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Zn(BH₄)₂/Al₂O₃: A new synthetic method for the efficient and convenient reduction of organic carbonyl compounds to their corresponding alcohols

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Abstract: Zn(BH₄)₂ (0.5–2 mmol) in the presence of Al₂O₃ (1 mmol) reduces a variety of organic carbonyl compounds such as aldehydes, ketones, acylolins, α -diketones and α,β -unsaturated carbonyl compounds to their corresponding alcohols. The reduction reactions were realized in THF at room temperature affording high to excellent yields of the products. The chemoselective reduction of aldehydes over ketones was successfully accomplished with this reducing system. In addition, regioselectivity and exclusive 1,2-reduction of conjugated carbonyl compounds to their corresponding allylic alcohols in high to excellent yields was successfully accomplished.

Keywords: Zn(BH₄)₂; Al₂O₃; reduction; carbonyl compounds; chemoselective; regioselectivity.

INTRODUCTION

It is well known that sodium borohydride reduces organic carbonyl compounds to their corresponding alcohols using enormously different reducing systems.¹ In order to control the reducing power of the reagent, hundreds of substituted borohydrides have been introduced in the chemical literature and many are now commercially available, *e.g.*, Li(BH₄),^{2a–c} K(BH₄),^{2d} Ca(BH₄)₂,^{3a} Cu(BH₄)₂,^{3b–d} Ti(BH₄)₃,⁴ Zr(BH₄)₄,^{5a,b} LiBH₄, Ca(BH₄)₂ and Zn(BH₄)₂ are the modified borohydride agents that have better solubility in aprotic solvents, so their uses and applications are of interest in organic synthesis. Among these reagents, zinc borohydride is unique because: a) Zn²⁺ is a soft Lewis acid in comparison to Ca²⁺, Li⁺ and Na⁺, which are hard acids and b) better coordination ability of Zn²⁺, which imparts selectivity in hydride transfer reactions. In addition, reduction of aldehydes and ketones with NaBH₄ impregnated on neutral

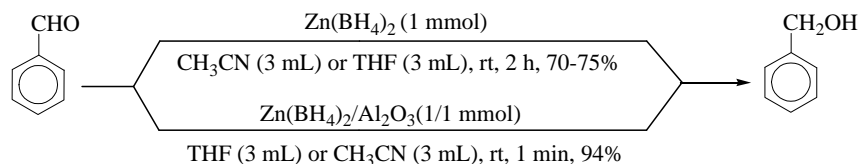
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Al_2O_3 under microwave irradiation has been reported. Although the reported method is fast for the reduction of aldehydes, in the case of ketones, the need for large amounts of NaBH_4 (eightfold) and the moderate yields of the products are major limitations.^{5c-d} On the other hand, zinc tetrahydroborate, $\text{Zn}(\text{BH}_4)_2$, as a non-conventional hydride transfer agent, has been reported to effect very efficient chemo-, regio- and stereoselective reductions. This potential reducing agent is neutral and can be used in a range of aprotic solvents, such as ether, THF and DMF. In spite of this, zinc tetrahydroborate has been used less than regular reducing agents in laboratories for the reduction of organic compounds, probably because of its non-availability as a commercial reagent, being freshly prepared in solution, and the problem of controlling its reducing power. To overcome these limitations, stable modifications of $\text{Zn}(\text{BH}_4)_2$ in the form of tertiary amino or phosphinoligand complexes, such as $[\text{Zn}(\text{BH}_4)_2(\text{dabco})]$ (dabco: 1,4-diazabicyclo [2.2.2.] octane,^{2,6} $[\text{Zn}(\text{BH}_4)_2(\text{pyz})]_n$ (pyz: pirazin),⁷ $[\text{Zn}(\text{BH}_4)_2(\text{Ph}_3\text{P})_{1-2}]$,⁸ $[\text{Zn}(\text{BH}_4)_2(\text{bpy})]$ (bpy: bipyridine),⁹ $[\text{Zn}(\text{BH}_4)_2(\text{py})]$ (py: pyridine),¹⁰ $[\text{Zn}(\text{BH}_4)_2\text{-XP}_4]$ (XP_4 : crosslinked 4-polyvinylpyridine),¹¹ $[\text{Zn}(\text{BH}_4)_2(\text{nmi})]$ ^{12a} (nmi: *N*-methylimidazole) and $[\text{Zn}(\text{BH}_4)_2(\text{nic})]$ (nic: nicotine)^{12b} have been made and used for the reduction of organic compounds. The challenge in chemistry to develop efficient processes, reaction media and conditions are some of the most important issues in the scientific community in this matter. In this context and in continuation of previous studies with modified reducing systems,¹² herein, $\text{Zn}(\text{BH}_4)_2/\text{Al}_2\text{O}_3$ is introduced as a new combination reducing system for the efficient and convenient reduction of carbonyl compounds to their corresponding alcohols.

