A Novel Method for the Deoxygenation of Sulfoxides with the $PPh_3/Br_2/CuBr$ System

Kiumars Bahrami,* Mohammad Mehdi Khodaei,* and Mohammad Khedri
Department of Chemistry, Razi University, Kermanshah 67149, Iran

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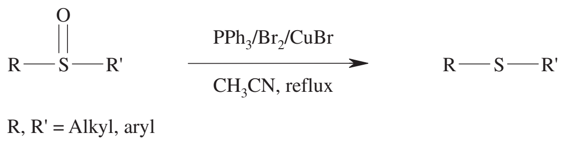
It was found that the combination of $PPh_3/Br_2/CuBr$ was an effective promoter for the deoxygenation of sulfoxides and gave the corresponding sulfides in excellent yield in acetonitrile under refluxing conditions. It is worth mentioning that this reagent system is chemoselective, tolerating various functional groups such as carbon–carbon double bond and ketone.

The deoxygenation of sulfoxides to the corresponding sulfides is an important reaction that has found considerable utility in organic synthesis[1] and in biochemical reactions.[2] In most cases, sulfoxides are removed from the target molecules and they are usually eliminated by a two-step process involving deoxygenation to sulfides,[3] which are then reductively cleaved by catalytic hydrogenation or other chemical methods.[4] This transformation has been accomplished in a variety of ways,[5–12] however, many of these transformations are limited by side reactions, low yields, the use of expensive reagents, functional group incompatibility, difficult work-up procedures, or harsh reaction conditions. For example, the use of hydrogen halides is somewhat restricted with acid-sensitive substrates, the reductions with the strong hydride systems $LiAlH_4$–$TiCl_4$ and $NaBH_4$–$CoCl_2$ are incompatible with several functional groups.

As a consequence, the introduction of new methods and/or further work on technical improvements to overcome the limitations is still an important experimental challenge. Herein, we describe the successful use of the $PPh_3/Br_2/CuBr$ system as a method to deoxygenation of sulfoxides to the corresponding sulfides. The route for the synthesis of sulfides is shown in Scheme 1.

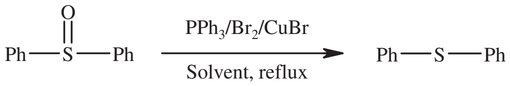
To evaluate the solvent effect, the deoxygenation of diphenyl sulfoxide was carried out under similar reaction conditions using various organic solvents such as toluene, dichloromethane, methanol, and acetonitrile (Table 1). Among the various solvents studied acetonitrile was found to be the best solvent for this transformation.

A ratio of 1:1.2:1.2:2.2 sulfoxide/PPh_3/Br_2/CuBr was found to be optimum for the deoxygenation of sulfoxides and the results are presented in Table 2. The applicability of the $PPh_3/Br_2/CuBr$ system was then examined for the deoxygenation of diaryl, dibenzyl, aryl benzyl, dialkyl, and cyclic sulfoxides in acetonitrile under refluxing conditions.[13] The results are presented in Table 2. As shown, all the reactions were completed within a short time and the sulfides were obtained in almost quantitative yields as the sole deoxygenation products.



Scheme 1.

Table 1.



Entry	Solvent[a]	Time/h	Yield/%[b]
1	CH_3CN	45	97
2	$PhCH_3$	45	20
3	CH_2Cl_2	45	25
4	MeOH	45	40

[a] Sulfoxide:PPh_3:Br_2CuBr = 1:1.2:1.2:2.2. [b] Isolated yields.

Table 2. Deoxygenation of sulfoxides to their corresponding sulfides using $PPh_3/Br_2/CuBr$ system

Entry	R	R′	Time/min	Yield/%[a,b]
1	C_6H_5	C_6H_5	41	98
2	C_6H_5	$C_6H_5CH_2$	30	97
3	$C_6H_5CH_2$	$C_6H_5CH_2$	45	94
4	C_6H_5	4-$MeC_6H_4CH_2$	34	97
5	C_6H_5	4-$BrC_6H_4CH_2$	30	96
6	C_6H_5	4-$NO_2C_6H_4CH_2$	36	93
7	4-MeC_6H_4	$C_6H_5CH_2$	29	96
8	4-BrC_6H_4	$C_6H_5CH_2$	26	97
9	4-ClC_6H_4	$C_6H_5CH_2$	27	95
10	4-MeC_6H_4	4-$BrC_6H_4CH_2$	35	93
11	4-BrC_6H_4	4-$BrC_6H_4CH_2$	27	96
12	4-MeC_6H_4	4-$MeC_6H_4CH_2$	35	95
13	C_6H_5	Me	30	92
14	C_6H_5	$CH_2CH=CH_2$	28	95
15	2-C_6H_4-CO-2-C_6H_4		39	90
16	n-C_4H_9	n-C_4H_9	48	93

[a] The products were characterized by comparison of their spectroscopic and physical data with those reported in literature. [b] Yields refer to pure isolated products.

