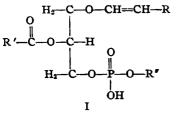
# Plasmalogens II

## Studies on Formation of Cyclic Acetals from Alkenyl Glycerol Ethers

### By CLAUDE PIANTADOSI, MICHAEL F. FROSOLONO\*, CARL E. ANDERSON and ALLEN F. HIRSCH

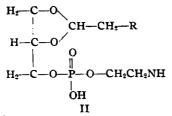
The 1-alkenyl glycerol ethers were converted to the corresponding cyclic glycerol acetals. The conditions necessary for their cyclization were studied, and no cleavage of the alkenyl linkage was observed. The compounds isolated from the cyclization reaction were identical with the synthetic cyclic glycerol acetals prepared by a different route.

T THE PRESENT TIME. naturally occurring A plasmalogens are thought to be derivatives of glycerylphosphoryl choline, ethanolamine or serine, containing a fatty acid residue and an enol ether linkage as typified by I, first proposed by Klenk and Debuch (1), where R and R' are long chain alkyl groups and R" represents ethanolamine, choline, or serine.

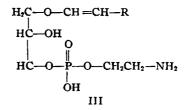


Evidence has recently been presented by Davenport and Dawson (2) that the cyclic acetal, II, isolated by Feulgen and Bersin (3) and Thannhauser, et al. (4), is an artifact formed by the acid hydrolysis of ethanolamine lysoplasmalogen, III; however, Landowne and Bergmann (5) have presented evidence for the occurrence of the cyclic form II in the sea anemone A. elegantissima, although Rapport and Alonzo (6) in a study of lipid extracts from the tissues of 11 marine invertebrates stated that their study did not produce proof either for or against an acetal structure.

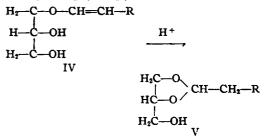
Since the synthesis of 3-(1-alkenyloxy)-1,2-



Received October 21, 1963, from the Departments of Medicinal Chemistry and Biochemistry, University of North Carolina, Chapel Hill. Accepted for publication November 11, 1963. The authors are indebted to the National Science Founda-tion (Grant G-9744, G-21305) and the Life Insurance Medical Research Fund for their support of this work. \* U. S. Public Health Service Training Grant No. 5TI-GM-404-03.



propanediols, IV, has been accomplished by this laboratory (7, 8), it was of interest to study the conditions necessary for their cyclization to the corresponding cyclic glycerol acetals, V.

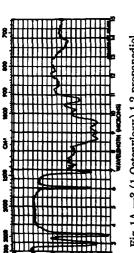


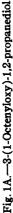
#### **EXPERIMENTAL'**

Cyclization of 3-(1-Octenyloxy)-1,2-propanediol (Table I).-The cyclization of 3-(1-octenyloxy)-1,2propanediol to 2-heptyl-4-hydroxymethyl-1,3-dioxolane is given as an example of the method used in the cyclization experiments. The other experiments were analogous, varying mainly in the choice of the cyclizing agent, reaction temperature, and time. To 5.0 ml. of 3-(1-octenyloxy)-1,2-propanediol dissolved in 10 ml. chloroform-isobutanol (1:1) mixture was added 10 ml. of aqueous 10% (w/v) trichloroacetic acid. The mixture was heated at 37° for 1 hour with vigorous stirring. The reaction mixture was allowed to stand at room temperature  $(25^{\circ})$ for approximately 17 hours. At the end of this time, sufficient N sodium hydroxide was added to neutralize the acid. The organic layer was extracted with diethyl ether, washed with water, and dried over anhydrous potassium carbonate. The solvent was removed in vacuo and the remaining oil distilled

GM-404-03.

<sup>&</sup>lt;sup>1</sup> All boiling points and melting points are uncorrected. Analyses were determined by G. Weiler and F. B. Strauss, Microanalytical Laboratory, Oxford, England, and by Spang Microanalytical Laboratory, Ann Arbor, Mich. All in-frared spectra were automatically recorded with a Perkin-Elmer infracord spectrophotometer, housed in an air-condi-tioned room. The instrument was calibrated by means of known absorption bands. The liquid samples were scanned in a sodium chloride mull cell. No solvent was used.





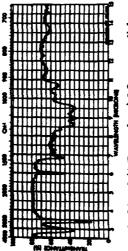


Fig. 2A.---3-(1-Decenyloxy)-1,2-propanediol.

