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Chloromethyl chlorosulfate: a new, catalytic method of preparation and reactions with some nucleophiles†

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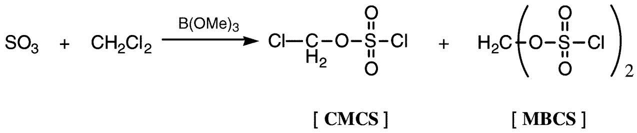
The reaction of liquid (γ-) SO_3 with CH_2Cl_2 at room temperature leads to SO_3 insertion into the C–Cl bonds, giving the useful chloromethylating agent chloromethyl chlorosulfate (CMCS). The process is very slow but becomes rapid on addition of catalytic quantities of trimethyl borate. The product mixture consists almost entirely of CMCS and the product of further sulfation, methylene bis(chlorosulfate) (MBCS), in a ratio of *ca.* 2 : 1, but typical yields of CMCS, isolated by distillation, are only 30–35%. The catalysed reaction in the homogeneous liquid phase at −45 °C has been followed as a function of time and of reactant concentration by ^1H nmr spectroscopy. It is observed that, besides CMCS and MBCS, three additional, transient products (designated A, B and C) are formed. Products A, B and C decompose slowly at −45 °C but much more rapidly if the reaction mixture is raised to room temperature, giving additional CMCS and MBCS. From an analysis of the SO_3 balance, it is inferred that products A, B and C arise from the reaction of one molecule of CH_2Cl_2 with respectively two, three and four molecules of SO_3; they are suggested to be chloromethyl chloropolysulfates. By measuring initial rates of CMCS formation or total CH_2Cl_2 consumption, it is shown that the reaction is first order in the catalyst and roughly third order in SO_3. A mechanistic scheme is proposed in which SO_3 forms equilibrating zwitterionic molecular complexes with CH_2Cl_2. of 1 : 1, 2 : 1 and higher stoichiometries. The boron-containing catalyst can activate these complexes towards nucleophilic attack at carbon by the negatively charged oxygen of another zwitterion. An analogous mechanism can be written for the conversion of CMCS into MBCS by SO_3 in the presence of trimethyl borate. CMCS reacts rapidly with anionic nucleophiles, such as halide or acetate ions (X^-), in homogeneous solution of their tetrabutylammonium salts in CD_3CN, or in a two-phase system ($CDCl_3/H_2O$) using alkali-metal salts in conjunction with a phase-transfer catalyst. In both situations the products ($ClCH_2X$) arise by rapid nucleophilic displacement of the chlorosulfate moiety; this then more slowly liberates chloride ion, which converts further CMCS into CH_2Cl_2. The reactivity of CMCS has been compared with that of MBCS and methyl chlorosulfate (MCS) in competitive experiments; the reactivity order is MCS > MBCS > CMCS >> CH_2Cl_2. Evidence is also presented suggesting that, in contrast to the halide nucleophiles, reaction of CMCS with sodium phenoxide in tetrahydrofuran solution leads to nucleophilic displacement of the sulfur-bound chloride.

Introduction

Chloromethyl chlorosulfate (CMCS) is a promising electrophilic reagent capable of chloromethylation, for example of simple carboxylic acids,[1] protected amino-acids,[2] and dialkyl phosphates,[3] without the generation of the potent carcinogen bischloromethyl ether as a by-product. Surprisingly, although the insertion of SO_3 into C–Cl bonds in, for example chloroethane[4a] and 1,1-dichloroethane,[4b] has long been known, the preparation of CMCS has been the subject of little previous research. The earliest literature reference concerns its synthesis from chlorosulfuric acid and formaldehyde by Fuchs and Katscher in 1927.[5] For this process high temperatures were required, CMCS yields were low and two side products were also present, bischloromethyl sulfate and bischloromethyl ether. A later synthetic process using chlorosulfuric acid and chloromethyl chloroformate resulted in increased yields of CMCS.[6] High temperatures were again required and the reaction was accompanied by effervescence of CO_2 and HCl. More recently Binderup and Hansen reported refluxing chlorosulfuric acid with bromochloromethane.[1] Another recent procedure due to Geering involved treating sulfur trioxide at room temperature with dichloromethane in the presence of a mixture of Na_2CO_3 and $NaHCO_3$.[7] However, yields of CMCS for both processes were low, with the latter giving methylenebis(chlorosulfate), MBCS, as the principal product.

In this paper we show that trimethyl borate acts as an efficient catalyst for the direct insertion of sulfur trioxide into the carbon–chlorine bonds of dichloromethane, providing a new, simple and reliable method of preparation of CMCS (Eqn. 1).



$$SO_3 + CH_2Cl_2 \xrightarrow{B(OMe)_3} Cl{-}CH_2{-}O{-}\overset{O}{\underset{O}{S}}{-}Cl + H_2C\left(O{-}\overset{O}{\underset{O}{S}}{-}Cl\right)_2 \quad (1)$$

[CMCS] **[MBCS]**

We report also on some studies of the kinetic form of this sulfonation process, and we suggest a mechanistic scheme, based on Lewis acid [SO_3 and $B(OMe)_3$] interactions with the Lewis base (CH_2Cl_2) consistent with the findings. Finally we examine the reactivity of CMCS towards some nucleophiles from which we suggest how, by a simple modification of the work-up, the efficiency of the preparative procedure can be improved. In studying the reactions of CMCS with nucleophiles, particular attention has been paid to regioselectivity. Nucleophilic attack at carbon could in principle involve displacement either of chloride or chlorosulfate ions, or might less probably involve concerted fragmentation to SO_3 and chloride ion, while attack at sulfur could displace chloride or, perhaps with fragmentation, chloromethoxide ion.[8] It has been found that the nature of the nucleophile affects regioselectivity, but halide ions usually displace chlorosulfate. Previous studies on

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† Electronic supplementary information (ESI) available: Tables S1–S4 and Scheme S1. See http://www.rsc.org/suppdata/ob/b4/b403338h/

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the hydrolysis of alkyl chlorosulfates in aqueous dioxan have indicated that the process involves a bimolecular displacement of chlorosulfate ion that can be accelerated by the presence of halide ions, hydroxide and by pyrrolidine in high concentration.[9]

Results

Preparation of CMCS

Preliminary attempts to prepare CMCS by the Geering procedure[7] from dichloromethane using γ-sulfur trioxide, the liquid modification, obtained from a number of different commercial suppliers, gave variable, usually low yields of the desired product. This form of SO_3 is usually maintained in the liquid state by the addition of small amounts of stabilisers,[10] which inhibit the formation of polymeric structures,[11] and it was established that the highest yields of CMCS were obtained using samples of SO_3 that contained trimethyl borate as the stabiliser. Subsequent investigation of reactions in which trimethyl borate was added in known amounts demonstrated that the reaction between dichloromethane and SO_3 at room temperature is indeed accelerated dramatically by very low concentrations (<1% by weight). This then formed the basis of the new preparative procedure in which SO_3 is slowly added to premixed dichloromethane (*ca.* 2-fold molar excess) and trimethyl borate (typically *ca.* 0.1 mol% with respect to SO_3) at a temperature of 20–30 °C. After allowing the reaction mixture to stand at ambient temperature for 10 minutes it is quenched by stirring it with aqueous sodium carbonate: this treatment lowers the level of the principal by-product MBCS which appears to have a deleterious effect on the CMCS yield from the subsequent distillation. The product, isolated from the dichloromethane layer by fractional distillation under reduced pressure is CMCS, later fractions being contaminated with MBCS. Overall the reaction under the conditions specified above appears to afford CMCS and MBCS as the sole products in an approximate ratio of 2 : 1, but after distillation isolated yields of CMCS were consistently only *ca.* 35% based on SO_3.

