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$B(C_6F_5)_3$-Catalyzed Deoxygenation of Sulfoxides and Amine *N*-Oxides with Hydrosilanes

Fangwei Ding,[a,b] Yanqiu Jiang,[a] Shaoyan Gan,[a,b] Robert Li-Yuan Bao,[a,b] Kaifeng Lin,[a] and Lei Shi *[a,b,c]

Dedication ((optional))

Abstract: An efficient strategy for the deoxygenation of sulfoxides and amine *N*-oxides using $B(C_6F_5)_3$ and hydrosilanes has been developed. The method affords the corresponding aromatic or aliphatic products in good to high yields, and shows good functional group tolerance under mild conditions.

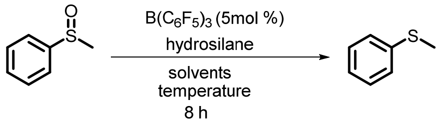
Introduction

Boron Lewis acids have spurred widespread interest as powerful tools for activation of hydrosilanes[1] and related transformations.[2] Meanwhile, hydrosilanes employed as low toxic, highly active and handling easily substances have also received considerable attention. Consequently, the combined use of $B(C_6F_5)_3$ and hydrosilanes is found to be a method for the deoxygenation of alcohols[3] and ethers[4] as well as carbonyl compounds and their derivatives.[5] The past decade has witnessed spectacular advances in metal-free catalytic reductions, particularly using $B(C_6F_5)_3$/silanes.[2] In addition, the reduction of sulfoxides and amine *N*-oxides into their corresponding sulfides and amines is an important reaction due to its considerable utility in organic synthesis. Over the past years, many systems have been employed for the deoxygenation of sulfoxides including reagents such as silane/MoO_2Cl_2,[6] oxo-complexes,[7] gold nanoparticle,[8] $Zn(OTf)_2/B_2(pin)_2$ or $Zn(OTf)_2$/boranes,[9] $SOCl_2$,[10] Fe powder,[11] ruthenium nanoparticle,[12] and I_2.[13] On the other hand, the deoxygenation of amine *N*-oxides involved In,[14] $Mo(CO)_6$,[15] Cu,[16] $NbCl_5$/Zn,[17] Raney nickel,[18] diboron reagents,[19] and gold nanoparticle.[20] However, many reagents employed for these deoxygenation processes are expensive,[6, 8, 12] sensitive to both air and moisture[15, 17] or using transition metal under harsh conditions. Herein, a novel method, $B(C_6F_5)_3$ deoxygenation of sulfoxides and amine *N*-oxides with hydrosilanes is presented.

Results and Discussion

The deoxygenation of methyl phenyl sulfoxide was chosen as the model reaction for studying the influence of hydrosilanes, and critical parameters such as solvents and temperature. In order to compare the catalytic activities of several hydrosilanes, phenylsilane, diethylsilane, and triphenylsilane as representative primary, secondary, and tertiary silanes were investigated. These reagents had a dramatic effect on the product yields. To our delight, the addition of small bulk of silane sources such as tetramethyldisiloxane (TMDS) and diethylsilane had positive effects. While there was no reaction in the presence of triphenylsilane, perhaps because the steric hindrance is involved in the Si–H bond cleavage. Fortunately, using $PhSiH_3$, the desired product was isolated in 85 % yield (Table 1, entry 2). The influence of solvents was investigated as well. Since tetrahydrofuran (THF) could interact with the $B(C_6F_5)_3$,[21] the catalyst activity was reduced, giving the desired product in 42 % yield. Using acetonitrile and 1,2-dichloroethane (DCE) as solvents, the substrates were converted into the expected products in 60 % and 75 % yields, respectively (Table 1, entries 8-9). Ultimately, the effect of temperature was studied. The yield could be slightly increased by elevating the temperature to 100 °C (Table 1, entry 10). However, when the reaction was carried out at room temperature (Table 1, entry 1), no product was obtained. Considering lower temperature may be good for functional group tolerance, and provide a mild condition, 60 °C was selected as the optimized temperature. As a result, (Table1, entry 2) was selected as the standard condition.

