Pergamon

Tetrahedron Vol. 51, No. 16, pp. 4723-4732, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00156-5

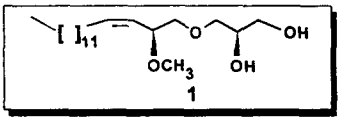
Stereoselective Total Synthesis of (2R,2'S,3Z)-1-O-(2-Methoxyhexadecenyl) glycerol And (2R,2'S)-1-(2'-Methoxyhexadecyl)glycerol-Potential Antitumour compounds From Shark Liver Oil

Mirza Hamed A.Baig, Subramanian Baskaran, Sharmila Banerjee and Girish K.Trivedi*

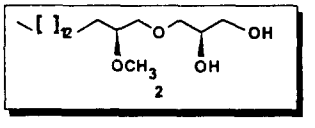
Department of Chemistry, Indian Institute of Technology, Powai, Bombay, India, 400 076.

Abstract: A simple and high yielding route for the stereoselective synthesis of alkyl glycerol ethers namely (2R,2'S,3Z)-1-O-(2-methoxyhexadecenyl)glycerol **1** and (2R,2'S)-1-(2'-methoxyhexadecyl) glycerol **2**, isolated form Shark liver oil is reported. The key reaction involves the Wittig olefination of the chiral aldehyde **12** with the ylide generated from tridecyl triphenyl phosphonium bromide results in the formation of compound **13**, a precursor for the title compounds **1** and **2**.

Several 2-methoxy alkyl glycerol ethers have been isolated from Greenland Shark liver oil[1-3] Among them, the title compounds **1** and **2** have been shown to exhibit antibacterial, anticholestermic, antimicrobial and antitumor activities[4-6] . Brohult et al.[7] have also reported the positive effect of alkyl glycerol ethers in the treatment of **AIDS**. However, to the best of our knowledge, no report of the synthesis of these compounds is available todate. Moreover, the first report[1] which deals with the isolation of these compounds does not comment on the optical activity or the absolute configuration of the two chiral centres in the molecule.



1



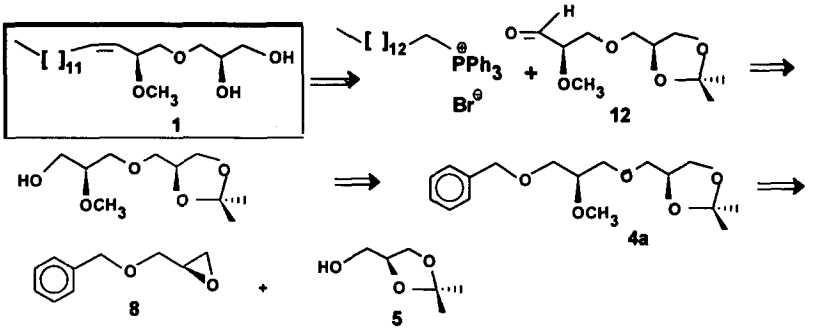
2

In connection with our work on the synthesis of alkyl glycerol ethers, we felt it desirable to provide an unambiguous synthetic route for this class of compounds. However, before embarking upon the synthesis of the chiral synthon **4a**, a key intermediate in total synthesis using the chiral alcohol **5**, it was felt pertinent to adopt the envisaged strategy using the achiral alcohol **4**. Herein we report the synthesis of a stereoisomer of 1-O-(2-methoxy hexadecyl) glycerol and its Δ^3-unsaturated derivative.

The retrosynthetic analysis of compound **1** (Retro Scheme-1) reveals that the molecule can be constructed via a Wittig coupling of the chiral aldehyde **12** and a C-13 Wittig salt. Compound

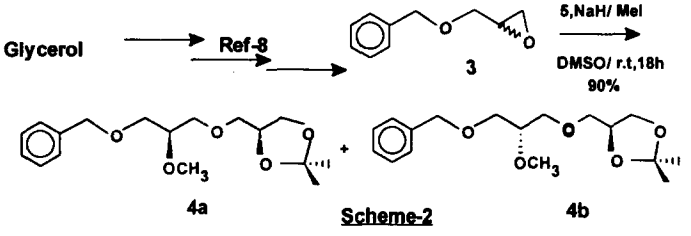
12, can in turn, be obtained from the chiral intermediate **4a**. Further disconnection of the intermediate **4a** provides the chiral key synthons, the epoxide **8** and the alcohol **5.**

The synthesis of the C-2' diastereomer of **4a** can therefore be envisaged from the achiral epoxide **3** and the chiral alcohol **5**. In the actual synthetic scheme, the achiral epoxide was derived from inexpensive and readily available glycerol (Scheme-2).



