Reduction of Sulfoxides with Sodium or Benzyl Bromide

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The reduction of dimethyl and diphenyl sulfoxides, and of alkyl and arylbenzyl sulfoxides to the corresponding sulfides can be carried out using sodium bromide without solvent or benzyl bromide in dimethylformamide, mostly through an oxidation–reduction cycle catalyzed by developing hydrobromic acid.

The sulfoxide–sulfide conversion, a very important reaction in organic synthesis, has been widely studied[1] and has recently been reviewed.[2] Many methods have been developed for the deoxygenation of sulfoxides, but only a few take place under mild conditions, in high yields, and with use of common laboratory reagents. Trivalent phosphorus compounds have been used successfully,[3] and more specifically, triphenylphosphine has been extensively exploited by using as coreactants carbon tetrachloride,[4] acids[5] and iodine/sodium iodide.[6] Recently polystyryldiphenylphosphine was used[7] to avoid the separation difficulties suffered from the previous phosphorus reagents. Halide ions have been used only in the form of the corresponding acid halides,[8,9] and as far as the authors are aware, the reduction of sulfoxides with tert-butyl bromide[10] represents the sole example of the use of organic halides for this kind of reaction.

We report herein the use of sodium or benzyl bromide for the reduction of sulfoxides in relatively mild conditions and with yields ranging from moderate to good. Our observation that sodium bromide, but not chloride,[11] triggered dimethyl sulfoxide decomposition, prompted us investigate this reaction with other sulfinyl derivatives.

The reaction is carried out by heating without solvent the derivatives 1a–g, with an equimolar amount of sodium bromide in the presence of catalytic amounts of para-

toluenesulfonic acid or tert-butyl hydroperoxide, until a vigorous reaction occurs (Scheme A). The phenylmethyl alkyl- and arylsulfinyl derivatives 1b–e, give the corresponding sulfides in particularly good yields however the GC analyses of their reaction mixtures always showed traces of benzyl bromide (Table 1).

Table 1. Reaction of Sodium Bromide with Sulfoxides 1a–g

Sulf-oxide	Temp. (°C)[a]	Product Sulfide[b]	Yield[c] (%)	mp (°C) or bp (°C)/Torr found	mp (°C) or bp (°C)/Torr reported
1a	–[d]	2a	70	37/760	38/760[17]
1b	130	2b	72	195/760	93–94/14[19]
1c	165	2c	69	48–49	49[17]
1d	135	2d	70[e]	115/22	114–115/22[18]
1e	135	2e	68	41–42	40[20]
1f	165	2f	35	99–101/0.1	296/760[17]
1g	165	2g	55	193/760	193/760[17]

[a] Temperature at which the reaction occurs instantaneously.

[b] ^{1}H-NMR and IR spectra of all the sulfides obtained are superimposable with those of authentic samples. The S—O vibration ($v = 1040$–$1060\,cm^{-1}$) is always absent in the IR spectra.
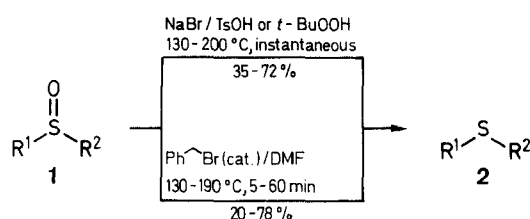
[c] Yields of isolated products are reported.

[d] The temperature reaches 190 °C and then drops very quickly to 65–67 °C in 40 min while Me_2S distills from the reaction mixture.

[e] Traces of 4-$CH_3C_6H_4CH_2Br$ are present in the GC of the reaction mixture.

The deoxygenation of 1a–g can also be carried out, though in very poor yields, by heating without solvent at high temperature (200 °C) probably through a Pummerer rearrangement.[12] The strong catalytic effect of sodium bromide (lower reaction temperatures, higher yields) is thought to be a consequence of the formation of benzyl bromide, by reaction of the halide with protonated sulfoxides.[13] Benzyl bromide thus formed could then undergo nucleophilic displacement more readily than the protonated sulfoxide (Scheme B).[14]

The role of benzyl bromide in the reduction is confirmed by the moderate yield of sulfides 2a–g (Table 2) obtained from the treatment of the corresponding sulfoxides with a catalytic amount of benzyl bromide in dimethylformamide solution or without solvent. The conditions are not particularly harsh, the temperatures being in the range 130–190 °C. We believe that the reaction is occurring mostly through an oxidation–reduction cycle[9] catalyzed by hydrobromic acid developing from the reaction along the path "b" of the

NaBr / TsOH or t-BuOOH
130-200 °C, instantaneous
35-72%

Ph⌢Br(cat.)/DMF
130-190 °C, 5-60 min
20-78%

1, 2	R^1	R^2	1, 2	R^1	R^2
a	CH$_3$	CH$_3$	e	CH$_2$Ph	Ph
b	CH$_2$Ph	CH$_3$	f	Ph	Ph
c	CH$_2$Ph	CH$_2$Ph	g	Ph	CH$_3$
d	4-CH$_3$C$_6$H$_4$CH$_2$	CH$_3$			

