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Communications

Bu$_3$SnH-Catalyzed Reduction of Nitroalkanes to Alkanes

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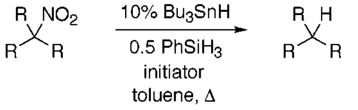
Since its discovery by Ono and Tanner in 1981,[1] the radical-mediated reduction of nitroalkanes to alkanes with stoichiometric Bu$_3$SnH has become the most widely employed method for effecting this useful transformation.[2−5] Because of the toxicity of certain tributyltin compounds,[6] as well as the purification problems that often accompany the use of Bu$_3$SnH,[7] the development of equally efficient, alternate methods that diminish the need for Bu$_3$SnH has obvious significance. Although silicon hydrides, in particular (Me$_3$Si)$_3$SiH, can serve as substitutes for Bu$_3$SnH in a number of radical-mediated processes,[8] Chatgilialoglu has established that (Me$_3$Si)$_3$SiH cannot effect the reduction of nitroalkanes to alkanes.[9]

We have recently reported the development of Bu$_3$SnH-catalyzed variants of several families of reactions that had previously been achieved with stoichiometric Bu$_3$SnH.[10,11] In the catalytic cycle for these processes, the first elementary steps involve the known stoichiometric reduction chemistry of Bu$_3$SnH, and the subsequent steps effect regeneration of the Bu$_3$SnH catalyst with an otherwise innocuous reductant. In this paper, we establish that this strategy can be applied to the conversion of nitroalkanes to alkanes, using 10% Bu$_3$SnH as the catalyst and PhSiH$_3$ as the stoichiometric reducing agent (eq 1).



(1)

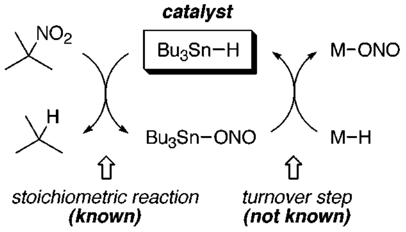


Figure 1. Proposed catalytic cycle for the Bu$_3$SnH-catalyzed reduction of nitroalkanes to alkanes.

Figure 1 provides a simplified version of a potential catalytic cycle for the Bu$_3$SnH-catalyzed reduction of a nitroalkane to an alkane. Initially, reaction of a nitroalkane with 1 equiv of Bu$_3$SnH produces an alkane and Bu$_3$SnONO (Figure 1, "stoichiometric reaction").[1,4] In the regeneration phase of the catalytic cycle, a second metal hydride (M−H) reduces Bu$_3$SnONO to Bu$_3$SnH (Figure 1, "turnover step").

In our earlier work on Bu$_3$SnH-catalyzed processes, we established that, for reactions that produce Bu$_3$SnOR in the "stoichiometric reaction" phase of the catalytic cycle, silanes (M−H = Si−H) serve as effective reducing agents in the "turnover step."[10] Because others had shown that the reduction of Sn−O bonds by silanes proceeds more slowly as the oxygen becomes less basic,[12] we were initially somewhat pessimistic about the likelihood that a silane would be able to reduce Bu$_3$SnONO to Bu$_3$SnH. In the case of nitroalkane reduction, the thermal instability of Bu$_3$SnONO (almost complete decomposition after several hours at 60 °C)[13] places a stringent requirement on the efficiency of the turnover step. Fortunately, our concern proved to be unfounded: Treatment of Bu$_3$SnONO with PhSiH$_3$ at room temperature leads to immediate and quantitative formation of Bu$_3$SnH (eq 2).[14]

$$\underset{\textbf{}^{119}\textbf{Sn NMR: }\boldsymbol{\delta}\textbf{ 83}}{\text{Bu}_3\text{Sn−ONO}} \quad \text{PhSiH}_3 \xrightarrow[\substack{\text{r.t.}\\ \text{<10 min.}\\ \textit{quantitative}}]{d_8\text{-toluene}} \underset{\textbf{}^{119}\textbf{Sn NMR: }\boldsymbol{\delta}\textbf{ -89}}{\text{Bu}_3\text{Sn−H}} \qquad (2)$$

Coupled with the previously reported stoichiometric reaction, this new Bu$_3$SnH-forming process provides the basis for a catalytic method for the reduction of nitroalkanes to alkanes (Figure 1). Thus, treatment of any of a variety of substrates with 10% Bu$_3$SnH and 0.5 equiv of PhSiH$_3$ in refluxing toluene furnishes the desired alkane in good yield (Table 1; catalyzed);[15−17] in the absence of Bu$_3$SnH under

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[1] (a) Ono, N.; Miyake, H.; Tamura, R.; Kaji, A. *Tetrahedron Lett.* **1981**, *22*, 1705−1708. (b) Tanner, D. D.; Blackburn, E. V.; Diaz, G. E. *J. Am. Chem. Soc.* **1981**, *103*, 1557−1559.

