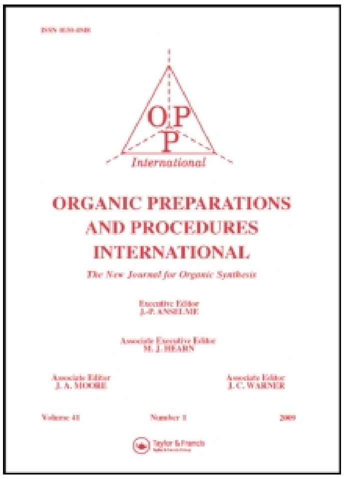

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4. H. Naemura, M. Komatsu, K. Adachi and H. Chikamatsu, *Chem. Commun.*, 1675 (**1986**).

5. A. H. Schroeder and S. Mazur, *J. Am. Chem. Soc.*, **100**, 7339 (1978).

6. R. Adams, S. Mac Kenzie Jr. and S. Loewe, *ibid.*, **70**, 664 (1948).

7. S. Shibata, E. Mosihita and Y. Arima, *Chem. Pharm. Bull. Jpn*, **15**, 1757 (1967).

8. A. I. Vogel, *"A Textbook of Practical Organic Chemistry"*, p. 782, Longmans, London, 1958.

9. M. J. Broadhurst, C. H. Hassal and G. S. Thomas, *J. Chem. Soc. Perkin Trans I*, 2502 (**1977**).

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RAPID OXIDATION OF SULFIDES AND SULFOXIDES WITH SODIUM HYPOCHLORITE

Submitted by
(07/14/95)

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Sulfones are important in organic synthesis. A number of reagents have been reported to oxidize sulfides and sulfoxides to the corresponding sulfones.[1] Sodium hypochlorite has been reported as an inexpensive and convenient oxidizing reagent for a variety of functional groups.[2] Sodium hypochlorite has also been used to oxidize sulfides and disulfides to sulfoxides and disulfoxides selectively[3] and in other cases it yields a mixture of sulfoxides and sulfones.[1b,c] While working on oxidations with hypochlorite,[4] we observed that dibenzyl sulfide was rapidly oxidized to the corresponding sulfone with sodium hypochlorite in acetonitrile at ambient temperature; prolonged oxidation resulted in a mixture of the products. Therefore, we decided to investigate the oxidation of different sulfides and sulfoxides with sodium hypochlorite in acetonitrile at ambient temperature. This paper reports a simple, rapid and convenient procedure for the oxidation of a variety of sulfides and sulfoxides to the corresponding sulfones with aqueous sodium hypochlorite at ambient temperature.

The oxidations were quite rapid and high yields of the sulfones were obtained by a simple work up. Most of the known reagents including hydrogen peroxide require more vigorous conditions (higher temperatures and long reaction times). This procedure is applicable to dibenzyl, dialkyl, diaryl, benzyl alkyl, benzyl aryl and aryl alkyl sulfides and sulfoxides; even a fatty sulfide such as benzyl n-dodecyl sulfide was easily oxidized using a somewhat higher molar ratio of substrate to NaOCl (Tables 1 and 2). In a separate reaction of **1a** with sodium hypochlorite at room temperature, aliquots were removed after 2 min, 10 min, 20 min and 30 min, quenched and analyzed. All these aliquots showed the presence of **2a** along with **3a**. HPLC analyses confirmed the presence of **2a** (10%) and **3a** (90%) in the aliquot removed after 2 min by comparison of retention time with authentic samples. Thus the oxidation of sulfides to the corresponding sulfones proceeds *via* the corresponding sulfoxides.

