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Catalytic dehydrogenative Si–N coupling of pyrroles, indoles, carbazoles as well as anilines with hydrosilanes without added base†

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A base-free, catalytic protocol for the dehydrogenative Si–N coupling of weakly nucleophilic N–H groups of heteroarenes or aryl-substituted amines with equimolar amounts of hydrosilanes is reported. Cooperative Si–H bond activation at a Ru–S bond generates a silicon electrophile that forms a Si–N bond prior to the N–H deprotonation by an intermediate Ru–H complex, only releasing H_2.

The formation of Si–N bonds is relevant to various areas of synthetic chemistry.[1] N–H bond silylation is one way to temporarily protect amino groups,[2] in particular the N–H group in indoles and pyrroles.[3] Their silylated derivatives are prevalent building blocks for the construction of heteroarene-based complex molecules. The Si–N bond is relatively labile though, and *N*-silylated anilines have been employed as silylating agents themselves.[4] The transition metal-catalysed synthesis of oligo-[5] or polysilazanes[6] is another significant application of Si–N coupling.

A silicon group is usually introduced at the nitrogen atom by a deprotonation/silylation sequence using a strong base and a halosilane.[2,7] The formation of stoichiometric amounts of salt is an issue in this approach. The direct coupling of N–H and Si–H bonds is an attractive alternative that, ideally, generates dihydrogen as the sole by-product. Several dehydrogenative Si–N couplings are known today[8] but generality and control of the chemoselectivity remain challenging. The latter was recently accomplished by Sadow *et al.*[9a] and Cui *et al.*[9b] in the direct catalytic mono-coupling of R_nSiH_{4-n} (with n = 1 and 2). Parallel to these current developments, progress has also been made toward the elusive dehydrogenative Si–N coupling of heteroarenes.[10] The methods reported by Tsuchimoto *et al.*[10b] and Mizuno *et al.*[10c] are broadly applicable and robust but require the addition of an external base (stoichiometric and catalytic, respectively) and a nitrile solvent as a H_2 acceptor. We disclose herein a base- and H_2 acceptor-free protocol for the catalytic dehydrogenative Si–N coupling of both N–H group-containing heteroarenes and aryl-substituted amines that follows an unusual silylation/deprotonation sequence.

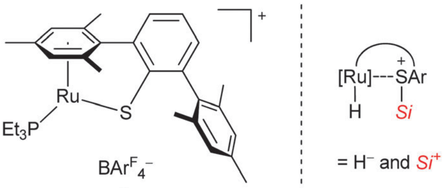

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Fig. 1 Tethered complex **1** with a polar Ru–S bond in Si–H bond activation [Ar^F = 3,5-bis(trifluoromethyl)phenyl and *Si* = triorganosilyl].

Our laboratory, in collaboration with Ohki and Tatsumi, introduced the cooperative activation of Si–H bonds at the polar Ru–S bond[11] of the coordinatively unsaturated, tethered ruthenium complex **1**[12] (left, Fig. 1). The heterolytic splitting of the Si–H bond (in analogy to H_2 activation[13]) results in the formation of a Ru–H complex and a silicon electrophile, a sulfur-stabilized silicon cation (right, Fig. 1). This catalytic entry into the chemistry of silicon cations has already allowed for the development of a regioselective Friedel–Crafts-type indole silylation[11] and a chemoselective, dehydrogenative silylation of enolizable carbonyl compounds.[14] The same reaction setup applied to weakly nucleophilic N–H groups now results in Si–N bond formation together with liberation of H_2.

Our investigation began with the *N*-silylation of indole (**2**) using Me_2PhSiH (**3a**) that we had used in our earlier C-3-silylation of *N*-protected indoles[11] (Scheme 1). For an equimolar mixture of indole and silane, full conversion was reached after 1 h at 60 °C using 1 mol% of **1**. The expected *N*-silylated indole **4a** was, however, contaminated with substantial amounts of the cognate indoline **5a** in a ratio of 76 : 24. This ratio improved with prolonged reaction times in favour of the protected indole, *e.g.*, 92 : 8 after 12 h. We have shown before that **1** is capable of (reversible) indoline-to-indole dehydrogenation.[11]

