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Cyanuric chloride as promoter for the oxidation of sulfides and deoxygenation of sulfoxides

Kiumars Bahrami [a,b,*], Mohammad M. Khodaei [a,*], Samira Sohrabnezhad [a]

[a] Department of Organic Chemistry, Faculty of Chemistry, Razi University, Kermanshah 67149-67346, Iran
[b] Nanoscience and Nanotechnology Research Center (NNRC), Razi University, Kermanshah 67149-67346, Iran

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ABSTRACT

This Letter discusses the use of cyanuric chloride as an efficient promoter for the chemoselective oxidation of sulfides to the corresponding sulfones in the presence of H_2O_2 as the terminal oxidant. Sulfoxides were also found to undergo deoxygenation to sulfides with cyanuric chloride and potassium iodide system. The reaction is broad in scope and easy to perform.

The wide-ranging chemistry of sulfones makes them very important reagents in organic synthesis in general and useful synthetic intermediates for the construction of various chemically and biologically significant molecules in particular.[1]

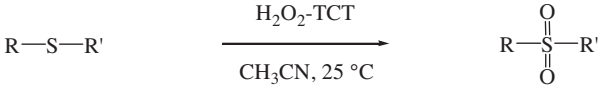
The direct oxidation of sulfides is an important and widely studied reaction for the preparation of sulfoxides and sulfones. However, the oxidation of sulfides to sulfones has been much less investigated as compared to the oxidation of sulfides to sulfoxides. For the selective oxidation of sulfides to sulfones, a range of oxidants have been studied.[2–4] Besides extended reaction times, some of these processes suffer from drawbacks, such as elevated temperatures, undesired side reactions occurring on other functional groups, the use of hazardous peracids, and toxic metallic compounds that generate waste streams. Therefore, convenient and environmentally benign methods for the oxidation of sulfides to sulfones are still required.

Inspired by our results using the H_2O_2–TAPC system for the oxidation of sulfides,[5] and following our recent interest in the use of hydrogen peroxide in organic synthesis,[6] we report here cyanuric chloride (TCT) as a selective and efficient promoter for the oxidation of sulfides into sulfones using H_2O_2 in acetonitrile at room temperature (Scheme 1).

Cyanuric chloride (2,4,6-trichloro-1,3,5-triazine, TCT), is an inexpensive and mild reagent that has been widely used in organic reactions.[7–12] This reagent is available as a white powder of high purity and due to its specific structure and electronic properties, is used extensively in the dye and pharmaceutical industries.[13] The preparation of sulfones using this reagent has not been reported to date.

A preliminary study with benzyl phenyl sulfide as a model substrate quickly established that this oxidation protocol produced the anticipated sulfone in excellent yield and in a short reaction time. A ratio of 1:2:1 (sulfide/H_2O_2/TCT) was found to be optimum for the complete conversion of sulfides (via sulfoxides) into sulfones. The reaction remained incomplete with smaller amounts, for example 1:1:0.7 (~20% contamination with the sulfoxide). A control experiment without catalyst showed that only a low yield of sulfoxide was obtained in the presence of 2 equiv of H_2O_2 after 6 h. In order to generalize the scope of the reaction, a series of structurally diverse sulfides were subjected to oxidation under the optimized reaction conditions, and the results are presented in Table 1. Oxidation of allyl phenyl, alkyl aryl, aryl benzyl, dialkyl, diaryl, cyclic, and heterocyclic sulfides produced excellent yields of the corresponding sulfones.