RESULTS AND DISCUSSION

Ranu *et al.* reported $\text{Zn}(\text{BH}_4)_2$ to be a reducing agent capable of reducing some organic carbonyl compounds.^{13a-c} To investigate the influence of alumina on the rate of reduction and the lack of systematic information on the reduction of carbonyl compounds with zinc borohydride in the presence of alumina without using any other agent directed the focus of the present study to an investigation of the influence of alumina as a moderator catalyst on this transformation. The preliminary experiments showed that the reduction of benzaldehyde (1 mmol) as a model compound with $\text{Zn}(\text{BH}_4)_2$ (1 mmol) in THF or CH_3CN was not completed after 1 h at room temperature. However, when this reaction was performed in the presence of neutral alumina (1 mmol), the rate of reduction was dramatically accelerated and the reaction was completed within 1 min (Scheme 1).

These results prompted an investigation of the optimum reaction conditions to examine the influence of alumina as a catalyst. For the selection of the appropriate solvent(s) and amount of catalyst in such reductions, a set of experiments was performed on the reduction of benzaldehyde and acetophenone as model compounds, the results of which are given in Tables I and II, respectively.



Scheme 1. Comparison of the reduction of benzaldehyde by $\text{Zn}(\text{BH}_4)_2$ in the presence and absence of neutral alumina.

TABLE I. Optimization reaction conditions for reduction of benzaldehyde with the $\text{Zn}(\text{BH}_4)_2$, neutral Al_2O_3 system at room temperature

Entry	Molar ratio ^a	Solvent (3 mL)	Time, h	Conversion ^b , %
1	(1/0.5/0)	THF	1	<100 ^c
2	(1/1/0)	THF	2	<100 ^c
3	(1/1/0)	CH_3CN	2	<100 ^c
4	(1/0.5/1) ^d	THF	0.08	100
5	(1/0.5/2)	THF	1.5	100
6	(1/0.5/1) ^d	CH_3CN	0.08	100
7	(1/1/1)	THF	0.016	100

^aMolar ratio benzaldehyde/ $\text{Zn}(\text{BH}_4)_2/\text{Al}_2\text{O}_3$; ^bcompletion of the reaction was monitored by TLC (eluent, CCl_4 , Et_2O : 5/2); ^cthe yields of isolated pure products were 50 % for entry 1, 75 % for entry 2 and 70 % for entry 3;

^dthe reduction reactions were performed in the presence of acidic, basic or neutral alumina and the same results were obtained

TABLE II. Optimization reaction conditions for the reduction of acetophenone with the $\text{Zn}(\text{BH}_4)_2$, neutral Al_2O_3 system at room temperature

Entry	Molar ratio ^a	Solvent (3 mL)	Time, h	Conversion ^b , %
1	(1/1/0)	THF	1	<100 ^c
2	(1/1/1) ^d	THF	1	100
3	(1/1/2)	THF	1	<100 ^c
4	(1/2/1) ^d	THF	0.8	100
5	(1/2/2)	THF	1.2	100

^aMolar ratio acetophenone/ $\text{Zn}(\text{BH}_4)_2/\text{Al}_2\text{O}_3$; ^bcompletion of the reaction was monitored by TLC (eluent, CCl_4 , Et_2O : 5/2), ^cthe yield of isolated pure products were 60 % for entry 1 and 80 % for entry 3; ^dthe reduction reactions were performed in the presence of acidic, basic or neutral alumina and the same results were obtained

The results showed that the reduction of benzaldehyde at room temperature with 0.5 molar amount of $\text{Zn}(\text{BH}_4)_2$ in the presence of 1 molar amount of neutral Al_2O_3 was very efficient (Table I, entries 4 and 6). In addition, it is noteworthy that the reduction reactions were performed in the presence of acidic and basic Alumina and the same results were obtained. Then these optimal conditions were applied for the reduction of structurally different aliphatic and aromatic aldehydes with neutral alumina. All the reactions were performed with 0.5 mol $\text{Zn}(\text{BH}_4)_2$ per mol aldehyde at room temperature and the corresponding primary alcohols were obtained in high to excellent yields (83–97 %), as could be seen in Table III.

