Cinnolines. Part XI.[1] Quaternisation of 3- and 4-Phenylcinnolines and Reduction of Some Methylcinnolinium Salts

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3-Phenylcinnoline quaternises with methyl iodide to give 1-methyl-3-phenylcinnolinium iodide and a small amount of its 2-methyl isomer, whereas only the 2-methiodide is isolated from quaternisation of 4-phenylcinnoline. 1-Methyl-3-phenylcinnolinium iodide is reduced electrolytically, or with sodium borohydride, to 1,4-dihydro-1-methyl-3-phenylcinnoline and this is reduced polarographically to 2-*o*-methylaminophenyl-1-phenylethylamine, which is also obtained directly from the quaternary salt by reduction with amalgamated zinc and hydrochloric acid. Reduction of 1,3-dimethylcinnolinium iodide by the Clemmensen method, however, gives 1,2-dimethylindole and 1,2-dimethylindoline while 2-methylcinnolinium iodides give the corresponding indole and indoline.

QUATERNISATION of 3-phenylcinnoline (I; X = H) in acetonitrile with methyl iodide gives a mixture of 1-methyl-3-phenylcinnolinium iodide (II; R^1 = Ph, R^2 = H, X = I) and the 2-methyl isomer (III; R^1 = Ph, R^2 = H, X = I), the ratio of the two products, as shown by the ^{1}H n.m.r. spectrum,[2] being 78 : 22. The quaternisation has now been carried out in ethanol and the products isolated in 60% and 14% yields respectively.

The major product (II; R^1 = Ph, R^2 = H, X = I) was reduced electrolytically, or with sodium borohydride, to give 1,4-dihydro-1-methyl-3-phenylcinnoline (IV), the ^{1}H n.m.r. spectrum of which showed singlets at τ 6·38 (2H, $4CH_2$) and at 6·54 (3H, 1Me). Polarographic and controlled-potential reduction in acid solution of the cyclic hydrazone (IV) gave a four-electron reaction, like other phenylhydrazones,[3] and led to the diamine (V), the structure of which was indicated by the failure of attempts to convert it through a diazonium salt into an azo-dye. In contrast, the minor quaternisation product (III; R^1 = Ph, R^2 = H, X = I), when similarly reduced, gave a solution which on diazotisation and coupling with β-naphthol yielded a red dye.

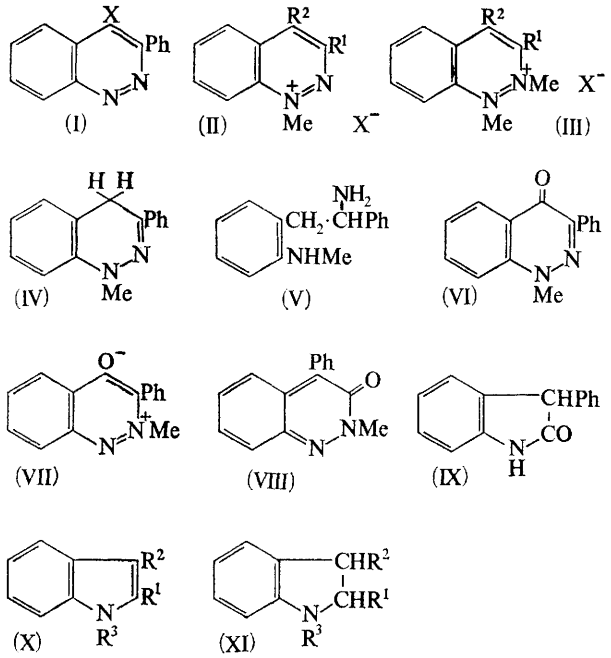
In acid solution, a difference has been found between the polarographic behaviour of cinnolines quaternised at N-1 and N-2. The former show two one-electron waves, where the half-wave potential of the first one is independent of pH, and an adsorption wave indicates a strong adsorption of the quaternary compound. Cinnolines quaternised at N-2 yield one two-electron wave. The assignment of structures (II; R^1 = Ph, R^2 = H, X = I) and (III; R^1 = Ph, R^2 = H, X = I) to the major and minor quaternisation products re-

[1] Part X, D. E. Ames, G. V. Boyd, R. F. Chapman, A. W. Ellis, A. C. Lovesey, and D. Waite, *J. Chem. Soc.* (*B*), 1967, 748.

