Electrophilic Aromatic Substitution. Part 16.[1] The Nitration of Anisole,[2] *o*-Methylanisole, and *p*-Methylanisole [2] in Aqueous Sulphuric Acid

By **James W. Barnett, Roy B. Moodie, Kenneth Schofield,** and **John B. Weston,** Department of Chemistry, The University, Exeter, Devon EX4 4QD
Robert G. Coombes,* John G. Golding, and **Geoffrey D. Tobin,** Department of Chemistry, The City University, St. John Street, London EC1V 4PB

In the quantitative mononitration of anisole in 54—82% sulphuric acid at 25° the *o* : *p* ratio varies from 1.8 to 0.7. It is suggested that the rate-limiting step is the formation of an encounter pair between the nitronium ion and an anisole molecule which is hydrogen-bonded to a hydronium ion. The change in the *o* : *p* ratio may be due to competition between direct formation of Wheland intermediates from the hydrogen-bonded encounter pair, and loss of the hydronium ion to give a nitronium ion–anisole encounter pair, with subsequent formation of Wheland intermediates. With *o*- and *p*-methylanisole the products, and changes in product ratios with acidity are interpreted by considering the fates of the *ipso*-Wheland intermediates formed at C–Me. 4-Methyl-2-nitrophenol is an important product of the nitration of *p*-methylanisole, and results from *ipso*-attack by nitronium at C–Me, followed by attack of water and loss of methoxy.

MANY reports on the nitration of anisole have appeared.[3] Attention has usually been concentrated on the *o* : *p* ratio of mononitroanisoles produced. The high *o* : *p* ratio reported for nitration with benzoyl nitrate and with nitric acid in acetic anhydride compared with other nitrating agents which involve the nitronium ion has been used in arguments about the mode of attack of the electrophile concerned,[4] the possible influence of hydrogen

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[1] Part 15, R. B. Moodie, K. Schofield, and J. B. Weston, *J.C.S. Perkin II*, 1976, 1089.

[2] Presented in part at the 169th National Meeting of the American Chemical Society, Philadelphia, April 1975; R. G. Coombes, J. G. Golding, L. W. Russell, and G. D. Tobin, in 'Laboratory and Industrial Nitrations,' A.C.S. Symposium Series No. 22, ed. L. F. Albright and C. Hanson, American Chemical Society, Washington, 1976, p. 73.

[3] (*a*) J. G. Hoggett, R. B. Moodie, J. R. Penton, and K. Schofield, 'Nitration and Aromatic Reactivity,' Cambridge University Press, Cambridge, 1971, p. 95; (*b*) S. R. Hartshorn and K. Schofield, *Progr. Org. Chem.*, 1971, **8**, 298.

[4] P. B. D. de la Mare and J. H. Ridd, 'Aromatic Substitution, Halogenation and Nitration,' Butterworths, London, 1959, p. 76; R. O. C. Norman and G. K. Radda, *Proc. Chem. Soc.*, 1960, 423; *J. Chem. Soc.*, 1961, 3030.

bonding on the mode of attack or on the substituent effect of the methoxy-group,[5] and the influence of the dielectric constant of the medium.[6]

The situation, however, appeared clarified when it was demonstrated that nitration involving fortuitous catalysis by nitrous acid could be responsible for low *o* : *p* ratios reported for nitration with nitric acid in aqueous sulphuric acid.[7] Nitration in the absence of nitrous acid in 65% sulphuric acid gave an *o* : *p* ratio of 1.5 whereas the presence of only *ca.* 4×10^{-2}M-nitrous acid gave an *o* : *p* ratio of 0.06. It then became a tenable hypothesis to believe that nitration by nitronium ion gave a high *o* : *p* ratio (*ca.* 60—70% of *o*-nitroanisole) and that low values observed under various circumstances were the result of varying amounts of fortuitous nitration catalysed by nitrous acid.[8] This possibility was suggested in 1957 by Halvarson and Melander.[9]

A rate profile for the nitration of anisole with nitric acid in 41—63% sulphuric acid, when nitrosation was precluded, was reported by Deno and Stein.[10] This indicated that anisole reacts *ca.* 70 times faster than does benzene in 57.3% sulphuric acid. More accurate data involving lower substrate concentrations are now available for most of the other substrates studied in this work.[11] A limiting rate of nitration corresponding to the rate of encounter of sufficiently reactive molecules with nitronium ions in this medium has been established,[11a] and Deno and Stein's data suggest that anisole reacts surprisingly at a rate a little less than the limiting one.

More recently the importance of *ipso*-attack at positions bearing alkyl groups,[12] and a methoxy-group,[13] has been amply demonstrated. Our interest in the nature of effective nitrating species under various conditions, the phenomenon of the encounter rate, and *ipso*-substitution have led us to investigate fully the kinetics and products of nitration of anisole, *o*-methylanisole, and *p*-methylanisole with nitric acid in aqueous sulphuric acid with the results presented in this paper. In the case of *p*-methylanisole nitration with nitric acid in acetic anhydride has been reported [14] to involve some demethylation, to form 4-methyl-2-nitrophenol, although no explanation was offered. It is clear that *ipso*-attack at C-Me should be of importance for this substrate particularly as it has been clearly demonstrated [15] for the nitration of 3,4-dimethylanisole in a similar medium. This point has also been made recently by Taylor.[16]

EXPERIMENTAL

Materials.—98% Sulphuric acid, 70% nitric acid, acetic acid, urea, and sulphanilic acid were AnalaR reagents. Concentrations of diluted sulphuric acid solutions were determined from density measurements. Anisole and *p*-methylanisole were commercial reagents purified by distillation. Sulphamic acid was G.P.R. grade. The nitroanisoles, *p*-nitroethylbenzene, 4-methyl-3-nitroanisole, 4-methyl-2-nitrophenol, 2-amino-4-methylanisole, and 2,4-dinitroanisole were redistilled or recrystallized commercial reagents. 4-Nitroveratrole was Koch–Light Ltd. Puris grade. *o*-Methylanisole was prepared by methylating *o*-cresol.[17] These compounds had physical properties corresponding to those in the literature.

