Chemistry. — Some Remarks on the Condensation Products of Polyoxy-Compounds with Chloral. By Prof. J. Böseken.

(Communicated at the meeting of November 27, 1926)

Our researches on the influence of poly-hydroxy-compounds on the conductivity of boric acid have led to closer examination of the complex compounds formed in the course of them. It then appeared that the mostly strongly acid compounds were often derivatives of boron, in which this atom had passed to a state of higher-valency (coordinate-value = 4). This is of hardly any consequence for the diagnosis of the position of the hydroxyl-groups in space, as also the formation of these higher-valency boron-compounds is dependent on the more or less easy appearance of five or six rings. Besides, it has been shown by Kolthoff 1) that in aqueous solutions these acids of the type B(O₂=R)₂H are for the greater part split up into HOBO₂=R₁, in which a simple ring system occurs.

Besides to the investigation of these boric-acid compounds we have also undertaken the study of the acetone compounds, which remain simpler of structure as a matter of course.

Both the boric-acid and the acetone compounds are hydrolized exceedingly easily and rapidly by diluted acids, so that they can mostly only be preserved with exclusion of acids. R. Willstätter 2) has succeeded in showing that acetone condensed with a-oxy acids to volatile compounds of the same type as the simple boric acid compounds:

\[
\begin{array}{c}
R-C-O \\
\text{O=C-O} \\
\text{C(CH₃)₂}
\end{array}
\]

which, however, could only be separated and kept, when all the water was carefully removed and excluded.

Of the a-hydroxy acids the corresponding condensation products with chloral, the chloralides, have already long been known. The first representative of this class of compounds was discovered by Städele 3) as reaction-product of chloral with strong sulphuric acid; it is the trichlor lactic acid chloralide:

\[
\begin{array}{c}
\text{H} \\
\text{CCl₃-C-O} \\
\text{O-C-O} \\
\text{CCl₃}
\end{array}
\]

1) Recueil 45, 607 (1926).
2) W. und Königberger. Berichte 56, 2107 (1923).
3) Ann. 61, 104 (1847).
the constitution of which has been determined by WALLACH ¹), and the formation of which was explained by me several years ago ²).

WALLACH has made a number of similar compounds with α-hydroxy acids synthetically by heating these with anhydrous chloral in sealed tubes.

As these compounds on the whole crystallize very well, and are very stable, and as for this reason they seemed very suitable to me for the determination of the constitution of polyoxy-compounds, I have started by making an improvement in the way of formation (see below), and I have examined whether these chloralides might possibly also be formed easily from other polyoxy compounds, as α-glycols, which appeared actually to be the case.

The simplification in the method of preparation is this: the α-hydroxy acid or the glycol were gently heated with chloral hydrate and strong sulphuric acid at ± 80° for some time, and the reaction mixture was extracted with ether, after the former had been diluted a little with water. In the case of hydroxy acids these first dissolve in the chloral sulphuric acid mixture, then the chloralide is separated, often already in crystallized state.

Besides the light that we expect the velocity of their formation or of their hydrolysis to throw in the future on the position of the hydroxyl groups, they are also of some interest from another stereo-chemical point of view. In consequence of the origin of a new asymmetric centre, the number of stereo-isomers becomes greater. Thus out of optically active lactic acid two optically active isomer dichloralides will be formed and from d-tartaric acids even three such isomeric dichloralides.

From pentaerythrite, if this possesses a tetrahedral configuration, a compound must be formed which in consequence of spirene-asymmetry will be decomposable into optical antipodes ³) etc.

By the side of the acetone compounds, these chloral compounds, may probably become of great importance for sugar chemistry.

The Preparation of Some Chloralides. Isomer d-Tartaric Acid Chloralides (with Miss J. BLOK).

Lactic acid chloralide. This was first made by WALLACH loc. cit. by heating lactic acid with anhydrous chloral in a sealed tube.

We have heated lactic acid (of 87 ⁰/₀) with the theoretic quantity of chloral hydrate, and an equal number of ccm of conc. H₂SO₄ at 35° for some hours, after first having come to the conclusion that these were the most favourable conditions. After the water had been poured off, a solid product was obtained which melted after distillation under diminished pressure at 45°. Yield 59 ⁰/₀.

¹) Ann. 193, 1 (1875).
³) If on the other hand it should be built up as a four-sided pyramid, it would have to be possible to separate two geometric isomers.
Though the lactic acid was feebly optically active, the compound appeared to be inactive, hence racemation has set in. We have got no indication of the formation of cis-trans isomers, though this must be possible according to our spatial conceptions.