[2] H. Lund, *Acta Chem. Scand.*, 1967, **21**, 2525.

[3] H. Lund, *Acta Chem. Scand.*, 1959, **13**, 249.

spectively, was confirmed by the observation that the former yields two one-electron waves in slightly acid solution whereas the latter yields a single two-electron wave.



In a limited number of quaternised cinnolines investigated, it has been found [2] that cinnolinium compounds quaternised at N-2 lost the methyl group in alkaline solution [4] at a rate depending on the substituents, whereas compounds quaternised at N-1 formed a pseudo-base. It has been found that the salt (III; $R^1 = Ph$, $R^2 = H$, $X = I$) loses the methyl group in alkaline solution (the reaction can be followed polarographically) but that isomer (II; $R^1 = Ph$, $R^2 = H$, $X = I$) does not.

The methods used previously [1] to determine the site of quaternisation of cinnolines have also been applied to 3- and 4-phenylcinnolines. Methylation of 4-hydroxy-3-phenylcinnoline (I; X = OH) with dimethyl sulphate and alkali gave 1-methyl-3-phenyl-4-cinnolone [(VI), 40%] and the anhydro-base [(VII), 16%] of 4-hydroxy-2-methyl-3-phenylcinnolinium hydroxide; no 4-methoxy-3-phenylcinnoline (I; X = OMe) could be isolated. Similar results were obtained by Lowrie [5] for methylation with methyl iodide and alkali. The structure of (VII) was confirmed by reduction with zinc and aqueous ethanolic ammonia to give *o*-aminophenyl benzyl ketone, isolated as its toluene-*p*-sulphonyl derivative. Similar reduction of the cinnolone (VI) gave no identifiable product. The u.v. spectrum of the anhydro-base (VII) closely resembled that of the anhydro-base of 4-hydroxy-2-methylcinnolinium hydroxide; [6] the very small effect of the conjugated 3-phenyl group is presumably due to the 2-methyl group forcing the 3-phenyl ring out of the plane of the rest of the molecule. In contrast, the u.v. spectrum of the cinnolone (VI) did show conjugation effects, the bands (at 267, 317, and 365 mμ) having lost the fine structure but having greater intensity than those in the spectrum of 1-methyl-4-cinnolone.[6] The u.v. spectrum of 4-hydroxy-3-phenylcinnoline (I; X = OH) in ethanol closely resembled that of the cinnolone (VI) and differed considerably from those of the anhydro-base (VII) and of 4-methoxy-3-phenylcinnoline (I; X = OMe) showing that, in ethanol, the tautomeric equilibrium involves predominantly 1-protonation (Figure 1).

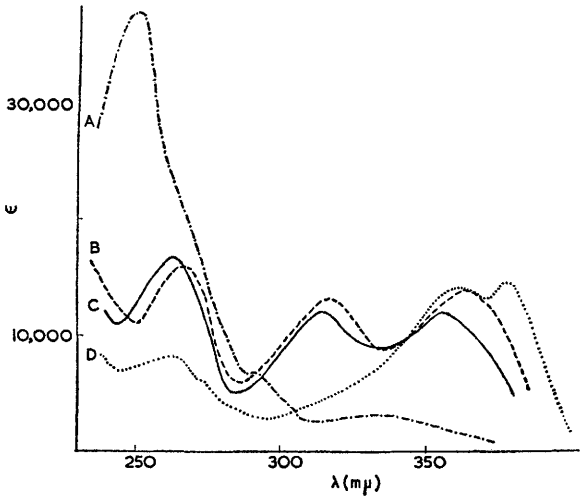


FIGURE 1 U.v. spectra (in EtOH): A, 4-methoxy-3-phenylcinnoline; B, 1-methyl-3-phenyl-4-cinnolone; C, 4-hydroxy-3-phenylcinnoline; D, anhydro-base of 4-hydroxy-2-methyl-3-phenylcinnolinium hydroxide

Reduction of the cinnolone (VI) with lithium aluminium hydride, and treatment of the crude di- or tetrahydrocinnoline formed with picric acid in boiling ethanol, gave 1-methyl-3-phenylcinnolinium picrate [II; $R^1 = Ph$, $R^2 = H$, $X = C_6H_2(NO_2)_3O$] which was also obtained from the major quaternisation product (II; $R^1 = Ph$, $R^2 = H$, $X = I$) by treatment with picric acid.

