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Reduction of nitrobenzene derivatives using sodium borohydride and transition metal sulfides

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ABSTRACT

Reported here is the reduction of aromatic nitro compounds using sodium borohydride and transition metal sulfides as catalysts. The reaction conditions were optimized using the reduction of nitrobenzene as a model reaction. The catalysts studied were iron sulfide (Fe_3S_4), copper sulfide (CuS), zinc sulfide (ZnS), cobalt sulfide (Co_3S_4), and nickel sulfide (NiS). The reduction was monitored using gas chromatography. Quantitative conversions were achieved using Co_3S_4 and NiS, representing a ten-fold increase in reactivity compared to the non-catalyzed reaction. Fe_3S_4 and ZnS had no apparent effect on the reduction of nitrobenzene while the reduction using CuS showed a marginal increase. The reduction method was applied to several aryl-nitro derivatives containing either electron-withdrawing or electron-donating groups. Halogen containing aryl-nitro compounds were reduced without dehalogenation. The reduction had no effect on other functional groups such as carboxylic acids, esters, amides, or alkenes, indicating that the reduction is highly chemoselective.

The reduction of nitroaromatic compounds to their corresponding aryl amines is an important reaction for the synthesis of various pharmaceuticals, dyes, and other industrially related compounds.[1] Additionally, diazotization of these aryl amines can easily yield important aromatic derivatives.[2]

Traditionally, nitroaromatic compounds are reduced using iron and hydrochloric acid[3] or via catalytic hydrogenation.[4] Some drawbacks, however, include the use of corrosive reagents and risks associated with highly flammable molecular hydrogen.

$NaBH_4$, a mild reducing agent, does not reduce nitroaromatic compounds under normal conditions. However, several $NaBH_4$ catalytic systems have been developed for the reduction of nitroaromatic compounds. Accordingly, $NaBH_4$/Raney nickel,[1] $NaBH_4/CuSO_4$,[5] $NaBH_4/Ni_2B$,[6] $NaBH_4/CoCl_2$,[7] $NaBH_4/Ni(OAc)_2{\cdot}4H_2O$,[8] and $NaBH_4/SnCl_2{\cdot}2H_2O$[9] have been proven successful in the reduction of nitroaromatic compounds.

In this work we studied the effect of several transition metal sulfides on the reduction of nitro-aromatic compounds using $NaBH_4$. The transition metal sulfides (Fe_3S_4, Co_3S_4, NiS, CuS, and ZnS) were synthesized hydrothermally.[10]

The reduction of nitrobenzene was studied to screen the catalysts. In a typical procedure, nitrobenzene (1 equiv) dissolved in ethanol was treated with $NaBH_4$ (3 equiv) in the presence of the corresponding catalyst (10 mol %). The reactions were carried out in a closed scintillation vial and sonicated for 60 min. The reaction was also performed without catalyst for comparison. Figure 1 shows the GC plots for the reduction of nitrobenzene using different catalysts.

The efficiency of each catalyst compared to the non-catalyzed reaction is shown in Table 1.

As seen from Figure 1 and Table 1, the reduction of nitrobenzene using $NaBH_4$ occurred in 9% conversion in the absence of a catalyst. No significant increase in the conversion was observed with Fe_3S_4 or ZnS. It should be noted that copper sulfate has been reported to catalyze the homogeneous reduction of aromatic nitro compounds.[5] However, we observed only marginal conversion using CuS. Co_3S_4 and NiS, on the other hand, increased the conversion by a factor of 10 compared with the non-catalyzed reaction.

After determining that only the cobalt and nickel sulfides produced an effect in the conversion, we studied the effect of the concentration of the catalyst. Table 2 summarizes the effect of Co_3S_4 and NiS concentration on the reduction of nitrobenzene. The reactions were carried out for 60 min using 3 equiv of sodium borohydride with respect to the nitrobenzene. It was observed that

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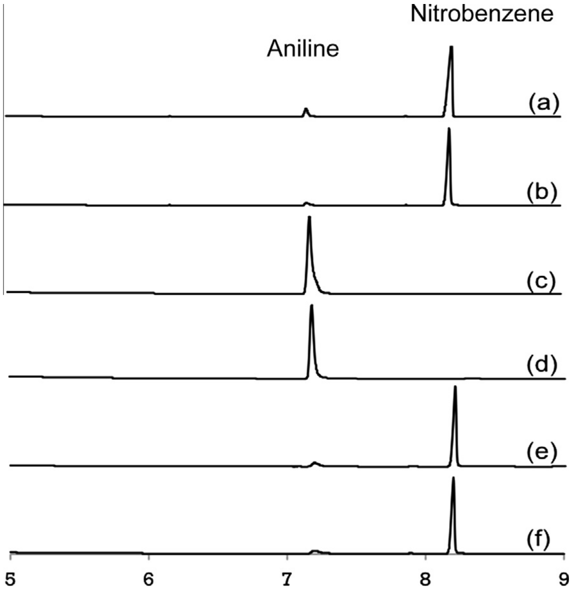


