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Research Article

Oxidation of sulfur compounds by *o*-xylylenebis (triphenylphosphonium peroxymosulfate) as a mild, selective and regenerable oxidant

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ABSTRACT

O-Xylylenebis(triphenylphosphonium peroxymosulfate) could be used for selective oxidation of sulfides and thiols to their corresponding sulfoxides and disulfides under nonaqueous and aprotic conditions without catalyst. Selective oxidation of thiols in the presence of sulfides at room temperature is also achieved with this reagent. The advantages of OXBTPPPMS are generality, high yield and selectivity, short reaction time and low cost.

Keywords: Sulfide; Sulfoxide; Selective oxidation; *o*-Xylylenebis(triphenylphosphonium peroxymosulfate)

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Introduction

Sulfur compounds are among the most versatile and reactive molecules in organic and bioinorganic chemistry. Their oxidation chemistry has attracted considerable attention due to its crucial role in the synthesis of pharmaceuticals, agrochemicals, fine chemicals, and in biological redox processes. Compounds such as thioethers (sulfides), thiols, and disulfides are widely present in natural and synthetic systems, and their controlled oxidation leads to sulfoxides or sulfones valuable intermediates with distinct physicochemical and biological properties. The oxidation of sulfides to sulfoxides and thiols to disulfides represents a fundamental transformation in sulfur chemistry. Sulfoxides are highly polarized molecules that exhibit stereochemical and electronic characteristics exploitable in asymmetric synthesis, drug design, and catalysis. Disulfides, on the other hand, play a critical role in biochemical systems; their reversible oxidation-reduction cycles modulate protein folding, enzymatic

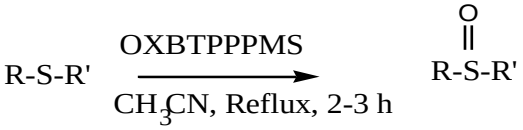
activity, and redox signaling in cellular environments. Understanding and controlling the oxidation pathways of sulfur compounds are therefore essential for both synthetic and biological applications [1-7].

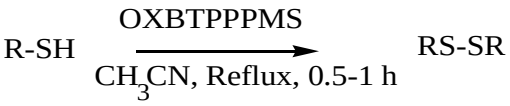
Several methods based on oxidative S-S coupling have already been reported [8-17]. Some of these methods suffer from disadvantages such as long reaction times, limited availability of oxidant, toxicity of reagents and isolation of products. Therefore, the introduction of readily available, safe and stable reagents for oxidation of thiols to disulfides is still a necessity.

On the other hand, the oxidation of sulfides to sulfoxides is the most straightforward synthetic route to the latter, and numerous reagents and oxidative procedures are available for this transformation. However, many of them cause over oxidation to the corresponsing sulfones. Therefore, control of the reaction conditions, that is, time, temperature and the relative amount of oxidants, plays an important role in avoiding the formation of oxidation side products, but this is often hard to achieve and therefore there is still considerable interest in the development of selective oxidants for this transformation [18-21].

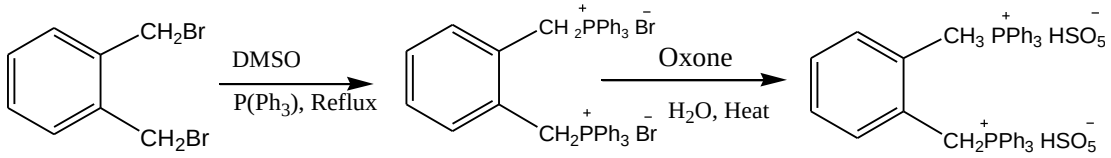
Oxone is an inexpensive, water-soluble, and stable oxidizing reagent that is commercially available, but this reagent is insoluble in organic solvents and buffering is needed due to its acidity [22]. Recently, we have reported *o*-xylylenebis(triphenylphosphonium Peroxymosulfate) OXBTPPPMS as a mild, inexpensive, and efficient oxidizing reagent for the conversion of oximes, phenylhydrazones and semicarbazones to the parent carbonyl compounds in a solvent-free system, oxidation of alcohols to aldehydes and ketones, hidroqinon to qinone under solvent-free [23]. In the course of our studies on the oxidation of organic sulfur compounds, we explored the utility of OXBTPPPMS as a mild and selective

oxidizing reagent for oxidation of sulfides **1** and thiols **3** to their corresponding sulfoxides **2** and disulfides **4** under nonaqueous conditions.





