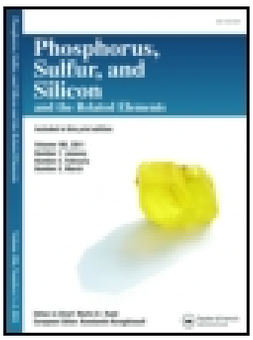

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ISSN: 1042-6507 (Print) 1563-5325 (Online) Journal homepage: http://www.tandfonline.com/loi/gpss20

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To cite this article: Byung Woo Yoo, Min Kyung Lee & Cheol Min Yoon (2016): A MILD, EFFICIENT AND SELECTIVE PROCEDURE FOR THE DEOXYGENATION OF SULFOXIDES WITH THE $TaCl_5$/INDIUM SYSTEM, Phosphorus, Sulfur, and Silicon and the Related Elements, DOI: 10.1080/10426507.2015.1119147

To link to this article: http://dx.doi.org/10.1080/10426507.2015.1119147

Accepted author version posted online: 29 Jan 2016.

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A MILD, EFFICIENT AND SELECTIVE PROCEDURE FOR THE DEOXYGENATION OF SULFOXIDES WITH THE $TaCl_5$/INDIUM SYSTEM

Byung Woo Yoo[1,*] Min Kyung Lee[1], and Cheol Min Yoon[1]

[1]Department of Advanced Materials Chemistry, Korea University, 2511 Sejong-ro, Sejong 339-700, Korea

[*]Corresponding Author Email: bwyoo@korea.ac.kr

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Abstract

The $TaCl_5$/In system was found to be a new reagent for reducing a wide range of structurally diverse sulfoxides to the corresponding sulfides with high yields under mild conditions. This protocol is chemoselective and tolerates several functional groups such as Br, Cl, OCH_3, CHO, and $CH = CH_2$.

Keywords

Deoxygenation; Sulfoxide; Sulfide; Tantalum(V) chloride; Indium

The deoxygenation of sulfoxides to sulfides is a valuable synthetic transformation that has attracted considerable attention in organic synthesis and biochemical reactions.[1] Sulfoxides are important intermediates in the synthesis of many bioactive and pharmaceutical compounds that often must be reduced to the corresponding sulfides during the reaction sequences.[2-5] Over the years, a good number of methods have been developed for the reduction of sulfoxides to the corresponding sulfides.[6-21] Although these methods are useful, they suffer from one or more drawbacks, such as low yields, long reaction times, complex experimental procedures, functional group incompatibility, or harsh reaction conditions. Therefore, there still exists a search for alternative new and efficient methods for the deoxygenation of sulfoxides.

The uses of oxophilic d-block metals (W, Mo, Ti, Zr) have become important in deoxygenation of various types of organic molecules.[22] In this regard, deoxygenations of sulfoxides are readily performed with low valent tungsten, molybdenum and titanium generated from WCl_6, $MoCl_5$ and $TiCl_4$ in the presence of a metal (Zn, In, Sm).[23-25] We envisioned that a combination of $TaCl_5$ with indium metal could bring about the deoxygenation of sulfoxides under mild conditions.

In recent years, indium metal has been the subject of active interest because of its unique properties such as low toxicity and high stability in water and air compared to other metals.[26-27]

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As in the case of zinc, the reduction potential of indium is not highly negative (In: E^o, In^{+3}/In = –0.345 V; Zn: E^o, Zn^{+2}/Zn = –0.763 V): thus, indium is not sensitive to water and does not form oxides readily in air.

The chemistry of $TaCl_5$ is one of the current interests in organic synthesis and has been extensively studied.[28-32] Tantalum species in low oxidation states serve as versatile one electron reductants, but their synthetic utility in this respect has been limited. Fortunately, tantalum(V) compounds generally exhibit low toxicity and are not considered particularly poisonous.[33] To the best of our knowledge, there is no report in which a $TaCl_5$/In system is used as a reagent for deoxygenation of sulfoxides to sulfides.

RESULTS AND DISCUSSION

In continuation of our studies on the utility of low valent metal reagents for organic transformations,[34-37] herein we report a mild and efficient procedure for the deoxygenation of sulfoxides using the $TaCl_5$/In system in acetonitrile at room temperature. The reaction can be generalized as shown in Scheme 1.

