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Chemoselective and efficient oxidation of sulfides to sulfoxides mediated by trimethylsilyl chloride and superoxide via a trimethylsilylperoxy radical

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Abstract

Chemoselective and efficient oxidation of various sulfides were mediated by Me_3SiCl and KO_2 in dry acetonitrile at –15°C to afford corresponding sulfoxides in excellent yields without any interference in the presence of ketone, olefin, ether and hydroxyl functionalities and without further oxidation to the sulfones. A trimethylsilylperoxy radical generated in situ from this new process is proposed.

Keywords: superoxide; trimethylsilyl chloride; trimethylsilylperoxy radical; oxidation.

Superoxide anion radical ($O_2^{-\cdot}$) is a reactive species easily generated in the body which can cause serious damage to living organisms.[1] Recently, much effort has been made not only on its biological toxicity but also on its application in organic synthesis.[2] In general, the four basic types of reactivities of superoxide have been documented as a base, an anion, a radical, and an electron-transfer reagent.[3] It also has been known that superoxide acts as a moderate reducing agent but a very weak oxidizing agent.[4] In the activation of oxidizing ability of superoxide, numerous studies have been reported to activate superoxide through the reaction of various organic substrates with superoxide to form a new peroxy intermediate that can act as a stronger oxidizing agent.[5] Although some sulfinyl, sulfonyl and phosphorous peroxy intermediates have been generated from the reaction of superoxide with each of the corresponding chlorides to testify their oxidizing abilities towards various organic substrates,[5] it is still of great interest to find out more strong-oxidizing agents, activated from superoxide, for use in organic synthesis. For instance, trialkylsilylperoxy radicals are likely to be good candidates for this purpose.

Trialkylsilylperoxy radicals have been prepared and studied by ESR spectroscopy by Howard's group.[6] Their results indicate that the structure of these silylperoxy radicals resembles the structure of alkylperoxy radicals and they exist in equilibrium with a tetroxide at temperature below

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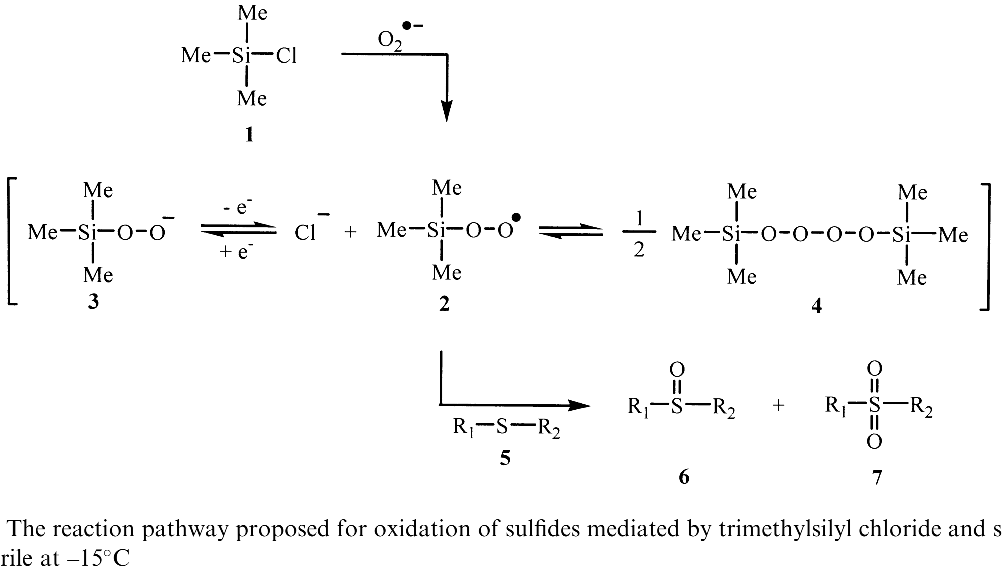
233°K.[6a] Surprisingly, no further works dealing with their applications in organic synthesis were reported. The reasons might be partly because the generation of silylperoxy radicals by photolysis of trialkylsilane in an oxygen-saturated solvent containing di-*tert*-butyl peroxide must produce a stronger oxidant of *tert*-butoxyl radical which might be expected to interfere the process of reaction studied before the formations of peroxy radicals in the course of reaction.[6a] For practical purposes, it is desirable to develop a new and efficient process for the preparation of these silylperoxy radicals. In this report, we demonstrate that chemoselective and efficient oxidation of various sulfides, bearing ketone, olefin, ether and hydroxyl functionalities, were mediated by trimethylsilyl chloride **1** and superoxide in dry acetonitrile at –15°C to give the corresponding sulfoxides exclusively in excellent yields. The reaction pathway is proposed to undergo through trimethylsilylperoxy radical **2** generated in situ from this new process.

