

H₂O₂ as a green and environmentally benign reagent for the oxidation of sulfides in the presence of {[K.18-Crown-6]X₃]_n (X= Br, I) compared with some other organic tribromides

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Abstract

In the presence of {[K.18-Crown-6]X₃]_n (X= Br, I)-as interesting trihalide reagents, organic sulfides were oxidized to their corresponding sulfoxides using H₂O₂ as a green reagent. {[K.18-Crown-6]X₃]_n activates H₂O₂ *via* in situ generation of HOX and variously substituted sulfides were selectively transformed into the corresponding sulfoxides. We compared the obtained results of {[K.18-Crown-6]X₃]_n with some other organic tribromides. Unexpectedly, in most cases, the results were similar.

Keywords: H₂O₂; {K.18-Crown-6]Br₃]_n; {K.18-Crown-6]I₃]_n; oxidation; sulfides; sulfoxides.

Introduction

A sulfoxide is a chemical substance containing a sulfinyl (S=O) functional group bound to two carbon atoms. S=O is a polar functional group. Sulfoxides are the oxidized derivatives of sulfides [1]. One of the important sulfoxides is alliin, a precursor to the compound that gives freshly chopped or crushed garlic its aroma [2], and DMSO with the formula (CH₃)₂SO, an important polar aprotic solvent. Organic sulfoxides are useful synthetic substrates for the preparation of various chemically and

biologically active structures [3]. They often play an important role as therapeutic factors such as anti-atherosclerotic, anti-ulcer, antibacterial, antifungal, antihypertensive, and cardiotoxic agents, as well as vasodilators and psychotonics [4].

Due to the importance of sulfoxides in synthetic organic reactions and biological chemistry, the oxidation of sulfides to their corresponding sulfoxides is important compared to some other organic reactions [5].

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Generally, oxidation reactions need stoichiometric amounts of toxic reagent/catalyst. Removal of the trace reagent from the reaction mixture is usually expensive and difficult. Thus, in green protocols [6], oxidation reactions using cheap green oxidants such as oxygen [7] or hydrogen peroxide (H_2O_2) have become increasingly popular [8].

Application of organic trihalide (Br_3^- and I_3^-) as reagents/catalysts are preferable to molecular bromine/iodine because of the high toxicity of these elements. Usage of organic tribromide reagents (OTBs) is very common. Some of these reagents include hexamethonium bis(tribromide) [9],

poly (4-vinylpyridinium tribromide) [10], and tribromide ion immobilized on magnetic nanoparticle [11]. Unlike the abundance of tribromide reagents, only one organic triiodide reagent has been reported so far. We reported $\{[\text{K.18-crown-6}]\text{Br}_3\}_n$ [12] and $\{[\text{K.18-crown-6}]\text{I}_3\}_n$ [13] as a particular trihalide structure (Figure 1). We have applied these compounds to the bromination of aromatic rings, conversion of thiols to disulfides, protection of amines, and alcohols [12-14]. Recently, we reported the oxidation of alcohols and protected alcohols using H_2O_2 in the presence of $\{[\text{K.18-crown-6}]\text{Br}_3\}_n$ [15].



Figure 1. Crystal's colors of $\{[\text{K.18-crown-6}]\text{Br}_3\}_n$ and $\{[\text{K.18-crown-6}]\text{I}_3\}_n$

Previously, we have studied the application of organic trihalides as reagent/catalyst [14,16] and also H_2O_2 and its derivatives such as UHP [17], melamine- H_2O_2 [18], and PVP- H_2O_2 [19] in organic functional groups transformations. Consequently, this study aimed to evaluate the effect of $\{[\text{K.18-crown-6}]\text{Br}_3\}_n$ and $\{[\text{K.18-crown-6}]\text{I}_3\}_n$ as two unique trihalide reagents for the oxidation of sulfides to sulfoxides in the presence of H_2O_2 .

Experimental

General

Chemicals were purchased from Merck, Fluka and Sigma-Aldrich companies. Products were characterized by comparison of their spectral (IR, $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$) with those of known samples. Preparation of $\{[\text{K.18-}$

crown-6] $\text{Br}_3\}_n$, $\{[\text{K.18-crown-6}]\text{I}_3\}_n$ and their recycling processes were performed according to our previously reported procedure [12,13].

