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The Mechanism of Nitration of Phenol and 4-Methylphenol by Nitrogen Dioxide in Solution

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Abstract: *The quantitative formation of nitrophenols from phenol by reaction with nitrogen dioxide in solution involves stages, the first being the abstraction of a hydrogen atom from the hydroxyl group by* $NO_2{\cdot}$ *and the second the reaction of the phenoxy radical formed with* NO_2*. The first stage is rate-limiting at high* $[NO_2{\cdot}]$*. In the case of 4-methylphenol a similar mechanism leads to both 4-methyl-4-nitrocyclohexa-2,5-dien-1-one and 4-methyl-6-nitrocyclohexa-2,4-dien-1-one intermediates and at high* $[NO_2{\cdot}]$ *the apparent rate of reaction can become the conversion of the latter intermediate into 4-methyl-2-nitrophenol.*

Our previous kinetic studies of the reaction of nitrogen dioxide in solution with phenols have concentrated on substituted phenols where the products are mainly nitrocyclohexa-2,5-dien-1-ones.[1,2] Kinetic[1,2] and other results[3] were rationalised by mechanisms involving initial hydrogen abstraction from the hydroxyl group, reaction of the phenoxy radical formed with $NO_2{\cdot}$ and, on occasion, the intermediacy of cyclohexa-2,4-dien-1-one intermediates.[2] These studies have now been extended to the formation of ring-substituted nitro-compounds from phenol and 4-methylphenol and demonstrate that the same general mechanism applies. Reactions between these substrates and nitrogen dioxide in cyclohexane and carbon tetrachloride were followed using the stopped-flow technique, monitoring the appearance of nitro-products by their UV absorptions.

The reaction of phenol (10^{-4} mol dm^{-3}) with a stoichiometric equivalent of $\{[N_2O_4] + 0.5[NO_2{\cdot}]\}$ in cyclohexane at 25°C gave a 97% yield of nitrophenols (54% *o*, 43% *p*). At a higher concentration of phenol (0.61 mol dm^{-3}) in carbon tetrachloride solution increasing quantities of *p*-benzoquinone are formed (30% with $[N_2O_4] + 0.5[NO_2{\cdot}] = 0.4$ mol dm^{-3}) by what seems to be a separate oxidation process.

Kinetic studies of the nitration in cyclohexane at 25°C were carried out under conditions of a large excess of nitrogen dioxide ([phenol], 0.5-2.5 x 10^{-5} mol dm^{-3}; $[NO_2{\cdot}]$, 0.9-7 x 10^{-4} mol dm^{-3}). The reaction was first order in phenol over more than 3 half-lives, giving k_1, and the extinction curve change indicated the formation of the nitrophenols in the above proportions. Figure 1, a plot of $\log_{10}k_1$ *vs* $\log_{10}[NO_2{\cdot}]$, shows that the order in $NO_2{\cdot}$ changes from 2 in the region below $[NO_2{\cdot}] = 2 \times 10^{-4}$ mol dm^{-3} to 1 above $[NO_2{\cdot}] = 3 \times 10^{-3}$ mol dm^{-3}, the corresponding third and second order rate coefficients being $k_3 = 7.6 \times 10^6$ dm^6 mol^{-2} s^{-1} and $k_2 = 2.5 \times 10^3$ dm^3 mol^{-1} s^{-1} respectively. A corresponding study of 2,4,6-[$^2H_3$]-phenol gave $k_3 = 3.8 \times 10^6$ dm^6 mol^{-2} s^{-1}

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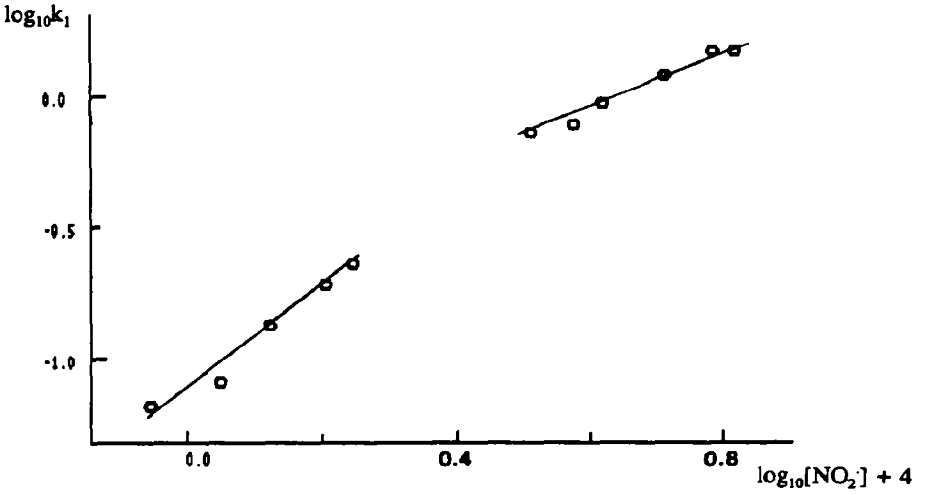


