290. *The Nitration of Some Simple Heterocyclic Nitrogen Compounds.*

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The qualitative nitration of 4-methylcinnoline, 4-hydroxyquinoline, and 1-methyl-4-cinnolone is described, and previous work on the nitration of quinazoline is confirmed. These and other qualitative results are discussed in the light of current views on modes of nitration.

Before a comprehensive application of electronic theory to the problem of substitution in heterocyclic systems can be made, especially in quantitative terms such as have been developed for benzene derivatives by Ingold and his school, it is necessary to examine to what extent qualitative regularities exist in this field. Many isolated observations have been recorded relating to such problems as the nitration of heterocyclic systems, but the stress has usually been on the synthesis of new compounds, and not on the comparative chemistry of different heterocyclic systems, even in the qualitative way which concerns us here. This being so, we have examined the nitration of some simple compounds of the triple series, quinolines, quinazolines, cinnolines. Some of the results have already been outlined (Schofield and Swain, *Nature*, 1948, **161**, 690), and in the present communication we supply the essential details and some extensions of the work.

Before our work was complete, Elderfield and his collaborators (*J. Org. Chem.*, 1947, **12**, 405) reported that 6-nitroquinazoline was the main product (56%) of nitration of quinazoline in sulphuric acid; our experiments confirm this. Before the work of Elderfield and his associates (*loc. cit.*) the only practicable route to quinazoline derivatives unsubstituted in the hetero-ring was that of Riedel (G.P. 174941; cf. Bogert and McColm, *J. Amer. Chem. Soc.*, 1927, **49**, 2650, and Reynolds and Robinson, *J.*, 1936, 196). By this method 5-chloro-2-nitrobenzaldehyde gave 5-*chloro*-2-*nitrobenzylidenebisformamide* and thence, by reduction, 6-*chloroquinazoline* in high yield. The same chloro-compound was obtained by a Sandmeyer reaction with the 6-aminoquinazoline resulting from the reduction of the major nitration product of quinazoline (see above). No homogeneous product could be isolated when quinazoline was nitrated with lithium nitrate (cf. 7-nitroquinoline; Bacharach, *Rec. Trav. chim.*, 1933, **52**, 413).

According to most of the available analogies, 4-methylcinnoline should nitrate in the same sense as cinnoline itself. Thus, quinoline (see, among others, Curd, Graham, Richardson, and Rose, *J.*, 1947, 1613) and quinaldine (Doebner and von Miller, *Ber.*, 1884, **17**, 1700; Decker and Remfrey, *Ber.*, 1905, **38**, 2773; Hammick, *J.*, 1926, 1302) give mixtures of the 5- and 8-derivatives, the latter predominating slightly, whilst from lepidine the major product is 8-nitrolepidine (Busch and Koenigs, *Ber.*, 1890, **23**, 2687; Johnson and Hamilton, *J. Amer. Chem. Soc.*, 1941, **63**, 2864) and a minor product, possibly the 5-isomer, has also been isolated (Buchman *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 380). The 4-methyl group thus appears to exert a steric effect, and this weight of analogy led us to expect 4-methylcinnoline to yield mainly 8-nitro-4-methylcinnoline. Thus, we nitrated 4-methylcinnoline as a prelude to cinnoline itself; under conditions similar to those used for lepidine (Johnson and Hamilton, *loc. cit.*) the only product so far isolated (50%) is 8-*nitro*-4-*methylcinnoline*; this was reduced to the *amine* and converted thence into 8-*chloro*-4-*methylcinnoline*, m. p. 126—127°; this last compound depressed the melting point of 6-chloro-, m. p. 136—137°, and 7-chloro-4-methylcinnoline, m. p. 119—120° (Atkinson and Simpson, *J.*, 1947, 808), and its structure was proved by synthesis. 3-Chloro-2-aminoacetophenone (Simpson *et al.*, *J.*, 1945, 646) with methylmagnesium iodide gave an oily compound (the carbinol or a mixture thereof with the olefin), yielding, on dehydration, the oily olefin, which was characterised as 2-(3′-*chloro*-2′-*acetamidophenyl*)*prop*-1-*ene* and converted by diazotisation into 8-chloro-4-methylcinnoline identical with the compound described above.

