Aliphatic Diether Analogs of Glyceride-Derived Lipids. I. Synthesis of D-α,β-Dialkyl Glyceryl Ethers*

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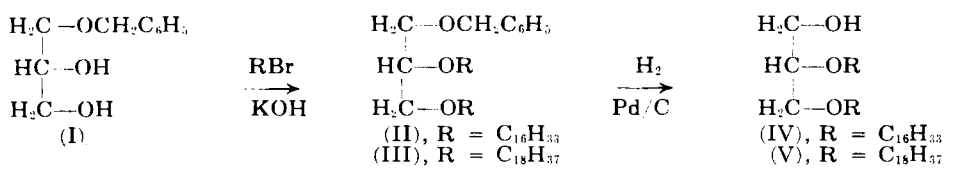
D-α,β-Di-*O*-hexadecyl and -di-*O*-octadecyl glycerol were synthesized by alkylation of L-α-*O*-benzyl glycerol with the corresponding alkyl bromide and potassium hydroxide in boiling benzene, followed by removal of the benzyl group by hydrogenolysis with palladium catalyst. The corresponding DL-α,β-di-*O*-alkyl glycerols were also synthesized by the same procedure, starting with DL-α-*O*-benzyl glycerol. The physical properties of these diethers are compared with those of the analogous diesters.

The existence of long-chain ethers of glycerol in naturally occurring lipids has been known for many years (Deuel, 1951; Hilditch, 1956). Until recently, the only types of ether-containing lipids found were α-glyceryl monoethers, such as batyl, chimyl, and selachyl alcohols in Elasmobranchs (Karnovsky *et al.*, 1946; Karnovsky and Brumm, 1955; Hallgren and Larsson, 1962a) and in mammals (Holmes *et al.*, 1941; Karnovsky *et al.*, 1946; Hallgren and Larsson, 1962b). These glyceryl ethers probably exist *in vivo* in the form of glycerides or phospholipids (Karnovsky, 1951), since they are obtained only after hydrolysis of the intact lipids. The presence of an ethanolamine phosphatide containing one ether-linked alkyl group has been demonstrated in egg yolk (Carter *et al.*, 1958), in brain (Svennerholm and Thorin, 1960; Ansell and Spanner, 1961), and in bovine red cells (Hanahan and Watts, 1961). Renkonen (1962) has recently found a lecithin having one alkyl ether group in human blood serum.

Since the diglyceride moieties of naturally occurring phosphatides have the α,β-structure and the D-configuration (Baer and Kates, 1950; see Kates, 1960), it was expected that the natural glyceryl diethers would also have the α,β-structure and the D-configuration.

The synthesis was carried out as follows (see Reaction Scheme):

L-α-Benzyl glyceryl ether (I), prepared from D-acetone glycerol (Baer and Fischer, 1939) by a modification of the procedures of Sowden and Fischer (1941) and Howe and Malkin (1951), was alkylated in boiling benzene with either *n*-hexadecyl bromide or *n*-octadecyl bromide, and potassium hydroxide. The D-α,β-dialkyl benzyl glyceryl ethers (II, III) were converted directly to the corresponding D-α,β-dialkyl glyceryl ethers (IV, V) by catalytic hydrogenolysis. The corresponding DL-α,β-dialkyl glyceryl ethers were also synthesized by the above procedure, starting with DL-α-benzyl glyceryl ether. The diethers were purified by crystallization from ethyl acetate and were shown to be homogeneous by paper and gas-liquid chromatography.



L-α-Benzyl Glycerol — D-α,β-Dialkyl Glyceryl Ether

Reaction Scheme

Recent studies in this laboratory (Sehgal *et al.*, 1962) have shown that the phosphatides of *Halobacterium cutirubrum* contain long-chain ether groups, rather than fatty acid ester groups. After hydrolysis of the total lipids of this bacterium, there was obtained in high yield a substance tentatively identified as a long-chain diether of glycerol.[1] This substance and the parent phosphatides (the major component of which resembles a polyglycerol phosphatide) thus constitute a new class of glycerol-derived lipids, one in which the glycerol has two ether-linked long-chain groups.

