

Catalytic metal-free Si–N cross-dehydrocoupling†

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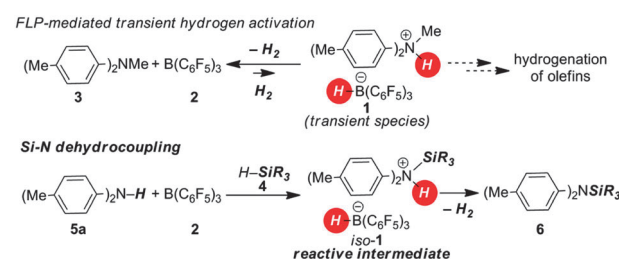
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The metal-free $\text{B}(\text{C}_6\text{F}_5)_3$ catalyzed dehydrocoupling of hydrosilanes with anilines, carbazoles and indoles is reported. For anilines and carbazoles the reaction proceeds by the liberation of H_2 as the sole Si–N coupling byproduct. Indoles react with diphenyl(methyl) hydrosilane to give *N*-silyl indolines with high diastereoselectivity (d.r. 10 : 1) in excellent yields. A mechanism for this Si–N coupling/hydrogenation sequence is proposed.

The cross-dehydrocoupling is an efficient methodology for the connection of two molecular entities.¹ Especially the dehydrocoupling of Si–H and N–H fragments provides an environmentally benign access to silyl-protected amines.² These ubiquitous structural motifs are usually obtained by the reaction of halosilanes with deprotonated amines, the generation of which often requires strong bases.³ This is not only of concern for atom efficiency but also for functional group tolerance. In light of this, the Si–N dehydrocoupling proved very useful, *e.g.* for the protection of indoles using $\text{Zn}(\text{OTf})_2$ (10 mol%) in the presence of 0.5–1.0 equiv. of pyridine.⁴ Oestreich's sulfur-bridged Ru–arene complex⁵ is particularly effective in the base-free dehydrocoupling of silanes with other nitrogen-containing heterocycles, *e.g.* indole, carbazole and pyrrole derivatives using only 1 mol% of catalyst loading.⁶ However, a metal-free variant has not yet been disclosed.⁷

We have shown earlier that the H_2 -activation product **1** of the frustrated Lewis pair (FLP) consisting of **2/3** is a transient species which readily releases H_2 at room temperature (Scheme 1, top).⁸ Accordingly, the isostructural intermediate iso-**1**, generated through the silyl-transfer from the silane **4** to the aniline **5a**, should readily liberate H_2 with concomitant release of the Si–N coupling product **6** (Scheme 1, bottom). As a potential silyl-transfer catalyst, borane **2** has attracted significant attention in hydrosilylation of aldehydes, ketones, imines and olefins.⁹ An analogous mechanism was only recently proposed by Oestreich as a competing pathway in the borane-promoted imine reduction with hydrosilanes.^{9a}



Scheme 1 Conceptual outline for the Si–N dehydrocoupling.

Indeed, when bis(4-toloyl)amine (**5a**) was reacted with diphenyl(methyl) silane (**4a**) in the presence of 5 mol% $\text{B}(\text{C}_6\text{F}_5)_3$ (**2**) at room temperature, the silylamine **6a** was obtained in 95% yield accompanied with the evolution of H_2 (Table 1, entry 1). In the absence of the catalyst, the formation of **6a** was not observed even when a mixture of **5a** and **4a** was heated to 90 °C for 12 h (Table 1, entry 2). The catalyst loading was reduced to 1 mol% with slight erosion in yield (73%, entry 3). Lower catalyst loadings of 0.1 mol% led to significantly reduced yields (entry 4). Further experiments were carried out with 1 mol% of **2** as catalyst.

The reaction displays a remarkable substrate scope. Besides diphenylamine derivatives (**5a** and **5b**, entries 3 and 5), carbazole derivatives **5c–f** also proved to be viable substrates and the products **6c–f** were obtained in 83–97% yields (entries 6–9). The dibromo derivative required 70 °C to undergo Si–N cross-dehydrocoupling in 51% yield without the observation of dehalogenation (entry 8). The reduced yield was attributed to the very low solubility of **5e** in toluene. Other silanes were also useful in the Si–N coupling reaction. Triethylsilane (**4b**) or 1,1,3,3-tetramethyldisiloxane (**4c**) readily reacted with carbazole (**5c**) or bis(4-tolyl)amine (**5a**) in high yields (entries 9 and 10). The silylation of primary aniline derivatives proceeded at 60–70 °C in excellent yields (88–97%, entries 11–15).¹⁰ The electron-deficient anilines **5m** and **5n** were reactive even at room temperature and **6m** and **6n** were obtained in 88% and 97% yields (entries 16 and 17). Also the two diamines *N,N'*-(diphenyl)-1,4-phenylene diamine (**5o**) and *N,N'*-(diphenyl)-ethylene diamine (**5p**) underwent silylation with diphenylmethyl silane (**4a**) in high yields (entries 18 and 19).

