Bond Scission Processes in Sulphur Compounds. Part IX.† Nucleophilic Catalysis in the Methanolysis of Methyl *p*-Nitrophenyl Sulphate

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Two consecutive processes are observed in the reaction of methyl *p*-nitrophenyl sulphate in methanol containing lithium perchlorate, as followed by u.v.–visible spectroscopy at 25°. In this solvolytic process, an initial conversion to *p*-nitrophenyl sulphate ion (carbon–oxygen scission) is followed by a further reaction to give *p*-nitrophenol (sulphur–oxygen scission). In reaction media containing perchloric acid the rate of the second stage is increased but the rate of the first stage remains unchanged. Therefore, there is no acid catalysis in the primary process yielding *p*-nitrophenyl sulphate ion. An apparent increase in the rate of this reaction which is observed in media containing hydrogen chloride can be ascribed to chloride ion catalysis. Similarly, nucleophilic catalysis is observed with bromide, fluoride, and azide ions. The reactivity order followed is typical of substitution at aliphatic carbon. A preference of alkyl aryl sulphates for reaction with nucleophiles at the alkyl carbon, rather than at aryl carbon or sulphonyl sulphur centres, is noted.

THOUGH esters of sulphuric acid enjoy wide utility as alkylating agents,[1,2] and they are also of biological importance,[3-5] past studies have been concerned chiefly with the common dialkyl sulphates. However, we reported recently [6] on the first quantitative study with a mixed alkyl aryl sulphate, methyl *p*-nitrophenyl sulphate. In that study, results were given for the alkaline methanolysis and also for the neutral methanolysis. Alkaline methanolysis was found to proceed solely by alkyl–oxygen scission, yielding *p*-nitrophenyl sulphate ion [reaction (1)]. Neutral methanolysis gave first *p*-nitrophenyl hydrogen sulphate (alkyl–oxygen scission), which was followed by its conversion to *p*-nitrophenol (sulphur–oxygen scission). The latter stage is an acid-catalysed reaction,[7,8] as given by reactions (2) and (3).

In order to explore further the reactivity, and modes of bond scission, of methyl *p*-nitrophenyl sulphate under various conditions we have now studied the reaction with a variety of nucleophiles. In addition, we have investigated the possibility of acid-catalysed processes;‡ hitherto there has been no report of the occurrence of acid catalysis in the solvolysis of dialkyl, or diaryl sulphates. The aspect of the work concerned with dilute acid media is considered first.

Experiments designed to test for Acid Catalysis.—The alkyl–oxygen and the sulphur–oxygen centres in methyl

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† Part VIII, E. Buncel, A. Raoult, and L.-I. Lancaster, *J. Amer. Chem. Soc.*, 1973, **95**, 5964.

‡ Some results of the reaction in methanolic HCl were included in a preliminary communication.[9]

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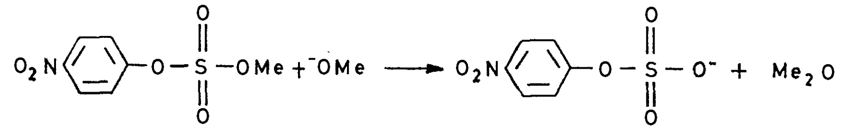
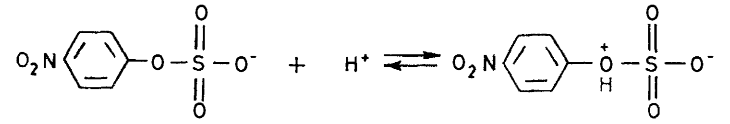
p-nitrophenyl sulphate could potentially serve as protonation sites, thus rendering the adjacent carbon and sulphur susceptible to acid-catalysed solvolytic displacement. It was decided to test for the occurrence of such acid-catalysed solvolysis, and since we had previously studied the alkaline and neutral methanolysis processes, we proceeded to examine the reaction of methyl *p*-nitrophenyl sulphate in methanol containing perchloric and hydrochloric acids. Accompanying control experiments were deemed necessary with lithium perchlorate and lithium chloride in order to test for ionic strength effects. The reaction was studied spectrophotometrically, by the method described previously.[6,10]



