Huygens Institute - Royal Netherlands Academy of Arts and Sciences (KNAW)

Chemistry. — *"On Milksugar".* II. By Prof. A. Smits and J. Gillis.
(Communicated by Prof. S. Hoogewerff.)

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The Ternary Pseudo T, x-figure.

When we draw up the pseudo-ternary T, x-figure, we come to
the following representation. (Fig. 9).
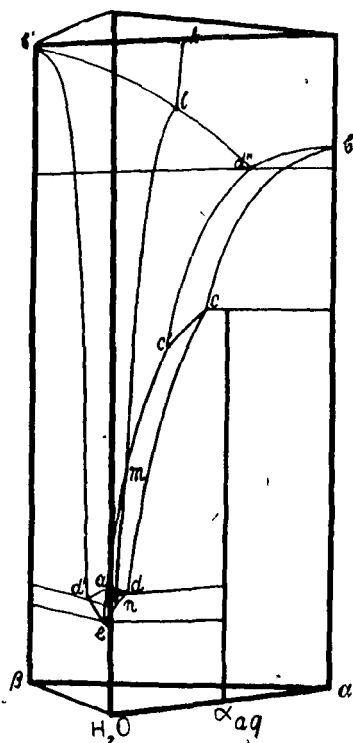

Fig. 9.

In the side plane for α-anhydride— H_2O
we know the initial solubility from $0°$
to $25°$ (determined by Hudson loc. cit.);
further the situation of the eutectic point
at $-0.3°$ and 0.27 mol. $°/_o$ α (point d).

We found the melting point of α at
$222°,8$ and that of α_{aq} at $201°,6$. With
regard to the real transformation point
of α_{aq}, i. e. the point where under the
pressure of 1 atm. the following con-
version takes place:

$$\alpha_{aq} \rightarrow \alpha + L$$
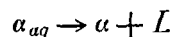
we have been able to ascertain that it
lies above $100°$; for when α-anhydride
was brought at $100°$ in a saturate milk-
sugar solution, a marked generation of
heat still took place, as a proof that at
this temperature hydration of the solid
α-anhydride still occurs.

If instead of a saturate milksugar
solution pure water of $100°$ is taken,
this generation of heat is not observed, because the velocity of
solution is very great at this temperature, and the negative heat
of solution then hides the smaller positive heat of hydration from us.

In the side plane of the system β-anhydride-water we know the
initial solubility at $0°$, the eutectic point d' lying at $-2°,3$ and $2,2$
mol. $°/_o$ β, and further the melting point of H_2O (point a), and the
melting point of β-anhydride b', lying at $252°,2$.

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In the side plane for α-anhydride $+$ β-anhydride we only know the meltings point b and b' of α and β-anhydride, it being assumed here that there occurs a eutectic point (point d'').

The melting surfaces in the space are clearly visible in the spacial figure. At the place where the melting surfaces or solubility surfaces intersect, there arises a three-phase line, and at the place where these three-phase lines meet — and this meeting always takes place by three three-phase lines at the same time — there arises a quadruple point.

Two quadruple points may be pointed out here in our spacial figure, first the point c' lying above $93°,5$, where coexist:

$$S_{\alpha_{aq}} + S_{\gamma} + S_{\beta} + L$$
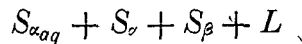
and secondly the ternary eutectic point e, where coexist:

$$S_{\alpha_{aq}} + S_{\beta} + S_{H_2O} + L$$
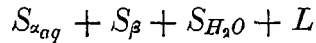
lying according to the calculation at $-2,6°$.

The T, x-spacial figure of the binary system.

In the ternary pseudo figure described here lies the binary system. We get this system, when we draw the surface of equilibrium for the equilibrium $\alpha \leqslant \beta$ in aqueous solution at different total concentrations and different temperatures through the axis for the component H_2O.

This surface of equilibrium intersects the melting point surface of β-anhydride along the line lm, from which it follows that in the binary system water-milksugar the saturate solutions in stable state coexist with β-anhydride from m to l. A change sets in in this in the point m, for below this point the equilibrium surface does not intersect the melting point surface of β-anhydride, but the melting point surface of α_{aq}, so that it is clear from this that the point m represents the found remarkable, *transition dehydration point* lying at $93°,5$, and for which on supply of heat the transformation

$$S_{\alpha_{aq}} \rightarrow S_\beta + L$$
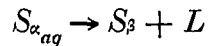
takes place.

