

Molybdate sulfuric acid (MSA): a novel and efficient solid acid reagent for the oxidation of thiols to symmetrical disulfides

Morteza Montazerzohori,* Bahador Karami, and Mahbobeh Azizi

Department of Chemistry, Yasouj University, Yasouj 75918-74831, P. O. Box-353 Iran

E- mail: mmzohori@mail.yu.ac.ir, mmzohory@yahoo.com

Abstract

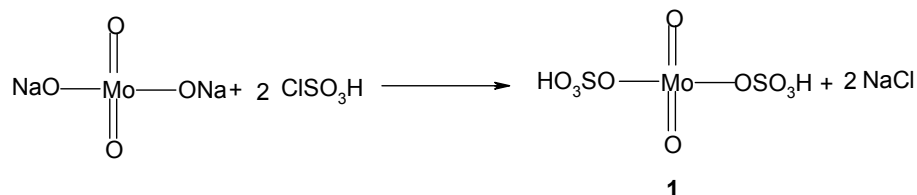
Wet molybdate sulfuric acid (MSA), as a new solid acid can be used in combination with sodium nitrite to transform a variety of thiols to the corresponding symmetric disulfides under mild and heterogeneous conditions. The process has several advantages: the reagents are inexpensive and non-hazardous, the reaction is clean, fast, high-yielding and MSA can be readily removed by filtration and re-used after treatment with HCl without loss of activity. Further, only thiol oxidation to disulfide was observed.

Keywords: Disulfides, oxidation, thiols, molybdate sulfuric acid

Introduction

Currently, the search about application of heterogeneous chemical systems is an active field both in industry and academia especially in view of simplified handling procedures, reduction of corrosion, avoidance of undesired by-products, clean and easily work-up procedures. With regard to the wide application of acids as reagents or catalysts in organic chemistry, the introduction of an inorganic solid acid can be useful in this direction. Several solid acids such as silica sulfuric acid¹ and *Nafion-H*² have been used for a wide variety of chemical transformations, *e.g.*, preparation of disulfides from thiols¹, oxidation of 1,4-dihydropyridines,³ *N*-nitrosation of secondary amines,⁴ acetal deprotection,⁵ oxidation of alcohols,⁶ alkylation and acylation,⁷ isomerization,⁸ transalkylation,⁹ nitration,¹⁰ ether and ester synthesis,¹¹ acetal formation,¹² and rearrangements.¹³ Disulfides have an important role in chemical synthesis. In biological systems they control the cellular redox potential and prevent oxidative damage.¹⁴⁻¹⁵ Several methods based on oxidative S-S coupling have been reported for the synthesis of disulfides from thiols and protected thiols including coupling with redox dyes¹⁶, diazo-compounds,¹⁷ sulfoxides,¹⁸ halogens,¹⁹ H₂O₂,²⁰ KMnO₄/CuSO₄,²¹ DMSO/I₂,²² sodium perborate,²³ Bismuth(III) Nitrate Pentahydrate,²⁴ 1,3-Dibromo-5,5-Dimethylhydantoin²⁵ and electrochemical methods.²⁶ In continuation of our recent studies²⁷ on the application of inorganic

solid acids, we herein present molybdate sulfuric acid (MSA) as a new solid acid. MSA (**1**) was prepared according to a previously published protocol²⁷ as shown in Scheme 1.



Scheme 1

This inorganic solid acid in combination with NaNO_2 was observed to be an efficient and heterogeneous system for the oxidation of thiols.

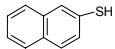
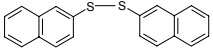
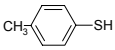
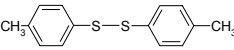
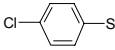
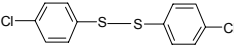
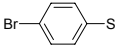
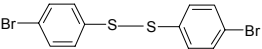
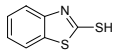
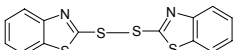

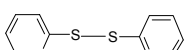

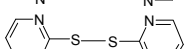

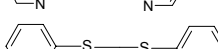
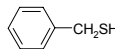
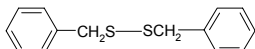
Results and Discussion

First, we were interested to examine MSA (**1**) as a H^+ source in combination with various oxidants in organic solvents. For this reason, we chose wet 10% (w/w) MSA/ NaNO_2 for the oxidative coupling of a series of aliphatic and aromatic thiols (**1-13a**) which were transformed to the corresponding disulfides (**1-13b**) in CH_2Cl_2 or methanol. All reactions were run under mild and heterogeneous conditions at room temperature and gave the expected disulfides in good-to-excellent yields (Table 1). Based on other literature reports,^{1a, 28-29} we propose that the reactions proceed *via* formation of NO^+ upon reaction of wet MSA(**1**) with NaNO_2 producing thionitrite **2** which converts to the related disulfides due to its instability under the reaction conditions according to Scheme 2.

