

Synthesis of Dialkyl Sulphites from Alcohols in the Halogen–Pyridine–Sulphur Dioxide System. Novel Behaviour of Alkyl Chlorosulphates in the Pyridine–Sulphur Dioxide System

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Dialkyl sulphites are formed selectively from alcohols in the halogen–pyridine–sulphur dioxide system. The behaviour of alkyl chlorosulphates in the pyridine–sulphur dioxide system has been investigated and the role of halogenosulphinat ion in this reaction is discussed.

IN the iodine–pyridine–sulphur dioxide system, carboxylic acids condense readily with amines to form amides. Amines alone in this system afford sulphamides in high yield, suggesting that iodine in liquid sulphur dioxide behaves like sulphuryl iodide, although this compound is not known.¹ In the same system the deoxygenation of sulphoxides to sulphides has also been performed with success.² Furthermore, iodine and bromine have been found to dissociate to give halogenosulphinat ion and halogen cation in pyridine–sulphur dioxide.²

We describe here a convenient and selective synthesis of dialkyl sulphites from alcohol in the halogen–pyridine–sulphur dioxide system, and also the role of halogenosulphite ion in this reaction.

RESULTS AND DISCUSSION

The alcohol reacted with iodine (0.5 mol. equiv.) in pyridine (1.5 mol. equiv.) and liquid sulphur dioxide (15 mol. equiv.) at room temperature. The results are summarized in Table 1. Primary and secondary alcohols afforded the corresponding dialkyl sulphites in good yield rather than the expected dialkyl sulphates. 1-Methylcyclohexanol gave 1-methylcyclohexene in 54% yield; this result is reasonable in view of the fact that the tertiary alcohol does not give the sulphite on treatment with thionyl chloride.³ This synthesis of dialkyl sulphites seems superior to the conventional use of thionyl chloride, since by-products such as alkyl iodides are not obtained. For example dinorbornyl sulphite was obtained quantitatively under these conditions, whereas the reaction with thionyl chloride gave only a 31.6% yield of the sulphite, along with by-products such as norbornyl chloride and other chlorides.⁴ In the

halogen–pyridine–sulphur dioxide system the dialkyl sulphite was the sole product, even when 1 mol. equiv. of iodine with respect to alcohol was used. For this reaction both iodide anions and iodine cations were necessary: dialkyl sulphite was not obtained when *N*-iodosuccinimide or tetraethylammonium iodide was used instead of iodine in this system.

TABLE 1
Synthesis of dialkyl sulphites by the reaction with iodine–pyridine–sulphur dioxide^a

Alcohol	Reaction time (h)	Yield of sulphite (%)	B.p. (°C) [mmHg]
Ethyl	1	84	156–158 [760] ^d
<i>n</i> -Butyl	1	92	118–120 [20] ^d
<i>n</i> -Hexyl	1	81	165–168 [19]
<i>s</i> -Butyl	12	91	74–75 [40]
Cyclohexyl	12	95	159–160 [10] ^d
1-Methylheptyl	12	90	168–172 [2] ^e
Norbornan-2- <i>endo</i> -yl	12	95 ^b	160–162 [2] ^f
Norbornan-2- <i>exo</i> -yl	12	92 ^c	160–162 [2] ^f

^aAlcohol (0.03 mol) reacted with iodine (0.015 mol) in pyridine–sulphur dioxide at 20 °C. ^bDinorbornan-2-*endo*-yl sulphite was obtained selectively. ^cThe product was dinorbornan-2-*exo*-yl sulphite. ^dA. I. Vogel and D. M. Cowan, *J. Chem. Soc.*, 1943, 16. ^eW. Gerrard, *J. Chem. Soc.*, 1944, 85. ^fJ. K. Stille and F. M. Sonnenberg, *J. Amer. Chem. Soc.*, 1966, **88**, 4914.

The reaction was also performed with bromine instead of iodine. The results are summarized in Table 2. Dialkyl sulphite, alkyl bromide, and olefin were obtained, and characterized by comparison of physical data with those of authentic samples.