OXBTPPPMS a mild, efficient, stable, and cheap reagent is a yellow powder that is quite soluble in chloroform and acetonitrile and insoluble in nonpolar solvents such as carbon tetrachloride, *n*-hexane, and diethyl ether. This reagent is readily prepared [23a] and could be stored for months without losing its potency.



2. Experimental

^{1}H NMR spectra were measured on Bruker Avance DRX 500 MHz spectrometers, using deuterated chloroform ($CDCl_3$) as solvent. Melting points were determined on Electro Thermal 9100. Materials were purchased from Fluka and Merck companies. All the products were characterized by ^{1}H NMR, and GC data and also by comparison with authentic samples.

2.1. General procedure:

To a solution of thiol or sulfide (1 mmol) in acetonitrile (5 mL), OXBTPPPMS (0.5 mmol) was added. The reaction mixture was refluxed for the appropriate time (Tables 1, 2). The progress of the reaction was monitored by TLC (eluent: n-hexane/ethyl acetate: 5/1). After disappearance of the starting material, the mixture was filtered through a sintered glass funnel and the solid residue was washed with acetonitrile (10 mL). Evaporation of the filtrates gave

products. All of the products were known compounds and characterized by comparing melting point and ^{1}H NMR spectra with does reported in the literature.

2.1.1. p-Methyl benzyl phenyl sulfoxide (Tabel 1 entry 1).

Yield 97%; mp 96-98 ºC; ^{1}H NMR (400 MHz, CDCl3): δ 2.42 (s, 3H), 4.0 (d, J = 12.6, 1H), 4.11 (d, J= 12.6, 1H), 7.02 (d, J = 7.6, 2H), 7.24-7.31 (m, 7H).

2.1..2. 1, 2- Diphenyl disulfide (Tabel 2 entry 1).

Yield 97%; mp 60-61 ºC; ^{1}H NMR (500 MHz, CDCl3): *δ* 7.26-7.31 (m, 2H), 7.35–7.40 (m, 4H), 7.57 (d, *J* = 8.3, 2H), 7.61 (d, *J* = 8.3, 2H).

3. Results and Discussion

o-xylylenebis(triphenylphosphonium Peroxymosulfate) is easily prepared from *o*-xylylenebis(triphenylphosphoniumbromid) and oxone [24]. Herein we report its utility for the oxidation of thiols and sulfides to disulfides and sulfoxides, respectively. Sulfides were oxidized in acetonitrile with OXTPPPMS to give the corresponding sulfoxides.

In our first experiments, methyl phenyl sulfide was chosen as a model substrate to determine the optimal reaction conditions. This reaction was carried out in different solvents such as CH2Cl2, THF, dioxane, ethanol, H2O and under solvent free condition the best results in terms of reaction time and yield of the product was obtained, when the reaction conducted in acetonitrile. The effect of catalyst amount was investigated using 1/0.25, 1/0.5 and 1/1molar ratios of OXBTPPPMS in the conversion of methyl phenyl sulfide. The results revealed that a 0.5 /1 molar ratio was optimum and a higher amount of catalyst did not have any effect on the completion of the reaction. The optimum ratio of sulfide to oxidant (1:0.5) is found to be ideal for complete conversion of sulfides **2** to sulfoxides **3** while the reaction remains incomplete with lesser ratio of substrate and oxidant, for example 1:1 and 1:1.2.

To show the generality of this procedure, a wide range of aromatic and aliphatic sulfoxides were transformed into the corresponding disulfides by treatment with OXBTPPPMS in acetonitrile (Table 1).