Molecular orbital calculations by Dr. G. V. Boyd, using a self-consistent version of the Hückel method [1] (ωβ technique), and assuming coplanarity of the phenyl group with the cinnoline nucleus, show that the 3-phenyl-2-*H*-cinnolinium ion is more stable than the 1-*H*-tautomer by 0·006β. The u.v. spectra of the methoperchlorates [(II) and (III); $R^1 = Ph$, $R^2 = H$, $X = ClO_4$], obtained from the corresponding methiodides, and of 3-phenylcinnolinium perchlorate are shown in Figure 2 but owing to steric effects these are of uncertain value in determining the site of protonation. Thus, the proton at C-4 exhibits a small steric hindrance for the phenyl group so that a small unknown angle between the planes of the phenyl and cinnoline rings must be expected in 3-phenylcinnoline. A proton at N-2 would not be expected to make the angle between the planes much

[4] *Cf.* J. C. E. Simpson, *J. Chem. Soc.*, 1947, 1653; J. S. Morley and J. C. E. Simpson, *J. Chem. Soc.*, 1949, 1354.

[5] H. S. Lowrie, *J. Medicin. Chem.*, 1966, **9**, 784.

[6] D. E. Ames, R. F. Chapman, H. Z. Kucharska, and D. Waite, *J. Chem. Soc.*, 1965, 5391.

greater, whereas a 2-methyl group would alter the angle considerably with loss of conjugation between the rings. It must, therefore, be considered that the shift of absorption maximum is mainly due to this loss of conjugation, *i.e.* the spectra reflect the steric requirements of the methyl group rather than the position of the charge. Polarographic reduction of 3-phenylcinnoline in acid solution gives two one-electron waves, similar to the 1-methylcinnolinium salt, but the distance between the waves is smaller than for the latter compound so that, although this suggests that a substantial part of protonation takes place at N-1, it is not possible to make a quantitative estimate.

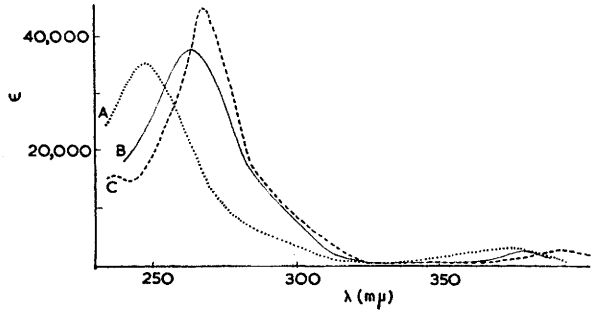


FIGURE 2 U.v. spectra (in 2·8% ethanolic perchloric acid): A, 2-methyl-3-phenylcinnolinium perchlorate; B, 3-phenylcinnolinium perchlorate; C, 1-methyl-3-phenylcinnolinium perchlorate

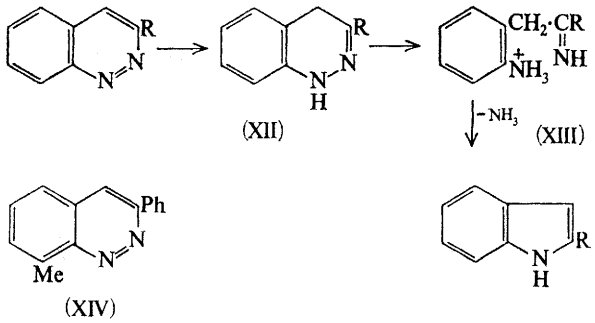
Methylation of 3-hydroxy-4-phenylcinnoline with dimethyl sulphate and alkali gave only 2-methyl-4-phenyl-3-cinnolone (VIII) the structure of which was shown, by reduction with phosphorus and hydriodic acid,[7] to form 3-phenyloxindole (IX). Reduction of cinnolone (VIII) with lithium aluminium hydride, and treatment of the crude product with ethanolic picric acid, gave 2-methyl-4-phenylcinnolinium picrate [III; $R^1 = H$, $R^2 = Ph$, $X = C_6H_2(NO_2)_3O$]. The same salt was obtained by quaternisation of 4-phenylcinnoline with methyliodide, followed by reaction of the methiodide with picric acid. Thus quaternisation of 4-phenylcinnoline occurs at N-2 (no other product could be isolated).

