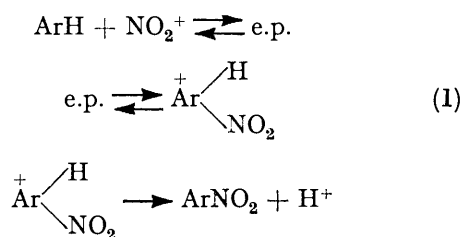


Electrophilic Aromatic Substitution. Part XIII.¹ Kinetics, Isomer Yields, and the Consequences of *ipso*-Attack in the Nitration of Toluene and Polymethylbenzenes in Aqueous Sulphuric Acid, and their Significance for the Mechanism of Aromatic Nitration

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Toluene, *o*-xylene, *m*-xylene, 1,2,4-, and 1,2,3-trimethylbenzene give yields of mononitro-isomers which vary with the percentage of sulphuric acid in a way which depends on (a) the medium dependence of the relative reactivities of the various substituted and unsubstituted positions in the molecule and (b) the partitioning of Wheland intermediates formed at substituted (*ipso*) positions between rearrangement and nucleophilic capture. Nitration of all the polymethylbenzenes studied occurs at closely similar rates, the encounter rate between the aromatic compound and the nitronium ion, yet positional selectivity does not disappear under these conditions, showing the necessity of including in the kinetic scheme an intermediate preceding Wheland intermediate formation.

NITRATION in aqueous sulphuric acid of aromatic compounds significantly more reactive than toluene occurs at the rate of encounter of the aromatic compound with the nitronium ion.² This circumstance has been represented by the inclusion in the nitration process of a separate, diffusion-controlled step, leading to the formation of an intermediate encounter pair, of undefined structure, prior to the Wheland intermediates [reactions (1)]. Such a representation follows from the



way in which such reactions are sometimes discussed.³ However, the necessity of postulating a distinct intermediate has not so far been demonstrated. The observation of a limiting rate of reaction, whether or not this approximates (as it does in the case of nitration in aqueous sulphuric acid) to the calculated diffusion rate, might be accounted for in terms of early transition states leading to Wheland intermediates; with the change in structure of the aromatic substrate in the direction of increasing reactivity, transition states produced by attack of nitronium ion upon activated positions would become 'earlier' until finally differences between individual activated positions would disappear. At this point a limiting rate of reaction would be reached, and selectivity both between activated positions and reactive substrates would disappear.

† In this paper 2,3,5-trimethyl-1-nitrobenzene will be referred to as 1,2,4-trimethyl-6-nitrobenzene, in order to facilitate comparison with the other nitroisomers formed on nitration of 1,2,4-trimethylbenzene.

¹ Part XII, *J.C.S. Perkin II*, 1972, 1652.

² R. G. Coombes, R. B. Moodie, and K. Schofield, *J. Chem. Soc. (B)*, 1968, 800.

The position might be illustrated by the cases of *p*-xylene and 1,2,4-trimethylbenzene. *p*-Xylene is nitrated at the limiting rate.² Its conversion into 1,2,4-trimethylbenzene would not, therefore, be expected to produce a compound capable of reacting faster (see below), and between *p*-xylene and 1,2,4-trimethylbenzene there would be no substrate selectivity. However, if the limiting rate produced in each case an intermediate which was subsequently transformed into Wheland intermediates in a distinct, product controlling step, there would be no reason why C-5 and C-6 † (positions very similar in their steric characteristics) in 1,2,4-trimethylbenzene should not reveal their different reactivities; thus, positional selectivities would be retained. Description of the limiting rate in terms of early transition states of the positionally oriented type would lead to the expectation that positional selectivity would also disappear.

The occurrence of intermediates in aromatic substitution prior to Wheland intermediates has been suggested to account for the retention of positional selectivity under conditions where substrate selectivity is appreciably lost.⁴ However, it has subsequently been shown that the apparent loss of substrate selectivity could have been due to incomplete mixing prior to reaction.⁵

In the light of the above considerations we were interested to determine whether or not reactive positions, in benzene derivatives which were nitrated at the encounter rate, retained selectivity, and have measured the rates of nitration in aqueous sulphuric acid and yields of nitro-compounds formed for a series of methylbenzenes.

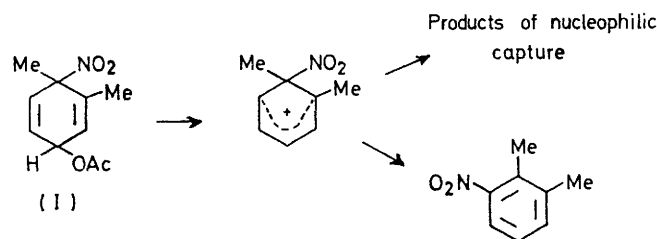
The prosecution of such studies and their interpretation has been considerably complicated by the demonstration for methylbenzenes of the importance of *ipso*-

³ I. Amdur and G. G. Hammes, 'Chemical Kinetics,' McGraw-Hill, London, 1966, p. 63; A. M. North, 'The Collision Theory of Chemical Reactions in Liquids,' Methuen, London, 1964.

⁴ G. A. Olah, S. J. Kuhn, and S. H. Flood, *J. Amer. Chem. Soc.*, 1961, 83, 4571; G. A. Olah, *Accounts Chem. Res.*, 1971, 4, 240.