Table 1. Optimization studies for the deoxygenation of methyl phenyl sulfoxide catalyzed by $B(C_6F_5)_3$.[a]



Entry	Hydrosilane	Solvent	*T* [°C]	Yield [%][b]
1	$PhSiH_3$	toluene	r.t.	trace
2	$PhSiH_3$	toluene	60	85
3	TMDS	toluene	60	75
4	Et_2SiH_2	toluene	60	73
5	PMHS	toluene	60	64
6	Ph_3SiH	toluene	60	trace
7	$PhSiH_3$	THF	60	42
8	$PhSiH_3$	MeCN	60	60
9	$PhSiH_3$	DCE	60	75

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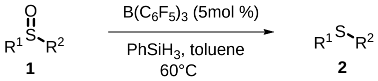
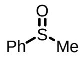
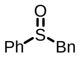
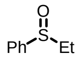
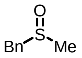
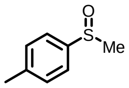
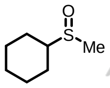
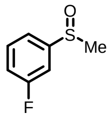
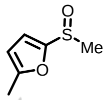
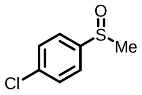
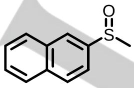
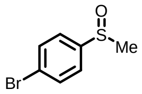
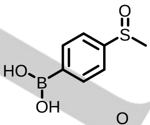
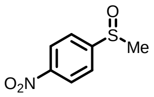
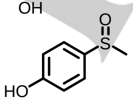
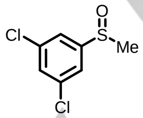
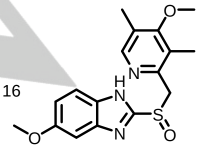
10	$PhSiH_3$	toluene	100	86

[a] Reaction conditions: sulfoxide 1a (0.5 mmol, 1 equiv.) and hydrosilane (1 mmol, 2 equiv.) with $B(C_6F_5)_3$ (5 mol %) in solvent (1.5 mL) at the investigated temperature for 8 h. [b] Yield of isolated product.

To probe the scope of the reaction, we applied the optimized conditions to a variety of sulfoxides. The deoxygenation of various sulfoxides to the corresponding sulfides was obtained in high yields, including sulfides bearing electronwithdrawing or electrondonating groups (Table 2). As shown in the Table 2, the deoxygenation of halogenated sulfoxides proceeded smoothly (Table 2, entries 4-6). Although the $B(C_6F_5)_3/Et_3SiH$ was reported to promote the hydrodefluorination of alkyl fluorides at room temperature,[22] substrate **1d** (Table 2, entry 4) was tolerated under the standard reaction conditions giving the desired product **2d** in 60 % yield. Chloro and bromo substituted sulfoxides afforded the corresponding products (**2e**, **2f,** and **2h**) in moderate to high yields, which might be employed for further structural manipulations such as the coupling reaction.

Table 2. Deoxygenation of various sulfoxides catalyzed by $B(C_6F_5)_3$.[a]



Entry	Substrate	Product	Yield[b] (%)	Entry	Substrate	Product	Yield (%)
1		**2a**	85	9		**2i**	72
2		**2b**	65	10		**2j**	62
3		**2c**	75	11		**2k**	60
4		**2d**	60	12		**2l**	82
5		**2e**	80	13		**2m**	82
6		**2f**	73	14		**2n**	81
7		**2g**	77	15		**2o**	87
8		**2h**	87	16		**2p**	71

[a] Reaction conditions: sulfoxides (0.5 mmol, 1 equiv.) and $PhSiH_3$ (1 mmol, 2 equiv.) with $B(C_6F_5)_3$ (5 mol %) in toluene (1.5 mL) at 60 °C for 8 h. [b] Yield of isolated product.

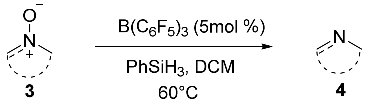
Particularly worth mentioning is the case that sulfoxide with $-NO_2$ was not reduced to $-NH_2$ (Table 2, entry 7), despite the $B(C_6F_5)_3/Et_3SiH$ could reduce of aromatic and aliphatic nitro groups with hydrosilanes,[23] perhaps because of the temperature and the amount of hydrosilanes. In other words, S–O bond is more active than the N–O bond. Furthermore, aliphatic and heterocyclic sulfoxides all underwent deoxygenation sufficiently, providing the corresponding sulfides in good yields (Table 2, entries 11-12). Sulfoxides with –OH afforded the desired products (**2n** and **2o**) in high yields. We also tried the reduction of omeprazole **1p** with the $PhSiH_3/B(C_6F_5)_3$ (5 mol %) system, ufiprazole **2p** was obtained in 71 % yield (Table 2, entry 16).

