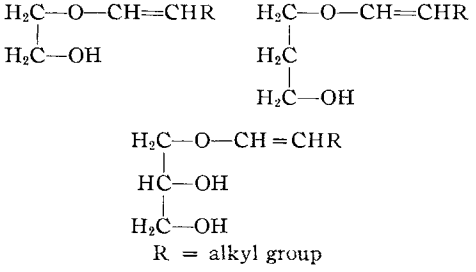
Synthesis of α,β-Unsaturated Ethers of Polyhydric Alcohols and Neutral Plasmalogens

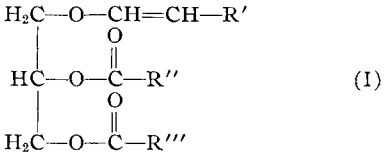
Sir:

Recent developments in the field of the plasmalogens have produced evidence that the aldehydogenic linkage in the plasmalogens is an α,β-unsaturated ether (1). We have prepared a series of α,β-unsaturated ethers of polyhydric alcohols with the following general formulas



The procedure involves a transacetalation reaction (2) between the polyhydric alcohol and an α-bromo dimethylacetal of a straight chain aldehyde. This α-bromo cyclic acetal is then refluxed with sodium in ether to yield the desired compounds. These compounds show an infrared absorption band of relatively strong intensity near 6 μ which is indicative of a —O—CH=CH— grouping (3). The elemental analysis and the 2,4-dinitrophenylhydrazone derivatives were correct. These derivatives formed immediately upon adding the reagent. The compounds show an α,β-unsaturated ether content of 80 to 96% upon assaying with iodine in methanol by the method of Siggia (4). The corresponding saturated ethers were prepared by hydrogenating the α,β-unsaturated ethers. As a means of structure proof one of the saturated ethers, 3-octyloxy-1,2-propanediol was prepared in a different manner. This consisted of reacting the sodium salt of isopropylidene glycerol with octyl bromide and then cleaving the ketal structure by acid hydrolysis. The physical constants of the two saturated ethers agreed favorably. The saturated ethers of glycerol gave a positive periodic acid test substantiating the α-position of the α,β-unsaturated ether linkage on the glycerol moiety.

In addition, several neutral plasmalogens (5) have been synthesized by a reaction of the above α,β-unsaturated ethers of glycerol with long chain acid chlorides in the presence of pyridine. A general plasmalogen formula:



(I)

The constants for 3-(1-octenyloxy)-1,2-propanediol are presented as typical for the entire series of α,β-unsaturated ethers prepared. A product, b_1 135–138°, n_D^{27} 1.4670 was obtained.

Anal.—Calcd. for $C_{11}H_{22}O_3$: C, 65.30; H, 10.96. Found: C, 65.19; H, 11.15. Infrared spectrum: 2.9 μ (O—H), 3.4 μ (C—H), 6 μ (—O—HC=CH—), 6.84 (C—H). The melting point of the 2,4-dinitrophenylhydrazone was found to be 95–96°. This agrees favorably with the literature (6).

The constants for 3-octyloxy-1,2-propanediol synthesized by hydrogenating the above compound are as follows: $b_{0.85}$ 135–136°, n_D^{25} 1.4503.

Anal.—Calcd. for $C_{11}H_{24}O_3$: C, 64.66; H, 11.84. Found: C, 64.29; H, 11.88. Infrared spectrum: 2.9 μ (O—H), 3.4 μ (C—H), 6.84 (C—H).

The constants for 3-octyloxy-1,2-propanediol synthesized by the alternate method are as follows: $b_{0.65}$ 130°, n_D^{28} 1.4490.

Anal.—Calcd. for $C_{11}H_{24}O_3$: C, 64.66; H, 11.84. Found: C, 64.70; H, 11.88. Infrared spectrum: 2.9 μ (O—H), 3.4 μ (C—H), 6.84 (C—H).

Compound (I), in which R′ is a hexyl radical, and R″ and R‴ are pentadecyl radicals, was found to be a low melting, white, waxy solid. Further work on these compounds is in progress in this laboratory.

Anal.—Calcd. for $C_{43}H_{82}O_5$: C, 76.05; H, 12.17. Found: C, 75.89; H, 12.24.

(1) Rapport, M. M., and Franzyl, R. E., *J. Neurochemistry*, **1**, 303(1957).
(2) Piantadosi, C., *et al.*, *J. Am. Chem. Soc.*, **80**, 6613 (1958).
(3) Rosenkrantz, H., and Gut, M., *Helv. Chim. Acta*, **36**, 1000(1953).
(4) Siggia, S., and Edsberg, R. L., *Anal. Chem.*, **20**, 762 (1948).
(5) Schogt, J. C. M., Begemann, P. H., and Koster, J., *J. Lipid Research*, **1**, 446(1960).
(6) Hodgman, C. D., "Tables for Identification of Organic Compounds," Chemical Rubber Publishing Co., Cleveland, Ohio, 1960, p. 70.

Claude Piantadosi
Allen F. Hirsch

University of North Carolina
School of Pharmacy
Chapel Hill, N. C.

Received August 28, 1961.
Accepted for publication September 18, 1961.
This work was supported by Research Grant G-9744 from the National Science Foundation.