Positional Selectivity in Aromatic Nitration occurring at the Diffusion Rate

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Summary Nitration of pseudocumene (1,2,4-trimethylbenzene) produces 5- and 6-nitropseudocumenes in the ratio 9 : 1 under conditions where there is evidence that both C-5 and C-6 are activated sufficiently to react upon encounter, showing the necessity for including in the kinetic scheme an intermediate preceding Wheland intermediate formation.

THE nitration of reactive aromatic compounds in 60—80% sulphuric acid containing nitric acid occurs at the rate of encounter of the nitronium ion (present in low equilibrium concentration) with the aromatic molecule.[1] It is important to enquire if positional selectivity is retained under such conditions. For this purpose we chose to investigate the nitration of pseudocumene, in which C-5 and C-6 have closely similar steric environments and are sufficiently reactive to react upon encounter, as the following argument shows. The rate constants for nitration of pseudocumene and *p*-xylene are closely similar to each other and to those of many other reactive aromatic compounds over the range of acidities studied, and comparable with that calculated for diffusion controlled reaction. *p*-Xylene is therefore nitrated at the encounter rate. Pseudocumene possesses an extra methyl group, and since methyl groups are activating at both *meta*- and *para*-positions C-5 and C-6 must each be more reactive than one position in *p*-xylene; each must therefore be sufficiently reactive to react upon encounter.

The yields of 3-, 5-, and 6-nitropseudocumene formed by nitrating pseudocumene long enough to give essentially complete mononitration, but insignificant dinitration, are shown in the Figure.

The variation in the yield of 6-nitropseudocumene with acidity recalls the behaviour of *o*-xylene.[2] In the latter case the results can be attributed[3] to initial attack by the nitronium ion not only at unsubstituted, but also at substituted (*ipso*[4]) positions. *ipso*-Attack can be followed either by nucleophilic capture of the Wheland intermediate, leading to products other than those of direct nitration, or by migration of the nitronium ion to an adjacent unsubstituted position. The latter fate predominates at high acidities.

The most reactive *ipso*-position in pseudocumene should be C-1, from which migration can enhance the yield of 6-nitropseudocumene (and perhaps of 3-nitropseudocumene[5]) with increasing acidity, as is observed (Figure). Thus the isomer proportions at low acidities give a clearer indication of positional selectivity. The ratio of 5- to 6-nitropseudocumene is found to approach 9 : 1, showing clearly that positional selectivity is retained in nitrations occurring at the encounter rate, provided that nucleophilic capture of Wheland intermediates formed at *ipso*-positions is under these conditions nearly complete.

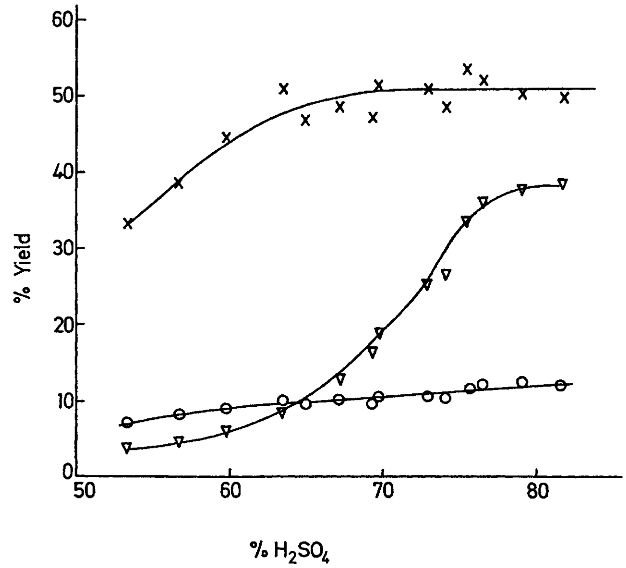

FIGURE. Yields, expressed as a percentage of the pseudocumene used, of 3-nitro-(○), 5-nitro-(×), and 6-nitro-(▽)-pseudocumenes, plotted against the composition of the aqueous sulphuric acid solvent, expressed as a weight percentage.

This persistence of positional selectivity excludes the explanation of the occurrence of the limiting rate in terms of 'early' transition states of the positionally oriented type.[6] Loss of substrate selectivity has been discussed in terms of the change of the rate-determining step to one in which a π-complex is formed,[7] or to one in which an encounter pair is formed;[1] regardless of the merits of the former suggestion the evidence on which it was based was unsound,[8] and the latter suggestion was made only by analogy with the way in which diffusion-controlled processes are sometimes discussed.[9] The present observations confirm the necessity of introducing into the mechanism of substitution an intermediate (I) preceding the Wheland intermediates formed at the nuclear positions. The formation of (I) is rate-determining (diffusion rate), and its rearrangement to Wheland intermediates is product determining. There are six different rate constants k_2 for formation of Wheland intermediates, and of these those for C-5 and C-6 must each considerably exceed k_{-1}, with one being about nine times the other. This degree of selectivity, whilst requiring the postulation of the extra step in the substitution gives no indication about the extent of attractive interaction between the aromatic and the electrophile in the intermediate. Even if this were zero, as in a non-interacting encounter pair, and if k_{-1} were taken to be[9a] as high as $10^{10}\ s^{-1}$, presumably k_2 could in the limit approach a vibration frequency, say 10^{12}—$10^{13}\ s^{-1}$, which would allow selectivity of the degree observed. Much higher selectivity would need to be observed before it became *necessary* to postulate some attractive interaction in the intermediate.

$$\mathrm{Ar} + \mathrm{NO_2^+} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{(I)} \xrightarrow{\Sigma k_2} \text{Wheland intermediates}$$

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