509. *The Reaction of Dialkyl Sulphites with Sodium Iodide in Acetone.*

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Known methods have been used to synthesise a series of dialkyl sulphites including several alkyl methyl sulphites and the carbohydrate derivatives 1 : 2-5 : 6-di-*O*-*iso*propylidene-D-glucofuranose 3-(methyl sulphite) and 1 : 2-3 : 4-di-*O*-*iso*propylidene-D-galactopyranose 6-(methyl sulphite). Unlike the dialkyl sulphates, which with sodium iodide in acetone give alkyl halide and sodium alkyl sulphate, sulphite esters give acetone sodium bisulphite. On reaction of dimethyl sulphite with sodium iodide in acetone rapid release of methyl iodide was followed by slower formation of acetone sodium bisulphite and methanol.

The reaction of dialkyl sulphates with sodium iodide in acetone follows a simple course and yields an alkyl halide and an alkyl sodium sulphate. Thus within ten seconds dimethyl sulphate and sodium iodide in acetone at room temperature give 93% of sodium methyl sulphate. Under identical conditions diethyl sulphate and di*iso*propyl sulphate [1] react less rapidly, to give sodium ethyl sulphate (83%) and sodium *iso*propyl sulphate (42%). Although no experimental details were given, methyl sulphate esters of some steroidal alcohols were reported [2] to yield the sodium salts of the corresponding steroid sulphates on reaction with sodium iodide in acetone.

An analogous reaction sequence with sulphite esters was expected to make accessible sodium alkyl sulphites (our especial interest was carbohydrate sulphites). To test this possibility a series of dialkyl sulphites and alkyl methyl sulphites have been prepared and their reactions with sodium iodide in acetone studied.

The dialkyl sulphites $SO(OR)_2$ listed in Table 2 were synthesised by the action of an excess of the appropriate alcohol with thionyl chloride by one of two methods.[3, 4] The alkyl methyl sulphites (MeO·SO·OR) (Table 1) were obtained by the reaction of methyl chlorosulphinate with the appropriate alcohol in the presence of pyridine,[5] along with a small amount of the dialkyl sulphite. Amongst the new compounds prepared were 1 : 2-5 : 6-di-*O*-*iso*propylidene-D-glucofuranose 3-(methyl sulphite) and 1 : 2-3 : 4-di-*O*-*iso*-propylidene-D-galactopyranose 6-(methyl sulphite). These appear to be the first examples

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[1] Cf. Garner and Lucas, *J. Amer. Chem. Soc.*, 1950, **72**, 5497.
[2] McKenna and Norymberski, *Chem. and Ind.*, 1954, 961.
[3] Price and Berti, *J. Amer. Chem. Soc.*, 1954, **76**, 1207.
[4] Voss and Blanke, *Annalen*, 1931, **485**, 258.
[5] Berti, *J. Amer. Chem. Soc.*, 1954, **76**, 1213.

of this class of compound in the carbohydrate field. Honeyman and Morgan[6] have described the related compound methyl 4 : 6-*O*-benzylidene-α-D-glucopyranoside 2 : 3-sulphite. All these sulphite esters decompose on short storage with the evolution of sulphur dioxide.

TABLE 1. *Alkyl methyl sulphites.*

No.	Sulphite	Yield (%)	B. p. (°/mm.)	$[\alpha]_D$ [a]	η (temp.)	Formula	Found (%) C	H	S	Required (%) C	H	S
VI	Me Pr^i	48	48—52°/ 17	—	1·4122 (20°)	$C_4H_{10}O_3S$	34·7	7·15	23·3	34·8	7·25	23·2
VII	Me *cyclo*pentyl [b]	44	97—100/ 15	—	1·4600 (20°)	$C_6H_{12}O_3S$	44·4	7·5	18·8	43·9	7·3	19·5
VIII	*cyclo*Hexyl Me	63	105—110/ 17	—	1·4630 (16°)	$C_7H_{14}O_3S$	47·4	8·1	18·1	47·2	7·9	18·0
IX	(−)-Menthyl Me [c, d]	64	86—88/ 0·2	−45·4°	1·4630 (20°)	$C_{11}H_{23}O_3S$	66·9	10·7	—	67·0	10·6	—
X	1 : 2-5 : 6-Di-*O*-*iso*propylidene-D-glucofuranose-3-(methyl sulphite)	65	122—130/ 0·01	−58·6	1·4621 (20°)	$C_{13}H_{21}O_8S$	46·2	6·6	9·5	46·15	6·5	9·5
XI	1 : 2-3 : 4-Di-*O*-*iso*propylidene-D-galactose-6-(methyl sulphite)	48	132—138/ 0·05	−58·6	1·4653 (20°)	$C_{13}H_{21}O_8S$	46·9	6·45	—	46·15	6·5	—

