Heteroaromatic Reactivity. Part VI.[1] Kinetics and Products of the Nitration of 4-Hydroxyquinoline, 1-Methyl-4-quinolone, 4-Methoxyquinoline, and 4-Hydroxycinnoline in Sulphuric Acid

By **R. B. Moodie, J. R. Penton,** and **K. Schofield,*** Department of Chemistry, University of Exeter, Exeter

The rates and products of nitration of the title compounds have been measured. The quinoline derivatives react as their conjugate acids, but with 4-hydroxycinnoline the free base may be involved to some extent. Surprisingly large proportions of 1-methyl-3-nitro-4-quinolone are formed from 1-methyl-4-quinolone. The 4-substituents in the cations from 4-hydroxy- and 4-methoxy-quinoline activate C(6) by factors of $3{\cdot}3 \times 10^3$ and $1{\cdot}6 \times 10^3$, and C(8) by factors of 29·5 and 23, respectively, the large effect at C(6) being noteworthy.

THE major product of the nitration of 4-hydroxyquinoline in mixed acid is 4-hydroxy-6-nitroquinoline.[2,3] 4-Hydroxycinnoline likewise gives mainly 4-hydroxy-6-nitrocinnoline, together with some of the 8-nitro-isomer.[4,5] These results, and similar ones obtained with 4-hydroxyquinaldine,[6] led to the suggestion [2,6,7]

[1] Part V, D. H. G. Crout, J. R. Penton, and K. Schofield, *J. Chem. Soc.* (*B*), 1971, 1254.
[2] K. Schofield and T. Swain, *J. Chem. Soc.*, 1949, 1367.
[3] A. Adams and D. H. Hey, *J. Chem. Soc.*, 1949, 255.
[4] K. Schofield and J. C. E. Simpson, *J. Chem. Soc.*, 1945, 512.
[5] J. C. E. Simpson, *J. Chem. Soc.*, 1947, 237.
[6] B. E. Halcrow and W. O. Kermack, *J. Chem. Soc.*, 1945, 415.
[7] K. Schofield, *Quart. Rev.*, 1950, **4**, 382.

that the entities being nitrated were the conjugate acids of the hydroxy-heterocycles.

From the nitration of 4-hydroxyquinoline in nitric acid alone at 95 °C only 4-hydroxy-3-nitroquinoline was isolated,[2] and 1-methyl-4-quinolone also gave the 3-nitro-compound.[8] From 4-hydroxycinnoline under these conditions the major product was still 4-hydroxy-6-nitrocinnoline[4] but a small proportion of the 3-nitro-compound was also produced.[2,9,10] The change in orientation might be due to either nitration of the heterocycles as free bases in nitric acid, or to nitration *via* nitrosation.[2,7]

We now report a study of the kinetics of nitration in sulphuric acid of 4-hydroxyquinoline, 1-methyl-4-quinolone, 4-methoxyquinoline, and 4-hydroxycinnoline, and a quantitative examination of the products formed under these and other conditions.

EXPERIMENTAL

Materials.—Quinolines. For the following compounds, prepared by standard methods, we give the name, solvent used for crystallisation (unless it was ethanol), description, and m.p.: 4-hydroxyquinoline, needles, 201 °C (lit.,[11] 200—201 °C); 4-hydroxy-3-nitroquinoline, brown plates, >325 °C (lit.,[12] >325 °C); 4-hydroxy-6-nitroquinoline, brown plates which powdered to a yellow solid, 325—327 °C (lit.,[3,13] 310—315 and 325 °C); 4-hydroxy-8-nitroquinoline, not recrystallised, 198 °C; 1-methyl-4-quinolone, cream-coloured needles, 152 °C (lit.,[14] 152 °C); 1-methyl-3-nitro-4-quinolone, cream-coloured needles, 227 °C (lit.,[8,15] 227—229 and 219·5—220·5 °C); 1-methyl-6-nitro-4-quinolone, yellow needles, 233 °C (lit.,[16] 233—234 °C); 4-methoxy-3-nitroquinoline, light petroleum (b.p. 40—60 °C), yellow needles, 100 °C (lit.,[15] 99—100 °C); 4-methoxy-8-nitroquinoline, methanol, needles, 182—183 °C (lit.,[16] 180—181 °C).