(1)



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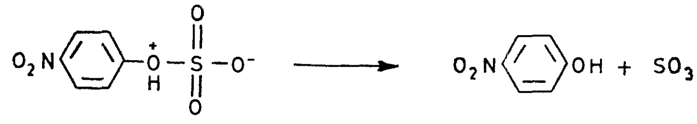

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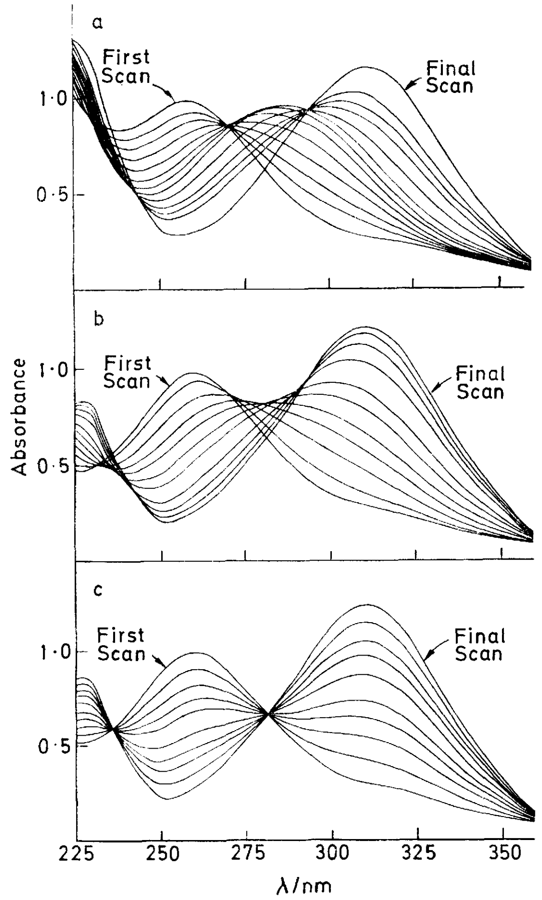

Spectral characteristics in the methanolysis of methyl *p*-nitrophenyl sulphate at 25°: a, reaction in the presence of 0·06M-$LiClO_4$; b, reaction with 1×10^{-4}M-$HClO_4$; c, reaction with 6×10^{-3}M-$HClO_4$

Two consecutive processes are observed in the reaction of methyl *p*-nitrophenyl sulphate in methanolic $LiClO_4$ solution. The spectral characteristics of the reaction are illustrated in Figure a. There is the initial conversion of methyl *p*-nitrophenyl sulphate to *p*-nitrophenyl sulphate ion (a decrease in absorbance at 260 nm, an increase at 283 nm, and isosbestic points at 230 and 270 nm), followed by the conversion of the intermediate *p*-nitrophenyl sulphate ion to *p*-nitrophenol (a decrease in absorbance at 283 nm, an increase at 311 nm, and isosbestic points at 243 and 295 nm). The final spectrum corresponds quantitatively with that of *p*-nitrophenol in this medium. The two processes are well defined in Figure a because the first stage of the reaction is appreciably more rapid than the second.

First-order rate constants (k_{obs}) for the conversion of methyl *p*-nitrophenyl sulphate to *p*-nitrophenyl sulphate ion were obtained from plots [10] of log ($A_t - A_\infty$) against *t* at 243 and 295 nm (the isosbestic points for the conversion of *p*-nitrophenyl sulphate ion to *p*-nitrophenol). The resulting rate data, given in Table 1, show that k_{obs} is invariant with changing lithium perchlorate concentration. The value of k_{obs} compares favourably with the value $5{\cdot}56 \times 10^{-4}$ s^{-1} previously obtained for the neutral reaction. Thus the kinetic results and spectral characteristics of the reaction of methyl *p*-nitrophenyl sulphate in methanolic $LiClO_4$ solutions are identical with those

