A Facile Synthesis of Sulfoxides by Oxidation of Sulfides with Sodium Bromite in an Aprotic Solvent in the Presence of Clay Minerals

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Synopsis. The title oxidation has been performed in dichloromethane in the presence of "wet"-montmorillonite and -kaolin. The substrates studied include dialkyl, alkyl aryl, diaryl, and cyclic sulfides, which give the corresponding sulfoxides in good yields under neutral and mild conditions.

Sulfoxide synthesis is a reaction of wide scope and has been the subject of considerable research,[1] partly due to the importance of a sulfoxide as a reaction intermediate in organic chemistry. Among these, the oxidation of a sulfide has been frequently used for this purpose owing to its easy accessibility.[2—4]

Recent success in isolating sodium bromite as a stable high-purity solid has developed its application to organic synthesis.[5] However, the reaction with sodium bromite in a water-free solvent has been only little investigated, compared with routine reactions under aqueous conditions.[5] This is because of the negligible solubility of sodium bromite in organic solvents except for lower alcohols. In the course of studies on the oxidation in an aprotic solvent, we have observed that inorganic supports serve as highly reactive sites for certain reagents in the oxidative transformation of various functional groups.[6—12] This led us to prospect the utility of sodium bromite for organic synthesis in an aprotic solvent in conjunction with clay minerals. We now present a facile and convenient synthesis of sulfoxides by means of the oxidation of sulfides with sodium bromite in dichloromethane in the presence of such clay minerals as montmorillonite and kaolin.

Results and Discussion

A cloudy mixture of a sulfide, sodium bromite trihydrate (hereafter referred simply as sodium bromite or $NaBrO_2$), and a clay mineral in an aprotic solvent was magnetically stirred under an inert atmosphere. The progress of reaction was readily followed by a GLC analysis of the supernatant. Effective stirring of the heterogeneous mixture is essential to ensure a smooth reaction and to obtain reproducible results. After complete consumption of a sulfide, filtration and washing of the residue with dichloromethane, followed by removal of the solvent, left the sulfoxide slightly contaminated with the corresponding sulfone.

One should be alerted to the complexity of the oxidation of a sulfide as well as appreciable side reactions characteristic of the halide oxidations, e.g. carbon–sulfur bond fission,[13] carbon–halogen bond formation,[14] aromatic halogenation.[15] Thus, the influence of the reaction conditions on the yield and selectivity of a sulfoxide was initially investigated.

Although the presence of a commercial clay mineral was essential for the reaction, it was sluggish, resulting only in the poor formation of a sulfoxide. While in the presence of a "wet"-clay mineral, a sulfide underwent smooth oxidation, selectively giving the corresponding sulfoxide. For example, upon the treatment of methyl phenyl sulfide (**1**) with sodium bromite ($[\mathbf{1}]/[NaBrO_2]$ $=0.8$; mole ratio) in dichloromethane at room temperature for 15 min, **1** was completely consumed and a mixture of methyl phenyl sulfoxide (**2**) (97%) and methyl phenyl sulfone (**3**) (3%; GLC selectivity) was formed in the presence of "wet"-montmorillonite (see the Experimental section); however, only 25% of **1** was converted with commercial montmorillonite under comparable conditions. Thus, the "wet"-clay mineral serves as a reactive site for $NaBrO_2$, playing an important role in facilitating the reaction in the aprotic solvent. However, a "wet"-montmorillonite with a greater or less water content than that indicated in Experimental has exhibited the inferior selectivity of the sulfoxide.

The effect of the solvent was then investigated in the presence of "wet"-montmorillonite. The reaction was strongly dependent on the solvent used. Among a variety of solvents examined (acetonitrile, tetrahydrofuran, acetone, benzene, ethyl acetate, hexane, ether, dichloromethane, chloroform, and carbon tetrachloride), only dichloromethane afforded a satisfactory result; that is, **1** was completely consumed and **2** was selectively formed (97%), along with only a minor amount of **3** (3%).