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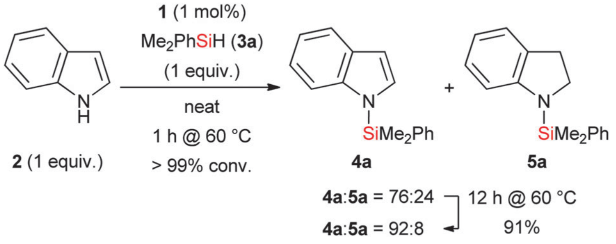
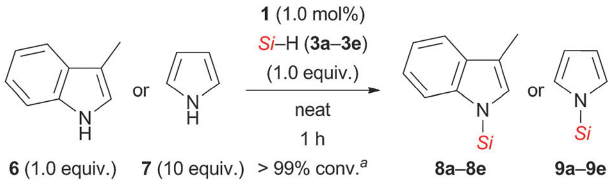
† Electronic supplementary information (ESI) available: Mechanistic proposal, preparation and characterisation data as well as ^1H and ^{13}C NMR spectra of all compounds. See DOI: 10.1039/c3cc38900f



Scheme 1 Dehydrogenative Si–N coupling of indole: reversible indoline-to-indole dehydrogenation catalysed by **1**.

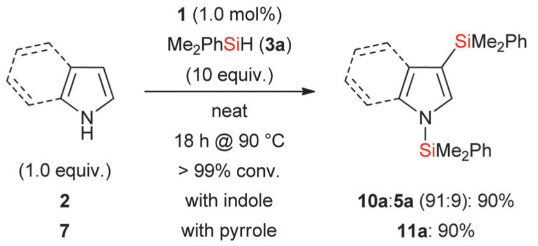
Table 1 Screening of different triorganosilanes



		3-Methylindole (6)			Pyrrole (7)		
Entry	*Si*–H	Temp. (°C)	Product	Yield[b] (%)	Temp. (°C)	Product	Yield[b] (%)
1	Me_2PhSiH (**3a**)	60	**8a**	97	90	**9a**	91
2	$MePh_2SiH$ (**3b**)	60	**8b**	90	90	**9b**	88
3[c]	$EtMe_2SiH$ (**3c**)	60	**8c**	94	90	**9c**	—[d]
4	Et_3SiH (**3d**)	90	**8d**	—[d]	90	**9d**	90
5	$i$$Pr_3SiH$ (**3e**)	90	**8e**	—[d]	90	**9e**	—[d]

[a] Conversion was monitored by GLC analysis and is based on the consumption of **3**. [b] Isolated yield after catalyst removal by filtration through a short plug of deactivated silica gel. [c] Volatile at elevated temperatures, used in toluene (0.5 M). [d] No reaction.

We then turned our attention to the screening of different triorganosilanes **3** in the dehydrogenative Si–N coupling of 3-methylindole[15] as well as pyrrole (**6** → **8** and **7** → **9**, Table 1). For the indole, sterically less demanding silanes **3a–3c** afforded excellent isolated yields whereas **3d** and **3e** did not react even at higher temperature (columns 3–5). For pyrrole, similar observations were made, yet requiring higher temperature and excess pyrrole (columns 6–8). It is somewhat unfortunate that $i$$Pr_3SiH$ (**3e**) is not activated by catalyst **1** for steric reasons because the $i$$Pr_3Si$ group is a commonly used protective group for these heteroarenes. By using an excess of **3a** (10 equiv.), we examined the possibility of double silylation, that is *N*-silylation and subsequent Friedel–Crafts C-3-silylation of indole and pyrrole (**2** → **10a** and **7** → **11a**, Scheme 2). Upon prolonging the reaction time (18 h instead of 1 h), doubly silylated **10a** (along with **5a**) and **11a** were formed in high yields.



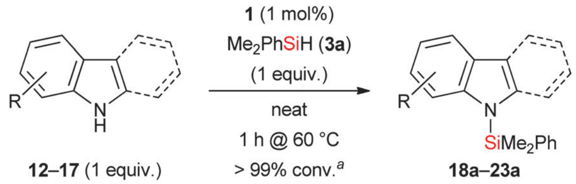
Scheme 2 Probing double silylation of indole and pyrrole.

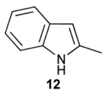
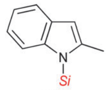
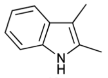
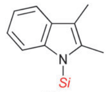
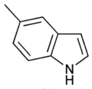
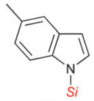
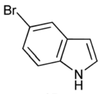
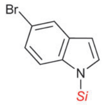
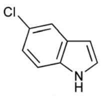
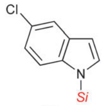
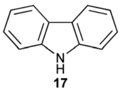
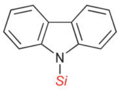
These findings are in accordance with previous results for *N*-protected indoles.[11]