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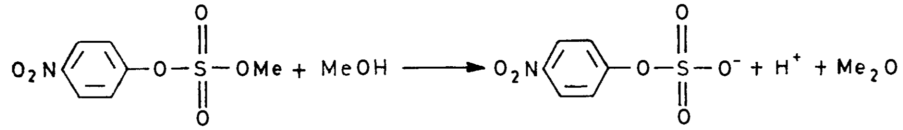
[10] E. Buncel, A. Raoult, and J. F. Wiltshire, *J. Chem. Educ.*, 1974, **51**, 814.

previously obtained[6] for the neutral methanolysis reaction [equation (4)]. The subsequent reaction of *p*-nitrophenyl sulphate ion to *p*-nitrophenol (Figure a) is an acid-catalysed process [equation (2) and (3)] and was characterized in the previous study.[6]


(4)

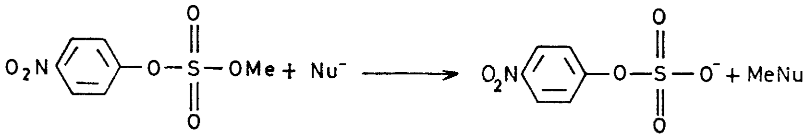
Kinetic runs with added perchloric acid exhibited a visual appearance that was quite different in character from that of the $LiClO_4$ runs. At low $HClO_4$ concentration (*ca.* 1 × 10^{-4}M), the spectral characteristics of the reaction are similar to those of Figure a, though the isosbestic points at 270 and 295 nm are somewhat less distinct (Figure b). As $HClO_4$ is gradually increased in concentration, these isosbestic points begin to merge, until finally ($HClO_4 \geqslant 6 \times 10^{-3}$M) the metamorphosis is complete and the reaction is characterized solely by a decrease in absorbance at 260 nm due to methyl *p*-nitrophenyl sulphate, a single sharp isosbestic point at 281 nm, and an increase in absorbance at 311 nm due to *p*-nitrophenol (Figure c). Table 1 lists the pseudo-first-order rate constants for the disappearance of methyl *p*-nitrophenyl sulphate obtained from plots of log ($A_\infty - A_t$) at 295 nm [the isosbestic point for the conversion of *p*-nitrophenyl sulphate ion to *p*-nitrophenol (Figure a)] or at 260 nm (with the spectral characteristics of Figure c). The rate of reaction is seen to be invariant with [$HClO_4$], the rate constant being identical to that obtained for the conversion of methyl *p*-nitrophenyl sulphate to *p*-nitrophenyl sulphate ion in methanolic $LiClO_4$ solution, and for the neutral methanolysis reaction.

TABLE 1

Kinetic data for the conversion of methyl *p*-nitrophenyl sulphate to *p*-nitrophenyl sulphate ion in methanol containing $LiClO_4$, $HClO_4$, and HCl at 25° [a]

Reagent	10^3[Reagent]/M	$10^4k_{obs}/s^{-1}$
$LiClO_4$	21·6	5·56
	30·7	5·50
	61·4	5·45
	100·1	5·60
$HClO_4$	0·10	5·29
	0·55	5·03
	6·06	5·27
	61·4	5·40
	122·8	5·42
	245·6	5·25
HCl	0·09	5·58
	0·50	5·78
	2·40	5·59
	6·00	6·07
	11·9	6·53
	15·5	7·14
	31·0	8·65
	61·4	11·4

[a] All runs were performed at a substrate concentration of 5 × 10^{-5}M. The reaction medium contained 1% ether and, in the case of the acid runs, ⩽0·5% water by volume.


(5)

A rationalization of these results may be given, in that the processes shown in the Figure represent the conversion of methyl *p*-nitrophenyl sulphate to *p*-nitrophenyl sulphate ion [neutral methanolysis, equation (4)], which is not acid catalysed, but which is followed by an acid-catalysed conversion of the intermediate to *p*-nitrophenol at a gradually increasing rate. At the high acid concentrations (Figure c) the rate constant for the second stage is considerably larger than for the first, so that the intermediate *p*-nitrophenyl sulphate ion cannot accumulate. The overall observed reaction is therefore the transformation of methyl *p*-nitrophenyl sulphate to *p*-nitrophenol.

