

Chemoselective Reduction of Carbonyl Compounds to Alcohols with Co-Doped Ammonia Borane

PENGMIAN HUANG^{1,2,3,*}, WENJUAN TANG³, GUISHAN TAN¹, WENBIN ZENG¹, YUANJIAN LI¹, QINGHUA ZHANG² and BO CHEN²

¹School of Pharmaceutical Sciences, Central South University, Changsha 410000, Hunan Province, P.R. China

²Fangsheng Pharmaceutical Co., Ltd. of Hunan, Changsha 410000, Hunan Province, P.R. China

³School of Chemistry and Biology Engineering, Changsha University of Science & Technology, Changsha 410000, Hunan Province, P.R. China

*Corresponding author: Fax: +86 731 85258733; Tel: +86 15973196958; E-mail: pengmianhuang@163.com

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Chemoselective reduction of various carbonyl compounds to alcohols with Co-doped ammonia borane was investigated in the present work. It was observed that Co-doped ammonia borane exhibited much better performance than ammonia borane. The Co-based catalysts could be reused up to four times with a slight decrease in activity. Thus, a mild and efficient method for chemoselective reduction of carbonyl compounds with Co-doped ammonia borane was established. The Co-doped ammonia borane sample was characterized by electron paramagnetic resonance. Electron paramagnetic resonance characterization revealed that Co element in a partially reduced state.

Keywords: Co-doped ammonia boarne, Chemoselective reduction, Carbonyl compounds.

INTRODUCTION

Ammonia borane (NH_3BH_3) has been a subject of intensive study¹ since 2000, because of its abnormally high hydrogen content ($19.6 \text{ wt } \%$)²⁻¹¹. In this study, 2 mol % nano-sized Co-based catalysts were introduced to ammonia borane through a "co-precipitation" method. We devoted to explore the chemoselective reduction of carbonyl compounds to alcohols with Co-doped ammonia borane. The reduction of carbonyl compounds by Co-doped ammonia borane was found much faster than by ammonia borane at room temperature. Therefore, a facile method for the preparation of alcohols by chemoselective reduction of carbonyl compounds with Co-doped ammonia borane was established. This is the first time to applied Co-doped ammonia borane in synthetic organic chemistry. The chemical state of Co element doped in ammonia borane was identified by electron paramagnetic resonance. Furthermore, the recyclability of Co-based catalysts was discussed.

EXPERIMENTAL

Synthesis of 2 mol % Co-doped ammonia borane: NH_3BH_3 was synthesized according to the procedure reported by Ramachandran and Gagare¹⁷. 0.4 mmol of CoCl_2 and 10 mL methanol were added into a sealed glass bottle at room temperature. The contents were sonicated for 20 min at room temperature, then, 20 mmol ammonia borane was added into that methanol solution. The solution or blending could be directly used in reduction reaction without further purification.

Co-doped ammonia borane could be preserved in solid form as well in methanol. When ammonia borane was added into that methanol solution containing CoCl_2 , immediately after, the resulting solution or blending was distilled at room temperature under a reduced pressure in a rotary evaporator within 5 min and the samples were continuously vacuumed to eliminate the rest solvent. After that, the samples were preserved in refrigerator to avoid self-decomposition.

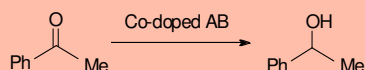
Chemoselective reduction of carbonyl compounds with ammonia borane or Co-doped ammonia borane: 10 mL of 5 mmol ammonia borane or 5 mmol Co-doped ammonia borane methanol solution was added into 5 mL of 10 mmol aldehydes or ketones solution in methanol in a sealed glass bottle and these contents stirred for an appropriate time at ambient pressure and temperature. The reaction was monitored by TLC. After the reaction, methanol was evaporated and then 30 mL hexane was added into the glass bottle to extract alcohol product three times. Then, clear hexane solution was collected after centrifugation. Next, hexane was evaporated by rotary evaporation, the residue was purified by silica gel column chromatography (elution by using petroleum ther : ethyl acetate = 5:1) to obtain the alcohol product and the product was characterized by ¹H NMR, ¹³C NMR. All of these mentioned reactions were carried out at least twice to check for reproducibility.