Further the said surface of equilibrium of course intersects also the ice-plane, and the line of intersection here indicates the melting point line of the ice in the binary system. This melting point line of the ice and the melting point line of the hydrate intersect in n (at $0,65°$ and $\pm 0,6$ mol. $°/_0$), where the surface of equilibrium meets the eutectic line de of the pseudo-ternary system.

It should be pointed out here that the shape of the surface of eqūilibrium could be derived from the final solubility of $S_{\alpha_{aq}}$ and S_β from 0° to 170°, and further from the projection of this line on the ground plane over the temperature range 0° to 100°.

Theory of the mutarotation.

On the ground of the new views to which we were led by our experimental investigation, we now. arrive at a theory on mutarotation which is essentially different from that drawn up by HUDSON.

As follows from the here given explanation of the behaviour of the system water-milksugar, this system must be considered to be pseudo ternary, in which water is then a component and α and β milksugar are the pseudo components. From this it follows immediately that it must be assumed that these different sorts of molecules occur side by side in the liquid phase, in which the phenomenon of the mutarotation takes place. We know further that for milksugar a hydrate α_{aq} is known in solid state. This alone would already point to the presence of this hydrate also in the solution, for which, as we' have seen, other phenomena plead too.

Now it is evident that when the_α-anhydride can combine with water to a hydrate, this will also be the case with the' β-modification. That we do not know this hydrate in solid state, does not plead at all against this assumption, for this tells us only in this connection, that the solubility of the β_{aq} must be greater than that of β-anhydride, which is just the reverse for the other pseudo-component.

In favour of the assumption of β_{aq} in the solution pleads further that for maltose, a substance which also presents mutarotation, the β_{aq} is known in solid state [1]), but the α_{aq} 'is not, and also that here, therefore, we find exactly what is still wanting for the milk sugar.

We assume, therefore, that in the aqueous solution 'the following equilibrium sets in:

$$\alpha + H_2O \rightleftarrows \alpha_{aq}$$
$$\downarrow\uparrow \qquad \downarrow\uparrow$$
$$\beta + H_2O \rightleftarrows \beta_{aq}.$$
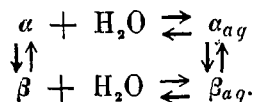
In this symbol there are two conversions of which we can say that they take place with great velocity.

First the reaction.

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1) J. Amer. Soc. **31** 76 (1909) en **32** p. 894 (1910).

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$$\alpha + H_2O \rightleftarrows \alpha_{aq}.$$
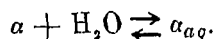
This follows from what was stated in the first communication. With regard to the conversion

$$\beta + H_2O \rightleftarrows \beta_{aq}$$
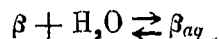
we must refer to the system H_2O-maltose, in which it was also found that this reaction proceeds very, rapidly. Hence it might be said that for the sugars the hydration equilibrium seems to set in very rapidly, and on this ground we assume that the hydration equilibrium of β-anhydride sets in very quickly.

In this way we come, therefore, to the conclusion that the setting in of the equilibria

$$\begin{array}{cc} \alpha & \alpha_{aq} \\ \uparrow\downarrow \text{ and } & \downarrow\uparrow \\ \beta & \beta_{aq} \end{array}$$

must be held responsible for the mutarotation, in other words that the establishment of these equilibria takes place *slowly*.

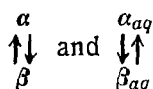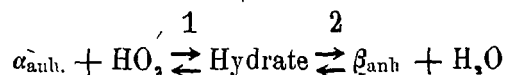In this view the difficulty that lies in the mutarotation theory of HUDSON, and is also acknowledged by himself, is entirely obviated. HUDSON namely assumed that we should have to do with the following equilibria:

$$\begin{array}{cc} 1 & 2 \\ \alpha_{anh.} + HO_2 \rightleftarrows \text{Hydrate} \rightleftarrows \beta_{anh} + H_2O \end{array}$$

in which the equilibrium 1 sets in with great velocity and 2 very slowly.

On account of this view HUDSON is forced to assume that for maltose 'exactly the reverse takes place, and that it is there exactly the equilibrium 2 that sets in very rapidly, and that 1 sets in very slowly.

HUDSON says about this: "Why the monohydrate should change instantly to the α-form for some sugars, but to the β-form for others, is entirely unknown, and is a most interesting problem."