⁵ J. H. Ridd, *Accounts Chem. Res.*, 1971, 4, 248.

nitration.⁶⁻⁸ The *ipso*-Wheland intermediates (W_i) may be captured by nucleophiles giving cyclohexa-1,4-dienes, capable of undergoing a variety of further reactions, or give by migration of the nitro-group to an unsubstituted position the nitro-compound which is also formed by direct nitration at that position.⁷ The latter, very important reaction was first demonstrated by Lewis and Robinson⁸ and re-discovered recently by Myhre,^{7a} who showed that (I) (formed by *ipso*-nitration and capture of the intermediate by acetate in the nitration of *o*-xylene in acetic anhydride) is solvolysed in aqueous sulphuric acid to give, in yields which increased with the acidity of the medium, 3-nitro-*o*-xylene. It was reasonably assumed that (I) underwent $A_{Al}I$ solvolysis⁹ to give the W_i , which was captured by nucleophiles (at low acidities mono- and di-nitro-3,4-dimethylphenols were formed), or which rearranged to 3-nitro-*o*-xylene. The higher the acidity the more successfully did the latter process compete, and Myhre's observations allowed him elegantly



to explain^{7a} the drastic variation with acidity of the proportions of 3- and 4-nitro-*o*-xylene formed by nitrating *o*-xylene in aqueous sulphuric acid. The absence of 4-nitro-*o*-xylene from amongst the products of solvolysis of (I) shows that neither further migration from an unsubstituted position, nor migration across an unsubstituted position, nor return of the W_i to reactants or prior intermediate (encounter pair or π -complex) can occur. The importance of this result for our own work led us to repeat Myhre's experiment with results completely in agreement with his. Migration across or from unsubstituted positions may occur in other systems and in different circumstances.^{6i,7b}

The general assumption behind our work is, therefore, that an unsubstituted position adjacent to a methyl group may be nitrated by direct nitration, and also by *ipso*-nitration followed by migration, and that by measuring yields of nitro-compounds at low acidities the consequences

of direct nitration may be disentangled from those of *ipso*-nitration, provided that at lower acidities nucleophilic capture of the *ipso*-intermediate can be made substantially complete.

EXPERIMENTAL

Materials.—Sulphuric acid and urea were AnalaR reagents. Concentrations of diluted acids were determined from density measurements. Pure nitric acid, prepared as described previously,¹⁰ was used. Toluene, the xylenes, 1,2,4-, and 1,2,3-trimethylbenzene were purified by fractional distillation, and their purities were checked by g.l.c. Nitrotoluenes, nitroxylenes, and 1,2,4-trimethyl-5-nitrobenzene were obtained from commercial sources. 1,2,3-Trimethyl-4- and -5-nitrobenzene were obtained by g.l.c. (Pye 105 instrument fitted with a 15 ft column of 15% Apiezon L on Chromosorb W; N_2 flow rate 40 ml min⁻¹; 195°) from the mixture formed by nitrating 1,2,3-trimethylbenzene with mixed acid. 4-Hydroxy-3-nitrotoluene was obtained from nitration of *p*-cresol in mixed acid.

1,2,4-Trimethyl-3-nitrobenzene.—1,2,4-Trimethyl-3,5,6-trinitrobenzene (5 g) was added to a solution of ammonia (*d* 0.88; 2 ml) in methanol (100 ml) which had been saturated with hydrogen sulphide. Hydrogen sulphide was passed in continuously as the mixture was boiled for 1 h. The reaction mixture was filtered, and methanol was removed from the filtrate. Crystallisation of the residue from water gave 2-amino-3,5,6-trimethyl-4-nitrobenzenesulphonic acid (4.1 g). This acid (3.9 g), ethylene glycol (50 ml), and concentrated hydrochloric acid (14 ml) were boiled together for 2 h. Neutralisation, filtration, and crystallisation from EtOH gave yellow needles of 5-amino-1,2,4-trimethyl-3-nitrobenzene (2.3 g), m.p. 136°. A suspension of this (1.1 g) in concentrated hydrochloric acid (18.5 ml) and water (18.5 ml) at 0° was diazotised with sodium nitrite (0.42 g) in water (20 ml). The solution was filtered into another prepared from 50% hypophosphorous acid (7 ml), water (3 ml), and a crystal of copper sulphate. After 12 h at 0° crude 1,2,4-trimethyl-3-nitrobenzene was collected and purified by column chromatography [basic alumina; light petroleum (b.p. 60–80°)] to give pale yellow needles (0.6 g), m.p. 28–29°.

1,2,4-Trimethyl-6-nitrobenzene.—The literature method¹¹ was used except that it was found most convenient to hydrolyse 6-acetylamino-2,3,5-trimethyl-1-nitrobenzene with boiling 6M-hydrochloric acid.

3,4-Dimethylbenzaldehyde.¹²—4-Bromo-*o*-xylene (10 g) in sodium-dried ether (10 ml) was added over 20 min to magnesium turnings (2.4 g; activated by washing twice with ether and drying at 105°), ether (10 ml), and a small crystal of iodine stirred in a three-necked flask protected against moisture. The mixture was boiled for 3 h and then ethyl orthoformate (10 g) in ether (10 ml) was added over 15 min. The mixture was stirred overnight at 25° and then freed from ether. The brown oil was boiled with 30%