RESULTS AND DISCUSSION

Effect of solvent in reduction reaction: The reduction of hypnone by Co-doped ammonia borane was studied in

different solvents to figure out the solvent effect. The result showed that reduction of carbonyl group was facilitated in protic solvents (Table-1). When the reaction was in aprotic solvents, precipitate was generated and the 1-phenylethanol was achieved only after hydrolysis of the precipitate in aqueous HCl solution or methanolysis of the precipitate in methanol. According to Berke and co-workers¹², the generated precipitate was borate ester. The reaction in alcohols solvents achieved higher yield of 1-phenylethanol than in water, which was probably due to the better solubility of reactant in alcohols. And the methanol mediated reaction showed the best performance.

TABLE-1
REDUCTION OF HYPNONE WITH Co-DOPED AMMONIA BORANE IN DIFFERENT SOLVENTS^a



Entry	Solvent	Yield ^b (%)
1	Neat water	81
2	Methanol	90
3	Ethanol	85
4	Isopropanol	82
5	Acetonitrile	58 ^c
6	Tetrahydrofuran	76 ^c
7	Dichloromethane	65 ^c
8	Toluene	78 ^c

^aAll reactions were carried out with Co-doped ammonia borane (5 mmol), hypnone (10 mmol) in solvent (15 mL) at room temperature for 3 h; ^bIsolated yields; ^cYield after hydrolysis

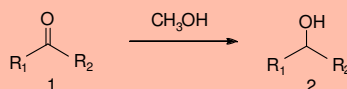
Chemoselective reduction of carbonyl compounds by ammonia borane and Co-doped ammonia borane: As shown in Table-2, several structurally different carbonyl compounds underwent reduction to corresponding alcohols with ammonia borane and 2 mol % Co-doped ammonia borane in methanol, respectively. The carbonyl group of carbonyl compounds was selectively reduced by ammonia borane or Co-doped ammonia borane while other unsaturated groups such as double bond (1a-1d, 1g), nitro (1e), ester group (1f) and phenyl group (1h) were retained. It is noteworthy that aromatic ketones reduced by Co-doped ammonia borane with high yields at room temperature within several hours.

Berke and co-workers have reported the reaction route of reduction of carbonyl compounds with ammonia borane in methanol¹². In this reaction route, the alcoholysis of ammonia borane was the rate-determined step. The addition of transition metal catalysts could accelerate the alcoholysis of ammonia borane¹³. Besides, cobalt element acted as a kind of Lewis acid could activate the carbonyl group¹⁴. Therefore, the doped Co-based catalysts could accelerate the reduction reaction.

Chemical state of cobalt in Co-doped ammonia borane:

Noting that ammonia borane was a reducing agent and the overall reaction environment was reductive, cobalt can hardly keep the Co²⁺ state. Electron paramagnetic resonance was employed to identify the chemical state of cobalt doped in ammonia borane. An absorption at $g = 2.14$ was observed (Fig. 1), which was far from that of metallic cobalt ($g = 1.41$)¹⁵ and close to that of Co⁺ ($g = 2.16$)^{15,16}. It was worth noting that paramagnetic Co²⁺ could not give a spectrum because of fast

TABLE-2
CHEMOSELECTIVE REDUCTION OF CARBONYL COMPOUNDS TO ALCOHOLS WITH AMMONIA BORANE AND Co-DOPED AMMONIA BORANE^a



Entry	Substrate	Product	Reductant	Time	Yield ^b (%)
1			AB	15 min	79
2	1a	2a	Co-doped AB	5 min	87
3			AB	15 min	90
4	1b	2b	Co-doped AB	5 min	98
5			AB	15 min	80
6	1c	2c	Co-doped AB	5 min	89
7			AB	15 min	82
8	1d	2d	Co-doped AB	5 min	92
9			AB	15 min	87
10	1e	2e	Co-doped AB	5 min	95
11			AB	15 min	90
12	1f	2f	Co-doped AB	5 min	97
13			AB	2 h	77
14	1g	2g	Co-doped AB	2 h	95
15			AB	16 h	86
16	1h	2h	Co-doped AB	3 h	90