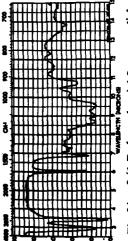
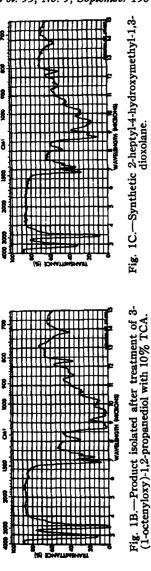


Fig. 3A.—3-(1-Dodecenyloxy)-1,2-propanediol.



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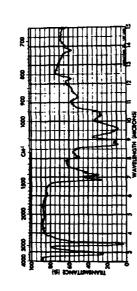
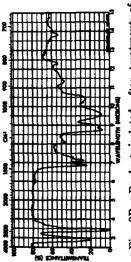


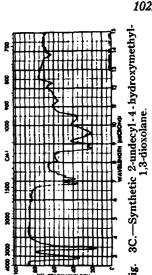
Fig. 2B.—Product isolated after treatment of 3-(1-decenyloxy)-1,2-propanediol with glacial acetic acid.

Fig. 2C.—Synthetic 2-nonyl-4-hydroxymethyl-1,3-dioxolane.



glacial ð treatment with Fig. 3B.-Product isolated after 3-(1-dodecenyloxy)-1,2-propanediol acetic acid.

Fig.



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TABLE I.—PHYSICAL CONSTANTS OF GLYCEROL ENOL ETHERS, ISOLATED CYCLIC GLYCEROL ACETALS, AND SYNTHETIC CYCLIC GLYCEROL ACETALS	cetal	Ű.	1.4531 (20.0)	1.4560	1.4575	Calcd. for CuHaO ith 1.40 Gm. HgCl Calcd. for CuHaO 11.70. Found: C
	c Glycerol A	°C/mm		95/0.02 1.4560 (20.0)	134/0.24 1.4575 (23.0)	28. c And. 28. c And. 0acetic acid w 13. f And. 13. f And. 13. f And. 13. f And. 13. f And. 14. f And. 14
			2-heptyl-4-hydroxy- methyl-1,3-dioxolane <sup>i</sup>	2-nonyl-4-hydroxy- methyl-1,3-dioxolane'	(20.0) <sup>A</sup> 2-undecyl-4-hydroxy- methyl-1,3-dioxolane <sup>k</sup>	<sup>b</sup> Anal.—Caled. for CuHMO:: C, 67,78; H, 11.38. Found: C, 67,94; H, 11.28. e Anal.—Caled. for CuHMO: 10% w/v trichoreacting acid: B, glacial acetic acid; C, 10% w/v trichoreactic acid with 146 Gu. HgCl3; isolated at end of 1 hour without allowing reaction mature to stand for 17 hours. / Anal.—Caled. for CuHHAO: 67.78; H, 11.38. Found: C, 68.23; H, 11.21. A Anal.—Caled. for CuHHAO:: C, 69.72; H, 11.70. Found: C, 66; H, 11.00. <i>i Anal.</i> —Caled. for CuHHAO:: C, 67.78; H, 11.38. Found: C, 67.86; H, 11.44. A Anal.—Caled. Go 66; H, 11.00. <i>i Anal.</i> —Caled. for CuHAO: C, 67.78; H, 11.38. Found: C, 67.86; H, 11.44. A Anal.—Caled.
	ated ion	(°C°)	0.000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.000000	(25.6) (25.6) (25.0) (25.0) (25.0) (25.0) (25.0)	(20.0)	78; H, 11 glacial ac owing reac i, H, 11.21. JaHaOa: C
	Compound Isolated after Cyclization	Da	1.4514 1.4514 1.4514 1.4514	$\begin{array}{c} 1.4526\\ 1.4538\\ 1.4540\\ 1.4530\\ 1.4539\\ 1.4538\\ 1.4538\end{array}$	1.4570	cd. for CuHHoD: C, 67.78. trichloroacetic acid; B, gla ad of I hour without allowi 38. Pound: C, 68.23; H .38. Pound: C, 68.23; H
	Com	° C./mm.	80/0.01 10.0/08 10.0/08 80/0.01	95/0.02 95/0.02 95/0.02 95/0.02 95/0.02	135/0.25	
	Conditions	hr.	-	1.0 0.1 0.0 0.5 0.5	1.0	AndiCal 10% w/v 1 01ated at er 778; H, 11.00.
		ι. Που Γ	37 86 87	37 37 37 37 37 37 37 37 37	8	I <1 + 1 → 2
		Solvent	CI None None	CI CI None None None	None	ound: C, 65.19; H, 11.15. Acid (cyclization agents): Tra-isolutanol. Compound ad. Calod. for CuHaO: C, 62 11; H, 10.96. Found: C, 62 H, 11.68.
		Acid	4848	400mmm	B	nd: C, 6 id (cyclia isobutan H, 10.96 11.68
		(; ()	(20.0)	(20.0)	(20.0)	1.96. Fou 74. d Ac hloroform 8. d Acd 8. 65.31; 99.90; H,
	, , , , , , , , , , , , , , , , , , ,	Q <b>n</b>	1.4657	1.4667	1.4684	31; H, 11 0; H, 11 nts: CI, 0 H, 11.0 CuH#O: cuH#O:
	Glycerol Enol Ether-	° C./mm.	120/0.02 1.4657 (20.0)	130/0.05 1.4667 (20.0	165/0.05	HarOs: C, 65 hund: C, 69.7 c acid. Solve und: C, 65.05 tiCalcd. for H, 11.70. Fo
TABLE I	Clycer		3-(1-Octenyloxy)- 1,2-propanediol <sup>a</sup>	3-(1-Decenyloxy)- 1,2-propanediol <sup>b</sup>	3-(1-Dodecenyloxy)- 165/0.05 1.4684 (20.0 1,2-propanediol	<sup>a</sup> A <i>wal</i> .—Caled. for C11HarOst. C, 65.31; H, 10.96. Found: C, 65.1 C, 69.72; H, 11.70. Found: C, 69.70; H, 11.74. A facia (cyclizati D) 90% VY glascial acetto acid. Solvents: C1. chloroform-isolutanol. C, 65.31; H, 103.96. Found: C, 60.65; H, 1108. A <i>axid</i> .—Caled. fo 69.54; H, 11.63. A <i>rasil</i> .—Caled. for C1.HarOls. C, 66.31; H, 10.96. for C4HarOst. C, 69.72; H, 11.70. Found: C, 69.90; H, 11.68.