*Citric acid chloralide.* This was prepared by heating citric acid with a small excess of chloral hydrate with conc. H₂SO₄ (e.g. 50 gr. acid + 52 gr. chloralhydrate + 50 ccm. H₂SO₄) between 40⁰—50⁰, and then diluting it with a little cold water. Then a semi solid mass is separated, which is washed with some ether, and is then recrystallized several times from chloroform. It appeared to be a mass consisting of blocks and needles (a total yield of 51 0/₀).

After repeated recrystallisation of the least soluble substance (the blocks) the melting-point was constant = 166⁰. It was strongly acid, dissolved in water, and also in the ordinary organic solvents in which citric acid does not dissolve.

<table>
<thead>
<tr>
<th>Found</th>
<th>Calc.</th>
</tr>
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<tbody>
<tr>
<td>0.0719 gr. equiv.</td>
<td>13.15 cc. AgNO₃</td>
</tr>
<tr>
<td>0.0685 „ „</td>
<td>12.60 „ „</td>
</tr>
</tbody>
</table>

This was, accordingly, the citric acid monochloralide, and to all probability:

\[
\left(\frac{\text{COOH}}{\text{CH}_2}\right)_2 = \text{CO}-\text{O}-\text{CHCCl}_3.
\]

The yield of the pure product melting at 166⁰ is pretty small; there are other substances among it, which will have to be studied further. The chlorine content of the mixture is, however, very near to the calculated value for a monochloralide, so that the possibility exists that by the side of the α-chloralide, also a β-chloralide is formed:

\[
\begin{align*}
\text{O} & \text{= CO} \\
\text{CH}_2 & \text{CHCCl}_3 \\
\text{HOOC} & \text{C-O} \\
\text{CH}_2 & \text{COOH}
\end{align*}
\]

β citric acid chloralide.
From the mother liquid another mixture was obtained, the chlorine-content of which was considerably higher, ± 40%. There is, therefore, an indication that there has also been formed a dichloralide, which may be expected to dissolve more easily in chloroform.

**d-Tartaric acid chloralides.** In the action of chloral on d-tartaric acid the formation of the dichloralide was at once taken into account.

1 Mol. of d-tartaric acid + 2 mol. of chloral hydrate + conc. H₂SO₄ is shaken while heated to 50°. At first it is a turbid liquid, which gradually solidifies; the dichloralide is insoluble in water, hence all the acid parts and remaining not converted chloral can be removed by washing with cold water. Yield: 71% of a perfectly white product. Though the chlorine content was in conformity with that calculated for dichloralide (found 51.1, calculated 52.0), it was unmistakably a mixture; melting range 129°-135°. This was to be expected; asymmetry centres are added; starting from d-tartaric acid, there are, therefore, three isomers to be expected:

<table>
<thead>
<tr>
<th>D (of the tartaric acid)</th>
<th>+</th>
<th>d</th>
<th>d</th>
<th>or trans-trans</th>
</tr>
</thead>
<tbody>
<tr>
<td>D</td>
<td>+</td>
<td>d</td>
<td>-1</td>
<td>for this case these</td>
</tr>
<tr>
<td>D</td>
<td>-1</td>
<td>+</td>
<td>d</td>
<td>are identical</td>
</tr>
<tr>
<td>D</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>cis-cis.</td>
</tr>
</tbody>
</table>

First the substance was sublimated in a locomotive according to EYKMAN: in 20 min. it already pretty rapidly went over at 130°; needles are, therefore, formed, which however appeared not to be homogeneous. As a considerable part was decomposed in this, we have further tried to bring about the separation by recrystallisation from chloroform and benzene. In this way we have succeeded in obtaining two substances with constant melting-point and constant rotatory power.

The least soluble isomer, melting-point = 159°-161°. Chlorine content = 52.0%. Rotation in chloroform, length of the tube = 2 dm.

- 0.6759 gr. in 25 cc. CHCl₃ at 16°.2 \(\alpha_D = -2.92\)
- 0.6747 " 24 cc. .. .. .. \(\alpha_D = -3.00\)
- \([\alpha]_D = -54°.0\) and \(-53°.7\) Mean = \(-53°.9\).

Lowest-melting modification, melting-point = 116°-118°. Chlorine content = 51.1%.

- 0.6786 gr. in 24 cc. CHCl₃ at 17°.0 \(\alpha_D = -1°.85\)
- 0.6271 " 22 .. .. .. 17°.0 \(\alpha_D = -1°.91\)
- \([\alpha]_D = -32°.8\) and \(-33°.5\) Mean = \(-33°.1\).

It is noteworthy that both modifications are levo-rotatory; it is, however, not astonishing, because pure anhydrous d-tartaric acid is also
levo-rotatory\(^1\)). As long as the third modification has not been found, it is not possible to draw further conclusions.

