The Homolytic Nitration of Quinoline with Pernitrous Acid.

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The decomposition of pernitrous acid in aqueous acid effects the nitration of quinoline in the 6- and the 7-position. This accords with the view that homolytic aromatic substitution initially involves the addition of radicals to the aromatic nucleus and not direct replacement of hydrogen.

HALFPENNY and ROBINSON (*J.*, 1952, 928, 939) have shown that pernitrous acid, which spontaneously decomposes to give free radicals capable of initiating vinyl polymerisation,

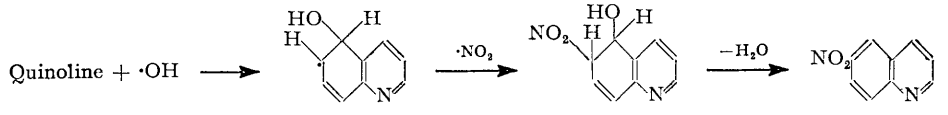
$$HO{\cdot}O{\cdot}N{:}O \longrightarrow HO{\cdot} + {\cdot}O{\cdot}N{:}O \longrightarrow HNO_3$$

can effect concurrent nitration and hydroxylation of aromatic liquids emulsified in dilute aqueous acid. In view of the natures of their reaction products they suggested that these aromatic substitutions were homolytic processes involving the successive additions of ·OH and $\cdot NO_2$ radicals to the aromatic nucleus and not the immediate abstraction of nuclear hydrogen by hydroxyl (compare Waters, *Discuss. Faraday Soc.*, 1953, **14**, 247; *Ann. Reports*, 1952, **49**, 122). Only small percentage yields of substitution products can be obtained by their procedure. This must be due mainly to the rapid recombination of vicinally produced ·OH and $\cdot NO_2$ radicals and not to the use of a two-phase system, since a further examination of the substitution of benzene has shown that addition of acetic acid to increase the solubility of the aromatic compound in the aqueous phase has little noticeable effect until the final reaction mixture contains at least 50% of acetic acid. In such solutions the reactivity of ·OH may be reduced considerably by radical transfer with

acetic acid molecules (Merz and Waters, *J.*, 1949, S 15) and, except that it does comprise a suitable buffer for regulating the rate of formation of pernitrous acid, the use of large quantities of acetic acid is undesirable for obvious practical reasons. The choice of other co-solvents is limited on account of the oxidising actions of hydroxyl radicals: alcohols, diethyl ether, and dioxan are attacked by decomposing pernitrous acid.

In view of these practical limitations to the study of reactions between pernitrous acid and aromatic compounds, the substitution of quinoline in aqueous acetic acid has been investigated, and a search has been made for reaction products diagnostic of the mode of attack on its benzenoid ring. The main reaction product is a brown alkali-soluble mixture, probably resulting from degradative oxidation of the pyridyl ring. No pure products could be isolated from this. The alkali-insoluble material contains, besides much unchanged quinoline, small amounts of both 6- and 7-nitroquinoline, which were isolated chromatographically and identified by comparison with authentic products of Skraup syntheses. No trace of either 5- or 8-nitroquinoline could be found. The latter are the normal products of heterolytic nitration of quinoline with nitric–sulphuric acid: their 6- and 7-substituted isomers are not formed under these conditions.

The isolation of only the two isomers in which the nitro-group occupies the deactivated β-positions in the benzenoid ring is, however, in full accord with the homolytic addition mechanism of Halfpenny and Robinson. Presumably, free hydroxyl radicals initially add to α-positions (compare the reactions between benzoyl peroxide and naphthalene derivatives: Dannley and Gippin, *J. Amer. Chem. Soc.*, 1952, **74**, 332) and thereby open up adjacent β-positions to combination of $\cdot NO_2$; thus:



Vicinal addition seems to be favoured, but this appears to be usual with free radicals.

