

**Chemistry.** — "*Cyclic Derivatives of Mannitol*". By Prof. P. VAN ROMBURGH and J. H. N. VAN DER BURG.

(Communicated at the meeting of October 28, 1922).

Many years ago the researches on the decomposition of the formates of polyhydric alcohols, and also those on the 1.3.5. hexatriene, induced one of us (v. R.) in collaboration with Mr. VAN MAANEN, to study the action of formic acid on mannitol.<sup>1)</sup>

After they had succeeded in preparing the hexaformate of mannitol it appeared against expectation that on being heated this substance yielded no hexatriene or only traces of it; on the other hand it yielded a product of the formula  $C_6H_8O$ , though in small quantities. This product, which boiled at  $107-109^\circ$ , had already been obtained by FAUCONNIER<sup>2)</sup>, together with isomannide, on heating mannitol with formic acid.

Also the tetraformate of mannitane and the diformate of isomannide were obtained by heating mannitol and formic acid, both in pure state. FAUCONNIER<sup>3)</sup> found already, that by heating the diformate of isomannide only carbon oxide was evolved, with formation of isomannide; when on the other hand the former was heated, carbonic acid gas was formed, and again the oxide  $C_6H_8O$  was obtained.

The following constants were found for this latter product, which is very strongly levo-rotatory. Bp.  $107^\circ$ ,  $d_{15}^{15} = 0,9226$ ,  $n_{D_{16}} = 1,3567$ . With bromine it gives a liquid dibromide,  $C_6H_8Br_2O$ ,  $d_{15}^{17,5} = 0,8622$ , Bp. 15 mm.  $118^\circ.5$ . A tetrabromide could not be obtained.

Reduction with hydrogen, according to SABATIER and SENDERENS, gave with  $C_6H_8O$ , both at  $110^\circ$  and at  $180^\circ$  a product of the formula  $C_6H_{10}O$ , which did not boil constantly under ordinary pressure but at  $16^\circ$  at 23 mm. Hence only 1 mol. of hydrogen had been absorbed.

In virtue of the decomposition of the di-formate of isomannide, in which only carbon oxide is formed, (so that it may be assumed not to

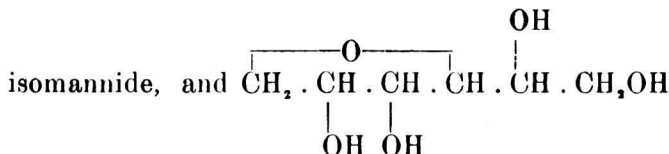
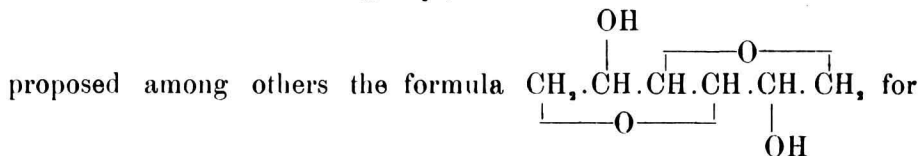
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<sup>1)</sup> VAN MAANEN, Diss. Utrecht, 1909.

<sup>2)</sup> C. r. 100, 914 (1885).

<sup>3)</sup> Bull. Soc. Chim. N.S. 41, 125 (1884).

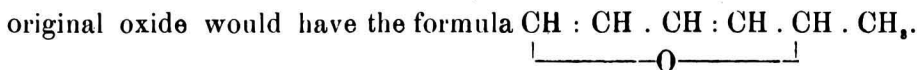
contain two vicinal OH-groups) VAN ROMBURGH and VAN MAANEN



for mannitane, the formate of which gave only carbon dioxide.

The compound  $\text{C}_6\text{H}_8\text{O}$  might therefore be represented by the formula  $\text{CH}_2 . \text{CH} : \text{CH} . \text{CH} . \text{CH} : \text{CH}_2$ , hence it would be  $\alpha$ -vinyldihydrofurane.

In 1917 WINDAUS and TOMICH<sup>1)</sup> too studied the compound  $\text{C}_6\text{H}_8\text{O}$ , and could obtain by its reduction with hydrogen under the influence of palladium, an addition of two mol. of hydrogen, so that  $\text{C}_6\text{H}_{10}\text{O}$  was formed, which substance according to them should be identical with a  $\delta$ -hexylene oxide described by LIPP<sup>2)</sup>, in which not a 5-ring, but a 6-ring occurs:



They concluded to the identity of the two saturated oxides by the equality of the boiling-point, both of the oxides and of the dibromides derived from them. WINDAUS rejects the possibility of the oxide being a furane-derivative, because then no asymmetric formula would be possible. This argument is, however, not valid with regard to the formula drawn up above.

