$Zn(BH_4)_2$/2NaCl: A Novel Reducing System for Efficient Reduction of Organic Carbonyl Compounds to Their Corresponding Alcohols

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ABSTRACT

$Zn(BH_4)_2$/2NaCl, obtained by the reaction of $ZnCl_2$ and $NaBH_4$,is a stable, efficient and selective reducing system in dry-THF. The $Zn(BH_4)_2$/2NaCl system (0.5–1 mmol) reduces a variety of carbonyl compounds to their corresponding alcohols in CH_3CN at room temperature in high to excellent yields.

KEYWORDS

Reduction, carbonyl compounds, $Zn(BH_4)_2$, chemoselective, regioselectivity, NaCl.

1. Introduction

Reduction is one of the most fundamental and useful reaction in organic synthesis. For the past 50 years, sodium borohydride has played an important role in modern synthetic organic chemistry.[1] This reagent is used widely and has gained commercial status, in spite of its poor solubility in organic solvents and low reactivity.[2] To overcome these drawbacks and for controlling its reducing power, soluble metal borohydrides have been realized through the variation of alkali-metal cations and transition metal cations in the hydride complex such as $LiBH_4$,[3] KBH_4, [4] $Ca(BH_4)_2$, [5] $Cu(BH_4)_2$, [6] $Zn(BH_4)_2$, [7] $Ti(BH_4)_3$, [8] $Zr(BH_4)_4$ and others.[8b] $LiBH_4$, $Ca(BH_4)_2$ and $Zn(BH_4)_2$ are the modified borohydride agents which have better solubility in aprotic solvents, so their uses and applications are interesting in organic synthesis. Among these reagents, zinc borohydride is unique because of the better coordination ability of Zn^{2+}, which imparts selectivity in hydride-transferring reactions. Zinc borohydride is moderately stable in ethereal solution and has many applications in organic synthesis.[9] Zinc borohydride, as a nonconventional hydride transferring agent, has been reported as an efficient chemo-, regio- and stereoselective reducing agent in several complex substrates. It can be used in a range of aprotic solvents such as, THF, Et_2O and DME. [10] Several combination reducing systems of $Zn(BH_4)_2$ such as $Zn(BH_4)_2$/TMEDA, [11a] $Zn(BH_4)_2$/Me_3SiCl, [11b] $Zn(BH_4)_2$/TFA/DME, [11c] $Zn(BH_4)_2/H_2O$, [11d] $Zn(BH_4)_2/Al_2O_3$, [11e] and $Zn(BH_4)_2$/C[11f] are interesting and have been used for different reduction purposes. Also, $Zn(BH_4)_2$ has been modified as stable tertiary amino or phosphinoligand complexes such as $[Zn(BH_4)_2(dabco)]$,[12] $[Zn(BH_4)_2(pyz)]_n$, [13] $[Zn(BH_4)_2(PPh_3)]$ and $[Zn(BH_4)_2(PPh_3)_2]$,[14] $[Zn(BH_4)_2(bpy)]$,[15] $[Zn(BH_4)_2(py)]$,[16] $[Zn(BH_4)_2XP_4]$,[17] $[Zn(BH_4)_2(nmi)]$[18a] and $[Zn(BH_4)_2(nic)]$[18b]. In this context we wish to introduce $Zn(BH_4)_2$/2NaCl as a new combination reducing system for fast and efficient reduction of a variety of carbonyl compounds such as aldehydes, ketones, acyloins, α-diketones and α,β-unsaturated carbonyl compounds to their corresponding alcohols at room temperature.

2. Experimental

2.1. General

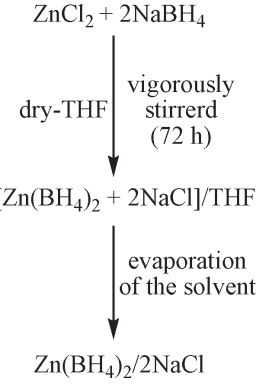
All substrates and reagents were purchased from commercial sources (Merck and Sigma-Aldrich) and used without further purification. IR and ^{1}H NMR spectra were recorded on Perkin-Elmer FT-IR RXI and (250, 300 & 400) MHz Bruker spectrometers, respectively. The products were characterized by their ^{1}H NMR or IR spectra and compared with authentic samples (melting points or boiling points). Organic layers were dried over anhydrous sodium sulfate. All yields refer to isolated pure products. TLC (silica gel 60 F_{254} aluminum sheet) was applied for the purity determination of substrates, products and reaction monitoring.

