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Silica sulfuric acid/$NaNO_2$ as a novel heterogeneous system for production of thionitrites and disulfides under mild conditions

Mohammad Ali Zolfigol*

Department of Chemistry, College of Science, Bu-Ali Sina University, P.O. Box 4135, Hamadan 65174, Iran

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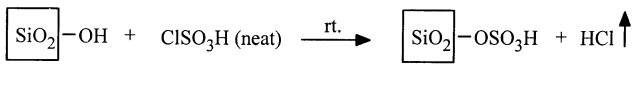
Abstract—Neat chlorosulfonic acid reacts with silica gel to give silica sulfuric acid in which sulfuric acid is immobilized on the surface of silica gel via covalent bond. Thiols can be readily converted to their corresponding thionitrites with a combination of silica sulfuric acid, wet SiO_2 and sodium nitrite in dichloromethane at room temperature. Disulfides result from the homolytic cleavage of the sulfur–nitrogen bond of the unstable thionitrites and subsequent coupling of the resultant thiyl radicals.

Any reduction in the amount of sulfuric acid needed and/or any simplification in handling procedures is required for risk reduction, economic advantage and environment protection.[1] In addition, there is current research and general interest in heterogeneous systems because of the importance such systems have in industry and in developing technologies.[2] In continuation of our studies on the application of inorganic acidic salts we found that silica gel reacts with chlorosulfonic acid to give silica sulfuric acid (**I**). It is interesting to note that the reaction is easy and clean without any work-up procedure because HCl gas is evolved from the reaction vessel immediately (Scheme 1).

We hoped that the silica sulfuric acid (**I**) would be a superior proton source to all of the reported acidic solid supports or acidic resins such as polystyrene sulfonic acid and Nafion-H[3] for running reactions under heterogeneous conditions. Therefore, we were interested in using this inorganic acidic resin (**I**) for the in situ generation of HNO_2 when used in conjunction with $NaNO_2$, wet SiO_2 and an organic solvent. On the other hand, thionitrites have not been as widely studied as their oxygen counterparts alkyl nitrites, generally because of their reduced stability.[4] However, in recent years there has been much interest generated in the chemistry and biochemistry of nitrosothiols,[4,5] since (a) they are being examined as possible drugs to effect vasodilatation and to reduce platelet aggregation, (b) they are now believed to play an important part in some of the physiological processes involving nitric oxide[5] and (c) they are being investigated as a source of thiyl radicals[6] or as nitrosating agents.[7]



I

Scheme 1.

The most general nitrosating reagent is nitrous acid, generated from sodium nitrite and mineral acid in water or in mixed alcohol–water solvents. Other nitrosating agents have been used successfully to synthesize thionitrites, notably alkyl nitrites, nitrosyl salts, dinitrogen trioxide, dinitrogen tetroxide,[4] oxalic acid dihydrate[8] or inorganic acidic salts[9] and sodium nitrite. Very recently, we among many others, have demonstrated that heterogeneous reagent systems have many advantages such as simple experimental procedures, mild reaction conditions and minimization of chemical wastes as compared to the liquid phase counterparts.[10] Therefore, we decided to apply silica sulfuric acid (**I**)/$NaNO_2$ as a new heterogeneous system for the nitrosation of thiols. We wish to report a simple, cheap and convenient method for the effective nitrosation of thiols and production of disulfides under mild and heterogeneous conditions (Scheme 2).

Different kinds of thiols were subjected to the nitrosation reaction in the presence of $NaNO_2$, wet SiO_2 (50% w/w) and silica sulfuric acid (**I**) in dichloromethane. The nitrosation reactions were performed under mild and completely heterogeneous conditions. A bright-red heterogeneous solution was obtained immediately due to the formation of thionitrite. Disulfides result from the homolytic cleavage of the sulfur–nitrogen bond of the unstable thionitrite and subsequent coupling of the resultant thiyl radicals.[11,12] Therefore, this method could be used for conversion of thiols to their corresponding disulfides quantitatively with increasing temperature (Scheme 2 and Table 1).