2,6-*Dinitroanisole.* This, m.p. 118° (lit.,[18] 118°), was prepared by boiling 1-chloro-2,6-dinitrobenzene with sodium methoxide in methanol.

4-*Methyl*-2-*nitroanisole.* This was prepared by oxidising the corresponding amino-compound.[19] Trifluoroacetic anhydride (8.5 cm^3) was added to 89% hydrogen peroxide (1.4 cm^3) in dichloromethane (25 cm^3) at 0°. After stirring for 5 min, 4-methyl-2-aminoanisole (1.7 g) in dichloromethane (15 cm^3) was added over 30 min, and the mixture was boiled for 1 h. The crude product was washed successively with 5N-hydrochloric acid (× 3), water, and 10% sodium carbonate solution. After drying ($MgSO_4$) and solvent removal a dark brown solid resulted. This was extracted with ether and, after drying and solvent removal, 4-methyl-2-nitroanisole was obtained as a dark yellow oil (Found: C, 58.4; H, 5.5; N, 7.8. Calc. for $C_8H_9NO_3$: C, 57.5; H, 5.4; N, 8.3%). It gave one peak on g.l.c. analysis and had ^{1}H n.m.r. and i.r. spectra consistent with its structure.

4-*Methyl*-2-*nitrophenol.* 70% Nitric acid (10 cm^3) was added to a solution of *p*-methylanisole (10 cm^3) in chloroform (100 cm^3) and the mixture was shaken vigorously. After a few minutes the solution was washed with water, and after drying ($MgSO_4$) the chloroform was removed. The resultant oil exhibited three peaks on g.l.c. analysis (Table 1) corresponding to *p*-methylanisole, 4-methyl-2-nitroanisole (A), and a third component (B). The ratio A : B was *ca.* 0.7. *p*-Methylanisole was removed by vacuum distillation and the residue was dissolved in chloroform and passed down a 12 in column of alkaline alumina (Brockmann activity 2). An initial fraction was discarded. Chloroform was removed from the yellow middle fraction to yield a yellow crystalline solid, m.p. 32.5—33.0° (Found: C, 54.8; H, 4.6; N, 9.1. Calc. for $C_7H_7NO_3$: C, 54.9; H, 4.6; N, 9.2%). The ^{1}H n.m.r. spectrum, τ (CCl_4) −0.5 (1 H), 2.0—3.0 (3 H), and 7.7 (3 H), and mass spectrum showed this compound to be 4-methyl-2-nitrophenol (lit.,[20] m.p. 32.5°). This sample which corresponded to the third g.l.c. peak was identical with the commercial sample of 4-methyl-2-nitrophenol.

2-*Methyl*-X-*nitroanisoles* (X = 3—6). These were prepared by diazotisation of the appropriate nitro-*o*-toluidine,

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[5] J. H. Ridd in 'Studies on Chemical Structure and Reactivity,' ed. J. H. Ridd, Methuen, London, 1966, p. 141.

[6] M. A. Paul, *J. Amer. Chem. Soc.*, 1958, **80**, 5332.

[7] J. G. Hoggett, R. B. Moodie, and K. Schofield, *Chem. Comm.*, 1969, 605.

[8] Ref. 3*b*, p. 299.

[9] K. Halvarson and L. Melander, *Arkiv. Kemi*, 1957, **11**, 77.

[10] N. C. Deno and R. Stein, *J. Amer. Chem. Soc.*, 1956, **78**, 578.

[11] (*a*) R. G. Coombes, R. B. Moodie, and K. Schofield, *J. Chem. Soc.* (*B*), 1968, 800; (*b*) R. G. Coombes, D. H. G. Crout, J. G. Hoggett, R. B. Moodie, and K. Schofield, *ibid.*, 1970, 347.

[12] S. R. Hartshorn, *Chem. Soc. Rev.*, 1974, **3**, 167.

[13] B. A. Collins, K. E. Richards, and G. J. Wright, *J.C.S. Chem. Comm.*, 1972, 1216.

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[15] A. Fischer and D. R. A. Leonard, *J.C.S. Chem. Comm.*, 1973, 300.

[16] R. Taylor in 'Specialist Periodical Report on Aromatic and Heteroaromatic Chemistry, Vol. 3,' The Chemical Society, London, 1975, p. 250.

[17] A. I. Vogel, 'A Textbook of Practical Organic Chemistry,' Longmans, London, 1948.

[18] M. J. ter Weel, *Rec. Trav. chim.*, 1915, **35**, 44.

[19] W. D. Emmons, *J. Amer. Chem. Soc.*, 1954, **76**, 3470.