In order to investigate the effect of the proportion of bromine, the reactions of octan-2-ol with various molar ratios of bromine were studied. The results are sum-

¹ M. Nojima, S. Hasegawa, and N. Tokura, *Bull. Chem. Soc. Japan*, 1973, **46**, 1254.

² M. Nojima, T. Nagata, and N. Tokura, *Bull. Chem. Soc. Japan*, 1975, **48**, 1343.

³ S. R. Sandler and W. Karo, 'Organic Functional Group Preparations,' vol. II, Academic Press, New York, 1971, p. 71.

⁴ J. K. Stille and F. M. Sonnenberg, *J. Amer. Chem. Soc.*, 1966, **88**, 4914.

marized in Table 3. When the ratio of bromine to alcohol was low, dialkyl sulphite was obtained as the major product, but the main products became alkyl bromide and dibromide as the proportion of bromine was increased. These results correspond with a result we obtained before: when an alcohol was added to a solution of bromine in sulphur dioxide, the alkyl bromide was obtained in good yield.⁵

TABLE 2
Reactions of alcohols in bromine-pyridine-sulphur dioxide^a

Alcohol	Product yield (%)		
	Sulphite	Bromide	Olefin
n-Butyl	20	Trace	<i>b</i>
n-Hexyl	54	Trace	<i>b</i>
s-Butyl	30	18	<i>b</i>
Cyclohexyl	0	62	37
1-Methylheptyl	41	30	8

^a Bromine (0.015 mol), alcohol (0.03 mol), and pyridine (0.045 mol) in sulphur dioxide (30 ml) kept at 20 °C for 1 h.

^b The yield of olefin was not investigated.

TABLE 3
Effect of the proportion of bromine in the reaction of octan-2-ol

Molar ratio of Br ₂ to ROH	Product yield (%)			
	Sulphite	Bromide	Olefin	Dibromide
0.5 : 1	41	30	8	Trace
1.0 : 1	0	37	Trace	51
2.0 : 1	0	24	Trace	72

The formation of diethyl sulphite with other reagents was also examined. The reaction of ethanol with thionyl chloride in pyridine-sulphur dioxide gave diethyl sulphite in 70% yield. With sulphuryl chloride, 25% yield of the sulphite was obtained without contamination by diethyl sulphate.

When norbornan-2-endo-ol reacted with sulphuryl chloride under the same conditions, norbornan-2-endo-yl chlorosulphite was obtained in 25% yield, with a 70% yield of norbornan-2-exo-yl chloride. This result is unexpected in that under conventional conditions an alcohol reacts with sulphuryl chloride to form an alkyl chlorosulphonate, and this reacts with an excess of alcohol giving dialkyl sulphate as the final product.⁶

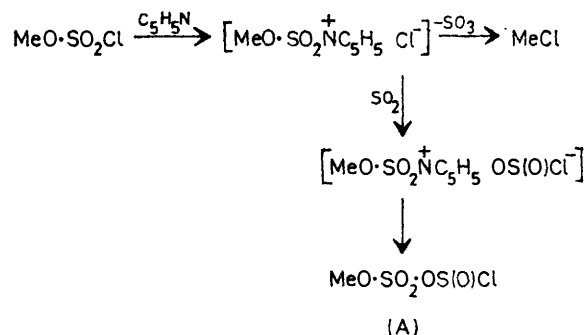
Interested in the behaviour of ethyl chlorosulphate in the pyridine-sulphur dioxide system, we kept a mixture of ethyl chlorosulphate and 1 : 1 pyridine-sulphur dioxide complex in acetonitrile at room temperature for 10 min, then added 1 equiv. of ethanol and kept the solution at room temperature for 1 h; diethyl sulphite was obtained in 10% yield.* A similar reaction in the presence of tetraethylammonium iodide gave diethyl sulphite in 15% yield.

