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Mohammad Mehdi Khodaei[ab]; Kiumars Bahrami[ab]; Mehdi Sheikh Arabi[a]
[a] Department of Chemistry, Razi University, Kermanshah, Iran [b] Nanoscience and Nanotechnology Research Center (NNRC), Razi University, Kermanshah, Iran

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Oxidation of sulfides to sulfoxides with H_2O_2/HNO_3 reagent system

Mohammad Mehdi Khodaei[a,b]*, Kiumars Bahrami[a,b]* and Mehdi Sheikh Arabi[a]

[a]*Department of Chemistry, Razi University, Kermanshah 67149, Iran;* [b]*Nanoscience and Nanotechnology Research Center (NNRC), Razi University, Kermanshah 67149, Iran*

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Selective oxidation of sulfides to sulfoxides is achieved by H_2O_2 using HNO_3 as the promotor. Aromatic and aliphatic sulfides are oxidized to sulfoxides in excellent yields and short reaction times. Different functional groups including C–C double bond, ester, ketone, acetal, alcohol, and oxime groups are tolerated under this reaction condition.

Keywords: nitric acid; hydrogen peroxide; sulfoxide synthesis; sulfides; chemoselectivity

1. Introduction

Much effort has been devoted to the development of highly efficient and atom-economical organic transformations in order to realize environmentally benign processes. Sulfoxides are useful synthetic intermediates in the synthesis of drugs and natural products (*1*, *2*). They have been utilized extensively in carbon–carbon bond-forming reactions, molecular rearrangements, and functional-group transformations (*3*, *4*). The increasing interest in, and applications of, sulfoxides have stimulated investigations on new methodologies of sulfoxide synthesis.

The direct oxidation of sulfides is one of the most important and widely studied reactions for the preparation of sulfoxides. The popularity of this method is due to the availability of a wide variety of sulfides that can be utilized in the oxidation of sulfides to the corresponding sulfoxides. Thus, the oxidation of sulfides to sulfoxides has been the subject of extensive studies, and a variety of procedures for this purpose are available (*5*–*7*).

Although different approaches have been reported, there are various limitations, such as long reaction times, hazardous organic solvents and reagents, transition metal catalysts, expensive oxidants, undesired side reactions at other functionalities accompanied by overoxidation to the sulfone, and low yields.

Aqueous hydrogen peroxide (30%) is an ideal oxidant in view of its high effective-oxygen content, its eco-friendly by-product (water), its relative safety in storage and operation, and its comparatively low cost of production and transportation (*8*, *9*).

*Corresponding authors. Email: Kbahrami2@hotmail.com; mmkhoda@razi.ac.ir

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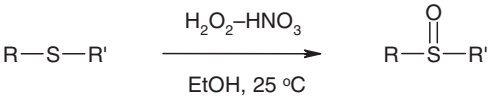
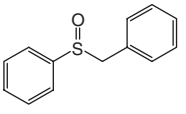
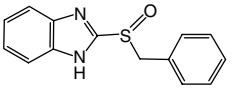
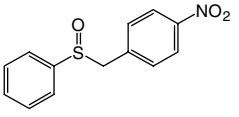
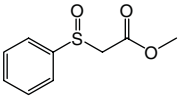
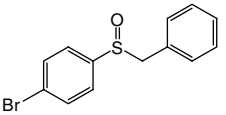
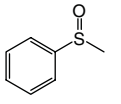
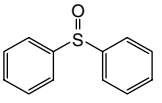
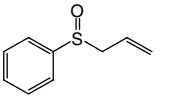
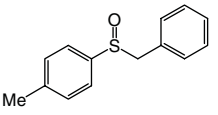
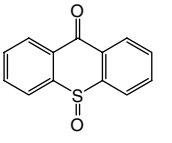
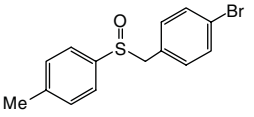
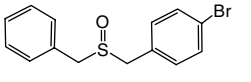
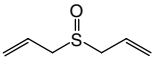
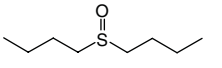


R, R′ = Alkyl, aryl

Scheme 1. Formation of sulfoxides from sulfides.