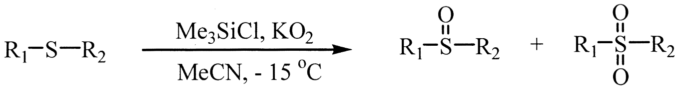
The new process for the oxidation of sulfides is represented in Scheme 1 with the results summarized in Table 1. In a general procedure (entry 1), a solution of Me_3SiCl (0.06 mL, 0.473 mmol) in dry acetonitrile (1 mL) was added slowly within 15 min to a heterogeneous solution of KO_2 (65 mg, 0.914 mmol) and methyl phenyl sulfide (0.05 mL, 0.426 mmol) in dry acetonitrile (3 mL) at –15°C with vigorous stirring under nitrogen. After stirring for 5 h at the same temperature, the reaction mixture was quenched by addition of 1N HCl (3 mL) and ice (2 g), and then extracted with ethyl acetate (3×15 mL) at room temperature. The combined organic portions were washed with water (15 mL) and brine (15 mL), dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by preparative TLC or column chromatography using ethyl acetate:hexane (2:1) as eluent to give methyl phenyl sulfoxide (55.3 mg, 93%). For a blank test, the oxidation of methyl phenyl sulfide to the corresponding sulfoxide underwent extremely slowly (98% of sulfide recovered) while the reaction was only treated with KO_2 without Me_3SiCl under the same reaction condition described above.



Scheme 1. The reaction pathway proposed for oxidation of sulfides mediated by trimethylsilyl chloride and superoxide in acetonitrile at –15°C

In all cases, only traceable amount of the sulfones were isolated or detected by ^1H NMR spectroscopy. Interestingly, the results indicate that silylperoxy radical **2**, rapidly generated in situ form Me_3SiCl and KO_2, is mild enough to allow the selective and high-yield oxidation of sulfides

Table 1
Oxidation of sulfides to the corresponding sulfoxides[a]



5 **6** **7**

Entry	R_1	R_2	Reactn. Time(h)	-SO- yield(%)[b]	$-SO_2-$ yield(%)[b]
1	C_6H_5	CH_3	5	93	1[c]
2	$4-CH_3OC_6H_4$	CH_3	2	92	1[c]
3	$CH_3C_6H_4$	CH_3	11	93	2[b]
4	$4-CH_3C(O)C_6H_4$	CH_3	9	97	trace
5	C_6H_5	CH_2Ph	10	95	1[c]
6	C_6H_5	CH_2CH_2OH	3.5	94	trace
7	$-CH_2CH_2CH_2CH_2-$		2	98	trace
8	Ph	Ph	18	94	1[c]
9	Ph	$CH_2CH_2CH_2CH{=}CH_2$	8	90	trace

[a] Molar ratio = sulfide : Me_3SiCl : KO_2 = 1 : 1.1 : 2.2

[b] Isolated yields. All compounds were characterized by IR, LRMS, and ^1H NMR spectroscopy

[c] Determined by ^1H NMR spectrum

to sulfoxides at lower temperature without any interference in the presence of ketone, olefin, ether and hydroxyl functionalities and with no further oxidation to sulfones. It has been known that oxidants commonly used for these reactions, such as *m*-chloroperoxybenzoic acid, hydrogen peroxide, iodosyl benzene, sodium periodate, oxone et al.,[7] require higher reaction temperatures than that needed by silylperoxy radical **2**. It is also remarkable that silylperoxy radical **2** oxidized sulfides to corresponding sulfoxides selectively in excellent yields as it has been known that a major difficulty encountered in the preparation of sulfoxides through oxidation of sulfides is the overoxidation to sulfones.[7]

It has also been rationalized that the oxidation of sulfides to sulfoxides is found to be electrophilic in contrast to the nucleophilic oxidation of sulfoxides to sulfones.[8] Besides the selective oxidation of sulfides to sulfoxides without further oxidation to sulfones, a competition oxidation of methyl 4-acetyl-, 4-methoxy- and nonsubstituted-phenyl sulfides was carried out under the same reaction condition described above for 1 h to give 4, 32 and 10% yields of the corresponding sulfoxides, respectively. The results indicate that the sulfur atom of these sulfides bearing an electron-donating group of 4-methoxy is oxidized more rapidly than that bearing an electron-withdrawing group of 4-acetyl due to its more nucleophilic character. Based on results mentioned above, silylperoxy radical **2** generated in situ from Me_3SiCl and KO_2 performs more likely to be electrophilic. It is noteworthy that the electrophilic oxidation of methyl phenyl sulfide to the corresponding sulfoxide mediated by Me_3SiCl and KO_2 was inhibited in the presence of 1,4-diazabicyclo[2.2.2]octane (DBACO) which is known to be a radical scavenger agent.[9] Certainly, the result shows that a radical species must exist and play an important role in the course of the oxidation reaction. Although trimethylsilylperoxy radical **2** formed from Me_3SiCl and KO_2 has not yet been confirmed in this study, it seems reasonable to propose that the strongly electrophilic oxidant generated from this new process is most likely to be silylperoxy radical **2** owing to its radical character as in the case of Howard's studies.[6] However, an alternative mechanism involving anion character **3** and silyl tetroxide **4** still cannot be ruled out.

In conclusion, we have demonstrated that silylperoxy radical **2**, rapidly generated in situ from Me_3SiCl and KO_2, performs a strongly electrophilic oxidizing ability to undergo the chemoselective and efficient oxidation of sulfides to corresponding sulfoxides in excellent yields without any interference in the presence of ketone, olefin, ether and hydroxyl functionalities and without further oxidation to the sulfones under mild conditions. The confirmation of **2** formed from this new process and its applications used more widely in organic synthesis have been under investigations.

Acknowledgements

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