$$\underset{\mathbf{1}}{R^1\text{-}S\text{-}R^2} \xrightarrow[CH_3CN,\ rt]{NaOCl} \underset{\mathbf{2}}{R^1\text{-}SO\text{-}R^2} \xrightarrow[CH_3CN,\ rt]{NaOCl} \underset{\mathbf{3}}{R^1\text{-}SO_2\text{-}R^2} \qquad (1)$$

a) $R^1 = PhCH_2$, $R^2 = PhCH_2$ b) $R^1 = PhCH_2$, $R^2 = CH_3$ c) $R^1 = PhCH_2$, $R^2 = n\text{-}C_3H_7$
d) $R^1 = PhCH_2$, $R^2 = n\text{-}C_{12}H_{25}$ e) $R^1 = Ph$, $R^2 = CH_3$ f) $R^1 = Ph$, $R^2 = n\text{-}C_3H_7$
g) $R^1 = n\text{-}C_3H_7$, $R^2 = n\text{-}C_3H_7$ h) $R^1 = n\text{-}C_4H_9$, $R^2 = n\text{-}C_4H_9$ i) $R^1 = PhCH_2$, $R^2 = Ph$
j) $R^1 = Ph$, $R^2 = Ph$ k) $R^1 = CH_3$, $R^2 = CH_3$

The Tables show that the oxidation of sulfides and sulfoxides bearing an aryl group proceeds more rapidly than the oxidation of sulfides and sulfoxides with a benzyl group. It was observed that if the reactions were allowed to proceed for a longer time, a mixture of products was obtained as observed by tlc, *i.e.*, benzoic acid was detected in the reaction of dibenzyl sulfide with NaOCl after ~4 hrs using 1:10 molar ratio of substrate to NaOCl. When the reaction was carried out for 24 hrs, 63% of benzoic acid was recovered. It is likely that the other products were obtained because of the acidity of α -methylene group of the sulfone formed initially. All our attempts to convert dibenzyl sulfide to stilbene by changing reaction conditions have failed so far though stilbene was observed to be present in the reaction mixture by tlc.

TABLE 1. Oxidation of Sulfides to Sulfones with Sodium Hypochlorite

Compd.	Yield of **3** (%)	Molar ratio Substrate:NaOCl	Time (min)	mp. (°C) obs.	mp. (°C) lit.
1a	89	1 : 10	30	149-150	150[5]
1b	70	1 : 10	30	122	127[5]
1c	55	1 : 10	30	84-85	85-89[6]
1d	83	1 : 15	30	86	87-88[7]
1e	94	1 : 10	5	87-88	88[5]
1f	83	1 : 10	5	46	46[5]
1g	86	1 : 5	60	27	29[5]
1h	98	1 : 10	30	43	44[5]

EXPERIMENTAL SECTION

Melting points were measured on a Tropical Labequip apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer Model 621 and Shimadzu model 435 spectrophotometers. NMR spectra were recorded on Perkin-Elmer model R-32 90 MHz and Hitachi FT-NMR 60 MHz with TMS as the internal standard. HPLC analyses were carried out using ODS-18 Zorbax (150mm x 46mm) column and methanol as eluent on Shimadzu model LC-4A. Sodium hypochlorite (Aldrich) and acetonirile

(E. Merck) were used in all the reactions; the concentration of sodium hypochlorite was estimated by iodometry.[8] Compounds **1a**, **1g** and **1h** were prepared from corresponding halides and sodium sulfide.[9] All other sulfides were prepared by coupling of halides with mercaptans in the presence of anhyd. K_2CO_3.[10] The sulfoxides were prepared by oxidation of the corresponding sulfides with sodium metaperiodate[11] except diphenyl sulfoxide which was obtained by Friedel-Crafts reaction of thionyl chloride with benzene in presence of anhydrous $AlCl_3$.[12]

Table 2. Oxidation of Sulfoxides with Sodium Hypochlorite

Compd.	Yield of **3** (%)	Molar ratio Substrate:NaOCl	Time (min)	mp. (°C) obs.	mp. (°C) lit.
2a	77	1 : 10	5	149-150	150[5]
2i	91	1 : 5	60	148	148[5]
2c	76	1 : 5	5	84-85	85-89[6]
2j	97	1 : 5	5	126	126[5]
2e	73	1 : 5	30	85-86	88[5]
2f	95	1 : 5	30	44	46[5]
2k	32	1 : 5	5	108	109[5]