TABLE III. Reduction of aldehydes (1 mmol) with the $\text{Zn}(\text{BH}_4)_2$ (0.5 mmol)/ Al_2O_3 (1 mmol) system in THF (3 mL) at room temperature; the reduction reactions were realized in the presence of neutral alumina

Entry	Substrate	Product	Time h	Yield ^a %	M.p. or B.p., °C	
					Found	Reported ¹⁴
1	Benzaldehyde	Benzyl alcohol	0.08	94	203–204	205
2	4-Chlorobenzaldehyde	4-Chlorobenzyl alcohol	0.08	92	71–73	70–72
3	3-Chlorobenzaldehyde	3-Chlorobenzyl alcohol	0.08	96	238	237
4	2,4-Dichlorobenzaldehyde	2,4-Dichlorobenzyl alcohol	0.08	90	56–58	55–58
5	4-Methylbenzaldehyde	4-Methylbenzyl alcohol	0.1	93	60–62	59–61
6	4-Methoxybenzaldehyde	4-Methoxybenzyl alcohol	0.1	93	258	259
7	4-Hydroxybenzaldehyde	4-Hydroxybenzyl alcohol	0.1	97	119–122	118–122
8	2-Hydroxybenzaldehyde	2-Hydroxybenzyl alcohol	0.1	92	84–85	83–85
9	3-Nitrobenzaldehyde	3-Nitrobenzyl alcohol	0.08	94	31–33	30–32
10	4-Nitrobenzaldehyde	4-Nitrobenzyl alcohol	0.08	94	92–94	92–94
11	4-Hydroxy-3-methoxybenzaldehyde	4-Hydroxy-3-methoxybenzyl alcohol	0.1	97	114–115	113–115
12	Furfural	Furfuryl alcohol	0.1	88	169–170	170
13	1-Naphthaldehyde	1-Naphthylmethanol	0.1	90	61–62	61–63
14	2,6-Dimethylhept-5-enal	2,6-Dimethylhept-5-en-1-ol	0.08	90	225–227	225–226
15	Heptanal	1-Heptanol	0.08	83	177	176

^aYields refer to isolated pure products

Next, attention was turned to the reduction of ketones using this reducing system. The low reactivities of ketones relative to those of aldehydes led to the reduction reactions being performed under different conditions, *i.e.*, the reductions were performed with 1 molar amounts of $\text{Zn}(\text{BH}_4)_2$ at room temperature in the presence of 1 molar amounts of neutral Al_2O_3 in THF (Table II, entry 2). The utility of this reducing system was further explored with the reduction of structurally different aliphatic and aromatic ketones using 1 mol $\text{Zn}(\text{BH}_4)_2$ in the presence of 1 mol neutral Al_2O_3 per mol ketone in THF at room temperature. Such reductions were also efficient and the corresponding secondary alcohols were obtained in high to excellent yields (87–98 %) (Table IV).

The synthetic applications of vicinal diols are well known and their preparations from the reduction of acyloins or α -diketones have attracted a great deal of attention. Reduction of α -diketones usually gives a mixture of α -hydroxy ketones and vicinal diols. Selective reduction of α -diketones to acyloins¹⁵ or vicinal diols¹⁶ can be undertaken with some chemical or biochemical reagents. Reduction of α -diketones to vicinal diols with modified hydroborate agents is also a subject of interest^{12,17} and this goal was easily achieved by $\text{Zn}(\text{BH}_4)_2$ (2 mol) in the presence of 1 mol neutral Al_2O_3 in THF at room temperature. The

reduction reactions were performed efficiently in short reaction times (20–40 min) (92–95 %) (Table V). Under different conditions, attempts to reduce α -diketones into acyloins were unsatisfactory and only vicinal diols were identified as the sole products. In addition, reduction of acyloins to vicinal diols is also a subject of interest in organic synthesis. The applications of non-hydridic reductants¹⁸ and modified hydroborate^{12,17} have also been reported for such reductions. Using $\text{Zn}(\text{BH}_4)_2$ (1 mol) in the presence of neutral Al_2O_3 (1 mol) in THF also easily provided this transformation at room temperature. Acyloin compounds were reduced to their corresponding vicinal diols in high to excellent yields with this reducing system (90–94 %) (Table V, entries 2 and 4).

