

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Studies in the Ketone Sugar Series. X. The Synthesis of a New Disaccharide, 1- β -Glucosidofractose, and the Structure of Turanose and Melezitose¹

BY EUGENE PACSU, E. JUSTIN WILSON, JR., AND LADISLAS GRAF

In 1926 Zemplén and Braun² prepared hendecamethylmelezitose which on controlled hydrolysis gave 2,3,4,6-tetramethylglucose and heptamethylturánose. On further hydrolysis the latter substance gave rise to the same tetramethylglucose and a sirupy trimethylfructose with $[\alpha]_D^{30}$ in water and 25° in alcohol solution. Using the method of elimination for structure determination, Zemplén and Braun concluded that their product was the 1,3,4-trimethylfructose. On this basis and on the assumption that melezitose was a derivative of sucrose which at that time was believed to possess a 2,6-ring in its fructose constituent, Zemplén and Braun also concluded that melezitose contained a glucosidic group at the fifth carbon atom of the fructose portion of the molecule and that turánose was a 5-glucosidofractose. After Haworth and Hirst³ had shown that the fructose constituent of sucrose did not belong to the pyranoid type but contained a 2,5-ring, Zemplén⁴ pointed out that in such case turánose was a 6-glucosidofractose and melezitose was the corresponding 6-glucosido derivative of sucrose. Zemplén's results and conclusions were later confirmed by Miss Leitch⁵ with the exception that she reported the rotation 55.5° in alcohol solution for the sirupy trimethylfructose. In 1931 Pacsu⁶ found that on treatment with triphenylmethyl chloride and subsequent acetylation turánose gave rise to a triphenylmethyl derivative and its pentaacetate. He considered this fact as evidence of the presence of three primary hydroxyl groups in turánose. This discovery together with the results of the methylation experiments of Zemplén and of Leitch led him to the conclusion that the formulas of turánose and melezitose originally suggested by Zemplén and Braun were the more probable. In

a series of investigations Pacsu⁷ subsequently prepared and studied the properties of the aceto-halogeno derivatives, the methylglycosides and the acetates of turánose. For reasons discussed in Part VII^{7e} several of these derivatives were described as ortho esters. Especially the existence of five octaacetates made it necessary that other than normal structures should be assigned to some of them in order to avoid conflict with the accepted structure of turánose. During the later phase of these investigations, however, it became increasingly difficult, if not impossible, to reconcile the new experimental facts with either the 5- or the 6-glucosidofractose formula of turánose. Striking difference between the properties of the true, crystalline 1,3,4-trimethylfructose⁸ (m. p. 75° ; $[\alpha]^{18D} -52^\circ$ in water solution) and those of the similarly named sirupy product of Zemplén and of Leitch also indicated that error must have been made in the structure determination of this important key substance and, consequently, the structures assigned to both turánose and melezitose were incorrect. If positions 5 and 6 in the fructose portion of turánose are thus eliminated from the possibilities where the disaccharide linkage might occur, there remain only carbon atoms 1, 3 and 4 for such union. If the glucosidic group were combined with carbon atom 4, the osazone of turánose⁹ would be identical with maltosazone. This, however, is not the case.¹⁰ Hence the glucosidic group must be attached on either carbon atom 1 or carbon atom 3. The fact that turánose gives an osazone does not *a priori* eliminate carbon atom 1 as a possible place for the disaccharide linkage. It is entirely conceivable that the ketone group and the adjacent secondary alcoholic group of a 1-glucosidofractose might react with phenylhydrazine to give a 2,3-osazone. Similarly constructed osazones have been reported¹¹ in the literature.

(1) This work was begun in the first semester of the academic year 1937-38 in the II. Chemical Institute of the Royal Hungarian University at Budapest, where the senior author spent his sabbatical leave. The experiments carried out in that Institute with Dr. Ladislav Graf, University Assistant, were later repeated and concluded in this Laboratory with Mr. E. Justin Wilson, Jr., Research Assistant on Special Funds from the Rockefeller Foundation.

(2) Zemplén and Braun, *Ber.*, **59**, 2230 (1926).

