Iron-catalyzed selective reduction of nitroarenes to anilines using organosilanes

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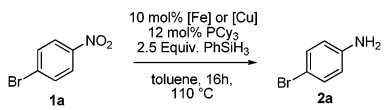
The iron-catalyzed reduction of aromatic nitro compounds to the corresponding anilines applying organosilanes is reported. In the presence of FeX_2–R_3P catalysts a series of nitroarenes is selectively reduced tolerating a wide range of functional groups.

Nitroarenes constitute central building blocks in organic synthesis.[1] Both in industry and academic laboratories, their reduction serves as an important method for the preparation of functionalized anilines, which are intermediates for agrochemicals, pharmaceuticals, dyes, and pigments.[2] Traditional non-catalytic processes using either Béchamp or sulfide reduction produce a large amount of waste.[3] Nowadays, in general recyclable heterogeneous catalysts are used for the catalytic hydrogenation of aromatic nitro compounds to anilines.[4] In addition to hydrogen, other reducing agents have been used for the preparation of anilines.[5] Obviously, hydrogenation of a variety of nitroarenes is well established applying commercially available heterogeneous catalysts. However, sometimes selectivity problems occur and the formation of (toxic) by-products or impurities is known.[6] Due to the easier tuning and milder reaction conditions homogeneous reduction of nitro compounds involving catalytic hydrogenation,[5,7] transfer hydrogenation,[8] and hydrosilylation has also been studied to some extent. In order to avoid the necessity to use autoclaves and/or to handle hydrogen, hydrosilylation offers an attractive alternative. However, with respect to nitro reduction this methodology has been largely ignored. Until now, only a handful of reports for the nitroarene reduction to amines with silanes has been published focussing on Pd,[9a,e–h] Pt,[9b] Rh,[9b,c] Sn,[9d] and Re catalysts.[9i] Due to the importance of selective reduction of aromatic nitro compounds, the search for improved chemoselective methods remains an actual goal. With respect to catalyst development iron-based complexes are more and more in the limelight of catalytic applications.[10] Due to their abundant availability, most iron compounds are inexpensive. Often they can be considered as biomimetic and some of them represent less-toxic alternatives to palladium, rhodium or ruthenium catalysts.

While iron-mediated hydrosilylations of carbonyl compounds have been investigated intensively,[11] to the best of our knowledge only very recently Nagashima and co-workers observed the reduction of the nitro moiety of a carboxamide with $[Fe_3(CO)_{12}]$ and TMDS.[12] Based on our background in iron-catalyzed reductions we became interested in the development of a hydrosilylation protocol for nitroarenes.[13] Herein, we present the first general method of this type. Preliminary experiments were carried out with *p*-nitrobromobenzene as model substrate using different iron(II) and iron(III) precursors, several phosphines, and different silanes in toluene (Tables 1–3). Obviously, no appreciable reaction takes place without catalyst (Table 1, entry 20) or silane (Table 1, entry 18), while in the presence of 10 mol% of simple iron(II) halides excellent yields (95–98%) of *p*-bromoaniline are detected (Table 1, entries 3 and 4). Applying $Fe(OAc)_2$, $Fe(acac)_2$, Fe(II)stearate, $[Fe(CO)_5]$, $FeCl_3{\cdot}6H_2O$, or $Fe(ClO_4)_3{\cdot}xH_2O$ the product is also formed but in lower yields (Table 1, entries 5, 7–9, 15 and 17).

In the absence of the phosphine, the reactivity is reduced significantly (Table 1, entry 19). To exclude the possibility of active copper traces as contaminants of iron salts in the hydrosilylation reaction, CuBr and CuI were tested directly as catalyst showing no significant conversion (Table 1, entries 21 and 22).[14] Next, we investigated the influence of different

Table 1 Applying different Fe and Cu precursors for the hydrosilylation of *p*-nitrobromobenzene[a]



