A Facile and Selective Oxidation of Organic Sulphides to Sulphoxides with Hydrogen Peroxide/Selenium Dioxide System[1]

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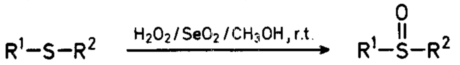
The use of sulphoxides as key intermediates for organic synthesis has drawn increasing interest in recent years. Therefore, new methods for the preparation of sulphoxides continue to be developed[2]. The standard methods involve the oxidation of organic sulphides by various oxidising reagents. The most common reagent to convert sulphides to sulphoxides is hydrogen peroxide alone or in the presence of various catalysts[3]. However, the major difficulty encountered in the preparation of sulphoxides by this method is over-oxidation to sulphones. Another drawback connected with the use of hydrogen peroxide is the relatively long reaction time which is needed for completion of the oxidation.

We report here a highly selective and rapid oxidation of organic sulphides **1** to sulphoxides **2** using hydrogen peroxide/selenium dioxide reagent.

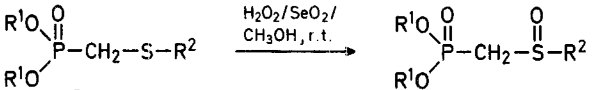


$$R^1-S-R^2 \xrightarrow{H_2O_2/SeO_2/CH_3OH,\,r.t.} R^1-\overset{O}{\overset{\|}{S}}-R^2$$

1 **2**

The reaction is very simple and takes place immediately upon addition of a solution of hydrogen peroxide and selenium dioxide to a solution of sulphide **1** in methanol at room temperature. The above oxidation procedure may be applied to dialkyl, alkyl aryl and diaryl sulphides **1**. Sulphoxides **2** are obtained in 80–95 % yield. Thin layer chromatography tests of the crude reaction products indicated that the oxidation of **1** is quantitative and the corresponding sulphones are not formed. Yields and physical constants for sulphoxides **2** are summarised in the Table.

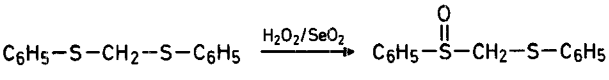
The utility of the hydrogen peroxide/selenium dioxide system is further demonstrated by the facile oxidation of α-phosphoryl sulphides to α-phosphoryl sulphoxides. The latter sulphoxides have attracted considerable attention in recent years[4-7] and have been prepared previously by the sodium metaperiodate oxidation of the corresponding sulphides. It has now been found that α-phosphoryl sulphides **3a–c** undergo very fast and clean oxidation to the corresponding sulphoxides **4a–c**, by hydrogen peroxide/selenium dioxide reagent.



3a-c **4a-c**

3, 4	R^1	R^2
a	C_2H_5	CH_3
b	C_2H_5	C_6H_5
c	CH_3	4-H_3C—C_6H_4

In an extension of this work we attempted also to oxidise selectively formaldehyde *S,S*-diphenyl acetal (**5**) to the monoxide **6** by means of the hydrogen peroxide/selenium dioxide system.



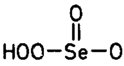
$$C_6H_5-S-CH_2-S-C_6H_5 \xrightarrow{H_2O_2/SeO_2} C_6H_5-\overset{O}{\overset{\|}{S}}-CH_2-S-C_6H_5$$

5 **6**

However, we found, that a small amount of the corresponding dioxide is formed when the oxidation reaction is complete. The full selectivity was observed only up to 50 % of the **5**→**6** conversion as evidenced by T.L.C. tests.

We would like to note that the present method is not suitable for the oxidation of α-halosulphides, most probably due to the fact that they react with selenium dioxide[8].

As far as the nature of the reagent concerns, it seems that perseleninic acid may be considered as the true oxidising agent formed from hydrogen peroxide and selenium dioxide.



$$HOO-\overset{O}{\overset{\|}{Se}}-OH$$

In this context it is interesting to note that Reich et al.[9] described very recently an example of the oxidation of methyl phenyl sulphide to methyl phenyl sulphoxide by means of phenylperseleninic acid. Further applications of the title reagent for oxidation of organic compounds are currently being studied in our laboratory.

General Procedure for Oxidation of Sulphides 1 to Sulphoxides 2 with Hydrogen Peroxide/Selenium Dioxide Reagent:

A round bottom flask is charged with methanol (20 ml) and sulphide **1** (10 mmol). The flask is immersed in a water bath. A solution of equimolar amounts of hydrogen peroxide and selenium dioxide in water (5 ml) is added slowly to the stirred reaction

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Table. Oxidation of Sulphides **1** or **3** to Sulphoxides **2** or **4** with Hydrogen Peroxide/Selenium Dioxide Reagent[a].

