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THE S_N MECHANISM IN AROMATIC COMPOUNDS. PART XIII

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Some reactions being investigated involving the reaction of nucleophilic reagents with cationic groups attached to the benzene ring were found to be "abnormal" in the sense that substitution did not take place at a ring carbon atom. The present investigation describes the large and important difference found between the "abnormal" reactions of aryl sulfonium and ammonium ions.

The reactions investigated were of SCN^- in absolute methanol with *p*-nitrophenyldimethylsulfonium and *p*-nitrophenyltrimethylammonium ions, to give, irreversibly, *p*-nitrothioanisole and *p*-nitrodimethylaniline respectively, together with methyl thiocyanate. The reaction with the sulfonium ion in water as solvent was also investigated.

The rate constants obtained are given and compared in Table I.

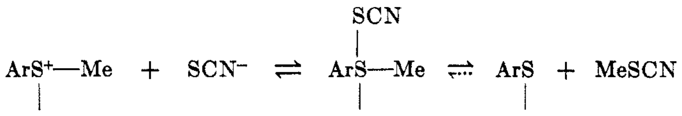
DISCUSSION

The methyl carbon atom in these compounds is susceptible to attack by a nucleophilic reagent by virtue of attachment to a positively charged hetero atom. Inasmuch as the inductive (−I) effect is concerned, the N^+ exerts the more powerful effect (*c.f.* Pauling's electronegativity indices (1a) which may be estimated as 3.3 and 2.8 for N^+ and S^+ respectively). Also while bond energies of $C—\overset{+}{N}$ and $C—S^+$ are not recorded, Pauling (1b) quotes C—S as being 6 K.cals. stronger than C—N and we may reasonably assume therefore that bond strength factors do not favor the demethylation of the sulfonium compound. If both are reacting by the same aliphatic S_N2 type reaction (I) the sulfonium compound should react more slowly, and not much faster as is found experimentally.

$$ArX^+ - Me + SCN^- \rightleftharpoons ArX——Me——SCN \rightleftharpoons ArX + MeSCN$$

(I)

The very large difference in magnitude and direction of the rate constants, and Arrhenius parameters, especially in activation energy, suggests that two different mechanisms are involved, and that while the ammonium compound reacts as shown (I), the sulfonium compound is able to react by a path (II) involving



$$\underset{|}{ArS^+}—Me + SCN^- \rightleftharpoons \underset{|}{\overset{SCN}{\overset{|}{ArS}}}—Me \rightleftharpoons \underset{|}{ArS} + MeSCN$$

(II)

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TABLE I

Compound	Rate Constant — $10^5 k_2$ — 1 moles^{-1} secs^{-1}							Activation Energy[a] (cals)	$\log_{10}$ Frequency Factor	Ratios at		100°
	(a) At temperatures shown in parenthesis				(b) Calculated at							
					0°	50°	100°			0°	50°	
p-Nitrotrimethyl ammonium chloride	21.9	165.5		685	0.04954	0.375	160	29000 ± 50	14.2	27200	3750	884 (SMe^+_2/NMe^+_3)
	(81.9)	(100.1)		(114.3)				22100 ± 200	13.1	138	106	88.1 ($MeOH/H_2O$)
p-Nitrodimethylsulfonium methosulfate												
(A)	77.5	262	283	827	2.59	1410	141800	23000 ± 250	11.7			
	(25.0)	(35.0)	(35.4)	(45.2)								
(B)	36.8	337		1740	0.0188	13.3	1610					
	(60.2)	(82.0)		(100.4)								

(A) methanol as solvent.

(B) water as solvent.

[a] Probable errors obtained by the method of least squares are to demonstrate the closeness of the plot of $\log_{10} k_2$ against 1/T to a straight line.

lower activation energy by virtue of forming a metastable intermediate involving a decet of electrons in the outer shell of the S atom; such a course is not available for the N compound.

The reactions of sulfonium and ammonium compounds with nucleophilic reagents usually investigated are elimination reactions, however Hughes, Ingold, *et al.* (2) investigated the S_N2 reaction of Me_3S^+ with OH^- and for reaction in pure ethanol found the rate 7.24×10^{-1} at 100° and in pure water as 3.69×10^{-5} at the same temperature. No rate for the corresponding reaction with Me_4N^+ could be found, but Vorlander and Spreckels (3) record Me_4N^+ as being stable to boiling 2% NaOH.