⁶ (a) D. J. Blackstock, A. Fischer, K. E. Richards, J. Vaughan, and G. J. Wright, *Chem. Comm.*, 1970, 641; (b) D. J. Blackstock, J. R. Cretney, A. Fischer, M. P. Hartshorn, K. E. Richards, J. Vaughan, and G. J. Wright, *Tetrahedron Letters*, 1970, 2793; (c) A. Fischer, C. C. Greig, A. L. Wilkinson, and D. R. Leonard, *Canad. J. Chem.*, 1972, 50, 2211; (d) A. Fischer and D. R. A. Leonard, *ibid.*, p. 3367; (e) A. Fischer and A. L. Wilkinson, *ibid.*, p. 3988; (f) D. J. Blackstock, A. Fischer, K. E. Richards, and G. J. Wright, *Austral. J. Chem.*, 1973, 26, 775; (g) A. Fischer and J. N. Ramsay, *J.C.S. Chem. Comm.*, 1973, 237; (h) A. Fischer and D. R. A. Leonard, *ibid.*, p. 300; (i) A. Fischer and C. G. Greig, *ibid.*, p. 396; (j) A. Fischer and C. G. Greig, *ibid.*, 1974, 50; (k) A. Fischer and J. N. Ramsay, *J. Amer. Chem. Soc.*, 1974, 96, 1614.

⁷ (a) P. C. Myhre, *J. Amer. Chem. Soc.*, 1972, 94, 7921; (b) R. C. Hahn and M. B. Groen, *ibid.*, 1973, 95, 6128; (c) R. C. Hahn and D. L. Strack, *ibid.*, 1974, 96, 4335.

⁸ H. J. Lewis and R. Robinson, *J. Chem. Soc.*, 1934, 1253.
⁹ K. Yates, *Accounts Chem. Res.*, 1971, 4, 136; K. Yates and R. A. McClelland, *J. Amer. Chem. Soc.*, 1967, 89, 2686.

¹⁰ J. G. Hoggett, R. B. Moodie, and K. Schofield, *J. Chem. Soc. (B)*, 1969, 1.

¹¹ L. Marion and C. W. Oldfield, *Canad. J. Res.*, 1947, 25B, 1.

¹² L. I. Smith and M. Bayliss, *J. Org. Chem.*, 1941, 6, 437.

sulphuric acid (20 ml) for 2 h. The cooled mixture was extracted with ether, and the aldehyde (5.8 g), b.p. 80—82° at 0.4 mmHg, was recovered by distillation, ν_{\max} 1690 cm^{-1} , τ (CDCl_3) 7.7, 2.4—2.75, and 0.10.

Kinetic Measurements.—The conventional technique described previously² was used.

Product Analysis.—(i) *From reaction in <70% sulphuric acid.* A solution of aromatic in acetic acid was prepared and a portion (typically, 0.25 ml of solution containing 1—2 mg of aromatic) was added to sulphuric acid (250 ml) of the required concentration containing urea (0.03M) and nitric acid (at least a 10-fold excess over the substrate) at 25°. The mixture was shaken vigorously for 10 half-lives and then quenched in ice-cold water (600—800 ml). A known amount of a reference standard was added and the mixture was extracted 10 times with dichloromethane. After drying (MgSO_4), the combined extracts were freed from solvent by fractional distillation (8 in glass column packed with glass helices). The column was rinsed into the distillation flask with a small volume of dichloromethane, giving a concentrated solution (2—3 ml) of the nitration products. Runs lasting >24 h were carried out in sealed tubes at 25°.

(ii) *From reactions in >70% sulphuric acid.* Reactions were of the scale described above. The aromatic in acetic acid was added to the solution of urea and nitric acid (in amount equimolar with the aromatic) in sulphuric acid stirred vigorously in a pleated flask.

Table 1 gives details of the g.l.c. procedure.

TABLE 1
G.l.c. conditions

Product	Reference standard	Column* ($T/^\circ\text{C}$)
Nitrotoluenes	Nitrobenzene	15% Polypropylene glycol (150)
Nitro- <i>o</i> -xylenes	<i>p</i> -Nitrotoluene	15% SE 30 silicone (140)
Nitro- <i>m</i> -xylenes	<i>p</i> -Nitrotoluene	15% SE 30 silicone (140)
Nitro- <i>p</i> -xylene	<i>p</i> -Nitrotoluene	15% SE 30 silicone (141)
Nitro-1,2,4-trimethylbenzene	1,3-Dimethyl-2-nitrobenzene	15% SE 30 silicone (147)
Nitro-1,2,3-trimethylbenzenes	Nitromesitylene	15% SE 30 silicone (154)

* All on Chromosorb W, 6 ft, nitrogen as carrier gas 40 ml min^{-1} . Pye 104 machine (flame ionisation detector).

Nitrations in Acetic Anhydride.—The following example is typical. A mixture of nitric acid (0.42 ml) and acetic anhydride (7 ml) was kept at 0° for 15 min. To the resulting solution was added at 0° another containing *o*-xylene (1.23 ml) and acetic anhydride (10 ml). The volume was brought to 25 ml by addition of acetic anhydride and the whole was maintained at 0° until signals from the aromatic protons of *o*-xylene had disappeared from the n.m.r. spectrum (*ca.* 24 h). Addition to water (100 ml), neutralisation with sodium carbonate, addition of a portion of a reference standard (*p*-nitrotoluene), extraction with dichloromethane (10 × 10 ml), drying (MgSO_4), and concentration (with the use of an 8 in-fractionating column packed with glass helices which were washed into the flask at the end) to *ca.* 10—15 ml gave a solution which was analysed by g.l.c., as described above.

RESULTS

Kinetics.—Second-order rate constants are given in Table 2; for some of the compounds these extend the range

of results previously reported.² (Rate profiles are in Figure 1.) To avoid complication of the product studies by dinitration it was necessary to study the rates of nitration of three trimethylnitrobenzenes; the results are in Table 2.