We failed to prepare 1-methyl-8-nitro-4-quinolone from 4-hydroxy-8-nitroquinoline, using methods which succeed for its isomers.[15,16]

4-Methoxyquinoline.—Sodium (1 g) was dissolved in methanol (20 ml) and the solution was added to another prepared from 4-chloroquinoline (3·7 g) and methanol (10 ml). The mixture was boiled until a sharp peak in its u.v. absorption spectrum at 316 nm disappeared (20 h; according to the literature[11] the reaction requires 3 h). The solvent was removed and a solution of the residue in 0·1N-sodium hydroxide (25 ml) was extracted continuously with ether for 24 h. Distillation of the dried ($MgSO_4$) extract gave 4-methoxyquinoline, b.p. 124 °C/0·8 mm. Further purification by column chromatography [silica gel (2 × 30 cm), elution with 1 : 1 benzene–chloroform] gave the product as a white solid (1·5 g) which was stored in absolute alcohol in the dark.

Cinnolines.—These are described in the same way as the quinolines. 4-Hydroxycinnoline, acetic acid, fawn solid, 235—236 °C (lit.,[4] 233·5—234 °C); 4-hydroxy-3-nitrocinnoline, not recrystallised, 285 °C (lit.,[10] 284·5—285·5 °C); 4-hydroxy-5-nitrocinnoline, fawn needles, 306 °C (lit.,[9] 304—305 °C); 4-hydroxy-6-nitrocinnoline, acetic acid, red-brown needles, >325 °C (lit.,[4] 330—331 °C); 4-hydroxy-7-nitrocinnoline, pale yellow needles, 295 °C (lit.,[9] 295—296 °C); 4-hydroxy-8-nitrocinnoline, yellow needles, 187 °C (lit.,[5] 185·5—186 °C).

Kinetic Methods.—Stock solutions (1—3 × 10^{-3}M) of 4-hydroxyquinoline, 1-methyl-4-quinolone, and 4-methoxyquinoline in ethanol were prepared. Samples (1 ml) were transferred to 10 ml graduated flasks, the solvent was removed, and the flasks were filled to the mark with sulphuric acid of the appropriate concentration. Samples (5 ml) of these solutions were thermally equilibrated with solutions of nitric acid in sulphuric acid of the required concentration, and the solutions were then thoroughly mixed. Rates of nitration for 4-hydroxyquinoline, 1-methyl-4-quinolone, and 4-methoxyquinoline were measured by following the increases in absorbance at 350, 350, and 334 nm, respectively.

For 4-hydroxycinnoline the small difference in the absorption spectra of the protonated form of the substrate and of 4-hydroxy-6-nitrocinnoline, the major product of nitration made the above method unsuitable. The following describes a typical run for this compound: a solution of 4-hydroxycinnoline (8·4 × 10^{-3}M) in 82·9% sulphuric acid (100 ml) was prepared in a 250 ml graduated flask by shaking the flask and its contents for 30 min. After equilibration at 25 °C for 20 min nitric acid (10 ml) was added. The solution was kept in a thermostat at 25 °C and samples (5 ml) were withdrawn at 10 min intervals and transferred to 500 ml graduated flasks containing water. The flasks were filled to the mark, and the absorbance of each solution was measured at 366 nm, water being used as a blank.

Chromatographic Methods.—Thin-layer chromatography (t.l.c.) was performed on glass plates coated with silica gel GF_{254} (Merck) or aluminium oxide G (Merck) in conjunction with the following solvent systems: (A) chloroform–methanol–benzene (9 : 1 : 2); (B) chloroform–methanol (1 : 1); (C) chloroform–methanol (1 : 2); (D) chloroform; (E) benzene–ether (1 : 3). Where stated Eastman Chromagram sheet 6060 (silica gel with fluorescent indicator) or 6062 (aluminium oxide) was used. R_F values obtained with Chromagram sheet are listed in Table 1. Similar values were obtained with glass plates.

Isomer Proportions.—The following method was used for determining isomer proportions formed in the nitrations of 4-hydroxyquinoline, 1-methyl-4-quinolone, and 4-methoxyquinoline.