Chloride Ion Catalysis.—Results obtained when the methanolysis was performed in the presence of hydrochloric acid show similarities, but also differences, when compared to the perchloric acid system. In the region of low HCl concentrations (0·1—2 × 10^{-3}M) the results follow closely those obtained with added $HClO_4$. Thus one observes spectrally an A ⟶ B ⟶ C consecutive reaction system which merges to an A ⟶ C process with increased acidity, once the B ⟶ C rate surpasses the A ⟶ B rate. In the meanwhile the measured k_{obs} remained at the 5·6 × 10^{-4} s^{-1} level, corresponding to the neutral methanolysis rate. On the other hand, with [HCl] ⩾ 6 × 10^{-3}M the k_{obs} values are found to increase (Table 1), though the visual appearance of the spectra during a given run retains the character of an A ⟶ C process (a single isosbestic point at 281 nm is maintained, as in Figure c). In view of the present results with added $HClO_4$, this increase in rate with added HCl, which was previously interpreted as evidence for the advent of an acid-catalysed process,[9] must now be ascribed to chloride ion catalysis [equation (5; $Nu^- = Cl^-$)].

Further evidence for chloride ion catalysis was sought by performing the reaction with added lithium chloride, in which case there should be no possibility of acid catalysis. The rate constant for the conversion of methyl p-nitrophenyl sulphate to p-nitrophenyl sulphate ion, in the presence of added LiCl, was in fact observed to increase with increasing LiCl concentration (Table 2). A plot of k_{obs} against [LiCl] is linear and the slope yields the second-order coefficient with respect to chloride ion, $k_{Cl^-} = 11{\cdot}0 \times 10^{-3}$ l mol^{-1} s^{-1} (from a similar plot of the HCl data, $k_{Cl^-} = 9{\cdot}7 \times 10^{-3}$ l mol^{-1} s^{-1}). The intercept in this plot has the value $5{\cdot}4 \times 10^{-4}$ s^{-1} and corresponds to the neutral methanolysis rate.

TABLE 2

Kinetic data for the nucleophile catalysed conversion of methyl p-nitrophenyl sulphate to p-nitrophenyl sulphate ion in methanol at 25° [a]

Reagent	10^3[Nucleophile]/ M	10^4k_{obs}/s^{-1} [b]	10^3k_2/l mol^{-1} s^{-1} [c]
Me_4NF	20·8	5·94	2·02
	36·2	6·35	
	41·9	6·50	
	60·0	6·76	
	72·5	6·91	
	108·7	7·89	
LiCl	30·0	8·52	11·0
	61·4	11·3	
	75·0	13·7	
	98·6	18·5	
LiBr	30·7	19·0	45·0
	61·4	37·5	
	115·9	57·3	
NaN_3	3·3	7·9	76·8
	16·4	18·3	
	32·8	29·9	
	36·1	33·4	
	61·4	52·8	
	112·0	91·8	

[a] Substrate concentration = 5×10^{-5}M. Reaction solutions contain 1% ether by volume. [b] The observed pseudo-first-order rate constant. [c] Calculated from slope of plot of k_{obs} against [Nucleophile].

In the kinetic runs performed with added LiCl the primary reaction ($A \longrightarrow B$) yielding p-nitrophenyl sulphate ion was seen to be followed by a much slower conversion of the latter to p-nitrophenol. The $B \longrightarrow C$ reaction [equations (2) and (3)] in this case is induced by the acid generated in the neutral methanolysis of methyl p-nitrophenyl sulphate to p-nitrophenyl hydrogen sulphate [equation (4)] which competes with the chloride ion catalysed reaction [equation (5)], which does not generate acid. The $B \longrightarrow C$ reaction was not investigated in detail, though it was noted that increasing the chloride ion concentration resulted in a reduced rate of the $B \longrightarrow C$ reaction, which is as would be expected.

