Convenient Reduction of Carbonyl Compounds to their Corresponding Alcohols with $NaBH_4/(NH_4)_2C_2O_4$ System

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ABSTRACT

Sodium borohydride (0.4–1.5 equivalents) in the presence of ammonium oxalate (0.2 equivalents) reduces varieties of organic carbonyl compounds such as aldehydes, ketones, acyloins, α-diketones and α,β-unsaturated carbonyl compounds to their corresponding alcohols. Reduction reactions were carried out in acetonitrile in high to excellent yields of products. The chemoselective reduction of aldehydes over ketones was accomplished successfully 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 achieved successfully with this reducing system.

KEYWORDS

Sodium borohydride, reduction, carbonyl compounds, ammonium oxalate, chemoselective, regioselectivity.

1. Introduction

Alcohols and their derivatives occupy an important position in organic synthesis. Preparation of alcohols and their derivatives from the reduction of carbonyl functional groups are of great importance in organic chemistry and there are numerous applications in the fine chemical industry and in the laboratory.[1] A large number of methods including catalytic reduction,[2] hydride homogeneous catalysis,[3] heterogeneous catalysis systems[4] and transfer reagents[5] have been reported to be effective towards carbonyl compounds reduction. In general, most synthetic chemists employ one of two reagents for this transformation, lithium aluminum hydride ($LiAlH_4$) or sodium borohydride ($NaBH_4$). $LiAlH_4$ is a powerful reducing agent which frequently displays poor selectivity for the reduction of multifunctional molecules, while sodium borohydride is a milder reducing agent. It has been used for the reduction of a number of organic functional groups[6] and the rates of reductions are sometimes quite slow with relatively low chemoselectivity. Controlling the reducing power of $NaBH_4$ has been achieved by different types of modifications, such as a) the use of hydride(s) with bulky substituents, i.e. electron-withdrawing or electron-releasing groups,[7] b) the change of the sodium cation to transition metal cations in the preparation of modified reducing reagents,[8] c) the use of quaternary ammonium and phosphonium tetrahydroborates,[9–10] d) the use of Lewis acids[11] and mixed solvent systems,[12] e) utilization of polymeric supports and anion exchange resin,[13a–e] and f) by performing the reduction reactions with sodium borohydride under unconventional energy sources such as microwave and ultrasound irradiations.[13g–h] A literature review also reveals that the reduction of carbonyl compounds can be achieved by $NaBH_4$ under protic conditions with some limitations.[13g] However, we realized that the use of $NaBH_4$ in the presence of ammonium salts (as mineral protic solids) has not been investigated. So, in continuing our efforts for the development of new reducing systems,[14] we decided to investigate the reducing properties of $NaBH_4$ in the presence of ammonium salts (which are convenient and readily available reagents) as the co-reagent for the reduction of a variety of carbonyl compounds. Herein, we thus wish to report a convenient method for reduction of aldehydes, ketones, α-diketones, acyloins and α,β-unsaturated carbonyl compounds to their corresponding alcohols with $NaBH_4/(NH_4)_2C_2O_4$ as new reducing system in CH_3CN.

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2. Experimental

2.1. General

All substrates and reagents were purchased from commercially sources with the best quality. IR and ^{1}H NMR spectra were recorded on PerkinElmer FT-IR RXI and 300 MHz Bruker spectrometers, respectively. The products were characterized by their ^{1}H NMR or IR spectra and comparison with authentic samples (melting or boiling points). Organic layers were dried over anhydrous sodium sulphate. All yields referred to isolated pure products. The purity of products was determined by TLC and ^{1}H NMR. Also, reactions were monitored by TLCs utilizing plates cut from silica gel 60 F_{254} aluminum sheets.