The effect of the temperature was also examined in the range of 0 °C—reflux temperature in dichloromethane. While the conversion of **1** was low (36%, 15 min) at 0 °C ($[NaBrO_2]/[\mathbf{1}]=0.8$), it increased with an elevation of the reaction temperature; at about 20—25 °C, **1** was completely consumed, and a highly selective formation of sulfoxide **2** (97%) was observed. However, a further elevation of the temperature resulted in an incomplete consumption of **1**, possibly due to an unproductive decomposition of sodium bromite.

Based on the results described above, the oxidation of various sulfides was conducted in dichloromethane in the presence of "wet"-montmorillonite at room temperature. The other reaction variables (the concentration of $NaBrO_2$ and reaction time) were determined on the basis of the reactivity of a sulfide and the selectivity of a sulfoxide. The results are summarized in Table 1. The aromatic ring (Entries 1—14), the allylic double bond (Entries 15 and 16), and the heterocyclic ring (Entries 29 and 30) were found to be intact under the reaction conditions employed. Interestingly, the influence of the electronic nature of the substituents on the

Table 1. Oxidation of Sulfides with Sodium Bromite in Dichloromethane in the Presence of "Wet"-Clay Minerals[a]

Entry No.	Sulfides	$[NaBrO_2]$[b] mmol	Time min	Sulfoxides[c] %	Solvents[d]
1	PhSMe	0.8	15	78	HE/EA (2:1)
2		[1.0]	[30]	[80]	
3	*p*-$MeOC_6H_4SMe$	0.7	15	70	HE/EA (1:1)
4		[0.8]	[30]	[82]	
5	*p*-MeC_6H_4SMe	0.8	30	86	HE/EA (3:2)
6		[0.8]	[30]	[82]	
7	*p*-BrC_6H_4SMe	0.7	15	75	HE/EA (3:2)
8		[0.6]	[15]	[82]	
9	*p*-$NO_2C_6H_4SMe$	1.0	60	71	DM
10		[1.1]	[60]	[72]	
11	Ph_2S	1.4	180	73	HE/EA (2:1)
12		[2.5]	[120]	[79]	
13	$(PhCH_2)_2S$	1.0	90	74	EtOH[e]
14		[0.7]	[90]	[80]	
15	$(CH_2CH{=}CH_2)_2S$	0.8	15	54	HE/EA (3:2)
16		[0.7]	[45]	[51]	
17	(*n*-C_8H_{17})SMe	0.7	15	70	HE/EA (7:3)
18		[0.8]	[30]	[73]	
19	(*n*-$C_6H_{13})_2S$	0.8	30	78	HE/EA (7:3)
20		[0.8]	[60]	[89]	
21	(*n*-Bu)$_2$S	0.8	15	78	HE/ET (1:1)
22		[0.8]	[60]	[74]	
23	(*s*-Bu)$_2$S	0.8	15	74	HE/EA (1:1)
24		[0.8]	[30]	[78]	
25	(*n*-Pr)$_2$S	0.7	15	80	HE/EA (3:2)
26		[0.8]	[30]	[82]	
27	(*i*-Pr)$_2$S	0.6	15	80	HE/EA (3:2)
28		[0.8]	[30]	[79]	
29	Tetrahydrothiophene	0.7	15	74	EA
30		[0.6]	[30]	[80]	

a) Under argon and at room temperature; 1 mmol of a sulfide, 1.0 g of a "wet"-montmorillonite, and 5 cm^3 (6 cm^3 in the cases of Entries 9 and 10) of CH_2Cl_2 were used in every run. For the oxidation using "wet"-kaolin (1.0 g), the reaction conditions and yields of the sulfoxides are indicated in square parentheses. b) Sodium bromite trihydrate was used. c) Isolated yields. d) Developing solvents used for the isolation of the sulfoxides by chromatography; numbers in parentheses are the mixture ratios of the solvents, where abbreviations, HE, EA, DM, and ET, stand for hexane, ethyl acetate, dichloromethane, and ether, respectively. e) Isolated by recrystallization from ethanol.

benzene ring or the carbon-chain length of the alkyl groups is small, and there was no appreciable difference in the yield of the sulfoxides. Oxidation in the presence of "wet"-kaolin, instead of "wet"-montmorillonite, in dichloromethane afforded a comparable or slightly superior yield of the sulfoxides, although, in general, a longer reaction time and a slightly larger amount of sodium bromite were required to complete the reaction.