Catalysis by Other Nucleophiles.—In order to establish the generality of nucleophilic catalysis in this system, the reaction of methyl p-nitrophenyl sulphate was extended to other common nucleophiles, namely Br^-, F^-, and N_3^-. In each case reaction was observed to yield cleanly the p-nitrophenyl sulphate ion, with pseudo-first-order kinetics.*

Second-order rate coefficients for the $A \longrightarrow B$ reaction with respect to the nucleophiles examined were obtained from linear plots of k_{obs} against [Nu^-].† The overall reactivity order obtained is $N_3^- > Br^- > Cl^- > F^-$, which is typical for substitution at an aliphatic carbon centre.[11-13] In contrast, reaction at sulphonyl centres is characterized by high reactivity of nonpolarizable nucleophiles.[14,15] Thus the sulphonyl centre has been termed ' hard ' [14] on the Pearson terminology.[16]

It is noteworthy that throughout this study, and the previous study [6] of the neutral and base-catalysed methanolysis reactions, no evidence was obtained for substitution at aromatic carbon or at sulphonyl sulphur. An S_NAr process [17-19] might have been expected in this system as a result of the presence of the activating nitro-substituent and since the $MeOSO_3^-$ ion is known to be a good leaving group. Methoxide and azide ions have been used as common nucleophiles in S_NAr reactions. With respect to the preference which has been observed in this system for reaction at alkyl carbon rather than at sulphonyl sulphur, the nucleophilic substitution reactions of mixed alkyl aryl sulphates appear to closely parallel those of the related dialkyl sulphates.[20,21] A further similarity between these two classes of compound lies in the absence of any report of an acid-catalysed solvolysis reaction.[20,21]

EXPERIMENTAL

The method of preparation and characterization of methyl p-nitrophenyl sulphate has been described previously.[22,23]

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* The suppression of the second stage of the reaction can be attributed to one or both of (a) the inability of the methanolysis reaction to compete effectively with the nucleophile catalysed reaction, and (b) neutralization of acid by the relatively basic nucleophiles. However, it was found that the second stage could be induced by the addition of an excess of acid.

† An estimate was made of the extent to which lyate ion contributes to the observed rate of the $A \longrightarrow B$ process by calculating the extent of the ionizations $Nu^- + MeOH \rightleftharpoons NuH + MeO^-$ using the acid dissociation constants of NuH and the autoprotolysis constant of the solvent. In no case was the contribution to the rate by the lyate ion significant.

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Potassium *p*-nitrophenyl sulphate (Sigma chemicals) showed no u.v. absorption due to *p*-nitrophenoxide ion in alkaline medium, and gave 98% *p*-nitrophenol after complete acid hydrolysis. Commercial absolute methanol was distilled from iodine-activated magnesium. Other reagents were of analytical quality.

Stock solutions of the substances listed below were prepared in methanol, except for the substrate in which case anhydrous ether was used. The following spectral characteristics were obtained: methyl *p*-nitrophenyl sulphate, $\lambda_{max.}$ 260 nm (ε 9430); *p*-nitrophenyl sulphate (potassium salt), $\lambda_{max.}$ 283 nm ($\varepsilon_{max.}$ 9200); *p*-nitrophenol, $\lambda_{max.}$ 311 nm ($\varepsilon_{max.}$ 10,600).

Spectral measurements were made on a Unicam SP 800 spectrophotometer in a thermostatted cuvette (20 mm). Reactions were followed by repeated scanning over the region 225—350 nm or, in the case of fast runs, absorbance was followed at the wavelength corresponding to the absorption maximum of the product species. Infinity spectra were obtained at the completion of the reactions.

Kinetics were performed under pseudo-first-order conditions, with the reagent present in excess. Runs were initiated by the addition, with a calibrated syringe, of the stock solution (60 μl) of the substrate (5×10^{-3}M) in ether to the methanolic reagent solution (5·94 ml) contained in the thermostatted cuvette. In the case of acidic media, stock $HClO_4$ and HCl solutions were prepared in aqueous medium and were of such concentration that the final methanolic reaction solution, on addition of a portion of the aqueous acid, contained a maximum of 0·5% water by volume.

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