We next examined the scope of the indole motif, substituted and unsubstituted at the C-3 atom (**12–16**, Table 2, entries 1–5). All of them underwent clean Si–N coupling in good to excellent yields. Aside from pyrrole and indole, carbazole also participated in this dehydrogenative *N*-silylation (**17**, Table 2, entry 6). These results compare well with the reports by Tsuchimoto *et al.*[10b] and Mizuno *et al.*[10c] (*vide supra*). The fact that these heteroarenes are sufficiently nucleophilic encouraged us to also test aryl-substituted amines with enhanced nucleophilicity (**24–30**, Table 3, entries 1–7). Indoline, essentially an aniline derivative, was dramatically more reactive than indole, yielding complete conversion in *n*-hexane after 5 min at ambient temperature (entry 1); indoline-to-indole oxidation only occurs at elevated temperatures (*cf.* Scheme 1).[11] Various substituted anilines displayed the same reactivity (Table 3, entries 2–7). It is worthy of note that the CF_3 group in **29** remains intact under these conditions.[16]

The chemoselectivity of our catalytic Si–N coupling was probed in the selective monoamination of dihydrosilane

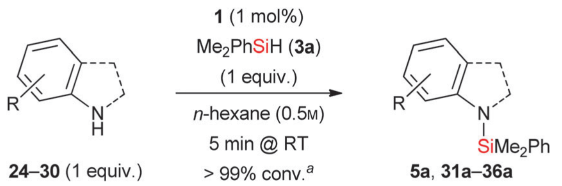
Table 2 Dehydrogenative Si–N coupling of indoles and carbazole

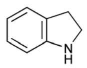
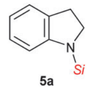
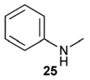
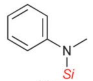
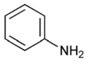
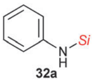
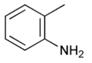
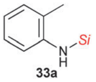
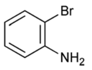
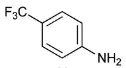
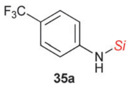
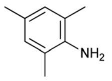
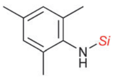


Entry	Substrate	Silylated product	Yield[b] (%)
1	 **12**	 **18a**	89[c]
2	 **13**	 **19a**	91
3	 **14**	 **20a**	96[d]
4	 **15**	 **21a**	89
5	 **16**	 **22a**	92
6	 **17**	 **23a**	76

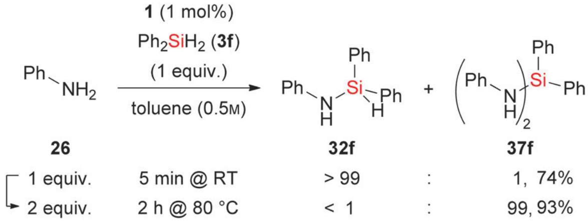
[a] See Table 1. [b] See Table 1. [c] Contaminated with trace amounts of $(Me_2PhSi)_2O$. [d] Approximately 10% of the cognate indoline detected.

Table 3 Dehydrogenative Si–N coupling of indoline and anilines



Entry	Substrate	Silylated product	Yield[b] (%)
1	 **24**	 **5a**	95
2	 **25**	 **31a**	92
3	 **26**	 **32a**	87
4	 **27**	 **33a**	85
5	 **28**	 **34a**	96
6	 **29**	 **35a**	85
7	 **30**	 **36a**	94

[a] See Table 1. [b] See Table 1.



Scheme 3 Probing chemoselective formation of silylamines with aniline (**26**) and Ph_2SiH_2 (**3f**).

Ph_2SiH_2 (**3f**) and aniline (**26** → **32f**, Scheme 3). With 1 equiv. of **26** at room temperature, only one Si–H bond of **3f** was cross-coupled. With subsequent addition of another equivalent of **26** at elevated temperature, the remaining Si–H bonds also underwent the cross-coupling (**26** → **37f**, Scheme 3).

To summarize, we accomplished an efficient protocol for the base-free dehydrogenative Si–N coupling of monohydrosilanes and weakly to moderately nucleophilic N–H groups. Pyrroles, indoles and carbazoles fall into the former and anilines into the latter category. Alkyl-substituted amines are not compatible with coordinatively unsaturated complex **1**, thwarting Si–H bond activation due to amine coordination (for a tentative mechanism, see the ESI†). Moreover, selective mono-coupling of a dihydrosilane and exactly 1.0 equiv. of aniline is feasible.

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15 Used to prevent its reduction (*cf.* Scheme 1) and possible double silylation (*cf.* Scheme 2).
16 Another version of **1** is also able to catalyse the hydrodefluorination of **29**: T. Stahl, H. F. T. Klare and M. Oestreich, *J. Am. Chem. Soc.*, DOI: 10.1021/ja311398j.