Cinnolines. Part II.[1] Reaction with Hydrogen Peroxide and Acetic Acid

By **M. H. Palmer** and **E. R. R. Russell**, Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh 9

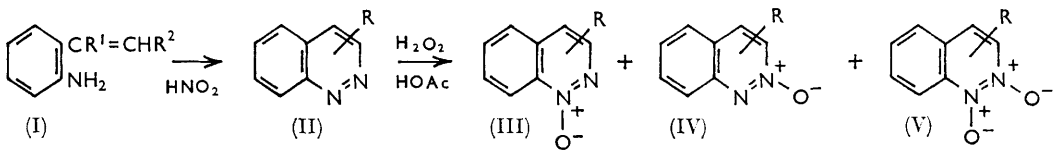
A number of new 4-alkyl- and 3,4-dialkyl-cinnolines have been prepared; they react with aqueous hydrogen peroxide in acetic acid to give the 1- and 2-oxides and the 1,2-dioxides. 4-Carboxy- and 4-methyl-3-nitrocinnolines give the corresponding 2- and 1-oxides respectively. The 4-alkyl- and 3,4-dialkyl-8-nitrocinnolines, in contrast, give the 8-nitro-cinnolin-4-ones. Under the same conditions, 4-methyl 8-nitroquinoline gives 2-amino-3-nitroacetophenone. Possible mechanisms of these and related reactions are discussed.

We recently reported [1] the synthesis of 4-methylcinnoline 1,2-dioxide by the reaction of 4-methylcinnoline with acetic acid and aqueous hydrogen peroxide; this is the first reference to the formation of a condensed pyridazine 1,2-dioxide by direct peroxidation, since benzo[*c*]cinnoline 5,6-dioxides are prepared by reductive cyclisation of 2,2′-dinitrobiphenyls.[2] More recently cinnoline, pyridazine, and benzo[*c*]cinnoline have been converted into the di-*N*-oxides by direct oxidation at higher temperatures.[3] We now give further details of our work on the oxidation of cinnolines and one related quinoline, and some observations on the nitration of some cinnoline 2-oxides.

Synthesis of Cinnolines.—A number of alkylcinnolines (IIa—f) were prepared by cyclisation of the *ortho*-aminophenylalkenes (I), obtained from Grignard reactions on *ortho*-aminoacetophenone or methyl anthranilate. Only the t-butyl compound (IIf) calls for comment: with an excess of t-butyl magnesium chloride (15 mol.) the Grignard reaction was virtually complete after two re-cycling processes (absence of absorption from the acetyl group at τ 7·55). The crude tertiary alcohol [τ 8·43 (Me), and 9·0 (Bu^t)] resisted dehydration by phosphoric oxide in benzene, the reagent used for all the other cinnolines (IIa—e), but was finally converted into the olefin (I; $R^1 = Bu^t$, $R^2 = H$) by distillation from potassium hydrogen sulphate (25% w/w) at 180°. There was evidence that some *o*-aminoacetophenone was formed (absorption at τ 7·55) under these conditions; the product could not be purified by chromatography on silica, and chromatography on alumina caused some decomposition. The crude olefin [τ 4·6 and 5·05 (each d, J 2 c./sec.)] was converted into the cinnoline, which was purified by chromatography on alumina; it did not crystallise, but the m.p. of 4-alkylcinnolines falls with increasing size of the 4-substituent. An unusual feature in the ^1H n.m.r. spectrum (CCl_4) of the 4-t-butylcinnoline is the marked deshielding of the 5-proton in comparison with that in 4-methylcinnoline; the two multiplets with centres at τ 1·4 and 1·65 correspond to the 5- and 8-protons respectively, the 3-proton signal (s) is at τ 0·8 and the 6- and 7-protons give a multiplet with centre at τ 2·25. Comparison with 4-methylcinnoline shows that the tertiary butyl group causes a difference in shielding of 0·2 p.p.m. for an *ortho*-proton and *ca.* 0·8 p.p.m. for the *peri*-proton; this is unlikely to be a conventional mesomeric or inductive effect, or to be associated with ring current or magnetic anisotropy variations. We conclude [4] that the major interference of the electron clouds of the two groups hinders precession and produces a downfield shift, which is no doubt partially relieved by out-of-plane bending.