To aid in establishing the structure of the bacterial diether (and also of the parent phosphatides), the synthesis of several dialkyl glyceryl ethers was undertaken.

Their infrared spectra showed the expected bands for OH, C—O—C, and CH_2 groups.

The nuclear magnetic resonance spectrum of DL-α,β-dihexadecyl glyceryl ether was examined to verify the α,β-structure of the diether. The following resonance bands (given as ppm, relative to tetramethylsilane taken as 10 ppm; see Hopkins, 1961) were found: 6.35 (unetherified CH_2); 6.5 (etherified CH_2); 7.75 (unidentified, possibly free OH); 8.7 (CH_2 in hydrocarbon chains); and 9.1 (terminal CH_3). The presence of the 6.35 ppm band, assigned to the hydrogens in an unetherified CH_2-group (Hopkins and Bernstein, unpublished), and the absence of a band at 6.2 ppm, assigned to the lone hydrogen on an unetherified CH-group (Hopkins and Bernstein, unpublished), would be consistent with the α,β-structure of the diether but not with the α,α′-structure (*c.f.* also Carter *et al.*, 1958). Final verification of the α,β-structure, however, must await further analysis of nuclear magnetic resonance spectra of various diether derivatives.

Because of the structural similarity between diethers and diesters of glycerol, it was of interest to compare their physical properties (see Table I). The melting points of the D-α,β-diethers were about 20° lower than

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[1] A similar substance had previously been obtained by Marinetti *et al.* (1959) after hydrolysis of hydrogenated beef heart phosphatides.

TABLE I
PHYSICAL PROPERTIES OF DIALKYL ETHERS AND DIESTERS OF GLYCEROL

Substance	M.p. (°C)	$[\alpha]_D$[a]	$[M]_D$[a]	Paper Chromatography (R_F)[b]	Gas-Liquid Chromatography (relative retention at 220°)[c]
Diethers					
D-α,β-di-O-hexadecyl glycerol	48.5–49.5	−7.5	−41	—	—
D-α,β-di-O-octadecyl glycerol	53.5–54.5	−6.9	−41	—	—
DL-α,β-di-O-hexadecyl glycerol	54.5–55.5	—	—	0.77	5.90
DL-α,β-di-O-octadecyl glycerol	63–64	—	—	0.77	17.9
Diglycerides					
D-α,β-dipalmitin	68–69[d]	−2.9[d]	−16.5[d]	—	—
D-α,β-distearin	76–77[d]	−2.8[d]	−17.5[d]	—	—
DL-α,β-dimyristin	58–59[d]	—	—	0.32	3.27
DL-α,β-dipalmitin	65–66[d]	—	—	0.30	9.89
DL-α,β-distearin	71.5–72.5[d]	—	—	0.28	—

[a] In chloroform. [b] Solvent, heptane–diisobutyl ketone, 96:6 (Marinetti *et al.*, 1958). [c] On a short (21-in.) column of silicone (SE-52) at 220° and 26 p.s.i.; reference standard, DL-α,β-dilaurin (retention time, 3.4 min.). The natural diether isolated from lipids of *H. cutirubrum* had a relative retention of 11.5; calcd. for α,β-diheptadecyl glyceryl ether, 10.5. [d] See Baer and Kates (1950).

those of the corresponding D-diesters, but the melting points of the DL-diethers were only 8–10° lower than those of the corresponding DL-diesters. The fact that the DL-diethers have higher melting points than the D-diethers indicated that the DL-forms are racemic *compounds*, and this was verified by the lowering of the m.p. of the DL-α,β-dioctadecyl glyceryl ether on admixture of a small amount of the D-isomer. In contrast, the DL- forms of the diglycerides are racemic *mixtures*, since they have lower melting points than the corresponding D-forms; this was verified by the rise in m.p. of the DL-α,β-distearin on admixture of a small amount of the D-isomer (see Eliel, 1962).