TABLE 2

Second-order rate coefficients for nitration in sulphuric acid at $25.0 \pm 0.1^\circ \text{C}$

H_2SO_4 (%) ^a	$[\text{HNO}_3]/\text{mol dm}^{-3}$ ^b	$k_2/\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$
Toluene		
52.5	0.40	2.8×10^{-5}
56.7	0.141	1.96×10^{-4}
57.5	1.28×10^{-2}	4.4×10^{-4}
60.1	1.12×10^{-2}	2.4×10^{-3}
61.0	2.1×10^{-2}	3.7×10^{-3}
64.0	3.2×10^{-2}	3.7×10^{-2}
<i>p</i> -Xylene		
56.7	0.27	1.79×10^{-3}
1,2,4-Trimethylbenzene		
56.8	2.0×10^{-1}	2.0×10^{-3}
60.9	7.0×10^{-2}	2.0×10^{-2}
64.1	9.6×10^{-3}	1.31×10^{-1}
65.4	4.2×10^{-3}	3.0×10^{-1}
67.3	2.2×10^{-3}	2.0
69.6	1.41×10^{-3}	4.3
70.3	1.38×10^{-3}	6.3
72.1	5.1×10^{-4}	14.2
74.0	5.0×10^{-4}	103
1,2,3-Trimethylbenzene		
64.0	5.5×10^{-2}	1.10×10^{-1}
69.2	2.9×10^{-3}	4.1
72.1	5.5×10^{-4}	30
1,2,4-Trimethyl-3-nitrobenzene		
69.2	0.20	1.16×10^{-2}
74.1	2.5×10^{-2}	0.55
1,2,4-Trimethyl-5-nitrobenzene		
69.2	0.20	2.5×10^{-3}
74.1	2.0×10^{-2}	9.6×10^{-2}
1,2,4-Trimethyl-6-nitrobenzene		
69.2	0.20	9.3×10^{-3}
74.1	5.2×10^{-3}	0.50

^a [Urea] *ca.* $3 \times 10^{-2} \text{ mol dm}^{-3}$, [ArH] *ca.* $5 \times 10^{-3} \text{ mol dm}^{-3}$. For toluene, measurements were made at 315 nm, for 1,2,3- and 1,2,4-trimethylbenzene, at 300 nm (or when $0.2M > [\text{HNO}_3] > 0.05M$ at 325 nm), for *p*-xylene, at 325 nm, for 1,2,4-trimethyl-5-nitrobenzene, at 335 nm, and for 1,2,4-trimethyl-3- and 1,2,4-trimethyl-6-nitrobenzene, at 350 nm. ^b $\pm 0.1\%$.

Yields of Mononitro Compounds.—These are in Table 3, and in Figures 2—5. It was not at first appreciated that the longer reaction times needed at low acidities can lead to interference by side reactions unless light is excluded. Subsequent nitrations in the dark in 53—55% sulphuric acid gave slightly improved yields of mononitro-compounds from toluene and 1,2,3-trimethylbenzene, but made little difference in the cases of *o*-xylene and 1,2,4-trimethylbenzene. From 1,2,4-trimethylbenzene, yields of mononitro-compounds improved markedly in 48—51% sulphuric acid when nitration was carried out in the dark, but at these acidities reaction times are very long (1—6 weeks) and the yields must be regarded as minimum figures. The side reactions were not investigated, but the following observations are of interest. (1) Of the mononitro-products, *m*-nitrotoluene, 4-nitro-*o*-xylene, and 1,2,3-trimethyl-5-nitrobenzene were the most reactive. They could not be recovered quantitatively when left in 57—59% sulphuric acid in the light for the time of a nitration experiment. (2) From *m*-nitrotoluene the major product

TABLE 3

Yields of nitro-compounds from the nitration of methylbenzenes in aqueous sulphuric acid at 25° a, b

Compound	H ₂ SO ₄ (%)	Yields of products (%)			Mass balance (%)
		1,2-Dimethyl- <i>x</i> -nitrobenzene			
<i>o</i> -Xylene		<i>x</i> = 3	<i>x</i> = 4		
	54.2	11.7	23.3		35
	63.5	29.3	31.4		61
	67.1	44.2	35.0		79
	72.8	57.0	40.0		97
	76.1	57.8	42.2		100
	79.9	56.0	43.4		99
	80.2	55.5	42.8		98
	82.7	53.2	46.8		100
	83.5	52.4	47.6		100
85.7	51.8	48.2		100	
<i>m</i> -Xylene		1,3-Dimethyl- <i>x</i> -nitrobenzene			
		<i>x</i> = 2	<i>x</i> = 4	<i>x</i> = 5	
	54.5	16.9	73.6	1.6	92
	64.0	18.2	77.9	2.2	98
	69.2	18.1	75.1	2.0	95
	79.0	17.2	76.7	2.3	96
	80.0	17.1	78.0	2.8	98
	81.9	16.8	78.6	2.6	98
<i>p</i> -Xylene		1,4-Dimethyl-2-nitrobenzene			
	57.9		47		47
	64.4		84		84
	72.1		96		96
1,2,4-Trimethylbenzene		1,2,4-Trimethyl- <i>x</i> -nitrobenzene			
		<i>x</i> = 3	<i>x</i> = 5	<i>x</i> = 6	
	47.8	6.6	27.5	2.6	37
	50.2	5.8	30.9	1.9	39
	53.8	9.0	35.9	3.3	48
	54.2	8.7	31.8	2.7	43
	56.7	8.2	38.2	4.6	51
	59.7	8.8	44.3	5.8	59
	62.5	9.9	50.8	8.3	69
	64.9	9.5	46.8	9.6	66
	67.1	9.9	48.3	12.8	71
	69.3	9.6	47.1	16.3	73
	69.7	10.3	51.2	18.5	80
	72.9	10.5	50.5	25.1	86
74.0	10.3	48.2	26.6	85	
75.4	11.6	53.5	33.6	99	
76.5	12.1	51.9	35.8	100	
79.1	12.3	50.1	37.6	100	
81.7	11.8	49.8	38.3	100	
1,2,3-Trimethylbenzene		1,2,3-Trimethyl- <i>x</i> -nitrobenzene			
		<i>x</i> = 4	<i>x</i> = 5		
	54.2	41.8	8.7		51
	57.9	43.2	8.9		52
	64.0	62.7	12.4		75
	69.2	79.3	13.7		93
	80.0	80.3	16.8		97
81.9	82.5	17.5		100	
Toluene		Nitrotoluene			
		<i>o</i>	<i>m</i>	<i>p</i>	
	54.9	61.0	3.7	30.9	95
	64.4	63.1	4.2	32.9	100
	65.0	63.3	3.8	32.9	97
	66.6	62.6	4.3	33.1	96
	67.1	62.7	3.8	33.4	98
	68.6	62.9	3.8	33.3	100
	73.4	61.0	3.6	35.3	102
	78.3	58.8	4.1	37.0	97
	78.4	58.9	3.8	37.3	99
86.8	56.4	3.8	39.8	99	
87.8	55.6	4.3	40.0	99	

