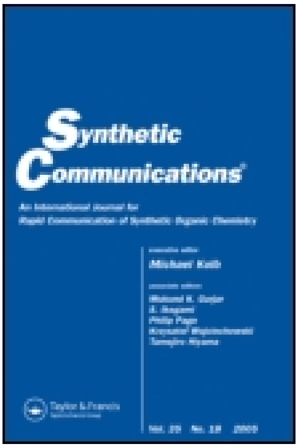

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Selective and Efficient Deoxygenation of Sulfoxides with $NbCl_5$/Indium System

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SELECTIVE AND EFFICIENT DEOXYGENATION OF SULFOXIDES WITH $NbCl_5$/INDIUM SYSTEM

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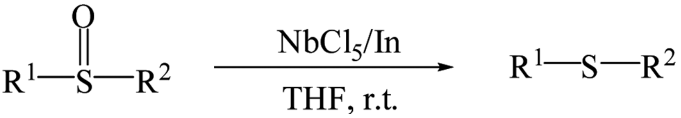
GRAPHICAL ABSTRACT



Abstract *It has been found that dialkyl, diaryl, and aryl alkyl sulfoxides can be selectively converted to the corresponding sulfides with a* $NbCl_5/In$ *system in good to excellent yields under mild conditions. Several functional groups (bromo, chloro, methoxy, aldehyde, and vinyl) were tolerated under the reaction conditions.*

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Keywords Deoxygenation; indium; niobium; sulfide; sulfoxide

INTRODUCTION

The deoxygenation of sulfoxides to the corresponding sulfides is a valuable transformation that has found utility in organic synthesis and biochemical reactions.[1] In Particular, sulfoxides deserve much attention as important chiral auxiliaries in asymmetric synthesis.[2] Therefore, a number of methods have been developed for the deoxgenation of sulfoxides. However, many of these methods are limited by undesirable side reactions, functional group incompatibility, difficult workup procedures, and harsh reaction conditions. Further, some of these methods are associated with limitations of poor yields and prolonged reaction times. As a consequence, the search for a new and efficient method for the deoxygenation of sulfoxides is still a worthwhile goal. Much effort has been devoted to the development of milder conditions where the presence of various sensitive and reducible functional groups can be tolerated. The use of low-valent oxophilic d-block metals has become important in deoxygenation of various types of organic substrates.[3] In this regard, deoxygenations of sulfoxides are readily performed with low-valent tungsten,

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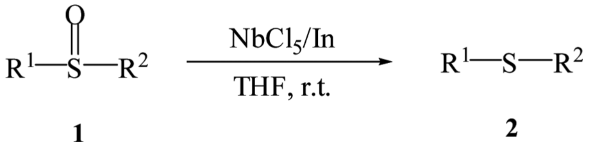
molybdenum, and titanium generated from WCl_6, $MoCl_5$, and $TiCl_4$ in the presence of metal (Zn, In, Sm).[4] In continuation of our efforts toward low-valent metal reagents for organic transformations,[5] we considered that a combination of $NbCl_5$ with indium could bring about the deoxygenation of sulfoxides under mild conditions. Recently, indium metal has drawn increasing attention for its unique properties such as low toxicity and high stability in water and air compared with other metals.[6] Herein, we report an efficient and chemoselective method for the deoxygenation of sulfoxides **1** to the corresponding sulfides **2** with a $NbCl_5$/In system at room temperature.

RESULTS AND DISCUSSION

We have investigated the reactions of $NbCl_5$/In system with various sulfoxides and found that they can be selectively reduced to the corresponding sulfides in good yields (Scheme 1). Metal–metal salt binary systems have long been used as reducing agents for many functional groups.[7] Recently we have reported that $TiCl_4$/In or Cp_2TiCl_2/In could be used for the deoxygenation of various sulfoxides.[8] In comparison with other procedures, the $NbCl_5$/In system reduces sulfoxides in better yields and shows good chemoselectivity. Some control experiments revealed that sulfoxides could not be deoxygenated by $NbCl_5$ or indium alone under the present condition and starting materials were recovered unchanged. The new reducing system was readily generated by the addition of indium powder to a stirred solution of niobium pentachloride in tetrahydrofuran (THF) under sonication. To assess the scope and limitations of this reagent system, the reaction was studied with various sulfoxides bearing other potentially labile functional groups. As shown in Table 1, the methodology is equally applicable to dialkyl, diaryl, and aryl alkyl sulfoxides. We have tried reduction of diphenylsulfone and methylphenylsulfone under the present reaction conditions. However, the starting materials were recovered intact.

Electron-donating or electron-withdrawing groups on the aromatic ring did not seem to affect the reaction significantly either in the yield of the product or the rate of the reaction. The functional group tolerance of this method is evident from entries 3–7, which show that bromo, chloro, methoxy, aldehyde, and vinyl functionalities are unaffected under the reaction conditions. Thus we have been able to demonstrate the utility of the easily accessible $NbCl_5$/In system as a useful reagent for effecting chemoselective deoxygenation of sulfoxides. Although the reaction mechanism is still unclear, it can be rationalized as the result of a two-step process. In the first step, it is assumed that reduction of niobium(V) chloride with indium provides low-valent niobium species, which are involved in complexation with the substrates. The complex weakens the S-O bond and renders the sulfur atom more



$$R^1-\overset{O}{\overset{\|}{S}}-R^2 \xrightarrow[\text{THF, r.t.}]{NbCl_5/In} R^1-S-R^2$$

Scheme 1. Conversion of sulfoxides to their corresponding sulfides.