[1] Part I, M. H. Palmer and E. R. R. Russell, *Chem. and Ind.*, 1966, 157.
[2] A. E. Blood and C. R. Noller, *J. Org. Chem.*, 1957, **22**, 711.
[3] I. Suzuki, M. Nakadate, T. Nakashima, and N. Nagasawa, *Tetrahedron Letters*, 1966, 2899.
[4] C. W. Haigh, M. H. Palmer, and B. Semple, *J. Chem. Soc.*, 1965, 6004.

An easy route to substituted 6-nitrocinnolines appeared to be nitration of the corresponding cinnoline 2-oxides, followed by reduction of the *N*-oxide group. In sulphuric acid (80% w/w) at 90° 4-methyl- and 4-ethyl-3-methyl-cinnoline *N*-oxides gave mixtures [5] of the 6- and 8-nitro-derivatives in which the former predominated; but there was also evidence of the 6,8-dinitro-compound from the reaction with the ethylmethyl-cinnoline (doublets, J 3 c./sec., at τ 1·08 and 1·31 in the spectrum of the crude product). Separation of the mixtures gave the 6- and 8-nitro-compounds, but attempts to reduce the *N*-oxide of the 6-nitro-compounds failed when phosphorus trichloride (neat or in chloroform) or triethyl phosphite at 150° was used. Under these conditions 4-nitropyridine also resists [6] reduction by these reagents; the reduced basicity of the *N*-oxide group resulting from the electron-attracting nitro-group can be interpreted as due to a quinoid canonical form. Such a structure should be detectable by the increased coupling constant ($J_{2,3}$) in comparison with that for 4-nitropyridine; however, the degeneracy of the system has made this impossible to measure.



a; R = 4-Me
b; R = 3-Me, 4-Et
c; R = 4-Me, 6-Br
d; R = 4,6-Me$_2$
e; R = 3,4-Me$_2$
f; R = 4-Bu^t

respectively]. In the reactions with 3,4-dialkyl-cinnolines (IIb and e) there was no evidence of the 1-oxide, but the 2-oxide and 1,2-dioxide (2 : 1) were isolated in each case.

Alkylation of the ethylmethylcinnoline (IIb) with methyl iodide gives the 1- and 2-methiodides (1 : 1); [6] since the alkylation and peroxidation steric requirements are probably not much different, this suggests that the dioxide is largely formed from the 1-oxide, as might be expected on steric grounds (N-1 of the 2-oxide is shielded by both the 8-proton and the oxide, whilst in the 1-oxide N-2 is less hindered by the oxide and the 3-proton).

The peroxidation of cinnoline-4-carboxylic acid gave a single product, which, since the characteristic lowfield resonance of the 8-proton in 1-oxides is absent, must be the 2-oxide. In contrast, the single product from 4-methyl-3-nitrocinnoline showed a multiplet at lower field than the 8-proton of the starting cinnoline, and this confirms the 1-oxide structure. Both results are consistent with the known electronic (and in the latter case steric) effects of the substituents.

4-Methyl-8-nitrocinnoline (VI; R = H) was expected to give the 2-oxide by analogy with the above results and with the behaviour of 8-nitrocinnoline itself,[8] although in the latter case 8-nitrocinnolin-4-one (VII; R = H) and 7-nitroindazole are also formed. The crude product showed the absence of methyl groups (^{1}H n.m.r. spectrum) and the presence of C=O and N–H groups (i.r. spectrum), and was identified as 8-nitrocinnolin-4-one (VII; R = H) by mass spectrometry and by synthesis from 2-amino-3-nitroacetophenone (VIII; R = Me). In similar experiments the next higher homologue (VI; R = Me) and 3,4-dimethyl-8-nitrocinnoline both gave the methylnitrocinnolinone (VII; R = Me), which was also synthesised from the propiophenone (VIII; R = Et). These experiments show that the carbon atoms lost during the oxidation are from the 4-alkyl group; thus ring-opening to the nitro-acetophenone diazonium salt (IX), followed by ring closure in a Borsche reaction does not occur.