Attempted nitration of 4-methylquinazoline has not so far yielded homogeneous material under a variety of conditions. This problem is still being examined. 4-Methylquinazoline was originally prepared by hydrolysis and decarboxylation of 4-methylquinazoline-2-carboxyamide

(Bogert and Nabenhauer, *J. Amer. Chem. Soc.*, 1924, **46**, 1932). We now find that treatment of *o*-formamidoacetophenone (Camps, *Ber.*, 1901, **34**, 2703; contrast Bischler, *Ber.*, 1893, **26**, 1352) with ammonia under pressure gives 4-methylquinazoline in good yield.

The nitration of 4-hydroxyquinoline in sulphuric acid was recently stated to give about 50% of 3-nitro-4-hydroxyquinoline (Mosher *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 303). This was unexpected in view of the behaviour of the closely related 4-hydroxyquinazoline (Bogert and Geiger, *J. Amer. Chem. Soc.*, 1912, **34**, 524; Morley and Simpson, *J.*, 1948, 360) and 4-hydroxycinnoline (Schofield and Simpson, *J.*, 1945, 512; Simpson, *J.*, 1947, 237). In fact, the compound, m. p. 144—145°, described by Mosher *et al.* as 4-chloro-3-nitroquinoline, strongly depresses the melting point of authentic 4-chloro-3-nitroquinoline, m. p. 121—122° (Bachman *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 365), and the two compounds differ considerably in stability: 4-chloro-3-nitroquinoline is very readily hydrolysed, *e.g.*, during attempted crystallisation from methanol, whilst the chloro-compound, m. p. 144—145°, survives such crystallisation. The derived 4-phenoxy-compounds were also different, *3-nitro-4-phenoxyquinoline*, m. p. 108—109°, strongly depressing the melting point (117—118°) of the phenoxy-derivative of the nitration product. On the other hand, 4-chloro-6-nitroquinoline, m. p. 144—145° (Riegel *et al.*, *J. Amer. Chem. Soc.*, 1946, **68**, 1264, 1267), and *6-nitro-4-phenoxyquinoline*, m. p. 117—118°, were identical with the corresponding derivatives of Mosher's nitration product.

The nitrations discussed above, and those of 4-hydroxyquinazoline and 4-hydroxycinnoline mentioned, were effected in sulphuric acid. Under similar conditions 4-hydroxyquinaldine also yields its 6-nitro-derivative (Kermack and Weatherhead, *J.*, 1939, 563), but, when the nitration is conducted in nitric acid at about 100°, the product is 3-nitro-4-hydroxyquinaldine (Conrad and Limpach, *Ber.*, 1887, **20**, 950; Halcrow and Kermack, *J.*, 1945, 415). Accordingly, we nitrated 4-hydroxyquinoline under the latter conditions, and from the total nitration product (obtained in 62% yield) the only homogeneous compound which we could characterise was 3-nitro-4-hydroxyquinoline (comprising 65% of the nitration product), isolated as its 4-chloro- and 4-phenoxy-derivatives.

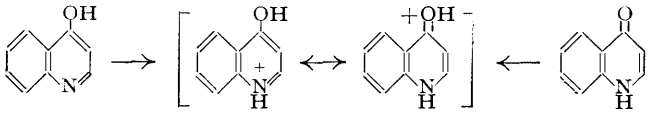
The qualitative evidence now available permits the distinguishing of two groups of compound among quinolines, quinazolines, and cinnolines, unsubstituted in the benz-ring, with regard to the direction of nitration:

(1*a*) α- and γ-Hydroxy-compounds, which are nitrated in sulphuric acid at C_6 or C_8 [4-hydroxyquinoline, 4-hydroxyquinazoline, 4-hydroxycinnoline, 4-hydroxyquinaldine, 2-hydroxylepidine (Balaban, *J.*, 1930, 2346), carbostyril(Friedlander and Lazarus, *Annalen*, 1885, **229**, 233; Decker, *J. pr. Chem.*, 1901, **64**, 85)]. (1*b*) Similar compounds, which are nitrated in the absence of sulphuric acid at the 3-position [4-hydroxyquinoline, 4-hydroxyquinaldine, 2 : 4-dihydroxyquinoline (Gabriel, *Ber.*, 1918, **51**, 1500. But see Ashley, Perkin and Robinson, *J.*, 1930, 382)].

