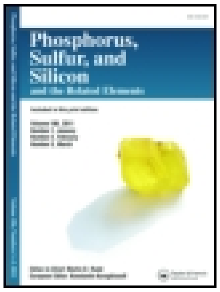

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EFFICIENT AND SELECTIVE OXIDATION OF THIOLS TO DISULFIDES BY 1,4-DIAZABICYCLO[2.2.2]OCTANE-DI-N-OXIDE-DI-PERHYDRATE UNDER NEUTRAL AND HETEROGENEOUS CONDITIONS

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EFFICIENT AND SELECTIVE OXIDATION OF THIOLS TO DISULFIDES BY 1,4-DIAZABICYCLO[2.2.2]OCTANE-DI-N-OXIDE-DI-PERHYDRATE UNDER NEUTRAL AND HETEROGENEOUS CONDITIONS

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1,4-Diazabicyclo[2.2.2]octane-di-N-oxide-di-perhydrate selectively oxidizes thiols to disulfides in acetonitrile in good yields. The method is generally useful for a wide variety of thiols.

Keywords: 1,4-Diazabicyclo[2.2.2]octane-di-N-oxide-di-perhydrate; disulfides; hydrogen peroxide; oxidation; thiols

Disulfides are important compounds from both synthetic and biological viewpoints.[1–3] Industrially, they find wide application as vulcanizing agents for rubber and elastomers, giving them excellent tensile strength.[4] The most important protocol for the preparation of disulfides is the oxidative coupling of thiols.[5] Since disulfides can be overoxidized in the oxidation medium, selective conversion of thiols to disulfides under mild conditions is important. Many reagents have been used for this purpose.[6–15]

1,4-Diazabicyclo[2.2.2]octane-di-N-oxide-di-perhydrate (DABCO-DNODP, Figure 1) is an inexpensive, stable, and easy to handle source of pure H_2O_2.[16] Although **I** has already been synthesized and fully

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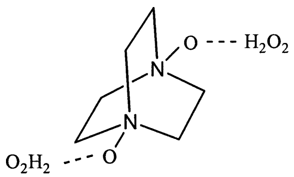
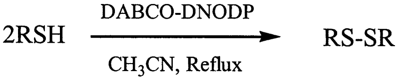


I

FIGURE 1 Structure of DABCO-DNODP.

characterized, unexpectedly we did not find any report on its application in organic synthesis except our recent report on its application in the oxidation of urazoles.[17]

In this article we wish to report a very efficient and simple procedure for selective oxidation of thiols to disulfides using DABCO-DNODP under heterogeneous conditions (Scheme 1).



SCHEME 1

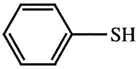
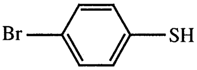
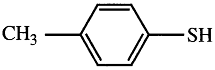
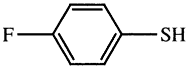
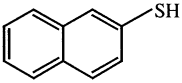
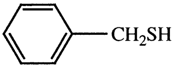
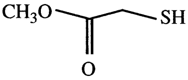
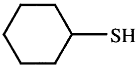
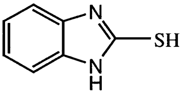
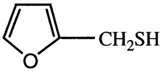
Table I collects the results derived from the oxidation of different kinds of thiols. The reagent was examined on a wide array of substrates, such as aromatic (homocyclic and heterocyclic) and aliphatic (cyclic and acyclic) thiols. As shown in Table I, coupling of aromatic thiols was easier than coupling of aliphatic thiols.

Hydrogen peroxide and its solid complexes are usually applied in the presence of acidic catalysts or co-oxidants; most of them are expensive, corrosive, or cause environmental pollution.[18–22] One of the important advantages of this method is the application of DABCO-DNODP without any acidic reagent. The medium is almost neutral, and acid-sensitive groups remain intact during the course of the reaction (Table I, entries 9, 13).

The reactions were easily carried out by stirring a mixture of thiol and DABCO-DNODP in acetonitrile under reflux conditions. The heterogeneous system allowed a simple workup to be performed merely by filtration, followed by evaporation of the solvent.

In conclusion, this is a very simple method for selective and efficient coupling of different types of thiols. Stability and ease of handling of the reagent, simple workup procedure, and neutrality of the reaction medium are among the advantages that make this new method an attractive addition to the previously reported procedures.

TABLE I Oxidative Coupling of Thiols to Disulfides by DABCO-DNODP (**I**) in Acetonitrile

Entry	Substrate	Time (h)	Oxid./sub. (mole ratio)	Yield[a] (%)
1		3.5	0.8	97
2		1	0.8	95
3		1	0.8	91
4		1.5	0.8	83
5		1	0.8	93
6		5	2.5	70
7	$CH_3(CH_2)_6CH_2$-SH	5	2.5	70
8	$CH_3(CH_2)_{10}CH_2$-SH	3	2.5	93
9		3.5	2.5	91
10	HOOC—CH_2-CH_2-SH	4	2.5	45
11		5.5	2.5	77
12		4	2.5	89
13		4	2.5	82

[a]Products were known and identified by comparison of their spectroscopic data (^{1}H NMR, IR) and physical properties with those of authentic samples.