The diethers had higher R_f values than the diesters in heptane-diisobutyl ketone on silicic acid–impregnated paper (Marinetti *et al.*, 1958) (Table I); they also had shorter retention times than the corresponding diesters when subjected to gas-liquid chromatography on a column of silicone (SE-52) at 220°. These results are consistent with the fact that the ether group is less polar than the ester group.

The unsaponifiable substance obtained from the lipids of *H. cutirubrum* was found to have an infrared spectrum and chromatographic properties (see Sehgal *et al.*, 1962) similar to those of the synthetic diethers. However, the nature of the alkyl groups of the natural compound has yet to be determined rigorously, although the analytical data (Sehgal *et al.*), the relative retention on SE-52 (Table I), and the absence of double-bond absorption in the infrared would suggest that the alkyl groups are saturated and have an average chain length not less than C_{17}. The results of detailed studies on the structure of the naturally occurring diether will be reported subsequently.

EXPERIMENTAL AND RESULTS[2]

L-α-*O*-*Benzyl Glycerol* (*I*).—This was prepared by a modification of the procedures of Sowden and Fischer (1941) and of Howe and Malkin (1951): a mixture of 19.1 g (0.145 moles) of D-acetone glycerol (Baer and Fischer, 1939), 38 g (0.3 moles) of benzyl chloride, and 17 g of powdered potassium hydroxide in 100 ml of dry benzene was refluxed with stirring for 16 hours. The water formed was removed by means of a phase-separating head. The cooled mixture was diluted with benzene (100 ml) and washed successively with water, 0.1 N hydrochloric acid, 2.5% potassium bicarbonate, and again water. The benzene phase was dried over sodium sulfate and the solvent removed under reduced pressure. Distillation of the residue yielded unreacted benzyl chloride, boiling below 100°/0.5 mm, and D-acetone glycerol benzyl ether, b.p. 107–8°/0.5 mm; yield, 28.0 g (87%). After hydrolysis of the isopropylidene group by the procedure of Howe and Malkin (1951), 22.8 g (84% over-all yield) of the L-α-*O*-benzyl glycerol was obtained; b.p. 142–146°/0.7 mm; $[\alpha]_D^{21}$ +5.5° (pure liquid) (Sowden and Fischer, 1941, gave $[\alpha]_D$ +5.3°).

D-α,β-*Di-O-Hexadecyl-α'-O-Benzyl Glycerol* (*II*).—A mixture of 3.46 g (0.02 mole) of L-α-*O*-benzyl glycerol, 24.4 g (0.08 mole) of 1-bromohexadecane, and 4.5 g of powdered potassium hydroxide in 50 ml of dry benzene was refluxed with stirring for 16 hours, the water formed being removed with a phase-separating head. The cooled mixture was diluted with 50 ml of ethyl ether and washed successively with water, 1 N hydrochloric acid, 2.5% potassium bicarbonate solution, and finally with water. The benzene solution was dried over sodium sulfate and the solvent evaporated under reduced pressure. The residue was subjected to distillation *in vacuo* to remove unreacted hexadecyl bromide (14.2 g) boiling between 120–135° 0.6 mm (bath, 155–165°). The residual oil (7.3 g, 58%) could not be crystallized and was not further purified. Its infrared absorption spectrum (liquid film), however, showed no OH band and had the required strong C—O—C— band at 1110 cm^{-1}, CH_2— bands at 2920 (*s*), 2850 (*s*), 1465 (*s*), and 1365 (*w*), and aryl absorption at 3020 (*w*), 1495 (*w*), 730 (*m*) and 695 (*m*) cm^{-1}. $[\alpha]_D^{27}$ − 0.12° (pure liquid); $[M]_D^{27}$, −0.76°; d^{27}, 0.961.