2.2. Preparation of $Zn(BH_4)_2$/2NaCl as Combination Reducing System

In a round-bottomed flask (500 mL) equipped with a magnetic stirrer bar and covered with foil, a solution of $ZnCl_2$ (5.452 g, 0.04 mol) and $NaBH_4$ (3.177 g, 0.084 mol) was prepared in dry THF (250 mL). The mixture was vigorously stirred for 72 hours at room temperature according to a literature procedure.[18a,b] Then the solvent was evaporated and the $Zn(BH_4)_2$/2NaCl was afforded as a grey solid (8.629 g, 100 %) as shown in Scheme 1.

2.3. Typical Procedure for the Reduction of Aldehydes with $Zn(BH_4)_2$/2NaCl System in CH_3CN

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer bar, a solution of benzaldehyde (0.106 g, 1 mmol) was prepared in CH_3CN (3 mL). To this solution, $Zn(BH_4)_2$/2NaCl (0.105 g, 0.5 mmol) was added and the mixture was stirred at room temperature for 1 min. The reaction was monitored by TLC (eluent; Hexane/EtOAc: 10/1). After completion of the



Scheme 1

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Table 1 Optimization of the reduction of benzaldehyde and acetophenone to their corresponding alcohols with the $Zn(BH_4)_2$/2NaCl system at room temperature.

Entry	Substrate	Molar ratio Substrate/[Zn(BH4)2/2NaCl]	Solvent	Time/min	Conversion [a]/%
1	PhCHO	1:1	Solvent free	60	10 [b]
2	PhCHO	1:1	*n*-Hexane	60	25 [b]
3	PhCHO	1:1	$CHCl_3$	60	35 [b]
4	PhCHO	1:1	CH_2Cl_2	60	40 [b]
5	PhCHO	1:1	Et_2O	60	70 [b]
6	PhCHO	1:1	DME	60	70 [b]
7	PhCHO	1:1	CH_3CN	*Im*	100
8	PhCHO	1:1	THF	4	100
9	PhCHO	1:0.5	CH_3CN	*Im*	100
10	PhCHO	1:0.5	THF	10	100
11	PhCHO	1:0.25	CH_3CN	60	35 [b]
12	PhCHO	1:0.5	CH_3OH	60	70 [b]
13	PhCHO	1:0.5	C_2H_5OH	60	60 [b]
14	$PhCOCH_3$	1:0.5	CH_3CN	60	25 [b]
15	$PhCOCH_3$	1:1	CH_3CN	60	100
16	$PhCOCH_3$	1:2	CH_3CN	40	100
17	$PhCOCH_3$	1:1	THF	90	100

[a] Completion of reactions was monitored by TLC (eluent; Hexane/EtOAc: 10/1).
[b] Conversions refer to isolated pure products. *Im*: immediately.

reaction, distilled water (5 mL) was added to the reaction mixture and stirred for 5 min. The mixture was extracted with CH_2Cl_2 (3 × 8 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed by column chromatography of the resulting crude material over silica gel (eluent; Hexane/EtOAc: 10/1) afforded liquid benzyl alcohol (0.102 g, 94 %, Table 2, entry 1).

2.4. Typical Procedure for the Reduction of Ketones with $Zn(BH_4)_2$/2NaCl System in CH_3CN

In a round-bottomed flask (10 mL), equipped with a magnetic stirrer bar, a solution of acetophenone (0.121 g, l mmol) was prepared in CH_3CN (3 mL). To this solution, $Zn(BH_4)_2$/2NaCl (0.210 g, 1 mmol) was added. The resulting mixture was stirred at room temperature for 60 min. The reaction was monitored by TLC (eluent; Hexane/EtOAc: 10/1). After completion of the reaction, distilled water (5 mL) was added to the reaction mixture and stirred for 5 min. The mixture was extracted with CH_2Cl_2 (3 × 8 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed column chromatography of the resulting crude material over silica gel (eluent; Hexane/EtOAc: 10/1) afforded crystals of 1-phenylethanol (0.l1 g, 93 % yield, Table 2, entry 11).