^a [ArH] ca. 5 × 10⁻⁵ mol dm⁻³. ^b [Urea] ca. 3 × 10⁻² mol dm⁻³. * ± 2%.

was *m*-nitrobenzaldehyde, which was formed whether or not nitric acid was present. (3) Although 1,2,4-trimethyl 5-nitrobenzene was unreactive its yield was improved by

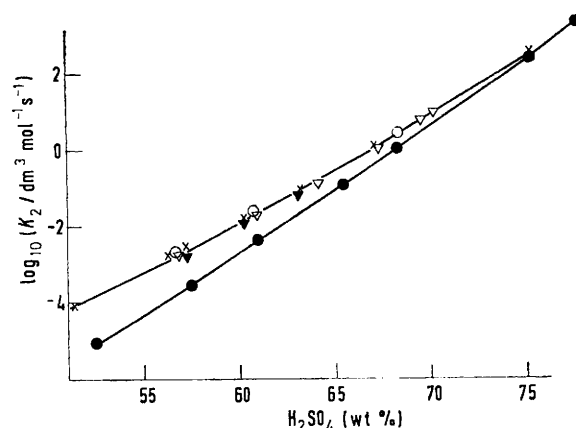


FIGURE 1 Variation of the logarithm of the second-order rate constant for nitration of mesitylene (x), 1,2,4-trimethylbenzene (∇), *p*-xylene (○), *o*-xylene (▼), and toluene (●) with the weight percentage of sulphuric acid

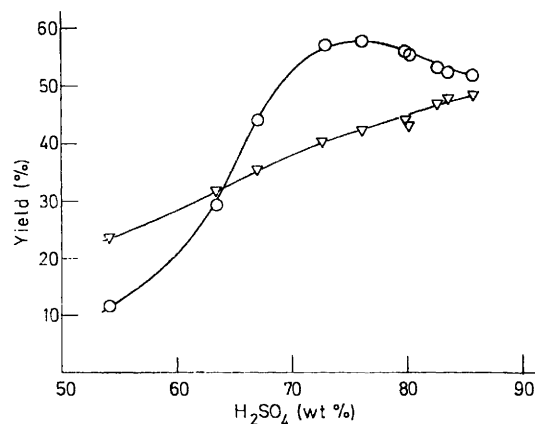


FIGURE 2 Nitration of *o*-xylene. Yields of 3-nitro- (○) and 4-nitro-*o*-xylene (∇), as a percentage of the starting substrate, plotted against the weight percentage of sulphuric acid

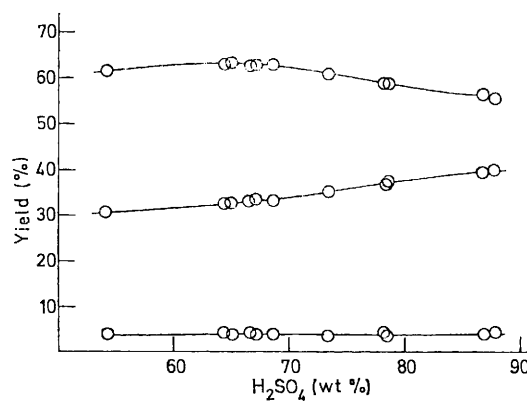


FIGURE 3 Nitration of toluene. Yields of *o*- (upper line), *m*- (middle line), and *p*-nitrotoluene (lower line) as a percentage of the starting substrate, plotted against the weight percentage of sulphuric acid

carrying out nitrations of 1,2,4-trimethylbenzene in <53% sulphuric acid in the dark, 1,2,4-trimethylbenzene itself being subject to photochemical decomposition.

