, 37.46, 37.51, 68.78, 69.89, 70.32, 70.98, 73.35, 77.95, 127.48, 127.57, 128.29, 138.42; IR (neat) 696, 735, 1115, 1377, 1462, 2858, 2925, 2951 cm^{-1}; EI-MS *m*/*z* 1481 (M^+), 1389 ($M^+ - CH_2Ph$), 1284, 91. Anal. Calcd for $C_{100}H_{184}O_6$: C, 81.01; H, 12.51. Found: C, 80.71; H, 12.81.

(2*S*,7*R*,11*R*,15*S*,19*S*,22*S*,26*S*,30*R*,34*R*,38*S*,43*R*,47*R*,51*S*,55*S*,58*S*,62*S*,66*R*,70*R*)-2,38-Bis(hydroxymethyl)-7,11,15,19,22,26,30,34,43,47,51,55,58,62,66,70-hexadecamethyl-1,4,37,40-tetraoxacyclodoheptacontane (3b). Compound **33** (74 mg, 0.050 mmol) was treated in the same manner as described for the preparation of **3a** to give **3b** (52 mg, 80%) as an oil: $[\alpha]^{25}_D$ +9.06 (*c* 1.74, $CHCl_3$); ^1H NMR (300 MHz) δ 0.80−0.92 (m, 48H), 0.97−1.68 (m, 104H), 2.18 (br, 2H), 3.42−3.74 (m, 18H); ^{13}C NMR (75 MHz) δ 19.76, 19.82, 19.85, 24.36, 24.44, 29.77, 29.81, 32.77, 33.04, 34.28, 36.55, 37.03, 37.35, 37.50, 63.03, 68.58, 70.07, 71.04, 78.35; IR (neat) 1049, 1115, 1377, 1462, 2858, 2925, 2952, 3452 cm^{-1}; EI-MS *m*/*z* 1301 (M^+), 1283 ($M^+ - H_2O$), 1271, 650. Anal. Calcd for $C_{86}H_{172}O_6$: C, 79.32; H, 13.31. Found: C, 79.38; H, 13.43.

Differencial Scanning Calorimetry (DSC) Measurement. All calorimetric measurements were performed on a SEIKO SSC-5200 differential scanning calorimeter. Each lipid (10−15 mg) was placed in an aluminum pan, and the pan was sealed to prevent adsorption of water during measurements. All thermograms were run at a scanning rate of 2 °C/min from −80 to 40 °C. Determinations of the transition points and of the enthalpy of the phase were performed on line by means of a microprocessor connected to the calorimeter.

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Supporting Information Available: ^1H NMR spectra for compounds **5**, **7**−**33**, **3a**, and **3b**, ^{13}C NMR spectra for compounds **21**−**25**, **29**−**33**, **3a**, and **3b**, and mass spectra for compounds **3a** and **3b** (44 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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