Oxidation with Mercury(II) Oxide–Iodine Reagent: Selective Oxidation of Sulfides to Sulfoxides

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A new method for selective oxidation of sulfides to sulfoxides with mercury(II) oxide–iodine reagent is reported.

In the course of our studies on the functionalizations of organic compounds with mercury(II) oxide–iodine reagent,[1] we have found that this reagent is useful for a mild, selective oxidation of alkyl sulfides to alkyl sulfoxides. This reaction can be carried out easily by stirring a suspension of the appropriate sulfide, HgO and I_2 in CH_2Cl_2 at room temperature under neutral conditions. The resultant bright scarlet, dense precipitate (HgI_2) was removed by filtration, and the product sulfoxide in the filtrate was isolated by distillation or crystallization. Under the conditions shown in the Table, primary and secondary alkyl sulfides including dibenzyl sulfide were readily oxidized to the corresponding sulfoxides as exclusive products. Di-*tert*-butyl sulfide failed to yield its sulfoxide, probably due to carbon–sulfur bond cleavage, which has been observed in the reaction of alkyl sulfides with Cl_2–H_2O[2] and halogen succinimides.[3,4] A six-membered cyclic sulfide, pentamethylene sulfide, was selectively converted to thiane 1-oxide in almost quantitative yield. The low yield of tetramethylene sulfoxide was caused by the competitive formation of the 1:1 complex of the sulfide–HgI_2.[5] Trimethylene sulfide remained unchanged. Dithianes were not oxidized to the corresponding oxides.[6] Oxidation rates of monophenyl sulfides were relatively slower than those of dialkyl sulfides, and diphenyl sulfide remained unchanged under these conditions. These results suggest that HgO–I_2 works as a mild, electrophilic reagent,[7] and not a nucleophile.[8] Attempts to convert thianaphthene and thiophene to the corresponding oxides resulted in the selective formations of 3-iodothianaphthene, 2- and 2,5-diiodothiophene, respectively, as previously reported.[9,10] In contrast, it is of interest that thianthrene exclusively yielded its monosulfoxide even with the use of excess of reagent.

All the crude sulfoxides obtained in the present experiments have not been contaminated with sulfones, except methyl phenyl sulfoxide. This product had a trace of methyl phenyl sulfone, which was easily removable by silica gel chromatography or distillation. The reaction mixtures were neutral in all cases: no acidic substances were produced in contrast to that of the reactions with other halogen reagents in aqueous media which liberated the corresponding hydrogen halides, such as HCl and HI.[2,3,11–13]

Identical oxidation of dibenzyl sulfide using yellow HgO, prepared from $HgCl_2$ and NaOH using water containing 20.25% of $H_2{}^{18}O$,[14] yielded 14.4% ^{18}O-incorporated dibenzyl sulfoxide. These results indicate that this reaction requires one equivalent each of HgO and I_2, and is accelerated with an enhanced nucleophilicity of sulfides and also with fewer steric hindrances. Therefore it is considered that the reaction proceeds via the formation of the iodo sulfinium cation, which has previously been suggested as an intermediate for the oxidation of sulfides by halogens,[3,11–13] followed by replacement of its iodine atom with an oxygen atom of HgO.

$$R_2S \xrightarrow{I_2} R_2\overset{+}{S}\text{-}I + I^- \xrightarrow{HgO} R_2SO + HgI_2$$

Thus, the mercury(II) oxide–iodine reagent provides a convenient procedure for the selective oxidation of sulfides to sulfoxides under neutral conditions.[15]

Table. Oxidation of Sulfides to Sulfoxides with HgO–I_2 reagent in CH_2Cl_2

Sulfide	HgO/I_2 (mol equiv)	Reaction time (h)	Yield (%)	bp (°C)/Torr or mp (°C) (solvent)	Lit. bp (°C)/Torr or mp (°C)
Pr_2S	1:1	0.5	95	75/0.5	63/0.3,[4] 80/0.3[16]
Bu_2S	1:1	0.5	94	72/0.5	87–89/1,[17] 105/3[18]
i-Pr_2S	1:1	0.5	92	87/15	60/3[16]
s-Bu_2S	1:1	0.5	92	65/0.5	72–74/1[17]
$(PhCH_2)_2S$	1:1	0.5	94	132–133 (MeOH)	134–136,[4] 135–136[19]
thiacyclopentane	1:1	0.5	38	89/0.5	97–103/1[17]
thiacyclohexane	1:1	0.5	94	66–67 (Et_2O–hexane)	67–68.2[19]
PhSMe	1:1	19	85	139–140/14	83–85/0.1,[19] 98–102/1[17]
p-ClC_6H_4SMe	2:2	24	92	180/15	46–48,[20] 47–48[21]
$PhSCH_2Ph$	2:2	13	92	117–121 (Et_2O–pet. ether)	123–124,[4] 122–123[18]
9,10-dithiaanthracene	2:2	20	90[a]	140–142 (MeOH)	143[18]

[a] 9,10-Dithiaanthracene monooxide was exclusively obtained.

