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THE STRUCTURE OF GLYCEROL ACETALS

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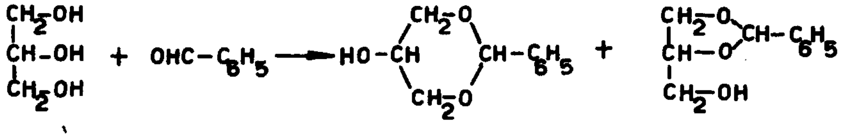
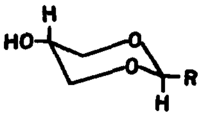
It is known that the condensation of carbonyl compounds with polyols yields cyclic acetals. Thus, it is known that by condensation of benzaldehyde with glycerol, a mixture of 2-phenyl-5-hydroxy-1,3-dioxane and 2-phenyl-4-hydroxymethyl-1,3-dioxolane is obtained[1]:

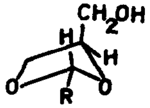


It has been accepted that by condensation of aldehydes with glycerol all the four possible geometrical isomers[2] of the cyclic glycerol acetals could be obtained:

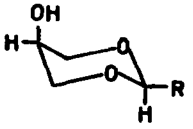
I



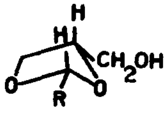
II



III



IV



However, up to now the separation and determination of the structure of cis and trans 2-phenyl-5-hydroxy-1,3-dioxanes was accomplished$^{3)}$, while the five-membered isomer with the dioxolane structure has not even been separated into its geometrical forms. Furthermore, it has been accepted that by condensation of carbonyl compounds with glycerol a dimeric or polymeric compound$^{4)}$ could also be obtained, but up to now the isolation and identificstion of such glycerol acetals has not been published. In general, while a good deal of work has been published on the subject of glycerol acetals, very few facts have been established with certainty, although the condesation products of glycerol with carbonyl compounds represent really interesting compounds not only in the theoretical field, but also as physiological active substances$^{5)}$ and as products for technical use$^{6)}$.

The object of this work was the investigation of methods for preparation of monomeric glycerol acetals, the separation of the structural and geometrical isomers and the determination of the stereochemical structure thereof. Accordingly, we prepared a series of glycerol acetals by the condensation of glycerol with eight n-alyphatic aldehydes from C_7 to C_{14}. These preparations were carried out by successive addition of the carbonyl compound to glycerol, heating the reaction mixture and eliminating the water formed in the reaction. The reaction conditions were as follows:

i) the reaction components were refluxed in xylene in presence of a catalyst (p-toluenesulfonic acid);

ii) the reaction components were mixed together and heated without any solvent added, either in the presence of a catalyst or without it; and

iii) the reaction components were refluxed in a pyridine solution, without any catalyst added.

The reaction products were distilled under reduced pressure and the cyclic acetals thus obtained boiled over a wide temperature range. The residue which could not be distilled without decomposition was not examined.

TABLE

Cond.Prod.of Glycerol and Carb. Comp.	Yields:				Boiling range °C/mmHg	n_D^{20} or M.P.
	Xylene sol.	Without solvent		Pyridine solution		
		+Catal.	-Catal.			
Enanthylid.-glycerol	96,2	94,1	96,0	98,4	$102\text{-}14_{0,5}$	1,4502
Octylidene-glycerol	90,1	79,2	82,0	89,4	$183\text{-}9_{30}$	1,4509
Nonylidene-glycerol	92,3			90,1	$169\text{-}79_{15}$	1,4524
Decylidene-glycerol	86,0			82,0	$175\text{-}85_{15}$	1,4540
Undecylid.-glycerol	81,3			88,2	$182\text{-}92_{14}$	1,4553
Dodecylid.-glycerol	94,9	88,0	82,1	95,0	$174\text{-}86_{1}$	1,4566
Tridecylid.-glycerol	84,1	74,0		88,1	$170\text{-}82_{0,4}$	M.P. 16-20
Tetradecyl.-glycerol	69,1	64,0	65,2	76,1	$199\text{-}218_{0,7}$	18-22

Satisfactory analytical data were obtained for all the compounds listed.