Solutions of the substrates (see Table 4) and nitric acid in sulphuric acid of the required concentration were equilibrated at 25 °C for 10 min, thoroughly mixed, and kept for 9 half-lives. The solution was poured on ice and the mixture was basified at <10 °C to *ca.* pH 7 with 5N-sodium hydroxide. Continuous extraction with chloroform (3 days), drying ($MgSO_4$), and removal of chloroform gave a solid which was dissolved in AnalaR acetone. Samples were applied to thin layer plates (silica gel, 10 × 20 cm) and

[8] J. R. Price, *Austral. J. Sci. Res.*, 1949, *A2*, 272.
[9] K. Schofield and R. S. Theobald, *J. Chem. Soc.*, 1949, 2404.
[10] H. E. Baumgarten, *J. Amer. Chem. Soc.*, 1955, **77**, 5109.
[11] G. F. Tucker and J. L. Irvin, *J. Amer. Chem. Soc.*, 1951, **73**, 1923.
[12] G. B. Bachman, D. E. Welton, G. L. Jenkins, and J. E. Christian, *J. Amer. Chem. Soc.*, 1947, **69**, 368.
[13] G. B. Bachman and D. E. Cooper, *J. Org. Chem.*, 1944, **9**, 302.
[14] 'Dictionary of Organic Compounds,' Eyre and Spottiswoode, London, 1965.
[15] W. J. Adams and D. H. Hey, *J. Chem. Soc.*, 1951, 1521.
[16] J. C. E. Simpson and P. H. Wright, *J. Chem. Soc.*, 1948, 1707.

development carried out with the appropriate solvent system. The bands were removed from the plates and extracted with ethanol. The solutions were filtered and the silica was washed with more ethanol. Filtrates and washings were combined and transferred to graduated flasks, which were filled to the mark with ethanol. The u.v. absorption spectrum of each solution was measured.

TABLE 1

Compound	Support *	Solvent system	R_F
4-Hydroxyquinoline	F	B	0·40
4-Hydroxy-3-nitroquinoline	G	A	0·49
4-Hydroxy-3-nitroquinoline	F	B	0·30
4-Hydroxy-6-nitroquinoline	G	A	0·53
4-Hydroxy-6-nitroquinoline	F	B	0·84
4-Hydroxy-8-nitroquinoline	G	A	0·73
4-Hydroxy-8-nitroquinoline	F	B	0·92
1-Methyl-3-nitro-4-quinolone	G	C	0·68
1-Methyl-6-nitro-4-quinolone	G	C	0·53
4-Methoxy-3-nitroquinoline	G	D	0·69
4-Methoxy-6-nitroquinoline	G	D	0·48
4-Methoxy-8-nitroquinoline	G	D	0·59
4-Hydroxy-3-nitrocinnoline	G	E	0·10
4-Hydroxy-5-nitrocinnoline	G	E	0·16
4-Hydroxy-6-nitrocinnoline	G	E	0·21
4-Hydroxy-7-nitrocinnoline	G	E	0·33
4-Hydroxy-8-nitrocinnoline	G	E	0·50

* F = Alumina; G = silica gel.

A similar method was used in the case of 4-hydroxycinnoline, but the insolubility of 4-hydroxy-6-nitrocinnoline made special precautions necessary. After 10 half-lives of the nitration the reaction solution was poured into ice–water (50 ml) contained in a continuous extractor for use with chloroform. Extraction was carried on overnight and the extract was adjusted to a volume of 1 l. Samples of this solution were then applied to thin-layer plates (20 × 20 cm, silica gel, solvent system E) and treated as described above. The bands containing the 6- and 8-nitro-compounds were removed and these isomers determined in the usual manner. The remainder of the chloroform extract was concentrated (*ca.* 15 ml) and the precipitate was collected and washed with chloroform. T.l.c. showed the solid to be pure 4-hydroxy-6-nitrocinnoline. The filtrate and washings were made up to 25 ml and samples (5 ml) were chromatographed as before. Bands containing the 3-, 5-, and 7-nitro-compounds were removed and extracted with chloroform. Each extract was concentrated to *ca.* 1 ml and chromatographed 3—4 times until the pure compounds were obtained. Concentrations were determined spectroscopically.