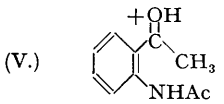
(2*a*) Unsubstituted heterocyclic compounds, or those with one α- or γ-methyl or -chloro-group, which are nitrated at C_5 and/or C_8 by mixed acids [quinoline, *iso*quinoline (Claus and Hoffmann, *J. pr. Chem.*, 1893, ii, **47**, 253; Fortner, *Monatsh.*, 1893, **14**, 146; Le Fèvre and Le Fèvre, *J.*, 1935, 1470; Andersag, *Chem. Zentr.*, 1934, I, 3595), quinaldine, lepidine, 4-methylcinnoline, 2-chloroquinoline (Deinet and Lutz, *J. Amer. Chem. Soc.*, 1946, **68**, 1325), 3-chloroquinoline (Baker *et al.*, *ibid.*, p. 1532), 4-chloroquinoline (Mosher *et al.*, *loc. cit.*)]. (2*b*) Heterocyclic compounds with both α- and γ-positions substituted either by methyl or chloro-groups, or by one each of these, which are nitrated most readily at C_8 and somewhat less readily at C_5, but also to some extent at C_6 [2 : 4-dimethylquinoline (Price, Velzen and Guthrie, *J. Org. Chem.*, 1947, **12**, 203; Vaughan, *J. Amer. Chem. Soc.*, 1948, **70**, 2294), 2-chlorolepidine (Johnson and Hamilton, *loc. cit.*; Krahler and Burger, *J. Amer. Chem. Soc.*, 1942, **64**, 2417), 4-chloroquinaldine (Halcrow and Kermack, *loc. cit.*)].

In discussing these facts it is essential to decide precisely what entity is being nitrated in any case and also what is the true nitrating agent. With regard to the facts under (1*a*) there can be no doubt that the nitrating agent here is the nitronium ion NO_2^+ (Bennett, Brand, and Williams, *J.*, 1946, 869 *et seq.*; Hughes, Ingold, and Reed, *Nature*, 1946, **158**, 448; Halberstadt, Hughes, and Ingold, *ibid.*, p. 514; Bunton, Hughes, Minkoff, and Reed, *ibid.*, p. 514; Westheimer and Kharasch, *J. Amer. Chem. Soc.*, 1946, **68**, 1871). As to the nature of the molecule being nitrated it might seem that the old problem of the tautomerism of compounds of this type would be a complication, but, taking 4-hydroxyquinoline as an example, it is probable that protonisation of either (I) or (II) occurs, giving the resonance hybrid (III ⟷ IV), and it is presumably the hybrid which is nitrated under these circumstances. In (III ⟷ IV),

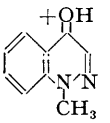
deactivation (with respect to an electrophilic reagent) occurs at C_5 and C_7, so that nitration is to be expected at C_6 and C_8. From another point of view the structure (IV) is seen to bear formal resemblance to protonated *o*-acetamidoacetophenone (V), which is known to give 5- and 3-nitro-2-acetamidoacetophenone when nitrated in sulphuric acid (Simpson *et al.*, *loc. cit.*), analogous to 6- and 8-nitro-4-hydroxyquinoline. Similar considerations apply to other compounds mentioned under (1*a*). In this connection we thought it of interest to nitrate 1-methyl-4-cinnolone (Schofield and Simpson, *loc. cit.*), in which the *p*-quinonoid structure (VI), similar to (IV), would be expected to exert a controlling influence; 8-nitro-1-methyl-4-cinnolone was the sole product (74%), identical with a specimen prepared from 8-nitro-4-hydroxycinnoline (Schofield



(I.) (III.) (IV.) (II.)