In the hope of developing a more convenient method for determination of the structures of quaternary cinnolinium salts, the chemical reduction of these salts has been further examined. Earlier work gave unsatisfactory results [8] because reduction was carried out under basic conditions which are known to cause degradation of cinnolinium salts to cinnoline as discussed above. Since reduction in an acidic medium was therefore necessary, the use of Clemmensen reduction conditions was examined.

2-Methylcinnolinium salts (III) were reduced by amalgamated zinc in hydrochloric acid to give the indoles (X; $R^3 = H$) and the corresponding indolines (XI; $R^3 = H$) (*cf.* formation of indoles in polarographic reduction [2]). Thus 2,3-dimethylcinnolinium iodide (III; $R^1 = Me$, $R^2 = H$, $X = I$) yielded 2-methylindole and 2-methylindoline (isolated as the benzoyl derivative). Similarly 2,4-dimethylcinnolinium iodide (III; $R^1 = H$, $R^2 = Me$, $X = I$) gave skatole and 3-methylindoline while 2-methyl-4-phenylcinnolinium iodide (III; $R^1 = H$, $R^2 = Ph$, $X = I$) was reduced to 3-phenylindole and 3-phenylindoline.

In contrast, reduction of 1,3-dimethylcinnolinium iodide (II; $R^1 = Me$, $R^2 = H$) with amalgamated zinc and hydrochloric acid gave 1,2-dimethylindole (X; $R^1 = R^3 = H$, $R^2 = Me$) and 1,2-dimethylindoline (XI; $R^1 = R^3 = Me$, $R^2 = H$). Under the same conditions, however, 1-methyl-3-phenylcinnolinium iodide (II; $R^1 = Ph$, $R^2 = H$, $X = I$) was reduced to the diamine (V) already described.

It therefore appears that the reduction of cinnolinium salts with amalgamated zinc and hydrochloric acid offers a useful method of determining the site of quaternisation. The results of these reductions may be considered in the light of the polarographic potentials and the reduction scheme [2] suggested previously. According to this, the primarily formed 1,4-dihydrocinnolines (XII) (or an *N*-alkyl derivative) are reduced in acid solution as phenylhydrazones [3] with initial hydrogenolysis of the N–N bond and formation of the imino-amine (XIII). The imine group may be either attacked by the amine, leading to ring contraction, or may be reduced further. When (XII; R = H or alkyl) is taken, the intermediate imine is reduced at a more negative potential than required for the hydrogenation of the N–N bond, but the imine is readily attacked by the amine; in the case of (XII; R = Ph) the further reduction takes place at the same potential as that of the original hydrogenolysis. The substituents at N-1, N-2, and C-4 are largely insignificant in this respect (as long as they are H, alkyl, or aryl). It is of interest that reduction by amalgamated zinc in hydrochloric acid gives the same results as would be expected from an electrolytic reduction in acid solution at a mercury electrode.



The site of the quaternisation of diaza-heterocyclic compounds is determined by both electronic and steric effects. For example, the latter is the dominant cause for the observed difference in the quaternisation of 3-phenylcinnoline and of 8-methyl-3-phenylcinnoline (XIV). The former produces, on reaction with methyl

[7] *Cf.* E. J. Alford and K. Schofield, *J. Chem. Soc.*, 1953, 1811.
[8] C. M. Atkinson and A. Taylor, *J. Chem. Soc.*, 1955, 4236; D. E. Ames and H. Z. Kucharska, *J. Chem. Soc.*, 1964, 283.

iodide, 78% of the isomer quaternised at N-1, whereas no detectable amount (<5%) of such an isomer is found on quaternisation of the latter.[2] The electronic influence of a methyl group at C-8 on the nitrogen atoms would be expected to be negligible so the observed difference must probably be ascribed to the steric effect of the methyl group.