Racemic acid chloralide was prepared in a perfectly analogous way to that in which tartaric acid chloralide had been made. Obtained was 20 gr. chloralide from 8 gr. racemic acid, i.e. the theoretic quantity. Very readily soluble in all org. solvents, except petroleum ether, insoluble in H\(_2\)O.

Original mельt point = 118°—128°; after repeated solution in alcohol and precipitation with water 164°—166°: in this the melting-point was never constant and much was lost. There have, undoubtedly, been formed isomers; the number of possible isomers is three, as with d-tartaric acid, all racemates or racemic mixtures; they may be indicated by R-trans-trans, R-cis-trans, and R-cis-cis.

Analysis:

\[
\begin{align*}
0.0341 \text{ gr. chloralide equiv.} & \quad 9.82 \text{ cc. AgNO}_3 \\
0.0531 \text{ . . . . . . . . . . . . 15.6} & \quad 52.3 \text{ . . . . . Cl} \\
& \quad \text{Cal. 52.0%}
\end{align*}
\]

Of the anti tartaric acid the di-chloralide was likewise obtained with excellent yield. This, too, was clearly a mixture; there may possibly be again three isomers here: i-trans-trans, i-cis-trans, and i-cis-cis; one of them was obtained after repeated recrystallisation with constant melting-point = 171°; Cl = 52.6\% Cal. 52.0\%. No attempts were made to isolate the other isomers, the purpose set by us, to find a simple method to convert the aliphatic \(\alpha\)-hydroxy acids into the corresponding chloralides, having been reached.

Salicylic acid chloralide. In the aromatic hydroxy acids a deviation may be expected, because the nucleus hydrogen atoms can be activated. This expectation proved true, for on application of the method described above, the product formed dissolved in diluted ammonia, which is not the case with the chloralide.

Hence a nucleus activator, as H\(_2\)SO\(_4\) is to be excluded here. 15 gr. salicylic acid was boiled with 23 gr. anhydrous chloral (excess) in connection with a reflux condenser, in which beautiful crystals were deposited. After 5 hours’ boiling the substance was poured out into H\(_2\)O, the mass was washed out with ammonia, and the residue was recrystallized from ether.

\[
\begin{align*}
\text{Melt. point} & = 124°—125°; \\
0.0718 \text{ gr.} & = 15.95 \text{ cc. AgNO}_3 0.0502 \text{ n.} = 39.6\% \text{ Cl; Cal. 39.8\% Cl.}
\end{align*}
\]

In view of this exceedingly easy six-ring formation one of the monochlorides observed in citric acid is very probably a \(\beta\)-chloralide (see before).

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\(^1\) I found this at Assen already in 1899, it may, for the rest, also be derived from the course of the rotation change with the concentration on one side, and from the change of the rotatory power of the alkylesters with diminishing molecular weight.
Amygdalic acid chloralide. WALLACH has already prepared this chloralide; he states that it melted at 82°—83°, and that he could obtain from the mother liquid a substance, melt. point 64°, with the chlorine content calculated for chloralide. We have prepared the substance by boiling amygdalic acid with anhydrous chloral (a small excess), as here too complications appeared with conc. H₂SO₄. In this way a solid light yellow substance was obtained, which was recrystallized from petroleum ether after being washed with H₂O.

The substance appeared to be perfectly homogeneous, and always melted sharply at 59°—60°, 0.06913 gr. = 14.55 cc. AgNO₃ 0.0502 n. = = 37.5% Cl. Calculated 37.8%. Accordingly we cannot confirm WALLACH’S communication.

It is advisable not to use H₂SO₄ as condensing substance; melting in with chloral is, however, not necessary; it may be boiled with a slight excess of anhydrous chloral.

Condensation of Glycols with chloral. (With Mr. J. STOK).

For this purpose the method with conc. H₂SO₄ appeared to yield excellent results at moderate temperature. In this way, i.e. as was described for citric acid and tartaric acid, glycerol and glycol were chloralized. The glycerol chloralide is a pretty viscid substance, which distils undecomposed, and is distinguished by a particularly great stability; it may be boiled without decomposition with 60% H₂SO₄, and is also proof to the action of HNO₃ 1.4 at boiling heat. By chromic acid in acid and KMnO₄ in alcalie solution oxidation sets in. Boiling point = 142°—144° Cl 0% found = 48.8 0% calc. = 48.1 0% d₁⁷₅/₄c. = = 1.5500, n₁⁰⁺ = 1.5053. The simplest chloralide, the glycol chloralide, the prototype of all these compounds, is also exceedingly resistant; it crystallizes beautifully and has a pleasant smell of camphor; solidifying point = 40°.

The communication of LESTER YODER ¹), who prepared the chloralide of glycerol by means of ZnCl₂ for an entirely different purpose, led me to think it desirable to make some communications of our researches.

Delft, November 1926.