TABLE IV. Reduction of ketones (1 mmol) with the $\text{Zn}(\text{BH}_4)_2$ (1 mmol)/ Al_2O_3 (1 mmol) system in THF (3 mL) at room temperature; the reduction reactions were realized in the presence of neutral alumina

Entry	Substrate	Product	Time h	Yield ^a %	M.p. or B.p., °C	
					Found	Reported ¹⁴
1	Benzophenone	Diphenylmethanol	3	96	65–67	65–67
2	Acetophenone	1-Phenylethanol	1	93	203	204
3	4-Bromoacetophenone	1-(4-Bromophenyl)ethanol	1	98	37–38	36–37
4	4-Methylacetophenone	1-(4-Methylphenyl)ethanol	3	93	219–221	218–220
5	4-Methoxybenzophenone	(4-Methoxyphenyl)phenylmethanol	4	90	68–69	67–69
6	2,3-Dihydro-1 <i>H</i> -inden-1-one	2,3-Dihydro-1 <i>H</i> -inden-1-ol	1.5	95	52–55	50–54
7	9 <i>H</i> -Fluoren-9-one	9 <i>H</i> -Fluoren-9-ol	1.6	93	153–154	153–154
8	4-Phenylcyclohexanone	4-Phenylcyclohexanol	1	87	58–60	58
9	4-Phenyl-2-butanone	4-Phenylbutan-2-ol	0.8	90	131–132	132

^aYields refer to isolated pure products

The chemoselective reduction of one functional group without affecting the other one is a well-known strategy for the preparation of molecules with ever-increasing complexity in organic synthesis.

This subject is of great interest and numerous modified hydroborate systems have been reported for it.^{6,8–10a–c,12,13b,17,19} Since under the defined conditions, the reduction of aldehydes and ketones with $\text{Zn}(\text{BH}_4)_2$ in the presence of Al_2O_3 is dependent on the molar ratio of $\text{Zn}(\text{BH}_4)_2$ to Al_2O_3 , it was thought that this system could have a chemoselectivity towards the reduction of aldehydes over ketones. This fact was demonstrated with the selective reduction of benzaldehyde in the presence of acetophenone using 0.5 mol $\text{Zn}(\text{BH}_4)_2$ in the presence of 1 mol neutral Al_2O_3 at room temperature in THF (Table VI, entry 3) (Scheme 2).

TABLE V. Reduction of acyloins and α -diketones with the $\text{Zn}(\text{BH}_4)_2/\text{Al}_2\text{O}_3$ (1 mmol) in THF (3 mL) at room temperature; the reduction reactions were realized in the presence of neutral alumina

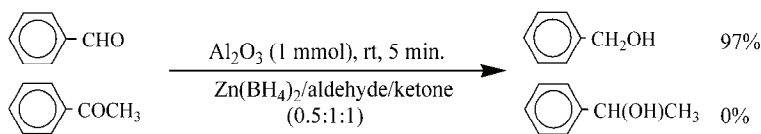
Entry	Substrate	Product	$\text{Zn}(\text{BH}_4)_2$ / Substrate	Time h	Yield ^a %	M.p. or B.p., °C	
						Found	Reported ¹⁴
1	Benzyl ^b	1,2-Diphenyl-ethane-1,2-diol	2/1	0.33	95	–	–
2	Benzoin ^b	1,2-Diphenyl-ethane-1,2-diol	1/1	0.33	90	–	–
3	1,2-Bis(4-methoxyphenyl)ethane-1,2-dione ^b	1,2-Bis(4-methoxyphenyl)-ethane-1,2-diol	2/1	0.58	92	–	–
4	2-Hydroxy-1,2-bis(4-methoxyphenyl)-ethanone ^b	1,2-Bis(4-methoxyphenyl)-ethane-1,2-diol	1/1	0.5	94	–	–
5	1,3-Diphenylpropane-1,2-dione	1,3-Diphenylpropane-1,2-diol	2/1	0.67	95	63–64	63–64

^aYields refer to isolated pure products; ^cthe pinacols were formed as *dl-meso* mixtures that were not separated