[20] M. O. de Vries, *Rec. Trav. chim.*, 1909, **28**, 276.

followed by decomposition to give the nitrocresol.[21] This was methylated with dimethyl sulphate and potassium carbonate in xylene.[22]

Kinetic Measurements.—The conventional technique described originally [11a] was used. The substrate was usually added to the aqueous sulphuric acid (25 cm^3) as a solution in acetic acid (0.100 cm^3). Sulphanilic acid, sulphamic acid, or urea were used as nitrous acid traps in both kinetic and product experiments as indicated. A Pye–Unicam SP 1800 or Perkin-Elmer PE 402 spectrophotometer was used.

Product Analyses.—(i) *From reactions in* $<$ *ca.* 70—73% *sulphuric acid.* The technique described previously [23] was used, sometimes with the following minor modifications. The substrate was added in acetic acid solution (1.0—1.5 cm^3); solutions were only shaken initially to ensure mixing (the dead space in reaction flasks was negligible); chloroform or dichloromethane were used for extraction; the reference standard was added after extraction; the column (12 in) was washed down with ether; sealed tubes were not used.

TABLE 1

G.l.c. conditions

Product	Reference standard	Column *	t/°C	Flow rate (cm^3 min^{-1})
Nitroanisoles	p-Nitroethylbenzene	A	140	60
	p-Nitrotoluene	B	165	40
2,4-Dinitroanisole	4-Nitroveratrole	C	208	60
2,6-Dinitroanisole	4-Nitroveratrole	C	145	60
4-Methylnitroanisoles	4-Nitroveratrole	A	154	40
4-Methyl-2-nitrophenol		C	168	90
2-Methylnitroanisoles	p-Nitrotoluene	D	165	40

* A, 1 m × 1/4 in, 5% PEGA on 1% phosphoric acid washed Chromasorb W, 60—85 mesh; B, 2.1 m × 1/4 in, 15% SE30 on Chromasorb W, 80—100 mesh; C, 1.5 m × 1/4 in, 1½% OV225 on universal support, 60—85 mesh; D, 2.1 m × 1/4 in, 15% Apiezon on Chromasorb W, 80—100 mesh. Pye 104 machine (flame ionisation detector).

(ii) *From reaction in* $>$ ca. 70—73% *sulphuric acid.* The equimolar technique described previously [23] was used, sometimes with the modifications described above. A pleated flask was not used for p-methylanisole or for some runs on anisole. Table 1 gives details of the g.l.c. procedure.

All nitro-products were identified by comparison of their retention times on g.l.c. analysis with those of independently identified authentic samples of the compounds. For the products from p-methylanisole two different columns were used and gave consistent results. In addition the appropriate peaks in the product from nitration of p-methylanisole in 58.1 and 73.5% sulphuric acid were subject to a g.l.c.–mass spectroscopic examination which confirmed their identities as 4-methyl-2-nitroanisole and 4-methyl-2-nitrophenol.

In 70—82% sulphuric acid 3—5% p-methylanisole was recovered. This amount was subtracted from the initial amount when calculating yields and mass balance.

(iii) *Silylation procedure.* It has been found possible to identify o-, m,- and p-nitrophenol, in 100, *ca.* 35, and *ca.* 25% yields respectively, after extraction from a *ca.* 1 × 10^{-4}M solution of these compounds in 67.6 and 87.0% sulphuric acid by the above procedure, treatment with an excess of *NO*-bis(trimethylsilyl)acetamide and g.l.c. analysis using a 1.5 m × ¼ in column of 1½% OV1 on 60—85 mesh universal support at 130° (60 ml min^{-1} N_2).

Activity Coefficients of Anisole and the Methylanisoles.—A solution of the anisole (20 cm^3, 2% by volume)in cyclohexane was stirred vigorously with water or with aqueous sulphuric acid (10 cm^3) of the required concentration at 25°. The layers were separated and the u.v. absorption of the aqueous or aqueous acid layer after appropriate dilution was compared with that of a solution of anisole of known concentration in the same medium. The activity coefficient is the ratio of the concentration in water to that in the aqueous acid, when extraction in each case is made from a cyclohexane solution of the same concentration.

RESULTS

Kinetics.—Second-order rate coefficients are given in Table 2 and rate profiles in Figure 1. For anisole, runs at most acidities were carried out in triplicate, with sulphanilic acid, sulphamic acid, and urea serving severally as nitrosation inhibitors. The triplicate experiments gave identical runs within experimental error.

Yields of Nitro-compounds.—These are given in Tables 3 and 4 and Figures 2—4.