The necessary spectroscopic data have been reported for 4-hydroxyquinoline,[17] 4-hydroxy-6-nitroquinoline,[17] 1-methyl-4-quinolone,[17] 1-methyl-3-nitro-4-quinolone,[8] 1-methyl-6-nitro-4-quinolone,[17] 4-methoxyquinoline,[17] 4-methoxy-6-nitroquinoline,[17] 4-hydroxycinnoline,[17] and 4-hydroxy-3-nitrocinnoline.[10] We report data ($\lambda_{max.}$/nm; log $\varepsilon_{max.}$ for ethanolic solutions) for 4-hydroxy-3-nitroquinoline (240, 313, 340; 4·07, 3·97, 3·82), 4-hydroxy-8-nitroquinoline (259, 386; 4·07, 3·97), 4-methoxy-3-nitroquinoline (253, 287, 335; 4·28, 3·84, 3·44), 4-methoxy-8-nitroquinoline (291, 310; 3·80, 3·68), 4-hydroxy-5-nitrocinnoline (234, 240, 249, 287, 298, 339, 350; 4·04, 4·06, 4·01, 3·62, 3·70, 4·03, 4·01), 4-hydroxy-6-nitrocinnoline (235, 265, 321, 365; 4·21, 3·93, 3·91, 4·04), 4-hydroxy-7-nitrocinnoline (239, 262, 304, 315, 369; 4·19, 4·12, 3·87, 3·87, 3·81), and 4-hydroxy-8-nitrocinnoline (229, 252, 389; 4·16, 4·00, 3·98).

The spectra of the following compounds ($\lambda_{max.}$/nm; log $\varepsilon_{max.}$) were determined in 81·45% sulphuric acid: 4-hydroxycinnoline (305, 342; 3·54, 3·69); 1-methyl-4-cinnolone (307, 343; 3·38, 3·62); and 4-hydroxy-2-methylcinnolinium hydroxide anhydro-base (298, 309, 349; 3·48, 3·50, 3·75). In the same order the spectra of these compounds also showed the following minima: (275, 314; 3·07, 3·45); (277, 313; 2·87, 3·33); (284, 303, 317; 3·31, 3·45, 3·38).

Qualitative Nitrations.—To a solution of 4-hydroxyquinoline (2 g) in 98% sulphuric acid (9 ml) at 0 °C was added during 45 min a solution of nitric acid (2 ml, *d* 1·42) in 98% sulphuric acid (2 ml). The solution was kept at 0 °C for 90 min more and at room temperature for 24 h, and then poured on ice (30 g). Neutralisation with ammonia, washing the precipitate with water, and drying gave a yellow solid (1·96 g, m.p. 265—280 °C). It was boiled with ethanol (1 l) for 1 h, and after cooling the solid was collected. Examination of the solid and of the filtrate by t.l.c. (Chromagram sheet 6060, solvent system A) showed the former to be 4-hydroxy-6-nitroquinoline and the latter to contain both the 6- and 8-nitro-compounds. Evaporation of the filtrate to *ca.* 10 ml gave more of the 6-nitro-compound, which was collected. The remaining filtrate was applied to a thick layer plate (20 × 20 cm, silica gel) which was developed with solvent system A. The bands corresponding to the 6- and 8-nitro-compounds were removed and extracted with chloroform. Working up in the usual way gave 4-hydroxy-8-nitroquinoline, m.p. 201° (decomp.) (25 mg), and 4-hydroxy-6-nitroquinoline, m.p. >325 °C (1·71 g *total*).

When nitration was carried out with nitric acid alone, with or without the addition of urea, the only products detected by chromatography were 4-hydroxy-6- and 4-hydroxy-3-nitroquinoline.

1-Methyl-4-quinolone (1·5 g) was nitrated in sulphuric acid by the method described above. The product (0·93 g, m.p. 239—243 °C) was boiled with ethanol (100 ml) for 1 h and the undissolved solid, m.p. 226 °C, was collected. Examination of the solid by t.l.c. (Chromagram sheet 6060, solvent system C) showed it to be mainly 1-methyl-6-nitro-4-quinolone. The filtrate contained the 3- and 6-nitro-compounds, accompanied by a number of unidentified substances.

RESULTS

The observed second-order rate constants are given in Table 2 and the Arrhenius parameters in Table 3. Sulphuric acid concentrations are corrected for water added with the nitric acid but not for that formed by ionisation of the nitric acid. Isomer proportions, recorded in Table 4 are, in general, means of two separate determinations.