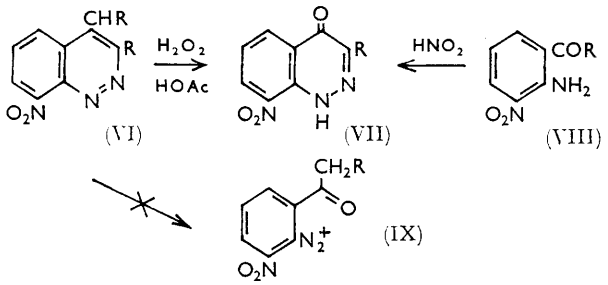
The formation of diazinones during the peroxidation of diazines occurs [9a] with pyrimidines, quinazolines,

Reactions with Hydrogen Peroxide.—The above alkylcinnolines were synthesised because the di-*N*-oxide is apparently formed [1,3] from 4-methylcinnoline as a stepwise process, and thus the introduction of a second oxygen atom should be facilitated by electron-releasing substituents; curiously only the mono-*N*-oxides have so far been identified from the reaction of 4-methoxycinnoline [7] with monoperphthalic acid. Treatment of the alkylcinnolines with hydrogen peroxide in acetic acid (30% w/w) gave products which extracted from neutral solution and were analysed by ^{1}H n.m.r. spectroscopy; the 8-proton in the *N*-oxides showed characteristic shifts relative to that in the parent cinnoline: 1-oxide and 1,2-dioxide downfield, and 2-oxide upfield (a detailed analysis of these shifts will be given elsewhere).

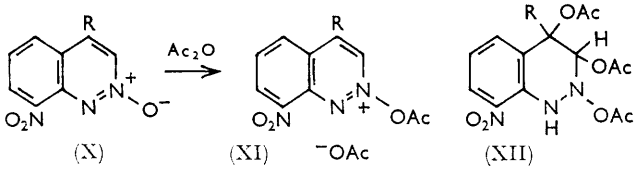
The mixtures were separated by chromatography on alumina and/or fractional crystallisation. In the reactions with the cinnolines (IIa, c, and d) the 1- to 2-oxide ratio was 1 : 2·5, and only the 4-methyl compound gave the dioxide [ratio 1 : 2·5 : 0·25 for (III), (IV), and (V)

[5] I. Suzuki, T. Nakashima, and N. Nagasawa, *Chem. and Pharm. Bull.* (*Japan*), 1966, **14**, 816.
[6] M. H. Palmer and P. S. McIntyre, to be published.
[7] I. Suzuki and T. Nakashima, *Chem. and Pharm. Bull.* (*Japan*), 1964, **12**, 619.
[8] I. Suzuki, T. Nakashima, and N. Nagasawa, *Chem. and Pharm. Bull.* (*Japan*), 1965, **13**, 713.
[9] M. H. Palmer, 'The Structure and Reactions of Heterocyclic Compounds,' Edward Arnold, London, 1967, (*a*) pp. 81, 189, 195; (*b*) pp. 54, 164; (*c*) pp. 152, 125.

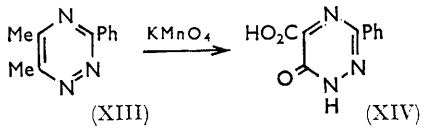
and quinoxalines; these products seem to result from nucleophilic substitution on the (possibly protonated) azine followed by oxidation. This mechanism will



