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A mild and convenient reduction of nitro compounds with $NaBH_4/SbF_3$ system in wet CH_3CN

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$NaBH_4$ in the presence of catalytic amounts of SbF_3 reduces a range of nitro compounds to their corresponding amines in high to excellent yields. Reduction reactions were carried out in wet CH_3CN within 2–30 minutes at room temperature.

Keywords: reduction, $NaBH_4$, SbF_3, nitro compounds

During the past decades, $NaBH_4$ has brought about revolutionary changes in the reduction of organo-functional groups in modern organic synthesis.[1] It is a relatively mild reducing agent and frequently used for the reduction of carbonyl compounds in protic solvents. Literature review shows that reduction of nitro compounds to their amines, a key synthetic transformation in organic synthesis has not been accomplished with sodium borohydride alone under ordinary conditions. However, the reducing power of $NaBH_4$ or its polymeric analogue (BER) undergoes a drastic change towards this transformation by the combination with transition metal and, rarely, main metal salts (halides). $NaBH_4/CoCl_2$,[2] $NaBH_4/FeCl_2$,[3] $NaBH_4/SnCl_2$,[4] $NaBH_4/CuSO_4$,[5] $NaBH_4/Pd/C$,[6] $NaBH_4/CuCl_2$,[7] $NaBH_4/TiCl_4$,[8] $NaBH_4/Cu(acac)_2$,[9] $NaBH_4/Me_3SiCl$,[10] $NaBH_4/NiCl_2$,[11] $NaBH_4/Ni(OAc)_2$[12a] and $BER/Ni(OAc)_2$[12b] are some of the systems which have been reported for the reduction of aliphatic or aromatic nitro compounds.

It was reported that by the combination of transition metal salts or halides with $NaBH_4$ in protic or aqueous solvent systems,[2,11-13] the formation of boride actively catalyses the decomposition of borohydride with the generation of H_2 gas and in conjunction with the hydride attack reduces nitro compounds to their corresponding amines. Literature survey shows that the boride-reduction of nitro compounds by the combination of main metal halides with $NaBH_4$ has been rarely investigated. Ren *et al.* reported that an ethanolic solution of $NaBH_4$ in the presence of molar equivalents of $BiCl_3$ or $SbCl_3$ through the boride formation reduces nitroarenes to their amines at room temperature.[14] Although the method was efficient for the reduction of nitro compounds, using the excess amounts of $NaBH_4$ (5–10 fold) is a major shortcoming.

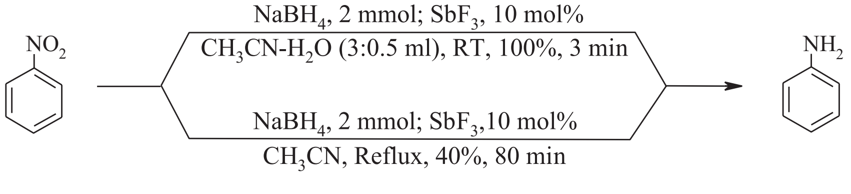
To expand the above-mentioned strategy in the reduction of nitro compounds by the $NaBH_4$/main metal halide system and our continuous efforts to develop modified borohydride agents in organic synthesis,[15] we report herein, SbF_3 as a more efficient promoter for a mild and convenient reduction of nitro compounds with sodium borohydride in wet CH_3CN at room temperature.

Our preliminary experiments showed that the reduction of nitrobenzene with 2 molar equivalents of $NaBH_4$ and catalytic amounts of SbF_3 (10 mol%) in CH_3CN (as an efficient aprotic solvent) without deposition of any precipitate was completed within 80 minutes under reflux conditions. However, a mixture of products with a 40% yield of aniline was obtained from the reduction. In another attempt, we found that by adding a small amount of water to the reaction mixture, when there was an immediate deposition of a fine black precipitate, the rate of reduction was dramatically increased and the reaction was completed within 3 minutes at room temperature. In the latter case, aniline was the sole product of reduction. The optimisation reactions showed that using 2 molar equivalents of $NaBH_4$ and 10 mol% of SbF_3 in a mixture of $CH_3CN–H_2O$ (3 : 0.5 ml) are the best conditions for the complete conversion of nitrobenzene into aniline (Scheme 1).