2. 5. Typical Procedure for the Reduction of α-Diketones and Acyloins with $Zn(BH_4)_2$/2NaCl System in CH_3CN

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer bar, a solution of benzil (0.21 g, l mmol) was prepared in CH_3CN (3 mL). To this solution, $Zn(BH_4)_2$/2NaCl (0.210 g, 1 mmol) was added. The resulting mixture was stirred at room temperature for 10 min. The reaction was monitored by TLC (eluent; Hexane/EtOAc: 10/1). After completion of the reaction, distilled water (6 mL) was added to the reaction mixture and stirred for 5 min. The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed by short column chromatography of the resulting crude material over silica gel (eluent; Hexane/EtOAc: 10/1) afforded crystals of 1,2-diphenyl ethane-1,2-diol (0.20 g, 95 % yield, Table 2, entry 19).

2.6. Typical Procedure for Competitive Reduction of Aldehydes and Ketones with $Zn(BH_4)_2$/2NaCl System in CH_3CN

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer bar, a solution of benzaldehyde (0.106 g, l mmol) and acetophenone (0.121 g, 1 mmol) was prepared in CH_3CN (3 mL). To this solution, $Zn(BH_4)_2$/2NaCl (0.105 g, 0.5 mmol) was added and the mixture was stirred at room temperature. The reaction was monitored by TLC (eluent; Hexane/EtOAc: 10/1). After 5 min, the reaction was quenched by the addition of distilled water (5 mL) and stirred for 5 min. The mixture was extracted with CH_2Cl_2 (3 × 15 mL) and dried over anhydrous Na_2SO_4. Evaporation of solvent followed by short column chromatography of the resulting crude material over silica gel (eluent; Hexane/EtOAc: 10/1) afforded liquid benzyl alcohol as a sole product (0.105 g, 97 %) and acetophenone (0.112 g, 93 %) an unused substrate (Table 3, entry 1).

2.7. Typical Procedure for Regioselective 1,2-Reduction of Conjugated Carbonyl Compounds with $Zn(BH_4)_2$/2NaCl System in CH_3CN

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer bar, a solution of benzylideneacetone (0.146 g, 1 mmol)) was prepared in CH_3CN (3 mL). To this solution $Zn(BH_4)_2$/2NaCl (0.210 g, 1 mmol) was added. The resulting mixture was stirred at room temperature. The reaction was monitored by TLC (eluent; Hexane/EtOAc: 10/1). After completion of the reaction within 40 min, distilled water (5 mL) was added to the reaction mixture and stirred for 5 min. The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed by short column chromatography of the resulting crude material over silica gel (eluent; Hexane/EtOAc: 10/1) afforded liquid 4-phenyl-3-buten-2-ol (0.l43 g, 96 % yield, Table 2, entry 24).

3. Results and Discussion

The $Zn(BH_4)_2$ reduces some carbonyl compounds[10a] with some peculiar chemoselectivities such as the reduction of aldehydes

Table 2 Reduction of carbonyl compounds to their corresponding alcohols with the $Zn(BH_4)_2$/2NaCl system in CH_3CN at room temperature.