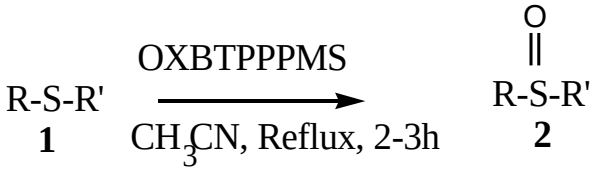


Table 1. Oxidation of sulfides with OXBTPPPMS

Entry	R	R’	Time(h)	Yield[a]	Mp(°C)[Ref]
1	p-Methyl benzyl	Phenyl	2	90	95-97 [25a]
2	Phenyl	Benzyl	3	88	123-125 [25b]
3	Benzyl	Benzyl	2	90	134-136 [25c]
4	Phenyl	Me	2	92	30-32 [25d]
5	Benzyl	Benzyl	2	93	134-136[25c]

In this method, oxidation of a sulfide is achieved by stirring a mixture of a sulfide and the reagent under reflux condition. The reaction time is usually between 2 and 3 h. The sulfoxides are isolated by filtering the reaction mixture and washing the filter cake with appropriate solvent. Evaporation of filtrate under vacuum often produces pure sulfoxide without any purification. All the reactions occurred with complete selectivity for sulfoxide formation; no over oxidation products such as sulfones were detected in the reaction mixtures. This method offers a simple, general, selective and highly efficient route for converting sulfides to the corresponding sulfoxides in the absence of complex catalyst.

Similarly when thiols 3 were treated with OXBTPPPMS in acetonitrile at reflux condition, a high yield of the corresponding disulfides 4 were obtained in 1 h (Table 2).

In most cases investigated, the optimum mole ratio between the thiol 3 and the oxidant is found to be 1:0.5, which produces pure disulfides **4** in high yields (Table 2). Aromatic and aliphatic thiols could be selectively oxidized within 0.5-1h to the corresponding disulfides in quantitative yields (Table 2, entries 1-9).

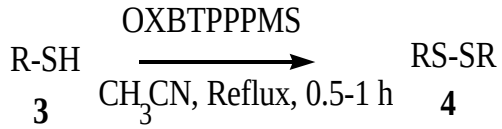
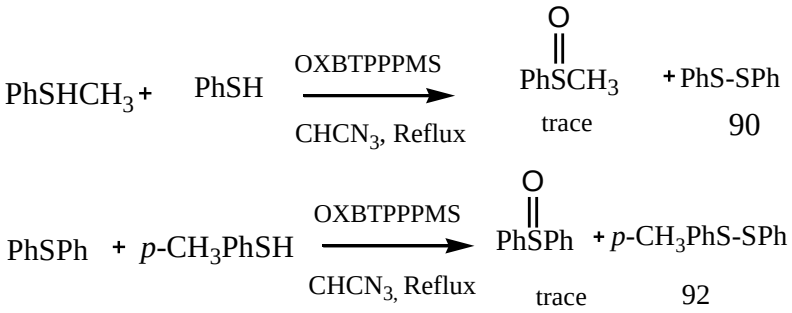


Table 2. Oxidation of thiols with OXBTPPPMS.

Entry	R	Time(h)	Yield%[a]	Mp(°C)[Ref]
1	Ph	0.5	94	59-61 [26a]
2	*p*-Methyl phenyl	0.5	94	44-46 [26b]
3	*P*-Methoxy phenyl	0.5	93	41-43 [26c]
4	*p*-Bromo phenyl	0.5	92	91-93 [26a]
5	Benzo thiazolyl	1	85	177-179 [26b]
6	Benzyl	1	88	70-72 [26b]
7	Cyclohexyl	1	82	Oil [26a]
8	Phenyl	1	90	60-61 [26a]
9	*β*-Naphtyl	1	90	143-144 [26a]

In order to study the selectivity of this method, a mixture of equimolar amounts of thiophenol or *p*-methoxythiophenol and phenylmethylsulfide was treated with 0.5 equivalents of OXBTPPPMS. After only 0.5h diphenyl and di(*p*-methoxyphenyl)disulfide were formed in 94% yield and a trace amount of phenylmethyl sulfoxide was detected.



4. Conclusion

In this paper, we have described a facile, mild and selective synthesis of disulfides and sulfoxides using OXBTPPPMS as a stable, safe and non-toxic oxidant. The several advantages of this method, including high yields of products, inexpensive, simple procedure, the easy and clean work-up, and unlike previous oxygenation methods, this one requires neither an aldehyde nor a transition metal complex , make this reaction convenient and efficient.

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