CCCLXXII.—*A Synthesis of Some Substituted 3-Methylquinolines.*

By STANLEY GORDON WILLIMOTT and IAN ALEXANDER SIMPSON.

THE earlier methods for the synthesis of 3-methylquinoline (Riedel, *Ber.*, 1883, **16**, 1610; Doebner and Miller, *Ber.*, 1884, **17**, 1714; 1885, **18**, 1642; Miller and Kinkelin, *Ber.*, 1887, **20**, 1916) give poor yields and are useless when substituted derivatives are required. Koenigs and Bischkopf (*Ber.*, 1901, **34**, 4330) claim to have synthesised 3-methylquinoline in good yield by condensing *o*-aminobenzaldehyde and propaldehyde in the presence of 1% potassium hydroxide. Under these conditions, however, Wislicenus and Elvert (*Ber.*, 1909, **42**, 1145) obtained only an oily intermediate product that gave no picrate; but they prepared the pure base in an 80% yield by heating together equimolecular quantities of *o*-aminobenzaldehyde and propaldehyde in a bomb tube at 220°. As 3-methylquinoline was required in quantity, the bomb-tube method of Wislicenus and Elvert was discarded, and a further modification of the Friedländer type of synthesis was attempted by condensing together equimolecular proportions of *o*-aminobenzaldehyde and propaldehyde in aqueous alcohol, piperidine being used as a condensing agent. The compound isolated was, however, a syrup which gave none of the characteristic reactions of a quinoline and resembled the intermediate oily compound obtained by Wislicenus and Elvert under similar conditions. The substance probably has the structure

$$NH_2\cdot C_6H_4\cdot CH(OH)\cdot CHMe\cdot CH{:}N\cdot C_6H_4\cdot CHO$$

analogous to that ascribed by Sonn and Benirschke (*Ber.*, 1921, **54**, 1731) to the compound obtained by condensing 6-aminopiperonal and acetaldehyde by means of dilute alkali.

Heller (*Ber.*, 1910, **43**, 1917) describes a synthesis of 3-methylquinoline from *o*-nitrobenzaldehyde and propaldehyde in which an excess of bisulphite solution is used as condensing agent and the intermediate aldol compound is reduced to the quinoline base by means of zinc dust and acetic acid. A modification of this method using piperidine instead of bisulphite as the condensing agent was found to be most suitable for the preparation of 3-methylquinoline and its substituted derivatives. In two cases, however, it was found preferable to form the styryl derivative by treatment of the aldol with acetic anhydride (compare Borsche and Quast, *Ber.*, 1919, **52**, 432) and reduce this with stannous chloride and hydrochloric acid. The substituted bases, which were only obtained in relatively poor yield, could usually be isolated as crystalline solids. They decompose rapidly to red oils on exposure to air, form characteristic quaternary salts, and, with the exception of 6:7-dimethoxy-3-methylquinoline, are volatile in steam. The dilute aqueous solutions of the hydrochlorides of these bases exhibit a characteristic bluish-green fluorescence.

EXPERIMENTAL.

β-o-*Nitrophenyl-α-methylhydracrylaldehyde*.—The deep red solution obtained by keeping an alcoholic solution of *o*-nitrobenzaldehyde

(1 mol.), propaldehyde ($1\frac{1}{2}$ mols.), and a few drops of piperidine for 5 days at room temperature was diluted with water. The aldol, isolated by means of ether and purified in alcoholic solution by charcoal, was obtained (yield, 80%) as a clear yellow syrup which showed no tendency to crystallise and could not be distilled under reduced pressure without decomposition (compare Heller, *loc. cit.*) (Found : C, 57·3; H, 5·9; N, 6·7. Calc. for $C_{10}H_{11}O_4N$: C, 57·4; H, 5·3; N, 6·7%).

3-Methylquinoline was obtained by reducing β-*o*-nitrophenyl-α-methylhydracrylaldehyde with zinc dust and acetic acid in the way described by Heller (yield, 25% calc. on the nitrobenzaldehyde).* The chloroplatinate crystallises in orange-red needles, m. p. 249° (compare Miller and Kinkelin, *Ber.*, 1887, **20**, 1917) [Found : Pt, 26·8; H_2O, 5·0. Calc. for $(C_{10}H_9N)_2,H_2PtCl_6,2H_2O$: Pt, 26·7; H_2O, 4·9%]. The *ethiodide* crystallises from absolute alcohol in yellow plates, m. p. 220° (decomp.) (Found : I, 43·2. $C_{12}H_{14}NI$ requires I, 42·4%). The *silver nitrate* double salt crystallises from alcohol in lustrous, silvery plates, m. p. 180°. The *dichromate* crystallises from hot water in red prisms, m. p. 134°.