For 4-hydroxy-3- and 4-hydroxy-6-nitroquinoline only a partial separation could be achieved by t.l.c. (silica gel, solvent system A). When the nitration product was examined by use of Chromagram sheet 6062 (solvent system B) no 4-hydroxy-3-nitroquinoline was observed. Attempts to detect this isomer on plates coated with alumina failed because of tailing of the band due to 4-hydroxy-6-nitroquinoline. In mixtures of known composition the 3-nitro-isomer (<2%) was easily detectable, and in view of these

[17] J. M. Hearn, R. A. Morton, and J. C. E. Simpson, *J. Chem. Soc.*, 1951, 3318.

TABLE 2

Nitrations in sulphuric acid

Compound	10^2[HNO_3]/ M	% H_2SO_4	T/ °C [a]	10^2k_2/ l mol^{-1} s^{-1}
4-Hydroxyquinoline [b]	5·3	80·7	25	0·691
	5·3	81·4	25	1·27
	5·3	81·4	35	2·59
	2·1	81·4	45	5·58
	2·1	83·2	25	6·98
	0·84	84·4	25	17·8
	0·42	85·4	25	52·9
1-Methyl-4-quinolone [b]	53	77·4	25	0·0165
	5·3	81·4	25	0·492
	5·3	81·4	35	1·03
	5·3	81·4	45	2·06
	2·1	83·9	25	4·24
	0·84	85·7	25	1·94
4-Methoxyquinoline [c]	5·3	81·4	25	0·6305
	5·3	81·4	35	1·31
	5·3	81·4	45	2·72
	5·7	82·6	25	2·07
	1·1	84·2	25	7·99
	1·1	85·1	25	19·3
4-Hydroxycinnoline [d]	144	81·2	25	0·0036
	144	81·2	35	0·0110
	144	81·2	45	0·0310
	144	82·9	25	0·0131
	75	84·4	25	0·0404
	16	85·6	25	0·1026

[a] ±0·2 °C. [b] [4-Hydroxyquinoline] = *ca.* $2·5 \times 10^{-4}$M. [c] [4-Methoxyquinoline] = *ca.* $1·7 \times 10^{-4}$M. [d] [4-Hydroxycinnoline] = *ca.* $8·0 \times 10^{-3}$M.

TABLE 3

Arrhenius parameters

Compound	% H_2SO_4	$\log_{10}$ (A/s^{-1})	E/kJ mol^{-1}
4-Hydroxyquinoline	81·4	8·3	59
1-Methyl-4-quinolone	81·4	7·9	59
4-Methoxyquinoline	81·4	8·0	59
4-Hydroxycinnoline	81·2	10·7	85

observations was assumed to be absent from the nitration mixture.

Preliminary investigations of the nitration of 1-methyl-4-quinolone showed that considerable decomposition occurred. In the experiments recorded in Table 4 conditions were adjusted to minimise this decomposition; basification was carried out so that the temperature did not rise above 0 °C, and light was excluded during the continuous extraction with chloroform. However, when samples of the nitration mixtures were applied in acetone to plates of silica gel and developed with solvent system C seven bands were observed, two corresponding to the 3- and 6-nitro-isomers. It is possible that 1-methyl-8-nitro-4-quinolone may have been formed but our failure to prepare this compound precluded its identification. When samples of 1-methyl-3- and 1-methyl-6-nitro-4-quinolone were dissolved in 84·1% sulphuric acid, and the solutions were treated as in the working up of a nitration, t.l.c. revealed no decomposition. Pseudo-first-order rate constants were, in general, calculated by the method of Guggenheim. However, in several experiments good, stable infinity readings were observed. It is, therefore, unlikely that decomposition of the nitro-product occurs *in situ*, but it is clear that the precise significance of the isomer proportions given in Table 4 for the nitration of 1-methyl-4-quinolone is doubtful.

T.l.c. showed that the nitration of 4-methoxyquinoline in 80·2 and 84·9% sulphuric acid gave only 4-methoxy-8- and 4-methoxy-6-nitroquinoline, the latter being identified by its u.v. spectrum.