Keywords: silica sulfuric acid; thiols; thionitrites; disulfides.

* Tel.: +98-811-8271075; fax: +98-811-8272404;
e-mail: zolfi@basu.ac.ir

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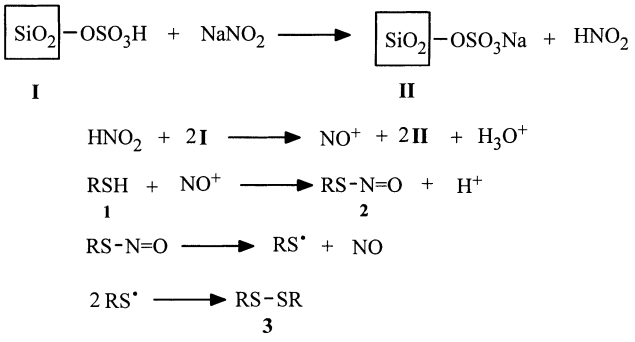
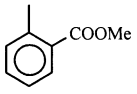
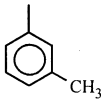


1, 2, 3	R	1, 2, 3	R
a	$PhCH_2$	f	C_2H_4OH
b	*n*-Bu	g	Ph
c	*n*-C_8H_{17}	h	C_3H_6SH
d	Cyclohexyl		
e		i	

Scheme 2.

Table 1. Nitrosation of thiols to their corresponding unstable nitrosothiols (**2**) and production of disulfides (**3**) with a combination of silica sulfuric acid (**I**), $NaNO_2$ (**II**) and wet SiO_2 (50% w/w) in dichloromethane at room temperature

Entry	Substrate	Product	Time (min)	Yields[a] (%)	Mp (°C)	
					Found	Reported
1	**1a**	**3a**	2	97	94–68	69–70[14]
2	**1b**	**3b**	1.5	98	Oil	
3	**1c**	**3c**	1.5	95	Oil	
4	**1d**	**3d**	3	99	Oil	
5	**1e**	**3e**	2	97	135–137	138[17]
6	**1f**	**3f**	5	98	25	24–24.5[14]
7	**1g**	**3g**	0.75	95	56–58	59–60[11–17]
8	**1h**	–[b]	1	–[b]	–	
9	**1i**	**3i**	3	98	42–45	45–47[17]

[a] Isolated yields.
[b] Polymerization occurred.

Although the reaction occurs without wet SiO_2, the reaction time period is very long and complete only after several days. Therefore we think that the presence of wet SiO_2 acts as a media and provides a heterogeneous effective surface area for in situ generation of HNO_2. Nitrosation did not occur in the absence of silica sulfuric acid (**I**).

In conclusion, silica sulfuric acid (**I**) is a good proton source in terms of convenience, cheapness, easy production, insolubility to all organic solvents. Practical and efficient nitrosation–oxidation of thiols were achieved by the present methodology. The cheapness and availability of the reagents, easy procedure and work-up make this method attractive for the large-scale operations.

1. Experimental

1.1. General

Chemicals were purchased from Fluka, Merck, Riedel-dehaen AG and Aldrich chemical companies. Disulfides were characterized by comparison of their spectral (IR, ^1H NMR, and TLC) and physical data with the authentic samples.[8,9,11–17]

1.2. Preparation of silica sulfuric acid

A 500 mL suction flask was used. It was equipped with a constant-pressure dropping funnel containing chlorosulfonic acid (23.3 g, 0.2 mol) and gas inlet tube for conducting HCl gas over an adsorbing solution i.e. water. Into it were charged 60.0 g of silica gel. Chlorosulfonic acid was added dropwise over a period of 30 min at room temperature. HCl gas evolved from the reaction vessel immediately (Scheme 1). After the addition was complete the mixture was shaken for 30 min. A white solid (silica sulfuric acid) of 76.0 g was obtained.

