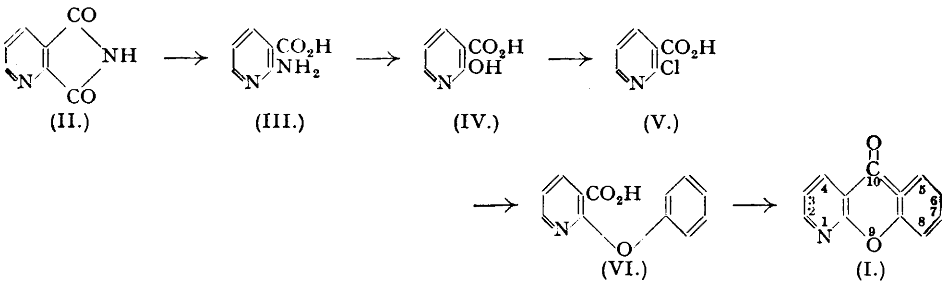
164. *Xanthones and Thioxanthones. Part III. The Synthesis of 9-Oxa-1-aza-anthrone (4-Azaxanthone).*

By Frederick G. Mann and J. Hedley Turnbull.

The synthesis of 9-oxa-1-aza-anthrone is described as part of a general investigation of the various isomeric aza-derivatives of xanthone and thioxanthone.

The replacement of one of the benzene rings in xanthone by a pyridine ring can theoretically give rise to four isomeric aza-9-oxa-anthrones. These novel heterocyclic systems may prove of considerable chemical and therapeutic interest, and we are now investigating their syntheses and properties. The present communication records briefly the synthesis of one of these compounds, namely 9-oxa-1-aza-anthrone (4-azaxanthone) (I).

2-Aminonicotinic acid (III) was prepared by Sucharda's method (*Ber.*, 1925, **58**, 1728), 8-hydroxyquinoline being converted into quinolinimide (II). This imide, when subjected to the Hofmann reaction, gave a mixture of 2-aminonicotinic acid (III) and 3-aminopicolinic acid. The former could be readily isolated by virtue of its lower solubility, and on treatment with nitrous acid gave 2-hydroxynicotinic acid (IV) (Philips, *Annalen*, 1895, **288**, 253) which in turn, with phosphorus pentachloride, yielded 2-chloronicotinic acid (V) (Wiedel and Strache, *Monatsh.*, 1886, **7**, 295). The sodium salt of this acid condensed with sodium phenoxide to give 2-phenoxynicotinic acid (VI), which on being heated with phosphorus oxychloride underwent cyclisation to (I); for success in the last two stages of this synthesis, however, very careful control of the conditions was essential. The oxa-aza-anthrone after sublimation formed fine, white needles, slightly soluble in water and readily soluble in strong mineral acids. Its pale yellow solution in concentrated sulphuric acid showed a faint green fluorescence.



EXPERIMENTAL.

2-*Aminonicotinic Acid* (III).—A solution of sodium hypochlorite (148 g.), prepared by passing chlorine (11·4 g.) into a mixture of sodium hydroxide (14·7 g.), water (27 c.c.), and ice (95 g.), was added to a solution of the imide (II) (23 g.) in cold 10% aqueous sodium hydroxide solution. The mixture was warmed to 80°, maintained at that temperature for 30 minutes, cooled, and acidified with 50% sulphuric acid (90 g.) and glacial acetic acid (*ca.* 5 c.c.); the aminonicotinic acid (5·7 g.) separated, and was recrystallised from water forming glistening pale-yellow plates (4 g.), m. p. 293° (decomp.). Philips (*loc. cit.*) records m. p. 310° (decomp.). The mother-liquors from the acidification contained 3-aminopicolinic acid which could be isolated as the copper salt (Sucharda, *loc. cit.*).

2-*Hydroxynicotinic Acid* (IV).—2-Aminonicotinic acid (4 g.) was dissolved in hot 10% sulphuric acid (32 c.c.), water (120 c.c.) added, and a solution of sodium nitrite (2 g.) in water (20 c.c.) run in at 40—50°. The clear solution was heated at 100° for 30 minutes and then cooled; the hydroxy-acid separated in long, white needles (2·5 g.), m. p. 255°.

2-*Chloronicotinic Acid* (V).—A mixture of the hydroxy-acid (1·0 g.), phosphorus oxychloride (0·5 c.c.), and phosphorus pentachloride (2·5 g.) was heated gradually to 140—145°. The clear melt was maintained at 140° for 10 minutes, cooled, and poured into ice-water, and the precipitated solid recrystallised from hot water giving pale yellow plates of the chloro-acid (V) (0·8 g.), m. p. 189° (decomp.). Wiedel and Strache (*loc. cit.*) record m. p. 193°.

2-*Phenoxynicotinic Acid* (VI).—2-Chloronicotinic acid (0·5 g.) and phenol (1 g.) were added in turn to methanol (4 c.c.) in which sodium (0·15 g.) had previously been dissolved. The mixture was evaporated to dryness at 100°, and the residue slowly heated to 170°, whereupon the mass melted and effervesced. The melt was cooled, dissolved in water, and extracted with ether, and the aqueous solution acidified with acetic acid. The phenoxynicotinic acid separated as a white solid (0·53 g.), m. p. 177—179°, which separated from dilute acetic acid in slender crystals, m. p. 179—180°, which were completely soluble in sodium hydrogen carbonate solution (Found: C, 67·1; H, 4·3; N, 6·8. $C_{12}H_9O_3N$ requires C, 67·0; H, 4·2; N, 6·5%).

9-*Oxa*-1-*aza-anthrone* (I).—A mixture of (VI) (100 mg.) and phosphorus oxychloride (2 c.c.) was heated under reflux for 30 minutes. The green solution was cooled and diluted with petroleum (b. p. 40—60°), and the precipitated solid collected, washed with water, dried (20 mg.), and sublimed at 170°/0·5 mm. The *oxa-aza-anthrone* was obtained as a white sublimate (15 mg.) which crystallised from dilute acetic acid in hair-like white needles, m. p. 182—183° (Found: C, 73·4; H, 3·7; N, 7·3. $C_{12}H_7O_2N$ requires C, 73·1; H, 3·6; N, 7·1%). The low solubility of this compound in cold dilute acetic acid indicates that it has only weakly basic properties.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE.
[*Received, October 21st*, 1950.]