Entry	Substrate	Product	Molar ratio Sub./Reg.	Time/min, Yield [a]/%	^{1}HNMR (δ ppm), IR (cm^{-1}) and Bp or Mp (°C)[23]	
1	Benzaldehyde	Benzyl alcohol	1:0.5	<1, 94	^{1}HNMR ($CDCl_3$)	7.33 (Ar, m, 5H), 4.71 (CH_2, s, 2H), 1.77 (OH, bs, 1H)
					IR (liquid film)	3339 (OH), 2926, 2874, 1608, 1453, 1205, 1015, 736, 696.
					Bp	205–206
2	3-Bromobenzaldehyde	3-Bromobenzyl alcohol	1:0.5	2, 97	^{1}HNMR ($CDCl_3$)	7.27 (Ar, m, 4H), 4.64 (CH_2, s, 2H), 2.29 (OH, bs, 1H)
					IR (liquid film)	3338 (OH), 2925, 2874, 1597, 1473, 1201, 1024, 776, 696
					Bp	165–166/16 mmHg
3	2,4-Dichlorobenzaldehyde	2,4-Dichlorobenzyl alcohol	1:0.5	2, 94	^{1}HNMR ($CDCl_3$)	7.45 (Ar, s, 1H), 7.39 (Ar, d, 1H, J=8.10 Hz), 7.28 (Ar, d, 1H, J=8.10 Hz), 4.76 (CH_2, s, 2H), 1.88 (OH,bs, 1H).
					IR (KBr)	3305 (OH), 2920, 2871, 1594, 1469, 1067, 813, 707
					Mp	57–58
4	4-Methylbenzaldehyde	4-Methylbenzyl alcohol	1:0.5	5, 93	HNMR ($CDCl_3$)	7.26 (Ar, 2H, d, J=6.00 Hz), 6.88 (Ar, 2H, d, J=6.00 Hz), 4.50 (CH_2, s, 2H), 3.77(CH_3, s, 3H), 2.82 (OH, ds, 1H)
					IR (KBr)	3359 (OH), 2935, 2836, 1586, 1463, 1033, 817
					Mp	59–60
5	4-Methoxybenzaldehyde	4-Methoxybenzyl alcohol	1:0.5	5, 95	^{1}HNMR ($CDCl_3$)	7.25 (Ar, d, 2H, J=8.40 Hz), 6.87 (Ar, d, 2H, J=8.40 Hz), 4.56 (CH_2, s, 2H), 3.79(OCH_3, s, 3H), 2.56 (OH, bs, 1H)
					IR (liquid film)	3365 (OH), 2937, 2878, 1612, 1462, 1033, 820, 737
					Bp	258–259
6	2-Methoxybenzaldehyde	2-Methoxybenzyl alcohol	1:0.5	5, 95	^{1}HNMR ($CDCl_3$)	7.32–6.93 (Ar, m,4H), 4.70 (CH_2, s, 2H), 3.88(OCH_3, s, 3H), 2.22 (OH, bs, 1H)
					IR (liquid film)	3398 (OH), 2940, 2840, 1601, 1463, 1243, 1034, 737
					Bp	249–251
7	3-Methylbenzaldehyde	3-Methylbenzyl alcohol	1:0.5	5, 97	^{1}HNMR ($CDCl_3$)	7.27–7.16 (Ar, m,4H), 4.65 (CH_2, s, 2H), 3.38(CH_3, s, 3H), 2.13 (OH, bs, 1H)
					IR (liquid film)	3348 (OH), 2925, 2874, 1597, 1473, 1217, 1025, 886, 759
					Bp	216–217
8	2-Methylbenzaldehyde	2-Methylbenzyl alcohol	1:0.5	5, 98	^{1}HNMR ($CDCl_3$)	7.36–7.24 (Ar, m, 4H), 4.69 (CH_2, s, 2H), 3.37 (CH_3, s, 3H), 1.94 (OH, bs, 1H)
					IR (KBr)	3326 (OH), 2909, 1604, 1487, 1052, 988, 743
					Mp	33–35
9	4-Nitrobenzaldehyde	4-Nitrobenzyl alcohol	1:0.5	<1, 93	^{1}HNMR ($CDCl_3$)	8.23 (Ar, d, 2H, J=8.60 Hz), 7.55 (Ar, d, 2H, J=8.60 Hz), 4.85 (CH_2, s, 2H), 1.87 (OH, bs, 1H)
					IR (KBr)	3519 (OH), 2870, 1602, 1508, 1339, 1057, 860, 835, 736
					Mp	92–94
10	1-Butanal	1-butanol	1:0.5	<1, 95	^{1}HNMR ($CDCl_3$)	3.65 (CH_2, m, 2H), 1.57(CH_2, m, 2H), 1.39 (CH_2 & OH, m, 3H) , 0.94 (CH_3, m, 3H)
					IR (liquid film)	3323, 2960, 2934, 2875, 1466, 1217, 1073, 847
					Bp	117–118