The new reducing system was generated by the reduction of tantalum(V) chloride with indium in CH_3CN under sonication. The addition of indium powder to a solution of tantalum(V)

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chloride in CH_3CN gave instantly a dark purple suspension., A kind of low-valent tantalum complex may be formed. Encouraged by the convenient generation of low-valent tantalum complexes from reduction of $TaCl_5$ with indium metal, we have investigated the reactions of the $TaCl_5$ /In system with a wide range of structurally diverse sulfoxides and found that the reductions smoothly proceeded with high yields and showed a good chemoselectivity over other labile substituents under mild conditions.

To ensure the role of indium, a control experiment was carried out using sulfoxide compounds with tantalum(V) chloride without indium metal, which failed to yield any reduced product. This result clearly indicates that the presence of indium is indispensable for the success of the reduction. In an effort to elucidate the scope and generality of this reagent system, the reaction was studied with various sulfoxides bearing other potentially labile functional groups. An inspection of the data in Table I reveals that dialkyl, diaryl, and aryl alkyl sulfoxides are all reduced smoothly giving sulfides in high yields (87-95%). This new methodology is highly chemoselective, tolerating a wide range of functional groups such as CHO, Br, Cl, OCH_3, and $CH = CH_2$ under the reaction conditions.

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Various solvents were screened for the reaction, and acetonitrile was found to be the most suitable. Dichloromethane, THF, benzene, and trichloromethane afforded the sulfide with only moderate conversions. A molar ratio of 1:2:4 (sulfoxide/$TaCl_5$/indium) was found to be optimum for the complete conversion of sulfoxides into sulfides in acetonitrile at room temperature. The reaction remained incomplete with smaller amounts. The reactions were clean, high-yielding and completed within 3 h depending on the substituents on the aryl rings. We have been able to demonstrate the utility of the easily accessible $TaCl_5$/In system as a useful reagent for effecting chemoselective deoxygenation of sulfoxides.

Although the detailed mechanism of the reaction requires more investigation, it can be rationalized as the result of a two-step process as illustrated in Scheme 2.[38-39] In the first step, it is assumed that reduction of tantalum(V) chloride with indium provides low-valent tantalum species, which are involved in complexation of the sulfoxide oxygen to the low-valent tantalum, $TaCl_3$. The complex weakens the S-O bond and renders the sulfur atom more susceptible to the reduction. In the subsequent step, the reduction proceeds by a reductive cleavage of the polarized S-O bond to form the sulfide. The residue of the reaction appears to contain tantalum(V) oxychloride, $TaOCl_3$.The good affinity of tantalum for heteroatoms and the high thermodynamic

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stability of the Ta-O bond facilitate the deoxygenative reduction of the sulfoxide group under mild conditions.

The efficiency of this new methodology is also demonstrated by the high yields obtained in the reduction of dibenzyl sulfoxide (Entry 6) and benzyl phenyl sulfoxide (Entry 7), since several methods fail completely with these substrates or only provide poor yields.[40-42] Our method offers several advantages such as mild reaction conditions, high yield, simple experimental operation, and tolerance of a variety of functional groups.

CONCLUSION

In conclusion, we believe that the present methodology using the $TaCl_5$/In system will represent a useful and efficient alternative to the conventional methods for the deoxygenation of sulfoxides. Further investigations of more useful applications with this system are currently underway in our laboratory.

EXPERIMENTAL

Materials and Methods

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All commercial reagents were purchased from Aldrich and Fluka Chemical Company and used without any further purification. NMR spectra were recorded on a FT-Bruker AF-300 (300 MHz for ^{1}H NMR; 75 MHz for ^{13}C NMR) in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded on a Shimadzu GC MS-QP 1000 PX at 70 eV. 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).

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General Procedure for the deoxygenation of sulfoxides

Indium powder (229 mg, 2.0 mmol) and tantalum(V) chloride (358 mg, 1.0 mmol) were mixed in CH_3CN (5 mL). The resulting mixture was sonicated for 0.5 h to produce a solution of the low-valent tantalum-indium complex. Diphenyl sulfoxide (101 mg, 0.5 mmol) was then added to this solution and the reaction mixture was stirred for 3.0 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, 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 silica gel (hexane:ethyl acetate = 2:1) to

afford diphenyl sulfide (86 mg, 92%). All of the products were identified by comparison of their spectroscopic data with authentic samples.[43]

Spectroscopic Data of Products

Diphenyl sulfide (Entry 1): ^{1}H NMR: δ 7.38-7.25 (m, 10H). ^{13}C NMR: δ 135.7, 131.1, 129.2, 127.1. GC/MS (*m/z*): 186 (M^+).

