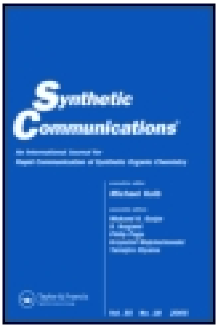

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# Caro's Acid Supported on Silica Gel. Part 1: Oxidative Coupling of Thiols to Disulfides

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# CARO'S ACID SUPPORTED ON SILICA GEL . PART 1 : OXIDATIVE COUPLING OF THIOLS TO DISULFIDES

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**Abstract**: Mild and efficient method for preparation of disulfides from thiols is described using Caro's acid supported on silica gel .

Amongst different methods of preparing disulfides, much attention have been paid to oxidation of thiols. Oxidation of thiols to disulfides without overoxidation is an important transformation in organic chemistry and biochemistry which is well investigated over the years. The disulfide bond formation is important in peptides[1] and bioactive molecules.[2]

Oxidation of thiols proceed stepwise , giving disulfides initially ; overoxidation of disulfides leads ultimately to sulfonic acids but several intermediates frequently can be obtained.[3] What happens in any particular oxidation depends on the disulfide , oxidant , possible catalyst and solvent .[4] Many reagents have been introduced to oxidize thiols to disulfides under controlled conditions.[5-20] Oxidative coupling of thiols have also been accomplished using clay - supported iron ( III )

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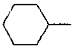
nitrate ( Clayfen )[21], calcium hypochlorite / montmorillonite K10 [22], and Fe ( III ) ion exchanged montmorillonite.[23] However, no studies are known in literature exploiting peroxysulfuric acid, Caro's acid, for this purpose. Although Caro's acid is a strong oxidizing agent, its utility in organic synthesis has been limited by its insolubility in common organic solvents, and its rapid deactivation on storage. This reagent is prepared in situ from potassium persulfate and sulfuric acid.[24]

We hereby report that Caro's acid supported on silica gel can be used to oxidize aliphatic as well as aromatic thiols to the corresponding disulfides in acetonitrile. The oxidation is carried out by stirring the reagent with thiol in acetonitrile at room temperature under air atmosphere giving in high yields (Table 1). The reagent selectively oxidizes thiols to the corresponding symmetric disulfides without overoxidation. The attractive features of this supported reagent include its modified activity and simple reaction work up to mere filtration and washing with the solvent. The reagent showed a good shelf life at least of one week. It can be stored as powder in a fridge. It did not show any loss of activity when compared with that of the freshly prepared reagent.

$$\underset{(1)}{2\,\mathrm{RSH}} \xrightarrow[\text{Acetonitrile, 20°C}]{\text{Caro's acid / SiO}_2} \underset{(2)}{\mathrm{RSSR}}$$

Two experiments are also conducted with p-methyl- and p-chlorothiophenol in nitrogen atmosphere under identical conditions and afforded the corresponding disulfides in 91 and 89% yields respectively. These results demonstrate the

**Table 1.** Oxidative Coupling of Thiols (**1**) to the Disulfides (**2**)

| Entry | R | Reaction Time(h) | Disulfide Yield[a](%) |
|---|---|---|---|
| a | Ph | 4.5 | 89 |
| b | 4-$MeC_6H_4$ | 5.5 | 92 |
| c | 4-$ClC_6H_4$ | 5.5 | 94 |
| d | 3-$MeC_6H_4$ | 6 | 95 |
| e | 2-$HO_2CC_6H_4$ | 24 | 69 |
| f | 2-$MeO_2CC_6H_4$ | 4.5 | 94 |
| g | $PhCH_2$ | 5 | 85 |
| h | n-$C_8H_{17}$ | 7 | 99 |
| i | iso-$C_4H_9$ | 4.5 | 77 (98)[b] |
| j | n-$C_4H_9$ | 4.5 | 84 (97)[b] |
| k |  | 8.5 | 96 (100)[b] |

[a] Yields refers to isolated product.
[b] Yields are based on GC analyses.

efficiency of Caro's acid-$SiO_2$ in an oxidative coupling in either inert or air atmosphere.

Summing up, the Caro's acid-silica gel system is shown to be a mild, efficient, and practical reagent for the oxidation of various thiols to the corresponding disulfides in high yields.

## EXPERIMENTAL SECTION :

Products were characterized by comparison of their physical data with those of authentic samples . $^1$H NMR spectra were recorded on a JEOL JNM-PMX-60SI spectrometer . IR spectra were obtained using a Shimadzu IR 470 instrument. The purity determination of the substrates and reaction monitoring were carried out by either analytical gas chromatography on a Shimadzu Chromatopac C-R6A instrument or TLC on a silica gel polygram SILG / UV 254 plates . Melting points were all corrected .