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Entry	Substrate	Product	Molar ratio Sub./Reg.	Time/min, Yield [a]/%	^{1}HNMR (δ ppm), IR (cm^{-1}) and Bp or Mp (°C)[23]	
11	Acetophenone	1-Phenylethanol	1:1	60, 93	^{1}HNMR ($CDCl_3$)	7.30 (Ar, m, 5H), 4.92(CH, q, 1H, J=6.30 Hz), 1.92 (OH, bs, 1H), 1.52 (CH_3, d, 3H, J=6.30 Hz)
					IR (liquid film)	3367 (OH), 2973, 2890, 1603, 1451, 1204, 1077, 898, 760, 699
					Bp	203–204
12	Benzophenone	Diphenylmethanol	1:1	90, 95	^{1}HNMR ($CDCl_3$)	7.31 (Ar, m, 10H), 5.84 (CH, s, 1H), 2.41 (OH, bs, 1H)
					IR (KBr)	3389 (OH), 3058, 3029, 1597, 1494, 1454, 1269, 1031, 763, 698
					Mp	65–67
13	4-Methylacetophenone	1-(4-Methylphenyl)ethanol	1:1	80, 98	^{1}HNMR ($CDCl_3$)	7.28 (Ar, d, 2H, J=7.80 Hz), 7.17 (Ar, d, 2H, J=7.80 Hz), 4.87 (CH, q, 1H, J=6.6 Hz), 2.36 (CH_3, s, 3H,), 2.03 (OH,bs, 1H), 1.49 (CH_3, d, 3H, J=8.56 Hz)
					IR (liquid film)	3350 (OH), 2972, 2924, 1612, 1447, 1201, 1084, 898, 817, 726
					Bp	219–220
14	4-Methoxyacetophenone	1-(4-Methoxylphenyl)ethanol	1:1	120, 95	^{1}HNMR ($CDCl_3$)	7.28 (Ar, d, 2H, J=8.40 Hz), 6.87 (Ar, d, 2H, J=8.40 Hz), 4.81 (CH, q, 1H, J=6.30 Hz), 3.78 (OCH_3, s, 3H), 2.53 (OH, bs, 1H), 1.45 (CH_3, d, 3H, J=6.30 Hz)
					IR (liquid film)	3378 (OH), 2969, 2839, 1611, 1513, 1454, 1088, 1034, 896, 831
					Bp	–
15	3-Nitroacetophenone	1-(3-Nitrophenyl)ethanol	1:1	40, 92	^{1}HNMR ($CDCl_3$)	8.24–7.51(Ar, m, 4H), 5.02 (CH, q, 1H, J=6.30 Hz), 2.50 (OH, bs, 1H), 1.53 (CH_3, d, 3H, J=6.30 Hz)
					IR (KBr)	3260 (OH), 2990, 1580, 1525, 1340, 1205, 1170, 810, 740, 690
					Mp	61–62
16	9H-fluoren-9-one	9H-fluoren-9-ol	1:1	60, 96	^{1}HNMR ($CDCl_3$)	7.66 (Ar, m, 4H), 7.37(Ar, m, 4H), 5.6 (CH, s, 1H), 1.66 (OH, bs, 1H)
					IR (KBr)	3304 (OH), 1608, 1452, 1301, 1188, 1024, 765, 738
					Mp	153–154
17	4-Phenylcyclohexanone	4-Phenylcyclohexanol	1:1	30, 93	^{1}HNMR ($CDCl_3$)	7.27 (Ar, m, 5H), 3.69 (CH, m, 1H), 2.50(CH, m, 1H), 2.12–1.45 (8H&OH)
					IR (KBr)	3419 (OH), 2922, 2851, 1600, 1493, 1452, 887, 756
					Mp	58–60
18	Cyclohexanone	Cyclohexanol	1:1	30, 97	^{1}HNMR ($CDCl_3$)	3.55 (CH, m, 1H), 2.40 (OH, bs, 1H), 1.8–1.19 (m, 10H)
					IR (liquid film)	3425 (OH), 2925, 2855, 1451, 1065, 969, 829
					Bp	160–162
19	Benzil	1,2-Diphenylethane-1,2-diol	1:1	10, 95	^{1}HNMR ($CDCl_3$)	7.33 (Ar, m, 10H), 4.83(2CH, s, 2H), 2.1 (2OH, bs, 2H)
					IR (KBr)	3370 (OH), 3315 (OH), 2939, 2900, 1605, 1449, 1270, 1030, 744, 699
					Mp	135–137
20	1,2-Bis(4-methoxy phenyl) ethane-1,2-dione	1,2-Bis(4-methoxyphenyl) ethane-1,2-diol	1:1	15, 93	^{1}HNMR ($CDCl_3$)	7.27–6.74 (Ar, m, 8H), 4.74 (CH, d, 1H, J=6.60Hz), (CH, d, 1H, J=6.60 Hz), 3.82 (OCH_3, s, 3H), 3.78 (OCH_3, s, 3H) 2.160 (bs, 2OH)
					IR (KBr)	3352 (OH), 2955, 2836, 1613,1252, 1036, 831
					Mp	–