General procedure for the oxidation of sulfides to sulfoxides

H_2O_2 30% (1.1 mmol) was added to a solution of sulfides (1 mmol) and $\{[\text{K.18-crown-6}]\text{X}_3\}_n$ (2 mmol) in CH_3CN (8 mL). The solution was stirred at reflux for the appropriate time (Table 2). The progress of the reaction was monitored by TLC. After the completion of the reaction, CH_3CN was removed by water-bath distillation. Column chromatography on a short pad of silica gel with CH_3CN afforded pure products in good to excellent yields. $\{[\text{K.18-Crown-6}]\text{X}_3\}_n$ can regenerate (70%) *via* adding the ethanolic solution

of X₂ to the residue of the reaction and recrystallization in acetonitrile.

Results and discussion

In this study, we report that {[K.18-crown-6]X₃]_n acts as efficient reagents for the oxidation of sulfides to sulfoxides. Control experiments were

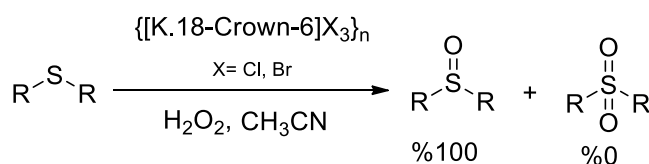
done to optimize the reaction conditions. First, oxidation of dibenzyl sulfide was used as a model reaction. This reaction was carried out in the presence of different amounts of {[K.18-crown-6]X₃]_n, H₂O₂, and different solvents. The optimized reaction conditions were 2 mmol of {[K.18-crown-6]X₃]_n, 1.1 mmol H₂O₂ and CH₃CN as the best solvent (Table 1).

Table 1. Optimization of the reaction condition for the oxidation of dibenzyl sulfide in the presence of {[K.18-crown-6]X₃]_n, H₂O₂ and diversity of solvents

Entry	{[K.18-crown-6]X ₃] _n (mmol)	H ₂ O ₂ (mmol)	Solvent (8 mL)	Temperature (°C)	Time (min.)	Isolated Yield (%)
1	2	--	--	25	30	Sluggish
2	2	--	CH ₃ CN	Reflux	50	Sluggish
3	1	1.1	CH ₃ CN	25	30	45
4	1.5	1.1	CH ₃ CN	Reflux	30	60
5	2	1	CH ₃ CN	Reflux	30	65
6	2	1.1	CH ₃ CN	Reflux	30	81
7	2	1.1	CHCl ₃	Reflux	45	55
8	2	1.1	EtOAc	Reflux	45	67
9	2	1.1	THF	Reflux	45	71
10	2	1.1	<i>n</i> -hexane	Reflux	45	44

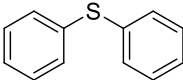
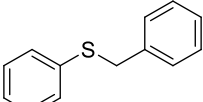
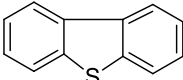
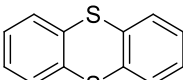
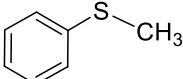
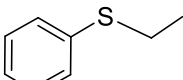
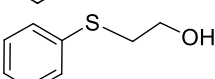
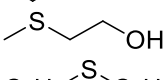
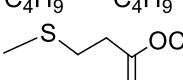
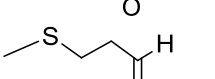
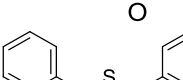
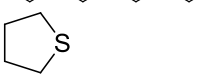

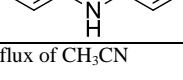
Secondly, we converted a range of sulfides to their corresponding sulfoxides under optimized reaction

conditions without any generation of sulfones as the by-product (Scheme 1 and Table 2).



Scheme 1. Oxidation of sulfides to sulfoxides using H₂O₂ in the presence of {[K.18-Crown-6]X₃]_n (X= Br, I)

Table 2. Oxidation of sulfides to sulfoxides using H₂O₂ in the presence of {[K.18-Crown-6]X₃}_n (X= Br, I)

Entry	Substrate	{[K.18-Crown-6]Br ₃ } _n		{[K.18-Crown-6]I ₃ } _n	
		Time (min.) ^a	Isolated Yield (%)	Time (min.) ^a	Isolated Yield (%)
1		35	80	30	88
2		35	90	40	78
3		40	88	35	85
4		40	78	35	75
5		40	83	30	74
6		35	74	30	69
7		35	70	45	83
8		35	66	30	73
9		25	75	25	70
10		35	77	30	81
11		28	83	40	85
12		30	81	35	73
13		25	76	30	80
14		30	67	35	75