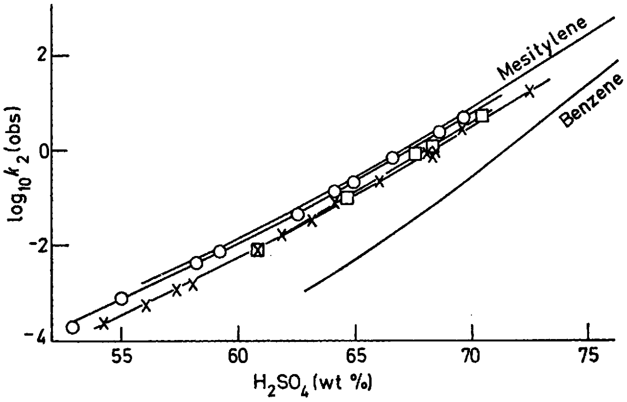

FIGURE 1 Rate profiles for nitration in aqueous sulphuric acid (○, o-methylanisole; □, p-methylanisole; ×, anisole)

Anisole. Yields of mononitroanisoles were not quantitative above 82% sulphuric acid. o- and p-Nitroanisoles (6 × 10^{-5}M) were recovered quantitatively by the extraction method used from their solutions in 89% sulphuric acid which had been kept at 25° for 1 h. 2,4- and 2,6-dinitroanisole were also extracted quantitatively from solutions in

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[21] M. J. Astle and W. P. Cropper, *J. Amer. Chem. Soc.*, 1943, **65**, 2395.

[22] M. S. Shah, C. T. Bhatt, and D. D. Kanga, *J. Chem. Soc.*, 1933, 1375.

[23] J. W. Barnett, R. B. Moodie, K. Schofield, and J. B. Weston, *J.C.S. Perkin II*, 1975, 648.

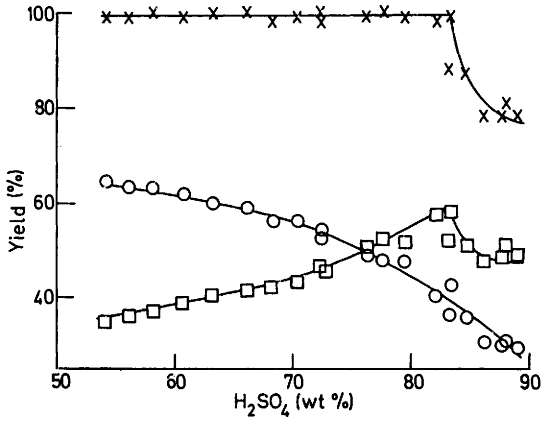


FIGURE 2 Nitration of anisole (○, *o*-mitroanisole; □, *p*-nitroanisole; ×, total)

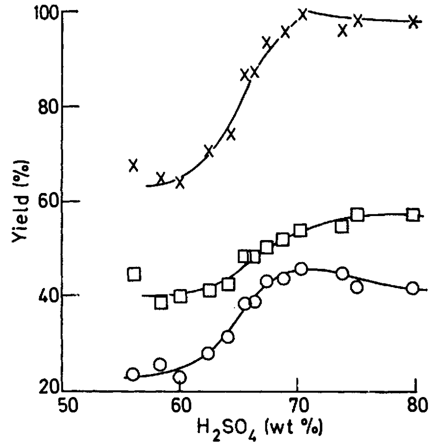


FIGURE 3 Nitration of *o*-methylanisole (○, 2-methyl-6-nitroanisole; □, 2-methyl-4-nitroanisole; ×, total)

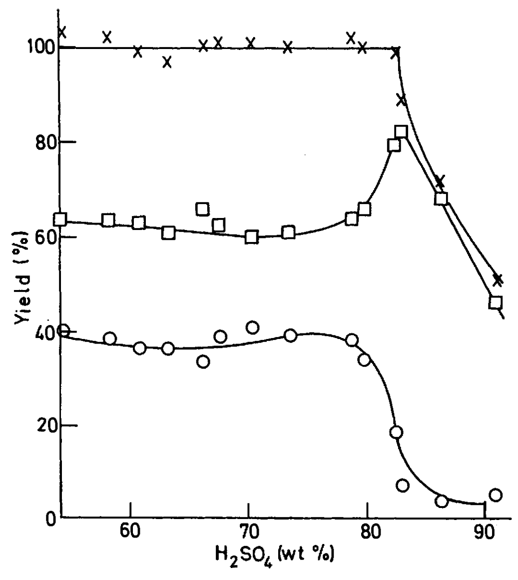


FIGURE 4 Nitration of *p*-methylanisole (○, 4-methyl-2-nitrophenol; □, 4-methyl-2-nitroanisole; ×, total)

sulphuric acid (between 82.8 and 91.3% by weight), which had been kept at 25° for the time of a nitration experiment.

The possibility that dinitration was affecting yields in >82% sulphuric acid (Table 4) was examined. Significant amounts of dinitration occurred in >86% sulphuric acid.

TABLE 2

Second-order rate coefficients for nitration in sulphuric acid at 25.0 ± 0.2 °C

H_2SO_4 (%) [a]	$10^2[HNO_3]$/M	k_2(obs)/dm^3 mol^{-1} s^{-1}
	Anisole [b–d]	
54.2	5.5	2.4×10^{-4}
56.1	5.5	5.3×10^{-4}
57.4	9.2	1.14×10^{-3}
58.1	5.5	1.39×10^{-3}
60.8	5.5	7.3×10^{-3}
61.9	5.3	1.56×10^{-2}
63.2	0.39	0.031
64.1	2.7	0.075
66.1	0.17	0.21
68.1	2.0	0.86
68.3	0.089	0.78
68.4	0.20	0.94
69.6	0.17	2.6
70.4	0.089	4.1
70.4	0.18	4.0
72.5	0.046	16.4
	o-Nitroanisole [e–g]	
72.5	5.5	8.3×10^{-3}
	p-Nitroanisole [e,g,h]	
72.5	5.5	7.7×10^{-3}
	p-Methylanisole [d,e,i]	
60.8	5.5	6.8×10^{-3}
64.6	0.33	9.8×10^{-2}
67.6	0.089	0.89
68.3	0.089	1.20
70.4	0.089	4.8
	4-Methyl-2-nitroanisole [e,d,j]	
74.4	0.089	1.00
75.3	0.089	1.77
	4-Methyl-3-nitroanisole [e,d,k]	
74.4	5.5	4.2×10^{-3}
	o-Methylanisole [b,d,l]	
52.9	3.7	2.4×10^{-4}
55.0	3.4	6.0×10^{-4}
58.2	5.5	4.1×10^{-3}
59.2	4.1	7.0×10^{-3}
62.5	4.5	0.043
64.1	3.7	0.13
64.9	4.2	0.20
66.6	2.7	0.69
68.6	1.4	2.4
69.7	0.56	4.5