3,4-Dimethylbenzaldehyde was a product of the nitration of 1,2,4-trimethylbenzene. It is unlikely to have been formed photochemically since its yield did not decrease when light was excluded. Its yield increased from 3.5%

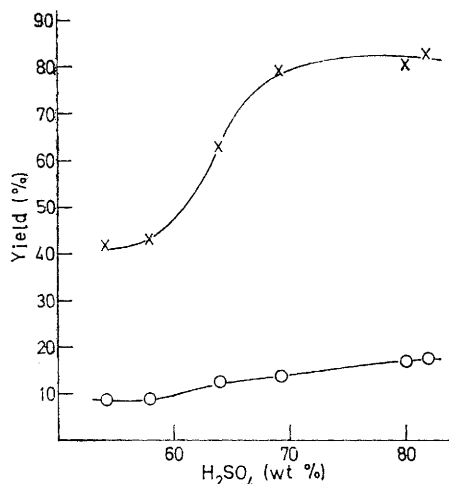


FIGURE 4 Nitration of 1,2,3-trimethylbenzene. Yields of 1,2,3-trimethyl-4- (x) and -5-nitrobenzene (O) as a percentage of the starting substrate, plotted against the weight percentage of sulphuric acid

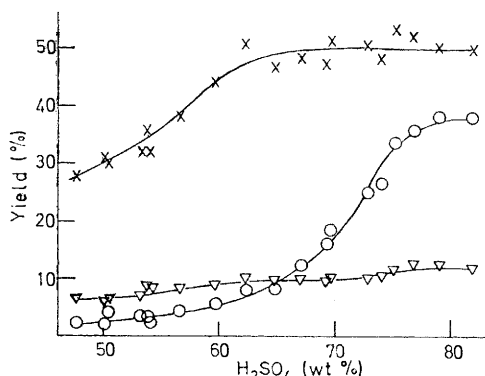


FIGURE 5 Nitration of 1,2,4-trimethylbenzene. Yields of 1,2,4-trimethyl-3- (∇), -5- (x), and -6-nitrobenzene (O), as a percentage of the starting substrate, plotted against the weight percentage of sulphuric acid

in 48% sulphuric acid to a maximum of 11% in 63% sulphuric acid, declined to zero in 74% sulphuric acid, and it was not observed at higher acidities.

4-Hydroxy-3-nitrotoluene (4.2%) was formed when toluene was nitrated in the dark in 54% sulphuric acid. Generally the very low concentrations of substrates which had to be used made the search for products other than mononitro-compounds impracticable.

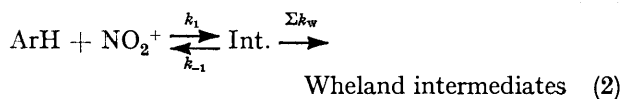
From Figures 2—5 it can be seen that even at acidities where the yields of mononitro-compounds are quantitative, their ratios are not independent of medium; thus, in the

case of toluene the *o* : *p* ratio changes from 1.9 in 64.4% sulphuric acid to 1.4 in 87.8% sulphuric acid.

DISCUSSION

Encounter Control.—The rate profiles for nitration of the dimethyl- and trimethyl-benzenes (Figure 1) show all these compounds to react at the limiting rate. We know of no compound which is nitrated at a rate exceeding this limiting rate. We have shown² that when an estimate is made of the low equilibrium concentration of nitronium ion the limiting rate is, within the error of the estimation, the rate of diffusion controlled reaction of the nitronium ion with the aromatic compound.

Positional Selectivity at the Encounter Rate.—The significance of the occurrence of positional selectivity between C-5 and C-6 in 1,2,4-trimethylbenzene was explained in the introduction; it would require the intervention of a common intermediate [Int. in reaction (2)] prior to the Wheland intermediates, which was formed at the diffusion rate, and whose rearrangement to Wheland intermediates was product-determining.



It remains to determine the proportions of the apparent reactivities of C-5 and C-6 which are derived from direct nitration and from rearrangement of the W_i s formed by attack at C-4 or C-1. The latter contribution is likely to be minimal at low acidities because it has to compete with nucleophilic capture. The yields of mononitro-compounds formed in 54% sulphuric acid are compared in Table 4 with our own and others'^{6,13,14} results for nitrations in acetic anhydride, a good capture medium.⁶ The close similarity may arise because the fractions of W_i s which are captured, rather than rearranging, are both less than unity and fortuitously similar in both media. If, as seems more likely, capture of W_i s is substantially complete in both solvents, then the considerable difference in the yields of 1,2,4-trimethyl-5- and -6-nitrobenzenes formed by nitration in 54% sulphuric acid arises only from direct nitration at these positions, and demonstrates the need for intermediate Int. in reaction (2). This degree of selectivity (*ca.* 10 : 1 in favour of C-5), whilst requiring the postulation of the extra step in the substitution, gives little information about the nature of the intermediate. Since the rate of the reaction approximates to the diffusion rate, the free energy of activation for its formation must be small, but the corresponding quantity for the reversal of this step cannot be gauged. An upper limit for the rate constant k_{-1} in reaction (2) would be that for a non-interacting encounter pair, and of the order^{3a} of 10^9 – 10^{10} s⁻¹. Since the step with rate constant k_1 is rate limiting, the values of k_w for

¹³ A. Fischer, J. Vaughan, and G. J. Wright, *J. Chem. Soc. (B)*, 1967, 368.

¹⁴ S. R. Hartshorn, R. B. Moodie, and K. Schofield, *J. Chem. Soc. (B)*, 1971, 1256.

formation of Wheland intermediates at C-5 and C-6 must both be greater than that of k_{-1} . However, an upper limit for k_w is a vibration frequency, say 10^{12} – 10^{13} s⁻¹, allowing selectivity of the degree observed even from a non-interacting encounter pair.