Retro-scheme-1

Nucleophilic opening of the epoxide using (2S)-1,2-isopropylidene glycerol was found to be regiospecific yielding intermediates which were methylated *in situ* affording the diastereomeric synthons **4a** and **4b** (**1:1**).

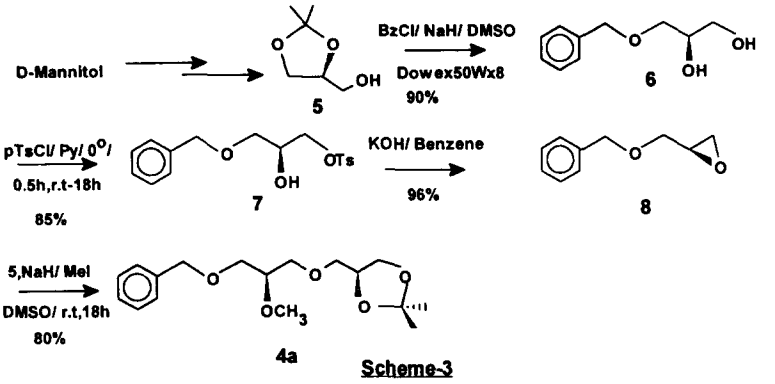


Scheme-2

On obtaining the two diastereomeric intermediates **4a** and **4b**, the next attempt was aimed at the synthesis of the chiral synthon **4a**. The chiral alcohol **6**[8] obtained from D-mannitol was subjected to selective tosylation. Conversion of the product alcohol to the epoxide **8**[9,10] was found to be quantitative using 2 equivalent of KOH in dry benzene under inert atmosphere. Regiospecific opening of the epoxide **8** with the chiral alcohol **5** yielded the optically active **4a**(Scheme-3)

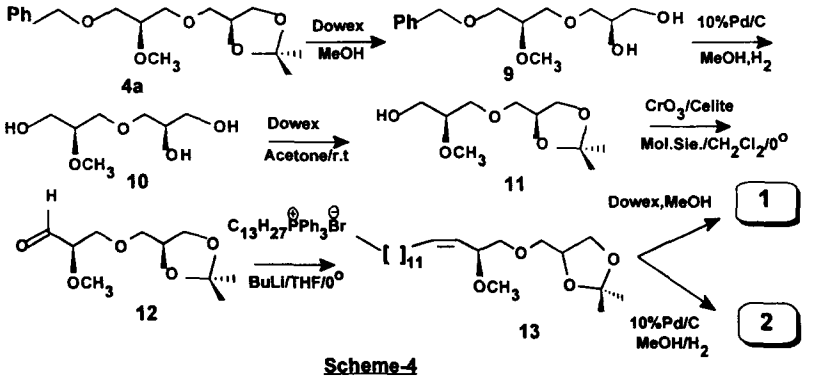
Having obtained (2S,2'S)-3-O-(3'-benzyloxy-2'-methoxy)propyl 1,2-isopropylidene glycerol **4a** as the key intermediate, the envisaged strategy required its conversion to the target molecule. In this direction debenzylation of **4a** by catalytic hydrogenation using 10% Pd/C as catalyst under hydrogen atmosphere was attempted(Scheme-4).

However, the reaction gave only unchanged starting material. Increase of hydrogen pressure to 5 psi was also of no avail and provided an intractible mixture of products on tlc. Therefore, removal of the isopropylidene group prior to the removal of benzyl group was attempted and the desired deprotection of the isopropylidene moiety was achieved in quantitative yield with Dowex50Wx 8.



Scheme-3

The diol **9**, thus obtained, was subjected to catalytic hydrogenation using 10% Pd/C under varying hydrogen pressure. Optimum yield (88%) of the triol **10** was obtained at 5 psi pressure of hydrogen for 36 hours. Presence of a broad IR band at 3450cm^{-1} , characteristic of hydroxy group and a three proton singlet at δ 3.45 in the ^{1}HNMR spectrum (-OCH_3 group) indicated the formation of compound **10**.