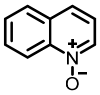
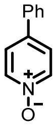
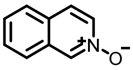
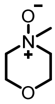
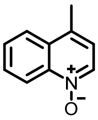
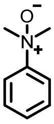
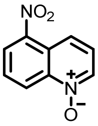
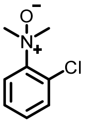
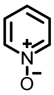
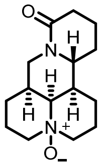
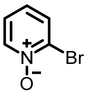
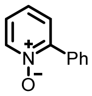
Due to the compatibility with a range of functional groups clarified in the reduction of sulfoxides, it seems possible to be suitable for reduction of other organoheteroatom oxides. To evaluate the general applicability of the $PhSiH_3/B(C_6F_5)_3$ (5 mol %) system, we also made an investigation of the deoxygenation of various aromatic and aliphatic amine *N*-oxides listed in the Table 3. The deoxygenation of quinoline *N*-oxide afforded quinoline **4a** in 84 % yield (Table 3, entry 1), and the reduction of isoquinoline *N*-oxide provided **4b** in 82 % yield under mild conditions (Table 3, entry 2). The remarkable functional group tolerance of our experimental conditions was observed in the deoxygenation of amine *N*-oxides with functional groups such as nitro, halogeno and carbonyl groups, to the corresponding amines in good to excellent yields (Table 3, entries 4, 6, 11, and 12).

Furthermore, examples for the deoxygenation of aliphatic amine *N*-oxides, including alicyclic and phenylic and substituted phenylic *N*-oxides to amines showed in high yields (65-75 %; Table 3, entries 9-11). This methodology had a positive effect on complex molecules. It worked well when we use this methodology to obtain complex natural products **4l** (Table 3, entry 12).

Based on previous reports[24] and our results, we assume that the $B(C_6F_5)_3$ acts as a Lewis acid (Figure 1). Initially, interaction of the hydrosilane with the Lewis-acidic boronic center activates the Si–H bond, in order to facilitate sulfoxides attacking at the silicon atom, thus an activation of the S=O bond occurs. Subsequently, the complex reacts further with another equivalent of hydrosilane to afford $[R^1R^2SH]^+$. Finally, protonation of $[HB(C_6F_5)_3]$ by the $[R^1R^2SH]^+$ liberates free H_2, sulfide and $B(C_6F_5)_3$. This mechanism is closely related to that described for the deoxygenation of phosphine oxide by Oestreich and Stephan.[25] In addition, the mechanism for the deoxygenation of amine *N*-oxides is similar to that reported by Namboothiri.[20] The activated silane reacts with the *N*-oxide substrate with simultaneous hydrogen transfer at C_2. The transient intermediate then rearomatizes with concomitant elimination of silanol, affording corresponding products.

Table 3. Deoxygenation of various amine *N*-oxides catalyzed by $B(C_6F_5)_3$.[a]



Entry	Substrate	Product	Yield (%)	Entry	Substrate	Product	Yield[b] (%)
1		**4a**	84	8		**4h**	78
2		**4b**	82	9		**4i**	65
3		**4c**	90	10		**4j**	75
4		**4d**	81	11		**4k**	70
5		**4e**	70	12		**4l**	82
6		**4f**	54				
7		**4g**	62				

[a] Reaction conditions: amine *N*-oxides (0.5 mmol, 1 equiv.) and $PhSiH_3$ (0.75 mmol, 1.5 equiv.) with $B(C_6F_5)_3$ (5 mol %) in DCM (1.5 mL) at 60 °C for 8 h. [b] Yield of isolated product.

