Sulphuryl Chloride as an Electrophile. Part II.[1] Substituted *m*-Di-methoxybenzenes

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The rates of reaction of sulphuryl chloride with a number of derivatives of *m*-dimethoxybenzene in chlorobenzene show good correlation with the Hammett equation. The high value of the reaction constant ($\rho = -4{\cdot}0$) confirms the heterolytic nature of the rate-determining step; further evidence of this mechanism is presented. Details are given for the preparation of pure derivatives of *m*-dimethoxybenzene.

SULPHURYL chloride reacts by a heterolytic reaction mechanism with 3,5-dimethylanisole in chlorobenzene at 25°.[1,2] The evidence includes the constancy of the second-order rate coefficient when reactions are carried out in the presence of iodine, of sulphur dioxide, and of benzoyl peroxide. The reaction rate also increased with increasing polarity of the solvent, in the order benzene < chlorobenzene < *o*-dichlorobenzene ⩽ nitrobenzene, and was strongly influenced by the nature of the aromatic ether. We now report the effects of substituents in the halogenation of *m*-dimethoxybenzene by sulphuryl chloride.

EXPERIMENTAL

Anisole, *m*-methylanisole, 2,3-dimethylanisole, and 2,3,5-trimethylanisole were prepared from the corresponding phenols by treatment with methyl iodide and sodium methoxide,[1] and purified by steam distillation from ferrous sulphate, followed by fractional distillation after being dried (Na); kinetically pure products resulted.

With *m*-dimethoxybenzene, whether prepared from resorcinol or commercial, a product was obtained (b.p. 214·5°/758 mm.; $n_D^{25} = 1{\cdot}5226$) which contained 10—20% of highly reactive impurities. These could not be completely removed, and kinetically pure *m*-dimethoxybenzene had to be prepared by a more devious route. *m*-Dichlorobenzene, in treatment with nitric acid (95%; 5 mol.) at 20°, gave 2,4-dichloronitrobenzene in 98% yield.[3] Treating this slowly, in methanol, with sodium methoxide (3 mol.) and then refluxing the suspension for 3 hr. gave, on dilution with water, 2,4-dimethoxynitrobenzene, m.p. 75·2—76·0° (ethanol) in 70% yield. This was reduced to the amine ($Fe/H_2O–CH_3{\cdot}CO_2H$) which was diazotised and deaminated in hypophosphorous acid (30%) to give *m*-dimethoxybenzene, b.p. 205·5°/756 mm.; $n_D^{25} = 1{\cdot}5236$. It is essential that a solid derivative, capable of recrystallisation to constant m.p., is prepared at some stage at or after methylation to obtain pure *m*-dimethoxybenzene derivatives. The impurities are probably methylcyclohexene-1,3-diones arising from *C*-alkylation of resorcinol. Pure *m*-dimethoxybenzene could also be prepared by the protodecarboxylation of either 2,4- or 2,6-dimethoxybenzoic acid.[4]

2,4-Dimethoxynitrobenzene with bromine (1 mol.) in chloroform gave 5-bromo-2,4-dimethoxynitrobenzene (95%), which on reduction and deamination gave 1-bromo-2,4-dimethoxybenzene, m.p. 23·0—23·5°; similarly, sulphuryl chloride and 2,4-dimethoxynitrobenzene gave the 5-chloro-analogue, which afforded 1-chloro-2,4-dimethoxybenzene, m.p. 4·8—5·0°, $n_D^{20} = 1{\cdot}5472$, on reduction and deamination. Direct replacement of the amino-group by halogen in 2,4-dimethoxyaniline gave much lower yields of these compounds. 1-Iodo-2,4-dimethoxybenzene, m.p. 40·0—40·8°, was obtained by direct halogenation of *m*-dimethoxybenzene.[5]

Methyl 2,4-dimethoxybenzoate, b.p. 150°/5 mm., was obtained from the corresponding acid; similarly methyl 3,5-dimethoxybenzoate, m.p. 40·2—40·6° (methanol). 1,2,4-Trimethoxybenzene, m.p. 19—21°, was best obtained from the combined hydrolysis and alkylation described by Baker; the required 1,2,4-triacetoxybenzene was prepared from benzoquinone.[6] 3,5-Dimethoxybenzonitrile, m.p. 92° (ethanol), was prepared by dehydration ($POCl_3$) of 3,5-dimethoxybenzamide.[7]

