Orientation Effects in the Sulphonation of Anisidinium Ions in Sulphuric Acid

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The rate and position of monosulphonation of the ions NN-dimethyl-m-anisidinium, NN-dimethyl-p-anisidinium, and NNN-trimethyl-p-anisidinium have been recorded in D_2SO_4. The reaction is of the first order with respect to the anisidinium ion. A limited comparison of orientation effects of sulphonation and hydrogen isotope exchange is given with respect to the additivity principle of partial rate factors associated with substituents.

THIS paper describes the concurrent sulphonation and demethylation of substituted anisidinium ions in concentrated sulphuric acid as part of a study of the electrophilic reactivity of anisidines.[1,2]

Monosulphonation of NN-dimethyl-m-anisidinium ion occurs at the 4- or 6-positions [N is at C(1)], and at the 3- or 5-positions for NN-dimethyl-p-anisidinium and NNN-trimethyl-p-anisidinium ions. Partial rate factors are illustrated in the Figure and are compared with the rate factors for H^+–D^+ exchange at the same positions. The rate of hydrogen exchange is approximately 10^2 times the rate for sulphonation with both kinetic processes under pseudo-first-order conditions and with both processes directed at the same ring positions.

EXPERIMENTAL

Materials.—Acids. Sulphuric acid (AnalaR; d 1·84 g cm^{-3}) was used. D_2SO_4 was prepared by adding deuterium oxide (Norsk-Hydro 99·7%) to sulphur trioxide distilled from 60% oleum. (*Caution:* addition of water to sulphur trioxide is explosive unless performed very slowly.) Stock solutions of 100% (w/w) D_2SO_4 were made up and diluted to the acidity required; each solution was standardised with sodium hydroxide.

Substrates. Anisidines and hydroxyanilines were methylated by standard procedures.[3] Hydrogen sulphates and methosulphates were stored over desiccants. Analyses are in Table 1.

Kinetics.—The results in Table 2 were evaluated from an average of four or five runs within the substrate concentration range 0·2—0·6M; the variance in rate constants was no greater than ±10% over this range. Exact quantities of substrate, sulphuric acid, and an inert standard

[1] J. R. Blackborow, Ph.D. Thesis, London, 1966.
[2] J. R. Blackborow and J. H. Ridd, *Chem. Comm.*, 1967, 132.
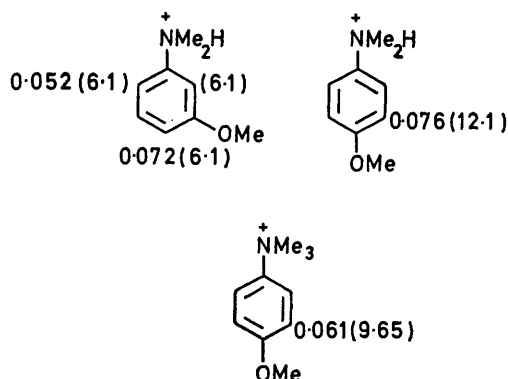[3] D. P. Evans and R. Williams, *J. Chem. Soc.*, 1949, 1199.

were introduced into an n.m.r. tube within a dry-box. The sealed tubes were kept in the preheater of a Perkin-Elmer R.10 spectrometer. Reaction rates were measured

$$\overset{+}{N}Me_2H \qquad \overset{+}{N}Me_2H$$

0·052 (6·1)   (6·1)   0·076(12·1)

0·072(6·1)   OMe   OMe

$$\overset{+}{N}Me_3$$

0·061(9·65)

OMe

Rate factors for sulphonation (35 ± 0·5 °C) (H–D exchange in parentheses) compared with a standard NNN-trimethyl-xylidinium hydrogen sulphate (for which the rate of H–D exchange in the ortho- and para-positions is taken as unity *). Solvent 97·0% D_2SO_4. Solute: 0·4M

* The actual first-order rate constant for H–D exchange is 20.5×10^{-5} s^{-1}.[1,2]

by estimating the change in the area of the aromatic proton magnetic resonance signal. A standard invariant

of NNN-trimethyl-3-sulpho-p-anisidinium tetraphenylborate (Found: C, 67·9; H, 6·0; N, 2·5; S, 5·45. $C_{34}H_{36}BNO_4S$ requires C, 72·2; H, 6·4; N, 2·5; S, 5·7%). p-Hydroxy-NNN-trimethylanilinium methosulphate similarly gave 4-hydroxy-NNN-trimethyl-3-sulphoanilinium tetraphenylborate (Found: C, 67·0; H, 6·3; N, 2·3; S, 5·7. $C_{33}H_{34}$-BNO_4S requires C, 71·9; H, 6·2; N, 2·55; S, 5·8%).