It is notable that the sulfides were chemoselectively oxidized in the presence of oxidation-prone functional groups, such as –OH and C=C. For example, oxidation of 2-(phenylthio)ethanol proceeded smoothly to produce the corresponding sulfone in 95% yield without interference from the alcohol functional group (Table 1, entry 7). In the case of allyl phenyl sulfide, hydrochlorination of the double bond was not observed, and only the corresponding sulfone was obtained in 95% yield (Table 1, entry 10). Methyl 2-(phenylthio)acetate containing a methyl ester group gave the desired sulfone in 98% yield, and its hydrolysis product was not formed under these reaction conditions (Table 1, entry 9). The acid sensitive sulfide 2-[(benzylthio)methyl]furan worked well without the formation of any side products (Table 1, entry 6). It was



R, R' = Alkyl, allyl, aryl

Scheme 1. Sulfones from sulfides.

* Corresponding authors. Fax: +98 831 4274559 (K.B.).
E-mail address: Kbahrami2@hotmail.com (K. Bahrami).

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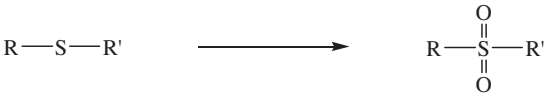
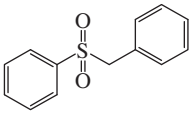
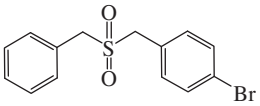
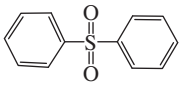
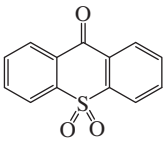
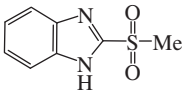
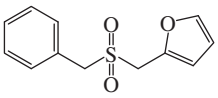
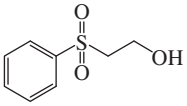
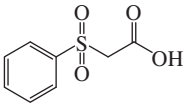
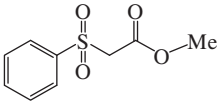
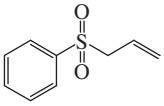
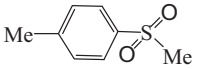
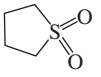
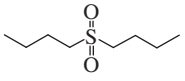
Table 1
Selective oxidation of sulfides into sulfones[a]

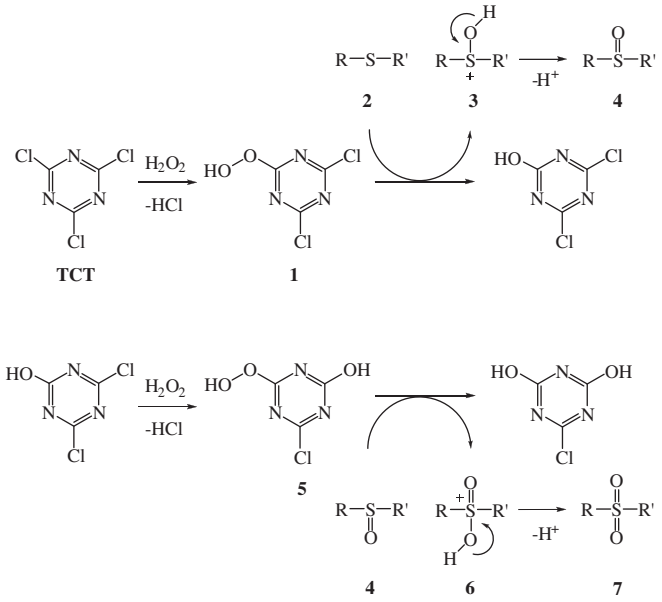


Entry	Product	Time (min)	Yield[b] (%)	Mp (°C)	Reference
1		17	97	148	5
2		30	98	177	6a
3		25	96	125–126	5
4[c]		15	97	186–188	5
5		20	97	199–201	14
6		15	95	84–85	5
7		15	95	Oil	15a
8		15	97	110–111	5
9		15	98	Oil	5
10		30	95	Oil	16
11		15	96	85–86	15b
12		15	92	Oil	17
13		30	95	44–45	17

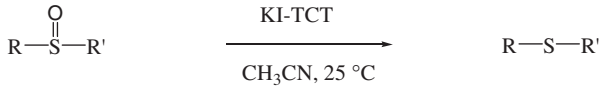
[a] The purified products were characterized by mp and ^{1}H NMR spectroscopy.
[b] Yields refer to pure isolated products.
[c] 1,4-Dioxane was used as the solvent.

significant that a ketone group was not oxidized using the present system (Table 1, entry 4).

