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A Convenient Synthesis of Sulfones by the Oxone Oxidation of Sulfides in an Aprotic Solvent in the Presence of Clay Minerals

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Synopsis. The title oxidation in dichloromethane in the presence of "wet"-montmorillonite and -kaolin afforded the corresponding sulfones in excellent to almost quantitative yield under neutral and mild conditions.

Sulfones are an important intermediate in organic synthesis and, thus, a large number of types of reactions have been developed.[1)] Among these, oxidative procedures have been readily accessible and there have been ample methods for this objective.[2)] However, there is still a need for effective, inexpensive, and manipulatively secure and simple methods that are performable under mild conditions.

Recently, Oxone[3)] has attracted considerable interest because of its versatility as an oxygen-donor for Baeyer–Villiger-type lactonization,[4)] the epoxidation of olefins,[5)] and the oxidation of sulfides to sulfoxides[6)] and sulfones.[4,7)] However, Oxone chemistry in a water-free solvent has been hardly explored compared with routine oxidation under aqueous conditions.[4—7)] In the course of studies on Oxone oxidation in non-aqueous media,[8)] we have disclosed that a montmorillonite clay serves as a highly reactive site for Oxone in the oxidation of sulfides to the sulfones,[8c)] which prompted us to search for an initiative and extensive application of various clay minerals for organic synthesis. This paper describes the oxidation of sulfides with Oxone in an aprotic solvent in the presence of such clay minerals as montmorillonite and kaolin, since the reaction offers a facile synthesis of sulfones, the results of which are comparable to chemoselective oxidation under aqueous conditions.[7)]

Results and Discussion

The oxidation of sulfides with Oxone in an aprotic solvent was carried out in an inert atmosphere in order to avoid autoxidation. A product study by GLC showed that in addition to a sulfoxide as an incipient product, the sulfone was concomitantly formed, even during the early stage of the reaction. It has been generally accepted that the priority of the formation of a sulfoxide or a sulfone depends on the concentration of the oxidant, as is typically observed in peroxy acid oxidations.[2)] In view of an analogous property of Oxone to peroxy acids,[4)] the effect of the concentration of Oxone on the selectivity of the products, **2** and **3**, in the oxidation of methyl phenyl sulfide (**1**) was examined. Upon treatment of **1** with one equiv of Oxone in dichloromethane (DM) at room temperature for 24 h, a mixture of **2** (40%) and **3** (18%) was formed, even though a considerable amount of **1** (42%; by GLC) still remained. The failure of the selective formation of **2** can be explained in terms of a relatively high susceptibility of **2** to a further oxidation to **3**; this phenomenon is distinctly in contrast with peroxy acid and periodate oxidations,[2)] where step 2 is much slower than step 1. Consequently, our interest has been focused on a selective and facile synthesis of the sulfones. To determine favorable conditions for the formation of a sulfone, the effects of the reaction variables on the reactivity of a sulfide, as well as on the selectivity and the yield of the sulfone, were initially investigated.

$$\underset{\mathbf{1}}{\mathrm{PhSMe}} \xrightarrow{\text{Step 1}} \underset{\mathbf{2}}{\mathrm{PhSOMe}} \xrightarrow{\text{Step 2}} \underset{\mathbf{3}}{\mathrm{PhSO_2Me}}$$

In the absence or presence of a commercial "dry"-clay mineral, the oxidation of a sulfide was considerably slow, giving a mixture of the sulfoxide and the sulfone. Indeed, the oxidation of **1** ([Oxone]/[**1**]=2.5; mole ratio) in DM at room temperature for 24 h in the absence or presence of a commercial montmorillonite gave 50 or 44% of **2** and 27 or 56% of **3**, respectively (by GLC); 23% of **1** remained in the former case. Whilst in the presence of "wet"-montmorillonite (see Experimental) **1** was completely consumed, even within 2 h under comparable conditions, solely giving **3**. These results indicate that "wet"-montmorillonite plays an important role in facilitating the oxidation. The use of a greater or less amount of "wet"-montmorillonite and of a reagent with a greater or smaller water content than that indicated in the Experimental section resulted in an inferior yield of the sulfone.

The effect of solvents was then examined in the presence of "wet"-montmorillonite. The reactivity of a sulfide was not so affected by the solvents, but the product distribution was strongly dependent on the solvents. For example, upon the oxidation of **1** in benzene, DM, and tetrahydrofuran at room temperature for 2 h ([Oxone]/[**1**]=2.5), **3** was selectively formed; **3** could be isolated in 92, 98, and 95% yields, respectively. Mixtures of **2** and **3**, however, were formed in other solvents in varying ratios: viz., in hexane, $CHCl_3$, CCl_4, ether, AcOEt, MeCN, and acetone, 88, 61, 90, 87, 89, 75, and 94% of **3**, along with 12, 39, 10, 13, 11, 25, and 6% of **2** were formed (by GLC), respectively.