Kinetic studies on the reaction of sulfur trioxide with dichloromethane

CMCS and MBCS are formally the result of insertion of a molecule of SO_3 into one or both of the C–Cl bonds of dichloromethane (Eqn. 1). Kinetic studies were undertaken with the aim of understanding this rather remarkable reaction better and so improving the efficiency of the preparation of CMCS. A separate study was carried out on the transformation of CMCS into MBCS by SO_3 in the presence of a catalytic amount of trimethyl borate. Monitoring of reaction mixtures by ^1H nmr spectroscopy seemed the obvious choice, but it was necessary to slow the reaction down compared with typical preparative experiments; most reactions were therefore followed at −45 °C. The use of nmr spectroscopy and the low temperature restricted the range of reactant concentrations that could be conveniently used to mol fractions of SO_3 in CH_2Cl_2 between 0.13 and 0.21; the lower value was determined by the limits of detection by nmr spectroscopy of the individual products formed, and the upper limit by the solubility of SO_3 in CH_2Cl_2 at −45 °C. The reactions were initiated by the introduction of a few microlitres of a CH_2Cl_2 solution of trimethyl borate into a mixture of the reactants in an nmr tube previously equilibrated at the reaction temperature. Spectra were recorded as a function of time, proton signals integrated, and the total integral including that for unchanged CH_2Cl_2 taken to be directly proportional to the total CH_2Cl_2 weighed into the reaction mixture.

Transient product formation. It was immediately apparent that, at −45 °C, in addition to CMCS and MBCS, identified by comparison of their chemical shifts with those of authentic specimens prepared by the method of Binderup and Hansen,[1] three further products, which we designate products A, B and C, were formed. Chemical shifts of all the components of the reaction mixtures, relative to external TMS, are collected in Table 1. From the start of the reaction CMCS was the product formed most rapidly, along with smaller amounts of products A, B and C, which were all produced without any detectable induction period. By contrast, MBCS was produced rather slowly at the start but its rate of formation increased somewhat as the reaction progressed. Fig. 1 shows the variation with time of the concentrations of the products (expressed in mol kg^{-1} in the reaction mixture) for a typical experiment. It is evident that the reaction began very rapidly at −45 °C but consumption of CH_2Cl_2 soon slowed down and the system reached a quasi-steady state around 2–3 hours after initiation of the reaction. At this point, the amount of CMCS produced was roughly equal to the combined amounts of compounds A, B and C, and it was much higher than the yield of MBCS. It was noted, however, that the yield of CMCS appeared to continue to rise slowly, while the yields of products B and C declined. Allowing the contents of the nmr tube to warm to room temperature and then cooling them again to −45 °C showed that the composition of the reaction mixture had changed appreciably (Table 2). Products B and C had disappeared completely, with a substantial increase in the amount of CMCS and MBCS; product A showed a much reduced yield and this could be removed completely if the nmr tube were held at room temperature for a few minutes. The total consumption of CH_2Cl_2 (assuming that all products contain only one carbon atom) increased by some 30% in going from the situation after 3 hours at −45 °C to the final reaction mixture; this indicates that additional sulfonation capability is released on raising the temperature of the reaction mixture after the initial reaction. Clearly Products A, B and C are transient (metastable) species and, on decomposition (slowly at −45 °C and much more rapidly at room temperature), give rise only to additional CMCS and MBCS. We hypothesise that the intermediate and final product compositions are reached when the level of SO_3 or other sulfonating capability is reduced virtually to zero at that temperature. In Table 2 the sums of the concentrations of the products

Table 1 Proton chemical shifts[a] of reactants and products in the reaction of SO_3 and CH_2Cl_2 at −45 °C measured *in situ*

Compound	CH_2Cl_2	CMCS	A	B	C	MBCS
δ/ppm	4.370	5.009	5.051	5.087	5.098	5.198

[a] Relative to external TMS and measured at 250 MHz.

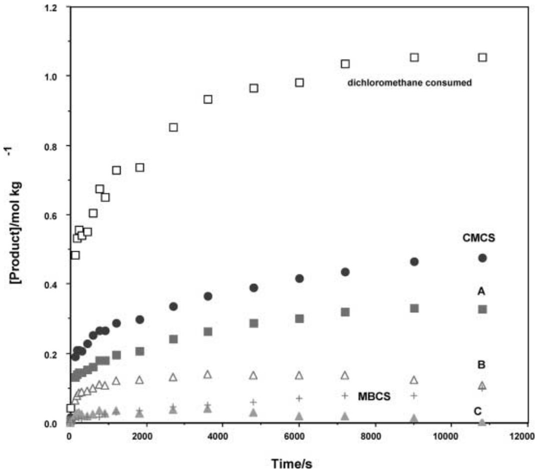


Fig. 1 Time dependence of product formation in the reaction of CH_2Cl_2 (9.71 mol kg^{-1}) with SO_3 (2.19 mol kg^{-1}) in the presence of $B(OMe)_3$ (2.39 mmol kg^{-1}) at −45 °C.

Table 2 Intermediate and final compositions of products of the reaction of SO_3, initially 2.171 mol kg^{-1}, and CH_2Cl_2 measured *in situ* at −45 °C

	Concentration/mol kg^{-1}		SO_3 Balance/mol kg^{-1}		
Product	Intermediate[a]	Final	SO_3/CH_2Cl_2[b]	Intermediate[a]	Final
CMCS	0.492	0.870	1	0.492	0.870
MBCS	0.093	0.331	2	0.186	0.662
Compound A	0.341	0.168	2	0.682	0.336
Compound B	0.107	0	3	0.321	0
Compound C	0.010	0	4	0.040	0
Totals	1.043	1.369		1.721	1.868

[a] After 3 hours at −45 °C. [b] Assumed stoichiometry.

Table 3 Reactant and product compositions (mol kg^{-1}) in the $B(OMe)_3$-catalysed reaction of SO_3 with CMCS measured by ^1H nmr spectroscopy *in situ* at −45 °C

Time/s	CMCS	SO_3	MBCS	CH_2Cl_2	Product A	
0	9.92	1.97	0	0	0	
0[a]	9.24	n.m.[b]	0.39	0.29	0	
9000	4.98	n.m.[b]	2.51	1.44	0.99	
SO_3 balance		[1.97] At $t = 0$	−2.51	+1.44	−0.99	= 2.06 consumed

[a] After standing overnight at room temperature in the absence of catalyst. [b] Not measured.