Scheme-4

In the ^{13}C NMR spectrum of **10**, the carbon atom bearing the -OCH_3 group appeared as a doublet at δ 82.22 ,while the C atoms bearing the hydroxy groups appeared at δ73.98(t), 72.25 (d) and 71.69(t). In the next step (2'S, 2S)-3-O-(1'-Hydroxy-2'-methoxypropyl)-1,2-isopropylidene glycerol ether **11** was obtained in a yield of 96 % via the protection of the two

vicinal hydroxy groups of **10**. The appearance of two, three-proton singlets at δ1.42 and 1.36 in the ^{1}H NMR spectrum of **7** indicated the formation of the isopropylidene moiety. The oxidation of **7** to the aldehyde **12** was best achieved[11] in a yield of 90% using pyridinium dichlorochromate prepared *in situ*, in presence of molecular sieves and celite. The doublet at δ9.7 in the ^{1}H NMR spectrum of **12** confirmed the presence of the aldehydic proton.

Wittig olefination of the aldehyde **12** was next effected with the ylide generated from tridecyl triphenyl phosphonium bromide using n-BuLi. The product obtained in an yield of 65% indicated the incorporation of the isopropylidene group by the presence of characteristic IR bands at 1390 and 1380 Cm^{-1}. The coupling constants of the olefinic proton signals at δ 5.67 (dt, J=11.14 Hz and 7.48 Hz) and δ 5.22 (dtd, J=11.1,7.78, 1.52 Hz) were also suggestive of the formation of the cis double bond in **13**.

It is pertinent to note that compound **13** is a single diastereomer, at the C-2' site. This has been ascertained with the help of **Eu**-shift reagent .This indicates that no epimerisation at the C-2' site of the chiral aldehyde takes place during the course of Wittig olefination. In keeping with the data reported in the literature[12] , the allylic carbon C-5' in **13** was observed at δ 27.82. This confirmed the stereospecific formation of the cis double bond.

The final step in the synthetic sequence involved the deprotection of the isopropylidene moiety with Dowex 50W x 8 affording (2S,2'S, 3Z)-1-O-(2'-methoxyhexadec-3-enyl)glycerol **1** in an overall yield of 47%. The ion peak observed at m/z 312(M -CH_3 OH) in the mass spectrum of compound **1** confirmed the formation of the desired product. The target compound **2** was obtained (overall yield 43%) in an one-pot reaction involving hydrogenation and deprotection using 10% Pd/C under 2 psi pressure even in the absence of Dowex.

The formation of **2** was indicated by the disappearance of the characteristic olefinic and isopropylidene methyl signals from the ^{1}H NMR and ^{13}C NMR spectra of the product. A down field shift of the ^{13}C NMR signal of C-2' from 76.02 to 80.29 indicated the removal of cis-olefinic effect. The mass spectrum of the product exhibited the base peak at m/z 241 corresponding to the fragment obtained via the cleavage of the α-bond of the C atom bearing the methoxy groups.

The synthetic strategy described here provides a simple and high yielding general route for the synthesis of alkyl glycerol ethers. The diastereomers of the novel chiral intermediate **4a** and **4b** can be utilised in a similar manner to synthesise the diastereomers of the target compound **1** & **2**.

EXPERIMENTAL:

Myristic acid, D. mannitol and glycerol were purchased from Aldrich Chemical Co., Dowex 50W X8 resin was purchased from Sigma Chemical Co. and Triphenylphosphine, 10% Pd/C catalyst and sodium hydride were purchased from Fluka Chemical Co. Melting points are reported uncorrected. Laboratory solvents were purified and predried before use according to standard procedures. Petroleum ether of b.p. 60-80° was used for column chromatography. Temperature is expressed in degree Celsius. I.R. spectra were recorded on Perkin Elmer 688 Spectrometer. NMR spectra were recorded either on Varian VXR 300S or Varian FT 60A or Varian 100 spectrometer using $CDCl_3$ as the solvent or $CDCl_3$:CD_3OD (9:1) solution containing TMS as an internal standard with chemical shifts (δ) expressed on ppm down field with respect to TMS. J values are given in Hz. Mass spectra were recorededon a CEC-21-110B double focusing mass spectrometer operating at 70 eV using direct inlet system. The optical rotations were measured with Shimadzu digital polarimeter. Purity was checked on Shimadzu GC-14A chromatogram.