The sulphonations were monitored by n.m.r. A 1 : 1 (w/w) mixture of the sulphonation products of trimethyl-p-anisidinium ion and p-hydroxytrimethylanilinium ion sulphonated in 97·8% (w/w) H_2SO_4 and subsequently diluted to 91% (w/w) H_2SO_4 produced an identical aromatic n.m.r. spectrum to that obtained from the ' sulphonation ' of trimethyl-p-anisidinium ion in 91% (w/w) H_2SO_4. These observations suggest that the anisidinium ion has been partially O-demethylated to yield the hydroxyanilinium ion which has subsequently been sulphonated to give the monosulphonic acid of p-hydroxytrimethylanilinium ion.

The combined monosulphonation products of NN-dimethyl-m-anisidinium ion have as yet proved too difficult to separate in quantities sufficient for estimating the position of substitution of the sulphonic acid group. NNN-Trimethyl-m-anisidinium methosulphonate was sulphonated in the same way as its para-isomer, white crystals of NNN-trimethyl-4-sulpho-m-anisidium tetraphenylboate being isolated (Found: C, 67·1; H, 6·4; N, 2·45; S, 5·6. $C_{34}H_{36}BNO_4S$ requires C, 72·2; H, 6·4; N, 2·5; S, 5·65%).

TABLE 1

Analysis

	Found (%)				Calc. (%)			
	C	H	N	S	C	H	N	S
m-MeO·C_6H_4·NMe$_2$H$^+$ HSO$_4^-$	43·5	6·2	5·5	12·85	43·3	6·07	5·62	12·86
p-MeO·C_6H_4·NMe$_2$H$^+$ HSO$_4^-$	43·0	6·3	5·5	12·69	43·3	6·07	5·62	12·86
p-MeO·C_6H_4·NMe$_3^+$ MeSO$_4^-$	46·6	7·0	4·9	11·72	47·6	6·90	5·05	11·57
p-HO·C_6H_4·NMe$_3^+$ MeSO$_4^-$	46·8	6·5	5·2	12·0	45·6	6·51	5·32	12·17
m-MeO·C_6H_4·NMe$_3^+$ MeSO$_4^-$	46·8	7·1	5·0	11·8	47·6	6·90	5·05	11·57

proton resonance signal from an inert substance introduced with the reactants was used to check instrument variation. Sulphonation was carried out in D_2SO_4 and results (Table 2) represent the rate-determining step in the displacement of a deuteron by the —SO$_3$D group.

TABLE 2

Substrate ion 0·4M	Acidity (% w/w) D_2SO_4	10^5 (Rate const.)/ s^{-1} (35 ± 0·5 °C)
NN-Dimethyl-m-anisidinium (overall rate of monosulphonation)	99·0	7·5
	97·0	2·55
NN-Dimethyl-p-anisidinium	99·0	4·49
	97·0	1·55
NNN-Trimethyl-p-anisidinium	99·0	3·70
	97·0	1·25

Isolation of Sulphonic Acids.—NNN-Trimethyl-p-anisidinium methosulphate (5 g, 0·018 mol) was dissolved in 97·8% (w/w) H_2SO_4 (50 ml); after four days the solution was poured into sodium carbonate solution (500 ml). The pH was adjusted to 8 with H_2SO_4. Sodium tetraphenylborate (5 g in 50 ml H_2O) was added and a white microcrystalline precipitate was obtained; filtration and recrystallisation from water–acetone gave white crystals