On a model, the hindrance towards a reagent approaching the nitrogen atoms in the plane of the cinnoline ring from a methyl group at C-8 and a phenyl substituent at C-3 coplanar with the cinnoline ring is about equal, but if the plane of the phenyl ring is about perpendicular to that of the cinnoline system, its steric hindrance is much less. It is thus probable that the phenyl group is not coplanar with the cinnoline ring during the bond formation in the quaternisation of (XIV), and it may be predicted that a bulky substituent at C-4 in (I), which would force the 3-phenyl substituent out of the plane of the cinnoline ring, would also cause a higher proportion of the isomer quaternised at N-2 to be formed.

The hydrogen at C-8 would be expected to produce approximately the same steric hindrance at N-1 as a methyl group at C-3 would do at N-2. This is substantiated by the rather small influence of the size of the quaternising reagent; thus the percentage quaternised at N-1 in 3-methylcinnoline alters from 30% to 34% to 37% when the reagent changes from methyl iodide to ethyl iodide to isopropyl iodide. Although the methyl group at C-3 thus seems to produce a slightly greater steric hindrance than the hydrogen at C-8, 3-methylcinnoline quaternises predominantly at N-2, which must be ascribed to the electronic effect of the benzene ring.

In the pyridazine [9] series, an estimation of the composition of a quaternisation mixture could be made from empirical 'substituent constants' which express the combined electronic and steric influence of a substituent on the rate of quaternisation at the nitrogen atom adjacent to the substituent. Although the relative weight of the electronic and steric influence is probably somewhat different in the cinnoline and pyridazine series due to the presence of the fused benzene ring, a similar approach using the 'substituent constants' from the pyridazine series may be applied to the cinnolines. From the quaternisation of cinnoline, 3- and 4-methylcinnoline the 'substituent constant' of the phenyl ring fused to the pyridazine ring in cinnoline may be roughly estimated at 0·12. By using this value, 3-phenylcinnoline is estimated to quaternise 83% at N-1 which compares reasonably well with the experimental value (78%). However, much more experimental material is needed before an estimate of the relative influence of the steric and electronic effects can be made.

EXPERIMENTAL

Evaporations were carried out under reduced pressure. U.v. spectra were measured on a Perkin-Elmer 137 spectrophotometer; ^{1}H n.m.r. spectra were determined at 60 Mc./sec. on a Varian Associates A-60 spectrometer with tetramethylsilane as internal standard. A recording polarograph Radiometer PO4 and a transistorised potentiostat (Tage Juhl Electronics, Copenhagen) were used for the electrolytic experiments.

Quaternisation of 3-*Phenylcinnoline*.—3-Phenylcinnoline [10] (5 g.) and methyl iodide (10 c.c.) in ethanol (40 c.c.) were heated under reflux for 2 hr. The crystals which separated when the solution was cooled were recrystallised from ethanol to give 1-*methyl*-3-*phenylcinnolinium iodide* (5·1 g.), deep red needles, m.p. 205—207° (Found: C, 51·6; H, 4·1; I, 36·4; N, 8·1. $C_{15}H_{13}IN_2$ requires C, 51·8; H, 3·8; I, 36·4; N, 8·0%). Concentration of the mother liquors and repeated recrystallisations from benzene–chloroform yielded 2-*methyl*-3-*phenylcinnolinium iodide* (1·2 g.), orange-red needles, m.p. 176—178° (Found: C, 51·7; H, 3·9; I, 36·5; N, 8·2%).

Reduction of 1-*Methyl*-3-*phenylcinnolinium Iodide with Sodium Borohydride*.—To the methiodide (1 g.) dissolved in methanol (10 c.c.), water (20 c.c.), and ether (30 c.c.) was added sodium borohydride (300 mg.) in small portions; the ethereal layer was separated and washed twice with water, dried (K_2CO_3), and evaporated. Recrystallisations from light petroleum (b.p. 40—60°) at −20° gave 1,4-*dihydro*-1-*methyl*-3-*phenylcinnoline* (625 mg.), m.p. 65—66° (Found: C, 80·8; H, 6·3; N, 12·6. $C_{15}H_{14}N_2$ requires C, 81·1; H, 6·4; N, 12·6%). The ^{1}H n.m.r. spectrum (in CCl_4) showed at τ 6·54 (3H, 1Me) and 6·38 (2H, $4CH_2$) and a multiplet at 3·45—2·1 (9H, ArH).