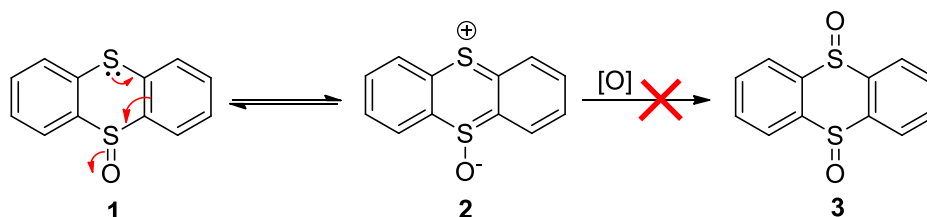
^aUnder the reflux of CH₃CN**Homoselectivity in the oxidation of thianthrene**

Previously, we introduced "homoselectivity" in the oxidation of

thianthrene. When the thianthrene exposes to the oxidation condition (Table 2, Entry 4), selective monosulfoxidation takes place and

further oxidation to disulfoxidation does not happen. We named this phenomenon "homoselectivity" [18]. We think that disulfoxidation does not

occur because lone pair electron of the second sulfur participates in resonance with the primary sulfoxide group (Scheme 2).

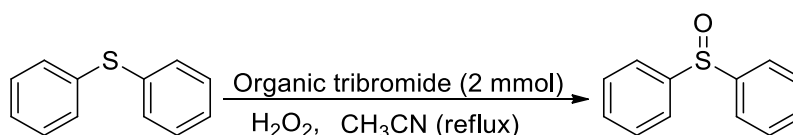


Scheme 2. Homoselectivity in the monooxidation of thiantherene

Effect of crown ether on the reaction acceleration

As we know, crown ethers are phase transfer catalysts [20], and we expect this catalyst to promote the reaction better than some other organic tribromides. Therefore, we applied some other reported organic tribromide i.e. Dabco-bromine [21], HMTA-bromine [22] and 1,1'-(Ethane-1,2-

diyl)dipyridinium bistr bromide (EDPBT) [23] for the oxidation of diphenyl sulfide under the reaction conditions and then comparison of their results with {[K.18-Crown-6]Br₃}_n. Unexpectedly, there was no distinguished difference between the results of these tribromides and {[K.18-Crown-6]Br₃}_n in terms of yields or reaction time (Scheme 3, Table 3).



Scheme 3. Oxidation of diphenyl sulfide using H₂O₂ in the presence of some organic tribromides

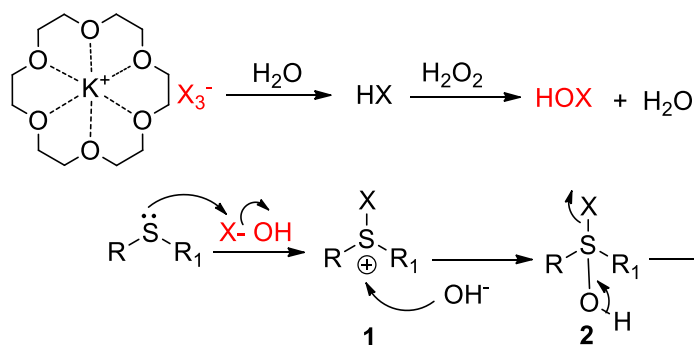
Table 3. Comparison of the results of some other organic tribromides with {[K.18-Crown-6]Br₃}_n in the oxidation of diphenyl sulfide using H₂O₂

Entry	Organic tribromide	Time (min.)	Isolated Yield (%)	References
1	{[K.18-Crown-6]Br ₃ } _n	35	80	This work
2	Dabco-bromine	35	83	[21]
3	HMTA-Bromine	40	81	[22]
4	EDPBT	40	78	[23]

Proposed mechanism

According to previously reported paper [24] and our obtained results, we propose that the mechanism for the oxidation of sulfides using H₂O₂ in the presence of {[K.18-Crown-6]X₃}_n can proceed by the in-situ formation of

HOX that causes this oxidation. Lone pair electron of sulfur attacks to X to form 1 and then OH⁻ bonds to 1 to form 2. H₂O removing from 2 produces the sulfoxide (Scheme 4).



Scheme 4. Suggested mechanism for the oxidation of sulfides to sulfoxides using H_2O_2 in the presence of $\{[\text{K.18-Crown-6}]\text{X}_3\}_n$

Conclusion

In summary, we explained the oxidation of sulfides to sulfoxides using H_2O_2 in the presence of $\{[\text{K.18-Crown-6}]\text{X}_3\}_n$. This protocol features good substrate scope, and excellent functional group compatibility, which holds promise for its convenient application in the preparation of sulfoxides without generation of sulfones as the by-product. The reaction is carried out at reflux conditions and yields of products are moderate to good. We compared the obtained results of $\{[\text{K.18-Crown-6}]\text{X}_3\}_n$ with some other organic tribromides. Unexpectedly, in most cases, the results were similar.

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