(V.)



(VI.)

and Theobald, unpublished). As to the reactions under (1*b*), it seems likely that nitric acid, although weaker than sulphuric acid (Hammett, " Physical Organic Chemistry," Chapter IX, New York, 1940), will still be strong enough to protonise the hydroxy-heterocyclic compounds (Bunton, Hughes, Minkoff, and Reed, *loc. cit.*, have made a similar point with regard to phenols), so that the different mode of substitution must be due to the substituting reagent. Nitration in this medium will still involve an electrophilic reagent (either nitronium or nitracidium ions; Halberstadt, Hughes, and Ingold, *loc. cit.*) which would again be expected to nitrate the molecule at C_6 or C_8 (with carbostyril ethers, 1-methyl-2-quinolone, etc., where nitration proceeds with relative ease, this is actually the case; Kaufmann and de Petherd, *Ber.*, 1917, **50**, 336), but the effect of nitrous acid may be important. With phenols in particular, the intervention of the latter can reverse completely the proportions of *o*- and *p*-isomers formed (Bunton *et al.*, *loc. cit.*). In connexion with this category of compounds it is noteworthy that 4-hydroxycinnoline yields 6-nitro- and a little 8-nitro-4-hydroxycinnoline when nitrated in sulphuric acid (Schofield and Simpson; Simpson, *locc. cit.*), but that in nitric acid at 50°, whilst the 6-nitro-compound is still the main product, an unidentified isomer is also produced in small amount. It is possible that the compound, which may be 3-nitro-4-hydroxycinnoline [it is not the 5- or 7-nitro-compound (Schofield and Theobald, unpublished)], would be formed in higher yield at higher temperatures; we are examining this point.

With regard to compounds grouped under (2) we have pointed out that the simple resonance picture is inadequate (Schofield and Swain, *loc. cit.*), as is also the semi-quantitative molecular-orbital model (Longuet-Higgins and Coulson, *Trans. Faraday Soc.*, 1947, **43**, 87). Recently, approximate calculations for quinazoline and cinnoline have appeared (Pullman, *Revue Scientifique*, 1948, **86**, 219) and it is interesting to notice that in the first case these lead us to expect electrophilic attack at C_6. With cinnoline the differences between the various positions in the benz-ring are small, and prediction would be difficult. It is becoming increasingly clear that the relative stabilities of the quinonoid transition complexes formed in these reactions may outweigh the initial distribution of electronic charge in determining the position of substitution (Waters, *J.*, 1948, 727). Quinazoline assumes special interest in this light, for perhaps here the *amphi*-quinonoid (C_2–C_6) form of the activated complex has particular importance, as is presumably the case with the compounds grouped under (2*b*). Waters (*loc. cit.*) stressed the importance of the oxidation–reduction potentials of relevant quinones for the present problem, and such measurements in the quinoline and *iso*quinoline fields support this view (Fieser and Martin, *J. Amer. Chem. Soc.*, 1935, **57**, 1840). We hope to make similar determinations in the quinazoline and cinnoline series.

Experimental.

(M. p.s are uncorrected.)

5-Chloro-2-nitrobenzylidenebisformamide.—5-Chloro-2-nitrobenzaldehyde (2 g.) (Mettler, *Ber.*, 1905, **38**, 2807) and formamide (10 c.c.) were treated with gaseous hydrogen chloride at 55°. Rapid dissolution occurred, heat was generated, and a solid quickly separated. The mixture was set aside for 2 hours, ethanol added (25 c.c.), and the product collected. Recrystallisation from boiling water gave 5-*chloro*-2-

nitrobenzylidenebisformamide as white needles, m. p. 206—207° (75%) (Found: C, 42·34; H, 3·4. $C_9H_8O_4N_3Cl$ requires C, 41·97; H, 3·1%).

