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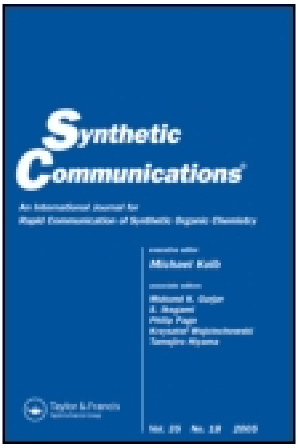

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Shigetaka Yakabe [a], Masao Hirano [b] & Takashi Morimoto [b]
[a] Nihon University, Narashino, Japan
[b] Tokyo University of Agriculture and Technology, Koganei, Japan

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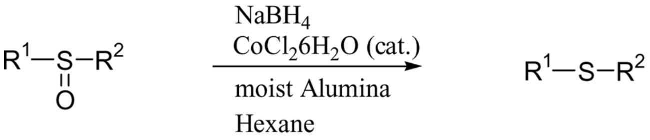
ONE-POT REDUCTION OF SULFOXIDES WITH $NaBH_4$, $CoCl_2 \cdot 6H_2O$ CATALYST, AND MOIST ALUMINA

Shigetaka Yakabe,[1] Masao Hirano,[2] and Takashi Morimoto[2]
[1]*Nihon University, Narashino, Japan*
[2]*Tokyo University of Agriculture and Technology, Koganei, Japan*

GRAPHICAL ABSTRACT



Abstract *Sulfoxides are reduced by a combination of sodium borohydride, a catalytic amount of cobalt(II) chloride hexahydrate, and chromatographic neutral alumina preloaded with a small amount of water (moist alumina) in hexane to produce the corresponding sulfides in good to excellent yields under mild conditions. An interesting structural influence of sulfoxides on their reactivity is observed.*

Keywords Cobalt(II) chloride hexahydrate; moist alumina; reduction; sodium borohydride; sulfoxide

INTRODUCTION

Reducing agents generated from sodium borohydride and transition metal halides (e.g., $NiCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$, $PdCl_2$) have successfully been used for the reduction of various functional groups including olefinic double bonds, carboxylic acids, nitro compounds, sulfoxides, and so on.[1,2]

We have recently examined the reduction of aldehydes and ketones with sodium borohydride in hexane in the presence of moist alumina ($NaBH_4$/moist alumina system),[3] upon which a synthetically very interesting reaction performance was observed; namely, the reducing system requires only stoichiometric to slightly excess amount of $NaBH_4$ for completion of the reaction and is amenable to a wide range of substrates having other reducible functional groups.[3a] The yields of the alcohols are excellent, and, in addition, the recovered alumina can be reused for several runs with no loss of its activity. Recently, this reaction system was used to develop a new one-pot reduction, which has been applied to the synthesis of chiral

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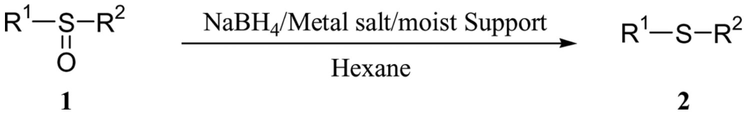
Address correspondence to Shigetaka Yakabe, Nihon University, Narashino 275-8575, Japan. E-mail: shige-yakabe@yahoo.co.jp

alcohols, β-azidoalcohols, allylic alcohols, 1,2-diols, and chiral lactones.[4] Encouraged by this success, our continued interest in $NaBH_4$ chemistry in aprotic solvents led us to extend the solid–solution biphasic system to sulfoxide-to-sulfide reduction, since there has been no general method achievable with this transformation in good yields under mild conditions with the use of common laboratory reagents.[5]

A preliminary experiment carried out using methyl phenyl sulfoxide (**1a**) as the test substrate with the $NaBH_4$/moist alumina system, however, failed to give methyl phenyl sulfide (**2a**), and starting **1a** was recovered quantitatively (Fig. 1). Consequently, we then looked for an efficient metal catalyst.[1] Of metal salts examined ($NiCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$, $PdCl_2$, and $CrCl_2$), $CoCl_2 \cdot 6H_2O$ was found to be the catalyst of choice for the present purpose. In addition, another comparative study using various solid-support materials (aluminas, silica gels, clays, zeolites) revealed that neutral alumina was superior to the others in terms of the conversion of **1a** as well as the yield of **2a**. These results are presented in Table 1.