D-α,β-*Di-O-Hexadecyl Glycerol* (*IV*).—A solution of the above benzyl ether (7.3 g) in 50 ml of ethyl acetate was shaken with 0.5 g of freshly prepared palladium on charcoal catalyst (Hessel *et al.*, 1954) in an atmosphere of hydrogen at room temperature and an initial pressure of about 40 cm of water. After 3 to 4 hours 240 ml of hydrogen was consumed (calcd. for 1 mole, 280 ml). Slower rates of hydrogenolysis were found to be due to incomplete removal of the alkyl bromide. In

[2] All melting points are uncorrected and were taken in Pyrex glass capillaries at a heating rate of 1°/minute. Infrared spectra were measured in carbon tetrachloride solution, unless otherwise noted, with a Perkin-Elmer Model 21 spectrophotometer (double-beam) with sodium chloride optics.

such cases, the catalyst was filtered off and hydrogenation resumed with fresh catalyst; when this did not suffice, the benzyl ether was again subjected to distillation as described above and again hydrogenated. After completion of the hydrogenolysis, the catalyst was removed by filtration and washed with chloroform, and the combined filtrates were evaporated to dryness under reduced pressure. The solidified residue was dried *in vacuo* in a desiccator (weight, 6.0 g; 55% over-all yield). Crystallization from 40 ml of ethyl acetate or from 50 ml of chloroform-methanol (1:4, v/v) at 5° yielded 3.4 g of D-α,β-di-*O*-hexadecyl glycerol with melting point 48.0–49.5°; recrystallization from ethyl acetate raised the melting point to 48.5–49.5°. $[\alpha]_D^{21}$, −7.5° (*c*, 7.5 in chloroform); $[M]_D$ −40.6°.

Anal. Calcd. for $C_{35}H_{72}O_3$ (541.6): C, 77.71; H, 13.42. Found: C, 77.44; H, 13.47.

The dihexadecyl ether is soluble in acetone, ethyl ether, chloroform, and benzene, and insoluble in cold methanol and cold ethyl acetate. Its infrared spectrum in carbon tetrachloride showed the following bands (cm^{-1}): OH, 3590 (sharp), 3480 (broad); CH_2—, 2920(*s*), 2850(*s*), 1465(*s*), 1377(*w*), 1350(*w*), 720(*m*); C—O—C—, 1112(*s*); C—O— (primary alcohol), 1045(*s*); other bands, 1395(*w*), 1300(*w*), and 1205(*w*).

D-α,β-*Di-O-Octadecyl-α'-Benzyl Glycerol* (*III*).—A mixture of 3.65 g (0.02 mole) of L-α-*O*-benzyl glycerol, 26.7 g (0.08 mole) of 1-bromo-octadecane, and 4.5 g of powdered potassium hydroxide in 50 ml of anhydrous benzene was refluxed with stirring for 16 hours, the water formed being removed by means of a phase-separating head. The cooled mixture was then diluted with 50 ml of ether and washed successively with water, 1 N hydrochloric acid, 2.5% potassium carbonate solution, and finally water. The dried benzene solution was evaporated under reduced pressure and the residue subjected to high-vacuum distillation to remove unreacted bromo-octadecane (12.4 g), boiling at 155–168°/0.7 mm (bath, 195–220°). The remaining oil (13.0 g, 95%), which solidified on cooling, was sufficiently pure for subsequent hydrogenolysis although still containing traces of bromo-octadecane. After two crystallizations from methanol-chloroform (1:1, v/v) at 5° the D-α,β-dioctadecyl benzyl ether melted at 35.5–36.5° and had $[\alpha]_D^{21}$ −0.29° (*c*, 7.5 in chloroform); $[M]_D^{21}$, −1.9°.

Anal. Calcd. for $C_{46}H_{86}O_3$ (687): C, 80.40; H, 12.62. Found: C, 79.90; H, 12.90.