The ¹H n.m.r. spectrum of methyl chlorosulphate in the pyridine-sulphur dioxide system consisted of two singlets, intensity ratio 6.3 : 3.7, at δ 2.88 and 4.34.

* Dialkyl sulphite was also obtained by the reaction of an alcohol with iodine in the presence of 1 : 1 sulphur dioxide-pyridine complex in acetonitrile.

⁵ N. Tokura, R. Tada, and R. Igarashi, *Bull. Chem. Soc. Japan*, 1960, **33**, 1176.

The former signal is identical with that of methyl chloride. The other appears at lower field than that of methyl chlorosulphate (δ 4.12) or methyl chlorosulphite (δ 3.99), and is considered to be due to the species MeO·SO₂·O·S(O)Cl, formed as in Scheme 1. It has been



SCHEME 1

suggested that a pyridinium salt is formed as an intermediate in the reaction of an alkyl chlorosulphate with pyridine, and then undergoes displacement by chloride ion.⁷ In liquid sulphur dioxide, chloride ion is well known to exist as chlorosulphite ion,⁸ and so the formation of the intermediate (A) in this system appears reasonable.

In terms of participation of this intermediate (A), the selective formation of dinorbornan-2-endo-yl sulphite from norbornan-2-endo-ol may be reasonably explained. The first step of the reaction of the alcohol with the iodine-sulphur dioxide reagent or with sulphuryl chloride is considered to be the formation of norbornan-2-endo-yl halogenosulphate (B), which gives a pyridinium salt (C) on reaction with pyridine. *exo*-Attack of halide ion on this intermediate then probably gives norbornan-2-*exo*-yl halide. Substitution by halogenosulphite ion on the sulphur atom of (B) will then give the intermediate (D), which could also be formed by the reaction of (C) with halogenosulphite ion. By attack of norbornan-2-endo-ol on (D), followed by elimination of sulphur trioxide as shown in Scheme 2, dinorbornan-2-endo-yl sulphite can reasonably be obtained. A path involving attack on norbornyloxysulphonylpyridinium ion or norbornyl cation by halosulphinate ion on the carbon atom to form a chlorosulphite, which is also a candidate for the precursor of dialkyl sulphite, is excluded for the following reason. If the reaction proceeds in this way, the formation of norbornan-2-*exo*-yl halogenosulphite would be expected,⁹ and as the final product norbornan-2-*exo*-yl norbornan-2-endo-yl sulphite should be obtained. The fact that methyl chlorosulphite was not observed as a product of the reaction of methyl chlorosulphate with pyridine in sulphur dioxide also supports the above consideration.

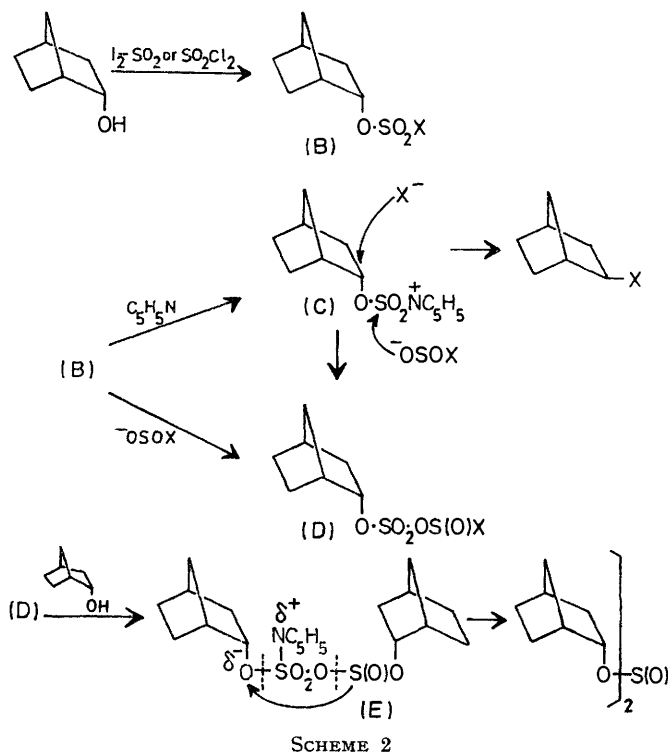
⁶ E. Buncel and J. P. Millington, *Canad. J. Chem.*, 1969, **47**, 2145.