From the nitration of 4-hydroxycinnoline in 84·9% sulphuric acid, t.l.c. revealed the formation of an unidentified compound (R_F 0·6), shown by u.v. spectroscopy to represent *ca.* 5% of the product.

DISCUSSION

4-Hydroxyquinoline and its Derivatives.—Application of the usual criteria [18] verifies the earlier conclusions regarding the nature of the substrate being nitrated. Thus, plots of $\log_{10} k_2$ against $-(H_R + \log_{10} a_w)$ (where w stands for H_2O) for 4-hydroxyquinoline, 4-methoxyquinoline, and 1-methyl-4-quinolone have slopes of 1·0, 1·0, and 0·97 respectively (Figure), as would be expected for reaction of the majority (cationic) species. The Arrhenius parameters are consistent with nitration of the conjugate acids. At a given acidity the similarity of the second-order rate constants for the nitrations of the quinolones and 4-methoxyquinoline support other evidence [19] for the view that the cations of these com-

TABLE 4

Proportions of isomers formed in the nitrations of 4-hydroxyquinoline, 1-methyl-4-quinolone, 4-methoxyquinoline, and 4-hydroxycinnoline in sulphuric acid at 25 °C

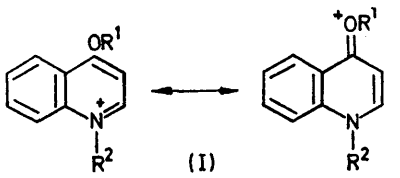
Compound	Substrate soln./ml	Concn. of substrate soln./M	HNO_3 soln./ml	Concn. of HNO_3 soln./M	% H_2SO_4	Nitro-compound/% 3	5	6	7	8	Total yield/%
4-Hydroxyquinoline	10	$5·8 \times 10^{-3}$	2	0·63	80·2			81·0		19·0	98
	10	$5·5 \times 10^{-3}$	1	0·63	81·4			80·8		19·2	96
	10	$5·3 \times 10^{-3}$	1	0·63	82·6			81·4		18·6	95
	10	2×10^{-3}	2	0·13	84·1			78·5		21·5	
1-Methyl-4-quinolone	10	3×10^{-2}	1	5·12	74·9	13·8		86·2		?	63
	10	$1·4 \times 10^{-2}$	1	1·58	80·2	4·5		95·5		?	82
	10	$1·4 \times 10^{-3}$	0·5	0·32	84·1	6·0		94·0		?	77
4-Methoxyquinoline	10	5×10^{-3}	1	1·57	80·2			72·3		27·7	89
	10	2×10^{-3}	2	0·13	84·9			73·9		26·1	97
4-Hydroxycinnoline	15	$1·8 \times 10^{-2}$	1	*a*	84·9	0·96	0·38	58·4	0·36	39·9	90

[a] *d* 1·42; 5% of an unidentified compound was also formed.

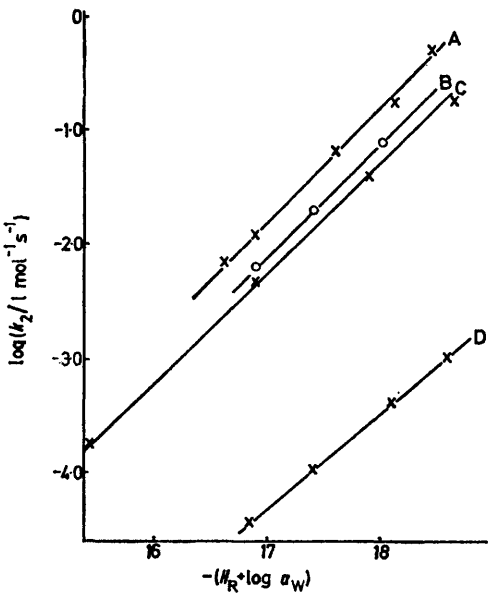
[18] J. G. Hoggett, R. B. Moodie, J. R. Penton, and K. Schofield, 'Nitration and Aromatic Reactivity,' ch. VIII, Cambridge Univ. Press, 1971.

[19] A. R. Katritzky and J. M. Lagowski, in 'Advances in Heterocyclic Chemistry,' vol. 1, Academic Press, New York, 1963; A. R. Katritzky, *Chimia*, 1970, **24**, 134.

pounds are of the type (I; $R^1 = R^2 = H$; $R^1 = Me$, $R^2 = H$; $R^1 = H$, $R^2 = Me$).