TABLE VI. Optimization of the reaction conditions for the competitive reduction of benzaldehyde (1 mmol) and acetophenone (1 mmol) with the $\text{Zn}(\text{BH}_4)_2$, Al_2O_3 system in THF (3 mL) at room temperature; the reduction reactions were performed in the presence of neutral alumina

Entry	Molar ratio ^a	Time, h	Yield of benzyl alcohol ^b , %	Yield of 1-phenylethanol ^b , %
1	1/1/0.5/0	1	50	30
2	1/1/0.5/0.5	1	79	6
3 ^c	1/1/0.5/1	0.08	97	0
4	1/1/1/1	1	94	30
5	1/1/2/1	1	96	51

^aMolar ratio as benzaldehyde, acetophenone, $\text{Zn}(\text{BH}_4)_2$, Al_2O_3 ; ^byields refer to isolated pure products by PLC (eluent, CCl_4 , Et_2O : 5/2); ^cGC analysis was also performed



Scheme 2. Competitive reduction of benzaldehyde and acetophenone with $\text{Zn}(\text{BH}_4)_2$ /neutral Al_2O_3 system in THF; the ratio in parentheses is in mmol.

The usefulness of this chemoselectivity of the reduction was further examined with the reduction of benzaldehyde in the presence of other ketones. As shown in Table VII, benzaldehyde was reduced exclusively, or nearly so.

Reduction of unsaturated carbonyl compounds with sodium borohydride, one of the most widely utilized reducing agents, is highly solvent dependent and generally does not result in useful regioselectivity.^{20a,b} To control the reducing potential and selectivity of NaBH_4 into regioselective 1,2-reduction of conju-

gated enones, numerous hydroborate agents have been developed in the following ways: a) by the replacement of hydride(s) with sterically bulky substituents or electron-withdrawing/releasing groups in order to discriminate between the structural and electronic environments of carbonyl groups;^{20c-f} b) combination with Lewis acids^{20g-k,3a} and mixed solvent systems;^{20a} c) use of transition metal hydroborates and their new modifications;^{20l} d) use of quaternary ammonium and phosphonium tetrahydroborates;^{19e-f,20m-n} e) and finally immobilization on an anion exchange resin.^{20o}

TABLE VII. Competitive reduction of benzaldehyde (1 mmol) in the presence of ketones (1 mmol) to their corresponding alcohols with $\text{Zn}(\text{BH}_4)_2$ (0.5 mmol), neutral Al_2O_3 (1 mmol) in THF (3 mL) at room temperature

Entry	Ketone	Time, h	Yield1 ^a , %	Yield2 ^b , %
1	Acetophenone	0.08	97	0
2	Benzophenone	0.08	93	2
3	9H-Fluoren-9-one	0.08	95	3
4	4-Phenylbutan-2-one	0.08	91	8

^aYield1 of benzyl alcohol refers to isolated pure products by PLC (eluent, CCl_4 , Et_2O : 5/2); ^byields of corresponding alcohols for ketones refer to isolated pure products by PLC (eluent, CCl_4 , Et_2O : 5/2)

The usefulness of the studied reducing system was further investigated with the regioselective 1,2-reduction of α,β -unsaturated carbonyl compounds. Thus, the reduction of cinnamaldehyde was examined. The reduction reaction occurred with 0.5 mmol $\text{Zn}(\text{BH}_4)_2$ in the presence of 1 mmol neutral Al_2O_3 in 5 min at room temperature in THF with a perfect regioselectivity and the product cinnamyl alcohol was obtained in high yield (Table VIII, entry 1). This procedure was also applied for the reduction of citral at room temperature and geraniol was obtained in 92 % yield (Table VIII, entry 2).

Furthermore, the reductions of conjugated enones with the studied reducing system were investigated. The results showed that the procedure was also regioselective and efficient, but the reduction reactions were performed using 1 molar amounts of $\text{Zn}(\text{BH}_4)_2$ in the presence of 1 molar amounts of neutral Al_2O_3 at room temperature in THF. Regioselective 1,2-reductions of benzylideneacetone and chalcone were successfully achieved, with high to excellent yields of the corresponding allylic alcohols (Table VIII, entries 3 and 4).