(3) Haworth and Hirst, *J. Chem. Soc.*, 1858 (1926).

(4) Zemplén, *Ber.*, **59**, 2539 (1926).

(5) Leitch, *J. Chem. Soc.*, 588 (1927).

(6) Pacsu, *THIS JOURNAL*, **53**, 3099 (1931).

(7) (a) Part I, Pacsu, *ibid.*, **54**, 3649 (1932); (b) Part II, Pacsu, *ibid.*, **55**, 2451 (1933); (c) Part III, Pacsu and Rich, *ibid.*, **55**, 3018 (1933); (d) Part VI, Cramer and Pacsu, *ibid.*, **59**, 711 (1937); (e) Part VII, Pacsu and Cramer, *ibid.*, **59**, 1059 (1937).

(8) (a) Hibbert and Tipson, *ibid.*, **52**, 2582 (1930); (b) Challinor, Haworth and Hirst, *J. Chem. Soc.*, 676 (1934).

(9) Fischer, *Ber.*, **17**, 583 (1884).

(10) Isbell and Pigman, *Bur. Standards J. Research*, **20**, 787 (1938).

(11) (a) De Bruyn and van Ekenstein, *Rec. trav. chim. de Pays-Bas*, **16**, 270, 277 (1897); (b) Nef, *Ann.*, **357**, 296 (1907).

For the investigation of this problem with all its implications regarding the structure of turanose and melezitose, 1- β -glucosidofructose was prepared in the following way. The starting material, 2,3-4,5-diacetone- β -fructopyranose¹² was condensed with tetraacetyl-1-bromoglucose by means of the Königs-Knorr reaction as modified by Reynolds and Evans.¹³ The product of the reaction was 1-tetraacetyl- β -glucosido-2,3-4,5-diacetone- β -fructopyranose with m. p. 162-163° and $[\alpha]^{20}_D -32.9^\circ$ in chloroform solution. Deacetylation of this compound resulted in the formation of 1- β -glucosido-2,3-4,5-diacetone- β -fructopyranose with m. p. 174-175° and $[\alpha]^{20}_D -45.6^\circ$ in water solution. On removal of the two acetone residues by controlled acid hydrolysis, this substance gave rise to the desired disaccharide, 1- β -glucosidofructose with m. p. 132-135° and $[\alpha]^{20}_D -59.2^\circ$ in water solution. The new sugar crystallized from its aqueous solution with two molecules of water, of which one was probably chemically bound. It reduced Fehling's solution but unlike turanose it was not fermented by yeast and no mutarotation could be observed in its aqueous solution. The latter fact lent support to the view that the substance represented a derivative of the open-chain fructose hydrate (I). Although the new disaccharide was obviously different from turanose there remained the possibility that the difference was caused by an α,β -isomerism similar to that in the cellobiose-maltose pair. The α -glucosidic linkage in turanose has been proved¹⁴ by Bridel and Aagaard and the presence of a β -glucosidic linkage in the new disaccharide follows from the fact that the sugar was prepared from acetyl-bromoglucose. It was, therefore, of great interest to investigate whether or not the 1- β -glucosidofructose will give an osazone as readily as turanose. It was found that under normal experimental conditions no osazone was formed from the new sugar. However, in the presence of an excess of acetic acid or if the heating with phenylhydrazine was extended to thirty minutes, a slight precipitation occurred and the isolated substance was identified as glucosazone.¹⁵

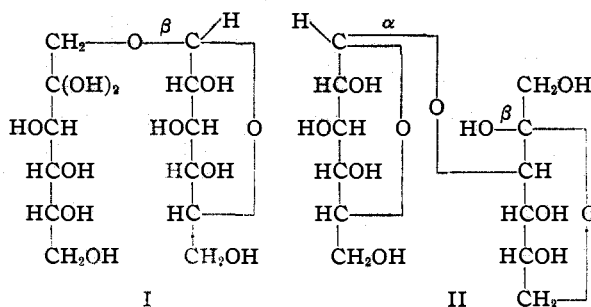
(12) (a) Fischer, *Ber.*, **23**, 1165 (1895); (b) Ohle and Koller, *ibid.*, **57**, 1571 (1924).