Application of the encounter rate criterion [18] (Table 5) eliminates the possibility that nitration involves the free base in the case of 4-methoxyquinoline, but for the other



Variation of the rate of nitration with acidity at 25 °C; A, 4-hydroxyquinoline; B, 4-methoxyquinoline; C, 1-methyl-4-quinolone; D, 4-hydroxycinnoline

TABLE 5

Comparison of the observed second-order rate constants for nitration with the calculated encounter rate constants for nitration *via* the free base in 81·4% sulphuric acid at 25 °C

Compound	$\log_{10}[k_2$(obs.)/ l mol^{-1} s^{-1}]	$\log_{10}[k_2$ (calc.)/ l mol^{-1} s^{-1}] [a]
4-Hydroxyquinoline	−1·90	−5·03, −2·16
4-Methoxyquinoline	−2·20	−9·41, −6·54
1-Methyl-4-quinolone	−2·31	−5·22, −2·35
4-Hydroxycinnoline	−2·44 [b]	−2·49, [b] 0·38 [b]

[a] The first column from H_0, the second column from H_A. [b] In 81·2% sulphuric acid.

two compounds is not decisive, because of the rather large uncertainty in k_2 (calc), the rate constant estimated for a reaction which occurred at every encounter of a nitronium ion and a molecule of the free base. The value of k_2 (calc) is derived from the formula (1) where

$$\log k_2 \text{ (calc)} = \log k_2 \text{ (mesitylene)} - pK_a + H_x \quad (1)$$

k_2 (mesitylene) is the rate constant for reaction of mesitylene (a substrate which reacts upon encounter [20]) in the same medium, and is obtained by short extrapolation of published rate constant data [20] to higher acidities. The main source of error comes from lack of knowledge about H_x, the appropriate acidity function for the protonation of the weak base in question. Table 5 reports values derived by use of H_0 and H_A.

For 4-hydroxyquinoline and 4-methoxyquinoline the predominance of 6-nitration supports the evidence adduced above for nitration *via* the cations. For both these compounds reaction of the free bases would be expected to occur to some extent at C(3) because of the directing properties of the hydroxy and methoxy groups. In this respect the case of 1-methyl-4-quinolone is puzzling, the considerable proportion of 3-nitration observed being unexpected in view of the behaviour of the analogous compounds, and of the strong evidence for nitration occurring through the cation.

4-Hydroxycinnoline.—For this compound the situation is not so clear. The slope of the plot of $\log_{10} k_2$ against $-(H_R + \log_{10} a_w)$ is 0·84 (Figure), a value slightly lower than is usually observed for compounds reacting *via* the majority species. The Arrhenius parameters appear at first sight not to be in accord with nitration *via* the cation, but strictly the data required for their evaluation are not available.[18] Application of the encounter rate criterion is unhelpful (Table 5).

The nitration of 4-hydroxycinnoline in sulphuric acid gives significant amounts of 4-hydroxy-3-nitrocinnoline (Table 4). In view of the obvious deactivation of the 3-position, and the fact that no 4-hydroxy-3-nitroquinoline could be detected in the nitration of 4-hydroxyquinoline under similar conditions, it seems likely that the 4-hydroxy-3-nitrocinnoline is formed by nitration of the free base. This conclusion would be consistent with the results of nitrating 4-hydroxycinnoline with nitric acid alone (Experimental section).

TABLE 6

Partial rate factors for nitrations in 80·0% sulphuric acid at 25 °C

	Position				
Compound	3	5	6	7	8
Quinolinium cation *	4·57 $\times 10^{-12}$	1·74 $\times 10^{-7}$	5·58 $\times 10^{-9}$	4·76 $\times 10^{-11}$	1·47 $\times 10^{-7}$
4-Hydroxyquinoline cation			1·84 $\times 10^{-5}$		4·34 $\times 10^{-6}$
4-Methoxyquinoline cation			8·84 $\times 10^{-6}$		3·34 $\times 10^{-6}$
1-Methyl-4-quinolone cation	3·85 $\times 10^{-7}$		8·14 $\times 10^{-6}$		
4-Hydroxycinnoline cation	8·35 $\times 10^{-10}$	3·31 $\times 10^{-10}$	5·08 $\times 10^{-8}$	3·13 $\times 10^{-10}$	3·47 $\times 10^{-8}$

* Ref. 1.