The analysis for carbon in NNN-trimethyl-3-sulpho-p-anisidinium, 4-hydroxy-NNN-trimethyl-3-sulphoanilinium, and NNN-trimethyl-4-sulpho-m-anisidinium tetraphenylboron salts is very low, and became lower on successive recrystallisations from concentrated aqueous acetone solutions. A constant set of analytical data was eventually obtained from crystals produced by from slow crystallisation from aqueous acetone. The spectra and analysis of these crystals was consistent with their structure being interpreted as the zwitterions (I)—(III) [Found: C, 41·3; H, 6·4; N, 4·8; S, 11·3. $C_{10}H_{19}NO_6S$ (I) requires C, 42·7; H, 6·8; N, 5·0; S, 11·4%. Found: C, 46·5; H, 5·7; N, 5·9; S, 13·8. $C_9H_{13}NO_4S$ (II) requires C, 46·75; H, 5·65; N, 6·05; S, 13·85%. Found: C, 48·7; H, 6·0; N, 5·6. $C_{10}H_{15}NO_4S$ (III) requires C, 49·0; H, 6·1; N, 5·7%]

Zwitterions (I) and (III) dissolve readily in water; (II) is only slightly soluble in water at 30 °C, but dissolves after reflux. Intermolecular hydrogen bonding between the —OH and —SO$_3^-$ groups is a possible reason for the low solubility of zwitterion (II) in cold water and absence of water of crystallisation from the solid. The i.r. spectrum of solid (II) shows a low-wavelength shift and broadening of the OH stretching mode when compared with the expected value of 3500—3400 cm^{-1} [(I), ν(OH) 3550 and 3485 cm^{-1}; (II), ν(OH) 3030 cm^{-1}].

The precipitation of zwitterions (I)—(III) with sodium tetraphenylborate from concentrated aqueous solutions produce white gels which after filtration yield microcrystalline material identical with our analysed *NNN*-trimethyl-3-sulpho-*p*-anisidinium, 4-hydroxy-*NNN*-trimethyl-3-sulphoanilinium, and *NNN*-trimethyl-4-sulpho-*m*-anisidinium
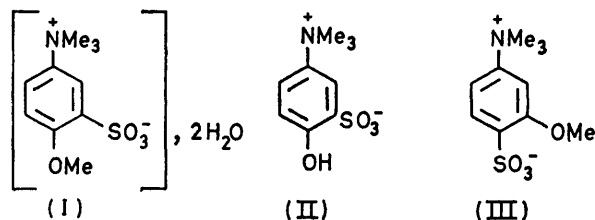
tetraphenylborate salts. The gels form more quickly in acid solutions (pH 5) but their carbon analysis is still low.

The sulphonation of *NNN*-trimethyl-*p*-anisidinium ion in 87% H_2SO_4 produces a mixture of *NNN*-trimethyl-3-sulpho-*p*-anisidinium and 4-hydroxy-*NNN*-trimethyl-3-sulphoanilinium ions (see Results section); these cations were precipitated as their tetraphenylborate salts. Fractional recrystallisation of these salts from aqueous acetone enabled the separation of the final products (I) and (II). This technique has not yet been successful in the separation of the products of sulphonation of *NN*-dimethyl-*m*-anisidinium ion.

RESULTS

A detailed description of the changes in the aromatic region of the n.m.r. spectra of *NN*-dimethyl-*m*-anisidinium, *NN*-dimethyl-*p*-anisidinium, and *NNN*-trimethyl-*p*-anisidinium ions as sulphonation and demethylation occur is given elsewhere.[1]

NN-Dimethyl-m-*anisidinium*.—At acidities above 97%, monosulphonation occurs with the production of two isomeric sulphonic acids in the approximate ratio 2 : 3. At lower acidities, *O*-demethylation accompanies sulphonation. The product of demethylation, *m*-hydroxydimethylanilinium, is sulphonated at a comparable rate with the substrate and produces two isomeric monosulphonic acids.

NN-Dimethyl-p-*anisidinium and* NNN-*Trimethyl*-p-*anisidinium*.—Similar behaviour was observed for both these compounds. Above acidities of 96%, monosulphonation occurs at the 3- or 5-position of the aromatic ring: at lower acidities *O*-demethylation accompanies sulphonation and the products of demethylation are again sulphonated at a similar rate to the substrate.

Diprotonation.—Evidence of *N,O*-diprotonation of *m*-hydroxy-*NN*-dimethylanilinium, *p*-hydroxy-*NNN*-trimethylanilinium, and the 3-sulpho-derivative of the latter was obtained and spectra could be interpreted in terms of a *N*-monoprotonation–*NO*-diprotonation equilibrium of these compounds.[4] Dimethyl-*m*- and -*p*-anisidinium ion and trimethyl-*p*-anisidinium ion are sulphonated too rapidly at acidities where such equilibrium could be detected.