[a] In $CHCl_3$. [b] Also obtained di*cyclo*pentyl sulphite, b. p. 147°/18 mm., η^{20} 1·4503 (Found: C, 54·7; H, 7·5; S, 14·2. $C_{10}H_{18}O_3S$ requires C, 55·0; H, 8·3; S, 14·7%). [c] Also obtained di-(−)-menthyl sulphite, b. p. 150—155°/0·2 mm., m. p. 53°, $[\alpha]_D$ −52·8° (*c*, 1·44 in $CHCl_3$) (Found: C, 66·9; H, 10·7. $C_{20}H_{38}O_3S$ requires C, 67·0; H, 10·6%). [d] Berti[5] reports b. p. 105—108° (bath)/1·0 mm., η^{20} 1·5640. Compounds VI, VII, VIII, X, and XI are new compounds.

Dimethyl sulphite was found to react very slowly with sodium iodide in dry acetone at room temperature but after two hours' boiling an appreciable amount of acetone sodium bisulphite had separated.

That this unexpected reaction of dimethyl sulphite was not specific for this substance was shown by the reaction of the methyl sulphite esters, detailed in Table 2, with sodium iodide in acetone, which in each case gave acetone sodium bisulphite, in yields of 55—75%. In compounds of the general formula MeO·SO·OR the yield of acetone sodium bisulphite is not greatly influenced by the nature of the residue R: thus (Table 2), when the hydroxyl group in the residue R was primary (I and XI), or secondary in an acyclic system (VI) or attached to a 5-membered ring (VII and X) or a 6-membered ring (VIII and IX), the yields of acetone sodium bisulphite did not differ greatly or vary according to an obvious pattern. The yields from diethyl sulphite and di*iso*propyl sulphite were much lower (12% and 0·73% respectively) than from dimethyl sulphite. These yields emphasise the resistance of the ethyl and the *iso*propyl group in the appropriate esters to attack by iodide ions and in this respect the benzyl group must facilitate attack by iodide ions.

TABLE 2. *Yields of acetone bisulphite following the action of sodium iodide in acetone on dialkyl sulphites under standard conditions.*

Sulphite	Yield (%)	Sulphite	Yield (%)
Me_2 (I)	75	Me *cyclo*pentyl (VII)	62
Et_2 (II)	12	(−)-Menthyl Me (IX)	60
Pr^i_2 (III)	0·73	1 : 2-5 : 6-Di-*O*-*iso*propylidene-D-glucofuranose 3-(methyl sulphite) (X)	58
$(CH_2Ph)_2$ (IV)	71	1 : 2-3 : 4-Di-*O*-*iso*propylidene-D-galactose 6-(methyl sulphite) (XI)	62
MePr^i (VI)	55		
*cyclo*Hexyl Me (VIII)	62		

Carbohydrate sulphites were not isolated after reaction of sodium iodide in acetone with methyl sulphites.

Under the standard conditions adopted for the reaction of sodium iodide (1 mol.), dimethyl sulphite (1 mol.), and acetone, a 75% yield of acetone sodium bisulphite was obtained after 2 hours. Prolongation of the reaction time gave further amounts of the same product. Likewise the first traces of material to separate were identified as acetone

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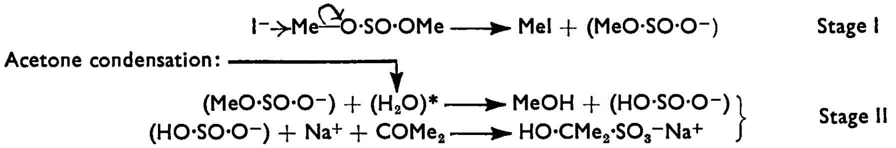
[6] Honeyman and Morgan, *J.*, 1955, 3660.

sodium bisulphite and there can be little doubt that this is the only product to separate from solution during the reaction.

