

Fused Heteroaromatic Dihydrosiloles:
Synthesis and Double-Fold Modification

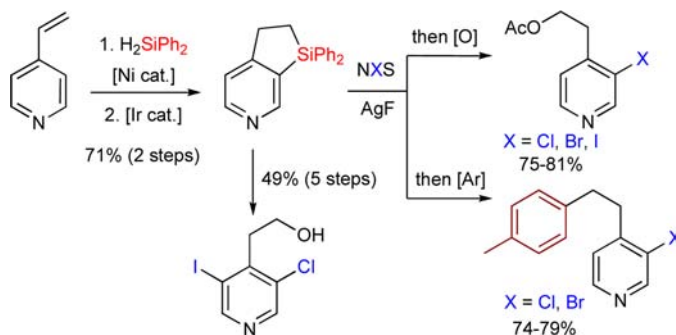
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ABSTRACT



An efficient method for the synthesis of fused heteroaromatic dihydrosiloles via Ni-catalyzed hydrosilylation/intramolecular Ir-catalyzed dehydrogenative coupling of the Si–H bond with the heteroaromatic C–H bond has been developed. The method is efficient for both electron-deficient and -rich heterocycles. It exhibits high functional group tolerance and good regioselectivity. Fused heteroaromatic dihydrosiloles can be smoothly halogenated and then oxidized or arylated. Application of these transformations allows obtaining highly functionalized heteroaromatic structures. A gram-scale synthesis of dihydropyridinosilole has also been accomplished using reduced amounts of Ni- and Ir-catalysts.

Transition-metal-catalyzed C–H silylation reactions¹ of aromatic and heteroaromatic systems serve as powerful tools for functionalization of these molecules.^{2–10} In recent years, a number of methodologies employing Ru,³ Ir,⁴

Rh,⁵ Pt,⁶ Pd,⁷ Re,⁸ and Lewis acid⁹ catalysis, have been developed for inter- and intramolecular dehydrogenative Si–H/C–H coupling reactions. Yet reports on analogous heteroaromatic C–H coupling are exceedingly rare.¹⁰ Recently, we reported a *one-pot* procedure for the efficient synthesis of dihydrobenzosiloles via hydrosilylation of

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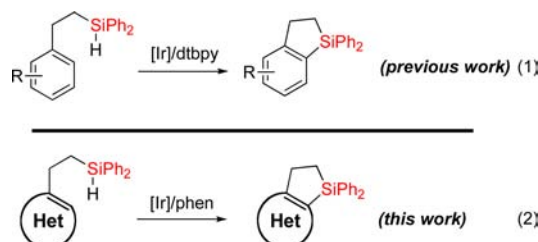
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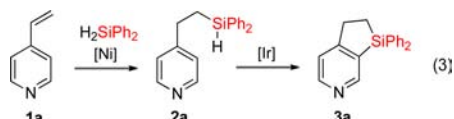
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styrenes with diphenylsilane followed by dehydrogenative cyclization (eq 1).¹¹ However, the heteroaromatic analogues of dihydrobenzosiloles are virtually unknown.¹² Given the importance of heteroaromatic molecules in various fields, herein we wish to report an efficient method for dehydrogenative Si–H/C–H cyclization of heteroaromatic molecules including pyridine, pyrrole, furan, and thiophene (eq 2). In this work, we also show that the resulted fused heteroaromatic dihydrosiloles can be readily transformed into valuable highly functionalized building blocks.



First, we attempted to apply the previously developed conditions¹¹ for the synthesis of dihydropyridinosilole **3a** from 4-vinylpyridine (eq 3). However, hydrosilylation of vinylpyridine **1a** with diphenylsilane in the presence of $\text{NiBr}_2 \cdot (\text{PPh}_3)_2$ produced traces of **2a**. Use of the $\text{Ni}(\text{cod})_2/\text{PPh}_3$ combination was more effective in this transformation to give **2a** in high yield. A subsequent *one-pot* addition of $[\text{Ir}(\text{cod})(\text{OMe})_2]$, dtbpy, and norbornene however did not provide any sufficient amounts of dihydropyridinosilole **3a**. Optimization of the dehydrogenative cyclization of **2a** revealed¹³ that use of 2% $[\text{Ir}(\text{cod})\text{OMe}]_2$ and 4% 1,10-phenanthroline gives a good yield of dihydropyridinosilole **3a** (Table 1, entry 1). We also found that the presence of PPh_3 , which is a requisite ligand for the hydrosilylation reaction, inhibits the cyclization step. Hence, the hydrosilylation/dehydrogenative coupling sequence was performed in two steps. Notably, both reactions can be easily scaled up to a gram-scale synthesis of dihydropyridinosilole **3a**, which can be accomplished using lower amounts of Ni- and Ir-catalysts (Table 1, entry 2).