Figure 1 The reaction of phenol with nitrogen dioxide in cyclohexane at 25°C; the slopes of the lines drawn are 2, for that at the lower values of $[NO_2]$, and 1, for that at the higher values.

and $k_2 = 2.1 \times 10^3$ dm^3 mol^{-1} s^{-1}, suggesting a primary kinetic isotope effect for the third order process only. The proportions of nitrophenols formed are similar to those reported for the nitrous acid catalysed nitration[4] of phenol in aqueous sulphuric acid (57% *o*, 43% *p*) and for nitration[5] of phenol by 2,3,5,6-tetrabromo-4-methyl-4-nitrocyclohexa-2,5-dien-1-one (56% *o*, 44% *p*), reactions where the product-determining stage is believed to involve reaction of $NO_2\cdot$ with the phenoxy radical. The intermediacy of this radical is also supported by the earlier work on the substituted phenols.[1,2,3] Considering the mechanism of Scheme 1, where

$$PhOH + NO_2\cdot \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} PhO\cdot + HNO_2$$

$$PhO\cdot + NO_2\cdot \xrightarrow{k_b} PRODUCTS$$

Scheme 1

$k_{-a} >> k_a$, if $k_b[NO_2\cdot] >> k_{-a}[HNO_2]$ then the reaction should be first order in $NO_2\cdot$ and PhOH, as is observed at the higher $[NO_2\cdot]$. If, however, $k_b[NO_2\cdot] << k_{-a}[HNO_2]$ a reaction second order in $NO_2\cdot$ should result as is observed at the lower $[NO_2\cdot]$. The observed kinetic isotope effects are consistent with Scheme 1 as only the reactions at lower $[NO_2\cdot]$ show a primary kinetic isotope effect indicating that hydrogen loss from the ring is at least partially rate-limiting under these conditions.

However, reaction according to Scheme 1 is not immediately consistent with the observed first order dependence on the concentration of phenol at low $[NO_2\cdot]$. The rate equation here should be

$$\frac{-d[PhOH]}{dt} = \frac{k_a k_b [PhOH][NO_2\cdot]^2}{k_{-a}[HNO_2]},$$

and so the linearity of the first order plots under these conditions implies that the concentration of nitrous acid is not increasing as the reaction proceeds. An effectively constant concentration of nitrous acid could be due to further equilibria which buffer this species at a low concentration. Alternative mechanistic schemes for the reaction which is second order in $NO_2^{\cdot}$ are unable to explain the lowering of order as $[NO_2^{\cdot}]$ is raised, and processes not involving the hydroxyl group are ruled out by the unreactivity of anisole under corresponding conditions $\{k_1 = 5 \times 10^{-6}$ s^{-1} for reaction of nitrogen dioxide ($[N_2O_4] + 0.5[NO_2^{\cdot}] = 0.13$ mol dm^{-3}) with anisole (0.014 mol dm^{-3}) at 25°C in carbon tetrachloride$\}$.

Reaction of 4-methylphenol and nitrogen dioxide at 25°C in cyclohexane gives 32% 4-methyl-4-nitrocyclohexa-2,5-dien-1-one and 68% 4-methyl-2-nitrophenol. The former then undergoes a slower first order conversion into the latter at a rate ($k_1 = 3.3 \times 10^{-4}$ s^{-1} in chloroform and 4.8×10^{-4} s^{-1} in cyclohexane at 25°C) similar to the rate established elsewhere[6] for this homolytic rearrangement.[7] Study of the corresponding rearrangement of 2,6-[$^2H_2$]-4-methyl-4-nitrocyclohexa-2,5-dien-1-one ($k_1 = 4.9 \times 10^{-4}$s^{-1} in cyclohexane at 25°C) demonstrated the absence of a primary kinetic isotope effect.