A possible mechanism for oxidation of the sulfide into the corresponding sulfone using H_2O_2 in the presence of TCT is outlined in Scheme 2. Nucleophilic attack of H_2O_2 on TCT leads to intermediate **1** in which the oxygen atom is more electrophilic. Next, nucleophilic attack of sulfide **2** on this intermediate gives intermediate **3** followed by the abstraction of hydrogen to yield the corresponding sulfoxide **4**. Sulfoxide **4** reacts with the intermediate **5** to form **6,** which follows the abstraction of hydrogen produces sulfone **7**.



Scheme 2. Proposed mechanism for the oxidation of sulfides.



R, R' = Alkyl, allyl, aryl

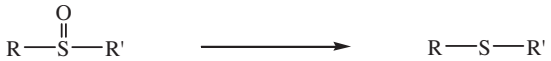
Scheme 3. Preparation of sulfides from sulfoxides.

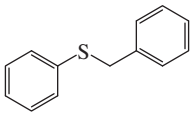
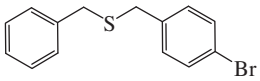
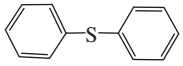
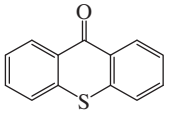
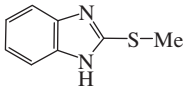
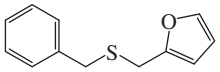
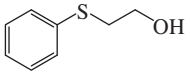
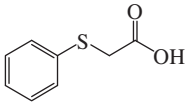
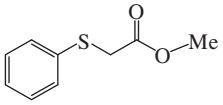
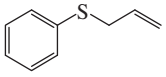
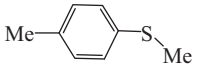
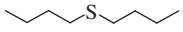
Deoxygenation of sulfoxides is a repeating theme in organic chemistry because of its use in various synthetic transformations and considerable utility in biochemical reactions.[18] A survey of the literature revealed that several methods have been reported for the reduction of sulfoxides.[19–22] Most of the procedures are impractical in some respects. Disadvantages include prolonged reaction times, low yields, poorly available reagents and harsh reaction conditions. Only a few methods allow the rapid and mild deoxygenation with inexpensive and common laboratory reagents. Therefore, a search for readily available reagents and universally applicable methods for this conversion is still a worthwhile goal.

In order to demonstrate the efficiency and applicability of TCT further, the chemoselective deoxygenation of sulfoxides to sulfides was also investigated with the KI–TCT system (Scheme 3).

The molar ratio of sulfoxide/TCT/KI (1:1:2.5) was found to be ideal for the complete conversion of sulfoxides into sulfides in acetonitrile at room temperature. Under the optimized conditions, the deoxygenation of various sulfoxides was carried out. The results are shown in Table 2. Both aromatic and aliphatic, cyclic and acyclic sulfoxides were reduced to sulfides in excellent yields. The reaction tolerates a variety of functional groups, including ketone, alcohol, carboxylic acid, ester, and alkene (Table 2, entries 4, and 7–10). The method is not suitable for the deoxygenation of aryl or alkyl sulfones into the corresponding sulfides.

