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OXIDATION USING DISTANNOXANE II.[1] SELECTIVE AND MILD OXIDATION OF SULPHIDES

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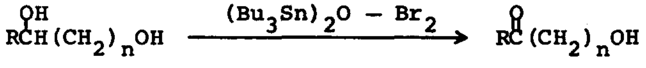
Recently, Trost developed the efficient route for the alkene synthesis involving the elimination of sulphinyl group, and successfully demonstrated the natural product synthesis.[2] In such natural product synthesis, however, we have encountered the difficulty for the sodium periodate oxidation of certain sulphides which have hydrophobic long alkyl chain, apparently because such hydrophobic sulphides are scarcely miscible with aqueous organic solvents.

While the hydrogen peroxide or peracid oxidation of sulphides require the special care to avoid the over-oxidation to sulphones or possible side reactions such as epoxidation of the olefin function. With this circumstance in mind, we have investigated the new oxidizing reagent which meets the following requirements;

(1) highly selective and mild oxidation to sulphoxides even in the presence of excess oxidizing reagent,

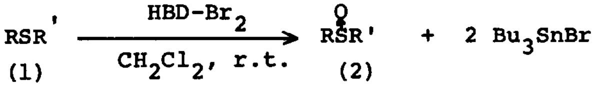
(2) oxidation in organic solvent without addition of water, which is suitable for hydrophobic sulphides such as intermediates for the natural product synthesis.

We have recently reported the selective oxidation of diols at the secondary hydroxy group using the combination of hexabutyldistannoxane (HBD) and bromine.[3]



$$\mathrm{R\overset{OH}{C}H(CH_2)_nOH} \xrightarrow{(Bu_3Sn)_2O\ -\ Br_2} \mathrm{R\overset{O}{\overset{\|}{C}}(CH_2)_nOH}$$

We wish to report here that this reagent satisfactorily meets the above requirements for the oxidation of sulphides. Upon treatment of various sulphides with HBD-Br_2 in methylene chloride at room temperature, the corresponding sulphoxides were obtained without sulphone contamination even in the presence of excess HBD-Br_2.



$$\underset{(1)}{RSR'} \xrightarrow[CH_2Cl_2,\ r.t.]{HBD\text{-}Br_2} \underset{(2)}{R\overset{O}{S}R'} + 2\ Bu_3SnBr$$

TABLE I. Oxidation of Sulphides[4]

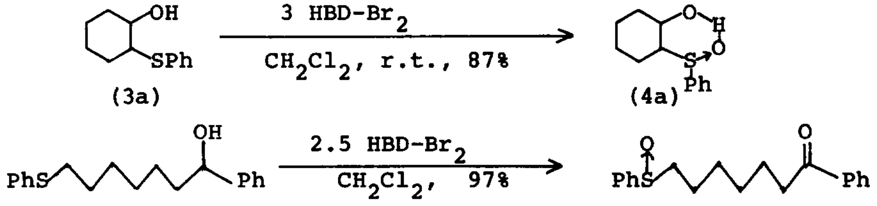
	Sulphides (1)	Sulphoxides (2)	Yield (%)	$\nu_{S=O}$ (cm^{-1})
a	$PhSCH_3$	$PhSOCH_3$	85	1040
b	$PhSCH_2Ph$	$PhSOCH_2Ph$	82	1035
c	$PhCH_2SCH_2Ph$	$PhCH_2SOCH_2Ph$	84 92[a)]	1032
d	CH_3SCH_2Cl	CH_3SOCH_2Cl	78[b)]	1050
e	$PhS(CH_2)_5CH_3$ [c)]	$PhSO(CH_2)_5CH_3$	85	1040
f	$[CH_3(CH_2)_{15}]_2S$	$[CH_3(CH_2)_{15}]_2SO$	90	1020
g	PhSPh	PhSOPh	18[d)] [5]	1045

a) By reverse addition; To a solution of HBD and Br_2 prepared at -78°C, sulphide 1c was added dropwise at the same temperature. b) at -78°C. c) Oxidation using sodium periodate in aq. MeOH-dioxane gave trace amount of sulphoxide 2e. d) Diphenyl sulphide was recovered in 81% yield. Dibutyltin oxide (Bu_2Sn=O) was also isolated.

