Asian Journal of Chemistry Vol. 21, No. 5 (2009), 3603-3610

(N-Methylimidazole)(tetrahydroborato)zinc Complex as a New Stable and Efficient Reducing Agent for Reduction of Carbonyl Compounds

BEHZAD ZEYNIZADEH* and DAVOOD SETAMDIDEH
Department of Chemistry, Faculty of Sciences, Urmia University, Urmia 57159-165, Iran
E-mail: bzeynizadeh@gmail.com

(N-Methylimidazole)(tetrahydroborato)zinc complex, as a stable white solid was prepared quantitatively by complexation of an equimolar amount of zinc tetrahydroborate and N-methylimidazole at room temperature. This reagent easily reduces a variety of carbonyl compounds such as aldehydes, ketones, acyloins, α-diketones and α,β-unsaturated carbonyl compounds to their corresponding alcohols in high to excellent yields. Reduction reactions were carried out under mild conditions in acetonitrile at room temperature.

Key Words: N-methylimidazole, $Zn(BH_4)_2$, Reduction, Carbonyl compounds.

INTRODUCTION

Zinc tetrahydroborate, $Zn(BH_4)_2$, as a non-conventional hydride transferring agent, has been reported to effect very efficient chemo-, regio- and stereoselective reductions in several complex substrates. In this context, the reducing abilities of zinc tetrahydroborate have been reviewed[1,2]. This potential reducing agent is a neutral and can be used in a range of aprotic solvents such as ether, THF and DMF. High coordination ability of zinc makes zinc tetrahydroborate more selective in its hydride transferring reactions. 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 non-availability as a commercial reagent, being freshly prepared solution just prior to use and limitation to handling and storage. To overcome these limitations, the stable modifications of $Zn(BH_4)_2$ as the form of tertiary amino or phosphino ligand complexes such as $[Zn(BH_4)_2(dabco)]$[3], $[Zn(BH_4)_2(pyz)]_n$[4], $[Zn(BH_4)_2(Ph_3P)_{1\text{-}2}]$[5], $[Zn(BH_4)_2(bpy)]$[6], $[Zn(BH_4)_2(py)]$[7] and the supported form as poly(4-vinylpyridine) supported zinc tetrahydroborate, $[Zn(BH_4)_2\text{-}XP_4]$[8] have been made and used for reduction of organic compounds.

The challenge in chemistry to develop efficient processes, reaction media and conditions is one of the most important issues in the scientific community. In this context and continuation of our earlier works with modified hydroborate agents, herein, we wish to introduce a new reducing agent as (N-methylimidazole)-(tetrahydroborato) zinc, $[Zn(BH_4)_2(nmi)]$ for reduction of carbonyl compounds such as aldehydes, ketones, acyloins, α-diketones, enals and enones to their corresponding alcohols at ambient temperature.

EXPERIMENTAL

All the reagents and substrates were purchased from commercial sources with the best quality and were used without further purification. The products were characterized by their $^{1}H/^{13}C$ NMR and IR spectra which were recorded on 300 MHz Bruker and Thermo Nicolet Nexus 670 FT-IR spectrometers, respectively. All yields refer to isolated pure products. TLC was applied for the purity determination of substrates, products and reaction monitoring over silica gel 60 F_{254} aluminum sheet.