The above proposed mechanism shows that the MSA (**1**) after a process remains as its sodium salt and therefore can be reusable acidic reagent. Thus, the recovered MSA from the oxidation reaction of, *e.g.*, **5a** was used again in another reaction with NaNO_2 , which afforded the related disulfide **5b** in 92% yield (compared to 98% in the first run; see Table 1).

For increasing the rate of the oxidation reaction one could use an excess of NaNO_2 , but because of the probable nitrosation of the formed disulfides, this was avoided (Table 1). Finally, it is noteworthy to point to the role of H_2O in the MSA/ NaNO_2 system. We decided to run a series of parallel reactions under anhydrous conditions or hydrous conditions (wet MSA(**1**)). The results clearly indicate that H_2O is essential for the generation of HNO_2 (see Scheme 2), since no oxidation was observed under strictly anhydrous conditions.

Table 1. Oxidation of thiols to the corresponding disulfides with wet MSA(1)/ NaNO₂ in dichloromethane or methanol at room temperature

Entry	Thiol (a)	Disulfide (b) ^a	Time (min.)	Yield ^b (%)	M.p.(°C) Found (Lit.)
1			10	94	144-146 (142-145) ²⁴
2			10	96	43-44 (44-45) ²⁴
3			20	95	72-73 (70-71) ²⁴
4			7	94	90-92 (91-93) ²⁴
5			15	90	177-179 (177-180) [*]
6			10	90	55-56 (55-67) ²⁴
7			10	90	133-135 (134-136) ³²
8			15	95	59-60 (58-59) ²⁴
9	CH ₃ (CH ₂) ₂ CH ₂ SH	(CH ₃ (CH ₂) ₂ CH ₂ S) ₂	18	85	Oil ²⁵
10	CH ₃ (CH ₂) ₆ CH ₂ SH	(CH ₃ (CH ₂) ₆ CH ₂ S) ₂	20	84	Oil ²⁵
11	n-BuSH	(n-BuS) ₂	20	90	Oil ²⁴
12	c-C ₆ H ₁₁ SH	(c-C ₆ H ₁₁ S) ₂	20	85	Oil ²⁴
13			16	90	68-70 (70-71) ²⁴

^a Identified by comparison with those reported in the literature. ^b Refers to isolated yields.

* Chemical and Reagents 2005-2007 MERCK.

water and not in the organic solvents. Characteristic IR bands (KBr, cm^{-1}); 3600-2200 (OH, bs), 1230-1150 (S=O, bs), 1050 (S-O, m), 1010 (S-O, m), 880-840 (Mo=O, m) and 450 (Mo-O, m).

Oxidation of thiols: a general procedure. To a solution of 2 mmol of thiol in 8 mL dichloromethane or methanol, 1 mmol of wet MSA (**1**) (10 % w/w) and 2 mmol of NaNO_2 were added. The reaction mixture was stirred at room temperature and a light-green heterogeneous solution was obtained rapidly and then disappeared. The reaction was monitored by TLC (n-hexane: ethyl acetate, 15: 5). The reaction mixture was filtered and washed with 2×4 mL dichloromethane or methanol (for some products). Dichloromethane or methanol was removed by water bath. The yields were summarized in Table 1.

Acknowledgements

The authors gratefully acknowledged partial support of this work by the Yasouj University, Yasouj, Iran.

References

1. (a) Zolfigol, M. A. *Tetrahedron* **2001**, *57*, 9509. (b) Shaabani, A.; Sol eimani, K.; Bazgir, A. *Synth. Commun.* **2004**, *34*, 3303.
2. Olah, G. A.; Molhotra, R. S.; Narang, C. *J. Org. Chem.* **1987**, *43*, 4628.
3. Zolfigol, M. A.; Shirini, F.; Ghorbani Choghamarani, A.; Mohammadpoor-Baltork, I. *Green Chem.* **2002**, *4*, 562.
4. Zolfigol, M. A.; Bamoniri, A. *Synlett* **2002**, 1621.
5. (a) Mirjalili, B. F.; Zolfigol, M. A.; Bamoniri, A. *J. Kor. Chem. Soc.* **2001**, *45*, 546. (b) Mirjalili, B. F.; Zolfigol, M. A.; Bamoniri, A. *Molecules* **2002**, *7*, 751.
6. (a) Mirjalili, B. F.; Zolfigol, M. A.; Bamoniri, A.; Zarei, A. *Bull. Kor. Chem. Soc.* **2003**, *24*, 400. (b) Mirjalili, B. F.; Zolfigol, M. A.; Bamoniri, A.; Zaghaghi, Z. *J. Chem. Res. (S)* **2003**, 273. (c) Mirjalili, B. F.; Zolfigol, M. A.; Bamoniri, A.; Zaghaghi, Z.; Hazar, A. *Acta Chem. Slov.* **2003**, *50*, 563. (d) Shirini, F.; Zolfigol, M. A.; Mohammadi, K. *Bull. Kor. Chem. Soc.* **2004**, *25*, 325.
7. Chitnis, S. R.; Sharma, M. M. *J. Catal.* **1996**, *160*, 84.
8. (a) Salomatina, O. V.; Yarovaya, O. I.; Korchagina, D. V.; Polovinka, M. P.; Barkhash, V. A. *Mendeleev Commun.* **2005**, 59. (b) Seen, A. J. *J. Chem. Educ.* **2004**, *81*, 383.
9. Takeuchi, G.; Shimoura, Y. *Catal. Surv. Jpn.* **1998**, *2*, 77.
10. Choudary, B. M.; Sateesh, M.; Lakshmi Kantam, M.; Koteswara Rao, K.; Ram Prasad, K. V.; Raghavan, K. V.; Sarma, J. A. R. P. *Chem. Commun.* **2000**, 25.
11. Yadav, G. D.; Rahuman, M. S. M. *Org. Pro. Res. Dev.* **2002**, *6*, 706.
12. Ledneczki, I.; Molnar, A. *Synth. Commun.* **2004**, *34*, 3683.

