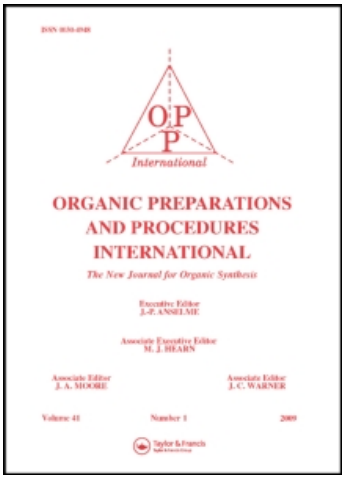

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A FACILE SYNTHESIS OF *rac*-1-O-ALKYLGLYCEROLS†

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Long chain 1-O-alkylglycerols are starting materials for synthesis of alkyl diacylglycerols and ether phospholipids,[1] which serve as model compounds in biophysical and biochemical studies.[2] 1-O-Alkylglycerols are synthesized by condensation of isopropylideneglycerol with alkyl halides, tosylates or mesylates followed by hydrolytic removal of the protecting groups.[3] A recent report describes conversion of alkylglycidyl ethers to corresponding dioxolanes or 1-O-alkyl-2,3-di-O-acetylglycerols followed by either acid or alkaline hydrolysis, respectively, to yield 1-O-alkylglycerols.[4] An earlier method reported for the synthesis of batyl alcohol $CH_2OHCHOHCH_2O(CH_2)_{17}CH_3$ was based on alkylation of sodium allyl alcoholate with octadecyl chloride or bromide followed by hydroxylation of the resulting allyl octadecyl ether with hydrogen peroxide in acetic acid and subsequent hydrolysis with alcoholic potassium hydroxide. The yield of batyl alcohol ranged from 35 to 55%.[5] These procedures involve several steps.

$$RCH_2OH \xrightarrow[TBAB,\ OH^-,\ 45°,\ 6\ hrs]{H_2C=CHCH_2Br,\ hexane} RCH_2OCH_2CH=CH_2$$

1

$$\xrightarrow[20°,\ 5\ hrs]{CTAP,\ CH_2Cl_2} RCH_2OCH_2CH(OH)CH_2OH$$

2

a) $R = CH_3(CH_2)_{10}$ b) $R = CH_3(CH_2)_{12}$
c) $R = CH_3(CH_2)_{14}$ d) $R = CH_3(CH_2)_{16}$

The present communication describes a simple two-step preparation of alkyl allyl ethers by reaction of normal long chain alcohols (C_{12}-C_{18}) in hexane with allyl bromide in the presence of phase-transfer catalyst, tetrabutylammonium bromide (TBAB), and aqueous alkali; direct hydroxylation with the recently developed novel reagent cetyltrimethylammonium permanganate (CTAP)[6] in dichloromethane yielded the corresponding *rac*-1-O-alkylglycerols (65-69% yield on the basis of alkyl allyl ether, see Table).

The use of TBAB gave higher yield of allyl dodecyl ether than cetyltrimethylammonium bromide (CTAB), benzyltriethylammonium chloride (TEBA), tetraethylammonium bromide

(TEAB), tetrabutylammonium chloride (TBACl); tetrabutylammonium iodide (TBAI) was as effective as TBAB. The unconverted alcohols were separated from the respective alkyl allyl ethers by gas chromatography (GC) on SE-30 column. For example, the relative retention time of dodecyl allyl ether was 1.6 with respect to dodecyl alcohol (1.0). The homologous alkyl allyl ethers were separated similarly. The retention times were 2.4, 5.4 and 12.2 for tetra-, hexa- and octadecyl allyl ethers, respectively relative to dodecyl allyl ether (1.0). GC was also used to check the purity of the alkyl allyl ethers isolated by silica gel column chromatography. The advantages of the present route are simplicity of the preparation of alkyl allyl ethers without recourse to protecting groups followed by direct hydroxylation to *rac*-1-O-alkylglycerols in fairly good yields.

TABLE. Yields and mps of *rac*-1-O-Alkylglycerols

Compound	Yield (%)[a]	mp (°C)	lit.[3] mp.
2a	69	48-49	49.5
2b	66	57-57.5	58.5
2c	65	64-64.5	65.5
2d	65	71-71.5	71-71.5

a) Yields are for isolated products and not optimized.

EXPERIMENTAL SECTION

Mps were determined on a Mettler FP 51 instrument and are uncorrected. Elemental analyses were carried out using CHN-600, LECO CORPORATION, USA. IR spectra were recorded on a Perkin-Elmer Model 283 B spectrophotometer. ^{1}H NMR spectra were obtained with JEOL FX 90Q and Varian 60-FT instruments in $CDCl_3$ solution using TMS as internal standard. Chemical shifts are given as δ values. Mass spectra were recorded on a V. G. Micromass 7070 H mass spectrometer at 70 ev. GC was carried out using Hewlett Packard 5840 A fitted with a 5% SE-30 (2' x 1/8") column, hydrogen flame detector and data processor. The column, injection port and detector temperatures were maintained at 170, 250 and 300° respectively. Flow rate of carrier gas (nitrogen) was 30 ml/min. Allyl bromide, the long chain alcohols and the phase transfer catalysts, were obtained from Aldrich Chemical Company, Inc., Milwaukee, WI, USA.