The infrared spectrum of the benzyl ether showed the following absorption bands (cm^{-1}): CH_2—, 2910(*s*), 2845(*s*), 1465(*m*), 1365–1375(*w*, doublet); C—O—C—, 1110(*s*); aryl bands, 3020(*w*), 1495(*w*), 730(*m*), and 695(*m*); other bands, 1300(*w*), 1200(*w*), 1028(*w*); no OH band.

D-α,β-*Di-O-Octadecyl Glycerol* (*V*).—The above benzyl ether (11.1 g) was hydrogenated in 85 ml of ethyl acetate with freshly prepared palladium on charcoal catalyst (1 g) as described for the hexadecyl derivative. Hydrogenation ceased after 3 hours with the consumption of 420 ml of hydrogen (calcd. for 1 mole, 460 ml). When the rate of hydrogenation was slow, the catalyst was removed by filtration and hydrogenation was resumed with fresh catalyst. After completion of the reaction, the diether was dissolved by addition of warm chloroform (40 ml), and the catalyst was filtered off and washed with chloroform. The combined filtrates were evaporated to dryness under reduced pressure and the solid residue was crystallized from 90–100 ml ethyl acetate, yielding 7.8 g (77% over-all yield) of D-α,β-di-*O*-octadecyl glycerol, m.p. 53.0–54.5°. Recrystallization from ethyl acetate or chloroform-methanol (1:5, v/v) at 5° raised the m.p. to 53.5–54.5°. $[\alpha]_D^{21}$ − 6.85° (*c*, 7.5 in chloroform): $[M]_D$,− 40.8.

Anal. Calcd. for $C_{39}H_{80}O_3$ (596): C, 78.45; H, 13.51. Found: C, 78.60; H, 13.84.

The dioctadecyl ether has solubilities similar to those of the dihexadecyl ether but is much less soluble in methanol, ethyl acetate, and petroleum ether. Its infrared spectrum in carbon tetrachloride solution was identical with that of the dihexadecyl ether.

DL-α-*O-Benzyl Glycerol*.—This substance was prepared in two ways: (1) by reaction of 1-chloro-propan-2,3-diol with benzyl alcohol in the presence of powdered sodium hydroxide at 90–100° by the procedure of Fairbourne *et al.* (1931); the product was obtained in a 53% yield and had b.p. 125–127°/0.2 mm and d^{27}, 1.129 (reported by Fairbourne *et al.*, 1931, b.p. 164°/2 mm; d^{25} 1.130); and (2) by the same procedure described above for the L-isomer, starting with DL-acetone glycerol, prepared according to the method of Newman and Renoll (1945); the product was obtained in an over-all yield of 70% and had b.p. 168–170°/0.8 mm.

DL-α,β-*Di-O-Hexadecyl Glycerol*.—This substance was prepared as described above for the D-isomer, but starting with DL-α-*O*-benzyl glycerol, and was obtained in an over-all yield of 50%; m.p. after recrystallization from methanol or ethyl acetate, 54.5–55.5°.

Anal. Calcd. for $C_{35}H_{72}O_3$ (541): C, 77.70; H, 13.42. Found: C, 77.23; H, 13.10.

The DL-isomer had similar solubilities and an identical infrared spectrum to those of the D-isomer.

DL-α,β-*Di-O-Octadecyl Glycerol*.—This substance was prepared as described above for the D-isomer, starting, however, with DL-α-*O*-benzyl glycerol; over-all yield, 50%; m.p. after recrystallization from ethyl acetate, 63–64°; admixture of a small amount of D-α,β-dioctadecyl ether lowered the m.p. to 61.5–63° (sintered, 59°). For comparison, the melting point of DL-α,β-distearin (69.5–70.5°) was determined after admixture of a small amount of D-α,β-distearin and found to be raised to 69.5–72.5°.

Anal. Calcd. for $C_{39}H_{80}O_3$ (596): C, 78.45; H, 13.51. Found: C, 78.06; H, 13.40.