[2] Based on a search of the Beilstein Crossfire database.

[3] For a review, see: Ono, N.; Kaji, A. *Synthesis* **1986**, 693−704. See also: Larock, Richard C. *Comprehensive Organic Transformations*; VCH: New York, 1989; p 26.

[4] For mechanistic studies, see: (a) Dupuis, J.; Giese, B.; Hartung, J.; Leising, M.; Korth, H.-G.; Sustmann, R. *J. Am. Chem. Soc.* **1985**, *107*, 4332−4333. Korth, H.-G.; Sustmann, R.; Dupuis, J.; Giese, B. *Chem. Ber.* **1987**, *120*, 1197−1202. (b) Kamimura, A.; Ono, N. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3629−3635. (c) Tanner, D. D.; Harrison, D. J.; Chen, J.; Kharrat, A.; Wayner, D. D. M.; Griller, D.; McPhee, D. J. *J. Org. Chem.* **1990**, *55*, 3321−3325.

[5] For applications of nitroalkanes in organic synthesis, see: Rosini, G.; Ballini, R. *Synthesis* **1988**, 833−847.

[6] (a) De Mora, S. J. *Tributyltin: Case Study of an Environmental Contaminant*; Cambridge University Press: Cambridge, UK, 1996. (b) Boyer, I. J. *Toxicology* **1989**, *55*, 253−298.

[7] For a succinct overview, see: Crich, D.; Sun, S. *J. Org. Chem.* **1996**, *61*, 7200−7201.

[8] For a review, see: Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188−194.

[9] Ballestri, M.; Chatgilialoglu, C. *J. Org. Chem.* **1992**, *57*, 948−952.

[10] (a) Barton−McCombie deoxygenation of alcohols: Lopez, R. M.; Hays, D. S.; Fu, G. C. *J. Am. Chem. Soc.* **1997**, *119*, 6949−6950. (b) Reduction of azides: Hays, D. S.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 2796−2797. (c) Reductive cyclization of enals and enones: Hays, D. S.; Fu, G. C. *J. Org. Chem.* **1996**, *61*, 4−5. (d) Conjugate reduction of enones: Hays, D. S.; Scholl, M.; Fu, G. C. *J. Org. Chem.* **1996**, *61*, 6751−6752.

[11] For the work of others, see: (a) Nitzsche, S.; Wick, M. *Angew. Chem.* **1957**, *69*, 96. Lipowitz, J.; Bowman, S. A. *Aldrichim. Acta* **1973**, *6*, 1−6. (b) Corey, E. J.; Suggs, J. W. *J. Org. Chem.* **1975**, *40*, 2554−2555. Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303−304.

[12] (a) Itoi, K. Fr. Patent 1,368,522, 1964. Itoi, K.; Kumano, S. *Kogyo Kagaku Zasshi* **1967**, *70*, 82−86. (b) Hayashi, K.; Iyoda, J.; Shiihara, I. *J. Organomet. Chem.* **1967**, *10*, 81−94. (c) Pijselman, J.; Pereyre, M. *J. Organomet. Chem.* **1973**, *63*, 139−157. (d) See also ref 10a.

[13] Kobayashi, K.; Kwanisi, M.; Kozima, S. *Synth. React. Inorg. Met.-Org. Chem.* **1978**, *8*, 75−82.

[14] In contrast, polymethylhydrosiloxane (TMSO−(SiHMeO)$_n$−TMS; PMHS) is ineffective for this reduction.

