160. *The Nitration Product of* 3 : 4-*Dihydro*-4-*methyl*-3-*oxo*-4 : 7-*phenanthroline*.

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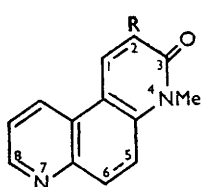
The mononitration product of 3 : 4-dihydro-4-methyl-3-oxo-4 : 7-phenanthroline is shown by various evidence, including unequivocal synthesis of the chloro-analogue, to be the unexpected 2-nitro-compound; hence this phenanthroline undergoes nitration as a cinnamic lactam.

The base 4 : 7-phenanthroline is not nitrated [1] by treatment with a mixture of fuming nitric acid and concentrated sulphuric acid at 100° but its dihydro-*N*-methyl-oxo-derivative (I; R = H) is converted thereby [2] into a mononitro-compound (*A*). Kaufmann and Radošević [2] reasoned from the 6-nitration [3] (quinoline numbering) of *N*-methylcarbostyril that (*A*) has the nitro-group in a *Bz*-position, probably 5 (phenanthroline numbering); a *Bz*-substitution would accord, also, with the proved 6-nitrations [4] (phenanthroline numbering) of 3-phenyl-4 : 7-phenanthroline and its 1-carboxylic acid derivative. However, it has been shown [5] that the amino-compound obtained by reducing the nitration product (*A*) is neither 5- nor 6-amino-3 : 4-dihydro-4-methyl-3-oxo-4 : 7-phenanthroline, and the work described here indicates which of the five available *Pyr*-positions is occupied by the substituent group.



(I)

[1] Haworth and Sykes, *J.*, 1944, 311.
[2] Kaufmann and Radošević, *Ber.*, 1909, **42**, 2612.
[3] Decker, *J. prakt. Chem.*, 1901, **64**, 85.
[4] Willgerodt and Jablonski, *Ber.*, 1900, **33**, 2918.
[5] Sykes, *J.*, 1953, 3543.

Oxidising the nitro-compound (*A*) with hot aqueous potassium permanganate gave quinolinic acid (in small yield). The same product was similarly obtained from the chloro-analogue (*B*), which was prepared by carrying out a Sandmeyer reaction on the amino-compound derived from (*A*) by reduction with ammonium sulphide.[5] An 8-, 9-, or 10-substituted compound would have been degraded to a substituted quinolinic or nicotinic acid, and the above finding therefore excluded further consideration of the three substituent positions in the unmodified pyridine ring; one of them (8) was also eliminated by the fact that the chloro-compound (*B*) is not identical with the 8-chloro-3 : 4-dihydro-4-methyl-3-oxo-4 : 7-phenanthroline prepared independently.[6] Evidence distinguishing between the remaining possibilities of 1- and 2-substitution was sought from the synthesis of a 2-substituted comparison compound as follows:

6-Nitroquinoline was converted by sulphur dichloride at 100° into its 3-chloro-derivative which was identified by degrading it to 3-chloroquinoline by way of the 6-amino-compound. (3-Chloroquinoline for comparison was prepared from 3-aminoquinoline by a Sandmeyer reaction; it had previously been prepared by chlorination of quinoline.[7]) The methiodide of 6-acetamido-3-chloroquinoline was converted by a Skraup reaction, into another quaternary salt which was isolated as the iodide and on oxidation with ferricyanide gave the compound (*B*), which must therefore have formula (I; R = Cl); and it follows that compound (*A*) is 3 : 4-dihydro-4-methyl-2-nitro-3-oxo-4 : 7-phenanthroline (I; R = NO_2).

The 2-nitration of the phenanthroline (I; R = H) by a reagent which provides oxides of nitrogen resembles nitration of certain unsaturated hydrocarbons,[8] which was invoked by Dewar and Maitlis [9] to account for the 3-nitration of quinoline by way of a postulated 1 : 2-adduct. It has a closer parallel in the α-nitration [10,11] of ethyl 3- and 4-nitrocinnamate. Further, 6-nitrocoumarin, a cinnamic lactone analogous to (I; R = H), is nitrated [12] in the corresponding position 3, and *N*-methyl-6-nitrocarbostyril, the equivalent lactam, is nitrated at both position 8 and a *Pyr*-position (unidentified).[13] Thus, cinnamic acid derivatives in which the benzene ring is suitably inactivated are nitrated in the side-chain, commonly, if not invariably, in the α-position; by conforming to this pattern, compound (I; R = H) manifests its character as a " pyridocinnamic lactam."