Scheme A
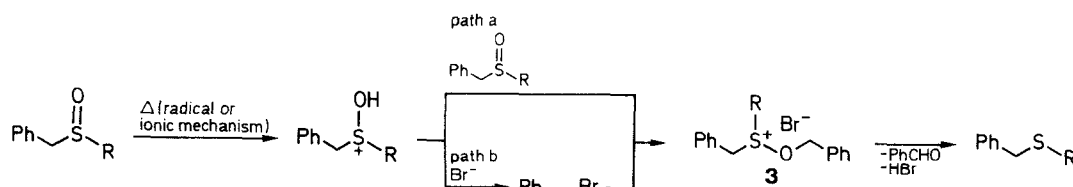
Scheme B

Table 2. Reduction of Sulfoxides 1a–f with a Catalytic Amount of Benzyl Bromide

Sulfoxide	Reaction Conditions			Product Sulfide[a]	Yield[b] (%)	mp (°C) or bp (°C)/Torr	
	Amount of DMF	Time (min)	Temp. (°C)			found	reported
1a	0	60	189	2a	70	37/760	38/760[17]
1b	3	60	155	2b	70[c]	196/760	93–94/14[19]
1b	0	–[d]	130	2b	72[c]	196/760	93–94/14[19]
1c	3	60	155	2c	50	48–49	49[17]
1c	0	–[d]	140	2c	70	48–49	49[17]
1d	2	60	155	2d	65[e]	155/22	114–115/22[18]
1d	0	5	150	2d	20[e]	155/22	114–115/22[18]
1e	3	60	155	2e	20	41–42	40[20]
1e	0	–[d]	140	2e	70	41–42	40[20]
1f	0	5	190	2f	78[f]	99–101/0.1	296/760[17]

[a] Refers to footnote b of Table 1.

[b] Yield of isolated products.

[c] Dibenzyl sulfide was detected by GC in the reaction mixture; 10% in the presence and 20% in the absence of the solvent.

[d] The reaction occurs instantaneously at the reported temperature.

[e] $(4\text{-}CH_3C_6H_4CH_2)_2S^{21}$ and $4\text{-}CH_3C_6H_4SCH_2Ph^{22}$ are detected in GC; 23% and 6% in the reaction with solvent, 52% and 10% in the reaction without solvent.

[f] A stoichiometric amount of benzyl bromide is used.

scheme. Evidence for this mechanism is that the reaction is almost completely inhibited[15] by sodium bicarbonate and that only catalytic[16] quantities of benzyl bromide are sufficient to carry out the reaction.

All compounds prepared were compared (mp, IR and ^{1}H-NMR spectra) with authentic samples prepared by known methods. The sulfoxides **1b,d,e,g** were readily prepared from the corresponding sulfides by standard procedures, whereas **1a,c,f** were purchased from Aldrich. Microanalyses were obtained on a Carlo Erba model 1106 Elemental analyzer. IR spectra were taken with a Perkin-Elmer 157-G spectrophotometer. ^{1}H-NMR were obtained on a Varian FT 80A spectrometer. GC analyses were performed on a Carlo Erba HRGC 5300 using SE-30 as a stationary phase and nitrogen as carrier gas. DMF was distilled under vacuum from BaO.

Reaction of the Sulfoxides 1a–g in the Presence of Sodium Bromide; General Procedure:

A mixture of the sulfoxide **1** (3 mmol), NaBr (0.31 g, 3 mmol) and a catalytic amount of TsOH is placed in a two-neck 50 mL flask fitted with a thermometer and a condenser. The mixture is slowly heated with an oil bath until the reaction becomes vigorous (see Table 1). The heating is stopped and the mixture is poured into water (2 mL), extracted with Et$_2$O (2 × 10 mL), dried (Na$_2$SO$_4$), and after GC analysis is chromatographed on a silica gel column, using light petroleum (bp 40–70°C)/Et$_2$O to give the sulfide **2**.

Reaction of Benzyl Methyl Sulfoxide with Benzyl Bromide; Typical Procedure:

A mixture of benzyl methyl sulfoxide (**1g**; 12.8 mmol), a catalytic amount of benzyl bromide and DMF (3 mL) is refluxed for 60 min in a 25 mL round-bottomed flask fitted with a condenser. The mixture is then poured into water (5 mL) and extracted with pentane (3 × 15 mL). The pentane layer is dried (Na$_2$SO$_4$), and evaporated. Percolation on a silica gel column using light petroleum as eluent gives the pure sulfide; yield: 0.6 g (70%).

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(12) When NaCl is used, the temperature at which some reduction occurs (190–200°C) is essentially the same as in the absence of NaCl. The yields are always very low except for 1b and 1d, which give 65% and 75% of the corresponding sulfides when heated until 200°C in the absence of any halide, and until 185°C in the presence of NaCl with catalytic amounts of p-toluenesulfonic acid. Benzyl chloride is always present in the GC of the reaction mixtures of all the benzyl sulfoxides.
(13) Methyl bromide could be formed in the case of 1a and 1g, whereas some other mechanism could operate in the case of 1f.
(14) A similar mechanism was proposed for DMSO decomposition:
Head, D. L.; McCarty, C. G. Tetrahedron Lett. 1973, 1405.
(15) Very small amounts of sulfides appearing in the GC of the reaction mixtures of 1b,c,e, when carrying out the reaction in the presence of NaHCO₃, are probably coming from the Pummerer rearrangement of the intermediate 3 of Scheme B.
(16) When using stoichiometric amount of benzyl bromide the normal products of reduction of sulfoxides 1b,d become negligible in comparison to new sulfides coming from other reaction paths. See Table 2 and relative footnotes.
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