Examination by mass spectrometry of the reaction solution after 2 hours showed the presence of methyl iodide and methanol, and in a parallel experiment with methyl *iso*propyl sulphite methyl iodide and a propanol were found in solution. In the latter case no methanol or propyl iodide could be detected, thus indicating that attack by the iodide ion occurred exclusively at the methyl group. Consequently, it seemed reasonable to suppose that the first stage in the reaction involved attack by iodide ions on the methyl groups of dimethyl sulphite to give methyl sulphite ions and methyl iodide, analogous to the reaction of dimethyl sulphate under the same conditions. Thereafter it is possible that further reactions occur as shown in Stage II.

Probable reaction pattern of dimethyl sulphite, sodium iodide, and acetone. The entities in parentheses have not been detected in the reaction mixture.



$$I^- \rightarrow Me{-}O{\cdot}SO{\cdot}OMe \longrightarrow MeI + (MeO{\cdot}SO{\cdot}O^-) \qquad \text{Stage I}$$

Acetone condensation:

$$\left.\begin{array}{l}(MeO{\cdot}SO{\cdot}O^-) + (H_2O)^* \longrightarrow MeOH + (HO{\cdot}SO{\cdot}O^-) \\ (HO{\cdot}SO{\cdot}O^-) + Na^+ + COMe_2 \longrightarrow HO{\cdot}CMe_2{\cdot}SO_3^-Na^+\end{array}\right\} \text{Stage II}$$

* Traces of water were detectable in the reaction mixture, but the precise origin is unknown; water may, *e.g.*, come from decomposition of the acetone bisulphite compound, in addition to the origin shown above.

The appearance of methyl iodide and methanol was followed by mass spectrometry (Table 3): formation of methyl iodide was relatively rapid, being complete within 20 minutes; that of methanol was slower, being *ca.* 65% complete after 2 hours. The early observation that the use of excess of sodium iodide with dimethyl sulphite did not significantly increase the yield of acetone sodium bisulphite after 2 hours is not now surprising since only Stage I of the reaction, which is not the rate-determining step, would be affected.

TABLE 3. *Release of methanol and methyl iodide in the reaction of sodium iodide and dimethyl sulphite in acetone.*

Time (min.)	MeI	MeOH (mol. %)	Acetone	Time (min.)	MeI	MeOH (mol. %)	Acetone
5	3·5 (4·7)	1·3 (1·3)	95·2 (94·0)	70	7·7	3·1	89·2
10	5·5 (6·2)	1·5 (2·1)	92·9 (91·7)	120	7·8	4·2	88·0
20	7·5 (7·6)	2·1 (3·1)	90·4 (89·3)	Max. theor.	6·8	6·8	86·4
40	7·5	2·7	89·8				

Traces of sulphur dioxide and water were present in each case. The figures in parentheses were obtained in duplicate experiments. Error $<\pm 0{\cdot}3$.

The kinetic study was made on a very small scale so that experimental error may have contributed to the difference in the amount of methanol released (*ca.* 65%) and the acetone sodium bisulphite precipitated (75%) after 2 hours and to the difference between observed and theoretical values.

From the evidence available it is not possible to decide which, after Stage I, is the rate-determining step in the formation of the acetone sodium bisulphite. The only reasonable source of water is from the condensation of acetone and it was observed that as the reaction proceeded non-volatile ether-soluble material accumulated in the reaction solution, from which mesityl oxide was isolated as its 2 : 4-dinitrophenylhydrazone.

In Stage II it is apparently the S–O linkage which is broken since (—)-menthol was recovered after reaction of (—)-menthyl methyl sulphite with sodium iodide in acetone. Cleavage of the C–O linkage would be expected to lead to inversion or racemisation at the asymmetric hydroxylic carbon atom in the (—)-menthol.

