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General and Practical One-Pot Synthesis of Dihydrobenzosiloles from Styrenes

Alexey Kuznetsov and Vladimir Gevorgyan*

*Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street,
Chicago, Illinois 60607-7061, United States*

vlad@uic.edu

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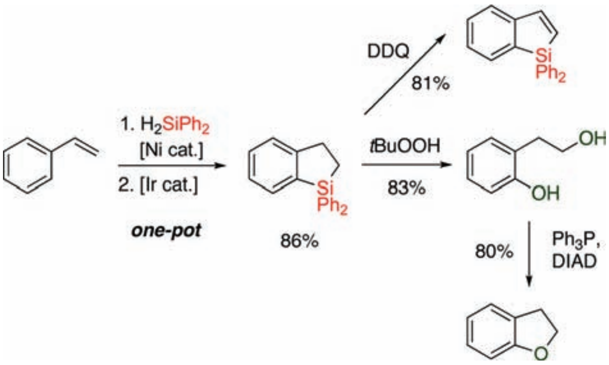
ABSTRACT



A one-pot synthesis of dihydrobenzosiloles from styrenes has been developed. The reaction involves the nickel-catalyzed hydrosilylation of styrene with diphenylsilane, followed by the iridium-catalyzed dehydrogenative cyclization. This method is efficient for both electron-rich and -deficient styrenes and exhibits good functional group tolerance, as well as excellent regioselectivity. The forming dihydrobenzosiloles can be efficiently converted into valuable benzosiloles or 2-hydroxyphenethyl alcohols.

Dehydrogenative coupling of the Si–H bond with aromatic C–H bonds is a powerful method for the synthesis of valuable aryl and hetaryl silanes. In recent years, several methods for SiH–CH coupling have been developed (Figure 1). Thus, in 2005 Hartwig showed the possibility of the formation of dihydrobenzosilole from dimethylphenethylsilane via an intramolecular platinum-catalyzed dehydrogenative cyclization reaction (eq 1).[1] However, the reaction required harsh conditions, and the scope of this approach toward dihydrobenzosiloles was not established. Later, Falck reported[2] a milder iridium-catalyzed intermolecular silylation of electron-rich aromatic heterocycles (eq 2). Then, Takai reported[3] the rhodium-catalyzed synthesis of dibenzosiloles from biarylhydrosilanes (eq 3). Very recently, Hartwig showed[4] that Falck's conditions can efficiently be used for *ortho*- C–H silylation of benzyl alcohol derivatives (eq 4). In 2009, Kawashima reported[5] the Lewis acid mediated intramolecular sila-Friedel–Crafts reaction leading to dibenzosiloles (eq 5). Dihydrobenzosiloles hold promise in becoming useful synthons for organic chemistry[6] (*vide infra*); however, to date, there are no efficient methods for their synthesis.[7] Herein, we wish to report a practical and general *one-pot* procedure for the synthesis of dihydrobenzosiloles **3** from styrenes **1** through the Ni-catalyzed hydrosilylation, followed by the Ir-catalyzed dehydrogenative cyclization (eq 6).

We aimed at developing a method for the synthesis of dihydrobenzosiloles via β-hydrosilylation of styrenes with dihydrosilanes, followed by dehydrogenative cyclization of the formed product. First, we turned our attention to

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[1] Tsukada, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 5022.
[2] Lu, B.; Falck, J. R. *Angew. Chem., Int. Ed.* **2008**, *47*, 7508.
[3] Ureshino, T.; Yoshida, T.; Kuninobu, Y.; Takai, K. *J. Am. Chem. Soc.* **2010**, *132*, 14324.
[4] Simmons, E. M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 17092.
[5] Furukawa, S.; Kobayashi, J.; Kawashima, T. *J. Am. Chem. Soc.* **2009**, *131*, 14192.
[6] For an example of hydrogenation of dihydrobenzosilole, see: Benkeser, R. A.; Mozdzen, E. C.; Muench, W. C.; Roche, R. T.; Siklosi, M. P. *J. Org. Chem.* **1979**, *44*, 1370.
[7] For selected examples of synthesis of dihydrobenzosiloles, see: (a) Belzner, J.; Dehnert, U.; Ihmels, H. *Tetrahedron* **2001**, *57*, 511. (b) Ando, W.; Sekiguchi, A. *J. Org. Chem.* **1980**, *45*, 5286. See also refs 1 and 6.

