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Nitric acid in the presence of supported P_2O_5 on silica gel: an efficient and novel reagent for oxidation of sulfides to the corresponding sulfoxides

Abdol R. Hajipour,[a,b,*] Behzad Kooshki[a] and Arnold E. Ruoho[a]

[a]*Pharmaceutical Research Laboratory, College of Chemistry, Isfahan University of Technology, Isfahan 84156, Iran*
[b]*Department of Pharmacology, University of Wisconsin Medical School, 1300 University Avenue, Madison, WI 53706-1532, USA*

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Abstract—This paper describes an efficient and easy method for oxidation of sulfides **1** to their corresponding sulfoxides **2** with nitric acid in the presence of supported P_2O_5 on silica gel under solvent-free conditions in high yields.

Sulfoxides play an important role in organic chemistry.[1–4] They have been utilized extensively in carbon–carbon bond formation reactions and as versatile building blocks in organic synthesis.[5,6] Oxidation of sulfides is a very useful route for preparation of sulfoxides. Several methods are available for conversion of sulfides to sulfoxides.[7–22] However, most of the existing methods use expensive, toxic, or rare oxidizing reagents that are difficult to prepare. Many of these procedures also suffer from poor selectivity and also often suffer from lack of generality and economic applicability. Therefore, there is a need for a simple, less expensive, general, and safer method for conversion of sulfides to sulfoxides. Reactions under solvent-free conditions have received increasing attention in recent years. The main advantage of these methods over conventional homogenous reactions is that they provide greater selectivity, proceed with enhanced reaction rates, give cleaner products, and involve simple manipulation.[23,24]

In continuation of our ongoing program to develop efficient reagents for oxidizing organic compounds,[23–26] we now wish to report a facile and selective method for oxidation of sulfides **1** to their corresponding sulfoxides **2** with 64% nitric acid in the presence of supported P_2O_5 on silica gel under solvent-free conditions. The P_2O_5/silica gel was prepared by mixing a mixture of P_2O_5 and silica gel (0.063–0.2 mm) in a mortar and grinding with a pestle for 1 min to obtain a homogenous mixture. This reagent is stable and can be kept at room temperature for months without losing its activity. Sulfides **1** are mixed with 1 equiv of P_2O_5/silica gel in a mortar and then oxidized with one equivalent of HNO_3 64% to the corresponding sulfoxides **2** (Table 1, Scheme 1).[27] After extraction of the product with ether and evaporating the solvent, the product was purified by column chromatography to produce the product in excellent yields and short a reaction time. This method offers a simple, general, selective, highly efficient, and green route for converting sulfides **1** to their corresponding sulfoxides **2** without over oxidation. As shown in Table 1 the reaction time for oxidation is short, the reaction time for aromatic sulfides with electron withdrawing groups is longer than aromatic sulfides with electron releasing groups.

The generality of the method was examined using alkyl aryl, dialkyl, diaryl, cyclic sulfides, and also aryl disulfides. It was discovered that a wide variety of sulfides can be selectively oxidized by this inexpensive reagent under mild conditions (Table 1). The rate of the reactions of arylalkyl and diaryl sulfides are not dependent on the substituents of the aromatic ring. The reagent was chemoselective, tolerating various functional groups, such as, methoxy, carbonyl, hydroxy, nitro, nitrile, C=C double bonds, and halide. This method is a versatile procedure for synthesis of α-chloro sulfoxides

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Keywords: Nitric acid; Supported P_2O_5; Sulfides; Sulfoxides.

* Corresponding author. Tel.: +983113913262; fax: +983113912350; e-mail: haji@cc.iut.ac.ir

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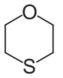
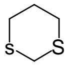
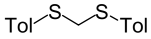
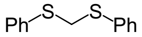
Table 1. Oxidation of sulfides to sulfoxides with 64% HNO_3 in the presence of P_2O_5/silica gel[a,b]

Entry	R_1	R_2	Reaction time (min)	Yield[c] (%)
1	Ph	Me	4	98
2	Ph	*n*-Bu	6	98
3	Ph	$PhCH_2$	6	95
4	$PhCH_2$	Me	6	96
5	$PHCH_2$	*n*-Bu	5	92
6	$PhCH_2$	$PhCH_2$	5	93
7	$4\text{-}MeC_6H_4$	Me	5	95
8	$4\text{-}ClC_6H_4$	Me	6	85
9	C_4H_9	C_4H_9	8	83
10	1-Naphthyl	Me	5	93
11	Pr	Pr	8	82
12	Allyl	Allyl	6	80
13	Ph	CH_2Cl	5	88
14	$4\text{-}MeC_6H_4$	CH_2Cl	5	87
15	1-Naphthyl	$PhCH_2$	5	90
16	1-Naphthyl	CH_2Cl	5	89
17	$4\text{-}NO_2C_6H_4$	Me	6	93
18	$4\text{-}CHOC_6H_4$	Me	5	97
19	$4\text{-}OHCH_2C_6H_4$	Me	7	94
20	$4\text{-}NCC_6H_4$	Me	6	92
21	Ph	CH_2CH_2OH	8	84
22	$4\text{-}MeOC_6H_4$	CH_2Cl	5	95
23	$–(CH_2)_4–$	—	8	90
23	$–(CH_2)_3–$	—	8	92
24		—	6	89
25		—		
26		—	5	80[d]
27		—	6	78[e]
28		—	6	74[f]