A typical procedure is as follows: deionized water (0.19 g) was added to commercial chromatographic neutral alumina (ICN Biomedical, Alumina N, Super I; 0.81 g) in portions, followed by a vigorous shaking of the mixture for a few minutes upon every addition of deionized water until a free-flowing powder was obtained and afforded a moist alumina (H_2O content, 19 wt%). Sulfoxides were prepared according to our own method.[6] Compound **1a** (0.140 g, 1 mmol), hexane (10 mL), $CoCl_2 \cdot 6H_2O$ (Kokusan Chemical; 0.024 g, 0.1 mmol), freshly prepared moist alumina (1 g), and $NaBH_4$ (Wako; 0.038 g, 1 mmol) were placed into a 30-mL round-bottom flask, and the resultant heterogeneous mixture was magnetically stirred at 30 °C. After 3 h, the reaction mixture was transferred onto a sintered glass filter funnel, and the filter cake was washed thoroughly with portions of dry ether (total *ca.* 60 mL). The sulfide **2a** was isolated and identified spectroscopically [^{1}H NMR, infrared (IR), gas chromatography–mass spectrometry (GC-MS)] via comparisons with commercial authentic samples.

The reduction of typical alkyl aryl, diaryl, and dialkyl sulfoxides was carried out with the $NaBH_4/CoCl_2 \cdot 6H_2O$ catalyst/moist alumina system in hexane, and the results are presented in Table 2. In the case of alkyl phenyl sulfoxide series (entries 1–5), the reactivity of the substrates decreased with an increase in the carbon chain length or the bulk of the alkyl groups. The same tendency was observed in the reduction of dialkyl sulfoxides (entries 8 and 9). So far as we are aware, such steric effect of alkyl groups on the reactivity of sulfoxides has not yet been reported. Certain $NaBH_4$-based reductions proceed without suffering from such remarkable structural influence of sulfoxides as observed herein; see, for example, Ref. 5(*d*) and 5(*g*). In fact, we have observed in our own experiments that certain sulfoxides show essentially the same reactivity upon the homogeneous $NaBH_4$ reduction in ethanol, giving the sulfides in almost equal yields. On the other hand, the difference in reactivities of unsubstituted (entry 1) and substituted thioanisoles (entries 10–12) is less apparent



$$R^1-\underset{\overset{\|}{O}}{S}-R^2 \xrightarrow[\text{Hexane}]{\text{NaBH}_4\text{/Metal salt/moist Support}} R^1-S-R^2$$

Figure 1. Sulfoxide reduction scheme in this reaction system.

Table 1. Effect of metal salts and supports on the reduction of methyl phenyl sulfoxide[a]

No.	Metal salt	Support	$NaBH_4$ (mmol)	GC yield (%) **1a**	**2a**
1	—	N-Alumina	1.0	>99	0
2	$CoCl_2 \cdot 6H_2O$	N-Alumina	1.0	2	95
3	$NiCl_2 \cdot 6H_2O$	N-Alumina	1.0	82	19
4	$PdCl_2$	N-Alumina	1.0	85	11
5	$CrCl_2$	N-Alumina	1.0	95	0
6	$CoCl_2 \cdot 6H_2O$	—	0.5	91	6
7	$CoCl_2 \cdot 6H_2O$	N-Alumina	0.5	43	66
8	$CoCl_2 \cdot 6H_2O$	Silica gel	0.5	92	16
9	$CoCl_2 \cdot 6H_2O$	Aluminum silicate	0.5	65	36
10	$CoCl_2 \cdot 6H_2O$	Bentonite	0.5	52	53
11	$CoCl_2 \cdot 6H_2O$	Montmorillonite K10	0.5	60	43
12	$CoCl_2 \cdot 6H_2O$	Hydrotalcite	0.5	72	35
13	$CoCl_2 \cdot 6H_2O$	Zeolite F9	0.5	81	19

[a] At 30 °C, for 3 h; 1 mmol of methyl phenyl sulfoxide, 1 g of moist support (H_2O content, 19 wt%), 0.1 mmol of metal salt, and 10 ml of hexane were used.

than that ascribed to the steric influence. The present reduction is assumed to occur on the alumina surface, since its absence resulted in a negligible conversion of **1a**. Therefore, moist alumina not only generates an active reducing species from $NaBH_4$ and $CoCl_2 \cdot 6H_2O$ but provides reaction sites unfavorable for bulky substrates, thus exerting a unique influence on the present system.