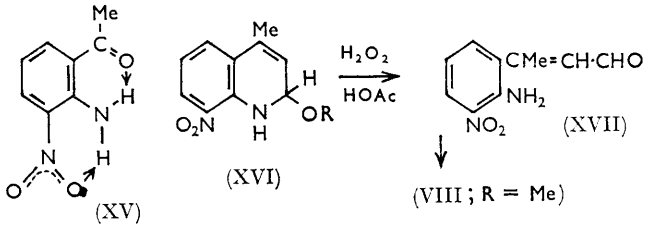
account for the formation [8] of the cinnolinone (VII; R = H) from 8-nitrocinnoline, but alternative mechanisms are (*a*) a 2,4-rearrangement of the 2-acetoxy- (or acetylperoxy-) cinnolinium salt (XI; R = H) as in the rearrangement [9b] of isoquinoline *N*-oxide to 4-hydroxy-



isoquinoline in the presence of toluene-*p*-sulphonyl chloride, or (*b*) formation of a 1,2,3,4-tetrahydrocinnoline derivative (XII) [by analogy with the bromination of isoquinolines (*etc.*) in acetic acid] and then further oxidation and hydrolysis. In both cases the characteristic reaction is migration of the *N*-substituent to a position *meta* to the reacting nitrogen atom.[9c] Such mechanisms do not in themselves account for the loss of the 4-substituent in the present reactions, unless this occurs before the nucleophilic substitution. The high reactivity of the 4-alkyl group towards oxidation is used in the synthesis of cinnoline by way of its 4-carboxy-derivative (II; R = 4-CO_2H). However, the ring of the latter is stable to hydrogen peroxide (*cf.* formation of the 2-oxide above), although the presence of an 8-nitro-group may facilitate decarboxylation. The failure of the 3-nitro-group (II; R = 4-Me, 3-NO_2) to behave like the 8-nitro-compound (II; R = 4-Me, 8-NO_2) can best be accounted for by stabilisation of the former through the 1-oxide. Stepwise oxidation of the side-chain to ketone (or aldehyde) followed by a Dakin reaction may be indicated by the reaction of crude 4-t-butyl-8-nitrocinnoline (IIf), where a product containing the t-butyl group was obtained; unfortunately this could not be fully characterised. The loss of a methyl group and substitution by a ' hydroxy-'group is not restricted to peroxide oxidation systems; various methyldiphenyl- and phenyldimethyl-1,2,4-triazines are oxidised to the triazinones [*e.g.* (XIII) ⟶ (XIV)] by permanganate ions,[10] and the mechanisms of the cinnoline and triazine processes could be similar. However, the major feature consistent with the participation of the 2-oxide (X; R = Me) as intermediate is the observation that (X; R = H) is formed from 8-nitrocinnoline, and the 4-alkyl group should not suppress its rate of formation relative to nucleophilic attack at the 4-position.

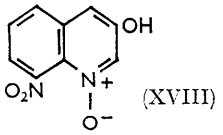


In an endeavour to assess the role of N-2 in these reactions, 4-methyl-8-nitroquinoline was treated with hydrogen peroxide in acetic acid under similar conditions to the cinnolines. Chromatography of the crude product gave a compound, slightly volatile in benzene vapour, which showed i.r. absorptions at 1730 (C=O) and 3300 (NH_2) cm.$^{-1}$; its ^{1}H n.m.r. spectrum ($CDCl_3$) had signals at τ 7·4 (s), 3·35 (t, J 8 c./sec.), 1·65 and 1·9 (two *ortho–meta* quartets, J 8 and 2 c./sec.), and 1·1 (NH_2). The evidence for the 1,2,3-trisubstituted benzene structure and synthesis showed the compound to be 2-amino-3-nitroacetophenone (VIII; R = Me); it is not readily extracted from benzene by strong hydrochloric acid, and this together with its volatility suggests a highly intramolecular hydrogen-bonded structure (XV). The



amino-ketone (XV) probably also arises from a preliminary 1,2-addition to give (XVI; R = H or Ac), ring-chain tautomerism to the amino-aldehyde (XVII), and oxidation to the amino-ketone (VIII).

In contrast, 8- and 6-nitroquinolines have been reported [11] to give the *N*-oxide and the 3-hydroxy-derivative (XVIII) of the *N*-oxide. Again the substitution *meta* to the nitrogen atom is reminiscent of the halogenation reactions in acetic acid, and may indicate the intermediate formation of a tetrahydroquinoline derivative of type (XII) arising from the dihydro-compound [*cf.* (XVI)].