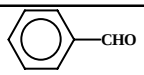
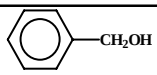
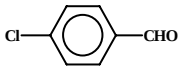
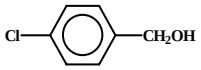
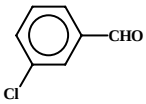
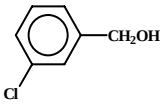
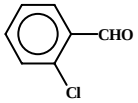
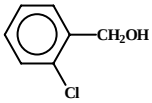
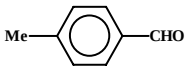
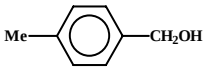
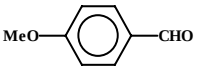
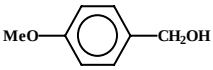
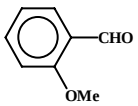
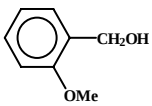
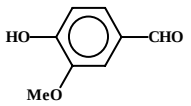
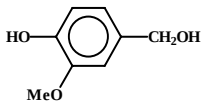
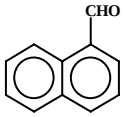
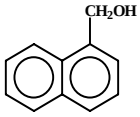
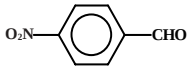
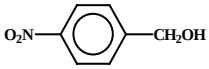
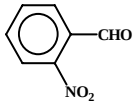
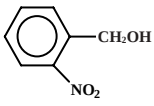
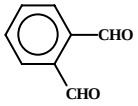
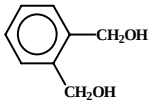
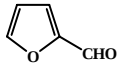
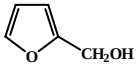
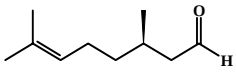
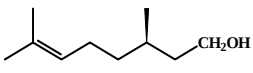
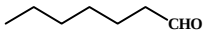
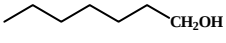
Preparation of (N-methylimidazole)(tetrahydroborato)zinc complex, [Zn(BH$_4$)$_2$(nmi)]: An ethereal solution of $Zn(BH_4)_2$ (0.16 M, 250 mL) was prepared from $ZnCl_2$ (5.452 g, 0.04 mol) and $NaBH_4$ (3.177 g, 0.084 mol) according to an available procedure in the literature[9]. Then, N-methylimidazole (3.28 g, 0.04 mol) in ether (50 mL) was added drop wise to the ethereal solution of $Zn(BH_4)_2$ and stirred for 0.5 h. Evaporation of the solvent under reduced pressure at room temperature gave $[Zn(BH_4)_2(nmi)]$ as a white powder in 95 % yield (6.73 g). This compound decomposed above 120 °C to a gray material. Found: Zn: 35.72 %, BH_4^-: 7.94 %. Calculated for $C_4H_{14}N_4B_2Zn$, Zn: 36.90 %, BH_4^-: 8.37 %.

A typical procedure for reduction of carbonyl compounds with [Zn(BH$_4$)$_2$(nmi)] complex: In a round-bottomed flask (10 mL), equipped with a magnetic stirrer, a solution of benzaldehyde (0.106 g, l mmol) in CH_3CN (2 mL) was prepared. The reducing agent (0.089 g, 0.5 mmol) was then added and the mixture was stirred at room temperature. TLC monitored the progress of the reaction (eluent, CCl_4/Et_2O: 5/2). After completion of the reaction in 5 min, a solution of HCl (2 %, 5 mL) was added to the reaction mixture and the mixture was stirred for additional 10 min. The mixture was extracted with CH_2Cl_2 (3 × 6 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent and short column chromatography of the resulting crude material over silica gel (eluent, CCl_4/Et_2O: 5/2) affords pure liquid benzyl alcohol (0.101 g, 94 % yield, Table-1).

RESULTS AND DISCUSSION

$[Zn(BH_4)_2(nmi)]$ is readily prepared by complexation of one to one equimolar ethereal solution of zinc tetrahydroborate and N-methylimidazole at room temperature. The complexation reaction is fast by immediate precipitation of the reagent. Evaporation of the solvent results in a stable white solid which could be stored in a sealed bottle for months without losing its activity. The Zn and BH_4^- contents in the complex were determined by atomic absorption[10] and iodometric titration[11] techniques, respectively. The measurements data are in best agreement with the proposed structure of the reagent as $[Zn(BH_4)_2(nmi)]$ (Fig. 1). The solubility behaviour of $[Zn(BH_4)_2(nmi)]$ in various aprotic solvents such as Et_2O, CH_2Cl_2, CH_3CN and THF was studied and observed that this reagent is slightly soluble in these solvents. This reagent in protic solvents such as methanol and ethanol is unstable and decomposed with the evolution of hydrogen gas. For the selection of appropriate solvent in

TABLE-1
REDUCTION OF ALDEHYDES WITH $[Zn(BH_4)_2(nmi)]$ COMPLEX[a]

Entry	Substrate	Product	Molar ratio Subs./Reag.	Time (min)	Yield (%)[b]
1			1:0.5	5	94
2			1:0.5	3	96
3			1:0.5	3	96
4			1:0.5	5	95
5			1:1	10	97
6			1:0.5	15	99
7			1:0.5	5	97
8			1:1	20	94
9			1:0.5	5	98
10			1:0.5	1	99
11			1:0.5	1	99
12			1:0.6	2	95
13			1:0.5	2	90
14			1:0.5	2	88
15			1:0.5	1	85

[a]All reactions were carried out in CH_3CN (2 mL) at room temperature.
[b]Yield refer to isolated pure products.