Methyl phenyl sulfide (Entry 2): ^{1}H NMR: δ 7.17-7.15 (m, 5H), 2.49 (s, 3H). ^{13}C NMR: δ 138.5, 128.8, 126.7, 125.0, 15.7. GC/MS (*m/z*): 124 (M^+).

Dibutyl sulfide (Entry 3): ^{1}H NMR: δ 2.65 (t, 4H, J = 7.2 Hz), 1.68-1.73 (m, 4H), 1.42-1.52 (m, 4H), 1.04 (t, 6H, J = 7.2 Hz). ^{13}C NMR: δ 32.0, 30.4, 22.2, 13.8. GC/MS (*m/z*): 146 (M^+).

Bis(4-methylphenyl) sulfide (Entry 4): ^{1}H NMR: δ 7.01-7.45 (m, 8H), 2.31 (s, 6H). ^{13}C NMR: δ: 139.8, 132.8, 131.3, 129.8, 21.4. GC/MS (*m/z*): 214 (M^+).

Methyl 4-tolyl sulfide (Entry 5): ^{1}H NMR: δ 7.54 (d, 2H, J = 11.1 Hz), 7.33 (d, 2H, J = 8.1 Hz), 2.70 (s, 3H), 2.41 (s, 3H). ^{13}C NMR: δ 134.9, 134.6, 129.6, 127.4, 20.9, 16.6. GC/MS (*m/z*): 138 (M^+).

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Dibenzyl sulfide (Entry 6): ^{1}H NMR: δ 7.35-7.25 (m, 10H), 3.61(s, 4H). ^{13}C NMR: δ 138.2, 129.2, 128.6, 127.2, 35.7. GC/MS (*m/z*): 214 (M^+).

Benzyl phenyl sulfide (Entry 7): ^{1}H NMR: δ 7.33-7.19 (m, 10H), 4.13 (s, 2H). ^{13}C NMR: δ 137.4, 136.3, 129.9, 128.8, 128.4, 127.8, 127.1, 125.4, 39.1. GC/MS (*m/z*): 200 (M^+).

Methyl 4-bromophenyl sulfide (Entry 8): ^{1}H NMR: δ 7.40 (d, 2H, J = 8.5 Hz), 7.12 (d, 2H, J = 8.6 Hz), 2.47 (3H). ^{13}C NMR: δ 138.5, 132.0, 128.9, 119.6, 15.0. GC/MS (*m/z*): 202 (M^+), 204 ($M+2^+$).

Bis(4-chlorophenyl) sulfide (Entry 9): ^{1}H NMR: δ 7.28-7.46 (m, 8 H). ^{13}C NMR: δ 134.0, 132.9, 130.8, 129.7. GC/MS (*m/z*): 254 (M^+), 258 ($M+2^+$).

Bis(4-methoxyphenyl) sulfide (Entry 10): ^{1}H NMR: δ 6.84-7.28 (m, 8H), 3.79 (s, 6H). ^{13}C NMR: δ 162.2, 137.4, 127.3, 115.1, 55.9. GC/MS (*m/z*): 246 (M^+).

4-(Methylthio)benzaldehyde (Entry 11): ^{1}H NMR: δ 9.93 (s, 1H), 7.78 (d, 2H, J = 8.4 Hz), 7.33 (d, 2H, J = 8.0 Hz), 2.54 (s, 3H). ^{13}C NMR: δ 191.0, 145.1, 133.2, 130.0, 127.1, 14.7. GC/MS (*m/z*): 152 (M^+).

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Phenyl vinyl sulfide (Entry 12): ^{1}H NMR: δ 7.42-7.27 (m, 5H), 6.55 (dd, 1H, J = 15.7 Hz, J = 10.4 Hz), 5.39-5.33 (m, 2H). ^{13}C NMR: δ 135.2, 132.3, 129.6, 129.1, 125.6, 114.7. GC/MS (*m/z*): 136 (M^+).

ACKNOWLEDGEMENT

This work was financially supported by Korea University.