Variation of Isomer Yields with Acidity.—As noted, two factors can be distinguished, the variation with acidity of the relative reactivities of all the nuclear positions (apparent under conditions where the aggregate yield of mononitro-compounds is quantitative),

with those for nitration in sulpholan¹² suggests that the two media are similar with regard to the relative reactivities of the positions, but that in sulpholan nucleophilic capture does not occur.

Nitrotoluenes are formed quantitatively in >64% sulphuric acid, showing that under these conditions W_i is not captured. Figure 3 shows that above 64% sulphuric acid the sum ($k_w^i + k_w^o$) diminishes relatively to k_w^p . Capture of W_i accounts for the small decrease in yield of *o*-nitrotoluene at low acidities, a conclusion

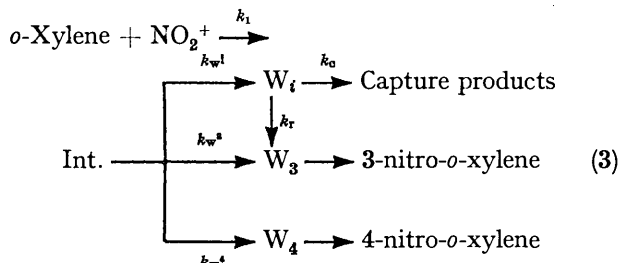
TABLE 4

Yields of nitro-isomers from nitrations in acetic anhydride, compared with those from nitrations in 54 (±1)% H₂SO₄

Medium	Nitro-toluenes			Nitro- <i>o</i> -xylenes		Nitro- <i>m</i> -xylenes			Nitro-1,2,4-trimethylbenzenes			Nitro-1,2,3-trimethylbenzenes	
	<i>o</i>	<i>m</i>	<i>p</i>	3	4	2	4	5	3	5	6	4	5
Ac ₂ O	60 ^a	3 ^a	34 ^a	13 ^b	24 ^b				7 ^b	38 ^b	4 ^b		
54 (±1)% H ₂ SO ₄	58 ^c	3 ^c	36 ^c	28 ^c	13 ^b	15 ^c	85 ^c	0 ^c	10 ^d	35 ^d	4 ^d	46 ^c	8 ^c
	61 ^b	4 ^b	31 ^b	12 ^b	23 ^b	17 ^b	74 ^b	2 ^b	9 ^b	34 ^b	3 ^b	41 ^b	9 ^b

^a Ref. 10. ^b This work, duplicate determinations, light was excluded from the reaction mixtures in aqueous sulphuric acid. ^c Ref. 9. ^d Ref. 2f.

and the medium-dependent partitioning of W_i s between rearrangement and nucleophilic capture. This can be illustrated by reference first to *o*-xylene (Figure 2) for which reactions (3) apply (Introduction and ref. 7a).



(W_3 means the Wheland intermediate for attack at C-3, and the other terms have similar meanings.) As already indicated, it is likely that none of the steps is significantly reversible (though the irreversibility of the first, diffusion-controlled step, is not relevant to the question of isomer yields). Thus, the two factors mentioned above are governed by $k_w^i : k_w^3 : k_w^4$, and k_r/k_o , respectively.

For *o*-xylene available results enable these two factors to be separated. Myhre^{7a} reported yields of 3-nitro-*o*-xylene resulting from solvolysis of ester (I) in 50, 60, and 70% sulphuric acid from which values for k_r/k_o for these media of 0.02, 0.18, and 4.0, respectively, follow. Combined with the nitration yields (interpolation or slight extrapolation of Figure 2) these values lead to the percentages of initial nitration at *C-*ipso** (C-1 + C-2), C-3, and C-4 shown in Table 5. Increasing acidity substantially increases the proportion of reaction at C-4, and to a smaller degree that at C-3, both at the expense of *ipso*-nitration; because of the need for interpolation and extrapolation in Figure 2 the values are approximate.

Comparison of the figures for 50% H₂SO₄ (Table 5)

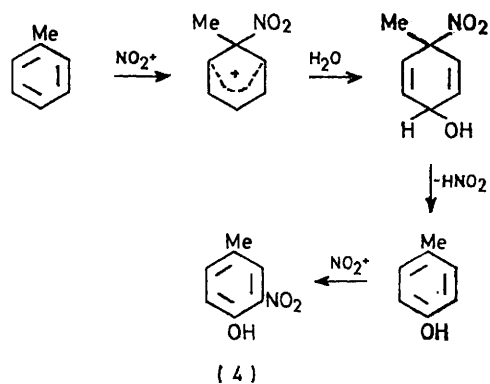
borne out by the consequent non-quantitative yield of mononitrotoluenes, and the appearance among the

TABLE 5

Percentages of initial attack at the various positions in *o*-xylene

	<i>C-<i>ipso</i></i>	C-3	C-4
50% H ₂ SO ₄	64	11	25
60% H ₂ SO ₄	55	15	30
70% H ₂ SO ₄	45	18	37

products of 4-hydroxy-3-nitrotoluene (g.l.c. identification). The latter is presumably formed as shown in reaction (4). It accounts for 4.2% of the total when



nitration is affected in 54% sulphuric acid, which may be compared with the reported 3–4% of *ipso*-capture when toluene is nitrated in acetic anhydride. This of course does not *prove* that capture is complete in either medium.