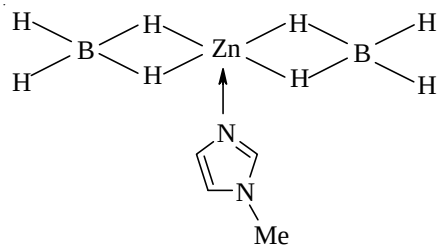


Fig. 1. (N-Methylimidazole)(tetrahydroborato)zinc complex

reduction reactions, benzaldehyde and acetophenone as model compounds were subjected to $[Zn(BH_4)_2(nmi)]$ in dry Et_2O, CH_2Cl_2, CH_3CN and THF. Our observation reveals that CH_3CN and THF were suitable solvents for reduction, but especially the reduction in CH_3CN provided a faster reaction rate and efficiency.

Reduction of aldehydes and ketones: Transformation of aldehydes and ketones to their alcohols is one of the most important reactions in organic synthesis[12]. $NaBH_4$ is usually used for the reduction of aldehydes and ketones to their corresponding alcohols in protic solvents such as ethanol or isopropanol under reflux condition. Consequently, the reductions encounter with low chemo- or regioselectivity. This goal could be easily achieved by $[Zn(BH_4)_2(nmi)]$ in CH_3CN under mild conditions. Reduction of structurally different aromatic and aliphatic aldehydes and ketones to their corresponding alcohols was carried out efficiently by the reagent (Tables 1 and 2). Aldehydes were reduced with 0.5-1.0 and ketones with 2-3 molar equivalents of the reagent in CH_3CN at room temperature. The product primary and secondary alcohols were obtained in high to excellent yields. The complete reduction of α-diketones and acyloins to *vicinal* diols was also easily achieved by $[Zn(BH_4)_2(nmi)]$. The reactions were efficiently carried out with 2 molar equivalents of the reagent in CH_3CN at room temperature (Table-2). The attempts for reduction of α-diketones to acyloins were unsatisfactory and only *vicinal* diols were detected as sole products. The work-up procedure of the reaction mixture is easy by employing dilute mineral acid (2 % HCl) and extraction with CH_2Cl_2 affords the crude product alcohols for further purification by a short column chromatography packed with silica gel.

1,2-Reduction of α,β-unsaturated carbonyl compounds: Reduction of conjugated carbonyl compounds by metal hydrides can follow two pathways *i.e.*, addition to carbonyl group (1,2-reduction) to give allylic alcohols or addition to the conjugated double bond (1,4-addition) to give saturated carbonyl compounds. In spite of substantial evidences, the tendency for $NaBH_4$ to reduce conjugated enals and enones is highly solvent-dependent and generally does not result in a useful regioselectivity[13]. Reduction of enals and enones was carried out by 0.5-3.0 molar equivalents of $[Zn(BH_4)_2(nmi)]$ in a perfect regioselectivity. The efficiency of the reductions was excellent by producing primary and secondary allylic alcohols in 92-98 % yields (Table-3).

TABLE-2
REDUCTION OF KETONES WITH $[Zn(BH_4)_2(nmi)]$ COMPLEX[a]

