HETEROCYCLIC COMPOUNDS

Part XI. The Application of the Pechmann and the Kostanecki
Reactions to γ-Orcacetophenone

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β-Oracetophenone has been shown to condense with aceto-acetic ester in the presence of phosphoryl chloride or anhydrous aluminium chloride by Desai and Ekhlas,¹ as well as Shah and Shah,² with the formation of 5-hydroxy-6-acetyl-4:7-dimethyl coumarin (I, R = CH₃CO) and 5-hydroxy-4:7-dimethylcoumarin (I, R = H), the latter being formed from orcinol which was produced by the deacetylation of oracetophenone. As we have worked out a satisfactory method of preparing γ-oracetophenone (II), we thought of applying the Pechmann and the Kostanecki Reactions to this interesting dihydroxy-ketone.

Acetoacetic ester condensed with γ-oracetophenone or 2:6-dihydroxy-4-methylacetophenone either in the presence of concentrated sulphuric acid or phosphoryl chloride giving 5-hydroxy-4:7-dimethylcoumarin (I, R = H), and not a trace of the expected 7-hydroxy-8-acetyl-4:5-dimethylcoumarin (III, R = CH₃) was formed. This ketone, thus resembled 4-acetyl-1-naphthol which, according to Desai and Ekhlas (loc. cit.) underwent de-acetylation in the course of the Pechmann condensation. However, its behaviour was quite different from that of 2-acetylresorcinol which was found by Limaye³ to condense readily forming 7-hydroxy-8-acetyl-4-methylcoumarin (III, R = H). Thus the presence of the methyl group in the para-position to the acetyl group brings about a marked change in the behaviour of γ-oracetophenone, and it will be interesting to study the influence of other positive as well as negative groups in the place of methyl.

\[
\begin{align*}
\text{CH}_3 & \text{O} \\
\text{O} & \\
\text{CO} & \\
\text{C} & \\
\text{CH} & \\
\text{CH}_3 & \\
\text{O} & \\
\text{CO} & \\
\text{COCH}_3 & \\
\text{CH} & \\
\text{CH}_3 & \\
\end{align*}
\]
Vigorous acetylation of \( \gamma \)-orcacetophenone according to Kostanecki's method gave two products, one neutral and the other acidic. The neutral product (A) had the composition \( \text{C}_{15}\text{H}_{14}\text{O}_{5} \) and melted at 103\(^\circ\), while the acidic product (B) having the composition \( \text{C}_{13}\text{H}_{12}\text{O}_{4} \) melted at 137\(^\circ\). On leaving (A) in contact with concentrated sulphuric acid according to the method of Sethna and Shah, an acidic product (C) melting at 141\(^\circ\) was obtained. The general reactions as well as the mixed melting point showed that (B) was essentially identical with (C), but slightly contaminated with a small amount of an impurity. Alkaline hydrolysis of (C) gave \( p \)-orsellinic acid (IV) which was identified by comparison with an authentic specimen kindly supplied by Dr. R. C. Shah. Therefore, the constitution of (C) was 3-acetyl-2: 7-dimethyl-5-hydroxychromone (V) while (A) was its 5-acetyl-derivative. When (B) was hydrolysed with alkali, \( p \)-orsellinic acid together with 5-hydroxy-4: 7-dimethylcoumarin was produced. Therefore, the impurity present in (B) must be 4-acetonyl-5-hydroxy-7-methylcoumarin (VI) which is isomeric with (V). Thus though the main product of the Kostanecki Reaction is 3-acetyl-2: 7-dimethyl-5-hydroxy-chromone, a small quantity of 4-acetonyl-5-hydroxy-7-methylcoumarin is also formed. Very recently Sethna and Shah (loc. cit.) have shown that substituted 4-acetonylcoumarins are exclusively produced during the Kostanecki acetylation of \( \beta \)-orcacetophenone. Thus it is quite clear that the course of this reaction is quite different in the case of the two isomeric orcacetophenones.