[4] D. D. Perrin, ' Dissociation Constants of Organic Bases in Aqueous Solution,' Butterworths, London, 1965.
[5] J. C. D. Brand, *J. Chem. Soc.*, 1950, 1004.
[6] J. C. D. Brand and W. C. Horning, *J. Chem. Soc.*, 1952, 3922.

DISCUSSION

Sulphonation.—The rate of sulphonation in concentrated sulphuric acid is dependent on acidity and sulphur trioxide activity.[5-8]

The rate profiles for *NN*-dimethyl-*p*- and -*m*-anisidinium ions have slopes identical with that of trimethyl-*p*-anisidinium ion which suggest that the first two react through the mono-*N*-protonated cations, not *via* small equilibrium concentrations of free anisidines.

Dimethyl- and trimethyl-*p*-anisidinium ions are sulphonated in the same ring positions (3 or 5), which is also indicative of reaction through the mono-*N*-protonated cations for both species. Hydrogen exchange is *ca*. 10^2 times faster than sulphonation (Figure), but the rate-factor ratios are very similar for all three ions, the difference in size and reactivity of the electrophiles being considered. This similarity suggests that positional discriminating power is not very different for either reactant. Sulphonation *via* a charged electrophile in the rate-determining step therefore seems more likely than that by a neutral species. There is however an anomaly in this comparison because of the absence of the third sulphonic acid isomer from *NN*-dimethyl-*m*-anisidinium ion compared with hydrogen exchange which occurs at an equal rate at the 2-, 4-, and 6-positions of the aromatic ring.[1,2] The same anomaly is observed in the sulphonation of *m*-hydroxy-*NN*-dimethylanilinium ion where the steric requirements would be expected to be less rigorous.

Steric Effects on Reactivity in Sulphonation Reactions.—Reaction of *NNN*-trimethylanisidinium ion in 98% D_2SO_4 leads first to its 2,6,4-trideuterio-derivative and subsequently to monosulphonic acids. Sulphonation in D_2SO_4 gives only a singlet n.m.r. peak for the proton in position 5 in the ring of the sulphonation product and sulphonation in 98% H_2SO_4 gives only one ABX system for the three ring protons of the trimethyl-sulpho-*m*-anisidinium ion (Table 3). The spectra do not change when the solvent is diluted to 90% acidity. The singlet spectrum may therefore indicate the formation of only one isomer. The bulky N^+Me_3 group would undoubtedly inhibit reactivity towards sulphonation at the positions *ortho* to itself more than at a position *para*. It is therefore reasonable to suggest that the isomer formed is the *para*-sulphonic acid.

The pair of resonances assigned to the n.m.r. spectra of the proton in the five position of the rings of *m*-hydroxy-*NN*-dimethyl-*X*-sulphoanilinium and *NN*-dimethyl-*X*-sulpho-*m*-anisidinium ions (Table 3) are hardly likely to arise from a diprotonation–monoprotonation equilibrium of one sulphonic acid isomer because the intensity ratio of the pair hardly changes over one unit of H_0. It seems likely therefore that the two resonances in each compound arise from two monosulphonic acid isomers, one of which contains the

[7] J. C. D. Brand, A. W. P. Jarvie, and W. C. Horning, *J. Chem. Soc.*, 1959, 3844.
[8] C. W. F. Kort and H. Cerfontain, *Rec. Trav. chim.*, 1968, **87**, 24.

sulphonic acid group *para* to the nitrogen substituent. The N^+Me_3 group therefore inhibits sulphonation at the 2- *and* 6-positions of the anisidine ring whereas the N^+Me_2H group inhibits sulphonation at the 2- *or* 6-position (whilst still reacting *via* the monoprotonated species) irrespective of whether the substituent in the 3-position is –OH as in the hydroxyanilinium ion or –OMe as in the anisidium ion.

proceed exclusively *para* yet in the sulphonation of the trimethylanilinium ion a *meta*-directing substituent yields a product ratio *ortho* : *meta* : *para* of 8 : 78 : 14 despite the greater size of the $-N^+Me_3$ group than of the –OMe substituent.[9] Such irregularities are possibly due to the action of differing sulphonating agents in each case or product isomerisation.