(2S)-1-O-Benzyl-2,3-epoxypropyl ether (8)

A mixture of (2S)-1-benzyloxy-1,2-propandiol-3-tosylate **(7)** (7.5 g, 22.3 mmol) and powdered KOH (5 g) in dry benzene (50 ml) was placed in a two necked 100 ml round bottom flask and the reaction mixture was stirred under nitrogen atmosphere for an hour. The reaction was monitored by TLC (1% EtOAc/petroleum ether). The reaction mixture was filtered through celite and the residue washed with dry benzene. Evaporation of solvent under reduced pressure gave a pale yellow oil which was distilled under vacuum at 180°C/0.8-0.9 torr to yield a pure compound 8 (3.45g, 94%). $[\alpha]_D^{28}$-10.9(neat),{Lit[10] $[\alpha]_D^{20}$-12.6 neat)}; ν_{max} (film)/cm^{-1}: 3050 (epoxy), 3020, 1800-1600 (Ar), 1500 (epoxy) ^1H NMR(300 MHz)δ: 7.3 (5H,s, Ar), 4.57 (2H, d, J = 7.3 , Ar-CH_2),3.75 (1H, dd, J = 3.05, 11.45, 3-H), 3.42 (1H, dd, J = 5.8, 11.45 , 3-H), 3.5-3.2 (1H, m, 2-H), 2.78 (1H, dd, J = 5.04, 4.2, 1-H), and 2.6 (1H, dd, J = 2.59, 5.04,1-H). ^{13}C NMR(75 MHz)δ :13.7 (s, C-1 of Ar), 128.26 (d, C-2 and C-6 of Ar), 127.58 (d, C-3 and C-5 of Ar), 73.12 (t, CH_2-Ar), 70.66 (t, C-1), 50.69 (d, C-2) and 44.08 (t, C-3).MS : m/z 164 (M)

(2'S,2S)-3-O-(3'-Benzyloxy-2'-methoxypropyl)-1,2-isopropylidine glyceryl ether (4a)

A solution of (2S)-1,2-isopropylidine glycerol **(5)** (0.63 g, 4.77 mmol) in DMSO (5 ml) was added dropwise to the solution of NaH 50% in petroleum wax (29 mg, 0.63 mmol) in DMSO (1 ml) for a period of 10 min. at 5° .The mixture was stirred and allowed to reach room temperature (~1h). To this solution epoxide 14 (0.57 g, 4.28 mmol) was added at 0-5° . It was allowed to reach room temperature in 1.5h and stirring was continued for additional 2h (Reaction was monitored by TLC, (5 and 30% EtOAc/petroleum. ether). When the TLC showed disappearance of the starting material, methyl iodide (2.5 g, 17.6 mmol) was added at 5°. It was allowed to reach room temperature in two hours and the reaction mixture was kept stirring at

room temperature for four hours. Water was added to the reaction mixture, extracted with ether, washed with brine, dried over and concentrated under *vacuo* to give an yellow oil. Purification was done by column chromatography using solvent CH_2Cl_2 and MeOH/CH_2Cl_2 mixture as eluant to yield compound 4a (1.48 g ,80%).
$[\alpha]_D^{30}$:+11.49 (c,8,$CHCl_3$);ν_{max} (film)/cm^{-1} : 3080, 3020, 1780-1600 (Ar), 1390, 1380 (>$C(CH_3)_2$), 1220, 1100, and 860. ^1H NMR(300 MHz)δ: 7.3 (5H,s, Ar), 4.55 (2H,s, CH_2 -Ar), 4.23 (1H,m, 2-H), 4.20 (1H, dd, J = 8.33, 6.43, 1-H), 3.72 (1H, dd,J=8.33, 6.24 , 1-H), 3.63-3.44 (7H,m,3-H, 1'-H, 2'-H and 3'-H), 3.45 (3H, s, OCH_3), 1.41 (3H,s,>$C(CH_3)_2$) and 1.35 (3H, s,>$C(CH_3)_2$);^{13}C NMR(75 MHz)δ :137.99 (s, C-1 of Ar), 128.08 (d, C-2 and C-6 of Ar), 127.37 (d, C-3, C-4 and C-5 of Ar), 109.03 (s, >$C(CH_3)_2$), 79.11 (d, C-2'), 74.41 (d, C-2), 73.15 (t, CH_2 -Ar), 72.24 (t, C-3'), 70.95 (t, C-1'), 69.28 (t, C-3), 66.52 (t, C-1), 57.70 (q, OCH_3), 26.51 (q, >$C(CH_3)_2$) and 25.18 (q, >$C(CH_3)_2$). Elemental (Calculated for $C_{17}H_{26}O_5$: C, 65.80; H, 8.35. Found : C, 65.68; H, 8.41%); MS : m/z 295 (M^+ -15).

