Est. 1984

ORIENTAL JOURNAL OF CHEMISTRY
An International Open Free Access, Peer Reviewed Research Journal

www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2015, Vol. 31, No. (2):
Pg. 1215-1218

Preparation of Arylamines form Aldehydes by $Zn(BH_4)_2/MgBr_2$

MINA MAHMOUDI and DAVOOD SETAMDIDEH*

Department of Chemistry, Mahabad Branch, Islamic Azad University, Mahabad, Iran.
*Corresponding author E-mail: davood.setamdideh@gmail.com; d.setamdideh@iau-mahabad.ac.ir

http://dx.doi.org/10.13005/ojc/310280

(Received: October 30, 2014; Accepted: January 12, 2015)

ABSTRACT

Reductive aminationa varietyof aldehydes with different anilines has been performed by$Zn(BH_4)_2$/$MgBr_2$as reducing system in THF at room temperature in high to excellent yields of the corresponding secondary amines (80-90%).

Key words:$Zn(BH_4)_2$, $MgBr_2$, Reductive amination, Aldehydes.

INTRODUCTION

One's famous of pharmaceutical intermediates for the synthesis of some drugs are amines. These compounds can be obtained by the reduction of cyano, azide, nitro, carboxamide derivatives. On the other hands, direct reductive amination (DRA) is a single operation can be carried out by some non-borohydride reducing system that they have been reviewed by our former works; alsosomeborohydrides systems have been used for DRA reaction [1].These methods have advantages and some disadvantages such as long reaction time, excess amount of reagents, using expensive reagents, toxic byproducts and higher reaction temperature. Therefore, there is interest in synthesis of amines under new systems. Recently, we have reported that $NaBH_4$/DOWEX(R)50WX4[1a], $NaBH_4$/$B(OH)_3$& $Al(OH)_3$[1b], $NaBH_4$/$Ga(OH)_3$[1c], $NaBH_4$/C [1d]and $NaBH_4$/$NaH_2PO_4.H_2O$[1e]can be used as convenient systems for reductive amination of aldehydes. So, in continuing our efforts for the development of new reducing systems[1-2],we have re-examined the DRA reaction.Thus, we introduce an efficient system*i.e.*$Zn(BH_4)_2$/$MgBr_2$in THF at room temperature for reductive amination of aldehydes.

RESULTS AND DISCUSSION

The model reaction has been chosen by reductive amination of benzaldehyde with aniline. This reaction was performed in different conditions as shown in table 1. By the testing ofthe different solvents, wehavefoundTHF is better solvent because itgives the highest yield of product. The optimization reaction conditions showed that using 1 molar equivalents of $Zn(BH_4)_2$ and 1 molar equivalents of$MgBr_2$in THF were the best conditions to complete the reductive amination of benzaldehye (1 mmol) and aniline (1 mmol) to *N*-benzylaniline (Table 1, Entry4). The reaction was

completed within 25 min with 90% yields of product as shown in scheme 1.

The efficiency of this protocol was further examined by using various structurally different aldehydes and anilines. In this approach, the correspondingsecondary amines were obtained in excellent yields (80-90%) and within appropriate times (20-45 min) as shown in Table 2.

The rate-determining step for reductive aminationsis Imine formation therefore additions ofco-reactants are desirable. It is notable, in the absence of $MgBr_2$, imine does not generate and benzyl alcohol has been produced as shown in scheme 1.

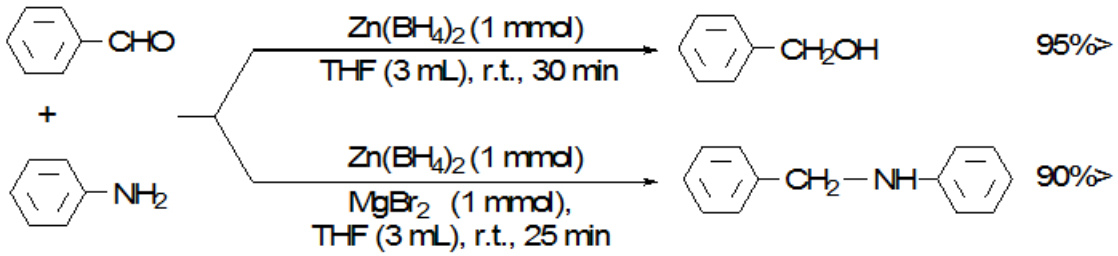
Also, the reductive amination of cinnamaldehyde with 1 molar equivalents of aniline and aniline by 1 molar equivalents of $Zn(BH_4)_2$ and 1 molar equivalents of $MgBr_2$ was carried out exclusively in 1,2-reduction manner within 20 minutes at room temperature.. In these reactions the corresponding cinnamylanilines were obtained in 80% yields (Table 2, entry 14).

The products were determined from the ^{1}H-chemical shift of the CH_2 group which appeared around 4.22-4.68 ppm as a singlet. Also the NH stretching frequency in FT-IR spectrum appeared around 3380-3427 cm^{-1}.

EXPERIMENTAL

General

All substrates and reagents were purchased from commercially sources with the best quality and used without further purification. IR and ^{1}H NMR spectra were recorded on PerkinElmer FT-IR RXI, 100 and 400 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



Scheme 1

Table 1: Optimization of the Reductive Amination of Benzaldehyde (1 mmol) and Aniline (1 mmol) to Benzylaniline with $Zn(BH_4)_2$ and $MgBr_2$at Room Temperature

Entry	$Zn(BH_4)_2$/mmol	$MgBr_2$/mmol	Solvent/3 mL	Time/min	Yields[a] /%
1	0.5	1	THF	60	50
2	0.5	0.5	THF	60	30
3	1	0.5	THF	60	50
4	1	1	THF	25	90
5	1	1.5	THF	20	85
6	1.5	1	THF	25	50
7	1	1	CH_3CN	60	50
8	1	1	Et_2O	60	50
9	1	1	CH_2Cl_2	60	20

[a]Yields refer to isolated pure benzylaniline.