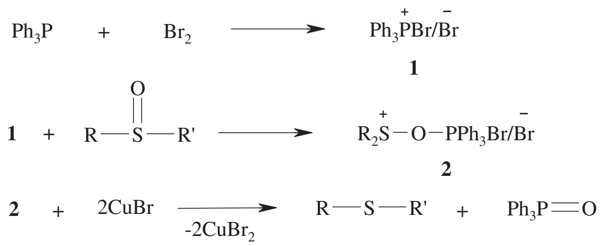
It is worth mentioning that the $Ph_3P/Br_2/CuBr$ system is chemoselective, tolerating various functional groups such as carbon–carbon double bond and ketone (Table 2, Entries 14 and 15). These observations clearly suggest that this method can be applied for the chemoselective deoxygenation of these sulfoxides in the presence of the above-mentioned functional groups in multifunctional molecules.

We investigated the deoxygenation of diphenyl sulfoxide (Table 2, Entry 1) as a model compound with Ph_3P, Ph_3P/Br_2, Ph_3P/CuBr, or CuBr in refluxing acetonitrile. Under these conditions, the reaction did not proceed at all after 2 h and the starting material was isolated intact from the reaction mixture.

In order to show the efficiency of this method, the results of deoxygenation of dibenzyl sulfoxide to dibenzyl sulfide (Table 2, Entry 3) by our method are compared with those reported by

Table 3. Comparison of deoxygenation of dibenzyl sulfoxide to dibenzyl sulfide (Table 2, Entry 3) by the $Ph_3P/Br_2/CuBr$ system with some of those reported in the literature

Reagent (Oxidant/Substrate)	Yield/% (Time)
$Ph_3P/Br_2/CuBr/CH_3CN$/reflux	94 (45 min)
$NiCl_2/NaBH_4$/THF/0 °C (3:9)[14]	81 (2 h)
$PhSiH_3/MoO_2Cl_2/PhCH_3$/reflux[15]	95 (20 h)
2,6-Dihydroxypyridine/CH_3CN/reflux[16]	98 (4 h)
$Ph_3P/TiCl_4$/THF/rt[17]	96 (2 h)
TiI_4/CH_3CN/0 °C[1f]	85 (10 min)
$BF_3 \cdot Et_2O/NaI/CH_3CN$/rt[18]	98 (20 min)
BBr_3/CH_2Cl_2/−23–0 °C[19]	91 (40 min)



Scheme 2. Proposed mechanism for the deoxygenation of sulfoxide.

other methods. The results show that this method is superior to some previously reported methods in terms of yields, reaction times, and the amount of the reagent used for successful deoxygenation (Table 3).

The enthalpies of formation of triphenylphosphine and triphenylphosphine oxide are $\Delta_f H^\circ = +207.02\,\mathrm{kJ\,mol^{-1}}$ and $\Delta_f H^\circ = -116.41\,\mathrm{kJ\,mol^{-1}}$, respectively.[20] On the basis of this fact, the formation of $Ph_3P{=}O$ is the major driving force in the proposed mechanism. Treatment of Ph_3P with Br_2 forms the intermediate **1**. Addition of sulfide to **1** produces the intermediate **2** and this intermediate in the presence of CuBr can then be converted to a sulfide (Scheme 2).

In conclusion, the present investigation has demonstrated the use of the $Ph_3P/Br_2/CuBr$ system as a very simple mixed-reagent system for the efficient deoxygenation of sulfoxides in excellent yields and short reaction times. In addition, wide applicability and also excellent chemoselectivity make this reagent system a good choice for the use in the deoxygenation of sulfoxides.

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13 General procedure for the deoxygenation of sulfoxides: To a flask containing a stirring mixture of Ph_3P (1.2 mmol, 0.314 g) and Br_2 (1.2 mmol, 0.07 mL) in dry acetonitrile (5 mL), sulfoxide (1 mmol) was added. CuBr (2.2 mmol, 0.315 g) was then added to the reaction mixture. The reaction mixture was stirred at reflux temperature for the time indicated in Table 2. The progress of the reaction was monitored periodically by TLC. Upon completion, the reaction mixture was evaporated and purified by silica-gel column chromatography with the appropriate mixture of *n*-hexane and ethyl acetate to afford the sulfides.

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