The DL-isomer had similar solubilities and an identical infrared spectrum to those of the D-isomer.

Paper Chromatography.—The diethers and diesters of glycerol were chromatographed on silicic acid–impregnated Whatman 3 MM paper with heptane–diisobutyl ketone (96:6, v/v) as solvent (Marinetti *et al.*, 1958). Each substance was applied to the paper in chloroform solution, approximately 200 μg/spot; the chromatograms were run in ascending direction for 5–6 hours and dried in the fume hood for 15 minutes, and the spots were detected with Rhodamine 6 G (see Marinetti *et al.*, 1958).

Gas-Liquid Chromatography.—The substances were chromatographed on a 21-in. column of 2% GE silicone (SE-52) on Gas-Chrom Z (80/100 mesh) at 220° with a pressure of 26 p.s.i., with argon as carrier gas. The apparatus used was a Pye Argon Chromatograph with a strontium 90-ionization detector. The column was preconditioned at 210–220° for 24 hours with gas flow, followed by 24 hours at 310° without gas flow.

Nuclear Magnetic Resonance Spectra.—These spectra were measured in deuterochloroform ($CDCl_3$) containing tetramethyl silane as internal reference standard, with a 60-mc Varian high-resolution spectrometer. Substrate concentration was about 10%. The chemical shifts are expressed as ppm relative to tetramethylsilane, which was taken as 10 ppm.

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References

Ansell, G. B., and Spanner, S. (1961), *Biochem. J. 81*, 36P.
Baer, E., and Fischer, H. O. L. (1939), *J. Biol. Chem. 128*, 463.
Baer, E., and Kates, M. (1950), *J. Am. Chem. Soc. 72*, 942.
Carter, H. E., Smith, D. B., and Jones, D. N. (1958), *J. Biol. Chem. 232*, 681.
Deuel, H. J., Jr. (1951), The Lipids, vol. 1, New York, Interscience Publishers, Inc., pp. 392–396.
Eliel, E. L. (1962), Stereochemistry of Carbon Compounds, New York, McGraw-Hill Book Co., pp. 44–45.
Fairbourne, A., Gibson, G. P., and Stephens, D. W. (1931), *J. Chem. Soc.* 445.
Hallgren, B., and Larsson, S. (1962a), *J. Lipid Research 3*, 31.
Hallgren, B., and Larsson, S. (1962b), *J. Lipid Research 3*, 39.
Hanahan, D. J., and Watts, R. (1961), *J. Biol. Chem. 236*, PC59.
Hessel, L. W., Morton, I. D., Todd, A. R., and Verkade, P. E. (1954), *Rec. Trav. Chim. 73*, 150.
Hilditch, T. P. (1956), The Chemical Constitution of Natural Fats, London, Chapman & Hall Ltd., pp. 33–37.
Holmes, H. N., Corbet, R. E., Geiger, W. B., Kornblum, N., and Alexander, W. (1941), *J. Am. Chem. Soc. 63*, 2607.
Hopkins, C. Y. (1961), *J. Am. Oil Chemists' Soc. 38*, 664.
Howe, R. J., and Malkin, T. (1951), *J. Chem. Soc.* 2663.
Karnovsky, M. L. (1951), *Biol. Bull. 107*, 238.
Karnovsky, M. L., Rapson, W. S., and Black, M. (1946), *J. Soc. Chem. Ind. (London) 65*, 425.
Karnovsky, M. L., and Brumm, A. F. (1955), *J. Biol. Chem. 216*, 689.
Kates, M. (1960), *in* Lipide Metabolism, Bloch, K., editor, New York, John Wiley and Sons, pp. 226–228.
Marinetti, G. V., Erbland, J., and Stotz, E. (1958), *J. Biol. Chem. 233*, 562.
Marinetti, G. V., Erbland, J., and Stotz, E. (1959), *J. Am. Chem. Soc. 81*, 861.
Newman, M. S., and Renoll, M. (1945), *J. Am. Chem. Soc. 67*, 1621.
Renkonen, O. (1962), *Biochim. Biophys. Acta 59*, 497.
Sehgal, S. N., Kates, M., and Gibbons, N. E. (1962), *Can. J. Biochem. Physiol. 40*, 69.
Sowden, J., and Fischer, H. O. L. (1941), *J. Am. Chem. Soc. 63*, 3244.
Svennerholm, L., and Thorin, H. (1960), *Biochim. Biophys. Acta 41*, 371.