The electronic effect of a ring substituent on the reactivity of a sulfide was also examined in the oxidation of the methyl phenyl sulfides. The time dependence of the product distribution in the oxidation of **1**, and the consumption curves of **1** and the *p*-MeO (**4**) and *p*-NO_2 derivatives, are illustrated in Fig. 1. The apparent reactivity order of the sulfides could be related to the electron-donating property of *para*-substituents, viz. MeO>H>NO_2, as observed in peroxy acid oxidations.[2b)] The conversion of sulfoxide (**5**) to the sulfone (**6**) was also faster than that of **7** to **8**; the reaction of

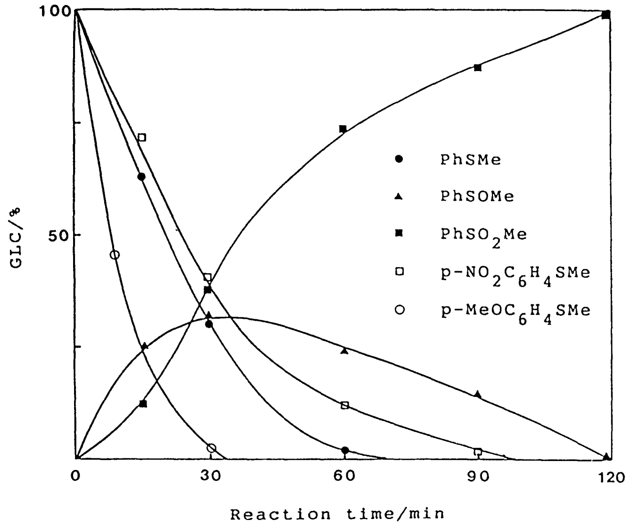

Fig. 1. Conversions and products distribution vs. reaction time in the oxidation of the methyl phenyl sulfides; reaction conditions are identical to those indicated in the oxidation procedure (see the Experimental section).

p-$\mathrm{MeOC_6H_4SOMe}$ (**5**) *p*-$\mathrm{MeOC_6H_4SO_2Me}$ (**6**)

p-$\mathrm{NO_2C_6H_4SOMe}$ (**7**) *p*-$\mathrm{NO_2C_6H_4SO_2Me}$ (**8**)

Table 1. Oxidation of Sulfides with an Oxone–"Wet"-Kaolin System[a)]

Entry No.	Sulfides	Time h	Eluents	Sulfones[b)] %
1	PhSMe	4	$\mathrm{CH_2Cl_2}$	97
2	*p*-$\mathrm{MeOC_6H_4SMe}$	3	AcOEt	99
3	*p*-$\mathrm{MeC_6H_4SMe}$	4	AcOEt	99
4	*p*-$\mathrm{BrC_6H_4SMe}$	5	$\mathrm{CH_2Cl_2}$	98
5	*p*-$\mathrm{NO_2C_6H_4SMe}$	4	AcOEt	96
6[c)]	PhSPh	24	AcOEt	75
7[c,d)]		3	AcOEt	90
8[c)]	$\mathrm{(PhCH_2)_2S}$	10	AcOEt	96
9	$\mathrm{(Allyl)_2S}$	3	$\mathrm{CH_2Cl_2}$	99
10[c)]	$\mathrm{(Octyl)_2S}$	10	$\mathrm{CH_2Cl_2}$	99
11	(Octyl)SMe	5	$\mathrm{CH_2Cl_2}$	99
12	$\mathrm{(Hexyl)_2S}$	5.5	$\mathrm{CH_2Cl_2}$	99
13	BuSBu	5	$\mathrm{CH_2Cl_2}$	97
14	(*s*-Bu)$_2$S	5	$\mathrm{CH_2Cl_2}$	98
15	(*t*-Bu)$_2$S	3	$\mathrm{CH_2Cl_2}$	95
16	PrSPr	4	$\mathrm{CH_2Cl_2}$	98
17	$\mathrm{(Isopropyl)_2S}$	4	$\mathrm{CH_2Cl_2}$	97
18	Tetrahydrothiophene	1	$\mathrm{CHCl_3}$	97

a) Under argon and under reflux; 1 mmol of sulfide, 1.2 g of "wet"-kaolin, 7 cm^3 of $\mathrm{CH_2Cl_2}$, and ca. 100 cm^3 of an eluent were used in every run; [Oxone]/[Sulfide]=2.5 (mole ratio). b) Isolated yields. c) [Oxone]/[Sulfide] =3.0 (mole ratio). d) In benzene (6 cm^3) at 333 K.