1a 2a

Entry	Precursor	PR_3	Silane	Yield (%)
1	FeF_2	PCy_3	$PhSiH_3$	3
2	$FeCl_2$	PCy_3	$PhSiH_3$	47
3	$FeBr_2$	PCy_3	$PhSiH_3$	**95**
4	FeI_2	PCy_3	$PhSiH_3$	**98**
5	$Fe(OAc)_2$	PCy_3	$PhSiH_3$	79
6	$FeSO_4{\cdot}7H_2O$	PCy_3	$PhSiH_3$	4
7	$Fe(acac)_2$	PCy_3	$PhSiH_3$	59
8	Fe(II)stearate	PCy_3	$PhSiH_3$	66
9	$[Fe(CO)_5]$	PCy_3	$PhSiH_3$	68
10	Fe(III)citrate	PCy_3	$PhSiH_3$	4
11	Fe_2O_3	PCy_3	$PhSiH_3$	2.5
12	Fe_3O_4	PCy_3	$PhSiH_3$	3
13	$Fe(NO_3)_3{\cdot}9H_2O$	PCy_3	$PhSiH_3$	46
14	$Fe(BF_4)_3$	PCy_3	$PhSiH_3$	19
15	$FeCl_3{\cdot}6H_2O$	PCy_3	$PhSiH_3$	67
16	$FePO_4{\cdot}4H_2O$	PCy_3	$PhSiH_3$	2
17	$Fe(ClO_4)_3{\cdot}xH_2O$	PCy_3	$PhSiH_3$	88
18[b]	$FeBr_2$	PCy_3	—	6
19[c]	$FeBr_2$	—	$PhSiH_3$	25
20[d]	—	PCy_3	$PhSiH_3$	5
21	CuBr	PCy_3	$PhSiH_3$	6
22	CuI	PCy_3	$PhSiH_3$	5

[a] Reaction conditions: 1 mmol *p*-nitrobromobenzene, 0.1 mmol Fe or Cu precursor, 0.12 mmol PCy_3, 2.5 equiv. $PhSiH_3$, 1.5 mL toluene, 110 °C, 16 h. [b] Without $PhSiH_3$. [c] Without PCy_3. [d] Without $FeBr_2$.

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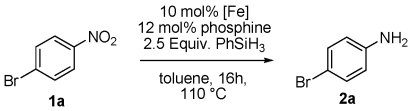
Table 2 Hydrosilylation of *p*-nitrobromobenzene: influence of different phosphines[a]



Entry	Precursor	PR_3	Yield (%)
1	$FeBr_2$	PPh_3	**99**
2	FeI_2	PPh_3	30
3	$FeBr_2$	PCy_3	95
4	$FeBr_2$	$(4\text{-MeO-Ph})_3P$	**99**
5	$FeBr_2$	$(4\text{-Me-Ph})_3P$	97
6	$FeBr_2$	$(4\text{-F-Ph})_3P$	90
7	$FeBr_2$	$(Bn)_3P$	10
8	$FeBr_2$	$n\text{BuPAd}_2$	97
9	$FeBr_2$	$MePPh_2$	**99**
10	$FeBr_2$	dppethene	20
11	$FeBr_2$	dppe	28
12	$FeBr_2$	dppb	84
13	$FeBr_2$	dpph	80
14	$FeBr_2$	dppf	14

[a] Reaction conditions: 1 mmol *p*-nitrobromobenzene, 0.1 mmol FeX_2, 0.12 mmol phosphine, 2.5 equiv. $PhSiH_3$, 1.5 mL toluene, 110 °C, 16 h.

phosphine ligands on the reduction of the model substrate. We were pleased to find a quantitative yield of *p*-bromoaniline by using a convenient *in situ* catalyst consisting of $FeBr_2$ and PPh_3 or other arylphosphines (Table 2, entries 1, 4 and 9). While most of the monodentate phosphines bearing aromatic or bulky substituents are highly reactive giving product yields above 90%, chelating phosphines reduce the reaction rate (Table 2, entries 10–14).

