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TBAF-catalyzed hydrosilylation for the reduction of aromatic nitriles†

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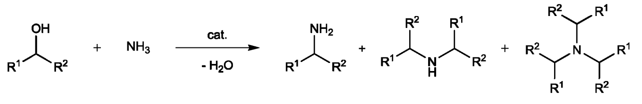
The selective catalytic hydrosilylation of functional groups is becoming an interesting tool for organic synthesis. In the present study, fluoride-catalyzed hydrosilylations of aromatic nitriles have been examined in detail. Using catalytic amounts of inexpensive tetra-*n*-butylammonium fluoride (TBAF) various aromatic nitriles are reduced in good yields under mild conditions.

Amines represent valuable intermediates for the fine and bulk chemical industries, agrochemicals, dyes as well as pharmaceuticals.[1] Among the various derivatives, primary amines are by far the synthetically most significant compounds.[2,3] The majority of industrially important primary amines are synthesized nowadays *via* amination of alcohols with ammonia or related reductive amination of carbonyl compounds (Scheme 1).[4] Despite large scale applications, there exists continuing interest in obtaining these products selectively under milder reaction conditions. Traditionally, on a laboratory scale primary amines have been prepared by the Gabriel synthesis[5] as well as reductive aminations.[6,7]

While the former reaction requires the use of phthalimides as protecting groups, in reductive aminations sometimes the formation of undesired secondary or tertiary amines cannot be avoided.[7,8] Notably, in the past decade other selective catalytic protocols using ammonia for primary amine synthesis such as hydroaminomethylations,[9,10] alcohol aminations,[11,12] and Buchwald–Hartwig aminations[13–15] have been developed.[16]

In addition to all these methodologies, the catalytic reduction of nitriles offers interesting access to primary amines. In general, nitriles are reduced with stoichiometric amounts of metal hydrides.[17] Advantageously, catalytic hydrogenation leads to lower amounts of waste products. However, to date only a few homogeneous catalysts are available for the reduction of nitriles to the corresponding primary amines.[18–22]

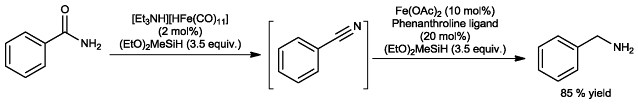


Scheme 1 Amination of alcohols with ammonia.

In particular, the catalytic hydrosilylation is a suitable tool for the selective reduction of nitriles.[23–26] It exhibits improved chemo- and regioselectivity under milder conditions compared to the conventionally used reducing agents.[27]

For the first time, Corriu *et al.*[28] reported transition metal catalyzed hydrosilylation of nitriles using Wilkinson's catalyst. In the past decades, different transition metals such as Re,[21] Ru[29] and Co[30] were found to activate the Si–H bond. Unfortunately, all these catalysts have drawbacks, for example high costs of the catalyst metals and in some cases a large excess of the hydrosilanes (up to 10 equiv.) is required. Recently, our group showed the first Fe-catalyzed hydrosilylation of nitriles, using a moderate excess of the hydrosilane (3.5 equiv.; Scheme 2).[24]

In addition to metal catalysis, a convenient approach is the use of fluoride ions as an activator for the hydrosilylation. Again, Corriu and co-workers were the first to report alkali fluoride salt mediated hydrosilylation of carbonyl compounds.[31] But since it requires stoichiometric amounts of the fluoride salt to sufficiently activate the hydrosilane, its utility was scarcely explored. The first fluoride-catalyzed hydrosilylation was performed by Fujita and Hiyama utilizing 2–5 mol% tetra-*n*-butylammonium fluoride (TBAF).[32] TBAF is a useful catalyst candidate since it offers a highly nucleophilic fluoride anion as an activator for the hydrosilylation. To date, fluoride activated hydrosilylations have been reported in the reduction of carbonyl derivatives like ketones,[32–37] aldehydes,[34,36,37] esters,[38] and rarely amides.[39]



Scheme 2 Iron-catalyzed hydrosilylation of benzamide.[24]

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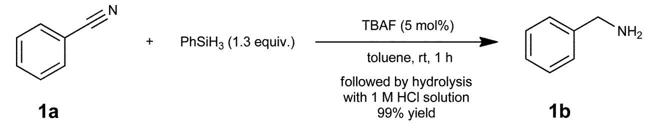


Scheme 3 TBAF-catalyzed hydrosilylation of benzonitrile.