Incidentally, other related halide species, $NaBrO_3$, $NaClO_2$, $NaClO_3$, $NaIO_3$, and $NaIO_4$, were found to be unattractive for sulfoxide synthesis; even when **1** was treated with these reagents in dichloromethane in the presence of "wet"-montmorillonite under more vigorous conditions (with 1.5 moles of the reagent per mole of **1**, under reflux, and for 2 h) than those of Entry 1, no reaction occurred.

In summary, the oxidation of sulfides with sodium bromite/"wet"-clay mineral systems in dichloromethane readily afforded sulfoxides in good yields within a reasonable period of time. All of the reagents used are inexpensive and safe to handle, and the reactions can be carried out under mild conditions. The system could be treated just like a clay-supported reagent,[16] permitting a facile isolation of sulfoxides. However, it should be noted that the present system requires no laborious preparation of a supported reagent, thus allowing an extended application of this procedure to such a thermally labile oxidant as sodium bromite. Thus, the present system may offer an improved alternative for a clay-supported reagent. The scope and utility of sodium bromite with the aid of an inorganic support for organic synthesis in an aprotic solvent is currently being extended in our laboratory.

Experimental

^{1}H NMR spectra were measured with a JEOL PMX-60 spectrometer for solutions in carbon tetrachloride or deuteriochloroform. IR spectra were recorded for thin films (neat) or KBr disks on a JASCO A-100 spectrophotometer. GLC was carried out on a Shimadzu GC-4C instrument with a 2 m column packed with 1.5% Silicone OV-17 on Shimalite WAW-DMCS, with temperature programming.

Starting Materials. All sulfides and clay minerals are commercially available and were used without purification. The purities of the former reagents were checked by GLC. Sodium bromite trihydrate was a gift from Nippon Silica Industrial Co., Ltd. Dichloromethane was dried over calcium chloride and fractionally distilled.17) The other solvents were purified according to methods described in the literature.18) The "wet"-clay mineral was prepared by adding distilled water (0.8 g) in portions to a commercial clay mineral (20 g), and by vigorous shaking of the mixture upon every addition for a few minutes until a free-flowing powder was obtained.

Oxidation Procedure. The following procedure is representative. To a cloudy slurry of "wet"-montmorillonite (1.0 g) and finely ground sodium bromite trihydrate (0.8 mmol) in dichloromethane (5 cm^3; 6 cm^3 of the solvent was used in the case of methyl *p*-nitrophenyl sulfide, owing to relatively low solubility of the sulfide) in a round-bottomed flask was added methyl phenyl sulfide (1 mmol) in a portion. The flask was flushed with dry argon and then capped with either a glass stopper or a silicone rubber septum, through which the supernatant was withdrawn by a microsyringe at intervals in order to follow the reaction. After magnetic stirring for 15 min at room temperature, the whole mixture was transferred onto a Pyrex Buchner funnel with a fritted glass disk; the product was thoroughly eluted with dichloromethane (required ca. 100 cm^3). Rotary evaporation of the combined clear solvent in vacuo left methyl phenyl sulfoxide contaminated slightly with methyl phenyl sulfone. Chromatography on silica gel (hexane–ethyl acetate; 2 : 1 by volume) gave 78% of pure (by GLC) methyl phenyl sulfoxide.

The sulfoxides, except for dibenzyl sulfoxide, thus obtained, were identified by a comparison of their NMR and IR spectra, as well as the GLC retention times with those of authentic samples prepared independently. Dibenzyl sulfoxide was isolated by recrystallization of a crude product from ethanol; mp 135 °C (lit:19) 134—135 °C).

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