⁷ J. Charalambous, M. J. Frazer, and W. Gerrard, *J. Chem. Soc.*, 1964, 5480.

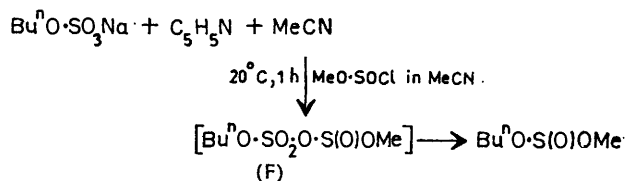
⁸ D. F. Burow, *Inorg. Chem.*, 1972, **11**, 574.

⁹ G. D. Sargent, *Quart. Rev.*, 1966, **20**, 301.

The possibility that the species (E) is the intermediate for the formation of dialkyl sulphite was confirmed by the following reaction. When sodium n-butyl sulphate



reacted with methyl chlorosulphite (1 mol. equiv.) in the presence of pyridine (1 mol. equiv.), n-butyl methyl sulphite was obtained in 55% yield, probably *via* the intermediate (F).



The selective formation of dialkyl sulphite in the reactions with iodine is explained as follows. The nucleophilicity of iodide ion in a dipolar aprotic solvent is weaker than that of bromide or chloride ion.¹⁰ Furthermore, iodide ion has been found to be solvated the most strongly by sulphur dioxide by measurements of electroconductivity of halide ions in liquid sulphur dioxide;¹¹ thus the nucleophilicity of iodide would be increased and the formation of alkyl iodide depressed. Iodosulphite ion may be reasonably considered as the sole nucleophilic reagent in this system.

EXPERIMENTAL

¹H N.m.r. spectra were obtained with a JEOL LNM 3H-60 instrument, i.r. spectra with a Hitachi 215 spectro-

¹⁰ A. J. Parker, *Chem. Rev.*, 1969, **69**, 1.

¹¹ S. Takezawa, Y. Kondo, and N. Tokura, *J. Phys. Chem.*, 1973, **76**, 2133.

¹² W. W. Binkley and E. F. Degering, *J. Amer. Chem. Soc.*, 1938, **60**, 2810.

meter, and mass spectra with a Hitachi RMU-6H spectrometer.

Methyl and ethyl chlorosulphates were prepared by the method of Binkley and Degering,¹² and methyl and ethyl chlorosulphites by the method of Berti.¹³ The preparation of norbornan-2-*exo*- and -*endo*-ols has been described.¹⁴

Reactions of Alcohols with Halogens in Pyridine-Sulphur Dioxide.—Into liquid sulphur dioxide (30 ml) in a high-pressure vessel, halogen (0.015 mol) in pyridine (0.045 mol) were added at -70°C . Then the alcohol (0.03 mol) was added slowly, and the vessel was sealed with a stainless cap and kept at 20°C . After the appropriate time the solution was cooled in acetone-solid CO_2 and poured into aqueous sodium hydroxide. The products were extracted with ether and the extract was washed with hydrochloric acid and saturated brine, dried (Na_2SO_4), and evaporated. The products were analysed by g.l.c. When necessary, products were isolated by column chromatography, and dialkyl sulphites were characterized by comparing physical data with those of authentic samples.¹⁵

For the reactions of alcohols with thionyl chloride and sulphuryl chloride, the same reaction conditions were used.

