THE REACTION OF *N*-CHLOROACETYLISATIN WITH ALKALI*

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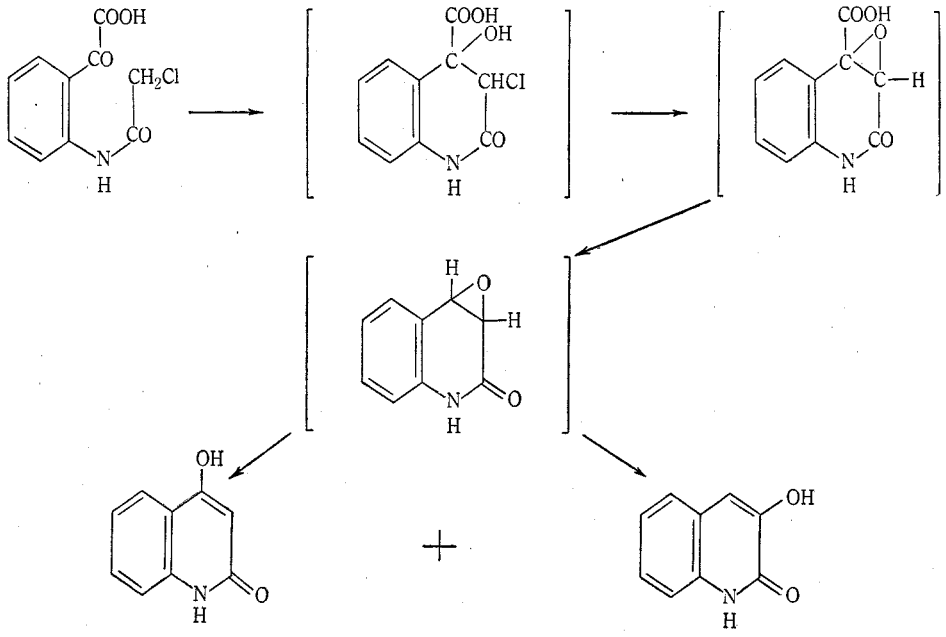
A simple laboratory synthesis of 4-hydroxy-2-quinolone based on the Camps method for preparing 2-quinolone-4-carboxylic acids from acylisatins has been described by Huntress and Bornstein (1949), who claim that reaction of *N*-chloroacetylisatin with alkali gives 56–70 per cent. yields of crude 4-hydroxy-2-quinolone. In our hands this reaction always leads to a mixture of 4-hydroxy-2-quinolone, in about 15 per cent. yield, with an approximately equal amount of an isomeric substance, m.p. 265 °C. The low yields of purified products are due to hydrolysis of the chloroacetyl compound, 55–65 per cent. being recoverable as isatin.



The second product is 3-hydroxy-2-quinolone (2,3-dihydroxyquinoline), the identity of which was established by comparison with a specimen prepared by the action of diazomethane on isatin (Arndt, Eistert, and Ender 1929). Formation of both 3- and 4-hydroxyquinolones in this reaction is of interest, particularly as *N*-acetylisatins (see, e.g. Halberkann 1921) give rise to 2-quinolone-4-carboxylic acids. A satisfactory explanation of the course of

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the reaction must therefore account for both the decarboxylation and the formation of an intermediate which can be converted to either 3- or 4-hydroxy-2-quinolone. These requirements are met by the following scheme* involving ethylene oxide formation and consequent ready decarboxylation of the intermediate glycidic acid (see, e.g. Barbier 1934).

Experimental

Microanalyses were carried out in the C.S.I.R.O. Microanalytical Laboratory. All melting points are corrected.

Reaction of *N*-chloroacetylisatin with alkali was carried out as described by Huntress and Bornstein (loc. cit.), but acidification was effected in two stages. 10N hydrochloric acid (6 ml) added to the reaction mixture from *N*-chloroacetylisatin (5 g), sodium hydroxide (5 g), and water (150 ml) gave a white precipitate (1·3 g, m.p. 250–320 °C) consisting mainly of 3- and 4-hydroxy-2-quinolones. A precipitate (2·2 g), which was essentially isatin, formed on further acidification.

Crude 4-hydroxy-2-quinolone was separated from the first precipitate by crystallization from methanol in which it is only sparingly soluble. Recrystallization from a large volume of methanol gave 4-hydroxy-2-quinolone as colourless needles, m.p. 361–362 °C (decomp.) (Found: C, 67·3; H, 4·4; N, 8·7%. Calc. for $C_9H_7O_2N$: C, 67·1; H, 4·4; N, 8·7%). The nitroso-derivative melted at 217 °C (decomp.), the acetyl-derivative at 221–222 °C. 4-Hydroxy-2-quinolone, prepared by the method of Ashley, Perkin, and Robinson (1930) from methyl acetylanthranilate, melted at 360–361 °C (decomp.), its nitroso derivative at 216 °C (decomp.), and its acetyl derivative at 221–222 °C. These melting points were unchanged in admixture with the corresponding materials prepared from *N*-chloroacetylisatin. 4-Hydroxy-2-quinolone gives a weak orange Fe^{3+} reaction.

Crude 3-hydroxy-2-quinolone from the methanolic liquors could not be further purified by crystallization. Acetylation with acetic anhydride and pyridine gave the acetyl-derivative, colourless needles from ethanol, m.p. 216·5–217·5 °C alone or mixed with authentic 3-acetoxy-2-quinolone, m.p. 217·5–218·5 °C (Found: C, 65·3; H, 4·5%. Calc. for $C_{11}H_9O_3N$: C, 65·0; H, 4·4%). Alkaline hydrolysis of the acetyl-derivative gave 3-hydroxy-2-quinolone, colourless needles from methanol, m.p. 264–265 °C, mixed m.p. with a specimen prepared according to Arndt, Eistert, and Ender (loc. cit.) 265–266 °C (Found: C, 67·1; H, 4·4; N, 9·0%. Calc. for $C_9H_7O_2N$: C, 67·1; H, 4·4; N, 8·7%). The substance gives a blue-green Fe^{3+} reaction.

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