Recently, we reported several new synthetic methods for environmentally benign reactions using aqueous 30% hydrogen peroxide (*10*). Now we wish to report a facile and selective method in which H_2O_2 has been used as the oxidizing agent in the presence of HNO_3 for the oxidation of sulfides to their sulfoxides in excellent yields (Scheme 1).

Table 1. Selective oxidation of sulfides using the H_2O_2 (2 equivalents)/HNO_3 (1 equivalent) system in ethanol.[a]

Entry	Sulfoxide	Yield %[b] (*t* (min))	Mp (°C) (ref.)	Entry	Sulfoxide	Yield %[b] (*t* (min))	Mp (°C) (ref.)
1		96 (7)	120–121 (*11a*)	8		95 (25)	171 (*11f*)
2[c]		97 (20)	162 (*10a*)	9		98 (14)	Oil (*11g*)
3		100 (18)	143 (*11b*)	10		98 (4)	28 (*10c*)
4		92 (40)	68 (*11c*)	11		100 (3)	Oil (*11d*)
5		98 (12)	121–122 (*11d*)	12[d]		93 (23)	201 (*11h*)
6		97 (20)	158 (*11e*)	13[c]		96 (14)	137 (*10a*)
7		97 (10)	Oil (*11f*)	14		97 (10)	30 (*10c*)

Notes: [a]The products were characterized by comparison of their spectroscopic and physical data with authentic samples synthesized by reported procedures. [b]Isolated yields. [c]Accompanied by sulfone <5%. [d]1,4-Dioxane was used as the solvent.

2. Result and discussion

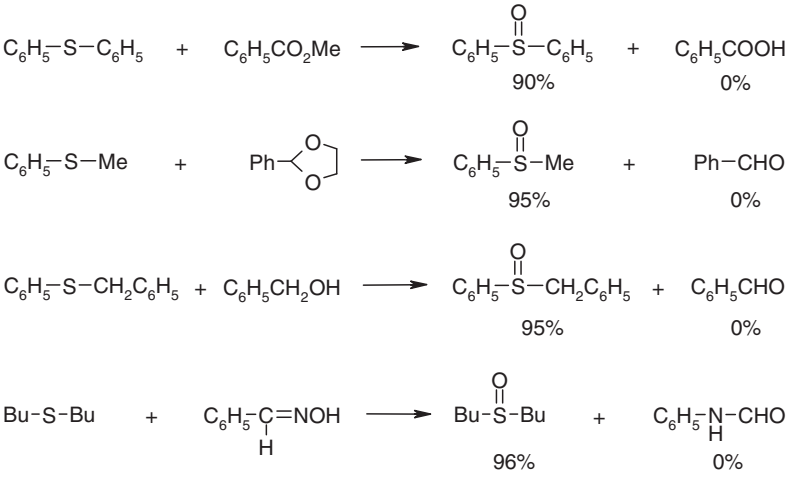
The choice of the organic solvent is of particular importance. Only ethanol was found suitable, giving rise to a relatively fast reaction rate at room temperature, while solvents such as dichloromethane, chloroform, toluene, and ethyl acetate had to be discarded.

The optimum ratio of sulfide to H_2O_2 to HNO_3 (1:2:1 equivalents) is found to be ideal for complete conversion of sulfides to sulfoxides, while with lesser amounts (for example, 1:2:0.75 and 1:1.5:1) the reaction remains incomplete. The use of excess oxidant (for example, 1:3:1 equivalents) increases the contamination of sulfone (<15%). Furthermore, HNO_3 is an effective agent only in the presence of H_2O_2. We studied the oxidation of 1 mmol of diphenyl sulfide as a model compound with 1 mmol of 65% HNO_3 as the oxidant. It was found that the reaction did not proceed at all after 2 h.