EXPERIMENTAL

Nuclear magnetic resonance spectra were recorded with a Perkin-Elmer R-10 (60 Mc./sec.) instrument, i.r. spectra

[10] R. Metze and S. Meyer, *Chem. Ber.*, 1957, **90**, 481.
[11] E. Ochiai, C. Kaneko, I. Shimada, Y. Murata, T. Kosuge, S. Miyashita, C. Kawasaki, *Chem. and Pharm. Bull.* (*Japan*), 1960, **8**, 126.

were recorded with a Unicam SP 200, and u.v. spectra with a Unicam SP 700. Alumina for chromatography was Spence type H.

4-Ethyl-3-methylcinnoline.—Addition of methyl anthranilate (75 g.) to the Grignard reagent from ethyl bromide (215 ml.) in ether (1800 ml.) gave 3-(2-aminophenyl)pentan-3-ol (100%), m.p. 58—59°, $\nu_{max.}$ 3300—3500 cm.$^{-1}$ (NH_2), τ (CCl_4) 3·3 (4H, m), 6·05 (s, NH_2 and OH), 8·15 (4H, q, *J* 8 c./sec.), and 9·25 (6H, t, *J* 8 c./sec.). The alcohol (85 g.) was dehydrated by boiling with phosphoric oxide (180 g.) in benzene (900 ml.) to give the crude olefin (I; R^1 = Et, R^2 = Me), $\nu_{max.}$ 3400 and 3500 cm.$^{-1}$ (NH_2), the n.m.r. spectrum (integration ratio aromatic–olefinic–methylene–methyl 4 : 1 : 2 : 6) of which showed the presence of a *cis–trans* mixture. Diazotisation of the amino-olefin (51 g.) in 6·5N-hydrochloric acid (380 ml.) at −10° for 3 days, and extraction of the basic oil with boiling light petroleum (b.p. 60—80°) gave the *cinnoline* (25 g.), m.p. 78° (Found: C, 76·7; H, 6·9; N, 17·0. $C_{11}H_{12}N_2$ requires C, 76·7; H, 7·0; N, 16·3%); for ^{1}H n.m.r. spectrum see Table 1.

Cognate Syntheses.—In a similar way the cinnolines (II; R = 4-Me, R = 4,6-Me_2, R = 4,8-Me_2, R = 6-Br, 4-Me, and R = 3-Me, 4-Et) were prepared. Physical data for the products are in Table 1.

4-t-Butylcinnoline.—Addition of the Grignard reagent from t-butyl chloride (70 g.) to *o*-aminoacetophenone (20 g.) gave, after hydrolysis, an oil (21 g.), the ^{1}H n.m.r. and i.r. spectra of which showed about 60% conversion into the alcohol. After two recyclisations the material showed no carbonyl absorption. The alcohol (20 g.) was recovered unchanged after being heated with phosphoric oxide (40 g.) in benzene (400 ml.), but when heated with potassium hydrogen sulphate (5 g.) at 180° for 1·5 hr. it gave an oil which was chromatographed on alumina to yield an oily mixture (9 g.) of olefinic materials (several absorptions in the 8—9·5 τ region). Diazotisation in 2N-hydrochloric acid and chromatography of the basic oil obtained on alumina gave the cinnoline as an oil (2·5 g.) which was nitrated without further purification (see Table 1 for ^{1}H n.m.r. spectrum).

4-Ethyl-3-methyl-8-nitrocinnoline.—The ethylmethylcinnoline (II; R = 3-Me, 4-Et) (7·3 g.) with concentrated sulphuric acid (35 ml.) and nitric acid (*d* 1·5; 2·3 ml.) below 0° gave the *nitro-compound* (7·7 g.), m.p. 102—103° (Found: C, 60·9; H, 4·8; N, 19·4. $C_{11}H_{11}N_3O_2$ requires C, 60·8; H, 5·1; N, 19·3%).

Cognate Preparations.—In a similar way the cinnolines (II; R = 4-Me, R = 3,4-Me_2, and R = 4-Bu^t) were converted into their 8-nitro-derivatives. Physical data for the products are given in Table 1.