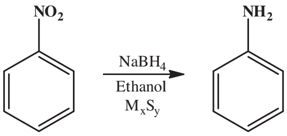
Figure 1. GC plots for nitrobenzene reduction attempts: (a) No catalyst; (b) Fe_3S_4; (c) Co_3S_4; (d) NiS; (e) CuS; (f) ZnS.

only 1 mol % Co_3S_4 caused significant increase in conversion (85%) compared to the non-catalyzed reaction. The conversion increased steadily up to 5 mol % and it remained relatively constant at 10 mol % and 20 mol %. The results suggest that 5 mol % of catalysts is the optimum concentration since the load of catalyst is relatively low while achieving excellent conversions. As it was the case with Co_3S_4, the conversion increases steadily with the concentration of NiS. However, the maximum conversion was achieved at 10 mol % catalyst and it remained relatively constant at 20 mol %. It should be noted that the results in Table 2 are from only one run at each catalyst concentration. Multiple studies are necessary to determine if catalyst saturation occurs at concentrations above 10 mol %.

Previous experiments demonstrated that using Co_3S_4 resulted in higher conversions compared with NiS. Therefore, the effect of the concentration of sodium borohydride on the Co_3S_4 catalyzed reduction of nitrobenzene was investigated. The experiments were conducted using 5 mol % Co_3S_4 with 60 min overall reaction time. The results are summarized in Table 3. As observed in Table 3, using 1 mol equiv of $NaBH_4$ resulted in 71% conversion. The results suggest that at least 2 equiv of $NaBH_4$ is needed to achieve quantitative conversions.

After determining the optimum concentration of catalyst and sodium borohydride, the effect of reaction time was investigated. The experiments were conducted using 5 mol % of Co_3S_4 and 3 equiv of sodium borohydride. The reaction mixtures were filtered using a Millipore syringe filter to eliminate the catalyst from the reaction mixture. This ensured that no further reaction was taking place. It was observed that 83% conversion was obtained at 10 min while quantitative conversions were achieved at 20 min.

Table 1
Reduction of nitrobenzene[a]



Catalyst	Conversion (%)
–	9 (±1.2)
Fe_3S_4	9.3
Co_3S_4	99.9
NiS	96.3
CuS	11.2
ZnS	10.9

[a] Ethanol, rt, sonication; substrate/$NaBH_4$/catalyst = 1:3:0.05, 1 h.

Table 2
Effect of catalyst concentration[a]

	Conversion[b] (%)	
Mole (%)	Co_3S_4	NiS
1	85	75
2.5	92	92.6
5	99.9	96.3
10	99.9	99.1
20	98.7	97.6

[a] Ethanol, rt, sonication; substrate/$NaBH_4$ = 1:3, 1 h.
[b] Monitored by gas chromatography.

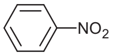
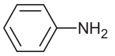
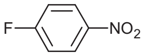
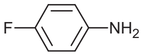
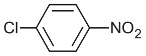
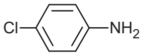
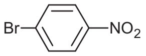
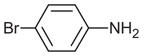
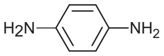
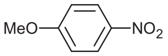
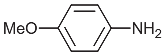
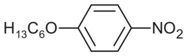
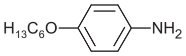
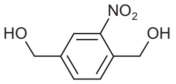
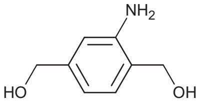
Table 3
Effect of $NaBH_4$ concentration

$NaBH_4$ (equiv)	Conversion (%)
1	71
1.5	99.6
2	99.9
3	99.9

The experiments described above demonstrated that quantitative conversions in the reduction of nitrobenzene were possible using Co_3S_4 and NiS. To demonstrate the scope of the newly developed method, the reduction of nitrobenzene derivatives containing both electron withdrawing and electron donating groups was investigated. The experiments were conducted using the optimum conditions of 5 mol % of Co_3S_4 (which was demonstrated to be the most efficient catalyst), 3 equiv of sodium borohydride, and the reaction time was 60 min.[11] Table 4 summarizes the results during the reduction of several nitrobenzene derivatives. It should be noted that the yields reported correspond to the isolated products.

