Catalytic metal-free Si–N cross-dehydrocoupling†

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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).

Notes and references

- For reviews, see: (a) C. S. Yeung and V. M. Dong, *Chem. Rev.*, 2011, **111**, 1215; (b) C. J. Scheuermann, *Chem.-Asian J.*, 2010, **5**, 436; (c) G. E. Dobereiner and R. H. Crabtree, *Chem. Rev.*, 2010, 681; (d) C. J. Li, *Acc. Chem. Res.*, 2009, **42**, 335; for recent examples, see: (e) X. M. Jie, Y. P. Shang, P. Hu and W. P. Su, *Angew. Chem., Int. Ed.*, 2013, **52**, 3630; (f) N. Kuhl, M. N. Hopkinson and F. Glorius, *Angew. Chem., Int. Ed.*, 2012, **51**, 8230.

- For reviews, see: (a) R. Waterman, *Chem. Soc. Rev.*, 2013, **42**, 5629; (b) E. M. Leitao, T. Jurca and I. Manners, *Nat. Chem.*, 2013, **5**, 817; (c) M. S. Hill, D. J. Liptrot, D. J. MacDougall, M. F. Mahon and T. P. Robinson, *Chem. Sci.*, 2013, **4**, 4212; (d) J. Y. Corey, *Chem. Rev.*, 2011, **111**, 863; (e) J. F. Harrod, *Coord. Chem. Rev.*, 2000, **206**, 493; (f) J. A. Reichl and D. H. Berry, *Adv. Organomet. Chem.*, 1998, **43**, 197; for pioneering work, see: (g) E. Matarasso-Tchiroukhine, *Chem. Commun.*, 1990, 681; for recent examples, see: (h) J. F. Dunne, S. R. Neal, J. Engelkemier, A. Ellern and A. D. Sadow, *J. Am. Chem. Soc.*, 2011, **133**, 16782; (i) C. K. Toh, H. T. Poh, C. S. Lim and W. Y. Fan, *J. Organomet. Chem.*, 2012, **717**, 9; (j) F. Buch and S. Harder, *Organometallics*, 2007, **26**, 5132; (k) A. Iida, A. Horii, T. Misaki and Y. Tanabe, *Synthesis*, 2005, 2677; (l) F. Lunzer, C. Marschner and S. Landgraf, *J. Organomet. Chem.*, 1998, **568**, 253; (m) H. Q. Liu and J. F. Harrod, *Can. J. Chem.*, 1992, **70**, 107; (n) H. Q. Liu and J. F. Harrod, *Organometallics*, 1992, **11**, 822; (o) W. D. Wang and R. Eisenberg, *Organometallics*, 1991, **10**, 2222; (p) Y. D. Blum, K. B. Schwartz and R. M. Laine, *J. Mater. Sci.*, 1989, **24**, 1707; (q) Y. Blum and R. M. Laine, *Organometallics*, 1986, **5**, 2081.
- (a) P. G. M. Wuts and T. W. Greene, *Protective Group in Organic Chemistry*, John Wiley & Sons, Inc., Hoboken, New Jersey, 4th edn, 2007; (b) S. Djuric, J. Venit and P. Magnus, *Tetrahedron Lett.*, 1981, **22**, 1787.
- T. Tsuchimoto, Y. Iketani and M. Sekine, *Chem.-Eur. J.*, 2012, **18**, 9500.
- (a) T. Stahl, H. F. T. Klare and M. Oestreich, *J. Am. Chem. Soc.*, 2013, **135**, 1248; (b) T. Stahl, K. Muether, Y. Ohki, K. Tatsumi and M. Oestreich, *J. Am. Chem. Soc.*, 2013, **135**, 10978; (c) C. D. F. Konigs, H. F. T. Klare, Y. Ohki, K. Tatsumi and M. Oestreich, *Org. Lett.*, 2012, **14**, 2842; (d) H. F. T. Klare, M. Oestreich, J.-i. Ito, H. Nishiyama, Y. Ohki and K. Tatsumi, *J. Am. Chem. Soc.*, 2011, **133**, 3312; (e) Y. Ohki, Y. Takikawa, H. Sadohara, C. Kesenheimer, B. Engendahl, E. Kapatina and K. Tatsumi, *Chem.-Asian J.*, 2008, **3**, 1625.
- C. D. F. Konigs, M. F. Mueller, N. Aiguabella, H. F. T. Klare and M. Oestreich, *Chem. Commun.*, 2013, **49**, 1506.
- For metal-free silylation of OH-groups, see: (a) D. J. Gao and C. M. Cui, *Chem.-Eur. J.*, 2013, **19**, 11143; (b) for metal-free silylation of P-P bonds, see: S. J. Geier and D. W. Stephan, *Chem. Commun.*, 2010, **46**, 1026.
- (a) L. Greb, S. Tussing, B. Schirmer, P. Oña-Burgos, K. Kaupmees, M. Lokov, I. Leito, S. Grimme and J. Paradies, *Chem. Sci.*, 2013, **4**, 2788; (b) L. Greb, P. Oña-Burgos, B. Schirmer, S. Grimme, D. W. Stephan and J. Paradies, *Angew. Chem., Int. Ed.*, 2012, **51**, 10164.
- (a) J. Hermeke, M. Mewald and M. Oestreich, *J. Am. Chem. Soc.*, 2013, **135**, 17537; (b) L. Greb, P. Oña-Burgos, A. Kubas, F. C. Falk, F. Breher, K. Fink and J. Paradies, *Dalton Trans.*, 2012, **40**, 9056; (c) W. E. Piers, A. J. V. Marwitz and L. G. Mercier, *Inorg. Chem.*, 2011, **50**, 12252; (d) A. Berkefeld, W. E. Piers and M. Parvez, *J. Am. Chem. Soc.*, 2010, **132**, 10660; (e) J. M. Blackwell, D. J. Morrison and W. E. Piers, *Tetrahedron*, 2002, **58**, 8247; (f) M. Rubin, T. Schwier and V. Gevorgyan, *J. Org. Chem.*, 2002, **67**, 1936; (g) D. J. Parks, J. M. Blackwell and W. E. Piers, *J. Org. Chem.*, 2000, **65**, 3090; (h) J. M. Blackwell, E. R. Sonmor, T. Scoccitti and W. E. Piers, *Org. Lett.*, 2000, **2**, 3921; (i) W. E. Piers and T. Chivers, *Chem. Soc. Rev.*, 1997, **26**, 345; (j) D. J. Parks and W. E. Piers, *J. Am. Chem. Soc.*, 1996, **118**, 9440.
- The elevated temperature of 60–70 °C was required to thermally cleave the aniline/B(C₆F₅)₃ adduct as evidenced by ¹¹B NMR.
- 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.
- For B(C₆F₅)₃-catalyzed 1,4-hydrosilylation of 2-phenyl quinoline, see: S. J. Geier, P. A. Chase and D. W. Stephan, *Chem. Commun.*, 2010, **46**, 4884.
- Determined by deprotection of **6v** and comparison of the ¹H NMR spectra of the resulting 1-*H* indoline with literature reported NMR data: F. O. Arp and G. C. Fu, *J. Am. Chem. Soc.*, 2006, **128**, 14264.
- Although the hydrogenation of *N*-methyl indoles is reported (10 mol% **2**, 103 bar H₂, 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 H₂) in the presence of 5 mol% **2** in toluene at 70 °C did not furnish indoline **6v**.