The typical experimental procedure is as follows; To a solution of n-hexadecyl sulphide (1f) (0.48g, 1 mmol) and hexabutyldistannoxane (HBD) (0.6 ml, 1.15 mmol) in dry methylene chloride (30 ml), bromine (0.06 ml, 1.15 mmol) solution in methylene chloride (5 ml) was added dropwise at room temperature with stirring (20-60 min). The mixture was stirred for additional 1-2 hr. Evapolation and addition of the small amount of n-hexane (or n-pentane) to the residue with cooling gave n-hexadecyl sulphoxide (2f), 0.45g (90%), m.p. 96.5-97.5°C (n-hexane).

In the case of liquid sulphoxides, separation of the sulphoxide was carried out using silica gel chromatography. As shown in TABLE I, the procedure has great value, especially, for the oxidation of hydrophobic sulphides such as (1e) and (1f), since the periodate oxidation of (1e) gave the trace amount of sulphoxide (2e).

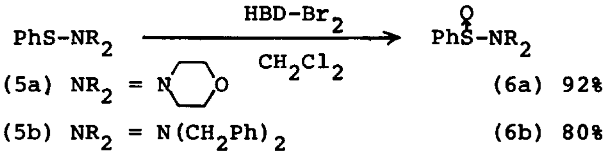
As an interesting application of the present method, we have examined the cooxidation of the bifunctional hydroxy-sulphides using excess HBD-Br_2. 2-Phenylthiocyclohaxanol (3a) gave 2-phenylsulphinylcyclohexanol (4a)[4] in 87% yield, m.p. 154-155°C (PhH), $\nu_{S=O}$ 990, 1008 cm^{-1}, ν_{OH} 3320 cm^{-1}. The ir spectrum of (4a) shows the strong hydrogen bonding, which seems to prevent the further oxidation of the hydroxy group.



(3a) (4a)
(3b) (4b)

On the other hand, hydroxy-sulphide (3b)[6] was cleanly oxidized at -75°C to keto-sulphoxide (4b)[4,7] in almost quantitative yield, m.p. 62-63°C (n-hexane). Consequently, the present HBD-Br_2 oxidation may provide a facile method for the preparation of keto-sulphoxides unless the strong intramolecular hydrogen bonding in the intermediate, hydroxy-sulphoxide is concerned.

Next we examined the oxidation of sulphenamides to sulphinamides, since the latter compounds were generally prepared on the reaction of sulphinyl chlorides with amines, and the direct oxidation of sulphenamides is known to give sulphonamides as main product by the usual oxidizing reagents.[8]



Sulphenamide (5a) and (5b) produced the corresponding sulphinamide (6a) [$\nu_{S=O}$ 1050 cm^{-1}, ν_{S-N} 902 cm^{-1}, m.p. 80.5-82°C] and (6b) [$\nu_{S=O}$ 1060 cm^{-1},

ν_{S-N} 890 cm^{-1}] in good yield, respectively, without sulphonamide contamination by the similar procedure either at -75°C (5a) or at room temperature (5b).[4]

The mildness and neutral conditions of the present oxidant may allow the selective oxidation of sulphenamides to sulphinamides and may constitute the preparative value.

In summary, the HBD-Br_2 reagent has potential utility due to the several aspects described above.

References

1) Part I. see ref. 3. Distannoxane (HBD) is available as a commercial product.
2) B. M. Trost, "Organic Sulfur Chemistry," Ed. C. J. M. Stirling, Butterworths, London, 1975, pp 237.
3) Y. Ueno and M. Okawara, Tetrahedron Lett., 4597 (1976).
4) All compounds obtained here had satisfactory physical, spectral, and analytical data.
5) Oae et al., reported the oxidation of certain sulphides with bromine-1,4-diazabicyclo-[2,2,2]octane complex, S. Oae, Y. Ohnishi, S. Kozuka, and W. Tagaki, Bull. Chem. Soc. Japan, 39, 364 (1966). Contrary to their results, the poor yield of diphenyl sulphoxide by our method indicates the more reduced (more mild) reactivity of our reagent, and this behaviour might suggest the possibility of the strong coordination of the bromine moiety to tin atom involving pentacoordinated organotin species prior to the formation of sulphoxides and n-tributyltin bromide.
6) This compound (3b) was prepared on the reaction of 6-phenylthiohexylmagnesium bromide with benzaldehyde, m.p. 50.0-51.5°C (n-pentane).
7) The procedure was similar except for the treatment with ammonium fluoride to remove the n-tributyltin bromide after evapolation of methylene chloride.
8) Y. Tanaka, T. Sugiyama, and Y. Tanaka, Chem. Pharm. Bull.(Tokyo), 13, 1384 (1965).