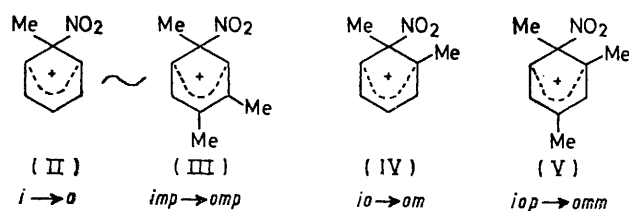
Only in >74% sulphuric acid do 1,2,3- and 1,2,4-trimethylbenzene give mononitro-derivatives quantitatively (Figures 4 and 5). The marked decrease

in the yield of 1,2,3-trimethyl-4-nitrobenzene at lower acidities indicates capture of the W_i formed at either C-1 or C-2, or both of these W_i s. Acetate adducts arising from both W_i s have been reported.^{6b,15} The yield of 1,2,4-trimethyl-6-nitrobenzene suffers a similar fate (Figure 5), presumably because of capture of the W_i formed at C-1. The accompanying appearance of 3,4-dimethylbenzaldehyde suggests that this is one of the products of such capture, though it cannot account for the whole of the decrease in the yield of 1,2,4-trimethyl-6-nitrobenzene. At lower acidities the yield of 1,2,4-trimethyl-5-nitrobenzene drops, showing that nitro-group migration from C-4 to C-5 can also be prevented by capture. Acetate adducts arising from W_i s formed at C-1 and C-4 in the nitration of 1,2,4-trimethylbenzene have been reported.^{6b} As expected,^{6b} the yield of nitro-*p*-xylene decreased with decreasing acidity (Table 3).

For toluene, 1,2,3-, and 1,2,4-trimethylbenzene the two factors controlling yields of nitro-compounds cannot yet be quantitatively separated because solvolysis of the appropriate esters [corresponding to (I)] has not been carried out. We are studying these reactions. In the meantime it is reasonable to suppose that $k_r:k_c$ is the quantity of primary importance, and that medium effects upon the ratios of rate constants for initial attack at the various positions are of secondary importance in determining yields.

Selectivity in the Migration Process.—The substantial increase in the yield of 1,2,4-trimethyl-6-nitrobenzene with increasing acidity is not matched by an increase in the yield of the 1,2,4-trimethyl-3-nitro-isomer. This suggests that the W_i formed at C-4 shows selectivity in rearranging, the nitro-group migrating preferentially to C-5 rather than to C-3. Of these two positions C-5 is the more reactive in direct nitration.

Migration versus Capture.—The acidities at which migration and capture compete equally for W_i s can be estimated approximately. Structures (II)–(V) are arranged in order of increasing acidity for equal partitioning, that is in order of decreasing ease of migration relative to that of capture.



It seems likely (see below, and ref. 15) that a methyl group activates positions in the order $p > o \gg i > m$,

¹⁵ A. Fischer and G. J. Wright, *Austral. J. Chem.*, 1974, **27**, 217.

¹⁶ A. F. Holleman, *Chem. Rev.*, 1924, **1**, 187.

and the above sequence is one in which migration is increasingly 'uphill.' This is illustrated by the code beneath the structure where, for instance, $iop \rightarrow omm$ means that the nitro-group migrates from a position activated by *i*-, *o*-, and *p*-methyl groups to one activated by *o*-, and two *m*-methyl groups. 1,2,3-Trimethylbenzene is not included because the proportions of migration to C-4 arising from C-1 and C-2 are unknown.

Selectivity in the Formation of the Various Wheland Intermediates.—Since all except toluene of the compounds studied are nitrated at the encounter rate relative aromatic reactivities cannot be investigated. However, positional selectivity is retained (see above) and it is interesting to examine the activating effect of the methyl group at nuclear positions and to enquire if it is additive.¹⁶ Relative positional reactivities change with the medium (see above) and clearly there can be no unique set of partial rate factors (p.r.f.) for all media. The ratio of p.r.f.s, $f_i:f_o:f_m:f_p$, of 2.2:20.8:1.0:25.6 has been deduced¹³ from the product yields from the nitration of toluene in acetic anhydride. Rather different ratios (3.1:14.1:1.0:23.2) were found¹⁵ to minimise the sum of the deviations between observed values of product distributions for the methylbenzenes in the same medium and those calculated on the basis of additivity,¹⁶ but their significance is less clear. Our product yields for the nitration of toluene in 54% sulphuric acid lead to the ratios (same order) 2.2:16.0:1.0:16.3. However, of all the compounds studied toluene is the one for which the lowest acidities are needed for capture to occur (Figures 2–5) so that there is the greatest uncertainty that nucleophilic capture at low acidities is complete. The ratios $f_i:f_m$ and $f_o:f_m$ should therefore be regarded as minimum and maximum figures respectively. We have calculated the product distributions to be expected in the methylbenzenes for a range of values of these p.r.f. ratios consistent with our data for toluene, both on the basis of additivity and using a modified version of the 'demand dependent free energy relationship'¹⁷ (without buttressing parameters). The latter is an attempt to fit the data with one adjustable parameter (the ratio $f_i:f_o$). The rather limited conclusions which can be drawn are that: (i) no ratio gives an excellent fit, but a wide range of ratios gives a reasonable fit (as good as that found with the best-fitting p.r.f.s for nitration in acetic anhydride¹⁵), so that $f_i:f_o$ cannot be chosen in this way, and (ii) the 'demand dependent' calculations give somewhat better fits than normal additivity. Further discussion is deferred until we have more information about *ipso*-attack in toluene.

[4/1979 Received, 26th September, 1974]

¹⁷ K. C. Richards, A. L. Wilkinson, and G. J. Wright, *Austral. J. Chem.*, 1972, **25**, 2369.