In our ongoing research on the development of novel hydrosilylations, here we report the first convenient fluoride-catalyzed reduction of different nitriles to primary amines. More specifically, the combination of a catalytic amount of TBAF with $PhSiH_3$ (1.3 equiv.) gave rise to a highly active system which allows the hydrosilylation of C–N-triple bonds to proceed at room temperature.

Initially, we investigated the reaction of benzonitrile **1a** with hydrosilanes in toluene as a model system (Scheme 3). To gain insights into factors responsible for the formation of primary amines we studied the influence of different fluoride sources, hydrosilanes and solvents. Throughout these studies we found that the use of only 5 mol% of commercially available TBAF as a fluoride source gave the desired benzylamine **1b** within 60 minutes.

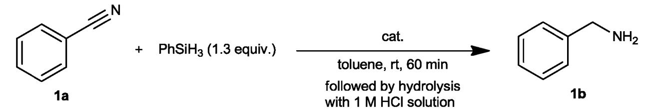
Using $PhSiH_3$, the primary amine was obtained exclusively without any formation of the undesired secondary amine. Notably, the small excess of $PhSiH_3$ used allows no quantitative bissilylation of the product. The resulting amine does not affect the selectivity of the reaction. Hence, we did not detect any secondary amine as a by-product.

The results illustrated in Table 1 show that the cheap and readily available fluoride source, TBAF, gave the best yield among the different explored fluoride catalysts (Table 1, entry 4). The obtained reactivity for the different fluoride sources (Table 1, entries 4 and 9–11) demonstrates nicely that the tetra-*n*-butylammonium (TBA) counter ion is essential for the catalytic reaction, since it offers a higher nucleophilicity to the fluoride. Furthermore, TBA is known to have an influence on the stabilisation of bulky penta-coordinated silicates[40] allowing a better fluoride exchange. The importance of fluoride is proved as no conversion is observed in the presence of the corresponding bromide (TBAB), chloride (TBAC) or hydrogen sulfate (TBAHS) as nucleophiles (Table 1, entries 6–8). In addition, iron(III)fluoride (Table 1, entry 9) gave no conversion within the observed reaction time. Afterwards, we explored the catalyst loading for the model reaction (Table 1, entries 2–5). We obtained the best yield using 5 mol% of the catalyst (Table 1, entry 4). Lowering the concentration gave worse conversion, while higher catalyst amounts led to unsatisfactory product yields, too (Table 1, entry 5). Apparently, selectivity is decreased using higher catalyst concentration, since secondary amines were detected in the reaction mixture (GC/MS). Among the different solvents investigated, toluene gave the best results. Other selected solvents led to rather low conversion and yield (Table 1, entries 12–15).

From the results of the hydrosilane screening (Table 2) it appears that di- and polymeric siloxanes are not useful to achieve appropriate conversions (Table 2, entries 4, 5, 14 and 15). The best yields were obtained with the initially used phenylsilane (Table 2, entries 8–12), which is known to be one of the most reactive hydrosilanes. Exhibiting only one phenyl residue the silicon atom lacks stabilisation possibilities and therefore allows a fast reaction using only a slight excess of the hydrosilane.