This product (400 mg.) was reduced at −0·90 v (SCE) in N-hydrochloric acid containing 40% ethanol. The reduction involved 4 electrons per molecule; when reduction was complete, the solution was evaporated. Crystallisation of the residue from ethanol–ether gave 2-*o*-methylaminophenyl-1-phenylethylamine dihydrochloride, m.p. and mixed m.p. (with sample described below), 216—218°; attempts to diazotise and couple with β-naphthol were unsuccessful.

2-Methyl-3-phenylcinnolinium iodide was reduced similarly at −1·1 v (SCE). The reduced solution was diazotised and coupled with β-naphthol to give a red azo-dye.

Methylation of 4-*Hydroxy*-3-*phenylcinnoline*.—A solution of 4-hydroxy-3-phenylcinnoline [11] (10·3 g.) in 4N-potassium hydroxide (250 c.c.) was stirred at 50° while dimethyl sulphate (10 c.c.) was added and then stirred at 70° for 2 hr. Isolation with chloroform and chromatography of the crude product in benzene on a column of alumina, followed by repeated recrystallisations from light petroleum (b.p. 60—80°), gave 1-methyl-3-phenyl-4-cinnolone (6·7 g.) as pale yellow needles, m.p. 117—119° (Found: C, 76·5; H, 5·3; N, 12·0. Calc. for $C_{15}H_{12}N_2O$: C, 76·3; H, 5·1; N, 11·9%). Elution of the column with chloroform then yielded the anhydro-base of 4-hydroxy-2-methyl-3-phenylcinnolinium hydroxide (2·7 g.), orange plates, m.p. 205—207°, from benzene–light petroleum (b.p. 60—80°) (Found: C, 76·6; H, 5·2; N, 12·0%) (lit.[5], m.p. 107—108° and 213—214° respectively for the two products).

2-*Toluene*-p-*sulphonamidophenyl Benzyl Ketone*.—*o*-Aminophenyl benzyl ketone [11] (1·9 g.), toluene-*p*-sulphonyl chloride (4 g.) and pyridine (25 c.c.) were heated

[9] H. Lund and P. Lunde, *Acta Chem. Scand.*, 1967, **21**, 1067.
[10] H. S. Lowrie, *J. Medicin. Chem.*, 1966, **9**, 664.
[11] D. W. Ockenden and K. Schofield, *J. Chem. Soc.*, 1953, 3440, 3706.

on a steam-bath for 1 hr. The solution was poured on ice and the solid was collected and washed with dilute acid. The *ketone* was obtained as plates (2·0 g.), m.p. 110—112° (Found: C, 68·8; H, 5·1; N, 3·8; S, 8·9. $C_{21}H_{19}NO_3S$ requires C, 69·0; H, 5·2; N, 3·8; S, 8·8%).

Reduction of the Anhydro-base of 4-Hydroxy-2-methyl-3-phenylcinnolinium Hydroxide with Zinc and Ammonia Solution.—The anhydro-base (0·7 g.), zinc dust (3 g.), ethanol (40 c.c.), and hydrobromic acid (4 drops; 48%) were heated under reflux for 1 hr. Aqueous ammonia (30 c.c.; *d* 0·88) was added and the mixture was heated under reflux for 8 hr. The filtered solution was concentrated, acidified, and washed with ethyl acetate; basification and isolation with ethyl acetate gave an oil which was dissolved in pyridine and stirred for 24 hr. with toluene-*p*-sulphonyl chloride. Addition of water, filtration, and recrystallisation from ethanol gave 2-toluene-*p*-sulphonamidophenyl benzyl ketone, m.p. and mixed m.p. 109—110°.