6-*Chloroquinazoline*.—(*a*) 6-Aminoquinazoline (0·1 g.; Elderfield *et al.*, *J. Org. Chem.*, 1947, **12**, 405), in hydrochloric acid (2 c.c. of 5N.) was diazotised at 0° with 5% aqueous sodium nitrite, and the solution treated with cuprous chloride (from 0·20 g. of copper sulphate; *Org. Synth.*, Coll. Vol. II, p. 130). After 4 hours at room temperature the mixture was warmed to 80°, cooled, basified, and extracted with ether. Removal of the ether after drying (Na_2SO_4) gave a white solid (0·11 g.), m. p. 143° after crystallisation from ether–ligroin (b. p. 40—60°), identical with the compound described in (*b*).

(*b*) The benzylidenebisformamide (1·5 g.) and zinc dust (4·3 g.) were treated with glacial acetic acid (5·7 g.) and crushed ice (18 g.) during 10 minutes. The flask was shaken for ½ hour, and, after stirring for a further 1½ hours with addition of small amounts of zinc dust (1·5 g. in all), the mixture was filtered, basified with sodium hydroxide, and extracted with ether. Removal of the ether after drying (Na_2SO_4) gave 6-*chloroquinazoline*, which crystallised from ether–ligroin (b. p. 40—60°) or from water as white needles, m. p. 143° (84%) (Found: C, 58·35; H, 3·3. $C_8H_5N_2Cl$ requires C, 58·38; H, 3·1%).

Nitration of 4-*Methylcinnoline*.—4-Methylcinnoline (0·5 g.) in concentrated sulphuric acid (2 c.c.) at 0° was treated with 1 c.c. of a nitrating mixture [from 1·85 c.c. of nitric acid (*d* 1·5) and 8·15 c.c. of concentrated sulphuric acid], added with stirring during 5 minutes. Stirring was continued for ½ hour at 0° and 2 hours at room temperature, the solution poured on ice and basified with ammonia, and the product (0·47 g.) crystallised from methanol, giving 8-*nitro*-4-*methylcinnoline* (0·32 g.; 49%), m. p. 138—139° (decomp.) (Found: C, 57·03; H, 3·6. $C_9H_7O_2N_3$ requires C, 57·12; H, 3·7%). The compound is difficult to free from a brown discoloration, but, when this is achieved, it gives yellow plates from methanol.

8-*Amino*-4-*methylcinnoline*.—The nitro-compound (0·5 g.) in hydrochloric acid (10 c.c. of 6N.) was treated with stannous chloride (2·5 g.) in concentrated hydrochloric acid (2·5 c.c.) at 50° for 10 minutes, and the mixture cooled, basified with concentrated potassium hydroxide solution, and extracted with ether. Removal of the ether after drying (Na_2SO_4) gave a yellow solid (0·38 g.), which formed orange prisms of 8-*amino*-4-*methylcinnoline*, m. p. 126—127°, on crystallisation from ether–ligroin (b. p. 40—60°) (Found: C, 67·64; H, 5·8; N, 26·2. $C_9H_9N_3$ requires C, 67·89; H, 5·7; N, 26·3%).

2-*Nitro*-3-*aminoacetophenone*.—When hydrolysing 2-nitro-3-acetamidoacetophenone to the amine (cf. Leonard and Boyd, *J. Org. Chem.*, 1946, **11**, 409) it proved essential to stop the reaction as soon as the acetamido-compound had dissolved in the acid, otherwise tars were formed and the required amine could not be isolated.

2-(3′-*Chloro*-2′-*aminophenyl*)*propan*-2-*ol*.—3-Chloro-2-aminoacetephenone (3 g.; from the amine described above, by the method of Simpson *et al.*, *J.*, 1945, 646) in ether (50 c.c.) was added during 10 minutes to a stirred Grignard reagent (from 1·71 g. of magnesium, 10·02 g. of methyl iodide, and 100 c.c. of ether) at room temperature. The resulting suspension was stirred and refluxed for ¾ hour, decomposed with ice and ammonium chloride, and extracted with ether. Removal of the ether after drying (Na_2SO_4) gave a yellow oil (3·2 g.). No crystalline product could be prepared from this material with acetyl chloride–pyridine, acetic anhydride, or picric acid. With phenyl *iso*cyanate a white solid resulted, but was not examined further.