2.2. Typical Procedure for Reduction of Aldehydes with the $NaBH_4/(NH_4)_2C_2O_4$ System

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer, a solution of benzaldehyde (0.106 g, 1 mmol) in CH_3CN (2 mL) was prepared. To this solution, $NaBH_4$ (0.019 g, 0.5 mmol) and then $(NH_4)_2C_2O_4$ (0.25 g, 0.2 mmol) was added and the mixture was stirred at room temperature for 15 min. Completion of the reaction was monitored by TLC (eluent; CCl_4:Et_2O = 5:2). Then, water (5 mL) was added to the reaction mixture and it was stirred for an additional 1 min. The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short-column chromatography of the resulting crude material over silica gel (eluent; CCl_4:Et_2O = 5:3) afforded the pure liquid benzyl alcohol (0.102 g, 94 %, Table 3, entry 1).

2.3. Typical Procedure for Reduction of Ketones to Alcohols with the $NaBH_4/(NH_4)_2C_2O_4$ System

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer and a condenser, a solution of acetophenone (0.12 g, l mmol) in CH_3CN (2 mL) was prepared and $NaBH_4$ (0.038 g,

1 mmol) and $(NH_4)_2C_2O_4$ (0.25 g, 0.2 mmol) were added and the mixture was stirred under reflux conditions for 55 min. TLC monitored the progress of the reaction (eluent; CCl_4:Et_2O = 5:2). After completion of the reaction distilled water (5 mL) was added to the reaction mixture and it was stirred for an additional 1 min. The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and dried over anhydrous sodium sulphate. Evaporation of the solvent and short-column chromatography of the resulting crude material over silica gel (eluent; CCl_4:Et_2O = 5:2) afforded the pure crystals of 1-phenylethanol (0.11 g, 96 % yield, Table 5, entry 2).

2.3. Typical Procedure for Competitive Reduction of Aldehydes and Ketones with the $NaBH_4/(NH_4)_2C_2O_4$ System

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer, a solution of benzaldehyde (0.106 g, 1 mmol) and acetophenone (0.12 g, 1 mmol) in CH_3CN (3 mL) was prepared. To this solution, $NaBH_4$ (0.019 g, 0.5 mmol) and $(NH_4)_2C_2O_4$ (0.25 g, 0.2 mmol) was added. The mixture was stirred at room temperature for 20 min. TLC monitored the progress of the reduction reaction. After 20 min, the reaction mixture was quenched by addition of distilled water (5 mL) and this mixture was then stirred for an additional 1 min. The mixture was extracted with CH_2Cl_2 (5 × 10 mL) and dried over anhydrous sodium sulphate. Evaporation of the solvent and short-column chromatography of the resulting crude materials over silica gel (eluent; CCl_4:Et_2O = 5:2), affords the pure liquid benzyl alcohol as a sole product of reduction reaction and acetophenone as an intact material (Table 6, entry 1).

2.4. Typical Procedure for Reduction of α-Diketones and Acyloins with the $NaBH_4/(NH_4)_2C_2O_4$ System

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer and a condenser, a solution of benzil (0.21 g, 1 mmol) in CH_3CN (2 mL) was prepared and $NaBH_4$ (0.057 g, 1.5 mmol) and $(NH_4)_2C_2O_4$ (0.25 g, 0.2 mmol) were added and the mixture was stirred under reflux conditions for 40 min. TLC monitored the progress of the reaction (eluent; CCl_4:Et_2O = 5:2). After completion of the reaction, distilled water (5 mL) was added to the reaction mixture and this combination was stirred for an additional 1 min. The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and dried over anhydrous sodium sulphate. Evaporation of the solvent and short-column chromatography of the resulting crude material over silica gel (eluent; CCl_4:Et_2O = 5:3) afforded the pure crystals of hydrobenzoin (0.20 g, 95 % yield, Table 7, entry 1).

2.5. Typical Procedure for Regioselective 1,2-Reduction of Conjugated Carbonyl Compounds with the $NaBH_4/(NH_4)_2C_2O_4$ System

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer and a condenser, a solution of benzylideneacetone (0.146 g, 1 mmol) in CH_3CN (2 mL) was prepared and $NaBH_4$ (0.046 g, 1.2 mmol) and $(NH_4)_2C_2O_4$ (0.25 g, 0.2 mmol) were added and the mixture was stirred under reflux conditions for 50 min. TLC monitored the progress of the reaction (eluent; CCl_4:Et_2O = 5:2). After completion of the reaction, distilled water (5 mL) was added to the reaction mixture and it was stirred for an additional 1 min. The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and dried over anhydrous sodium sulphate. Evaporation of the solvent and short-column chromatography of the resulting crude material over silica gel (eluent; CCl_4:Et_2O = 5:2) afforded the pure liquid 4-phenyl-3-buten-2-ol (0.141 g, 95 % yield, Table 8, entry 3).