Reduction of 1-Methyl-3-phenyl-4-cinnolone With Lithium Aluminium Hydride.—The cinnolone (3 g.) in benzene (100 c.c.) was added to lithium hydride (6 g.) in ether (300 c.c.) and the mixture was heated under reflux for 4 hr. and left overnight. Potassium hydroxide (5 g.) in water (12 c.c.) was added cautiously and the mixture was heated under reflux for 1·5 hr. and filtered, the solid being washed twice with boiling ethyl acetate. The combined filtrates were evaporated; picric acid (15 g.) and ethanol (200 c.c.) were added and the solution was heated under reflux for 3 hr. and then poured into ether (600 c.c.). Filtration and recrystallisations from ethanol yielded *1-methyl-3-phenylcinnolinium picrate* (3·5 g.), m.p. 172—173° (Found: C, 56·5; H, 3·6; N, 15·9. $C_{21}H_{15}N_5O_7$ requires C, 56·1; H, 3·4; N, 15·6%).

1-Methyl-3-phenylcinnolinium iodide (0·4 g.) was dissolved in boiling ethanol and a saturated ethanolic solution of picric acid was added. The product, which separated on cooling, was washed with ether and crystallised from ethanol to give 1-methyl-3-phenylcinnolinium picrate, m.p. and mixed m.p. 171—173°.

Perchlorate Salts.—The following salts were prepared: *3-phenylcinnolinium perchlorate*, yellow needles, m.p. 162—164° (from ethanol–ether) (Found: C, 54·6; H, 3·5; N, 8·9. $C_{14}H_{11}ClN_2O_4$ requires C, 54·8; H, 3·6; N, 9·2%); *4-Phenylcinnolinium perchlorate*, pale yellow needles, m.p. 202—204° (from ethanol–ether) (Found: C, 55·1; H, 3·6; N, 9·4%); *2-methyl-3-phenylcinnolinium perchlorate*, yellow needles, m.p. 208—210° (from acetone–ether) (Found: C, 56·3; H, 4·0; N, 8·7. $C_{15}H_{13}ClN_2O_4$ requires C, 56·2; H, 4·1; N, 8·7%); *1-methyl-3-phenylcinnolinium perchlorate*, m.p. 228—230° (from acetone–ether) (Found: C, 56·4; H, 4·2; N, 8·8%); and *2-methyl-4-phenylcinnolinium perchlorate*, m.p. 184—186° (from acetone–ether) (Found: C, 55·9; H, 4·2; N, 8·7%).

2-Methyl-4-phenyl-3-cinnolone.—Methylation of 3-hydroxy-4-phenylcinnoline [12] with dimethyl sulphate as described gave the *cinnolone*, orange–yellow needles, m.p. 173—175° (from ethanol) (Found: C, 76·3; H, 5·0; N, 12·1. $C_{15}H_{12}N_2O$ requires C, 76·4; H, 5·1; N, 11·9%). Chromatography of the mother liquors in benzene on alumina revealed no trace of another isomer.

The cinnolone (0·8 g.), red phosphorus (0·8 g.), and hydriodic acid (12 c.c.; *d* 1·7) were heated under reflux for 8 hr. Water was added and the mixture was neutralised with sodium hydroxide solution and extracted with ether. Evaporation gave a solid from which 3-phenyloxindole [13] was isolated, m.p. and mixed m.p. 186—188° (from ethanol). The aqueous solution was strongly basified with sodium hydroxide solution and distilled into hydrochloric acid. The acid solution was evaporated to dryness and the residue in hot water was treated with picric acid to give methylamine picrate, m.p. and mixed m.p. 207—209°.

Reduction of 2-Methyl-4-phenyl-3-cinnolone with Lithium Aluminium Hydride.—The cinnolone (4·0 g.) was reduced in the same manner as the isomeric compound described above and the crude product was similarly treated with picric acid to give *2-methyl-4-phenylcinnolinium picrate*, m.p. 128—130° (from ethanol) (Found: C, 56·3; H, 3·6; N, 15·5. $C_{21}H_{15}N_5O_7$ requires C, 56·1; H, 3·4; N, 15·6%). Quaternisation of 4-phenylcinnoline [14] with methyl iodide gave 2-methyl-4-phenylcinnolinium iodide m.p. 224—226° (lit.,[14] 220°); no other product could be isolated. 2-Methyl-4-phenylcinnolinium picrate (2·1 g.), obtained from the methiodide had m.p. and mixed m.p. 130—132°.