Entry	Substrate	Product	Molar ratio Subs./Reag.	Time (min)	Yield (%)[b]
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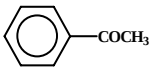
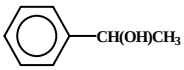
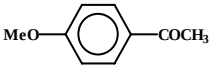
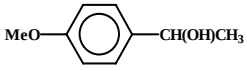
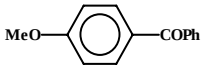
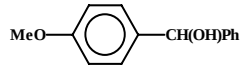
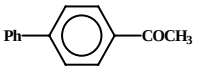
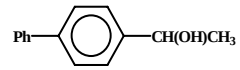
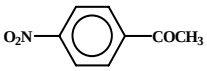
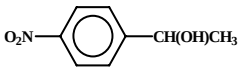
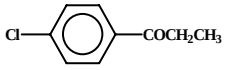
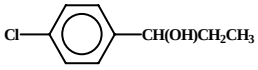
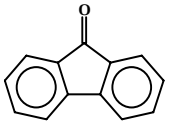
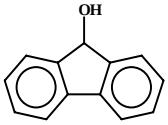
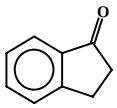
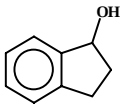
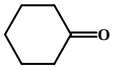
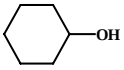
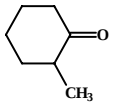
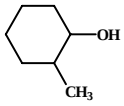
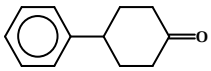
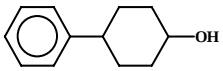
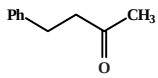
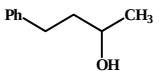
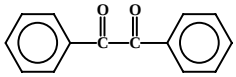
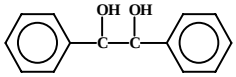
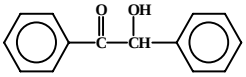
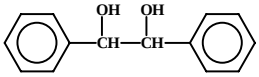
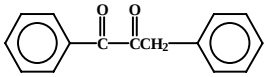
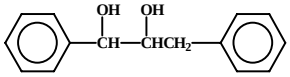
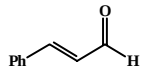
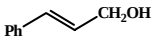
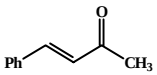
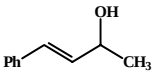
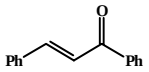
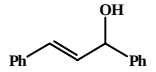
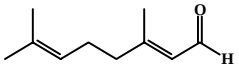
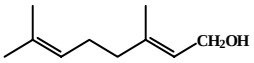
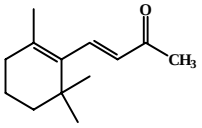
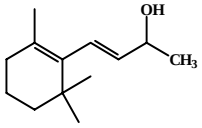
2			1:2	1.30	97
3			1:3	1.80	99
4			1:3	3.00	97
5			1:3	1.30	98
6			1:1.5	0.8	95
7			1:2	1.00	94
8			1:2.5	1.00	99
9			1:2	1.00	97
10			1:1	0.08	90
11			1:1	0.13	91
12			1:1	0.25	96
13			1:2	0.30	98
14			1:2	0.08	94
15			1:2	0.08	96
16			1:2	0.20	93

[a]All reactions were carried out in CH_3CN (2 mL) at room temperature.
[b]Yield refer to isolated pure products.

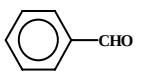
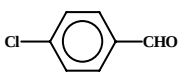
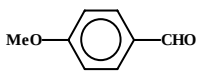
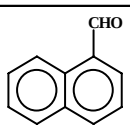
In order to show the efficiency of $[Zn(BH_4)_2(nmi)]$, we compared some of present results with those of reported for $[Zn(BH_4)_2(dabco)]$[3], $[Zn(BH_4)_2(pyz)]_n$[4], $[Zn(BH_4)_2(Ph_3P)_{1-2}]$[5], $[Zn(BH_4)(bpy)]$[6], $[Zn(BH_4)(py)]$[7], $[Zn(BH_4)_2$-XP4$]$[8] and $Zn(BH_4)$[14] (Table-4). As it's seen that the present reagent shows high to comparable efficiency under mild conditions at ambient temperature.

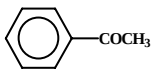
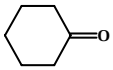
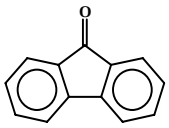
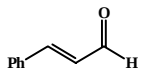
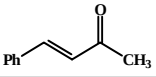
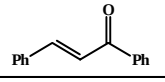
TABLE-3
REDUCTION OF CONJUGATED CARBONYL COMPOUNDS WITH $[Zn(BH_4)_2(nmi)]$ COMPLEX[a]

Entry	Substrate	Product	Molar ratio Subs./Reag.	Ratio of 1,2:1,4	Time (min)	Yield (%)[b]
1			1:0.5	100:0	10	98
2			1:2	100:0	60	96
3			1:3	100:0	90	97
4			1:0.5	100:0	5	89
5			1:2	100:0	90	91

[a]All reactions were carried out in CH_3CN (2 mL) at room temperature.
[b]Yield refer to isolated pure products.