Table 4 Influence of trimethyl borate concentration on the initial rate of formation of CMCS (v_{CMCS}) and of consumption of CH_2Cl_2 (v_{tot}) at −45 °C[a]

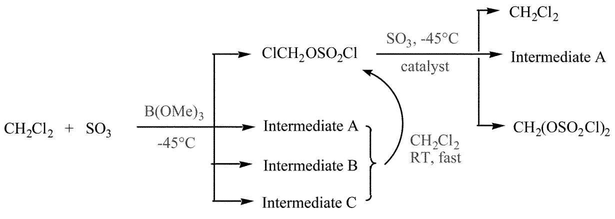
$[B(OMe)_3]$/mmol kg^{-1}	0	1.65	2.20	2.39	3.31	4.40	5.48
v_{CMCS}/mmol kg^{-1} s^{-1}	*ca.* 0	0.60	1.7	2.0	2.4	3.4	4.2
v_{tot}/mmol kg^{-1} s^{-1}	*ca.* 0	1.0	2.6	4.5	5.8	6.7	7.2

[a] Initial reactant concentrations: CH_2Cl_2 9.71; SO_3 2.19 mol kg^{-1}.

after 3 hours and at the end of reaction falls far short of the initial concentration of SO_3 weighed into the reaction tube. This indicates that, after allowance is made for the MBCS produced, the stoichiometry of the transient products cannot all be $SO_3 : CH_2Cl_2 = 1 : 1$ as it is for CMCS; indeed it is difficult to conceive of enough plausible isomeric structures with that stoichiometry. Accordingly we present in Table 2 possible stoichiometries for the products A, B and C that would account for most of the SO_3 initially present. Stoichiometries are known for CMCS and MBCS, and we have separate evidence for the SO_3/CH_2Cl_2 ratio for product A as detailed below. The agreement between the amount of SO_3 present at the start of the reaction and the amount tied up in the products at the intermediate stage and at the end of the reaction can be improved by adjustment to the SO_3/CH_2Cl_2 ratio for products A, B and C, but, for present purposes, minimum values have been chosen.

Experiments carried out in which CMCS (25 mol percent with respect to SO_3) was present at the start of the reaction of SO_3 and CH_2Cl_2 led to a large reduction in the conversion of CH_2Cl_2 into CMCS at the steady state, but substantial increases in the production of MBCS and product A, with smaller increases for products B and C. In a further experiment, allowing a 5 : 1 mixture of CMCS and SO_3 to stand overnight at room temperature without a catalyst led to significant conversion (*ca.* 20% based on SO_3) of CMCS into MBCS and, surprisingly, the production of a rather smaller amount of CH_2Cl_2 (Table 3). When a catalytic amount of trimethyl borate was added to the mixture at −45 °C, the MBCS and CH_2Cl_2 formation, measured after 150 min increased dramatically, accompanied by a substantial yield of product A. From the product analysis in Table 3 it can be seen that the SO_3 balance can only be maintained if formation of product A from CMCS consumes one molecule of SO_3. Thus the SO_3/CH_2Cl_2 ratio in A is 2 : 1, making it isomeric with MBCS.

The pattern of these observations is represented in Scheme 1.



Scheme 1

Kinetic form. The time-dependence of the consumption of CH_2Cl_2 at −45 °C could not be fitted to a simple kinetic expression with an integral kinetic order. Accordingly the problem was approached by measurements of the initial rate of reaction under a range of conditions. Concentration/time curves for both CMCS appearance and CH_2Cl_2 consumption were fitted to a second order polynomial (with $r > 0.99$ in most cases), and the expressions differentiated with respect to time, setting $t = 0$. Because of the need to adjust the spectrometer after introduction of the sample tube, no concentrations could be satisfactorily measured during the first 2 minutes after initiation of the reaction, and data for the next 5 minutes were used in the fitting. The catalyst concentration could be varied conveniently over a substantial range of values, but, as explained earlier, the relative concentrations of SO_3 and CH_2Cl_2 were constrained within a rather narrow range. All reaction mixtures were made up by weight, and concentrations are expressed as mol kg^{-1}.

Table 4 shows the variation of the initial rate of CMCS formation, v_{CMCS}, and of total CH_2Cl_2 consumption, v_{tot}, with the trimethyl borate concentration in a series of reactions carried out with constant initial reactant concentrations. The results fit the expression v_{CMCS}/mol kg^{-1} s^{-1} = $800[B(OMe)_3]$ with $r = 0.98$ and v_{tot}/mol kg^{-1} s^{-1} = $1480[B(OMe)_3]$ with $r = 0.95$, satisfactorily demonstrating a first order dependence, with a negligible uncatalysed reaction. It should be noted that no evidence was found to indicate the nature of the catalytic entity under the reaction conditions, but addition of further SO_3 after completion of the reaction showed the catalytic activity to be little diminished.

Table 5 Influence of reactant concentrations on the initial rate of formation of CMCS (v_{CMCS}) and disappearance of CH_2Cl_2 (v_{tot}) at −45 °C

$[SO_3]$/mol kg^{-1}	$[CH_2Cl_2]$/mol kg^{-1}	$[B(OMe)_3]$/mmol kg^{-1}	v_{CMCS}/mmol kg^{-1} s^{-1}	v_{tot}
1.554	10.31	2.17	0.4	0.93
1.955	9.931	2.17	0.8	1.4
2.043	9.848	2.05	0.6	1.5
2.171	9.738	2.18	1.2	2.0
2.193	9.707	2.20	1.7	2.5
2.480	9.454	2.47	1.6	4.4

Table 6 Product analysis after 5 minutes in competitive reactions of halide ions with CMCS (0.3 M) and MCS (0.3 M) in CD_3CN at 25 °C

		[CMCS]/M	$[CH_2Cl_2]$/M	$[CH_2BrCl]$/M	[MCS]/M	[MeCl]/M	[MeBr]/M
Halide (init. conc.)	δ_H	6.13	5.44	5.31	4.23	3.02	2.67
Chloride (0.15 M)		0.300	0.009	0	0.119	0.093	0
Bromide (0.15 M)		0.300	0.013	0	0.118	0.015	0.140
Bromide (0.30 M)		0.247[a]	0.077[a]	0[a]	0	0.011	0.257

[a] After 240 min. [CMCS] = 0.193. $[CH_2Cl_2]$ = 0.084, $[CH_2BrCl]$ = 0.012 M.

Variation of the initial CH_2Cl_2 and SO_3 concentrations within the constraints referred to above, using catalyst levels that were kept as close to constant as the experimental procedure allowed, led to changes in the initial rates detailed in Table 5. The precision of the values of v, for CMCS formation and CH_2Cl_2 consumption was not high and we approach the results with due caution. Logarithmic plots of $v' = v/[\text{catalyst}]$ and $v'' = v/[\text{catalyst}][CH_2Cl_2]$ against log $[SO_3]$ were roughly linear but with random scatter; linear regression analysis indicated that a marginally better fit was achieved with log v'' [r = 0.896(CMCS formation) and 0.964(CH_2Cl_2 consumption)] compared with log v' [r = 0.884(CMCS) and 0.961(CH_2Cl_2)]. We cannot therefore say with confidence whether the order of the reaction in CH_2Cl_2 is zero or one. The effect of changing $[SO_3]$ on both v_{CMCS} and v_{tot} is pronounced, the slope of the logarithmic plots being 3.1 (log v') and 3.2 (log v''), which represents the formal order of the reaction with respect to that reactant.