Having the optimized conditions for dehydrogenative cyclization in hand, we examined the scope of the

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(13) See Supporting Information for details.

Table 1. Scope of Electron-Deficient Heterocycles in Hydrosilylation–Dehydrogenative Cyclization^a

entry	intermediate	2, yield ^b	product	3, yield ^b
1		84%		83%
2 ^c		83%		74–82%
3		86%		87%
4		86%		68% (5:1)
5		61%		64%
6		95%		traces
7		93%		79%
8		90%		86%
9		83%		75%
10		dec.		N/A
11		48%		36%
12		76% ^d		73%
13		67%		72%
14		76%		77%
15		97%		74%
16		96%		78%
17		90%		74% ^e
18		94%		56% ^e

^a Hydrosilylation reaction conditions: **1** (1.0 mmol), H_2SiPh_2 (1.02 mmol), $\text{Ni}(\text{cod})_2$ (5 mol %), PPh_3 (20 mol %), and THF (1.0 mL) were stirred at 90 °C for 2 h under nitrogen. Dehydrogenative coupling reaction conditions: **2** (0.5 mmol), $[\text{Ir}(\text{cod})\text{OMe}]_2$ (2 mol %) and 1,10-phenanthroline (4 mol %), norbornene (1.2 equiv), and THF (1.0 mL) were stirred at 100 °C for 12 h under nitrogen. ^b Isolated yield. ^c Reaction was performed on 10 mmol scale using 2.5 mol % Ni-catalyst and 0.25–0.5 mol % Ir-catalyst. ^d 10 mol % $\text{Ni}(\text{cod})_2$ was used. ^e 48 h at 100 °C.

hydrosilylation–dehydrogenative cyclization reaction starting with 4-vinylpyridines bearing a substituent at the C2 position of the ring (Table 1, entries 3–5). It was found that both electron-donating and -withdrawing groups were tolerable at this position leading to a dehydrogenative Si–H/C–H coupling reaction at a less hindered site. Hydrosilylation of 4-methyl-3-vinylpyridine worked well (entry 6). However, attempts at the cyclization step resulted in traces of cyclized product only, probably due to the inhibition of the Ir catalyst by its complexation with the pyridine nitrogen atom.

On the other hand, 2-methyl-3-vinylpyridine and its derivatives were converted into the cyclization products in good yield (entries 7–9). 2-Vinylpyridine underwent a smooth hydrosilylation reaction, as judged by GC/MS analysis of the crude reaction mixture; however it decomposed upon purification into 2-ethylpyridine (entry 10). This result can be explained by intramolecular pyridine nitrogen-assisted hydrolysis of the hydrosilylation product **2i**. Hence, next, we examined reactions of more sterically hindered substrates possessing a substituent at the C6 position of the pyridine ring. Thus, the hydrosilylation of 6-methyl-2-vinylpyridine lead to the corresponding hydrosilylation product **2j** in moderate yield (entry 11). A subsequent dehydrogenative cyclization reaction of **2j** allowed **3j** to be obtained in low yield. Introduction of fluorine at the C5 position of 6-methyl-2-vinylpyridine gave improved results (entry 12). Employment of substrates possessing MeO- and CF₃- groups at the C6 position of 2-vinylpyridine gave comparable good yields for both steps (entries 13–14). Having explored the

Table 2. Scope of Electron-Rich Heterocycles in Hydrosilylation–Dehydrogenative Cyclization^a

entry	intermediate	2, yield ^b	product	3, yield ^b
1		93%		88%
2		70%		67%
3		91%		84%
4		94%		63%
5		92%		61% (10:1)
6		89%		94% (10:1)
7		85%		52% (7:1)
8		84%		59%