Next, we optimized the model reaction by varying the phenylsilane equivalents (Table 2, entries 8–12). Best results

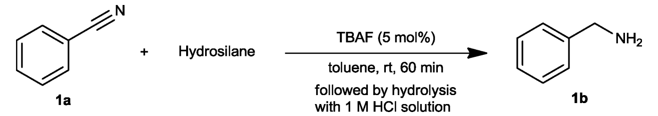
Table 1 Fluoride-catalyzed reduction of benzonitrile[a]



Entry	Catalyst	Mol%-catalyst	Conversion[b,c] [%]	Yield[b] [%]
1	/	/	0	0
2	TBAF	1	52	30
3	TBAF	3	91	54
4	*TBAF*	*5*	*99*	*99*
5	TBAF	10	100	55
6	TBAB	5	0	0
7	TBAHS	5	0	0
8	TBAC	5	0	0
9	FeF_3	5	0	0
10	NaF	5	4	0
11	CsF	5	3	0
12	TBAF	5	5 (DCM)	1
13	TBAF	5	78 (THF)	44
14	TBAF	5	60 (NMP)	23
15	TBAF	5	70 (DMSO)	45

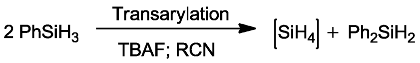
[a] Reaction conditions: (i) **1a** (1.0 mmol), catalyst (1–10 mol%), phenylsilane (1.3 equiv.) in toluene (2 mL) at rt for 60 min. (ii) The reaction mixture is then quenched with 1 M HCl solution for 90 min. [b] Determined by GC with hexadecane as an internal standard. [c] Solvent in brackets where no toluene was used.

Table 2 Reduction of benzonitrile using different hydrosilanes[a]



Entry	Hydrosilane	Hydrosilane [equiv.]	Conversion[b] [%]	Yield[b] [%]
1	$(EtO)_3SiH$	3	66	50
2	Et_3SiH	3	9	0
3	$(EtO)_2MeSiH$	3	58	23
4	Pentamethyldisiloxane	3	10	4
5	Tetramethyldisiloxane	3	0	0
6	$MePh_2SiH$	3	5	2
7	Me_2PhSiH	3	0	0
8	$PhSiH_3$	1.1	91	86
9	$PhSiH_3$	1.2	96	83
10	*$PhSiH_3$*	*1.3*	*99*	*99*
11	$PhSiH_3$	1.4	99	99
12	$PhSiH_3$	1.5	100	92
13	Ph_2SiH_2	2	60	22
14	PMHS	5	25	0
15	Bis(trimethylsiloxy)-methylsilane	3	40	0

[a] Reaction conditions: (i) **1a** (1.0 mmol), TBAF (5 mol%), hydrosilane (1.1–5 equiv.) in toluene (2 mL) at rt for 60 min. (ii) The reaction mixture is then quenched with 1 M HCl solution for 90 min. [b] Determined by GC with hexadecane as an internal standard.



Scheme 4 Transarylation of phenylsilane.

were obtained with an excess of 1.3 to 1.4 equivalents (Table 2, entries 10 and 11). A larger excess of the hydrosilane again led to lower yields since side reactions occur.

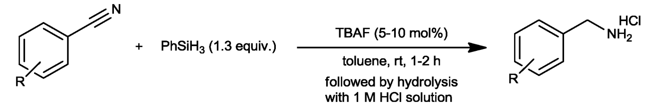
Interestingly, more than one hydride equivalent is derived from one molecule of phenylsilane. In order to investigate this effect, we performed ^{29}Si NMR spectroscopic studies after the hydrolysis of a typical reaction mixture. Besides Si–O species resulting from hydrolysis, no phenylsilane was detected. Instead, to our surprise diphenylsilane was identified as a side product in this reaction. Additional experiments proved that the presence of fluoride, nitrile and the counter ion is necessary for this unusual transarylation of the phenyl group from $PhSiH_3$ (Scheme 4). We assume that penta-coordinated $[FSiR_3H]^-$ (R = Ph, H, N) intermediates offer the additional hydrides for the quantitative reduction of the different nitrile substrates. Notably, the nitrile moiety plays a significant role in this odd transformation, since there is no transarylation observed in the presence of TBAF alone (GC/MS analysis). To the best of our knowledge reported transarylations between silanes do not proceed under such mild conditions.[41]