6 : 7-*Methylenedioxy*-3-*methylquinoline*.—A solution of 6-nitropiperonal (35 g.), propaldehyde (20 g.), and piperidine (2 c.c.) in 70% alcohol (2 l.) having been kept for 5 days at room temperature, the alcohol was distilled off and the resultant heavy red oil, presumably β-6-nitro-3 : 4-methylenedioxyphenyl-α-methylhydracrylaldehyde, reduced as previously described. The mixture was made alkaline and the base distilled in steam. The green, milky distillate slowly deposited 6 : 7-*methylenedioxy*-3-*methylquinoline* in long, colourless needles (+ $2H_2O$), m. p. 74°, which, when dried over sulphuric acid, crumbled to a fine, white powder, the anhydrous base melting at 105—106° (yield, 18% calc. on 6-nitropiperonal) (Found for the hydrated base: H_2O, 16·0. $C_{11}H_9O_2N,2H_2O$ requires H_2O, 16·1%. Found for the anhydrous base: C, 70·4; H, 4·8; N, 7·5. $C_{11}H_9O_2N$ requires C, 70·6; H, 4·8; N, 7·5%). The *chloroplatinate* crystallises from water in orange-yellow plates [Found : Pt, 24·7. $(C_{11}H_9O_2N)_2,H_2PtCl_6$ requires Pt, 24·9%]. The *chloroaurate* separates from dilute hydrochloric acid in golden-yellow needles (Found : Au, 37·3. $C_{11}H_9O_2N,HAuCl_4$ requires Au, 37·4%). The *picrate* forms yellow needles, m. p. 259°. The *methiodide*, prepared by refluxing equimolecular proportions of the base and methyl iodide in anhydrous benzene, crystallises from

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* It has since been found that by reducing this substance with stannous chloride and hydrochloric acid in the way described in the preparation of 6 : 7-dimethoxy-3-methylquinoline the yield of 3-methylquinoline can be increased to 80%.

absolute alcohol in yellow needles, m. p. 240° (Found: I, 38·6. $C_{12}H_{12}O_2NI$ requires I, 38·5%). The *ethiodide* forms yellow needles, m. p. 195°.

β-6-*Nitro*-3 : 4-*dimethoxyphenyl*-α-*methylhydracrylaldehyde* can be obtained in extremely poor yield from 6-nitroveratraldehyde by the method previously described. By using an excess of propaldehyde and no other solvent, however, the aldol is obtained, in 30% yield, as a pale brown syrup with a characteristic odour. Its alcoholic solution exhibits a strong green fluorescence.

6-*Nitro*-3 : 4-*dimethoxy*-α-*methylcinnamaldehyde*.—The preceding aldol (5 g.) was boiled with acetic anhydride (25 g.) under reflux for 3 hours and the cooled, dark brown solution was poured into excess of dilute sodium hydroxide solution, cooled with ice. The brown solid which slowly separated crystallised from benzene in yellow needles, m. p. 165—166° (Found: C, 57·3; H, 5·1. $C_{12}H_{13}O_5N$ requires C, 57·4; H, 5·2%).

6 : 7-*Dimethoxy*-3-*methylquinoline* can be obtained in very poor yield by direct reduction of the aldol compound with zinc dust and acetic acid. A more satisfactory method is as follows: 6-Nitro-3 : 4-dimethoxy-α-methylcinnamaldehyde (2 g.) was added slowly to a boiling solution of stannous chloride (20 g.) in concentrated hydrochloric acid (50 c.c.). The cooled, dark red solution was made alkaline, and the base extracted with ether. The ethereal solution was shaken with dilute hydrochloric acid (traces of tarry matter, which increase greatly if the initial material is not pure, are retained by the ether), and the base, after being liberated, was again dissolved in ether and dried over anhydrous sodium sulphate; the ethereal solution was then saturated at 0° with dry hydrogen chloride. The precipitated *hydrochloride* crystallised from alcohol in small, colourless needles, m. p. 220—223° (decomp.) (Found: Cl, 14·9. $C_{12}H_{13}O_2N,HCl$ requires Cl, 14·8%). The base, which rapidly decomposes to a dark brown oil on exposure to air, crystallises from ether in long, colourless needles, m. p. 81—83°. The *methiodide* forms pale yellow needles, m. p. 245° (decomp.).

6-*Nitro*-3-*methoxy*-α-*methylcinnamaldehyde*.— 6-Nitro-3-methoxybenzaldehyde (Heilbron, Kitchen, Parkes, and Sutton, J., 1925, **127**, 2172), treated with propaldehyde and piperidine by the method for the preparation of β-6-nitro-3 : 4-dimethoxyphenyl-α-methylhydracrylaldehyde, gave a golden-yellow oil, presumably β-3-methoxyphenyl-α-methylhydracrylaldehyde. This was converted, by means of acetic anhydride, into the *cinnamaldehyde*, which crystallised from benzene in pale yellow plates, m. p. 115—116° (Found: C, 60·0; H, 5·1. $C_{11}H_{11}O_4N$ requires C, 59·7; H, 5·0%).

6-*Methoxy*-3-*methylquinoline*.—The above aldehyde was reduced with stannous chloride and concentrated hydrochloric acid and the reaction mixture was made alkaline and distilled in steam. The distillate was extracted with ether, and the *hydrochloride* precipitated from the dried ethereal solution. It crystallised from alcohol in colourless plates, m. p. 213—215° (Found : Cl, 16·7. $C_{11}H_{11}ON,HCl$ requires Cl, 16·9%). Attempts to isolate the base produced a colourless oil which could not be crystallised and rapidly developed a red colour on exposure to air. The *methiodide* crystallises from methyl alcohol in yellow needles, m. p. 280—283° (decomp.) (Found : I, 39·9. $C_{12}H_{11}ONI$ requires I, 40·3%). The *chloroplatinate* forms golden needles [Found : Pt, 25·5. $(C_{11}H_{11}ON)_2,H_2PtCl_6$ requires Pt, 25·8%].

The authors desire to thank Professor I. M. Heilbron, D.S.O., D.Sc., for his interest in this work and his valuable advice. They are also indebted to the Advisory Council of the Department of Scientific and Industrial Research and to the Trustees of the late Professor Campbell Brown for grants which enabled the work to be carried out.

THE UNIVERSITY, LIVERPOOL. [*Received, July* 16*th*, 1926.]