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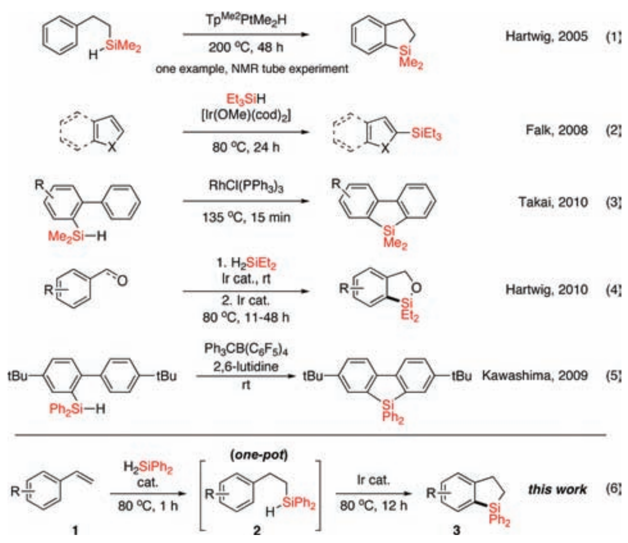
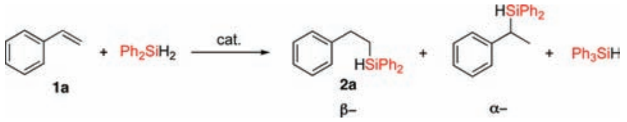


Figure 1. Methods for SiH−CH coupling.

hydrosilylation of styrenes, as the first step of the proposed sequence. Although several methods for hydrosilylation of styrene with diphenylsilane using Au,[8] Zr,[9] Yb,[10] and Rh[11] complexes exist, methods employing cheap and readily available catalysts are still in demand. On the other hand, it is known that nickel(II) salts with phosphine ligands are effective catalysts for hydrosilylation of olefins.[12] Since there are no reports on nickel-catalyzed β-hydrosilylation of styrene with dihydrosilanes, we verified the possibility of hydrosilylation of styrene with diphenylsilane in the presence of nickel catalysts (Table 1). When 5 mol % $\mathrm{NiCl_2{\bullet}(PCy_3)_2}$ was employed, only triphenylsilane, a product of disproportionation of diphenylsilane,[13] was formed (entry 1). Using 5 mol % $\mathrm{NiCl_2{\bullet}dppe}$, the desired hydrosilylated product **2a** was obtained in 6% yield (entry 2). Other nickel catalysts, such as $\mathrm{NiCl_2{\bullet}dppf}$ and $\mathrm{NiCl_2{\bullet}dppp}$, provided **2a** in 10% and 55% yields, respectively (entries 3, 4). We were pleased to find that $\mathrm{NiCl_2{\bullet}(PPh_3)_2}$ and $\mathrm{NiBr_2{\bullet}(PPh_3)_2}$ gave **2a** in high yield and high regioselectivity (entries 5−7). When $\mathrm{NiBr_2}$ without triphenylphosphine was used, no hydrosilylated product was formed (entry 8). Employment of phosphine-free $\mathrm{Ni(cod)_2}$ resulted in the mixture of regioisomers (entry 9). However, a combination of triphenylphosphine with $\mathrm{Ni(cod)_2}$ gave the desired hydrosilane **2a** in high yield and regioselectivity (entry 10).