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Entry	Substrate	Product	Molar ratio Sub./Reg.	Time/min, Yield [a]/%	^{1}HNMR (δ ppm), IR (cm^{-1}) and Bp or Mp (°C)[23]	
21	Benzoin	1,2-Diphenylethane-1,2-diol	1:1	5, 96	^{1}HNMR ($CDCl_3$)	–
					IR (KBr)	–
					Mp	–
22	2-Hydroxy-1,2-bis(4-methoxy phenyl) ethanone	1,2-Bis(4-methoxyphenyl) ethane-1,2-diol	1:1	8, 92	^{1}HNMR ($CDCl_3$)	–
					IR (KBr)	–
					Mp	–
23	Cinnamaldehyde	3-Phenyl-2-propen-1-ol	1:0.5	5, 97	^{1}HNMR ($CDCl_3$)	7.29(Ar, m, 5H), 6.58 (CH, d, 1H, J=15.90 Hz), 6.34 (CH, dd, 1H, J_1=15.90, J_2=5.10 Hz), 4.28 (CH_2, d, 2H, J=5.10 Hz), 2.71 (OH, bs, 1H)
					IR (KBr)	3337 (OH), 2925, 2857, 1449, 1216, 1093, 967, 757
					Mp	30–33
24	Benzylideneacetone	4-Phenyl-3-butene-2-ol	1:1	40, 96	^{1}HNMR ($CDCl_3$)	7.41–7.23 (Ar, m, 5H), 6.27 (CH, d, 1H, J=15.90 Hz), 6.58 (CH, dd, 1H, J_1=15.90 Hz, J_2=6.30 Hz), 4.49 (CH, q, 1H, J=6.30 Hz), 1.76 (OH, bs, 1H), 1.39(CH_3, d, 3H, J=6.60 Hz)
					IR (KBr)	3360 (OH), 2972, 2873, 1598, 1449, 1058, 967, 749
					Mp	55–56
25	Chalcone	1,3-Diphenyl-2-propen-1-ol	1:1	45, 95	^{1}HNMR ($CDCl_3$)	7.42–7.18 (Ar, m, 10H), 6.48 (CH, d, 1H, J=15.90 Hz), 6.41 (CH, dd, 1H, J_1=15.90 Hz, J_2=6.30 Hz), 5.38 (CH, d, 1H, J=6.30 Hz), 2.18 (OH, bs, 1H)
					IR (KBr)	3359 (OH), 3027, 2876, 1600,1450, 1067, 966, 745
					Mp	57–58

[a] Completion of reactions was monitored by TLC (eluent; Hexane/EtOAc: 10/1). Yields refer to isolated pure products.

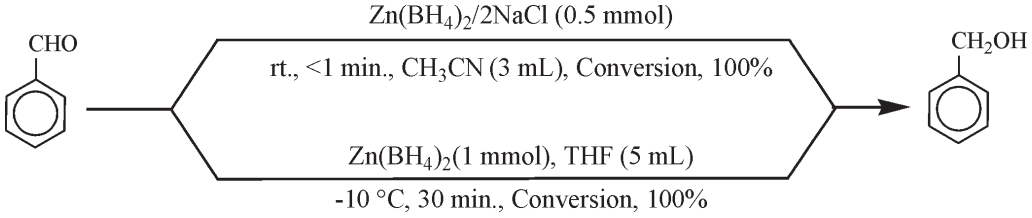
Table 3 Competitive the reduction of aldehydes and ketones to the corresponding alcohols with the$Zn(BH_4)_2$/2NaCl (0.5 mmol) system in CH_3CN (3 mL) at room temperature.

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

[a] Molar Ratio as: Substrate 1/Substrate 2.
[b] Conversion refer to TLC monitoring (eluent; Hexane/EtOAc: 10/1) and isolated pure products.

Table 4 Comparison of the reduction of aldehydes and ketones by the$Zn(BH_4)_2$/2NaCl system in CH_3CN with other reported reducing systems.