2-(3′-*Chloro*-2′-*aminophenyl*)*prop*-1-*ene*.—The above-named carbinol (3·1 g.), phosphoric oxide (6·2 g.), and benzene (50 c.c.) were heated under reflux for 3 hours, and the mixture decomposed with ice, basified with ammonia, and extracted with ether. Removal of the solvent after drying (Na_2SO_4) gave a yellow oil (2·7 g.). Treatment for 1 hour at 95° with acetic anhydride converted this into 2-(3′-*chloro*-2′-*acetamidophenyl*)*prop*-1-*ene*, which formed crisp, colourless prisms, m. p. 125—126°, from ether–ligroin (b. p. 40—60°) (Found: C, 62·88; H, 5·9. $C_{11}H_{12}ONCl$ requires C, 62·99; H, 5·8%).

8-*Chloro*-4-*methylcinnoline*.—(*a*) 8-Amino-4-methylcinnoline (0·2 g.) in hydrochloric acid (2 c.c. of 6N.) was diazotised at 0° with 5% aqueous sodium nitrite, and the solution treated dropwise with cuprous chloride solution (from 0·36 g. of copper sulphate). After 4 hours at room temperature the mixture was heated to 80°, cooled, basified, and extracted with ether. Removal of the solvent from the dried (Na_2SO_4) extract, and crystallisation of the residue (0·05 g.) from ligroin (b. p. 60—80°) gave a product, m. p. 126—127°, identical with that described in (*b*).

(*b*) The olefin described above (from 3·2 g. of carbinol) was dissolved in hydrochloric acid (16 c.c. of 2N- and 5 c.c. of concentrated acid) and diazotised at 0° with sodium nitrite (1·3 g. in 5 c.c. of water). When kept at room temperature, the solution became red and finally green. After 8 days, some tar had appeared, and addition of sodium hydroxide solution precipitated first more tar and then a grey solid. The latter was collected and, by extracting the tar with warm ether, a little more was obtained. The combined crops (1·44 g.) were extracted with ligroin (b. p. 60—80°) in a Soxhlet apparatus, a dark blue solid (0·37 g.; m. p. indefinite) remaining undissolved, and concentration of the extract gave a yellow solid (0·9 g.). Several crystallisations of this last from ligroin (b. p. 60—80°) gave yellow needles of 8-*chloro*-4-*methylcinnoline*, m. p. 126—127° (Found: C, 60·23; H, 4·1. $C_9H_7N_2Cl$ requires C, 60·50; H, 3·9%). The *picrate* formed stout green needles from ethanol; several crystallisations from ethanol served to decrease the intensity of the colour without removing it completely; the pure compound had m. p. 179—180° (decomp.) (Found: C, 44·86; H, 2·3. $C_{15}H_{10}O_7N_5Cl$ requires C, 44·20; H, 2·5%). The formation of strongly coloured impurities has been observed in other examples of this reaction (Atkinson and Simpson, *J.*, 1947, 808; Jacobs *et al.*, *J. Amer. Chem. Soc.*, 1946, **68**, 1310), and it is possible that the reported colours of 4-methylcinnoline picrates are due to impurities, since 8-chloro-4-methylcinnoline picrate prepared from material obtained by nitration appeared to be yellow although available quantities were too small fully to establish this point.

o-*Formamidoacetophenone*.—*o*-Aminoacetophenone (6 g.) was boiled under reflux for 10 minutes with anhydrous formic acid (8 g.), the solution poured into water, and the precipitate collected; the product (4·73 g.) had m. p. 77—78° (Camps, *Ber.*, 1901, **34**, 2703, gives m. p. 79°).

4-*Methylquinazoline*.—The formamido-compound (2 g.), aqueous ammonia (4 c.c.; *d* 0·880), and alcohol (10 c.c.) were heated in a sealed tube for 4 hours at 140°, and the solution concentrated, giving a pale brown oil which did not crystallise. Distillation gave 4-methylquinazoline (1·32 g., b. p.

