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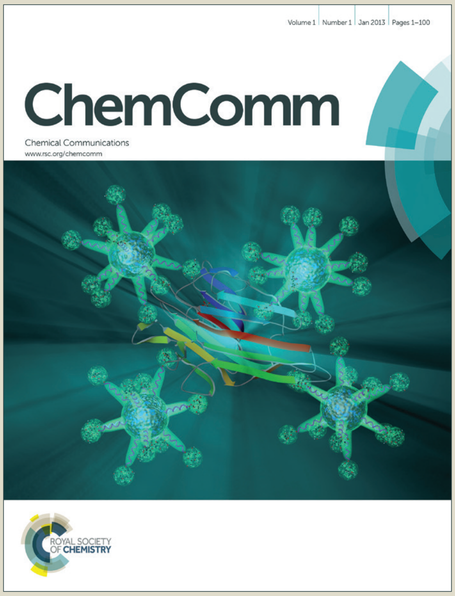

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Catalytic metal-free Si-N cross-dehydrocoupling

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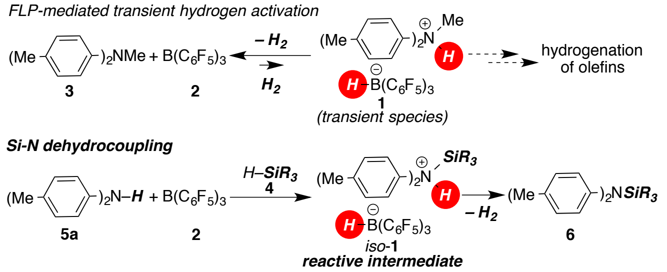
The metal-free $B(C_6F_5)_3$ catalyzed dehydrocoupling of hydrosilanes with anilines, carbazoles and indoles is reported. For anilines and carbazoles the reaction proceeds by the liberation of H_2 as sole Si–N coupling byproduct. Indoles react with diphenyl(methyl) hydrosilane to N-silyl indolines with high diastereoselectively (d.r. 10:1) in excellent yields. A mechanism of 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 motives are usually obtained by the reaction of halosilanes with deprotonated amines, which generation often requires strong bases.[3] This is not only of concern for atom efficiency but also for functional group tolerance. In this light 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. 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 pyrrol 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 potential silyl-transfer catalyst borane **2** has attracted significant attention in hydrosilylations of aldehydes, ketones, imines and olefins.[9] An analogous mechanism was only recently proposed by Oestreich as competing pathway in the borane-promoted imine reduction with hydrosilanes.[9a]

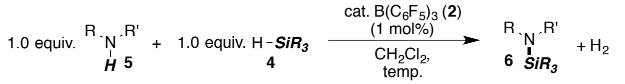
Indeed, when bis(4-toloyl)amine (**5a**) was reacted with diphenyl(methyl) silane (**4a**) in the presence of 5 mol% $B(C_6F_5)_3$ (**2**) at room temperature the silylamine **6a** was obtained in 95% yield accompanied with the evolution of H_2 (Table 1, entry 1). In the absence of the catalyst the formation 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.

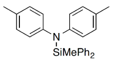
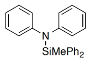
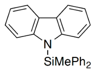
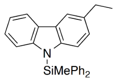
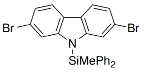
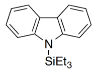
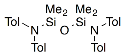
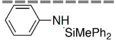
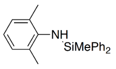
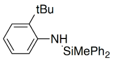
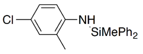
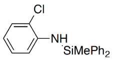
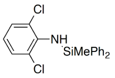
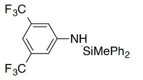
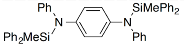
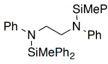
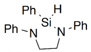
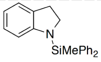
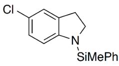
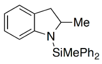
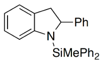
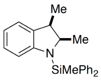


Scheme 1 Conceptional outline for the Si–N dehydrocoupling.

The reaction displays remarkable substrate scope. Besides diphenyl amine derivatives (**5a** and **5b**, entries 3 and 5) also carbazole derivatives **5c-f** proved as viable substrates and the products **6c-f** were obtained in 83-97% yield (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% yield (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 diphenyl-methyl silane (**4a**) in high yields (entries 18 and 19).

