

TRANSITION METAL CATALYZED/NaBH₄/MeOH REDUCTION OF NITRO, CARBONYL, AROMATICS TO HYDROGENATED PRODUCTS AT ROOM TEMPERATURE

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ABSTRACT

Reduction of nitrobenzene, 4-ethyl nitrobenzene, 4-isopropyl nitrobenzene, 4-nitro 1-phenyl acetate, acetophenone, with CuCl₂/MeOH/NaBH₄ provided hydrogenated products in quantitative yields. In order to evaluate the best catalytic systems various transition metal catalysts were examined for the first time and CuCl₂ catalysts was superactive system. And a solvent system was also studied with methanol being the best solvent evolved. The reactions were exceedingly clean with no byproduct formation, negating the need for further purification. Most reactions provided moderate to excellent yields.

KEYWORDS: Reduction, CuCl₂, NaBH₄, nitrobenzene, aniline.

I. INTRODUCTION

The pioneering discovery by Brown describing the use of Ni borides in accelerating CuCl₂-mediated reactions has resulted in widespread applications of NiCl₂-NaBH₄ catalysts. This combination is utilized in several reduction reactions. Due to its ability to enhance reaction outcomes, NaBH₄ is the preferred reducing agent in CuCl₂-mediated reactions.

Homogeneous catalysts have attracted interest for reductions reactions due its conversions and high selectivity [1,2]. H.C. Brown [3] and A. Rahman [4] co-workers have explored the use of Ni-Boride[3], Ni-Boride silica catalysts[4,5] Au complexes[6], Ni[7],Pt, Ru[8], Fe[9] for reduction of nitroaromatics, and other aromatics to hydrogenated products at room temperature and at low temperature (0-5°C) methanol co-solvents in reduction reactions.

Comparison with other reported protocols with Pd, Ni complexes, Ru, Rh[4] using raney nickel catalysts (which is pyrophoric) reveals some interesting trends were observed with longer reaction times, use of sophisticated instruments, high pressure, temperature precludes the wide use of these reagents and conditions.

The effects of water and DMPU[2] in the reduction of ketones. These additives have proven to be useful in several reactions but unfortunately do not have the broad applicability of HMPA, and as a consequence, the search for an alternative is ongoing. The major drawback of using HMPA is carcinogenic. The use of Sml₂/H₂O/Et₃N mixture in the reduction of ketones [10,11]. The use of the above mentioned catalysts requires stringent conditions and the authors developed a new CuCl₂/NaBH₄ system for these reduction reactions. These reactions are instantaneous and provide yields of reduced products. The author studied the comparison of the H₂O/NaBH₄ method and the NaBH₄/MeOH method in reduction of ketones indicates that MeOH/NaBH₄/CuCl₂ is approximately 100 times faster. This method has also been applied in the reduction of nitroaromatics, ketones,

aldehydes, olefins. These examples clearly show the utility of $\text{CuCl}_2/\text{MeOH}/\text{NaBH}_4$ mixtures in reduction of several functional groups.

II. EXPERIMENTAL SECTION:

2.1 Materials Used:

All these materials were purchased from fluka company, CuCl_2 , NaBH_4 , EtOH, MeOH, ethylacetate, THF.

2.2 Experimental Procedure:

In a 25 ml single neck round bottom flask 5ml of methanol is added to 2mmol substrate to it CuCl_2 and NaBH_4 is added with more 5 ml of MeOH and the reaction mixture is stirred for 5-10min monitoring through TLC. Upon completion of reaction mixture it is quenched with water and extracted with organic solvent ethyl acetate upon evaporation of ethyl acetate affording product which is subjected to column chromatography affording pure product which is analyzed by GC, H NMR and compared with the standard samples.

III. RESULTS AND DISCUSSION:

Moreover, they provide better yields and require less time than the HMPA/alcohol systems. The workup and the subsequent purification of the products are straight forward during the course of the reaction. Therefore, the combination of $\text{CuCl}_2/\text{NaBH}_4/\text{MeOH}$ provides an excellent alternative to HMPA[12-17] in SmI_2 -based reactions.

Initial mechanistic studies show that water and NaBH_4 do not accelerate the reactions separately. The acceleration is a result of the $\text{CuCl}_2/\text{NaBH}_4/\text{MeOH}$ mixture.

Other borohydrides such as KBH_4 , KCNBH_4 have the same effect as NaBH_4 but required more quantity of these borides for the reaction to be completed compared to NaBH_4 , while replacement of water by alcohols has a deleterious impact on the rates of reduction. It has been proposed that rapid precipitation of $\text{Cu}(\text{OH})_3$ and NaBH_4 , provides the driving force for the reduction[11-12]. To expand the applicability of the $\text{CuCl}_2/\text{MeOH}/\text{NaBH}_4$ reagent and to determine its general utility in important single electron- transfer-promoted reactions, the reduction of nitro aromatics to aromatic amines was studied. Recent work in our laboratory has shown that solvation also plays an important role in determining the outcome of these reductions¹³. In order to check the best suitable solvents the author analyzed with H_2O , MeOH, ethanol and THF for reduction of nitroaromatics in four solvents showed that, in most cases, MeOH provided superior solvent for reduction reactions over ethanol, THF and H_2O .