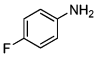
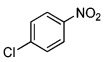
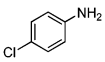
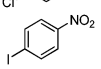
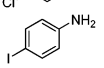
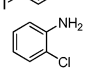
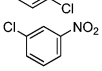
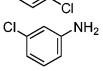
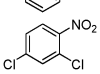
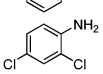
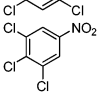
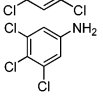
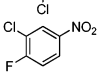
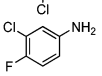
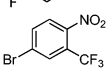
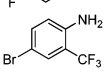
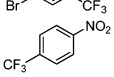
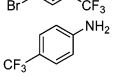
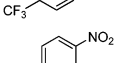
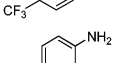
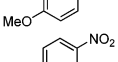
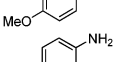
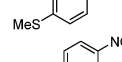
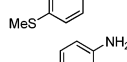
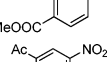
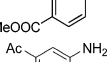
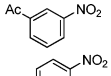
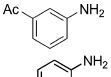
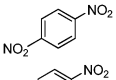
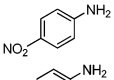
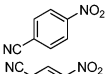
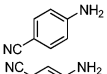
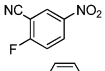
The reduction of *p*-nitrobromobenzene was also studied in the presence of different arylsilanes, polymethylhydrosiloxane (PMHS), trichlorosilane, and alkoxysilanes. Nevertheless, phenylsilane remains the reagent of choice leading to quantitative yield (Table 3, entry 1). While alkoxysilanes showed similar reactivity (60–66% yield), aryl- or alkylsilanes containing only one Si–H group gave poorer results. Finally, we were interested in the functional group tolerance of our protocol. Hence, 26 different nitro-substituted arenes and heteroarenes were reacted under the previously optimized reaction conditions ($FeBr_2$, Ph_3P, 2.5 equivalents of $PhSiH_3$ in toluene at 110 °C). The results are summarized in Table 4.[15]

Table 3 Hydrosilylation of *p*-nitrobromobenzene: influence of different silanes[a]

Entry	Silane	Yield (%)
1	$PhSiH_3$	**99**
2[b]	$PhSiH_3$	78
3	Ph_2SiH_2	48
4	Me_2PhSiH	8
5	Et_3SiH	9
6	Cl_3SiH	5
7	PMHS	31
8	$(EtO)_3SiH$	66
9	$Me(EtO)_2SiH$	64
10	$(MeO)_3SiH$	60

[a] Reaction conditions: 1 mmol *p*-nitrobromobenzene, 0.1 mmol $FeBr_2$, 0.12 mmol PPh_3, 2.5 equiv. silane, 1.5 mL toluene, 110 °C, 16 h. [b] Up scaling by factor 5 and isolated yield is given.

Table 4 $FeBr_2$-catalyzed hydrosilylation of nitroarenes to anilines[a]

Entry	Substrate	Amine	Yield (%)
1			85
2			89
3[b]			42
4			99
5[b]			96
6			94
7			91
8			93
9			84
10			99
11			99
12			72
13			99 71[e]
14			50
15[b]			99
16			84
17[b,c]			83
18			59 58[e]
19			82
20			77
21[b]			25
22			61
23			80
24			76
25[d]			40
26[d]			85

[a] Reaction conditions: 1 mmol nitroarene, 0.1 mmol $FeBr_2$, 0.12 mmol PPh_3, 2.5 equiv. $PhSiH_3$, 1.5 mL toluene, 110 °C, 16 h. [b] Working up procedure without MeOH. [c] 2–3% of the diamine were detected. [d] 1% of C=C hydrogenation was detected. [e] Up scaling by factor 5 and isolated yields are given.

Non-substituted nitrobenzene and -toluene are effectively reduced in 85–89% yield (Table 4, entries 1 and 2). Except for fluorine substituents, high yields of the corresponding anilines are achieved in the presence of halide substituents irrespective of their ring position (Table 4, entries 3–11). Even 3,4,5-trichoro-nitrobenzene produced selectively the respective aniline in 84% yield (Table 4, entry 9). In none of these cases significant amounts (>2%) of dehalogenation have been observed. Notably, other reducible functional groups such as cyano, nitro, ester groups as well as C=C double bonds are not affected under these conditions. The reduction of 1,4-dinitrobenzene proceeds chemoselectively affording 83% of 4-nitroaniline (Table 4, entry 17). The reduction of cyano-substituted nitrobenzenes, which are important transformations in organic chemistry, gave 56–82% of cyanoanilines (Table 4, entries 18 and 19). To our delight the nitro group is highly chemoselectively reduced in ethyl *p*-nitrocinnamate and *p*-nitrostilbene (Table 4, entries 25 and 26). However, no aniline was formed in the hydrosilylation of 3-nitrostyrene and 4-nitrophenylacetate.