As seen in Table 4, the newly developed system was employed successfully in the reduction of nitrobenzene derivatives in moderate (58%) to high (>90%) isolated yields. The isolated yield was independent of the nature of the substituents. Thus, high yields were observed for nitrobenzene containing electron withdrawing groups (entries 2, 3, 4, and 8), and for nitrobenzene containing electron donating groups (entries 5, 6, and 7). The seemingly low

Table 4
Reduction of nitrobenzene derivatives

Entry	Substrate structure	Product structure	Isolated yield (%)
1			73
2			81
3			91
4			86
5			58
6			93
7			90
8			84

yield observed for entry 5 can be attributed to the high solubility of the product in the solvents used during recrystallization.

Products 1–6 are available commercially. Their physical properties and their IR and NMR spectra correspond to those for the respective chemicals available from Sigma Aldrich Chemical Co (see Supporting information). The ^1H NMR and ^{13}C NMR spectra of *p*-hexyloxy-aniline (entry 7) correspond to the literature.[12] A new compound was obtained used the procedure reported here (entry 8). The new compound, 2-amino-p-xylylene glycol, was obtained as a white powder (mp = 130–132 °C). Its structure was confirmed by its ^1H NMR, ^{13}C NMR, ^{13}C DEPT-135, and FTIR spectra (see Supporting information).

It should also be noted that the newly developed reduction procedure did not result in dehalogenation as in the case of entries 2, 3, and 4. Thus, only reduction of the nitro group was observed under the conditions studied. Furthermore, the $NaBH_4$/metal sulfide system did not affect other functional groups like alkenes, carboxylic acids, esters, or amides, indicating the selectivity of the reduction toward the nitro group.

The method reported here compares favorably with other literature methods which use $NaBH_4$ in the presence of cobalt or nickel salts. For instance, when the system $CoCl_2/NaBH_4$ is used, the reactions proceed in relatively low percent yields (35% to 50%), and required high temperature (>200 °C).[7] Furthermore, $CoCl_2$ was used in 200% mole ratio (i.e., 2 equiv relative to the substrate) while quantitative conversions are obtained in the method reported here using only 5 mol % of catalyst with respect to the substrate. Reduction of nitro derivatives using $NaBH_4/Ni(OAc)_2{\cdot}4H_2O$ (20 mol % with respect to the substrate) proceeds in high yields (>90%) for the optimized reaction. However, the reduction requires careful monitoring of the amount of water in the reaction mixture. Accordingly, the reduction proceeds in 10% yield in the absence of water and varies between 60% and 92% depending on the amount of water added to the solvent.[8] An additional advantage of the method reported here is that the use of heterogeneous catalysts allows for easy separation from the reaction mixture.

In summary, quantitative conversions were achieved for the reduction of nitrobenzene utilizing $NaBH_4/Co_3S_4$ and $NaBH_4$/NiS systems. Reduction of various nitroaromatic compounds was successfully carried out in moderate to high yields. The heterogenous reduction system allows for simple filtration of transition metal catalysts simplifying the work-up. The newly developed method also affords a mild and selective alternative for the effective conversion of nitroaromatic compounds to their corresponding aryl amines.

Acknowledgments

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Supplementary data

Supplementary data (detailed experimental procedures as well as characterization data) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.08.068.

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10. Metal sulfide catalysts were synthesized hydrothermally using Teflon lined autoclaves placed inside stainless steel jackets. Fe_3S_4 was synthesized by dissolving 30 mmol of $FeCl_3$ and 60 mmol of thiourea in 20 mL of ethylene glycol and 5 mL of H_2O. The solution was then autoclaved at 180 °C for 1 h. ZnS_2 was synthesized by dissolving 2 mmol of $Zn(NO_3)_2$ and 12 mmol of Na_2S in 15 mL of H_2O. The solution was then autoclaved at 140 °C for 1 h. Ni_3S_4, Co_3S_4, and CuS_2 were synthesized by dissolving 2 mmol of MCl_2 and 12 mmol Na_2S in 15 mL of H_2O. The solution was then autoclaved for 1 h at 140 °C. The precipitate from each reaction was filtered, washed with water, followed by a methanol wash, and then oven dried.
11. Typical reduction procedure: In a scintillation vial containing 8 mL reagent alcohol, 2 mmol of the corresponding nitrobenzene derivative, 5 mol % of Co_3S_4, and 0.227 g (6 mmol) of sodium borohydride were added. The vial was capped and placed in the sonication bath for 1 h. The reaction mixture was filtered using a Celite cake, washed with methanol, and the solvent evaporated under reduced pressure. The residue was partitioned between water and ethyl acetate. The layers were separated and the aqueous layer was back extracted with ethyl acetate (2 × 15 ml). The organic layers were combined, washed with water, dried over $MgSO_4$, and the solvent evaporated under reduced pressure. The resulting product was dried under vacuum for 1 h.
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