1.3. Typical experimental procedure

To a solution of thiophenol (0.220 g, 2 mmol) in CH_2Cl_2

(10 mL), **I** (1.520 g, 4 mmol), wet SiO_2 (50% w/w) (0.4 g) and $NaNO_2$ (0.257 g, 4 mmol) were added. The resulting mixture was stirred at room temperature and a bright red heterogeneous solution was obtained immediately. Thionitrites were characterized by comparison of their UV spectra with those reported in the literature.[11,12] Typical spectra are as follows: λ_{max} (CH_2Cl_2): PhSNO, 380, 529, 570 nm]. A pale yellow solution was also obtained after 30 min and then filtered. The residue was washed with CH_2Cl_2 (2×10 mL). Anhydrous Na_2SO_4 (3 g) was added to the filtrate. After 15 min, the resulting mixture was filtered again. Dichloromethane was removed by water bath (40–50°C) and simple distillation. The yield was 0.210 g (95%) of crystalline brownish solid (**3g**), mp 56–58°C [Lit.[11–17] mp 58–60°C].

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References

1. Riego, J. M.; Sedin, Z.; Zaldivar, J. M.; Marziano, N. C.; Tortato, C. *Tetrahedron Lett.* **1996**, *37*, 513.
2. Turro, N. J. *Tetrahedron* **1987**, *43*, 1589.
3. Olah, G. A.; Molhotra, R.; Narang, S. C. *J. Org. Chem.* **1987**, *43*, 4628.
4. (a) Williams, D. L. H. *Supplement F2: The Chemistry of Amino, Nitroso, Nitro and Related Groups*; Wiley: New York, 1996 pp 665–682 and references cited therein. (b) Keefer, L. K.; Williams, D. L. H. *Methods in Nitric Oxide Reseach*; Wiley: New York, 1996; pp 509–519.
5. (a) Williams, D. L. H. *Transition Met. Chem.* **1996**, *21*, 189. (b) Beloso, P. H.; Williams, D. L. H. *Chem. Commun.* **1997**, 89. (c) Nobel, D. R.; Swift, H. R.; Williams, D. L. H. *Chem. Commun.* **1999**, 2317. (d) Munro, A. P.; Williams, D. L. H. *Can. J. Chem.* **1999**, *77*, 550. (e) Munro, A. P.; Williams, D. L. H. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1989. (f) Holmes, A. J.; Williams, D. L. H. *Chem. Commun.* **1998**, 1711. (g) Amado, S.; Dicks, A. P.; Williams, D. L. H. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1869. (h) Coupe, P. J.; Williams, D. L. H. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1057. (i) Williams, D. L. H. *Acc. Chem. Res.* **1999**, 869. (j) Fukuto, J. M.; Ignarro, L. J. *Acc. Chem. Res.* **1997**, 149.
6. Oae, S.; Kim, Y. H.; Fukushima, D. *Chem. Lett.* **1977**, 893.
7. Cornelis, A.; Depaye, N.; Gerstmans, A.; Laszlo, P. *Tetrahedron Lett.* **1983**, *24*, 3103.
8. Zolfigol, M. A.; Nematollahi, D.; Mallakpour, S. E. *Synth. Commun.* **1999**, *29*, 2277.
9. Zolfigol, M. A. *Synth. Commun.* **2000**, *30*, 1593.