Reaction of CMCS with SO_3. In the reaction of CH_2Cl_2 with SO_3 it was noted that the formation of MBCS always began very slowly and accelerated as the reaction progressed. As mentioned above, introducing CMCS into a reaction mixture containing CH_2Cl_2 and SO_3, led to the production of increased amounts of MBCS and compound A. Both observations are consistent with MBCS being a consecutive product formed by sulfonation of the initially formed CMCS. In order to check that such an interpretation was correct, we investigated, using ^1H nmr spectroscopy, the reaction of CMCS and SO_3 in the presence of trimethyl borate at −45 °C. Surprisingly, as well as producing MBCS and compound A, the reaction mixture also gave rise to substantial quantities of CH_2Cl_2. The time variation of concentrations is shown in Fig. 2, confirming that the timescale of this reaction is much the same as the reaction of CH_2Cl_2 with SO_3.

Reactions of CMCS with nucleophiles

The reactions studied were mainly with anionic nucleophiles and were undertaken either in homogeneous solutions of tetrabutylammonium salts in CD_3CN or in a two-phase $CDCl_3$–H_2O system using alkali-metal salts with tetraoctylammonium bromide as a phase-transfer catalyst. For purposes of comparison some reactions were carried out using MBCS or methyl chlorosulfate (MCS) as the substrate in place of CMCS. In most cases the anionic nucleophile was used in deficit with respect to CMCS so as to provide information on the stoichiometry of the reaction, and a few competitive experiments were undertaken using mixtures of nucleophiles or of substrates in order to assess relative reactivities. Reactions were monitored as a function of time by ^1H nmr spectroscopy taking advantage of the fact that all the substrates and their reaction products give rise to readily distinguishable singlet signals. Proton chemical shifts (δ_H) of the reaction products are given in Tables 6 and 7 and in Tables S1–S4 of the supplementary information.† 1,2-Dichloroethane or 1,2-dimethoxyethane or toluene were present at known concentration in the reaction mixtures and used as an internal standard in converting the integrated nmr signals into product concentrations.

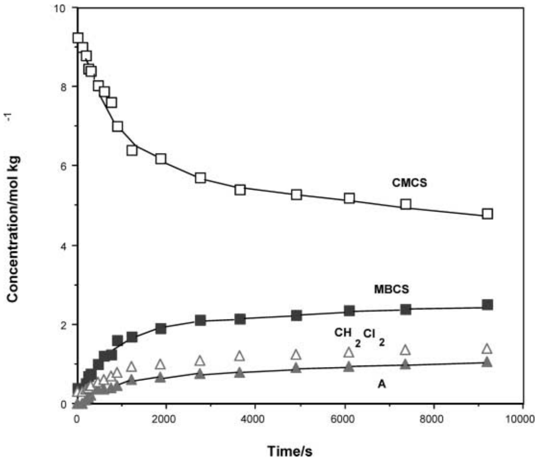


Fig. 2 Time dependence of product formation at −45 °C on addition of $B(OMe)_3$ (1.65 mmol kg^{-1}) to a mixture of CMCS (9.92 mol kg^{-1}) and SO_3 (1.97 mol kg^{-1}) that had been allowed to stand overnight at room temperature (see Table 3).

Reactions in homogeneous solution in CD_3CN. Reactions at 25 °C were rapid over the first 10 min, but a slower process that produced additional substitution product followed this initial phase. The detailed results of experiments using chloride, bromide and iodide ions as nucleophiles at 25 °C are in the supplementary information (Table S1),† but the product analysis in the reaction of CMCS with 25 mol% tetrabutylammonium bromide illustrates the pattern of behaviour (Fig. 3). After a few hours, 25% of the CMCS had been converted into bromochloromethane but this was accompanied by an amount of dichloromethane corresponding to some 14% additional conversion of CMCS. A similar additional reaction was observed in the reaction of CMCS with 25 mol% tetrabutylammonium chloride; 39% conversion into dichloromethane. A competitive experiment using 12.5 mol percent of chloride and 12.5 mol percent of bromide ions together showed that after 10 min dichloromethane had been formed in quantitative yield based on the chloride concentration, but the bromochloromethane yield

Table 7 Time variation of the composition (M) of the organic layer in a reaction mixture in which MBCS is treated with potassium chloride[a] in $CDCl_3/H_2O$ containing tetraoctylammonium bromide[b] at 25 °C

	MBCS	CMCS	BMCS[c]	CH_2Cl_2	CH_2BrCl
Time/min δ_H	6.14	5.97	6.04	5.30	5.17
0	0.300	0	0	0	0
5	0.211	0.061	0.007	0	0
30	0.019	0.204	0.010	0.004	0
60	0	0.175	0.010	0.045	0
120	0	0.099	0.008	0.114	0
180	0	0.041	0.001	0.165	0.002
240	0	0.014	0	0.246	0.004

[a] Initially, molar ratio KCl : MBCS = 0.25. [b] Initially, molar ratio $(C_8H_{17})_4N^+Br^-$: MBCS = 0.05. [c] Bromomethyl chlorosulfate; δ_H 6.04.

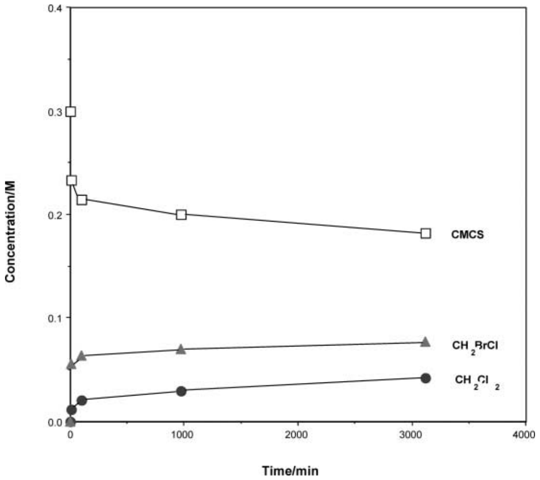


Fig. 3 Product development in the reaction of CMCS (0.30 M) with tetrabutylammonium bromide (0.075 M) in CD_3CN solution at 25 °C.

was substantially short of quantitative. On storage of the solution for 26 h, quantitative conversion into the bromo-product was achieved, but by then the dichloromethane yield had risen, again by an amount equivalent to 13% conversion of CMCS. The source of the excess dichloromethane is clearly the further reaction of displaced chlorosulfate ions, presumably by transfer of SO_3 to the solvent,[12] liberating additional chloride ions. Kinetic studies have shown that, in water at 25 °C, the half-life for hydrolysis of chlorosulfate ion is about 3 ms, unaffected by pH in the range 3.5 to 9.[13] This observation is of more direct relevance to the two-phase experiments described below, but SO_3-transfer to less basic solvents is likely to be facile. The competitive reactions of chloride and bromide ions showed that chloride ion was significantly more reactive than bromide ion, in keeping with expectation for nucleophilic reactions in a dipolar aprotic solvent.[14] Reactions of CMCS with tetrabutylammonium iodide led to consumption of CMCS in more than the stoichiometric amount and this continued on prolonged storage during which time small concentrations of dichloromethane could be detected. No other new ^1H nmr signals were observed, but the reaction solution took on a pale red-brown colour. Cyclic voltammetry of CMCS (1.06 mM) in CH_3CN/tetrabutylammonium perchlorate (0.1 M) showed that it underwent irreversible electrochemical reduction with a peak potential of −0.142 V (*vs.* SCE; scan rate 200 mV s^{-1}) suggesting that CMCS would be likely to oxidise iodide ion. The UV/visible spectrum of reaction mixtures, however, showed only very weak absorbance at wavelengths corresponding to iodine + tetrabutylammonium iodide in CD_3CN. This matter has not been pursued further.