[a] ±0.1%. [b] Urea (*ca.* 3×10^{-2}M), sulphanilic acid (*ca.* 1×10^{-2}M), or sulphamic acid (*ca.* 2×10^{-2}M) present. [c] Measurements at 330 nm. [d] [ArH] *ca.* 1×10^{-4}M. [e] [Sulphanilic acid] *ca.* 1×10^{-2}M. [f] Measurements at 320 nm. [g] [ArH] *ca.* 6×10^{-5}M. [h] Measurements at 350 nm. [i] Measurements at 295 or 300 nm. [j] Measurements at 260 nm. [k] Measurements at 285 nm. [l] Measurements at 335 nm.

In calculating these yields allowance was made for the anisole which must be unchanged when dinitration occurs in equimolar reactions.

Neither *o*- nor *p*-nitrophenol (>0.1% would have been detected) was detected when the product from nitration in 92% sulphuric acid was examined by g.l.c. after silylation.

Nitration solutions in >82% sulphuric acid were noticeably yellow.

o-*Methylanisole*. The major products at all acidities were 2-methyl-4- and 2-methyl-6-nitroanisole (Table 3 and Figure 3), but traces of the 3- (<0.2%) and 5-nitro-isomer (<0.5%) were also detected. Separate experiments established that even at the lowest acidity (55% sulphuric acid) the products were unchanged in the reaction solution during the time of a nitration experiment.

TABLE 3

Yields of nitro-compounds from the nitration of anisoles in aqueous sulphuric acid at 25 °C

Compound	H_2SO_4 (%)	Yield of products (%)		Mass balance (%)
Anisole [a–e]		Nitroanisoles [d]		
		o-	p-	
	54.2	64.1	34.8	99
	56.1	63.1	36.0	99
	58.1	63.0	37.0	100
	60.8	61.7	38.7	99
	63.2	59.8	40.2	100
	66.1	58.8	41.2	100
	68.3	57.4	42.0	99
	70.4	56.0	43.0	99
	72.4	53.8	46.2	100
	72.5	52.5	45.3	98
	76.3 [e]	48.9	50.5	99
	77.7 [e]	47.7	52.3	100
	79.5 [e]	47.4	51.5	99
	82.1 [e]	40.5	57.3	98
	83.2 [c]	36.4	51.9	88
	83.3 [e]	42.6	56.4	99
	84.7 [e]	35.6	51.0	87
	86.2 [e]	30.3	47.6	78
	87.8 [e]	29.7	48.4	78
	88.0 [e]	30.4	50.6	81
	89.0 [e]	29	49	78
p-Methylanisole [c,f]		4-Methyl-2-nitrophenol	4-Methyl-2 2-nitroanisole	
	46.0 [g,h]	40.0	61.1	101
	54.2 [g]	40.0	63.6	104
	58.1 [g]	38.2	63.4	102
	60.8 [g]	36.2	63.1	99
	63.2 [g]	36.1	60.7	97
	66.1 [g]	33.9	65.7	100
	67.6 [g]	39.0	62.4	101
	70.3 [e,g]	40.8	59.8	101
	73.5 [e,g]	39.2	60.8	100
	78.8 [e,g]	38.2	64.3	102
	79.8 [e,b]	34.2	65.7	100
	82.5 [e,g]	18.7	79.9	99
	83.0 [e,b]	7.0	82.3	89
	86.3 [e,b]	4.0	68.1	72
	90.8 [e,b]	5.0	46.2	51
o-Methylanisole [a–c]		2-Methyl-6-nitroanisole [i]	2-Methyl-4-nitro anisole [i]	
	56.1	23.2	44.3	67.5
	58.4	25.2	38.6	64.7
	60.0	23.2	39.9	64.0
	62.5	27.8	41.4	70.5
	64.1	31.3	42.4	74.0
	65.6	38.4	48.2	86.8
	66.3	38.9	48.4	87.1
	67.4	43.2	50.2	93.4
	68.8	43.8	51.8	95.6
	70.3 [e]	45.7	53.8	99.5
	73.8 [e]	44.7	54.6	96.0
	75.0 [e]	42.0	57.3	98.0
	79.8 [e]	41.7	57.1	98.0