The separation of all the four possible geometrical isomers of enanthylideneglycerol and dodecylideneglycerol was successfully carried out both by chromatographical methods and by distillation on a Podbielniak column.

The TL-chromatography was attempted both on thin layers of alumina of various activity and pH, and on thin layers of silicagel. According to our results, the best separation is obtained on thin layers of silicagel with an elluent consisting of ligroin (90-120°C), tert.-butanol and ethyl acetate in a ratio of 40:7:4. The development of the TLC was carried out by iodine, phosphomolybdenic acid or by antimonpentachloride. The sulfuric acid does not develop one of the isomers. On the chromatograms four spots were obtained ("compounds 1-4") in ratios which depended upon the reaction conditions of the synthesis of the glycerol acetal. Thus, it could be shown that two of the isomers (compounds "2" and "4") were the major products providing that the preparation of the cyclic acetal was performed under kinetic control, while the other two isomers ("1" and "3") were the major products prowiding that the preparation was performed under thermodynamic control.

The above mentioned glycerol acetals were separated both by gas-chromatography and by column chromatography on silicagel (Merck 0,08; the elluation carried out with the aforesaid mixture of solvents) and further by distillation on a Podbielniak column.

A series of compounds ("1" to "4", according to their

Rf values on silicagel) was thus obtained from each of the glycerol acetals and it was shown that they represent the pure isomers with the structures I, II, III and IV respectively. A study of the dependance of ratios of these isomers from the reaction conditions is in course.

The determination of the ring structure of these compounds was carried out by the method established by Hill, Whelen and Hibbert[1)], and it was found that "1" and "3" represent compounds with the dioxane structure, while "2" and "4" represent compounds with the dioxolane structure. The determination of the stereochemistry of all the four isomers of enanthylideneglycerol was carried out by means of the IR and NMR spectra.

The NMR spectra of "1" and "3" are completely in accordance with the proposed structures I and III respectively. Namely, both spectra indicate that these compounds are of the dioxane structure. The hydroxylic hydrogen signal in the NMR spectrum of "3" is shifted to the lower field relative to the same signal in NMR spectrum of "1". This is in accordance with their IR spectra (5.10^{-3}M in CCl_4), where sharp bands for the hydroxylic groups appear: for compound "3" at 3590 cm^{-1} and for compound "1" at 3600 (weak) and at 3635 cm^{-1} (much stronger). Since the possibility of an intramolecular assotiation exists only in the cis-dioxane structure (III), it was concluded that the compound "3" represents the cis-2-n-hexyl-5-hydroxy-1,3-dioxane. Accordingly, the compound "1" of the enanthylideneglycerol series represents the trans-2-n-hexyl-5-

hydroxy-1,3-dioxane. The weak band for the hydroxylic group at 3600 cm^{-1} in the IR spectrum of this compound, not shifted by further dilution, indicate that an equilibrium between the diequatorial and diaxial form exists. Further evidence was found in the NMR spectrum of this compound, where weak signals appeared due to the presence of the diaxial isomer.

The NMR and IR spectra of compounds "2" and "4" of this series are completely in accordance with the structures II and IV respectively. Namely, the signals for the hydroxylic hydrogen in the NMR spectra of "2" and "4" are both shifted to a lower field, relative to the same signals in the spectra of the dioxane isomers, which indicates a much stronger intramolecular O-H....O bonding than in the compounds "1" and "3". The doublet at τ 7,8 in the spectrum of "4" corresponds to the $-CH_2-R$ hydrogens and is evidently caused by the magnetic anysothropie of the molecule existing only if the compound has the structure IV, and could not be observed in the NMR spectrum of the compound "2", indicating that the compound "4" is the cis-2-n-hexyl-4-hydroxymethyl-1,3-dioxolane, and that compound "2" is the trans-2-n-hexyl-4-hydroxymethyl-1,3-dioxolane. Further evidence was found in the IR spectra of these compounds, where the bands of the hydroxylic groups are at 3600 and 3585 cm^{-1} respectively, indicating that the distance between the hydroxylic group and the ring oxygen is somewhat shorter in the cis than in the trans isomer.

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