A broadly similar pattern of behaviour was found for the reactions of methyl chlorosulfate (MCS) with tetrabutylammonium chloride and bromide under the same conditions (CD_3CN; 25 °C). Product analyses were probably less quantitatively reliable because of the volatility of methyl chloride (bp −24 °C) and methyl bromide (4 °C) but both were readily detected by nmr spectroscopy; the concentrations of residual MCS are believed to be accurate. The results (supplementary information Table S2 †) support the view that displaced chlorosulfate ions can give rise to additional chloride-substitution product. Moreover, when bromide was used, appreciable concentrations of methyl chloride were formed, just as dichloromethane appeared in reactions of CMCS with bromide ion. With iodide ion, methyl iodide is formed indicating that, unlike the situation with CMCS, iodide behaves as a simple nucleophile towards MCS (for which the peak reduction potential for irreversible reduction under the same conditions as for CMCS was −0.422 V *vs.* SCE). Reactions in which CMCS and MCS, both initially 0.30 M, were allowed to compete for a deficiency of tetrabutylammonium chloride or bromide showed that MCS is by far the more reactive (Table 6). Only when the nucleophile was present at a concentration such that essentially all the MCS was first consumed did the concentration of CMCS show any subsequent diminution.

Tetrabutylammonium acetate proved to be a rather disappointing nucleophile towards both CMCS and MCS under homogeneous conditions. Yields of substitution products were only 64% for CMCS with acetate (25 mol%) and 50% for MCS with 50 mol% acetate, even after prolonged reaction times. Again strong competition was provided by chloride ion, especially in the case of CMCS. Nevertheless the procedure provides a better route from CMCS to chloromethyl acetate than the two-phase procedure described in the report of Binderup and Hansen,[1] who obtained no product (see below).

Reactions in a two-phase system $CDCl_3/H_2O$. The behaviour of anionic nucleophiles (as their alkali-metal salts) towards CMCS was also studied in the two-phase system $CDCl_3/H_2O$, using tetraoctylammonium bromide (5% with respect to CMCS) as a phase-transfer catalyst. Samples of the organic layer were removed at intervals from the reaction mixtures and analysed quantitatively by ^1H nmr spectroscopy.

Potassium bromide appears to be a well-behaved nucleophile under these conditions in that CH_2BrCl was formed in close to quantitative yield in 3 h. Contamination of this product by CH_2Cl_2 was only serious in the case where the amount of KBr present was below one molar equivalent with respect to CMCS, and this then arose only in the late stages of the reaction when the bromide level had become low. Details are in the supplementary information (Table S3). † Competitive reactions using KBr and KCl indicated that relative reactivities were very similar. By contrast the attempt to generate chloromethyl acetate by using sodium acetate as the nucleophile under phase transfer conditions led to disappointing results (*cf.* ref. 1). At best, by using a twofold molar excess of sodium acetate over CMCS, the conversion of CMCS into the desired ester was only 24%, the major product being CH_2Cl_2. An important reason could be the protonation of acetate ions by acid generated by the interaction of displaced chlorosulfate ions with water. Yields of chloromethyl acetate were only slightly increased (to some 36%) by having a threefold excess of sodium bicarbonate with respect to CMCS in the aqueous phase. A contributory factor to the low ester yields was our use of tetraoctylammonium bromide as the phase-transfer catalyst, since bromide ions efficiently displaced chlorosulfate from CMCS and this in turn was transformed into chloride ion.

A similar pattern of reactivity was established for MCS under two-phase conditions, using KCl, KBr, KI and sodium acetate (25 mol% with respect to MCS) in the aqueous phase and tetraoctylammonium bromide (5% with respect to MCS) as the phase transfer catalyst. The results of product analyses are in the supplementary information (Table S4).† Yields of methyl bromide and methyl iodide were close to quantitative, but accompanied by methyl chloride in a large quantity despite its volatility. Acetate ion proved an ineffective nucleophile; although all the MCS was consumed, no chloromethyl acetate was detected, conversion being largely to methyl chloride.

Interestingly, the timescale for completion of two-phase reactions was an order of magnitude shorter for MCS than CMCS, and a series of competitive experiments established that the sequence of decreasing reactivity towards bromide ion was MCS > MBCS > CMCS. The substantial rate difference between MBCS and CMCS offers a method of enhancing the CMCS content of the product mixture from the standard preparative process; preferential reaction of MBCS with chloride ion in an aqueous wash generates CMCS, while over-reaction produces mainly the readily separable CH_2Cl_2. We have not attempted to optimise this procedure, but an example of the time variation of the composition of a reaction mixture in which MBCS is treated with KCl in the presence of a little tetraoctylammonium bromide is in Table 7.

Reaction of CMCS with sodium phenoxide. In addition to the quantitative conversion/time studies using halide and acetate anions, the reaction of CMCS with sodium phenoxide in tetrahydrofuran was examined preparatively with a view to studying the regiochemistry not only of CMCS but also of phenoxide ion, in particular whether alkylation of the aromatic nucleus might occur. The only identifiable product, isolated by distillation of the oily material obtained after work-up in 37% yield corresponded to $C_7H_7O_4SCl$, that is the product of substitution, not of chlorosulfate, but of chlorine by phenoxy in CMCS. This chloride displacement could have been by substitution of the C-bound Cl by phenoxide O, giving PhO–CH_2–OSO_2Cl, or by displacement of the S-bound Cl, giving PhO–SO_2–O–CH_2Cl. Of these two possibilities, we prefer the latter principally because of the close similarity of the chemical shifts of the methylene carbon (δ_C 76.56) and the attached protons (δ_H 5.81) to those of CMCS (77.32 and 5.96 ppm respectively). The alternative product has some structural similarity to MBCS for which the relevant methylene signals are found at 92.18 and 6.14 ppm. Thus the more polarisable phenoxide nucleophile appears to react preferentially at sulfur and in this regard is similar to amine nucleophiles.

