Mechanism of Formation of 4-Methyl- and 4-Chloro-2-nitrophenol in the Nitration of 4-Methyl- and 4-Chloro-anisole, Respectively, in Aqueous Sulphuric Acid

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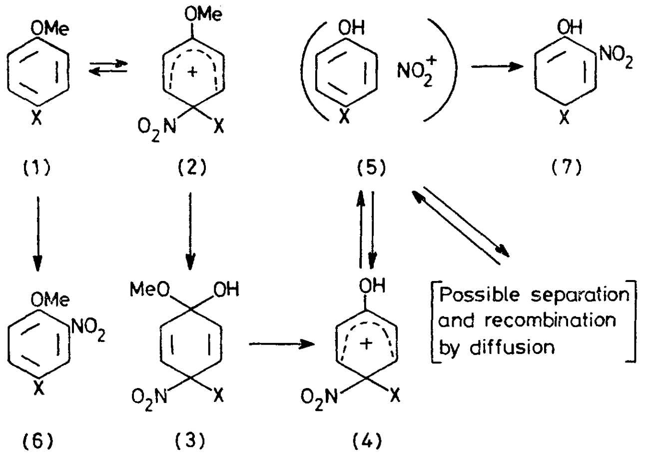
Summary The title reactions involve capture by water of the *ipso*-Wheland intermediates, followed by loss of methanol, then of nitronium ion to give solvent-caged ion pairs of *para*-substituted phenol and nitronium ion which can combine before or after diffusion apart.

NITRATION of *p*-methylanisole (**1**; X = Me) in 50—75% H_2SO_4 gives (**6**; X = Me) (60%) and (**7**; X = Me) (40%).[1] Similarly, *p*-chloroanisole (**1**; X = Cl) gives (**6**; X = Cl) (60%) and (**7**; X = Cl) (40%) in 58—62% H_2SO_4. Use of more concentrated acid reduces the yields of phenols. Compound (**1**; X = Cl) also gives (**7**; X = Cl) with mixtures of acetic acid, nitric acid, and water, the yield reaching a maximum (40%) in more aqueous mixtures.[2]

It has been concluded[1,2] that (**7**) is formed *via* the *ipso*-Wheland intermediate (**2**). We suggested[1] that demethoxylation occurs *via* (**3**), rather than S_N2 demethylation of (**2**), and that nitro-group migration proceeds through the solvent-caged pair (**5**) (Scheme). These suggestions are now confirmed.

With (X = Cl) but not with (X = Me) we detected the 4-X-phenol (g.l.c.–m.s. following extraction) as an intermediate in the nitration. In 66% H_2SO_4 the concentration of *p*-chlorophenol reached 2% of the starting concentration of *p*-chloroanisole after one half-life for nitration, and then diminished. Combined with kinetic data this shows the intermediacy of (**5**). For nitration in 66% H_2SO_4 the second-order rate constants for mesitylene, *p*-cresol,[3] and *p*-chlorophenol are in the ratios 1:0·5:0·2. These vary slightly with acidity. Mesitylene reacts at the limiting rate of encounter of the nitronium ion with the aromatic ring in aqueous sulphuric acid;[4] clearly *p*-cresol reacts close to this limit, but *p*-chlorophenol does not. Consequently the phenol could separate from (**5**; X = Cl) but not, or to a much smaller degree (see below), from (**5**; X = Me). Our results exclude an alternative mechanism[5] (held to explain the ability of the nitro-group to undergo 1,3-migration) in which (**4**) would go to (**7**) *via* solvent-caged nitrogen dioxide and phenol radical cation. Escape from the solvent cage could not then give *p*-chlorophenol.



SCHEME

TABLE. Products from the nitration of *p*-methylanisole (10^{-2} mol dm^{-3}) in aqueous sulphuric acid enriched in $H_2{}^{18}O$

		% ^{18}O-Enrichment	
% H_2SO_4	Product studied[a]	Found	Expected per oxygen atom enriched
63·5[b]	(7; X = Me)	11·6	4·4
63·5[b]	(7; X = Me)	13·0	4·4
66·8[c]	(7; X = Me)	8·4	3·5
	(6; X = Me)	1·3	
71·1[c]	(7; X = Me)	3·6	3·5
71·3[c]	(7; X = Me)	3·8	3·5
	(6; X = Me)	0·6	
74·9[d]	(7; X = Me)	8·3	2·8
	(6; X = Me)	5·7	

[a] By comparison of the molecular ion peak (M^+) with the ($M^+ + 2$) peak in the mass spectrum. [b] Aromatic compound added last, nitric acid in excess. [c] Equimolar conditions, nitric acid added last. [d] Equimolar conditions, aromatic compound added last.

Use of ^{18}O-enriched water in the solvent, and mass spectrometry of the products, provides evidence (Table) for the sequence (**2** → **3** → **4**). When nitric acid was pre-equilibrated with 63·5 and 74·9% H_2SO_4, both the nitro-group and hydroxy group in the phenol formed were ^{18}O-enriched.

The other results (Table) give fresh evidence for the onset at high acidities of nitration which is zeroth order in aromatic concentration.[6] When nitric acid is added last to the reaction mixture, ^{18}O-enrichment of the 4-methyl-2-nitroanisole occurs to a degree which declines with increasing acidity; nitronium ion is increasingly likely to react with *p*-methylanisole rather than with water in the solvent. The enrichment of the 4-methyl-2-nitrophenol in 66·8% H_2SO_4, but not in 71·3% H_2SO_4, exceeds that expected from the sum of the partial enrichment of the nitro-group and the full enrichment of the hydroxy group. This indicates that in the less viscous acid there is enough leakage from the solvent-caged pair (**5**; X = Me) to allow further equilibration of the nitronium ion with the solvent. Clearly, the relative rate constant for nitration of *p*-cresol quoted above signifies reaction close to, but not at, the diffusion-controlled limit. The reactivity of the phenol is probably reduced by hydrogen-bonding.[1]

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