Entry	Reducing systems	Molar ratio (reagent./substrate), time/h					
		Benzaldehyde	Acetophenone	Benzophenone	Cyclohexanone	9H-fluoren-9-one	Benzoin
1	$Zn(BH_4)_2$/2NaCl	0.5, *Im*	1, 1	1, 1.5	0.5, 0.25	1, 1	1, 0.08
2[10a–c]	$Zn(BH_4)_2$	1, 0.5 [a]	1, *N.R* [a]	–	1, 0.08 [b]	–	–
3[11e]	$Zn(BH_4)_2/Al_2O_3$	0.5, 0.08	1, 1	1, 3	–	1, 1.6	1, 1
4[11d]	$Zn(BH_4)_2/H_2O$	1, 0.02	2, 1.5	2, 3	2, 1	2, 2	2, 0.33
5[11f]	$Zn(BH_4)_2$/C	1, 0.08	1, 1.25	1, 3	1, 0.5	1, 2	1, 0.5
6[12]	$[Zn(BH_4)_2(dabco)]$	0.75, 0.7	1.2, 5.4	1.5, 8.5	–	1.5, 2.3	1, 0.17
7[14]	$[Zn(BH_4)_2(Ph_3P)]$	–	2, 1.25	–	2, 1	2, 0.5	–
8[15]	$[Zn(BH_4)_2(bpy)]$	0.25, 0.2	0.35, 0.17	1, 0.75	0.5, 0.15	1, 1.5	0.5, 0.08
9[16]	$[Zn(BH_4)_2(py)]$	1, 0.5	2, 2	2, 4.3	2, 2	2, 5.3	0.5, 0.5
10[13]	$[Zn(BH_4)_2(pyz)_n]$	1, 2.5	4, 30	–	4, 18	–	3, 5
11[18a]	$[Zn(BH_4)_2(nmi)]$	1, *Im*	1, *Im*	–	1, 1	1.6, 18	–
12[18b]	$[Zn(BH_4)_2(nic)]$	1, 0.25	2, 0.8	2, 21.5	–	–	–
13[17]	$[Zn(BH_4)_2XP_4]$	1, 8	2, 15	2, 48	2, 24	–	–

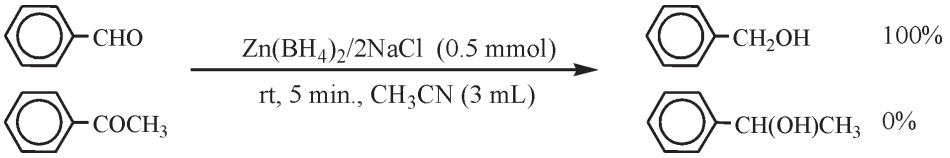


Scheme 2

over aromatic ketones[10b] and the reduction of ketones and conjugated aldehydes over enones.[10c] In order to determine the most appropriate reaction conditions and evaluate the efficiency of the addition of NaCl, we first examined the reduction of benzaldehyde as a model compound as shown in Table 1. Among the tested aprotic and protic solvents i.e. *n*-hexane, $CHCl_3$, CH_2Cl_2, Et_2O, DME, CH_3CN, THF, CH_3OH, C_2H_5OH and solvent-free conditions, benzaldehyde reduction was better in CH_3CN. The optimization study showed that using 0.5 molar equivalents of $Zn(BH_4)_2$/2NaCl in CH_3CN (3 mL) is the best conditions as shown in Scheme 2.

This procedure was also applied to the reduction of various aliphatic and aromatic aldehydes (Table 2, entries 1–10). All reductions were completed within 1–5 min by 0.5 molar equivalents of $Zn(BH_4)_2$/2NaCl with excellent yield of products (93–98 %). Our next attempt was the reduction of ketones to the corresponding secondary alcohols. We optimized the reaction conditions with acetophenone as model compound (Table 1, entries 14–17). Due to the lower reactivity of ketones relative to aldehydes, the reduction require a higher molar amounts of $Zn(BH_4)_2$/2NaCl. The reduction reactions were carried out with 1 molar equivalents of $Zn(BH_4)_2$/2NaCl at room temperature in CH_3CN. All reductions were completed within 30–120 min with high to excellent yield of products (92–98 %) as shown in Table 2 (entries11–18). Since the reduction of aldehydes and ketones is dependent on molar ratio $Zn(BH_4)_2$/2NaCl and aldehydes reduce faster than ketones by this reducing system, therefore, we thought that this system has a chemoselectivity towards reduction of aldehydes over ketones. Therefore, a 1:1 mixture (1 mmol of each) of benzaldehyde and acetophenone was treated with 0.5 molar equivalents of $Zn(BH_4)_2$/2NaCl at room temperature in CH_3CN as shown in Scheme 3. The selectivity ratio for the reduction of aldehyde was 100 %. 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 3.