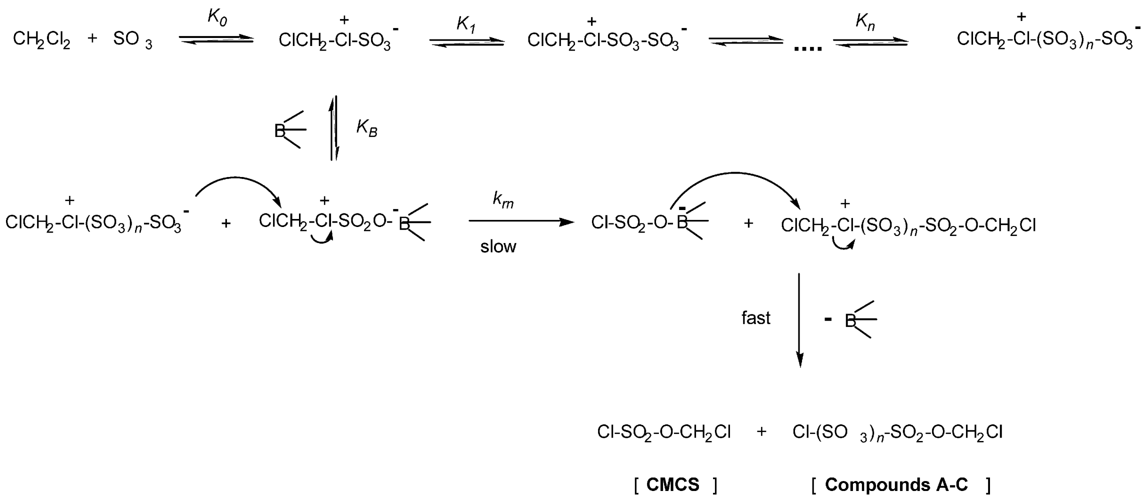
Discussion

Formation of CMCS

Dichloromethane reacts rather slowly with sulfur trioxide at room temperature, and it is evident that $B(OMe)_3$ catalyses the reaction giving rise to CMCS and MBCS in the proportion of roughly 2 : 1 when CH_2Cl_2 is in twofold excess over SO_3. We have no evidence of the nature of trimethyl borate when dissolved in SO_3, but our results make it clear that a true catalyst is present in that, on completion of the reaction, further addition of SO_3 to the reaction mixture leads to continued reaction with little diminution in activity. Sulfur trioxide exists in three modifications, α-, β- and γ-, of which the last is a low-melting, ice-like form (mp 16.8 °C) formed by condensation of the vapour at temperatures above 27 °C and generally believed to consist of a mixture of monomeric SO_3 together with lower oligomers, particularly the trimer.[11,15] In dilute solution in organic solvents such as carbon tetrachloride the monomeric form is claimed to predominate on the basis of infra-red spectroscopic evidence.[16] It may be noted that B-compounds are added commercially to stabilise γ-SO_3 in the liquid form by inhibiting SO_3-polymerisation initiated by nucleophiles such as water. We presume that it does this by competing with SO_3 to bind to the weakly nucleophilic end of the growing chain, thereby stopping further SO_3 attack. We believe that catalysis of CMCS formation also occurs as a result of the Lewis acidic character of the boron centre. Catalysis by $B(OMe)_3$ is not restricted to CMCS formation since, as we have shown, it also catalyses transformation of CMCS into MBCS.

Kinetics and mechanism of the trimethyl borate-catalysed reactions. In the present kinetic investigation, SO_3 was present in CH_2Cl_2 at concentrations at the upper limit of the range in which only monomeric SO_3 was detectable in CCl_4. In the absence of trimethyl borate the rate of formation of CMCS in such solutions is slow at room temperature and is negligible at −45 °C. The kinetic form of the consumption of CH_2Cl_2 at −45 °C is $v_{tot} = k_{tot}[B(OMe)_3][SO_3]^3$ with the order in CH_2Cl_2 uncertain, as is often the case where the solvent is also a reactant. The initial products appear to be CMCS and the metastable compounds A, B and C which, we have argued, contain more than one molecule of SO_3. Our observations on MBCS on the other hand indicate that this is a product of further sulfonation of CMCS. Since the pattern of behaviour that we have observed, both in the formation and reactions of CMCS and MBCS, does not suggest the involvement of radical species, we offer a polar interpretation of our findings on the catalysis by trimethyl borate, the formation and composition of the observed intermediates, and the kinetic form of the conversion of CH_2Cl_2 into CMCS (Scheme 2). This interpretation is based on the known, strongly electrophilic (Lewis acidic) nature of SO_3, the weaker Lewis acidity of $B(OMe)_3$ and the weak basicity of the chloro-substituents in CH_2Cl_2. We recognise that the interpretation is speculative, but we believe that Scheme 2 provides a self-consistent approach to understanding both the course and the kinetic features of this interesting reaction and designing future experiments.

Key features of the proposed mechanism are (i) the representation of the state of SO_3 in CH_2Cl_2 solution as a rapidly equilibrating mixture of complexes in which the solvent first binds a molecule of SO_3 by way of a Cl–S bond, further molecules then being attached by way of the sulfonate end; (ii) the formulation of the metastable species A, B and C as chloromethyl chloropolysulfates; and (iii) the catalytic role of trimethyl borate as a means of activating the CH_2Cl_2/SO_3 complexes towards nucleophilic attack at carbon by other complexes. Because SO_3 is such a powerful electrophile, we assume that it does not exist in the free state in solution to any significant degree; instead it is envisaged that polymeric forms of SO_3 complexed to CH_2Cl_2 are produced by rapid SO_3-transfer between the various complexes present in solution. The complexes are formulated as being chloronium species, a category of intermediates that is well-documented, particularly for cyclic structures, in which a chlorine lone pairs bind intramolecularly to a nearby carbocation centre,[17a] although more recently an example of an intermolecular attachment of an electrophile has been described.[17b] All the complexes are thought to interact with the boron-containing catalyst to varying degrees; for simplicity we represent only the interaction with the 1 : 1 complex in Scheme 2. This situation could explain the use of trimethyl borate as a stabiliser for the low-melting γ-form of SO_3, which on exposure to traces of water is prone to undergo polymerisation with transformation into the higher melting α- and β-forms. We offer no views on the structure of the catalytic species during the



Scheme 2 Proposed pathways to CMCS and compounds A–C.

course of the present reactions and use the noncommittal formalism $\mathrm{B}\!\lessdot$, nevertheless Scheme 2 represents a boron-containing entity as a true catalyst. The proposal that the metastable products A, B and C are chloro-polysulfates (chloropyrosulfates) is supported as follows. We have evidence that CMCS on treatment with SO_3 and $B(OMe)_3$ gives rise to two products each containing two molecules of SO_3; since the first, MBCS, is the product of insertion of SO_3 into the C–Cl bond of CMCS, it is not unreasonable that the second isomer should arise by insertion into the S–Cl bond. Analogous polysulfates have been implicated as transient intermediates in aromatic sulfonation by SO_3, reactions which show kinetic orders in SO_3 of two or more.[18]

On the basis of Scheme 2, assuming that all the Lewis acid/base equilibria are rapidly established, we can express the total concentration of SO_3 weighed into the reaction mixture by Eqn. (2), where, for simplicity, charges have been omitted from the representations of the species:

$$[\mathrm{SO_3}]_{\mathrm{tot}} = [\mathrm{SO_3}] + [\mathrm{ClCH_2ClSO_3}] + 2[\mathrm{ClCH_2ClSO_3SO_3}] + 3[\mathrm{ClCH_2ClSO_3SO_3SO_3}] + \ldots etc. \qquad (2)$$

$$= [\mathrm{ClCH_2ClSO_3}]\ \{1/K_0[\mathrm{CH_2Cl_2}] + 1 + 2K_1[\mathrm{ClCH_2ClSO_3}]/[\mathrm{CH_2Cl_2}] + 3K_2K_1[\mathrm{ClCH_2ClSO_3}]^2/[\mathrm{CH_2Cl_2}] + \ldots etc.\} \qquad (3)$$

If $K_0 >> 1$, the first term can be neglected, and provided that $[SO_3]_{tot}$ is small enough then Eqn. (4) applies.