(13) Reynolds and Evans, *This Journal*, **60**, 2559 (1938).

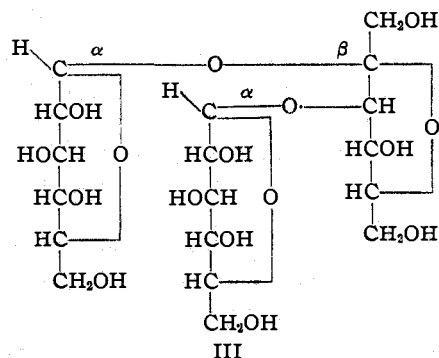
(14) (a) Bridel and Aagaard, *Bull. soc. chim. biol.*, **9**, 384 (1927); (b) Aagaard, *Tidshr. Kemi Bergvaesen*, **3**, 5, 16, 35 (1928).

(15) By condensation of 12 g. of their supposed [Bridel and Schinle, *Ber.*, **66**, 325 (1933); Part II, Note 9, Pacsu, *This Journal*, **55**, 2451 (1933)] 2,3,4,5-tetraacetylfructopyranose with 6 g. of acetyl-bromoglucose Helferich and Brederick [*Ann.*, **465**, 166 (1928)] obtained 0.2 g. of a crystalline octaacetate (m. p. 129° and $[\alpha]^{20}_D$

From the results of these experiments it became evident that turanose and 1- β -glucosidofructose were two entirely different sugars. Consequently the α -glucosidic group in turanose must be attached on carbon atom 3 of the fructose constituent as the only possible position left for the disaccharide linkage. Since Isbell and Pigman¹⁰ have shown that crystalline turanose exhibits a pyranose-furanose mutarotation, the structure of this sugar has now become definitely established as 3- α -glucosido- β -fructopyranose represented by formula II.



As to the structure of melezitose, the identity of the potential disaccharide fructose < > glycopyranose presents an interesting problem. Unlike turanose this disaccharide cannot be isolated in a free state and it may be sucrose with a 2,5-ring in the fructose part or a ring isomer of sucrose with a fructopyranose constituent. This problem is now under investigation in this Laboratory and the results so far obtained indicate that in all probability the structure of melezitose corresponds to formula III.



With the recognition of the true structure of turanose as 3- α -glucosidofructose, it became necessary to revise the chemical formulas assigned to all the 14.1° in chloroform solution) of 1- β -glucosidofructose. On deacetylation of this acetate the authors obtained a small quantity of an amorphous product which was found to give glucosazone in a very small yield when treated with phenylhydrazine "in the customary manner."

TABLE I

DESIGNATION OF THE INCORRECT AND THE TRUE STRUCTURAL FORMULAS OF TURANOSE DERIVATIVES AND THE M. P. AND SPECIFIC ROTATION OF THE SUBSTANCES