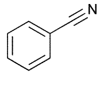
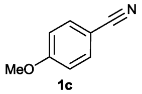
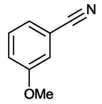
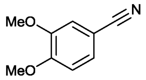
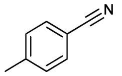
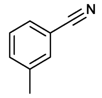
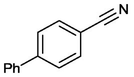
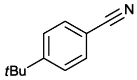
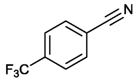
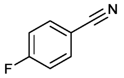
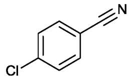
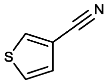
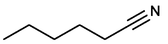
It is well known that SiH_4 is a dangerous gas, which ignites when it is exposed to air. Thus, we carefully investigated the limitations of this formation. Exposing a 20 mmol-scale reaction after one hour to air led to no ignition of the reaction mixture.

Using our optimized conditions we studied the scope and limitations of the TBAF-catalyzed hydrosilylation of nitriles. For this purpose various aromatic, heteroaromatic and aliphatic nitriles were examined (Table 3).

In general, aromatic substrates with several electron-donating substituents were found to be hydrosilylated in good isolated yields at room temperature (67–80%; Table 3, entries 2–6). However, *ortho*-substituted substrates showed no reactivity. The steric demand of the *ortho*-substituents seems to hinder the addition of the active silane species. 3,4-Dimethoxy-benzylamine (Table 3, entry 4) was obtained in better yields at 60 °C (70%) compared to the reaction at room temperature (40%). At higher temperature (110 °C) with this substrate as well as other aromatic nitriles the reaction gave no conversion. Apart from electron-rich benzonitriles, some electron-deficient substituents were also tolerated (Table 3, entries 9–11). Unfortunately, testing heterocyclic nitriles (3-thiophenecarbonitrile or picolinonitrile) as well as hexanenitrile did not show any reactivity under the described conditions. It is important to note that in cases where no conversion of the substrate was observed ignition of the gas phase can occur after exposing the reaction mixture to air.‡

Table 3 Scope and limitations[a]



Entry	Substrate	Time [h]	Isolated yield [%]
1	 **1a**	1	95
2	 **1c**	1.5	80
3	 **1d**	1.5	79[b]
4	 **1e**	1.5	70[c]
5	 **1f**	2	67
6	 **1g**	1.5	73
7	 **1h**	2	76[b]
8	 **1i**	2	73
9	 **1j**	2	62[b]
10	 **1k**	2	79
11	 **1l**	2	81[b]
12		2	0
13		1	0

[a] Reaction conditions (i) nitrile (1.0 mmol), TBAF (5–10 mol%), phenylsilane (1.3 equiv.) in toluene (2 mL) at rt for 1–2 h. (ii) The reaction mixture is then quenched with 1 M HCl solution for 90 min. [b] Second catalyst addition (5 mol%) after half of the reaction time. [c] Reaction at 60 °C.

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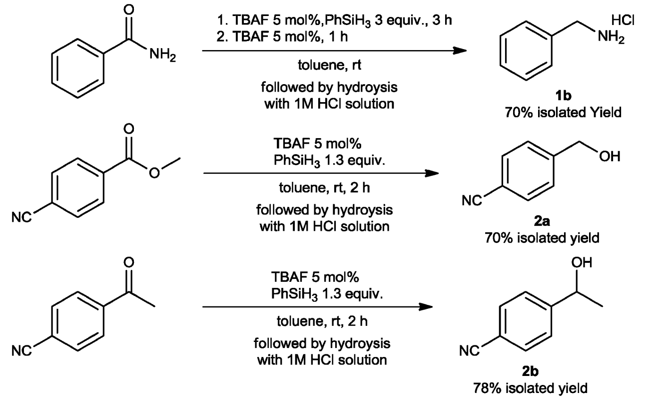
‡ In the reaction of hexanenitrile ignition of the gas phase was observed after exposing the reaction mixture to air. We assume the formation of significant amounts of SiH_4 to be responsible for this effect.