Table 2: Reductive Amination of Aldehydes (1 mmol) with Anlines (1 mmol) by $Zn(BH_4)_2$ (1 mmol) in the presence of $MgBr_2$ (1 mmol) in THF (3 mL) at Room Temperature.

Entry	Aldehydes	Anilines	Products	Time / min	Yields [a] / %
1	benzaldehyde	aniline	*N*-benzylaniline	25	90
2	benzaldehyde	4-bromoaniline	*N*-benzyl-4-bromoaniline	20	87
3	benzaldehyde	4-methoxyaniline	*N*-benzyl-4-methoxyaniline	20	90
4	2-nitrobenzaldehyde	4-methylaniline	*N*-(2-nitrobenzyl)- 4-methylaniline	20	89
5	4-bromobenzaldehyde	aniline	*N*-(4-bromobenzyl)aniline	20	82
6	2-methoxybenzaldehyde	aniline	*N*-(2-methoxybenzyl)aniline	30	89
7	4-methylbenzaldehyde	4-bromoaniline	*N*-(4-methylbenzyl)-4-bromoaniline	30	90
8	2-nitrobenzaldehyde	4-methoxyaniline	*N*-(2-nitrobenzyl)- 4-methoxyaniline	20	90
9	4-methylbenzaldehyde	4-methylaniline	*N*-(4-methylbenzyl)- 4-methylaniline	20	83
10	4-methylbenzaldehyde	4-methoxyaniline	*N*-(4-methylbenzyl)- 4-methoxyaniline	40	89
11	4-methoxybenzaldehyde	4-methylaniline	*N*-(4-methoxybenzyl)-4-methylaniline	20	90
12	2-methoxybenzaldehyde	4-bromoaniline	*N*-(2-methoxybenzyl)-4-bromoaniline	45	89
13	4-nitrobenzaldehyde	aniline	*N*-(4-nitrobenzyl)aniline	20	85
14	cinnamaldehyde	aniline	*N*-cinnamylaniline	20	80

[a] Yields referee to isolated pure products.

over anhydrous sodium sulfate. All yields referred 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.

Reductive amination of benzaldehyde and aniline with $Zn(BH_4)_2/MgBr_2$, A typical procedure:

In a round-bottomed flask (10 mL) equipped with a magnetic stirrer, a solution of benzaldehyde (0.106 g, 1 mmol) , aniline (0.093 g, 1 mmol) and $MgBr_2$(0.182g, 1 mmol) in THF (3 mL) was prepared. The resulting mixture was stirred for 5 min at room temperature. Then $Zn(BH_4)_2$(0.275 g, 1 mmol) was added to the reaction mixture and stirred at room temperature. TLC monitored the progress of the reaction (eluent; CCl_4/Ether: 5/2). The reaction was filtered after completion within 25 min. Evaporation of the solvent and short column chromatography of the resulting crude material over sil-ica gel (eluent; CCl_4/ Ether: 5/2) afforded the *N*-benzylaniline (0.l64 g, 90% yield, Table 2, entry 1).

CONCLUSIONS

In this context, we have shown that $Zn(BH_4)_2/MgBr_2$is suitable for the reductive amination of a variety of aldehydes and anilines to their corresponding secondary amines in high to excellent yields. Reduction reactions were carried out with 1 molar equivalents of $Zn(BH_4)_2$in the presence of 1 molar equivalents of $MgBr_2$in THF at room temperature. High efficiency of the reductions, shorter reaction times and easy work-up procedure makes as an attractive new protocol for reductive amination of aldehydes.

ACKNOWLEDGMENTS

The authors gratefully appreciated the financial support of this work by the research council of Islamic Azad University branch of Mahabad.

REFERENCES

1. a) Setamdideh, D.; Sepehraddin . D. *J. Mex. Chem. Soc*. **2014**, *57*, 22-25. b) Setamdideh, D.; Hasani, S.; Noori, S. *J. Chin. Chem. Soc.***2013**, *60*, 1267-1271. c) Pourhanafi, S.; Setamdideh, D.;Khezri, B. *Orient. J. Chem*. **2013**, *29*, 709-712.d) HsanloieTaie, S.;

Setamdideh, D. *Orient. J. Chem*. **2014**, *30*, 341-344. e) S.; Arefi, H.; Setamdideh, D. *Orient. J. Chem*. **2014**, *30*, 299-302.

2. a) Setamdideh, D.; Rafigh, M. *E-J. Chem*.**2012**, *4*, 2338-2345. b) Setamdideh, D.; Rahmatollahzadeh, M. *J. Mex. Chem. Soc*. **2012**, *56*, 169-175.c) Setamdideh, D.; Ghahremani, S. *S. Afr. J. Chem.***2012**, *65*, 91-97. d) Setamdideh, D.; Khezri, B.; Rahmatollahzadeh, M. *J. Serb. Chem. Soc.***2013**, *78*, 1-13e) Mohamadi, M.; Setamdideh, D.; Khezri, B. *Org. Chem. Inter.***2013**, 2, doi:10.1155/2013/127585.f) Setamdideh, D.; Khaledi, L. *S. Afr. J. Chem.***2013**, *66*, 150-157.g) AziziAsl, P.; Setamdideh, D, *J. Chin. Chem. Soc.***2014**, *61*, 940-944.