EXPERIMENTAL SECTION

General

Products are known compounds and characterized by comparison of their spectral data (^{1}H-NMR, IR) and physical properties with authentic samples. Monitoring of the reactions was accomplished by TLC using precoated aluminium sheets, Merck, silica gel 60 F_{254} (eluent: MeOH/HOAc: 5/1). DABCO-DNODP was prepared according to the reported procedure,[16] and its hydrogen peroxide content was determined by titration with $KMnO_4$.[23] All yields refer to isolated products.

General Procedure for the Oxidation of Thiols by DABCO-DNODP

DABCO-DNODP (1.6–5.0 mmol) was added to a stirred solution of thiol (2 mmol) in acetonitrile (7 ml). The mixture was stirred magnetically under reflux condition for the appropriate period of time (Table I). Progress of the reaction was followed by TLC. The mixture was cooled and filtered over a sintered glass funnel. Evaporation of the solvent under reduced pressure followed by preparative thin layer chromatography on silica gel afforded the pure products in 45–97% yield.

REFERENCES

[1] B. Schmidt, S. Lindman, W. Tong, G. Lindeberg, A. Gogoll, Z. Lai, M. Thornwall, B. Synnergren, A. Nilson, C. J. Welch, M. Sohtell, C. Westerlund, F. Nyberg, A. Karlen, and A. Hallberg, *J. Med. Chem.*, **40,** 903 (1997).

[2] K. W. Li, J. Wu, W. Xing, and J. A. Simon, *J. Am. Chem. Soc.*, **118,** 7237 (1996).

[3] B. D. Palmer, G. W. Newcastle, A. M. Thompson, M. Boyd, H. D. H. Showalter, A. D. Sercel, D. W. Fry, A. J. Kraker, and W. A. Dennyyrosine, *J. Med. Chem.*, **38,** 58 (1995).

[4] K. Ramadas and N. Srinivasan, *Synth. Commun.*, **25,** 227 (1995).

[5] G. Capozzi and G. Modena, *The Chemistry of Thiol Group*, edited by S. Patai (John Wiley and Sons, New York, 1974), Part 2, pp. 785–839.

[6] B. Karimi, H. Hazarkhani, and D. Zareyee, *Synthesis*, 2513 (2002).

[7] B. Karimi and D. Zareyee, *Synlett*, 346 (2002).

[8] S. Raghavan, A. Rajender, S. C. Joseph, and M. A. Rasheed, *Synth. Commun.*, **31,** 1477 (2001).

[9] R. S. Varma, H. M. Meshram, and R. Dahiya, *Synth. Commun.*, **30,** 1249 (2000).

[10] P. Salehi, A. Farrokhi, and M. Gholizadeh, *Synth. Commun.*, **31,** 2777 (2001).

[11] N. Iranpoor, P. Salehi, and F. Shirini, *Org. Prep. Proc. Int.*, **27,** 216 (1995).

[12] B. Movassagh, M. M. Lakouraj, and K. Ghodrati, *Synth. Commun.*, **29,** 3597 (1999).

[13] N. Iranpoor, H. Firouzabadi, and M. A. Zolfigol, *Synth. Commun.*, **28,** 367 (1998).

[14] A. R. Hajipour and N. Mahboubghah, *Indian J. Chem.*, **37B,** 1041 (1998).

[15] V. Kesavan, D. Bonnet-Delpon, and J. P. Begue, *Synthesis*, 223 (2000).

[16] A. A. Oswald and D. L. Guertin, *J. Org. Chem.*, **28,** 651 (1963).

[17] M. A. Zolfigol, P. Salehi, S. E. Mallakpour, and M. Torabi, *Bull. Chem. Soc. Jpn.*, **76,** 1673 (2003).

[18] G. S. Owens and M. M. Abu-Omar, *J. Chem. Soc., Chem. Commun.*, 1165 (2000).

[19] T. R. Boehlow and C. D. Spilling, *Tetrahedron Lett.*, **37,** 2717 (1996).
[20] R. Balicki and J. Golinski, *Synth. Commun.*, **30,** 1529 (2000).
[21] C. J. Moody and J. L. O'Connell, *J. Chem. Soc. Chem. Commun.*, 1311 (2000).
[22] M. Giurg, J. Mlochowski, and A. Ambrozak, *Polish J. Chem.*, **76,** 1713 (2002).
[23] J. Bassett, J. Mendham, G. H. Jeffery, and R. C. Denney, *Vogel's Textbook of Quantitative Chemical Analysis*, 5th ed. (John Wiley, New York, 1989), p. 372.