Peroxidation Reactions.—Typical procedures for the peroxidation of alkyl- and alkylnitro-cinnolines are given for 4-methyl- and 4-ethyl-3-methyl-8-nitro-cinnolines. The physical constants for the oxides are given in Table 2.

4-Methylcinnoline 1-Oxide, 2-Oxide, and 1,2-Dioxide.—4-Methylcinnoline (10 g.) with acetic acid (50 ml.) and 30% hydrogen peroxide (25 ml.) was heated at 70° for 3 hr. The solution was evaporated to half volume, more peroxide (25 ml.) and acetic acid (25 ml.) were added, and the mixture was heated for 3 hr. more. It was then evaporated to half volume, neutralised with sodium carbonate, and extracted with chloroform (3 × 100 ml.). The extract was washed with ferrous sulphate solution and gave a solid (7 g.), the ^{1}H n.m.r. spectrum of which showed the presence of *N*-oxide functions at N-1 and N-2. Chromatography on alumina gave (*a*) 4-methylcinnoline 1-oxide (1·3 g.), m.p. 94—95° (lit.,[12] 95—96°) by elution with benzene–light petroleum (b.p. 60—80°); (*b*) 4-methylcinnoline-2-oxide (3·5 g.), m.p. 147—148° (lit.,[12] 150—151°) by elution with chloroform–benzene (25% v/v); and (*c*) *4-methylcinnoline 1,2-dioxide* (0·35 g.), m.p. 171—172° (Found:

TABLE 1

Physical data for cinnolines (II)

R	M.p.	^{1}H N.m.r. absorptions (τ values) 3-H	4-H	5-H	6-H	7-H	8-H
4-Me	72° [a]	1·0 [b,c]	7·42	2·25 [d]	2·25 [d]	2·25 [d]	1·6 [e]
4,6-Me_2	75—76	0·95 [b,c]	7·35	2·40	7·40	2·40	1·65 [g]
4,8-Me_2	90—91 [h]	1·00 [b,c]	7·38	2·45 [i]	2·45 [i]	2·45 [i]	7·08
3,4-Me_2	119—120 [j]	7·12 [b]	7·42	2·25 [d]	2·25 [d]	2·25 [d]	1·65 [e]
6-Br, 4-Me	128—129 [k]	0·95 [b,c]	7·35	1·95 [l]		2·18 [g,l]	1·65 [g]
3-Me, 4-Et	78 [m]	7·12 [b]	7·0,[n] 8·75 [o]	2·35 [d]	2·35 [d]	2·35 [d]	1·72 [e]
4-CMe_3	Oil [p]	0·8 [b]	8·35	1·55 [i]	2·25	2·25 [i]	1·55 [i]
4-Me, 8-NO_2 ...	136 [q]	0·7 [r,c]	7·24	2·0 [i]	2·0 [i]	2·0 [i]	
4-Et, 3-Me, 8-NO_2	102—103 [s]	7·02 [r]	6·85,[n] 8·70 [o]	1·95 [l,t]	2·15 [u]	1·65 [l,]	
3,4-Me_2, 8-NO_2	150—151 [v]	7·02 [r]	7·31	2·00 [l,t]	2·25 [u]	1·77 [l,t]	
4-Bu^t, 8-NO_2 ...	195	2·0 [w]	8·35	2·0 [i]	2·0 [i]	2·0 [i]	
4-Me, 3-NO_2 ...	182 [x]		7·15 [r]	1·9 [i]	1·9 [i]	1·9 [i]	1·35 [e]