Reductions of 2-Methylcinnolinium Salts with Amalgamated Zinc and Hydrochloric Acid.—(a) *2,3-Dimethylcinnolinium iodide.* Granulated zinc (5 g.) was shaken for 5 min. with mercuric chloride (1 g.) in water (20 c.c.) and concentrated hydrochloric acid (1 c.c.); after decantation of the acid, the amalgamated zinc was washed with water and then heated under reflux for 4·5 hr. with the methiodide (1 g.), concentrated hydrochloric acid (15 c.c.), and water (10 c.c.). After addition of water, the solution was extracted six times with ether; evaporation of the extracts yielded an oil which was shown by t.l.c. to contain 2-methylindole. The aqueous layer was basified with potassium hydroxide (15 g.) in water (50 c.c.). Isolation with ether gave an oil which was shaken with benzoyl chloride and 2N-sodium hydroxide to form 1-benzoyl-2-methylindoline, m.p. 88·5—89·5° (from methanol) identical with authentic sample.[15]

(b) *2,4-Dimethylcinnolinium iodide.* The methiodide gave 3-methylindole, which collected in the condenser, and had m.p. and mixed m.p. 94—96°. The basic fraction was benzoylated as before to produce *1-benzoyl-3-methylindoline*, m.p. 101—103°, from ethanol (Found: C, 81·3; H, 6·4; N, 5·9. $C_{16}H_{15}NO$ requires C, 81·1; H, 6·4; N, 5·9%). This product was identical (mixed m.p.) with a sample prepared from 3-methylindoline.[16]

(c) *2-Methyl-4-phenylcinnolinium iodide.* Reduction yielded 3-phenylindole, which was recrystallised from light petroleum (b.p. 60—80°) and had m.p. and mixed m.p. 85—86°. The basic fraction gave *3-phenyl-1-toluene-p-sulphonylindoline*, m.p. 141—142° (from ethanol) (Found: C, 72·1; H, 5·3; N, 4·0. $C_{21}H_{19}NO_2S$ requires C, 72·2; H, 5·5; N, 4·0%) identical with a sample prepared from 3-phenylindole.[17]

Reduction of 1,3-Dimethylcinnolinium Iodide.—The quaternary salt was reduced in the manner described. Isolation with ether gave an oil which was shown to contain 1,2-dimethylindole by t.l.c. in ethyl acetate on silica. The basic product was isolated with ether; treatment with methyl iodide in methanol gave 1,2-dimethylindoline methiodide,

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m.p. and mixed m.p. 193—194° (decomp.) (Found: C, 45·5; H, 5·4; N, 5·1; I, 44·0. Calc. for $C_{11}H_{16}IN$: C, 45·7; H, 5·6; N, 4·9; I, 43·9%). Despite careful purification and drying, both samples had lower m.p. than the literature values (200—202°,[18] and 211°,[15]). In another experiment, 1,2-dimethylindoline was isolated as the picrate, m.p. and mixed m.p. 126—127° (decomp.) (lit.,[19] 131—133°) (Found: C, 50·7; H, 4·2; N, 14·9. Calc. for $C_{16}H_{16}N_4O_7$: C, 51·1; H, 4·3; N, 14·9%).

Reduction of 1-*Methyl*-3-*phenylcinnolinium Iodide*.—This methiodide was similarly reduced; basification and isolation with ether gave an oil which was dried by addition of benzene followed by evaporation. Dissolution in dry ether and treatment with hydrogen chloride gave 2-o-*methylaminophenyl*-1-*phenylethylamine dihydrochloride*, m.p. 217—219° (from ethanol–ether) (Found: C, 60·2; H, 6·6; Cl, 23·6; N, 9·4. $C_{15}H_{20}Cl_2N_2$ requires C, 60·2; H, 6·8; Cl, 23·7; N, 9·4%). The base also gave the *dibenzoyl derivative*, m.p. 167—169° (from ethanol) (Found: C, 80·1; H, 6·0; N, 6·3. $C_{29}H_{26}N_2O_2$ requires C, 80·2; H, 6·0; N, 6·5%).

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