Scheme 5 Selective hydrosilylation of different carbonyl groups.

Adding a second amount of catalyst improved product yields and conversion (Table 3, entries 3, 7, 9 and 11). While exploring different functional groups, we discovered that our methodology is also a useful tool for selective reduction of esters (70% isolated yield) and ketones (79% isolated yield) in the presence of a nitrile moiety (Scheme 5). This is possible since these carbonyl groups are more reactive compared to the C–N triple bond.

Additionally, we found that benzamide can be reduced to yield the primary amine easily with only adding the catalyst twice during the reaction time (Scheme 5). Since we optimized the reaction conditions for the hydrosilylation of nitriles, the obtained yields for the reduction of different functional groups are not optimized and further variations might offer increased yields.

In summary, we presented the first metal-free hydrosilylation of aromatic nitriles to the corresponding primary amines. The procedure makes use of simple TBAF as a commercially available catalyst and phenylsilane as a hydride source. Interestingly, under very mild reaction conditions a rare transarylation of the phenylsilane occurs. In addition, this protocol can be applied for the reduction of different carbonyl moieties (amides, esters, ketones), too.

Notes and references

1 H. A. Wittcoff, B. G. Reuben and J. S. Plotkin, in *Industrial Organic Chemicals*, John Wiley & Sons, Inc., 2005, pp. 15–56.

2 H. Zollinger, *Color Chemistry: Syntheses, Properties, and Applications of Organic Dyes and Pigments*, WILEY-VCH GmbH & Co. KGaA, Weinheim, 3rd revised edn, 2003.

3 K. Weissermel and H.-J. Arpe, *Industrial Organic Chemistry*, WILEY-VCH Verlag & Co. KGaA, Weinheim, 2003.

4 S. A. Lawrence, *Amines: Synthesis. Properties and Applications*, Cambridge University, Cambridge, 2004.

5 M. S. Gibson and R. W. Bradshaw, *Angew. Chem., Int. Ed.*, 1968, **7**, 919–930.

6 E. M. Dangerfield, C. H. Plunkett, A. L. Win-Mason, B. L. Stocker and M. S. M. Timmer, *J. Org. Chem.*, 2010, **75**, 5470–5477.