3. Results and Discussion

Reduction of benzaldehyde as a model compound took place with one molar equivalent of $NaBH_4$ in CH_3CN (the optimal aprotic solvent) within 90 min at room temperature. By adding 1 molar equivalent of different ammonium salts to the mentioned reaction, the reduction reaction was accelerated (Table 1, entry 1, 8 and 10). These results promoted us to investigate the influence of $(NH_4)_2C_2O_4$ and the optimum reaction conditions for reduction of aldehydes. In order to determine the most appropriate reaction conditions and evaluate the catalytic efficiency of $(NH_4)_2C_2O_4$, a model study was carried out on the reduction of benzaldehyde (Table 2). Among the tested aprotic solvents such as *n*-hexane, $CHCl_3$, CH_2Cl_2, Et_2O, THF, CH_3CN, DMF and solvent-free conditions, the benzaldehyde reduction reaction was most facile and proceeded to give the highest yield in CH_3CN (Table 2, entry 13). The optimization reaction conditions showed that using 0.5 molar equivalents of $NaBH_4$ and 0.2 molar equivalents of $(NH_4)_2C_2O_4$ in CH_3CN were the best conditions to complete the reduction of benzaldehye to benzyl alcohol as shown in Scheme 1.

The efficiency of this protocol was further examined by the reduction of structurally different aliphatic and aromatic aldehydes with $NaBH_4/(NH_4)_2C_2O_4$ as new reducing system in CH_3CN. All reductions were completed within 5–40 min as shown in Table 3. The molar ratio of $NaBH_4$ is different according to the nature of the substrates. 0.4–0.6 molar equivalents of $NaBH_4$ and 0.2 molar equivalents of ammonium oxalate per one equivalents of the substrate were sufficient to complete conver-

Table 1 Reduction of benzaldehyde to benzyl alcohol with $NaBH_4$ and ammonium salts in CH_3CN (2 mL) at room temperature.

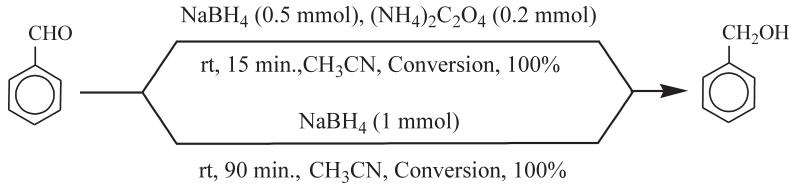
Entry	Ammonium salts	Molar ratio Substrate:$NaBH_4$:ammonium salts	Time/min	Conversion [a]/%
1	NH_4I	1:1:1	60	100
2	NH_4Cl	1:1:1	60	90 [b]
3	NH_4NO_3	1:1:1	60	40 [b]
4	$CH_3CO_2NH_4$	1:1:1	60	60 [b]
5	$(NH_4)_2HPO_4$	1:1:1	60	50 [b]
6	$(NH_4)_2SO_4$	1:1:1	60	45 [b]
7	$CH_3CO_2NH_4$	1:1:1	60	50 [b]
8	$(NH_4)_2C_2O_4$	1:1:1	<2	100
9	HCO_2NH_4	1:1:1	60	80 [b]
10	$NH_4.HF_2$	1:1:1	35	100

[a] Completion of the reactions were monitored by TLC (eluent; CCl_4:Et_2O = 5:2).
[b] Conversions refer to isolated pure products.

Table 2 Optimization of reduction of benzaldehyde to benzyl alcohol with $NaBH_4$ and $(NH_4)_2C_2O_4$ in aprotic solvent at room temperature.