TABLE-4
COMPARISON OF REDUCTION OF CARBONYL COMPOUNDS WITH $[Zn(BH_4)_2(nmi)]$ COMPLEX AND OTHER REPORTED REAGENTS

Entry	Substrate	Molar ratio (reag./subs.); Time (h) and Yield (%)								
		I	II[7a]	III[6]	IV[3a]	V[4]	VI[5]	VII[5]	VIII[14]	IX[8]
1		0.5 (0.08) (94)	1 (0.5) (91)	0.25 (0.02) (95)	0.75 (0.7) (90)	1 (2.5) (73)	–	–	1 (0.5) (100)	1 (8) (80)
2		0.5 (0.05) (96)	1 (0.2) (99)	0.25 (0.08) (98)	0.75 (0.4) (97)	1 (3) (95)	–	1 (a) (88)	1 (0.5) (100)	1 (5) (95)
3		0.5 (0.25) (99)	1 (1.3) (96)	0.35 (0.17) (99)	0.75 (12) (96)	2 (1.5) (96)	–	1 (0.17) (89)	–	1 (12) (75)
4		0.5 (0.08) (98)	1 (0.8) (95)	0.25 (0.13) (99)	–	–	2 (0.5) (90)	1.5 (a) (100)	–	1 (8) (84)

Entry	Substrate	Molar ratio (reag./subs.); Time (h) and Yield (%)								
		I	II[7a]	III[6]	IV[3a]	V[4]	VI[5]	VII[5]	VIII[14]	IX[8]
5		2 (1.3) (97)	2 (2) (94)	0.5 (2.15) (97)	1.2 (5.4) (92)	4 (30) (85)	2 (1.25) (75)	2 (0.5) (80)	1 (0.5) (0)	2 (15) (0)
6		3 (1) (95)	2 (4.3) (97)	1 (0.75) (99)	1.5 (8.5) (94)	–	–	–	–	2 (48) (0)
7		1 (0.08) (90)	2 (2) (89)	0.5 (0.15) (88)	–	4 (18) (85)	2 (1) (100)	1 (1) (95)	1 (0.08) (100)	2 (24) (0)
8		2.5 (1) (99)	2 (5.3) (98)	1 (1.5) (94)	1.5 (2.3) (95)	–	2 (0.5) (88)	2 (0.33) (85)	–	–
9		0.5 (0.17) (98)	1 (1.5) (97)	0.5 (0.03) (92)	0.75 (4.5) (94)	3 (6) (93)	1.5 (0.4) (100)	1 (0.25) (90)	1 (0.5) (100)	1 (9) (90)
10		2 (1) (96)	2 (1) (97)	1 (1.3) (97)	1.2 (2.2) (92)	4 (8) (95)	2 (2.5) (87)	2 (0.5) (90)	1 (0.5) (15)	2 (15) (10)
11		3 (1.5) (97)	2 (3) (94)	1 (3) (98)	1.3 (7.5) (95)	4 (30) (90)	–	–	–	2 (24) (0)

[I][Zn(BH$_4$)$_2$(nmi)]; [II][Zn(BH$_4$)$_2$(py)]; [III][Zn(BH$_4$)$_2$(bpy)]; [IV][Zn(BH$_4$)$_2$(dabco)]; [V][Zn(BH$_4$)$_2$(pyz)]; [VI][Zn(BH$_4$)$_2$(Ph$_3$P)]; [VII][Zn(BH$_4$)$_2$(Ph$_3$P)$_2$]; [VIII]Zn(BH$_4$)$_2$; [I][Zn(BH$_4$)$_2$(XP4)]; a: Immediately.

Conclusion

In this study, we have quantitatively prepared (N-methylimidazole)(tetrahydroborato)zinc complex, [Zn(BH$_4$)$_2$(nmi)] and utilized it as an efficient reducing agent for the reduction of structurally different carbonyl compounds at ambient temperature. The perfect regioselectivity was observed for 1,2-reduction of α,β-unsaturated carbonyl compounds. The stability, ease of handling and storage of the reagent, mild reaction conditions and perfect regioselectivity are the advantages which make this new modified zinc tetrahydroborate as synthetically useful reducing agent.

ACKNOWLEDGEMENT

The authors gratefully acknowledge the financial support of this work by the Research Council of Urmia University.

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(*Received*: 9 June 2008; *Accepted*: 10 February 2009) AJC-7231