A metastable intermediate is not a transition state, but whatever the exact form of the transition state for the sulfonium compound, it is clear that in going to it from reactants there is a reduction of total electrical charge, and on the Hughes-Ingold theory of solvent action (4) a change from methanol to water as solvent should cause a large decrease in rate. The work of Hughes, Ingold, *et al.* (2) confirms this for reaction of Me_2S^+ with OH^-, the change from ethanol to water giving a ratio of 19620/1. This value is probably somewhat too large since much of the reaction in ethanol would be due to OEt^-. In the present work a smaller ratio is to be expected since the change is from methanol to water and because the SCN^- is a mesomeric ion with the negative charge considerably distributed as compared with OH^- or OEt^-. From Table I the ratio is seen to be 106/1 at 50°. The effect is due to a change both in frequency factor (entropy term) and activation energy. Substituents in the ring are expected to have a considerably smaller effect on the "abnormal" side chain reaction than for ring substitution [Miller (5); Heppolette and Miller (6)]. The p-NO_2 compounds were used as having been already prepared for other investigations.

This discussion may throw some light on biological methylations involving sulfonium and ammonium compounds. Useful references are articles by Cantoni (7, 8a, b, and 9). The isolation of naturally occurring sulfonium compounds by Challenger, *et al.* (10 and 11) and McRorie, *et al.* (12) is also of interest.

EXPERIMENTAL

Solvents and thermostats were as in previous papers in this series. Rates for the sulfonium methosulfate were obtained by putting aliquots into excess standard $AgNO_3$ solution containing nitrous-free nitric acid, and back-titrating with standard thiocyanate using ferric alum indicator. The ammonium chloride was followed by titrating aliquots against standard $AgNO_3$ using an Ag/AgCl electrode, with separate estimation of the constant amount of Cl^-.

Reaction products obtained direct from reaction mixtures were p-nitrothioanisole (m.p. 72°; lit. 72°) and p-nitrodimethylaniline (m.p. 164°; lit. 164°).

Preparation of materials. p-Nitrothioanisole. An alkaline solution containing sodium p-nitrothiophenoxide was prepared from p-chloronitrobenzene by the method of Price and Stacy (13). The p-nitrothiophenoxide was converted in solution to p-nitrothioanisole with dimethyl sulfate by the method of Brand and Stallman (14); the over-all yield being 63%. The product on recrystallization from ethanol had m.p. 72° (lit. 72°).

p-Nitrophenyldimethylsulfonium methosulfate was obtained from p-nitrothioanisole by the method of Baker and Noffit (15) in 64% yield. The product recrystallized from methanol had m.p. 159° (lit. m.p. 157–158.5°).

p-Nitrodimethylaniline was prepared from *p*-chloronitrobenzene by the method of Campbell (16) in 96% yield. The product recrystallized from methanol had m.p. 162.5–163.5° (lit. 164°).

p-Nitrotrimethylammonium picrate (a) and *chloride* (b). Compound (a) was prepared from *p*-nitrodimethylaniline by the method of Zaki and Fahim (17) in 50% yield. The product when recrystallized from water had m.p. 182–183° (lit. 182–183°).

Compound (b) was obtained by decomposition of the picrate (17) in 66% yield. The product when recrystallized from ether-ethanol had m.p. 183–184° (lit. 183–184°).

All m.p.s. are corrected.

Typical runs

Sulfonium salt with excess SCN^- in methanol at 25°

Time (mins.)	0	30	60	105	150	210	270
Titer	13.74	14.21	14.51	15.10	15.51	16.11	16.57
Log term	0.1709	1814	1886	2050	2182	2410	2619
	330	420	"infinity"				
	16.96	17.32	20.50	20.54	20.51		
	2830	3135					

k = $7.87_5 \pm 0.06_3 \times 10^{-4}$ l moles^{-1} secs^{-1}.

Ammonium salt with equimolar amount of SCN^- in methanol at 81.9°

Time (hrs.)	0	5	10	16	22	30
Titer	14.19	13.62	13.17	12.62	12.11	11.77
Reciprocal term	0.1410	1534	1647	1812	1996	2141
	37	46				
	11.31	11.02				
	2375	2551				

k = $2.20_0 \pm 0.03_2 \times 10^{-4}$ l moles^{-1} secs^{-1}.

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SUMMARY

The dealkylation by SCN^- of SMe_2^+ and NMe_3^+ attached directly to a benzene ring has been investigated. The sulfonium ion reacts much faster, and this is ascribed to an alternative mechanism of lower activation energy involving the ability of the S atom to hold 10 electrons in its outer shell. The solvent effect was also investigated and shown to agree with the Hughes-Ingold theory of solvent effects (4). The reactions throw some light on biological methylations.

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