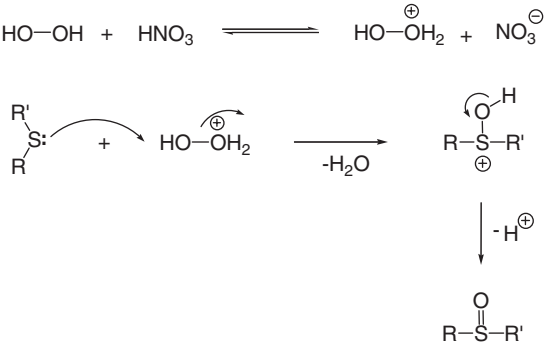
The generality of the method was examined using alkyl aryl, dialkyl, diaryl, cyclic, and heterocyclic sulfides (Table 1). It was discovered that a wide variety of sulfides can be selectively oxidized by this inexpensive system under mild conditions. The reagent system was chemoselective, tolerating various functional groups, such as carbonyl, nitro, C−C double bonds, and halide. Diphenyl sulfide may exert a little steric hindrance for oxidation as exhibited by the longer time of 40 min with 92% yield (Entry 4). The protocol worked efficiently in oxidizing 2-(benzylthio)benzimidazole to afford the corresponding sulfoxide (Entry 8). Interestingly, the presence of the ester group did not interfere with the oxidation process of the sulfide and desired sulfoxide was obtained in excellent yield (Entry 9).

In order to show the chemoselectivity of this method, we have also carried out several competitive reactions. The experimental results show that the reaction tolerates sensitive functional groups such as ester, acetal, alcohol, and oxime, and only the sulfur atom is selectively oxidized (Scheme 2). These observations clearly show that the method is applicable to the selective oxidation of sulfides in the presence of the earlier-mentioned functional groups and can be considered as a useful practical achievement for this transformation.

To access the feasibility of applying this method in a preparative scale, we carried out the oxidation of benzyl phenyl sulfide on a 30 mmol scale. As expected, the reaction proceeded smoothly, similar to the case on a smaller scale (Entry 1), and the desired product was obtained in 97% isolated yield.



Scheme 2. Reagents and conditions: molar ratio of substrates to H_2O_2 to HNO_3 (1:1:2:1), EtOH, 25 °C.



Scheme 3. Proposed mechanism for the oxidation of sulfides.

The possible mechanism for oxidation of sulfides to the corresponding sulfoxides using H_2O_2 in the presence of HNO_3 is outlined in Scheme 3.

3. Conclusion

In conclusion, nitric acid promotes the chemoselective and efficient oxidation of sulfides to sulfoxides with the environmentally friendly 30% H_2O_2, under mild reaction conditions. This method offers the advantage of shorter reaction times, excellent yields, large-scale synthesis, high chemoselectivity, and easy work-up. Therefore, our method can be considered the most outstanding methodology of sulfoxidation.

4. Experimental

4.1. *General procedure*

The sulfide (3 mmol) dissolved in EtOH (15 mL) was treated with 30% H_2O_2 (6 mmol, 0.6 mL) and 65% HNO_3 (3 mmol, 0.2 mL). After stirring at 25 °C for the time required, the reaction mixture was quenched by adding water (30 mL), extracted with ethyl acetate, and the extract dried with anhydrous $MgSO_4$. The filtrate was evaporated and the corresponding sulfoxide was obtained as the only product. Spectral data for selected compounds follow.

4.1.1. *Entry 1, Table 1: benzyl phenyl sulfoxide*

IR (KBr): 1034 cm^{-1}.
^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 3.99$ (d, $J = 12.53$ Hz, 1H), 4.11 (d, $J = 12.53$ Hz, 1H), 7.96–7.00 (m, 2H), 7.22–7.30 (m, 3H), 7.36–7.46 (m, 5H).
^{13}C NMR (50 MHz, $CDCl_3$): δ 63.5, 124.4, 128.2, 128.4, 128.8, 129.1, 130.4, 131.2, 142.7.

4.1.2. *Entry 7, Table 1: diallyl sulfoxide*

IR (neat): 1035, 1621 cm^{-1}.
^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 3.04$ (m, 2H), 3.07 (m, 2H), 5.00–5.09 (m, 4H), 5.66–5.80 (m, 2H).
^{13}C NMR (50 MHz, $CDCl_3$): δ 33.6, 117.5, 134.6.