Table 2
Selective deoxygenation of sulfoxides into sulfides[a]



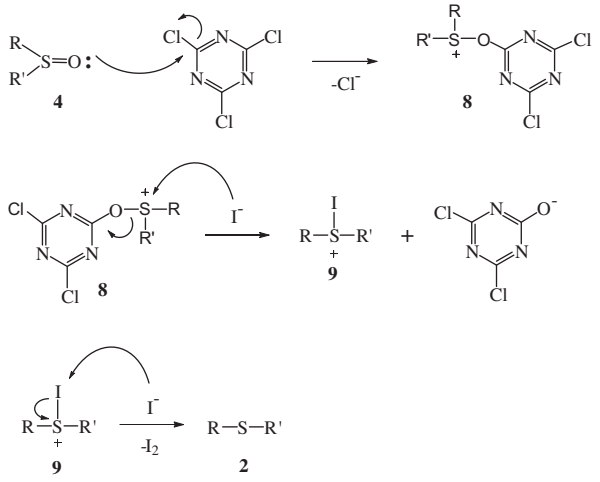
Entry	Product	Time (min)	Yield[b] (%)	Mp (°C)	Reference
1		10	97	44–46	5
2		10	95	Oil	5
3		5	94	Oil	5
4		10	95	206–207	5
5		15	99	199–200	23
6		15	93	Oil	5
7		8	95	Oil	24
8		7	94	60–61	5
9		5	96	Oil	5
10		7	97	Oil	5
11		10	96	Oil	25
12		12	96	Oil	26
13		8	95	Oil	5

[a] The purified products were characterized by mp and ^{1}H NMR spectroscopy.
[b] Yields refer to pure isolated products.

Olah et al. previously reported the deoxygenation of diarylsulfoxides with cyanuric chloride.[20a] A comparison of two systems shows that in this work there are sufficient advantages over the Olah system, both in terms of substrate scope and mild conditions.

A plausible mechanism for the deoxygenation is shown in Scheme 4. Initially, coordination of TCT to the oxygen atom of sulfoxide **4** produces intermediate **8** in which the sulfur atom is more electrophilic. Next, nucleophilic attack of the iodide on the sulfur in **8** leads to intermediate **9**. The resultant iodinated species **9** is in turn attacked by another iodide anion to give the sulfide **2** and iodine.

In conclusion, we have shown that TCT can promote the selective oxidation of a variety of sulfides into the corresponding sulfones in the presence of H_2O_2 as the terminal oxidant. Furthermore, the combination of TCT and KI reagent was applied



Scheme 4. Proposed mechanism for the deoxygenation of sulfoxides into sulfides with the KI–TCT system.

for the deoxygenation of a series of sulfoxides. Although the literature reports a number of procedures for the oxidation of sulfides and deoxygenation of sulfoxides, the excellent yields, simplicity, good availability of starting materials, compatibility with a variety of functionalities, and ease of isolation of the products make our procedure a practical alternative.

General procedure for the preparation of sulfones

To a mixture of sulfide (1 mmol) and TCT (1 mmol, 0.184 g) in acetonitrile (5 mL) was added 30% H_2O_2 (2 mmol, 0.2 mL). The mixture was stirred at room temperature for the appropriate period of time until complete consumption of the starting material as observed by TLC. After completion of the reaction, H_2O (10 mL) was added to the reaction mixture which was then extracted with EtOAc (4 × 5 mL) and the combined extracts were dried ($MgSO_4$). The filtrate was evaporated and the corresponding sulfone was obtained as the only product (Table 1).

General procedure for the preparation of sulfides

To a flask containing a stirred mixture of sulfoxide (1 mmol) in acetonitrile (5 mL), TCT (1 mmol, 0.184 g) and KI (2.5 mmol, 0.42 g) were added. The mixture was stirred at room temperature and monitored by TLC. On completion of the reaction, H_2O (10 mL) was added to the reaction mixture which was then extracted with EtOAc (4 × 5 mL) and the combined extracts were dried ($MgSO_4$). The filtrate was evaporated and the corresponding sulfide was obtained as the sole product (Table 2).

All of products are known compounds and were characterized by the comparison with authentic samples (^{1}H NMR and mp).

Acknowledgment

We are thankful to Razi University Research Council for partial support of this work.

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