[a] C. M. Atkinson and J. C. E. Simpson (*J. Chem. Soc.*, 1947, 808) give m.p. 72—73°. [b] In CCl_4. [c] Poorly defined 1:3:3:1 quartet (*J* 1·0 c./sec.) which on irradiation of the 4-methyl signal collapsed to a singlet. [d] Centre of multiplet of ABC part of ABCX spectrum—approximate chemical shifts only. [e] Characteristic X part of ABCX spectrum. [f] Found: C, 75·8; H, 6·3; N, 17·4. $C_{10}H_{10}N_2$ requires C, 76·0; H, 6·3; N, 17·7%. [g] Doublet, *J* 9 c./sec. [h] Found: C, 76·1; H, 6·2; N, 17·6. $C_{10}H_{10}N_2$ requires C, 76·0; H, 6·3; N, 17·7%. [i] Degenerate multiplets which are not interpretable at 60 Mc./sec. [j] D. I. Haddlesey, P. A. Mayor, and S. S. Szinai (*J. Chem. Soc.*, 1964, 5269) give m.p. 119—120°. [k] Found: C, 48·4; H, 3·1; Br, 35·8; N, 12·4. $C_9H_7BrN_2$ requires C, 48·4; H, 3·1; Br, 35·8; N, 12·6%. [l] Doublet *J ca.* 2 c./sec. [m] Analytical data in text. [n] Quartet, *J* 7 c./sec. [o] Triplet, *J* 7 c./sec. [p] Nitrated without further purification. [q] L. Mackenzie and C. S. Hamilton (*J. Org. Chem.*, 1951, **16**, 1414) give m.p. 137—138°. [r] In $CDCl_3$. [s] Found: C, 60·9; H, 4·8; N, 19·4. $C_{11}H_{11}N_3O_2$ requires C, 60·8; H, 5·1; N, 19·3%. [t] Doublet, *J* 8 c./sec. [u] Triplet, *J* 8 c./sec. [v] Found: C, 58·8; H, 4·4; N, 19·8. $C_{10}H_9N_3O_2$ requires C, 59·1; H, 4·5; N, 20·7%. [w] In CF_3CO_2H. [x] H. E. Baumgarten and M. R. de Brunner (*J. Amer. Chem. Soc.*, 1954, **76**, 3489) give m.p. 183°.

[12] M. Ogata, H. Kano, and K. Tori, *Chem. and Pharm. Bull.* (*Japan*), 1963, **11**, 1123, 1527.

TABLE 2

Physical data for cinnoline oxides

R	M.p.	^{1}H N.m.r. spectra (τ values) 3-H	4-H	5-H	6-H	7-H	8-H
1-Oxides (III)							
4,6-Me_2...	160—161 [a]	1·90	7·40	2·40	7·44	2·40	1·45
4-Me.....	94—95 [b]	1·83	7·42	←	2·3 [c]	→	1·33
H	107 [d]	1·80	2·53	←	2·3 [c]	→	1·33
4-Me, 3-NO_2	170		7·0	←	1·70 [c]	→	1·10 [f]
2-Oxides (IV)							
H	126 [d]	1·80	1·90	←	2·3 [c]	→	
4-Me.....	147—148 [b]	1·90	7·38	←	2·3 [c]	→	
4,6-Me_2...	230—231 [g]	1·90	7·40	2·35	7·42	2·35	2·20
3-Me, 4-Et	98—99 [h]	7·35	6·88, 8·35	←	2·30 [c]	→	
3,4-Me_2...	160—161 [i]	7·4	7·40	←	2·37 [c]	→	
4-CO_2H	242 [j]	1·40 [k]		←	2·10 [c]	→	
1,2-Dioxides							
4-Me ...	171—172 [l]	1·90	7·40	←	2·20 [c]	→	1·70
3-Me, 4-Et	171—172 [m]	7·32	6·95, 8·70	←	2·20 [c]	→	1·60
3,4-Me_2...	171—172 [n]	7·36	7·36	←	2·30 [c]	→	1·70