Experimental

Degradation of Kaufmann and Radošević's Nitro-compound.—The nitro-compound [2] (1 g.) was refluxed with potassium permanganate (7 g.) in water (200 c.c.) until all the permanganate had disappeared (several hours). The precipitated manganese dioxide was filtered off and the filtrate together with hot-water washings was concentrated to small volume and acidified with acetic acid. Copper acetate solution was added, and the blue deposit which was formed very slowly was suspended in hot water and freed from copper with hydrogen sulphide. The crystalline residue (0·1 g.) which remained when the filtrate was evaporated to dryness recrystallised from water as colourless prisms, m. p. about 220° after a transition at about 185°. Quinolinic acid decomposes at about 190°, depending on the rate of heating, to nicotinic acid which has m. p. 232°.

A batch of crude degradation product was heated to its decomposition point (carbon dioxide evolved; lime-water test). The residue crystallised from alcohol (charcoal) as colourless needles, m. p. 231° with previous softening, alone and in admixture with authentic nicotinic acid (m. p. 232°).

[6] Sykes, *J.*, 1956, 3087.
[7] Edinger and Lubberger, *J. prakt. Chem.*, 1896, **54**, 340.
[8] Hückel, " Theoretical Principles of Organic Chemistry," Elsevier, Amsterdam, 1955, Vol. I, pp. 750, 751.
[9] Dewar and Maitlis, *J.*, 1957, 944.
[10] Friedländer and Lazarus, *Annalen*, 1885, **229**, 233.
[11] Friedländer and Mähly, *ibid.*, p. 210.
[12] Clayton, *J.*, 1910, 1388.
[13] Kaufmann and de Petherd, *Ber.*, 1917, **50**, 342.

3-*Chloro*-6-*nitroquinoline*.—6-Nitroquinoline (4 g.) was heated with sulphur dichloride (10 c.c.) in a sealed tube at 100° for 4 hr. The solid product was washed free from sulphur chlorides with ether, then dissolved in hot, dilute hydrochloric acid and precipitated with aqueous ammonia from the filtered solution. The *chloronitroquinoline* crystallised slowly from alcohol (charcoal) as almost colourless prismatic needles (2 g.), m. p. 145° (Found: C, 51·9; H, 2·7; Cl, 16·9. $C_9H_5O_2N_2Cl$ requires C, 51·8; H, 2·4; Cl, 17·0%). Bachmann and Cooper [14] give m. p. 145° (corr.) for a chloro-6-nitroquinoline which they suggest might be the 3-chloro-compound.

6-*Amino*-3-*chloroquinoline*.—3-Chloro-6-nitroquinoline (4 g.) was reduced with aqueous ammonium sulphide as described [6] for reduction of 6-nitroquinoline. The mixture was decomposed with hydrochloric acid, filtered, and made alkaline with aqueous ammonia; the precipitated *aminochloroquinoline* (2·6 g.) crystallised from chlorobenzene as yellow prismatic needles, m. p. 170—171° (Found: C, 60·0; H, 4·0. $C_9H_7N_2Cl$ requires C, 60·5; H, 4·0%).

The *acetyl* derivative, obtained in excellent yield by heating the amine in glacial acetic acid with excess of acetic anhydride for 10 min., crystallised from alcohol as colourless prisms, m. p. 213—214° (Found: C, 59·4; H, 4·3. $C_{11}H_9ON_2Cl$ requires C, 59·9; H, 4·1%).