$$[\mathrm{ClCH_2ClSO_3}] \approx [\mathrm{SO_3}]_{\mathrm{tot}} \qquad (4)$$

The rate-limiting step is taken to be the attack of $ClCH_2Cl^+SO_3(SO_3)_nSO_3^-$ on a complex of $ClCH_2Cl^+SO_3^-$ and the catalyst (rate constant k_{rn}) so that, bearing in mind that for $n = 0$ two molecules of CMCS result whereas for other values of n only one molecule is formed together with a molecule of compound A, B or C, the rate of conversion of CH_2Cl_2 into products is given by (Eqn. 5):

$$-\mathrm{d}[\mathrm{CH_2Cl_2}]/\mathrm{d}t = K_B[\mathrm{B}]\ \{2k_{r0}[\mathrm{ClCH_2ClSO_3}]^2 + K_1 k_{r1}[\mathrm{ClCH_2ClSO_3}]^3/[\mathrm{CH_2Cl_2}] + K_1K_2k_{r2}[\mathrm{ClCH_2ClSO_3}]^4/[\mathrm{CH_2Cl_2}]^2 + \ldots etc.\} \qquad (5)$$

From this expression it is evident that the observed order in SO_3 of the CMCS forming reaction is predicted to be 2 or greater depending on the relative magnitudes of the terms within the braces in (Eqn. 4). Analogous rate expressions can be derived for reactions involving attack of $ClCH_2Cl^+(SO_3)_nSO_3^-$ on complexes of the catalyst with $ClCH_2Cl^+(SO_3)_nSO_3^-$ ($n \neq 0$); these predict orders ≥3 in SO_3 and 1 in the catalyst. The apparent order in SO_3 on this basis will depend on the balance of reactivities of the various pathways, but our observed value around 3, together with the first order dependence on the catalyst, appears to be consistent with a multiplicity of reaction pathways of the type shown in Scheme 2.

A possible route to MBCS by consecutive sulfonation of CMCS consistent with the observation of its accelerating rate of formation in the initial stages of the reaction of SO_3 with CH_2Cl_2 can be formulated in an analogous fashion to Scheme 2 (supplementary information: Scheme S1 †). The significant intermediate here is the complex of SO_3 with CMCS *via* the carbon-bound chlorine atom. The alternative complexation using the sulfur-bound chlorine can give rise to compound A. What cannot be easily accommodated using reaction pathways of this type is the observation of substantial amounts of CH_2Cl_2 in the reaction of CMCS with SO_3. It could be that one of the intermediates postulated above, $\mathrm{ClSO_3B}\!\lessdot^-$, which is formally the adduct of chlorosulfate anion and the catalyst, may function in these reactions in a rather similar way to chlorosulfate ion generated by nucleophilic displacement from CMCS, providing or otherwise transferring a chloride ion to CMCS with formation of CH_2Cl_2 and regeneration of chlorosulfate. We have at this time no additional evidence to support or dismiss such a side reaction.

Reactions of CMCS, MCS and MBCS with nucleophiles. The reactions of CMCS with nucleophilic anions always seems to involve displacement of chlorosulfate. Although the use of bromide ion as the nucleophile results in substantial amounts of CH_2Cl_2 along with the CH_2BrCl, there is no evidence that this arises by displacement of Cl^- from the –O–SO_2–Cl group; the similarity of the excess yield of CH_2Cl_2 in reactions of chloride ion with CMCS in CD_3CN and the yield of CH_2Cl_2 in analogous reactions of bromide ion with CMCS appears to be solely a consequence of the formation of chloride ion from displaced chlorosulfate ions by transfer of SO_3 to the solvent. On the basis of the present observations, this transfer process in CD_3CN appears to be slow compared with the nucleophilic displacement at carbon. The same is unlikely to be true in water where SO_3 transfer is evidently very fast.[12] Relative reactivities of the halide ions towards CMCS in homogeneous solution in CD_3CN and in a two-phase ($CDCl_3/H_2O$) liquid system are in keeping with established patterns for nucleophilic displacements in dipolar aprotic and aqueous systems respectively. The success of acetate as a nucleophile in the homogeneous phase displacement of chlorosulfate from CMCS contrasts with the failure of the reaction in the two-phase system $CDCl_3/H_2O$. This is to be compared with the report of Binderup and Hansen,[1] who, under similar two-phase conditions, obtained yields of 64–80% of chloromethyl esters of pivalic, hexanoic, octanoic and benzoic acids, but no chloromethyl acetate. Presumably, in the partly aqueous conditions of the $CDCl_3/H_2O$ system, the nucleophilic reactivity of halide ions exceeds that of acetate ion, a situation that does not obtain in the dipolar aprotic solvent CD_3CN where acetate ions compete quite successfully with chloride.

Though anionic, phenoxide ion in tetrahydrofuran as solvent appears, on the basis of the only isolated product, to lead to substantial attack at the sulfur atom of CMCS with displacement of chloride ion. It should be noted, however, that, in reactions of methyl chlorosulfate with sodium 3-methylphenoxide in aqueous dioxan, the product is 3-methylanisole, indicating nucleophilic displacement of chlorosulfate in this case.[9a] Leaving aside the effect of the change of solvent, our present results indicate that the presence of the chloro-substituent on carbon in CMCS slows down nucleophilic attack (by halide ions) on carbon by some two orders of magnitude relative to MCS. The rate of nucleophilic attack on sulfur could be less affected by the chloro-substituent, making attack at sulfur by sodium phenoxide more likely in CMCS than in MCS. This situation is reminiscent of the behaviour of aniline towards ethyl chlorosulfate where products of displacement of chlorosulfate, mono- and di-ethylanilines, and products attributable to chloride displacement from sulfur, phenylsulfamic acids, have been reported.[19] Interestingly attack at sulfur seems to be favoured by tertiary bases such as pyridine.[20]

Finally, the trimethyl borate catalysed procedure for CMCS preparation, although rapid and clean, produces a substantial amount of MBCS; this is hydrolysed and the hydrolysis product discarded. In this investigation, competitive reactivity studies have demonstrated that MBCS is very much more reactive towards Cl^- than CMCS; the complete reactivity sequence is MCS > MBCS > CMCS >> CH_2Cl_2. It is evident therefore that, in the $B(OMe)_3$-catalysed preparative process for CMCS described in the Experimental, the yield of CMCS could be substantially improved if the standard procedure were modified by inclusion of an aqueous sodium chloride wash (in the presence of a phase-transfer catalyst) in place of the lengthy sodium carbonate wash in the work-up procedure prior to distillation.

Experimental

Safety

Because of the possibility of the formation of chloromethyl ether in the course of operations to prepare and study the reactions of CMCS, all operations were conducted in efficient fume hoods. In addition, personnel carried individual monitors that continuously sampled the atmosphere close to their faces with adsorption of organic compounds on Tenax®TA (supplied by Perkin Elmer, Seer Green, Buckinghamshire). The presence of chloromethyl ether in the adsorbate was checked periodically by thermal desorption (ATD400) and GC/mass spectrometry ("Turbomass"). None was detected.

Materials

Sulfur trioxide was distilled from fuming sulfuric acid (30% SO_3 by weight), to which had been added 10% potassium persulfate, using an air condenser (condensation temperature 42 °C). For the kinetic experiments, it was collected in previously weighed vessels containing CH_2Cl_2. Ground glass surfaces were avoided since these seemed to catalyse a reaction between the two components. Dichloromethane (100 cm^3) was washed three times with concentrated sulfuric acid (10 cm^3), then with water (10 cm^3), followed by 10% aqueous sodium hydrogen carbonate (10 cm^3) and a further portion of water (10 cm^3). After drying over calcium chloride, it was distilled from calcium hydride. Trimethyl borate was a commercial sample used without further purification. All salts were commercial samples of the highest available purity, dried and stored in a desiccator before use. Acetonitrile (HPLC grade) and CD_3CN were passed through a short column of activated alumina immediately prior to use in the nucleophilic reactions and for electrochemical measurements. Deuterochloroform was used as received.