It has appeared from investigations on the action of ozone on the oxide  $\text{C}_6\text{H}_8\text{O}$ , undertaken by Mr. BRUINS in the Utrecht Laboratory after the publishing of WINDAUS and TOMICH's paper, that in this reaction only carbonic acid, formaldehyde, and formic acid could be found, but no products in which a  $\text{CH}_2$ -group occurs, which pleads against WINDAUS's formula. This, however, did not give a rigorous proof for the  $\alpha$ -vinyldihydrofurane-formula. To obtain perfect certainty, we have followed another course,

First of all by reduction of  $\text{C}_6\text{H}_8\text{O}$  with hydrogen of a pressure of two atmospheres in the presence of palladiumsol the saturated

<sup>1)</sup> Göttinger Nachrichte Math. Phys. Kl. 1917, S. 462.

<sup>2)</sup> B. 18, 3275 (1885).

oxide  $C_6H_{12}O$  was prepared. We used for this purpose an apparatus as indicated by SKITA<sup>1)</sup>, in which the process of the reaction can be easily followed. During the fractionation the substance polymerizes partially, so that a perfectly pure product only can be obtained at the expense of considerable loss.

In spite of careful purification the possibility exists therefore that a small quantity of unsaturated product is left behind.

The substance was optically inactive, and showed the following constants:

$$\text{bp. } 103^{\circ}_x\text{—}106^{\circ} \quad d_{16}^{16} 0.8693 \quad n_D 1.42797$$

(analysis: found C 71.8 H 12.3; calc. C 72.0 H 12.0).

In the way indicated by LIPP loc. cit. we have further prepared the  $\sigma$ -hexylene oxide, with the following constants:

$$\text{bp}_{767} 106^{\circ}\text{—}106^{\circ}.2, \quad d_{16}^{16} 0.8617, \quad n_D 1.41887.$$

Since on reduction  $\alpha$ -vinylidihydrofuran must yield  $\gamma$ -hexylene oxide, we have also prepared this oxide according to WOHLGEMUTH<sup>2)</sup>, who however, only gives its boiling-point, viz.  $106^{\circ}\text{—}108^{\circ}$  at 770 mm.

The following constants were found:  $\text{Bp}_{780} 106^{\circ}.5\text{—}107^{\circ}$ ,  $d_{16}^{16} 0.8609$ ,  $n_D 1.41685$ .

The corresponding bromides were obtained by treatment of these oxides with the 8-10-fold volume of hydrobromic acid (48 %) in a sealed tube for 1 to 2 hours at  $100^{\circ}$ . The 1-5-dibromo hexane boiled at 15 mm. at  $105^{\circ}\text{—}108^{\circ}$  (analysis found Br. 65.3 %, calc. 65.5), the 1-4-dibromo hexane at  $106^{\circ}\text{—}108^{\circ}$  at 15 mm. (Br. found 65.4). The boiling-point of the di-bromide obtained from the reduced oxide  $C_6H_{12}O$  was  $106^{\circ}\text{—}110^{\circ}$  at 14 mm. (Br. found 65.6). It is evident that from the equation of the physical constants, both of the oxides and of their di-bromides, no conclusion can be drawn about the structure of the reduced oxide  $C_6H_{12}O$ , unless there are large quantities of the substances at our disposal. It was, therefore, necessary to try to obtain crystallized compounds. An attempt to prepare crystallized benzoates of the glycols corresponding with the dibromides did not meet with success. The action of piperidine on the di-bromides, on the other hand, in which quaternary ammonium bromides were formed, had a favourable result.

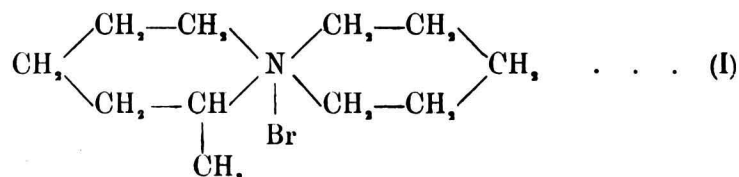
In analogy with VON BRAUN<sup>3)</sup>, who made act 1-5-dibromo pentane

<sup>1)</sup> B. **45**, 3595 (1912).

<sup>2)</sup> C.r. **159**, 80 (1914).

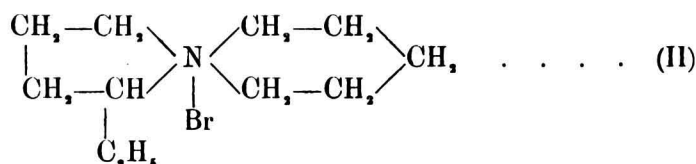
<sup>3)</sup> B. **39**, 4347 (1906).

on piperidine in excess, we prepared, from the 1-5-dibromide, the  $\alpha$ -methylpentamethylene piperidinium bromide:



By recrystallisation from alcohol-ether it is obtained as a white crystalline substance, melting above  $290^\circ$  (Br found 32.63, calc. 32.5).

In an analogous way the 1-4-dibromide yielded the  $\alpha$ -ethyltetramethylene piperidinium bromide:



This substance melted at  $270^\circ$  corr. (Br 32.58 found, 32.5 calc.).