In order to show the efficiency of the reducing system $\text{Zn}(\text{BH}_4)_2/\text{Al}_2\text{O}_3$, the results obtained in the present were compared with those of reported in the literature for $\text{NaBH}_4/\text{MoCl}_5$,^{21a} $\text{NaBH}_4/\text{Dowex1-x8}$,^{21b} $[\text{Zn}(\text{BH}_4)_2(\text{bpy})]$,⁹ $[\text{Zn}(\text{BH}_4)_2(\text{py})]$,¹⁰ $[\text{Zn}(\text{BH}_4)_2(\text{Ph}_3\text{P})_2]$,⁸ $\text{Ph}_3\text{PMe}(\text{BH}_4)$ ^{20m} and $[\text{PhCH}_2(\text{dabco})\text{BH}_4]$ ^{19e}, as given in Table IX.

TABLE VIII. Reduction of conjugated carbonyl compounds with $Zn(BH_4)_2$, Al_2O_3 (1 mmol) in THF (3 mL) at room temperature; the reduction reactions were performed in the presence of neutral alumina

Entry	Substrate	Product	$Zn(BH_4)_2$ / Substrate	Time h	Yield ^a %	M.p. or B.p., °C	
						Found	Reported ¹⁴
1	Cinnamaldehyde	3-Phenyl-2-propen-1-ol	0.5/1	0.08	96	33–34	33–35
2	<i>Cis</i> and <i>trans</i> citral	<i>Cis</i> and <i>trans</i> -3,7-dimethyl-2,6-octadien-1-ol ^b	0.5/1	0.08	92	–	–
3	Benzylideneacetone	4-Phenyl-3-butene-2-ol	1/1	1	95	55–56	55–57
4	Chalcone	1,3-Diphenylprop-2-en-1-ol	1/1	3	91	33–34	33–34

^aYields refer to isolated pure products; ^b*cis* and *trans* geraniol were not separated

TABLE IX. Comparison of the reductions of aldehydes and ketones with $Zn(BH_4)_2/Al_2O_3$ system and with other reported reducing systems; I – $Zn(BH_4)_2/Al_2O_3$, II – $NaBH_4/MoCl_5$, III – $NaBH_4/Dowex1-x8$, IV – $[Zn(BH_4)_2(bpy)]$, V – $[Zn(BH_4)_2(py)]$, VI – $[Zn(BH_4)_2(Ph_3P)_2]$, VII – $Ph_3PMe(BH_4)$, VIII – $[PhCH_2(dabco)]BH_4$

Entry	Substrate	Molar ratio (reagent/substrate), time, h, yield, %							
		I	II ^{21a}	III ^{21b}	IV ⁹	V ¹⁰	VI ⁸	VII ^{20m}	VIII ^{19e}
1	Benzaldehyde	0.5, 0.08, 94	0.5, 0.03, 96	1, 0.05, 96	0.25, 0.02, 95	1, 0.5, 91	–	1, Im ^a , 90	1, 0.25, 90
2	4-Methoxybenzaldehyde	0.5, 0.1, 93	1.5, 3, 99	1.5, 3, 99	0.35, 0.17, 99	1, 1.3, 96	1, 0.17, 89	1, Im, 83	2, 0.8, 85
3	4-Chlorobenzaldehyde	0.5, 0.08, 92	1, 0.15, 99	1, 0.15, 99	0.25, 0.08, 98	1, 0.2, 99	1, Im, 88	1, Im, 86	1, 0.23, 90
4	Benzophenone	1, 3, 96	3, 3.2, 98	3, 3.2, 98	1, 0.75, 99	2, 4.3, 97	–	–	2, 21.5, 90
5	9 <i>H</i> -Fluoren-9-one	1, 1.6, 93	2, 1.8, 94	2, 1.8, 94	1, 1.5, 94	2, 5.3, 98	2, 0.33, 85	1.6, 18, 80	–
6	Benzoin	1, 0.33, 90	2, 0.17, 96	2, 0.17, 96	0.5, 0.08, 91	0.5, 0.5, 97	–	–	–

^aImmediately

EXPERIMENTAL

All substrates and reagents of the best available quality were purchased from commercial sources and used without further purification. IR and ¹H-NMR spectra were recorded on a PerkinElmer FT-IR RXI and a 300 MHz Bruker spectrometers, respectively. Agilent 6890N gas chromatograph equipped with a FID detector was used in this study. The products were characterized by their ¹H-NMR or IR spectra and comparison with authentic samples (melting points or boiling points). The organic layers were dried over anhydrous sodium sulfate. All

yields refer to isolated pure products. TLC on silica gel 60 F₂₅₄ aluminum sheets was applied for purity determination of the substrates and products and to monitor the reactions.

