

**EFFICIENT, HIGH YIELD OXIDATION OF THIOLS AND SELENOLS  
TO DISULPHIDES AND DISELENIDES**

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**Abstract:** Thiols and selenols are smoothly oxidised in high yield to disulphides and diselenides by sodium perborate at room temperature.

Thiols and selenols are among the most easily oxidised of all functional groups, and air, or oxygen, can often be used satisfactorily for their high yield conversion into the corresponding disulphides and diselenides. These reactions are, however, generally rather slow in the absence of basic catalysts, especially for medium or large scale operations, and in the case of phenylselenol, for example, time consuming monitoring of the reaction is required.<sup>1</sup> Consequently, disulphides and diselenides are most frequently prepared by oxidation of thiols and selenols with hydrogen peroxide, and yields are usually excellent if the correct amount of oxidant is used and care taken to avoid over-oxidation.<sup>2</sup>

We now show that sodium perborate, a very cheap, safe and easily handled oxidant,<sup>3,4</sup> smoothly converts thiols and selenols into disulphides and diselenides in excellent yield at room temperature. No over-oxidation has been observed in any instance, even when the reactions were carried out with an excess of the reagent and in different solvent media.

Data for oxidation of thiols to disulphides are given in Table I. Reactions are conveniently carried out on a 10 mmolar scale with respect to

thiol using 20 mmol of sodium perborate in aqueous methanol, but water or aqueous acetic acid can also be used. All reactions were complete within two hours. For aromatic thiols, the reaction is essentially insensitive to the nature or position of other substituent groups, although with pentafluorothiophenol, oxidation in aqueous methanol gave only a 20% yield of disulphide after two hours compared with 87% when aqueous acetic acid was used.

**Table I**  
Oxidation of thiols to disulphides with sodium perborate



| R  | Conditions <sup>a</sup> | Yield, % <sup>b,c</sup> | R   | Conditions <sup>a</sup> | Yield, % <sup>a,b</sup> |
|--|-------------------------|-------------------------|---|-------------------------|-------------------------|
| n-C <sub>4</sub> H <sub>9</sub>                                  | A                       | 93                      | 4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>  | B                       | 96                      |
| sec-C <sub>4</sub> H <sub>9</sub>                                | A                       | 72                      | 2-ClC <sub>6</sub> H <sub>4</sub>                 | B                       | 96                      |
| C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>                    | B                       | 93                      | 3-ClC <sub>6</sub> H <sub>4</sub>                 | B                       | 88                      |
| HOOCCH <sub>2</sub> CH <sub>2</sub>                              | B                       | 78                      | 4-ClC <sub>6</sub> H <sub>4</sub>                 | B                       | 99                      |
| L-HOOC(H <sub>2</sub> N)CHCH <sub>2</sub>                        | C                       | 77                      | 2,6-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> | B                       | 98                      |
| C <sub>6</sub> H <sub>5</sub>                                    | B                       | 92                      | 2-FC <sub>6</sub> H <sub>4</sub>                  | B                       | 82                      |
| 2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>                  | B                       | 95                      | 3-FC <sub>6</sub> H <sub>4</sub>                  | B                       | 96                      |
| 3-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>                  | B                       | 86                      | 4-FC <sub>6</sub> H <sub>4</sub>                  | B                       | 97                      |
| 4-(CH <sub>3</sub> ) <sub>3</sub> CC <sub>6</sub> H <sub>4</sub> | B                       | 96                      | C <sub>6</sub> F <sub>5</sub>                     | C                       | 87                      |
| 2-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>                 | B                       | 93                      | 2-Pyridyl   | C                       | 75                      |
| 3-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>                 | B                       | 89                      |   |                         |                         |

<sup>a</sup> A: 10 mmol RSH in 40 ml H<sub>2</sub>O for 2h at room temperature. B: 10 mmol RSH in 25 ml CH<sub>3</sub>OH and 10 ml H<sub>2</sub>O for 2h at room temperature. C: 10 mmol RSH in 25 ml CH<sub>3</sub>COOH and 10 ml H<sub>2</sub>O for 2h at room temperature. <sup>b</sup> No attempt was made to optimise yields. <sup>c</sup> Refers to pure, isolated material.

For oxidation of selenols, reactions were initially carried out in ethanol at 20°C on a 20-80 mmolar scale and using one molar equivalent of sodium perborate. This gave the diselenides in 70-97% yield (Table II, entries 1-7). In the case of phenylselenol, the yield of diphenyl diselenide decreased dramatically from 97 to 64% when the reaction was performed on a larger (0.7 mol) scale due to the presence of substantial amounts of sodium phenylselenolate.<sup>5</sup> The yield can, however, be increased to 93% on the larger scale if the reaction is carried out in ethanol

containing one molar equivalent of acetic acid. Use of ethanol containing one molar equivalent of acetic acid proved, in fact, to be more effective than use of ethanol alone, especially for aromatic selenols (Table II, entries 8-14).