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REFERENCES

1. Firouzabadi, H.; Jamalian, A. *J. Sulfur Chem.* **2008**, 29, 53-97.

2. Carreno, M. C. *Chem. Rev.* **1995**, 95, 1717-1760.

3. Madesclaire, M. *Tetrahedron* **1988**, 44, 6537-6580.

4. Solladie, G. In *Asymmetric Synthesis*; Morrison, J. D.; Ed.; Academic: New York, 1983; Vol. 2, pp. 157-199.

5. Walker, A. J. *Tetrahedron*: *Asymmetry* **1992**, 3, 961-998.

6. Khurana, J. M.; Sharma, V.; Chacko, S. A. *Tetrahedron* **2007**, 63, 966-969.

7. Bhatia, G. S.; Graczyk, P. P. *Tetrahedron Lett*. **2004**, 45, 5193-5195.

8. Bahrami, K.; Khodaei, M. M.; Sheikh Arabi, M. *J. Org. Chem.* **2010**, 75, 6208-6213.

9. Bahrami, K.; Khodaei, M. M.; Sohrabnezhad, S. *Tetrahedron Lett.* **2011**, 52, 6420-6423.

10. Yadav, J. S.; Reddy, B. V. S.; Srinivas, C.; Srihari, P. *Synlett* **2001**, 854-855.

11. Yoo, B. W.; Min, S. K. *Synth. Commun.* **2011**, 41, 2993-2996.

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12. Miller, S. J.; Collier, T. R.; Wu, W. *Tetrahedron Lett.* **2000**, 41, 3781-3783.

13. Hua, G.; Woolin, J. D. *Tetrahedron Lett*. **2007**, 48, 3677-3679.

14. Cabrita, I.; Sousa, S. C. A.; Fernandes, A. C. *Tetrahedron Lett*. **2010**, 51, 6132-6135.

15. Sousa, S. C. A.; Bernardo, J. R.; Romao, C. C.; Fernandes, A. C. *Tetrahedron* **2012**, 68, 8194-8197.

16. Bahrami, K.; Khodaei, M. M.; Karimi, A. *Synthesis* **2008**, 40, 2543-2546.

17. Zarei, M.; Ameri, M. A.; Jamaleddini, A. *J. Sulfur Chem.* **2013**, 34, 259-263.

18. Bahrami, K.; Khodaei, M. M.; Khedri, M. *Chem. Lett.* **2007**, 36, 1324-1325.

19. Reis, P. M.; Costa, P. J.; Romao, C. C.; Fernandes, J. A.; Calhorda, M. J.; Royo, B. *Dalton Trans*. **2008**, 1727-1733.

20. Fernandes, A. C.; Romao, C. C. *Tetrahedron* **2006**, 62, 9650-9654.

21. Harrison, D. J.; Tam, N. C.; Vogels, C. M.; Langler, R. F.; Baker, R. T.; Decken, A.; Westcott, S. A. *Tetrahedron Lett.* **2004**, 45, 8493-8496.

22. Cintas, P. *Activated Metals in Organic Synthesis*, CRC: Boca Raton, FL., 1993.

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23. Yoo, B. W.; Song, M. S.; Park, C. M. *Synth. Commun.* **2007**, 37, 3089-3093.

24. Firouzabadi, H.; Karimi, B. *Synthesis* **1999**, 31, 500-502.

25. Wang, J. Q.; Zhang, Y. M. *Synth. Commun.* **1995**, 25, 3545-3547.

26. Nair, V.; Ros, S.; Jayan, C. N.; Pillia, B. S. *Tetrahedron* **2004**, 60, 1959-1982.

27. Cintas, P. *Synlett* **1995**, 1087-1096.

28. Kataoka, Y.; Miyai, J.; Oshima, K.; Takai, K.; Utimoto, K. *J. Org. Chem.* **1992**, 57, 1973-1981.

29. Shibata, I.; Kano, T.; Kanazawa, N.; Fukuoka, S.; Baba, A. *Angew. Chem. Int. Ed.* **2002**, 41, 1389-1392.

30. Shmizu, H.; Kobayashi, S. *Tetrahedron Lett.* **2005**, 46, 7593-7595.

31. Kirihara, M.; Noguchi, T.; Okajima, N.; Naito, S.; Ishizuka, Y.; Harano, A.; Tuukiji, H.;Takizawa, R. *Tetrahedron* **2012**, 68, 1515-1520.

32. Kirihara, M.; Yamamoto, J.; Takuya, N.; Hirai, Y. *Tetrahedron Lett.* **2009**, 50, 1180-1183.

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33. Lewis, R. J. S. R. *Dangerous properties of Industrial Materials*, 8th ed., Vol. 3; Van Nostrand Reinhold: New York, **1989**.