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through a 5-in. Vigreux column to yield one product. The structures assigned were supported by their infrared spectra (Figs. 1-3). The 2,4-dinitrophenylhydrazone of the aldehyde was prepared from the isolated product, m.p. 106°. Reported m.p. 106° (9). The 2,4-dinitrophenylhydrazones of the aldehydes obtained from the isolated cyclization products of 3-(1-decenyloxy)-1,2-propanediol and 3-(1-dodecenyloxy)-1,2-propanediol were also prepared and the melting points were, respectively, 104° and 106°, which agreed with the iterature values (9).

Preparation of 2-Alkyl-4-hydroxymethyl-1.3-dioxolanes .-- The 2-alkyl-4-hydroxymethyl-1,3-dioxolanes used as reference compounds were synthesized by a completely independent procedure described in the literature (10).

The 3-(1-alkenyloxy)-1,2-propanediols (Figs. 1A, 2A, 3A) show a characteristic absorption in the infrared region at 1653 cm.<sup>-1</sup> attributed to the -O--CH==CH-- group (11). As expected, this absorption is absent in the infrared pattern of the cyclic glycerol acetals, thus the use of the infrared spectrophotometer enabled one to demonstrate cyclization very readily. The infrared patterns (Figs. 1B, 2B, 3B) of the material resulting from the cyclization of the alkenyl glycerol ethers showed no absorbance in the 1650 cm.<sup>-1</sup> region and were in all respects identical to the infrared patterns of the appropriate reference compounds. The refractive indices, boiling points, and elemental compositions of the materials isolated from the cyclization procedure agreed favorably with the reference compounds (Table I).

#### DISCUSSION

The results presented here support the conclusions reached by Davenport and Dawson in their work with ethanolamine lysoplasmalogen. In the experiment conducted with 10% aqueous trichloroacetic acid with 1.40 Gm. mercuric chloride as the cyclization agent, and 3-(1-decenyloxy)-1,2-propanediol (Table I), only one product was formed, 2-nonyl-4-hydroxymethyl-1,3-dioxolane, and no free aldehyde could be detected. Davenport and Dawson, however, state that the free aldehyde is generated from ethanolamine lysoplasmalogen in the presence of the mercuric ion, although a small amount of the cyclic form remains. This may be due to the fact that the experiments reported in the present work were based on the synthetic, 3-(1-alkenyloxy)-1,2-propanediols, as compared with the ethanolamine lysoplasmalogen utilized by the above authors.

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