EXPERIMENTAL

Starting Materials.—The alkyl methyl sulphites in Table 1 were obtained by the procedure given by Berti.[5] Other dialkyl sulphites were prepared according to the methods described by Voss and Blanke [4] and Price and Berti.[3]

Action of Sodium Iodide in Acetone on Dialkyl Sulphates.—To a solution of the dialkyl sulphate (0·01 mole) in acetone (10 ml.) was added a solution of sodium iodide (0·01 mole) in acetone (10 ml.). The solution in each case became yellow and after a few seconds at room temperature the sodium alkyl sulphate crystallised. It was collected, washed with acetone, and dried *in vacuo* over phosphoric oxide. The sodium alkyl sulphates were deliquescent. The yields of alkyl sodium sulphate were: methyl 93%, ethyl 83%, *iso*propyl 42%.

Action of Sodium Iodide in Solvents other than Acetone on Dialkyl Sulphates.—A solution of sodium iodide (0·5 g.) in the appropriate solvent (5 ml.) was added to one of dimethyl sulphate (0·42 g.) in the same solvent (5 ml.). The precipitated sodium methyl sulphate was collected, washed with a little of the reaction solvent, and dried as above. The yields of sodium methyl sulphate were: from ethyl methyl ketone 0·45 g. (100%), acetylacetone 0·4 g. (89%), acetonylacetone 0·4 g. (89%). Dimethylformamide was unsatisfactory as solvent since sodium methyl sulphate was appreciably soluble in it.

Action of Sodium Iodide in Acetone on Methyl Alkyl and Other Dialkyl Sulphites.—A solution of sodium iodide (0·01 mole) in acetone (10 ml.; dried over K_2CO_3) was added to one of dialkyl sulphite (0·01 mole) in acetone (10 ml.). The solution rapidly became yellow but at room temperature solid separated only slowly. The yields recorded in Table 3 were obtained after the solutions had been boiled under reflux for 3 hr. and the resultant precipitates collected, washed with acetone, and dried *in vacuo* (P_2O_5). *X*-Ray powder photographs of the precipitates showed them to be identical with each other and with authentic acetone sodium bisulphite. The precipitates were heated at 100°/17 mm. until of constant weight (loss, *ca.* 60%; theor. for sodium acetone bisulphite 62%). *X*-Ray powder photographs of the residues showed that they were identical with each other and with authentic sodium sulphite. The volatile material from the preceding decompositions was collected in a liquid-air-cooled trap and examined by mass spectrometry (Metropolitan Vickers MS 2 mass spectrometer) which revealed the presence of water, acetone, and sulphur dioxide.

Release of Methanol and Methyl Iodide in the Reaction of Dimethyl Sulphite with Sodium Iodide in Acetone.—Sodium iodide was allowed to react with dimethyl sulphite under the conditions described above. The dimethyl sulphite was added to a boiling solution of the sodium iodide in acetone. Aliquots were withdrawn at suitable time intervals, cooled immediately in liquid air, and examined by mass spectrometry for methanol and methyl iodide. The results are summarised in Table 3.

Reactions of Sodium Iodide in Dimethylformamide and Other Solvents with Methyl Alkyl Sulphites.—A solution of sodium iodide (0·01 mol.) in dimethylformamide (10 ml.) was added to one of sulphite (0·01 mole) in dimethyl formamide (10 ml.) and the mixture boiled under reflux for 3 hr. Thereafter it was diluted with ether and filtered, and sodium iodide was removed by washing the collected precipitate with acetone. The products (yield 0·42—0·58 g.) obtained from the sulphites, I, VI, VIII, IX, X, and XI gave identical *X*-ray powder photographs. There was negligible loss of weight on heating. Analyses were obtained as follows: C, 12·1—14·0; H, 2·9—3·8; S, 17·6—24·3%. The C and H range included 8 analyses, S included 3. In the reaction with (−)-menthyl methyl sulphite (−)-menthol was recovered in 50% yield from the mother-liquors.

When the reaction was carried out in methyl cyanide, ethyl methyl ketone, acetylacetone, or acetonylacetone, unidentified products were obtained different from that obtained in dimethyl formamide.

Stability of Alkyl Sulphites and Alkyl Sulphates.—On storage under normal conditions all the derivatives listed in Tables 1 and 2, and also the dialkyl sulphates, underwent some decomposition with the development of acidic products and evolution of sulphur dioxide. It was essential to wash an ethereal solution of the sulphite or sulphate with aqueous sodium hydrogen carbonate and fractionally distil the product before experiments were carried out.

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