34. Yoo, B. W.; Min, S. K. *Synth. Commun.* **2011**, 41, 2993-2996.

35. Yoo, B. W.; Choi, J. W. *Synth. Commun.* **2009**, 39, 3550-3554.

36. Yoo, B. W.; Lee, S. J.; Park, Y. K.; Choi, J. Y.; Ahn, Y. S. *Bull. Korean Chem. Soc.* **2013**, 34, 1951-1952.

37. Yoo, B. W.; Choi, J. W.; Kim, Y. S. *Bull. Korean Chem. Soc.* **2008**, 29, 1655-1656.

38. Oh, K.; Knabe, W. E. *Tetrahedron* **2009**, 65, 2966-297.

39. Ho, T. L.; Hall, T. W.; Wong, C. M. *Synthesis* **1973**, 206-207.

40. Alper, H.; Keung, E. C. H. *Tetrahedron Lett.* **1970**, 11, 53-56.

41. Chasar, D. W. *J. Org. Chem*. **1971**, 36, 613-614.

42, Drabowicz, J.; Mikolajczyk, M. *Synthesis* **1976**, 527-528.

43. The Aldrich Library of ^{13}C and ^{1}H FT-NMR spectra; Pouchert, C. J., Behnke, J. Eds.; Aldrich: Milwaukee, 1992.

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Table 1 Deoxygenation of sulfoxides to sulfides with the $TaCl_5$/In system.

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	95
3	nC_4H_9	nC_4H_9	$(nC_4H_9)_2s$	1.0	91
4	4-$CH_3c_6H_4$	4-$CH_3c_6H_4$	(4-$CH_3c_6H_4)_2s$	0.5	92
5	4-$CH_3c_6H_4$	CH_3	4-$CH_3c_6H_4SCH_3$	0.5	94
6	$PhCH_2$	$PhCH_2$	$(PhCH_2)_2S$	1.5	91
7	$PhCH_2$	Ph	$PhCH_2SPh$	2.0	92
8	4-BrC_6H_4	CH_3	4-BrC_6H_{4SMe}	1.5	90
9	4-$C1C_6H_4$	4-$C1C_6H_4$	(4-$C1C_6H_4)_2S$	1.0	92
10	4-$CH_3OC_6H_4$	4-$CH_3OC_6H_4$	(4-$CH_3OC_6H_4)_2S$	3.0	90
11	4-OHC-C_6H_4	CH_3	4-OHC-$C_6H_4SCH_3$	1.0	87
12	Ph	$CH_2 = CH$	$PhSCH = CH_2$	1.5	89

[a]Refers to isolated yields.

[b]All the products were characterized by comparison of their spectral data with authentic samples.

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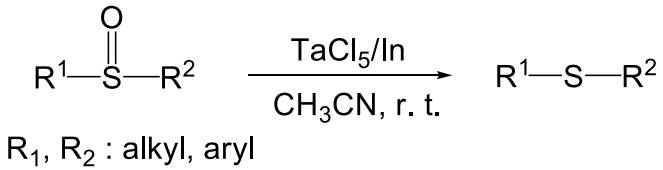

Scheme 1. Deoxygenation of sulfoxides to sulfides.

Scheme 1 Deoxygenation of sulfoxides to sulfides.

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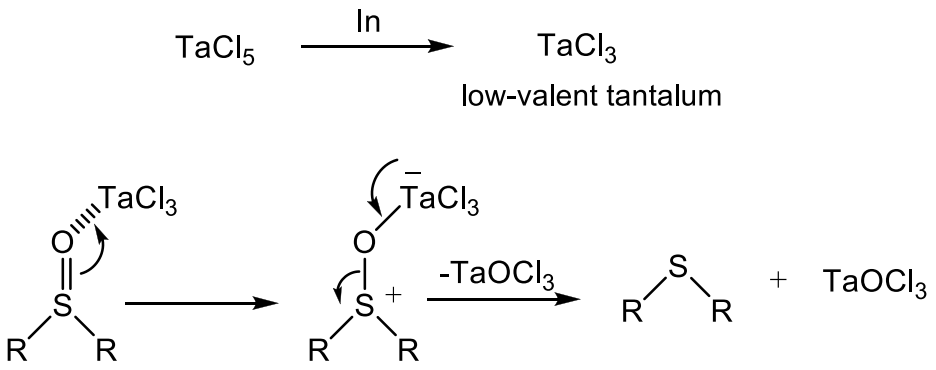

Scheme 2. Proposed mechanism for the deoxygenation of sulfoxide.

Scheme 2 Proposed mechanism for the dexygenation of sulfoxide

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