126—128/12 mm.) which crystallised in the ice-chest. It was characterised as the picrate, m. p. 181·5—182° (Bogert and Nabenhauer, *J. Amer. Chem. Soc.*, 1924, **46**, 1932, give m. p. 183·5°) (Found : C, 48·5; H, 3·3. Calc. for $C_{15}H_{11}O_7N_5$: C, 48·3; H, 3·0%).

Nitration of 4-*Hydroxyquinoline.*—(*a*) Nitration under the conditions given by Mosher and his co-workers (*J. Amer. Chem. Soc.*, 1947, **69**, 303) proceeded as they describe. The derived chloro-nitroquinoline, m. p. 144—145°, was identical with 4-chloro-6-nitroquinoline, m. p. 144—145° (Riegel *et al.*, *J. Amer. Chem. Soc.*, 1946, **68**, 1264), and under the conditions described below gave 6-nitro-4-phenoxyquinoline, identical with the authentic compound.

(*b*) 4-Hydroxyquinoline (1 g.) in nitric acid (10 c.c.; *d* 1·42) was heated at 95° for 1 hour. Dilution of the solution with ice gave a yellow solid, m. p. (320) 326—328° (0·82 g.), which was boiled under reflux for 2 hours with phosphorus oxychloride (8 c.c.); the solution was decomposed with ice, neutralised with sodium acetate, and extracted with ether. Removal of the solvent after drying (Na_2SO_4) provided a yellow solid (0·79 g.), m. p. (95) 101—104°, which on warming in methanol (20 c.c.) rapidly precipitated a white solid (0·54 g.), m. p. >310°. Rechlorination with phosphorus oxychloride, and crystallisation of the product from ether–ligroin (b. p. 40—60°) gave 4-chloro-3-nitroquinoline, m. p. 119—120°, identical with an authentic specimen (Bachman *et al.*, *J. Amer. Chem. Soc.*, 1947, **68**, 365). This was readily converted into 3-nitro-4-phenoxyquinoline as described below.

3-*Nitro*-4-*phenoxyquinoline.*—4-Chloro-3-nitroquinoline (0·65 g.) and phenol (3 g.) were heated at 180° for 4 hours (cf. Backeberg and Marais, *J.*, 1942, 381), and the solution poured into sodium hydroxide solution (100 c.c. of 2N.) and extracted with ether. Removal of the ether after drying (Na_2CO_3) gave a pale yellow solid (0·5 g.). 3-*Nitro*-4-*phenoxyquinoline* separated from ether–ligroin (b. p. 40—60°) in pale yellow needles, m. p. 108—109° (Found : C, 64·11; H, 4·31. $C_{15}H_{10}O_3N_2,H_2O$ requires C, 63·41; H, 4·26%).

6-*Nitro*-4-*phenoxyquinoline.*—In the same way, 4-chloro-6-nitroquinoline (0·3 g.) gave 6-*nitro*-4-*phenoxyquinoline* (0·28 g.), forming colourless plates from ether–ligroin (b. p. 40—60°), m. p. 117—118° (Found : C, 66·6; H, 4·0. $C_{15}H_{10}O_3N_2$ requires C, 67·6; H, 3·8%).

Nitration of 1-*Methyl*-4-*cinnolone.*—The compound (0·5 g.) in concentrated sulphuric acid (2 c.c.) was treated during 15 minutes at 0° with 1 c.c. of nitration mixture [from 1·6 c.c. of nitric acid (*d* 1·5) and 8·4 c.c. of concentrated sulphuric acid] with stirring, and the solution stirred for a further 15 minutes at 0° and 1½ hours at room temperature, and poured on ice. Recrystallisation of the granular precipitate (0·47 g.) from methanol gave glistening, yellow plates of 8-nitro-1-methyl-4-cinnolone, m. p. 238—239°, identical with a specimen from 8-nitro-4-hydroxycinnoline (Schofield and Theobald, unpublished).

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