HUDSON's view was somewhat forced, as he was obliged to assume for two perfectly analogous reactions, viz. hydrations of sterioisomers, that one proceeds very rapidly, the other very slowly. According to our view it is assumed that the reaction velocity of the said perfectly analogous conversions differs but little, whereas a great difference is assumed to exist between reaction velocities, one of which is a hydration and the other an intra-molecular conversion.

Mutarotation would, therefore, not be due to a slow dehydration process in the sugar series, as was assumed by HUDSON, but to the slow

establishment of the internal equilibrium between two stereo-isomeric forms.

Constitution of the mono-hydrates in the sugar series.

TOLLENS was the first who ascribed a lacton structure to the α- and β-modifications of the sugar series:

For glucose we should e.g. have the two following configurations:

$$CH_2OH \cdot CHOH \cdot CH \cdot CHOH \cdot CHOH \cdot C{<}^H_{OH} \text{ and}$$
$$\underset{\underline{\qquad\qquad O \qquad\qquad}}{}$$
$$CH_2OH \cdot CHOH \cdot CH \cdot CHOH \cdot CHOH \cdot C{<}^{OH}_{H}$$
$$\underset{\underline{\qquad\qquad O \qquad\qquad}}{}$$

which, therefore, only differ by the asymmetry of the final carbon atom. These compounds contain, therefore, no aldehyde-group, and it is in accordance with this that they do not colour fuchsine sulphuric acid, form no bi-sulphite compounds, and do not exhibit any tendency to polymerisation.

SIMON, and especially ARMSTRONG have succeeded in showing the probability of this structure, the latter by demonstrating that the two methylglucosides α and β, which certainly do not contain an aldehyde group, are converted to α and β glucose by hydrolysis with enzymes.

HUDSON [1]) advanced facts in 1909, which gave a very great probability to this formula.

He says namely this: if we assume that the α- and β-modifications of the aldoses possess the structure proposed by TOLLENS, the molecular rotation of one may be represented by the sum $+ A + B$ ($A =$ rotation of the asymmetric final carbon atom, $B =$ rotation of the rest of the molecule) and of the other by $- A + B$ (rotation of the group B diminished by that of the levo-rotatory final carbon atom).

The difference between the molecular rotations of the α- and β-modifications is therefore $2A$ and the sum $2B$. From this it follows that all the aldoses not substituted at the final carbon atom will have to exhibit a constant difference of $2A$, whereas the same aldoses with different groups at the final carbon atom must all yield the same values of $2B$.

HUDSON found this prediction actually confirmed, not only for the

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[1]) The signification of certain numerical relations in the sugar group. J. Amer. Chem. Soc. **81** 66.
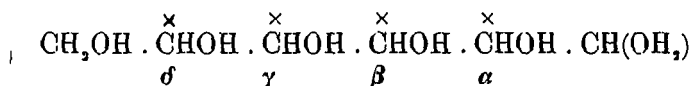
unsubstituted sugars, but also for the glucosides, the acetates, the hydrazons, and the compound sugars, so that this gives a very weighty support to the validity of the assumed structure for the α- and β-modifications.

HUDSON, however, has overlooked a very important point as far as the structure of the sugar mono-hydrates is concerned.

In this he has not been very consistent, as he assumes e.g. for the sugars lactose, glucose, arabinose, and galactose as rotation for the α-modification (a rotation which is not directly to be determined because the α-modification of those sugars passes into hydrate on contact with water), that calculated from the rotation of the hydrate, for which he gives the structure as follows e.g. for glucose:

$$CH_2OH. \ CHOH.CHOH.CHOH \ CHOH. \ CH(OH)_2.$$
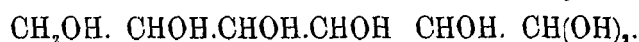
This formula cannot be correct, as in this way the asymmetric final carbon atom of TOLLENS's formula disappears, which means that the rotation of this hydrate will no longer be $A + B$, but only B', which quantity is equal to the algebraic sum of the rotations of the asymmetric carbon atoms indicated by $\times$:

$$\underset{\delta}{CH_2OH} . \overset{\times}{C}HOH . \underset{\gamma}{\overset{\times}{C}HOH} . \underset{\beta}{\overset{\times}{C}HOH} . \underset{\alpha}{\overset{\times}{C}HOH} . CH(OH_2)$$

and this sum is no longer equal to B, because the asymmetric carbon atom has changed now too.