At $[NO_2^{\cdot}]$ less than ~1.2×10^{-4} mol dm^{-3} the initial nitration reaction, measured by the formation of 2-nitro-4-methylphenol, is first order in 4-methylphenol and second order in $[NO_2^{\cdot}]$ ($k_3 = 5.0 \times 10^7$ dm^6 mol^{-2} s^{-1}), similar behaviour to that of phenol. However, above $[NO_2^{\cdot}] =$ ~1.4×10^{-4} mol dm^{-3} the rate, which is still first order in substrate, becomes independent of nitrogen dioxide concentration ($k_1 = 0.78$ s^{-1}), an observation consistent with a change to rate limiting reaction of an intermediate formed in bulk. Such intermediates formed in the reaction of substituted phenols have been identified as 6-nitrocyclohexa-2,4-dien-1-ones.[3] An *ortho* secondary dienone has previously been observed from reaction of 2,5-dimethylphenol with nitrogen dioxide,[8] but such an intermediate was not observed in previous studies of 4-methylphenol.[8,9] Figure 2 is a plot of first order rate coefficients (k_1) for 4-methylphenol and 2,6-[$^2H_2$]-4-methylphenol *vs* $[NO_2^{\cdot}]^2$. The kinetic isotope effect is 3.3 at $[NO_2^{\cdot}] <$ ~1×10^{-4} mol dm^{-3} and 4.9 at $[NO_2^{\cdot}] >$ ~1×10^{-4} mol dm^{-3}.

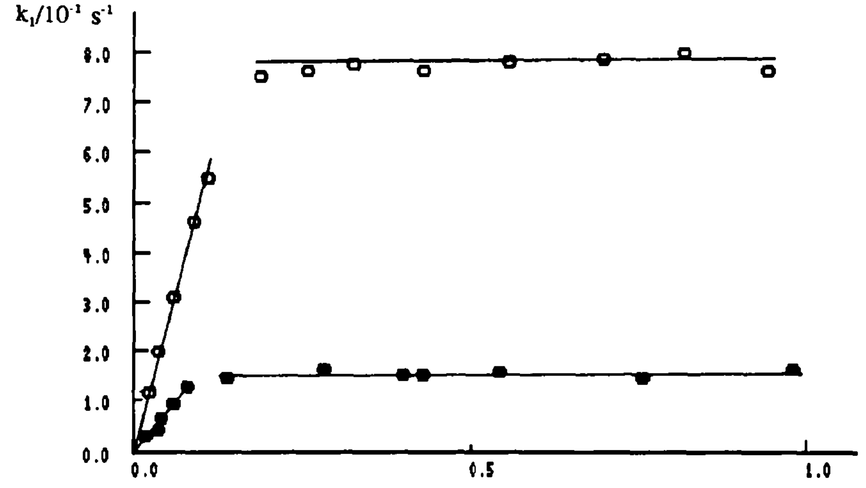
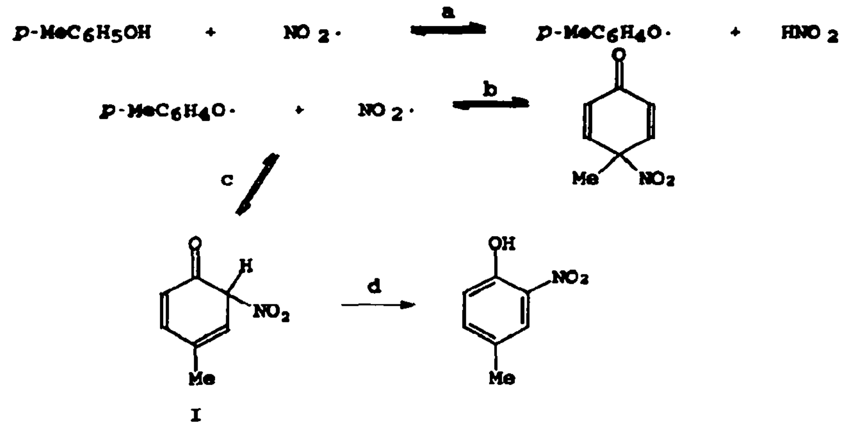


Figure 2 The reactions of 4-methylphenol and 2,6-[$^2H_2$]-4-methylphenol with nitrogen dioxide in cyclohexane at 25°C.

These results can be discussed in terms of the mechanism of Scheme 2. The third order process, which is faster than that for phenol, involves a pre-equilibrium lying to the left followed by the other steps involving at least partially rate limiting step **d**. The process, zeroth order in nitrogen dioxide, which is observed at higher [$NO_2\cdot$] is step **d** when the 6-nitrocyclohexa-2,4-dien-1-one **I** is formed in bulk. Although the full details are not clear, step **c** must be reversible as when 2,6-[$^2H_2$]-4-methylphenol reacts at the [$NO_2\cdot$] > ~1x10^{-4} mol dm^{-3} the proportion of 2-nitro-4-methylphenol formed apparently decreases to 26% and to 8% at [$NO_2\cdot$] = 0.42 x 10^{-4} mol dm^{-3}.



Scheme 2

We conclude that the difference between the behaviour of phenol and 4-methylphenol is that, for the former, less reactive substrate, cyclohexadien-1-one intermediates do not become bulk species at higher [$NO_2\cdot$], but that the hydroxyl hydrogen abstraction stage can become rate limiting.

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