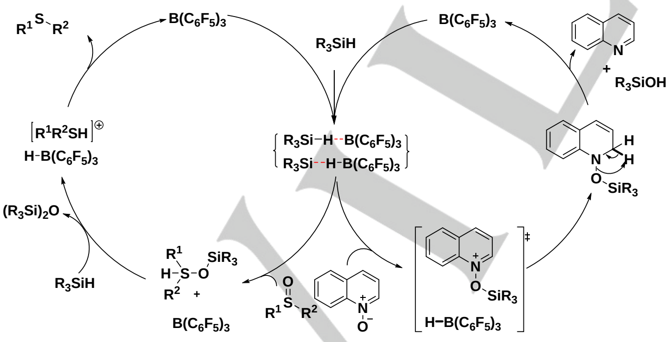


Figure 1. Proposed catalytic cycle for the reduction of sulfoxides and *N*-oxides.

Conclusions

In conclusion, the $PhSiH_3/B(C_6F_5)_3$ system serves as an efficient methodology for deoxygenation of a wide range of sulfoxides and amide *N*-oxides with other reducible substituents intact (such as –F and –NO_2) in good to excellent yields without any additives. This approach also features a mild condition, high chemical selectivity, and good functional group tolerance to obtain drug intermediate and natural product. This protocol should be very useful in future because of the ease of operation, the environmentally friendly reaction conditions, and its wide scope.

Experimental Section

General Procedure for the Deoxygenation of Sulfoxides and Amine *N*-oxides: To a mixture of an appropriate sulfoxides or amine *N*-oxides (0.5 mmol) and $B(C_6F_5)_3$ (5 mol %) in a standard Schlenk tube, 1 mmol of $PhSiH_3$ for sulfoxides (0.75 mmol for amine *N*-oxides) was added. The mixture was evacuated and backfilled with N_2 (3 times). Then, the solvent (1.5 mL) was added via syringe, and the mixture was stirred at 60 °C for 8 h. The resulting reaction mixture was concentrated under reduced pressure and purified by column chromatography using petroleum ether/ethyl acetate to afford the corresponding products.

Acknowledgements

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Keywords: Deoxygenation • $B(C_6F_5)_3$ • Hydrosilane • Sulfide • Amine

[1] Y. Ma, B. Wang, L. Zhang, Z. Hou, *J. Am. Chem. Soc.* **2016**, *138*, 3663-3666.

[2] M. Oestreich, J. Hermeke, J. Mohr, *Chem. Soc. Rev.* **2015**, *44*, 2202-2220.

[3] V. Gevorgyan, J.-X. Liu, M. Rubin, S. Benson, Y. Yamamoto, *Tetrahedron Lett.* **1999**, *40*, 8919-8922.

[4] a) V. Gevorgyan, M. Rubin, J.-X. Liu, Y. Yamamoto, *J. Org. Chem.* **2001**, *66*, 1672-1675; b) L. L. Adduci, M. P. McLaughlin, T. A. Bender, J J. Becker, M. R. Gagné, *Angew. Chem. Int. Ed.* **2014**, *53*, 1646-1649; *Angew. Chem.* **2014**, *126*, 1672-1675. c) K. Saito, K. Kondo, T. Akiyama, *Org. Lett.* **2015**, *17*, 3366-3369.

[5] a) R. D. Nimmagadda, C. McRae, *Tetrahedron Lett.* **2006**, *47*, 5755-5758; b) M. Tan, Y. Zhang. *Tetrahedron Lett.* **2009**, *50*, 4912-4915; c) D. Bezier, S. Park, M. Brookhart, *Org. Lett.* **2013**, *15*, 496-499; d) K. Sakata, H. Fujimoto, *J. Org. Chem.* **2013**, *78*, 12505-12512; e) E. Blondiaux, T. Cantat, *Chem. commun.* **2014**, *50*, 9349-9352; f) R. C. Chadwick, V. Kardelis, P. Lim, A. Adronov, *J. Org. Chem.* **2014**, *79*,

7728-7733; g) M. Mehta, M. H. Holthausen, I. Mallov, M. Perez, Z.-W. Qu, S. Grimme, D. W. Stephan, *Angew.Chem.Int. Ed.* **2015**, *54*, 8250-8254; *Angew. Chem.* **2015**, *127*, 8368-8372.

[6] A. C. Fernandes, C. C. Romão, *Tetrahedron* **2006**, *62*, 9650-9654.

[7] a) S. C. A. Sousa, A. C. Fernandes, *Tetrahedron Lett.* **2010**, *51*, 6132-6135; b) S. C. A. Sousa, J. R. Bernardo, M. Wolff, B. Machura, A. C. Fernandes, *Eur. J. Org. Chem.* **2014**, 1855-1859.