We applied the optimal conditions for the reduction of a variety of aromatic and aliphatic nitro compounds to their corresponding amines. As shown in Table 1, the product amines were obtained in high to excellent yields within 2–30 minutes. The chemoselective reduction of nitro group in the presence of carboxylic acid was proven with the reduction of 2-nitrobenzoic acid to anthranilic acid in 93% yield (entry 4). Our attempts to reduce C=O over nitro group in 3-nitrobenzaldehyde and 3′-nitroacetophenone were unsatisfactory and under the different conditions both of the functional groups were reduced (entries 5,6). The complete reduction of nitroarenes with two and three nitro groups was also achieved perfectly by this protocol: using 4–6 molar equivalents of $NaBH_4$ in the presence of 10 mol% of SbF_3 were the requirements for these transformations (entries 14–17). All attempts to perform chemoselective reduction of one nitro group in the presence of the other one were unsuccessful and the mixture of products was identified from the reaction mixture. Table 1 also shows that the reduction of aliphatic nitro compounds as well as nitroarenes was performed perfectly within 2–3 minutes (entries 18–20).

To highlight the efficiency of this synthetic methodology, we compared some of our results with the reported reagents such as $NaBH_4/SbCl_3$,[14] $NaBH_4/BiCl_3$,[14] and $BER/Ni(OAc)_2$.[12b] The comparison shows that in the number of molar equivalents of $NaBH_4$ and catalyst, the time needed and the efficiency of the reductions, this protocol is more efficient (Table 2).

The exact mechanism of this protocol is not clear; however, in our experiments, some results are noteworthy. In all reductions, by the combination of $NaBH_4$ with SbF_3 (10 mol%)



Scheme 1

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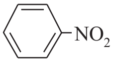
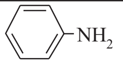
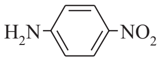
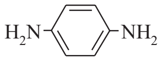
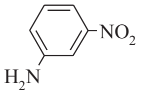
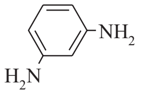
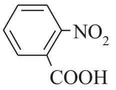
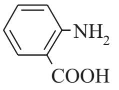
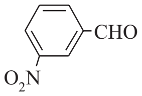
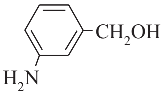
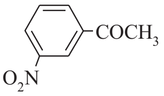
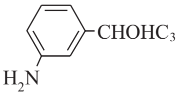
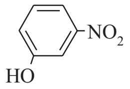
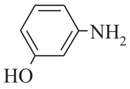
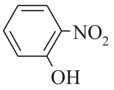
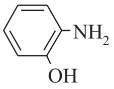
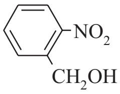
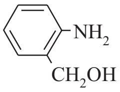
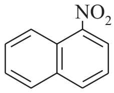
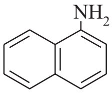
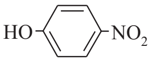
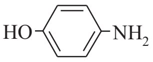
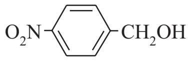
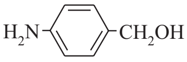
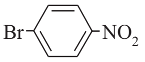
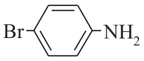
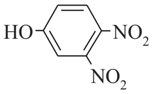
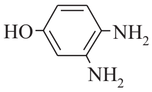
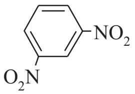
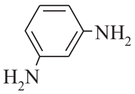
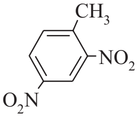
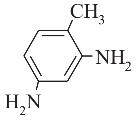
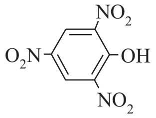
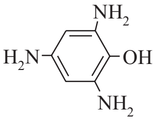
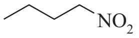
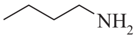
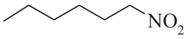
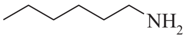
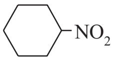
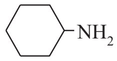
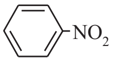
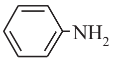
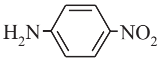
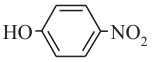
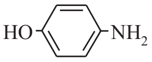
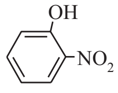
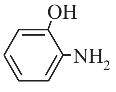
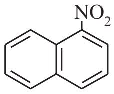
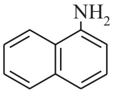
Table 1 Reduction of nitro compounds with the $NaBH_4/SbF_3$ system[a]