Reductions of α-diketones and acyloins to the corresponding vicinal diols are an interesting subject in organic synthesis.[19] In this context, we decided to use the $Zn(BH_4)_2$/2NaCl system for the reduction of α-diketones and acyloins. Reduction of α-diketones to their corresponding vicinal diols took place with 1 molar equivalents of $Zn(BH_4)_2$/2NaCl at room temperature in CH_3CN. Vicinal diols were obtained in excellent yields (93–95 %) (Table 2, entries 19 & 20). All attempts to reduce α-diketones into acyloins were not satisfactory. The reduction of acyloins to their corresponding vicinal diols (92–96 %) was also obtained successfully by 1 molar equivalents of $Zn(BH_4)_2$/2NaCl at room temperature in CH_3CN (Table 2, entries 21 & 22). Preparation of allyl alcohols from conjugated carbonyl compounds is an important synthetic method in organic synthesis.[20] However, regioselective 1,2-reduction of α,β-unsaturated aldehydes and ketones with metal hydride reducing agents is often difficult to achieve due to the competing 1, 4-reduction.[21] On the other hand, 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 potential of the 1,2-reduction of α,β-unsaturated aldehydes and ketones with the $Zn(BH_4)_2$/2NaCl system. The reduction of cinnamaldehyde with 0.5 molar



Scheme 3

Table 5 Comparison of the reduction of benzaldehyde with the $Zn(BH_4)_2$/2NaCl (0.5mmol) (stored under different conditions) in CH_3CN at room temperature.

Entry	Light	Open door container	Storage time/week	Time/min	Conversion [a]/%
1	–	–	12	*Im*	100
2	+	–	12	10	100
3 [b]	+	+	4	70	100
4	+	+	6	90	85
5	+	+	12	120	45 [c]

[a] Completion of reactions was monitored by TLC (eluent; Hexane/EtOAc: 10/1).
[b] A stock solution of $Zn(BH_4)_2$ in THF or DME prepared can be stored in a refrigerator in a closed container for several weeks.Whereas, $Zn(BH_4)_2$/2NaCl can be stored in a opened container for several weeks at room temperature.
[c] Yield refer to isolated pure product.

equivalents of the $Zn(BH_4)_2$/2NaCl exclusivity afforded the 1,2-reduction product after 5 min at room temperature in CH_3CN. In this reaction, cinnamyl alcohol was obtained in 97 % yield (Table 2, entry 23). Under this protocol, reduction of conjugated ketones such as benzylidenacetone (Table 2, entry 24) and chalcone (Table 2, entry 25) were achieved efficiently with 1 molar equivalents of $Zn(BH_4)_2$/2NaCl at room temperature in CH_3CN in excellent yields (95–97 %).

In order to show the efficiency of this reducing system, we compared our results with other reported reducing systems (Table 4). In all cases, the $Zn(BH_4)_2$/2NaCl has a greater potential for the reduction of organic carbonyl compounds. Only $Zn(BH_4)_2$(bpy) (Table 4, entry 8) has some advantages over $Zn(BH_4)_2$/2NaCl. But the synthesis of $Zn(BH_4)_2$(bpy) is more costly than $Zn(BH_4)_2$/2NaCl. Also, in our experience,[18] reducing complexes (Table 4, entries 6–13) release a ligand during reduction reactions. The isolation of organic ligands is costly and time-consuming exercise. Whereas, the $Zn(BH_4)_2$/2NaCl has no such limitations and does not require any other additives. The stability and shelf-life of the $Zn(BH_4)_2$/2NaCl was investigated by comparing the reduction reactions of benzaldehye as model compound under different conditions as shown in Table 5. Experiments show that, in adverse conditions, this reducing system is stable and its reducing power remains significant (Table 5, entry 3). The effect of the NaCl is not clear, but most probably NaCl protects $Zn(BH_4)_2$ from the direct effect of oxygen, humidity and light.[22] It is notable that NaCl does not interfere with the reduction and extraction processes. In the work-up process, water is added to the reaction mixture to hydrolyze of the resulting borates. The NaCl is dissolved in water and the resulting brine increases the yield of products, since the solubility of alcohols decreases in brine.

4. Conclusion

In this investigation, we have shown the reducing properties of $Zn(BH_4)_2$/2NaCl remained intact for several months. Consequently, it is much easier to use than other similar reducing agents. Also, we have shown that the $Zn(BH_4)_2$/2NaCl reduces a variety of carbonyl compounds to their corresponding alcohols in high to excellent yields. Reduction reactions were carried out with 0.5–1 molar equivalents of $Zn(BH_4)_2$/2NaCl at room temperature in CH_3CN without any other additive. 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. Reduction of acyloins and α-diketones by this reducing system also produced the corresponding vicinal diols. Moreover, features such as: a) high efficiency of the reduction reactions, b) shorter reaction times, c) ease of preparation, handling and storage, d) very good stability, e) low reaction temperature, f) easy work-up procedure and g) possible to produce commercially make this reducing system an attractive protocol for the reduction of carbonyl compounds, therefore it could be a useful addition to the present methodologies.

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