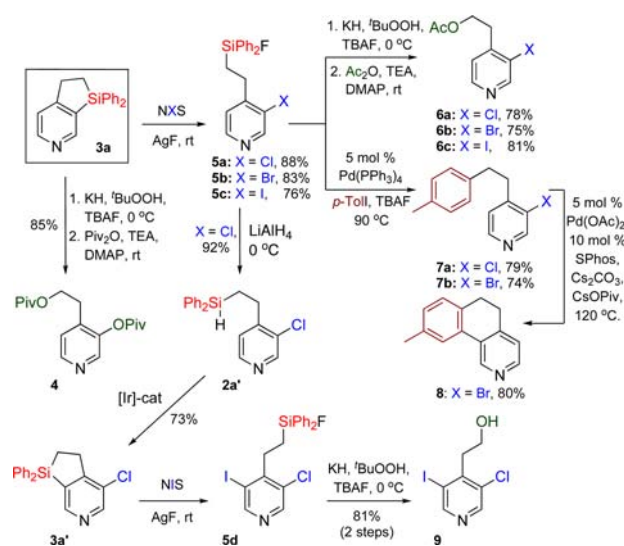
^a Hydrosilylation reaction conditions: **1** (1.0 mmol), H₂SiPh₂ (1.02 mmol), Ni(cod)₂ (5 mol %), PPh₃ (20 mol %), and THF (1.0 mL) were stirred at 90 °C for 2 h under nitrogen. Dehydrogenative coupling reaction conditions: **2** (0.5 mmol), [Ir(cod)OMe]₂ (2 mol %) and 1,10-phenanthroline (4 mol %), norbornene (1.2 equiv), and THF (1.0 mL) were stirred at 100 °C for 12 h under nitrogen. ^b Isolated yield.

dehydrogenative cyclization of pyridine substrates with a Si-tether at different positions, we turned our attention to other electron-deficient heterocycles. It was found that quinoline, isoquinoline, and quinoxaline systems provided high yields for the hydrosilylation reaction and good yields for a subsequent cyclization step (entries 15–18).

Next, we examined the possibility of using substrates possessing electron-rich heterocycles in this hydrosilylation–dehydrogenative coupling reaction sequence (Table 2). We were pleased to find that furan, thiophene, and pyrrole systems worked well in both reactions producing the corresponding cyclization products in good yields (entries 1–3). In the case of pyrrole with a Si-tether at the C4 position, the cyclization selectively occurred at the C3 position (entry 3). Expectedly, benzothiophene with a tether at the C3 position cyclized at the C2 site (entry 4). Cyclization of fused hetero-aromatic systems at the phenyl ring were efficient, as well. Thus, employment of benzothiophene with a tether at C5 resulted in the cyclization product at the C6 position as a major regioisomer (entry 5). Similarly, indole and *N*-Ts indazole with an alkylsilyl tether at C5 gave the C6 cyclization products as major regioisomers (entries 6–7). On the other hand, *N*-Me indazole with a Si-tether at C5 cyclized at the C6 exclusively (entry 8).

Finally we explored the synthetic usefulness of this method by transforming the obtained fused hetero-aromatic dihydrosiloles into valuable heterocyclic building blocks (Scheme 1). Thus, dihydropyridinosilole **3a** upon treatment with ^tBuOOH/KH and TBAF¹⁴ can be oxidized into 4-(2-hydroxyethyl)pyridin-3-ol derivative **4** in

Scheme 1. Further Modifications of Dihydropyridinosilole



85% yield. Upon reaction with *N*-halosuccinimides and AgF, the C(Het)–Si bond of dihydropyridinosilole **3a** can be cleaved selectively over the C(Ph)–Si bond to produce 3-halopyridinefluorosilanes **5a–c** in good yields.

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The Si-group in **5a–c** can be further oxidized to **6a–c**, or replaced with an aryl-¹⁵ group to form **7a,b** in good yields. Compound **7b** can undergo efficient intramolecular direct arylation with formation of tricyclic dihydrobenzoquinoline **8**. Moreover, upon reaction with LiAlH₄,¹⁶ 3-chloropyridinefluorosilane **5a** was converted to hydrosilane **2a'**, which was cyclized into **3a'** under the Ir-catalyzed dehydrogenative cyclization reaction conditions. Subsequent dihydrosilole ring opening with NIS and AgF, and oxidation of the Si-group in the resulted 3-chloro-5-iodopyridinefluorosilane **5d** using ^tBuOOH/KH and TBAF, led to the highly functionalized 2-(3-chloro-5-iodopyridin-4-yl)ethanol **9**.

In summary, we developed an efficient method for the synthesis of fused heteroaromatic dihydrosiloles via the Ni-catalyzed hydrosilylation of heteroaromatic styrenes,

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followed by the Ir-catalyzed dehydrogenative Si–H/C–H coupling sequence. This method proved to be very effective for electron-deficient and -rich heterocycles. These newly formed fused heteroaromatic dihydrosiloles can be further transformed into valuable heterocyclic building blocks, possessing halogen, hydroxyl, and aryl functionalities.

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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>.

The authors declare no competing financial interest.