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Table 1 Si–N cross-dehydrocoupling of aromatic amines with hydrosilanes^a

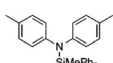
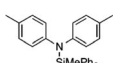
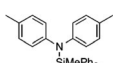
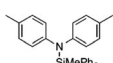
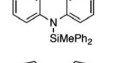
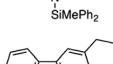
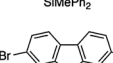
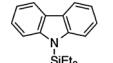
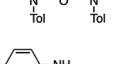
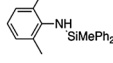
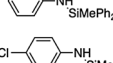
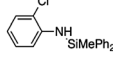
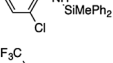
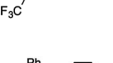
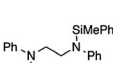
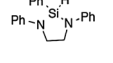
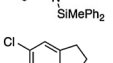
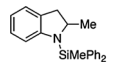
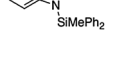
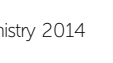
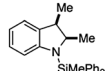
$1.0 \text{ equiv. } \begin{array}{c} \text{R} \quad \text{R}' \\ \quad \\ \text{N} \\ \\ \text{H} \end{array} \text{ 5} + 1.0 \text{ equiv. H-SiR}_3 \xrightarrow[\text{CH}_2\text{Cl}_2, \text{ temp.}]{\text{cat. B(C}_6\text{F}_5)_3 \text{ (2) (1 mol\%)}} \begin{array}{c} \text{R} \quad \text{R}' \\ \quad \\ \text{N} \\ \\ \text{SiR}_3 \end{array} \text{ 6} + \text{H}_2$					
Entry	<i>t</i> [h]	<i>T</i> [°C]	Product	Yield [%]	
Diarylamines					
1	1	25		95 ^b	
2	12	90		0 ^c	
3	1	25		73	
4	10	25		32 ^d	
5	1	25		91	
6	1	25		97	
7	1	25		83	
8	24	25		95 ^e	
9	1	25		95 ^e	
10	1	25		97	
Anilines					
11	72	70		90 ^b	
12	48	70		90	
13	48	70		93	
14	36	60		97	
15	24	60		91	
16	36	25		88	
17	24	25		97	
Diamines					
18	24	25		26 ^f	
19	24	70		92 ^b	
20	24	60		83	
Indoles					
21	144	70		50 ^e	
22	24	70		81	
23	24	70		96	
24	24	70		97	

Table 1 (continued)

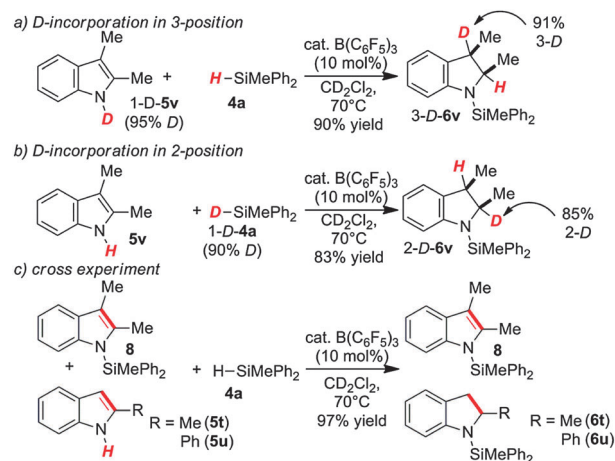
$1.0 \text{ equiv. } \begin{array}{c} \text{R} \quad \text{R}' \\ \quad \\ \text{N} \\ \\ \text{H} \end{array} \text{ 5} + 1.0 \text{ equiv. H-SiR}_3 \xrightarrow[\text{CH}_2\text{Cl}_2, \text{ temp.}]{\text{cat. B(C}_6\text{F}_5)_3 \text{ (2) (1 mol\%)}} \begin{array}{c} \text{R} \quad \text{R}' \\ \quad \\ \text{N} \\ \\ \text{SiR}_3 \end{array} \text{ 6} + \text{H}_2$					
Entry	<i>t</i> [h]	<i>T</i> [°C]	Product	Yield [%]	
25	24	70		92	

^a Reactions were performed on a 1.0 mmol scale, 3 M in CH₂Cl₂. ^b 5 mol% 2. ^c Absence of 2. ^d 0.1 mol% B(C₆F₅)₃. ^e 10 mol% 2, 0.1 mmol scale, 3 M in CD₂Cl₂, yield determined by ¹H NMR. ^f 2 mol% 2.

Accordingly, the reaction of **5p** with phenylsilane (**4d**) provided the cyclic product **6q** in 83% yield (entry 20).