Coupling reaction of 1-O-benzyl-2,3-epoxypropyl ether (3) with (2S)-1,2-isopropylidene glycerol (5)

A solution of (2S)-1,2-isopropylidene glycerol **(5)** (3.3 g, 25 mmol) in DMSO (30 ml) was added dropwise to the solution of NaH 50% in petroleum wax (1.15 g, 24 mmol) in DMSO (10 ml) for a period of 15 min. at 5°. The mixture was stirred and allowed to reach room temperature in one hour. To the reaction mixture, epoxide **3** (3 g, 22 mmol) was added dropwise over 30 min. at 0-5° . It was allowed to reach room temperature in 1.5h and kept stirring for additional 2 h. Reaction was monitored by TLC (5 and 30% EtOAc/petroleum ether). When the disappearance of starting material was indicated on TLC, methyl iodide (12.5 g, 88 mmol) was added at 0° and the reaction mixture was allowed to reach room temperature in two hours. It was kept stirring at room temperature for further 4 h. After usual workup, a yellow oil was obtained. Yield : 5.4 g (90%). The product showed two spots on TLC (1%, MeOH/$CHCl_3$). These were separated by column chromatography using $CHCl_3$ and $CHCl_3$/MeOH mixture. Compound 4a and4b were the two required diastereomers obtained in the yield of 3.16 g (63.5%) and 1.62 g (31.7%) respectively of the crude product.

(2'R,2S)-3-O-(3'-Benzyloxy-2'-methoxypropyl)-1,2-isopropylidene glyceryl ether (4b)

$[\alpha]_D^{28}$ +4.37 (c 12.8,$CHCl_3$); ν_{max} (film)/cm^{-1}: 3080, 3020, 1800-1600 (Ar), 1390, 1380 (>$C(CH_3)_2$) 1260, 1220, 1110, 860 and 720 .
^1H NMR(60MHz)δ: 7.3 (5H, s, Ar), 4.52 (2H, s, CH_2 -Ar), 4.35-3.2 (9H, m, 1-H, 2-H, 3-H, 1'-H, 2'-H and 3'-H).3.42 (3H, s, OCH_3), 1.4 (3H, s, >$C(CH_3)_2$) and 1.35 (3H, s,>$C(CH_3)_2$). ^{13}C NMR(75 MHz)δ : 138.2 (s, C-1 of Ar), 128.29 (d, C-2 and C-6 of Ar), 127.57 (d, C-3, C-4 and C-5 of Ar), 109.29 (s, >$C(CH_3)_2$), 78.50 (d, C-2'). 74.58 (d, C-2), 73.35 (t, CH_2 -Ar), 73.31 (t, C-3), 71.66 (t, C-3'), 69.90 (t, C-1'), 66.74 (t, C-1), 57.9 (q, O-CH_3), 26.72 (q, >$C(CH_3)_2$) and 25.38 (q, >$C(CH_3)_2$).

(Calculated $C_{17}H_{26}O_5$: C 65.80 H 8.34 Found : C 65.78 H 8.44%);
MS : m/z 295(M^+ -15).

(2'R,2R)-3-O-(3'-Benzyloxy-2'-methoxypropyl)-1,2-dihydroxy glyceryl ether (9)

To a solution of compound **4a** (3 g, 9.68 mmol) in methanol (50 ml), Dowex 50W X8 (1:1 eq. w/w) was added and stirred for 2h at room temperature. Reaction was monitored by TLC (1% and 10%MeOH/$CHCl_3$).The reaction mixture was then filtered through a G-4 sintered crucible to recover the resin and the filtrate was evaporated to furnish the free diol **9**(2.6 g, 100%). ν_{max} (film)/cm^{-1}: 3450 (OH), 3080, 3020, 1800-1600 (Ar), 1460, 1280, 1100, 760 and 720 . ^1H NMR(60MHz)δ: 7.3 (5H, s, Ar), 4.5 (2H, s, CH_2 -Ar), 4.4-3.0 (12H, m, 3'-H, 2'-H, 1'-H, 3-H, 2-H, 1-H, 1-OH, 2-OH), 3.4 (3H, s, OCH_3). ^{13}C NMR(75 MHz)δ : 137.93 (s, C-1 of Ar), 128.38 (d, C-2 and C-5 of Ar), 127.68 (d, C-3, C-4 and C-5 of Ar), 79.28 (d, C-2'), 73.43 (t, CH_2 -Ar), 73.03 (t, C-3'), 71.04 (t, C-1'), 70.62 (d, C-2), 69.11 (t, C-3), 63.83 (t, C-1), and 57.86 (q, OCH_3).