The reaction of norbornan-2-*endo*-ol (3.36 g) with iodine (2.67 g) and pyridine (3.84 g) in liquid sulphur dioxide (30 ml) at 20°C for 12 h gave dinorbornan-2-*endo*-yl sulphite (3.85 g, 95%),⁴ b.p. $160\text{--}162^\circ$ at 2 mmHg, ν_{max} 1 200, 980, 960, 835, and 742 cm^{-1} ; δ 4.72 (2 H, complex m). From norbornan-2-*exo*-ol a 92% yield of dinorbornan-2-*exo*-yl sulphite⁴ was obtained, b.p. $160\text{--}162^\circ$ at 2 mmHg, ν_{max} 1 205, 980, 963, 860, 840, and 742 cm^{-1} ; δ 4.35 (2 H, complex m). The reaction of norbornan-2-*endo*-ol with sulphuryl chloride (2.01 g) afforded dinorbornan-2-*endo*-yl sulphite (1.01 g, 25%) and norbornan-2-*exo*-yl chloride (2.73 g, 70%), δ 6.20 (1 H, complex m).¹⁶

The ¹H N.m.r. Spectrum of Methyl Chlorosulphate in Pyridine-Sulphur Dioxide.—Into a solution of methyl chlorosulphate (130 mg, 1.0 mmol) and (10 mg; internal standard) sulphur dioxide (1.0 ml) cooled in solid CO_2 -acetone, pyridine (79 mg, 1.0 mmol) was slowly added. After warming to 20°C during 5 min the ¹H spectrum consisted of two singlets, ratio 6.3 : 3.7, at δ 2.88 and 4.34. The spectra of methyl chlorosulphate, methyl chlorosulphite, and methyl chloride in sulphur dioxide were obtained similarly.

Reaction of Ethyl Chlorosulphate with Ethanol in Pyridine-Sulphur Dioxide.—Into a solution of the 1:1 sulphur dioxide-pyridine complex (10 ml) in acetonitrile (50 ml), ethyl chlorosulphate (0.03 mol) was added during 10 min, followed, during 10 min, by ethyl alcohol (0.03 mol) dissolved in acetonitrile (20 ml), and the mixture was kept at 20°C for 1 h. Evaporation left diethyl sulphite (0.40 g, 3 mmol).

Reaction of Diethyl Sulphate with Iodine in Pyridine-Sulphur Dioxide.—Diethyl sulphate (0.03 mol) was dissolved in a solution of iodine (0.015 mol) and pyridine (0.045 mol) in sulphur dioxide (30 ml), and the mixture was kept for 1 h at 20°C . Conventional work-up afforded unchanged diethyl sulphate quantitatively.

Reaction of Sodium n-Butyl Sulphate with Methyl Chlorosulphite.—Into a solution of sodium n-butyl sulphate

¹³ G. Berti, *J. Amer. Chem. Soc.*, 1954, **76**, 1213.

¹⁴ J. P. Schaefer and D. S. Weinberg, *J. Org. Chem.*, 1964, **30**, 2635.

¹⁵ W. Gerrard and B. D. Shepherd, *J. Chem. Soc.*, 1955, 2069.

¹⁶ L. Schmerling, *J. Amer. Chem. Soc.*, 1946, **68**, 1195.

(3.52 g, 0.02 mol)¹⁷ and pyridine (1.58 g, 0.02 mol) in acetonitrile (50 ml), methyl chlorosulphite (2.28 g, 0.02 mol) dissolved in acetonitrile (30 ml) was added at 20 °C during 10 min, and stirring was continued for 50 min. The mixture afforded n-butyl methyl sulphite¹⁸ (1.07 g,

55%), b.p. 86–88° at 14 mmHg, ν_{\max} 1 207, 990, 960, 924, and 860 cm^{-1} ; δ 0.94 (3 H, t), 1.2–1.8 (4 H, m), 3.55 (3 H, s), and 3.92 (2 H, t); *m/e* 152.

This work was partially supported by a grant-in-aid from the Ministry of Education, Japan.

¹⁷ P. Baumgarten, *Chem. Ber.*, 1926, **59B**, 1976.

¹⁸ P. Carre and D. Libermann, *Bull. Soc. chim. France*, 1933, 1050.