13. (a) Harmer, M. A.; Sun, Q. *Appl. Catal. A: General* **2001**, *45*, 221 and references therein. (b) Elings, J. A.; Lempers, H. E. B.; Sheldon, R. A. *Eur. J. Org. Chem.* **2000**, 1905.
14. Pe'er, I. C.; Felder, E.; Man, O.; Silman, I.; Sussman, J. L. *Proteins* **2004**, *54*, 20.
15. Bardwell, J. C. *Mol. Microbiol.* **1994**, *14*, 199.
16. Kharasch, N.; Arora, A. S. *Phosphorus Sulfur Silicon* **1976**, *2*, 1.
17. Kosower, E. M.; Kosower, N. S. *Nature* **1969**, *224*, 117.
18. (a) Wallace, T. T. *J. Am. Chem. Soc.* **1964**, *86*, 2018. (b) Wallace, T. T.; Wein, H. A. *Chem. Ind. (London)* **1966**, 1558.
19. Small, D. L.; Bailey, J. H.; Cavallito, G. J. *J. Am. Chem. Soc.* **1947**, *69*, 1711.
20. Evans, B. J.; Doi, J. T.; Musker, W. K. *J. Org. Chem.* **1990**, *55*, 2337.
21. Noureldin, N. A.; Caldwell, M.; Hendry, J.; Lee, D. G. *Synthesis* **1998**, 1587.
22. (a) Aida, T.; Akasaka, T.; Furukawa, N.; Oae, S. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1441. (b) Fristad, W. E.; Peterson, J. R. *Synth. Commun.* **1985**, *15*, 1.
23. McKillop, A.; Koyuncu, D. *Tetrahedron Lett.* **1990**, *31*, 5007.
24. Khodaei, M. M.; Mohammadpoor-Baltork, I.; Nikoofar, K. *Bull. Kor. Chem. Soc.* **2003**, *24*, 885 and references therein.
25. Khazaei, A.; Zolfigol, M. A.; Rostami, A. *Synthesis* **2004**, 2959.
26. Leite, S. L. S.; Pardini, V. L.; Viertler, H. *Synth. Commun.* **1990**, *20*, 393.
27. (a) Karami, B.; Montazertozohori, M.; Habibi, M. H. *Bull. Kor. Chem. Soc.* **2005**, *26*, 1125. (b) Karami, B.; Montazertozohori, M.; Karimipour, Gh.; Habibi, M. H. *Bull. Kor. Chem. Soc.* **2005**, *26*, 1431. (c) Karami, B.; Montazertozohori, M.; Habibi, M. H.; Zolfigol, M. A. *Heterocyclic Commun.* **2005**, *11*, 513. (d) Karami, B.; Montazertozohori, M.; Habibi, M. H. *Phosphorus, Sulfur, Silicon and Related Elements*, **2006**, *181*, 2825. (e) Montazertozohori, M.; Karami, B. *Helv. Chim. Acta* **2006**, *89*, 2922.
28. Iranpoor, N.; Firouzabadi, H.; Zolfigol, M. A. *Synth. Commun.* **1998**, *28*, 367.
29. Firouzabadi, H.; Iranpoor, N.; Zolfigol, M. A. *Synth. Commun.* **1998**, *28*, 1179.
30. Zolfigol, M. A.; Nematollahi, D.; Mallakpour, S. E. *Synth. Commun.* **1999**, *29*, 2277.
31. Zolfigol, M. A. *Synth. Commun.* **2000**, *30*, 1593.
32. Jensen, G. B.; Smith, G.; Sagatys, D. S.; Healy, P. C.; White, J. M. *Acta Cryst.*, **2004**, *E60*, 2438