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

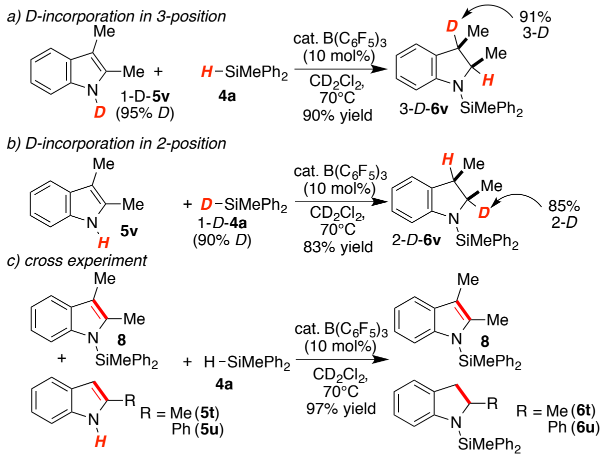
[a] reactions were performed on 1.0 mmol scale, 3 M in CH_2Cl_2; [b] 5 mol% **2**; [c] absence of **2**; [d] 0.1 mol% $B(C_6F_5)_3$; [e] 10 mol% **2**, 0.1 mmol scale, 3 M in CD_2Cl_2, yield determined by ^1H NMR; [f] 2 mol% **2**.

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

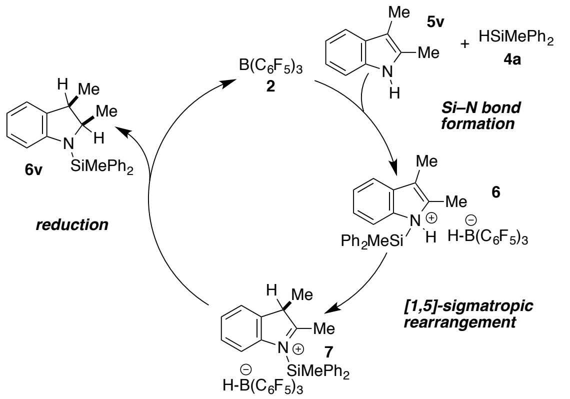
Finally we investigated the potential of the Si–N dehydrocoupling for pyrrol and indole derivatives. While pyrrol-derivatives were unreactive under our reaction conditions[11] the indole-derivatives **5r-v** displayed high reactivity. The indoles **5r-v** were chemospecifically converted into the 1-silylated 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 2-position 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 for FLP-activated H_2 nor the resonance for 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** 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/re-arrangement/reduction mechanism (Scheme 3). The product of the $B(C_6F_5)_3$-catalyzed silyl-transfer to **5v** gives 1-silyl-1-*H*-indol-1-ium **6** and 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 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–$B(C_6F_5)_3$] 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 diastereo-selectivity (d.r. 10:1).



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



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

Notes and references

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Electronic Supplementary Information (ESI) available: experimental procedures, analytical data. See DOI: 10.1039/c000000x/

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10. The elevated temperature of 60-70 °C was required to thermally cleave the aniline/$B(C_6F_5)_3$ 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.*, 2013, DOI: 10.1039/c3cc47372d.
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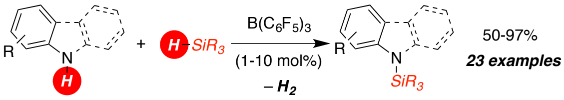
14. Although the hydrogenation of N-methyl indoles is reported (10 mol% **2**, 103 bar H_2, 80 °C, see D. W. Stephan, S. Greenberg, T. W. Graham, P. Chase, J. J. Hastie, S. J. Geier, J. M. Farrell, C. C. Brown, Z. M. Heiden, G. C. Welch and M. Ullrich, *Inorg. Chem.*, 2011, **50**, 12338) the hydrogenation of 1-silyl-2,3-dimethyl indole (4 bar H_2) in the presence of 5 mol% **2** in toluene at 70 °C did not furnish indoline **6v**.

Graphical for Table of Contents



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The $B(C_6F_5)_3$ catalyzed cross-dehydrocoupling of hydrosilanes with anilines, carbazoles and indoles is reported and provides an metal-free access to silyl-protected amines.