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NaBH$_4$/Charcoal: A New Synthetic Method for Mild and Convenient Reduction of Nitroarenes

Behzad Zeynizadeh [a] & Davood Setamdideh [a]
[a] Department of Chemistry, Faculty of Sciences, Urmia University, Urmia, Iran

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$NaBH_4$/Charcoal: A New Synthetic Method for Mild and Convenient Reduction of Nitroarenes

Behzad Zeynizadeh and Davood Setamdideh
Department of Chemistry, Faculty of Sciences, Urmia University,
Urmia, Iran

Abstract: $NaBH_4$ in the presence of charcoal (0.4–0.8 g) reduces varieties of nitroarenes to their corresponding amines. Reduction reactions were carried out in a mixture of H_2O-THF (1:0.5 mL) at 50–60°C with high to excellent yields of products.

Keywords: Amines, charcoal, $NaBH_4$, nitroarenes, reduction

Arylamines are widely used as antioxidants and intermediates for dyes, photographic materials, pharmaceuticals, and agricultural chemicals. So, reduction of aromatic nitro compounds is one of the important methods for the preparation of arylamines. During the past decades, the application of $NaBH_4$ as a mild reducing agent has brought about fundamental changes in the reduction of functional groups in modern organic synthesis.[1] It is known that solely sodium borohydride does not reduce nitro compounds under ordinary conditions. However, the reducing power of this reagent or its polymeric analogue (BER) undergoes a drastic change toward reduction of nitro groups by the combination with metal halides or salts[2] such as $NaBH_4/CoCl_2$, $NaBH_4/FeCl_2$, $NaBH_4/SnCl_2$, $NaBH_4/CuSO_4$, $NaBH_4/Ni(OAc)_2$, $NaBH_4/NiCl_2$, $NaBH_4/BiCl_3$ or $SbCl_3$, $NaBH_4$/Co(pyridyl), $NaBH_4/Cu(acac)_2$, and BER/$Ni(OAc)_2$.

The application of carbon in its palladium-supported form to modify the reducing capability of $NaBH_4$ toward reduction of nitro compounds was first

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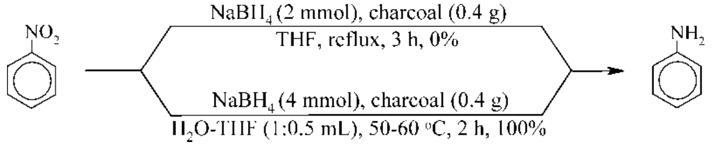
Address correspondence to Behzad Zeynizadeh, Department of Chemistry, Faculty of Sciences, Urmia University, Urmia 57159-165, Iran. E-mail: b.zeynizadeh@mail.urmia.ac.ir

reported in a brief note at 1962.[3] In this report, the transformation of nitro compounds to amines with sodium borohydride by adding it to a mixture of palladium on carbon in alkaline water or methanol was investigated. The combination system of $NaBH_4$ and Pd/C was also reported for the reduction of this functional group in THF at room temperature.[4]

In the reported methods, a mixture of carbon and palladium showed an activity; however, our literature review did not show any application for the use of carbon alone as a promoter in the reduction of functional groups with $NaBH_4$. This subject and our continuous efforts to explore the synthetic utilities of modified hydroborate agents in organic synthesis[5] encouraged us to investigate reduction of nitroarenes by the combination of sodium borohydride and charcoal in a mixture of H_2O-THF.

Our preliminary experiments showed that the reduction of nitrobenzene as a model compound with 2 molar equiv of $NaBH_4$ in the presence of charcoal (0.4 g) in THF did not show any activity under reflux conditions. However, we found that by adding a few drops of water to the reaction mixture, the rate of reaction accelerated extremely at room temperature with the evolution of hydrogen gas.

The reaction conditions were optimized, and they showed that using 4 molar equiv of $NaBH_4$ per 1 molar equiv of substrate in the presence of charcoal (0.4 g), in a mixture of H_2O-THF (1:0.5 mL) at 50–60°C is optimal for the complete conversion.



To explore the synthetic utility of this combination system, we studied the reduction of structurally different nitroarenes to their amines. Table 1 shows the results of these transformations. Reduction reactions were completed within 1–5 h with high to excellent yields of the corresponding amines. The results show that selective reduction of the nitro group in the presence of carboxylic acid can be achieved perfectly with the reduction of 2-nitrobenzoic acid to anthranilic acid in 93% yield (entry 4). Chemoselective reduction of carboxaldehyde or keto groups over nitro in a molecule was demonstrated with the selective reduction of C=O in 2-nitrobenzaldehyde and 2′-nitroacetophenone by the use of 1 molar equiv of $NaBH_4$ in the presence of charcoal (0.4–0.5 g) within 5–10 min at 50–60°C (entries 10,12). This utility was also effective for the reduction of dinitro or trinitroarenes using 8–12 molar equiv of $NaBH_4$ in the presence of 0.6–0.8 g of charcoal (entries 15–19).