Short-Chain Fatty Acid (C_6,C_8,C_{10}) Phosphatidyl Ethanolamines*

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Condensation of the appropriate α-iodo diglyceride with monosilver salt of monophenylphosphoryl *N*-carbobenzoxyethanolamine gave dihexanoyl-, dioctanoyl-, and didecanoyl-DL-α-glycerylmonophenylphosphoryl *N*-carbobenzoxyethanolamines. Removal of the protective phenyl and carbobenzoxy groups by catalytic hydrogenolysis in the presence of palladium and platinum produced short-chain fatty acid phosphatidyl ethanolamines in yields ranging from 48.4% to 60.5% of theory. The required, but unknown, α-iodo diglycerides of hexanoic, octanoic, and decanoic acids are also described in detail. Dihexanoylphosphatidyl ethanolamine promises to be a suitable aqueous substrate for biological and chemical investigations.

Saturated long-chain fatty acid phosphatidyl ethanolamines have been synthesized by Rose (1947), Hunter *et al.* (1948), Bevan and Malkin (1951), Baylis *et al.* (1958), and Baer *et al.* (1952).

Recently Baer and Grof (1960) synthesized dihexanoyl L-α-phosphatidyl ethanolamine. Purification of the final product was achieved by the use of chromatography on a silicic acid column. The low absorptive capacity of silicic acid for phospholipids, the slow elution time, and the large volumes of eluting fluid required make this elegant method impractical for the preparation of the large quantities of phospholipids which are required for biological studies being carried out in this laboratory.

The procedure reported in this paper utilized monophenylphosphoryl dichloride as the phosphorylating agent (first applied to the synthesis of phospholipids and their biological intermediates by Baer and coworkers, 1948, 1950, 1952, 1953, 1955) and utilized the condensation of the monosilver salt of phosphoric acid diester with alkyl halide introduced by Malkin and co-workers for the synthesis of long-chain fatty acid phosphatidyl serine (Bevan *et al.*, 1957) and phosphatidyl ethanolamines (Baylis *et al.*, 1958).

The three required α-iodo diglycerides containing hexanoic, octanoic, and decanoic acids have not been described in the literature. They were prepared from α-iodo glycerol (Baer and Fischer, 1948) *via* acetone glycerol (Newman and Renall, 1945) and esterified with the appropriate fatty acid chloride as described by Baer and Mahadevan (1959) for the preparation of α-benzyl ether didecanoylglycerol. In the past, biological investigations of phospholipids have been limited to lecithins, since synthetic phosphatidyl ethanolamines were unsuitable because of their very low solubility in aqueous solutions. The DL-α-phosphatidyl ethanolamines described here containing hexanoic, octanoic, and decanoic acids were found to be highly soluble in methanol and ethanol, but only sparingly soluble in water. Of these three compounds, only DL-α-(dihexanoyl)-phosphatidyl ethanolamine promises to become useful as a substrate for biological studies in homogeneous aqueous systems. It was found to be soluble to the extent of 0.4 g per 100 ml of water. The racemic α-phosphatidyl ethanolamines have been obtained in over-all yields ranging from 48.4% to 60.5%. Studied by the technique of Marinetti and Stotz (1956), the three compounds described here appeared to be chromatographically pure.

Experimental Procedures and Results

Materials

Synthetic quinoline and barium oxide were shaken for eight hours and the quinoline distilled *in vacuo*.

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