7 S. Gomez, J. A. Peters and T. Maschmeyer, *Adv. Synth. Catal.*, 2002, **344**, 1037–1057.

8 J. Bódis, L. Lefferts, T. Müller, R. Pestman and J. Lercher, *Catal. Lett.*, 2005, **104**, 23–28.

9 B. Zimmermann, J. Herwig and M. Beller, *Angew. Chem., Int. Ed.*, 1999, **111**, 2515–2518.

10 H. Klein, R. Jackstell, M. Kant, A. Martin and M. Beller, *Chem. Eng. Technol.*, 2007, **30**, 721–725.

11 C. Gunanathan and D. Milstein, *Angew. Chem., Int. Ed.*, 2008, **47**, 8661–8664.

12 D. Pingen, C. Müller and D. Vogt, *Angew. Chem., Int. Ed.*, 2010, **122**, 8307–8310.

13 Q. Shen and J. F. Hartwig, *J. Am. Chem. Soc.*, 2006, **128**, 10028–10029.

14 D. S. Surry and S. L. Buchwald, *J. Am. Chem. Soc.*, 2007, **129**, 10354–10355.

15 R. J. Lundgren, B. D. Peters, P. G. Alsabeh and M. Stradiotto, *Angew. Chem., Int. Ed.*, 2010, **49**, 4071–4074.

16 J. L. Klinkenberg and J. F. Hartwig, *Angew. Chem., Int. Ed.*, 2011, **50**, 86–95.

17 J. Seyden-Penne, *Reductions by Alumino and Borohydrides in Organic Synthesis*, Wiley-VCH, New York, 2nd edn, 1997.

18 C. Gunanathan, M. Hölscher and W. Leitner, *Eur. J. Inorg. Chem.*, 2011, 3381–3386.

19 S. Enthaler, D. Addis, K. Junge, G. Erre and M. Beller, *Chem.–Eur. J.*, 2008, **14**, 9491–9494.

20 D. Addis, S. Enthaler, K. Junge, B. Wendt and M. Beller, *Tetrahedron Lett.*, 2009, **50**, 3654–3656.

21 I. Cabrita and A. C. Fernandes, *Tetrahedron*, 2011, **67**, 8183–8186.

22 R. Reguillo, M. Grellier, N. Vautravers, L. Vendier and S. Sabo-Etienne, *J. Am. Chem. Soc.*, 2010, **132**, 7854–7855.

23 S. Das, S. Zhou, D. Addis, S. Enthaler, K. Junge and M. Beller, *Top. Catal.*, 2010, **53**, 979–984.

24 S. Das, B. Wendt, K. Möller, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2012, **51**, 1662–1666.

25 S. Laval, W. Dayoub, A. Favre-Reguillon, M. Berthod, P. Demonchaux, G. Mignani and M. Lemaire, *Tetrahedron Lett.*, 2009, **50**, 7005–7007.

26 A. M. Caporusso, N. Panziera, P. Pertici, E. Pitzalis, P. Salvadori, G. Vitulli and G. Martra, *J. Mol. Catal. A: Chem.*, 1999, **150**, 275–285.

27 D. Addis, S. Das, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2011, **50**, 6004–6011.

28 R. J. P. Corriu, J. J. E. Moreau and M. Pataud-Sat, *J. Organomet. Chem.*, 1982, **228**, 301–308.

29 D. V. Gutsulyak and G. I. Nikonov, *Angew. Chem., Int. Ed.*, 2010, **49**, 7553–7556.

30 T. Murai, T. Sakane and S. Kato, *J. Org. Chem.*, 1990, **55**, 449–453.

31 J. Boyer, R. J. P. Corriu, R. Perz and C. Reye, *Tetrahedron*, 1981, **37**, 2165–2171.

32 M. Fujita and T. Hiyama, *J. Am. Chem. Soc.*, 1984, **106**, 4629–4630.

33 D. Yang and D. D. Tanner, *J. Org. Chem.*, 1986, **51**, 2267–2270.

34 M. Fujita and T. Hiyama, *J. Org. Chem.*, 1988, **53**, 5405–5415.

35 M. D. Drew, N. J. Lawrence, W. Watson and S. A. Bowles, *Tetrahedron Lett.*, 1997, **38**, 5857–5860.

36 Y. Goldberg, K. Rubina, M. Shymanska and E. Lukevics, *Synth. Commun.*, 1990, **20**, 2439–2446.

37 Y. Goldberg, E. AbĀbele, M. Shymanska and E. Lukevics, *J. Organomet. Chem.*, 1989, **372**, C9–C11.

38 J. Boyer, R. J. P. Corriu, R. Perz, M. Poirier and C. Reye, *Synthesis*, 1981, 558–559.

39 S. Zhou, K. Junge, D. Addis, S. Das and M. Beller, *Org. Lett.*, 2009, **11**, 2461–2464.

40 S. Deerenberg, M. Schakel, A. H. J. F. d. Keijzer, M. Kranenburg, M. Lutz, A. L. Spek and K. Lammertsma, *Chem. Commun.*, 2002, 348–349.

41 A. Schäfer, M. Reißmann, A. Schäfer, W. Saak, D. Haase and T. Müller, *Angew. Chem., Int. Ed.*, 2011, **123**, 12845–12848.