[a] [ArH] *ca.* 1—2 × 10^{-4}M. [b] [Sulphamic acid] *ca.* 2 × 10^{-2}M or [Urea] *ca.* 3 × 10^{-2}M. [c] [HNO_3] = 2 × 10^{-4}—5 × 10^{-2}M. [d] <10^{-3}% *m*-Nitroanisole was found. [e] Equimolar proportions of ArH and HNO_3. [f] [ArH] *ca.* 2 × 10^{-4}M. [g] [Sulphanilic acid] *ca.* 1 × 10^{-2}M. [h] At 60°. [i] 2-Methyl-3-nitroanisole (<0.2%) and 2-methyl-5-nitroanisole (<0.5%) were also detected by g.l.c.

p-*Methylanisole*. 4-Methyl-2-nitrophenol and 4-methyl-2-nitroanisole were formed in approximately constant proportions and quantitative yields in 46—80% sulphuric acid. 4-Methyl-3-nitroanisole could not have been present to the extent of >0.2%. The ratio of the products was constant during the course of a run (Table 5). It was confirmed separately that the products and 4-methyl-3-nitroanisole were recovered quantitatively from simulated reaction solutions by the extraction method employed. Thus, 4-methyl-2-nitroanisole, 4-methyl-3-nitroanisole, and 4-methyl-2-nitrophenol (each 4 × 10^{-5}M) were recovered in 99, 100, and 99% yields respectively from 68% sulphuric acid containing 9 × 10^{-4}M-nitric acid and 2 × 10^{-2}M-sulphamic acid after 100 min at 25° (*ca.* 10 half-lives for the nitration of *p*-methylanisole).

TABLE 4

Yields of nitro-compounds from the nitration of anisole in >82% sulphuric acid [a] at 25 °C

H_2SO_4 (%)	Yield of products (%)				Mass balance (%)
	o-Nitroanisole	p-Nitroanisole	2,4-Dinitroanisole	2,6-Dinitroanisole	
83.2	36.4	51.9	<0.1	b	88
86.2	31.8	49.8	5.0	b	87
90.3	26.2	39.6	6.7	b	73
91.8	20.5	40.6	8.5	0.2	70
94.3	20.5	39.8	21.9	2.2	84

[a] [ArH] = [HNO_3] = 2.2 × 10^{-4}M; [Sulphamic acid] *ca.* 2 × 10^{-2}M. [b] <10^{-2}%.

TABLE 5

Ratios of products formed in the nitration [a] of *p*-methylanisole in 68.5% sulphuric acid at 25 °C

Extent of reaction (%)	[4-methyl-2-nitrophenol]/[4-methyl-2-nitroanisole]
30	0.67
45	0.72
70	0.73
90	0.72

[a] [ArH] 9.5 × 10^{-5}M, [HNO_3] 8.2 × 10^{-4}M, and [sulphamic acid] 2 × 10^{-2}M.

TABLE 6

Activity coefficients of anisole and the methylanisoles at 25 °C

H_2SO_4 (%)	10^3E/dm^3 mol^{-1} cm^{-1}	$\log_{10}y$[a]
Anisole ($\lambda_{max.}$ 268 nm)		
56.6	1.33	0.137
65.9	1.14	−0.044
73.2	1.04	−0.332
o-Methylanisole ($\lambda_{max.}$ 270 nm)		
39.3	1.27	0.387
50.0	1.30	0.401
57.6	1.16	0.286
69.0	1.09	0.127
76.4	0.86	−0.284
p-Methylanisole ($\lambda_{max.}$ 276 nm)		
39.3	1.51	0.494
50.0	1.43	0.474
57.6	1.42	0.492
69.0	1.34	0.350
76.4	1.22	0.144

[a] *y* is the molar activity coefficient, with water as the standard state.

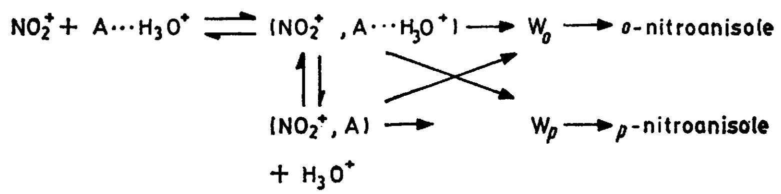
In >82% sulphuric acid, yields fell although 4-methyl-2-nitroanisole, 4-methyl-3-nitroanisole, and 4-methyl-2-nitrophenol were unchanged after 40 min in 86.3% sulphuric acid at 25°.

p-Cresol was not detected (>1% would have been detected) in the extract from a solution of *p*-methylanisole (1×10^{-4}M) in 82.5% sulphuric acid which had been kept at 25° for 3 h. *p*-Cresol could be extracted in 94% yield from a solution containing initially *p*-cresol (*ca.* 1×10^{-4}M).

Activity Coefficients.—Our data for anisole (Table 6) in 55—75% sulphuric acid follow on smoothly from data [24] for 0—50% sulphuric acid, and show that strong ' salting in ' occurs at higher acidities. This behaviour is similar to that of other organic molecules which can act as hydrogen-bonding bases, and different from that of such compounds as benzene and chlorobenzene.[24] The methylanisoles are similarly, but less markedly salted in (Table 6). In each case, salting in was accompanied by a marked decrease in the molar absorptivity at the wavelength of maximum absorption (Table 6).