**Table II**  
Oxidation of selenols to diselenides with sodium perborate

| R - SeH  |       |                         | →                                 | R - Se - Se - R |                         |                         |
|--|-------|-------------------------|-----------------------------------|-----------------|-------------------------|-------------------------|
| R  | Entry | Conditions <sup>a</sup> | Yield, % <sup>b,c</sup>           | Entry           | Conditions <sup>a</sup> | Yield, % <sup>a,b</sup> |
| CH <sub>3</sub>                                  | 1     | A, 5h                   | 86                                | 8               | B, 5h                   | 75                      |
| n-C <sub>4</sub> H <sub>9</sub>                  | 2     | A, 3h                   | 93                                | 9               | B, 3h                   | 97                      |
| C <sub>6</sub> H <sub>5</sub>                    | 3     | A, 6h                   | 97 <sup>d</sup> , 64 <sup>e</sup> | 10              | B, 5h                   | 93 <sup>e</sup>         |
| 4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>  | 4     | A, 6h                   | 73                                | 11              | B, 2h                   | 96                      |
| 4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> | 5     | A, 6h                   | 81                                | 12              | B, 2h                   | 96                      |
| 4-ClC <sub>6</sub> H <sub>4</sub>                | 6     | A, 6h                   | 70                                | 13              | B, 2h                   | 93                      |
| 2-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>  | 7     | A, 6h                   | 70                                | 14              | B, 2h                   | 96                      |

<sup>a</sup>A: C<sub>2</sub>H<sub>5</sub>OH, 20°C. B: 1 eq CH<sub>3</sub>COOH in C<sub>2</sub>H<sub>5</sub>OH, 20°C. <sup>b</sup>No attempt was made to optimise yields.

<sup>c</sup>Refers to pure, isolated material. <sup>d</sup>20 mmol scale. <sup>e</sup>0.7 mol scale.

Using the above method we have tried, in a procedure which parallels one described by Reich,<sup>6</sup> to oxidise directly with sodium perborate the crude phenylselenolate magnesium bromide resulting from the reaction of metallic selenium with phenylmagnesium bromide. Diphenyl diselenide was obtained in about 65% yield but was contaminated with a significant amount of polyselenides.<sup>6</sup> Unfortunately, however, metallic selenium was slowly released from this material on recrystallisation, and it was impossible to obtain the pure diselenide by this method. This is not a consequence of the oxidation reaction but of reaction of the Grignard reagent with selenium, and in our hands similar problems were encountered with the Reich procedure.

Oxidation of selenols to diselenides may involve formation of seleninic acids,<sup>7</sup> and attempts were made in the present study to trap such intermediates as  $\beta$ -hydroxyalkyl selenides by performing the reaction in the presence of olefins. All such attempts were unsuccessful irrespective of the conditions used.

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**References**

1. A. Krief, A.F. de Mahieu, W. Dumont and M. Trabelsi, *Synthesis*, 131 (1988).
2. It is well known that selenols and diselenides react with hydrogen peroxide to produce, depending on the amount of hydrogen peroxide used (2 eq or more), seleninic (H. Rheinboldt, in: *Houben-Wehl*, Vol. IX, Georg Thieme Verlag, Stuttgart, 1967, p 917; D.L. Klayman and W.W.H. Gunther, in: *Organic Selenium Compounds: Their Chemistry and Biology*, John Wiley and Sons, New York, 1973) or perseleninic acid (A. Krief, W. Dumont and A.F. de Mahieu, *Tetrahedron Lett.*, **29**, 3269 (1988) and references therein) respectively.
3. A. McKillop and J. Tarbin, *Tetrahedron*, **43**, 1753 (1987).
4. A. McKillop and D. Kemp, *Tetrahedron*, **45**, 3299 (1989).
5. Sodium phenyl selenolate is also oxidised to diphenyl diselenide (68% yield) under these conditions.
6. H.J. Reich, M.L. Cohen and P.S. Clark, *Org. Synthesis*, **59**, 141 (1979).
7. D. Labar and A. Krief, *Bull. Soc. Chim. Belg.*, **93**, 1005 (1984); T. Hori and K.B. Sharpless, *J. Org. Chem.*, **43**, 1968 (1978); D. Labar, A. Krief and L. Hevesi, *Tetrahedron Lett.*, 3967 (1978); H.J. Reich, S. Wollowitz, J.E. Trend, F. Chow, and D.F. Wendelborn, *J. Org. Chem.*, **43**, 1697 (1978); J.L. Kice, F. Mc Afec and M. Slebocka-Tilk, *Tetrahedron Lett.*, **23**, 3323 (1982).

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