It may be noted that Schorigin and Topchiev (*Ber.*, 1936, **69**, 1874) obtained 7-nitroquinoline by the action of nitrogen peroxide on quinoline at 100°, and that Bacharach, Haut, and Caroline (*Rec. Trav. chim.*, 1933, **52**, 413) also obtained this isomer by using a nitrating agent which is prone to form free nitrogen peroxide. Homolytic additions of $\cdot NO_2$ radicals to quinoline may perhaps occur in both these instances.

Experimental

Oxidations with Pernitrous Acid.—N-Sodium nitrite solution (30 c.c.) was added dropwise with shaking to methanol (5 c.c.) in water (50 c.c.) and hydrogen peroxide (20 c.c. of 6%), slightly acidified with sulphuric acid (2 c.c. of 2N). When admixture was complete, further equal volumes of hydrogen peroxide and sodium nitrite solutions were added in the same way. The solution was then warmed and volatile products were sucked by a slow stream of air into a little distilled water. Spot tests and the dimedone reaction established the production of formaldehyde. Oxidations also followed the simultaneous dropwise additions of sodium nitrite and hydrogen peroxide solutions to methanol in 75% acetic acid. No formaldehyde could be detected after addition of hydrogen peroxide, sodium nitrite, or dilute nitric acid individually to similarly weakly-acidified aqueous methanol.

Corresponding oxidations were effected with ethanol, *n*- and *iso*-propanol, *tert.*-butanol, ethylene glycol, diethyl ether, and dioxan, the oxidation products, which were identified as described by Merz and Waters (*loc. cit.*), being those resulting from the action of hydroxyl radicals.

Modifications of Procedure for Aromatic Nitration.—Repetition of the exact procedure of Halfpenny and Robinson (*loc. cit.*) gave a conversion into nitrobenzene of 0·4% of the benzene originally taken and 4% of the sodium nitrite: much benzene could of course be recovered. No increase of yields followed replacement of water by 25% acetic acid. The optimum yields of nitrobenzene (4·5% of benzene taken = 25% of benzene not recovered; 6% of sodium nitrite taken) were obtained by the simultaneous slow drop-wise additions of hydrogen peroxide (100-vol.; 80 c.c.) and concentrated aqueous sodium nitrite (30 g. in 40 c.c. of water) to a well-

stirred solution of benzene (50 c.c.) in glacial acetic acid (200 c.c.) and water (80 c.c.), temperature rise above 35° being prevented by external cooling.

On addition of hydrogen peroxide and sodium nitrite to this concentration of acetic acid the yellow colour of pernitrous acid appears immediately and fades after about 2 sec. No additional mineral acid need be used. Blank experiments verified that the dilute nitric acid resulting from the foregoing reaction does not nitrate benzene. Acetic acid of similar concentration did not noticeably increase the yield in a corresponding nitration of chlorobenzene and was of little value for the nitration of naphthalene or for attack on *cyclo*hexane.

Nitration of Quinoline.—Best yields were obtained by use of cold concentrated solutions containing just enough acid to prevent hydrolysis of quinolinium salt at any stage of the reaction.

Colourless quinoline (100 c.c.), purified by distillation under reduced pressure and subsequent passage through activated alumina, was dissolved in a mixture of acetic acid (16 c.c.), sulphuric acid (10 c.c.), and water (80 c.c.) and stirred in a three-necked flask cooled in ice. Solutions of hydrogen peroxide (120 c.c. of 100-vol. diluted with 20 c.c. of water and 3 c.c. of concentrated sulphuric acid) and sodium nitrite (48 g. in 140 c.c. of water) were simultaneously added dropwise at equal rates during 2 hr., the peroxide being initially in very slight excess. Sodium hydroxide solution (30%) was then added until the mixture became neutral to Congo-red, and then saturated potassium carbonate solution until the mixture was neutral to litmus. The quinoline phase was separated, and the remainder extracted with benzene. The quinoline and extracts were shaken with sodium hydroxide solution (30%) to remove phenolic products, solvent and unchanged quinoline were removed under diminished pressure, and the dark residue (4 g.) in benzene (25 c.c.) was adsorbed on a 3-foot alumina column. This was eluted with benzene–light petroleum (1 : 1; b. p. 60—80°). Pale yellow material moved down the column, following a little unchanged quinoline, and, when viewed with ultra-violet light was seen to have separated into three main light-sensitive bands. After extrusion of the alumina, the contents of each of the three bands were extracted with alcohol and examined separately by further chromatography and eventual crystallisation. The first band gave 0·01 g. only of a pale yellow solid, m. p. 149—157°, probably consisting of dinitroquinolines (Found: C, 47·3; H, 3·2. Calc. for $C_9H_5O_4N_3$: C, 50·2; H, 2·3%). There was too little for complete purification.