Partial Rate Factors.—Partial rate factors for the nitration of 4-hydroxyquinoline, 1-methyl-4-quinolone, 4-methoxyquinoline, and 4-hydroxycinnoline in 80·05% sulphuric acid at 25 °C are given in Table 6. They were

[20] R. G. Coombes, R. B. Moodie, and K. Schofield, *J. Chem. Soc.* (*B*), 1968, 800.

calculated by use of data for benzene [20] and for *p*-dichlorobenzene.[21] The error involved in the small extrapolation of the rate data for 4-hydroxy- and 4-methoxy-quinoline is negligible. For 4-hydroxycinnoline it has been assumed that the isomer proportions do not vary with acidity, an assumption which the discussion above shows may not be justified. The partial rate factors for C(6) and C(8) should not be much affected.

The hydroxy group is slightly more activating than the methoxy group. Introduction of these substituents at the 4-position of the quinolinium ion activates C(6) by factors of $3{\cdot}3 \times 10^3$ and $1{\cdot}6 \times 10^3$, and C(8) by factors of 29·5 and 23, respectively (Table 6). The greater effect produced at C(6) than at C(8) is not surprising, substitution at the former position involving a structure for which a *para*-quinonoid form can be written as against an *ortho*-quinonoid form in the latter case, but the magnitude of the effect is noteworthy. Comparable data for other systems are lacking.

For the 3-positions in the cations of 4-hydroxy- and 4-methoxy-pyridine and 1-methyl-4-pyridone partial rate factors of *ca.* 10^{-11} have been reported,[22] indicating considerably smaller reactivities than that now reported for C(3) in the cation of 1-methyl-4-quinolone.

For 4-hydroxycinnoline comparison with the cinnolinium ion is possible only if the two cations have similar structures. The dominant monocation of cinnoline is protonated at N(2).[23] However, there is no evidence to indicate the position of the proton in the 4-hydroxycinnolinium ion, although it has been suggested that the tautomerism of 4-hydroxycinnoline involves N(1).[24] Comparison of the u.v. spectra of solutions in sulphuric acid of 4-hydroxycinnoline, 1-methyl-4-cinnolone, and the anhydro-base of 4-hydroxy-2-methylcinnolinium hydroxide could clarify the position, and accordingly these spectra (81·5% sulphuric acid) were measured. Qualitatively the spectra indicated (Experimental section) that the predominant cation from 4-hydroxycinnoline is similar to that from 1-methyl-4-cinnolone, but there are indications of the formation of 4-hydroxy-2-cinnolinium cation though the proportion of this form is difficult to estimate.

Clearly, comparison of the partial rate factors for nitration of the 4-hydroxycinnolinium ion with those for the cinnolinium ion is precluded. If protonation is assumed to occur at N(1) an estimate of the influence of the unprotonated nitrogen atom N(2) in the former on the reactivities of C(6) and C(8) can be made. Comparison (Table 6) of the figures for 4-hydroxyquinolinium with those for 4-hydroxycinnolinium cation show that in the latter C(6) and C(8) are deactivated by factors of *ca.* 360 and 125, respectively. The effect of the unprotonated N(1) upon the cinnolinium cation can be deduced from the partial rate factors for the nitration of the 2-cinnolinium and isoquinolinium [25] cations. Rate data for nitration of 2-cinnolinium cation at 25 °C are not available. However, use of the Arrhenius parameters determined for reaction in 76·14 and 81·1% sulphuric acid,[26] and extrapolation of rate data to 25 °C gives k_2(obs.) $= 5 \times 10^{-7}$ l mol^{-1} s^{-1} for 80·05% sulphuric acid. Assumption of 50% of 8-nitration gives a partial rate factor of *ca.* $1{\cdot}47 \times 10^{-9}$. Comparison with the value for the 8-nitration of isoquinolinium cation ($1{\cdot}0 \times 10^{-6}$) gives 680 as the factor by which unprotonated N(1) deactivates C(8) in the cinnolinium cation.

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