A typical procedure for reduction of aldehydes with the Zn(BH₄)₂/Al₂O₃ system in THF

Zn(BH₄)₂ was prepared from ZnCl₂ and NaBH₄ according to an established procedure from the literature.⁵ In a round-bottomed flask (10 mL) equipped with a magnetic stirrer, a solution of benzaldehyde (0.106 g, 1 mmol) in THF (3 mL) was prepared. To this solution, Zn(BH₄)₂ (0.048 g, 0.5 mmol) and then neutral Al₂O₃ (0.101 g, 1 mmol) were added and the mixture was stirred at room temperature for 5 minutes. Completion of the reaction was monitored by TLC (eluent, CCl₄/Et₂O: 5/2). Then, distilled water (1 mL) was added to the reaction mixture and stirring was continued for 5 min.. The mixture was extracted with CH₂Cl₂ (3×6 mL) and dried over anhydrous Na₂SO₄. Evaporation of the solvent and a short column chromatography of the resulting crude material over silica gel (0.015–0.040 mm, eluent, CCl₄/Et₂O: 5/3) afforded the pure liquid benzyl alcohol (0.102 g, 94 %, Table III, entry 1).

A typical procedure for reduction of ketones to alcohols with the Zn(BH₄)₂/Al₂O₃ system in THF

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer, a solution of acetophenone (0.121 g, 1 mmol) in THF (3 mL) was prepared. To this solution, Zn(BH₄)₂ (0.095 g, 1 mmol) and then neutral Al₂O₃ (0.101 g, 1 mmol) were added. The resulting mixture was stirred at room temperature for 60 min. The progress of the reaction was monitored by TLC (eluent, CCl₄/Et₂O: 5/2). After completion of the reaction, distilled water (1 mL) was added to the reaction mixture and then stirring was continued for an additional 5 min. The mixture was extracted with CH₂Cl₂ (3×8 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and short column chromatography of the resulting crude material over above mentioned silica gel afforded pure crystals of 1-phenylethanol (0.11 g, 93 % yield, Table IV, entry 2).

A typical procedure for reduction of α-diketones and acyloins with the Zn(BH₄)₂/Al₂O₃ system in THF

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer, a solution of benzil (0.21 g, 1 mmol) in THF (3 mL) was prepared. To this solution, Zn(BH₄)₂ (0.190 g, 2 mmol) and then neutral Al₂O₃ (0.101 g, 1 mmol) were added. The resulting mixture was stirred at room temperature for 20 min. The progress of the reaction was monitored by TLC (eluent, CCl₄/Et₂O: 5/2). After completion of the reaction, distilled water (1 mL) was added to the reaction mixture and stirring was continued for an additional 5 min. The mixture was extracted with CH₂Cl₂ (3×10 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and short column chromatography of the resulting crude material over above mentioned silica gel afforded pure crystals of 1,2-diphenylethane-1,2-diol (0.20 g, 95 % yield, Table V, entry 1).

A typical procedure for the competitive reduction of aldehydes and ketones with the Zn(BH₄)₂/Al₂O₃ system in THF (method A)

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer, a solution of benzaldehyde (0.106 g, 1 mmol) and acetophenone (0.120 g, 1 mmol) in THF (3 mL) was prepared. To this solution, Zn(BH₄)₂ (0.048 g, 0.5 mmol) and then neutral Al₂O₃ (0.101 g, 1 mmol) were added and the mixture was stirred at room temperature. The progress of the reaction was monitored by TLC. After 5 min, the reaction mixture was quenched by addition of distilled water (1 mL) and this mixture was then stirred for an additional 5 min. The mixture was extracted with CH₂Cl₂ (3×8 mL) and dried over anhydrous sodium sulfate. After

the evaporation of solvent, the resulting crude products (0.223 g) were separated by plate layer chromatography (PLC) over silica gel (60 F₂₅₄ (0.063–0.200 mm), eluent, CCl₄/Et₂O: 5/2), which afforded pure liquid benzyl alcohol as the sole product (0.106 g, 97 %) and acetophenone (0.108 g, 89 %) as intact material (Table VI, entry 3).

