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THIOPHOSPHORYL BROMIDE: A NEW REAGENT FOR THE REDUCTION OF SULFOXIDES TO SULFIDES

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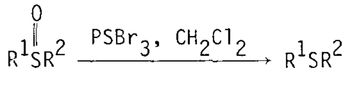
Summary: Thiophosphoryl bromide ($PSBr_3$) has been found to be a mild, effective reagent for the reduction of sulfoxides of widely differing structural types to the corresponding sulfides.

A number of new procedures for the reduction of sulfoxides have recently been reported[1-6] and at least two excellent reviews of this synthetic conversion have also appeared recently.[7,8] We ourselves have recently described the use of phosphorus pentasulfide as a versatile reagent not only for reducing sulfoxides but also for the reduction of related classes of compounds, such as sulfimides (sulfilimines) and selenoxides.[9] We now wish to report the successful application of a simple new reagent for the sulfoxide to sulfide conversion, namely, thiophosphoryl bromide ($PSBr_3$).[10] To our knowledge, this represents the first general application of thiophosphoryl bromide as a reagent in organic synthesis.

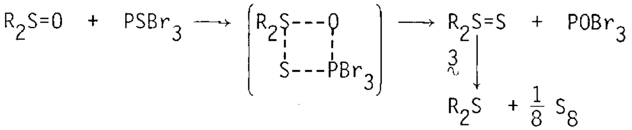
As the results in the Table indicate, thiophosphoryl bromide has proved to be, in several ways, a superior reagent to phosphorus pentasulfide for the reduction of sulfoxides. It is readily available commercially, or it may conveniently be synthesized from red phosphorus, bromine and phosphorus pentasulfide, in 67% yield.[11] The reagent, although a low-melting solid, is only moderately hygroscopic and does not require extreme precautions in handling. It is readily soluble in organic solvents such as dichloromethane and thus is not subject to possible variations in surface activity arising from the method of purification of the reagent, which may characterize a heterogeneous reagent system such as phosphorus pentasulfide suspended in an organic solvent.[12] Although the reaction times required were somewhat more variable with thiophosphoryl bromide, the yields were, in most cases better and, in some cases, very much better, than in the analogous reactions with phosphorus pentasulfide (Table, entries 2a-c, 2e, 2f). Curiously, the formally analogous thiophosphoryl chloride ($PSCl_3$)[13] was found to be almost totally ineffective for the reduction of sulfoxides.



$$R^1\overset{O}{\overset{\|}{S}}R^2 \xrightarrow{PSBr_3,\ CH_2Cl_2} R^1SR^2$$

1 2a-h

The results obtained are summarized in the Table. All reactions proceeded smoothly in dichloromethane at 25°, using a 1:1 molar ratio of the reactants. Any vestigial traces of thiophosphoryl bromide were conveniently destroyed by washing with dilute sodium carbonate solution. The sulfoxide corresponding to 2h, 2,2-dimethylthiochroman-4-one 1-oxide, was chosen to illustrate the impressive selectivity of the reagent in attacking exclusively the sterically hindered sulfoxide group, in preference to the more accessible carbonyl group.[14] The final entry in the Table indicates that the reaction with thiophosphoryl bromide is also capable of extension to selenoxides and, in fact, that selenoxides react faster than their sulfoxide counterparts, as already noted by us in an earlier investigation.[9] As previously observed with the phosphorus pentasulfide reagent and with almost all other reagents tried to date, however, thiophosphoryl bromide (or the chloride) shows no reaction with simple sulfones, even after several days. Although no direct mechanistic evidence is yet available, it seems probable that, by analogy with the phosphorus pentasulfide reaction, the reduction of sulfoxides may proceed through formation of the four-centre transition state shown, possibly leading to the unstable thiosulfoxide 3 and phosphoryl bromide. Recent mechanistic studies of the phosphorus pentasulfide reaction of sulfoxides have shown that the thiosulfoxides are likely intermediates, which would lose sulfur readily to give the sulfides.[15] The by-product expected in our reaction, phosphoryl bromide, is known to be readily hydrolyzed in aqueous media[16] and would thus not survive our work-up procedure. The greater electron-withdrawing effect of chlorine may render the P=S, in thiophosphoryl chloride, insufficiently reactive towards the polar sulfoxide bond.



The method herein reported constitutes a versatile, mild procedure for the deoxygenation of sulfoxides in high yield, using a readily obtainable, simple reagent. The reaction appears to be capable of extension to selenoxides and may also be used to reduce keto-sulfoxides to keto-sulfides, without concomitant attack at the carbonyl group. A typical procedure is described below.

Reduction of Dibenzyl Sulfoxide to Dibenzyl Sulfide: Dibenzyl sulfoxide (0.46 g, 2.0 mmol) was dissolved in dichloromethane (16 ml) in a pre-dried flask equipped with stirrer, drying tube, and septum-cap inlet. Thiophosphoryl bromide (0.6 g = 0.2 ml, 2.0 mmol) was carefully added, using a syringe, and the reaction mixture stirred at 25° for 2 h. The dichloromethane solution was then washed with 5% sodium carbonate solution (2x) and the organic layer dried ($MgSO_4$) and evaportated. The pure sulfide (0.29 g, 66%) was isolated after preparative T.L.C. No sulfoxide band at 1040 cm^{-1} (Nujol) was present in the I.R., while the ^1H N.M.R. showed only $\delta(CDCl_3)$ 3.53 (4H,s), 7.23 (10H,s) ppm. (Corresponding singlets in the sulfoxide appear at $\delta(CDCl_3)$ 3.90 and 7.33 ppm.)

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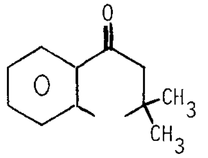
Table: Reduction of Sulfoxides (**1**)[a] to Sulfides (**2a**-**h**) with thiophosphoryl bromide[b] at 25°C in dichloromethane.

Product	R^1	R^2	Yield[c] [%]	Reaction Conditions
2a	CH_3	CH_3	99	10 min/25°
2b	n-C_4H_9	n-C_4H_9	90	2 h/25°
2c	$C_6H_5CH_2$	$C_6H_5CH_2$	66	2 h/25°
2d[d]	CH_2=$CHCH_2$[d]	C_6H_5[d]	99	2 h/25°
2e	(p-)$CH_3C_6H_4$	(p-)$CH_3C_6H_4$	84	6 h/25°
2f	C_6H_5	C_6H_5	98	4 h/25°
2g	(p-)ClC_6H_4	(p-)ClC_6H_4	78	24 h/25°
2h[e,f]		[e,f]	99	2 h/25°
2i[g]	C_6H_5[g]	C_6H_5[g]	88	5 min/25°

[a] With the exception of 2,2-dimethylthiochroman-4-one 1-oxide (see **2h**) the sulfoxides used in this investigation were commercially available and were used as supplied.

[b] Thiophosphoryl bromide was obtained from Ventron Corporation, and used without purification.

[c] The purity of all products, confirmed by T.L.C., N.M.R., I.R., and by mp and mixed mp with an authentic sample where appropriate, was >99%. The literature mp's and bp's of the sulfides in the Table, except those for **2d** and **2h** (q.v.), have been cited previously.[9]

[d] The sulfide is a liquid, lit.[17] bp 114°/25 torr.

[e] The required sulfoxide has been reported previously.[18]

[f] The sulfide had mp 42-44°, lit.[19] mp 44-45°.

[g] Conversion of diphenyl selenoxide[20] to diphenyl selenide. The selenide is a liquid, lit.[21] bp 159°/10 torr.

References and Notes

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