4 was thus completed in a shorter period.

Based on the data described above, a synthetic reaction of sulfones was performed at room to reflux temperature in DM in the presence of "wet"-montmorillonite. Using 2.5 moles of Oxone per mole of a sulfide is recommended, since the reaction with two equiv or with a slightly greater amount of Oxone is rather slow. It should be noted that efficient stirring is essential to ensure a smooth oxidation and also to obtain a reproducible result. Under these conditions, the reactions were completed in one to several hours and there was no detectable amount of by-products, giving pure sulfones in usually better than 90% yields.[8c)] In order to obtain a high yield of the sulfones, an appropriate choice of an eluent is necessary (see also the forth column in Table 1), since the yield of a sulfone strongly depends on the eluent used. Indeed, **8** was isolated in 70, 60, 67, 96, and 91% yields when DM, ether, $\mathrm{CHCl_3}$, AcOEt, and acetone were used as eluents, respectively.

The oxidation of sulfides was also carried out in the presence of "wet"-kaolin in DM in a manner similar to that with an Oxone–"wet"-montmorillonite system, except that the reaction was conducted at an elevated temperature (reflux) and for a longer period, since the efficiency of kaolin is slightly inferior to that using montmorillonite. The results are presented in Table 1. The aromatic-ring (Entries 1—8) and the heterocyclic-ring (Entry 18), as well as the allylic double bond (Entry 9) were found to be intact, leading to a selective formation of the sulfones in excellent yields. The electronic effect of the substituents on the benzene-ring regarding the yield of the sulfones was small (Entries 1—5); they afforded almost quantitative yields of the sulfones. In all instances, some differences in the concentration of Oxone and the reaction times could be mainly ascribed to a difference in the reactivity of the sulfides. Although diphenyl sulfide showed an exceptionally low reactivity in DM (Entry 6), which gave only 75% of the sulfone (**9**), along with 22% of the sulfoxide, the reaction in benzene at 333 K for 3 h exclusively yielded **9** in 90% yield (Entry 7).

The present system is closely related to a conventional clay-supported reagent[9)] in the sense that the reaction should be considered to occur on an external surface and/or in an interlayer of a clay mineral, because of the negligible solubility of Oxone in organic solvents, although a relative significance of the phases is obscure. Since the present purpose was synthetic, clear information concerning the observed effects of water and solvents on the reactivity of the sulfides and of the eluents on the yield of sulfones has not yet been obtained. It is well known[9,10)] that in addition to water, inorganic as well as organic molecules are adsorbed on a clay surface, and the resultant swelling of the clay, complexation of the clay with these species etc. exert a modified activity of the clay and/or a specific product selectivity. The present reaction may be affected by diverse combinations of possible interactions of a clay with Oxone, a sulfide and/or a sulfone, as well as a solvent (or an eluent), the elucidation of which would provide a satisfactory explanation for the results.

In summary, the oxidation of sulfides with Oxone–"wet"-clay mineral systems in dichloromethane efficiently afforded sulfones in excellent yields. All of the reagents used are inexpensive and safe to handle, and the reaction is fairly clean. The system can be treated just like a clay-supported reagent and, thus, the procedures for isolating the sulfones are facile; it can be emphasized, however, that the reaction is performable instantly without any preparation of a supported reagent. The present system thus constitutes an improved version not only of a clay-supported reagent, but of the previous method under aqueous conditions,[7] owing to there being no need to buffer the reaction medium or to carry out tedious work-up procedures. An estimation of the scope and limitations of the systems for organic synthesis is now being undertaken.

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-4CM instrument with a 2 m column packed with Silicone OV-17 on Shimalite WAW-DMCS, with temperature programming.

Starting Materials. All sulfides are commercially available and were used without purification. Oxone and clay minerals are also commercially available. The solvents were rigorously dried and distilled. The "wet"-clay mineral was prepared by adding distilled water (2 g) in eight portions to a commercial clay mineral (10 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 typical procedure is as follows. To a cloudy slurry of "wet"-montmorillonite (1.2 g) and Oxone (2.5 moles of a sulfide) in dichloromethane (6 cm^3; 7 cm^3 of the solvent was used in the case of "wet"-kaolin) in a round-bottommed 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 silicon-rubber septum, through which the supernatant was withdrawn by a microsyringe at intervals in order to follow the progress of the reaction. After magnetic stirring for 2 h 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 pure (100% by GLC) methyl phenyl sulfone.

The sulfones, thus prepared, had satisfactory purities (over 98%) and were identified by their NMR and IR spectra, as well as the GLC retention times with those of authentic samples.

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