A Novel Direct Synthesis of the *N*-Oxides of Quinoline Derivatives

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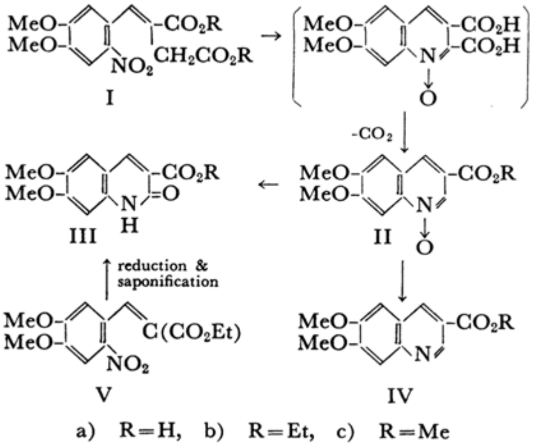
The *N*-oxides of quinoline compounds are usually obtained by the oxidation of corresponding quinoline derivatives. No synthesis resulting in the direct formation of the *N*-oxide of quinoline derivatives seems to have been recorded so far. Perhaps the only exception is the report of Loudon et al.[1] regarding the syntheses of some 1, 4-dihydro-1-hydroxy-4-oxoquinolines, which in their tautomeric form can be regarded as 4-hydroxyquinoline *N*-oxide derivatives.

We record below a novel quinoline synthesis, in which the nitro group of a benzene derivative interacts with the side chain in the ortho position, in the presence of a base, and results in the direct formation of the *N*-oxide of a quinoline derivative.



a) R=H, b) R=Et, c) R=Me

Veratraldehyde was condensed with ethyl succinate to obtain veratrylidenesuccinic acid,[2] m. p. 174—175°C, which on nitration gave *o*-nitroveratrylidenesuccinic acid[3] (Ia) as yellow needles, m. p. 214—415°C. Ia, on being warmed with 20% aqueous potassium hydroxide, gave an acid (m. p. 282—283°C decomp.) which was then purified by precipitation with acid from its sodium bicarbonate solution. The constitution of this acid was confirmed to be 6,7-dimethoxyquinoline-1-oxide-3-carboxylic acid (IIa), as it underwent the known rearrangement[4] of the *N*-oxides of quinoline to carbostyrils on being heated with acetic anhydride, and gave 2-hydroxy-6, 7-dimethoxyquinoline-3-carboxylic acid (IIIa) as yellow needles (m. p. 310°C decomp.), an acid which was identical (delete infrared spectrum and mixed melting point) with an authentic sample[5], synthesised through a previously-reported unambiguous route, involving the reduction of the intermediate (V) and its simultaneous cyclisation, followed by the saponification of the resulting ester. IIIa obtained by either of the routes, on sublimation in vacuo, decarboxylated to the same 6, 7-dimethoxycarbostyril (III, H for CO_2R) (m. p. 232—234°C); the two samples had identical infrared spectra, and their melting point and mixed melting point were the same. On esterification, 6, 7-dimethoxyquinoline-1-oxide-3-carboxylic acid (IIa) gave the ethyl ester (IIb), as white needles (m. p. 214—215°C) and the methyl ester (IIc), as white needles (m. p. 211—212°C). The ethyl ester, on deoxygenation[6] with PCl_3, gave ethyl 6, 7-dimethoxyquinoline-3-carboxylate (IVb) as white needles, m. p. 140—141°C; on saponification this gave 6, 7-dimethoxyquinoline-3-carboxylic acid (IVa), as white micro-needles (m. p. 267—268°C). All the compounds reported above gave satisfactory C, H and N analyses.

Similar work in an analogous series has been completed; it will be described in detail in a subsequent publication.

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