Dibromoborane-dimethyl sulfide: A new, mild, chemoselective reagent for the rapid deoxygenation of sulfoxides to sulfides†

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Dibromoborane-dimethyl sulfide chemoselectively deoxygenates aliphatic and aromatic sulfoxides to the corresponding sulfides in excellent chemical yields in CH_2Cl_2 solvent in 15 minutes at both 0°C and room temperature, in the presence of reducible functional groups, such as alkene, ketone, ester, lactone, nitrile, amide, azide, sulfone, and *N*-oxide.

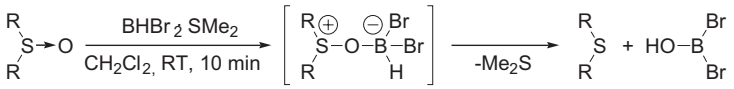
Keywords: dibromoborane-DMS, sulfoxides, sulfides, deoxygenation and chemoselectivity

Sulfoxides have proved to be highly useful synthetic intermediates, especially as a chiral auxiliaries in organic synthesis.[1] The growing significance of organosulfur compounds in natural product synthesis has stimulated the development of numerous useful mild and selective methods for the deoxygenation of sulfoxides to sulfides.[2] We and others have developed several boron-based reducing reagents, which successfully reduce sulfoxides to sulfides.[3] Tungsten hexachloride (WCl_6), Zr-Ru heterometallic complexes (at low temperature) and TiI_4 have also been used to effect deoxygenation of sulfoxides to sulfides.[4] 2,6-Dihydroxypyridine, Tebbe reagent, Ph_3P/Lewis acid, $NaBH_4$/I_2, NBS/I_2, oxalyl chloride, phosphite/dichlorodioxomolybdenum (VI), and silphos have also been reported as effective reagents for the reduction.[5] Recently Westcott and coworkers[6] reported the deoxygenation of sulfoxides using the boron-based reagent, catecholborane.

Among the haloboron reagents, dichloroborane ($BHCl_2$) rapidly and chemoselectively deoxygenated dialkyl and alicyclic sulfoxides to sulfides in THF under mild conditions whereas the reaction took 24 h to reach 90% completion with diphenyl sulfoxide. Guindon *et al.*[3j] studied the comparative deoxygenation of dialkyl, arylalkyl, diaryl, and heterocyclic sulfoxides with three boron bromide reagents – boron tribromide (BBr_3), 9-borabicyclo[3.3.1]nonyl bromide (*B*-Br-9-BBN), and dimethylboron bromide (Me_2BBr) and found that these reagents are very efficient and rapid at lower temperatures (–23 to 0°C) in the presence of propene (bromine trap). However, the reaction of BBr_3 with diaryl sulfoxide was slow and low yielding.

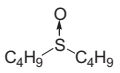
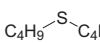
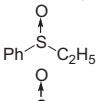
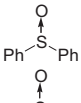
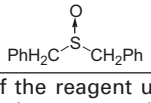
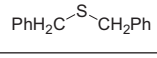
Monobromoborane-dimethyl sulfide ($BH_2Br{\cdot}SMe_2$) and dibromoborane–dimethyl sulfide ($BHBr_2{\cdot}SMe_2$) have mainly been utilised as hydroborating agents.[7,8] Recently we explored the synthetic utilities of these reagents as highly stereo-, regio-, and chemoselective reagents for the cleavage of epoxides to bromohydrins.[9,10] Our longstanding interests in developing new synthetic methodologies based on boron reagents persuaded us to examine the synthetic utility of $BHBr_2{\cdot}SMe_2$ for the deoxygenation of sulfoxides to sulfides. We now report a new application of $BHBr_2{\cdot}SMe_2$ as a practical, mild, chemoselective reagent for the deoxygenation of sulfoxides to sulfides at both 0°C and room temperature in short reaction time.[11]

Reaction of sulfoxides with 1.0 equiv of $BHBr_2{\cdot}SMe_2$ in CH_2Cl_2 at room temperature or 0°C for 10–15 min resulted in complete deoxygenation of the sulfoxides to the corresponding sulfides in excellent yield with high chemical purity (Scheme 1) (Table 1). Significantly, the reaction is found to be very



Scheme 1 Deoxygenation of organic sulfoxide to sulfide.

Table 1 Deoxygenation of sulfoxide to sulfides by $BHBr_2{\bullet}SMe_2$[a] via Scheme 1

Entry	Sulfoxides	Reaction conditions	Product sulfide	Yield/%[b]	Isolated yield/%
1		25°C, 10 min		96	90
2		0°C, 15 min		83[c]	–
3		25°C, 10 min		96	92
4		25°C, 10 min		90	86
5		0°C, 15 min		96	90
6		0°C, 15 min		96	91

[a]1.0 Equiv of the reagent used. [b]Yield determined by ^{1}H NMR spectroscopy using biphenyl as an internal standard. [c]The crude product was clean as seen by ^{1}H NMR (no chromatographic purification due to its volatile nature).

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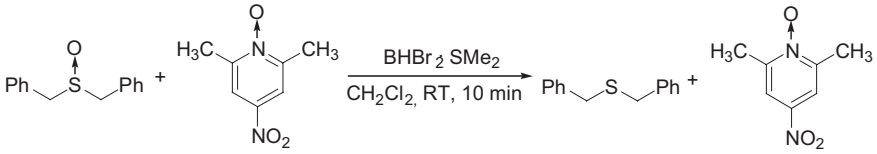
rapid for all the sulfoxides studied, *e.g.*, dialkyl, alicyclic, arylalkyl, and diaryl sulfoxides. ^{1}H NMR spectra showed the complete absence of halogenated byproducts and Pummerer-type products. The relatively lower yield of the tetrahydrothiophene (83%) is probably due to the volatile nature of the product.