### Preparation of Caro's acid - silica gel reagent

To ice cooled 98% sulfuric acid ( 4.7 g ) is added in small portions potassium persulfate ( 4.5 g ) with stirring ; to this is added crushed ice ( 13 g ) and water ( 4 g ) and the temperature is kept below 15°C . Silica gel ( 5 g , TLC grade , Kieselgel 60G, particle size 15 μm ) is added in portions to the mixture and stirred for 4 h in ice-water bath . The mixture is then filtered under suction and dried in a desiccator to give a white free flowing powder.

### Typical oxidation procedure

p -Chlorothiophenol ( **1c** , 0.51 g , 3.5 mmol ) is dissolved in acetonitrile ( 20 ml ) and Caro's acid - silica gel ( 2.1 g , Caro's acid content 3.5 mmol) added in small portions to the solution . The heterogenous mixture is magnetically stirred at room temperature for 5.5 h . The mixture is then filtered through a sintered glass funnel and the residue is washed thoroughly with acetonitrile . The filtrate is evaporated and redissolved in dichloromethane , washed with 5% sodium hydroxide solution and water . Drying ( $MgSO_4$ ) and evaporation of the organic layer gave the crude disulfide ( **2c** ) which recrystallized from methanol ; yield 0.47 g, m.p. 68-69°C ( Lit.[25] m.p. 71°C ) .

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**References :**

1. Bodanszky,M." Principles of Peptide Synthesis ", Springer-Verlag, Berlin, **1984**, chapter 4.
2. Johnson, J.R.; Bruce, W. F. and Dutcher, J. D. *J. Am. Chem. Soc.,* **1943**, *65*, 2005 .
3. Oae, S. " Organic Chemistry of Sulfur " , Plenum press, New York, **1977**, chapter 7 .
4. Kharasch, N. and Meyers, C. Y. ( Editors ), " The Chemistry of Organic Sulfur Compounds ",Pergamon press, New York, **1966**, *Vol. 2,* pp. 367-402 .
5. Uemura,S.; Tanaka, S. and Okano, M. *Bull. Chem. Soc. Jpn.*,**1977**, *50* , 220.
6. Kim, Y. H. ; Shinhama , K.; Fukushima , D. and Oae, S. *Tetrahedron Lett.* , **1978**, *14* , 1211.
7. Drabowicz , J. and Mikolajczyk , M. *Synthesis* , **1980** , 32 .
8. Huang , M. and Chan, C. C. *Ibid.*, **1982** , 1091 .

9. Firouzabadi, H.; Mottaghinejad, E. and Seddighi, M. *Ibid.*, **1989**, 378.

10. Pryor, W. A.; Church, D. F.; Govindan, C. K. and Crank, G. *J. Org. Chem.*, **1982**, *47*, 156.

11. Fujihara, H.; Akaishi, R. and Furukawa, N. *Bull. Chem. Soc. Jpn.*, **1989**, *62*, 627.

12. Firouzabadi, H. and Baltork, I. M. *Ibid.*, **1992**, *65*, 1185.

13. Matsuda, F.; Matsumoto, T.; Ohsaki, M.; Ito, Y. and Terashima, S. *Ibid.*, **1992**, *65*, 360.

14. McKillop, A.; Koyuncu, D.; Krief, A.; Dumont, W.; Renier, P. and Trabelsi, M. *Tetrahedron Lett.*, **1990**, *31*, 5007.

15. Sato, T.; Otera, J. and Nozaki, H. *Ibid.*, **1990**, *31*, 3591.

16. Dick, A. P.; Swift, H. R.; Williams, D. L. H.; Butler, A. R.; Al-Sa'doni, H. H. and Cox, B. G. *J. Chem. Soc. Perkin Trans. 2*, **1996**, 481.

17. Barnet, D. J.; Rios, A. and Williams, D. L. H. *Ibid.*, **1995**, 1279.

18. Ramadas, K. and Srinivasan, N. *Synthetic Commun.*, **1995**, *25*, 227.

19. Wu, X.; Ricke, R. D. and Zhu, L. *Ibid.*, **1996**, *26*, 191.

20. Iranpoor, N.; Firouzabadi, H. and Zolfigol, M. A. *Ibid.*, **1998**, *28*, 367.

21. Cornelis, A. and Laszlo, P. *Synthesis*, **1985**, 909.

22. Hirano, M.; Yakabe, S.; Fukami, M. and Morimoto, T. *Synthetic Commun.*, **1997**, *27*, 2783.

23. Meshram, H. M. and Kache, R. *Ibid.*, **1997**, *27*, 2403.

24. Langley, W. D. *Org. Syn. Coll. Vol.*, **1955**, *3*, 334.

25. "*Beilstein's Handbuch der Organischen Chemie* ", Springer- Verlag, Berlin, **1923** , Bd VI, pp. 330.

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