Nmr spectrometers

Most measurements were made at 250 MHz on a Bruker AC 250 spectrometer. Some additional measurements were made at 300 and 200 MHz using respectively Varian Gemini 300 and Bruker AC 200 instruments.

Reaction of dichloromethane with sulfur trioxide

Sulfur trioxide (196.8 g; 2.46 mol) was added dropwise over 100 minutes to premixed dichloromethane (418.4 g; 4.93 mol) and trimethyl borate (0.2 g; 1.92 mmol) keeping the temperature between 20 and 30 °C. The reaction was rapid and produced a dark brown colouration. After allowing the reaction mixture to stand at ambient temperature for 10 minutes it was quenched by adding it slowly to cold water (400 g) containing sodium carbonate (47.8 g) and a little tetrabutylammonium hydrogen sulfate (3.0 g). The mixture was stirred for 90 min until CO_2evolution had completely stopped. The dichloromethane layer was then separated, dried with $MgSO_4$ and CH_2Cl_2 removed under reduced pressure, yielding crude CMCS (223 g). Distillation of the crude product under reduced pressure gave CMCS (136 g; 33% of theoretical) as a dense colourless liquid, bp 85–89 °C/76 mm Hg. Analysis: found C 7.21, H 1.17, Cl 42.8, S 19.2%; $CH_2Cl_2SO_3$ requires C 7.28, H 1.22, Cl 42.98, S 19.43%. Nmr: $\delta_H = 5.01$ in $(CD_3)_2CO$; $\delta_H = 5.96$, $\delta_C = 77.32$ in $CDCl_3$. Higher boiling fractions contained further CMCS but were contaminated with MBCS, detectable by nmr spectroscopy ($\delta_H = 5.20$ in $(CD_3)_2CO$; see below).

Methylene bis(chlorosulfate) (MBCS)

Trimethyl borate (20 μl; 0.18 mmol) was syringed into a mixture of CMCS (21.2 g; 0.129 mole) and sulfur trioxide (16.3 g; 0.203 mole) at 0 °C. An exothermic reaction took place immediately. When this subsided, the reaction mixture was left at room temperature for 30 min. After quenching the mixture with ice (50 g), CH_2Cl_2 (50 cm^3) was added, the organic layer separated and washed three times with water (60 cm^3) and dried ($MgSO_4$). Removal of the solvent followed by distillation under vacuum afforded MBCS (41% yield), bp 86 °C/9 mm Hg. Analysis: found C 5.1, H 0.90, Cl 28.4, S 25.3%; $CH_2O_6S_2Cl_2$ requires C 4.9, H 0.82, Cl 28.9, S 26.2%. Nmr spectra: δ_H 6.14 (200 MHz in $CDCl_3$/TMS); δ_C 92.18 (300 MHz in $CDCl_3$/TMS). CIMS: found 261.90177; [M + CH_4] requires 261.90136.

Methyl chlorosulfate

In a three-necked flask equipped with an argon gas inlet, dropping funnel and drying tube and cooled to −78 °C was placed methanol (8.00 g; 0.25 mol). Sulfuryl chloride (33.74 g; 0.25 mol) was added dropwise over 60 min, the stream of argon agitating the solution and carrying away the HCl produced. After completion of the addition, the flask was allowed to warm up to 0 °C and the reaction mixture quenched by the addition of ice water. Separation of the organic layer and two further washings with ice water gave the product, which was dried ($MgSO_4$) and distilled under vacuum. Yield 9.58 g (29%), bp 48–49 °C/22 mm Hg. Nmr spectra: δ_H 4.21 (200 MHz in $CDCl_3$/TMS); δ_C 61.14 (300 MHz in $CDCl_3$/TMS).

Reactions of CMCS, MCS and MBCS with anionic nucleophiles

For reactions in homogeneous solution stock solutions were prepared containing CMCS or MCS (7.5 mmol), internal standard (1,2-dimethoxyethane or 1,2-dichloroethane; 1.5 mmol) and made up to 25 cm^3 by addition of CD_3CN at 25 °C.

Aliquots of these solutions (1.5 cm^3) were then added to weighed amounts of quaternary ammonium salts in nmr tubes and thoroughly mixed (t = 0). ^{1}H nmr spectra were then recorded at intervals.

For reactions in the $CDCl_3/H_2O$ two phase system, stock solutions of CMCS, MBCS or MCS together with the same internal standards in $CDCl_3$ were prepared with concentrations as specified above. Weighed amounts of the salt of the nucleophile together with tetraoctylammonium bromide (5 mol% with respect to the organic chlorosulfate) were placed in a small flask together with water (5 cm^3) and equilibrated at 25 °C. An aliquot of the $CDCl_3$ solution (5 cm^3) was added with vigorous magnetic stirring (t = 0) and the spectrum of the organic layer recorded at appropriate intervals.

Reaction of CMCS with sodium phenoxide

Phenol (5.08 g) was added to tetrahydrofuran (20 cm^3) containing sodium hydride (7.3 g of a 60% dispersion in oil, prewashed with cyclohexane) under a positive pressure of argon. After hydrogen evolution had ceased, a solution of CMCS (17.86 g) in tetrahydrofuran (20 cm^3) was added dropwise at room temperature over a period of one hour and the mixture allowed to stir overnight. The reaction mixture was then diluted with ethyl acetate and the insoluble salts removed by centrifugation and then filtration. Removal of the solvent left a gelatinous material that was redissolved in ethyl acetate, the solution washed with water and dried ($MgSO_4$). Rotary evaporation left a red oil (8.96 g), TLC of which showed two spots, one corresponding to phenol and the other to the product, the R_f-value of which was close to that of CMCS. Vacuum distillation of the oil afforded phenoxymethyl chlorosulfate (4.37 g; 37% yield) bp128 °C/9 mm Hg as a colourless oil. Analysis: found, C 37.9, H 3.2, S 14.2, Cl 16.4%; $C_7H_7O_4SCl$ requires C 37.8, H 3.2, S 14.4, Cl 15.9%. Mass spectrum: accurate mass: found, 221.97544; calculated, 221.97536; fragmentation 222 (M^+), 187 (– Cl), 107 (– SO_3), 93 (– CH_2), [77 (– CH_2O)]. Nmr spectra (300 MHz/ $CDCl_3$): δ_H 5.81 (s; 2H), 7.21–7.43(m; 5H): δ_C 76.55, 121.32, 128.02, 130.20, 150.26 ppm.

Cyclic voltammetry

Cyclic voltammograms were recorded on solutions of CMCS (1.06 mM), MBCS (3.0 mM) or MCS (5.9 mM) in CH_3CN containing tetrabutylammonium perchlorate (0.1 M) at room temperature using a platinum working electrode (1 mm diameter), a coil of platinum wire as counter electrode and a saturated calomel electrode as reference. The electrode system was controlled by an EcoChemie PGSTAT20 combined waveform generator/potentiostat.

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