Evidence for 3-*Chlorination of* 6-*Nitroquinoline*.—6-Amino-3-chloroquinoline (1·2 g.) was diazotised and reduced with ethanol as described [15] for the 8-amino-isomer. A yellowish oil was obtained by steam-distilling the basified reaction mixture; it formed a picrate (0·6 g.), yellow needles, m. p. 186—187°, from alcohol. Baker *et al.*[15] give m. p. 187—189°, and Meisenheimer [16] gives m. p. 182° for the picrate of 3-chloroquinoline obtained in both cases by chlorinating quinoline with sulphur dichloride.[7] The structure of this presumed 3-chloro-derivative has not been satisfactorily proved, because the degradation product claimed [7] to be 5-chloronicotinic acid cannot in fact be this acid; [17] the analytical results quoted for the product do not agree with the requirements for a chloroquinolinic acid. On the other hand, although the b. p. (255°/743 mm.) is not sharply differentiated from those of the other monochloroquinolines (b. p.s of all seven fall within the range 255—290°), the m. p. of the picrate is well removed at least from those of 2- and 4-chloroquinoline picrate. We were unable to obtain a sample of 3-chloroquinoline of satisfactory purity by Edinger and Lubberger's [7] method on a reduced scale, but prepared the compound by a Sandmeyer reaction from 3-aminoquinoline (crude yield 1 g. from 5 g.). A chief fraction, b. p. 259°/770 mm. (Found: Cl, 21·1. Calc. for C_9H_6NCl: Cl, 21·7%), distilled from several combined preparations, formed a picrate, m. p. 186—187° not depressed by admixture with the first-mentioned picrate, above.

6-*Acetamido*-3-*chloro*-1-*methylquinolinium Iodide*.—6-Acetamido-3-chloroquinoline (2 g.) was heated in a sealed tube with an excess of methyl iodide in methanol for 30 min. at 100°; the yellow *methiodide* (3 g.) crystallised from water (charcoal) as needles, m. p. (decomp.) about 250° with previous darkening (Found: I, 35·0. $C_{12}H_{12}ON_2ClI$ requires I, 35·0%).

2-*Chloro*-4-*methyl*-4 : 7-*phenanthrolinium Iodide*.—6-Acetamido-3-chloroquinoline methiodide (4 g.) was subjected to a Skraup reaction in the conditions described [5] for the 8-chloro-isomer, and the *chlorophenanthroline methiodide* (1·6 g.) was isolated by adding potassium iodide solution to the diluted, nearly neutralised reaction mixture. The new methiodide crystallised from water (charcoal) as orange prisms which darkened and softened above 240° and decomposed at about 260° (Found: I, 35·6. $C_{13}H_{10}N_2ClI$ requires I, 35·6%).

2-*Chloro*-3 : 4-*dihydro*-4-*methyl*-3-*oxo*-4 : 7-*phenanthroline*.—(*a*) The preceding methiodide (1·0 g.) was oxidised with potassium ferricyanide in alkaline solution. The *dihydro*-N-*methyl*-*oxo*-*compound* (0·6 g.) was precipitated promptly when the reagents were mixed, and was purified by way of the sulphate which crystallised on cooling of a solution of the base in hot, dilute sulphuric acid (charcoal); it crystallised from chlorobenzene as almost colourless needles, m. p. 240° (Found: C, 63·5; H, 3·8; Cl, 14·8. $C_{13}H_9ON_2Cl$ requires C, 63·8; H, 3·7; Cl, 14·5%).

(*b*) Kaufmann and Radošević's amino-compound [2,5] (4·5 g.) in hot, concentrated hydrochloric acid was cooled in ice, to produce a finely crystalline suspension of the hydrochloride, and sodium nitrite (1·5 g.) in water was added gradually with vigorous shaking between additions. The deep red diazotised solution was added gradually to cuprous chloride (2 g.) in concentrated hydrochloric acid (20 c.c.) at 0° (copious frothing) and the mixture was set aside for ½ hr. A

[14] Bachmann and Cooper, *J. Org. Chem.*, 1944, **9**, 302.
[15] Baker, Albisetti, Dodson, Lappin, and Riegel, *J. Amer. Chem. Soc.*, 1946, **68**, 1532.
[16] Meisenheimer, *Ber.*, 1926, **59**, 1848.
[17] von Pechmann and Mills, *Ber.*, 1904, **37**, 3829.

hot, aqueous solution (charcoal) of the precipitated hydrochloride was decomposed with aqueous ammonia; the precipitated base (3 g.), crystallised from chlorobenzene, had m. p. 241°, unchanged by admixture with the above dihydro-*N*-methyl-oxo-compound.

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