Table 1. Table 1. Optimization of the Reaction Conditions for Ni-Catalyzed Hydrosilylation of Styrene with Diphenysilane[a]



		GC yield, %		
entry	cat.	β-	α-	$\mathrm{Ph_3SiH}$
1	$\mathrm{NiCl_2{\bullet}(PCy_3)_2}$	–	–	34
2	$\mathrm{NiCl_2{\bullet}dppe}$	6	13	8
3	$\mathrm{NiCl_2{\bullet}dppf}$	10	3	3
4	$\mathrm{NiCl_2{\bullet}dppp}$	55	37	11
5	$\mathrm{NiCl_2{\bullet}(PPh_3)_2}$	87	<2	<2
6	$\mathrm{NiBr_2{\bullet}(PPh_3)_2}$	90	<2	<1
7[b]	**$\mathrm{NiBr_2{\bullet}(PPh_3)_2}$**	**92 (87)**[c]	**<1**	**<1**
8	$\mathrm{NiBr_2}$	–	–	–
9	$\mathrm{Ni(cod)_2}$	53	30	6
10[d]	$\mathrm{Ni(cod)_2/PPh_3}$	89	<2	<1

[a] Conditions: 5 mol % cat., 0.2 mmol of styrene, 0.22 mmol of $\mathrm{Ph_2SiH_2}$ in 0.2 mL of THF were stirred at 80 °C for 6 h under a $\mathrm{N_2}$ atmosphere. The reaction was monitored by GC-MS analysis. [b] 2 mol % cat. was used. The reaction was analyzed after 1 h. [c] Isolated yield is given in parentheses. [d] 5 mol % cat. and 20 mol % $\mathrm{PPh_3}$ were used.

After a convenient method for β-hydrosilylation of styrene with diphenylsilane was established, we searched for efficient conditions for intramolecular dehydrogenative cyclization. It was found that, under Falck's conditions,[2] the hydrosilane **2a** underwent smooth dehydrogenative cyclization into the dihydrobenzosilole **3a**. Moreover, it was found that the dehydrocyclization can be performed in a one-pot manner after completion of the hydrosilylation step to produce dihydrobenzosilole **3a** in 86% overall yield.

Next we examined the scope of this one-pot transformation (Table 2). It was found that this method is quite general, as diverse styrenes, possessing MeO, Me, F, Cl, and $\mathrm{CO_2Me}$ groups in *ortho*-, *meta*- and *para*-positions, were well tolerated under the reaction conditions to give the corresponding dihydrobenzosiloles **3** in good yields. Generally, when *meta*-substituted styrenes were used, dehydrocyclization occurred at the least hindered *para*-position to the substituent. Only when a small group, such as fluorine, was employed, a 2:1 mixture of *para*- and *ortho*-cyclized products **3i** was obtained. In the case of *ortho*-methylstyrene, 36 h were required for the completion of the dehydrocyclization step toward **3g**.

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(8) For selected examples of Au-catalyzed hydrosilylation of styrene with $\mathrm{Ph_2SiH_2}$, see: (a) Corma, A.; Gonzalez-Arellano, C.; Iglesias, M.; Sanchez, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 7820. (b) Debono, N.; Iglesias, M.; Sanchez, F. *Adv. Synth. Catal.* **2007**, *349*, 2470.

(9) For an example of Zr-catalyzed hydrosilylation of styrene with $\mathrm{Ph_2SiH_2}$, see: Takahashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 8564.

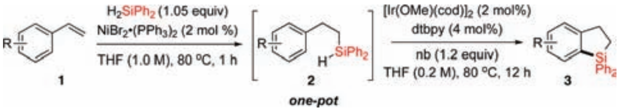
(10) For an example of Yb-catalyzed hydrosilylation of styrene with $\mathrm{Ph_2SiH_2}$, see: Takaki, K.; Sonoda, K.; Kousaka, T.; Koshoji, G.; Shishido, T.; Takehira, K. *Tetrahedron Lett.* **2001**, *42*, 9211.