Preparation of Allyl Dodecyl Ether (1a).- To a vigorously stirred mixture of 1-dodecanol (4.65 g, 25 mmol), 48% aq. NaOH (75 mmol), TBAB (0.40 g, 1.25 mmol) and hexane (30 ml), allyl bromide (4.3 ml, 50 mmol) was added dropwise for 30 min at 25-30°. Then the mixture was stirred vigorously at 45° for 6 hrs, cooled and the organic layer was separated. The solvent was evaporated under reduced pressure and the product was chromatographed on a silica gel column using n-hexane:diethyl ether (90:10, v/v) to yield pure allyl dodecyl ether

(4.58 g) in 81% yield. Unconverted alcohol was eluted using diethyl ether. IR (neat): 3080 (C=C-H), 1645 (C=C), 1100 (C-O-C) cm^{-1}. ^1H NMR: δ 6.19-5.71 (m, 1H, -CH=), 5.35-5.10 (m, 2H, $=CH_2$), 4.25-3.87 (m, 2H, $-OCH_2-C=C$), 3.42 (t, 2H, $-CH_2-O-$), 1.35 [b s, 2OH, $-(CH_2)_{10}-$], 0.88 (t, 3H, $-CH_3$). MS: m/z (rel. int.) 226 (M, 0.8), 198 (M-28, 1.7), 197 (M-29, 7.5), 169 (M-57, 1.7), 71 ($CH_2=CH-CH_2-O=CH_2^+$ and/or $C_5H_{11}^+$, 94.2), 58 ($CH_2=CH-CH_2OH^+$, 75.8), 57 ($CH_2=CH-CH_2O^+$ and/or $C_4H_9^+$, 100), 41 ($CH_2-CH=CH_2^+$, 71.7).

Anal. Calcd. for $C_{15}H_{30}O$: C, 79.58; H, 13.36. Found: C, 79.75; H, 13.02

Allyl Tetradecyl Ether (1b).- 1-Tetradecanol (5.35 g, 25 mmol) provided 4.95 g (78%) of the title ether.

Anal. Calcd. for $C_{17}H_{34}O$: C, 80.24; H, 13.47. Found: C, 80.64; H, 13.11

Allyl Hexadecyl Ether (1c).- 1-Hexadecanol (6.05 g, 25 mmol) provided 5.26 g (75%) of the title ether.

Anal. Calcd. for $C_{19}H_{38}O$: C, 80.78; H, 13.56. Found: C, 81.04; H, 13.20

Allyl Octadecyl Ether (1d).- 1-Octadecanol (6.75 g, 25 mmol) provided 5.64 g (73%) of the title ether.

Anal. Calcd. for $C_{21}H_{42}O$: C, 81.22; H, 13.63. Found: C, 80.98; H, 13.33

The spectral patterns (IR, ^1H NMR and MS) of 1b, 1c and 1d are similar to that of 1a.

Synthesis of *rac*-1-O-dodecylglycerol (2a).- CTAP, prepared[6] from CTAB and potassium permanganate, was added dropwise (2.02 g, 5 mmol) in dichloromethane (30 ml) to allyl dodecyl ether (1.13 g, 5 mmol) in dichloromethane (15 ml) at 20°. Stirring was continued for 5 hrs and the mixture was concentrated to half of its volume. The residual solution was diluted with ether (100 ml) and filtered through a pad of Celite and anhydrous sodium sulfate. The filtrate was evaporated under reduced pressure and *rac*-1-O-dodecylglycerol was purified by silica gel column chromatography. The unconverted allyl dodecyl ether was eluted with n-hexane:diethyl ether (90:10, v/v) and the *rac*-1-O-dodecylglycerol with ethyl acetate, (0.89 g). IR (KBr): 3600-3120 [$-CH(OH)CH_2OH$], 1120 (C-O-C) cm^{-1}. ^1H NMR: δ 3.87-3.33 [m, 7H, $-CH_2-O-CH_2-CH(OH)CH_2OH$], 1.58 (s s, 2H, D_2O exchangeables), 1.31 [b s, 2OH, $-(CH_2)_{10}-$], 0.88 (t, 3H, $-CH_3$). MS: m/z (rel. int.) 260 (M, absent), 229 ($M-CH_2OH$, 1.7), 199 [$M-CH(OH)CH_2OH$, 6.7], 169 [$M-OCH_2CH(OH)CH_2OH$, 7.9], 97 (13.3), 85 (38.3), 71 (58.3), 57 (100).

Anal. Calcd. for $C_{15}H_{32}O_3$: C, 69.18; H, 12.39. Found: C, 69.50; H, 12.09

rac-1-O-Tetradecylglycerol (2b).- Allyl tetradecyl ether (1.27 g, 5 mmol) provided 0.95 g of the title product.

Anal. Calcd. for $C_{17}H_{36}O_3$: C, 70.78; H, 12.58. Found: C, 70.98; H, 12.31

rac-1-O-Hexadecylglycerol (2c).- Allyl hexadecyl ether (1.41 g, 5 mmol) provided 1.03 g of the title product.

Anal. Calcd. for $C_{19}H_{40}O_3$: C, 72.10; H, 12.74. Found: C, 71.92; H, 12.38

rac-1-O-Octadecylglycerol (2d).- Allyl octadecyl ether (1.55 g, 5 mmol) provided 1.11 g of the title product.

Anal. Calcd. for $C_{21}H_{44}O_3$: C, 73.20; H, 12.87. Found: C, 72.90; H, 12.52

The spectral patterns (IR, ^1H NMR and MS) of 2b, 2c and 2d are similar to that of 2a.

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N-(DIPHENYLMETHYLENE)–α,β-DIDEHYDROAMINO ACID ESTERS. THERMAL AND LEWIS ACID INDUCED DIMERIZATIONS

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N-Protected α,β-didehydroamino acid esters are useful synthons in the synthesis of α-amino acids.[1] N-(Arylidene)-α,β-didehydroalaninates have been used as Michael acceptors