The observed regularities for the aldoses are, therefore, no longer to be explained in this way. We should e.g. have for glucose:

$$\begin{array}{lll} \alpha\text{-hydrate}: & B' & \text{sum} \\ \beta\text{-anhydride}: & -A+B & -A+B+B' \end{array}$$

On the other hand we have e.g. for the ethylglucosides α and β (both anhydrides)

$$\begin{array}{lll} \alpha\text{-ethylglucoside}: & +A'+B & \text{sum} \\ \beta\text{-ethylglucoside}: & -A'+B & 2B \end{array}$$

Hence the sum of the molecular rotations of the α and β glucose cannot be equal to that of the α and the β ethyl glucoside, 23200 and 25230 being found, hence a pretty good agreement. The same thing holds for galactose and ethyl galactoside, for which is found 34700 and 36400.

For other glucosides e. g. methyl-d-glucoside, methyl-d-galactoside, and methyl-d-xyloside, of which the β-modifications of the two first contain resp. $\frac{1}{2}$ H_2O and 1 H_2O, and of the third the α and β modifications are anhydrous, HUDSON's law holds good in spite of

this, though the rotations of these substances are taken as if they -were really anhydrous.

It is therefore evident that the optical superposition takes place here whether these substances contain water or not, and that for all the asymmetric final carbon atom with the lacton ring occurs.

Accordingly we arrive at the result in this way *that for the unsubstituted aldoses e. g. glucose, galactose, milksugar etc. the presence of H_2O does not change amything at all in the structure of the asymmetric final carbon atom.*

No more, therefore, than for methyl glucoside will the water be bound to the final carbon atom in glucose itself. We may now question how it is that Hudson notwithstanding this inconsistency, has arrived at satisfactory results. The answer to this question is very simple. In his calculations for the rotation of the anhydride Hudson has namely taken the rotation of the hydrate, which is only allowed 'when the water is bound in such a way that it cannot influence the rotation of the final carbon atom.

' If e. g. milk sugar hydrate is a molecular compound of $C_{12} H_{22} O_{11}$ with one mol. of water, and quite to be compared with $CuSO_4H_2O$, then it is clear that the water bound to the sugar molecule does not affect its rotation or only very slightly. If we, therefore, know the rotation of α-milksugar hydrate, this rotation is the same as that of milksugar anhydride, as nothing has been changed in the grouping of the active carbon atoms, and thus it may be understood that though Hudson has executed his calculations with the rotations of hydrates, they have yet led to good results; but in this way it has been proved very convincingly that the hydrates do not contain the group $-C\genfrac{}{}{0pt}{}{=(OH)_2}{-H}$.

SUMMARY.

The results of this research may be summarized as follows:

1. The final solubility curve was determined between 89° and 200°, starting both from β-anhydride and from α-anhydride, and this curve, in connection with Hudson's determinations, proved the existence of a break at 93°.5.

2. From the fact that α-anhydride is always converted into β-anhydride above 93°.5, and also from the melting-points of α-anhydride (222°.8) and of β-anhydride (252°.2) determined for the first time follows with certainty that above 93°.5 the α-modification is metastable.

3. It could be established by dehydration experiments of the solid hydrate at different temperatures that this hydrate is a hydrate of the α-modification.

4. It was demonstrated by experiment that 93°.5 in the system water-milksugar is no ordinary transformation point, but a point that we propose to call a *transition-dehydration point*, as at this temperature the hydrate of the α-modification under the pressure of 1 atm. *dehydrates and is also converted to the β-modification.*

5. The observed phenomena have suggested that for milksugar two kinds of molecules α and β have to be assumed, on account of which the system water-milksugar must be considered to be pseudo-ternary. Of this system the isotherms have been determined under the pressure of 1 atm. at different temperatures. By also indicating the curve which represents the situation of the equilibrium between α and β milksugar at different total concentrations the situation of the binary equilibrium diagram at different temperatures could be pointed out in the pseudo ternary system, which enabled us to explain in a simple way all the phenomena observed.

6. Then the pseudo ternary T-x-figure of the system $H_2O + \alpha$ milksugar $+ \beta$ milksugar with the surface of equilibrium lying in it was constructed.

7. A new theory was drawn up for the mutarotation, and in conclusion it was still proved that the monohydrates in the sugar series cannot contain the group $-C\begin{smallmatrix}=(OH)_2 \\ -H\end{smallmatrix}$.

Amsterdam, June 29, 1917.   *Anorg. Chem Laboratory
of the University.*