Entry	Molar ratio Benzaldehyde:$NaBH_4$:$(NH_4)_2C_2O_4$	Solvent	Time/min	Conversion [a]/%
1	1:1:1	Solvent-free	30	10 [b]
2	1:1:1	*n*-Hexane	30	<5 [b]
3	1:1:1	$CHCl_3$	30	5 [b]
4	1:1:1	CH_2Cl_2	30	10 [b]
5	1:1:1	Et_2O	30	40 [b]
6	1:1:1	THF	5	100
7	1:1:1	CH_3CN	<2	100
8	1:1:1	DMF	20	100
9	1:1:0.5	CH_3CN	6	100
10	1:1:0.2	CH_3CN	8	100
11	1:0.5:1	CH_3CN	10	100
12	1:0.5:0.5	CH_3CN	12	100
13	1:0.5:0.2	CH_3CN	15	100
14	1:0.5:0.1	CH_3CN	60	70 [b]
15	1:0.5:0.2	THF	23	100

[a] Completion of the reactions were monitored by TLC (eluent; CCl_4:Et_2O = 5:2).
[b] Conversion refers to isolated pure products.



Scheme 1

sion of aldehydes to the corresponding alcohols in excellent yields (93–97 %).

Our next attempt was the reduction of ketones to the corresponding secondary alcohols with the $NaBH_4/(NH_4)_2C_2O_4$ system. We optimized the reaction conditions with the reduction of the model compound acetophenone by $NaBH_4/(NH_4)_2C_2O_4$ under different conditions as shown in Table 4. Reduction of ketones was obtained with this reducing system, but due to the lower reactivity of ketones relative to aldehydes, the reduction require higher molar amounts of $NaBH_4$ at higher temperatures (Table 4, entry 8). The reduction reactions were performed with 1–1.2 molar amounts of $NaBH_4$ in presence of 0.2 molar amounts of ammonium oxalate under reflux conditions in CH_3CN. All reductions were completed within 10–80 min with high to excellent yields (91–98 %) as shown in Table 5. The results (Tables 3 and 5) show that the substrates with electron withdrawing groups were reduced faster than the substrates with electron-releasing groups.

Table 3 Reduction of aldehydes with the $NaBH_4/(NH_4)_2C_2O_4$ [a] system in CH_3CN at room temperature.

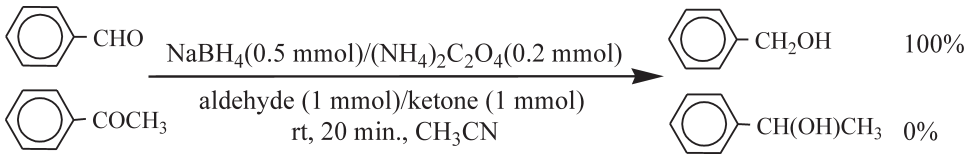
Entry	Substrate	Product	Molar ratio Substrate:$NaBH_4$	Time/min	Yield [b]/%	Mp or Bp/°C Found	Mp or Bp/°C Reported [15]
1	Benzaldehyde	Benzyl alcohol	1:0.5	15	94	203–204	205
2	4-Chlorobenzaldehyde	4-Chlorobenzyl alcohol	1:0.5	10	97	71–73	70–72
3	3-Chlorobenzaldehyde	3-Chlorobenzyl alcohol	1:0.5	10	95	238	237
4	2,4-Dichlorobenzaldehyde	2,4-Dichlorobenzyl alcohol	1:0.5	10	94	56–58	55–58
5	4-Methylbenzaldehyde	4-Methylbenzyl alcohol	1:0.6	25	93	60–62	59–61
6	4-Methoxybenzaldehyde	4-Methoxybenzyl alcohol	1:0.6	30	96	258	259
7	4-Hydroxybenzaldehyde	4-Hydroxybenzyl alcohol	1:0.6	30	94	119–122	118–122
8	2-Hydroxybenzaldehyde	2-Hydroxybenzyl alcohol	1:0.6	35	95	84–85	83–85
9	3-Nitrobenzaldehyde	3-Nitrobenzyl alcohol	1:0.5	5	93	31–33	30–32
10	4-Nitrobenzaldehyde	4-Nitrobenzyl alcohol	1:0.5	5	97	92–94	92–94
11	4-Hydroxy-3-methoxy-benzaldehyde	4-Hydroxy-3-methoxybenzyl alcohol	1:0.6	40	95	114–115	113–115
12	Furfural	Furfuryl alcohol	1:0.5	15	94	169–170	170
13	1-Naphthaldehyde	1-Naphthylmethanol	1:0.5	15	95	61–62	61–63
14	2,6-Dimethylhept-5-enal	2,6-Dimethylhept-5-en-1-ol	1:0.4	10	96	225–227	225–226
15	Heptanal	1-Heptanol	1:0.4	10	95	177	176