(2'S,2R)-3-O-(1'-Hydroxy-2'-methoxypropyl)-1,2-dihydroxyglyceryl ether (10)

To a solution of compound **9** (2 g, 7.4 mmol) in methanol (50 ml), 10% Pd/C (100 mg) was added under N_2 atmosphere and then kept stirring for 36 h at 5psi pressure of H_2. Deprotection of benzyl group was found to be complete after 36h (Reaction was monitored by TLC. (10% and 15% MeOH/$CHCl_3$). The reaction mixture was filtered through G-4 sintered crucible and the filtrate was concentrated under *vacuo* to give an yellow oil. It was purified by column chromatography using 10-20% of MeOH in $CHCl_3$ as an eluant to yield compound **10**(1.15 g, 88%).
$[\alpha]_D^{29}$ -3.53 (c 1.14, MeOH).ν_{max} (film)/cm^{-1} : 3450 (br OH), 1580, 1520, 1220 and 1110; ^1H NMR(CD_3OD,60MHz)δ: 4.9 (3H, brs,1-OH, 2-OH, 1-OH), 3.58-3.43 (10H, m, 1-H, 2-H, 3-H, 3'-H, 2'-H, 1'-H) and 3.45 (3H, s, OCH_3). ^{13}C NMR(75 MHz, CD_3OD) : 82.22 (d, C-2'), 73.98 (t, C-3'), 72.25 (d, C-2), 71.69 (t, C-3), 64.48 (t, C-1'), 62.17 (t, C-1) and 58.15 (q, OCH_3).

(2'S,2S)-3-O-(1'-Hydroxy-2'-methoxypropyl)-1,2-isopropylidene glyceryl ether (11)

To a solution of compound **10**(1 g, 5.5 mmol) in dry acetone (50 ml), catalytic amount of Dowex 50W X8 (10-15 granules) was added and stirred for six hours. When starting material was not detectable on TLC, the reaction mixture was filtered through G-4 sintered crucible and the filtrate concentrated under vacuum to give a light yellow oil (1.2 g,, 100%). It was purified further by column chromatography using $CHCl_3$ as a solvent to get compound **11** (1.15 g, 96%). Purity was checked by GC. (98% pure)
$[\alpha]_D^{30}$ +7.57 (c 7,$CHCl_3$). ν_{max} (film)/cm^{-1} : 3450 (brOH), 1390, 1380 ($C(CH_3)_2$), 1260, 1220, 1110 (br) and 860 . ^1H NMR(300 MHz)δ: 4.27 (1H, tt, J = 5.8, 6.2, 2-H), 4.05 (1H, dd, J = 8.24, 6.41 , 1-H), 3.74 (1H, dd, J = 8.24, 6.25, 1-H), 3.79-3.42 (7H, m, 3-H, 3'-H, 2'-H and 1'-H), 3.46 (3H, s, OCH_3), 2.3 (1H, brs, 1'-OH), 1.42 (3H, s, $>C(CH_3)_2$) and 1.36 (3H, s, $>C(CH_3)_2$

). ^{13}C NMR(75 MHz)δ : 109.24 (s, >C(CH_3)$_2$), 80.08 (d, C-2'), 74.55 (d, C-2, 72.38 (t, C-3), 71.01 (t, C-3'), 66.44 (t, C-1), 61.85 (t, C-1'), 57.64 (q, OCH), 26.54 (q, >C(CH_3)$_2$) and 25.2 (q,>C(CH_3)$_2$).

(2'R,2S)-3-O-(1'-axo-2'-methoxypropyl)-1,2-isopropylidene glyceryl ether (12)

To a suspension of celite (2g) and activated powdered molecular sieves (1g) in dry CH_2Cl_2 (20 ml), dry pyridine (1 ml, 13 mmol) was added and cooled in an ice bath. To this cold solution (0°), CrO_3 (0.6 g, 0.6 m.mol) was added in three portions over a period of 15 min. and stirred for about half an hour at the same temperature. To the reaction mixture a solution of alcohol **11**(220 mg, 1 mmol) in dry CH_2Cl_2(2 ml) was added and stirred for 45 min. Ether (50 ml) was next added and stirred further for 10 min. The supernatant solution was decanted and the residue washed with more ether (3 x 60 ml). The combined extracts were concentrated under reduced pressure to afford the crude aldehyde 12 (200 mg, 90%); ν_{max} (film)/cm^{-1} : 1730 (CHO), 1390, 1380 (>C(CH_3)$_2$);^1H NMR(60MHz)δ: 9.7 (1H, d, CHO), 4.5-3.00 (8H, m, 1-H, 2-H, 3-H, 3'-H and 2'-H), 3.5 (3H, s,OCH_3), 1.42 (3H, s, 3H, CH_3), and 1.36 (3H, s, CH_3).