A typical procedure for competitive reduction of aldehydes and ketones with Zn(BH₄)₂/Al₂O₃ system in THF (method B)

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer, a solution of benzaldehyde (0.106 g, 1 mmol) and acetophenone (0.121 g, 1 mmol) in THF (3 mL) was prepared. A sample of reaction mixture in THF is injected (0.1 μL) onto a HP5 30 m×25 μm capillary column. The initial column temperature (100 °C) was held for 2 min, then increased at 15 °C min⁻¹ to 240 °C and held for 15 min. Benzaldehyde eluted first (7.28 min) followed by acetophenone (10.29 min) with a relative response ratio of about 1:1 (Instrument parameters: injector temperature, 250 °C; detector temperature, 300 °C; flow rate (He), 45 mL min⁻¹, with He as the make-up gas). Then, to this solution, Zn(BH₄)₂ (0.048 g, 0.5 mmol) and then neutral Al₂O₃ (0.101 g, 1 mmol) were added and the mixture was stirred at room temperature. The progress of the reaction was monitored by TLC. After 5 min, the reaction mixture was quenched by the addition of distilled water (0.5 mL) and the stirring was continued for an additional 5 min, and dried over anhydrous sodium sulfate. Again, a sample of reaction mixture in THF is injected (0.1 μL) onto the GC column under the same conditions. Benzyl alcohol eluted first (9.71 min) followed by acetophenone (10.29 min) with a relative response ratio of about 1:1. The reduction procedure afforded pure liquid benzyl alcohol as the sole product and acetophenone as unreacted material.

The typical procedure for the regioselective 1,2-reduction of conjugated carbonyl compounds with the Zn(BH₄)₂/Al₂O₃ system in THF

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer, a solution of benzylideneacetone (0.146 g, 1 mmol) in THF (3 mL) was prepared. To this solution, Zn(BH₄)₂ (0.095 g, 1 mmol) and then neutral Al₂O₃ (0.101 g, 1 mmol) were added. The resulting mixture was stirred at room temperature. The progress of the reaction was monitored by TLC (eluent, CCl₄/Et₂O: 5/2). After completion of the reaction within 60 min, distilled water (1 mL) was added to the reaction mixture and this mixture was then stirred for an additional 5 min. The mixture was extracted with CH₂Cl₂ (3×10 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and short column chromatography of the resulting crude material over silica gel (eluent, CCl₄/Et₂O: 5/2) afforded pure liquid 4-phenyl-3-buten-2-ol (0.140 g, 95 % yield, Table VIII, entry 3).

CONCLUSIONS

In this investigation, it was shown that the combination system of Zn(BH₄)₂/Al₂O₃ in THF reduces a variety of carbonyl compounds to their corresponding alcohols in high to excellent yields. The reduction reactions were performed with 0.5–2 mmol Zn(BH₄)₂ in the presence of 1 mmol Al₂O₃ in THF. Reduction of acyls and α-diketones by this reducing system also efficiently produced the corresponding vicinal diols. In addition, the chemoselective reduction of aldehydes over ketones was successfully accomplished with this reducing system. Regioselectivity of this system was also investigated with exclusive 1,2-reduction of conjugated carbonyl compounds to their corresponding allylic alcohols in high

to excellent yields. All reductions were realized at room temperature. The high efficiency of the reductions, short reaction times and easy work-up procedure makes this combined reductant an attractive new protocol for the reduction of carbonyl compounds and it could be a useful addition to the existing methodologies.

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ИЗВОД

Zn(BH₄)₂/Al₂O₃: НОВ СИНТЕТИЧКИ ПОСТУПАК ЗА ЕФИКАСНУ РЕДУКЦИЈУ ОРГАНСКИХ КАРБОНИЛНИХ ЈЕДИЊЕЊА ДО ОДГОВАРАЈУЋИХ АЛКОХОЛА

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Zn(BH₄)₂ (0,5–2 mmol) у присуству Al₂O₃ (1 mmol) редукује различита карбонилна једињења, као што су алдехиди, кетони, ацилоини, α-дикетони и α,β-незасићена карбонилна једињења, до одговарајућих алкохола. Реакција се одвија у тетраhydroфурану као растварачу, на собној температури, а принос производа је висок до одличан. Хемиоселективна редукација алдехида у присуству кетона извршена је успешно. Осим тога, постигнута је региоселективност и селективна 1,2-редукција конјугованих карбонилних једињења до одговарајућих алилних алкохола у високом до одличном приносу.

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