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Catalytic metal-free Si–N cross-dehydrocoupling†

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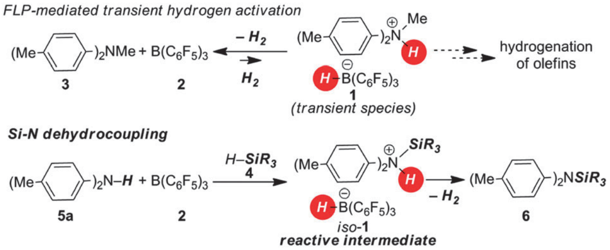
The metal-free $B(C_6F_5)_3$ catalyzed dehydrocoupling of hydrosilanes with anilines, carbazoles and indoles is reported. For anilines and carbazoles the reaction proceeds by the liberation of H_2 as the sole Si–N coupling byproduct. Indoles react with diphenyl(methyl) hydrosilane to give *N*-silyl indolines 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 $Zn(OTf)_2$ (10 mol%) in the presence of 0.5–1.0 equiv. of pyridine.[4] Oestreich's sulfur-bridged Ru–arene complex[5] 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 Conceptional 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% $B(C_6F_5)_3$ (**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 bibromo 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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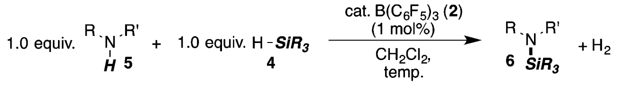
Table 1 Si–N cross-dehydrocoupling of aromatic amines with hydrosilanes[a]



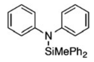
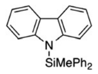
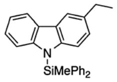
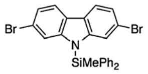
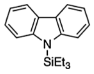
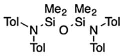
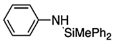
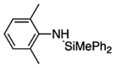
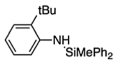
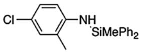
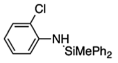
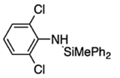
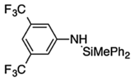
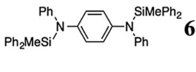
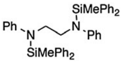
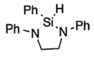
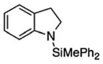
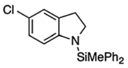
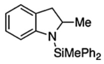
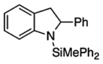
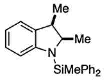
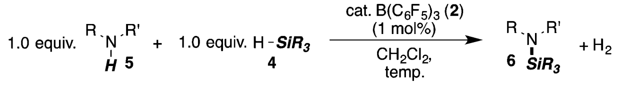
	Entry	t [h]	T [°C]	Product		Yield [%]
Diarylamines	1	1	25		**6a**	95[b]
	2	12	90			0[c]
	3	1	25			73
	4	10	25			32[d]
	5	1	25		**6b**	91
	6	1	25		**6c**	97
	7	1	25		**6d**	83
	8	24	25		**6e**	95[e]
	9	1	25		**6f**	95[e]
	10	1	25		**6g**	97
Anilines	11	72	70		**6h**	90[b]
	12	48	70		**6i**	90
	13	48	70		**6j**	93
	14	36	60		**6k**	97
	15	24	60		**6l**	91
	16	36	25		**6m**	88
	17	24	25		**6n**	97
Diamines	18	24	25		**6o**	26[f]
	19	24	70		**6p**	92[b]
	20	24	60		**6q**	83
Indoles	21	144	70		**6r**	50[e]
	22	24	70		**6s**	81
	23	24	70		**6t**	96
	24	24	70		**6u**	97
	25	24	70		**6v**	92

Table 1 (continued)

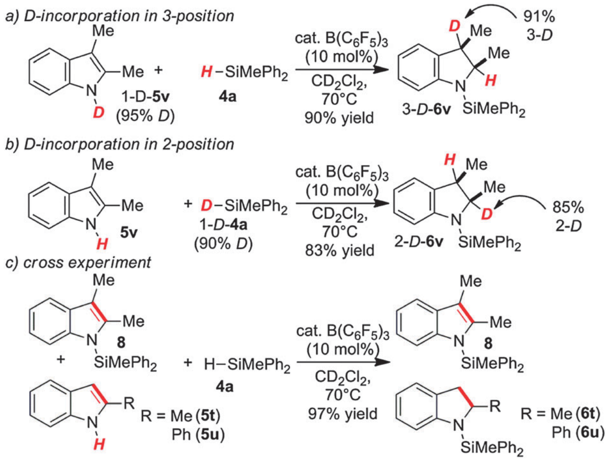


[a] Reactions were performed on a 1.0 mmol scale, 3 M in CH_2Cl_2. [b] 5 mol% **2**. [c] Absence of **2**. [d] 0.1 mol% $B(C_6F_5)_3$. [e] 10 mol% **2**, 0.1 mmol scale, 3 M in CD_2Cl_2, yield determined by ^1H NMR. [f] 2 mol% **2**.

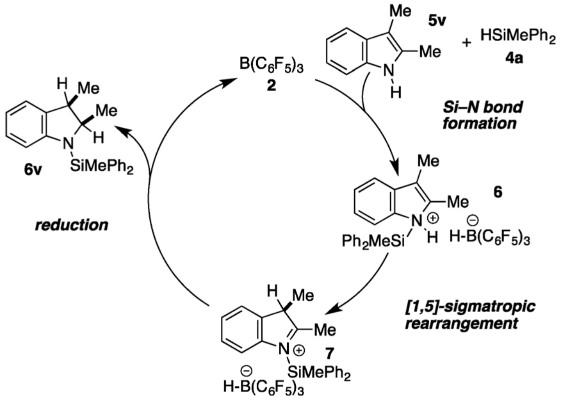
Accordingly, the reaction of **5p** with phenylsilane (**4d**) provided the cyclic product **6q** in 83% yield (entry 20).

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**, [D_8]-toluene). Neither the resonance of FLP-activated H_2 nor the resonance of dissolved H_2 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-SiMePh$_2$ (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–SiMePh$_2$ (**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–SiMePh$_2$ (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 chemoselective deuteration and the absence of dissolved or FLP-activated H$_2$ or HD[14] strongly support a *N*-silylation/rearrangement/reduction mechanism (Scheme 3). The product of the B(C$_6$F$_5$)$_3$-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(C$_6$F$_5$)$_3$] 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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10 The elevated temperature of 60–70 °C was required to thermally cleave the aniline/B(C$_6$F$_5$)$_3$ adduct as evidenced by ^{11}B NMR.

11 Neither *N*- nor C3-silylation products were observed, see: L. D. Curless, E. R. Clark, J. J. Dunsford and M. J. Ingleson, *Chem. Commun.*, 2014, DOI: 10.1039/c3cc47372d.

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