(2S,2'S,3'Z)-3-O-(2'-Methoxyhexadec-3'-ethyl)-1,2-isopropylidene glycerol (13)

To an ice cold solution of tridecyl triphenyl phosphonium bromide (1.47 g, 2.8 mmol) in THF (20 ml), n-butyl lithium (1.75 ml, 2.5 mmol) was added. After stirring for one hour at 0-5° the mixture was cooled to -10° . To the stirred solution at -10° the crude aldehyde **12** (200 mg, 0.95 mmol) in THF (3 ml) was added dropwise for half an hour. The reaction mixture was allowed to reach at 0° in an hour. The reaction mixture was then quenched with brine and extracted with ether (3 x 50 ml). The combined organic layer was dried over anhydrous , concentrated and chromatographed over silica gel column using solvent petroleum ether:ethyl acetate mixture as eluant to yield compound 13 (220 mg 65%). Purity was checked by GC.; $[\alpha]_D^{28}$+9.16 (c 1.2, $CHCl_3$); ν_{max} (film)/cm^{-1} : 3010, 1650 (C=C), 1390, 1380 (>C(CH_3)$_2$) 1220, 1100, 1050, 850, 730 and 720 . ^1H NMR(300 MHz)δ: 5.67 (1H, dt, J = 11.14 , 7.48 , 4'-H), 5.22 (1H, dtd, J = 11.1, 7.78, 1.52 , 3'-H), 4.28 (1H, m, 2-H), 4.2 (1H, m, 2'-H), 4.05 (1H, dd, J = 8.24, 6.4 , 1-H), 3.74 (1H, dd, J = 8.24, 6.25 , 1-H), 3.66-3.42 (4H, m, 3-H and 1'-H), 2.08 (2H, m, 5'-H), 1.42 (3H, s, >C(CH_3)$_2$), 1.36 (3H, s,>C(CH_3)$_2$), 1.26 (20H, s, 6'-H to 15'-H), and 0.88 (3H, t, 16'-H).
^{13}C NMR(75 MHz)δ :136.38 (d, C-3'), 126.7 (d, C-4'), 109.29 (s, >C(CH_3)$_2$), 76.02 (d, C-2'), 74.61 (t, C-3'), 74.55 (d, C-2), 72.43 (t, C-3), 66.87 (t, C-1), 56.16 (q, OCH_3), 31.85 (t, C-14'), 29.43 (t, C-6' to C-13'), 27.82 (t, C-5'), 26.71 (q, >C(CH_3)$_2$), 25.35 (q, >C(CH_3)$_2$), 22.60 (t, C-15'), and 14.00 (q, C-16'). MS : m/z 369 (M^+-15), 131(M^+-$C_6H_{31}O_3$,base peak)

(2R,2'S,3Z)-1-O-(2'-Methoxyhexadec-3-enyl)glycerol (1)

To a solution of compound **13** (100 mg, 0.27 mmol) in methanol (10 ml), Dowex 50W x8 (1:1 eq. w/w) was added and stirred for an hour at room temperature. Reaction was

monitored by TLC (1% MeOH in $CHCl_3$). After usual workup, compound **1** was obtained which was further purified by column chromatography using $CHCl_3$ and MeOH/$CHCl_3$ mixture as eluants(75 mg, 85%); $[\alpha]_D^{28}$-3.14 (c 3.5,$CHCl_3$); ν_{max} (film)/cm^{-1} : 3450 (OH), 3020, 1650,(C=C), 1460, 1110 (br), 860, 740 and 720,^{1}H NMR(300 MHz)δ: 5.70 (1H, dt, J = 11.1, 8.1 , 4'-H), 5.21 1H, ddt, J = 9.4, 11.1, 1.5 , 3'-H), 4.24-4.17 (1H, m, 2'-H), 3.87 (1H, m, 2-H), 3.74-3.45 (6H, m, 1-H, 3-H, and 1'-H), 3.31 (3H, s, OCH_3), 2.45 (1H, brs, 2-OH), 2.07 (2H, m, 5'-H), 1.8 (1H, brs, 1-OH), 1.26 (2H, s, 6-H to 15-H), and 0.88 (3H, t, J = 6.56 , 16'-H).
^{13}C NMR(75 MHz)δ : 135.9 (d, C-3'), 126.1 (d, C-4'), 76.07(d, C-2'), 74.36 (t, C-1'), 73.15 (t, C-1), 70.71 (d, C-2), 63.91 (t, C-3), 56.01 (q, OCH_3), 31.85 (t, C-14'), 29.42 (t, C-6 to C-13'), 27.80 (t, C-5'), 22.60 (t, C-15') and 14.00 (q, C-16'). MS : m/z 315 (M^+-15), 241 (M^+-C_4 H_9 O_3, base peak).