Scanning electron microscopy (SEM) images of the commercial alumina and the metal-supported aluminas are shown in Fig. 2. SEM images of (b) and (c) show some small grains on alumina particles compared with the SEM image of (a); therefore, Co compounds during this reaction are present in a homogeneous dispersion on alumina particles.

Table 2. Reduction of various sulfoxides[a]

No.	Sulfoxide R^1	R^2	$NaBH_4$ (mmol)	$CoCl_2$ (mmol)	Al_2O_3[b] (g)	Temp. (°C)	Isolated yield (%) **1**	**2**
1	Ph	Me(1a)	1.0	0.1	1.0	30	2	95
2	Ph	Et	2.5	0.2	2.5	30	0	90
3	Ph	Bu	4.0	0.4	4.0	60	34	51
4	Ph	*s*-Bu	4.0	0.4	4.0	60	68	27
5	Ph	C_6H_{13}	4.0	0.4	4.0	60	52	39
6	Ph	Ph	4.0	0.4	4.0	60	51	48
7	$PhCH_2$	$PhCH_2$	2.0	0.2	2.0	60	86	12
8	Me	C_8H_{17}	2.0	0.2	2.0	30	0	>99
9	C_6H_{13}	C_6H_{13}	3.0	0.3	3.0	60	72	18
10	$4\text{-}CH_3C_6H_4$	Me	1.0	0.1	1.0	30	0	79
11	$4\text{-}ClC_6H_4$	Me	1.0	0.1	1.0	30	5	90
12	$4\text{-}EtOCOC_6H_4$	Me	1.0	0.1	1.0	30	24	53

[a] For 3 h; sulfoxide 1 mmol and hexane 10 ml were used.

[b] Moist alumina (H_2O content, 19 wt%).

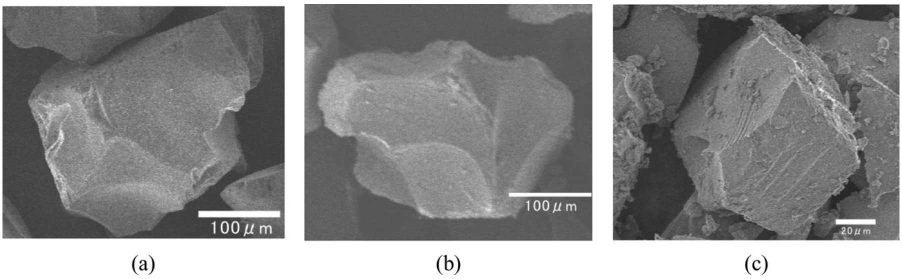


Figure 2. SEM images of (a) the commercial alumina and the metal-supported aluminas (b) before the reduction (residue of reaction according to typical procedure without sulfoxide and $NaBH_4$, for 10 min stirring) and (c) after the reduction.

The color of insoluble materials in this reaction turned from pale pink to gray a short time later. This color change presumes that CoO and/or Co_3O_4 were produced on alumina. Co compounds on alumina could not be identified but might become clear in further analysis by x-ray diffraction,[7] Fourier transform infrared (FT-IR) spectroscopy,[8] and so on.

In summary, a new, experimentally simple reduction of numbers of sulfoxides can be achieved using easily available, inexpensive, and safe reagents ($NaBH_4$, $CoCl_2 \cdot 6H_2O$, and chromatographic alumina), giving the corresponding sulfides moderate to excellent yields under mild and neutral conditions. A further application of the present heterogeneous system in a variety of organic transformations is now under way in our laboratory.

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