4.1.3. *Entry 8, Table 1: (benzimidazol-2-yl) benzyl sulfoxide*

IR (neat): 1023 cm^{-1}.
^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 4.32$ (d, $J = 13.2$ Hz, 1H), 4.56 (d, $J = 13.2$ Hz, 1H,), 7.04–7.40 (m, 8H), 7.61–7.64 (m, 2H).
^{13}C NMR (50 MHz, $CDCl_3$): δ 60.3, 115.3, 122.8, 123.2, 127.3, 127.6, 127.8, 129.4, 150.9.

4.1.4. *Entry 9, Table 1: Methyl 2-(phenylsulfinyl)acetate*

IR (neat): 1038 cm^{-1}.
^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 3.65$ (d, $J = 13.6$ Hz, 1H), 3.68 (s, 3H), 3.83 (d, $J = 13.6$ Hz, 1H), 7.50–7.53 (m, 3H), 7.64–7.67 (m, 2H).
^{13}C NMR (50 MHz, $CDCl_3$): δ 51.8, 60.5, 123.0, 128.4, 130.8, 141.9, 164.2.

4.1.5. *Entry 11, Table 1: allyl phenyl sulfoxide*

IR (neat): 1043, 1660 cm^{-1}.
^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 3.37$–3.57 (m, 2H), 5.08–5.28 (m, 2H), 5.47–5.68 (m, 1H), 7.42–7.54 (m, 5H).
^{13}C NMR (50 MHz, $CDCl_3$): δ 60.7, 123.9, 124.3, 125.2, 129.0, 131.1, 142.8.

4.1.6. *Entry 13, Table 1: Benzyl 4-bromobenzyl sulfoxide*

IR (KBr, cm^{-1}) 1029.
^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.78 (d, $J = 13.1$ Hz, 1H), 3.89 (d, $J = 13.1$ Hz, 1H), 3.95 (s, 2H), 7.2 (d, $J = 8.3$ Hz, 2H), 7.32–7.33 (m, 2H), 7.40–7.44 (m, 3H), 7.54 (d, $J = 8.3$ Hz, 2H).
^{13}C NMR (50 MHz, $CDCl_3$): δ 56.2, 57.5, 122.6, 128.4, 129.1, 129.2, 129.8, 130.1, 131.8, 132.1.

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References

(1) Patai, S.; Rappoport, Z.; Stirling, C.J.M., Eds. *The Chemistry of Sulphones and Sulphoxides*; John Wiley: New York, 1988; Vol. 3, p 56.
(2) Page, P.C.B., Ed. *Organosulfur Chemistry II*. Springer: Berlin, 1999.
(3) Huang, J.-Y.; Li, S.-J.; Wang, Y.-G. *Tetrahedron Lett*. **2006,** *47,* 5637–5640.
(4) Gross, Z.; Mahammed, A. *J. Mol. Catal. A Chem*. **1999,** *142*, 367–372.
(5) (a) Kowalski, P.; Mitka, K.; Ossowska, K.; Kolarska, Z. *Tetrahedron* **2005,** *61,* 1933–1953; (b) Baciocchi, E.; Gerini, M.F.; Lapi, A. *J. Org. Chem*. **2004,** *69*, 3586–3589; (c) Xu, W.L.; Li, Y.Z.; Zhang, Q.S.; Zhu, H.S. *Synthesis* **2004,** 227–232; (d) Sabir, H.M.; Chandrasekar, D.M.; Madhavi, A.K. *Synth. Commun*. **1998,** *28,* 939–943; (e) Koposov, A.Y.; Zhdankin, V.V. *Synthesis* **2005,** 22–24.
(6) (a) Kim, S.S.; Rajagopal, G. *Synthesis* **2003,** 2461–2463; (b) Li, Z.; Xia, C.-G.; Xu, C.-Z. *Tetrahedron Lett*. **2003,** *44,* 9229–9232; (c) Li, Z.; Xia, C.-G. *J. Mol. Catal. A Chem*. **2004,** *214,* 95–101; (d) Jeyakumar, K.; Chand, D.K. *Tetrahedron Lett*. **2006,** *47*, 4573–4576.
(7) (a) Yuan, Y.; Bian, Y. *Tetrahedron Lett*. **2007,** *48,* 8518–8520; (b) Tohma, H.; Takizawa, S.; Watanabe, H.; Kita, Y. *Tetrahedron Lett*. **1998,** *39,* 4547–4550; (c) Ochiai, M.; Nakanishi, A.; Ito, T. *J. Org. Chem*. **1997,** *62,* 4253–4259; (d) Mohammadpoor-Baltork, I.; Memarian, H.R.; Bahrami, K. *Can. J. Chem*. **2005,** *83,* 115–121; (e) Prasanth, K.L.; Maheswaran, H. *J. Mol. Catal. A Chem*. **2007,** *268*, 45–49.
(8) Jones, C.W., Ed. *Applications of Hydrogen Peroxide and Derivatives*; Royal Society of Chemistry: Cambridge, 1999.
(9) Strukul, G., Ed. *Catalytic Oxidations with Hydrogen Peroxide as Oxidant*; Kluwer Academic Publishers: Dordrecht, 1992.
(10) (a) Bahrami, K. *Tetrahedron Lett*. **2006,** *47,* 2009–2012; (b) Khodaei, M.M.; Bahrami, K.; Khedri, M. *Can. J. Chem*. **2007,** *85,* 7–11; (c) Khodaei, M.M.; Bahrami, K.; Karimi, A. *Synthesis* **2008,** 1682–1684; (d) Bahrami, K.; Khodaei,