Present incorrect designation	M. p., °C.	$[\alpha]^{20}_D$ in chloro- form solution	Designation of the correct structural formula
"First octaacetylturanose" ^a (Hexaacetyl- β -turanose<2,6>-2,3-l-semiorthoacetic anhydride)	216-217	20.5°	Octaacetyl-3- α -glucosido- β -fructopyranose
"Fourth octaacetylturanose" ^a (Hexaacetyl- β -turanose<2,6>-2,3-d-semiorthoacetic anhydride)	194-195	103.2°	Octaacetyl-3- α -glucosido- α -fructopyranose
"Fifth octaacetylturanose" ^b (β -Octaacetylturanose)	Sirup	67.4°	Octaacetyl-3- α -glucosido- β -fructofuranose
"Second octaacetylturanose" ^a (α -Octaacetylturanose)	158	107.0°	Octaacetyl-3- α -glucosido- α -fructofuranose
"Third octaacetylturanose" ^{a,c} (Octaacetyl- <i>keio</i> -turanose)	96	126.2°	Octaacetyl-3- α -glucosido- <i>keio</i> -fructose
"Stable chloroacetylturanose" ^a (Hexaacetyl- β -turanose<2,6>-2,3-l-orthoacetyl chloride)	185	-0.4°	Heptaacetyl-2-chloro-3- α -glucosido- β -fructopyranose
"Stable bromo-acetylturanose" ^a (Hexaacetyl- β -turanose<2,6>-2,3-l-orthoacetyl bromide)	133-134	-30.5°	Heptaacetyl-2-bromo-3- α -glucosido- β -fructopyranose
"Stable iodo-acetylturanose" ^a (Hexaacetyl- β -turanose<2,6>-2,3-l-orthoacetyl iodide)	105-106	-54.2°	Heptaacetyl-2-iodo-3- α -glucosido- β -fructopyranose
Heptaacetylturanose ^d (ortho ester structure with l-configuration)	140-141	37.0°	Heptaacetyl-3- α -glucosido- β -fructopyranose
"Normal" β -methylturanoside heptaacetate ^d	188-189	27.5°	Heptaacetyl-3- α -glucosido- β -methylfructopyranoside
"Normal" β -methylturanoside ^{d,e}	173-174	3.6° ^f	3- α -Glucosido- β -methylfructopyranoside
Heptaacetyl- β -methylturanoside with ortho ester structure ^d	162-164	80.0°	Hexaacetyl-1,2-[methoxyl-ethylidene]-3- α -glucosido- β (?)fructopyranose
" γ -(3)-Monoacetyl- β -methylturanoside ^d	137	114.6° ^f	1,2-[Methoxyl-ethylidene]-3- α -glucosido- β (?)fructopyranose

^a Note (7a). ^b Note (7d). ^c Note (7c). ^d Note (7b). ^e This substance was originally described as a sirup. Later it was obtained in long needles from alcohol solution and showed the indicated constants. ^f In water solution.

derivatives which were previously prepared from this sugar. In this revisionary work it was found that all the experimental facts accumulated during the past investigations could be interpreted excellently on the basis of the new formula. In Table I a list is given of the more important turanose derivatives with their incorrect designations as they now appear in the literature. The last column contains the names of the correct chemical formulas which are based on experimental facts and on the true structure of turanose. Since it is impractical to designate turanose derivatives possessing the furanoid or pyranoid fructose constituent by retaining the word "turanose," the scientific name of 3- α -glucosidofructose has been used throughout because this permits the precise designation of any structural difference.

The acetohalogeno derivatives, the methylglycosides and the acetates of 1- β -glucosidofructose are now being investigated in this Laboratory.

Experimental Part

2,3-4,5-Diacetone- β -fructopyranose.—This substance was prepared by a slightly modified procedure of Ohle and Koller.^{12b} Forty cc. of concentrated sulfuric acid was added drop by drop with mechanical stirring to one liter of acetone in an ice-salt mixture. The solution was then shaken on the machine at room temperature with 50 g. of fructose. After three hours of shaking the solution became clear and it was made alkaline with concentrated ammonia solution; the ammonium sulfate was filtered off and the clear filtrate was evaporated *in vacuo* yielding a solid residue or a sirup. This was dissolved in hot water

containing about 25% ethyl alcohol and the hot solution was filtered with activated carbon. The resulting clear, orange-colored solution was treated with water until a slight cloudiness developed; then it was warmed up again and allowed to cool and crystallize. Large prismatic crystals of pure β -diacetonefructose were obtained. On concentration *in vacuo* the mother liquor yielded additional crystals. After one recrystallization from dilute alcohol, the substance had m. p. 96-97° and $[\alpha]^{20}_D$ -33.0° in water solution. These values are in good agreement with those recorded^{12a,b} in the literature; total yield, 47 g.

