Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 47 (2006) 3509–3510

Tetrahedron Letters

Oxidation of thiols to disulfides with monochloro poly(styrenehydantoin) beads

Akin Akdag, Thomas Webb and S. D. Worley*

Auburn University, Department of Chemistry and Biochemistry, Auburn, AL 36849, United States

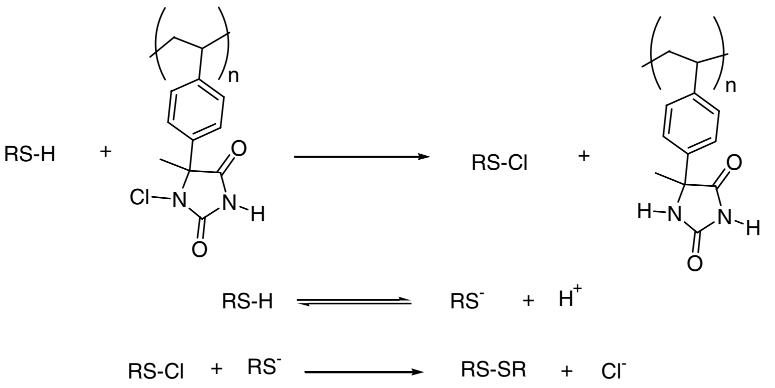
Received 1 March 2006; accepted 15 March 2006
Available online 5 April 2006

Abstract—Various thiols were converted to symmetrical disulfides. This facile and reproducible method uses water as a solvent, and monochloro poly(styrenehydantoin) beads as an oxidizing agent.

© 2006 Elsevier Ltd. All rights reserved.

Disulfide bonds play crucial roles in biology and chemistry.[1] Disulfides are primarily produced from thiols, which are readily available and facile to prepare.[2] However, synthesis of disulfides from thiols sometimes can be problematic due to the overoxidation of thiols, that is, the reaction not terminating at the disulfide stage and proceeding further to sulfoxides and sulfones.[3] On the other hand, many successful reagents have been developed for the synthesis of disulfides from thiols; for example, 1,3-dibromo-5,5-dimethylhydantoin, cerium (IV) salts, permanganates, transition metal oxides, sodium chlorite, peroxides, and halogens are examples of reagents used in disulfide bond formation from thiols.[4]

In this study, which was prompted by the need to identify products from the use of a convenient oxidizing agent to remove noxious odor from cutting oil fluids, we have employed monochloro poly(styrenehydantoin) beads[5] in water to form disulfides from thiols.[6] Previously, Sun and Worley had reported that an amorphous form of the dichloro derivative oxidized aryl sulfides to the sulfoxides and the sulfones.[5d] The beads did not overoxidize the thiols; the sole product isolated from these experiments was disulfides. This was because the dissociation constant for amide *N*-halamine in water to produce free chlorine is very low.[7] Presumably, the reactions proceed through halogen transfer from amide *N*-halamine to thiols to yield sulfenyl chlorides, which react with thiolate anion to yield disulfides and hydrochloric acid (see Scheme 1). The proposed mechanism is in agreement with the experimental observation that water becomes acidic at the end of the reaction, as well



Scheme 1. Proposed mechanism for formation of a disulfide from a thiol.

---

* Corresponding author. Tel.: +1 334 844 6944; fax: +1 334 844 6959; e-mail: worlesd@auburn.edu

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.03.105

Table 1. Thiols used in this experiment and the yield of conversion to disulfides

	Thiol	Isolated yield (%)
a	Ethanethiol	85
b	Butanethiol	81
c	2-Mercaptoethanol	91
d	2-Propanethiol	86
e	2-Methyl-2-propanethiol[a]	60
f	Thiophenol	90
g	4-Methoxythiophenol	93
h	Benzylthiol	92

[a] Only 50% conversion was observed by NMR even after 24 h.

as formation of disulfide bonds and the prior literature.[4g]

Different types of thiols were employed in this study: primary, secondary, tertiary, phenylic, and benzylic thiols. Except for *tert*-butyl thiol, excellent conversion of thiols to disulfides has been observed. The low yield using *tert*-butyl thiol may be due to the low acidity of the *tert*-butyl thiol, or to steric hindrance caused by the bulky *tert*-butyl group.[8] The reaction products were analyzed with ^{1}H and ^{13}C NMR spectroscopy (Table 1). All of the spectra are in excellent agreement with the literature[9].