10. (a) Zolfigol, M. A.; Kiany-Borazjani, M.; Sadeghi, M. M.; Mohammadpoor-Baltork, I.; Memarian, H. R. *Synth. Commun.* **2000**, *30*, 551. (b) Zolfigol, M. A.; Kiany-Borazjani, M.; Sadeghi, M. M.; Memarian, H. R.; Mohammadpoor-Baltork, I. *Synth. Commun.* **2000**, *30*, 2945. (c) Zolfigol, M. A.; Kiany-Borazjani, M.; Sadeghi, M. M.; Memarian, H. R.; Mohammadpoor-Baltork, I. *J. Chem. Res. (S)* **2000**, 197. (d) Zolfigol, M. A.; Mallakpour, S. E. *Synth. Commun.* **1999**, *29*, 4061. (e) Zolfigol, M. A.; Kiany-Borazjani, M.; Mallackpour, S. E.; Nassr-Isfahani, H. *Synth. Commun.* **2000**, *30*, 2573. (f) Zolfigol, M. A.; Madrakian, E.; Ghaemi, E. *Indian J. Chem.* **2000**, *39B*, 308. (g) Zolfigol, M. A.; Mallakpour, S. E.; Ghaemi, E.; Madrakian, E. *Synth. Commun.* **2000**, *30*, 1689. (h) Zolfigol, M. A.; Kiany-Borazjani, M.; Sadeghi, M. M.; Mohammadpoor-Baltork, I.; Memarian, H. R. *Synth. Commun.* **2000**, *30*, 3919. (i) Zolfigol, M. A. *Synth. Commun.* **1999**, *29*, 905. (j) Zolfigol, M. A.; Ghaemi, E.; Madrakian, E.; Kiany-Borazjani, M. *Synth. Commun.* **2000**, *30*, 2057. (k) Zolfigol, M. A.; Shirini, F.; Ghorbani Choghamarani, A.; Taqian-nasab, A.; Keypour, H.; Salehzadeh, S. *J. Chem. Res. (S)* **2000**, 420. (l) Zolfigol, M. A.; Ghorbani Choghamarani, A.; Shirini, F.; Keypour, H.; Salehzadeh, S. *Synth. Commun.* **2001**, *31*, 359. (m) Zolfigol, M. A.; Zebarjadian, M. H.; Chehardoli, G.; Mallakpor, S. E.; Shamsipur, M. *Tetrahedron* **2001**, *57*, 1627. (n) Zolfigol, M. A.; Ghaemi, E.; Madrakian, E. *Molecules* **2001**, *6*, 614. (o) Zolfigol, M. A.; Bagherzadeh, M.; Madrakian, E.; Ghaemi, E.; Taqian-nasab, A. *J. Chem. Res. (S)* **2001**, 140. (p) Zolfigol, M. A.; Sadeghi, M. M.; Mohammadpoor-Baltork, I.; Ghorbani Choghamarani, A.; Taqian-nasab, A. *Asian J. Chem.* **2001**, *13*, 887. (q) Zolfigol, M. A.; Shirini, F.; Ghorbani Choghamarani, A.; Shiri, A.; Keypour, H.; Salehzadeh, S. *Asian J. Chem.* **2001**, *13*, 849. (r) Zolfigol, M. A. *Molecules* **2001**, *6*, 694. (s) Zolfigol, M. A.; Bagherzadeh, M.; Ghorbani Choghamarani, A.; Keypour, H.; Salehzadeh, S. *Synth. Commun.* **2001**, *31*, 1661. (t) Zolfigol, M. A.; Bagherzadeh, M.; Chehardoli, G.; Mallakpor, S. E. *Synth. Commun.* **2001**, *31*, 1149.
11. Iranpoor, N.; Firouzabadi, H.; Zolfigol, M. A. *Synth. Commun.* **1998**, *28*, 367.
12. Firouzabadi, H.; Iranpoor, N.; Zolfigol, M. A. *Synth. Commun.* **1998**, *28*, 1179.
13. Wallace, T. J. *J. Org. Chem.* **1966**, *31*, 3071.
14. Ogura, F.; Yamaquchi, H.; Otsubo, T.; Tanaka, H. *Bull. Chem. Soc. Jpn* **1982**, *55*, 641.
15. Hirano, M.; Yakabe, S.; Fukami, M.; Mirimoto, T. *Synth. Commun.* **1997**, *27*, 2783.
16. Ramadas, K.; Srinivasan, N. *Synth. Commun.* **1995**, *25*, 227.
17. *Dictionary of Organic Compounds*, 5th ed.; 1982.