In summary, a new inexpensive and convenient iron-based catalytic system consisting of $FeBr_2$–Ph_3P has been discovered for the reduction of nitroarenes with organosilanes. The procedure is general and the selectivity of the catalyst has been demonstrated applying challenging substrates with C=O, C≡N, C=C, and OH groups.

Notes and references

1 N. Ono, *The Nitro Group in Organic Synthesis*, Wiley-VCH, New York, 2001.

2 (*a*) H. U. Blaser, A. Baiker and R. Prins, in *Heterogeneous Catalysis and Fine Chemicals*, ed. H. U. Blaser, E. Schmidt, Elsevier, Amsterdam, 1997, vol. IV, pp. 17–30; (*b*) R. S. Downing, P. J. Kunkeler and H. van Bekkum, *Catal. Today*, 1997, **37**, 121–136; (*c*) G. Wegener, M. Brandt, L. Duda, J. Hofmann, B. Klesczewski, D. Koch, R. Kumpf, H. Orzesek, H. Pirkl, C. Six, C. Steinlein and M. Weisbeck, *Appl. Catal., A*, 2001, **221**, 303–335.

3 H. U. Blaser, U. Siegrist and M. Studer, in *Fine Chemicals Through Heterogeneous Catalysis*, ed. R. A. Sheldon, H. van Bekkum, Wiley-VCH, Weinheim, 2001, p. 389.

4 For an excellent review on recent advances on heterogeneous hydrogenation of functionalized nitroarenes see: H. U. Blaser, H. Steiner and M. Studer, *ChemCatChem*, 2009, **1**, 210–221.

5 P. Rylander, in *Catalytic Hydrogenation in Organic Synthesis*, ed. P. Rylander, Academic Press, New York, 1979, pp. 113–137.

6 (*a*) P. Baumeister, H. U. Blaser and M. Studer, *Catal. Lett.*, 1997, **49**, 219–222; (*b*) H. U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner and M. Studer, *Adv. Synth. Catal.*, 2003, **345**, 103–151.

7 (*a*) J. F. Knifton, *J. Org. Chem.*, 1976, **41**, 1200–1206; (*b*) S. G. Harsy, *Tetrahedron*, 1990, **46**, 7403–7412; (*c*) P. M. Reis and B. Royo, *Tetrahedron Lett.*, 2009, **50**, 949–952; (*d*) A. Corma, C. González-Arellano, M. Iglesias and F. Sánchez, *Appl. Catal., A*, 2009, **356**, 99–102.

8 (*a*) H. Imai, T. Nishiguchi and K. Fukuzumi, *Chem. Lett.*, 1976, 655–656; (*b*) Y. Watanabe, T. Ohta, Y. Tsuji, T. Hiyoshi and Y. Tsuji, *Bull. Chem. Soc. Jpn.*, 1984, **57**, 2440–2444; (*c*) A. B. Taleb and G. Jenner, *J. Mol. Catal.*, 1994, **91**, L149–L153.

9 (*a*) J. Lipowitz and S. A. Bowman, *J. Org. Chem.*, 1973, **38**, 162–165; (*b*) K. A. Andrianov, V. I. Sidorov and M. I. Filimonova, *Zh. Obshch. Khim.*, 1977, **47**, 485; (*c*) H. R. Brinkman, W. H. Miles, M. D. Hilborn and M. C. Smith, *Synth. Commun.*, 1996, **26**, 973–980; (*d*) J. Tormo, D. S. Hays and G. C. Fu, *J. Org. Chem.*, 1998, **63**, 5296–5297; (*e*) I. Jovel, L. Golomba, M. Fleisher, J. Popelis, S. Grinberga and E. Lukevics, *Chem. Heterocycl. Compounds*, 2004, **40**, 701–714; (*f*) R. J. Rahaim, Jr. and R. E. Maleczka, Jr., *Org. Lett.*, 2005, **7**, 5087–5090; (*g*) R. J. Rahaim, Jr. and R. E. Maleczka, Jr., *Synthesis*, 2006, 3316–3340; (*h*) S. Srinivasan and X. Huang, *Chirality*, 2008, **20**, 265–277; (*i*) R. G. de Noronha, C. C. Romão and A. C. Fernandes, *J. Org. Chem.*, 2009, **74**, 6960–6964.