(2R,2'S)-1-O-(2'methoxyhexadecyl) glycerol (2)

To a solution of compound **13** (80 mg, 0.21 mmol) in methanol (15 ml), 10% Pd/C (50 mg) was added and stirred vigorously under 2psi pressure of H_2 for 20 min. Reaction was monitored by TLC (10% MeOH/$CHCl_3$). After the reaction was over, the resultant solution was filtered through G-4 sintered crucible and the filtrate was concentrated under *vacuo* to give a compound **2**(66 mg, 92%).
$[\alpha]_D^{30}$ 2.02 (c 3.46, MeOH); ν_{max} (film)/cm^{-1} : 3450 (OH), 1460, 1110 (br) and 720; ^{1}H NMR(300 MHz)δ: 3.87 (1H, m, 2-H), 3.72-3.44 (6H, m, 3-H, 1-H and 1'-H), 3.39 (3H, s, OCH_3), 3.32 (1H, m, 2'-H), 2.5 (2H, brs, 2-OH and 3-OH), 1.15 (2H, m, 3-H), 1.27 (24H, s, 4-H to 15-H), and 0.89 (3H, t, J = 6.56 , 16'-H).
^{13}C NMR(75 MHz)δ : 80.29 (d, C-2'), 73.40 (t, C-1'), 73.14 (t, C-1), 70.64 (d, C-2), 63.9 (t, C-3), 57.17 (q, -OCH_3), 31.87 (t, C-14'), 30.83 (t, C-3'), 29.25 (t, C-5' to C-11' and C-13'), 29.29 (t, C-12'), 25.32 (t, C-4'), 22.63 (t, C-15') and 14.03 (t, -15'). MS : m/z 313 (M^+-15), 239 (M^+- C_4 H_9 O_3 , base peak).

Acknowledgement:
We thank CSIR , New Delhi (MHAB,SB & SB) for the award of Senior Research Fellowship. We wish to thank RSIC, I.I.T, Bombay for the spectral facilities.

References and Notes:

1. Hallgren,B.; Stallberg,G, *Acta Chem. Scand Ser B.*, **1967**,21,1519-1529.
2. Hallgren,B.; Nikalsson,A.; Stallberg,G.;Thorin,H, *Acta. Chem. Scand.*, **1974**, 28, 1029-1034.
3. Hallgren,B.;Stallberg,G, *Acta Chem. Scand. Ser. B.*, **1974**, 28, 1074-1076.
4. Ved,H.S.; Gustow,E.; Pieringer,R.A, *J. biol. Chem.*, **1984**, 259, 8122-8124.
5. Boeryd,B.; Hallgren,B.; Stallberg,G, *Br. J. exp. Path.*, **1971**, 52, 221.
6. Zaiden,H, Jpn. patent 81.07,715, *Chem. Abst.*, **1981**,94, 15057z

7. Brohult,S.;Brohult,A.; Eu.Patent.app. 321, 428 *Chem Abst.*,**1990**, 112, 151889d.
8. Pallavivini,M.;Villa,L.;Cesaroti,E.;Antogmazza,P, *J.Chem.Res(s)*,**1994**, 232-233.
9. Jurczak,J.;Pikul,S.;Baier,T,*Tetrahedron.*,**1986**,42, 447-488 (furthur references cited therein).
10. Takano,S.;Saya,K.;Goto,E.;Hirama,M.;Ogasawara,K, *Synthesis*, **1983**,116-117.
11. Oxidation of the primary alcohol 17 with pyridinium dichromate in $CHCl_3$ did not furnish the desired product. A mere 10% of **12** was obtained under Swern oxidation conditions.
12. Levy,G.C,*Topics in Carbon- 13 NMR Spectroscopy.*, John Wiley and Sons Inc., New york. **1976**, 2, 83.

(*Received in UK* 5 *January* 1995; *revised* 16 *February* 1995; *accepted* 17 *February* 1995)