The exact mechanism of this protocol is not clear; however, we think that the following factors may play a role in the reductions: a) Charcoal is a very fine porous material and the use of sodium borohydride in the presence of water makes it finely disperse on the surface of charcoal and therefore more

Table 1. Reduction of nitroarenes with NaBH$_4$/charcoal system[a]

Entry	Substrate	Product	Molar ratio subs./NaBH$_4$	Charcoal (g)	Time (h)	Yield (%)[b]	Mp or Bp (°C)	
							Found	Reported[6]
1	Nitrobenzene	Aniline	1:4	0.4	2	95	183–184	184
2	4-Nitroaniline	1,4-Phenylenediamine	1:4	0.4	3	96	143–145	143–145
3	3-Nitroaniline	1,3-Phenylenediamine	1:4	0.4	3	85	65–67	64–66
4	2-Nitrobenzoic acid	Anthranilic acid	1:5	0.5	3	93	146–148	144–148
5	4-Nitrophenol	4-Aminophenol	1:4	0.4	3	95	188–190	188–190
6	2-Nitrophenol	2-Aminophenol	1:4	0.4	3	95	175–177	174–177
7	4-Nitrobenzyl alcohol	4-Aminobenzyl alcohol	1:4	0.4	2	95	61–63	60–63
8	2-Nitrobenzyl alcohol	2-Aminobenzyl alcohol	1:4	0.4	3	90	84–85	83–85
9	1-Nitronaphthalene	1-Naphthylamine	1:4	0.4	2	95	49–51	48–50
10	2-Nitrobenzaldehyde	2-Nitrobenzyl alcohol	1:1	0.4	5 min	90	70–71	70–72
11	2-Nitrobenzaldehyde	2-Aminobenzyl alcohol	1:5	0.5	3	85	84–85	83–85
12	2′-Nitroacetophenone	1-(2-Nitrophenyl)-1-ethanol	1:1	0.5	10 min	87	—	—
13	2′-Nitroacetophenone	1-(2-Aminophenyl)-1-ethanol	1:5	0.5	3	90	—	—

(*continued*)

Table 1. Continued

Entry	Substrate	Product	Molar ratio subs./$NaBH_4$	Charcoal (g)	Time (h)	Yield (%)[b]	Mp or Bp (°C)	
							Found	Reported[6]
14	1-Bromo-4-nitrobenzene	4-Bromoaniline	1:4	0.4	2	95	63–65	62–64
15	1,3-Dinitrobenzene	1,3-Phenylenediamine	1:8	0.6	1	97	65–67	64–66
16	2,4-Dinitrotoluene	2,4-Diaminotoluene	1:8	0.6	3	94	97–100	97–99
17	2,4-Dinitrophenol	2,4-Diaminophenol	1:8	0.6	5	97[c]	221–223	222 (dec.)
18	2,4-Dinitroaniline	1,2,4-Triaminobenzene	1:8	0.6	5	95	—	—
19[d]	Picric acid	2,4,6-Triaminophenol	1:12	0.8	4	97	—	—

[a] All reactions were carried out in H_2O-THF (1:0.5 mL) at 50–60°C.

[b] Yields refer to isolated pure products.

[c] The product was isolated as a salt of dihydrochloride.

[d] The reaction was carried out in H_2O-THF (1:1.25 mL) at 50–60°C.

interaction with the substrate produces the efficiency in the reductions. b) In our experiments, we saw that $NaBH_4$ in the presence of charcoal in a mixture of H_2O-THF gently liberates hydrogen gas, therefore H_2 in a synergic sense with the hydride attack performs reductions. c) The hydrolysis of the produced amino-borate intermediate by the presence of water in the reaction mixture makes a promotion in the reductions.

In conclusion, we have shown that $NaBH_4$ in the presence of charcoal is an efficient protocol for the reduction of nitroarenes. Reduction reactions were carried out in a mixture of H_2O-THF (1:0.5 mL) at 50–60°C under mild conditions. The product amines were obtained in high to excellent yields. Reduction of dinitro or trinitroarenes was also achieved successfully with this protocol. The chemoselective reduction of carbonyl groups over nitro groups was also achieved perfectly. The simplicity of the method, cheapness and availability of the reagents, mild reaction conditions, high yields of products, and the easy workup procedure are the advantages that could make this protocol a useful addition to the present methodologies.

EXPERIMENTAL

General

All reagents and substrates were purchased from commercial sources, are of the best quality, and were used without further purification. IR and ^1H NMR spectra were recorded on Thermo Nicolet Nexus 670 FT-IR and 300-MHz Bruker spectrometers, respectively. The products were characterized by a comparison with authentic samples (melting or boiling points) and their ^1H 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 $NaBH_4$/Charcoal System: A Typical Procedure

In a round-bottomed flask (15 mL) equipped with magnetic stirrer and condenser, a solution of nitrobenzene (0.123 g, 1 mmol) in a mixture of H_2O-THF (1:0.5 mL) was prepared. Charcoal (0.4 g) was then added, and the reaction mixture was stirred with magnetic stirrer for 10 min at room temperature. To the resulted mixture, $NaBH_4$ (0.151 g, 4 mmol) was added portionwise for 2 h with stirring at 50–60°C. TLC monitored the progress of the reaction (eluent, CCl_4/Et_2O:5:2). At the end of the reaction, the reaction mixture was simply filtered and dried over anhydrous sodium sulfate. Evaporation of the solvent and a 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%, Table 1).

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