In our hands the Sandmeyer reaction of 3,5-dimethoxyaniline gave poor yields of 1-bromo-3,5-dimethoxybenzene; (cf. 7) this, and the corresponding chloro-compound, were prepared from *p*-nitrosophenol. A solution of *p*-nitrosophenol in methanol–ether (1 : 1, v/v) was saturated with hydrogen bromide at 20—25°. The precipitate of 6-bromo-2,4-dimethoxyaniline hydrobromide was deaminated to give 1-bromo-3,5-dimethoxybenzene, m.p. 66°, in 31% yield overall. This is an adaptation of a reported process [8] by which 1-chloro-3,5-dimethoxybenzene, m.p. 37° (45%), was also prepared.

Kinetic Procedure.—The purification of chlorobenzene and of sulphuryl chloride has been described;[1] standard solutions were made up by weight. Hydrolysis showed these solutions to be 99·7—99·9% pure; each solution was shown to contain neither an excess of molecular chlorine, nor an excess of sulphur dioxide, nor equimolecular amounts of these two decomposition products of sulphuryl chloride.[1]

Weighed amounts of the aromatic compound were dissolved in standard solutions of sulphuryl chloride which were at 25°; samples were withdrawn at intervals to be discharged into excess of standard iodine solution, which were then back-titrated with standard sodium thiosulphate.

DISCUSSION

The rates of reaction of the various ethers with sulphuryl chloride are strongly influenced by the effects of the substituents; the Table shows the experimental results, which fit a Hammett plot well. In the case of

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[1] Part I, R. Bolton and P. B. D. de la Mare, *J. Chem. Soc.* (*B*), 1967, 1044.

[2] R. Bolton, P. B. D. de la Mare, and H. Suzuki, *Rec. Trav. chim.*, 1966, **85**, 1206.

[3] A. F. Holleman, *Rec. Trav. chim.*, 1912, **31**, 280.

[4] R. W. Hay and K. R. Tate, personal communication.

[5] H. Kauffmann and F. Kieser, *Ber.*, 1912, **45**, 2333.

[6] W. Baker, E. H. T. Jukes, and C. A. Subrahmanyam, *J. Chem. Soc.*, 1934, 1681.

[7] N. B. Dean and W. B. Whalley, *J. Chem. Soc.*, 1954, 4638.

[8] S. Goldschmidt and L. Suchanek, *Chem. Ber.*, 1957, **90**, 19.

sulphuryl chloride, as with molecular chlorine, Brown's σ^+ is the more appropriate constant than the original Hammett–Jaffe σ; use of σ^+ gives a reaction constant, ρ, of $-4\cdot0 \pm 0\cdot2$. This high value indicates that considerable charge is being developed in the transition states of the reactions, and hence that a heterolytic mechanism is involved.

Rate constants for the reaction of sulphuryl chloride with some aromatic ethers in chlorobenzene at 25°

Aromatic ether	$\Sigma\sigma^+$	k_2 (l. mole^{-1} sec.$^{-1}$)
Anisole	$-0\cdot778$	*ca.* 6×10^{-7}
m-Methylanisole	$-1\cdot092$	2×10^{-5}
2,3-Dimethylanisole	$-1\cdot158$	$2\cdot4 \times 10^{-5}$
3,5-Dimethylanisole	$-1\cdot410$	$3\cdot8 \times 10^{-4}$
2,3,5-Trimethylanisole	$-1\cdot479$	$1\cdot7 \times 10^{-3}$
m-Dimethoxybenzene	$-1\cdot556$	$5\cdot8 \times 10^{-4}$
1-Bromo-2,4-dimethoxybenzene	$-1\cdot151$	$1\cdot8 \times 10^{-5}$
1-Chloro-2,4-dimethoxybenzene	$-1\cdot157$	$1\cdot6 \times 10^{-5}$
1-Iodo-2,4-dimethoxybenzene	$-1\cdot197$	$2\cdot9 \times 10^{-4}$
2,4-Dimethoxynitrobenzene	$-0\cdot882$	$1\cdot4 \times 10^{-6}$
1,2,4-Trimethoxybenzene	$-1\cdot509$	$5\cdot5 \times 10^{-4}$
Methyl 2,4-dimethoxybenzoate	$-1\cdot188$	$4\cdot2 \times 10^{-5}$
Methyl 3,5-dimethoxybenzoate	$-1\cdot067$	$6\cdot2 \times 10^{-6}$
1-Bromo-3,5-dimethoxybenzene	$-1\cdot406$	$2\cdot6 \times 10^{-4}$
1-Chloro-3,5-dimethoxybenzene	$-1\cdot442$	$2\cdot7 \times 10^{-4}$
3,5-Dimethoxybenzonitrile	$-0\cdot897$	$2\cdot6 \times 10^{-5}$