Product	R^1	R^2	Yield [%][b]	b.p./torr or m.p.[c]	n_D^{20}[c]	Lit. b.p./torr or m.p.	Lit. n_D^{20}
2a	CH_3	*i*-C_4H_9	82 (75)	45–46°/0.2	—	40°/0.1[10]	1.4640
2b	*n*-C_4H_9	*n*-C_4H_9	90	32–34°	—	32°[11]	—
2c	$C_6H_5CH_2$	$C_6H_5CH_2$	94 (88)	132–135°[d]	—	132–133°[12]	—
2d	CH_3	C_6H_5	95	30–31°	—	29.5°[13]	—
2e	*i*-C_3H_7	C_6H_5	97 (90)	88–90°/0.05	1.5618	101–102°/0.01[14]	1.5620
2f	*i*-C_4H_9	C_6H_5	95 (90)	110–111°/0.1	—	102–103°/0.01[14]	—
2g	CH_3	4-$H_3C—C_6H_4$	94 (91)	41–42°[e]	—	41–42°[15]	—
2h	C_6H_5	C_6H_5	92 (86)	68–71°[f]	—	69–71°[15]	—
4a	C_2H_5	CH_3	95	—	1.4768[g]		1.4766[4]
4b	C_2H_5	C_6H_5	93	—	1.5305[h]		1.5307[7]
4c	CH_3	4-$H_3C—C_6H_4$	100	—	1.5226[i]		1.5236[4]

[a] All reaction were carried out using 10 mmol of sulphide **1** or **3**.

[b] Yield of the crude product. In parenthesis the yield of sulphoxide **2** after purification (distillation or crystallization) is given.

[c] M.p. and n_D^{20} for the crude oxidation product.

[d] M.p. 133–134° after crystallization from ethanol.

[e] M.p. 42–43° after crystallization from ether/hexane (1 : 2).

[f] M.p. 69–70° after crystallization from ether/hexane (1 : 1).

[g] ^{31}P-N.M.R. ($CHCl_3$): $\delta = -16.7$ ppm [Lit. [4], ^{31}P-N.M.R. (neat): $\delta = -17.6$ ppm].

[h] ^{31}P-N.M.R. ($CHCl_3$): $\delta = -19.0$ ppm [Lit. [7], ^{31}P-N.M.R. ($CHCl_3$): $\delta = -20.8$ ppm].

[i] ^{31}P-N.M.R. ($CHCl_3$): $\delta = -15.95$ ppm [Lit. [4], ^{31}P-N.M.R. (neat): $\delta = -16.5$ ppm].

solution. A minute after an addition of the oxidising reagent a T.L.C. test [silica gel GF_{24} plates; benzene/ethanol (9 : 1); iodine vapour as developer] shows the quantitative formation of sulphoxide **2**. Then water (100 ml) is added to the reaction mixture. After saturation with sodium chloride the aqueous phase is extracted with chloroform (3 × 30 ml). The chloroform extract is dried over magnesium sulphate and evaporated to give virtually pure sulphoxide **2** as evidenced by I.R., N.M.R. spectroscopy, and T.L.C. analysis.

Diethylphosphorylmethyl Methyl Sulphoxide (4a):

To a solution of sulphide **3a** (2 g, 10 mmol) in methanol (20 ml) a solution of selenium dioxide (1.1 g, 10 mmol) and hydrogen peroxide (10 mmol) in methanol (5 ml) is added dropwise. The reaction mixture is stirred for another 5 min and water (100 ml) added. After saturation with sodium chloride the aqueous layer is extracted with chloroform (3 × 30 ml). The chloroform solution is dried and evaporated to give sulphoxide **4a**; yield: 2.05 g (95 %); n_D^{22}: 1.4760 (Lit. [4], n_D^{20}: 1.4766); ^1H-N.M.R. consistent with structure.

^{31}P-N.M.R. ($CHCl_3$): $\delta = -16.7$ ppm [Lit. [4], ^{31}P-N.M.R. (neat): $\delta = -17.6$ ppm].

Partial Oxidation of *S,S*-Acetal 5:

To a solution of *S,S*-acetal **5** (1.15 g, 5 mmol) in methanol (10 ml) a solution of selenium dioxide (0.25 g, 2.5 mmol) and hydrogen peroxide (3 mmol) in methanol (3 ml) is added dropwise. After 5 min water (70 ml) is added and the resultant solution is extracted with chloroform (2 × 30 ml). The chloroform solution is dried and evaporated to give a mixture containing **5** and **6**; (T.L.C. analysis); yield: 1.15 g. Chromatography of the crude reaction product on silica gel (100–200 mesh) column with ether/hexane/benzene (2 : 1 : 1) as eluent gives unreacted **5**; yield: 0.45 g (39 %); m.p. 39–40° (Lit. [16], m.p. 38–40°).

^1H-N.M.R. (CCl_4): $\delta = 4.20$ [s, 2H, $\underline{H}_2C(SC_6H_5)_2$] 7.1–7.5 ppm (m, 10 H_{arom}).

and with chloroform as eluent gives monoxide **6**[17]; yield: 0.65 g (53 %); oil; n_D^{22}: 1.6310.

^1H-N.M.R. (CCl_4): $\delta = 4.02$ [s, 2H, $C_6H_5—S—C\underline{H}_2—S(O)C_6H_5$]; 6.9–7.7 ppm (m, 10 H_{arom}).

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