[a] All reactions were carried out in the presence of 0.2 molar equivalents of $(NH_4)_2C_2O_4$.
[b] Completion of the reactions were monitored by TLC (eluent; CCl_4:Et_2O = 5:2), yield refers to isolated pure products.

Table 4 Optimization of reduction of acetophenone to 1-phenylethanol with $NaBH_4$ and $(NH_4)_2C_2O_4$ system.

Entry	Molar ratio Acetophenone:$NaBH_4$:$(NH_4)_2C_2O_4$	Solvent	Condition	Time/min	Conversion [a]/%
1	1:2:0.2	THF	r.t.	60	10[b]
2	1:2:0.2	CH_3CN	r.t.	60	25[b]
3	1:2:0.2	THF	Reflux	60	85[b]
4	1:2:0.2	CH_3CN	Reflux	35	100
5	1:2:0.5	CH_3CN	r.t.	60	35[b]
6	1:2:0.5	CH_3CN	Reflux	25	100
7	1:1:0.5	CH_3CN	Reflux	50	100
8	1:1:0.2	CH_3CN	Reflux	55	100
9	1:1.5:0.2	CH_3CN	Reflux	45	100

[a] Completion of the reactions were monitored by TLC (eluent; CCl_4:Et_2O = 5:2).
[b] Conversions refer to isolated pure product.



Scheme 2

Aldehydes are reduced faster than ketones with lower molar ratio of $NaBH_4$ and lower temperature by this reducing system. Therefore, this reducing system can act as a chemoselective system for the discrimination of aldehydes over ketones. In order to show the chemoselectivity of the system, we performed the reduction of one molar equivalent acetophenone in the presence of one molar equivalent of benzaldehyde with 0.5 molar equivalents $NaBH_4$ and 0.2 molar equivalents of $(NH_4)_2C_2O_4$ at room temperature, as shown in Scheme 2. The selectivity ratio for the reduction of aldehyde with respect to ketone was 100 %. This is a general trend for the reduction of various aldehydes in the presence of ketones as shown in Table 6; in most cases the selectivity ratios were excellent.

Vicinal diols are useful in synthetic organic chemistry and their preparation by the reduction of α-diketones and acyloins have attracted a great deal of attention. In this context, we decided to use the $NaBH_4/(NH_4)_2C_2O_4$ system for the reduction of α-diketones and acyloins. Reduction of α-diketones to their corresponding vicinal diols took place with the application of 1.5 molar equivalents of $NaBH_4$ in the presence of 0.2 molar equivalents $(NH_4)_2C_2O_4$ in CH_3CN under reflux conditions. Vicinal diols were obtained in excellent yields and all attempts to reduce α-diketones into acyloins were unsatisfactory by this reducing system (Table 7, entries 1, 3 and 5). Reduction of acyloins to vicinal diols was also obtained by this reducing system in CH_3CN. Using 1.2 molar equivalents of $NaBH_4$ was the requirement for the excellent yields of the corresponding vicinal diols under reflux conditions (Table 7, entries 2 and 4).

Allyl alcohols are important synthetic materials and their preparations from the reduction of conjugated carbonyl compounds

Table 5 Reduction of ketones with the $NaBH_4/(NH_4)_2C_2O_4$ [a] system in CH_3CN under reflux conditions.

