Structures of the Anhydrides of 3- and 5-Hydroxylaevulic Acid

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Submitted in honour of the sixtieth birthday of my teacher, Professor Arne Fredga

The anhydrides of 3- and 5-hydroxylaevulic acid are studied, and new structures (VI and VII) are proposed.

Studying 2- and 3-hydroxylaevulic acid Wolff¹ found that these compounds lost water when heated to give crystalline products with high melting points. Wolff suggested that the products were the lactides of the two acids and he proposed the structures I and II for these compounds.

\[
\begin{align*}
\text{I} & \quad \text{II} \\
\text{CH}_3\text{COCH}_2\text{CHCH}_2\text{COCH}_3 & \quad \text{CH}_3\text{COCHCH}_2\text{COCH}_3 \\
\text{O=C-OCH=CHCH}_2\text{COCH}_3 & \quad \text{O=C-OCH=CHCH}_2\text{COCH}_3
\end{align*}
\]

However, in a recent paper² the present author has pointed out, that Wolff’s 2-hydroxylaevulic acid was in fact the 5-isomer. The structure I must therefore be incorrect.

The ethyl ester of the real 2-hydroxylaevulic acid was prepared by Rossi and Lauchenauer³ and by Wynn and Corwin⁴. These authors found that this ester very easily dehydrated intramolecularly to give β-acetylethacrylic acid (III).

\[
\text{III} \quad \text{CH}_3\text{COCHCH}_2\text{COOC}_2\text{H}_5 \rightarrow \text{CH}_3\text{COCH=CHCOOC}_2\text{H}_5 + \text{H}_2\text{O}
\]

Since 5-hydroxylaevulic acid is both a γ-keto and a δ-hydroxy acid and 3-hydroxylaevulic acid is a γ-keto-β-hydroxy acid it would be interesting to study how these acids dehydrate.
Fig. 1. Infrared spectrum of anhydride of 5-hydroxylaevulic acid (VI). Solid in KBr.

Fig. 2. Infrared spectrum of anhydride of 3-hydroxylaevulic acid (VII). Solid in KBr.

Wolff\textsuperscript{1} made no determination of the molecular weights of the anhydrides, but proposed that they were dimers on the grounds of their high melting points. In the present work the molecular weights were determined by the Rast method, and the values 230 (5-anhydride) and 212 (3-anhydride) were obtained showing that the anhydrides are dimers.

The infrared spectra of the anhydrides, Figs. 1 and 2, gave further information about their structures. No peaks were found in the region 5.79—5.88 μ (1725—1700 cm\(^{-1}\)) where carbonyl and carboxyl groups are known to have strong vibration absorption bands, \textit{cf.} Bellamy\textsuperscript{5,6}. On the other hand, both spectra have strong peaks near the region 5.61—5.68 μ (1780—1760 cm\(^{-1}\)) where saturated \(\gamma\)-lactones absorb\textsuperscript{7}.

Some \(\gamma\)-keto acids, for instance \(\gamma\)-oxopimelic acid and 3-acetylglutaric acid, form bicyclic anhydrides containing two \(\gamma\)-lactone rings IV\textsuperscript{8} and V\textsuperscript{8}.

\[
\text{IV} \quad \text{V}
\]

The infrared spectra of these also have peaks in the same region as the anhydrides of the two hydroxylaevulic acids, see Table 1. These data indicate that the studied anhydrides also possess γ-lactone rings and the structure VI for the 5-hydroxylaevulic acid anhydride and the structure VII for the 3-isomer anhydride seem probable.

![Structures VI and VII](image)

Although these structures seem rather complex, they can be more easily understood if it is supposed that, as in the dehydration of laevulic acid to α-angelica lactone \(^\text{10}\), intermediates in their formation are the lactols (VIII and IX) of the corresponding acids, and these dehydrate giving the dimer anhydrides VI and VII.

\[
\begin{align*}
\text{OH} & \quad \text{OH} \\
2 \text{CH}_2\text{CO-CH}_2\text{CH}_2\text{COOH} & \rightarrow 2 \text{CH}_2\text{C-CH}_2\text{CH}_2\text{C}=\text{O} & \rightarrow \text{VI} + 2\text{H}_2\text{O} \\
\text{VIII} \\
\text{OH} & \quad \text{OH} \\
2 \text{CH}_2\text{CO-CH-CH}_2\text{COOH} & \rightarrow 2 \text{CH}_3\text{C-CH}_2\text{COOH} & \rightarrow \text{VII} + 2\text{H}_2\text{O} \\
\text{IX} \\
\end{align*}
\]

Other 1,2-diols, for instance 1,2-propanediol and 1,2-butanediol can also dehydate in a similar way to 2,5- (and not 2,6-) derivatives of p-dioxane \(^\text{11,12}\).

The spectra of the anhydrides VI and VII also contain a series of bands in the region 8.90—9.71 \(\mu\) (1124—1030 cm\(^{-1}\)) where dioxane derivatives absorb \(^\text{13}\). However bands in this region are not specific for dioxane derivatives and therefore this information is of minor importance.

\begin{table}[h]
\centering
\begin{tabular}{|l|c|}
\hline
Substance & Band in the region 5.5—6.0 \(\mu\) \\
\hline
5-Hydroxylaevulic acid & 5.81, 5.90 \\
Anhydride of 5-hydroxyalaevulic acid (VI) & 5.61 \\
Anhydride of 3-hydroxylaevulic acid (VII) & 5.59 \\
γ-Oxopimelic acid & 5.82, 5.90 \\
Anhydride of γ-oxopimelic acid (IV) & 5.58 \\
Anhydride of 3-acetylgluutaric acid (V) & 5.56 \\
\hline
\end{tabular}
\caption{Table 1.}
\end{table}

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EXPERIMENTAL

The micro analyses were carried out by the Analytical Laboratory of the Chemical Institute, University of Uppsala. The melting point measurements were performed by means of the Kofler microscopic method and the infrared spectra were obtained with a Perkin Elmer Model 137 spectrophotometer provided with a sodium chloride prism.

_Anhydride of 5-hydroxyalaevic acid (VI)._ This compound was prepared according to Wolff 1. M.p. 265–268°C. The infrared spectrum is given in Fig. 1. (Found: C 52.69; H 5.32; M.W. 230. Calc. for C_{14}H_{13}O_4(228.1): C 52.61; H 5.30; M.W. 228).

_Anhydride of 3-hydroxyalaevic acid (VII)._ This compound was prepared according to Wolff 1. M.p. 238–240°C. The infrared spectrum is given in Fig. 2. (Found: C 52.41; H 5.39; M.W. 212. Calc. for C_{14}H_{13}O_4(228.1): C 52.61; H 5.30; M.W. 228).

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REFERENCES

6. Ref. 5, p. 162.
7. Ref. 5, p. 179.
13. Ref. 5, p. 119.

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