The second band gave 0·38 g. of white feathery crystals of 6-nitroquinoline, m. p. 148—150° unchanged after admixture with authentic material (m. p. 150—151°) prepared from *p*-nitroaniline by the Skraup reaction (Found: C, 62·3; H, 3·5; N, 15·8. Calc. for $C_9H_6O_2N_2$: C, 62·1; H, 3·5; N, 16·1%). The third band gave 0·39 g. of 7-nitroquinoline, m. p. 131—132°, identical with material (same m. p.) prepared from *m*-nitroaniline by the Skraup reaction. Repeated elution of the original alumina column, as well as chromatography of mother-liquors, failed to separate any trace of other nitroquinoline isomers. The identities of the 6- and 7-nitroquinoline were confirmed by comparative measurements of their infra-red spectra, using paraffin pastes. The distinctive absorption bands of these spectra are listed below.

Infra-red spectra of 6- *and* 7-*nitroquinoline.*

6-Nitroquinoline			7-Nitroquinoline			6-Nitroquinoline			7-Nitroquinoline		
λ, μ	ν, cm.$^{-1}$	*I* *	λ, μ	ν, cm.$^{-1}$	*I* *	λ, μ	ν, cm.$^{-1}$	*I* *	λ, μ	ν, cm.$^{-1}$	*I* *
6·17	1621	m	6·17	1621	w	9·27	1079	s	9·35	1070	s
6·23	1606	s	6·26	1597	m	9·74	1026	m	9·73	1028	m
6·59	1514	s	6·59	1514	s	10·12	988	w	10·07	994	m
6·71	1490	s	6·70	1493	s	10·51	952	m	10·50	952	s
7·04	1428	m	6·99	1432	s	11·10	901	s	11·04	906	m
7·28	1373	m	7·28	1373	m				11·17	896	s
7·37	1351	s	7·37	1351	s	11·74	852	s	11·84	845	s
7·46	1341	s	7·49	1335	s	12·38	808	s	12·41	806	s
7·57	1321	s	7·57	1321	m	12·53	798	m	12·57	791	s
8·79	1138	m	8·78	1139	m	12·66	781	s			
8·96	1116	s	8·88	1126	s	12·89	776	s	12·97	770	s
						13·60	735	s	13·56	738	s

* *I* = intensity; s = strong; m = medium; w = weak intensity.

It is significant that, although the characteristic frequencies for bond stretching are almost identical throughout the whole range of 6—8 μ, yet the bending frequencies, though still similar, have systematic wave-length differences of 0·05—0·1 μ. The absorption in the 8·5—14 μ wave-band is confined to the few very sharply marked positions noted in the Table.

Attempts were made to isolate phenolic products from the aqueous phase. Extraction, after acidification to pH 6, gave 0·5 g. of dark viscous oil which did not contain any of the known sparingly-soluble hydroxyquinolines. Concentration, followed by acidification to Congo-red, gave a brown powder (*ca.* 5 g.), moderately soluble in water and easily soluble in both weak acid or weak alkali such as ammonia, which tarred when dried and decomposed when vacuum-distillation was attempted. Benzoylation and methylation (Me_2SO_4) in alkali both failed to yield tractable products.

A corresponding reaction with pyridine gave similar intractable material.

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