1 - Tetraacetyl - β - glucosido - 2,3 - 4,5 - diacetone - β - fructopyranose.—The condensation of β -diacetonefructose with acetylbromoglucose was carried out according to the procedure of Reynolds and Evans¹³ for the preparation of gentiobiose. Twenty-six g. of β -diacetonefructose, 25 g. of silver oxide prepared according to Helferich and Klein,¹⁶ 100 g. of Drierite and 100 g. of absolute chloroform were placed in a 500-cc. three-necked flask equipped with a mercury-sealed stirrer, calcium chloride tube and a separatory funnel. The mixture was stirred for one hour to ensure the absence of moisture, then 5 g. of iodine was added after the manner of Helferich and co-workers.¹⁷ A solution of 42 g. of acetylbromoglucose in 150 cc. of absolute chloroform was then added in one hour to the reaction mixture under vigorous stirring at room temperature. After twenty-four hours of continuous stirring the apparatus was fitted with a condenser and the stirring was continued at 55-60° for one hour. The reaction mixture was filtered through a layer of activated carbon, the filtrate was concentrated *in vacuo* and the crystalline residue was dissolved in 200 cc. of hot ethyl alcohol. Upon cooling the disaccharide derivative separated in colorless needles which were recrystallized from alcohol; yield, 30

(16) Helferich and Klein, *Ann.*, **450**, 219 (1926).

(17) Helferich, Bohn and Winkler, *Ber.*, **63**, 990 (1930).

to 35 g.; m. p. 162–163°; $[\alpha]^{20}_D -32.9^\circ$ in chloroform solution (*c*, 2.374). The substance was insoluble in cold water, slightly soluble in hot water and petroleum ether, soluble in cold ether. In an acetyl estimation 0.4666 g. of the substance was dissolved in 22 cc. of pure acetone. This solution required 31.75 cc. of decinormal alkali, whereas the value calculated for tetraacetyl-1-glucosido- β -diacetonfructose is 31.63 cc.

Anal. Calcd. for $C_{26}H_{48}O_{16}$: C, 52.85; H, 6.48. Found: C, 53.14; H, 6.47.

1- β -Glucosido-2,3-4,5-diacetone- β -fructopyranose.—The deacetylation of the tetraacetate was carried out by a small quantity of sodium methoxide according to the method of Zemplén and Pacsu.¹⁸ Sixty grams of the acetate in 300 cc. of methyl alcohol was heated on the water-bath for thirty minutes with 15 cc. of a 0.2 *N* methyl alcoholic sodium methoxide solution. After treatment with activated carbon the solution was concentrated *in vacuo* and the solid residue was crystallized from hot absolute alcohol. From the mother liquor, after treatment with activated carbon, additional crystals were obtained; yield, 42 g.; m. p. 174–175°; $[\alpha]^{20}_D -45.6^\circ$ in water solution (*c*, 0.986).

Anal. Calcd. for $C_{18}H_{30}O_{11}$: C, 51.15; H, 7.16. Found: C, 51.27; H, 7.22.

1- β -Glucosidofructose.—The conditions for the removal of the two acetone residues without simultaneously hydrolyzing the disaccharide linkage were established by quantitative estimation of the increase during hydrolysis of the reducing power of the acid solution. A 0.5179-g. sample of the diacetone derivative was dissolved in 50 cc. of 5% acetic acid, then the solution was transferred to a flask for heating in the water-bath. For reduction determination by the Bertrand method, 4-cc. samples were withdrawn at certain intervals of time and diluted to 20 cc. The permanganate solution used was standardized against a solution containing 0.3010 g. of pure glucose in 100 cc. of water. Twenty cc. of this solution required 18.22 cc. of the potassium permanganate solution, so that 1 cc. of the latter was equivalent to 6.2 mg. of copper. The results are summarized in Table II.