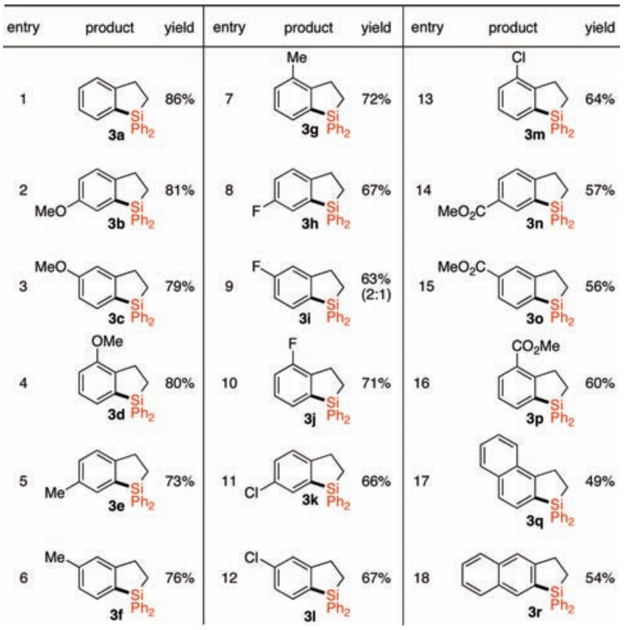
(11) For selected examples of Rh-catalyzed hydrosilylation of styrene with $\mathrm{Ph_2SiH_2}$, see: (a) Nielsen, L.; Skrydstrup, T. *J. Am. Chem. Soc.* **2008**, *130*, 113145. (b) Betley, T. A.; Peters, J. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 2385.

(12) For examples of Ni(II) and Ni(0) catalyzed hydrosilylation of olefins, see: (a) Belyakova, Z. V.; Pomerantseva, M. G.; Efimova, L. A.; Chernyshev, E. A.; Storozhenko, P. A. *Rus. J. Gen. Chem.* **2010**, *80*, 728. (b) Gareau, D.; Sui-Seng, C.; Groux, L. F.; Brisse, F.; Zargarian, D. *Organometallics* **2005**, *24*, 4003. (c) Yamamoto, K.; Hayashi, T.; Uramoto, Y.; Ito, R.; Kumada, M. *J. Organomet. Chem.* **1976**, *118*, 331.

(13) For examples of Rh-catalyzed disproportionation of diphenylsilane, see: (a) Rodenberg, L.; Davis, C. W.; Yao *J. Am. Chem. Soc.* **2001**, *123*, 5120. (b) Chang, L. S.; Corey, J. Y. *Organometallics* **1989**, *8*, 1885.

Table 2. Scope of the One-Pot Hydrosilylation Dehydrocyclization Reaction[a]





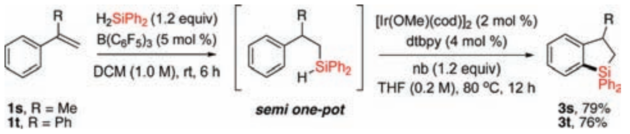
entry	product	yield	entry	product	yield	entry	product	yield
1	**3a**	86%	7	**3g**	72%	13	**3m**	64%
2	**3b**	81%	8	**3h**	67%	14	**3n**	57%
3	**3c**	79%	9	**3i**	63% (2:1)	15	**3o**	56%
4	**3d**	80%	10	**3j**	71%	16	**3p**	60%
5	**3e**	73%	11	**3k**	66%	17	**3q**	49%
6	**3f**	76%	12	**3l**	67%	18	**3r**	54%

[a] Conditions: 2 mol % Ni cat., 0.50 mmol of styrene, 0.53 mmol of Ph_2SiH_2 in 0.5 mL of THF were stirred at 80 °C for 1 h under a N_2 atmosphere. Then, 2 mol % Ir cat., 4 mol % dtbpy, 0.6 mmol of norbornene, and 2.0 mL of THF were added. Reaction was stirred at 80 °C for 12 h.