The validity of the Hammett equation under these conditions is suspect for the following reasons: (*a*) it is assumed that the substituent effect of an *ortho*-group is linearly related to that of the same group in the *para*-position; (*b*) the steric effects at the reaction sites are not the same; for example, the primary steric effect in the attack on 1-bromo-3,5-dimethoxybenzene is unlikely to be the same as that for attack on anisole. Also (*c*) substitution is unlikely to occur to give the same isomer ratio in each aromatic ether. While substitution of *m*-dimethoxybenzene involves attack almost entirely at the 4-position, presumably owing to steric inhibition at the 2-position, it seems unlikely that halogenation of a 5-substituted 1,3-dimethoxybenzene will occur preferentially at any particular site. In the absence of any knowledge of the isomer ratios for the reactions, the overall rate constant has been used in constructing the Hammett plot. While this is subject to criticism, since it takes no account of the equivalence of some reaction sites (*e.g.*, the 4- and 6-positions of *m*-dimethoxybenzene), it is unlikely that this would alter the value of ρ by more than a few percent., and would certainly not vitiate the conclusions drawn from it.

While most of the aromatic ethers lie close to the line in the Hammett plot, 1-iodo-2,4-dimethoxybenzene reacts considerably more rapidly than predicted. The effect is not due to the halogen group as such, since the bromo- and chloro-analogues show no such increase in reactivity; it may be due to a change in the nature of the reaction. A sequence in which attack occurs first at the iodine atom, giving an iodosodichloride which subsequently acts as a chlorinating agent in its own right, would not be experimentally distinguishable from the direct attack of the aromatic ring by sulphuryl chloride; it is quite probable that an iodosodichloride would be as effective a chlorinating agent as the sulphuryl chloride molecule.

The evidence that these reactions are not proceeding by the homolytic mechanism has been negative. Although the susceptibility of the rate to changes of the solvent and to changes of the structure of the aromatic ether are more consistent with a heterolytic mechanism, only one rate of reaction could be found for each compound under the same conditions, and no acceleration could be produced by free-radical initiators such as benzoyl peroxide.[1] We now believe that we have observed the homolytic reaction in the following situations: In some cases where the aromatic ether was isolated by distillation from a solution in diethyl ether, anomolously high second-order rate constants were found. Such behaviour occurred with 1-bromo-2,4-dimethoxybenzene ($k_2' = 1\cdot5 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$ at 25°), 1-chloro-2,4-dimethoxybenzene ($k_2' = 1\cdot6 \times 10^{-2}$), methyl 2,4-dimethoxybenzoate ($k_2' = 5 \times 10^{-2}$), and anisole ($k_2' = 2 \times 10^{-2}$). In no case was the order of the reaction strictly defined, although good second-order plots were obtained during 70% reaction. In general the compounds could be purified by steam-distillation from ferrous sulphate, in which case the observed second-order rate coefficient dropped sharply.

In this anomalous reaction, the structures of the ethers play a much smaller part in determining the rate, and we tentatively ascribe this to the incursion of the homolytic process involving attack of the ether by chlorine radicals. Kharasch and Brown [9] found that the reaction of sulphuryl chloride with cyclohexene, which normally proceeds violently, takes place very slowly with 'peroxide-free' reagents in the dark at room temperature and they noted that a similar acceleration in the presence of peroxides with the reactions of other hydrocarbons. The initiator of our 'fast' reactions was not light; it was probably diethyl peroxide. Although we have found that benzoyl peroxide had no effect upon the reaction of sulphuryl chloride on 3,5-dimethylanisole, an alkyl peroxide might be expected to be a more efficient initiator; this has been shown in some reactions of sulphuryl chloride.[9]

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