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

**Experimental**

**Condensation of \( \gamma \)-orcacetophenone with acetoo-acetic ester.**—(1) A mixture of \( \gamma \)-orcacetophenone (1 g.), acetoo-acetic ester (1 g.) and concentrated \( \text{H}_2\text{SO}_4 \) (5 c.c.) was left at the ordinary temperature for 24 hours, and poured over ice. The sticky solid on crystallisation from alcohol gave short needles, m.p. 256–58\(^\circ\), which was identified as 5-hydroxy-4: 7-dimethylcoumarin by comparison with an authentic specimen. The mother-liquor did not furnish any other product. The same result was obtained on using 73 per cent. \( \text{H}_2\text{SO}_4 \).
(2) A mixture of the ketone (1 g.), aceto-acetic ester (1 g.), phosphoryl chloride (1 c.c.) and dry benzene (10 c.c.) was heated on water-bath under reflux for three hours. The benzene solution was poured out from some black, sticky precipitate that was formed at the bottom of the flask, and the residue extracted with three lots of benzene (10 c.c. each). After removing benzene from the combined extracts, the residue was crystallised from dilute alcohol when needles, m.p. 256°, were obtained, and were identified as 5-hydroxy 4: 7-dimethylcoumarin.

Kostanekki reaction with γ-oraceto-phenone.—A mixture of γ-oraceto-phenone (3 g.), anhydrous sodium acetate (3 g.) and acetic anhydride (15 c.c.) after being heated in an oil-bath at 175-80° for 20 hours, was poured into water, and the solid that slowly separated out was filtered off. The dry solid (1·4 g.) was shaken up with cold 5 per cent. NaOH, when part of it dissolved.

The insoluble portion A (0·5 g.) crystallised from dilute alcohol in cluster of needles, m.p. 103°. 5-Acetoxy-3-acetyl-2: 7-methylchromone was soluble in most of the organic solvents, and its alcoholic solution did not give any coloration with ferric chloride. (Found: C, 65·6; H, 5·2; C_{13}H_{12}O_{4} requires C, 65·7; H, 5·1 per cent.)

5-Hydroxy-3-acetyl -2: 7-dimethylchromone (V).—A pale-brown solution of the above product (0·3 g.) in concentrated H_{2}SO_{4} (10 c.c.) was kept overnight, and poured over ice. The product which separated out crystallised from hexane in colourless needles, m.p. 141°. (Found: C, 67·5; H, 5·2; C_{13}H_{12}O_{4} requires C, 67·2; H, 5·2 per cent.).

The chromone was soluble in most of the organic solvents, while its alcoholic solution gave a deep-violet coloration with ferric chloride. Its solution in dilute caustic soda solution as well as concentrated H_{2}SO_{4} was yellow and non-fluorescent.

Hydrolysis of 5-hydroxy-3-acetyl-2: 7-dimethylchromone.—A solution of the chromone (0·2 g.) in 5 per cent. caustic soda (10 c.c.) was heated on sand-bath under reflux for one-and-half hours, cooled, filtered and acidified with concentrated HCl. The solid which was purified through a dilute sodium bicarbonate solution crystallised from hot water in needles, m.p. 165-66°, and identified as p-orSELLinic acid by comparison with an authentic specimen.

The alkali-soluble substance (B) from the Kostanecki Reaction was recovered after acidification, and crystallised from alcohol in needles, m.p. 137°. This m.p. could not be raised by subsequent recrystallisations. Its
alcoholic solution gave a deep-violet coloration with ferric chloride, while its mixed m.p. with 5-hydroxy-3-acetyl-2:7-dimethylchromone was 139°. (Found: C, 67.6; H, 5.1; C_{13}H_{12}O requires C, 67.2; H, 5.2 per cent.)

Hydrolysis of B with 5 per cent. caustic soda and formation of p-orsellinic acid and 5-hydroxy-4:7-dimethylcoumarin.—A solution of the product B (0.7 g.) in 5 per cent. caustic soda (15 c.c.) was heated on sand-bath under reflux for one-and-half hours. The solid (m.p. 143-46°) obtained on acidification of the mixture with concentrated HCl was treated with a solution of sodium bicarbonate which dissolved most of the solid leaving a residue (0.1 g.) which was identified as 5-hydroxy-4:7-dimethylcoumarin while the alkaline solution gave, on acidification, p-orsellinic acid.

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Summary

γ-Orcacetophenone undergoes deacetylation when condensed with acetoacetic ester in the presence of concentrated H$_2$SO$_4$ or phosphoryl chloride. Acetylation in presence of anhydrous sodium acetate gave a mixture of 5-acetoxy-2:7-dimethyl-3-acetylchromone, 5-hydroxy-2:7-dimethyl-3-acetylchromone, and 4-acetonyl-5-hydroxy-7-methylcoumarin. Thus it differs essentially from its isomer β-orcacetophenone with respect to these reactions.

REFERENCES

3. Limaye .. Rasayanam, 1936, 1, 65.