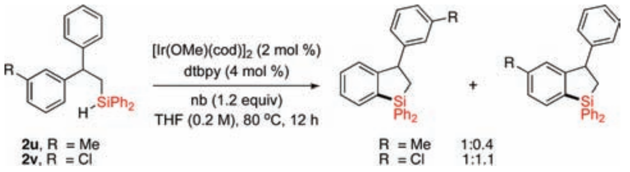
Next, we examined the possibility of employment of this one-pot method for synthesis of substituted dihydrobenzosiloles (Scheme 1). To this end, hydrosilylation of α-substituted styrenes was examined. Unfortunately hydrosilylation reaction of α-methyl- **1s** and α-phenyl styrene **1t** in the presence of a $NiBr_2•(PPh_3)_2$ catalyst system was not effective. However, the corresponding hydrosilylated products were obtained in high yields employing a Lewis acid catalyst, $B(C_6F_5)_3$.[14] Subsequently, after removing $B(C_6F_5)_3$ and the solvent, the dehydrocyclization step was performed using standard dehydrogenative coupling conditions. Thus, 3-methylbenzosilole **3s** and 3-phenyldehydrobenzosilole **3t** were obtained using this semi-one-pot procedure in 79% and 76% yields, respectively (Scheme 1).

In order to gain some insight into the mechanism of the dehydrocyclization reaction, we first performed an intermolecular competitive cyclization study. It was found that the substrates possessing electron-withdrawing groups at the aromatic ring cyclized faster then those possessing electron-donating groups. Thus, the following reactivity trend was found for the rates of cyclization of *meta*-substituted styrenes: MeO < Me < H < Cl < CO_2Me. Likewise, intramolecular competitive cyclization experiments of **2u** and **2v** indicated a similar reactivity trend (Scheme 2). Hence, cyclization of **2u**, possessing a Me- group in one of the aromatic rings, preferentially occurred at the unsubstituted ring, whereas there was a slight preference for cyclization into the Cl-substituted aromatic ring in **2v**. Thus, in all cases, the reaction preferentially occurs at the electron-deficient C–H bond, thereby supporting the C–H activation path rather than the electrophilic metalation pathway.[4] Furthermore, the performed intermolecular kinetic isotope effect studies of **2a** and **2a-*d*$_5$**[15] revealed $k_H/k_D = 1.6$, which suggests that cleavage of the aromatic C–H bond may occur at the rate-determining step.[16]

Scheme 1. Hydrosilylation–Dehydrocyclization Reaction of α-Substituted Styrenes



Scheme 2. Intermolecular Competitive Cyclization



Based on the above-mentioned observations, the following mechanistic pathways were proposed (Scheme 3). First, the iridium species undergo oxidative addition into the Si–H bond of hydrosilane **2** with formation of iridium hydride **A**. Hydrometalation of the double bond of norbornene gives intermediate **B**, which then undergoes insertion into the aromatic C–H bond to give intermediate **C** (**Path A**, similar to Falck's mechanism[2]). The following reductive elimination of norbornane gives intermediate **D**. Alternatively (**Path B**), the concerted metalation–deprotonation of the intermediate **B** through the transition state **E**[17] can occur to give the same intermediate **D** upon elimination of the norbornane. The reductive elimination from **D** leads to the cyclized product **3** and regenerates the iridium catalyst.

