Chemoselective Oxidation of Sulfides to Sulfoxides Using *N*-*t*-Butyl-*N*-chlorocyanamide

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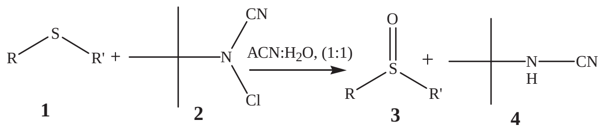
A simple, efficient and highly chemoselective method has been developed for the synthesis of sulfoxides from sulfides using *N*-*t*-butyl-*N*-chlorocyanamide as an oxidant in a mixed acetonitrile–water solution with a 1:1 mol ratio of oxidant to sulfides. *N*-*t*-butyl-*N*-chlorocyanamide, a source of positive chlorine, has been used for conversion of the variety of sulfides into their corresponding sulfoxides in quantitative yields.

Sulfoxides have attracted the attention of organic chemists for a long time owing to their varied reactivity as a functional group for the transformations into variety of organosulfur compounds. These transformations are useful for the synthesis of drugs and sulfur-substituted natural products.[1,2] Sulfoxides are also useful for the stereocontrol in the construction of chemically and biologically important molecules.[3–5] These compounds are usually prepared by the oxidation of sulfides and several oxidative procedures are applicable for this transformation.[6,7] Generally, it is important to stop the oxidation at the sulfoxide stage by controlling the electrophilic character of the oxidant, but this requirement is often hard to meet and the failure results in over-oxidation of sulfoxides to sulfones. Therefore, there is still considerable interest in the development of selective oxidants for this important transformation.[6] There is significant difference in the nuleophilicity of the sulfides compared to the sulfoxides,[8] although several methods are known[6,7] for oxidizing sulfides to sulfoxides, very few are sufficiently selective to terminate oxidation at the sulfoxides stage and prevent over-oxidation to sulfones.[9] The most recent reports on sulfoxides synthesis include formation from thionyl chloride and arenes employing trifluoromethanesulfonic acid[10] or scandium triflate[11] as the catalyst. The direct preparation of sulfoxides often suffers from the formation of mixture of the products containing sulfonium salt and chlorinated by-products along with desired sulfoxides.[12] Copper-catalyzed (TEMPO) oxidation of sulfides to sulfoxides has just been reported.[13] No doubt this method works at ambient temperature with improved selectivity, but time-consuming. A variety of the existing methods have disadvantages of being expensive, using toxic chemicals, or suffering from moderate selectivity. In the course of our studies on *N*-*t*-butyl-*N*-chlorocyanamide[14] **2** for oxidation of sulfides, we have explored a rapid, efficient, economic, and easy-to-use method for chemoselective and quantitative transformation of sulfides to their corresponding sulfoxide.



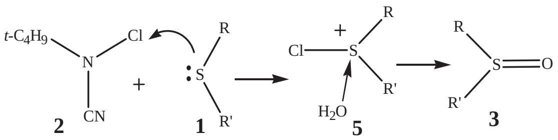
Scheme 1. Synthesis of sulfoxides from sulfides.

This protocol uses **2** as positive chlorine donor for the oxidation of sulfides to sulfoxides in a mixed acetonitrile–water solution (Scheme 1). The reaction was almost instantaneous at 25 °C and took less than a minute for complete transformation of sulfides to sulfoxides. A series of experiments established that one mol of **2** per mol of sulfides were required to obtain maximum yield of the sulfoxides. Using standard conditions, the oxidation of a series of sulfides was examined (Table 1). Many factors such as change in the alkyl aryl group and the choice of the reaction medium also have profound effect on the progress of the reaction. The sulfides were chosen to reflect a variety of structural types. Dialkyl, alkyl aryl, diaryl, cyclic, dibenzothiophene and sulfide with ester moiety reacted with **2** under these reaction conditions to produce the corresponding sulfoxides in excellent yields in less than a min along with quantitative recovery of *t*-butylcyanamide **4**. The reactivity was almost the same for all the sulfides used in this study. The choice of reaction medium is important. The best results were obtained in acetonitrile–water (1:1). However, in case of phenyl methyl sulfide, 4-chlorophenyl methyl sulfide, diphenyl sulfide, and dibezothiophene (Table 1, Entrys 1, 2, 4, and 13) which are insoluble in 1:1 acetonitrile–water solution, this solution in the ratio of 7:3 was used to get maximum yield. Generally, electron-withdrawing group attached to sulfides reduces the reactivity against oxidation. The notable feature of this method is the efficient oxygenation of even those sulfides, which are linked to electron-withdrawing group (Table 1, Entry 5). The formation of sulfoxide is thought to proceed via the formation of sulfonium ion **5**, which is formed by the attack of sulfur on the electrophilic chlorine, which then

Table 1. Preparation of sulfoxides[15] by **2**

Entry	R	R′	Yield/%[b]
1[a]	CH_3	C_6H_5	94
2[a]	CH_3	p-Cl-C_6H_5	95
3	i-C_3H_7	C_6H_5	95
4[a]	C_6H_5	C_6H_5	96
5	p-Ac-C_6H_5	p-Ac-C_6H_5	94
6	C_3H_7	C_3H_7	96
7	i-C_3H_7	i-C_3H_7	94
8	C_4H_9	C_4H_9	96
9	$(CH_2)_2$-OH	$(CH_2)_2$-OH	92
10	$(CH_2)_2$-OH	C_2H_5	94
11	C_2H_5	COOMe	95
12	Tetrahydrothiophene	—	95
13[a]	Dibenzothiophene	—	92
14	1,4-Dithiane	1,4-Dithiane-1-oxide	90

All products had satisfactory spectroscopic data and were compared with authentic samples.
[a]Acetonitrile–water ratio is 7:3. [b]Isolated yield.



Scheme 2.

decomposes to sulfoxide with the elimination of HCl gas (Scheme 2).

In conclusion, we have investigated the potential use of **2** for the highly chemoselective and very fast oxidation of sulfide. An advantage of this method is the short reaction time (i.e. less than a min), mild reaction conditions with operational simplicity and no over-oxidation of sulfoxide to sulfone.

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15 Experimental: To a stirred solution of *N*-*t*-butyl-*N*-chlorocyanamide[14] (1.0 mmol), in a mixed acetonitrile–water solution (1:1), sulfide (1.0 equiv.) was added. The reaction was carried out at room temperature and was monitored by TLC. After completion of reaction, water (50 mL) was added to the solution, which was then extracted with DCM, dried over anhydrous Na_2SO_4. On evaporation of the solvent on rotary evaporator gave mixture of sulfoxide and *t*-butylcyanamide (bp 53–54 °C/8 mmHg). The pure sulfoxide was obtained either by recrystallization in DCM/pet. ether (40–60 °C) (in case of solid products) or distillation (in case of liquid products).

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