M.M.; Kavianinia, I. *Synthesis* **2007,** 547–550; (e) Bahrami, K.; Khodaei, M.M.; Naali, F. *J. Org. Chem*. **2008,** *73*, 6835–6837; (f) Bahrami, K.; Khodaei, M.M.; Naali, F. *Synlett* **2009,** 569–572; (g) Bahrami, K.; Khodaei, M.M.; Tirandaz, Y. *Synthesis* **2009,** 369–371; (h) Khodaei, M.M.; Bahrami, K.; Tirandaz, Y. *J. Sulfur Chem*. **2009,** *30*, 581–584; (i) Bahrami, K.; Khodaei, M.M.; Farrokhi, A. *Tetrahedron* **2009,** *65*, 7658–7661; (j) Bahrami, K.; Khodaei, M.M.; Soheilizad, M. *Synlett* **2009,** 2773–2776; (k) Bahrami, K.; Khodaei, M.M.; Soheilizad, M. *J. Org. Chem*. **2008,** *74*, 9287–9291.

(11) (a) Ali, M.H.; Leach, D.R.; Schmitz, C.E. *Synth. Commun*. **1998,** *28*, 2969–2983; (b) Clark, N.G.; Cranham, J.E.; Greenwood, D.; Marshall, J.R.; Stevenson, H.A. *J. Sci. Food Agric*. **1957,** *8*, 566–570; (c) Kim, S.S.; Nehru, K.; Kim, S.S.; Kim, D.W.; Jung, H.C. *Synthesis* **2002,** 2484–2486; (d) Choudary, B.M.; Bharathi, B.; Reddy, C.V.; Kantam, M.L. *J. Chem. Soc. Perkin Trans. I*, **2002,** 2069–2074; (e) Brookes, R.F.; Clark, N.G.; Cranham, J.E.; Greenwood, D.; Marshall, J.R.; Stevenson, H.A. *J. Sci. Food Agric*. **1958,** *9*, 111–115; (f) Rafiee, E.; Mohammadpoor Baltork, I.; Tangestaninejad, S.; Azada, A.; Moinee, S. *Z. Nat. B: Chem. Sci*. **2006,** *61*, 601–606; (g) Batigalhia, F.; Zaldini-Hernandes, M.; Ferreira, A.G.; Malvestiti, I.; Cass, Q.B. *Tetrahedron* **2001,** *57*, 9669–9676; (h) Ali, M.H.; Stricklin, S. *Synth. Commun*. **2006,** *36*, 1779–1786.