[a] Found: C, 68·9; H, 5·8; N, 16·1. $C_{10}H_{10}N_2O$ requires C, 68·9; H, 5·8; N, 16·1%. [b] Ref. 12 gives 1-oxide, m.p. 95—96°; 2-oxide, m.p. 150—151°. [c] Centre of degenerate multiplet. [d] Ref. 12 gives 1-oxide, m.p. 110—111°; 2-oxide, m.p. 125—126°. [e] Found: C, 52·3; H, 3·6; N, 20·3. $C_9H_7N_3O_3$ requires C, 52·7; H, 3·4; N, 20·5%. [f] In CF_3CO_2H. [g] Found: C, 68·6; H, 5·4; N, 16·4. $C_{10}H_{10}N_2O$ requires C, 68·9; H, 5·8; N, 16·1%. [h] Found: C, 70·2; H, 6·4; N, 14·8. $C_{11}H_{12}N_2O$ requires C, 70·2; H, 6·4; N, 14·9%. [i] Found: C, 68·9; H, 5·6; N, 15·6. $C_{10}H_{10}N_2O$ requires C, 68·9; H, 5·8; N, 16·1%. [j] Found: C, 56·4; H, 3·2; N, 15·0. $C_9H_6N_2O_3$ requires C, 56·8; H, 3·2; N, 14·7%. [k] In Me_2SO. [l] Found: C, 61·2; H, 4·5; N, 15·6. $C_9H_8N_2O_2$ requires C, 61·3; H, 4·5; N, 15·9%. [m] Found: C, 64·8; H, 5·7; N, 13·6. $C_{11}H_{12}N_2O_2$ requires C, 64·7; H, 5·9; N, 13·7%. [n] Found: C, 63·3; H, 6·0; N, 14·6. $C_{10}H_{10}N_2O_2$ requires C, 63·1; H, 5·3; N, 14·7%.

C, 61·2; H, 4·5; N, 15·6. $C_9H_8N_2O_2$ requires C, 61·3; H, 4·5; N, 15·9%).

3-Methyl-8-nitrocinnolin-4(1H)-one.— 4-Ethyl-3-methyl-8-nitrocinnoline (7·5 g.) with acetic acid (38 ml.) and 30% hydrogen peroxide (19 ml.) was heated at 70° as before. Evaporation and neutralisation gave the crude cinnolinone contaminated with 5% of the starting cinnoline (from relative abundances of ions at *m/e* 205 and 233 in the mass spectrum). Recrystallisation gave the *cinnolinone* (3·15 g.), m.p. 235—236° (Found: C, 52·4; H, 3·7; N, 20·6. $C_9H_7N_3O_3$ requires C, 52·7; H, 3·5; N, 20·4%), $\nu_{max.}$ ($CHCl_3$) 3350 (NH), 2450 (Me), 1640 (NH–C=C–CO), and 1540 (NO_2) cm.$^{-1}$, τ (CF_3CO_2H) 0·9 and 1·1 (H-5 and -7), 2·25 (H-6), and 7·36 (3-Me), *m/e* (principal ions) 205 (M^+), 190 (M — CH_3), 164 (M — MeCN), 118, 90, 78, and 63.

2-Amino-3-nitroacetophenone.— 4-Methyl-8-nitroquinoline (8·8 g.) in acetic acid (30 ml.) and 30% hydrogen peroxide (8 ml.) was heated at 70—75° for 2·5 hr.; after addition of more hydrogen peroxide (9·5 ml.) the mixture was heated for a further 17 hr. concentrated *in vacuo*, and neutralised with sodium carbonate. It was then extracted with chloroform, and separated into fractions soluble and insoluble in strong alkali. The neutral material, after chromatography on alumina and elution with benzene, gave the acetophenone, m.p. 89—91° (lit.,[13] 92—93°), $\nu_{max.}$ 1730 cm.$^{-1}$, τ ($CDCl_3$) 1·1br (s, NH_2), 1·65 and 1·9 (*ortho* and *meta* quartets, 4- and 6-H), 3·35 (t, *J* 7 c./sec., 5-H), and 7·37 (s, Me); the semicarbazone had m.p. 225—226° (lit.,[13] 223°). The alkali-soluble fraction on acidification gave a solid, m.p. 195—200°, $\nu_{max.}$ 3300 (OH), 1730 (C=O), 1630 (C=C ?), and 1530 (NO_2) cm.$^{-1}$. The compound was very insoluble, but its ^{1}H n.m.r. spectrum (Me_2SO) showed a singlet at τ 7·1 as well as poorly defined aromatic proton resonances. No further identification was possible.

[8/926 *Received, July 2nd,* 1968]

[13] E. Bamberger, *Ber.*, 1915, **48**, 537.