Oxidation of Sulfides to Sulfoxides in the Presence of HgO and Iodine; General Procedure:

A suspension of the appropriate sulfide (5 mmol), HgO (red, 5 mmol, Kanto Chem. Co.) and iodine (5 mmol) in CH_2Cl_2 (20 mL) was stirred at r.t. for the time noted in the Table, monitoring the reaction by TLC (silica gel; CH_2Cl_2). The preciptate was removed by suction filtration. The filtrate was washed with 5% aq $Na_2S_2O_3$ solution (20 mL) and water (30 mL), dried ($MgSO_4$), and evaporated to dryness. The residue was crystallized from the appropriate solvent, or distilled under reduced pressure.

The ^{18}O Labelling Experiment on the Formation of Dibenzyl Sulfoxide in the Oxidation of Dibenzyl Sulfide in the Presence of HgO–I_2:

A suspension of dibenzyl sulfide (107 mg, 0.5 mmol) and yellow HgO (109 mg, 0.5 mmol, prepared by the reaction of a solution of $HgCl_2$ in water containing 20.25% of $H_2{}^{18}O$ with NaOH)[14] in CH_2Cl_2 (5 mL) was flushed with nitrogen for 15 min. After addition of I_2 (127 mg, 0.5 mmol), the suspension was stirred under N_2 for 45 min. The resultant colorless solution was separated from the scarlet precipitate and worked up as described above to give dibenzyl sulfoxide (113 mg) as a colorless solid. The analysis of the incorporation of ^{18}O to this crude sulfoxide by FI mass spectrometry (JEOL JMS-DX300 spectrometer) indicated that the sulfoxide contained 14.4% ^{18}O.

(1) Preceeding paper on a related subject, see: Orito, K.; Hatakeyama, T.; Takeo, M.; Suginome, H. *Synthesis* **1995**, 1273.
(2) Kwart, J.; Miller, R.K. *J. Am. Chem. Soc.* **1956**, *78*, 5008.
(3) Tagaki, W.; Kikukawa, K.; Ando, K.; Oae, S. *Chem. Ind. (London)* **1964**, 1624.
(4) Harville, R.; Read, S.F., Jr. *J. Org. Chem.* **1968**, *33*, 3976.
(5) Tetramethylene sulfide–HgI_2 complex is a colorless solid, which decomposes gradually during usual isolation, such as filtration and recrystallization, to a colorless liquid (tetramethylene sulfide) and a scarlet precipitate (HgI_2).
(6) 1,2-Dithiane was unreactive, and 1,3- as well as 1,4-dithiane gave a 1:1 complex with HgI_2 as a white precipitate.
(7) Greco, A.; Modena, G.; Todesco, P.E. *Gazz. Chim. Ital.* **1960**, *90*, 671, *Chem. Abstr.* **1961**, *55*, 16510f.
(8) Modena, G.; Todesco, P.E. *J. Chem. Soc.* **1962**, 4920.
(9) Gaertner, R. *J. Am. Chem. Soc.* **1952**, *74*, 4950.
(10) Campaigne, E.; Foye, W.O. *J. Am. Chem. Soc.* **1948**, *70*, 3941.
(11) Higuchi, T.; Gensch, K.-H. *J. Am. Chem. Soc.* **1966**, *88*, 3874; 5486.
(12) Gensch, K.-H.; Pitman, I.H.; Higuchi, T. *J. Am. Chem. Soc.* **1968**, *90*, 2096.
(13) Miotti, U.; Modena, G.; Sedea, L. *J. Chem. Soc. (B)* **1970**, 802.
(14) Suginome, H.; Senboku, H. *Tetrahedron* **1994**, *50*, 13101.
(15) Treatment of dibenzyl sulfide with Ag_2O–I_2 also gave dibenzyl sulfoxide, but at a slower reaction rate.
(16) Addison, C.C.; Sheldon, J.C. *J. Chem. Soc.* **1956**, 2705.
(17) Liu, K.-T.; Tong, T.-C. *J. Org. Chem.* **1978**, *43*, 2717.
(18) Oae, S.; Ohnishi, Y.; Kozuka, S.; Tagaki, Y. *Bull. Chem. Soc. Japan* **1966**, *39*, 364.
(19) Leonard, N.J.; Johnson, C.R. *J. Org. Chem.* **1962**, *27*, 282.
(20) Andersen, K.K.; Edmonds, W.H.; Biasotti, J.B.; Strecker, R.A. *J. Org. Chem.* **1966**, *31*, 2859.
(21) Cerniáni, A.; Modena, G. *Gazz. Chim. Ital.* **1959**, *89*, 843 *Chem. Abstr.* **1960**, *54*, 22446i.