[15] Experimental procedure: A solution of Bu$_3$SnH (0.026 mL, 0.10 mmol), PhSiH$_3$ (0.061 mL, 0.50 mmol), and 1,1′-azobis(cyclohexanecarbonitrile) (ACHN; 49 mg, 0.20 mmol) in toluene (0.3 mL) was added to a solution of the nitroalkane (1.00 mmol) in toluene (0.2 mL). The resulting mixture was immersed in a 110 °C oil bath and stirred for 5 h. Additional ACHN (49 mg, 0.20 mmol) was then added, and the mixture was stirred for 3 more hours at 110 °C. The reaction product was then purified by flash chromatography.

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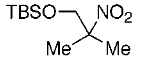
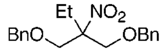
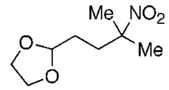
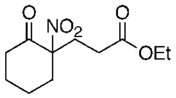
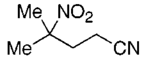
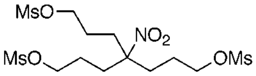
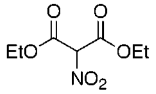
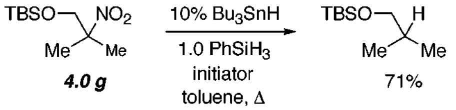
Table 1. Bu_3SnH-Catalyzed Reduction of Nitroalkanes to Alkanes (Eq 1)

Entry	Substrate	Isolated Yield (%)[a] *Catalyzed*[b]	*Stoich.*[c]
1[d]		76	77
2		71	74
3		75	78
4[e]		76	79
5		70	67
6		61	58[f]
7[g]		67	70

[a] Average of two runs. [b] (1) 10% Bu_3SnH, 0.5 equiv of $PhSiH_3$, 0.2 equiv of ACHN, toluene, 110 °C, 5 h; (2) 0.2 equiv of ACHN, 3 h. [c] (1) 1.5 equiv of Bu_3SnH, 0.2 equiv of ACHN, toluene, 110 °C, 5 h; (2) 0.2 equiv of ACHN, 3 h. [d] Yields by GC vs an internal standard: catalytic Bu_3SnH, 90%; stoichiometric Bu_3SnH, 93%. [e] These reactions were run at 80 °C with AIBN as the initiator. [f] Based on 76% conversion. This reaction is slower than the catalytic reaction, due to the low solubility of the substrate under the stoichiometric reduction conditions. [g] These reactions were run at 80 °C with AIBN as the initiator (8 h for the catalytic reaction; 2 h for the stoichiometric reaction). The yields were measured by GC vs an internal standard.

otherwise identical conditions, <10% reduction is observed. Importantly, the new catalytic reaction proceeds with efficiency comparable to the stoichiometric Bu_3SnH method (Table 1). Like the stoichiometric method, the catalytic reaction is effective for the reduction of tertiary nitroalkanes and activated secondary nitroalkanes and is compatible with functionality such as ethers, acetals, ketones, esters, nitriles, and mesylates.[3]

For the reduction of the TBS ether of 2-methyl-2-nitro-1-propanol (Table 1, entry 1), we have determined that the concentration of Bu_3SnH remains constant throughout the course of the reaction, consistent with our understanding of the catalytic cycle. Reduction of this substrate on a 4-g scale provides a 71% yield of the alkane (eq 3), illustrating the practicality of the new catalytic process.



(3)

In conclusion, we have described the development of a new Bu_3SnH-catalyzed method for the reduction of nitroalkanes to alkanes. The catalytic cycle is based on a known stoichiometric reaction and a previously unknown catalyst-regeneration step. We have established that the catalytic process is comparable to the stoichiometric in terms of efficiency and that it is amenable to scale-up. In view of the fact that the conversion of nitroalkanes to alkanes is currently most often accomplished with stoichiometric Bu_3SnH, we anticipate that this environmentally friendlier, Bu_3SnH-catalyzed variant may become the method of choice for effecting this important transformation.

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Supporting Information Available: Experimental procedures and compound characterization data (8 pages).

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(16) Reductions can be achieved with lower catalyst loadings, but longer reaction times are required. The use of smaller amounts of initiator sometimes leads to incomplete reduction.

(17) In several of our earlier studies of Bu_3SnH-catalyzed reactions, we established that the presence of a primary alcohol can facilitate regeneration of Bu_3SnH (ref 10a–c). However, added primary alcohol is *detrimental* in the case of Bu_3SnH–catalyzed reductions of nitroalkanes to alkanes (possibly due to the formation of HNO_2).