DISCUSSION

Rate Profiles.—Mesitylene is representative of a number of compounds, more reactive than toluene, which give almost exactly the same rate profile,[11a,13] identified as that for the limiting rate of encounter of aromatic with nitronium ion. The rate profiles for anisole and *p*-methylanisole fall slightly below, whilst that for *o*-methylanisole is closely similar to that for mesitylene. Substituent constants [25] suggest that the anisoles should be reactive enough to be nitrated at the encounter rate. If the anisoles are hydrogen-bonded in strongly acidic solutions (Table 6), presumably to the hydronium ion, this would reduce the rate of encounter (for electrostatic reasons [26]) and the intrinsic reactivity. Either or both of these effects could explain the apparent departures from the limiting encounter rate.



SCHEME 1

Isomer Proportions.—In 54—82% sulphuric acid, anisole is quantitatively mononitrated, but the $o:p$ ratio varies steadily from 1.84 to 0.71 (Table 3 and Figure 2). If, as seems likely, the initial encounter involves a hydrogen-bonded species ($A\cdots H_3O^+$ in Scheme 1), it is possible that the encounter pair [23] (e.p.) so formed (NO_2^+, $A\cdots H_3O^+$) can form W_o and W_p* either directly or after loss of the hydronium ion. Since the latter process is likely to compete less effectively as the acidity increases, the marked change in isomer proportions may be from those characteristic of (NO_2^+,A) to those characteristic of (NO_2^+,$A\cdots H_3O^+$). In the latter, *o*-substitution, needing close approach of two positive charges, would be relatively disfavoured. It is noteworthy that nitration in acetic anhydride, where hydrogen-bonding can hardly be significant, produces a high (2.3) $o:p$ ratio.

With the methylanisoles, isomer proportions are relatively constant, except when they show the relatively sudden changes associated with a change in the fate of W_i^{Me}, as discussed below. This may be because loss of the hydrogen-bonded hydronium ion, if the latter is present, competes less effectively with W formation in these more reactive compounds.

The nitration of *o*-methylanisole leads to a mixture of 2-methyl-4- and 2-methyl-6-nitroanisoles, and the overall yield of mononitro-products increases from 65 to 100% in the region 62—68% sulphuric acid (Figure 3). It seems likely that the e.p. formed initially proceeds directly to W_i^{Me}, W_4, and W_6. W_i^{Me} is captured by water at low acidities (as are the similar W_is formed from toluene and polymethylbenzenes),[23] but at high acidities leads to the formation of nitro-products. This latter process however does not occur by 1,2-migration of the nitro-group, as it certainly does in the case of *o*-xylene,[23,27] because that could not lead to the observed increase in the yield of 2-methyl-4-nitroanisole (Figure 3). The fact that the yields of both major nitro-isomers increase, and that there is no increase in the yield of the 3-nitro-isomer, suggests that instead W_i^{Me} expels nitronium ion to return to the e.p. It is possible that the hydrogen-bonded hydronium ion has by this stage been lost, which would account for the higher proportions of the 6-nitro-isomer at high acidities. Scheme 2 is a possible mechanism, in which (NO_2^+,*o*-MeA $\cdots H_3O^+$) represents the first formed e.p., and (NO_2^+,*o*-MeA) that which is formed from W_i^{Me}.

1,2-Migration in the W_i^{Me} from *o*-methylanisole presumably fails to occur because it would be from a position *ortho* to methoxy to a position *meta* to it, and therefore relatively ' uphill '.[23] A similar situation obtains with *p*-methylanisole (see below). The alternative 1,2-migration to give W_i^{OMe}, and thence W_6 may occur to some extent (W_i^{OMe}s are known to occur in other cases),[13] but cannot be the exclusive pathway.

From *p*-methylanisole quantitative yields of mononitro-compounds are observed in 46—82.5% sulphuric

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* We use W to represent a Wheland intermediate, and suffixes to designate particular Ws in an obvious way. W_i^{R} indicates an *ipso*-Wheland intermediate with the electrophile attached to C–R.

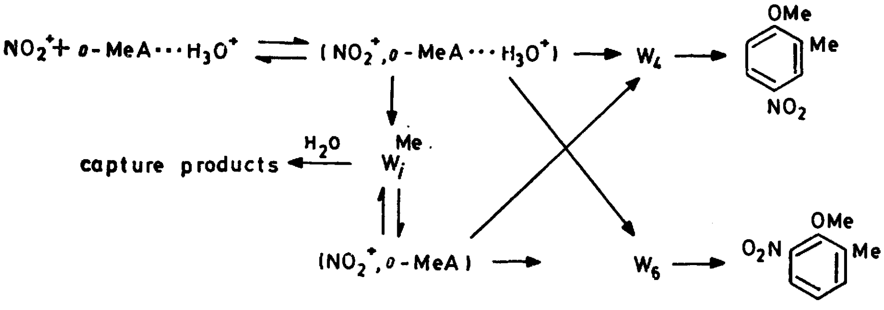
[24] K. Yates and R. A. McClelland, *Progr. Phys. Org. Chem.*, 1974, **11**, 323.

[25] C. D. Johnson, ' The Hammett Equation,' Cambridge University Press, Cambridge, 1973.