Entry	Substrate	Product	Molar ratio Substrate:$NaBH_4$	Time/min	Yield [b]/%	Mp or Bp/°C Found	Mp or Bp/°C Reported [15]
1	Benzophenone	Diphenylmethanol	1:1.2	50	95	65–67	65–67
2	Acetophenone	1-Phenylethanol	1:1	55	96	203	204
3	4-Bromoacetophenone	1-(4-Bromophenyl)ethanol	1:1	50	95	37–38	36–37
4	4-Methoxyacetophenone	1-(4-Ethoxyaphenyl)ethanol	1:1.2	75	98	–	–
5	4-Methylacetophenone	1-(4-Methylphenyl)ethanol	1:1.2	70	93	219–221	218–220
6	4-Methoxybenzophenone	(4-Methoxyphenyl) (phenyl) methanol	1:1.2	80	94	68–69	67–69
7	4-Nitroacetophenone	1-(4-Nitrophenyl)ethanol	1:1	40	92	–	–
8	4-Chloroacetophenone	1-(4-Chlorophenyl)ethanol	1:1	50	95	–	–
9	2,3-Dihyroinden-1-one	2,3-Dihydro-1H-inden-1-ol	1:1	65	95	52–55	50–54
10	9H-fluoren-9-one	9H-fluoren-9-ol	1:1	60	97	153–154	153–154
11	2-Methylcyclohexanone	2-Methylcyclohexanol	1:1	10	92	164–166	163–166
12	Cyclohexanone	Cyclohexanol	1:1	15	94	160–162	160–161
13	4-Phenylcyclohexanone	4-Phenylcyclohexanol	1:1	10	91	58–60	58
14	3-Pentanone	3-Pentanol	1:1	10	92	115	115
15	4-Phenyl-2-butanone	4-Phenylbutan-2-ol	1:1	10	96	131–132	132

[a] All reactions were carried out in the presence of 0.2 molar equivalents of $(NH_4)_2C_2O_4$.
[b] Completion of the reactions were monitored by TLC (eluent; CCl_4:Et_2O = 5:2), yield refers to isolated pure products.

Table 6 Competitive reduction of aldehydes and ketones to alcohols with $NaBH_4$ (0.5 mol) and $(NH_4)_2C_2O_4$ (0.2 mol) at room temperature in CH_3CN.

Entry	Substrate 1	Substrate 2	Molar ratio [a]	Time/min	Convertion 1:Convertion 2 [b]/%
1	Benzaldehyde	Acetophenone	1:1	20	100:0
2	Benzaldehyde	Benzophenone	1:1	20	100:0
3	Benzaldehyde	Cyclohexanone	1:1	30	100:5
4	Benzaldehyde	4-Phenylcyclohexanone	1:1	25	100:5
5	Benzaldehyde	9H-fluoren-9-one	1:1	20	100:0

[a] Molar ratio as substrate 1:substrate 2.
[b] Conversion refer to TLC monitoring (eluent; CCl_4:Et_2O =5:2) and isolated pure products.

Table 7 Reduction of acyloins and α-diketones with the $NaBH_4/(NH_4)_2C_2O_4$ [a] system in CH_3CN under reflux conditions.

Entry	Substrate	Product	Molar ratio Substrate:$NaBH_4$	Time/min	Yield [b]/%
1	Benzil	1,2-Diphenyl ethane-1,2-diol	1:1.5	40	95
2	Benzoin	1,2-Diphenyl ethane-1,2-diol	1:1.2	30	98
3	1,2-Bis(4-methoxyphenyl) ethane-1,2-dione	1,2-Bis(4-methoxyphenyl)ethane-1,2-diol	1:1.5	60	92
4	2-Hydroxy-1,2-bis (4-methoxyphenyl) ethanone	1,2-Bis(4-methoxyphenyl)ethane-1,2-diol	1:1.2	40	94
5	1,3-Diphenylpropane-1,2-dione	1,3-Diphenylpropane-1,2-diol	1:1.5	50	95

[a] All reactions were carried out in the presence of 0.2 molar equivalents of $(NH_4)_2C_2O_4$.
[b] Yield refer sto isolated pure products.
The pinacols are formed as dl-meso mixtures which were not separated.