TABLE II

HYDROLYSIS AT 100° OF THE ACETONE GROUPS IN 0.5179 G. OF 1- β -GLUCOSIDO- β -DIACETONEFRUCTOSE DISSOLVED IN 50 CC. OF 5% ACETIC ACID. OPTICAL ROTATIONS AND COPPER REDUCING POWER

Hours	Observed rotation	$[\alpha]^{20}_D$	Cc. of permanganate soln. for 4-cc. samples	Mg. of Cu	Mg. of sugar (calcd. as glucose)
0.16	-0.45°	-43.4°
0.42	- .38
1.50	- .38	..	2.35	14.6	7.0
3.5	- .48	..	4.0	24.8	12.0
5.5	- .50	-59.8 (calcd. as free sugar)	4.40	27.3	13.5
17.7	- .38	..	4.45	27.6	13.8
23.0	- .30	..	4.85	30.1	15.0
41.5	- .24	..	5.00	31.0	15.4

It is seen from the table that in the presence of 5% acetic acid about six hours of heating is sufficient to remove

the acetone residues. At that time a 4-cc. sample of the solution, as used for the reduction determination, should contain 33.4 mg. of the new sugar. From the figure (13.5 mg.) obtained it follows that the reducing power of the disaccharide is only 40% of that of glucose. For the conversion of 40 g. of the diacetone derivative into the free sugar, eight 5-g. samples were dissolved each in 500 cc. of 5% acetic acid and the solutions were heated on the water-bath at 100° for six hours. After this time the batches were united and the solution was concentrated *in vacuo* at 45° to a crystalline mass. This was treated repeatedly with water, each time the solvent being evaporated *in vacuo* to ensure the removal of the acetic acid. Finally the hot aqueous solution of the residue was allowed to stand at 0° and crystallize. Colorless, fine needles of pure 1- β -glucosidofructose dihydrate were obtained. On concentration *in vacuo* the mother liquor yielded additional crystals: total yield, 30.5 g. After one recrystallization from water the substance had m. p. 132–135° and $[\alpha]^{20}_D -59.2^\circ$ in water solution (*c*, 1.3328; first reading, eight minutes after addition of solvent). The rotation remained constant during an observation period of one day. The new sugar is difficultly soluble in cold water, hot methyl alcohol and hot dioxane, and practically insoluble in ethyl alcohol. It is regarded as an open-chain derivative of fructose hydrate (I).

Experiments carried out in fermentation saccharimeters showed that while yeast was capable of fermenting turanose very readily in distilled water to give carbon dioxide, it was without any effect on the new disaccharide.

On account of the difficult solubility of the sugar in suitable solvents the usual methods of molecular weight determination could not be employed. Finally by the aid of Menzies' differential thermometer¹⁹ the molecular weight of the sugar in methyl alcohol was determined in a special ebullioscopic apparatus²⁰ as being 381 instead of the calculated value of 378. For analysis the substance was dried at room temperature over concd. sulfuric acid in a vacuum desiccator to constant weight.

Anal. Calcd. for $C_{12}H_{22}O_{11} \cdot 2H_2O$: C, 38.07; H, 6.93. Found: C, 37.76; H, 6.73.

Osazone Test on 1- β -Glucosidofructose.—When 0.5 g. of the sugar in 5 cc. of hot water was heated on the water-bath with a filtered solution of 0.5 g. of phenylhydrazine (3 moles) and 0.3 g. of glacial acetic acid (3 moles) in 5 cc. of water, the solution remained almost colorless for ten minutes. On continued heating the solution became yellow and after thirty minutes a very small precipitation of osazone took place. After filtration the solution was heated with 1 cc. of glacial acetic acid for thirty minutes, during which time a somewhat larger quantity of osazone separated. In another experiment 0.2 g. of the sugar was heated in 10 cc. of water with 0.4 g. of phenylhydrazine (6 moles) and the same amount of glacial acetic acid (10 moles). In twelve minutes a brown colored osazone separated which was filtered off. After additional heating for twenty minutes, the solution again deposited a brown colored substance. The combined solids were purified with moist ethyl acetate; yield, 70 mg. of light yellow crystals; m. p. 204–206°; $[\alpha]^{20}_D -65.5^\circ$, in a mixture of

(19) Menzies, *THIS JOURNAL*, **43**, 2309 (1921).

(20) Menzies and Wright, Jr., *ibid.*, **43**, 2314 (1921).

(18) Zemplén and Pacsu, *Ber.*, **62**, 1613 (1929).

six parts of absolute alcohol and four parts of pyridine (c , 0.58). After one day the rotation became constant at -34.5° . On the basis of these data the substance was identified as pure glucosazone.