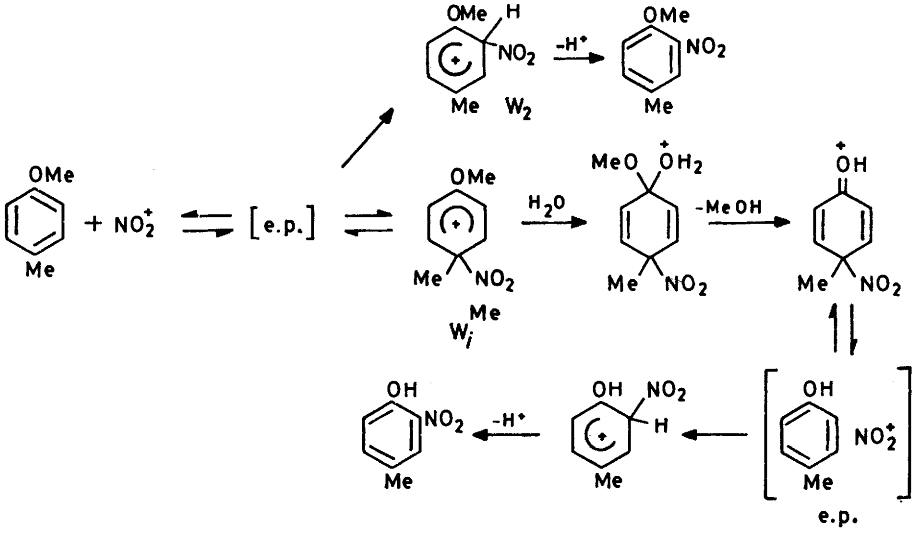
[26] M. Eigen, *Angew. Chem. Internat. Edn.*, 1964, **3**, 1.

[27] P. C. Myhre, *J. Amer. Chem. Soc.*, 1972, **94**, 7921.

acid (Figure 4). The ratio of 4-methyl-2-nitroanisole to 4-methyl-2-nitrophenol is constant up to *ca.* 80% H_2SO_4 but above this acidity the proportion of demethylated product rapidly diminishes. The behaviour of the 4-methyl-2- and -3-nitroanisoles and of *p*-methylanisole in simulated reaction media demonstrates that demethylation does not occur prior or subsequent to nitration and this conclusion is supported by the constant ratio over the wide range of acidity. Demethylation of W_2 cannot be occurring as it would have to compete with proton loss from W_2 and the ratio of products would vary with acidity. It is therefore suggested that the demethylated product is formed *via* W_i^{Me} with a *p*-methoxy-group (Scheme 3). Demethylation leads to W_i^{Me} with a *p*-hydroxy-group. Loss of nitronium ion from this species would yield an e.p., and in view of the probable reactivity of *p*-cresol the formation of 4-methyl-2-nitrophenol from it would be expected to be faster than the dissociation of the e.p. In accord with the conclusion that free *p*-cresol would not be present, the ratio of products remains constant during the course of an individual run (Table 5).



SCHEME 2



SCHEME 3

The analogy with the mechanism of acid hydrolysis of anisoles [28] suggests that demethylation may involve aryl–oxygen fission by attack of water at the carbon atom bearing the methoxy-group to give an adduct, and subsequent loss of methanol. In 80—82.5% sulphuric acid, as the water concentration falls the rate of this process becomes too slow to compete with the return to the e.p., the yield of demethylated product falls, and it is replaced by 4-methyl-2-nitroanisole. The absence of 4-methyl-3-nitroanisole under any of the conditions suggests not only that direct formation of W_3 does not occur to a significant extent, but also that the rearrangement of W_i^{Me} to W_3 does not occur, in agreement with the results from *o*-methylanisole.

The drop in yield of mononitro-compounds observed for both anisole and *p*-methylanisole in >82.5% sulphuric acid can be partly explained by dinitration, even though product studies at these acidities were performed with equimolar proportions of reactants to minimise this problem. Approximate calculations indicate that at the highest acidities the rate of dinitration is so large that significant dinitration could occur during the mixing process. The data in Table 4 show that both expected dinitro-products are formed from anisole. The measured relative rates of nitration of nitro-compounds (Table 2)

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[28] W. M. Schubert and R. H. Quacchia, *J. Amer. Chem. Soc.*, 1963, **85**, 1284.

show that dinitration will become important for *p*-methylanisole at lower acidities than for anisole, and it is possible but not certain that this is a complete explanation of the drop in yield for this substrate. Of the anisole nitrated in $>82.5\%$ sulphuric acid, however, 12—30% remains unaccounted for (Table 4) and we have at present no explanation for this. Nitration should obey a zeroth-order rate law at these acidities;[29] the estimated half-life is *ca.* 10^4 times smaller than the measured half-life for sulphonation in 89% sulphuric acid,[30] which excludes sulphonation as the cause of the low yields. Sulphonation does, however, prevent direct study of the rate of possible demethylation of these compounds at the highest acidities, but one cannot conceive that the demethylation reaction, which is insignificant for *p*-methylanisole in 82.5% sulphuric acid could become faster than the estimated rate of nitration ($t_{\frac{1}{2}}$ *ca.* 4×10^{-3} s in 89% sulphuric acid). In agreement with this no nitrophenols were detected from nitration of anisole in 92% sulphuric acid. Demethylation of the nitro-compounds also does not occur.

We thank the S.R.C. for support (J. W. B., J. G. G., and J. B. W.) and for the use of the Physico-Chemical Measurements Unit at Harwell.

[6/718 *Received, 12th April, 1976*]

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[29] J. W. Chapman and A. N. Strachan, *J.C.S. Chem. Comm.*, 1974, 293.

[30] R. G. Coombes and G. P. Tucker, unpublished results.