Table 8 Reduction of α,β-unsaturated carbonyl compounds to their corresponding allyl alcohols with the $NaBH_4/(NH_4)_2C_2O_4$ [a] system in CH_3CN.

Entry	Substrate	Product	Molar ratio Substrate:$NaBH_4$	Time/min	Yield [b]/%	Mp or Bp/°C Found	Mp or Bp/°C Reported [15]
1 [c]	Cinnamaldehyde	3-Phenyl-2-propen-1-ol	1:0.5	20	98	33–34	33–35
2 [c]	Citral	3,7-Dimethyl-2,6-octadien-1-ol	1:0.5	20	97	228–230	229–230
3 [d]	Benzylideneacetone	Phenyl-3-butene-2-ol	1:1.2	50	95	55–56	55–57
4 [d]	Chalcone	4-Phenyl-3-butene-2-ol	1:1.2	45	93	33–34	33–34
5 [d]	β-Ionone	4-(2,6,6-Trimethylcyclohex-1-enyl)-3-buten-2-ol	1:1.2	40	96	–	–

[a] All reactions were carried out in the presence of 0.2 molar equivalents of $(NH_4)_2C_2O_4$.
[b] Completion of the reactions were monitored by TLC (eluent; CCl_4:Et_2O = 5:2); yield refers to isolated pure products.
[c] The reaction was carried out at room temperature.
[d]The reactions was carried out under reflux conditions.

are one of the easiest in organic synthesis. Regioselective 1,2-reduction of α,β-unsaturated aldehydes and ketones with metal hydride reducing agents due to competing 1,2- *vs.* 1,4-attack by the hydride is often difficult to achieve in organic synthesis. The tendency of sodium borohydride to reduce enones or enals in a conjugate sense is highly dependent on solvent and often ignored.[9] However, need for allylic alcohols has led to the development of several specific reagents and some of them are commercially available.[13] In this context, we also investigated the possibility of the 1,2-reduction of α,β-unsaturated aldehydes and ketones with the $NaBH_4/(NH_4)_2C_2O_4$ system. The reduction of cinnamaldehyde by 0.5 molar equivalents of $NaBH_4$ in the presence of 0.2 molar equivalents of $(NH_4)_2C_2O_4$ was thus carried out exclusively in 1,2-reduction manner within 20 min at room temperature. In this reaction, cinnamyl alcohol was obtained in 98 % yield (Table 8, entry 1). This achievement prompted us to evaluate the behavior of other enals and enones in respect to this transformation. Citral also showed the best efficiency and regioselectivity under this protocol. Reduction of conjugated ketones such as benzalacetone, β-ionone and benzalacetophenone were achieved efficiently with 1–1.2 molar equivalents of $NaBH_4$ in the presence of 0.2 molar equivalents $(NH_4)_2C_2O_4$ as shown in Table 8.

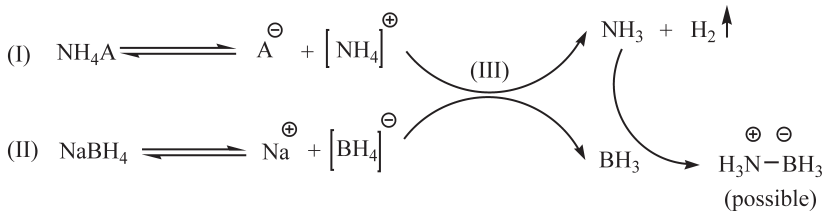
In order to show the efficiency of this reducing system, we compared our results with those of reported in the literature for $NaBH_4/MoCl_5$,[16a] $NaBH_4$/Dowex1-x8,[16b] $[Zn(BH_4)_2(bpy)]$,[16c] $[Zn(BH_4)_2(py)]$,[16d] $[Zn(BH_4)_2(Ph_3P)_2]$,[16e] $Ph_3PMe(BH_4)$[9b] and $[PhCH_2(dabco)]BH_4$[9a] as shown in Table 9.