Our results represent an attempt to correlate the

TABLE 3

¹H N.m.r. spectra at 60 MHz. Values/p.p.m. from $Me_2SO_4 = 0.0$ [99·0% D_2SO_4 (w/w)]

Ion	Solvent 99·0% (w/w)	Aromatic		NMe	Coupling const./Hz
NN-Dimethyl-m-anisidinium	D_2SO_4	$-(3\cdot2—3\cdot8)$		$\left.{0\cdot73 \atop 0\cdot81}\right\} d$	$^3J(NH–CH_3)$ 4·8
NN-Dimethyl-p-anisidinium	D_2SO_4	$\left.{-3\cdot50 \atop -3\cdot19}\quad{-3\cdot66 \atop -3\cdot34}\right\}$ (AA¹BB¹)		$\left.{0\cdot72 \atop 0\cdot82}\right\} d$	$^3J(NH–CH_3)$ 6·0
NNN-Trimethyl-p-anisidinium	D_2SO_4	$\left.{-3\cdot62 \atop -3\cdot18}\quad{-3\cdot78 \atop -3\cdot34}\right\}$ (AA¹BB¹)		0·60	J_{AB} 9·6
m-Hydroxy-NN-dimethylanilinium	D_2SO_4	$-3\cdot57$(s) †		0·77	
m-Hydroxy-NN-dimethyl-X-sulphoanilinium	D_2SO_4	$-4\cdot1$(s) †*	$-4\cdot05$(s) †*	0·63	
NN-Dimethyl-X-sulpho-m-anisidinium	D_2SO_4	$-4\cdot11$(s) †*	$-4\cdot10$(s) †*	0·63	
NNN-Trimethyl-3-sulpho-p-anisidinium	H_2SO_4	$-(3—4)$ (ABX)		0·70	J_{BX} 8·5
4-Hydroxy-NNN-trimethyl-3-sulphoanilinium	H_2SO_4	$-(3—4)$ (ABX)		0·70	J_{BX} 8·5
O-Protonated 4-hydroxy-NNN-trimethyl-3-sulpho-anilinium	H_2SO_4 (110%)	$\left.{-3\cdot3 \atop -2\cdot90}\quad{-3\cdot5 \atop -3\cdot10}\right\}$ (ABX)?			
p-Hydroxy-NNN-trimethylanilinium	H_2SO_4	$\left.{-3\cdot43 \atop -3\cdot07}\quad{-3\cdot58 \atop -3\cdot21}\right\}$ (AA¹BB¹)			J_{AB} 8·4
O-Protonated p-hydroxy-NNN-trimethylanilinium	H_2SO_4	$\left.{-3\cdot83 \atop -3\cdot59}\quad{-3\cdot67 \atop -3\cdot43}\right\}$ (AA¹BB¹)			J_{AB} 9·6
NNN-Trimethyl-m-anisidinium	H_2SO_4	$-(3—4)$		0·60	
NNN-Trimethyl-4-sulpho-m-anisidinium	H_2SO_4	$-(3\cdot0—4\cdot5)$ (ABX)		0·5	J_{BX} 10·0
NNN-Trimethyl-4-sulpho-m-anisidinium	D_2SO_4	$-4\cdot39$(s) †			

* Two monosulphonic acid isomers. † 2,4,6-Trideuterio-derivative.

Conclusion.—The similarity in the rate-factor ratios of hydrogen-isotope exchange and sulphonation particularly with respect to NN-dimethyl-m-anisidinium ion reinforce the view that the position *ortho* to the nitrogen pole is not deactivated with respect to the *para*-position. A direct comparison of H^+–D^+ exchange and sulphonation in these systems is open to criticism because of the unusual steric factors involved in sulphonation. The curious nature of steric interactions in sulphonation is not restricted to anisidinium ions; for example, the sulphonation of anisole appears to

orientations of differing electrophiles under identical experimental conditions. As such, they support no more than a superficial argument in favour of the limitations of the additivity principle of substituents.

⁹ H. Cerfontain, ' Mechanistic Aspects in Aromatic Sulphonation and Desulphonation,' Wiley, New York, 1968.