Summary

The present structures of turanose and melezitose are based on the supposed 1,3,4-trimethylfructose, a sirupy product obtained by Zemplén and by Leitch from the fully methylated melezitose. The existence of the true, crystalline 1,3,4-trimethylfructose and the number and properties of the octaacetates and other derivatives of turanose indicate that neither carbon atom 5 nor carbon atom 6 of the fructose part of turanose can carry the glucosidic linkage. Carbon atom 4 is also eliminated because turanosazone

is not identical with maltosazone. If carbon atom 1 were the position of the linkage, 1- β -glucosidofructose would be the β -glycosidic isomer of turanose. This new disaccharide has been synthesized by condensation of acetylbromoglucose with β -diacetonefructose and subsequent hydrolysis of the acetyl and isopropylidene groups. The synthetic sugar is entirely different from turanose and unlike the latter it does not give an osazone except for a small quantity of glucosazone. Turanose, therefore, must be 3- α -glucosidofructose and melezitose the corresponding sucrose derivative. Based on the true formula of turanose the correct structures of the more important turanose derivatives are given.

PRINCETON, NEW JERSEY RECEIVED AUGUST 1, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Infrared Absorption Studies of Some Glycols and Ethoxyalcohols

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It has been recognized for some time that hydroxy compounds such as the alcohols and acids can undergo association through the formation of hydrogen bonds.^{1,2} This association can lead to the formation of well-defined dimers in certain cases, or to the formation of polymers of indefinite size. Thus the monocarboxylic acids form definite dimers,³ whereas water and the alcohols can associate to form aggregates of varying sizes.⁴

It has been observed further that certain hydroxy compounds such as water not only can associate with themselves,⁵ but also can bond to other molecules such as the ethers.⁶ Ethyl ether has no active hydrogens, and so cannot form hydrogen bonds by itself, but its oxygen readily can take part in the formation of a hydrogen bond by serving as an acceptor for an active hydrogen atom from another molecule.

In addition to molecules bonding to others of the same kind or to suitable molecules of a different kind, it also has been found that internal bonding, giving rise to ring formation, can occur in certain cases. This type of bonding known as "intramolecular" bonding (to be distinguished from

"intermolecular" bonding) occurs, for example, in *o*-nitrophenol,⁷ and salicyl aldehyde,⁸ in which cases a stable six-membered ring containing a hydrogen bond is formed.

Evidence for the above-described effects has been provided in numerous ways, but one of the most convenient methods is through the study of infrared absorption. Infrared studies show that, whereas a certain absorption frequency to be associated with an OH group is generally present in hydroxy compounds, that frequency is shifted by an appreciable amount when hydrogen bonding occurs.^{1,8} The shifted or hydrogen bond frequency occurs at wave lengths higher than is found for the fundamental OH, and the magnitude of the shift is usually sufficiently large so as to leave no doubt that a change in the nature of the hydroxyl group has taken place.

The effects discussed above were first observed for the simple hydroxy compounds, by themselves or in combination with simple ethers. It was accordingly felt desirable to investigate by means of infrared absorption studies the association of the glycols and ethoxyalcohols. It is clear from their structures that these molecules offer the possibility of not only associating with one another,

(1) Errera, *Helv. Chim. Acta*, **20**, 1373 (1937).

(2) Buswell, Rodebush and Roy, *THIS JOURNAL*, **60**, 2239 (1938).

(3) Pauling and Brockway, *Proc. Natl. Acad. Sci.*, **20**, 336 (1934).

(4) Zachariasen, *J. Chem. Phys.*, **3**, 158 (1935).

(5) Morgan and Warren, *J. Chem. Phys.*, **6**, 666 (1938).

(6) Unpublished work of Mr. I. T. Krohn of this Laboratory.

(7) Buswell, Dietz and Rodebush, *J. Chem. Phys.*, **5**, 501 (1937).

(8) Hilbert, Wulf, Hendricks and Liddell, *Nature*, **135**, 147 (1935).