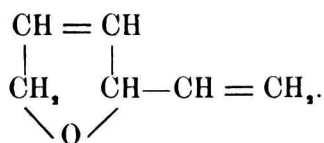
The dibromide obtained from the reduced oxide,  $\text{C}_6\text{H}_{11}\text{O}$ , treated in the same way, yielded a substance melting at  $269^\circ$  (corr.). (III). A mixture of this substance and the preceding one melted sharply at  $269^\circ$  corr.

Hence the 1-4-hexane dibromide and the dibromo derivative of the reduced oxide are identical.

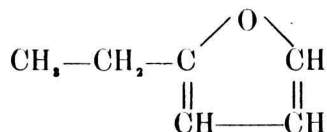
Moreover we prepared double salts with platinum chloride which likewise present the same analogy in their melting-points and in those of their mixtures.

From (I)	$(\text{C}_{11}\text{H}_{22}\text{NBr})_2 \text{PtCl}_4$	Pt. found	23.4	} calc. 23.5
	M.P. $247^\circ$ corr.			
From II	M.P. $260^\circ$ ,,	,, ,,	23.5	
From III	M.P. $259^\circ$ ,,	,, ,,	23.4	
	Mixed melting-point	I and II	$246^\circ$ corr.	
	,, ,,	II and III	$260^\circ$ ,,	

Here again appears the analogy between the compound obtained from the 1-4-oxide and that which was prepared from the reduced oxide,  $\text{C}_6\text{H}_{11}\text{O}$ . Consequently this reduced oxide may really be regarded as  $\alpha$ -ethyltetrahydrofuran and the unsaturated oxide  $\text{C}_6\text{H}_8\text{O}$  of FAUCONNIER as  $\alpha$ -vinyldihydrofuran:



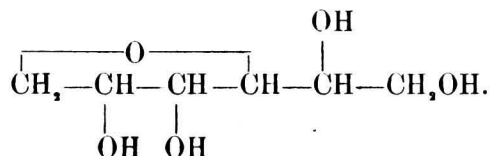
The place of the double bonds in this compound is now exactly known. The substance being optically active, an asymmetric carbon atom must be present in it; a formula, e. g. as the following:



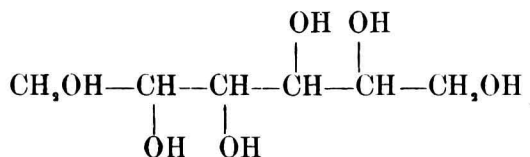
would not satisfy, as has also been remarked by WINDAUS.

As  $\alpha$ -vinylidihydrofuran is formed from mannitane tetra formate, it is now possible to draw up a structure formula for the anhydrides of mannitol, viz. mannitane and isomannide.

We then arrive at the following scheme for mannitane:



In connection with the spatial formula of mannitol:

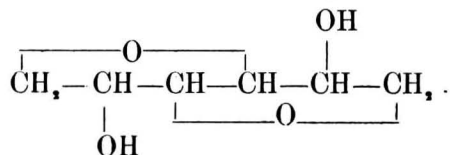


We see that as soon as the oxide-ring is formed between the C-atoms 1 and 4, the OH-groups at 2 and 3 will be at the same side. Besides the molecule contains two OH-groups situated beside each other at 5 and 6 (in perfect accordance with the pyrogenic decomposition of the tetra-formate, in which formic acid and carbon dioxide are split off from OH-groups placed beside each other), so that here a possibility must be for the formation of a di-acetone compound. In fact this compound was obtained as a colourless substance crystallizing in glossy leaflets, melting-point  $155^\circ$  (analysis C 58.83, H 8.38; calculated C 59.0 H 8.2).

The conductivity of boric acid will also be increased greatly by mannitane. <sup>1)</sup>

<sup>1)</sup> BÖESEKEN, Rec. 40, 553 (1921).

Through the formation of a second oxide ring, we then arrive at the following formula for the second anhydride



The places of the OH-groups here are at 2.5; hence no acetone derivative can be formed, nor will the conductivity of boric acid be raised. On treatment with acetone and 1% hydrochloric acid the isomannide was actually recovered. The results of the measurements of the conductivity are recorded in the following table:

Capacity of the vessel 0.4106. Conductivity of the boric acid 0.5 mol. Litre $30 \times 10^{-6} = K_3$ .							
	In water			In boric acid sol.			$K_1 - (K_2 + K_3)$ .
	A.	W.	$K_2 \times 10^{-6}$	A.	W.	$K_1 \times 10^{-6}$	
Mannitol	500	5660	72.5	500	1037	396	294
Mannitane	500	3240	126.8	500	440	933	776
Isomannide				480	11000	34.4	4.4

The concentrations were 0,2 mol./Litre.

After deduction of the conductivity for water  $3 \times 10^{-6}$ , we find therefore that iso-mannide in a very small, quite negligible degree increases the conductivity, whereas this increase for mannitane exceeds that of mannitol more than  $2\frac{1}{2}$  times.

Of the forgoing we may conclude that the structure of the unsaturated oxide  $C_6H_8O$  is proved, likewise that of mannitane. The given formula for isomannide seems to be exceedingly probable.

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