^aAll reactions were carried out with ammonia borane (AB) or Co-doped ammonia borane (AB) (5 mmol), aldehyde or ketone (10 mmol) in methanol (15 ml) at room temperature. ^bIsolated yields

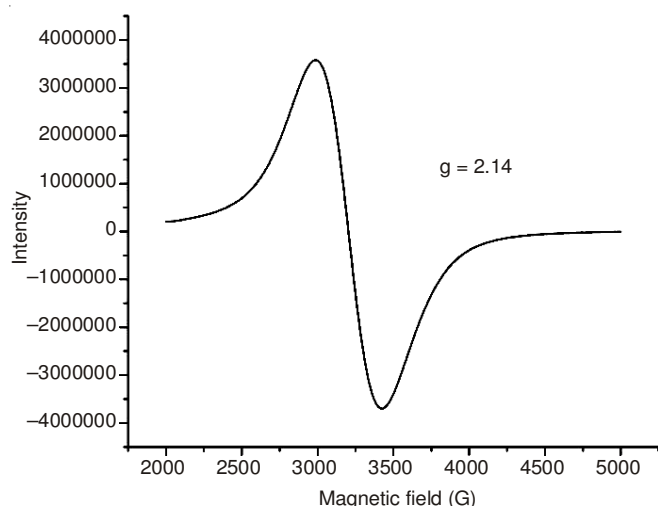


Fig. 1. Electron paramagnetic resonance curve of the Co-doped ammonia borane sample

spin-lattice relaxation at room temperature. It was very likely that part of Co element was in Co^+ state.

When the reaction completed, the cobalt was back to Co^{2+} state, according to electron paramagnetic resonance characterization. Further investigations on the chemical state of Co element and the reaction mechanism are needed.

Recyclability of Co-based catalysts: The reusability of Co-based catalysts was investigated in the model reaction of reduction of hypnone. When the reduction reaction completed, methanol was evaporated and hexane was used to extract the alcohol. The residue was dried over anhydrous magnesium sulfate and achieved red solid of which the main components was CoCl_2 . The solid was reused for the next reduction reaction. As shown in Fig. 2, the Co-based catalysts could be reused up to 4 times without significant loss in activity.

Conclusion

Here we have reported a selective and new procedure for chemoselective reduction of carbonyl compounds to corresponding alcohols by Co-doped ammonia borane. The advantages offered by this method include readily available and stable reagent, excellent yields, mild conditions, operational simplicity and applicability to a wide range of substrates. Characterization results of Co-doped ammonia borane show that the Co element in partially reduced chemical state, could catalyze the reduction reaction.

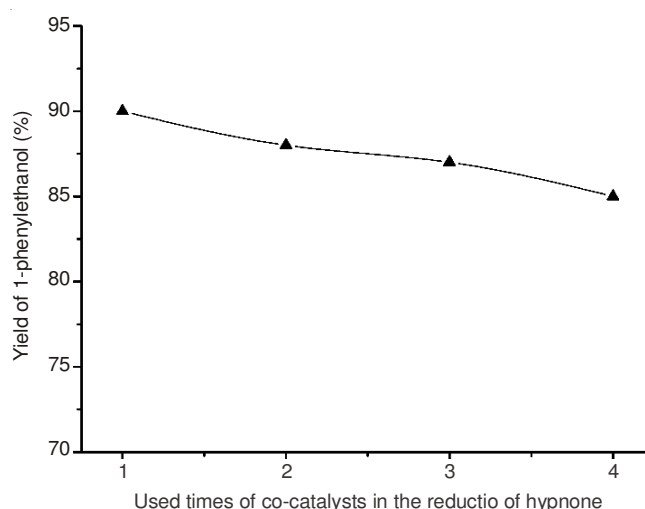


Fig. 2. Recyclability of Co-based catalysts

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