[8] Y. Mikami, A. Noujima, T. Mitsudome, T. Mizugaki, K. Jitsukawa, K. Kaneda, *Chem. Eur. J.* **2011**, *17*, 1768-1772.

[9] a) S. Enthaler, *Catal. Lett.***2012**, *142*, 1306-1311; b) S. Enthaler, S. Krackl, E. Irran, S. Inoue, *Catal Lett.* **2012**, *142*, 1003-1010.

[10] Y. Jang, K. T. Kim, H. B. Jeon, *J. Org. Chem.* **2013**, *78*, 6328-6331.

[11] R. Ma, A.-H. Liu, C.-B. Huang, X.-D. Li, L.-N. He, *Green Chem.* **2013**, *15*, 1274-1279.

[12] T. Mitsudome, Y. Takahashi, T. Mizugaki, K. Jitsukawa, K. Kaneda, *Angew. Chem. Int. Ed.* **2014**, *53*, 8348-8351; *Angew. Chem.* **2014**, *126*, 8488-8491.

[13] M. Abbasi, M. R. Mohammadizadeh, Z. Moradi, *Tetrahedron Lett.* **2015**, *56*, 6610-6613.

[14] J. S. Yadav, B. V. S. Reddy, M. M. Reddy, *Tetrahedron Lett.* **2000**, *41*, 2663-2665.

[15] B. W. Yoo, J. W. Choi, C. M. Yoon, *Tetrahedron Lett.* **2006**, *47*, 125-126.

[16] S. K. Singh, M. S. Reddy, M. Mangle, K. R. Ganesh, *Tetrahedron* **2007**, *63*, 126-130.

[17] K. Oh, W. E. Knabe, *Tetrahedron* **2009**, *65*, 2966-2974.

[18] N. B. Gowda, G. K. Rao, R. A. Ramakrishna, *Tetrahedron Lett.* **2010**, *51*, 5690-5693.

[19] H. P. Kokatla, P. F. Thomson, S. Bae, V. R. Doddi, M. K. Lakshman, *J. Org. Chem.* **2011**, *76*, 7842-7848.

[20] S. Donck, E. Gravel, N. Shah, D. V. Jawale, E. Doris, I. N. N. Namboothiri, *RSC Adv.* **2015**, *5*, 50865-50868.

[21] D. W. Stephan, G. Erker, *Angew. Chem. Int. Ed.* **2010**, *49*, 46-76; *Angew. Chem.* **2010**, *122*, 50-81.

[22] C. B. Caputo, D. W. Stephan, *Organometallics* **2012**, *31*, 27-30.

[23] D. Porwal, M. Oestreich, *Eur. J. Org. Chem.* **2016**, 3307-3309.

[24] a) D. J. Parks, W. E. Piers, *J. Am. Chem. Soc.* **1996**, *118*, 9440-9441; b) D. J. Parks, J. M. Blackwell, Warren E. Piers, *J. Org. Chem.* **2000**, *65*, 3090-3098; c) J. M. Blackwell, E. R. Sonmor, T. Scoccitti, W. E. Piers, *Org. Lett.* **2000**, *24*, 3921-3923; d) J. Hermeke, M. Mewald, M. Oestreich, *J. Am. Chem. Soc.* **2013**, *135*, 17537-17546.

[25] M. Mehta, I. Garcia de la Arada, M. Perez, D. Porwal, M. Oestreich, D. W. Stephan, *Organometallics* **2016**, *35*, 1030-1035.

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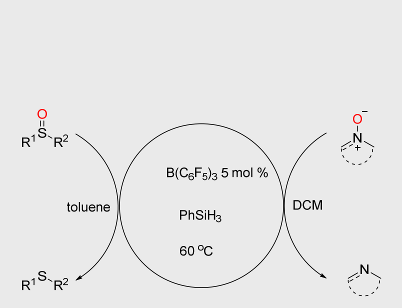

Deoxygenation

*Fangwei Ding, Yanqiu Jiang, Shaoyan Gan, Robert Li-Yuan Bao, Kaifeng Lin, and Lei Shi **

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$B(C_6F_5)_3$-Catalyzed Deoxygenation of Sulfoxides and Amine *N*-Oxides with Hydrosilanes

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