General Procedure.- In a dried round-bottomed flask fitted with a stir bar, was placed a mixture of **1** or **2** (0.2 g) and acetonitrile (2 mL). Sodium hypochlorite (0.63 M) was added . The contents of the flask were stirred at ambient temperature. The progress of the reaction was monitored by tlc using benzene as eluent in case of sulfides and benzene/EtOAc (90:10, v/v) as eluent in case of sulfoxides. After the disappearance of the starting material, the reaction mixture was acidified with 3N HCl and was extracted with ether (2 x 15 mL). The combined extract was dried over $MgSO_4$, concentrated on a rotary evaporator and dried in a desiccator. The products were identified by mp., IR and NMR spectra.

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REFERENCES

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1. a) S. R. Sandler and W. Karo *"Organic Functional Group Preparations"*, p. 500, Academic Press, New York, 1968; b) M. Madesclaire, Tetrahedron **42**, 5459 (1986) and references cited therein; c) S. Patai and Z. Rappoport (Ed.), *"The Synthesis of Sulphones, Sulphoxides and Cyclic Sulphides"*, Wiley, New York, p. 1, 69 (1994).

2. S. K. Chakraborty, *"Oxidations in Organic Chemistry" Part C*, p. 243, Academic Press, New York, 1978.

3. V. Ceré, A. Guenzi, S. Pollicino, E. Sandri and A. Fava, *J. Org. Chem.*, **45**, 261 (1980); b) L. S. S. Réamonn and W. Ivo O'Sullivan, *Chem. Commun.*, 1012 (**1976**); c) R. Siedlecka and J.

Skarzewski, *Synthesis*, 401 (**1994**) and references cited therein.

4. a) J. M. Khurana, P. K. Sahoo, S. S. Titus and G. C. Maikap, *Synth. Commun.*, **20**, 1357 (1990), and references cited therein; b) J. M. Khurana, A. Ray and P. K.Sahoo, *Bull. Chem. Soc. Jpn*, **67**, 1901 (1994).

5. S. Buckingham, (Ed.) *"Dictionary of Organic Chemistry"*, 5th edition, Chapman and Hall, New York, 1988.

6. US Patent, 2682544 (1954); *C.A.*, **49**, P7006a (1955)

7. M. Uchino, K. Suzuki and M. Sekiya, *Chem. Pharm. Bull. Jpn*, **26**, 1837 (1978).

8. A. I. Vogel *"Quantitative Inorganic Analysis"*, p. 396, ELBS/Longman, 1975.

9. A. I. Vogel's *"Textbook of Practical Organic Chemistry"*, 4th ed., p. 374, ELBS/Longman, 1987.

10. J. M., Khurana and P. K. Sahoo, *Synth. Commun.*, **22**, 1691 (1992).

11. Ref. 9, p. 587.

12. *"Methoden der Organische Chemie"*, Houben Weyl, **9**, 136 (1955).

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MIXED DISULFIDES OF L-CYSTEINE AND ITS DERIVATIVES WITH 2-MERCAPTOETHANOL

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The mixed disulfide (**5a**), of L-cysteine (**4a**) and 2-mercaptoethanol (ME) has been shown to function as a transport form of L-cysteine in mouse lymphoma cells in culture.[1] Whereas L-cysteine was not taken up by these cells, the presence of ME in the medium resulted in a thiol-disulfide exchange reaction producing **5a.** This compound was taken up by the lymphoma cells *via* the "L" amino acid transport system and the disulfide bond subsequently reduced by intracellular enzymes to liberate L-cysteine, thereby promoting cell growth. Murray and Rathbun[2] have also observed that not