Table 1. Deoxygenation of various sulfoxides with $NbCl_5$/indium

Entry	R^1	R^2	Products	Time (h)	Yield (%)[a,b]
1	Ph	Ph	PhSPh	3.0	92
2	Ph	CH_3	$PhSCH_3$	1.0	96
3	$4\text{-}BrC_6H_4$	Me	$4\text{-}BrC_6H_4SMe$	3.0	94
4	$4\text{-}ClC_6H_4$	$4\text{-}ClC_6H_4$	$(4\text{-}ClC_6H_4)_2S$	2.5	90
5	$4\text{-}CH_3OC_6H_4$	$4\text{-}CH_3OC_6H_4$	$(4\text{-}CH_3OC_6H_4)_2S$	3.0	93
6	$4\text{-}CHOC_6H_4$	CH_3	$4\text{-}CHOC_6H_4SCH_3$	3.0	89
7	Ph	$CH_2{=}CH$	$PhSCH{=}CH_2$	1.5	88
8	$4\text{-}CH_3C_6H_4$	$4\text{-}CH_3C_6H_4$	$(4\text{-}CH_3C_6H_4)_2S$	0.5	91
9	$4\text{-}CH_3C_6H_4$	CH_3	$4\text{-}CH_3C_6H_4SCH_3$	0.5	90
10	$PhCH_2$	$PhCH_2$	$(PhCH_2)_2S$	4.0	95
11	$PhCH_2$	Ph	$PhCH_2SPh$	3.5	93
12	nC_4H_9	nC_4H_9	$(nC_4H_9)_2S$	2.0	92

[a] Refers to isolated yields.

[b] The products were characterized by comparison of their spectroscopic and physical data with reported values.

susceptible to the reduction. In the subsequent step, the reduction proceeds by a reductive cleavage of the polarized S-O bond through a single electron transfer from indium metal to the niobium-substrate complex.[9] The in situ generation of deoxygenating reagent, $NbCl_3$ (or $NbCl_4$), from the $NbCl_5$/indium system would present the possibility of regeneration of the reagent from the oxidized form $NbOCl_3$. The resulting $NbOCl_3$ can be recycled upon reduction with indium to NbOCl. The substoichiometric use of $NbCl_5$ supports the possibility of such reagent regeneration. The reducing property exhibited by metal–metal salt combinations proceeds through transfer of one electron from the metal surface to the substrate. In such combinations, the elementary metal part needs to be more electropositive than the metal part of the salt. The method offers advantages such as mild reaction conditions, simple experimental operation, and tolerance of some functional groups. The utility of $NbCl_5$/In system as a new reducing agent is also demonstrated by the good yields of dibenzyl sulfide (entry 10) and phenyl benzyl sulfide (entry 11) obtained after the reduction of the corresponding sulfoxides. Usually the sulfoxides that contain a benzyl group are difficult to reduce by other reagents.[10]

EXPERIMENTAL

Melting points were determined by the open glass capillary method and are uncorrected. All reagents were used as received. THF was distilled from sodium benzophenone immediately prior to use. The ^1H NMR spectra were recorded on a FT-Bruker AF-300 (300 MHz for ^1H NMR; 75 MHz for ^{13}C NMR) using tetramethyl silane (TMS) as an internal standard. Thin-layer chromatographic (TLC) analysis was performed on silica gel plates (Merck, 60 F-254). All products were purified by flash column chromatography using silica gel 60 (79–230 mesh, Merck).

A general procedure for the deoxygenation of sulfoxides is as follows: Indium powder (230 mg, 2.0 mmol) and niobium pentachloride (135 mg, 0.5 mmol) were mixed in freshly distilled THF (5 mL). The resulting mixture was sonicated for

0.5 h to produce a solution of the low-valent niobium–indium complex. Diphenylsulfoxide (202 mg, 1.0 mmol) was then added to this solution, and the reaction mixture was stirred for 3 h at room temperature. The progress of the reaction was followed by TLC. On completion, the solvent was removed under reduced pressure, and the residue was extracted successively with ethyl acetate and washed with water and brine. The organic layer was separated and dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on a silica gel (hexane–ethyl acetate = 2:1) to give a pale yellow liquid, which was identified as diphenylsulfide (171 mg, 92%).[11a] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.25 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.7, 131.1, 129.2, 127.1. GC/MSD (*m*/*z*): 186 (M^+). All of the products were characterized by comparison of their spectroscopic and physical data with reported values. Please see the spectroscopic data of products, available online.

CONCLUSION

In conclusion, we have discovered that $NbCl_5$/In system mediates an efficient and selective conversion of sulfoxides to the corresponding sulfides with good yields under mild conditions. We believe that this procedure will present a useful and practical alternative to the conventional methods for the deoxygenation of sulfoxides to sulfides. Further investigations of more useful applications are currently in progress.

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