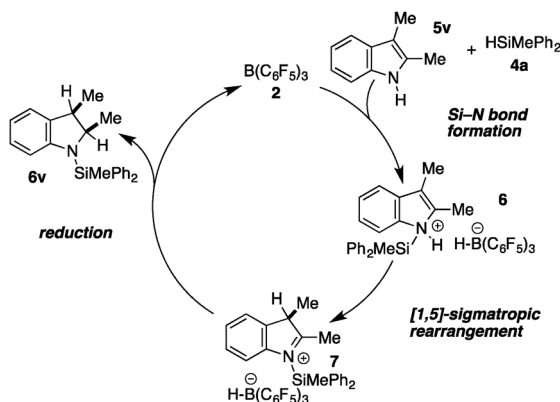
Finally, we investigated the potential of the Si–N dehydrocoupling for pyrrole and indole derivatives. While pyrrole-derivatives were unreactive under our reaction conditions,¹¹ the indole-derivatives **5r–v** displayed high reactivity. The indoles **5r–v** were chemospecifically converted into the 1-silylated indoline derivatives **6r–v** (entries 21–25) without the formation of unsaturated side products arising from N or C3-silylation.¹² Indole (**5r**) required prolonged reaction time (144 h, entry 21) for the domino silylation/reduction sequence and indoline (**6r**) was obtained in 50% yield. The less electron-rich 6-chloroindole (**5s**) was transformed into **6s** in excellent yield in only 24 h (95%, entry 22). Substituents in position 2 were well tolerated and the 2-methyl and 2-phenyl indolines **5t** and **5u** were obtained in quantitative yields (96% and 97%, entries 3–5). 2,3-dimethylindole (**5v**) was diastereoselectively reduced to *cis*-2,3-dimethyl indoline (**6v**) in quantitative yield (98%, d.r. 10 : 1).¹³

The high chemospecificity and diastereoselectivity prompted us to investigate the Si–N cross coupling/hydrogenation reaction of **5v** with **4a** in detail (Scheme 2). Only resonances of the starting materials and the product **6v** were observed when the reaction was monitored by ¹H NMR (1 mol% 3, [D₈]-toluene). Neither the resonance of FLP-activated H₂ nor the resonance of dissolved H₂ was observed by ¹H NMR. Deuterium labeling experiments were conducted to investigate the fate of the hydridic and protic hydrogen atoms in silane **4a**



Scheme 2 Isotope labelling experiments with (a) 1-D-2,3-dimethylindole (1-D-**4v**), with (b) D-SiMePh₂ (D-**4a**) and (c) cross experiment.





Scheme 3 Proposed catalytic cycle for the Si-N coupling/hydrogenation domino reaction.

and indole 5v. The reaction of 1-D,2,3-dimethyl indole (1-D-5v, 95% D) with H-SiMePh₂ (4a) gave exclusively *cis*-3-D,2,3-dimethyl indoline (3-D-6v) in high yields (97%, 92% D-incorporation, Scheme 2a). The reaction of D-SiMePh₂ (D-2a, 95% D) with 5v provided exclusively *cis*-2-D,2,3-dimethyl indoline (2-D-6v) in 96% yield with 92% D-incorporation at position 2. Together the chemo-selective deuteration and the absence of dissolved or FLP-activated H₂ or HD¹⁴ strongly support a *N*-silylation/rearrangement/reduction mechanism (Scheme 3). The product of the B(C₆F₅)₃-catalyzed silyl-transfer to 5v is 1-silyl-1-*H*-indol-1-ium 6, which rearranges to the more stable 1-silyl-3-*H*-indol-1-ium 7. Alternatively, an intermolecular proton-transfer might be conceivable. However, according to our cross experiment using 5t-u and 1-silyl-indole 8, the sigmatropic rearrangement mechanism is more likely (Scheme 2c). The indole derivatives 5t and 5u were equally reactive as 5v (96–98%, 24 h, see Table 1, entries 23–25) and should be readily protonated by transiently formed 6 (formed by the reaction of 5 and 4a, compare Scheme 3). However, the reaction of an equimolar mixture of 8, 5t-u, and 4a in the presence of 10 mol% 2 produced 6t or 6u as the product (6u/6v >95:5; 6t:6v >90:10). This is a strong indication that intermolecular proton-transfer is not operative in the silylation/hydrogenation reaction sequence. The final step in the catalytic cycle is the hydride transfer from [H-B(C₆F₅)₃] to the highly electrophilic iminium species 7 from the least hindered side liberating *cis*-6v and the catalyst 2.

In summary, we have developed the metal-free Si-N cross-dehydrocoupling for primary and secondary aryl amines having solely molecular hydrogen as byproduct. Indole derivatives undergo *N*-silylation followed by a rearrangement/reduction sequence to furnish indolines in high yields and high diastereoselectivity (d.r. 10:1).

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