After developing a practical method for the synthesis of dihydrobenzosiloles from styrenes, the initial studies of

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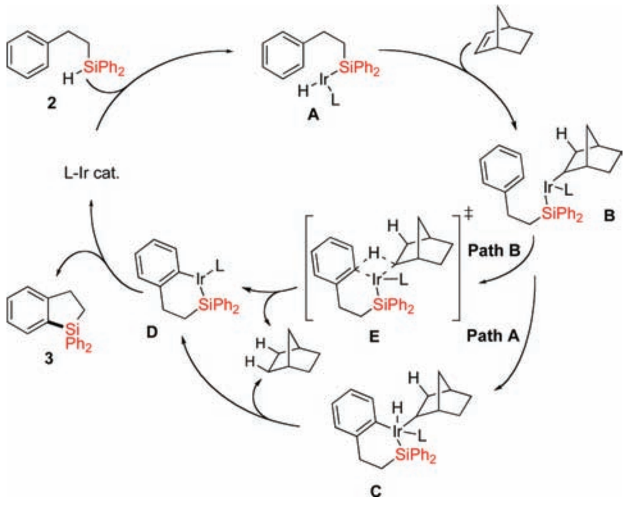
[14] For $B(C_6F_5)_3$-catalyzed hydrosilylation of alkenes, see: Rubin, M.; Schwier, T.; Gevorgyan, V. *J. Org. Chem.* **2002**, *67*, 1936.

[15] See Supporting Information for details.

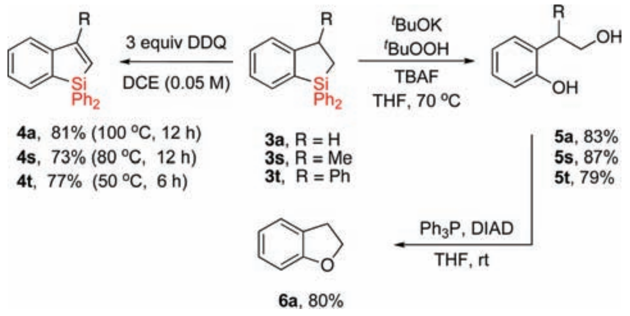
[16] (a) Livendahl, M.; Echavarren, A. M. *Isr. J. Chem.* **2010**, *50*, 630. (b) Wei, Y.; Kan, J.; Wang, M.; Su, W.; Hong, M. *Org. Lett.* **2009**, *11*, 3346.

[17] For a very recent study on the CMD-type mechanism in the Ir-catalyzed C–H arylation, see: Garcia-Melchor, M.; Gorelsky, S. I.; Woo, T. K. *Chem.—Eur. J.* **2011**, *17*, 13847.

Scheme 3. Proposed Mechanistic Pathways



Scheme 4. Further Transformations of Dihydrobenzosiloles



their synthetic utility were performed. It was found that compounds **3a**, **3s**, and **3t** in the presence of DDQ can be effectively oxidized into valuable benzosiloles **4**[18] (Scheme 4). Expectedly, oxidation of 3-phenyl derivative **3t** is more facile than that of 3-methyl derivative **3s**, which in turn is more reactive than the unsubstituted dihydrobenzosilole **3a**. It has also been shown that dihydrobenzosiloles **3a**, **3s**, and **3t** can readily be converted into 2-hydroxyphenethyl alcohols **5** in 79−87% yield when treated with *tert*-butylperoxide and TBAF. By application of standard Mitsunobu-type reaction conditions, 2-hydroxyphenethyl alcohol **5a** was smoothly transformed into dihydrobenzofuran **6a**.

In summary, we have developed a general and practical method for a one-pot synthesis of synthetically valuable dihydrobenzosiloles from styrenes. The method implies a nickel-catalyzed hydrosilylation reaction followed by the irridium-catalyzed dehydrogenative cyclization process. The obtained dihydrobenzosiloles can be readily converted into benzosiloles or 2-hydroxyphenethyl alcohols.

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Supporting Information Available. Detailed experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[18] (a) Wong, W. W. H.; Hooper, J. F.; Holmes, A. B. *Aust. J. Chem.* **2009**, *62*, 393. (b) Wong, W. W. H.; Holmes, A. B. *Adv. Polym. Sci.* **2008**, *212*, 85. (c) Tamao, K.; Uchida, M.; Izumizawa, T.; Furukawa, K.; Yamaguchi, S. *J. Am. Chem. Soc.* **1996**, *118*, 11974.

The authors declare no competing financial interest.