Entry	Substrate	Product	Molar ratio	Time/min	Yield (%)[b]	M.p. or B.p./°C	
			Subs./$NaBH_4$/SbF_3			Found	Reported[16]
1			1:2:0.1	3	95	183–184	184
2			1:2:0.1	2	96	143–145	143–145
3			1:2:0.1	2	94	65–67	64–66
4			1:2:0.1	2	93	146–148	144–148
5			1:2:0.1	5	96	94–95	93–95
6			1:4:0.2	5	95	67–69	66–69
7			1:2:0.1	2	92	124–126	124–126
8			1:2:0.1	2	96	175–177	174–177
9			1:2:0.1	2	95	84–85	83–85
10			1:2:0.1	2	94	49–51	48–50
11			1:2:0.1	3	96	188–190	188–190
12			1:2:0.1	5	95	61–63	60–63
13			1:2:0.1	2	97	63–65	62–64
14			1:4:0.1	20	93[c]	222	222
15			1:4:0.1	10	94	65–67	64–66
16			1:4:0.1	15	95	97–100	97–99
17			1:6:0.1	30	90	–	–
18			1:2:0.1	2	89	78–79	78
19			1:2:0.1	3	92	130–132	131–132
20			1:2:0.1	3	92	134	134

[a]All reactions were carried out in CH_3CN-H_2O (3:0.5 ml) at room temperature; [b]yields refer to isolated pure products; [c]the product was isolated as a salt of dihydrochloride (entry 14).

Table 2 Comparison of reduction of nitro compounds with the $NaBH_4/SbF_3$ system and some other reported reagents

Entry	Substrate	Product	(Molar equivalent of reductant) (Time/h) (Yield/%)			
			I	II[14]	III[14]	IV[12b]
1			(2:0.1)(0.05)(95)	(10:2)(2)(86)	(8:1.5)(0.5)(90)	(5:0.1)(1)(94)
2			(2:0.1)(0.03)(96)	(10:2)(1.5)(85)	(8:1.5)(0.33)(91)	–
3			(2:0.1)(0.05)(96)	(10:2)(1.5)(90)	(8:1.5)(0.17)(85)	(5:0.1)(1)(96)
4			(2:0.1)(0.03)(96)	(10:2)(1.5)(95)	(8:1.5)(0.17)(88)	–
5			(2:0.1)(0.03)(94)	–	–	(5:0.1)(1)(96)

$^{\mathrm{I}}NaBH_4/SbF_3$; $^{\mathrm{II}}NaBH_4/SbCl_3$; $^{\mathrm{III}}NaBH_4/BiCl_3$; $^{\mathrm{IV}}$BER/Ni$(OAc)_2$

in wet CH_3CN, the immediate deposition of a fine black precipitate and the subsequent evolution of hydrogen gas were observed. We think that reduction of nitro compounds is probably due to formation of the black precipitate which catalyses the decomposition of $NaBH_4$, strongly adsorbs nitro compounds and activates them towards reduction by $NaBH_4$. This black precipitate may be boride, zerovalent metal or a mixture of these.

In conclusion we have shown that a variety of aliphatic and aromatic nitro compounds were reduced efficiently to their corresponding amines by the combination of $NaBH_4$ with catalytic amounts of SbF_3 in wet CH_3CN. The reductions were completed within 2–30 minutes at room temperature. We think that in the view points of molar equivalents of $NaBH_4$ and catalyst, high efficiency, shorter reaction times, easy work-up procedure, and presentation of SbF_3 as a more efficient catalyst for the probable boride-catalysed reduction of nitro compounds, this protocol is a synthetically useful addition to the present methodologies.

Experimental

All reagents and substrates were purchased from commercial sources with the best quality and were used without further purification. IR and ^{1}H NMR spectra were recorded on Thermo Nicolet Nexus 670 FT–IR and 300 MHz Bruker Avance spectrometers, respectively. The products were characterised by a comparison with authentic samples (melting or boiling points) and their ^{1}H NMR or IR spectra. All yields refer to isolated pure products. TLC was applied for the purity determination of substrates, products and reaction monitoring over silica gel 60 F_{254} aluminum sheet.

Reduction of nitrobenzene to aniline with $NaBH_4/SbF_3$ system; typical procedure

In a round-bottomed flask (15 ml) equipped with a magnetic stirrer, a solution of nitrobenzene (0.123 g, 1 mmol) in CH_3CN-H_2O (3:0.5 ml) was prepared. To the resulting solution, SbF_3 (0.018 g, 0.1 mmol) was added and the mixture was then stirred for 2 min. Afterwards, $NaBH_4$ (0.076 g, 2 mmol) as a fine powder was added to the reaction mixture and a fine black precipitate was immediately deposited. The mixture continued to be stirred for 3 min and the progress of the reaction was monitored by TLC (eluent; CCl_4/Et_2O: 5/2). At the end of reaction, distilled water (5 ml) was added to the reaction mixture and the mixture stirred for 10 min. The mixture was extracted with CH_2Cl_2 (3 × 8 ml) and dried over anhydrous sodium sulfate. Evaporation of the solvent and short column chromatography of the resulting crude material over silica gel (eluent; CCl_4/Et_2O: 5/3) gave the pure liquid aniline (0.088 g, 95%, entry 1, Table 1).

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