Transition metal chemistry have attracted interest for chemists over decades for hydrogenation reactions, since the nature of metals is known to influence its outcome in $\text{CuCl}_2/\text{MeOH}/\text{NaBH}_4$ -mediated reactions a series of lewis acid catalysts ZnCl_2 , ZnNO_3 , CuSO_4 , CuNO_3 , CaCl_2 , BaCl_2 , CoCl_2 , FeSO_4 , FeCl_3 , MgCl_2 , BiNO_3 , [14-16] were used for nitrobenzene reduction to evaluate the best catalytic system. With these systems only starting material was recovered upon continuation of reaction for 24 h. From these results its evident that the best catalytic system was CuCl_2 based lewis acid system the results are presented in table 1.

Table 1 Reduction of nitrobenzene to aniline with various lewis acids with NaBH_4 in MeOH at room temperature.

S. No	Catalysts	Time	Conversion%	Result
1.	ZnCl_2	20h	-	No reaction
2.	CuSO_4	20m	96	
3.	$\text{Cu}(\text{NO}_3)_2$	20m	96	
4.	CaCl_2	20h	20	
5.	BaCl_2	24h	-	No reaction
6.	CoCl_2	24h	-	No reaction

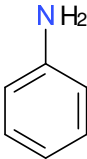
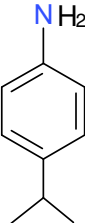
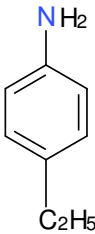
7.	FeSO ₄	24h	-	No reaction
8.	FeCl ₃	24h	-	No reaction
9.	MgCl ₂	24h	-	No reaction
10.	Bi(NO ₃) ₂	20h	30	

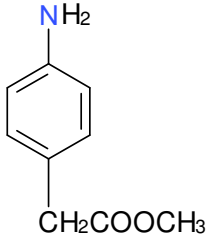
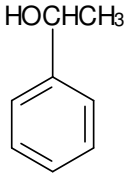
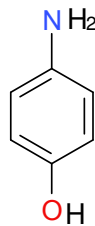
Means duplicate runs

The results obtained with Cu lewis acids catalysts encouraged the author to run reactions with a series of substituted aromatics were reduced to hydrogenation products presented in table 2. 4-Isopropyl nitrobenzene, 4-Ethyl nitrobenzene, 4-Nitro-1-phenylacetate, acetophenone, 4-nitrophenol, 1-nitronaphthalene. These reactions were performed at room temperature, and all the reactions were completed within 5-10min after 5 min of addition of the NaBH₄ to CuCl₂. The products were determined by gas chromatography, and utilizing the protocol described by A Rahman².

All reactions were quantitative, and the precipitation of byproducts Cu(OH)₃ made purification quite simple. Filtration of the precipitate and extraction with organic solvent then evaporating the solvent on rotary evaporator provided clean product, and no further purification was necessary. Inspection of the results in Table 2 shows a number of interesting trends. Most reactions provided selective product.

Table 2 Reduction of substituted aromatics to hydrogenated products with CuCl₂/NaBH₄/MeOH at room temperature.

S. No	Substrates	Time	Conv%	Products
1.	C ₆ H ₅ -NO ₂	5 min	98	
2.	(CH ₃) ₂ -CH-C ₆ H ₅ -NO ₂	10 min	90	
3.	4-C ₂ H ₅ -C ₆ H ₄ -NO ₂	5 min	95	
4.	4-NO ₂ -C ₆ H ₄ -CH ₂ COOCH ₃	10 min	80	

5.	$C_6H_5-COCH_3$	5 min	98	
6.	4-HO-C ₆ H ₄ -NO ₂	5 hr	50	
7.	$C_{12}H_{10}-NO_2$	5min	97	 $C_{12}H_{10}-NH_2$

Means duplicate runs

All the substrates were reduced with greater selectivity by $CuCl_2/MeOH/NaBH_4$ but with entry no 6 showed less conversion to 50% in 5h duration this owing to its hydroxyl group present at the para position. It's important to assess various mechanistic scenarios responsible for reaction outcomes so that practitioners can make judicious choices best suited to their system of interest. The reduction of ketones by $CuCl_2$ in the presence of proton sources likely proceeds through a House-type mechanism,[16] and recent mechanistic work has shown that the rate-limiting step is the first proton transfer to the initially formed ketyl radical anion[17-25]. The radical produced after protonation of the ketyl is reduced to a carbanion by a second equivalent of $Cu(II)$.

IV. CONCLUSION

Nitrobenzene, substituted nitro benzene and other aromatics was reduced to aniline with $CuCl_2/NaBH_4/MeOH$ system in 5min and various transition metal lewis acid catalysts were examined for this transformation and the best catalytic system evolved to be $CuCl_2$. And variety of substrates were reduced to its hydrogenated product notable being 4-Isopropyl nitrobenzene, 4-ethyl nitrobenzene, 4-nitro-1-phenyl acetate and 1-nitro naphthalene. Methanol was the best solvent evolved among other solvents tested THF, EtOH and H_2O . Regardless of the exact mechanistic details of the present reductions, the data presented herein show the utility and ease of $CuCl_2/MeOH/NaBH_4$

reducing system in the reduction reactions. This methodology is simple, economic, eco friendly and requires less time for the reaction to complete.

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