10 (*a*) *Iron Catalysis in Organic Chemistry*, ed. B. Plietker, Wiley-VCH, Weinheim, 1st edn., 2008; (*b*) S. Enthaler, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2008, **47**, 3317–3321; (*c*) S. Gaillard and J.-L. Renaud, *ChemSusChem*, 2008, **1**, 505–509.

11 (*a*) H. Brunner, R. Eder, B. Hammer and U. Klement, *J. Organomet. Chem.*, 1990, **394**, 555–567; (*b*) H. Nishiyama and A. Furuta, *Chem. Commun.*, 2007, 760–762; (*c*) H. Nishiyama and A. Furuta, *Tetrahedron Lett.*, 2008, **49**, 110–113; (*d*) D. V. Gutsulyak, L. G. Kuzmina, J. A. K. Howard, S. F. Vyboishchikov and G. I. Nikonov, *J. Am. Chem. Soc.*, 2008, **130**, 3732–3733; (*e*) B. K. Langlotz, H. Wadepohl and L. H. Gade, *Angew. Chem., Int. Ed.*, 2008, **47**, 4670–4674; (*f*) A. M. Tondreau, E. Lobkovsky and P. J. Chirik, *Org. Lett.*, 2008, **10**, 2789–2792; (*g*) C. Dal Zotto, D. Virieux and J.-M. Campagne, *Synlett*, 2009, 276–278; (*h*) A. M. Tondreau, J. M. Darmon, B. M. Wile, S. K. Floyd, E. Lobkovsky and P. J. Chirik, *Organometallics*, 2009, **28**, 3928–3940.

12 Y. Sunada, H. Kawakami, T. Imaika, Y. Motoyama and H. Nagashima, *Angew. Chem.*, 2009, **121**, 9675–9678.

13 (*a*) S. Enthaler, B. Hagemann, G. Erre, K. Junge and M. Beller, *Chem.–Asian J.*, 2006, **1**, 598–604; (*b*) S. Enthaler, G. Erre, M. K. Tse, K. Junge and M. Beller, *Tetrahedron Lett.*, 2006, **47**, 8095–8099; (*c*) N. Shaikh, K. Junge and M. Beller, *Org. Lett.*, 2007, **9**, 5429–5432; (*d*) S. Enthaler, B. Spilker, G. Erre, K. Junge, M. K. Tse and M. Beller, *Tetrahedron*, 2008, **64**, 3867–3876; (*e*) N. Shaikh, K. Junge, S. Enthaler and M. Beller, *Angew. Chem., Int. Ed.*, 2008, **47**, 2497–2501; (*f*) S. L. Zhou, D. Addis, K. Junge, S. Das and M. Beller, *Chem. Commun.*, 2009, 4883–4885; (*g*) S. L. Zhou, K. Junge, D. Addis, S. Das and M. Beller, *Org. Lett.*, 2009, **11**, 2461–2464; (*h*) S. Zhou, K. Junge, D. Addis, S. Das and M. Beller, *Angew. Chem., Int. Ed.*, 2009, **48**, 9507–9510.

14 (*a*) S. L. Buchwald and C. Bolm, *Angew. Chem.*, 2009, **121**, 5694–5695; (*b*) P.-F. Larsson, A. Correa, M. Carril, P.-O. Norrby and C. Bolm, *Angew. Chem.*, 2009, **121**, 5801–5803.

15 General procedure for the hydrosilylation of nitroarenes: 0.12 mmol (31.5 mg) PPh_3, 0.1 mmol (21.6 mg) $FeBr_2$, and 1 mmol of the corresponding nitroarene are mixed in a pressure tube and flashed three times with vacuum and argon. Then, 2.5 mmol $PhSiH_3$ (308 μL) and 1.5 mL dry toluene are added. The mixture is stirred for 16 hours in a preheated oil bath at 110 °C. After cooling the pressure tube to room temperature diglyme or hexadecane are added as internal standard and the mixture is diluted with 4 mL THF. The reactionis quenched with 2 mL NaOH (2 N) and stirred for 30 minutes. By adding 4 mL MeOH the two phases were homogenized. The yield was determined by GC (HP5: 50-8-260/5-8-280/5-8-300). All amines are analyzed by GC–MS and identified by comparison with authentic primary amines. The reaction was scaled up by factor 5 for three substrates. The corresponding amines were isolated and purified by column chromatography (pentane–ethyl acetate = 5 : 1 → 2 : 1).