[a] Confirmed by comparison with authentic samples.[14–19]

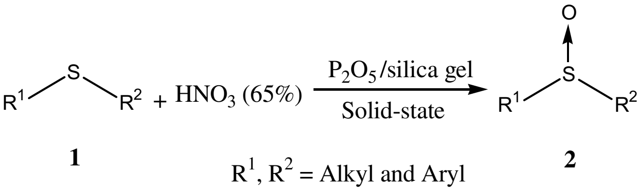
[b] Substrate/oxidant (1:1.2 mmol).

[c] Yield of isolated pure products.

[d] 10% disulfoxide.

[e] 15% disulfoxide.

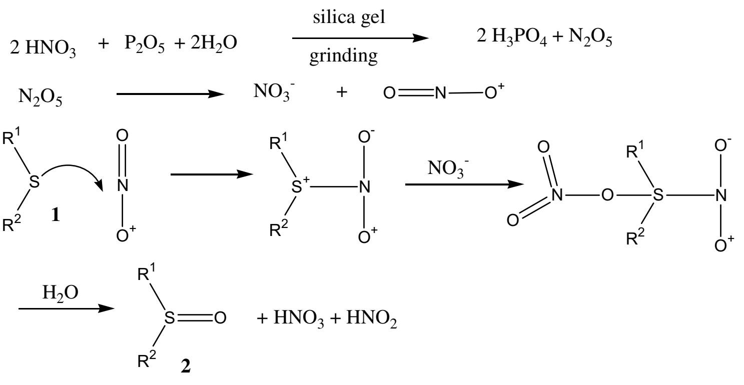
[f] 12% disulfoxide.



Scheme 1.

from their corresponding sulfides (Table 1, entries 13 and 14). Also this procedure is useful for partial oxidation of formaldehyde *S*,*S*-diphenyl acetal to the corresponding monosulfoxides in good yields (Table 1, entries 26–28).

The possible mechanism for oxidation of sulfides **1** to the corresponding sulfoxides **2** using nitric acid in the



Scheme 2.

presence of supported P_2O_5 on silica gel under solvent-free conditions is outlined in Scheme 2.

In conclusion, we report an easy and versatile method for converting sulfides to their corresponding sulfoxides with the following advantages: (a) our reagent is inexpensive and can be easily handled, can be stored for months without losing its activity. (b) The procedure is simple and occurs under solvent-free conditions at room temperature. (c) The yield of sulfoxide is high and the reaction time is short. (d) The isolation of the product is straightforward.

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27. Preparation of reagent [P_2O_5/silica gel (64%, w/w)]: In a mortar 4.5 g of P_2O_5 (31.69 mmol) and 2.5 g of silica gel (0.063–0.2 μm) was ground for 1 min to a homogeneous mixture.

Typical procedure for oxidation of sulfides **2** to sulfoxides **3** with reagent **1**: In a mortar, 0.2 g of P_2O_5/silica gel (64%, w/w) (1 mmol) and thioanisole (1 mmol, 0.124 g) was ground for 30 s and then 0.5 ml of HNO_3 65% was added and the mixture was ground with a pestle for 4 min. After disappearance of the starting sulfide monitored by TLC using EtOAc–cyclohexane (2:8), the product was extracted by Et_2O (2×10 ml) and filtered through a sintered glass funnel, and dried ($MgSO_4$). The solvent was removed under reduced pressure. The residue was purified by column chromatography using silica gel (EtOAc–cyclohexane, 2:8) to afford methyl phenyl sulfoxide as a colorless oil in 98% yield as revealed from ^1H NMR analysis, mp 30–32 °C [Lit.[16] mp 32–33 °C]. ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 2.7$ (s, 3H), 7.48–7.56 (m, 3H), 7.64–7.67 (m, 2H). IR (film): 692, 754, 954, 1046, 1092, 1415, 1446, 1477, 2915, 3000, 3062 cm^{-1}.