There are several advantages of this reaction over other methods in the literature. The used monochloro beads can easily be regenerated by exposure to free chlorine (bleach).[5c] The reactions were very clean, gave excellent reproducible yields, and were facile to apply to various thiols. Moreover, excellent selectivity was obtained from these reactions.

In conclusion, the method for oxidizing thiols with monochloro poly(styrenehydantoin) beads, as reported in this paper, is a simple, efficient, facile to handle, very mild procedure for the conversion of thiols to disulfides.

Acknowledgments

This work has been supported by The US Air Force and the Vanson HaloSource company. The monochloro beads were kindly supplied by the Vanson HaloSource Company. The authors thank Dr. J. F. Williams for helpful discussions during the course of this work.

References and notes

1. (a) *Organosulfur Chemistry Synthetic Aspects*; Page, P., Ed.; Academic Press: San Diego, 1995; (b) *Organic Sulfur Chemistry: Structure and Mechanism*; Oae, S., Ed.; CRC: Boca Raton, FL, 1991.
2. Vogel, A. I. *Vogel's Textbook of Practical Organic Chemistry*; Longman Scientific & Technical; Wiley: New York, 1989.
3. Some examples are: (a) Iranpoor, N.; Mohajer, D.; Rezaeifard, A.-R. *Tetrahedron Lett.* **2004**, *45*, 3811–3815; (b) Lazzaro, F.; Crucianelli, M.; De Angelis, F.; Neri, V.; Saladino, R. *Tetrahedron Lett.* **2004**, *45*, 9237–9240; (c) Freeman, F.; Angeletakis, C. N. *J. Am. Chem. Soc.* **1983**, *105*, 4039–4049.
4. Some examples: (a) Khazaei, A.; Zolfigol, M. A.; Rostami, A. *Synthesis* **2004**, 2959–2961; (b) Joshi, A. V.; Bhusare, S.; Baidossi, M.; Qafisheh, N.; Sasson, Y. *Tetrahedron Lett.* **2005**, *46*, 3583–3585; (c) Ali, M. H.; McDermott, M. *Tetrahedron Lett.* **2002**, *43*, 6271–6273; (d) Patel, S.; Mishra, B. K. *Tetrahedron Lett.* **2004**, *45*, 1371–1372; (e) Leino, R.; Lönnqvist, J.-E. *Tetrahedron Lett.* **2004**, *45*, 8489–8491; (f) Laszlo, P.; Delaude, L. *J. Org. Chem.* **1996**, *61*, 6360–6370; (g) Peskin, A. V.; Winterbourn, C. C. *Free Radical Biol. Med.* **2001**, *30*, 572–579.
5. (a) Sun, G.; Wheatley, W. B.; Worley, S. D. *Ind. Eng. Chem. Res.* **1994**, *33*, 168–170; (b) Chen, Y.; Worley, S. D.; Kim, J.; Wei, C.-I.; Chen, T.-Y.; Santiago, J. I.; Williams, J. F.; Sun, G. *Ind. Eng. Chem. Res.* **2003**, *42*, 280–284; (c) Chen, Y.; Worley, S. D.; Kim, J.; Wei, C.-I.; Chen, T.-Y.; Suess, J.; Kawai, H.; Williams, J. F. *Ind. Eng. Chem. Res.* **2003**, *42*, 5715–5720; (d) Sun, G.; Worley, S. D. *Chem. Oxid.* **1997**, 134–144.
6. The following general oxidation procedure was applied to all thiols presented in Table 1. To a mixture of monochloro polystryrene hydantoin beads (3 g) (obtained from HaloSource Company) in water (50 mL) was added a thiol (1 g). The mixture was stirred at room temperature for 6 h. Then, the mixture was filtered, and the residue was washed with methylene chloride (DCM). The water was extracted with DCM (50 mL × 2). The combined organic phase was dried over anhydrous sodium sulfate, filtered, and the solvent evaporated to provide a disulfide.
7. Akdag, A.; Okur, S.; Mckee, M. L.; Worley, S. D. *J. Chem. Theory Comput.*, in press.
8. Arnett, E. M.; Small, L. E. *J. Am. Chem. Soc.* **1977**, *99*, 808–816.
9. Freeman, F.; Angeletakis, C. N. *J. Org. Chem.* **1982**, *47*, 4194–4200.