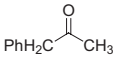
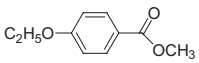
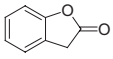
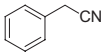
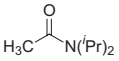
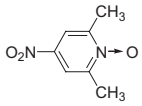
In order to explore the chemoselectivity of this reagent, a study of deoxygenation of dibenzyl sulfoxide in the presence of an equivalent amount of reducible compound was undertaken. The dibenzyl sulfoxide was chemoselectively reduced and most of the added "reducible" compounds, such as ketone, ester, lactone, nitrile, amide, *N*-oxide, alkene, sulfone and azide, were recovered almost quantitatively (Scheme 2). The results are summarised in Table 2. In order to show the relative effectiveness of this reagent $BHBr_2{\cdot}SMe_2$, the result achieved from the deoygenation of dibenzyl sulfoxide with $BHBr_2{\cdot}SMe_2$ is compared with some of the boron reagents reported in the literature (Table 3). It is very obvious from Table 3 that $BHBr_2{\cdot}SMe_2$ very cleanly and efficiently deoxygenates in a shorter reaction time.

In summary, dibromoborane-dimethyl sulfide rapidly and cleanly deoxygenates dialkyl, alicyclic, aryl alkyl and diaryl sulfoxides at ambient temperature or at 0°C in <15 min. Several reducible functional groups, such as alkene, ketone, ester, lactone, nitrile, amide, *N*-oxide, azide, and sulfone, survive during the deoxygenation process. This new procedure does not require the bromine trap (alkene) as needed in the case of $(CH_3)_2BBr$ and *B*-Br-9-BBN. Therefore, dibromoborane-dimethyl sulfide ($BHBr_2{\cdot}SMe_2$) should serve as an excellent, mild, chemoselective deoxygenating reagent for the reduction of sulfoxides to sulfides, complementing the current synthetic methodologies.



Scheme 2 Chemoselective deoxygenation of dibenzyl sulfoxide by $BHBr_2{\cdot}SMe_2$ in CH_2Cl_2 in the presence of 4-nitro-2,6-dimethylpyridine-1-oxide.

Table 2 Chemoselective deoxygenation of dibenzyl sulfoxide by $BHBr_2{\cdot}SMe_2$ in CH_2Cl_2 in the presence of other "reducible" compounds

Entry	Reducible compound	Conditions	Sulfide/%[a]	Recovery of reducible compound/%[a]
1		25°C, 10 min	99	90
2		25°C, 10 min	97	99
3		0°C, 15 min	99	99
4		0°C, 15 min	98	88
5		25°C, 15 min	97	86
6		25°C, 10 min	96	94
7		0°C, 15 min	98	99
8		25°C, 15 min	91	99

[a]Yield determined by ^{1}H NMR spectroscopy using biphenyl as an internal standard.

Table 3 Deoxygenation of dibenzyl sulfoxide with various boron reagents: a comparison

Entry	Reagent/mmol	Conditions	% Isolated yield	Refer.
1	$BHCl_2$ (1.0)	25°C, 4 h	37	3a
2	$BHCl_2$ (1.0)	25°C, 24 h	90	3a
3	$BF_3{\bullet}OEt_2$–NaI	0°C to RT, 5 h	96	2a
4	BBr_3 (1.0)	–25 to 0°C, 40 min	83	3j
5	*B*–Br–9–BBN (1.0)[a]	–25 to 0°C, 40 min	96	3j
6	$(CH_3)_2BBr$ (1.0)[a]	–25 to 0°C, 40 min	94	3j
7	$ThxCHCl{\bullet}S(CH_3)_2$ (1.0)	25°C, 4 h	89	3f
8	$BHBr_2{\bullet}S(CH_3)_2$ (1.0)	0°C, 15 min	91	This work
9	$BHBr_2{\bullet}S(CH_3)_2$ (1.0)	25°C, 10 min	90	This work

[a]Reaction was conducted in the presence of propene which functions as a bromine trap.

Experimental

All starting materials were purchased from the Aldrich Chemical Company. All products are known compounds; they were identified by comparison of their spectroscopic data with those of authentic samples.[5i]

A representative procedure for the deoxygenation of dibenzyl sulfoxide to dibenzyl sulfide with $BHBr_2{\cdot}SMe_2$

Dibromoborane–dimethyl sulfide (1.0 ml, 1 mmol, 1.0 M in CH_2Cl_2) was added slowly to a stirred solution of dibenzyl sulfoxide (0.23 g, 1 mmol) in CH_2Cl_2 (2.0 ml) at room temperature under a nitrogen atmosphere. The reaction took place instantaneously (as seen by ^{11}B NMR). After 10 min, the reaction mixture was quenched with 3M NaOH (2.5 ml) with cooling (ice) and extracted with CH_2Cl_2 (3 × 25 ml), washed with water (10 ml) and brine solution (2 ×10 ml). The organic layer was dried (anhydrous Na_2SO_4) and concentrated *in vacuo* to obtain the crude dibenzyl sulfide (0.206 g, 96%) which was found to be spectroscopically pure. The chemical yield of the product sulfide was determined by ^1H NMR spectroscopy using biphenyl as an internal standard. The product sulfide was also purified by silica gel column chromatography and the chemical yield (90%) of the isolated product was determined (Table 1).

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