It is notable that due to the low solubility of ammonium salts in CH_3CN, the reaction takes place under heterogeneous conditions. The mechanism for the influence of ammonium salts is not clear, but as shown in Scheme 3, we observed that with the addition of ammonium salts (as a proton donors) to the reaction mixture (substrate & $NaBH_4$ in CH_3CN), hydrogen gas slowly is liberated *in situ* (Scheme 3, step III).

Hydrogen gas generation seems to be directly related to the solubility of the $NaBH_4$ (Scheme 3, step II) and ammonium salts (Scheme 3, step I) in the reaction solvent. The synergistically

Table 9 Comparison of reductions of aldehydes and ketones with $NaBH_4/(NH_4)_2C_2O_4$ system and other reported reducing systems.

Entry	Reducing systems	Molar ratio (reagent:substrate), time/h					
		Benzaldehyde	4-Methoxy-benzaldehyde	Benzophenone	Cyclohexanone	9H-fluoren-9-one	Benzoin
1	$NaBH_4/(NH_4)_2C_2O_4$	0.5, 0.25	0.6, 0.5	1.20, 0.83	1, 0.25	1, 1	1.2, 0.5
2 [16a]	$NaBH_4/MoCl_5$	0.5, 0.3	1.5, 3	3, 3.2	1.5, 1.25	2, 1.8	2, 0.17
3 [16b]	$NaBH_4$/Dowex1-x8	1, 0.05	1.5, 3	3, 3.2	1.5, 1.25	2, 1.8	2, 0.17
4 [16c]	$[Zn(BH_4)_2(bpy)]$	0.25, 0.2	0.35, 0.17	1, 0.75	0.5, 0.15	1, 1.5	0.5, 0.08
5 [16d]	$[Zn(BH_4)_2(py)$	1, 0.5	1, 1.3	2, 4.3	2, 2	2, 5.3	0.5, 0.5
6 [16e]	$[Zn(BH_4)_2(Ph_3P)_2]$	–	1, 0.17	–	1, 1	2, 0.33	–
7 [9b]	Ph3Me(BH4)	1, *Im*	1, *Im*	–	1, 1	16, 18	–
8 [9a]	[PhCH2(dabco)]BH_4	–1, 0.25	2, 0.8	2, 21.5	–	–	–



Scheme 3

generated molecular hydrogen combines with the hydride attack from the borohydride and thus accelerates the rate of reduction reaction.

In the presence of small amounts of water (2–3 drops), due to increased solubility of ammonium salts and $NaBH_4$, hydrogen gas generation increase dramatically. Water has a levelling effect on the influence of ammonium salts on the reduction reaction rate, i.e. the use of the ammonium salts mentioned in Table 1 (entries 5–6, 8) are not beneficial when carrying out the reduction reactions in wet solvents, because water causes an increase in solubility of the ammonium salts and $NaBH_4$. Consequently, the $NaBH_4$ rapidly decomposes before the reduction reactions are complete. Also, experiments show that the chemoselectivity of the $NaBH_4/(NH_4)_2C_2O_4$ system in wet media decreases and that its regioselectivity is reduced.

4. Conclusions

In this investigation, we have shown that the combination system of $NaBH_4/(NH_4)_2C_2O_4$ in CH_3CN reduces a variety of carbonyl compounds to their corresponding alcohols in high to excellent yields. Reduction reactions were carried out with 0.4–1.5 molar equivalents of $NaBH_4$ in the presence of 0.2 molar equivalents of $(NH_4)_2C_2O_4$ in CH_3CN. Reduction of acyloins and α-diketones by the $NaBH_4/(NH_4)_2C_2O_4$ system also produced efficiently the corresponding vicinal diols in CH_3CN. The chemoselective reduction of aldehydes over ketones was accomplished successfully with this reducing system. In addition, 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 accomplished with high efficiency of the reductions, using the appropriate molar ratios of $NaBH_4$ and $(NH_4)_2C_2O_4$, shorter reaction times and easy work-up procedure. Therefore this new protocol for reduction of carbonyl compounds could be a useful addition to the present methodologies.

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